Development of Highly Regioselective Functionalizations of Arenes, Heteroarenes and Alkynes

Submitted in partial fulfillment of the requirements
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by

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Under the Supervision of

Prof. D. Maiti (IIT Bombay)
&
Prof. David W. Lupton (Monash University)

The course of study for this award was developed jointly by
Monash University, Australia and the Indian Institute of Technology, Bombay
and was given academic recognition by each of them.
The programme was administrated by The IITB-Monash Research Academy

(Year 2018)

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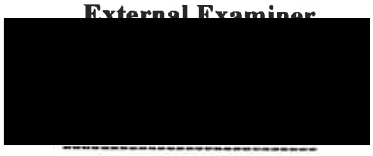

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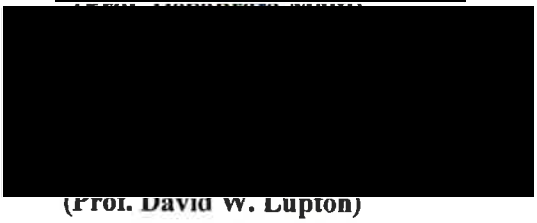

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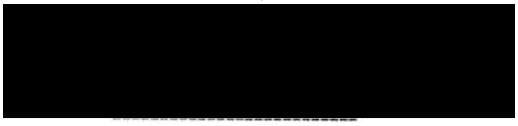

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List of abbreviations

°C	Degree Celsius
atm	Atmosphere
Ar	Aryl
^{i}Pr	Iso propyl
^{t}Bu	Tertiary butyl
Cy	Cyclohexyl
cat.	Catalyst
acac	Acetylacetonate
dba	Dibenzylidineacetone
DCM	Dichloromethane
DMF	Dimethyl Formamide
DMSO	Dimethyl Sulfoxide
TFT	Trifluorotoulene
ESI MS	Electrospray Ionization Mass Spectrometry
Et_2O	Diethyl ether
EtOAc	Ethyl acetate
EtOH	Ethanol
EWG	Electron-withdrawing group
EDG	Electron-donating group
etc.	Et cetera
L	Ligand
MeOH	Methanol
et al.	Etalii
NMP	N-methylpyrrolidone
OAc	Acetate
OMe	Methoxy
Ph	Phenyl
h	Hour
Ar	Aryl

COD	1, 5-cyclooctadiene
mL	Milli liter
mmol	Milli mole
M.P.	Melting point
NMR	Nuclear Magnetic Resonance
DTBP	Di-tertiary-butyl peroxide
equiv.	Equivalent
MS	Molecular sieves
phen	1, 10-phenanthroline
SET	Single electron transfer
rt	Room temperature
***t*-BuOH**	Tertiary butyl alcohol
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TFE	Trifluoroethanol
XRD	X-Ray Diffraction
***t*-Amy-OH**	Tertiary amyl alcohol
IR	Infrared spectroscopy
DCE	Dichloroethane
GC	Gas chromatography
HRMS	High resolution mass spectrometry
KIE	Kinetic isotope effect

Chapter 1

Introduction and Scope of the Thesis

1.1. Introduction:

Innovation and technologies are the key parameter to define the socio-economic background of a nation. Development of natural sciences is one the major segments that boost up the growth of scientific development. Chemistry, a prime component of natural sciences, has contributed enormously towards the paramount progress of human civilization. Complexity of the biologically active molecules and the underlying mechanistic intricacies fascinated the synthetic chemists over the centuries. The provocation to understand the mechanism and their artificial synthesis leads to the innovation and evolution of different synthetic tools. The practical and industrial synthesis of value added products, pharmaceutically and naturally occurring compounds demands a simple, step economic, atom economic and eco-friendly strategies. Over the decades, numerous research groups across the globe have invested an enormous amount of effort in finding such strategy. As an outcome, a wide range of methodologies has been developed. Some of these strategies have been marked as a landmark in the history of synthetic chemistry for their simplicity and wide applicability for synthesizing complex target molecules, on the other hand, many others are failed to make any mark because of their tedious procedure and limited scope.

Structurally C–H and C–C bonds are the fundamental backbone of organic molecules. Hence, the expansion of synthetic scope in organic chemistry is largely dependent on devising a suitable protocol in a simple and environmentally binging way. In this regard, cross-coupling reaction is considered to be one of the most remarkable strategies to form a C–C bond. Before the era of transition metal catalyzed cross-coupling reactions, organometallic reagents, such as, Grignard reagent, Hillmann reagents are the only way to form C–C bonds. Unambiguously, discovery of Grignard reagent is one of the greatest inventions in the history of organic synthesis. However, use of Grignard reagent found to be difficult in many cases where a target molecule consists of various functional groups. Under this circumstance, metal catalyzed cross-coupling reaction provides alternative avenues for synthesizing structurally and functional group enriched complex molecules. Cross-coupling reactions are typically defined as the coupling between aryl, alkyl, vinyl, alkynyl halides or pseudohalidesand an organometallic reagent, such as organo-boron, organo-zinc or oragnosilane etc. in presence of a transition metal. The most famous cross-coupling reaction include the

name of Heck, Suzuki, Negishi, Hiyama and Sonogashira reactions, which are the most fundamental strategy to generate C–C bonds. Despite the huge success of the cross-coupling reactions, the major drawback of these methods is the use of prefunctionalized coupling partners. In contrast to that, direct C–H functionalization is always step economic and sustainable. Hence the direct C–H activation and/or functionalization have drawn tremendous attention in the emerging frontiers of synthetic chemistry over last few decades. The major challenges associated with the C–H functionalization is; a) inertness of C–H and C–C bonds, b) regioselectivity and c) chemoselectivity. Despite the challenges, a wide variety of strategy has been adopted to achieve selective C–H and C–C functionalization.

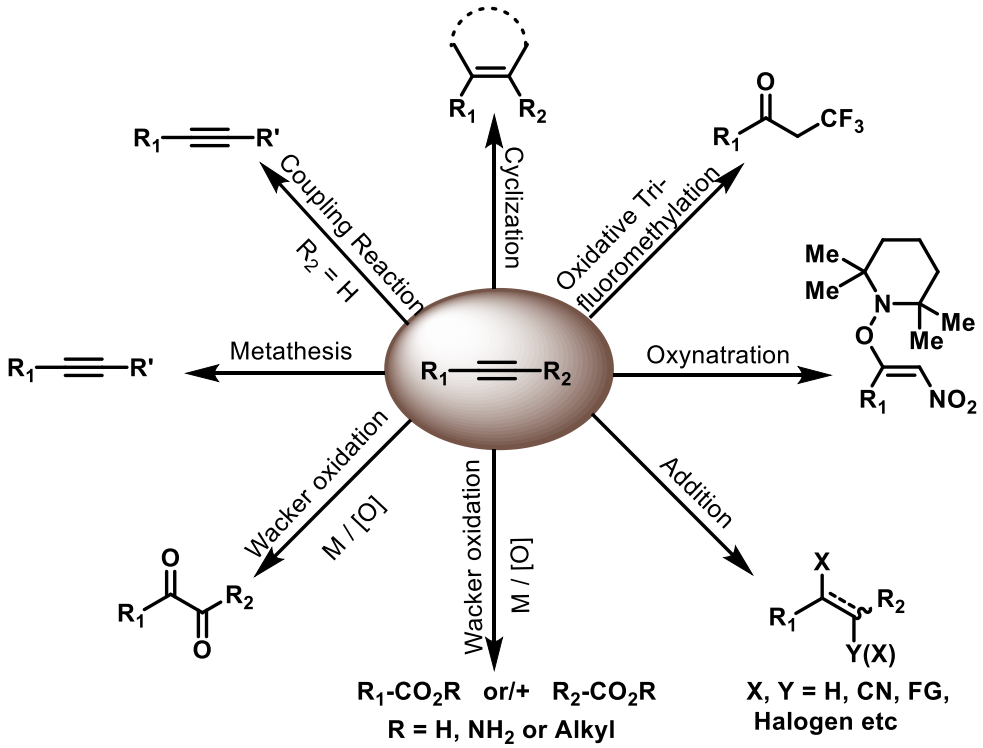
Although the transition metal catalyzed C–H activation has been acclaimed as one of the most successful path to carry out C–H functionalization, but free radical based approach is also found to be one of the classical path in functionalizing C–H or C–C bond. The current study is focused on developing new methods to carry out C–H and C–C bond functionalization in a regioselective manner embracing both free radical and transition metal catalyzed C–H activation path. The first three chapter of this thesis is about the regioselective C–C and C–H functionalization following a radical based approach. Whereas the chapter 5 and 6 delineates a directing group assisted regioselective distal *meta*- and *para*-C–H functionalization.

1.2. Background

Although transition metal catalysis has evolved tremendously to construct complex building block, natural products to fulfill the demand of human kind in broad prospect over last few decades, but the parallel complementary study on radical process has also drawn a significant attention to construct C–C or C–X bond by cleaving the C–H C–C and/or C–X bonds. The intrinsic advantages of radical reactions are; a) the reaction conditions are usually less hazardous, b) environment friendly c) reaction conditions are usually mild d) many cases the reactions are metal free. The current study is initially (Chapter 2, 3 and 4) focused on development of novel methods to achieve C–H and C–C functionalization in a regioselective manner, which follows the radical pathway. In the later part (Chapter 5 and 6) of the thesis delineates the transition metal catalyzed distal *meta*-, and *para*-C–H functionalization.

1.2.1. Aerobic Oxynitration of Alkynes with ^{t}BuONO and TEMPO: An Effort to Trap the Unstable Vinyl Radical

Scheme 1.1. Important transformations of alkynes

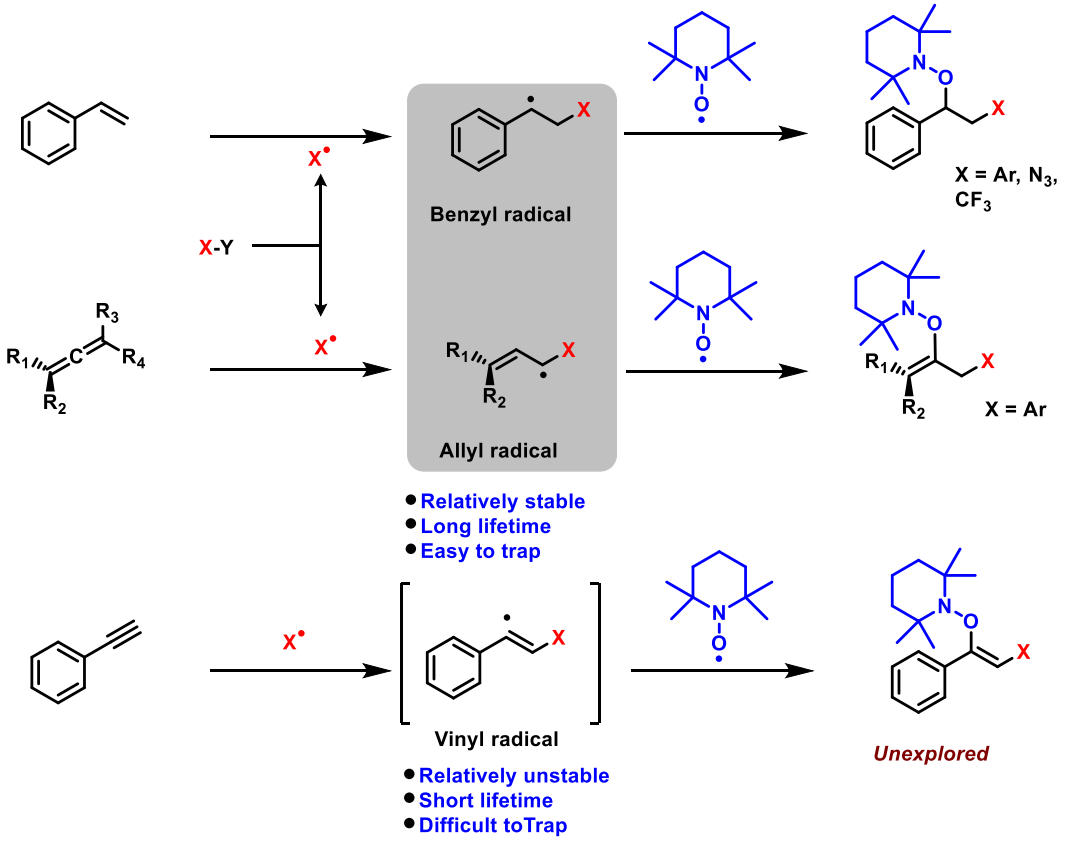


Alkynes are considered as one of the most ubiquitous and valuable feedstock motif to provide a plethora of synthetic transformations (Scheme 1.1).[1] Over the decades, it has

been utilized as a precursor for preparing building blocks in material sciences, natural product synthesis, pharmaceutically important drug molecule preparation, sensors, semiconductors, liquid crystals and polymers. In biology, pharmacology, medicine, biotechnology and nanotechnology, alkynes and their derivatives are found to be important in significant magnitude. Owing to the undeniable significance, alkyne functionalization has been a subject of extensive research both in industry as well as in academia for prolong time. Back in early nineteenth century, alkyne chemistry has been started to explore. Ketones generation *via* hydration of alkynes[2] or the addition reactions[3] are the early examples in this class. Cyclo-addition or cyclization (click chemistry) reactions of alkynes are another important class of reactions, which revolutionize the synthetic chemistry.[4] Needless to say that alkyne metathesis reactions,[5] Pd-catalyzed Wacker-type oxidations to generate 1,2-diketones[6] has empowered the strategic arsenal of chemist. Glaser-Hay coupling[7] and Sonogashira coupling reaction[8] provide a route to form C–C bond. C–C bond cleavage of alkynes to produce carboxylic acids or it's derivatives is also an alternative way to functionalize the alkynes.[9] Despite the huge effort that has been employed over the centuries to cultivate alkyne functionalizations, yet it's paramount importance and wide applicability demands to explore new methods to achieve unexplored functionalizations.

In this regard, we were interested in inventing a radical process to functionalize the alkynes. Radical chemistry has displayed a huge potential to perform C–H functionalization,[10] cascade cyclization[11] and photochemical transformations.[12] We envisioned utilizing alkynes as the radical acceptor in presence of any radical initiator. As an outcome we anticipate producing substituted alkenes or complete C–C bond cleavage to produce a nitrile moiety in presence of a proper nitrogenating source. In oppose to the alkenes, alkynes are very much inert towards radical acceptor. A radical attack to olefins or allenes produces stable alkyl radicals. The stability of the alkyl radical allows enough lifetimes to couple with another radical donor, which resulted a 1,2-disubstituted-alkyl moiety. In a sharp contrast, interaction of an alkyne to a radical donor results an unstable vinyl radical, which have a very short lifetime and belongs to the σ radicals (Scheme 1.2). The instability of the vinyl radical prompts to undergo hydrogen abstraction reaction. Hence, trapping of these vinyl radical with a right radical scavenger is utmost challenging.

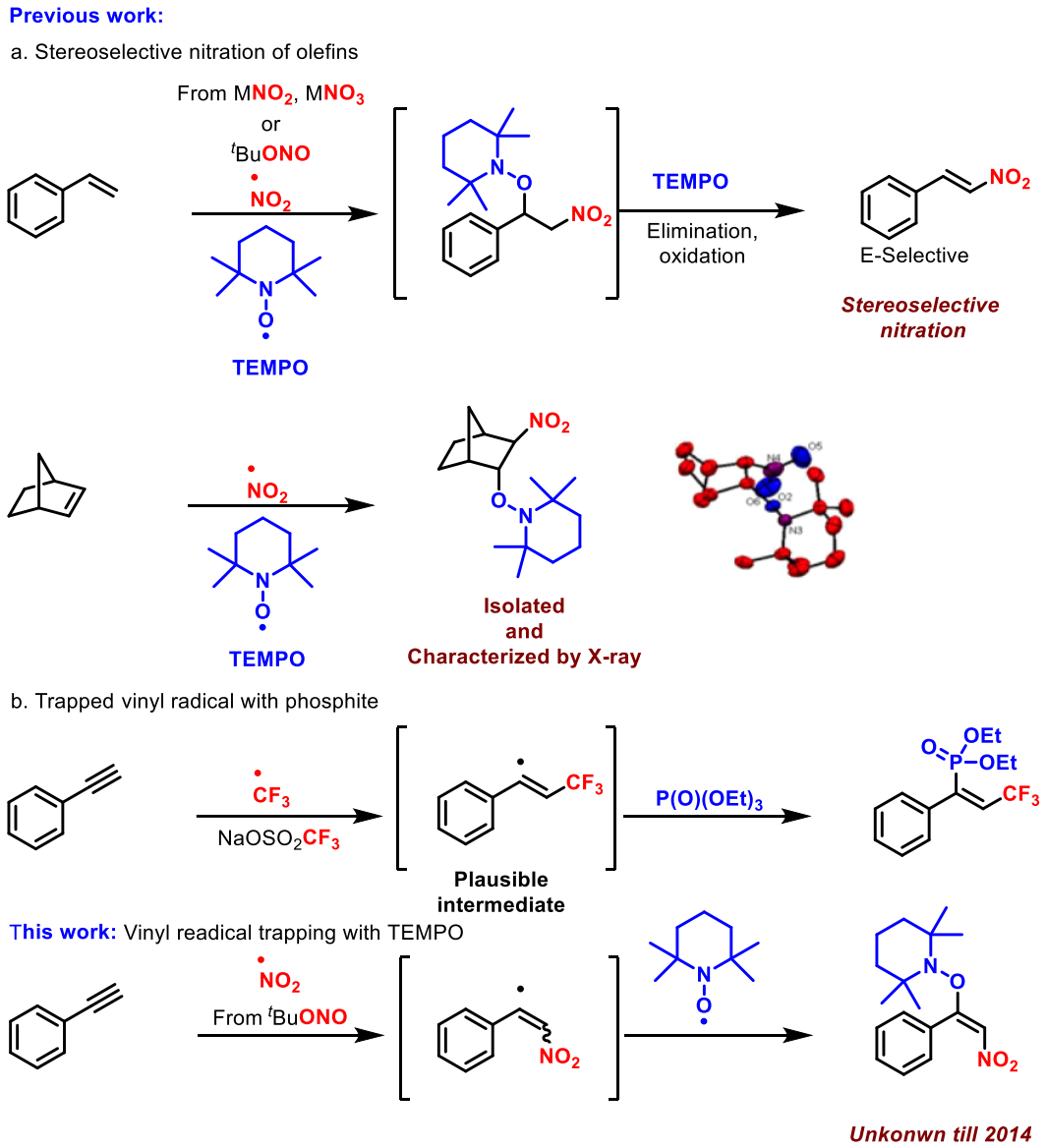
Scheme 1.2. Stability of benzyl or allyl radical *vs* vinyl radical



Preparation of *α, β*-difunctionalized alkane from a alkene following a radical based pathway has been well explored in recent years. Different metals namely, Cu, Au, Ti, Sn has been employed to perform *α, β*-difunctionalization of alkenes. A primitive example in this domain is the Meerwein arylation back in 1939. In the process copper (I) has been used as a catalyst and aryl diazonium salt is used to produce aryl radical which oxidatively added to the alkene.[13] In 2007, Henrich and co-workers has reported a Fe (II) mediated oxyarylation of alkenes using aryl diazonium salt as aryl radical source.[14] They have successfully trapped the intermediate by 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO).[15] An unprecedented result has been published by Studer and co-workers in 2012, where they reported the transition metal free oxyarylation of alkenes with aryl diazonium salt and TEMPONa.[16] Following oxyarylation of alkenes, the same group has utilized different other potential radical sources which can easily oxidatively add to the alkene and the resultant alkyl radical can be trapped by the suitable radical scavenger such as TEMPO. In all these reports, a suitable radical such as aryl,[16] azide[17]or trifluoromethyl[18] oxidatively added to the

alkene and an alkyl radical is generated. The resulted alkyl radical then trapped by the TEMPO and *α, β*-difunctionalized alkane is received as an outcome (Scheme 1.2).

Scheme 1.3. Overview of current work



However, our group disclosed an unprecedented report for selective synthesis of (*E*)-nitro alkene in the year of 2012 (Scheme 1.3).[19] Silver nitrite has been used a nitro radical source which oxidatively add to the alkenes and the resulted radical intermediate is trapped by the TEMPO. Upon anti-elimination of TEMPOH, the *E*-selective nitro olefin is obtained. Detail mechanistic study showed that the nitro radical generated from $AgNO_2$ add to the olefin and generated the alkyl radical which then trap the TEMPO. Such TEMPO-alkane-NO_2 adduct has been isolated and characterized by X-ray crystallography when norbornene was used as the substrate. The absence of anti-*β*-

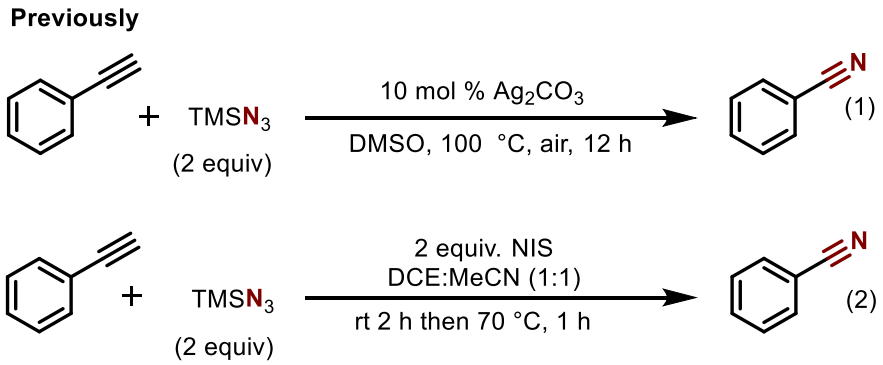
hydrogen prevents the further elimination. This method definitely provides an alternative way to conventional Henry reaction which is used to prepare nitro-olefin *via* condensation reaction. [20] In search of new metal-free nitrating reagents, our group has come up with *tert*-butyl nitrite (^{t}BuONO) as an alternative nitrating reagent which is equally effective in producing *E*-selective nitro olefins.[21]

Though, the radical addition towards alkene are well explored, in a sharp contrast the same chemistry of alkynes remain less unexplored. In this regard, we envisaged to use ^{t}BuONO as the nitrating reagent which upon interaction with alkynes produce the vinyl radicals. TEMPO has been utilized to trap this vinyl radical. As a result, nitroaminooxylated alkene was obtained. Despite numerous reports on alkyl or allyl radical trapping methods, to the best of our knowledge, this is the first time we remain successful in trapping vinyl radical. A wide range of functional group containing terminal olefins has been successfully employed to nitroaminoxylated olefins. The reaction is equally compatible with aryl and alkyl acetylene. TEMPO adds to the vinyl radical always in a *trans*-manner to the nitro group. The stereochemistry is confirmed by the X-ray crystallography.

1.2.2. Aryl Nitriles from Alkynes Using tert-Butyl Nitrite: Metal-Free Approach to C≡C Bond Cleavage

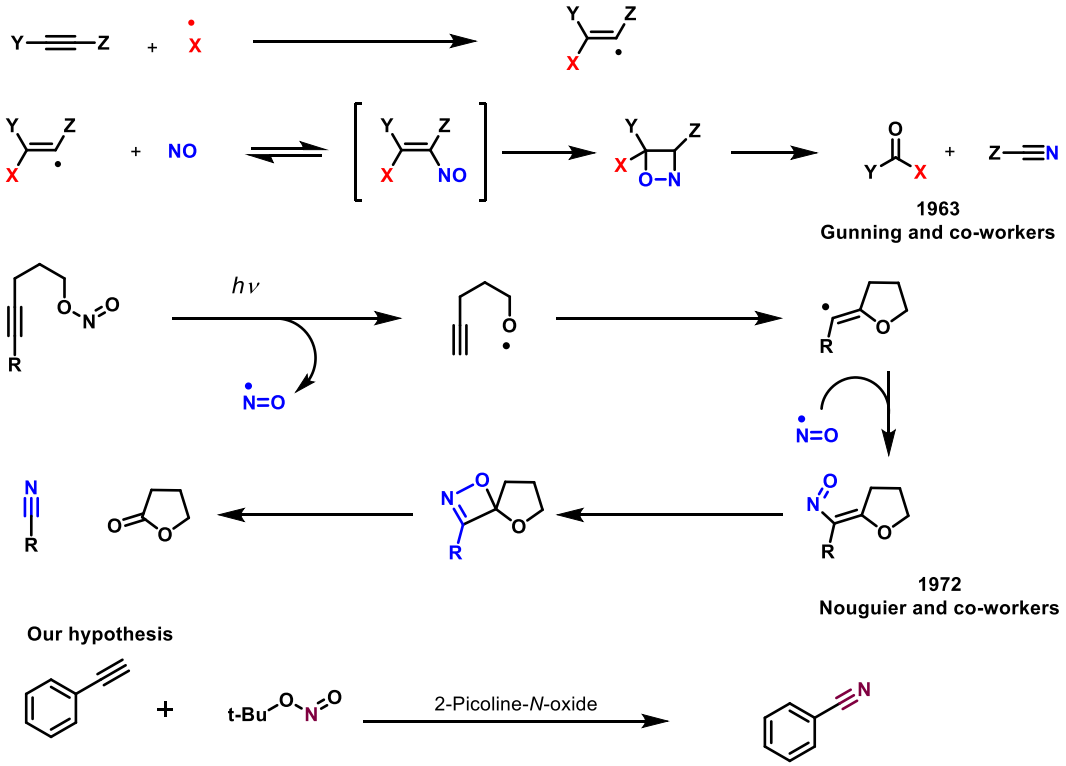
As discussed earlier, alkynes are immensely important fundamental motifs which are used to produce a wide variety of functional groups. However, the C≡C bond cleavage of an alkyne is tremendously challenging. The high bond energy posed the major challenge in the process of C–C bond breaking. Although metal catalyzed alkyne metathesis is text book chemistry and well explored. But direct C-C bond cleavage of alkyne to nitrile remains unexplored. In this regard, Jiao and co-workers first disclosed a silver catalyzed protocol to transform the alkyne to nitrile in 2013 (Scheme 1.4).[22] They used trimethylsilylazide ($TMSN_3$) as the nitrogenating reagent. Nevertheless, a broad substrate scope and functional group tolerance make the method attractive and important, but the use of coinage silver metal and DMSO as solvent limited the scope of acceptability. Hence, a more green and mild condition was yet to be developed. Almost at the same time, Yanada and co-workers revealed a metal free protocol to transform alkynes to nitrile (Scheme 1.4).[23] However, they have used $TMSN_3$ as the nitrogenating reagent.

Scheme 1.4. Formation of benzonitrile from alkynes using $TMSN_3$



As a part of our radical based reaction development, we planned to perform alkyne bond cleavage using a radical initiator. We inspired from a primitive discovery by Gunning and co-workers in the year of 1963,[24] where they have stated that "we have recently examined the gas phase reactions, at room temperature, of nitric oxide with vinyl and substituted vinyl radicals, where the radicals were formed in situ by the addition of an inducer radical (Y) to an alkyne (X—C≡C—Z). The results suggest a new family of free-radical reactions involving degradation, at the triple bond, of the parent alkynyl structure.(Scheme 1.5)" They utilized the nitric oxide as the source of nitoso radical. We thought to employ ^{t}BuONO as the source of nitroso radical which can add across the alkyne triple bond and intramolecular cyclization can generate the nitrile compounds at ease. ^{t}BuONO is very prone to produce the NO radical. Very recently, Wang group has disclosed a report on transformation of toluene to benzonitrile using ^{t}BuONO as the nitrogenting source.[25] Mechanistically, ^{t}BuONO homolytically cleaved to nitroso and *tert*-butoxy radical, which abstract a proton from the toluene to generate the benzyl radical. The benzyl radical captured the NO radical which upon isomerization produce the aldoxime. The aldoxime finally transform to nitrile by palladium (Pd) catalysis. All these precedent reports lead us to rationalize and designing a method to prepare the nitrile compounds *via* complete breakage of alkynes. We hypothesized that the *tert*-butoxy radical can interact with alkyne at the terminal position which will generate a vinyl radical. The vinyl radical can then capture the nitroso, which then undergo a four membered cyclic intermediate formation. Finally presence of a suitable base prompt elimination of formamide to produce nitrile compounds.

Scheme 1.5. Overview of our approach with respect to the literature precedence

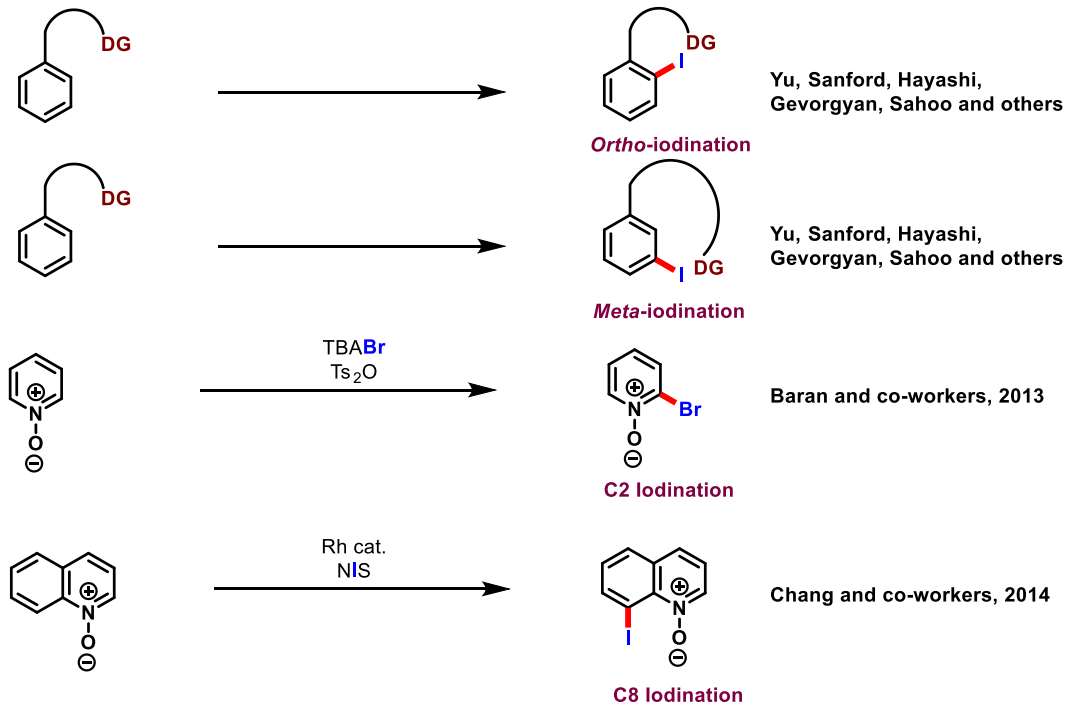


1.2.3. The Regioselective Iodination of Heterocycles *via* a Radical Mechanism

As a part of our ongoing research interest about radical based reaction discovery, we were interested in regioselective C–H functionalization of heterocycles. In particular, regioselective iodination of heterocycle is immensely important in organic synthesis. It is considered as one of the most important synthons in organic synthesis. Beyond its application in traditional synthetic methods such as metalation,[26] aromatic nucleophilic substitution reaction,[27] they are played undeniably major role in cross-coupling reactions.[28] Because of the low bond energy of C–I bond and facile nature to the oxidative addition, it is found to be superior coupling partner over the bromo or chloro congeners. Besides the synthetic utility, (hetero)aryl iodides have been found to be widely applicable in thyroid disease, anticancer treatment, X-ray imaging, and several pharmacokinetics studies.[29] In-spite of the synthetic and medicinal applicability of heteroaryl iodides, they are hugely expensive and limited in commercial availability. Hence, considerable effort has been invested in finding a suitable protocol to prepare heteroaryl iodides under a milder and greener reaction conditions with exclusive

regioselectivity. Sandmeyer reaction is one of the conventional ways to prepare the aryliodides. But the process demands prefunctionalized aromatic amines or nitro compounds.[30] Direct iodination of aromatic setup demands a Lewis acid or protonic acids, but the condition is not compatible with heterocycles as well as the regioselective cannot be achieve.[31]

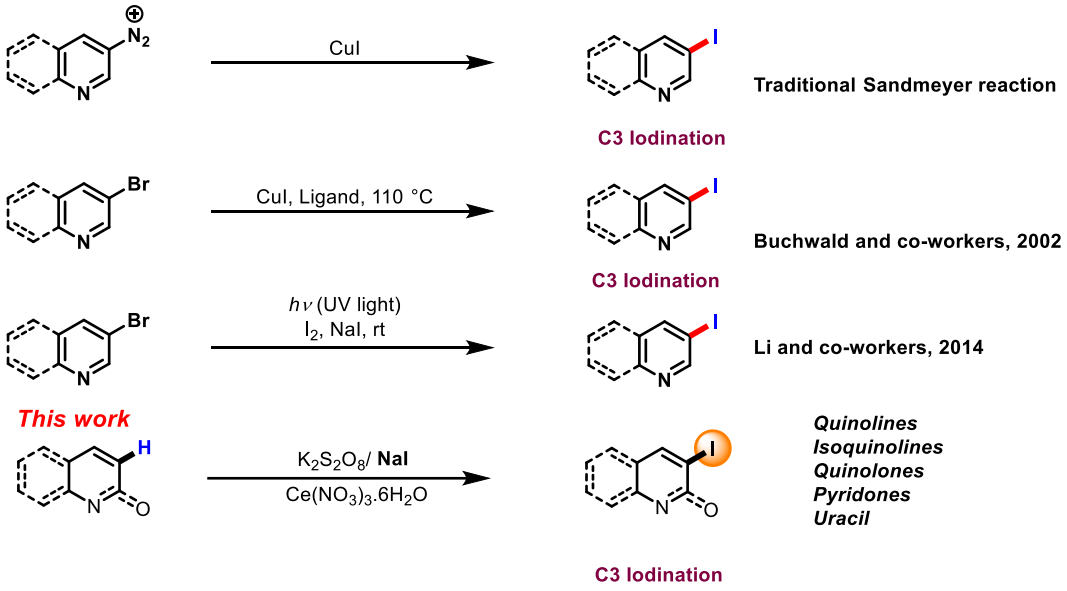
Scheme 1.6. Directing group assisted iodination protocols



However, directing group assisted C–H iodination is well explored using palladium, rhodium and other transition metals as the catalyst (Scheme 1.6).[32] Copper catalyzed aromatic Finkelstein reaction to transform bromo to iodo compounds has been reported by Buchwald and co-workers (Scheme 1.7).[33] More recently, Li group has reported a photo-induced Finkelstein reaction to access C3 and C4 iodinated quinolines.[34] Unfortunately, such approach demands the prefunctionalized aryl and heteroaryl compounds. In 2013, Baran and co-workers has reported C2 bromination of pyridine and quinoline using Bu_4NBr as a nucleophilic bromide source.[35] Chang's group has reported rhodium catalyzed C8 iodination of quinoline-*N*-oxide using NIS as the iodinating reagent.[36] Though significant effort has been employed in developing regioselective iodination of pyridine or quinolines but most of the methods are often limited by several factors that include poor selectivity, prefunctionalization or harsh reaction conditions. The lack of a mild hassle free reaction condition to achieve regioselective C3 iodination is yet to be addressed. As part of broader studies on the

functionalization of heterocycles, we commenced studies focused on C3 selective iodination of quinolines and related heterocycles. We envisaged a direct radical iodination approach enabled by the mild generation of the iodo radical. It was postulated that such an approach should allow predictable C3 iodination due to the stability of the first formed radical intermediate. Very recently a related concept was communicated by Sun[37] and Jain[38] group, which allowed the iodination of different quinoline derivatives in a regioselective manner.

Scheme 1.7. Traditional way of heterocycle C3-iodination and our approach

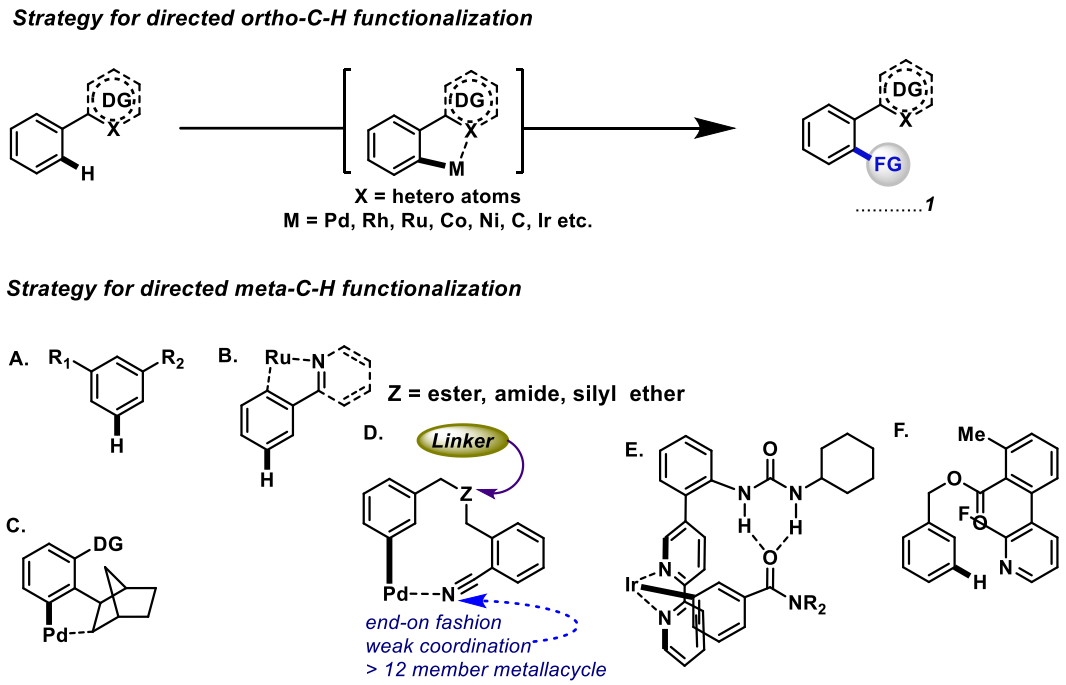


1.2.4. Development of Selective *meta*-C–H Functionalization Exploiting a Strong Coordinating Based Directing Group

Transformation of inert carbon-hydrogen (C−H) bonds into carbon-carbon (C−C) and/or carbon-heteroatom (C−X) bonds is arguably the best strategy during the synthesis of functional groups enriched arenes, which are ubiquitous in pharmaceuticals, agrochemicals, material sciences and complex natural products.[39] Functionalization of arenes using aromatic electrophilic or radical substitution reaction involving traditional Friedel-Crafts or Minisci reactions engrossed with selectivity issues.[40] A continuous effort to resolve the selectivity problems has prompted tremendous development of transition metal catalyzed cross coupling reaction,[41] but the detrimental effect on multistep synthesis of prefunctionalized starting materials limited the strategy. To avoid the prefunctionalization, directing group (DG)-assisted transition metal catalyzed C−H functionalization[42] has been acclaimed as a successful

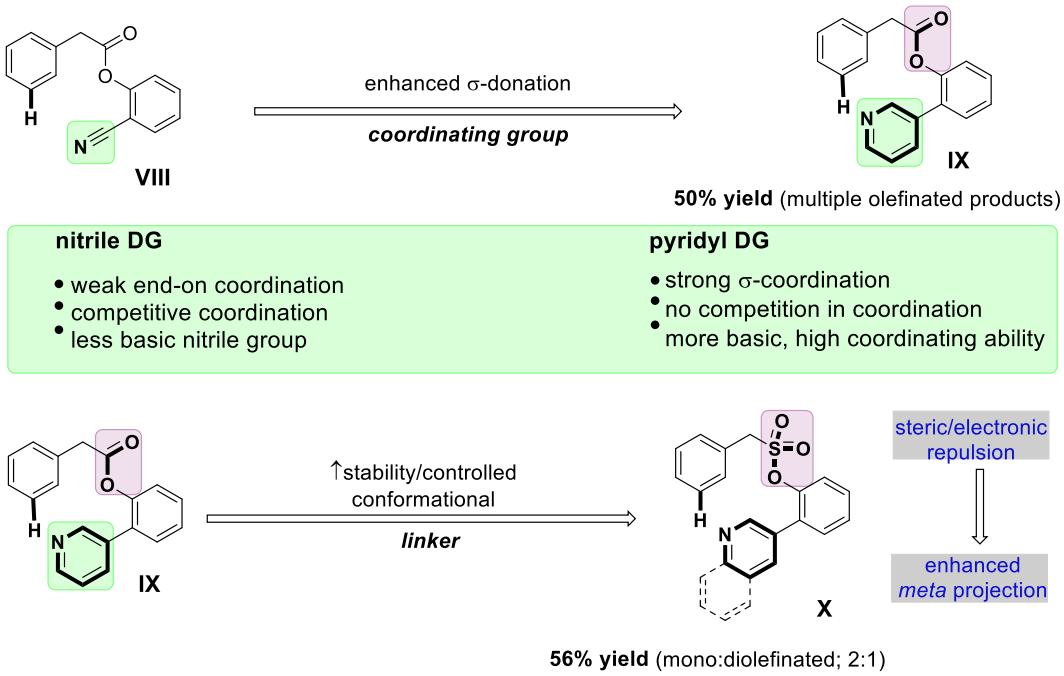
strategy in discerning energetically comparable C−H bonds present in the arene substrates of interest. Chelation assistance by heteroatom bearing directing group (DG) successfully guided the metals to the core of an energetically and conformationaly favourable rigid 5-6 membered metallacycle for proximal C−H activation to execute a plethora of *ortho*-C−H functionalization (Scheme 1.8, eq 1).[43] In a sharp contrast, beyond *ortho*-, distal *meta*- and *para*-C−H activation remained much less explored because of the requirement of a large macro-cyclophane type intermediate.[44] Nevertheless, distal C−H activation, dictated by the steric and electronic control (Scheme 1.8, A and B) has been achieved.[45] To overcome the intrinsic biasness, a staunch protocol is expected which demands a prudent combinations of chain length, directing group, ligands and metals.

Scheme 1.8. Strategies for directed C–H functionalization

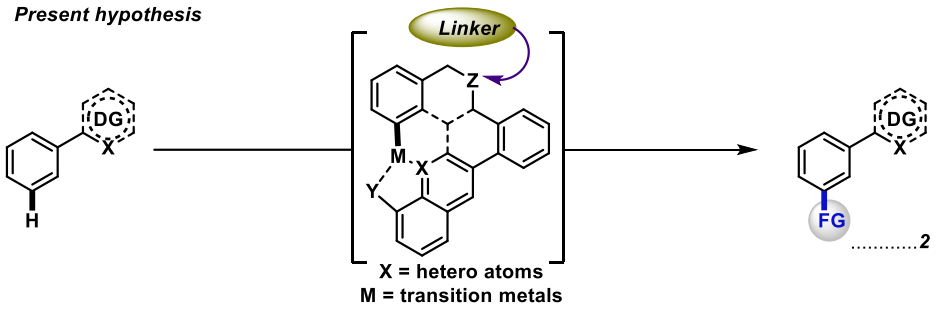


In this endeavor, pioneering approach has been disclosed by Yu and co-workers using cyano based template for *meta*-C−H functionalization.[46] Extending the concept, a significant progress has been made by one example from Tan group[47] and several examples from our[48] as well as Li group[49] by relying on the weakly end-on coordination of cyano group (Scheme 1.8, D). More recently, independent concepts has been implemented using hydrogen bonding approach (Kanai, Scheme 1.8, E),[50] Catelani approach (Yu and Dong, Scheme 1.8, C)[51] and by employing pyridine containing DG (Yu, Scheme 1.8, F)[52] etc.

Scheme 1.9. Limitation of weak coordinating cyano DG

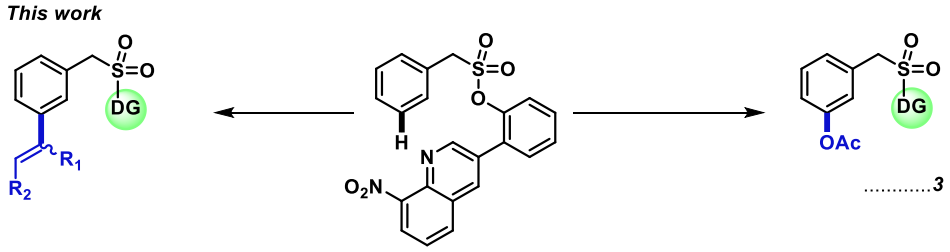


Scheme 1.10. Our hypothesis in order to develop a strong coordinating DG



Although, previous directing templates favored the formation of strain free cyclophane type macrocyclic intermediate and executed distal *meta*-C−H activation but it suffers from the intrinsic limitations owing to the weak coordination of cyano to Pd(II) centre via end-on fashion. This weak coordination is inherently competitive with solvents and other coordinating reagent present in the reaction and efficacy of the DG is eventually affected (Scheme 1.9).

Scheme 1.11. Overview of present work



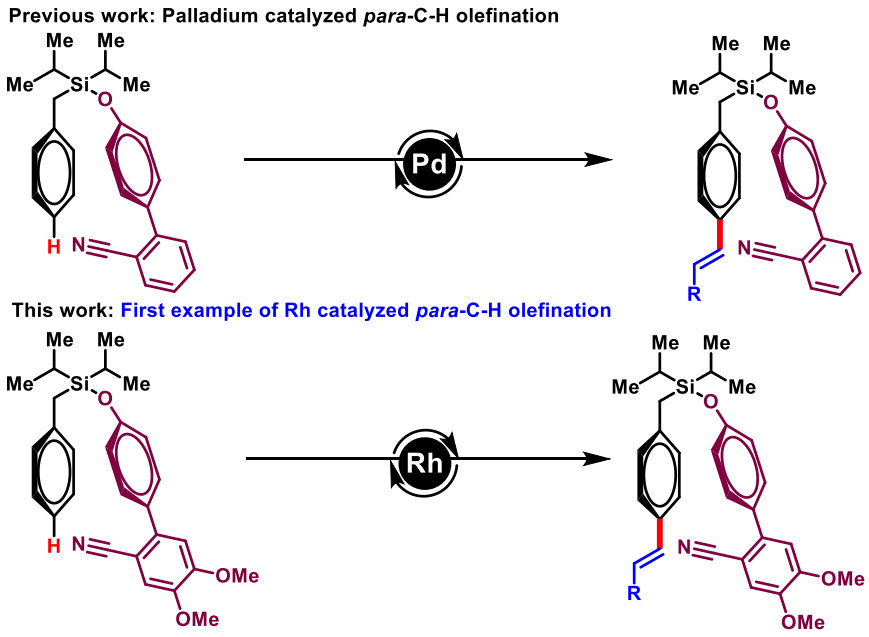
Under these circumstances, the potential of quinoline scaffold in designing a robust directing group for distal C−H activation through strong σ-coordination could be beneficial. According to the hypothesis (Scheme 1.10, eq 2), a planar yet rigid skeleton is the prerequisite where the heteroatom containing DG can hold the metal perfectly in a close proximity towards the *meta*-position of the arene ring to carry out the desired functionalization in an effective manner. Hence, a judicious engineering of quinoline-based template has been designed using the sulfonate linker to carry out the olefination and acetoxylation reaction at distal *meta*-position (Scheme 1.11, eq. 3).

1.2.5. Introducing a New Transition Metal in the Realm of Directing Group Assisted Distal *para*-C–H Functionlization

Upon successful accomplishment of *meta*-C–H functionalization, we envisaged to extend the concept to achieve the selective *para*-C–H functionalization. Based on our knowledge, gained from *meta*-template designing, we decided to modify the directing group, linker length and spacer. Upon thorough screening of linker length, and atom connectivity we come up with a cyano based biphenyl template to carryout *para*-C–H olefination and acetoxylation reaction for the first time back in 2015.[53] Switching the atom connectivity, we successfully performed the *para*-C–H olefination of phenol. [54] Further extension to perform other novel functionalizations selectively at *para*-position, make us realizing the incompetence of the existing template. As a consequence, we tried to control the steric and electronic factors that can enhance the efficacy of the DG. Finally we come up with dimethoxysubstituted cyano based biphenyl template, which proves to be superior in terms of yields and selectivity. With this 2nd generation DG we successfully accomplished the silylation and acylation reaction selectively at *para*- position of toluene based scaffold.[55]

However, the previous protocol utilizes the catalytic activity of Pd(II)/(0) and Pd(II)/(IV) to perform the desired *para*-functionalization. In addition to the development Pd catalyzed distal C–H functionalization, it is highly desirable to extend the concept of template assisted C–H functionalization using other transition metals. Recent and rapid development of Rh catalysis, employed for *ortho*-C–H activation,[56] stimulated us to explore its reactivity in template assisted distal *meta*- and *para*-C–H functionalization. Few facts that encourage us to use Rh as an alternative or complementary to Pd are; a) Rh catalyzed $C_{(sp^2)}$–H activation is well known at proximal position, b) C–H activation often occurred *via* chelation assisted DG, c) the ligands that is used for Pd-catalysis are usually different from the Rh-catalysis, hence the discovery might will open up a new avenue for developing new class of stereo-selective reactions that is controlled by the ligands, d) the redox potential for Rh and Pd is completely different, hence utilization of Rh may demand a new oxidant instead of Ag, which has often used in super stoichiometric amount in Pd catalysis. It implies that Rh catalysis may provide economically cheaper alternative compare to the Pd.

Scheme 1.12. Overview of present work



Very recently, our group[57] and Yu[58] group have parallelly disclosed a novel rhodium catalyzed distal *meta*-C–H olefination of phenylacetic acids and hydrocinnamic acids respectively. However, utilization of Rh to achieve the distal *para*-C–H

functionalization is yet to be explored. Hence we started investigating with our 2nd generation DG, and found that [Rh(COD)Cl_2] in association with $CuCl_2$ as oxidant and V_2O_5 as co-oxidant provide the desired product in good yield and selectivity (Scheme 1.12). In the last part of the thesis describe the development of Rh-catalyzed *para*-C–H olefination.

1.3. Reference

(1) (a) Trost B. M.; Li, C.-J. *Modern Alkyne Chemistry: Catalytic and Atom-Economic Transformations, ed*. Wiley, New York, 2014; (b) Stang, P. J.; Diederich, F. *Modern Acetylene Chemistry, ed*. Wiley, New York, 2008; (c) Diederich, F.; Stang, P. J.; Tykwinski, R. R. *Acetylene Chemistry. Chemistry, Biology and Material Science, ed*. Wiley-VCH, Weinheim, 2005.

(2) (a) Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Org. Lett*. **2001**, *3*, 735. (b) Tokunaga, M.; Suzuki, T.; Koga, N.; Fukushima, T.; Horiuchi, A.; Wakatsuki, Y. *J. Am. Chem. Soc.* **2001**, *123*, 11917. (c) Marion, N.; Ramon, R. S.; Nolan, S. P.´ *J. Am. Chem. Soc.* **2009**, *131*, 448. (d) Grotjahn, D. B.; Lev, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 12232.

(3) (a) Ding, S.; Yan, Y.; Jiao, N. *Chem. Commun*. **2013**, *49*, 4250. (b) Song, S.; Li, X.; Sun, X.; Yuan, Y.; Jiao, N. *Green Chem*. **2015**, *17*, 3285. (c) Peng, H.; Akhmedov, N. G.; Liang, Y.-F.; Jiao, N.; Shi, X. *J. Am. Chem. Soc*. **2015**, *137*, 8912. (d) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *J. Am. Chem. Soc*. **2005**, *127*, 9260. (e) Shen, H. C. *Tetrahedron* **2008**, *64*, 3885. (f) Beletskaya, I.; Moberg, C. *Chem. Rev*. **1999**, *99*, 3435. g) Oestreich, M. *Sci. Synth*. **2006**, *25*, 199.

(4) (a) Gilmore, K.; Alabugin, I. V. *Chem. Rev.* **2011**, *111*, 6513. (b) Amblard, F.; Cho, J. H.; Schinazi, R. F. *Chem. Rev*. **2009**, *109*, 4207. (c) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed*. **2001**, *40*, 2004. (d) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302. (e) Meldal, M.; Tornøe, C. W. *Chem. Rev*. **2008**, *108*, 2952. (f) Demko, Z. P.; Sharpless, K. B. *Angew. Chem., Int. Ed*. **2002**, *41*, 2113. (g) Friscourt, F.; Boons, G.-J. *Org. Lett*. **2010**, *12*, 4936. (h) Rodionov, V. O.; Presolski, S. I.; Gardinier, S.; Lim, Y.-H.; Finn, M. G. *J. Am. Chem. Soc*. **2007**, *129*, 12696. (i) Rasmussen, L. K.; Boren, B. C.; Fokin, V. V. *Org. Lett*. **2007**, *9*, 5337. (j) Nakamura, T.; Terashima, T.; Ogata, K.; Fukuzawa, S.-i. *Org. Lett*. **2011**, *13*, 620. (k) Shin, J.-A.; Lim, Y.-G.; Lee, K.-H. *J. Org. Chem*. **2012**, *77*, 4117. (l) Kamata, K.; Nakagawa, Y.; Yamaguchi, K.; Mizuno, N. *J. Am. Chem. Soc.* **2008**, *130*, 15304. (m) Barral, K.;

Moorhouse, A. D.; Moses, J. E. *Org. Lett*. **2007**, *9*, 1809. (n) Park, I. S.; Kwon, M. S.; Kim, Y.; Lee, J. S.; Park, J. *Org. Lett*. **2008**, *10*, 497. (o) Ö zcubukc ¸u, S.; Ozkal, E.; ¸ Jimeno, C.; Pericas, M. A.` *Org. Lett*. **2009**, *11*, 4680. (p) Liu, M.; Reiser, O. *Org. Lett*. **2011**, *13*, 1102. (q) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed*. **2002**, *41*, 2596. (r) Lipshutz, B. H.; Taft, B. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 8235. (s) Yamada, Y. M. A.; Sarkar, S. M.; Uozumi, Y. *J. Am. Chem. Soc*. **2012**, *134*, 9285.

(5) (a) Wang, T.; Jiao, N. *Acc. Chem. Res.* **2014**, *47*, 1137. (b) Furstner, A.; Davies, P. W. *Chem. Commun*. **2005**, 2307. (c) Villar, H.; Frings, M.; Bolm, C. *Chem. Soc. Rev*. **2007**, *36*, 55. (d) Deshmukh, P. H.; Blechert, S. *Dalton Trans*. **2007**, 2479. (e) Zhang, W.; Moore, J. S. *Adv. Synth. Catal*. **2007**, *349*, 93. (f) Lozano-Vila, A. M.; Monsaert, S.; Bajek, A.; Verpoort, F. *Chem. Rev*. **2010**, *110*, 4865. (g) Fü rstner, A. *Angew. Chem., Int. Ed*. **2013**, *52*, 2794. (h) Astruc, D. *New J. Chem*. **2005**, *29*, 42.

(6) (a) Kotov, V.; Scarborough, C. C.; Stahl, S. S. *Inorg. Chem*. **2007**, *46*, 1910. (b) Cornell, C. N.; Sigman, M. S. *Inorg. Chem*. **2007**, *46*, 1903. (c) Jung, M. E.; Deng, G. *Org. Lett.* **2014**, *16*, 2142. (d) Zhang, C.; Jiao, N. *J. Am. Chem. Soc*. **2010**, *132*, 28. (e) Michel, B. W.; Steffens, L. D.; Sigman, M. S. *Organic Reactions; John Wiley & Sons, Inc.:* **2004**. (f) Wan, Z.; Jones, C. D.; Mitchell, D.; Pu, J. Y.; Zhang, T. Y. *J. Org. Chem*. **2006**, *71*, 826. (g) Ren, W.; Xia, Y.; Ji, S.-J.; Zhang, Y.; Wan, X.; Zhao, J. *Org. Lett*. **2009**, *11*, 1841.

(7) (a)Sindhu, K. S.; Anilkumar, G. *RSC Adv*., **2014**, 4, 27867. (b) Su, L.; Dong, J.; Liu, L.; Sun, M.; Qiu, R.; Zhou, Y.; Yin, S.-F. *J. Am. Chem. Soc.*, **2016**, *138*, 12348. (c) Balaraman, K.; Kesavan, V. *Synthesis*, **2010**, 3461. (d) Bédard, A.-C.; Collins, S. K. *J. Am. Chem. Soc.*, **2011**, *133*, 19976. (e) Yan, S.; Pan, S.; Osako, T.; Uozumi, Y. *Synlett*, **2016**, *27*, 1232. (f) Luu, T.; Morisaki, Y.; Cunningham, N.; Tykwinski, R. R. *J. Org. Chem.*, **2007**, *72*, 9622.

(8) (a) Chinchilla, R.; Najera, C.´ *Chem. Rev.* **2007**, *107*, 874. (b) Dudnik, A. S.; Gevorgyan, V. *Angew. Chem., Int. Ed*. **2010**, *49*, 2096. (c) Sun, C.-L.; Shi, Z.-J. *Chem. Rev*. **2014**, *114*, 9219. (d) Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed*. **2003**, *42*, 5993. (e) Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc*. **2003**, *125*, 13642. (f) Gallop, C. W. D.; Chen, M.-T.; Navarro, O. *Org. Lett*. **2014**, *16*, 3724. (g) Dong, J.; Wang, F.; You, J. *Org. Lett*. **2014**, *16*, 2884. (h) Sanchez-Sanchez, C.; Orozco, N.; Holgado, J. P.; Beaumont, S. K.; Kyriakou, G.; Watson, D. J.; Gonzalez-Elipe, A. R.; Feria, L.;

Fernandez Sanz, J.; Lambert, R. M.´ *J. Am. Chem. Soc*. **2015**, *137*, 940. (i) Ahammed, S.; Dey, R.; Ranu, B. C. *Tetrahedron Lett*. **2013**, *54*, 3697.

(9) Kolle, S.; Batra, S. *Org. Biomol. Chem*., **2016**, *14*, 11048.

(10) (a) Wang, J.; Liu, C.; Yuan, J.; Lei, A. *Angew. Chem., Int. Ed*. **2013**, *52*, 2256. (b) Li, Y.-M.; Sun, M.; Wang, H.-L.; Tian, Q.-P.; Yang, S.- D. *Angew. Chem., Int. Ed*. **2013**, *52*, 3972. (c) Liu, W.; Groves, J. T. *Angew. Chem., Int. Ed*. **2013**, *52*, 6024. (d) Qvortrup, K.; Rankic, D. A.; MacMillan, D. W. C. *J. Am. Chem. Soc*. **2014**, *136*, 626. (e) Wei, W.-T.; Zhou, M.-B.; Fan, J.-H.; Liu, W.; Song, R.-J.; Liu, Y.; Hu, M.; Xie, P.; Li, J.-H. *Angew. Chem., Int. Ed*. **2013**, *52*, 3638.

(11) (a) Wille, U. *Chem. Rev.* **2013**, *113*, 813. (b) Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed*. **2013**, *52*, 12975. (c) Zhu, R.; Buchwald, S. L. *Angew. Chem., Int. Ed*. **2013**, *52*, 12655. (d) Zhang, B.; M.-Lichtenfeld, C.; Daniliuc, C. G.; Studer, A. *Angew. Chem., Int. Ed*. **2013**, *52*, 10792.

(12) (a) Miyake, Y.; Nakajima, K.; Nishibayashi, Y. *J. Am. Chem. Soc.* **2012**, *134*, 3338. (b) Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. *Angew. Chem., Int. Ed*. **2014**, *53*, 539. (c) Winston, M. S.; Wolf, W. J.; Toste, F. D. *J. Am. Chem. Soc*. **2014**, *136*, 7777. (d) Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D. W. C. *Science* **2013**, *339*, 1593. (e) Terrett, J. A.; Clift, M. D.; MacMillan, D. W. C. *J. Am. Chem. Soc*. **2014**, *136*, 6858.

(13) (a) Meerwein, H.; Buchner, E.; van Emsterk, K. *J. Prakt. Chem*. **1939**, *152*, 237. (b) Rondestvedt, C. S. *Org. React.* **1976**, 225. (c) Molinaro, C.; Mowat, J.; Gosselin, F.; O'Shea, P. D.; Marcoux, J.-F.; Angelaud, R.; Davies, I. W. *J. Org. Chem.* **2007**, *72*, 1856.

(14) (a) Heinrich, M. R.; Wetzel, A.; Kirschstein, M. *Org. Lett.* **2007**, *9*, 3833. (b) Heinrich, M. R. *Chem. Eur. J*. **2009**, *15*, 820.

(15) (a) Vogler, T.; Studer, A. *Synthesis* **2008**, *13,* 1979. (b) Tebben, L.; Studer, A. *Angew. Chem., Int. Ed*. **2011**, *50*, 5034.

(16) Hartmann, M.; Li, Y.; Studer, A. *J. Am. Chem. Soc*. **2012**, *134*, 16516.

(17) Zhang, B.; Studer, A. *Org. Lett*. **2013**, *15*, 4548.

(18) Li, Y.; Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8221.

(19) Maity, S.; Manna, S.; Rana, S.; Togati, N.; Mallick, A; Maiti, D. *J. Am. Chem. Soc.* **2013**, *135*, 3355.

(20) (a) Kurti, L.; Czako, B. *Strategic Applications of Named Reactions in Organic Synthesis; Elsevier Academic Press: Amsterdam,* 2005. (b) Fioravanti, S.; Pellacani, L.; Tardella, P. A.; Vergari, M. C. *Org. Lett*. **2008**, *10*, 1449.

(21) Maity, S.; Togati, N.; Sharma, U.; Maiti, D. *Org. Lett*. **2013**, *15*, 3384.

(22) Shen, T.; Wang, T.; Qin, C.; Jiao, N. *Angew. Chem., Int. Ed*. **2013**, *52*, 6677.

(23) Okamoto, N.; Ishikura, M.; Yanada, R. *Org. Lett*. **2013**, *15*, 2571.

(24) (a) Sherwood, A. G.; Gunning, H. E. *J. Am. Chem. Soc*. **1963**, *85*, 3506. (b) Surzur, J. M.; Dupuy, C.; Bertrand, M. P.; Nouguier, R. *J. Org. Chem*. **1972**, *37*, 2782.

(25) Shu, Z.; Ye, Y.; Deng, Y.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed*. **2013**, *52*, 10573.

(27) (a) Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 4302. (b) Tilly, D.; Chevallier, F.; Mongin, F.; Gros, P. C. *Chem. Rev.* **2014**, *114*, 1207.

27. (a) Bunnett, J. F.; Zahler, R. *Chem. Rev.* **1951**, *49*, 273. (b) Hartwig, J. F. *Synlett* **2006**, *9*, 1283. (c) Crampton, M. R. *Organic Reaction Mechanisms*; Wiley: New York, 2003, 275.

(28) (a) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (b) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450. (c) Popov, I.; Lindeman, S.; Daugulis, O. *J. Am. Chem. Soc.* **2011**, *133*, 9286.

(29) (a) Pimlott, S. L.; Sutherland, A. *Chem. Soc. Rev*., **2011**, *40*, 149. (b) Goldsby R. E.; Fitzgerald, P. A. *Nucl. Med. Biol*., **2008**, *35*, S49. (c) Seevers, R. H.; Counsell, R. E. *Chem. Rev*., **1982**, *82*, 575. (d) Ceusters, M.; Tourwe, D.; Callaerts, J.; Mertens, J.; Peter, A. *J. Org. Chem*., **1995**, *60*, 8324. (e) DeNardo, G. L.; DeNardo, S. J.; O'Donnell, R. T.; Kroger, L. A.; Kukis, D. L.; Meares, C. F.; Goldstein, D. S.; Shen, S. *Clin. Lymphoma*, **2000**, *1*, 118.

(30) (a) Hodgson, H. H.; *Chem. Rev*., **1947**, *40*, 251. (b) Galli, C. *Chem. Rev*., **1988**, *88*, 765.

(31) (a) Paul, V.; Sudalai, A.; Daniel, T.; Srinivasan, K. V. *Tetrahedron Lett*., **1994**, *35*, 7055. (b) Zanka, A.; Kubota, A. *Synlett*, **1999**, *12,* 1984 (c) Olah, G. A.; Wang, Q.; Sandford, G.; Prakash, G. K. S. *J. Org. Chem.*, **1993**, *58*, 3194. (d) Prakash, G. K. S.; Mathew, T.; Hoole, D.; Esteves, P. M.; Wang, Q.; Rasul G.; Olah, G. A. *J. Am. Chem. Soc.*, **2004**, *126*, 15770. (e) Stavber, S.; Jereb, M.; Zupan, M. *Synthesis*, **2008**, *10*, 1487.

(32) For Pd-catalyzed reactions, please see: (a) Kalyani, D.; Dick, A. R.; Anani W. Q.; Sanford, M. S. *Org. Lett*., **2006**, *8*, 2523; (b) Mei, T.-S.; Giri, R.; Maugel N.; Yu, J.-Q.

Angew. Chem., Int. Ed., **2008**, *47*, 5215; (c) Ma, X. T.; Tian, S. K. *Adv. Synth. Catal.*, **2013**, *355*, 337. (d) Schroeder, N.; Wencel-Delord J.; Glorius, F. *J. Am. Chem. Soc*., **2012**, *134*, 8298. (e) Schroeder, N.; Lied, F.; Glorius, F. *J. Am. Chem. Soc*., **2015**, *137*, 1448. (f) Partridge B. M.; Hartwig, J. F. *Org. Lett*., **2012**, *15*, 140. (g) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc*., **2006**, *128*, 6790. (h) Wang, W.; Pan, C.; Chen, F.; Cheng, J. *Chem. Commun*., **2011**, *47*, 3978. (i) Wang, L.; Ackermann, L. *Chem. Commun*., **2014**, *50*, 1083. (j) Wang, X.-C.; Hu, Y.; Bonacorsi, S.; Hong, Y.; Burrell, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 10326. (k) Imazaki, Y.; Shirakawa, E.; Ueno, R.; Hayashi, T. *J. Am. Chem. Soc*. **2012**, *134*, 14760. (l) Dudnik, A. S.; Chernyak, N.; Huang, C.; Gevorgyan, V. *Angew. Chem., Int. Ed*. **2010**, *49*, 8729. (m) Newman, S. G.; Howell, J. K.; Nicolaus, N.; Lautens, M. *J. Am. Chem. Soc*. **2011**, *133*, 14916. (n) Cant, A. A.; Bhalla, R.; Pimlott, S. L.; Sutherland, A. *Chem. Commun*. **2012**, *48*, 3993. (o) Casitas, A.; Canta, M.; Sola, M.; Costas, M.; Ribas, X. *J. Am. Chem. Soc.* **2011**, *133*, 19386. (p) Bissember, A. C.; Banwell, M. G. *J. Org. Chem.* **2009**, *74*, 4893.

(33) (a) Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844. (b) Chen, M.; Ichikawa, S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2015**, *54*, 263.

(34) Li, L.; Liu, W.-B.; Zeng, H.-Y.; Mu, X.-Y.; Cosa, G.; Mi, Z.-T.; Li, C.-J. *J. Am. Chem. Soc.* **2015**, *137*, 8328.

(35) Wengryniuk, S. E.; Weickgenannt, A.; Reiher, C.; Strotman, N. A.; Chen, K.; Eastgate, M. D.; Baran, P. S. *Org. Lett.* **2013**, *15*, 792.

(36) Hwang, H.; Kim, J.; Jeong, J.; Chang, S. *J. Am. Chem. Soc*. **2014**, *136*, 10770.

(37) Sun, K.; Lv, Y.; Wang, J.; Sun, J.; Liu, L.; Jia, M.; Liu, X.; Li, Z.; Wang, X. *Org. Lett.* **2015**, *17*, 4408.

(38) Sharma, K. K.; Patel, D. I.; Jain, R. *Chem. Commun.,* **2015**, *51*, 15129.

(39) (a) Giri, R.; Shi, B.-F.; Engle, K. M.; Maugel, N.; Yu, J.-Q. *Chem. Soc. Rev.* **2009**, *38*, 3242; (b) Chao, J.; Li, H.; Cheng, K.-W.; Yu, M.-S.; Chang, R. C.-C.; Wang, M. *J. Nutr. Biochem.* **2010**, *21*, 482; (c) Jazzar, R.; Hitce, J.; Renaudat, A.; Sofack-Kreutzer, J.; Baudoin, O. *Chem. Eur. J.* **2010**, *16*, 2654; (d) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885; (e) Newhouse, T.; Baran, P. S. *Angew. Chem. Int. Ed.* **2011**, *50*, 3362; (f) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451; (g) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; (h) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369; (i) Brückl, T.; Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826.

(40) (a) Minisci, F.; Bernardi, R.; Bertini, F.; Galli, R.; Perchinummo, M. *Tetrahedron* **1971**, *27*, 3575; (b) Minisci, F.; Citterio, A.; Giordano, C. *Acc. Chem. Res.* **1983**, *16*, 27; (c) Li, J. J. In *Name Reactions: A Collection of Detailed Mechanisms and Synthetic Applications*; Springer Berlin Heidelberg: Berlin, Heidelberg, 2009, p 361; (d) Manna, S.; Maity, S.; Rana, S.; Agasti, S.; Maiti, D. *Org. Lett.* **2012**, *14*, 1736; (e) Seo, S.; Slater, M.; Greaney, M. F. *Org. Lett.* **2012**, *14*, 2650; (f) Deb, A.; Manna, S.; Maji, A.; Dutta, U.; Maiti, D. *Eur. J. Org. Chem.* **2013**, *2013*, 5251; (g) Presset, M.; Fleury-Brégeot, N.; Oehlrich, D.; Rombouts, F.; Molander, G. A. *J. Org. Chem.* **2013**, *78*, 4615; (h) Hammer, S. G.; Heinrich, M. R. In *Comprehensive Organic Synthesis II (Second Edition)*; Elsevier: Amsterdam, 2014, p 495; (i) Zheng, Q.-Z.; Jiao, N. *Chem. Soc. Rev.* **2016**, *45*, 4590.

(41) (a) Cahiez, G.; Moyeux, A. *Chem. Rev.* **2010**, *110*, 1435; (b) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111*, 1596; (c) Chinchilla, R.; Najera, C. *Chem. Soc. Rev.* **2011**, *40*, 5084; (d) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417; (e) Knappke, C. E. I.; Jacobi von Wangelin, A. *Chem. Soc. Rev.* **2011**, *40*, 4948; (f) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780; (g) Molnár, Á. *Chem. Rev.* **2011**, *111*, 2251; (h) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346; (i) Selander, N.; J. Szabó, K. *Chem. Rev.* **2011**, *111*, 2048; (j) Sore, H. F.; Galloway, W. R. J. D.; Spring, D. R. *Chem. Soc. Rev.* **2012**, *41*, 1845; (k) Su, W.; Zhang, M.; Wu, G. In *C-H and C-X Bond Functionalization: Transition Metal Mediation*; The Royal Society of Chemistry: 2013, p 328; (l) Szostak, M.; Fazakerley, N. J.; Parmar, D.; Procter, D. J. *Chem. Rev.* **2014**, *114*, 5959; (m) Ahrens, T.; Kohlmann, J.; Ahrens, M.; Braun, T. *Chem. Rev.* **2015**, *115*, 931; (n) Johansson Seechurn, C. C. C.; Li, H.; Colacot, T. J. In *New Trends in Cross-Coupling: Theory and Applications*; The Royal Society of Chemistry: 2015, p 91; (o) Cheng, C.; Hartwig, J. F. *Chem. Rev.* **2015**, *115*, 8946; (p) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *Chem. Rev.* **2015**, *115*, 9587; (q) Liu, C.; Yuan, J.; Gao, M.; Tang, S.; Li, W.; Shi, R.; Lei, A. *Chem. Rev.* **2015**, *115*, 12138; (r) Petrone, D. A.; Ye, J.; Lautens, M. *Chem. Rev.* **2016**, *116*, 8003; (s) Hesp, K. D.; Genovino, J. In *Synthetic Methods in Drug Discovery: Volume 1*; The Royal Society of Chemistry: 2016; Vol. 1, p 170.

(42) (a) Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403; (b) Dick, A. R.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 2300; (c) Shabashov, D.; Daugulis, O. *Org. Lett.* **2005**, *7*, 3657; (d) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.*

2009, *48*, 9792; (e) Ackermann, L. *Chem. Commun.* **2010**, *46*, 4866; (f) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147; (g) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315; (h) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315; (i) Rousseau, G.; Breit, B. *Angew. Chem. Int. Ed.* **2011**, *50*, 2450; (j) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293; (k) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740; (l) Haibach, M. C.; Kundu, S.; Brookhart, M.; Goldman, A. S. *Acc. Chem. Res.* **2012**, *45*, 947; (m) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936; (n) Powers, D. C.; Ritter, T. *Acc. Chem. Res.* **2012**, *45*, 840; (o) Gallardo-Donaire, J.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 9350; (p) Louillat, M.-L.; Patureau, F. W. *Chem. Soc. Rev.* **2014**, *43*, 901; (q) Ros, A.; Fernandez, R.; Lassaletta, J. M. *Chem. Soc. Rev.* **2014**, *43*, 3229; (r) Wang, X.; Yu, D.-G.; Glorius, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 10280.

(43) (a) Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Chem. Commun.* **1994**, 2267; (b) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604; (c) Wang, X.; Truesdale, L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 3648; (d) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879; (e) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814; (f) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788; (g) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651; (h) Zhang, F.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906; (i) Huang, Z.; Lim, H. N.; Mo, F.; Young, M. C.; Dong, G. *Chem. Soc. Rev.* **2015**, *44*, 7764.

(44) Schranck, J.; Tlili, A.; Beller, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 9426.

(45) (a) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E.; Smith, M. R. *Science* **2002**, *295*, 305; (b) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390; (c) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593; (d) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072; (e) Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Köhn, G.; Whittlesey, M. K.; Frost, C. G. *J. Am. Chem. Soc.* **2011**, *133*, 19298; (f) Hofmann, N.; Ackermann, L. *J. Am. Chem. Soc.* **2013**, *135*, 5877; (g) Luo, J.; Preciado, S.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 4109; (h) Luo, J.; Preciado, S.; Larrosa, I. *Chem. Commun.* **2015**, *51*, 3127; (i) Paterson, A. J.; St John-Campbell, S.; Mahon, M. F.; Press, N. J.; Frost, C. G. *Chem. Commun.* **2015**, *51*, 12807; (j) Teskey, C. J.; Lui, A. Y. W.; Greaney, M. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 11677; (k) Bisht, R.; Chattopadhyay, B. *J. Am. Chem. Soc.* **2016**, *138*, 84; (l) Fan, Z.; Ni, J.; Zhang, A. *J.*

Am. Chem. Soc. **2016**, *138*, 8470; (m) Cheng, C.; Hartwig, J. F. *Science* **2014**, *343*, 853; (n) Martínez-Martínez, A. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T. *Science* **2014**, *346*, 834; (o) Tobisu, M.; Chatani, N. *Science* **2014**, *343*, 850; (p) Ackermann, L.; Li, J. *Nat Chem* **2015**, *7*, 686.

(46) (a) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518; (b) Wan, L.; Dastbaravardeh, N.; Li, G.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 18056; (c) Cheng, G.-J.; Yang, Y.-F.; Liu, P.; Chen, P.; Sun, T.-Y.; Li, G.; Zhang, X.; Houk, K. N.; Yu, J.-Q.; Wu, Y.-D. *J. Am. Chem. Soc.* **2014**, *136*, 894; (d) Tang, R.-Y.; Li, G.; Yu, J.-Q. *Nature* **2014**, *507*, 215; (e) Yang, G.; Lindovska, P.; Zhu, D.; Kim, J.; Wang, P.; Tang, R.-Y.; Movassaghi, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136*, 10807; (f) Yang, Y.-F.; Cheng, G.-J.; Liu, P.; Leow, D.; Sun, T.-Y.; Chen, P.; Zhang, X.; Yu, J.-Q.; Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **2014**, *136*, 344; (g) Deng, Y.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2015**, *54*, 888.

(47) Lee, S.; Lee, H.; Tan, K. L. *J. Am. Chem. Soc.* **2013**, *135*, 18778.

(48) (a) Bera, M.; Modak, A.; Patra, T.; Maji, A.; Maiti, D. *Org. Lett.* **2014**, *16*, 5760; (b) Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc.* **2015**, *137*, 11888; (c) Bera, M.; Maji, A.; Sahoo, S. K.; Maiti, D. *Angew. Chem. Int. Ed.* **2015**, *127*, 8635; (d) Bera, M.; Sahoo, S. K.; Maiti, D. *ACS Catal.* **2016**, *6*, 3575; (e) Maji, A.; Bhaskararao, B.; Singha, S.; Sunoj, R. B.; Maiti, D. *Chem. Sci.* **2016**, *7*, 3147; (f) Patra, T.; Bag, S.; Kancherla, R.; Mondal, A.; Dey, A.; Pimparkar, S.; Agasti, S.; Modak, A.; Maiti, D. *Angew. Chem. Int. Ed.* **2016**, *55*, 7751; (g) Patra, T.; Watile, R.; Agasti, S.; Naveen, T.; Maiti, D. *Chem. Commun.* **2016**, *52*, 2027.

(49) (a) Li, S.; Cai, L.; Ji, H.; Yang, L.; Li, G. *Nat. Commun.* **2016**, *7*; (b) Li, S.; Ji, H.; Cai, L.; Li, G. *Chem. Sci.* **2015**, *6*, 5595.

(50) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. *Nat. Chem.* **2015**, *7*, 712.

(51) (a) Dong, Z.; Dong, G. *J. Am. Chem. Soc.* **2013**, *135*, 18350; (b) Shen, P.-X.; Wang, X.-C.; Wang, P.; Zhu, R.-Y.; Yu, J.-Q. *J. Am. Chem. Soc.* **2015**, *137*, 11574; (c) Wang, X.-C.; Gong, W.; Fang, L.-Z.; Zhu, R.-Y.; Li, S.; Engle, K. M.; Yu, J.-Q. *Nature* **2015**, *519*, 334.

(52) Chu, L.; Shang, M.; Tanaka, K.; Chen, Q.; Pissarnitski, N.; Streckfuss, E.; Yu, J.-Q. *ACS Cent. Sci.* **2015**, *1*, 394.

(53) Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc*. **2015**, *137*, 11888.

(54) Patra, T.; Bag, S.; Kancherla, R.; Mondal, A.; Dey, A.; Pimparkar, S.; Agasti, S.; Modak, A.; Maiti, D. *Angew. Chem., Int. Ed*. **2016**, *55*, 7751.

(55) Maji, A.; Guin, S.; Feng, S.; Dahiya, A.; Singh, V. K.; Liu, P.; Maiti, D. *Angew. Chem., Int. Ed.* **2017**, *56*, 14903.

(56) a) Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc*. **2010**, *132*, 9982. b) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Org. Lett*. **2011**, *13*, 540. c) Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc*. **2011**, *133*, 2350. d) Gong, T.-J.; Xiao, B.; Liu, Z.-J.; Wan, J.; Xu, J.; Luo, D.-F.; Fu, Y.; Liu, L. *Org. Lett*. **2011**, *13*, 3235. e) Park, S. H.; Kim, J. Y.; Chang, S. *Org. Lett*. **2011**, *13*, 2372. f) Hyster, T. K.; Knçrr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500. g) Zhao, P.; Wang, F.; Han, K.; Li, X. *Org. Lett*. **2012**, *14*, 3400. h) Feng, C.; Feng, D.; Loh, T.-P. *Org. Lett*. **2013**, *15*, 3670. i) Zhang, T.; Wu, L.; Li, X. *Org. Lett*. **2013**, *15*, 6294. j) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. *Org. Lett*. **2013**, *15*, 3366. k) Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. *Org. Lett*. **2013**, *15*, 1528. l) Zhou, J.; Li, B.; Hu, F.; Shi, B.-F. *Org. Lett*. **2013**, *15*, 3460. m) Zhang, X.-S.; Zhu, Q.-L.; Zhang, Y.-F.; Li, Y.- B.; Shi, Z.-J. *Chem. Eur. J.* **2013**, *19*, 11898. n) Han, S.; Shin, Y.; Sharma, S.; Mishra, N. K.; Park, J.; Kim, M.; Kim, M.; Jang, J.; Kim, I. S. *Org. Lett*. **2014**, *16*, 2494. o) Otley, K. D.; Ellman, J. A. *Org. Lett*. **2015**, *17*, 1332.

(57) Bera, M.; Agasti, S.; Chowdhury, R.; Mondal, R.; Pal, D.; Maiti, D. *Angew. Chem., Int. Ed.* **2017**, *56*, 5272.

(58) Xu, H.-J.; Lu, Y.; Farmer, M. E.; Wang, H.-W.; Zhao, D.; Kang, Y.-S. Sun, W.-Y. Yu, J.-Q. *J. Am. Chem. Soc*. **2017**, *139*, 2200.

Chapter 2

Aerobic Oxynitration of Alkynes with ^{t}BuONO and TEMPO: Expanding the Scope of Metal-free Nitration

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Aerobic Oxynitration of Alkynes with ^{t}BuONO and TEMPO: Expanding the Scope of Metal-free Nitration

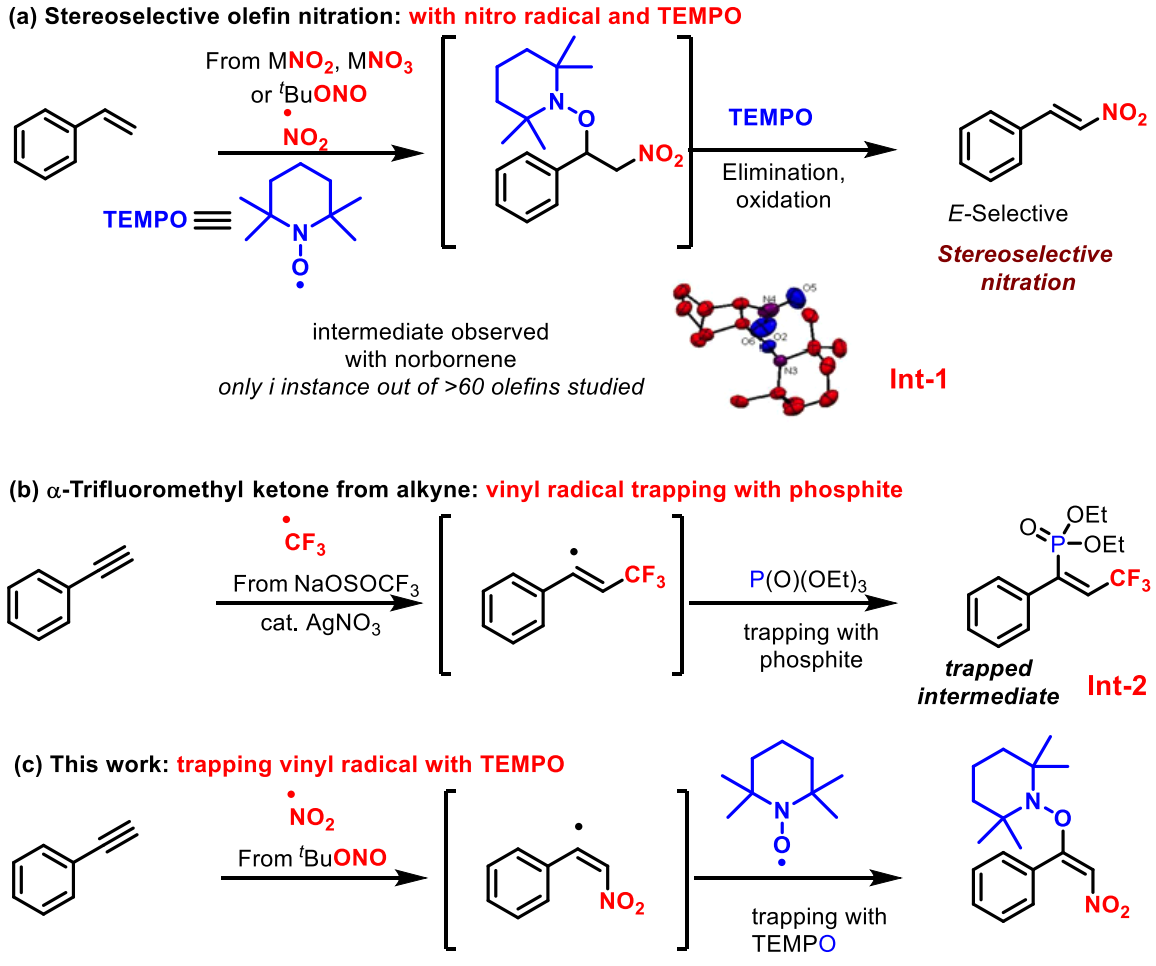
Abstract: An efficient method for stereoselective nitroaminoxylation of alkyne has been reported. The reaction enjoys a broad substrate scope, good functional group tolerance and high yields. Synthetically useful α–nitroketones can be accessed through these products in a single step. This method expands the scope of metal-free nitration to feed-stock chemical, alkynes.

2.1. Introduction

Olefins and alkynes are considered as feedstock chemicals in organic chemistry. Synthetic transformations of these unsaturated systems under mild aerobic conditions are of utmost importance. In this context, development of sustainable radical reactions seems to be the key to achieve such purpose.[1]

Recently we reported a series of radical based stereoselective nitration of olefins with TEMPO as the oxidizing agent.[2] Nitro radicals derived from shelf-stable precursors are likely to interact with the olefin to generate a nitroalkane radical intermediate.[3] Such transient radical species might be trapped with a 'persistent radical' such as TEMPO (plausible intermediate, Scheme 2.1a).[4] However, among more than 60 olefins studied, we observed such an intermediate only with a strained olefin, norbornene (**Int-1**, Scheme 2.1a). In other cases, subsequent oxidation proceeded faster to give olefin nitration in a stereoselective manner.[2a]

Scheme 2.1. Our previous work with unsaturated systems and radicals

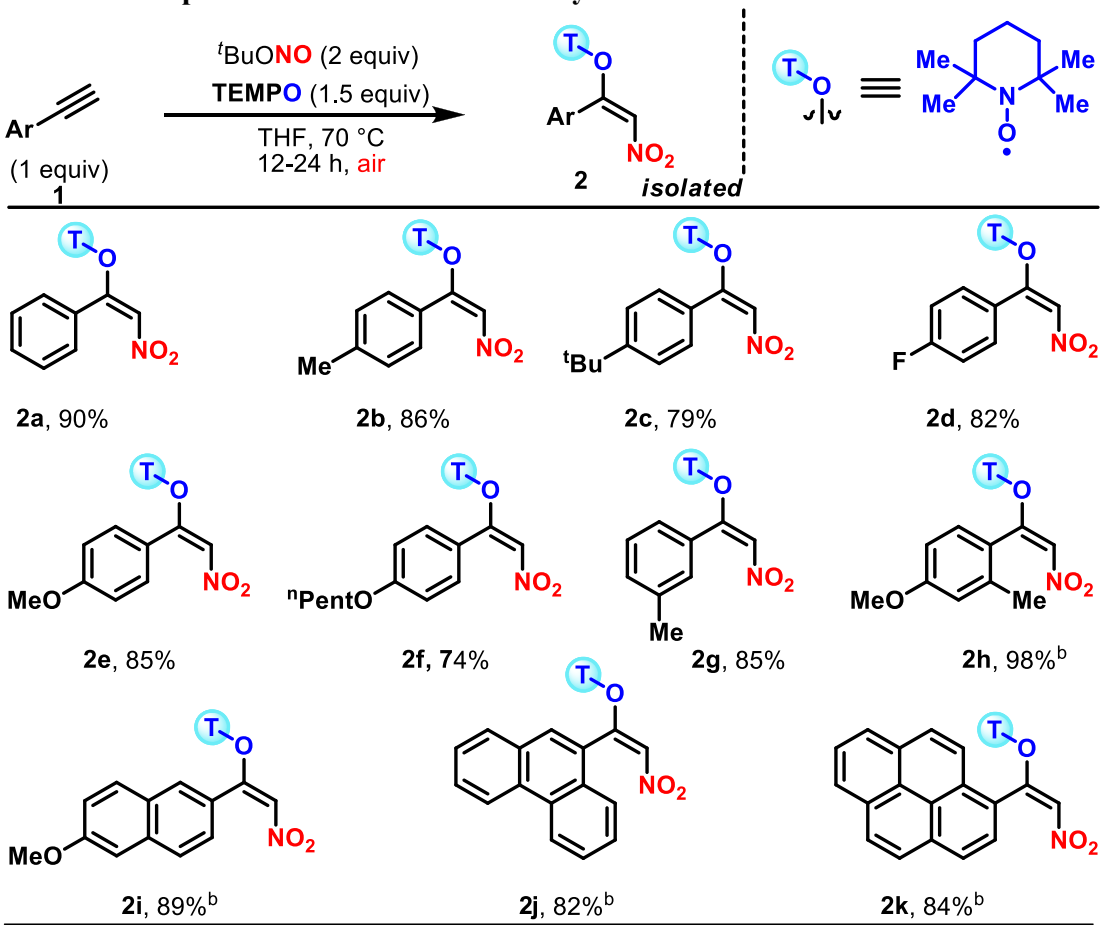


This observation was followed by a related development wherein an incipient trifluoromethyl radical[5] from NaOSOCF3 reacted with an alkyne to afford a highly reactive vinyl radical, which in the presence of $P(OEt)_3$ underwent an Arbuzov type[6] reaction to give intermediate 2 (**Int-2**, Scheme 2.1b).[7] This result showed us that selective functionalization of alkynes could be performed without having the Glaser-Hay homo-coupling product.[8] Furthermore, a highly reactive vinyl radical (σ radical) with a lower lifetime could be trapped in the laboratory set-up to provide bis-functionalized product.[9]

2.2. Result and Discussion

These observations motivated us to explore further and we decided to apply our previously established *metal-free* nitration conditions on terminal alkynes.[2b, 10] Interestingly, ^{t}BuONO provided the desired oxynitro product in considerable synthetic yield. Careful choice of solvents, temperature and more importantly nitro radical source consisted optimized reaction condition where slight excess of TEMPO provided the nitro product in excellent yields.

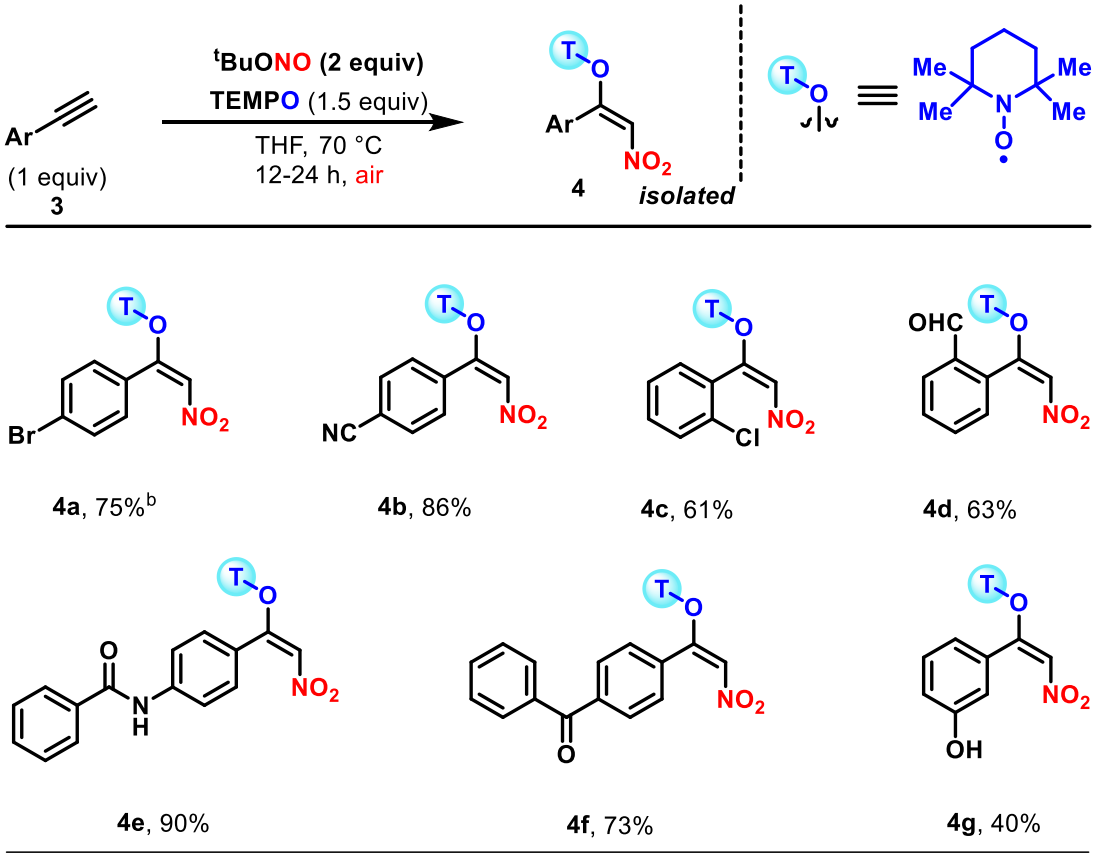
Table 2.1. Scope with aromatic terminal alkynes[a]



[a]General reaction condition: alkyne (0.5 mmol), ^{t}BuONO (1 mmol), TEMPO (0.75 mmol), THF (3 mL), 70 ºC, 24 h; [b]12 h.

Next, we started to explore the scope and limitation of this reaction. Phenylacetylene gave the product in 90% isolated yield (GC 95%; Table 2.1, **2a**). Differentially substituted alkynes with 4-Me (**2b**, 86%) and 4-F (**2d**, 82%) groups did not alter the outcome of the reaction. Likewise, a 4-OMe (**2e**, 85%) and a 4-alkoxy group (**2f**, 74%) were well tolerated. *Meta*- and *ortho*- substituted phenylacetylenes also underwent the reaction successfully (**2g** and **2h**). Notably, alkynes based on naphthalene (**2i**, 89%), phenanthrene (**2j**, 82%), and pyrene (**2k**, 84%) gave the desired products in excellent yields.

Table 2.2. Scope with functionalized aromatic terminal alkynes[a]

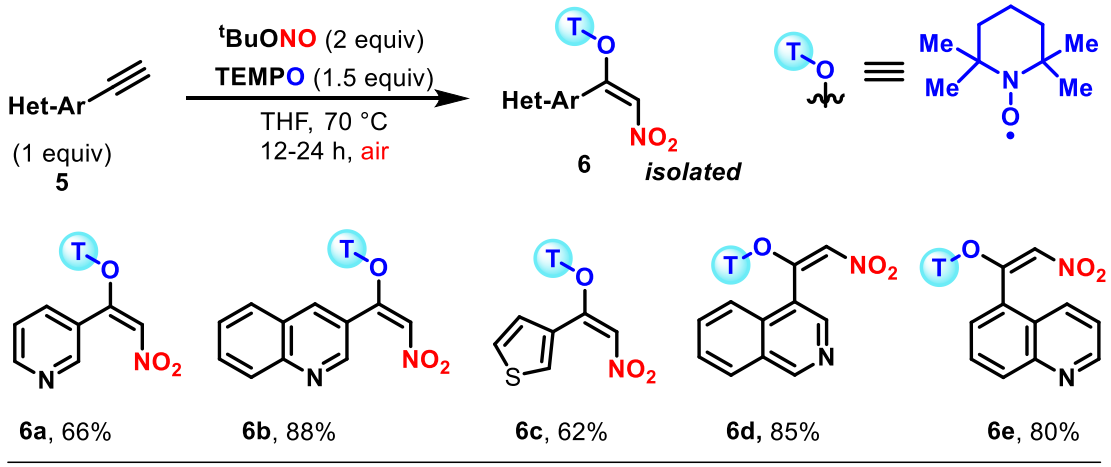


[a]General reaction condition: alkyne (0.5 mmol), ^{t}BuONO (1 mmol), TEMPO (0.75 mmol), THF (3 mL); [b]24 h.

A number of functionalized terminal alkynes underwent successful oxynitration under standard conditions (Table 2.2). The 4-bromo phenylacetylene gave the product in 75% yield (**4a**). Similarly, a cyano group at the *para*- position was found to be compatible under this ^{t}BuONO/TEMPO condition (**4b**, 86%). Sterically congested 2-Cl (**4c**, 61%) and 2-CHO (**4d**, 63%) substituted phenylacetylene provided the desired product. Likewise, a NHCO- (**4e**, 90%) and a keto- (**4f**, 73%) moiety remained intact while undergoing oxynitration. Moreover, a 3-

OH group was also tolerated (**4g**, 40%). Note that minor amount of ring nitration product was detected in this case.[11]

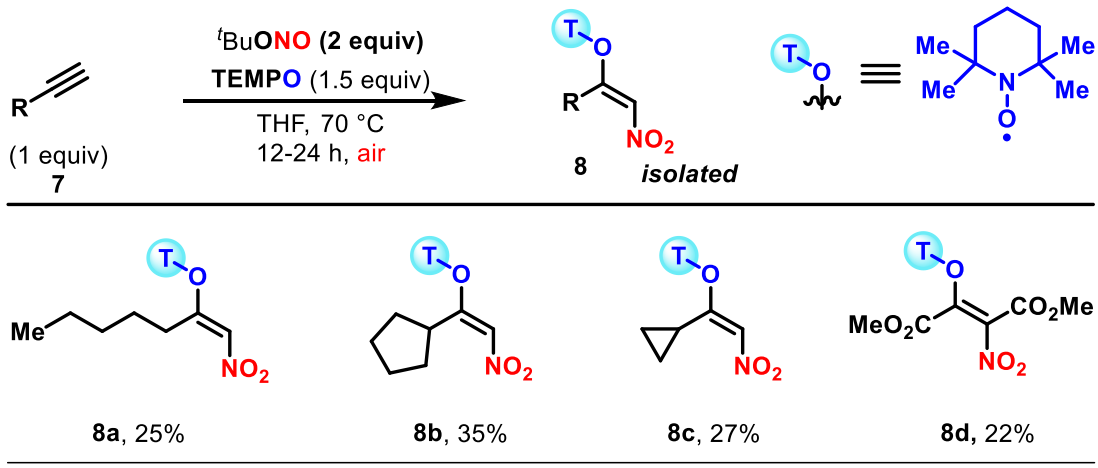
Table 2.3. Scope with heteroaromatic terminal alkynes



[a]General reaction condition: alkyne (0.5 mmol), ^{t}BuONO (1 mmol), TEMPO (0.75 mmol), THF (3 mL).

Next, the scope of this reaction was extended to heteroaromatic alkynes, which reacted efficiently in usual conditions (Table 2.3). Quinoline (**6b**) and isoquinoline derivatives (**6d** and **6e**) were particularly interesting as excellent yields were obtained with the corresponding alkynes (80-88%). With pyridine 3-alkyne, slight decrease of yield was observed (**6a**, 66%). On the other hand, electron rich thiophene derivative gave the desired product in synthetically useful yield (**6c**, 62%).

Table 2.4. Scope with aliphatic terminal alkynes[a]

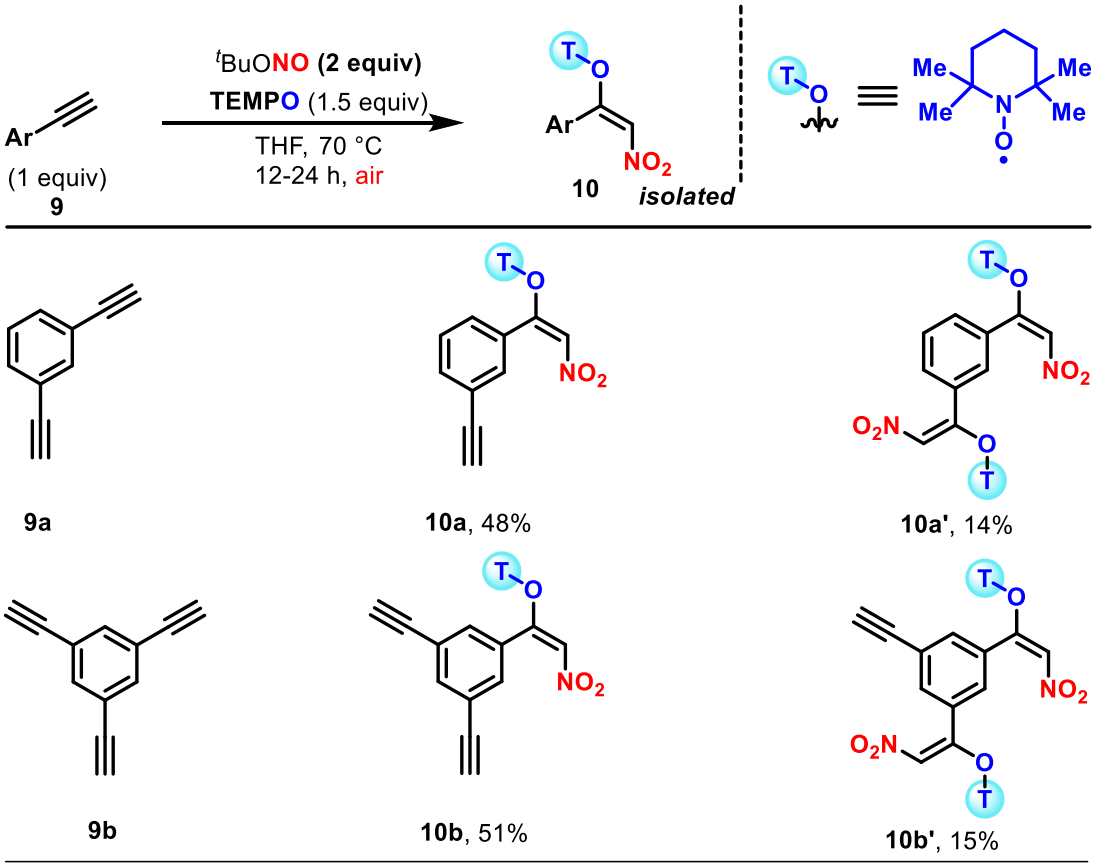


[a]General reaction condition: alkyne (0.5 mmol), ^{t}BuONO (1 mmol), TEMPO (0.75 mmol), THF (3 mL).

Aliphatic alkynes are distinct from their aromatic counterpart. Particularly in radical mechanism, the electronic difference often plays a major role in terms of reactivity.

Nevertheless, we investigated a number of such alkynes under the standard condition (Table 2.4). Aliphatic terminal alkyne such as 1-heptyne reacted with the ensuing nitro radical although the reactivity was diminished significantly (**8a**, 25%). This might be attributed to the lack of stabilization of the vinyl radical in absence of an aromatic system. Interestingly, both cyclopentyl (**8b**, 35%) and cyclopropyl (**8c**, 27%) acetylene gave the usual oxynitro product. Absence of any rearrangement or allene type product indeed suggests that the TEMPO trapping step is fast. Isolation of unreacted TEMPO from the reaction mixture further indicated the lack of undesired reactions in these cases. Notably, internal alkyne dimethylacetylenedicarboxylate underwent successful oxynitration under the standard condition (**8d**).

Table 2.2. Oxynitration trials on substrates containing multiple terminal alkynes[a]



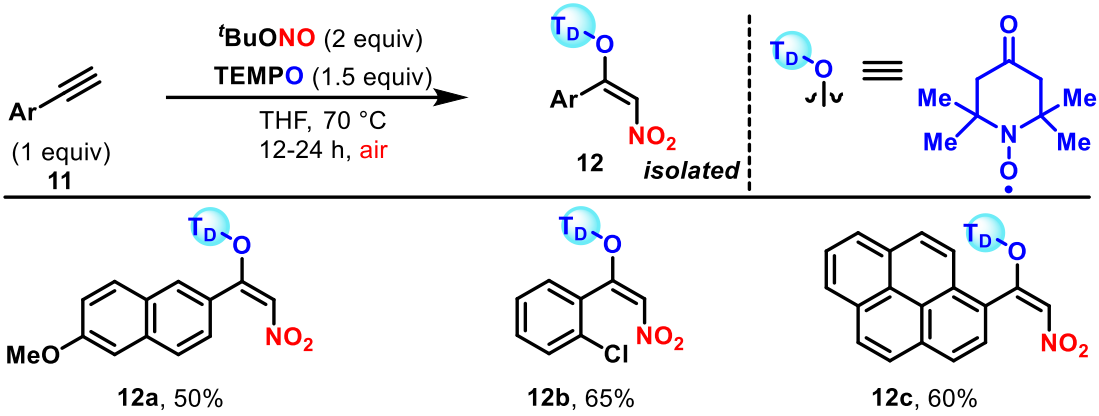
[a]General reaction condition: alkyne (0.5 mmol), ^{t}BuONO (1 mmol), TEMPO (0.75 mmol), THF (3 mL).

Another interesting class of substrates is *bis*- and *tris*- alkynes (Scheme 2.2). Under the usual condition, preference for mono-functionalization was evident in 1,3-diethynylbenzene and 1,3,5-triethynylbenzene. In case of *tris*-alkyne only trace amount tri-functionalized product was detected.

We next investigated the reaction with 4-oxo TEMPO (Table 2.5). The 6-methoxynaphthalene can be coupled in50% yield (**12a**). Similarly, 2-chlorophenylacetylene (**12b**,65%) and 1-ethynylpyrene (**12c**,60%) provided the desired product in preparatively useful yields.

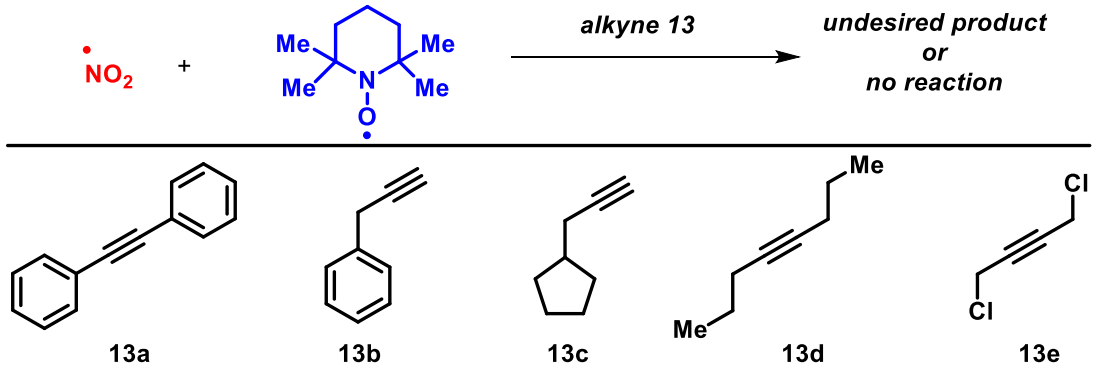
The present method is not without limitation. We realized that internal alkynes such as diphenyl acetylene (**13a**) and 4-octyne (**13d**) did not produce the expected oxynitration compounds. In case of diphenyl acetylene, 20% of benzil was isolated without a trace of the desired nitro compound.

Table 2.5. Scope of different TEMPO derivatives[a]



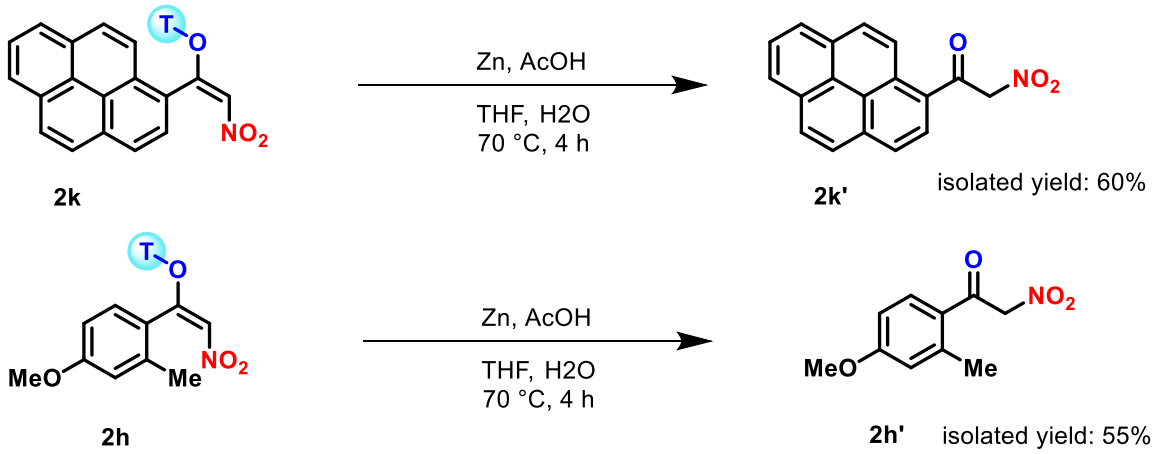
[a]General reaction condition: alkyne (0.5 mmol), ^{t}BuONO (1 mmol), TEMPO derivative (0.75 mmol), THF (3 mL).

Table 2.6. Unsuccessful substrates



The nitroaminoxylated products can be easily converted to useful α-nitroketones in high yields and purity in a single step (Scheme 2.3). These examples further signify the synthetic utility of nitroaminoxylated products derived through this present method.

Scheme 2.3. Synthetic Applications: Synthesis of α-Nitro Ketones



We confirmed the formation of (*E*)-product by X-ray crystallographic characterization of compounds **2i** (CCDC 1029301) and **4b (**CCDC 1029302). Interestingly, these compounds are containing aryl rings perpendicular to the plane of olefin double bonds and hence to the plane of vinyl radical. This might attribute to the relatively longer lifetime of vinyl radical which is sufficient in this case for trapping with TEMPO to get the anticipated nitroaminoxylated product.

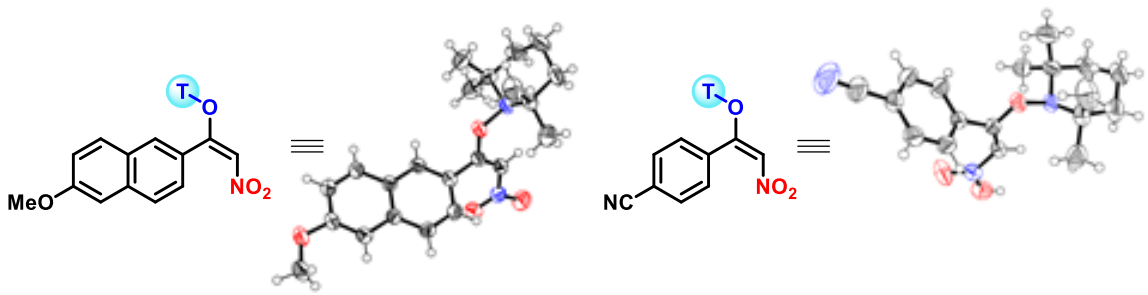


Figure 2.1. ORTEP diagram of compounds 2i and 4b

In conclusion, we have developed an efficient method for oxynitration of simple unactivated alkynes. Generation of the nitro radical, reaction with alkyne and subsequent trapping of the vinyl radical with TEMPO comprise the reaction sequence. This newly developed process is tolerant of a wide variety of functional groups and excellent yields have been obtained in most of the cases. Even aliphatic alkynes can be functionalized albeit in low yield. Owing to its mild nature and broad substrate scope, this method is expected to find applications in academic and industrial settings.

2.3. Experimental details

2.3.1. General Consideration:

2.3.1.a. Reagent Information. Unless otherwise stated, all reactions were carried out under air atmosphere in screw cap reaction tubes. All solvents were bought from Merck in sure-seal bottle and were used as received. *tert*-Butyl nitrite was purchased from Sigma Aldrich. 2,2,6,6-Tetramethyl-1-piperidinyloxy, free radical (TEMPO) was obtained from Spectrochem. Alkynes were bought from Aldrich and Alfa-Aesar. Some alkynes were synthesized from commercially available compounds by Sonogashira coupling and desilylation following literature procedures. For column chromatography, silica gel (100–200 mesh) obtained from SRL Co. was used. A gradient elution using pet ether and ethyl acetate was performed, based on Merck aluminum TLC sheets (silica gel 60F254).

2.3.1.b. Analytical Information: All isolated compounds were characterized by ^{1}H, ^{13}C-NMR spectroscopy, IR spectroscopy, Gas chromatography mass spectra (GC–MS)/HR-MS. Unless otherwise stated, all Nuclear Magnetic Resonance spectra were recorded on a Bruker 400 and 500 MHz instrument. The references used for the NMR are tetramethylsilane (TMS) for ^{1}H and ^{13}C-NMR. Some Nuclear Magnetic Resonance was taken on a VARIAN 400 MHz instrument. All ^{1}H-NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C-NMR spectra were reported in ppm relative to deuterochloroform (77.23 ppm), unless otherwise stated, and all were obtained with 1H decoupling. The melting points were measured in Büchi Melting Point Model B-545 apparatus. All GC analyses were performed on an Agilent 7890A GC system with an FID detector using a J & W DB–1 column (10 m, 0.1 mm I.D.) using *n*-decane as the internal standard. GCMS analysis was done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

2.3.1.c. Description of Reaction Tube:

Fig.1. Pictorial description of reaction tube for nitro aminoxylation of alkyne: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left hand side]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E) [right hand side, top]; Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A) [right hand side, bottom].

2.3.2. Optimization of the reaction condition for nitro aminoxylation of alkyne

2.3.2.a. Optimization by varying solvent

Sr. No.	Solvent	GC Yield (%)
1	Toluene	60
2	MeOH	-
3	Cyclohexane	46
4	DCM	54
5	DCE	73
6	$CHCl_3$	35
7	**THF**	**80**
8	1,4-Dioxane	79
9	DMSO	-
10	DMF	-
11	Chlorobenzene	40
12	MeCN	42

2.3.2.b. Optimization by varying Nitro Source

Sr. No.	Nitro source	GC Yield (%)
1	-	-
2	KNO_3	-
3	$NaNO_2$	-
4	$AgNO_2$	41
5	$AgNO_3$	62
6	$Bi(NO_3)_3.5H_2O$	75
7	$NiNO_3.6H_2O$	30
8	**^{t}BuONO**	**80**
9	$(NH_4)_2Ce(NO_3)_6$	10
10	ZrO(NO3)2	-
11	Ce(NO3)3.6H2O	2
12	Pb(NO3)2	5

Among the different nitro sources, ^{t}BuONO was found to be excellent for the transformation.

2.3.2.c. Optimization by varying solvent amount

Sr. No.	solvent amount (mL)	GC Yield (%)
1	0.5	54
2	1.0	80
3	**1.5**	**85**
4	2.0	72
5	3.0	75

After having the suitable solvent in hand we optimized amount of solvent and was found 1.5 mL solvent is sufficient to achieve the excellent conversion.

2.3.2.d. Optimization by varying TEMPO amount

Sr. No.	TEMPO (equiv)	GC Yield (%)
1	-	-
2	0.5	30
3	1.0	63
4	**1.5**	**92**
5	2.0	85
6	3.0	86

Different loadings of TEMPO proven that, 1.5 equivalent of TEMPO with respect to alkyne is perfectly fine for the excellent yield.

2.3.2.e. Optimization by varying *t*BuONO amount

Sr. No.	*t*BuONO (equiv)	GC Yield (%)
1	-	-
2	0.5	28
3	1.0	80
4	1.5	82
5	**2.0**	**92**
6	3.0	93

Varying the amount of ^{t}BuONO revealed that 2.0 equivalent of ^{t}BuONO is required for achieving excellent yield.

2.3.2.f. Optimization by varying temperature

Sr. No.	Temperature (˚C)	GC Yield (%)
1	RT	30
2	50	60
3	**70**	**94**
4	90	92
5	100	90

After screening the amount of solvent, TEMPO and *t*BuONO we tried to see the effect of temperature and it was found that 70 ˚C is good for transformation.

2.3.2.g. Optimization by varying time

Sr. No.	Time (h)	GC Yield (%)
1	6	30
2	12	87
3	18	89
4	22	91
5	**24**	**94**

Time optimization revealed that 12 hour to 24 hour yield is almost consistent. So, we ran the reactions from 12 to 24 hour depending on the substrate.

2.3.3. General Procedure A: Synthesis of (*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-phenylvinyl)-oxy)piperidine derivatives from terminal alkyne

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, TEMPO (0.375 mmol, 58.5 mg) and corresponding alkyne (0.25 mmol). Solid reagents were weighed first followed by liquid reagents. Addition of 1.5 mL of THF was followed by the addition requisite amount of *tert*-Butyl nitrite (0.5 mmol, 59.5 μL). The reaction mixture was stirred vigorously on a preheated oil bath at 70 °C for 12-24 h depending on the substrate. After completion of the reaction the mixture was diluted with EtOAc (2 mL) and evaporated under vacuum. The crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

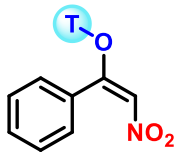
General Procedure B: Synthesis of terminal alkyne (starting material)

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar [$Pd(PPh_3)_2Cl_2$] (0.02 mmol; 14 mg), CuI (0.04 mmol; 7.6 mg) and bromo-substrate (1 mmol). To that, dry THF (1 mL) followed by triethylamine (1.55 mmol; 216 μL) was added under nitrogen atmosphere with stirring at room temperature. Under nitrogen atmosphere, trimethylsilylacetylene (1.25 mmol; 176 μL) was added to the reaction mixture slowly. Gradually the reaction turned dark. The reaction was stirred continuously for 24 h at room temperature. The progress of the reaction was monitored by TLC. Once the reaction was done, the mixture was diluted with 5 mL EtOAc and filtered through the celite. The filtrate was evaporated under reduced pressure and the compound was isolated through silica column (100-200 mesh).[12]

Terminal alkyne was obtained through hydrolysis of 4-(trimethysilyl)ethynyl-substrates. The TMS-ethynyl substrates were dissolved in 1.5 mL MeOH and anhydrous K_2CO_3 were added to it under N_2 atmosphere. The reaction mixture was stirred at room temperature for 3 h. Upon completion, the reaction was filtered through celite and the filtrate was evaporated under reduced pressure and purified through silica column (100-200 mesh).

2.3.4. Characterization data:

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-phenylvinyl)oxy)piperidine: (Scheme 3, entry 2a)



(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-phenylvinyl)oxy)piperidine was synthesized using the general procedure A from phenylacetylene in 0.5 mmol scale. Yield: 90% (137 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 6H), 1.23 (s, 6H), 1.59 – 1.68 (m, 6H), 7.45 (d, J = 4.6 Hz, 4H), 7.47 – 7.52 (m, 1H), 7.83 (s, 1H).

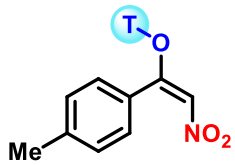
^{13}C NMR (101 MHz, $CDCl_3$) δ 16.82, 20.81, 32.15, 39.70, 61.66, 123.52, 128.26, 130.70, 131.93, 171.81.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{17}H_{24}N_2O_3Na$ is 327.1679, found: 327.1674.

IR (thin film) 3142, 2977, 2936, 1625, 1597, 1499, 1486, 1366, 1341, 1174, 1119, 797, 695 cm^{-1}.

Melting Point: 103-105 ºC

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(*p*-tolyl)vinyl)oxy)piperidine: (Scheme 3, entry 2b)



(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(*p*-tolyl)vinyl)oxy)piperidine was synthesized using the general procedure A from 1-ethynyl-4-methylbenzene in 0.5 mmol scale. Yield: 86% (137 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99.5:0.5 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.20 (s, 6H), 1.22 (s, 6H), 1.59 – 1.66 (m, 6H), 2.42 (s, 3H), 7.27 (d, J = 7.9 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.82 (s, 1H).

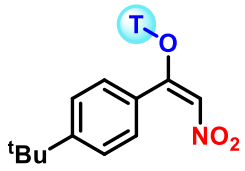
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.86, 20.84, 21.74, 32.17, 39.72, 61.63, 123.35, 128.33, 128.91, 129.15, 141.17, 172.03.

HRMS (ESI): $[M + H]^+$ calculated for: 319.2022, found: 319.2034.

Melting Point: 100-101 ºC

IR (thin film) 3144, 2977, 2936, 1621, 1605, 1513, 1489, 1366, 1339, 1172, 1117, 824 cm^{-1}.

(*E*)-1-((1-(4-(*tert*-butyl)phenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 3, entry 2c)



(*E*)-1-((1-(4-(*tert*-butyl)phenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A from 1-tert-butyl-4-ethynylbenzene in 0.5 mmol scale. Yield: 79% (142 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.21 (d, J = 1.3 Hz, 12H), 1.36 (s, 9H), 1.59 – 1.65 (m, 6H), 7.40 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 8.6 Hz, 2H), 7.82 (s, 1H).

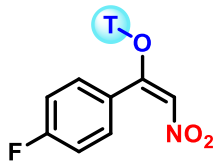
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.93, 20.95, 31.40, 32.22, 35.16, 39.81, 61.70, 123.40, 125.42, 128.34, 128.77, 154.24, 172.04.

HRMS (ESI): $[M + H]^+$ calculated for $C_{21}H_{33}N_2O_3$: 361.2491, found: 361.2482.

Melting Point: 125-126 ºC.

IR (thin film) 2967, 1623, 1604, 1514, 1493, 1339, 1173, 1129, 840 cm^{-1}.

(*E*)-1-((1-(4-fluorophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 3, entry 2d)



(*E*)-1-((1-(4-fluorophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A from 1-ethynyl-4-fluorobenzene in 0.5 mmol scale. Yield: 82% (132 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

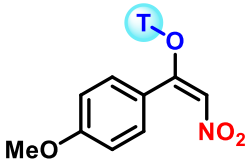
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.19 (s, 6H), 1.20 (s, 6H), 1.58 – 1.67 (m, 6H), 7.13 (t, J = 8.6 Hz, 2H), 7.42 – 7.48 (m, 2H), 7.81 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.79, 20.80, 32.13, 39.67, 61.70, 115.60, 115.78, 123.66, 127.80, 127.83, 130.58, 130.65, 163.11, 165.11, 170.71.

HRMS (ESI): $[M + H]^+$ calculated for $C_{17}H_{24}N_2O_3F$: 323.1771, found: 323.1891.

Melting Point: 110-111 ºC.

(*E*)-1-((1-(4-methoxyphenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 3, entry 2e)



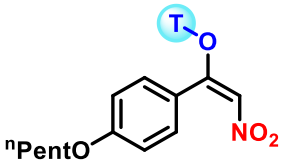
(*E*)-1-((1-(4-methoxyphenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A from 1-ethynyl-4-methoxybenzene in 0.5 mmol scale. Yield: 85% (142 mg). Yellow oil. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm)1.20 (s, 6H), 1.20 (s, 6H), 1.59 – 1.66 (m, 6H), 3.86 (s, 3H), 6.96 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 7.81 (s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.86, 20.88, 32.15, 39.73, 55.51, 61.61, 113.83, 123.02, 123.64, 130.36, 161.73, 171.66.

HRMS (ESI): $[M + H]^+$ calculated for $C_{18}H_{27}N_2O_4$: 335.1971, found: 335.1982.

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(4-(pentyloxy)phenyl)vinyl)oxy)piperidine: (Scheme 3, entry 2f)



(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(4-(pentyloxy)phenyl)vinyl)oxy)piperidine was synthesized using the general procedure A from 1-ethynyl-4-(pentyloxy)benzene 0.5 mmol scale. Yield: 74% (144 mg). Yellow oily liquid. Eluent: petroleum ether: ethyl acetate = 99.3:0.7 (v/v).

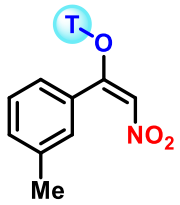
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.94 (t, J = 7.1 Hz, 3H), 1.19 (s, 6H), 1.20 (s, 6H), 1.41 (s, 3H), 1.62 (d, J = 4.5 Hz, 6H), 1.81 (s, 3H), 4.00 (t, J = 6.5 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.80 (s, 1H).

^{13}C NMR (101MHz, $CDCl_3$) δ (ppm) 14.23, 16.93, 20.95, 22.65, 26.29, 28.39, 29.07, 32.21, 39.80, 61.67, 68.31, 114.33, 123.02, 123.38, 130.41, 161.47, 171.80.

HRMS (ESI): $[M + H]^+$ calculated for $C_{22}H_{35}N_2O_4$: 391.2597, found: 391.2636.

IR (thin film) 3144, 2934, 2872, 1607, 1574, 1512, 1490, 1366, 137, 1254, 1172, 1120, 835 cm^{-1}.

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(*m*-tolyl)vinyl)oxy)piperidine: (Scheme 3, entry 2g)



(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(*m*-tolyl)vinyl)oxy)piperidine was synthesized using the general procedure A from 1-ethynyl-3-methylbenzene in 0.5 mmol scale. Yield: 85% (135 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v). m. p.

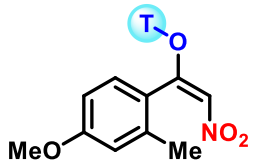
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.20 (s, 6H), 1.23 (s, 6H), 1.60 – 1.66 (m, 6H), 2.41 (s, 3H), 7.21 – 7.25 (m, 2H), 7.29 – 7.37 (m, 2H), 7.81 (s, 1H).

^{13}C NMR (126MHz, $CDCl_3$) δ (ppm) 16.86, 20.86, 21.59, 32.19, 39.73, 61.66, 123.46, 125.32, 128.38, 128.70, 131.55, 131.91, 138.21, 172.17.

HRMS (ESI): $[M + H]^+$ calculated for $C_{18}H_{27}N_2O_3$: 319.2022, found: 319.2025.

Melting Point: 94-96 ºC.

(*E*)-1-((1-(4-methoxy-2-methylphenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 3, entry 2h)



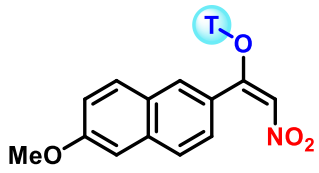
(*E*)-1-((1-(4-methoxy-2-methylphenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A from 1-ethynyl-4-methoxy-2-methylbenzene in 0.5 mmol scale. Yield: 98% (171 mg). Yellow oily liquid. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17 (s, 6H), 1.25 (s, 6H), 1.62 (s, 6H), 2.31 (s, 3H), 3.79 (s, 3H), 6.78 (d, J = 9.5 Hz, 2H), 7.19 (d, J = 8.1 Hz, 1H), 7.91 (s, 1H).

^{13}C NMR (101MHz, $CDCl_3$) δ (ppm) 16.83, 20.82, 32.13, 39.71, 61.71, 115.37, 118.10, 120.22, 123.34, 129.79, 133.08, 156.02, 172.06.

HRMS (ESI): $[M + H]^+$ calculated for $C_{19}H_{29}N_2O_4$: 349.2127, found: 349.2131.

(*E*)-1-((1-(6-methoxynaphthalen-2-yl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 3, entry 2i)



(*E*)-1-((1-(6-methoxynaphthalen-2-yl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A from 2-ethynyl-6-methoxynaphthalene 0.5 mmol scale. Yield: 89% (171 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.23 (s, 6H), 1.28 (s, 6H), 1.59 – 1.68 (m, 6H), 3.92 (s, 3H), 7.17 (d, J = 2.5 Hz, 1H), 7.20 (dd, J = 8.9, 2.5 Hz, 1H), 7.49 (dd, J = 8.5, 1.8 Hz, 1H), 7.80 (dd, J = 8.7, 5.6 Hz, 2H), 7.93 (s, 1H), 7.94 (d, J = 1.9 Hz, 1H).

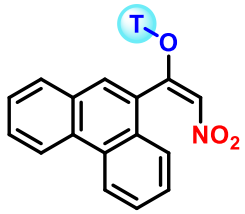
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm)16.73, 20.75, 32.09, 39.60, 55.39, 61.57, 105.83, 119.55, 123.38, 125.86, 126.77, 128.04, 128.22, 130.20, 135.79, 159.02, 172.03.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{22}H_{28}N_2NaO_4$: 407.1941, found: 407.1944.

Melting Point: 138-139 ºC

IR (thin film) 3140, 2976, 2935, 1628, 1598, 1509, 1480, 1337, 1264, 1215, 1170, 1129, 1030, 866, 755 cm^{-1}.

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(phenanthren-9-yl)vinyl)oxy)piperidine: (Scheme 3, entry 2j)



(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(phenanthren-9-yl)vinyl)oxy)piperidine was synthesized using the general procedure A from 9-ethynylphenanthrene 0.5 mmol scale. Yield: 82% (166 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.12 (s, 3H), 1.27 (s, 3H), 1.44 (d, J = 7.8 Hz, 6H), 1.68 (q, J = 13.8, 13.3 Hz, 6H), 7.64 (q, J = 7.1 Hz, 2H), 7.72 (dt, J = 13.1, 7.7 Hz, 2H), 7.83 (s, 1H), 7.97 (t, J = 8.5 Hz, 2H), 8.19 (d, J = 2.8 Hz, 1H), 8.75 (dd, J = 22.3, 8.3 Hz, 2H).

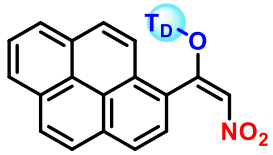
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.89, 20.78, 20.92, 32.55, 39.94, 40.00, 61.62, 62.30, 122.92, 123.48, 124.76, 125.58, 127.14, 127.25, 127.46, 127.52, 128.18, 128.94, 129.41, 130.07, 130.36, 130.81, 131.21, 170.74.

HRMS (ESI): $[M + H]^+$ calculated for $C_{25}H_{29}N_2O_3$: 405.2178, found: 405.2076.

Melting Point: 195-196 ºC.

IR (thin film) 2980, 1633, 1494, 1447, 1340, 1164, 865, 811, 762 cm^{-1}.

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(pyren-4-yl)vinyl)oxy)piperidine: (Scheme 3, entry 2k)



(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(pyren-4-yl)vinyl)oxy)piperidine was synthesized using the general procedure A from 1-ethynyl-1,3a2-dihydropyrene in 0.5 mmol scale. Yield: 84% (186 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v). m. p.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.12 (s, 3H), 1.26 (d, J = 4.1 Hz, 3H), 1.47 (d, J = 3.6 Hz, 6H), 1.58 (s, 1H), 1.70 (qd, J = 12.6, 12.1, 3.1 Hz, 5H), 8.00 – 8.07 (m, 2H), 8.11 (dd, J = 9.1, 4.4 Hz, 2H), 8.15 (d, J = 2.7 Hz, 2H), 8.16 – 8.22 (m, 1H), 8.22 – 8.24 (m, 1H), 8.26 (d, J = 2.2 Hz, 2H).

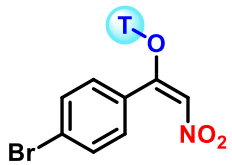
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.97, 20.89, 32.66, 40.05, 123.54, 124.67, 124.75, 124.79, 125.56, 125.82, 126.05, 126.22, 126.51, 127.03, 127.38, 129.00, 129.11, 129.33, 130.94, 131.37, 132.81, 171.12.

HRMS (ESI): $[M + H]^+$ calculated for $C_{27}H_{29}N_2O_3$: 429.2178, found: 429.2146.

Melting Point: 190-192 ºC.

IR (thin film) 3138, 2977, 2935, 1615, 1598, 1509, 1492, 1366, 1339, 1295, 1169, 1146, 847, 758 cm^{-1}.

(*E*)-1-((1-(4-bromophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 4, entry 4a)



(*E*)-1-((1-(4-bromophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A from 1-bromo-4-ethynylbenzene in 0.5 mmol scale. Yield: 75% (143 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.18 (s, 6H), 1.20 (s, 6H), 1.62 (d, J = 7.6 Hz, 6H), 7.31 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.80 (s, 1H).

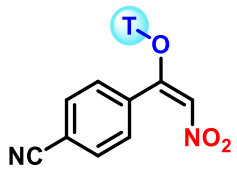
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.85, 20.87, 32.22, 39.74, 61.81, 123.83, 125.32, 129.96, 130.83, 131.84, 170.71.

HRMS (ESI): $[M + H]^+$ calculated for $C_{17}H_{23}N_2O_3Br$: 382.0892, found: 382.1236.

Melting Point: 76-78 ºC.

IR (thin film) 3141, 2977, 2936, 1626, 1587, 1497, 1367, 1340, 1173, 1119, 833, 814 cm^{-1}.

(*E*)-4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)benzonitrile: (Scheme 4, entry 4b)



(*E*)-4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)benzonitrile was synthesized using the general procedure A from 1-bromo-4-ethynylbenzene in 0.5 mmol scale. Yield: 86% (142 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm)1.18 (s, 6H), 1.21 (s, 6H), 1.63 (s, 6H), 7.51 – 7.54 (m, 2H), 7.73 – 7.77 (m, 2H), 7.81 (s, 1H).

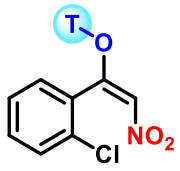
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.79, 20.85, 32.23, 39.73, 61.99, 114.42, 118.25, 124.36, 132.36, 136.58, 169.70.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{18}H_{24}N_3O_3Na$: 352.1632, found: 352.1638.

Melting Point: 165-167 ºC.

IR (thin film) 3130, 2981, 2942, 2871, 2229, 1628, 1601, 1506, 1342, 1322, 1174, 1119, 844, 761 cm^{-1}.

(*E*)-1-((1-(2-chlorophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidin: (Scheme 4, entry 4c)



(*E*)-1-((1-(2-chlorophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidin was synthesized using the general procedure A from 1-chloro-2-ethynylbenzene in 0.5 mmol scale. Yield: 61% (103mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99.3:0.7 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.18 (s, 6H), 1.29 (d, J = 22.9 Hz, 6H), 1.63 (s, 6H), 7.30 – 7.39 (m, 2H), 7.37 – 7.46 (m, 1H), 7.48 (dd, J = 7.9, 1.3 Hz, 1H), 7.89 (s, 1H).

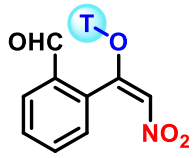
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.92, 20.78, 32.19, 39.99, 61.90, 125.17, 127.08, 129.42, 130.00, 131.27, 132.27, 132.88, 169.09.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{17}H_{23}ClNaN_2O_3$: 361.1289, found: 361.1288.

Melting Point: 137- 138 ºC

IR (thin film) 3144, 2979, 2937, 1629, 1589, 1498, 1472, 1367, 1344, 1322, 1177, 1131, 1053, 796, 755 cm^{-1}.

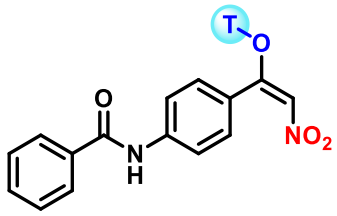
(*E*)-2-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)benzaldehyde: (Scheme 4, entry 4d)



(*E*)-2-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)benzaldehyde was synthesized using the general procedure A from 2-ethynylbenzaldehyde in 0.5 mmol scale. The compound is found to be getting decomposed in contact with silica inside the column. Efforts to obtain the compound in pure form did not help us. So, the NMR of the crude reaction mixture was recorded by using 1,3,5-trimethoxybenzene as the internal standard.

NMR Yield: 63% (Internal Ref: 1,3,5-trimethoxybenzene)

(*E*)-*N*-(4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)phenyl)benzamide: (Scheme 4, entry 4e)



(*E*)-*N*-(4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)phenyl)benzamide was synthesized using the general procedure A from N-(4-ethynylphenyl)benzamide in 0.5 mmol scale. Yield: 90% (191 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.18 (d, J = 2.4 Hz, 12H), 1.60 (d, J = 7.5 Hz, 6H), 7.39 (d, J = 2.3 Hz, 1H), 7.39 – 7.45 (m, 3H), 7.51 (tt, J = 7.0, 1.8 Hz, 1H), 7.70 – 7.75 (m, 2H), 7.80 (s, 1H), 7.82 – 7.87 (m, 2H), 8.42 (d, J = 19.1 Hz, 1H).

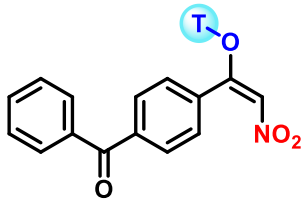
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 14.32, 16.83, 20.84, 21.19, 32.16, 39.70, 60.59, 61.70, 119.87, 123.28, 127.34, 128.85, 129.42, 132.14, 134.71, 140.63, 166.32, 171.79.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{24}H_{29}N_3O_4Na$: 446.2056, found: 446.2034.

Melting Point: 147-148 ºC

IR (thin film) 2978, 2936, 1661, 1603, 1516, 1405, 1326, 1246, 1173, 1128, 757, 715 cm^{-1}.

(*E*)-(4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)phenyl)(phenyl)methanone: (Scheme 4, entry 4f)



(*E*)-(4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)phenyl)(phenyl)methanone was synthesized using the general procedure A from (4-ethynylphenyl)(phenyl)methanone 0.5 mmol scale. Yield: 73% (149 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 98.5:1.5 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (s, 6H), 1.24 (s, 6H), 1.60 – 1.69 (m, 6H), 7.48 – 7.56 (m, 4H), 7.59 – 7.66 (m, 1H), 7.83 – 7.89 (m, 5H).

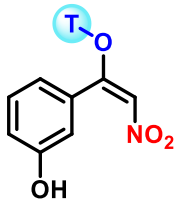
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.90, 20.93, 32.31, 39.81, 61.94, 124.13, 128.36, 128.64, 130.12, 130.34, 133.01, 135.86, 137.29, 139.42, 170.88.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{24}H_{29}N_2O_4Na$: 432.2055, found: 432.1921.

Melting Point: 165-167 ºC.

IR (thin film) 3144, 2977, 2937, 2874, 1663, 1628, 1600, 1507, 1490, 1341, 1323, 1277, 1175, 1118, 801, 753, 709 cm^{-1}.

(*E*)-3-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)phenol: (Scheme 4, entry 4g)



(*E*)-3-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)phenol was synthesized using the general procedure A from 3-ethynylphenol 0.5 mmol scale. Yield: 40% (64 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 98:2 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (s, 6H), 1.15 (s, 6H), 1.52 – 1.61 (m, 6H), 6.87 (s, 1H), 6.92 (d, J = 7.7 Hz, 2H), 7.23 (d, J = 7.6 Hz, 1H), 7.75 (s, 1H).

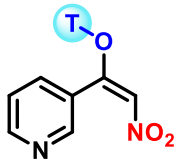
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.83, 20.82, 32.13, 39.71, 61.71, 115.37, 118.10, 120.22, 123.34, 129.79, 133.08, 156.02, 172.06.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{17}H_{24}N_2NaO_4$: 343.1628, found: 343.1630.

Melting Point: 131-132 ºC.

IR (thin film) 3398, 2977, 2937, 1587, 1495, 1367, 1337, 1245, 1171, 1113, 921, 795, 696 cm^{-1}.

(*E*)-3-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)pyridine: (Scheme 5, entry 6a)



(*E*)-3-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)pyridine was synthesized using the general procedure A from 3-ethynylpyridine 0.5 mmol scale. Yield: 66% (101 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 98.5:1.5 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.15 (s, 6H), 1.17 (s, 6H), 1.59 (d, J = 6.1 Hz, 6H), 7.36 (dd, J = 7.9, 4.9 Hz, 1H), 7.73 (dt, J = 7.9, 2.0 Hz, 1H), 7.82 (s, 1H), 8.64 – 8.69 (m, 2H).

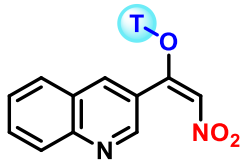
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.69, 20.71, 32.12, 39.60, 61.77, 123.14, 124.48, 128.30, 136.03, 148.61, 151.39, 168.81.

HRMS (ESI): $[M + H]^+$ calculated for $C_{16}H_{24}N_3O_3$: 306.1812, found: 306.1816.

Melting Point: 87-89 ºC

IR (thin film) 3142, 2977, 2937, 2875, 1626, 1585, 1495, 1339, 1246, 1175, 1129, 867, 812, 758, 708 cm^{-1}.

(*E*)-3-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)quinoline: (Scheme 5, entry 6b)



(*E*)-3-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)quinoline was synthesized using the general procedure A from 3-ethynylquinoline 0.5 mmol scale. Yield: 88% (157 mg). Yellow oily liquid. Eluent: petroleum ether: ethyl acetate = 95:5 (v/v).

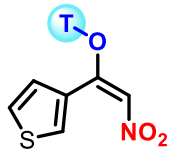
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (s, 6H), 1.27 (s, 6H), 1.65 (s, 6H), 7.62 (ddd, J = 8.0, 6.9, 1.1 Hz, 1H), 7.77 – 7.86 (m, 1H), 7.90 (dd, J = 8.3, 1.3 Hz, 1H), 7.95 (s, 1H), 8.13 – 8.20 (m, 1H), 8.27 (d, J = 2.2 Hz, 1H), 8.92 (d, J = 2.3 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.85, 20.91, 32.35, 39.78, 61.97, 124.79, 125.46, 127.08, 127.60, 128.66, 129.62, 131.31, 136.42, 148.66, 148.92, 169.11.

HRMS (ESI): $[M + H]^+$ calculated for $C_{20}H_{26}N_3O_3$: 356.1974, found: 356.1695.

IR (thin film) 3141, 2977, 2935, 1627, 1592, 1494, 1368, 1340, 1309, 1253, 1172, 1105, 783, 755 cm^{-1}.

(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(thiophen-3-yl)vinyl)oxy)piperidine: (Scheme 5, entry 6c)

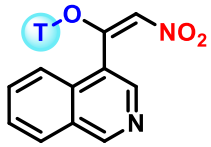


(*E*)-2,2,6,6-tetramethyl-1-((2-nitro-1-(thiophen-3-yl)vinyl)oxy)piperidine was synthesized using the general procedure A from 3-ethynylthiophene 0.5 mmol scale. Yield: 62% (96 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.17 (s, 6H), 1.22 (s, 6H), 1.58 – 1.66 (m, 6H), 7.30 (dd, J = 5.1, 1.3 Hz, 1H), 7.35 (dd, J = 5.1, 3.0 Hz, 1H), 7.83 (s, 1H), 7.85 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.87, 21.00, 32.11, 39.70, 61.67, 123.29, 125.26, 127.99, 129.61, 131.12, 166.02.
HRMS (ESI): $[M + H]^+$ calculated for $C_{15}H_{23}N_2O_3S$: 311.1429, found: 311.1424.

Melting Point: 108-110 ºC.
IR (thin film) 3141, 2977, 2936, 1614, 1488, 1411, 1335, 1302, 1163, 1109, 807, 682 cm^{-1}.

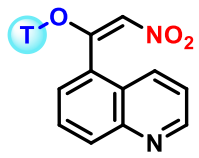
(*E*)-4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)isoquinoline: (Scheme 5, entry 6d)



(*E*)-4-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)isoquinoline was synthesized using the general procedure A from 4-ethynylisoquinoline 0.25 mmol scale. Yield: 85% (75 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 90:10 (v/v). m. p.
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.07 – 1.25 (m, 6H), 1.36 (s, 6H), 1.67 (dd, J = 4.7, 2.5 Hz, 6H), 7.68 (ddd, J = 8.1, 6.7, 1.3 Hz, 1H), 7.75 (ddd, J = 8.4, 6.7, 1.4 Hz, 1H), 7.81 (dd, J = 8.4, 1.2 Hz, 1H), 8.07 (dd, J = 8.2, 1.1 Hz, 1H), 8.13 (s, 1H), 8.58 (s, 1H), 9.35 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.92, 20.87, 32.59, 39.97, 123.20, 125.05, 126.39, 128.06, 128.12, 128.72, 131.98, 133.23, 142.14, 154.80, 168.17.
HRMS (ESI): $[M + H]^+$ calculated for $C_{20}H_{26}N_3O_3$: 356.1974, found: 356.1459.

Melting Point: 155-156 ºC.
IR (thin film) 3134, 2975, 2932, 1616, 1573, 1486, 1380, 1340, 1229, 1170, 1128, 907, 798, 773, 750 cm^{-1}.

(*E*)-5-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)isoquinoline: (Scheme 5, entry 6e)



(*E*)-5-(2-nitro-1-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)vinyl)isoquinoline was synthesized using the general procedure A 6-ethynylquinoline 0.25 mmol scale. Yield: 80% (71 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 90:10 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.06 – 1.19 (m, 6H), 1.34 (s, 6H), 1.59 – 1.70 (m, 6H), 7.59 – 7.71 (m, 2H), 7.74 (dd, J = 7.2, 1.3 Hz, 1H), 8.05 – 8.11 (m, 2H), 8.55 (d, J = 5.9 Hz, 1H), 9.31 (d, J = 1.0 Hz, 1H).

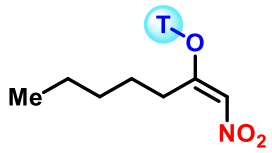
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.79, 20.76, 32.45, 39.83, 116.89, 125.71, 126.72, 128.35, 129.84, 130.28, 133.32, 144.40, 153.30, 168.85.

HRMS (ESI): $[M + H]^+$ calculated for $C_{20}H_{26}N_3O_3$: 356.1974, found: 356.1495.

Melting Point:137-139 ºC.

IR (thin film) 3142, 2978, 2935, 1627, 1581, 1495, 1342, 1325, 1263, 1169, 1141, 817, 780, 758, 623 cm^{-1}.

(*E*)-2,2,6,6-tetramethyl-1-(1-nitrohept-1-en-2-yloxy)piperidine: (Scheme 7, entry 8a)



S18

(*E*)-2,2,6,6-tetramethyl-1-(1-nitrohept-1-en-2-yloxy)piperidine was synthesized using the general procedure A 1-heptyne 0.5 mmol scale. Yield: 25% (38 mg). Yellow oily liquid. Eluent: pet ether.

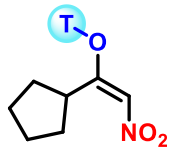
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.91 (t, J = 7.1 Hz, 3H), 1.04 (s, 6H), 1.18 (s, 6H), 1.31 – 1.36 (m, 2H), 1.51 – 1.62 (m, 6H), 1.61 – 1.73 (m, 4H), 2.81 – 2.89 (m, 2H), 7.67 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 14.09, 16.88, 20.72, 22.45, 27.04, 31.42, 32.10, 39.70, 61.35, 123.18, 177.55.

HRMS (ESI): $[M + H]^+$ calculated for $C_{16}H_{31}N_2O_3$: 299.2335, found: 299.2326.

IR (thin film) 2934, 2873, 1614, 1495, 1338, 1174, 1087, 918, 813, 724 cm^{-1}.

(*E*)-1-(1-cyclopentyl-2-nitrovinyloxy)-2,2,6,6-tetramethylpiperidine: (Scheme 7, entry 8b)



(*E*)-1-(1-cyclopentyl-2-nitrovinyloxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A 1-heptyne 0.5 mmol scale. Yield: 35% (52 mg). Yellow solid compound. Eluent: pet ether.

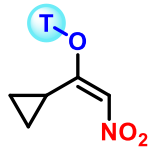
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.03 (s, 6H), 1.17 (s, 6H), 1.47 – 1.60 (m, 6H), 1.64 – 1.68 (m, 2H), 1.73 – 1.81 (m, 4H), 1.92 – 2.02 (m, 2H), 4.10 – 4.21 (m, 1H), 7.68 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.78, 20.87, 26.29, 30.65, 31.96, 39.71, 40.00, 61.46, 122.72, 178.94.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{16}H_{29}N_2NaO_3$: 320.2076, found: 320.2080.

Melting Point: m. p. 71-73 ºC.

(*E*)-1-(1-cyclopropyl-2-nitrovinyloxy)-2,2,6,6-tetramethylpiperidine: (Scheme 7, entry 8c)



(*E*)-1-(1-cyclopropyl-2-nitrovinyloxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A cyclopropyne 0.5 mmol scale. Yield: 27% (36 mg). Yellow liquid compound. Eluent: pet ether.

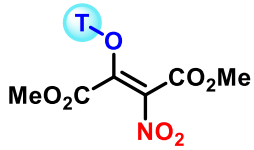
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.01 (s, 6H), 1.03 – 1.07 (m, 2H), 1.11 (s, 6H), 1.14 – 1.19 (m, 2H), 1.47 – 1.71 (m, 6H), 3.30 (tt, J = 8.4, 5.2 Hz, 1H), 7.81 (s, 1H). S19

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 9.09, 11.49, 16.80, 20.87, 31.88, 39.65, 61.48123.92, 176.03.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{14}H_{25}N_2NaO_3$: 292.1763, found: 292.1722.

IR (thin film) 3149, 2938 1594, 1489, 1365, 1337, 1182, 1069, 920, 762 cm^{-1}.

Dimethyl 2-nitro-3-(2,2,6,6-tetramethylpiperidin-1-yloxy)fumarate: (Scheme 7, entry 8d)



Dimethyl 2-nitro-3-(2,2,6,6-tetramethylpiperidin-1-yloxy)fumarate was synthesized using the general procedure A dimethyl but-2-ynedioate 0.5 mmol scale. Yield: 22% (38 mg). Yellow solid compound. Eluent: pet ether.

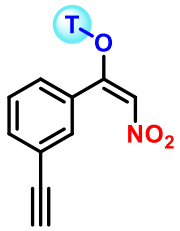
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.12 (s, 6H), 1.17 (s, 6H), 1.52 – 1.64 (m, 6H), 3.68 (s, 3H), 3.90 (s, 3H), 5.93 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 16.99, 20.73, 32.08, 39.87, 51.56, 53.09, 61.64, 95.82, 163.88, 165.73, 167.56.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{15}H_{25}N_2O_7Na$: 368.1559, found: 368.1562.

Melting Point: 130-131 ºC

(*E*)-1-(1-(3-ethynylphenyl)-2-nitrovinyloxy)-2,2,6,6-tetramethylpiperidine: (Scheme 8, entry 10a)



(*E*)-1-(1-(3-ethynylphenyl)-2-nitrovinyloxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A 1,3-diethynylbenzene0.5 mmol scale. Yield: 48% (79 mg). Yellow oily liquid. Eluent: petroleum ether: ethyl acetate = 99.5:0.5 (v/v).

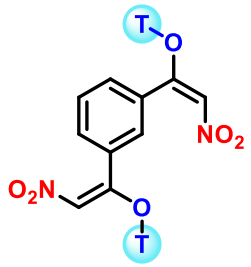
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.16 (s, 6H), 1.19 (s, 6H), 1.58 (d, J = 1.2 Hz, 6H), 3.12 (s, 1H), 7.36 – 7.40 (m, 2H), 7.51 (q, J = 1.3 Hz, 1H), 7.58 (ddd, J = 5.4, 3.4, 1.6 Hz, 1H), 7.78 (d, J = 1.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.74, 26.12, 32.09, 39.62, 61.68, 78.48, 82.72, 109.63, 122.61, 123.77, 128.52, 131.59, 134.10, 170.61.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{19}H_{24}N_2NaO_3$: 351.1679, found: 351.1686.

IR (thin film) 3289, 3142, 2976, 2936, 2874, 1626, 1497, 1367, 1341, 1260, 1167, 901, 809, 694 cm^{-1}.

1-((*E*)-2-nitro-1-(2,2,6,6-tetramethylpiperidin-1-yloxy)vinyl)-3-((Z)-2-nitro-1-(2,2,6,6-tetramethylpiperidin-1-yloxy)vinyl)benzene: (Scheme 8, entry 10a')



1-((*E*)-2-nitro-1-(2,2,6,6-tetramethylpiperidin-1-yloxy)vinyl)-3-((Z)-2-nitro-1-(2,2,6,6-tetramethylpiperidin-1-yloxy)vinyl)benzenewas synthesized using the general procedure A 1,3- diethynylbenzene0.5 mmol scale. Yield: 14% (37 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 98:2 (v/v).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.21 (d, J = 2.2 Hz, 24H), 1.57 – 1.68 (m, 12H), 7.50 – 7.58 (m, 2H), 7.60 (dd, J = 7.1, 1.6 Hz, 2H), 7.84 (s, 2H).

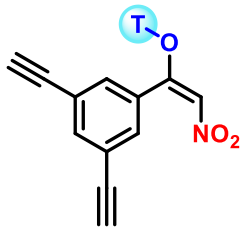
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 16.84, 20.86, 32.22, 39.76, 61.83, 123.85, 128.35, 128.55, 130.88, 131.79, 170.42.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{28}H_{42}N_4NaO_6$: 553.2997, found: 554.2998.

Melting Point: 162-164 ºC.

IR (thin film) 2931, 1631, 1500, 1340, 1171 cm^{-1}.

(*E*)-1-((1-(3,5-diethynylphenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 8, entry 10b)



(*E*)-1-((1-(3,5-diethynylphenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A 1,3,5-triethynylbenzene 0.5 mmol scale. Yield: 51% (90 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99.5:0.5 (v/v).

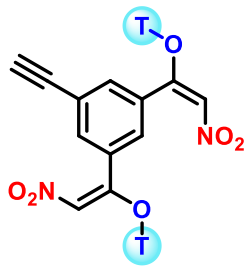
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.18 (s, 6H), 1.20 (s, 6H), 1.62 (s, 6H), 3.15 (s, 2H), 7.47 (d, J = 1.5 Hz, 2H), 7.70 (t, J = 1.6 Hz, 1H), 7.79 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 20.88, 32.22, 39.74, 61.88, 79.29, 81.85, 109.75, 123.18, 131.81, 137.43, 169.72.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{21}H_{24}N_2NaO_3$: 375.1679, found: 375.1673.

Melting Point: 152-154 ºC.

(*E*)-1-((1-(3,5-diethynylphenylacetylene)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine: (Scheme 8, entry 10b')



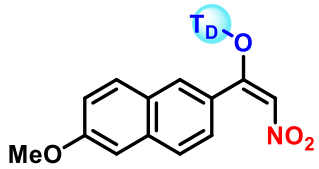
(*E*)-1-((1-(3,5-diethynylphenylacetylene)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidine was synthesized using the general procedure A 1,3,5-triethynylbenzene 0.5 mmol scale. Yield: 15% (42 mg). Yellow viscous compound. Eluent: petroleum ether: ethyl acetate = 97:3 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21 (s, 24H), 1.57 (s, 12H), 3.19 (s, 1H), 7.49 (t, *J* = 1.7 Hz, 1H), 7.67 (d, *J* = 1.6 Hz, 2H), 7.83 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 20.95, 29.92, 32.31, 39.83, 61.99, 124.22, 128.82, 132.35, 134.00, 169.49.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{30}H_{42}N_4NaO_6$: 577.2997, found: 577.2992

(*E*)-1-((1-(6-methoxynaphthalen-2-yl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidin-4-one: (Scheme 9, entry 12a)



(*E*)-1-((1-(6-methoxynaphthalen-2-yl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidin-4-one was synthesized using the general procedure A from 2-ethynyl-6-methoxynaphthalene 0.5 mmol scale. Yield: 50% (100 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v)..

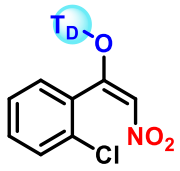
^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 1.30 (s, 6H), 1.43 (s, 6H), 2.37 – 2.42 (m, 2H), 2.74 (d, *J* = 13.1 Hz, 2H), 3.95 (s, 3H), 7.16 – 7.23 (m, 2H), 7.45 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.78 – 7.81 (m, 2H), 7.89 – 7.91 (m, 1H), 7.95 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 23.28, 31.56, 52.90, 55.45, 64.56, 105.84, 119.77, 123.66, 125.60, 125.84, 126.97, 127.99, 128.33, 130.22, 135.91, 159.21, 171.01, 205.60.

HRMS (ESI): $[M + H]^+$ calculated for $C_{22}H_{27}N_2O_5$: 399.1920, found: 399.1925.

Melting Point: m. p. 140-142 ºC

(*E*)-1-((1-(2-chlorophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidin-4-one: (Scheme 9, entry 12b)



(*E*)-1-((1-(2-chlorophenyl)-2-nitrovinyl)oxy)-2,2,6,6-tetramethylpiperidin-4-one was synthesized using the general procedure A from 1-chloro-2-ethynylbenzene 0.5 mmol scale. Yield: 65% (115 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

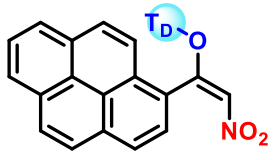
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.14 (s, 3H), 1.25 (s, 6H), 1.28 (s, 3H), 1.46 (s, 6H), 7.33 (dd, J = 7.6, 1.8 Hz, 1H), 7.38 (td, J = 7.4, 1.2 Hz, 1H), 7.45 (td, J = 7.7, 1.8 Hz, 1H), 7.48 – 7.52 (m, 1H), 7.95 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 23.00, 31.91, 53.51, 64.95, 125.54, 127.25, 129.48, 130.19, 131.68, 132.94, 161.19, 168.22, 205.60.

HRMS (ESI): $[M + H]^+$ calculated for $C_{17}H_{22}ClN_2O_4$: 353.1263, found: 353.1262.

Melting Point: 129-130 ºC

(*E*)-2,2,6,6-tetramethyl-1-(2-nitro-1-(pyren-1-yl)vinyloxy)piperidin-4-one: (Scheme 9, entry 12c)



(*E*)-2,2,6,6-tetramethyl-1-(2-nitro-1-(pyren-1-yl)vinyloxy)piperidin-4-one was synthesized using the general procedure A 1-ethynylpyrene 0.5 mmol scale. Yield: 60% (133 mg). Yellow solid compound. Eluent: petroleum ether: ethyl acetate = 95:5 (v/v).

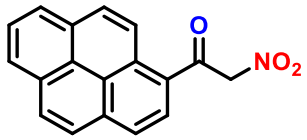
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 1.20 (s, 3H), 1.35 (s, 3H), 1.61 (s, 6H), 2.41 (s, 2H), 2.82 (d, J = 13.5 Hz, 2H), 8.01 (d, J = 7.9 Hz, 1H), 8.06 (dd, J = 14.1, 6.4 Hz, 2H), 8.09 – 8.14 (m, 2H), 8.17 (dd, J = 9.1, 7.0 Hz, 2H), 8.25 (dd, J = 10.2, 7.6 Hz, 3H), 8.32 (s, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 0.21, 23.29, 32.16, 53.28, 123.16, 124.71, 124.79, 125.51, 126.00, 126.12, 126.25, 126.47, 126.66, 127.35, 129.18, 129.28, 129.63, 130.86, 131.36, 133.08, 170.21, 205.66.

HRMS (ESI): $[M + H]^+$ calculated for $C_{27}H_{27}N_2O_4$: 443.1971, found: 443.1974.

IR (thin film) 2980, 1722, 1619, 1598, 1494, 1370, 1341, 1299, 1236, 1144, 849, 757 cm^{-1}.

Melting Point: 184-186 ºC

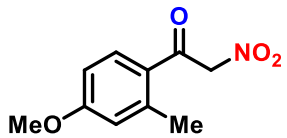
2-nitro-1-(pyren-1-yl)ethanone: (Scheme 11, entry 2k')[13]



2-nitro-1-(pyren-1-yl)ethanone was synthesized according to the literature method.[3] A solution of **2k** (65 mg, 0.15 mmol) in 5 mL 3:1:1 HOAc/H_2O/THF was treated with Zn powder (390 mg, 6.0 mmol) and the resulting suspension was stirred at 70 °C in a sealed reaction tube for 4 h. The reaction mixture was cooled to RT, and the Zn was removed by filtration through Celite. The solution was concentrated under reduced pressure and purified by column chromatography of silica gel (100–200 mesh) to provide **2k'** (26 mg, 60%) as yellow solid. Eluent: petroleum ether: ethyl acetate = 90:10 (v/v).
^{1}H NMR (400 MHz, Methanol-*d*4) δ 2.94 (s, 2H), 8.04 (t, J = 7.6 Hz, 0H), 8.09 – 8.14 (m, 1H), 8.16 (d, J = 9.5 Hz, 1H), 8.20 (s, 1H), 8.22 – 8.26 (m, 1H), 8.26 – 8.30 (m, 2H), 8.31 (d, J = 8.3 Hz, 1H), 8.33 – 8.38 (m, 2H), 8.45 (d, J = 9.4 Hz, 0H), 8.57 (d, J = 8.0 Hz, 1H), 9.02 (d, J = 9.4 Hz, 1H).
HRMS (ESI): $[M + Na]^+$ calculated for $C_{18}H_{11}NNaO_3$: 312.0637, found: 312.0634.

Melting Point: 145-147 ºC.

1-(4-methoxy-2-methylphenyl)-2-nitroethanone: (Scheme 11, entry 2h')[13]



1-(4-methoxy-2-methylphenyl)-2-nitroethanone was synthesized according to the literature method.[3] A solution of **2h** (53 mg, 0.15 mmol) in 5 mL 3:1:1 HOAc/H_2O/THF was treated with Zn powder (390 mg, 6.0 mmol) and the resulting suspension was stirred at 70 °C in a sealed reaction tube for 4 h. The reaction mixture was cooled to RT, and the Zn was removed by filtration through Celite. The solution was concentrated under reduced pressure and purified by column chromatography of silica gel (100–200 mesh) to provide **2h'** (17 mg, 55%) as yellow solid. Eluent: petroleum ether: ethyl acetate = 99:1 (v/v).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.61 (s, 3H), 3.88 (s, 3H), 5.82 (s, 2H), 6.76 – 6.85 (m, 2H), 7.52 (d, J = 8.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 22.97, 55.75, 82.71, 111.54, 118.58, 125.45, 131.94, 144.97, 163.75, 185.47.
HRMS (ESI): $[M + Na]^+$ calculated for $C_{10}H_{11}NNaO_4$: 232.0580, found: 232.0582.
Melting Point: 115-117 ºC.

2.4. Conclusion

In conclusion, we have developed an efficient method for oxynitration of simple unactivated alkynes. Generation of the nitro radical, reaction with alkyne, and subsequent trapping of the vinyl radical with TEMPO comprise the reaction sequence. This newly developed process is tolerant of a wide variety of functional groups, and excellent yields have been obtained in most of the cases. Even aliphatic alkynes can be functionalized albeit in low yield. Owing to its mild nature and broad substrate scope, this method is expected to find applications in academic and industrial settings.

2.4. Reference

(1) (a) Tellis, J. C.; Primer, D. N.; Molander, G. A. *Science* **2014**, *345*, 433. (b) Zuo, Z.; Ahneman, D. T.; Chu, L.; Terrett, J. A.; Doyle, A. G.; MacMillan, D. W. C. *Science* **2014**, *345*, 437. (c) Girard, S. A.; Knauber, T.; Li, C.-J. *Angew. Chem. Int. Ed.* **2014**, *53*, 74. (d) Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D. W. C. *Science* **2013**, *339*, 1593. (e) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**,*113*, 5322. (f) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. *Chem. Rev.* **2013**, *113*, 6234. (g) Creutz, S. E.; Lotito, K. J.; Fu, G. C.; Peters, J. C. *Science* **2012**, *338*, 647. (h) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (i) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (j) Chudasama, V.; Fitzmaurice, R. J.; Caddick, S. *Nat. Chem.* **2010**, *2*, 592. (k) Li, C.-J. *Acc.*

Chem. Res. **2010**, *43*, 581. (l) Maji, A.; Rana, S.; Akanksha; Maiti, D. *Angew. Chem. Int. Ed.* **2014**, *53*, 2428. (m) Modak, A.; Dutta, U.; Kancherla, R.; Maity, S.; Bhadra, M.; Mobin, S. M.; Maiti, D. *Org. Lett.* **2014**, *16*, 2602. (n) Manna, S.; Maity, S.; Rana, S.; Agasti, S.; Maiti, D. *Org. Lett.* **2012**, *14*, 1736.

(2) (a) Maity, S.; Manna, S.; Rana, S.; Naveen, T.; Mallick, A.; Maiti, D. *J. Am. Chem. Soc.* **2013**, *135*, 3355. (b) Maity, S.; Naveen, T.; Sharma, U.; Maiti, D. *Org. Lett.* **2013**, *15*, 3384. (c) Naveen, T.; Maity, S.; Sharma, U.; Maiti, D. *J. Org. Chem.* **2013**, *78*, 5949. (d) Gemotes, H. P. L.; Hessel, V.; Noel, T. *Org. Lett.* **2014**, *16*, 5800. (e) Campbell, A. N.; Stahl, S. S. *Acc. Chem. Res.* **2012**, *45*, 851.

(3) Maity, S.; Naveen, T.; Sharma, U.; Maiti, D. *Synlett* **2014**, *25*, 603.

(4) (a) Studer, A. *Chem. Soc. Rev.***2004**, *33*, 267. (b) Hartmann, M.; Li, Y.; Studer, A. *J. Am. Chem. Soc.* **2012**, *134*, 16516. (c) Li, Y.; Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8221.

(5) (a) Deb, A.; Manna, S.; Modak, A.; Patra, T.; Maity, S.; Maiti, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 9747. (b) Patra, T.; Deb, A.; Manna, S.; Sharma, U.; Maiti, D. *Eur. J. Org. Chem.* **2013**, 5247.

(6) (a) Ganapathy, S.; Sekhar, B. B. V. S.; Cairns, S. M.; Akutagawa, K.; Bentrude, W. G. *J. Am. Chem. Soc* **1999**, *121*, 2085. (b) Jiao, X. Y.; Bentrude, W. G. *J. Am. Chem. Soc.* **1999**, *121*, 6088. (c) Jiao, X. Y.; Bentrude, W. G. *J. Org. Chem.* **2003**, *68*, 3303.

(7) Maji, A.; Hazra, A.; Maiti, D. *Org. Lett.* **2014**, *16*, 4524.

(8) (a) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem. Int. Ed.* **2000**, *39*, 2633. (b) Bedard, A.-C.; Collins, S. K. *J. Am. Chem. Soc.* **2011**, *133*, 19976. (c) Hamada, T.; Ye, X.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130*, 833. (d) Peng, H.; Xi, Y.; Ronaghi, N.; Dong, B.; Akhmedov, N. G.; Shi, X. *J. Am. Chem. Soc.* **2014**, *136*, 13174.

(9) (a) Sargent, G. D.; Browne, M. W. *J. Am. Chem. Soc* **1967**, *89*, 2788. (b) Lu, Q.; Zhang, J.; Zhao, G.; Qi, Y.; Wang, H.; Lei, A. W. *J. Am. Chem. Soc.* **2013**, *135*, 11481.

(10) Manna, S.; Jana, S.; Saboo, T.; Maji, A.; Maiti, D. *Chem. Commun.* **2013**, *49*, 5286.

(11) Koley, D.; Colon, O. C.; Savinov, S. N. *Org. Lett.* **2009**, *11*, 4172.

(12) (a) Gulykina, N. S.; Dolgina, T. M.; Bondarenko, G. N.; Beletskaya, I. P. *Russian J.Org. Chem.* **2003**, *39*, 797. (b) Gelman, D.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2003**, *42*, 5993.

(13) Boger, D. L.; Garbaccio, R. M.; Qing Jin. *J. Org. Chem.* **1997**, *62*, 8875.

Chapter 3

Aryl Nitriles from Alkynes using *tert*-butyl Nitrite: Metal-Free Approach to C≡C Bond Cleavage

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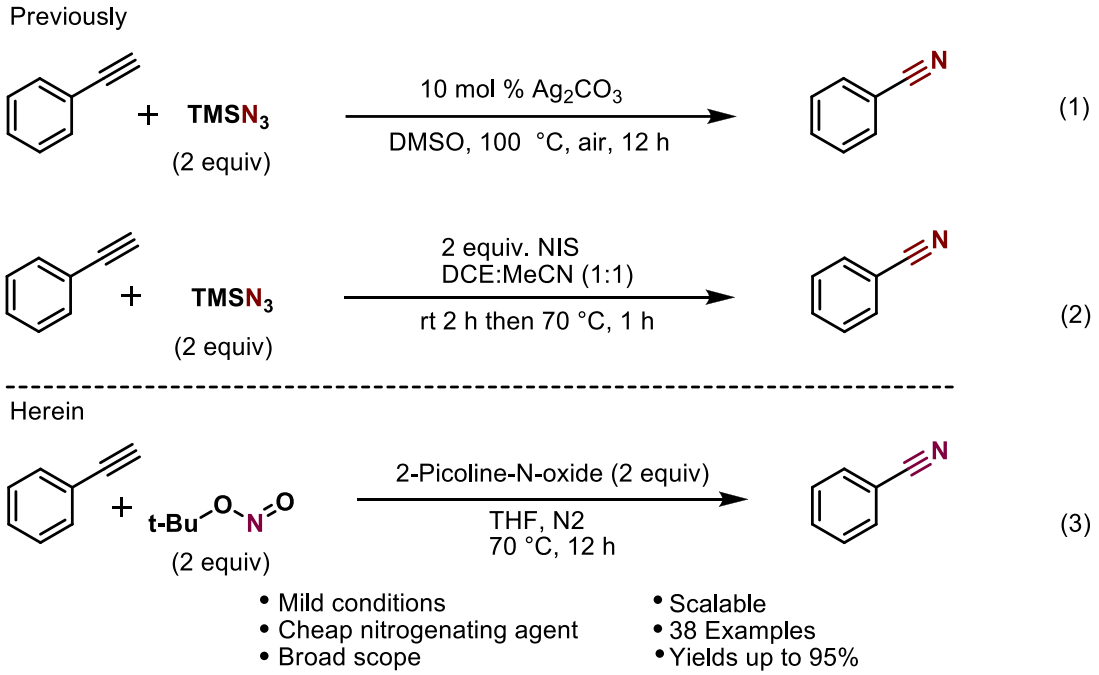
Aryl Nitriles from Alkynes using *tert*-butyl Nitrite: Metal-Free Approach to C≡C Bond Cleavage

Abstract: Alkyne C≡C bond breaking, outside of alkyne metathesis, remains an underdeveloped area in reaction discovery. Recently, nitrogenation has been reported to allow nitrile formation from alkynes. A new protocol for the metal-free C≡C bond cleavage of terminal alkynes to produce nitriles is reported. This method provides an opportunity to synthesize a vast range of nitriles containing aryl, heteroaryl and natural product derivatives (38-examples). In addition, the potential of ^{t}BuONO is demonstrated to act as a powerful nitrogenating agent for terminal aryl alkynes.

3.1. Introduction

Alkyne derivatizations are widely used in organic synthesis. Some important transformations of alkynes include addition[1] and hydration reactions,[2] while alkynes have been employed in industrially useful processes such as the Pd-catalyzed Wacker oxidation to produce 1,2-diketones,[3] and the Sonogashira coupling to achieve C(*sp*)–C(sp^2) bond formation.[4] Academically and industrially, perhaps the most widely used reaction is the (3 + 2) cycloaddition (click chemistry).[5] In the modern era, fragmentation of alkynes has received increasing attention. For example carboxylic acids have been prepared by the cleavage of carbon-carbon triple bond,[6] while alkyne metathesis is the most important reaction within this class.[7]

Scheme 3.1. Transformation of alkynes



Although reactions involving C≡Cbondcleavage are difficult owing to high bond energy, reaction design using this event is possible. Recently, Jiao and coworkers reported an unprecedented silver catalyzed synthesis of nitriles from alkynes using TMS-N_3 as the nitrogenating reagent (eq. 1).[8] The potential utility of this new entry to nitrile[9] is significant with the nitrile group prevalent in natural products,[10]drug molecules,[11] dyes,[12] and in the polymer industry.[13] Specifically, more than thirty nitrile containing drugs have been approved for the treatment of depression, breast cancer and Parkinson's disease, while twenty more are in clinical trials.[14] In addition nitrile groups can be used as synthetic precursor to install acids, amides, ketones *etc*.or as directing groups for remote C–H activation through weak coordination.[15]Yanada reported a related C≡Ccleavage by exploiting TMS-N_3 as the

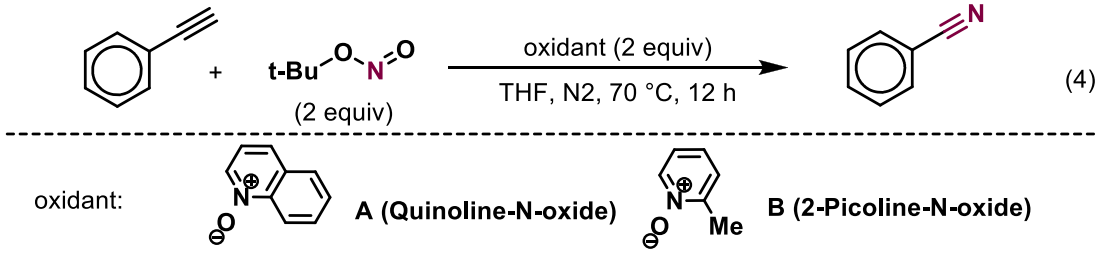
nitrogenating agent, however this reaction is designed to cleave both internal as well as terminal alkynes (eq. 2).[16]

Following our recent success with α-trifluoromethylation[17] and oxynitration[18] of alkynes, we planned to achieve a related terminal alkyne nitrogenation using *tert*-butyl nitrite (eq. 3).[19] Such a strategy would address safety and cost concerns that can plague reactions with azides, defining the first metal free approach to aryl nitriles from terminal alkynes.

3.2. Result and discussion

Initial investigations were carried out with phenyl acetylene to identify optimal conditions. Under aerobic condition exploiting quinoline-*N*-oxide as oxidant, and at temperatures suited to the homolysis of *tert*-butyl nitrite, we were pleased to form benzonitrile in 30% yield (Table 3.1, entry 1). Subsequently, variation of oxidant showed that 2-picoline-*N*-oxide can produce the desired cyanobenzene in improved yield (Table 3.1, entry 2). Though the reaction is compatible in non-polar aprotic solvent (Table 3.1, entries 1-4), THF is found to be the best. While yield has decreased under an oxygen atmosphere, it was drastically improved when the reaction was carried out under inert atmosphere (Table 3.1, entry 11). This may well be due to inhibition of alkyne oxidation under inert atmosphere.

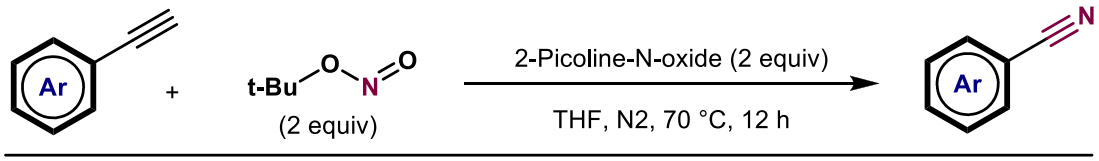
Table 3.1. Optimization of Reaction Conditions

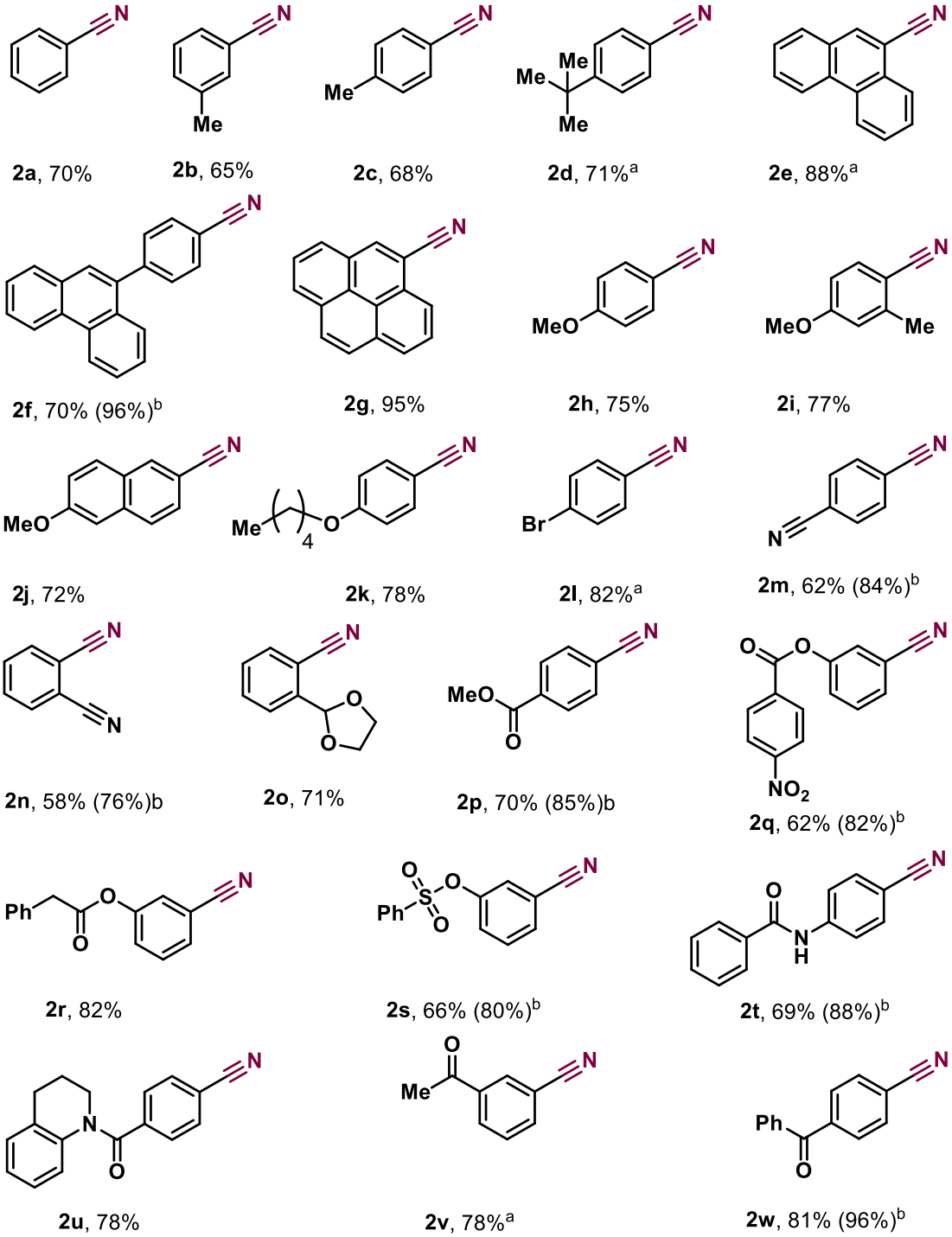


entry	solvent	oxidant (equiv)	cond[n]	yield (%)[a]
1	DCE	**A** (2)	air	30
2	DCM	**B** (2)	air	35
3	DCE	**B** (2)	air	39
4	THF	**B** (2)	air	45
5	MeOH	**B** (2)	air	<1
6	THF	**B** (2)	air	25
7	THF	**B** (2)	air	32
8	THF	**B** (2)	air	45
9	THF	**B** (2)	O_2	10
10	**THF**	**B** (2)	**N_2**	**76 (70)**[b]

[a]yield calculated by GC except as noted. [b]isolated yield.

Table 3.2. Synthesis of nitriles from arylacetylenes





2a, 70% **2b**, 65% **2c**, 68% **2d**, 71%[a] **2e**, 88%[a]

2f, 70% (96%)[b] **2g**, 95% **2h**, 75% **2i**, 77%

2j, 72% **2k**, 78% **2l**, 82%[a] **2m**, 62% (84%)[b]

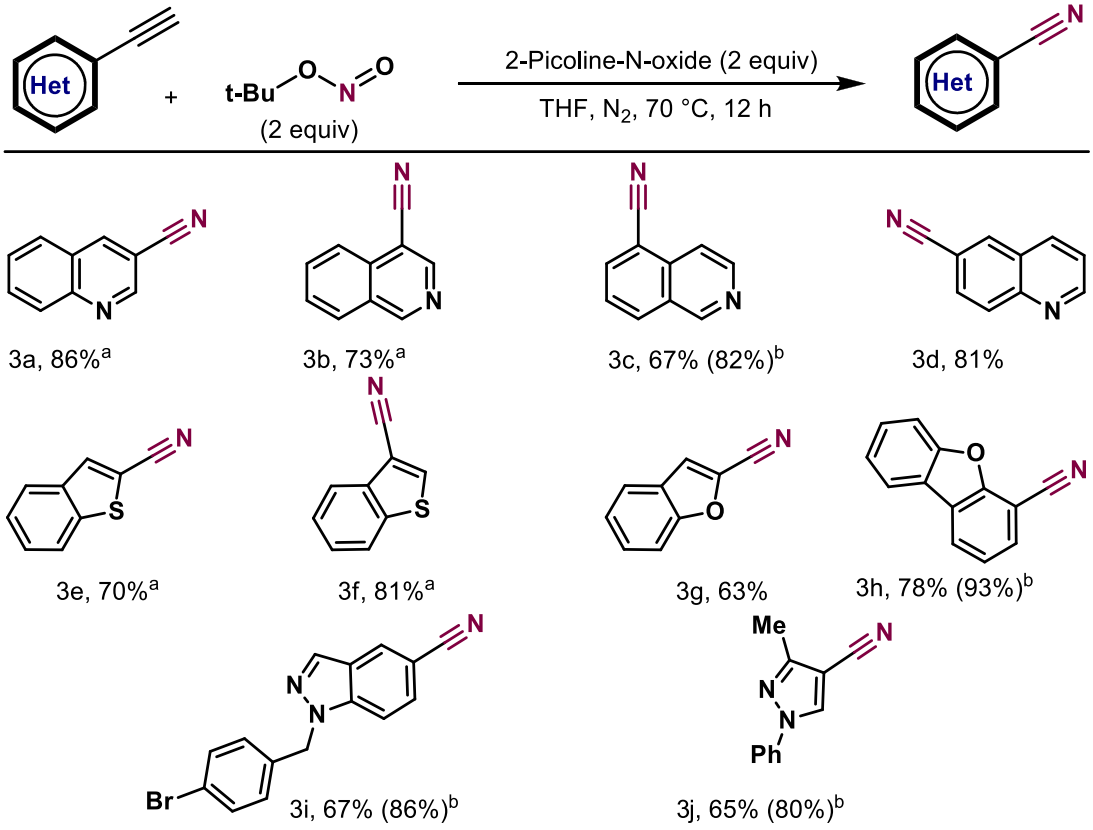
2n, 58% (76%)b **2o**, 71% **2p**, 70% (85%)b **2q**, 62% (82%)[b]

2r, 82% **2s**, 66% (80%)[b] **2t**, 69% (88%)[b]

2u, 78% **2v**, 78%[a] **2w**, 81% (96%)[b]

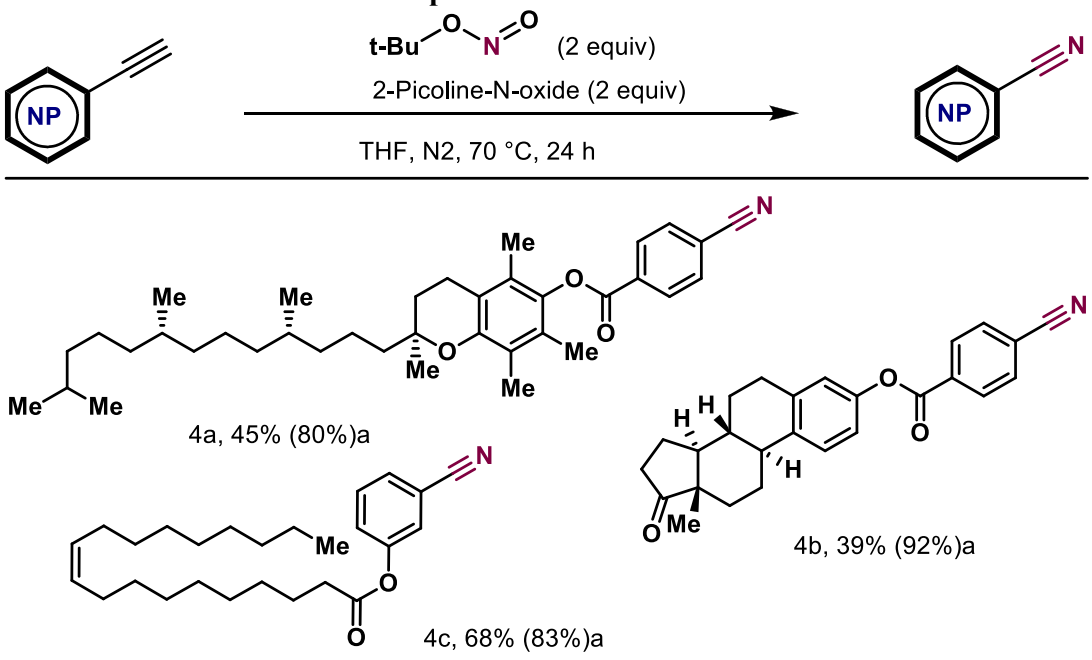
[a]6 h,[b]yield based on recovered starting material

Table 3.3. Synthesis of heterocyclic nitriles



[a]6 h,[b]yield based on recovered starting material

Table 3.4. Nitriles based on natural products



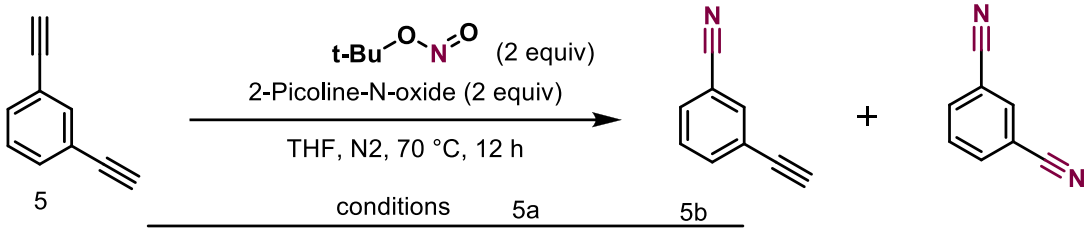
[a]yield based on recovered starting material

Next, the nitrogenation of alkynes was examined in the context of natural product derivatives. Specifically we focused our attention on application to various natural product

derived esters. Thus, the alkynyl ester of *vitamin*-E was converted to nitrile **4a** in45% yield, while the estrone derivative **4b** was prepared in 39% isolated yield. Finally oleic acid derivative **4c** was prepared in 68% isolated yield.

Despite our best efforts, different internal alkynes including prop-1-ynylbenzene, 1,2-diphenylethyne, ethyl-3-phenylpro-piolate, trimethyl-(phenylethynyl) silane and terminal alkyl alkynes such as oct-1-yne, ethynylcyclopentane, prop-2-ynylbenzene failed to deliver nitriles under standard reaction conditions.

Scheme 3.2. Nitrile from 1,3-diethynylbenzene, 5

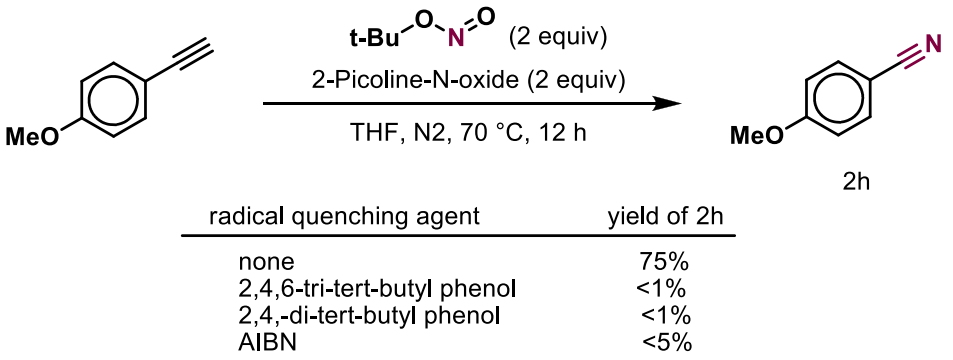


conditions	5a	5b
"2 equiv" (as above)	58%	15%
"4 equiv"	7%	70%

To further expand the scope of this reaction and gain mechanistic insight, the nitrogenation of 1,3-dialkynyl benzene **5** was examined. We expected that a mixture of product formation is likely due to the presence of multiple alkynes, and the ratio will potentially clarify the roles of electronic substituent on the reaction. With 1,3-diethynylbenzene (**5**) under standard reaction condition, the *mono*-cyanoarene**5a** as the major product (58%) suggesting that the second nitrogenation is impeeded by the first. Addition of twice the stoichiometry of nitrogenating reagent allowed *di*-cyanoarene**5b** to form as the major product (70%) from 1,3-diethynylbenzene **5**.

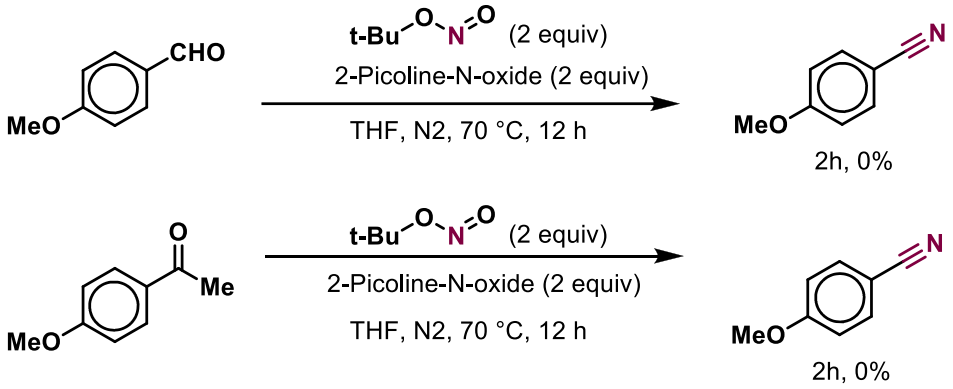
In order to understand the mechanism of the nitrile formation, a number of control experiments were performed (Scheme 3.3). Firstly to probe the formation of free radical intermediates, the reaction was repeated in presence of a number of radical quenchers (eq. 6). Thus, 2,4,6-*tri*-tertiarybutyl phenol, 2,4-*di*-tertiarybutyl phenol and AIBN all lead to significant retardation of the reaction suggested that it is likely proceeding *via* a radical pathway. To test whether aldehyde or ketone intermediates are formed, various aryl aldehydes and ketones were examined (eq. 7 and 8). In none of these cases was the expected benzonitrile compound formed.

Scheme 3.3. Control studies to elucidate the mechanism



(6)

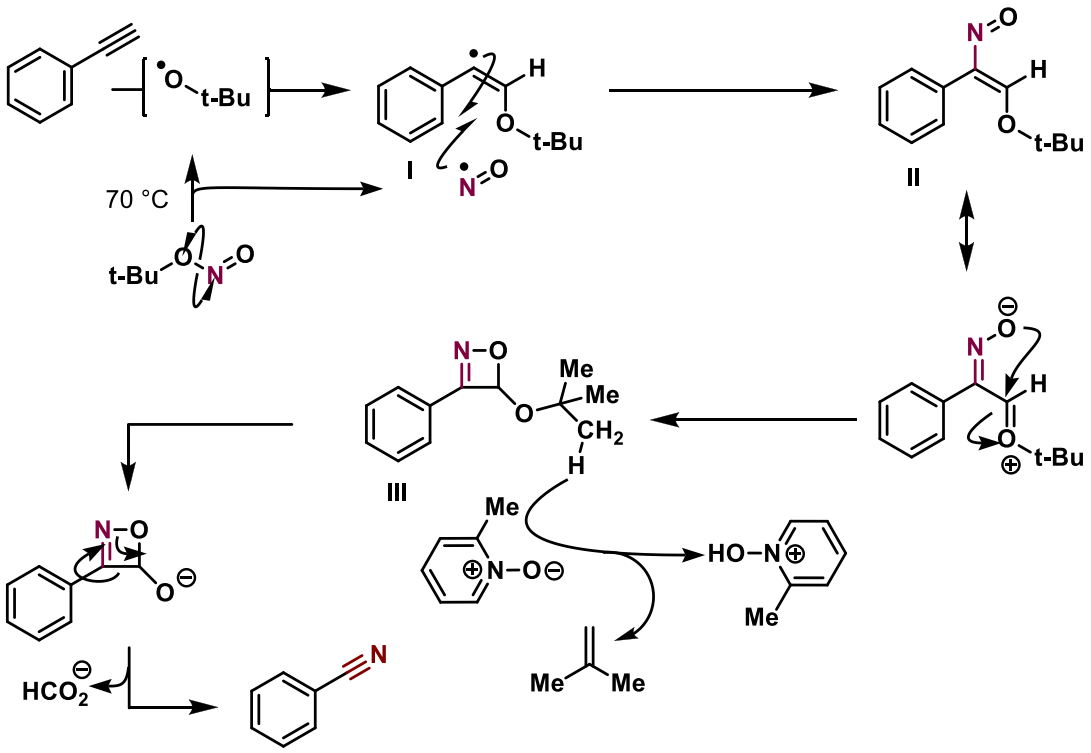
radical quenching agent	yield of 2h
none	75%
2,4,6-tri-tert-butyl phenol	<1%
2,4,-di-tert-butyl phenol	<1%
AIBN	<5%



(7)

(8)

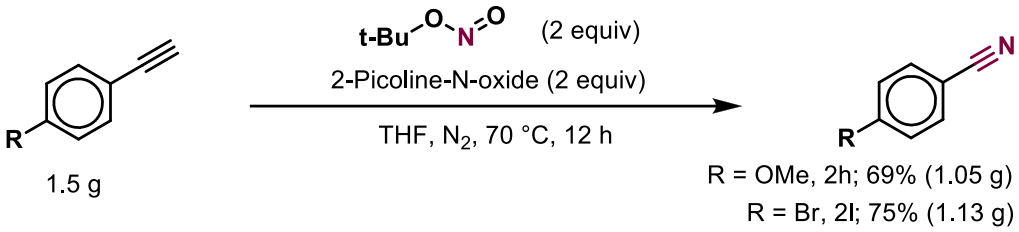
Scheme 3.4. Plausible reaction mechanism



Based on these observations, a plausible mechanism has been outlined (Scheme 3.4). First *in-situ*homolysis of *tert*-butyl nitrite yields the *tert*-butyl oxy radical and nitroso radical.

Addition of the formerto the alkyne forms a phenyl-substituted vinyl radical **I** which is trapped by nitroso radical to yield **II**. Cyclisation of **II** then provides the strained four membered intermediate **III** with elimination of formic acid lead to the formation of benzonitrile.[20] Presumably a *tert*-butyl cation is formed in the conversion of **III** to the final product and a proton abstraction by the 2-picoline-*N*-oxide resulted isobutylene.

Scheme 3.5. Gram-scale reactions



Scalability of the reaction was tested successfully by preparing **2h** and **2l** in 69% and 75% yields, respectively.

3.3. Experimental details

3.3.1. General Consideration

3.3.1.a.Reagent Information: Unless otherwise stated, all the reactions were carried out under N_2 atmosphere in screw cap reaction tubes. All the solvents were bought from Aldrich in a sure-seal bottle and were used as received. ^{t}BuONO and 2-Picoline-*N*-oxide were purchased from Sigma Aldrich . All the alkynes were bought from Aldrich and Alfa-Aesar. For column chromatography, silica gel (100–200 mesh) from SRL Co. was used. A gradient elution using pet ether and ethyl acetate was performed based on Merck aluminium TLC sheets (silica gel $60F_{254}$).

3.3.1.b. Analytical Information: All isolated compounds are characterized by ^{1}H NMR, ^{13}C NMR spectroscopy, gas chromatography mass spectra (GCMS). Nuclear magnetic resonance spectra were recorded either on a Bruker 500, 400 MHz instrument. All ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C NMR spectra were reported in ppm relative to deuteron chloroform (77.23 ppm), unless otherwise stated, and all were obtained with ^{1}H decoupling. All GC analysis were performed on Agilent 7890A GC system with an FID detector using a J & W DB–1 column (10 m, 0.1 mm I.D.) with n-octadecane as the internal standard. All GCMS analysis was done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). High-resolution

mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

3.3.1.c. Description of Reaction Tube:

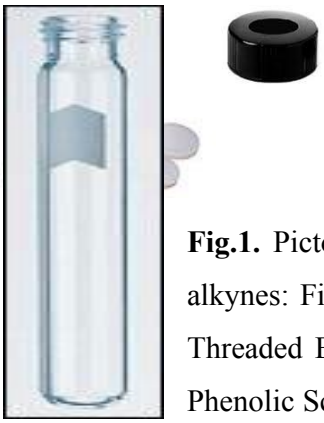
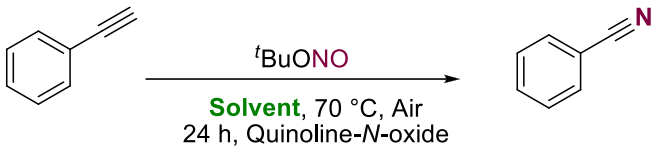


Fig.1. Pictorial description of reaction tube for aryl nitriles formation from alkynes: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E) [right]; Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A) [right].

3.3.2. Optimization of Reaction Condition

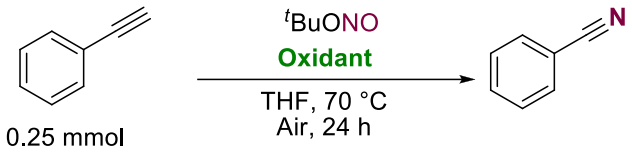
3.3.2.a. Optimization by varying solvent: A thorough screening of solvent has been carried out with 0.25 mmol of phenyl acetylene and 0.5 mmol of tBuONO and 0.5 mmol of quinoline-*N*-oxide. Reactions were carried out for 24 h under aerobic condition at 70 °C and found that THF is the best solvent for the required transformation. And further studies have been done with THF as solvent.



Sr. No.	Solvent	GC Yield (%)
1	DCE	26
2	DCM	21
3	$CHCl_3$	15
4	CCl_4	20
5	**THF**	**30**
6	1,4-Dioxane	18

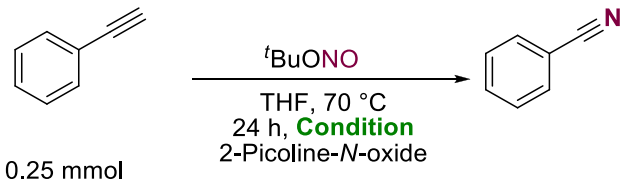
7	Toluene	18
8	*o*-Xylene	14
9	Benzene	16
10	Cyclohexane	20
11	EtOAc	18
12	Acetone	23
13	MeCN	24
14	MeOH	-
15	DMSO	-
16	DMF	-

3.3.2.b. Oxidant Optimization: After finding THF as the best solvent, we performed the reaction using oxidants and among the oxidants screened 2-picoline-N-oxide was found to give the product in satisfactory yield. And we proceed further with 2-picolne-*N*-oxide as the oxidant.



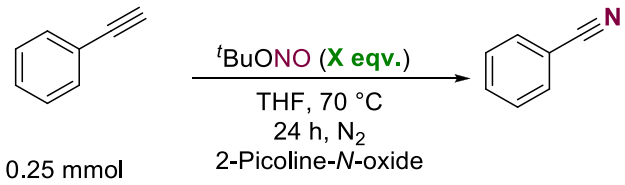
Sr. No.	Oxidant	GC Yield (%)
1	No Oxidant	7
2	Quinoline-*N*-Oxide	30
3	Benzoquinone	22
4	$K_2Cr_2O_7$	28
5	$KMnO_4$	23
6	MnO_2	29
7	TBHP	-
8	DTBP	30
9	H_2O_2	20
10	$K_2S_2O_8$	21
11	Oxone	16
12	**2-Picoline-*N*-Oxide**	**45**

3.3.2.c. Condition Variation: Inert atmosphere is important for the desired transformation.



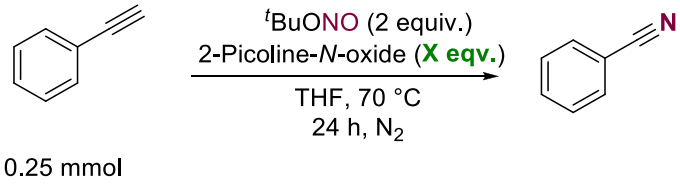
Sr. No.	Atmosphere	GC Yield (%)
1	Air	45
2	**N_2**	**76**
3	O_2	14

3.3.2.d. Amount of ^{t}BuONO: After variation of solvent, oxidant and atmosphere required for the reaction. We focus on the quantity of the reagent important for the transformation. First we start variation of nitrogenating source i.e. ^{t}BuONO. And a thorough variation shows that 2 equivalent of ^{t}BuONO is foremost for the desired transformation.

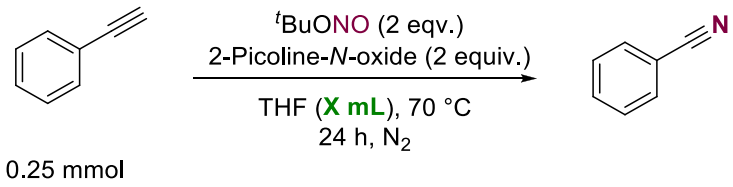


Sr. No.	Amount of ^{t}BuONO (equiv.)	Amount of ^{t}BuONO (mmol)	GC Yield (%)
1	1	0.25	40
2	**2**	**0.50**	**76**
3	3	0.75	75
4	4	1.00	73
5	6	1.50	72

3.3.2.e. Amount of Picoline-*N*-oxide: Similarly, we optimized the amount of oxidant i.e. 2-picoline-*N*-oxide and found that 2 equivalents of oxidant is required to achieve the best yield in 76%.

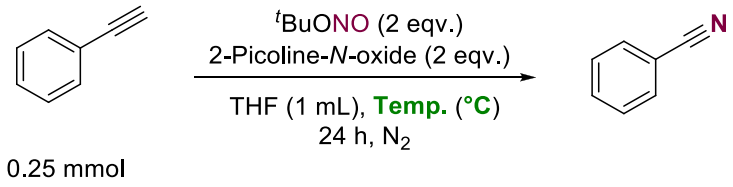


Sr. No.	Amount of Picolin-*N*-Oxide (eqv.)	Amount of Picolin-*N*-Oxide (mmol)	GC Yield (%)
1	1	0.25	35
2	**2**	**0.50**	**76**
3	3	0.75	70
4	4	1.00	65
5	6	1.50	60



3.3.2.f. Amount of Solvent: Solvent amount optimization showed that 1.0 mL THF is good enough for 0.25 mmol scale reaction.

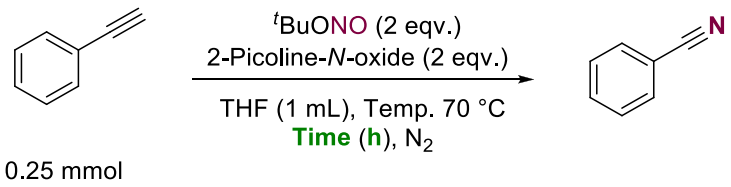
Sr. No.	Solvent Amount (mL)	GC Yield (%)
1	0.5	68
2	**1.0**	**76**
3	1.5	75
4	2.0	74
5	2.5	75
6	3.0	70



3.3.2.g. Temperature Variation: We traversed a temperature from room temperature to 100 °C and found that 70 °C is sufficient for the transformation to give excellent yield.

Sr. No.	Temperature (°C)	GC Yield (%)
1	RT	40
2	50	55
3	60	67
4	65	70
5	**70**	**76**
6	75	75
7	80	76
8	90	74
9	100	70

3.3.2.h. Time Optimization: 6-12 hour is required to achieve the maximum yield.



0.25 mmol

Sr. No.	Time (h)	GC Yield (%)
1	2	30
2	4	60
3	**6**	**74**
4	8	75
5	10	76
6	**12**	**76**
7	16	75
8	20	74
9	24	73
10	36	75

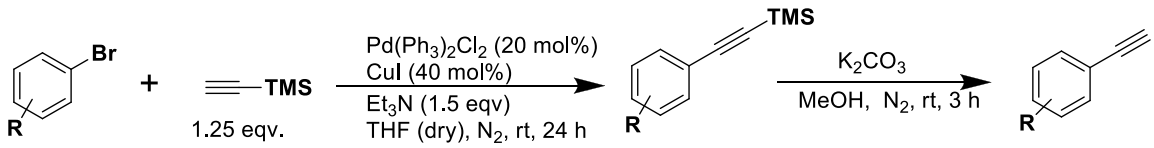
3.3.3. General Procedure

General Procedure A: Synthesis of nitriles from terminal alkynes

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, corresponding alkyne (0.5 mmol), ^{t}BuONO (1.0 mmol, 103 mg, 119 µL) and 2-Picoline-*N*-Oxide (1.0 mmol, 109 mg) under N_2 atmosphere. 2 mL of THF was added using syringe at the end. The reaction mixture was stirred vigorously on a preheated oil bath at 70 °C. Unless mentioned the reaction was taken out after 6-12 h (monitored by TLC) and the reaction mixture was directly used for the isolation through column chromatography. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

Precaution for gram scale reaction: As ^{t}BuONO boiling point is 63 °C and during gram scale reaction proper precaution need to be taken. The reactions have been carried out in the fume hood following the procedure described here. An oven-dried round bottom flask was charged with a magnetic stir-bar and corresponding alkyne (1.5 g ; 11.4 mmol, 4-methoxyphenylacetylene). Under N_2 atmosphere, 23 mL THF was added to it and ^{t}BuONO (22.8 mmol, 1.71 mL) and 2-Picoline-*N*-Oxide (22.8 mmol, 2.49 g) was added slowly drop wise under ice cold condition. The reaction mixture was placed in a preheated oil bath maintaining 60 °C. The reaction mixture was used directly for purification and 1.05 g 4-methoxybenzonitrile (**2h**) was obtained in 69% yield. Same procedure was followed for entry no **2l**.

General Procedure B: Synthesis of terminal alkynes [21]



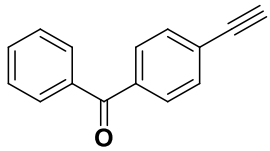
An oven-dried screw cap reaction tube was charged with a magnetic stir-bar [$Pd(PPh_3)_2Cl_2$] (0.02mmol; 14mg), CuI (0.04 mmol; 7.6 mg) and bromo-substrate (1 mmol). Freshly distil dry THF (2 mL) was added to the reaction tube under nitrogen atmosphere using syringe. Triethylamine (1.55 mmol; 216 µl) was injected in it and the reaction was stirred at room temperature. Under nitrogen atmosphere trimethylsilylacetylene (1.25 mmol; 176 µl) was added to the reaction mixture slowly. Gradually the reaction turned dark. The reaction was

stirred continuously for 24 h at room temperature. The progress of the reaction was monitored by TLC. Once the reaction was over the mixture was diluted with 5 ml EtOAc and filtered through the celite. The filtrate was evaporated under low pressure and the compound was isolated through silica column (100-200 mesh).

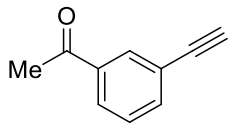
Terminal alkyne was obtained through hydrolysis of 4-(trimethysilyl)ethynyl-substrates. The TMS-ethynyl substrates were dissolved in 1.5 ml MeOH and 2.5 equiv. of anhydrous K_2CO_3 were added to it under N_2 atmosphere. The reaction mixture was stirred at room temperature for 3 h. Upon completion the reaction was filtered through celite and the filtrate was evaporated under low pressure and purified through silica column (100-200 mesh).

3.3.4. Characterization Data

The following substrates were synthesized using this protocol.

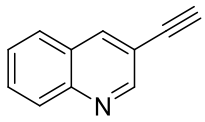


(4-ethynylphenyl)(phenyl)methanone: The compound has been synthesized following the general procedure B from the corresponding bromo analogue. Colourless solid isolated with 88% yield. Eluent: petroleum ether: ethyl acetate - 99:1 (v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.74 (tt, *J* = 7.9, 1.5 Hz, 4H), 7.63 – 7.57 (m, 3H), 7.52 – 7.46 (m, 2H), 3.36 – 3.16 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 80.31, 83.01, 126.45, 128.58, 130.13, 130.18, 132.19, 132.84, 137.43, 137.61, 196.07.

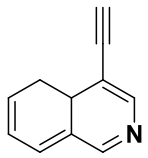


1-(3-ethynylphenyl)ethanone: The compound has been synthesized following the general procedure B from the corresponding bromo analogue. Colourless solid isolated with 80% yield. Eluent: petroleum ether: ethyl acetate - 99:1 (v/v). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.08 – 8.00 (dt, *J* = 2.0, 1.1 Hz, 1H), 7.97 – 7.87 (ddq, *J* = 7.9, 1.9, 1.0 Hz, 1H), 7.70 – 7.60 (dp, *J* = 7.7, 1.2 Hz, 1H), 7.46 – 7.36 (td, *J* = 7.7, 0.9 Hz, 1H), 3.24 – 3.01 (s, 1H), 2.70 – 2.46 (d, *J*

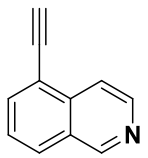
= 1.0 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 26.77, 78.48, 82.74, 122.90, 128.54, 128.86, 132.22, 136.48, 137.31, 197.31.



3-ethynylquinoline: The compound has been synthesized following the general procedure B from the corresponding bromo analogue. Solid compound isolated in 92% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.94 – 8.84 (t, *J* = 1.9 Hz, 1H), 8.24 – 8.12 (d, *J* = 2.2 Hz, 1H), 8.10 – 7.97 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.68 – 7.62 (m, 2H), 7.50 – 7.43 (m, 1H), 3.38 – 3.07 (s, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 80.66, 81.01, 116.27, 127.00, 127.36, 127.61, 129.44, 130.36, 139.30, 147.10, 152.23.

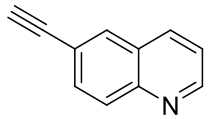


4-ethynyl-4a,5-dihydroisoquinoline: The compound has been synthesized following the general procedure B from the corresponding bromo analogue. Solid compound isolated in with 92% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.26 – 9.14 (d, *J* = 1.1 Hz, 1H), 8.79 – 8.66 (s, 1H), 8.33 – 8.17 (dq, *J* = 8.3, 1.0 Hz, 1H), 8.02 – 7.94 (dp, *J* = 8.2, 1.2 Hz, 1H), 7.86 – 7.70 (ddq, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.70 – 7.58 (ddt, *J* = 8.2, 5.7, 1.3 Hz, 1H), 3.60 – 3.50 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 79.08, 84.68, 114.99, 125.11, 127.87, 128.11, 128.15, 131.47, 136.02, 147.51, 152.75.



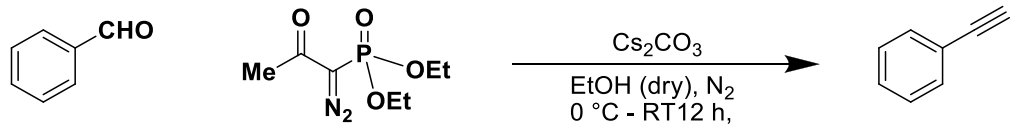
5-ethynylisoquinoline: The compound has been synthesized following the general procedure B from the corresponding bromo analogue. Colourless solid isolated with 90% yield. Eluent: petroleum ether: ethyl acetate – 99.5:0.5 (v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.41 – 9.34 (d, *J* = 0.9 Hz, 1H), 8.78 – 8.73 (d, *J* = 5.9 Hz, 1H), 8.29 – 8.20 (dt, *J* = 8.3, 1.1 Hz, 1H),

8.16 – 8.10 (dd, *J* = 7.3, 1.2 Hz, 1H), 8.05 – 7.98 (dt, *J* = 5.8, 1.0 Hz, 1H), 7.75 – 7.64 (dd, *J* = 8.3, 7.2 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 109.83, 116.66, 117.85, 126.80, 128.11, 133.06, 135.46, 136.76, 145.80, 153.25.



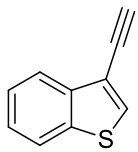
6-ethynylquinoline: The compound has been synthesized following the general procedure B from the corresponding bromo analogue. Solid compound isolated in 89% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.88 – 8.80 (dq, *J* = 4.3, 2.0 Hz, 1H), 8.02 – 7.94 (dt, *J* = 9.7, 3.3 Hz, 2H), 7.92 – 7.86 (q, *J* = 2.3 Hz, 1H), 7.74 – 7.65 (dq, *J* = 8.7, 1.9 Hz, 1H), 7.36 – 7.27 (ddd, *J* = 8.5, 4.3, 2.1 Hz, 1H), 3.28 – 3.04 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 78.62, 83.25, 120.44, 121.83, 127.84, 129.67, 132.07, 132.32, 135.81, 147.83, 151.22.

General Procedure C: Synthesis of alkynes from aldehydes:[22]

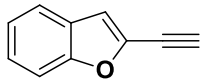


To a stirred solution of aldehyde (75.5 mg, 0.5 mmol) and BOR (Bestman-Ohira Reagent) (275 mg, 1.25 mmol) in dry EtOH (10 mL) was added Cs_2CO_3 (480 mg, 1.5 mmol) at 0 °C and the resulting mixture was stirred until complete consumption of aldehyde (monitored by TLC). After complete conversion of aldehyde, solvent was evaporated completely under low pressure and 10 mL of ethylacetate and 5 mL brine solution was added and the organic portion was collected passing through anhydrous Na_2SO_4. Water part was extracted two more times. Organic portion was evaporated and directly used for purification using silica gel (100-200 mesh) column and petroleum ether and ethyl acetate as the eluent.

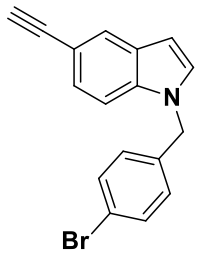
The following substrates were synthesized using this protocol.



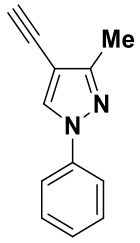
The compound has been synthesized following the general procedure C from the corresponding aldehyde. Yellow liquid isolated with 75% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.03 – 7.95 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.90 – 7.83 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.74 – 7.69 (s, 1H), 7.50 – 7.45 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.44 – 7.39 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 3.43 – 3.24 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 77.63, 79.97, 117.48, 122.78, 123.14, 125.01, 125.33, 131.58, 138.92, 139.40.



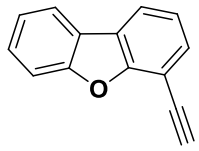
The compound has been synthesized following the general procedure C from the corresponding aldehyde. Liquid compound isolated in 70% yield. Eluent: petroleum ether: ethyl acetate – 99.5:0.5 (v/v). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.68 – 7.52 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.52 – 7.43 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.43 – 7.32 (ddt, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.30 – 7.23 (td, *J* = 7.5, 7.1, 1.0 Hz, 1H), 7.04 – 7.01 (t, *J* = 1.0 Hz, 1H), 3.65 – 3.41 (d, *J* = 1.1 Hz, 1H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 74.32, 83.61, 111.54, 112.83, 121.56, 123.59, 126.12, 127.39, 137.90, 154.98.



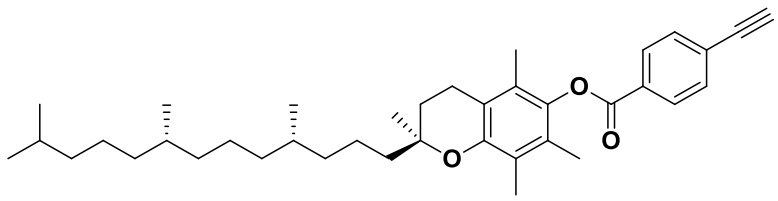
The compound has been synthesized following the general procedure C from the corresponding aldehyde. Solid compound isolated in 78% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.05 – 8.01 (d, *J* = 1.0 Hz, 1H), 7.96 – 7.90 (t, *J* = 1.2 Hz, 1H), 7.49 – 7.39 (m, 3H), 7.28 – 7.24 (m, 1H), 7.07 – 7.02 (m, 2H), 5.69 – 5.40 (s, 2H), 3.16 – 2.92 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 52.65, 76.16, 76.91, 77.55, 84.09, 109.45, 114.86, 122.14, 124.41, 126.05, 129.05, 130.44, 132.15, 134.10, 135.64, 139.18.



The compound has been synthesized following the general procedure C from the corresponding aldehyde. Solid compound isolated in 80% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.99 – 7.88 (d, *J* = 1.6 Hz, 1H), 7.67 – 7.53 (m, 2H), 7.46 – 7.35 (m, 2H), 7.29 – 7.21 (ddt, *J* = 8.6, 7.4, 1.2 Hz, 1H), 3.38 – 2.99 (s, 1H), 2.53 – 2.29 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 12.43, 80.83, 103.87, 119.07, 126.67, 129.54, 130.24, 139.58, 153.30.

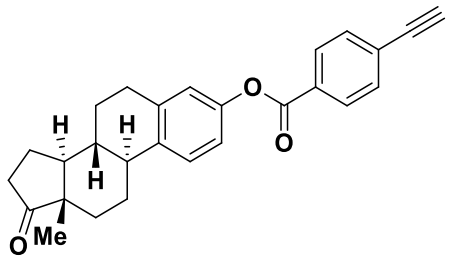


The compound has been synthesized following the general procedure C from the corresponding aldehyde. Solid compound isolated in 83% yield. Eluent: petroleum ether: ethyl acetate – 99:1 (v/v). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.99 – 7.92 (ddd, *J* = 7.7, 2.6, 1.2 Hz, 2H), 7.69 – 7.64 (d, *J* = 8.2 Hz, 1H), 7.62 – 7.57 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.52 – 7.46 (ddd, *J* = 8.4, 7.3, 1.4 Hz, 1H), 7.40 – 7.34 (td, *J* = 7.6, 0.9 Hz, 1H), 7.34 – 7.28 (t, *J* = 7.6 Hz, 1H), 3.50 – 3.45 (s, 1H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 82.41, 106.81, 112.27, 121.00, 121.67, 122.88, 123.34, 124.03, 124.73, 127.89, 131.24, 156.40, 156.76.

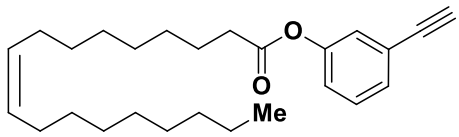


The compound has been synthesized esterification of 4-ethynylbenzoic acid with α-tocopherol. 4-ethynylbenzoic acid (2 mmol, 292mg), α-tocopherol (2 mmol, 860 mg), DCC (2 mmol, 412 mg), DMAP (2 mmol, 244 mg) and DCM (10 mL) were taken in a round bottom flask and

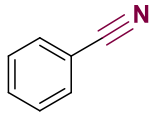
stirred at room temperature for overnight. Reaction mixture was concentrated then and corresponding ester was purified through silica gel (100–200 mesh). Colourless solid isolated with 75% yield. Eluent: petroleum ether: ethyl acetate – 99.5:0.5 (v/v). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.24 – 8.20 (m, 2H), 7.66 – 7.62 (m, 2H), 3.31 – 3.25 (s, 1H), 2.67 – 2.60 (t, *J* = 6.8 Hz, 2H), 2.17 – 2.12 (s, 3H), 2.11 – 2.05 (s, 3H), 2.05 – 2.00 (s, 3H), 1.94 – 1.71 (dq, *J* = 16.0, 5.5, 4.3 Hz, 2H), 1.69 – 1.49 (dh, *J* = 19.9, 6.6, 6.0 Hz, 2H), 1.48 – 1.00 (m, 16H), 0.94 – 0.83 (t, *J* = 6.6 Hz, 14H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 12.08, 12.41, 13.26, 19.83, 19.91, 19.98, 20.85, 21.26, 22.85, 22.94, 24.67, 25.04, 28.20, 31.24, 32.92, 33.00, 37.52, 37.62, 37.69, 37.76, 39.60, 75.32, 80.55, 82.98, 117.71, 123.39, 125.24, 127.01, 127.49, 129.82, 130.20, 132.46, 140.74, 149.76, 164.71.



The compound has been synthesized esterification of 4-ethynylbenzoic acid with estrone. 4-ethynylbenzoic acid (2 mmol, 292mg), estrone (2 mmol, 540 mg), DCC (2 mmol, 412 mg), DMAP (2 mmol, 244 mg) and DCM (10 mL) were taken in a round bottom flask and stirred at room temperature for overnight. Reaction mixture was concentrated then and corresponding ester was purified through silica gel (100–200 mesh) eluting with pet ether– ethyl acetate mixture (95:5 v/v). Colourless solid isolated with 70% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.19 – 8.10 (dd, *J* = 8.3, 1.5 Hz, 2H), 7.65 – 7.57 (dd, *J* = 8.2, 1.5 Hz, 2H), 7.38 – 7.31 (d, *J* = 8.5 Hz, 1H), 7.05 – 6.87 (m, 2H), 3.31 – 3.24 (d, *J* = 1.2 Hz, 1H), 2.99 – 2.88 (dt, *J* = 9.0, 4.4 Hz, 2H), 2.58 – 2.46 (dd, *J* = 18.9, 8.6 Hz, 1H), 2.46 – 2.38 (dd, *J* = 11.8, 4.6 Hz, 1H), 2.37 – 2.24 (td, *J* = 10.9, 4.1 Hz, 1H), 2.22 – 1.93 (m, 5H), 1.57 – 1.43 (m, 4H), 1.32 – 1.20 (m, 2H), 0.98 – 0.88 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 14.06, 21.82, 26.00, 26.57, 29.65, 31.78, 36.08, 38.23, 44.40, 48.18, 50.66, 80.70, 82.93, 118.98, 121.82, 126.72, 127.58, 129.83, 130.21, 132.43, 137.81, 138.36, 148.90, 164.99.



The compound has been synthesized esterification of oleic acid with 3-ethynylphenol. Oleic acid (2 mmol, 564 mg), 3-ethynylphenol (2 mmol, 236 mg), DCC (2 mmol, 412 mg), DMAP (2 mmol, 244 mg) and DCM (10 mL) were taken in a round bottom flask and stirred at room temperature for overnight. Reaction mixture was concentrated then and corresponding ester was purified through silica gel (100–200 mesh). Pale yellowish liquid has been isolated with 77% yield. Eluent: petroleum ether: ethyl acetate – 97:3 (v/v). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.40 – 7.32 (m, 2H), 7.25 – 7.23 (t, *J* = 1.9 Hz, 1H), 7.12 – 7.09 (dt, *J* = 7.8, 1.9 Hz, 1H), 5.47 – 5.31 (m, 2H), 3.17 – 3.05 (s, 1H), 2.65 – 2.51 (t, *J* = 7.5 Hz, 3H), 2.16 – 1.97 (m, 5H), 1.85 – 1.71 (p, *J* = 7.5 Hz, 3H), 1.67 – 1.57 (s, 1H), 1.49 – 1.19 (m, 28H), 0.98 – 0.84 (m, 4H). **^{13}C NMR** (126 MHz, Chloroform-*d*) δ 14.33, 22.90, 25.09, 27.36, 27.43, 29.27, 29.29, 29.36, 29.54, 29.74, 29.89, 29.98, 31.74, 32.12, 34.52, 78.17, 82.80, 122.63, 123.60, 125.45, 129.51, 129.71, 129.90, 130.24, 150.67, 172.18.



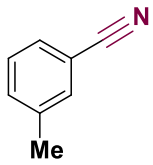
Benzonitrile (Table 3.2, Entry 2a):[23] Reaction was done following general procedure A with ethynylbenzene (0.5 mmol, 51 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 μL). Yellowish viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 70% (36 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.65 (dt, *J* = 8.1, 1.1 Hz, 2H), 7.62 – 7.58 (m, 1H), 7.47 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 132.94, 132.29, 129.28, 119.00, 112.58.

GC-MS (m/z): 103.0 $[M]^{+}$.

IR (Neat): 3067, 2229, 1681, 1599, 1490, 1447, 1287, 1178, 1026, 927, 758, 688, 548 cm^{-1}.

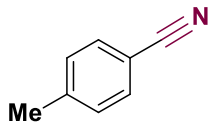


3-methylbenzonitrile (Table 3.2, Entry 2b):[24] Reaction was done following general procedure A with 1-ethynyl-3-methylbenzene (0.5 mmol, 58 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Yellowish viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 65% (38 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 (d, 2H), 7.44-7.39 (m, 1H), 7.33-7.36 (m, 1H), 2.38 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 21.33, 112.43, 119.22, 129.17, 129.46, 132.67, 133.83, 139.40.

GC-MS (m/z): 117.1 $[M]^{+}$.



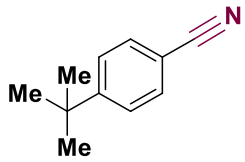
4-methylbenzonitrile (Table 3.2, Entry 2c):[24] Reaction was done following general procedure A with 1-ethynyl-4-methylbenzene (0.5 mmol, 58 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Yellowish viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 68% (40 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 (dd, J = 8.1, 1.3 Hz, 1H), 7.30 – 7.24 (m, 1H), 2.42 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 143.84, 132.15, 129.96, 119.29, 109.40, 21.96.

GC-MS (m/z): 117.0 $[M]^{+}$.

IR (Neat): 3037, 2926, 2253, 2229, 1915, 1672, 1608, 1508, 1449, 1177, 1022, 911, 817, 735, 649, 547 cm^{-1}.

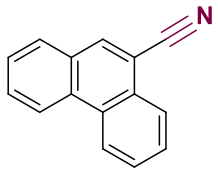


4-tert-butylbenzonitrile (Table 3.2, Entry 2d):[23]Reaction was done following general procedure A with 4-tert-butylbenzonitrile (0.5 mmol, 79 mg) with 2 eqv. ^{t}BuONO (1.0 mmol,

119 µL). Yellowish viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 71% (57 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.62 – 7.55 (m, 2H), 7.52 – 7.44 (m, 2H), 1.44 – 1.25 (m, 12H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 31.13, 35.46, 109.46, 119.37, 126.35, 132.15, 156.82. **GC-MS** (m/z): 159.1 $[M]^+$.



Phenanthrene-9-carbonitrile (Table 3.2, Entry 2e):[25] Reaction was done following general procedure A with 9-ethynylphenanthrene (0.25 mmol, 50.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL)**.** Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 88% (45 mg).

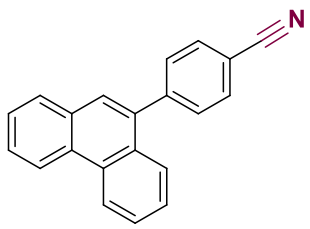
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.67 – 8.61 (m, 2H), 8.28 – 8.24 (m, 1H), 8.20 – 8.16 (s, 1H), 7.90 – 7.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.80 – 7.71 (m, 3H), 7.68 – 7.63 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 109.62, 118.15, 123.07, 123.30, 126.32, 127.84, 128.32, 128.42, 129.07, 129.71, 129.99, 130.04, 130.23, 131.99, 135.86.

GC-MS (m/z): 203.2 $[M]^+$.

IR (Neat): 3073, 2924, 2225, 1955, 1613, 1448, 1247, 1220, 1020, 950, 917, 862, 759, 744, 719, 621, 473 cm^{-1}.

Melting point: 111-113 °C.



4-(phenanthren-9-yl)benzonitrile (Table 3.2, Entry 2f):[26] Reaction was done following general procedure A with 9-(4-ethynylphenyl)phenanthrene (0.25 mmol, 69.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL)**.** Yellowish solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (98:2 v/v) mixture as eluent. Isolated yield 70% (49 mg).

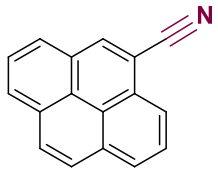
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.83 – 8.78 (d, *J* = 8.3 Hz, 1H), 8.77 – 8.71 (d, *J* = 8.3 Hz, 1H), 7.94 – 7.88 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.83 – 7.76 (td, *J* = 8.4, 1.4 Hz, 4H), 7.74 – 7.69 (dddd, *J* = 8.3, 6.8, 4.4, 1.4 Hz, 2H), 7.68 – 7.62 (m, 4H), 7.60 – 7.54 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 111.44, 119.10, 122.79, 123.34, 126.36, 127.04, 127.07, 127.33, 127.44, 128.11, 129.03, 130.35, 130.43, 130.87, 130.99, 131.32, 132.34, 136.98, 145.89.

GC-MS (m/z): 279.3 $[M]^{+}$.

IR (Neat): 3064, 2925, 2853, 2227, 1605, 1450, 1265, 1022, 863, 839, 754, 732, 591 cm^{-1}.

Melting point: 176-178 °C.



Pyrene-4-carbonitrile (Table 3.2, Entry 2g):[27] Reaction was done following general procedure A with 4-ethynylpyrene (0.25 mmol, 56.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 95% (54 mg).

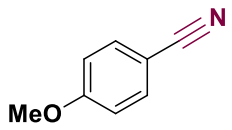
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 – 8.14 (dq, *J* = 15.2, 8.2 Hz, 4H), 8.12 – 8.00 (m, 4H), 7.98 – 7.87 (dd, *J* = 29.0, 8.6 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 105.52, 118.91, 123.36, 123.80, 124.33, 126.82, 126.99, 127.07, 129.45, 130.44, 130.79, 132.80, 134.07.

GC-MS (m/z): 227.1 $[M]^{+}$.

IR (Neat): 3043, 2922, 2215, 1929, 1595, 1185, 970, 840, 824, 757, 711, 610 cm^{-1}.

Melting point: 149-151 °C.



4-methoxybenzonitrile (Table 3.2, Entry 2h):[23] Reaction was done following general procedure A with 1-ethynyl-4-methoxybenzene (0.5 mmol, 66 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL)**.** Colourless Solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 75% (50 mg).

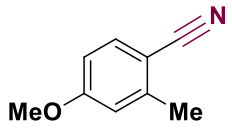
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 – 7.53 (m, 2H), 6.95 – 6.90 (m, 2H), 3.89 – 3.77 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 55.65, 103.98, 114.86, 119.32, 134.04, 162.95.

GC-MS (m/z): 133.1 $[M]^{+}$.

IR (Neat): 2976, 2843, 2222, 1606, 1575, 1510, 1304, 1261, 1173, 1025, 843, 739, 683, 547 cm^{-1}.

Melting point: 58-60 °C.

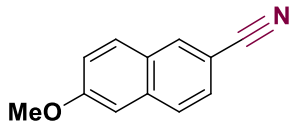


4-methoxy-2-methylbenzonitrile (Table 3.2, Entry 2i):[28] Reaction was done following general procedure A with 1-ethynyl-4-methoxy-2-methylbenzene (0.5 mmol, 73 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Yellowish solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 77% (57 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 – 7.45 (d, J = 8.5 Hz, 1H), 6.79 – 6.77 (d, J = 2.5 Hz, 1H), 6.77 – 6.74 (dd, J = 8.5, 2.6 Hz, 1H), 3.83 – 3.82 (s, 3H), 2.54 – 2.45 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 20.84, 55.61, 104.63, 112.24, 115.81, 118.73, 134.32, 144.21, 162.85.

GC-MS (m/z): 147.1 $[M]^{+}$.



6-methoxy-2-naphthonitrile (Table 3.2, Entry 2j):[29] Reaction was done following general procedure A with 2-ethynyl-6-methoxynaphthalene (0.5 mmol, 91 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL)**.** Light yellow solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 72% (66 mg).

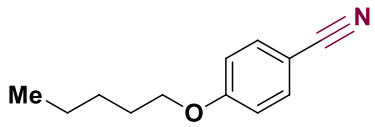
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 – 8.11 (m, 1H), 7.80 – 7.75 (dd, *J* = 8.7, 2.2 Hz, 2H), 7.59 – 7.53 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.29 – 7.20 (dd, *J* = 9.7, 3.2 Hz, 1H), 7.17 – 7.13 (d, *J* = 2.5 Hz, 1H), 3.97 – 3.93 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 55.70, 106.07, 106.91, 119.79, 120.87, 127.26, 127.92, 127.99, 130.16, 133.94, 136.60, 160.20.

GC-MS (m/z): 183.1 $[M]^{+}$.

IR (Neat): 2939, 2221, 1622, 1602, 1390, 1267, 1228, 1025, 892, 870, 811 cm^{-1}.

Melting point: 105-107 °C.



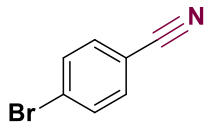
4-(pentyloxy)benzonitrile (Table 3.2, Entry 2k):[30] Reaction was done following general procedure A with 2-ethynyl-6-methoxynaphthalene (0.5 mmol, 94 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL)**.** Pale yellow oily compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 78% (74 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 – 7.51 (m, 2H), 6.99 – 6.84 (m, 2H), 4.04 – 3.91 (t, *J* = 6.6 Hz, 2H), 1.84 – 1.72 (dq, *J* = 8.2, 6.5 Hz, 2H), 1.51 – 1.27 (m, 4H), 0.97 – 0.87 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 14.14, 22.54, 28.22, 28.82, 68.54, 103.72, 115.31, 119.49, 134.08, 162.60.

GC-MS (m/z): 189.2 $[M]^{+}$.

IR (Neat): 2935, 2872, 2561, 2224, 1606, 1574, 1508, 1470, 1302, 1260, 1171, 1113, 1049, 1014, 834, 548 cm^{-1}.



4-bromobenzonitrile (Table 3.2, Entry 2l):[24] Reaction was done following general procedure A with 1-bromo-4-ethynylbenzene (0.5 mmol, 89.5 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 82% (74 mg).

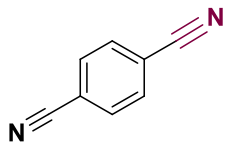
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 – 7.61 (m, 2H), 7.55 – 7.49 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 111.41, 118.23, 128.19, 132.82, 133.58.

GC-MS (m/z): 181.0 $[M]^{+}$.

IR (Neat): 2985, 2945, 2231, 1742, 1481, 1374, 1243, 1048, 938, 847, 608 cm^{-1}.

Melting point: 110-112 °C.



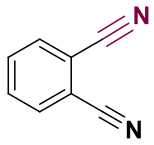
Terephthalonitrile (Table 3.2, Entry 2m):[25] Reaction was done following general procedure A with 4-ethynylbenzonitrile (0.5 mmol, 63.5 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (95:5 v/v) mixture as eluent. Isolated yield 62% (40 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.79 (s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 116.91, 117.20, 132.99.

IR (Neat): 3096, 3053, 2232, 1400, 1276, 1200, 841, 763, 557 cm^{-1}. GC-MS (m/z): 128.0 $[M]^{+}$.

Melting point: More than 200 °C.

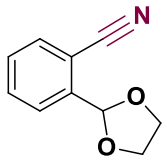


Phthalonitrile (Table 3.2, Entry 2n):[31] Reaction was done following general procedure A with 4-ethynylbenzonitrile (0.5 mmol, 63.5 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield 58% (37 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 5.8, 3.3 Hz, 2H), 7.76 (dd, *J* = 5.9, 3.3 Hz, 2H).

^{13}C NMR (126 MHz, Chloroform-d) δ 133.79, 133.33, 116.24, 115.50.

GC-MS (m/z): 128.1 $[M]^{+}$.



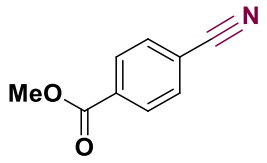
2-(1,3-dioxolan-2-yl)benzonitrile (Table 3.2, Entry 2o): Reaction was done following general procedure A with 2-(2-ethynylphenyl)-1,3-dioxolane (0.25 mmol, 43.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (95:5 v/v) mixture as eluent. Isolated yield 71% (31 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.75 – 7.67 (m, 1H), 7.66 – 7.56 (qd, *J* = 7.7, 1.6 Hz, 2H), 7.52 – 7.43 (td, *J* = 7.3, 2.0 Hz, 1H), 6.02 – 5.95 (s, 1H), 4.30 – 4.21 (m, 2H), 4.13 – 4.07 (m, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 66.17, 102.21, 111.54, 117.31, 128.09, 129.91, 132.79, 133.86, 141.26.

GC-MS (m/z): 175.1 $[M]^{+}$. **HRMS** (ESI): $[M + Na]^{+}$ calculated for $C_{10}H_9NaNO_2$: 198.0525, found: 198.0531.

IR (thin film): 3076, 2957, 2894, 2229, 1728, 1595, 1488, 1454, 1398, 1277, 1143, 1078, 763 cm^{-1}.



Methyl 4-cyanobenzoate (Table 3.2, Entry 2p):[32] Reaction was done following general procedure A with methyl 4-ethynylbenzoate (0.5 mmol, 80 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (98:2 v/v) mixture as eluent. Isolated yield 70% (57 mg).

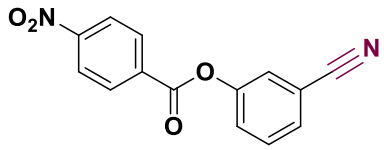
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 – 8.04 (m, 2H), 7.79 – 7.64 (m, 2H), 3.99 – 3.90 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 52.88, 116.55, 118.11, 130.25, 132.38, 134.08, 165.58.

GC-MS (m/z): 161.1 $[M]^{+}$.

IR (Neat): 3428, 3074, 3009, 2957, 2850, 2230, 1951, 1728, 1440, 1405, 1286, 1181, 1109, 960, 865, 764, 740, 692, 546 cm^{-1}.

Melting point: 65-67 °C.



3-cyanophenyl 4-nitrobenzoate (Table 3.2, Entry 2q): Reaction was done following general procedure A with 3-ethynylphenyl 4-nitrobenzoate (0.25 mmol, 67 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Pale Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (96:4 v/v) mixture as eluent. Isolated yield 62% (42 mg).

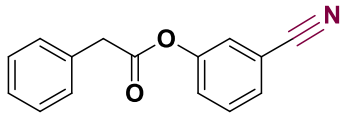
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 – 8.37 (s, 4H), 7.66 – 7.55 (m, 3H), 7.54 – 7.49 (dt, *J* = 8.0, 2.0 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 114.00, 117.81, 124.09, 125.51, 126.67, 130.37, 130.89, 131.63, 134.19, 150.76, 151.38, 162.94.

HRMS (ESI): $[M + H]^{+}$ calculated for $C_{15}H_{13}N_2O_5$: 301.0818, found: 301.085.

IR (Neat): 3110, 2926, 2232, 1741, 1607, 1582, 1524, 1349, 1265, 1234, 1145, 1078, 897, 799, 714, 680 cm^{-1}.

Melting point: 125-127 °C.



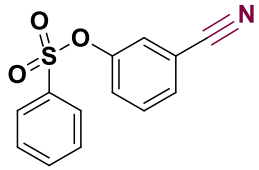
3-cyanophenyl 2-phenylacetate (Table 3.2, Entry 2r): Reaction was done following general procedure A with 3-ethynylphenyl 2-phenylacetate (0.25 mmol, 59 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (95:5 v/v) mixture as eluent. Isolated yield 82% (49mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 – 7.49 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.43 (t, *J* = 7.9 Hz, 1H), 7.42 – 7.36 (m, 5H), 7.36 – 7.31 (m, 2H), 4.07 – 3.72 (s, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 41.39, 113.55, 117.94, 125.42, 126.66, 127.78, 129.02, 129.42, 129.76, 130.51, 132.93, 150.91, 169.56.

HRMS (ESI): $[M + H]^{+}$ calculated for $C_{15}H_{12}NO_2$: 238.0863, found: 238.0858.

IR (Neat): 3066, 3034, 2234, 1769, 1584, 1481, 1432, 1230, 1141, 1117, 951, 897, 738, 473 cm^{-1}.



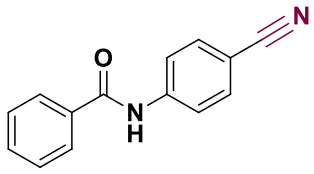
3-cyanophenyl benzenesulfonate (Table 3.2, Entry 2s):[33] Reaction was done following general procedure A with 3-ethynylphenyl benzenesulfonate (0.25 mmol, 64.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (93:7 v/v) mixture as eluent. Isolated yield 66% (43 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.81 (m, 2H), 7.75 – 7.68 (m, 1H), 7.60 – 7.52 (m, 3H), 7.47 – 7.40 (t, *J* = 8.0 Hz, 1H), 7.33 – 7.23 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 113.96, 117.39, 126.14, 127.51, 128.59, 129.64, 130.95, 131.06, 134.87, 135.02, 149.66.

GC-MS (m/z): 259.1 $[M]^+$. **HRMS** (ESI): $[M + H]^+$ calculated for $C_{13}H_{10}NO_3S$: 260.0376, found: 260.0370.

IR (Neat): 3077, 2927, 2235, 1605, 1582, 1481, 1373, 1227, 1190, 1127, 1092, 938, 805, 681, 588, 557 cm^{-1}.



***N*-(4-cyanophenyl)benzamide (Table 3.2, Entry 2t):**[34] Reaction was done following general procedure A with N-(4-ethynylphenyl)benzamide (0.25 mmol, 55.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59 μL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (75:25v/v) mixture as eluent. Isolated yield 69% (38.5 mg).

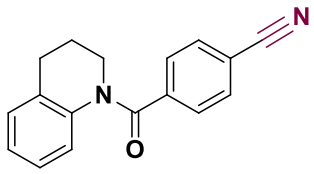
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 – 8.00 (d, *J* = 11.6 Hz, 1H), 7.92 – 7.83 (m, 2H), 7.83 – 7.76 (dd, *J* = 8.7, 2.9 Hz, 2H), 7.69 – 7.62 (m, 2H), 7.62 – 7.55 (td, *J* = 7.8, 2.6 Hz, 1H), 7.55 – 7.42 (qd, *J* = 7.5, 6.6, 2.9 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 107.62, 119.01, 120.13, 127.32, 129.20, 132.72, 133.56, 134.32, 142.22, 166.09.

GC-MS (m/z): 222.1 $[M]^+$.

IR (Neat): 3349, 2986, 2226, 1742, 1593, 1522, 1448, 1374, 1243, 1047, 938, 847, 608 cm^{-1}.

Melting point: 164-166 °C.



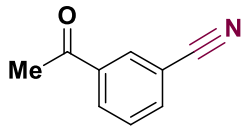
4-(1,2,3,4-tetrahydroquinoline-1-carbonyl)benzonitrile (Table 3.2, Entry 2u): Reaction was done following general procedure A with (3,4-dihydroquinolin-1(2H)-yl)(4-ethynylphenyl)methanone (0.25 mmol, 65 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 μL). Colourless crystalline solid was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (85:15 v/v) mixture as eluent. Isolated yield 78% (51 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 – 7.52 (m, 2H), 7.46 – 7.38 (m, 2H), 7.21 – 7.14 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.07 – 6.99 (td, *J* = 7.5, 1.2 Hz, 1H), 6.90 – 6.82 (m, 1H), 6.61 – 6.49 (s, 1H), 3.97 – 3.84 (t, *J* = 6.6 Hz, 2H), 2.90 – 2.80 (t, *J* = 6.6 Hz, 2H), 2.13 – 1.99 (p, *J* = 6.5 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 24.20, 27.08, 44.51, 113.82, 118.33, 125.55, 126.17, 128.78, 129.42, 132.14, 132.41, 138.65, 140.79, 168.25.

GC-MS (m/z): 262.1 [M]+. **HRMS** (ESI): $[M + Na]^+$ calculated for $C_{17}H_{14}N_2NaO$: 285.0998, found: 285.0983.

Melting point: 104-106 °C.



3-acetylbenzonitrile (Table 3.2, Entry 2v):[35] Reaction was done following general procedure A with 1-(3-ethynylphenyl)ethanone (0.5 mmol, 72 mg) with 2 eqv. ^{t}BuONO (1.0 mmol,119 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield 78% (57 mg).

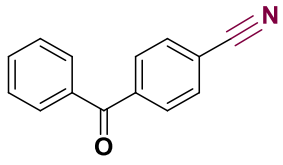
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 – 8.20 (d, *J* = 1.7 Hz, 1H), 8.20 – 8.14 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.87 – 7.81 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.64 – 7.58 (t, *J* = 7.8 Hz, 1H), 2.70 – 2.55 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 26.75, 113.33, 118.08, 129.86, 132.18, 132.38, 136.16, 137.89, 195.99.

GC-MS (m/z): 145.1 $[M]^+$.

IR (Neat): 3351, 3070, 2925, 2229, 1689, 1418, 1369, 1273, 1186, 1024, 964, 910, 801, 679, 607, 537 cm^{-1}.

Melting point: 95-97 °C.



4-benzoylbenzonitrile (Table 3.2, Entry 2w):[36] Reaction was done following general procedure A with (4-ethynylphenyl)(phenyl)methanone (0.25 mmol, 51.5 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (98.5:0.5 v/v) mixture as eluent. Isolated yield 81% (42 mg).

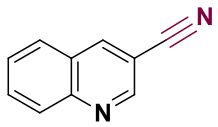
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.89 – 7.84 (m, 2H), 7.81 – 7.75 (m, 4H), 7.68 – 7.60 (m, 1H), 7.55 – 7.47 (m, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 115.80, 118.17, 128.79, 130.21, 130.38, 132.32, 133.48, 136.47, 141.37, 195.17.

GC-MS (m/z): 207.1 $[M]^{+}$.

IR (Neat): 3088, 3063, 2228, 1651, 1597, 1446, 1403, 1310, 1278, 1114,929, 857, 794, 736, 694, 678, 593, 541 cm^{-1}.

Melting point: 113-115 °C.



Quinoline-3-carbonitrile (Table 3.3, Entry 3a):[37] Reaction was done following general procedure A with 3-ethynylquinoline (0.5 mmol, 76.5 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield 86% (66 mg).

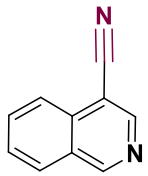
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.11 – 8.95 (d, J = 2.2 Hz, 1H), 8.67 – 8.41 (m, 1H), 8.22 – 8.12 (m, 1H), 8.01 – 7.86 (m, 2H), 7.79 – 7.60 (ddd, J = 8.0, 6.9, 1.2 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 106.74, 117.27, 126.36, 128.43, 128.67, 130.01, 132.96, 141.65, 148.95, 149.90.

GC-MS (m/z): 154.0 $[M]^{+}$.

IR (Neat): 3064, 2928, 2853, 2229, 1862, 1620, 1598, 1489, 1371, 1266, 1129, 922, 745, 475 cm^{-1}.

Melting point: 107-109 °C.



Isoquinoline-4-carbonitrile (Table 3.3, Entry 3b):[38] Reaction was done following general procedure A with 4-ethynylisoquinoline (0.25 mmol, 38 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield 73% (28 mg).

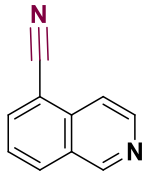
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.45 – 9.37 (d, *J* = 0.9 Hz, 1H), 8.95 – 8.85 (s, 1H), 8.23 – 8.14 (dq, *J* = 8.4, 0.9 Hz, 1H), 8.14 – 8.06 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.97 – 7.89 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.82 – 7.74 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 106.16, 116.09, 124.29, 127.77, 128.67, 129.40, 133.24, 134.67, 148.51, 156.46.

GC-MS (m/z): 154.1 $[M]^{+}$.

IR (Neat): 3061, 2921, 2850, 2231, 1864, 1620, 1567, 1499, 1380, 1270, 1153, 910, 779, 757, 464 cm^{-1}.

Melting point: 93-95 °C.



isoquinoline-5-carbonitrile (Table 3.3, Entry 3c): Reaction was done following general procedure A with 5-ethynylisoquinoline (0.5 mmol, 76.5 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Pale colourless solid was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 67% (52 mg).

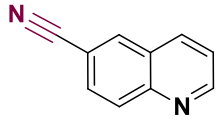
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.41 – 9.34 (d, *J* = 0.9 Hz, 1H), 8.78 – 8.73 (d, *J* = 5.9 Hz, 1H), 8.29 – 8.20 (dt, *J* = 8.3, 1.1 Hz, 1H), 8.16 – 8.10 (dd, *J* = 7.3, 1.2 Hz, 1H), 8.05 – 7.98 (dt, *J* = 5.8, 1.0 Hz, 1H), 7.75 – 7.64 (dd, *J* = 8.3, 7.2 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 109.83, 116.66, 117.85, 126.80, 128.11, 133.06, 135.46, 136.76, 145.80, 153.25.

GC-MS (m/z): 154.1 $[M]^+$.

IR (Neat): 3061, 2925, 2226, 1617, 1584, 1569, 1372, 1273, 1031, 920, 827, 764, 470 cm^{-1}.

Melting point: 135-137 °C.



quinoline-6-carbonitrile (Table 3.3, Entry 3d):[39] Reaction was done following general procedure A with 6-ethynylquinoline (0.25 mmol, 38 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 µL). Colourless solid was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (87:13 v/v) mixture as eluent. Isolated yield 81% (31 mg).

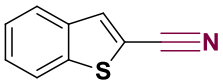
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.07 – 9.00 (m, 1H), 8.27 – 8.14 (m, 3H), 7.87 – 7.81 (dq, *J* = 8.7, 1.7 Hz, 1H), 7.56 – 7.50 (ddd, *J* = 8.3, 4.2, 1.5 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 110.55, 118.65, 122.90, 127.70, 130.28, 131.22, 134.28, 136.54, 149.26, 153.42.

GC-MS (m/z): 154.1 $[M]^+$.

IR (Neat): 3050, 2925, 2229, 1795, 1320, 1029, 899, 838, 797, 551, 474 cm^{-1}.

Melting point: 133-136 °C.



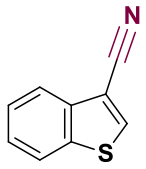
Benzo[b]thiophene-2-carbonitrile (Table 3.3, Entry 3e):[40] Reaction was done following general procedure A with 2-ethynylbenzo[b]thiophene (0.5 mmol, 79 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Redish viscous compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 70% (56 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 – 7.85 (m, 3H), 7.57 – 7.51 (ddd, *J* = 8.2, 7.1, 1.4 Hz, 1H), 7.51 – 7.45 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 109.94, 114.68, 122.61, 125.51, 125.95, 128.09, 135.20, 137.69, 141.53.

GC-MS (m/z): 159.1 $[M]^+$.

IR (Neat): 3090, 3063, 2925, 2850, 2216, 1951, 1713, 1595, 1510, 1427, 1252, 1190, 1160, 1106, 944, 867, 7749, 558 cm^{-1}.



Benzo[b]thiophene-3-carbonitrile (Table 3.3, Entry 3f):[41] Reaction was done following general procedure A with 3-ethynylbenzo[b]thiophene (0.5 mmol, 79 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Yellowish solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 81% (65 mg).

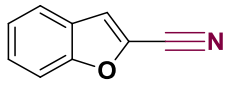
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (s, 1H), 8.01-7.99 (d, J = 8 Hz, 1H), 7.92-7.90 (d, J = 8 Hz, 1H), 7.52 – 7.56 (t, J = 16 Hz, 1H), 7.51-7.47 (t, J = 16 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 107.36, 114.51, 122.76, 123.04, 126.19, 126.40, 137.49, 137.72, 138.71.

GC-MS (m/z): 159.1 $[M]^+$.

IR (Neat): 3108, 2929, 2851, 2224, 1954, 1623, 1497, 1461, 1426, 1256, 856, 812, 754, 728, 710, 508 cm^{-1}.

Melting point: 70-72 °C.



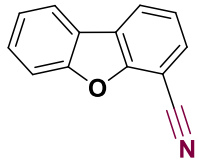
Benzofuran-2-carbonitrile (Table 3.3, Entry 3g):[41] Reaction was done following general procedure A with 2-ethynylbenzofuran (0.5 mmol, 71 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59 µL) and 2 equiv. 2-picoline-*N*-oxide (0.5 mmol, 54.5 mg). Redish viscous liquid was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5 : 0.5 v/v) mixture as eluent. Isolated yield 50% (36 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.59 – 7.48 (m, 2H), 7.47 (d, *J* = 0.9 Hz, 1H), 7.37 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.90, 128.65, 127.54, 125.71, 124.76, 122.78, 118.67, 112.32, 112.04.

GC-MS (m/z): 143.1 $[M]^+$.

IR (Neat): 3054, 2924, 2854, 2301, 1650, 1454, 1377, 1264, 1022, 743 cm^{-1}.



Dibenzo[b,d]furan-4-carbonitrile (Table 3.3, Entry 3h):[27] Reaction was done following general procedure A with 4-ethynyldibenzo[b,d]furan (0.25 mmol, 48 mg) with 2 eqv. ^{t}BuONO (0.5 mmol, 59.5 μL). Colourless solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99:1 v/v) mixture as eluent. Isolated yield 78% (38 mg).

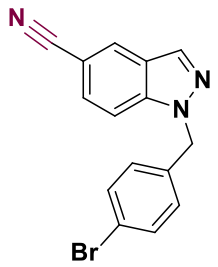
^{1}H NMR (400 MHz, Chloroform-d) δ 8.18 – 8.11 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.01 – 7.91 (m, 1H), 7.75 – 7.68 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.68 – 7.63 (dt, *J* = 8.3, 0.8 Hz, 1H), 7.60 – 7.49 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.47 – 7.37 (m, 2H).

^{13}C NMR (101 MHz, Chloroform-d) δ 96.83, 112.41, 115.21, 121.20, 123.01, 123.17, 124.00, 125.60, 125.80, 128.80, 130.55, 156.30, 156.51.

GC-MS (m/z): 193.1 $[M]^+$.

IR (Neat): 3063, 2231, 1604, 1448, 1420, 1268, 1192, 754 cm^{-1}.

Melting point: 128-130 °C.



1-(4-bromobenzyl)-1*H*-indazole-5-carbonitrile (Table 3.3, Entry 3i): Reaction was done following general procedure A with 1-(4-bromobenzyl)-5-ethynyl-1*H*-indazole (0.2 mmol, 62 mg) with 2 eqv. ^{t}BuONO (0.4 mmol, 47.5 µL). Yellowish solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield 67% (42 mg).

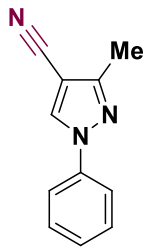
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 – 8.10 (d, *J* = 1.9 Hz, 2H), 7.58 – 7.52 (dd, *J* = 8.7, 1.4 Hz, 1H), 7.49 – 7.42 (m, 2H), 7.42 – 7.37 (d, *J* = 8.7 Hz, 1H), 7.10 – 7.04 (m, 2H), 5.58 – 5.55 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 52.93, 76.91, 77.55, 104.81, 110.52, 119.61, 122.51, 124.22, 127.95, 128.95, 129.12, 132.33, 134.84, 134.98, 140.38.

GC-MS (m/z): 311.1 [M]+. **HRMS** (ESI): $[M + Na]^{+}$ calculated for $C_{15}H_{10}BrN_3Na$: 333.9950, found: 333.9916.

IR (Neat): 2928, 2356, 2221, 1615, 1590, 1485, 1337, 1302, 1283, 1169, 1119, 891, 826, 808, 795, 746, 496 cm^{-1}.

Melting point: 133-135 °C.



3-methyl-1-phenyl-1*H*-pyrazole-4-carbonitrile (Table 3.3, Entry 3j): Reaction was done following general procedure A with 4-ethynyl-3-methyl-1-phenyl-1*H*-pyrazole (0.5 mmol, 91 mg) with 2 eqv. ^{t}BuONO (1.0 mmol, 119 µL). Colorless crystalline solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (97:3 v/v) mixture as eluent. Isolated yield 65% (60 mg).

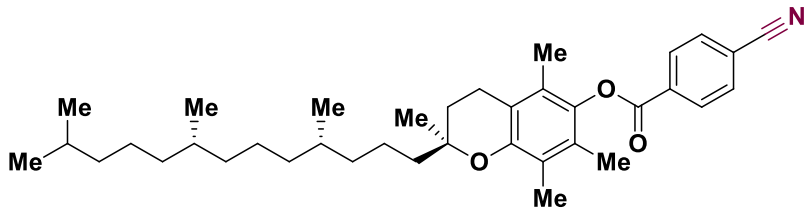
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 – 8.17 (s, 1H), 7.65 – 7.61 (m, 2H), 7.50 – 7.45 (m, 2H), 7.39 – 7.34 (m, 1H), 2.51 – 2.42 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 12.74, 76.98, 77.48, 94.39, 113.63, 119.83, 128.08, 129.89, 132.20, 139.02, 153.66.

GC-MS (m/z): 183.2 $[M]^+$. **HRMS** (ESI): $[M + H]^+$ calculated for $C_{11}H_{10}N_3$: 184.0869, found: 184.0862.

IR (Neat): 3150, 2927, 2227, 1598, 1553, 1446, 1383, 1216, 830, 751, 684, 668 cm^{-1}.

Melting point: 96-98 °C.



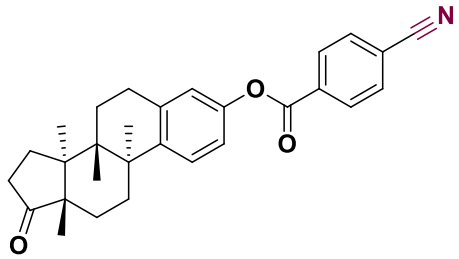
(S)-2,5,7,8-tetramethyl-2-((4S,8S)-4,8,12-trimethyltridecyl)chroman-6-yl 4-cyanobenzoate(Table 3.4, Entry 4a): Reaction was done following general procedure A with (S)-2,5,7,8-tetramethyl-2-((4S,8S)-4,8,12-trimethyltridecyl)chroman-6-yl 4-ethynylbenzoate (0.2 mmol, 111 mg) with 2 eqv. ^{t}BuONO (0.4 mmol, 48 µL).Yellowish crystalline solid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99: 1 v/v) mixture as eluent. Isolated yield 45% (50 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 – 8.28 (m, 2H), 7.89 – 7.77 (m, 2H), 2.66 – 2.55 (t, *J* = 6.8 Hz, 2H), 2.18 – 2.08 (s, 3H), 2.06 – 2.02 (s, 3H), 2.02 – 1.97 (s, 3H), 1.90 – 1.72 (m, 2H), 1.61 – 1.50 (d, *J* = 23.9 Hz, 9H), 1.31 – 1.22 (d, *J* = 4.9 Hz, 15H), 1.17 – 1.01 (m, 3H), 0.88 – 0.83 (t, *J* = 7.0 Hz, 15H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 12.10, 12.44, 13.28, 14.35, 19.92, 20.86, 21.27, 22.86, 22.95, 24.68, 25.04, 28.21, 29.59, 29.93, 32.15, 33.01, 37.52, 37.62, 37.69, 39.60, 75.45, 76.91, 77.43, 77.55, 117.08, 117.87, 118.15, 123.59, 125.07, 126.79, 130.83, 132.65, 133.70, 140.57, 149.99, 163.82.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{37}H_{53}NNaO_3$: 582.3918, found: 582.3915.

Melting point: 64-66 °C.



(8R,9S,13S,14S)-8,9,13,14-tetramethyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl 4-cyanobenzoate (Table 3.4, Entry 4b): Reaction was done following general procedure A with (8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]ph -enanthren-3-yl 4-ethynylbenzoate(0.2 mmol, 88 mg) with 2 eqv. ^{t}BuONO (0.4 mmol, 48 µL). Colourless solid was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (90:10 v/v) mixture as eluent. Isolated yield 39% (35 mg).

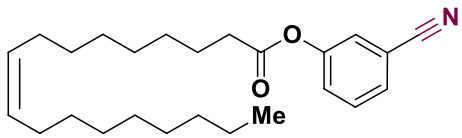
^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.33 – 8.27 (m, 2H), 7.85 – 7.77 (m, 2H), 7.38 – 7.33 (d, *J* = 8.5 Hz, 1H), 7.01 – 6.96 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.96 – 6.93 (d, *J* = 2.5 Hz, 1H), 2.99 – 2.91 (dd, *J* = 9.5, 4.4 Hz, 2H), 2.58 – 2.48 (dd, *J* = 19.1, 8.7 Hz, 1H), 2.48 – 2.40 (m, 1H), 2.38 – 2.29 (td, *J* = 10.9, 3.7 Hz, 1H), 2.22 – 2.11 (dt, *J* = 18.6, 8.9 Hz, 1H), 2.11 – 1.95 (m, 3H), 1.62 – 1.41 (m, 11H), 1.32 – 1.20 (d, *J* = 2.6 Hz, 1H), 1.07 – 1.02 (s, 0H), 0.99 – 0.90 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 14.05, 21.80, 25.98, 26.52, 29.65, 29.91, 31.75, 36.06, 38.19, 44.39, 48.16, 50.64, 117.15, 118.08, 118.77, 121.62, 126.85, 130.83, 132.59, 133.72, 138.20, 138.55, 148.63, 164.07.

HRMS (ESI): $[M + H]^+$ calculated for $C_{29}H_{32}NO_3$: 442.2376, found: 442.2393.

IR (Neat): 2930, 2855, 2225, 1740, 1608, 1493, 1297, 1224, 1175, 1149, 1074, 1020, 893, 738 cm^{-1}.

Melting point: More than 200 °C.



3-cyanophenyl oleate (Table 3.4, Entry 4c): Reaction was done following general procedure A with 3-ethynylphenyl oleate (0.2 mmol, 76 mg) with 2 eqv. ^{t}BuONO (0.4 mmol, 48 µL). Pale yellowish viscous liquid compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 68% (52 mg).

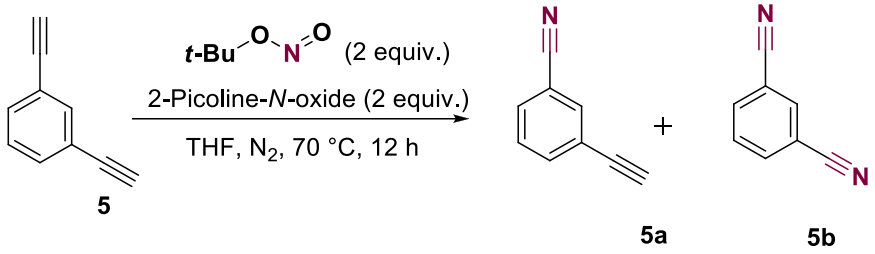
^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.55 – 7.44 (m, 2H), 7.43 – 7.39 (t, *J* = 1.9 Hz, 1H), 7.37 – 7.32 (dt, *J* = 8.1, 1.8 Hz, 1H), 5.54 – 5.16 (m, 2H), 2.61 – 2.53 (t, *J* = 7.5 Hz, 2H), 2.05 –

1.92 (dp, *J* = 24.4, 6.5 Hz, 4H), 1.79 – 1.70 (p, *J* = 7.5 Hz, 2H), 1.50 – 1.15 (m, 18H), 0.91 – 0.84 (t, *J* = 6.8 Hz, 3H).

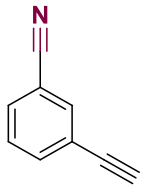
^{13}C NMR (126 MHz, Chloroform-*d*) δ 14.30, 22.88, 24.97, 29.10, 29.22, 29.27, 29.38, 29.51, 29.69, 29.74, 29.85, 32.10, 32.73, 32.80, 34.43, 76.98, 77.48, 113.66, 118.03, 125.59, 126.79, 129.61, 130.32, 130.51, 130.75, 151.07, 171.80.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{26}H_{39}NNaO_2$: 420.2873, found: 420.2802.

IR (Neat): 2926, 2854, 2234, 1769, 1584, 1481, 1464, 1432, 1377, 1238, 1141, 968, 797, 681, 471 cm^{-1}.



3-ethynylbenzonitrile (Scheme 3.2, Entry 5a): Reaction was done following general procedure A with 1,3-diethynylbenzene (1.0 mmol, 127 mg) with 2 eqv. ^{t}BuONO (2.0 mmol, 240 µL) and Picoline-*N*-oxide (1.0 mmol, 218 mg)**.** Pale yellowish viscous liquid (**5a**) compound was isolated through 100-120 mesh silica gel using pet ether: ethyl acetate (99.5:0.5 v/v) mixture as eluent. Isolated yield 58% (74 mg). Another fraction (**5b**) was isolated as solid compound in 15% yield (20 mg). The same compound was treated with 4 eqv. ^{t}BuONO (4.0 mmol, 480 µL) and Picoline-*N*-oxide (4.0 mmol, 436 mg) and 5a and 5b was isolated in 7% and 70% yield respectively.

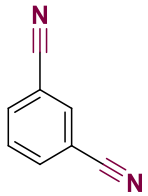


3-ethynylbenzonitrile (Scheme 3.2, Entry 5a):[42]

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (td, *J* = 1.6, 0.6 Hz, 1H), 7.70 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.63 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.45 (td, *J* = 7.8, 0.6 Hz, 1H), 3.19 (s, 1H), 0.07 (s, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.38, 135.67, 132.25, 129.50, 123.98, 118.08, 113.15, 81.38, 79.98.

GC-MS (m/z): 127.0 $[M]^+$.



Isophthalonitrile (Scheme 3.2, Entry 5b):[41]

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.00 – 7.94 (m, 1H), 7.90 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.66 (t, *J* = 7.9 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 136.19, 135.63, 130.54, 116.79, 114.43.

GC-MS (m/z): 128.0 $[M]^+$.

IR (Neat): 3078, 3046, 2921, 2855, 2235, 1692, 1480, 1423, 1361, 1271, 1183, 904, 804, 678, 50 cm^{-1}.

Melting point: 160-162 °C.

3.4. Conclusion

In conclusion, we have developed the first metal-free nitrogenation of terminal alkynes to provide arylnitrile under mild conditon. This is the first example where *tert*-butyl nitrite is used as the nitrogenating reagent for alkynes. A wide range of functional groups are compatible with the reaction conditions. This metal-free nitrile synthesis avoids the use of hazardous materials, allowing potential application in industry and academia.

3.5. References

(1) (a) Ding, S.; Yan, Y.; Jiao, N. *Chem. Commun.***2013**, *49*, 4250. (b) Song, S.; Li, X.; Sun, X.; Yuan, Y.; Jiao, N. *Green Chem.* **2015**, *17*, 3285. (c) Peng, H.; Akhmedov, N. G.; Liang, Y.-F.; Jiao, N.; Shi, X. *J. Am. Chem. Soc.***2015**, *137*, 8912. (d) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *J. Am. Chem. Soc.***2005**, *127*, 9260. (e) Shen, H. C. *Tetrahedron* **2008**, *64*, 3885. (f) Irina, B.; Christina, M. *Chem. Rev.***1999**, *99*, 3435.

(2) (a) Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Org. Lett.* **2001**, *3*, 735. (b) Tokunaga, M.; Suzuki, T.; Koga, N.; Fukushima, T.; Horiuchi, A.; Wakatsuki, Y. *J. Am. Chem. Soc.* **2001**, *123*, 11917. (c) Marion, N.; Ramón, R. S.; Nolan, S. P. *J. Am. Chem. Soc.* **2009**, *131*, 448. (d) Grotjahn, D. B.; Lev, D. A. *J. Am. Chem. Soc.* **2004**, *126*, 12232. (e) Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem., Int. Ed.* **2002**, *114*, 4745.

(3) (a) Kotov, V.; Scarborough, C. C.; Stahl, S. S. *Inorg. Chem.* **2007**, *46*, 1910. (b) Cornell, C. N.; Sigman, M. S. *Inorg. Chem.* **2007**, *46*, 1903. (c) Jung, M. E.; Deng, G. *Org. Lett.* **2014**, *16*, 2142. (d) Zhang, C.; Jiao, N. *J. Am. Chem. Soc.* **2010**, *132*, 28. (e) Michel, B. W.; Steffens, L. D.; Sigman, M. S. In *Organic Reactions*; John Wiley & Sons, Inc.: 2004. (f) Wan, Z.; Jones, C. D.; Mitchell, D.; Pu, J. Y.; Zhang, T. Y. *J. Org. Chem.* **2006**, *71*, 826. (g) Ren, W.; Xia, Y.; Ji, S.-J.; Zhang, Y.; Wan, X.; Zhao, J. *Org. Lett.* **2009**, *11*, 1841.

(4) (a) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874. (b) Dudnik, A. S.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2010**, *49*, 2096. (c) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219. (d) Gelman, D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 5993. (e) Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 13642. (f) Gallop, C. W. D.; Chen, M.-T.; Navarro, O. *Org. Lett.* **2014**, *16*, 3724. (g) Dong, J.; Wang, F.; You, J. *Org. Lett.* **2014**, *16*, 2884 (h) Sanchez-Sanchez, C.; Orozco, N.; Holgado, J. P.; Beaumont, S. K.; Kyriakou, G.; Watson, D. J.; Gonzalez-Elipe, A. R.; Feria, L.; Fernández Sanz, J.; Lambert, R. M. *J. Am. Chem. Soc.* **2015**, *137*, 940. (i) Ahammed, S.; Dey, R.; Ranu, B. C. *Tetrahedron Lett.* **2013**, *54*, 3697.

(5) (a) Gilmore, K.; Alabugin, I. V. *Chem. Rev.* **2011**, *111*, 6513. (b) Amblard, F.; Cho, J. H.; Schinazi, R. F. *Chem. Rev.* **2009**, *109*, 4207. (c) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *113*, 2056. (d) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302. (e) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952. (f) Demko, Z. P.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2113.(g) Friscourt, F.; Boons, G.-J. *Org. Lett.* **2010**, *12*, 4936. (h) Rodionov, V. O.; Presolski, S. I.; Gardinier, S.; Lim, Y.-H.; Finn, M. G. *J. Am. Chem. Soc.* **2007**, *129*, 12696. (i) Rasmussen, L. K.; Boren, B. C.; Fokin, V. V. *Org. Lett.* **2007**, *9*, 5337. (j) Nakamura, T.; Terashima, T.; Ogata, K.; Fukuzawa, S.-i. *Org. Lett.* **2011**, *13*, 620. (k) Shin, J.-A.; Lim, Y.-G.; Lee, K.-H. *J. Org. Chem.* **2012**, *77*, 4117. (l) Kamata, K.; Nakagawa, Y.; Yamaguchi, K.; Mizuno, N. *J. Am. Chem. Soc.* **2008**, *130*, 15304. (m) Barral, K.; Moorhouse, A. D.; Moses, J. E. *Org. Lett.* **2007**, *9*, 1809. (n) Park, I. S.; Kwon, M. S.; Kim, Y.; Lee, J. S.; Park, J. *Org. Lett.* **2008**, *10*, 497. (o) Özçubukçu, S.; Ozkal, E.; Jimeno, C.; Pericàs, M. A. *Org. Lett.* **2009**, *11*, 4680. (p) Liu, M.; Reiser, O. *Org. Lett.* **2011**, *13*, 1102. (q) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596.(r) Lipshutz,

B. H.; Taft, B. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 8235.(s) Yamada, Y. M. A.; Sarkar, S. M.; Uozumi, Y. *J. Am. Chem. Soc.* **2012**, *134*, 9285.

(6) (a) Shimada, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 6646. (b) Datta, S.; Chang, C.-L.; Yeh, K.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2003**, *125*, 9294.(c) Liu, Y.; Song, F.; Guo, S. *J. Am. Chem. Soc.* **2006**, *128*, 11332. (d) Wang, A.; Jiang, H. *J. Am. Chem. Soc.* **2008**, *130*, 5030. (e) Das, A.; Chaudhuri, R.; Liu, R.-S. *Chem. Commun.* **2009**, 4046. (f) Liu, H.; Feng, M.; Jiang, X. *Chem. Asian J.* **2014**, *9*, 3360.

(7) (a) Wang, T.; Jiao, N. *Acc. Chem. Res.* **2014**, *47*, 1137. (b) Furstner, A.; Davies, P. W. *Chem. Commun.* **2005**, 2307. (c) Villar, H.; Frings, M.; Bolm, C. *Chem. Soc. Rev.* **2007**, *36*, 55. (d) Deshmukh, P. H.; Blechert, S. *Dalton Trans.* **2007**, 2479. (e) Zhang, W.; Moore, J. S. *Adv. Synth. Catal.***2007**, *349*, 93. (f) Lozano-Vila, A. M.; Monsaert, S.; Bajek, A.; Verpoort, F. *Chem. Rev.***2010**, *110*, 4865. (g) Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 2794. (h) Astruc, D. *New J. Chem.***2005**, *29*, 42.

(8) (a) Shen, T.; Wang, T.; Qin, C.; Jiao, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 6677. (b) Qin, C.; Su, Y.; Shen, T.; Shi, X.; Jiao, N. *Angew. Chem., Int. Ed.***2016**, *55*, 350. (c) Chen, F.; Wang, T.; Jiao, N. *Chem. Rev.* **2014**, *114*, 8613.

(9) Bisseret, P.; Duret, G.; Blanchard, N. *Org. Chem. Front.* **2014**, *1*, 825.

(10) F. Fleming, F. *Nat. Prod. Rep.* **1999**, *16*, 597.

(11) Fleming, F. F.; Yao, L.; Ravikumar, P. C.; Funk, L.; Shook, B. C. *J. Med. Chem.* **2010**, *53*, 7902.

(12) An, M.; Sarker, A. K.; Jung, D.-C.; Hong, J.-D. *Bull. Korean Chem. Soc.* **2011**, *32*, 2083.

(13) Goujon, L. J.; Khaldi, A.; Maziz, A.; Plesse, C.; Nguyen, G. T. M.; Aubert, P.-H.; Vidal, F.; Chevrot, C.; Teyssié, D. *Macromolecules* **2011**, *44*, 9683.

(14) Cohen, D. T.; Buchwald, S. L. *Org. Lett.* **2015**, *17*, 202.

(15) (a) Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc.* **2015**, *137*, 11888. (b) Bera, M.; Maji, A.; Sahoo, S. K.; Maiti, D. *Angew. Chem., Int. Ed.* **2015**, *127*, 8635. (c) Bera, M.; Modak, A.; Patra, T.; Maji, A.; Maiti, D. *Org. Lett.***2014**, *16*, 5760.

(16) Okamoto, N.; Ishikura, M.; Yanada, R. *Org. Lett.* **2013**, *15*, 2571.

(17) Maji, A.; Hazra, A.; Maiti, D. *Org. Lett.* **2014**, *16*, 4524.

(18) Dutta, U.; Maity, S.; Kancherla, R.; Maiti, D. *Org. Lett.* **2014**, *16*, 6302.

(19) (a) Wille, U. *Chem. Rev.* **2013**, *113*, 813. (b) Hartung, J. *Chem. Rev.* **2009**, *109*, 4500. (c) Maity, S.; Manna, S.; Rana, S.; Naveen, T.; Mallick, A.; Maiti, D. *J. Am. Chem. Soc.* **2013**, *135*, 3355. (d) Maity, S.; Naveen, T.; Sharma, U.; Maiti, D. *Org. Lett.* **2013**, *15*, 3384. (e) Shu, Z.; Ye, Y.; Deng, Y.; Zhang, Y.; Wang, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 10573. (f) Manna, S.; Jana, S.; Saboo, T.; Maji, A.; Maiti, D. *Chem. Commun.* **2013**, *49*, 5286. (g) Naveen, T.; Maity, S.; Sharma, U.; Maiti, D. *J. Org. Chem.* **2013**, *78*, 5949. (h) Ji, Y.-f.; Yan, H.; Jiang, Q.-b. *Eur. J. Org. Chem.* **2015**, *2015*, 2051. (i) Yang, X.-H.; Ouyang, X.-H.; Wei, W.-T.; Song, R.-J.; Li, J.-H. *Adv. Synth. Catal.* **2015**, *357*, 1161. (j) Yan, H.; Mao, J.; Rong, G.; Liu, D.; Zheng, Y.; He, Y. *Green Chem.* **2015**, *17*, 2723.(k) Hao, X.-H.; Gao, P.; Song, X.-R.; Qiu, Y.-F.; Jin, D.-P.; Liu, X.-Y.; Liang, Y.-M. *Chem. Commun.***2015**, *51*, 6839. (l) Zhao, J.; Li, P.; Xia, C.; Li, F. *RSC Adv.* **2015**, *5*, 32835.

(20) (a) Sherwood, A. G.; Gunning, H. E. *J. Am. Chem. Soc.* **1963**, *85*, 3506. (b) Surzur, J. M.; Dupuy, C.; Bertrand, M. P.; Nouguier, R. *J. Org. Chem.***1972**, *37*, 2782.

(21) (a) A. Maji, A. Hazra, D. Maiti, *Org. Lett.* **2014**, *16*, 4524. (b) D. Gelman, S. L. Buchwald, *Angew. Chem., Int. Ed.* **2003**, *42*, 5993.

(22) R. Kumar, D. Verma, S. M. Mobin, I. N. N. Namboothiri, *Org. Lett.* **2012**, *14*, 4070.

(23) T. Shen, T. Wang, C. Qin, N. Jiao, *Angew. Chem., Int. Ed.* **2013**, *52*, 6677.

(24) M. Sundermeier, A. Zapf, M. Beller, *Angew. Chem., Int. Ed.* **2003**, *42*, 1661.

(25) J. Kim, J. Choi, K. Shin, S. Chang, *J. Am. Chem. Soc.* **2012**, *134*, 2528.

(26) K. Pati, C. Michas, D. Allenger, I. Piskun, P. S. Coutros, G. d. P. Gomes, I. V. Alabugin, *J. Org. Chem.* **2015**, *80*, 11706.

(27) K. Okamoto, N. Sakata, K. Ohe, *Org. Lett.* **2015**, *17*, 4670.

(28) Z. Shu, Y. Ye, Y. Deng, Y. Zhang, J. Wang, *Angew. Chem., Int. Ed.* **2013**, *52*, 10573.

(29) P. Anbarasan, H. Neumann, M. Beller, *Chem. Eur. J.* **2010**, *16*, 4725.

(30) X. Zong, Q.-Z. Zheng, N. Jiao, *Org. Biomol. Chem.* **2014**, *12*, 1198.

(31) S. Laulhé, S. S. Gori, M. H. Nantz, *J. Org. Chem.* **2012**, *77*, 9334.

(32) O. Grossman, D. Gelman, *Org. Lett.* **2006**, *8*, 1189.

(33) A. C. Babtie, M. F. Lima, A. J. Kirby, F. Hollfelder, *Org. Biomol. Chem.* **2012**, *10*, 8095.

(34) W. Fan, Y. Yang, J. Lei, Q. Jiang, W. Zhou, *J. Org. Chem.* **2015**, *80*, 8782.

(35) A. V. Ushkov, V. V. Grushin, *J. Am. Chem. Soc.* **2011**, *133*, 10999.

(36) G. Meng, M. Szostak, *Org. Lett.* **2015**, *17*, 4364.

(37) T. D. Senecal, W. Shu, S. L. Buchwald, *Angew. Chem., Int. Ed.* **2013**, *52*, 10035.

(38) Y. Zhu, L. Li, Z. Shen, *Chem. Eur. J.* **2015**, *21*, 13246.

(39) P. Y. Yeung, C. M. So, C. P. Lau, F. Y. Kwong, *Org. Lett.* **2011**, *13*, 648.

(40) S. Zhou, K. Junge, D. Addis, S. Das, M. Beller, *Org. Lett.* **2009**, *11*, 2461.

(41) D. T. Cohen, S. L. Buchwald, *Org. Lett.* **2015**, *17*, 202.

(42) H. C. Bertrand, M. Schaap, L. Baird, N. D. Georgakopoulos, A. Fowkes, C. Thiollier, H. Kachi, A. T. Dinkova-Kostova, G. Wells, *J. Med. Chem.* **2015**, *58*, 7186.

Chapter 4

The Regioselective Iodination of Quinolines, Quinolones, Pyridones, Pyridines and Uracil

Chapter 4

The Regioselective Iodination of Quinolines, Quinolones, Pyridones, Pyridines and Uracil

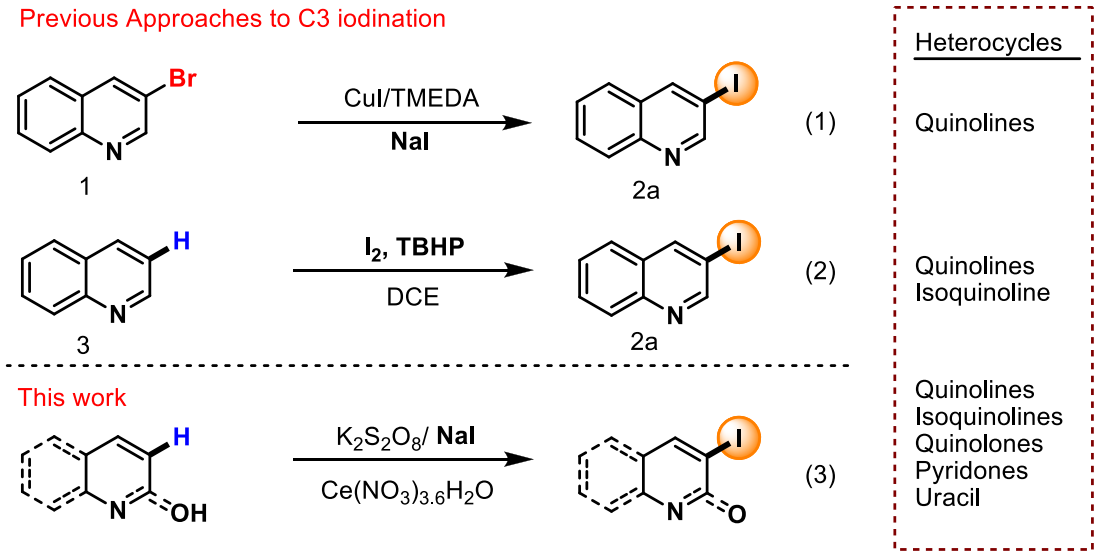
Abstract: A radical based direct C–H iodination protocol for quinolines, quinolones, pyridones, pyridines, and uracil has been developed. The iodination occurs in a C3 selective manner for quinolines and quinolones. Pyridones and pyrdines undergo C3 and C5 iodination, while dimethyl uracil undergoes C5 iodination. Scope of the method was demonstrated through the rapid synthesis of both electron rich as well as electron poor heteroaromatic iodides. The protocol was found to be scalable and general, while a mechanism has been proposed.

4.1. Introduction

Iodine containing compounds are integral to synthetic organic chemistry. Beyond applications in traditional synthetic methods such as metalation[1] and aromatic nucleophilic substitution,[2] they are now ubiquitous in cross-coupling chemistry.[3] Furthermore, radiolabeled iodide analogues play a vital role in medicinal and radiotherapeutic science.[4] As a consequence, extensive efforts have been made to develop useful protocols for preparing aryl iodides.[5-7] However, their synthesis remains difficult, with limitations relating to the use of expensive transition metals, need for highly polar solvents, prefunctionalization, and modest regioselectivity, plaguing many reported approaches.[8] On contrary to simple aryl iodide, the synthesis of heteroaromatic iodides is increasingly difficult.

Quinoline, pyridone and other nitrogen containing heterocyclic iodides are highly important structural motifs due to their presence in innumerable natural products and pharmaceutical agents.[9] In recent years, much efforts have been devoted towards the regioselective synthesis of iodinated heterocycles.[10-12] Aromatic Finkelstein reaction from bromides (i.e. 1) have developed as popular method for accessing iodo-quinolines (2) (eq. 1, Scheme 4.1).[13] Recently Li et al. have disclosed a photo induced metal free Finkelstein reaction to access C3 and C4 iodinated quinoline.[14] Unfortunately, such an approach demands prefunctionalization, and therefore limit generality. Direct regioselective functionalization of heterocycles arguably has the greatest potential to deliver broadly applicable iodination methods. However, selectivity with substrates bearing multiple C–H bonds makes this approach more challenging.

Scheme 4.1. C3 selective iodination by C–H functionalization

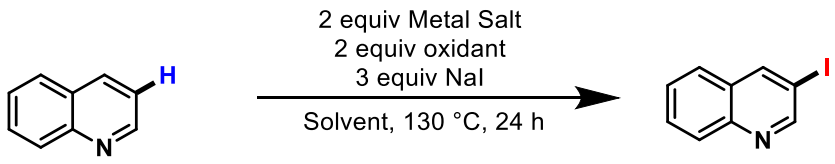


With pyridyl and quinoline, halogenation can be addressed by exploiting the N oxide thereby allowing selective C2 halogenation.[15] While in an orthogonal approach recently reported by Chang and co-workers C8 iodination was achievable by rhodium catalyzed C–H iodination of quinoline-N-oxide with NIS.[16] While selective C2 and C8 halogenation of quinolines can be achieved, mild regioselective methods for other iodinations remain limited. As part of broader studies on the functionalization of heterocycles[17] in 2013 we commenced studies focused on C3 selective halogenation of quinolines, and related heterocycles. We envisaged a direct radical iodination approach enabled by the mild generation of the iodo radical. It was postulated that such an approach should allow predictable C3 iodination due to the stability of the first formed radical intermediate. Very recently a related concept was communicated by Sun and Jain which allowed the iodination of different quinolone derivatives in a regioselective manner (3) (eq. 2, Scheme 4.1).[10f,g] Stimulated by this report we wish to report our approaches on this topic. While our conditions are related to those of Sun and Jain, we have been able to achieve mild iodination of both electron rich and poor quinolines, as well as pyridones, uracil and pyridines. Mechanistically we believe that in-situ generation of the iodo radical leads to selective C3 iodination, although with highly electron rich substrates alternate mechanistic pathways are possible.

4.2. Result and discussion

To achieve selective C3 iodination we commenced by reacting quinoline with $K_2S_2O_8$ and sodium iodide in the presence of $MnSO_4$ in dichloroethane (DCE) heated at 130 °C. Unfortunately, these conditions, and those in which the manganese was replaced by either tin or cobalt failed to provide 3-iodo-quinoline (**2a**) (Table 4.1, entries 1-3). In contrast the reaction in the presence of either bismuth, nickel or cerium salts gave promising yields of the expected product with $Ce(NO_3)_3.6H_2O$ optimal with 40% yield of **2a** (Table 4.1, entries 4-6). Addition of 1 equivalent of TFA increased the yield, while an examination of alternate oxidants confirmed that potasiumperoxodisulphate was ideal (Table 4.1, entry 7), although other common oxidants were also viable (Table 4.1, entries 8-11). Finally, increasing the stoichiometry of sodium iodide to three equivalents increased the yield further to 85% (Table 4.1, entry 12). Finally, control experiments demonstrated that each reagent is necessary for the formation of 3-iodoquinoline in synthetically useful yields (See the experimental details for more information).

Table 4.1. Selected optimization of iodination



3a **2a**

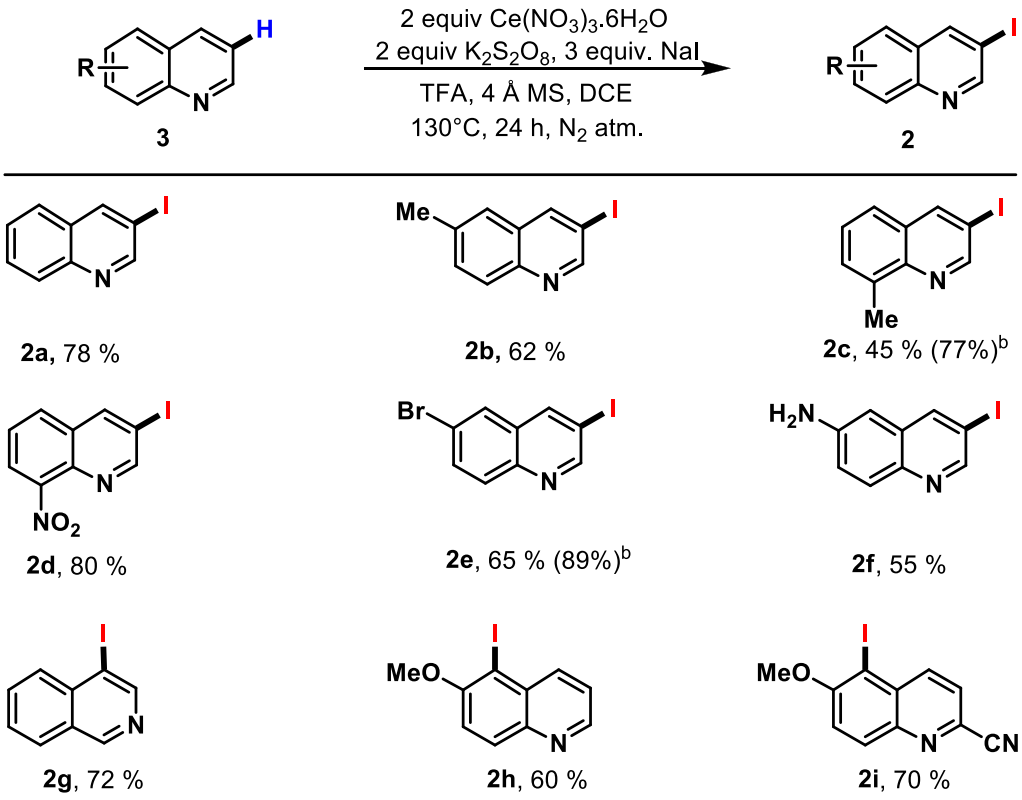
Entry	Metal salt	Oxidant	Solvent[a]	Yield[b]
1	$MnSO_4.H_2O$	$K_2S_2O_8$	DCE	-
2	$SnCl_2.2H_2O$	$K_2S_2O_8$	DCE	-
3	$CoCl_2.6H_2O$	$K_2S_2O_8$	DCE	1
4	$Bi(NO_3)_3.5H_2O$	$K_2S_2O_8$	DCE	30
5	$Ni(NO_3)_2$	$K_2S_2O_8$	DCE	37
6	$Ce(NO_3)_3.6H_2O$	$K_2S_2O_8$	DCE	40
7[c]	$Ce(NO_3)_3.6H_2O$	$K_2S_2O_8$	DCE	62
8[c]	$Ce(NO_3)_3.6H_2O$	TBHP	DCE	61
9[c]	$Ce(NO_3)_3.6H_2O$	$K_2S_2O_8$	1,2,3-TCP	45
10[c]	$Ce(NO_3)_3.6H_2O$	$K_2S_2O_8$	^tBuOH	20
11[c]	$Ce(NO_3)_3.6H_2O$	DTBP	DCE	59
12[c,d]	**$Ce(NO_3)_3.6H_2O$**	**$K_2S_2O_8$**	**DCE**	**85(78)[e]**

[a]All reactions performed at 130 °C. [b]GC yield except as noted. [c]1 equiv TFA added. [d]3 equivNaI. [e]Isolated yield.

With the optimized reaction condition, the generality of the regioselective iodination was examined with the halogenation of various quinoline derivatives (Table 4.2). In contrast to the studies of Sun and Li who reported solely the iodination of electron poor substrates our conditions allowed 6-methyl (**2b**, 62%) and 8-methyl (**2c**, 45%), as well as electron deficient 8-NO_2 (**2d**, 80%) iodoquinolines to be prepared in acceptable isolated yields after column chromatography. Similarly 6-bromoquinoline and electron rich 6-amino quinoline gave C3 iodinated **2e** and **2f** in 65% and 55% yields respectively. Isoquinoline gave C4-iodinated product **2g** in 72% yield, as reported by Sun and Li. When the 6-methoxy quinolineswere examined the selectivity switches to C5-iodinated products (**2h**, 60% and **2i**, 70%).

Next, we thought to examine the related iodination of N-benzyl quinolones (i.e. **4a**) under the optimized reaction condition (Table 4.3). To our delight, we obtained the C3 iodinated N-benzyl quinolone derivative **5a** in 65% yield.

Table 4.2. Scope of iodination for various quinolines[a]

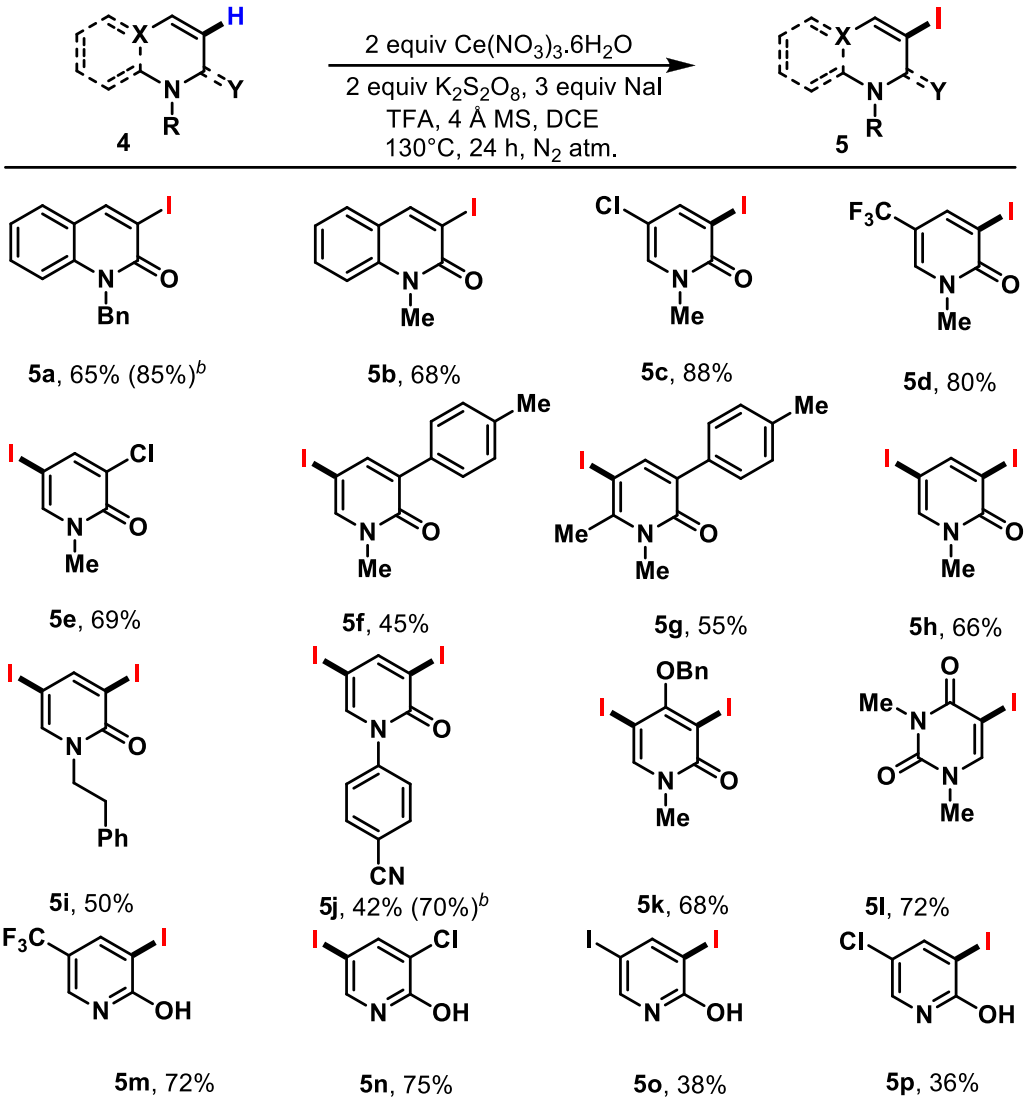


[a]Isolated yield. [b]Yield based on recovered starting material.

Similar results were obtained in the preparation of the *N*-methyl quinolone **5b**, while C5 blocked (Cl, **4c** or CF_3, **4d**) iodinated pyridones (**5c** and **5d**) were also prepared in excellent yield. When C3 blocked pyrdiones were subjected to the reaction condition (Cl, **4e**; *p*-tolyl, **4f**) the C5 iodinated products formed smoothly. The reaction was insensitive to steric congestion with the C5 iodinated C6-methyl-C3-*p*-tolyl pyridone prepared in 55% yield.

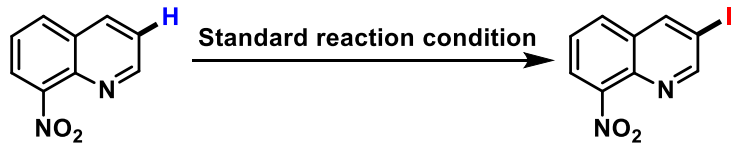
With *N*-phenylethyl, *N*-methyl or *N*-aryl pyridones bearing no additional substituents the diiodinated pyridones **5h**, **5i** and **5j** were prepared in 66, 50 and 42% yields respectively. The electron deficient pyridine **4j** was diiodinated to give **5j** smoothly, while dimethyl uracil (**4k**) provided the product of monoiodination. Finally a series of 2-hydroxy iodopyridines **5m**-**5p** bearing either C3 or C5 substituents were smoothly formed in acceptable yields.

Table 4.3. Scope of the iodination of pyridones, quinolones, uracil and pyridines[a]



[a]Isolated yield.bYield based on recovered starting material.

Scheme 4.2. Scaled up iodination of 8-nitro quinoline

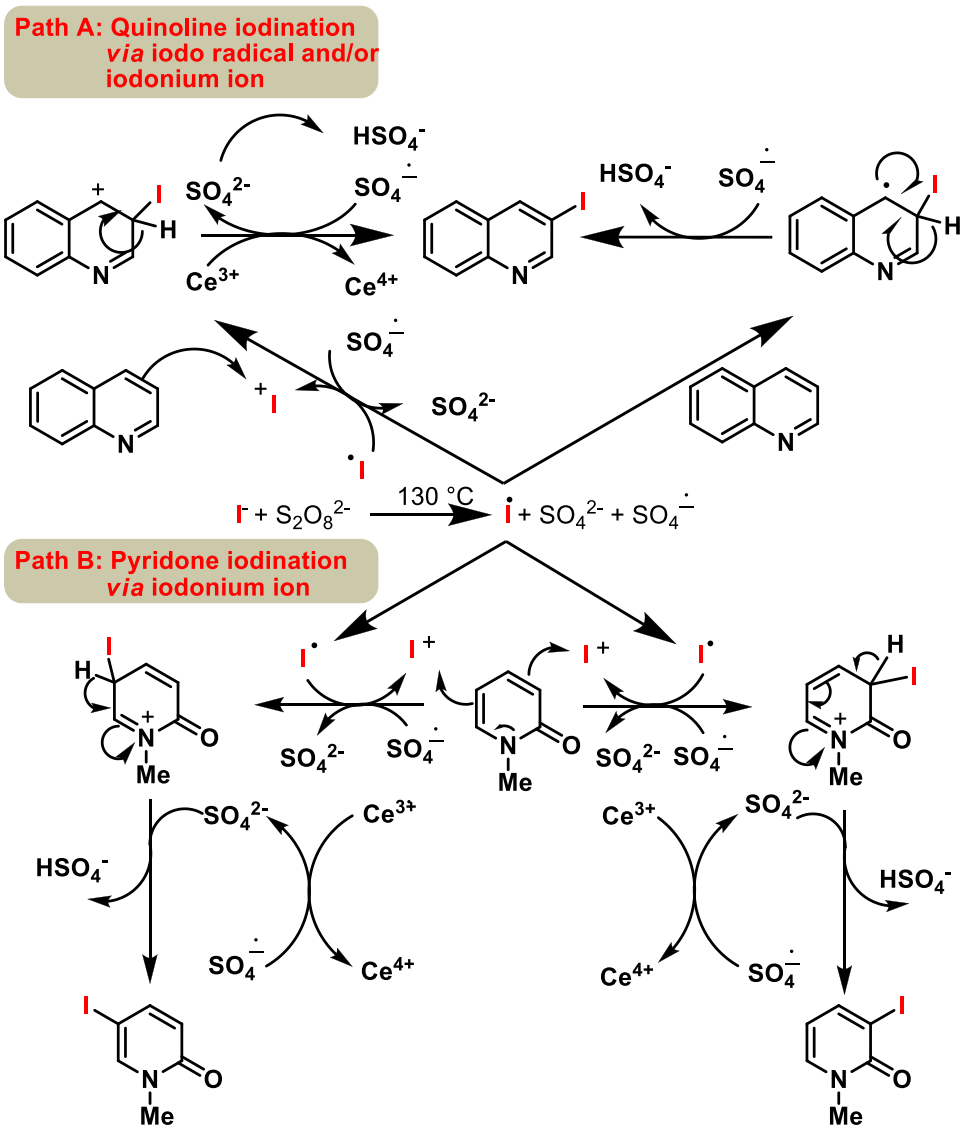


To assess the scalability of the protocol conversion of 8-NO_2quinoline to 3-iodo-8-nitro quinoline (**2d**) was performed with 1.3 g of substrate. The expected iodide **2d** was obtained in 77% yield, only slightly lower than the yield achieved with the submilimolar scale reaction (Scheme 4.2).

In order to gain insight into the reaction mechanism, a number of control experiments were performed. When a radical quencher (*e.g.* TEMPO) was introduced this suppressed the

iodination reaction with only a trace of the iodinated product of quinoline **2a**. Based on this observation, it may be assumed that one of the steps for iodination is proceeding *via* a radical pathway.

Scheme 4.3. Plausible mechanism



Previous studies with pyridone demonstrated selective functionalization at C3 position via a radical based transformation.[18] The observed C5-functionalized products, as in 6-methoxy quinoline **2h**, likely forms by electrophilic iodination. Therefore, the present protocol can promote iodination reaction both by a radical or electrophilic path. By considering the C3 and C5 selectivity for quinoline and pyridone, a mechanism is proposed in Scheme 4.3.

4.3.Experimental details

4.3.1. General considerations

2.3.1.a. Reagent Information: All solvents were bought from Merck/Aldrich in sure-seal bottle and were used as received. For column chromatography, silica gel (60–120 mesh or 100–200 mesh) obtained from SRL Co.. A gradient elution using pet ether and ethyl acetate was performed, based on Merck aluminum TLC sheets (silica gel 60F254).

4.3.1.b. Analytical Information: All isolated compounds were characterized by ^{1}H, ^{13}C NMR spectroscopy, gas chromatography mass spectra (GC-MS) and HRMS (ESI). Nuclear Magnetic Resonance spectra were recorded on a Bruker 400 MHz or 500 MHz instrument. Unless mentioned, all ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform-d (7.26 ppm) in the deuterated solvent and all ^{13}C NMR spectra were reported in ppm relative to chloroform-d ($CDCl_3$) (77.23 ppm). All GC analyses were performed on an Agilent 7890A GC system with an FID detector using a J & W DB-1 column (10 m, 0.1 mm I.D.) using *n*-decane as the internal standard. GCMS analysis was done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

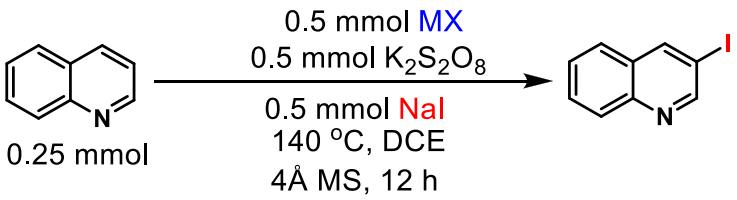
4.3.1.c. Description of Reaction Tube:

Fig.1. Pictorial description of reaction tube for oxidative α-trifluoromethylation: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E) [right]; Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A) [right].

4.3.2. Experimental Section

4.3.2. Optimization of Reaction Condition

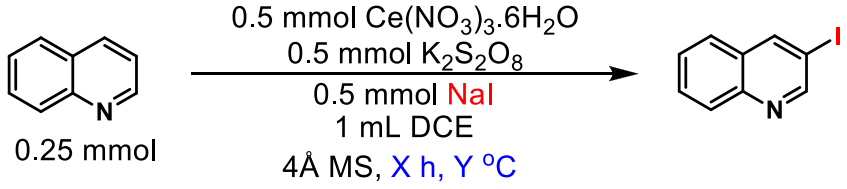
4.3.2.a. Variation of Metal Sources -As found from the control experiment use of metal is obvious to achieve the desire product. We started screening different metal salts.



Entry	Metal Sources	GC Yield (%)
1	$Bi(NO_3)_3.5H_2O$	30
1	$Ni(NO_3)_2$	35
2	CuBr	5
3	**$Ce(NO_3)_3.6H_2O$**	**40**
4	$CoCl_2.6H_2O$	1
5	$NiSO_4$	-
6	$SnCl_2.2H_2O$	-
7	$MnSO_4.H_2O$	-
8[a]	$Ni(NO_3)_2$	37
9[b]	$Pd(Oac)_2$	6

[a]1 mmol NH_4I ; [b] 20 mol%

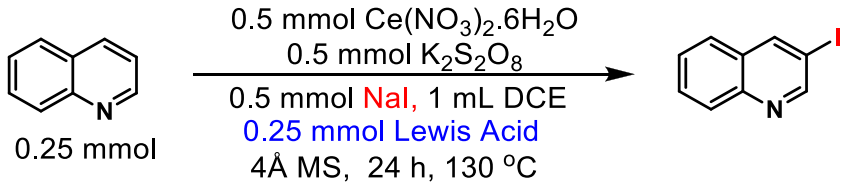
4.3.2.b. Variation of Temperatureand Time: From metal salt screening it has been found that $Ce(NO_3)_3.6H_2O$ is the best metal salt for the conversion. Later on we optimized the temperature and time simultaneously along with the $Ce(NO_3)_3.6H_2O$ as the metal salt. The optimized data is tabulated below.



Entry	Temperature	Time	GC Yield (%)
1	110 °C	16 h	2
2	120 °C	16 h	6
3	130 °C	12 h	48
4	130 °C	16 h	50
5	**130 °C**	**24 h**	**55**
6	140 °C	24 h	56

Following the result further optimization was carried out at 130 °C for 24 hour.

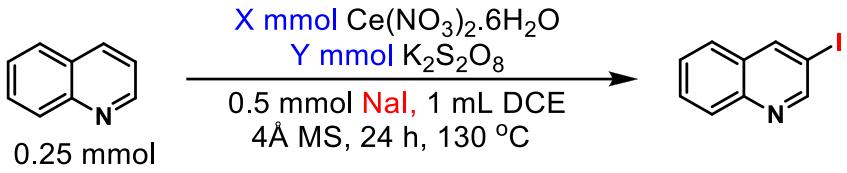
4.3.2.c. Variation of Lewis Acids: a series of Lewis acids was then varied and tried to figure out whether Lewis acid has any effect on the reaction. The optimized results are shown in the following table.



Entry	Lewis Acids	GC Yield (%)
1	-	55
2	**TFA**	**62**
3	$AlMe_3$	54
4	PTSA	35
5	$BF_3.OEt_2$	13
6	$FeCl_3.6H_2O$	20
7	$B(O^iPr)_3$	1
8[a]	-	5

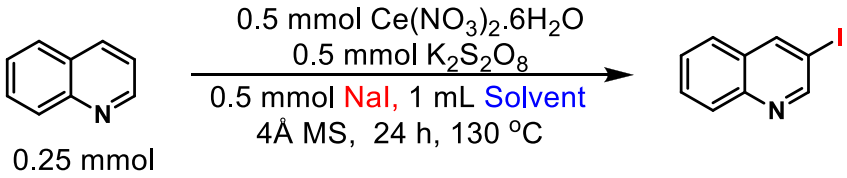
[a]I_2 in place of NaI

4.3.2.d. Variation of Amount of $Ce(NO_3)_2.6H_2O$ & $K_2S_2O_8$: So, TFA, $AlMe_3$ or PTSA can enhance the reaction. Further screening was made on the equivalent ration of metal salt and amount of oxidizing agent, i.e. $K_2S_2O_8$. Optimization data tabulated below.



Entry	$Ce(NO_3)_2.6H_2O$(mmol)	$K_2S_2O_8$(mmol)	GC Yield (%)
1	0.25	-	9
2	0.50	-	22
3	0.75	-	26
4	1.00	-	28
5	0.25	0.50	26
6	**0.50**	**0.50**	**62**
7	0.75	0.50	61
8	1.00	0.50	55
9	1.00	1.00	36

From the above result it is clear that 0.50 mmol$Ce(NO_3)_3.6H_2O$ and 0.50 mmol $K_2S_2O_8$ is proper ratio to get a good conversion for 0.25 mmol of substrate.

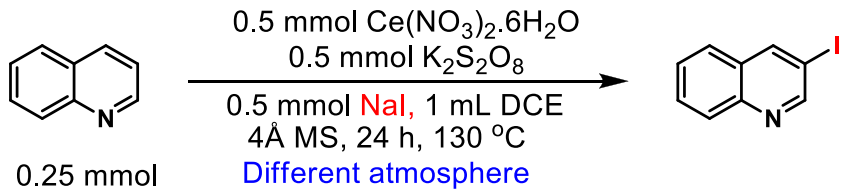


4.3.2.e. Variation of Solvents -we then tried to find the best solvent required for the maximum conversion. A series of solvent has been used for the solvent screening. The optimized condition is shown below.

Entry	Solvent	GC Yield (%)
1	Cyclohexane	2
2	Toluene	0
3	DMF	0
4	Decalin	0
5	Trifluorotoluene	-
6	**DCE**	**62**

So, DCE is the best solvent for the reaction.

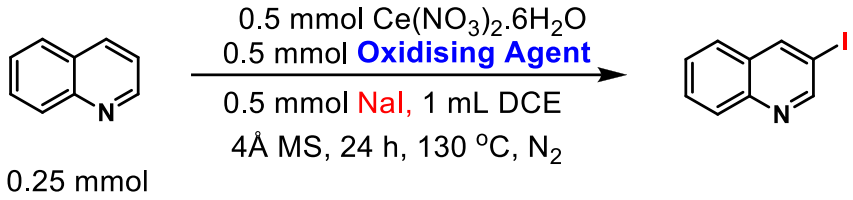
4.3.2.f. Reaction atmosphere variation -After that we put the reaction in N_2, O_2 and air. The optimization data is shown below.



Entry	Atmosphere	GC Yield (%)
1	**N_2**	**75**
2	O_2	74
3	Air	65

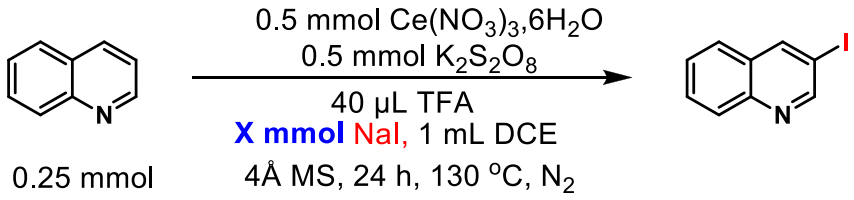
So, maintaining N_2 atmosphere enhances the reaction. So further studies have been carried out in N_2 atm.

4.3.2.g. Variation of different oxidising source -Different oxidizing agent was then screened to know the best oxidizing agent for the iodination. The optimized data is given below.



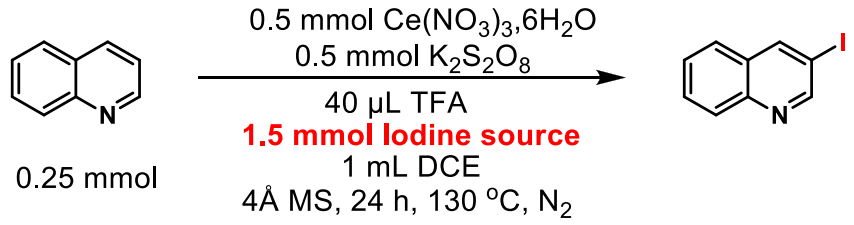
Entry	Oxidising agent	GC Yield(%)
1	**$K_2S_2O_8$**	**75**
2	$(NH_4)_2S_2O_8$	34
3	TEMPO	4
4	Para benzoquinone	0

4.3.2.h. Variation of NaI amount - Amount of Sodium iodide is varied to achieve the improve reaction condition.



Entry	Amount of $Ce(NO_3)_3$ (mmol)	Amount of $K_2S_2O_8$ (mmol)	Amount of NaI (mmol)	GC Yield (%)
1	0.5	0.5	0.25	40
2	0.5	0.5	0.5	75
3	**0.5**	**0.5**	**0.75**	**86**
4	0.5	0.5	1.0	82

4.3.2.i. Variation of iodine source- Different iodine sources has been varied and it is found that sodium iodide is most effective iodinating reagent for this transformation.



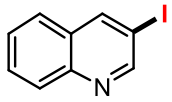
Entry	Iodine Source	GC Yield(%)
1	**NaI**	**85**
2	KI	68
3	NIS	20
4	Molecular iodine	40
5	TBAI	0

2.3.3. <u>General Procedure</u> for Iodination of Quinolines, Pyridones, Pyridines and Uracil

In a clean, oven–dried screw cap reaction tube, with previously placed magnetic stir–bar heterocycle (0.5 mmol) (for solid compounds); NaI (3.0equiv, 1.5 mmol, 224.8 mg); Cerus nitrate hexahydrate ($Ce(NO_3)_3.6H_2O$) (2.0 equiv, 1.0 mmol 434mg); Potassium perdisulphate

($K_2S_2O_8$) (2.0 equiv, 1.0 mmol270 mg); molecular shieves4 Å (150 mg) andTrifluoroacetic acid (80 μL) were taken. The reaction tube was tightly sealed and allowed for vacuum by high vacuum pump and nitrogen gas was passed using Schlenk line. Thus making the reaction tube completely N_2 atmosphere, solvent DCE (2 mL) was added by syringe (for liquid starting material substrate was added by micro syringe). The tube was placed in a preheated oil bath at 130 ˚C. The reaction mixture was vigorously stirred for 24h. Upon completion of the reaction the reaction mixture was cooled to room temperature, and dried, then the residue was diluted with ethyl acetate (3x10 mL) and transferred to separating funnel. Ethyl acetate (10 mL) and water (15 mL) were added to the filtrate. The combined organic extract was dried over Na_2SO_4 and solvent evaporated on a rotary evaporator. The mixture was purified by column chromatography over silica gel (60-120/100-200 mesh size) and petroleum ether/ethyl acetate.

2.3.4. Characterization Data

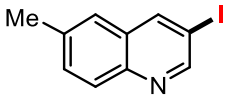


3-iodoquinoline (Table 2, Entry 2a):[19,20] Iodinated product was obtained following the general procedureon a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (99:1 v/v). Colorless solid compound obtained. Yield 78% (99 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.03 (d, *J* = 2.1 Hz, 1H), 8.54 (dd, *J* = 2.1, 0.8 Hz, 1H), 8.06 (dq, *J* = 8.5, 1.0 Hz, 1H), 7.76 – 7.68 (m, 2H), 7.56 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 90.0, 127.0, 127.6, 129.7, 130.2, 137.3, 143.9, 146.5, 155.8.

HRMS (ESI): $[M + H]^+$ calculated for C_9H_7IN is 255.9623, found: 255.9625.



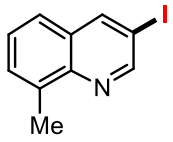
3-iodo-6-methylquinoline (Table 4.2, Entry 2b):[19,20] Iodinated product was obtained following the general procedure on a 0.5 mmol (71.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel

column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). Colorless crystalline solid compound. Yield 62% (83 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 8.47 – 8.42 (m, 1H), 7.97 (t, *J* = 6.2 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.47 – 7.41 (m, 1H), 2.53 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 21.9, 89.7, 125.8, 128.9, 130.2, 132.9, 138.0, 143.8, 144.5, 154.5.

HRMS (ESI): $[M + H]^+$ calculated for $C_{10}H_9IN$ is 269.9780, found: 269.9791.

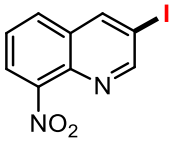


3-iodo-8-methylquinoline (Table 4.2, Entry 2c):[19] Iodinated product was obtained following the general procedure on a 0.5 mmol (71.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (97:3 v/v). Brownish solid compound. Yield 45% (61 mg).

^{1}H NMR (400 MHz; Chloroform-*d*): δ = 2.79 (s, 3H), 7.45 (d, J = 7.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 2H), 8.51 (d, J = 2.0 Hz, 1H), 9.06 (d, J = 2.0 Hz, 1H).

^{13}C NMR (100 MHz; Chloroform-*d*): δ = 17.8, 89.9, 124.9, 127.3, 130.0, 130.2, 137.5, 143.8, 145.5, 154.4.

HRMS (ESI): $[M + H]^+$ calculated for $C_{10}H_9IN$ is 269.9780, found: 269.9773.

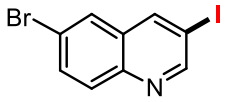


3-iodo-8-nitroquinoline (Table 4.2, Entry 2d):[20] Iodinated product was obtained following the general procedure on a 0.5 mmol (87 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). Yellow solid. Yield 80% (120 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.17 (d, *J* = 2.1 Hz, 1H), 8.65 (d, *J* = 2.1 Hz, 1H), 8.06 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.93 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.64 (dd, *J* = 8.3, 7.5 Hz, 1H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 92.3, 124.4, 126.6, 130.6, 131.2, 137.9, 143.9, 148.5, 158.1.

HRMS (ESI): $[M + H]^+$ calculated for $C_9H_6IN_2O_2$ is 300.9474, found: 300.9454.

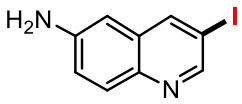


6-bromo-3-iodoquinoline (Table 4.2, Entry 2e):[19,20] iodinated product was obtained following the general procedure on a 0.5 mmol (104 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (98:2 v/v). Colorless solid.
Yield 65% (108 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.06 – 9.00 (d, *J* = 2.1 Hz, 1H), 8.47 – 8.41 (dd, *J* = 2.2, 0.8 Hz, 1H), 7.96 – 7.90 (d, *J* = 9.0 Hz, 1H), 7.89 – 7.84 (d, *J* = 2.1 Hz, 1H), 7.82 – 7.74 (dd, *J* = 9.0, 2.2 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 91.15, 121.61, 128.96, 130.97, 131.38, 133.77, 142.87, 145.04, 156.16.

HRMS (ESI): $[M + H]^+$ calculated for C_9H_6BrIN is 333.8723, found: 333.8725.

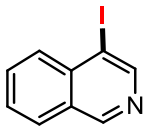


5-iodoquinolin-6-amine (Table 4.2, Entry 2f):[20] Iodinated product was obtained following the general procedure on a 0.5 mmol (72 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (96:4 v/v) Brownish solid compound. Yield 55% (74 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.61 (dd, *J* = 4.1, 1.4 Hz, 1H), 8.22 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H), 7.37 (dd, *J* = 8.5, 4.2 Hz, 1H), 7.22 (d, *J* = 8.9 Hz, 1H), 4.58 (s, 2H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 81.1, 120.3, 123.0, 131.0, 131.5, 138.2, 143.9, 146.2, 147.1.

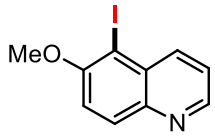
HRMS (ESI): $[M + H]^+$ calculated for $C_9H_8IN_2$ is 270.9732, found: 269.9748.



4-iodoisoquinoline (Table 4.2, Entry 2g):[19,20] iodinated product was obtained following the general procedure on a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). Colorless solid was obtained. Yield 72% (92 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.22 (s, 1H), 8.93 (s, 1H), 8.06 – 8.02 (m, 1H), 7.96 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.86 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.72 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.55, 148.84, 137.88, 133.27, 131.06, 129.45, 129.16, 128.89, 97.20.

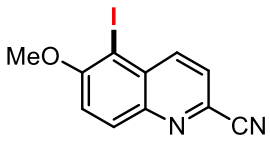


5-iodo-6-methoxyquinoline (Table 4.2, Entry 2h): iodinated product was obtained following the general procedure on a 0.5 mmol (79.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (90:10 v/v). Yellowish Solid. Yield 60% (85 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.04 – 8.98 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.90 – 8.85 (m, 1H), 8.51 – 8.46 (m, 1H), 7.80 – 7.73 (dd, *J* = 8.7, 4.7 Hz, 1H), 7.63 – 7.58 (d, *J* = 9.3 Hz, 1H), 4.14 – 4.09 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 57.72, 86.45, 118.73, 123.01, 126.65, 132.13, 138.38, 144.45, 145.51, 158.85.

Melting point: 112-114 °C.



5-iodo-6-methoxyquinoline-2-carbonitrile (Table 4.2, Entry 2i): iodinated product was obtained following the general procedure on a 0.5 mmol (92 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica

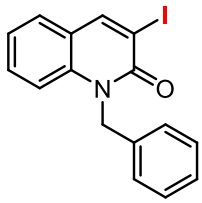
gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Colorless solid was obtained. Yield 70% (109 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.58 – 8.52 (dd, *J* = 8.8, 0.8 Hz, 1H), 8.19 – 8.13 (dd, *J* = 9.4, 0.8 Hz, 1H), 7.71 – 7.66 (d, *J* = 8.7 Hz, 1H), 7.56 – 7.52 (d, *J* = 9.3 Hz, 1H), 4.21 – 3.92 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 57.54, 85.76, 117.44, 118.30, 125.14, 132.04, 132.22, 132.42, 140.91, 144.71, 159.10. Calculated mass 310.9681 (Molecular formula – $C_{11}H_8IN_2O$), Observed mass 310.9673.

HRMS (ESI): $[M + H]^+$ calculated for $C_{11}H_8IN_2O$ is 310.9681, found: 310.9673.

Melting point: above 200 °C.

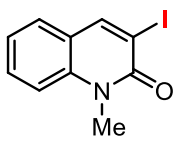


1-benzyl-3-iodoquinolin-2(1*H*)-one (Table 4.3, Entry 5a): iodinated product was obtained following the general procedure on a 0.5 mmol (117.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (90:10 v/v). Colorless solid was obtained. Yield 65% (117 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 2.0 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.34 – 7.21 (m, 3H), 7.21 – 7.16 (m, 2H), 7.00 (d, *J* = 8.9 Hz, 1H), 6.80 (d, *J* = 9.5 Hz, 1H), 5.51 (s, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.23, 139.19, 139.15, 138.42, 137.27, 136.05, 129.09, 127.65, 126.69, 123.14, 122.92, 117.22, 85.32, 46.13.

Melting point: 162-164 °C.



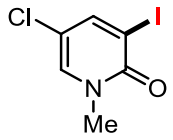
3-iodo-1-methylquinolin-2(1*H*)-one (Table 4.3, Entry 5b): iodinated product was obtained following the general procedure on a 0.5 mmol (79.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Colorless solid was obtained. Yield 68% (97 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.88 – 7.86 (d, *J* = 2.0 Hz, 1H), 7.83 – 7.79 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.59 – 7.55 (d, *J* = 9.5 Hz, 1H), 7.15 – 7.09 (d, *J* = 8.9 Hz, 1H), 6.74 – 6.70 (d, *J* = 9.5 Hz, 1H), 3.80 – 3.60 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 29.74, 85.27, 116.37, 122.87, 137.21, 137.96, 139.21, 139.70, 162.19.

HRMS (ESI): $[M + H]^+$ calculated for $C_{10}H_9INO$ is 285.9723, found: 285.9723.

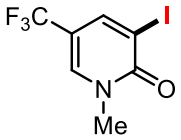
Melting point: 132-134 °C.



5-chloro-3-iodo-1-methylpyridin-2(1*H*)-one (Table 4.3, Entry 5c): iodinated product was obtained following the general procedure on a 0.25 mmol (35.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v) yellowish crystalline solid compound. Yield 88% (59 mg)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 2.4 Hz, 1H), 7.73 (dq, *J* = 2.5, 1.2 Hz, 1H), 3.64 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 40.0, 93.0, 110.7, 138.3, 144.1, 159.9.



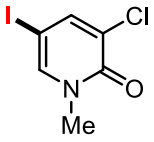
3-iodo-1-methyl-5-(trifluoromethyl)pyridin-2(1*H*)-one (Table 4.3, Entry 5d): Iodinated product was obtained following the general procedure on a 0.5 mmol (88.5 mg) scale reaction.

The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v) Colorless crystalline solid was obtained. Yield 80% (121 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (d, *J* = 2.5 Hz, 1H), 7.75 (dq, *J* = 2.5, 1.2 Hz, 1H), 3.62 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 40.0, 92.8, 110.7 (q, *J*= 35.6 Hz), 122.37 (q, *J*= 271.3 Hz), 138.4, 144.1, 159.8.

HRMS (ESI): $[M + H]^+$ calculated for $C_7H_6INOF_3$ is 303.9446, found: 303.9443.

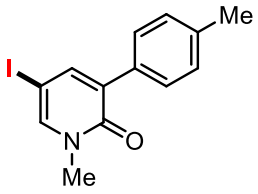


3-chloro-5-iodo-1-methylpyridin-2(1*H*)-one (Table 4.3, Entry 5e): iodinated product was obtained following the general procedure on a 0.25 mmol (71.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v) sluggish Colorless solid compound was obtained. Yield 69% (93 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 2.2 Hz, 1H), 7.48 (d, *J* = 2.4 Hz, 1H), 3.55 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 38.6, 61.7, 127.4, 142.0, 144.5, 158.1.

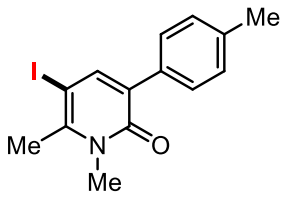
HRMS (ESI): $[M + H]^+$ calculated for C_6H_6INOCl is 269.9183, found: 269.9170.



5-iodo-1-methyl-3-p-tolylpyridin-2(1*H*)-one (Table 4.3, Entry 5f): iodinated product was obtained following the general procedure on a 0.25 mmol (50 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (93:17 v/v). Colorless solid compound was obtained. Yield 60% (49 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.68 – 8.55 (d, *J* = 3.1 Hz, 1H), 8.28 – 8.14 (d, *J* = 3.0 Hz, 1H), 7.67 – 7.49 (m, 2H), 7.35 – 7.14 (d, *J* = 7.9 Hz, 2H), 3.75 – 3.63 (s, 3H), 2.43 – 2.33 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 21.48, 39.57, 128.57, 129.31, 130.05, 130.58, 130.65, 131.91,138.37, 139.21, 161.48.

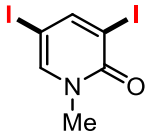


5-iodo-1,6-dimethyl-3-p-tolylpyridin-2(1*H*)-one (Table 4.3, Entry 5g): iodinated product was obtained following the general procedure on a 0.25 mmol (53 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Colorless solid compound was obtained. Yield 55% (47 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 – 8.14 (s, 1H), 7.60 – 7.56 (m, 2H), 7.26 – 7.21 (d, *J* = 8.0 Hz, 2H), 3.82 – 3.60 (s, 3H), 2.99 – 2.75 (s, 3H), 2.50 – 2.26 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 18.54, 21.49, 33.13, 100.19, 127.99, 128.61, 129.31, 131.80, 132.26, 138.84, 148.02, 161.66.

Melting point: 130-131 °C.

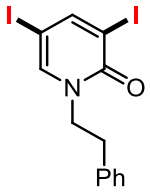


3,5-diiodo-1-methylpyridin-2(1*H*)-one (Table 4.3, Entry 5h): Iodinated product was obtained following the general procedure on a scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (88:12 v/v) Black solid compound. Yield 66% (118 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.07 (d, *J* = 2.3 Hz, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 3.57 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 39.4, 63.7, 94.3, 143.8, 154.9, 159.2.

HRMS (ESI): $[M + H]^+$ calculated for $C_6H_6I_2NO$ is 361.8539, found: 361.8539.

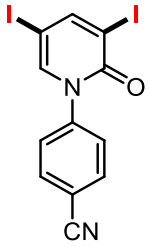


3,5-diiodo-1-phenethylpyridin-2(1*H*)-one (Table 4.3, Entry 5i): iodinated product was obtained following the general procedure on a 0.5 mmol (99.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (95:5 v/v). Brownish solid. Yield 50% (112 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 – 8.03 (d, *J* = 2.3 Hz, 1H), 7.33 – 7.24 (m, 3H), 7.16 – 7.14 (d, *J* = 1.7 Hz, 1H), 7.14 – 7.10 (dd, *J* = 4.0, 1.7 Hz, 2H), 4.15 – 4.09 (m, 2H), 3.05 – 2.99 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 35.12, 54.05, 63.46, 94.51, 127.26, 129.02, 129.11, 137.37, 143.41, 154.83, 158.56.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{13}H_{11}I_2NNaO$ is 473.8822, found: 473.8822.

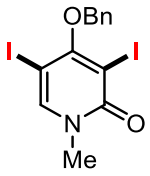


4-(3,5-diiodo-2-oxopyridin-1(2*H*)-yl)benzonitrile(Table 4.3, Entry 5j): iodinated product was obtained following the general procedure on a 0.5 mmol (98 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (98:2 v/v). Yellow Solid. Yield 42% (93 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.22 – 8.16 (d, *J* = 2.3 Hz, 1H), 7.84 – 7.77 (m, 2H), 7.58 – 7.48 (m, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 29.90, 65.31, 95.64, 113.41, 117.80, 127.56, 133.57, 141.87, 143.67, 155.71.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{12}H_6I_2N_2NaO$ is 470.8462, found: 473.8822.



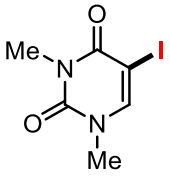
4-(benzyloxy)-3,5-diiodo-1-methylpyridin-2(1*H*)-one (Table 4.3, Entry 5k): iodinated product was obtained following the general procedureon a 0.5 mmol (107.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v). Yellow Solid. Yield 68% (158 mg).

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 – 7.66 (s, 1H), 7.65 – 7.60 (m, 2H), 7.46 – 7.36 (m, 3H), 5.09 – 5.03 (s, 2H), 3.62 – 3.58 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*) δ 38.82, 64.88, 74.64, 86.55, 128.74, 128.95, 128.96, 135.41, 144.13, 161.63, 167.00.

HRMS (ESI): $[M + Na]^+$ calculated for $C_{13}H_{11}I_2NNaO_2$ is 489.8771, found: 489.8774.

Melting point: 1549-151 °C.



5-iodo-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione(Table 4.3, Entry 5l): iodinated product was obtained following the general procedureon a 0.5 mmol (70 mg) scale reaction. The

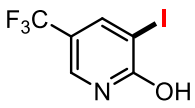
reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v) Brownish solid compound. Yield 72% (97 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (s, 1H), 3.42 (s, *J* = 3.0 Hz, 6H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 29.7, 37.4, 67.3, 147.6, 160.6.

HRMS (ESI): $[M + H]^+$ calculated for $C_6H_8IN_2O_2$ is 266.9631, found: 266.9644.

Melting point: above 200 °C.



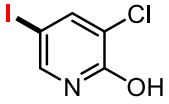
3-iodo-5-(trifluoromethyl)pyridin-2-ol (Table 4.3, Entry 5m): iodinated product was obtained following the general procedureon a 0.5 mmol (81.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (80:20 v/v) Colorless solid compound was obtained. Yield 72% (104 mg).

^{1}H NMR (400 MHz, Methanol-d_4) δ 8.31 – 8.18 (m, 1H), 7.93 – 7.81 (m, 1H).

^{13}C NMR (101 MHz, Methanol-d_4) δ 162.37, 146.97, 136.58, 124.15 (q, *J*= 270.54 Hz), 112.54(q, *J*= 35.2 Hz), 93.52.

HRMS (ESI): $[M + H]^+$ calculated for C_6H_4INO is 289.9290, found: 289.9288.

Melting point: 182-183 °C.



3-chloro-5-iodopyridin-2-ol (Table 4.3, Entry 5n): iodinated product was obtained following the general procedureon a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-

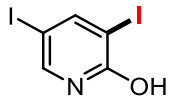
200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Colorless solid compound was obtained. Yield 75% (96 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.64 – 8.55 (d, *J* = 2.8 Hz, 1H), 8.47 – 8.41 (d, *J* = 2.8 Hz, 1H).

^{13}C NMR (126 MHz, Methanol-d_4) δ 126.60, 132.35, 133.95, 136.71, 160.84.

HRMS (ESI): $[M + H]^+$ calculated for C_5H_3ClINO is 255.8940, found: 255.8955.

Melting point: More than 200 °C.



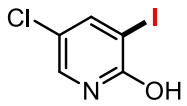
3,5-diiodopyridin-2-ol (Table 4.3, Entry 5o): iodinated product was obtained following the general procedureon a 0.5 mmol (110 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (85:15 v/v). Yellow Solid.Yield 38% (66 mg).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.79 – 8.70 (dd, *J* = 3.0, 1.2 Hz, 1H), 8.56 – 8.46 (dd, *J* = 2.8, 1.2 Hz, 1H).

^{13}C NMR (126 MHz, Methanol-d_4) δ 91.54, 133.15, 138.28, 144.53, 162.19.

HRMS (ESI): $[M + H]^+$ calculated for $C_5H_3I_2NO$ is 347.8370, found: 347.833.

Melting point: above 200 °C.



5-chloro-3-iodopyridin-2-ol (Table 4.3, Entry 5p): iodinated product was obtained following the general procedureon a 0.5 mmol (64.5 mg) scale reaction. The reaction was continued for 24 h. Pure product was isolated by column chromatography through a silica gel column (100-200 mesh). Eluent: pet ether: ethyl acetate (83:17 v/v). Yellow Solid. Yield 36% (46 mg).

^{1}H NMR (400 MHz, DMSO-d_6) δ 13.23 (s, 1H), 8.52 (d, *J* = 2.9 Hz, 1H), 8.16 (d, *J* = 2.9 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 153.28, 141.93, 139.45, 137.87, 109.00.

HRMS (ESI): $[M + H]^+$ calculated for C_5H_3ClINO is 255.8940, found: 255.8924.

Melting point: above 200 °C.

4.4. Conclusion

In conclusion, a variety of heterocyles can be iodinated in a predictable and selective manner using simple reaction conditions. This method is operationally simple and scalable. Due to high demand of heterocyclic iodides, this protocol is expected to find application in industry and academia.

4.5. References

(1) (a) Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 4302. (b) Tilly, D.; Chevallier, F.; Mongin, F.; Gros, P. C. *Chem. Rev.* **2014**, *114*, 1207.

(2) (a) Bunnett, J. F.; Zahler, R. *Chem. Rev.* **1951**, *49*, 273. (b) Hartwig, J. F. *Synlett* **2006**, *9*, 1283. (c) Crampton, M. R. *Organic Reaction Mechanisms*; Wiley: New York, **2003**, 275.

(3) (a) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (b) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450. (c) Popov, I.; Lindeman, S.; Daugulis, O. *J. Am. Chem. Soc.* **2011**, *133*, 9286.

(4) (a) Bunevicˇius, R.; Kazˇanavicˇius, G.; zˇalinkevicˇius, R. ; J. Pran-ge, A. Jr. *N. Engl. J. Med.* **1999**, *340*, 424. (b) Klein, I.; Ojamaa, K. *N. Engl. J. Med.* **2001**, *344*, 501. (c) Roberts, C. G.P.; Ladenson, P. W. *Lancet* **2004**, *363*, 793. (d) Cerchietti, L. C.; Lopes, E. C.; Yang, S. N.; Hatzi, K.; Bunting, K. L.; Tsikitas, L. A.; Mallik, A.; Robles, A. I.; Walling, J.; Varticovski, L.; Shaknovich, R.; Bhalla, K. N.; Chiosis, G.; Melnick, A. *Nat. Med.* **2009**, *15*, 1369. (e) Pimlott, S. L.; Sutherland, A. *Chem. Soc. Rev.* **2011**, *40*, 149. (f) Hallouard, F.; Anton, N.; Choquet, P.; Constantinesco, A.; Vandamme, T. *Biomaterials* **2010**, *31*, 6249. (g) Seevers, R. H.; Counsell, R. E. *Chem. Rev.* **1982**, *82*, 575. (h) Goldsby, R. E.; Fitzgerald, P. A. *Nucl. Med. Biol.* **2008**, *35*, S49.

(5) Hennessy, E. J.; Buchwald, S. L. *Org. Lett.* **2002**, *4*, 269.

(6) (a) Merkushev, E. B.; *Synthesis* **1988**, 923. (b) Sheppard, T. D. *Org. Biomol. Chem.* **2009**, *7*, 1043.

(7) (a) Takagi, K.; Hayama, N.; Inokawa, S. *Bull. Chem. Soc. Jpn.***1980**, *53*, 3691. (b) Tsou, T. T.; Kochi, J. K. *J. Org. Chem.***1980**, *45*,1930. (c) Meyer, G.; Rollin, Y.; Perichon, J. *Tetrahedron Lett.* **1986**, *27*, 3497. (d) Clark, J. H.; Jones, C. W.; *J. Chem. Soc. Chem. Commun.* **1987**, 1409. (e) Yang, S. H.; Li, C. S.; Cheng, C. H. *J. Org. Chem.* **1987**, *52*, 691. (f) Yamashita, K.-I.; Tsuboi, M.; Asano, M. S.; Sugiura, K.-I. *Synth. Commun.* **2012**, *42*, 170.

(8) (a) Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Org. Lett.* **2006**, *8*, 2523. (b) Du, B.; Jiang, X.; Sun, P. *J. Org. Chem*. **2013**, *78*, 2786. (c) Qiu, D.; Mo, F.; Zheng, Z.; Zhang, Y.; Wang, J. *Org. Lett.* **2010***, 12*, 5474. (d) Hubbard, A.; Okazaki, T.; Laali, K. K. *J. Org. Chem.* **2008,** *73,* 316. (e) Filimonov, V. D.; Semenischeva, N. I.; Krasnokutskaya, E. A.; Tretyakov, A. N.; Hwang, H. Y.; Chi, K. W. *Synthesis* **2008**, *2*, 185. (f) Krasnokutskaya, E. A.; Semenischeva, N. I.; Filimonov, V. D.; Knochel, P. *Synthesis* **2007**, *1*, 81.

(9) (a) Pierce, J. B.; Ariyan, Z. S.; Ovenden, G. S. *J. Med. Chem.* **1982**, *25*, 131. (b) Earl, R. A.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 4786. (c) Mirkin, C. A.; Lu, K. L.; Snead, T. E.; Geoffroy, G. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 2809. (d) Egan, T. J.; Ross, D. C.; Adams, P. A. *FEBS Lett.* **1994**, *352*, 54. (e) Foley, M.; Tilley, L. *Pharmacol. Ther.* **1998**, *79*, 55. (f) Adam, W.; Hartung, J.; Okamoto, H.; Marquardt, S.; Nau, W. M.; Pischel, U.; Saha-Möller, C. R.; Spehar, K. *J. Org. Chem.* **2002**, *67*, 6041. (g) Kouznetsov, V. V.; Mendez, L. Y.; Gomez, C. M. *Curr. Org. Chem.* **2005**, *9*, 141. (h) Vu, A. T.; Cohn, S. T.; Manas, E. S.; Harris, H. A.; Mewshaw, R. E. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 4520. (i) Surup, F.; Wagner, O.; Frieling, J. V.; Schleicher, M.; Oess, S.; Muller, P.; Grond, S. *J. Org. Chem.* **2007**, *72*, 5085. (j) Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166. (k) Solomon, V. R.; Lee, H. *Curr. Med. Chem.* **2011**, *18*, 1488. (l) Fotiadou, A. D.; Zografos, A. L. *Org. Lett.* **2011**, *13*, 4592.

(10) (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (b) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (c) Wasa, M.; Worrell, B. T.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 1275. (d) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (e) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (f) Sun, K.; Lv, Y.; Wang, J.; Sun, J.; Liu, L.; Jia, M.; Liu, X.; Li, Z.; Wang, X. *Org. Lett.* **2015**, *17*, 4408.

(11) (a) Taylor, E. C.; Crovetti, A. J. *J. Org. Chem.* **1954**, *19*, 1633. (b) Chambers, R. J.; Marfat, A. *Synth. Commun.* **1997**, *27*, 515. (c) Nicolaou, K. C.; Namoto, K.; Ritzen, A.; Ulven, T.; Shoji, M.; Li, J.; D'Amico, G.; Liotta, D.; French, C. T.; Wartmann, M.; Altmann, K. H.; Giannakakou, P. *J. Am. Chem. Soc.* **2001**, *123*, 9313. (c) Ji, J. G.; Li, T.; Bunnelle, W. H. *Org.*

Lett. **2003**, *5*, 4611. (d) Inglis, S. R.; Stojkoski, C.; Branson, M. M.; Cawthray, J. F.; Fritz, D.; Wiadrowski, E.; Pyke, S. M.; Booker, G. W. *J. Med. Chem.* **2004**, *47*, 5405.

(12) (a) Clark, R. B.; He, M. S.; Fyfe, C.; Lofland, D.; O'Brien, W. J.; Plamondon, L.; Sutcliffe, J. A.; Xiao, X. Y. *J. Med. Chem.* **2011***,* 54, 1511. (b) Heitman, L. H.; Goblyos, A.; Zweemer, A. M.; Bakker, R.; Mulder-Krieger, T.; van Veldhoven, J. P. D.; de Vries, H.; Brussee, J.; Ijzerman, A. P. *J. Med. Chem.* **2009**, *52*, 926. (c) Lumeras, W.; Caturla, F.; Vidal, L.; Esteve, C.; Balague, C.; Orellana, A.; Dominguez, M.; Roca, R.; Huerta, J. M.; Godessart, N.; Vidal, B. *J. Med. Chem.* **2009**, *52*, 5531. (d) Paudler, W. W.; Jovanovic, M. V. *J. Org. Chem.* **1983**, *48*, 1064. (e) Petitjean, A.; Kyritsakas, N.; Lehn, J. M. *Chem. - Eur. J.* **2005**, *11*, 6818.

(13) (a) Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844. (b) Chen, M.; Ichikawa, S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2015**, *54*, 263.

(14) Li, L.; Liu, W.-B.; Zeng, H.-Y.; Mu, X.-Y.; Cosa, G.; Mi, Z.-T.; Li, C.-J. *J. Am. Chem. Soc.* **2015**, *137*, 8328.

(15) Wengryniuk, S. E.; Weickgenannt, A.; Reiher, C.; Strotman, N. A.; Chen, K.; Eastgate, M. D.; Baran, P. S. *Org. Lett.* **2013**, *15*, 792.

(16) Hwang, H.; Kim, J.; Jeong, J.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 10770.

(17) Deb, A.; Manna, S.; Maji, A.; Dutta, U.; Maiti, D. *Eur. J. Org. Chem*. **2013**, *24*, 5251.

(18) (a) Deb, A.; Agasti, S.; Saboo, T.; Maiti, D. *Adv. Synth. Catal.* **2014**, *356,* 705. (b) Modak, A.; Rana, S.; Maiti, D. *J. Org. Chem.* **2015**, *80*, 296.

(19) Sun, K.; Lv, Y.; Wang, J.; Sun, J.; Liu, L.; Jia, M.; Liu, X.; Li, Z.; Wang, X. *Org. Lett.,* **2015**, *17*, 4408.

(20) Sharma, K. K.; Patel D. I.; Jain, R. *Chem. Commun.***, 2015**, ***51***, 15129.

Chapter 5

Catalytic Arene *meta*-C–H Functionalization Exploiting a Quinoline Based Template

Chapter 2

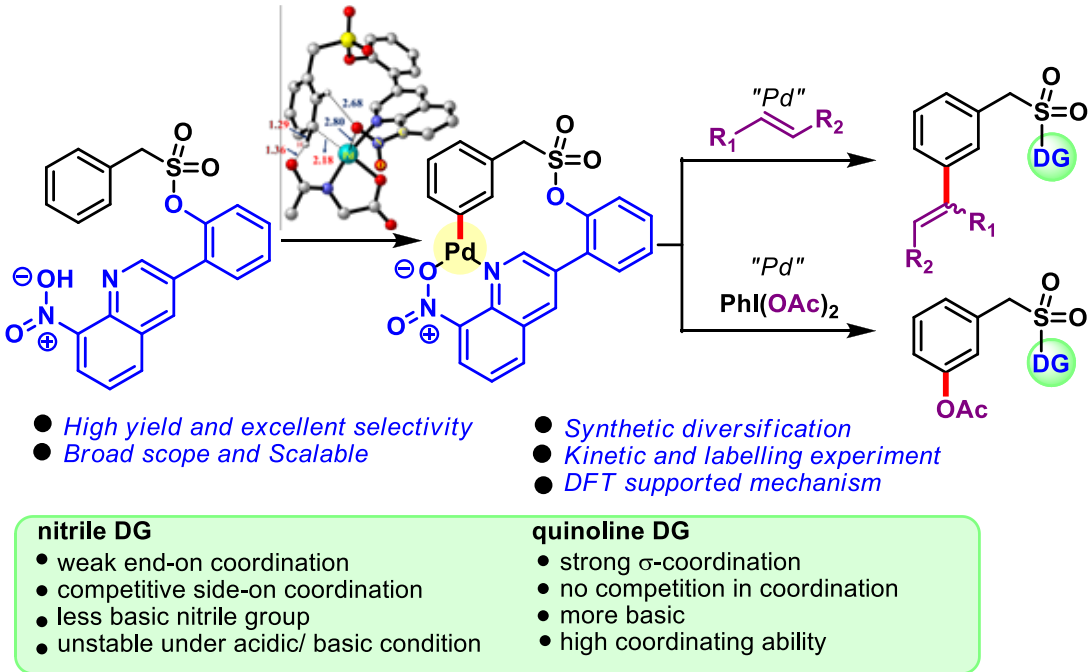
Catalytic Arene *meta*-C–H Functionalization Exploiting a Quinoline Based Template

Abstract: An efficient method for stereoselective nitroaminoxylation of alkyne has been reported. The reaction enjoys a broad substrate scope, good functional group tolerance and high yields. Synthetically useful α–nitroketones can be accessed through these products in a single step. This method expands the scope of metal-free nitration to feed-stock chemical, alkynes.

5.1. Introduction

Transformation of inert carbon-hydrogen (C–H) bonds into carbon-carbon (C–C) and/or carbon-heteroatom (C–X) bonds arguably defines one of the most concise approaches for the synthesis of functional group enriched arenes which are ubiquitous in pharmaceuticals, agrochemical, material science and complex natural products.[1] Selective C–H functionalization posed the major challenge in this realm. In this context, DG-assisted transition metal catalyzed C–H functionalization have been developed to discriminate energetically comparable C–H bonds in the arene. In case of ortho functionalization, chelation assistance by heteroatom bearing DGs successfully allow energetically favourable 5 or 6 membered metallacycle formation.[2] In this regard, pioneering work has been carried out by Daugulish and co-workers for arylation using 8-aminoquinoline as directing group.[3] Since then, pyridine and quinoline has been significantly utilized in directed *ortho*-C–H functionalization as well as aliphatic C–H activation.[4] In sharp contrast, *meta*- and *para*-C–H activation remains much less explored.[5] Nevertheless, such C–H activation can be achieved by exploiting non directed steric and electronic control.[6]

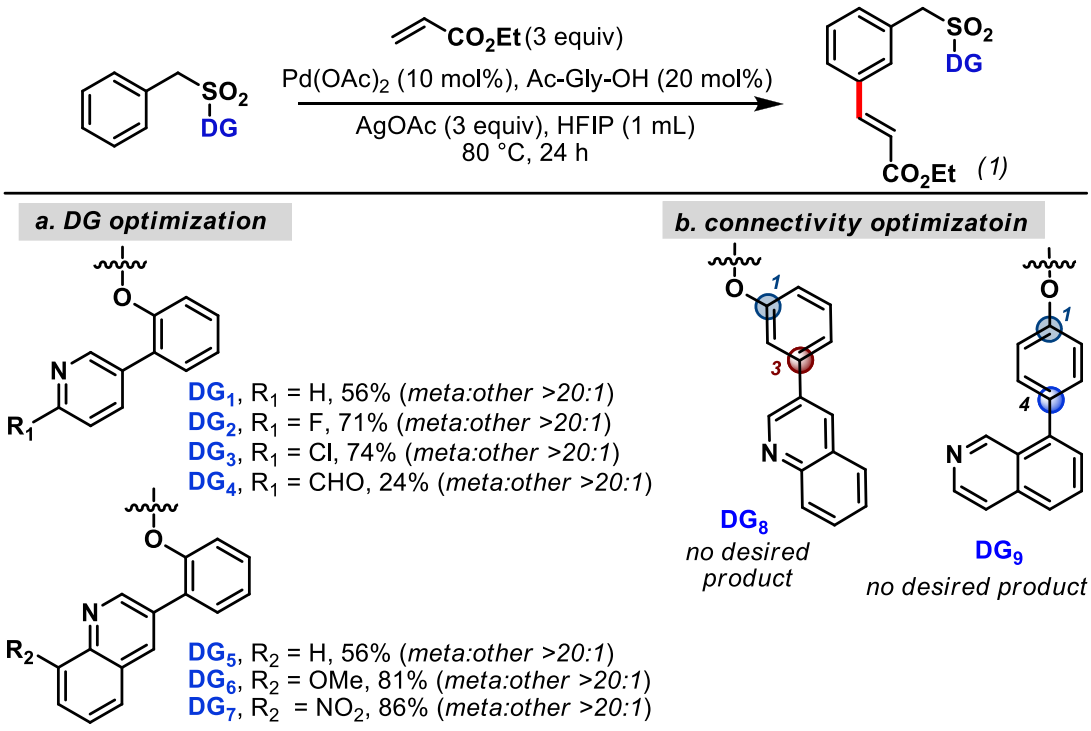
Scheme 5.1. Overview of present work



In addition, directed *ortho*-metallations can be exploited that either perturb electronic properties,[7,8,9] or are coupled with Catelani chemistry,[10,11,12] to ultimately allow *meta*-functionalization. Recently, hydrogen bonding strategies have been developed by Kanai, to

allow *meta*-C–H activation via transiently formed intermediate.[13] The capacity to form macrocyclic structures represents an alternative approach to the challenge of directed *meta*-C–H functionalization. Elegant approaches from Yu and co-workers using nitrile based templates for *meta*-C–H functionalization have been instrumental in the development of the field.[5a-c,14] Extending this concept, progress has been made, with one example from the Tan group,[15] several examples from our group,[16] as well as the Li group[17] relying on the weak end-on coordination of the cyano group. This weak coordination is inherently competitive with solvents and other coordinating reagents, thus the efficacy of the DG can be undesirably affected. To address this limitation the Yu and our group demonstrated the use of pyridyl DGs which allow *meta*-C–C bond and C–I bond formation.[18] Herein, we wish to report the discovery of the sulfonate linked 8-nitroquinoline based strong σ donating DG for *meta*-C–H functionalization. The methodology used in C–C and C–O bond forming reactions as well as computational and mechanistic studies, derivatization and scale up are examined.

Table 5.1. DG and connectivity optimization



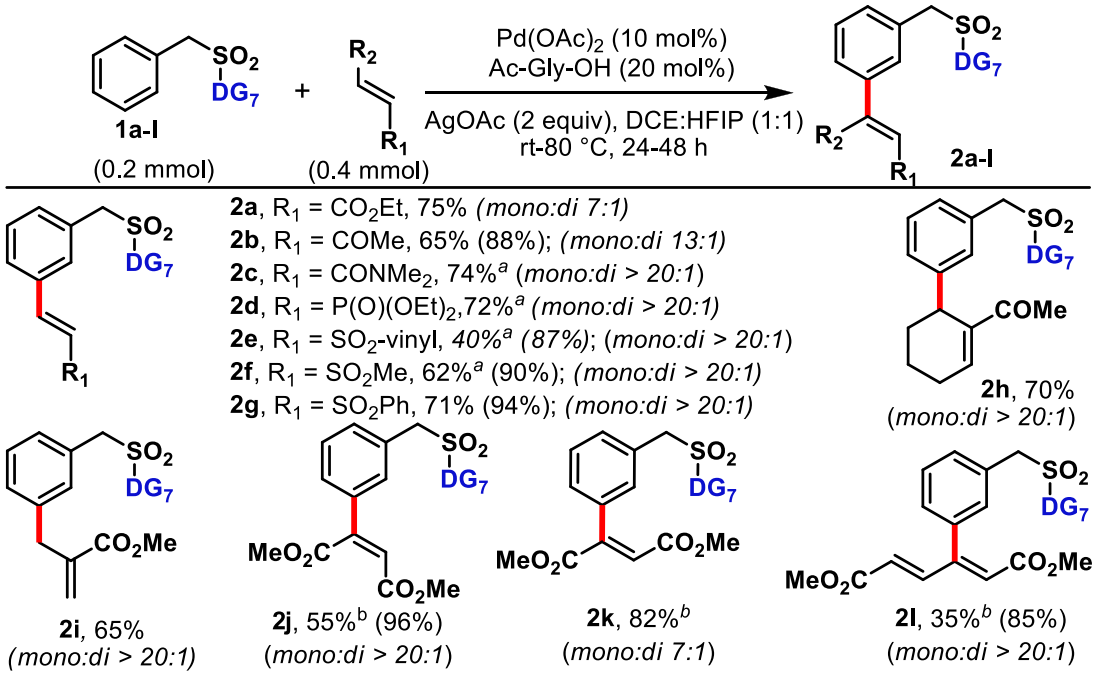
Yields and ratio determined by ^{1}H-NMR using trimethoxybenzene as internal standard

5.2. Result and discussion

Design of the quinoline scaffold for *meta*-C–H activation builds upon our, and others, earlier studies exploiting ester linked nitrile materials.[12-15] While linking the pyridyl DG *via* an ester was examined, we observed the formation of *meta*-alkenylated products with very low selectivity and transesterification caused premature removal of the DG. As a replacement; we envisaged the incorporation of a sulfonyl linker. It was postulated that steric and electronic repulsion between the two oxygen atoms, and the sp^3 nature of the sulfur should enhance *meta*-projection and establish close vicinity between the donor atom and the phenyl ring. To our delight, a remarkable improvement in *meta*-selectivity was obtained using the sulfonyl linker, allowing a 56% yield of *meta*-olefinated product.

Encouraged by this finding, we examined substituted pyridyl DGs **DG2**-**DG4** (Table 5.1). Switching to quinoline directing group **DG5** gave good yields and selectivity. Finally, introduction of 8-substituents, in the form of either a methoxy or nitro group enhanced the yield to 81% and 86%, respectively. It was reasoned that the secondary assistance by the oxygen atom of the nitro or the methoxy group can help metal binding and hence facilitate the formation of *meta*-olefinated product. Finally, the importance of connectivity was examined with 1,3- and 1,4- linked substrates (**DG8** and **DG9**) proving inadequate for the reaction.

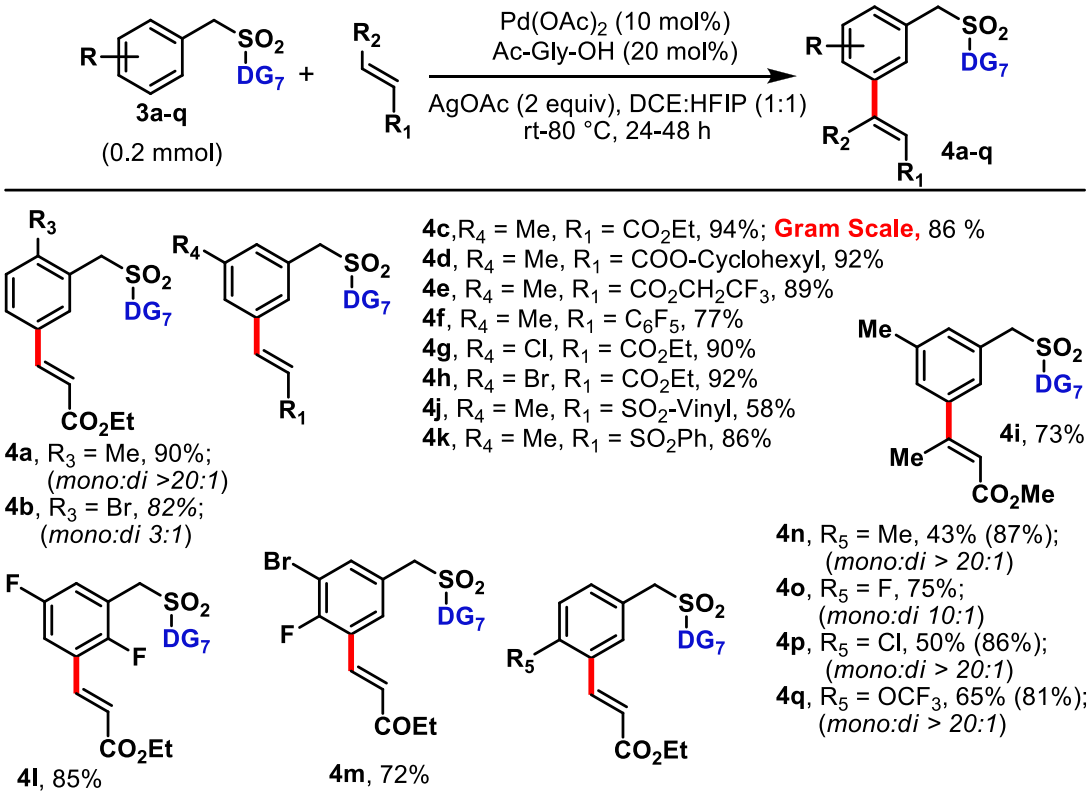
Table 5.2. Olefination scope



Yields in paranthesis are based on recovered starting material, a. 80 °C, b. 120 °C in HFIP, mono:di ratio determined by ^{1}H-NMR

Subsequent optimization was performed with the 8-nitroquinoline DG (i.e. **DG7**). Changing the standard conditions (*eq. 1*) to room temperature with a decrease in silver acetate (2 equiv.) as oxidant and exploiting a mixture of HFIP and DCE as the solvent were required to achieve the desired functionalization of **1a** in synthetically useful yields and selectivity.[19] Various terminal olefins and internal olefins (Table 5.2) were successfully employed with excellent selectivity for *meta*-olefination using the present scaffold.

Table 5.3. Scope of benzyl sulfonate ester



Yields in parenthesis are based on recovered starting material; mono:di ratio determined by ^{1}H-NMR

The scope with substituted arenes was examined to probe the electronic and/or steric influence on the product distribution (Table 5.3). A gram scale reaction was performed with 3-methyl sulfonate ester moiety (**4c**) to demonstrate the scalability of the method. The compatibility of the protocol with substrates bearing complex partner such as acrylic ester of α-tocoferol, thymol acrylate, isoboronyl acrylate and dicyclopentanyl acrylate provided the olefinated product in good to excellent yields (Table 5.4) and with complete *meta* selectivity.

The mono olefinated products were further treated with olefins and produced the desired *meta*-diolefinated product with exclusive *meta*-selectivity (Table 5.5).

Table 5.4. Scope with appended complex molecule

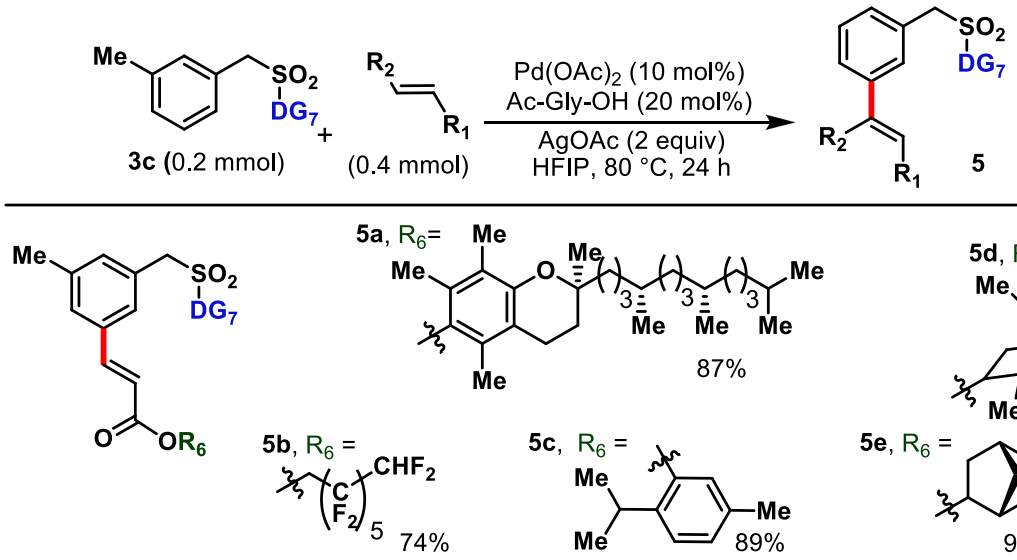


Table 5.5. Scope of homo- and hetero-diolefination

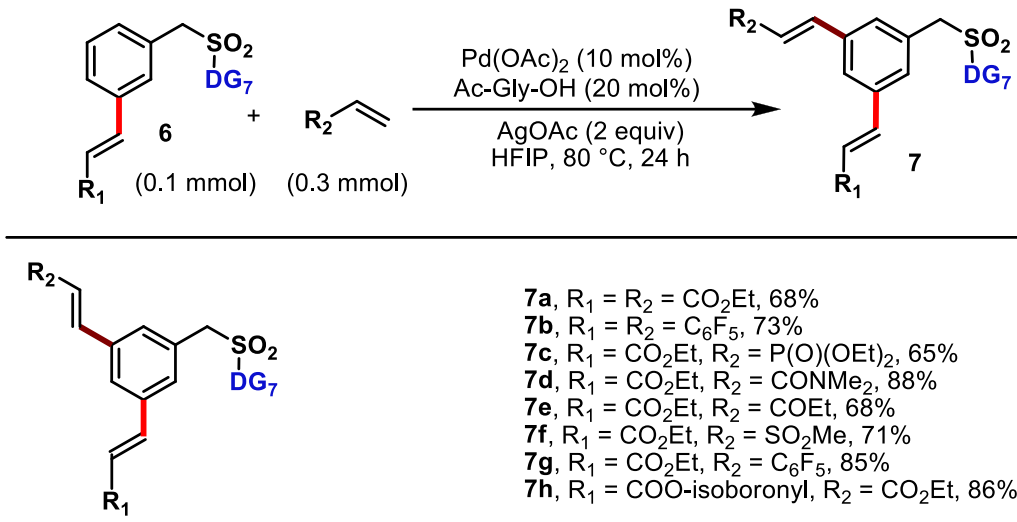
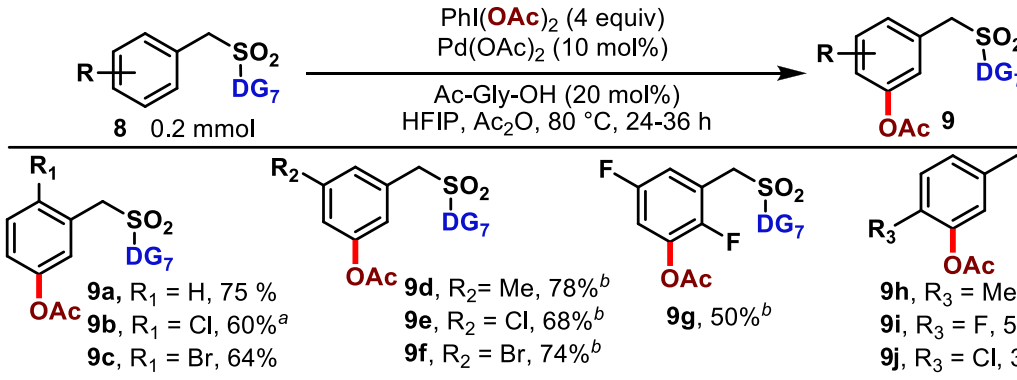
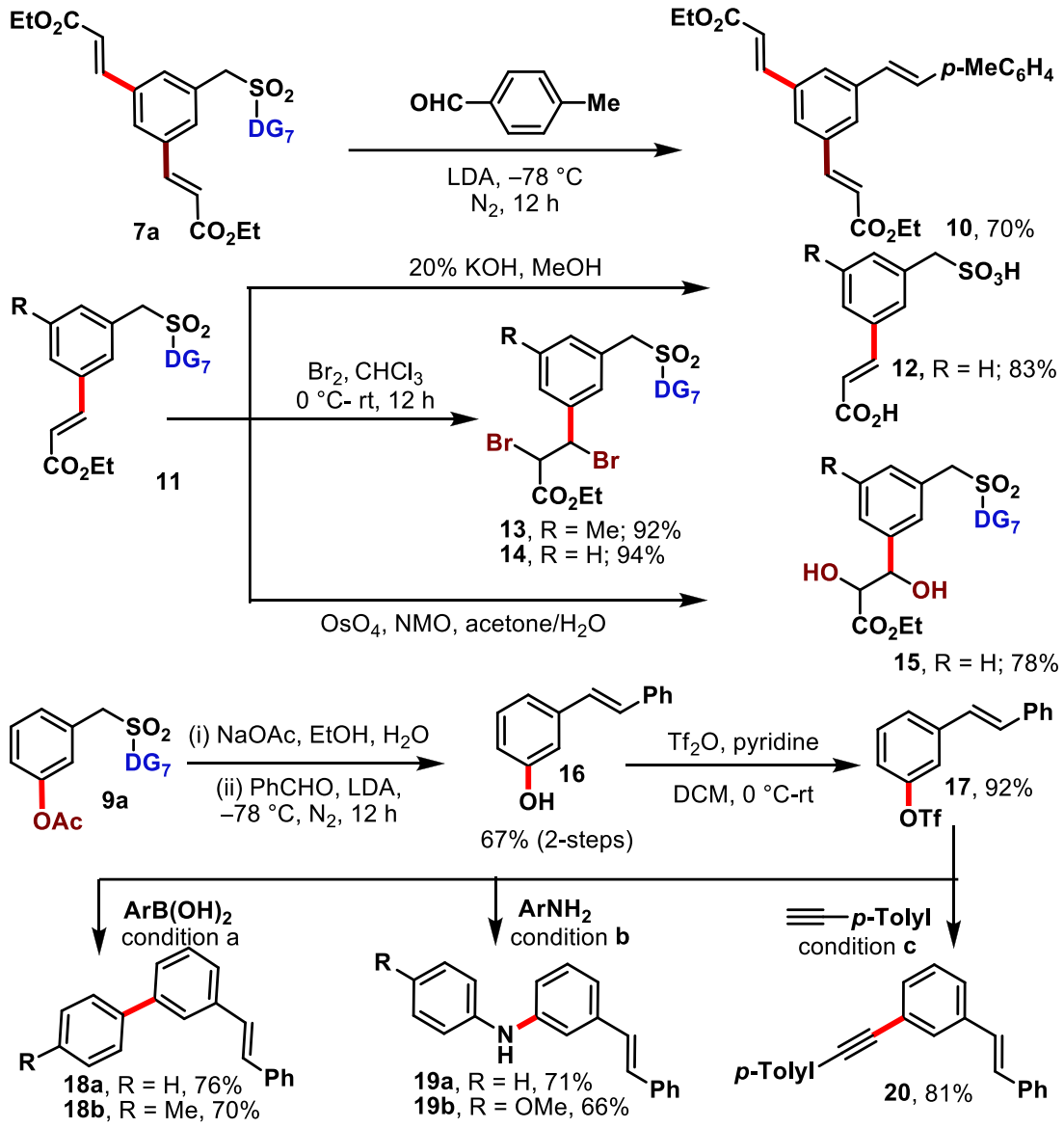


Table 5.6. Scope of acetoxylation



[a]reaction performed at 100 °C, [b]reaction run for 36 h

Scheme 5.2. Utility of *meta*-functionalized products



Condition a: $Pd(PPh_3)_2Cl_2$, PPh_3, K_2CO_3, toluene, 100 °C; Condition b: $Pd_2(dba)_3$, DPPF, ^tBuONa, toluene, 100 °C; Condition c: $Pd(OAc)_2$, PPh_3, K_3PO_4, DMSO, 80 °C

After succeeding in olefination reaction we examined the versatility of the scaffold and successfully achieved the *meta*-acetoxylation products in useful yields. Initial study was carried out with unsubstituted phenyl methane sulphonate and 75% acetoxylated product was isolated with excellent *meta*-selectivity using $PhI(OAc)_2$ as the acetoxylating reagent. Under the optimized conditions, the substrate scope with differently substituted arenes was explored (Table 3.6).

Utilization of the *meta*-functionalized products generated from this protocol can be further demonstrated by converting the olefinated and acetoxylated intermediates to synthetically versatile compounds (Scheme 3.2).

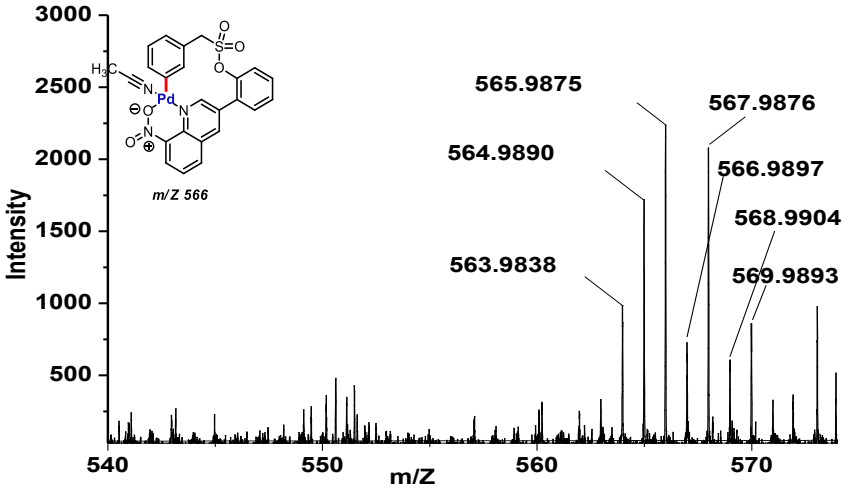


Figure 5.1. ESI-MS study to detect Pd-arene complex with substrate 1a in CH_3CN

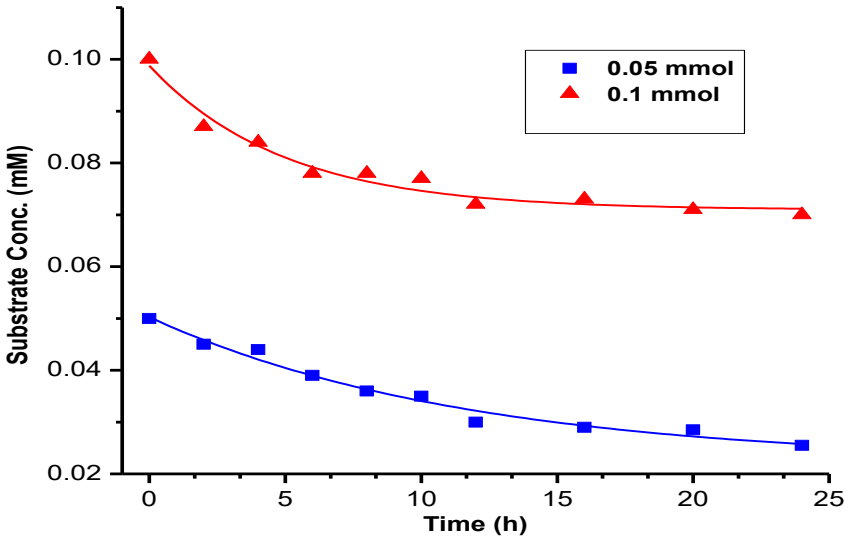
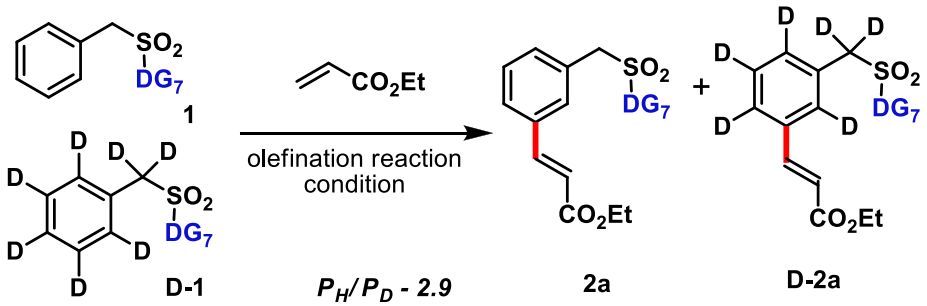


Figure 5.2. Order determination with respect to substrate

In order to gain mechanistic insight, the reaction progress was monitored by NMR.[19] Stoichiometric addition of palladium acetate and ligand to the model substrate **1a** resulted in a downfield shift of 8-nitroquinoline protons indicating the involvement of quinoline group in the coordination to the metal. ESI-MS study reveals the formation of C–H activated complex, [**CH_3CN-Pd-1a**] with palladium acetate, ligand and model substrate **1a** in CH_3CN (Figure 3.1). Observation was further confirmed by solvated $Pd(OAc)_2$ in CD_3CN with **1a** as well as with *m*-tolylmethanesulfonate ester substrate (**3c**) in CH_3CN.[19] Kinetic studies revealed the first order rate dependency on substrate (Figure 3.2) and zero order dependency with respect to the

olefin.[19-20] From intermolecular competition experiment, ***pH/pD*** is found to be 2.9 (Scheme 3.3) and K_H/K_D is 1.9.

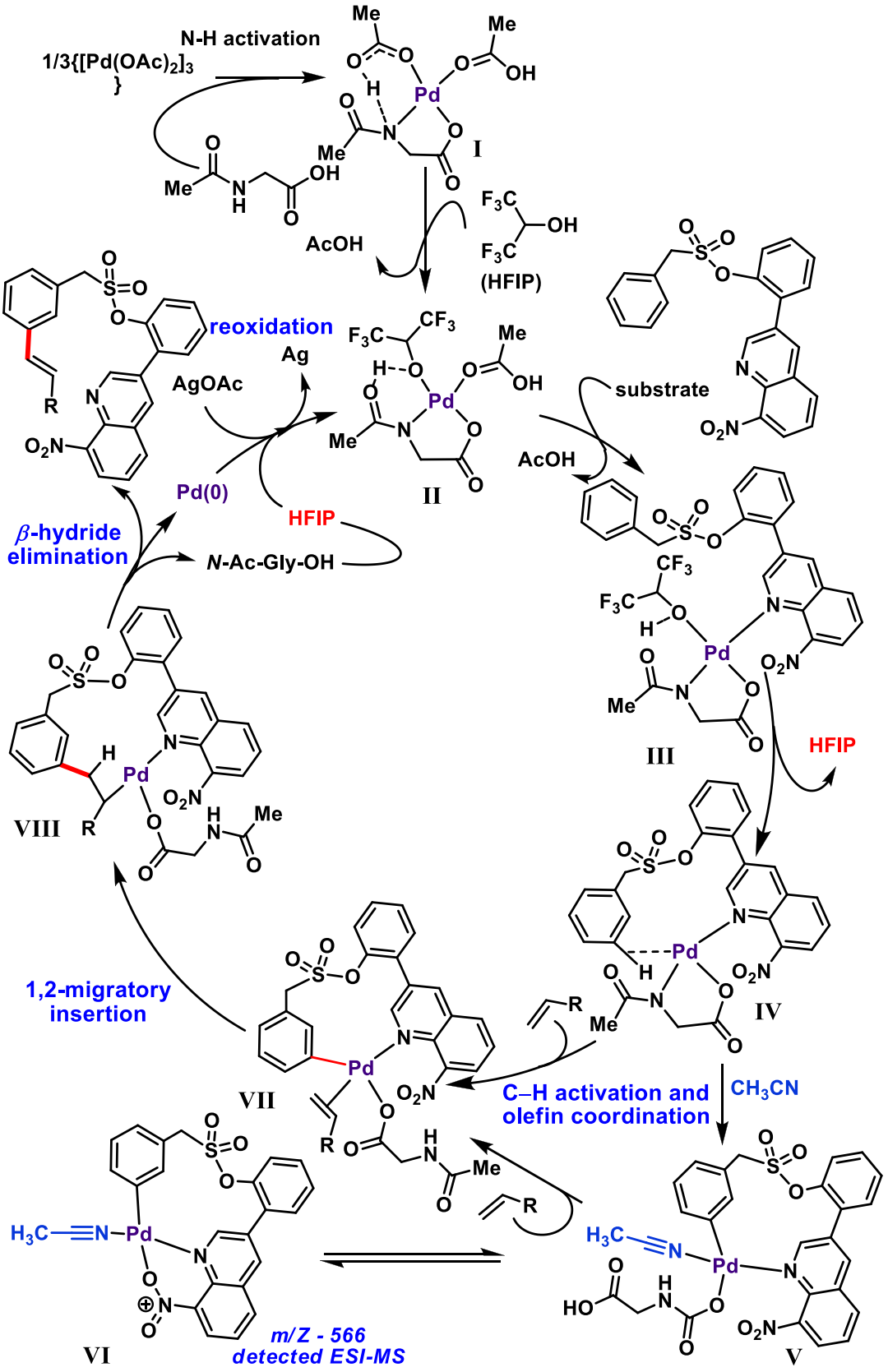
Scheme 5.3. Intermolecular labelling experiment

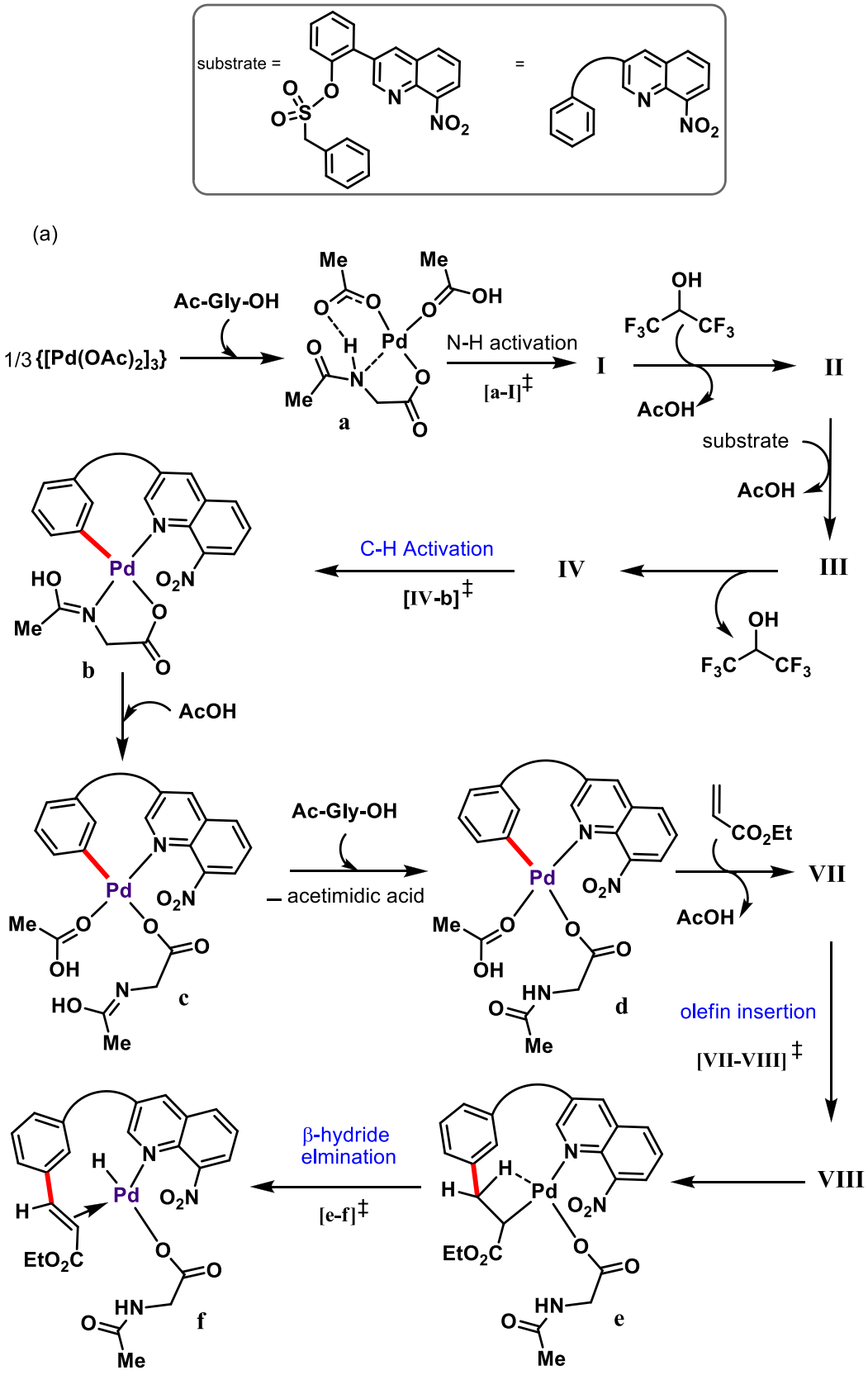


The mechanistic investigations on the catalytic cycle (Scheme 3.4 and Figure 3.3) was carried out by using DFT method with the M06 functional.[21] In line with earlier reports on Pd-catalyzed *meta*-C–H activation, we have examined the role of the *N*-protected amino acid by computing the energies of various intermediates and transition states involved in the catalytic cycle.[14b,c] As noted earlier, the solvent HFIP is considered as a coordinating ligand in the early states of the reaction.[16d] While the mechanism of the reaction can be broadly viewed as consisting of three major steps such as the C–H activation, olefin insertion and *β*-hydride elimination, other elementary steps are equally important to develop a comprehensive view of the actual catalytic event.

The combination of palladium acetate and *N*-acyl amino acid is considered first toward the formation of a chelated species **I** (Scheme 3.4).[19] Species **I** can undergo a ligand exchange wherein the AcOH is displaced by a molecule of HFIP. The uptake of a molecule of substrate by the resulting intermediate **II** can then be accomplished through the exchange of the second molecule of bound AcOH. The resulting catalyst-substrate complex **III** can now create an open coordination site by the expulsion of the weakly bound HFIP. This will enable the Pd center to develop a desirable and vital interaction with the aryl C–H bond, as shown in intermediate **IV**. In the next step, *meta*-C–H activation gives a palladated intermediate **b**, with weakly chelating iminol nitrogen.

Scheme 5.4. A plausible catalytic cycle




substrate =
=
(a)
1/3 {[Pd(OAc)2]3}
Ac-Gly-OH
N-H activation
[a-I]‡
I
II
AcOH
substrate
III
IV
C-H Activation
[IV-b]‡
a
b
c
d
e
f
Ac-Gly-OH
– acetimidic acid
CO2Et
VII
olefin insertion
[VII-VIII] ‡
VIII
β-hydride
elimination
[e-f]‡

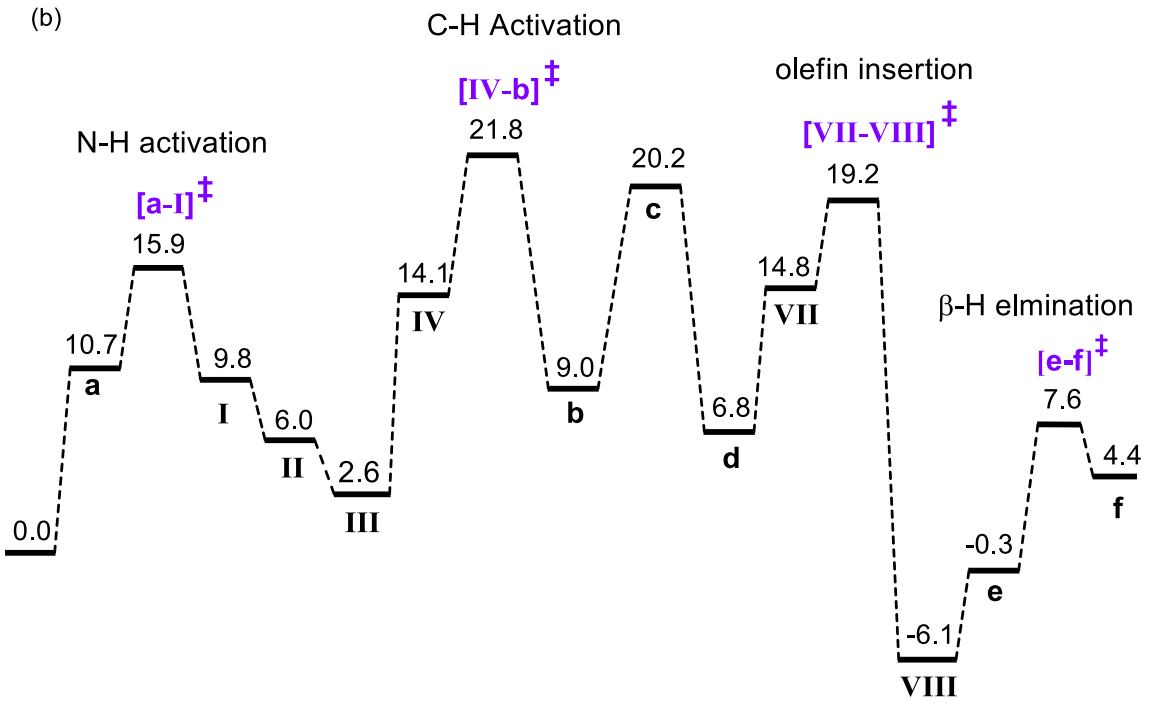
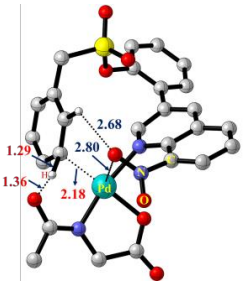
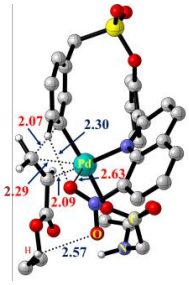


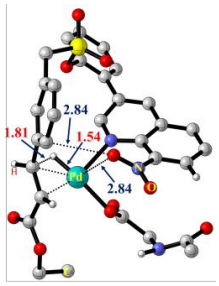
Figure 5.3: (a) Detailed mechanism of olefination using the *meta*-C–H bond activation, and **(b)** the corresponding Gibbs free energy profile (kcal/mol) obtained at the SMD/M06/6-31G**,SDD(Pd)//M06/6-31G**,SDD(Pd) level of theory (The structures shown using the Roman numbers are described in Scheme 3.4)



C–H activation [**IV-b**]‡



Olefin insertion [**VII-VIII**]‡



β-hydride elimination [**e-f**]‡

Figure 5.4. Optimized geometries of the important transition states obtained at the SMD/M06/6-31G**,SDD(Pd)//M06/6-31G**,SDD(Pd) level of theory.

It can be noticed that in the ligand assisted C–H activation transition state **[IV-b]**‡, the abstraction of the *meta*-C_{aryl}–H proton is facilitated by the carbonyl group of the amido moeity of the amino acid ligand.[22] We note that the order of preference, based on the relative energies of the transition states, is *meta* > *para* > *ortho*.[22] Computed relative Gibbs free energy barriers (in kcal/mol) follows the trend, meta(0.0) < para(1.0) << ortho(11.0). Iminol coordination is displaced by the olefin to provide intermediate **VII**. Olefin insertion resulted *meta*-alkylated intermediate **VIII**. A conformational change in **VIII** helps in *β*-hydride elimination that

resulted in the desired product. This leads to the formation of a Pd(0) complex, which upon oxidation by the silver salt regenerates the catalytic Pd(II) species (Scheme 3.4).

The overall energetic features of the reaction can be understood using the Gibbs free energy profile provided in Figure 3.3. Evidently, the most energy demanding step in the catalytic event is the *meta*-C–H activation. This is in agreement with ***pH/pD*** value 2.9. The activation barrier for this elementary step is found to be about 19 kcal/mol. The transition state geometries convey an important interaction between the quinoline nitro group and the palladium (Figure 3.4). The contact distances between the $–NO_2$ group and Pd are found to be in the range from 2.6 to 2.8 Å. Another week interaction between the $–NO_2$ oxygen and the C–H of the aryl ring of the substrates is also observed. A graphical illustration of these weak interactions, generated using the non-covalent interaction plot, is provided in figure 3.5.[23] Natural charge calculation illustrates that the incorporation of as $–NO_2$ and –OMe at the C-8 position of the quinoline ring influence the charge on palladium and are beneficial for the C–H activation (Table 3.7). The NO_2 and OMe substituents in the quinoline ring help polarize the C2-H3 bond due to the Pd/C-H agostic interactions. We noticed that the Pd(1)-C(2) distances in the pre-reacting complexes are relatively shorter when C8 quinoline is substituted ($–NO_2$ or –OMe) than when it is unsubstituted.

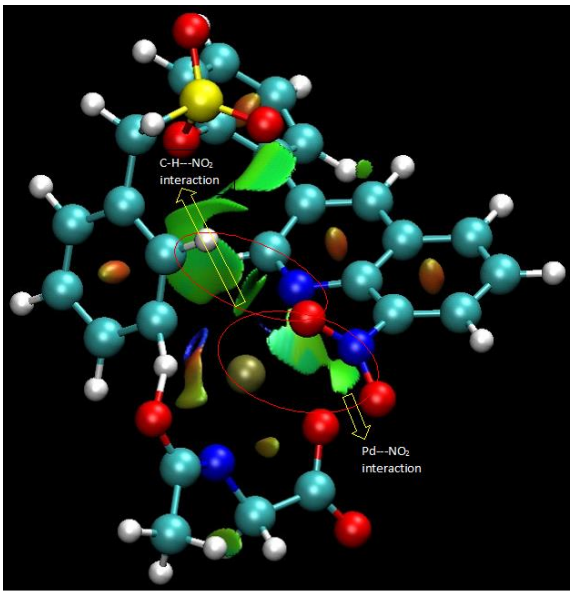
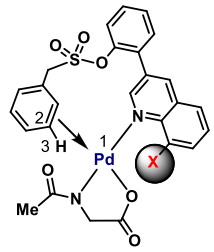


Figure 5.5. *meta*-C–H activation transition state plot is generated from NCI program for showing non-covalent interactions

Table 5.7. Natural Charges on Key Atoms and Pd-Aryl Bond Distances (angstroms) in the Respective Pre-reacting Complexes of the *meta*-C–H Activation Transition States

	X=	Pd (1)	C (2)	H (3)	Pd (1)- C (2)
	$-NO_2$	0.513	-0.282	0.328	2.44
	-OMe	0.530	-0.257	0.310	2.46
	-H	0.522	-0.243	0.304	2.55

5.3. Experimental details

5.3.1. General Consideration

5.3.1.a. Reagent Information: Unless otherwise stated, all the reactions were carried out under aerobic condition in screw cap reaction tubes. All the solvents were bought from Aldrich/Alfa Aesar (India)/TCI (India)/Merck in a sure-seal bottle and were used as received. Palladium acetate was purchased from Alfa Aesar. Silver acetate was bought from LobaChemicals and *N*-Ac-gly-OH is obtained from Alfa aesar (India). HFIP was received from TCI (India). All the benzyl chlorides and bromides were bought from Aldrich/Alfa Aesar (India)/TCI (India)/Spectrochem. For column chromatography, silica gel (100–200 mesh) from SRL Co. was used. A gradient elution using pet ether and ethyl acetate was performed based on Merck aluminium TLC sheets (silica gel $60F_{254}$).

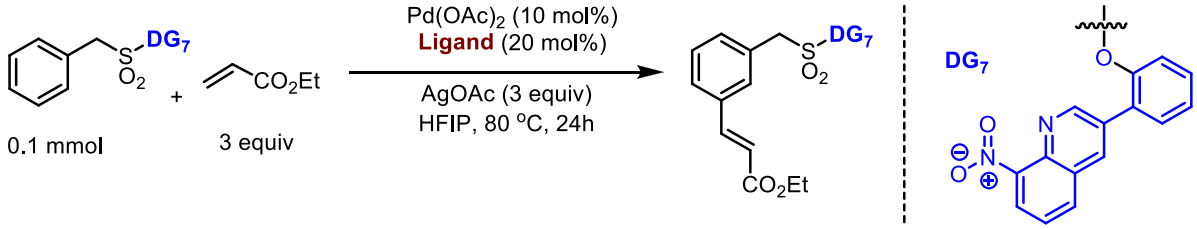
5.3.1.b. Analytical Information: All isolated compounds are characterized by ^{1}H NMR, ^{13}C NMR spectroscopy. Nuclear magnetic resonance spectra were recorded either on a Bruker 500 or 400 MHz instrument. All ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.23 ppm), unless otherwise stated, and all were obtained with ^{1}H decoupling. High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

5.3.1.c. Description of Reaction Tube:

Pictorial description of reaction tube for *meta*-olefination and acetoxylation reaction: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E) [right]; Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A) [right].

5.3.2. Optimization

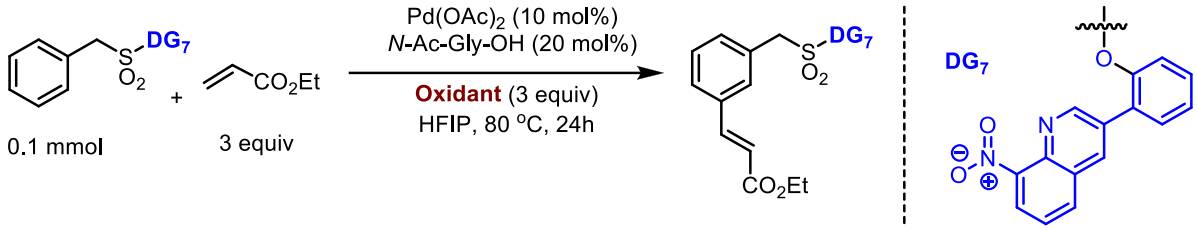
5.3.2.I. Optimization for *meta*-olefination reaction:



5.3.2.I.a. Optimization by varying ligands:

Entry	Ligands	% Yield (NMR)	Ratio (mono:di)
1	***N*-Ac-Gly-OH**	**86**	**1.5:1**
2	*N*-Ac-Phe-OH	37	11:1
3	*N*-Ac-Val-OH	18	8:1
4	*N*-Ac-Leu-OH	38	15:1

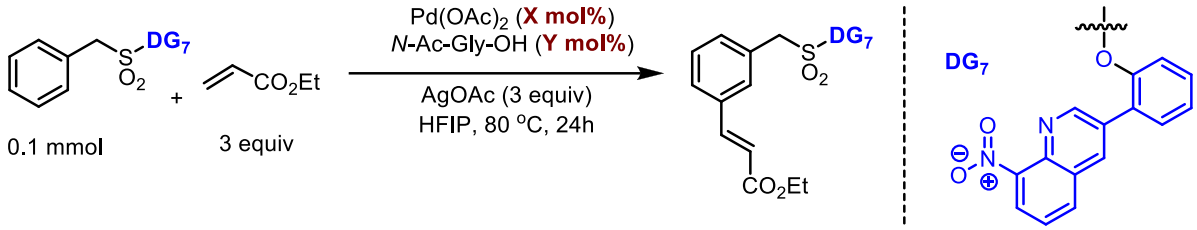
5	*N*-Boc-Leu-OH	32	15:1
6	*N*-Boc-Phe-OH	28	>20:1
7	*N*-Ac-Ala-OH	<10	-
8	Boc-Gly-OH	15	>20:1
9	Boc-isoleucine	<5	-
10	For-Gly-OH	<5	-
11	Boc-Val-OH	<10	-
12	Boc-Ala-OH	<10	-
13	*N*-acetyl methionine	<10	-
14	Ac-Gly-ethylester	-	-
15	Glycine	<5	-
16	*Z*-Phe-OH	<5	-



5.3.2.I.b. Oxidant optimization:

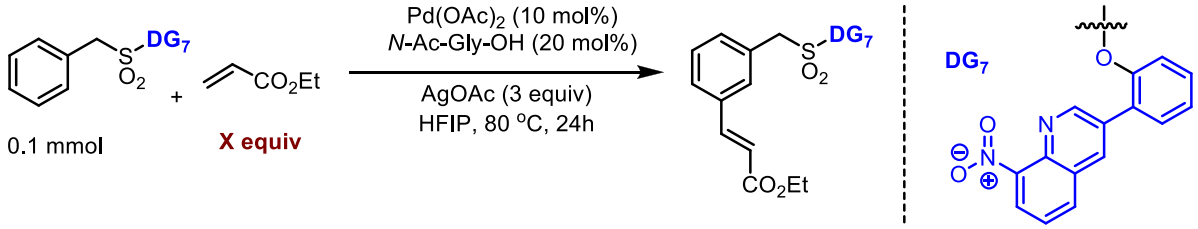
Entry	**Oxidant**	**% Yield(NMR)**	**Ratio (*mono:di*)**
1	**AgOAc**	**86**	**1.5:1**
2	Ag_2CO_3	70	2:1
3	$AgSO_4$	45	5:1

4	AgO	<20	-
5	$K_2S_2O_8$	-	-
6	*p*-Benzoquinone	-	-
7	$Cu(OAc)_2$	-	-
8	$CuCl_2$	-	-
9	MnO_2	-	-



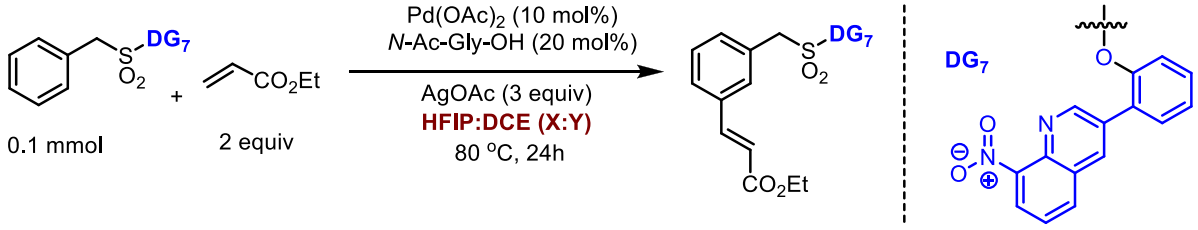
5.3.2.I.c. Optimization by varying catalyst loading (palladium and ligand amount):

Entry	**Pd- Loading (mol%)**	**Ligand Amount (mol%)**	**% Yield (NMR)**	**Ratio (*mono:di*)**
1	2	4	50	7:1
2	4	8	70	2:1
3	6	12	74	2:1
4	8	16	79	2:1
5	**10**	**20**	**86**	**1.5:1**
6	15	30	87	1:1
7	20	40	87	1:1



5.3.2.I.d. Olefin amount variation:

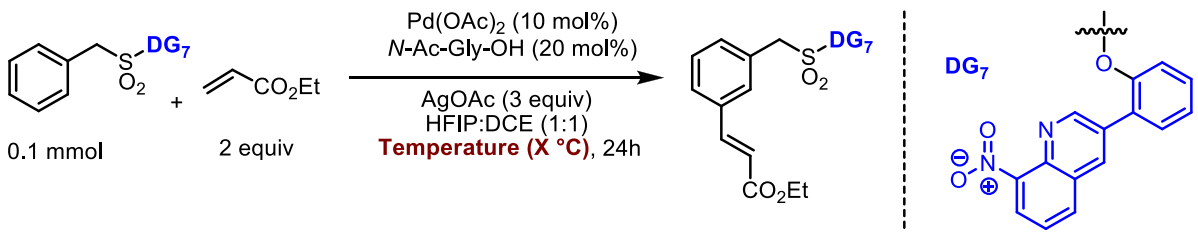
Entry	Olefin Amount (equiv)	% Yield (NMR)	Ratio (*mono:di*)
1	1	57	7:1
2	1.2	65	3:1
3	1.4	76	3:1
4	1.6	80	2.5:1
5	1.8	85	2:1
6	**2.0**	**86**	**2:1**
7	2.5	87	1.5:1
8	3.0	86	1.5:1



5.3.2.I.e. Solvent combination screening:

Entry	HFIP/DCE (µl)	% Yield (NMR)	Ratio (*mono:di*)

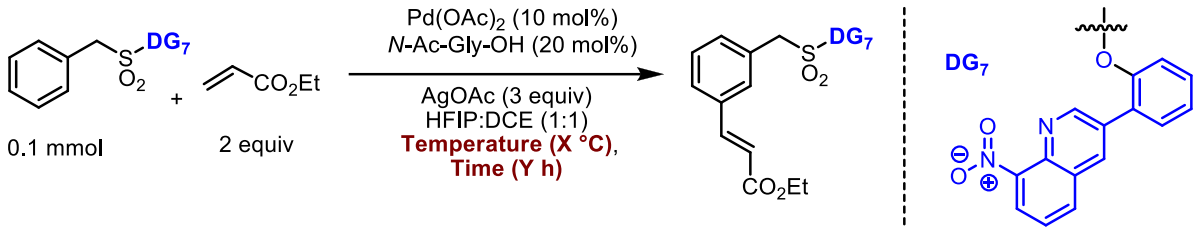
1	500:0	86	2:1
2	400:100	85	3:1
3	300:200	81	3:1
4	**250:250**	**80**	**3:1**
5	200:300	78	3:1
6	100:400	72	3.5:1
7	50:450	64	5:1
8	0:500	0	-



5.3.2.I.f. Temperature optimization:

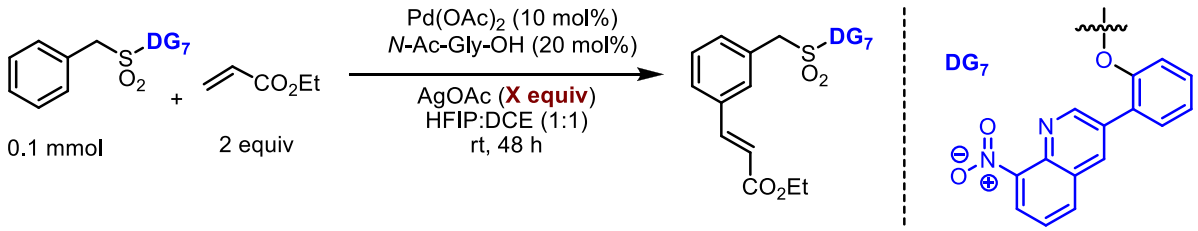
Entry	Temperature (°C)	% Yield (NMR)	Ratio (*mono:di*)
1	**RT**	**55**	**>10:1**
2	35	68	2:1
3	40	70	2:1
4	45	75	2:1
5	50	78	2:1
6	80	80	3:1
7	100	87	1:1

8	130	61	1:1



5.3.2.I.g. Temperature and time optimization:

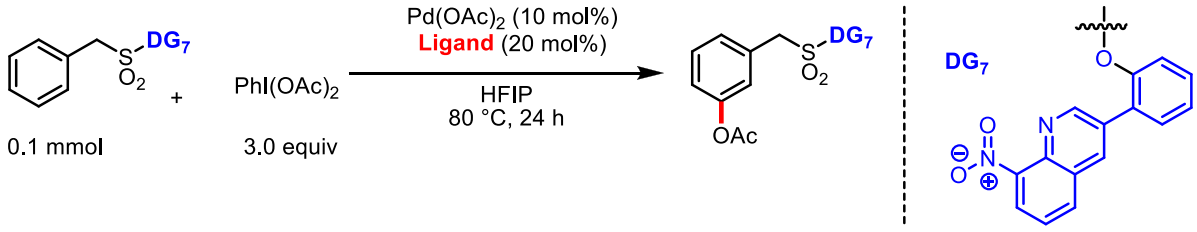
Entry	Temperature (°C)	Time (h)	% Yield (NMR)	Ratio (*mono:di*)
1	RT	12	34	>20:1
2	RT	24	55	>10:1
3	RT	30	63	>10:1
4	RT	36	70	10:1
5	**RT**	**48**	**75**	**7:1**
6	50	48	87	1:1
7	80	48	90	1:1
8	100	48	89	1:1



5.3.2.I.h. Oxidant amount optimization:

Entry	Oxidant Amount (equiv)	% Yield (NMR)	Ratio (*mono:di*)
1	0.5	35	10:1
2	1.0	70	7:1
3	1.5	70	7:1
4	**2.0**	**75**	**7:1**
5	2.5	75	7:1
6	3.0	75	7:1

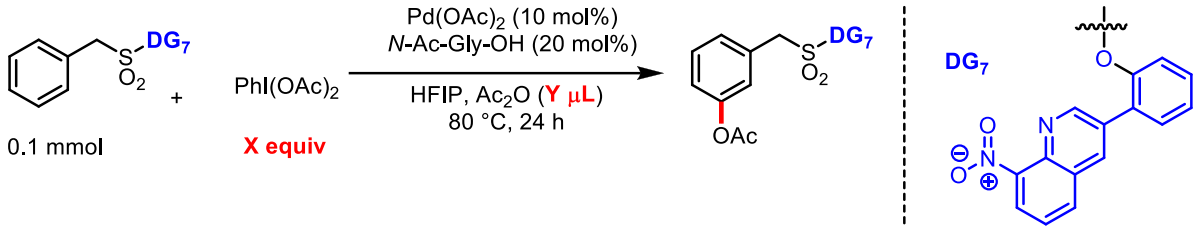
5.3.2.II. Optimization for *meta*-acetoxylation reaction:



5.3.2.II.a. Oxidant optimization:

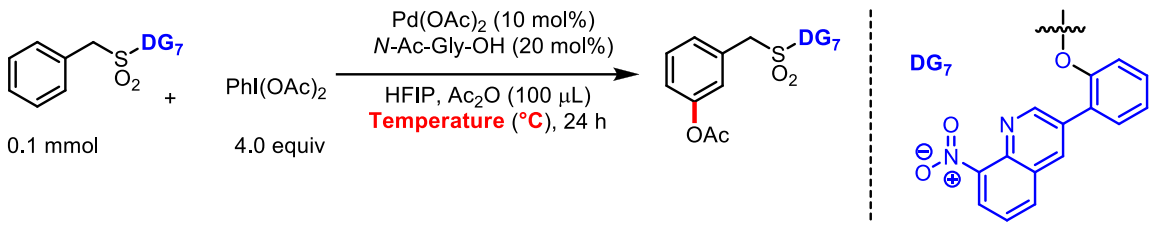
Entry	Ligands	% Yield (NMR)	Ratio (mono:di)
1	***N*-Ac-Gly-OH**	**60**	**>20:1**
2	*N*-For-Gly-OH	36	>20:1
3	*N*-Ac-Val-OH	18	>20:1
4	*N*-Ac-Phe-OH	44	>20:1
5	*N*-Ac-Ala-OH	20	>20:1
6	*N*-Boc-Phe-OH	<10	-
7	*N*-Boc-Val-OH	<5	-

8	*N*-Boc-Gly-OH	<5	-
9	*N*-Boc-isoleucine	<5	-
10	Ac-Gly-ethylester	<10	-
11	Glycine	<10	-
12	N-Ac-Leu-OH	54	>20:1



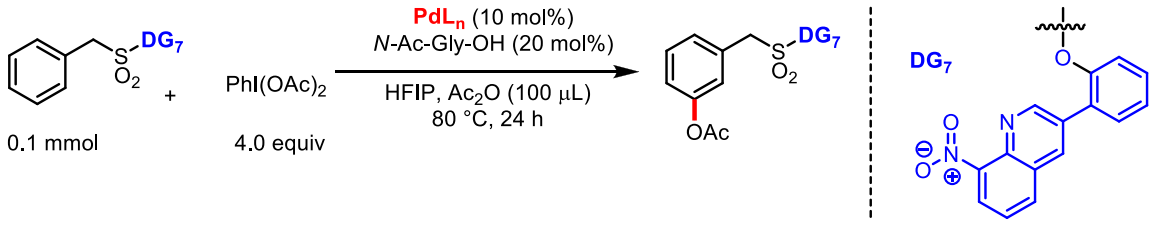
5.3.2.II.b. $PhI(OAc)_2$ and Ac_2O amount variation:

Entry	$PhI(OAc)_2$(equiv)	Ac_2O (µL)	% Yield (NMR)	Ratio (mono:di)
1	1.0	-	25	>20:1
2	2.0	-	32	>20:1
3	2.5	-	50	>20:1
4	3.0	-	60	>20:1
5	3.5	-	65	>20:1
6	4.0	-	69	>20:1
7	5.0	-	65	>20:1
9	4.0	50	70	>20:1
10	4.0	75	71	>20:1
11	**4.0**	**100**	**75**	**>20:1**
12	4.0	120	76	<20:1



5.3.2.II.c. Temperature optimization:

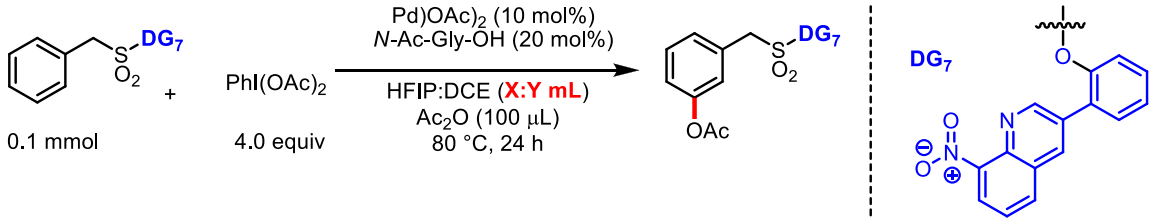
Entry	Temperature (°C)	% Yield (NMR)	Ratio (mono:di)
1	RT	<10%	-
2	50	30	>20:1
3	60	52	>20:1
4	70	68	>20:1
5	**80**	**75**	**>20:1**
6	90	76	>20:1
7	100	80	<20:1



5.3.2.II.d. Pd-salt variation:

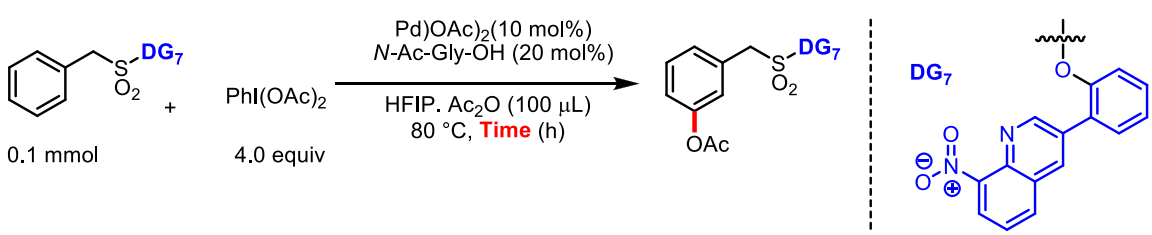
Entry	Pd-Salt	% Yield (NMR)	Ratio (mono:di)
1	**$Pd(OAc)_2$**	**75**	**>20:1**
2	$PdSO_4$	-	>20:1

3	$Pd(PPh_3)_4$	40	>20:1
4	$Pd(CH_3CN)_2Cl_2$	20	>20:1
5	$Pd_2(dba)_3$	35	>20:1
6	$PdCl_2$	-	>20:1



5.3.2.II.e. Oxidant optimization:

Entry	HFIP:DCE (mL)	% Yield (NMR)	Ratio (mono:di)
1	**1.0:0**	**75**	**>20:1**
2	0.8:0.2	70	>20:1
3	0.6:0.4	61	>20:1
4	0.5:0.5	56	>20:1
5	0.4:0.6	40	>20:1
6	0.2:0.8	20	>20:1
7	0:1.0	-	-



5.3.2.II.f. Time optimization:

Entry	Time (h)	% Yield (NMR)	Ratio (mono:di)
1	12	40	>20:1
2	16	53	>20:1
3	**24**	**75**	>20:1
4	30	76	>20:1
5	**36**	**78**	**<20:1**
6	48	80	<20:1

5.3.3. General Procedure

5.3.3.a. General Procedure A: *meta*-mono-olefination of sulphonic esters

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, substrate (0.2 mmol, 1.0 equiv), olefin (0.4 mmol, 2.0 equiv), $Pd(OAc)_2$ (10 mol%, 0.02 mmol, 4.4 mg), *N*-Ac-Gly-OH (20 mol%, 0.04 mmol, 4.7 mg), and AgOAc (2.0 equiv, 0.4 mmol, 66.7 mg) were taken. Subsequently, HFIP:DCE (1:1, 2 mL) was added and the reaction mixture was stirred vigorously for 24-48 h at rt-80 °C. The reaction mixture was then diluted with EtOAc and filtered through celite pad. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent. (Olefination reactions with 3-substituted arene compounds have been carried out in only HFIP solvent for improved yield)

5.3.3.b. General Procedure B: *meta*-di-olefination of sulphonic esters

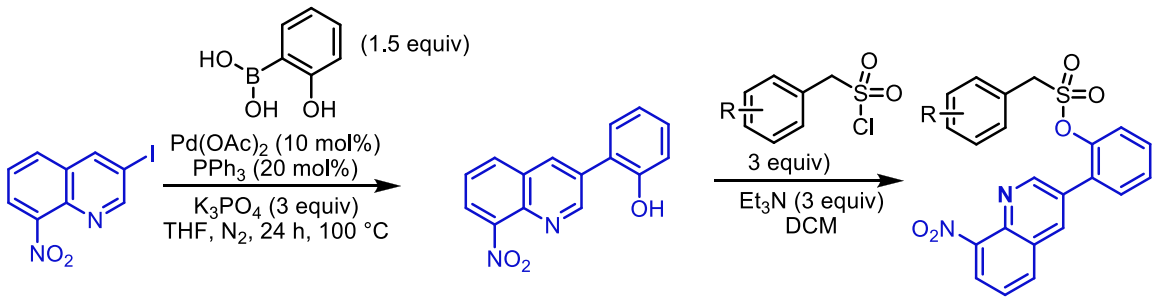
The *mono*-olefinated product has been utilized as the substrate for the hetero-di-olefination. An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, mono-olefianted product as substrate (0.1 mmol, 1.0 equiv), olefin (0.3 mmol, 3.0 equiv), $Pd(OAc)_2$ (10 mol%, 2.2 mg), *N*-Ac-Gly-OH (20 mol%, 2.3 mg), and AgOAc (0.2mmol, 2.0 equiv, 33 mg) were taken. Subsequently, HFIP (1 mL) was added and the reaction mixture was stirred vigorously for 24 h at a preheated oil bath of 80 °C. The reaction mixture was then diluted with EtOAc

and filtered through celite pad. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

5.3.3.c. General Procedure C: *meta*-acetoxylation of sulphonic esters

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, substrate (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (10 mol%, 0.02 mmol, 4.4 mg), *N*-Ac-Gly-OH (20 mol%, 0.04 mmol, 4.7 mg) and $PhI(OAc)_2$(0.8 mmol, 4.0 equiv, 257.6 mg) were taken. Subsequently, HFIP (2 mL) and 100 μL Ac_2O were added. The reaction mixture was placed on a preheated oil bath of 80 °C and stirred vigorously for 24-36 h. The reaction mixture was then diluted with EtOAc and filtered through celite pad. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

5.3.3.d. Procedure D: Synthesis of directing group and substrates

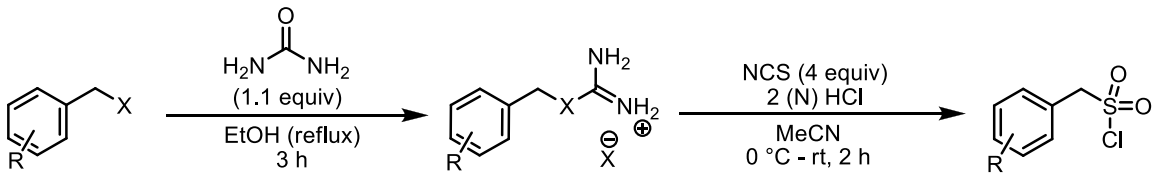


Step 1: In an oven-dried screw cap reaction tube, charged with a magnetic stir-bar,3-iodo-8-nitroquinoline (1.0 equiv), 2-hydroxyphenylboronic acid (1.5 equiv), $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%) and K_3PO_4 (3.0 equiv) were added. Then the closed reaction tube was evacuated and backfilled with N_2 for three times and THF (3 mL per 1 mmol) as solvent was added using syringe. The reaction mixture was submerged in a preheated 100 °C oil bath and allowed for vigorous stirring for 24 hours. After 24 hour, reaction mixture was allowed to cool and diluted with EtOAc and extracted with brine solution. The organic layer was dried over $Na_2SO_4$and concentrated by evaporation. Concentrated organic part was purified by column chromatography. Yellow crystalline compound was isolated in 75% yields using 15% ethyl acetate and pet ether mixture as an eluent.

Step 2: In an oven dried 100 mL round bottom flask, phenol (1 equiv) was dissolved in DCM (5 mL DCM permmol phenol) and Et_3N (3.0 equiv) was added drop wise and allowed to stir

for 15 min at room temperature. Followed by, sulphonyl chloride (3.0 equiv) was added portion wise very slowly at 0 °C. The reaction mixture was then stirred at room temperature for overnight and upon complete consumption of phenol DCM was dried under vacuum. The residue was diluted with EtOAc and was with brine solution. The organic part was dried over Na_2SO_4, and purified by column chromatography.

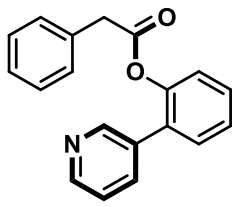
5.3.3.e. Procedure E: Synthesis of sulfonyl chloride from benzyl chloride/bromide[24]



Step 1: In an oven dried 250 mL round bottomed flask charged with magnetic stir-bar, thiourea (11 mmol , 1.1 equiv, 836 mg) was taken in absolute ethanol (30 mL) followed by the corresponding benzyl chloride/bromide (10 mmol , 1.0 equiv) was added. The reaction mixture was refluxed for 3 h. After cooling the reaction mixture, the solvent was dried under reduced pressure which result a white solid. The solid was directly used for the next step directly.

Step 2: In a clean round bottomed flask charged with stirbar, *N*-chlorosuccinimide (40 mmol, 4.0equiv, 5.34 g) was added to MeCN (20 mL). 2(N) HCl(2.8 mL) was then added to the solution. The reaction mixture was stirred on an ice cooled water bath for 15 min. The solid salt obtained from the first step was added slowly to this reaction mixture and stirred vigorously. The addition led to an exothermic reaction. However the temperature was maintained below 25 °C. Upon forming a clear solution the mixture was warmed to the room temperature and stirred for 2 h. The reaction was evaporated under reduced pressure to remove the acetonitrile. The remaining solution was diluted with water and extracted with ethyl acetate. The organic portion was dried over anhydrous Na_2SO_4. The solution was concentrated under reduced pressure and purified through column chromatography.

5.3.4. Characterization:

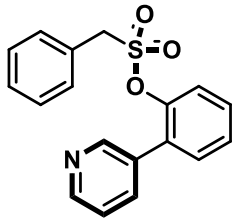


2-(pyridin-3-yl)phenyl 2-phenylacetate :

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 2.2, 0.7 Hz, 1H), 8.52 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.65 (d, *J* = 7.3 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.43 (q, *J* = 7.3 Hz, 3H), 7.36 (dd, *J* = 5.0, 1.7 Hz, 3H), 7.23 (dd, *J* = 6.9, 3.3 Hz, 3H), 3.76 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.78, 148.12, 136.91, 132.97, 130.94, 129.74, 129.57, 129.41, 128.87, 128.68, 127.50, 127.06, 126.85, 123.14, 41.44.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{19}H_{16}NO_2$: 290.1175, found 290.1170.

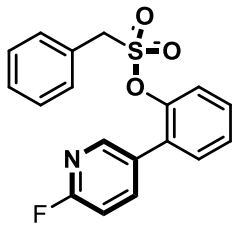


2-(pyridin-3-yl)phenylphenylmethanesulfonate (DG_1):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 – 8.73 (m, 1H), 8.63 (dd, *J* = 4.7, 1.6 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.46 – 7.30 (m, 9H), 7.28 (s, 1H), 4.17 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.97, 149.01, 146.33, 136.94, 132.93, 131.95, 131.43, 130.84, 129.87, 129.36, 129.04, 127.66, 126.81, 123.36, 123.29, 57.55.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{18}H_{16}NO_3S$: 326.0845, found 326.0841.

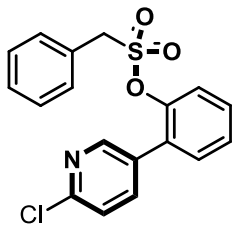


2-(6-fluoropyridin-3-yl)phenylphenylmethanesulfonate (DG_2):

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 2.3 Hz, 1H), 7.83 (td, *J* = 8.1, 2.5 Hz, 1H), 7.44 – 7.36 (m, 6H), 7.35 – 7.31 (m, 3H), 7.27 (dd, *J* = 6.1, 4.6 Hz, 2H), 6.89 (dd, *J* = 8.5, 2.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.77, 146.21, 142.21, 142.13, 131.51, 131.13, 130.91, 130.08, 129.53, 129.17, 127.75, 126.89, 123.36, 109.49, 109.12, 57.70.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{18}H_{15}FNO_3S$: 344.0751, found 344.0755.

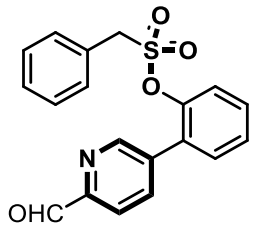


2-(6-chloropyridin-3-yl)phenylphenylmethanesulfonate(DG$_3$):

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, *J* = 2.1 Hz, 1H), 7.68 (dd, *J* = 8.2, 2.4 Hz, 1H), 7.43 – 7.33 (m, 7H), 7.30 – 7.26 (m, 3H), 4.31 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 150.97, 150.01, 149.75, 146.05, 139.62, 131.85, 131.45, 130.91, 130.28, 129.57, 129.20, 127.81, 126.83, 124.06, 123.44, 57.70.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{18}H_{14}ClNNaO_3S$: 382.0275, found 382.0278.

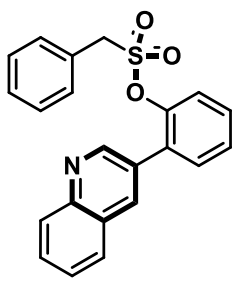


2-(6-formylpyridin-3-yl)phenylphenylmethanesulfonate (DG$_4$):

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.12 (s, 1H), 8.88 – 8.71 (m, 1H), 7.96 – 7.79 (m, 2H), 7.53 – 7.13 (m, 9H), 4.30 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.19, 151.69, 150.46, 145.98, 137.81, 137.19, 131.44, 131.32, 130.89, 130.69, 129.55, 129.17, 127.91, 126.79, 123.58, 121.39, 57.66.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{19}H_{16}NO_4S$: 354.0800, found 354.0790.

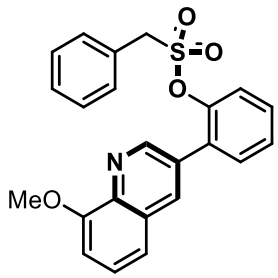


2-(quinolin-3-yl)phenylphenylmethanesulfonate(DG$_5$):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (d, *J* = 2.2 Hz, 1H), 8.25 (d, *J* = 1.9 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.78 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.61 (ddd, *J* = 14.1, 7.6, 4.1 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.46 – 7.36 (m, 3H), 7.24 – 7.13 (m, 5H), 4.15 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 151.12, 147.51, 146.59, 136.30, 132.13, 131.91, 130.78, 130.22, 130.14, 129.97, 129.53, 129.33, 128.98, 128.37, 127.81, 127.75, 127.33, 126.79, 123.37, 57.72.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{22}H_{18}NO_3S$: 376.1007, found: 376.1005.

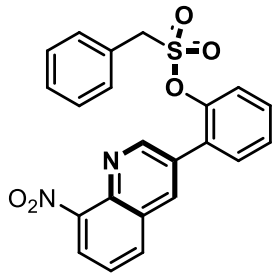


2-(8-methoxyquinolin-3-yl)phenylphenylmethanesulfonate(DG$_6$):

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.24 (s, 1H), 7.52 (dd, *J* = 17.1, 8.9 Hz, 2H), 7.44 (d, *J* = 6.4 Hz, 4H), 7.20 (dt, *J* = 16.7, 6.7 Hz, 5H), 7.12 (d, *J* = 7.6 Hz, 1H), 4.14 (s, 3H), 4.11 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.88, 146.59, 136.21, 132.00, 131.91, 130.87, 130.84, 130.01, 129.30, 128.98, 128.96, 127.76, 127.61, 126.76, 123.49, 120.08, 108.25, 77.48, 77.23, 76.98, 57.70, 56.29.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{23}H_{20}NO_4S$: 406.1113, found: 406.1112.

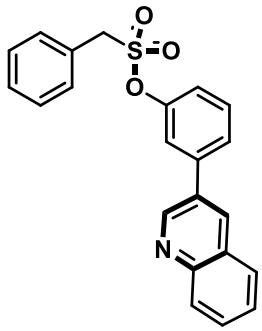


2-(8-nitroquinolin-3-yl)phenylphenylmethanesulfonate(DG$_7$):

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (d, *J* = 2.1 Hz, 1H), 8.28 (d, *J* = 2.1 Hz, 1H), 8.07 (d, *J* = 7.5 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.49 – 7.40 (m, 3H), 7.37 (d, *J* = 7.6 Hz, 1H), 7.22 – 7.15 (m, 5H), 4.30 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.26, 148.28, 146.21, 138.57, 136.15, 132.61, 131.97, 131.75, 131.24, 130.66, 130.49, 129.28, 128.93, 128.55, 127.87, 126.67, 125.88, 124.19, 123.40, 57.63.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{22}H_{17}N_2O_5S$: 421.0858, found: 421.0853.

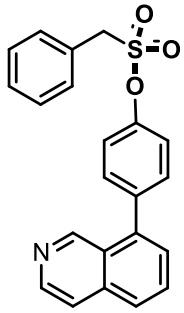


3-(quinolin-3-yl)phenylphenylmethanesulfonate (DG$_8$):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (d, *J* = 2.2 Hz, 1H), 8.24 (d, *J* = 1.9 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.80 – 7.71 (m, 1H), 7.61 (t, *J* = 7.8 Hz, 2H), 7.54 – 7.46 (m, 3H), 7.46 – 7.40 (m, 3H), 7.35 – 7.28 (m, 1H), 7.18 (dd, *J* = 8.1, 1.6 Hz, 1H), 4.60 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.98, 149.49, 147.67, 140.07, 133.94, 132.40, 131.17, 130.78, 130.12, 129.81, 129.65, 129.28, 128.27, 128.02, 127.53, 127.39, 126.21, 121.78, 121.15, 115.72, 57.36.

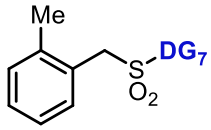
HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{22}H_{18}NO_3S$: 376.1001, found: 376.1006.



4-(isoquinolin-8-yl)phenylphenylmethanesulfonate(DG$_9$):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.59 – 8.54 (m, 1H), 7.88 – 7.81 (m, 1H), 7.76 – 7.68 (m, 2H), 7.55 – 7.40 (m, 8H), 7.26 (s, 2H), 4.61 (s, 2H).

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{22}H_{18}NO_3S$: 376.1001, found: 376.1004.

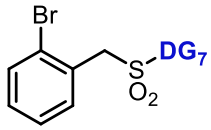


2-(8-nitroquinolin-3-yl)phenyl o-tolylmethanesulfonate (3a)

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (d, *J* = 2.2 Hz, 1H), 8.31 (t, *J* = 5.8 Hz, 1H), 8.07 (t, *J* = 6.9 Hz, 1H), 8.02 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.36 – 7.32 (m, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.09 (tt, *J* = 6.8, 3.4 Hz, 1H), 7.05 – 6.98 (m, 2H), 4.36 (s, 2H), 2.20 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.31, 146.17, 138.69, 138.27, 136.20, 132.61, 132.11, 131.85, 131.74, 131.52, 131.05, 130.58, 129.60, 128.57, 127.94, 126.51, 125.91, 125.12, 124.23, 123.64, 55.18, 19.56.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{23}H_{19}N_2O_5S$: 435.1015, found: 435.1010.

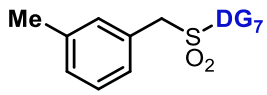


2-(8-nitroquinolin-3-yl)phenyl (2-bromophenyl)methanesulfonate (3b):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, *J* = 2.2 Hz, 1H), 8.30 (d, *J* = 2.2 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.03 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.50 – 7.42 (m, 4H), 7.38 (dt, *J* = 6.8, 3.4 Hz, 1H), 7.30 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.09 (td, *J* = 7.5, 1.3 Hz, 1H), 7.02 (td, *J* = 7.7, 1.7 Hz, 1H), 4.57 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.28, 148.43, 145.92, 138.68, 136.19, 133.46, 132.62, 132.50, 132.02, 131.84, 131.58, 130.88, 130.59, 128.53, 128.05, 127.91, 126.91, 125.86, 125.63, 124.14, 123.69, 56.91.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{22}H_{15}BrN_2NaO_5S$: 520.9777, found: 520.9771.



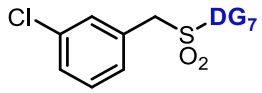
2-(8-nitroquinolin-3-yl)phenyl m-tolylmethanesulfonate (3c):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (d, *J* = 2.2 Hz, 1H), 8.31 (d, *J* = 2.2 Hz, 1H), 8.09 (d, *J* = 7.5 Hz, 1H), 8.02 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.66 (t, *J* = 7.9 Hz, 1H), 7.49 – 7.43 (m, 3H), 7.40 (dd, *J* = 7.0, 5.7 Hz, 1H), 7.09 – 6.97 (m, 4H), 4.25 (s, 2H), 2.22 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.34, 146.28, 138.87, 138.68, 136.18, 132.67, 132.01, 131.79, 131.41, 131.32, 130.56, 130.18, 128.87, 128.59, 127.93, 127.77, 126.48, 125.88, 124.74, 124.27, 123.54, 57.68, 21.35.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{23}H_{19}N_2O_5S$: 435.1015, found: 435.1008.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{22}H_{14}F_2N_2NaO_5S$: 479.0483, found: 479.0485.

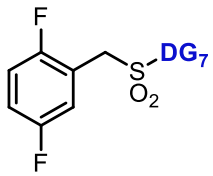


2-(8-nitroquinolin-3-yl)phenyl (3-chlorophenyl)methanesulfonate (3g):

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.30 (d, *J* = 1.4 Hz, 1H), 8.13 (d, *J* = 7.5 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.55 – 7.46 (m, 4H), 7.23 (d, *J* = 4.1 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 4.28 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.25, 146.01, 138.72, 136.13, 134.84, 132.62, 131.95, 131.37, 130.68, 130.65, 130.26, 129.64, 128.86, 128.58, 128.11, 126.11, 126.04, 124.32, 123.51, 56.98.

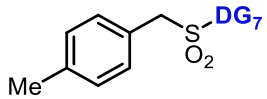
HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{22}H_{15}ClN_2NaO_5S$: 477.0282, found: 477.0285.



2-(8-nitroquinolin-3-yl)phenyl (2,5-difluorophenyl)methanesulfonate (3l):

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (d, *J* = 2.2 Hz, 1H), 8.31 (d, *J* = 2.2 Hz, 1H), 8.09 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.09 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.05 (dd, *J* = 8.3, 1.2 Hz, 1H), 8.05 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.48 – 7.44 (m, 1H), 6.98 (ddd, *J* = 8.2, 5.4, 2.8 Hz, 1H), 6.87 (tdt, *J* = 9.3, 8.0, 4.7 Hz, 1H), 4.35 (s, 2H

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.15, 145.91, 138.69, 136.14, 132.80, 132.57, 132.25, 132.17, 131.96, 131.90, 131.45, 130.64, 128.99, 128.89, 128.51, 128.18, 126.00, 124.27, 123.45, 118.63, 117.18, 50.31.

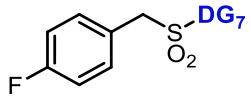


2-(8-nitroquinolin-3-yl)phenyl p-tolylmethanesulfonate (3n):

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.32 (s, 1H), 8.08 (d, *J* = 7.5 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.50 – 7.36 (m, 4H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.01 (d, *J* = 7.8 Hz, 2H), 4.26 (s, 2H), 2.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.39, 148.32, 146.36, 139.46, 138.65, 136.20, 132.63, 132.02, 131.77, 131.15, 130.62, 130.53, 129.74, 128.62, 127.88, 125.89, 124.27, 123.57, 123.45, 57.47, 21.34.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{22}H_{15}FN_2NaO_5S$: 461.0577, found: 461.0570.

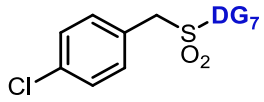


2-(8-nitroquinolin-3-yl)phenyl (4-fluorophenyl)methanesulfonate (3o):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, *J* = 2.2 Hz, 1H), 8.28 (d, *J* = 2.2 Hz, 1H), 8.11 (dt, *J* = 4.6, 2.3 Hz, 1H), 8.02 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.67 (dd, *J* = 8.2, 7.6 Hz, 1H), 7.52 – 7.40 (m, 4H), 7.21 – 7.16 (m, 2H), 6.91 – 6.85 (m, 2H), 4.26 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.32, 148.31, 146.09, 138.66, 136.13, 132.62, 132.55, 131.99, 131.85, 131.26, 130.62, 128.55, 128.04, 126.06, 124.43, 123.49, 122.61, 116.25, 116.07, 56.83.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{23}H_{19}N_2O_5S$: 435.1015, found: 435.1008.

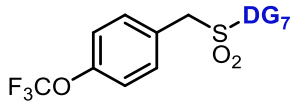


2-(8-nitroquinolin-3-yl)phenyl (4-chlorophenyl)methanesulfonate (3p):

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (t, *J* = 3.7 Hz, 1H), 8.28 (d, *J* = 2.1 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.00 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.66 (t, *J* = 7.9 Hz, 1H), 7.49 – 7.39 (m, 4H), 7.17 – 7.11 (m, 4H), 4.26 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.25, 148.21, 146.08, 138.58, 136.08, 135.59, 132.53, 131.99, 131.88, 131.84, 131.13, 130.57, 129.23, 128.50, 128.04, 126.07, 125.25, 124.45, 123.39, 56.84.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{22}H_{15}ClN_2NaO_5S$: 477.0282, found: 477.0288.

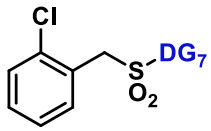


2-(8-nitroquinolin-3-yl)phenyl (4-(trifluoromethoxy)phenyl)methanesulfonate (3q):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 2.2 Hz, 1H), 8.32 (d, *J* = 2.2 Hz, 1H), 8.04 (ddd, *J* = 12.7, 7.9, 1.2 Hz, 2H), 7.67 – 7.60 (m, 1H), 7.50 – 7.42 (m, 3H), 7.36 – 7.32 (m, 1H), 7.26 (s, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.29 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.24, 149.87, 148.18, 146.19, 138.53, 136.10, 132.49, 132.37, 131.92, 131.81, 131.08, 130.54, 128.52, 128.04, 126.06, 125.45, 124.32, 123.23, 121.25, 56.70.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{23}H_{15}F_3N_2NaO_6S$: 527.0495, found: 527.0492.

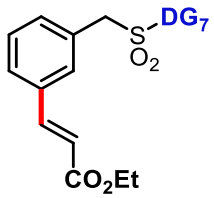


2-(8-nitroquinolin-3-yl)phenyl (2-chlorophenyl)methanesulfonate (8b):

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 – 9.03 (m, 1H), 8.29 (d, *J* = 2.1 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.05 – 7.98 (m, 1H), 7.67 – 7.61 (m, 1H), 7.50 – 7.42 (m, 4H), 7.30 – 7.27 (m, 1H), 7.20 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.10 (td, *J* = 7.7, 1.7 Hz, 1H), 7.04 (td, *J* = 7.5, 1.3 Hz, 1H), 4.54 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.24, 148.40, 145.95, 138.65, 136.17, 135.17, 132.59, 132.52, 132.01, 131.83, 131.53, 130.74, 130.56, 130.08, 128.52, 128.00, 127.27, 125.86, 125.11, 124.13, 123.58, 54.40.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{22}H_{15}ClN_2NaO_5S$: 477.0282, found: 477.0280.



(E)-ethyl 3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (2a):

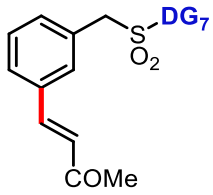
The compound was synthesized following the general procedure A in 0.2 mmol scale at room temperature for 48 hour. The pure compound was purified through silica column using ethyl acetate: petroleum ether (20:80) mixture as the eluent. Yield 75%; (mono:di 7:1) 68 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (d, *J* = 2.0 Hz, 1H), 8.26 (d, *J* = 2.0 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.48 (m, 5H), 7.34 (d, *J* = 4.5 Hz, 2H), 7.24 – 7.16 (m, 2H), 6.29 (d, *J* = 16.0 Hz, 1H), 4.30 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.70, 153.17, 148.34, 146.03, 143.23, 138.58, 136.02, 135.22, 132.54, 132.18, 131.90, 131.87, 131.33, 130.56, 130.08, 129.57, 128.76, 128.49, 128.02, 127.60, 125.91, 124.19, 123.46, 119.55, 60.78, 57.21, 14.46.

HRMS (*m*/*z*): $[M + H]^+$calcd for $C_{27}H_{23}N_2O_7S$: 519.1226, found: 519.1224



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-(3-oxobut-1-enyl)phenyl)methanesulfonate(2b):

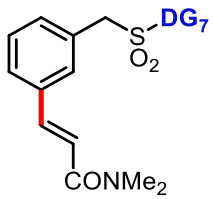
The compound was synthesized following the general procedure A in 0.2 mmol scale at room temperature for 48 hour. The pure compound was purified through silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 65%; (mono:di 13:1) 59 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (d, *J* = 1.8 Hz, 1H), 8.25 (d, *J* = 2.1 Hz, 1H), 8.05 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.98 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.52 – 7.39 (m, 4H), 7.37 – 7.33 (m, 2H), 7.29 (d, *J* = 16.3 Hz, 1H), 7.20 (dd, *J* = 7.8, 5.5 Hz, 2H), 6.55 (d, *J* = 16.3 Hz, 1H), 4.31 (s, 2H), 2.33 (d, *J* = 11.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.37, 153.15, 148.29, 145.91, 142.05, 138.51, 136.00, 135.23, 132.56, 132.40, 131.89, 131.29, 130.58, 130.26, 129.62, 128.99, 128.49, 128.07, 128.04, 127.66, 125.92, 124.16, 123.47, 57.14, 27.75.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{26}H_{20}N_2NaO_6S$: 511.0934, found: 511.0937.



(E)-2-(8-nitroquinolin-3-yl)phenyl(3-(3-(dimethylamino)-3-oxoprop-1-enyl)phenyl)-methanesulfonate(2c):

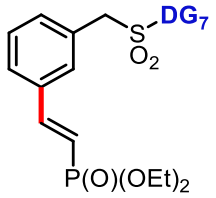
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (50:50) mixture as the eluent. Yield 74%, 77 mg mono olefinated product was isolated.

Appearance: Brown viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.25 (d, *J* = 2.1 Hz, 1H), 8.05 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.97 (d, *J* = 4.8 Hz, 1H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.48 – 7.38 (m, 5H), 7.37 – 7.30 (m, 2H), 7.15 (dd, *J* = 6.5, 2.2 Hz, 2H), 6.81 (d, *J* = 15.5 Hz, 1H), 4.29 (s, 2H), 3.15 (s, 3H), 3.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.43, 153.14, 148.20, 145.99, 141.03, 138.50, 136.12, 136.05, 132.63, 131.87, 131.81, 131.46, 131.27, 130.53, 129.75, 129.38, 128.69, 128.48, 128.00, 127.39, 125.94, 124.21, 123.43, 118.69, 57.24, 37.60, 36.09.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{23}N_3NaO_6S$: 540.1200, found: 540.1191.



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-(2-(diethoxyphosphoryl)vinyl)phenyl)methane-sulfonate(2d):

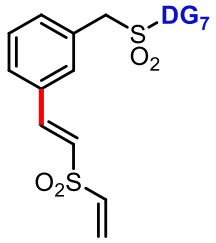
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (60:40) mixture as the eluent. Yield 72%, 84 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, J = 2.0 Hz, 1H), 8.28 (d, J = 2.1 Hz, 1H), 8.07 (dd, J = 7.5, 1.3 Hz, 1H), 8.01 (dd, J = 8.3, 1.1 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.48 – 7.42 (m, 4H), 7.38 – 7.31 (m, 3H), 7.19 (dd, J = 4.8, 1.7 Hz, 2H), 6.24 – 6.15 (m, 1H), 4.28 (s, 2H), 4.17 – 4.07 (m, 4H), 1.34 (t, J = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.20, 148.37, 147.40, 147.34, 146.09, 138.61, 136.09, 135.83, 135.60, 132.56, 132.21, 131.95, 131.86, 131.36, 130.61, 129.86, 129.57, 128.52, 128.50, 128.08, 127.56, 126.05, 124.24, 123.51, 116.65, 114.75, 62.20, 62.14, 57.26, 16.61, 16.55.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{28}H_{27}N_2NaO_8PS$: 605.1118: 372.1795, found: 605.1111.



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-(2-(vinylsulfonyl)vinyl)phenyl)methanesulfonate (2e):

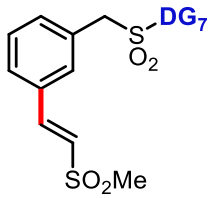
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (35:65) mixture as the eluent. Yield 40%, 43 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, *J* = 2.1 Hz, 1H), 8.26 (d, *J* = 2.1 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.01 (dt, *J* = 7.0, 3.5 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.51 – 7.47 (m, 2H), 7.46 – 7.42 (m, 2H), 7.42 – 7.36 (m, 1H), 7.34 (s, 1H), 7.31 (dt, *J* = 6.9, 1.7 Hz, 1H), 7.26 – 7.18 (m, 2H), 6.76 – 6.61 (m, 2H), 6.51 – 6.40 (m, 1H), 6.15 – 6.08 (m, 1H), 4.30 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.14, 148.35, 145.85, 143.06, 138.55, 137.62, 136.03, 133.28, 133.14, 132.58, 131.95, 131.39, 130.67, 130.54, 129.89, 129.38, 128.50, 128.18, 127.99, 126.88, 126.17, 124.30, 123.54, 57.03.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{26}H_{20}N_2NaO_7S_2$: 559.0604, found: 559.0598.



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-(2-(methylsulfonyl)vinyl)phenyl)methanesulfonate (2f):

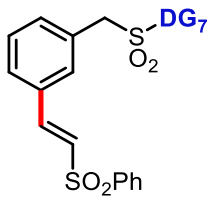
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (40:60) mixture as the eluent. Yield 62%, 65 mg mono olefinatedsolid product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (d, *J* = 2.1 Hz, 1H), 8.26 (d, *J* = 2.1 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.1 Hz, 1H), 8.03 – 8.00 (m, 1H), 7.66 (t, *J* = 7.9 Hz, 1H), 7.49 (q, *J* = 3.7 Hz, 2H), 7.47 – 7.42 (m, 2H), 7.40 (t, *J* = 11.1 Hz, 1H), 7.36 (s, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.25 (s, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 15.5 Hz, 1H), 4.30 (s, 2H), 3.04 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.14, 148.28, 145.79, 142.53, 138.49, 136.03, 133.19, 132.95, 132.62, 131.93, 131.36, 130.66, 130.53, 129.82, 129.36, 128.48, 128.17, 127.99, 127.64, 126.13, 124.28, 123.53, 57.02, 43.32.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{25}H_{20}N_2NaO_7S_2$: 547.0604, found: 547.0611.



(E)-8-nitro-3-(2-((3-(2-(phenylsulfonyl)vinyl)benzylsulfonyl)methyl)phenyl)quinoline (2g):

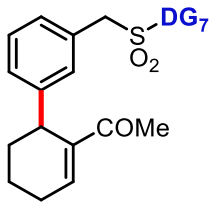
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (50:50) mixture as the eluent. Yield 71%, 83 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, *J* = 2.1 Hz, 1H), 8.25 (d, *J* = 2.1 Hz, 1H), 8.05 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.99 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.95 – 7.90 (m, 2H), 7.66 – 7.59 (m, 2H), 7.55 (t, *J* = 7.5 Hz, 2H), 7.46 (ddd, *J* = 12.2, 5.9, 3.9 Hz, 5H), 7.32 – 7.27 (m, 2H), 7.20 (dd, *J* = 6.3, 4.2 Hz, 2H), 6.81 – 6.76 (m, 1H), 4.28 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.14, 148.35, 145.85, 143.06, 138.55, 137.62, 136.03, 133.28, 133.14, 132.58, 131.95, 131.39, 130.67, 130.54, 129.89, 129.38, 128.50, 128.18, 127.99, 126.88, 126.17, 124.30, 123.54, 57.03.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{30}H_{23}N_2O_7S_2$: 587.0947, found: 587.0947.



(S)-2-(8-nitroquinolin-3-yl)phenyl (3-(2-acetylcyclohex-2-enyl)phenyl)methanesulfonate (2h):

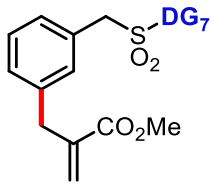
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 70%, 76 mg mono olefinated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 2.1 Hz, 1H), 8.35 (d, *J* = 2.1 Hz, 1H), 8.11 – 8.04 (m, 2H), 7.68 – 7.63 (m, 1H), 7.44 (tdt, *J* = 11.2, 7.5, 3.9 Hz, 3H), 7.18 – 7.06 (m, 4H), 7.01 (d, *J* = 8.7 Hz, 2H), 4.26 (d, *J* = 2.4 Hz, 2H), 3.95 (s, 1H), 2.37 (dd, *J* = 16.9, 5.1 Hz, 1H), 2.18 (s, 3H), 1.80 (tdd, *J* = 12.9, 5.6, 3.2 Hz, 2H), 1.67 – 1.59 (m, 1H), 1.40 (dddd, *J* = 23.4, 13.1, 10.4, 7.1 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.63, 153.43, 148.41, 146.54, 146.29, 142.98, 140.75, 138.70, 136.21, 132.70, 132.09, 131.66, 131.23, 130.56, 130.14, 129.12, 128.98, 128.71, 128.41, 127.85, 126.51, 125.92, 124.21, 123.50, 57.93, 38.35, 31.18, 26.26, 25.89, 16.87.

HRMS (*m*/*z*): $[M + Na]^+$ calculated. for $C_{30}H_{26}N_2NaO_6S$: 565.1404, found: 565.1399.



Methyl 2-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)benzyl)acrylate (2i):

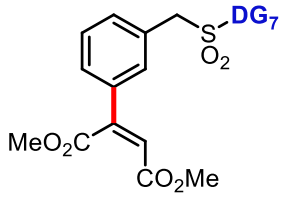
The compound was synthesized following the general procedure A in 0.2 mmol scale at room temperature for 48 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 65%, 67 mg mono olefinated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (d, *J* = 2.1 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H), 8.08 (ddd, *J* = 7.0, 3.9, 1.0 Hz, 1H), 8.03 (t, *J* = 6.2 Hz, 1H), 7.66 (dd, *J* = 10.2, 5.5 Hz, 1H), 7.45 (qd, *J* = 9.0, 4.4 Hz, 3H), 7.33 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.14 – 7.04 (m, 4H), 6.19 (s, 1H), 5.43 (d, *J* = 0.9 Hz, 1H), 4.26 (s, 2H), 3.67 (s, 3H), 3.51 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.28, 153.33, 148.35, 146.30, 139.80, 139.59, 138.66, 136.17, 132.65, 132.02, 131.77, 131.46, 131.29, 130.55, 130.11, 129.12, 128.81, 128.60, 127.95, 126.90, 126.77, 125.94, 124.27, 123.52, 57.64, 52.11, 37.95.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{27}H_{22}N_2NaO_7S$: 541.1040, found: 541.1041.



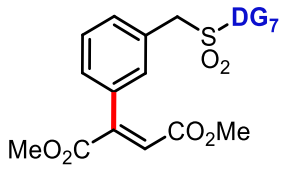
Dimethyl 2-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)maleate (2j):

The compound was synthesized following the general procedure A in 0.2 mmol scale at 120 °C for 36 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 55%, 62 mg mono olefinated product was isolated.

Appearance: Pale white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (d, *J* = 2.2 Hz, 1H), 8.38 (d, *J* = 2.2 Hz, 1H), 8.09 – 8.05 (m, 2H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.50 – 7.41 (m, 4H), 7.25 – 7.23 (m, 2H), 7.22 – 7.18 (m, 2H), 7.02 (s, 1H), 4.28 (d, *J* = 6.5 Hz, 2H), 3.76 (s, 3H), 3.55 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.38, 165.43, 153.43, 148.33, 146.45, 143.13, 138.69, 136.24, 134.76, 132.69, 132.05, 131.67, 131.44, 131.25, 130.98, 130.61, 130.08, 129.66, 128.67, 128.60, 127.96, 126.48, 125.98, 124.31, 123.64, 57.60, 53.19, 52.16.



Dimethyl 2-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)maleate (2k):

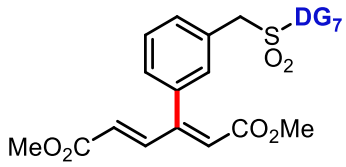
The compound was synthesized following the general procedure A in 0.2 mmol scale at 120 °C for 36 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 82% (mon:di – 7:1), 80 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (d, *J* = 2.0 Hz, 1H), 8.27 (d, *J* = 2.0 Hz, 1H), 8.09 – 8.06 (m, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.48 – 7.40 (m, 4H), 7.35 (s, 1H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.25 – 7.17 (m, 2H), 6.21 (s, 1H), 4.29 (s, 2H), 3.89 (s, 3H), 3.78 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.03, 165.35, 153.25, 148.38, 147.76, 146.03, 138.66, 136.09, 134.09, 132.63, 131.94, 131.92, 131.39, 130.64, 129.78, 128.99, 128.56, 128.14, 127.92, 127.73, 126.02, 124.29, 123.57, 118.51, 57.20, 53.04, 52.38.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{28}H_{22}N_2NaO_9S$: 585.0938, found: 585.0933.



(2Z,4Z)-dimethyl3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)hexa-2,4-dienedio-ate (2l):

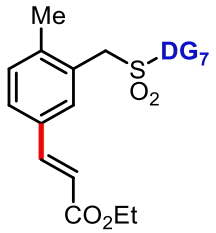
The compound was synthesized following the general procedure A in 0.2 mmol scale at 120 °C for 36 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (28:72) mixture as the eluent. Yield 35%, 41 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 – 9.05 (m, 1H), 8.65 (dd, *J* = 16.1, 0.8 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.04 (dt, *J* = 12.2, 3.9 Hz, 1H), 7.68 – 7.60 (m, 1H), 7.52 – 7.43 (m, 4H), 7.41 – 7.37 (m, 1H), 7.21 – 7.12 (m, 3H), 5.94 – 5.87 (m, 1H), 5.74 (d, *J* = 16.1 Hz, 1H), 4.30 (s, 2H), 3.79 (s, 3H), 3.74 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.78, 165.71, 153.27, 151.36, 148.33, 146.12, 140.06, 139.19, 138.63, 136.09, 132.56, 132.07, 131.89, 131.36, 131.31, 131.01, 130.63, 129.82, 129.41, 128.61, 128.11, 128.04, 127.31, 126.05, 124.34, 123.72, 123.50, 57.35, 52.16, 52.03.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{30}H_{24}N_2NaO_9S$: 611.1095, found: 611.1097.



(*E*)-ethyl 3-(4-methyl-3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4a):

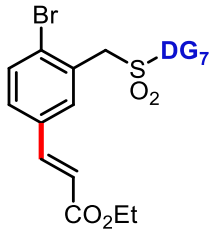
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 90%, 96 mg mono olefinated product was isolated.

Appearance: Pale white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (d, J = 1.9 Hz, 1H), 8.26 (d, J = 1.8 Hz, 1H), 8.07 (d, J = 7.5 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.62 (t, J = 7.9 Hz, 1H), 7.49 (ddd, J = 10.8, 6.5, 3.4 Hz, 1H), 7.43 (dd, J = 18.0, 10.2 Hz, 4H), 7.28 (s, 1H), 7.20 (t, J = 10.9 Hz, 1H), 7.06 (d, J = 7.9 Hz, 1H), 6.23 (d, J = 16.0 Hz, 1H), 4.35 (s, 2H), 4.25 (dd, J = 14.0, 6.8 Hz, 2H), 2.21 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.92, 153.14, 148.40, 145.93, 143.26, 140.55, 138.64, 136.07, 132.86, 132.54, 132.02, 131.88, 131.70, 131.62, 131.44, 130.64, 128.80, 128.49, 128.08, 125.95, 125.91, 124.20, 123.67, 118.54, 60.72, 54.74, 19.58,14.51.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{28}H_{24}N_2NaO_7S$: 555.1196, found: 555.1198.



(*E*)-ethyl 3-(4-bromo-3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4b):

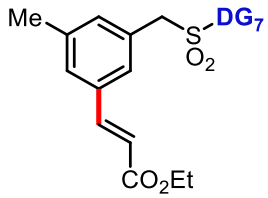
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 82%, 74 mg mono olefinated product was isolated.

Appearance: Pale white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (d, *J* = 2.1 Hz, 1H), 8.23 (d, *J* = 2.1 Hz, 1H), 8.03 (d, *J* = 7.4 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.49 (ddd, *J* = 12.8, 7.9, 6.6 Hz, 2H), 7.45 – 7.36 (m, 4H), 7.29 (t, *J* = 10.7 Hz, 1H), 7.12 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.21 (d, *J* = 16.0 Hz, 1H), 4.53 (s, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.52, 153.11, 145.69, 141.95, 138.58, 136.07, 134.29, 134.09, 132.57, 131.97, 131.93, 131.64, 131.58, 130.66, 129.74, 128.44, 128.19, 127.67, 127.15, 125.87, 124.16, 123.70, 120.16, 60.95, 56.40, 14.50.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{27}H_{22}BrN_2O_7S$: 597.0326, found: 597.0324.



(*E*)-ethyl 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4c):

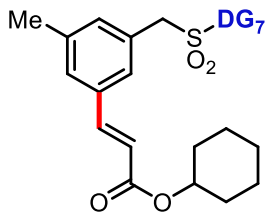
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 94%, 100 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (d, *J* = 2.1 Hz, 1H), 8.27 (d, *J* = 2.1 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.45 (tt, *J* = 18.7, 10.5 Hz, 5H), 7.14 (s, 2H), 7.02 (s, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 4.28 – 4.21 (m, 4H), 2.22 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.83, 153.19, 148.29, 146.03, 143.48, 139.62, 138.56, 136.05, 135.11, 133.08, 132.65, 131.89, 131.35, 130.59, 129.64, 128.48, 128.06, 127.34, 125.90, 124.31, 123.55, 119.24, 60.77, 57.18, 21.20, 14.49.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{28}H_{24}N_2NaO_7S$: 555.1196, found: 555.1199.



(*E*)-cyclohexyl 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)-acrylate (4d):

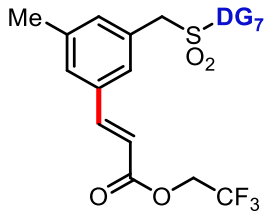
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 92%, 54 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (d, *J* = 2.2 Hz, 1H), 8.27 (d, *J* = 2.2 Hz, 1H), 8.06 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.98 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.60 (dt, *J* = 12.2, 6.1 Hz, 1H), 7.48 – 7.42 (m, 4H), 7.42 – 7.36 (m, 1H), 7.14 (s, 2H), 7.01 (s, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 4.91 – 4.82 (m, 1H), 4.26 (s, 2H), 2.22 (s, 3H), 1.90 (dd, *J* = 9.1, 4.0 Hz, 2H), 1.76 (dd, *J* = 8.8, 3.6 Hz, 2H), 1.60 – 1.52 (m, 1H), 1.50 – 1.42 (m, 2H), 1.42 – 1.32 (m, 2H), 1.32 – 1.24 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.22, 153.13, 148.21, 146.01, 143.12, 139.55, 138.51, 136.02, 135.14, 132.98, 132.63, 131.86, 131.83, 131.31, 130.55, 129.59, 128.44, 128.03, 127.27, 125.88, 124.27, 123.51, 119.79, 73.00, 57.13, 31.86, 25.54, 23.94, 21.16.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{32}H_{30}N_2NaO_7S$: 609.1666, found: 609.1666.



(*E*)-2,2,-difluoroethyl3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4e):

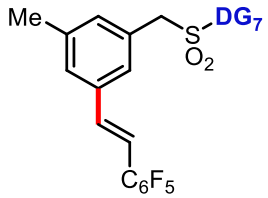
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 89%, 52 mg mono olefinated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 2.1 Hz, 1H), 8.27 (d, *J* = 2.2 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.98 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.64 – 7.59 (m, 1H), 7.53 – 7.47 (m, 3H), 7.47 – 7.44 (m, 2H), 7.18 (s, 1H), 7.16 (s, 1H), 7.07 (s, 1H), 6.32 (d, *J* = 16.0 Hz, 1H), 4.72 (t, *J* = 13.7 Hz, 2H), 4.27 (s, 2H), 2.26 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.99, 153.17, 148.34, 146.00, 145.96, 139.85, 138.56, 136.01, 134.48, 133.74, 132.59, 131.95, 131.92, 131.37, 130.63, 129.93, 128.50, 128.11, 127.56, 127.53, 125.90, 124.27, 123.57, 116.85, 60.57 (q, *J* = 365 Hz), 57.10, 21.20.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{32}H_{30}N_2NaO_7S$: 609.1666, found: 609.1664.



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-methyl-5-(perfluorostyryl)phenyl)methanesulfonate (4f):

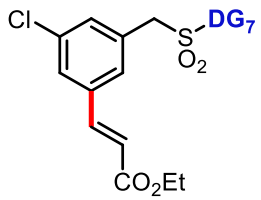
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (15:85) mixture as the eluent. Yield 77%, 96 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (d, *J* = 1.9 Hz, 1H), 8.30 (d, *J* = 1.9 Hz, 1H), 8.05 (d, *J* = 6.9 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.52 – 7.42 (m, 4H), 7.22 – 7.12 (m, 3H), 6.98 (s, 1H), 6.82 (d, *J* = 16.8 Hz, 1H), 4.29 (s, 2H), 2.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.20, 148.26, 146.10, 139.50, 138.57, 137.13, 136.25, 136.17, 136.07, 132.64, 131.88, 131.31, 130.59, 128.52, 128.45, 128.05, 127.25, 126.41, 125.79, 124.23, 123.55, 113.61, 57.31, 21.25.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{31}H_{20}F_5N_2O_5S$: 627.1008, found: 627.0999.



(*E*)-ethyl 3-(3-chloro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)-acrylate (4g)

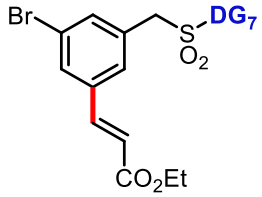
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 90%, 99 mg mono olefinated product was isolated.

Appearance: Pale white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, *J* = 1.9 Hz, 1H), 8.30 (dd, *J* = 12.7, 2.1 Hz, 1H), 8.09 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.01 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.65 (dd, *J* = 8.1, 7.6 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.47 (dt, *J* = 4.0, 2.2 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.32 (t, *J* = 1.6 Hz, 1H), 7.20 (dd, *J* = 3.2, 1.6 Hz, 2H), 6.32 – 6.27 (m, 1H), 4.30 – 4.22 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.32, 153.13, 148.28, 145.87, 141.64, 138.63, 136.90, 136.03, 135.49, 132.63, 132.00, 131.80, 131.32, 130.67, 129.24, 128.67, 128.47, 128.33, 128.25, 126.04, 124.46, 123.51, 121.03, 61.01, 56.56, 14.45.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{21}ClN_2NaO_7S$: 575.0650, found: 575.0654.



(*E*)-ethyl 3-(3-bromo-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4h):

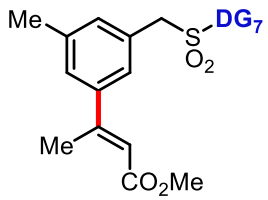
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 92%, 110 mg mono olefinated product was isolated.

Appearance: Yellowish solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (s, 1H), 8.28 (s, 1H), 8.08 (d, J = 7.4 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.52 – 7.42 (m, 5H), 7.36 (d, J = 18.5 Hz, 2H), 7.25 (s, 1H), 6.29 (d, J = 16.0 Hz, 1H), 4.28 – 4.20 (m, 4H), 1.33 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.28, 153.12, 148.26, 145.88, 141.53, 138.62, 137.10, 136.03, 134.65, 132.65, 131.99, 131.77, 131.60, 131.30, 130.66, 129.45, 128.76, 128.47, 128.24, 126.04, 124.46, 123.49, 123.40, 121.04, 60.99, 56.48, 14.44.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{27}H_{22}BrN_2O_7S$: 597.0326, found: 597.0368.



(*E*)-methyl 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)but-2-enoate (4i):

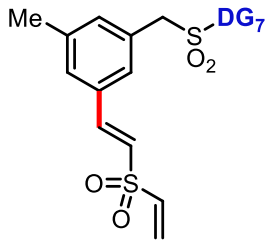
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 73%, 74 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (t, *J* = 4.2 Hz, 1H), 8.32 (d, *J* = 2.2 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.01 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.51 – 7.42 (m, 4H), 7.15 (s, 1H), 7.12 (s, 1H), 7.02 (s, 1H), 5.97 (d, *J* = 1.2 Hz, 1H), 4.25 (s, 2H), 3.74 (s, 3H), 2.44 (d, *J* = 1.2 Hz, 3H), 2.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.17, 154.81, 153.25, 148.27, 146.18, 142.84, 139.26, 138.59, 136.08, 132.62, 132.01, 131.96, 131.88, 131.29, 130.61, 128.54, 128.22, 128.08, 126.86, 125.95, 125.87, 124.34, 123.55, 117.37, 57.42, 51.38, 21.36, 18.02.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{28}H_{24}N_2NaO_7S$: 555.1196, found: 555.1199.



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-methyl-5-(2-(vinylsulfonyl)vinyl)phenyl)methanesulfonate (4j):

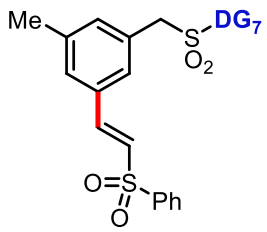
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP. The pure compound was purified by silica column using ethyl acetate: pet ether (40:60) mixture as the eluent. Yield 58%, 64 mg mono olefinated product was isolated.

Appearance: Brownish solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, *J* = 1.4 Hz, 1H), 8.27 (d, *J* = 2.1 Hz, 1H), 8.11 – 8.05 (m, 1H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.66 (td, *J* = 8.2, 1.9 Hz, 1H), 7.53 – 7.43 (m, 4H), 7.34 (d, *J* = 15.4 Hz, 1H), 7.13 (s, 1H), 7.11 (s, 1H), 7.07 (s, 1H), 6.74 – 6.59 (m, 2H), 6.43 (dd, *J* = 16.6, 2.0 Hz, 1H), 6.10 (dd, *J* = 9.8, 1.3 Hz, 1H), 4.26 (s, 2H), 2.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.08, 148.26, 145.88, 143.27, 140.01, 138.48, 137.69, 136.02, 134.14, 133.01, 132.61, 131.93, 131.89, 131.38, 130.63, 130.13, 129.16, 128.45, 128.14, 127.80, 127.75, 126.51, 126.14, 124.33, 123.54, 56.98, 21.16.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{22}N_2NaO_7S_2$: 573.0761, found: 573.0766.



(*E*)-2-(8-nitroquinolin-3-yl)phenyl (3-methyl-5-(2-(phenylsulfonyl)vinyl)phenyl)methan-esulfonate (4k):

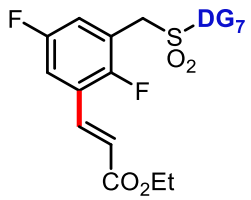
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate:pet ether (50:50) mixture as the eluent. Yield 86%, 103 mg mono olefinated product was isolated.

Appearance: Brown solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, *J* = 1.5 Hz, 1H), 8.27 (d, *J* = 2.0 Hz, 1H), 8.05 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.94 – 7.88 (m, 2H), 7.64 – 7.59 (m, 2H), 7.57 – 7.51 (m, 2H), 7.51 – 7.46 (m, 2H), 7.46 – 7.38 (m, 3H), 7.10 (s, 2H), 7.04 (s, 1H), 6.77 (d, *J* = 15.4 Hz, 1H), 4.24 (s, 2H), 2.21 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.04, 148.20, 145.90, 141.36, 140.59, 139.94, 138.45, 136.04, 134.00, 133.67, 132.97, 132.61, 131.91, 131.83, 131.34, 130.60, 130.02, 129.54, 128.41, 128.23, 128.12, 127.84, 127.62, 126.14, 124.34, 123.51, 56.92, 21.12.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{31}H_{24}N_2NaO_7S_2$: 623.0917, found: 623.0915.



(*E*)-ethyl 3-(2,5-difluoro-3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)-acrylate (4l):

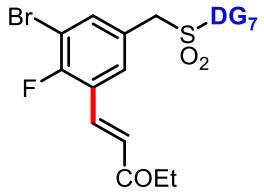
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour in HFIP solvent. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 85%, 94 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.31 (s, 1H), 8.09 (d, *J* = 7.3 Hz, 1H), 8.04 (d, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 16.2 Hz, 1H), 7.51 (s, 2H), 7.48 (d, *J* = 11.2 Hz, 2H), 7.11 (s, 1H), 7.01 (s, 1H), 6.40 (d, *J* = 16.2 Hz, 1H), 4.37 (s, 2H), 4.28 (q, *J* = 7.0 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.19, 153.10, 148.34, 145.83, 138.66, 136.10, 134.84, 132.55, 132.05, 131.88, 131.47, 130.69, 128.49, 128.30, 126.07, 124.40, 123.49, 123.18, 123.14, 120.23, 120.03, 116.33, 116.13, 61.15, 50.27, 14.46.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{20}F_2N_2NaO_7S$: 577.0857, found: 577.0852.



(*E*)-ethyl 3-(3-bromo-2-fluoro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-phenyl)acrylate (4m):

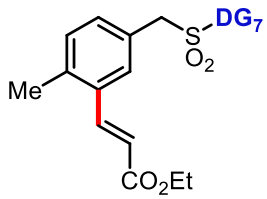
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (32:68) mixture as the eluent. Yield 72%, 86 mg mono olefinated product was isolated.

Appearance: Yellowish solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (d, *J* = 2.0 Hz, 1H), 8.29 (dd, *J* = 17.3, 2.2 Hz, 1H), 8.10 (d, *J* = 7.5 Hz, 1H), 7.99 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.67 (t, *J* = 7.9 Hz, 1H), 7.55 – 7.50 (m, 2H), 7.48 (dt, *J* = 5.8, 2.3 Hz, 2H), 7.43 (dd, *J* = 9.1, 7.0 Hz, 2H), 7.36 – 7.32 (m, 1H), 6.66 (d, *J* = 16.4 Hz, 1H), 4.22 (s, 2H), 2.70 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 200.45, 153.17, 148.30, 145.83, 138.66, 136.52, 136.02, 132.53, 132.37, 132.36, 132.02, 131.81, 131.32, 130.75, 130.22, 130.17, 130.07, 128.47, 128.36, 126.20, 124.94, 124.55, 123.60, 110.95, 56.05, 34.65, 8.14.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{20}BrFN_2NaO_6S$: 621.0102, found: 621.0109.



(*E*)-ethyl 3-(2-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4n):

The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 43%, 46 mg mono olefinated product was isolated.

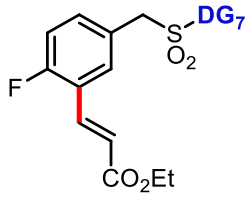
Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (d, *J* = 2.1 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H), 8.09 (d, *J* = 7.5 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.78 (d, *J* = 15.9 Hz, 1H), 7.65 (td, *J* = 7.8, 3.8 Hz, 1H),

7.50 – 7.43 (m, 4H), 7.39 (d, J = 1.1 Hz, 1H), 7.09 (dd, J = 7.8, 1.5 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.23 (d, J = 15.9 Hz, 1H), 4.30 – 4.21 (m, 4H), 2.32 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.90, 153.33, 148.30, 146.26, 141.26, 139.00, 138.63, 136.22, 134.31, 132.65, 131.98, 131.87, 131.56, 131.20, 130.65, 128.66, 128.61, 128.07, 125.97, 124.83, 124.41, 124.39, 123.54, 120.62, 60.87, 57.18, 19.75, 14.51.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{28}H_{24}N_2NaO_7S$: 555.1196, found: 555.1197.



(*E*)-ethyl 3-(2-fluoro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4o):

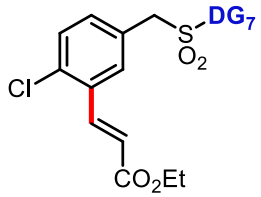
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (28:72) mixture as the eluent. Yield 75% (mono:di – 10:1), 73 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (d, J = 2.0 Hz, 1H), 8.26 (d, J = 2.1 Hz, 1H), 8.09 (dd, J = 7.5, 1.2 Hz, 1H), 7.98 (dd, J = 8.2, 0.9 Hz, 1H), 7.65 (t, J = 7.9 Hz, 1H), 7.57 (d, J = 16.2 Hz, 1H), 7.52 – 7.44 (m, 4H), 7.39 (dd, J = 6.7, 2.1 Hz, 1H), 7.21 – 7.15 (m, 1H), 6.92 (dd, J = 9.9, 8.7 Hz, 1H), 6.40 (d, J = 16.2 Hz, 1H), 4.30 – 4.22 (m, 4H), 1.33 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.57, 162.57, 160.53, 153.22, 148.21, 145.94, 138.57, 136.08, 135.98, 133.74, 133.66, 132.53, 131.91, 131.39, 131.37, 131.28, 130.66, 128.49, 128.16, 126.09, 124.51, 123.54, 123.33, 123.24, 122.18, 122.12, 117.15, 116.97, 60.98, 56.52, 14.46.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{21}FN_2NaO_7S$: 559.0946, found: 559.0949.



(*E*)-ethyl 3-(2-chloro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (4p):

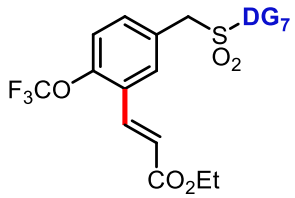
The compound was synthesized following the general procedure Ain 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 50%, 55 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, *J* = 2.1 Hz, 1H), 8.27 (d, *J* = 2.1 Hz, 1H), 8.10 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.98 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.87 (d, *J* = 16.0 Hz, 1H), 7.70 – 7.63 (m, 1H), 7.53 – 7.43 (m, 5H), 7.24 (d, *J* = 4.2 Hz, 1H), 7.15 – 7.11 (m, 1H), 6.30 (d, *J* = 16.0 Hz, 1H), 4.30 – 4.22 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.29, 153.25, 146.01, 139.27, 138.65, 136.06, 133.58, 132.78, 132.53, 131.93, 131.84, 131.22, 130.86, 130.68, 129.78, 128.49, 128.22, 126.15, 126.07, 124.58, 123.54, 122.19, 61.04, 56.68, 14.46.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{27}H_{21}ClN_2NaO_7S$: 575.0650, found: 575.0651.



(*E*)-ethyl 3-(5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-2-(trifluoromethoxy)-phenyl)acrylate (4q):

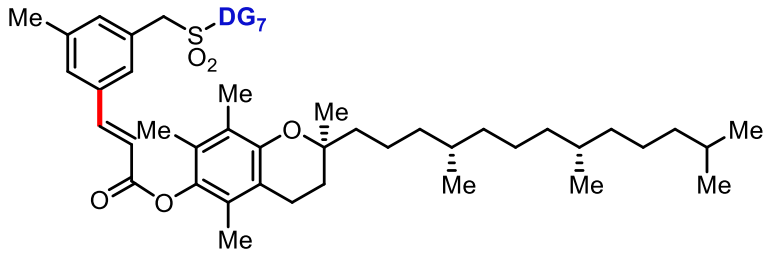
The compound was synthesized following the general procedure A in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 65%, 78 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14 (d, *J* = 1.8 Hz, 1H), 8.30 (t, *J* = 13.4 Hz, 1H), 8.12 – 7.98 (m, 2H), 7.79 – 7.69 (m, 1H), 7.69 – 7.62 (m, 1H), 7.57 – 7.38 (m, 5H), 7.28 (dd, *J* = 9.7, 7.6 Hz, 1H), 7.16 (dd, *J* = 8.5, 1.4 Hz, 1H), 6.38 (d, *J* = 16.1 Hz, 1H), 4.35 – 4.20 (m, 4H), 1.35 – 1.31 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.24, 153.31, 148.38, 148.05, 146.17, 136.18, 136.09, 133.30, 132.48, 131.96, 131.93, 131.24, 130.72, 130.47, 128.62, 128.26, 126.19, 126.02, 124.49, 123.46, 122.66, 121.74, 61.07, 56.66, 14.44.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{28}H_{21}F_3N_2NaO_8S$: 625.0863, found: 625.0868.



(*E*)-((S)-2,5,7,8-tetramethyl-2-((4S,8S)-4,8,12-trimethyltridecyl)chroman-6-yl) 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (5a):

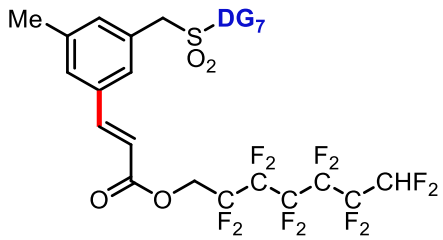
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by through silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 87%, 76 mg mono olefinated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (d, *J* = 2.2 Hz, 1H), 8.32 (d, *J* = 2.2 Hz, 1H), 8.09 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.02 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.66 (dd, *J* = 15.9, 8.2 Hz, 2H), 7.51 (ddd, *J* = 5.9, 3.9, 1.4 Hz, 2H), 7.49 – 7.45 (m, 2H), 7.26 – 7.25 (m, 1H), 7.23 (s, 1H), 7.07 (s, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 4.28 (s, 2H), 2.61 (t, *J* = 6.7 Hz, 2H), 2.27 (s, 3H), 2.11 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.86 – 1.74 (m, 3H), 1.63 (d, *J* = 17.5 Hz, 3H), 1.59 – 1.47 (m, 4H), 1.47 – 1.32 (m, 6H), 1.18 – 1.02 (m, 8H), 0.86 (dd, *J* = 8.7, 6.8 Hz, 14H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.49, 153.25, 149.68, 148.39, 146.11, 145.16, 140.62, 139.81, 138.63, 136.11, 135.06, 133.44, 132.62, 131.98, 131.91, 131.41, 130.66, 129.89, 128.55, 128.13, 127.61, 127.44, 126.97, 126.02, 125.23, 124.34, 123.63, 123.28, 118.39, 117.63, 75.29, 57.26, 39.57, 37.60, 37.49, 32.98, 28.19, 25.02, 24.66, 22.93, 22.84, 21.27, 20.83, 19.96, 19.90, 13.26, 12.41, 12.07.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{55}H_{68}N_2NaO_8S$: 939.4594, found 939.4511.



(*E*)-2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)-phenoxysulfonyl)methyl)phenyl)acrylate (5b):

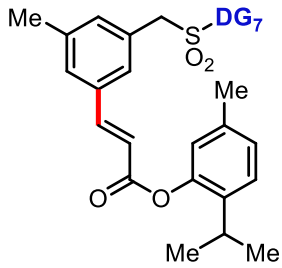
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 74%, 65 mg mono olefinated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, *J* = 2.1 Hz, 1H), 8.27 (d, *J* = 2.2 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.98 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.64 – 7.59 (m, 1H), 7.53 – 7.42 (m, 5H), 7.18 (s, 1H), 7.16 (s, 1H), 7.07 (s, 1H), 6.32 (d, *J* = 16.0 Hz, 1H), 6.07 (tt, *J* = 51.9, 5.1 Hz, 1H), 4.72 (t, *J* = 13.7 Hz, 2H), 4.27 (s, 2H), 2.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.05, 153.20, 148.37, 146.13, 145.97, 139.88, 138.59, 136.03, 134.49, 133.79, 132.60, 131.96, 131.39, 130.65, 129.98, 128.52, 128.14, 127.61, 127.53, 125.91, 124.29, 123.61, 116.80, 57.11, 21.21.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{33}H_{23}F_{12}N_2O_7S$: 819.1029, found: 819.1007.



(*E*)-2-isopropyl-5-methylphenyl 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (5c):

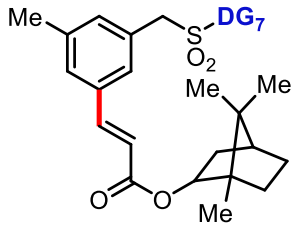
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (27:73) mixture as the eluent. Yield 89%, 57 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (d, *J* = 2.1 Hz, 1H), 8.32 (d, *J* = 2.1 Hz, 1H), 8.09 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.54 – 7.45 (m, 4H), 7.26 (d, *J* = 1.0 Hz, 1H), 7.23 (dt, *J* = 11.5, 5.8 Hz, 2H), 7.10 – 7.03 (m, 2H), 6.89 (s, 1H), 6.55 (dd, *J* = 16.0, 2.7 Hz, 1H), 4.28 (s, 2H), 3.03 (dt, *J* = 13.7, 6.8 Hz, 1H), 2.34 (s, 3H), 2.27 (s, 3H), 1.22 (dd, *J* = 6.9, 2.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.57, 153.21, 148.34, 148.05, 146.06, 145.37, 139.79, 138.59, 137.31, 136.78, 136.08, 134.90, 133.52, 132.61, 131.94, 131.91, 131.37, 130.64, 129.91, 128.52, 128.12, 127.61, 127.46, 127.38, 126.66, 125.97, 124.31, 123.58, 122.91, 118.32, 57.19, 29.88, 27.31, 23.28, 21.24, 21.05.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{36}H_{32}N_2NaO_7S$: 659.1822, found: 659.1823.



(*E*)-2-isopropyl-5-methylphenyl 3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)acrylate (5d):

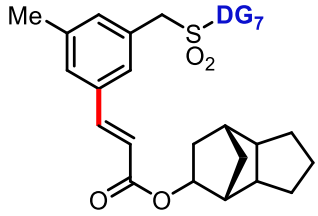
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 80%, 51 mg mono olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, *J* = 2.2 Hz, 1H), 8.29 (d, *J* = 2.2 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.99 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.50 – 7.45 (m, 4H), 7.38 (d, *J* = 16.0 Hz, 1H), 7.15 (s, 2H), 7.01 (s, 1H), 6.27 (d, *J* = 16.0 Hz, 1H), 4.79 (dd, *J* = 7.5, 4.0 Hz, 1H), 4.26 (s, 2H), 2.24 (s, 3H), 1.93 – 1.80 (m, 2H), 1.78 (t, *J* = 4.0 Hz, 1H), 1.62 – 1.54 (m, 1H), 1.25 (d, *J* = 5.0 Hz, 1H), 1.23 – 1.16 (m, 1H), 1.15 – 1.08 (m, 1H), 1.06 (s, 3H), 0.90 (s, 3H), 0.87 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.43, 153.21, 146.07, 143.20, 139.65, 138.60, 136.09, 135.22, 133.06, 132.66, 131.91, 131.38, 130.63, 129.74, 128.51, 128.10, 127.33, 127.28, 125.94, 124.34, 123.60, 119.85, 81.47, 57.22, 49.10, 47.20, 45.26, 39.06, 33.95, 27.26, 21.23, 20.34, 20.27, 11.74.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{37}H_{40}N_2NaO_6S$: 663.2499, found: 663.2499.



(*E*)-dicyclopentanyl-3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-phenyl)acryl-ate (5e):

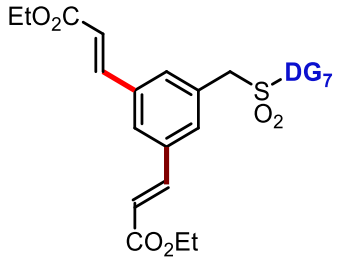
The compound was synthesized following the general procedure A in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by through silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 95%, 61 mg mono olefinatedproduct was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (d, *J* = 2.0 Hz, 1H), 8.28 (d, *J* = 2.1 Hz, 1H), 8.11 – 8.06 (m, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.63 (td, *J* = 7.9, 2.0 Hz, 1H), 7.50 – 7.44 (m, 4H), 7.38 (d, *J* = 16.0 Hz, 1H), 7.14 (s, 2H), 7.01 (s, 1H), 6.27 (d, *J* = 16.0 Hz, 1H), 4.67 (t, *J* = 10.9 Hz, 1H), 4.25 (s, 2H), 2.23 (s, 3H), 2.22 – 2.12 (m, 2H), 2.10 – 2.03 (m, 1H), 1.89 – 1.71 (m, 5H), 1.52 – 1.46 (m, 1H), 1.37 (q, *J* = 11.0 Hz, 2H), 1.23 (dt, *J* = 12.3, 5.9 Hz, 1H), 1.04 – 0.91 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.67, 153.21, 148.32, 146.05, 143.12, 139.63, 138.60, 136.07, 135.21, 133.02, 132.66, 131.91, 131.38, 130.62, 129.68, 128.50, 128.08, 127.29, 125.93, 124.33, 123.59, 119.80, 57.22, 47.48, 46.41, 43.20, 39.80, 39.33, 32.22, 31.88, 29.66, 27.93, 21.23.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{36}H_{34}N_2NaO_7S$: 661.1979, found: 661.1955.



(2*E*,2'*E*)-diethyl 3,3'-(5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-1,3-phenylene)diacrylate (7a):

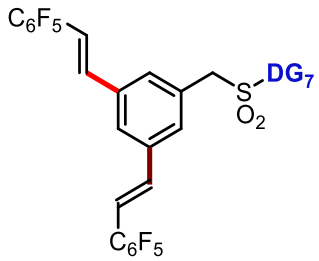
The compound was synthesized following the general procedure B in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (25:75) mixture as the eluent. Yield 68%, 42 mg homo-di-olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (d, *J* = 2.0 Hz, 1H), 8.26 (d, *J* = 2.0 Hz, 1H), 8.09 – 8.06 (m, 1H), 8.00 – 7.96 (m, 1H), 7.62 (t, *J* = 7.9 Hz, 1H), 7.50 (dd, *J* = 7.3, 4.5 Hz, 4H), 7.46 (t, *J* = 3.6 Hz, 3H), 7.34 (s, 2H), 6.35 (d, *J* = 16.1 Hz, 2H), 4.31 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.51, 153.12, 148.32, 145.88, 142.39, 138.59, 136.05, 136.00, 132.58, 132.00, 131.85, 131.38, 131.15, 130.68, 128.47, 128.44, 128.28, 128.24, 125.99, 124.40, 123.59, 120.57, 60.97, 56.89, 14.49.

HRMS (*m*/*z*): $[M + H]^+$calcd for $C_{32}H_{29}N_2O_9S$: 617.1594, found: 617.1587



2-(8-nitroquinolin-3-yl)phenyl (3,5-bis(perfluorostyryl)phenyl)methanesulfonate (7b):

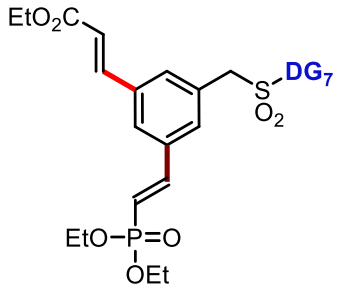
The compound was synthesized in 0.1 mmol scale at 80 °C for 24 hour. The di-olefnated product was obtained while the model substrate, phenylmethanesulfonate (**1**),was treated with the standard condition of procedure B. The pure compound was purified by silica column using ethyl acetate: pet ether (18:82) mixture as the eluent. Yield 73%, 59 mg homo-di-olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (d, *J* = 2.2 Hz, 1H), 8.29 (d, *J* = 2.2 Hz, 1H), 8.03 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.95 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.61 – 7.50 (m, 3H), 7.50 – 7.44 (m, 2H), 7.42 (s, 1H), 7.32 (s, 2H), 7.28 (s, 1H), 7.24 (s, 1H), 6.90 (d, *J* = 16.8 Hz, 2H), 4.36 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.15, 148.35, 145.98, 138.62, 137.98, 136.02, 135.52, 135.47, 135.39, 132.60, 132.01, 131.87, 131.38, 130.69, 129.06, 128.53, 128.22, 126.40, 125.78, 124.21, 123.64, 114.75, 112.01, 57.16.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{38}H_{18}F_{10}N_2NaO_5S$: 827.0669, found: 827.0647.



(*E*)-ethyl 3-(3-((E)-2-(diethoxyphosphoryl)vinyl)-5-((2-(8-nitroquinolin-3-yl)phenoxy-sulfonyl)meth-yl)phenyl)acrylate (7c):

The compound was synthesized following the general procedure Bin 0.1 mmol scale at 80 °C for 24 hour. The pure compound was by silica column using ethyl acetate: pet ether (55:45) mixture as the eluent. Yield 65%, 44 mg hetero-di-olefinated product was isolated.

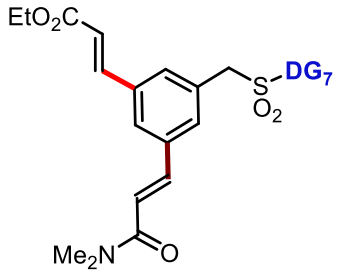
Appearance: Brown solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, *J* = 2.0 Hz, 1H), 8.29 (d, *J* = 2.0 Hz, 1H), 8.07 (d, *J* = 7.4 Hz, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.50 – 7.45 (m, 5H), 7.43 – 7.29

(m, 4H), 6.35 – 6.22 (m, 2H), 4.29 – 4.23 (m, 4H), 4.17 – 4.10 (m, 4H), 1.35 (dt, *J* = 10.6, 7.1 Hz, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.46, 153.08, 148.30, 146.52, 146.46, 145.90, 142.34, 138.55, 136.03, 135.99, 132.56, 131.96, 131.85, 131.38, 131.13, 131.06, 130.68, 128.46, 128.37, 128.26, 127.89, 126.09, 124.37, 123.60, 120.51, 62.29, 62.25, 60.94, 56.87, 16.63, 16.58, 14.47.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{33}H_{34}N_2O_{10}PS$: 681.1666, found: 681.1666



(*E*)-ethyl 3-(3-((E)-3-(dimethylamino)-3-oxoprop-1-enyl)-5-((2-(8-nitroquinolin-3-yl)-phenoxysulfonyl)meth-yl)phenyl)acrylate (7d):

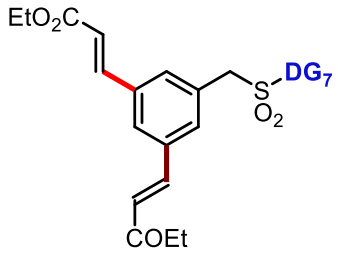
The compound was synthesized following the general procedure B in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (50:50) mixture as the eluent. Yield 88%, 54 mg hetero-di-olefinated product was isolated.

Appearance: Brownish solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (d, *J* = 2.1 Hz, 1H), 8.24 (d, *J* = 2.0 Hz, 1H), 8.04 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.50 – 7.47 (m, 3H), 7.46 – 7.38 (m, 4H), 7.33 (s, 1H), 7.28 (s, 1H), 6.89 (d, *J* = 15.4 Hz, 1H), 6.30 (d, *J* = 16.0 Hz, 1H), 4.31 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.20 (s, 3H), 3.06 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.52, 166.29, 153.03, 148.21, 145.80, 142.54, 140.31, 138.46, 136.96, 135.97, 135.73, 132.60, 131.95, 131.82, 131.34, 131.31, 130.63, 130.36, 128.43, 128.25, 128.17, 127.88, 125.96, 124.32, 123.52, 120.14, 119.73, 60.88, 56.82, 37.71, 36.20, 14.47.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{32}H_{30}N_3O_8S$: 616.1748, found: 616.1742.



(*E*)-ethyl 3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-5-((E)-3-oxopent-1-enyl)phenyl)acrylate (7e):

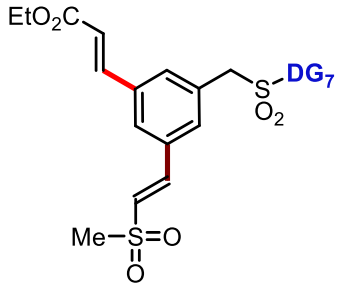
The compound was synthesized following the general procedure B in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 68%, 41 mg hetero-di-olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, *J* = 2.1 Hz, 1H), 8.25 (d, *J* = 2.0 Hz, 1H), 8.06 (d, *J* = 7.5 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 7.51 – 7.43 (m, 6H), 7.35 (t, *J* = 7.6 Hz, 3H), 6.66 (d, *J* = 16.2 Hz, 1H), 6.34 (d, *J* = 16.0 Hz, 1H), 4.32 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.70 (q, *J* = 7.3 Hz, 2H), 1.34 (dd, *J* = 9.4, 4.8 Hz, 3H), 1.16 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 200.68, 166.50, 153.08, 148.28, 145.77, 142.39, 139.90, 138.51, 136.27, 135.96, 132.59, 132.00, 131.87, 131.32, 131.17, 130.68, 128.46, 128.24, 127.75, 125.97, 124.31, 123.58, 120.49, 60.96, 56.84, 34.53, 14.48, 8.23.

HRMS (*m*/*z*): $[M+Na]^+$ calculated for $C_{32}H_{28}N_2NaO_8S$: 623.1464, found: 623.1468.



(*E*)-ethyl 3-(3-((E)-2-(methylsulfonyl)vinyl)-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-phenyl)acrylate (7f):

The compound was synthesized following the general procedure Bin 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (40:60) mixture as the eluent. Yield 71%, 44 mg hetero-di-olefinated product was isolated.

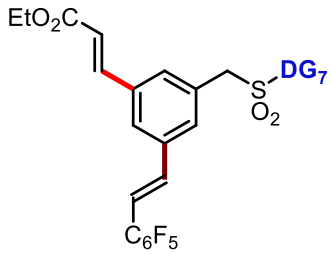
Appearance: Yellowish solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, *J* = 2.1 Hz, 1H), 8.24 (d, *J* = 2.1 Hz, 1H), 8.08 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.00 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.66 – 7.61 (m, 1H), 7.55 (ddd, *J* = 8.8, 7.6,

1.7 Hz, 2H), 7.48 – 7.41 (m, 5H), 7.37 (d, J = 4.2 Hz, 2H), 7.01 – 6.97 (m, 1H), 6.34 – 6.29 (m, 1H), 4.32 (s, 2H), 4.27 (q, J = 7.1 Hz, 2H), 3.10 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.36, 153.03, 145.56, 141.93, 141.70, 136.24, 135.94, 133.89, 132.62, 132.06, 131.98, 131.93, 131.72, 131.43, 130.77, 128.85, 128.75, 128.57, 128.47, 128.34, 126.16, 124.41, 123.66, 120.89, 77.55, 77.23, 76.91, 61.04, 56.71, 43.32, 14.50.

HRMS (*m*/*z*): $[M + H]^+$calcd for $C_{30}H_{27}N_2O_9S_2$: 623.1152, found: 623.1153



(*E*)-ethyl 3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-5-(perfluorostyryl)-phenyl)acrylate (7g):

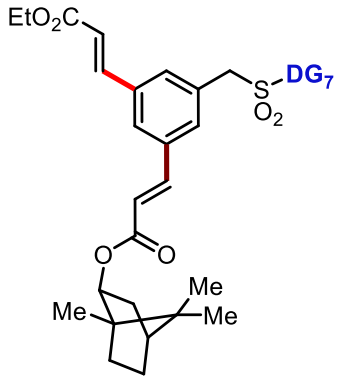
The compound was synthesized following the general procedure B in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 85%, 60 mg hetero-di-olefinatedproduct was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, J = 2.2 Hz, 1H), 8.27 (d, J = 2.1 Hz, 1H), 8.04 (dd, J = 7.5, 1.3 Hz, 1H), 7.96 (dd, J = 8.3, 1.1 Hz, 1H), 7.62 – 7.56 (m, 1H), 7.54 – 7.48 (m, 3H), 7.48 – 7.43 (m, 3H), 7.34 (s, 1H), 7.30 (s, 1H), 7.23 (t, J = 11.1 Hz, 1H), 6.89 (d, J = 16.8 Hz, 1H), 6.36 (d, J = 16.0 Hz, 1H), 4.34 (s, 2H), 4.27 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.57, 153.11, 148.28, 145.90, 142.68, 138.56, 138.04, 135.99, 135.90, 135.13, 132.60, 131.99, 131.83, 131.35, 130.66, 130.33, 130.01, 128.48, 128.34, 128.20, 127.17, 125.87, 124.29, 123.58, 120.27, 114.94, 60.94, 56.97, 14.48.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for$C_{35}H_{23}F_5N_2NaO_7S$: 733.1038, found: 733.1035.



(*E*)-ethyl 3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)-5-((E)-3-oxo-3-((2R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yloxy)prop-1-enyl)phenyl)acrylate (7h):

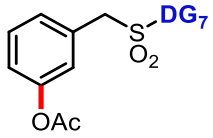
The compound was synthesized following the general procedure B in 0.1 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (30:70) mixture as the eluent. Yield 86%, 62 mg hetero-di-olefinated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (d, *J* = 2.2 Hz, 1H), 8.28 (d, *J* = 2.2 Hz, 1H), 8.07 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.99 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.52 – 7.39 (m, 7H), 7.35 (s, 1H), 7.33 (s, 1H), 6.37 (d, *J* = 7.8 Hz, 1H), 6.33 (d, *J* = 7.8 Hz, 1H), 4.80 (dd, *J* = 7.3, 4.2 Hz, 1H), 4.33 – 4.22 (m, 4H), 1.86 (dd, *J* = 6.9, 3.8 Hz, 1H), 1.80 – 1.69 (m, 4H), 1.63 – 1.55 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.18 – 1.11 (m, 1H), 1.07 (s, 3H), 0.90 (s, 3H), 0.87 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.50, 166.08, 153.12, 145.95, 142.41, 142.12, 136.16, 136.07, 136.01, 132.55, 131.99, 131.87, 131.40, 131.17, 130.68, 128.49, 128.41, 128.27, 128.24, 126.02, 124.37, 123.60, 121.15, 120.58, 81.69, 60.96, 49.13, 47.22, 45.29, 39.05, 33.97, 27.26, 20.33, 14.49, 11.73.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{40}H_{41}N_2O_9S$: 725.2527, found: 725.2521.



3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9a):

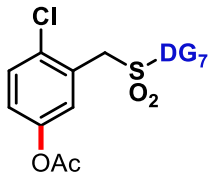
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 75%: 72 mg *meta*-acetoxylated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (dd, *J* = 7.2, 2.2 Hz, 1H), 8.29 (dd, *J* = 6.7, 2.2 Hz, 1H), 8.07 (dt, *J* = 7.5, 1.9 Hz, 1H), 8.03 – 7.99 (m, 1H), 7.66 – 7.59 (m, 1H), 7.49 – 7.40 (m, 3H), 7.37 (ddd, *J* = 8.2, 4.8, 2.6 Hz, 1H), 7.19 (dd, *J* = 13.3, 5.4 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 7.02 (t, *J* = 1.9 Hz, 1H), 6.98 – 6.92 (m, 1H), 4.28 (s, 2H), 2.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.31, 153.27, 150.88, 148.31, 146.12, 138.63, 136.09, 132.66, 131.91, 131.80, 131.30, 130.56, 129.95, 128.55, 128.18, 128.08, 128.00, 125.88, 124.22, 123.95, 123.51, 122.73, 57.11, 21.20.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{24}H_{19}N_2O_7S$: 479.0913, found: 479.0910.



4-chloro-3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9b):

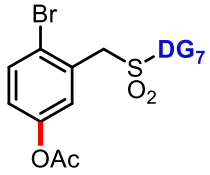
The compound was synthesized following the general procedure C in 0.2 mmol scale at 100 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 60%: 62 mg *meta*-acetoxylated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 – 9.03 (m, 1H), 8.35 – 8.27 (m, 1H), 8.12 – 8.06 (m, 1H), 8.03 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.69 – 7.61 (m, 1H), 7.51 – 7.43 (m, 4H), 7.21 (dd, *J* = 9.7, 6.5 Hz, 1H), 7.12 (d, *J* = 2.7 Hz, 1H), 6.88 (td, *J* = 8.5, 2.5 Hz, 1H), 4.50 (d, *J* = 8.4 Hz, 2H), 2.25 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.09, 153.27, 149.26, 148.41, 145.89, 138.70, 136.14, 132.68, 132.02, 131.96, 131.90, 131.54, 130.84, 130.65, 128.55, 128.14, 126.23, 125.87, 125.57, 124.24, 123.68, 54.16, 21.19.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{17}ClKN_2O_7S$: 551.0082, found: 551.0084.



4-bromo-3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9c):

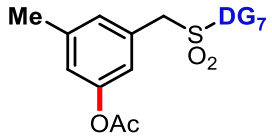
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 64%: 71 mg *meta*-acetoxylated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (d, *J* = 2.0 Hz, 1H), 8.31 (dd, *J* = 9.1, 2.0 Hz, 1H), 8.12 – 8.05 (m, 1H), 8.05 – 8.01 (m, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.51 – 7.42 (m, 4H), 7.38 (d, *J* = 8.7 Hz, 1H), 7.13 (d, *J* = 2.7 Hz, 1H), 6.81 (dt, *J* = 8.2, 4.1 Hz, 1H), 4.54 (s, 2H), 2.25 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.00, 153.27, 149.90, 145.85, 138.68, 136.16, 134.15, 132.69, 131.95, 131.89, 131.54, 130.65, 128.53, 128.15, 128.09, 125.86, 125.59, 124.42, 124.23, 123.72, 121.96, 56.64, 21.19.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{17}BrKN_2O_7S$: 594.9571, found: 594.9593.



3-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9d):

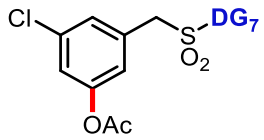
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 36hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 78%: 77 mg *meta*-acetoxylated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (dd, *J* = 8.3, 2.2 Hz, 1H), 8.32 (dd, *J* = 6.2, 2.3 Hz, 1H), 8.11 – 8.07 (m, 1H), 8.05 – 8.00 (m, 1H), 7.68 – 7.60 (m, 1H), 7.52 – 7.39 (m, 4H), 6.88 (t, *J* = 3.4 Hz, 1H), 6.82 (s, 1H), 6.77 (s, 1H), 4.24 (s, 2H), 2.25 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.47, 152.34, 149.86, 147.38, 145.21, 139.51, 137.69, 135.11, 131.69, 130.96, 130.82, 130.37, 129.60, 127.96, 127.59, 127.03, 126.82, 124.87, 123.27, 122.62, 122.48, 120.04, 56.22, 28.89, 20.25.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{25}H_{20}KN_2O_7S$: 531.0623, found: 531.0628.



3-chloro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9e):

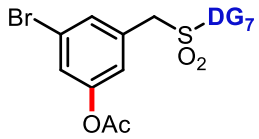
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 36hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 68%: 70 mg *meta*-acetoxylated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (d, *J* = 2.2 Hz, 1H), 8.28 (dd, *J* = 7.9, 2.2 Hz, 1H), 8.11 (dt, *J* = 8.5, 4.3 Hz, 1H), 8.03 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.48 (ddd, *J* = 11.6, 3.9, 2.9 Hz, 4H), 7.07 (t, *J* = 1.6 Hz, 1H), 6.95 (t, *J* = 1.9 Hz, 1H), 6.91 (t, *J* = 1.7 Hz, 1H), 4.24 (s, 2H), 2.27 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.96, 153.25, 151.25, 145.89, 138.70, 136.08, 135.23, 132.74, 131.95, 131.82, 131.37, 130.68, 129.37, 128.53, 128.22, 128.08, 126.02, 124.49, 123.58, 123.38, 122.46, 56.55, 21.18.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{17}ClKN_2O_7S$: 551.0082, found: 551.0079.



3-bromo-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9f):

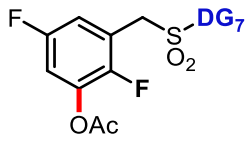
The compound was synthesized following the general procedure C in 0.2 mmol scale at 90 °C for 36hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 74%: 82 mg *meta*-acetoxylated product was isolated.

Appearance: Yellowish solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.05 (t, *J* = 14.9 Hz, 1H), 8.27 (d, *J* = 10.9 Hz, 1H), 8.15 – 8.07 (m, 1H), 8.02 (t, *J* = 9.6 Hz, 1H), 7.66 (dt, *J* = 11.6, 7.9 Hz, 1H), 7.56 – 7.40 (m, 4H), 7.20 (s, 1H), 7.09 (d, *J* = 11.1 Hz, 1H), 6.95 (d, *J* = 10.8 Hz, 1H), 4.25 – 4.19 (m, 2H), 2.24 (dd, *J* = 20.7, 17.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.95, 153.26, 151.26, 148.34, 145.92, 138.73, 136.08, 132.76, 131.97, 131.83, 131.41, 130.94, 130.69, 129.65, 128.55, 128.23, 126.23, 126.04, 124.50, 123.59, 122.95, 122.82, 56.48, 21.17.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{17}BrKN_2O_7S$: 594.9571, found: 594.9591.



2,5-difluoro-3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9g):

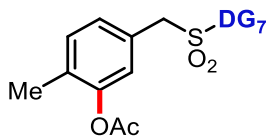
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 36 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 50%: 51 mg *meta*-acetoxylated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (d, *J* = 2.2 Hz, 1H), 8.32 (d, *J* = 2.2 Hz, 1H), 8.12 – 8.09 (m, 1H), 8.05 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.51 – 7.45 (m, 4H), 6.89 (ddd, *J* = 8.0, 4.9, 3.1 Hz, 1H), 6.80 (ddd, *J* = 8.7, 8.0, 5.0 Hz, 1H), 4.37 (s, 2H), 2.32 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.83, 153.20, 148.55, 148.36, 145.86, 138.73, 136.12, 132.66, 131.99, 131.89, 131.55, 131.33, 130.69, 128.54, 128.29, 128.22, 125.99, 124.43, 123.56, 115.59, 115.78, 113.31, 113.11, 96.33, 50.19, 20.60.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{16}F_2KN_2O_7S$: 553.0278, found: 553.0279.



2-methyl-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9h):

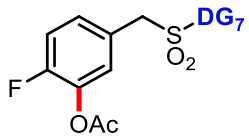
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 36 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 43%: 43 mg *meta*-acetoxylated product was isolated.

Appearance: Colourless solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (d, J = 2.0 Hz, 1H), 8.32 (d, J = 1.8 Hz, 1H), 8.09 (d, J = 6.8 Hz, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.50 – 7.42 (m, 3H), 7.42 – 7.37 (m, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.98 (d, J = 7.9 Hz, 1H), 6.95 (s, 1H), 4.25 (s, 2H), 2.29 (s, 3H), 2.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 169.20, 153.39, 149.54, 146.24, 138.66, 136.18, 132.70, 131.95, 131.89, 131.79, 131.73, 131.20, 130.59, 129.78, 128.62, 128.31, 128.00, 125.87, 125.50, 124.29, 123.58, 56.99, 20.92, 16.17.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{25}H_{20}KN_2O_7S$: 531.0623, found: 531.0625.



2-fluoro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9i):

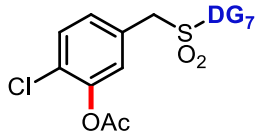
The compound was synthesized following the general procedure C in 0.1mmol scale at 80 °C for 36 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 52%: 26mg *meta*-acetoxylatedproduct was isolated.

Appearance: Viscous liquid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.28 (s, 1H), 8.10 (d, J = 7.3 Hz, 1H), 8.02 (d, J = 8.1 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 7.47 (dd, J = 13.7, 7.6 Hz, 3H), 7.40 (d, J = 7.9 Hz, 1H), 7.12 – 7.01 (m, 2H), 6.96 (t, J = 9.0 Hz, 1H), 4.34 – 4.18 (m, 2H), 2.31 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.24, 153.37, 136.11, 132.61, 131.95, 131.89, 131.30, 130.67, 129.56, 129.50, 128.59, 128.12, 127.33, 126.34, 126.04, 124.90, 124.42, 123.56, 117.42, 117.31, 56.61, 20.62.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{17}FKN_2O_7S$: 535.0372, found: 535.0377.



2-chloro-5-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl acetate (9j):

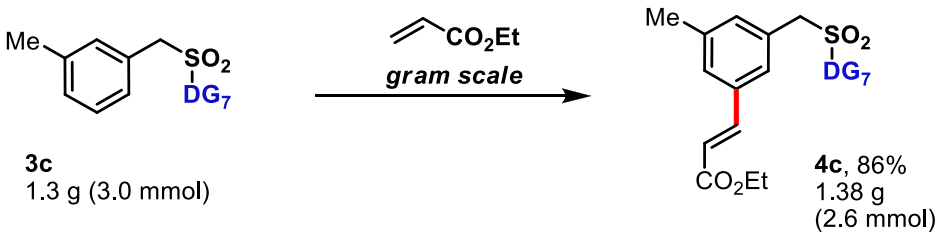
The compound was synthesized following the general procedure C in 0.2 mmol scale at 80 °C for 24 hour. The pure compound was purified by silica column using ethyl acetate: pet ether (20:80) mixture as the eluent. Yield 39%: 40 mg *meta*-acetoxylated product was isolated.

Appearance: Viscous liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, *J* = 2.2 Hz, 1H), 8.28 (d, *J* = 2.1 Hz, 1H), 8.12 – 8.09 (m, 1H), 8.01 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.51 – 7.45 (m, 3H), 7.42 (t, *J* = 5.6 Hz, 1H), 7.15 (tdd, *J* = 6.5, 4.2, 2.2 Hz, 1H), 7.08 (d, *J* = 2.0 Hz, 1H), 7.03 (dd, *J* = 8.3, 2.1 Hz, 1H), 4.25 (s, 2H), 2.32 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.45, 153.35, 148.30, 147.35, 146.05, 138.69, 136.11, 132.64, 132.02, 131.88, 131.23, 130.87, 130.67, 129.35, 129.19, 128.58, 128.16, 126.85, 126.08, 126.06, 124.50, 123.57, 56.63, 20.74.

HRMS (*m*/*z*): $[M + K]^+$ calculated for $C_{24}H_{17}ClKN_2O_7S$: 551.0082, found: 551.0086.

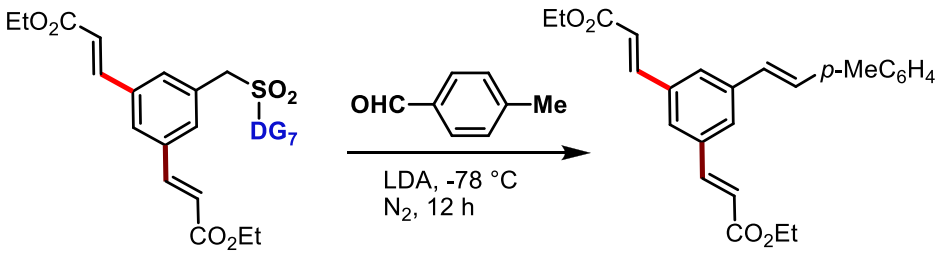


3c
1.3 g (3.0 mmol)

4c, 86%
1.38 g
(2.6 mmol)

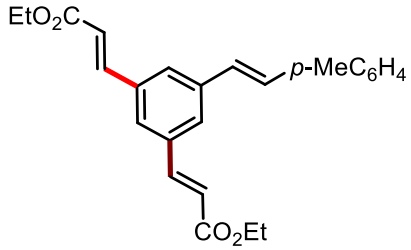
Procedure for gram scale reaction: In an oven dry round bottomed flask all the solid reagents were added sequentially; $Pd(OAc)_2$ (10 mol%, 67 mg), *N*-Ac-Gly-OH (20 mol%, 70 mg), and AgOAc (2.0 equiv, 6.0 mmol, 1.0 g) was taken and followed by 3.0 mmol (1.3 g) of *m*-tolylmethanesulfonate ester (**3c**) was added. To the mixture 6 mL of HFIP and ethyl acrylate (3.0 equiv, 9.0 mmol, 0.95 mL) were added. The reaction mixture was then placed on a preheated 80 °C oil bath and stirred for 24 hour. The reaction mixture was then diluted with EtOAc and filtered through celite pad. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and pure compound was isolated as colourless solid by petroleum ether/ethyl acetate (75:25) as the eluent. Yield: 86% (1.38 g).

3.3.2.d. Application



Procedure:[25] 0.25 mL freshly prepared LDA solution (2M in THF) was diluted with THF (5 mL) in a flame dry round bottomed flask, charged with a magnetic stir bar. The solution was then cooled to -78 °C. In an another round bottomed flask a solution of 4-methylbenzaldehyde

(0.3 mmol) and homo-di-olefinated product (**7a**, 0.2 mmol) was made in 20 mL dry THF. The solution was added slowly to the LDA/THF solution at -78 °C. Then the reaction mixture was allowed to attain room temperature and stirred overnight. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic layer was dried over Na_2SO_4. The desired compound was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.



(2*E*,2'*E*)-diethyl 3,3'-(5-(4-methylstyryl)-1,3-phenylene)diacrylate (10):

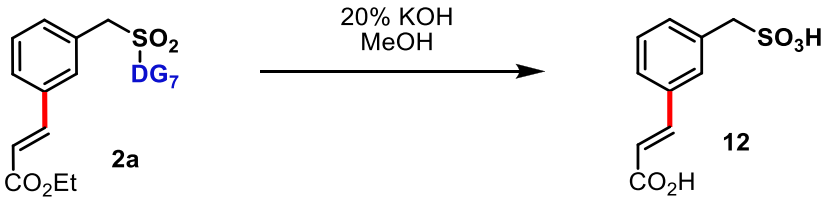
Pure compuoud was isolated in 70% yield, 82 mg by column chromatography using ethylacetate:petroleum ether (1:99) as eluent.

Appearance: Colourless solid.

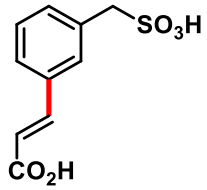
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 16.0 Hz, 2H), 7.62 (d, *J* = 1.2 Hz, 2H), 7.51 (s, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 7.16 – 7.00 (m, 2H), 6.50 (d, *J* = 16.0 Hz, 2H), 4.28 (q, *J* = 7.1 Hz, 4H), 2.37 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.88, 143.81, 139.02, 138.38, 135.64, 134.04, 130.63, 129.70, 127.43, 126.81, 126.36, 126.15, 119.61, 60.84, 21.48, 14.50.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{25}H_{26}NaO_4$: 413.1723, found: 413.1728.



Procedure:[16b] Olefinated compound **2a** (0.2 mmol, 103 mg) was dissolved in 5 mL of 20% KOH in MeOH solution and the reaction mixture was stirred for overnight at room temperature. After completion of the reaction (checked by TLC), methanol was removed in vacuo and a white solid appeared. Then the crude solid was washed with ethyl acetate for three times. After washing, solid di-acid **12** was obtained quantitatively.

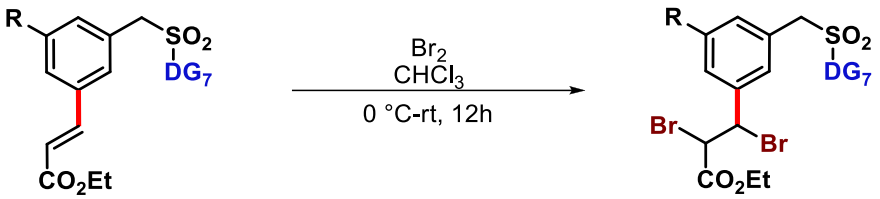


(*E*)-3-(3-(sulfomethyl)phenyl)acrylic acid (12):

Yield 83% (40 mg)

^{1}H NMR (400 MHz, D_2O) δ 7.41 (d, *J* = 11.0 Hz, 2H), 7.34 – 7.16 (m, 3H), 6.38 (d, *J* = 16.0 Hz, 1H), 4.03 (s, 2H).

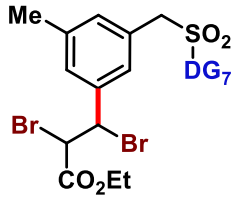
^{13}C NMR (101 MHz, D_2O) δ 175.27, 160.62, 140.02, 135.52, 132.69, 131.26, 129.45, 127.12, 125.05, 56.65.



11

R = Me; **13**, 92%
R = H; **14**, 94%

Procedure:[26] Bromine (2.0 equiv, 0.2 mmol) was added dropwise to a solution of olefinated product **11** (0.1 mmol) in chloroform (2 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred until complete consumption of starting material. The mixture was quenched with saturated sodium thiosulfate solution, and then the layers were separated. The aqueous layer was extracted with chloroform. Then the combined organic extract was dried ($MgSO_4$) and purified by column using EtOAc/petroleum ether (15:85). And colourless solid was obtained in quantitative yield.



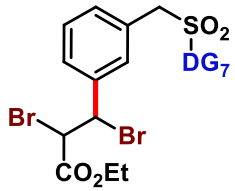
Ethyl 2,3-dibromo-3-(3-methyl-5-((2-(8-nitroquinolin-3-yl)phenylsulfonyl)methyl)phenyl)propane-ate (13):

Yield: 92%,(63.5 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (t, *J* = 3.1 Hz, 1H), 8.26 (d, *J* = 2.2 Hz, 1H), 7.96 (ddd, *J* = 5.0, 3.3, 1.3 Hz, 2H), 7.57 – 7.51 (m, 1H), 7.41 – 7.38 (m, 1H), 7.36 – 7.32 (m, 2H), 7.23 – 7.19 (m, 1H), 7.10 – 7.07 (m, 1H), 7.05 (s, 1H), 6.97 (s, 1H), 5.15 (d, *J* = 11.7 Hz, 1H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.27 – 4.21 (m, 2H), 4.16 (s, 2H), 2.18 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.75, 153.36, 148.35, 146.33, 139.87, 138.67, 138.61, 136.13, 132.58, 132.48, 131.99, 131.74, 131.24, 130.56, 129.98, 128.63, 128.03, 127.66, 127.49, 126.02, 124.29, 123.57, 62.84, 57.35, 50.01, 46.90, 21.31, 14.03.

HRMS (*m/z*): $[M + H]^+$ calculated for $C_{28}H_{25}Br_2N_2O_7S$: 690.9749 found: 690.9743.



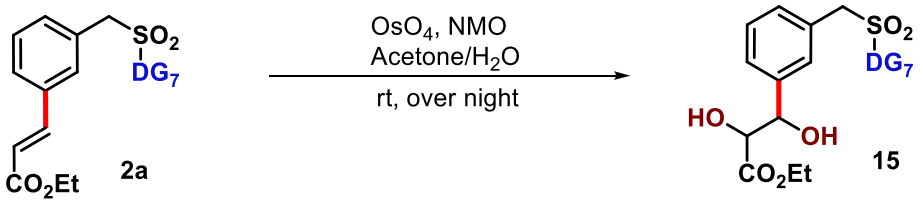
Ethyl2,3-dibromo-3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)propanoate (14):

Yield: 94% (63.5 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (d, *J* = 2.1 Hz, 1H), 8.34 (d, *J* = 2.1 Hz, 1H), 8.11 – 8.05 (m, 2H), 7.71 – 7.65 (m, 1H), 7.51 – 7.43 (m, 3H), 7.37 – 7.32 (m, 2H), 7.31 – 7.26 (m, 2H), 7.24 (t, *J* = 5.7 Hz, 1H), 5.25 (d, *J* = 11.7 Hz, 1H), 4.74 (d, *J* = 11.7 Hz, 1H), 4.38 – 4.28 (m, 4H), 1.38 – 1.34 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.76, 153.43, 148.46, 146.31, 138.85, 138.76, 136.18, 132.64, 132.05, 131.80, 131.66, 131.30, 130.64, 130.57, 129.77, 129.27, 128.70, 128.08, 127.73, 126.08, 124.34, 123.58, 62.95, 57.43, 49.82, 46.96, 14.10.

HRMS (*m/z*): $[M + H]^+$ calculated for $C_{27}H_{23}Br_2N_2O_7S$: 676.9593, found: 676.9587.



Ethyl 2,3-dihydroxy-3-(3-((2-(8-nitroquinolin-3-yl)phenoxysulfonyl)methyl)phenyl)propaneate (15):[27]

Yield:78%(43 mg)

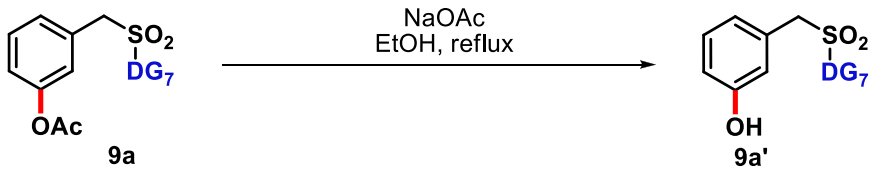
Procedure: To a solution of **cinnamate (2a)** (0.1 mmol, 52 mg) in a mixture of acetone (1 mL), and H_2O (1 mL) were added NMO (0.2 mmol, 2.0 equiv, 23.4 mg) and OsO_4 (2% by *wt*in H_2O, 0.01 mmol, 125 mg) and the mixture was stirred at room temperature for overnight. After completion of the reaction EtOAc and saturated solution of $Na_2S_2O_3$ were added to the reaction mixture. The aqueous layer was extracted with EtOAc, and the combined organic layer was washed with brine solutioin, and dried over Na_2SO_4. The solvent was removed under reduced pressure and the pure compound was obtained by column chromatography on silica

gel eluted with petroleum ether/EtOAc (30:70) to afford the 1,2-dihydroxy compound **15** as colourless solid.

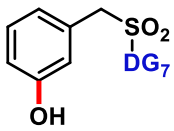
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 2.2 Hz, 1H), 8.24 (d, *J* = 2.2 Hz, 1H), 8.10 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.03 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.66 – 7.61 (m, 1H), 7.53 – 7.47 (m, 3H), 7.47 – 7.40 (m, 2H), 7.26 (s, 1H), 7.04 (dt, *J* = 7.5, 2.9 Hz, 2H), 5.09 – 5.04 (m, 1H), 4.43 – 4.35 (m, 3H), 4.34 – 4.28 (m, 2H), 3.82 (d, *J* = 6.4 Hz, 1H), 3.62 (t, *J* = 6.3 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.61, 153.35, 147.79, 145.33, 141.84, 138.00, 136.21, 132.98, 132.28, 131.89, 131.47, 130.68, 130.15, 129.06, 128.80, 128.79, 128.19, 127.70, 126.97, 125.93, 124.76, 124.24, 74.71, 74.18, 62.33, 57.57, 14.37.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{27}H_{25}N_2O_9S$: 553.1281, found: 553.1281.



Procedure:[28] To the stirred solution of acetoxylated compound (**9a,** 1.0 equiv) in EtOH (5 mL/mmol), NaOAc (10 equiv) in H_2O (2.5 mL/mmol) was added and the reaction mixture was refluxed for overnight. After completion of reaction, The mixture was diluted with H_2O and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and the pure product was isolated as colourless solid by column chromatography using petroleum:ethyl acetate (75:25) as eluent.

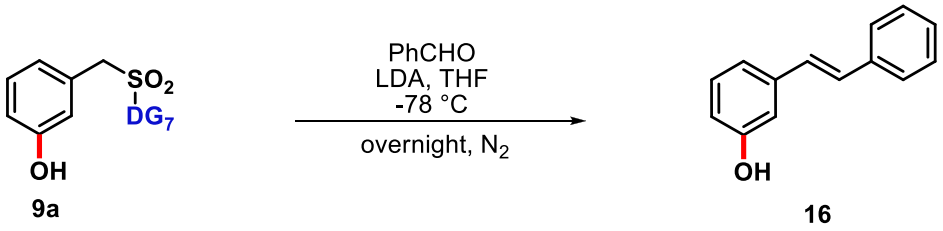


2-(8-nitroquinolin-3-yl)phenyl (3-hydroxyphenyl)methanesulfonate(9a'):

^{1}H NMR (400 MHz, MeOD) δ 8.98 (d, *J* = 2.1 Hz, 1H), 8.42 (d, *J* = 2.0 Hz, 1H), 8.13 (t, *J* = 7.8 Hz, 2H), 7.70 (t, *J* = 7.9 Hz, 1H), 7.56 (dd, *J* = 6.7, 2.5 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.36 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.93 (t, *J* = 7.9 Hz, 1H), 6.69 (s, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 6.58 (dd, *J* = 8.2, 1.8 Hz, 1H), 4.44 (s, 2H).

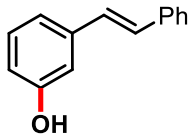
^{13}C NMR (101 MHz, CD_3CN): δ 158.32, 154.41, 149.66, 147.86, 139.33, 137.63, 133.68, 133.31, 133.25, 132.80, 131.80, 131.17, 130.04, 129.80, 129.23, 127.56, 124.90, 124.36, 123.54, 118.83, 117.36, 58.00.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{22}H_{17}N_2O_6S$: 437.0807, found: 437.0803.



9a **16**

Procedure:[16b] Freshly prepared LDA solution (0.15 mL/mmol; 2M in THF) was taken in a flame dry round bottomed flask, charged with a magnetic stir bar. The solution was then cooled to -78 °C. In an another round bottomed flask a solution of benzaldehyde (2.0 equiv) and phenol (**9a'**, 1.0 equiv) was made in dry THF (10 mL/mmol). The solution was added slowly to the LDA/THF solution at -78 °C. Then the reaction mixture was allowed to attain room temperature and stirred overnight. The reaction mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic layer was dried over Na_2SO_4. The desired compound was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate(98:2) as the eluent.

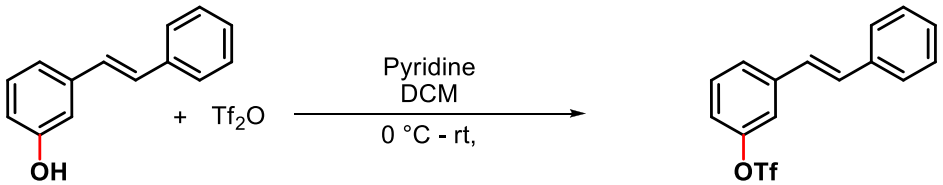


(*E*)-3-styrylphenol (16):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 2H), 7.39 – 7.32 (m, 2H), 7.26 (s, 2H), 7.13 – 7.04 (m, 3H), 7.01 – 6.97 (m, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.83 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.00, 139.33, 137.36, 130.09, 129.43, 128.91, 128.45, 127.96, 126.78, 119.69, 114.88, 113.17.

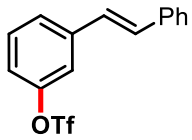
HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{14}H_{13}O$: 197.0966, found:197.9627.



16 **17**

Procedure:[29] To a solution of (*E*)-3-styrylphenol **16** (1 equiv) in dry dichloromethane anhydrous pyridine (1.5equiv) was added at 0 °C and stirred for 15 min, followed by triflic anhydride (2.0 equiv) was added. After allowing the reaction mixture to attain room

temperature, the reaction mixture was stirred for overnight. The reaction was quenched with saturated aqueous bicarbonate solution and extracted with DCM. The organic layer was dried over sodium sulfate, concentrated to dryness under reduced pressure, and purified by column chromatography using petroleum ether as eluent. Pure compound was isolated as colourlessliquid in 92% yield.

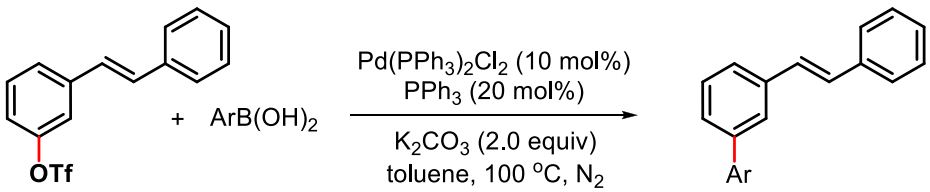


(E)-3-styrylphenyl trifluoromethanesulfonate (17):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.49 (m, 3H), 7.47 – 7.35 (m, 4H), 7.31 (t, *J* = 7.3 Hz, 1H), 7.19 – 7.03 (m, 3H).

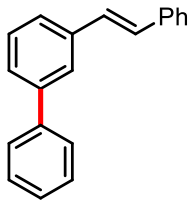
^{13}C NMR (101 MHz, $CDCl_3$) δ 150.27, 140.44, 136.63, 131.50, 130.60, 129.03, 128.60, 127.00, 126.70, 126.55, 120.10, 119.12.

GC-MS (*m/z*): 328.1 $[M]^+$.



17 18

Procedure: In an oven dried reaction tube charged with magnetic stir bar, triflate (**17**, 0.1 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (10 mol%, 0.01 mmol, 7.0 mg), PPh_3 (20 mol%, 0.02 mmol, 5.2 mg), K_2CO_3 (0.2 mmol, 2.0 equiv, 27.6 mg) and aryl boronic acid (0.15 mmol, 1.5 equiv) have been taken. The reaction tube was closed by a screw capfor evacuation and back filled with N_2 for three times. Then 2 mL of dry toluene was added to the reaction mixture and placed in a preheated oil bath at 100 °C. The reaction mixture was stirred vigorously for 24 h. The reaction mixture was allowed to cool to room temperature and filtered through the celite pad. The filtrate was concentrated under reduced pressure and pure product was isolated by column chromatography using petroleum ether as the eluent.



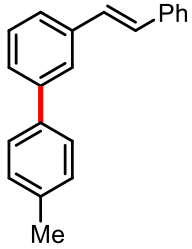
(*E*)-3-styrylbiphenyl (18a):

Yield: 76%, (19.5 mg)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.68 – 7.62 (m, 2H), 7.60 – 7.42 (m, 7H), 7.39 (t, J = 7.6 Hz, 3H), 7.29 (t, J = 7.4 Hz, 1H), 7.20 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.93, 141.32, 138.00, 137.47, 129.31, 129.26, 128.99, 128.92, 128.79, 127.92, 127.62, 127.42, 126.77, 126.74, 125.64, 125.59.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{20}H_{16}Na$: 279.1150, found: 279.1153.



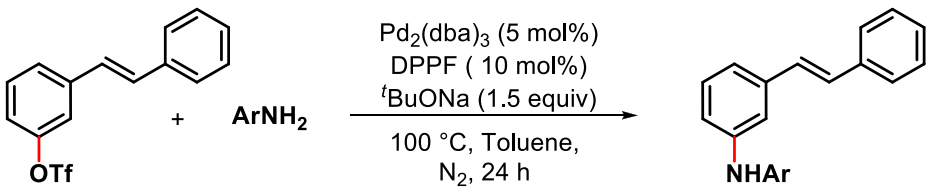
(*E*)-4'-methyl-3-styrylbiphenyl (18b):

Yield: 70% (19 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (t, J = 1.6 Hz, 1H), 7.57 – 7.51 (m, 4H), 7.48 (ddt, J = 7.3, 5.5, 1.5 Hz, 2H), 7.43 (d, J = 7.4 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.28 (ddd, J = 5.6, 3.1, 1.2 Hz, 3H), 7.17 (s, 2H), 2.41 (s, 3H).

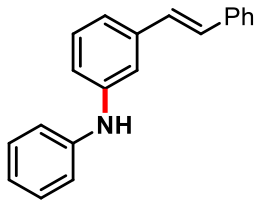
^{13}C NMR (101 MHz, $CDCl_3$) δ 141.86, 138.44, 137.97, 137.53, 137.42, 129.72, 129.27, 129.19, 128.92, 128.90, 127.89, 127.25, 126.77, 126.58, 125.48, 125.32, 21.34.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{21}H_{18}Na$: 293.1306, found: 293.1301.



Procedure:[30] In an oven dried reaction tube charged with magnetic stir bar, aryl amine (0.2 mmol, 2.0 equiv), $Pd_2(dba)_3$ (5mol%, 0.005 mmol, 4.5 mg), DPPF (10 mol%, 0.01 mmol, 5.5 mg), ^{t}BuONa (0.15 mmol, 1.5equiv, 14.4 mg) have been taken. The reaction tube was closed

by a screw cap for evacuation and back filled with N_2 for three times. Then 2 mL of dry toluene was added to the reaction mixture was stirred vigorously at 85 °C. In another reaction tube a solution of triflate (0.1 mmol, 1.0 equiv) was made in degassed toluene and added drop wise to the previous mixture.The reaction mixture was stirred vigorously for 24 h. The reaction mixture was allowed to cool to room temperature and filtered through the celite pad. The filtrate was concentrated under reduced pressure and pure product was isolated by column chromatography using petroleum ether as the eluent.



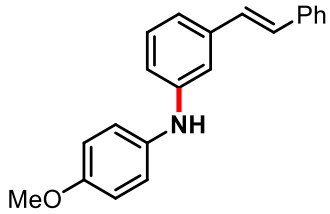
(*E*)-N-phenyl-3-styrylaniline (19a):

Yield: 71% (19.5 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.4 Hz, 3H), 7.37 (t, *J* = 7.6 Hz, 3H), 7.31 – 7.26 (m, 1H), 7.24 – 7.21 (m, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.08 (dd, *J* = 10.9, 5.8 Hz, 4H), 6.99 (s, 1H), 6.77 – 6.71 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.06, 139.27, 137.35, 130.07, 129.55, 129.35, 128.90, 128.46, 127.94, 126.76, 119.60, 119.28, 115.71, 114.91, 113.17.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{20}H_{17}NNa$: 294.1256, found: 294.1259.



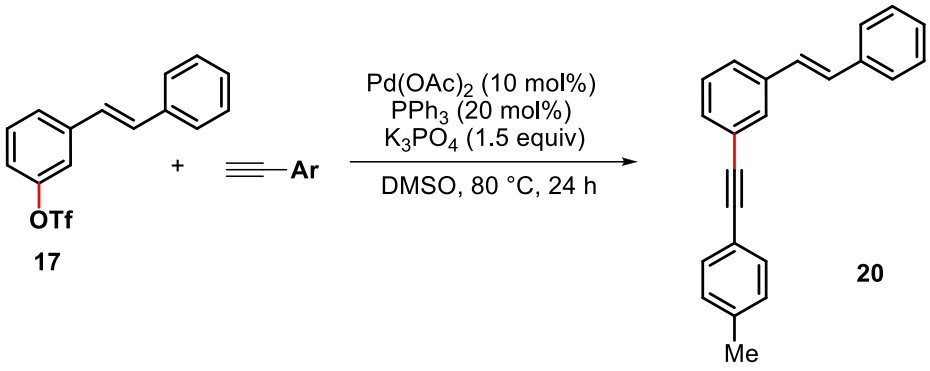
(*E*)-N-(4-methoxyphenyl)-3-styrylaniline (19b):

Yield: 66% (20 mg)

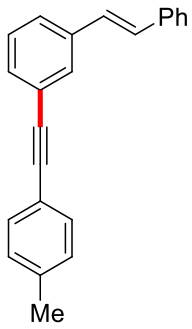
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 16.0 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.42 (dd, *J* = 5.0, 1.8 Hz, 2H), 7.35 (dd, *J* = 10.3, 4.7 Hz, 2H), 7.20 (t, *J* = 7.9 Hz, 1H), 7.11 (dd, *J* = 6.9, 1.9 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 1H), 7.04 (s, 1H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.90 – 6.87 (m, 2H), 5.53 (s, 1H), 3.82 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.56, 137.57, 135.04, 130.73, 129.20, 129.08, 128.87, 128.62, 127.78, 126.72, 125.65, 122.68, 118.24, 115.38, 114.95, 113.75, 55.81.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{21}H_{20}NO$: 302.1545, found: 302.1530.



Procedure:[31] Aryl triflate (**17**, 0.1 mmol, 1.0 equiv), 4-ethynyltoluene (0.15 mmol, 1.5 equiv), $Pd(OAc)_2$ (10 mol%, 0.01 mmol, 2.2 mg), PPh_3 (20 mol%, 0.02 mmol, 5.2 mg) and K_3PO_4, (0.15 mmol, 1.5 equiv, 31.8 mg) was taken in a reaction tube and 2 mL of DMSO was added under N_2 atmosphere. The reaction mixture was stirred for 24 h at 80 °C. After completion of the reaction the reaction mixture was diluted with water and extracted with diethyl ethr. The organic layer was washed with brine and dried over Na_2SO_4. Evaoration of the solvent followed by purification have been done by column chromatography and the pure compound (**20**) was isolated as solid using petroleum ether as the eluent.



(*E*)-1-styryl-3-(p-tolylethynyl)benzene (20):

Yield: 81% (24 mg)

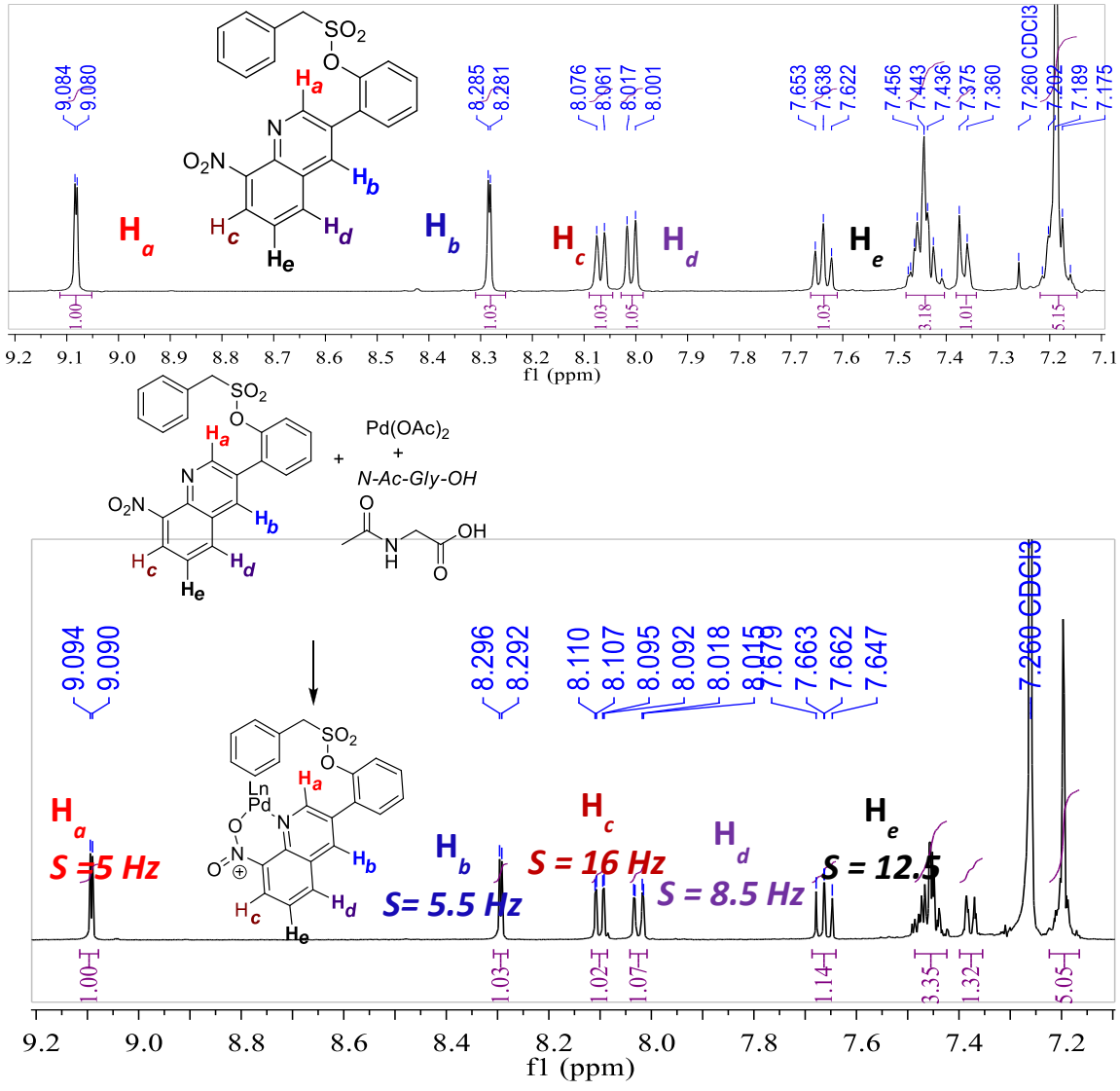
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.56 – 7.51 (m, 2H), 7.48 (t, J = 8.4 Hz, 3H), 7.45 – 7.41 (m, 1H), 7.41 – 7.32 (m, 3H), 7.31 – 7.27 (m, 1H), 7.19 (t, J = 8.8 Hz, 2H), 7.16 – 7.06 (m, 2H), 2.39 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.71, 137.73, 137.32, 131.77, 130.82, 129.70, 129.69, 129.38, 128.96, 128.91, 128.06, 126.83, 126.57, 124.09, 120.34, 89.91, 88.85, 21.76.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{23}H_{18}Na$: 317.1306, found: 317.1305.

5.3.5. NMR study:

In an oven dry reaction tube charged with clean magnetic stir bar equimolar amount of substrate (0.05mmol, 21 mg, 1.0 equiv), *N*-Ac-Gly-OH (0.1 mmol, 11 mg, 2.0 equiv) and $Pd(OAc)_2$ (0.05 mmol, 11 mg, 1.0 equiv) was taken and to that 0.5 mL HFIP was added. The reaction mixture was then stirred vigorously for 3 h at 80 °C. Then the reaction mixture was taken out and NMR of the mixture was analyzedimmediately. Comparing the proton shift of the reaction mixture and substrate, we concluded that the reasonable ^1H shift of directing groups (specifically the ^1H shift of 8-nitroquinoline moiety) indicating a weak coordiantion may be operative during the course of the reaction. In other word, quinoline group could be involved in coordinating to the palladium centre during the reaction which resulted a down field shift in proton NMR.



**(S stands for the shift in Hz)*

Figure 5.3.5: NMR study to interfere metal-directing group interaction

5.3.6. ESI-MS study:

$Pd(OAc)_2$ was dissolved in CH_3CN and HFIP mixture (1:1, 1 mL) in a oven dried reaction tube then substrate (**1a**, 0.05 mmol, 21 mg), *N*-Ac-Gly-OH (0.1 mmol, 11 mg), was added to the solution of $Pd(OAc)_2$. The mixture was stirred for 3 h at 80 °C. After that ESI-MS spectrum was recorded. In mass spectrum, a CH_3CN-Pd-substrate adduct such as [**CH_3CN-Pd-1a**] was appeared as a possible intermediate species with desired isotopic pattern.

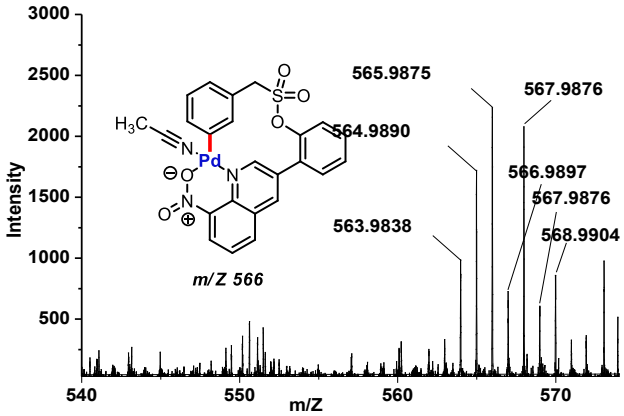


Figure 5.3.6a: Palladium-Substrate (**1a**) adduct in ESI-MS study [**CH_3CN-Pd-1a**] m/Z = 566.

To verify further the observed intermediate of the reaction, **1a** was replaced with a methyl substituted substrate (**3c**). Similar adduct has been detected. The observation found to be consistent while solvent, CH_3CN has been replaced by CD_3CN.

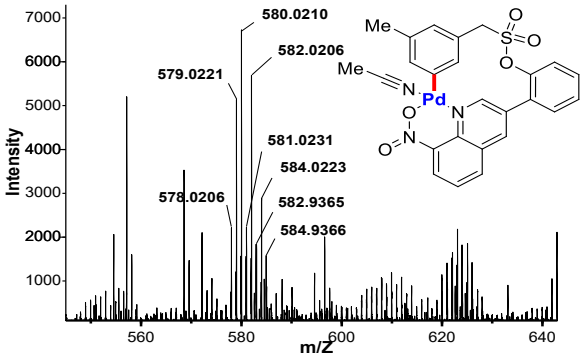


Figure 5.3.6b: Palladium-Substrate (**3c**) adduct in ESI-MS study [**CH_3CN-Pd-3c**] m/Z = 580.

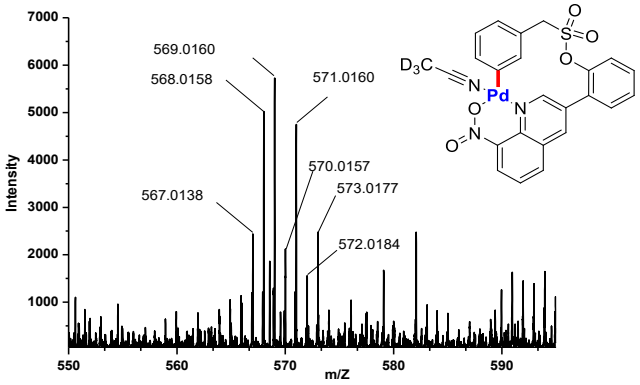


Figure 5.3.6c: Palladium-Substrate (**1**) adduct in CD_3CN in ESI-MS study **[CD_3CN-Pd-1a**]: m/Z = 569

5.3.7. Kinetic Experiment:

Table S15: Kinetic experiment

	Substrate	Olefin	$Pd(OAc)_2$	*N*-Ac-Gly-OH	AgOAc	HFIP:DCE
Run 1	**0.1mmol**	0.1 mmol	10 mol%	20 mol%	0.1 mmol	1 mL
Run 2	**0.05mmol**	**0.1 mmol (2 equiv)**	10 mol%	20 mol%	0.1 mmol	1 mL
Run 3	0.05 mmol	**0.2 mmol (4 equiv)**	10 mol%	20 mol%	0.1 mmol	1 mL
Run 4 (**D-1**)	**0.05 mmol (Deuterated substrate D-1)**	0.1 mmol (2 equiv)	10 mol%	20 mol%	0.1 mmol	1 mL

*Reaction carried out at room temperature to avoid the formation of *di*-product.

Determination of order with respect to substrate: Comparing Run 1 and Run 2

Run 1: 0.1 mmol

x_1- 0.1559, y_1- 0.0979

x_2- 1.2714, y_2- 0.0924

$dx = x_2-x_1 = (1.2714 - 0.1559) = 1.1155$

$dy = y_2-y_1 = (0.0924 - 0.0979) = -0.0055$

$R_1 = dy/dx = -0.0055/1.1155 = -0.0049$

Run 2: 0.05 mmol

X_1- 0.3284, Y_1- 0.0494

X_2- 2.2892, Y_2- 0.0452

DX = X_2-X_1 = (2.2892 - 0.3284) = 1.9608

DY = Y_2-Y_1 = (0.0452 - 0.0494) = -0.0042

R_2 = DY/DX = -0.0042/1.9608 = -0.0021

We know

Rate = dy/dx= k[substrate]^a[olefin]^b

Now, R_1/R_2 ={dy/dx}$_{run1}$/{DY/DX}$_{run2}$ =

{k[substrate] $^a{}_{Run1}$[olefin]$^b{}_{run1}$}/{k[substrate]$^a{}_{run2}$[olefin]$^b{}_{run2}$}

At t=0; [olefin] $_{run1}$= [olefin] $_{run2}$

- ⇨ R_1/R_2 = [substrate]$^a{}_{run1}$/[substrate]$^a{}_{run2}$
- ⇨ -0.0049/-0.0021 = [substrate]$^a{}_{run1}$/[substrate]$^a{}_{run2}$
- ⇨ 2.33 = [substrate]$^a{}_{run1}$/[substrate]$^a{}_{run2}$

At t=0; [substrate]$^a{}_{run1}$/[substrate]$^a{}_{run2}$ = [0.1/0.05]^a = 2^a

So, $2.33 = 2^a$

log(2.33) = alog(2)

0.3673 = a*0.3010

So, a = 1.22

Which indicates that the reaction rate with respect to substrate is **one**.

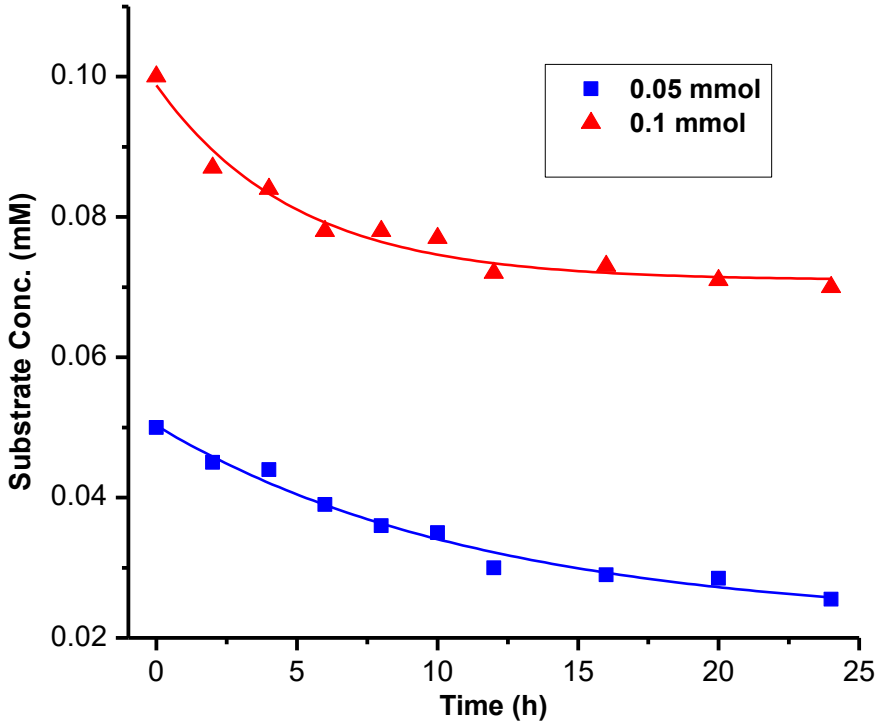


Figure 5.3.7a: Determination of order with respect to substrate

Determination of order with respect to olefin: Comparing Run 2 and Run 3

From Run 2 we have seen that

R_2 = DY/DX = -0.0042/1.9608 = -0.0021

From Run 3:

X_1' = 0.2022, Y_1' = 0.0497

X_2' = 1.7091, Y_2' = 0.0465

$DX' = X_2' - X_1'$ = (1.7091 - 0.2022) = 1.5069

$DY' = Y_2' - Y_1'$ = (0.0465 - 0.0497) = -0.0032

Hence, $R_3 = DY'/DX'$ = (-0.0032/1.5069) = -0.002123

So slope of Run 2 and Run 3 is same following the same route to calculate the order with respect to olefin;

Rate = dx/dy= $k[substrate]^a[olefin]^b$

Now, $R_2/R_3=\{dy/dx\}_{run2}/\{DY/DX\}_{run3} = \{k[substrate]^a{}_{Run1}\ [olefin]^b{}_{run1}\}/\{k[substrate]^a{}_{run2}\ [olefin]^b{}_{run2}\}$

At t=0; $[Substrate]_{run1} = [Substarate]_{run2}$

- ⇨ $R_2/R_3 = [olefin]^b{}_{run2}[olefin]^b{}_{run3}$
- ⇨ $-0.0021/-0.0021 = [olefin]^b{}_{run2}/[olefin]^b{}_{run3}$

⇨ $1 = [olefin]^{b}_{run2}/[olefin]^{b}_{run3}$

At t=0; $[olefin]^{b}_{run2}/[olefin]^{b}_{run3} = 2$

So, $1 = 2^{b}$

log(1) = blog(2)

0 = b*0.3010

So, b = 0

Which implies that the reaction order with respect to olefin is **zero**, i.e.the rate is independent on the amount of olefin.

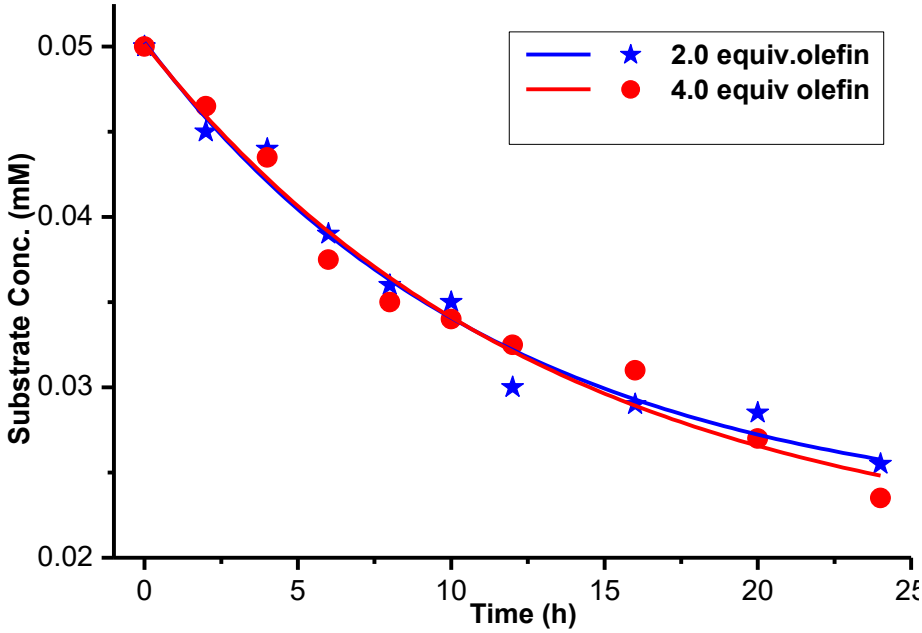
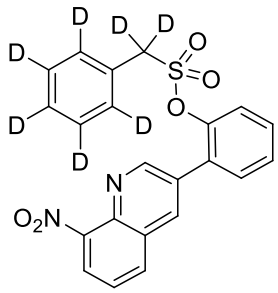


Figure 5.3.7b: Determination of order with respect to olefin

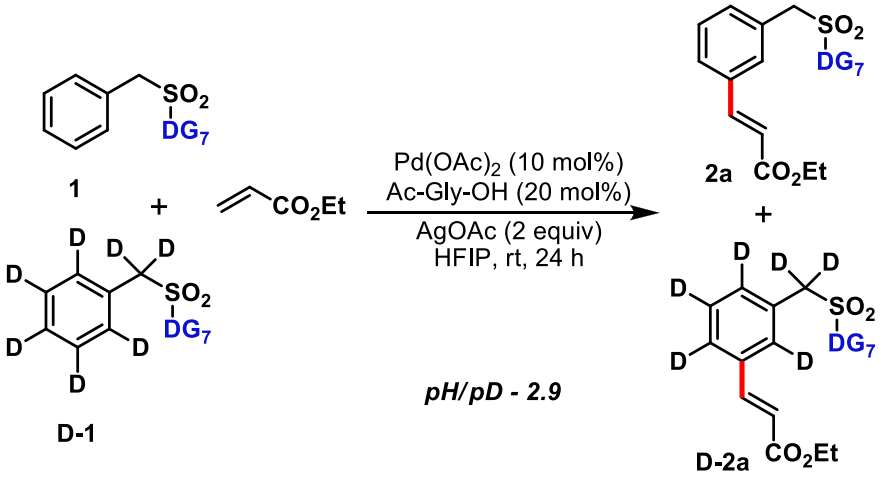
5.3.8. Intermolecular KIE experiment:



^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 2.0 Hz, 1H), 8.29 (d, *J* = 2.1 Hz, 1H), 8.08 (d, *J* = 7.5 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.49 – 7.41 (m, 3H), 7.39 – 7.34 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.31, 147.40, 145.24, 137.68, 135.14, 131.61, 131.01, 130.79, 130.30, 129.53, 129.13 (d), 127.77 (d), 127.58, 127.35 (d), 126.91, 125.43 (d), 124.90, 123.20, 122.46, 56.33 (t).

HRMS (*m*/*z*): $[M + H]^{+}$ calculated for $C_{22}H_{10}D_7N_2O_5S$: 428.1298, found: 428.1295.



An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, phenylmethanesulfonate ester **1**,(0.1 mmol, 42 mg), deuterated-phenylmethanesulfonate ester**D-1** (0.1 mmol, 43 mg), olefin (0.4 mmol, 2.0 equiv), $Pd(OAc)_2$ (10 mol%, 4.4 mg), *N*-Ac-Gly-OH (20 mol%, 4.7 mg), and AgOAc (2.0 equiv, 66 mg) were taken. Subsequently, HFIP:DCE (1:1, 2 mL) was added and the reaction mixture was stirred vigorously for 48 h at room temperature. The reaction mixture was then diluted with EtOAc and filtered through celite pad. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and 20:80 petroleum ether:ethyl acetate was used as the eluent. $P_H/P_D$was calculated from 1H NMR spectrum of the isolated product.From NMR spectrum product distribution *pH/pD*was found 2.9.

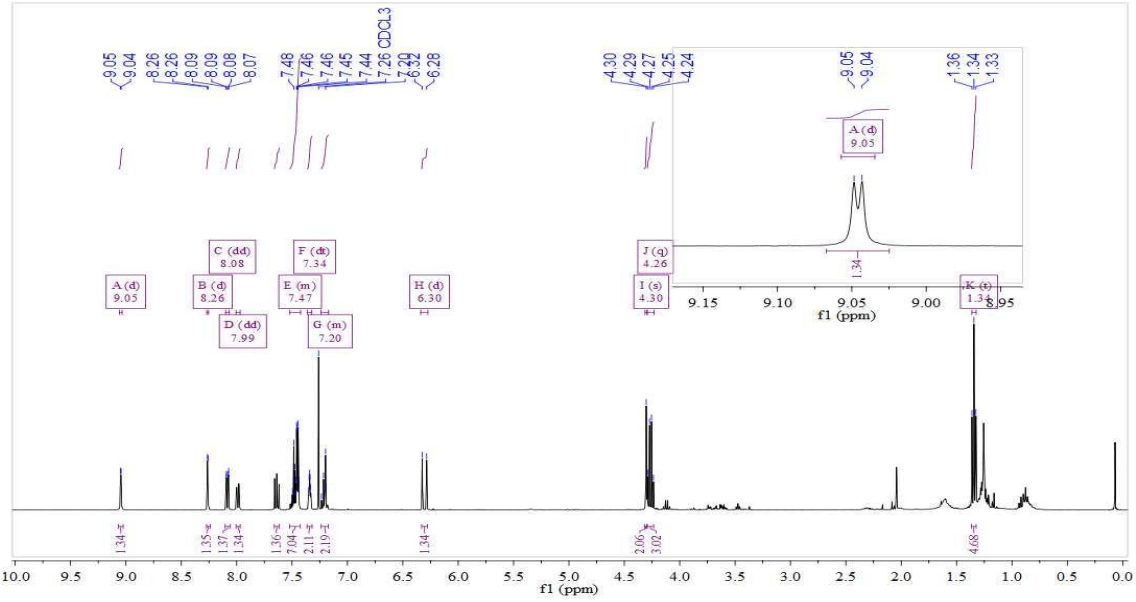


Figure 5.3.8: Determination ofP_H/P_D

In this spectrum peak at 9.05 ppm is corresponds to the nitroquinoline group and total integration is 1.34 which is also true for the doublet (at 6.30 ppm) coming from the styrenyl proton. Among this 1.34 proton, one proton is coming from compound **2a** is rest 0.34 is the contribution of deutarated substrate **D-2a**. And hence $[pH/pD] = 1/0.0.34 = 2.9$

Determination of K_H/K_D: Comparing Run 2 and Run 4

Run 2: 0.05 mmol

X_1- 0.3284, Y_1- 0.0494

X_2- 2.2892, Y_2- 0.0452

DX = X_2-X_1 = (2.2892 - 0.3284) = 1.9608

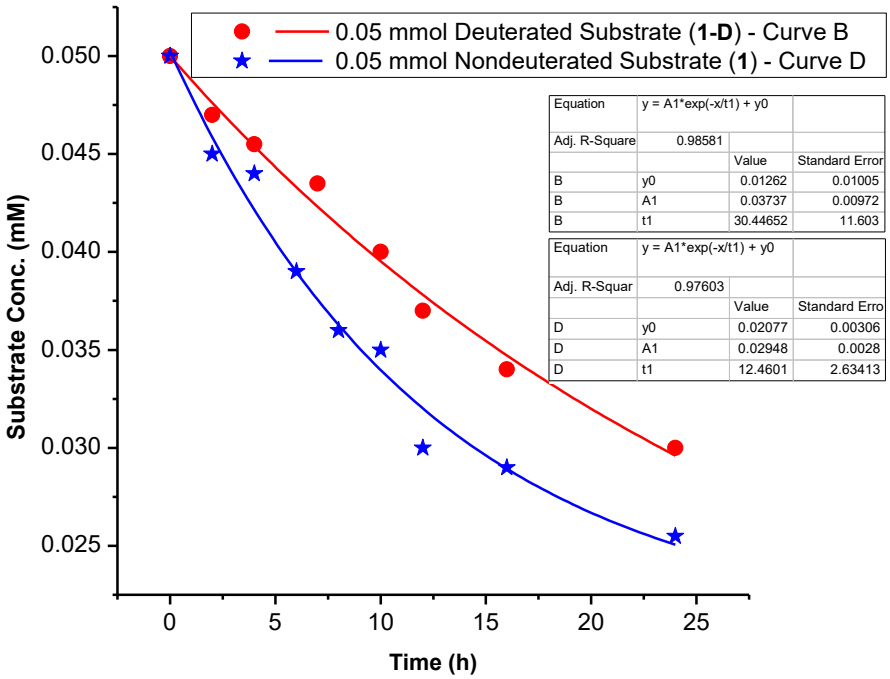
DY = Y_2-Y_1 = (0.0452 - 0.0494) = -0.0042

R_2 = DY/DX = -0.0042/1.9608 = -0.0021

Run 4: 0.05 mmoldeuterated substrate (D-1)

x_1= 1.5050, y_1 = 0.0482
x_2= 2.9088, y_2 = 0.0466
dx = x2 – x1 = 2.9088 - 1.5050 = 1.4038
dy= y2 – y1 = 0.0490 – 0.0479 = -0.0016
R_4 = dy/dx = -0.0016/1.4038 = -0.0011
We know
Rate = dy/dx= k[substrate]^a[olefin]^b
Now, R_2/R_4 ={ DY/DX }$_{run2}$/{dy/dx }$_{run4}$ = {K_H[substrate] ^{a} $_{Run2}$ [olefin] ^{b} $_{run2}$}/{K_D[substrate] ^{a} $_{run4}$ [olefin] ^{b} $_{run4}$}
At t=0; [olefin] $_{run2}$= [olefin] $_{run4}$ and [substrate] $_{run2}$ = [substrate] $_{run4}$

⇨ $R_2/R_4 = K_H/K_D$ = -0.0021/-0.0011 = 1.9



Equation	y = A1*exp(-x/t1) + y0		
Adj. R-Square	0.98581		
		Value	Standard Error
B	y0	0.01262	0.01005
B	A1	0.03737	0.00972
B	t1	30.44652	11.603

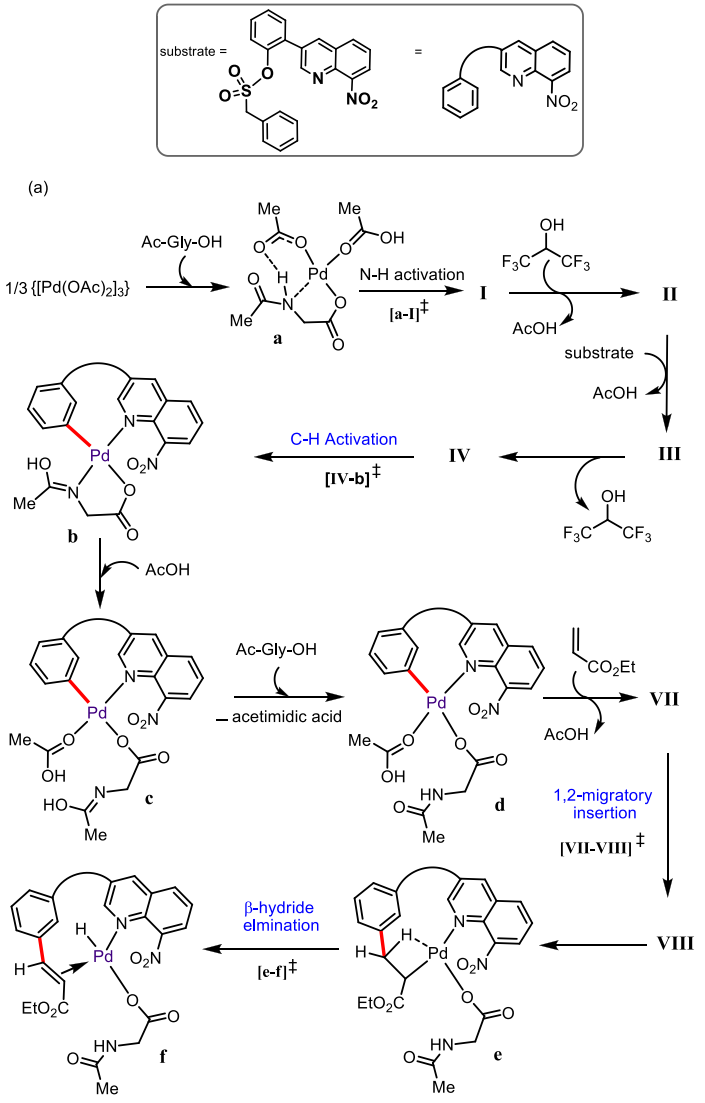
Equation	y = A1*exp(-x/t1) + y0		
Adj. R-Squar	0.97603		
		Value	Standard Erro
D	y0	0.02077	0.00306
D	A1	0.02948	0.0028
D	t1	12.4601	2.63413

Figure S7: Determination of K_H/K_D

5.3.9. Computational Methods

Computations were performed using Gaussian09 (Revision D.01) suite of quantum chemical program.[32] The transition states were verified by examining whether it has a unique imaginary frequency representing the desired reaction coordinate. Intrinsic reaction coordinate (IRC) calculations were additionally carried out to further characterize the true nature of the important transition states.[33] Graphical representation of the optimized geometries are created by using CYLView.[34] All the relative energies (kcal/mol) were calculated with respect to the separated reactants.

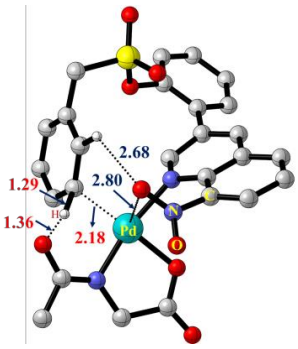
5.3.9a. Detailed mechanistic steps involved in olefination reaction



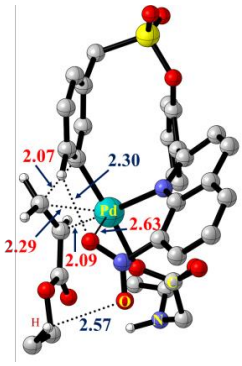
Scheme 5.3.9a: Detailed intermediate steps

5.3.9b. Optimized geometries of the important transition states

Table 5.3.9b: Optimized geometries

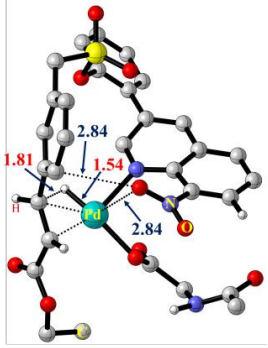


C–H activation [**IV-b**]‡



Olefin insertion

[**VII-VIII**]‡

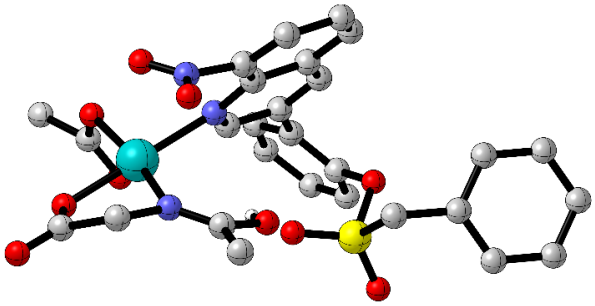


β-hydride elimination [**e-f**]‡

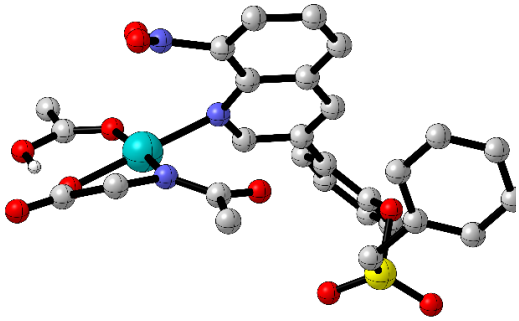
***Transiton state geometries obtained at the M06/6-31G**, SDD(Pd) level of theory**

5.3.9c. Different binding modes between palladium acetate, *N*-acetylglycine ligand and substrate

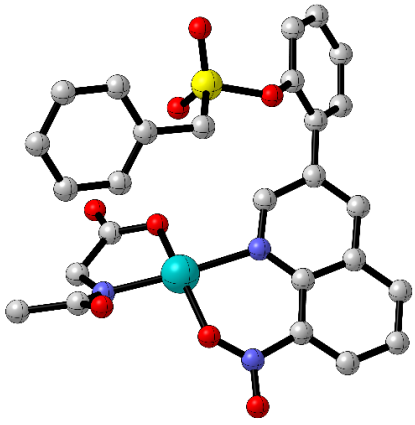
Table 5.3.9c: Optimized geometries of different binding modes between palladium acetate, N-acetyl glycine ligand and the substrate obtained at the $SMD_{(\varepsilon=16.7)}$/M06/6-31G**//M06/6-31G** level of theory and the corresponding Gibbs free energies (in kcal/mol).

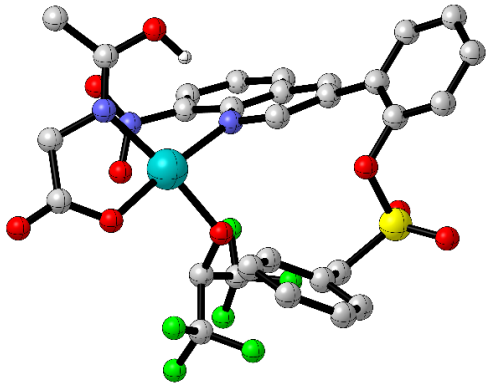


III(a) (9.6)

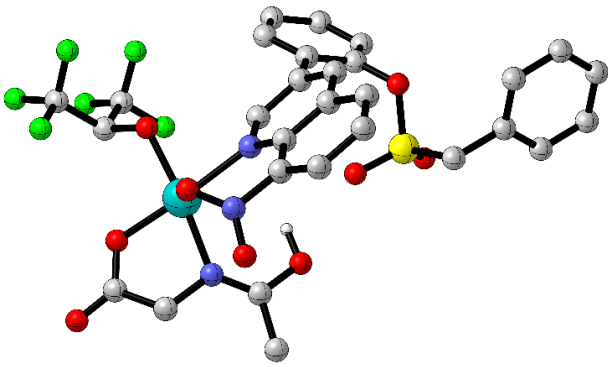


III(b) (8.5)

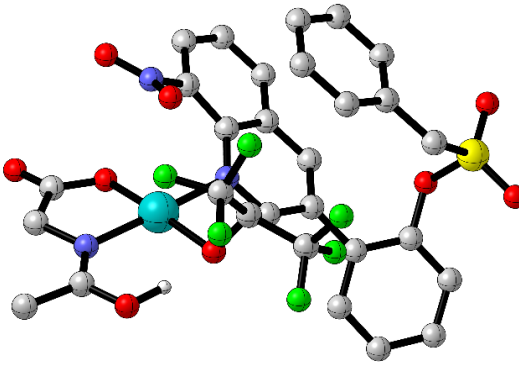




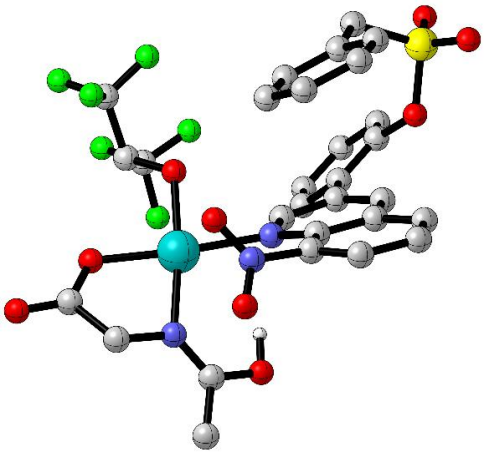
III(c) (14.0)



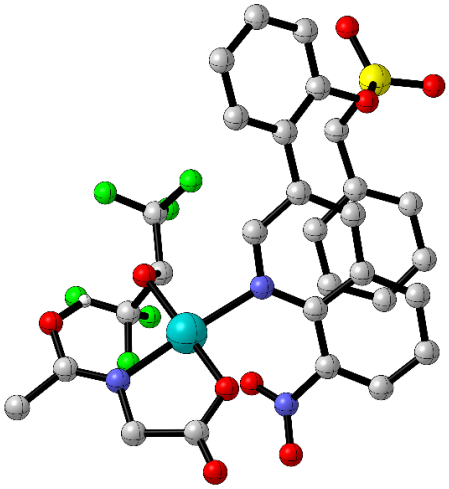
III(d) (10.3)



III(e) (10.4)

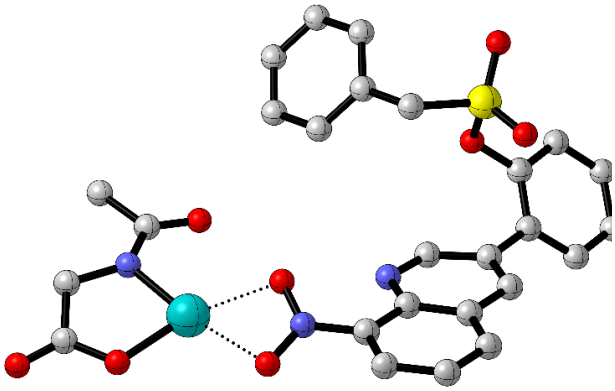


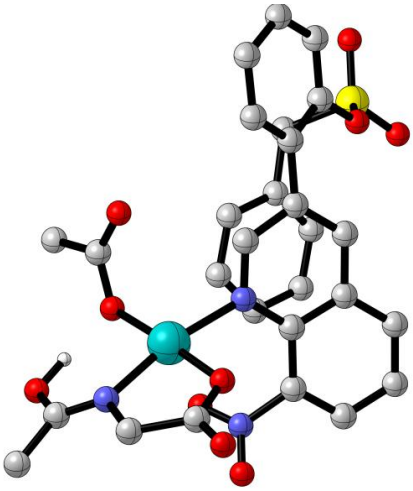
III (2.6)



III(f) (11.6)

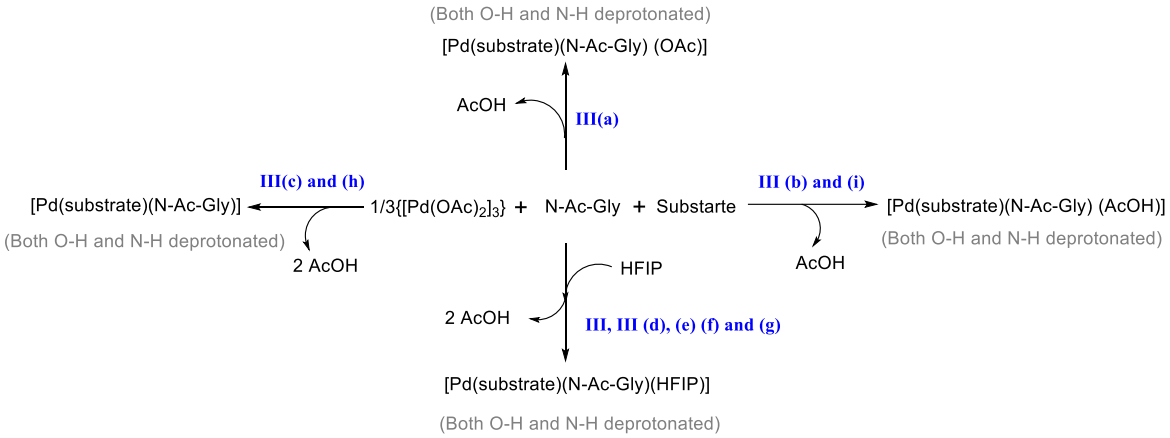
III(g) (3.0)





III(h) (30.4)

III(i) (4.7)



Scheme S2: Illustration of how the relative Gibbs free energies of different binding modes (as shown in Table S17) of catalyst, ligand and substrates are computed

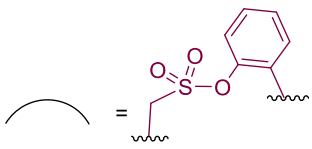
5.3.9d. C–H Activation Models

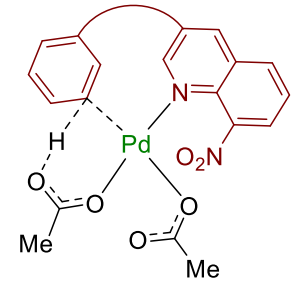
Table 5.3.9d: Relative Gibbs Free Energies (in kcal/mol) of the C–H Activation Transition States at the *meta-, ortho*-and *para-* Positions Obtained at the $SMD_{(\varepsilon=16.7)}$/M06/6-31G**//M06/6-31G** Level of Theory

Mode of C–H activation[a]	*meta-*	*ortho-*	*para-*
A	25.6	33.2	22.6
B	25.0	36.5	22.2
C	**21.8**	32.8	22.9
D	37.0	33.5	36.7
E	26.1	36.6	27.4
F	56.1	62.6	57.5
G	26.3	36.1	27.8

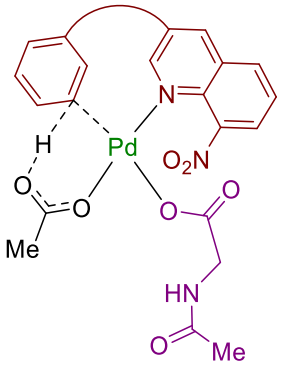
[a]SeeTable S19for details of these binding modes. The lowest energy possibility (**C**) is shown in bold font type.

Table 5.3.9e: *meta* C-H bond activation transition states obtained at the $SMD_{(\varepsilon=16.7)}$/M06/6-31G**//M06/6-31G** level of theory. (Similar possibilities for the *ortho*- and *para*-C–H bond activation were also examined and the computed data is provided in Table S17).

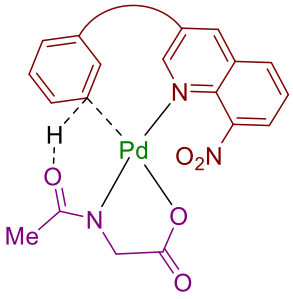




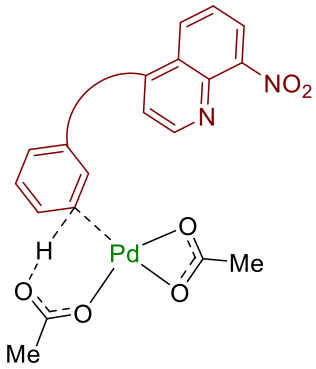
(A)



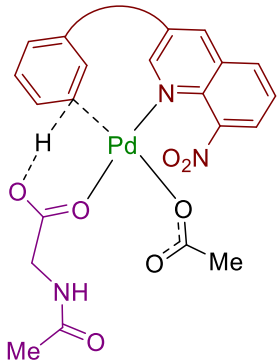
(B)



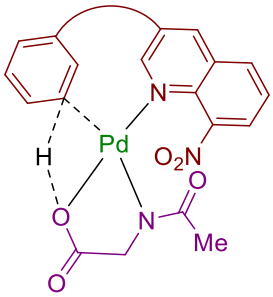
(C) [4-5]‡



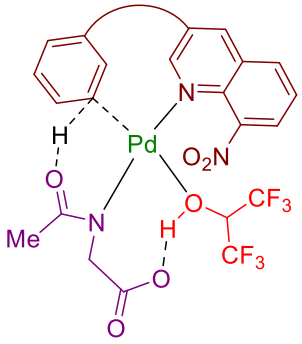
(D)



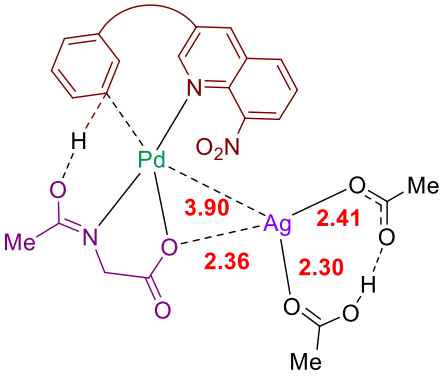
(E)



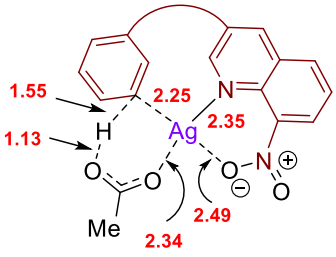
(F)



(G)



(H) 23.1 kcal/mol



(I) 28.8 kcal/mol[35]

Table 5.3.9e: Energetics of Various Species Involved in the Catalytic Cycle Computed at the $SMD_{(\varepsilon=16.7)}$/M06/6-31G**,SDD(Pd)//M06/6-31G**,SDD(Pd) Level of Theory

Stationary Points	Total Energy	Stationary Points	Total Energy
$[Pd(OAc)_2]_3$	-1754.125986	**II**	-1582.142215
Substrate-**1**	-1730.762457	**III**	-3083.949447
Ligand	-436.8757687	**IV**	-2294.368782

HFIP	-789.5300087	**[IV-b]‡**	-2294.35374
AcOH	-228.9731031	**b**	-2294.379387
Substrate-**2** (olefin)	-345.5744617	**c**	-2523.354903
$[AgOAc]_2$	-750.8489252	**d**	-2523.374801
AgOAc	-375.3915089	**VII**	-2639.977314
$[AgOAc.HFIP]_2$	-2329.958543	**[VII-VIII]‡**	-2639.969199
		VIII	-2640.009943
a	-1021.576704	**e**	-2639.996198
[a-I]‡	-1021.564145	**[e-f]‡**	-2639.981611
I	-1021.577629	**f**	-2639.984206

Table 5.3.9f: Energetics of Various Species of Stationary Point **(III)** Computed at the $SMD_{(\varepsilon=16.7)}$/M06/6-31G**,SDD(Pd)//M06/6-31G**,SDD(Pd) Level of Theory

Stationary Point **(III)**	Total Energy	Stationary Point **(III)**	Total Energy
III(a)	-2523.370273	**III**	-3083.949697
III(b)	-2523.372453	**III(f)**	-3083.935267
III(c)	-2294.368028	**III(g)**	-3083.949447
III(d)	-3083.932562	**III(h)**	-2294.339047
III(e)	-3083.929150	**III(i)**	-2523.382959

Table 5.3.9g: Energetics of Various Mode of C–H activation are Computed at the $SMD_{(\varepsilon=16.7)}$/M06/6-31G**,SDD(Pd)//M06/6-31G**,SDD(Pd) Level of Theory

Mode of C-H activation	*meta*	*ortho*	*para*
	Total Energy		
A	-2315.43694	-2315.425049	-2315.438938
B	-2523.345309	-2523.328582	-2523.350687
C	-2294.35374	-2294.336536	-2294.353957

D	-2315.410802	-2315.419308	-2315.416384
E	-2523.338294	-2523.322493	-2523.341104
F	-2294.299699	-2294.288701	-2294.297372
G	-3083.905376	-3083.888413	-3083.902035
H	-2898.784668		
I	-2106.14555		

5.3.10: *meta*-C–H activation transition state plot for showing non-covalent interactions

The transition state geometries, as given in 3.b, convey an important interaction between the quinoline nitro group and the palladium centre. The contact distances between the $–NO_2$ group and Pd are found to be in the range from 2.6 to 2.8 Å. Another interaction is between the $–NO_2$ oxygen and the $C_{sp2/sp3}$–H of the aryl ring of the substrates. A graphical illustration of these weak interactions, generated using the non-covalent interaction plot, is shown below.[36] It is interesting to note that the substituents such as $–NO_2$ and –OMe at the C-8 position of the quinoline ring offers improved yields of *meta*-olefinated products as compared to unsubstituted quinolines.

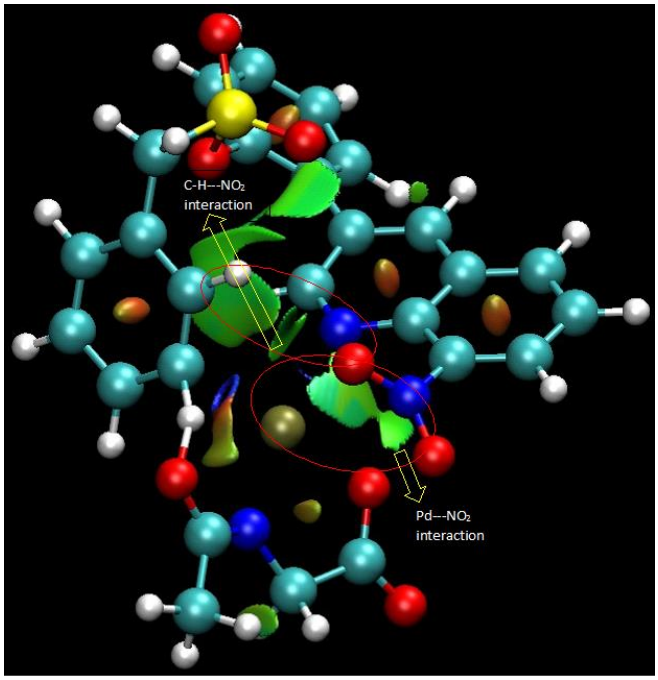


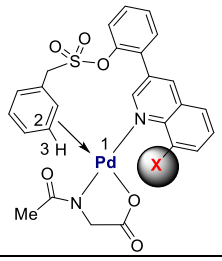
Figure S8:*meta*-C–H activation transition state plot

5.3.11: Calculation of natural charges

We have computed the natural charges on the carbon and hydrogen atoms of the pre-reacting complexes of the C–H activation transition states, shown as C-2 and H-3 in Table S23, by using natural population analysis (NPA).[37] The relative nucleophilicities and electrophilicities of the C-2 and H-3 atoms of the aryl ring can be approximately compared using the computed NPA

changes. It appears that the C-8 substituent on the quinoline ring is able to influence the charge on palladium, which in turn, results in a minor change in C-2 and H-3 atoms that are involved in the C–H activation (Table S23). In both $–NO_2$ and –OMe substituted quinolines, H-3 becomes more protic while C-2 becomes relatively more nucleophilic as compared to the theunsubstituted case. These trends suggest that the substituted quinolines are likely to be better directing groups for improving efficiency of *meta*-C–H activation of arenes.

Table 5.3.11: Natural charges on important atoms in the respective pre-reacting complexes of the *meta*-C–H activation transition states

	X=	Pd(1)	C(2)	H (3)
	-NO2	0.513	-0.282	0.328
	-OMe	0.530	-0.257	0.310
	-H	0.522	-0.243	0.304

Cartesian Coordinates of the Optimized Geometries at the M06/6-31G**,SDD(Pd) Level of Theory

---

$[Pd(OAc)_2]_3$

Number of imaginary frequencies : 0

Electronic energy : =-1754.0916027
Zero-point correction= 0.315972
Thermal correction to Energy= 0.349810
Thermal correction to Enthalpy= 0.350755
Thermal correction to Gibbs Free Energy= 0.246926
Sum of electronic and zero-point Energies= -1753.775631
Sum of electronic and thermal Energies= -1753.741792
Sum of electronic and thermal Enthalpies= -1753.740848
Sum of electronic and thermal Free Energies= -1753.844676

.....

Cartesian Coordinates

.....

46	1.539985	-0.981241	-0.002552
8	1.051330	-2.022629	-1.678608
8	0.923281	-2.488570	1.233357
6	-0.163708	-2.587758	1.864606
8	-1.227084	-1.932937	1.670977
46	-1.622140	-0.842778	0.000920
6	-0.065629	-2.579881	-1.877150
8	-1.139747	-2.391083	-1.244603
8	2.289926	-0.103781	1.671800
8	2.645890	0.216109	-1.237609

6	2.272752	1.243469	-1.866804
8	1.227372	1.926579	-1.671702
46	0.079639	1.820792	0.003059
6	2.323470	1.144185	1.869452
8	1.692841	2.037335	1.241374
8	-1.054404	2.025777	1.677153
8	-1.508622	2.181868	-1.233330
6	-2.153149	1.433130	1.874026
6	-2.213948	1.349208	-1.865662
8	-2.614270	0.442686	1.243837
8	-2.293796	0.103739	-1.669052
6	-0.101719	-3.607873	-2.972941
1	0.228167	-4.567075	-2.559914
1	-1.115336	-3.721983	-3.360703
1	0.592480	-3.330353	-3.769070
6	3.191332	1.733023	-2.950665
1	3.911776	2.427404	-2.505158
1	3.741617	0.899358	-3.390597
1	2.625316	2.274286	-3.711340
6	3.248583	1.614785	2.956354
1	2.911219	2.570480	3.361210
1	3.320633	0.859688	3.741976
1	4.246860	1.748798	2.526066
6	-3.023581	1.993318	2.963478
1	-3.605318	1.197526	3.432504
1	-2.416947	2.522411	3.700803
1	-3.720092	2.709920	2.515151
6	-3.084188	1.908704	-2.955899
1	-3.993258	2.314298	-2.499117
1	-2.569977	2.724552	-3.468166
1	-3.370516	1.123621	-3.657954
6	-0.214479	-3.624957	2.951093
1	0.774728	-3.767847	3.389873
1	-0.943748	-3.340275	3.712130
1	-0.538018	-4.573214	2.508624

Substrate-**1**

Number of imaginary frequencies : 0

Electronic energy : =-1730.7331268
Zero-point correction= 0.343243
Thermal correction to Energy= 0.367179
Thermal correction to Enthalpy= 0.368123
Thermal correction to Gibbs Free Energy= 0.288484
Sum of electronic and zero-point Energies= -1730.389884
Sum of electronic and thermal Energies= -1730.365948
Sum of electronic and thermal Enthalpies= -1730.365004
Sum of electronic and thermal Free Energies= -1730.444643

.....

Cartesian Coordinates

.....

6	-0.888234	-1.480143	1.394561
1	0.096457	-1.071560	1.134634
1	-0.856963	-1.818108	2.438881
8	-1.294041	1.045694	2.120439
6	-2.274700	1.584264	-0.500177
6	-1.161299	2.368557	-0.823762
6	-3.566861	2.084235	-0.539541
6	-1.393587	3.691882	-1.206725
6	-3.771455	3.403493	-0.927448
1	-4.386403	1.428157	-0.257394
6	-2.684222	4.205046	-1.261857
1	-0.543865	4.316133	-1.478172
1	-4.780694	3.804822	-0.966929
1	-2.841722	5.235413	-1.570312
8	-2.082761	0.256341	-0.137358
16	-1.985393	-0.059214	1.482363
8	-3.305029	-0.456966	1.933255
6	-1.322774	-2.554120	0.445408
6	-0.515752	-2.863567	-0.650943
6	-2.509463	-3.260165	0.654684
6	-0.895597	-3.872868	-1.529345
1	0.420975	-2.325796	-0.804380
6	-2.887337	-4.261617	-0.230826
1	-3.139860	-3.011070	1.506397
6	-2.081543	-4.569575	-1.323599
1	-0.258396	-4.116077	-2.376127
1	-3.813941	-4.806148	-0.064817
1	-2.377318	-5.357862	-2.012181
6	1.198627	2.474229	-0.031198
6	2.450713	1.849718	0.169104
6	0.196358	1.813873	-0.698660
6	3.519824	2.486401	0.841142
6	2.595861	0.513540	-0.299247
6	0.509727	0.530653	-1.230155
6	4.710176	1.832884	1.041328
1	3.379372	3.505962	1.195989
6	3.822167	-0.140529	-0.009148
1	-0.235622	0.014846	-1.838574
6	4.864254	0.502430	0.609241
1	5.532791	2.328125	1.549295
1	5.790672	-0.039171	0.776037
7	1.637569	-0.103316	-1.033675
7	3.999626	-1.563730	-0.317141
8	5.091303	-1.906711	-0.742718
8	3.066447	-2.309126	-0.079032
1	1.023798	3.463496	0.391837

N-Acetylglycine

Number of imaginary frequencies : 0

Electronic energy : =-436.8568818

Zero-point correction= 0.117817
Thermal correction to Energy= 0.126678
Thermal correction to Enthalpy= 0.127622
Thermal correction to Gibbs Free Energy= 0.082579
Sum of electronic and zero-point Energies= -436.739065
Sum of electronic and thermal Energies= -436.730204
Sum of electronic and thermal Enthalpies= -436.729259
Sum of electronic and thermal Free Energies= -436.774303

Cartesian Coordinates

6	-1.857377	0.142291	0.002734
8	-1.946766	1.347414	0.016304
8	-2.913670	-0.679120	0.012116
1	-3.703094	-0.116823	0.030914
6	-0.569045	-0.625148	-0.028230
1	-0.564878	-1.283972	-0.908956
1	-0.527492	-1.300069	0.838945
7	0.530805	0.294681	-0.039221
1	0.299243	1.279659	-0.040359
6	1.812412	-0.166552	-0.002702
8	2.064102	-1.359775	0.023368
6	2.883978	0.894167	0.009681
1	2.499515	1.913806	-0.088791
1	3.446780	0.814480	0.944666
1	3.585146	0.693456	-0.805081

HFIP

Number of imaginary frequencies : 0

Electronic energy : =-789.5215432
Zero-point correction= 0.063926
Thermal correction to Energy= 0.072853
Thermal correction to Enthalpy= 0.073798
Thermal correction to Gibbs Free Energy= 0.029122
Sum of electronic and zero-point Energies= -789.457617
Sum of electronic and thermal Energies= -789.448690
Sum of electronic and thermal Enthalpies= -789.447746
Sum of electronic and thermal Free Energies= -789.492421

Cartesian Coordinates

6	1.283713	-0.135097	-0.030952
6	0.002827	0.542958	-0.499058
6	-1.262275	-0.164995	-0.025527
1	0.002331	0.474558	-1.600561
9	2.325094	0.424653	-0.642081
9	1.260268	-1.431272	-0.348172
9	1.459475	-0.025078	1.277991
9	-1.448667	-1.315362	-0.664812
9	-1.262854	-0.395704	1.279953

9	-2.307652	0.632927	-0.303789
8	0.045916	1.843754	-0.018262
1	-0.746224	2.306744	-0.311941

AcOH

Number of imaginary frequencies : 0

Electronic energy : =-228.963173
Zero-point correction= 0.062295
Thermal correction to Energy= 0.066778
Thermal correction to Enthalpy= 0.067722
Thermal correction to Gibbs Free Energy= 0.035401
Sum of electronic and zero-point Energies= -228.900878
Sum of electronic and thermal Energies= -228.896395
Sum of electronic and thermal Enthalpies= -228.895451
Sum of electronic and thermal Free Energies= -228.927772

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Cartesian Coordinates

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6	-0.092416	0.124236	0.000363
8	-0.652166	1.192424	-0.000094
8	-0.762605	-1.046342	-0.000050
1	-1.703301	-0.812817	-0.000202
6	1.386716	-0.099499	-0.000074
1	1.676548	-0.681724	0.880034
1	1.675962	-0.682999	-0.879520
1	1.903161	0.860462	-0.000894

Substarate-**2** (olefin)

Number of imaginary frequencies : 0

Electronic energy : =-345.5669177
Zero-point correction= 0.123848
Thermal correction to Energy= 0.131628
Thermal correction to Enthalpy= 0.132572
Thermal correction to Gibbs Free Energy= 0.091621
Sum of electronic and zero-point Energies= -345.443069
Sum of electronic and thermal Energies= -345.435290
Sum of electronic and thermal Enthalpies= -345.434346
Sum of electronic and thermal Free Energies= -345.475297

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Cartesian Coordinates

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6	-2.976719	-0.323139	-0.000018
6	-1.720198	-0.760002	0.000025
1	-3.823727	-1.002692	-0.000092
1	-3.176050	0.746458	0.000043

1	-1.462560	-1.816613	0.000031
6	-0.600963	0.206513	0.000008
8	-0.710578	1.411903	-0.000040
8	0.580011	-0.435719	0.000029
6	1.737250	0.408899	0.000052
6	2.948170	-0.485571	-0.000060
1	1.701139	1.062044	0.881073
1	1.701011	1.062185	-0.880842
1	3.863447	0.114667	0.000546
1	2.957705	-1.128272	0.886115
1	2.958321	-1.127441	-0.886829

$[AgOAc]_2$

Number of imaginary frequencies : 0

Electronic energy : =-750.8299419
Zero-point correction= 0.104041
Thermal correction to Energy= 0.116995
Thermal correction to Enthalpy= 0.117940
Thermal correction to Gibbs Free Energy= 0.061784
Sum of electronic and zero-point Energies= -750.725901
Sum of electronic and thermal Energies= -750.712946
Sum of electronic and thermal Enthalpies= -750.712002
Sum of electronic and thermal Free Energies= -750.768158

Cartesian Coordinates

47	-0.004084	-1.381193	0.001918
8	2.123865	1.122851	0.002249
6	2.682131	-0.012676	0.003384
6	4.188999	-0.000462	-0.012535
1	4.559213	0.679848	0.759186
1	4.595495	-1.001990	0.134411
1	4.528430	0.392574	-0.976341
8	2.119195	-1.144244	0.003647
8	-2.123894	-1.122842	0.002297
6	-2.682132	0.012695	0.003375
6	-4.189002	0.000534	-0.012519
1	-4.559230	-0.679709	0.759254
1	-4.595462	1.002086	0.134360
1	-4.528462	-0.392564	-0.976290
8	-2.119164	1.144253	0.003566
47	0.004085	1.381173	0.001936

AgOAc

Number of imaginary frequencies : 1

Electronic energy : =-375.3640073
Zero-point correction= 0.050347
Thermal correction to Energy= 0.055651
Thermal correction to Enthalpy= 0.056595
Thermal correction to Gibbs Free Energy= 0.019804
Sum of electronic and zero-point Energies= -375.313660
Sum of electronic and thermal Energies= -375.308357
Sum of electronic and thermal Enthalpies= -375.307412
Sum of electronic and thermal Free Energies= -375.344204

Cartesian Coordinates

47	-1.097908	-0.002149	-0.000033
8	0.901291	-1.104269	0.000195
6	1.499613	0.011175	-0.000064
6	3.008025	-0.004801	-0.000228
1	3.361708	-0.555448	-0.876917
1	3.414869	1.007317	-0.005370
1	3.361683	-0.545941	0.882420
8	0.900910	1.123870	0.000200

$[AgOAc.HFIP]_2$

Number of imaginary frequencies : 0

Electronic energy : =-2329.9327226
Zero-point correction= 0.237429
Thermal correction to Energy= 0.270233
Thermal correction to Enthalpy= 0.271177
Thermal correction to Gibbs Free Energy= 0.167851
Sum of electronic and zero-point Energies= -2329.695294
Sum of electronic and thermal Energies= -2329.662490
Sum of electronic and thermal Enthalpies= -2329.661545
Sum of electronic and thermal Free Energies= -2329.764872

Cartesian Coordinates

1	1.099823	-3.458615	-0.301052
6	0.418032	-3.046296	-1.046892
6	0.146275	-1.588449	-0.804087
1	0.863453	-3.156384	-2.041265
1	-0.521839	-3.603557	-1.051334
8	0.865965	-0.985037	0.041261
8	-0.777749	-1.056958	-1.487191
47	-1.259383	1.081561	-1.420965
47	0.678844	1.116607	0.591889
1	-0.110822	5.721618	0.281927
6	-1.049546	5.160221	0.272483
6	-0.760376	3.707224	-0.005614
1	-1.486010	5.250539	1.272016
1	-1.731865	5.578778	-0.468345
8	0.054522	3.150739	0.785564

8	-1.351242	3.180179	-0.989096
8	-3.482347	-0.910327	-1.280152
8	3.052461	-1.452992	1.566214
6	4.183644	-0.972124	0.942135
1	5.015268	-0.998829	1.659050
1	-2.578001	-1.286206	-1.314139
6	-4.038936	-1.091499	-0.025502
1	-5.110738	-0.861499	-0.084473
6	-3.920236	-2.553513	0.397505
6	-3.458702	-0.127814	1.014734
9	-4.186865	-0.111381	2.124346
9	-3.438213	1.112752	0.520271
9	-2.199894	-0.451873	1.343207
9	-4.353638	-2.755763	1.637008
9	-2.643479	-2.958287	0.330094
9	-4.628492	-3.316931	-0.426843
1	2.292384	-1.457942	0.943830
6	4.582396	-1.877904	-0.222068
6	4.051809	0.493226	0.516830
9	3.474707	1.201987	1.493475
9	5.233558	1.039182	0.259248
9	5.581678	-1.366219	-0.939426
9	4.968668	-3.060017	0.248489
9	3.546603	-2.084306	-1.042642
9	3.282553	0.632517	-0.576074

All the stationary points of the energy profile diagram as shown in Figure 4.

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a

Number of imaginary frequencies : 0

Electronic energy : =-1021.5484806
Zero-point correction= 0.224294
Thermal correction to Energy= 0.243903
Thermal correction to Enthalpy= 0.244847
Thermal correction to Gibbs Free Energy= 0.174248
Sum of electronic and zero-point Energies= -1021.324187
Sum of electronic and thermal Energies= -1021.304577
Sum of electronic and thermal Enthalpies= -1021.303633
Sum of electronic and thermal Free Energies= -1021.374233

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Cartesian Coordinates

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46	-0.164950	-0.214858	0.007257
8	2.621132	-1.155365	-1.150487
6	2.529752	-3.473417	-0.573147
6	2.009440	-2.058438	-0.564509
8	0.901861	-1.928859	0.093044
6	0.826492	2.228513	-1.070110
6	-0.638245	2.488763	-0.732265

8	-1.242138	1.477670	-0.122096
8	-1.190540	3.512164	-1.045473
1	1.395144	3.146712	-0.899176
1	0.886000	1.964397	-2.131434
1	3.561338	-3.493876	-0.928859
1	2.455253	-3.915198	0.424107
1	1.906171	-4.076798	-1.240991
7	1.399563	1.109192	-0.296893
1	2.034750	0.454350	-0.806302
6	1.898033	1.477270	1.011095
8	1.596489	2.541859	1.485238
6	2.766310	0.446865	1.663300
1	3.290306	0.911014	2.500094
1	2.143519	-0.373464	2.038807
1	3.472562	0.010884	0.949060
6	-3.033195	-1.054699	0.281778
6	-4.122177	-2.053405	0.478069
1	-4.789194	-2.034423	-0.389162
1	-3.703904	-3.050787	0.611456
1	-4.719797	-1.770853	1.349944
8	-1.846299	-1.422845	0.274175
8	-3.448436	0.164991	0.128135
1	-2.696380	0.821522	0.001334

[a-I]‡

Number of imaginary frequencies : 1
The smallest frequency is : -910.1520 cm(-1)

Electronic energy : =-1021.5366058
Zero-point correction= 0.219451
Thermal correction to Energy= 0.238680
Thermal correction to Enthalpy= 0.239624
Thermal correction to Gibbs Free Energy= 0.169963
Sum of electronic and zero-point Energies= -1021.317155
Sum of electronic and thermal Energies= -1021.297926
Sum of electronic and thermal Enthalpies= -1021.296981
Sum of electronic and thermal Free Energies= -1021.366643

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Cartesian Coordinates

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46	-0.222757	-0.250287	0.017313
8	2.462179	-1.315078	-1.110764
6	2.417881	-3.586256	-0.425698
6	1.820588	-2.213602	-0.504960
8	0.698050	-2.060268	0.078177
6	1.075406	1.944840	-1.132061
6	-0.317216	2.465374	-0.775118
8	-1.070850	1.571319	-0.149682
8	-0.685768	3.578817	-1.058071
1	1.789517	2.774935	-1.117554

1	1.032768	1.579054	-2.166134
1	3.012500	-3.788307	-1.319131
1	3.088077	-3.612265	0.440360
1	1.644779	-4.344065	-0.288112
7	1.498732	0.822630	-0.282594
1	2.038618	-0.130054	-0.776270
6	2.081014	1.089997	0.997640
8	2.548363	0.175069	1.635533
6	2.095931	2.514615	1.477314
1	2.434132	2.517500	2.514269
1	2.788298	3.119706	0.880709
1	1.108723	2.985702	1.408975
6	-3.174450	-0.745772	0.257376
6	-4.383735	-1.595920	0.447902
1	-4.887802	-1.299604	1.373229
1	-5.086834	-1.421475	-0.371622
1	-4.104299	-2.648155	0.496063
8	-2.043470	-1.255731	0.260068
8	-3.432238	0.519351	0.103706
1	-2.605433	1.074316	-0.019134

I

Number of imaginary frequencies : 0

Electronic energy : =-1021.5510532
Zero-point correction= 0.223400
Thermal correction to Energy= 0.243142
Thermal correction to Enthalpy= 0.244086
Thermal correction to Gibbs Free Energy= 0.172692
Sum of electronic and zero-point Energies= -1021.327653
Sum of electronic and thermal Energies= -1021.307911
Sum of electronic and thermal Enthalpies= -1021.306967
Sum of electronic and thermal Free Energies= -1021.378361

Cartesian Coordinates

46	0.197557	-0.001698	0.164164
8	-0.737909	2.671219	-1.059563
6	0.242808	4.201302	0.495564
6	-0.190206	2.833126	0.044853
8	0.061717	1.890621	0.880889
6	-1.772582	-1.983090	0.598674
6	-0.543036	-2.734716	0.089083
8	0.436790	-1.948429	-0.315236
8	-0.498216	-3.940931	0.088565
1	-1.771612	-2.061959	1.695501
1	-2.658819	-2.510645	0.231626
1	1.318259	4.303612	0.314953
1	-0.285595	4.972479	-0.067721
1	0.078809	4.321606	1.569267

7	-1.735892	-0.581979	0.193674
1	-1.879045	1.654346	-0.903076
6	-2.797969	0.029983	-0.235219
8	-2.791298	1.214642	-0.759047
6	-4.164202	-0.582670	-0.170543
1	-4.905089	0.197290	-0.351034
1	-4.276220	-1.349257	-0.945911
1	-4.352931	-1.051764	0.798895
6	3.162687	-0.411597	-0.194802
6	4.581806	0.043967	-0.234616
1	4.976876	-0.097892	-1.245435
1	4.652633	1.093206	0.051117
1	5.183143	-0.577177	0.435632
8	2.254678	0.390962	0.071137
8	3.002873	-1.673677	-0.459072
1	2.038289	-1.954954	-0.430447

II

Number of imaginary frequencies : 0

Electronic energy : =-1582.1186916
Zero-point correction= 0.225809
Thermal correction to Energy= 0.249905
Thermal correction to Enthalpy= 0.250849
Thermal correction to Gibbs Free Energy= 0.169044
Sum of electronic and zero-point Energies= -1581.892883
Sum of electronic and thermal Energies= -1581.868787
Sum of electronic and thermal Enthalpies= -1581.867842
Sum of electronic and thermal Free Energies= -1581.949648

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Cartesian Coordinates

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46	-0.913041	0.236333	-0.202064
6	-2.995910	-1.764177	0.067830
6	-3.650841	-0.407061	0.301927
8	-2.837720	0.627222	0.207128
8	-4.827557	-0.325112	0.556262
1	-3.572699	-2.263184	-0.722811
1	-3.135767	-2.351443	0.986373
7	-1.584070	-1.661937	-0.283182
6	-0.898166	-2.722087	-0.594035
8	0.356747	-2.678614	-0.921773
8	0.989229	-0.231723	-0.695320
1	0.730377	-1.730625	-0.877381
6	1.970212	0.223578	0.155044
6	3.220102	0.484896	-0.683198
6	2.223328	-0.762244	1.295319
1	1.719762	1.189623	0.626457
9	3.545059	-0.564734	-1.431198

9	2.995312	1.517713	-1.495597
9	4.270265	0.787584	0.085377
9	2.790456	-1.888160	0.862047
9	2.995022	-0.240201	2.246817
9	1.054593	-1.096972	1.864697
8	-0.357060	2.253773	-0.089194
6	-1.112564	3.233082	0.030583
8	-2.398993	3.173791	0.190720
6	-0.563439	4.617676	-0.010420
1	-1.005901	5.150902	-0.857645
1	-0.856543	5.155385	0.896018
1	0.521527	4.596601	-0.109403
1	-2.745470	2.231189	0.227650
6	-1.500824	-4.088311	-0.604129
1	-1.909335	-4.338805	0.380878
1	-2.325417	-4.143319	-1.323256
1	-0.737080	-4.817986	-0.875032

III

Number of imaginary frequencies : 0

Electronic energy : =-3083.9002238
Zero-point correction= 0.509990
Thermal correction to Energy= 0.552768
Thermal correction to Enthalpy= 0.553712
Thermal correction to Gibbs Free Energy= 0.435259
Sum of electronic and zero-point Energies= -3083.390234
Sum of electronic and thermal Energies= -3083.347456
Sum of electronic and thermal Enthalpies= -3083.346512
Sum of electronic and thermal Free Energies= -3083.464965

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Cartesian Coordinates

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46	-2.341289	0.038113	-0.732209
6	4.191113	-0.540799	1.453620
1	3.559497	-1.357337	1.075939
1	4.733861	-0.932775	2.324945
8	6.096175	-1.693122	0.089825
6	4.050451	-0.993909	-1.892031
6	2.665259	-0.915126	-2.100762
6	4.823911	-1.984876	-2.485621
6	2.083476	-1.897117	-2.914762
6	4.214200	-2.949083	-3.276535
1	5.894364	-1.994761	-2.311359
6	2.840432	-2.907570	-3.488337
1	1.017468	-1.844417	-3.125299
1	4.818959	-3.725919	-3.736432
1	2.358576	-3.650796	-4.117646
6	-5.076651	0.651841	-1.438903
6	-4.213456	1.850393	-1.831764

8	-2.925647	1.733650	-1.606063
8	-4.732578	2.832881	-2.312330
1	-5.714949	0.409458	-2.298591
7	-4.274404	-0.490522	-1.018636
6	-4.797935	-1.663402	-0.858918
8	-4.101209	-2.699129	-0.475721
8	4.659456	0.000872	-1.133224
16	5.499906	-0.381703	0.234758
8	6.310502	0.791521	0.467913
6	3.377813	0.676959	1.789035
6	2.015178	0.494971	2.037622
6	3.936387	1.946694	1.955850
6	1.220008	1.558157	2.450924
1	1.583615	-0.499945	1.930995
6	3.134026	3.013029	2.348693
1	4.996382	2.100201	1.776427
6	1.779399	2.823273	2.601390
1	0.160635	1.400371	2.646963
1	3.578720	3.997997	2.473353
1	1.161301	3.657449	2.926431
1	-3.152119	-2.445527	-0.242138
1	-5.737903	0.982687	-0.624859
6	2.208260	1.482177	-1.451254
6	1.320296	2.453495	-0.948699
6	1.825501	0.161180	-1.543290
6	1.707072	3.814710	-0.889114
6	0.028996	2.048923	-0.504620
6	0.501445	-0.133610	-1.157140
6	0.841339	4.770708	-0.430307
1	2.707959	4.077179	-1.225975
6	-0.792335	3.060923	0.067694
1	0.120548	-1.150762	-1.228311
6	-0.416060	4.381381	0.063069
1	1.127002	5.817960	-0.408340
1	-1.105273	5.106772	0.485087
7	-0.359758	0.749471	-0.678599
7	-2.014643	2.759202	0.818164
8	-2.898064	3.591051	0.830546
8	-2.032387	1.702987	1.442605
1	3.196622	1.799075	-1.777175
6	-6.243682	-1.945662	-1.103810
1	-6.509216	-1.737573	-2.146130
1	-6.453514	-2.992368	-0.880512
1	-6.872094	-1.307076	-0.473514
8	-1.748130	-1.758639	0.072244
6	-1.262310	-1.706393	1.354918
1	-0.786550	-0.739220	1.605045
6	-2.373678	-1.890285	2.390524
6	-0.160935	-2.757276	1.495701
9	-1.951033	-1.618519	3.625146
9	-3.382482	-1.060310	2.112860
9	-2.858441	-3.133950	2.379320
9	0.870272	-2.430517	0.688545
9	0.324935	-2.804802	2.738510
9	-0.562307	-3.972180	1.151693

IV

Number of imaginary frequencies : 0

Electronic energy : =-2294.3142914
Zero-point correction= 0.439776
Thermal correction to Energy= 0.474080
Thermal correction to Enthalpy= 0.475025
Thermal correction to Gibbs Free Energy= 0.373210
Sum of electronic and zero-point Energies= -2293.874515
Sum of electronic and thermal Energies= -2293.840211
Sum of electronic and thermal Enthalpies= -2293.839267
Sum of electronic and thermal Free Energies= -2293.941082

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Cartesian Coordinates

.....

46	-1.778382	-0.408311	0.418663
6	-1.210337	-2.309208	-1.007197
6	-1.293660	-2.819285	0.296665
6	-0.121496	-3.220634	0.970968
6	1.091660	-3.168887	0.323486
6	1.185652	-2.682320	-0.999786
6	0.048576	-2.227874	-1.640504
1	1.994674	-3.515446	0.823153
6	2.513110	-2.700400	-1.693253
1	2.416168	-2.734013	-2.784753
1	3.144651	-3.537770	-1.376051
8	2.856996	-0.050547	-1.902998
6	4.085030	-0.323284	0.979076
6	3.465298	0.899725	1.265938
6	5.339416	-0.650015	1.472990
6	4.156155	1.783573	2.102167
6	6.003637	0.248830	2.297830
1	5.772700	-1.607739	1.198401
6	5.405263	1.463751	2.617681
1	3.685711	2.729509	2.364014
1	6.984097	-0.002283	2.693233
1	5.911895	2.165785	3.274593
6	-4.037553	-0.041878	2.157447
6	-3.264997	1.267594	2.155379
8	-2.232279	1.313622	1.335486
8	-3.571167	2.195169	2.871862
1	-5.098556	0.220389	2.070625
7	-3.594790	-0.933925	1.101713
6	-4.451550	-1.658365	0.342612
8	-4.107224	-2.283910	-0.662299
8	3.410702	-1.285410	0.232595
8	4.902358	-1.511887	-1.779251
16	3.527189	-1.240216	-1.413532
1	-3.908094	-0.490055	3.156367

6	2.032083	2.551082	0.111483
6	0.858982	2.896802	-0.585971
6	2.189732	1.295694	0.643091
6	0.684662	4.196728	-1.117122
6	-0.142129	1.901771	-0.756499
6	1.088523	0.412740	0.529530
6	-0.461439	4.533092	-1.785415
1	1.479814	4.924484	-0.968895
6	-1.276995	2.279291	-1.522503
1	1.126475	-0.561984	1.014933
6	-1.452923	3.557500	-1.987155
1	-0.605307	5.535518	-2.177023
1	-2.362047	3.785612	-2.535774
1	2.832121	3.286508	0.187707
7	-0.016035	0.686126	-0.136395
7	-2.292401	1.311197	-1.953142
8	-3.458602	1.647827	-1.893051
8	-1.875859	0.255191	-2.407975
1	-2.271205	-3.031696	0.717085
1	-0.189305	-3.623425	1.978265
1	0.111413	-1.835548	-2.654425
1	-2.137763	-2.127175	-1.548151
6	-5.899960	-1.722989	0.796836
1	-6.002839	-1.910280	1.870928
1	-6.416011	-0.782190	0.570806
1	-6.383299	-2.524851	0.236140

[IV-b]‡

Number of imaginary frequencies : 1
The smallest frequency is : -1634.1550 cm(-1)

Electronic energy : =-2294.3008456
Zero-point correction= 0.434972
Thermal correction to Energy= 0.468509
Thermal correction to Enthalpy= 0.469453
Thermal correction to Gibbs Free Energy= 0.370436
Sum of electronic and zero-point Energies= -2293.865873
Sum of electronic and thermal Energies= -2293.832337
Sum of electronic and thermal Enthalpies= -2293.831392
Sum of electronic and thermal Free Energies= -2293.930409

Cartesian Coordinates

46	-1.811817	-0.354608	0.450258
6	-0.888114	-2.212063	-0.229305
6	-0.709079	-3.087256	0.857072
6	0.478619	-3.788432	1.034761
6	1.508047	-3.623840	0.118013
6	1.357261	-2.774101	-0.982883
6	0.160631	-2.082574	-1.155911

1	2.452173	-4.150057	0.256027
6	2.519927	-2.564399	-1.900403
1	2.229592	-2.442867	-2.950971
1	3.265797	-3.363150	-1.828968
8	2.658130	0.110184	-1.960320
6	4.084527	-0.252028	0.852424
6	3.479458	0.948442	1.247788
6	5.370197	-0.593249	1.246532
6	4.218372	1.788612	2.088311
6	6.082391	0.262721	2.076284
1	5.789115	-1.527908	0.884150
6	5.499743	1.452084	2.503616
1	3.761305	2.715048	2.431314
1	7.088682	-0.001022	2.390356
1	6.045035	2.120758	3.164396
6	-4.445832	-0.240542	1.651917
6	-3.773550	1.113531	1.899137
8	-2.586446	1.276327	1.366507
8	-4.343557	1.956716	2.558481
1	-5.421999	-0.028744	1.195339
7	-3.628934	-1.103910	0.817324
6	-4.120709	-2.041476	0.024856
8	-3.405515	-2.667159	-0.809198
8	3.371923	-1.173220	0.093288
8	4.816702	-1.182646	-1.969207
16	3.434424	-1.047435	-1.554288
1	-4.640317	-0.691731	2.636433
6	1.981681	2.661743	0.281123
6	0.777764	3.043584	-0.342318
6	2.168233	1.376235	0.726839
6	0.576969	4.366723	-0.803105
6	-0.223780	2.053053	-0.529259
6	1.057471	0.502470	0.633677
6	-0.585815	4.719477	-1.433464
1	1.367482	5.096059	-0.638457
6	-1.366545	2.443300	-1.278999
1	1.110535	-0.495091	1.068014
6	-1.563378	3.739329	-1.680950
1	-0.749451	5.738324	-1.771296
1	-2.474200	3.978601	-2.221760
1	2.785431	3.393070	0.358007
7	-0.080326	0.818590	0.046021
7	-2.349988	1.471555	-1.772843
8	-3.524206	1.786471	-1.743629
8	-1.904121	0.430663	-2.237839
1	-1.530409	-3.223873	1.560093
1	0.603975	-4.461340	1.879591
1	0.049754	-1.397499	-1.997070
1	-2.119017	-2.240149	-0.622790
6	-5.581204	-2.396865	0.099704
1	-5.938331	-2.454634	1.132414
1	-6.171533	-1.630074	-0.415833
1	-5.739097	-3.352011	-0.403162

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b

Number of imaginary frequencies : 0

Electronic energy : =-2294.3258093
Zero-point correction= 0.441162
Thermal correction to Energy= 0.475054
Thermal correction to Enthalpy= 0.475998
Thermal correction to Gibbs Free Energy= 0.375678
Sum of electronic and zero-point Energies= -2293.884647
Sum of electronic and thermal Energies= -2293.850756
Sum of electronic and thermal Enthalpies= -2293.849811
Sum of electronic and thermal Free Energies= -2293.950131

Cartesian Coordinates

46	-1.780206	-0.329825	0.438875
6	-0.682037	-1.951152	-0.057501
6	-0.644384	-3.031940	0.835644
6	0.376112	-3.979013	0.775089
6	1.397366	-3.841408	-0.156445
6	1.360908	-2.792638	-1.074925
6	0.298588	-1.886023	-1.054193
1	2.233910	-4.538891	-0.165175
6	2.534540	-2.556925	-1.970486
1	2.263090	-2.358895	-3.015275
1	3.262488	-3.374317	-1.940078
8	2.796348	0.117408	-1.995485
6	4.028071	-0.276023	0.884446
6	3.473646	0.957886	1.257879
6	5.286225	-0.672487	1.315866
6	4.237424	1.773353	2.100757
6	6.022920	0.159553	2.148240
1	5.667378	-1.633160	0.981709
6	5.493606	1.383850	2.544497
1	3.816751	2.722800	2.427115
1	7.006830	-0.151122	2.489300
1	6.058381	2.035543	3.205907
6	-4.295000	-0.510191	1.830622
6	-3.913289	0.986729	1.851757
8	-2.834054	1.301879	1.208989
8	-4.627535	1.738234	2.488000
1	-5.382253	-0.581384	1.717712
7	-3.573405	-1.242059	0.794353
6	-4.148272	-2.092076	0.018123
8	-3.505542	-2.644162	-0.995958
8	3.296495	-1.169623	0.108528
8	4.884998	-1.274527	-1.847757
16	3.482991	-1.076179	-1.534571
1	-4.033534	-0.922710	2.815109
6	1.995969	2.725324	0.323770
6	0.784058	3.127867	-0.273570

6	2.174971	1.430661	0.745196
6	0.591522	4.461195	-0.707903
6	-0.229246	2.149518	-0.472316
6	1.048664	0.579038	0.667212
6	-0.568189	4.833765	-1.332680
1	1.387741	5.181328	-0.530402
6	-1.359680	2.555882	-1.235651
1	1.101586	-0.419907	1.095119
6	-1.543784	3.861493	-1.614228
1	-0.725907	5.860401	-1.649040
1	-2.443158	4.112051	-2.168510
1	2.806458	3.449406	0.399494
7	-0.095874	0.910700	0.097527
7	-2.324283	1.598196	-1.789288
8	-3.484490	1.945159	-1.889233
8	-1.871188	0.525393	-2.172596
1	-1.407225	-3.121579	1.609309
1	0.392923	-4.807368	1.480524
1	0.293892	-1.060232	-1.766187
1	-2.593146	-2.277390	-1.023069
6	-5.563220	-2.550925	0.141848
1	-5.801947	-2.829770	1.171829
1	-6.245568	-1.746406	-0.154663
1	-5.727324	-3.405402	-0.516183

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c

Number of imaginary frequencies : 0

Electronic energy : =-2523.3021371
Zero-point correction= 0.504439
Thermal correction to Energy= 0.544090
Thermal correction to Enthalpy= 0.545034
Thermal correction to Gibbs Free Energy= 0.431331
Sum of electronic and zero-point Energies= -2522.797698
Sum of electronic and thermal Energies= -2522.758047
Sum of electronic and thermal Enthalpies= -2522.757103
Sum of electronic and thermal Free Energies= -2522.870806

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Cartesian Coordinates

.....

46	-1.351213	0.359551	-0.642277
6	-0.562987	-1.322846	-1.302298
6	-1.068235	-2.549412	-0.864958
6	-0.336992	-3.718707	-1.070321
6	0.915786	-3.666134	-1.668655
6	1.412699	-2.446155	-2.125644
6	0.646435	-1.286025	-1.994985
1	1.522567	-4.566182	-1.757727
6	2.834714	-2.346805	-2.575738
1	2.973512	-1.773952	-3.501405

1	3.318477	-3.323464	-2.680860
8	3.618635	-0.009450	-1.500695
6	3.752332	-1.698986	1.204877
6	3.399450	-0.544170	1.920780
6	4.659541	-2.620137	1.709959
6	3.983114	-0.366056	3.180022
6	5.226522	-2.414887	2.960701
1	4.906721	-3.486878	1.103706
6	4.881495	-1.287452	3.699763
1	3.703283	0.508136	3.765432
1	5.933290	-3.138126	3.358692
1	5.309770	-1.127377	4.685766
6	-5.237619	-1.397459	-0.706460
6	-3.967453	-0.705999	-0.220263
8	-3.203474	-0.341521	-1.174493
8	-3.735956	-0.601244	0.998945
1	-4.895391	-2.363319	-1.124160
7	-6.269394	-1.530177	0.281376
6	-6.143953	-2.403971	1.194412
8	-7.097554	-2.485767	2.144071
8	3.142994	-1.982450	-0.010064
8	5.230099	-1.938789	-1.425156
16	3.869767	-1.436612	-1.397143
1	-5.608319	-0.825238	-1.564046
6	2.821822	1.827251	1.468056
6	2.052258	2.797624	0.793918
6	2.520141	0.493873	1.354030
6	2.369247	4.172296	0.906786
6	0.990123	2.358335	-0.047671
6	1.329593	0.173051	0.658883
6	1.670695	5.112966	0.198535
1	3.187640	4.458526	1.564522
6	0.371987	3.362141	-0.849009
1	0.976727	-0.855961	0.661682
6	0.679159	4.693146	-0.704322
1	1.905559	6.169303	0.288912
1	0.156272	5.403547	-1.337139
1	3.694513	2.152000	2.033836
7	0.593202	1.044724	-0.009529
7	-0.516892	3.051767	-1.976724
8	-1.354355	3.880154	-2.281439
8	-0.312038	1.999365	-2.564318
1	-2.014814	-2.596059	-0.328946
1	-0.732646	-4.670581	-0.721577
1	1.054422	-0.337393	-2.342631
1	-7.722806	-1.775415	1.932141
6	-5.059125	-3.408504	1.412230
1	-4.727546	-3.841083	0.461617
1	-4.197848	-2.905074	1.864336
1	-5.402330	-4.207502	2.072634
8	-2.091728	2.261026	0.276883
6	-2.332264	2.377284	1.482581
6	-2.127369	3.693838	2.164470
1	-2.892679	4.393126	1.812614
1	-2.194389	3.602174	3.249448

1	-1.155964	4.103378	1.866563
8	-2.766791	1.421471	2.246693
1	-3.032274	0.594711	1.708254

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d

Number of imaginary frequencies : 0

Electronic energy : =-2523.3216406
Zero-point correction= 0.504618
Thermal correction to Energy= 0.544280
Thermal correction to Enthalpy= 0.545224
Thermal correction to Gibbs Free Energy= 0.429890
Sum of electronic and zero-point Energies= -2522.817022
Sum of electronic and thermal Energies= -2522.777360
Sum of electronic and thermal Enthalpies= -2522.776416
Sum of electronic and thermal Free Energies= -2522.891750

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Cartesian Coordinates

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46	-1.358064	0.480978	-0.140450
6	-0.864852	-1.370186	-0.621502
6	-1.415565	-2.458675	0.057399
6	-0.859160	-3.727899	-0.094105
6	0.268125	-3.910217	-0.884724
6	0.799899	-2.831394	-1.589643
6	0.196951	-1.574822	-1.501850
1	0.747338	-4.886247	-0.945575
6	2.108266	-2.980677	-2.297604
1	2.118346	-2.561664	-3.311782
1	2.454415	-4.018756	-2.334964
8	3.362215	-0.653320	-1.797102
6	3.800676	-1.863342	1.088653
6	3.701985	-0.562231	1.604026
6	4.701631	-2.785748	1.602486
6	4.535129	-0.232646	2.679232
6	5.518495	-2.429913	2.667395
1	4.746582	-3.770988	1.147280
6	5.429208	-1.151915	3.210485
1	4.457420	0.763134	3.112483
1	6.221590	-3.151883	3.074016
1	6.055196	-0.870629	4.053201
6	-5.226121	-0.794568	1.215059
6	-3.868188	-0.118018	1.124811
8	-3.321247	-0.138440	-0.024047
8	-3.423234	0.385372	2.170951
1	-5.973430	0.010352	1.320404
7	-5.482850	-1.651893	0.089347
6	-6.534074	-2.510629	-0.066013
8	-6.692907	-3.154527	-1.088657
8	2.948711	-2.282393	0.075553
8	4.710358	-2.770902	-1.662096

16	3.452178	-2.070737	-1.489778
1	-5.234463	-1.345768	2.164712
6	3.297323	1.730700	0.753742
6	2.511080	2.659377	0.042383
6	2.834412	0.462244	0.994774
6	3.003348	3.960647	-0.217297
6	1.242954	2.240926	-0.455931
6	1.495643	0.198024	0.621172
6	2.278954	4.847286	-0.967669
1	3.976277	4.231609	0.187835
6	0.575805	3.163946	-1.313355
1	1.042518	-0.749471	0.903073
6	1.064591	4.428778	-1.534874
1	2.650705	5.848366	-1.164499
1	0.493055	5.081946	-2.187281
1	4.302990	2.019700	1.056903
7	0.726178	1.031188	-0.062594
7	-0.598095	2.808152	-2.119981
8	-1.380003	3.697683	-2.399249
8	-0.679119	1.647282	-2.495226
1	-2.270000	-2.323772	0.716367
1	-1.292787	-4.571803	0.438110
1	0.623787	-0.738680	-2.054453
6	-7.472899	-2.614386	1.113642
1	-6.945982	-2.944025	2.017009
1	-7.935737	-1.646750	1.341970
1	-8.252227	-3.336912	0.867978
8	-1.750740	2.613441	0.359976
6	-1.757772	3.139495	1.476768
6	-1.315252	4.558454	1.645418
1	-1.886552	5.060495	2.429201
1	-0.259961	4.563854	1.946540
1	-1.408124	5.082653	0.691467
8	-2.102684	2.534965	2.572593
1	-2.514463	1.621204	2.372785
1	-4.871398	-1.540285	-0.711886

VII

Number of imaginary frequencies : 0

Electronic energy : =-2639.9271617
Zero-point correction= 0.569995
Thermal correction to Energy= 0.611326
Thermal correction to Enthalpy= 0.612270
Thermal correction to Gibbs Free Energy= 0.499994
Sum of electronic and zero-point Energies= -2639.357167
Sum of electronic and thermal Energies= -2639.315836
Sum of electronic and thermal Enthalpies= -2639.314892
Sum of electronic and thermal Free Energies= -2639.427168

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Cartesian Coordinates

46	0.615763	-0.095244	0.772892
6	-2.554387	2.116418	2.608126
6	-1.274737	1.721367	2.217988
6	-1.057597	0.412352	1.790459
6	-2.102357	-0.501400	1.812577
6	-3.398806	-0.083945	2.123866
6	-3.622817	1.229877	2.532754
1	-1.934574	-1.535717	1.503596
1	-0.455111	2.438139	2.209929
1	-4.634215	1.560307	2.761726
6	-4.531152	-1.011137	1.840333
1	-4.230841	-2.063602	1.802964
1	-5.380233	-0.910203	2.527295
1	-2.723255	3.139256	2.938620
6	3.683474	-1.053749	-2.296009
6	2.563197	-0.229315	-1.647759
8	2.297715	-0.598357	-0.440333
8	2.042384	0.679021	-2.286826
1	4.621975	-0.491268	-2.226709
1	3.438520	-1.161472	-3.355869
7	3.860774	-2.362296	-1.708127
1	4.297817	-2.386895	-0.791544
6	2.839598	-3.254330	-1.866728
8	1.952924	-3.098012	-2.699141
6	2.859737	-4.441012	-0.940437
1	2.416696	-5.300353	-1.449949
1	3.862052	-4.686053	-0.578375
1	2.249789	-4.197559	-0.061044
6	0.989084	-0.793663	2.903504
6	1.648557	-1.629437	2.033092
1	0.039925	-1.085892	3.339205
1	1.510192	0.043751	3.363723
1	1.208982	-2.577246	1.718918
6	3.113537	-1.526550	1.768674
8	3.762192	-2.434296	1.293841
8	3.614340	-0.368301	2.185992
6	4.965587	-0.077451	1.800469
6	5.354609	1.213999	2.466966
1	4.985215	0.011373	0.704672
1	5.607542	-0.918139	2.089656
1	6.386479	1.473060	2.209051
1	4.697567	2.021848	2.129014
1	5.283740	1.126775	3.556291
16	-5.284387	-0.644337	0.231068
8	-6.018894	-1.812029	-0.216027
8	-5.904059	0.659009	0.271273
8	-3.981004	-0.393223	-0.745382
6	-2.980227	-1.330064	-0.983150
6	-3.210550	-2.699190	-0.953427
6	-1.700020	-0.811918	-1.256191
6	-2.152130	-3.574312	-1.189287
1	-4.211394	-3.075335	-0.764951
6	-0.670359	-1.717640	-1.533160

6	-0.884963	-3.091322	-1.489093
1	-2.340674	-4.645186	-1.170908
1	0.303965	-1.345350	-1.838872
1	-0.058625	-3.748681	-1.750885
6	0.055266	2.430077	-1.092108
6	-1.421040	0.636960	-1.366909
6	1.285213	3.028785	-0.680677
6	-0.733969	3.235017	-1.965927
6	-2.273676	1.411144	-2.188164
6	1.699582	4.254673	-1.142837
6	-0.322263	4.524649	-2.371628
6	-1.938488	2.698668	-2.468504
1	-3.164823	0.951112	-2.600000
6	0.887741	5.029208	-1.983060
1	2.672117	4.617067	-0.822993
1	-0.982889	5.089720	-3.026097
1	-2.560496	3.315412	-3.114143
1	1.225173	6.006666	-2.313837
7	-0.334355	1.151143	-0.783948
7	2.212603	2.458180	0.302138
8	1.741948	2.145531	1.390852
8	3.395886	2.420074	0.019306

[VII-VIII]‡

Number of imaginary frequencies : 1
The smallest frequency is : -284.7410 cm(-1)

Electronic energy : =-2639.9174577
Zero-point correction= 0.568806
Thermal correction to Energy= 0.609740
Thermal correction to Enthalpy= 0.610684
Thermal correction to Gibbs Free Energy= 0.498813
Sum of electronic and zero-point Energies= -2639.348651
Sum of electronic and thermal Energies= -2639.307718
Sum of electronic and thermal Enthalpies= -2639.306773
Sum of electronic and thermal Free Energies= -2639.418644

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Cartesian Coordinates

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46	0.647348	-0.211669	0.676239
6	-2.383157	1.883671	2.800439
6	-1.095476	1.430985	2.524052
6	-0.907297	0.140078	2.024316
6	-2.006838	-0.704515	1.869866
6	-3.297868	-0.235166	2.104098
6	-3.484573	1.066540	2.575215
1	-1.859057	-1.728509	1.517922
1	-0.240882	2.091366	2.652450
1	-4.493713	1.437604	2.743502
6	-4.463865	-1.099274	1.753648

1	-4.187373	-2.147595	1.600355
1	-5.283473	-1.054863	2.481277
1	-2.528125	2.893828	3.176999
6	3.730667	-0.970226	-2.353685
6	2.570774	-0.186807	-1.725400
8	2.295111	-0.609914	-0.538422
8	2.036949	0.727610	-2.342799
1	4.659685	-0.406664	-2.207060
1	3.543977	-1.037013	-3.428527
7	3.887295	-2.299365	-1.802106
1	4.293216	-2.343049	-0.871312
6	2.844415	-3.164802	-1.988059
8	1.966952	-2.965467	-2.820563
6	2.836722	-4.372074	-1.090122
1	2.315260	-5.191027	-1.591389
1	3.842416	-4.686503	-0.795377
1	2.301250	-4.109508	-0.168877
6	0.701275	-0.844622	2.880601
6	1.452847	-1.645129	1.978928
1	-0.071580	-1.330533	3.467404
1	1.214154	-0.027708	3.387573
1	1.059289	-2.625929	1.699935
6	2.927995	-1.569244	1.818142
8	3.576613	-2.458180	1.306812
8	3.448513	-0.444778	2.310541
6	4.817168	-0.187246	1.960842
6	5.230503	1.073044	2.669326
1	4.866507	-0.078170	0.867094
1	5.426581	-1.053789	2.244471
1	6.269408	1.318375	2.426670
1	4.593169	1.903964	2.352823
1	5.148766	0.955149	3.755068
16	-5.264803	-0.559390	0.223927
8	-6.055028	-1.657717	-0.296155
8	-5.839799	0.752373	0.410391
8	-3.988746	-0.266020	-0.767112
6	-3.001345	-1.204634	-1.056912
6	-3.250264	-2.570605	-1.097499
6	-1.722125	-0.684751	-1.316354
6	-2.204342	-3.443676	-1.391284
1	-4.255285	-2.944727	-0.926031
6	-0.707896	-1.585037	-1.663135
6	-0.936912	-2.957200	-1.685449
1	-2.404088	-4.512107	-1.425970
1	0.264120	-1.211039	-1.974521
1	-0.117938	-3.607228	-1.986777
6	0.079226	2.509708	-1.028901
6	-1.433833	0.767926	-1.354415
6	1.323921	3.057778	-0.596860
6	-0.684262	3.361270	-1.880731
6	-2.274975	1.588097	-2.144377
6	1.782257	4.279640	-1.025116
6	-0.228763	4.646583	-2.251616
6	-1.905305	2.873170	-2.392874
1	-3.180331	1.163866	-2.564309

6	0.997111	5.099891	-1.848022
1	2.764215	4.603049	-0.692369
1	-0.868272	5.251252	-2.891763
1	-2.511537	3.522496	-3.021516
1	1.366564	6.073926	-2.153940
7	-0.336087	1.232721	-0.756654
7	2.211479	2.418353	0.375734
8	1.706522	2.074620	1.438517
8	3.397716	2.345710	0.111985

VIII

Number of imaginary frequencies : 0

Electronic energy : =-2639.9599159
Zero-point correction= 0.570867
Thermal correction to Energy= 0.612305
Thermal correction to Enthalpy= 0.613249
Thermal correction to Gibbs Free Energy= 0.499308
Sum of electronic and zero-point Energies= -2639.389049
Sum of electronic and thermal Energies= -2639.347611
Sum of electronic and thermal Enthalpies= -2639.346667
Sum of electronic and thermal Free Energies= -2639.460608

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Cartesian Coordinates

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46	0.659983	-0.322810	0.383047
6	-1.278435	0.483766	2.889962
6	-0.243852	-0.434490	2.631368
6	-0.531175	-1.663526	2.006017
6	-1.865023	-1.939402	1.647275
6	-2.881876	-1.047004	1.940561
6	-2.581278	0.180147	2.560276
1	-2.093158	-2.883558	1.151191
1	0.755440	-0.253882	3.025276
1	-3.385386	0.884008	2.767905
6	-4.294723	-1.402625	1.604727
1	-4.372963	-2.377976	1.116416
1	-4.950191	-1.404355	2.485722
1	-1.038422	1.428762	3.368730
6	3.372442	-0.256773	-2.946985
6	2.255175	0.360056	-2.095493
8	2.282957	-0.084963	-0.883004
8	1.476938	1.168418	-2.589538
1	4.264440	0.376614	-2.889218
1	3.027606	-0.265545	-3.984592
7	3.723292	-1.600160	-2.540243
1	4.280521	-1.677274	-1.694647
6	2.767434	-2.568326	-2.671992
8	1.718335	-2.378804	-3.278320
6	3.129335	-3.900953	-2.066506

1	2.229102	-4.517004	-1.996197
1	3.852996	-4.415192	-2.708769
1	3.581835	-3.773843	-1.076428
6	0.571632	-2.691385	1.836587
6	1.545329	-2.120578	0.819301
1	0.143607	-3.634839	1.476637
1	1.048744	-2.888827	2.804698
1	1.539010	-2.632354	-0.148861
6	2.936828	-1.818843	1.237431
8	3.937588	-2.096800	0.606535
8	2.973639	-1.165967	2.413355
6	4.255650	-0.674585	2.830933
6	4.014226	0.246761	3.996164
1	4.720562	-0.154213	1.985286
1	4.895372	-1.528292	3.090329
1	4.963709	0.642615	4.370820
1	3.386360	1.087620	3.681608
1	3.514303	-0.279599	4.816988
16	-5.144321	-0.222899	0.525813
8	-6.184811	-0.937819	-0.185894
8	-5.437640	0.984155	1.265350
8	-3.982078	0.250876	-0.527725
6	-3.126662	-0.657681	-1.146312
6	-3.518527	-1.940719	-1.507247
6	-1.832011	-0.186500	-1.392858
6	-2.581519	-2.794625	-2.085960
1	-4.547158	-2.258147	-1.357976
6	-0.928674	-1.048995	-2.025877
6	-1.288066	-2.356356	-2.342106
1	-2.885252	-3.801062	-2.364920
1	0.046297	-0.680233	-2.336520
1	-0.544640	-2.987700	-2.823201
6	0.138394	2.777996	-0.471904
6	-1.444864	1.229526	-1.164374
6	1.343875	3.160877	0.185060
6	-0.441450	3.780338	-1.301604
6	-2.148567	2.210375	-1.903057
6	1.964737	4.363837	-0.047786
6	0.175153	5.038944	-1.477187
6	-1.640070	3.470496	-1.979840
1	-3.042550	1.919290	-2.445417
6	1.376342	5.323901	-0.884238
1	2.905731	4.562216	0.457312
1	-0.317616	5.765825	-2.120018
1	-2.116270	4.236670	-2.588505
1	1.866882	6.279919	-1.040441
7	-0.383629	1.514682	-0.416779
7	1.977014	2.350621	1.225210
8	1.239770	1.930634	2.107074
8	3.186003	2.211279	1.199702

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e

Number of imaginary frequencies : 0

Electronic energy : =-2639.931112
Zero-point correction= 0.568918
Thermal correction to Energy= 0.610528
Thermal correction to Enthalpy= 0.611472
Thermal correction to Gibbs Free Energy= 0.494846
Sum of electronic and zero-point Energies= -2639.362194
Sum of electronic and thermal Energies= -2639.320584
Sum of electronic and thermal Enthalpies= -2639.319640
Sum of electronic and thermal Free Energies= -2639.436266

Cartesian Coordinates

46	1.016098	-1.059422	-0.480479
6	-0.857170	-3.100928	3.430284
6	-0.073025	-3.334285	2.304722
6	-0.586269	-3.089811	1.033698
6	-1.904277	-2.644406	0.913344
6	-2.691351	-2.396102	2.032742
6	-2.152901	-2.617795	3.300964
1	-2.316379	-2.443481	-0.077967
1	0.950244	-3.682957	2.424365
1	-2.751764	-2.411567	4.186346
6	-4.094865	-1.900048	1.884325
1	-4.706167	-2.503951	1.203591
1	-4.615716	-1.851904	2.848002
1	-0.442893	-3.277975	4.419411
6	4.021897	1.854200	-1.202473
6	2.872768	0.860322	-1.315201
8	2.763482	0.050571	-0.313862
8	2.145101	0.897882	-2.303439
1	3.601670	2.866894	-1.183327
1	4.618436	1.775217	-2.121929
7	4.836651	1.701390	-0.021807
1	4.997876	0.750541	0.284778
6	4.902412	2.678945	0.927844
8	4.420931	3.795325	0.776630
6	5.628702	2.297003	2.191837
1	6.355712	3.078268	2.429681
1	4.900744	2.253461	3.008472
1	6.139052	1.331154	2.129833
6	0.227691	-3.183005	-0.229735
6	1.691866	-2.963888	-0.202149
1	-0.213132	-2.340391	-0.931922
1	-0.049753	-4.011279	-0.900544
1	2.241241	-2.979832	0.739842
6	2.444238	-3.342588	-1.413836
8	1.933284	-3.686807	-2.461179
8	3.763371	-3.186449	-1.221560
6	4.566189	-3.102758	-2.409704
6	4.590792	-1.672713	-2.896434
1	4.160510	-3.784686	-3.164386

1	5.558599	-3.452337	-2.109141
1	5.220514	-1.579835	-3.787567
1	3.581717	-1.323768	-3.148917
1	4.989457	-1.012372	-2.116717
16	-4.285403	-0.217001	1.261935
8	-5.682983	0.149852	1.379168
8	-3.242214	0.658553	1.754921
8	-3.985503	-0.538173	-0.342026
6	-4.483390	0.386022	-1.265083
6	-5.761553	0.181143	-1.763812
6	-3.690550	1.464281	-1.684196
6	-6.277384	1.055816	-2.710850
1	-6.337810	-0.659286	-1.387507
6	-4.235218	2.331059	-2.637306
6	-5.511326	2.132733	-3.146972
1	-7.277187	0.897052	-3.105848
1	-3.627336	3.160202	-2.994894
1	-5.906285	2.817695	-3.892709
6	0.959986	4.442242	1.092521
6	-0.190596	4.340301	0.357022
6	-0.684536	3.073229	-0.037705
6	0.028336	1.889400	0.299472
6	1.109104	2.033624	1.219043
6	1.582508	3.274586	1.569340
1	-2.519486	3.825377	-0.892260
1	1.368740	5.409901	1.366273
1	-0.744613	5.227900	0.056979
6	-1.910101	2.937484	-0.725347
1	2.433307	3.339826	2.239203
6	-1.445083	0.628677	-0.952079
6	-2.355103	1.697925	-1.113789
1	-1.669165	-0.329341	-1.419922
7	-0.312391	0.707284	-0.292119
7	1.649426	0.899593	1.980457
8	2.734407	1.038390	2.518677
8	0.942530	-0.092258	2.092821

[e-f]‡

Number of imaginary frequencies : 1
The smallest frequency is : -189.9069 cm(-1)

Electronic energy : =-2639.9200626
Zero-point correction= 0.565857
Thermal correction to Energy= 0.607126
Thermal correction to Enthalpy= 0.608071
Thermal correction to Gibbs Free Energy= 0.492706
Sum of electronic and zero-point Energies= -2639.354206
Sum of electronic and thermal Energies= -2639.312936
Sum of electronic and thermal Enthalpies= -2639.311992
Sum of electronic and thermal Free Energies= -2639.427356

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Cartesian Coordinates

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46	1.015584	-1.082210	-0.557403
6	-0.735297	-2.638237	3.572234
6	0.086764	-2.939980	2.493126
6	-0.428837	-2.938344	1.196957
6	-1.788325	-2.665988	1.009950
6	-2.610120	-2.340520	2.082031
6	-2.071712	-2.319222	3.370674
1	-2.200256	-2.657848	-0.001467
1	1.139380	-3.157571	2.658579
1	-2.705358	-2.055027	4.215660
6	-4.049849	-2.002483	1.866574
1	-4.555354	-2.654498	1.145570
1	-4.622617	-2.023371	2.801287
1	-0.322606	-2.632142	4.577511
6	4.019649	1.782595	-1.226063
6	2.910420	0.744766	-1.219050
8	2.852122	-0.024055	-0.194313
8	2.119967	0.703068	-2.172049
1	3.565474	2.779427	-1.277564
1	4.601042	1.651818	-2.149526
7	4.858925	1.743245	-0.053250
1	5.033572	0.821259	0.327249
6	4.899499	2.789507	0.822574
8	4.391481	3.879573	0.589436
6	5.622177	2.512779	2.115659
1	6.231551	3.382652	2.373242
1	4.874889	2.375210	2.904831
1	6.253938	1.620084	2.079090
6	0.413514	-3.126464	-0.006112
6	1.815770	-2.985455	-0.067478
1	-0.219099	-1.823428	-1.105421
1	-0.029837	-3.701721	-0.822788
1	2.419347	-2.770308	0.814734
6	2.532680	-3.430446	-1.285107
8	1.999753	-3.859856	-2.286091
8	3.851342	-3.236321	-1.138952
6	4.621881	-3.188496	-2.350427
6	4.616160	-1.772025	-2.876739
1	4.202568	-3.897916	-3.071438
1	5.625533	-3.519101	-2.066512
1	5.221553	-1.694157	-3.785889
1	3.595443	-1.443462	-3.110811
1	5.022963	-1.085729	-2.123704
16	-4.372166	-0.332574	1.257301
8	-5.795292	-0.076989	1.364103
8	-3.405960	0.619448	1.765850
8	-4.030097	-0.620188	-0.342596
6	-4.541181	0.303293	-1.259358
6	-5.815036	0.079550	-1.762274
6	-3.766338	1.397947	-1.670494
6	-6.345992	0.951618	-2.703187
1	-6.376229	-0.774819	-1.394889

6	-4.326365	2.259999	-2.619682
6	-5.598485	2.044559	-3.131350
1	-7.342283	0.777348	-3.100497
1	-3.731623	3.100283	-2.973282
1	-6.003822	2.727407	-3.873445
6	0.929963	4.494130	0.892155
6	-0.235531	4.354804	0.187335
6	-0.735588	3.070262	-0.136273
6	-0.013550	1.901046	0.236909
6	1.084491	2.093095	1.127807
6	1.561074	3.350557	1.411332
1	-2.584466	3.790694	-0.988633
1	1.343492	5.473804	1.110257
1	-0.798950	5.226005	-0.142068
6	-1.975801	2.908639	-0.790511
1	2.421254	3.447888	2.064660
6	-1.518418	0.591585	-0.920268
6	-2.429823	1.654208	-1.112757
1	-1.762798	-0.382484	-1.335986
7	-0.367472	0.690542	-0.290945
7	1.641628	1.000037	1.935645
8	2.715975	1.184566	2.481500
8	0.956053	-0.001482	2.076325

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f

Number of imaginary frequencies : 0

Electronic energy : =-2639.9307687
Zero-point correction= 0.566293
Thermal correction to Energy= 0.608684
Thermal correction to Enthalpy= 0.609629
Thermal correction to Gibbs Free Energy= 0.490187
Sum of electronic and zero-point Energies= -2639.364476
Sum of electronic and thermal Energies= -2639.322084
Sum of electronic and thermal Enthalpies= -2639.321140
Sum of electronic and thermal Free Energies= -2639.440582

Cartesian Coordinates

46	1.162771	-1.467583	-0.712877
6	-1.110542	-1.143144	3.552106
6	-0.238292	-1.786738	2.687340
6	-0.722100	-2.426984	1.541986
6	-2.100527	-2.428716	1.301264
6	-2.979892	-1.779444	2.163152
6	-2.474559	-1.127682	3.289461
1	-2.484025	-2.915481	0.402873
1	0.827400	-1.760397	2.896081
1	-3.156591	-0.600376	3.954230
6	-4.441865	-1.736112	1.862052

1	-4.782039	-2.564847	1.231961
1	-5.063055	-1.713783	2.765665
1	-0.715056	-0.629777	4.424376
6	3.298893	1.815016	-1.596140
6	2.564489	0.545725	-1.251356
8	2.954927	-0.179359	-0.295507
8	1.549036	0.226845	-1.949547
1	2.630525	2.675886	-1.452360
1	3.537474	1.789217	-2.669065
7	4.467365	1.985180	-0.772891
1	4.815085	1.140847	-0.333674
6	4.754901	3.185094	-0.187881
8	4.149549	4.213649	-0.455918
6	5.866944	3.140735	0.827340
1	6.360859	4.114133	0.856986
1	5.430284	2.938391	1.812443
1	6.602486	2.358374	0.616071
6	0.155457	-3.073577	0.562923
6	1.542230	-3.126461	0.587857
1	0.005800	-2.079099	-1.505883
1	-0.328228	-3.758567	-0.134848
1	2.137081	-2.678753	1.385244
6	2.249040	-4.066961	-0.322803
8	1.708245	-4.850129	-1.071662
8	3.572775	-3.899729	-0.211382
6	4.378087	-4.584241	-1.185873
6	4.404893	-3.800124	-2.475793
1	3.979036	-5.593567	-1.333228
1	5.368394	-4.654101	-0.727096
1	5.087760	-4.265857	-3.193964
1	3.407133	-3.765586	-2.925752
1	4.740573	-2.773722	-2.291519
16	-4.950531	-0.251883	0.981534
8	-6.348181	-0.380712	0.616218
8	-4.470235	0.943722	1.644096
8	-4.019818	-0.523232	-0.349917
6	-4.194783	0.330717	-1.441011
6	-5.284917	0.099614	-2.270519
6	-3.255038	1.338109	-1.700100
6	-5.467020	0.879120	-3.403881
1	-5.979218	-0.691737	-2.004208
6	-3.457792	2.089820	-2.867247
6	-4.543113	1.874757	-3.703556
1	-6.318371	0.699024	-4.054581
1	-2.720665	2.843709	-3.134024
1	-4.657935	2.477762	-4.600523
6	1.259929	4.764623	0.719085
6	0.081718	4.516781	0.068223
6	-0.449778	3.206120	0.009669
6	0.205231	2.118555	0.659397
6	1.412250	2.437833	1.358106
6	1.926556	3.712151	1.367626
1	-2.144891	3.760146	-1.193512
1	1.701031	5.756221	0.730434
1	-0.454576	5.316617	-0.440010

6	-1.622168	2.929051	-0.720961
1	2.864075	3.895135	1.881461
6	-1.343145	0.640054	-0.167681
6	-2.092024	1.641586	-0.842820
1	-1.653871	-0.401005	-0.257913
7	-0.263834	0.852190	0.548838
7	2.167155	1.441591	2.127838
8	3.365993	1.635716	2.277206
8	1.556634	0.507697	2.613392

III (a)

Number of imaginary frequencies : 0

Electronic energy : =-2523.2998982
Zero-point correction= 0.504807
Thermal correction to Energy= 0.544612
Thermal correction to Enthalpy= 0.545556
Thermal correction to Gibbs Free Energy= 0.429721
Sum of electronic and zero-point Energies= -2522.795092
Sum of electronic and thermal Energies= -2522.755286
Sum of electronic and thermal Enthalpies= -2522.754342
Sum of electronic and thermal Free Energies= -2522.870177

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Cartesian Coordinates

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46	-2.775580	0.230467	-0.222075
6	2.987994	-1.228664	-0.922821
1	2.347617	-1.354145	-0.040225
1	2.545165	-1.810981	-1.740712
8	1.276732	0.716480	-1.486009
6	2.866828	2.502700	0.127726
6	1.707401	2.684626	0.888185
6	3.565936	3.566602	-0.417859
6	1.242500	3.987267	1.070402
6	3.102837	4.859066	-0.194142
1	4.449711	3.363511	-1.016600
6	1.941100	5.067249	0.542868
1	0.316212	4.144439	1.619904
1	3.641506	5.703646	-0.615317
1	1.566818	6.075599	0.696465
6	-3.814783	-2.007961	-1.628487
6	-4.738125	-0.822360	-1.936030
8	-4.377227	0.318045	-1.413976
8	-5.733919	-0.999045	-2.604870
1	-3.801902	-2.675098	-2.496991
7	-2.482790	-1.523477	-1.269263
6	-1.426476	-2.183377	-1.568756
8	-0.207047	-1.678270	-1.383244
8	3.325043	1.202329	-0.105316
16	2.712485	0.466552	-1.446684
8	3.536397	0.808848	-2.585356

6	4.422869	-1.554655	-0.665539
6	4.902281	-1.606110	0.643265
6	5.295499	-1.800821	-1.726263
6	6.235277	-1.907134	0.892833
1	4.216440	-1.407370	1.467206
6	6.629967	-2.096887	-1.477301
1	4.926313	-1.752760	-2.749017
6	7.100901	-2.152004	-0.168883
1	6.600399	-1.949393	1.916052
1	7.304566	-2.287371	-2.308127
1	8.144766	-2.387154	0.024215
1	-0.239764	-0.711212	-1.248453
1	-4.239236	-2.558372	-0.775366
6	1.500206	0.506569	2.115198
6	0.764897	-0.673724	2.367554
6	0.954180	1.508084	1.357654
6	1.337802	-1.733777	3.109720
6	-0.543133	-0.796149	1.812313
6	-0.347230	1.311259	0.844945
6	0.668500	-2.916426	3.285623
1	2.331237	-1.586476	3.530652
6	-1.212732	-2.024860	2.065337
1	-0.802784	2.070252	0.195948
6	-0.618692	-3.060475	2.745581
1	1.115767	-3.733646	3.843256
1	-1.182514	-3.979931	2.873708
7	-1.058657	0.209493	1.034949
7	-2.603572	-2.261857	1.669419
8	-2.853395	-3.340349	1.145544
8	-3.410389	-1.382295	1.905073
1	2.515237	0.592591	2.502665
6	-1.413821	-3.563648	-2.132738
1	-1.741186	-3.551817	-3.178662
1	-0.401240	-3.968817	-2.094172
1	-2.093151	-4.213253	-1.572859
8	-3.464963	1.856971	0.766243
6	-3.144456	3.009451	0.261283
6	-4.024574	4.131756	0.756831
1	-3.543324	5.097048	0.584102
1	-4.966970	4.100208	0.199775
1	-4.267515	4.001030	1.814936
8	-2.229707	3.211095	-0.538931

III (b)

Number of imaginary frequencies : 0

Electronic energy : =-2523.3258699
Zero-point correction= 0.504618
Thermal correction to Energy= 0.544280
Thermal correction to Enthalpy= 0.545224
Thermal correction to Gibbs Free Energy= 0.430156

Sum of electronic and zero-point Energies= -2522.821252
Sum of electronic and thermal Energies= -2522.781590
Sum of electronic and thermal Enthalpies= -2522.780646
Sum of electronic and thermal Free Energies= -2522.895714

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Cartesian Coordinates

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46	2.583906	0.286346	0.370259
6	-3.202651	-0.682943	1.779941
1	-2.122280	-0.671033	1.572409
1	-3.349521	-0.915501	2.843913
8	-2.699329	1.867126	2.274353
6	-3.253404	2.468296	-0.389349
6	-2.003160	2.556021	-1.008219
6	-4.051974	3.586416	-0.195306
6	-1.565361	3.816789	-1.422622
6	-3.598324	4.829061	-0.620685
1	-5.012749	3.463981	0.299406
6	-2.353178	4.945229	-1.231251
1	-0.598130	3.902079	-1.916181
1	-4.218217	5.708782	-0.469358
1	-1.996390	5.915840	-1.565559
6	3.163308	-2.047715	1.906885
6	4.267821	-1.048370	2.221674
8	4.081319	0.156676	1.696659
8	5.232702	-1.340171	2.885429
1	2.888856	-2.524433	2.855445
7	2.029562	-1.422087	1.246515
6	0.754856	-1.788910	1.458836
8	-0.217158	-1.179761	0.984643
8	-3.685771	1.226009	0.044279
16	-3.725792	1.022795	1.696262
8	-5.110984	1.166457	2.105670
6	-3.932349	-1.634460	0.879415
6	-3.179373	-2.451279	0.033067
6	-5.323694	-1.756694	0.896261
6	-3.813899	-3.385296	-0.781111
1	-2.092176	-2.353241	0.037279
6	-5.952068	-2.679924	0.069102
1	-5.912040	-1.116031	1.550278
6	-5.199884	-3.498856	-0.768938
1	-3.217646	-4.032331	-1.422926
1	-7.036069	-2.765149	0.083933
1	-5.694857	-4.228088	-1.406365
1	3.615895	-2.828720	1.273855
6	-1.642272	0.211176	-1.817777
6	-0.769219	-0.861184	-2.088211
6	-1.170236	1.361076	-1.227673
6	-1.233954	-2.042655	-2.712479
6	0.591419	-0.745572	-1.695835
6	0.174356	1.352556	-0.799300
6	-0.393286	-3.104573	-2.922292
1	-2.282847	-2.092274	-2.998207
6	1.441727	-1.839927	-2.001516
1	0.558702	2.192977	-0.222048

6	0.961613	-2.997749	-2.562245
1	-0.756208	-4.017915	-3.385097
1	1.659757	-3.808404	-2.749464
7	1.005002	0.345086	-0.989035
7	2.896142	-1.768031	-1.826808
8	3.461404	-2.766735	-1.415714
8	3.443554	-0.724563	-2.146935
1	-2.692849	0.116164	-2.089330
6	0.508382	-3.026186	2.303373
1	0.743047	-2.833386	3.357049
1	-0.551918	-3.280087	2.226430
1	1.112244	-3.881605	1.982188
8	3.311976	2.101779	-0.447833
6	4.431200	2.594644	-0.232409
6	4.881392	3.804441	-0.980392
1	5.204197	4.575227	-0.274804
1	5.751428	3.540556	-1.590025
1	4.081964	4.178742	-1.619674
8	5.301842	2.143143	0.616058
1	4.972679	1.332287	1.121521

III (c)

Number of imaginary frequencies : 0

Electronic energy : =-2294.3079895
Zero-point correction= 0.440241
Thermal correction to Energy= 0.474535
Thermal correction to Enthalpy= 0.475479
Thermal correction to Gibbs Free Energy= 0.372286
Sum of electronic and zero-point Energies= -2293.867748
Sum of electronic and thermal Energies= -2293.833455
Sum of electronic and thermal Enthalpies= -2293.832511
Sum of electronic and thermal Free Energies= -2293.935703

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Cartesian Coordinates

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46	-1.344126	1.060537	0.688065
6	0.355015	-2.149676	-1.852095
1	0.238010	-1.073160	-1.678408
1	0.898987	-2.308249	-2.791351
8	2.006820	-4.028469	-0.886389
6	3.689280	-1.408013	-0.019962
6	3.862587	-0.118665	0.497332
6	4.564607	-2.440079	0.289628
6	4.968150	0.123897	1.314741
6	5.638717	-2.181766	1.133603
1	4.397467	-3.424070	-0.140270
6	5.847841	-0.901736	1.637810
1	5.110371	1.121829	1.726270
1	6.323022	-2.986609	1.388789
1	6.692990	-0.703463	2.291356

6	-2.999343	-0.059410	2.751725
6	-1.551592	-0.352700	3.117535
8	-0.659089	0.007132	2.205736
8	-1.236570	-0.861223	4.168239
1	-3.384163	0.661190	3.491753
7	-3.092927	0.442744	1.395871
6	-4.062764	0.089027	0.523899
8	-3.959523	0.247696	-0.694941
8	2.665355	-1.591520	-0.935909
16	1.483323	-2.712174	-0.574920
8	0.981789	-2.408811	0.749523
6	-0.958438	-2.866080	-1.787256
6	-2.110948	-2.156751	-1.451686
6	-1.042152	-4.229053	-2.082568
6	-3.343949	-2.800766	-1.426902
1	-2.075448	-1.089541	-1.225813
6	-2.272176	-4.872960	-2.035823
1	-0.143151	-4.783592	-2.346507
6	-3.423926	-4.159351	-1.712164
1	-4.228544	-2.209352	-1.200796
1	-2.333186	-5.934811	-2.262323
1	-4.386800	-4.665074	-1.691437
1	-3.559248	-0.991726	2.900932
6	3.262467	2.145910	-0.390528
6	2.280994	3.092227	-0.764722
6	2.900047	0.945033	0.161795
6	2.661071	4.319928	-1.347896
6	0.903481	2.769901	-0.570912
6	1.523971	0.750265	0.420250
6	1.715784	5.224880	-1.755926
1	3.722775	4.526377	-1.468469
6	-0.052746	3.718461	-1.051967
1	1.186549	-0.129987	0.973539
6	0.359639	4.910411	-1.616471
1	2.003088	6.171437	-2.202975
1	-0.401935	5.597281	-1.967819
7	0.580409	1.610732	0.071583
7	-1.516886	3.530509	-1.065526
8	-2.193234	4.453428	-1.468559
8	-2.045275	2.459400	-0.731711
1	4.311065	2.372909	-0.581972
6	-5.321967	-0.523444	1.109432
1	-5.657686	-0.018412	2.021299
1	-6.104374	-0.469312	0.349247
1	-5.151442	-1.579479	1.356053

III (d)

Number of imaginary frequencies : 0

Electronic energy : =-3083.8724255
Zero-point correction= 0.508222

Thermal correction to Energy= 0.551954
Thermal correction to Enthalpy= 0.552899
Thermal correction to Gibbs Free Energy= 0.430001
Sum of electronic and zero-point Energies= -3083.364203
Sum of electronic and thermal Energies= -3083.320471
Sum of electronic and thermal Enthalpies= -3083.319527
Sum of electronic and thermal Free Energies= -3083.442424

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Cartesian Coordinates

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46	1.549145	-0.541848	-0.751275
6	-2.932832	-1.303733	0.798285
1	-1.867873	-1.051278	0.881493
1	-3.256483	-1.731397	1.756416
8	-3.205068	1.153807	1.779616
6	-3.394391	2.113742	-0.992506
6	-2.420989	3.081764	-0.714672
6	-4.622447	2.452763	-1.544360
6	-2.718491	4.411550	-1.033916
6	-4.895035	3.781314	-1.845380
1	-5.347084	1.660986	-1.711962
6	-3.940815	4.761838	-1.591123
1	-1.963074	5.176325	-0.861157
1	-5.854041	4.049656	-2.280588
1	-4.144881	5.800992	-1.835410
6	3.888394	-1.321947	-2.257480
6	3.177473	-2.597579	-1.805362
8	2.061269	-2.428817	-1.142084
8	3.673390	-3.674629	-2.053005
1	4.260394	-1.479764	-3.276669
7	3.009558	-0.160334	-2.163282
6	3.294934	0.931056	-2.774880
8	2.498926	1.991145	-2.687410
8	-3.128778	0.788821	-0.705597
16	-3.754255	0.276901	0.760796
8	-5.192327	0.159505	0.606002
6	-3.214195	-2.183881	-0.379360
6	-2.174489	-2.478361	-1.264195
6	-4.479807	-2.733008	-0.592067
6	-2.401009	-3.316837	-2.350062
1	-1.180687	-2.071166	-1.075839
6	-4.704449	-3.561973	-1.684674
1	-5.289961	-2.502101	0.097367
6	-3.665397	-3.856003	-2.563569
1	-1.580370	-3.556849	-3.022098
1	-5.692562	-3.987135	-1.845564
1	-3.841136	-4.513899	-3.411850
1	1.743966	1.759461	-2.117284
1	4.758004	-1.175932	-1.598829
6	-0.531098	3.564042	0.827368
6	0.787694	3.336692	1.269218
6	-1.114133	2.754239	-0.119511
6	1.395642	4.201067	2.209858
6	1.514032	2.247235	0.710034
6	-0.353950	1.643380	-0.549616

6	2.709964	4.044048	2.559930
1	0.795207	5.003130	2.633362
6	2.875053	2.137378	1.095243
1	-0.790402	0.925600	-1.243070
6	3.463333	3.014788	1.969549
1	3.180076	4.712593	3.274548
1	4.517992	2.893294	2.202439
7	0.898770	1.404154	-0.179587
7	3.770091	1.099819	0.559341
8	4.635763	1.475185	-0.216828
8	3.599902	-0.047406	0.930411
1	-1.085707	4.404353	1.242492
6	4.507851	1.153946	-3.606431
1	4.547255	0.443099	-4.438386
1	4.510210	2.170926	-4.000475
1	5.402094	0.998276	-2.992346
8	0.208914	-1.152079	0.610203
6	0.747558	-1.836995	1.670481
1	1.839101	-1.997360	1.592850
6	0.523659	-1.010902	2.937972
6	0.147151	-3.243425	1.778625
9	0.937245	-1.632715	4.042979
9	1.210638	0.141176	2.847761
9	-0.757779	-0.683178	3.105631
9	0.228542	-3.873905	0.618036
9	0.792186	-3.973324	2.693846
9	-1.147810	-3.209623	2.134673

III (e)

Number of imaginary frequencies : 0

Electronic energy : =-3083.8668801
Zero-point correction= 0.507531
Thermal correction to Energy= 0.551612
Thermal correction to Enthalpy= 0.552556
Thermal correction to Gibbs Free Energy= 0.426653
Sum of electronic and zero-point Energies= -3083.359349
Sum of electronic and thermal Energies= -3083.315268
Sum of electronic and thermal Enthalpies= -3083.314324
Sum of electronic and thermal Free Energies= -3083.440227

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Cartesian Coordinates

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46	-2.365656	-0.708560	-0.340025
6	4.572884	-1.064790	-0.631080
1	3.973070	-1.370376	0.235171
1	4.478864	-1.839042	-1.402653
8	2.274936	-0.057248	-1.475018
6	3.020999	2.460365	-0.050339
6	1.740202	2.398461	0.509554
6	3.518099	3.615694	-0.630570

6	0.945501	3.545713	0.452358
6	2.721331	4.755578	-0.647618
1	4.512321	3.594991	-1.068492
6	1.437810	4.717449	-0.110974
1	-0.068364	3.512125	0.847865
1	3.100387	5.670778	-1.094576
1	0.808008	5.602416	-0.138289
6	-3.442213	-2.998692	-1.679325
6	-4.457270	-1.865326	-1.850065
8	-4.095999	-0.713633	-1.340965
8	-5.511405	-2.075325	-2.407991
1	-3.474179	-3.630124	-2.574025
7	-2.113558	-2.454012	-1.418350
6	-1.051197	-3.041964	-1.828461
8	0.150536	-2.496929	-1.661200
8	3.824853	1.317553	-0.032240
16	3.672755	0.319716	-1.336704
8	4.386156	0.902938	-2.452669
6	5.992675	-0.749219	-0.289631
6	6.340404	-0.407263	1.017321
6	6.976789	-0.772133	-1.278378
6	7.657145	-0.100716	1.336539
1	5.565784	-0.374228	1.783632
6	8.293646	-0.463001	-0.960088
1	6.704080	-1.024278	-2.301797
6	8.635257	-0.128938	0.346891
1	7.920754	0.161926	2.358072
1	9.055580	-0.483744	-1.735100
1	9.666492	0.110207	0.595068
1	0.054995	-1.587844	-1.324806
1	-3.755631	-3.609534	-0.819873
6	1.896141	0.281585	1.865558
6	1.375952	-0.997015	2.161152
6	1.215691	1.123669	1.023925
6	2.099443	-1.896799	2.980238
6	0.129448	-1.383286	1.585348
6	-0.011335	0.664939	0.503983
6	1.642305	-3.167714	3.209826
1	3.037860	-1.554011	3.413055
6	-0.322710	-2.693641	1.895269
1	-0.567564	1.307844	-0.173502
6	0.419004	-3.569434	2.649216
1	2.206533	-3.860520	3.826759
1	0.023015	-4.566344	2.820880
7	-0.533630	-0.527353	0.744855
7	-1.639170	-3.187032	1.480994
8	-1.674935	-4.282190	0.936374
8	-2.600109	-2.481842	1.727576
1	2.858883	0.570830	2.285320
6	-1.011263	-4.371297	-2.499891
1	-1.510651	-4.325568	-3.473898
1	0.024266	-4.679332	-2.650341
1	-1.532341	-5.115386	-1.888590
8	-2.800153	0.968649	0.646865
6	-3.712216	1.818729	0.081005

1	-4.220803	1.413414	-0.813220
6	-4.819723	2.100085	1.091838
6	-2.987726	3.082348	-0.370205
9	-5.714403	2.975375	0.616953
9	-5.464084	0.969343	1.371081
9	-4.341291	2.593481	2.236104
9	-1.996481	2.750558	-1.221874
9	-3.776474	3.946678	-1.004245
9	-2.409739	3.733098	0.651205

III

Number of imaginary frequencies : 0

Electronic energy : =-3083.9008127
Zero-point correction= 0.509265
Thermal correction to Energy= 0.552173
Thermal correction to Enthalpy= 0.553117
Thermal correction to Gibbs Free Energy= 0.434803
Sum of electronic and zero-point Energies= -3083.391548
Sum of electronic and thermal Energies= -3083.348640
Sum of electronic and thermal Enthalpies= -3083.347696
Sum of electronic and thermal Free Energies= -3083.466009

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Cartesian Coordinates

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46	-2.322309	-0.009302	-0.754543
6	3.978914	-0.488229	1.471529
1	3.453293	-1.321196	0.983158
1	4.481663	-0.914047	2.351326
8	6.081075	-1.380029	0.226429
6	4.110748	-0.722809	-1.858392
6	2.740634	-0.689200	-2.156192
6	4.956967	-1.670691	-2.422475
6	2.244428	-1.670659	-3.023738
6	4.432919	-2.633869	-3.274052
1	6.012970	-1.649617	-2.176680
6	3.074418	-2.637617	-3.571419
1	1.191120	-1.651681	-3.295707
1	5.093959	-3.376827	-3.712049
1	2.662234	-3.382601	-4.246545
6	-5.118725	0.478852	-1.309308
6	-4.340493	1.741463	-1.679028
8	-3.039896	1.690752	-1.507898
8	-4.933587	2.711754	-2.094276
1	-5.767603	0.230698	-2.159619
7	-4.239055	-0.629431	-0.957204
6	-4.697979	-1.827500	-0.781883
8	-3.934543	-2.833499	-0.452720
8	4.624558	0.269298	-1.027564
16	5.363745	-0.133718	0.392289
8	6.046158	1.082835	0.769206

6	3.027952	0.612950	1.859260
6	1.785583	0.203747	2.355889
6	3.337012	1.973100	1.847278
6	0.859137	1.130000	2.818724
1	1.556030	-0.860145	2.409535
6	2.407161	2.899912	2.314548
1	4.304372	2.310774	1.484111
6	1.169922	2.487445	2.795464
1	-0.103970	0.788660	3.193808
1	2.661241	3.957794	2.305068
1	0.452718	3.217878	3.164892
1	-2.980025	-2.539721	-0.285183
1	-5.773267	0.739535	-0.465117
6	2.149521	1.675980	-1.508711
6	1.212487	2.593882	-0.994765
6	1.834244	0.339839	-1.617082
6	1.520667	3.974689	-0.930587
6	-0.046663	2.111266	-0.535669
6	0.521160	-0.025109	-1.256732
6	0.614847	4.872119	-0.432614
1	2.492228	4.301254	-1.296389
6	-0.901077	3.063669	0.088281
1	0.188826	-1.054829	-1.375600
6	-0.598787	4.402688	0.099276
1	0.838744	5.934264	-0.405725
1	-1.310095	5.079786	0.562556
7	-0.377100	0.800526	-0.745872
7	-2.068124	2.679536	0.888455
8	-2.985809	3.470024	0.975190
8	-2.001959	1.607971	1.478782
1	3.122016	2.046003	-1.827474
6	-6.141778	-2.170979	-0.946565
1	-6.478211	-1.952709	-1.966066
1	-6.291253	-3.230558	-0.736020
1	-6.758881	-1.574434	-0.265888
8	-1.600320	-1.815627	-0.086876
6	-0.981363	-1.791736	1.136841
1	-0.454838	-0.840239	1.332823
6	-1.957886	-1.962779	2.301903
6	0.101448	-2.872367	1.144579
9	-1.389803	-1.589345	3.453945
9	-3.038525	-1.204578	2.116906
9	-2.370143	-3.225707	2.428763
9	1.101119	-2.507487	0.319216
9	0.642792	-3.031223	2.359995
9	-0.347103	-4.048463	0.733749

III (f)

Number of imaginary frequencies : 0

Electronic energy : =-3083.8821453
Zero-point correction= 0.509582
Thermal correction to Energy= 0.552756
Thermal correction to Enthalpy= 0.553700
Thermal correction to Gibbs Free Energy= 0.434830
Sum of electronic and zero-point Energies= -3083.372563
Sum of electronic and thermal Energies= -3083.329390
Sum of electronic and thermal Enthalpies= -3083.328445
Sum of electronic and thermal Free Energies= -3083.447315

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Cartesian Coordinates

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46	2.343812	0.300407	0.249708
6	-4.284253	0.235104	-1.490757
1	-4.958023	0.478047	-2.323655
1	-4.029401	1.180491	-0.994864
8	-5.671766	-1.957205	-0.768150
6	-3.992549	0.238430	1.752456
6	-2.611413	0.300635	2.008913
6	-4.881077	1.155788	2.302009
6	-2.162923	1.338985	2.837729
6	-4.397006	2.182347	3.102157
1	-5.939967	1.055075	2.090424
6	-3.036365	2.273905	3.371414
1	-1.105588	1.407809	3.083139
1	-5.091792	2.902616	3.525852
1	-2.652983	3.066622	4.007671
6	5.134271	-0.351930	0.354379
6	5.031520	1.114072	-0.074364
8	3.812955	1.597024	-0.125790
8	6.030711	1.736821	-0.354543
1	6.035546	-0.474474	0.965257
7	3.919401	-0.762196	1.048342
6	3.925242	-1.646153	1.975864
8	2.803528	-1.952614	2.622871
8	-4.454586	-0.824112	0.987129
16	-5.398049	-0.601106	-0.351622
8	-6.470846	0.322746	-0.043550
6	-3.072348	-0.526656	-1.930159
6	-3.187091	-1.776624	-2.547084
6	-1.814224	0.065815	-1.805441
6	-2.054434	-2.421690	-3.029941
1	-4.166197	-2.239887	-2.646869
6	-0.683777	-0.573162	-2.308111
1	-1.702331	1.043575	-1.333085
6	-0.803872	-1.819473	-2.915063
1	-2.153080	-3.393048	-3.510053
1	0.282571	-0.082609	-2.209804
1	0.082922	-2.311859	-3.310149
1	2.097137	-1.365013	2.295998
1	5.251447	-0.963260	-0.552670
6	-1.906037	-1.985615	1.167203
6	-0.913092	-2.805317	0.593348
6	-1.645649	-0.659867	1.441514

6	-1.181518	-4.169870	0.329656
6	0.356863	-2.242581	0.279541
6	-0.337398	-0.210335	1.160111
6	-0.222246	-4.986401	-0.208252
1	-2.172244	-4.550278	0.568883
6	1.292828	-3.113407	-0.339836
1	-0.076903	0.826449	1.348330
6	1.030606	-4.446102	-0.544001
1	-0.424945	-6.036013	-0.398014
1	1.801333	-5.060835	-1.000578
7	0.630490	-0.945278	0.626693
7	2.563772	-2.637149	-0.891892
8	3.574807	-3.254304	-0.588734
8	2.519049	-1.673758	-1.638720
1	-2.877504	-2.422648	1.381058
6	5.111964	-2.429293	2.415101
1	5.874838	-1.769614	2.842161
1	4.816253	-3.162002	3.167050
1	5.553773	-2.944025	1.554879
8	0.965531	1.450565	-0.623192
6	1.172946	2.801292	-0.682655
1	2.216473	3.114492	-0.495269
6	0.840255	3.273734	-2.093442
6	0.311668	3.463332	0.387600
9	1.033177	4.586825	-2.241605
9	1.620360	2.641765	-2.967329
9	-0.432186	3.012592	-2.418731
9	0.717321	3.031771	1.600743
9	0.385879	4.790645	0.391470
9	-0.980544	3.122695	0.280320

III (g)

Number of imaginary frequencies : 0

Electronic energy : =-3083.9002238
Zero-point correction= 0.509990
Thermal correction to Energy= 0.552768
Thermal correction to Enthalpy= 0.553712
Thermal correction to Gibbs Free Energy= 0.435259
Sum of electronic and zero-point Energies= -3083.390234
Sum of electronic and thermal Energies= -3083.347456
Sum of electronic and thermal Enthalpies= -3083.346512
Sum of electronic and thermal Free Energies= -3083.464965

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Cartesian Coordinates

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46	-2.341289	0.038113	-0.732209
6	4.191113	-0.540799	1.453620
1	3.559497	-1.357337	1.075939
1	4.733861	-0.932775	2.324945
8	6.096175	-1.693122	0.089825

6	4.050451	-0.993909	-1.892031
6	2.665259	-0.915126	-2.100762
6	4.823911	-1.984876	-2.485621
6	2.083476	-1.897117	-2.914762
6	4.214200	-2.949083	-3.276535
1	5.894364	-1.994760	-2.311359
6	2.840432	-2.907570	-3.488338
1	1.017468	-1.844417	-3.125299
1	4.818959	-3.725919	-3.736432
1	2.358576	-3.650796	-4.117646
6	-5.076651	0.651841	-1.438903
6	-4.213457	1.850393	-1.831764
8	-2.925647	1.733649	-1.606063
8	-4.732578	2.832881	-2.312330
1	-5.714949	0.409458	-2.298591
7	-4.274404	-0.490522	-1.018636
6	-4.797935	-1.663402	-0.858917
8	-4.101209	-2.699129	-0.475720
8	4.659456	0.000872	-1.133224
16	5.499905	-0.381703	0.234758
8	6.310502	0.791521	0.467913
6	3.377813	0.676959	1.789035
6	2.015177	0.494971	2.037622
6	3.936387	1.946693	1.955849
6	1.220008	1.558156	2.450924
1	1.583614	-0.499945	1.930996
6	3.134025	3.013029	2.348693
1	4.996382	2.100201	1.776427
6	1.779398	2.823273	2.601390
1	0.160635	1.400371	2.646963
1	3.578720	3.997997	2.473353
1	1.161300	3.657449	2.926431
1	-3.152118	-2.445527	-0.242138
1	-5.737903	0.982687	-0.624859
6	2.208260	1.482176	-1.451254
6	1.320296	2.453495	-0.948699
6	1.825501	0.161180	-1.543290
6	1.707072	3.814710	-0.889114
6	0.028996	2.048923	-0.504620
6	0.501445	-0.133610	-1.157140
6	0.841339	4.770708	-0.430308
1	2.707959	4.077179	-1.225975
6	-0.792335	3.060923	0.067694
1	0.120548	-1.150762	-1.228311
6	-0.416060	4.381381	0.063069
1	1.127002	5.817960	-0.408340
1	-1.105273	5.106772	0.485087
7	-0.359758	0.749471	-0.678599
7	-2.014643	2.759202	0.818164
8	-2.898064	3.591051	0.830546
8	-2.032387	1.702987	1.442605
1	3.196622	1.799075	-1.777175
6	-6.243682	-1.945662	-1.103810
1	-6.509216	-1.737573	-2.146130
1	-6.453514	-2.992368	-0.880512

1	-6.872094	-1.307076	-0.473514
8	-1.748130	-1.758640	0.072243
6	-1.262310	-1.706393	1.354918
1	-0.786550	-0.739220	1.605045
6	-2.373678	-1.890285	2.390524
6	-0.160935	-2.757276	1.495701
9	-1.951033	-1.618519	3.625146
9	-3.382481	-1.060310	2.112860
9	-2.858441	-3.133950	2.379321
9	0.870272	-2.430517	0.688545
9	0.324935	-2.804802	2.738510
9	-0.562307	-3.972180	1.151693

III (h)

Number of imaginary frequencies : 1

Electronic energy : =-2294.2823009
Zero-point correction= 0.438555
Thermal correction to Energy= 0.472682
Thermal correction to Enthalpy= 0.473626
Thermal correction to Gibbs Free Energy= 0.369315
Sum of electronic and zero-point Energies= -2293.843746
Sum of electronic and thermal Energies= -2293.809619
Sum of electronic and thermal Enthalpies= -2293.808675
Sum of electronic and thermal Free Energies= -2293.912986

Cartesian Coordinates

46	3.983123	-0.586664	0.057397
6	-2.374653	1.421614	-1.772766
1	-1.837063	0.498638	-1.518749
1	-2.395000	1.519905	-2.866660
8	-4.405672	-0.283872	-1.830873
6	-4.834651	0.216349	0.938261
6	-4.448211	-1.092025	1.247011
6	-6.080351	0.716427	1.283040
6	-5.362056	-1.896443	1.930875
6	-6.970698	-0.100718	1.970686
1	-6.328555	1.735833	0.999350
6	-6.611311	-1.405817	2.293483
1	-5.075338	-2.913789	2.192468
1	-7.947806	0.282924	2.251945
1	-7.305087	-2.044378	2.833947
6	6.070302	1.385473	0.360881
6	6.733814	0.024842	0.241025
8	5.896666	-0.995350	0.129090
8	7.932889	-0.123532	0.252030
1	6.455907	2.019035	-0.452924
7	4.632915	1.238528	0.307096
6	3.736149	2.163458	0.722103
8	2.538595	1.909825	0.850452

8	-3.939660	1.035972	0.265034
16	-4.089840	1.061662	-1.385123
8	-4.958101	2.168593	-1.734428
6	-1.796372	2.618668	-1.082357
6	-0.669980	2.461775	-0.273750
6	-2.349859	3.888925	-1.262045
6	-0.095309	3.565370	0.349842
1	-0.219280	1.477186	-0.137519
6	-1.784228	4.985661	-0.624941
1	-3.230473	4.010327	-1.889716
6	-0.658216	4.825346	0.179167
1	0.800689	3.411736	0.947255
1	-2.221949	5.971960	-0.761942
1	-0.214765	5.690098	0.668400
1	6.413830	1.833656	1.305327
6	-2.996752	-2.775276	0.126227
6	-1.721015	-3.198756	-0.309681
6	-3.133255	-1.596930	0.818693
6	-1.524539	-4.409969	-1.010364
6	-0.617072	-2.344332	-0.029638
6	-1.944908	-0.861881	1.088947
6	-0.268886	-4.803875	-1.412636
1	-2.392310	-5.030561	-1.226920
6	0.659013	-2.783179	-0.494835
1	-2.008813	0.056746	1.674578
6	0.838024	-3.987784	-1.146012
1	-0.126998	-5.738614	-1.946219
1	1.836388	-4.273272	-1.463458
7	-0.746147	-1.205509	0.682413
7	1.822660	-1.980032	-0.294526
8	2.945328	-2.527211	-0.237606
8	1.759647	-0.751062	-0.192834
1	-3.872957	-3.374186	-0.120546
6	4.288044	3.542803	1.013442
1	4.838993	3.543014	1.961777
1	4.973924	3.890879	0.233714
1	3.448769	4.236662	1.097846

III (i)

Number of imaginary frequencies : 0

Electronic energy : =-2523.3312742
Zero-point correction= 0.506352
Thermal correction to Energy= 0.545429
Thermal correction to Enthalpy= 0.546373
Thermal correction to Gibbs Free Energy= 0.434577
Sum of electronic and zero-point Energies= -2522.824922
Sum of electronic and thermal Energies= -2522.785845
Sum of electronic and thermal Enthalpies= -2522.784901
Sum of electronic and thermal Free Energies= -2522.896697

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Cartesian Coordinates

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46	-2.451179	-0.524157	-0.194933
6	4.398384	-0.178366	1.742009
1	4.183883	-1.247857	1.623619
1	5.088156	-0.078409	2.590908
8	6.561072	-0.711834	0.361156
6	4.036189	-1.290738	-1.287256
6	2.653005	-1.438389	-1.486080
6	4.923633	-2.341902	-1.486277
6	2.197955	-2.706425	-1.872951
6	4.434577	-3.587092	-1.860013
1	5.985086	-2.171906	-1.341502
6	3.069960	-3.770128	-2.051839
1	1.136379	-2.853324	-2.057283
1	5.128176	-4.409508	-2.013791
1	2.681489	-4.738159	-2.355973
6	-5.128717	-0.674269	-1.300880
6	-4.234001	0.039151	-2.313356
8	-2.986722	0.231153	-1.958054
8	-4.699911	0.385128	-3.376334
1	-5.493766	-1.594746	-1.778156
7	-4.434725	-0.975320	-0.052859
6	-5.100610	-1.270240	1.016067
8	-4.526687	-1.483155	2.173458
8	4.503008	-0.023051	-0.953128
16	5.468014	0.239739	0.353979
8	5.713391	1.661906	0.286336
6	3.157212	0.642473	1.905993
6	1.917206	0.003178	1.983178
6	3.223093	2.029888	2.061184
6	0.759591	0.737854	2.223675
1	1.852354	-1.080014	1.855404
6	2.063698	2.763978	2.284139
1	4.186126	2.532104	2.001640
6	0.832477	2.120277	2.369406
1	-0.209167	0.241926	2.275263
1	2.125340	3.843926	2.398089
1	-0.079181	2.687451	2.546354
1	-3.532092	-1.378326	2.111086
1	-5.998205	-0.024942	-1.135747
6	1.946382	0.992493	-1.554572
6	0.963818	1.972405	-1.302435
6	1.691068	-0.336111	-1.298066
6	1.226383	3.336628	-1.572455
6	-0.289007	1.571347	-0.760818
6	0.395245	-0.650374	-0.828120
6	0.275136	4.294577	-1.342306
1	2.202837	3.600479	-1.973169
6	-1.217263	2.608838	-0.475778
1	0.124065	-1.677703	-0.588360
6	-0.962002	3.920230	-0.790102
1	0.470910	5.339119	-1.565135
1	-1.725995	4.662082	-0.575262

7	-0.545237	0.241199	-0.573659
7	-2.456310	2.383781	0.280526
8	-3.485320	2.860934	-0.157251
8	-2.348670	1.776295	1.338169
1	2.905677	1.314770	-1.950152
6	-6.588765	-1.388752	1.046730
1	-6.956028	-1.992636	0.211648
1	-6.898813	-1.836924	1.991709
1	-7.046101	-0.395926	0.962337
8	-1.987098	-1.299864	1.672375
6	-1.166825	-2.309373	1.832513
6	-1.068809	-2.752428	3.272919
1	-2.065581	-2.911617	3.698122
1	-0.479300	-3.667797	3.348648
1	-0.592163	-1.960747	3.862874
8	-0.509096	-2.835760	0.945147

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meta-C-H-activation –OMe substituted quinoline -**PRC** (Pre reacting Complex)

Number of imaginary frequencies : 0

Electronic energy : =-2204.3835631
Zero-point correction= 0.470828
Thermal correction to Energy= 0.504605
Thermal correction to Enthalpy= 0.505549
Thermal correction to Gibbs Free Energy= 0.406582
Sum of electronic and zero-point Energies= -2203.912735
Sum of electronic and thermal Energies= -2203.878958
Sum of electronic and thermal Enthalpies= -2203.878014
Sum of electronic and thermal Free Energies= -2203.976981

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Cartesian Coordinates

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46	1.800512	-0.393504	-0.411269
6	1.240575	-2.088016	1.283599
6	1.469300	-2.713007	0.047176
6	0.379442	-3.226120	-0.689858
6	-0.890612	-3.178423	-0.163050
6	-1.121218	-2.606506	1.106784
6	-0.070232	-2.033193	1.800618
1	-1.728991	-3.605935	-0.710738
6	-2.496987	-2.674524	1.694419
1	-2.482978	-2.718644	2.789936
1	-3.069478	-3.531392	1.322874
8	-2.920011	-0.046591	1.891746
6	-4.033668	-0.323751	-1.026527
6	-3.441881	0.922074	-1.270437
6	-5.270486	-0.671434	-1.548618
6	-4.147999	1.815108	-2.082467
6	-5.947989	0.234668	-2.355011
1	-5.682452	-1.647340	-1.307330
6	-5.382388	1.477586	-2.622826

1	-3.701031	2.782889	-2.302461
1	-6.915493	-0.030877	-2.772434
1	-5.903376	2.187864	-3.259530
6	3.887838	-0.284925	-2.327130
6	3.272905	1.113087	-2.313481
8	2.300270	1.272432	-1.439073
8	3.639600	1.988120	-3.068592
1	4.959268	-0.192235	-2.535525
7	3.603785	-0.976892	-1.083469
6	4.542771	-1.341871	-0.186977
8	4.265732	-1.658361	0.979506
8	-3.350459	-1.281956	-0.275030
8	-4.916303	-1.563219	1.670745
16	-3.536125	-1.247234	1.362007
1	3.443374	-0.824222	-3.178686
6	-2.041986	2.523047	0.003486
6	-0.879297	2.832226	0.736318
6	-2.173381	1.311408	-0.630587
6	-0.718710	4.071214	1.398609
6	0.136188	1.842827	0.815322
6	-1.061705	0.437857	-0.594250
6	0.423177	4.314861	2.114031
1	-1.507716	4.815502	1.319260
6	1.278681	2.099134	1.632293
1	-1.080421	-0.495726	-1.155610
6	1.421630	3.329334	2.237714
1	0.563312	5.270757	2.612352
1	2.303978	3.535318	2.836141
1	-2.862714	3.239820	-0.008775
7	0.032894	0.682331	0.095779
1	2.486102	-2.937985	-0.257214
1	0.558553	-3.706178	-1.648580
1	-0.247522	-1.567112	2.769374
1	2.099084	-1.778039	1.875661
6	5.986560	-1.405583	-0.650497
1	6.098964	-1.922204	-1.609310
1	6.403097	-0.397604	-0.765817
1	6.557647	-1.932001	0.116321
8	2.146378	1.082421	1.784732
6	3.498646	1.377995	2.099044
1	3.600648	1.736956	3.131539
1	4.038773	0.434268	1.979534
1	3.890358	2.129768	1.400656

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meta-C-H-activation –OMe substituted quinoline -**TS**

Number of imaginary frequencies : 1
The smallest frequency is : -1662.1547 cm(-1)

Electronic energy : =-2204.3628419
Zero-point correction= 0.464588
Thermal correction to Energy= 0.498251

Thermal correction to Enthalpy= 0.499195
Thermal correction to Gibbs Free Energy= 0.399815
Sum of electronic and zero-point Energies= -2203.898254
Sum of electronic and thermal Energies= -2203.864591
Sum of electronic and thermal Enthalpies= -2203.863646
Sum of electronic and thermal Free Energies= -2203.963027

Cartesian Coordinates

46	1.853701	-0.318029	-0.391081
6	0.919784	-2.145144	0.334267
6	0.771729	-3.060556	-0.723431
6	-0.399707	-3.789890	-0.893382
6	-1.444645	-3.613423	0.002897
6	-1.326268	-2.725329	1.077066
6	-0.144754	-2.006479	1.241772
1	-2.377372	-4.160584	-0.130847
6	-2.508390	-2.508732	1.967385
1	-2.240226	-2.352640	3.019252
1	-3.238266	-3.322814	1.905601
8	-2.686554	0.158402	1.959570
6	-4.044590	-0.287528	-0.875169
6	-3.442617	0.911732	-1.276940
6	-5.314867	-0.653731	-1.295566
6	-4.172436	1.729459	-2.146691
6	-6.016559	0.178696	-2.157885
1	-5.731529	-1.587224	-0.927287
6	-5.439112	1.369553	-2.587814
1	-3.718668	2.657494	-2.489719
1	-7.010852	-0.103808	-2.493360
1	-5.977086	2.021557	-3.271069
6	4.440399	-0.361923	-1.686906
6	3.921383	1.078942	-1.786965
8	2.725684	1.287713	-1.302943
8	4.612814	1.933130	-2.305507
1	5.500173	-0.315520	-1.407500
7	3.649278	-1.134507	-0.747502
6	4.139037	-2.027661	0.090528
8	3.427802	-2.554424	0.999200
8	-3.341170	-1.185810	-0.077085
8	-4.826684	-1.165446	1.953678
16	-3.438975	-1.016824	1.561101
1	4.390580	-0.795942	-2.697418
6	-2.003520	2.638127	-0.251610
6	-0.818741	3.041335	0.393446
6	-2.145737	1.360137	-0.736074
6	-0.657923	4.348042	0.908707
6	0.212800	2.076600	0.547245
6	-1.018417	0.508761	-0.651186
6	0.494987	4.679676	1.568590
1	-1.458922	5.070287	0.768749
6	1.358664	2.427823	1.322723
1	-1.046964	-0.483853	-1.099145
6	1.499778	3.717892	1.786726
1	0.634765	5.685026	1.957588

1	2.386260	3.987151	2.353883
1	-2.833755	3.341357	-0.311064
7	0.106372	0.847685	-0.050018
1	1.603499	-3.202744	-1.412510
1	-0.501598	-4.491938	-1.717447
1	-0.058907	-1.293309	2.063417
1	2.149751	-2.148931	0.763047
6	5.578719	-2.458074	-0.006998
1	5.856860	-2.708744	-1.035555
1	6.240581	-1.649784	0.326199
1	5.733103	-3.324097	0.637777
8	2.230535	1.440590	1.598978
6	3.591658	1.779566	1.785253
1	3.763946	2.232450	2.770564
1	4.144539	0.837080	1.725340
1	3.930516	2.455309	0.989191

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meta-C-H-activation –OMe substituted quinoline -**Product**

Number of imaginary frequencies : 0

Electronic energy : =-2204.3874156
Zero-point correction= 0.471356
Thermal correction to Energy= 0.505071
Thermal correction to Enthalpy= 0.506015
Thermal correction to Gibbs Free Energy= 0.405931
Sum of electronic and zero-point Energies= -2203.916060
Sum of electronic and thermal Energies= -2203.882345
Sum of electronic and thermal Enthalpies= -2203.881401
Sum of electronic and thermal Free Energies= -2203.981484

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Cartesian Coordinates

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46	1.828943	-0.280624	-0.352219
6	0.710283	-1.883460	0.153502
6	0.699238	-2.985760	-0.715224
6	-0.305659	-3.948114	-0.646522
6	-1.339798	-3.807154	0.269531
6	-1.335741	-2.735255	1.161602
6	-0.289345	-1.810384	1.131746
1	-2.163831	-4.519217	0.284906
6	-2.528837	-2.503660	2.032398
1	-2.279319	-2.275021	3.076306
1	-3.235237	-3.339913	2.010787
8	-2.860413	0.158330	2.008306
6	-3.988475	-0.311172	-0.905354
6	-3.431420	0.916349	-1.292421
6	-5.231358	-0.728956	-1.360535
6	-4.180770	1.708222	-2.169748
6	-5.952528	0.079114	-2.229578
1	-5.614104	-1.685411	-1.015997
6	-5.422929	1.299701	-2.636385

1	-3.759016	2.655460	-2.501041
1	-6.924752	-0.247082	-2.589420
1	-5.976440	1.934055	-3.323863
6	4.328842	-0.556409	-1.760609
6	4.091517	0.968495	-1.666561
8	2.964787	1.314037	-1.140671
8	4.952643	1.709321	-2.108904
1	5.406245	-0.750220	-1.730531
7	3.596613	-1.259158	-0.711750
6	4.146949	-2.150630	0.033579
8	3.495810	-2.689037	1.052839
8	-3.270021	-1.179908	-0.087013
8	-4.907741	-1.289726	1.826386
16	-3.504077	-1.057019	1.543967
1	3.952190	-0.886164	-2.739315
6	-2.024006	2.700432	-0.298360
6	-0.834137	3.136188	0.317126
6	-2.149142	1.411280	-0.757181
6	-0.686501	4.458476	0.794946
6	0.213583	2.189929	0.487030
6	-1.003297	0.587568	-0.678966
6	0.467313	4.822189	1.436098
1	-1.497878	5.166199	0.641335
6	1.351747	2.570331	1.261414
1	-1.024665	-0.409132	-1.114399
6	1.481138	3.877402	1.682481
1	0.599071	5.840521	1.792920
1	2.363653	4.174024	2.241457
1	-2.866179	3.389372	-0.357504
7	0.123006	0.948831	-0.088727
1	1.473445	-3.079537	-1.477064
1	-0.299867	-4.791947	-1.333550
1	-0.315610	-0.962870	1.818210
1	2.586809	-2.311371	1.067320
6	5.533344	-2.681447	-0.131237
1	5.687262	-3.062841	-1.145253
1	6.271927	-1.890705	0.038798
1	5.703549	-3.484667	0.586877
8	2.219569	1.596581	1.584933
6	3.564024	1.959160	1.835958
1	3.671239	2.456189	2.809560
1	4.131294	1.024173	1.852278
1	3.945464	2.597987	1.029746

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meta-C-H-activation quinoline -**PRC**

Number of imaginary frequencies : 0

Electronic energy : =-2089.9179663
Zero-point correction= 0.437437
Thermal correction to Energy= 0.469141
Thermal correction to Enthalpy= 0.470085

Thermal correction to Gibbs Free Energy= 0.373433
Sum of electronic and zero-point Energies= -2089.480529
Sum of electronic and thermal Energies= -2089.448825
Sum of electronic and thermal Enthalpies= -2089.447881
Sum of electronic and thermal Free Energies= -2089.544534

Cartesian Coordinates

46	-1.996074	-0.220151	0.365609
6	-1.341891	-2.007398	-1.345042
6	-1.770079	-2.527424	-0.112782
6	-0.819409	-3.040587	0.795600
6	0.510845	-3.099981	0.441097
6	0.933127	-2.657023	-0.827670
6	0.018746	-2.077090	-1.693535
1	1.243697	-3.523913	1.126052
6	2.356302	-2.882159	-1.236211
1	2.450007	-3.133664	-2.299759
1	2.839216	-3.673999	-0.653736
8	2.900816	-0.341917	-1.824174
6	3.851816	-0.174300	1.149695
6	3.297609	1.111002	1.164033
6	5.069259	-0.461371	1.748197
6	4.015237	2.112603	1.822925
6	5.760818	0.552773	2.399628
1	5.457788	-1.473780	1.681535
6	5.230865	1.838690	2.438476
1	3.595547	3.116278	1.858888
1	6.714622	0.337684	2.873941
1	5.765240	2.633518	2.952313
6	-4.260162	0.039216	2.067028
6	-3.511377	1.367586	2.156230
8	-2.450003	1.457046	1.376582
8	-3.853720	2.253107	2.908952
1	-5.335099	0.243289	2.126222
7	-3.884153	-0.686485	0.868325
6	-4.715130	-0.871725	-0.185437
8	-4.293313	-1.144379	-1.316270
8	3.152092	-1.218888	0.538742
8	4.813223	-1.867881	-1.233138
16	3.433056	-1.458579	-1.068026
1	-3.999220	-0.538621	2.967122
6	2.001920	2.410873	-0.504179
6	0.855262	2.585438	-1.303496
6	2.053234	1.406625	0.431986
6	0.772297	3.579187	-2.306634
6	-0.238645	1.699108	-1.113262
6	0.898369	0.607695	0.599474
6	-0.349586	3.683971	-3.087539
1	1.617382	4.250779	-2.445439
6	-1.384158	1.822213	-1.931261
1	0.873568	-0.164065	1.367435
6	-1.431384	2.797378	-2.897292
1	-0.410634	4.448903	-3.857266
1	-2.316957	2.889059	-3.520665

1	2.871936	3.044252	-0.676202
7	-0.185811	0.739846	-0.133867
1	-2.829904	-2.673095	0.068845
1	-1.152150	-3.431989	1.753641
1	0.351247	-1.708455	-2.663080
1	-2.096067	-1.662185	-2.049979
6	-6.208803	-0.790045	0.058873
1	-6.516396	-1.297257	0.979056
1	-6.528209	0.256550	0.131419
1	-6.711543	-1.245307	-0.796367
1	-2.227090	1.148443	-1.773711

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meta-C-H-activation quinoline -**TS**

Number of imaginary frequencies : 1
The smallest frequency is : -1643.3572 cm(-1)

Electronic energy : =-2089.9016341
Zero-point correction= 0.431804
Thermal correction to Energy= 0.462982
Thermal correction to Enthalpy= 0.463926
Thermal correction to Gibbs Free Energy= 0.369684
Sum of electronic and zero-point Energies= -2089.469831
Sum of electronic and thermal Energies= -2089.438652
Sum of electronic and thermal Enthalpies= -2089.437708
Sum of electronic and thermal Free Energies= -2089.531950

Cartesian Coordinates

46	-2.053558	-0.070521	0.235549
6	-1.162450	-1.974554	-0.344898
6	-1.138565	-2.810230	0.787414
6	-0.031129	-3.594769	1.086542
6	1.070947	-3.563350	0.242898
6	1.072072	-2.764040	-0.904501
6	-0.042429	-1.980014	-1.192917
1	1.952667	-4.159934	0.474769
6	2.307273	-2.712516	-1.746183
1	2.100221	-2.644596	-2.820885
1	2.975389	-3.561137	-1.566792
8	2.658933	-0.075988	-1.984590
6	3.845279	-0.327790	0.955170
6	3.308050	0.938344	1.217171
6	5.069932	-0.731533	1.466400
6	4.056617	1.791384	2.035033
6	5.790439	0.135376	2.278010
1	5.438894	-1.720600	1.209728
6	5.278926	1.397380	2.564344
1	3.652098	2.774974	2.267137
1	6.748664	-0.175863	2.685254
1	5.833086	2.078124	3.205327
6	-4.738892	0.031315	1.330383

6	-4.090471	1.396307	1.587751
8	-2.890588	1.567974	1.091643
8	-4.695614	2.236713	2.219600
1	-5.727502	0.222769	0.892384
7	-3.908127	-0.795925	0.475467
6	-4.375024	-1.719992	-0.344280
8	-3.628497	-2.327586	-1.167095
8	3.114502	-1.247359	0.206809
8	4.705248	-1.517334	-1.724746
16	3.311498	-1.247378	-1.430736
1	-4.908252	-0.439826	2.310428
6	2.018561	2.612414	-0.062820
6	0.859355	3.024995	-0.744456
6	2.053691	1.406209	0.596605
6	0.802337	4.234629	-1.476383
6	-0.275854	2.170467	-0.719998
6	0.869498	0.630801	0.602055
6	-0.332365	4.575201	-2.164683
1	1.680328	4.877855	-1.486180
6	-1.431413	2.541218	-1.441504
1	0.845001	-0.322424	1.130012
6	-1.453244	3.717581	-2.147764
1	-0.372205	5.503563	-2.728586
1	-2.348873	3.994838	-2.697570
1	2.911207	3.236242	-0.106128
7	-0.241353	0.993919	-0.011041
1	-2.017894	-2.844611	1.429970
1	-0.024789	-4.230867	1.968377
1	-0.035944	-1.345657	-2.080487
1	-2.348193	-1.948188	-0.860284
6	-5.835411	-2.083562	-0.320850
1	-6.207014	-2.211673	0.700642
1	-6.426966	-1.288887	-0.790619
1	-5.980200	-3.005407	-0.885753
1	-2.299918	1.888343	-1.409411

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meta-C-H-activation quinoline -**Product**

Number of imaginary frequencies : 0

Electronic energy : =-2089.9276526
Zero-point correction= 0.438326
Thermal correction to Energy= 0.469720
Thermal correction to Enthalpy= 0.470664
Thermal correction to Gibbs Free Energy= 0.375735
Sum of electronic and zero-point Energies= -2089.489326
Sum of electronic and thermal Energies= -2089.457932
Sum of electronic and thermal Enthalpies= -2089.456988
Sum of electronic and thermal Free Energies= -2089.551918

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Cartesian Coordinates

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46	-2.030367	0.000703	0.252490
6	-0.960164	-1.671668	-0.117559
6	-1.071753	-2.731878	0.796024
6	-0.149367	-3.775065	0.805166
6	0.919894	-3.763742	-0.081543
6	1.037003	-2.735416	-1.015179
6	0.078077	-1.719815	-1.054667
1	1.677413	-4.545243	-0.041171
6	2.267794	-2.654338	-1.861561
1	2.064931	-2.474637	-2.924877
1	2.903299	-3.540473	-1.765659
8	2.783995	-0.030117	-1.979915
6	3.801064	-0.400072	0.981664
6	3.312728	0.881942	1.266072
6	5.005324	-0.858367	1.496982
6	4.086885	1.690517	2.104538
6	5.751886	-0.034907	2.329924
1	5.339367	-1.855292	1.223148
6	5.289074	1.241084	2.635664
1	3.718978	2.685600	2.348596
1	6.694445	-0.390823	2.737421
1	5.865311	1.888759	3.291333
6	-4.680530	-0.143644	1.389590
6	-4.301910	1.352163	1.417334
8	-3.164200	1.651200	0.880226
8	-5.080904	2.116643	1.955803
1	-5.754529	-0.219107	1.188020
7	-3.873637	-0.889126	0.428268
6	-4.379314	-1.798141	-0.327972
8	-3.655900	-2.409252	-1.251519
8	3.049258	-1.273327	0.198875
8	4.722666	-1.598109	-1.656365
16	3.331549	-1.256522	-1.428440
1	-4.502232	-0.542665	2.398322
6	2.102240	2.602255	-0.037963
6	0.949161	3.070253	-0.693822
6	2.078907	1.415055	0.654608
6	0.950258	4.265184	-1.451533
6	-0.238048	2.289331	-0.621383
6	0.851850	0.716928	0.710690
6	-0.178924	4.666322	-2.115275
1	1.868245	4.848083	-1.498971
6	-1.389477	2.724492	-1.314126
1	0.791754	-0.217244	1.265752
6	-1.353137	3.887136	-2.043301
1	-0.174666	5.583516	-2.698599
1	-2.247648	4.215771	-2.566067
1	3.031084	3.165618	-0.126122
7	-0.253155	1.122187	0.106935
1	-1.880466	-2.731240	1.527036
1	-0.249072	-4.583483	1.526653
1	0.201153	-0.907826	-1.772982
1	-2.733199	-2.074585	-1.190790
6	-5.795711	-2.268457	-0.279994
1	-6.083444	-2.543273	0.738999

1	-6.473237	-1.474456	-0.612822
1	-5.915941	-3.130742	-0.937111
1	-2.304115	2.145094	-1.227121

Mode of C-H Activation

***meta* C-H activation**

A

Number of imaginary frequencies : 1
The smallest frequency is : -1593.1595 cm(-1)

Electronic energy : =-2315.3862971
Zero-point correction= 0.443437
Thermal correction to Energy= 0.478512
Thermal correction to Enthalpy= 0.479457
Thermal correction to Gibbs Free Energy= 0.377340
Sum of electronic and zero-point Energies= -2314.942860
Sum of electronic and thermal Energies= -2314.907785
Sum of electronic and thermal Enthalpies= -2314.906840
Sum of electronic and thermal Free Energies= -2315.008957

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Cartesian Coordinates

.....

46	1.743349	-0.554976	-0.656214
6	0.802611	-2.328038	0.183187
6	0.564360	-3.229780	-0.869359
6	-0.652388	-3.891729	-0.995603
6	-1.656894	-3.652974	-0.067797
6	-1.444140	-2.779127	1.003013
6	-0.215487	-2.134782	1.131144
1	-2.627188	-4.137183	-0.174950
6	-2.579575	-2.483463	1.931549
1	-2.269034	-2.371582	2.977604
1	-3.377068	-3.232078	1.877399
8	-2.552810	0.197412	1.987996
6	-4.033141	-0.065546	-0.801293
6	-3.364649	1.100352	-1.198674
6	-5.344941	-0.323115	-1.172675
6	-4.065526	1.993282	-2.016416
6	-6.018283	0.583124	-1.981462
1	-5.814271	-1.233456	-0.810346
6	-5.372786	1.739277	-2.409586
1	-3.558366	2.893586	-2.358768
1	-7.044344	0.383913	-2.278691
1	-5.888706	2.446139	-3.054026
8	2.303361	0.980715	-1.887814
8	-3.363607	-1.034591	-0.061098
8	-4.784233	-0.962215	2.017414
16	-3.400111	-0.911890	1.588808

6	-1.720020	2.691120	-0.241673
6	-0.490268	2.957402	0.393936
6	-2.019039	1.432828	-0.700318
6	-0.199667	4.254307	0.878094
6	0.425998	1.883837	0.584926
6	-0.973560	0.482029	-0.648803
6	0.961183	4.498781	1.560634
1	-0.925006	5.045386	0.698304
6	1.554777	2.155234	1.414592
1	-1.097574	-0.489706	-1.125308
6	1.821455	3.428887	1.854509
1	1.197887	5.494906	1.922342
1	2.703984	3.569879	2.469833
1	-2.457595	3.490511	-0.305854
7	0.186428	0.694180	-0.057576
7	2.400314	1.104910	2.011969
8	3.442471	1.438107	2.533603
8	1.943233	-0.030798	2.023773
1	1.352589	-3.406057	-1.600890
1	-0.822751	-4.582743	-1.817750
1	-0.057358	-1.432026	1.949035
1	2.076925	-2.329683	0.544666
6	3.332572	1.647502	-1.458354
6	3.906241	2.583762	-2.498756
1	3.108951	3.112914	-3.028632
1	4.592544	3.292692	-2.030829
1	4.453159	1.993290	-3.241398
8	3.821443	1.549133	-0.336539
8	3.399913	-1.587887	-1.274744
6	3.928296	-2.329672	-0.385458
6	5.345220	-2.755270	-0.630771
1	5.583177	-3.654680	-0.060531
1	5.519771	-2.906519	-1.698162
1	5.998811	-1.942315	-0.296711
8	3.352464	-2.703513	0.669447

B

Number of imaginary frequencies : 1
The smallest frequency is : -1625.0778 cm(-1)

Electronic energy : =-2523.2903564
Zero-point correction= 0.499783
Thermal correction to Energy= 0.538796
Thermal correction to Enthalpy= 0.539740
Thermal correction to Gibbs Free Energy= 0.429287
Sum of electronic and zero-point Energies= -2522.790573
Sum of electronic and thermal Energies= -2522.751560
Sum of electronic and thermal Enthalpies= -2522.750616
Sum of electronic and thermal Free Energies= -2522.861070

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Cartesian Coordinates

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46	-1.098092	1.507974	-0.545124
6	0.559143	2.796566	-0.032593
6	1.087416	3.364088	-1.205863
6	2.460477	3.461180	-1.402963
6	3.322617	2.978161	-0.427980
6	2.828677	2.418398	0.755744
6	1.453143	2.344659	0.954029
1	4.399909	3.016462	-0.586426
6	3.789147	1.808777	1.727550
1	3.501584	1.955237	2.775649
1	4.815958	2.163069	1.588560
8	2.685529	-0.605782	2.102009
6	4.028011	-1.257079	-0.708552
6	2.929021	-2.078952	-0.990890
6	5.315882	-1.587905	-1.103380
6	3.174498	-3.244384	-1.724463
6	5.531580	-2.755895	-1.823261
1	6.128245	-0.920515	-0.829384
6	4.455769	-3.578967	-2.142275
1	2.332143	-3.883487	-1.982360
1	6.537828	-3.018948	-2.138052
1	4.614613	-4.486055	-2.719421
6	-3.512472	-1.715548	-2.004405
6	-2.351200	-0.725163	-1.875964
8	-2.630788	0.245706	-1.068816
8	-1.310276	-0.907491	-2.492983
1	-3.098819	-2.665500	-2.352902
7	-4.201491	-1.884796	-0.743563
6	-4.602994	-3.037550	-0.145931
8	-5.073800	-3.041744	0.985928
8	3.834883	-0.034615	-0.070786
8	5.196033	-0.459225	2.003158
16	3.891670	0.009416	1.578672
1	-4.190337	-1.343866	-2.789000
6	0.852572	-2.795296	0.148581
6	-0.355826	-2.503400	0.809511
6	1.588759	-1.800568	-0.445534
6	-1.117957	-3.527561	1.425755
6	-0.776363	-1.148342	0.878025
6	1.010314	-0.512479	-0.472998
6	-2.279982	-3.237323	2.085904
1	-0.756414	-4.551383	1.349526
6	-1.940543	-0.888369	1.653673
1	1.485101	0.279812	-1.048412
6	-2.690197	-1.896805	2.203121
1	-2.898638	-4.017799	2.517101
1	-3.610103	-1.645515	2.721419
1	1.222542	-3.819881	0.163094
7	-0.112166	-0.197684	0.147243
7	-2.381119	0.473203	1.967960
8	-3.578336	0.692119	1.976828
8	-1.510123	1.287070	2.245710
1	0.400871	3.731212	-1.968066
1	2.859072	3.898468	-2.315077

1	1.059665	1.893737	1.865575
1	-0.535178	3.396229	0.346670
6	-4.406894	-4.315980	-0.924375
1	-4.824672	-4.260226	-1.935217
1	-3.337801	-4.545312	-1.018312
1	-4.891902	-5.122986	-0.373033
1	-4.330414	-1.040835	-0.193437
8	-2.216335	3.061274	-1.269434
6	-2.283972	4.091760	-0.523754
8	-1.524976	4.317761	0.452604
6	-3.367947	5.076073	-0.852758
1	-3.147029	6.052196	-0.418198
1	-3.500170	5.147315	-1.934591
1	-4.305674	4.702927	-0.427745

D

Number of imaginary frequencies : 1
The smallest frequency is : -1551.7513 cm(-1)

Electronic energy : =-2315.3680329
Zero-point correction= 0.442064
Thermal correction to Energy= 0.478058
Thermal correction to Enthalpy= 0.479002
Thermal correction to Gibbs Free Energy= 0.369439
Sum of electronic and zero-point Energies= -2314.925969
Sum of electronic and thermal Energies= -2314.889975
Sum of electronic and thermal Enthalpies= -2314.889031
Sum of electronic and thermal Free Energies= -2314.998594

Cartesian Coordinates

46	4.241675	-0.312983	0.521360
6	2.884662	0.774279	-0.689570
6	2.557238	2.023421	-0.128105
6	1.249400	2.491355	-0.142591
6	0.250248	1.722647	-0.729409
6	0.556321	0.491990	-1.321148
6	1.860652	0.014782	-1.282570
1	-0.777595	2.088215	-0.753975
6	-0.536416	-0.309242	-1.954673
1	-0.240628	-0.793137	-2.892029
1	-1.437187	0.292482	-2.121312
8	-1.424645	-1.120653	0.432407
6	-3.388696	-2.772397	-1.070675
6	-4.381814	-2.132531	-0.315500
6	-3.361905	-4.149672	-1.232889
6	-5.366783	-2.937376	0.263770
6	-4.355473	-4.925571	-0.647649
1	-2.558055	-4.589490	-1.817197
6	-5.360083	-4.316922	0.098254
1	-6.157782	-2.460444	0.840143

1	-4.343570	-6.004706	-0.775591
1	-6.143479	-4.918300	0.552239
8	4.969380	-1.738016	1.943933
8	-2.415273	-2.014736	-1.713450
8	-0.130949	-2.768733	-0.967718
16	-1.039299	-1.644765	-0.862700
6	-4.464329	-0.164293	1.192839
6	-4.260846	1.213852	1.422368
6	-4.334227	-0.680933	-0.072280
6	-4.385647	1.792456	2.706275
6	-3.880844	2.014349	0.307685
6	-4.073255	0.243505	-1.122061
6	-4.163924	3.133439	2.895864
1	-4.664056	1.152302	3.541603
6	-3.619294	3.386789	0.565869
1	-4.063010	-0.121082	-2.151040
6	-3.786251	3.942906	1.809412
1	-4.269609	3.577151	3.881716
1	-3.607459	5.006745	1.935670
1	-4.667576	-0.818786	2.040088
7	-3.835084	1.520166	-0.954350
7	-3.141979	4.277843	-0.496365
8	-3.622324	5.398973	-0.532330
8	-2.270001	3.863252	-1.241211
1	3.349237	2.629961	0.310471
1	1.001778	3.456750	0.291749
1	2.087389	-0.960542	-1.715098
1	4.005510	0.807608	-1.327169
6	3.821920	-2.274606	1.920484
6	3.489969	-3.464542	2.750526
1	2.633242	-3.233115	3.390499
1	3.192975	-4.290876	2.097520
1	4.347389	-3.757414	3.359462
8	2.931645	-1.767542	1.154461
8	5.825247	0.922094	0.157992
6	5.996828	1.337116	-1.033536
6	7.312372	2.002791	-1.317607
1	7.247215	2.612018	-2.220319
1	7.623713	2.603633	-0.460266
1	8.068451	1.225184	-1.468308
8	5.157588	1.210073	-1.959294

E

Number of imaginary frequencies : 1
The smallest frequency is : -1525.6145 cm(-1)

Electronic energy : =-2523.2789563
Zero-point correction= 0.498533
Thermal correction to Energy= 0.538331
Thermal correction to Enthalpy= 0.539275
Thermal correction to Gibbs Free Energy= 0.424042

Sum of electronic and zero-point Energies= -2522.780423
Sum of electronic and thermal Energies= -2522.740625
Sum of electronic and thermal Enthalpies= -2522.739681
Sum of electronic and thermal Free Energies= -2522.854915

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Cartesian Coordinates

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46	-1.332180	0.009109	0.211629
6	-0.706842	-1.961049	-0.421287
6	-0.795710	-2.832743	0.678274
6	0.203779	-3.761904	0.944934
6	1.314412	-3.822629	0.114108
6	1.426068	-2.980497	-0.997564
6	0.410964	-2.065741	-1.267368
1	2.120519	-4.522352	0.332475
6	2.686665	-3.006829	-1.803901
1	2.519800	-2.882409	-2.880716
1	3.276701	-3.914318	-1.638596
8	3.262565	-0.396062	-1.916887
6	4.369445	-0.881659	1.033082
6	3.944505	0.412415	1.361043
6	5.542945	-1.420759	1.539857
6	4.738427	1.140954	2.252843
6	6.316226	-0.671626	2.417133
1	5.830061	-2.421110	1.227873
6	5.906768	0.607609	2.780633
1	4.411532	2.136964	2.545526
1	7.235080	-1.089611	2.819590
1	6.498673	1.192896	3.479331
6	-5.301002	-1.444377	-0.343393
6	-3.800338	-1.280274	-0.353504
8	-3.274546	-0.595417	0.570466
8	-3.176482	-1.838141	-1.293848
1	-5.503832	-2.523748	-0.398613
7	-5.903981	-0.830088	0.804686
6	-7.228965	-0.864043	1.145328
8	-7.653842	-0.265385	2.116608
8	3.573009	-1.690289	0.226744
8	5.175568	-2.014763	-1.687373
16	3.802598	-1.643539	-1.407480
1	-5.652703	-1.019175	-1.297886
6	2.849835	2.311095	0.214855
6	1.788725	2.853809	-0.538369
6	2.776637	1.035461	0.714596
6	1.854051	4.166616	-1.062311
6	0.663053	2.028873	-0.801138
6	1.546531	0.355989	0.552473
6	0.832962	4.671120	-1.824038
1	2.734896	4.765587	-0.840044
6	-0.324972	2.562431	-1.670004
1	1.379663	-0.592997	1.058282
6	-0.265867	3.851743	-2.135090
1	0.876412	5.683937	-2.212988
1	-1.073091	4.206323	-2.769061
1	3.754115	2.903393	0.349387

7	0.545599	0.819456	-0.169861
7	-1.421124	1.743598	-2.198795
8	-2.513752	2.264585	-2.309828
8	-1.139567	0.602191	-2.540901
1	-1.664742	-2.770491	1.333271
1	0.126892	-4.426965	1.801526
1	0.500067	-1.389313	-2.118758
1	-1.896995	-1.733662	-0.971548
6	-8.113268	-1.697040	0.247817
1	-8.068298	-1.356350	-0.793437
1	-7.812405	-2.751576	0.260273
1	-9.139098	-1.615096	0.609373
1	-5.308261	-0.246886	1.381613
8	-1.845685	1.846438	0.936577
6	-1.133171	2.267408	1.942732
8	-0.234105	1.643828	2.497706
6	-1.489078	3.682746	2.343471
1	-1.050155	3.921451	3.314448
1	-1.088469	4.372503	1.589528
1	-2.573111	3.821420	2.366295

F

Number of imaginary frequencies : 1
The smallest frequency is : -1225.7352 cm(-1)

Electronic energy : =-2294.2524701
Zero-point correction= 0.434632
Thermal correction to Energy= 0.468054
Thermal correction to Enthalpy= 0.468998
Thermal correction to Gibbs Free Energy= 0.370915
Sum of electronic and zero-point Energies= -2293.817838
Sum of electronic and thermal Energies= -2293.784416
Sum of electronic and thermal Enthalpies= -2293.783472
Sum of electronic and thermal Free Energies= -2293.881555

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Cartesian Coordinates

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46	1.616785	-0.908476	-0.586517
6	0.355047	-2.610584	-0.150896
6	-0.107443	-3.387129	-1.225799
6	-1.390408	-3.928213	-1.226090
6	-2.254097	-3.626558	-0.182495
6	-1.832001	-2.834644	0.889981
6	-0.518042	-2.370979	0.921925
1	-3.282945	-3.985010	-0.205277
6	-2.834869	-2.390679	1.906423
1	-2.440944	-2.364017	2.929757
1	-3.750127	-2.991700	1.891955
8	-2.361157	0.242890	2.067778
6	-4.009530	0.313570	-0.693173
6	-3.239120	1.409226	-1.108156

6	-5.356451	0.202925	-1.007145
6	-3.876911	2.382115	-1.885826
6	-5.965085	1.187295	-1.774583
1	-5.904896	-0.657820	-0.634823
6	-5.219645	2.273955	-2.221812
1	-3.292187	3.227989	-2.242899
1	-7.018762	1.102443	-2.026353
1	-5.685001	3.040428	-2.835927
6	4.438216	-0.670739	-0.688557
6	4.058614	-2.100027	-0.286420
8	2.846709	-2.513363	-0.793442
8	4.764859	-2.829436	0.345775
1	5.118793	-0.781597	-1.550530
7	3.297737	0.171632	-0.971246
6	3.386361	1.415612	-1.488109
8	2.398359	2.104778	-1.752059
8	-3.412718	-0.737845	-0.004185
8	-4.755471	-0.528515	2.117800
16	-3.393003	-0.687930	1.648707
1	5.045475	-0.294320	0.151146
6	-1.409707	2.812166	-0.196043
6	-0.134987	2.943209	0.388417
6	-1.846294	1.598363	-0.665222
6	0.311124	4.194049	0.873653
6	0.674406	1.781988	0.519530
6	-0.898426	0.549249	-0.672080
6	1.524901	4.312447	1.495364
1	-0.336168	5.058131	0.738602
6	1.862624	1.928562	1.290171
1	-1.141708	-0.393604	-1.159419
6	2.292322	3.159284	1.722925
1	1.878483	5.274272	1.854075
1	3.222572	3.206217	2.280508
1	-2.067807	3.680118	-0.213250
7	0.299516	0.632216	-0.123318
7	2.656671	0.793305	1.766159
8	3.853414	0.964586	1.929402
8	2.057347	-0.240355	2.031667
1	0.555321	-3.571531	-2.071811
1	-1.728816	-4.550661	-2.051229
1	-0.190691	-1.743608	1.753001
1	1.861850	-2.831106	-0.197691
6	4.783673	1.976353	-1.681914
1	5.306048	2.044921	-0.718671
1	5.394813	1.347270	-2.339743
1	4.698783	2.973073	-2.118428

G

Number of imaginary frequencies : 1
The smallest frequency is : -1406.7498 cm(-1)

Electronic energy : =-3083.853044
Zero-point correction= 0.502996
Thermal correction to Energy= 0.545782
Thermal correction to Enthalpy= 0.546726
Thermal correction to Gibbs Free Energy= 0.428251
Sum of electronic and zero-point Energies= -3083.350048
Sum of electronic and thermal Energies= -3083.307262
Sum of electronic and thermal Enthalpies= -3083.306318
Sum of electronic and thermal Free Energies= -3083.424793

Cartesian Coordinates

46	1.119465	-0.918918	-0.067094
6	-0.120659	-2.690155	-0.175854
6	-0.173428	-3.082953	-1.525570
6	-1.375085	-3.459457	-2.116347
6	-2.538511	-3.452395	-1.359406
6	-2.513831	-3.089646	-0.007945
6	-1.307459	-2.716807	0.577747
1	-3.488694	-3.724250	-1.818086
6	-3.801672	-3.031115	0.751771
1	-3.711173	-3.375791	1.789010
1	-4.607384	-3.589305	0.263388
8	-3.603914	-0.598235	1.849385
6	-4.535980	0.392305	-1.011247
6	-3.735137	1.520610	-0.785045
6	-5.746089	0.475148	-1.684189
6	-4.194370	2.743636	-1.285496
6	-6.178846	1.703079	-2.167801
1	-6.329871	-0.431783	-1.813470
6	-5.397439	2.837792	-1.972140
1	-3.577847	3.629460	-1.143822
1	-7.124073	1.771695	-2.699391
1	-5.724328	3.799441	-2.358521
6	3.793836	-1.378022	-1.479575
6	5.021115	-0.825819	-0.752277
8	4.786671	0.097202	0.170315
8	6.133491	-1.229396	-0.996137
1	4.156477	-2.109700	-2.212014
7	2.783008	-1.961813	-0.609575
6	3.021914	-3.089116	0.067351
8	2.139061	-3.637873	0.779926
8	-4.100132	-0.866409	-0.608919
8	-5.879099	-1.371486	1.101244
16	-4.440021	-1.354008	0.934265
1	3.324293	-0.566508	-2.042232
6	-2.245962	2.398816	0.991895
6	-1.136959	2.266204	1.852014
6	-2.503580	1.458480	0.022556
6	-0.858207	3.225529	2.855612
6	-0.308023	1.121767	1.701753
6	-1.545097	0.430385	-0.142039
6	0.216968	3.073165	3.689673
1	-1.515011	4.088657	2.940699
6	0.741996	0.967596	2.643461

1	-1.642604	-0.280159	-0.962595
6	1.022365	1.924141	3.583967
1	0.440781	3.817382	4.447848
1	1.860600	1.760930	4.255105
1	-2.929410	3.233748	1.141781
7	-0.493465	0.273609	0.641130
7	1.521315	-0.273130	2.736663
8	2.725988	-0.177618	2.859952
8	0.878641	-1.314379	2.742226
1	0.746232	-3.089750	-2.108184
1	-1.407094	-3.754565	-3.162128
1	-1.279859	-2.414787	1.624935
1	0.949735	-2.997404	0.430495
6	4.372447	-3.748326	0.020350
1	4.882419	-3.642081	-0.940082
1	5.016638	-3.278405	0.772782
1	4.251635	-4.801508	0.278632
8	2.217372	0.831032	-0.168446
1	3.850433	0.412001	0.140738
6	1.716667	1.924137	-0.807419
1	0.669859	2.179467	-0.534989
6	2.539726	3.140016	-0.378476
6	1.688404	1.754826	-2.329520
9	0.998670	0.643842	-2.647142
9	2.911551	1.624246	-2.844726
9	1.082730	2.772140	-2.942443
9	2.149952	4.256189	-1.002975
9	3.835158	2.967316	-0.610515
9	2.372821	3.336407	0.933075

H

Number of imaginary frequencies : 1
The smallest frequency is : -1675.6873 cm(-1)

Electronic energy : =-2898.7265958
Zero-point correction= 0.552159
Thermal correction to Energy= 0.598185
Thermal correction to Enthalpy= 0.599129
Thermal correction to Gibbs Free Energy= 0.472137
Sum of electronic and zero-point Energies= -2898.174437
Sum of electronic and thermal Energies= -2898.128411
Sum of electronic and thermal Enthalpies= -2898.127467
Sum of electronic and thermal Free Energies= -2898.254459

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Cartesian Coordinates

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46	1.848021	-1.000018	-0.129117
6	1.122080	-3.006624	-0.401416
6	0.938111	-3.242871	-1.776506
6	-0.215571	-3.853167	-2.256125
6	-1.210731	-4.220760	-1.361927

6	-1.060015	-4.003188	0.013120
6	0.109178	-3.414456	0.486911
1	-2.135373	-4.665610	-1.728711
6	-2.205735	-4.313429	0.924224
1	-1.892026	-4.679840	1.909165
1	-2.913960	-5.027410	0.490416
8	-2.438609	-1.961689	2.179108
6	-4.008042	-1.120217	-0.474637
6	-3.490279	0.168971	-0.283349
6	-5.266932	-1.332450	-1.018013
6	-4.291176	1.246102	-0.681181
6	-6.039812	-0.245387	-1.404717
1	-5.618486	-2.354731	-1.127438
6	-5.545690	1.045156	-1.241058
1	-3.896861	2.255811	-0.573699
1	-7.023494	-0.407524	-1.837346
1	-6.137734	1.901321	-1.553721
6	4.351201	-0.100413	-1.311899
6	3.477273	1.116540	-1.043425
8	2.517804	0.950240	-0.176390
8	3.670156	2.187386	-1.603610
1	5.303280	0.065321	-0.784576
7	3.683111	-1.312092	-0.870317
6	4.308124	-2.448380	-0.611675
8	3.706016	-3.451204	-0.132822
8	-3.231305	-2.243314	-0.201486
8	-4.546178	-3.248854	1.694400
16	-3.199021	-2.859523	1.328420
1	4.572432	-0.117943	-2.388016
6	-2.042155	1.427067	1.285098
6	-0.843869	1.568256	2.016267
6	-2.194959	0.411403	0.374962
6	-0.667316	2.609897	2.956759
6	0.181977	0.608956	1.808737
6	-1.053422	-0.387119	0.112951
6	0.491502	2.715572	3.680460
1	-1.473064	3.330698	3.086122
6	1.323490	0.703568	2.648526
1	-1.066463	-1.101157	-0.706542
6	1.494332	1.743102	3.528322
1	0.632004	3.524793	4.390533
1	2.404467	1.775966	4.119867
1	-2.862880	2.114871	1.487612
7	0.074071	-0.296623	0.786995
7	2.350301	-0.345170	2.683185
8	3.514183	0.004026	2.763315
8	1.957727	-1.503801	2.673076
1	1.718889	-2.937277	-2.471731
1	-0.346455	-4.028294	-3.320976
1	0.223469	-3.220773	1.554008
1	2.377132	-3.134140	-0.082332
47	1.192318	2.764432	-0.915208
8	-0.724343	2.493013	-2.169587
6	-0.753146	1.267474	-2.567961
6	-1.968399	0.851665	-3.373347

1	-1.688186	0.813189	-4.431836
1	-2.287283	-0.156529	-3.084408
1	-2.800307	1.552466	-3.259305
8	0.144060	0.444318	-2.349525
8	-0.137856	4.397137	0.266794
6	-1.343006	4.595548	0.168898
6	-2.061321	5.571987	1.053056
1	-3.001718	5.144175	1.415864
1	-1.421262	5.867476	1.886268
1	-2.321270	6.460831	0.468381
8	-2.142760	4.005600	-0.690003
1	-1.631574	3.389753	-1.322848
6	5.781034	-2.570802	-0.889036
1	6.063857	-3.623798	-0.863316
1	6.051081	-2.135708	-1.856227
1	6.344317	-2.038727	-0.113064

I

Number of imaginary frequencies : 1
The smallest frequency is : -405.3770 cm(-1)

Electronic energy : =-2106.1052534
Zero-point correction= 0.389902
Thermal correction to Energy= 0.421153
Thermal correction to Enthalpy= 0.422097
Thermal correction to Gibbs Free Energy= 0.323841
Sum of electronic and zero-point Energies= -2105.715352
Sum of electronic and thermal Energies= -2105.684100
Sum of electronic and thermal Enthalpies= -2105.683156
Sum of electronic and thermal Free Energies= -2105.781412

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Cartesian Coordinates

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6	1.520783	-2.533623	0.128283
6	1.257204	-3.224367	-1.071291
6	0.047392	-3.870133	-1.321692
6	-0.972519	-3.796664	-0.382378
6	-0.770860	-3.102478	0.812255
6	0.466831	-2.503894	1.061832
1	-1.938883	-4.262492	-0.576429
6	-1.905065	-2.948966	1.773397
1	-1.592268	-2.974083	2.824972
1	-2.701347	-3.686447	1.623317
8	-1.869272	-0.277234	2.075906
6	-3.733641	-0.463428	-0.606018
6	-3.369072	0.844233	-0.956846
6	-4.990402	-0.977710	-0.896258
6	-4.321972	1.599731	-1.654911
6	-5.917629	-0.199327	-1.573743
1	-5.216539	-1.991055	-0.577049
6	-5.575996	1.092564	-1.961507

1	-4.054626	2.601174	-1.986282
1	-6.899442	-0.603586	-1.804920
1	-6.284865	1.705371	-2.512097
8	-2.814084	-1.312585	-0.012668
8	-4.094193	-1.449723	2.152550
16	-2.739118	-1.355659	1.643215
6	-2.015055	2.790116	-0.251940
6	-0.785765	3.407198	0.056291
6	-2.076261	1.461475	-0.599514
6	-0.711753	4.786755	0.359749
6	0.385988	2.600968	0.047082
6	-0.841239	0.758080	-0.623920
6	0.494551	5.385709	0.613912
1	-1.634824	5.363205	0.372830
6	1.605018	3.260146	0.368460
1	-0.828005	-0.294897	-0.909209
6	1.666591	4.611166	0.606841
1	0.553805	6.447953	0.831155
1	2.635899	5.057018	0.810355
1	-2.923126	3.388842	-0.195588
7	0.325454	1.288421	-0.312976
7	2.871261	2.535452	0.509528
8	3.863928	3.033939	0.016051
8	2.848096	1.497808	1.163453
1	2.044112	-3.270773	-1.829055
1	-0.108538	-4.418724	-2.249144
1	0.599229	-1.980684	2.012492
1	3.068477	-2.427437	0.237088
47	1.998988	-0.360887	-0.261918
8	4.178420	-0.659882	-1.063959
6	4.750593	-1.649608	-0.578977
6	6.225452	-1.851874	-0.793193
1	6.739564	-1.778911	0.170805
1	6.410955	-2.857987	-1.180748
1	6.620506	-1.099377	-1.477533
8	4.188017	-2.568374	0.133965

***ortho* C-H activation**

A

Number of imaginary frequencies : 1
The smallest frequency is : -1623.4187 cm(-1)

Electronic energy : =-2315.3767705
Zero-point correction= 0.443761
Thermal correction to Energy= 0.478780
Thermal correction to Enthalpy= 0.479724
Thermal correction to Gibbs Free Energy= 0.377605
Sum of electronic and zero-point Energies= -2314.933009
Sum of electronic and thermal Energies= -2314.897991

Sum of electronic and thermal Enthalpies= -2314.897047
Sum of electronic and thermal Free Energies= -2314.999165

Cartesian Coordinates

46	1.725079	-0.421336	-0.561796
6	0.932061	-3.169956	-1.267197
6	0.052028	-4.176203	-1.636362
6	-1.077909	-4.412221	-0.859597
6	-1.338527	-3.615505	0.247032
6	-0.494086	-2.555629	0.580986
6	0.690538	-2.331218	-0.158770
1	-2.226442	-3.799562	0.850405
6	-0.849925	-1.678441	1.747851
1	-0.220581	-0.783788	1.799642
1	-0.783641	-2.207837	2.707629
8	-2.603419	0.289874	2.235908
6	-3.836189	-0.264421	-0.400772
6	-3.472360	0.982271	-0.931765
6	-5.136680	-0.739509	-0.465246
6	-4.464745	1.734069	-1.563350
6	-6.107549	0.030534	-1.095514
1	-5.359788	-1.708001	-0.025348
6	-5.768240	1.260617	-1.652318
1	-4.200788	2.694343	-2.002928
1	-7.128693	-0.335743	-1.159369
1	-6.523545	1.855024	-2.159624
6	2.845114	3.110196	-2.623403
6	2.131539	1.838179	-2.218819
8	2.686358	1.264714	-1.189062
8	1.117932	1.454851	-2.793257
1	2.566398	3.388493	-3.642073
6	3.822566	-2.173268	0.108730
8	3.042345	-2.530597	1.025845
8	-2.848930	-1.079792	0.133643
8	-3.436872	-2.086424	2.343889
16	-2.563804	-1.082236	1.765386
6	-1.878284	2.764480	-0.224995
6	-0.624506	3.101006	0.333027
6	-2.120142	1.490387	-0.667403
6	-0.354948	4.407983	0.802375
6	0.326716	2.061385	0.515070
6	-1.007793	0.615200	-0.716617
6	0.818526	4.694229	1.450137
1	-1.107364	5.177621	0.642389
6	1.468916	2.377146	1.296275
1	-1.069163	-0.316937	-1.270948
6	1.728982	3.657980	1.716803
1	1.030740	5.700342	1.799041
1	2.635050	3.834802	2.288646
1	-2.672086	3.510569	-0.217882
7	0.134721	0.854762	-0.111520
7	2.362490	1.343976	1.827052
8	3.541683	1.610790	1.941143
8	1.834685	0.296643	2.182407

1	0.260997	-4.792420	-2.507433
1	-1.758782	-5.221674	-1.112347
1	1.778179	-2.181036	0.538305
6	5.257961	-2.607299	0.153676
1	5.661890	-2.708610	-0.855644
1	5.829027	-1.827336	0.668557
1	5.358207	-3.538236	0.714611
1	1.849827	-3.029472	-1.835243
8	3.483726	-1.436489	-0.877015
1	2.540196	3.916329	-1.944174
1	3.928698	2.998660	-2.535494

B

Number of imaginary frequencies : 2
The smallest frequency is : -1606.6926 cm(-1)

Electronic energy : =-2523.2777793
Zero-point correction= 0.500019
Thermal correction to Energy= 0.538170
Thermal correction to Enthalpy= 0.539114
Thermal correction to Gibbs Free Energy= 0.430936
Sum of electronic and zero-point Energies= -2522.777761
Sum of electronic and thermal Energies= -2522.739609
Sum of electronic and thermal Enthalpies= -2522.738665
Sum of electronic and thermal Free Energies= -2522.846844

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Cartesian Coordinates

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46	1.808477	-0.423086	-0.502707
6	1.402397	-3.020402	-1.785981
6	0.655988	-4.026570	-2.379652
6	-0.414011	-4.581329	-1.684705
6	-0.750984	-4.097473	-0.428136
6	-0.046849	-3.038395	0.146820
6	1.081188	-2.496193	-0.515138
1	-1.593491	-4.529283	0.110526
6	-0.499328	-2.515365	1.480544
1	0.016368	-1.594315	1.769400
1	-0.364138	-3.253333	2.282425
8	-2.480029	-0.954206	2.390369
6	-3.702175	-1.038160	-0.308503
6	-3.528925	0.338319	-0.521673
6	-4.927958	-1.659254	-0.486858
6	-4.633219	1.077572	-0.946897
6	-6.013891	-0.900508	-0.909838
1	-5.007080	-2.725850	-0.293632
6	-5.863632	0.463009	-1.147501
1	-4.513539	2.144428	-1.128930
1	-6.978799	-1.377960	-1.058994
1	-6.710931	1.052113	-1.488432
6	4.175044	-1.930991	-0.258244

8	3.499336	-2.616052	0.547326
8	-2.594744	-1.811324	0.021571
8	-3.001653	-3.375880	1.926735
16	-2.276904	-2.159525	1.608764
6	-2.159007	2.069194	0.641756
6	-0.947214	2.387617	1.292425
6	-2.248106	0.943380	-0.136206
6	-0.832925	3.549563	2.092253
6	0.136420	1.479492	1.178265
6	-1.039900	0.263085	-0.414157
6	0.318197	3.808309	2.790816
1	-1.674100	4.236605	2.112867
6	1.262580	1.732005	2.005681
1	-1.002873	-0.490081	-1.196108
6	1.369733	2.875759	2.757794
1	0.412033	4.705649	3.394867
1	2.269923	3.018935	3.348327
1	-3.031469	2.691811	0.830669
7	0.083596	0.477485	0.237549
7	2.312981	0.735187	2.209072
8	3.461485	1.119184	2.312474
8	1.942348	-0.427915	2.323411
1	0.923652	-4.395655	-3.366641
1	-0.988443	-5.395815	-2.119708
1	2.166476	-2.357604	0.185691
6	5.662794	-2.116521	-0.314011
1	6.041741	-1.903286	-1.315464
1	6.114544	-1.398291	0.378878
1	5.934593	-3.124131	0.005431
1	2.276277	-2.629581	-2.303935
8	3.686500	-1.048381	-1.042786
6	1.803785	3.568506	-1.875232
6	1.708076	2.042332	-1.803617
8	2.379529	1.534972	-0.823494
8	0.963387	1.438071	-2.572663
1	1.697249	3.889915	-2.916102
7	0.752045	4.158109	-1.062209
6	-0.564478	4.324485	-1.400107
8	-1.382184	4.689054	-0.562682
1	2.769937	3.916047	-1.498554
6	-0.937715	4.047679	-2.830511
1	-0.411333	4.727999	-3.510710
1	-0.664118	3.023962	-3.111189
1	-2.012550	4.202639	-2.937051
1	0.943130	4.308898	-0.078648

C

Number of imaginary frequencies : 1
The smallest frequency is : -1509.6559 cm(-1)

Electronic energy : =-2294.2865697
Zero-point correction= 0.434951
Thermal correction to Energy= 0.468454
Thermal correction to Enthalpy= 0.469398
Thermal correction to Gibbs Free Energy= 0.370762
Sum of electronic and zero-point Energies= -2293.851619
Sum of electronic and thermal Energies= -2293.818116
Sum of electronic and thermal Enthalpies= -2293.817172
Sum of electronic and thermal Free Energies= -2293.915808

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Cartesian Coordinates

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46	1.620462	-0.344434	-0.539162
6	0.900559	-3.152981	-1.156146
6	0.029223	-4.162727	-1.536871
6	-1.143998	-4.356320	-0.814058
6	-1.453320	-3.518971	0.249798
6	-0.616439	-2.454618	0.587027
6	0.605455	-2.265607	-0.100149
1	-2.368812	-3.682077	0.816473
6	-1.000077	-1.531388	1.710205
1	-0.398011	-0.615532	1.708702
1	-0.902216	-2.006450	2.695749
8	-2.819174	0.393318	2.138005
6	-4.033387	-0.281715	-0.464035
6	-3.688716	0.940510	-1.060596
6	-5.330675	-0.769828	-0.487164
6	-4.698924	1.650382	-1.713443
6	-6.318460	-0.040846	-1.139163
1	-5.538142	-1.717726	0.002475
6	-5.999208	1.163681	-1.760022
1	-4.451482	2.590681	-2.203187
1	-7.336781	-0.419062	-1.169120
1	-6.767269	1.726611	-2.283740
6	4.420772	-0.351638	-1.284519
6	3.860407	1.029970	-1.635302
8	2.608117	1.247725	-1.302510
8	4.561287	1.845797	-2.193623
1	5.342551	-0.180548	-0.714196
7	3.457161	-1.151979	-0.550414
6	3.770086	-1.940850	0.470352
8	2.888420	-2.449986	1.215638
8	-3.033615	-1.062838	0.094947
8	-3.561752	-2.007213	2.346126
16	-2.732326	-0.993576	1.722344
1	4.710163	-0.834516	-2.229517
6	-2.118105	2.800535	-0.532653
6	-0.858340	3.219685	-0.054651
6	-2.339339	1.485214	-0.856867
6	-0.606543	4.572617	0.276967
6	0.131440	2.226311	0.175869
6	-1.206355	0.635398	-0.857273
6	0.586740	4.945091	0.836107
1	-1.384710	5.306655	0.078146

6	1.288930	2.638929	0.889881
1	-1.269241	-0.361704	-1.286227
6	1.533538	3.959293	1.168324
1	0.790406	5.985310	1.071554
1	2.452810	4.214158	1.687013
1	-2.932464	3.523635	-0.566117
7	-0.044434	0.963053	-0.332314
7	2.201549	1.678311	1.518406
8	3.387339	1.939998	1.547327
8	1.680224	0.697068	2.037223
1	0.278381	-4.817938	-2.368101
1	-1.818388	-5.169904	-1.070967
1	1.650577	-2.095891	0.622777
6	5.211400	-2.259742	0.763151
1	5.781273	-2.472770	-0.146188
1	5.680986	-1.403449	1.262087
1	5.251315	-3.116968	1.436572
1	1.858314	-3.050270	-1.663660

D

Number of imaginary frequencies : 1
The smallest frequency is : -1558.5451 cm(-1)

Electronic energy : =-2315.3774657
Zero-point correction= 0.441958
Thermal correction to Energy= 0.477719
Thermal correction to Enthalpy= 0.478663
Thermal correction to Gibbs Free Energy= 0.372434
Sum of electronic and zero-point Energies= -2314.935508
Sum of electronic and thermal Energies= -2314.899747
Sum of electronic and thermal Enthalpies= -2314.898802
Sum of electronic and thermal Free Energies= -2315.005031

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Cartesian Coordinates

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46	-2.423578	-0.440726	0.835748
6	-2.883407	-3.201135	0.170508
6	-2.398522	-4.489378	0.360814
6	-1.082460	-4.770500	0.015318
6	-0.253069	-3.790126	-0.532914
6	-0.724712	-2.495279	-0.700474
6	-2.058307	-2.182950	-0.335687
1	0.755698	-4.053740	-0.838233
6	0.056776	-1.380641	-1.345170
1	-0.011790	-0.446206	-0.769205
1	-0.342338	-1.158389	-2.346193
8	2.315414	-0.355323	-2.208647
6	3.611489	-1.391909	0.219198
6	3.972446	-0.080013	0.560654
6	4.536599	-2.424278	0.187246
6	5.310002	0.151198	0.892768
6	5.860868	-2.165534	0.521580
1	4.197344	-3.414270	-0.106103

6	6.244802	-0.876915	0.878918
1	5.610896	1.157578	1.179319
1	6.590328	-2.970855	0.502914
1	7.277244	-0.670178	1.148973
6	-0.372985	0.965234	3.883131
6	-1.193496	0.429737	2.762144
8	-2.266961	0.996395	2.408791
8	-0.814660	-0.616593	2.126003
1	0.201230	1.819830	3.508415
6	-4.134629	0.014900	-1.404384
8	-3.308933	-0.648308	-2.084642
8	2.281619	-1.691331	-0.069395
8	2.114402	-2.857590	-2.285170
16	1.805249	-1.591135	-1.647914
6	3.272639	2.210013	-0.128217
6	2.239046	3.142830	-0.374565
6	2.988790	1.011230	0.479519
6	2.461257	4.392211	-0.999754
6	0.917688	2.750396	-0.026876
6	1.660097	0.824595	0.953568
6	1.411729	5.231087	-1.282058
1	3.481044	4.673583	-1.256766
6	-0.138735	3.607124	-0.425526
1	1.414594	-0.053788	1.553778
6	0.091073	4.830888	-1.000380
1	1.587333	6.194155	-1.752988
1	-0.756314	5.459157	-1.259572
1	4.277838	2.425091	-0.490557
7	0.663132	1.634192	0.698266
7	-1.532467	3.157317	-0.331920
8	-2.359180	3.964243	0.053726
8	-1.771218	2.026114	-0.726082
1	-3.038863	-5.267188	0.769214
1	-0.688985	-5.775255	0.153561
1	-2.619672	-1.362302	-1.158694
6	-5.191331	0.813506	-2.106955
1	-4.837170	1.849287	-2.157023
1	-5.352669	0.439749	-3.119213
1	-6.118729	0.808646	-1.530447
1	-3.918144	-2.962361	0.415875
8	-4.132888	0.084149	-0.135267
1	-1.023658	1.321542	4.685790
1	0.318065	0.205107	4.255981

E

Number of imaginary frequencies : 1
The smallest frequency is : -1625.0002 cm(-1)

Electronic energy : =-2523.2654961
Zero-point correction= 0.498597
Thermal correction to Energy= 0.538170

Thermal correction to Enthalpy= 0.539115
Thermal correction to Gibbs Free Energy= 0.424964
Sum of electronic and zero-point Energies= -2522.766899
Sum of electronic and thermal Energies= -2522.727326
Sum of electronic and thermal Enthalpies= -2522.726382
Sum of electronic and thermal Free Energies= -2522.840532

Cartesian Coordinates

46	1.135366	0.035332	-0.413495
6	1.017616	-2.820117	-1.098243
6	0.419689	-4.009957	-1.485808
6	-0.666489	-4.492782	-0.762521
6	-1.168985	-3.764126	0.307008
6	-0.615656	-2.531521	0.656555
6	0.526160	-2.046069	-0.025209
1	-2.022208	-4.142677	0.868653
6	-1.237040	-1.752948	1.781776
1	-0.828043	-0.741288	1.868774
1	-1.124946	-2.257315	2.750761
8	-3.409639	-0.217196	2.108124
6	-4.313813	-1.043364	-0.578725
6	-4.199813	0.250708	-1.108316
6	-5.474526	-1.790042	-0.706606
6	-5.293409	0.766295	-1.806370
6	-6.551792	-1.251238	-1.401146
1	-5.509057	-2.781384	-0.262760
6	-6.455761	0.020589	-1.959144
1	-5.218692	1.759669	-2.245334
1	-7.464661	-1.830080	-1.512990
1	-7.292177	0.434975	-2.515694
6	5.012487	-1.327170	0.627163
6	3.519608	-1.199455	0.437637
8	3.108232	-0.569096	-0.583716
8	2.782162	-1.725179	1.307421
1	5.227575	-2.398604	0.749782
7	5.745923	-0.740413	-0.458351
6	7.104233	-0.747728	-0.625148
8	7.635232	-0.169762	-1.555980
8	-3.206021	-1.621498	0.027276
8	-3.703616	-2.719127	2.216377
16	-3.038212	-1.550351	1.672597
1	5.229780	-0.858800	1.601247
6	-3.079933	2.346249	-0.349098
6	-1.964327	2.956848	0.265933
6	-3.011076	1.045924	-0.775736
6	-2.013922	4.300037	0.706452
6	-0.819186	2.155921	0.524399
6	-1.733928	0.436975	-0.742903
6	-0.964969	4.853883	1.392861
1	-2.907362	4.880709	0.486125
6	0.187139	2.734450	1.343389
1	-1.560580	-0.491210	-1.278856
6	0.136972	4.050888	1.731264
1	-0.995568	5.890038	1.715783

1	0.953852	4.437111	2.333430
1	-4.016426	2.900167	-0.403443
7	-0.708665	0.928093	-0.082095
7	1.265227	1.941615	1.941922
8	2.336621	2.481143	2.129703
8	0.984729	0.793784	2.269333
1	0.815204	-4.572362	-2.327938
1	-1.124218	-5.442810	-1.028207
1	1.521568	-1.673111	0.743942
6	7.885721	-1.520387	0.410719
1	7.735092	-1.106609	1.415055
1	7.581803	-2.573486	0.441045
1	8.944183	-1.460640	0.154176
1	1.907949	-2.477375	-1.623184
1	5.217240	-0.189952	-1.125615
8	1.753679	1.893295	-0.973823
6	1.138762	2.383486	-2.015601
6	1.580365	3.796228	-2.325161
1	2.670249	3.877592	-2.299492
1	1.194849	4.107092	-3.298186
1	1.186755	4.465705	-1.549665
8	0.263646	1.817445	-2.660343

F

Number of imaginary frequencies : 1
The smallest frequency is : -1347.9962 cm(-1)

Electronic energy : =-2294.2437088
Zero-point correction= 0.434141
Thermal correction to Energy= 0.467510
Thermal correction to Enthalpy= 0.468454
Thermal correction to Gibbs Free Energy= 0.370414
Sum of electronic and zero-point Energies= -2293.809568
Sum of electronic and thermal Energies= -2293.776199
Sum of electronic and thermal Enthalpies= -2293.775255
Sum of electronic and thermal Free Energies= -2293.873294

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Cartesian Coordinates

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46	1.392475	-0.894690	-0.532842
6	-0.142044	-3.481887	-1.290649
6	-1.190435	-4.387114	-1.410080
6	-2.185697	-4.404382	-0.440985
6	-2.147156	-3.495877	0.610909
6	-1.115426	-2.563469	0.711804
6	-0.054594	-2.562097	-0.225725
1	-2.948986	-3.484525	1.348664
6	-1.197164	-1.528223	1.795633
1	-0.364625	-0.817471	1.765102
1	-1.252526	-1.967059	2.800362
8	-2.408405	0.850627	2.103603

6	-3.859140	0.350846	-0.451118
6	-3.314714	1.490902	-1.065178
6	-5.221715	0.094236	-0.461752
6	-4.192072	2.357499	-1.719958
6	-6.073863	0.976722	-1.115900
1	-5.589055	-0.797430	0.038887
6	-5.557335	2.101398	-1.752587
1	-3.788815	3.237175	-2.218842
1	-7.142380	0.779512	-1.134225
1	-6.221345	2.783575	-2.276872
6	4.223986	-0.894301	-0.357623
6	3.706369	-2.271056	0.064894
8	2.491560	-2.597750	-0.473553
8	4.330348	-3.035221	0.743902
1	5.001022	-1.091815	-1.114136
7	3.187018	-0.004877	-0.830633
6	3.418925	1.113010	-1.554886
8	2.514883	1.830384	-1.986331
8	-3.005444	-0.585054	0.120717
8	-3.793564	-1.231625	2.409286
16	-2.710771	-0.524314	1.750937
1	4.741112	-0.494041	0.531424
6	-1.428043	3.033353	-0.512213
6	-0.121512	3.184749	0.001254
6	-1.890981	1.793822	-0.868669
6	0.362570	4.459176	0.375308
6	0.654956	2.015603	0.237690
6	-0.937456	0.750759	-0.882243
6	1.575461	4.594529	0.996340
1	-0.257428	5.327389	0.161419
6	1.827551	2.191244	1.023638
1	-1.180980	-0.198279	-1.351003
6	2.294683	3.442489	1.348438
1	1.957397	5.573214	1.270193
1	3.211663	3.507990	1.925804
1	-2.085252	3.902117	-0.533287
7	0.252971	0.829867	-0.324193
7	2.544714	1.082868	1.656284
8	3.734504	1.227301	1.881525
8	1.885628	0.107431	1.996877
1	-1.217534	-5.086984	-2.241843
1	-3.001113	-5.121247	-0.503979
1	1.347672	-2.760671	0.012593
6	4.872265	1.490731	-1.778727
1	5.403917	1.602457	-0.825638
1	5.402438	0.727802	-2.361378
1	4.900590	2.435532	-2.324297
1	0.669201	-3.512153	-2.017291

G

Number of imaginary frequencies : 1

The smallest frequency is : -1234.1205 cm(-1)

Electronic energy : =-3083.8379585
Zero-point correction= 0.502472
Thermal correction to Energy= 0.545710
Thermal correction to Enthalpy= 0.546654
Thermal correction to Gibbs Free Energy= 0.427010
Sum of electronic and zero-point Energies= -3083.335486
Sum of electronic and thermal Energies= -3083.292249
Sum of electronic and thermal Enthalpies= -3083.291304
Sum of electronic and thermal Free Energies= -3083.410949

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Cartesian Coordinates

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46	-0.937036	0.816505	0.021262
6	0.034830	3.152219	-1.464171
6	0.936562	3.871059	-2.234744
6	2.232999	4.064521	-1.768051
6	2.626984	3.500829	-0.562936
6	1.748940	2.711818	0.181551
6	0.408477	2.551016	-0.242025
1	3.641524	3.656613	-0.198588
6	2.238145	2.078794	1.452652
1	1.521500	1.360214	1.865538
1	2.467558	2.822678	2.227036
8	3.771300	-0.047793	2.050291
6	4.504236	-0.217372	-0.822767
6	3.899524	-1.470630	-1.000106
6	5.812906	0.027298	-1.208888
6	4.650802	-2.476982	-1.609372
6	6.541071	-0.992483	-1.811589
1	6.234249	1.013751	-1.033718
6	5.956950	-2.238897	-2.019715
1	4.195924	-3.453092	-1.770285
1	7.565517	-0.809970	-2.124777
1	6.522304	-3.031147	-2.503123
6	-3.674459	1.846766	-0.968419
6	-4.881186	1.235371	-0.251281
8	-4.676809	0.077896	0.355415
8	-5.952207	1.796919	-0.233778
1	-4.022473	2.777244	-1.435157
7	-2.522984	2.090529	-0.111641
6	-2.505190	3.115770	0.747438
8	-1.474105	3.397744	1.411483
8	3.743082	0.823781	-0.312728
8	4.922458	2.119064	1.470524
16	3.818408	1.193881	1.301469
1	-3.363658	1.177293	-1.777997
6	2.308643	-2.801760	0.378331
6	1.186278	-2.815966	1.235081
6	2.581805	-1.700497	-0.393151
6	0.901554	-3.930212	2.059452
6	0.406984	-1.630853	1.333194
6	1.586410	-0.693192	-0.435650
6	-0.113711	-3.880493	2.978260

1	1.514777	-4.822301	1.951632
6	-0.555185	-1.589726	2.374326
1	1.643220	0.102015	-1.176660
6	-0.834347	-2.686097	3.150491
1	-0.341401	-4.739355	3.602134
1	-1.605117	-2.596230	3.910343
1	3.005249	-3.638795	0.413256
7	0.570349	-0.632629	0.401007
7	-1.214301	-0.341724	2.768999
8	-2.382816	-0.389560	3.090215
8	-0.502519	0.655641	2.803060
1	0.620346	4.305497	-3.179858
1	2.939344	4.660864	-2.340631
1	-0.437519	2.697883	0.684946
6	-3.703608	4.016088	0.885725
1	-3.759936	4.674659	0.009693
1	-4.648861	3.470139	0.942760
1	-3.567523	4.634369	1.773740
1	-0.997138	3.062078	-1.796600
8	-2.217018	-0.797774	-0.174241
1	-3.775236	-0.285473	0.167537
6	-1.899495	-1.778365	-1.068898
1	-0.853606	-2.146005	-0.996273
6	-2.760727	-3.006366	-0.764712
6	-2.051481	-1.304135	-2.516230
9	-2.516951	-4.006285	-1.616924
9	-4.057374	-2.726978	-0.811057
9	-2.471422	-3.452194	0.461619
9	-3.299754	-0.916715	-2.780953
9	-1.703879	-2.233305	-3.403905
9	-1.248457	-0.242295	-2.727644

***para* C-H activation**

A

Number of imaginary frequencies : 1
The smallest frequency is : -1480.5125 cm(-1)

Electronic energy : =-2315.3898191
Zero-point correction= 0.443137
Thermal correction to Energy= 0.478603
Thermal correction to Enthalpy= 0.479547
Thermal correction to Gibbs Free Energy= 0.374618
Sum of electronic and zero-point Energies= -2314.946682
Sum of electronic and thermal Energies= -2314.911216
Sum of electronic and thermal Enthalpies= -2314.910272
Sum of electronic and thermal Free Energies= -2315.015201

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Cartesian Coordinates

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46	-1.942789	-0.495802	0.505825
6	-0.575689	-2.064646	-1.742307
6	-1.106427	-2.254850	-0.455099
6	-0.303143	-2.894259	0.506651
6	1.017209	-3.220597	0.229996
6	1.550174	-2.941393	-1.030369
6	0.735095	-2.410468	-2.033051
1	1.658641	-3.646156	1.000875
6	3.017066	-3.081064	-1.260673
1	3.276960	-3.405666	-2.275743
1	3.515013	-3.737488	-0.539415
8	3.343156	-0.525169	-2.050270
6	3.789980	0.034320	0.972417
6	3.086871	1.240196	0.877636
6	4.988146	-0.071229	1.665426
6	3.635888	2.345471	1.541090
6	5.513381	1.045015	2.301701
1	5.493001	-1.032777	1.680794
6	4.830366	2.255281	2.241278
1	3.087510	3.285012	1.528689
1	6.449557	0.966539	2.847757
1	5.221960	3.131141	2.751888
6	-2.350223	2.849161	3.087608
6	-1.778367	1.668437	2.331917
8	-2.587473	1.221711	1.417778
8	-0.670675	1.208361	2.599145
1	-1.563312	3.349613	3.656213
6	-3.991875	-2.469931	0.923162
8	-3.588223	-3.008223	-0.143591
8	3.268717	-1.117370	0.388374
8	5.291115	-1.724346	-0.998956
16	3.863203	-1.495597	-1.105639
1	-3.116261	2.487116	3.781393
6	1.609397	2.548773	-0.612228
6	0.362987	2.793320	-1.220879
6	1.827882	1.413127	0.127091
6	0.140670	3.997830	-1.928547
6	-0.672335	1.826210	-1.072531
6	0.748103	0.504186	0.221497
6	-1.090974	4.288981	-2.450131
1	0.971071	4.693818	-2.028994
6	-1.924533	2.160022	-1.663225
1	0.858818	-0.396755	0.819416
6	-2.132385	3.360455	-2.298856
1	-1.270014	5.220460	-2.978536
1	-3.122711	3.559672	-2.697568
1	2.399790	3.288824	-0.730380
7	-0.435239	0.693024	-0.341577
7	-3.074005	1.249187	-1.701228
8	-4.174728	1.726374	-1.505990
8	-2.846757	0.078166	-1.975577
1	-0.714472	-3.089850	1.497509
1	1.155173	-2.212254	-3.018026
1	-2.404032	-2.512496	-0.370381

1	-1.189126	-1.586221	-2.502868
6	-5.251513	-2.984714	1.555691
1	-5.204272	-2.874522	2.640892
1	-6.087572	-2.377709	1.192556
1	-5.427014	-4.023848	1.272086
8	-3.420584	-1.499678	1.506324
1	-2.837860	3.550116	2.404248

B

Number of imaginary frequencies : 1
The smallest frequency is : -1493.5533 cm(-1)

Electronic energy : =-2523.2984439
Zero-point correction= 0.500647
Thermal correction to Energy= 0.539506
Thermal correction to Enthalpy= 0.540450
Thermal correction to Gibbs Free Energy= 0.430249
Sum of electronic and zero-point Energies= -2522.797797
Sum of electronic and thermal Energies= -2522.758938
Sum of electronic and thermal Enthalpies= -2522.757994
Sum of electronic and thermal Free Energies= -2522.868195

Cartesian Coordinates

46	2.026657	-0.531386	-0.563893
6	0.984241	-2.896139	1.069898
6	1.440563	-2.583723	-0.222487
6	0.625659	-2.931683	-1.316427
6	-0.643412	-3.458900	-1.122467
6	-1.111064	-3.680520	0.175540
6	-0.271882	-3.449779	1.268272
1	-1.299335	-3.654858	-1.969791
6	-2.541677	-4.044631	0.396557
1	-2.696584	-4.732547	1.236568
1	-3.029486	-4.456150	-0.493262
8	-3.038041	-1.989758	2.062478
6	-3.716100	-0.447952	-0.592514
6	-3.087590	0.728436	-0.167218
6	-4.944445	-0.436172	-1.240254
6	-3.736536	1.936558	-0.459914
6	-5.575090	0.774184	-1.495455
1	-5.385774	-1.385087	-1.530950
6	-4.961570	1.962438	-1.112079
1	-3.229730	2.865500	-0.199496
1	-6.535134	0.786554	-2.004725
1	-5.432502	2.918164	-1.331044
6	1.415352	3.619712	-1.250224
6	1.311032	2.096738	-1.387215
8	2.328506	1.490753	-0.875566
8	0.314398	1.591434	-1.896490
1	1.379609	3.866341	-0.182216

6	4.220519	-1.991592	-1.704155
8	3.954561	-2.899221	-0.870644
8	-3.076409	-1.677237	-0.431082
8	-4.941278	-2.937462	0.715086
16	-3.535607	-2.607706	0.848628
6	-1.585919	1.756084	1.504878
6	-0.316185	1.935720	2.084241
6	-1.802816	0.789717	0.554123
6	-0.091430	3.003045	2.983666
6	0.745715	1.078640	1.687569
6	-0.691480	-0.005589	0.203099
6	1.160646	3.253836	3.478026
1	-0.936504	3.636257	3.244967
6	2.017199	1.344755	2.270013
1	-0.792679	-0.750982	-0.581671
6	2.222700	2.413866	3.108832
1	1.339758	4.085847	4.152152
1	3.225888	2.577690	3.490355
1	-2.385837	2.430332	1.802669
7	0.517868	0.129345	0.725849
7	3.189168	0.488388	2.060787
8	4.274642	1.030804	1.971860
8	3.001468	-0.721020	2.031899
1	0.982130	-2.736674	-2.328356
1	-0.640290	-3.638094	2.275679
1	2.746605	-2.657708	-0.438822
1	1.604929	-2.644834	1.926416
6	5.479603	-2.107334	-2.512472
1	5.356563	-1.621875	-3.482541
1	6.278864	-1.588077	-1.972964
1	5.765155	-3.154399	-2.628130
8	3.509895	-0.960180	-1.906576
1	2.379968	3.969321	-1.630881
7	0.328793	4.289630	-1.922255
1	0.353744	4.229403	-2.931571
6	-0.924686	4.243877	-1.377880
8	-1.129886	4.030067	-0.189545
6	-2.044190	4.475333	-2.358628
1	-1.742454	5.081846	-3.218417
1	-2.375217	3.495660	-2.726420
1	-2.884797	4.954861	-1.850482

C

Number of imaginary frequencies : 1
The smallest frequency is : -1609.9168 cm(-1)

Electronic energy : =-2294.3018992
Zero-point correction= 0.436051
Thermal correction to Energy= 0.469297
Thermal correction to Enthalpy= 0.470241
Thermal correction to Gibbs Free Energy= 0.372299

Sum of electronic and zero-point Energies= -2293.865848
Sum of electronic and thermal Energies= -2293.832603
Sum of electronic and thermal Enthalpies= -2293.831658
Sum of electronic and thermal Free Energies= -2293.929600

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Cartesian Coordinates

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46	-1.855994	-0.434615	0.372784
6	-0.419317	-1.947920	-1.830680
6	-0.975006	-2.203188	-0.565467
6	-0.169885	-2.852351	0.389715
6	1.162092	-3.141751	0.128808
6	1.714781	-2.800410	-1.108259
6	0.910189	-2.237674	-2.100924
1	1.793673	-3.596650	0.891141
6	3.184604	-2.931644	-1.328327
1	3.452883	-3.191894	-2.359522
1	3.670813	-3.637589	-0.646812
8	3.514085	-0.320682	-1.912254
6	3.969756	-0.032347	1.162532
6	3.273686	1.182479	1.176506
6	5.153539	-0.215094	1.864875
6	3.812502	2.207662	1.966595
6	5.670404	0.825563	2.624016
1	5.652215	-1.177479	1.796462
6	4.991575	2.038454	2.678189
1	3.271610	3.148629	2.042126
1	6.594988	0.685024	3.177257
1	5.374112	2.853840	3.286359
6	-4.309073	-0.343741	1.912664
6	-3.628017	1.017391	2.064448
8	-2.506119	1.180170	1.405926
8	-4.132451	1.868376	2.765919
1	-5.316611	-0.151019	1.516546
7	-3.554081	-1.238874	1.052833
6	-4.048488	-2.361967	0.569373
8	-3.414459	-3.092689	-0.247999
8	3.450365	-1.119030	0.467088
8	5.466147	-1.605313	-0.975005
16	4.038359	-1.367647	-1.056942
1	-4.435032	-0.758365	2.923997
6	1.838902	2.668992	-0.182551
6	0.618040	2.988923	-0.806016
6	2.034859	1.446476	0.415613
6	0.407886	4.274516	-1.360333
6	-0.410627	2.006168	-0.827801
6	0.955255	0.532004	0.348983
6	-0.805810	4.619176	-1.889243
1	1.229916	4.986848	-1.332277
6	-1.632946	2.394969	-1.445728
1	1.048631	-0.451385	0.809371
6	-1.837844	3.665186	-1.920853
1	-0.977516	5.612189	-2.293413
1	-2.808462	3.904162	-2.345539
1	2.630013	3.417506	-0.177113

7	-0.207666	0.792658	-0.225806
7	-2.734053	1.459155	-1.707407
8	-3.864467	1.829343	-1.459692
8	-2.432277	0.390125	-2.220099
1	-0.603438	-3.111958	1.356014
1	1.346978	-1.984423	-3.065963
1	-2.235849	-2.521730	-0.463403
1	-1.028899	-1.467957	-2.591997
6	-5.421603	-2.810834	0.988697
1	-5.532099	-2.798395	2.077853
1	-6.178478	-2.134292	0.574900
1	-5.600184	-3.817607	0.609610

D

Number of imaginary frequencies : 1
The smallest frequency is : -1555.1570 cm(-1)

Electronic energy : =-2315.3738871
Zero-point correction= 0.442897
Thermal correction to Energy= 0.478239
Thermal correction to Enthalpy= 0.479184
Thermal correction to Gibbs Free Energy= 0.374522
Sum of electronic and zero-point Energies= -2314.930990
Sum of electronic and thermal Energies= -2314.895648
Sum of electronic and thermal Enthalpies= -2314.894703
Sum of electronic and thermal Free Energies= -2314.999366

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Cartesian Coordinates

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46	-3.085436	-0.381983	0.670139
6	-1.343870	-0.864525	-1.738380
6	-1.943670	-1.560524	-0.676939
6	-1.246324	-2.640651	-0.099003
6	-0.010130	-3.027176	-0.588101
6	0.566513	-2.337626	-1.661955
6	-0.102052	-1.250590	-2.227913
1	0.520712	-3.867520	-0.142945
6	1.894130	-2.786102	-2.188952
1	1.977921	-2.673388	-3.276701
1	2.119269	-3.825690	-1.928381
8	3.209791	-0.458090	-1.970512
6	3.795700	-1.499610	0.973797
6	3.662237	-0.194695	1.473292
6	4.752324	-2.383462	1.454644
6	4.526415	0.164569	2.517329
6	5.602923	-1.988798	2.477735
1	4.810454	-3.373242	1.010522
6	5.480177	-0.711610	3.015041
1	4.423261	1.152307	2.962021
1	6.349165	-2.680091	2.859973
1	6.125014	-0.397434	3.831774

6	-2.862087	3.443936	1.568619
6	-3.000391	1.999787	1.235373
8	-3.777055	1.232821	1.881724
8	-2.299551	1.490846	0.296638
1	-2.668996	4.018430	0.657004
6	-4.676624	-2.713556	0.389823
8	-4.359328	-2.637795	-0.822687
8	2.906542	-1.985717	0.016638
8	4.522889	-2.598361	-1.811758
16	3.304567	-1.848970	-1.575157
1	-2.005958	3.569378	2.241422
6	3.052188	2.123534	0.830779
6	2.162662	3.053440	0.248927
6	2.716048	0.792724	0.919811
6	2.444838	4.437936	0.191588
6	0.957636	2.540876	-0.309264
6	1.423678	0.431146	0.436669
6	1.553942	5.310108	-0.381965
1	3.379023	4.799168	0.618924
6	0.103184	3.475787	-0.955344
1	1.071496	-0.592163	0.569806
6	0.367595	4.822686	-0.960942
1	1.765069	6.375274	-0.412326
1	-0.338239	5.492847	-1.443015
1	4.021421	2.478781	1.179908
7	0.604021	1.242947	-0.176836
7	-1.072900	3.037168	-1.712782
8	-2.081169	3.722991	-1.627519
8	-0.942730	2.065865	-2.432560
1	-1.703269	-3.190036	0.722849
1	0.361475	-0.688593	-3.037464
1	-3.194652	-1.868449	-0.808239
1	-1.846954	-0.006206	-2.177793
6	-5.734431	-3.688205	0.819236
1	-5.840144	-4.487481	0.084015
1	-5.502598	-4.090701	1.807675
1	-6.686159	-3.151670	0.894274
8	-4.166236	-1.994930	1.311131
1	-3.759087	3.802954	2.077966

E

Number of imaginary frequencies : 1
The smallest frequency is : -1495.9395 cm(-1)

Electronic energy : =-2523.2839673
Zero-point correction= 0.500866
Thermal correction to Energy= 0.539601
Thermal correction to Enthalpy= 0.540545
Thermal correction to Gibbs Free Energy= 0.428990
Sum of electronic and zero-point Energies= -2522.783101
Sum of electronic and thermal Energies= -2522.744366

Sum of electronic and thermal Enthalpies= -2522.743422
Sum of electronic and thermal Free Energies= -2522.854977

.....

Cartesian Coordinates

.....

46	-1.318209	-0.312663	-0.017051
6	0.346533	-1.410409	-2.355812
6	-0.449062	-1.852547	-1.284576
6	0.105441	-2.788710	-0.391929
6	1.436219	-3.173458	-0.495809
6	2.230268	-2.653421	-1.520704
6	1.665520	-1.814241	-2.484241
1	1.879155	-3.844432	0.239331
6	3.703277	-2.888212	-1.515293
1	4.139003	-2.985001	-2.517387
1	4.011019	-3.748444	-0.911343
8	4.293386	-0.257199	-1.525692
6	4.218052	-0.530484	1.559506
6	3.629366	0.737610	1.643015
6	5.235266	-0.927152	2.417537
6	4.104576	1.593392	2.645570
6	5.689284	-0.054208	3.396728
1	5.659413	-1.919405	2.293873
6	5.119964	1.209568	3.510210
1	3.640485	2.571087	2.759520
1	6.483194	-0.363922	4.070855
1	5.458937	1.895891	4.281606
6	-5.056781	-2.118622	-0.457276
6	-3.565577	-1.902456	-0.606071
8	-2.957358	-1.441277	0.405905
8	-3.024975	-2.164514	-1.713848
1	-5.501255	-2.092974	-1.458109
6	-3.120001	1.487220	1.365965
8	-3.947284	1.263520	0.485068
8	3.763780	-1.449698	0.618525
8	5.965676	-1.865823	-0.550267
16	4.592131	-1.484647	-0.812929
6	2.589232	2.504656	0.253343
6	1.519332	3.017433	-0.504323
6	2.559229	1.224211	0.749167
6	1.562952	4.355753	-0.961545
6	0.393537	2.180665	-0.768866
6	1.408144	0.463950	0.445748
6	0.507414	4.898451	-1.640348
1	2.452885	4.942526	-0.743023
6	-0.661969	2.778618	-1.522459
1	1.320994	-0.552368	0.827077
6	-0.610773	4.095668	-1.913583
1	0.528021	5.929513	-1.979675
1	-1.458824	4.491179	-2.463680
1	3.447685	3.147352	0.444033
7	0.376521	0.909430	-0.257860
7	-1.840833	2.055931	-2.033888
8	-2.873973	2.684098	-2.144227
8	-1.677805	0.893459	-2.376110

1	-0.511385	-3.184382	0.415192
1	2.283784	-1.432691	-3.295365
1	-1.753634	-1.934707	-1.533228
1	-0.071468	-0.705408	-3.069611
6	-3.478508	2.295019	2.596030
1	-2.668350	2.978482	2.864784
1	-4.404805	2.849453	2.427179
1	-3.620297	1.610340	3.439896
8	-1.885924	1.082344	1.380403
1	-5.239050	-3.110331	-0.021676
7	-5.632549	-1.146863	0.429067
1	-5.296968	-0.190375	0.318240
6	-5.990482	-1.526029	1.695086
8	-6.089989	-2.691869	2.042520
6	-6.304158	-0.376807	2.620309
1	-6.011147	0.594830	2.209479
1	-7.378442	-0.369140	2.831027
1	-5.789463	-0.546803	3.570493

F

Number of imaginary frequencies : 1
The smallest frequency is : -1156.1567 cm(-1)

Electronic energy : =-2294.251112
Zero-point correction= 0.435328
Thermal correction to Energy= 0.468740
Thermal correction to Enthalpy= 0.469684
Thermal correction to Gibbs Free Energy= 0.370939
Sum of electronic and zero-point Energies= -2293.815784
Sum of electronic and thermal Energies= -2293.782372
Sum of electronic and thermal Enthalpies= -2293.781428
Sum of electronic and thermal Free Energies= -2293.880173

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Cartesian Coordinates

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46	1.643221	-0.937001	-0.571804
6	0.046893	-2.553150	1.343647
6	0.464776	-2.642182	0.006671
6	-0.489373	-2.997025	-0.963001
6	-1.826639	-3.158428	-0.628503
6	-2.237538	-2.946509	0.690287
6	-1.290893	-2.703839	1.686910
1	-2.571810	-3.364302	-1.396488
6	-3.690986	-2.803361	0.992968
1	-3.978009	-3.175079	1.984325
1	-4.344870	-3.255754	0.240073
8	-3.469607	-0.354789	2.094950
6	-3.910489	0.602480	-0.930319
6	-3.019318	1.683686	-0.880346
6	-5.148615	0.698274	-1.553602
6	-3.428064	2.866914	-1.512424

6	-5.531844	1.891359	-2.149369
1	-5.797693	-0.172004	-1.552843
6	-4.663767	2.977944	-2.132372
1	-2.738155	3.707588	-1.539600
1	-6.500783	1.965930	-2.635658
1	-4.941763	3.910281	-2.616670
6	4.384176	-0.720321	-1.260208
6	4.043655	-2.159701	-0.859586
8	2.755634	-2.516974	-1.209349
8	4.806194	-2.929698	-0.355978
1	4.824136	-0.790871	-2.271271
7	3.240979	0.164564	-1.200951
6	3.282590	1.469726	-1.538343
8	2.300005	2.213386	-1.472808
8	-3.533992	-0.629647	-0.405256
8	-5.630633	-0.979227	0.965706
16	-4.185709	-1.065712	1.053858
1	5.194391	-0.420502	-0.577556
6	-1.235303	2.768452	0.453778
6	0.051677	2.791414	1.021826
6	-1.701474	1.659640	-0.212636
6	0.531345	3.965096	1.650259
6	0.865366	1.629829	0.922508
6	-0.806113	0.570028	-0.311500
6	1.798283	4.018512	2.162468
1	-0.129529	4.828257	1.697270
6	2.140696	1.704857	1.552638
1	-1.101230	-0.320520	-0.864119
6	2.603682	2.869528	2.112918
1	2.178285	4.924749	2.624076
1	3.599923	2.867452	2.544442
1	-1.861240	3.653401	0.558315
7	0.414142	0.556814	0.204395
7	3.030181	0.553060	1.719281
8	4.230527	0.748400	1.638304
8	2.510153	-0.523207	1.980370
1	-0.183197	-3.087409	-2.006237
1	-1.619233	-2.548314	2.713631
1	1.953055	-2.947803	-0.506183
6	4.630923	2.019832	-1.966862
1	5.336578	1.988769	-1.126400
1	5.073323	1.441994	-2.786769
1	4.499001	3.055343	-2.285409
1	0.766770	-2.273115	2.110896

G

Number of imaginary frequencies : 1
The smallest frequency is : -1470.7899 cm(-1)

Electronic energy : =-3083.8517483
Zero-point correction= 0.502336

Thermal correction to Energy= 0.545277
Thermal correction to Enthalpy= 0.546221
Thermal correction to Gibbs Free Energy= 0.427331
Sum of electronic and zero-point Energies= -3083.349412
Sum of electronic and thermal Energies= -3083.306472
Sum of electronic and thermal Enthalpies= -3083.305528
Sum of electronic and thermal Free Energies= -3083.424417

Cartesian Coordinates

46	1.190837	-1.037419	-0.036896
6	-0.820294	-2.724858	1.532459
6	-0.076141	-2.750928	0.338516
6	-0.748253	-3.044824	-0.862599
6	-2.127784	-3.200055	-0.881931
6	-2.855725	-3.102370	0.306122
6	-2.192324	-2.912091	1.521383
1	-2.654254	-3.361324	-1.821757
6	-4.347155	-3.079178	0.261722
1	-4.821428	-3.602873	1.100842
1	-4.761183	-3.463238	-0.676453
8	-4.613537	-0.796793	1.666198
6	-4.286160	0.563737	-1.145479
6	-3.457067	1.588309	-0.672260
6	-5.332749	0.808212	-2.024685
6	-3.711306	2.880569	-1.152263
6	-5.573461	2.103130	-2.462988
1	-5.946499	-0.027316	-2.347539
6	-4.754973	3.140549	-2.029253
1	-3.048212	3.688516	-0.849085
1	-6.390398	2.296507	-3.152833
1	-4.918522	4.153706	-2.386604
6	3.448401	-1.579123	-2.000335
6	4.817330	-1.053793	-1.560363
8	5.823086	-1.369188	-2.150123
8	4.832631	-0.258701	-0.499474
1	3.640061	-2.312898	-2.793281
7	2.637469	-2.148115	-0.936642
6	2.997461	-3.298884	-0.365137
8	2.299067	-3.847655	0.529169
8	-4.029365	-0.753941	-0.776908
8	-6.367960	-1.374568	-0.043327
16	-4.988973	-1.399866	0.402679
1	2.877092	-0.768112	-2.465638
6	-2.073610	2.322519	1.249012
6	-0.914772	2.232360	2.043798
6	-2.338137	1.393709	0.270952
6	-0.621484	3.237136	2.996460
6	-0.026967	1.137594	1.838462
6	-1.394430	0.352173	0.123528
6	0.537704	3.198789	3.721977
1	-1.335159	4.048839	3.121965
6	1.132813	1.109722	2.664494
1	-1.538753	-0.391970	-0.658606
6	1.421832	2.121571	3.545740

1	0.775386	3.980085	4.437330
1	2.344389	2.056765	4.114661
1	-2.753652	3.157179	1.413814
7	-0.291913	0.231656	0.845368
7	2.081259	-0.009574	2.685099
8	3.262508	0.253052	2.787912
8	1.607241	-1.138057	2.643779
1	-0.178494	-3.119967	-1.788050
1	-2.765285	-2.858471	2.445611
1	1.107652	-3.183259	0.493278
1	-0.305659	-2.521906	2.468541
6	4.269940	-3.990198	-0.773002
1	4.375257	-4.063626	-1.859851
1	5.136164	-3.424886	-0.410151
1	4.282190	-4.986080	-0.329243
8	2.356735	0.686491	-0.226809
1	3.918209	0.018792	-0.225725
6	2.388595	1.657930	-1.180069
1	3.145021	1.482658	-1.978820
6	2.845307	2.956190	-0.500741
6	1.080678	1.856882	-1.951690
9	4.051089	2.771950	0.024849
9	2.022675	3.327499	0.485206
9	2.921557	3.972943	-1.365613
9	0.628774	0.678108	-2.412446
9	0.102921	2.384268	-1.202404
9	1.249270	2.648615	-3.008381

5.4. Conclusion

In conclusion, we have successfully introduced 8-nitroquinoline as a DG for *meta*-C–H functionalization which mimics the traditional *ortho*-C–H functionalization *via* strong σ-coordination. The protocol is capable in performing olefination and acetoxylation with ease which can be diversified to different synthetically important compounds in late stage. High yielding gram scale *meta*-olefination reaction made this protocol more general and attractive. Removal of the DG resulted a trialkenylated product which is difficult to synthesize by other traditional methods. The kinetic studies, order determination, NMR, ESI-MS and DFT studies shed light into the mechanism.

5.5. Reference

(1) (a) Newhouse, T.; Baran, P. S. *Angew. Chem. Int. Ed.* **2011**, *50*, 3362-3374. (b) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885-1898. (c) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009. (d) Brückl, T.;

Baxter, R. D.; Ishihara, Y.; Baran, P. S. *Acc. Chem. Res.* **2012**, *45*, 826-839. (e) Wencel-Delord, J.; Glorius, F. *Nat. Chem.* **2013**, *5*, 369-375.

(2) (a) Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Chem. Commun.* **1994**, 2267-2268. (b) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604-2610. (c) Wang, X.; Truesdale, L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 3648-3649. (d) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879-5918. (e) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814-825. (f) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788-802. (g) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651-3678. (h) Zhang, F.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906-6919. (i) Huang, Z.; Lim, H. N.; Mo, F.; Young, M. C.; Dong, G. *Chem. Soc. Rev.* **2015**, *44*, 7764-7786.

(3) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154-13155.

(4) (a) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074-1086. (b) Rouquet, G.; Chatani, N. *Angew. Chem. Int. Ed.* **2013**, *52*, 11726-11743. (c) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, *135*, 5308-5311. (d) Aihara, Y.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *J. Am. Chem. Soc.* **2014**, *136*, 15509-15512. (e) Matsubara, T.; Asako, S.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2014**, *136*, 646-649. (f) Ilies, L.; Matsubara, T.; Ichikawa, S.; Asako, S.; Nakamura, E. *J. Am. Chem. Soc.* **2014**, *136*, 13126-13129. (g) Song, W.; Lackner, S.; Ackermann, L. *Angew. Chem. Int. Ed.* **2014**, *53*, 2477-2480. (h) Daugulis, O.; Roane, J.; Tran, L. D. *Acc. Chem. Res.* **2015**, *48*, 1053-1064. (i) Zhang, S.-Y.; Li, Q.; He, G.; Nack, W. A.; Chen, G. *J. Am. Chem. Soc.* **2015**, *137*, 531-539. (j) Wu, X.; Zhao, Y.; Ge, H. *J. Am. Chem. Soc.* **2014**, *136*, 1789-1792. (k) Fruchey, E. R.; Monks, B. M.; Cook, S. P. *J. Am. Chem. Soc.* **2014**, *136*, 13130-13133. (l) Rouquet, G.; Chatani, N. *Chem. Sci.* **2013**, *4*, 2201-2208.

(5) (a) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518-522. (b) Tang, R.-Y.; Li, G.; Yu, J.-Q. *Nature* **2014**, *507*, 215-220. (c) Yang, G.; Lindovska, P.; Zhu, D.; Kim, J.; Wang, P.; Tang, R.-Y.; Movassaghi, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136*, 10807-10813. (d) Schranck, J.; Tlili, A.; Beller, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 9426-9428.

(6) (a) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E.; Smith, M. R. *Science* **2002**, *295*, 305-308. (b) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390-391. (c) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072-5074. (d) Luo, J.; Preciado, S.; Larrosa, I. *J. Am. Chem. Soc.* **2014**, *136*, 4109-4112. (e) Cheng, C.; Hartwig, J. F. *Science* **2014**, *343*, 853-857. (f) Martínez-Martínez, A. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T. *Science* **2014**, *346*, 834-837. (g) Tobisu,

M.; Chatani, N. *Science* **2014**, *343*, 850-851. (h) Luo, J.; Preciado, S.; Larrosa, I. *Chem. Commun.* **2015**, *51*, 3127-3130. (i) Bisht, R.; Chattopadhyay, B. *J. Am. Chem. Soc.* **2016**, *138*, 84-87.

(7) (a) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593-1597. (b) Duong, H. A.; Gilligan, R. E.; Cooke, M. L.; Phipps, R. J.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 463-466. (c) Teskey, C. J.; Lui, A. Y. W.; Greaney, M. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 11677-11680. (d) Fan, Z.; Ni, J.; Zhang, A. *J. Am. Chem. Soc.* **2016**, *138*, 8470-8475.

(8) (a) Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Köhn, G.; Whittlesey, M. K.; Frost, C. G. *J. Am. Chem. Soc.* **2011**, *133*, 19298-19301. (b) Paterson, A. J.; St John-Campbell, S.; Mahon, M. F.; Press, N. J.; Frost, C. G. *Chem. Commun.* **2015**, *51*, 12807-12810.

(9) (a) Hofmann, N.; Ackermann, L. *J. Am. Chem. Soc.* **2013**, *135*, 5877-5884. (b) Li, J.; Warratz, S.; Zell, D.; De Sarkar, S.; Ishikawa, E. E.; Ackermann, L. *J. Am. Chem. Soc.* **2015**, *137*, 13894-13901. (c) Ackermann, L.; Li, J. *Nat Chem* **2015**, *7*, 686-687. (d) Kumar, N. Y. P.; Bechtoldt, A.; Raghuvanshi, K.; Ackermann, L. *Angew. Chem. Int. Ed.* **2016**, *55*, 6929-6932.

(10) (a) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem. Int. Ed.* **1997**, *36*, 119-122. (b) Cárdenas, D. J.; Martín-Matute, B.; Echavarren, A. M. *J. Am. Chem. Soc.* **2006**, *128*, 5033-5040. (c) Ferraccioli, R. *Synthesis* **2013**, *45*, 581-591.

(11) (a) Dong, Z.; Dong, G. *J. Am. Chem. Soc.* **2013**, *135*, 18350-18353. (b) Dong, Z.; Wang, J.; Dong, G. *J. Am. Chem. Soc.* **2015**, *137*, 5887-5890. (c) Dong, Z.; Wang, J.; Ren, Z.; Dong, G. *Angew. Chem. Int. Ed.* **2015**, *54*, 12664-12668.

(12) (a) Wang, X.-C.; Gong, W.; Fang, L.-Z.; Zhu, R.-Y.; Li, S.; Engle, K. M.; Yu, J.-Q. *Nature* **2015**, *519*, 334-338. (b) Shen, P.-X.; Wang, X.-C.; Wang, P.; Zhu, R.-Y.; Yu, J.-Q. *J. Am. Chem. Soc.* **2015**, *137*, 11574-11577. (c) Wang, P.; Li, G.-C.; Jain, P.; Farmer, M. E.; He, J.; Shen, P.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2016**, *138*, 14092-14099. (d) Wang, P.; Farmer, M. E.; Huo, X.; Jain, P.; Shen, P.-X.; Ishoey, M.; Bradner, J. E.; Wisniewski, S. R.; Eastgate, M. D.; Yu, J.-Q. *J. Am. Chem. Soc.* **2016**, *138*, 9269-9276. (e) Shi, H.; Wang, P.; Suzuki, S.; Farmer, M. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2016**, *138*, 14876-14879.

(13) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. *Nat. Chem.* **2015**, *7*, 712-717.

(14) (a) Wan, L.; Dastbaravardeh, N.; Li, G.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 18056-18059. (b) Cheng, G.-J.; Yang, Y.-F.; Liu, P.; Chen, P.; Sun, T.-Y.; Li, G.; Zhang, X.; Houk, K. N.; Yu, J.-Q.; Wu, Y.-D. *J. Am. Chem. Soc.* **2014**, *136*, 894-897. (c) Yang, Y.-F.; Cheng, G.-J.; Liu, P.; Leow, D.; Sun, T.-Y.; Chen, P.; Zhang, X.; Yu, J.-Q.; Wu, Y.-D.; Houk, K. N.

J. Am. Chem. Soc. **2014**, *136*, 344-355. (d) Deng, Y.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2015**, *54*, 888-891.

(15) Lee, S.; Lee, H.; Tan, K. L. *J. Am. Chem. Soc.* **2013**, *135*, 18778-18781.

(16) (a) Bera, M.; Modak, A.; Patra, T.; Maji, A.; Maiti, D. *Org. Lett.* **2014**, *16*, 5760-5763. (b) Bera, M.; Maji, A.; Sahoo, S. K.; Maiti, D. *Angew. Chem. Int. Ed.* **2015**, *127*, 8635-8639. (c) Bera, M.; Sahoo, S. K.; Maiti, D. *ACS Catal.* **2016**, *6*, 3575-3579. (d) Maji, A.; Bhaskararao, B.; Singha, S.; Sunoj, R. B.; Maiti, D. *Chem. Sci.* **2016**, *7*, 3147-3153. (e) Patra, T.; Watile, R.; Agasti, S.; Naveen, T.; Maiti, D. *Chem. Commun.* **2016**, *52*, 2027-2030. (f) Modak, A.; Mondal, A.; Watile, R.; Mukherjee, S.; Maiti, D. *Chem. Commun.* **2016**, *52*, 13916-13919. (g) Maity, S.; Hoque, E.; Dhawa, U.; Maiti, D. *Chem. Commun.* **2016**, *52*, 14003-14006.

(17) (a) Li, S.; Ji, H.; Cai, L.; Li, G. *Chem. Sci.* **2015**, *6*, 5595-5600 (b) Li, S.; Cai, L.; Ji, H.; Yang, L.; Li, G. *Nat. Commun.* **2016**, *7*, 10443.

(18) (a) Chu, L.; Shang, M.; Tanaka, K.; Chen, Q.; Pissarnitski, N.; Streckfuss, E.; Yu, J.-Q. *ACS Cent. Sci.* **2015**, *1*, 394-399. (b) Bag, S.; Jayarajan, R.; Mondal, R.; Maiti, D. *Angew. Chem. Int. Ed.* **2017**, *56*, 3182-3186.

(19) See the experimental details for more information.

(20) Sharma, U.; Naveen, T.; Maji, A.; Manna, S.; Maiti, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 12669-12673.

(21) (a) Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. *J. Chern. Phys.* **1987**, *86*, 866-872. (b) Andrae, D.; Häußermann, U.; Dolg, M.; Stoll, H.; Preuß, H. *Theor. Chim. Acta.* **1990**, *77*, 123-141. (c) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215-241(d) Frisch, M. J. e. a. G., Revision D.01; Gaussian, Inc.: Wallingford, CT, 2013. (Full details of the computational methods are provided in the experimental section). **2013**.

(22) *Alternative possibilities were found to be more higher energy. See experimental details*.

(23) (a) Johnson, E. R.; Keinan, S.; Mori-Sánchez, P.; Contreras-García, J.; Cohen, A. J.; Yang, W. *J. Am. Chem. Soc.* **2010**, *132*, 6498-6506. (b) Contreras-García, J.; Johnson, E. R.; Keinan, S.; Chaudret, R.; Piquemal, J.-P.; Beratan, D. N.; Yang, W. *J. Chem. Theory Comput.* **2011**, *7*, 625-632.

(24) Zhanhui Yang, Y. Z., Jiaxi Xu *Synlett***2013**, *24*, 2165.

(25) (a) Keck, G. E.; Savin, K. A.; Weglarz, M. A. *J. Org. Chem.***1995**, *60*, 3194. (b) Blakemore, P. R. *J. Chem. Soc., Perkin Trans. 1***2002**, 2563.

(26) Wang, S.; Chen, Y.; Zhao, S.; Xu, X.; Liu, X.; Liu, B.-F.; Zhang, G. *Bioorg. Med. Chem.***2014**, *24*, 1766.

(27) Horiuchi, T.; Nagata, M.; Kitagawa, M.; Akahane, K.; Uoto, K. *Bioorg. Med. Chem.***2009**, *17*, 7850.

(28) Narender, T.; Reddy, K. P.; Madhur, G. *Synth. Commun.***2009**, *39*, 1949.

(29) Marchais-Oberwinkler, S.; Wetzel, M.; Ziegler, E.; Kruchten, P.; Werth, R.; Henn, C.; Hartmann, R. W.; Frotscher, M. *J. Med. Chem.***2011**, *54*, 534.

(30) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.***1997**, *62*, 1268.

(31) Shirakawa, E.; Kitabata, T.; Otsuka, H.; Tsuchimoto, T. *Tetrahedron***2005**, *61*, 9878.

(32)Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.;Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09 (Revision D. 01); Gaussian, Inc.: Wallingford, CT, 2013.

(33)Fukui, K. *Acc. Chem. Res.*, **1981**, 14, 363.

(34) Legault, C. Y. CYLview, 1.0b, Université de Sherbrooke, Quebec (Canada), **2009**, (http://www.cylview.org).

(35) Whitaker, D.; Bures, J.; Larrosa, I. *J. Am. Chem. Soc.***2016**, *138*, 8384.

(36) (a) Johnson, E. R.; Keinan, S.; Mori-Sánchez, P.; Contreras-García, J.; Cohen, A. J.; Yang, W. *J. Am. Chem. Soc.***2010**, *132*, 6498. (b) Contreras-García, J.; Johnson, E. R.; Keinan, S.; Chaudret, R.; Piquemal, J.-P.; Beratan, D. N.; Yang, W. *J. Chem. Theory Comput.***2011**, *7*, 625.

(37) Glendening, E. D. R., A.E.; Carpenter, J.E.; Weinhold, F. NBO Version 3.1, TCI, University of Wisconsin, Madison, 1998. **2013**.

Chapter 6

Rhodium Catalyzed Template-Assisted Distal *para*-C–H Olefination

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Rhodium Catalyzed Template-Assisted Distal *para*-C–H Olefination

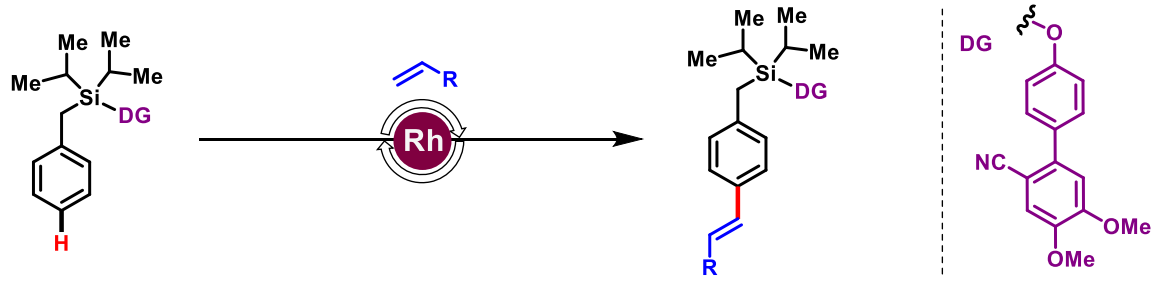
Abstract: Site selective C–H functionalization strategy relying on template assistance has been evolved in significant magnitude over the last few decades. Catalytic potential of transition metals has been utilized to perform a wide range of functionalization in this regard. Despite tremendous progress in directed *ortho*-C–H functionalization, selective distal*para*-C–H functionalizationremain elusive till 2015. Although, Pd-catalyzed DG assisted *para*-C–H functionalization is little explored, but utilization of other transition metals to perform such distal *para*-functionalization is yet to be addressed. Here in we disclosed a novel Rh-catalyzed directing group assisted *para*-C–Halkenylation method. A wide variety of substrates and olefin coupling partners are employed to carryout *para*-C–Holefination in a regioselctive fashion.

6.1. Introduction

The transformation of carbon-hydrogen (C–H) bonds into diverse classes of carbon-carbon (C–C) and carbon-heteroatom (C–X) bonds is a cornerstone of organic synthesis. There is intense interest in the discovery of new strategies for regioselective C–H functionalization.[1] A daunting challenge is imposed by the innate inertness of C−H bonds combined with the subtle reactivity differences among the C−H bonds of a given substrate. Directing group (DG)-assisted transition metal-catalyzed C−H activation has proven a successful strategy for regioselective C−H functionalizations in a general and predictable manner.[2] Most commonly coordination of a directing group to a transition metal to form a kinetically and thermodynamically stable 5- or 6-membered metallacycle is used to achieve *ortho*-C–H functionalization. In sharp contrast, distal C−H activation of *meta*[3] and *para*[4] sites is more challenging. In particular, *para*-C–H activation, which entails the formation of large macrocyclophane type metallacyclic intermediates, has remained elusive.[5] In a recent breakthrough, palladium-catalyzed systems employing a carefully designed 'D-shaped' directing group/linker template, based on a cyanobiphenyl motif, led to the first examples of distal *para*-C–H olefinations and acetoxylations.[5-6] Subsequent modifications of the 1st generation DGs through steric and electronic tuning led to 2nd generation DGs capable of effecting *para*-selective silylations[7] and acylations.[8]

Scheme 6.1. Rh-Catalyzed *para*-C–H Olefination

Present work: First example of Rh catalyzed *para*-C–H olefination



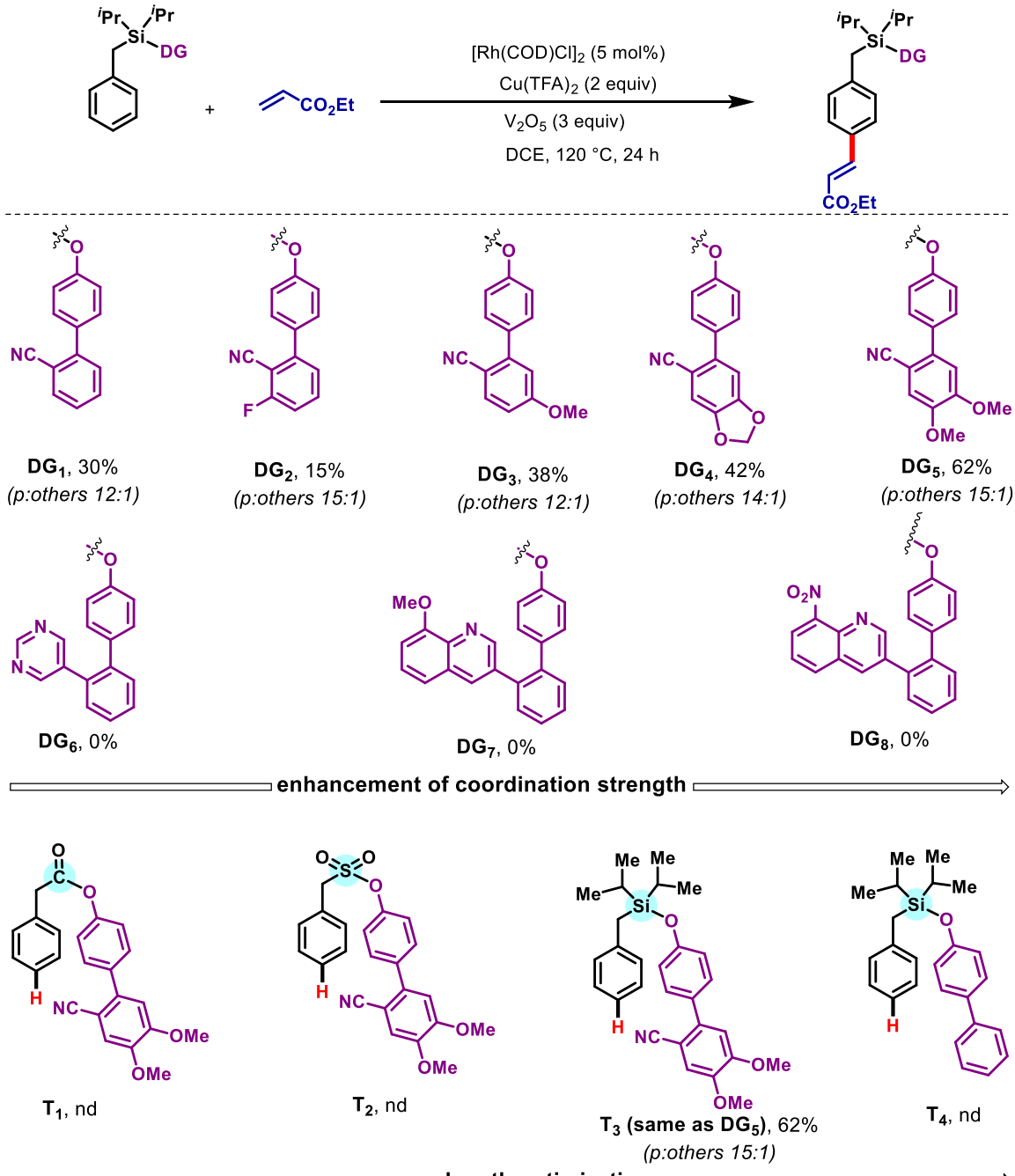
- *Introducing Rh in para-C–H activation*
- *Easily removable DG*
- *Diversification of products*

- *47 examples*
- *High yield and excellent selectivity*
- *DFT supported mechanism*

To the best of our knowledge, for template assisted *para*-selective functionalization palladium catalyst has been employed so far; albeit, other transition metals are also known to deliver *para*-selective functionalization relying on steric and electronic governance.[5-9] As part of our ongoing interest in C–H functionalization, we have now

translated this reaction into the realm of rhodium catalysis and we report here the first example of a Rh-catalyzed *para*-C–H olefination. Existing Rh-catalyzed approaches to C–H activation,[10] using Rh(I)/Rh(III) redox cycles, are complementary to the Pd(0)/Pd(II) or Pd(II)/Pd(IV) cycles prevalent in palladium catalysis.

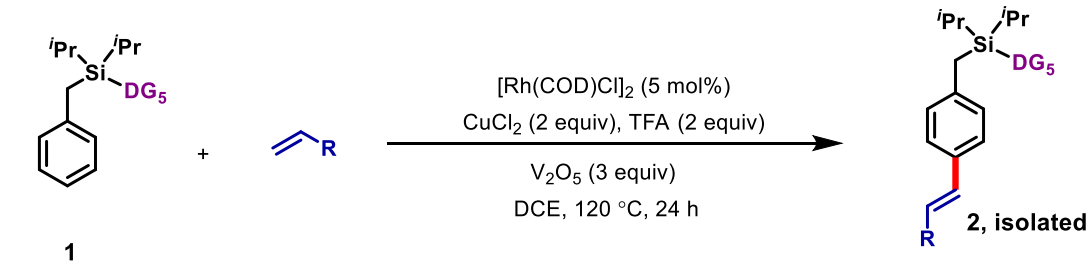
Scheme 6.2. Evaluation of Directing Groups[11]

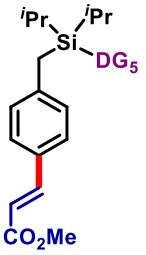


Yield and selectivity (*p:others)* determined by the ^{1}H NMR of crude reaction mixture using trimethoxybenzene (TMB) as internal standard

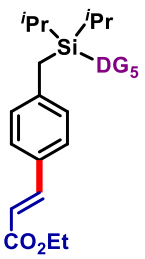
The use of Rh offers benefits over Pd: (a) in contrast to Pd catalysis, which usually requires super-stoichiometric quantities of silver salts, Rh catalysis can be performed with alternative, often cheaper, oxidants; (b) compared with Pd catalysis, which employ monoprotected amino acids (MPAA) as ligands, the different coordination environment of Rh is expected to provide advantageous opportunities for stereoselective synthesis; and (c) importantly, Rh-catalysis does not require use of hexafluoroisopropanol (HFIP), often unavoidable in Pd-catalysed distal C–H activation. With these thoughts in mind, we set about examining a Rh-catalyzed, DG-assisted distal *para*-C–H olefination, as shown in Scheme 6.1.

Table 6.1. Scope of Olefin Coupling Partners[11]

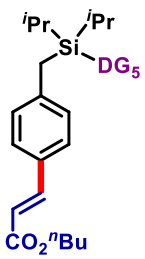




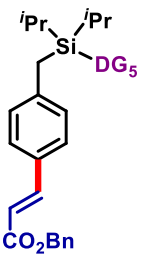
2a, 75% (12:1)



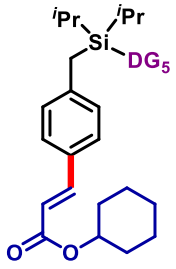
2b, 78% (15:1)



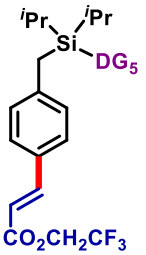
2c, 74% (7:1)



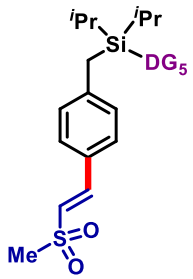
2d, 71% 10:1)



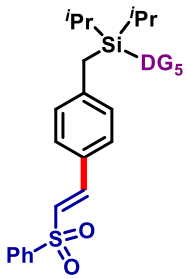
2e, 77% (9:1)



2f, 69% (8:1)



2g, 48% (15:1)

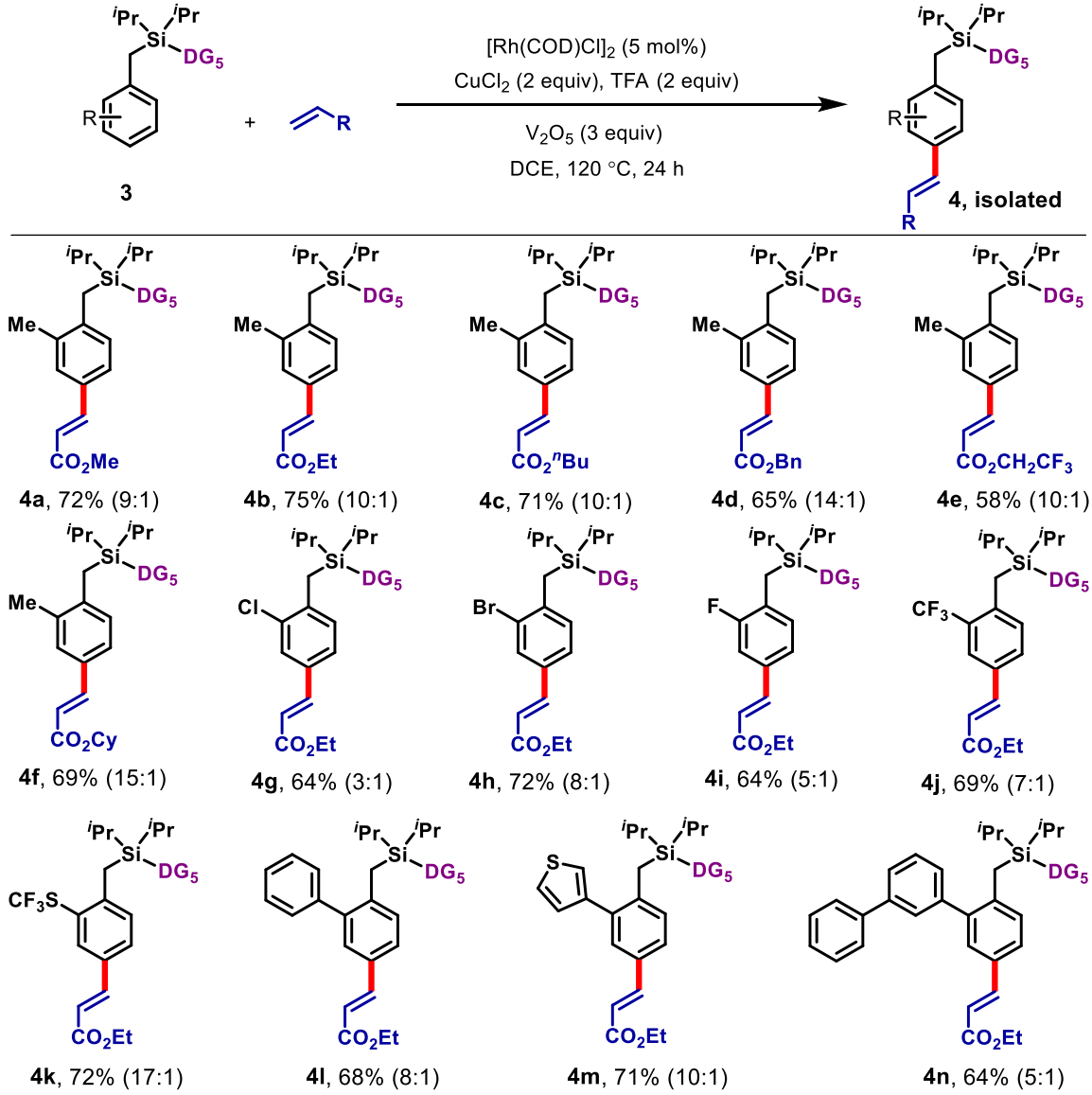


2h, 62% (15:1)

Ratio of *para:others* determined by the ^{1}H NMR of crude reaction mixture

6.2. Result and discussion

Table 6.2. Scope of Monosubstituted Toluene Derivatives[11]



Ratio of *para:others* determined by the ^{1}H NMR of crude reaction mixture

We commenced with the olefination of toluene scaffold **DG$_1$** by ethyl acrylate (Scheme 6.2). Our first attempt, using [Rh(COD)Cl]$_2$ (5 mol%) as catalyst, *N*-Ac-Gly-OH (10 mol%) as ligand, and AgOAc (3 equiv) as oxidant, was unsuccessful. However, use of copper trifluoroacetate [Cu(TFA)$_2$] as oxidant with V_2O_5 as a co-oxidant provided the desired *para*-olefinated product in 30% yield. Encouraged by this initial result, we examined how the outcome could be improved by modifying the DG (Scheme 6.2). Analysis of cyano-based DGs (**DG$_1$-DG$_5$**) showed that the presence of an electron-withdrawing fluorine substituent (**DG$_2$**) diminished the yield to 15% whereas an electron

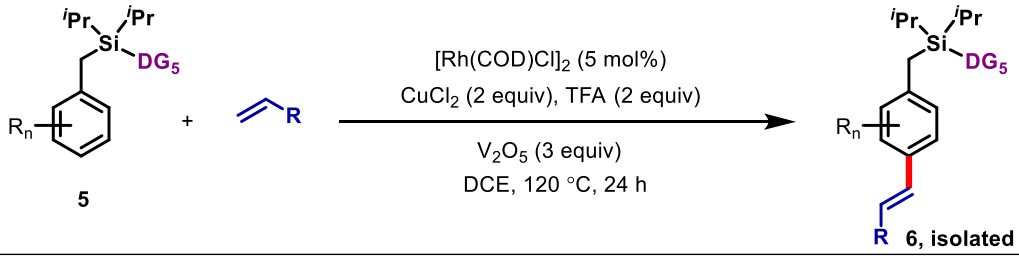
donating methoxy group (**DG$_3$**) elevated the yield to 38%. By further enhancing the electron richness of the DG, the piperonal derivative **DG$_4$** afforded a 42% yield of the olefinated product.

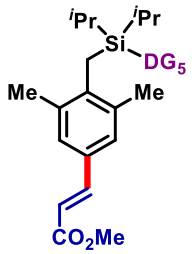
The dimethoxy-substituted **DG$_5$** gave a further improvement in yield, to 62%, with 15:1 *para* selectivity. The strong σ-donating DGs **DG$_6$**-**DG$_8$** failed to provide any of the desired olefinated products. A range of different tethers, containing carbonyl (**T$_1$**), sulfonyl (**T$_2$**), and silyl (**T$_3$**) linkers, were tested, as was a nitrile-free biphenyl template (**T$_4$**); only the silyl-based template **T$_3$** successfully delivered the desired olefinated product under the Rh-catalyzed conditions. These results indicate that the combination of sterically bulky silyl linker, nitrile group, and alkoxy groups present in **DG$_5$** is crucial for obtaining good yields of the *para*-olefinated product.

Using best-performing directing group **DG$_5$**, we optimized the reaction with respect to oxidants. A wide variety of silver and copper salts were tested.[11] In contrast to Pd-catalyzed olefinations, silver salts were found to be ineffectual in these Rh-catalyzed reactions, delivering the olefinated products in only trace amounts. Use of $Cu(TFA)_2$ as the oxidant in conjunction with V_2O_5 as a co-oxidant gave a 62% yield of olefinated product with excellent (15:1) *para* selectivity. Use of $CuCl_2$ provided a lower (30%) yield of product, but a combination of $CuCl_2$, V_2O_5 and trifluoroacetic acid (TFA) furnished the olefinated product in excellent (85%) yield, with 15:1 *para* selectivity.[11] Interestingly, in the absence of either V_2O_5 or TFA, the yield was significantly lower (40% and 30%, respectively). Other acidic additives such as acetic acid (AcOH), triflic acid (CF_3SO_3H) and pivalic acid (Piv-OH) failed to yield the *para*-olefinated product.[11]

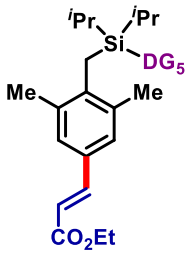
With optimized conditions in hand, we explored the scope of the reaction with respect to olefin (Table 6.1), arene (Table 6.2 and 6.3), and benzylic substituents (Table 6.4). With respect to the olefin coupling partner (Table 6.1), a range of acrylates reacted efficiently, including alkyl acrylates **2a**-**2d**, cyclohexyl acrylate **2e**, and trifluoroethyl acrylate **2f**. The olefinated products were obtained in excellent yields with synthetically useful *para*-selectivities ranging from 7:1 to 15:1. Apart from acrylates, vinyl sulfones including methyl vinyl sulfone (**2g**) and phenyl vinyl sulfone (**2h**) also gave the olefinated products, in 48% and 62% yields, respectively.

Table 6.3. Scope of Disubstituted Toluene Derivatives in Rh-Catalyzed *para*-C–H Olefination[11]

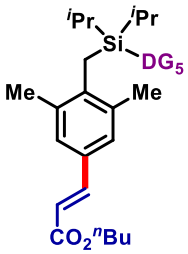




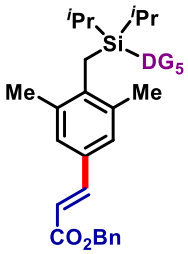
6a, 70% (>20:1)



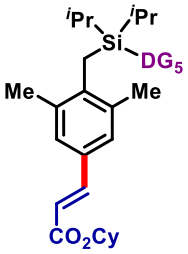
6b, 72% (>20:1)



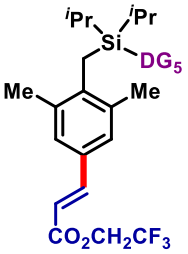
6c, 65% (>20:1)



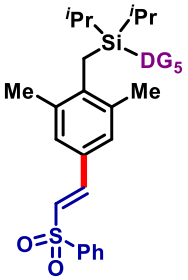
6d, 81% (>15:1)



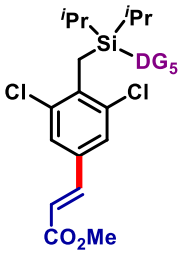
6e, 67% (>20:1)



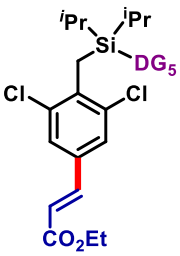
6f, 73% (>20:1)



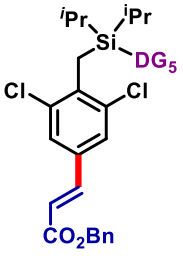
6g, 54% (>20:1)



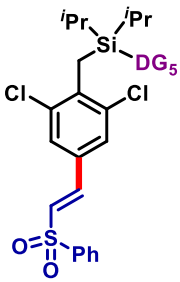
6h, 59% (>20:1)



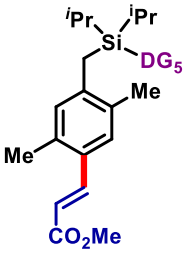
6i, 62% (>20:1)



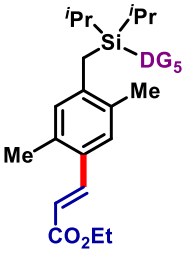
6j, 71% (>20:1)



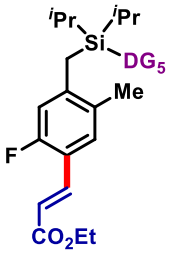
6k, 55% (>20:1)



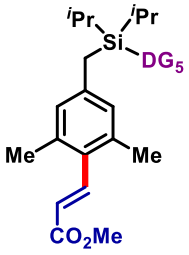
6l, 71% (>20:1)



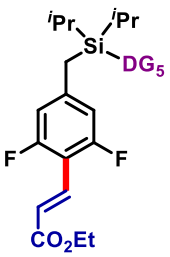
6m, 70% (>20:1)



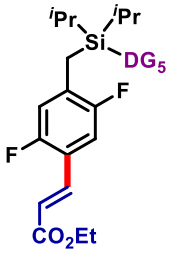
6n, 65% (>20:1)



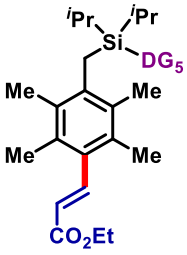
6o, 56%(15:1)



6p, 63% (>20:1)



6q, 61% (>20:1)

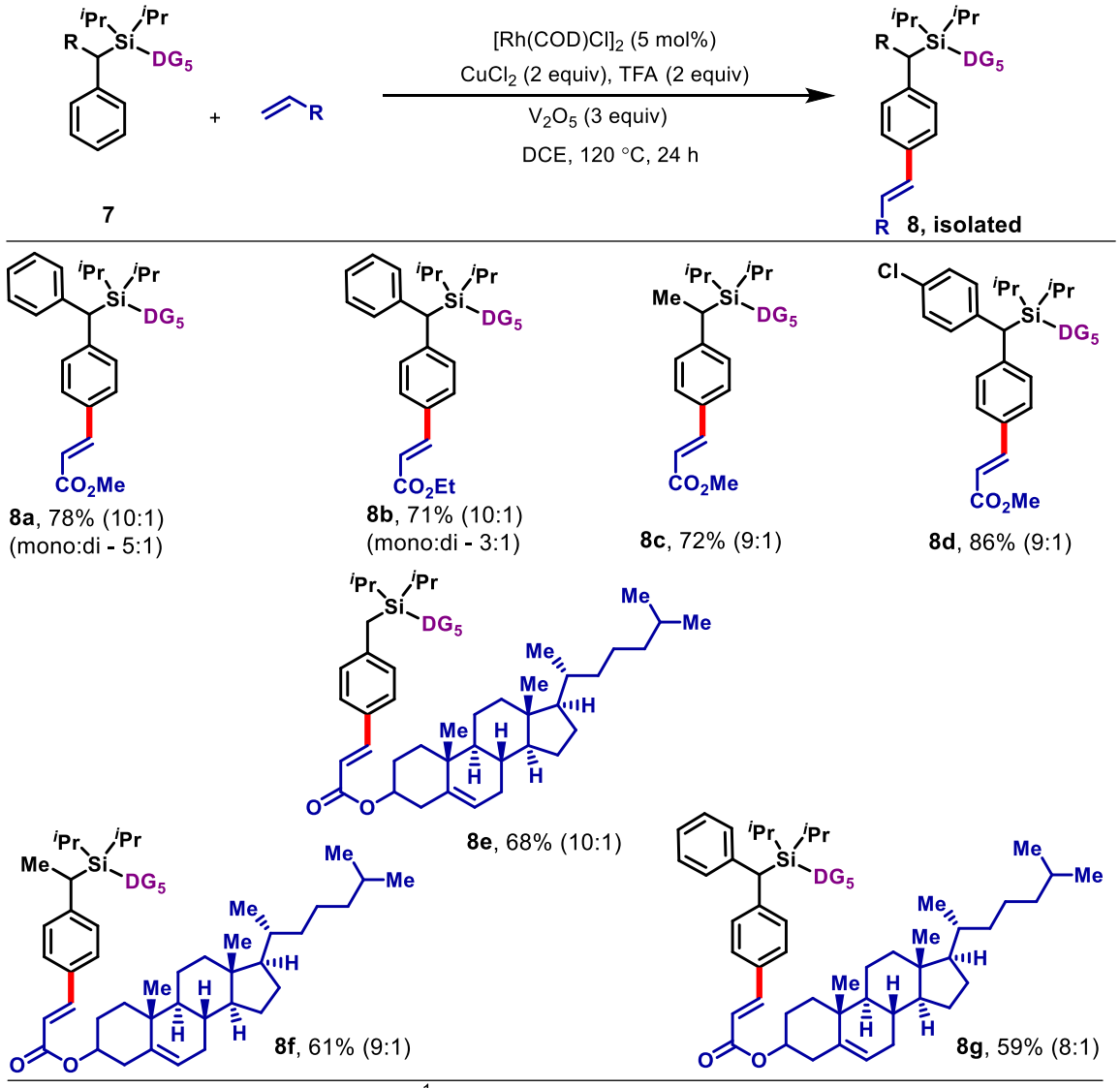


6r, 61%

Ratio of *para:others* determined by the ^{1}H NMR of crude reaction mixture

Next an array of substituted arenes was examined (Tables 6.2 and 6.3). For monosubstituted arenes, excellent yields and selectivities were obtained irrespective of the electronic nature of the substituent (Table 6.2). Both Electron-rich and Electron-deficient arenes were well tolerated, providing yields of up to 75% with upto 17:1 *para* selectivity.

Table 6.4. Scope of α-substituted Toluene Derivatives and More Complex Olefin Coupling Partners[11]

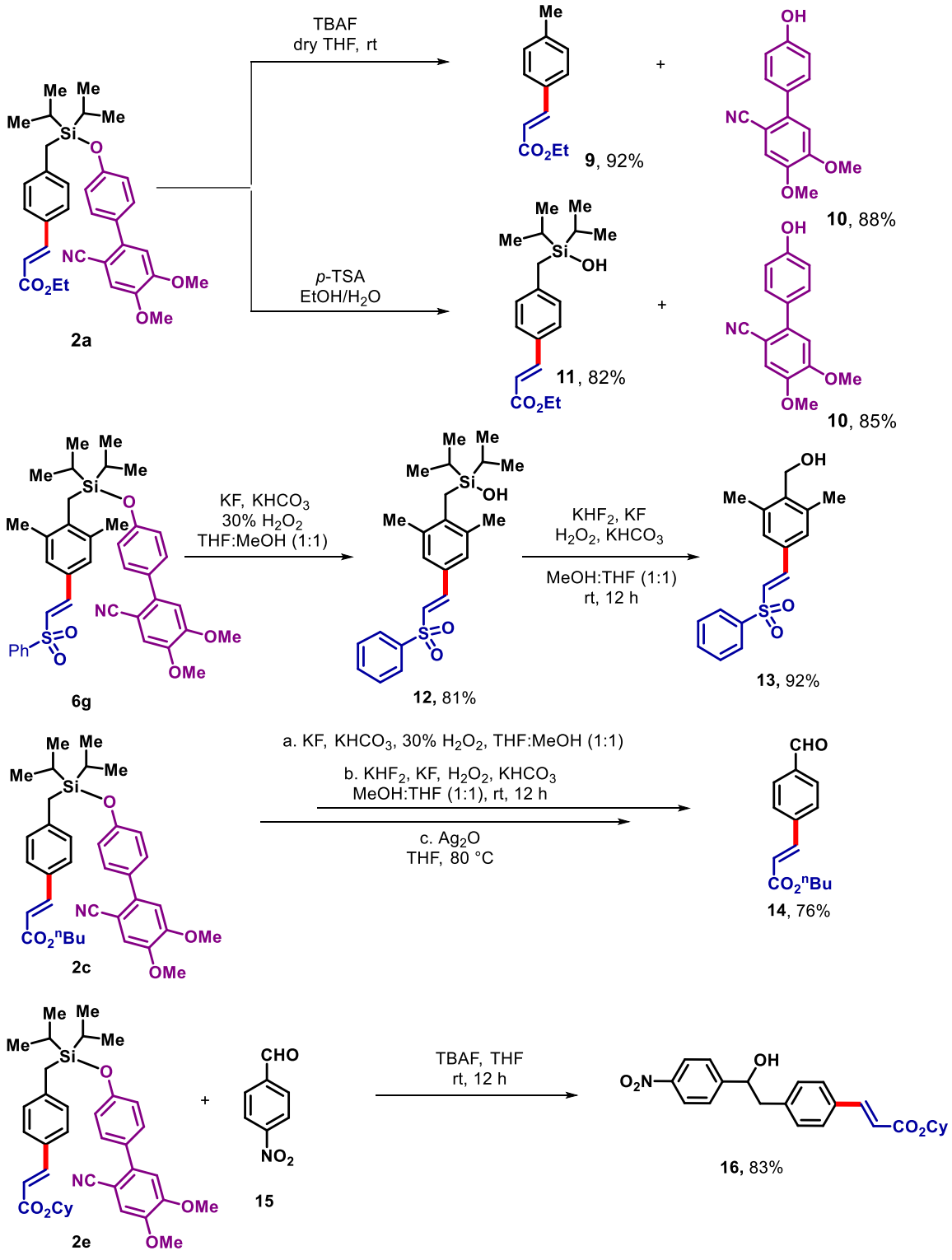


Ratio of *para:others* determined by the ^{1}H NMR of crude reaction mixture

Disubstituted arenes were also extremely well tolerated (Table 6.3). The reaction was successfully applied to a range of 2,2-, 2,5, 3,5 and 2,6-disubstituted toluenes containing methyl, fluoro, and/or chloro substituents (**6a-6q**). The selectivities of these reactions were generally higher than those observed for monosubstituted arenes, with all ≥15:1

para selective. Even a tetramethyl-substituted arene was tolerated, reacting with ethyl acrylate to give **6r** in 61% yield.

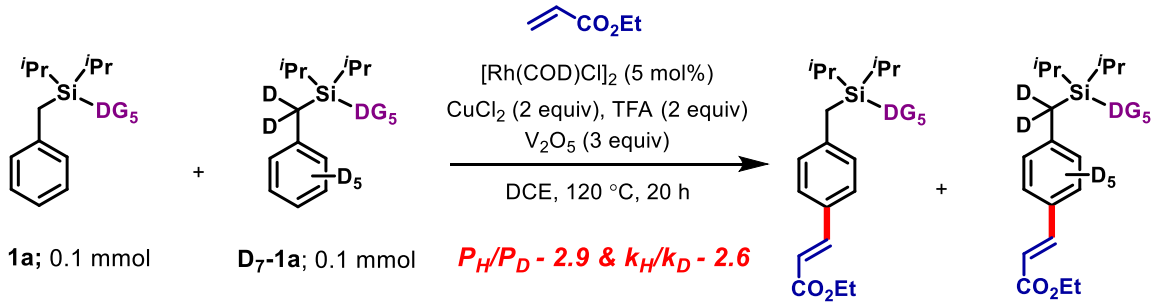
Scheme 6.3. Removal of the Directing Group and Diversification of the *para*-Olefinated Products[11]



The protocol is also applicable to α-substituted toluene derivatives (Table 6.4). Substrates bearing methyl, phenyl, or substituted phenyl substituents at the benzylic α-position reacted with methyl or ethyl acrylate to afford *para*-olefinated products **8a-8d**. The reaction also worked well with a more complex olefin coupling partner, namely, the acrylate derived from cholesterol, which furnished **8e-8g** in 59-68% yield.

The **DG5** directing group can be readily removed from the olefinated product in several ways (Scheme 6.3). Treatment of **2b** with TBAF furnished the desilylated product **9** in 92% yield and allowed the **DG5** alcohol **10** to be recovered in 88% yield for reutilization. Alternatively, treatment of **2b** with *p*-TSA generated the corresponding silanol derivative **11** in 82% yield along with an 85% recovery of the **DG5** alcohol. In principle, silanol **11** could be further used as a directing group for *ortho* functionalization. Therefore, the silyl-linked **DG5** represents a traceless directing group enabling access to multi-functionalized arenes. While the *para*-olefinated product **6g** has been treated with KF, $KHCO_3$ and H_2O_2, it produced the corresponding silanol (**12**). The silanol derivative was then employed under modified Tamao's oxidation condition to produce corresponding benzyl alcohol (**13**). Another derivative **2c** was treated under similar condition to provide the benzyl alcohol which subsequently oxidized to the corresponding benzaldehyde derivative (**14**) in 76% yield. The silyl based template can act as a nucleophile in presence of TBAF. To demonstrate that, 4-nitrobenzaldehyde (**15**) and 2-naphthaldehyde (**17**) was treated with *para*-olefinated product **2e** and **6c,** respectively to produce corresponding benzyl alcohols (**16** and **18** in 83% and 72%, respectively).

Scheme 6.4. Experiments with a Deuterium-Labeled Substrate[11]



A plausible catalytic cycle for the *para*-olefination is shown in Scheme 6.5. In this mechanism, the Rh(I) catalyst precursor is first oxidized to Rh(III). The main steps in

the cycle consist of C–H activation, migratory insertion, *β*-hydride elimination, and reductive elimination.[11]

Scheme 6.5. Possible Catalytic Cycle for *para*-Selective Rh-Catalyzed Olefination

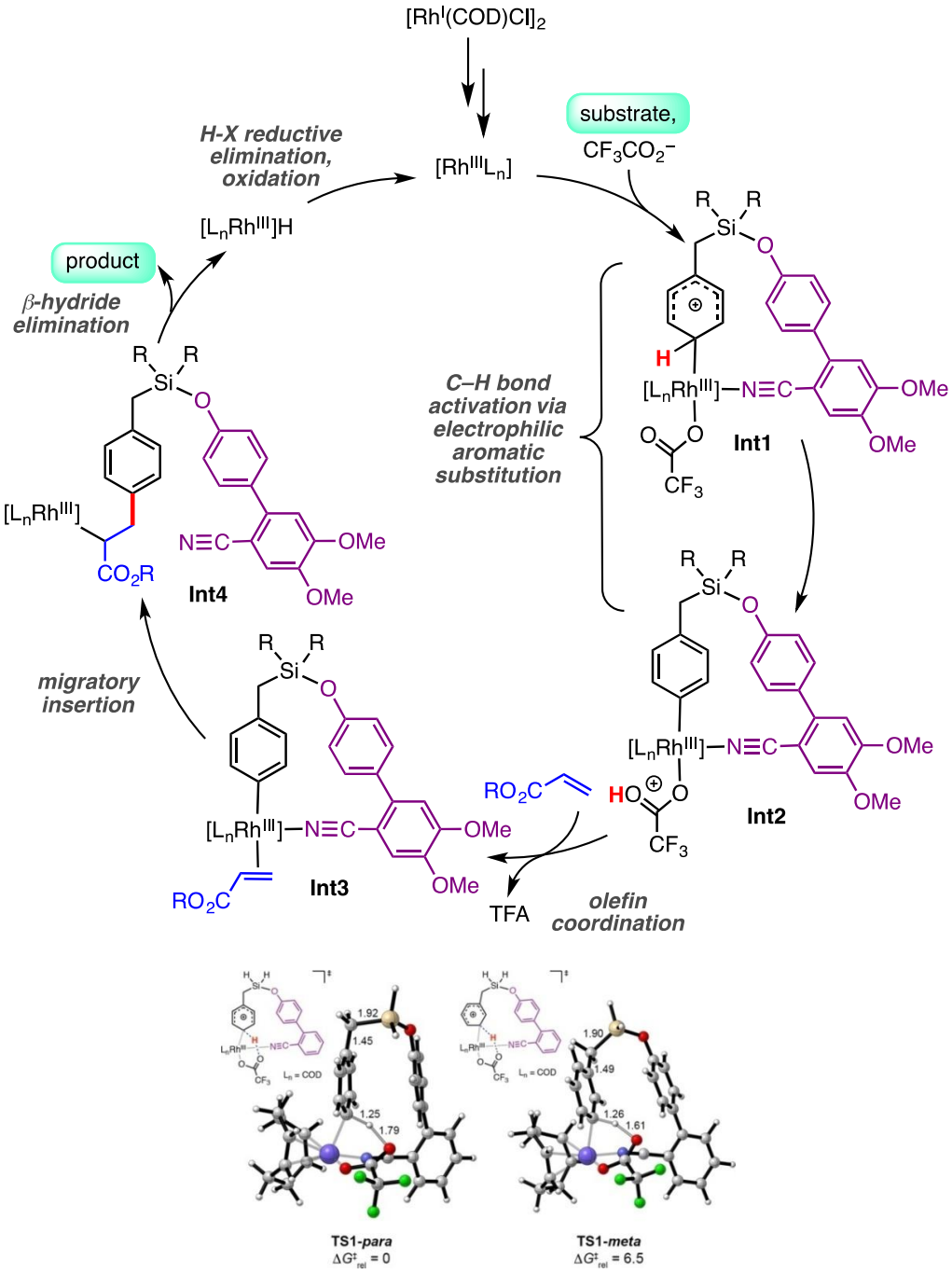


Figure 6.1. Transition states for Rh(III)-mediated *para*-C–H and *meta*-C–H bond activation, computed with M06/6-311+G(d,p)-SDD//M06/6-31G(d,p)-LANL2DZ in SMD dichloroethane. Distances in Å, $\Delta G^{\ddagger}_{rel}$ in kcal/mol.

We explored the C–H activation process using density functional theory (DFT) (Figure 6.1). Computations with the M06 functional using a model of **DG1** with trifluoroacetate anion as the base predicted that the C–H bond activation follows an electrophilic aromatic substitution pathway, with a distinct intermediate **Int1**, rather than a concerted metalation-deprotonation pathway.[10p, 12,] Transition structures for C–H bond breaking at the *para* and *meta* positions are shown in Figure 6.1.

The *para* transition state, **TS1-*para***, is 6.5 kcal/mol lower in energy than the *meta* transition state **TS1-*meta***. A fragment-based analysis of the TSs[12] reveals that the preference for *para*-C–H activation is due to a *β*-silicon effect. The interaction of the arene with Rh(III) endows it with arenium cation character, and this interaction is strengthened in **TS1-*para***because the C–Si bond (which lies perpendicular to the ring) stabilizes the positive charge through hyperconjugation. Computations also revealed the roles of the DG methoxy and nitrile substituents.[12] Incorporation of two methoxy groups on the DG activates the substrate toward C–H bond breaking, lowering the barrier by 1.6 kcal/mol relative to **TS1-*para***. A TS in which the nitrile is not bound to Rh was computed to be 23 kcal/mol higher in energy than **TS1-*para***, indicating that the coordination of the nitrile to Rh strongly stabilizes the C–H activation transition state.

6.3. Experimental details

6.3.1. General Consideration

6.3.1a. Reagent Information: Unless otherwise stated, all the reactions were carried out under aerobic condition in screw cap reaction tubes. All the solvents were bought from Aldrich/Alfa Aesar (India)/TCI (India)/Merck in a sure-seal bottle and were used as received. Chloro(1,5-cyclooctadiene)rhodium(I) dimer [Rh(COD)Cl_2] was bought from Ark Pharma.Cupric chloride ($CuCl_2$) and vanadium pentoxide (V_2O_5) is obtained from Sigma Aldrich. Palldiumacetate, used for study material preparation, was purchased from Alfa Aesar. All the benzyl chlorides and bromides were bought from Aldrich/Alfa Aesar (India)/TCI (India)/Spectrochem. For column chromatography, silica gel (100–200 mesh) from SRL Co. was used. A gradient elution using pet ether and ethyl acetate was performed based on Merck aluminium TLC sheets (silica gel 60F_{254}).

6.3.1b. Analytical Information: All isolated compounds are characterized by ^{1}H NMR, ^{13}C NMR spectroscopy. Copies of the ^{1}H NMR, ^{13}C NMR can be found in the supporting information. Nuclear magnetic resonance spectra were recorded either on a Bruker 500 or 400 MHz instrument. All ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.23 ppm), unless otherwise stated, and all were obtained with ^{1}H decoupling. High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.

6.3.1c. Description of Reaction Tube:

Pictorial description of reaction tube for *para*-olefination: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E); Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A).

6.3.2. Optimization of the reaction condition

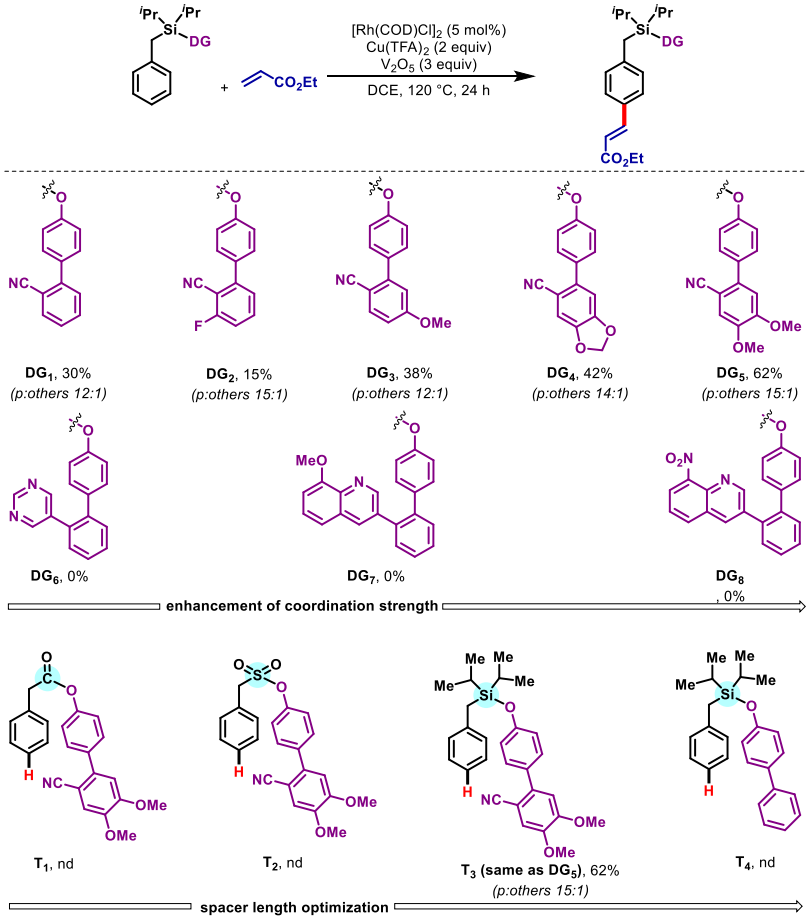
6.3.2.I. Optimization (yields and selectivity is determined by ^{1}H NMR of crude reaction mixture using trimethoxy benzene as internal standard)**:**

6.3.2.I.a: Initial finding

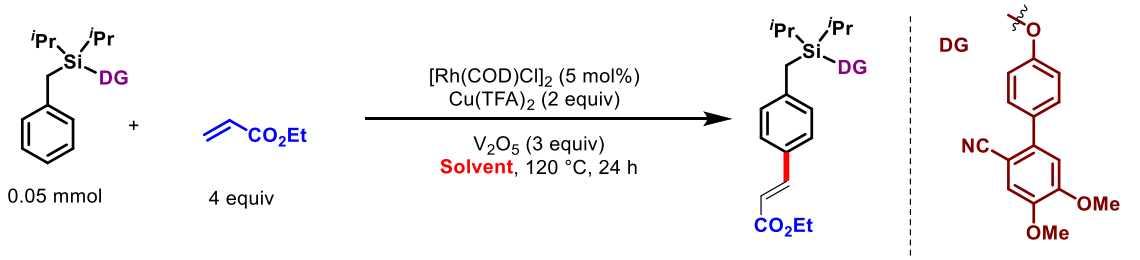
#	**Rh Salt**	**Oxidant**	**Ligand**	**Solvent**	**Yiled (%) (*p:others*)**
1	$[Rh(COD)Cl]_2$	AgOAc	*N*-Ac-Gly-OH	HFIP	nd
2	$[Rh(COD)Cl]_2$	Ag_2CO_3	*N*-Ac-Gly-OH	HFIP	nd
3	$[Rh(COD)Cl]_2$	AgOAc	*N*-Ac-Gly-OH	DCE	nd
4	$[Rh(COD)Cl]_2$	Ag_2CO_3	*N*-Ac-Gly-OH	DCE	nd
5	$[Rh(COD)Cl]_2$	$CuCl_2$	*N*-Ac-Gly-OH	DCE	nd
6	$[Rh(COD)Cl]_2$	CuCl	*N*-Ac-Gly-OH	DCE	nd

7	$[Rh(COD)Cl]_2$	$Cu(OAc)_2$	*N*-Ac-Gly-OH	DCE	nd
8	$[Rh(COD)Cl]_2$	Cu(TFA)	*N*-Ac-Gly-OH	DCE	trace
9	$[Rh(COD)Cl]_2$	Cu(TFA)	-	DCE	trace
10	**$[Rh(COD)Cl]_2$**	**Cu(TFA) & V_2O_5**	**-**	**DCE**	**30 (10:1)**
11	$[RhCp^*Cl]_2$	Cu(TFA)	-	DCE	trace

6.3.2.I.b: DG optimization

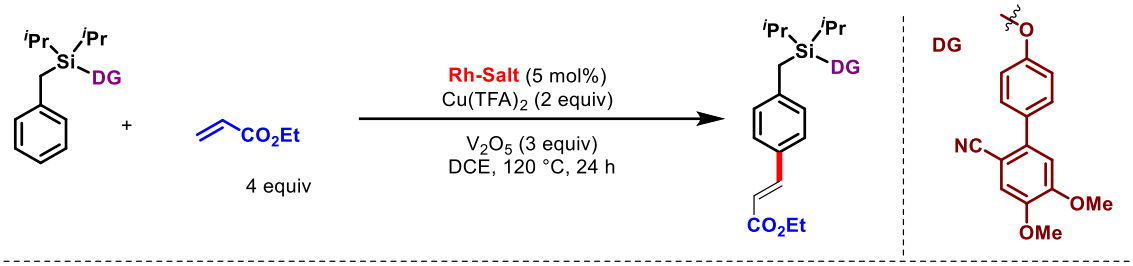


6.3.2.I.c: Solvent optimization



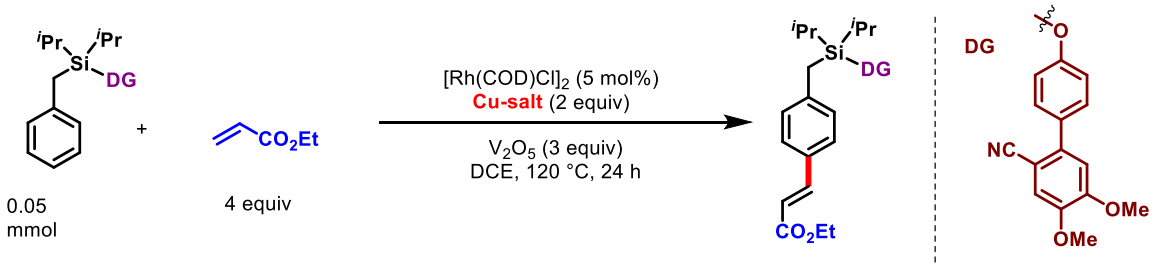
Sr. No.	Solvents	Yield (%)(*p:others*)
1	**DCE**	**62 (15:1)**
2	DCM	16 (14:1)
3	$CHCl_3$	trace
4	HFIP	nd
5	TFE	nd
6	TFT	nd
7	Toluene	nd
8	*m*-Xylene	nd
9	NMP	nd
10	TBME	nd
11	1,4-Dioxane	trace
12	THF	trace
13	MeOH	nd
14	^{i}PrOH	nd
15	Chlorobenzene	trace
16	TCP	7 (10:1)
17	MeCN	nd
18	PhCN	nd
19	DMF	nd
20	DMSO	nd
21	2-Me-THF	nd

6.3.2.I.d: Rh-Salt Optimization



#	Rh-Salt	Yield (%)(*p:others*)
1	No-Rh cat.	n.d.
2	$[RhCp^*Cl_2]_2$	20 (10:1)
3	**$[Rh(COD)Cl]_2$**	**62 (15:1)**
4	$Rh(OAc)_2$	trace
5	$Rh(PPh_3)_3Cl$	n.d.
6	[Rh(COD)(*S*)-BINAP]BF_4	trace

6.3.2.I.e: Cu-Salt Optimization

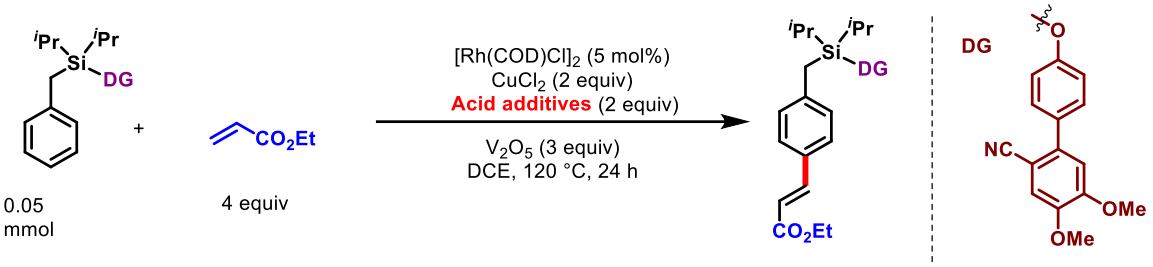


#	Cu-Salt	Yield (%)(*p:others*)
1	No Cu-Salt	20 (13:1)
2	$CuCl_2$	30 (10:1)
3	CuCl	trace
4	**$Cu(TFA)_2$**	**62 (15:1)**
5	$Cu(OAc)_2.H_2O$	24 (7:1)
6	Cu_2O	nd
7	$Cu(OTf)_2$	trace

8	$CuSO_4$	trace

Notably silver salts as oxidant remain ineffective to produce desired product

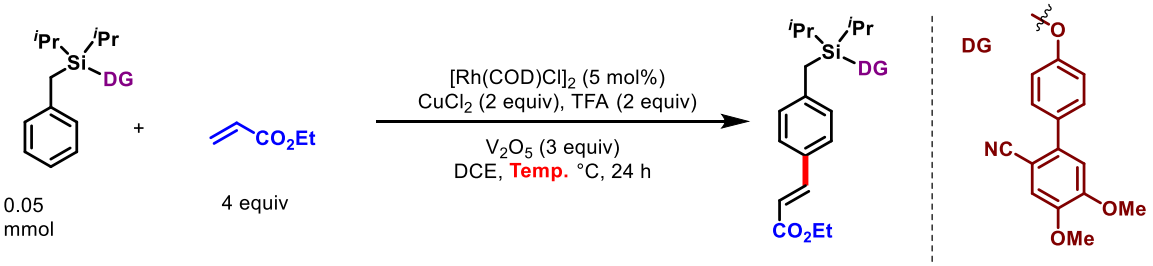
6.3.2.I.f: Cu-Salt and Acid Additive Optimization



#	Cu-Salt	Acid additives	Yield (%)(*p:others*)
1	$Cu(TFA)_2$	TFA	43 (8:1)
2	$Cu(TFA)_2$	AcOH	40 (10:1)
3	$Cu(TFA)_2$	Piv-OH	26 (12:1)
4	$Cu(TFA)_2$	Adamantane-1-carboxylic acid	55 (16:1)
5	**$CuCl_2$**	**TFA**	**85 (15:1)**
6	$CuCl_2$	AcOH	38 (11:1)
7	$CuCl_2$	Piv-OH	trace
8	$CuCl_2$	Adamantane-1-carboxylic acid	trace
9	$CuCl_2$	-	40
10	$CuCl_2$	TFA	30*

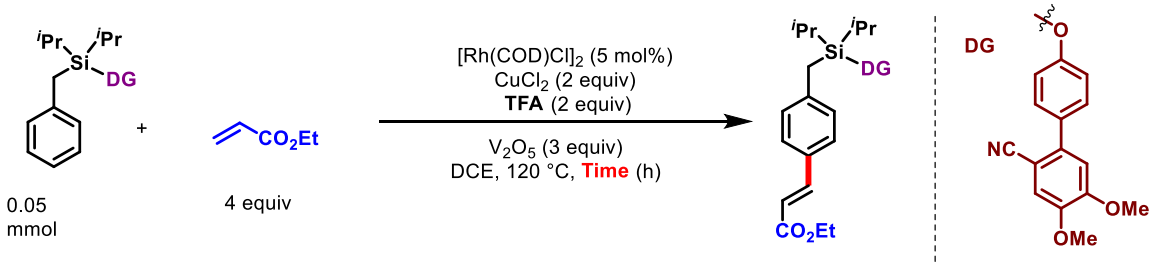
*the reaction was conducted in absence of V_2O_5

6.3.2.I.g: Temperature Optimization



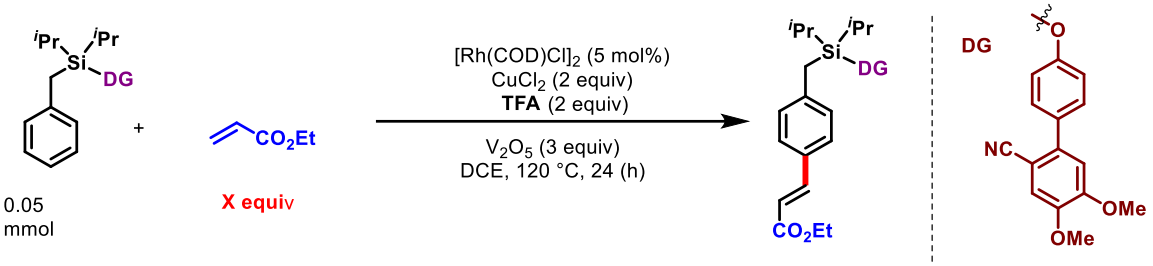
#	Temperature (°C)	Yield (%)(*p:others*)
1	50	n.d.
2	70	trace
3	80	20 (>20:1)
4	90	26 (18:1)
5	100	35 (16:1)
6	110	72 (15:1)
7	**120**	**85 (15:1)**
8	130	70 (7:1)

6.3.2.I.h: Time Optimization



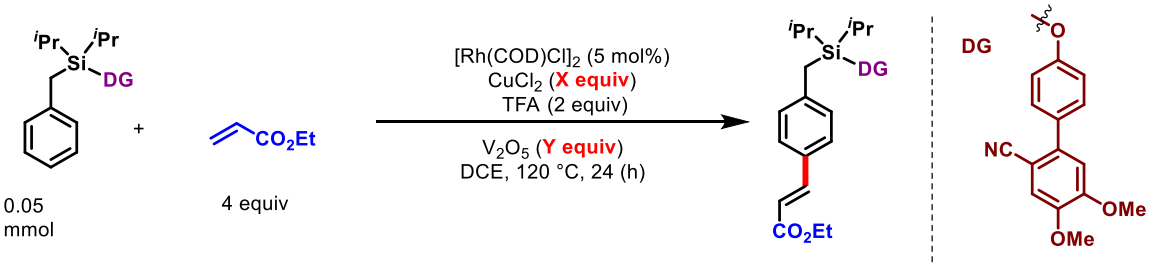
#	Time (h)	Yield (%)(*p:others*)
1	12	60 (18:1)
2	16	68 (18:1)
3	20	76 (16:1)
4	**24**	**85 (15:1)**
5	36	86 (12:1)
6	48	80 (10:1)

6.3.2.I.i: Olefin Amount Optimization



#	Olefin amount (equiv.)	Yield (%)(*p:others*)
1	1.0	34 (>20:1)
2	1.5	42 (>20:1)
3	2.0	58 (>16:1)
4	2.5	64 (15:1)
5	3.0	70 (15:1)
6	3.5	77 (15:1)
7	**4.0**	**85 (15:1)**
8	5	84 (10:1)

6.3.2.I.j: Amount of $CuCl_2$ and V_2O_5 Optimization



#	$CuCl_2$ amount (equiv.)	V_2O_5 amount (equiv.)	Yield (%)(*p:others*)
1	1.0	3.0	52 ((16:1)
2	1.5	3.0	72 (15:1)
3	**2.0**	**3.0**	**85 (15:1)**
4	2.5	3.0	70 (12:1)

5	3.0	3.0	62 (10:1)
6	2.0	1.0	68 (15:1)
7	2.0	1.5	72 (15:1)
8	2.0	2.0	74 (15:1)
9	2.0	2.5	80 (14:1)
10	2.0	3.5	84 (12:1)
11	2.0	4.0	85 (10:1)

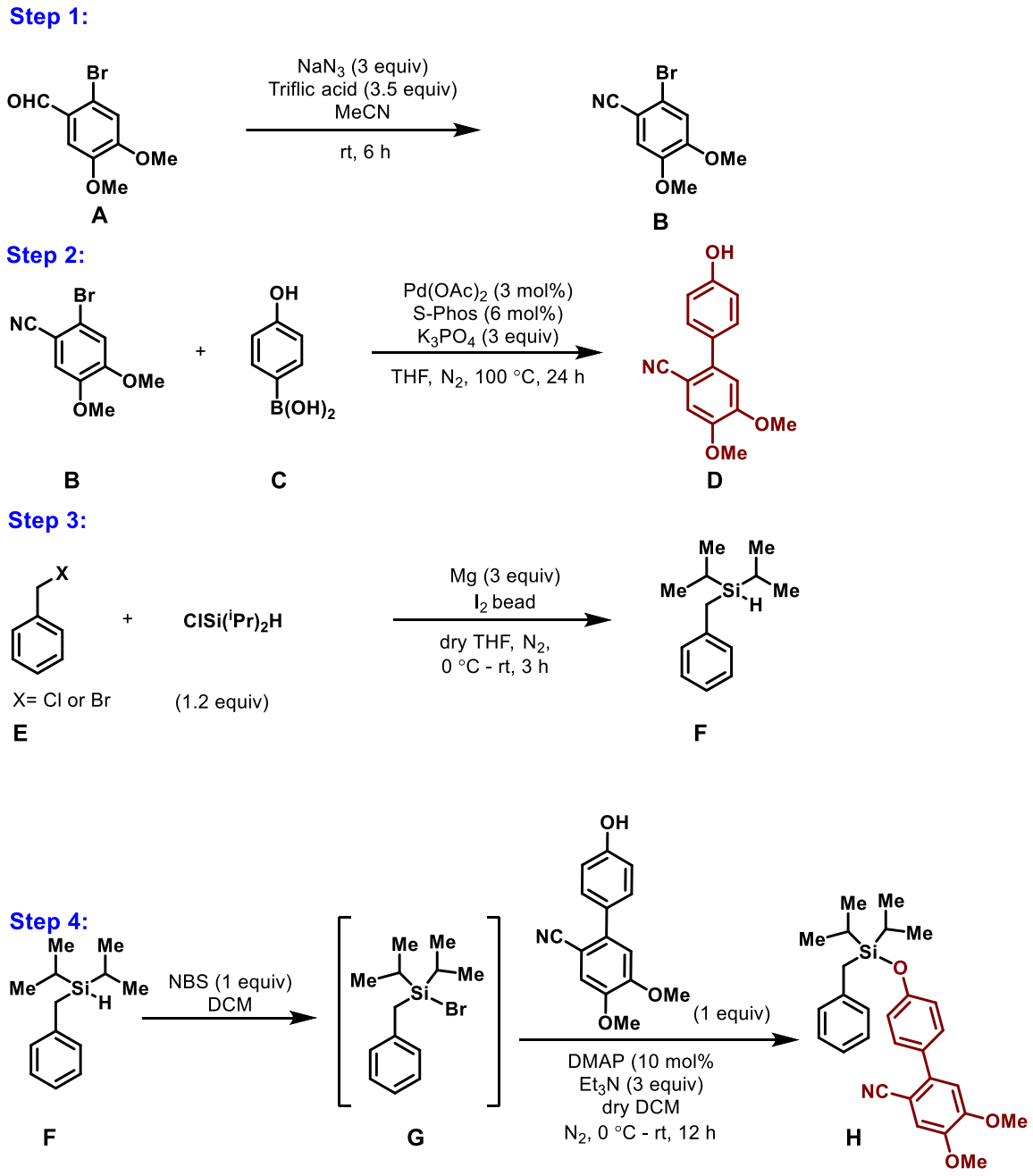
6.3.3. Optimization of the reaction condition

6.3.3.a. Procedure A: General Procedure for *para*-Olefination

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, substrate (0.2 mmol, 1.0 equiv.), [Rh(COD)Cl_2] (5mol%, 0.01mmol, 4.9 mg), $CuCl_2$ (0.4 mmol, 2 equiv, 53.6 mg), and V_2O_5 (0.6mmol, 3 equiv, 109.1 mg) were taken. Subsequently, DCE (2 mL), olefin (0.8mmol, 4.0 equiv) and trifluoroacetic acid (0.4 mmol, 2 equiv., 30.6 μL) was added. The reaction tube was capped tightly and placed on a preheated 120 °C oil bath. The reaction mixture was stirred vigorously for 24h. The reaction mixture was then diluted with DCM. 10 mL dilute ammonia solution was added to the reaction mixture; the organic part was extracted with DCM and dried over magnesium sulfate. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

6.3.3.b. Procedure B: Synthesis of directing group and substrates

Step-1: In an oven dried round bottom flask (250 mL), charged with stir-bar, aldehyde substrate (A) (20 mmol) and NaN_3 (3 equiv.) were taken. MeCN (60 mL) was added to it and stirred at room temperature for 15 mins. 3.5 equiv. of triflic acid was added to the mixture in portion with a plastic dropper. After the addition the reaction was allowed to stir at room temperature for 6 hour. Upon completion the reaction was diluted with ethyl acetate and the organic solvent was evaporated under reduced pressure. The solid residue was dissolved in ethyl acetate and washed with saturated $NaHCO_3$ solution (3 times). The organic fraction was then dried over anhydrous Na_2SO_4 and purified through column chromatography.[13] Quantitative conversion; white solid.



Step-2:[5] In an oven dried reaction tube, charged with stir-bar, Pd $(OAc)_2$ (3 mol%), S-phos (6 mol%), **B** (3 mmol), 4-hydroxyphenyl boronic acid (3.5 mmol) and K_3PO_4 (3 equiv.) were added. The reaction tubes were capped with Teflon cap and purged with N_2 using schlenk line set up. THF was added to the reaction mixture (5 mL) and submerged in a preheated 100 °C oil bath and allowed for vigorous stirring for 24 hours. After 24 hour, reaction mixture was allowed to cool and diluted with EtOAc and extracted with brine solution. The organic layer was dried over $Na_2SO_4$and concentrated by evaporation. Concentrated organic part was

purified by column chromatography. Pale yellow crystalline compound was isolated in 75% yields using ethyl acetate and petroleum ether mixture (20:80) as an eluent.

Step 3:[5] In a clean, oven-dried screw cap reaction tube, charged with magnetic stir–bar, activated magnesium turnings (15 mmol, 3 equiv.) and I_2 (one bead) were taken. The reaction tube was evacuated and back filled with nitrogen three times. Dry THF (15 mL) was added to it followed by di-isopropylchlorosilane (6 mmol, 1.2 equiv) in drop wise fashion and stirred at room temperature for 15 mins. A solution of benzyl chloride/bromide (5 mmol) in dry THF (10 mL) was added to the solution drop wise over a period of 15 minutes under ice cold condition. The mixture was vigorously stirred for 3 hours. Upon completion, the reaction mixture was quenched and washed with brine solution (3X10 mL). Aqueous part was washed thrice with ethyl acetate (3X20 mL). The combined organic layer was then dried over anhydrous Na_2SO_4. The compound (**F**) was purified using chromatography [silica gel (60-120/100-200 mesh size)] and petroleum-ether as the eluent. Benzyldiisopropylsilane (**F**) was collected and used for next step.

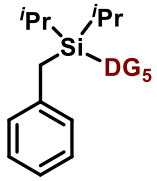
Step 4:[5] To an ice cold suspension of *N*-bromosuccinimide (5.0 mmol, 1.0 equiv) in 10 mL dry DCM, benzyldiisopropylsilane (**F**) (5.0 mmol, 1.0 equiv) was added drop wise under N_2 atmosphere. The reaction was kept on stirring for 3 hours at room temperature. In an another clean round bottomed flask, charged with magnetic stir–bar, 4'-hydroxy-4, 5-dimethoxybiphenyl-2-carbonitrile (**D**) (5 mmol, 1.0 equiv) and 4-dimethylaminopyridine (10 mol%) were taken. The set up was evacuated and refilled with N_2. 5 mL dry DCM was added to the mixture followed by triethylamine (15 mmol, 3.0 equiv) in a drop wise fashion. The entire solution was kept for stirring at room temperature until 4'-hydroxy-4,5-dimethoxybiphenyl-2-carbonitrile gets dissolved completely. The aforementioned solution of benzylbromodiisopropylsilane was added drop wise under the ice-cold condition. The reaction mixture was then stirred overnight at room temperature. Upon completion, the mixture was quenched with water (20 mL) and extracted with ethyl acetate thrice (3X30 mL). The organic layer was combined and dried over anhydrous Na_2SO_4. The final substrate (**H**) was purified through column chromatography using silica gel (60-120/100-200 mesh size) and petroleum-ether/ethyl acetate (90/10, v/v) as the eluent. Isolated compound turned into colourless crystalline solid upon drying. Yield: 73%

6.3.4. Characterization

6.3.4.a. Characterization of starting material

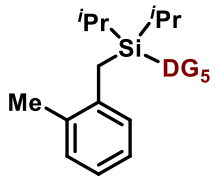
Characterization of starting materials (all the starting material and templates have been prepared by the previous literature report):[7]

4'-((benzyldiisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile:



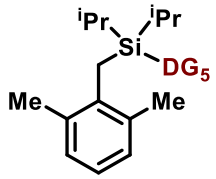
The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (90: 10)
Yield: 73%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 2H), 7.15 – 7.12 (m, 3H), 7.09 (t, *J* = 7.3 Hz, 1H), 6.90 (s, 1H), 6.87 (d, *J* = 8.5 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.40 (s, 2H), 1.23 (m, 2H), 1.05 (m, 12H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 156.2, 152.7, 148.2, 140.2, 138.7, 131.4, 130.0, 129.1, 128.5, 124.7, 120.2, 119.5, 115.2, 112.5, 102.3, 56.5, 56.3, 21.2, 17.6, 17.6, 13.1.

4'-((diisopropyl(2-methylbenzyl)silyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile:

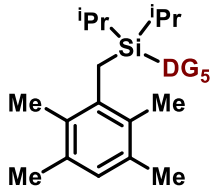


The substrate was prepared following the procedure B.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (90: 10)
Yield: 70%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 10 Hz, 2H), 7.14 (d, *J* = 5 Hz, 1H), 7.11 (s, 1H), 7.08 (t, *J* = 6.6 Hz, 2H), 7.01 (t, *J* = 5 Hz, 1H), 6.87 (s, 1H), 6.69 (d, *J* = 10 Hz, 2H), 3.96 – 3.93 (m, 3H), 3.92 (s, 3H), 2.37 (s, 2H), 2.30 (s, 3H), 1.31 – 1.24 (m, 2H), 1.08 (d, *J* = 10 Hz, 6H), 1.03 (d, *J* = 10 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 152.7, 148.1, 140.2, 137.4, 135.7, 131.2, 130.5, 129.9, 129.4, 125.9, 124.9, 119.9, 119.5, 115.2, 112.5, 102.2, 56.4, 56.3, 20.6, 18.1, 17.7, 17.5, 13.4.

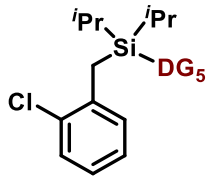
4'-(((2,6-dimethylbenzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether: ethyl acetate (90:10)
Yield: 72%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.13 (s, 1H), 7.00 – 6.90 (m, 3H), 6.88 (s, 1H), 6.73 (d, *J* = 8.4 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.40 (s, 2H), 2.33 (s, 6H), 1.28 – 1.21 (m, 2H), 1.11 – 1.08 (m, 6H), 1.11 – 1.08 (m, 6H), 0.99 – 0.96 (m, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 152.6, 148.1, 140.1, 136.5, 135.4, 131.1, 129.9, 128.2, 124.4, 119.8, 119.3, 115.1, 112.4, 102.2, 56.3, 56.2, 21.5, 17.6, 17.3, 15.8, 14.1.
4'-((diisopropyl(2,3,5,6-tetramethylbenzyl)silyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



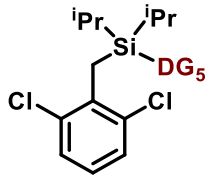
The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (90:10)
Yield: 72%
Physical appearance: Colourless solid
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 1H), 6.87 (s, 1H), 6.75 (s, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.48 (s, 2H), 2.20 (s, 6H), 2.18 (s, 6H), 1.28 – 1.19 (m, 2H), 1.11 – 1.07 (m, 6H), 1.00 – 0.95 (m, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1, 152.7, 148.1, 140.3, 136.2, 133.7, 131.6, 130.9, 129.8, 128.4, 119.8, 119.5, 115.2, 112.5, 102.3, 56.5, 56.3, 21.0, 17.7, 17.5, 17.1, 16.5, 14.2.
4'-(((2-chlorobenzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile:



The substrate was prepared following the procedure B.
Column material: 100-200 mesh silica

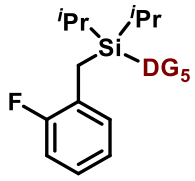
Eluent: pet ether:ethyl acetate (88:12)
Yield: 68%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 10 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 1H), 7.14 – 7.08 (m, 1H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.89 (s, 1H), 6.85 (d, *J* = 10 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 2.56 (s, 2H), 1.33 – 1.26 (m, 2H), 1.09 – 1.03 (m, 12H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 152.7, 148.1, 140.1, 137.1, 133.2, 131.3, 130.7, 129.9, 129.6, 126.7, 126.1, 119.9, 119.4, 115.1, 112.4, 102.2, 56.3, 56.2, 18.5, 17.5, 17.4, 13.5.

4'-(((2,6-dichlorobenzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



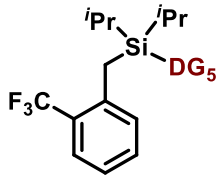
The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (85:15)
Yield: 68%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 10 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 1H), 6.94 (t, *J* = 8.0 Hz, 1H), 6.87 (s, 1H), 6.80 (d, *J* = 10 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.75 (s, 2H), 1.41 – 1.33 (m, 2H), 1.11 (d, *J* = 10 Hz 6H), 1.06 (d, *J* = 10 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 152.7, 148.1, 140.3, 136.8, 134.5, 131.1, 129.8, 128.2, 126.3, 119.8, 119.5, 115.2, 112.5, 102.3, 56.5, 56.3, 18.0, 17.6, 17.5, 14.4.

4'-(((2-fluorobenzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile:



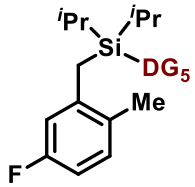
The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (88:12)
Yield: 68%
Physical appearance: Colourless solid
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 12 Hz, 2H), 7.19 – 7.11 (m, 2H), 7.09 – 7.03 (m, 1H), 7.01 – 6.94 (m, 2H), 6.90 (s, 1H), 6.87 (d, , *J* = 10 Hz, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 2.38 (s, 2H), 1.29 – 1.21 (m, 2H), 1.10 – 1.02 (m, *J* = 7.3 Hz, 12H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5 (d, *J* = 243.41), 156.0, 152.6, 148.1, 140.1, 131.3, 131.1 (d, *J* = 4.04), 131.1, 129.9, 126.2 (d, *J* = 8.08), 125.8(d, *J* = 17.17), 123.9 (d, *J* = 3.03), 120.1, 119.4, 115.4, 115.1, 115.1, 112.4, 102.2, 56.3, 56.2, 17.4, 17.4, 13.4, 13.3, 13.2.

4'-((diisopropyl(2-(trifluoromethyl)benzyl)silyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



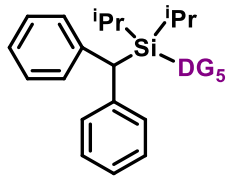
The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (85:15)
Yield: 68%
Physical appearance: White solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.36 (m, 4H), 7.21 – 7.16 (m, 1H), 7.13 (s, 1H), 6.89 (s, 1H), 6.86 (d, *J* = 5.0 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.59 (s, 2H), 1.32 – 1.25 (m, 2H), 1.07 – 1.03 (m, 6H), 0.99 – 0.96 (m, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 152.7, 148.2, 140.2, 138.4, 131.6, 131.5, 130.1, 127.9 (q, *J* = 28.98 Hz), 126.4 (q, *J* = 5.88 Hz), 126.1, 124.8, 123.9, 120.1, 119.5, 115.2, 112.5, 102.3, 56.5, 56.3, 17.9, 17.6, 17.4, 13.4.

4'-(((5-fluoro-2-methylbenzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (85:15)
Yield: 69%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 5.7 Hz, 2H), 7.12 (s, 1H), 7.01 (t, *J* = 8.1, 6.4 Hz, 1H), 6.88 (s, 1H), 6.84 (dd, *J* = 10.2, 2.7 Hz, 1H), 6.75 – 6.67 (m, 3H), 3.94 (s, 3H), 3.92 (s, 3H), 2.34 (s, 2H), 2.24 (s, 3H), 1.32 – 1.24 (m, 2H), 1.09 (d, *J* = 7.5 Hz, 6H), 1.04 (d, *J* = 7.4 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ 161.3 (d, *J* = 243.18), 155.8, 152.7, 148.1, 140.1, 139.6 (d, *J* = 7.56), 131.5, 131.4, 131.4, 131.2 (d, *J* = 2.52), 129.9, 119.9, 119.4, 115.7 (d, *J* = 21.42), 115.2, 112.5, 111.4 (d, *J* = 20.16), 102.3, 56.4, 56.3, 19.8, 18.5, 17.7, 17.5, 13.4.

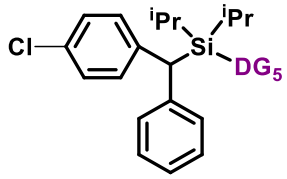
4'-((benzhydryldiisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (80:10)
Yield: 71%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.48 (m, 4H), 7.41 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.38 (d, *J* = 10.0, 2H), 7.30 – 7.26 (m, 3H), 7.16 (m, 2H), 7.14 (s, 1H), 6.90 (s, 1H), 6.86 (d, *J* = 10.0, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 3.80 (s, 1H), 1.31 – 1.24 (m, 2H), 0.94 – 0.90 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1, 152.7, 148.2, 142.7, 142.2, 140.2, 131.4, 130.1, 129.7, 129.2, 128.7, 128.7, 125.8, 125.6, 120.1, 119.5, 115.2, 112.5, 102.4, 56.5, 56.4, 42.9, 18.1, 17.8, 17.8, 17.7, 13.8, 13.3.

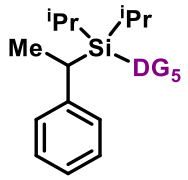
4'-((((4-chlorophenyl)(phenyl)methyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (80:10)
Yield: 65%
Physical appearance: Colourless solid
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.38 (m, 6H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.14 (s, 1H), 6.90 (s, 1H), 6.87 (d, 10.0 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 3.77 (s, 1H), 1.31 – 1.24 (m, 2H), 0.97 – 0.87 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 152.7, 148.2, 141.7, 140.9, 140.1, 131.6, 130.9, 130.1, 129.5, 128.8, 128.7, 126.1, 119.9, 119.5, 115.2, 112.5, 102.4, 56.5, 56.3, 42.1, 18.1, 18.1, 17.8, 17.8, 13.8, 13.8.

4'-((diisopropyl(1-phenylethyl)silyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



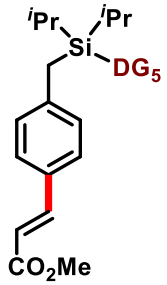
The substrate was prepared following the procedure **B**.
Column material: 100-200 mesh silica
Eluent: pet ether:ethyl acetate (80:10)
Yield: 75%
Physical appearance: Colourless solid

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, 10.0 Hz, 2H), 7.29 – 7.21 (m, 5H), 7.14 (s, 1H), 6.91 (s, 1H), 6.89 (d, 10.0 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.63 (q, *J* = 10.0 Hz, 1H), 1.55 (d, *J* = 7.6 Hz, 2H), 1.38 – 1.32 (m, 1H), 1.25 – 1.17 (m, 1H), 1.11 – 1.00 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 152.7, 148.1, 144.9, 140.2, 131.2, 129.9, 128.4, 128.4, 128.2, 127.6, 125.1, 124.8, 120.1, 119.5, 115.1, 112.5, 102.2, 77.5, 77.2, 76.9, 56.4, 56.3, 27.6, 18.1, 18.0, 17.8, 17.8, 17.6, 16.4, 13.1, 12.9.

6.3.4.b. Characterization of *para*-olefinated products:

2a. methyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4- yl)oxy)diisopropyl-silyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 75% (*para:others* = 12:1)

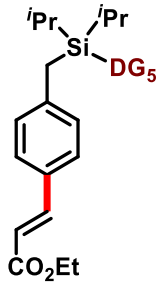
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 16.0 Hz, 1H), 7.38 (dt, *J* = 4.9, 2.8 Hz, 4H), 7.15 – 7.12 (m, 3H), 6.91 – 6.84 (m, 3H), 6.36 (d, 1H), 3.95 (d, *J* = 3.6 Hz, 3H), 3.92 (s, 3H), 3.78 (s, 3H), 2.42 (s, 2H), 1.26 – 1.18 (m, 3H), 1.05 (dd, *J* = 7.4, 2.6 Hz, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 156.0, 152.7, 148.2, 145.1, 142.0, 140.1, 131.5, 130.9, 130.1, 129.5, 128.4, 120.1, 119.5, 116.4, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 56.4, 56.3, 51.8, 21.6, 17.6, 17.6, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{32}H_{37}NNaO_5Si$ 566.2333: found: 566.2329.

2b. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)-methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 78% (*para:others* = 15:1)

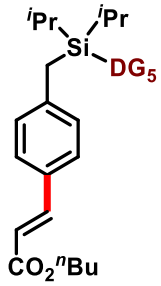
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, CDCl3) δ 7.63 (d, 1H), 7.41 – 7.36 (m, 4H), 7.16 – 7.12 (m, *J* = 4.1 Hz, 3H), 6.89 (s, 1H), 6.86 (d, 2H), 6.36 (d, 1H), 4.24 (q, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.43 (s, 2H), 1.32 (t, *J* = 9.5, 4.8 Hz, 3H), 1.25 – 1.20 (m, *J* = 14.7, 7.3 Hz, 2H), 1.06 (d, *J* = 2.7 Hz, 6H), 1.04 (d, *J* = 2.6 Hz, 6H).

^{13}C NMR (126 MHz, CDCl3) δ 167.4, 156.0, 152.7, 148.2, 144.8, 141.9, 140.1, 131.5, 131.0, 130.1, 129.5, 128.4, 120.1, 119.5, 116.9, 115.2, 112.5, 102.3, 60.5, 56.5, 56.3, 21.6, 17.6, 17.6, 14.5, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{39}NNaO_5Si$ 580.2490: found: 580.2485.

2c. butyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4yl)oxy)diisopropylsil-yl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure Ain 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 74% (*para:others* = 7:1)

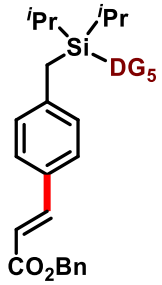
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 1H), 7.39 (dt, *J* = 8.5, 2.7 Hz, 4H), 7.13 (d, *J* = 7.7 Hz, 3H), 6.90 – 6.83 (m, 3H), 6.39 – 6.31 (m, 1H), 4.21 – 4.15 (m, 2H), 3.94 (dd, *J* = 13.3, 12.6 Hz, 7H), 2.41 (d, *J* = 8.2 Hz, 2H), 1.71 – 1.64 (m, 3H), 1.42 (dq, *J* = 14.5, 7.3 Hz, 2H), 1.25 – 1.19 (m, 2H), 1.05 (dd, *J* = 7.4, 2.5 Hz, 14H), 0.95 (td, *J* = 7.4, 4.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 156.0, 152.7, 148.2, 144.8, 141.9, 140.1, 131.5, 131.0, 130.1, 129.5, 128.3, 120.1, 120.1, 119.4, 116.9, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 64.4, 56.4, 56.3, 30.9, 21.6, 19.4, 17.6, 17.5, 13.9, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{35}H_{43}NNaO_5Si$ 608.2803: found: 608.2796.

2d. benzyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 71% (*para:others* = 10:1)

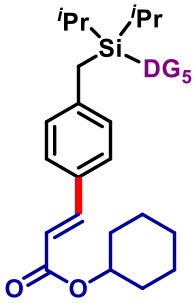
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 16.0 Hz, 1H), 7.43 – 7.36 (m, 8H), 7.35 – 7.31 (m, *J* = 7.0, 3.6, 1.4 Hz, 1H), 7.16 – 7.12 (m, *J* = 7.8 Hz, 3H), 6.90 – 6.85 (m, 3H), 6.42 (d, 1H), 5.24 (s, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.43 (s, 2H), 1.26 – 1.19 (m, *J* = 14.1, 6.6 Hz, 2H), 1.06 (d, *J* = 2.5 Hz, 6H), 1.04 (d, *J* = 2.4 Hz, 6H).

^{13}C NMR (126 MHz, CDCl3) δ 167.2, 155.9, 152.7, 148.2, 145.4, 142.1, 140.1, 136.4, 131.5, 130.9, 130.1, 129.5, 128.7, 128.4, 128.4, 128.3, 120.1, 119.5, 116.4, 115.2, 112.5, 102.3, 66.4, 56.4, 56.3, 21.6, 17.6, 17.5, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{38}H_{41}NNaO_5Si$ 642.2720: found: 642.2720.

2e. cyclohexyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 77% (*para:others* = 9:1)

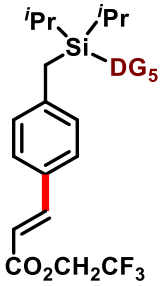
Physical appearance: Colourless viscous compound

^{1}H NMR(500 MHz, $CDCl_3$) δ 8.22 (d, J = 15.9 Hz, 1H), 8.01 – 7.96 (m, 4H), 7.75 – 7.72 (m, 3H), 7.49 (s, 1H), 7.46 (d, J = 10.0 Hz, 2H), 6.96 (d, J = 15.0 Hz, 1H), 5.50 – 5.44 (m, 1H), 4.55 (s, 3H), 4.52 (s, 3H), 3.02 (s, 2H), 2.55 – 2.46 (m, 2H), 2.39 – 2.32 (m, 2H), 2.18 – 2.13 (m, 1H), 2.11 – 1.95 (m, 5H), 1.85 – 1.78 (m, 2H), 1.66 – 1.63 (m, 12H).

^{13}C NMR(126 MHz, $CDCl_3$) δ 166.9, 156.0, 152.7, 148.2, 144.5, 141.8, 140.1, 131.5, 131.1, 130.1, 129.5, 128.3, 120.1, 119.4, 117.5, 115.2, 112.5, 102.4, 77.5, 77.2, 76.9, 72.7, 56.5, 56.3, 31.9, 25.6, 23.9, 21.6, 17.6, 17.6, 13.1 .

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{37}H_{45}NNaO_5Si$ 634.2959: found: 634.2957.

2f. 2,2,2-trifluoroethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)-diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 69% (*para:others* = 8:1)

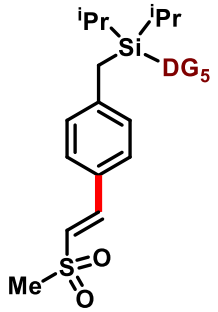
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, 1H), 7.40 (m, 4H), 7.15 (dd, *J* = 12.3, 5.5 Hz, 3H), 6.91 – 6.84 (m, 4H), 6.41 (d, 1H), 4.57 (q, *J* = 8.5 Hz, 2H), 3.95 (s, 3H), 3.93 (s, 3H), 2.44 (s, 1H), 1.25 – 1.20 (m, *J* = 14.9, 7.5 Hz, 3H), 1.07 – 1.04 (m, *J* = 7.4, 1.6 Hz, 13H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 156.0, 152.8, 148.3, 147.4, 142.9, 140.1, 131.6, 130.4, 130.1, 129.6, 128.7, 120.1, 119.5, 115.2, 114.5, 112.5, 102.4, 77.5, 77.2, 76.9, 56.5, 56.3, 21.8, 17.6, 17.6, 13.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{36}F_3NNaO_5Si$ 634.2207: found: 634.2209.

2g. (*E*)-4'-((diisopropyl(4-(2-(methylsulfonyl)vinyl)benzyl)silyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile:



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (82:18)

Yield: 48% (*para:others* = 15:1)

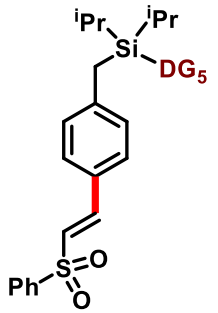
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 15.4 Hz, 1H), 7.37 (t, *J* = 8.3 Hz, 4H), 7.17 – 7.12 (m, 3H), 6.89 (s, 1H), 6.86 – 6.82 (m, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.01 (s, 3H), 2.44 (s, 2H), 1.22 (mzz, *J* = 14.8, 6.8 Hz, 4H), 1.07 – 1.03 (m, *J* = 7.2 Hz, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 152.8, 148.2, 144.2, 143.5, 140.1, 131.6, 130.1, 129.8, 128.9, 128.6, 124.7, 120.1, 119.5, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 56.5, 56.3, 43.6, 21.8, 17.6, 17.6, 13.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{31}H_{37}NNaO_5SSi$ 586.2054: found: 586.2053.

2h. (*E*)-4'-((diisopropyl(4-(2-(phenylsulfonyl)vinyl)benzyl)silyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (82:18)

Yield: 62% (*para:others* = 15:1)

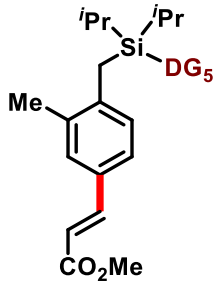
Physical appearance: Colourless solid compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 – 7.92 (m, *J* = 7.1, 3.1, 1.8 Hz, 1H), 7.63 (d, *J* = 15.3 Hz, 1H), 7.59 (dd, *J* = 3.8, 2.5 Hz, 1H), 7.55 – 7.51 (m, 1H), 7.38 (d, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.13 (t, *J* = 4.1 Hz, 2H), 6.89 (s, 1H), 6.85 (d, 1H), 6.78 (d, *J* = 15.4 Hz, 1H), 3.96 (s, 1H), 3.93 (s, 2H), 2.43 (s, 1H), 1.24 – 1.16 (m, 1H), 1.05 – 1.03 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.9, 152.8, 148.3, 143.4, 142.9, 141.3, 140.1, 133.4, 131.7, 130.1, 129.7, 129.5, 128.9, 127.8, 125.8, 120.1, 119.5, 115.2, 112.5, 102.4, 77.5, 77.2, 76.9, 56.5, 56.3, 29.9, 21.8, 17.6, 17.6, 13.2.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{36}H_{39}NNaO_5SSi$ 648.2210: found: 648.2211.

4a. methyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleum ether:ethyl acetate (90: 10)

Yield: 72% (*para:others* = 9:1)

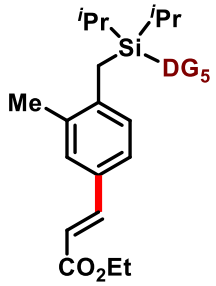
Physical appearance: Colourless viscous compound

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 16.0 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.26 (s, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.12 (s, 1H), 6.86 (s, 1H), 6.69 (d, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.78 (s, 3H), 2.40 (s, 2H), 2.30 (s, 3H), 1.32 – 1.23 (m, *J* = 14.6, 7.3 Hz, 2H), 1.09 (d, *J* = 7.4 Hz, 6H), 1.03 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 155.8, 152.7, 148.2, 145.4, 141.0, 140.2, 136.3, 131.4, 131.1, 130.4, 129.9, 129.9, 125.8, 119.9, 119.5, 116.2, 115.2, 112.5, 102.3, 56.5, 56.3, 51.8, 20.6, 18.8, 17.8, 17.5, 13.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{39}NNaO_5Si$ 580.2490: found: 580.2492.

4b. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleum ether:ethyl acetate (90: 10)

Yield: 75% (*para:others* = 10:1)

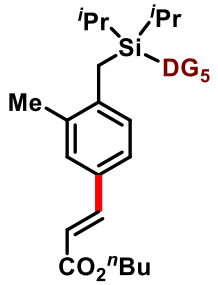
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 13.1 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 2.8 Hz, 2H), 7.15 (d, *J* = 8.5 Hz, 1H), 7.12 (s, 1H), 6.86 (s, 1H), 6.70 (d, *J* = 8.6 Hz, 2H), 4.24 (q, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.40 (s, 2H), 2.30 (s, 3H), 1.32 (t, *J* = 7.1, 3.4 Hz, 3H), 1.29 – 1.24 (m, *J* = 15.0, 7.4 Hz, 2H), 1.09 (d, 6H), 1.04 (d, *J* = 7.3, 2.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 155.9, 152.7, 148.2, 145.1, 140.9, 140.2, 136.3, 131.4, 131.2, 130.4, 129.9, 129.9, 125.8, 119.9, 119.5, 116.7, 115.2, 112.5, 102.4, 77.5, 77.2, 76.9, 60.4, 56.5, 56.3, 20.6, 18.8, 17.7, 17.5, 14.5, 13.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{34}H_{41}NNaO_5Si$ 594.2646: found: 594.2647.

4c. butyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleum ether:ethyl acetate (90: 10)

Yield: 71% (*para:others* = 10:1)

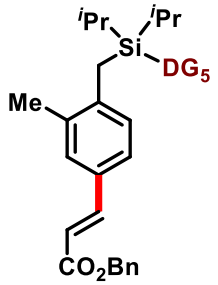
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 16 Hz 1H), 7.33 – 7.30 (m, 2H), 7.28 – 7.26 (m, 2H), 7.16 – 7.14 (m, 1H), 7.12 (s, 1H), 6.86 (s, 1H), 6.71 – 6.68 (m, 2H), 6.37 (d, *J* = 16.0 Hz, 1H), 4.18 (t, *J* = 7.5 Hz 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.40 (s, 2H), 2.30 (s, 3H), 1.70 – 1.64 (m, 2H), 1.47 – 1.39 (m, 2H), 1.30 – 1.24 (m, 2H), 1.09 (d, *J* = 5 Hz, 6H), 1.04 – 1.02 (d, *J* = 10 Hz, 6H), 0.95 (t, *J* = 7.4, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 155.8, 152.7, 148.2, 145.0, 140.9, 140.2, 136.3, 131.4, 131.2, 130.4, 129.9, 129.9, 125.8, 119.9, 119.5, 116.7, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 64.4, 56.5, 56.3, 31.0, 20.6, 19.4, 18.8, 17.7, 17.5, 13.9, 13.5.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{36}H_{45}NNaO_5Si$ 622.2959: found: 622.2959.

4d. benzyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (87:13)

Yield: 65% (*para:others* = 14:1)

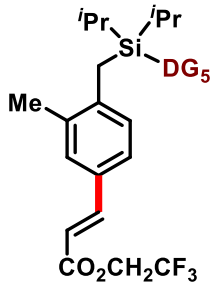
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.65 (d, *J* = 16.0 Hz, 1H), 7.43 – 7.27 (m, 9H), 7.15 (d, *J* = 10.0 Hz, 1H), 7.11 (s, 1H), 6.86 (s, 1H), 6.69 (d, *J* = 10.0 Hz, 2H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.23 (s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 2.40 (s, 2H), 2.30 (s, 3H), 1.29 – 1.24 (m, 2H), 1.09 (d, *J* = 7.5 Hz, 6H), 1.03 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 155.8, 152.7, 148.2, 145.7, 141.1, 140.2, 136.4, 136.3, 131.4, 131.1, 130.4, 129.9, 129.9, 128.8, 128.4, 128.3, 125.9, 119.9, 119.5, 116.2, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 66.4, 56.5, 56.3, 20.6, 18.8, 17.7, 17.5, 13.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{39}H_{43}NNaO_5Si$ 656.2803: found: 656.2797.

4e. 2,2,2-trifluoroethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)-diisopropylsilyl)methyl)-3-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleum ether:ethyl acetate (90: 10)

Yield: 58% (*para:others* = 10:1)

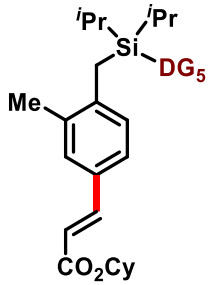
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 15.0 Hz, 1H), 7.33 – 7.28 (m, 4H), 7.17 (d, *J* = 10.0 Hz,1H), 7.12 (s, 1H), 6.86 (s, 1H), 6.71 – 6.69 (d, *J* = 10.0 Hz, 2H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.56 (qd, *J* = 8.5, 2.7 Hz, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.41 (s, 2H), 2.31 (s, 3H), 1.30 – 1.25 (m, 2H), 1.09 (m, 6H), 1.04 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6, 155.9, 152.7, 148.2, 147.4, 142.9, 140.1, 131.6, 130.5, 130.1, 129.6, 128.7, 120.1, 120.1, 119.5, 115.2, 114.4, 112.5, 102.3, 77.5, 77.2, 76.9, 60.9, 60.6, 60.3, 60.0, 56.4, 56.3, 21.8, 17.6, 17.5, 13.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{34}H_{38}F_3NNaO_5Si$ 648.2471: found: 648.2475.

4f. cyclohexyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diiso-propylsilyl)methyl)-3-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleum ether:ethyl acetate (90: 10)

Yield: 69% (*para:others* = 15:1)

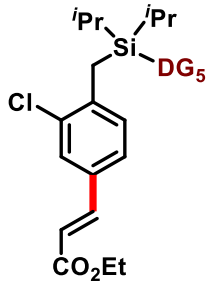
Physical appearance: Colourless viscous compound

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, , *J* = 16.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 4.7 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.12 (s, 2H), 6.86 (s, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 4.90 – 4.83 (m, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 2.39 (s, 2H), 2.30 (s, 3H), 1.94 – 1.87 (m, 2H), 1.79 – 1.72 (m, 2H), 1.50 – 1.37 (m, 4H), 1.30 – 1.23 (m, 4H), 1.08 (d, *J* = 8.0 Hz, 6H), 1.03 (d, *J* = 8.0 Hz,6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 155.9, 152.7, 148.2, 144.7, 140.8, 140.2, 136.3, 131.4, 131.3, 130.3, 129.9, 129.9, 125.8, 119.9, 119.5, 117.3, 115.2, 112.5, 102.3, 77.6, 77.2, 76.9, 72.7, 56.5, 56.4, 31.9, 25.7, 24.0, 20.6, 18.8, 17.7, 17.5, 13.5.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{38}H_{47}NNaO_5Si$ 648.3116: found: 648.3117.

4g. ethyl (*E*)-3-(3-chloro-4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diiso-propylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure Ain 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (86:14)

Yield: 64% (*para:others* = 3:1)

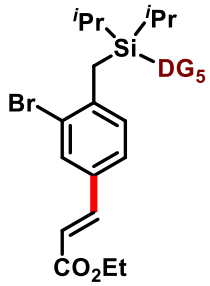
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 16.0, 8.1 Hz, 1H), 7.48 (s, 1H), 7.40 – 7.35 (m, 2H), 7.34 – 7.27 (m, 1H), 7.21 (s, 1H), 7.13 (s, 1H), 6.91 – 6.82 (m, 3H), 6.36 (d, *J* = 16.0 Hz, 1H), 4.24 (q, *J* = 6.6, 2H), 3.95 (s, 3H), 3.93 (s, 3H), 2.58 (s, 2H), 1.35 – 1.28 (m, 5H), 1.10 – 1.03 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 155.9, 152.7, 148.2, 143.3, 140.2, 140.0, 133.9, 132.8, 131.5, 131.1, 130.1, 129.1, 126.3, 120.0, 119.9, 118.4, 115.2, 112.5, 102.4, 77.5, 77.2, 76.9, 60.7, 56.5, 56.4, 19.2, 17.6, 17.5, 14.5, 13.7.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{38}ClNNaO_5Si$614.2105;found: 614.2109

4h. ethyl (*E*)-3-(3-bromo-4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (87:13)

Yield: 72% (*para:others* = 8:1)

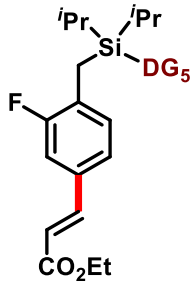
Physical appearance: Colourless viscous compound

^{1}H NMR(500 MHz, $CDCl_3$) δ 7.64 (d, J = 16.0 Hz, 1H), 7.41 – 7.37 (m, 4H), 7.16 – 7.12 (m, 3H), 6.89 (s, 1H), 6.86 (d, J = 8.6 Hz, 2H), 6.36 (d, J = 16.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.43 (s, 2H), 1.32 (t, J = 7.5 Hz, 3H), 1.24 – 1.20 (m, 2H), 1.07 – 1.03 (m, 12H).

^{13}C NMR(126 MHz, $CDCl_3$) δ 167.5, 156.1, 152.7, 148.2, 144.9, 141.9, 140.2, 131.6, 131.0, 130.1, 129.5, 128.4, 120.2, 119.5, 116.9, 115.2, 112.5, 102.3, 60.6, 56.5, 56.4, 21.6, 17.6, 17.6, 14.6, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{38}BrNNaO_5Si$: 658.1600 found658.1559.

4i. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-fluorophenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (87:13)

Yield: 64% (*para:others* = 5:1)

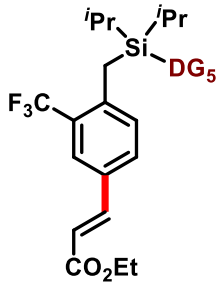
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 16.0 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.32 – 7.24 (m, 1H), 7.20 – 7.11 (m, 3H), 6.92 – 6.83 (m, 3H), 6.35 (d, *J* = 16.0 Hz, 1H), 4.25 (q, , *J* = 6.6 Hz, 2H), 3.95 (s, 3H), 3.93 (s, 3H), 2.40 (s, 2H), 1.32 (t, *J* = 5.0 Hz, 3H), 1.27 – 1.21 (m, 2H), 1.08 – 1.03 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 155.9, 152.7, 148.2, 143.9, 143.7, 140.1, 131.5, 131.5, 130.1, 130.1, 124.2, 120.1, 119.5, 118.3, 115.2, 114.4, 114.2, 112.5, 102.3, 77.5, 77.2, 76.9, 60.7, 56.5, 56.3, 17.5, 17.4, 14.5, 14.0, 13.4.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for C33H38FNNaO5Si598.2395; found: 598.2393.

4j. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-(trifluoromethyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (86:14)

Yield: 69% (*para:others* = 7:1)

Physical appearance: Colourless viscous compound

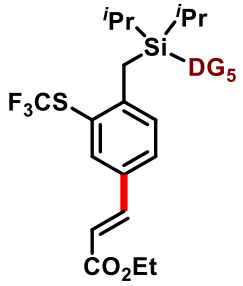
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.63 (d, *J* = 16.0 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.42 – 7.37 (m, 3H), 7.13 (s, 1H), 6.90 – 6.83 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 4.25 (q, *J* =

14.3, 7.2 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.60 (s, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.29 – 1.26 (m, 2H), 1.07 – 1.04 (m, 6H), 0.99 – 0.96 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 155.8, 152.7, 148.2, 143.2, 141.0, 140.1, 132.3, 131.6, 131.3, 130.5, 130.2, 130.1, 120.0, 119.9, 119.5, 118.8, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 60.8, 56.5, 56.3, 18.5, 17.6, 17.3, 14.5, 13.4.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{34}H_{38}F_3NNaO_5Si$ 648.2364: found: 648.2368.

4k. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)-methyl)-3-((trifluoromethyl)thio)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 72% (*para:others* = 17:1)

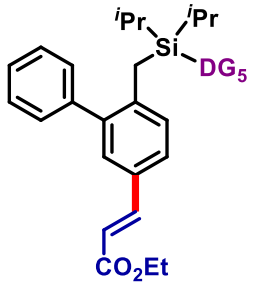
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.61 (d, J = 10.1 Hz, 1H)), 7.51 (dd, J = 8.1, 1.9 Hz, 1H), 7.34 (m, 3H), 7.12 (s, 1H), 6.87 (s, 1H), 6.76 – 6.73 (m, 2H), 6.40 (d, J = 10.1 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.79 (s, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.27 (dd, J = 12.7, 5.2 Hz, 2H), 1.08 (d, J = 7.4 Hz, 6H), 1.05 (d,J = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 155.7, 152.7, 148.2, 147.9, 143.1, 140.0, 138.1, 132.5, 131.6, 131.1, 130.2, 130.1, 119.8, 118.7, 115.2, 112.5, 102.3, 60.8, 56.5, 56.3, 20.5, 17.7, 17.5, 14.5, 13.6.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{34}H_{39}F_3NOSSi$: 658.2265: found: 658.2266.

4l. ethyl (*E*)-3-(6-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsil-yl)methyl)-[1,1'-biphenyl]-3-yl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 68% (*para:others* = 8:1)

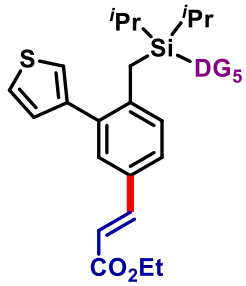
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, 1H), 7.39 – 7.34 (m, *J* = 13.6, 6.5 Hz, 3H), 7.33 – 7.26 (m, *J* = 19.8, 5.7 Hz, 6H), 7.21 (s, 1H), 7.08 (s, 1H), 6.83 (s, 1H), 6.83 (s, 1H), 6.59 (d, *J* = 8.2 Hz, 2H), 6.35 (d, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 2.47 (s, 2H), 1.27 (t, *J* = 7.0 Hz, 3H), 1.05 – 0.99 (m, *J* = 14.4, 7.2 Hz, 2H), 0.84 – 0.78 (m, *J* = 11.6, 7.4 Hz, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 155.9, 152.7, 148.2, 144.7, 142.0, 141.5, 140.2, 139.6, 131.3, 131.2, 130.6, 130.5, 129.9, 129.7, 128.6, 127.3, 126.9, 119.9, 119.5, 117.3, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 60.5, 56.5, 56.3, 18.4, 17.4, 17.3, 14.5, 13.2.

HRMS (*m/z*): $[M + H]^+$ calculated for $C_{39}H_{44}NO_5Si$: 634.2989; found: 634.2980.

4m. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3-(thiophen-3-yl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 71% (*para:others* = 10:1)

Physical appearance: Colourless viscous compound

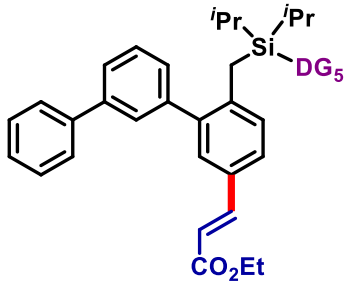
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 15.7 Hz, 1H), 7.34 – 7.27 (m, 5H), 7.18 – 7.16 (m, *J* = 4.6, 1.8 Hz, 2H), 7.12 (s, 1H), 7.00 (s, 1H), 6.88 (s, 1H), 6.63 (d, *J* = 8.5 Hz, 2H), 6.11 (d,

J = 15.7 Hz, 1H), 4.22 (q, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.39 (s, 2H), 1.31 (t, J = 7.1 Hz, 3H), 0.93 (d, 6H), 0.90 (d, J = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 155.9, 152.7, 148.1, 140.6, 140.2, 137.9, 136.5, 136.3, 133.3, 132.5, 131.3, 130.8, 130.2, 129.9, 129.4, 128.7, 124.9, 119.9, 119.5, 117.4, 115.2, 112.5, 102.3, 60.8, 56.5, 56.3, 18.4, 17.5, 17.4, 14.5, 13.1.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{37}H_{41}NO_5SSi$: 639.2475; found: 639.2478.

4n. ethyl (*E*)-3-(6-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-[1,1':3',1''-terphenyl]-3-yl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 64% (*para:others* = 5:1)

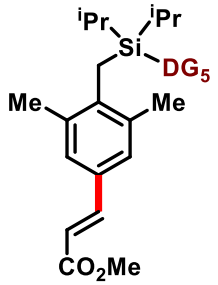
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, 1H), 7.59 – 7.54 (m, J = 9.8, 6.8, 1.4 Hz, 4H), 7.49 (t, J = 7.1 Hz, 1H), 7.44 – 7.40 (m, J = 12.8, 5.5 Hz, 4H), 7.35 – 7.31 (m, 2H), 7.29 (d, 3H), 7.13 (s, 1H), 6.84 (s, 1H), 6.63 (d, 2H), 6.41 (d, 1H), 4.24 (q, 2H), 3.94 (s, 3H), 3.93 (s, 3H), 0.88 (d, J = 7.4 Hz, 6H), 0.85 (d, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 155.8, 152.7, 148.1, 144.6, 142.0, 141.9, 141.6, 141.1, 140.1, 139.7, 131.3, 131.3, 130.6, 130.4, 129.9, 128.9, 128.6, 128.6, 127.7, 127.5, 127.4, 127.1, 126.1, 119.9, 119.5, 117.4, 115.2, 112.5, 102.2, 60.5, 56.5, 56.3, 18.6, 17.4, 17.3, 14.5, 13.2.

HRMS (*m*/*z*): $[M + H]^+$ calculated for $C_{45}H_{48}NO_5Si$: 710.3302 found: 710.3305.

6a. methyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 70% (*para:others* = >20:1)

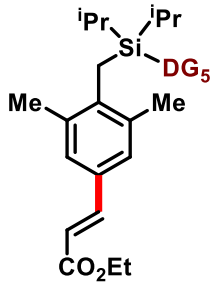
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 16.0 Hz, 1H), 7.32 – 7.29 (m, 2H), 7.14 (s, 2H), 7.11 (s, 1H), 6.85 (s, 1H), 6.74 – 6.70 (m, 2H), 6.34 (d, *J* = 16.0 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.77 (s, 3H), 2.42 (s, 2H), 2.34 (s, 6H), 1.29 – 1.21 (m, 3H), 1.09 (d, *J* = 7.4 Hz, 6H), 1.02 – 0.95 (m, 7H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 155.8, 152.7, 148.1, 145.5, 140.3, 140.1, 136.2, 131.3, 130.5, 129.9, 128.1, 119.7, 119.5, 115.9, 115.2, 112.4, 102.3, 77.5, 77.2, 76.9, 56.4, 56.3, 51.7, 21.5, 17.6, 17.4, 16.6, 14.3.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{34}H_{41}NNaO_5Si$ 594.2646: found: 594.2642.

6b. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 72% (*para:others* = >20:1)

Physical appearance: Colourless viscous compound

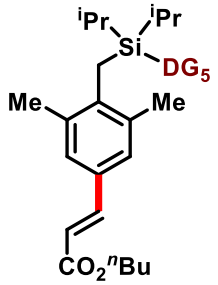
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.31 (d, 2H), 7.15 (s, 2H), 7.12 (s, 1H), 6.86 (s, 1H), 6.72 (d, 2H), 6.35 (d, *J* = 16.0 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 3.92 (s,

3H), 2.42 (s, 2H), 2.34 (s, 6H), 1.31 (t, J = 7.1 Hz, 3H), 1.24 – 1.20 (m, J = 9.3, 5.0 Hz, 2H), 1.09 (d, J = 7.0 Hz, 6H), 0.97 (d, J = 3.0 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 155.8, 152.7, 148.1, 145.2, 140.2, 140.1, 136.2, 131.3, 130.6, 129.9, 128.1, 119.8, 119.5, 116.4, 115.2, 112.4, 102.3, 77.5, 77.2, 76.9, 60.4, 56.4, 56.3, 21.6, 17.7, 17.4, 16.6, 14.5, 14.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{35}H_{43}NNaO_5Si$ 608.2803: found: 608.2804.

6c. butyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure Ain 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 65% (*para:others* = >20:1)

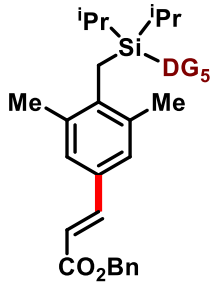
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J = 16.0 Hz, 1H), 7.33 – 7.30 (m, 2H), 7.15 (s, 2H), 7.11 (s, 1H), 6.85 (s, 1H), 6.74 – 6.70 (m, 2H), 6.35 (d, J = 16.0 Hz, 1H), 4.17 (t, J = 6.7 Hz, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 2.42 (s, 2H), 2.34 (s, 6H), 1.69 – 1.64 (m, 2H), 1.46 – 1.38 (m, 2H), 1.25 (td, J = 7.3, 3.3 Hz, 2H), 1.09 (d, J = 3.1 Hz, 6H), 0.96 (dd, J = 7.4, 3.8 Hz, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 155.8, 152.7, 148.1, 145.1, 140.2, 140.1, 136.2, 131.3, 130.6, 129.9, 128.0, 119.8, 119.5, 116.4, 115.2, 112.4, 102.3, 77.5, 77.2, 76.9, 64.4, 56.4, 56.3, 30.9, 21.5, 19.4, 17.6, 17.4, 16.6, 14.2, 13.9.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{37}H_{47}NNaO_5Si$ 636.3116: found: 636.3110.

6d. benzyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure Ain 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 81% (*para:others* = >15:1)

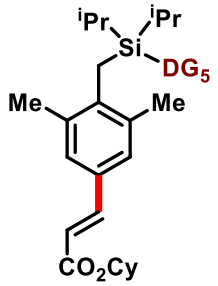
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 16.0 Hz, 1H), 7.42 – 7.34 (m, 5H), 7.34 – 7.30 (m, 3H), 7.15 (s, 2H), 7.11 (s, 1H), 6.86 (s, 1H), 6.73 (d, *J* = 8.6 Hz, 2H), 6.41 (d, *J* = 16.0 Hz, 1H), 5.23 (s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 2.43 (s, 2H), 2.34 (s, 6H), 1.26 – 1.21 (m, 2H), 1.09 (d, *J* = 7.4 Hz, 6H), 0.97 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 155.8, 152.7, 148.2, 145.8, 140.4, 140.1, 136.5, 136.3, 131.3, 130.5, 129.9, 128.7, 128.3, 128.1, 119.8, 119.5, 116.0, 115.2, 112.5, 102.3, 66.3, 56.5, 56.3, 21.6, 17.7, 17.4, 16.7, 14.3.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{40}H_{45}NNaO_5Si$ 670.2959: found: 670.2945.

6e. cyclohexyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-3,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure Ain 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 67% (*para:others* = >20:1)

Physical appearance: Colourless viscous compound

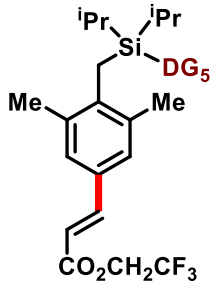
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 16.0 Hz, 1H), 7.32 – 7.30 (m, 2H), 7.15 (s, 2H), 7.11 (s, 1H), 6.85 (s, 1H), 6.73 – 6.71 (m, 2H), 6.35 (d, *J* = 16.0 Hz, 1H), 4.88 – 4.83 (m, 1H),

3.93 (s, 3H), 3.91 (s, 3H), 2.42 (s, 2H), 2.33 (s, 6H), 1.89 (dd, *J* = 8.3, 4.2 Hz, 2H), 1.75 (dd, *J* = 8.5, 3.6 Hz, 2H), 1.55 (dd, *J* = 8.9, 3.7 Hz, 1H), 1.50 – 1.45 (m, 2H), 1.44 – 1.35 (m, 3H), 1.25 – 1.21 (m, 2H), 1.08 (d, *J* = 7.4 Hz, 6H), 0.96 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 155.8, 152.6, 148.1, 144.8, 140.1, 140.0, 136.1, 131.3, 130.7, 129.9, 127.9, 119.7, 119.4, 116.9, 115.1, 112.4, 102.2, 77.5, 77.2, 76.9, 72.5, 56.4, 56.3, 31.9, 25.6, 23.9, 21.5, 17.6, 17.3, 16.6, 14.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{39}H_{49}NNaO_5Si$ 662.3272: found: 662.3276.

6f. 2,2,2-trifluoroethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)di-isopropyl-silyl)methyl)-3,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 73% (*para:others* = >20:1)

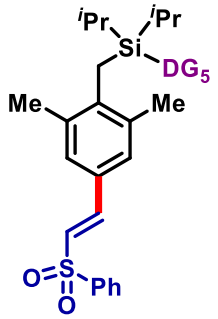
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 16.0 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.17 (s, 2H), 7.12 (s, 1H), 6.86 (s, 1H), 6.74 – 6.71 (m, 2H), 6.40 (d, *J* = 16.0 Hz, 1H), 4.56 (q, *J* = 8.5 Hz, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.44 (s, 2H), 2.35 (s, 6H), 1.25 (dd, *J* = 13.7, 6.2 Hz, 2H), 1.10 (d, *J* = 7.4 Hz, 6H), 0.98 (dk, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7, 155.6, 152.7, 148.2, 147.8, 141.2, 140.1, 136.4, 131.4, 130.1, 129.9, 128.3, 123.4 (q, *J* = 278.4 Hz), 119.7, 119.5, 115.2, 113.9, 112.4, 102.3, 77.5, 77.2, 76.9, 60.4 (q, *J* = 36.5 Hz), 56.4, 56.3, 21.5, 17.6, 17.4, 16.8, 14.3.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{35}H_{40}F_3NNaO_5Si$ 662.2520: found: 662.2524.

6g. (*E*)-4'-(((2,6-dimethyl-4-(2-(phenylsulfonyl)vinyl)benzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphenyl]-2-carbonitrile



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (80:20)

Yield: 54% (*para:others* = >20:1)

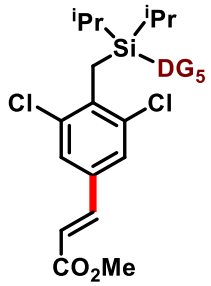
Physical appearance: Colourless solid compound

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.60 – 7.54 (m, 2H), 7.54 – 7.48 (m, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.12 (s, 1H), 7.11 (s, 2H), 6.86 (s, 1H), 6.86 (s, 1H), 6.77 (d, J = 16 Hz, 1H), 6.72 (d, J = 12.0 Hz, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.42 (s, 2H), 2.32 (s, 6H), 1.25 – 1.20 (m, 2H), 1.07 (d, J = 7.3 Hz, 6H), 0.95 (d, J = 7.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 152.7, 148.2, 143.2, 141.6, 141.4, 140.1, 136.5, 133.3, 131.4, 129.9, 129.4, 128.5, 128.5, 127.7, 125.2, 119.7, 119.5, 115.2, 112.45, 102.3, 56.5, 56.3, 21.5, 17.6, 17.4, 16.9, 14.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{38}H_{43}NNaO_5SSi$676.2529; found:676.2530.

6h. methyl (*E*)-3-(3,5-dichloro-4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)-diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 59% (*para:others* = >20:1)

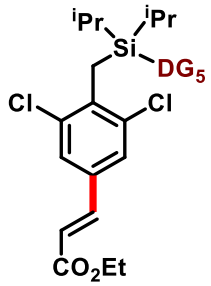
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 16.0 Hz, 1H), 7.37 (s, 2H), 7.31 (d, *J* = 10.0 Hz, 2H), 7.12 (s, 1H), 6.85 (s, 1H), 6.79 (d, *J* = 10.0 Hz, 2H), 6.34 (d, *J* = 16.0 Hz, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.77 (s, 2H), 2.77 (s, 2H), 1.41 – 1.35 (m, 2H), 1.13 – 1.10 (m, 6H), 1.09 – 1.06 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.1, 155.8, 152.7, 148.1, 142.2, 140.2, 139.1, 134.9, 132.9, 131.2, 129.8, 127.4, 119.7, 119.5, 119.1, 115.2, 112.4, 102.3, 77.5, 77.2, 76.9, 56.5, 56.3, 52.0, 18.7, 17.6, 17.5, 14.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{32}H_{35Cl2}NNaO_5Si$ 634.1550: found: 634.1555.

6i. ethyl (*E*)-3-(3,5-dichloro-4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)-diisopropylsilyl)methyl)-phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 62% (*para:others* = >20:1)

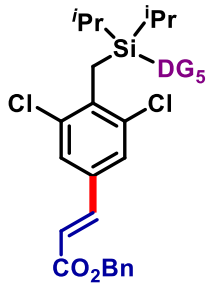
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, 1H), 7.38 (s, 2H), 7.31 (d, 1H), 7.12 (s, 1H), 6.85 (s, 1H), 6.81 – 6.79 (m, 2H), 6.34 (d, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.77 (s, 2H), 1.38 (dd, *J* = 14.9, 7.4 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.12 (d, 6H), 1.07 (d, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 155.9, 152.7, 148.1, 141.9, 140.2, 139.0, 134.9, 132.9, 131.2, 129.9, 127.4, 119.8, 119.7, 119.5, 115.2, 112.4, 102.3, 77.5, 77.2, 76.9, 60.9, 56.5, 56.3, 18.7, 17.6, 17.5, 14.5, 14.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{37}Cl_2NNaO_5Si$ 648.1710: found: 648.1716.

6j. benzyl (*E*)-3-(3,5-dichloro-4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 71% (*para:others* = >20:1)

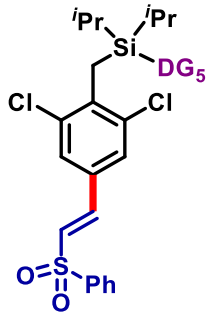
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, 1H), 7.40 – 7.34 (m, 7H), 7.33 – 7.30 (m, 2H), 7.10 (s, 1H), 6.85 (s, 1H), 6.79 (d, 2H), 6.39 (d, J = 15.8 Hz, 1H), 5.22 (s, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 2.77 (s, 2H), 1.38 (dq, J = 14.6, 7.3 Hz, 1H), 1.11 (d, J = 7.5 Hz, 6H), 1.07 (d, J = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4, 155.7, 152.7, 148.1, 142.4, 140.1, 139.1, 136.0, 134.9, 132.8, 131.2, 129.8, 128.8, 128.4, 128.3, 127.4, 119.7, 119.5, 119.2, 115.2, 112.4, 102.3, 66.6, 56.4, 56.3, 18.6, 17.6, 17.4, 14.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{38}H_{39}Cl_2NNaO_5Si$ 710.1867; found: 710.1860.

6k. (*E*)-4'-(((2,6-dichloro-4-(2-(phenylsulfonyl)vinyl)benzyl)diisopropylsilyl)oxy)-4,5-dimethoxy-[1,1'-biphen-yl]-2-carbonitrile



The compound was synthesized following the general procedure Ain 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (80:20)

Yield: 55% (*para:others* = >20:1)

Physical appearance: Colourless solid compound

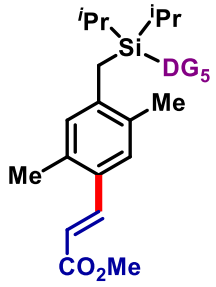
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.7 Hz, 2H), 7.47 (d, J = 15.4 Hz, 1H), 7.30 (d, J = 8.6 Hz, 2H), 7.26 (s, 1H), 7.13 (s, 1H), 6.85 (s,

1H), 6.81 (d, *J* = 15.4 Hz, 1H), 6.78 (d, *J* = 8.6 Hz, 2H), 3.95 (s, 3H), 3.93 (s, 3H), 2.77 (s, 2H), 1.37 (dt, *J* = 14.8, 7.5 Hz, 2H), 1.11 (d, *J* = 7.4 Hz, 6H), 1.06 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.7, 152.7, 148.2, 140.5, 140.3, 140.1, 139.7, 135.1, 133.7, 131.3, 130.7, 129.8, 129.6, 128.7, 127.9, 127.9, 119.7, 119.5, 115.3, 112.4, 102.3, 56.5, 56.3, 18.9, 17.6, 17.5, 14.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{36}H_{37}Cl_2NNaO_5SSi$ 716.1436; found: 716.1430.

6l. methyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropyl-silyl)methyl)-2,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 71% (*para:others* = >20:1)

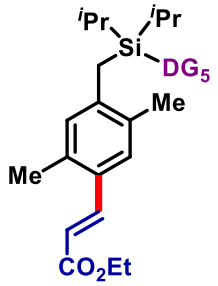
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 15.9 Hz, 1H), 7.32 (d, 2H), 7.30 (s, 1H), 7.12 (s, 1H), 6.95 (s, 1H), 6.86 (s, 1H), 6.72 (d, 2H), 6.30 (d, *J* = 15.9 Hz, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 3.78 (s, 3H), 2.35 (s, 3H), 2.26 (s, 3H), 1.29 – 1.25 (m, 2H), 1.09 (d, 6H), 1.04 (d, *J* = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 155.9, 152.7, 148.1, 142.8, 140.6, 140.1, 135.3, 133.7, 131.9, 131.3, 129.9, 129.7, 128.4, 119.9, 119.5, 116.9, 115.2, 112.5, 102.3, 56.5, 56.3, 51.7, 20.2, 19.5, 18.5, 17.7, 17.5, 13.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{35}H_{43}NNaO_5Si$ 608.2803; found: 608.2805.

6m. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropyl-silyl)methyl)-2,5-dimethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 70% (*para:others* = >20:1)

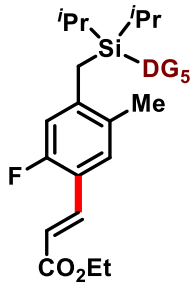
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 15.9 Hz, 1H), 7.34 – 7.30 (m, *J* = 8.6, 1.9 Hz, 3H), 7.12 (s, 1H), 6.95 (s, 1H), 6.86 (s, 1H), 6.72 (d, 2H), 6.30 (d, *J* = 15.9 Hz, 1H), 4.24 (q, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.35 (s, 3H), 2.26 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.28 – 1.23 (m, *J* = 7.4 Hz, 2H), 1.08 (d, *J* = 7.5 Hz, 6H), 1.03 (d, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 155.9, 152.7, 148.1, 142.5, 140.5, 140.1, 135.2, 133.6, 131.9, 131.3, 129.9, 129.8, 128.4, 119.9, 119.5, 117.4, 115.2, 112.4, 102.3, 60.5, 56.4, 56.3, 20.2, 19.5, 18.4, 17.7, 17.5, 14.5, 13.5.

HRMS (*m/z*): $[M + H]^+$ calculated $C_{34}H_{41}NNaO_5Si$ 594.2646; found: 594.2645.

6n. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-2-fluoro-5-methylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (86:14)

Yield: 65% (*para:others* = >20:1)

Physical appearance: colourless solid

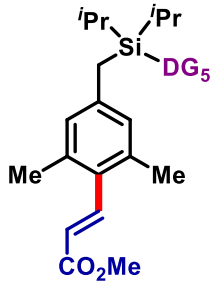
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 16.2 Hz, 1H), 7.33 (d, *J* = 10.0 Hz, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.12 (s, 1H), 6.89 – 6.84 (m, 2H), 6.74 – 6.71 (d, *J* = 10.0 Hz, 2H), 6.45 (d, *J* =

16.2, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 2.36 (s, 2H), 2.25 (s, 3H), 1.34 – 1.26 (m, 5H), 1.09 (d, *J* = 5.0 Hz, 6H), 1.04 (d, *J* = 5.0 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 160.9, 158.9, 155.7, 152.7, 148.2, 143.0, 142.9, 140.1, 137.8, 131.9, 131.9, 131.6, 130.6, 130.6, 130.0, 119.8, 119.5, 119.2, 119.2, 118.8, 118.7, 116.5, 116.3, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 60.6, 56.4, 56.3, 19.8, 19.1, 17.7, 17.5, 14.5, 13.5.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{38}H_{43}NNaO_5SSi$676.2529; found:676.2530.

6o. methyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropyl-silyl)methyl)-2,6-dimethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 56% (*para:others* = >15:1)

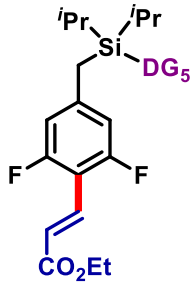
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 16.4 Hz, 1H), 7.39 (d, 2H), 7.13 (s, 1H), 6.89 (s, 1H), 6.87 – 6.85 (m, 2H), 6.81 (s, 2H), 6.05 (d, *J* = 16.4 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.80 (s, 3H), 2.32 (s, 2H), 2.29 (s, 6H), 1.25 – 1.18 (m, *J* = 14.3, 7.3 Hz, 2H), 1.07 (d, *J* = 3.8 Hz, 6H), 1.05 (d, *J* = 3.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.8, 156.2, 152.7, 148.2, 143.6, 140.1, 139.4, 137.1, 131.4, 130.1, 130.0, 129.3, 122.4, 120.2, 119.5, 115.2, 112.5, 102.3, 56.5, 56.3, 51.8, 21.4, 20.9, 17.7, 17.6, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{35}H_{43}NNaO_5Si$ 608.2803; found: 608.2808.

6p. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropyl-silyl)methyl)-2,6-difluorophenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

Yield: 63% (*para:others* = >20:1)

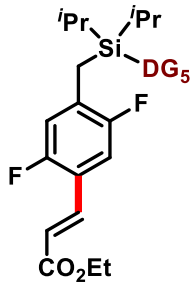
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 16.4 Hz, 1H), 7.41 (d, 2H), 7.13 (s, 1H), 6.90 (s, 1H), 6.88 (d, 2H), 6.68 (d, *J* = 10.0 Hz, 2H), 6.64 (d, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 2.39 (s, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.28 – 1.22 (m, 2H), 1.07 (d, *J* = 2.1 Hz, 6H), 1.06 (d, *J* = 2.1 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 162.7, 162.6, 160.7, 160.6, 155.7, 152.7, 148.2, 144.7, 144.7, 144.6, 139.9, 131.9, 131.1, 130.2, 122.9, 122.8, 122.8, 120.0, 119.4, 115.2, 112.5, 112.4, 112.2, 108.9, 108.9, 108.8, 102.3, 60.7, 56.4, 56.3, 22.1, 17.6, 17.5, 14.5, 13.2.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{33}H_{37}F_2NNaO_5Si$ 616.2301; found: 617.2316.

6q. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-2,5-difluoro-phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 61% (*para:others* = >20:1)

Physical appearance: Colourless viscous compound

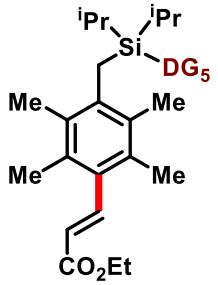
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 16.2 Hz, 1H), 7.39 (d, *J* = 10.0 Hz, 2H), 7.16 – 7.11 (m, 2H), 6.92 – 6.84 (m, 4H), 6.42 (d, *J* = 16.2 Hz, 1H), 4.25 (q, *J* = 6.6 Hz, 2H), 3.95 (s, 3H),

3.92 (s, 3H), 2.37 (s, 2H), 1.32(t, J = 7.5 Hz, 2H), 1.26 (m, 3H), 1.07 (d, J = 3.2 Hz, 6H), 1.06 (d, J = 3.2 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 157.8 (d, J = 86.94), 155.9 (d, J = 79.38), 155.7, 152.7, 148.2, 140.1, 136.4, 131.7,131.1 (dd, J = 21.42, J = 8.82), 131.1, 131.0, 130.9 130.1, 120.5 (d, J = 6.3), 119.9, 119.4, 117.9 (dd, J = 23.94, J = 5.04) 115.2, 114.3 (dd, J = 25.83, J =5.04), 112.5, 102.3, 60.8, 56.5, 56.3, 17.5, 17.4, 14.5, 14.4, 13.4.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{37}F_2NNaO_5Si$ 616.2301: found: 616.2303.

6r. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)-2,3,5,6-tetramethylphenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (88:12)

Yield: 61%

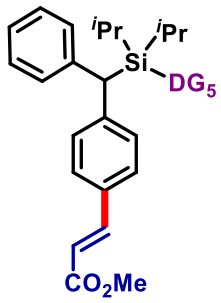
Physical appearance: Colourless solid compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J = 16.3 Hz, 1H), 7.28 (d, J = 8.6 Hz, 2H), 7.12 (s, 1H), 6.85 (s, 1H), 6.66 (d, J = 8.6 Hz, 2H), 5.82 (d, J = 16.3 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.52 (s, 2H), 2.24 (s, 6H), 2.17 (s, 6H), 1.32 (t, J = 7.1 Hz, 3H), 1.26 – 1.22 (m, J = 12.5, 4.9 Hz, 2H), 1.10 (d, J = 7.4 Hz, 6H), 0.99 (d, J = 7.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 155.9, 152.7, 148.1, 146.7, 140.2, 136.8, 132.0, 132.0, 131.8, 131.1, 129.8, 124.5, 119.7, 119.5, 115.2, 112.5, 102.3, 77.5, 77.2, 76.9, 60.6, 56.5, 56.3, 18.4, 17.7, 17.5, 17.1, 14.5, 14.2.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{37}H_{47}NNaO_5Si$ 636.3121: found: 636.3126.

8a. methyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)(phenyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 78% (*para:others* = 10:1) (mono:di = 5:1)

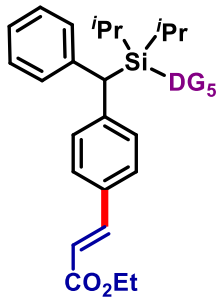
Physical appearance: Colourless viscous compound

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 16.0 Hz, 1H), 7.54 – 7.42 (m, 6H), 7.38 (d, *J* = 8 Hz, 2H), 7.29 (t, *J* = 8 Hz, 2H), 7.18 (t, *J* = 8 Hz, 1H), 7.14 (s, 1H), 6.89 (s, 1H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.38 (d, *J* = 16.0 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.82 (s, 1H), 3.79 (s, 3H), 1.32 – 1.27 (m, 2H), 0.95 – 0.90 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 155.9, 152.8, 148.3, 145.2, 144.9, 141.4, 140.1, 132.0, 131.6, 130.1, 130.0, 129.7, 128.8, 128.5, 126.1, 120.0, 119.5, 117.0, 115.2, 112.5, 102.4, 56.5, 56.4, 51.8, 43.0, 18.1, 18.1, 17.8, 13.9.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{38}H_{41}NNaO_5Si$: 642.2646: found: 642.2649.

8b. ethyl (*E*)-3-(4-((((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)(phenyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 71% (*para:others* = 10:1) (mono:di = 3:1)

Physical appearance: Colourless viscous compound

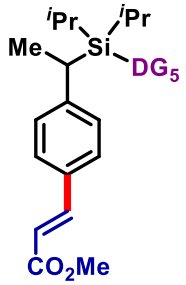
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 16.0 Hz, 1H), 7.52 – 7.47 (m, 4H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.38 (d, 5 Hz, 2H), 7.29 (t, *J* = 7.7 Hz, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.14 (s, 1H), 6.89

(s, 1H), 6.86 (d, *J* = 10.0 Hz, 2H), 6.38 (d, *J* = 16.0 Hz, 1H), 4.24 (q, *J* = 6.6 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 3.83 (s, 1H), 1.32 (t, *J* = 7.5 Hz, 3H), 1.30 – 1.28 (m, 2H), 0.96 – 0.91 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 155.9, 152.8, 148.3, 145.1, 144.6, 141.5, 140.2, 132.1, 131.7, 130.1, 130.0, 129.7, 128.8, 128.5, 126.1, 120.0, 119.5, 117.5, 115.3, 112.6, 102.4, 60.6, 56.5, 56.4, 43.1, 18.1, 18.1, 17.8, 17.8, 14.5, 14.3, 13.9.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{39}H_{43}NNaO_5Si$: 656.2802: found: 642.2805.

8c. methyl (*E*)-3-(4-(1-(((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropyl-silyl)ethyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:1)

Yield: 72% (*para:others* = 9:1)

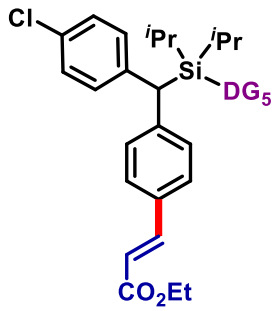
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.13 (s, 1H), 6.89 (s, 1H), 6.86 (d, *J* = 8.5 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.79 (s, 3H), 2.66 (q, *J* = 5.0 Hz, 1H), 1.54 (d, *J* = 10.0 Hz, 3H), 1.34 (dt, *J* = 14.9, 7.5 Hz, 1H), 1.20 (dt, *J* = 11.5, 7.4 Hz, 1H), 1.07 (dd, *J* = 7.5, 2.5 Hz, 6H), 1.01 (d, *J* = 7.4 Hz, 3H), 0.96 (d, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 156.2, 152.7, 148.2, 145.2, 140.2, 131.4, 131.4, 130.1, 128.8, 128.3, 120.1, 119.5, 116.6, 115.2, 112.5, 102.4, 56.5, 56.4, 51.8, 28.1, 18.2, 18.1, 17.8, 17.8, 16.2, 13.2, 13.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{33}H_{39}NNaO_5Si$: 580.2489: found: 580.2495.

8d. methyl (*E*)-3-(4-((4-chlorophenyl)(((2'-cyano-4',5'-dimethoxy-[1,1'-biphenyl]-4-yl)oxy)diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (84:16)

Yield: 86% (*para:others* = 9:1)

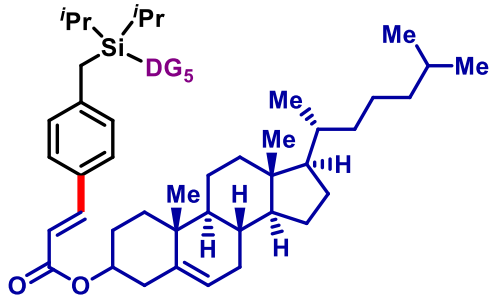
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 16.0 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.46 (d, J = 4.2 Hz, 2H), 7.44 – 7.38 (m, 4H), 7.27 (s, 1H), 7.25 (s, 1H), 7.14 (s, 1H), 6.89 (s, 1H), 6.86 (d, J = 10.0 Hz, 2H), 6.39 (d, J = 16.0 Hz, 1H), 4.25 (q, J = 6.6 Hz, 2H), 3.96 (s, 3H), 3.93 (s, 3H), 3.78 (s, 1H), 1.32 (t, J = 7.5 Hz, 3H), 1.29 – 1.26 (m, 2H), 0.96 – 0.90 (m, 12H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 155.7, 152.7, 148.3, 144.8, 144.5, 140.2, 140.0, 132.3, 131.9, 131.8, 130.9, 130.8, 130.2, 129.9, 128.9, 128.6, 125.7, 119.9, 119.5, 117.7, 115.2, 112.5, 102.4, 60.6, 56.5, 56.4, 42.2, 18.1, 18.0, 17.8, 17.8, 14.5, 13.9, 13.8.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{39}H_{42}ClNNaO_5Si$: 690.2413 found: 690.2415.

8e. (*E*)-((8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl) 3-(4-(((2'-cyanobiphenyl-4-yloxy)diisopropylsilyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 68%(*para:others* = 10:1)

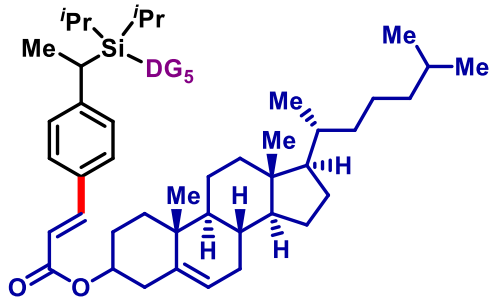
Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 15.9 Hz, 1H), 7.40 – 7.36 (m, 4H), 7.15 – 7.12 (m, 3H), 6.89 (s, 1H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.35 (d, *J* = 16.0 Hz, 1H), 5.40 (d, *J* = 4.0 Hz, 1H), 4.73 (s, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 2.42 (s, 2H), 2.39 (d, *J* = 7.3 Hz, 2H), 2.04 – 1.78 (m, 6H), 1.55 – 1.42 (m, 6H), 1.24 – 1.08 (m, 10H), 1.08 – 1.03 (m, *J* = 9.4, 6.7 Hz, 17H), 1.02 – 0.97 (m, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.88 – 0.84 (m, 7H), 0.68 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.9, 156.1, 152.8, 148.2, 144.7, 141.9, 140.2, 139.9, 131.6, 131.1, 130.1, 129.5, 128.4, 122.9, 120.2, 119.5, 117.4, 115.2, 112.5, 102.4, 74.1, 56.9, 56.5, 56.4, 56.4, 50.3, 42.5, 39.9, 39.7, 38.5, 37.3, 36.9, 36.4, 36.0, 32.1, 32.1, 28.5, 28.2, 28.1, 24.5, 24.0, 23.0, 22.8, 21.6, 21.3, 19.6, 18.9, 17.6, 17.6, 13.2, 12.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{58}H_{79}NNaO_5Si$: 920.5625found: 920.5630.

8f. (*E*)-((8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl) 3-(4-(((2'-cyanobiphenyl-4-yloxy)diisopropylsilyl)ethyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 61% (*para:others* = 9:1)

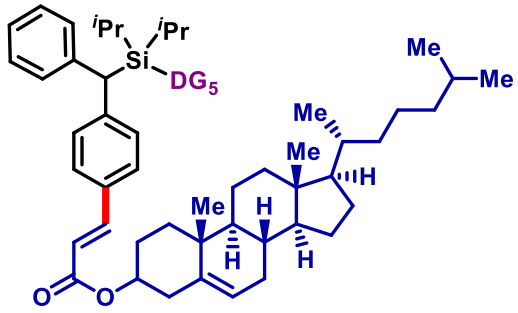
Physical appearance: Colorless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 15.9 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.38 (d, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.13 (s, 1H), 6.89 (s, 1H), 6.86 (d, 2H), 6.37 (d, 1H), 5.40 (d, *J* = 3.9 Hz, 1H), 4.78 – 4.69 (m, 1H), 3.95 (s, 3H), 3.92 (s, 3H), 2.66 (q, *J* = 7.4 Hz, 1H), 2.39 (d, *J* = 7.2 Hz, 2H), 2.06 – 1.80 (m, 6H), 1.71 – 1.42 (m, 13H), 1.23 – 1.11 (m, 7H), 1.09 – 1.04 (m, 11H), 1.03 – 0.99 (m, 6H), 0.96 (d, *J* = 7.5 Hz, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.89 – 0.85 (m, 7H), 0.68 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 156.2, 152.7, 148.2, 147.9, 144.7, 140.2, 139.9, 131.5, 131.4, 130.0, 128.7, 128.2, 122.8, 120.0, 119.5, 117.5, 115.2, 112.5, 102.3, 74.1, 56.9, 56.5, 56.3, 50.2, 42.5, 39.9, 39.7, 38.5, 37.2, 36.8, 36.4, 35.9, 32.1, 32.1, 28.4, 28.2, 28.1, 28.0, 24.5, 24.0, 23.0, 22.8, 21.2, 19.5, 18.9, 18.1, 18.0, 17.9, 17.8, 16.1, 13.2, 13.1, 12.1.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{59}H_{81}NNaO_5Si$: 934.5782 found: 934.5788.

8g. (*E*)-((8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl) 3-(4-(((2'-cyanobiphenyl-4-yloxy)diisopropylsilyl)(phenyl)methyl)phenyl)acrylate



The compound was synthesized following the general procedure A in 0.2 mmol scale.

Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 59% (*para:others* = 8:1)

Physical appearance: Colourless viscous compound

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 15.9 Hz, 1H), 7.52 – 7.46 (m, 4H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.14 (s, 1H), 6.89 (s, 1H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.39 (d, *J* = 4.1 Hz, 1H), 4.79 – 4.69 (m, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.82 (s, 1H), 2.39 (d, *J* = 7.5 Hz, 2H), 2.04 – 1.82 (m, 6H), 1.75 – 1.63 (m, 4H), 1.60 – 1.43 (m, 7H), 1.20 – 1.07 (m, 7H), 1.04 (d, *J* = 5.6 Hz, 4H), 0.92 (dd, *J* = 14.6, 7.5 Hz, 17H), 0.86 (dd, *J* = 6.6, 2.2 Hz, 7H), 0.68 (s, 3H).

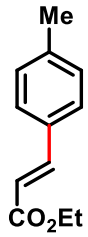
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 155.9, 152.8, 148.2, 144.9, 144.5, 141.8, 140.2, 139.9, 132.2, 131.6, 130.1, 129.9, 129.7, 128.8, 128.5, 126.1, 122.9, 120.0, 119.5, 117.9, 115.2, 112.5, 102.4, 74.2, 56.9, 56.5, 56.4, 50.3, 43.0, 42.5, 39.9, 39.7, 38.5, 37.3, 36.9, 36.4, 36.0, 32.1, 32.1, 29.9, 28.5, 28.2, 28.1, 24.5, 24.0, 23.0, 23.0, 22.8, 21.3, 19.6, 18.9, 18.1, 18.1, 17.8, 17.8, 13.9, 12.1.

HRMS (*m/z*): $[M + Na]^+$ calculated for $C_{64}H_{83}NNaO_5Si$: 996.5938found: 934.5792.

6.3.5. Removal of directing group:

Method 1: In a clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar, compound **2a** (278 mg, 0.5 mmol) was dissolved in 10 mL of THF, a solution of 1M TBAF (1.0 mL, 2.0 eq.) in THF was added drop wise at RT. The solution was stirred for 3 hours at room temperature. After completion of reaction, solvent was evaporated to dryness, and the residue was purified by chromatography using silica gel.

9. Ethyl (*E*)-3-(p-tolyl)acrylate:[4]



Column material: 100-200 mesh silica

Eluent: petroleum ether:ethyl acetate (98:2)

Yield: 92%

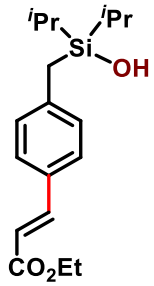
Physical appearance: Colourless liquid

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 6.39 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 1.33 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 144.7, 140.7, 131.9, 129.7, 128.2, 117.3, 77.6, 77.2, 76.9, 60.5, 21.5, 14.5.

Method 2: In a clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar, compound 2a (111 mg, 0.2 mmol) and *p*-toluenesulfonic acid (10 mol%) were dissolved in 3 mL of EtOH and 1 mL H_2O (EtOH/H_2O: 3/1). The solution was stirred at 110 °C for 16 hours. After being stirred, reaction mixture was removed from oil-bath and kept at room temperature. Ethanol was removed under reduced pressure and aqueous part was extracted by EtOAc. Organic part was evaporated to dryness and the residue was purified by column chromatography silica gel.

11. Ethyl (E)-3-(4-((hydroxydiisopropylsilyl)methyl)phenyl)acrylate:



Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (95:5)

Yield: 82%

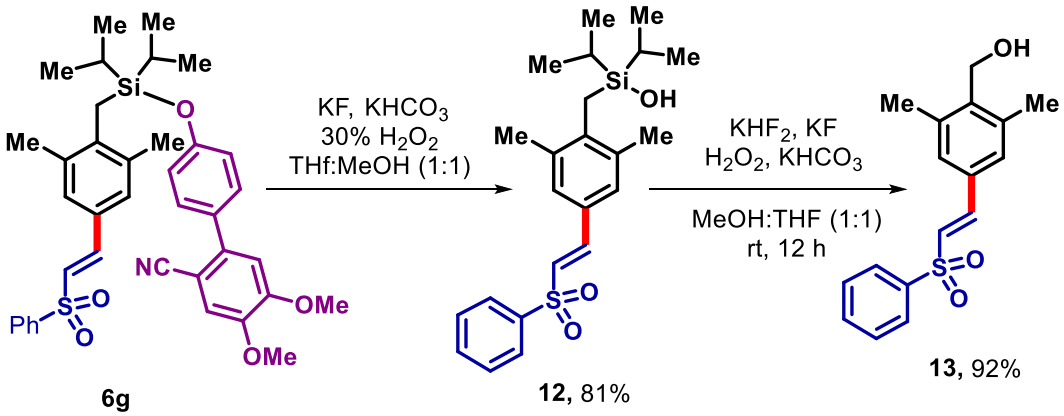
Physical appearance: Crystalline yellowish solid

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 16.0 Hz, 1H), 7.39 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 6.36 (d, J = 16.0 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 2.24 (s, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.03 – 0.98 (m, J = 10.8, 5.5 Hz, 14H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 167.5, 144.9, 142.8, 130.9, 129.2, 128.5, 116.8, 60.6, 22.2, 17.5, 17.4, 14.6, 12.9.

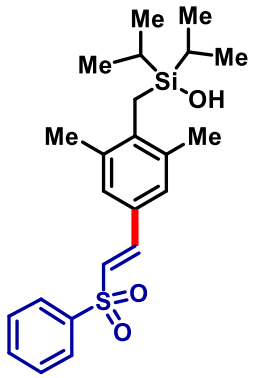
HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{18}H_{28}NaO_3Si$ 343.1700: found: 343.1694.

Diversification of *para*-olefinated products: Preparation of *para*-olefinated benzyl alcohol



Procedure: Procedure modified from literature:[12] The *para*-olefinated product **6g** (0.2 mmol) was added to a mixture of KF (0.4 mmol) and $KHCO_3$ (0.4 mmol) in MeOH (0.5 mL) and THF (0.5 mL). 30% H_2O_2 in THF (4 mmol) was added to the reaction mixture and stirred at 60 °C for 12 h. After being cooled to room temperature, the reaction mixture was treated with H_2O (2 mL). The mixture was then extracted with EtOAc (20 mL) and the combined organic phase was dried over Na_2SO_4 and removal of solvents under reduced pressure afforded the silanol in quantitive amount. The silanol derivative was dissolved in THF:MeOH (2 mL:2 mL). KHF_2 (125 mg, 1.6 mmol), KF (23 mg, 0.4 mmol), H_2O_2 (30% in THF, 0.15 mL, 1.6 mmol), and $KHCO_3$ (160 mg, 1.6 mmol) were added, and the mixture was stirred at room temperature for 12 h. The reaction was quenched with saturated solution of Na_2SO_3 and the resulting mixture was extracted with EtOAc (20 mL, then 2 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated by rotary evaporation. The crude benzyl alcohol derivative (**12**) was further purified by column chromatography.

12. (*E*)-(2,6-dimethyl-4-(2-(phenylsulfonyl)vinyl)benzyl)diisopropylsilanol



Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (93:7)

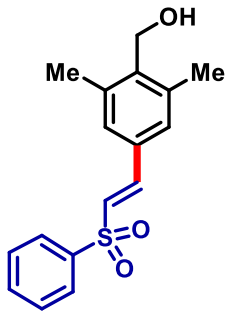
Yield: 81%

Physical appearance: Yellowish solid

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.4 Hz, 2H), 7.62 – 7.51 (m, 4H), 7.11 (s, 2H), 6.75 (d, *J* = 15.3 Hz, 1H), 2.31 (s, 6H), 2.25 (s, 2H), 1.03 (d, *J* = 6.5 Hz, 6H), 1.00 – 0.95 (m, 2H), 0.91 (d, *J* = 6.4 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 142.2, 141.5, 136.4, 133.3, 129.5, 128.5, 128.2, 127.8, 125.1, 21.5, 17.5, 17.5, 17.3, 14.0.

13. (*E*)-(2,6-dimethyl-4-(2-(phenylsulfonyl)vinyl)phenyl)methanol



Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (93:7)

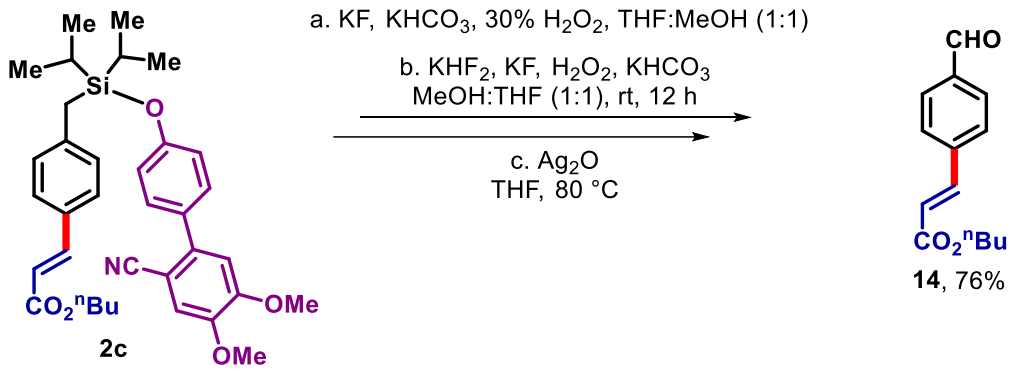
Yield: 92%

Physical appearance: Colourless solid

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.6 Hz, 2H), 7.63 – 7.58 (m, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.13 (s, 2H), 6.98 (s, 1H), 6.78 (d, *J* = 15.3 Hz, 1H), 2.84 (s, 1H), 2.27 (s, 6H), 2.18 (s, 2H).

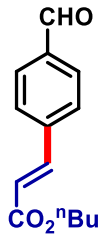
^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 141.3, 139.5, 137.5, 135.9, 133.4, 129.5, 128.0, 127.8, 125.8, 125.7, 77.5, 77.2, 76.9, 49.7, 20.7.

Diversification of *para*-olefinated products: Preparation of *para*-olefinated benzaldehyde



Procedure: As stated above the *para*-olefinated product **2c** was treated with **condition a** and **condition b** to produce the corresponding benzyl alcohol. The benzyl alcohol was then oxidized to benzaldehyde derivative **14** using silver oxide. In a closed cap reaction tube the benzyl alcohol (0.1 mmol) and Ag_2O (34 mg, 0.15 mmol) was taken and dissolved in THF (1 mL). the reaction mixture was stirred at 80 °C for overnight. The resulting reaction mixture was taken out and cooled to room temperature. Then the reaction mixture was filtered the celite pad and purified by column chromatography.

14. butyl (*E*)-3-(4-formylphenyl)acrylate



Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (90:10)

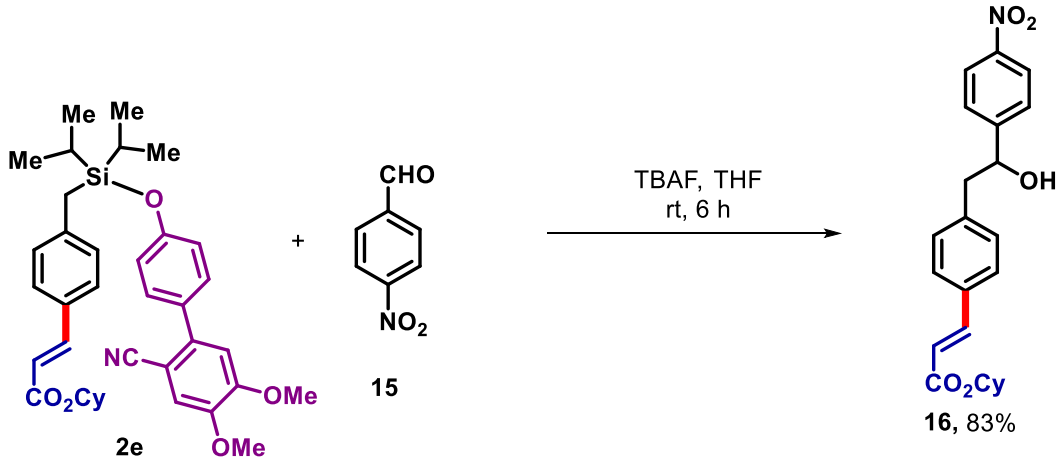
Yield: 76%

Physical appearance: Colourless solid

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.90 (d, J = 8.1 Hz, 2H), 7.73 – 7.66 (m, J = 12.4 Hz, 3H), 6.55 (d, J = 8.7 Hz, 1H), 4.23 (t, J = 6.7 Hz, 2H), 1.73 – 1.67 (m, 2H), 1.48 – 1.41 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H).

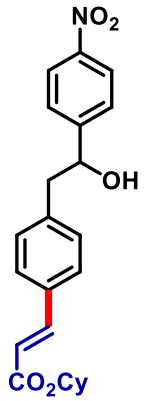
^{13}C NMR (126 MHz, $CDCl_3$) δ 191.7, 166.7, 143.0, 140.4, 137.4, 130.4, 128.7, 121.8, 77.5, 77.2, 76.9, 65.0, 30.9, 19.4, 13.9.

Diversification of *para*-olefinated products: Nucleophilic addition of silyl motif to aldehyde



Procedure modified from literature:[14] In a closed cap reaction tube, *para*-olefinated product (0.2 mmol, 1.0 equiv.) and corresponding aryl aldehyde (0.24 mmol, 1.2 equiv.) were dissolved in THF (1 mL). To the reaction mixture TBAF (1 (M) solution in THF, 0.2 mmol, 1 equiv) was added. The reaction mixture was stirred at room temperature for 12 hour. The reaction mixture was then extracted with ethyl acetate (20 mL, then 2 x 10 mL). were dried over Na_2SO_4 and concentrated by rotary evaporation. The crude benzyl alcohol derivatives (**16**) were further purified by column chromatography.

16. cyclohexyl (*E*)-3-(4-(2-hydroxy-2-(4-nitrophenyl)ethyl)phenyl)acrylate



Column material: 100-200 mesh silica

Eluent: petroleumether:ethyl acetate (85:15)

Yield: 83%

Physical appearance: Crystalline yellow solid

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 16.0 Hz, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 6.40 (d, J = 16.0 Hz, 2H), 5.04 (t, J = 5.7 Hz, 1H), 4.92 – 4.85 (m, 1H), 3.10 – 2.97 (m, 2H), 2.28 (s, 1H), 1.96 – 1.87 (m, 2H),

1.80 – 1.73 (m, 2H), 1.60 – 1.55 (m, 1H), 1.53 – 1.45 (m, 2H), 1.45 – 1.36 (m, 2H), 1.34 – 1.27 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 160.0, 147.6, 143.9, 139.3, 133.6, 130.3, 128.5, 126.9, 123.9, 119.1, 74.4, 73.0, 46.0, 31.9, 25.6, 24.0.

HRMS (*m*/*z*): $[M + Na]^+$ calculated for $C_{23}H_{25}NNaO_5$ 418.1625: found: 418.1624.

6.3.6. Kinetic Experiment:

Table 6.3.6.a: Kinetic experiment

	Substrate	Olefin	$[Rh(COD)Cl]_2$	$CuCl_2$+TFA	V_2O_5	DCE
Run 1	**0.1mmol**	0.2mmol	5 mol%	2 equiv	3equiv	1 mL
Run 2	**0.05mmol**	**0.2mmol (4equiv)**	5mol%	2 equiv	3 equiv	1 mL
Run 3	0.05 mmol	**0.3mmol (6equiv)**	5mol%	2 equiv	3 equiv	1 mL
Run 4 (**D_7-1a**)	**0.05 mmol (Deuterated substrate D_7-1a)**	0.2mmol (4equiv)	5mol%	2 equiv	3 equiv	1 mL

*the yield has been determined by 1H NMR of crude reaction mixture using trimethoxy benzene as internal standard

Determination of order with respect to substrate: Comparing Run 1 and Run 2

Run 1: 0.1 mmol of substrate

x_1 – 0.1021

y_1 – 3.4175

x_2 – 0.7448

y_2 – 11.3716

Slope $= R_1 = dy/dx = y_2 - y_1 / x_2 - x_1$

$= (11.3716 – 3.4575)/(0.7448 - 0.1021)$

$= 7.9141/0.6427 = 12.3138$

Run 2: 0.05 mmol of substrate

X_1 – 0.0955

Y_1 – 0.5603

X_2 – 0.7179

Y_2 – 4.5374

Slope = $R_2 = dY/dX = Y_2 - Y_1/X_2 - X_1$

$= (4.5374 - 0.5603)/(0.7179 - 0.0955)$

$= 3.9771/0.6224 = 6.3899$

We know

Rate = $dy/dx = k[substrate]^a[olefin]^b$

Now, $R_1/R_2 = \{dy/dx\}_{run1}/\{DY/DX\}_{run2} =$

$\{k[substrate]^a{}_{Run1}[olefin]^b{}_{run1}\}/\{k[substrate]^a{}_{run2}[olefin]^b{}_{run2}\}$

At t=0; $[olefin]_{run1} = [olefin]_{run2}$

- ⇨ $R_1/R_2 = [substrate]^a{}_{run1}/[substrate]^a{}_{run2}$
- ⇨ $12.3138/6.3899 = [substrate]^a{}_{run1}/[substrate]^a{}_{run2}$
- ⇨ $1.92 = [substrate]^a{}_{run1}/[substrate]^a{}_{run2}$
- ⇨ So $[substrate]^a{}_{run1}/[substrate]^a{}_{run2}$ is nearly equal to 2.0

At t=0; $[substrate]^a{}_{run1}/[substrate]^a{}_{run2} = [0.1/0.05]^a = 2^a$

So, $2.0 = 2^a$

log(2) = a*log(2)

So, a = 1.0

Which indicates that the reaction rate with respect to substrate is **one**.

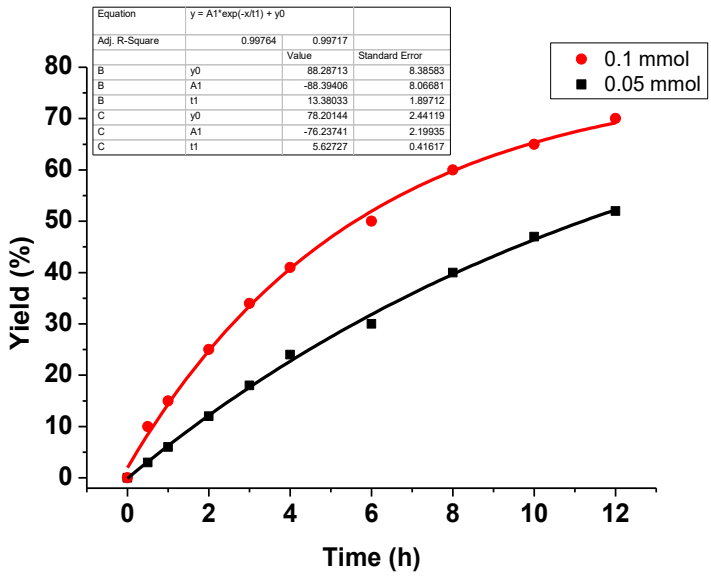


Figure 6.3.6.i.: Order determination with respect to the substrate

Determination of order with respect to olefin: Comparing Run 2 and Run 3

Run 2: 0.05 mmol and 4 equiv of olefin

x_1 – 0.1053

y_1 – 0.0198

x_2 – 0.6184

y_2 – 5.5119

Slope = $R_2 = y_2 - y_1 / x_2 - x_1$

$= (5.5119 – 0.0198)/(0.6184 - 0.1053)$

$= 5.4921/0.5131 = 10.7038$

Run3: 0.05 mmol and 6 equiv of olefin

X_1 – 0.1123

Y_1 – 0.8362

X_2 – 0.8390

Y_2 – 9.1008

Slope = $R_3 = dY/dX = Y_2 – Y_1 / X_2 – X_1$

$= (9.1008 – 0.8362)/(0.8390 - 0.1123)$

= 8.2646/0.7267

= 11.37

We know

Rate = dy/dx= k[substrate]^{a}[olefin]^{b}

Now, R_3/R_2={dY/dX}$_{run3}$ /{dy/dx}$_{run2}$ =

{k[substrate] ^{a}$_{Run3}$[olefin]^{b}$_{run3}$}/{k[substrate]^{a} $_{run2}$[olefin]^{b} $_{run2}$}

At t=0; [ssubstrate] $_{run2}$= [substrate] $_{run3}$

- ⇨ R_3/R_2 = [olefin]^{a} $_{run3}$/[olefin]^{a} $_{run2}$
- ⇨ 11.37/10.70 = [olefin]^{a} $_{run3}$/[olefin]^{a} $_{run2}$
- ⇨ 1.03 = [olefin]^{a} $_{run3}$/[olefin]^{a} $_{run2}$

At t=0; [olefin]^{a} $_{run3}$/[olefin]^{a} $_{run2}$ = [0.3/0.2]^{a} = 1.5^{a}

So, 1.06 which is nearly equal to 1= 1.5^{a}

So, log(1.06) = alog(1.5)

=> 0.0253 = a*0.1760

So, a = 0.14, Which indicates that the reaction rate with respect to olefin is zero, i.e. rate is independent on the amount of olefin.

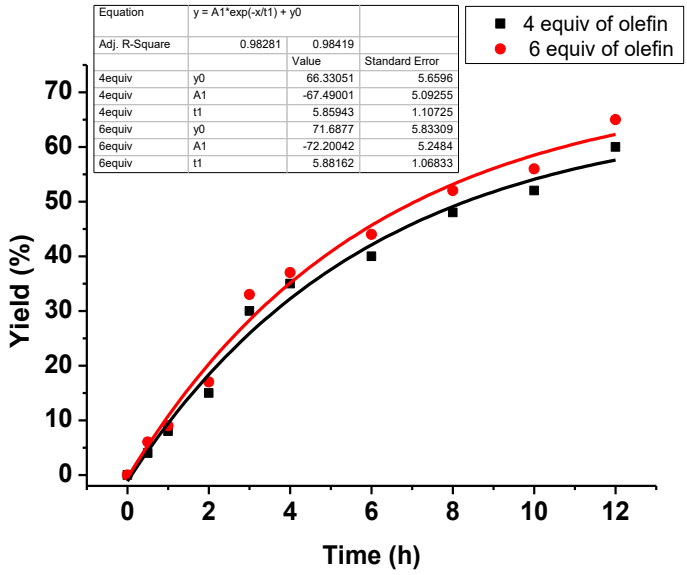


Figure 6.3.6.ii: Order determination with respect to the olefin

Determination of k_H/k_D: Comparing Run 2 and Run 4

Run 2: 0.05 mmol and 4 equiv. of olefin

x_1- 0.3834, y_1- 2.8772

x_2- 1.1783, y_2- 11.4023

dx = x_2 - x_1 = (1.1783 - 0.3834) = 0.7949

dy = y_2 - y_1 = (11.4023 - 2.8772) = 8.5251

Slope = R_2 = dy/dx = 8.5251/0.7949= 10.7247

Run 4: 0.05 mmol deuterated substrate (D_7-1a)

X_1= 0.2914, Y_1 = 0.8157
X_2= 1.6594, Y_2 = 6.3031
dX = X_2 – X_1 = 1.6594 - 0.2914= 1.368
dY= Y_2 – Y_1 = 6.3031– 0.8157= 5.4874
R_4 = dY/dX = 5.4874/1.368= 4.0112
We know
Rate = dy/dx= k[substrate]^a[olefin]^b
Now, R_2/R_4 ={ DY/DX }$_{run2}$/{dy/dx }$_{run4}$ = {K_H[substrate] ^{a} $_{Run2}$ [olefin] ^{b}$_{run2}$}/{K_D[substrate] ^{a} $_{run4}$ [olefin] ^{b} $_{run4}$}
At t=0; [olefin] $_{run2}$= [olefin] $_{run4}$ and [substrate] $_{run2}$ = [substrate] $_{run4}$

⇨ $R_2/R_4 = k_H/k_D$= 10.7247/4.0112 = 2.6

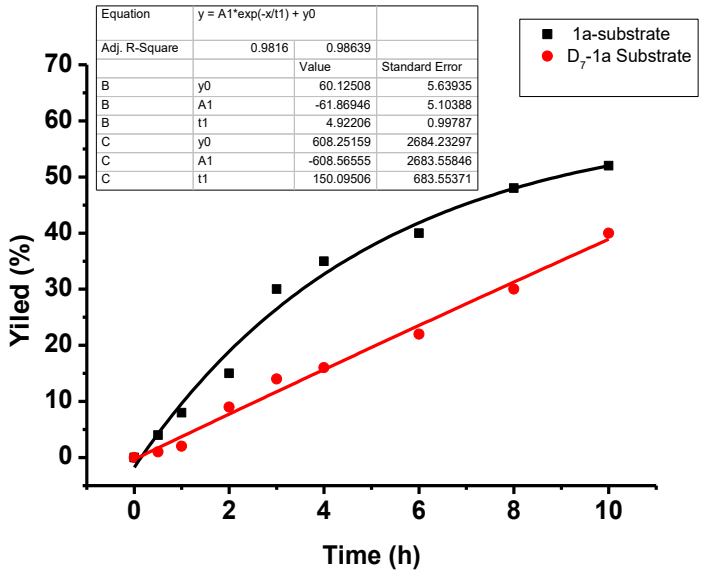


Figure 6.3.6.iii: k_H/k_D determination

Intermolecular KIE experiment:

An oven-dried screw cap reaction tube was charged with a magnetic stir-bar, **1a**(0.1 mmol, 45.9 mg), deuterated-**1aD_7-1a** (0.1 mmol, 46.6 mg), olefin (0.8mmol, 4.0 equiv), $[Rh(COD)Cl]_2$ (5mol%), $CuCl_2$ and TFA (2.0 equiv) and V_2O_5 (3 equiv) were taken. Subsequently, DCE (2 mL) was added and the reaction mixture was stirred vigorously for 20 h at 120 °C. The reaction mixture was then diluted with DCM.10 mLdilute ammonia

solutionwas added to the reaction mixture; the organic part was extracted with DCM and dried over magnesium sulfate. After evaporation of the solvent, the crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent. $P_H/P_D$was calculated from ^{1}H NMR spectrum of the isolated product. From NMR spectrum product distribution $P_H/P_D$was found 2.9.

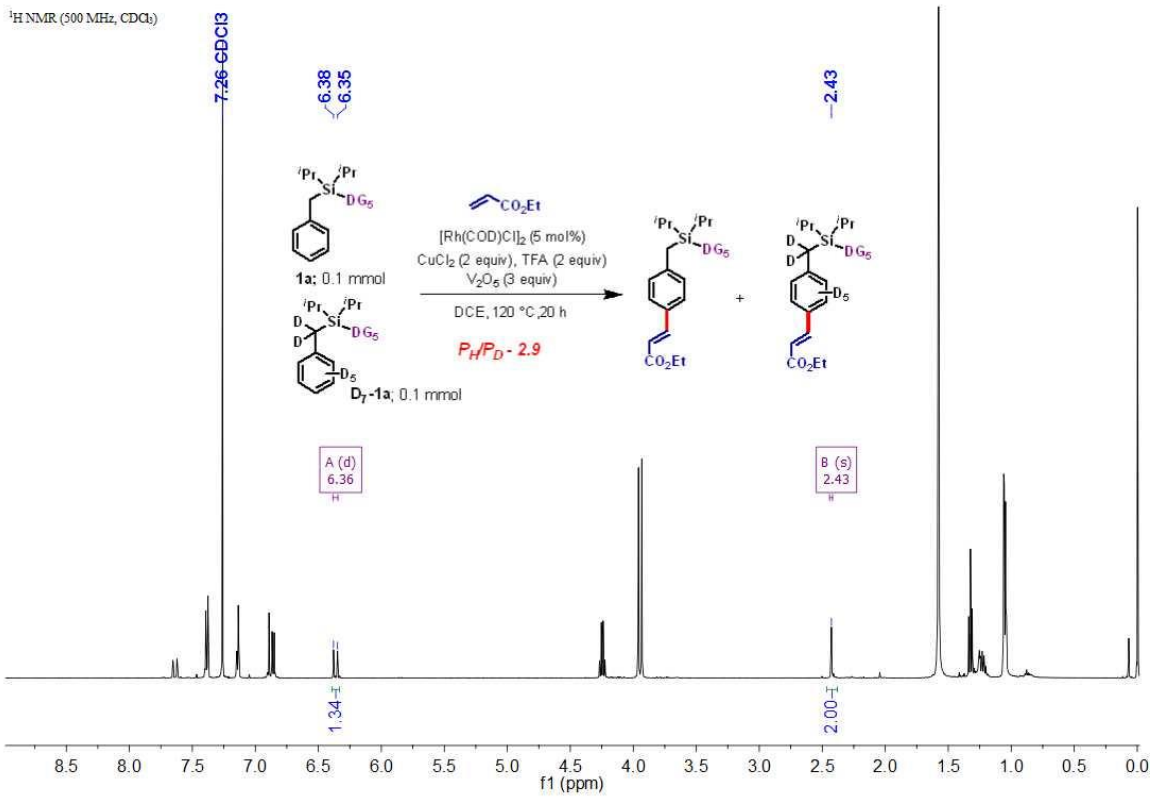


Figure 6.3.6.iv: P_H/P_D determination

In this spectrum peak at 2.43 ppm is corresponds to benzylic proton and total integration is 2.0and the doublet at 6.36 ppm coming from the styrenyl proton. Among this 1.34 proton, one proton is coming from compound **2a** is rest 0.34 is the contribution of deutarated substrate **D$_7$-1a**. And hence [P_H/P_D] = 1/0.34 = 2.9.

6.3.7. Computational Study

6.3.7.a. Analysis of the Origins of Regioselectivity in Rh-Catalyzed C–H Activation

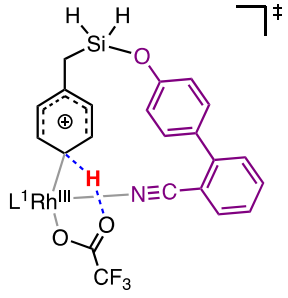
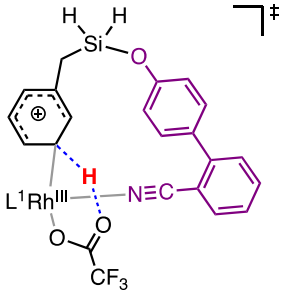
The origins of the *para*-regioselectivity in the Rh-catalyzed C–H activation reaction were explored by performing computations on a series of fragment structures derived from transition states **TS1-*para*** and **TS1-*meta***. The structures are shown in Table S12. Entry A of the table compares the energy (*E*) of the intact**TS1-*para***with that of **TS1-*meta***, showing the former to be 7.7 kcal/mol lower in energy. Entry B showsthe energies of the substrates alone, in the same geometry as found in the TS. The substrate fragment from**TS1-*para*** is 1.0 kcal/mol lower in energy than that from**TS1-*meta***. Entry C shows the$[RhL_n(CF_3CO_2)]^{2+}$unit. This fragment is

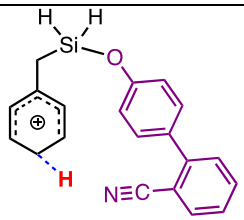
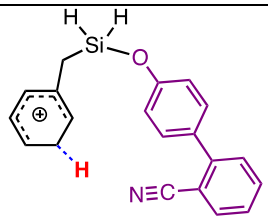
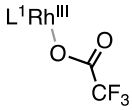
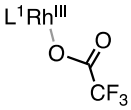
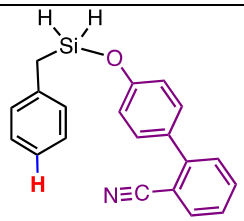
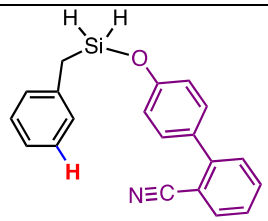
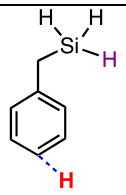
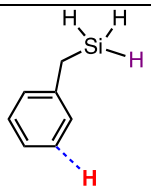
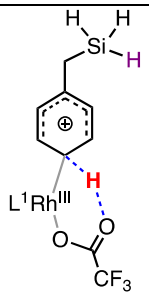
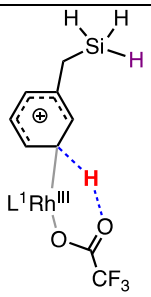
equienergetic in the two TSs. The results in entries B and C imply that, out of the total 7.7 kcal/mol energy difference between **TS1-*para*** and **TS1-*meta***, 1.0 kcal/mol is attributable to distortions of the substrate, no differences are ascribable to the $[RhL_n(CF_3CO_2)]^{2+}$unit, and the remainder, 6.7 kcal/mol, is therefore ascribed to differences in the strength of the interaction between the substrate and $[RhL_n(CF_3CO_2)]^{2+}$in the two TSs.

Entry D of the table contains structures wherein the substrate fragment was subjected to a partial optimization, allowing the reacting CH group and the two neighbouring CH groups to relax. For these structures, the *meta* fragment is found to be 0.4 kcal/mol lower in energy than the *para* fragment. This indicates that the conformational preorganization of the DG is approximately equivalent in *meta* vs *para* attack, in fact slightly favouring *meta* attack. Therefore, the origin of the 1 kcal/mol energy difference between the unrelaxed substrate fragments (entry B) must be localized near the site of reactivity rather than within the rest of the scaffold.

In entry E, the substrate has been truncated by replacing the DG with an H atom (positioned at a distance of 1.09 Å from the Si atom). This silylmethylarene fragment is 2.7 kcal/mol lower in energy in the *para* TS than in the *meta* TS. In entry F, the samesilylmethylareneis bound to $[RhL_n(CF_3CO_2)]^{2+}$. This fragment differs by 8.9 kcal/mol between the two TSs, favouring *para*. This result suggests that the main origin of the *para*-regioselectivity lies in the interaction between the silylmethylarene moiety and $[RhL_n(CF_3CO_2)]^{2+}$. The silylmethylarene has arenium character in the TS and its interaction with $[RhL_n(CF_3CO_2)]^{2+}$ is enhanced in the *para* TS, becausethe C–Si bond can stabilize the areniumcation, in a variant of the β-silicon effect.[15]

Table 6.3.7.i. Energy comparison of structural fragmentsof**TS1-*para*** and **TS1-*meta***.[a]

Structure	***Para***	***Meta***	**□*E* (*meta* – *para*)**
A.Full TS			7.7

B. Substrate			1.0
C.$[RhL_n(CF_3CO_2)]^{2+}$			0.0
D. Substrate after allowing reacting CH group and two neighbouring CH groups to relax			–0.4
E. Truncated substrate after removal of DG			2.7
F. Truncated substrate bound to RhL_n			8.9

[a]L^1 = COD. Δ*E* (*meta* – *para*) calculated with M06/6-311+G(d,p)-SDD in SMD dichloroethane (kcal/mol).

6.3.7.b. Computational Investigations of DG Preorganization inSeveral C–H Activation Mechanisms

Many Rh(III)-catalyzed C–H functionalizations utilize a Rh(III) catalyst precursor such as $[RhCp^*Cl_2]_2$. In the chemistry reported herein, however, the catalyst precursor is a Rh(I) species, $[Rh(COD)Cl]_2$. In our mechanistic study, we therefore considered the possibility that C–H activation may occur either before or after the oxidation of Rh(I) to Rh(III). We performed DFT calculations on three different C–H activation processes, as follows:

Mechanism **1**: A Rh(III)-mediated electrophilic aromatic substitution pathway mediated by $[Rh^{III}(COD)(CF_3CO_2)]^{2+}$

Mechanism **2**: A Rh(I)-mediated concerted metalation–deprotonation pathway mediated by $[Rh^{I}(COD)(CF_3CO_2)]$

Mechanism **3**: A Rh(I)-mediated oxidative addition pathway mediated by $[Rh^{I}(COD)Cl]$.

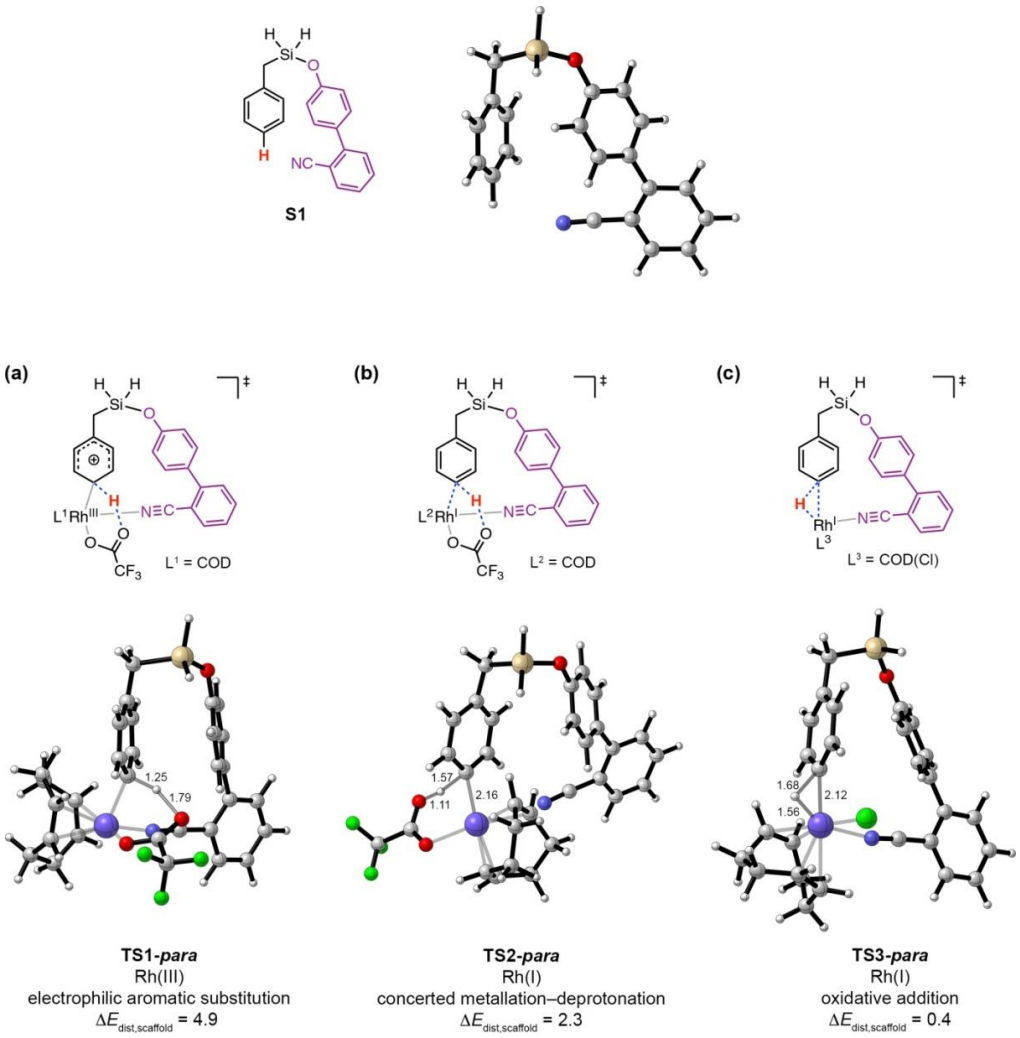


Figure 6.3.7.i. Model substrate **S1** and the transition states for*para*-C–H bond activation of **S1**according to (a) mechanism **1**, (b) mechanism **2**, and (c) mechanism **3**.The energy required to distort the **S1** scaffold into each TS geometry ($\Delta E_{dist,scaffold}$) is shown. Distances in Å, $\Delta E_{dist,scaffold}$ in kcal/mol.

A full computational characterization of these three mechanisms will be reported in due course. For the present study, however, we have examined the transition states for *para*-C–H bond

activation of the model substrate **S1**in each of the three mechanisms **1**–**3**. The transition states, calculated with M06, are shown in Figure S4.

For each TS, a calculation was performed to quantify the amount of conformational reorganization that the substrate undergoes on going from its ground-state geometry to the TS.The atoms of the RhL_n unit were deleted from each TS, leaving the substrate remaining. A partial geometry optimization was then performed in which the *para*–CH group and the two adjacent CH groups were allowed to relax while holding the remainder of the substrate fixed in the TS geometry. This was done in order to determine the energy associated withthe reorganization of the scaffold, as opposed to the reorganization of the atoms involved in bond-forming and bond-breaking. The energy of the resulting partially-relaxed substrate was calculated with M06/6-311+G(d,p) in SMD dichloroethane. The energies associated with distortion of the scaffold, $\Delta E_{\text{dist,scaffold}}$, are shown in Figure S4.The scaffold distortion energies in **TS1-*para***, **TS2-*para***, and **TS3-*para*** are all small:4.9, 2.3, and 0.4 kcal/mol, respectively, indicating that the preorganization of the DG for distal *para*-C–H activation is quite general for a range of Rh-catalyzed C–H activation mechanisms.

Returning to mechanism **1**, electrophilic aromatic substitution by Rh(III), we also performed calculations to determine how the C–H activation barrier is influenced by (a) the nitrile group and (b) the methoxy groups on the DG. Figure S5(a) shows a transition state calculated for the Rh(III)-catalyzed C–H activation wherein the nitrile group is not coordinated to rhodium (**TS1-*para*-2**). This TS is 22.8 kcal/mol higher in energy than the corresponding TS that has the nitrile bound to rhodium (**TS1-*para***). Thus, the coordination of the nitrile to Rh strongly activates the substrate toward C–H activation. Figure S5(b) shows a transition state (**TS1-*para*-3**) corresponding to the C–H activation of a dimethoxy-substituted substrate, **S2**. The barrier for C–H activation of this substrate is 1.6kcal/mol lower than that for the methoxy-free **TS1-*para***, consistent with the greater catalytic activity of the dimethoxy-substituted directing group $\mathbf{DG_5}$ relative to the unsubstituted $\mathbf{DG_1}$.

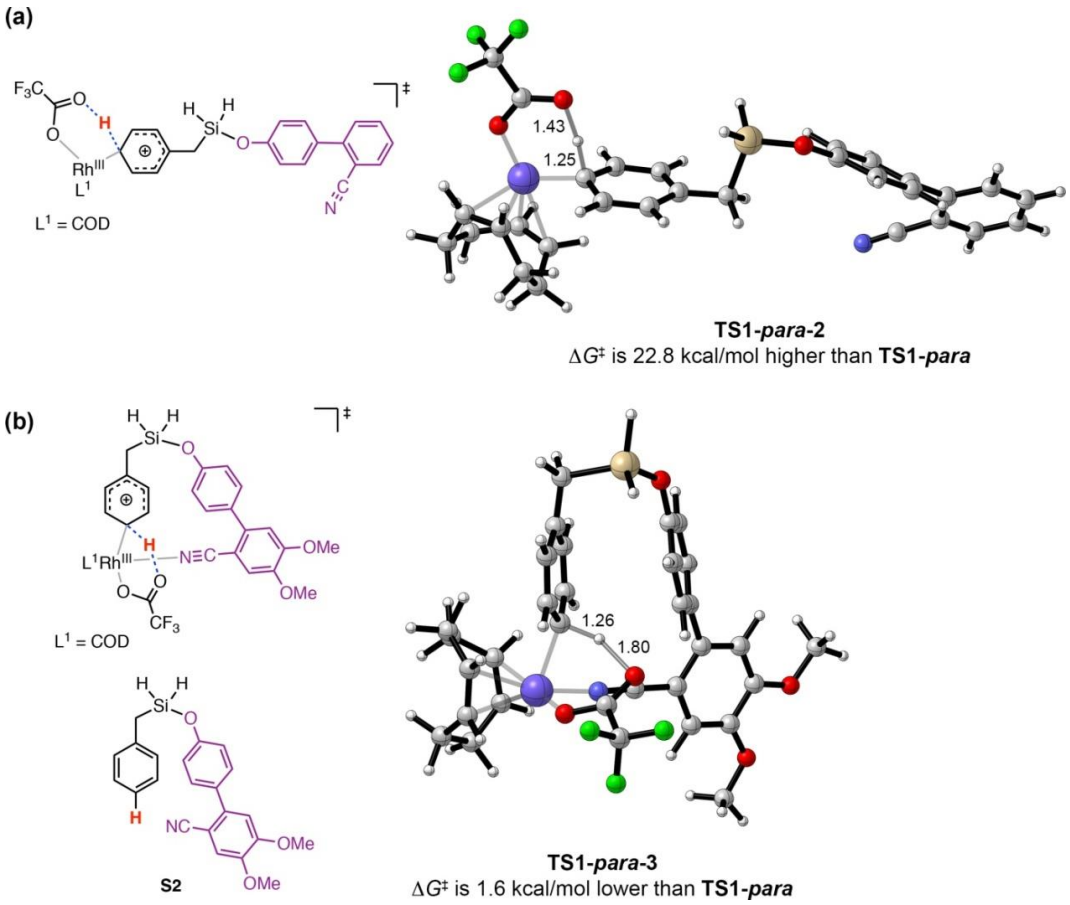


Figure 6.3.7.ii. Transition states for *para*-C–H bond activation of (a) the model substrate **S1**without Rh–nitrile coordination, and (b) the dimethoxy-substituted substrate **S2**. Distances in Å, $\Delta G^{\ddagger}$ in kcal/mol.

6.3.8. Computational Methods

Density functional theory calculations were performed in Gaussian 09[16] and Gaussian 16.[17] The M06 functional[18] was used, as has been previously used in other computational studies of Rh-catalyzed C–H activation.[19] For geometry optimizations, a mixed basis set consisting of 6-31G(d,p) on non-metal atoms and LANL2DZ on rhodium was used, in conjunction with the SMD implicit model[20] to simulate the solvent, dichloroethane. Vibrational frequency calculations were performed to characterize each species as a ground state or transition state and to obtain thermochemical quantities.Errors in computed entropies, introduced by the treatment of low frequency modes as harmonic motions, were minimized by use of Truhlar's approximation[21] in which all harmonic frequencies below 100 cm^{-1} were raised to exactly 100 cm^{-1} before evaluation of the vibrational component of the thermal contribution to entropy. Subsequently, single-point energy calculations were performed with M06 using a mixed basis

set consisting of 6-311+G(d,p) on non-metal atoms and SDD on rhodium, in SMD dichloroethane. Gibbs free energies were obtained by adding the thermochemical corrections derived from the M06/6-31G(d,p)-LANL2DZ(SMD) frequency calculations (after application of Truhlar's approximation) to the M06/6-311+G(d,p)-SDD(SMD) single-point energies and are reported at a standard state of 1 mol/L and 298.15 K.

The following section lists the Cartesian coordinates of optimized species along with the following energies (in Hartree):

E: Sum of M06/6-31G(d,p)-LANL2DZ electronic potential energy and free energy of solvation in dichloroethane

G: M06/6-31G(d,p)-LANL2DZ Gibbs free energy in solution at 1 mol/L and 298.15 K after correction of low-frequency vibrational modes

E_{LBS}: Sum of M06/6-311+G(d,p)-SDD electronic potential energy and free energy of solvation in dichloroethane

G_{tot}: Total M06/6-311+G(d,p)-SDD Gibbs free energy in dichlorethaneat 1 mol/L and 298.15 K

6.3.9. Computed Geometries and Energies

S1

C	-1.653563	-2.971560	0.032224
C	-1.623161	-2.181174	-1.113560
C	-2.542075	-1.150200	-1.277412
C	-3.507754	-0.890156	-0.300558
C	-3.537746	-1.698362	0.840802
C	-2.619400	-2.730681	1.006254
C	1.636268	0.951209	0.048536
C	1.282007	2.077380	-0.706442
C	-0.030575	2.515473	-0.767215
C	-1.028195	1.839218	-0.062472
C	-0.689179	0.732324	0.716891
C	0.626719	0.293664	0.760187
C	5.758602	-0.272166	0.218719
C	5.400785	1.070013	0.315796
C	4.066065	1.448718	0.258086
C	3.043201	0.508294	0.099468
C	3.423794	-0.846445	-0.015575
C	4.770892	-1.228260	0.050121
C	2.466202	-1.878280	-0.267416
N	1.731755	-2.752914	-0.491194
C	-4.421113	0.291831	-0.421906
Si	-3.733565	1.779552	0.494952
H	-3.515442	1.436163	1.922694
H	-4.629271	2.948393	0.367257
O	-2.294131	2.307743	-0.184581

```
H   -0.924511   -3.767838    0.163236
H   -0.870986   -2.361721   -1.878729
H   -2.504457   -0.519824   -2.166218
H   -4.286619   -1.506130    1.609777
H   -2.656289   -3.347875    1.901621
H    2.046754    2.602332   -1.275929
H   -0.308532    3.377401   -1.369004
H   -1.450580    0.192542    1.276716
H    0.865631   -0.571241    1.376582
H    6.801826   -0.571079    0.268435
H    6.167745    1.829326    0.447721
H    3.798087    2.498006    0.360918
H    5.026628   -2.280395   -0.046796
H   -4.580594    0.570553   -1.471499
H   -5.409364    0.081076    0.011716
0 imaginary frequencies
E = -1191.232450
G = -1190.963920
E_LBS = -1191.463731
G_tot = -1191.195201
```

[Rh(COD)(CF_3CO_2)]$^{2+}$

```
Rh   0.396952   -0.054225    0.061793
C    2.173447    0.306583   -1.556173
C    3.327659   -0.601013   -1.372725
C    2.905466   -1.802926   -0.505688
C    2.205468   -1.459775    0.754658
C    2.272927   -0.276975    1.476707
C    3.147682    0.918064    1.275228
C    2.376467    1.942510    0.447502
C    1.809108    1.450553   -0.823629
O   -1.464978    0.612742   -0.710204
C   -2.152412   -0.066770    0.115041
O   -1.617676   -0.760123    0.999847
C   -3.676170   -0.012124   -0.054225
F   -4.083488    1.250203   -0.007559
F   -3.995100   -0.517812   -1.241474
F   -4.282758   -0.704351    0.891880
H    1.513404    0.076945   -2.400419
H    1.102075    2.123974   -1.315162
H    2.267958   -2.483748   -1.082725
H    4.188361   -0.082870   -0.948541
H    3.609320   -0.988618   -2.356835
H    3.801780   -2.393383   -0.251838
H    1.525919    2.357682    1.027906
H    2.975446    2.849703    0.241061
H    4.111999    0.668873    0.828476
H    3.350606    1.357771    2.256607
H    1.625025   -2.265966    1.206916
H    1.640754   -0.242318    2.370958
0 imaginary frequencies
E = -946.885595
G = -946.713694
E_LBS = -948.150660
G_tot = -947.978759
```

TS1-*para*

```
C   -1.341052   -3.328249   -0.317161
C   -1.464547   -2.262029   -1.248590
C   -0.682277   -1.152698   -1.134329
```

C	0.307357	-1.051002	-0.088275
C	0.517629	-2.211715	0.751997
C	-0.313830	-3.287997	0.663885
Rh	1.970260	0.196370	-0.558481
C	4.056331	-0.796928	-0.737431
C	4.712598	-0.273837	-1.981222
C	3.958438	0.920147	-2.574063
C	2.479648	0.758702	-2.707850
C	1.749726	-0.409081	-2.827626
C	2.292662	-1.793494	-3.088667
C	2.603091	-2.608566	-1.833654
C	3.125335	-1.813540	-0.676457
N	0.502386	1.682140	-0.572571
C	-0.428211	2.375751	-0.545609
O	2.331755	0.331979	1.489218
C	1.463465	0.616938	2.382117
O	0.241121	0.651738	2.303854
C	2.143362	0.906681	3.738603
F	2.810425	-0.174170	4.148516
F	3.014273	1.908464	3.617637
F	1.256851	1.229709	4.667848
H	-0.879010	-0.293212	-1.768571
H	4.457106	-0.442906	0.214557
H	2.977704	-2.251404	0.309966
C	-2.350087	-4.371073	-0.270134
H	-2.252507	-2.310215	-1.997055
H	-0.071309	-0.218606	0.765645
H	1.250829	-2.167131	1.553954
H	-0.230975	-4.106758	1.375358
H	4.136564	1.810624	-1.952715
H	4.823250	-1.075947	-2.716842
H	5.721512	0.058983	-1.718966
H	4.366833	1.180289	-3.562774
H	1.700265	-3.138024	-1.508752
H	3.336939	-3.396162	-2.059704
H	3.177293	-1.705461	-3.727958
H	1.546347	-2.335693	-3.677874
H	1.930496	1.692151	-2.846709
H	0.697167	-0.258834	-3.059243
C	-1.528881	3.273467	-0.589738
C	-1.233520	4.633744	-0.777990
C	-2.263320	5.542906	-0.940886
C	-3.581949	5.093594	-0.930231
C	-3.871968	3.749115	-0.736322
C	-2.862119	2.804396	-0.545590
H	-0.196032	4.955802	-0.806454
H	-2.040112	6.595947	-1.083785
H	-4.395544	5.801945	-1.062484
H	-4.907243	3.418534	-0.700259
C	-3.227467	1.395293	-0.293601
C	-4.182989	0.766318	-1.104438
C	-4.594013	-0.530208	-0.844261
C	-4.062299	-1.223128	0.244132
C	-3.133847	-0.606045	1.082386
C	-2.715478	0.690548	0.802896
H	-4.598265	1.299783	-1.957184
H	-5.322560	-1.028101	-1.479062
O	-4.503560	-2.497020	0.441252
H	-2.735087	-1.131840	1.949444
H	-2.006148	1.174592	1.472708
Si	-3.701751	-3.843233	0.994374

```
H   -4.713562   -4.906194    1.055760
H   -3.020948   -3.597690    2.282841
H   -1.970958   -5.316191    0.141431
H   -2.855136   -4.532321   -1.228829
```

This TS was located as the maximum in a plot of Δ*G* vs C–H distance in the precursor complex (arenium ion) corresponding to a reaction coordinate in which the C–H bond stretches and the proton moves towards the trifluoroacetate oxygen.

0 imaginary frequencies

E = -2138.224828

G = -2137.757646

E_{LBS} = -2139.717803

G_{tot} = -2139.250621

TS1-*meta*

```
C   -0.053579   -3.736779    1.573572
C   -0.755972   -3.199841    0.476895
C   -0.342975   -1.969264   -0.007474
C    0.739728   -1.257188    0.601896
C    1.428529   -1.856560    1.709416
C    0.993514   -3.063617    2.206296
C   -1.909943   -3.944356   -0.111266
Si  -3.464145   -4.020593    0.971611
O   -4.540833   -2.812999    0.538514
C   -4.210814   -1.521339    0.281974
C   -4.903377   -0.861477   -0.733327
C   -4.577316    0.446047   -1.053007
C   -3.547955    1.116744   -0.379719
C   -2.890802    0.456782    0.664272
C   -3.222404   -0.849035    1.002575
C   -3.182703    2.489985   -0.769174
C   -1.838702    2.873668   -0.978804
C   -1.492062    4.186598   -1.336562
C   -2.488351    5.131507   -1.502005
C   -3.820963    4.764267   -1.321410
C   -4.160602    3.465915   -0.962533
C   -0.794647    1.915693   -0.899252
N    0.082673    1.156454   -0.866648
Rh   1.831025    0.065181   -0.649970
C    1.817872   -0.248146   -2.924949
C    3.150094    0.339291   -3.254670
C    4.343866   -0.212414   -2.461724
C    4.077289   -0.324733   -0.986549
C    3.583373   -1.433441   -0.327805
C    3.218798   -2.749533   -0.943987
C    2.516344   -2.651566   -2.296311
C    1.547143   -1.502906   -2.415824
O    2.329899    1.091059    1.099949
C    1.458205    1.461804    1.949303
O    0.296319    1.073367    2.090020
C    2.017013    2.518434    2.924148
F    2.468710    3.570771    2.243880
F    1.094555    2.929931    3.776838
F    3.032623    1.996570    3.610957
H    4.444721    0.491107   -0.359814
H    3.724852   -1.437328    0.752809
H   -0.891774   -1.509741   -0.828541
H    2.224020   -1.314530    2.212684
H    1.470003   -3.497233    3.080290
H   -0.350210   -4.715132    1.951393
```

H	3.078499	1.425598	-3.101831
H	4.661588	-1.181968	-2.856739
H	5.182592	0.476964	-2.598098
H	3.325372	0.216225	-4.334364
H	2.580013	-3.293098	-0.238379
H	4.135926	-3.350560	-1.029996
H	3.244427	-2.580469	-3.110961
H	1.957567	-3.577406	-2.466147
H	0.959686	0.348342	-3.239167
H	0.489974	-1.757384	-2.374009
H	-0.446924	4.441787	-1.490850
H	-2.230300	6.150330	-1.774976
H	-4.606249	5.504271	-1.452296
H	-5.202869	3.201062	-0.800298
H	-5.103899	0.947719	-1.862434
H	-5.682141	-1.395991	-1.271274
H	-2.721905	-1.338285	1.838427
H	-2.124630	0.974490	1.241463
H	-4.210365	-5.267880	0.733451
H	-3.061021	-3.897013	2.394157
H	-1.617527	-4.990938	-0.278644
H	-2.187234	-3.535746	-1.091373
H	0.243321	-0.271291	1.211243

This TS was located as the maximum in a plot of ΔG vs C–H distance in the precursor complex (arenium ion) corresponding to a reaction coordinate in which the C–H bond stretches and the proton moves towards the trifluoroacetate oxygen.
1 imaginary frequency
E = -2138.213864
G = -2137.748546
E_{LBS} = -2139.705546
G_{tot} = -2139.240228

TS2-*para*

C	-0.841716	2.052584	1.366300
C	0.010549	0.978608	1.137394
C	1.266393	1.137364	0.522770
C	1.648329	2.461121	0.224434
C	0.787753	3.536157	0.412608
C	-0.485807	3.342453	0.962076
Rh	2.127959	-0.335420	-0.801641
C	0.729176	0.361575	-2.260979
C	1.411048	0.385674	-3.603300
C	2.312300	-0.827216	-3.858670
C	3.036051	-1.264095	-2.605569
C	2.592756	-2.258560	-1.740806
C	1.300563	-3.025104	-1.844341
C	0.097819	-2.151958	-2.216917
C	0.182368	-0.761653	-1.618628
C	-2.305336	-2.517671	0.884028
N	-1.154111	-2.345204	0.906019
H	1.730244	-1.663490	-4.264185
H	3.047522	-0.570360	-4.630439
H	2.021498	1.298675	-3.641408
H	0.663408	0.490040	-4.406985
H	-0.016773	-2.084257	-3.306228
H	-0.814248	-2.635071	-1.844058
H	1.111831	-3.475305	-0.860401
H	1.401788	-3.864480	-2.551279
H	3.333423	-2.693057	-1.064193

```
H     4.086224   -0.973754   -2.528890
H    -0.537083   -0.558497   -0.822763
H     0.365983    1.338067   -1.926144
C    -3.703489   -2.813424    0.888064
H     2.348239    0.470978    1.446816
H     2.636730    2.649524   -0.202231
H     1.091503    4.542612    0.120092
H    -1.816981    1.885675    1.827288
H    -0.322972   -0.019836    1.426074
C    -4.680873   -1.814299    0.696208
C    -6.020192   -2.206704    0.794298
C    -6.378105   -3.522153    1.057511
C    -5.401026   -4.498516    1.230803
C    -4.065277   -4.142880    1.149000
H    -6.794820   -1.459918    0.635045
H    -7.430458   -3.788522    1.117090
H    -5.677688   -5.529525    1.432314
H    -3.282901   -4.883136    1.296361
C    -4.361043   -0.402444    0.399298
C    -3.421372   -0.036464   -0.572689
C    -5.070451    0.616767    1.048679
C    -4.857793    1.950140    0.736004
H    -5.793570    0.357341    1.819569
C    -3.931189    2.296304   -0.247487
H    -5.405799    2.741162    1.242313
C    -3.208910    1.296990   -0.901989
H    -2.872735   -0.805208   -1.116164
H    -2.491509    1.560487   -1.678413
O    -3.804428    3.611744   -0.564508
Si   -2.426784    4.561627   -0.615033
C    -1.472730    4.467137    1.006731
H    -1.538955    4.135264   -1.727642
H    -2.966889    5.912843   -0.877097
H    -0.971882    5.434491    1.150535
H    -2.195091    4.349468    1.826478
O     4.107981   -0.460340    0.208702
C     4.135479   -0.221696    1.414832
O     3.176268    0.217049    2.136895
C     5.433006   -0.436799    2.204071
F     6.382851   -0.956928    1.442931
F     5.212957   -1.255469    3.230132
F     5.861891    0.729098    2.684671
1 imaginary frequency
E = -2138.597866
G = -2138.136824
```

TS3-*para*

```
C    -1.307027    2.824618    1.233049
C    -0.138530    2.075572    1.123146
C     0.501286    1.886661   -0.110119
C    -0.055404    2.549323   -1.216316
C    -1.207502    3.320117   -1.102160
C    -1.864674    3.461385    0.123392
Rh    2.131143    0.540396   -0.272376
C     2.439488    0.140964    1.873749
C     3.127886   -1.183710    2.064448
C     4.222461   -1.504063    1.039089
C     3.946021   -0.953523   -0.339368
C     4.366939    0.279616   -0.780765
C     5.098750    1.319848    0.024884
```

```
C     4.571321    1.507375    1.449392
C     3.069155    1.348585    1.573976
Cl    1.731793    0.276173   -2.672608
C     0.088462   -2.391691   -0.137636
N     0.852119   -1.518737   -0.073090
H     5.194532   -1.133394    1.388062
H     4.327838   -2.592984    0.970725
H     2.359035   -1.963076    2.028106
H     3.542436   -1.216371    3.085167
H     5.057181    0.805868    2.139192
H     4.846702    2.508914    1.798723
H     5.010400    2.272042   -0.512816
H     6.174792    1.084319    0.047505
H     4.339177    0.457554   -1.855258
H     3.591242   -1.654852   -1.095027
H     2.512129    2.258487    1.798339
H     1.438272    0.180462    2.302453
C    -0.807112   -3.502675   -0.194555
H     2.141455    2.098744   -0.396547
H     0.423799    2.455125   -2.187787
H    -1.611578    3.817767   -1.985357
H    -1.798667    2.914374    2.202500
H     0.251264    1.625217    2.033277
C    -2.198133   -3.332352   -0.022109
C    -2.984127   -4.488343   -0.000715
C    -2.425144   -5.749688   -0.159522
C    -1.053117   -5.898457   -0.348358
C    -0.243700   -4.775006   -0.362329
H    -4.060668   -4.386135    0.117781
H    -3.069279   -6.625529   -0.146960
H    -0.617228   -6.884753   -0.479770
H     0.831986   -4.864793   -0.491401
C    -2.820467   -2.003896    0.132660
C    -2.458368   -0.926201   -0.683374
C    -3.817197   -1.795185    1.095385
C    -4.416724   -0.555490    1.249206
H    -4.110906   -2.613999    1.749845
C    -4.036116    0.512308    0.433589
H    -5.180556   -0.390798    2.005292
C    -3.056722    0.317125   -0.541198
H    -1.712468   -1.056966   -1.465918
H    -2.743889    1.134123   -1.187785
O    -4.651224    1.701729    0.640823
Si   -4.610733    3.109694   -0.271999
C    -3.165501    4.197306    0.229763
H    -4.518230    2.755016   -1.709527
H    -5.900687    3.768880    0.022875
H    -3.184437    5.078365   -0.428031
H    -3.337596    4.554087    1.253431
1 imaginary frequency
E = -2072.770140
G = -2072.332453
```

TS1-*para*-2

```
C    11.019850   -1.287974   -0.820350
C    10.962910    0.000279   -0.295261
C     9.738824    0.593356   -0.012751
C     8.534309   -0.076151   -0.242932
C     8.608531   -1.386584   -0.762379
C     9.843383   -1.982332   -1.050850
```

C	7.249601	0.578484	0.074662
C	7.097779	1.270956	1.283070
C	5.898822	1.882160	1.611766
C	4.824318	1.815273	0.727118
C	4.962631	1.158220	-0.494460
C	6.166810	0.542635	-0.809831
O	3.667405	2.432163	1.101065
Si	2.118595	2.084721	0.609587
C	1.742105	0.248178	0.973898
C	0.313953	0.031624	0.733302
C	-0.150541	-0.275903	-0.568688
C	-1.493465	-0.399006	-0.807891
C	-2.438881	-0.113670	0.224113
C	-1.969672	0.090511	1.555127
C	-0.620524	0.224214	1.774664
Rh	-4.211013	-0.919004	-0.543576
O	-5.147900	0.978341	-0.566011
C	-4.571637	2.099373	-0.515356
C	-5.525270	3.277549	-0.796937
F	-6.029901	3.147881	-2.022682
C	7.431549	-2.175598	-0.954730
N	6.492455	-2.844990	-1.110230
C	-5.904582	-1.488428	0.687895
C	-4.855730	-1.150153	1.562921
C	-4.075564	-2.157327	2.348342
C	-3.548087	-3.329861	1.522000
C	-3.244594	-2.979197	0.087726
C	-4.119549	-3.125185	-0.972505
C	-5.581053	-3.451319	-0.889456
C	-6.315182	-2.892522	0.343646
O	-3.377419	2.338022	-0.282171
F	-6.531079	3.261563	0.074121
F	-4.904617	4.441464	-0.711830
H	-6.163447	-3.535067	1.217433
H	-7.386859	-2.890135	0.126757
H	-6.057982	-3.066595	-1.799895
H	-5.706426	-4.543340	-0.932922
H	-4.252151	-4.168728	1.532616
H	-2.625751	-3.698836	1.979888
H	-3.251762	-1.661748	2.865892
H	-4.745405	-2.513677	3.146528
H	-4.860503	-0.124514	1.938577
H	-6.598482	-0.689709	0.418976
H	-2.191660	-2.858572	-0.170008
H	-3.688052	-3.136230	-1.975890
H	-2.801838	1.053682	-0.021617
H	-1.848204	-0.642508	-1.813096
H	0.568368	-0.421708	-1.372115
H	-0.259202	0.490775	2.765794
H	-2.666482	0.302688	2.361218
H	2.374504	-0.348502	0.305187
H	2.023338	0.069568	2.018562
H	1.911734	2.315361	-0.838002
H	1.243151	2.939360	1.430089
H	5.771925	2.405227	2.556090
H	4.142135	1.140460	-1.210478
H	7.927433	1.307698	1.986214
H	6.270280	0.049840	-1.774526
H	9.706080	1.608517	0.377025
H	11.880923	0.552366	-0.109675
H	9.862966	-2.996287	-1.441998

```
H   11.976841   -1.751363   -1.043082
1 imaginary frequency
E = -2138.181856
G = -2137.721315
E_LBS = -2139.674901
G_tot = -2139.214360
```

S2

```
C    1.514330    2.858456    0.277779
C    1.555154    1.903827    1.290993
C    2.698064    1.133843    1.481593
C    3.818654    1.299497    0.662027
C    3.768317    2.267300   -0.347493
C    2.627625    3.039190   -0.539582
C   -0.265109   -1.096941   -0.220719
C    0.570415   -0.535375   -1.194086
C    1.918781   -0.852606   -1.255953
C    2.467174   -1.720040   -0.310700
C    1.645979   -2.311714    0.647969
C    0.294718   -2.000226    0.690436
C   -4.368108    0.203251    0.005697
C   -3.307197    1.129998   -0.161000
C   -1.999013    0.674008   -0.232957
C   -1.680887   -0.687474   -0.141764
C   -2.739309   -1.592710    0.020534
C   -4.072756   -1.143271    0.093368
C   -2.516264   -3.000498    0.065139
N   -2.367645   -4.155087    0.099905
C    5.017101    0.408250    0.807577
Si   5.064210   -0.953230   -0.489304
H    5.028773   -0.342533   -1.842064
H    6.262419   -1.805031   -0.342556
O    3.792759   -2.029119   -0.295168
H    0.621605    3.463776    0.129091
H    0.691012    1.756715    1.937162
H    2.723664    0.381546    2.269702
H    4.636668    2.410439   -0.991123
H    2.608864    3.787468   -1.329199
H    0.153030    0.156216   -1.924097
H    2.549858   -0.409905   -2.024456
H    2.088312   -2.991968    1.371778
H   -0.326460   -2.440678    1.467906
O   -5.606289    0.732145    0.067049
O   -3.669912    2.421098   -0.228529
H   -1.184280    1.385209   -0.338055
H   -4.864556   -1.876726    0.210359
H    5.049364   -0.053285    1.802971
H    5.950570    0.977796    0.687201
C   -2.644897    3.391425   -0.355923
C   -6.688086   -0.165574    0.229034
H   -3.146369    4.359660   -0.404430
H   -2.061168    3.241612   -1.273546
H   -1.972158    3.376418    0.512560
H   -7.593026    0.444666    0.249652
H   -6.609966   -0.725026    1.171005
H   -6.752149   -0.874234   -0.607562
E = -1420.163238
G = -1419.833927
E_LBS = -1420.454631
G_tot = -1420.125320
```

TS1-*para*-3

C	-2.907043	2.628999	0.410922
C	-2.221195	3.371569	-0.586773
C	-1.325734	2.702917	-1.463913
C	-1.043687	1.380843	-1.290045
C	-1.647190	0.632946	-0.212820
C	-2.666835	1.296480	0.571123
C	-2.322885	4.821053	-0.614576
Si	-1.109363	5.550038	0.686641
O	0.459753	5.219220	0.253836
C	1.115938	4.027920	0.165526
C	2.044580	3.891005	-0.867100
C	2.750956	2.708047	-1.008528
C	2.541028	1.634213	-0.131644
C	1.617961	1.795171	0.908157
C	0.912971	2.983457	1.066812
C	3.362088	0.410236	-0.248877
C	2.828016	-0.890516	-0.299183
C	3.664267	-2.029109	-0.361656
C	5.035060	-1.881632	-0.380341
C	5.588973	-0.571437	-0.353904
C	4.752445	0.536633	-0.291667
C	1.433691	-1.107391	-0.386941
N	0.297530	-1.324981	-0.506849
Rh	-1.783040	-1.475714	-0.517080
C	-1.654755	-2.368260	-2.591855
C	-2.493489	-3.592773	-2.419202
C	-3.880088	-3.367077	-1.804730
C	-3.850066	-2.436929	-0.624545
C	-4.048679	-1.071221	-0.668333
C	-4.320024	-0.247389	-1.890103
C	-3.485390	-0.621025	-3.115912
C	-2.078281	-1.069924	-2.805749
O	5.926063	-2.884982	-0.428572
C	5.424413	-4.209811	-0.426778
O	6.921288	-0.514126	-0.376404
C	7.542354	0.763948	-0.332792
O	-1.951048	-1.664804	1.547498
C	-1.185661	-1.132364	2.419548
O	-0.368674	-0.227675	2.293197
C	-1.417570	-1.751990	3.815059
F	-1.209482	-3.068619	3.779496
F	-0.611578	-1.224332	4.723210
F	-2.678979	-1.541611	4.196972
H	-0.271422	0.918408	-1.897994
H	-3.842196	-2.897823	0.365081
H	-4.295567	-0.606947	0.285612
H	-0.815928	3.278602	-2.233224
H	-0.777142	0.445095	0.679287
H	-3.146421	0.761521	1.385908
H	-3.593047	3.146391	1.078570
H	-1.926783	-4.297601	-1.795283
H	-4.587790	-2.994594	-2.551543
H	-4.261558	-4.334307	-1.463698
H	-2.585339	-4.086476	-3.398831
H	-4.150278	0.806219	-1.638923
H	-5.393368	-0.322940	-2.119137
H	-3.978307	-1.403245	-3.703375
H	-3.420132	0.254057	-3.770248
H	-0.585061	-2.554240	-2.704744

```
H   -1.283579   -0.375181   -3.068254
H    3.210867   -3.014809   -0.405045
H    5.182792    1.532567   -0.235672
H    3.472630    2.606526   -1.817032
H    2.192134    4.721170   -1.553105
H    0.215663    3.092842    1.896534
H    1.471617    0.998070    1.634157
H   -1.226092    7.013892    0.654021
H   -1.464379    4.959516    1.994094
H   -3.301719    5.185035   -0.273050
H   -2.057072    5.259043   -1.582971
H    8.616766    0.576968   -0.356520
H    7.260154    1.372363   -1.200816
H    7.287128    1.298214    0.590513
H    6.296389   -4.865889   -0.439733
H    4.834336   -4.412388    0.476555
H    4.812161   -4.408117   -1.316170
This TS was located as the maximum in a plot of ΔG vs C–H distance in the
precursor complex (arenium ion) corresponding to a reaction coordinate in
which the C–H bond stretches and the proton moves towards the
trifluoroacetate oxygen.
0 imaginary frequencies
E = -2367.157781
G = -2366.629915
E_LBS = -2368.711109
G_tot = -2368.183243
```

6.4. Conclusion

In summary, herein we have reported the first example of a Rh-catalyzed distal *para*-C–H functionalization reaction. The Rh-catalyzed olefination of toluenes using the Si-linked DG5 directing group displays broad substrate tolerance. Electron-rich and electron-deficient arenes are coupled with electron-deficient olefins in high yield and selectivity. Mechanistic studies are consistent with a catalytic cycle in which the C–H bond activation is rate-determining. This work reveals the potential of Rh catalysis to diversify the scope of functionalizations in the realm of remote *para*-C–H activation.

6.5. Reference

1. (a) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.*, **2011**, *40*, 5068-5083. (b) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633-639. (c) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem. Int. Ed.* **2012**, *51*, 10236-10254. (d) Mkhalid, I. A. I.; Barnard, J. H.; Marder, T. B.; Murphy, J. M.; Hartwig, J. F. *Chem. Rev.* **2010**, *110*, 890-931. (e) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173-1193. (f) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293-1314. (g) Yi, H.; Zhang, G.; Wang, H.; Huang, Z.; Wang, J.; Singh, A. K.; Lei, A. *Chem. Rev.* **2017**, *117*, 9016-9085. (h) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 9792-9826. (i) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900-2936.
2. (a) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281-295. (b) Arockiam, P. B.; Bruneau, C.; P. H. Dixneuf, *Chem. Rev.* 2012, **112**, 5879-5918. (c) Chen, X.; Engle, K. M.; Wang, D.-H. Yu, J.-Q. *Angew. Chem. Int. Ed.*, 2009, **48**, 5094-5115. (d) Daugulis, O.; Do, H.-Q.;

Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074-1086. (e) Engle, K. M.; Yu, J.-Q. *J. Org. Chem.* **2013**, *78*, 8927-8955. (f) Giri, R.; Thapa, S.; Kafle, A. *Adv. Synth. Catal.* **2014**, *356*, 1395-1411. (g) Huang, Z.; Lim, H. N.; Mo, F.; Young, M. C.; Dong, G. *Chem. Soc. Rev.*, **2015**, ***44***, 7764-7786. (h) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147-1169. (i) Neufeldt, S. R. Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936-946. (j) Drapeau, M. P.; Gooßen, L. J. *Chem. Eur. J.* **2016**, *22*, 18654-18677. (k) Ros, A.; Fernandez, R.; Lassaletta, J. M. *Chem. Soc. Rev.* **2014**, *43*, 3229-3243. (l) Satoh, T.; Miura, M. *Synthesis*, **2011**, 3395-3409. (m) Shi, G.; Zhang, Y. *Adv. Synth. Catal.* **2014**, *356*, 1419-1442. (n) Topczewski, J. J.; Sanford, M. S. *Chem. Sci.* **2015**, *6*, 70-76. (o) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichimica Acta*, 2013. (p) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215-1292. (q) Zhang, F.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906-6919. (r) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107-1295. (s) Zhang, M.; Zhang, Y.; Jie, X.; Zhao, H.; Li, G.; Su, W. *Org. Chem. Front.* **2014**, *1*, 843-895. (t) Rej, S.; Chatani, N. *Angew. Chem. Int. Ed*. **2019**, *58*, 2–28. (u) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature,* **1993**, *366*, 529–531. (v) Kakiuchi, F.; Murai, S. *Acc. Chem. Res*. **2002**, *35*, 826-834. (w) Ogiwara, Y.; Tamura, M.; Kochi, T.; Matsuura, Y.; Chatani, N.; Kakiuchi, F. *Organometallics* **2014**, *33*, 402−420. (x) Kakiuchi, F.; Kochi, T.; Mizushima, E.; Murai, S. *J. Am. Chem. Soc*. **2010**, *132*, 17741–17750.

3. (a) Shi, H.; Wang, P.; Suzuki, S.; Farmer, M. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2016**, *138*, 14876-14879. (b) Xu, H.-J.; Lu, Y.; Farmer, M. E.; Wang, H.-W.; Zhao, D.; Kang, Y.-S.; Sun, W.-Y.; Yu, J.-Q. *J. Am. Chem. Soc.* **2017**, *139*, 2200-2203. (c) Xu, H.-J.; Kang, Y.-S.; Shi, H.; Zhang, P.; Chen, Y.-K.; Zhang, B.; Liu, Z.-Q.; Zhao, J.; Sun, W.-Y.; Yu, J.-Q.; Lu, Y. *J. Am. Chem. Soc.* **2019**, *141*, 76-79. (d) Lee, S.; Lee, H.; Tan, K. L. *J. Am. Chem. Soc.* **2013**, *135*, 18778-18781. (e) Li, S.; Cai, L.; Ji, H.; Yang, L. Li, G. *Nat. Commun*. **2016**, *7*. (f) Li, S.; Ji, H.; Cai, L.; Li, G. *Chem. Sci.* **2015**, *6*, 5595-5600. (g) Mi, R.-J.; Sun, Y.-Z.; Wang, J.-Y.; Sun, J.; Xu, Z.; Zhou, M.-D. *Org. Lett.* **2018**, *20*, 5126-5129. (h) Zhang, L.; Zhao, C.; Liu, Y.; Xu, J.; Xu, X.; Jin, Z. *Angew. Chem. Int. Ed.* **2017**, *56*, 12245-12249. (i) Bag, S.; Jayarajan, R.; Dutta, U.; Chowdhury, R.; Mondal, R.; Maiti, D. *Angew. Chem. Int. Ed.* **2017**, *56*, 12538-12542. (j) Bera, M.; Agasti, S.; Chowdhury, R.; Mondal, R.; Pal, D.; Maiti, D. *Angew. Chem. Int. Ed.* **2017**, *56*, 5272-5276. (k) Bera, M.; Maji, A.; Sahoo, S. K.; Maiti, D. *Angew. Chem. Int. Ed.* **2015**, *54*, 8515-8519. (l) Dutta, U.; Modak, A.; Bhaskararao, B.; Bera, M.; Bag, S.; Mondal, A.; Lupton, D. W.; Sunoj, R. B.; Maiti, D. *ACS Catal.* **2017**, *7*, 3162-3168. (m) Jayarajan, R.; Das, J.; Bag, S.; Chowdhury, R.; Maiti, D. *Angew. Chem. Int. Ed.* **2018**, *57*, 7659-7663. (n) Modak, A.; Patra, T.; Chowdhury, R.; Raul, S.; Maiti, D. *Organometallics*, **2017**, *36*, 2418-2423. (o) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518-522. (p) Tang, R.-Y.; Li, G.; Yu, J.-Q. *Nature*, **2014**, *507*, 215-220. (q) Chu, L.; Shang, M.; Tanaka, K.; Chen, Q.; Pissarnitski, N.; Streckfuss, E. Yu, J.-Q. *ACS Cent. Sci*. **2015**, *1*, 394-399. (r) Jin, Z.; Chu, L.; Chen, Y.-Q.; Yu, J.-Q. *Org. Lett.* **2018**, *20*, 425-428. (s) Phipps, R. J.; Gaunt, M. J. *Science* **2009**, *323*, 1593-1597. (t) Duong, H. A.; Gilligan, R. E.; Cooke,V; Phipps, R. J.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 463-466. (u) Leitch, J. A.; Bhonoah, Y.; Frost, C. G. *ACS Catal.* **2017**, *7*, 5618-5627. (v) Saidi, O.; Marafie, J.; Ledger, A. E. W.; Liu, P. M.; Mahon, M. F.; Kociok-Köhn, G.; Whittlesey, M. K.; Frost, C. G. *J. Am. Chem. Soc.* **2011**, *133*, 19298-19301. (w) Hofmann, N.; Ackermann, L. *J. Am. Chem. Soc.* **2013**, *135*, 5877-5884. (x) Li, J.; Warratz, S.; Zell, D.; De Sarkar, S.; Ishikawa, E. E.; Ackermann, L. *J. Am. Chem. Soc.* **2015**, *137*, 13894-13901. (y) Fumagalli, F.; Warratz, S.; Zhang, S.-K.; Rogge, T.; Zhu, C.; Stückl, A. C.; Ackermann, L. *Chem. Eur. J.* **2018**, *24*, 3984-3988. (z) Mihai, M. T.; Davis, H. J.; Genov, G. R.; Phipps, R. J. *ACS Catal.* **2018**, *8*, 3764-3769. (aa) Mihai, M. T.; Genov, G. R.; Phipps, R. J. *Chem. Soc. Rev.* **2018**, *47*, 149-171. (ab) Ferraccioli, R. *Synthesis*, **2013**, *45*, 581-591. (ac) Catellani,

M.; Frignani, F.; Rangoni, A. *Angew. Chem. Int. Ed.* **1997**, *36*, 119-122. (ad) Faccini, F.; Motti, E.; Catellani, M. *J. Am. Chem. Soc.* **2004**, *126*, 78-79. (ae) Dong, Z.; Dong, G. *J. Am. Chem. Soc.* **2013**, *135*, 18350-18353. (af) Dong, Z.; Wang, J.; Dong, G. *J. Am. Chem. Soc.* **2015**, *137*, 5887-5890. (ag) Dong, Z.; Wang, J.; Ren, Z.; Dong, G. *Angew. Chem. Int. Ed.* **2015**, *54*, 12664-12668. (ah) Wang, X.-C.; Gong, W.; Fang, L.-Z.; Zhu, R.-Y.; Li, S.; Engle, K. M.; Yu, J.-Q. *Nature* **2015**, *519*, 334-338. (ai) Li, G.-C.; Wang, P.; Farmer, M. E.; Yu, J.-Q. *Angew. Chem. Int. Ed.* **2017**, *56*, 6874-6877. (aj) Kuninobu, Y.; Ida, H.; Nishi, M.; Kanai, M. *Nat. Chem*. **2015**, *7*, 712-717. (ak) Bisht, R.; Chattopadhyay, B. *J. Am. Chem. Soc.* **2016**, *138*, 84-87. (al) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E.; Smith, M. R. *Science* **2002**, *295*, 305-308. (am) Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390-391. (an) Robbins, D. W.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2013**, *52*, 933-937.

4. (a) Haines, B. E.; Saito, Y.; Segawa, Y.; Itami, K.; Musaev, D. G. *ACS Catal.* **2016**, *6*, 7536-7546. (b) Hoque, M. E.; Bisht, R.; Haldar, C.; Chattopadhyay, B. *J. Am. Chem. Soc.* **2017**, *139*, 7745-7748. (c) Leitch, J. A.; McMullin, C. L.; Paterson, A. J.; Mahon, M. F.; Bhonoah, Y. Frost, C. G. *Angew. Chem. Int. Ed.* **2017**, *56*, 15131-15135. (d) Okumura, S.; Nakao, Y. *Org. Lett.* **2017**, *19*, 584-587. (e) Yang, L.; Semba, K.; Nakao, Y. *Angew. Chem. Int. Ed.* **2017**, *56*, 4853-4857. (f) Tian, C.; Yao, X.; Ji, W.; Wang, Q.; An, G.; Li, G. *Eur. J. Org. Chem.* **2018**, 5972-5979. (g) Zhu, L.; Qi, X.; Li, Y.; Duan, M.; Zou, L.; Bai, R.; Lan, Y. *Organometallics* **2017**, *36*, 2107-2115.
5. Bag, S.; Patra, T.; Modak, A.; Deb, A.; Maity, S.; Dutta, U.; Dey, A.; Kancherla, R.; Maji, A.; Hazra, A.; Bera, M.; Maiti, D. *J. Am. Chem. Soc.* **2015**, *137*, 11888-11891.
6. Patra, T.; Bag, S.; Kancherla, R.; Mondal, A.; Dey, A.; Pimparkar, S.; Agasti, S.; Modak A.; Maiti, D. *Angew. Chem. Int. Ed.* **2016**, *55*, 7751-7755.
7. Maji, A.; Guin, S.; Feng, S.; Dahiya, A.; Singh, V. K.; Liu, P.; Maiti, D. *Angew. Chem. Int. Ed.* **2017**, *56*, 14903-14907.
8. Maji, A.; Dahiya, A.; Lu, G.; Bhattacharya, T.; Brochetta, M.; Zanoni, G.; Liu, P.; Maiti, D. *Nat. Commun.* **2018**, *9*, 3582.
9. (a) Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A.; *Science* **2012**, *337*, 1644-1648. (b) Ciana, C.-L.; Phipps, R. J.; Brandt, J. R.; Meyer, F.-M.; Gaunt, M. J. *Angew. Chem. Int. Ed.* **2011**, *50*, 458-462. (c) Berzina, B.; Sokolovs, I.; Suna, E. *ACS Catal.* **2015**, *5*, 7008-7014. (d) Yu, Z.; Ma, B.; Chen, M.; Wu, H.-H.; Liu, L.; Zhang, J. *J. Am. Chem. Soc.* **2014**, *136*, 6904-6907.

   10.(a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624-655. (b) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2012**, *45*, 814-825. (c) Cui, S.; Zhang, Y.; Wu, Q. *Chem. Sci.* **2013**, *4*, 3421-3426. (d) Feng, C.; Feng, D.; Loh, T.-P. *Org. Lett.* **2013**, *15*, 3670-3673. (e) Hyster, T. K.; Knörr, L.; Ward, T. R.; Rovis, T. *Science* **2012**, *338*, 500-503. (f) Kuhl, N.; Schröder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443-1460. (g) Li, B.; Ma, J.; Xie, W.; Song, H.; Xu, S.; Wang, B. *Chem. Eur. J.* **2013**, *19*, 11863-11868. (h) Li, G.; Ding, Z.; Xu, B. *Org. Lett.* **2012**, *14*, 5338-5341. (i) Li, X.; Zhao, M. *J. Org. Chem.* **2011**, 76, 8530-8536. (j) Liu, B.; Fan, Y.; Gao, Y.; Sun, C.; Xu, C.; Zhu, J. *J. Am. Chem. Soc.* **2013**, *135*, 468-473. (k) Park, S. H.; Kim, J. Y.; Chang, S. *Org. Lett.* **2011**, *13*, 2372-2375. (l) Mishra, N. K.; Park, J.; Sharma, S.; Han, S.; Kim, M.; Shin, Y.; Jang, J.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Chem. Commun.* **2014**, *50*, 2350-2352. (m) Nobushige, K.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2014**, *16*, 1188-1191. (n) Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9982-9983. (o) Presset, M.; Oehlrich, D.; Rombouts, F.; Molander, G. A. *Org. Lett.* **2013**, *15*, 1528-1531. (p) Qi, X.; Li, Y.; Bai, R.; Lan, Y. *Acc. Chem. Res.* **2017**, *50*, 2799-2808. (q) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. *Org. Lett.* **2013**, *15*, 3366-3369. (r) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2011**, 13, 540-542. (s) Wang, F.; Song, G.; Li, X. *Org. Lett.* **2010**, *12*, 5430-

5433. (t) Zhang, X.-S.; Zhu, Q.-L.; Zhang, Y.-F.; Li, Y.-B.; Shi, Z.-J. *Chem. Eur. J.* **2013**, *19*, 11898-11903. (u) Zhou, J.; Li, B.; Hu, F.; Shi, B.-F. *Org. Lett.* **2013**, *15*, 3460-3463. (v) Zhu, C.; Falck, J. R. *Chem. Commun.* **2012**, *48*, 1674-1676. (w) Shibata, K.; Natsui, S.; Chatani, N. *Org. Lett*. **2017**, *19*, 2234−2237. (x) Kita, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2010**, *12*, 1864-1867.

11. See the Supporting Information for detailed descriptions.
12. We also considered several other mechanisms in which the CH bond cleavage step is mediated by either Rh(III) or Rh(I). Details are provided in the Supporting Information.
13. Rokade, B. V.; Prabhu, K. R. *J. Org. Chem*. **2012**, *77*, 5364.
14. Wang, C.; Ge, H. *Chem. Eur. J*. **2011**, *17*, 14371-14374.
15. Liu, P.; Tang, J.; Zeng, X. *Org. Lett*. **2016**, *18*, 5536-5539.
16. Wierschke, S. G.; Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 1496.
17. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Jr. Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision E.01; Gaussian, Inc., Wallingford, CT, **2013**.
18. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16, Revision A.03, Gaussian, Inc., Wallingford CT, **2016**.
19. Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215–241.
20. Sperger, T.; Sanhueza, I. A.; Kalvet, I.; Schoenebeck, F. *Chem. Rev.* **2015**, *115*, 9532.
21. Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378.