Auxiliary-Assisted C-H Functionalization: Exploring the Realm of C-C and C-Heteroatom Bond Formation

A Thesis Submitted

in Partial Fulfilment of the Requirements

for the Degree of

Doctor of Philosophy in Chemistry

By

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karmaṇy-evādhikāras te mā phaleṣhu kadāchana

mā karma-phala-hetur bhūr mā te saṅgo ’stvakarmaṇi

“Bhagavad Gita: Chapter 2, Verse 47”

Dedicated to the unwavering pillars of my journey – my parents

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

Department of Chemistry

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati, India under the supervision of Prof. Tharmalingam Punniyamurthy.

In accordance with the established protocol for reporting scientific observations, proper acknowledgments have been provided whenever the work described relies on the discoveries made by other researchers.

Guwahati — Kangkan Talukdar

January 2024

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CERTIFICATE

This is to certify that Mr. Kangkan Talukdar has been working under my supervision since January 2017. I am forwarding his thesis entitled "*Auxiliary-Assisted C-H Functionalization: Exploring the Realm of C-C and C-Heteroatom Bond Formation*" being submitted for the Ph.D. degree of this institute. I certify that he has fulfilled all the requirements according to the rules of this institute, and regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

Guwahati

January 2024

Supervisor

Prof. Tharmalingam Punniyamurthy

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"Guru Brahma, Guru Vishnu, Guru Devo Maheshwara;

Guru Sakshat Parabrahma, Tasmai Shri Guruve Namaha."

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Kangkan Talukdar

List of Abbreviations

acac	acetylacetone
Å	angstrom (10^{-8} cm)
Bn	benzyl
Boc	*tert*-butoxycarbonyl
BQ	benzoquinone
Bz	benzoyl
Cp*	1,2,3,4,5-pentamethylcyclopentadiene
CCDC	Cambridge crystallographic data center
p-cymene	4-isopropyltoluene
DG	directing group
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMSO	dimethylsulfoxide
DMF	*N*,*N*-dimethylformamide
dtbpy	4,4′-di-*tert*-butyl-2,2′-bipyridyl
EDG	electron donating group
eq	equation
equiv	equivalent
ESI	electrospray ionization
EWG	electron wthdrawing group
FT-IR	Fourier transform infrared spectroscopy
FG	functional group
HFIP	hexafluoroisopropanol
het	heterocyclic
HRMS	high-resolution mass spectrometry
Hz	hertz
LG	leaving group
m/z	mass to charge ratio
mp	melting point
mA	milliampere

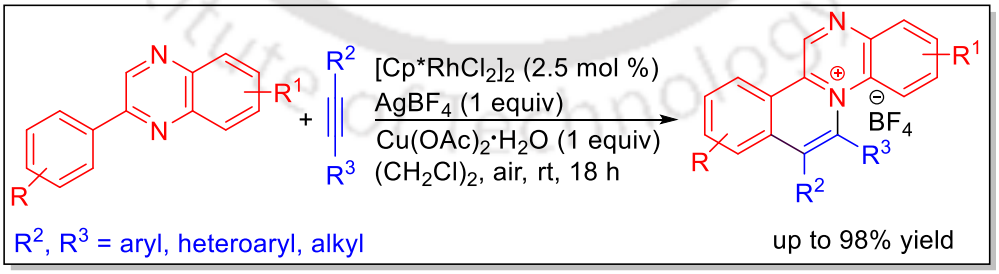
MesCOOH	2,4,6-trimethylbenzoic acid
MsOH	methanesulfonic acid
MHz	megahertz
NMR	nuclear magnetic resonance
NMP	*N*-methyl-2-pyrrolidone
NMO	*N*-methylmorpholine-N-oxide
NHPI	*N*-Hydroxyphthalimide
ORTEP	oak ridge thermal ellipsoid plot
R_f	retardation factor
rt	room temperature
PIDA	(Diacetoxyiodo)benzene
Piv	pivaloyl
py	pyridine
pym	pyrimidine
1, 10-Phen	1, 10-phenanthroline
PivOH	pivalic acid
SET	single-electron transfer
TBN	*tert*-Butyl nitrite
TCP	1,2,3-Trichloropropane
TFE	2,2,2-trifluoroethanol
TMEDA	tetramethylethylenediamine
TLC	thin layer chromatography
TsOH	*p*-toluenesulfonic acid
TMS	trimethylsilyl
TM	transition metal
μL	microliter

Abstract

The thesis is segmented into four chapters. The initial chapter delineates a Rh-catalyzed tandem C-C/C-N bond formation of quinoxalines with alkynes leading to heterocyclic ammonium salts. The second chapter explores the Pd-catalyzed sp^3 C-H alkoxycarbonylation of 8-methylquinolines using $Mo(CO)_6$ as a CO surrogate. The third chapter showcases the Rh-catalyzed alkenylation of aryl 2-pyridyl ethers with vinyl acetate *via* sp^2 C-H activation. Lastly, the fourth chapter delves into on Ru-catalyzed site selective acetoxylation of aryl 2-pyridyl ethers exploiting vinyl acetate as acetoxylating agent.

Chapter I. Rh-Catalyzed Tandem C-C/C-N Bond Formation of Quinoxalines with Alkynes Leading to Heterocyclic Ammonium Salts

The quaternary ammonium salts with substitutions hold significant importance as they are commonly found in numerous natural products displaying diverse bioactivities. The conventional methods for synthesizing these salts often face challenges related to the need for pre-functionalized substrate precursors, harsh reaction conditions, and a restricted substrate scope. The increasing demand for quaternary ammonium salts in pharmaceutical and materials sciences has propelled the active exploration of synthetic routes in recent research endeavors. The present chapter describes an efficient Rh-catalyzed oxidative coupling of quinoxalines with alkynes via a tandem C-H activation and *N*-annulation to provide a diverse variety of quaternary ammonium salts at room temperature (Scheme 1). The mild reaction conditions, substrate scope and functional group diversity are the salient practical features.

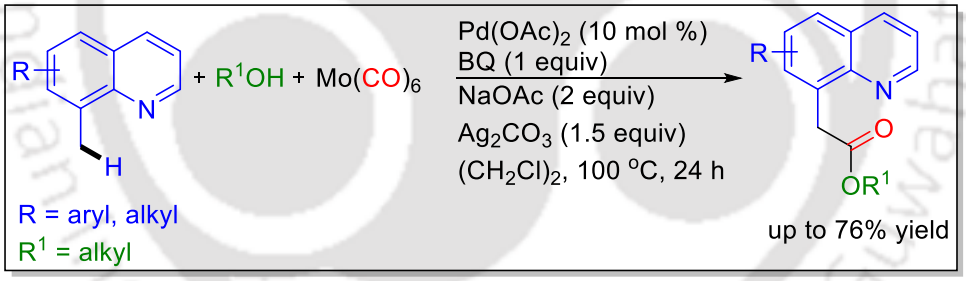


Org. Biomol. Chem. **2019**, *17*, 2148.

Scheme 1. Rh(III)-Catalyzed Tandem C-C/C-N Bond formation of Quinoxalines

Chapter II. Pd-Catalyzed sp^3 C-H Alkoxycarbonylation of 8-methylquinolines using $Mo(CO)_6$ as a CO Surrogate

The exploration of C-O bond formation holds pivotal importance in organic synthesis, given the widespread presence of this structural element in a multitude of biologically and pharmaceutically significant molecules. Recent focus on atom-efficient processes and green chemistry has elevated transition-metal-catalyzed direct C-H activation as a leading protocol in modern synthetic chemistry. This method has significantly prospered in constructing site-selective C-C and C-heteroatom bonds. Regioselective functionalization of sp^3 C-H bonds faces significant challenges due to the absence of π-bonds and the high bond dissociation energy associated with them. Due to the remarkable significance of quinolines in alkaloids and medicinal science, their functionalization has garnered considerable attention in the field of synthetic chemistry. In this chapter, we present a Pd(II)-catalyzed three-component sp^3 C-H alkoxycarbonylation of 8-methylquinoline (8-MQ) derivatives, utilizing $Mo(CO)_6$ as a bench stable, non-toxic alternate for CO (Scheme 2). The selectivity, functional group tolerance and late-stage natural product mutations are the important practical features.



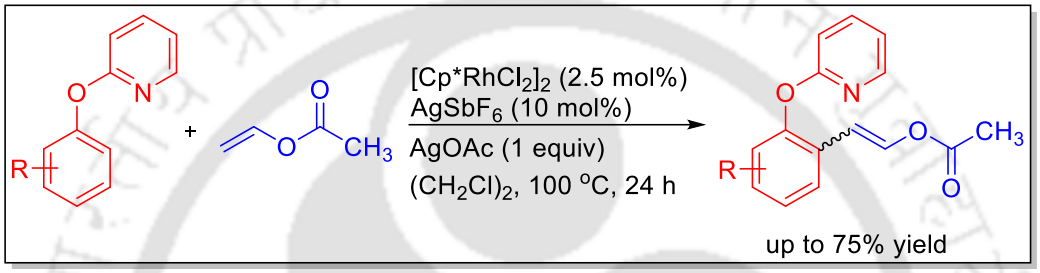
Chem. Commun. **2021**, *57*, 3359.

Scheme 2. Pd(II)-Catalyzed Alkoxycarbonylation of 8-MQs using $Mo(CO)_6$ as CO Surrogate

Chapter III. Rh-Catalyzed Site-Selective Alkenylation of Aryl 2-Pyridyl Ethers with Vinyl Acetate

Direct C-H functionalization catalyzed by transition metals has revolutionized the transformation of basic compounds into intricate molecules, fostering structural diversity and enhancing atom efficiency. Olefins, a prevalent functional group, can undergo straightforward modifications to create complex organic molecules. The unique reactivity of olefins emphasizes the significance of

alkene functionalization in the realm of organic synthesis. In recent times, diverse transition metal catalysts, including Pd, Rh, Ru, Ir, and Co, have been employed for akenylation reaction. Nonetheless, most current techniques are limited to activated alkenes such as acrylates, enones, and styrenes. However, achieving direct sp^2 C-H functionalization in electron-rich alkenes remains uncommon, despite being a highly sought-after goal. This chapter elucidates a method for site selective alkenylation of aryl 2-pyridyl ethers utilizing vinyl acetate as alkenylating agent using Rh(III)-catalysis (Scheme 3). The site-selectivity, utilization of unactivated alkene and mechanistic investigations are salient features of the protocol.



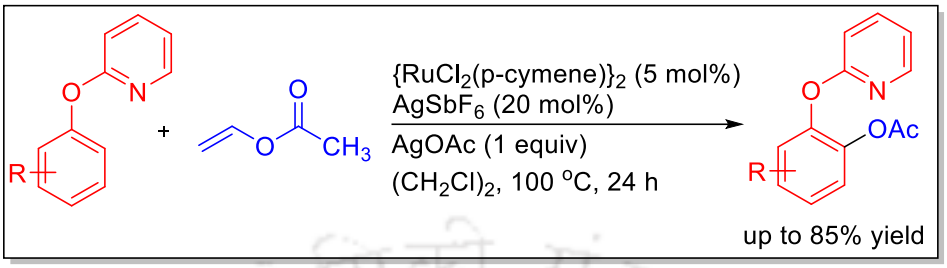
Manuscript under preparation.

Scheme 3. Rh-Catalyzed Alkenylation of Aryl 2-Pyridyl Ethers with Vinyl Acetate

Chapter IV. Ru-Catalyzed *ortho*-Selective Acetoxylation of Aryl 2-Pyridyl Ethers Exploiting Vinyl Acetate as an Acetoxylating Agent

Establishing C-C and C-O bonds is a fundamental goal in the field of synthetic organic chemistry. Significantly, heterocycles containing nitrogen and oxygen serve as crucial structural motifs, prominently contributing to a diverse range of biologically active natural compounds and synthetic pharmaceuticals. Given the contemporary focus on atom-economical procedures and a green chemistry approach, transition-metal-catalyzed direct C-H activation has emerged as a reliable protocol at the forefront of current synthetic chemistry. In recent times, the remarkable growth of transition metal-catalyzed C-H bond functionalization has been evident, primarily attributed to the convenient accessibility of C-H bonds. Within the array of C-H functionalization reactions, considerable attention has been devoted to transition metal catalyzed C-O bond formation reaction although restricted to employment of hypervalent iodine reagents along with $Cu(OAc)_2$. This chapter outlines a Ru-catalyzed site-selective oxygenation of aryl 2-pyridyl ethers employing vinyl acetate as the acetoxylating agent (Scheme 4). Aryl 2-pyridyl ethers with versatile functional

groups are well tolerated the reaction protocol and the suggested mechanism has been supported by a combination of experimental mechanistic inquiries and DFT calculations.



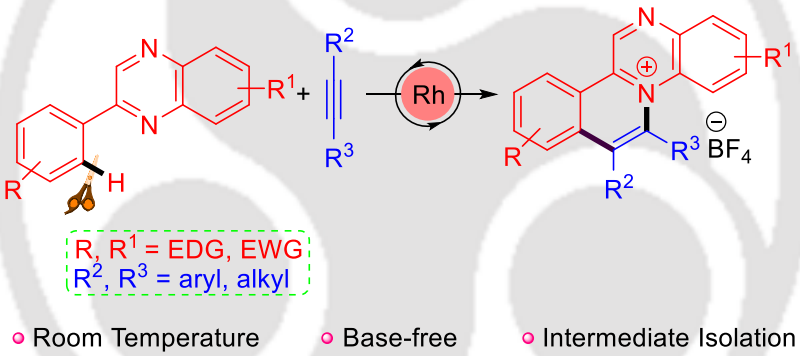
Manuscript under preparation.

Scheme 4. Ru-Catalyzed *ortho*-Selective Acetoxylation of Aryl 2-Pyridyl Ethers

Contents

Chapter I

Rh-Catalyzed Tandem C-C/C-N Bond Formation of Quinoxalines with Alkynes Leading to Heterocyclic Ammonium Salts



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Chapter I

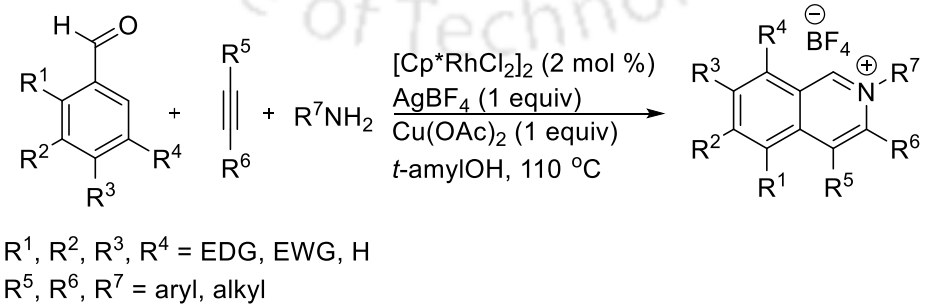
Rh-Catalyzed Tandem C-C/C-N Bond Formation of Quinoxalines with Alkynes Leading to Heterocyclic Ammonium Salts

Substituted quaternary ammonium salts are important class of compounds as their occurrence is prevalent in many natural products that exhibit diverse bioactivities.[1] The traditional protocols for the synthesis of quaternary ammonium salts are, however, often suffer due to the requirement of pre-functionalized substrate precursors, harsh reaction conditions and limited substrate scope.[2] In accordance with the growing concerns on the development of sustainable chemistry,[3] transition-metal-catalyzed oxidative annulation *via* C-H bond activation has emerged as a powerful synthetic tool for the step and atom-economical organic syntheses.[4] Owing to the high efficiency, selectivity and lenity towards the different functional groups, Rh-catalyzed C-H activation[5] followed by *N*-annulation affords an effective synthetic strategy for the synthesis of heterocyclic structural scaffolds. Due to the high demand of the quaternary ammonium salts in the area of pharmaceutical and material sciences, designing of their synthetic routes have become an active topic of research in recent times.[6]

1.1 Literature Study

1.1.1 Rh-Catalyzed C-H Bond Activation/Annulation

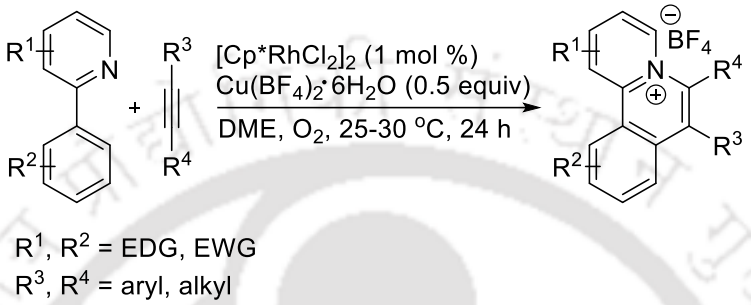
Cheng and co-workers disclosed a Rh(III)-catalyzed regioselective synthesis of substituted isoquinolinium salts involving benzaldehydes, amines, and alkynes *via* C-H bond activation and annulation (Scheme 1).[7] The procedure was effectively employed for the total synthesis of oxychelerythrine with excellent yield.



R^1, R^2, R^3, R^4 = EDG, EWG, H
R^5, R^6, R^7 = aryl, alkyl

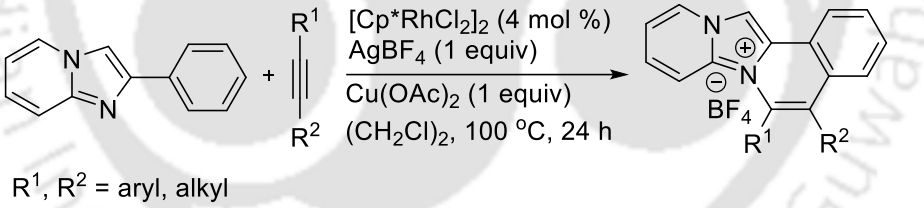
Scheme 1. Rh-Catalyzed Oxidative C-H Activation/Annulation

A Rh(III)-catalyzed C-H activation/annulation under O_2 atmosphere for the synthesis of polycyclic pyridinium salts was reported by Cheng and co-workers (Scheme 2).[8] This mechanism was supported by the isolation of a five membered rhodacycle. Furthermore, pyridinium salts have been identified as promising candidates for application in the electron-injection layer within organic light-emitting diodes (OLEDs).



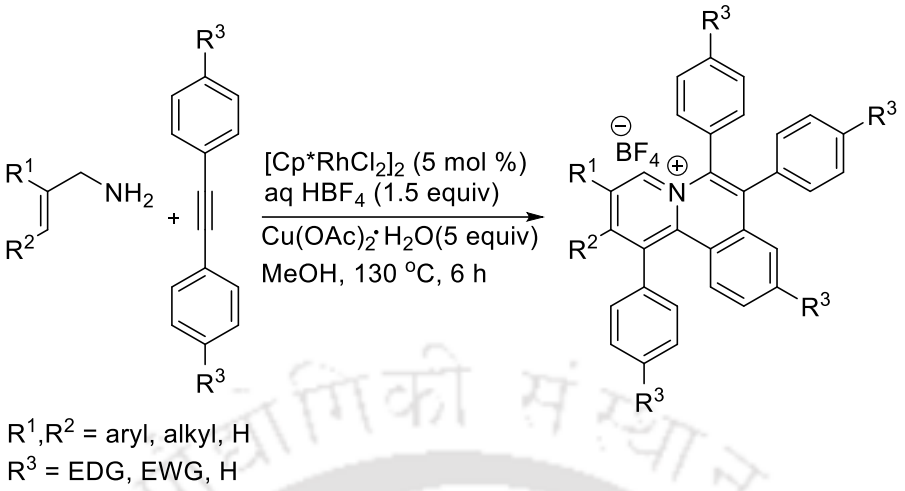
Scheme 2. Rh-Catalyzed Synthesis of Polycyclic Pyridinium Salts

A divergent oxidative coupling of alkynes with 2-phenylimidazo[1,2-a]pyridines *via* Rh(III)-catalyzed C-H activation to afford a fused isoquinolinium salts has been successfully accomplished by Li and co-workers (Scheme 3).[9] A rhodacyle has been isolated as a reactive intermediate.



Scheme 3. Rh-Catalyzed Synthesis of Fused Isoquinolinium Salts

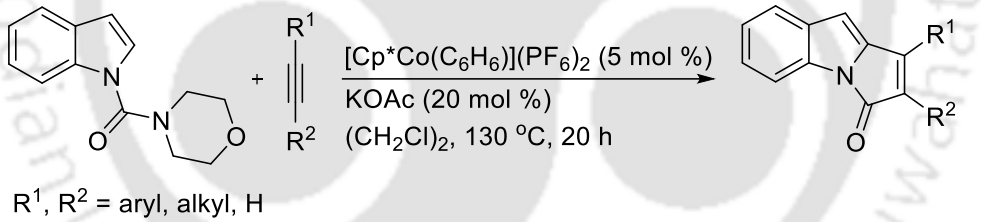
Jun and co-workers demonstrated a Rh(III)-catalyzed cascade double *N*-annulation of allylamines, diarylacetylenes, and HBF_4 for the synthesis of benzoquinolizinium salts (Scheme 4).[10] Crucially, the benzoquinolizinium salts obtained act as fluorescent materials, and their emission wavelengths can be adjusted by choosing suitable substituents.



Scheme 4. Rh-Catalyzed Cascade Double *N*-annulation Reactions

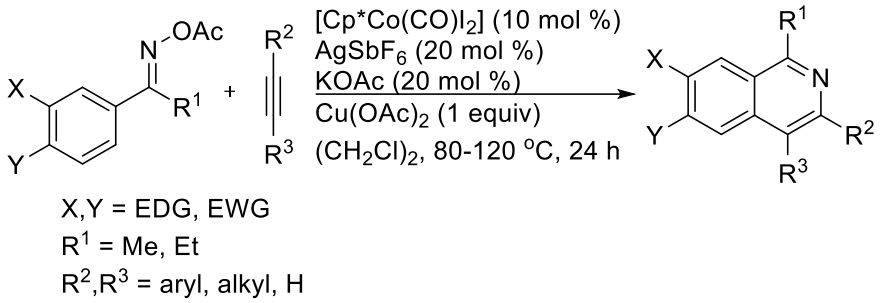
1.1.2 Co-Catalyzed C-H Bond Activation/Annulation

Kanai and co-workers accomplished a Co-catalyzed C2 selective alkenylation/annulation of *N*-carbamoyl indole to afford pyrroloindolones in one-pot (Scheme 5).[11] The protocol accommodated broad range of alkynes including terminal alkynes.



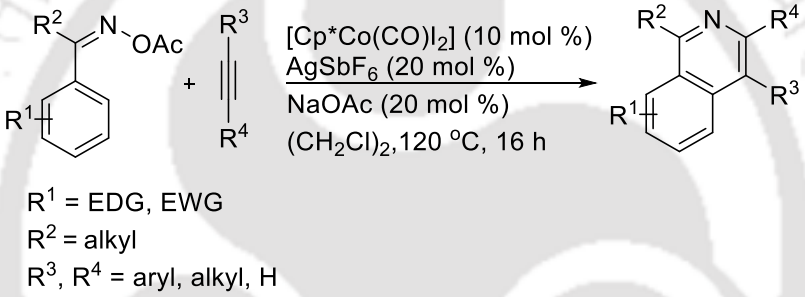
Scheme 5. Co-Catalyzed Redox-Neutral C-H Alkenylation/Annulation

Matsunaga and co-workers developed a Cp*Co(III)-catalyzed site-selective C-H activation of unsymmetrical *O*-acyl oximes for the synthesis of multisubstituted isoquinolines from terminal and internal alkynes (Scheme 6).[12] It is worth mentioning that Cp*Co(III) catalyst exhibited much higher site selectivity for unsymmetrical *O*-acyl oximes and higher reactivity towards terminal alkynes than the Cp*Rh(III) catalyst.



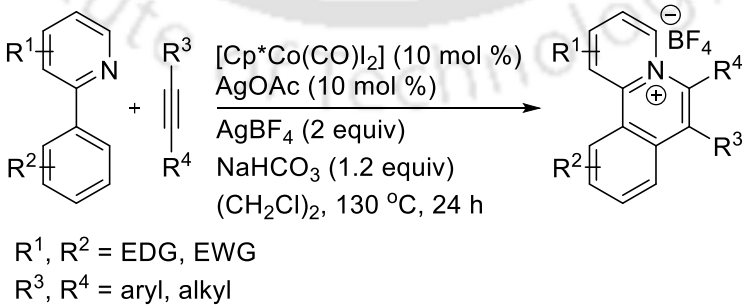
Scheme 6. Co-Catalyzed Site-Selective C-H Activation of Unsymmetrical *O*-Acyl Oximes

A highly efficient Co(III)-catalyzed C-H/N-O functionalizations of *O*-acyl oximes with alkynes is reported by Ackermann and co-workers (Scheme 7).[13] This methodology exhibits remarkable tolerance towards various functional groups, internal alkynes as well as the terminal ones.



Scheme 7. Co-Catalyzed C-H/N-O Functionalization of *O*-Acyl Oximes

Cheng and co-workers described a Co(III)-catalyzed oxidative annulation of nitrogen containing arenes with alkynes for the synthesis of heterocyclic quaternary ammonium salts (Scheme 8).[14] The outcomes closely resemble reactions catalyzed by Rh and Ru complexes. Additionally, the conversion of salts into diverse *N*-heterocycles has been successfully showcased.

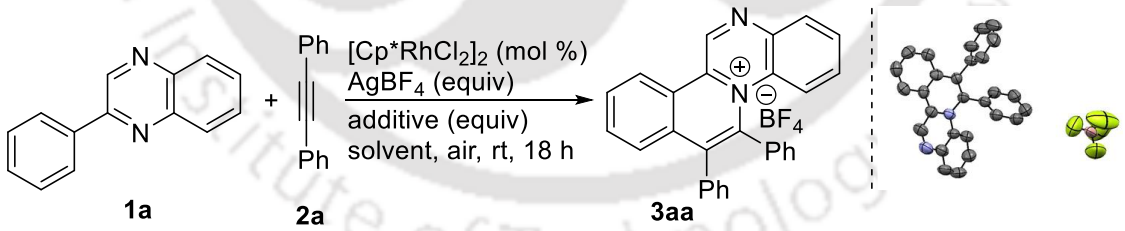


Scheme 8. Co-Catalyzed Oxidative Annulation of Nitrogen Containing Arenes with Alkynes

1.2 Present Study

We here present an efficient Rh-catalyzed oxidative coupling of quinoxalines with alkynes *via* a tandem C-H activation and *N*-annulation to provide a diverse quaternary ammonium salts at room temperature under air. We initiated the reaction screening with 2-phenylquinoxaline **1a** and 1,2-diphenylethyne **2a** as the model substrates using $[Cp^*RhCl_2]_2$ as a catalyst in the presence of additives (Table 1). To our delight, 6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium salt **3aa** was produced in 41% yield when the substrates **1a** and **2a** were stirred with 2.5 mol % of $[Cp^*RhCl_2]_2$, 1 equiv of $Cu(OAc)_2{\cdot}H_2O$ and 1 equiv of $AgBF_4$ at room temperature in THF under air (entry 1). Recrystallization of **3aa** in DMSO gave single crystal whose structure was determined using an X-ray analysis. The yield was increased to 98% employing 1,2-dichloroethane as a solvent, whereas the reactions using 1,4-dioxane, CH_3CN, methanol, toluene, *m*-xylene, DMSO and CH_2Cl_2 yielded inferior results (entries 2-9). In a set of additives screened, $Cu(OAc)_2{\cdot}H_2O$, $Cu(OAc)_2$, AgOAc, NaOAc, KOAc, $K_2S_2O_8$ and O_2, the former furnished the best result (entries 9-15). Decreasing the catalyst loading (1 mol %) led to drop the yield to 65%, whereas the absence of the additive produced **3aa** in 10% yield (entries 16 & 17). When $AgBF_4$ (2 equiv) was used, the product **3aa** was observed in 18% yield (entry 18). The use of aq. HBF_4 in place of $AgBF_4$ led to no annulation (entry 19). Control experiments confirmed that the combination of $[Cp^*RhCl_2]_2$ and $AgBF_4$ is crucial for the annulation to produce **3aa** (entries 20 and 21).

Table 1. Optimization of Reaction Conditions[a]



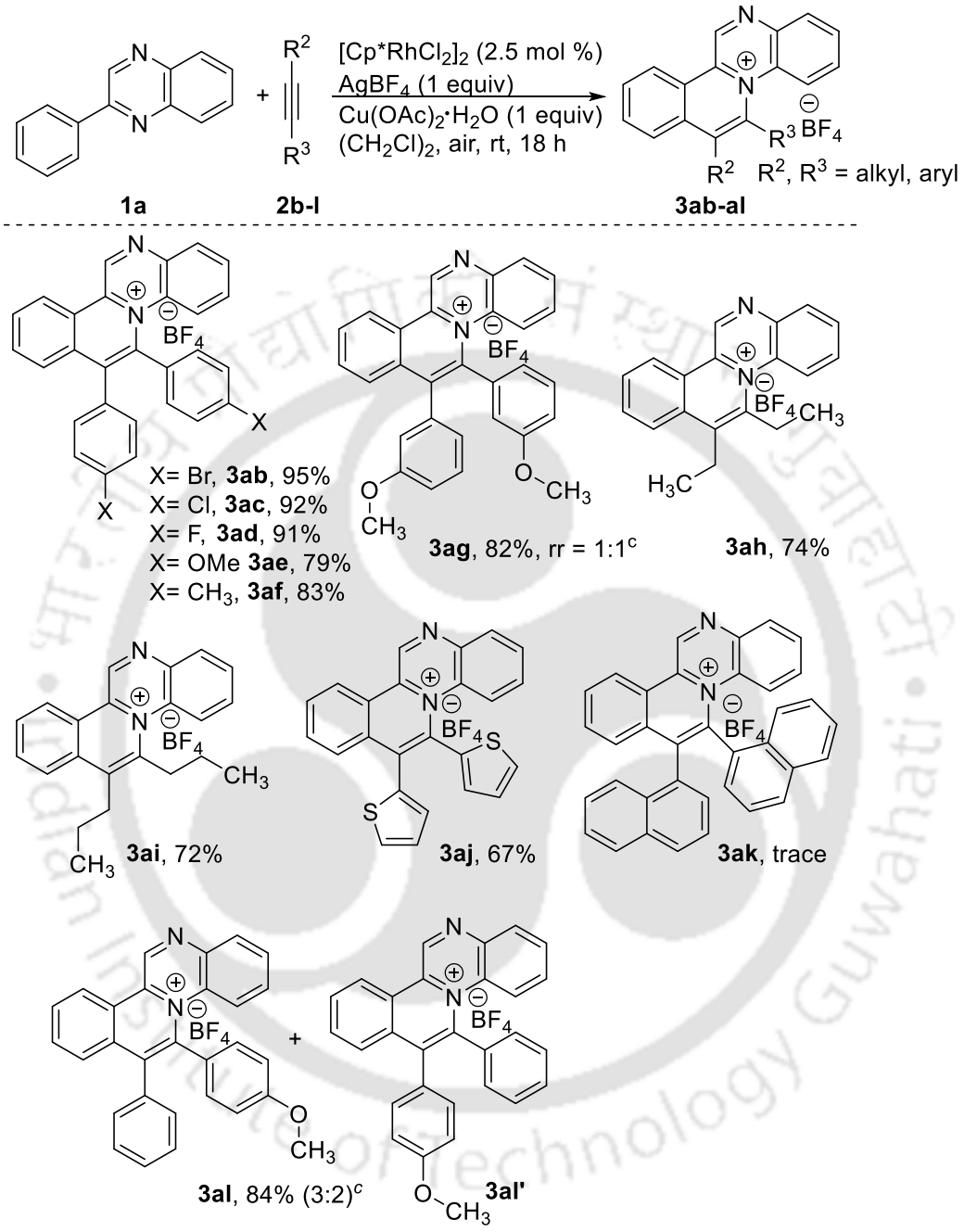
Entry	Catalyst	Additive	Solvent	Yield [%][b]
1	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	THF	41
2	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	1,4-dioxane	37
3	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	CH_3CN	trace
4	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	MeOH	32
5	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	toluene	n.d.
6	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	*m*-xylene	n.d.

7	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	DMSO	trace
8	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	CH_2Cl_2	71
9	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	98
10	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	$(CH_2Cl)_2$	75
11	$[Cp^*RhCl_2]_2$	AgOAc	$(CH_2Cl)_2$	58
12	$[Cp^*RhCl_2]_2$	NaOAc	$(CH_2Cl)_2$	15
13	$[Cp^*RhCl_2]_2$	KOAc	$(CH_2Cl)_2$	8
14	$[Cp^*RhCl_2]_2$	$K_2S_2O_8$	$(CH_2Cl)_2$	trace
15	$[Cp^*RhCl_2]_2$	O_2	$(CH_2Cl)_2$	15
16[c]	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	65
17[d]	$[Cp^*RhCl_2]_2$	---	$(CH_2Cl)_2$	10
18[e]	$[Cp^*RhCl_2]_2$	---	$(CH_2Cl)_2$	18
19[f]	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	n.d.
20[g]	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	n.d.
21	---	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	n.d.

[a]Reaction condition: **1a** (0.25 mmol), **2a** (0.25 mmol), [Rh] (2.5 mol %), $AgBF_4$ (0.25 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol), solvent (3 mL), rt, 18 h, air. [b]Isolated yield. [c][Rh] (1 mol %). [d]Without $Cu(OAc)_2{\cdot}H_2O$. [e]2.0 equiv $AgBF_4$. [f]aq. HBF_4 in place of $AgBF_4$. [g]Without $AgBF_4$. n.d.= not detected.

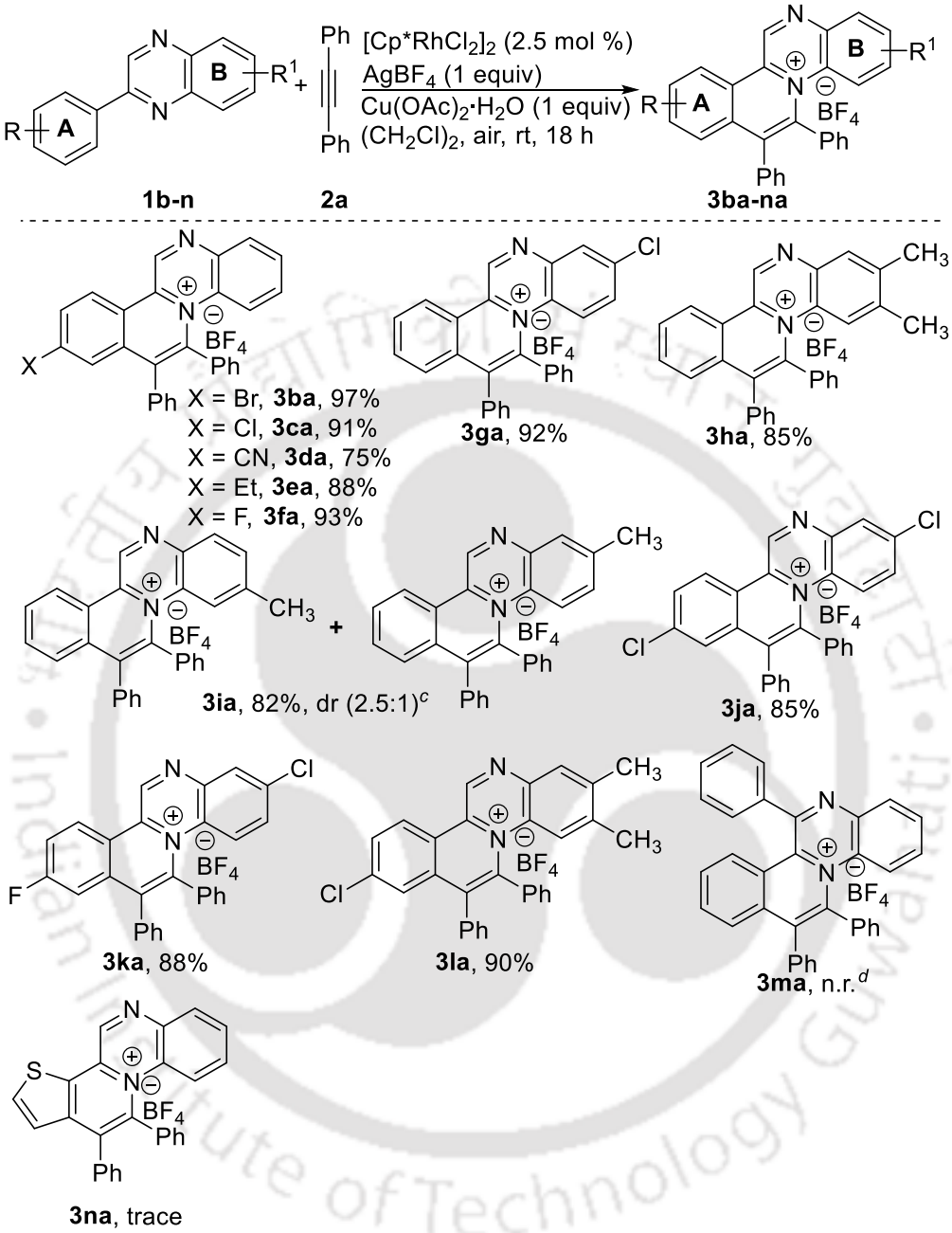
Having optimized the reaction condition, the scope of the procedure was explored for a series of substituted alkynes **2b-l** with 2-phenylquinoxaline **1a** as a standard substrate (Table 2). Diarylalkynes with functional groups at the 4-position of the aryl ring such as bromo **2b**, chloro **2c**, fluoro **2d**, methoxy **2e** and methyl **2f** groups were compatible, affording **3ab-af** in 79-95% yields, whereas alkynes bearing substitution at the 3-position of the aryl ring such as methoxy **2g** group gave **3ag** in 82% yield as a 1:1 mixture of rotational isomers. In addition, dialkylalkynes can be coupled to deliver the ammonium salts **3ah-i** in good yields, although comparatively a slightly lower efficiency was observed with dithienyl **2j** and dinaphthyl **2k** acetylenes due to electronic and steric factors. Furthermore, the unsymmetrical alkyne, 1-methoxy-4-(phenylethynyl)benzene **2l** underwent reaction to give **3al** and **3al'** as a 3:2 mixture of regioisomers, which indicates that Rh preferentially reacts at the sterically less hindered side of the unsymmetrical alkyne.[15]

Table 2. Substrate Scope of Internal Alkynes[a]



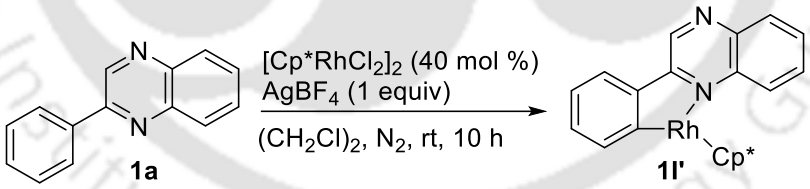
[a]Reaction conditions: **1a** (0.25 mmol), **2b-l** (0.25 mmol), [Rh] (2.5 mol %), $AgBF_4$ (0.25 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.25 mmol), $(CH_2Cl)_2$ (3 mL), rt, 18 h, air. [b]Isolated yield. [c]Determined from 400 MHz ^1H NMR.

Table 3. Substrate Scope of 2-Phenylquinoxalines [a]

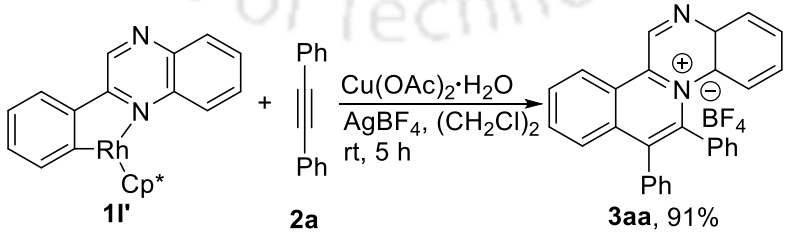


[a]Reaction conditions: **1b-n** (0.25 mmol), **2a** (0.25 mmol), [Rh] (2.5 mol %), $AgBF_4$ (0.25 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol), $(CH_2Cl)_2$ (3 mL), rt, 18 h, air. [b]Isolated yield. [c]dr was determined using 400 MHz ^1H NMR. [d]n.r.= no reaction.

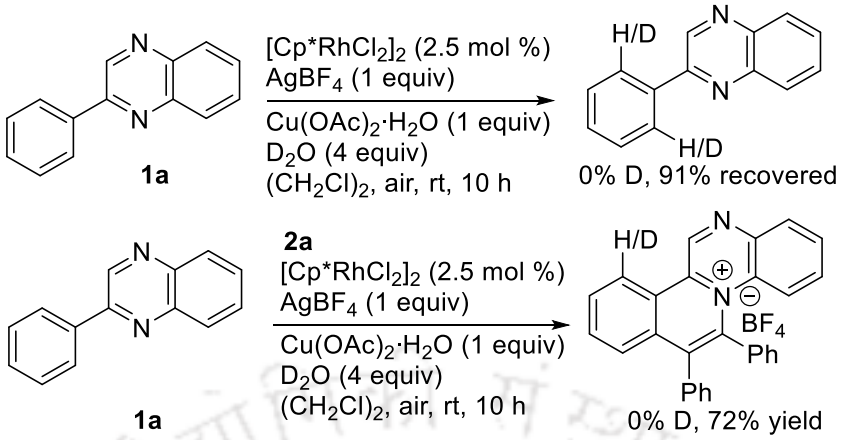
The scope of the procedure was extended to the coupling of a series of 2-phenylquinoxalines **1b-n** with diphenylacetylene **2a** as a standard substrate (Table 3). The substrates bearing the substitution at the 4-position of the aryl ring **A** such as bromo **1b**, chloro **1c**, cyano **1d**, ethyl **1e** and fluoro **1f** groups were tolerant, furnishing the quaternary ammonium salts **3ba-fa** in 75-97% yields. Similar results were obtained with the substrates bearing the substitution at the ring **B** with chloro **1g** and dimethyl **1h** groups producing **3ga** and **3ha** in 85 and 92% yields respectively, while **1i** underwent annulation to afford **3ia** (82%) as a 5:2 mixtures of diastereomers as the precursor **1i** was an inseparable mixture of two regioisomers. In addition, the substrates having the substitution at both the rings **A** and **B** could be annulated to give **3ja**, **3ka** and **3la** in 85-90% yields. Next, the reaction of 2,3-diphenylquinoxaline **1m** and 2-thiophenylquinoxaline **1n** was carried out with diphenylacetylene **2a**, no product was observed in case of former while as the later yielded trace amount of product. To get insight into the reaction pathway, the intermediate **1I′** was isolated by the treatment of 40 mol % $[Cp^*RhCl_2]_2$ with **1a** in $(CH_2Cl)_2$ for 10 h (Scheme 9), which was characterized by ^1H NMR and ESI-HRMS. The treatment of **1I′** with **2a** in presence of $Cu(OAc)_2{\cdot}H_2O$ and $AgBF_4$ produced the quaternary ammonium salt **3aa** in 91% yield (Scheme 10).[5f,8,15] This experimental result indicates that the reaction proceeds through the formation of a 5-membered rhodacycle **1I′**. Next, we performed the isotope labelling experiments to understand the nature of the C-H activation. In this regard, the reaction of **1a** with or without **2a** using D_2O as a co-solvent does not exhibit any H/D scrambling at the *ortho*-position, which clearly suggests that



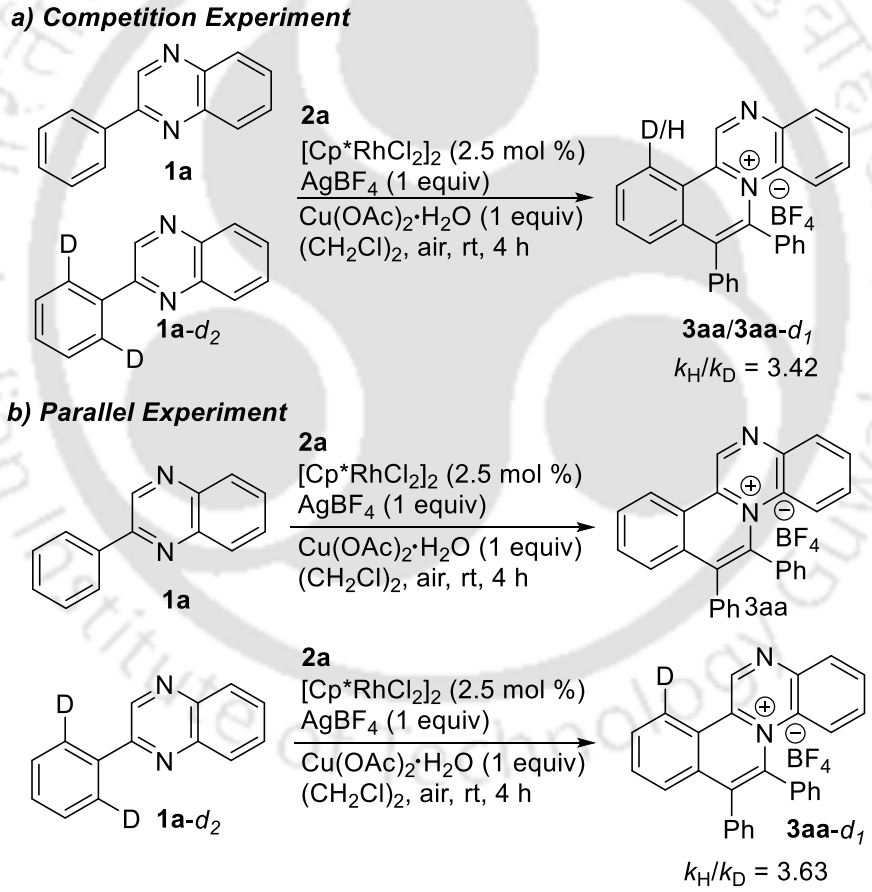
Scheme 9. Isolation of Intermediate **1I′**



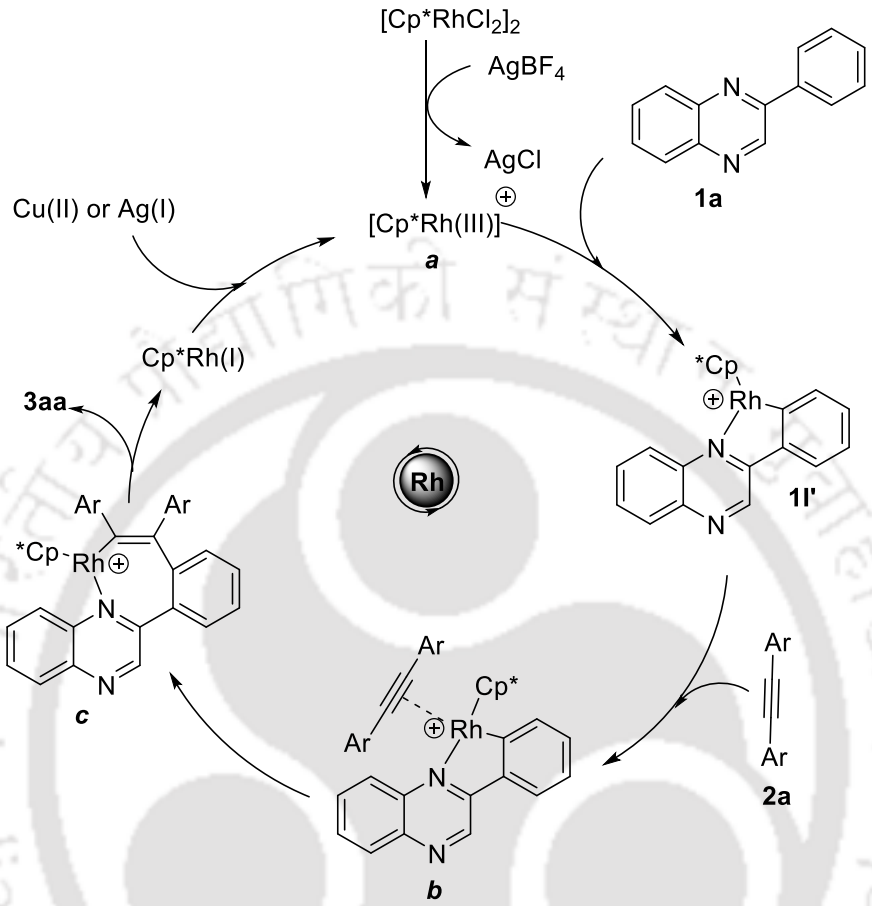
Scheme 10. Reaction of Intermediate **1I′** with Diphenylacetylene **2a**



Scheme 11. H/D Scrambling Experiments



Scheme 11. Kinetic Isotope Experiments



Scheme 11. Plausible Reaction Mechanism

the C-H bond activation step may be irreversible (Scheme 11).[16a] Furthermore, the intermolecular competition experiment of **1a** and **1a**-d_2 with **2a** produced the k_H/k_D = 3.42, while the parallel experiment gave k_H/k_D = 3.63 (Scheme 12), which indicate that the C-H bond cleavage may be the rate-determining step.[16b,c] Based on these experimental results, a plausible catalytic cycle is depicted in Scheme 13. The reaction of $[Cp^*RhCl_2]_2$ with $AgBF_4$ may produce a cationic Rh(III) species ***a***, which may activate the C-H bond of **1** to form a five-membered rhodacycle **1I′** (Scheme 13).[15,17] Subsequent co-ordination of acetylene **2** with rhodacycle **1I′** may lead to the formation of the Rh(III)-species ***b***, which can undergo migratory insertion to form ***c***. The latter may undergo reductive elimination to deliver the heterocycles **3** and a Rh(I) species, which can be oxidized using Cu(II)/Ag(I) to generate the active Rh(III) species ***a*** and complete the catalytic cycle.

Finally, we investigated the photophysical properties **3aa**, **3ad**, **3ga**, **3fa** and **3ha** as the representative examples.[6b,8,9] Figure 1 shows the photoluminescence spectra and the Table 4 presents emission wavelength, which unveil that irrespective of the substitution, all the heterocyclic salts showed a sharp green photoluminescence with emission wavelength in the range of 500-570 nm. This observation reveals that the qunoxalin-5-ium salts can be potent candidates for the development of green organic light-emitting diodes (OLEDs) and ionic dopants.[18]

Table 4. Fluorescence Emission Wavelength Maxima of Selected Salts

Entry	Quinoxalin-5-ium salts	Emission wavelength (nm)
1	**3aa**	521
2	**3ad**	526
3	**3ga**	532
4	**3fa**	535
5	**3ha**	519

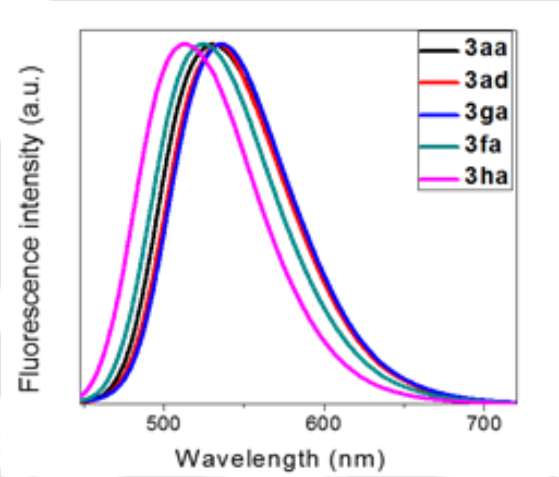


Figure 1. Photoluminescence Spectra of Selected Salts in CH_2Cl_2 (1.0×10^{-5} M)

In summary, we have successfully developed an efficient Rh-catalyzed oxidative coupling of 2-arylquinoxalines with alkynes to furnish a diversely substituted quaternary ammonium salts via oxidative C-H bond activation, followed by annulation under mild reaction condition. The reaction pathway is demonstrated using the isolation of the five-membered rhodacycle **1I′** and kinetic isotope studies. The preliminary photophysical studies suggests that these structural scaffolds can be useful towards the development of organic light emitting diodes (OLEDs).

1.3 Experimental Section

General Information. $[Cp^*RhCl_2]_2$, $AgBF_4$ (98%) and $Cu(OAc)_2 \cdot H_2O$ (≥98%) were purchased from Aldrich and used as received. 2-Arylqunoxalines **1a-l** and alkynes **2a-l** were prepared according to literature.[19,20] Merck silica gel G/GF 254 plates were used for analytical TLC and Rankem silica gel (60-120 mesh) was used for column chromatography. NMR (^1H and ^{13}C) spectra were recorded in Bruker 300, Bruker Avance III 400 and 600 spectrometers using $CDCl_3$/DMSO-d_6 as a solvent and TMS as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively and other data are reported as follows: s = singlet, d = doublet, dd= doublet of doublet, t = triplet, m = multiplet, q = quartet. PerkinElmer IR instrument was used for recording FT-IR spectra. Using Q-Tof ESI-MS instrument (model HAB 273), mass spectra were recorded. Single crystal X-ray data were collected using Bruker SMART APEX-II CCD diffractometer, which is equipped with 1.75 kW sealed-tube Mo-Kα irradiation (λ = 0.71073 Å) at 296(2) K. The crystal structure was solved by direct method using *SHELLX-97* (Göttingen, Germany) and refined with full-matrix least squares on F^2 using *SHELXL*-97.

Procedure for the Synthesis of Rhodacycle 1I′. To a 10 mL round bottom flask, 2-phenylquinoxaline **1a** (0.25 mmol, 52 mg), $[Cp^*RhCl_2]_2$ (0.10 mmol, 62 mg) and $AgBF_4$ (0.25 mmol, 48.6 mg) were added. The flask was purged with nitrogen three times followed by the addition of 3 mL of $(CH_2Cl)_2$. The mixture was stirred at room temperature for 10 h and was then passed through a short pad of celite using MeOH. The filtrate was concentrated in vacuo and the residue washed with EtOAc (1 x 5 mL). The resultant yellow solid was dried and isolated in 55% yield. The formation of the rhodacycle **1I′** was confirmed by ^1H NMR and HRMS analysis.

Procedure for the Reaction of 1I′ with 1,2-diphenylethyne 2a. To a 10 mL round bottom flask, 1,2-diphenylethyne **2a** (0.05 mmol, 9 mg), **1I′** (0.05 mmol, 26 mg), $AgBF_4$ (0.05 mmol, 9.7 mg) and $Cu(OAc)_2 \cdot H_2O$ (0.05 mmol, 10 mg) were added in 1.5 mL of $(CH_2Cl)_2$ and stirred at room temperature for 5 h. The reaction mixture was then diluted with CH_2Cl_2 (5 mL) and passed through a short pad of celite using CH_2Cl_2 (3 x 5 mL). The combined filtrate was concentrated in vacuo and the residue was purified on silica gel column chromatography employing CH_2Cl_2/MeOH (96:4) as an eluent to afford **3aa** in 91% yield.

Procedure for the Synthesis of 1a-*d*$_2$.[21] In an oven-dried 10 mL round bottom flask, 2-phenylqunoxaline **1a** (0.25 mmol, 52 mg), $[Cp^*RhCl_2]_2$ (5 mol %, 7.6 mg), AgOTf (0.05 mmol, 12.8 mg), Ag_2CO_3 (0.25 mmol, 68.8 mg), toluene (1.5 mL) and D_2O (0.5 mL) were stirred at 130 °C for 14 h under air. The solvent was then removed on a rotary evaporator and the residue was dissolved with EtOAc and passed through a short pad of celite. The filtrate was concentrated and the residue was purified on silica gel column chromatography using EtOAc/hexane (1:10) as an eluent to afford **1a-*d*$_2$** as a pale yellow solid. The deuterium incorporation was determined using 400 MHz ^{1}H NMR as 96.5%.

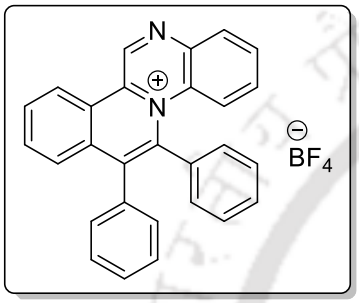
H/D Exchange Experiment with D_2O. 2-Phenylquinoxaline **1a** (0.25 mmol, 52 mg), $[Cp^*RhCl_2]_2$ (2.5 mol %, 3.8 mg), $AgBF_4$ (0.25 mmol, 48.6 mg), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol, 49.9 mg) and D_2O (1 mmol) were stirred at room temperature for 10 h in $(CH_2Cl)_2$ (3 mL) under air. The reaction mixture was then diluted with CH_2Cl_2 (5 mL), and passed through a short pad of celite using CH_2Cl_2 (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent on vacuo produced a residue, which was purified on silica gel column chromatography using EtOAc/hexane (1:10) as eluent. No deutration incorporation was observed from 400 MHz ^{1}H NMR.

H/D Exchange Experiment with D_2O in Presence of Alkyne. 2-Phenylquinoxaline **1a** (0.25 mmol, 52 mg), 1,2-diphenylethyne **2a** (0.25 mmol, 44.5 mg), $[Cp^*RhCl_2]_2$ (2.5 mol %, 3.8 mg), $AgBF_4$ (0.25 mmol, 48.6 mg), $Cu(OAc)_2{\cdot}H_2O$ (0.25 mmol, 49.9 mg) and D_2O (1 mmol) were stirred at room temperature for 10 h in $(CH_2Cl)_2$ (3 mL) under air. The reaction mixture was diluted with CH_2Cl_2 (5 mL), and passed through a short pad of celite using CH_2Cl_2 (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent on vacuo produced a residue, which was purified on silica gel column chromatography using CH_2Cl_2/MeOH (96:4) as an eluent. No deutration incorporation was observed from 400 MHz ^{1}H NMR.

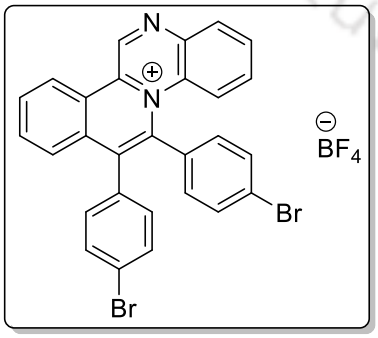
Competition Isotope Experiment. Compound **1a** (0.25 mmol, 52 mg) and **1a-*d*$_2$** (0.25 mmol, 52 mg) were subjected to the standard reaction conditions for 4 h. The reaction mixture was diluted with CH_2Cl_2 (5 mL) and passed through a short pad of celite using CH_2Cl_2 (3 x 5 mL). The filtrate was concentrated on vacuo and the residue was purified on silica gel column chromatography using CH_2Cl_2/MeOH (96:4) as an eluent. The k_H/k_D was determined using 300 MHz ^{1}H NMR as 3.42.

Parallel Kinetic Isotope Experiment. Compound **1a** (0.25 mmol, 52 mg) and **1a**-d_2 (0.25 mmol, 52 mg) were separately subjected to the standard reaction conditions for 4 h. The reaction mixtures were diluted with CH_2Cl_2 (5 mL). Both the reaction mixtures were combined together and the resultant solution was passed through a short pad of celite using CH_2Cl_2 (3 x 5 mL). The filtrate was concentrated on vacuo and the residue was purified on silica gel column chromatography using CH_2Cl_2/MeOH (96:4) as an eluent. The k_H/k_D was determined using 400 MHz ^{1}H NMR as 3.63.

1.4 Characterization data

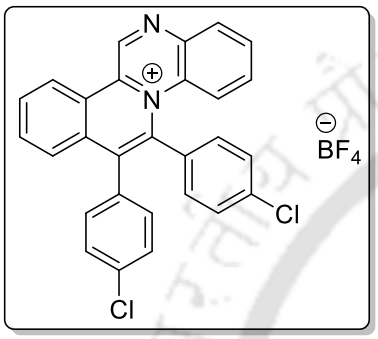


6,7-Diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3aa. Yellow solid; yield 98% (115 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.04 (s, 1H), 9.75 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 8.0 Hz, 1H), 8.34-8.29 (m, 2H), 7.91 (t, J = 8.0 Hz, 1H), 7.79-7.72 (m, 2H), 7.52-7.44 (m, 4H), 7.33-7.21 (m, 7H); ^{13}C NMR (150 MHz, DMSO-d_6/$CDCl_3$, 1:10) δ 144.95, 144.93, 142.0, 141.6, 140.2, 136.1, 136.0, 135.7, 134.3, 132.6, 132.1, 130.8, 130.4, 129.7, 129.44, 129.42, 128.5, 128.4, 128.0, 127.4, 127.1, 125.8, 124.4, 123.4; FT-IR (KBr) 2924, 2853, 1612, 1572, 1520, 1495, 1464, 1345, 1261, 1061, 766, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{19}N_2^+$: 383.1543, found: 383.1548.

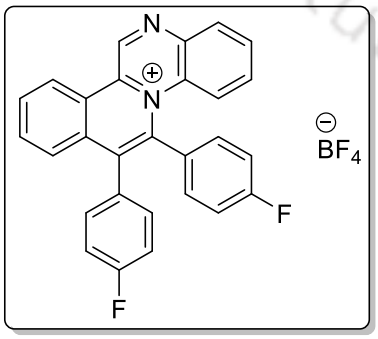


6,7-Bis(4-bromophenyl)isoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ab. Yellow solid; yield 95% (149 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.05 (s, 1H), 9.75 (d, J = 8.0 Hz,

1H), 8.47-8.44 (m, 1H), 8.38-8.28 (m, 2H), 7.97-7.93 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.75-7.70 (m, 3H), 7.64-7.59 (m, 1H), 7.56-7.53 (m, 2H), 7.31-7.28 (m, 2H), 7.21-7.18 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.1, 141.7, 139.7, 139.3, 137.8, 137.1, 135.4, 134.3, 132.8, 132.5, 132.4, 132.1, 131.8, 131.7, 131.5, 130.1, 127.38, 127.31, 127.0, 124.8, 124.2, 123.4, 122.4; FT-IR (KBr) 2924, 2853, 1590, 1490, 1437, 1396, 1346, 1250, 1081, 1058, 1013, 820, 775, 735 cm^{-1}; HRMS (ESI) *m/z* [M-BF_4]$^+$ calcd for $C_{28}H_{17}Br_2N_2^+$: 540.9733, found: 540.9753.

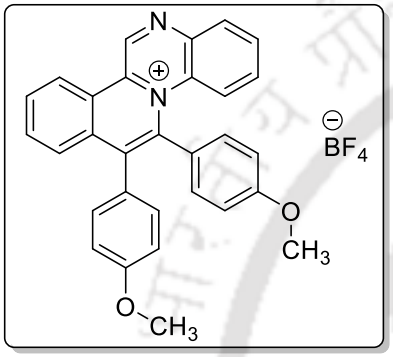


6,7-Bis(4-chlorophenyl)isoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ac. Yellow solid; yield 92% (124 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.06 (s, 1H), 9.75 (d, *J* = 8.4 Hz, 1H), 8.46 (d, *J* = 7.8 Hz, 1H), 8.36 (t, *J* = 8.4 Hz, 1H), 8.31 (t, *J* = 7.8 Hz, 1H), 7.96-7.94 (m, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.59-7.57 (m, 2H), 7.41-7.36 (m, 4H), 7.27 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.1, 141.7, 139.7, 139.4, 137.8, 137.1, 135.4, 134.5, 134.0, 133.7, 132.46, 132.42, 131.8, 131.4, 130.1, 128.9, 128.8, 127.37, 127.31, 127.0, 124.8, 124.2; FT-IR (KBr) 2924, 2853, 1598, 1519, 1493, 1439, 1347, 1212, 1083, 1061, 968, 823, 769, 755, 669 cm^{-1}; HRMS (ESI) *m/z* [M-BF_4]$^+$ calcd for $C_{28}H_{17}Cl_2N_2^+$: 451.0763, found: 451.0769.

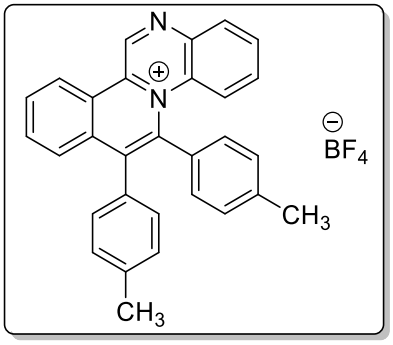


6,7-Bis(4-fluorophenyl)isoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ad. Yellow solid; yield 91% (115 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.04 (s, 1H), 9.74 (d, *J* = 8.4 Hz, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 8.36-8.29 (m, 2H), 7.93 (t, *J* =

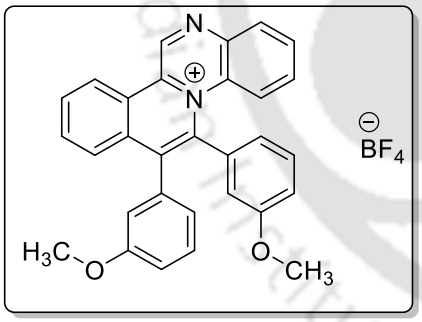
7.8 Hz, 1H), 7.76 (t, *J* = 7.8 Hz, 2H), 7.58 (t, *J* = 8.4 Hz, 1H), 7.39 (s, 2H), 7.33 (t, *J* = 8.4 Hz, 2H), 7.27 (s, 1H), 7.16 (t, *J* = 8.4 Hz, 2H), 6.56 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 162.9 (J_{C-F} = 247.6 Hz), 162.7 (J_{C-F} = 245.1 Hz), 147.2, 147.0, 141.6, 140.0, 139.8, 137.6, 136.9, 135.6, 133.0, 132.28, 132.20, 131.7, 131.3, 130.0, 129.9, 127.4, 127.2 (J_{C-F} = 6.7 Hz), 127.0 (J_{C-F} = 5.4 Hz), 124.7, 124.1, 115.9 (J_{C-F} = 22.2 Hz), 115.8 (J_{C-F} = 24.1 Hz); FT-IR (KBr) 2924, 2854, 1604, 1509, 1437, 1375, 1336, 1230, 1162, 1059, 969, 832, 776, 698 cm^{-1}; HRMS (ESI) *m/z* [M-BF_4]$^+$ calcd for $C_{28}H_{17}F_2N_2^+$: 419.1354, found: 419.1356.



6,7-Bis(4-methoxyphenyl)isoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ae. Yellow solid; yield 79% (105 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.97 (s, 1H), 9.68 (d, *J* = 8.4 Hz, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.30-8.25 (m, 2H), 7.90 (t, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 8.4 Hz, 1H), 7.24 (d, *J* = 9.0 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 3.80 (s, 3H), 3.71 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.7, 159.2, 147.1, 141.6, 141.1, 140.9, 137.5, 136.7, 136.4, 132.1, 132.0, 131.4, 131.2, 130.1, 129.7, 127.99, 127.92, 127.1, 127.0, 125.8, 124.8, 124.0, 114.18, 114.13, 55.38, 55.31; FT-IR (KBr) 2960, 2925, 2839, 1611, 1573, 1512, 1439, 1335, 1246, 1179, 1061, 1029, 964, 826, 797 cm^{-1}; HRMS (ESI) *m/z* [M-BF_4]$^+$ calcd for $C_{30}H_{23}O_2N_2^+$: 443.1754, found: 443.1764.

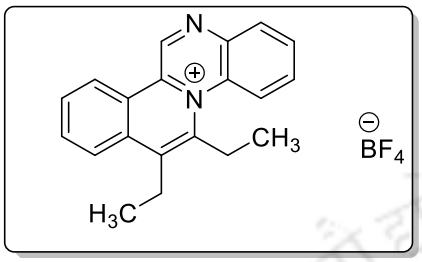


6,7-Di-*p*-tolylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3af. Yellow solid; yield 83% (103 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 9.72 (d, *J* = 8.4 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.33-8.25 (m, 2H), 7.90 (t, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.53-7.48 (m, 1H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.10 (q, *J* = 6.8 Hz, 4H), 2.37 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6/$CDCl_3$,1:10) δ 144.8, 142.2, 141.6, 140.5, 139.7, 138.3, 136.3, 135.9, 135.6, 131.9, 131.5, 130.6, 130.3, 129.6, 129.2, 129.0, 128.7, 127.4, 127.3, 125.7, 124.3, 123.4, 20.85, 20.80; FT-IR (KBr) 2927, 2838, 1611, 1573, 1512, 1465, 1439, 1335, 1288, 1185, 1060, 1028, 964, 826, 772, 755 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{30}H_{23}N_2^+$: 411.1856, found: 411.1860.

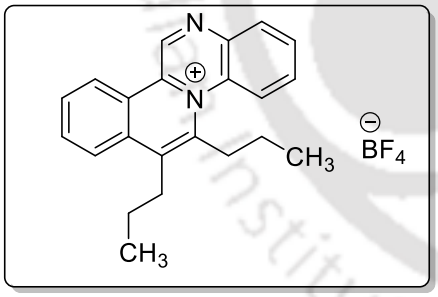


6,7-Bis(3-methoxyphenyl)isoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ag. (Rotational isomers 1:1) Yellow solid; yield 82% (109 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.04 (s, 2H), 9.74 (d, *J* = 8.4 Hz, 2H), 8.45 (d, *J* = 8.4 Hz, 2H), 8.35-8.29 (m, 5H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.92-7.89 (m, 2H), 7.81 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.08 (s, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 6.6 Hz, 2H), 6.92-6.88 (m, 4H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.70 (s, 1H), 6.68 (d, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 3.66 (s, 3H), 3.54 (s, 3H), 3.52 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.09, 159.06, 159.03, 158.9, 147.1, 141.6, 140.48, 140.45, 140.1, 137.6, 136.9, 136.42, 136.40, 135.6, 135.07, 135.05, 132.3, 131.3, 130.1,

130.0, 129.9, 129.89, 129.82, 127.7, 127.1, 124.8, 123.9, 122.6, 122.5, 122.4, 122.0, 115.98, 115.92, 115.87, 115.84, 115.7, 115.6, 114.2, 55.3, 55.2; FT-IR (KBr) 2924, 2853, 1601, 1589, 1519, 1458, 1425, 1322, 1264, 1157, 1059, 940, 769, 695 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{30}H_{23}O_2N_2^+$: 443.1754, found: 443.1752.

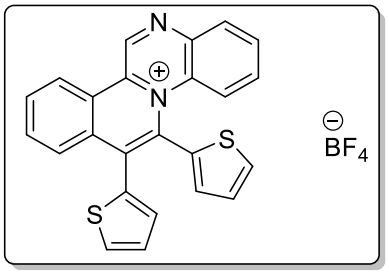


6,7-Diethylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ah. Yellow solid; yield 74% (69 mg); ^1H NMR (400 MHz, DMSO-d_6) δ 10.79 (s, 1H), 9.53 (d, *J* = 8.8 Hz, 1H), 8.61 (t, *J* = 8.0 Hz, 2H), 8.48 (d, *J* = 8.0 Hz, 1H), 8.36 (t, *J* = 8.0 Hz, 1H), 8.22 (t, *J* = 7.6 Hz, 1H), 8.12 (t, *J* = 8.0 Hz, 1H), 8.05 (t, *J* = 8.0 Hz, 1H), 3.68 (q, *J* = 7.2 Hz, 2H), 3.50 (q, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.9, 143.8, 142.0, 141.1, 136.9, 136.6, 134.7, 131.7, 131.3, 130.6, 129.7, 127.5, 127.1, 125.0, 124.3, 124.0, 26.9, 22.5, 14.9, 13.8; FT-IR (KBr) 2924, 2853, 1610, 1589, 1517, 1435, 1384, 1335, 1212, 1129, 1092, 1050, 898, 781, 761, 699 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{20}H_{19}N_2^+$: 287.1543, found: 287.1546.

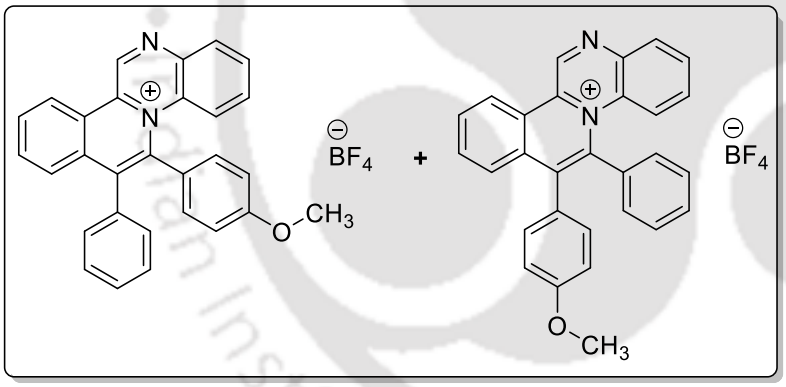


6,7-Dipropylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ai. Yellow solid; yield 72% (72 mg); ^1H NMR (400 MHz, DMSO-d_6) δ 10.81 (s, 1H), 9.54 (d, *J* = 8.4 Hz, 1H), 8.62 (q, *J* = 6.0 Hz, 2H), 8.48 (q, *J* = 6.8 Hz, 1H), 8.36 (t, *J* = 7.6 Hz, 1H), 8.22 (t, *J* = 8.0 Hz, 1H), 8.13 (t, *J* = 7.6 Hz, 1H), 8.06 (t, *J* = 8.8 Hz, 1H), 3.67 (t, *J* = 8.0 Hz, 2H), 3.43 (t, *J* = 8.0 Hz, 2H), 1.83 (q, *J* = 8.0 Hz, 2H), 1.37 (q, *J* = 7.6 Hz, 2H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.70 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.0, 142.9, 141.26, 141.21, 136.9, 136.8, 135.2, 132.0, 131.6, 130.9, 129.9, 127.7, 127.2, 125.4, 124.3, 124.2, 35.6, 31.3, 24.2, 22.7, 14.3, 13.8; FT-IR (KBr) 2924, 1610, 1588, 1516, 1459, 1435, 1384, 1335, 1262, 1084, 1050, 898, 781, 760 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{22}H_{23}N_2^+$: 315.1856, found:

315.1857.

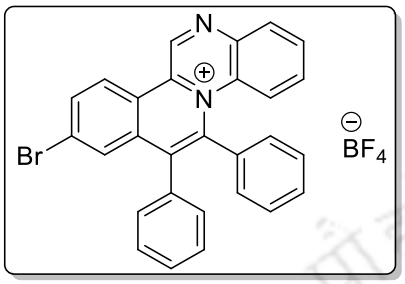


6,7-Di(thiophen-2-yl)isoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3aj. Yellow solid; yield 67% (81 mg); ^{1}H NMR (400 MHz, DMSO- d_6) δ 10.97 (s, 1H), 9.69-9.66 (m, 1H), 8.44 (q, *J* = 7.2 Hz, 1H), 8.35-8.32 (m, 2H), 7.96-7.93 (m, 3H), 7.87 (d, *J* = 6.0 Hz, 1H), 7.81 (d, *J* = 6.0 Hz, 1H), 7.63-7.59 (m, 1H), 7.47-7.46 (m, 1H), 7.32-7.29 (m, 1H), 7.20-7.19 (m, 1H), 7.02-7.00 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.0, 141.5, 138.2, 137.2, 136.5, 136.2, 135.6, 135.5, 133.4, 132.68, 132.60, 132.2, 132.1, 131.4, 130.16, 130.13, 129.9, 128.0, 127.5, 127.3, 127.2, 127.0, 124.8, 122.6; FT-IR (KBr) 2927, 2845, 1578, 1509, 1481, 1443, 1321, 1201, 1067, 964, 812, 783, 721, 651 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{24}H_{15}S_2N_2^+$: 395.0671, found: 395.0683.

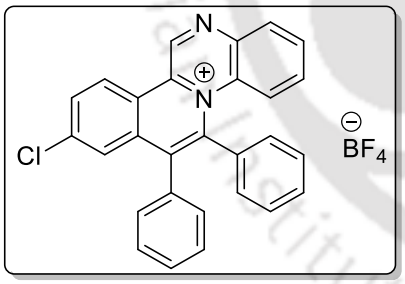


6-(4-Methoxyphenyl)-7-phenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate and 7-(4-Methoxyphenyl)-6-phenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate.(3:2) 3al. Yellow solid; yield 84% (105 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.03 (s, 0.9H), 11.01 (s, 0.6H), 9.72 (t, *J* = 7.8 Hz, 1.6H), 8.43 (t, *J* = 7.8 Hz, 1.6H), 8.34-8.27 (m, 3.4 H), 7.91 (t, *J* = 7.8 Hz, 1.7H), 7.83 (d, *J* = 9.0 Hz, 0.7H), 7.79 (d, *J* = 9.0 Hz, 2H), 7.72 (d, *J* = 9.0 Hz, 0.7H), 7.54 (t, *J* = 9.0 Hz, 0.8H), 7.51-7.48 (m, 3.2H), 7.34 (t, *J* = 7.2 Hz, 3.3H), 7.28 (t, *J* = 7.8 Hz, 2.2H), 7.25 (d, *J* = 9.0 Hz, 2.9H), 7.16 (d, *J* = 8.4 Hz, 2.1H), 7.03 (d, *J* = 8.4 Hz, 2.1H), 6.82 (d, *J* = 9.0 Hz, 1.4H), 3.79 (s, 3H), 3.70 (s, 1.9H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 159.7, 159.2, 147.2, 141.7, 140.96, 140.91, 140.88, 140.86, 137.69, 137.60, 136.8, 136.3, 135.8, 135.5, 133.9, 132.2, 132.15, 132.10, 131.4, 131.3,

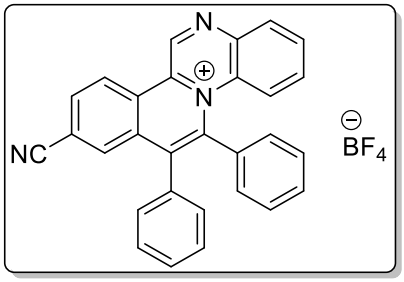
131.2, 130.6, 130.15, 130.13, 130.0, 129.8, 129.7, 129.6, 128.7, 128.6, 127.9, 127.7, 127.2, 127.19, 127.17, 127.0, 125.6, 124.9, 124.8, 124.2, 124.0, 114.1, 114.0, 55.36, 55.31; FT-IR (KBr) 2955, 2924, 2853, 1609, 1586, 1512, 1439, 1397, 1337, 1292, 1249, 1177, 1059, 1028, 771, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{29}H_{21}ON_2^+$: 413.1648, found: 413.1654.



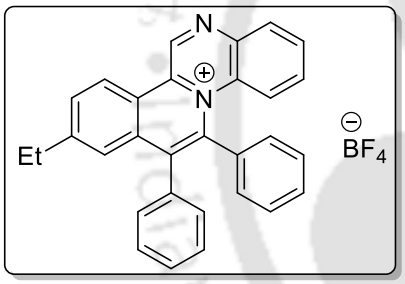
9-Bromo-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ba. Yellow solid; yield 97% (133 mg); ^1H NMR (600 MHz, DMSO-d_6) δ 11.02 (s, 1H), 9.67 (d, *J* = 9.0 Hz, 1H), 8.55 (d, *J* = 10.2 Hz, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 7.93 (t, *J* = 7.8 Hz, 1H), 7.77-7.75 (m, 2H), 7.52-7.46 (m, 4H), 7.32 (t, *J* = 9.0 Hz, 3H), 7.26-7.23 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.1, 141.8, 141.7, 139.4, 137.7, 136.6, 135.2, 135.1, 133.1, 131.8, 131.5, 131.1, 130.4, 130.1, 130.0, 129.8, 129.3, 129.2, 129.0, 128.8, 128.7, 127.6, 124.0, 123.8; FT-IR (KBr) 2923, 2853, 1596, 1519, 1462, 1445, 1396, 1328, 1261, 1083, 1030, 785, 759 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{18}BrN_2^+$: 461.0648, found: 461.0639.



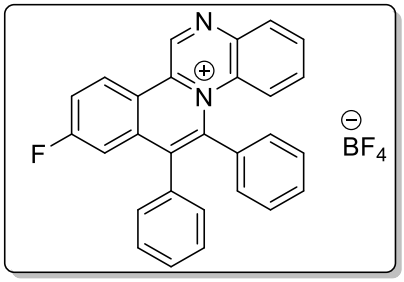
9-Chloro-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ca. Yellow solid; yield 91% (114 mg); ^1H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 9.76 (d, *J* = 9.2 Hz, 1H), 8.45-8.40 (m, 2H), 7.92 (t, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 9.2 Hz, 1H), 7.59 (s, 1H), 7.47-7.46 (m, 3H), 7.32-7.23 (m, 8H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.1, 142.2, 141.86, 141.80, 139.6, 137.6, 136.8, 135.1, 133.2, 132.6, 131.5, 131.2, 130.5, 130.2, 130.07, 130.06, 129.8, 129.7, 129.0, 128.7, 127.6, 125.7, 124.1, 123.6; FT-IR (KBr) 2924, 2854, 1607, 1519, 1462, 1377, 1083, 824, 759, 700 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{18}ClN_2^+$: 417.1153, found: 417.1160.



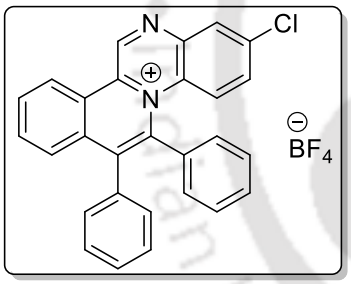
9-Cyano-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3da. Yellow solid; yield 75% (93 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.11 (s, 1H), 9.89 (d, *J* = 8.4 Hz, 1H), 8.70 (d, *J* = 10.2 Hz, 1H), 8.49 (d, *J* = 7.8 Hz, 1H), 8.10 (s, 1H), 7.97 (t, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.55 (t, *J* = 8.4 Hz, 1H), 7.48-7.47 (m, 3H), 7.34-7.31 (m, 3H), 7.26-7.23 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.2, 142.4, 142.0, 140.4, 137.4, 135.1, 134.8, 132.9, 132.7, 132.09, 132.06, 130.4, 130.3, 130.2, 130.1, 129.9, 129.1, 128.7, 128.6, 128.5, 127.6, 126.7, 124.2, 118.1, 117.3; FT-IR (KBr) 2923, 2853, 1618, 1588, 1517, 1462, 1439, 1372, 1330, 1131, 1084, 1028, 970, 831, 762, 699 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{29}H_{18}N_3^+$: 408.1495, found: 408.1500.



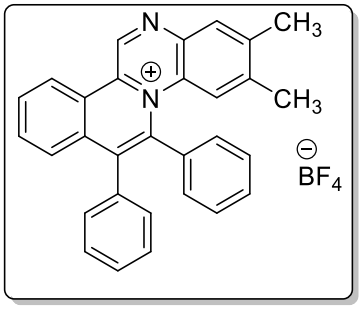
9-Ethyl-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ea. Yellow solid; yield 88% (110 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.98 (s, 1H), 9.66 (d, *J* = 9.0 Hz, 1H), 8.41 (d, *J* = 9.0 Hz, 1H), 8.25 (d, *J* = 9.0 Hz, 1H), 7.88 (t, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.48-7.44 (m, 5H), 7.31 (t, *J* = 8.4 Hz, 3H), 7.25-7.21 (m, 4H), 2.89 (q, *J* = 7.2 Hz, 2H), 1.19 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 154.3, 147.3, 141.5, 140.7, 140.4, 137.4, 136.3, 135.4, 133.8, 133.2, 131.1, 130.6, 130.1, 130.0, 129.7, 129.6, 128.79, 128.72, 128.6, 127.7, 127.3, 124.7, 124.1, 123.4, 29.0, 14.9; FT-IR (KBr) 2963, 2924, 2854, 1614, 1571, 1523, 1462, 1436, 1331, 1213, 1144, 1056, 928, 832, 769, 700 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{30}H_{23}N_2^+$: 411.1856, found: 411.1861.



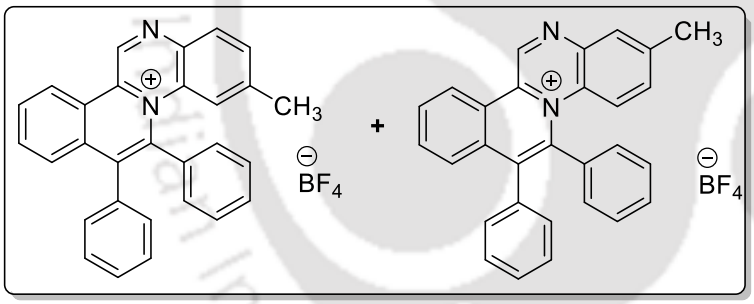
9-Fluoro-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3fa. Yellow solid; yield 93% (113 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.01 (s, 1H), 9.87 (d, *J* = 9.6 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.34-8.29 (m, 1H), 7.91 (t, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.52-7.45 (m, 4H), 7.34-7.31 (m, 4H), 7.27-7.21 (m, 4H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.0 (J_{C-F} = 258.9 Hz), 147.2, 141.5, 141.4, 140.0 (J_{C-F} = 4.9 Hz), 138.5, 138.4, 137.5, 135.1, 133.3, 131.8, 131.7, 131.3, 130.5, 130.1, 129.9, 129.8, 129.0, 128.7, 127.5, 124.1, 122.3, 122.2, 111.6 (J_{C-F} = 23.2 Hz); FT-IR (KBr) 2924, 2853, 1619, 1524, 1463, 1428, 1404, 1376, 1330, 1209, 1179, 1083, 1035, 765, 701 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{18}FN_2^+$: 401.1449, found: 401.1433



2-Chloro-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ga. Yellow solid; yield 92% (116 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.06 (s, 1H), 9.76 (d, *J* = 8.4 Hz, 1H), 8.47 (d, *J* = 8.4 Hz, 1H), 8.37-8.31 (m, 2H), 8.01 (q, *J* = 6.6 Hz, 1H), 7.75-7.73 (m, 2H), 7.47-7.45 (m, 3H), 7.39-7.37 (m, 3H), 7.31 (t, *J* = 8.4 Hz, 2H), 7.24-7.23 (m, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 147.7, 140.9, 140.6, 140.4, 137.9, 137.3, 136.0, 134.8, 134.2, 133.6, 132.4, 131.7, 131.6, 130.6, 130.03, 130.00, 128.9, 128.8, 128.6, 128.1, 127.4, 127.1, 124.8, 124.0; FT-IR (KBr) 2924, 2853, 1602, 1584, 1508, 1444, 1397, 1335, 1164, 1081, 1032, 918, 751, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{18}ClN_2^+$: 417.1153, found: 417.1155.

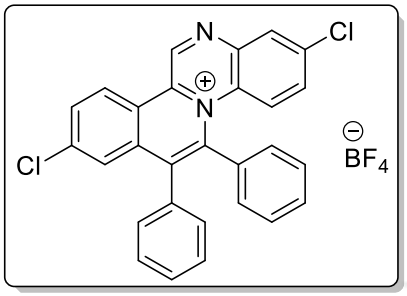


2,3-Dimethyl-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ha. Yellow solid; yield 85% (106 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.98 (s, 1H), 9.73 (d, *J* = 9.2 Hz, 1H), 8.33-8.23 (m, 3H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.48-7.44 (m, 4H), 7.37-7.33 (m, 3H), 7.30-7.26 (m, 2H), 7.24-7.22 (m, 2H), 2.44 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 145.7, 141.6, 140.7, 140.6, 140.4, 140.0, 136.6, 136.3, 135.3, 135.1, 133.8, 132.0, 130.5, 129.9, 129.4, 129.3, 128.6, 128.5, 128.4, 126.9, 126.8, 125.6, 124.9, 123.8, 20.0, 19.0; FT-IR (KBr) 2924, 2853, 1609, 1583, 1507, 1443, 1398, 1375, 1337, 1229, 1149, 1082, 1030, 869, 766, 696 cm^{-1}; HRMS (ESI) *m/z* [M-BF_4]$^+$ calcd for $C_{30}H_{23}N_2^+$: 411.1856, found: 411.1866.

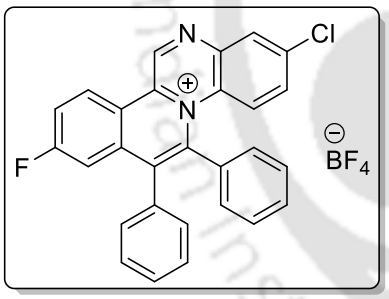


3-Methyl-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate and 2-Methyl-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate (2.5:1) 3ia. Yellow solid; yield 82% (99 mg); ^{1}H NMR (400 MHz, DMSO-d_6) 11.02 (s, 0.4H), 10.99 (s, 1H), 9.72 (t, *J* = 8.0 Hz, 1.6H), 8.34-8.25 (m, 5.1 H), 7.79 (d, *J* = 8.0 Hz, 1.2H), 7.71 (t, *J* = 8.0 Hz, 1.6H), 7.66 (d, *J* = 9.2 Hz, 0.5H), 7.51 (s, 1.1H), 7.46-7.44 (m, 4.9H), 7.35-7.22 (m, 12.3H), 2.12 (s, 3.3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.9, 145.8, 142.0, 141.8, 140.8, 140.7, 140.5, 140.2, 137.3, 136.9, 136.6, 136.5, 135.4, 135.3, 135.2, 133.7, 132.6, 132.0, 131.2, 130.5, 130.4, 129.97, 129.90, 129.7, 129.4, 129.2, 128.64, 128.61, 128.5, 128.4, 127.3, 127.0, 126.9, 125.6, 124.88, 124.82, 123.9, 123.5, 21.4, 20.4; FT-IR (KBr) 2924, 2854, 1608, 1519, 1444, 1375, 1339, 1209, 1161, 1083, 1061, 839, 777, 696 cm^{-1}; HRMS (ESI) *m/z* [M-BF_4]$^+$ calcd for $C_{29}H_{21}N_2^+$: 397.1699, found:

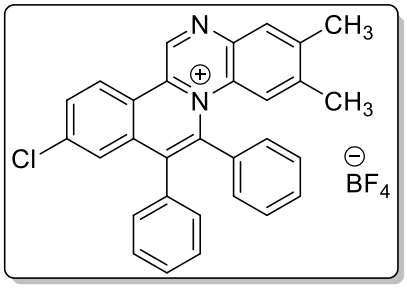
397.1699.



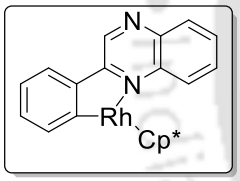
2,9-Dichloro-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ja. Yellow solid; yield 85% (114 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.04 (s, 1H), 9.79 (d, *J* = 9.2 Hz, 1H), 8.48-8.45 (m, 2H), 8.03 (dd, *J* = 9.2, 6.4 Hz, 1H), 7.73-7.72 (m, 1H), 7.62-7.61 (m, 1H), 7.48-7.47 (m, 3H), 7.39-7.36 (m, 3H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.26-7.24 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.5, 142.5, 141.7, 140.4, 139.6, 137.7, 136.8, 134.5, 134.3, 132.8, 132.7, 131.7, 131.6, 130.4, 130.0, 129.9, 129.7, 129.0, 128.8, 128.6, 127.9, 125.6, 123.9, 123.4; FT-IR (KBr) 2924, 2853, 1597, 1510, 1434, 1393, 1331, 1205, 1187, 1096, 1056, 1033, 973, 851, 729, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{17}Cl_2N_2^+$: 451.0763, found: 451.0763.



2-Chloro-9-fluoro-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3ka. Yellow solid; yield 88% (115 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.03 (s, 1H), 9.89 (q, *J* = 4.4 Hz, 1H), 8.47 (d, *J* = 8.8 Hz, 1H), 8.37-8.32 (m, 1H), 8.01 (dd, *J* = 8.8, 6.8 Hz, 1H), 7.71 (s, 1H), 7.48-7.46 (m, 3H), 7.39-7.31 (m, 6H), 7.25-7.22 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.6 ($J_{C\text{-}F}$ = 260.6 Hz), 147.6, 141.4, 140.2, 138.7, 137.5, 134.4, 134.2, 133.0, 131.9, 131.8, 131.6 ($J_{C\text{-}F}$ = 4.5 Hz), 130.5, 130.0, 129.8, 128.9, 128.8, 128.6, 127.9, 123.9, 122.5, 122.3, 122.0, 111.6 ($J_{C\text{-}F}$ = 23.1 Hz); FT-IR (KBr) 2924, 2853, 1617, 1519, 1463, 1377, 1329, 1288, 1199, 1062, 1031, 909, 831, 765, 697 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{28}H_{17}ClFN_2^+$: 435.1059, found: 435.1071.



9-Chloro-2,3-dimethyl-6,7-diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate 3la. Yellow solid; yield 90% (120 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.95 (s, 1H), 9.75 (d, *J* = 9.2 Hz, 1H), 8.41 (dd, *J* = 8.8, 6.8 Hz, 1H), 8.24 (s, 1H), 7.57-7.56 (m, 1H), 7.47-7.46 (m, 4H), 7.36-7.28 (m, 5H), 7.26-7.23 (m, 2H) 2.44 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 145.6, 141.9, 141.4, 141.2, 140.9, 140.8, 139.2, 136.5, 136.1, 135.1, 133.1, 132.3, 130.4, 129.9, 129.6, 129.33, 129.31, 128.8, 128.6, 125.59, 125.55, 123.69, 123.64, 20.1, 19.0; FT-IR (KBr) 2923, 1599, 1508, 1451, 1396, 1346, 1333, 1224, 1154, 1096, 1083, 1032, 968, 826, 751, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{30}H_{22}ClN_2^+$: 445.1466, found: 445.1466.



Rhodacycle 1I′. Yellow solid; yield 55 % (29 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.59 (s, 1H), 8.35 (dd, *J* = 8.0, 6.4 Hz, 2H), 8.17-8.12 (m, 2H), 7.92-7.83 (m, 2H), 7.62-7.58 (m, 2H), 1.71 (s, 3H), 1.61 (s, 1H), 1.54 (s, 11H); HRMS (ESI) *m/z* $[M\text{-}BF_4]^+$ calcd for $C_{24}H_{24}RhN_2^+$: 443.0995, found: 443.0995.

Crystal Structure and Data of 3aa

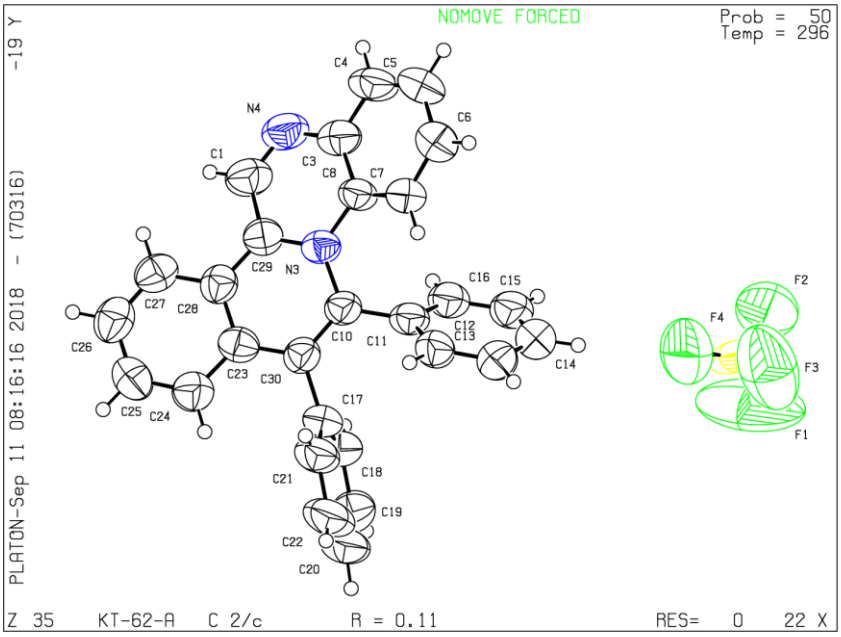


Figure 2. ORTEP Diagram of 6,7-Diphenylisoquinolino[2,1-a]quinoxalin-5-ium tetrafluoroborate **3aa** with 50% Thermal Ellipsoids (CCDC 1867227).

Identification code	**3aa**
Empirical formula	$C_{28}H_{19}N_2BF_4$
Formula weight	470.26
Crystal habit, colour	block/yellow
Crystal size, mm^3	0.32 x 0.25 x 0.16
Temperature, T/K	296(2)
Wavelength, λ/Å	0.71073
Crystal system	monoclinic
Space group	'C 2/c'
Unit cell dimensions	a = 31.900(4) Å b = 9.7621(10) Å c = 15.5417(16) Å $\alpha = \gamma = 90.00°$ $\beta = 107.394(14)$
Volume, V/$Å^3$	4618.5(9)
Z	8
Calculated density, $Mg \cdot m^{-3}$	1.353
Absorption coefficient, μ/mm^{-1}	0.101
F(000)	1936
θ range for data collection	1.338 to 25.048 °
Limiting indices	$-37 \leq h \leq 37, -11 \leq k \leq 11, -18 \leq l \leq 18$
Reflection collected / unique	4093/ 1585 [R(int) = 0.0742]

Completeness to θ	1.000 (θ = 25.048 °)
Refinement method	SHELXL-97 (Sheldrick, 1997)
Data / restraints / parameters	4093 / 0 / 316
Goodness–of–fit on F^2	1.349
Final R indices [I>2sigma(I)]	R1 = 0.1092, wR2 = 0.2628
R indices (all data)	R1 = 0.2352, wR2 = 0.3187

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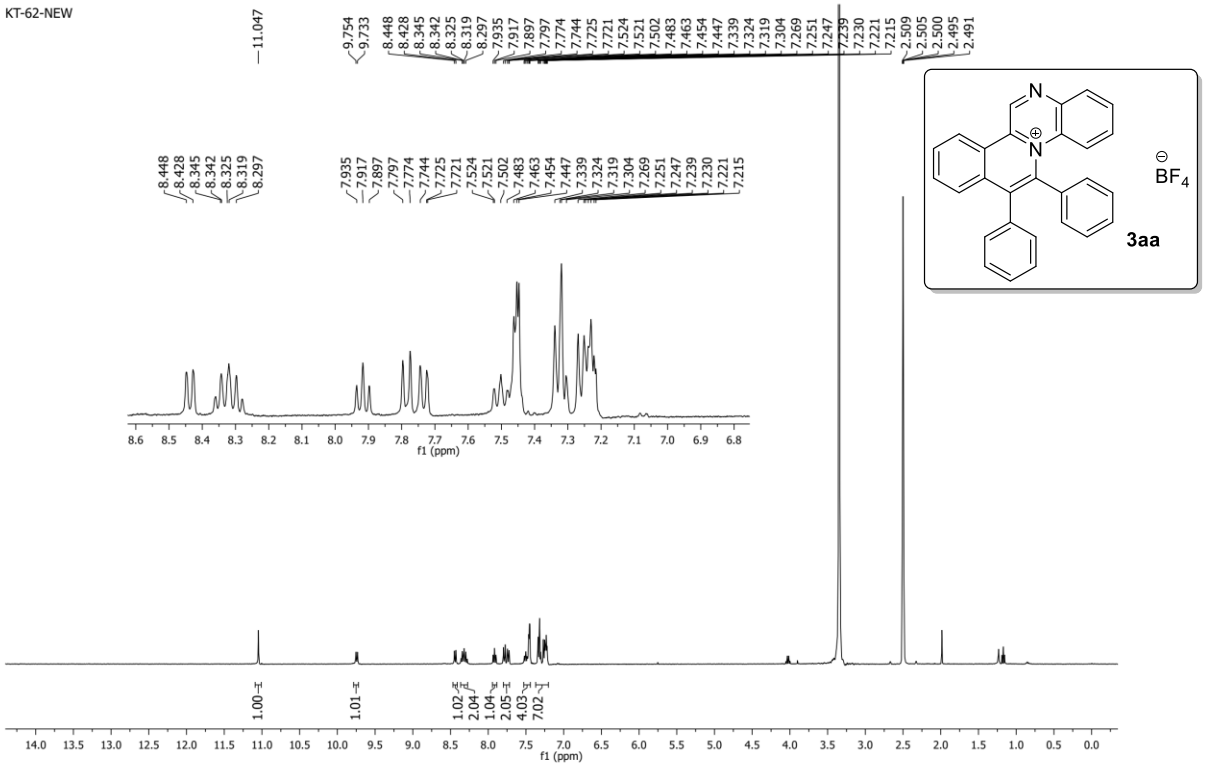
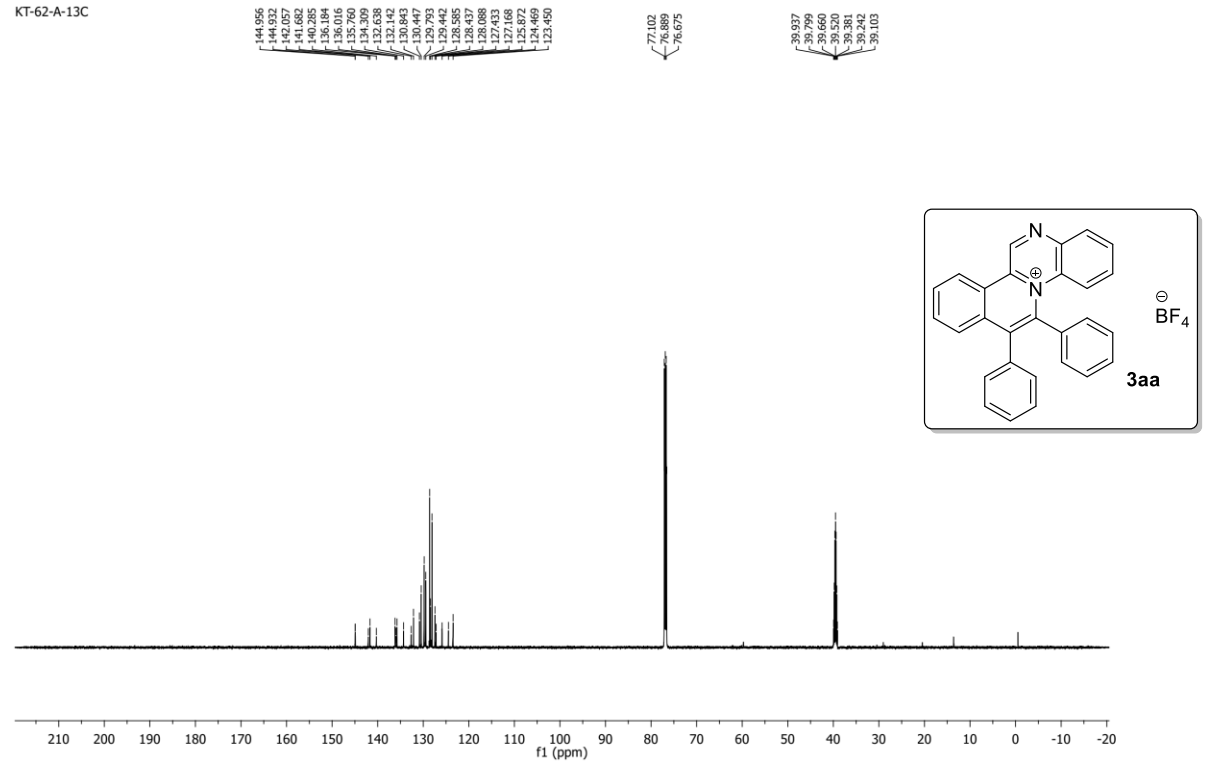
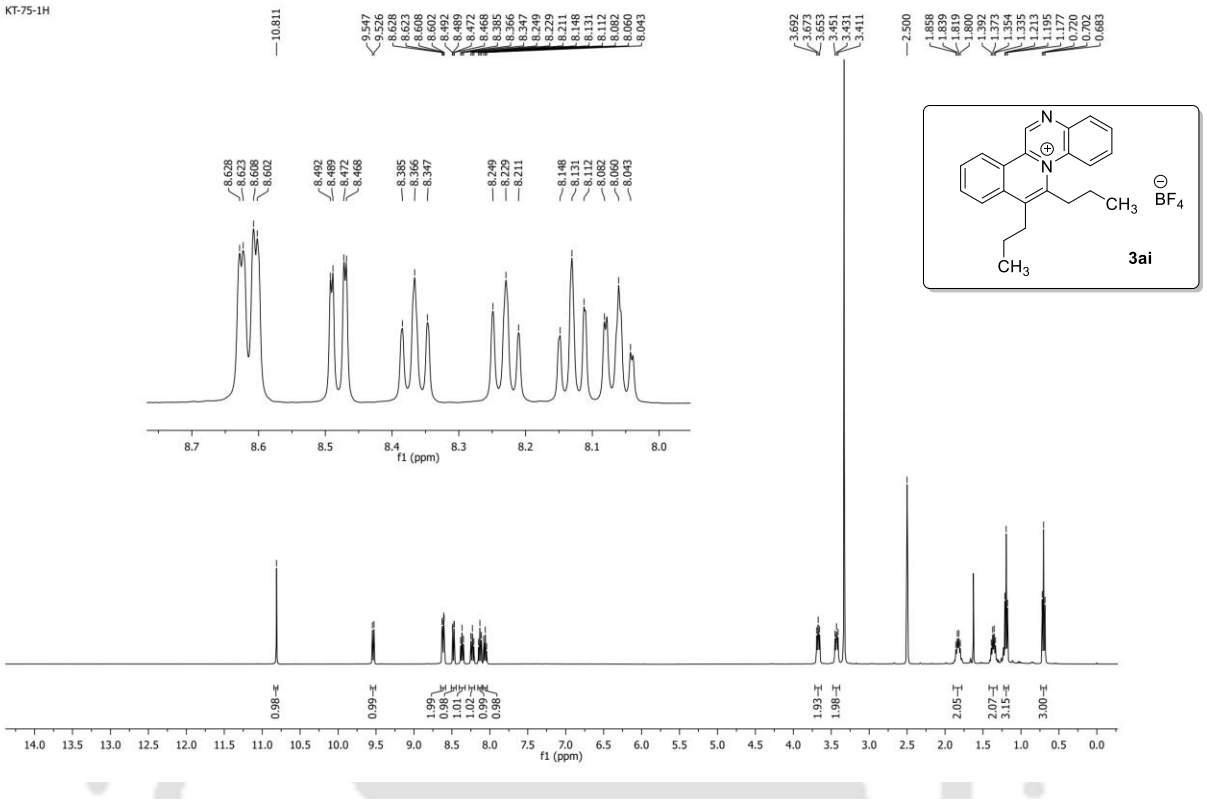
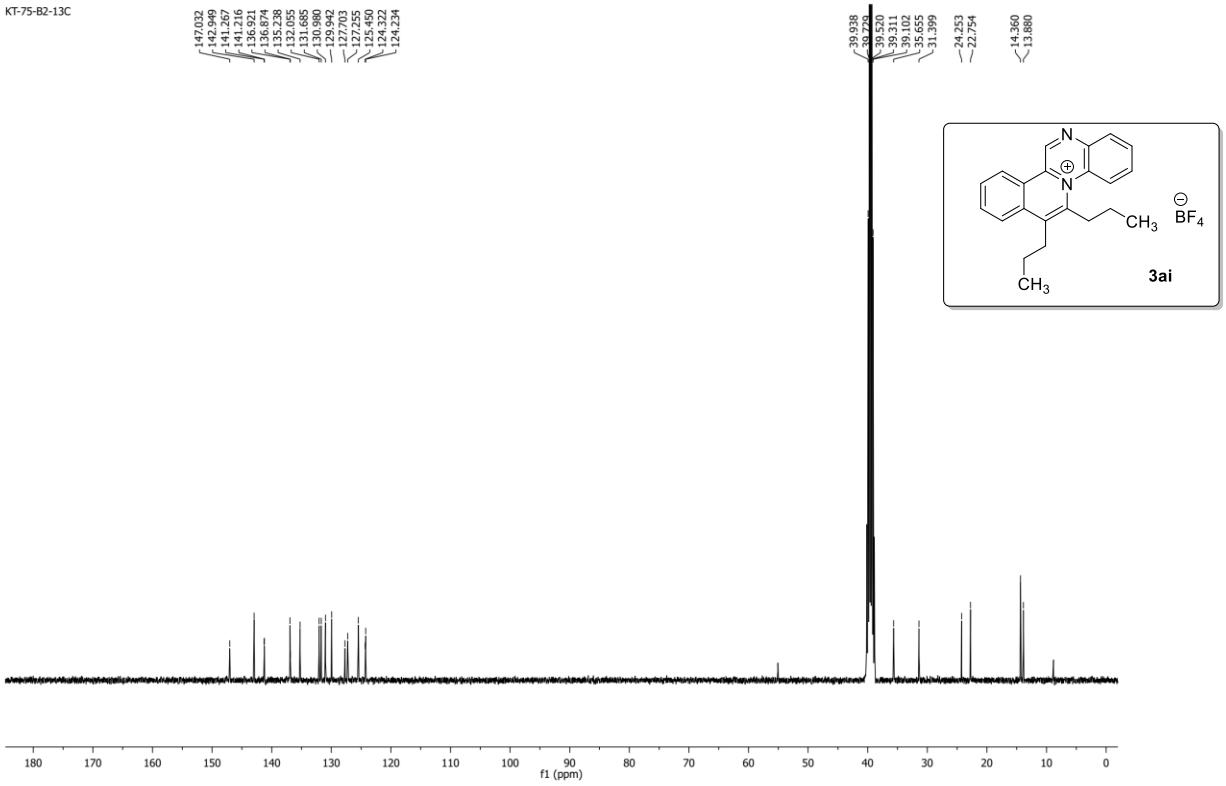
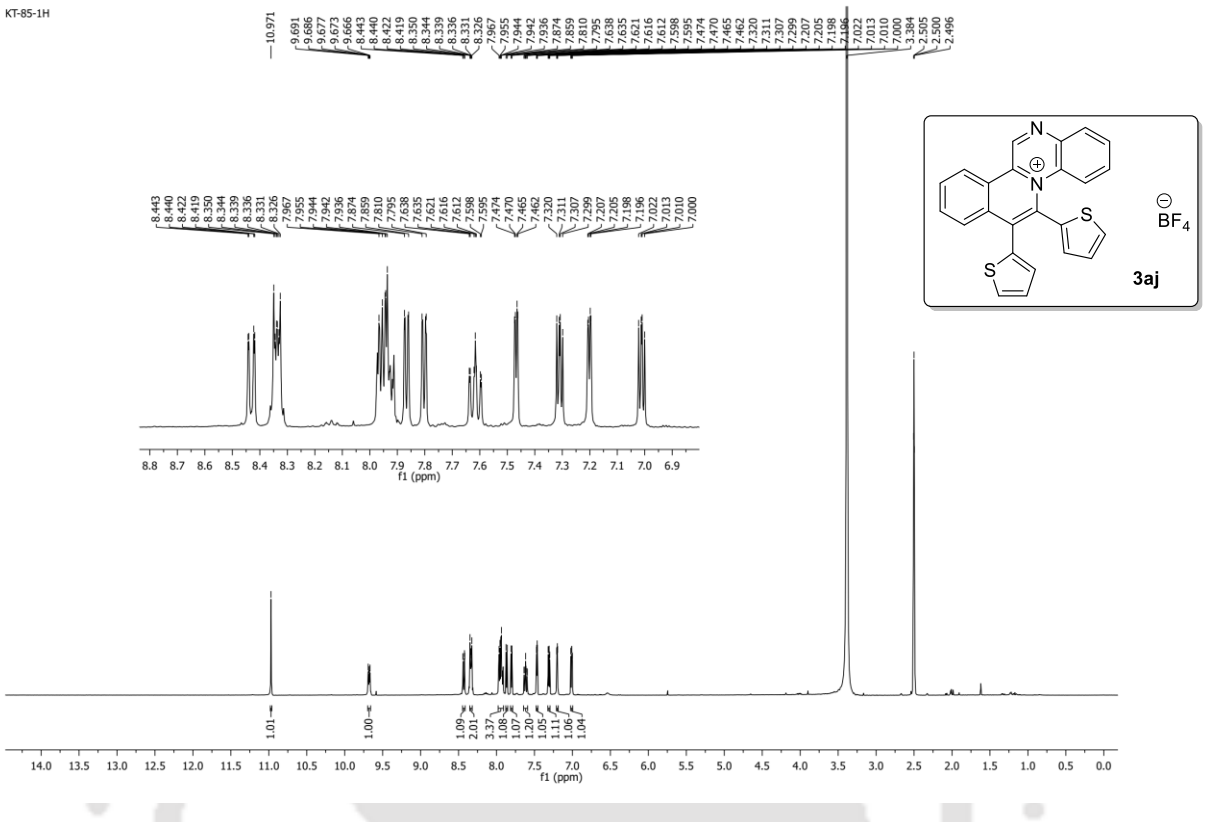
1.6 Selected NMR Spectra

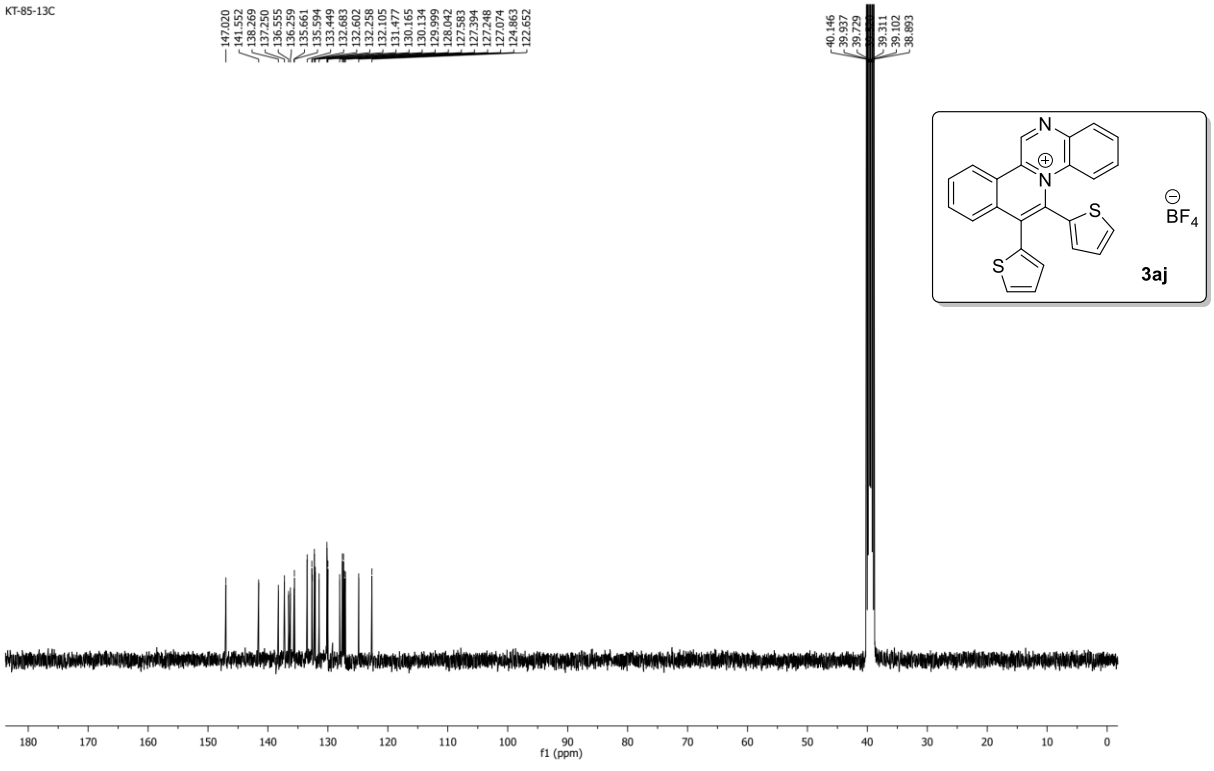


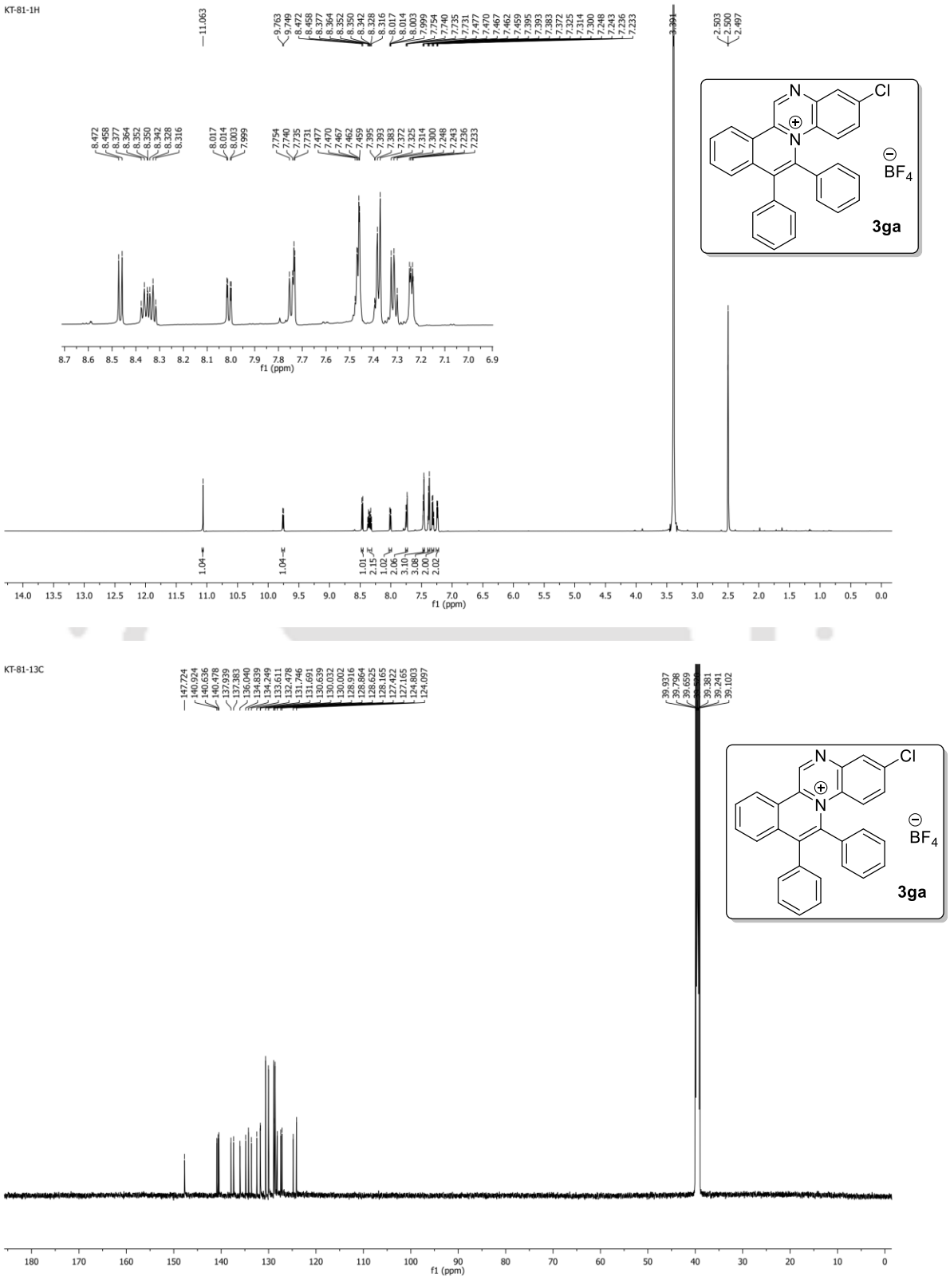






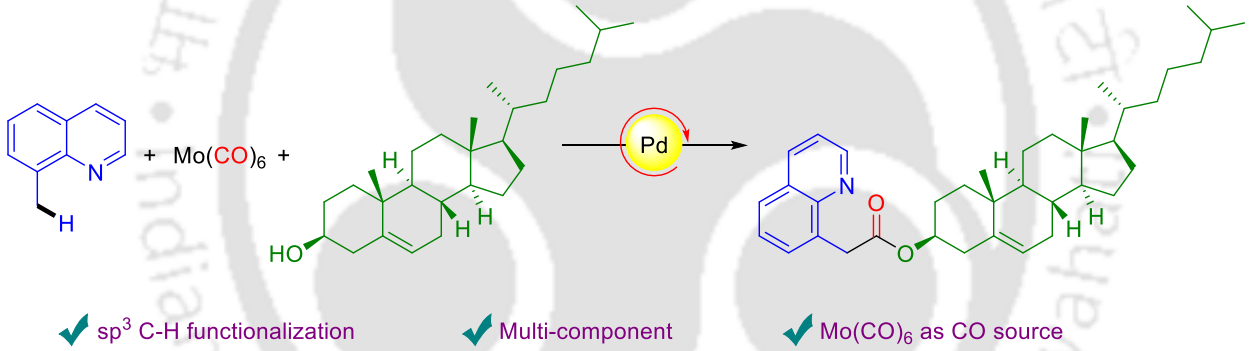






Chapter II

Pd-Catalyzed sp^3 C-H Alkoxycarbonylation of 8-methylquinolines using $Mo(CO)_6$ as CO Surrogate



Chem. Commun. **2021**, *57*, 3359.

Chapter II

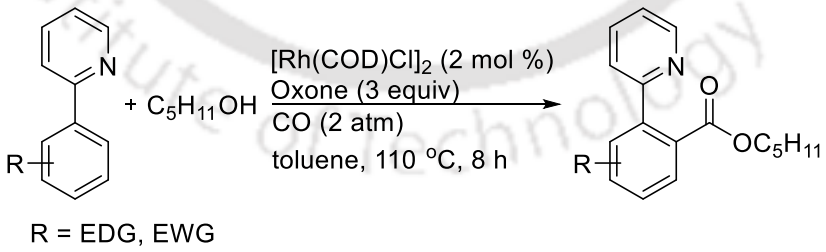
Pd-Catalyzed sp^3 C-H Alkoxycarbonylation of 8-Methylquinolines using $Mo(CO)_6$ as CO Surrogate

The construction of C-O bond is a key quest in organic synthesis, due to the ubiquity of this structural unit in myriad of molecules of biological and pharmaceutical significance.[1] With recent attention towards the atom economical process and green chemistry perspective, transition-metal-catalyzed direct C-H activation has emerged as a reliable protocol that holds the prime locus in modern synthetic chemistry and has immensely thrived for the construction of site-selective C-C and C-heteroatom bond.[2] Highly regioselective functionalization of sp^3 C-H bonds encounters tremendous challenges due to the non-availability of π-bonds as well as high bond dissociation energy associated with it.[3] The merger of carbonylation and C-H functionalization has shined as a lucrative alternative for ester synthesis as compared to trivial protocols, which demand pre-activated starting materials. Driven by the astounding importance of quinolines in alkaloids and medicinal science,[4] their functionalization has earned enormous attention in synthetic chemistry.

2.1 Literature Study

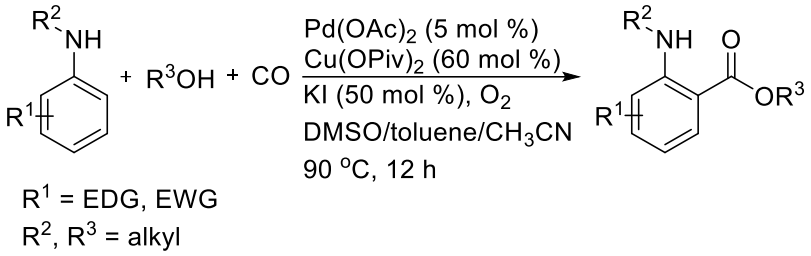
2.1.1 Transition-Metal-Catalyzed sp^2 C-H Carbonylation

Zhang and co-workers reported a Rh-catalyzed *ortho*-selective carbonylation of aromatic C-H bond with CO and alcohols (Scheme 1).[5] The carbonylation of electron-rich, electron-poor, and heterocyclic arenes has been successfully demonstrated with a broad substrate scope. The reaction exhibits excellent regioselectivities and displays wide functional group tolerance.



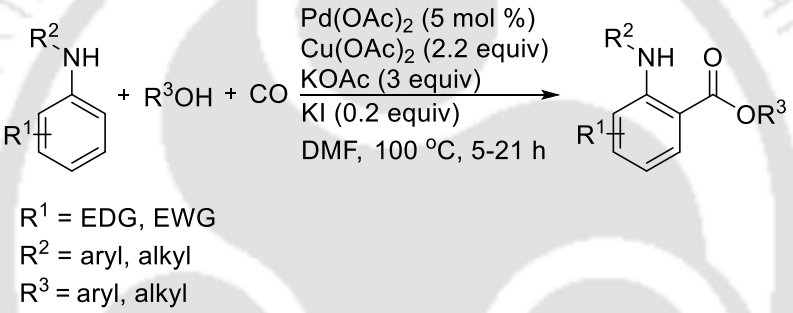
Scheme 1. Rh-Catalyzed *ortho*-Selective Alkoxycarbonylation of Aromatic C-H Bond

The synthesis of *o*-aminobenzoate derivatives was achieved through a Pd/Cu-catalyzed oxidative C-H alkoxycarbonylation of *N*-substituted anilines by Lei and co-workers (Scheme 2).[6] The methodology accommodated a wide range of *N*-substituted anilines and alcohols.



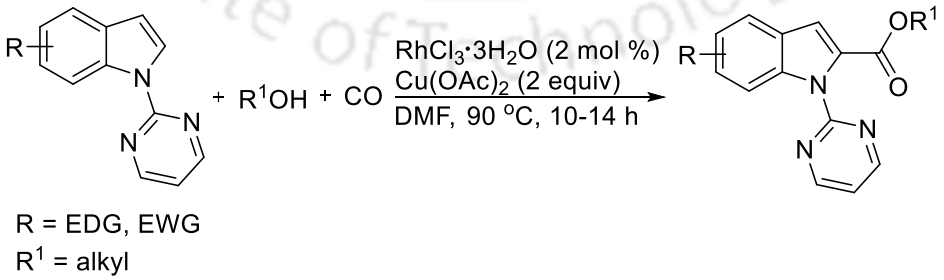
Scheme 2. Pd/Cu-Catalyzed Oxidative Alkoxycarbonylation of *N*-Substituted Anilines

Guan and co-workers demonstrated a Pd(II)-catalyzed C-H monocarbonylation of *N*-substituted anilines for the synthesis of *o*-aminobenzoates under mild balloon pressure of CO (Scheme 3).[7] The reaction demonstrated tolerance towards various aliphatic alcohols and phenol, providing the corresponding o-aminobenzoates in good yields.



Scheme 3. Pd-Catalyzed Monocarbonylation of *N*-Substituted Anilines

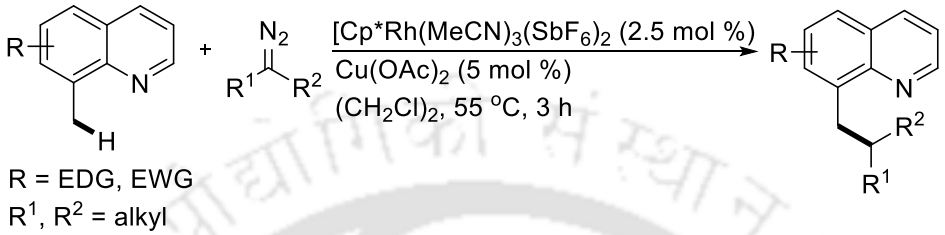
Yang and co-workers disclosed a $RhCl_3 \cdot 3H_2O$ catalyzed C2-selective C-H alkoxycarbonylation of indoles with alcohols and CO catalyzed for the synthesis of diverse indole-2-carboxylic esters (Scheme 4).[8] This protocol was found to be applicable for the synthesis of pyrrole-2-carboxylic esters, enabling intramolecular C-H alkoxycarbonylation.



Scheme 4. Rh-Catalyzed C2-Selective Alkoxycarbonylation of Indoles

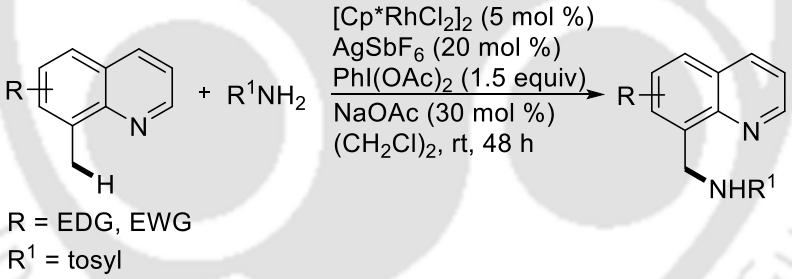
2.1.1 Rh-Catalyzed sp^3 C-H Functionalization of 8-Methylquinoline

Zhou group employed 8-methylquinoline as a substrate in the intermolecular chelation-assisted Rh-catalyzed C(sp^3)-H alkylation with α-diazocarbonyl compounds as the alkylating source (Scheme 5).[9] Key attributes of this approach include mild reaction conditions and highly regioselective primary C(sp^3)-H functionalization.



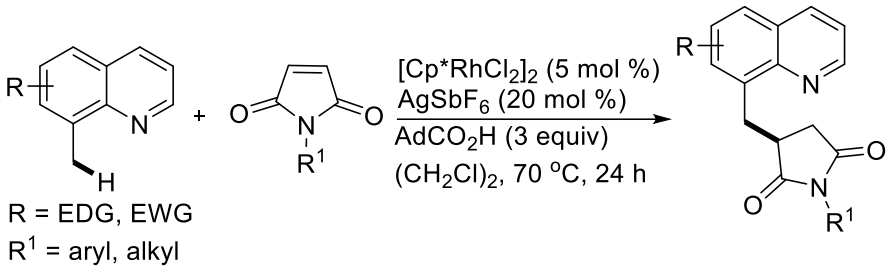
Scheme 5. Rh-Catalyzed Alkylation

A Rh(III)-catalyzed regioselective C(sp^3)-H amidation of 8-methylquinolines using aryl sulfonamides as amidating agent was demonstrated by You and co-workers (Scheme 6).[10] The protocol tolerated a wide range of aryl sulfonamides containing electron-neutral, electron-donating, and electron-withdrawing groups.



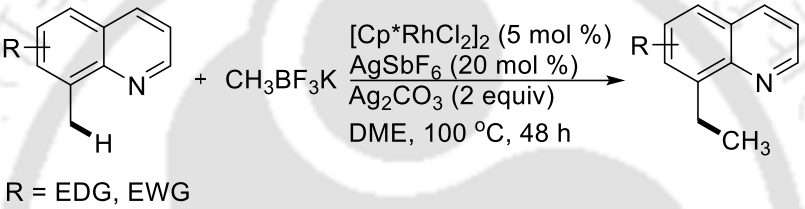
Scheme 6. Rh-Catalyzed Amidation

In an elegant manner, Kim and co-workers accomplished a Rh-catalyzed selective C8 alkylation of 8-methylquinolines, employing maleimide as the alkylating reagent *via* C(sp^3)-H activation (Scheme 7).[11] The described protocol exhibited a wide substrate scope in high yield, while demonstrating exceptional tolerance to various functional groups and remarkable chemoselectivity.



Scheme 7. Rh-Catalyzed Alkylation

Sharma and co-workers reported a Rh-catalyzed alkylation strategy for the C(sp^3)-H methylation of 8-methylquinolines exploiting air-stable potassium methyltrifluoroborates as methylating agent (Scheme 8).[12] This marks the inaugural C(sp^3)-H methylation reaction of 8-methylquinoline under Rh-catalysis, achieving complete regioselectivity.

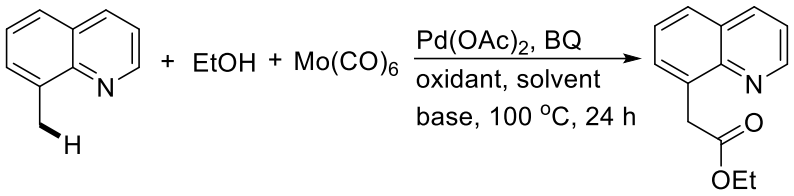


Scheme 8. Rh-Catalyzed Methylation

2.2 Present Study

We here report a Pd(II)-catalyzed three-component sp^3 C-H alkoxycarbonylation of 8-methylquinoline (8-MQ) derivatives using $Mo(CO)_6$ as CO surrogate. The initial investigation was carried out employing 8-MQ **1a** and ethanol **2a** as the model substrates with $Pd(OAc)_2$ as a catalyst and $Mo(CO)_6$ as a CO source in presence of base and oxidant (Table 1). To our delight, the carbonylation took place to give **3aa** in 55% yield when substrates **1a** and **2a** were stirred in presence of $Pd(OAc)_2$ (10 mol %), BQ (1.0 equiv), $Mo(CO)_6$ (1 equiv), NaOAc (2 equiv) and Ag_2CO_3 (2 equiv) in *m*-xylene at 100 °C utilizing a sealed tube (entry 1). The presence of BQ was crucial as it can facilitate the reductive elimination step.[13] In a set of oxidants studied, Ag_2CO_3, Ag_2O, $AgNO_3$, $Cu(OAc)_2{\cdot}H_2O$, $Cu(OAc)_2$, $K_2S_2O_8$ and O_2, the former gave the best result (entries 2-8). In case of the base, NaOAc yielded superior results compared to KOAc, Cs_2CO_3 and DBU (entries 9-11). The yield increased to 76% employing 1,2-dichloroethane as the solvent, whereas EtOH, CH_2Cl_2, DMSO, AcOH and toluene produced inferior results (entries 12-17). Control experiment suggests that the presence of base and $Mo(CO)_6$ are crucial for the formation of **3aa** (entries 18-19). It is worth to mention that the reduction in loading of $Mo(CO)_6$ impeded the overall

Table 1. Optimization of the Reaction Condition.[a]



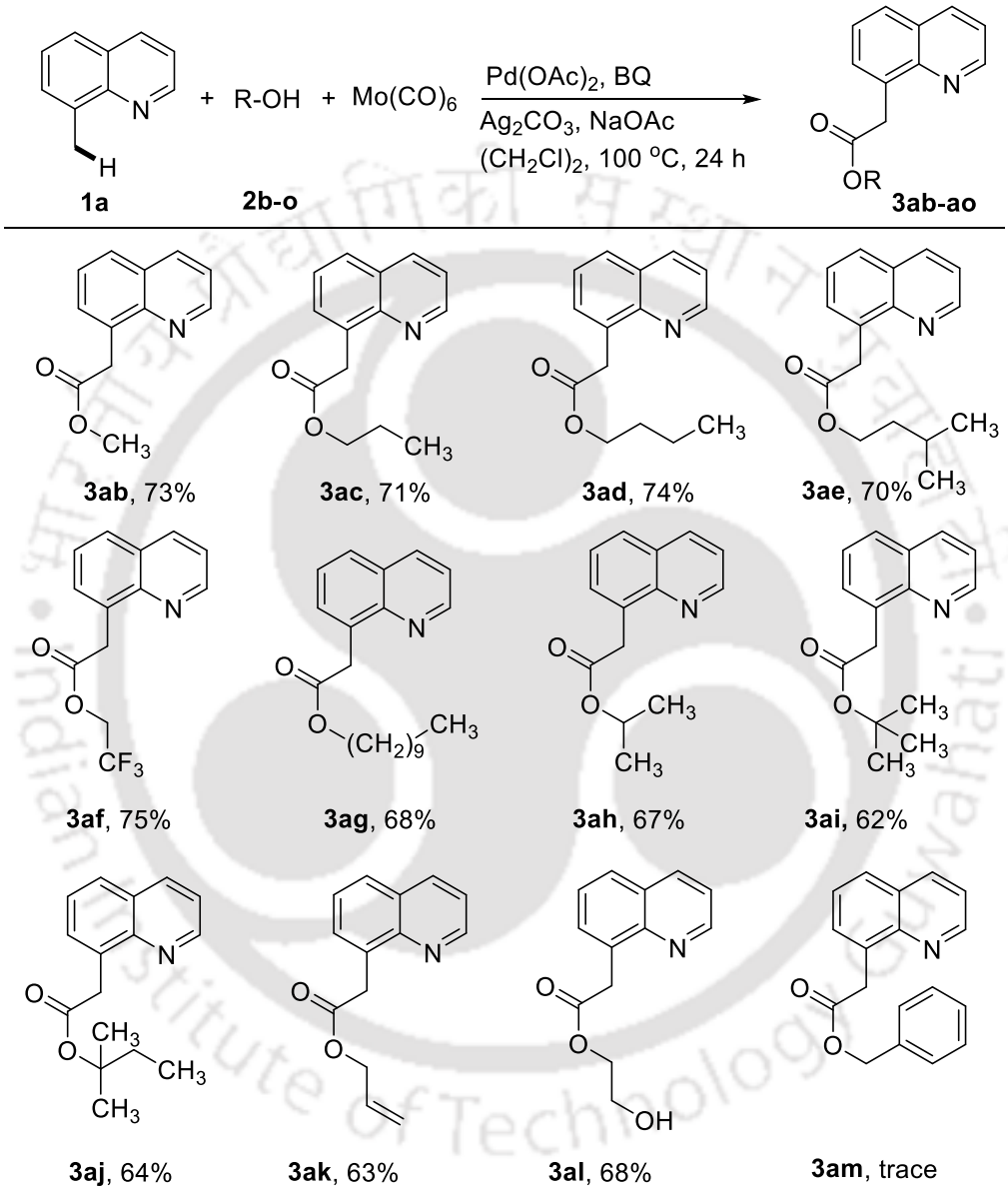
1a **2a** **3aa**

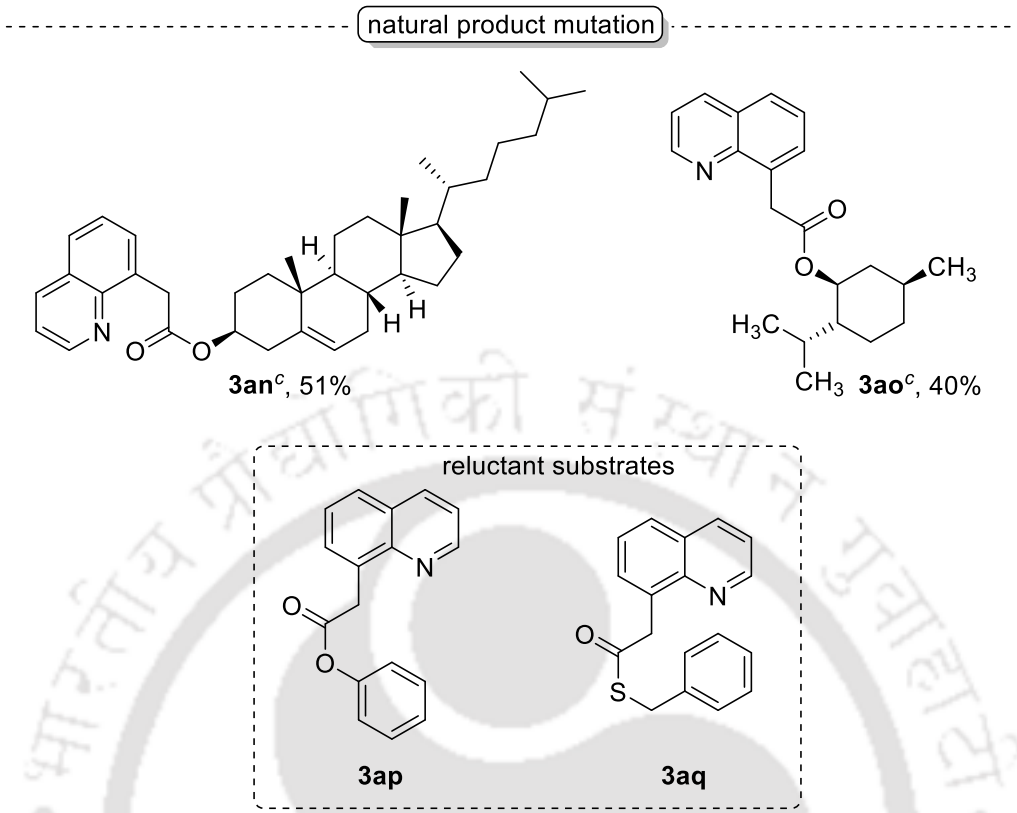
Entry	Base	Oxidant	Solvent	Yield[b]
1	NaOAc	Ag_2CO_3	*m*-xylene	55
2	NaOAc	Ag_2O	*m*-xylene	15
3	NaOAc	$AgNO_3$	*m*-xylene	22
4	NaOAc	$Cu(OAc)_2$	*m*-xylene	trace
5	NaOAc	$Cu(OAc)_2{\cdot}H_2O$	*m*-xylene	trace
6	NaOAc	$K_2S_2O_8$	*m*-xylene	trace
7	NaOAc	O_2	*m*-xylene	n.d.
8	NaOAc	-	*m*-xylene	19
9	KOAc	Ag_2CO_3	*m*-xylene	12
10	Cs_2CO_3	Ag_2CO_3	*m*-xylene	n.d.
11	DBU	Ag_2CO_3	*m*-xylene	n.d.
12	NaOAc	Ag_2CO_3	EtOH	38
13[c]	NaOAc	Ag_2CO_3	CH_2Cl_2	49
14	NaOAc	Ag_2CO_3	$(CH_2Cl)_2$	76
15	NaOAc	Ag_2CO_3	DMSO	n.d.
16	NaOAc	Ag_2CO_3	AcOH	n.d.
17	NaOAc	Ag_2CO_3	toluene	52
18	-	Ag_2CO_3	$(CH_2Cl)_2$	31
19[d]	NaOAc	Ag_2CO_3	$(CH_2Cl)_2$	n.d.
20[e]	NaOAc	Ag_2CO_3	$(CH_2Cl)_2$	36
21[f]	NaOAc	Ag_2CO_3	$(CH_2Cl)_2$	n.d.
22[g]	NaOAc	Ag_2CO_3	$(CH_2Cl)_2$	25

[a]Reaction conditions: **1a** (0.20 mmol), **2a** (2 mmol), $Pd(OAc)_2$ (10 mol %), $Mo(CO)_6$ (0.20 mmol), BQ (0.20 mmol), base (0.40 mmol), oxidant (0.30 mmol), solvent (2 mL), 100 °C, 24 h, pressure tube. [b]Isolated

yield. [c]Reaction was carried out at 80 °C. [d]Without $Mo(CO)_6$. [e]With $Mo(CO)_6$ (0.10 mmol). [f]With CO gas. [g]With $Co_2(CO)_8$. n.d. = not detected. BQ = 1,4-benzoquinone.

Table 2. Substrate scope of alcohols.[a,b]



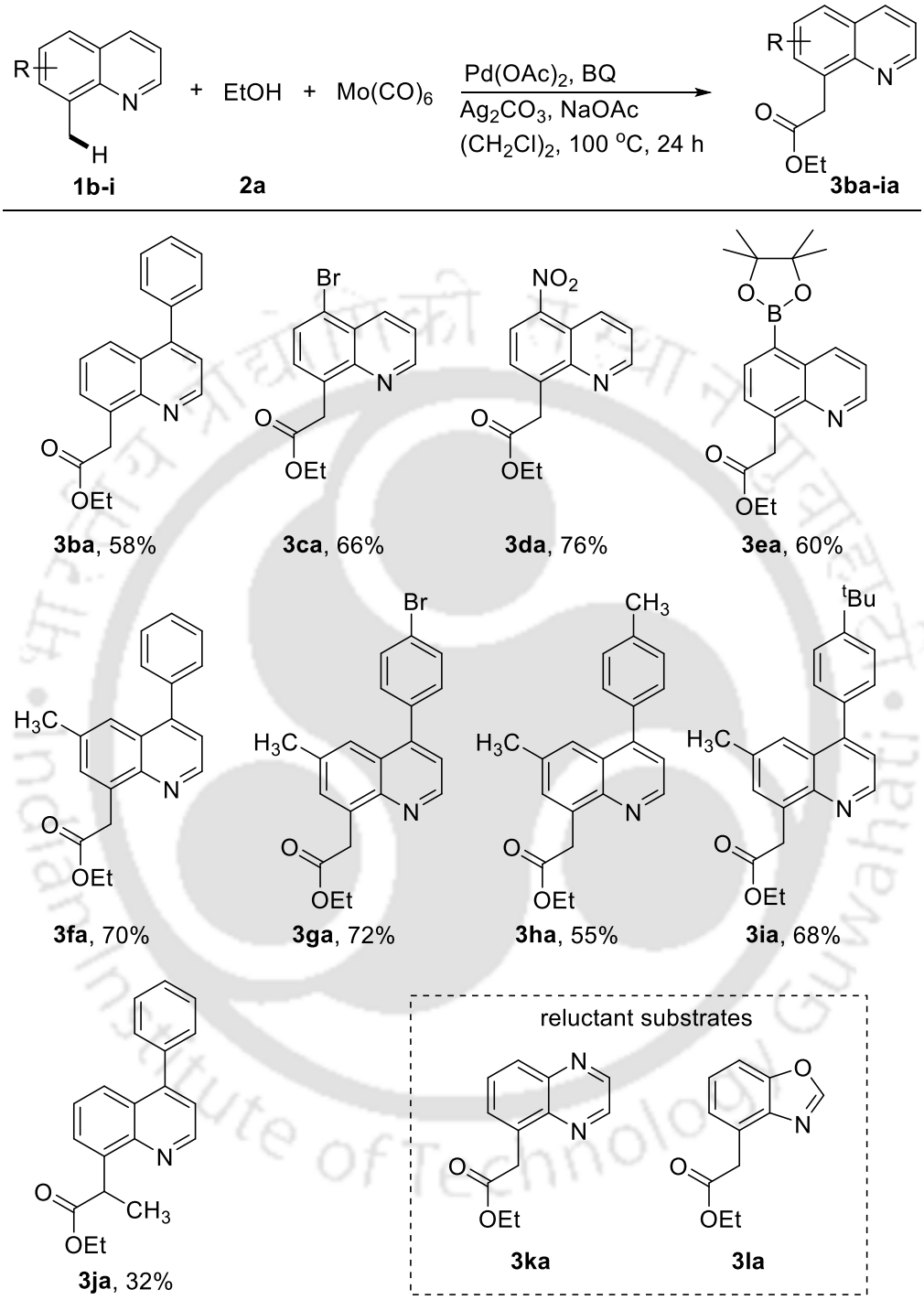


[a]Reaction conditions: **1a** (0.20 mmol), **2b-m** (2 mmol), $Pd(OAc)_2$ (10 mol %), $Mo(CO)_6$ (0.20 mmol), BQ (0.20 mmol), NaOAc (0.40 mmol), Ag_2CO_3 (0.30 mmol), $(CH_2Cl)_2$ (2 mL), 100 °C, 24 h, pressure tube. [b]Isolated yield. [c]Employing 1 mmol of **2n-o**.

yield and delivered only 36% (entry 20). Remarkably, the use of CO gas failed to produce the carbonylated product while $CO_2(CO)_8$ afforded the target adduct in 25% yield (entries 21-22).

Having the optimized condition in hand, the scope of the protocol was studied to a series of primary, secondary and tertiary alcohols **2b-l** with 8-methylquinoline **1a** as a standard substrate (Table 2). Primary alcohols such as methanol **2b**, propan-1-ol **2c**, butan-1-ol **2d**, 3-methylbutan-1-ol **2e**, 2,2,2- trifluoroethanol **2f** and decan-1-ol **2g** were compatible, affording **3ab-ag** in 68-75% yields, whereas secondary and tertiary alcohols, isopropanol **2h**, *tert*-butanol **2i** and 2-methylbutan-2-ol **2j**, were well tolerated to give the desired **3ah-aj** in 62-67% yields. Intriguingly, the allyl alcohol **2k** provided the alkoxycarbonylated **3ak** in 63% yield instead of alkenylated one, whereas mono-alkoxycarbonylated **3al** was obtained in 68% yield in case of ethylene glycol **2l**. Next, the strategy was extended towards the installation of diverse biomolecules such as cholesterol **2n**, an essential structural component of cell membrane to furnish **3an** in 51% yield,

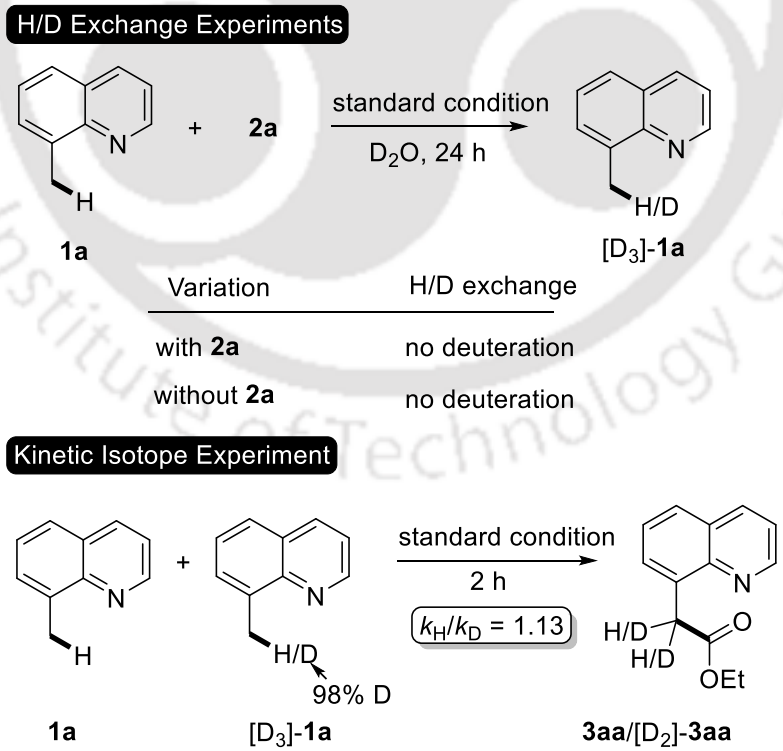
Table 3. Substrate scope of 8-Methylquinoline.[a,b]



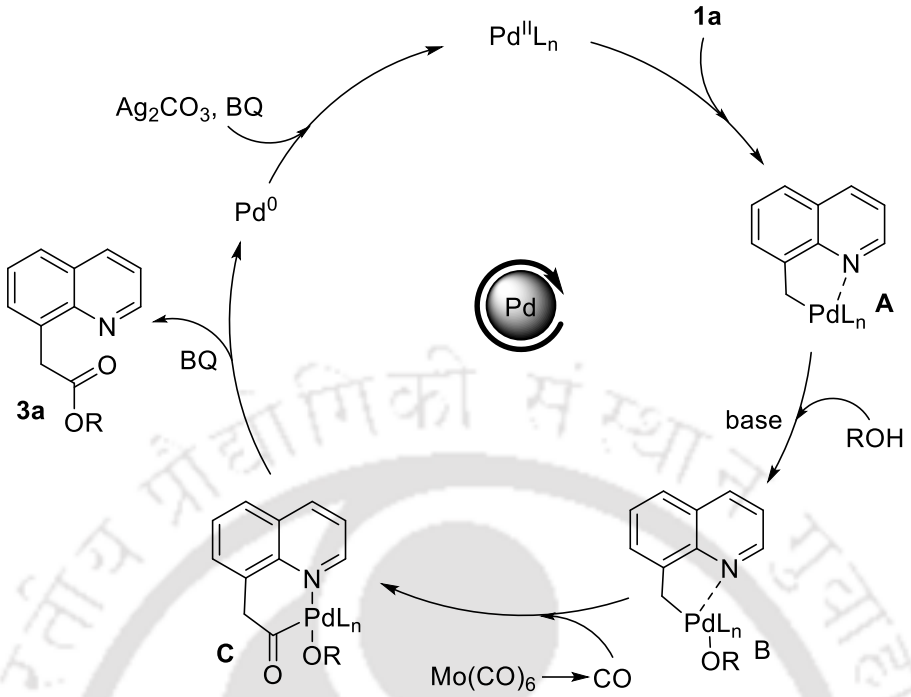
[a]Reaction conditions: **1b-i** (0.20 mmol), **2a** (2 mmol), $Pd(OAc)_2$ (10 mol %), $Mo(CO)_6$ (0.20 mmol), BQ (0.20 mmol), NaOAc (0.40 mmol), Ag_2CO_3 (0.30 mmol), $(CH_2Cl)_2$ (2 mL), 100 °C, 24 h, pressure tube. [b]Isolated yield.

whereas, κ-opioid receptor agonist L-menthol **2o** was found to be well tolerated, delivering the anticipated **3ao** in 40% yield. Intriguingly, the reaction of **1a** with phenol **2p** and benzyl mercaptan **2q** failed to produce the target products. Fascinated by the effective outcomes, our attention was shifted towards the diversification of 8-MQs exploiting EtOH **2a** as the standard substrate (Table 3). It was observed that, substituent like phenyl at the C4-site of 8-MQ was successfully participated in the reactions, furnishing **3ba** in 58% yield, while substitution in C5-position such as bromo **1c**, nitro **1d** and pinacolborane **1e** produced the desired **3ca-ea** in good yields (60-76%). Delightfully, substitutions at both C4 and C6-positions **2f-i** successfully transformed to alkoxycarbonylated **3fa-ia** in 55-72% yields. 8-Ethyl-4-phenylquinoline **1j** participated to assemble **3ja** in 32% yield, while 5-methylquinoxaline **1k** and 4-methylbenzo[d]oxazole **1l** were reluctant to deliver the corresponding products.

To gain insight into the mechanistic pathway, H/D exchange and kinetic-isotope experiments were performed (Scheme 9). Deuterium labelling experiments using D_2O as a co-solvent did not exhibit any significant H/D scrambling, which suggest the irreversible nature of the C-H bond activation step,[14] while the kinetic isotope experiment using **1a** and [D_3]-**1a** with **2a**, furnished a k_H/k_D = 1.13,

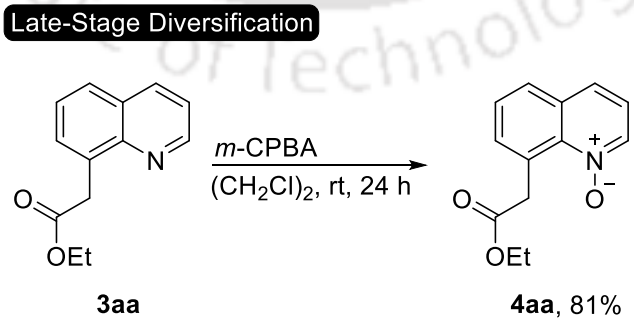


Scheme 9. Preliminary Mechanistic Investigations

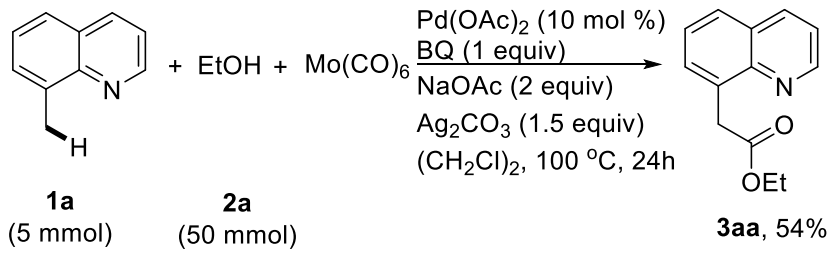


Scheme 10. Proposed Reaction Mechanism

which suggests that the C-H bond cleavage might not be involved in rate-determining step. Based on these experiments and literature precedent,[15] a plausible mechanism is depicted in Scheme 10. The activation of the benzylic C-H bond of **1a** by an active Pd(II) species can form an intermediate **A**, which in turn in presence of base can undergo ligand exchange with alcohol to yield a five membered palladacycle **B**. Subsequently, a six-membered cyclic intermediate **C** is induced *via* coordination/insertion of CO into the Pd-C bond. The latter may undergo reductive elimination, facilitated by BQ or Ag_2CO_3 to deliver the target **3a** with the concomitant generation of Pd(0) species, which in presence of Ag(I) can be oxidized to the active Pd(II) species to complete the catalytic cycle.



Scheme 11. Post-Synthetic Utilities



Scheme 12. Scale up synthesis

To demonstrate the synthetic utility, **3aa** was reacted, as a representative example, with *m*-CPBA to produce *N*-oxide **4aa** in 81% yield (Scheme 11).[16a] The resultant quinoline *N*-oxide can serve as a functional handle for the synthetic modifications.[16b,c] Finally, the scale-up of the reaction was invested utilizing **1a** (5 mmol), as a representative example (Scheme 12). The esterification occurred to furnish **3aa** in 54% yield, which suggests that the reaction is scalable.

In summary, we have presented a Pd(II)-catalyzed three-component C-H carbonylation of 8-MQs with readily available alcohols exploiting $Mo(CO)_6$ as the CO surrogate. The selectivity, functional group tolerance and late-stage natural product mutations are the important practical features.

2.3 Experimental Section

General Information. $Pd(OAc)_2$ (≥99.9%), benzoquinone, $Mo(CO)_6$, NaOAc, Ag_2CO_3 (99%), 8-methylquinoline, 5-methylquinoxaline, benzylmercaptan and alcohols were purchased from Aldrich and used as received. The substituted 8-MQs **1b-i**, 8-ethyl-4-phenylquinoline **1j** and 4-methylbenzo[d]oxazole **1l** were prepared according to literature.[17] Merck silica gel G/GF 254 plates were used for analytical TLC and Rankem silica gel (60-120 mesh) was used for column chromatography. NMR (^1H and ^{13}C) spectra were recorded in Bruker Avance III 400 and 600 spectrometers using $CDCl_3$ as solvent and TMS as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively, and other data are reported as follows: s = singlet, d = doublet, dd= doublet of doublet, t = triplet, m = multiplet and q = quartet. Melting points were determined using a Büchi B-540 apparatus and are uncorrected. IR spectra were collected on a PerkinElmer Fourier transform infrared (FT-IR) spectrometer. Quadrupole time-of-flight electrospray ionization (ESI) mass spectrometer (model HAB 273) was used for mass analysis.

General Procedure for the sp^3 C-H Alkoxycarbonylation of 8-MQs. 8-MQ **1** (0.2 mmol), alcohol **2** (2 mmol), $Pd(OAc)_2$ (10 mol %, 4.4 mg), BQ (0.2 mmol, 21.2 mg), $Mo(CO)_6$ (0.2 mmol, 52.8 mg) and Ag_2CO_3 (0.3 mmol, 83 mg) were stirred at 100 ^oC for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The mixture was diluted with dichloromethane (10 mL) and passed through a short pad of celite. The organic layer was washed with brine (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane/EtOAc (10:2) as eluent to afford the desired **3**.

Scale-up Synthesis of 3aa. 8-Methylquinoline **1a** (5 mmol, 715 mg), EtOH **2** (50 mmol, 2.3 g), $Pd(OAc)_2$ (10 mol %, 110 mg), BQ (5 mmol, 530 mg), $Mo(CO)_6$ (5 mmol, 1.32 g) and Ag_2CO_3 (7.5 mmol, 2 g) were subjected to the above described standard reaction condition. The mixture was diluted with dichloromethane (20 mL) and passed through a celite pad and washed with brine (5 mL) and water (5 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated to produce a residue, which was purified by column chromatography on silica gel using *n*-hexane/EtOAc (10:2) as eluent to afford **3aa** in 54% (580 mg) yield.

Synthesis of 4aa.[18] 3-Chloroperbenzoic acid (0.2 mmol, 34.5 mg) was added to a stirred solution of ethyl 2-(quinolin-8-yl)acetate **3aa** (0.2 mmol, 43 mg) in CH_2Cl_2 (1 mL) at 0 ^oC. The reaction mixture was allowed to stir at room temperature for 24 h and then treated with an aqueous $NaHCO_3$. The resultant mixture was extracted with CH_2Cl_2 (10 mL) and the organic phase was washed with brine (3 mL) and water (3 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure to give the residue, which was purified by column chromatography on silica gel using EtOAc /MeOH (8:1) as an eluent.

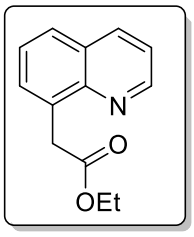
Synthesis of [D_3]-**1a**.[19] 8-MQ **1a** (0.3 mmol, 43.0 mg), $[RhCp^*Cl_2]_2$ (2.5 mol %, 4.6 mg), AcOD (0.9 mmol, 54.1 mg), $Cu(OAc)_2$ (0.6 mmol, 109.0 mg) and D_2O (1 mL) were stirred at 100 ^oC for 20 h. The resultant mixture was extracted with EtOAc (10 mL) and the organic layer was dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane/EtOAc (10:1) to afford [D_3]-**1a** in 90% yield. The deuterium incorporation was determined using 400 MHz ^1H NMR as 98%.

H/D Exchange Experiment with D_2O. 8-MQ **1a** (0.2 mmol, 28.6 mg), $Pd(OAc)_2$ (10 mol %, 4.4 mg), BQ (0.2 mmol, 21.2 mg), $Mo(CO)_6$ (0.2 mmol, 52.8 mg), Ag_2CO_3 (0.3 mmol, 83 mg) and D_2O (2 mmol) were stirred in 1,2-dichloroethane at 100 ^oC for 24 h in a sealed tube. The work-up and purification were performed as described in the general procedure. 400 MHz ^1H NMR spectrum of the product showed no deuterium incorporation.

H/D Exchange Experiment with D_2O in Presence of Alcohol. 8-Methylquinoline **1a** (0.2 mmol, 28.6 mg), EtOH (2 mmol, 92 mg), $Pd(OAc)_2$ (10 mol %, 4.4 mg), BQ (0.2 mmol, 21.2 mg), $Mo(CO)_6$ (0.2 mmol, 52.8 mg), Ag_2CO_3 (0.3 mmol, 83 mg) and D_2O (2 mmol) were stirred in 1,2-dichloroethane at 100 ^oC for 24 h. The work-up and purification was performed as above, and the 400 MHz ^1H NMR spectrum of the product revealed no deuterium incorporation.

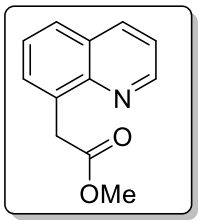
Kinetic Isotope Effect Experiment. A mixture of 8-Methylquinoline **1a** (0.2 mmol, 28.6 mg) and [D_3]-**1a** (0.2 mmol, 29.2 mg) was reacted with EtOH **2a** (2 mmol, 92 mg) for 2 h under standard reaction conditions. The reaction mixture was diluted with DCM (5 mL), and passed through a short pad of celite using DCM (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent on vacuo produced a residue, which was purified on silica gel column chromatography on silica gel using *n*-hexane and EtOAc (10:2) as eluent to afford **3aa**/[D_2]-**3aa**. The intermolecular k_H/k_D was found to be 1.13, based on the 400 MHz ^1H NMR spectroscopy.

2.4 Characterization data

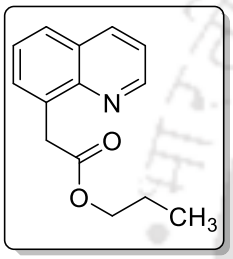


Ethyl 2-(quinolin-8-yl)acetate 3aa. Yellow liquid; yield 76% (33 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.40 (q, *J* = 4.0 Hz, 1H), 4.27 (s, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 149.7, 146.8, 136.3, 133.6, 130.4, 128.4, 127.5, 126.3, 121.2, 60.8, 37.3, 14.3; FT-IR (neat) 2980, 2924, 2852, 1729, 1499, 1367, 1026, 830, 797 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{14}NO_2^+$:

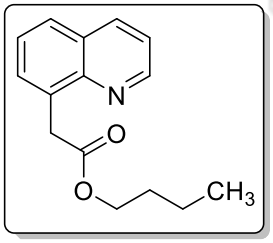
216.1019, found: 216.1025.



Methyl 2-(quinolin-8-yl)acetate 3ab. Yellow liquid; yield 73% (29 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.0 Hz, 6.4 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.41 (q, *J* = 4.0 Hz, 1H), 4.29 (s, 2H), 3.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 149.8, 146.8, 136.3, 133.5, 130.4, 128.5, 127.6, 126.3, 121.3, 52.1, 37.0; FT-IR (neat) 2952, 2921, 2852, 1734, 1499, 1259, 1171, 1014, 794, 733 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{12}H_{12}NO_2^+$: 202.0863, found: 202.0868.

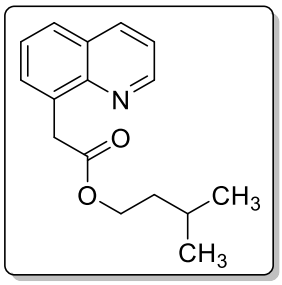


Propyl 2-(quinolin-8-yl)acetate 3ac. Yellow liquid; yield 71% (32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.40 (q, *J* = 4.4 Hz, 1H), 4.29 (s, 2H), 4.07 (t, *J* = 6.4 Hz, 2H), 1.66-1.58 (m, 2H), 0.85 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 149.7, 146.9, 136.3, 133.7, 130.3, 128.4, 127.4, 126.3, 121.2, 66.4, 37.3, 22.0, 10.4; FT-IR (neat) 2965, 2934, 2877, 1730, 1499, 1336, 1153, 1059, 794, 762 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{16}NO_2^+$: 230.1176, found: 203.1175.

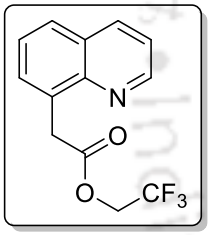


Butyl 2-(quinolin-8-yl)acetate 3ad. Yellow liquid; yield 74% (36 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.0 Hz, 6.4 Hz, 1H), 7.77 (d, *J* = 9.2 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.40 (q, *J* = 4.0 Hz, 1H), 4.27 (s, 2H), 4.11 (t, *J* = 6.8 Hz, 2H), 1.61-1.54 (m, 2H), 1.33-1.25 (m, 2H), 0.86 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 149.7, 146.9, 136.3, 133.7, 130.3, 128.4, 127.4, 126.3, 121.2,

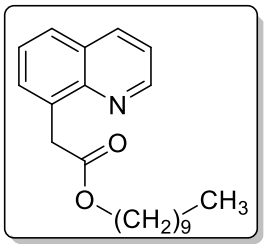
64.7, 37.3, 30.7, 19.1, 13.8; FT-IR (neat) 2958, 1730, 1499, 1338, 1258, 1172, 1061, 794, 763 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{18}NO_2^+$: 244.1332, found: 244.1337.



Isopentyl 2-(quinolin-8-yl)acetate 3ae. Yellow liquid; yield 70% (36 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.0 Hz, 6.4 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 6.8 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.40 (q, *J* = 4.0 Hz, 1H), 4.27 (s, 2H), 4.14 (t, *J* = 6.8 Hz, 2H), 1.61-1.53 (m, 1H), 1.49 (q, *J* = 6.8 Hz, 2H), 0.85 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 149.7, 146.9, 136.3, 133.7, 130.3, 128.4, 127.5, 126.3, 121.2, 63.5, 37.4, 25.1, 22.5; FT-IR (neat) 2956, 1731, 1499, 1367, 1258, 1154, 1049, 981, 794, 761 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{20}NO_2^+$: 258.1489, found: 258.1493.

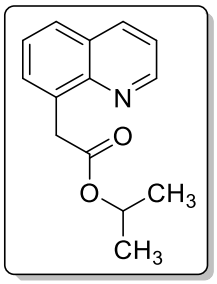


2,2,2-Trifluoroethyl 2-(quinolin-8-yl)acetate 3af. Colorless liquid; yield 75% (40 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (q, *J* = 2.4 Hz, 1H), 8.16 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 6.4 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.42 (q, *J* = 4.0 Hz, 1H), 4.52 (q, *J* = 7.6 Hz, 2H), 4.36 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 149.8, 146.7, 136.3, 132.5, 130.4, 128.4, 127.9, 126.3, 124.5 (q, J_{C-F} = 275.7), 121.4, 60.8 (q, J_{C-F} = 36.3), 36.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -73.6; FT-IR (neat) 2921, 2852, 1716, 1595, 1401, 1279, 979, 812, 764 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{11}F_3NO_2^+$: 270.0736, found: 270.0740.

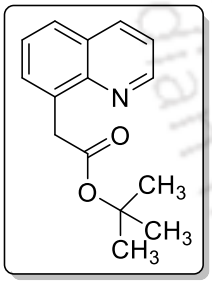


Decyl 2-(quinolin-8-yl)acetate 3ag. Yellow liquid; yield 68% (44 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.40 (q, *J* = 4.0 Hz, 1H), 4.27 (s,

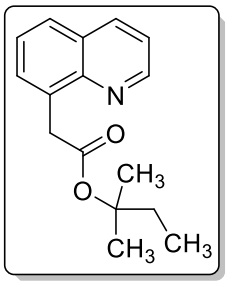
2H), 4.10 (t, *J* = 6.8 Hz, 2H), 1.59-1.54 (m, 1H), 1.31-1.28 (m, 15H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 149.7, 146.9, 136.3, 133.8, 130.3, 128.4, 127.4, 126.3, 121.2, 65.0, 37.3, 32.0, 29.6, 29.4, 29.3, 28.7, 25.9, 22.8, 14.2; FT-IR (neat) 2923, 2853, 1734, 1595, 1338, 1171, 1028, 795, 783 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{30}NO_2^+$: 328.2271, found: 328.2287.



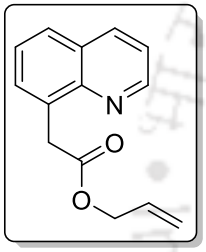
Isopropyl 2-(quinolin-8-yl)acetate 3ah. Yellow liquid; yield 67% (31 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (q, *J* = 2.4 Hz, 1H), 8.14 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 6.8 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.39 (q, *J* = 4.4 Hz, 1H), 5.11-5.01 (m, 1H), 4.24 (s, 2H),1.24 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 149.6, 146.8, 136.2, 133.9, 130.3, 128.4, 127.4, 126.3, 121.2, 68.1, 37.6, 21.9; FT-IR (neat) 2978, 2934, 1725, 1499, 1372, 1241, 1104, 957, 794, 763 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{16}NO_2^+$: 230.1176, found: 230.1181.



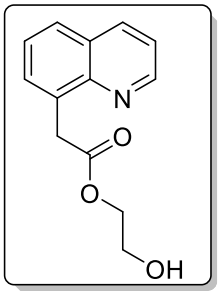
***tert*-Butyl 2-(quinolin-8-yl)acetate 3ai**. Yellow liquid; yield 62% (30 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.14 (dd, *J* = 8.0 Hz, 6.4 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.40 (q, *J* = 4.4 Hz, 1H), 4.19 (s, 2H),1.44 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.7, 149.6, 146.9, 136.3, 134.2, 130.3, 128.4, 127.3, 126.3, 121.2, 80.7, 38.5, 28.2; FT-IR (neat) 2977, 1731, 1499, 1392, 1345, 1367, 1256, 797 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{18}NO_2^+$: 244.1332, found: 244.1329.



***tert*-Pentyl 2-(quinolin-8-yl)acetate 3aj**. Yellow liquid; yield 64% (33 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (q, *J* = 2.0 Hz, 1H), 8.14 (dd, *J* = 8.4 Hz, 6.8 Hz, 1H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.39 (q, *J* = 4.0 Hz, 1H), 4.19 (s, 2H), 1.72 (q, *J* = 7.2 Hz, 2H) 1.40 (s, 6H), 0.78 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 149.6, 146.9, 136.2, 134.3, 130.3, 128.4, 127.2, 126.3, 121.2, 83.0, 38.5, 33.6, 25.6, 8.1; FT-IR (neat) 2973, 2925, 2855, 1726, 1499, 1196, 1142, 1060, 949, 829, 762 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{20}NO_2^+$: 258.1489, found: 258.1486.

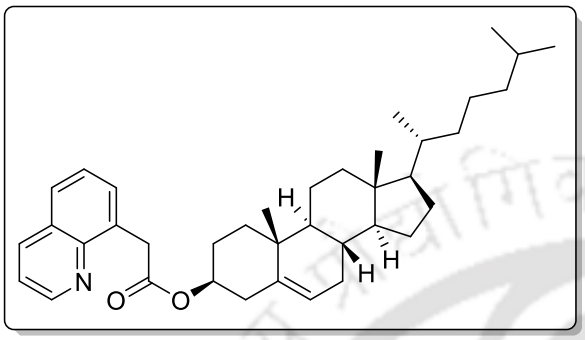


Allyl 2-(quinolin-8-yl)acetate 3ak. Yellow liquid; yield 63% (28 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.0 Hz, 6.8 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.41 (q, *J* = 4.0 Hz, 1H), 5.95-5.86 (m, 1H), 5.29-5.24 (m, 1H), 5.20-5.16 (m, 1H), 4.64-4.62 (m, 2H), 4.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 149.8, 146.8, 136.3, 133.4, 132.4, 130.4, 128.4, 127.6, 126.3, 121.3, 118.0, 65.4, 37.2; FT-IR (neat) 2926, 2854, 1731, 1499, 1365, 1239, 1150, 987, 828, 794, 764 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{14}NO_2^+$: 228.1019, found: 228.1020.

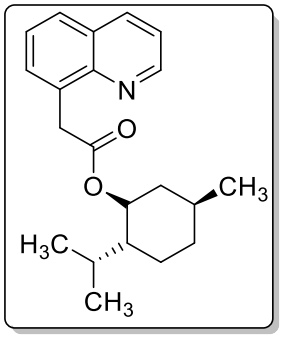


2-Hydroxyethyl 2-(quinolin-8-yl)acetate 3al. Yellow liquid; yield 68% (31 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (q, *J* = 2.8 Hz, 1H), 8.18 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.43 (q, *J* = 4.0 Hz,

1H), 4.29 (t, *J* = 4.4 Hz, 2H), 4.26 (s, 2H), 3.79 (t, *J* = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 149.9, 146.6, 136.7, 133.3, 130.8, 128.6, 127.8, 126.5, 121.4, 66.4, 61.2, 37.9; FT-IR (neat) 3406, 2924, 2854, 1732, 1500, 1259, 1173, 1077, 794, 765 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{14}NO_3^+$: 232.0968, found: 232.0976.

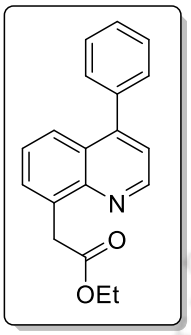


(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 2-(quinolin-8-yl)acetate 3an. Colorless solid; mp 155-157 °C; yield 51% (57 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (q, *J* = 2.4 Hz, 1H), 8.15 (dd, *J* = 8.4 Hz, 6.4 Hz, 1H), 7.76 (d, *J* = 6.8 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.40 (q, *J* = 4.4 Hz, 1H), 5.35 (d, *J* = 5.2 Hz, 1H), 4.70-4.62 (m, 1H), 4.25 (s, 2H), 2.34-2.30 (m, 2H), 2.04-1.97 (m, 2H), 1.92-1.77 (m, 3H), 1.60-1.57 (m, 4H), 1.54-1.51 (m, 2H), 1.47-1.41 (m, 4H), 1.33-1.32 (m, 2H), 1.25 (s, 1H), 1.15-1.03 (m, 7H), 0.99 (s, 4H), 0.91 (d, *J* = 4.8 Hz, 3H), 0.86 (dd, *J* = 6.8 Hz, 4.8 Hz, 6H), 0.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 149.6, 146.9, 139.9, 136.2, 133.9, 130.3, 128.4, 127.4, 126.3, 122.6, 121.2, 74.4, 56.8, 56.2, 50.1, 42.4, 39.8, 39.6, 38.1, 37.6, 37.1, 36.7, 36.3, 35.9, 32.05, 32.00, 28.3, 28.1, 27.8, 24.4, 23.9, 22.9, 22.7, 21.1, 19.4, 18.8, 12.0; FT-IR (neat) 2933, 2867, 2852, 1732, 1499, 1260, 1172, 1028, 796, 764, 703 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{38}H_{54}NO_2^+$: 556.4149, found: 556.4149.

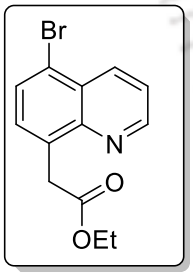


(1R,2S,5S)-2-Isopropyl-5-methylcyclohexyl 2-(quinolin-8-yl)acetate 3ao. Yellow solid; mp 85-87 °C; yield 40% (26 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (q, *J* = 2.8 Hz, 1H), 8.17 (dd, *J* = 8.0 Hz, 6.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 6.8 Hz, 1H),

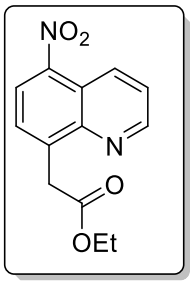
7.49 (t, *J* = 8.0 Hz, 1H), 7.40 (q, *J* = 4.0 Hz, 1H), 4.72-4.65 (m, 1H), 4.23 (s, 2H), 1.66-1.59 (m, 3H), 1.34-1.25 (m, 3H), 0.97 (q, *J* = 6.0 Hz, 1H), 0.91 (t, *J* = 6.0 Hz, 2H), 0.88 (d, *J* = 6.8 Hz, 3H), 0.79 (d, *J* = 6.8 Hz, 3H), 0.67 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 149.6, 146.9, 136.2, 134.0, 130.2, 128.4, 127.3, 126.3, 121.2, 74.6, 47.1, 40.9, 38.0, 34.4, 31.5, 26.0, 23.5, 22.1, 20.8, 16.4; FT-IR (neat) 2953, 2925, 2868, 1729, 1499, 1368, 1259, 1173, 985, 811, 795 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{28}NO_3^+$: 326.2115, found: 326.2116.



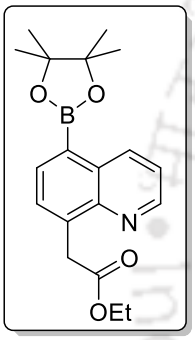
Ethyl 2-(4-phenylquinolin-8-yl)acetate 3ba. Yellow liquid; yield 58% (34 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d *J* = 4.4 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.52-7.47 (m, 6H), 7.33 (d, *J* = 4.4 Hz, 1H), 4.31 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4, 149.1, 148.6, 147.1, 138.2, 133.8, 130.2, 129.5, 128.5, 128.3, 126.8, 126.1, 125.5, 121.4, 60.7, 37.6, 14.2; FT-IR (neat) 2918, 2849, 1731, 1490, 1396, 1252, 1154, 1030, 853, 765 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{18}NO_2^+$: 292.1332, found: 292.1334.



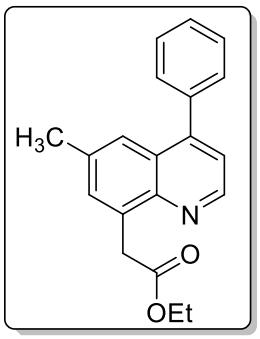
Ethyl 2-(5-bromoquinolin-8-yl)acetate 3ca. Yellow solid; mp 104-106 ºC; yield 66% (39 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (q, *J* = 2.8 Hz, 1H), 8.54 (dd, *J* = 8.4 Hz, 6.8 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.52-7.49 (m, 2H), 4.22 (s, 2H), 4.18 (q, *J* = 6.8 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 150.3, 147.5, 135.8, 133.8, 130.6, 130.1, 127.8, 122.3, 121.2, 60.9, 37.2, 14.3; FT-IR (neat) 2978, 2988, 2937, 1718, 1568, 1496, 1343, 1179, 1028, 934, 847, 789 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{13}BrNO_2^+$: 294.0124, found: 294.0131.



Ethyl 2-(5-nitroquinolin-8-yl)acetate 3da. Yellow solid; mp 66-67 ºC; yield 76% (39 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04-9.00 (m, 2H), 8.36 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.65 (q, *J* = 4.4 Hz, 1H), 4.33 (s, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 1.24 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 150.7, 146.6, 144.9, 141.7, 132.3, 128.6, 124.4, 124.0, 121.3, 61.2, 37.9, 14.3; FT-IR (neat) 2930, 2854, 1734, 1521, 1336, 1275, 1176, 1028, 815, 764 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{13}H_{13}N_2O_4^+$: 261.0870, found: 261.0882.

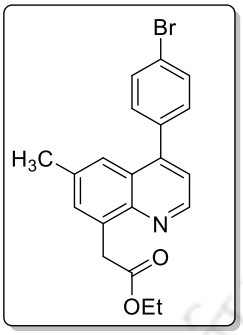


Ethyl 2-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinolin-8-yl)acetate 3ea. Yellow liquid; yield 60% (41 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (dd, *J* = 8.4 Hz, 2.8 Hz, 1H), 8.89 (q, *J* = 2.4 Hz, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 6.8 Hz, 1H), 7.43 (q, *J* = 4.4 Hz, 1H), 4.28 (s, 2H), 4.16 (q, *J* = 7.2 Hz, 2H), 1.41 (s, 12H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 149.2, 146.7, 137.2, 137.0, 135.9, 132.2, 130.4, 129.6, 121.4, 84.0, 60.8, 37.8, 25.1, 14.3; FT-IR (neat) 2979, 2927, 2854, 1733, 1502, 1368, 1259, 1111, 1029, 976, 856, 795 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{19}H_{25}BNO_4^+$: 342.1871, found: 342.1886.

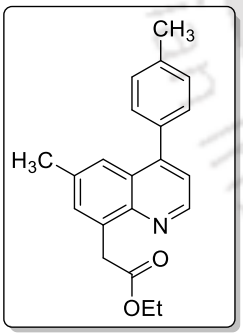


Ethyl 2-(6-methyl-4-phenylquinolin-8-yl)acetate 3fa. Yellow liquid; yield 70% (43 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 4.4 Hz, 1H), 7.59 (s, 1H), 7.55-7.47 (m,

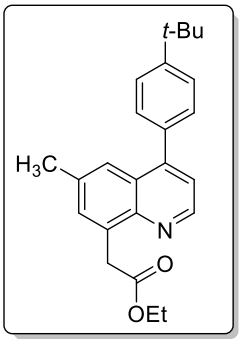
6H), 7.28 (d, *J* = 4.4 Hz, 1H), 4.27 (s, 2H), 4.22 (q, *J* = 6.4 Hz, 2H), 2.44 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 148.3, 147.9, 145.8, 138.6, 136.0, 133.5, 132.6, 129.6, 128.6, 128.3, 126.9, 124.3, 121.6, 60.8, 37.7, 21.9, 14.3; FT-IR (neat) 2980, 2919, 2849, 1731, 1491, 1366, 1253, 1160, 1031, 867, 764 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{20}NO_2^+$: 306.1489, found: 306.1486.



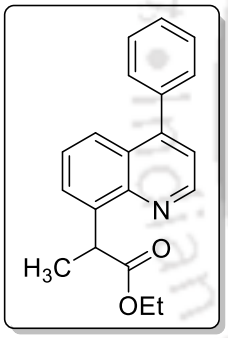
Ethyl 2-(4-(4-bromophenyl)-6-methylquinolin-8-yl)acetate 3ga. Yellow liquid; yield 72% (55 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.2 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 13.2 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 4.2 Hz, 1H), 4.26 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.5, 148.2, 146.6, 145.8, 137.4, 136.4, 133.7, 132.8, 131.8, 131.2, 126.6, 123.9, 122.7, 121.4, 60.9, 37.7, 21.9, 14.3; FT-IR (neat) 2978, 2924, 2865, 1731, 1485, 1387, 1160, 1009, 827, 764, 749 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{19}BrNO_2^+$: 384.0594, found: 384.0595.



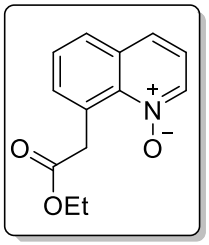
Ethyl 2-(6-methyl-4-(*p*-tolyl)quinolin-8-yl)acetate 3ha. Yellow liquid; yield 55% (35 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (d, *J* = 4.4 Hz, 1H), 7.62 (s, 1H), 7.48 (s, 1H), 7.39-7.32 (m, 4H), 7.27 (d, *J* = 4.4 Hz, 1H), 4.26 (s, 2H), 4.22 (q, *J* = 7.2 Hz, 2H), 2.47 (s, 3H), 2.44 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 148.3, 148.0, 145.8, 138.2, 135.9, 135.6, 133.5, 132.5, 129.5, 129.3, 127.1, 124.4, 121.6, 60.8, 37.7, 21.9, 21.4, 14.3; FT-IR (neat) 2980, 29128, 2850, 1731, 1498, 1439, 1386, 1159, 1029, 908, 867, 817, 729 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{21}H_{22}NO_2^+$: 320.1645, found: 320.1659.



Ethyl 2-(4-(4-(tert-butyl)phenyl)-6-methylquinolin-8-yl)acetate 3ia. Yellow liquid; yield 68% (49 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 4.4 Hz, 1H), 7.59 (s, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.41 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.19 (t, *J* = 4.4 Hz, 1H), 4.19 (s, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.38 (s, 3H), 1.34 (s, 9H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.7, 151.4, 148.3, 147.9, 145.8, 135.9, 135.6, 133.4, 132.6, 129.4, 127.0, 125.5, 124.5, 121.6, 60.8, 37.7, 34.8, 31.5, 21.9, 14.3; FT-IR (neat) 2961, 2906, 2867, 1733, 1498, 1365, 1254, 1160, 1031, 834, 750 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{24}H_{28}NO_2^+$: 362.2115, found: 362.2116.



Ethyl 2-(4-phenylquinolin-8-yl)propanoate 3ja. Colorless liquid; yield 32% (19 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, *J* = 4.4 Hz, 1H), 7.83 (dd, *J* = 8.4 Hz, 2.4 Hz, 1H), 7.67 (dd, *J* = 6.8 Hz, 1.2 Hz, 1H), 7.52-7.44 (m, 6H), 7.33 (d, *J* = 4.4 Hz, 1H), 5.08 (q, *J* = 7.2 Hz, 1H), 4.18 (q, *J* = 6.8 Hz, 2H), 1.66 (d, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 149.0, 146.3, 140.4, 138.4, 129.7, 128.6, 128.4, 127.3, 127.0, 126.4, 125.1, 121.5, 60.7, 40.4, 18.5, 14.3; FT-IR (neat) 2977, 2922, 2850, 1730, 1490, 1395, 1189, 1096, 855, 767 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{20}NO_2^+$: 306.1489, found: 306.1489.



8-(2-Ethoxy-2-oxoethyl)quinoline 1-oxide 4aa. Brown solid; 109-110 ^{o}C; yield

81% (37 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 6.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 6.8 Hz, 1H), 7.22 (q, *J* = 2.4 Hz, 1H), 4.39 (s, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 149.7, 137.2, 134.7, 132.5, 129.4, 128.6, 128.2, 126.5, 121.1, 60.7, 43.5, 14.4; FT-IR (neat) 3415, 3070, 2983, 2905, 1730, 1575, 1370, 1301, 1228, 1180, 1024, 817, 762 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{14}NO_3^+$: 232.0968, found: 232.0982.

2.5 References

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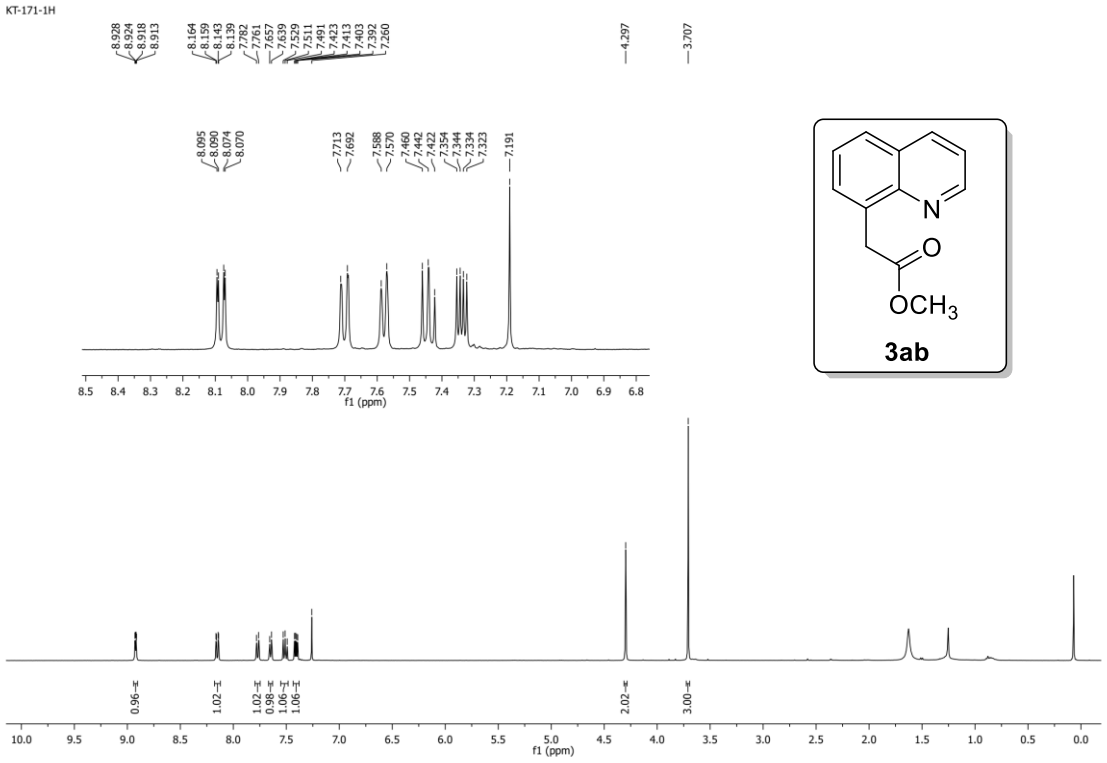
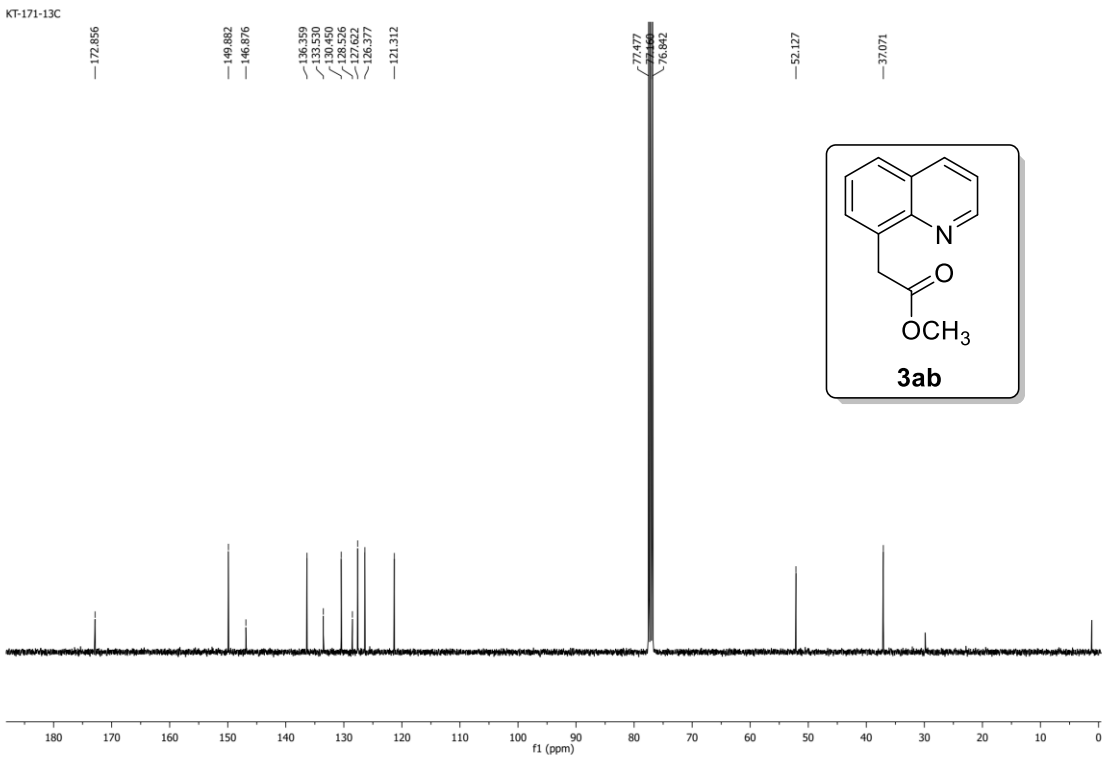
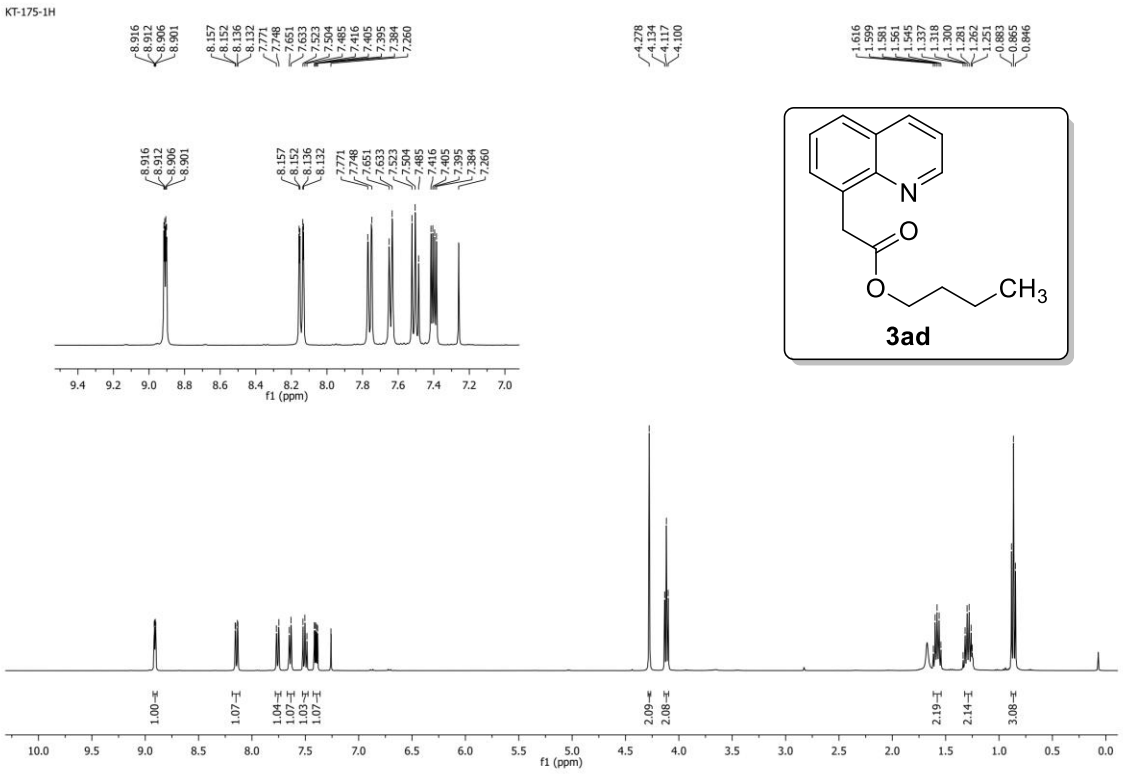
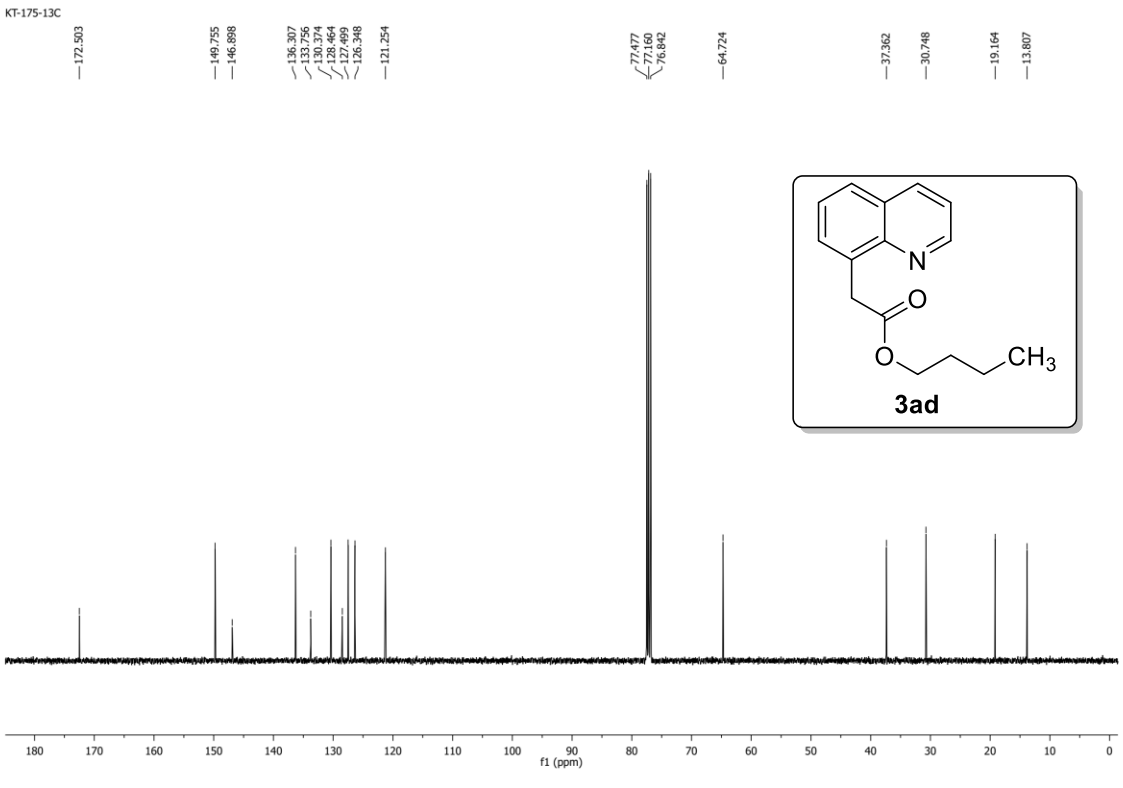
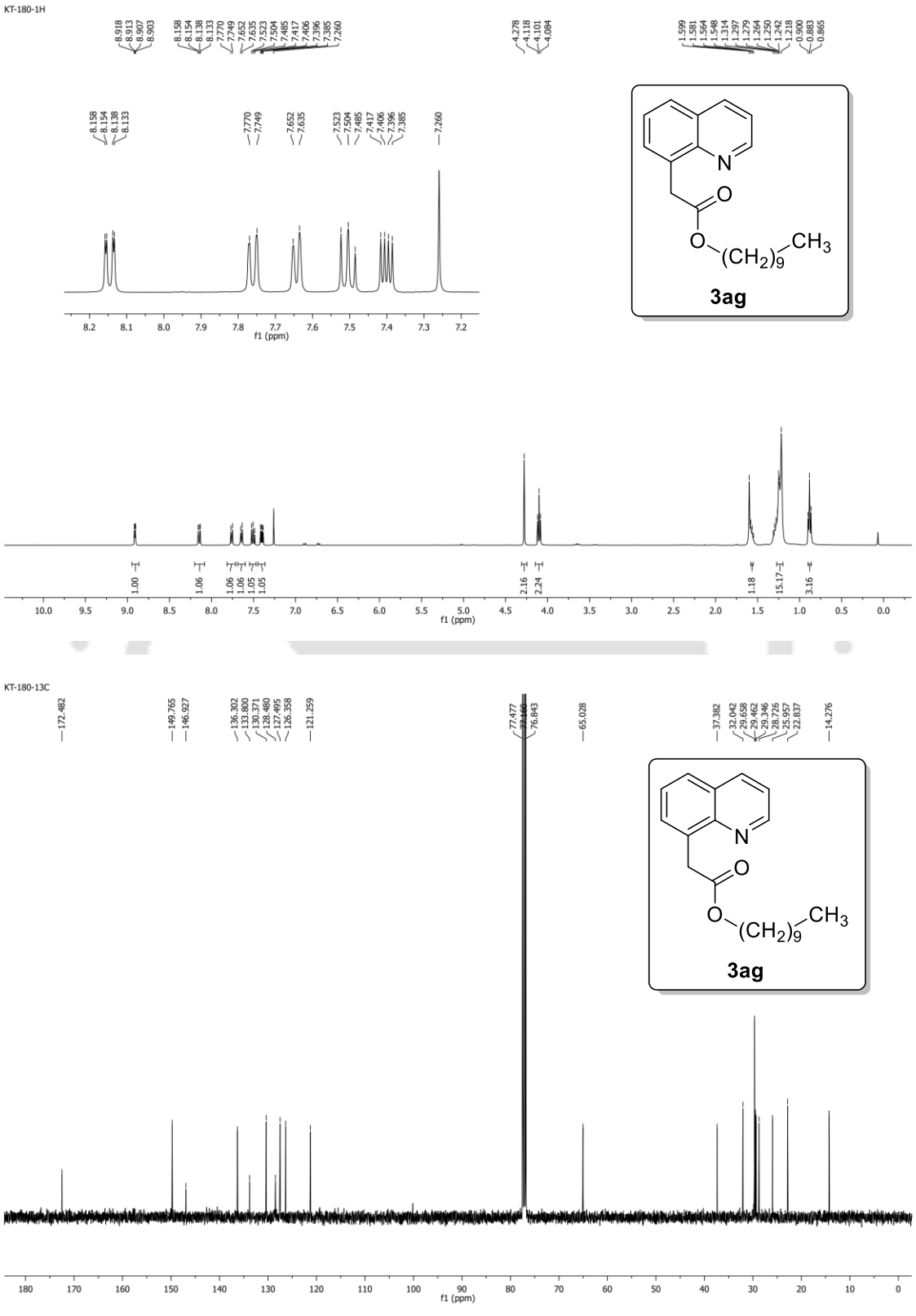
2.6 Selected NMR Spectra

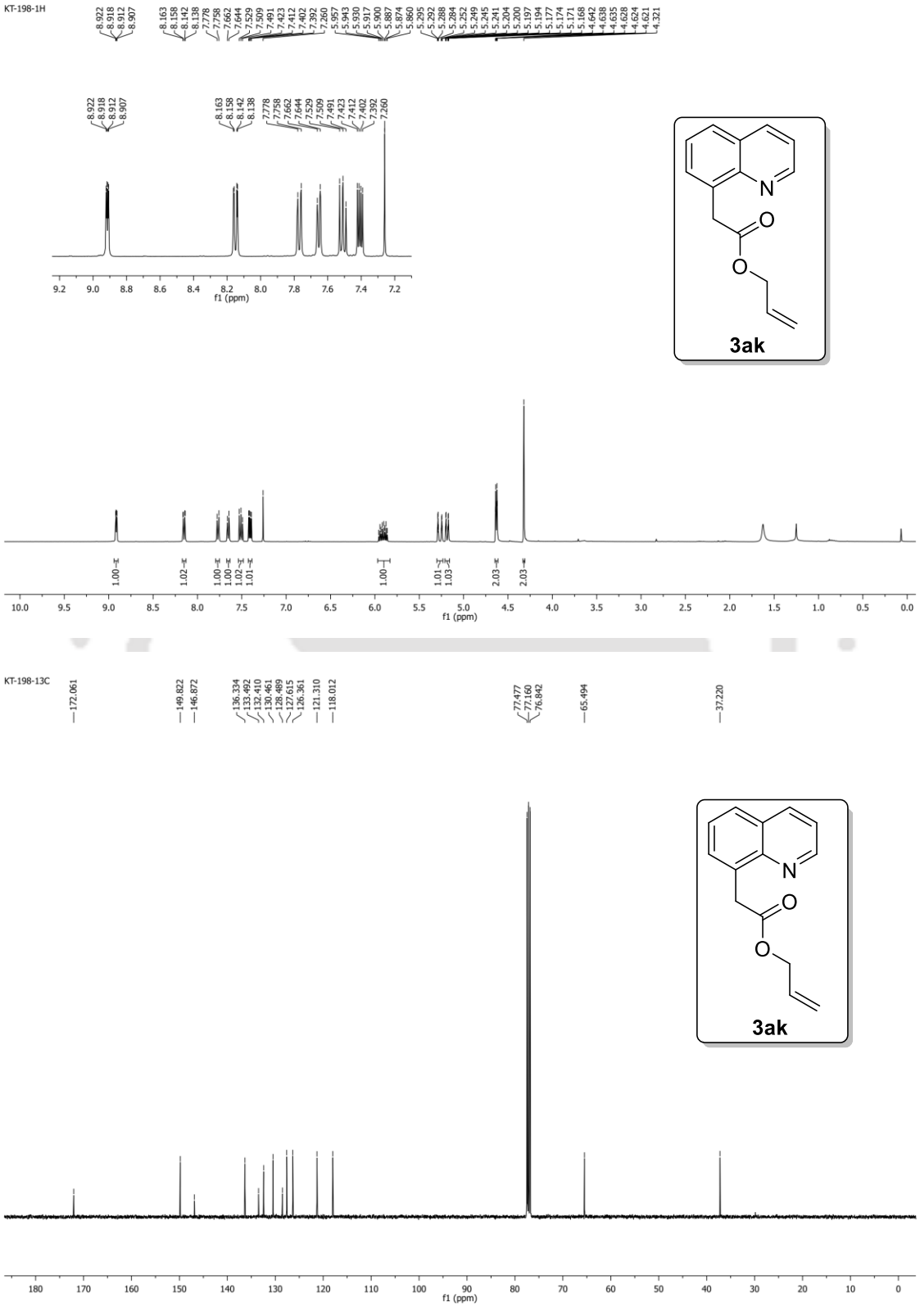






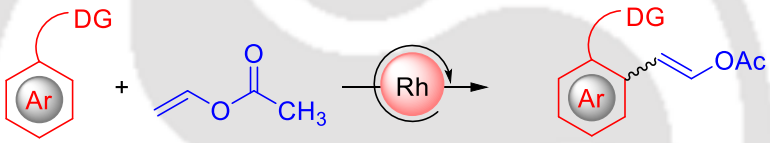






Chapter III

Rh-Catalyzed Site-Selective Alkenylation of Aryl 2-Pyridyl Ethers with Vinyl Acetate



✔ Unactivated Alkene ✔ Gram Scale Synthesis ✔ DFT Studies

Manuscript under preparation.

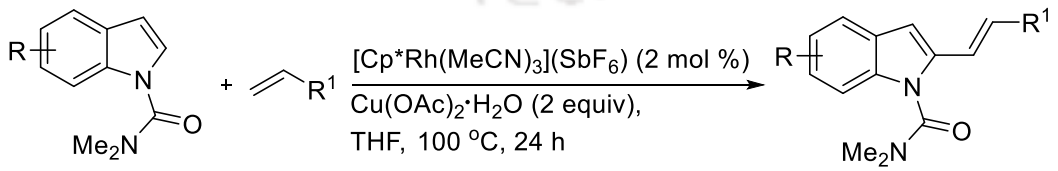
Rh-Catalyzed Site-Selective Alkenylation of Aryl 2-Pyridyl Ethers with Vinyl Acetate

Olefins, a widespread functional group, can be easily modified to form intricate organic molecules. The distinctive reactivity of olefins underscores the importance of alkene functionalization in organic synthesis.[1] In this scenario, the chelation-assisted transition-metal-catalyzed functionalization of olefins through C-H activation has become a crucial technique. This method facilitates the formation of new C-C bonds in a highly atom- and step-economical fashion.[2] Recently, various transition-metal-catalysts, such as Pd, Rh, Ru, Ir, and Co, have been utilized for this particular transformation. However, the majority of existing methods are restricted to activated alkenes like acrylates, enones, and styrenes. Significantly, the direct oxidative C-H olefination of arenes with electron-rich olefins, such as vinyl acetates, enamides, and vinyl ethers, remains a challenging task. Only recently have a few instances of direct C-H alkenylation of arenes with activated olefins been documented.[3] Nevertheless, the direct sp^2 C-H functionalization of electron-rich alkenes is still infrequent despite being highly sought after.

3.1 Literature Study

3.1.1 Rh-Catalyzed Alkenylation of sp^2 C-H Bond

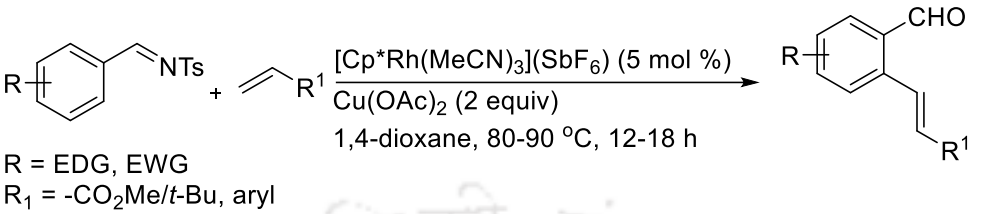
Wang and co-workers reported a regioselective C2 oxidative alkenylation of indoles *via* cationic Rh(III)-catalyzed C-H bond activation (Scheme 1).[4] The alkenylation was effectively applied to a diverse range of olefins and indole derivatives featuring both electron-donating and electron-withdrawing groups. The outcome of this protocol resulted in exclusive regioselectivity, producing C2-*E*-olefinated indoles.



R = EDG, EWG
R^1 = $-CO_2Me$, -Ar, $-SO_2Ph$, -CN

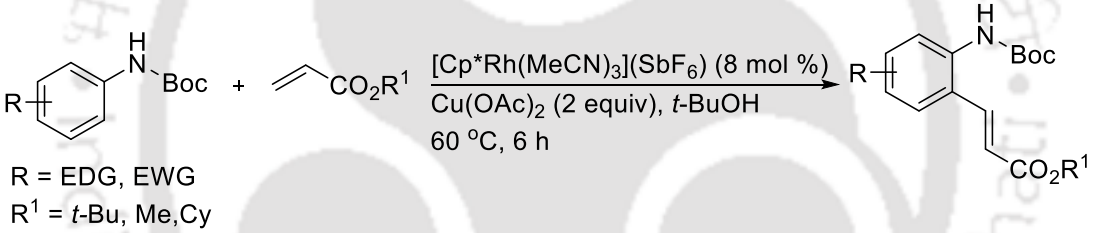
Scheme 1. Rh-Catalyzed C2 Alkenylation of Indoles

Li group described a Rh(III)-catalyzed olefination protocol for the synthesis of *ortho*-olefinated benzaldehydes using *N*-sulfonyl imines (Scheme 2).[5] The reaction tolerated a wide range of activated alkenes such as styrenes and acrylates.



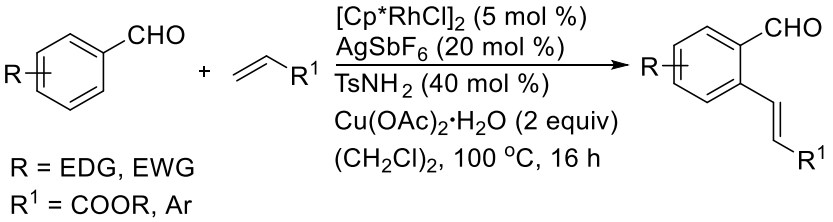
Scheme 2. Rh-Catalyzed Olefination of Benzaldehydes

A Rh(III)-catalyzed *ortho*-alkenylation of anilines, directed by a removable Boc-protecting group was elucidated by Miura and co-workers (Scheme 3).[6] The resulting *ortho*-alkenylanilines can be easily converted into nitrogen-containing fused heteroaromatic compounds, including indoles and quinolines.



Scheme 3. Rh-Catalyzed *ortho*-Alkenylation of Anilines

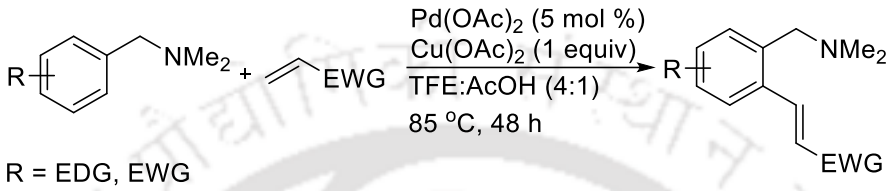
Wang and co-workers demonstrated a Rhodium-catalyzed *ortho*-C-H olefination of aromatic aldehydes employing transient directing strategy (Scheme 4).[7] Both electron-rich and electron-deficient aromatic aldehydes were accommodated, affording the corresponding products in moderate to good yields. Significantly, this protocol offers a straightforward approach to obtaining olefinated aromatic aldehydes using aldehydes as the simple starting materials.



Scheme 4. Rh-Catalyzed *ortho*-C-H Olefination of Aromatic Aldehydes

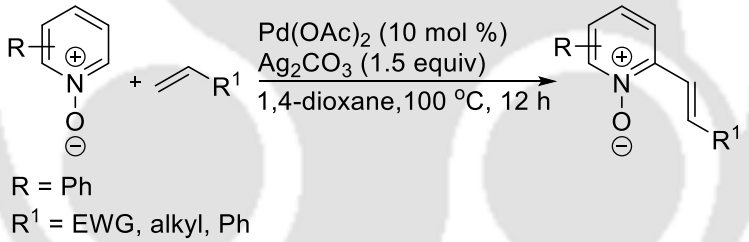
3.1.2 Pd-Catalyzed Alkenylation of sp^2 C-H Bond

Shi and co-workers described an elegant *ortho*-olefination of *N*,*N*-dimethylbenzylamines exploiting Pd(II)-catalytic system tuned by the acidity of the reaction conditions (Scheme 5).[8] Mechanistic investigations revealed that a crucial step in this catalytic transformation involved electrophilic attack on the phenyl ring by the Pd(II) ion, assisted by the *N*,*N*-dimethylaminomethyl group. The acidity of the reaction conditions played a controlling role in this process.



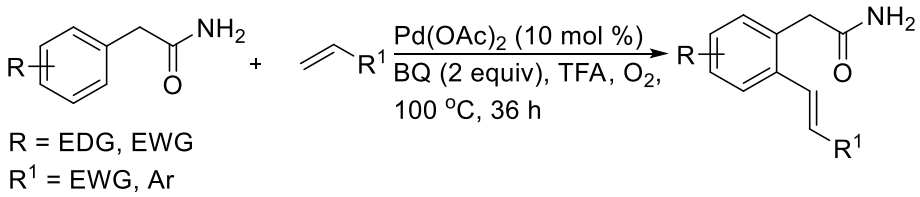
Scheme 5. Pd-Catalyzed *ortho*-Olefination of *N*,*N*-dimethylbenzylamines

An efficient Palladium-catalyzed site-selective alkenylation of pyridine *N*-oxides was described by Chang and co-workers (Scheme 6).[9] The reaction tolerated both activated and unactivated olefins generating moderate to good yield.



Scheme 6. Pd-Catalyzed Site-Selective Alkenylation of Pyridine *N*-Oxides

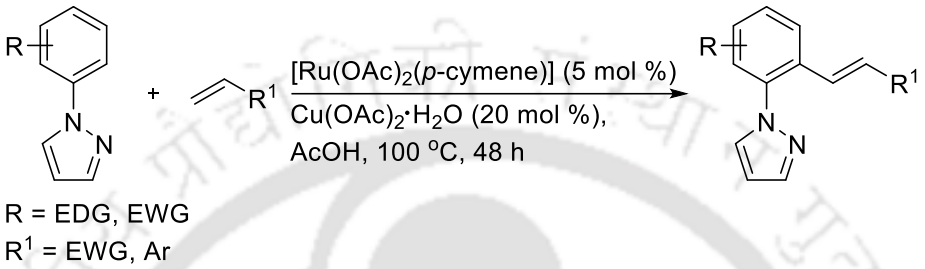
Kumar and co-workers described a Pd(II)-catalyzed regioselective C-H alkenylation of arylacetamides *via* distal weakly coordinating primary amides as chelating groups (Scheme 7).[10] This approach facilitates the integration of a synthetically adaptable olefin into the final products, yielding moderate to good amounts with both regio- and stereoselectivity.



Scheme 7. Pd-Catalyzed Regio-Selective Alkenylation of Arylacetamides

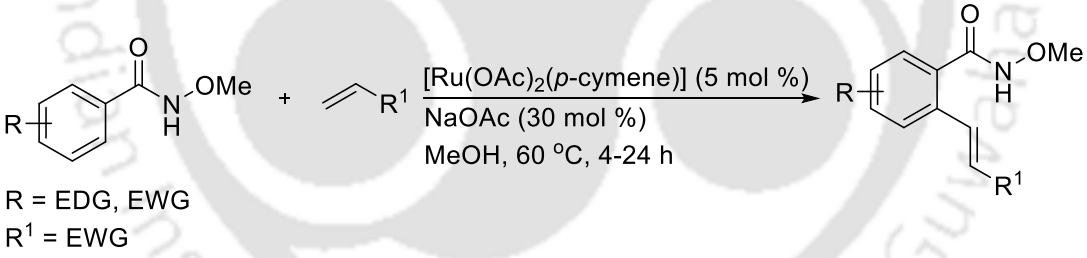
3.1.3 Ru-Catalyzed Alkenylation of sp^2 C-H Bond

A Ruthenium diacetate-catalyzed oxidative alkenylation of *N*-aryl pyrazoles by styrene and alkyl acrylates for the synthesis of alkenyl *N*-arylpyrazoles was demonstrated by Dixneuf and co-workers (Scheme 8).[11] It is worth mentioning that Alkenylation using electrophilic acrylates necessitates a stoichiometric quantity of oxidant, while the process with styrene is simpler and employs a catalytic amount of $Cu(OAc)_2 \cdot H_2O$ in acetic acid.



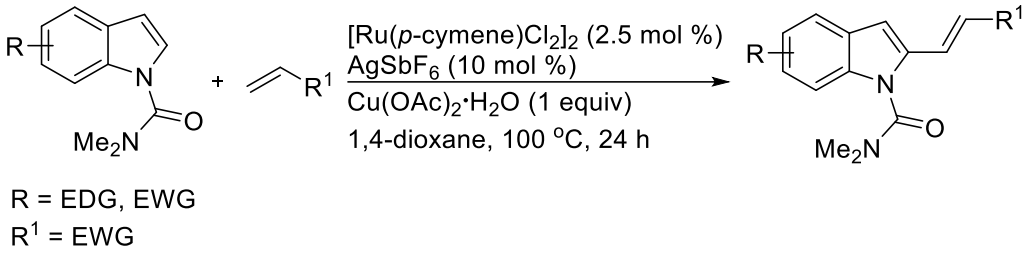
Scheme 8. Ru-Catalyzed Oxidative Alkenylation of *N*-Aryl Pyrazole

Wang and colleagues demonstrated a Ru-catalyzed oxidative C-H bond olefination of *N*-methoxybenzamides using an oxidizing directing group (Scheme 9).[12] The catalytic reaction selectively targets *ortho*- and mono-olefination exclusively.



Scheme 9. Ru-Catalyzed Oxidative Alkenylation of *N*-Methoxybenzamides

Wang and co-workers reported an effective ruthenium-catalyzed oxidative coupling of indoles with diverse alkenes at the C2-position displaying excellent stereo- and regio-selectivity (Scheme 10).[13] This process is facilitated by the use of the *N*,*N*-dimethylcarbamoyl moiety as a directing group.



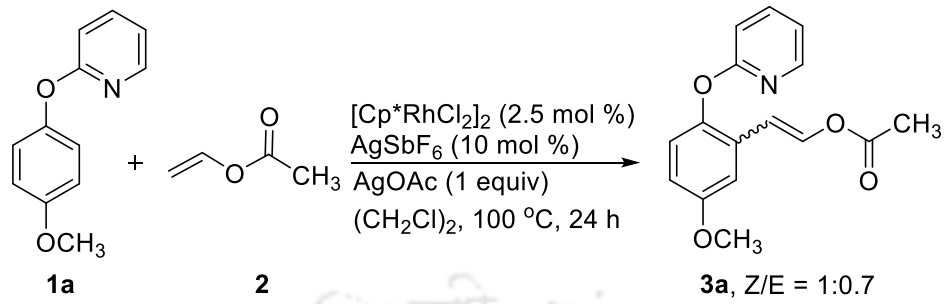
Scheme 10. Ru-Catalyzed Oxidative C2-Alkenylation of Indoles

3.2 Present Study

Herein we report a Rh-catalyzed site selective alkenylation of aryl 2-pyridyl ethers utilizing vinyl acetate as alkenylating agent. The initial investigation was conceded out by employing 2-(4-methoxyphenoxy)pyridine **1a** and vinyl acetate **2** as model substrates and $[Cp^*RhCl_2]_2$ as catalyst and $AgSbF_6$ as additive in presence of oxidant (Table 1). To our delight, the alkenylated product **3a** was formed in 46% isolated yield when substrates **1a** and **2** were subjected to react in presence of $[Cp^*RhCl_2]_2$ (2.5 mol%), $AgSbF_6$ (10 mol%), $Cu(OAc)_2{\cdot}H_2O$ (1 equiv) in TFE at 100 °C for 24 h (entry 1). 1,2-Dichloroethane came out as the solvent of choice, yielding up to 57% whereas CH_3CN, toluene, *m*-xylene, DMSO, EtOH and CH_2Cl_2 were all found to be inferior (entry 2-8). In a set of oxidants screened such as AgOAc, Ag_2CO_3, NaOAc, CsOAc, AcOH and PivOH, the former furnished the best result, yielding up to 75% (entry 9-14). However, in the absence of an oxidant, the procedure proved unsuccessful in delivering the desired product (entry 15). Additionally, a control experiment indicated that both vinyl acetate **2** and $AgSbF_6$ are essential for achieving the expected product **3a** in a satisfactory yield (entry 16-18).

Once the optimized condition was obtained, the methodology's applicability was assessed for electronically diverse substituents at various positions of the aryl ring **1b**-**j** (Table 2). In this instance, the unmodified directing group resulted in the formation of 57% of the *ortho*-selective alkenylated product **3b** without any diastereoselectivity. It was noted that when electron- donating methyl groups were present at both the *meta*-positions relative to directing group **1c**, a yield of 62% for the alkenylated product **3c** was achieved with 1:0.6 (*Z*/*E*)-diastereoselectivity. In contrast, a bulkier electron-donating *t*-butyl group at the *ortho*-position, as in the case of **1d**, only resulted in a yield of 47% (*Z*/*E* = 1:0.5) for **3d**, whereas in case of bromo **1e**, the protocol was reluctant to deliver the target product in significant amount. Nevertheless, when electron-withdrawing groups like chloro **1f** and bromo **1g** were positioned at the *para*-position, they resulted in relatively higher

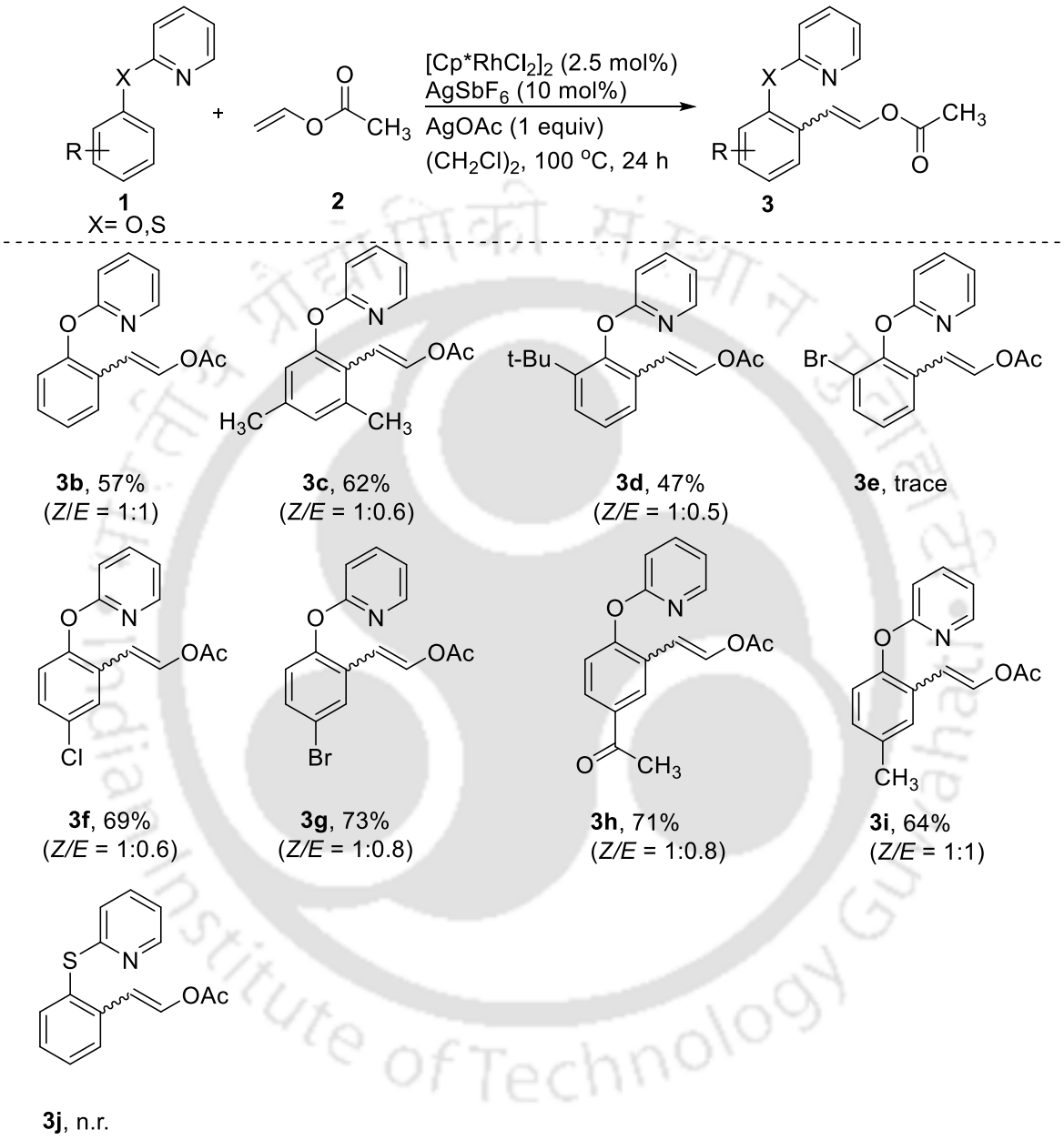
Table 1. Optimization of Rh-catalyzed Alkenylation[a]



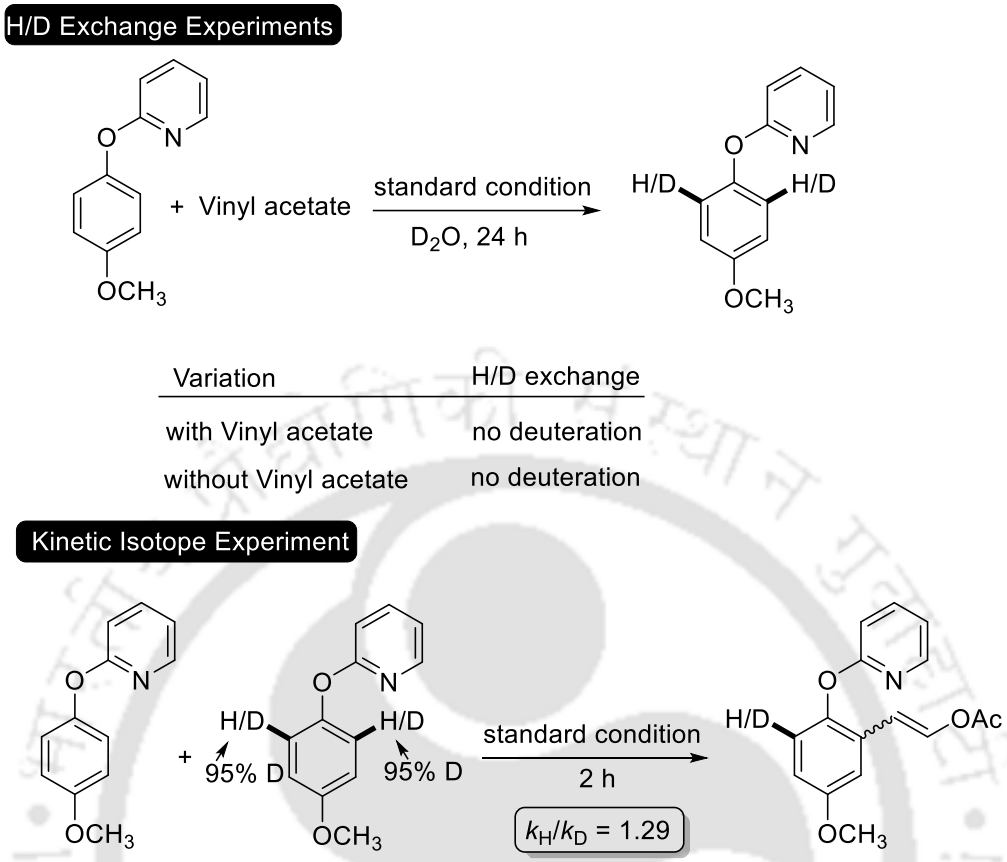
Entry	Catalyst	Additive	Oxidant	Solvent	Yield[b]
1	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	TFE	46
2	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	CH_3CN	n.d.
3	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	toluene	n.d.
4	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	*m*-xylene	n.d.
5	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	DMSO	n.d.
6	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	methanol	n.d.
7	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	CH_2Cl_2	53
8	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	57
9	$[Cp^*RhCl_2]_2$	$AgSbF_6$	Ag_2CO_3	$(CH_2Cl)_2$	n.d.
10	$[Cp^*RhCl_2]_2$	$AgSbF_6$	NaOAc	$(CH_2Cl)_2$	trace
11	$[Cp^*RhCl_2]_2$	$AgSbF_6$	$AgBF_4$	$(CH_2Cl)_2$	trace
12	$[Cp^*RhCl_2]_2$	$AgSbF_6$	AgOAc	$(CH_2Cl)_2$	75
13	$[Cp^*RhCl_2]_2$	$AgSbF_6$	AcOH	$(CH_2Cl)_2$	trace
14	$[Cp^*RhCl_2]_2$	$AgSbF_6$	PivOH	$(CH_2Cl)_2$	n.d.
15	$[Cp^*RhCl_2]_2$	$AgSbF_6$	---	$(CH_2Cl)_2$	n.d.
16[c]	$[Cp^*RhCl_2]_2$	$AgSbF_6$	AgOAc	$(CH_2Cl)_2$	n.d.
17[d]	$[Cp^*RhCl_2]_2$	---	AgOAc	$(CH_2Cl)_2$	trace

[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.6 mmol), [Rh] (2.5 mol %), $AgSbF_6$ (0.02 mmol), oxidant (0.2 mmol), solvent (2 mL), 100 °C, 24 h, sealed tube. [b]Isolated yield. [c]Without **2a**. [d]Without $AgSbF_6$. n.d. = not detected.

Table 2. Substrate scope for alkenylation reaction.[a,b]



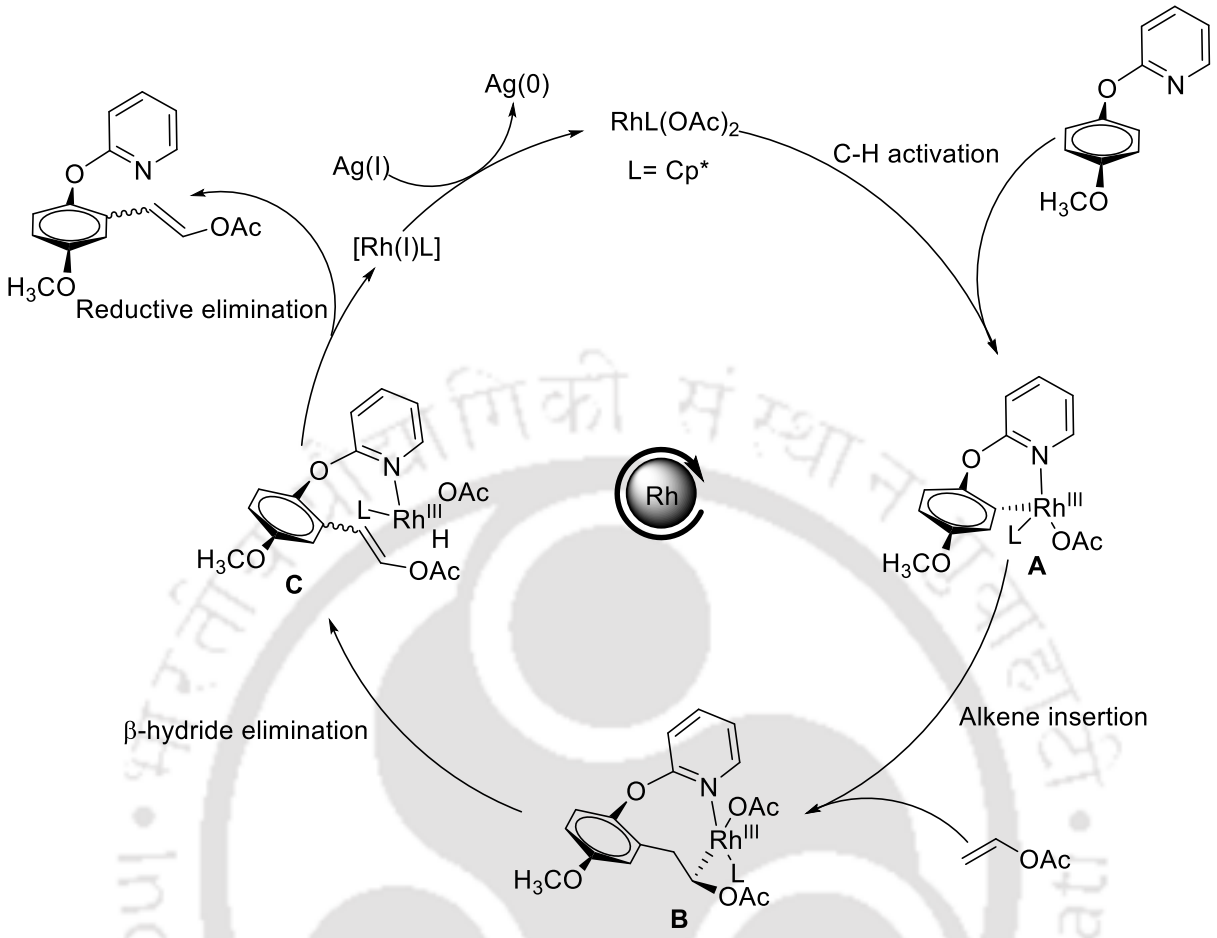
[a]Reaction conditions: **1b-j** (0.20 mmol), **2** (0.6 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), $AgSbF_6$ (10 mol %), AgOAc (0.20 mmol), $(CH_2Cl)_2$ (2 mL), 100 °C, 24 h, pressure tube. [b]Isolated yield.



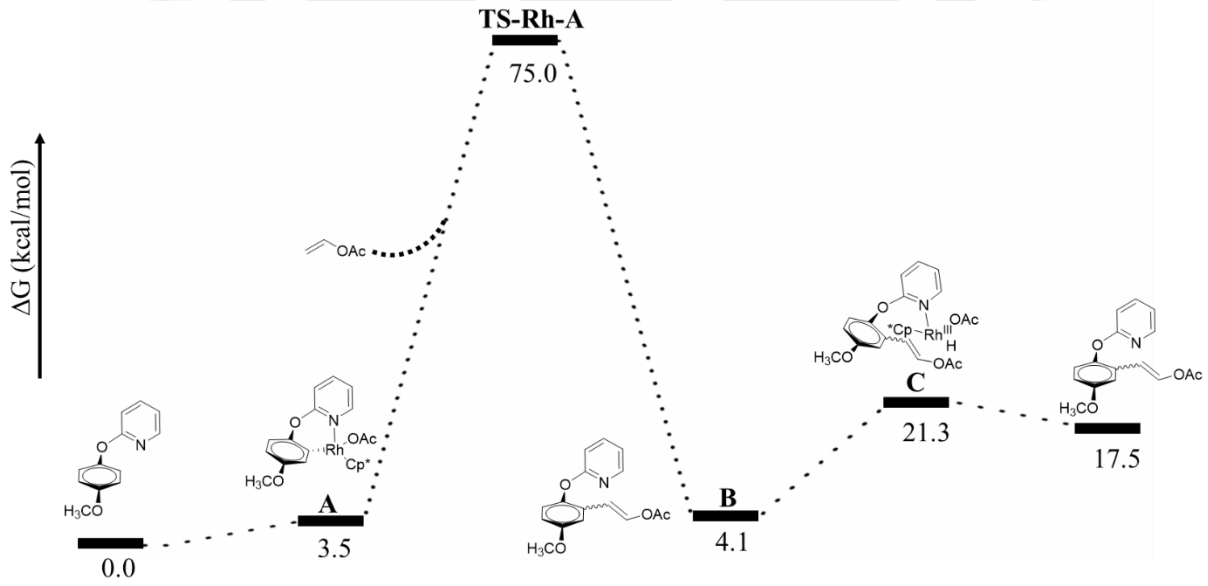
Scheme 11. Preliminary Mechanistic Investigations

yields of 69% and 73% respectively (**3f**, *Z*/*E* = 1:0.6 and **3g**, *Z*/*E* =1:0.8). This enhancement in yield could potentially be attributed to the stabilization of the chelated intermediate *via* the electron-withdrawing effect. However, in the case of *para*-substituted acetoxy group **1h**, a 71% yield of the desired product **3h** was obtained, whereas methyl group **1i** yielded 64% of the expected product **3i** without showing any diastereoselectivity. The protocol was found to be ineffective for 2-(phenylthio)pyridine **1j** to deliver the expected outcome **3j**, possibly due to catalyst poisoning.

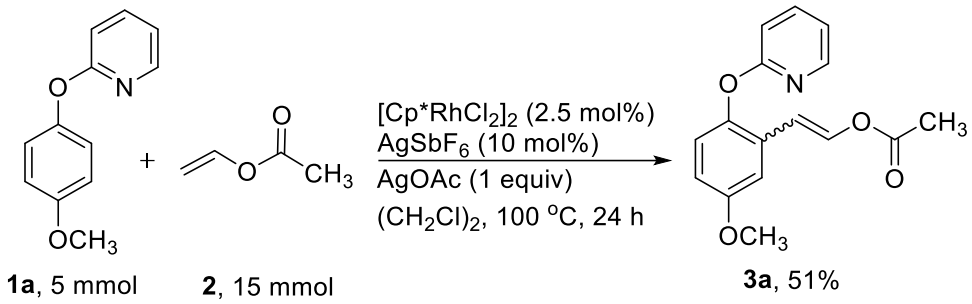
In order to unravel the mechanistic pathway, H/D exchange and kinetic-isotope experiments were performed (Scheme 11). The Deuterium labelling experiments using D_2O as a co-solvent did not exhibit any significant H/D scrambling, which suggest the irreversible nature of the C-H bond activation step.[14] Additionally, the kinetic isotope experiment furnished a k_H/k_D ratio of 1.29, which implies that the rate-determining step might not entail C-H bond cleavage. In order to delve deeper



Scheme 12. Proposed Reaction Mechanism



Scheme 13. Energy Profile Diagram of Rh-catalysed Alkenylation



Scheme 14. Scale up Synthesis

into the mechanistic pathway of these reactions, we conducted DFT calculations. All calculations were executed at the B3LYP level of theory. From the experimental observations and DFT calculations, a plausible catalytic pathway has been formulated (Scheme 12).[15] The associated energy profile diagram is illustrated in Scheme 13. In the process of forming the alkenylated product, the catalyst initially undergoes transformation into the active Rh(III) species under the experimental conditions. Subsequently, the Rh-centre is inserted into the *o*-C-H bond of the substrate relative to the directing group, in a slightly uphill process (ΔG = 3.5 kcal/mol) to form **A**. Following that, the alkene is introduced into the Rh-C bond *via* a transition state TS-Rh-A ($\Delta G^{\neq}$ = 75 kcal/mol) to generate species B. Subsequently, β-hydride elimination leads to the formation of species C. The latter may undergo reductive elimination to yield the desired alkenylated product, and the process is observed to be endothermic (ΔG = 17.5 kcal/mol) in nature. Finally, the Rh-catalysed alkenylation reaction was successfully scaled up using 2-(4-methoxyphenoxy)pyridine (5 mmol) as a representative case, as depicted in Scheme 14. The alkenylation proceeded to deliver the desired product in a 51% yield, affirming the scalability of the reaction.

In summary, we have established an effective cross-coupling protocol for alkenylation of aryl 2-pyridyl ethers with vinyl acetate through transition-metal-catalyzed sp^2 C-H activation. The proposed mechanism has been substantiated through a combination of experimental mechanistic investigations and DFT calculations. The selectivity, functional group tolerance and scalability are the important practical features.

3.3 Experimental Section

General Information. $[Cp^*RhCl_2]_2$, $AgSbF_6$ (98%), AgOAc (99%), and vinyl acetate were purchased from Aldrich and used as received. The substituted Aryl 2-Pyridyl Ethers **1a-j** were prepared according to literature.[16] Merck silica gel G/GF 254 plates were used for analytical TLC and Rankem silica gel (60-120 mesh) was used for column chromatography. NMR (^1H and ^{13}C) spectra were recorded in Bruker Avance III 400, 500 and 600 spectrometers using $CDCl_3$ as solvent and TMS as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively, and other data are reported as follows: s = singlet, d = doublet, dd= doublet of doublet, t = triplet, m = multiplet and q = quartet. IR spectra were collected on a PerkinElmer Fourier transform infrared (FT-IR) spectrometer. Quadrupole time-of-flight electrospray ionization (ESI) mass spectrometer (model HAB 273) was used for mass analysis.

General Procedure for the Alkenylation of Aryl 2-Pyridyl Ethers. Aryl 2-Pyridyl Ethers **1** (0.2 mmol), vinyl acetate **2** (0.6 mmol, 51.7 mg), $[Cp^*RhCl_2]_2$ (2.5 mol%, 3 mg), $AgSbF_6$ (20 mol%, 13.7 mg) and AgOAc (0.2 mmol, 33.4 mg) were stirred at 100 ^oC for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The mixture was diluted with dichloromethane (10 mL) and passed through a short pad of celite. The organic layer was washed with brine (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane/EtOAc (10:1) as eluent to afford the desired product **3**.

Scale-up Synthesis of 3a. 2-(4-methoxyphenoxy)pyridine **1a** (5 mmol, 1.1 g), vinyl acetate **2** (15 mmol, 1.3 g), $[Cp^*RhCl_2]_2$ (2.5 mol%, 77 mg), $AgSbF_6$ (20 mol%, 343 mg) and AgOAc (5 mmol, 835 mg) were subjected to the above described standard reaction condition. The mixture was diluted with dichloromethane (20 mL) and passed through a celite pad and washed with brine (5 mL) and water (5 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated to produce a residue, which was purified by column chromatography on silica gel using *n*-hexane/EtOAc (10:1) as eluent to afford **3a** in 51% (726 mg) yield.

Synthesis of $[D_2]$**-1a**.[17] 2-(4-methoxyphenoxy)pyridine **1a** (40.2 mg, 0.2 mmol), $\{RuCl_2(p\text{-cymene})\}_2$ (6 mg, 5.0 mol %), $AgSbF_6$ (13.7 mg, 20 mol %), AcOH (5.0 μL, 50.0 mol %), and Ag_2CO_3 (110 mg, 0.4 mmol) were stirred at 110 °C for 3 h in $(CH_2Cl)_2/D_2O$ (1.8:0.2) under N_2.

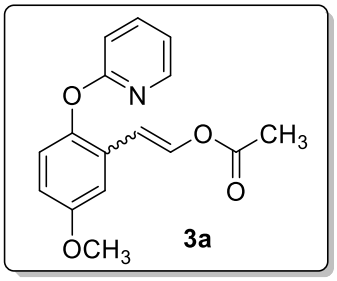
The reaction mixture was cooled to room temperature, diluted with dichloromethane (10 mL), and passed through a short pad of Celite using dichloromethane (50 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified using column chromatography on silica gel to yield [D_2]-**1a** in 59% yield (23.9 mg) as a colorless liquid. Deuterium incorporation in the *ortho*-position was found to be 95% as estimated from 400 MHz ^{1}H NMR.

H/D Exchange Experiment with D_2O. Aryl 2-Pyridyl Ethers **1** (0.2 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%, 3 mg), $AgSbF_6$ (20 mol%, 13.7 mg) and AgOAc (0.2 mmol, 33.4 mg) and D_2O (2 mmol) were stirred at 100 ^{o}C for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The work-up and purification were performed as described in the general procedure. 400 MHz ^{1}H NMR spectrum of the product showed no deuterium incorporation.

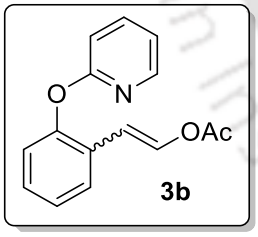
H/D Exchange Experiment with D_2O in Presence of Vinyl acetate. Aryl 2-Pyridyl Ethers **1** (0.2 mmol), vinyl acetate **2** (0.6 mmol, 51.7 mg), $[Cp^*RhCl_2]_2$ (2.5 mol%, 3 mg), $AgSbF_6$ (20 mol%, 13.7 mg) and AgOAc (0.2 mmol, 33.4 mg) and D_2O (2 mmol) were stirred at 100 ^{o}C for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The work-up and purification were performed as described in the general procedure. 400 MHz ^{1}H NMR spectrum of the product showed no deuterium incorporation.

Kinetic Isotope Effect Experiment. A mixture of 2-(4-methoxyphenoxy)pyridine **1a** (0.2 mmol, 40.2 mg) and [D_2]-**1a** (0.2 mmol, 40.6 mg) was reacted with Vinyl acetate **2** (0.6 mmol, 51.7 mg) for 2 h under standard reaction conditions. The reaction mixture was diluted with DCM (5 mL), and passed through a short pad of celite using DCM (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent on vacuo produced a residue, which was purified on silica gel column chromatography on silica gel using *n*-hexane and EtOAc (20:1) as eluent to afford **4a**/[D_1]-**4a**. The intermolecular k_H/k_D was found to be 1.29, based on the 400 MHz ^{1}H NMR spectroscopy.

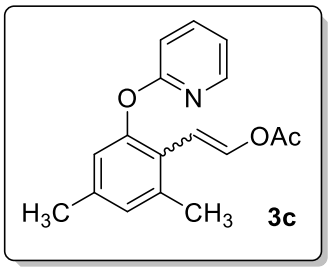
3.4 Characterization Data



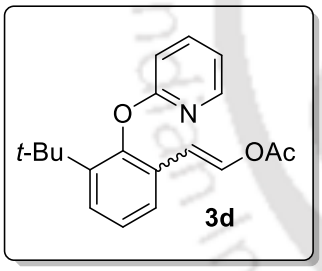
5-Methoxy-2-(pyridin-2-yloxy)styryl acetate 3a. Yellow liquid; yield 75% (30 mg); major diastereomer (*Z*/*E* = 1:0.7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.15 (m, 1.6H, major + minor), 7.86 (d, *J* = 12.8 Hz, 0.6H, minor), 7.68-7.63 (m, 1.7H, major + minor), 7.56 (d, *J* = 3.1 Hz, 1H, major), 7.24 (d, *J* = 7.4 Hz, 1H, major), 7.03 (d, *J* = 8.8 Hz, 1H, major), 7.00-6.99 (m, 0.6H, minor), 6.97-6.93 (m, 1.7H, major + minor), 6.87-6.82 (m, 3.3H, major + minor), 6.45 (d, J = 12.8 Hz, 0.6H, minor), 5.83 (d, J = 7.4 Hz, 1H, major), 3.84 (s, 3H, major), 3.82 (s, 1.6H, minor), 2.23 (s, 3H, major), 2.13 (s, 1.7H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 167.4, 164.3, 164.1, 156.9, 156.6, 147.9, 144.8, 144.7, 139.6, 139.5, 137.7, 135.0, 128.2, 127.9, 123.8, 123.2, 118.3, 118.2, 115.6, 114.7, 114.2, 111.2, 110.8, 110.7, 110.1, 105.4, 55.8, 55.6, 21.0, 20.9; FT-IR (neat) 1729, 1499, 1367, 1026, 830 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{16}NO_4^+$: 286.1074, found: 286.1076.



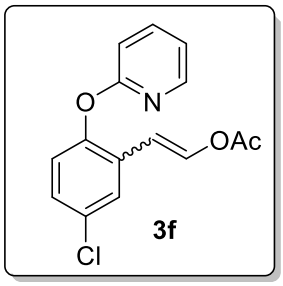
2-(Pyridin-2-yloxy)styryl acetate 3b. Yellow liquid; yield 57% (22 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18-8.17 (m, 2H), 7.99 (d, *J* = 7.8 Hz, 2H), 7.88 (d, *J* = 12.9 Hz, 1H), 7.70-7.66 (m, 2H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.32-7.28 (m, 2H), 7.24-7.23 (m, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 8.4 Hz, 2H), 7.01-6.96 (m, 2H), 6.91-6.87 (m, 2H), 6.49 (d, *J* = 14.0 Hz, 1H), 5.90 (d, *J* = 7.4 Hz, 1H), 2.23 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 167.6, 151.23, 151.22, 148.03, 148.02, 139.7, 139.6, 137.6, 134.9, 130.8, 128.7, 128.6, 127.2, 127.1, 125.5, 125.2, 122.6, 122.2, 118.6, 118.5, 111.2, 111.1, 110.1, 105.4, 21.0, 20.9; FT-IR (neat) 1719, 1215, 1160, 1026, 790 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{14}NO_3^+$: 256.0968, found: 256.0965.



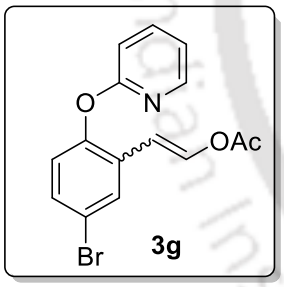
2,4-Dimethyl-6-(pyridin-2-yloxy)styryl acetate 3c. Yellow liquid; yield 62% (25 mg); major diastereomer (*Z/E* = 1:0.6); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17-8.14 (m, 1.6H, major + minor), 7.71 (d, *J* = 12.8 Hz, 1H, major), 7.67-7.61 (m, 1.6H, major + minor), 7.14 (d, *J* = 7.0 Hz, 0.6H, minor), 6.96-6.93 (m, 1H, major), 6.93-6.90 (m, 3.2H, major + minor), 6.82-6.80 (m, 1H, major), 6.76 (s, 1H, major), 6.30 (d, *J* = 12.8 Hz, 1H, major), 5.61 (d, *J* = 7.0 Hz, 0.6H, minor), 2.35 (s, 3H, major), 2.32 (s, 1.8H, minor), 2.29 (s, 3H, major), 2.25 (s, 1.8H, minor), 2.10 (s, 3H, major), 1.95 (s, 1.8H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 167.9, 163.8, 163.6, 151.6, 151.4, 147.9, 147.8, 139.5, 139.4, 138.44, 138.41, 138.1, 137.9, 135.3, 128.5, 127.7, 123.1, 120.9, 120.1, 118.3, 118.0, 111.6, 111.3, 108.6, 107.1, 21.3, 21.2, 21.1, 20.9, 20.8, 20.4; FT-IR (neat) 1725, 1234, 1060, 957, 722 cm^{-1} HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{18}NO_3^+$: 284.1281, found: 284.1299.



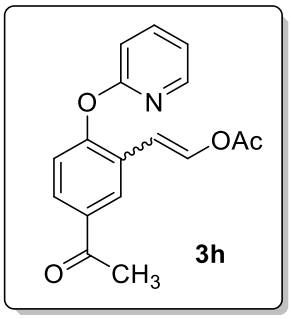
3-(*tert*-Butyl)-2-(pyridin-2-yloxy)styryl acetate 3d. Yellow liquid; yield 47% (19 mg); major diastereomer (*Z/E* = 1:0.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17-8.13 (m, 1.5H, major + minor), 7.74-7.71 (m, 0.5H, minor), 7.69 (d, *J* = 12.7 Hz, 1.5H, major + minor), 7.66-7.60 (m, 1H, major), 7.41-7.39 (m, 1H, major), 7.38-7.35 (m, 2H, major + minor), 7.24-7.16 (m, 2H, major), 7.04 (d, *J* = 7.4 Hz, 0.5H, minor), 6.95-6.87 (m, 2H, major), 6.75 (d, *J* = 8.3 Hz, 1.5H, major + minor), 6.21 (d, *J* = 12.7 Hz, 1H, major), 5.58 (d, *J* = 7.4 Hz, 0.5H, minor), 2.19 (s, 1.5H, minor), 2.08 (s, 3H, major), 1.32 (s, 4.5H, minor), 1.31 (s, 9H, major); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 164.3, 164.1, 149.6, 149.5, 148.2, 148.1, 143.1, 142.7, 139.5, 139.4, 137.3, 134.5, 129.1, 129.0, 127.2, 127.0, 125.9, 125.7, 125.3, 125.2, 118.4, 118.0, 111.0, 110.9, 110.5, 110.4, 107.2, 35.1, 35.0, 30.80, 30.77, 21.0, 20.8; FT-IR (neat) 1730, 1458, 1338, 1222, 1172, 763 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{22}NO_3^+$: 312.1594, found: 312.1601.



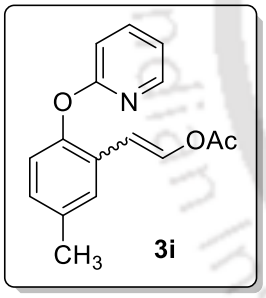
5-Chloro-2-(pyridin-2-yloxy)styryl acetate 3f. Yellow liquid; yield 69% (28 mg); major diastereomer (*Z/E* = 1:0.6); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-8.14 (m, 1.6H, major + minor), 7.98 (d, *J* = 2.6 Hz, 1H, major), 7.88 (d, *J* = 12.9 Hz, 0.6H, minor), 7.73-7.67 (m, 1.6H, major + minor), 7.47 (d, *J* = 2.5 Hz, 0.6H, minor), 7.28-7.25 (m, 1.6H, major + minor), 7.24-7.21 (m, 1H, major + minor), 7.04-6.97 (m, 3.2H, major + minor), 6.94-6.89 (m, 1.6H, major + minor), 6.41 (d, *J* = 12.9 Hz, 0.6H, minor), 5.82 (d, *J* = 7.4 Hz, 1H, major + minor), 2.25 (s, 3H, major), 2.14 (s, 1.6H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 167.3, 163.5, 163.3, 149.6, 147.9, 147.7, 139.84, 139.81, 138.4, 135.7, 130.7, 130.5, 130.3, 129.2, 129.1, 128.7, 128.5, 128.4, 126.9, 124.0, 123.5, 118.8, 118.6, 111.3, 111.2, 109.1, 104.3, 21.0, 20.8; FT-IR (neat) 1728, 1356, 1258, 1120, 1048, 981, 761 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{13}ClNO_3^+$: 290.0578, found: 290.0581.



5-Bromo-2-(pyridin-2-yloxy)styryl acetate 3g. Yellow liquid; yield 73% (30 mg); major diastereomer (*Z/E* = 1:0.8); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.12 (m, 3H, major + minor), 7.87 (d, *J* = 12.8 Hz, 0.8H, minor), 7.73-7.67 (m, 2H, major), 7.63 (d, *J* = 2.4 Hz, 0.8H, minor), 7.42-7.35 (m, 2H, major + minor), 7.28 (s, 0.7H, minor), 7.04 – 6.89 (m, 6H, major + minor), 6.40 (d, *J* = 12.9 Hz, 0.8H, minor), 5.82 (d, *J* = 7.4 Hz, 1H, major), 2.25 (s, 3H, major), 2.14 (s, 2H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 167.3, 163.5, 163.3, 150.2, 147.9, 139.8, 138.4, 135.7, 133.5, 131.4, 129.8, 129.6, 129.2, 124.3, 123.9, 118.8, 118.4, 118.1, 111.4, 111.3, 109.0, 104.2, 77.5, 77.2, 76.8, 21.0, 20.8; FT-IR (neat) 1729, 1424, 1240, 1021, 980, 794 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{13}BrNO_3^+$: 334.0073, found: 334.0073.



5-Acetyl-2-(pyridin-2-yloxy)styryl acetate 3h. Colorless liquid; yield 71% (28 mg); major diastereomer (*Z*/*E* = 1:0.6); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H, major), 8.18 (s, 2H, major + minor), 8.10 (s, 0.6H, minor), 7.98 (d, *J* = 12.8 Hz, 0.7H, minor), 7.91-7.83 (m, 2H, major), 7.77-7.70 (m, 2H, major), 7.33 (d, *J* = 7.4 Hz, 1H, major), 7.14 (dd, *J* = 8.4, 5.1 Hz, 2H, major), 7.07-6.96 (m, 4H, major + minor), 6.53 (d, *J* = 12.8 Hz, 0.6H, minor), 5.95 (d, *J* = 7.4 Hz, 1H, major), 2.62-2.61 (m, 5H, major + minor), 2.26 (s, 3H, major), 2.16 (s, 1.8H, minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 196.2, 168.5, 162.5, 153.7, 149.9, 147.8, 147.0, 143.0, 142.5, 140.8, 140.7, 140.0, 134.4, 130.9, 130.5, 127.7, 127.4, 124.2, 123.0, 122.7, 119.7, 119.6, 118.5, 115.4, 112.6, 111.7, 77.5, 77.2, 76.8, 26.6, 26.4, 20.5; FT-IR (neat) 1716, 1595, 1401, 1279, 812, 761 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{16}NO_4^+$: 298.1074, found: 298.1082.



5-Methyl-2-(pyridin-2-yloxy)styryl acetate 3i. Colorless liquid; yield 64% (26 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17-8.15 (m, 2H), 7.86 (d, *J* = 12.8 Hz, 1H), 7.77-7.76 (m, 1H), 7.68-7.64 (m, 2H), 7.32 (s, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 7.12-7.07 (m, 2H), 7.04-6.93 (m, 4H), 6.89-6.85 (m, 2H), 6.45 (d, *J* = 12.8 Hz, 1H), 5.84 (d, *J* = 7.4 Hz, 1H), 2.38 (s, 3H), 2.35 (s, 3H), 2.22 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.5, 168.0, 167.6, 164.1, 163.9, 149.0, 148.9, 148.0, 148.0, 139.6, 139.5, 137.4, 135.1, 134.7, 131.2, 129.5, 129.5, 127.5, 127.0, 126.8, 122.5, 122.1, 118.3, 118.3, 111.0, 110.9, 110.0, 105.6, 21.4, 21.1, 21.0, 20.9; FT-IR (neat) 1712, 1385, 1277, 972, 805, 764 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{16}H_{16}NO_3^+$: 270.1125, found: 270.1134.

3.5 Computation Studies

All calculations were performed using the Gaussian-16 program package[18]. Full geometry optimizations were carried out using Kohn-Sham hybrid-DFT B3LYP[19] level of theory and BS1 basis set. BS1 is defined as an SDD[20] basis set for Ru atom and 6-31G* Pople basis set[21] for all other atoms. Frequency calculations at the same method and basis set were performed to distinguish transition state structures (one imaginary frequency) and minima structures (no imaginary frequency) on the potential energy surface. The transition states were verified by the intrinsic reaction coordinate (IRC) calculations, wherever necessary.[22] Free energies were calculated by using frequency calculations at 100 °C to match the experimental conditions.

Table 3. Free Energies (G) and Total Energies (E) of all the optimized structures given in Hartree along with the number of imaginary frequencies

Species	**Free energy (G)**	**Total energy (E)**	**Imaginary Frequency (NImag)**
For Rh-cycle			
1a-Rh	-1932.753135	-1933.2497284	0
AcOH	-229.055286	-229.0817864	0
A-Rh	-1703.692273	-1704.1513698	0
TS-Rh-A	-1703.578252	-1704.0279338	1
B-Rh	-1703.691289	-1704.1638268	0
C-Rh	-1703.663873	-1704.1199715	0
3a	-1474.614742	-1475.0170137	0

Table 4. The Cartesian Coordinates (xyz) for All Optimized Structures Are Presented

1a-Rh				H	3.69465	-0.60036	0.38245
C	-0.17906	4.00006	-0.23415	H	6.90494	1.51876	2.31447
C	-0.10304	4.0018	-1.6327	H	5.89233	-0.66545	1.54656
C	1.15285	3.92009	-2.25741	N	3.48382	1.45374	0.48165
C	2.31119	3.81701	-1.49745	O	-1.17592	4.07291	-2.46937
C	2.22397	3.79674	-0.10411	C	-2.47739	4.15067	-1.89267
C	0.99034	3.89582	0.52572	H	-3.17081	4.17704	-2.73535
H	-1.13585	4.05597	0.26969	H	-2.69444	3.27974	-1.26371
H	1.19327	3.9357	-3.34206	H	-2.59282	5.07125	-1.30362
H	3.28373	3.75299	-1.97545	C	7.08857	-2.56434	-1.11057
H	0.94302	3.89086	1.61036	H	6.95666	-1.5006	-0.9427
O	3.3881	3.77547	0.66894	H	8.04918	-2.92025	-1.46438
C	4.03167	2.59218	0.88635	C	6.1047	-3.42869	-0.88487
C	5.26529	2.67861	1.55447	H	6.20061	-4.49903	-1.03317
C	4.16467	0.31879	0.7231	O	4.89449	-2.98704	-0.38151
C	5.94843	1.49675	1.79873	C	3.72819	-3.69508	-0.49296
H	5.64641	3.64793	1.8564	O	2.73475	-3.22192	0.00396
C	5.39338	0.28224	1.37343	C	3.755	-5.01419	-1.23396

H	4.1691	-4.89936 -2.24123	C	-1.55749	-1.60195 -1.3465
H	4.36417	-5.75481 -0.7029	C	-1.2566	-2.5105 0.7747
H	2.73142	-5.38316 -1.29932	C	-1.98105	-2.65226 -0.46042
Rh	-2.38364	-0.70653 0.45708	C	-2.99444	-3.7077 -0.78305
O	-2.86878	1.4409 0.37243	H	-3.80621	-3.29049 -1.38173
O	-4.42918	-0.88634 0.74863	H	-2.51481	-4.51939 -1.34771
C	-2.91639	1.47706 1.64515	H	-3.42488	-4.14109 0.12369
C	-5.25514	-1.05155 -0.24745	C	-2.0298	-1.39182 -2.75295
O	-4.95424	-1.2258 -1.43123	H	-1.7591	-0.39534 -3.11269
O	-2.55884	0.44922 2.30171	H	-1.56908	-2.12841 -3.42653
C	-3.43331	2.69606 2.36643	H	-3.11667	-1.48721 -2.8014
H	-3.33557	3.59043 1.74634	C	0.26751	0.26998 -1.30551
H	-4.49591	2.5448 2.58961	H	0.91293	0.78838 -0.59383
H	-2.90573	2.83049 3.31429	H	0.90793	-0.12454 -2.10599
C	-6.71866	-0.99046 0.18872	H	-0.40458	1.0059 -1.75576
H	-7.36414	-1.36735 -0.60767	C	0.67607	-0.97593 1.65856
H	-6.87549	-1.56283 1.10808	H	0.22496	-0.97358 2.65568
H	-6.98834	0.05074 0.40155	H	1.52569	-1.66948 1.66214
C	-0.31197	-1.40815 0.61954	H	1.06066	0.02644 1.45721
C	-0.49558	-0.85694 -0.67994	C	-1.35214	-3.39701 1.97943

H	-2.32263	-3.89678	2.03416	H	3.02365	-0.71906	2.00232
H	-0.57128	-4.16926	1.9481	H	5.69868	2.68016	1.87254
H	-1.21779	-2.82427	2.90166	H	5.13937	0.3945	2.78598
A-Rh				N	2.48731	0.83035	0.75066
C	-1.57536	3.74857	-0.28706	O	-3.58012	2.4116	0.15665
C	-2.2186	2.52904	-0.05188	C	-4.34075	3.60594	0.24522
C	-1.48472	1.33511	-0.01259	H	-5.36655	3.29865	0.46059
C	-0.0993	1.32087	-0.19838	H	-3.97865	4.25299	1.05475
C	0.51969	2.55919	-0.38744	H	-4.32523	4.16814	-0.698
C	-0.18814	3.75454	-0.44769	C	-4.87648	-1.27378	2.7325
H	-2.12038	4.68388	-0.33087	H	-5.06565	-0.65128	3.59972
H	-2.00921	0.40703	0.19087	H	-4.94886	-2.35087	2.84245
H	0.34706	4.68603	-0.60805	C	-4.54214	-0.71352	1.57456
O	1.91847	2.6921	-0.5487	H	-4.42932	0.35601	1.42202
C	2.75237	2.07018	0.30882	O	-4.20066	-1.50274	0.48535
C	3.91476	2.76163	0.67906	C	-4.60951	-1.19301	-0.78427
C	3.33223	0.26134	1.64653	O	-4.12891	-1.81237	-1.70425
C	4.79624	2.15975	1.56407	C	-5.63855	-0.09864	-0.94312
H	4.07642	3.75512	0.27692	H	-6.45005	-0.19632	-0.21528
C	4.49204	0.89152	2.0717	H	-5.15358	0.87223	-0.78832

H	-6.03346	-0.14375	-1.95871	H	-0.85913	-4.01871	-1.35866
Rh	1.00997	-0.37938	-0.18023	H	-0.82924	-3.28946	0.25172
O	0.04701	-0.71097	1.67766	C	3.97448	-1.47841	-1.52189
C	0.51681	-1.50848	2.58325	H	4.40073	-1.88729	-2.44819
O	1.60247	-2.11029	2.54618	H	4.31689	-0.44172	-1.43903
C	-0.39709	-1.644	3.80184	H	4.39565	-2.03984	-0.68392
H	-0.11985	-2.52468	4.38612	C	2.08985	0.42591	-3.23709
H	-0.28506	-0.75438	4.43377	H	2.29062	-0.00564	-4.22854
H	-1.44675	-1.70028	3.49907	H	1.3413	1.21303	-3.36308
C	0.27732	-2.21084	-1.24085	H	3.0127	0.9023	-2.89286
C	1.6694	-2.52537	-0.9192	C	-0.9242	-0.58621	-2.9102
C	2.47628	-1.56224	-1.55291	H	-0.90259	0.50373	-2.99707
C	0.25992	-1.10619	-2.14945	H	-0.92107	-1.00341	-3.92713
C	1.61719	-0.62901	-2.27648	H	-1.86938	-0.87235	-2.44395
C	2.10803	-3.72309	-0.12843	TS-Rh-A			
H	3.19168	-3.72964	0.01851	C	2.97374	-3.18304	1.20519
H	1.64896	-3.73533	0.86292	C	3.84944	-2.48283	0.36435
H	1.83837	-4.64845	-0.65613	C	3.62529	-1.12576	0.10085
C	-0.88278	-3.062	-0.81735	C	2.51347	-0.44962	0.62747
H	-1.84792	-2.59299	-1.01779	C	1.66226	-1.17134	1.4883

C	1.88174	-2.51189	1.76544	C	2.89238	1.33408	1.19309
H	3.13022	-4.22929	1.43803	C	2.16969	2.43261	0.57482
H	4.32917	-0.60782	-0.54494	O	1.17954	3.01307	1.40508
H	1.19741	-3.03115	2.42946	C	0.77198	4.28294	1.10674
O	0.62919	-0.55234	2.19332	O	1.2394	4.94777	0.21236
C	-0.38981	0.13487	1.61333	C	-0.32292	4.71744	2.0507
C	-1.4898	0.38843	2.4393	H	-0.57281	5.76127	1.85725
C	-1.3886	1.23209	-0.15927	H	-1.20798	4.0899	1.90091
C	-2.56371	1.09869	1.92067	H	-0.00394	4.5929	3.09044
H	-1.48192	-0.00152	3.45057	Rh	1.58302	0.92751	-0.65732
C	-2.50869	1.53935	0.59302	O	0.70933	1.82424	-2.38839
H	-1.28333	1.55209	-1.18884	C	0.73224	0.74627	-3.09531
H	-3.43043	1.30581	2.54085	O	1.14155	-0.33073	-2.58744
H	-3.32852	2.08421	0.13951	H	2.63242	1.14157	2.23205
N	-0.3239	0.55084	0.34026	H	3.96291	1.31206	1.00718
O	4.95119	-3.02397	-0.23109	H	2.70726	3.18859	0.00449
C	5.21531	-4.40248	-0.02829	C	0.23531	0.81287	-4.52117
H	6.11531	-4.62274	-0.60514	H	-0.86009	0.86824	-4.52252
H	5.40057	-4.62759	1.0308	H	0.61053	1.71619	-5.0108
H	4.3897	-5.02862	-0.39156	H	0.54414	-0.07607	-5.07463

C	-4.53955	-1.56894	0.71981	H	-3.26132 -3.20036 2.54223
C	-4.8181	-0.88075	-0.56075	C	-5.48501 -1.55719 1.87809
C	-3.77367	-1.1415	-1.4177	H	-6.42129 -2.08714 1.64207
C	-3.32508	-2.24038	0.60723	H	-5.058 -2.03249 2.76637
C	-2.82374	-1.98554	-0.7029	H	-5.78141 -0.53518 2.15535
C	-1.54764	-2.49968	-1.2709	B-Rh	
H	-1.6609	-2.7993	-2.32123	C	5.15057 0.81067 0.34838
H	-0.75495	-1.7321	-1.26402	C	5.15877 -0.58364 0.24261
H	-1.16453	-3.35719	-0.70727	C	3.97799 -1.26456 -0.0929
C	-3.60066	-0.70268	-2.84279	C	2.77541 -0.59625 -0.32598
H	-2.65662	-0.16144	-2.99701	C	2.80283 0.80557 -0.22472
H	-3.58416	-1.5553	-3.5372	C	3.95771 1.49961 0.10865
H	-4.41193	-0.04182	-3.16463	H	6.04394 1.36528 0.60974
C	-6.05401	-0.07338	-0.81145	H	4.01912 -2.34757 -0.16289
H	-6.15648	0.75971	-0.09903	H	3.91948 2.58198 0.18899
H	-6.06307	0.35631	-1.81794	O	1.61735 1.53759 -0.35751
H	-6.96831	-0.67646	-0.7066	C	0.95379 1.49314 -1.54764
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H	-2.45787	-4.11537	1.26908	C	-1.06782 1.15067 -2.61193
H	-1.67794	-2.69064	1.95453	C	0.79888 1.95592 -3.89031

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C	-0.54395	1.57939	-3.82578	O	-2.23125	-1.18143	-0.76538
H	-2.10766	0.86376	-2.49944	C	-3.3287	-0.93045	-1.40616
H	1.24087	2.28819	-4.82537	O	-3.84535	0.1858	-1.57581
H	-1.18444	1.60958	-4.70054	H	1.15975	-1.1162	-1.67306
N	-0.32139	1.07932	-1.48547	H	1.82031	-2.42837	-0.7536
O	6.25438	-1.37244	0.44617	H	0.86203	-1.1422	1.35356
C	7.4764	-0.74414	0.7939	C	-3.99047	-2.18533	-1.975
H	8.20545	-1.54834	0.90888	H	-3.23618	-2.86682	-2.37838
H	7.81659	-0.05722	0.00711	H	-4.52276	-2.71186	-1.17272
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C	1.52404	-1.37887	-0.67681	C	-1.62236	0.07836	2.4854
C	0.38814	-1.28571	0.37967	C	-0.60424	1.09415	2.34023
O	-0.26608	-2.56886	0.57106	C	-2.81251	0.56436	1.82108
C	-0.65085	-3.36847	-0.44544	C	-1.1682	2.15631	1.55509
O	-0.33192	-3.2517	-1.61066	C	-2.54529	1.847	1.25765
C	-1.52446	-4.48765	0.08517	C	-0.48601	3.44999	1.21607
H	-1.1348	-4.88319	1.02775	H	0.59832	3.33454	1.17241
H	-2.52698	-4.08951	0.27597	H	-0.82325	3.84169	0.25158
H	-1.59174	-5.2826	-0.6598	H	-0.71907	4.20824	1.97643

C	0.72968 1.11052 3.02726	C	3.28249 -0.20627 -0.2903
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H	1.13552 0.10147 3.15071	C	2.03162 -2.31164 -0.33414
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H	-4.67494 0.08781 0.86105	O	0.94793 -0.29068 0.36065
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C	-3.53556 2.72064 0.54158	C	1.45195 -0.60656 2.71159
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H	-0.51949 -1.54925 3.37705	H	-2.31034 -0.17574 3.20323
H	-1.82827 -0.91434 4.386	H	1.62683 -0.78407 4.84444
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C-Rh		N	-0.76426 -0.25334 1.84563
C	3.14975 -2.98834 -0.82375	O	5.50071 -2.83615 -1.49525
C	4.34133 -2.28069 -1.03588	C	5.50944 -4.22345 -1.79178
C	4.39851 -0.90881 -0.76661	H	6.51997 -4.44891 -2.13739

H	5.28741	-4.82845 -0.90257	H	2.52329	1.62802 0.63408
H	4.79168	-4.47186 -2.58467	H	4.90525	1.76163 -1.31468
C	3.28558	1.2404 -0.02487	C	-4.15115	1.39214 -1.1966
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O	4.2763	3.45209 -0.44708	C	-2.09982	0.44164 -1.8616
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O	2.58596	3.79077 1.0548	C	-1.8589	1.68159 -1.20803
C	3.8995	5.66266 0.25711	C	-3.3309	3.69907 -0.38533
H	4.95837	5.77267 0.51286	H	-2.92803	3.74911 0.63849
H	3.77369	6.01368 -0.77271	H	-2.78662	4.45111 -0.97237
H	3.28803	6.26469 0.92987	H	-4.37881	4.01148 -0.3395
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O	-2.9421	-1.96521 1.14839	H	-5.9412	0.83304 -0.141
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O	-1.36287	-2.5748 -0.2854	H	-6.20149	1.17999 -1.84959
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C	1.49736 -1.9323 2.23464	H	1.41547 6.1088 1.57458

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H	-2.41054	2.47037	1.22931
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H	-3.50871	1.45982	2.17042

3.6 References

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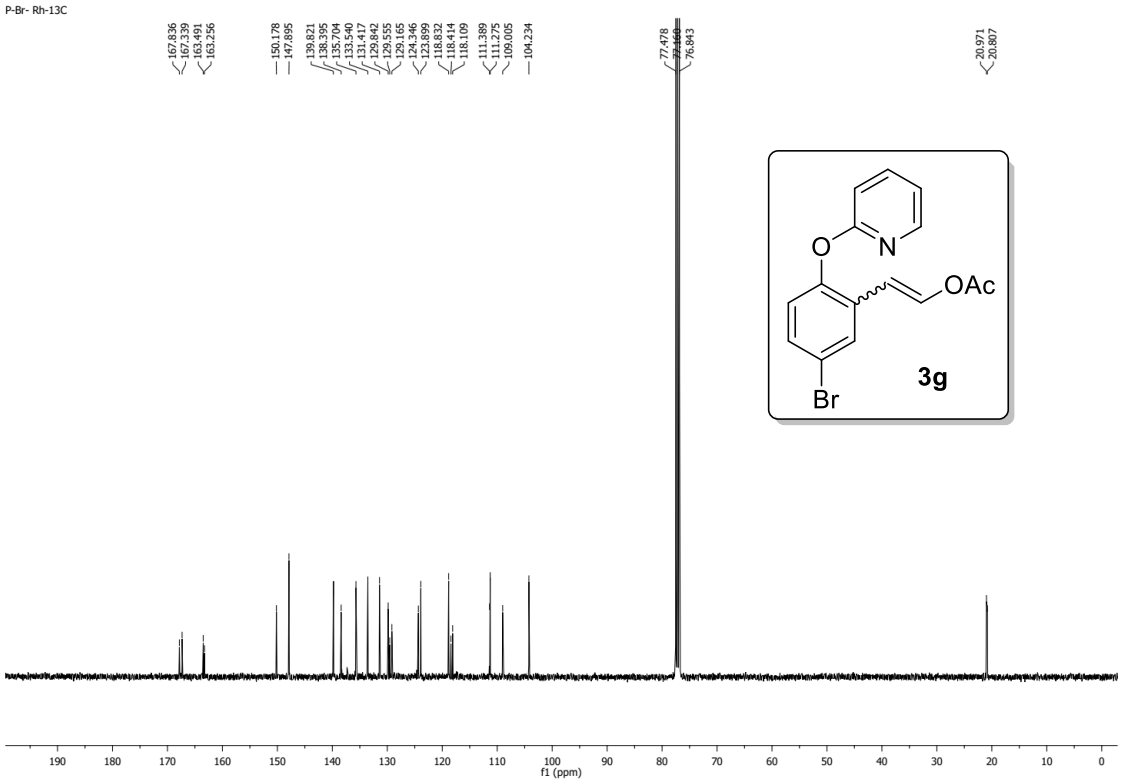
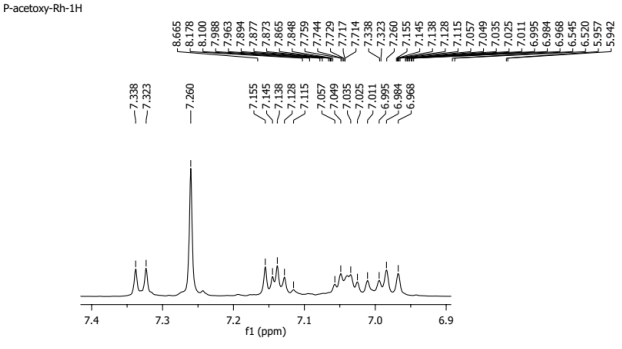
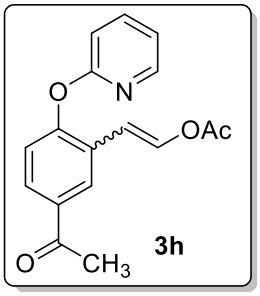
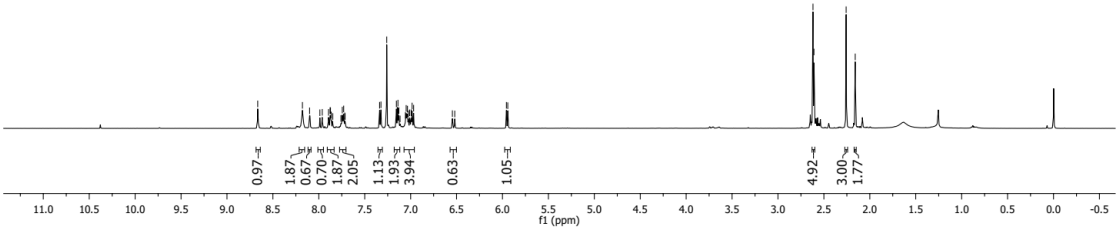
3.7 Selected NMR Spectra



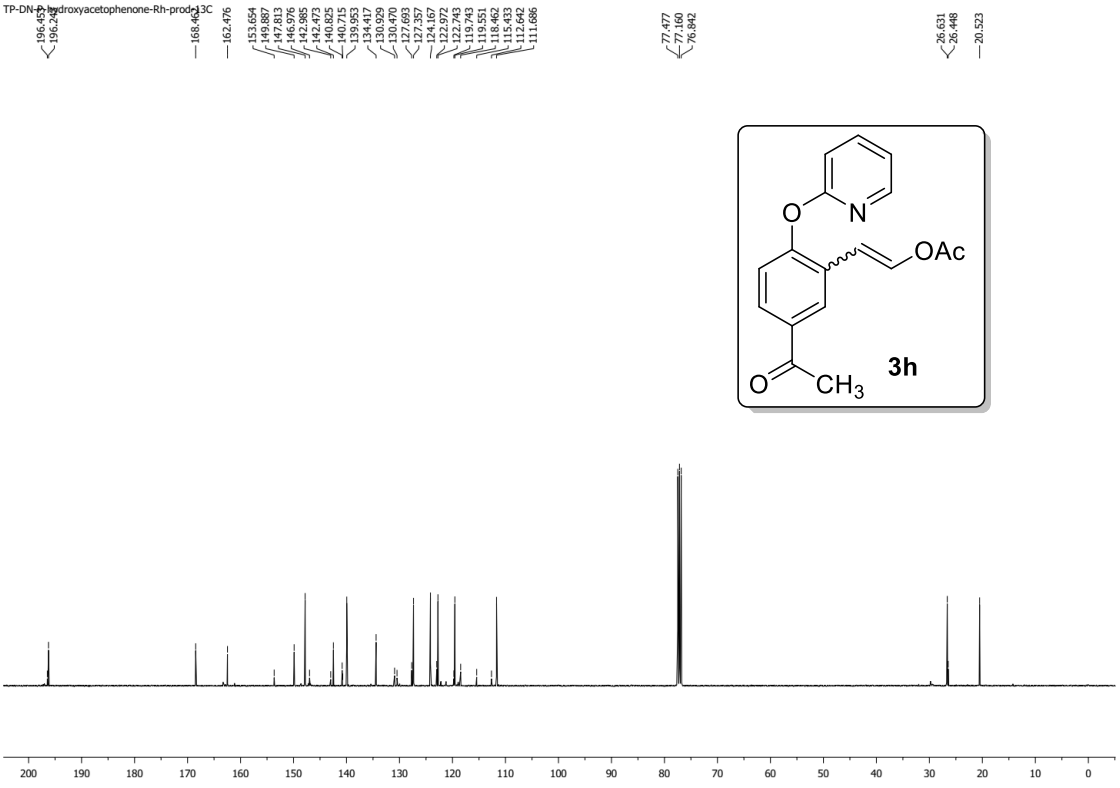
P-acetoxy-Rh-1H



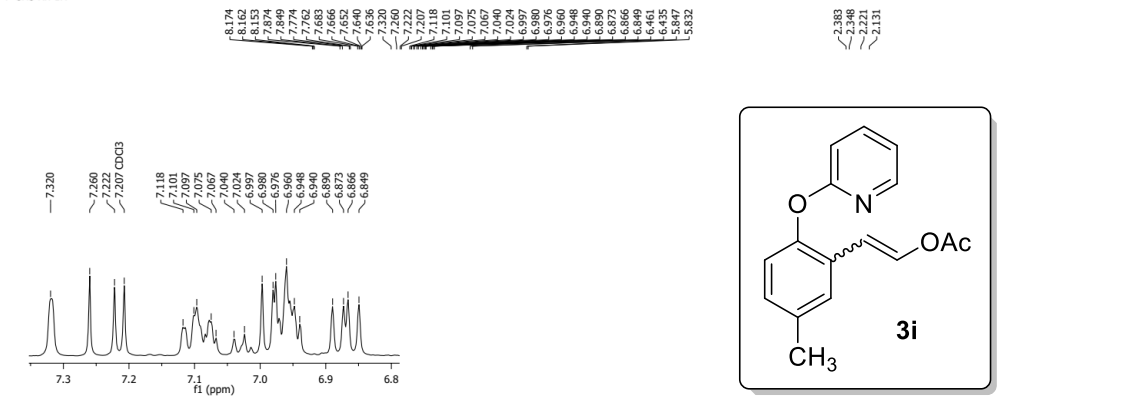




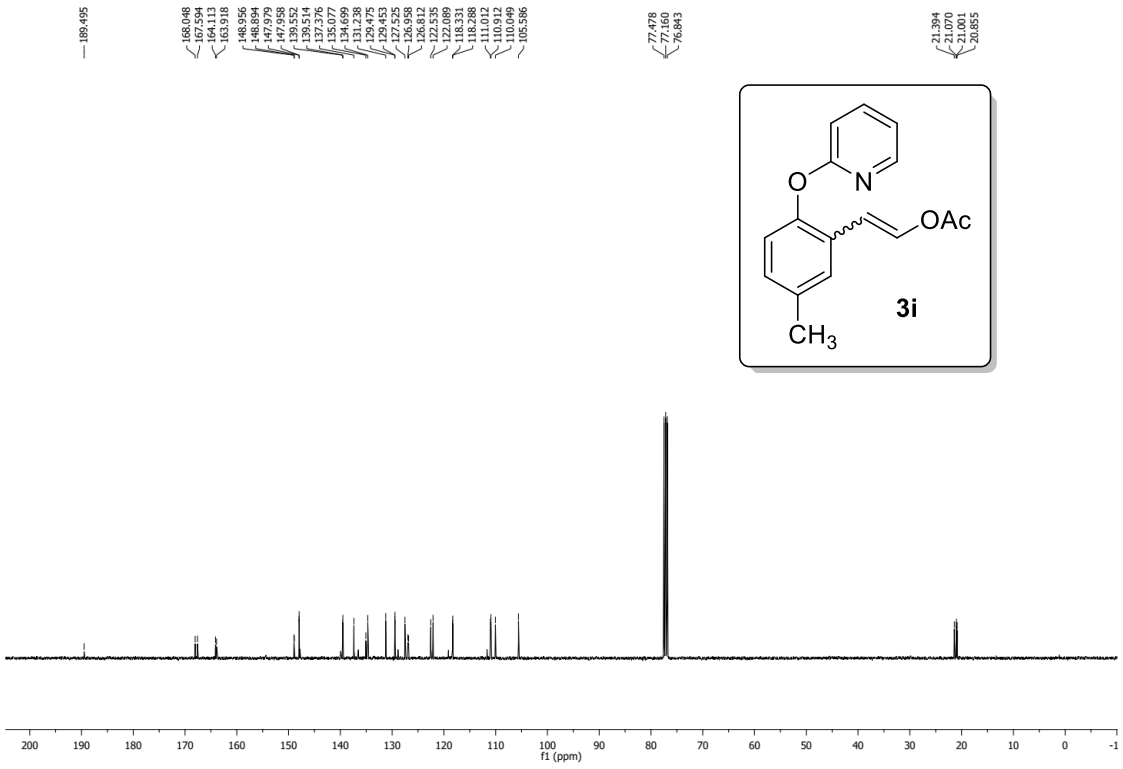
TP-DN-P-hydroxyacetophenone-Rh-prod-13C



P-CH3 Rh-1H

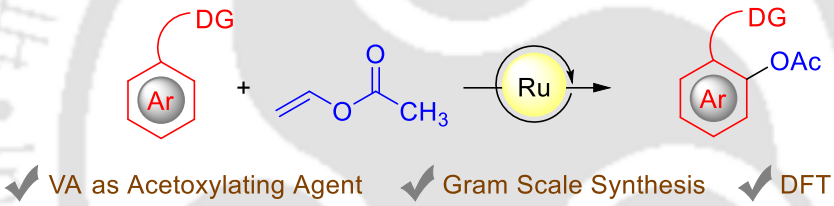


P-CH3 Rh-13C



Chapter IV

Ru-Catalyzed ortho-Selective Acetoxylation of Aryl 2-Pyridyl Ethers Exploting Vinyl Acetate as an Acetoxylating Agent



✔ VA as Acetoxylating Agent ✔ Gram Scale Synthesis ✔ DFT Studies

Manuscript under preparation.

Chapter IV

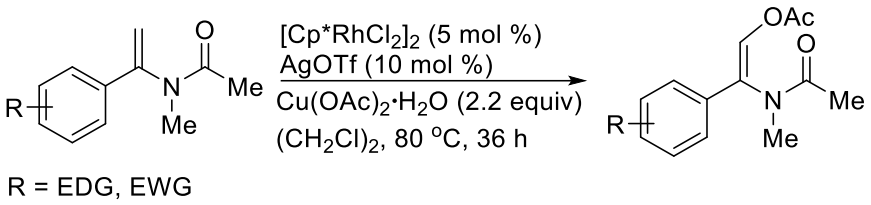
Ru-Catalyzed Acetoxylation of Aryl 2-Pyridyl Ethers with Vinyl Acetate as an Acetoxylating Agent

The formation of C-C and C-O bonds stands as a fundamental objective within the realm of synthetic organic chemistry. Notably, nitrogen and oxygen-containing heterocycles serve as pivotal structural motifs, playing a prominent role in a wide array of biologically active natural compounds and synthetic pharmaceuticals.[1] With recent emphasis on atom-economical processes and a green chemistry perspective, transition-metal-catalyzed direct C-H activation has risen to prominence as a dependable protocol at the forefront of modern synthetic chemistry.[2] The chelation-assisted transition-metal-catalyzed C-H functionalization of olefins is now considered an indispensable method, as it facilitates the formation of new C-C bonds with exceptional atom and step efficiency. In recent times, the remarkable growth of transition metal-catalyzed C-H bond functionalization has been evident, primarily attributed to the convenient accessibility of C-H bonds. Among various C-H functionalization reactions, significant focus has been directed towards the formation of C-O bonds.[3] This particular transformation has garnered considerable attention due to its capacity to induce polar nature and its distinctive role as a hydrogen bond donor-acceptor. Recently, the scope of transition metal-catalyzed directing group-assisted C-H acetoxylation reactions has been restricted to employing hypervalent iodine reagents like phenyliodine(III)diacetate and $PhI(OCOAr)_2$, acetic acid along with $Cu(OAc)_2$. Nevertheless, the utilization of vinyl acetate as an acetylating agent is infrequent within the realm of synthetic organic chemistry.

4.1 Literature

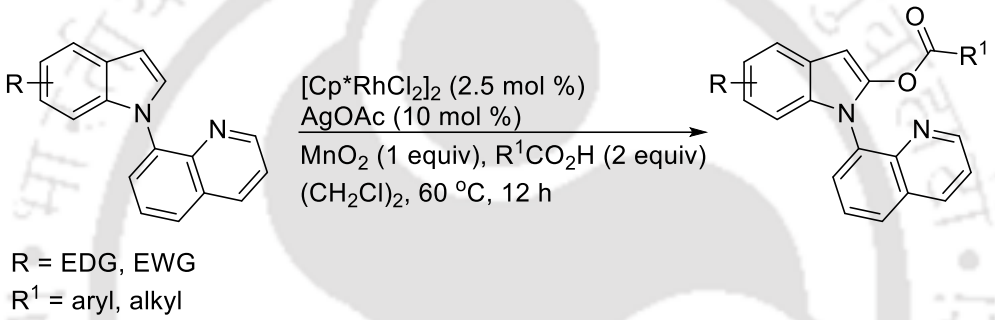
4.1.1 Rh-Catalyzed Acetoxylation/Acyloxylation of sp^2 C-H bond

A Rh(III)-catalyzed direct regioselective acetoxylation of enamides was achieved by Zhang and co-workers (Scheme 1).[4] It is worth noting that the $Cu(OAc)_2$ serves as an oxidant as well as source of acetate in the reaction.



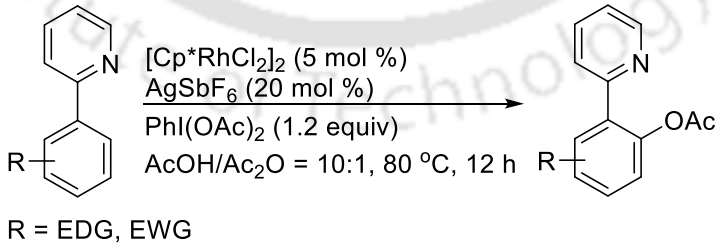
Scheme 1. Rh-Catalyzed Amide-Assisted Acetoxylartion

Wu and co-workers described a regio- and chemoselective C2 C-H acyloxylation of indoles under Rh-catalysis with *N*-quinolinyl auxiliary (Scheme 2).[5] This approach is suitable for a broad spectrum of indoles and structurally diverse carboxylic acids, exhibiting high reaction efficiencies to produce functionalized indoles.



Scheme 2. Rh-Catalyzed C2 C-H Acyloxylation of Indoles

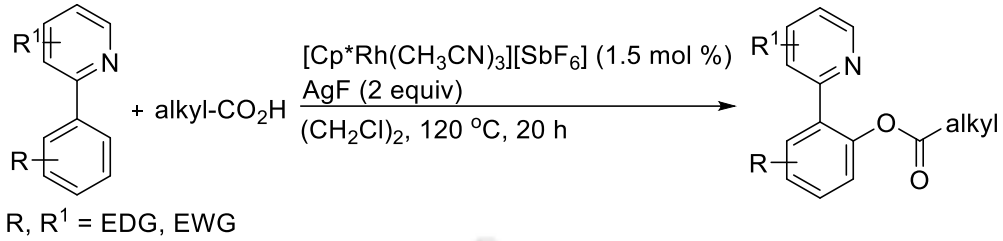
An efficient Cp*Rh(III)-catalyzed, chelation-assisted C(sp^2)-H acetoxylation of 2-arylpyridines was reported by Zhou and co-workers (scheme 3).[6] The protocol is characterized by its relatively mild reaction conditions, tolerance towards a variety of synthetically useful functional groups, and the selective preparation of acetoxylation, highlighting its significant features.



Scheme 3. Rh-Catalyzed sp^2 C-H Acetoxylation of 2-Arylpyridines

A versatile Rh(III)-catalysis for direct acyloxylation of aryl C-H bonds with carboxylic acids was demonstrated by Li and co-workers (Scheme 4).[7] The protocol's synthetic usefulness was

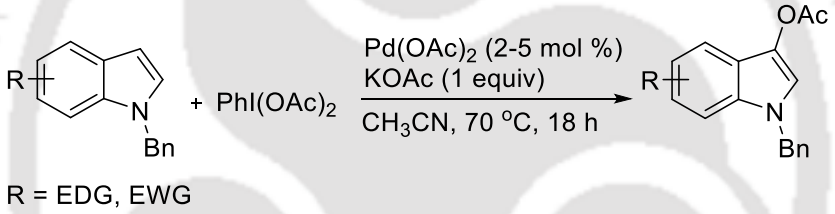
showcased through the late-stage functionalization and modification of biologically active compounds.



Scheme 4. Rh-Catalyzed sp^2 C-H Acyloxylation of 2-Arylpyridines

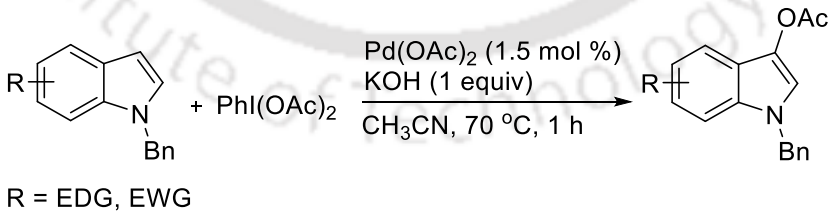
4.1.2 Pd-Catalyzed Acetoxylation of sp^2 C-H bond

Kwong and co-workers demonstrated a Pd(II)-catalyzed regioselective C3 C-H acetoxylation of indoles (Scheme 5).[8] Under mild reaction conditions, this protocol offers an easy and direct pathway to a diverse range of pharmaceutically valuable 3-oxyindole scaffolds.



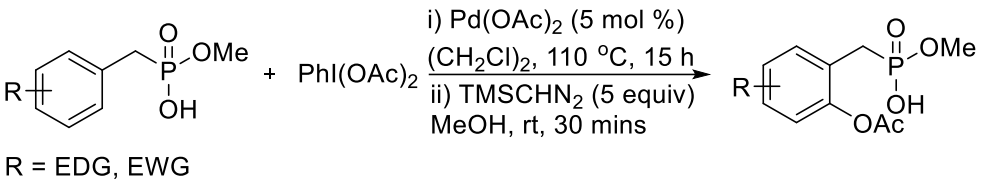
Scheme 5. Pd-Catalyzed sp^2 C-H Acetoxylation of Indoles

A similar Pd(II)-catalyzed C3 acetoxylation of indoles was disclosed by Lei and co-workers (Scheme 6).[9] It is worth mentioning that the selectivity was implemented without the assistance of directing groups.



Scheme 6. Pd-Catalyzed C3 Acetoxylation of Indoles

Kim and co-workers described a Pd(II)-catalyzed *ortho*-acetoxylation of phosphonic and phosphoric monoacids, providing easy access to various acetoxy benzylic phosphonic acids along with catechol derivatives (Scheme 7).[10]



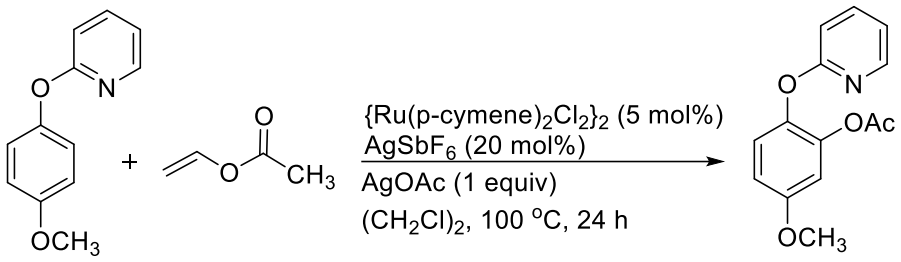
Scheme 7. Pd-Catalyzed sp^2 C-H Acetoxylation of Phosphonic and Phosphoric Monoacids

4.2 Present Study

In this line, we here present a Ru-catalyzed site-selective oxygenation of aryl 2-pyridyl ethers employing vinyl acetate as the acetoxylating agent. The initial investigation was conceded out by employing 2-(4-methoxyphenoxy)pyridine **1a** and vinyl acetate **2** as model substrates and $\{RuCl_2(p\text{-cymene})\}_2$ as catalyst and $AgSbF_6$ as additive in presence of oxidant (Table 1). To our delight, the acetoxylated product **3a** was formed in 43% isolated yield when substrates **1a** and **2** were subjected to react in presence of $\{RuCl_2(p\text{-cymene})\}_2$ (5 mol%), $AgSbF_6$ (20 mol%) and $Cu(OAc)_2{\cdot}H_2O$ (1 equiv) in TFE at 100 °C for 24 h (entry 1). 1,2-Dichloroethane came out as the solvent of choice, yielding up to 61% whereas CH_3CN, toluene, *m*-xylene, DMSO, EtOH and CH_2Cl_2 were found to be inferior (entry 2-8). In a set of oxidants screened such as AgOAc, Ag_2CO_3, NaOAc, CsOAc, AcOH and PivOH, the former furnished the best result, yielding up to 85% (entry 9-14). However, in the absence of an oxidant, the procedure proved unsuccessful in delivering the desired product (entry 15). Additionally, a control experiment indicated that both vinyl acetate **2** and $AgSbF_6$ are essential for achieving the expected product **3a** in a satisfactory yield (entry 16-18).

The devised monodentate chelation-assisted *ortho*-selective C-H acetoxylation approach was found to deliver satisfactory to moderate yields of the desired products, regardless of whether electron-donating or electron-withdrawing substituents were part of the aryl ring (Table 2). When substituents, like 3,5-dimethyl **1b** as well as *t*-butyl **1c**, bromo **1d**, iodo **1e** and methyl **1f** were introduced at the *ortho*-position of the aryl ring, they proved to be compatible, resulting in the formation of the products with yields ranging from 59% to 68%. Nonetheless, substituents such as 2,3-dimethyl **1g** and 4-chloro **1h** found to be effective in yielding **3g** and **3h** with 59% and 71% of yields, respectively. Gratifyingly, the synthesis of the desired **3i** was successful with a 55% yield using 2-(phenylthio)pyridine **1i**. However, 4-acetoxy **1j** produced **3j** in 66% yield, whereas 4-methyl **1k** did not yield the expected product in significant amount.

Table 1. Optimization of Reaction Conditions[a]

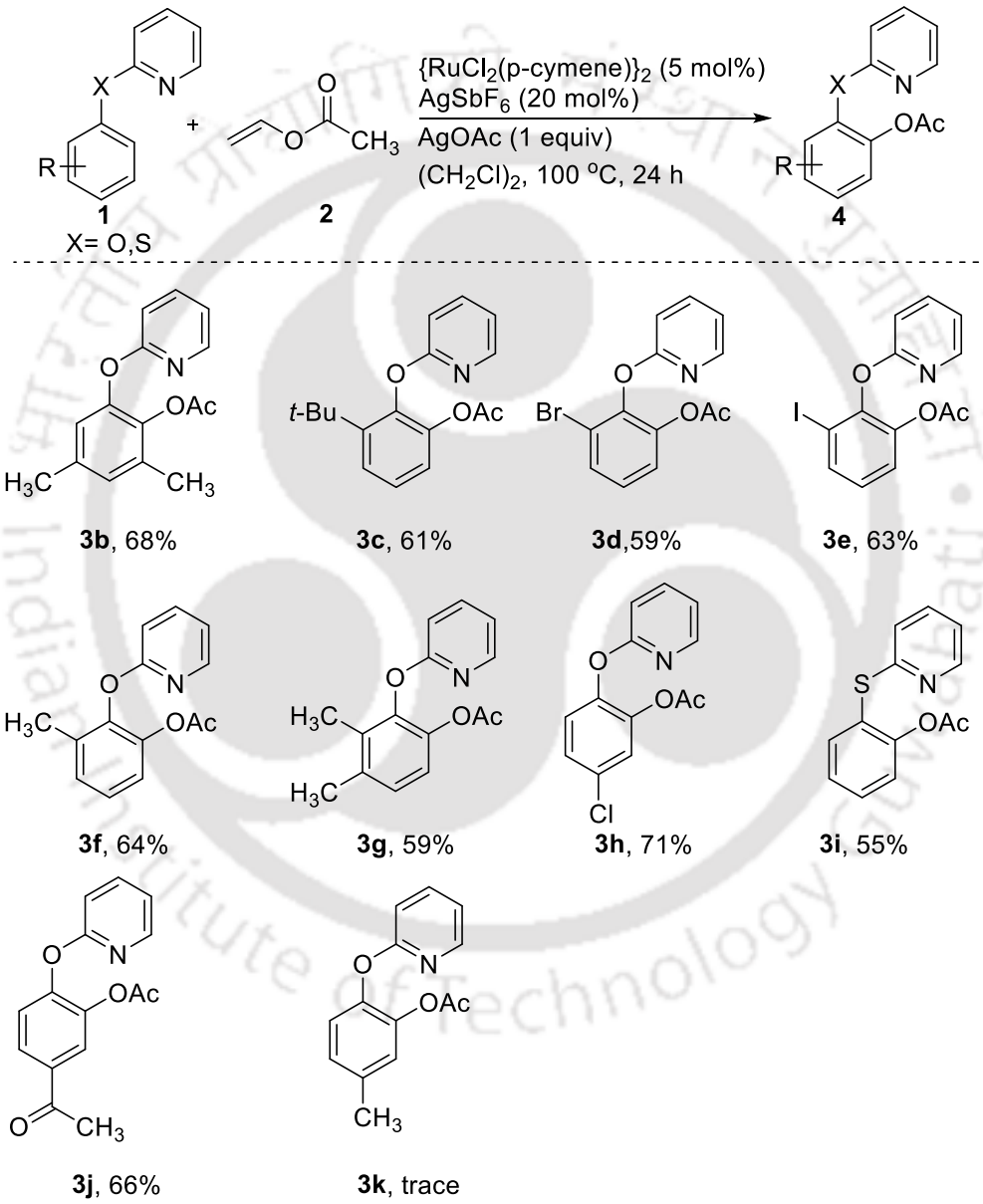


1a **2** **3a**

Entry	Catalyst	Additive	Oxidant	Solvent	Yield[b]
1	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	TFE	43
2	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	CH_3CN	n.d.
3	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	toluene	n.d.
4	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	*m*-xylene	n.d.
5	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	DMSO	n.d.
6	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	ethanol	n.d.
7	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	CH_2Cl_2	trace
8	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	$Cu(OAc)_2{\cdot}H_2O$	$(CH_2Cl)_2$	61
9	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	AgOAc	$(CH_2Cl)_2$	85
10	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	NaOAc	$(CH_2Cl)_2$	trace
11	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	CsOAc	$(CH_2Cl)_2$	trace
12	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	Ag_2CO_3	$(CH_2Cl)_2$	n.d.
13	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	AcOH	$(CH_2Cl)_2$	trace
14	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	PivOH	$(CH_2Cl)_2$	n.d.
15	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	---	$(CH_2Cl)_2$	n.d.
16[c]	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	AgOAc	$(CH_2Cl)_2$	n.d.
17[d]	$\{RuCl_2(p\text{-cymene})\}_2$	---	AgOAc	$(CH_2Cl)_2$	trace
18[e]	$\{RuCl_2(p\text{-cymene})\}_2$	$AgSbF_6$	AgOAc	$(CH_2Cl)_2$	n.d.

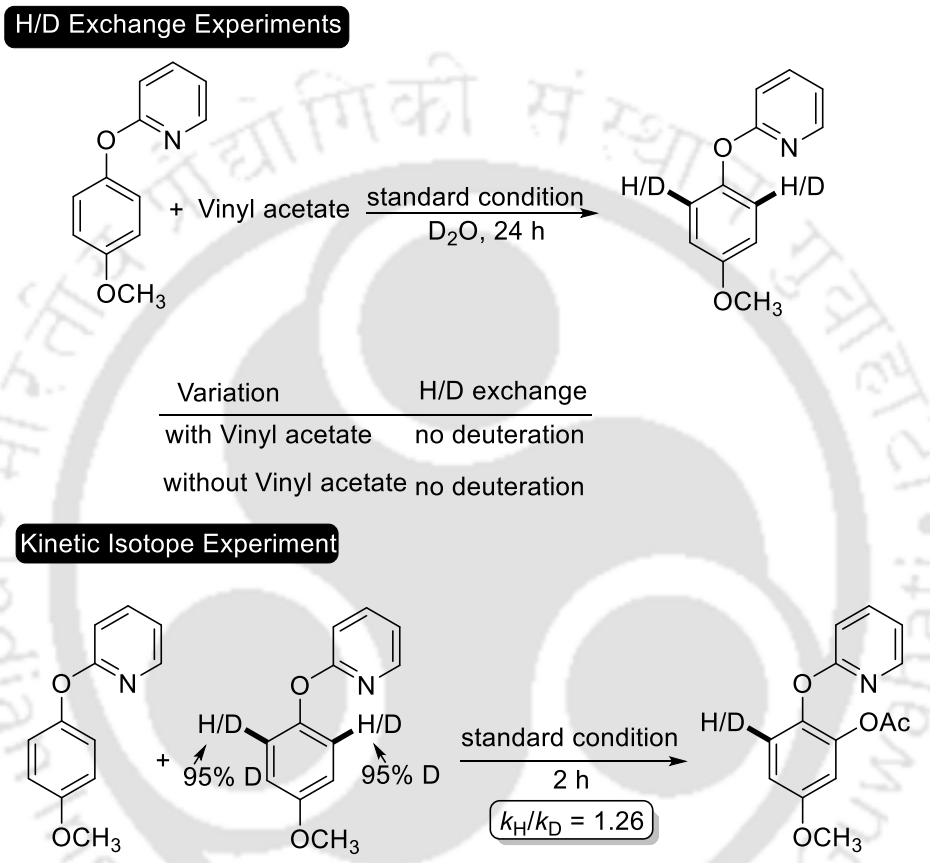
[a]Reaction conditions: **1a** (0.2 mmol), **2** (0.6 mmol), [Ru] (5 mol %), $AgSbF_6$ (0.04 mmol), oxidant (0.2 mmol), solvent (2 mL), 100 °C, 24 h, sealed tube. [b]Isolated yield. [c]Without **2**. [d]Without $AgSbF_6$. [e]With allyl acetate instead of **2**. n.d. = not detected.

Table 2. Substrate Scope of Acetoxylation Reaction.[a,b]



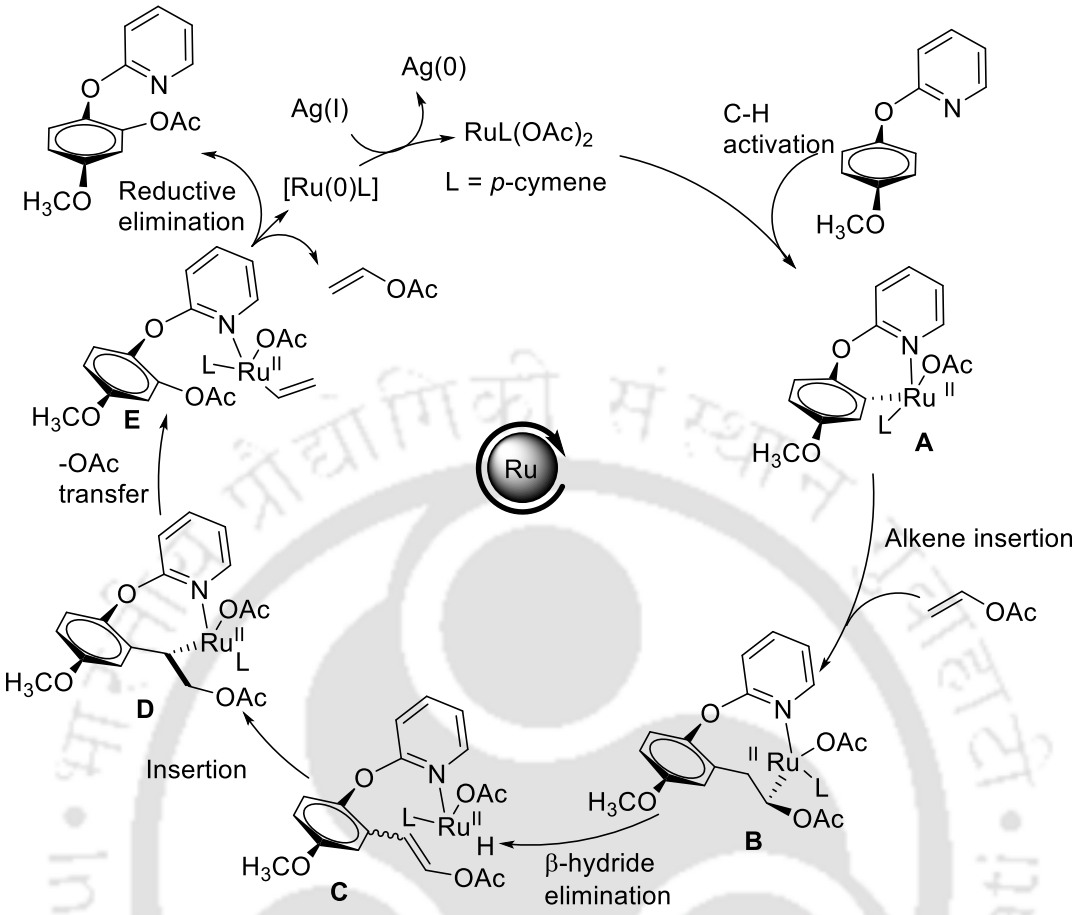
[a]Reaction conditions: **1** (0.20 mmol), **2** (0.6 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%), AgOAc (0.20 mmol), $(CH_2Cl)_2$ (2 mL), 100 °C, 24 h, pressure tube. [b]Isolated yield.

To elucidate the mechanistic pathway, we conducted H/D exchange and kinetic isotope experiments (Scheme 8). The deuterium labeling experiments, utilizing D_2O as a co-solvent, did not reveal substantial H/D scrambling, indicating the irreversible nature of the C-H bond activation step.[11] Furthermore, the kinetic isotope experiment yielded a k_H/k_D ratio of 1.26, suggesting that the rate-determining step may not involve C-H bond cleavage. To further explore the mechanistic

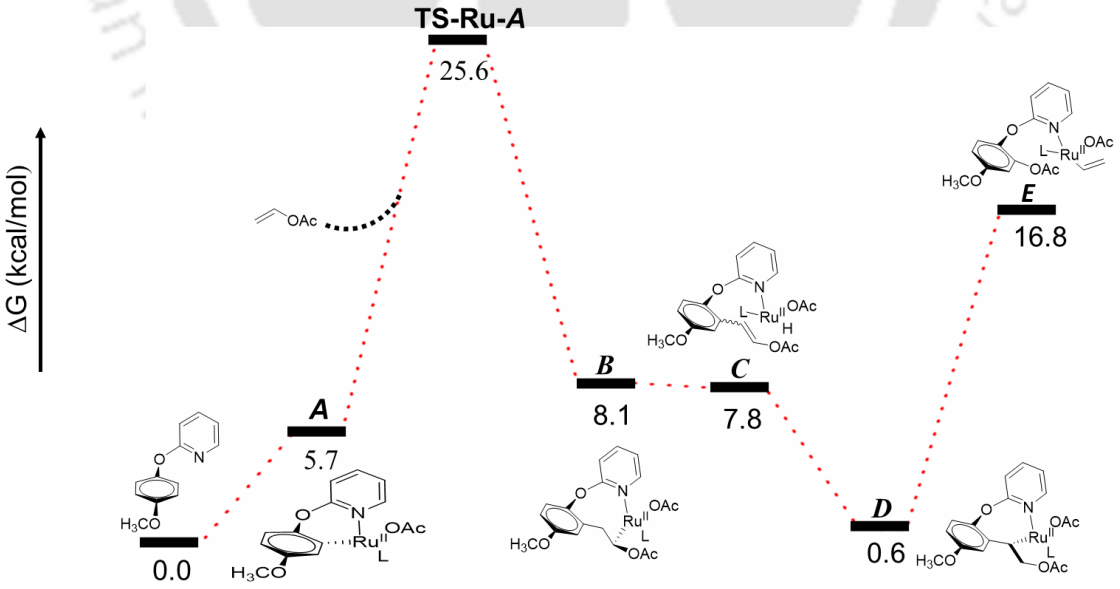


Scheme 8. Preliminary Mechanistic Investigations

pathway of these reactions, we performed density functional theory (DFT) calculations. All computations were carried out at the B3LYP level of theory. Based on both experimental observations and DFT calculations, we have developed a plausible catalytic pathway (Scheme 9).[12] The corresponding energy profile diagram depicts in Scheme 10. During the generation of the acetoxylated product, the catalyst undergoes an initial conversion into the active Ru(II) species under the experimental conditions. Subsequently, the Ru center is inserted into the *o*-C-H bond of the substrate, relative to the directing group, in an endothermic process (ΔG = 5.7 kcal/mol) to yield **A.** Subsequently, alkene insertion occurs to generate species **B** through a transition state with

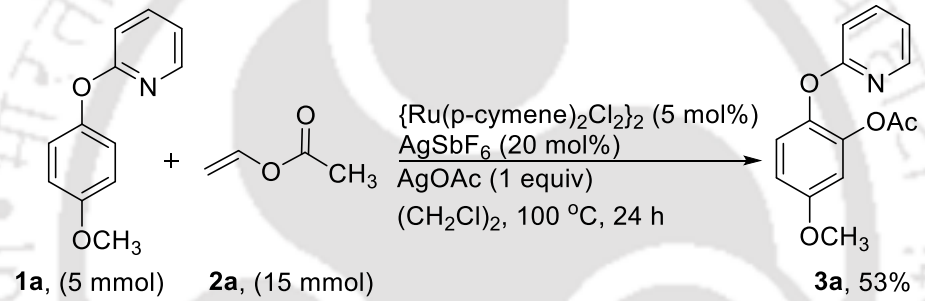


Scheme 9. Proposed Reaction Mechanism



Scheme 10. Energy Profile Diagram of Ru-catalyzed Acetoxylation

an energy barrier **TS-Ru-A** of 25.6 kcal/mol. The subsequent step involves β-hydride elimination leading to the formation of species **C**, which is a somewhat downhill process (ΔG = 7.8 kcal/mol). Afterward, the Ru-center reinserts into the C=C bond at the more electron-rich carbon atom to generate **D**, which is an energetically favorable step (ΔG = 0.6 kcal/mol). Next, the transfer of the acetate group to the aryl ring, accompanied by the simultaneous cleavage of the C-C bond, resulting in the formation of intermediate **E** in an endothermic step (ΔG = 16.8 kcal/mol). This intermediate will proceed to undergo reductive elimination, leading to the formation of the final product and the regeneration of the catalyst under the given reaction conditions. Finally, the Ru-catalyzed acetoxylation reaction was successfully scaled up using 2-(4-methoxyphenoxy)pyridine (5 mmol) as a representative case, as depicted in Scheme 11. The acetoxylation proceeded to yield the desired product in a 53% yield, affirming the scalability of the reaction.



Scheme 11. Scale up synthesis

In conclusion, we have developed an efficient oxidative cross-coupling method for acetoxylating aryl 2-pyridyl ethers with vinyl acetate through transition metal-catalyzed sp^2 C-H activation. The suggested mechanism has been supported by a combination of experimental and DFT calculations. Noteworthy practical features include selectivity, functional group tolerance, and scalability.

4.3 Experimental Section

General Information. $\{RuCl_2(p\text{-cymene})\}_2$ (97%), $AgSbF_6$ (98%), AgOAc (99%), and vinyl acetate were purchased from Aldrich and used as received. The substituted Aryl 2-Pyridyl Ethers **1a-k** were prepared according to literature.[13] Merck silica gel G/GF 254 plates were used for analytical TLC and Rankem silica gel (60-120 mesh) was used for column chromatography. NMR (^1H and ^{13}C) spectra were recorded in Bruker Avance III 400, 500 and 600 spectrometers using $CDCl_3$ as solvent and TMS as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively, and other data are reported as follows: s = singlet, d = doublet, dd= doublet of doublet, t = triplet, m = multiplet and q = quartet. IR spectra

were collected on a PerkinElmer Fourier transform infrared (FT-IR) spectrometer. Quadrupole time-of-flight electrospray ionization (ESI) mass spectrometer (model HAB 273) was used for mass analysis.

General Procedure for the Acetoxylation of Aryl 2-Pyridyl Ethers. Aryl 2-Pyridyl Ethers **1** (0.2 mmol), vinyl acetate **2** (0.6 mmol, 51.7 mg), $\{RuCl_2(p\text{-cymene})\}_2$ (5 mol%, 6 mg), $AgSbF_6$ (20 mol%, 13.7 mg) and AgOAc (0.2 mmol, 33.4 mg) were stirred at 100 °C for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The mixture was diluted with dichloromethane (10 mL) and passed through a short pad of celite. The organic layer was washed with brine (5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane/EtOAc (20:1) as eluent to afford the desired product **3**.

Scale-up Synthesis of 3a. 2-(4-methoxyphenoxy)pyridine **1a** (5 mmol, 1.1 g), vinyl acetate **2** (15 mmol, 1.3 g), $\{RuCl_2(p\text{-cymene})\}_2$ (5 mol%, 153 mg), $AgSbF_6$ (20 mol%, 343 mg) and AgOAc (5 mmol, 835 mg) were subjected to the above described standard reaction condition. The mixture was diluted with dichloromethane (20 mL) and passed through a celite pad and washed with brine (5 mL) and water (5 mL). The organic layer was dried over Na_2SO_4 and the solvent was evaporated to produce a residue, which was purified by column chromatography on silica gel using *n*-hexane/EtOAc (20:1) as eluent to afford **3a** in 53% (686 mg) yield.

Synthesis of $[D_2]$**-1a**.[14] 2-(4-methoxyphenoxy)pyridine **1a** (40.2 mg, 0.2 mmol), $\{RuCl_2(p\text{-cymene})\}_2$ (6 mg, 5.0 mol %), $AgSbF_6$ (13.7 mg, 20 mol %), AcOH (5.0 μL, 50.0 mol %), and Ag_2CO_3 (110 mg, 0.4 mmol) were stirred at 110 °C for 3 h in $(CH_2Cl)_2/D_2O$ (1.8:0.2) under N_2. The reaction mixture was cooled to room temperature, diluted with dichloromethane (10 mL), and passed through a short pad of Celite using dichloromethane (50 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified using column chromatography on silica gel to yield $[D_2]$-**1a** in 59% yield (23.9 mg) as a colorless liquid. Deuterium incorporation in the *ortho*-position was found to be 95% as estimated from 400 MHz ^{1}H NMR.

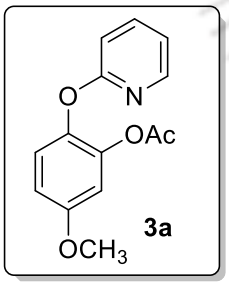
H/D Exchange Experiment with D_2O. Aryl 2-Pyridyl Ethers **1** (0.2 mmol), $\{RuCl_2(p\text{-cymene})\}_2$ (5 mol%, 6 mg), $AgSbF_6$ (20 mol%, 13.7 mg) and AgOAc (0.2 mmol, 33.4 mg) and D_2O (2 mmol)

were stirred at 100 °C for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The work-up and purification were performed as described in the general procedure. 400 MHz ^{1}H NMR spectrum of the product showed no deuterium incorporation.

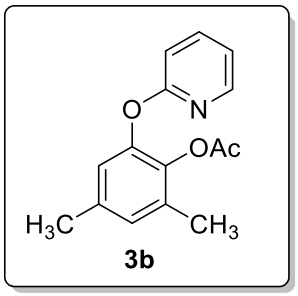
H/D Exchange Experiment with D_2O in Presence of Vinyl acetate. Aryl 2-Pyridyl Ethers **1** (0.2 mmol), vinyl acetate **2** (0.6 mmol, 51.7 mg), $\{RuCl_2(p\text{-cymene})\}_2$ (5 mol%, 6 mg), $AgSbF_6$ (20 mol%, 13.7 mg) and AgOAc (0.2 mmol, 33.4 mg) and D_2O (2 mmol) were stirred at 100 °C for 24 h in 1,2-dichloroethane (2 mL) in a sealed tube. The work-up and purification were performed as described in the general procedure. 400 MHz ^{1}H NMR spectrum of the product showed no deuterium incorporation.

Kinetic Isotope Effect Experiment. A mixture of 2-(4-methoxyphenoxy)pyridine **1a** (0.2 mmol, 40.2 mg) and [D_2]-**1a** (0.2 mmol, 40.6 mg) was reacted with Vinyl acetate **2** (0.6 mmol, 51.7 mg) for 2 h under standard reaction conditions. The reaction mixture was diluted with DCM (5 mL), and passed through a short pad of celite using DCM (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent on vacuo produced a residue, which was purified on silica gel column chromatography on silica gel using *n*-hexane and EtOAc (20:1) as eluent to afford **3a**/[D_1]-**3a**. The intermolecular k_H/k_D was found to be 1.26, based on the 400 MHz ^{1}H NMR spectroscopy.

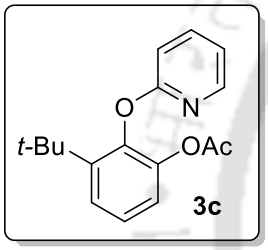
4.4 Characterization data



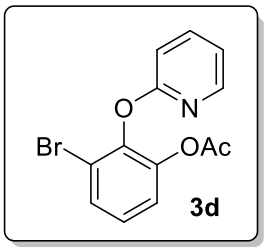
5-Methoxy-2-(pyridin-2-yloxy)phenyl acetate 3a. Yellow liquid; yield 85% (34 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16-8.15 (m, 1H), 7.68-7.64 (m, 1H), 7.15 (d, *J* = 8.9 Hz, 1H), 6.98-6.96 (m, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 6.82 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.76 (d, J = 2.9 Hz, 1H), 3.80 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 163.6, 157.2, 147.8, 143.4, 139.5, 138.9, 123.8, 118.5, 112.4, 110.7, 109.6, 55.9, 20.6; FT-IR (neat) 1722, 1252, 1142, 1060, 949, 830, 760 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{14}NO_4^+$: 260.0917, found: 260.0911.



2,4-Dimethyl-6-(pyridin-2-yloxy)phenyl acetate 3b. Yellow liquid; yield 68% (27 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21-8.17 (m, 1H), 7.70-7.64 (m, 1H), 7.00-6.96 (m, 1H), 6.90 (d, *J* = 7.4 Hz, 2H), 6.85 (s, 1H), 2.30 (s, 3H), 2.17 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 163.5, 147.9, 145.4, 139.5, 139.3, 136.5, 132.0, 128.1, 121.1, 118.6, 111.1, 21.2, 20.3, 16.3; FT-IR (neat) 1730, 1497, 1195, 1140, 1062, 945, 762 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{16}NO_3^+$: 258.1125, found: 258.1122.

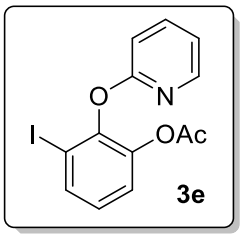


3-(*tert*-Butyl)-2-(pyridin-2-yloxy)phenyl acetate 3c. Yellow liquid; yield 61% (24 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 4.7 Hz, 1H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.98-6.95 (m, 1H), 6.90 (d, *J* = 8.2 Hz, 1H), 1.78 (s, 3H), 1.36 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 163.3, 148.0, 144.1, 143.8, 143.4, 139.4, 125.0, 124.7, 121.7, 118.2, 110.4, 35.2, 30.5, 20.4; FT-IR (neat) 1734, 1594, 1335, 1170, 1022, 795, 780 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{20}NO_3^+$: 286.1438, found: 286.1431.

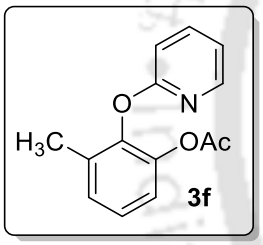


3-Bromo-2-(pyridin-2-yloxy)phenyl acetate 3d. Colorless liquid; yield 59% (24 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.72 (dd, *J* = 8.9, 4.2 Hz, 1H), 7.53 (d, *J* = 5.6 Hz, 1H), 7.16 (dt, *J* = 19.1, 9.1 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 2.03 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 163.1, 147.7, 145.4, 142.6, 139.5, 126.9, 125.6, 123.7, 123.2, 118.7,

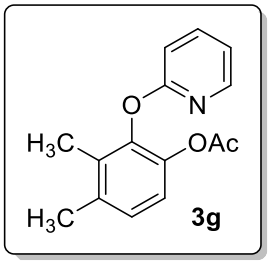
111.0, 20.5; FT-IR (neat) 1732, 1590, 1338, 1171, 1025, 795, 783 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{11}BrNO_3^+$: 307.9917, found: 307.9911.



3-Iodo-2-(pyridin-2-yloxy)phenyl acetate 3e. Brown liquid; yield 63% (25 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.19-8.15 (m, 1H), 7.69 (ddd, *J* = 8.3, 7.2, 2.0 Hz, 1H), 7.29-7.26 (m, 1H), 7.24 (q, *J* = 1.8 Hz, 1H), 7.22-7.19 (m, 1H), 7.00 (ddd, *J* = 7.2, 5.0, 0.8 Hz, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 163.2, 147.8, 145.5, 142.8, 139.6, 127.0, 125.7, 123.9, 123.3, 118.8, 111.1, 20.6; FT-IR (neat) 1725, 1580, 1325, 1170, 1082, 790, 783 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{11}INO_3^+$: 355.9778, found: 355.9786.

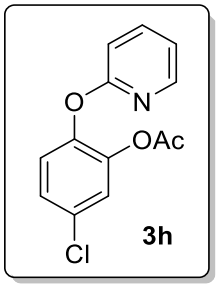


3-Methyl-2-(pyridin-2-yloxy)phenyl acetate 3f. Yellow liquid; yield 64% (26 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 5.2, 1.5 Hz, 1H), 7.69-7.66 (m, 1H), 7.16 (d, *J* = 5.1 Hz, 2H), 7.04 (t, *J* = 4.8 Hz, 1H), 6.96 (dd, *J* = 6.7, 5.4 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 2.20 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 163.0, 147.9, 143.6, 143.3, 139.5, 133.3, 128.6, 125.5, 121.1, 118.3, 110.1, 20.6, 16.5; FT-IR (neat) 1726, 1484, 1372, 1239, 1105, 957, 762 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{14}H_{14}NO_3^+$: 244.0968, found: 244.0972.

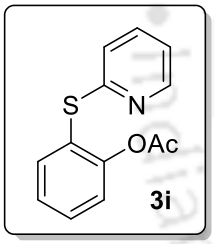


3,4-Dimethyl-2-(pyridin-2-yloxy)phenyl acetate 3g. Yellow liquid; yield 59% (24 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 8.14-8.13 (m, 1H), 7.69-7.65 (m, 1H), 7.05 (d, J = 8.2 Hz, 1H), 6.98-6.89 (m, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (150 MHz,

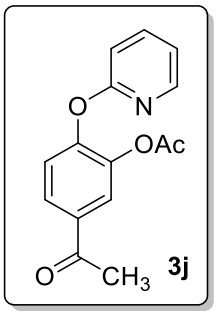
$CDCl_3$) δ 169.0, 163.2, 147.9, 143.2, 141.2, 139.5, 136.0, 131.7, 126.9, 120.2, 118.3, 110.1, 20.6, 20.1, 13.1; FT-IR (neat) 1731, 1501, 1367, 1245, 1150, 828, 762 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ $C_{15}H_{16}NO_3^+$: 258.1125, found: 258.1122.



5-Chloro-2-(pyridin-2-yloxy)phenyl acetate 3h. Yellow liquid; yield 71% (28 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 5.2, 2.2 Hz, 1H), 7.73 – 7.67 (m, 1H), 7.23 (q, *J* = 2.2 Hz, 2H), 7.18 (d, *J* = 8.7 Hz, 1H), 7.01 (ddd, *J* = 7.2, 5.0, 0.8 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 2.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 162.9, 147.8, 144.3, 143.2, 139.8, 130.3, 127.1, 124.3, 124.2, 119.1, 111.1, 20.5; FT-IR (neat) 1725, 1485, 1372, 1240, 1104, 959, 761 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{11}ClNO_3^+$: 264.0422, found: 264.0429.



2-(Pyridin-2-ylthio)phenyl acetate 3i. Yellow liquid; yield 55% (22 mg); ^1H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, J = 4.8 Hz, 1H), 7.66 (dd, J = 7.7, 1.5 Hz, 1H), 7.49-7.44 (m, 2H), 7.30 (td, J = 7.6, 1.2 Hz, 1H), 7.23-7.21 (m, 1H), 7.01 (dd, J = 7.4, 5.8 Hz, 1H), 6.89 (d, J = 8.1 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.2, 160.3, 152.2, 149.6, 137.0, 136.9, 131.0, 127.2, 124.6, 123.8, 121.7, 120.3, 20.8; FT-IR (neat) 1735, 1445, 1390, 1325, 1256, 790 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{13}H_{12}NO_2S^+$: 246.0583, found: 246.0584.



5-Acetyl-2-(pyridin-2-yloxy)phenyl acetate 3j. Yellow liquid; yield 66% (26 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.87 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.80 (d, *J* = 2.1 Hz, 1H), 7.77 – 7.71 (m, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.05 (dd, *J* = 7.2, 5.0 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 2.58 (s, 3H), 2.10 (s, 3H). δ 8.14 (d, J = 6.0 Hz, 1H), 7.67 (t, J = 8.7 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 6.98 – 6.88 (m, 3H), 2.30 (s, 3H), 2.10 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 168.5, 162.5, 149.9, 147.8, 142.5, 140.0, 134.4, 127.3, 124.2, 122.7, 119.5, 111.7, 26.6, 20.5; FT-IR (neat) 1731, 1426, 1365, 1237, 1139, 985, 829, 794 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{15}H_{14}NO_4^+$: 272.0917, found: 272.0925.

4.5 Computation Studies

All calculations were performed using the Gaussian-16 program package[15]. Full geometry optimizations were carried out using Kohn-Sham hybrid-DFT B3LYP[16] level of theory and BS1 basis set. BS1 is defined as an SDD[17] basis set for Ru atom and 6-31G* Pople basis set[18] for all other atoms. Frequency calculations at the same method and basis set were performed to distinguish transition state structures (one imaginary frequency) and minima structures (no imaginary frequency) on the potential energy surface. The transition states were verified by the intrinsic reaction coordinate (IRC) calculations, wherever necessary.[19] Free energies were calculated by using frequency calculations at 100 °C to match the experimental conditions.

Table 3. Free Energies (G) and Total Energies (E) of all the optimized structures given in Hartree along with the number of imaginary frequencies

Species	**Free energy (G)**	**Total energy (E)**	**Imaginary Frequency (NImag)**
For Ru-cycle			
1a-Ru	-1916.49713	-1916.9895861	0
A-Ru	-1687.432687	-1687.8879294	0
AcOH	-229.055286	-229.0817864	0

TS-Ru-A	-1687.401079	-1687.8590505	1
B-Ru	-1687.428886	-1687.8955337	0
D-Ru	-1687.429389	-1687.8812501	0
E-Ru	-1687.440869	-1687.9039539	0
F-Ru	-1687.415132	-1687.8713321	0

Table 4. The Cartesian Coordinates (xyz) for All Optimized Structures are Presented

1a-Ru				H	3.59149	4.42399	2.7728
C	0.81636	4.26535	0.02627	H	3.33608	3.60833	1.20604
C	0.66774	3.97748	1.38761	H	3.02138	5.37283	1.37529
C	-0.57558	3.53497	1.86756	C	-7.16573	-1.05777	1.85894
C	-1.65	3.37046	1.00417	H	-6.95385	-0.21891	1.20446
C	-1.49032	3.64207	-0.35856	H	-8.03307	-1.00718	2.50674
C	-0.26843	4.0938	-0.84258	C	-6.38844	-2.13564	1.87475
H	1.76022	4.62233	-0.36917	H	-6.56938	-2.99588	2.51023
H	-0.67803	3.32679	2.92786	O	-5.30891	-2.22308	1.01673
H	-2.60635	3.02583	1.38118	C	-4.27653	-3.10546	1.18766
H	-0.17064	4.32282	-1.8995	O	-3.39359	-3.09696	0.36376
O	-2.55623	3.59247	-1.25214	C	-4.29968	-4.02375	2.38957
C	-3.3403	2.47744	-1.35548	H	-4.38581	-3.45712	3.3228
C	-4.56904	2.65541	-2.01108	H	-5.14264	-4.72268	2.34059
C	-3.72963	0.25445	-1.00823	H	-3.3694	-4.59161	2.39407
C	-5.3906	1.54542	-2.15023	O	1.3913	-0.61383	1.70156
H	-4.84393	3.63683	-2.38145	O	3.71874	-1.70521	0.8466
C	-4.97174	0.31358	-1.63267	C	2.14626	0.33676	2.08484
H	-3.36791	-0.68432	-0.59671	C	4.46846	-2.68188	0.40636
H	-6.35073	1.6395	-2.6508	O	4.49092	-3.13467	-0.73951
H	-5.58499	-0.57785	-1.70838	O	2.91549	0.86911	1.21612
N	-2.91483	1.31666	-0.8739	C	2.86881	0.3085	-2.17739
O	1.6526	4.10961	2.32473	C	1.57763	0.78457	-1.75412
C	2.97147	4.39623	1.87496	C	0.53999	-0.11336	-1.43053

C	0.74794	-1.53702	-1.49975
C	2.01267	-2.00504	-1.93451
C	3.0609	-1.08929	-2.2745
H	1.42657	1.84543	-1.58271
H	-0.39372	0.27739	-1.03439
H	2.25329	-3.05879	-1.9042
H	4.04433	-1.492	-2.48042
C	-0.38173	-2.46892	-1.09707
H	-0.9903	-1.93137	-0.36035
C	-1.2731	-2.74363	-2.32675
H	-2.14648	-3.32988	-2.02538
H	-1.63087	-1.81228	-2.78063
H	-0.72178	-3.30405	-3.09214
C	0.07982	-3.77773	-0.44153
H	0.74854	-3.58404	0.4035
H	-0.79767	-4.31867	-0.07297
H	0.60155	-4.43169	-1.1507
C	3.98732	1.27809	-2.45766
H	3.8919	1.6843	-3.47341
H	3.96481	2.11726	-1.75523
H	4.96213	0.78869	-2.3774
C	2.14677	0.81166	3.51137
H	2.0168	1.89786	3.53638
H	1.35079	0.32301	4.07697
H	3.11381	0.57301	3.96793
C	5.37068	-3.25297	1.49912
H	5.99147	-4.05467	1.09392
H	6.00791	-2.46282	1.91084
H	4.76054	-3.63902	2.32306
Ru	2.33781	-0.63023	-0.24063
A-Ru			
C	1.41946	3.77575	-0.22884
C	2.15685	2.59048	-0.15385
C	1.50513	1.35266	-0.07126
C	0.10777	1.24154	-0.06224
C	-0.59238	2.44692	-0.17601
C	0.02528	3.69018	-0.24589
H	1.89604	4.74697	-0.28705
H	2.11134	0.45323	-0.03846
H	-0.58335	4.5867	-0.32233
O	-2.00832	2.50169	-0.19606
C	-2.71431	1.65783	-0.97085
C	-3.86413	2.1808	-1.58249
C	-3.08024	-0.41722	-1.94252
C	-4.62739	1.35777	-2.39447
H	-4.10606	3.22398	-1.4149
C	-4.21736	0.03409	-2.59317
H	-2.6985	-1.42643	-2.06639
H	-5.51587	1.74542	-2.88488
H	-4.76467	-0.64066	-3.24232
N	-2.35168	0.37101	-1.1092
O	3.54029	2.54713	-0.15774
C	4.23888	3.76819	-0.33713
H	5.30098	3.51314	-0.35033
H	3.96995	4.24899	-1.28679
H	4.04814	4.46966	0.48611
C	5.34921	-1.37937	-1.91782
H	5.70386	-0.85966	-2.80071
H	5.45206	-2.45883	-1.87637
C	4.78342	-0.69529	-0.92898
H	4.63149	0.38014	-0.93531
O	4.23716	-1.36008	0.16122

C	4.36847	-0.87907	1.43847
O	3.71125	-1.39803	2.30973
C	5.33122	0.26262	1.66124
H	6.27874	0.10053	1.13788
H	4.88386	1.18877	1.28094
H	5.50349	0.36158	2.73359
O	0.1569	-0.91747	-1.71936
C	-0.11203	-1.91463	-2.50637
O	-1.00954	-2.75742	-2.35234
C	-2.0663	-0.72079	2.01707
C	-0.69502	-0.51096	2.30237
C	0.31788	-1.39809	1.81503
C	-0.03487	-2.49213	0.99049
C	-1.42382	-2.74688	0.72268
C	-2.39661	-1.86542	1.2055
H	-0.39087	0.35745	2.87557
H	1.36281	-1.20963	2.03564
H	-1.69739	-3.55182	0.05239
H	-3.43588	-2.01904	0.92409
C	1.01923	-3.41122	0.432
H	1.99742	-2.92608	0.40627
C	-3.19289	0.12356	2.5989
H	-3.93131	0.26803	1.79681
C	0.8127	-1.97475	-3.72178
H	0.59416	-2.86027	-4.32256
H	0.67826	-1.07507	-4.33289
H	1.85892	-1.99041	-3.39824
Ru	-0.86346	-0.56186	0.0895
H	1.09989	-4.30124	1.07081
H	0.74647	-3.74056	-0.57385
C	-3.88891	-0.65877	3.73398
H	-4.74635	-0.09443	4.11871
H	-4.25195	-1.63477	3.39323
H	-3.19579	-0.83114	4.56637
C	-2.75974	1.51125	3.09053
H	-2.08948	1.4399	3.95585
H	-2.2558	2.07872	2.30368
H	-3.6397	2.08049	3.41057

AcOH

O	-2.52284	-2.81554	-0.90273
C	-2.87734	-3.97688	-0.32959
O	-2.87061	-4.17398	0.87464
C	-3.31463	-4.9966	-1.35858
H	-3.46869	-5.96158	-0.87383
H	-4.25086	-4.66264	-1.81918
H	-2.57111	-5.0846	-2.15628
H	-2.14521	-2.07518	-0.42225

TS-Ru-A

C	4.68158	-0.10115	0.62679
C	3.92862	0.93246	1.19812
C	2.55193	0.77843	1.37214
C	1.84453	-0.36593	0.93551
C	2.65396	-1.41315	0.43261
C	4.02295	-1.27852	0.26171
H	5.7519	-0.01887	0.48432
H	2.0231	1.58031	1.87841
H	4.5773	-2.11246	-0.15788
O	2.16783	-2.69278	0.16505
C	1.02521	-3.03994	-0.45367
C	0.95566	-4.40077	-0.80565
C	-1.09039	-2.67213	-1.30945
C	-0.17778	-4.88305	-1.4295

H	1.80961	-5.02741	-0.57661
C	-1.22789	-3.99249	-1.69234
H	-1.86789	-1.942	-1.48728
H	-0.24597	-5.92946	-1.712
H	-2.13976	-4.31369	-2.18393
N	0.02073	-2.17871	-0.69129
O	4.44652	2.12255	1.63403
C	5.84172	2.33038	1.50053
H	6.03747	3.32591	1.90376
H	6.41833	1.58942	2.07106
H	6.1573	2.29807	0.44894
C	0.50448	-0.80018	2.02414
C	-0.92428	-0.73188	1.60514
O	-1.55853	-2.0286	1.70488
C	-2.90269	-2.06973	1.80544
O	-3.62293	-1.09247	1.83422
C	-3.38903	-3.50111	1.88352
H	-4.47566	-3.51071	1.97835
H	-3.08826	-4.04799	0.98356
H	-2.9366	-4.00995	2.74124
O	-1.30308	0.13408	-1.80422
C	-0.37847	0.30364	-2.6846
O	0.82718	0.26727	-2.33385
C	0.03202	3.26354	-1.45236
C	0.2705	2.62372	-0.21452
C	-0.78456	2.30685	0.65017
C	-2.12943	2.62036	0.31193
C	-2.3476	3.2376	-0.91351
C	-1.28529	3.55862	-1.7766
H	1.29705	2.46978	0.09505
H	-0.56222	1.97079	1.66011
H	-3.3568	3.49807	-1.21593
H	-1.50334	4.06839	-2.71349
C	-3.24774	2.3494	1.31125
H	-3.08167	1.34912	1.72664
C	-3.19049	3.36347	2.47465
H	-3.95434	3.12991	3.22596
H	-2.21474	3.35692	2.97401
H	-3.37101	4.38299	2.1116
C	-4.65127	2.32809	0.68961
H	-4.70495	1.62559	-0.14865
H	-5.3823	2.00994	1.44061
H	-4.95835	3.31906	0.33153
C	1.18481	3.6168	-2.35981
H	1.66358	2.70688	-2.7394
H	0.85093	4.21424	-3.21489
H	1.95105	4.19353	-1.8266
H	0.81182	-1.81547	2.27943
H	0.74186	-0.11054	2.83297
H	-1.54368	-0.00647	2.12845
C	-0.79148	0.55108	-4.11809
H	-1.26104	1.53808	-4.19276
H	0.07734	0.51327	-4.77824
H	-1.53377	-0.18937	-4.43295
Ru	-0.03784	-0.18231	-0.13446
B-Ru			
C	5.01719	-0.28652	-0.90452
C	5.01967	0.0653	0.44863
C	3.83802	-0.04491	1.19627
C	2.63789	-0.49112	0.6385
C	2.66913	-0.84524	-0.72286
C	3.82958	-0.74569	-1.4804

H	5.91164	-0.21491	-1.51196	C	-1.97651	0.44932	-2.6522
H	3.87426	0.23292	2.24566	C	-0.54717	0.62065	-2.5759
H	3.79642	-1.02362	-2.52967	C	0.05271	1.63983	-1.79732
O	1.50773	-1.2105	-1.40864	C	-0.75846	2.48366	-0.96355
C	0.69215	-2.1858	-0.91581	C	-2.1449	2.21825	-0.93233
C	1.12956	-3.50922	-0.86774	C	-2.74893	1.23808	-1.79428
C	-1.43245	-2.77703	-0.23908	H	0.09284	-0.04167	-3.14873
C	0.23001	-4.4939	-0.47609	H	1.13164	1.75769	-1.80269
H	2.15315	-3.73389	-1.14624	H	-2.78031	2.75646	-0.23908
C	-1.07971	-4.11926	-0.17614	H	-3.8106	1.04021	-1.70316
H	-2.4443	-2.44703	-0.05274	C	-0.11705	3.62719	-0.19446
H	0.53986	-5.53388	-0.42862	H	0.89464	3.30051	0.08284
H	-1.82856	-4.85027	0.10842	C	0.03744	4.84112	-1.13646
N	-0.55344	-1.80409	-0.57572	H	0.56439	5.65454	-0.62455
O	6.11049	0.52155	1.13327	H	0.60372	4.58408	-2.03866
C	7.33443	0.6493	0.43071	H	-0.94362	5.21753	-1.45035
H	8.05995	1.02239	1.15602	C	-0.85138	4.01848	1.09601
H	7.67929	-0.31723	0.0387	H	-0.98806	3.15595	1.75464
H	7.25247	1.36429	-0.39933	H	-0.27056	4.77605	1.63414
C	1.39661	-0.59399	1.50018	H	-1.834	4.45737	0.88393
C	0.28636	0.44808	1.18568	C	-2.59548	-0.60477	-3.53164
O	-0.42516	0.76795	2.4236	H	-2.84895	-0.19313	-4.5178
C	-0.97976	-0.18708	3.19116	H	-1.90422	-1.43945	-3.69082
O	-0.83488	-1.3858	3.05215	H	-3.50679	-0.99581	-3.07074
C	-1.78641	0.44707	4.30689	H	0.99694	-1.60811	1.50139
H	-1.21244	1.23545	4.80406	H	1.71509	-0.41092	2.53384
H	-2.68535	0.90506	3.88238	H	0.80969	1.39102	1.00809
H	-2.07445	-0.31791	5.03011	C	-4.65334	-0.67869	1.97763
O	-2.55478	-0.17401	1.01338	H	-4.18694	-1.25012	2.78731
C	-3.73071	-0.65878	0.75896	H	-4.81345	0.34062	2.34771
O	-4.12234	-1.10185	-0.33199	H	-5.61514	-1.12531	1.717

Ru	-1.10258	0.28307	-0.46373
D-Ru			
C	5.00059	-1.45661	-1.06058
C	5.51244	-0.25153	-0.56175
C	4.65326	0.68048	0.03295
C	3.28246	0.43183	0.17455
C	2.7941	-0.79511	-0.32445
C	3.63211	-1.71339	-0.94269
H	5.63929	-2.18345	-1.5478
H	5.0776	1.62614	0.3532
H	3.2119	-2.63545	-1.33328
O	1.41906	-1.03378	-0.27602
C	0.88464	-1.7956	0.71741
C	1.66121	-2.57542	1.58213
C	-1.07442	-2.58289	1.66429
C	1.01621	-3.38679	2.50757
H	2.74088	-2.54361	1.51223
C	-0.37794	-3.40822	2.53702
H	-2.15904	-2.55416	1.64462
H	1.59964	-4.0021	3.18682
H	-0.92597	-4.04134	3.2262
N	-0.46041	-1.76256	0.77776
O	6.82375	0.11829	-0.62755
C	7.74122	-0.76362	-1.25432
H	8.71403	-0.27197	-1.19889
H	7.79378	-1.72923	-0.73379
H	7.4814	-0.93508	-2.30739
C	2.34279	1.39167	0.76506
C	2.69361	2.35956	1.61865
O	1.82472	3.26209	2.20533
C	0.80647	3.86074	1.49491
O	0.65308	3.75553	0.30456
C	-0.06767	4.64796	2.43796
H	-0.71078	3.95169	2.98922
H	0.53364	5.19626	3.16801
H	-0.69463	5.33145	1.864
O	-2.68497	-0.00553	1.51739
C	-3.71632	-0.69502	1.8962
O	-4.13325	-1.73961	1.37218
C	-2.49562	-1.81771	-2.08187
C	-1.22141	-1.17445	-2.32224
C	-1.07615	0.23449	-2.32103
C	-2.17323	1.07693	-1.91853
C	-3.36752	0.4193	-1.5312
C	-3.55025	-1.00466	-1.67502
H	-0.35537	-1.78896	-2.55054
H	-0.11395	0.67734	-2.55664
H	-4.18386	0.99971	-1.11675
H	-4.4858	-1.44832	-1.3543
C	-2.00817	2.58899	-1.91735
H	-0.95703	2.79217	-1.67992
C	-2.29645	3.14314	-3.32806
H	-2.11114	4.22313	-3.36005
H	-1.66115	2.66931	-4.08538
H	-3.34234	2.97041	-3.6112
C	-2.85438	3.30611	-0.85669
H	-2.69159	2.86817	0.13286
H	-2.57587	4.36496	-0.81847
H	-3.92651	3.25798	-1.08617
C	-2.62923	-3.31382	-2.19181
H	-2.71288	-3.62228	-3.24281
H	-1.75248	-3.82091	-1.77238

H	-3.51591	-3.66985	-1.65957
C	-4.41765	-0.10983	3.12326
H	-3.70261	0.0126	3.94417
H	-4.81051	0.88603	2.888
H	-5.23689	-0.75884	3.44032
H	-0.72537	0.69809	0.32817
H	1.30033	1.27778	0.48755
H	3.69875	2.50363	2.00258
Ru	-1.69554	-0.37724	-0.3216
E-Ru			
C	4.09028	0.28812	-1.75352
C	4.08392	0.80497	-0.45572
C	2.92957	0.68708	0.33089
C	1.75568	0.06867	-0.12323
C	1.79928	-0.4457	-1.43556
C	2.93429	-0.33544	-2.22927
H	4.96188	0.35854	-2.39334
H	2.96109	1.08913	1.33902
H	2.90187	-0.73555	-3.2381
O	0.67792	-0.96708	-2.10203
C	-0.14267	-1.93058	-1.60701
C	0.06623	-3.25507	-1.99315
C	-2.13078	-2.48101	-0.55188
C	-0.87084	-4.21613	-1.63279
H	0.95531	-3.49523	-2.56409
C	-2.00022	-3.81491	-0.91764
H	-2.99266	-2.1135	-0.00543
H	-0.72802	-5.25483	-1.91597
H	-2.77437	-4.52058	-0.63579
N	-1.20384	-1.54603	-0.87078
O	5.14332	1.43516	0.13939
C	6.34074	1.56871	-0.60565
H	7.04667	2.08504	0.04796
H	6.75555	0.59064	-0.88523
H	6.18827	2.16554	-1.5155
C	0.56851	-0.03727	0.80467
C	0.57311	-1.3689	1.5644
O	1.80513	-1.50755	2.34429
C	2.7179	-2.40631	1.92626
O	2.57417	-3.16035	0.9844
C	3.96331	-2.33966	2.78463
H	4.53153	-1.43972	2.52235
H	3.70402	-2.27012	3.84488
H	4.58175	-3.21949	2.6
O	-2.0958	-0.35257	1.72838
C	-3.34221	-0.6576	1.93389
O	-4.22775	-0.73787	1.07008
C	-2.86535	1.23417	-1.70773
C	-1.48288	1.35527	-2.10507
C	-0.54551	2.08174	-1.33538
C	-0.92523	2.6636	-0.07334
C	-2.25052	2.44123	0.35773
C	-3.22081	1.76794	-0.46468
H	-1.15018	0.87334	-3.01881
H	0.48155	2.15926	-1.67558
H	-2.55369	2.76155	1.34761
H	-4.20981	1.58016	-0.06414
C	0.08977	3.47284	0.71704
H	1.05694	2.96579	0.60158
C	0.22588	4.87841	0.09327
H	1.00506	5.45052	0.60989
H	0.4932	4.82538	-0.96792

H	-0.71537	5.43532	0.17651
C	-0.21492	3.56999	2.21857
H	-0.3611	2.58162	2.6664
H	0.61805	4.05914	2.73519
H	-1.1129	4.16987	2.41118
C	-3.85449	0.49017	-2.56535
H	-4.27361	1.15116	-3.33577
H	-3.37668	-0.35099	-3.07933
H	-4.67768	0.10101	-1.95978
H	-0.23239	-1.37818	2.29449
C	-3.65527	-0.9551	3.40002
H	-3.04267	-1.7931	3.75143
H	-3.40228	-0.08986	4.02271
H	-4.71253	-1.19978	3.52106
H	0.69005	0.73665	1.5716
H	0.50496	-2.24309	0.92005
Ru	-1.35299	0.4394	-0.09991
F-Ru			
C	-4.26991	-2.05357	-0.44459
C	-5.24104	-1.11173	-0.08324
C	-4.86529	0.22044	0.1534
C	-3.53789	0.59672	0.03445
C	-2.56004	-0.34057	-0.33094
C	-2.93497	-1.65728	-0.56698
H	-4.53359	-3.08687	-0.63433
H	-5.61811	0.95089	0.42741
H	-2.16919	-2.37362	-0.84791
O	-1.2177	0.00401	-0.35496
C	-0.70318	0.71937	-1.39537
C	-1.46113	1.04715	-2.52443
C	1.1445	1.79705	-2.23406
C	-0.86282	1.7881	-3.53376
H	-2.4906	0.72027	-2.59558
C	0.46753	2.17733	-3.38323
H	2.18065	2.05612	-2.0816
H	-1.42938	2.05498	-4.42134
H	0.98196	2.75876	-4.14049
N	0.58483	1.06835	-1.23838
O	-6.56752	-1.3779	0.06245
C	-7.01472	-2.70912	-0.15038
H	-8.09164	-2.69283	0.02441
H	-6.81862	-3.0398	-1.17869
H	-6.54297	-3.40848	0.55193
O	-3.20044	1.93923	0.18125
C	-2.58136	2.34087	1.34272
O	-2.36229	1.60007	2.26903
C	-2.22037	3.80038	1.25663
H	-1.30855	3.90521	0.65657
H	-3.01161	4.37345	0.76672
H	-2.02981	4.18616	2.25896
O	3.29124	0.14067	-1.26437
C	3.07779	-0.79107	-2.15019
O	2.11681	-1.56708	-2.17667
C	2.07748	-1.95054	1.16692
C	0.77788	-1.51404	1.38235
C	0.51537	-0.24036	2.00412
C	1.53983	0.53593	2.58624
C	2.88849	0.1246	2.31721
C	3.13475	-1.03437	1.54545
H	-0.06284	-2.09966	1.0326
H	-0.51162	0.08431	2.11982
H	3.7188	0.73749	2.65342

H	4.15977	-1.28136	1.28458	H	0.88627	-3.34509	-0.95554
C	1.23597	1.72241	3.46109	H	1.64063	-4.91507	-0.62978
H	0.19821	2.04434	3.33405	C	3.05749	-4.20517	1.6346
C	2.44401	-3.29023	0.55196	H	2.31641	-4.44783	2.40625
H	3.21639	-3.08941	-0.20112	H	3.40108	-5.14545	1.18787
C	4.15633	-0.84274	-3.23381	H	3.91469	-3.73524	2.13007
H	4.09207	0.05462	-3.86079	C	2.7392	2.26296	0.30896
H	5.1546	-0.85051	-2.78407	H	3.77562	2.27102	-0.05119
H	4.02071	-1.72654	-3.86109	C	2.18272	3.44198	0.62451
H	1.37469	1.44871	4.51613	H	2.73086	4.38333	0.5439
H	1.8987	2.56243	3.23692	H	1.15383	3.52645	0.97562
C	1.28407	-3.98819	-0.1665	Ru	1.9528	0.38436	0.35232
H	0.48068	-4.26102	0.53049				

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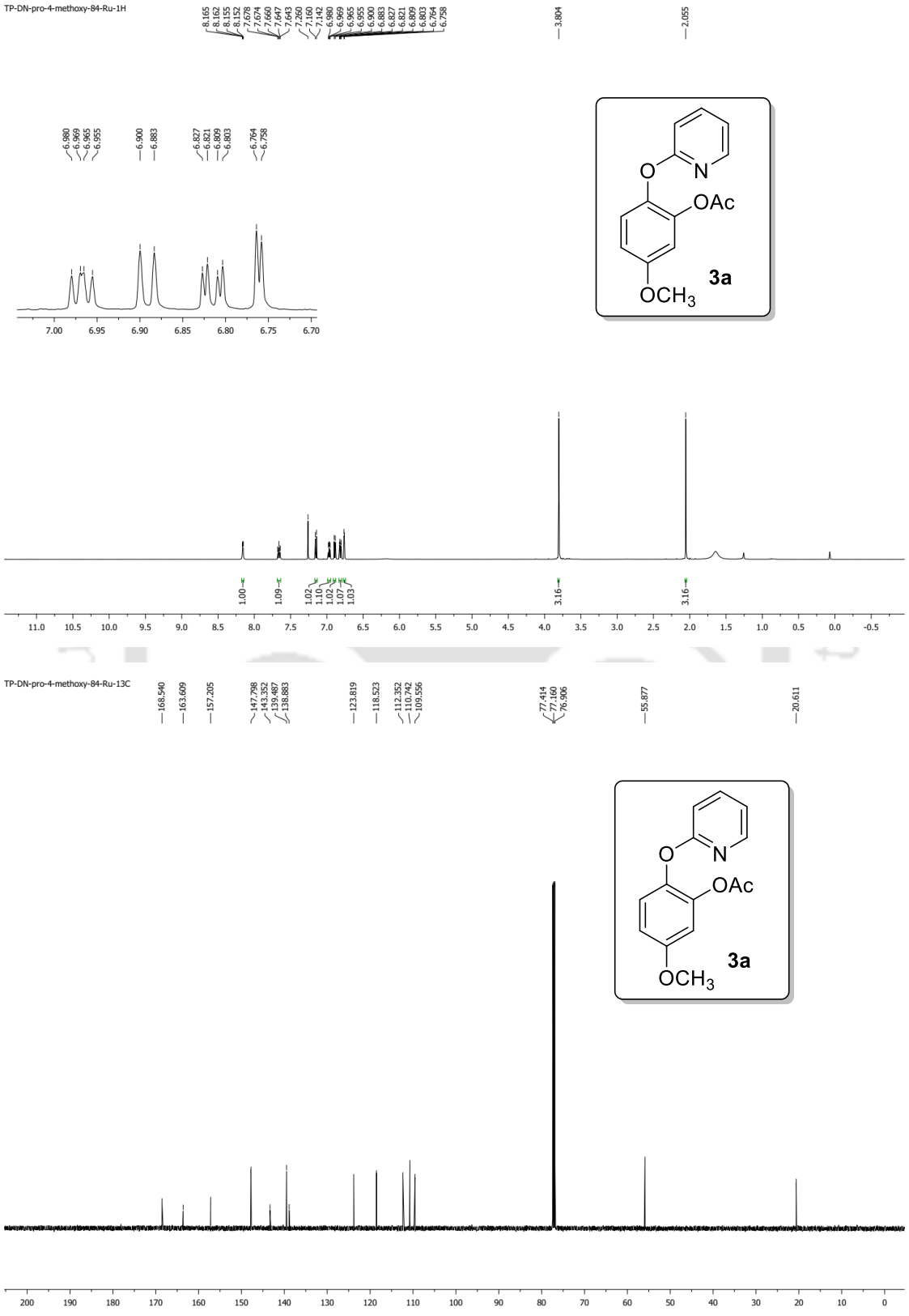
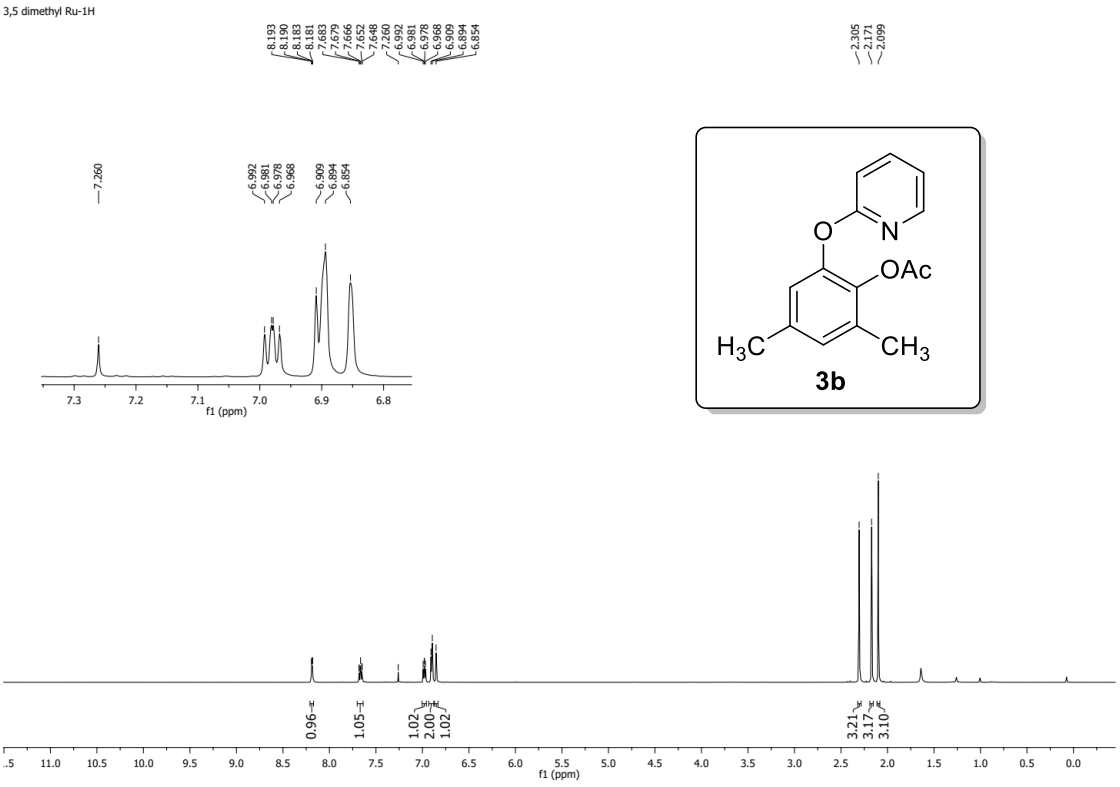
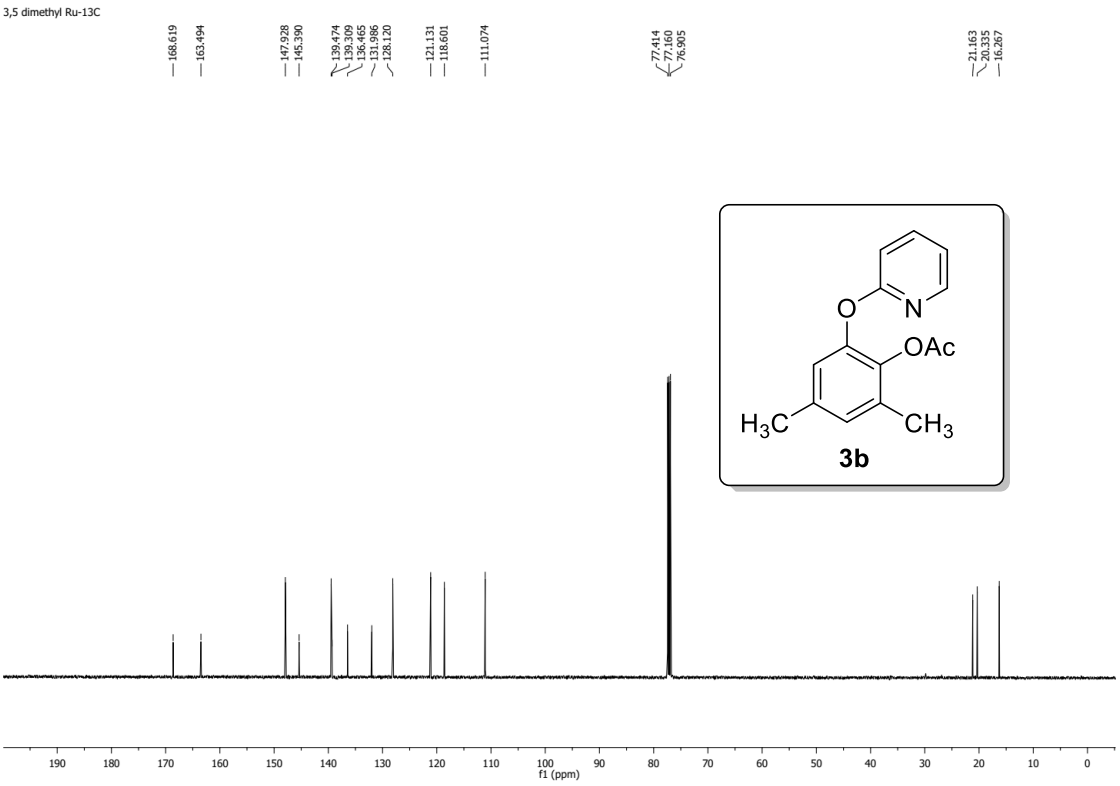
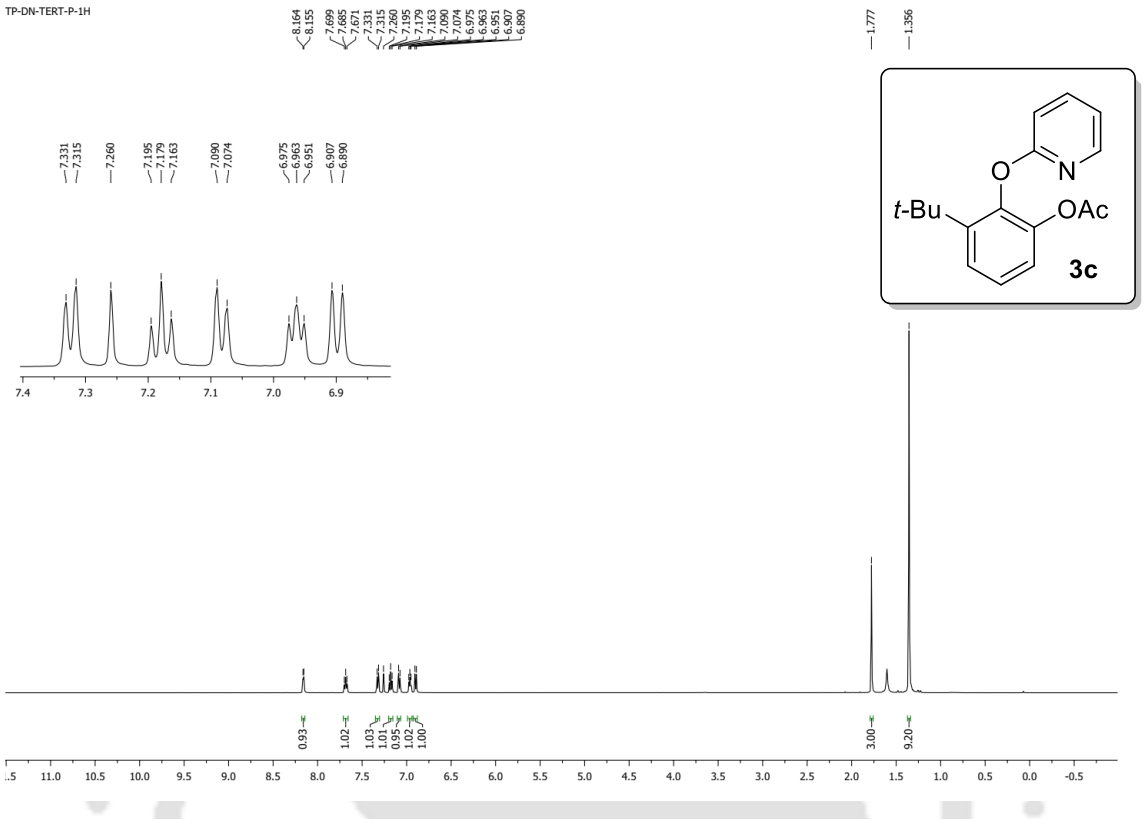
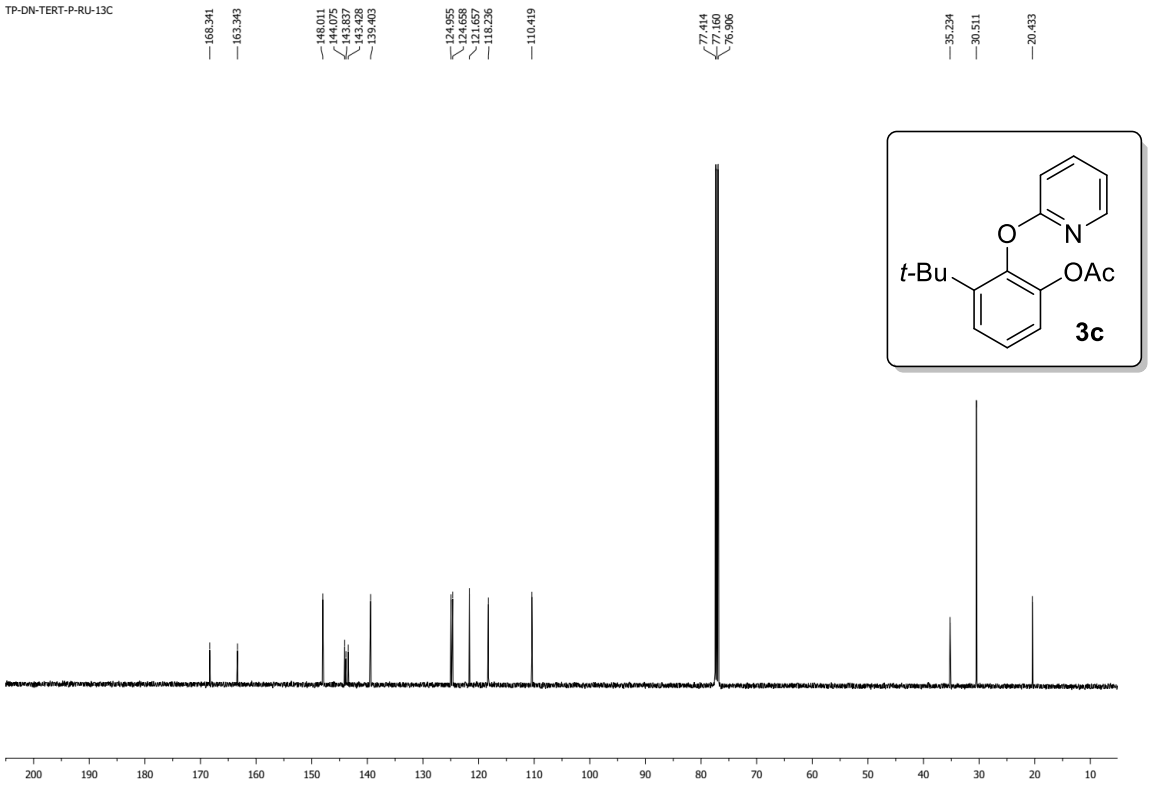
4.7 Selected NMR Spectra

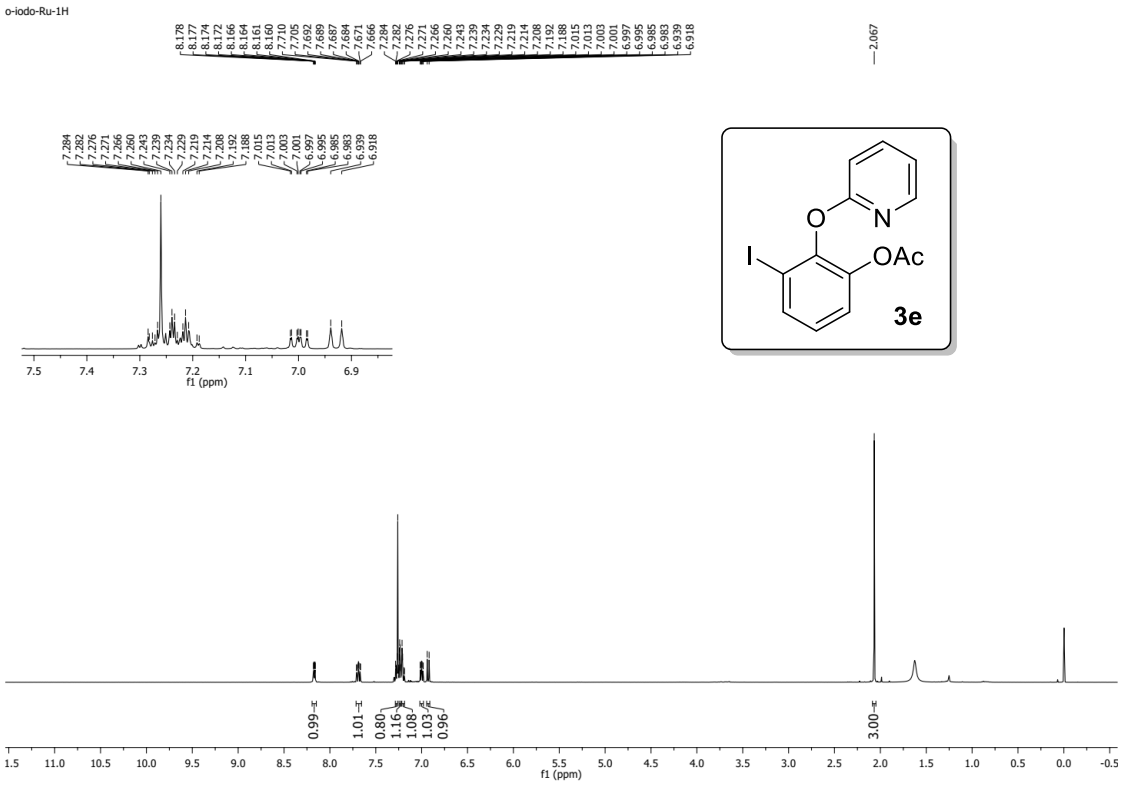


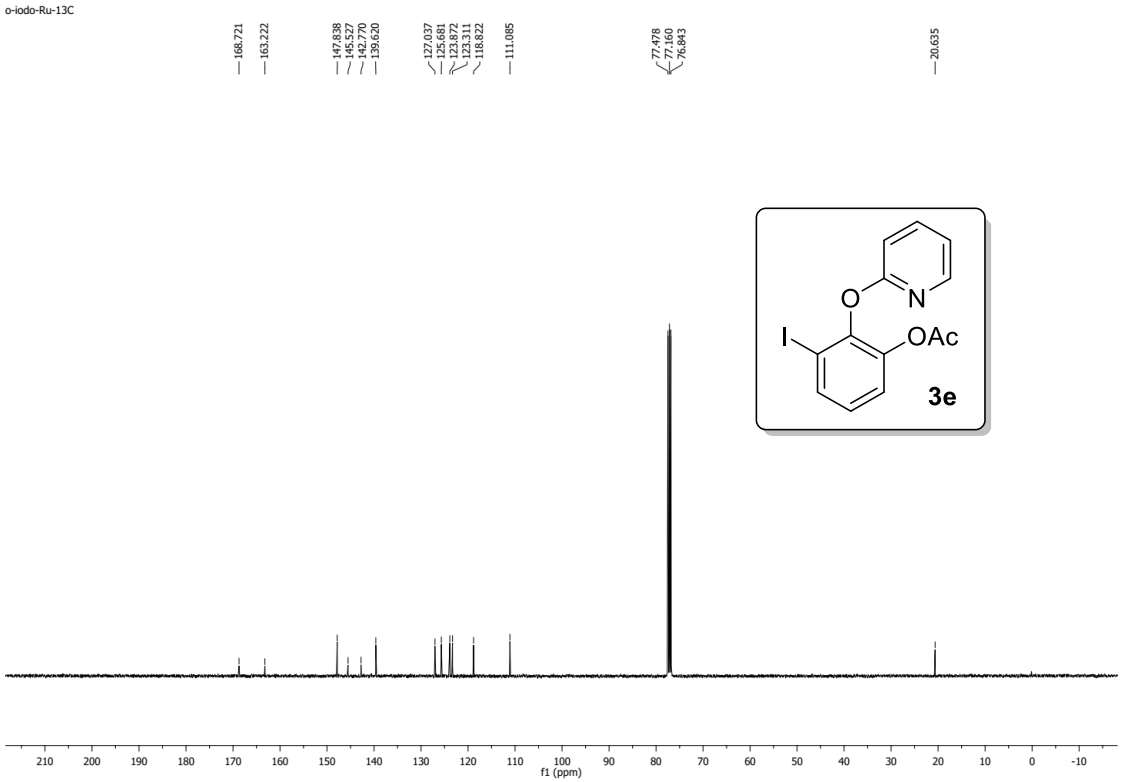


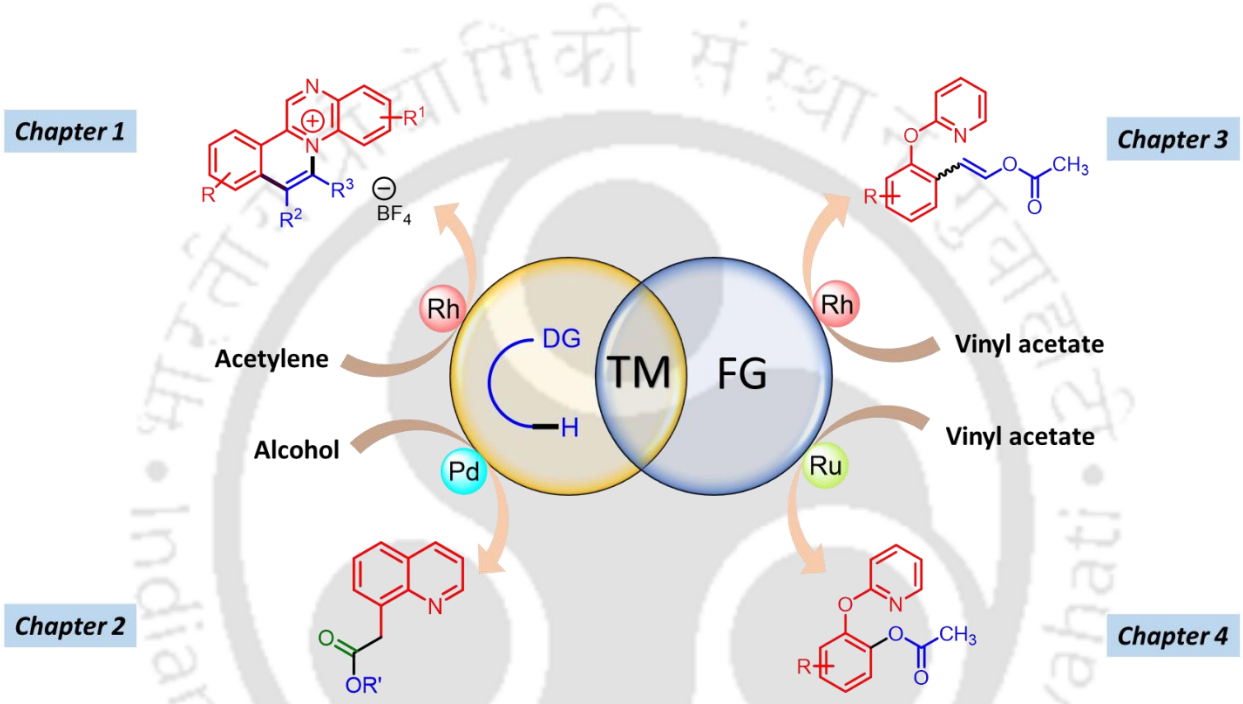












In Chapter I, we have introduced a Rh(III)-catalyzed tandem C-C/C-N bonds formation of quinoxalines with alkynes, resulting in the formation of heterocyclic quaternary ammonium salts. Under optimal reaction conditions, the process advances through the formation of a 5-membered rhodacycle, which was subsequently isolated. The approach allowed for the incorporation of both diaryl and dialkylalkenes, yielding good to excellent results. Moreover, the initial photophysical investigations suggest the potential utility of these structural frameworks in the advancement of organic light-emitting diodes (OLEDs).

In Chapter II, we have presented Pd(II)-catalyzed three component alkoxycarbonylation of sp^3 C-H bonds in 8-methylquinolines, employing $Mo(CO)_6$ as a substitute for carbon monoxide. The remarkable selectivity, functional group tolerance and late-stage natural product mutations are important practical findings.

In Chapter III, a Rh(III)-catalyzed site-selective alkenylation of aryl 2-pyridyl ether derivatives was showcased exploring electron-rich olefins like vinyl acetate. This novel reaction pathway offers a promising approach for achieving C2-alkenylation of aryl 2-pyridyl ether, serving as a feedstock for subsequent valuable modifications.

In Chapter IV, we have showcased a Ru(II)-catalyzed acetoxylation of aryl 2-pyridyl ethers utilizing vinyl acetate as an acetoxylating agent. aryl 2-pyridyl ethers featuring a variety of functional groups are well endured, leading to the formation of the desired acetoxylated products. The notable aspects of our findings include outstanding site-selectivity, functional group tolerance, and scalability.

List of Publications

1. **Kangkan Talukdar**, Subhasish Roy, Raghunath Bag and Tharmalingam Punniyamurthy, Rh-Catalyzed tandem C-C/C-N bond formation of quinoxalines with alkynes leading to heterocyclic ammonium salts, *Org. Biomol. Chem*. **2019**, *17*, 2148.
2. Raghunath Bag, Tanumay Sarkar, Sundaravel Vivek Kumar, **Kangkan Talukdar** and Tharmalingam Punniyamurthy, BINOL accelerated Ru(II)-catalyzed regioselective C-H functionalization of arenes with disulfides and diselenides, *J. Chem. Sci*. **2019**, *131*, 1.
3. Tanumay Sarkar, Bijay Ketan Das, **Kangkan Talukdar**, Tariq A. Shah and Tharmalingam Punniyamurthy, Recent Advances in Stereoselective Ring Expansion of Spirocyclopropanes: Access to the Spirocyclic Compounds, *ACS Omega*. **2020**, *5*, 26316.
4. Tanumay Sarkar, **Kangkan Talukdar**, Subhasish Roy and Tharmalingam Punniyamurthy, Expedient iron-catalyzed stereospecific synthesis of triazines *via* cycloaddition of aziridines with diaziridines, *Chem. Commun*. **2020**, *56*, 3381.
5. **Kangkan Talukda**r, Tanumay Sarkar, Subhasish Roy and Tharmalingam Punniyamurthy, Pd-Catalyzed sp^3 C-H alkoxycarbonylation of 8-methylquinolines using $Mo(CO)_6$ as CO surrogate, *Chem. Commun*. **2021**, *57*, 3359.
6. Tanumay Sarkar, **Kangkan Talukdar**, Bijay Ketan Das, Tariq A. Shah, Bijoy Debnath and Tharmalingam Punniyamurthy, The transition-metal-catalyzed stereoselective ring-expansion of vinylaziridines and vinyloxiranes, *Org. Biomol. Chem*. **2021**, *19*, 3776.
7. **Kangkan Talukdar**, Tariq A. Shah, Tanumay Sarkar, Subhasish Roy, Prabhat Kumar Maharana and Tharmalingam Punniyamurthy, Pd-catalyzed bidentate auxiliary assisted remote C(sp^3)-H functionalization, *Chem. Commun*. **2021**, *57*, 13221.
8. Tanumay Sarkar, Tariq A. Shah, Prabhat Kumar Maharana, **Kangkan Talukdar**, Bijay Ketan Das and Tharmalingam Punniyamurthy, *Chem. Rec*. **2021**, *21*, 1.
9. Pallab Karjee, Tanumay Sarkar, **Kangkan Talukdar**, Tariq A. Shah, Bijay K. Das and Tharmalingam Punniyamurthy, Copper-Catalyzed sp^3 C-H Bond Functionalization, Handbook of C-H-Functionalization, First Edition. Edited by Debabrata Maiti, *WILEY-VCH GmbH*, 2022, DOI: 10.1002/9783527834242.chf0057.
10. Sharajit Saha, Bijoy Debnath, **Kangkan Talukdar**, Pallab Karjee, Santu Mandal, and Tharmalingam Punniyamurthy, Cascade C-H Activation/Annulation of Sulfoxonium

Ylides with Vinyl Cyclopropanes: Access to Cyclopropane-Fused α-Tetralones, *Org. Lett*. **2023**, *25*, 3352.

11. Tariq A. Shah, Tanumay Sarkar, Subhradeep Kar, Prabhat Kumar Maharana, **Kangkan Talukdar** and Tharmalingam Punniyamurthy, *Chem Asian J*. **2023**, e202300815.

Conference Attended

1. Participated in Full agenda of American Chemical Society on campus in 2017.
2. Presented poster in TEQIP-III sponsored national conference in Recent Advances in Applied Sciences (RAAS'19), organized by Gauhati University in 2019.
3. Participated in a one-day international webinar "Recent trends in chemistry in the fields of medicine and industry", organized by Presidency University in 2020.
4. Presented a poster in the international conference "Recent trends in chemical sciences (RTCS-2020)", organized by Indian Chemical Society in 2020.
5. Presented a poster in the international conference "The present and future of excellence in organic synthesis (PFEOS-2021)", organized by Tezpur University in 2021.