Studies Toward C-O, C-S and C-Se Bonds Formation: Synthesis of Chalcogenated Compounds

A Thesis Submitted

in Partial Fulfilment of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

by

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Dedicated To

My Family Members

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 keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

Guwahati — Raghunath Bag

October 2018

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CERTIFICATE

This is to certify that Mr. Raghunath Bag has been working under my supervision since July 2013. I am forwarding his thesis entitled *"Studies Toward C-O, C-S and C-Se Bonds Formation: Synthesis of Chalcogenated Compounds"* 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

October 2018

Prof. Tharmalingam Punniyamurthy

Supervisor

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Raghunath Bag

List of Abbreviations

AcOH	acetic acid
Ac_2O	acetic anhydride
acac	acetylacetone
Å	angstrom (10^{-8} cm)
$AgBF_4$	silver tetrafluoroborate
AgOTf	silver trifluoromethanesulfonate
$AgSbF_6$	silver hexafluoroantimonate
Ag_2CO_3	silver carbonate
aq.	aqueous
aq. HCl	aqueous hydrochloric acid
Ar	aryl
BHT	2,6-di-*tert*-butyl-4-methylphenol
BINOL	(*R*)-(+)-1,1′-bi(2-naphthol)
Bipyridyl	2,2′-bipyridine
Boc-Phe-OH	*N*-(*tert*-butoxycarbonyl)-L-phenylalanine
CCDC	cambridge crystallographic data centre
CH_3CN	acetonitrile
C_6H_5Cl	chlorobenzene
$CHCl_3$	chloroform
CH_2Cl_2	dichloromethane
$(CH_2Cl)_2$	1,2-dichloroethane
CFL	compact fluorescent lamp
DABCO	1,4-diazabicyclo[2.2.2]octane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicarboxylate
DLP	dilauroyl peroxide
DMSO	dimethylsulfoxide
DMAP	4-(dimethylamino)pyridine
DMF	*N*,*N*-dimethylformamide

DTBP	di-*tert*-butyl peroxide
dr	diastereomeric ratio
EDG	electron donating group
equiv	equivalent
EtOH	ethanol
Et_2O	diethyl ether
Et_3N	triethylamine
ESI	electrospray ionization
Et	ethyl
EWG	electron wthdrawing group
FT-IR	fourier transform infrared spectroscopy
HOBt	*N*-hydroxybenzotriazole
H_2O_2	hydrogen peroxide
HRMS	high-resolution mass spectrometry
Hz	hertz
*i*PrOH	isopropyl alcohol
KBr	potassium bromide
KPF_6	potassium hexafluorophosphate
KTFA	potassium trifluoroacetate
K_2CO_3	potassium carbonate
K_3PO_4	Potassium phosphate tribasic
$K_2S_2O_8$	potassium persulfate
LED	light-emitting diode
LiO*t*Bu	lithium *tert*-butoxide
*m*CPBA	3-chloroperoxybenzoic acid
m/z	mass to charge ratio
mp	melting point
MesCOOH	2,4,6-trimethylbenzoic acid
Me	methyl
MeOH	methanol
Me_2S	dimethyl sulfide

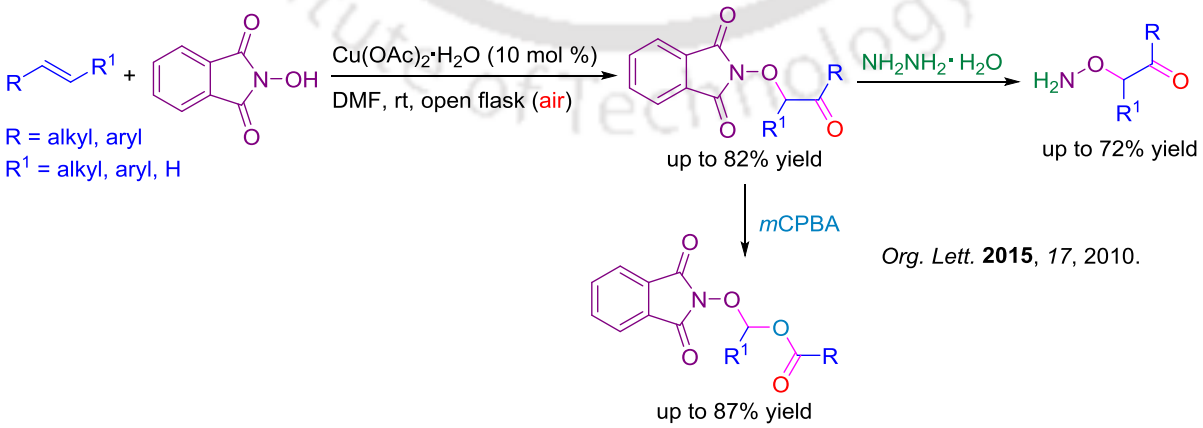
MHz	megahertz
$Mn^{III}TPPCl$	manganese (III) tetraphenylporphyrin chloride
$Mo(CO)_6$	molybdinumhexacarbonyl
NMR	nuclear magnetic resonance
$NH_2NH_2{\cdot}H_2O$	hydrazine monohydrate
NHPI	*N*-hydroxyphthalimide
NHSI	*N*-hydroxysuccinimide
nm	nanometer
o-NBA	*ortho*-nitrobenzoic acid
ORTEP	oak ridge thermal ellipsoid plot
Ph	phenyl
R_f	retardation factor
rt	room temperature
PCy_3	tricyclohexylphosphine
PCC	pyridinium chlorochromate
PIDA	phenyliodonium diacetate
PPh_3	triphenyphosphine
$P(2,4,6\text{-}Me_3C_6H_2)_3$	tris(2,4,6-trimethylphenyl)phosphine
PivOH	pivalic acid
SET	single-electron transfer
*t*AmOH	*tert*-amyl alcohol
TBAI	tetrabutylammonium iodide
TBHP	*tert*-butyl hydroperoxide
TEMPO	2,2,6,6-tetramethylpiperidine 1-oxyl
THF	tetrahydrofuran
TLC	thin-layer chromatography
TsOH	*p*-toluenesulfonic acid
TMS	trimethylsilyl
W	watt
Zn dust	Zinc dust

Abstract

The thesis is divided into four chapters. The first chapter describes a Cu(II)-catalyzed direct dioxygenation of alkenes with *N*-hydroxyphthalimide (NHPI) to furnish *β*-keto-*N*-alkoxyphthalimides employing air as an oxidant. The second chapter deals with the Fe(III)-catalyzed hydroperoxydation of alkenes with air using NHPI and HOBt at room temperature. The third chapter focuses on the metal-free dioxygenation for the synthesis of organic nitrate esters from the reaction of alkenes with *N*-hydroxylamines (NHPI, NHSI and HOBt) and *t*BuONO under air. The fourth chapter discusses the Ru(II)-catalyzed *ortho*-selective C(sp^2)-H chalcogenation of arenes tethered with 7-azaindoles using disulfides and diselenides in presence of BINOL under air.

Chapter I. Copper-Catalyzed Aerobic Dioxygenation of Alkenes with *N*-Hydroxyphthalimide

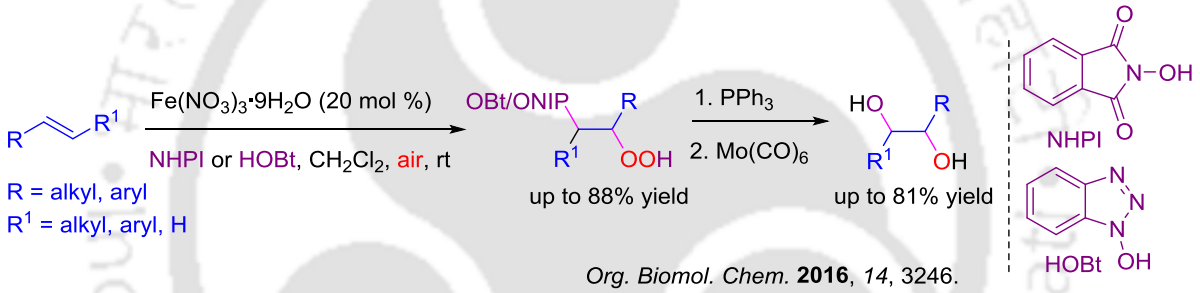
Direct radical dioxygenation of alkenes has emerged as a fascinating and powerful tool for the construction of functionalized compounds in pharmaceutical and agrochemical industries. The use of molecular oxygen from air as terminal oxidant for this purpose is highly attractive due to the inexpensive and natural abundance of air. This chapter deals with, a direct aerobic dioxygenation of alkenes with *N*-hydroxyphthalimide employing air as a sole oxidant at room temperature (Scheme 1). This general protocol offers a series of dioxygenated compounds in good yields with wide variety of substrate scope and functional group tolerance. The dioxygenated compounds are transformed into esters and *β*-ketoalkoxyamines in high yields.



Scheme 1. Cu-Catalyzed Oxidation of Alkenes with Air and *N*-Hydroxyphthalimide

Chapter II. Iron-Catalyzed Aerobic Dioxygenation of Alkenes with *N*-Hydroxylamines

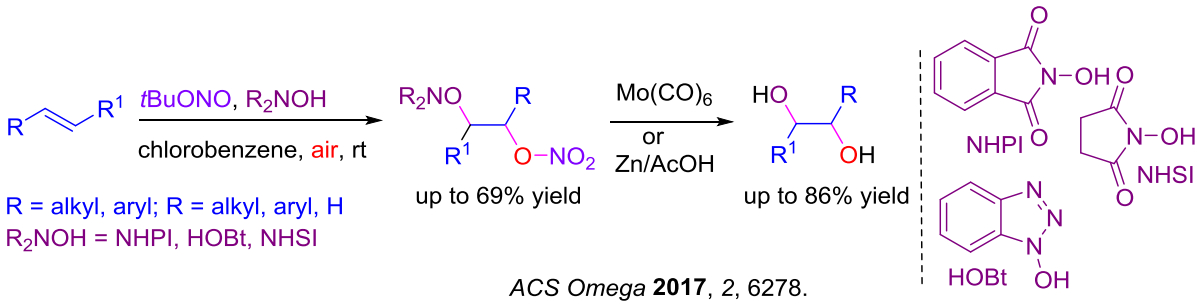
Selective and sustainable dioxygenation of alkenes using molecular oxygen from air as sole oxidant is an important process in both academia and industry since molecular oxygen is most abundant, cheap, green and sustainable oxidant in nature, which makes this process attractive. This chapter describes a Fe(III)-catalyzed hydroperoxidation of alkenes with *N*-hydroxylamines (NHPI and HOBt) employing air as sole oxidant at room temperature (Scheme 2). The hydroperoxide compounds are further converted into corresponding alcohols, which on reduction in presence of $Mo(CO)_6$ delivers synthetically useful 1,2-diols. The protocol is simple and uses non-toxic and inexpensive iron salt as the catalyst and air as sole oxidant.



Scheme 2. Fe-Catalyzed Oxidation of Alkenes with Air and *N*-Hydroxylamines

Chapter III. Metal-Free Aerobic Dioxygenation of Alkenes with *tert*-Butyl Nitrite and *N*-Hydroxylamines

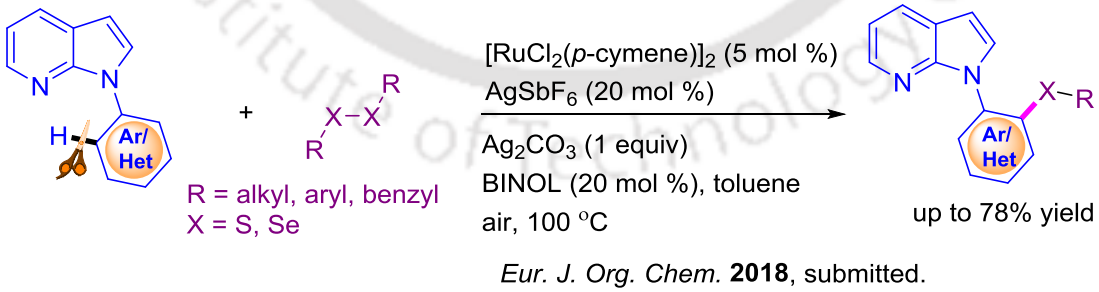
Organic nitrate esters are widely applied in medicinal chemistry as leading therapeutic class of drugs, found in natural products. Therefore, development of an efficient protocol for selective and sustainable dioxygenation of alkenes to synthesis nitrate esters will be attractive using molecular oxygen from air as clean and cheap oxidant. In this chapter, we disclose a metal-free protocol for aerobic dioxygenation of alkenes with *tert*-butyl nitrite and *N*-hydroxylamines to provide nitrate esters at room temperature (Scheme 3). The reaction proceeds through a radical pathway using readily accessible starting materials to provide nitrate esters in moderate to good yields. The utility of the protocol was reflected by transforming the nitrate esters into 1,2-diols, 1,2-diketone and *β*-aminoxy nitrates in high yields.



Scheme 3. *tert*-Butyl Nitrite Mediated Aerobic Dioxygenation of Alkenes

Chapter IV. Ruthenium-Catalyzed 7-Azaindole Directed *Ortho*-Selective C-H Chalcogenation of Arenes

7-Azaindole moieties are important structural motifs, found in plethora of bio-active natural products and pharmaceuticals as therapeutic agents due to their unique structural feature bearing electron-rich azole and electron-deficient azine rings. Thus, development of transition-metal catalyzed regioselective functionalization of unactivated arene C-H bonds tethered with 7-azaindole through C-H activation, as a reliable synthetic toolbox is desirable. In this chapter, we present a Ru-catalyzed *ortho*-selective C-H chalcogenation of arenes tethered with 7-azaindoles using disulfides and diselenides in presence of BINOL as ligand under air (Scheme 4). This developed protocol provides a potential route for the synthesis of a series of *ortho*-chalcogenated arenes in high yields. The regioselectivity, functional group tolerance, broad substrate scope, gram-scale synthesis and mechanistic studies are the important features.



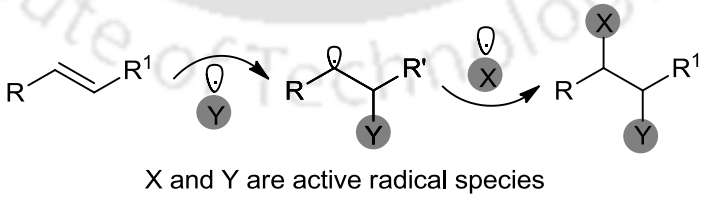
Scheme 4. Ru-Catalyzed Regioselective C-H Chalcogenation of Arenes

Contents

Chapter I

Copper-Catalyzed Aerobic Dioxygenation of Alkenes with *N*-Hydroxyphthalimide

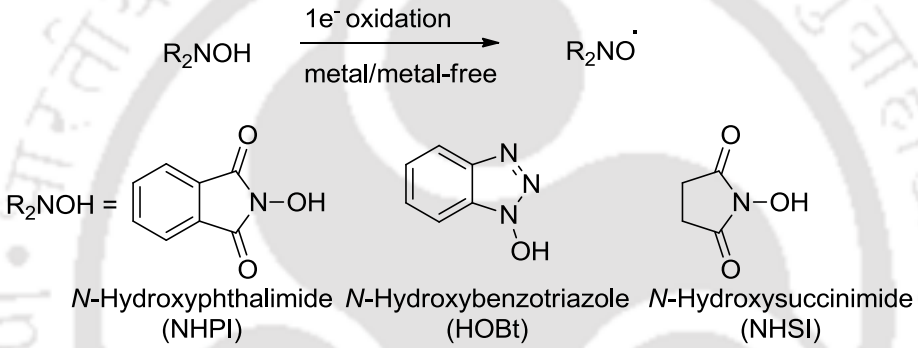
Direct 1,2-difunctionalization of alkenes has emerged as a powerful synthetic tool for the construction of functionalized organic compounds in pharmaceutical and agrochemical industries. The pioneering work of Prevost,[1a] Woodward,[1b] Upjohn[1c] and Sharpless[1d] dihydroxylation of alkenes are proven to be practical and adopted industrially. However, these reactions often employ toxic metals, which limit their practicality. Thus, several radical difunctionalization[2] of alkenes, dioxygenation,[3] oxytrifluoromethylation,[4] halosulfonylation,[5] oxyamination,[6] oxyhalogenation,[7] oxyphosphorylation,[8] aminohalogenation[9] and oxysulfonylation[10] have been developed. These difunctionalization reactions proceed through a common radical pathway, first an active radical species is generated *in situ*, which undergoes addition with the double bond of alkene to form a stable carbon-centered radical that couples with another active radical species (Scheme 1). Thus, two active radical species couple with the double bond in a vicinal fashion. Among them, the selective and catalytic vicinal dioxygenation of alkenes is one of the most valuable synthetic strategies for the preparation of diols[11] and *α*-oxygenated ketones[12] *via* multiple-electron oxidation, which are found in natural products as well as used as building blocks in synthetic chemistry. In addition, aerobic dioxygenation of alkenes is a vital and useful process. Therefore, the direct dioxygenation of alkenes utilizing air as an oxidant is a valuable synthetic tool, since air is environment friendly, clean and inexpensive.[13]



Scheme 1. General Mechanism for the Radical Difunctionalization of Alkenes

N-Hydroxylamines are suitable organic compounds to generate active catalytic species, which can undergo C-H bond functionalization under the oxidizing conditions. The radical generated from *N*-hydroxylamines under metal or metal-free condition, through one-electron

oxidation process is an active radical species, which serves as *O*-centered radical surrogates in organic synthesis (Scheme 2).[14] Recently, *N*-hydroxylamines (NHPI, HOBt and NHSI) have been exploited as stoichiometric starting materials for the construction of the *C*-*O* bond with alkenes, alkynes and hydrocarbons. Therefore, the radical dioxygenation of alkenes with *O*-centered radical surrogates such as NHPI, HOBt and NHSI utilizing air as sole oxidant is highly desirable for the formation of *C*-*O* bonds to synthesis of oxygenated ketones, peroxides and alcohols, which are important synthons in synthetic chemistry. In this chapter, we present a direct aerobic dioxygenation of alkenes with *N*-hydroxyphthalimide (NHPI) employing air as a terminal oxidant.

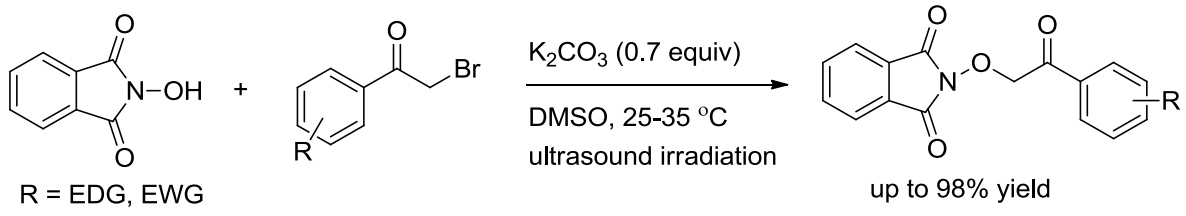


Scheme 2. *O*-Centered Radical Surrogates

1.1 Literature

1.1.1 Base-Mediated Synthesis of *β*-Keto-*N*-Alkoxyphthalimide

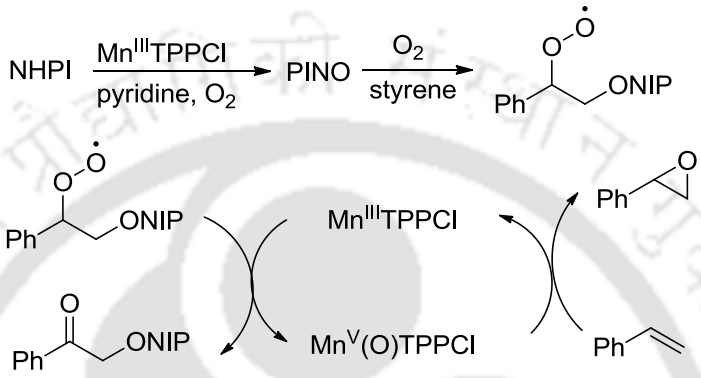
Wang and co-workers reported K_2CO_3-mediated alkylation NHPI with alkyl halide to give *β*-keto-*N*-alkoxyphthalimide in presence of ultrasound irradiation in good yields (Scheme 3).[15]



Scheme 3. K_2CO_3-Mediated Synthesis of *β*-Keto-*N*-Alkoxyphthalimides

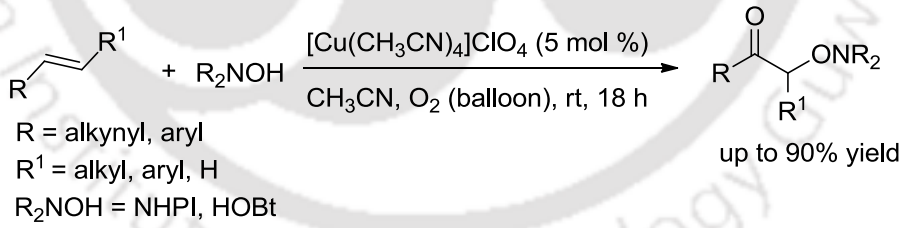
1.1.2 Metal-Catalyzed Aerobic Radical Dioxygenation of Alkenes

Masui and co-workers reported a Mn^{III}TPPCl-catalyzed epoxidation of styrene with NHPI using molecular oxygen (Scheme 4).[16] The reaction proceeds *via* a radical pathway through the formation of the peroxy radical, which is converted into the *β*-oxygenated ketone in presence of Mn^{III}TPPCl. This is the first report where *β*-keto-*N*-alkoxyphthalimide is observed along with target epoxidation.



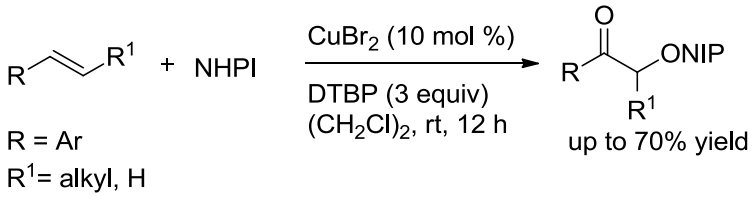
Scheme 4. Mn-Catalyzed Oxidation of Styrenes with Molecular Oxygen

Woerpel and co-workers reported a Cu-catalyzed aerobic dioxygenation of alkenes and enynes with NHPI as well as *N*-hydroxybenzotriazole (HOBt) to furnish oxygenated ketones at room temperature. Synthetic utility of the dioxygenated compounds is reported (Scheme 5).[17]



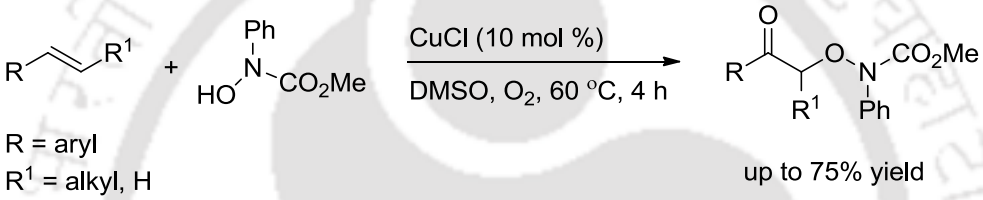
Scheme 5. Cu-Catalyzed Oxidation of Alkenes and Enynes

Xia and co-workers described a Cu-catalyzed direct dioxygenation of alkenes with NHPI using di-*tert*-butyl peroxide (DTBP) as an oxidant at room temperature to furnish *β*-keto-*N*-alkoxyphthalimides in moderate to good yields (Scheme 6).[18]



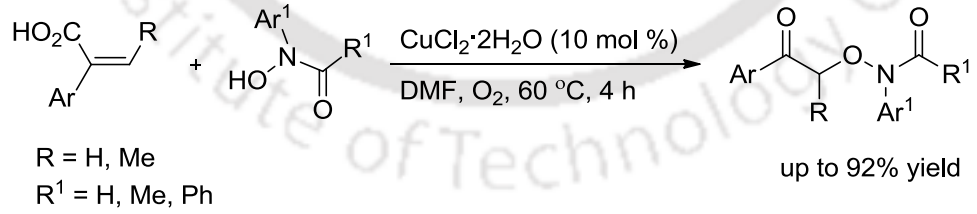
Scheme 6. Cu-Catalyzed Direct Dioxygenation of Alkenes

Lei and co-workers developed a Cu-catalyzed radical dioxygenation of alkenes with *N*-phenyl hydroxamic acid in the presence of molecular oxygen as a sole oxidant to produce *α*-oxygenated ketones in moderate to good yields (Scheme 7).[19] To understand the mechanism of this protocol, mechanistic studies have been well explored. The $^{18}O_2$ labeling experiment suggests that the ketonic oxygen source is molecular oxygen.



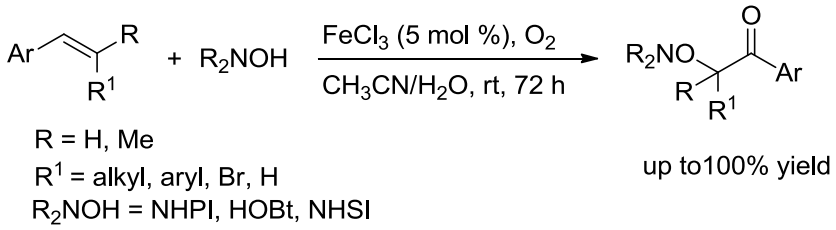
Scheme 7. Cu-Catalyzed Radical Dioxygenation of Alkenes

A Cu-catalyzed aerobic decarboxylation/ketooxygenation of electron-deficient alkenes with of *N*-aryl hydroxamic acids has been described to deliver *α*-oxygenated ketones in high yields (Scheme 8).[20] This protocol provides an aerobic ketooxygenation of electron deficient alkenes *via* successive O-H alkylation, aerobic decarboxylation and oxygenation in a single process.



Scheme 8. Cu-Catalyzed Aerobic Decarboxylation/Ketooxygenation of Alkenes

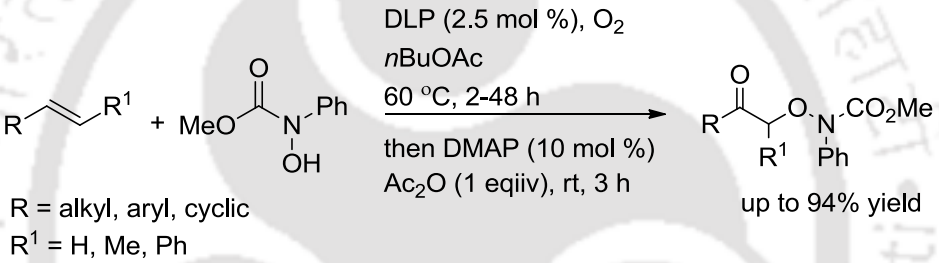
Tang and co-workers described a Fe-catalyzed oxidation of aryl alkenes utilizing NHPI, HOBt and NHSI (*N*-hydroxysuccinimide) in the presence of oxygen to form dioxygenated compounds in high yields (Scheme 9).[21] Post synthetic modification of the dioxygenated compounds have been demonstrated to show the synthetic utility of the protocol.



Scheme 9. Fe-Catalyzed Radical Dioxygenation of Aryl Alkenes

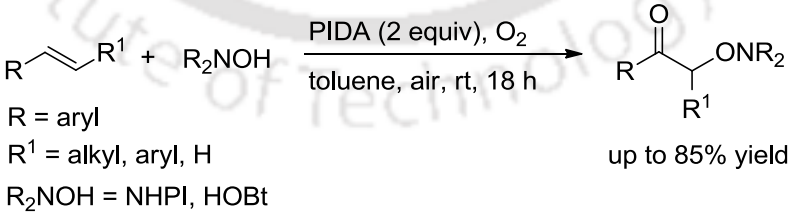
1.1.3 Metal-Free Aerobic Radical Dioxygenation of Alkenes

Alexanian and co-workers reported a metal-free dilauroyl peroxide (DLP) catalyzed inter- and intramolecular aerobic ketooxygenation of alkenes using *N*-hydroxamic acids (Scheme 10).[22] A hefty array of substrates such as aromatic and cyclic alkenes with *N*-aryl hydroxamic acids deliver *α*-oxygenated ketones with high level of regio- and stereoselectivities.



Scheme 10. DLP-Catalyzed Radical Ketooxygenation of Alkenes

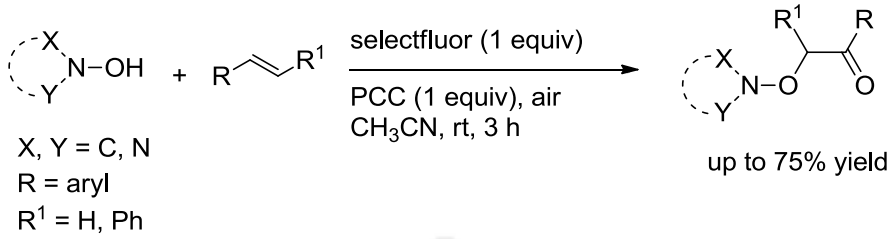
A metal-free phenyliodonium diacetate (PIDA) mediated dioxygenation of alkenes with *N*-hydroxylamines under oxygen atmosphere has been demonstrated to give *α*-oxygenated ketones (Scheme 11).[23] This protocol is applicable for a wide range of alkenes with a variety of functional groups to deliver *α*-oxygenated ketones in good yields.



Scheme 11. PIDA-Mediated Aerobic Dioxygenation of Alkenes

An operationally simple protocol for the selectfluor mediated radical oxidation of styrenes with *N*-hydroxylamines has been described in the presence of air (Scheme 12).[24] A series of styrenes bearing electron donating and withdrawing groups with NHPI, HOBt and NHSI

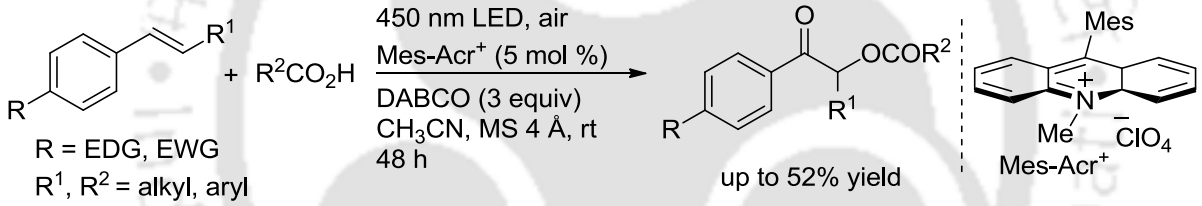
were amenable under these conditions to produce the dioxygenated compound in moderate to good yields.



Scheme 12. Selectfluor-Mediated Aerobic Dioxygenation of Styrenes

1.1.4 Photo-Catalyzed Aerobic Radical Dioxygenation of Alkenes

A metal-free organo photoredox catalytic oxo-acyloxylation of aryl alkenes with carboxylic acids and molecular oxygen has been developed to give *α*-acyloxy ketones using blue LED (Scheme 13).[25] 9-Mesityl-10-methylacridinium perchlorate (Mes-Acr$^+$) is used as the photocatalyst in this protocol.

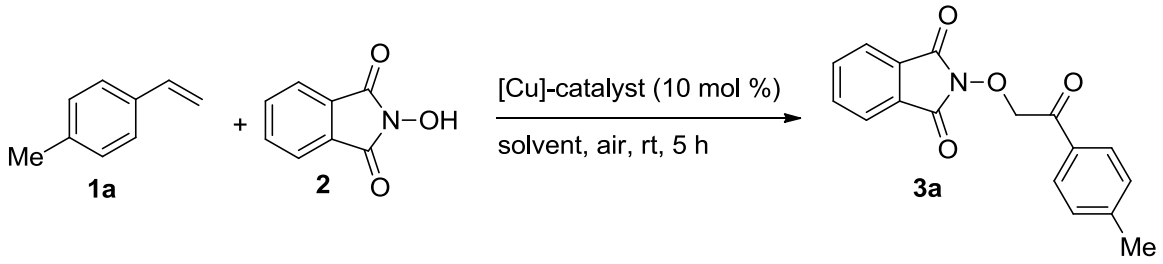


Scheme 13. Photoredox Catalytic Synthesis of *α*-Acyloxy Ketones

1.2 Present Study

We present here a copper-catalyzed direct dioxygenation of alkenes with NHPI to synthesis of *β*-keto-*N*-alkoxyphthalimides under air. The reaction proceeds through a radical pathway to provide dioxygenated compounds. First, we carried out the optimization of the reaction using 4-methylstyrene **1a** and NHPI **2** as model substrates at room temperature in presence of different solvents and varied copper catalysts under air (Table 1). Pleasantly, the reaction of 4-methylstyrene **1a** with NHPI **2** furnished *β*-keto-*N*-alkoxyphthalimide **3a** in 54% yield when these substrates were stirred in presence of 10 mol % $Cu(OAc)_2 \cdot H_2O$ in $(CH_2Cl)_2$ under air (entry 1). Molecular oxygen produced similar result, while TBHP, $K_2S_2O_8$ and 30% H_2O_2 ended with inferior results (entries 2-5). In contrast, N_2 balloon furnished the product **3a** in a

Table 1. Optimization of the Reaction Conditions[a]



Entry	[Cu]-catalyst	Solvent	Yield (%)[b,c]
1	$Cu(OAc)_2·H_2O$	$(CH_2Cl)_2$	54
2	$Cu(OAc)_2·H_2O$	$(CH_2Cl)_2$	52[d]
3	$Cu(OAc)_2·H_2O$	$(CH_2Cl)_2$	23[e]
4	$Cu(OAc)_2·H_2O$	$(CH_2Cl)_2$	16[f]
5	$Cu(OAc)_2·H_2O$	$(CH_2Cl)_2$	39[g]
6	$Cu(OAc)_2·H_2O$	$(CH_2Cl)_2$	trace[h]
7	$Cu(OAc)_2·H_2O$	toluene	28
8	$Cu(OAc)_2·H_2O$	CH_3CN	36
9	$Cu(OAc)_2·H_2O$	THF	37
10	$Cu(OAc)_2·H_2O$	EtOH	45
11	$Cu(OAc)_2·H_2O$	DMSO	32
12	$Cu(OAc)_2·H_2O$	H_2O	n.d.
13	**$Cu(OAc)_2·H_2O$**	**DMF**	**70**
14	CuI	DMF	15
15	$CuCl_2$	DMF	54
16	$CuBr_2$	DMF	35
17	CuO nano	DMF	27
18	$Cu(OTf)_2$	DMF	18
19	$Cu(OAc)_2·H_2O$	DMF	53[i]
20	$Cu(OAc)_2·H_2O$	DMF	66[j]
21	-	DMF	n.d.

[a] Reaction conditions: 4-Methylstyrene **1a** (1.5 mmol), NHPI **2** (0.5 mmol), $Cu(OAc)_2·H_2O$ (10 mol %), solvent (2.5 mL), rt, air (open flask), 5 h.

[b] Isolated yield.

[c] Trace of *p*-tolualdehyde obtained as a by-product due to oxidative cleavage of the double bond.

[d] O_2 balloon.

[e] TBHP (0.5 mmol) used.

[f] $K_2S_2O_8$ (0.5 mmol) used.

[g] H_2O_2 (0.5 mmol) used.

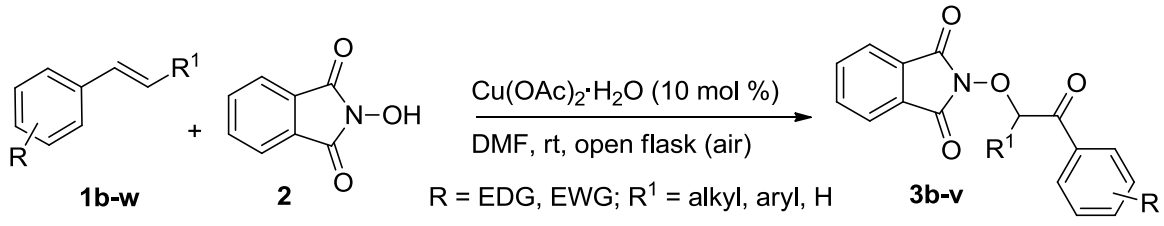
[h] N_2 balloon.

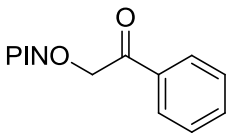
[i] $Cu(OAc)_2 \cdot H_2O$ (5 mol %) used. [j] 4-Methylstyrene **1a** (1 mmol) used. n.d. = not detected.

trace amount (entry 6). In a set of solvents screened, toluene, CH_3CN, THF, EtOH, DMSO, H_2O and DMF, the latter produced the best result (entries 7-13). Among the copper salts screened, $Cu(OAc)_2 \cdot H_2O$, CuI, $CuCl_2$, $CuBr_2$, CuO nanoparticle and $Cu(OTf)_2$, the former gave the superior yield (entries 13-18). Decreasing the amount of the catalyst (5 mol %) or 4-methylstyrene (2 equiv) led to drop the yield to <66% (entries 19 and 20). In the absence of copper source, the formation of **3a** was not observed (entry 21).

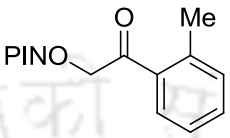
Next, the scope of the procedure was studied for the reaction of substituted alkenes with NHPI (Table 2). The reaction of styrene **1b** produced the dioxygenated **3b** in 65% yield, whereas 2-substituted styrene **1c** with methyl group underwent reaction to provide **3c** in 80% yield. Similarly, the reactions of the 3-substituted styrenes bearing substituents with bromo **1d**, chloro **1e**, methoxy **1f** and methyl **1g** functional groups produced the dioxygenated **3d-g** in 62-82% yields. Styrenes having substitution at the 4-position with acetoxy **1h**, bromo **1i**, chloro **1j**, chloromethyl **1k**, fluoro **1l**, methoxy **1m** and phenyl **1n** groups oxidized to furnish **3h-n** in 36-68% yields. Di- and trisubstituted styrenes **1o-q** having methyl or methoxy groups at 2,4- or 3,4,5- or 2,4,6-positions were amenable, furnishing **3o-q** in 60-68% yields. The reaction of *trans*-*β*-methylstyrene **1r** with NHPI afforded **3r** in 61% yield. Similar results were observed with *cis*-stilbene **1s** and *trans*-stilbene **1t**, delivering **3s** in 15 and 45% yields, respectively. Likewise, 1- and 2-vinylnaphthalenes **1u-v** underwent oxidation to produce **3t** and **3u** in 55 and 57% yields, respectively. However, aliphatic alkene, 1-octene **1w** was an unsuccessful substrate and the dioxygenation was not observed. The compound **3d** in CH_2Cl_2 gave single crystal whose structure was determined using X-ray analysis (Figure 1).

Table 2. Reaction of Acyclic Alkenes with NHPI[a-c]

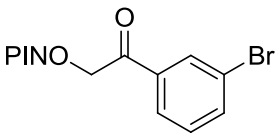




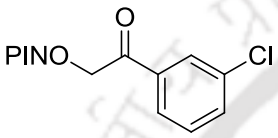
3b, 5 h, 65%



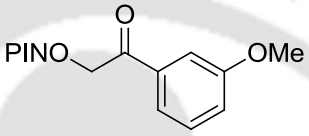
3c, 7 h, 80%



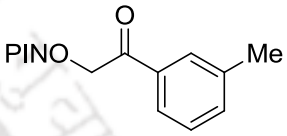
3d, 10 h, 64%



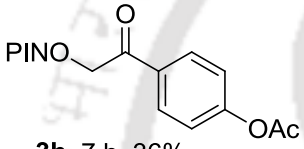
3e, 10 h, 62%



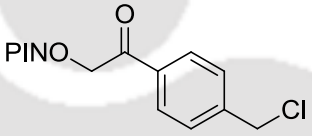
3f, 5 h, 82%



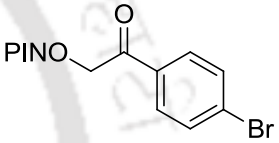
3g, 5 h, 64%



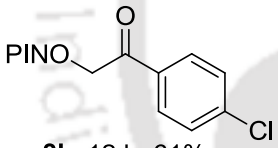
3h, 7 h, 36%



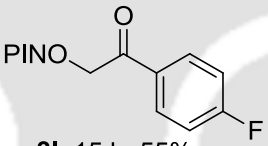
3i, 6 h, 68%



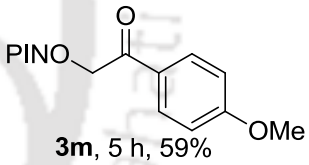
3j, 12 h, 59%



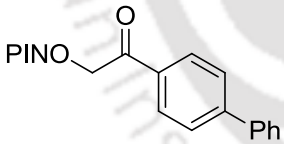
3k, 12 h, 61%



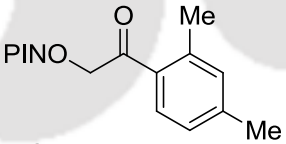
3l, 15 h, 55%



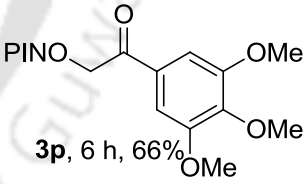
3m, 5 h, 59%



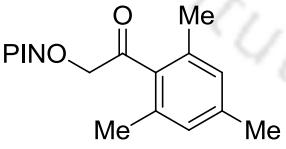
3n, 7 h, 50%



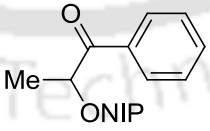
3o, 5 h, 68%



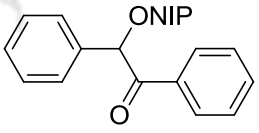
3p, 6 h, 66%



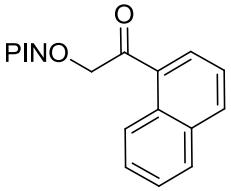
3q, 5 h, 60%



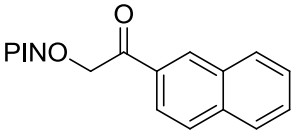
3r, 5 h, 61%



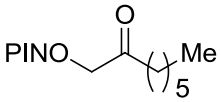
3s, 32 h, 15%[d], 45%[e]



3t, 9 h, 55%



3u, 6 h, 57%



3v, 72 h, 0%

[a] Reaction conditions: Alkenes **1b-w** (3 mmol), NHPI **2** (1 mmol), $Cu(OAc)_2 \cdot H_2O$ (10 mol %), DMF (3 mL), rt, air.

[b] Isolated yield.

[c] Aldehyde obtained as a by-product in trace due to oxidative cleavage of the double bond.

[d] Using *cis*-stilbene.

[e] Using *trans*-stilbene.

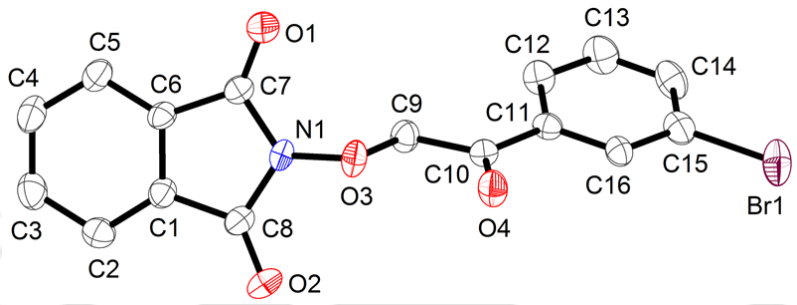
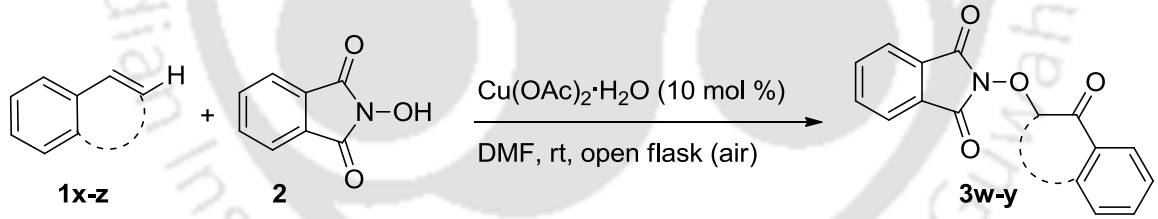
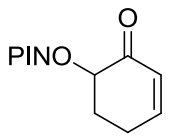


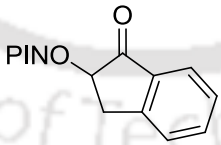
Figure 1. ORTEP diagram of 2-(2-(3-bromophenyl)-2-oxoethoxy)isoinoline-1,3-dione **3d** with 50% ellipsoid. H-Atoms are omitted for clarity (CCDC 1048261).

Table 3. Reaction of Cyclic Alkenes[a,b]

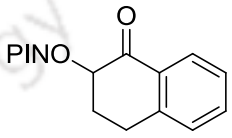




3w, 24 h, 55%



3x, 24 h, 34%



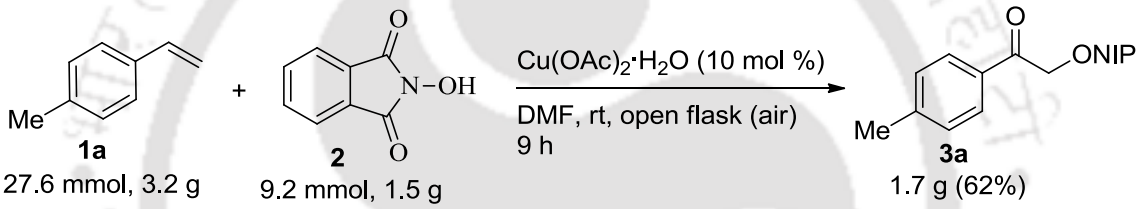
3y, 24 h, 55%

[a] Reaction conditions: Alkenes **1x-z** (3 mmol), NHPI **2** (1 mmol), $Cu(OAc)_2 \cdot H_2O$ (10 mol %), DMF (3 mL), rt, air.

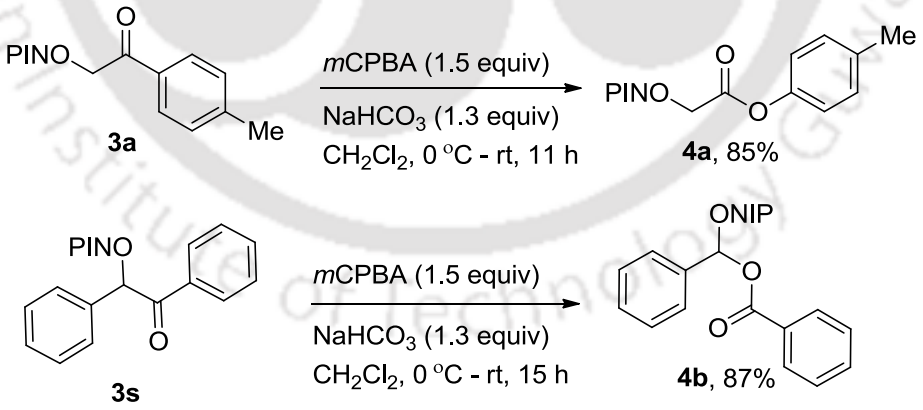
[b] Isolated yield.

The scope of the protocol was next extended for the reaction of cyclic alkenes (Table 3). These substrates were slightly less reactive compared to the acyclic one. 1,3-Cyclohexadiene **1x** underwent oxidation with NHPI to produce **3w** in 55% yield. Indene **1y** and 1,2-dihydronaphthalene **1z** oxidized to furnish **3x** and **3y** in 34 and 55% yields, respectively. These results suggest that broad range of substrates can be oxidized.

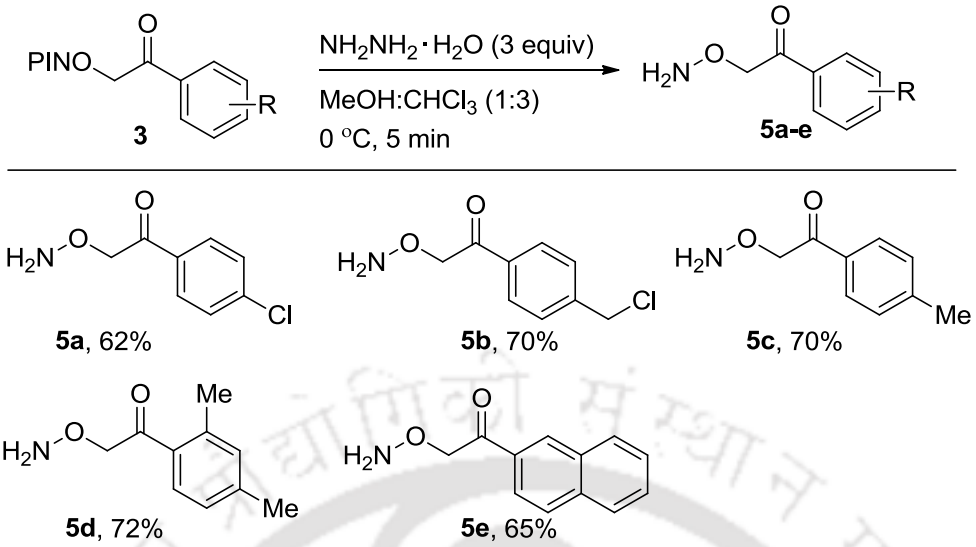
The reaction of 4-methylstyrene **1a** and NHPI **2** was examined for the gram scale synthesis (Scheme 14). The oxidation occurred to provide **3a** in 62% yield, which suggests that the protocol is scalable. Further, the oxidation of *β*-keto-*N*-alkoxyphthalimides can be performed utilizing 3-chloroperbenzoic acid (*m*CPBA) to deliver esters (Scheme 15).[26] For examples, the oxidation of **3a** and **3s** can be performed to give **4a** and **4b** in 85 and 87% yields, respectively.



Scheme 14. Gram-Scale Synthesis



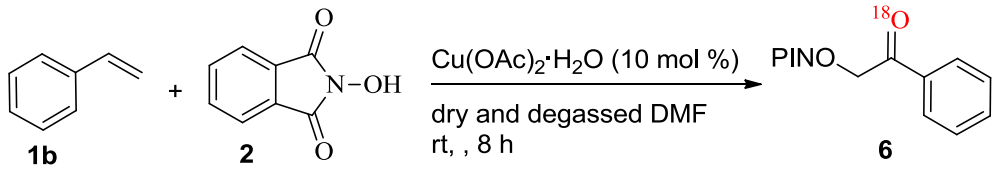
Scheme 15. Oxidation of *β*-Keto-*N*-Alkoxyphthalimides to Esters



Scheme 16. Hydrolysis of *β*-Keto-*N*-Alkoxyphthalimides to *β*-Ketoalkoxyamines

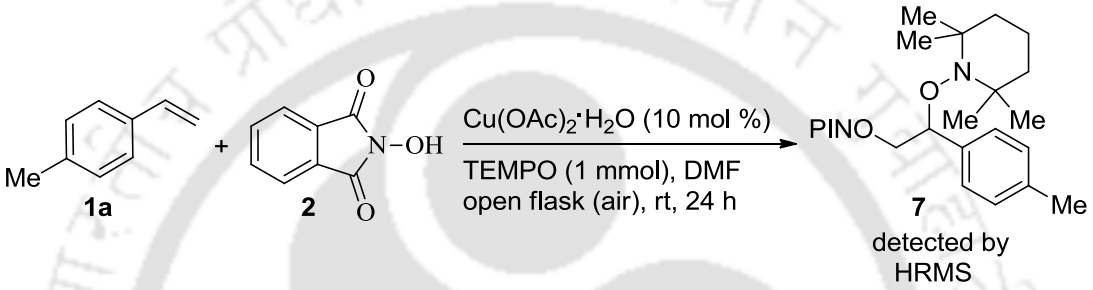
Finally, the hydrolysis of *β*-keto-*N*-alkoxyphthalimides was studied using hydrazine hydrate to afford *β*-ketoalkoxyamines in good yields (Scheme 16).[27,28] The hydrolysis of **3k** delivered **5a** in 62% yield. Similarly, **3k**, **3a**, **3o** and **3u** underwent hydrolysis to provide alkoxyamines **5b-e** in 65-72% yields.

To investigate the reaction mechanism, isotope labeling experiment was conducted to realize the source of ketonic oxygen atom in the final product (Scheme 17). The reaction using $^{18}O_2$ incorporated ^{18}O in the product, while $H_2{}^{18}O$ failed to produce ^{18}O incorporation, which suggests that the oxygen source can be the atmospheric oxygen from air.[29] In addition, the treatment of TEMPO[30] on the standard conditions afforded the TEMPO adduct **7**, which was characterized by HRMS (Scheme 18). This experiment suggests that the reaction may proceed *via* a radical pathway. Thus, the reaction of NHPI with $Cu(OAc)_2$ can produce PINO radical,[7] which can add to alkene terminally to form the stable secondary radical intermediate ***a*** (Scheme 19). The latter in presence of Cu(OAc) and air can produce the Cu(II)-peroxo intermediate ***b***, which can rearrange to furnish **3** along with Cu(OAc)(OH), which in presence of AcOH can regenerate the catalyst to complete the catalytic cycle.

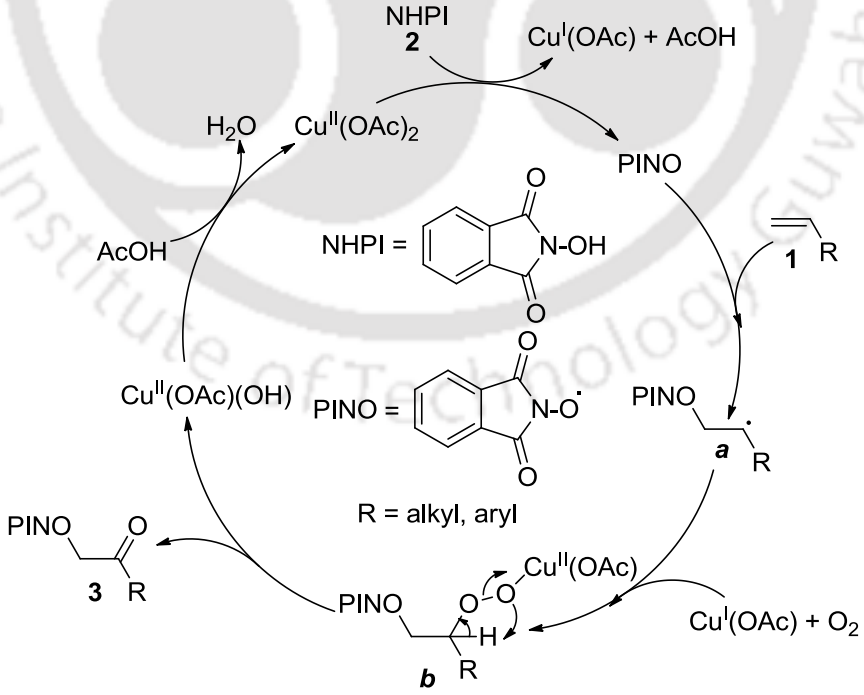


Oxygen	Solvent	Observation
$^{18}O_2$	DMF	^{18}O- incorporated
O_2	DMF + $H_2{}^{18}O$ (5 µL)	no isotope labeling

Scheme 17. Isotope Labeling Studies



Scheme 18. Trapping of Styrenyl Radical by TEMPO



Scheme 19. Proposed Catalytic Cycle

In summary, we have presented a copper-catalyzed simple aerobic dioxygenation of alkenes with NHPI at room temperature. The products can be converted into esters and *β*-ketoalkxoyamines, which can serve as useful building blocks in synthetic chemistry. The mild reaction condition, greater reactivity, functional group tolerance and the use of air as the oxidant are the important practical features.

1.3 Experimental Section

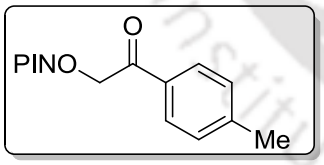
General Information. Alkenes, NHPI (97%), 2,2,6,6-tetramethylpiperdine-1-oxyl (99%) (TEMPO) and 3-chloroperoxybenzoic acid (*m*CPBA) (<77%) of Aldrich were used as received. $Cu(OAc)_2 \cdot H_2O$ (>98%) and hydrazine hydrate (90-100%) were purchased from Merck. Merck silica gel G/GF 254 plates were used for analytical TLC. Rankem silica gel (60-120 mesh) was used for column chromatography. NMR (^1H and ^{13}C) spectra were recorded on DRX-400 Varian spectrometer and Bruker Avance III 600 spectrometer using $CDCl_3$ and DMSO-d_6 as the solvent and TMS as an internal standard. Chemical shifts (δ) are reported in ppm and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, br s = broad singlet and *J* = spin-spin coupling constant (Hz). Melting points were measured with a Büchi B-540 apparatus. PerkinElmer IR spectrometer was used for recording IR spectra. Q-Tof ESI-MS instrument (model HAB 273) was used for collecting HRMS. Single crystal X-ray data were determined using Bruker SMART APEX-II CCD diffractometer, which is equipped with 1.75 kW sealed-tube Mo-Kα irradiation (λ = 0.71073 Å) at 298(2) K. The structure was solved by the direct method using SHELXL-97 (Göttingen, Germany) and refined with full-matrix least squares on F^2 using SHELXL-97.

General Procedure for the Synthesis of *β*-Keto-*N*-Alkoxyphthalimides. Alkene **1** (3 mmol), NHPI **2** (1 mmol, 163 mg) and $Cu(OAc)_2 \cdot H_2O$ (10 mol %, 20 mg) were stirred in DMF (3 mL) at room temperature under air (open flask). The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The resultant mixture was extracted with ethyl acetate (3 x 15 mL) and successively washed with brine (1 x 10 mL) and ice-cold water (1 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

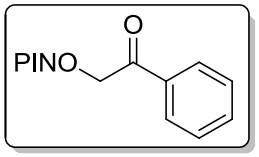
General Procedure for the Oxidation of 3 to Esters 4. To a solution of **3** (0.14 mmol) CH_2Cl_2 (2 mL) was added $NaHCO_3$ (0.18 mmol, 16 mg) and *m*CPBA (0.21 mmol, 36 mg) at 0 °C and the resultant mixture was stirred at room temperature. The progress of the reaction was monitored by TLC. After completion, the solvent was evaporated on a rotary evaporator and the residue was treated with $NaHCO_3$ solution (3 mL). The mixture was extracted with ethyl acetate (3 x 15 mL) and washed with brine (1 x 10 mL) and water (1 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

General Procedure for the Hydrolysis of 3 to *β*-Ketoalkoxyamines 5. To a solution of **3** (0.37 mmol) in MeOH/$CHCl_3$ (1:3) was added hydrazine monohydrate (1.11 mmol, 56 mg). The reaction mixture was stirred at 0 °C for 5 minutes under air. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion, the colorless precipitate was filtered and washed with a 1:5 mixture of Et_2O:hexane (10 mL). The combined solution was evaporated under reduced pressure and the resultant oil was dissolved in Et_2O (4 mL). When the solution was subjected to dry HCl gas, a colorless precipitate was formed that was filtered and washed with Et_2O (3 x 10 mL) to give the pure HCL salt of **5**.[27]

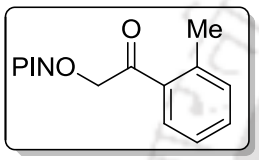
1.4 Characterization Data



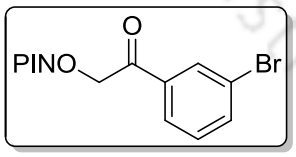
2-(2-Oxo-2-*p*-tolylethoxy)isoindoline-1,3-dione 3a. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 163-164 °C; yield 70% (206 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.85-7.84 (m, 2H), 7.76-7.75 (m, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 5.42 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.9, 163.1, 145.2, 134.7, 132. 0, 129.6, 128.9, 128.5, 123.7, 78.5, 21.8; FT-IR (KBr) 2955, 2909, 1788, 1730, 1701, 1606, 1467, 1430, 1357, 1244, 1185, 1129, 956, 876, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_4$: 296.0923, found: 296.0918.



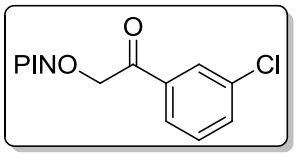
2-(2-Oxo-2-*p*-phenylethoxy)isoindoline-1,3-dione 3b. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.43; colorless solid; mp 137-138 °C; yield 65% (183 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.85-7.84 (m, 2H), 7.76-7.75 (m, 2H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 5.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 163.1, 134.8, 134.5, 134.2, 129.0, 128.9, 128.4, 123.8, 78.6; FT-IR (KBr) 3060, 2979, 2939, 1793, 1723, 1447, 1378, 1226, 1186, 1136, 1059, 967, 875, 697 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{11}NO_4$: 282.0766, found: 282.0769.



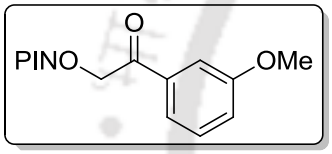
2-(2-Oxo-2-*o*-tolylethoxy)isoindoline-1,3-dione 3c. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 127-128 °C; yield 80% (236 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.84 (m, 2H), 7.76-7.74 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.30 (t, *J* = 7.2 Hz, 2H), 5.33 (s, 2H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 163.1, 139.7, 134.7, 134.2, 132.6, 132.4, 129.3, 128.8, 125.8, 123.7, 79.5, 21.4; FT-IR (KBr) 2923, 1794, 1745, 1725, 1690, 1602, 1466, 1373, 1187, 1044, 978, 877, 695cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_4$: 296.0923, found: 296.0923.



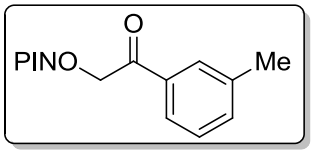
2-(2-(3-Bromophenyl)-2-oxoethoxy)isoindoline-1,3-dione 3d. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.45; colorless solid; mp 152-153 °C; yield 64% (230 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.86-7.84 (m, 2H), 7.77–7.73 (m, 3H), 7.39 (t, *J* = 8.0 Hz, 1H), 5.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2, 163.0, 137.0, 136.2, 134.9, 131.5, 130.5, 128.8, 127.1, 123.9, 123.2, 78.7; FT-IR (KBr) 3091, 2923, 1787, 1728, 1701, 1563, 1463, 1426, 1358, 1187, 1131, 1067, 995, 876, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{10}BrNO_4$: 359.9871, found: 359.9873.



2-(2-(3-Chlorophenyl)-2-oxoethoxy)isoindoline-1,3-dione 3e. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.45; colorless solid; mp 139-140 °C; yield 62% (202 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.84-7.82 (m, 2H), 7.77-7.75 (m, 2H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 5.38 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.4, 163.1, 136.0, 135.4, 134.9, 134.2, 130.3, 128.9, 128.7, 126.7, 123.9, 78.8; FT-IR (KBr) 2925, 1788, 1727, 1696, 1374, 1360, 1230, 1187, 1137, 1081, 983, 877, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{10}ClNO_4$: 316.0377, found: 316.0377.

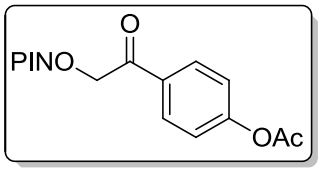


2-(2-(3-Methoxyphenyl)-2-oxoethoxy)isoindoline-1,3-dione 3f. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.40; colorless solid; mp 158-159 °C; yield 82% (255 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.83 (m, 2H), 7.77-7.74 (m, 2H), 7.55-7.54 (m, 2H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.16-7.14 (m, 1H), 5.44 (s, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.1, 163.1, 160.0, 135.7, 134.8, 129.9, 128.9, 123.8, 121.0, 120.9, 112.4, 78.6, 55.6; FT-IR (KBr) 3096, 2932, 1786, 1726, 1697, 1595, 1463, 1358, 1267, 1187, 1172, 1131, 1017, 1002, 960, 875, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_5$: 312.0872, found: 312.0868.

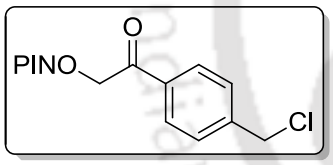


2-(2-Oxo-2-*m*-tolylethoxy)isoindoline-1,3-dione 3g. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; colorless solid; mp 140-141 °C; yield 64% (189 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.84 (m, 2H), 7.81 (s, 1H), 7.79 (d, *J* = 7.8 Hz, 1H), 7.77-7.75 (m, 2H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 5.44 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 163.1, 138.8, 135.0, 134.8, 134.5,

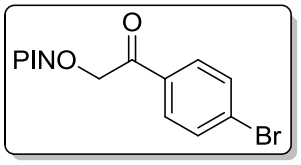
128.9, 128.89, 128.85, 125.5, 123.8, 78.5, 21.4; FT-IR (KBr) 3096, 2922, 1787, 1726, 1696, 1603, 1462, 1356, 1254, 1187, 1171, 1129, 1068, 1022, 979, 876, 704 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_4$: 296.0923, found: 296.0929.



4-(2-(1,3-Dioxoisoindolin-2-yloxy)acetyl)phenyl acetate 3h. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.34; colorless solid; mp 164-165 °C; yield 36% (122 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.0 Hz, 2H), 7.85-7.84 (m, 2H), 7.77-7.75 (m, 2H), 7.26 (d, *J* = 9.2 Hz, 2H), 5.41 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.3, 168.8, 163.2, 155.3, 134.9, 132.2, 130.4, 129.0, 123.9, 122.3, 78.7, 21.3; FT-IR (KBr) 3089, 2960, 1788, 1757, 1741, 1694, 1598, 1467, 1366, 1203, 1166, 1135, 1064, 1012, 987, 851, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{18}H_{13}NO_6$: 340.0821, found: 340.0817.

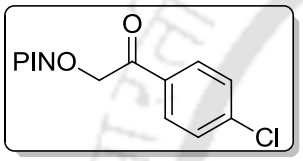


2-(2-(4-(Chloromethyl)phenyl)-2-oxoethoxy)isoindoline-1,3-dione 3i. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 182-183 °C; yield 68% (224 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 2H), 7.86-7.84 (m, 2H), 7.77-7.75 (m, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 5.41 (s, 2H), 4.62 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.9, 163.1, 143.6, 134.9, 134.4, 129.08, 129.06, 128.9, 123.9. 78.7, 45.3; FT-IR (KBr) 2925, 2853, 1791, 1745, 1727, 1692, 1609, 1359, 1245, 1186, 1132, 1082, 980, 878, 694 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{12}ClNO_4$: 330.0533, found: 330.0524.



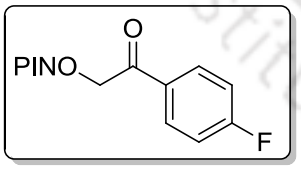
2-(2-(4-Bromophenyl)-2-oxoethoxy)isoindoline-1,3-dione 3j.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.45; colorless solid; mp 166-167 °C; yield 59% (212 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.85-7.84 (m, 2H), 7.77-7.75 (m, 2H), 7.66 (d, *J* = 9.0 Hz, 2H), 5.35 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.7, 163.1, 134.9, 133.4, 132.4, 130.2, 129.6, 128.9, 123.9, 78.8; FT-IR (KBr) 2923, 1789, 1729, 1691, 1585, 1464, 1363, 1240, 1189, 1174, 1138, 1069, 986, 877, 696 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{10}BrNO_4$: 359.9871, found: 359.9875.



2-(2-(4-Chlorophenyl)-2-oxoethoxy)isoindoline-1,3-dione 3k.

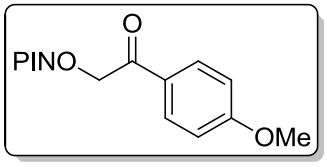
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.45; colorless solid; mp 164-165 °C; yield 61% (192 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.85-7.84 (m, 2H), 7.77-7.76 (m, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 5.36 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.5, 163.1, 140.8, 134.9, 133.0, 130.1, 129.4, 128.9, 123.9, 78.8; FT-IR (KBr) 3083, 2972, 2928, 1789, 1727, 1706, 1587, 1402, 1373, 1227, 1184, 1133, 1089, 967, 803, 696 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{10}ClNO_4$: 316.0377, found: 316.0370.



2-(2-(4-Fluorophenyl)-2-oxoethoxy)isoindoline-1,3-dione 3l.

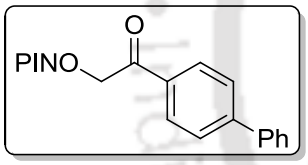
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.46; colorless solid; mp 155-156 °C; yield 55% (164 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10-8.08 (m, 2H), 7.86-7.83 (m, 2H), 7.78-7.75 (m, 2H), 7.20-7.16 (m, 2H), 5.37 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 167.7 (d, *J* = 255.5 Hz), 163.1, 134.9, 131.5, 131.4, 128.9, 123.9, 116.3 (d, *J* = 22.1 Hz), 78.8; FT-IR (KBr) 3068, 2978, 2942, 1790, 1722, 1597, 1507, 1410, 1377, 1220, 1185,

1133, 1062, 972, 876, 697 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{16}H_{10}FNO_4$: 300.0672, found: 300.0672.



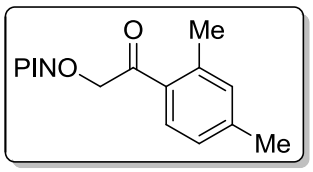
2-(2-(4-Methoxyphenyl)-2-oxoethoxy)isoindoline-1,3-dione 3m.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.40; colorless solid; mp 145-146 °C; yield 59% (183 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.0 Hz, 2H), 7.85-7.84 (m, 2H), 7.76-7.74 (m, 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 5.38 (s, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9, 164.4, 163.2, 134.8, 131.0, 129.0, 127.7, 123.8, 114.2, 78.6, 55.7; FT-IR (KBr) 3061, 2937, 2915, 2844, 1789, 1727, 1689, 1602, 1513, 1431, 1372, 1247, 1175, 1129, 1062, 1014, 981, 876, 698 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_5$: 312.0872, found: 312.0874.



2-(2-(Biphenyl-4-yl)-2-oxoethoxy)isoindoline-1,3-dione 3n.

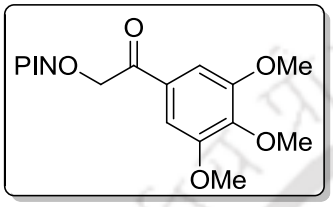
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; colorless solid; mp 165-166 °C; yield 50% (178 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.8 Hz, 2H), 7.85-7.83 (m, 2H), 7.76-7.73 (m, 2H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.62-7.60 (m, 2H), 7.47-7.44 (m, 2H), 7.41 (d, *J* = 7.2 Hz, 1H), 5.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.0, 163.2, 146.9, 139.8, 134.8, 133.3, 129.1, 129.0, 128.9, 128.6, 127.6, 127.4, 123.9, 78.7; FT-IR (KBr) 3026, 2922, 1793, 1744, 1686, 1603, 1466, 1357, 1236, 1188, 1131, 1080, 1062, 980, 876, 769, 693 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{22}H_{15}NO_4$: 358.1079, found: 358.1073.



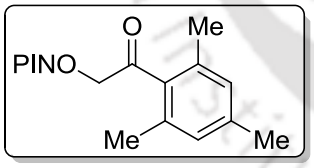
2-(2-(2,4-Dimethylphenyl)-2-oxoethoxy)isoindoline-1,3-dione 3o.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.43; colorless solid; mp 156-157

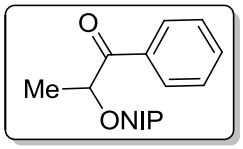
°C; yield 68% (210 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.83 (m, 2H), 7.76-7.75 (m, 2H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.10 (s, 2H), 5.32 (s, 2H), 2.54 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 163.2, 143.5, 140.3, 134.8, 133.3, 131.4, 129.7, 129.0, 126.5, 123.8, 79.5, 21.6; FT-IR (KBr) 3098, 2924, 2854, 1787, 1733, 1691, 1609, 1465, 1371, 1357, 1224, 1187, 1138, 1081, 1052, 986, 877, 703 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{18}H_{15}NO_4$: 310.1079, found: 310.1068.



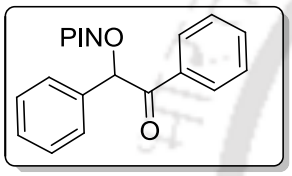
2-(2-Oxo-2-(3,4,5-trimethoxyphenyl)ethoxy)isoindoline-1,3-dione 3p. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.38; colorless solid; mp 147-148 °C; yield 66% (245 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.85 (m, 2H), 7.78-7.76 (m, 2H), 7.36 (s, 2H), 5.35 (s, 2H), 3.94 (s, 6H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 163.2, 153.4, 143.6, 134.9, 129.7, 128.9, 123.9, 106.3, 79.0, 61.1, 56.6; FT-IR (KBr) 2927, 1788, 1734, 1692, 1585, 1466, 1416, 1324, 1237, 1186, 1127, 1081, 1018, 991, 877, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{19}H_{17}NO_7$: 372.1083, found: 372.1088.



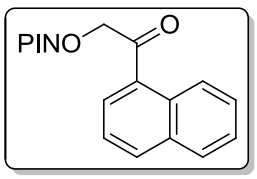
2-(2-Mesityl-2-oxoethoxy)isoindoline-1,3-dione 3q. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 167-168 °C; yield 60% (194 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.83 (m, 2H), 7.76-7.75 (m, 2H), 6.85 (s, 2H), 5.07 (s, 2H), 2.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 162.9, 139.8, 135.2, 134.8, 134.0, 128.8, 128.7, 123.7, 80.8, 21.2, 19.2; FT-IR (KBr) 2964, 2924, 2855, 1788, 1732, 1698, 1608, 1425, 1356, 1230, 1184, 1137, 1081, 1013, 992, 878, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{19}H_{17}NO_4$: 324.1236, found: 324.1238.



2-(1-Oxo-1-phenylpropan-2-yloxy)isoindoline-1,3-dione 3r. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 179-180 °C; yield 61% (180 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.8 Hz, 2H), 7.82-7.80 (m, 2H), 7.74-7.73 (m, 2H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 5.74 (q, *J* = 6.6 Hz, 1H), 1.68 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.5, 163.8, 134.9, 134.8, 133.9, 129.4, 128.9, 128.8, 123.8, 83.8, 16.3; FT-IR (KBr) 3059, 2932, 2854, 1788, 1737, 1679, 1595, 1451, 1374, 1232, 1188, 1129, 1036, 977, 877, 698 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_4$: 296.0923, found: 296.0917.

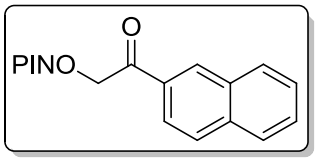


2-(2-Oxo-1,2-diphenylethoxy)isoindoline-1,3-dione 3s. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; colorless solid; mp 165-166 °C; yield 45% (161 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.78-7.74 (m, 2H), 7.72-7.69 (m, 2H), 7.62-7.60 (m, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.36-7.35 (m, 3H), 6.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.9, 163.4, 134.9, 134.6, 133.8, 132.8, 130.2, 129.6, 129.3, 129.1, 128.9, 128.8, 123.7, 88.6; FT-IR (KBr) 3085, 3062, 2930, 1788, 1733, 1687, 1597, 1448, 1377, 1347, 1226, 1188, 1134, 1081, 977, 877, 698 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{22}H_{15}NO_4$: 358.1079, found: 358.1075.

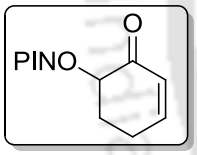


2-(2-(Naphthalen-1-yl)-2-oxoethoxy)isoindoline-1,3-dione 3t. Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.42; colorless solid; mp 174-175 °C; yield 55% (182 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, *J* = 8.4 Hz, 1H), 8.05-8.03 (m, 2H), 7.87-7.82 (m, 3H), 7.75-7.72 (m, 2H), 7.61-7.59 (m, 1H), 7.55-7.50 (m, 2H), 5.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 163.2, 134.8, 134.3, 134.2, 131.9, 130.6,

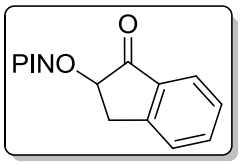
129.5, 129.0, 128.78, 128.74, 126.9, 125.9, 124.4, 123.9, 79.7; FT-IR (KBr) 3053, 2926, 1782, 1725, 1689, 1508, 1462, 1419, 1361, 1245, 1185, 1108, 1079, 1032, 981, 876, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{20}H_{13}NO_4$: 332.0923, found: 332.0922.



2-(2-(Naphthalen-2-yl)-2-oxoethoxy)isoindoline-1,3-dione 3u. Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 173-174 °C; yield 57% (189 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.03-8.00 (m, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.92-7.82 (m, 4H), 7.77-7.73 (m, 2H), 7.63-7.59 (m, 1H), 7.57-7.53 (m, 1H), 5.55 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.4, 163.2, 136.2, 134.9, 132.6, 131.9, 130.9, 130.0, 129.2, 129.08, 129.03, 128.1, 127.2, 123.9, 123.7, 78.9; FT-IR (KBr) 3064, 2929, 1789, 1732, 1694, 1466, 1375, 1190, 1139, 1083, 1062, 991, 878, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{20}H_{13}NO_4$: 332.0923, found: 332.0921.

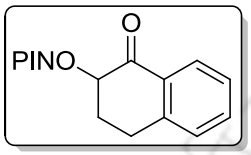


2-(2-Oxocyclohexyloxy)isoindoline-1,3-dione 3w. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.49; yellow solid; mp 110-111 °C; yield 55% (141 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.79-7.77 (m, 2H), 7.16-7.14 (m, 1H), 6.12 (d, *J* = 10.2 Hz, 1H), 5.04-5.02 (m, 1H), 2.80-2.76 (m, 1H), 2.49-2.44 (m, 1H), 2.42-2.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.9, 164.2, 145.6, 135.0, 131.9, 128.9, 123.9, 81.0, 34.7, 28.0; FT-IR (KBr) 3046, 2927, 1788, 1731, 1681, 1465, 1376, 1251, 1187, 1127, 1081, 1016, 983, 877, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{14}H_{11}NO_4$: 258.0766, found: 258.0774.

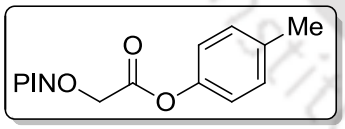


2-(1-Oxo-2,3-dihydro-1*H*-inden-2-yloxy)isoindoline-1,3-dione 3x. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.47; yellow solid; mp 191-192

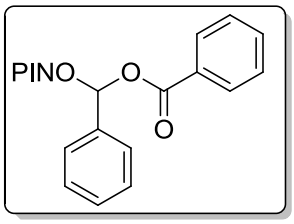
°C; yield 34% (100 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.86 (m, 2H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.77-7.76 (m, 2H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 5.13-5.12 (m, 1H), 3.65-3.61 (m, 1H), 3.44-3.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 163.4, 151.0, 136.3, 134.8, 134.7, 129.1, 128.4, 126.8, 125.1, 123.9, 83.0, 32.7; FT-IR (KBr) 3091, 3067, 2938, 1787, 1729, 1713, 1604, 1466, 1420, 1365, 1298, 1252, 1183, 1117, 1082, 1014, 994, 968, 874, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{11}NO_4$: 294.0766, found: 294.0765.



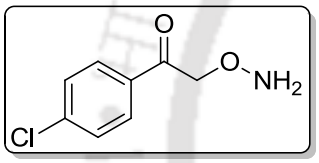
2-(1-Oxo-1,2,3,4-tetrahydronaphthalen-2-yloxy)isoindoline-1,3-dione 3y. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.46; yellow solid; mp 170-171 °C; yield 55% (169 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.8 Hz, 1H), 7.84-7.83 (m, 2H), 7.75-7.73 (m, 2H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 4.96-4.94 (m, 1H), 3.36-3.31 (m, 1H), 3.04-2.99 (m, 1H), 2.63-2.57 (m, 1H), 2.55-2.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 163.4, 143.4, 134.6, 134.2, 131.4, 129.0, 128.8, 128.1, 127.2, 123.8, 84.5, 28.4, 25.9; FT-IR (KBr) 3070, 2945, 2844, 1790, 1734, 1679, 1597, 1454, 1352, 1295, 1241, 1184, 1152, 1116, 1063, 1027, 978, 878, 703 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{18}H_{13}NO_4$: 308.0923, found: 308.0927.



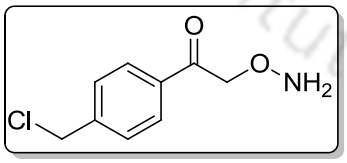
***p*-Tolyl 2-(1,3-dioxoisoindolin-2-yloxy)acetate 4a.** Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.55; colorless solid; mp 148-149 °C; yield 85% (37 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.77-7.76 (m, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 5.04 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 163.1, 147.8, 136.2, 134.9, 130.2, 129.0, 124.0, 121.1, 73.3, 21.0; FT-IR (KBr) 2973, 2939, 2863, 1771, 1736, 1507, 1466, 1430, 1375, 1212, 1199, 1187, 1140, 1048, 877, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{17}H_{13}NO_5$: 312.0872, found: 312.0876.



***p*-Tolyl 2-(1,3-dioxoisoindolin-2-yloxy)-2-phenylacetate 4b.** Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.58; colorless solid; mp 123-124 °C; yield 87% (45 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.2 Hz, 2H), 7.85-7.81 (m, 4H), 7.75-7.72 (m, 2H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.53 (s, 1H), 7.49-7.46 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6, 163.2, 134.7, 134.0, 133.5, 130.5, 130.4, 129.1, 129.0, 128.84, 128.80, 127.5, 124.0, 100.7; FT-IR (KBr) 2922, 2850, 1787, 1741, 1452, 1377, 1262, 1180, 1137, 1088, 1069, 957, 873, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{22}H_{15}NO_5$: 374.1028, found: 374.1025.

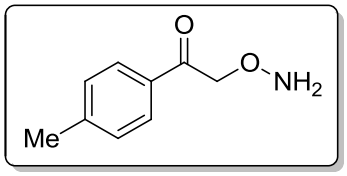


2-(Aminooxy)-1-(4-chlorophenyl)ethanone 5a. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.52; yellow liquid; yield 62% (42 mg); ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.26 (br s, 2H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 5.55 (s, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 193.0, 139.0, 132.4, 129.7, 129.1, 75.6; FT-IR (neat) 3429, 3201, 2887, 2818, 2645, 1683, 1591, 1490, 1471, 1407, 1242, 1091, 1066, 984, 828 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_8ClNO_2$: 186.0322, found: 186.0322.

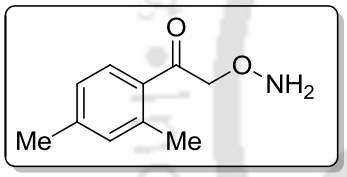


2-(Aminooxy)-1-(4-chlorophenyl)ethanone 5b. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.49; yellow liquid; yield 70% (51 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.25 (br s, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 2H), 5.57 (s, 2H), 4.84 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 193.4, 143.7, 133.4, 129.3, 128.2, 75.7, 45.1; FT-IR (neat) 3433, 2895, 2818, 2610, 1681, 1609, 1472, 1409, 1384, 1267,

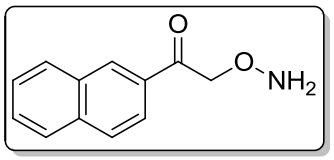
1235, 1067, 985, 678 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_9H_{10}ClNO_2$: 200.0478, found: 200.0472.



2-(Aminooxy)-1-*p*-tolylethanone 5c. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.47; yellow liquid; yield 70% (43 mg); ^1H NMR (600 MHz, DMSO-d_6) δ 11.17 (br s, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 5.52 (s, 2H), 2.39 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 193.4, 144.8, 131.2, 129.5, 127.9, 75.5, 21.2; FT-IR (neat) 3431, 3030, 2919, 2822, 2610, 1680, 1609, 1476, 1408, 1384, 1237, 1186, 1039, 994, 896, 813 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_9H_{11}NO_2$: 166.0868, found: 166.0867.



2-(Aminooxy)-1-(2,4-dimethylphenyl)ethanone 5d. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.45; yellow liquid; yield 72% (48 mg); ^1H NMR (600 MHz, DMSO-d_6) δ 11.18 (br s, 2H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 9.0 Hz, 2H), 5.40 (s, 2H), 2.46 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 196.1, 142.9, 138.6, 132.7, 130.8, 129.3, 126.5, 76.4, 20.9; FT-IR (neat) 3429, 3120, 2920, 2831, 2659, 1678, 1613, 1465, 1403, 1229, 1142, 1059, 982, 830 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{10}H_{14}NO_2$: 180.1025, found: 180.1014.



2-(Aminooxy)-1-(naphthalen-2-yl)ethanone 5e. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.49; yellow liquid; yield 65% (48 mg); ^1H NMR (600 MHz, DMSO-d_6) δ 11.19 (br s, 2H), 8.66 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.97-7.95 (m, 1H), 7.71 (t, *J* = 7.2 Hz, 1H), 7.66 (t, *J* =

7.8 Hz, 1H), 5.68 (s, 2H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 193.8, 135.4, 131.9, 130.0, 129.6, 129.1, 128.6, 127.7, 127.2, 122.9, 75.7; FT-IR (neat) 3433, 2923, 2854, 2662, 1678, 1627, 1468, 1403, 1378, 1019, 820, 744 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{12}H_{11}NO_2$: 202.0868, found: 202.0868.

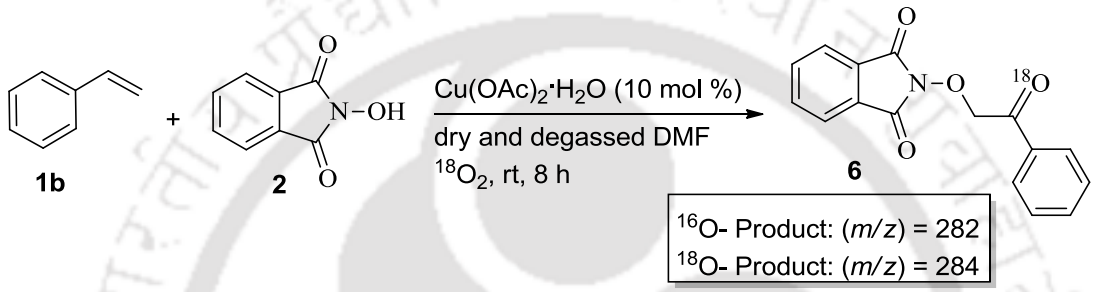
Crystal Data for 3d at 298(2) K

Identification code	**3d**
Empirical formula	$C_{16}H_{10}BrNO_4$
Formula weight	360.15
Crystal habit, colour	block / colorless
Crystal size, mm^3	0.41 x 0.37 x 0.23
Temperature, *T*/K	298(2)
Wavelength, *λ*/Å	0.71073
Crystal system	monoclinic
Space group	'$P2_1/c$'
Unit cell dimensions	a = 12.4447(11) Å
	b = 15.6502(13) Å
	c = 7.9646(7) Å
	$\alpha = \gamma$ = 90.00°,
	β = 105.739(6)°
Volume, *V*/Å^3	1493.0(2)
Z	4
Calculated density, Mg·m^{-3}	1.602
Absorption coefficient, *μ*/mm^{-1}	2.770
F(000)	720
θ range for data collection	1.70 to 28.33°
Limiting indices	$-16 \le h \le 16, -20 \le k \le 19, -10 \le l \le 10$
Reflection collected / unique	25315 / 3667 [*R*(int) = 0.0735]
Completeness to *θ*	98.5 % (*θ* = 28.33°)
Max. and min. transmission	0.529 and 0.334

Refinement method	'SHELXL–97 (Sheldrick, 1997)'
Data / restraints / parameters	3667 / 0 / 119
Goodness-of-fit on F^2	1.052
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0738, *wR*2 = 0.1947
R indices (all data)	*R*1 = 0.1404, *wR*2 = 0.2308

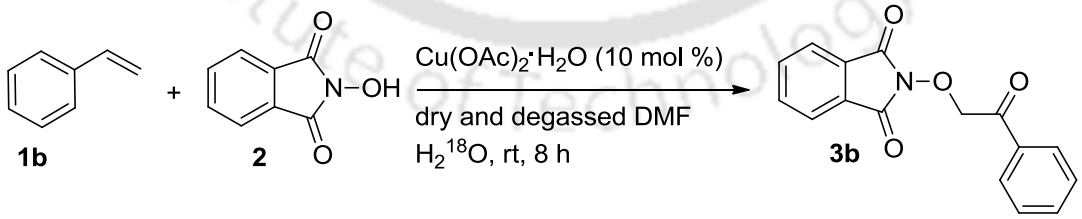
1.5 Isotope Labeling Experiments

$^{18}O_2$ Experiment



A schlenk tube was charged with a magnetic bar, styrene (0.75 mmol, 78 mg), NHPI (0.25 mmol, 40.7 mg), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol, 5 mg) and dry DMF (1 mL) in a glove box. The reaction mixture was then removed from the glove box and allowed to freeze using liquid N_2 and degassed. The solid was allowed to melt and the solution was purged with $^{18}O_2$ for 1-2 times and the solution was allowed to stir at room temperature. After 8 h, a small amount of the reaction mixture was taken out and diluted with 1 mL of CH_3CN and analyzed by HRMS (Figure 2).

$H_2{}^{18}O$ Experiment



A schlenk tube was charged with a magnetic bar, styrene (0.75 mmol, 78 mg), NHPI (0.25 mmol, 40.7 mg), $Cu(OAc)_2 \cdot H_2O$ (0.025 mmol, 5 mg), dry DMF (1 mL) and $H_2{}^{18}O$ **(**5 µL) in glove box. The reaction was removed from the glove box, purged with normal O_2 balloon and

stirred at room temperature. After 8 h, a small amount of reaction mixture was taken out and diluted with CH_3CN (1 mL) and analyzed by HRMS (Figure 3).

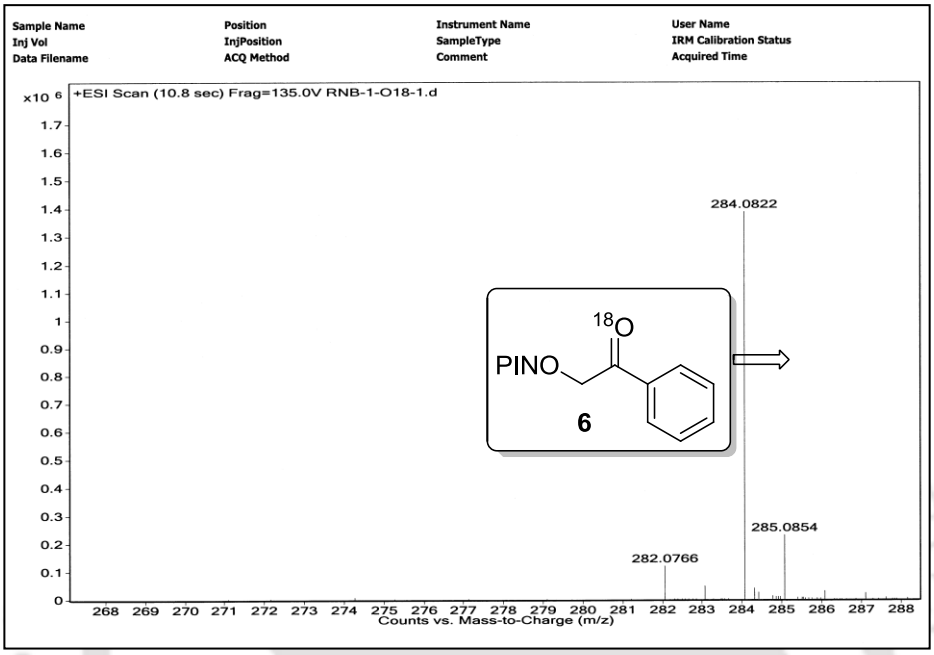


Figure 2. HRMS Spectra of ^{18}O product

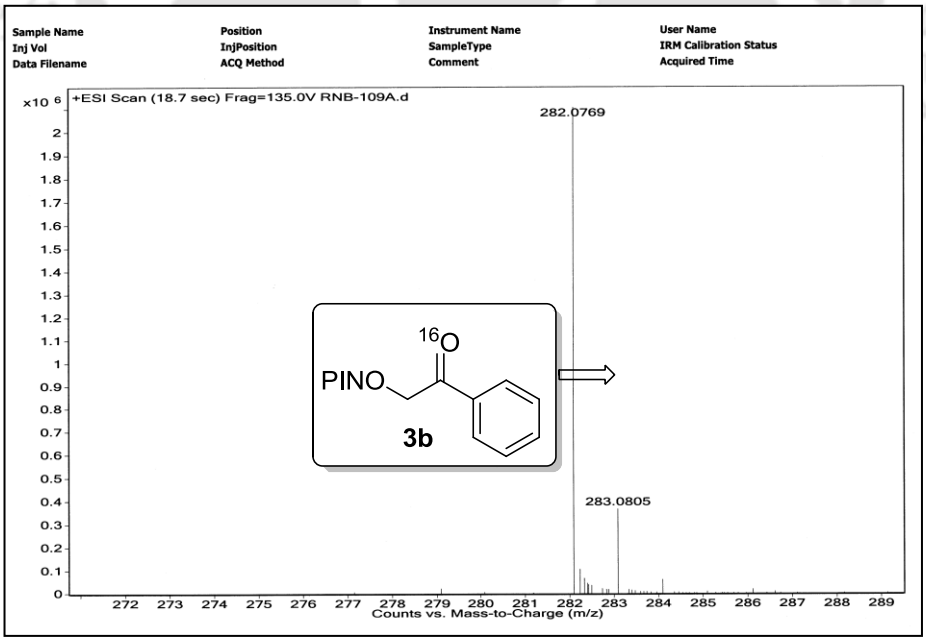


Figure 3. HRMS Spectra of ^{16}O product

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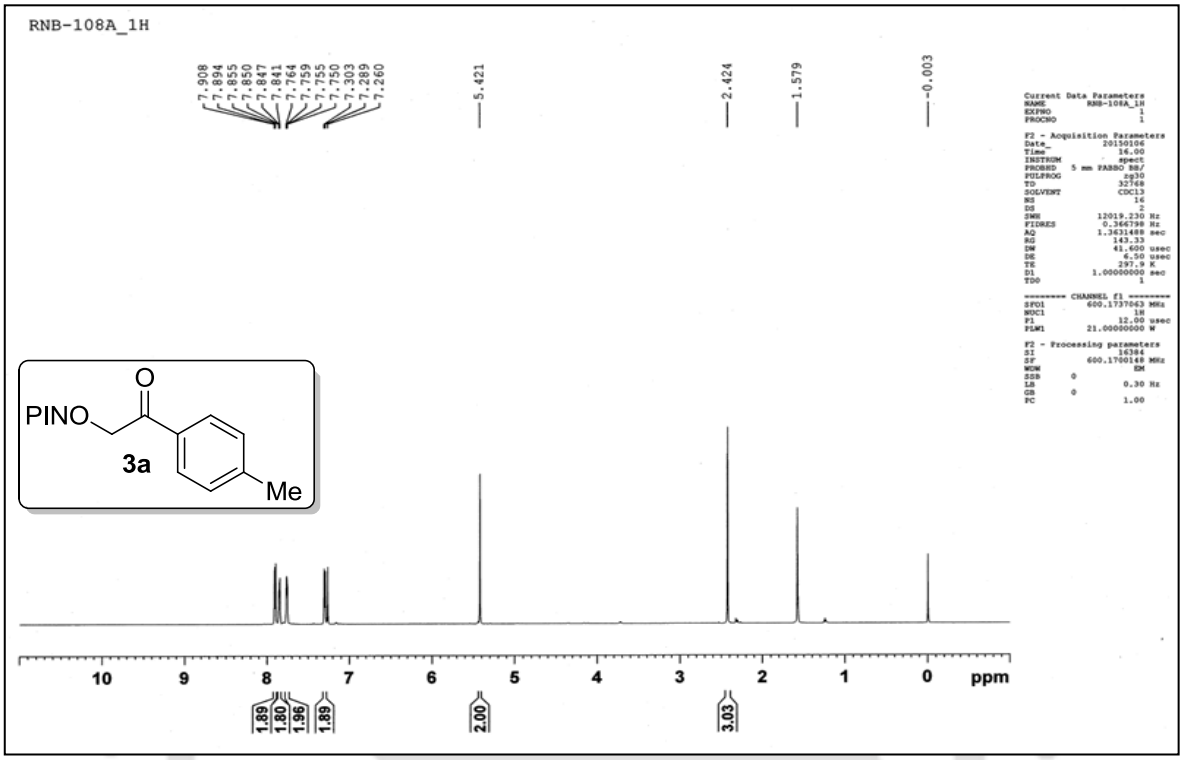
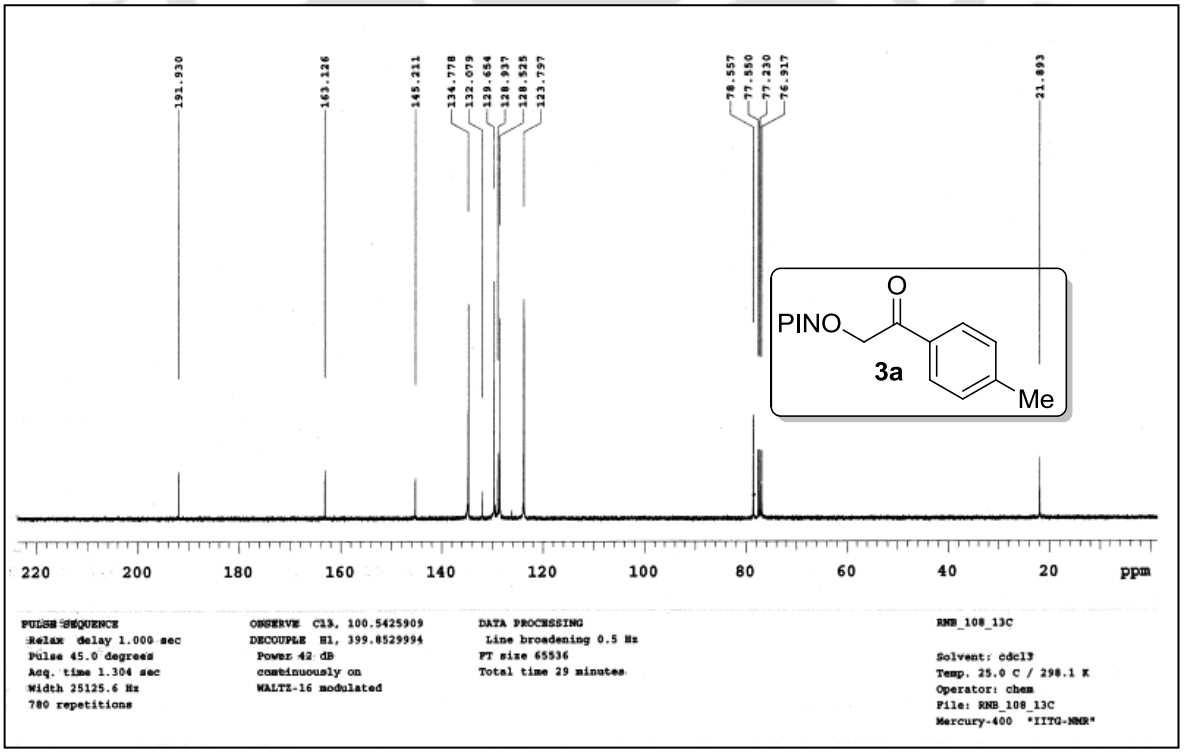
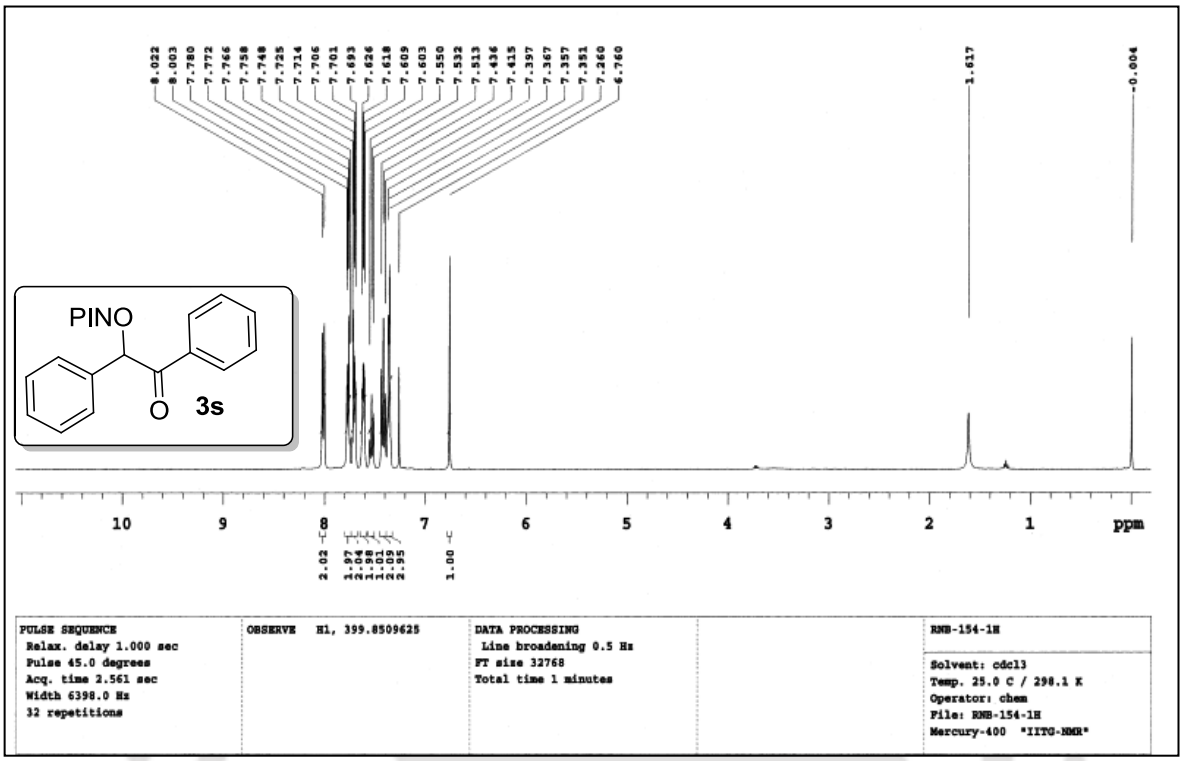
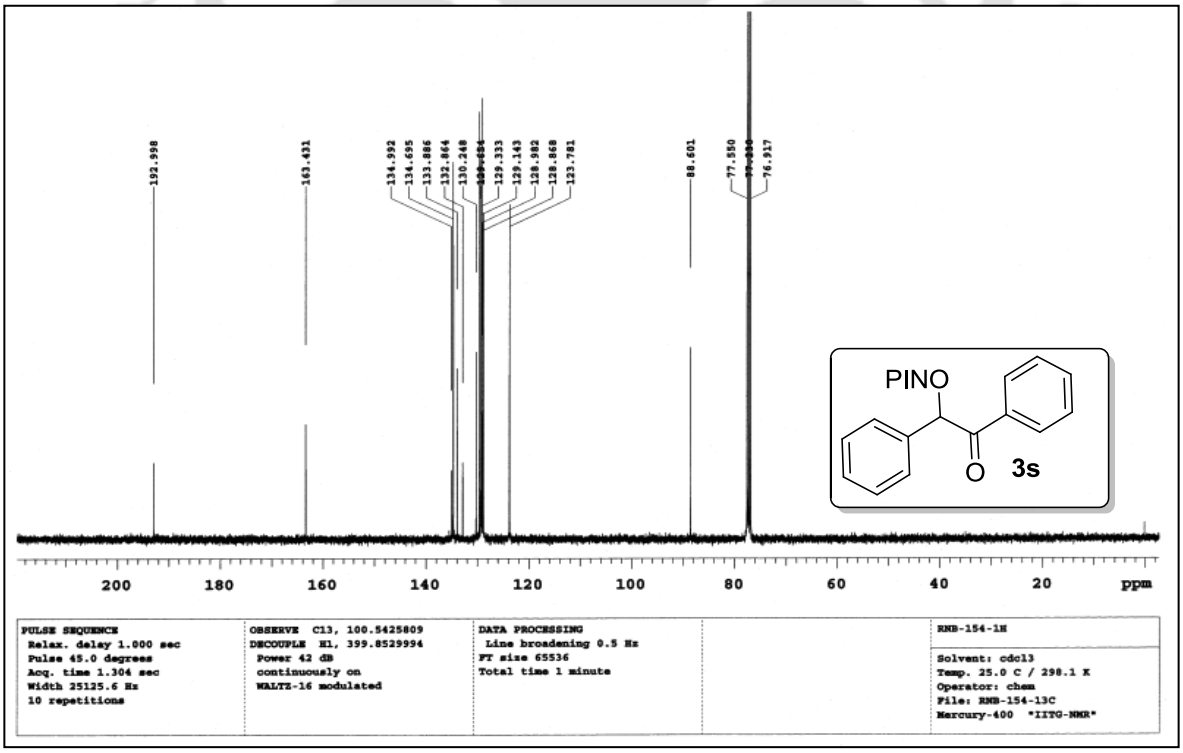
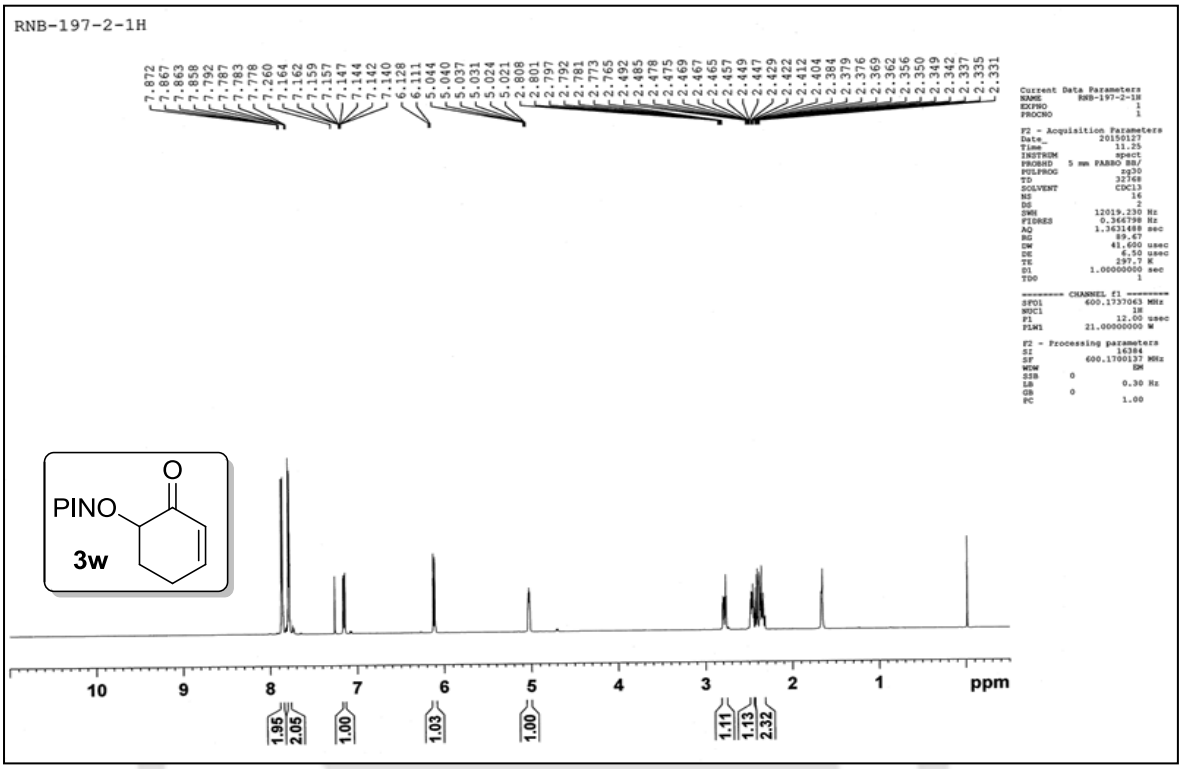
1.7 Selected NMR Spectra

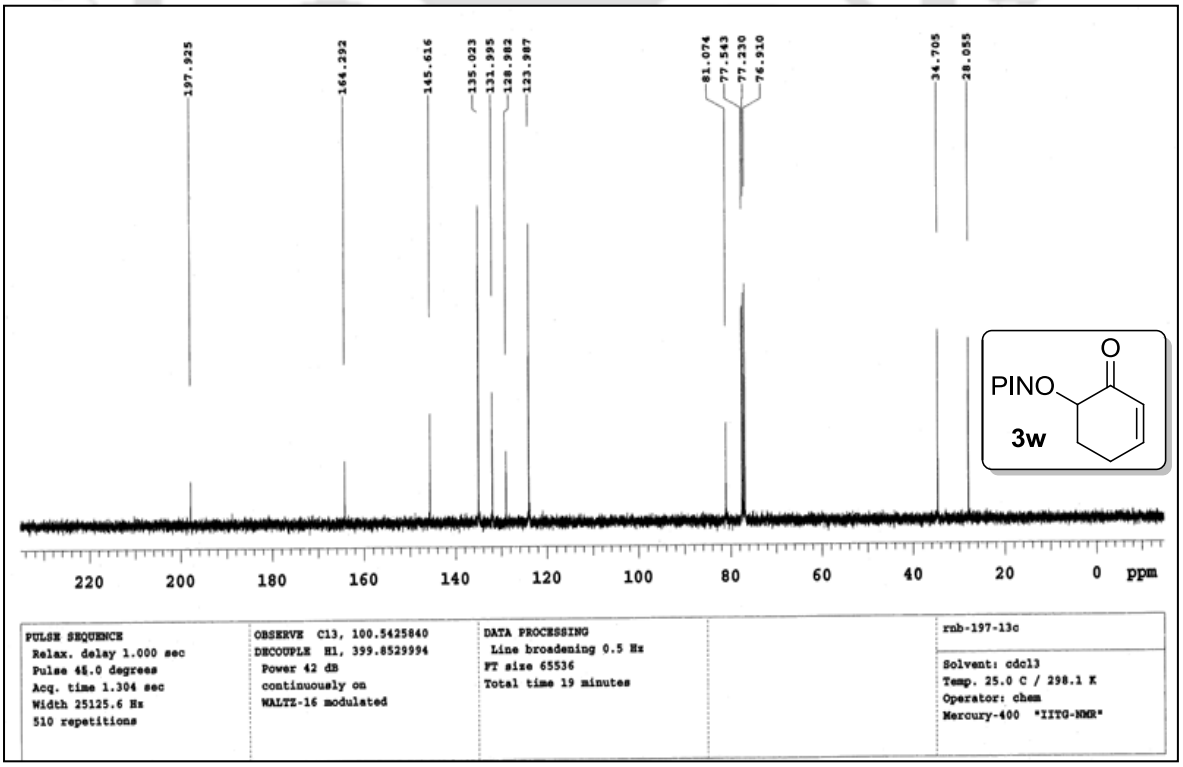


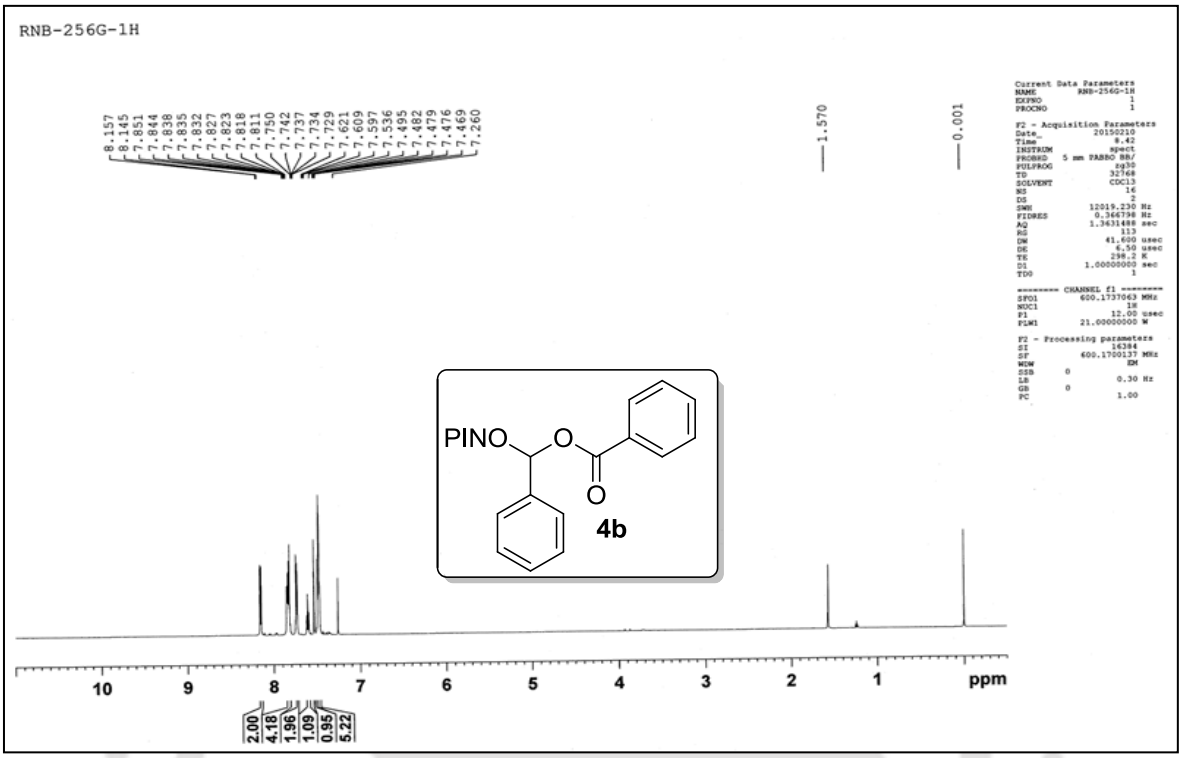


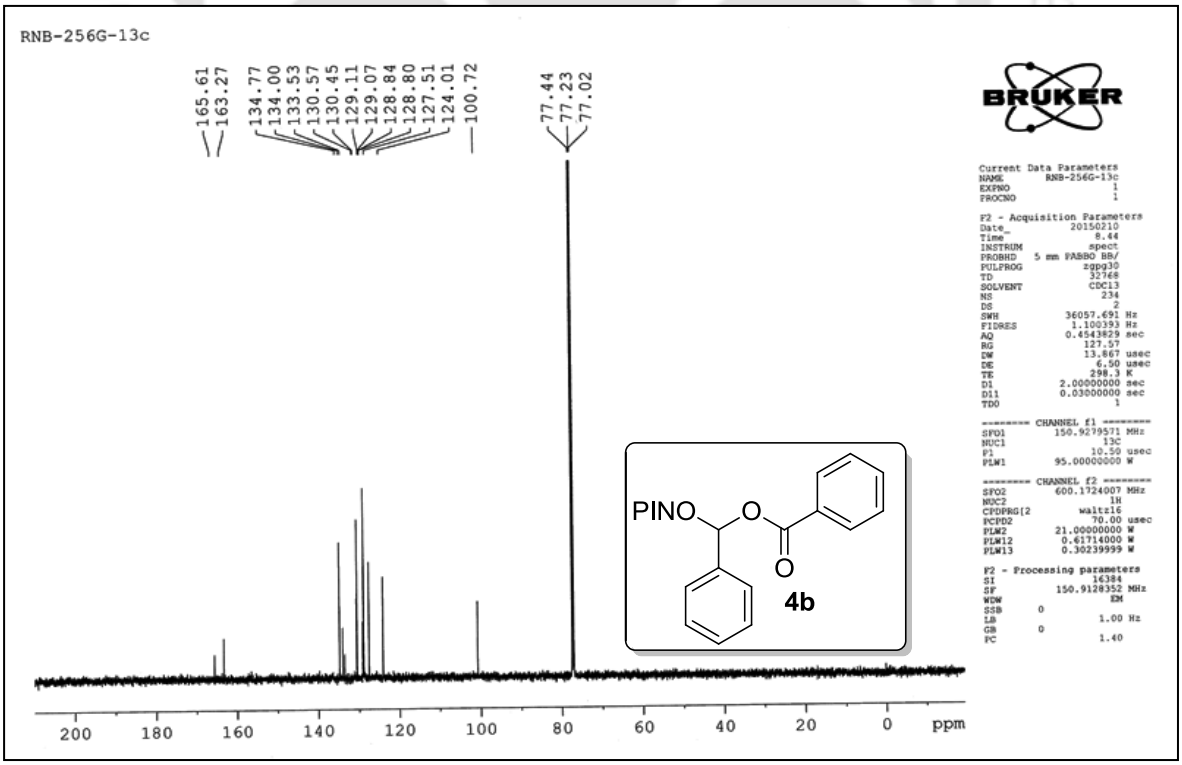


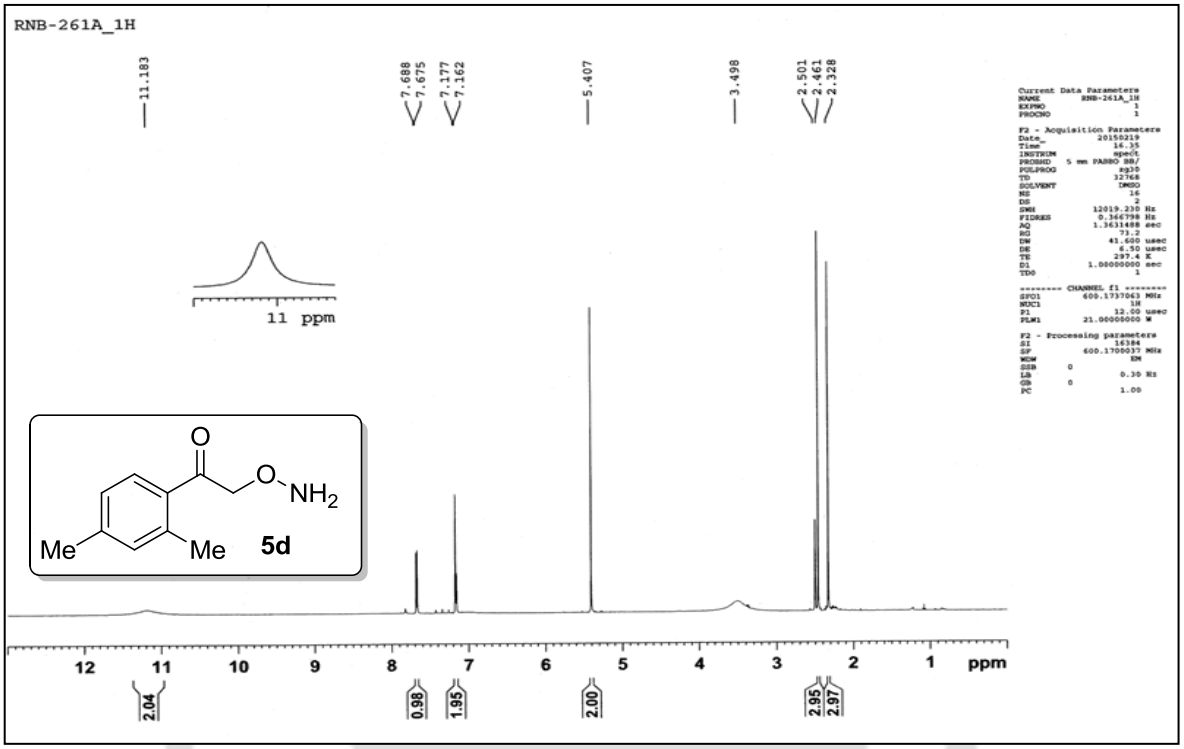


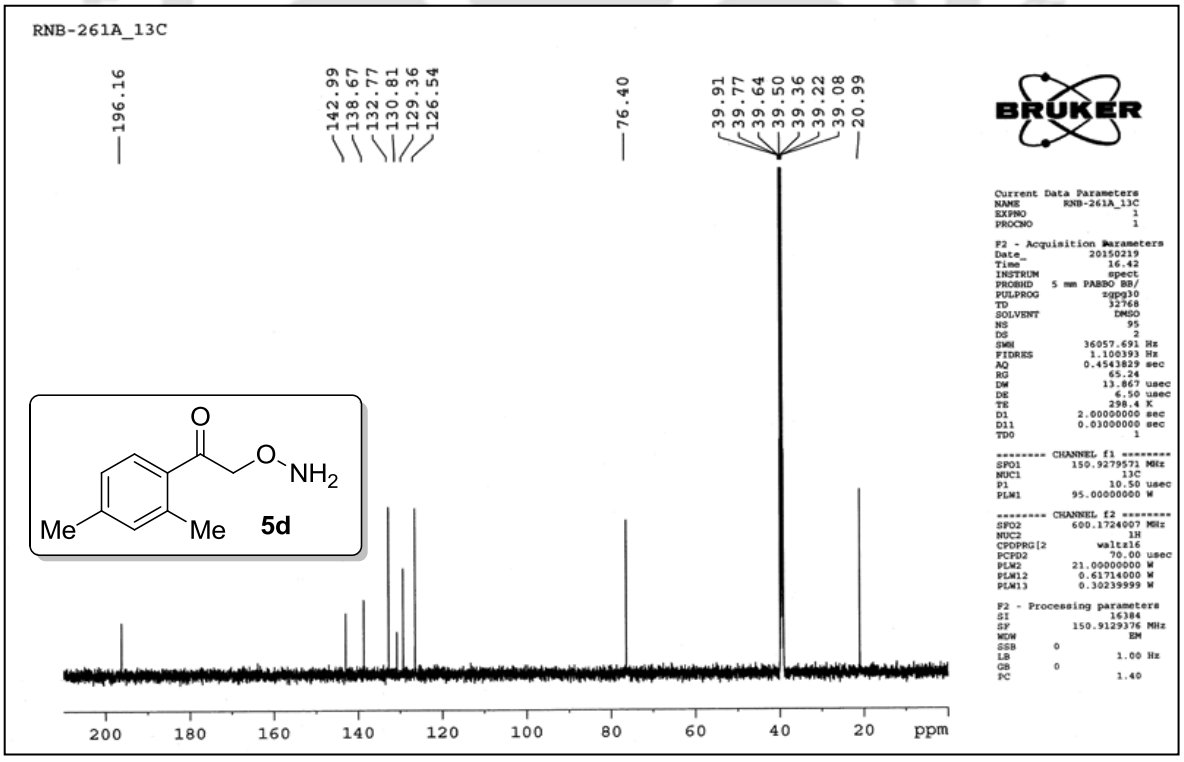












Chapter II

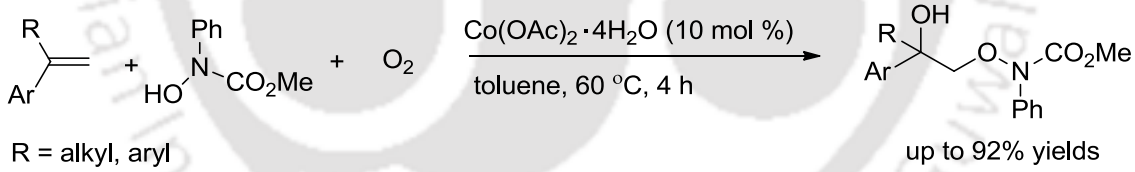
Iron-Catalyzed Aerobic Dioxygenation of Alkenes with *N*-Hydroxylamines

Iron has recently tempted considerable attention in synthetic organic chemistry as it is non-toxic, inexpensive, environmentally benign and second most abundant (4.7 wt %) element in the earth crust.[1] In addition, iron-containing enzymes play important role in biological systems[2] and several functional models containing iron complexes[3] have thus been developed for the formation of carbon-heteroatom bonds as the replacement of expensive transition metals. Further, $Fe(NO_3)_3{\cdot}9H_2O$ is well known to generate radical from organic substrate during oxidation in presence of molecular oxygen.[4] Therefore, exploration of iron based catalytic systems for the sustainable dioxygenation of alkenes using air would be valuable.

2.1 Literature

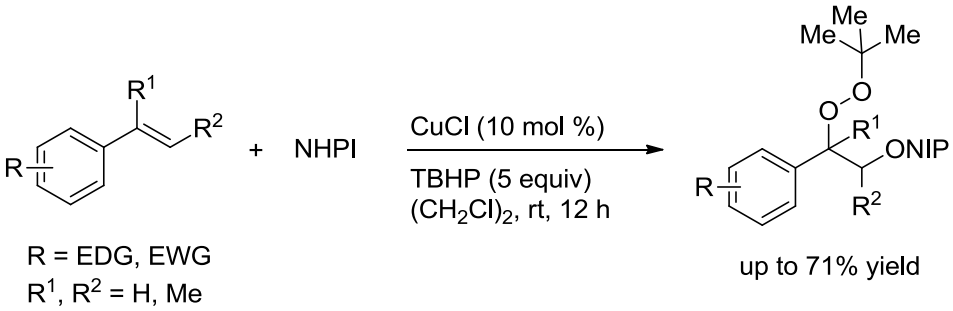
2.1.1 Metal-Catalyzed Aerobic Radical Dioxygenation of Alkenes

Lei and co-workers reported a Co-catalyzed radical dioxygenation of 1,1,-disubstituted styrenes with molecular oxygen using *N*-hydroxamic acid to produce α-oxo-tertiary alcohols (Scheme 1).[5]



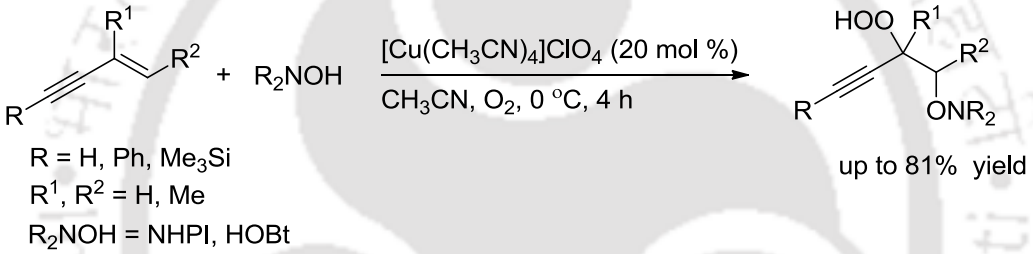
Scheme 1. Co-Catalyzed Aerobic Dioxygenation of 1,1-Disubstituted Styrenes

A Cu-catalyzed oxidation of styrenes with *tert*-butyl hydroperoxide (TBHP) employing NHPI is demonstrated at room temperature to provide α-oxygenated peroxides (Scheme 2).[6] The reaction involves a radical addition process and TEMPO is used for trapping the radical intermediate.



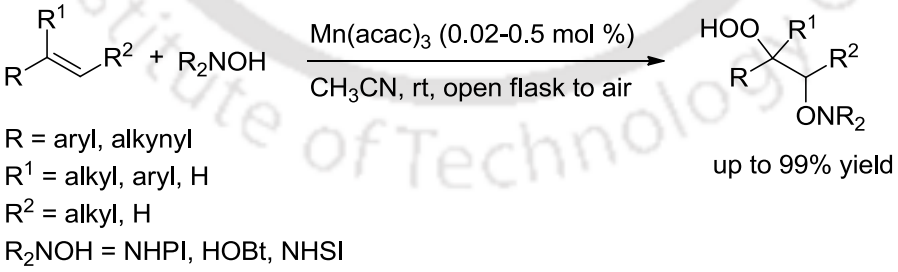
Scheme 2. Cu-Catalyzed Synthesis of Peroxides

Woerpel and co-workers described a Cu-catalyzed radical oxygenation of 1,3-enynes with NHPI and HOBt in the presence molecular oxygen to yield propargyl hydroperoxides (Scheme 3).[7] Protection of the hydroperoxide has been developed due to the weak nature of peroxide bond to avoid difficulty in isolation and characterization of the compounds.



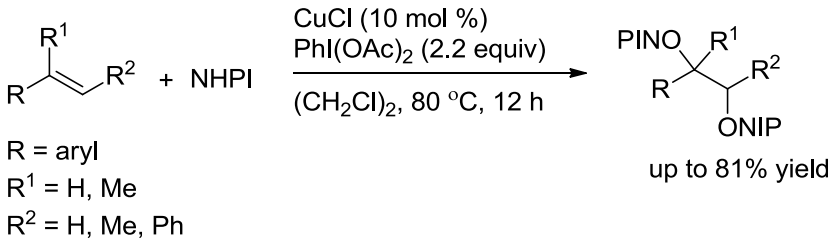
Scheme 3. Aerobic Hydroperoxidation of 1,3-Enynes

An efficient protocol for Mn-catalyzed hydroperoxidation of alkenes with molecular oxygen using *N*-hydroxylamines is demonstrated at room temperature (Scheme 4).[8] The protocol is explored for the hydroperoxidation of conjugated enynes and dienes.



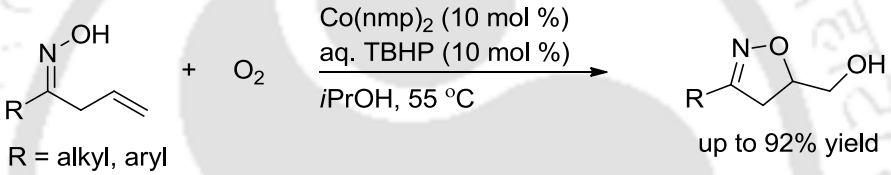
Scheme 4. Mn-Catalyzed Aerobic Hydroperoxidation of Alkenes

A Cu-catalyzed oxidation of styrenes with NHPI employing $PhI(OAc)_2$ as oxidant is described to provide dioxygenated compounds at ambient conditions (Scheme 5).[9] The current protocol offers 1,2-dihydroxylamination of styrenes in low to high yields.



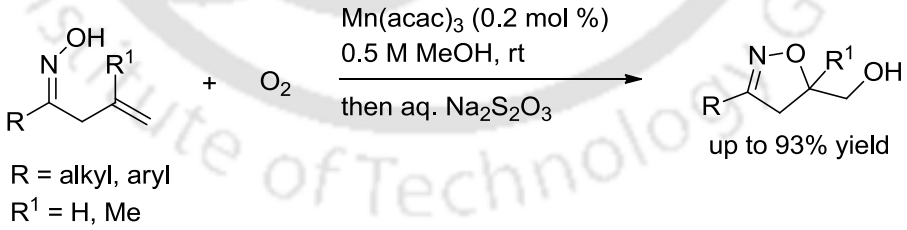
Scheme 5. Cu-Catalyzed 1,2-Dihydroxylamination of Styrenes

An intramolecular dioxygenation of *β,γ*-unsaturated oximes with molecular oxygen is reported for the construction of dihydroisoxazoles in presence of Co-catalyst under ambient conditions (Scheme 6).[10] In case of *β,γ* and *α,β*-unsaturated oximes, this protocol is smoothly effective.



Scheme 6. Co-Catalyzed Aerobic Oxidative Cyclization of Unsaturated Oximes

Makino and co-workers described an intramolecular oxidative cyclization of unsaturated oximes under Mn-catalysis to yield 4,5-dihydroisoxazoline alcohols (Scheme 7).[11] This protocol is applicable for the synthesis of hydroxamic acid A, an antitrypanosonal agent, used for the management of Chagas disease.

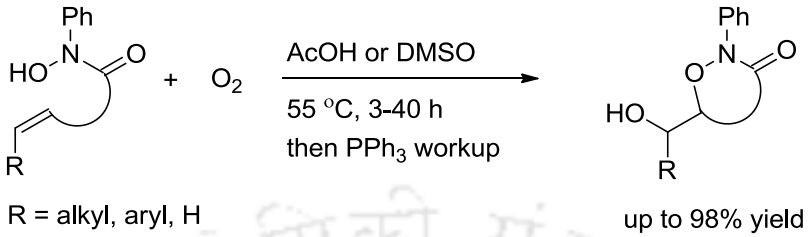


Scheme 7. Mn-Catalyzed Oxidative Cyclization of Unsaturated Oximes

2.1.2 Metal-Free Radical Dioxygenation of Alkenes

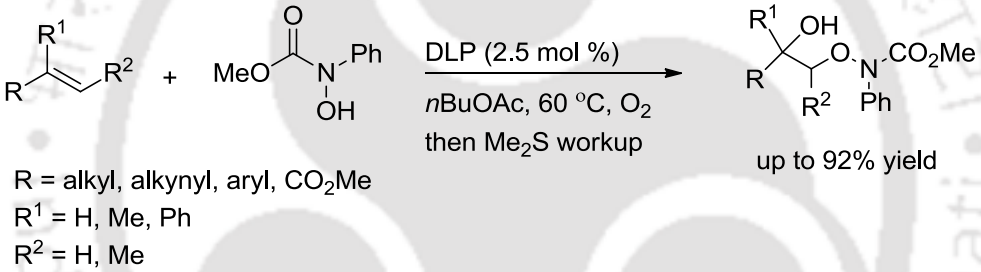
Alexanian and co-workers developed an intramolecular dioxygenation of alkenyl *N*-aryl hydroxamic acids with molecular oxygen under metal-free conditions (Scheme 8).[12] This

protocol is extended for the synthesis of 1,2-diol by the reduction of the *N*-*O* bond in good yield.



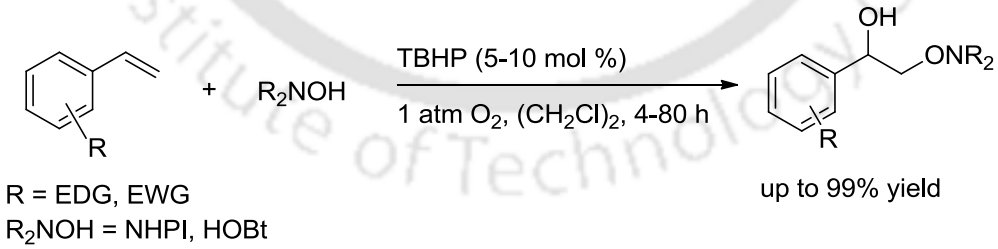
Scheme 8. Aerobic Dioxygenation of Alkenyl *N*-Aryl Hydroxamic Acids

Dilauroyl peroxide (DLP) catalyzed dioxygenation of alkenes with molecular oxygen using *N*-hydroxamic acid derivatives has been disclosed (Scheme 9).[13] Conjugated dienes and enynes are amenable to yield the corresponding dioxygenated products.



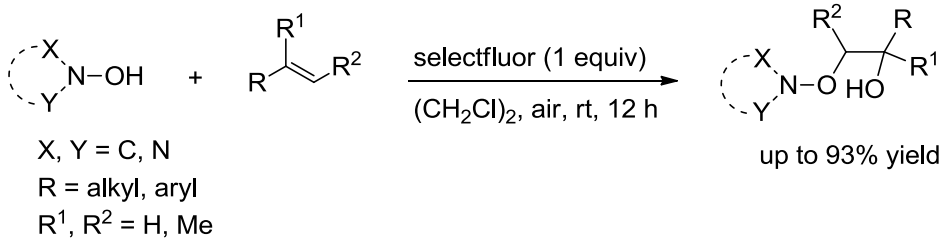
Scheme 9. Aerobic Dioxygenation of Alkenes with *N*-Aryl Hydroxamic Acids

A metal-free radical dioxygenation of styrenes with *N*-hydroxylamines has been reported utilizing TBHP at room temperature under oxygen atmosphere (Scheme 10).[14]



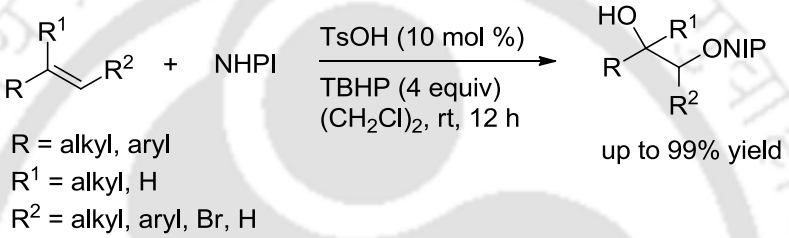
Scheme 10. Peroxide-Catalyzed Dioxygenation of Styrenes with *N*-Hydroxylamines

A selectfluor-mediated selective radical dioxygenation of alkenes has been described with air employing *N*-hydroxylamines at room temperature to generate *β*-oxo alcohols (Scheme 11).[15]



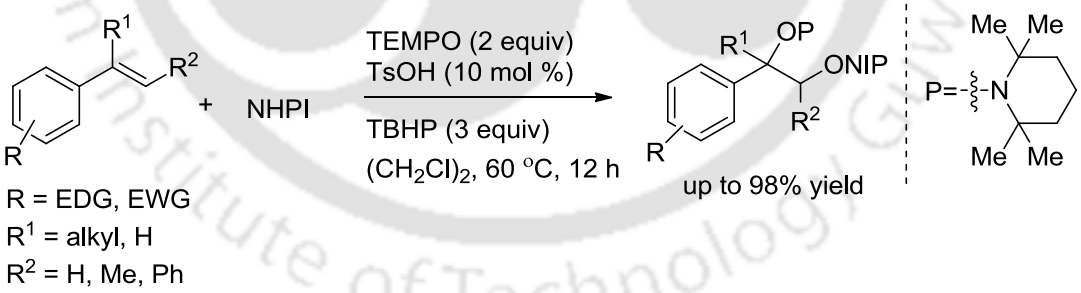
Scheme 11. Selectfluor-Mediated Oxidation of Alkenes to *β*-Oxo Alcohols

Xia and co-workers reported an acid catalyzed radical dioxygenation of alkenes with NHPI employing TBHP as oxidant (Scheme 12).[6] This protocol offers a library of substituted alcohols in good to excellent yields.



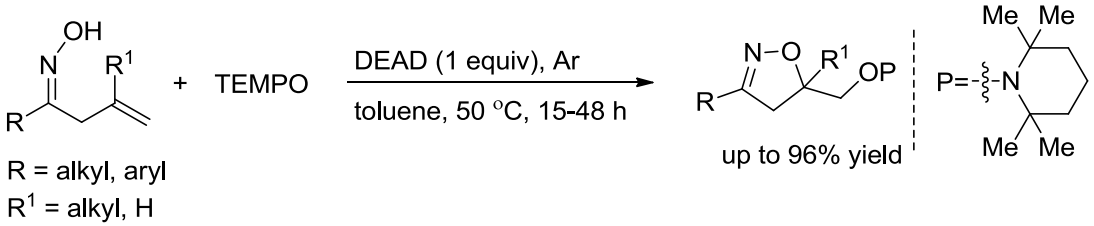
Scheme 12. Acid-Catalyzed Synthesis of Alcohols

The acid catalyzed 1,2-dihydroxylamination of alkenes with NHPI and TEMPO is reported to produce dioxygenated compounds, which can been converted into ketones using *m*CPBA (Scheme 13).[16]



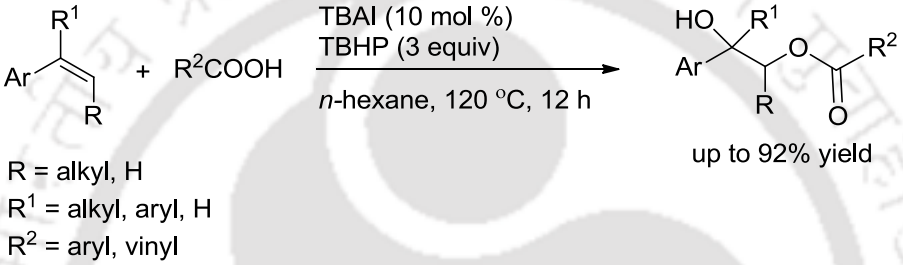
Scheme 13. Acid-Catalyzed Dioxygenation of Alkenes

The oxygenation of *β,γ*-unsaturated oximes has been demonstrated employing TEMPO and DEAD at ambient conditions (Scheme 14).[17] This reaction proceeds through a 5-exo-trig cyclization of an oxime radical followed by TEMPO trapping to deliver the 4,5-dihydroisoxazoles, which are important building blocks in synthetic chemistry.



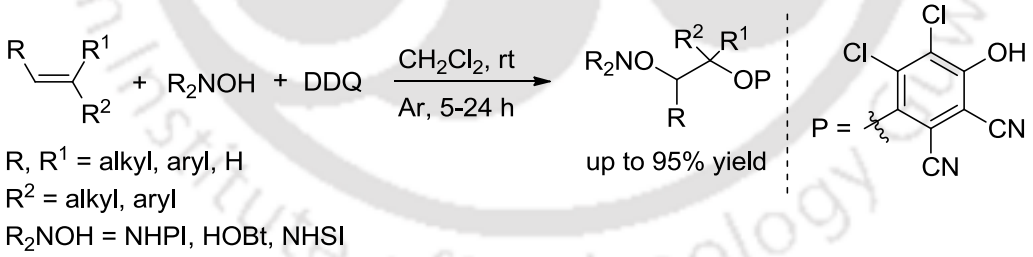
Scheme 14. Oxime Radical Promoted Oxygenation of Alkenes

TBAI-catalyzed regioselective oxygenation of alkenes with organic acids as an *O*-centered radical source has been developed employing TBHP (70% in water) as an oxidant (Scheme 15).[18]



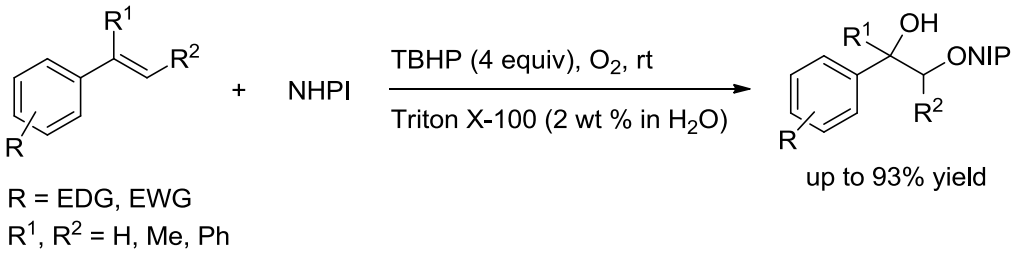
Scheme 15. TBAI-Catalyzed Dioxygenation of Alkenes

Jiang and co-workers developed a metal-free DDQ-mediated oxygenation of alkenes with *N*-hydroxylamines to provide dioxygenated compounds at room temperature (Scheme 16).[19] In this protocol, DDQ plays a dual role, a dehydrogenating reagent and a coupling partner.



Scheme 16. DDQ-Mediated Dioxygenation of Alkenes

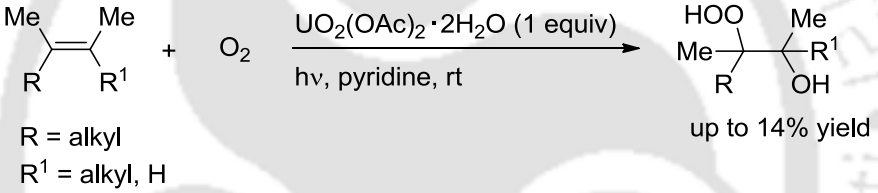
Bihel and co-workers developed a peroxide mediated dioxygenation of styrenes with NHPI and molecular oxygen in presence of Triton X-100 as a surfactant to give the dioxygenated compounds at room temperature (Scheme 17).[20]



Scheme 17. Peroxide-Mediated Dioxygenation of Styrenes

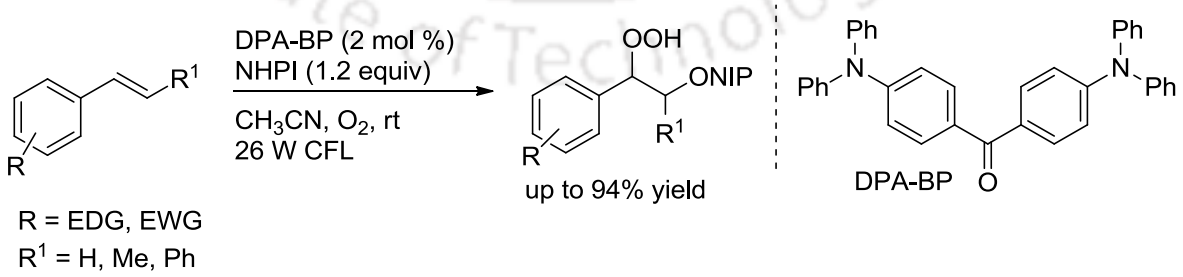
2.1.3 Photo-Catalyzed Aerobic Radical Dioxygenation of Alkenes

The first radical photo oxidation of alkenes with molecular oxygen is reported employing uranyl acetate to provide *β*-hydroxy hydroperoxides (Scheme 18).[21] Isotope labeling studies suggest that the water is the source of oxygen atom of hydroxyl group and the molecular oxygen is the source of the oxygen atoms in the hydroperoxyl group.



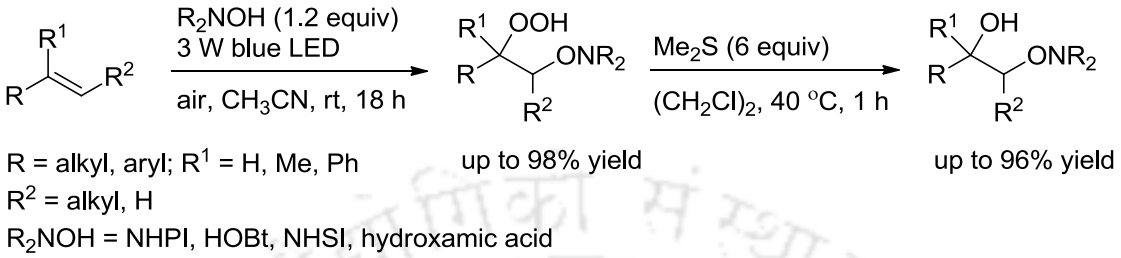
Scheme 18. Photooxidation of Alkenes

A photoinduced proton-coupled electron transfer process is reported for the aerobic dioxygenation of styrenes with molecular oxygen and NHPI in the presence of 4,4'-bis(diphenylamino)benzophenone (DPA-BP) at room temperature (Scheme 19).[22] The donor-substituted benzophenone i.e. DPA-BP under photochemical irradiation activates NHPI *via* a unidirectional proton coupled electron transfer (PCET) process.



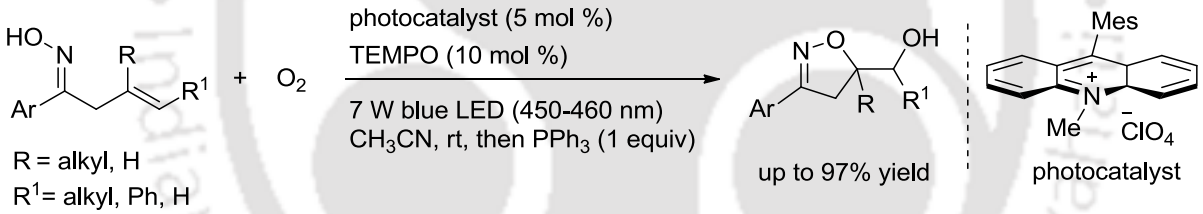
Scheme 19. Photoinduced Dioxygenation of Styrenes

A visible light promoted oxidation of alkenes with oxygen (air) and *N*-hydroxylamines is developed for the synthesis of alkyl hydroperoxides (Scheme 20).[23] These hydroperoxides are transformed to synthetically useful alcohols under ambient conditions.



Scheme 20. Visible-Light-Promoted Dioxygenation of Alkenes

Xiao and co-workers developed the dioxygenation/cyclization of *β,γ*-unsaturated oximes with molecular oxygen using TEMPO/photocatalytic system at room temperature (Scheme 21).[24] First, alkyl hydroperoxide is formed, which on reduction with PPh_3 produces the hydroxyl compound.

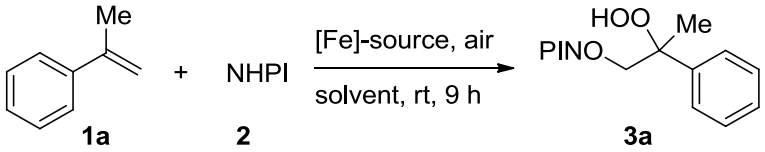


Scheme 21. Oxidative Radical Dioxygenation/Cyclization of *β,γ*-Unsaturated Oximes

2.2 Present Study

We here present a Fe-catalyzed dioxygenation of alkenes using air and *N*-hydroxylamines to afford *N*-(*β*-hydroperoxyalkoxy)amines that can be converted to *N*-(*β*-hydroxyalkoxy)amines in the presence of PPh_3 in quantitative yield. Initially, we carried out the optimization of the reaction using *α*-methylstyrene **1a** and NHPI **2** as the model substrates employing different Fe-sources at room temperature (Table 1). Delightfully, the reaction readily occurred to furnish the *N*-(*β*-hydroperoxyalkoxy)phthalimide **3a** in 81% yield when the substrates **1a** and **2** were stirred with 20 mol % $Fe(NO_3)_3{\cdot}9H_2O$ in $(CH_2Cl)_2$ under air (entry 1). Subsequent

Table 1. Optimization of the Reaction Conditions[a]



Entry	[Fe]-source	Solvent	Yield (%)[b]
1	$Fe(NO_3)_3{\cdot}9H_2O$	$(CH_2Cl)_2$	81
2	$Fe(NO_3)_3{\cdot}9H_2O$	toluene	22
3	**$Fe(NO_3)_3{\cdot}9H_2O$**	**CH_2Cl_2**	**84**
4	$Fe(NO_3)_3{\cdot}9H_2O$	DMSO	trace
5	$Fe(NO_3)_3{\cdot}9H_2O$	H_2O	n.d.
6	$Fe(NO_3)_3{\cdot}9H_2O$	CH_2Cl_2	78[c]
7	$Fe(NO_3)_3{\cdot}9H_2O$	CH_2Cl_2	trace[d]
8	$Fe(acac)_3$	CH_2Cl_2	72
9	$FeBr_2$	CH_2Cl_2	n.d.
10	$K_3Fe(CN)_6$	CH_2Cl_2	34
11	$Fe(NO_3)_3{\cdot}9H_2O$	CH_2Cl_2	67[e]
12	$Fe(NO_3)_3{\cdot}9H_2O$	CH_2Cl_2	71[f]
13	-	CH_2Cl_2	n.d.

[a] Reaction conditions: *α*-methylstyrene **1a** (0.5 mmol), NHPI **2** (0.25 mmol), $Fe(NO_3)_3{\cdot}9H_2O$ (20 mol %), solvent (1.5 mL), rt, 9 h, air.

[b] Isolated yield.

[c] O_2 balloon used.

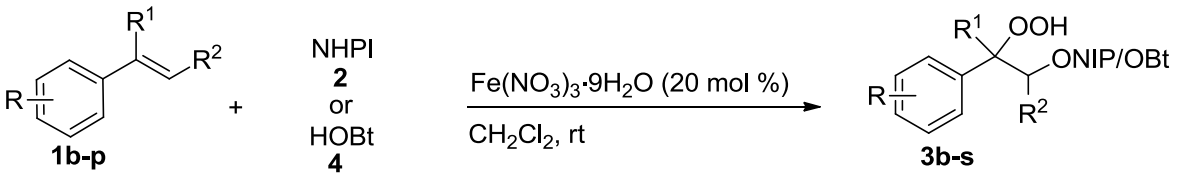
[d] N_2 balloon used.

[e] 15 mol % $Fe(NO_3)_3{\cdot}9H_2O$ was used.

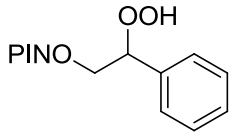
[f] 1.5 Equiv **1a** was used. n.d.= not detected.

screening of solvents led an increase in the yield to 84% using CH_2Cl_2, while DMSO, toluene and H_2O produced inferior results (entries 2-5). Similar result was observed with oxygen balloon while N_2 furnished the target product in a trace amount (entries 6 and 7). Among the iron sources screened, $Fe(NO_3)_3{\cdot}9H_2O$, $FeBr_2$, $Fe(acac)_3$ and $K_3Fe(CN)_6$, the former produced

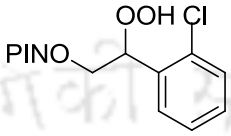
Table 2. Reaction of Alkenes with NHPI and HOBt[a,b]



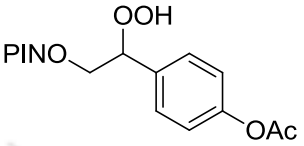
R = EDG, EWG; R^1 = alkyl, aryl, H; R^2 = alkyl, H



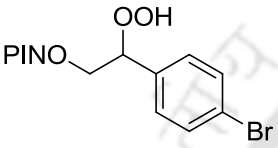
3b, 15 h, 80%



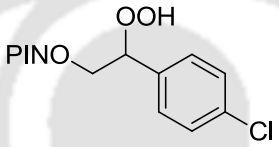
3c, 20 h, 74%



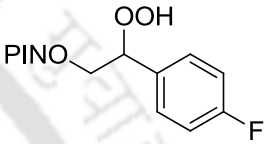
3d, 22 h, 68%



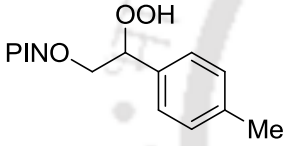
3e, 11 h, 74%



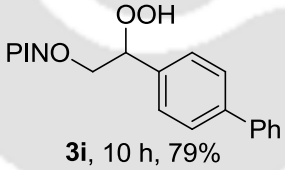
3f, 10 h, 71%



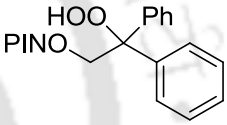
3g, 11 h, 71%



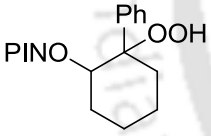
3h, 18 h, 88%



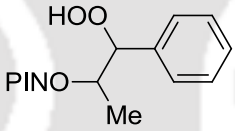
3i, 10 h, 79%



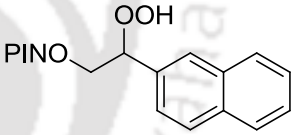
3j, 14 h, 73%



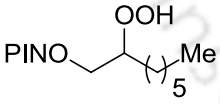
3k, 9 h, 69%



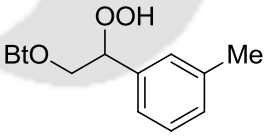
3l, 12 h, 78%, *dr* = 3:1[c]



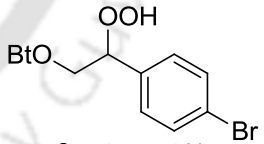
3m, 11 h, 74%



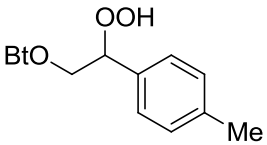
3n, 72 h, 16%



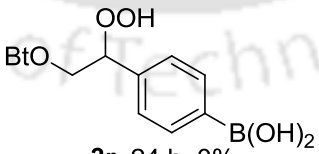
3o, 7 h, 46%



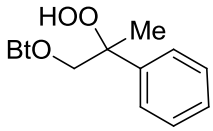
3p, 9 h, 52%



3q, 6 h, 61%



3r, 24 h, 0%



3s, 6 h, 63%

[a] Reaction conditions: Alkenes **1b-p** (0.5 mmol), NHPI **2** or HOBt **4** (0.25 mmol), $Fe(NO_3)_3 \cdot 9H_2O$ (20 mol %), CH_2Cl_2 (1.5 mL), rt, air.

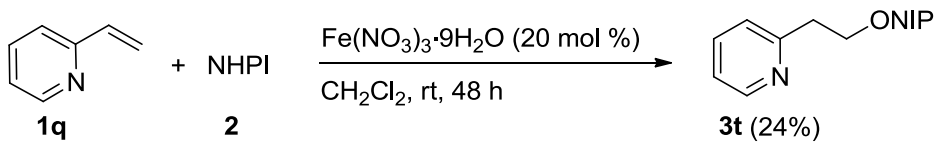
[b] Isolated yield.

[c] *dr* Determined by ^1H NMR.

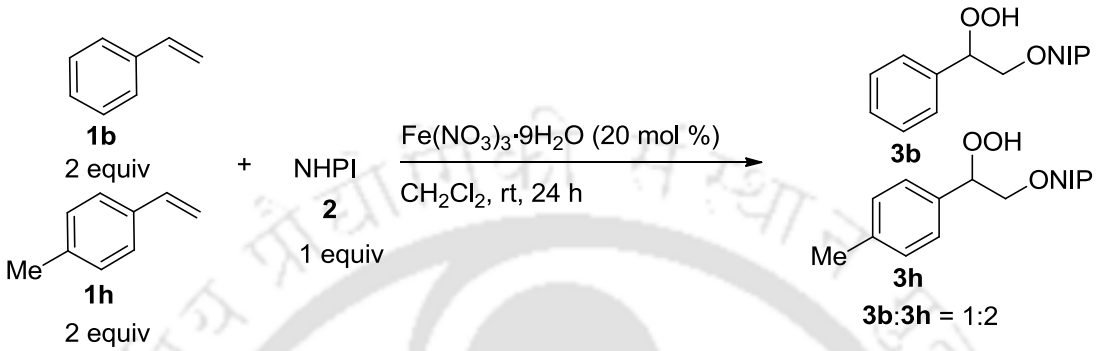
the best result (entries 3 and 8-10). Decreasing the amount of the iron source (15 mol %) or *α*-methylstyrene (1.5 equiv) led to drop the yield to <71% (entries 11 and 12). A control experiment confirmed that without the $Fe(NO_3)_3 \cdot 9H_2O$ the product **3a** was not formed (entry 13).

Next, the scope of the procedure was studied for the reaction of a series of substituted alkenes with NHPI (Table 2). The reaction of styrene **1b** produced **3b** in 80% yield. The substrates **1c** bearing substitution at the 2-position with chloro group exhibited slightly lesser reactivity to provide **3c** in 74% yield, while **1d-g** having electron withdrawing substituents at the 4-position with acetoxy **1d**, bromo **1e**, chloro **1f** and fluoro **1g** groups oxidized to furnish **3d-g** in 68-74% yields. The reaction of the substrate **1h** containing electron donating group at the 4-position with methyl group produced the peroxide **3h** in 88% yield. The substrate **1i** bearing substitution at the 4-position with phenyl oxidized to provide **3i** in 79% yield. In addition, 1-phenylstyrene **1j** underwent reaction to furnish **3j** in 73% yield. Likewise, 1-phenylcyclohexene **1k** oxidized to give **3k** in 69% yield. Further, *β*-methylstyrene **1l** underwent oxidation to afford **3l** in 78% yield as a 3:1 diastereoisomers. Moreover, 2-vinylnaphthalene **1m** oxidized to peroxide **3m** in 74% yield, whereas the reaction of aliphatic alkene such as 1-octene **1n** produced **3n** in 16% yield. Under these conditions, the reaction of 2-vinylpyridine **1q** with NHPI delivered alkoxyamine **3t** in 24% yield (Scheme 22). The substrates bearing electron donating group exhibited greater reactivity compared to unsubstituted one (Scheme 23).

The scope of the protocol was further examined for the reaction of styrenes with HOBt (Table 2). Selectivity of these reactions were less compared to NHPI based reactions. For example, the substrate **1o** bearing 3-methyl group on phenyl ring oxidized to **3o** in 46% yield, while the substrates bearing the substitution at the 4-position with bromo **1e** and methyl **1h** groups on aryl ring produced **3p** and **3q** in 52 and 61% yields, respectively, along with ketones (~5%) as by-product. However, the substrate bearing boronic acid **1p** failed to react and the formation of the target product was not observed, whereas *α*-methylstyrene **1a** readily oxidized to produce the target peroxide **3s** in 63% yield.



Scheme 22. Reaction of 2-Vinylpyridine with NHPI.



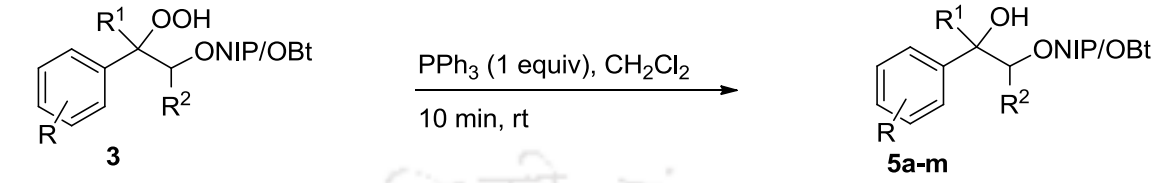
Scheme 23. Cross-Over Experiment

Next, the scale up of the protocol was studied using **1a** and NHPI **2** as model substrates under optimized conditions. The reaction readily occurred to afford the peroxide **3a** in 72% yield (Scheme 24). This result suggests that the protocol is scalable. Moreover, the peroxides can be readily converted into the corresponding alcohols in quantitative yields (Table 3). For examples, the reactions of the peroxides **3a**, **3c**, **3e-l**, **3p-q** and **3s** were examined with PPh_3 to produce the hydroxyl **5a-m** in 93-99% yields.[25] Recrystallization of compound **5i** produced single crystal whose structure was confirmed using X-ray analysis (Figure 1). We next studied the one pot conversion of alkenes to hydroxyl compound using alkene **1a** as a representative example (Scheme 25). The reaction readily occurred to furnish the hydroxyl derivative in 82% yield.

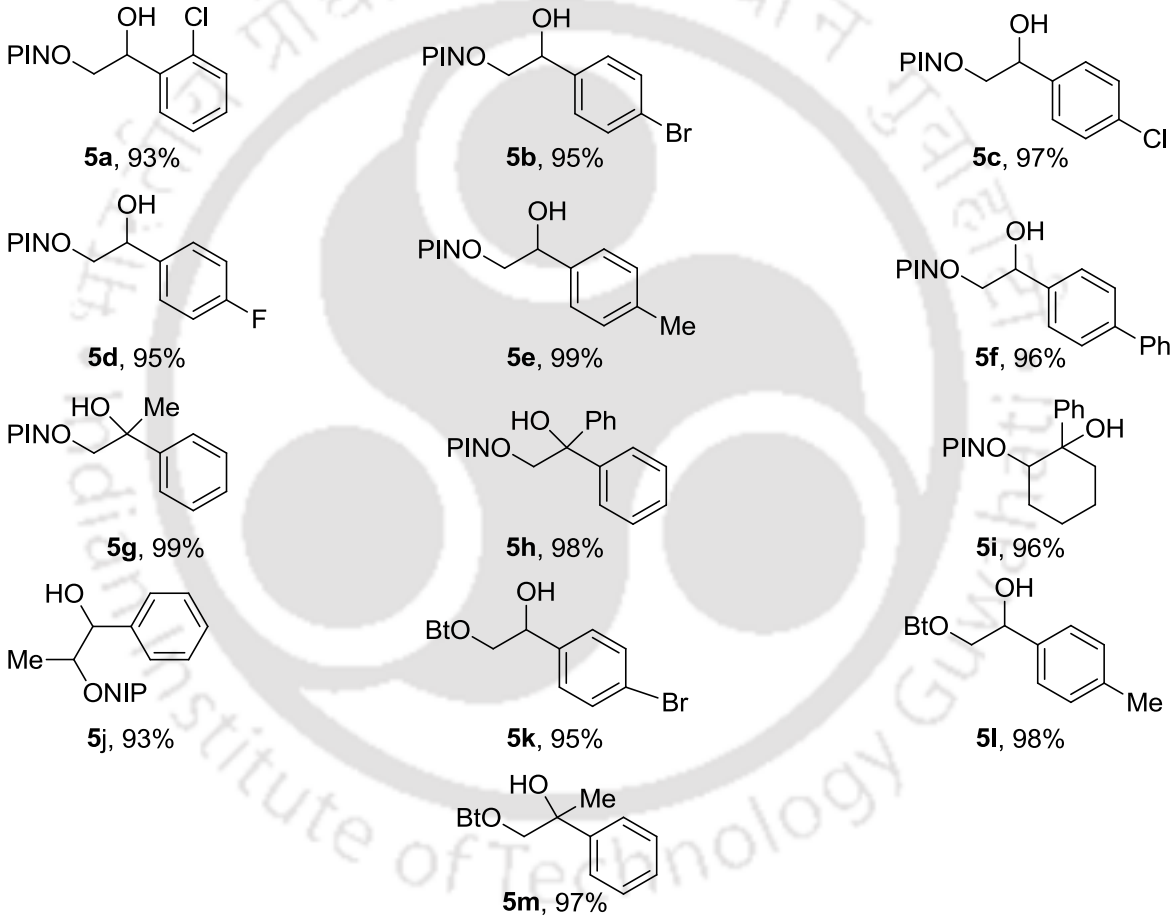
The hydrolysis of the hydroxyl compounds **5e** and **5g** were investigated with hydrazine hydrate (Scheme 26).[26] The reaction efficiently occurred to produce the *β*-hydroxy-*N*-alkoxyamines **6a** and **6b** in 77 and 79% yields, respectively, which are important in medicinal chemistry.[27] In addition, the reductive cleavage of *N*-*O* bond of the hydroxyl compounds **5** was performed using $Mo(CO)_6$ to produce 1,2-diols (Table 4).[28] For examples, the hydroxyl compounds **5a-g** and **5j** readily underwent reduction in presence of $Mo(CO)_6$ to deliver the target 1,2-diols **7a-h** in 61-81% yields.[29] Finally, *β*- hydroxy-*N*-alkoxyamines **6a**

and **6b** can be converted into 1,2-diols **7e** and **7g** in 71 and 77% yields, respectively (Scheme 27).[28]

Table 3. Reduction of Peroxides with PPh_3[a,b]

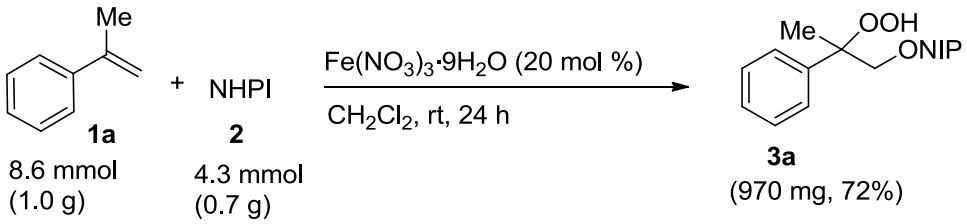


R = alkyl, aryl, H, halo; R^1 = alkyl, aryl, H; R^2 = alkyl, H

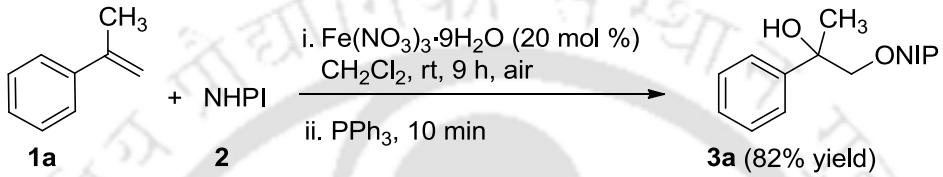


[a] Reaction conditions: Peroxides **3** (0.1 mmol), PPh_3 (0.1 mmol), CH_2Cl_2 (1.5 mL), 10 min, rt.

[b] Isolated yields.



Scheme 24. Gram-scale Synthesis



Scheme 25. One-Pot Synthesis of Alcohol

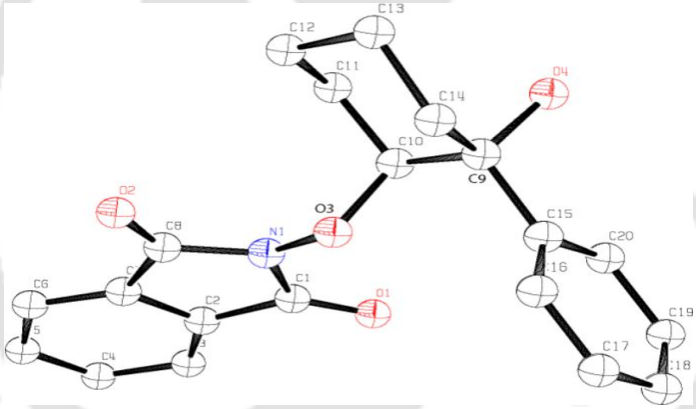
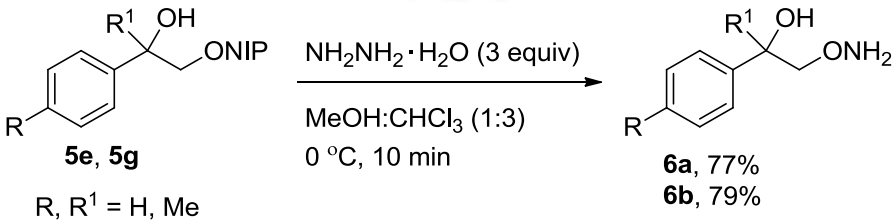
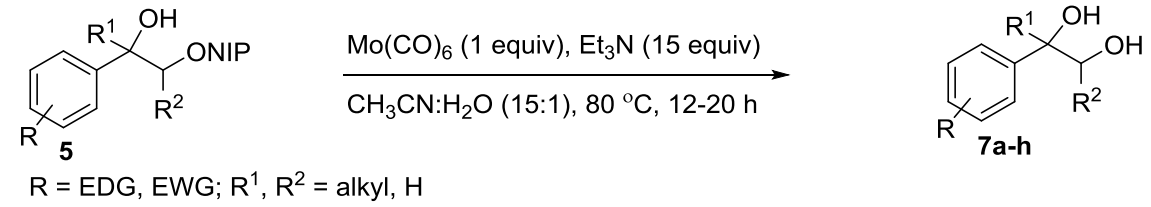


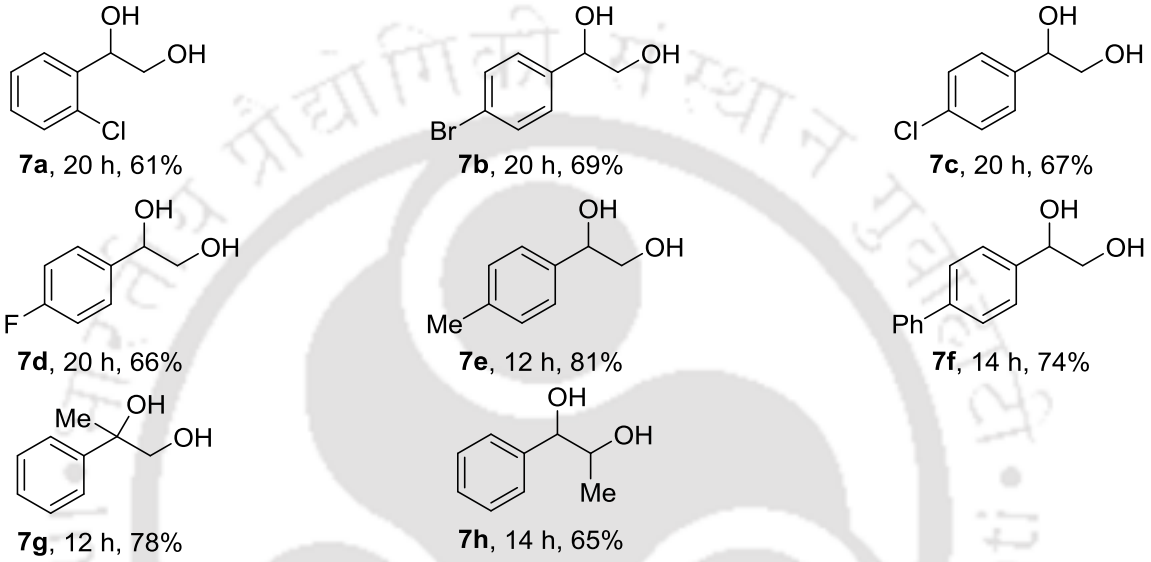
Figure 1. ORTEP diagram of 2-(2-hydroxy-2-phenylcyclohexyloxy)isoindoline-1,3-dione **5i** with 50% ellipsoid. H-Atoms are omitted for clarity (CCDC 1431312).



Scheme 26. Synthesis of *β*-Hydroxy-*N*-Alkoxyamines

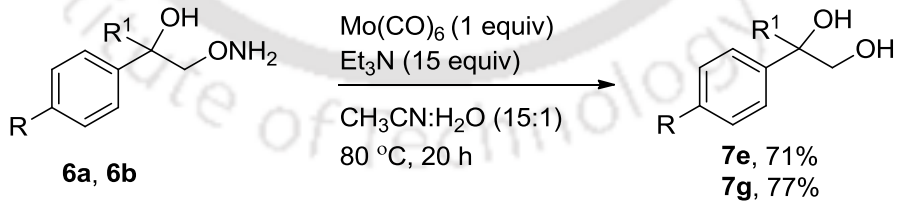
Table 4. Synthesis of 1,2-Diols[a,b]



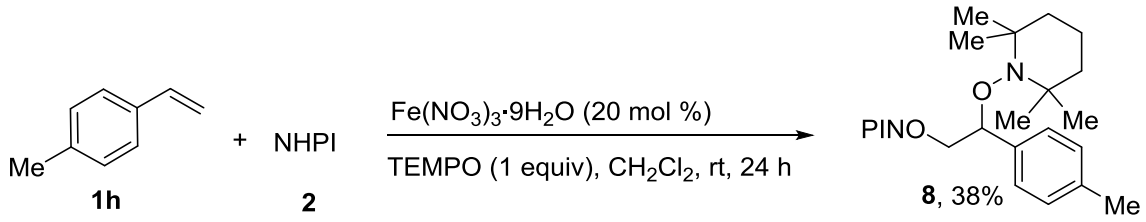


[a] Reaction conditions: Alcohols **5** (0.2 mmol), $Mo(CO)_6$ (0.2 mmol), Et_3N (3.0 mmol), $CH_3CN:H_2O$ (15:1, 2 mL), 80 °C, 12-20 h.

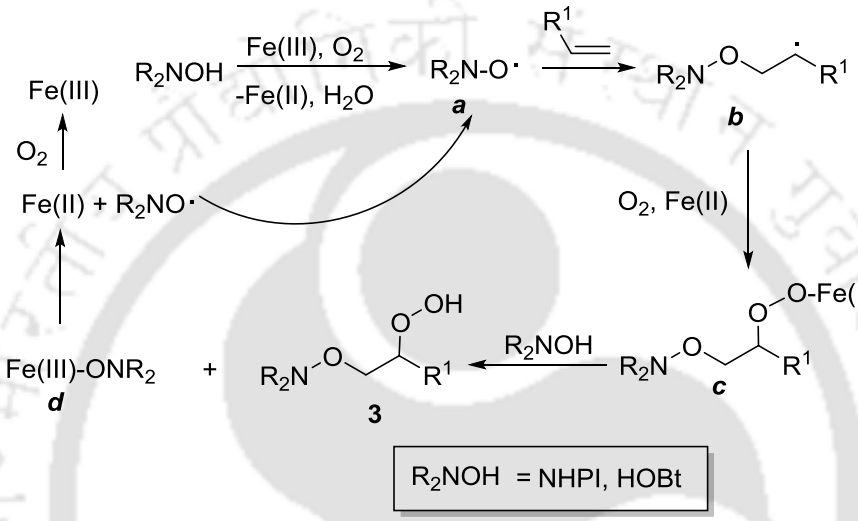
[b] Isolated yield.



Scheme 27. Synthesis of 1,2-Diols from *β*-Hydroxy-*N*-Alkoxyamines



Scheme 28. Radical-Scavenger Experiment



Scheme 29. Proposed Catalytic Pathway

To understand the mechanistic pathway, the radical trapping experiment of **1h** was performed with TEMPO and the TEMPO-adduct **8** was isolated in 38% yield, which suggests that the reaction may proceed *via* a radical pathway (Scheme 28).[29] Thus, NHPI and HOBt[30] in presence of Fe(III) and air can produce the radical species ***a***, which may react with alkene to produce a stable secondary radical ***b*** (Scheme 29). The radical ***b*** may add with molecular oxygen from air and Fe(II) to generate Fe(III)-peroxo intermediate ***c***, which may react with *N*-hydroxylamine to yield the peroxide **3** and R_2NO-Fe(III) species ***d***. The latter may undergo homolytic bond cleavage to form $R_2NO\cdot$ radical ***a*** and Fe(II) species that may be oxidized to Fe(III) by air to complete the catalytic process.[31]

In summary, we have established an operationally simple and practical method for aerobic dioxygenation of alkenes with *N*-hydroxylamines using iron catalyst at room temperature. Molecular oxygen from air acts as sole oxidant, which makes this process

synthetically important. Moreover, mild reaction condition, selectivity, iron salt as the non-toxic and inexpensive catalyst and dioxygen from air as the oxygen source are the significant practical features.

2.3 EXPERIMENTAL SECTION

General Information. $Fe(NO_3)_3 \cdot 9H_2O$ (98%) and hydrazine hydrate (90-100%) of Merck were used as received. Other materials, purification and analyses are followed as presented in chapter 1.

General Procedure for the Dioxygenation of Alkenes. Alkene **1** (0.5 mmol), NHPI **2** or HOBt **4** (0.25 mmol) and $Fe(NO_3)_3 \cdot 9H_2O$ (20 mol %, 20.2 mg) were stirred in CH_2Cl_2 (1.5 mL) at room temperature under air. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The resultant mixture was extracted with CH_2Cl_2 (3 x 10 mL) and successively washed with brine (1 x 10 mL). The organic solution was dried over Na_2SO_4 and evaporated on a rotary evaporator to produce a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

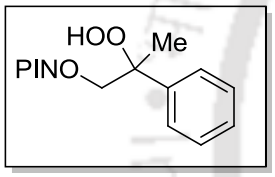
General Procedure for the Synthesis of *α*-Oxygenated-*β*-Hydroxy Compounds. To a solution of peroxide **3** (0.1 mmol) in CH_2Cl_2 (1.5 mL) was added PPh_3 (0.1 mmol, 26.2 mg). The reaction mixture was stirred for 10 minutes at room temperature. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The resultant mixture was extracted with CH_2Cl_2 (3 x 10 mL) and successively washed with brine (1 x 10 mL). The organic solution was dried over Na_2SO_4 and evaporated on a rotary evaporator to give a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

General Procedure for the Hydrolysis of 5 to *β*-Hydroxyalkoxyamines 6. To a solution of **5** (0.34 mmol) in $MeOH/CHCl_3$ (1:3) was added hydrazine hydrate (1.01 mmol, 51 mg). The reaction mixture was stirred at 0 °C for 10 minutes under air. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion, the reaction mixture was evaporated. The colorless precipitate was filtered and washed with Et_2O (10 mL). The combined solution was evaporated under reduced pressure and the resultant oil was

dissolved in Et_2O (4 mL). When the solution was subjected to HCl gas, a colorless precipitate was formed that was filtered and washed with Et_2O (3 x 10 mL) to give the pure HCL salt of **6**.[26]

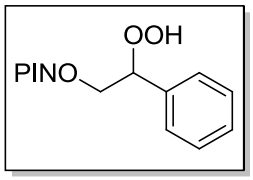
General Procedure for the Synthesis of 1,2-Diols. To a solution of **5** or **6** (0.2 mmol) in CH_3CN/H_2O (15:1, 2 mL) was added $Mo(CO)_6$ (0.2 mmol, 53 mg) and Et_3N (3.0 mmol, 0.42 mL). The reaction mixture was stirred at 80 °C for 12-20 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The resultant mixture was neutralized by using aqueous NH_4Cl and extracted with ethyl acetate (3 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

2.4 Characterization Data



2-(2-Hydroperoxy-2-phenylpropoxy)isoindoline-1,3-dione 3a.

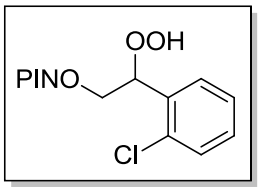
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.36; colorless solid; mp 118-119 °C; yield 84% (66 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (br s, 1H), 7.87-7.85 (m, 2H), 7.79-7.77 (m, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 4.72-4.63 (m, 2H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 140.9, 135.0, 128.8, 128.7, 128.1, 125.5, 124.0, 84.6, 79.9, 23.0; FT-IR (KBr) 3371, 2993, 2924, 1782, 1720, 1494, 1446, 1400, 1379, 1186, 1141, 1082, 1019, 1003, 965, 878, 763, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{17}H_{15}NO_5$: 336.0848, found: 336.0849.



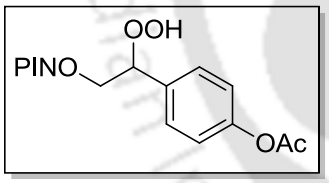
2-(2-Hydroperoxy-2-phenylethoxy)isoindoline-1,3-dione 3b.

Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.38; liquid; yield 80% (60 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (br s, 1H), 7.87-7.85 (m, 2H), 7.78-7.76 (m, 2H), 7.41-

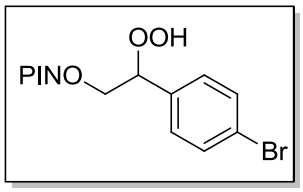
7.33 (m, 5H), 5.43-5.40 (m, 1H), 4.51-4.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 135.8, 135.0, 129.0, 128.9, 128.8, 127.2, 124.0, 85.6, 79.1; FT-IR (neat) 3439, 1788, 1731, 1494, 1467, 1454, 1375, 1187, 1134, 1082, 1018, 997, 877, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{16}H_{13}NO_5$: 322.0691, found: 322.1780.



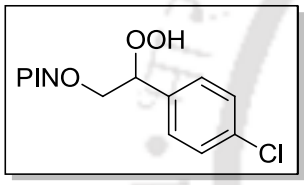
2-(2-(2-Chlorophenyl)-2-hydroperoxyethoxy)isoindoline-1,3-dione 3c. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.39; liquid; yield 74% (62 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.97 (br s, 1H), 7.86-7.84 (m, 2H), 7.78-7.76 (m, 2H), 7.58 (d, *J* = 6.4 Hz, 1H), 7.34-7.32 (m, 1H), 7.31-7.24 (m, 2H), 5.84 (d, *J* = 6.0 Hz, 1H), 4.51-4.47 (m, 1H), 4.29-4.26 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.9, 134.9, 133.6, 132.6, 129.89, 129.8, 128.7 128.1, 127.3, 123.9, 83.1, 77.8; FT-IR (neat) 3441, 1789, 1729, 1467, 1443, 1374, 1187, 1134, 1081, 1034, 1018, 997, 877, 759, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{16}H_{12}ClNO_5$: 356.0302, found: 356.0297.



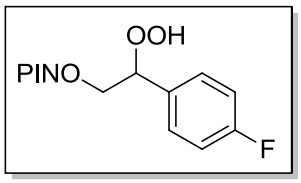
4-(2-(1,3-Dioxoisoindolin-2-yloxy)-1-hydroperoxyethyl)phenyl acetate 3d. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.32; liquid; yield 68% (61 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (br s, 1H), 7.88-7.85 (m, 2H), 7.79-7.77 (m, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 5.42-5.39 (m, 1H), 4.50-4.48 (m, 2H) 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 163.9, 151.1, 135.0, 133.5, 128.8, 128.5, 124.0, 122.1, 85.0, 78.8, 21.3; FT-IR (neat) 3409, 3066, 2945, 1784, 1751, 1736, 1722, 1606, 1509, 1465, 1373, 1224, 1202, 1169, 1137, 1082, 1015, 990, 911, 878, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{18}H_{15}NO_5$: 380.0746, found: 380.0740.



2-(2-(4-Bromophenyl)-2-hydroperoxyethoxy)isoindoline-1,3-dione 3e. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.37; colorless solid; mp 114-115 °C; yield 74% (70 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (br s, 1H), 7.83-7.81 (m, 2H), 7.77-7.75 (m, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.38-5.34 (m, 1H), 4.47 (d, *J* = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 134.9, 131.9, 131.7, 129.0, 128.6, 123.9, 122.9, 84.7, 78.4; FT-IR (KBr) 3452, 2948, 2918, 1783, 1717, 1486, 1465, 1378, 1187, 1132, 1080, 1016, 995, 877, 818, 697 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{16}H_{12}BrNO_5$: 399.9797, found: 399.9796.

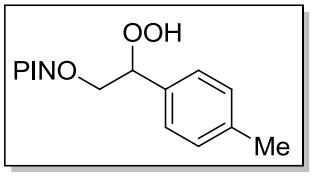


2-(2-(4-Chlorophenyl)-2-hydroperoxyethoxy)isoindoline-1,3-dione 3f. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.36; liquid; yield 71% (60 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.72 (br s, 1H), 7.86-7.84 (m, 2H), 7.78-7.77 (m, 2H), 7.36-7.33 (m, 4H), 5.38-5.36 (m, 1H), 4.50-4.44 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.9, 135.0, 134.9, 134.4, 129.1, 128.8, 128.7, 124.0, 84.8, 78.6; FT-IR (neat) 3370, 3036, 2938, 1784, 1716, 1492, 1464, 1359, 1190, 1121, 1082, 1015, 987, 909, 876, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{16}H_{12}ClNO_5$: 356.0302, found: 356.0302.

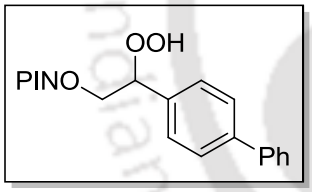


2-(2-(4-Fluorophenyl)-2-hydroperoxyethoxy)isoindoline-1,3-dione 3g. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.37; liquid; yield 71% (57 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.67 (br s, 1H), 7.87-7.85 (m, 2H), 7.79-7.77 (m, 2H), 7.41-7.38 (m, 2H), 7.07-7.04 (m, 2H), 5.39-5.37 (m, 1H), 4.52-4.46 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.99, 163.9 (d, J_{C-F} = 246.4 Hz), 135.0, 131.7, 129.28 (d, J_{C-F} = 7.8

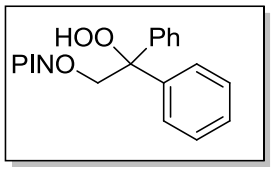
Hz), 128.8, 124.0, 115.9 (d, $J_{C\text{-}F}$ = 21.9 Hz), 84.8, 78.8; FT-IR (neat) 3434, 2923, 1789, 1732, 1605, 1511, 1467, 1375, 1225, 1187, 1160, 1132, 1082, 1018, 905, 878, 837, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{16}H_{12}FNO_5$: 340.0597, found: 340.0596.



2-(2-Hydroperoxy-2-*p*-tolylethoxy)isoindoline-1,3-dione 3h. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.36; liquid; yield 88% (69 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 9.57 (br s, 1H), 7.87-7.85 (m, 2H), 7.78-7.76 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 5.37 (t, *J* = 6.4 Hz, 1H), 4.50-4.49 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 138.8, 134.8, 132.8, 129.4, 128.7, 127.2, 123.9, 85.3, 78.9, 21.3; FT-IR (neat) 3439, 2922, 1788, 1729, 1631, 1515, 1467, 1375, 1186, 1132, 1082, 1018, 996, 877, 814, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{17}H_{15}NO_5$: 336.0848, found: 336.0852.

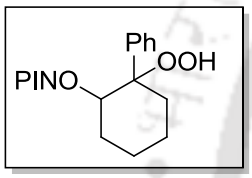


2-(2-(Biphenyl-4-yl)-2-hydroperoxyethoxy)isoindoline-1,3-dione 3i. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.35; liquid; yield 79% (74 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 9.72 (br s, 1H), 7.85-7.83 (m, 2H), 7.76-7.73 (m, 2H), 7.59-7.54 (m, 4H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.2 Hz, 1H), 5.47-5.46 (m, 1H), 4.55-4.53 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 141.9, 140.6, 134.9, 134.8, 128.9, 128.8, 127.7, 127.68, 127.63, 127.2, 124.0, 85.3, 78.9; FT-IR (neat) 3439, 1787, 1728, 1632, 1487, 1374, 1187, 1133, 1081, 1018, 996, 877, 731, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{17}NO_5$: 398.1004, found: 398.1004.



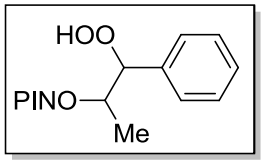
2-(2-Hydroperoxy-2,2-diphenylethoxy)isoindoline-1,3-dione 3j.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.37; colorless solid; mp 173-174 °C; yield 73% (69 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.34 (br s, 1H), 7.87-7.85 (m, 2H), 7.78-7.77 (m, 2H), 7.50 (d, *J* = 7.2 Hz, 4H), 7.35 (t, *J* = 7.2 Hz, 4H), 7.30-7.27 (m, 2H), 5.12 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.0, 140.1, 135.1, 128.8, 128.6, 128.3, 127.0, 124.1, 88.4, 79.4; FT-IR (KBr) 3381, 3058, 2914, 1792, 1716, 1467, 1450, 1384, 1137, 1073, 1028, 985, 879, 744, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{22}H_{17}NO_5$: 398.1004, found: 398.1007.



2-(2-Hydroperoxy-2-phenylcyclohexyloxy)isoindoline-1,3-dione 3k.

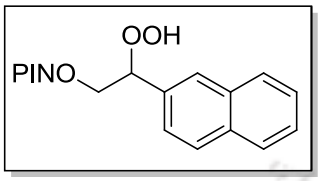
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.38; liquid; yield 69% (61 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (br s, 1H), 7.82-7.79 (m, 3H), 7.77-7.73 (m, 3H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 4.73-4.70 (m, 1H), 2.41-2.35 (m, 1H), 2.23-2.12 (m, 2H), 1.95-1.71 (m, 3H), 1.47-1.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 138.3, 134.9, 128.8, 128.6, 128.4, 127.1, 123.8, 88.2, 86.8, 31.8, 28.0, 22.4, 21.8; FT-IR (neat) 3439, 2937, 2866, 1788, 1725, 1630, 1467, 1376, 1188, 1127, 1081, 1016, 984, 878, 762, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{19}NO_5$: 376.1161, found: 376.1165.



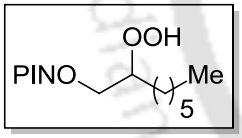
2-(1-Hydroperoxy-1-phenylpropan-2-yloxy)isoindoline-1,3-dione 3l.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.36; *dr* = 3:1, liquid; yield 78% (61 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.09 (br s, 1H), 9.79 (br s, 0.26H), 7.88-7.86 (m, 2.3H), 7.80-7.78 (m, 2.4H), 7.45-7.42 (m, 2H), 7.38-7.33 (m, 4H), 5.16-5.15 (m, 1H), 5.12-5.10 (m, 0.34H), 4.82-4.79 (m, 1H), 4.66-4.59 (m, 0.27H), 1.29 (d, *J* = 6.8 Hz, 3H), 1.20 (d,

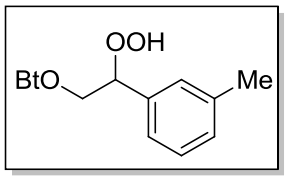
J = 6.4 Hz, 0.73H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 164.7, 135.05, 135.01, 134.9, 128.9, 128.89, 128.84, 128.6, 128.3, 128.0, 124.03, 124.0, 88.2, 84.5, 17.1, 14.2; FT-IR (neat) 3415, 2926, 1788, 1730, 1632, 1467, 1454, 1381, 1188,1124, 1081, 1016, 979, 878, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{17}H_{15}NO_5$: 336.0848, found: 336.0848.



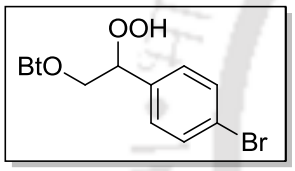
2-(2-Hydroperoxy-2-(naphthalen-2-yl)ethoxy)isoindoline-1,3-dione 3m. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.38; liquid; yield 74% (65 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (br s, 1H), 7.90-7.88 (m, 1H), 7.83-7.78 (m, 5H), 7.75-7.72 (m, 2H), 7.49-7.45 (m, 3H), 5.58 (t, *J* = 6.0 Hz, 1H), 4.59 (d, *J* = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 134.9, 133.5, 133.3, 133.2, 128.8, 128.7, 128.3, 127.8, 126.7, 126.6, 126.5, 124.6, 123.9, 85.7, 79.0; FT-IR (neat) 3415, 3052, 2922, 1786, 1719, 1465, 1372, 1188, 1142, 1126, 1081, 1021, 1003, 952, 878, 822, 752, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{20}H_{15}NO_5$: 372.0848, found: 372.0850.



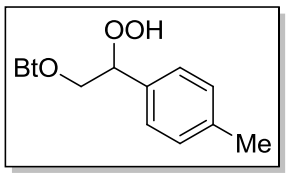
2-(2-Hydroperoxyoctyloxy)isoindoline-1,3-dione 3n. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.43; liquid; yield 16% (12 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (br s, 1H), 7.88-7.85 (m, 2H), 7.79-7.77 (m, 2H), 4.50 (q, *J* = 6.4 Hz, 1H), 4.27-4.21 (m, 2H), 1.70-1.64 (m, 2H), 1.33-1.25 (m, 8H), 0.90-0.87 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.1, 135.0, 128.9, 124.0, 82.6, 79.0, 31.8, 29.3, 29.0, 25.7, 22.7, 14.2; FT-IR (neat) 3438, 2926, 2854, 1789, 1731, 1637, 1466, 1376, 1187, 1124, 1075, 1018, 877, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{16}H_{21}NO_5$: 330.1317, found: 330.1318.



1-(2-Hydroperoxy-2-*m*-tolylethoxy)-1*H*-benzo[*d*][1,2,3]triazole 3o. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.36; liquid; yield 46% (33 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (br s, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.50 (t, *J* = 6.8 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 7.18-7.14 (m, 3H), 5.38 (t, *J* = 6.0 Hz, 1H), 4.80 (d, *J* = 6.4 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 138.8, 135.4, 130.1, 128.9, 128.4, 128.0, 127.6, 125.1, 124.4, 120.2, 109.2, 84.6, 80.5, 21.5; FT-IR (neat) 3439, 2920, 2850, 1610, 1489, 1445, 1361, 1265, 1241, 1159, 1098, 971, 782, 744, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{15}N_3O_3$: 286.1192, found: 286.1193.

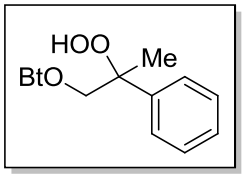


1-(2-(4-Bromophenyl)-2-hydroperoxyethoxy)-1*H*-benzo[*d*][1,2,3]triazole 3p. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.38; liquid; yield 52% (45 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (br s, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.55-7.51 (m, 3H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.39 (t, *J* = 6.0 Hz, 1H), 4.79 (d, *J* = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 134.6, 132.2, 129.1, 128.6, 127.5, 125.2, 123.4, 120.3, 109.0, 84.0, 79.9; FT-IR (neat) 3471, 2923, 2853, 1640, 1486, 1445, 1362, 1265, 1241, 1099, 1071, 1011, 972, 821, 782, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{14}H_{12}BrN_3O_3$: 350.0140, found: 350.0141.

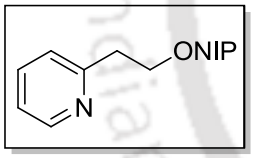


1-(2-Hydroperoxy-2-*p*-tolylethoxy)-1*H*-benzo[*d*][1,2,3]triazole 3q. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.36; liquid; yield 61% (43 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (br s, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 2H), 7.16 (d, *J* =

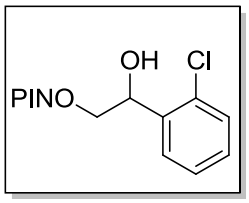
8.0 Hz, 2H), 5.38-5.35 (m, 1H), 4.85-4.76 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 139.2, 132.5, 129.6, 128.4, 127.6, 127.3, 125.0, 120.1, 109.2, 84.3, 80.4, 21.3; FT-IR (neat) 3439, 2921, 1615, 1515, 1445, 1362, 1265, 1240, 1157, 1098, 969, 815, 766, 744 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{15}N_3O_3$: 286.1192, found: 286.1190.



1-(2-Hydroperoxy-2-phenylpropoxy)-1*H*-benzo[*d*][1,2,3]triazole 3s Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.37; liquid; yield 63% (45 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.36 (br s, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 3H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 2H), 4.97-4.91 (m, 2H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 140.3, 128.9, 128.4, 128.3, 127.2, 125.7, 125.0, 120.2, 109.2, 84.6, 82.7, 22.1; FT-IR (neat) 3439, 2987, 2850, 1640, 1496, 1446, 1373, 1264, 1159, 1099, 983, 844, 764, 744, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{15}N_3O_3$: 286.1192, found: 286.1191.

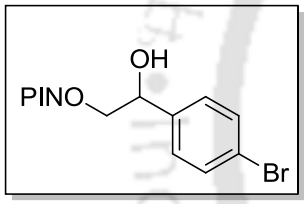


2-(2-(Pyridin-2-yl)ethoxy)isoindoline-1,3-dione 3t. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.22; liquid; yield 24% (16 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 6.8 Hz, 1H), 7.83-7.81 (m, 2H), 7.75-7.73 (m, 2H), 7.66-7.62 (m, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 6.4 Hz, 1H), 4.64 (t, *J* = 6.8 Hz, 2H), 3.32 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 157.5, 149.5, 136.7, 134.6, 129.0, 123,9, 123.7, 121.9, 77.4, 37.1; FT-IR (neat) 2924, 1789, 1732, 1592, 1570, 1467, 1437, 1373, 1187, 1129, 1082, 1017, 991, 877, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{12}N_2O_3$: 269.0926, found: 269.0934.



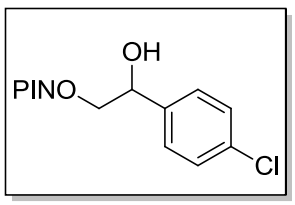
2-(2-(2-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione 5a.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.44; liquid; yield 93% (29.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.89 (m, 2H), 7.82-7.80 (m, 2H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.34-7.29 (m, 2H), 7.26-7.21 (m, 1H), 5.38 (d, *J* = 8.8 Hz, 1H), 4.53 (d, *J* = 11.2 Hz, 1H), 3.96 (t, *J* = 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 135.7, 135.1, 131.7, 129.4, 129.3, 128.8, 128.0, 127.5, 124.2, 82.1, 67.9; FT-IR (neat) 3525, 2945, 2922, 1781, 1726, 1465, 1436, 1381, 1361, 1305, 1283, 1187, 1136, 1082, 1062, 1031, 994, 957, 879, 763, 704, 694 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{16}H_{12}ClNO_4$: 300.0427, found: 300.0428.



2-(2-(4-Bromophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione 5b.

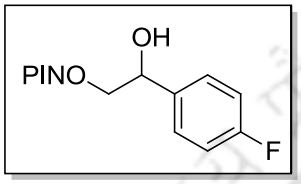
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 113-114 °C; yield 95% (34.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.86 (m, 2H), 7.82-7.79 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.98 (d, *J* = 10.0 Hz, 1H), 4.35 (d, *J* = 11.6 Hz, 1H), 4.06 (t, *J* = 11.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 137.2, 135.1, 131.8, 128.8, 128.0, 124.1, 122.2, 83.5, 70.3; FT-IR (KBr) 3509, 3089, 2941, 1782, 1732, 1716, 1488, 1466, 1399, 1374, 1313, 1186, 1129, 1076, 1009, 991, 877, 837, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{16}H_{12}BrNO_4$: 343.9922, found: 343.9919.



2-(2-(4-Chlorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione 5c.

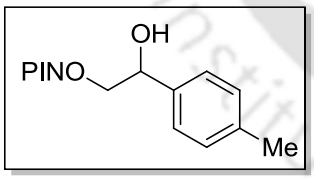
Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.45; colorless solid; mp 119-120

°C; yield 97% (30.8 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.87 (m, 2H), 7.81-7.79 (m, 2H), 7.34-7.29 (m, 4H), 4.99 (d, *J* = 7.6 Hz, 1H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.07 (t, *J* = 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 136.7, 135.1, 134.0, 128.9, 128.8, 127.7, 124.1, 83.6, 70.3; FT-IR (KBr) 3504, 3093, 2984, 2941, 1787, 1733, 1716, 1491, 1466, 1403, 1373, 1365, 1319, 1236, 1184, 1128, 1087, 1076, 1017, 993, 889, 877, 837, 700, 692 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{16}H_{12}ClNO_4$: 300.0427, found: 300.0429.



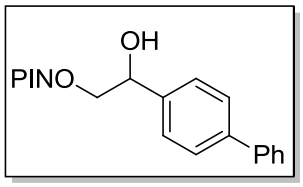
2-(2-(4-Fluorophenyl)-2-hydroxyethoxy)isoindoline-1,3-dione 5d.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 101-102 °C; yield 95% (28.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.87 (m, 2H), 7.81-7.79 (m, 2H), 7.38-7.34 (m, 2H), 7.03 (t, *J* = 8.4 Hz, 2H), 4.99 (d, *J* = 7.6 Hz, 1H), 4.35 (d, *J* = 11.6 Hz, 1H), 4.08 (t, *J* = 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 163.9 (d, $J_{C\text{-}F}$ = 245.0 Hz), 135.1, 134.0, 128.8, 128.1 (d, $J_{C\text{-}F}$ = 8.0 Hz), 124.1, 115.7 (d, $J_{C\text{-}F}$ = 22.0 Hz), 83.7, 70.3; FT-IR (KBr) 3504, 2942, 2898, 1787, 1726, 1606, 1512, 1466, 1410, 1366, 1317, 1225, 1186, 1177, 1160, 1124, 1110, 1077, 1015, 995, 876, 831, 787, 704 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{16}H_{12}FNO_4$: 284.0723, found: 284.0721.

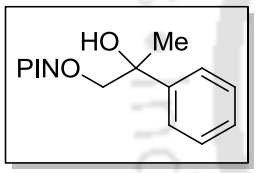


2-(2-Hydroxy-2-*p*-tolylethoxy)isoindoline-1,3-dione 5e.

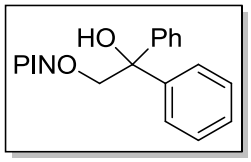
Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 104-105 °C; yield 99% (29.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.86 (m, 2H), 7.80-7.78 (m, 2H), 7.27 (d, *J* = 7.6 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 4.98 (d, *J* = 9.6 Hz, 1H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.18 (br s, 1H), 4.11 (t, *J* = 11.6 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 138.0, 135.2, 135.0, 129.4, 128.9, 126.3, 124.0, 83.8, 70.8, 21.3; FT-IR (KBr) 3525, 2920, 1784, 1719, 1466, 1379, 1314, 1187, 1137, 1018, 994, 877, 815, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{17}H_{15}NO_4$: 280.0974, found: 280.0967.



2-(2-(Biphenyl-4-yl)-2-hydroxyethoxy)isoindoline-1,3-dione 5f. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.40; colorless solid; mp 129-130 °C; yield 96% (34.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82-7.80 (m, 2H), 7.72-7.70 (m, 2H), 7.52 (t, *J* = 7.2 Hz, 4H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 5.06 (d, *J* = 9.6 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 4.16 (t, *J* = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 141.0, 140.6, 137.2, 134.9, 128.8, 128.7, 127.4, 127.3, 127.1, 126.7, 123.9, 83.6, 70.6; FT-IR (KBr) 3508, 3027, 2919, 1784, 1722, 1466, 1485, 1378, 1314, 1231, 1187, 1133, 1082, 1066, 1018, 992, 876, 767, 735, 699 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{22}H_{17}NO_4$: 342.1130, found: 342.1130.

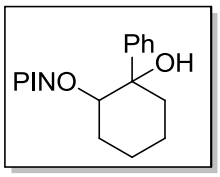


2-(2-Hydroxy-2-phenylpropoxy)isoindoline-1,3-dione 5g. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.41; liquid; yield 99% (29.4 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75-7.74 (m, 2H), 7.71-7.69(m, 2H), 7.50 (d, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 7.8 Hz, 2H), 7.13 (t, *J* = 7.8 Hz, 1H), 4.79 (br s, 1H), 4.58 (d, *J* = 10.8 Hz, 1H), 4.31 (d, *J* = 10.8 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.8, 143.9, 134.7, 128.6, 128.3, 127.1, 125.0, 123.7, 86.3, 73.4, 26.9; FT-IR (neat) 3316, 2982, 1790, 1717, 1627, 1496, 1464, 1446, 1370, 1255, 1178, 1134, 1082, 1022, 1004, 976, 961, 891, 874, 786, 765, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{17}H_{15}NO_4$: 280.0974, found: 280.0974.



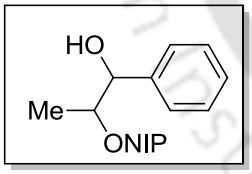
2-(2-Hydroxy-2,2-diphenylethoxy)isoindoline-1,3-dione 5h. Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.42; liquid; yield 98% (35.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.73 (m, 2H), 7.69-7.67 (m, 2H), 7.52 (d, *J* = 7.6 Hz, 4H), 7.28 (t,

J = 7.2 Hz, 4H), 7.18 (t, *J* = 7.2 Hz, 2H), 4.80 (s, 2H), 4.77 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 143.0, 134.8, 128.5, 128.4, 127.5, 126.5, 123.8, 84.6, 77.4; FT-IR (neat) 3536, 3027, 2948, 2888, 1790, 1722, 1492, 1464, 1449, 1383, 1335, 1257, 1187, 1170, 1124, 1060, 1028, 1011, 977, 908, 875, 772, 697 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{22}H_{17}NO_4$: 342.1130, found: 342.1132.



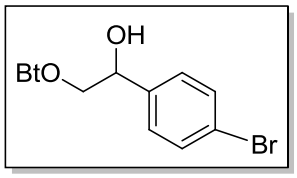
2-(2-Hydroxy-2-phenylcyclohexyloxy)isoindoline-1,3-dione 5i.

Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.39; colorless solid; mp 156-157 °C; yield 96% (32.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.69 (m, 6H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.27-7.25 (m, 1H), 4.47-4.44 (m, 1H), 3.01 (br s, 1H), 2.55-2.49 (m, 1H), 2.32-2.24 (m, 1H), 2.11-1.96 (m, 1H), 1.83-1.69 (m, 3H), 1.54-1.45 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.1, 144.2, 134.6, 128.9, 128.1, 127.6, 127.2, 123.6, 92.1, 74.1, 35.2, 27.5, 21.6, 21.5; FT-IR (KBr) 3434, 3030, 2935, 2867, 1781, 1720, 1493, 1465, 1446, 1377, 1276, 1189, 1163, 1119, 1081, 1043, 1020, 996, 979, 880, 762, 699 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{20}H_{19}NO_4$: 320.1287, found: 320.1291.

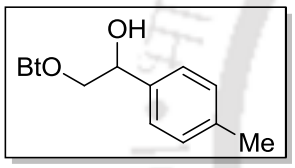


2-(1-Hydroxy-1-phenylpropan-2-yloxy)isoindoline-1,3-dione 5j.

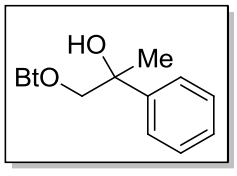
Analytical TLC on silica gel, 1:3 ethyl acetate/hexane R_f = 0.40; liquid; yield 96% (27.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.89 (m, 2H), 7.82-7.79 (m, 2H), 7.34-7.32 (m, 4H), 7.27-7.24 (m, 1H), 5.027-5.021 (m, 1H), 4.50-4.45 (m, 1H), 4.06 (br s, 1H), 1.22 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 138.7, 135.1, 129.0, 128.4, 127.5, 126.0, 124.1, 88.3, 71.7, 11.3; FT-IR (neat) 3504, 2989, 2938, 1787, 1728, 1612, 1494, 1467, 1450, 1375, 1327, 1187, 1125, 1082, 1057, 1015, 977, 878, 747, 700 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_{17}H_{15}NO_4$: 280.0974, found: 280.0975.



2-(1*H*-Benzo[*d*][1,2,3]triazol-1-yloxy)-1-(4-bromophenyl)ethanol 5k. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.41; liquid; yield 95% (31.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 5.21-5.18 (m, 1H), 4.63-4.49 (m, 2H), 3.56 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 137.7, 132.0, 128.5, 128.1, 127.3, 125.1, 122.6, 120.4, 108.9, 84.5, 70.8; FT-IR (neat) 3439, 2925, 2854, 1632, 1488, 1445, 1401, 1360, 1264, 1240, 1157, 1088, 1010, 973, 821, 782, 743, cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{14}H_{12}BrN_3O_2$: 334.0191, found: 334.0192.

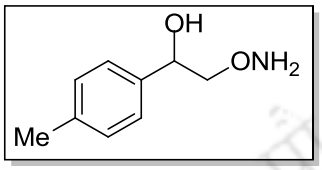


2-(1*H*-Benzo[*d*][1,2,3]triazol-1-yloxy)-1-*p*-tolylethanol 5l. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.41; liquid; yield 98% (26.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.15-7.13 (m, 2H), 5.18-5.15 (m, 1H), 4.64-4.53 (m, 2H), 4.37 (br s, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 138.4, 135.7, 129.5, 128.4, 127.4, 126.3, 125.1, 120.2, 109.1, 84.8, 71.2, 21.3; FT-IR (neat) 3439, 2921, 1613, 1514, 1446, 1359, 1264, 1240, 1179, 1158, 1090, 1020, 971, 900, 816, 781, 744 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{15}N_3O_2$: 270.1243, found: 270.1243.

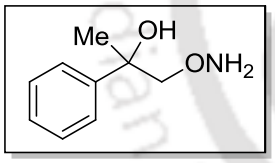


1-(1*H*-Benzo[*d*][1,2,3]triazol-1-yloxy)-2-phenylpropan-2-ol 5m. Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.42; liquid; yield 97% (26 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.46 (t, *J* =

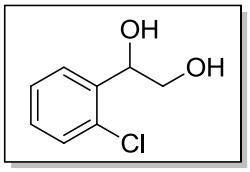
7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 3H), 7.36 (t, *J* = 8.4 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 4.70-4.63 (m, 2H), 3.28 (br s, 1H), 1.80 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.58, 143.54, 128.7, 128.2, 127.9, 127.1, 125.3, 124.9, 120.3, 108.8, 87.7, 73.9, 26.6; FT-IR (neat) 3413, 2977, 2926, 2850, 1617, 1494, 1446, 1375, 1263, 1240, 1158, 1097, 974, 743, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{15}N_3O_2$: 270.1243, found: 270.1241.



2-(Aminooxy)-1-*p*-tolylethanol 6a. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.46; liquid; yield 77% (44 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.99 (br s, 2H), 7.26 (d, *J* = 7.6 Hz, 2H), 7.16 (d, *J* = 7.6 Hz, 2H), 4.87-4.84 (m, 1H), 4.07-3.96 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 138.1, 136.7, 128.7, 126.1, 78.6, 69.9, 20.7; FT-IR (neat) 3439, 3258, 2920, 2690, 1592, 1554, 1342, 1076, 1060, 1026, 946, 890, 814 cm^{-1}; HRMS (ESI) *m/z* $[M-OH]^+$ calcd for $C_9H_{13}NO_2$: 150.0919, found: 150.0919.

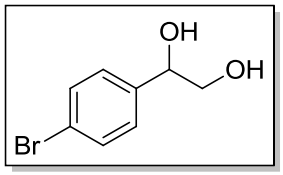


1-(Aminooxy)-2-phenylpropan-2-ol 6b. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.47; liquid; yield 79% (45 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.05 (br s, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 4.09 (s, 2H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 145.2, 127.9, 126.8, 125.3, 80.9, 73.0, 26.2; FT-IR (neat) 3471, 1632, 1554, 1538, 1505, 1382, 1226, 1091, 1015, 917, 700 cm^{-1}; HRMS (ESI) *m/z* $[M-OH]^+$ calcd for $C_9H_{13}NO_2$: 150.0919, found: 150.0919.

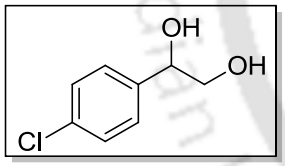


1-(2-Chlorophenyl)ethane-1,2-diol 7a.[29a] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.46; colorless solid; mp 106-107 °C; yield 61% (21 mg); ^{1}H

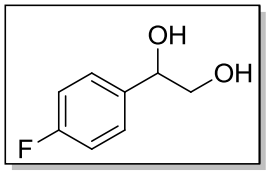
NMR (400 MHz, $CDCl_3$) δ 7.61-7.58 (m, 1H), 7.35-7.29 (m, 2H), 7.26-7.21 (m, 1H), 5.26-5.23 (m, 1H), 3.92-3.88 (m, 1H), 3.59-3.55 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 131.7, 129.0, 128.4, 127.8, 126.8, 71.2, 66.4; FT-IR (KBr) 3280, 2924, 2855, 1637, 1470, 1437, 1364, 1265, 1129, 1096, 1070, 1031, 899, 758 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_8H_9ClO_2$: 195.0189, found: 195.0188.



1-(4-Bromophenyl)ethane-1,2-diol 7b.[29a] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.43; colorless solid; mp 99-100 °C; yield 69% (30 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51-7.47 (m, 2H), 7.27-7.24 (m, 2H), 4.81-4.78 (m, 1H), 3.76-3.73 (m, 1H), 3.63-3.59 (m, 1H), 2.69 (br s, 1H), 2.17 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 140.7, 130.5, 127.5, 120.3, 73.3, 67.5; FT-IR (KBr) 3406, 2931, 2895, 1651, 1590, 1483, .1458, 1394, 1347, 1228, 1196, 1093, 1068, 1035, 1011, 899, 823 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_8H_9BrO_2$: 238.9684, found: 238.9683.

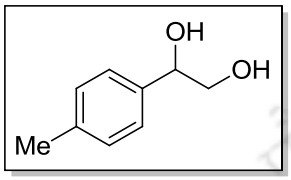


1-(4-Chlorophenyl)ethane-1,2-diol 7c.[29a] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.42; liquid; yield 67% (23 mg); ^1H NMR (400 MHz, DMSO-d_6) δ 7.37-7.32 (m, 4H), 5.36 (d, *J* = 4.4 Hz, 1H), 4.77 (t, *J* = 6.0 Hz, 1H), 4.52 (q, *J* = 5.6 Hz, 1H), 3.38 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.5, 131.2, 128.2, 127.7, 73.0, 67.2; FT-IR (neat) 3643, 3437, 2926, 2848, 1634, 1490, 1193, 1083, 1016, 818 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_8H_9ClO_2$: 195.0189, found: 195.0187.

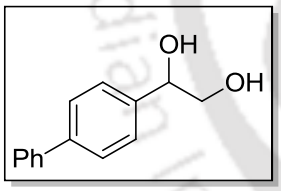


1-(4-Fluorophenyl)ethane-1,2-diol 7d.[29b] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.43; liquid; yield 66% (21 mg); ^1H NMR (400 MHz, $CDCl_3$) δ

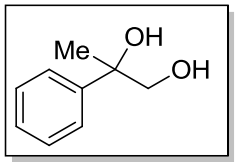
7.34-7.29 (m, 2H), 7.06-7.01 (m, 2H), 4.79-4.77 (m, 1H), 3.71-3.68 (m, 1H), 3.62-3.59 (m, 1H), 3.02 (br s, 1H), 2.00 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (d, J_{C-F} = 244.4 Hz), 136.3, 127.9 (d, J_{C-F} = 8.3 Hz), 115.7 (d, J_{C-F} = 21.7 Hz), 74.2, 68.2; FT-IR (neat) 3416, 2956, 2922, 1637, 1606, 1510, 1379, 1225, 1078, 1025, 891, 834 cm^{-1}; HRMS (ESI) *m/z* [M-OH]$^+$ calcd for $C_8H_9FO_2$: 139.0559, found: 139.0564.



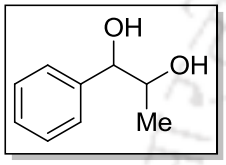
1-(*p*-Tolyl)ethane-1,2-diol 7e.[29a] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 69-70 °C; yield 81% (25 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 4.76- 4.73 (m, 1H), 3.69-3.60 (m, 2H), 3.05 (br s, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 137.6, 129.3, 126.2, 74.7, 68.2, 21.3; FT-IR (KBr) 3259, 3158, 2919, 2858, 1514, 1461, 1348, 1234, 1198, 1096, 1070, 1032, 899, 819, 774 cm^{-1}; HRMS (ESI) *m/z* [M-OH]$^+$ calcd for $C_9H_{12}O_2$: 135.0810, found: 135.0811.



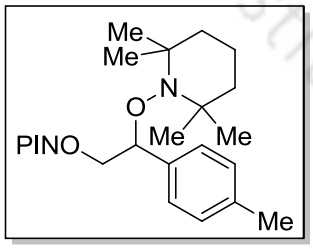
1-([1,1'-Biphenyl]-4-yl)ethane-1,2-diol 7f. Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 147-148 °C; yield 74% (32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, *J* = 7.6 Hz, 4H), 7.44 (t, *J* = 7.6 Hz, 4H), 7.35 (t, *J* = 7.6 Hz, 1H), 4.90-4.88 (m, 1H), 3.84-3.69 (m, 2H), 1.80 (br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 142.7, 140.2, 138.7, 128.9, 127.2, 126.9, 126.6, 126.2, 73.5, 67.4; FT-IR (KBr) 3349, 3025, 2925, 1634, 1565, 1485, 1404, 1363, 1247, 1191, 1097, 1074, 1043, 899, 845, 759, 725, 689 cm^{-1}; HRMS (ESI) *m/z* [M-OH]$^+$ calcd for $C_{14}H_{14}O_2$: 197.0966, found: 197.0967.



2-Phenylpropane-1,2-diol 7g.[29c] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.44; liquid; yield 78% (24 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.29 (d, *J* = 7.2 Hz, 1H), 3.79 (d, *J* = 11.2 Hz, 1H), 3.63 (d, *J* = 11.2 Hz, 1H), 2.85 (br s, 1H), 2.20 (br s, 1H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 128.6, 127.3, 125.2, 75.0, 71.2, 26.2; FT-IR (neat) 3442, 2954, 2923, 2870, 1766, 1716, 1638, 1494, 1448, 1377, 1240, 1156, 1125, 1045, 955, 864, 764, 701 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_9H_{12}O_2$: 135.0810, found: 135.0810.



1-Phenylpropane-1,2-diol 7h.[29a] Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.45; liquid; yield 65% (20 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 4.68 (d, *J* = 4.0 Hz, 1H), 4.02-3.99 (m, 1H), 2.67 (br s, 1H), 2.04 (br s, 1H), 1.08-1.06 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 128.5, 128.0, 126.8, 77.6, 71.4, 17.3; FT-IR (neat) 3414, 2959, 2921, 1639, 1452, 1379, 1259, 1199, 1126, 1080, 1043, 991, 930, 852, 746, 700 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ calcd for $C_9H_{12}O_2$: 135.0810, found: 135.0814.



2-(2-(2,2,6,6-Tetramethylpiperidin-1-yloxy)-2-*p*-tolylethoxy)isoindoline-1,3-dione 8. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.56; liquid; yield 38% (42 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77-7.76 (m, 2H), 7.70-7.69 (m, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 7.8 Hz, 2H), 5.09 (t, *J* = 7.2 Hz, 1H), 4.74-4.71 (m, 1H), 4.48 (t, *J* = 9.6 Hz, 1H), 2.29 (s, 3H), 1.46-1.25 (m, 9H), 1.17 (s, 3H), 1.03 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.1, 137.3, 137.0, 134.2, 128.7,

128.6, 127.8, 123.2, 82.9, 79.9, 60.0, 40.3, 34.0, 21.1, 20.2, 17.0; FT-IR (neat) 2930, 1791, 1735, 1514, 1466, 1375, 1361, 1257, 1186, 1132, 1081, 1017, 997, 877, 817, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{32}N_2O_4$: 437.2440, found: 437.2441.

Crystal Data of 5i at 298(2) K

Identification code	**5i**
Empirical formula	$C_{20}H_{19}NO_4$
Formula weight	337.36
Crystal habit, colour	Needle / colorless
Crystal size, mm^3	0.32 x 0.24 x 0.12
Temperature, *T*/K	298 (2)
Wavelength, *λ*/Å	0.71073
Crystal system	monoclinic
Space group	'*C* c'
Unit cell dimensions	*a* = 14.19(3)Å
	b = 16.50(3)Å
	c = 7.736(15)Å
	α = *γ* = 90.00°,
	β = 101.18(3)°
Volume, *V*/$Å^3$	1776(6)
Z	4
Calculated density, $Mg·m^{-3}$	1.261
Absorption coefficient, *μ*/mm^{-1}	0.088
F(000)	712
θ range for data collection	2.94 to 25.00°
Limiting indices	$-17 \le h \le 17, -18 \le k \le 19, -9 \le l \le 9$
Reflection collected / unique	2990 / 2404 [*R*(int) = 0.0397]
Completeness to *θ*	99.1 % (*θ* = 25.25°)
Max. and min. transmission	0.975 and 0.989

Refinement method	SHELXL-97 (Sheldrick, 1997)'
Data / restraints / parameters	2990/2/ 230
Goodness-of-fit on F^2	1.045
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0449, *wR*2 = 0.1044
R indices (all data)	*R*1 = 0.0642, *wR*2 = 0.1269

2.5 References

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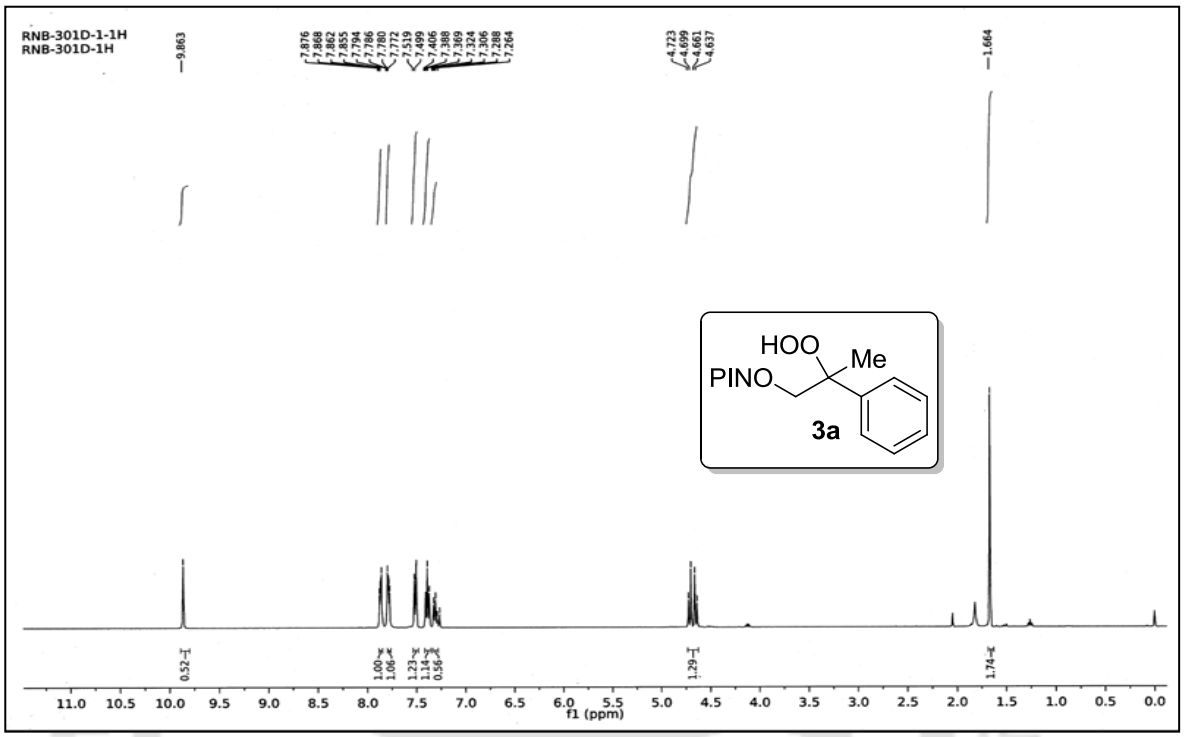
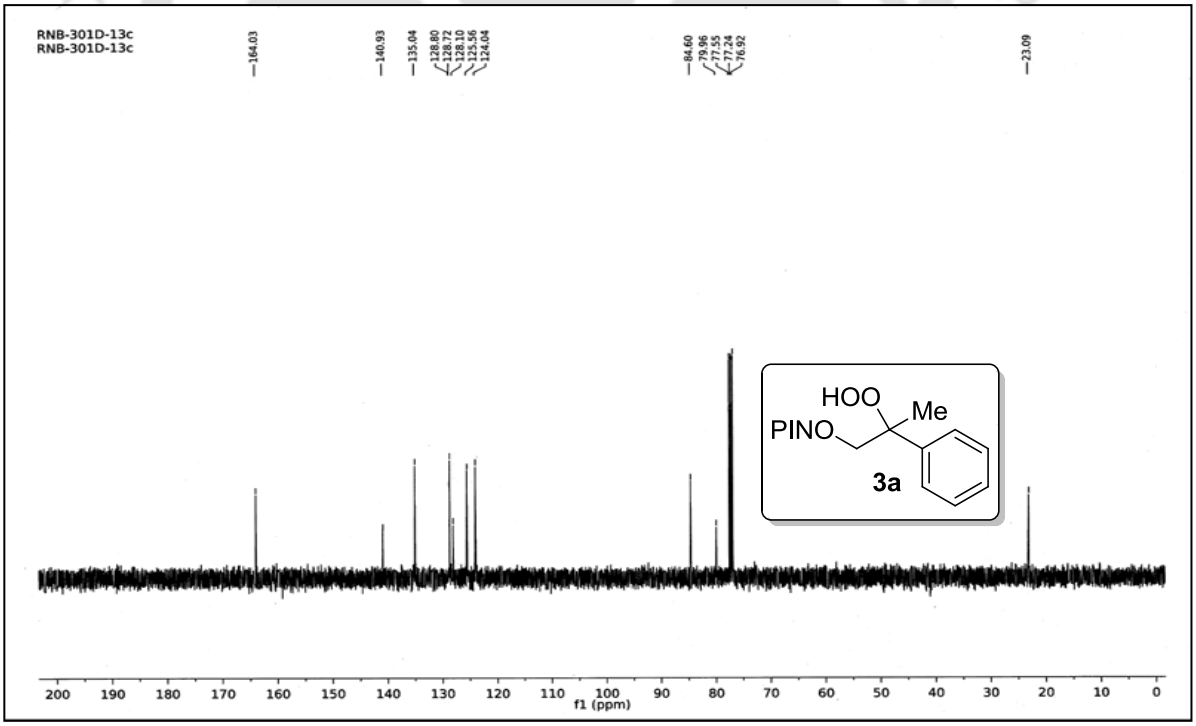
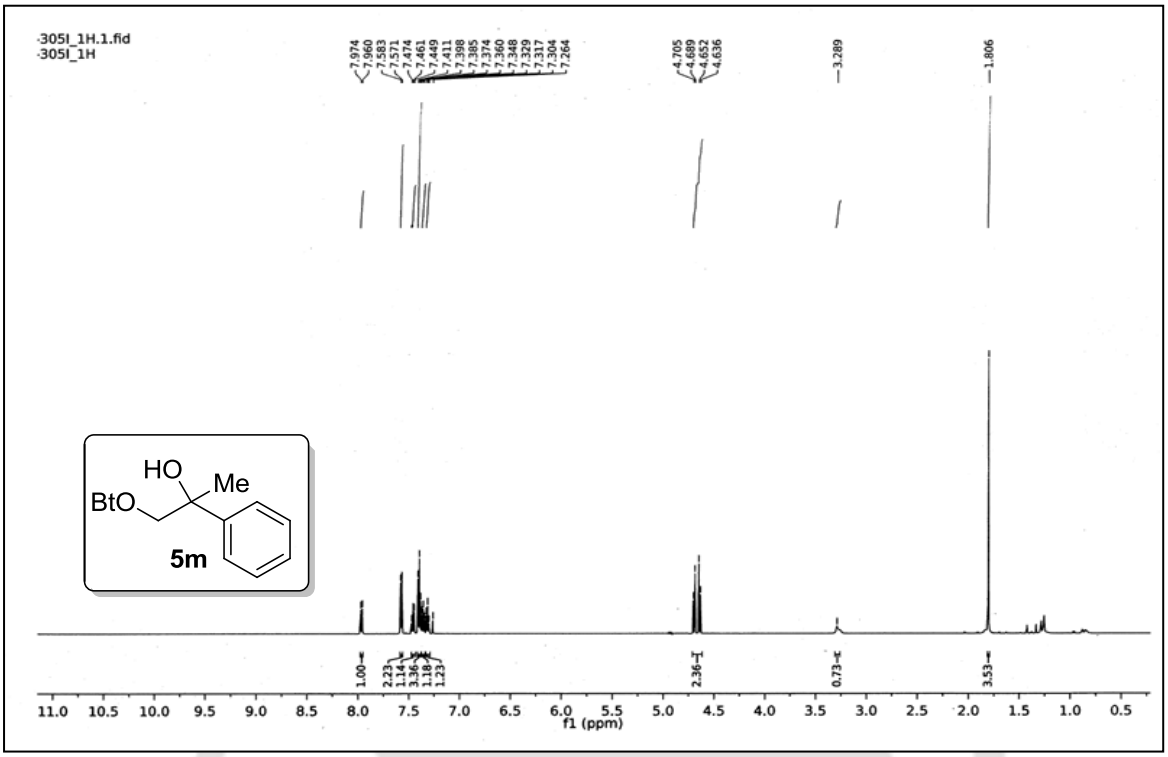
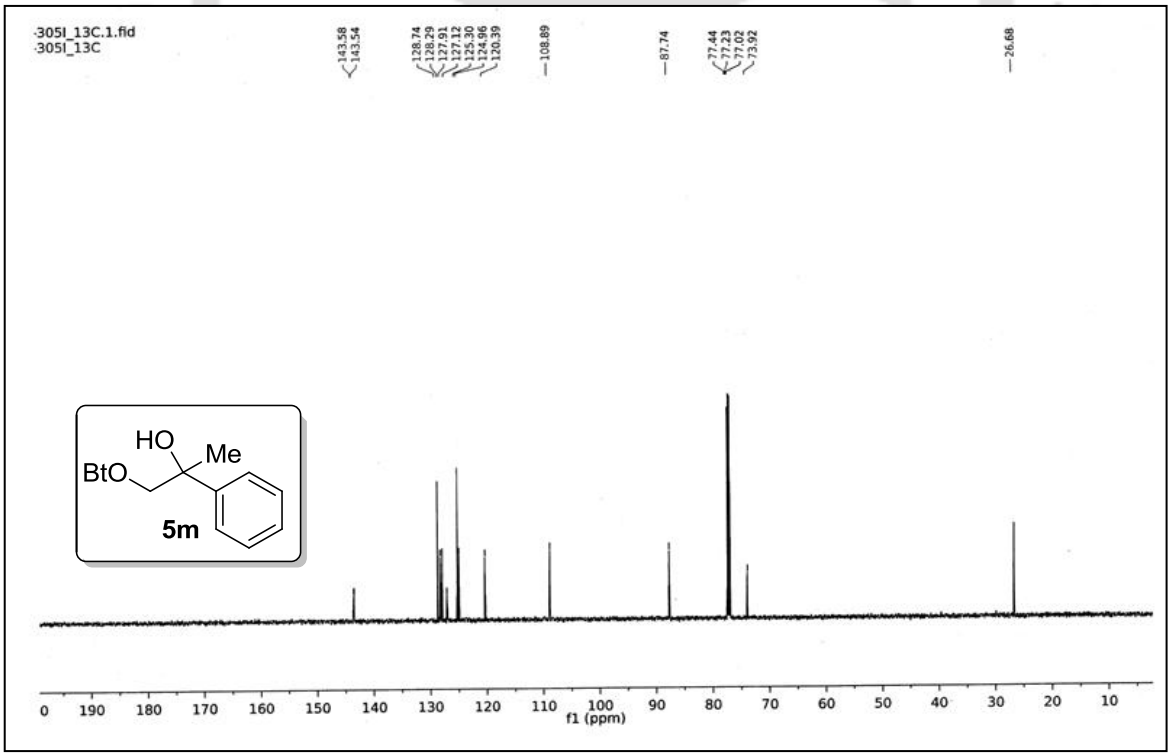
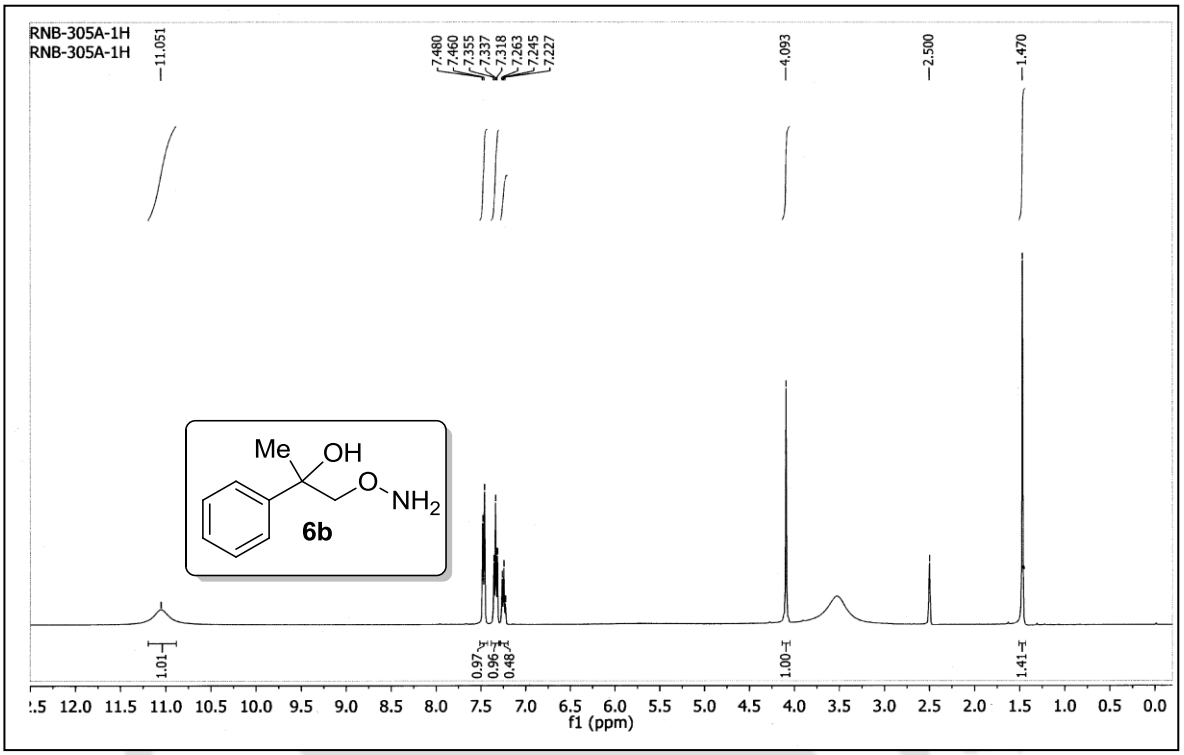
2.6 Selected NMR Spectra

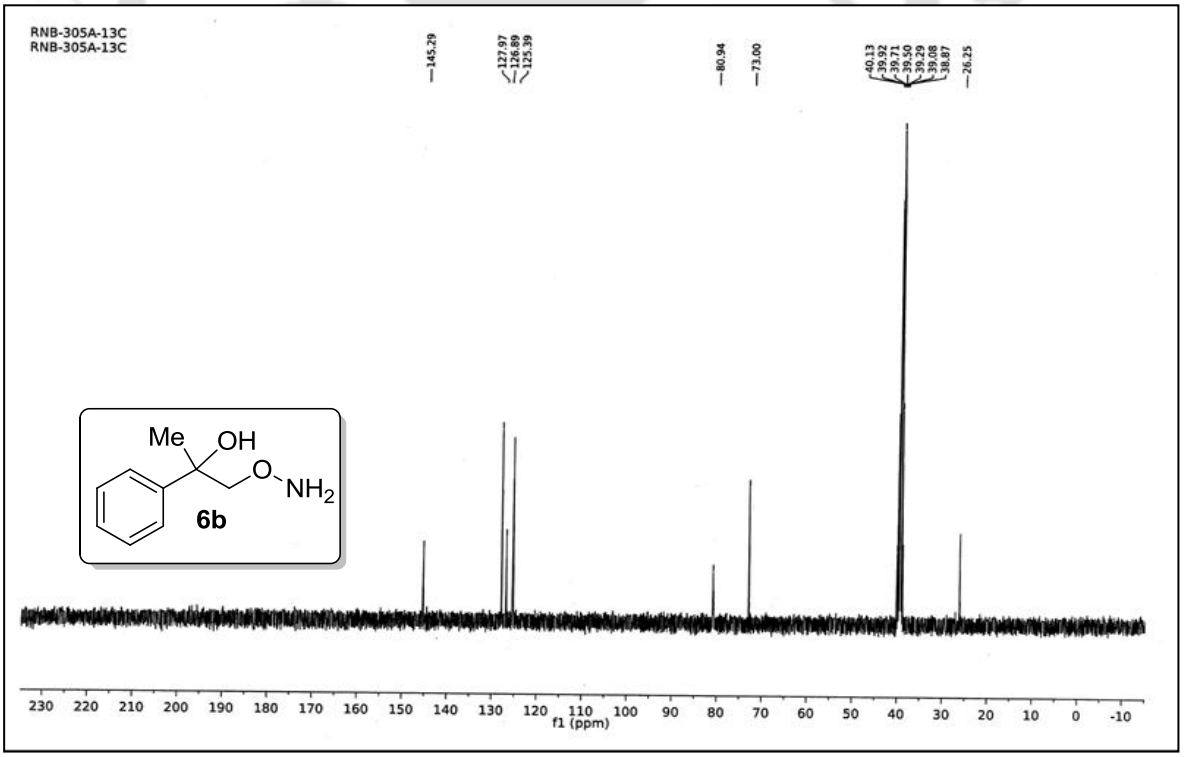


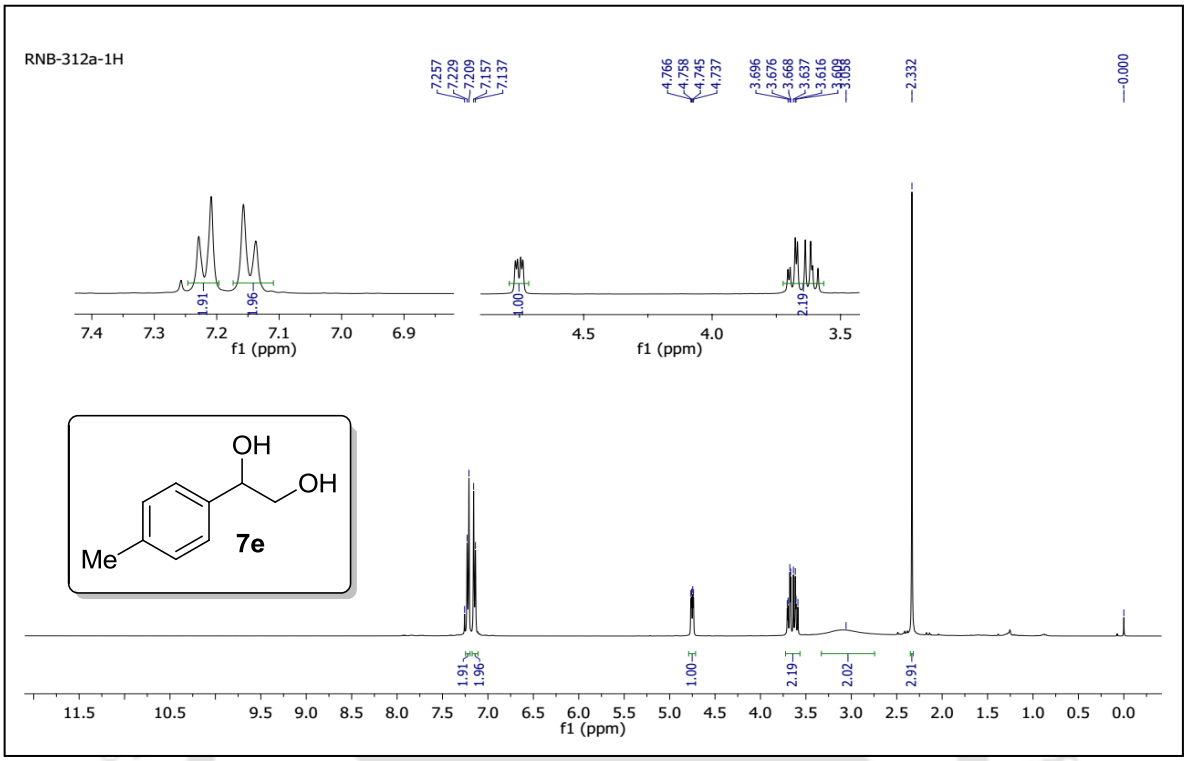


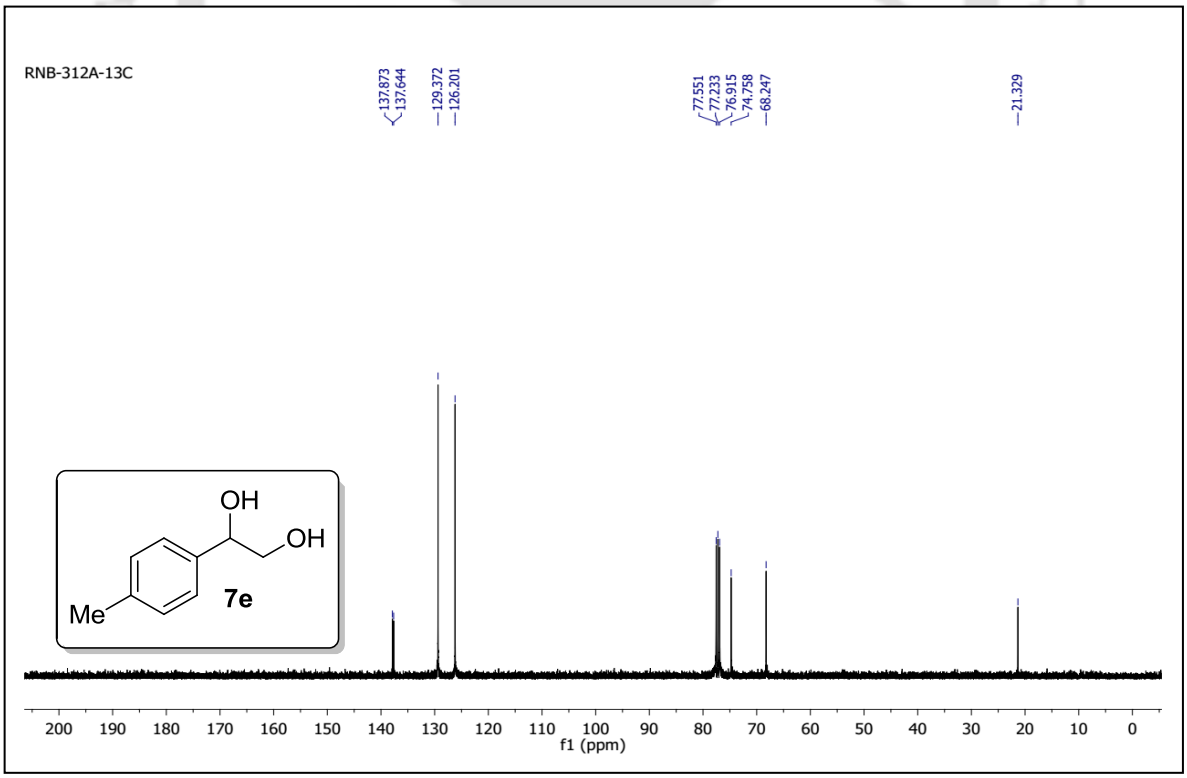


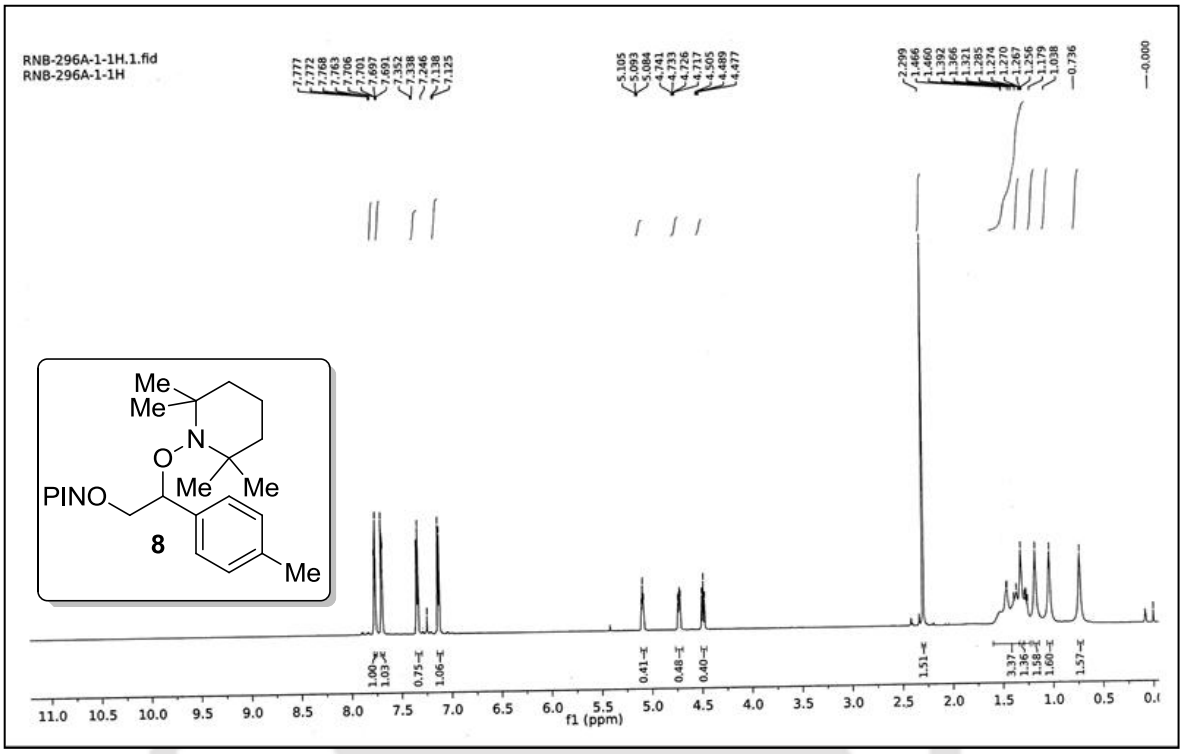


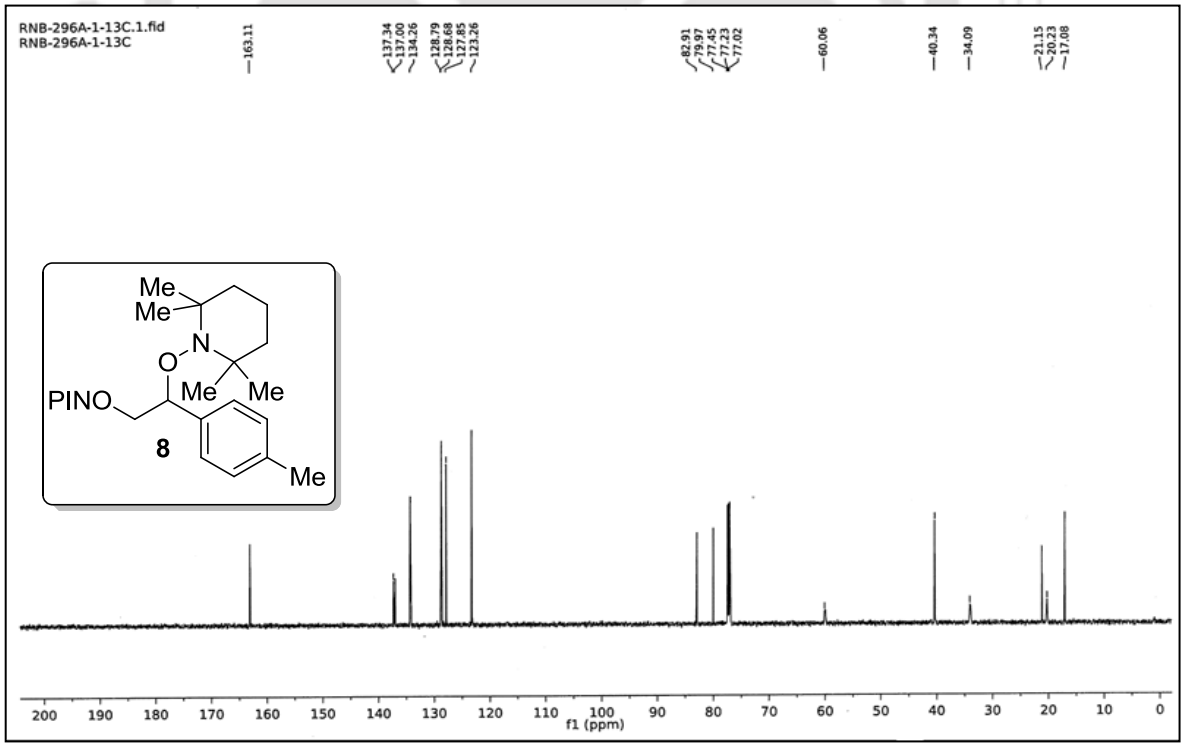












Chapter III

Metal-Free Aerobic Dioxygenation of Alkenes with *tert*-Butyl Nitrite and *N*-Hydroxylamines

Organic nitrate esters are oldest class of NO donors and found in numerous natural products.[1] They are also widely applied in medicinal chemistry as a leading therapeutic class of drugs.[2] These are commonly applied for the treatment of angina pectoris, preeclampsia and pulmonary hypertension, etc. For example, first organic nitrate ester glyceryl trinitrate (GTN), known as the main representative of the class of nitrate esters, has been used for the treatment of angina pectoris. In addition, isosorbide dinitrate (ISDN) and isosorbide 5-mononitrate (ISMN) are used for the improvement of left ventricular function with congestive heart failure and pulmonary hypertension (Figure 1).[3] Therefore, considering the medicinal importance of nitrate esters, the development of a new protocol for the aerobic synthesis of nitrate esters would be valuable.

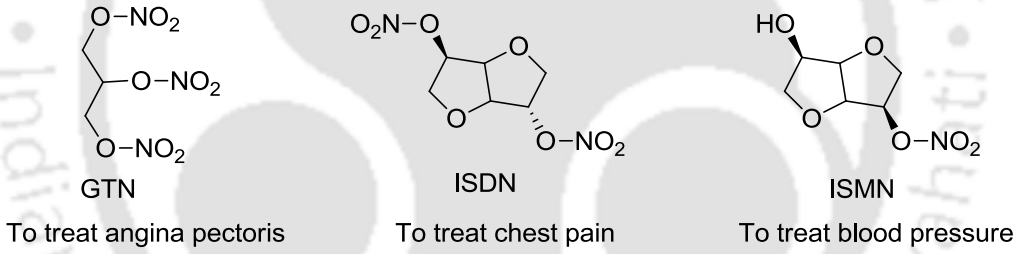
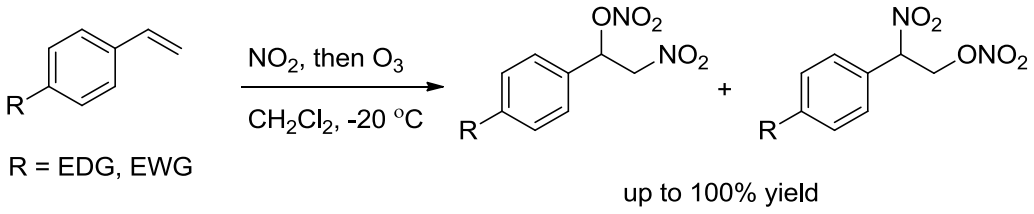


Figure 1. Examples of Some Medicinally Important Nitrate-Ester Drugs

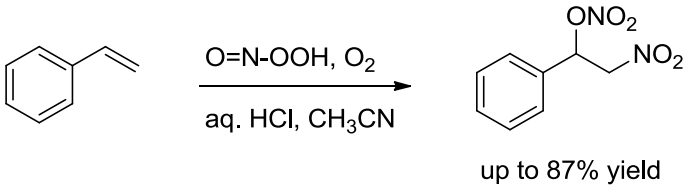
3.1 Literature

In 1997, Suzuki and co-workers reported the nitration of styrenes with a combination of nitrogen dioxide (NO_2) and ozone (O_3) in CH_2Cl_2 at -20 °C to produce isomeric nitro-nitrates (Scheme 1).[4] This nitration procedure is known as Kyodai nitration.



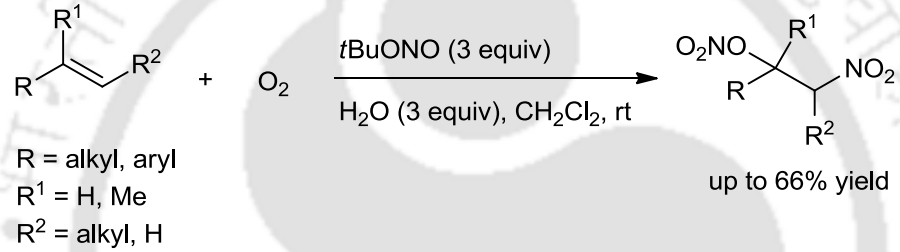
Scheme 1. Nitration of Styrenes with Nitrogen Dioxide and Ozone

A radical nitration of styrene using peroxynitrous acid HPN (O=N-OOH) and oxygen is known in aqueous acidic medium to provide nitro-nitrates in moderate yield (Scheme 2).[5]



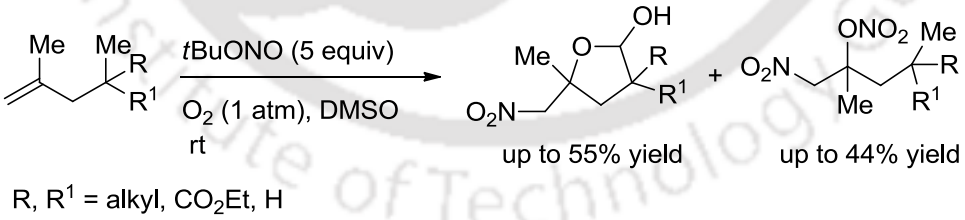
Scheme 2. Nitration of Styrene with Peroxynitrous Acid and Oxygen

Ishibashi and co-workers developed a metal-free oxidative nitration of alkenes with a combination of molecular oxygen and *tert*-butyl nitrite (*t*BuONO) to produce nitrate esters at room temperature (Scheme 3).[6]



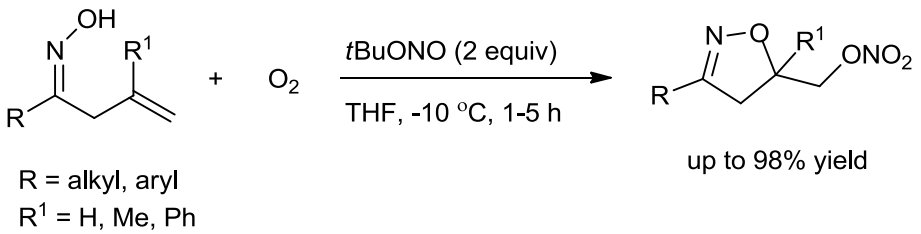
Scheme 3. Oxidative Nitration of Alkenes with Molecular Oxygen

A direct sp^3 C-H oxidation of aliphatic alkenes with *tert*-butyl nitrite and molecular oxygen is described to give γ-lactone and nitrate ester at room temperature (Scheme 4).[7] This metal-free multifunctionalization has been performed employing molecular oxygen as an oxidant.



Scheme 4. Aerobic Nitration of Alkenes with *tert*-Butyl Nitrite

Kang and co-workers reported a *t*BuONO-mediated nitrooxylation of alkenyl oximes with molecular oxygen to give nitrooxyisoxazolines in good yields (Scheme 5).[8] In this method, *t*BuONO acts as a NO source and radical initiator. This protocol is utilized for the synthesis of diol and 1,3-oxazinane in high yields.



Scheme 5. Aerobic Autoxidative Nitrooxylation of Alkenyl Oximes

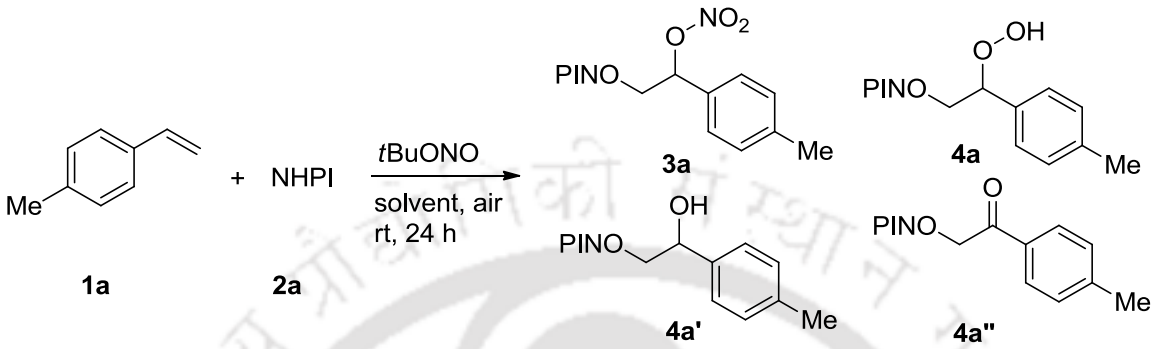
3.2 Present Study

We report here a metal-free dioxygenation for the synthesis of nitrate esters from the reaction of alkenes with *N*-hydroxylamines and *t*BuONO under aerobic conditions. These compounds can be transformed to 1,2-diols, *β*-aminoxy nitrate esters and 1,2-diketone. We commenced our optimization studies using 4-methylstyrene **1a** and NHPI **2a** as standard substrates employing *t*BuONO in presence of air at room temperature (Table 1). The oxidation occurred to produce the nitrate ester **3a** in 63% yield in $(CH_2Cl)_2$, whereas peroxide **4a** (5%), alcohol **4a′** (6%) and ketone **4a′′** (7%) were obtained as by-products (entry 1). In a set of solvents screened, chlorobenzene, CH_2Cl_2, toluene, CH_3CN, THF, DMSO and DMF, the former gave the best result (entries 2-8). Increasing or decreasing the amount of the 4-methylstyrene or *t*BuONO led to drop the yield (entries 9-12). The reaction using oxygen balloon instead of air produced 59% yield**,** while the N_2 balloon furnished the target product in a trace amount (entries 13 and 14).

With the optimized condition, the generality of the procedure was studied for the reaction of a series of diversely substituted styrenes with NHPI (Table 2). For example, styrene **1b** underwent oxidation to produce **3b** in 55% yield. The substrates bearing substitution at *ortho*-position of phenyl ring with chloro **1c** and methyl **1d** groups delivered the nitrate esters **3c** and **3d** in 60 and 62% yields, respectively. The reaction of styrenes having substitution at *meta*-position with bromo **1e**, methoxy **1f**, methyl **1g** and nitro **1h** furnished the esters **3e-h** in 47-66% yields. Likewise, the substrates containing the substitution at *para*-position with bromo **1i**, chloromethyl **1j**, chloro **1k** and phenyl **1l** underwent oxidation to deliver the **3i-l** in 57-67% yields. In addition, *β*-methylstyrene **1m** underwent oxidation to give **3m** in 61% yield with a 18:1 mixture of diastereomers. Similar results observed with *trans* and *cis*-stilbenes producing the nitrate ester **3m** in 56 and 51% yields, respectively, in a 17:1 mixture of diastereomers. In contrast, tri-substituted styrene such as *trans*-*α*-methylstilbene **1p** was

ineffective and no nitrate ester was observed. However, 2-vinylnapthalene **1q** underwent oxidation to give **3n** in 61% yield.

Table 1. Optimization of the Reaction Conditions[a]



Entry	**1a** (equiv)	Solvent	Yield (%)[b]			
			3a	**4a**	**4a′**	**4a′′**
1	2	$(CH_2Cl)_2$	63	<5	6	7
2	2	CH_2Cl_2	59	trace	10	12
3	**2**	**chlorobenzene**	**69**	**trace**	**<5**	**<5**
4	2	toluene	53	5	11	16
5	2	CH_3CN	42	-	trace	16
6	2	THF	55	trace	11	15
7	2	DMSO	-	-	-	trace
8	2	DMF	-	-	-	trace
9	3	chlorobenzene	61	trace	5	12
10	1.5	chlorobenzene	47	trace	trace	12
11	2	chlorobenzene	60[c]	trace	10	13
12	2	chlorobenzene	58[d]	trace	trace	trace
13	2	chlorobenzene	62[e]	trace	12	18
14	2	chlorobenzene	trace[f]	-	-	-

[a] Reaction conditions: 4-Methylstyrene **1a** (1.0 mmol), NHPI **2a** (0.5 mmol), *t*BuONO (1.0 mmol), solvent (2 mL), air, rt, 24 h.

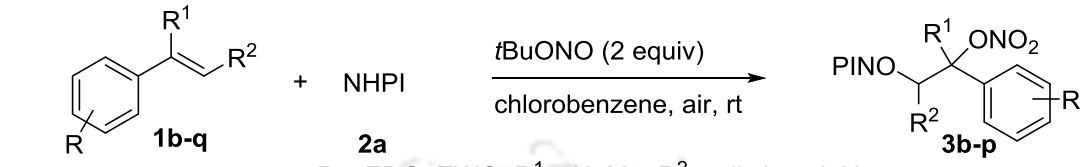
[b] Isolated yield.

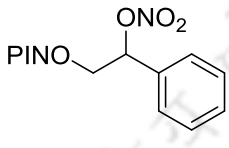
[c] 3 Equiv *t*BuONO used.

[d] 1.5 Equiv *t*BuONO used.

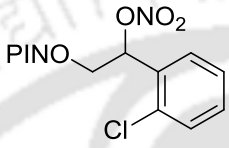
[e] O_2 balloon used. [f] N_2 balloon used.

Table 2. Reaction of Styrenes with NHPI[a-c]

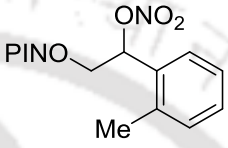




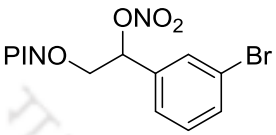
3b, 20 h, 58%



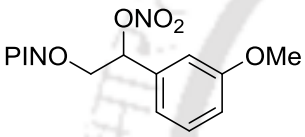
3c, 30 h, 60%



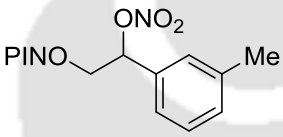
3d, 28 h, 62%



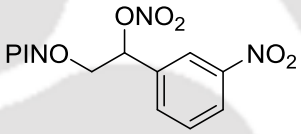
3e, 30 h, 61%



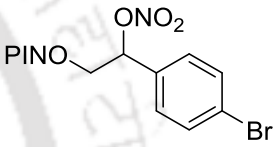
3f, 24 h, 63%



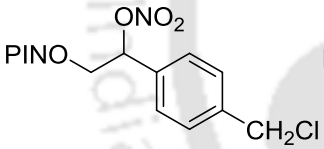
3g, 28 h, 66%



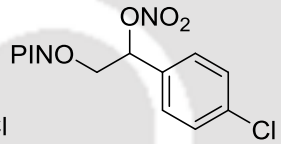
3h, 36 h, 47%



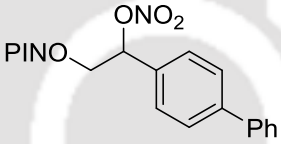
3i, 28 h, 62%



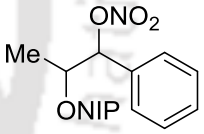
3j, 26 h, 57%



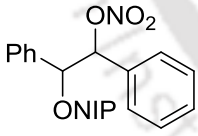
3k, 30 h, 61%



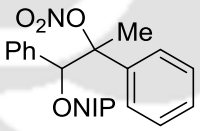
3l, 28 h, 65%



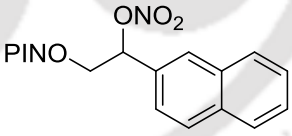
3m, 26 h, 61%
dr = 18:1[d]



3n, 31 h, 56%[e]
51%[f], *dr* = 17:1[d]



3o, 30 h, 0%



3p, 28 h, 61%

[a] Reaction conditions: Styrenes **1b-q** (1.0 mmol), NHPI **2a** (0.5 mmol), *t*BuONO (1.0 mmol), chlorobenzene (2 mL), air, rt.

[b] Isolated yield.

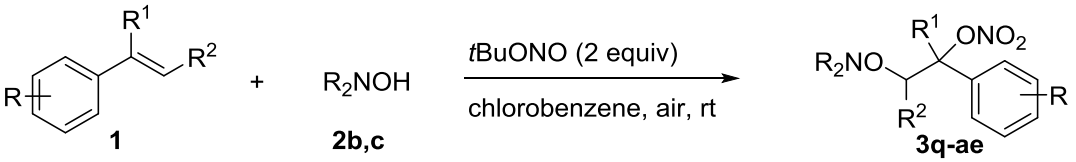
[c] Accompanied <5% of ketones and alcohols.

[d] *dr* determined by ^{1}H NMR.

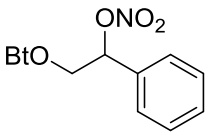
[e] *trans*-Stilbene used.

[f] *cis*-Stilbene used.

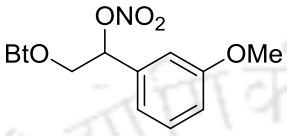
Table 3. Reaction of Styrenes with HOBt and NHSI[a-c]



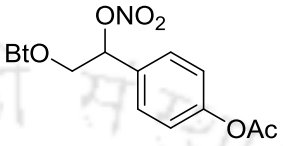
R = EDG, EWG; R^1 = H, Me; R^2 = alkyl, aryl, H; R_2NOH = HOBt, NHSI



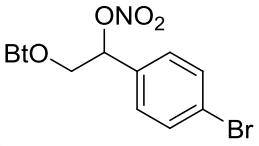
3q, 20 h, 51%



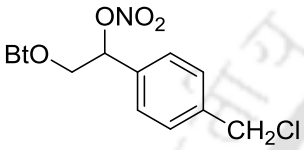
3r, 18 h, 57%



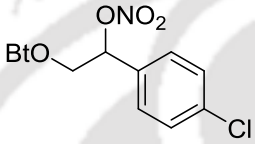
3s, 24 h, 47%



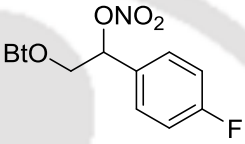
3t, 21 h, 51%



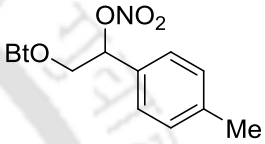
3u, 26 h, 49%



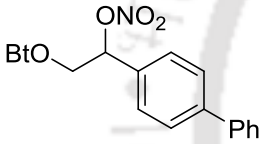
3v, 22 h, 51%



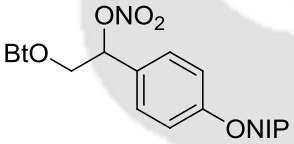
3w, 22 h, 50%



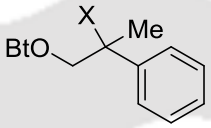
3x, 18 h, 53%



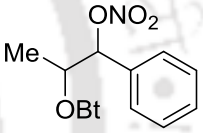
3y, 18 h, 58%



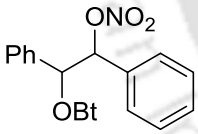
3z, 18 h, 58%



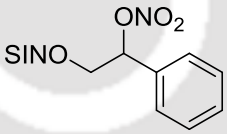
X = ONO_2, **3aa**, 26 h, trace
X = NO_2, **5**, 26 h, 26%
X = OH, **4b'**, 26 h, 48%



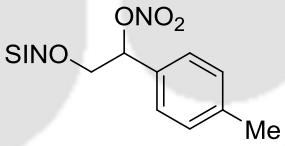
3ab, 19 h, 52%
dr = 5:1[d]



3ac, 26 h, 47%
dr = 17:1[d]



3ad, 20 h, 57%



3ae, 20 h, 59%

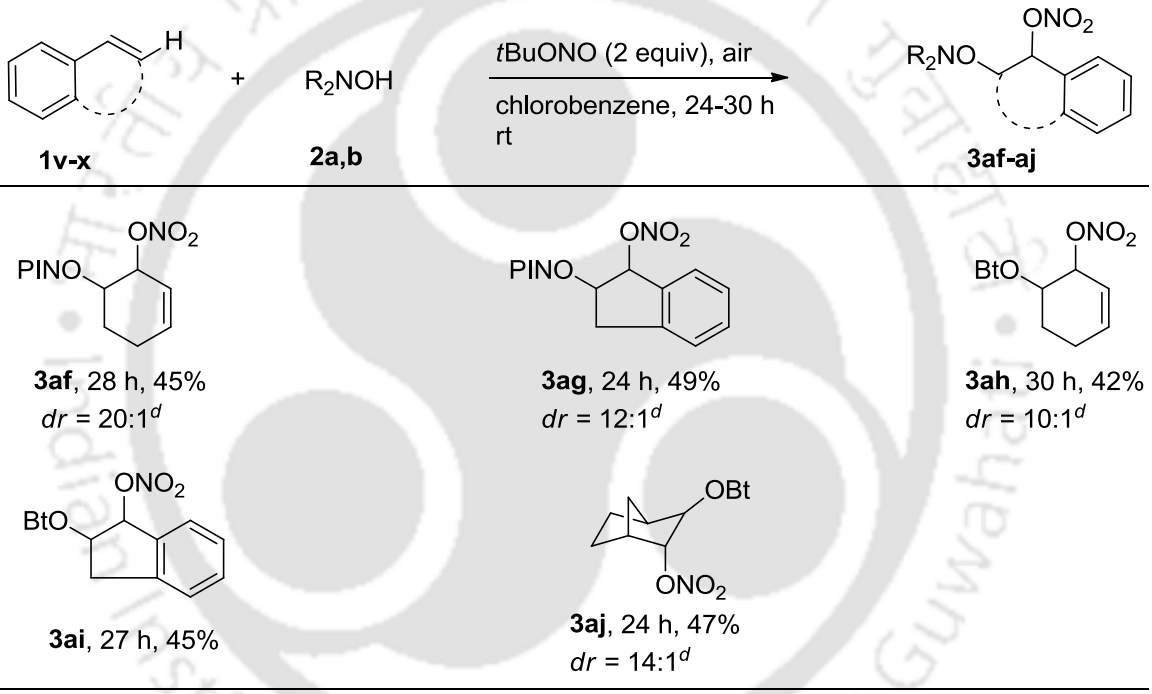
[a] Reaction conditions: Styrenes **1** (1.0 mmol), **2b** or **2c** (0.5 mmol), *t*BuONO (1.0 mmol), chlorobenzene (2 mL), air, rt.

[b] Isolated yield. [c] Accompanied <5% of ketones and alcohols. [d] *dr* determined by ^{1}H NMR.

The procedure was further extended for the reaction of HOBt and *N*-hydroxysuccinimide (NHSI) (Table 3). Styrene **1b** underwent reaction with HOBt **2b** to furnish **3q** in 51% yield, while styrene **1f** with methoxy functionality at *meta*-positon delivered the ester **3r** in 57% yield. Similarly, the reaction of the substrates bearing substitution at *para*-position with

acetoxy **1r**, bromo **1i**, chloromethyl **1j**, chloro **1k**, fluoro **1s**, methyl **1a**, phenyl **1l** and PINO **1t** functionalities produced **3s-z** in 47-58% yields. However, α-methyl styrene **1u** underwent reaction to produce a trace amount of the ester **3aa** along with 48% alcohol **4b′**[9b] and 26% nitroalkane **5**, whereas β-methylstyrene **1m** and *trans*-stilbene **1n** underwent oxidation to furnish the nitrate esters **3ab** and **3ac** in 52 (*dr* = 5:1) and 47% (*dr* = 17:1) yields, respectively. Further, the oxidation of styrenes **1b** and **1a** can be accomplished with NHSI **2c** to produce the nitrate esters **3ad** and **3ae** in 57 and 59% yields, respectively.

Table 4. Reaction of Cyclic Alkenes[a-c]



[a] Reaction conditions: Alkenes **1v-x** (1.0 mmol), **2a** or **2b** (0.5 mmol), *t*BuONO (1.0 mmol), chlorobenzene (2 mL), air, rt.

[b] Isolated yield.

[c] Accompanied <5% alcohols and ketones. [d] *dr* determined by ^{1}H NMR.

Next, the reaction of cyclic alkenes was studied (Table 4). The reaction of cyclohexadiene **1v** and indene **1w** with NHPI furnished **3af** and **3ag** in 45% (*dr* = 20:1) and 49% (*dr* = 12:1) yields, respectively. In addition, the reaction of **1v**, **1w** and 1-norbornene **1x** with HOBt

produced the esters **3ah-aj** in 42-47% (*dr* = 10:1-14:1) yields. The nitrate ester **3ag** in CH_2Cl_2 produced single crystal, whose structure was determined using X-ray analysis (Figure 2).

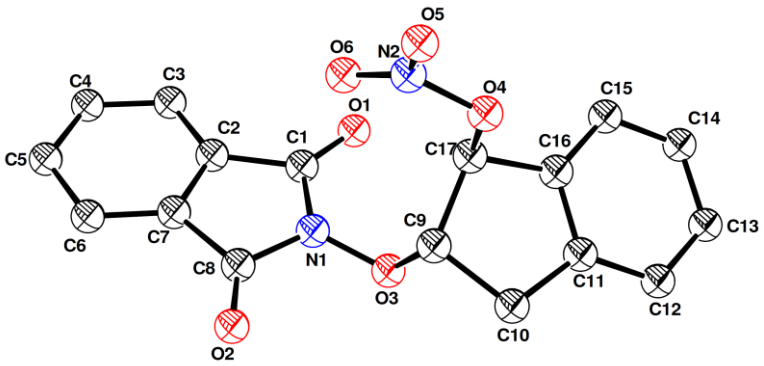
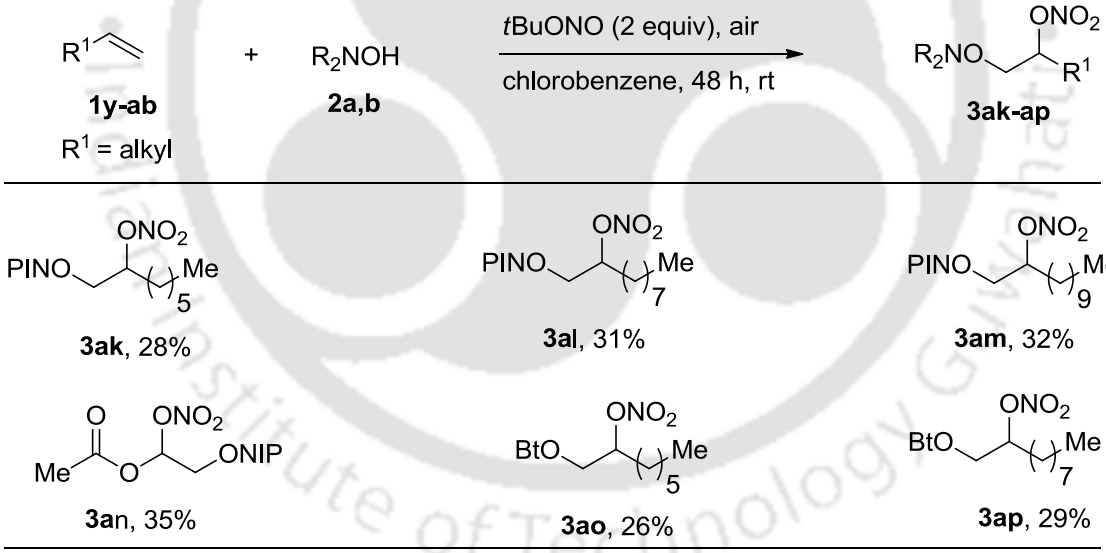


Figure 2. ORTEP diagram of 2-((1,3-dioxoisoindolin-2-yl)oxy)-2,3-dihydro-1*H*-inden-1-yl nitrate **3ag** with 50% ellipsoid. H-Atoms are omitted for clarity (CCDC 1534002).

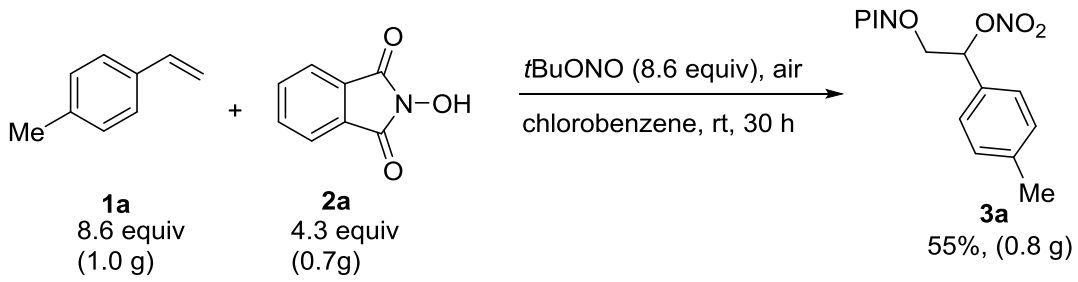
Table 5. Reaction of Aliphatic Alkenes[a-c]



[a] Reaction conditions: Alkenes **1y-ab** (1.0 mmol), **2a** or **2b** (0.5 mmol), *t*BuONO (1.0 mmol), chlorobenzene (2 mL), air, 48 h, rt.

[b] Isolated yield.

[c] Accompanied a trace amount of alcohols and ketones.

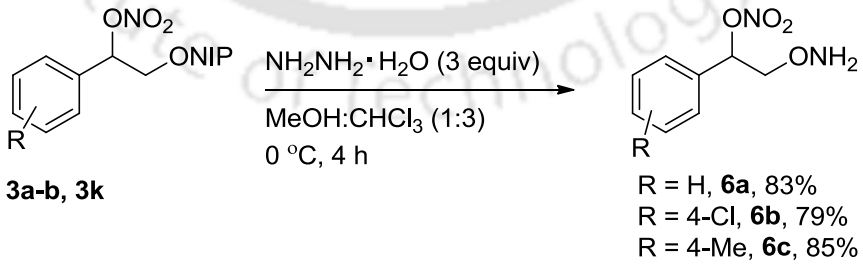


Scheme 6. Gram-Scale Synthesis

The protocol was further applied for the oxidation of aliphatic alkenes (Table 5). For example, 1-octene **1y**, 1-decene **1z** and 1-dodecene **1aa** oxidized to give the esters **3ak-3am** in 28-32% yields. The reaction of vinyl acetate **1ab** with NHPI furnished nitrate ester **3an** in 35% yield. In addition, **1y** and **1z** underwent oxidation with HOBt to furnish **3ao** and **3ap** in 26 and 29% yields, respectively. The lesser reactivity of aliphatic alkenes compared to aryl alkenes may be due to the less stability of the radical intermediate in case of aliphatic alkenes that are formed during the course of the dioxygenation process.

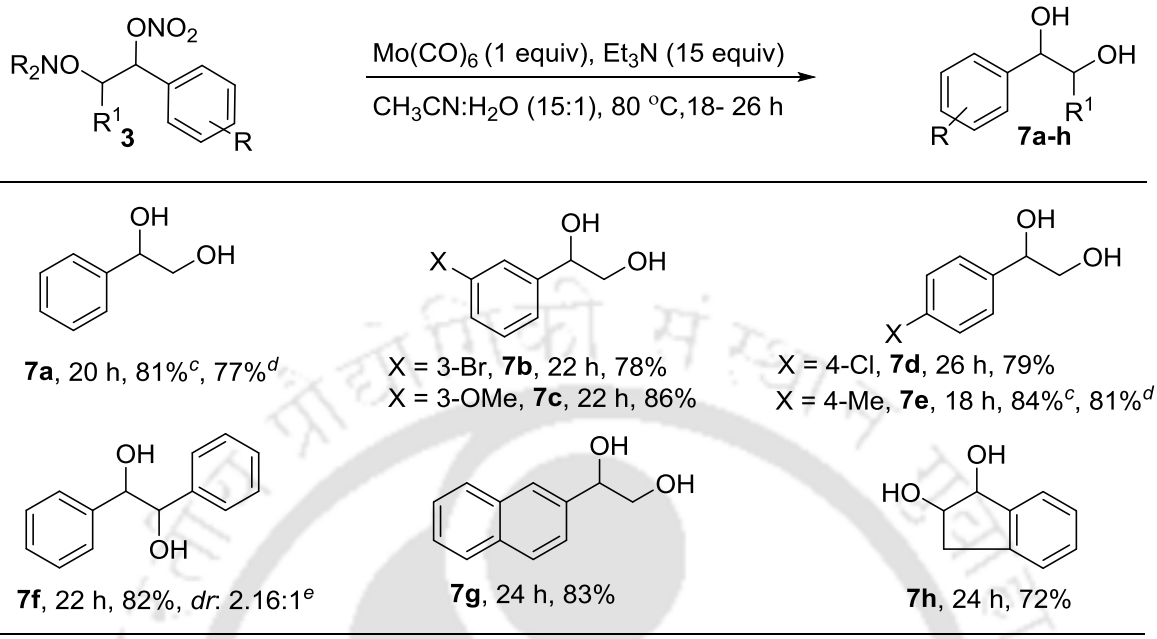
To reveal the scale up of the protocol, a gram-scale synthesis of nitrate ester was performed employing **1a** and **2a** as the representative examples (Scheme 6). As above, the oxidation readily occurred to furnish the nitrate ester **3a** in 55% yield, which suggests that this protocol can be utilized for gram-scale synthesis.

To show the utility of the developed protocol, hydrolysis of the nitrate esters **3a**, **3b** and **3k** were studied with hydrazine hydrate at 0 °C (Scheme 7).[9b] The reaction efficiently occurred to furnish the *β*-aminoxy nitrate esters **6a-c** in 79-85% yields, which are important in medicinal chemistry.[10]



Scheme 7. Synthesis of *β*-Aminoxy Nitrate Esters

Table 6. Synthesis of 1,2-Diols using $Mo(CO)_6$[a,b]



[a] Reaction conditions: **3** (0.25 mmol), $Mo(CO)_6$ (0.25 mmol), Et_3N (3.75 mmol), $CH_3CN:H_2O$ (2 mL), 18-26 h, 80 °C.

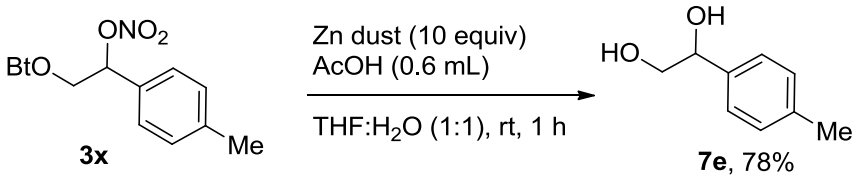
[b] Isolated yield.

[c] Diol obtained from breaking PINO bond.

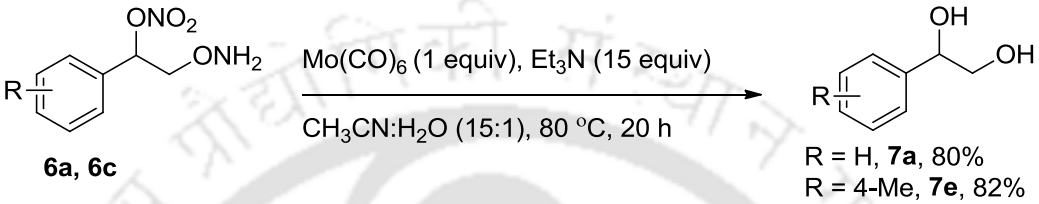
[d] Diol obtained from breaking of SINO bond.

[e] *dr* determined by ^1H NMR.

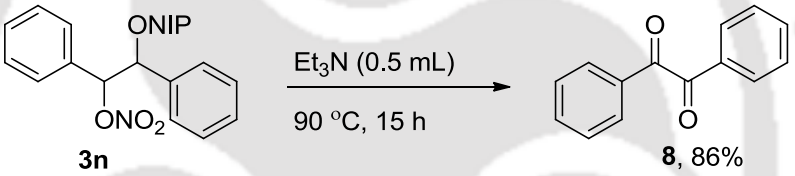
Next, reductive cleavage of *N-O* bond of the nitrate esters was performed using $Mo(CO)_6$ to produce 1,2-diols (Table 6).[11] The nitrate esters **3a-b**, **3e-f**, **3k**, **3n**, **3p** and **3ag** can be easily cleaved to give the 1,2-diols **7a-h** in 72-86% yields.[12] The nitrate ester **3ad** and **3ae** produced similar results to deliver **7a** and **7e** in 77 and 81% yields, respectively. In addition, the direct reduction of *N-O* bond of **3x** using Zn/AcOH furnished vicinal diol **7e** in 78% yield (Scheme 8).[13] Moreover, the *β*-aminoxy nitrate esters **6a** and **6c** underwent reductive cleavage using $Mo(CO)_6$ to furnish **7a** and **7e** in high yields (Scheme 9).[11] Finally, the compound **3n** under basic medium produced benzil **8**, which is an important building block in synthetic chemistry (Scheme 10).[14]



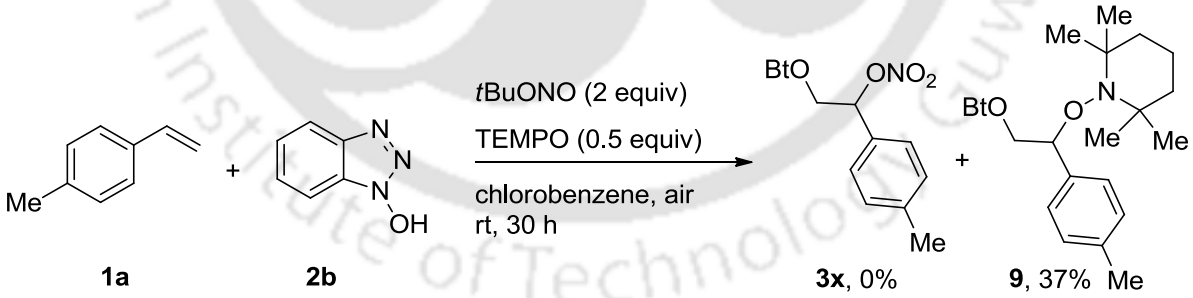
Scheme 8. Synthesis of 1,2-Diol from **3x**



Scheme 9. Synthesis of 1,2-Diols from *β*-Aminoxy Nitrate Esters

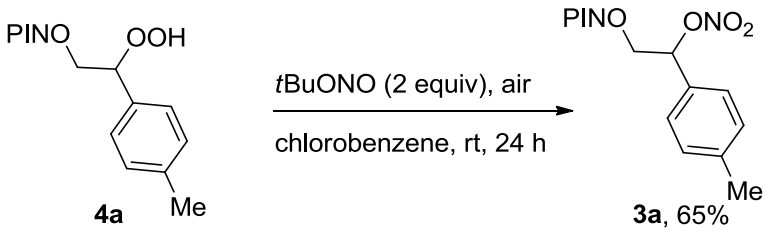


Scheme 10. Synthesis of Benzil

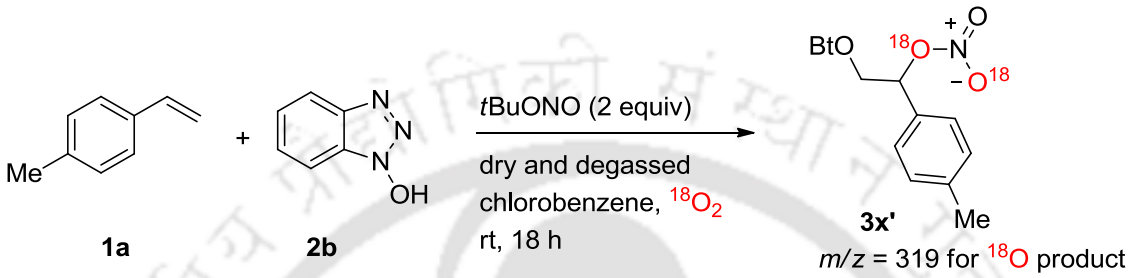


Scheme 11. Radical Trapping Experiment

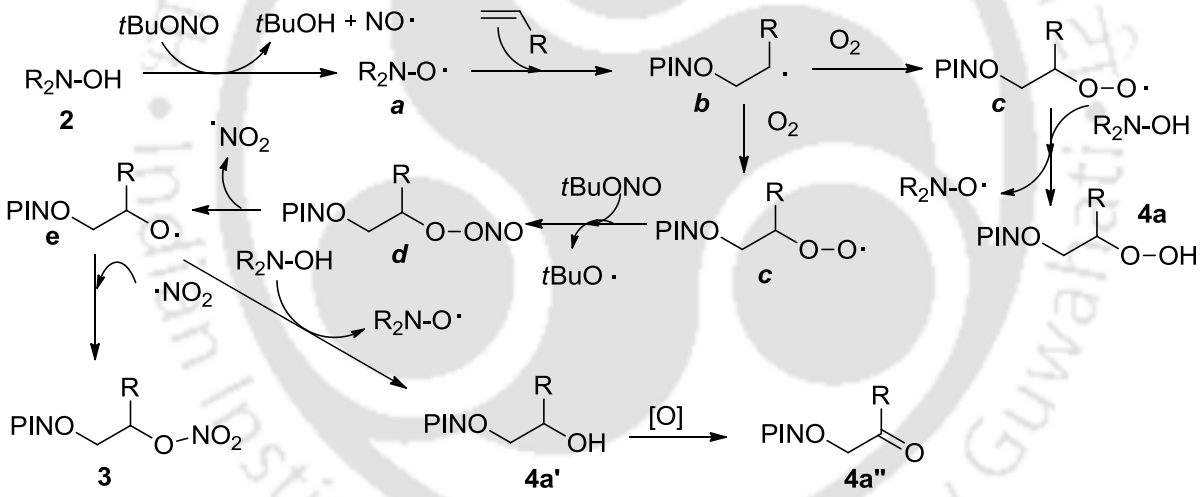
To reveal the reaction mechanism, the reaction of 4-methylstyrene **1a** with HOBt **2b** was performed using TEMPO (Scheme 11).[15] The reaction produced the TEMPO adduct **9** as a sole product and the nitrate ester **3x** was not observed, which suggests that the reaction may proceeds *via* a radical pathway. In addition, the treatment of the peroxide **4a** with *t*BuONO produced the ester **3a** in 65% yield, which indicates the formation of peroxy intermediate



Scheme 12. Conversion of **4a** into **3a**



Scheme 13. Isotope Labeling Study



Scheme 14. Proposed Reaction Mechanism

during the course of reaction (Scheme 12). In addition, the reaction of **1a** with **2b** was studied employing $^{18}O_2$ and the two labeled oxygen atoms from $^{18}O_2$ were incorporated in the ester **3x′**, which indicates that air is the source of the two oxygen atoms in the nitrate ester (Scheme 13). Thus, *N*-hydroxylamine (R_2N-OH) in presence of *t*BuONO may generate *N*-oxyl radical ***a*** under air,[16] which may undergo addition with alkene to provide a stable secondary radical intermediate ***b*** (Scheme 14). The radical ***b*** in presence of oxygen from air may generate peroxy radical species ***c***, which with *t*BuONO can produce peroxo species ***d***.

Homolytic cleavage of O-O bond of ***d*** generates alkoxy radical ***e***, which on coupling with NO_2· radical affords the ester **3**. On the other hand, the peroxy species ***c*** on reaction with *N*-hydroxylamine generates peroxide **4a**, while the alkoxy radical ***e*** in presence of *N*-hydroxylamine may provide the alcohol **4a′** which on oxidation produces the ketone **4a′′**. In this protocol, *t*BuONO with air plays dual role, a radical initiator as well as NO_2 source.

In summary, a metal-free dioxygenation for the synthesis of organic nitrate esters from alkenes using *N*-hydroxylamines and *t*BuONO has been described under air. The nitrate esters can be transformed to 1,2-diols, *β*-aminoxy nitrate esters and 1,2-diketone in high yields. Metal-free mild condition, greater reactivity, functional group diversity and the use of air as the terminal oxidant are significant practical features.

3.3 EXPERIMENTAL SECTION

General Information. *tert*-Butyl nitrite (90%) and $Mo(CO)_6$ (98%) of Aldrich, hydrazine hydrate (90-100%) of Merck and zinc dust (90%) of Rankem were used as received. The styrene 2-(4-vinylphenoxy)isoindoline-1,3-dione was prepared according to literature.[9a] The other materials and analysis are performed as reported in chapter1.

General Procedure for the Synthesis of Nitrate Esters. Alkene **1** (1.0 mmol), *N*-hydroxylamine **2** (0.5 mmol) and *t*BuONO (1.0 mmol, 119 μL) were stirred in chlorobenzene (2.0 mL) at room temperature under air. The reaction mixture was treated with CH_2Cl_2 (30 mL) and successively washed with brine (1 x 10 mL) and water (1 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent produced a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

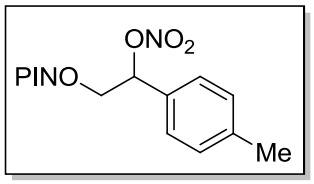
General Procedure for the Synthesis of *β*-Aminoxy Nitrate Esters. To a stirred solution of nitrate ester **3** (0.25 mmol) in MeOH/$CHCl_3$ (1:3, 2 mL) was added hydrazine hydrate (0.75 mmol, 37.6 mg). The resultant mixture was stirred at 0 ^oC for 4 h under air, and the solvent was evaporated on a rotatory evaporator. The residue was treated with Et_2O (30 mL) and the solid was filtered. The filtrate was evaporated under reduced pressure to give a pure colorless oil.

General Procedure for the Synthesis of 1,2-Diols using $Mo(CO)_6$. To a stirred solution of **3** or **6** (0.25 mmol) in CH_3CN/H_2O (15:1, 2 mL) were added $Mo(CO)_6$ (0.25 mmol, 66 mg) and Et_3N (3.75 mmol, 0.52 mL). The reaction mixture was stirred at 80 °C for 18-26 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion, the resultant mixture was neutralized using saturated NH_4Cl and extracted with ethyl acetate (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent provided a residue, which was purified on silica gel column chromatography using hexane and ethyl acetate as an eluent.

Procedure for the Synthesis of 1,2-Diol using Zn/AcOH. To a stirred solution of nitrate ester **3x** (0.25 mmol, 78.6 mg) in THF/H_2O (1:1, 2 mL) were added Zn dust (2.5 mmol, 163.5 mg) and AcOH (0.6 mL). The reaction mixture was stirred at room temperature for 1 h. The resultant mixture was neutralized using saturated $NaHCO_3$ and extracted with ethyl acetate (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

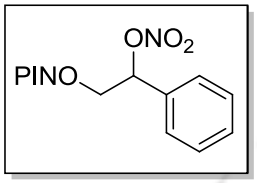
Procedure for the Synthesis of Benzil. A mixture of nitrate ester **3n** (0.2 mmol, 80.9 mg) and Et_3N (0.5 mL) was stirred at 90 °C for 15 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The resultant mixture was neutralized using saturated NH_4Cl and extracted with ethyl acetate (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as an eluent.

3.4 Characterization Data

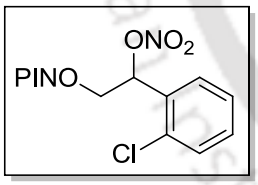


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(*p*-tolyl)ethyl nitrate 3a. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.40; colorless solid; mp 120-121 °C; yield 69% (118 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.79-7.77 (m, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.28 (dd, *J* = 9.6, 6.8 Hz, 1H), 4.55

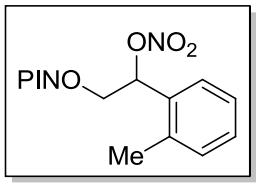
(dd, *J* = 12.8, 3.2 Hz, 1H), 4.34 (dd, *J* = 12.4, 9.6 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 140.0, 134.9, 130.6, 129.9, 128.9, 126.9, 124.0, 82.8, 77.3, 21.4; FT-IR (KBr) 2955, 2923, 1791, 1735, 1636, 1556, 1515, 1467, 1374, 1275, 1186, 1129, 1081, 1019, 1000, 877, 856, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{14}N_2O_6$: 360.1196, found: 360.1194.



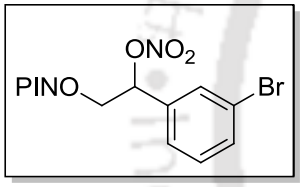
2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-phenylethyl nitrate 3b. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.41; liquid; yield 58% (95 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.84 (m, 2H), 7.79-7.76 (m, 2H), 7.41-7.38 (m, 5H), 6.31 (dd, *J* = 9.6, 6.8 Hz, 1H), 4.58-4.52 (m, 1H), 4.36 (dd, *J* = 12.8, 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 135.0, 133.6, 129.9, 129.2, 128.8, 126.9, 123.9, 82.7, 77.3; FT-IR (neat) 3065, 2943, 1791, 1732, 1639, 1560, 1494, 1467, 1373, 1275, 1187, 1131, 1081, 1020, 1000, 877, 855, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{12}N_2O_6$: 346.1039, found: 346.1038.



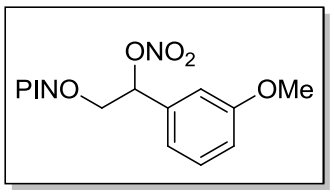
1-(2-Chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)oxy)ethyl nitrate 3c. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.43; liquid; yield 60% (109 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89-7.87 (m, 2H), 7.80-7.78 (m, 2H), 7.47-7.45 (m, 1H), 7.42-7.40 (m, 1H), 7.34-7.32 (m, 2H), 6.72 (dd, *J* = 7.2, 3.0 Hz, 1H), 4.42 (t, *J* = 4.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 135.0, 132.5, 131.6, 130.8, 130.3, 128.8, 127.8, 127.1, 124.0, 79.5, 76.1; FT-IR (neat) 3066, 2937, 1792, 1731, 1644, 1468, 1440, 1373, 1277, 1128, 1081, 1019, 1002, 877, 848, 759, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{11}ClN_2O_6$: 380.0649, found: 380.0647.



2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(*o*-tolyl)ethyl nitrate 3d. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 109-110 °C; yield 62% (106 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.78-7.77 (m, 2H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 3H), 6.27 (dd, *J* = 9.0, 6.6 Hz, 1H), 4.54 (dd, *J* = 12.6, 3.0 Hz, 1H), 4.34 (dd, *J* = 12.6, 9.6 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 139.2, 135.0, 133.6, 130.7, 129.2, 128.9, 127.5, 124.0, 123.8, 82.9, 77.4, 21.5; FT-IR (KBr) 3029, 2923, 1792, 1736, 1638, 1556, 1489, 1467, 1374, 1275, 1187, 1161, 1131, 1081, 1019, 999, 877, 853, 787, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{14}N_2O_6$: 360.1196, found: 360.1190.

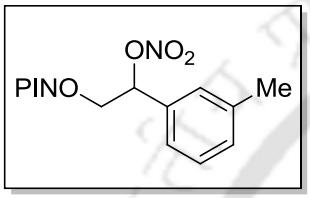


1-(3-Bromophenyl)-2-((1,3-dioxoisoindolin-2-yl)oxy)ethyl nitrate 3e. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.43; liquid; yield 61% (124 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.86 (m, 2H), 7.79-7.78 (m, 2H), 7.56 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 6.25 (dd, *J* = 9.6, 6.6 Hz, 1H), 4.52 (dd, *J* = 12.6, 3.0 Hz, 1H), 4.35 (dd, *J* = 12.6, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 136.0, 135.0, 133.1, 130.9, 130.0, 128.9, 125.5, 124.0, 123.4, 81.7; FT-IR (neat) 3065, 2941, 1791, 1735, 1640, 1571, 1468, 1430, 1373, 1274, 1187, 1130, 1080, 1020, 1000, 877, 849, 786, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{11}BrN_2O_6$: 424.0144, found: 424.0143.

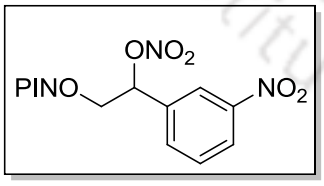


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(3-methoxyphenyl)ethyl nitrate 3f. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.39; colorless solid;

mp 121-122 °C; yield 63% (113 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.79-7.77 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 7.2 Hz, 2H), 6.27 (dd, *J* = 9.6, 6.8 Hz, 1H), 4.53 (dd, *J* = 12.8, 3.2 Hz, 1H), 4.36 (dd, *J* = 12.4, 9.6 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 160.2, 135.2, 135.0, 130.4, 128.9, 124.0, 119.0, 115.4, 112.3, 82.7, 77.4, 55.5; FT-IR (KBr) 2944, 2839, 1792, 1734, 1638, 1604, 1491, 1467, 1373, 1274, 1187, 1129, 1081, 1020, 1002, 877, 853, 785, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{14}N_2O_7$: 376.1145, found: 376.1142.

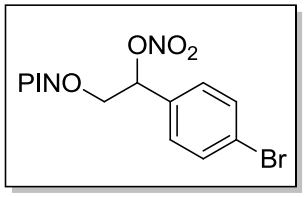


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(*m*-tolyl)ethyl nitrate 3g. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.40; colorless solid; mp 109-110 °C; yield 66% (113 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.78-7.77 (m, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 3H), 6.27 (dd, *J* = 9.0, 6.6 Hz, 1H), 4.54 (dd, *J* = 12.6, 3.0 Hz, 1H), 4.34 (dd, *J* = 12.6, 10.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 139.2, 134.9, 133.6, 130.6, 129.1, 128.9, 127.5, 124.0, 123.9, 82.9, 21.5; FT-IR (KBr) 2922, 1791, 1734, 1636, 1561, 1467, 1373, 1274, 1187, 1130, 1081, 1019, 999, 877, 853, 787, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{14}N_2O_6$: 360.1196, found: 360.1197.

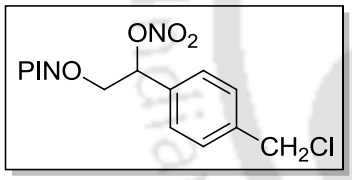


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(3-nitrophenyl)ethyl nitrate 3h. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.30; liquid; yield 47% (88 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (t, *J* = 2.0 Hz, 1H), 8.29-8.26 (m, 1H), 7.89-7.86 (m, 2H), 7.85-7.82 (m, 1H), 7.81-7.79 (m, 2H), 7.65 (t, *J* = 8.0 Hz, 1H), 6.39 (dd, *J* = 8.4, 5.2 Hz, 1H), 4.59 (dd, *J* = 12.8, 4.0 Hz, 1H), 4.43 (dd, *J* = 12.4, 8.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.5, 148.7, 136.0, 135.1, 133.0, 130.6, 128.7, 124.8, 124.1, 122.2, 81.1, 76.9; FT-IR (neat) 2918, 2850, 1791, 1734, 1642, 1531, 1467, 1352, 1309, 1274, 1186, 1128, 1081,

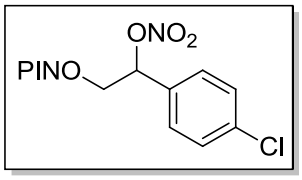
1020, 1001, 876, 847, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{16}H_{11}N_3O_8$: 391.0890, found: 391.0909.



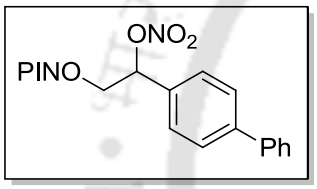
1-(4-Bromophenyl)-2-((1,3-dioxoisoindolin-2-yl)oxy)ethyl nitrate 3i. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.42; colorless solid; mp 121-122 °C; yield 62% (126 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.80-7.78 (m, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.26 (dd, *J* = 9.0, 6.0 Hz, 1H), 4.52 (dd, *J* = 12.6, 3.6 Hz, 1H), 4.34 (dd, *J* = 12.6, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 135.0, 132.8, 132.6, 128.9, 128.6, 124.2, 124.0, 82.0, 77.1; FT-IR (KBr) 2923, 2851, 1791, 1731, 1593, 1556, 1490, 1467, 1372, 1274, 1187, 1129, 1080, 1011, 877, 850, 785, 700 cm^{-1}. HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{16}H_{11}BrN_2O_6$: 424.0144, found: 424.0144.



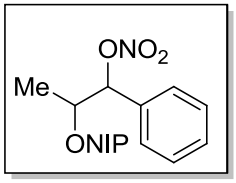
1-(4-(Chloromethyl)phenyl)-2-((1,3-dioxoisoindolin-2-yl)oxy)ethyl nitrate 3j. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.38; liquid; yield 57% (107 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.80-7.78 (m, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 6.31 (dd, *J* = 9.6, 6.6 Hz, 1H), 4.57 (s, 2H), 4.54 (dd, *J* = 12.6, 3.0 Hz, 1H), 4.35 (dd, *J* = 12.6, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 139.3, 135.0, 133.9, 129.5, 128.9, 127.4, 124.0, 82.3, 77.3, 45.5; FT-IR (neat) 2923, 2852, 1791, 1734, 1637, 1555, 1515, 1467, 1373, 1275, 1186, 1081, 1019, 1002, 877, 853, 791, 701 cm^{-1}. HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{17}H_{13}ClN_2O_6$: 394.0806, found: 394.0803.



1-(4-Chlorophenyl)-2-((1,3-dioxoisoindolin-2-yl)oxy)ethyl nitrate 3k. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.43; liquid; yield 61% (111 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.80-7.78 (m, 2H), 7.40-7.35 (m, 4H), 6.27 (dd, *J* = 9.2, 6.0 Hz, 1H), 4.53 (dd, *J* = 12.8, 3.6 Hz, 1H), 4.34 (dd, *J* = 12.8, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 136.0, 135.0, 132.3, 129.6, 128.9, 128.4, 124.0, 81.9; FT-IR (neat) 2924, 1791, 1735, 1639, 1588, 1493, 1467, 1374, 1274, 1187, 1092, 1015, 877, 851, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{16}H_{11}ClN_2O_6$: 380.0649, found: 380.0641.

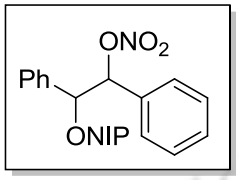


1-([1,1'-Biphenyl]-4-yl)-2-((1,3-dioxoisoindolin-2-yl)oxy)ethyl nitrate 3l. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.37; colorless solid; mp 123-124 °C; yield 65% (131 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.87 (m, 2H), 7.80-7.78 (m, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.48-7.42 (m, 5H), 7.37 (t, *J* = 7.2 Hz, 1H), 6.36 (dd, *J* = 9.6, 6.4 Hz, 1H), 4.60 (dd, *J* = 12.8, 3.2 Hz, 1H), 4.41 (dd, *J* = 12.4, 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 142.8, 140.1, 135.0, 132.4, 129.0, 128.8, 127.9, 127.4, 127.2, 124.0, 123.7, 82.6, 77.3; FT-IR (KBr) 3059, 3032, 2926, 2854, 1791, 1733, 1639, 1559, 1487, 1467, 1373, 1275, 1187, 1130, 1080, 1019, 877, 852, 766, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{22}H_{16}N_2O_6$: 422.1352, found: 422.1345.

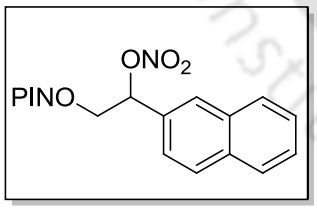


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-phenylpropyl nitrate 3m. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.40; liquid; yield 61% (104 mg); *dr* = 18:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88-7.85 (m, 1.99H), 7.80-7.77 (m, 2.08H), 7.40

(d, *J* = 4.2 Hz, 3.97H), 7.37-7.34 (m, 1.09H), 6.21 (d, *J* = 3.6 Hz, 1H), 6.08 (d, *J* = 7.8 Hz, 0.04H), 4.69-4.62 (m, 0.04H), 4.61-4.58 (m, 1.06H), 1.44 (d, *J* = 6.6 Hz, 3.25H), 1.21 (d, *J* = 6.6 Hz, 0.10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.2, 134.9, 134.3, 129.2, 129.1, 129.0, 126.6, 124.0, 84.7, 83.7, 13.1; FT-IR (neat) 2923, 2851, 1791, 1735, 1638, 1496, 1467, 1454, 1373, 1279, 1187, 1120, 1080, 981, 858, 754, 700 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{17}H_{14}N_2O_6$: 360.1196, found: 360.1185.

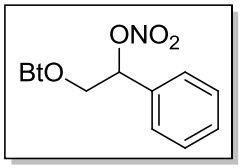


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1,2-diphenylethyl nitrate 3n. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.38; colorless solid; mp 146-147 °C; yield 56% (113 mg); *dr* = 17:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74-7.70 (m, 2.13H), 7.69-7.65 (m, 1.95H), 7.39-7.37 (m, 1.97H), 7.35-7.32 (m, 3.95H), 7.30-7.28 (m, 3.12H), 7.22-7.16 (m, 0.90H), 6.41 (d, *J* = 11.2 Hz, 0.09H), 6.36 (d, *J* = 5.6 Hz, 1H), 6.04 (d, *J* = 10.4 Hz, 1H), 5.70 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 134.7, 133.5, 132.5, 129.9, 129.5, 129.2, 128.8, 128.7, 128.3, 127.9, 123.7, 88.1, 83.9; FT-IR (KBr) 3065, 3033, 2922, 1790, 1735, 1640, 1455, 1373, 1277, 1187, 1126, 1081, 1016, 982, 876, 732, 698 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{22}H_{16}N_2O_6$: 422.1352, found: 422.1356.

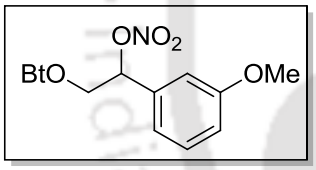


2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(naphthalen-2-yl)ethyl nitrate 3p. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.40; liquid; yield 61% (115 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 13.2 Hz, 2H), 7.86-7.83 (m, 4H), 7.77-7.76 (m, 2H), 7.52-7.51 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 1H), 6.47 (dd, *J* = 9.0, 6.0 Hz, 1H), 4.65 (dd, *J* = 12.6, 3.6 Hz, 1H), 4.44 (dd, *J* = 12.6, 9.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 135.0, 133.8, 133.2, 131.0, 129.4, 128.9, 128.3, 128.0, 127.2, 127.0, 126.8, 124.0, 123.7, 82.9; FT-IR (neat) 3060, 2925, 1790, 1733, 1637, 1467, 1373, 1274, 1187, 1127, 1081,

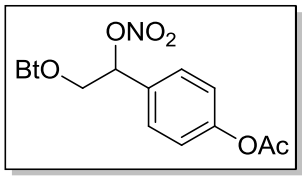
1019, 1002, 877, 852, 750, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{20}H_{14}N_2O_6$: 396.1196, found: 396.1191.



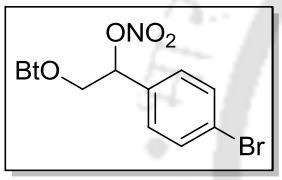
2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-phenylethyl nitrate 3q. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.44; liquid; yield 51% (77 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 4.4 Hz, 2H), 7.44-7.40 (m, 6H), 6.30 (t, *J* = 6.4 Hz, 1H), 4.83 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 133.0, 130.2, 129.4, 128.7, 127.3, 126.9, 125.1, 120.5, 108.4, 81.4, 79.1; FT-IR (neat) 3066, 3036, 2948, 1639, 1495, 1455, 1445, 1363, 1318, 1275, 1238, 1157, 1088, 1026, 972, 903, 853, 765, 744, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{14}H_{12}N_4O_4$: 301.0937, found: 301.0942.



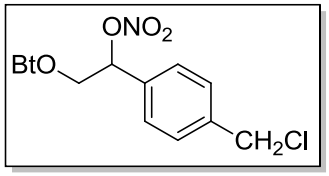
2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(3-methoxyphenyl)ethyl nitrate 3r. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.42; liquid; yield 57% (94 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.56-7.52 (m, 2H), 7.44-7.40 (m, 1H), 7.34-7.30 (m, 1H), 6.99-6.91 (m, 3H), 6.27 (dd, *J* = 7.6, 2.4 Hz, 1H), 4.80 (t, *J* = 4.8 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 143.5, 134.4, 130.6, 128.7, 127.3, 125.1, 120.5, 118.9, 115.5, 112.4, 108.4, 81.3, 79.1, 55.5; FT-IR (neat) 3066, 3005, 2943, 2838, 1642, 1603, 1588, 1491, 1456, 1437, 1363, 1274, 1158, 1089, 1038, 976, 851, 780, 744, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{15}H_{14}N_4O_5$: 331.1042, found: 331.1045.



4-(2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(nitrooxy)ethyl)phenyl acetate 3s. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.33; liquid; yield 47% (84 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04-8.02 (m, 1H), 7.56-7.51 (m, 2H), 7.44-7.41 (m, 3H), 7.17-7.15 (m, 2H), 6.31 (t, *J* = 6.0 Hz, 1H), 4.81 (dd, *J* = 6.6, 5.4 Hz, 2H), 2.30 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.2, 152.0, 143.5, 130.5, 128.8, 128.3, 127.3, 125.2, 122.8, 120.5, 108.5, 80.7, 78.9, 21.2; FT-IR (neat) 2924, 1643, 1605, 1540, 1509, 1445, 1368, 1275, 1203, 1169, 1090, 1016, 972, 911, 847, 781, 766, 745 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{16}H_{14}N_4O_6$: 359.0992, found: 359.0989.

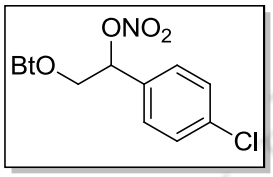


2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(4-bromophenyl)ethyl nitrate 3t. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.42; liquid; yield 57% (97 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-8.02 (m, 1H), 7.57-7.54 (m, 4H), 7.44-7.41 (m, 1H), 7.31 (d, *J* = 5.6 Hz, 2H), 6.26 (t, *J* = 4.0 Hz, 1H), 4.80 (d, *J* = 4.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 132.7, 132.1, 128.9, 128.6, 127.3, 125.2, 124.5, 120.6, 108.4, 80.7, 78.7; FT-IR (neat) 3067, 2920, 2851, 1643, 1592, 1554, 1445, 1409, 1363, 1311, 1274, 1239, 1157, 1088, 1073, 1011, 975, 903, 850, 781, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{14}H_{11}BrN_4O_4$: 379.0042, found: 379.0037.

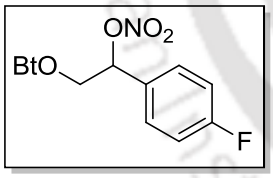


2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(4-(chloromethyl)phenyl)ethyl nitrate 3u. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.39; liquid; yield 49% (85 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.56-7.52 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.42 (t, *J* = 8.4 Hz, 2H), 6.30 (t, *J*

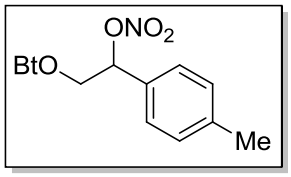
= 6.0 Hz, 1H), 4.81 (d, *J* = 6.0 Hz, 2H), 4.57 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.6, 139.7, 133.2, 129.6, 128.8, 127.4, 127.3, 125.2, 120.6, 108.4, 81.0, 78.9, 45.4; FT-IR (neat) 2923, 2850, 1642, 1515, 1444, 1424, 1384, 1363, 1275, 1239, 1157, 1089, 1034, 973, 904, 851, 781, 766, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{15}H_{13}ClN_4O_4$: 349.0704, found: 349.0701.



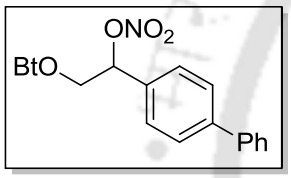
2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(4-chlorophenyl)ethyl nitrate 3v. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.43; liquid; yield 51% (85 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-8.03 (m, 1H), 7.56-7.55 (m, 2H), 7.45-7.40 (m, 3H), 7.38-7.36 (m, 2H), 6.27 (t, *J* = 6.4 Hz, 1H), 4.81 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 136.4, 131.5, 129.8, 128.9, 128.4, 127.3, 125.2, 120.6, 108.4, 80.6, 78.8; FT-IR (neat) 2922, 2849, 1639, 1597, 1493, 1444, 1413, 1384, 1362, 1312, 1273, 1238, 1156, 1090, 1014, 974, 903, 844, 781, 766, 742 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{14}H_{11}ClN_4O_4$: 335.0547, found: 335.0543.



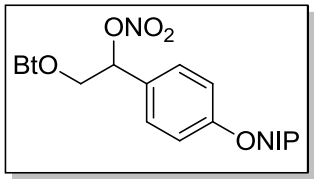
2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(4-fluorophenyl)ethyl nitrate 3w. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.44; liquid; yield 50% (80 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 3.6 Hz, 2H), 7.43-7.41 (m, 3H), 7.12 (t, *J* = 8.4 Hz, 2H), 6.30 (dd, *J* = 7.8, 3.0 Hz, 1H), 4.81 (t, *J* = 4.2 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.5 (d, J_{C-F} = 249 Hz), 143.5, 129.1 (d, J_{C-F} = 9 Hz), 128.9, 128.8, 127.3, 125.2, 120.6, 116.7 (d, J_{C-F} = 21 Hz), 108.4, 80.7, 78.9; FT-IR (neat) 3072, 2953, 2917, 2851, 1642, 1606, 1512, 1445, 1364, 1312, 1276, 1236, 1161, 1089, 1033, 975, 903, 841, 781, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{14}H_{11}FN_4O_4$: 319.0843, found: 319.0841.



2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(*p*-tolyl)ethyl nitrate 3x. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.43; liquid; yield 53% (83 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.57-7.52 (m, 2H), 7.44-7.41 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.26 (dd, *J* = 6.8, 1.2 Hz, 1H), 4.81 (t, *J* = 5.6 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 140.4, 130.1, 129.9, 128.7, 127.3, 126.9, 125.1, 120.5, 108.5, 81.4, 79.1, 21.4; FT-IR (neat) 3028, 2923, 2857, 1639, 1555, 1515, 1445, 1383, 1363, 1274, 1239, 1180, 1089, 855, 817, 744, 695 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{15}H_{14}N_4O_4$: 315.1093, found: 315.1092.

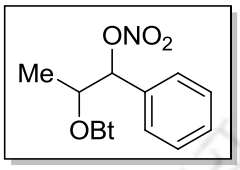


2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-([1,1'-biphenyl]-4-yl)ethyl nitrate 3y. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.38; liquid; yield 58% (109 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.57-7.51 (m, 4H), 7.48-7.40 (m, 5H), 7.39-7.34 (m, 1H), 6.34 (t, *J* = 6.4 Hz, 1H), 4.86 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 143.2, 140.0, 131.7, 129.0, 128.7, 128.1, 128.0, 127.4, 127.3, 127.2, 125.1, 120.5, 108.4, 81.2, 79.0; FT-IR (neat) 3032, 2924, 1641, 1487, 1445, 1362, 1274, 1238, 1157, 1088, 973, 902, 849, 781, 765, 743, 698 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{20}H_{16}N_4O_4$: 377.1250, found: 377.1253.

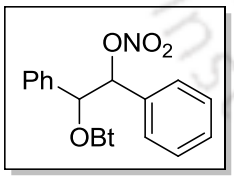


2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-(4-((1,3-dioxoisoindolin-2-yl)oxy)phenyl)ethyl nitrate 3z. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.35; colorless solid; mp 184-185 °C; yield 58% (134 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (d, *J* = 9.0 Hz, 1H), 7.94-7.92 (m, 2H), 7.84-7.83 (m, 2H), 7.56 (t, *J* =

7.8 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 3H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.28 (t, *J* = 7.2 Hz, 1H), 4.79 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.9, 160.1, 143.6, 135.3, 129.3, 128.9, 128.8, 127.3, 125.2, 124.3, 120.6, 115.2, 108.4, 80.6, 78.9; FT-IR (KBr) 2965, 2923, 2849, 1791, 1737, 1634, 1500, 1255, 1204, 1153, 1116, 1019, 970, 900, 862, 826, 766, 716, 696 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{22}H_{15}N_5O_7$: 462.1050, found: 462.1053.

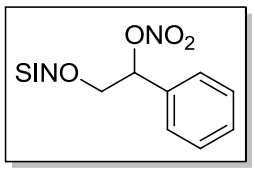


2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1-phenylpropyl nitrate 3ab. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.42; liquid; yield 52% (82 mg); *dr* = 5:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 1.13H), 7.58-7.47 (m, 1.47H), 7.43-7.41 (m, 5.98H), 7.40-7.37 (m, 2.44H), 6.16 (d, *J* = 8.4 Hz, 0.20H), 6.13 (d, *J* = 4.0 Hz, 1H), 5.07-5.01 (m, 1.06H), 4.96-4.89 (m, 0.23H), 1.51 (d, *J* = 6.4 Hz, 3.15H), 1.35 (d, *J* = 6.4 Hz, 0.51H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 133.8, 133.6, 129.6, 129.4, 129.2, 128.7, 128.1, 127.6, 126.9, 125.0, 120.5, 108.6, 86.9, 83.3, 14.0; FT-IR (neat) 3066, 2991, 2924, 2851, 1642, 1549, 1496, 1454, 1382, 1367, 1277, 1240, 1158, 1088, 1054, 968, 855, 744, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{15}H_{14}N_4O_4$: 315.1093, found: 315.1094.

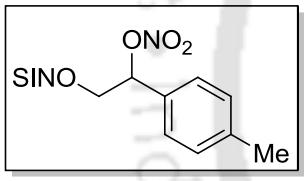


2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-1,2-diphenylethyl nitrate 3ac. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.40; liquid; yield 47% (88 mg); *dr* = 17:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 1H), 7.40-7.35 (m, 4.16H), 7.34-7.31 (m, 4.15H), 7.30 (d, *J* = 4.2 Hz, 2.71H), 7.28-7.27 (m, 1.92H), 7.17 (d, *J* = 8.4 Hz, 1.10H), 6.51 (d, *J* = 5.4 Hz, 0.06H), 6.45 (d, *J* = 5.4 Hz, 1H), 5.89 (d, *J* = 6.0 Hz, 0.07H), 5.86 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.3, 133.3, 132.3, 130.3, 129.9, 128.98, 128.91, 128.7, 128.3, 127.9, 127.8, 124.8, 120.3, 108.8, 91.5, 83.5; FT-IR (neat) 3066, 3036, 2924, 1734, 1643, 1532, 1496, 1455, 1444, 1382, 1317, 1277, 1239, 1199, 1157,

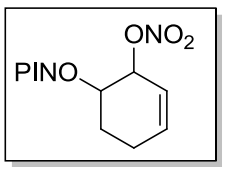
1086, 961, 847, 743, 699 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$calcd for $C_{20}H_{16}N_4O_4$: 377.1250, found: 377.1252.



2-((2,5-Dioxopyrrolidin-1-yl)oxy)-1-phenylethyl nitrate 3ad. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.32; liquid; yield 57% (80 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.28 (m, 5H), 6.24 (d, *J* = 8.0 Hz, 1H), 4.45 (t, *J* = 12.4 Hz, 1H), 4.25 (d, *J* = 12.4 Hz, 1H), 2.73 (s, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.1, 133.5, 129.9, 129.2, 126.8, 83.2, 75.9, 25.5; FT-IR (neat) 2924, 2853, 1788, 1730, 1634, 1556, 1495, 1455, 1430, 1382, 1276, 1203, 1078, 1026, 996, 903, 858, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{12}H_{12}N_2O_6$: 298.1039, found: 298.1041.

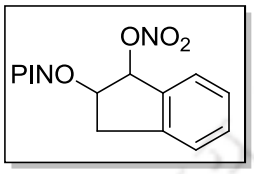


2-((2,5-Dioxopyrrolidin-1-yl)oxy)-1-(*p*-tolyl)ethyl nitrate 3ae. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.31; liquid; yield 59% (87 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.22 (d, *J* = 9.2 Hz, 1H), 4.45 (t, *J* = 9.6 Hz, 1H), 4.23 (d, *J* = 10.0 Hz, 1H), 2.74 (s, 4H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.0, 140.1, 130.5, 129.9, 126.9, 83.4, 75.9, 25.5, 21.4; FT-IR (neat) 2946, 2924, 1788, 1734, 1636, 1556, 1515, 1493, 1430, 1380, 1276, 1202, 1074, 1041, 996, 901, 858, 816, 721 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{13}H_{14}N_2O_6$: 312.1196, found: 312.1191.

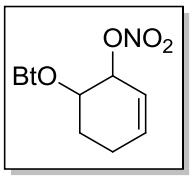


6-((1,3-Dioxoisoindolin-2-yl)oxy)cyclohex-2-en-1-yl nitrate 3af. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.44; liquid; yield 45% (68 mg); *dr* = 20:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.84 (m, 2.01H), 7.78-7.76 (m, 2.01H), 6.35

(dd, *J* = 10.0, 6.4 Hz, 1H), 6.11 (dd, *J* = 10.4, 6.4 Hz, 1H), 6.04-6.00 (m, 0.05H), 5.87-5.82 (m, 0.09H), 5.54-5.51 (m, 1.15H), 4.81-4.77 (m, 1.18H), 2.53-2.44 (m, 1.10H), 2.17-2.02 (m, 2.05H), 1.93-1.83 (m, 1.43H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.4, 134.9, 131.6, 129.0, 128.3, 123.9, 79.4, 76.4, 24.0, 23.3; FT-IR (neat) 2926, 2854, 1788, 1732, 1628, 1548, 1467, 1383, 1275, 1187, 1127, 1080, 1016, 973, 877, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{14}H_{12}N_2O_6$: 322.1039, found: 322.1037.

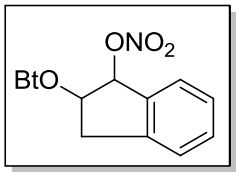


2-((1,3-Dioxoisoindolin-2-yl)oxy)-2,3-dihydro-1*H*-inden-1-yl nitrate 3ag. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.43; colorless solid; mp 160-161 °C; yield 49% (83 mg); *dr* = 12:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 1.99H), 7.79-7.77 (m, 2.21H), 7.70-7.66 (m, 0.18H), 7.49 (d, *J* = 7.6 Hz, 1.01H), 7.42 (t, *J* = 7.6 Hz, 1.08H), 7.34 (t, *J* = 6.8 Hz, 2.23H), 7.22-7.16 (m, 0.14H), 6.65 (s, 0.92H), 6.56 (d, *J* = 15.2 Hz, 0.07H), 5.15 (d, *J* = 7.2 Hz, 0.99H), 5.05-5.00 (m, 0.08H), 3.63 (dd, *J* = 17.6, 10.8 Hz, 1.13H), 3.54-3.45 (m, 0.11H), 3.36 (d, *J* = 17.6 Hz, 1.13H), 3.27-3.19 (m, 0.10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.0, 142.1, 135.0, 134.1, 131.1, 128.8, 128.1, 126.9, 125.4, 124.0, 90.2, 89.5, 36.1; FT-IR (KBr) 2965, 2920, 2850, 1792, 1733, 1636, 1467, 1374, 1310, 1271, 1187, 1126, 1082, 1019, 974, 857, 788, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{17}H_{12}N_2O_6$: 358.1039, found: 358.1035.

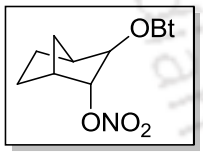


6-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)cyclohex-2-en-1-yl nitrate 3ah. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.45; liquid; yield 42% (58 mg); *dr* = 10:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.4 Hz, 1.01H), 7.55 (d, *J* = 4.0 Hz, 1.94H), 7.43-7.39 (m, 1.11H), 6.31 (dd, *J* = 10.0, 6.4 Hz, 1H), 6.18 (dd, *J* = 10.0, 6.4 Hz, 1.07H), 5.98 (dd, *J* = 9.2, 6.8 Hz, 0.15H), 5.87-5.81 (m, 0.19H), 5.77-5.74 (m, 0.12H), 5.59-5.55 (m, 0.97H), 5.20-5.17 (m, 0.98H), 5.10 (d, *J* = 4.0 Hz, 0.10H), 2.48-2.40 (m, 1.17H),

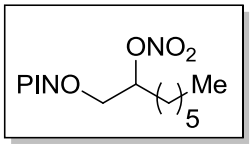
2.20-2.16 (m, 2.26H), 2.01-1.93 (m, 1.31H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 130.8, 129.1, 128.5, 128.3, 125.0, 120.6, 108.7, 81.9, 75.7, 24.0, 23.3; FT-IR (neat) 2961, 2924, 2850, 1634, 1497, 1460, 1384, 1263, 1194, 1096, 785, 749 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{12}H_{12}N_4O_4$: 277.0937, found: 277.0938.



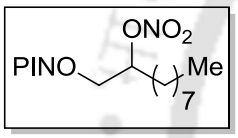
2-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)-2,3-dihydro-1*H*-inden-1-yl nitrate 3ai. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.44; liquid; yield 45% (70 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.4 Hz, 1H), 7.57-7.51 (m, 3H), 7.49-7.43 (m, 2H), 7.41-7.36 (m, 2H), 6.67 (s, 1H), 5.51 (d, *J* = 6.4 Hz, 1H), 3.63-3.46 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 141.8, 133.7, 131.5, 128.8, 128.4, 127.8, 127.0, 125.7, 125.1, 120.7, 108.4, 91.8, 88.0, 36.1; FT-IR (neat) 2922, 2850, 1726, 1639, 1464, 1444, 1384, 1353, 1275, 1239, 1156, 1089, 1011, 945, 847, 744 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{15}H_{12}N_4O_4$: 313.0937, found: 313.0937.



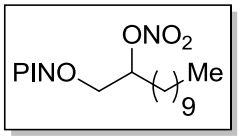
3-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)bicyclo[2.2.1]heptan-2-yl nitrate 3aj. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.41; colorless solid; mp 106-107 °C; yield 47% (68 mg); *dr* = 14:1; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 0.93H), 7.58 (d, *J* = 8.4 Hz, 0.96H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 8.4 Hz, 1H), 5.13 (d, *J* = 5.4 Hz, 1H), 4.80 (d, *J* = 5.4 Hz, 1.01H), 4.63 (m, 0.08H), 4.09 (d, *J* = 16.8 Hz, 0.07H), 2.84 (d, *J* = 4.8 Hz, 1.01H), 2.80 (d, *J* = 4.8 Hz, 0.07H), 2.57 (d, *J* =3.6 Hz, 1H), 2.52 (d, *J* = 11.4 Hz, 0.05H), 2.34 (d, *J* = 10.8 Hz, 1.14H), 2.25 (d, *J* = 4.8 Hz, 0.06H), 1.74-1.61 (m, 2.77H), 1.47 (d, *J* = 10.8 Hz, 1.15H), 1.33-1.29 (m, 1.18H), 1.11-1.06 (m, 1.11H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.5, 128.5, 127.7, 125.0, 120.4, 108.9, 91.4, 84.2, 40.6, 39.7, 33.7, 25.2, 23.2; FT-IR (KBr) 2922, 2850, 1726, 1639, 1464, 1444, 1384, 1353, 1275, 1239, 1156, 1089, 1011, 945, 847, 744 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{13}H_{14}N_4O_4$: 291.1093, found: 291.1092.



1-((1,3-Dioxoisoindolin-2-yl)oxy)octan-2-yl nitrate 3ak. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.51; liquid; yield 28% (47 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.83 (m, 2H), 7.78-7.76 (m, 2H), 5.40-5.35 (m, 1H), 4.38-4.29 (m, 2H), 1.86-1.78 (m, 2H), 1.46-1.40 (m, 2H), 1.36-1.25 (m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 134.9, 128.9, 123.9, 81.2, 77.1, 31.6, 29.6, 29.1, 25.0, 22.6, 14.2; FT-IR (neat) 2927, 2856, 1791, 1736, 1633, 1554, 1467, 1375, 1276, 1187, 1121, 1081, 1020, 877, 853, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{16}H_{20}N_2O_6$: 354.1665, found: 354.1663.

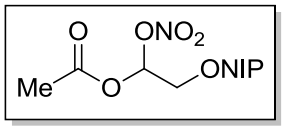


1-((1,3-Dioxoisoindolin-2-yl)oxy)decan-2-yl nitrate 3al. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.50; liquid; yield 31% (56 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.84 (m, 2H), 7.77-7.76 (m, 2H), 5.40-5.36 (m, 1H), 4.45-4.37 (m, 1H), 4.35-4.30 (m, 1H), 1.85-1.76 (m, 2H), 1.47-1.41 (m, 2H), 1.31-1.25 (m, 10H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 134.9, 128.9, 123.9, 81.2, 77.1, 33.9, 32.0, 29.7, 29.4, 29.3, 25.0, 22.8, 14.3; FT-IR (neat) 2926, 2855, 1792, 1737, 1633, 1554, 1467, 1383, 1276, 1187, 1128, 1081, 1022, 877, 856, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+ NH_4]^+$calcd for $C_{18}H_{24}N_2O_6$: 382.1978, found: 382.1990.

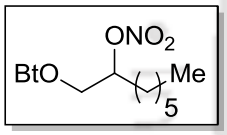


1-((1,3-Dioxoisoindolin-2-yl)oxy)dodecan-2-yl nitrate 3am. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.49; liquid; yield 32% (63 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86-7.84 (m, 2H), 7.77-7.76 (m, 2H), 5.40-5.36 (m, 1H), 4.39-4.30 (m, 2H), 1.87-1.76 (m, 2H), 1.47-1.41 (m, 2H), 1.29-1.26 (m, 14H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.4, 134.9, 128.9, 123.9, 81.2, 77.1, 33.9, 32.0, 29.74, 29.71,

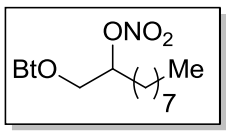
29.6, 29.52, 29.50, 25.0, 22.8, 14.3; FT-IR (neat) 2926, 2854, 1792, 1737, 1634, 1554, 1466, 1374, 1276, 1188, 1081, 1021, 1002, 877, 855, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{20}H_{28}N_2O_6$: 410.2291, found: 410.2294.



2-((1,3-Dioxoisoindolin-2-yl)oxy)-1-(nitrooxy)ethyl acetate 3an. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.42; liquid; yield 35% (54 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87-7.86 (m, 2H), 7.80-7.78 (m, 2H), 7.31 (dd, *J* = 6.6, 1.8 Hz, 1H), 4.40-4.35 (m, 2H), 2.15 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.5, 163.4, 135.1, 128.8, 124.1, 92.0, 74.2, 20.7; FT-IR (neat) 2924, 2852, 1736, 1666, 1557, 1468, 1374, 1286, 1210, 1188, 1124, 1082, 1028, 937, 877, 821, 702 cm^{-1}; HRMS (ESI) *m/z* $[M+NH_4]^+$calcd for $C_{12}H_{10}N_2O_8$: 328.0781, found: 328.0758.

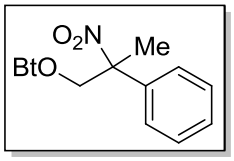


1-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)octan-2-yl nitrate 3ao. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.52; liquid; yield 26% (40 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.4 Hz, 1H), 7.56-7.55 (m, 2H), 7.44-7.40 (m, 1H), 5.52-5.46 (m, 1H), 4.77 (dd, *J* = 11.2, 8.4 Hz, 1H), 4.65 (dd, *J* = 11.2, 4.4 Hz, 1H), 1.89-1.83 (m, 2H), 1.50-1.43 (m, 2H), 1.34-1.28 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.6, 128.7, 127.1, 125.1, 120.6, 108.5, 80.4, 79.2, 31.6, 29.6, 29.0, 25.0, 22.6, 14.1; FT-IR (neat) 2928, 2857, 1637, 1458, 1369, 1277, 1239, 1157, 1088, 850, 781, 766, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{14}H_{20}N_4O_4$: 309.1563, found: 309.1560.

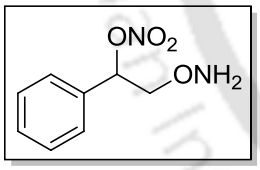


1-((1*H*-Benzo[*d*][1,2,3]triazol-1-yl)oxy)decan-2-yl nitrate 3ap. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.51; liquid; yield 29% (49 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.57-7.53 (m, 2H), 7.43-7.40 (m, 1H), 5.49-5.47 (m, 1H), 4.76 (dd, *J* = 11.4, 8.4 Hz, 1H), 4.64 (dd, *J* = 11.4, 4.8 Hz, 1H), 1.87-

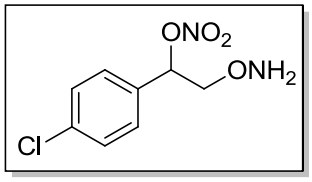
1.83 (m, 2H), 1.48-1.44 (m, 2H), 1.29-1.25 (m, 10H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.6, 128.7, 127.1, 125.1, 120.6, 108.5, 80.4, 79.2, 31.9, 29.6, 29.4, 29.3, 25.1, 22.8, 14.3; FT-IR (neat) 2927, 2855, 1638, 1556, 1463, 1370, 1276, 1239, 1157, 1088, 853, 781, 766, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{16}H_{24}N_4O_4$: 337.1876, found: 337.1878.



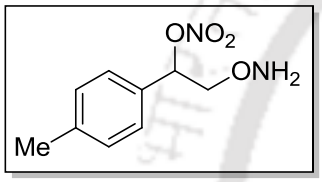
1-(2-Nitro-2-phenylpropoxy)-1*H*-benzo[*d*][1,2,3]triazole 5. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.35; liquid; yield 26% (39 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.44-7.42 (m, 5H), 7.35-7.32(m, 1H), 5.46 (d, *J* = 10.0 Hz, 1H), 4.95 (d, *J* = 9.6 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 135.2, 130.3, 129.5, 128.7, 126.3, 125.3, 125.2, 120.4, 109.0, 91.0, 82.7, 21.3; FT-IR (neat) 2923, 2850, 1736, 1637, 1549, 1383, 1264, 1085, 1020, 988, 744, 697 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{15}H_{14}N_4O_3$: 299.1144, found: 299.1145.



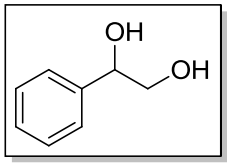
2-(Aminooxy)-1-phenylethyl nitrate 6a. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.39; liquid; yield 83% (40 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.34 (m, 5H), 6.24 (dd, *J* = 8.8, 5.6 Hz, 1H), 5.61 (br s, 2H), 4.04 (dd, *J* = 12.8, 3.6 Hz, 1H), 3.86 (dd, *J* = 12.4, 9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.7, 129.4, 129.1, 126.9, 82.8, 76.3; FT-IR (neat) 3428, 3063, 3032, 2925, 1636, 1555, 1494, 1451, 1358, 1275, 1026, 855, 758, 699 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_{10}N_2O_4$: 199.0719, found: 199.0717.



2-(Aminooxy)-1-(4-chlorophenyl)ethyl nitrate 6b. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.40; liquid; yield 79% (46 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 6.20 (dd, *J* = 9.0, 5.4 Hz, 1H), 5.61 (br s, 2H), 4.00 (dd, *J* = 12.6, 3.6 Hz, 1H), 3.83 (dd, *J* = 12.6, 9.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.4, 133.3, 129.3, 128.3, 81.9, 76.0; FT-IR (neat) 3429, 3032, 2926, 2716, 1638, 1598, 1556, 1492, 1274, 1091, 1044, 1014, 826, 752, 721 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_8H_9ClN_2O_4$: 233.0329, found: 233.0333.

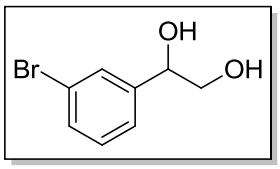


2-(Aminooxy)-1-(*p*-tolyl)ethyl nitrate 6c. Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.38; liquid; yield 85% (45 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 7.6 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.21 (dd, *J* = 8.8, 5.6 Hz, 1H), 5.52 (br s, 2H), 4.05-4.00 (m, 1H), 3.85-3.81 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.5, 131.6, 129.7, 126.9, 82.8, 76.2, 21.4; FT-IR (neat) 3324, 3030, 2922, 2854, 1632, 1554, 1515, 1456, 1378, 1275, 1201, 1117, 1017, 858, 815, 755, 721 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_9H_{12}N_2O_4$: 213.0875, found: 213.0880.

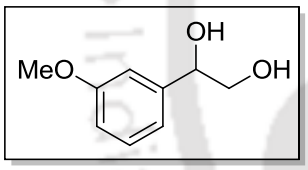


1-Phenylethane-1,2-diol 7a.[12a] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.37; colorless solid; mp 61-62 °C yield 81% (28 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.33 (m, 3H), 7.31-7.27 (m, 2H), 4.80 (dd, *J* = 8.4, 5.6 Hz, 1H), 3.73 (dd, *J* = 10.4, 8.0 Hz, 1H), 3.63 (dd, *J* = 11.2, 3.2 Hz, 1H), 3.09 (br s, 1H), 2.29 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 128.6, 128.1, 126.2, 74.8, 68.2; FT-IR (KBr) 3448,

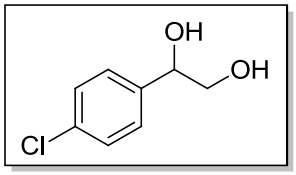
2924, 2854, 1637, 1449, 1382, 1263, 1100, 756, 700 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_8H_{10}O_2$: 121.0654, found: 121.0650.



1-(3-Bromophenyl)ethane-1,2-diol 7b.[12c] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.41; liquid; yield 78% (42 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 4.79 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.75 (dd, *J* = 11.4, 7.8 Hz, 1H), 3.62 (dd, *J* = 11.4, 3.0 Hz, 1H), 2.40 (br s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.0, 131.2, 130.3, 129.4, 124.9, 122.9, 74.1, 68.0; FT-IR (neat) 3400, 2925, 2873, 1658, 1595, 1569, 1475, 1426, 1191, 1100, 1071, 1030, 899, 783, 734, 696 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_8H_9BrO_2$: 198.9759, found: 198.9760.

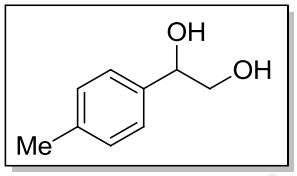


1-(3-Methoxyphenyl)ethane-1,2-diol 7c.[12b] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.33; liquid; yield 86% (36 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 2H), 6.83 (d, *J* = 8.4 Hz, 1H), 4.77 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.79 (s, 3H), 3.74-3.71 (m, 1H), 3.65-3.61 (m, 1H), 2.05 (br s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.9, 142.4, 129.7, 118.5, 113.5, 111.8, 74.7, 68.2, 55.4; FT-IR (neat) 3393, 2933, 2836, 1602, 1586, 1488, 1455, 1435, 1318, 1264, 1155, 1075, 1042, 932, 876, 786, 757, 699 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_9H_{12}O_3$: 151.0759, found: 151.0754.

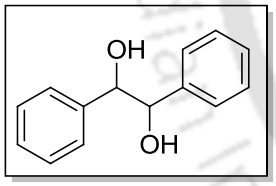


1-(4-Chlorophenyl)ethane-1,2-diol 7d.[12a] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.40; liquid; yield 79% (34 mg); ^1H NMR (600 MHz,

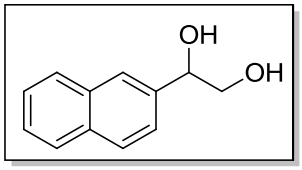
$CDCl_3$) δ 7.33 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 4.78 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.72 (dd, *J* = 11.4, 7.8 Hz, 1H), 3.60 (dd, *J* = 10.8, 3.0 Hz, 1H), 2.90 (br s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.1, 133.9, 128.8, 127.6, 74.2, 68.1; FT-IR (neat) 3422, 2924, 2871, 1643, 1598, 1492, 1405, 1194, 1089, 1013, 890, 824 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_8H_9ClO_2$: 155.0264, found: 155.0266.



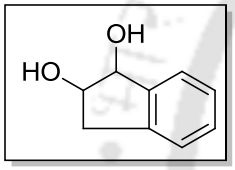
1-(*p*-Tolyl)ethane-1,2-diol 7e.[12a] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.35; colorless solid; mp 70-71 °C; yield 84% (32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 4.79 (dd, *J* = 7.6, 4.8 Hz, 1H), 3.75-3.70 (m, 1H), 3.67-3.61 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 137.7, 129.4, 126.2, 74.7, 68.2, 21.3; FT-IR (KBr) 3400, 2923, 2870, 1771, 1719, 1613, 1514, 1453, 1261, 1180, 1080, 1020, 890, 771, 719 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_9H_{12}O_2$: 135.0810, found: 135.0808.



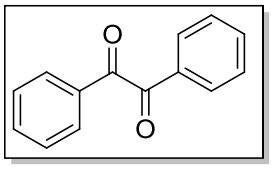
1,2-Diphenylethane-1,2-diol 7f.[12a] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.32; liquid; yield 82% (44 mg); dr : 2.16:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.28 (m, 5.86H), 7.24-7.21 (m, 7.20H), 7.11-7.09 (m, 2H), 4.81 (s, 1.99H), 4.68 (s, 0.92H), 2.97 (br s, 0.95H), 2.33 (br s, 2.42H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.0, 139.9, 128.4, 128.33, 128.30, 128.1, 127.3, 127.1, 79.3, 78.3; FT-IR (neat) 3390, 3059, 3030, 2920, 2850, 1635, 1491, 1452, 1260, 1201, 1037, 845, 765, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_{14}H_{14}O_2$: 197.0967, found: 197.0961.



1-(Naphthalen-2-yl)ethane-1,2-diol 7g.[12a] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.34; colorless solid; mp 133-134 °C; yield 83% (39 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85-7.83 (m, 4H), 7.50-7.46 (m, 3H), 5.01 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.87 (dd, *J* = 11.4, 8.4 Hz, 1H), 3.76 (dd, *J* = 11.4, 3.0 Hz, 1H), 2.62 (br s, 1H), 2.07 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.1, 133.4, 133.3, 128.5, 128.1, 127.9, 126.5, 126.2, 125.2, 124.1, 74.9, 68.2; FT-IR (KBr) 3414, 3057, 3020, 2932, 2844, 1700, 1603, 1453, 1384, 1260, 1005, 915, 845, 766, 698 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_{12}H_{12}O_2$: 171.0810, found: 171.0811.

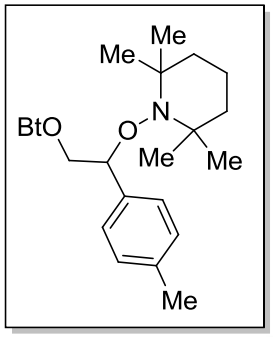


2,3-Dihydro-1*H*-indene-1,2-diol 7h.[12a] Analytical TLC on silica gel, 1:2 ethyl acetate/hexane R_f = 0.37; colorless solid; mp 92-93 °C; yield 72% (27 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.42 (m, 1H), 7.29-7.25 (m, 3H), 5.02 (d, *J* = 4.8 Hz, 1H), 4.53 (t, *J* = 5.2 Hz, 1H), 3.15 (dd, *J* = 16.4, 10.4 Hz, 1H), 2.98 (dd, *J* = 16.4, 12.8 Hz, 1H), 2.47 (br s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.1, 140.3, 129.1, 127.4, 125.6, 125.2, 76.1, 73.7, 38.9; FT-IR (KBr) 3441, 2951, 2922, 2850, 1637, 1474, 1459, 1432, 1319, 1254, 1187, 1154, 1104, 1063, 1052, 1041, 987, 815, 735 cm^{-1}; HRMS (ESI) *m/z* $[M\text{-}OH]^+$ Calcd for $C_9H_{10}O_2$: 133.0654, found: 133.0655.



Benzil 8.[14] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.56; yellow solid; mp 94-95 °C; yield 86% (36 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.8 Hz, 4H), 7.66 (t, *J* = 7.8 Hz, 2H), 7.51 (t, *J* = 7.8 Hz, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.7, 135.1, 133.1, 130.1, 129.2; FT-IR (KBr) 3064, 2925, 2853, 2000, 1976,

1915, 1785, 1659, 1595, 1579, 1490, 1450, 1323, 1210, 1172, 1098, 1072, 998, 875, 795, 696 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{14}H_{10}O_2$: 211.0759, found: 211.0755.



1-(2-((2,2,6,6-Tetramethylpiperidin-1-yl)oxy)-2-(*p*-tolyl)ethoxy)-1*H*-benzo[*d*][1,2,3]triazole 9. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.52; liquid; yield 37% (75.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.4 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.34-7.31 (m, 3H), 7.20 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 1H), 5.16 (t, *J* = 6.0 Hz, 1H), 5.02 (dd, *J* = 9.0, 4.2 Hz, 1H), 4.77 (dd, *J* = 9.6, 3.0 Hz, 1H), 2.38 (s, 3H), 1.66-1.39 (m, 6H), 1.35 (s, 3H), 1.20 (s, 3H), 1.07 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.5, 137.9, 136.9, 129.1, 127.88, 127.83, 127.1, 124.6, 120.1, 108.9, 83.1, 82.4, 60.3, 40.5, 34.2, 21.3, 20.5, 17.2; FT-IR (neat) 2972, 2931, 2871, 1614, 1564, 1514, 1446, 1376, 1361, 1262, 1239, 1181, 1132, 1086, 1018, 972, 817, 781, 742 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ Calcd for $C_{24}H_{32}N_4O_2$: 409.2604, found: 409.2608.

Crystal Data of 3ag at 298 (2) K

Identification code	**3ag**
Empirical formula	$C_{17}H_{12}N_2O_6$
Formula weight	340.29
Crystal habit, colour	Needle / colorless
Crystal size, mm^3	0.32 x 0.24 x 0.12
Temperature, T/K	298 (2)
Wavelength, λ/Å	0.71073
Crystal system	monoclinic
Space group	'P 21/n'

Unit cell dimensions	a = 14.3090(9)Å b = 5.7406(6)Å c = 19.1631(9)Å $\alpha = \gamma = 90.00°$, $\beta = 98.798(6)°$
Volume, V/Å^3	1555.6(2)
Z	4
Calculated density, Mg·m^{-3}	1.453
Absorption coefficient, μ/mm^{-1}	0.112
F(000)	704
θ range for data collection	3.72 to 27.03°
Limiting indices	$-17 \leq h \leq 16$, $-4 \leq k \leq 6$, $-22 \leq l \leq 13$
Reflection collected / unique	2802 / 1954 [R(int) = 0.0239]
Completeness to θ	99.90 % (θ = 25.25°)
Max. and min. transmission	0.968 and 0.987
Refinement method	SHELXL-97 (Sheldrick, 1997)'
Data / restraints / parameters	2802/0/ 226
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0950, wR2 = 0.0566
R indices (all data)	R1 = 0.0818, wR2 = 0.1076

3.5 References

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3.6 HRMS Spectra of 3x and 3x′

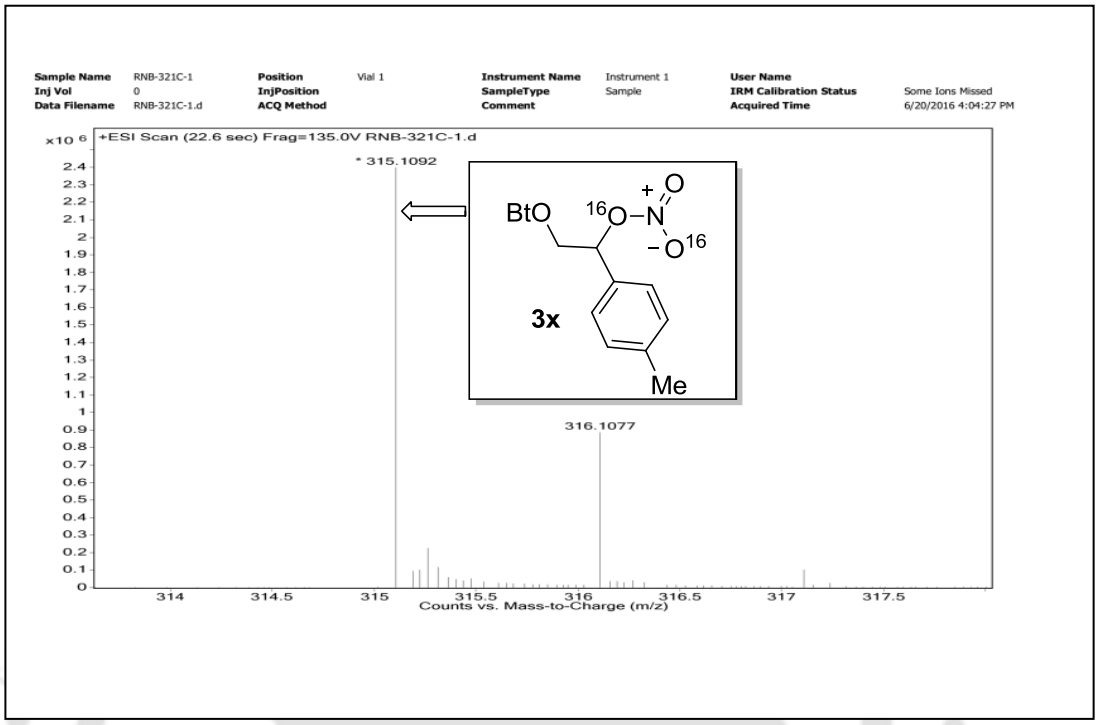


Figure 3. HRMS Spectra of 3x (^{16}O Product)

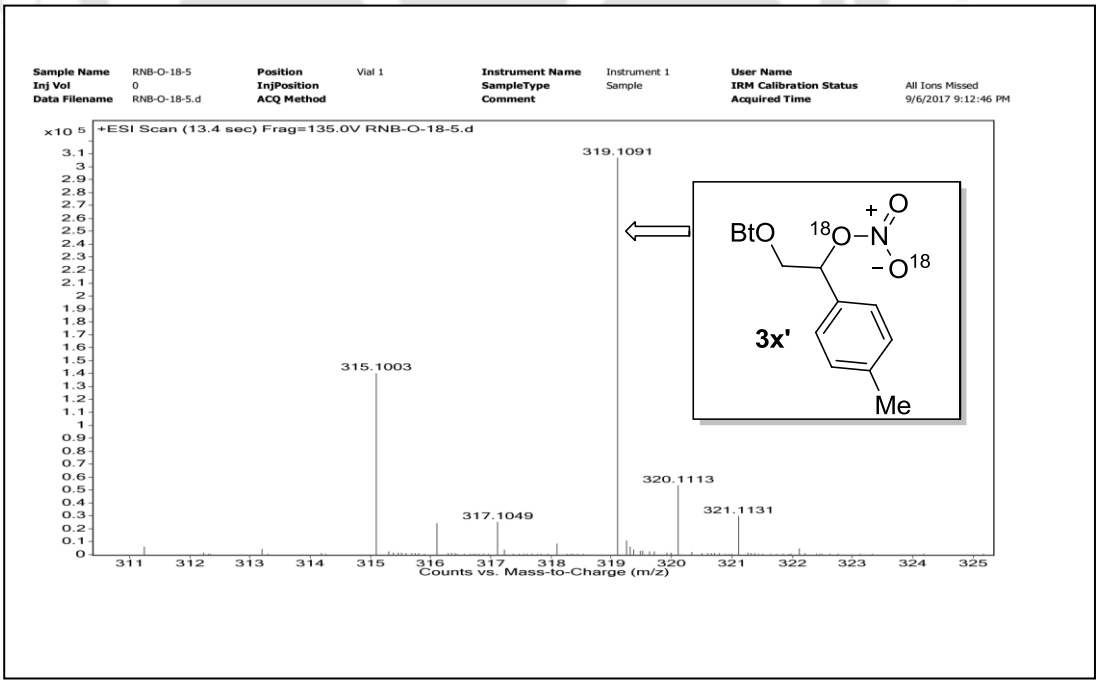
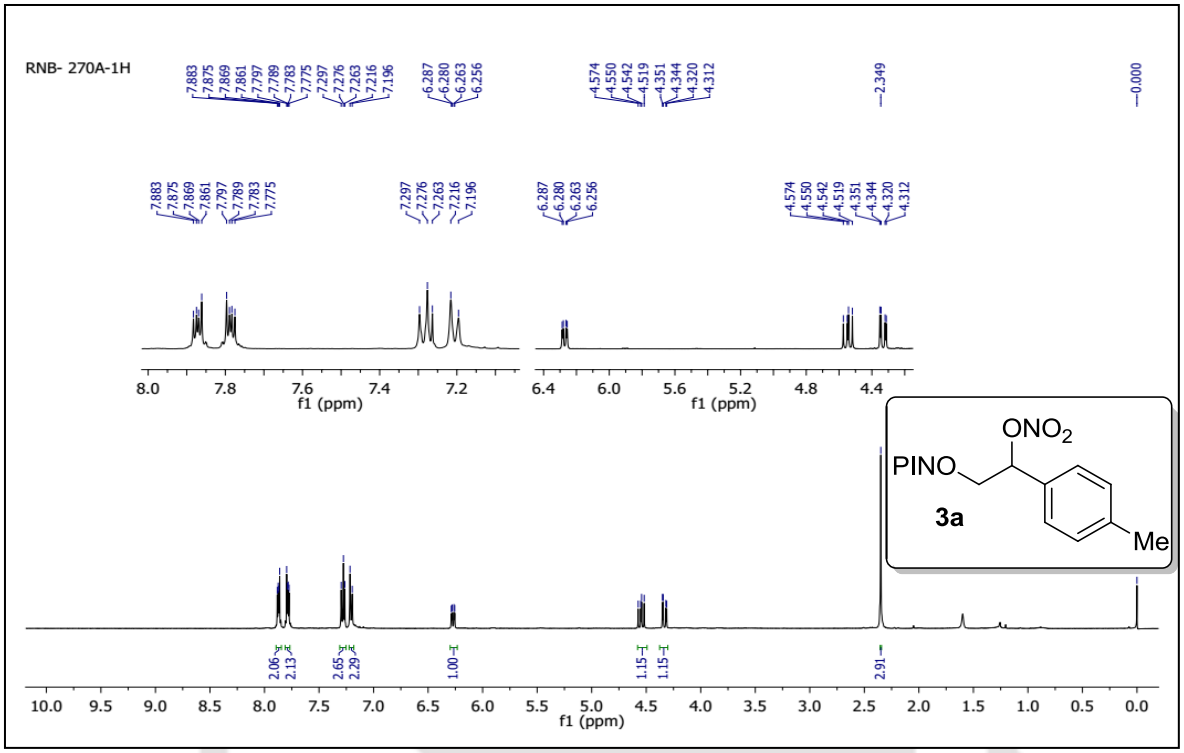
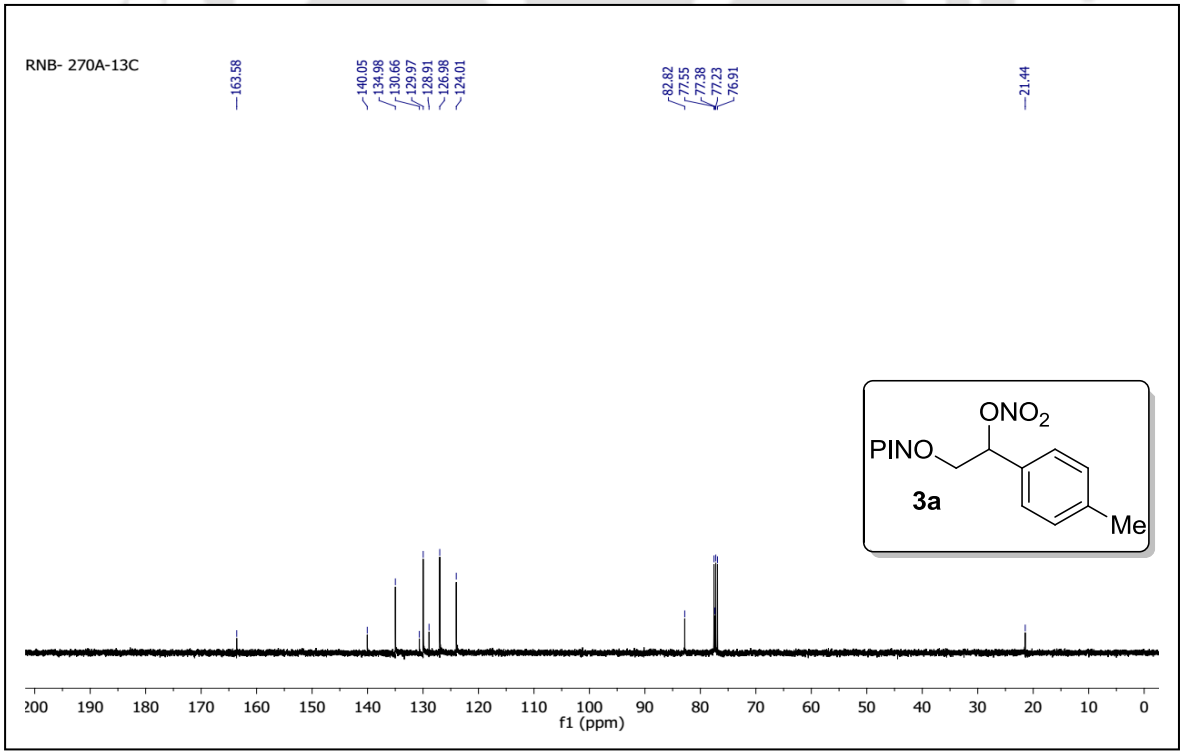
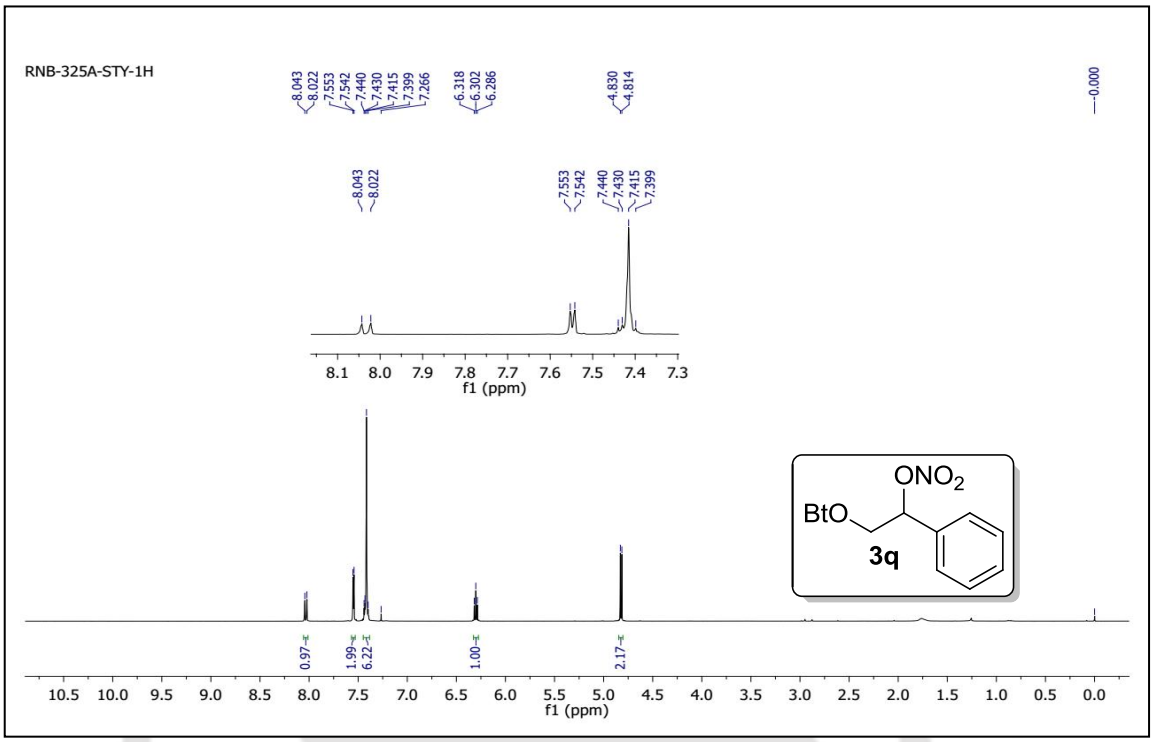


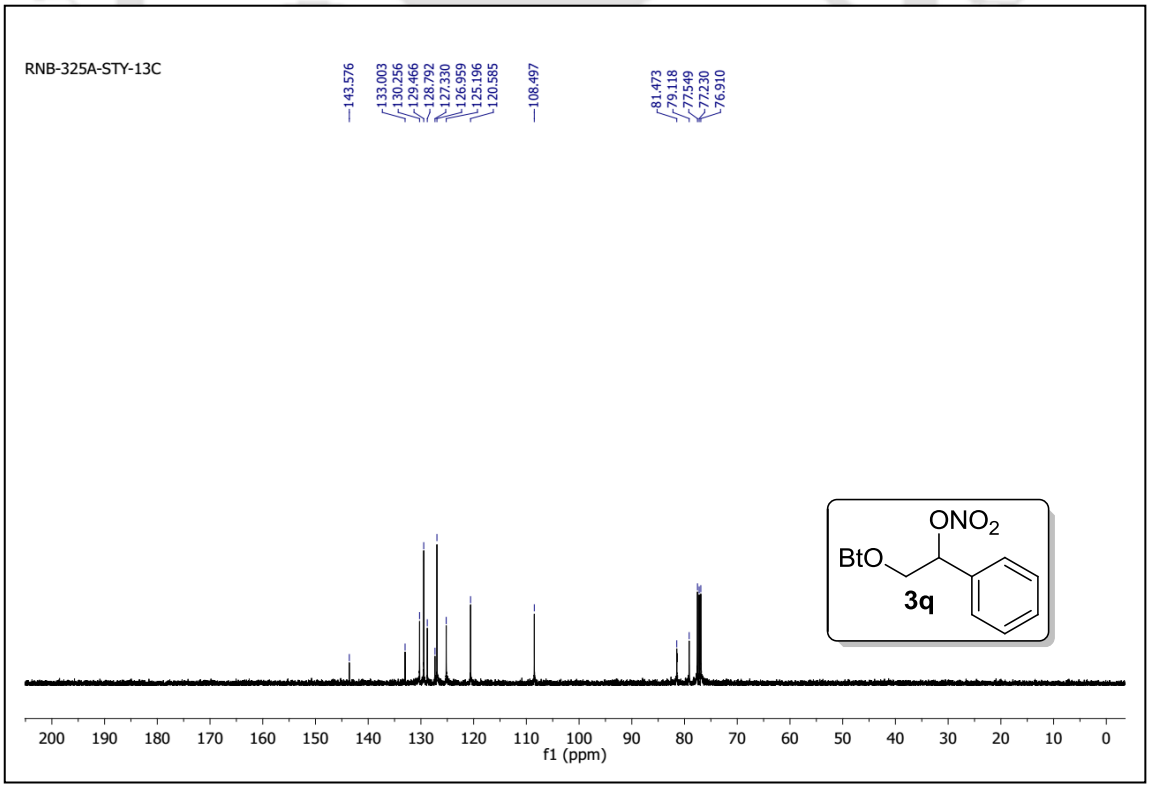
Figure 4. HRMS Spectra of 3x′ (^{18}O Product)

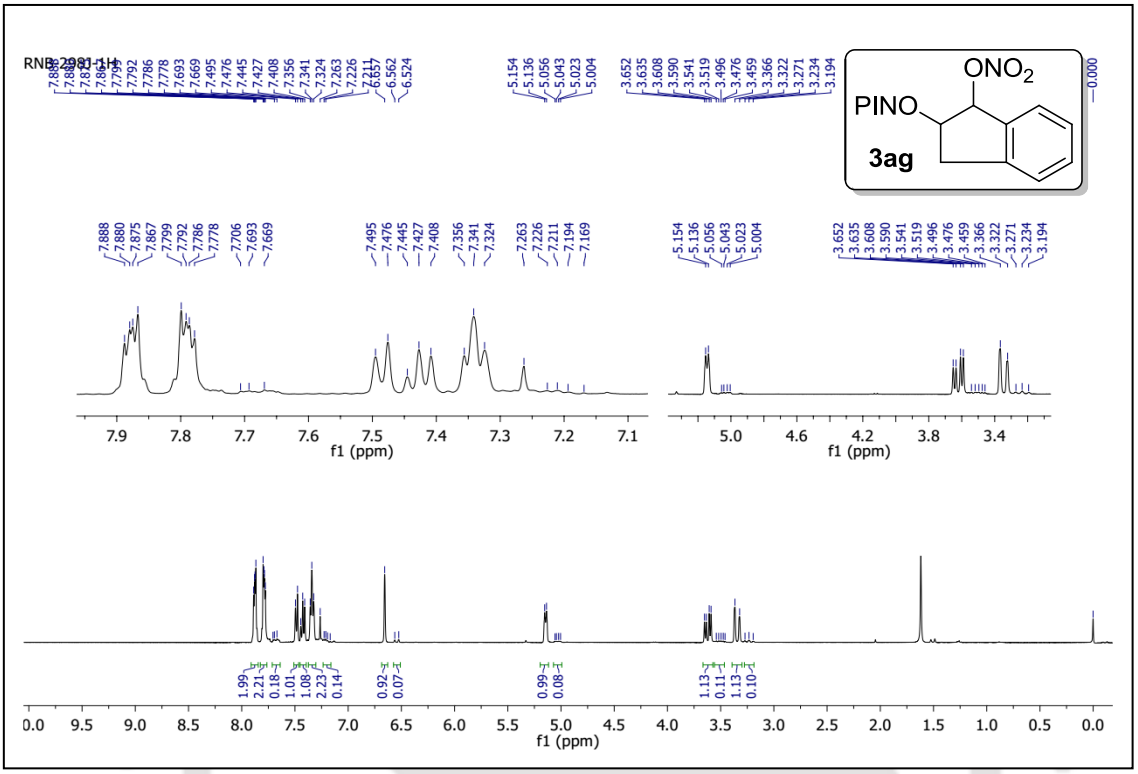
3.7 Selected NMR Spectra

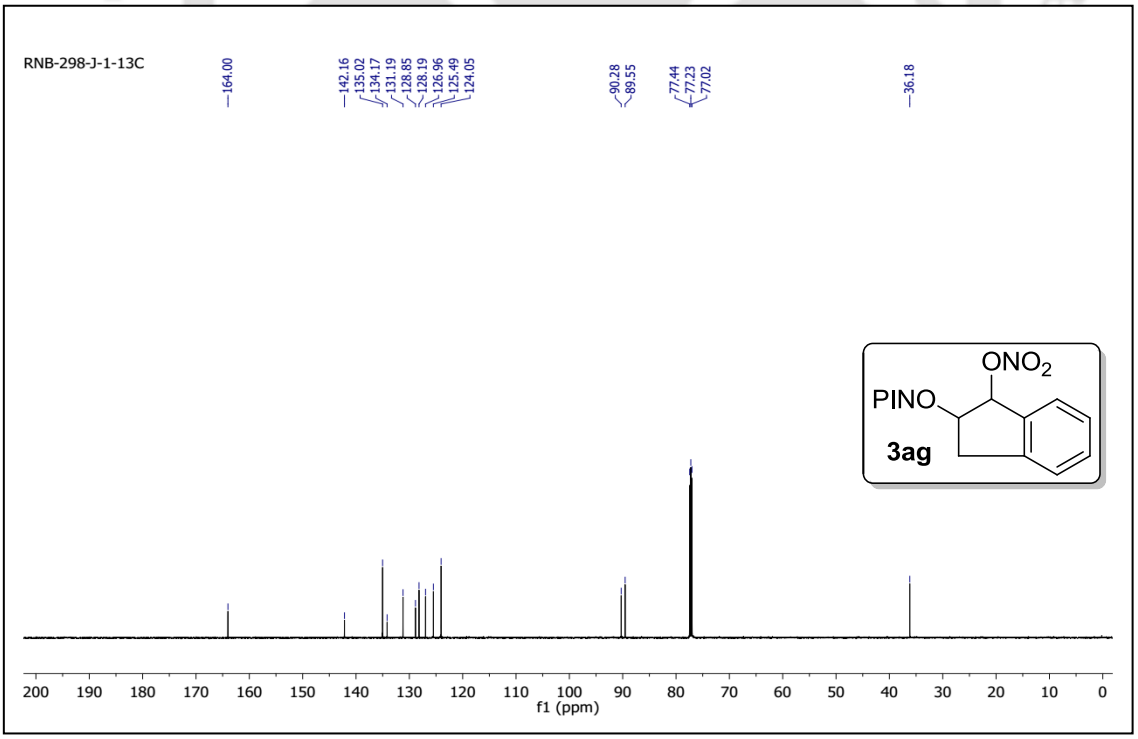


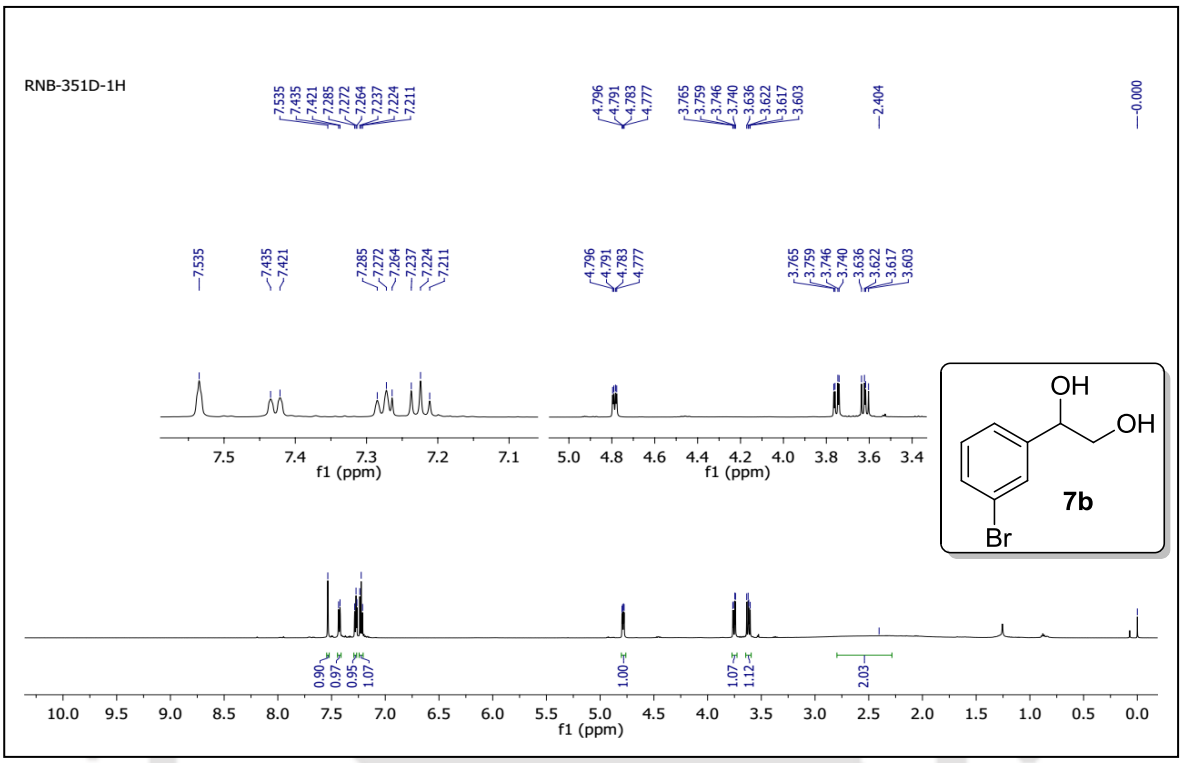


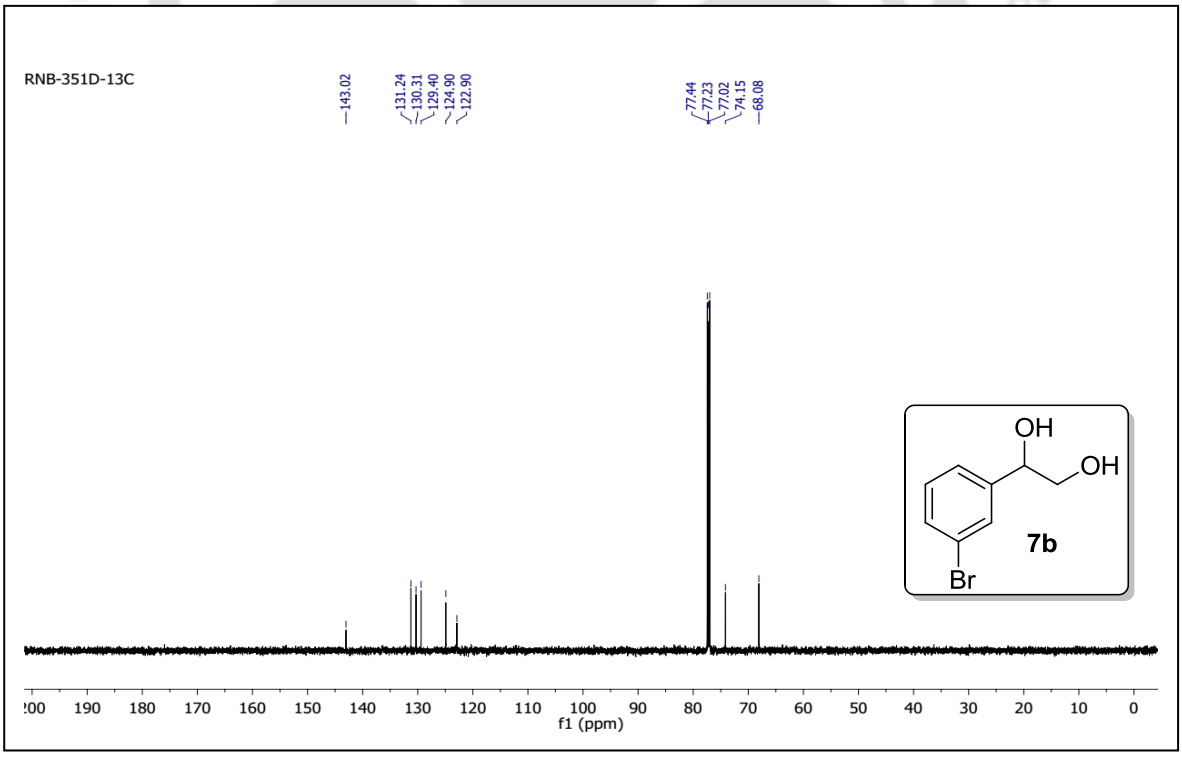


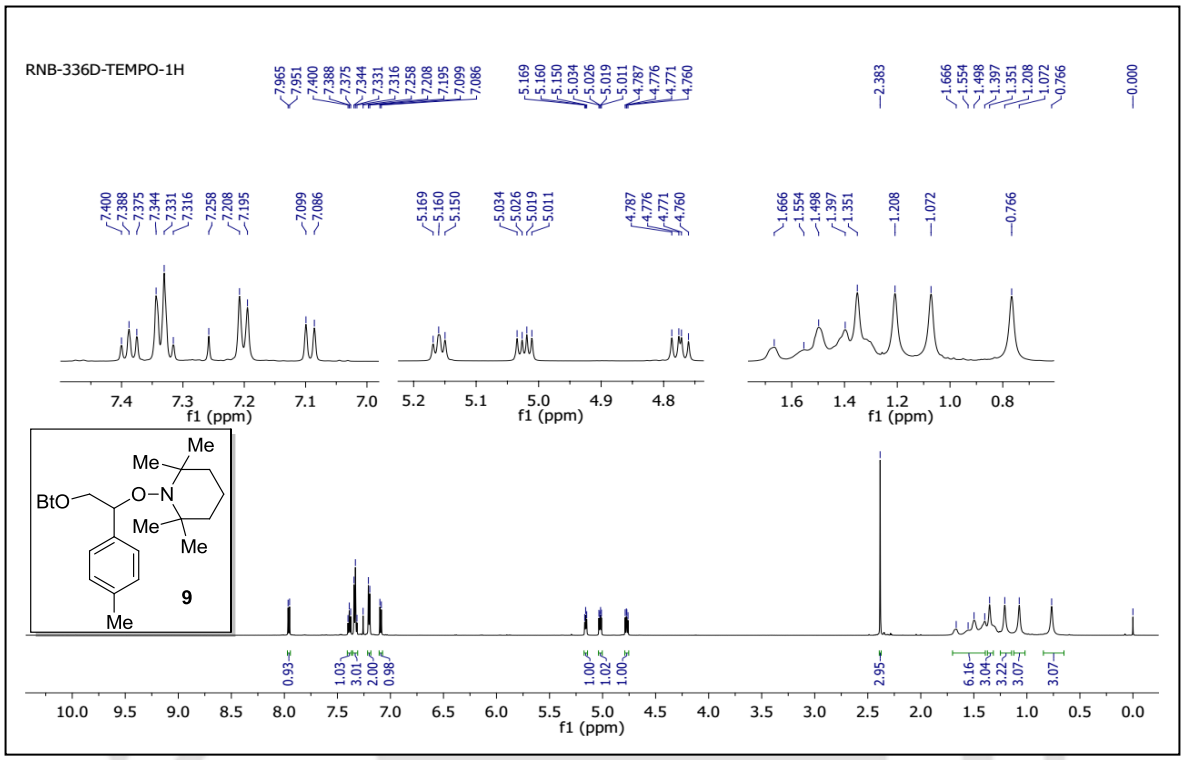


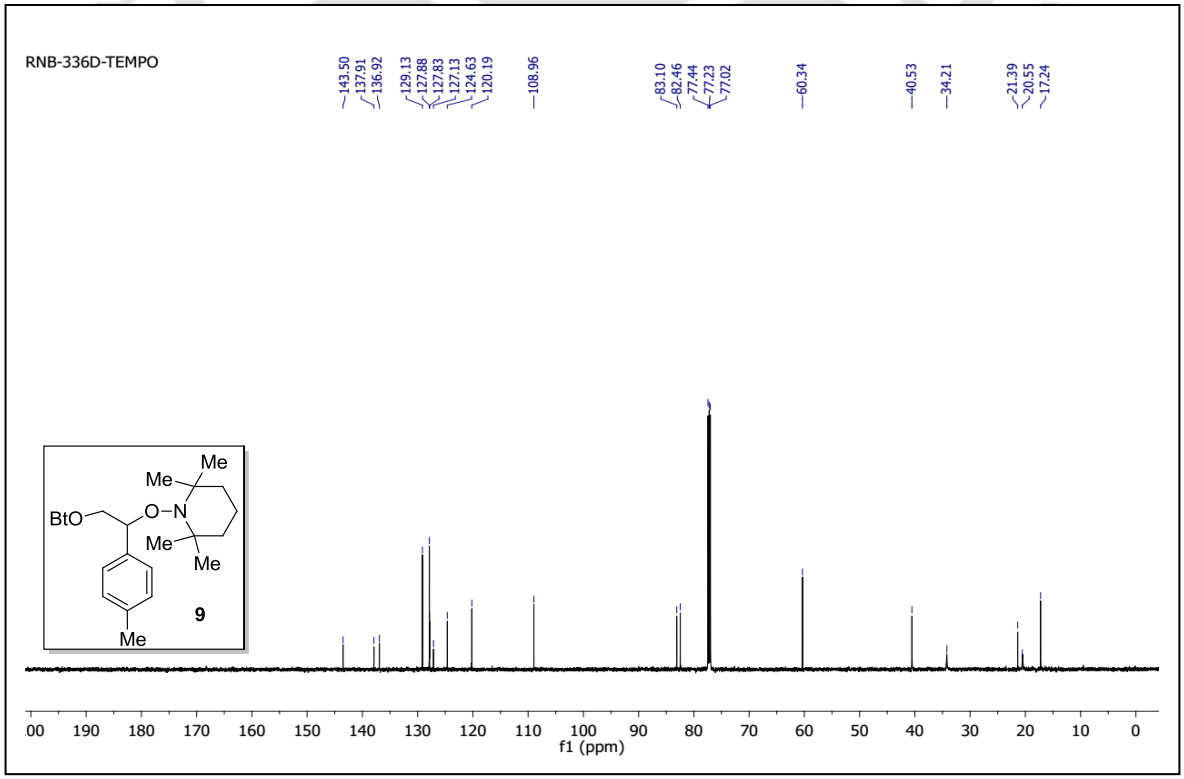












Chapter IV

Ruthenium-Catalyzed 7-Azaindole Directed *Ortho*-Selective C-H Chalcogenation of Arenes

7-Azaindole moieties are important structural motifs and found in numerous bio-active natural products and pharmaceuticals.[1] 7-Azaindoles also display diverse biological properties, such as antitumor, anti-inflammatory and antibacterial activities. Thus, various 7-azaindole derivatives are made in medicinal chemistry. Moreover, their unique structural properties bearing electron-rich azole and electron-deficient azine rings make them important as the therapeutic agents, such as the marketed anti-cancer vemurafenib, PKM2 activator and glucokinase activator (Figure 1).[1] Keeping in mind the biological activity of 7-azaindole motifs, considerable effort is thus made on C-H functionalization [2,3] of *N*-aryl-7-azaindoles.

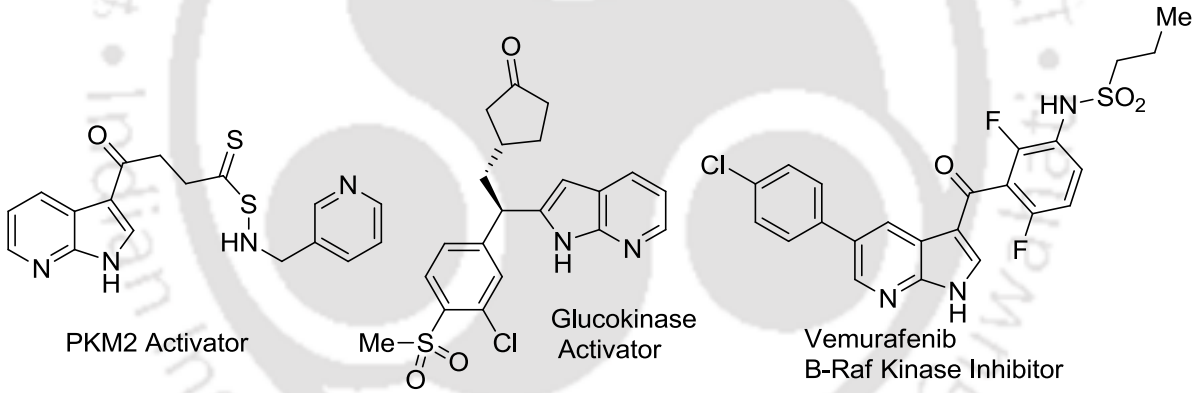


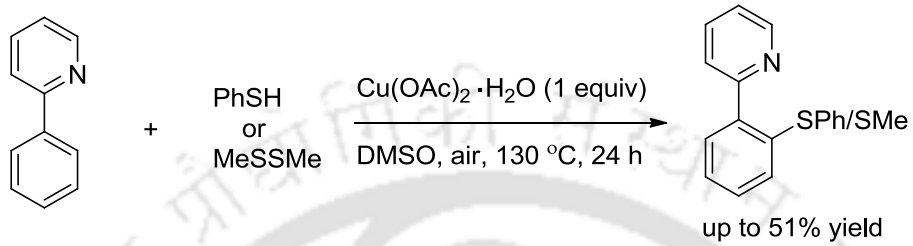
Figure 1. Examples of Some Bio-Active 7-Azaindoles

Aryl and alkyl chalcogenated compounds are core building blocks in material and medicinal sciences.[4] Therefore, the synthesis of aryl thioethers and selenylated molecules have been an immense subject of current synthetic methodology. In this regard, several metal[5] mediated traditional cross-coupling and metal-free[6] protocols are developed for this purpose. Most of these methods, however, often suffer from the requirement of prefunctionalized substrate precursors and regioselectivity. Development of transition-metal[7] catalyzed regioselective chalcogenation of arene C-H bonds as a reliable synthetic toolbox is thus desirable.

4.1 Literature

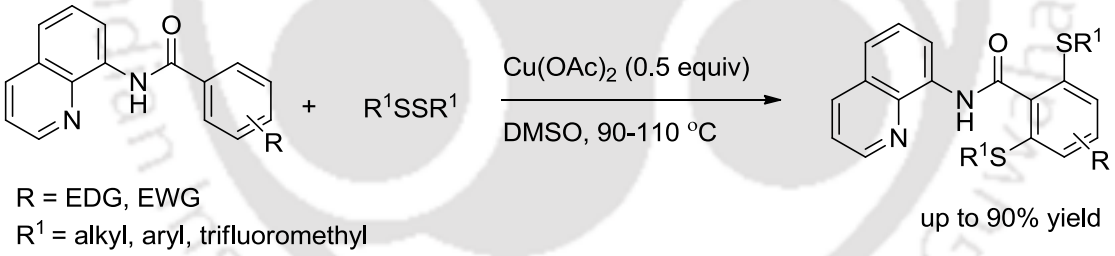
4.1.1 Cu-Mediated/Catalyzed C-H Chalcogenation of Arenes

In 2006, Yu and co-workers disclosed a Cu-mediated *ortho*-directed C-H thiolation of 2-phenylpyridine employing thiophenol or dimethyl disulfide as the thiolating agent in presence of aerobic oxygen (Scheme 1).[8]



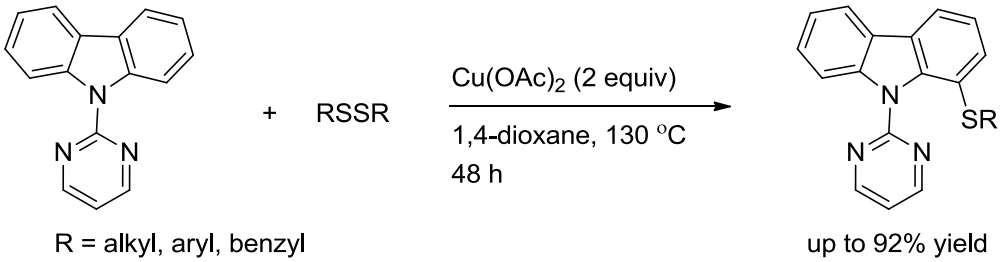
Scheme 1. Cu-Mediated Thiolation of 2-Phenylpyridine

Daugulis and co-workers developed a Cu-mediated auxiliary-assisted sulfenylation of *β*-sp^2 C-H bonds of benzoic acid derivatives employing disulfides as the sulfenylating agents at ambient conditions (Scheme 2).[9] This protocol provides a straightforward method for the preparation of aryl trifluoromethyl thioethers, which are important for the synthesis of trifluoromethyl sulfones and sulfoxides.



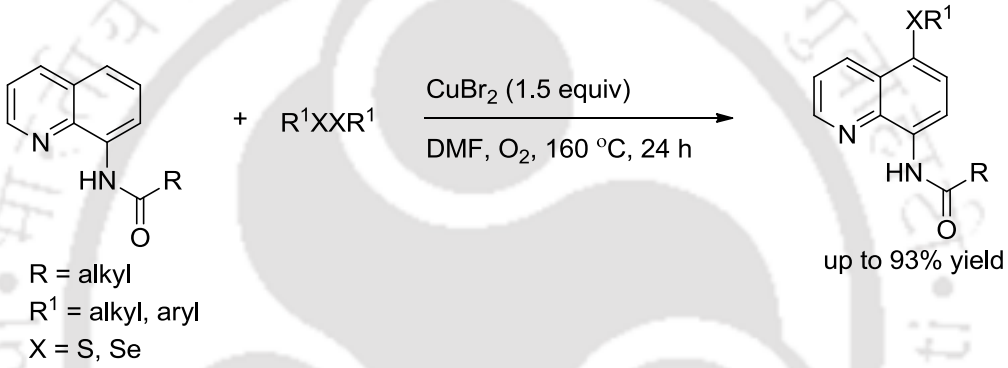
Scheme 2. Cu-Catalyzed Auxiliary-Assisted Sulfenylation of Arenes

Kambe and co-workers established a Cu-mediated C-H thiolation of carbazoles with disulfides using pyrimidyl auxiliary to obtain *ortho*-thiolated carbazoles (Scheme 3).[10] This protocol has been extended for *N*-heterocycles such as benzo[*h*]quinoline, 2-phenylquinoline and indole moieties.



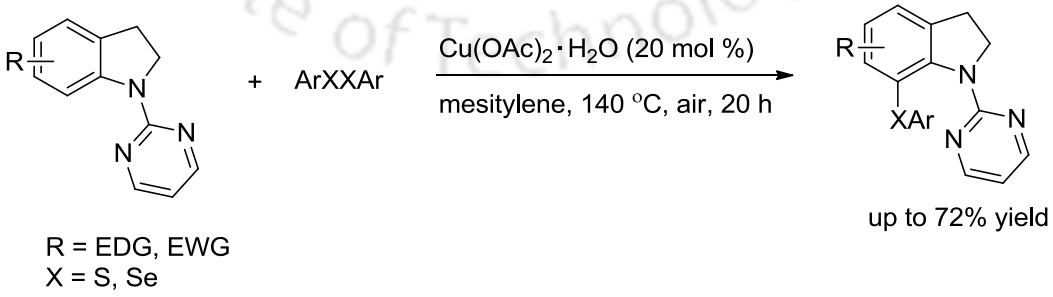
Scheme 3. Cu-Mediated *Ortho*-Thiolation of Carbazole

Yin and co-workers reported a Cu-mediated C5-chalcogenation of 8-aminoquinoline scaffolds with disulfides and diselenides to afford chalcogenoethers in good yields (Scheme 4).[11]



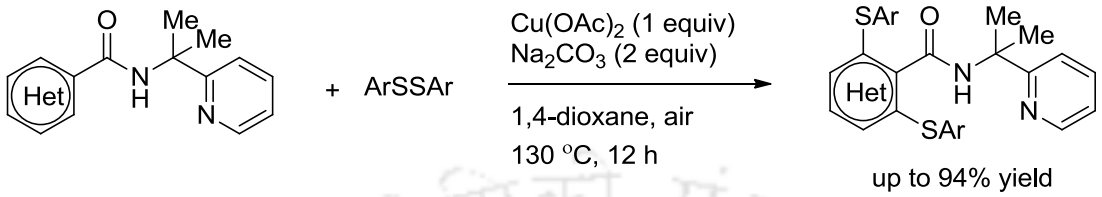
Scheme 4. Cu-Mediated C-H Chalcogenation of Quinolines

Ackermann and co-workers developed a Cu-catalyzed C-H chalcogenation of indolines at the C7-position using pyrimidyl auxiliary (Scheme 5).[12] This protocol is extended for indoles to provide C2-thiolated indoles. The formation of *C-S* and *C-Se* bonds of indolines and indoles has been presented with excellent levels of positional and chemoselectivity.



Scheme 5. Cu-Catalyzed C-H Chalcogenation of Indolines

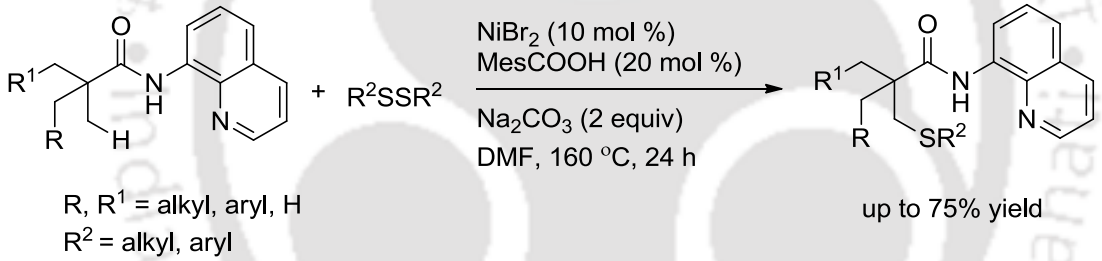
Shi and co-workers reported a Cu-mediated *ort*ho-C-H thiolation of heteroarenes assisted by PIP amine (2-(pyridin-2-yl)isopropylamine) auxiliary under ligand and oxidant-free conditions (Scheme 6).[13]



Scheme 6. Cu-Mediated Thiolation of Heteroarenes

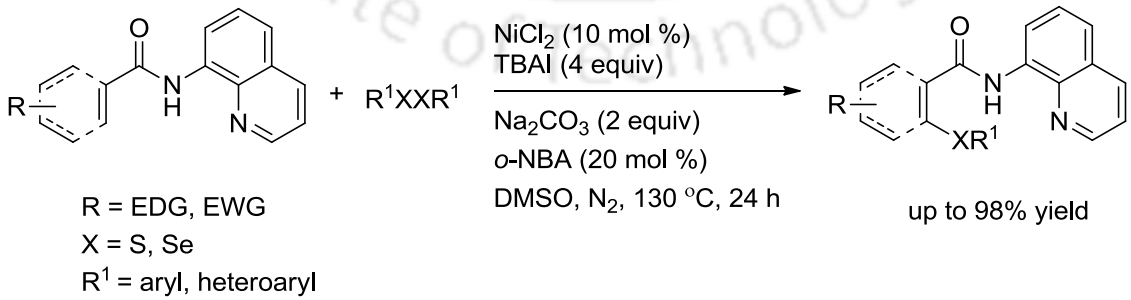
4.1.2 Ni-Catalyzed C-H Chalcogenation of Arenes

Ni-catalyzed *ortho*-thiolation of methyl C(sp^3)-H bonds in aliphatic amides containing 8-aminoquinoline as a bidentate chelating group has been disclosed (Scheme 7).[14] This method involves the removal of 8-aminoquinoline moiety to provide the carboxylic acid, which is an important key precursor for the construction of biological molecules.



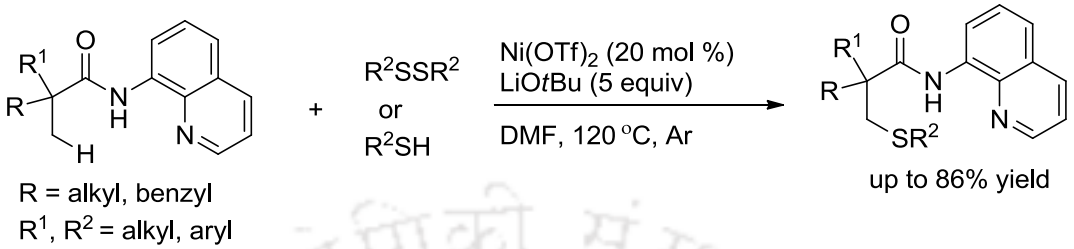
Scheme 7. Ni-Catalyzed C(sp^3)-H Thiolation of Arenes

Zhang and co-workers reported a Ni-catalyzed chalcogenation of arene and alkene C(sp^2)-H bonds with aryl disulfides and diselenides utilizing 8-aminoquinolyl auxiliary under ambient conditions (Scheme 8).[15]



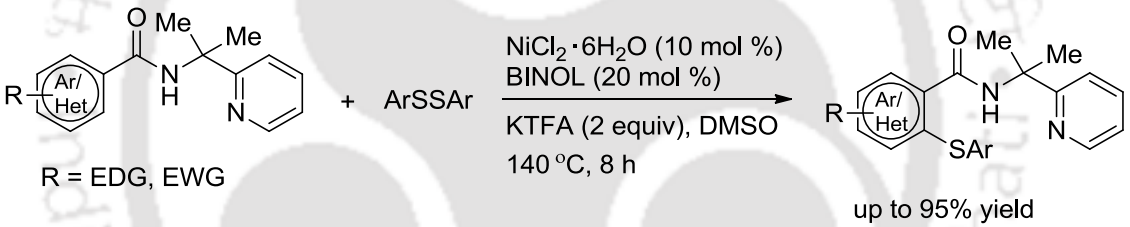
Scheme 8. Ni-Catalyzed Direct C-H Chalcogenation of Arenes

Ni-catalyzed thiolation of sp^3 C-H bond of arenes has been developed with disulfides or thiols as thiolating agent in presence of quinoline directing group (Scheme 9).[16] This method is applicable for the thiolation of sp^2 C-H bonds of arenes in good yields.



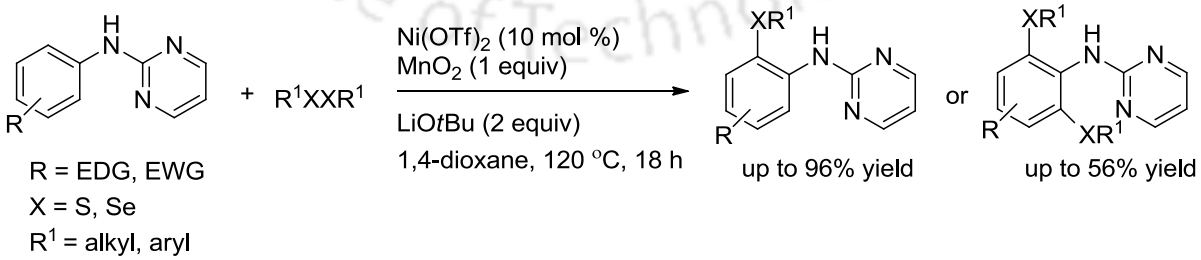
Scheme 9. Ni-Catalyzed Thiolation of sp^3 C-H Bond of Arenes

Shi and co-workers reported a Ni-catalyzed thiolation of unactivated (hetero)aryl C-H bonds with aryl disulfides using 2-(pyridine-2-yl)isopropylamine (PIP-amine) as directing group (Scheme 10).[17] This protocol is extended for the reaction of thiophenol to provide aryl sulfide in moderate yield.



Scheme 10. Ni-Catalyzed Thiolation of Unactivated Aryl C-H Bonds

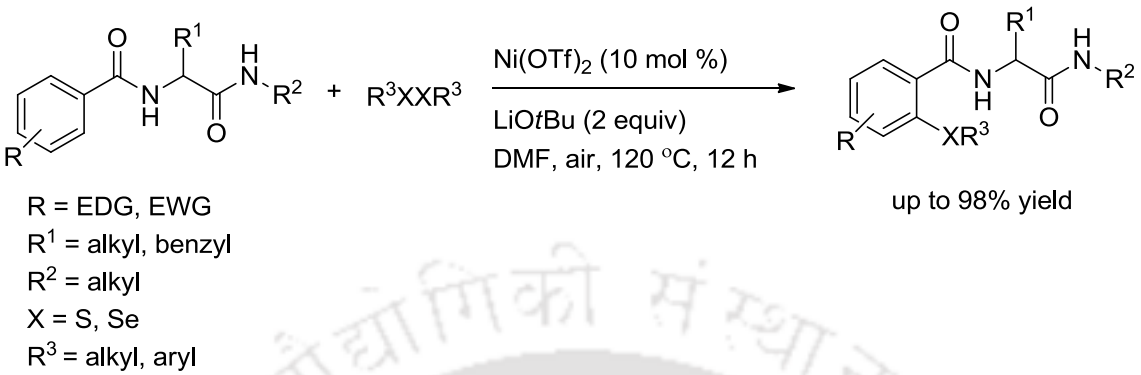
Ackermann and co-workers developed a Ni-catalyzed C-H chalcogenation of anilines using pyrimidine as the directing group under ligand free condition (Scheme 11).[18] This method provides a well explored mechanistic studies, indicating the evidence for SET-type process and a rate-limiting C-H activation.



Scheme 11. Ni-Catalyzed C-H Chalcogenation of Aniline Derivatives

Liu and co-workers reported a Ni-catalyzed C(sp^2)-H chalcogenation of *N*-benzoyl *α*-amino acids with disulfides and diselenides under ambient conditions (Scheme 12).[19] This method

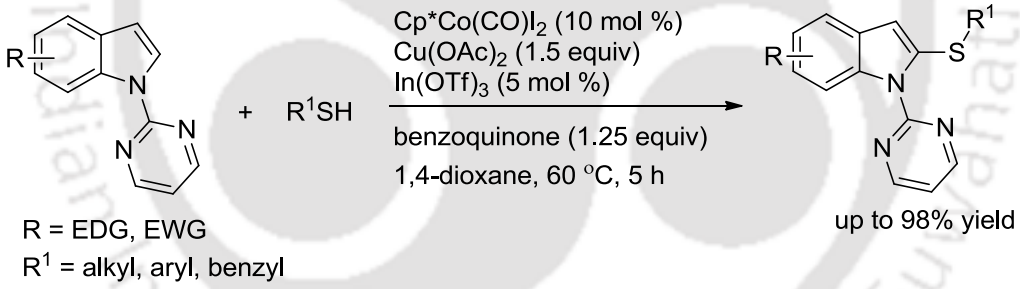
provides a direct approach for the construction of *ortho*-thiolated *N*-benzoyl *α*-amino acids, which are important in pharmaceuticals and medicinal sciences.



Scheme 12. Ni-Catalyzed C(sp^2)-H Chalcogenation of *N*-Benzoyl *α*-Amino Acid Derivatives

4.1.3 Co-Catalyzed C-H Thiolation of Arenes

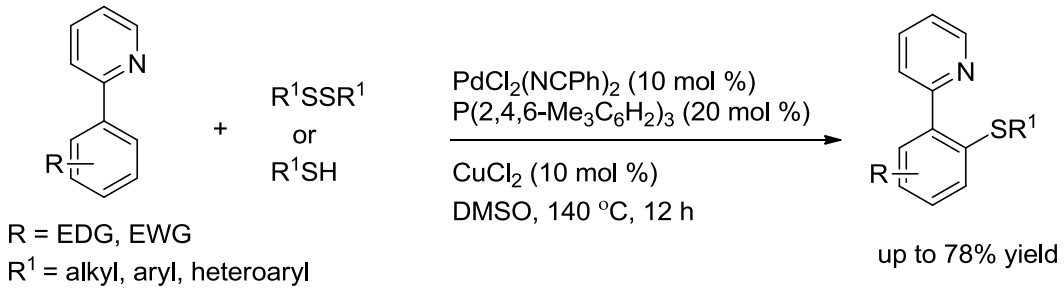
Glorius and co-workers reported a Co-catalyzed dehydrogenative coupling of thiols with indoles using pyrimidyl moiety as the directing group (Scheme 13).[20] For this regioselective and robust transformation, a co-operative reactive mechanism has been proposed.



Scheme 13. Co-Catalyzed C-H Thiolation of Indoles

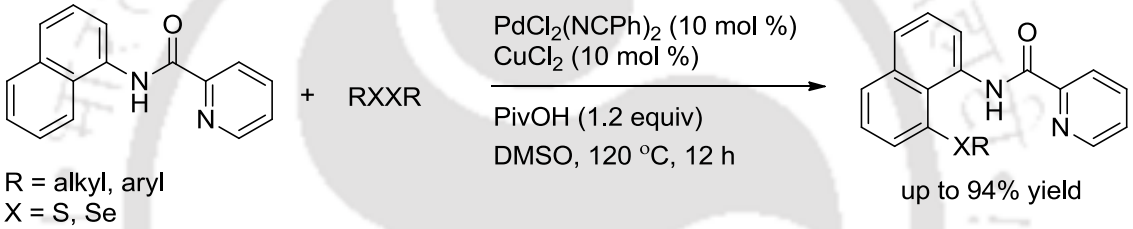
4.1.4 Pd-Catalyzed C-H Chalcogenation of Arenes

Thiolation of aryl C-H bond with disulfides or thiols has been developed using Pd/Cu co-catalysis (Scheme 14).[21] The reaction produced exclusively *ortho*-selective thiolated product induced by pyridine directing group.



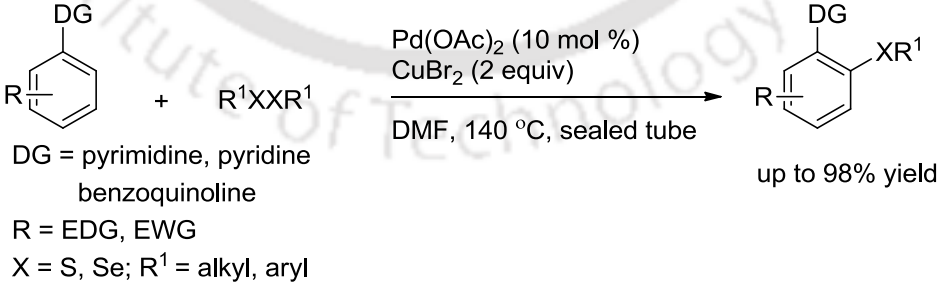
Scheme 14. Pd-Catalyzed Direct *Ortho*-Thiolation of 2-Phenylpyridine

Nishihara and co-workers reported a Pd-catalyzed *peri*-selective chalcogenation of arenes with the assistance of picolinamide directing group to provide 8-sulfenyl-1-naphthylamines (Scheme 15).[22] Removal of picolinamide directing group produces the thiolated napthylamine under base hydrolysis.



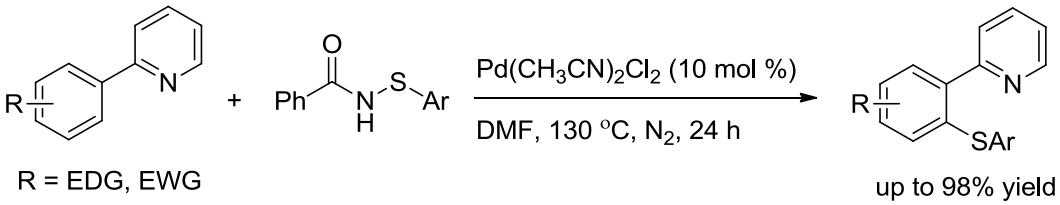
Scheme 15. Pd-Catalyzed Site-Selective Chalcogenation of Naphthylamines

Kambe and co-workers developed a Pd-catalyzed intermolecular C-H chalcogenation of arenes with disulfides and diselenides under ligand and additive free conditions (Scheme 16).[23] This method gives the chalcogenated carbazole, 2-phenylpyridine, benzo[*h*]quinoline and indoles in good to high yields.



Scheme 16. Pd-Catalyzed Direct C-H Chalcogenation of Arenes

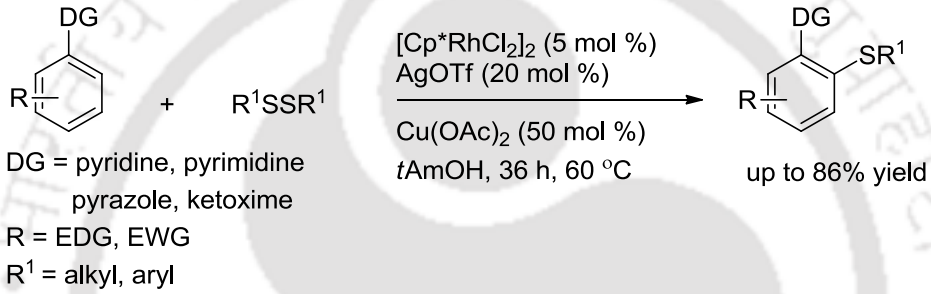
Zhang and co-workers reported a Pd-catalyzed C-H thiolation of 2-phenylpyridine with *N*-arylthiobenzamide as thiolating reagent and oxidant for the synthesis of aryl sulfides in good yields (Scheme 17).[24]



Scheme 17. Pd-Catalyzed *Ortho*-Thiolation of Arene C-H Bonds

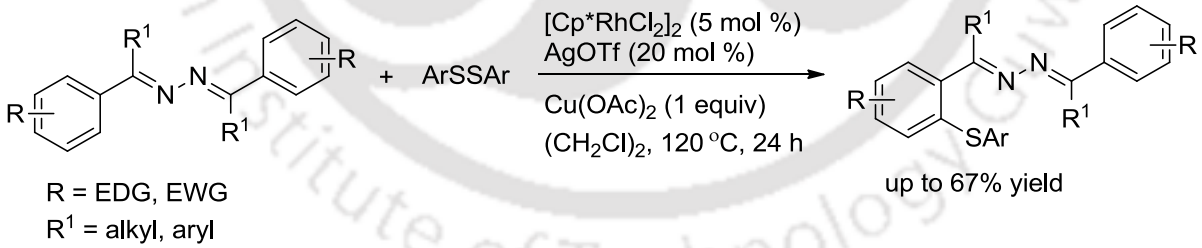
4.1.5 Rh-Catalyzed C-H Chalcogenation of Arenes

Li and co-workers reported a Rh-catalyzed intermolecular C-H thiolation of arenes with aryl and alkyl disulfides to provide aryl thioethers (Scheme 18).[25] This method utilizes different directing groups such as pyridine, pyrimidine, pyrazole and ketoximes for direct thiolation.



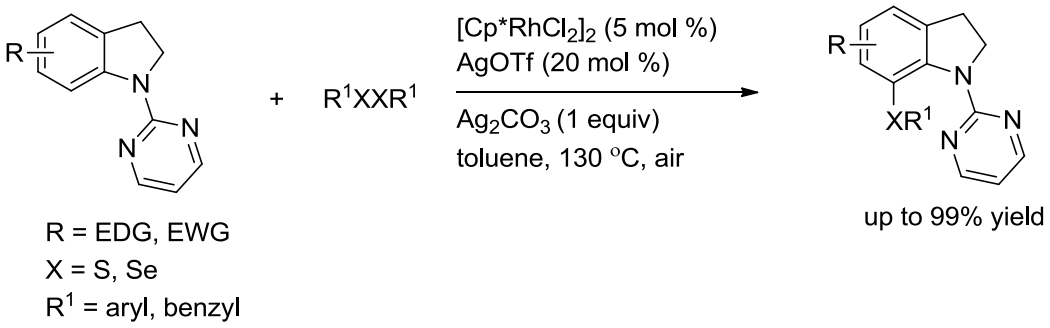
Scheme 18. Rh-Catalyzed *Ortho*-Thiolation of Arenes

A Rh-catalyzed *ortho*-thiolation of aromatic ketazines with aryl disulfides has been described to achieve *ortho*-thiolated ketazines under ambient conditions (Scheme 19).[26]



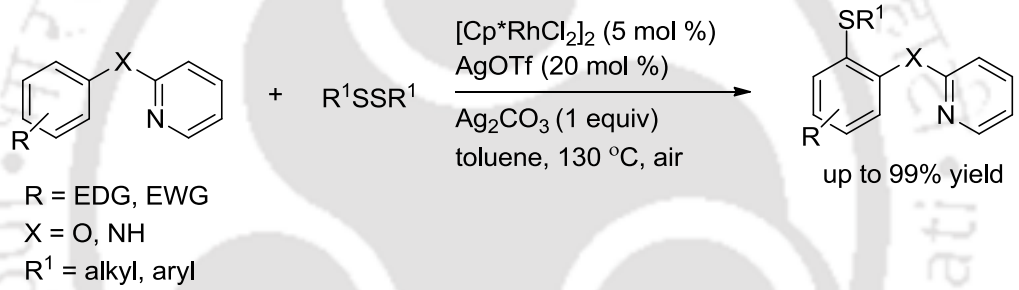
Scheme 19. Rh-Catalyzed *Ortho*-Thiolation of Aromatic Ketazines

Rh-catalyzed C7-chalcogenation of indolines with disulfides and diselenides has been developed utilizing pyrimidyl directing group (Scheme 20).[27] Removal of the pyrimidyl directing group provides the valuable C7-functionalized indoline scaffolds.



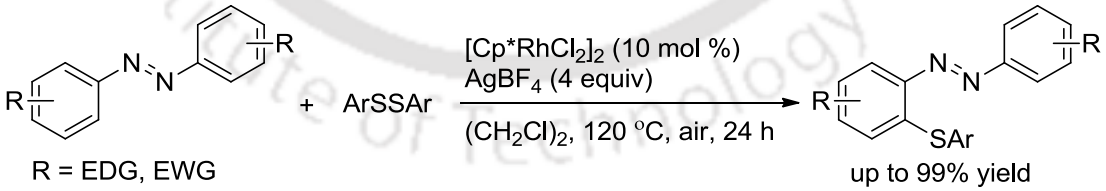
Scheme 20. Rh-Catalyzed C7-Chalcogenation of Indolines

Zhang and co-workers reported a Rh-catalyzed thiolation of phenols and anilines using disulfide with the assistance of 2-pyridyl group under air (Scheme 21).[28] The removal of the directing group generates 2-hydroxythiophenols and 2-aminothiophenol, which bear high synthetic value in medicinal, material and natural product sciences.



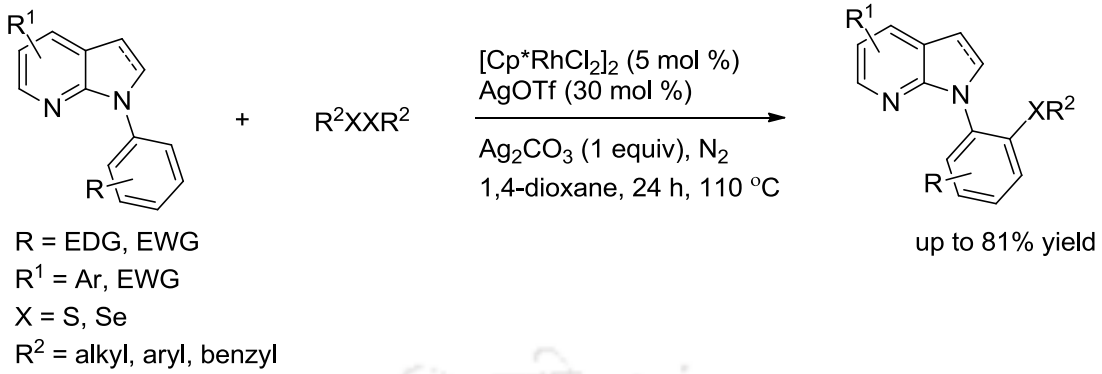
Scheme 21. Rh-Catalyzed Direct Thiolation of Phenols and Anilines

Zhou and co-workers reported a Rh-catalyzed thiolation of azobenzenes with disulfides to obtain *ortho*-thiolated azobenzenes (Scheme 22).[29] The azobenzene directing group has been detached under acidic conditions to form thiol free aniline in high yield.



Scheme 22. Rh-Catalyzed O*rtho*-Thiolation of Azobenzenes

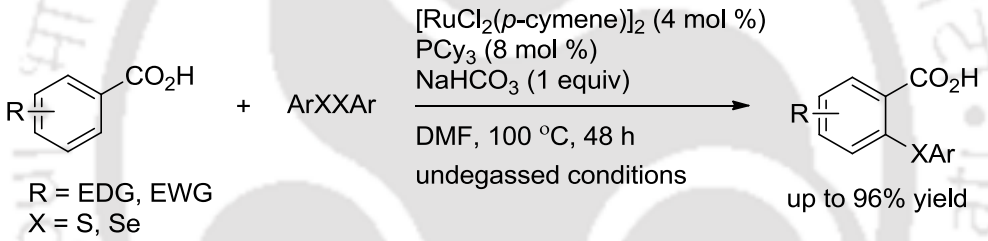
Rh-catalyzed chalcogenation of arenes with disulfides and diselenides has been recently established employing 7-azaindoles and 7-azaidolenes as the directing groups in presence of silver triflate (AgOTf) and silver carbonate (Ag_2CO_3) in moderate to good yields (Scheme 23).[30]



Scheme 23. Rh-Catalyzed Chalcogenation of Arenes C-H Bond

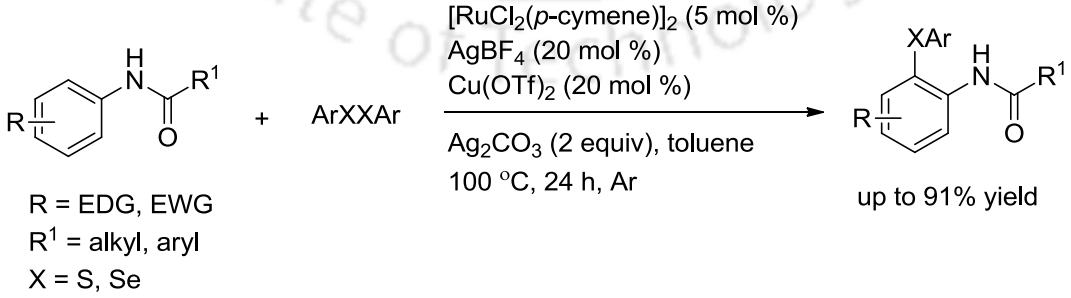
4.1.6 Ru-Catalyzed C-H Chalcogenation of Arenes

Ru-catalyzed C-H chalcogenation of aromatic carboxylic acids has been described to produce *ortho*-chalcogenated carboxylic acids (Scheme 24).[31] This protocol has been extended for the sequential synthesis of chalcogenoxanthones in good yields.



Scheme 24. Ru-Catalyzed O*rtho*-Chalcogenation of Carboxylic Acids

Ru-catalyzed C-H chalcogenation of anilides with disulfides and diselenides has been developed to afford *ortho*-thiolated and selenylated anilides under ambient condition (Scheme 25).[32]



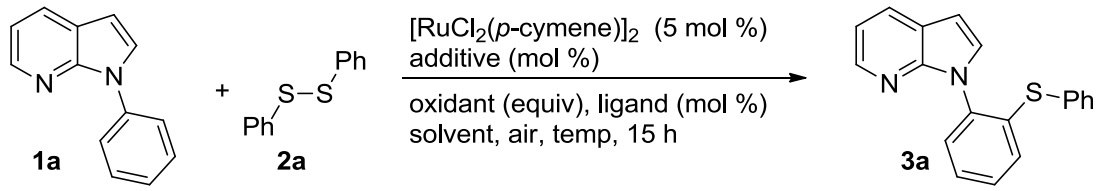
Scheme 25. Ru-Catalyzed C-H Chalcogenation of Anilides

4.2 Present Study

We present here a Ru-catalyzed *ortho*-selective C-H chalcogenation of arenes tethered with 7-azaindoles using disulfides and diselenides in presence of BINOL under air. This reaction includes the advantages of broad substrate scope and functional group diversity. First, we initiated our studies using *N*-phenyl-7-azaindole **1a** and diphenyl disulfide **2a** as standard substrates (Table 1). To our delight, the C-H activation and *C*-*S* bond formation occurred to deliver the *ortho*-thiolated **3a** in 35% yield when the substrates were stirred with 5 mol % $[RuCl_2(p\text{-cymene})]_2$, 20 mol % $AgSbF_6$ and 1 equiv of Ag_2CO_3 in toluene at 100 ^oC for 15 h under air (entry 1). The use of the ligands led to accelerate the yield to 72% employing BINOL, whereas PCy_3, bipyridyl and Boc-Phe-OH produced inferior results (entries 2-5). Of the solvents screened, toluene, 1,4-dioxane, DMF, $(CH_2Cl)_2$, *m*-xylene and chlorobenzene, the former furnished the best yield (entries 6-10). In a set of oxidants investigated such as Ag_2CO_3, AgOAc, $Cu(OAc)_2$ and $K_2S_2O_8$, the former produced the superior result (entries 2 and 11-13). Subsequent screening of additives, $AgBF_4$ and KPF_6 led to produce less yields (entries 14 and 15). A similar result was observed when the reaction temperature was lowered (entry 16). Control experiments confirmed that the thiolation was not observed in the absence of additive or Ru-catalyst (entries 17 and 18).

Having optimized the reaction condition, we envisaged the substrates scope using a diversely substituted disulfides **2b-n** with **1a** as a standard substrate (Table 2). Disulfide bearing substitution at *ortho*-position of the aryl ring with bromo **2b**, chloro **2c** and methyl **2d** functionalities underwent thiolation to afford the thioehers **3b-d** in 60-66% yields. Similarly, *meta*-substituted disulfide bearing methoxy **2e** group underwent reaction with **1a** to furnish **3e** in 69% yield. The reaction of the disulfides having *para*-substitution with bromo **2f**, chloro **2g**, methoxy **2h**, methyl **2i** and nitro **2j** functionalities delivered **3f-j** in 65-75% yields. Similar result was observed with dinaphthyl disulfide **2k**, producing the thioether **3k** in 71% yield. In addition, benzyl disulfide **2l** underwent reaction to deliver **3l** in 70% yield, whereas didodecyl **2m** and dihexadecyl **2u** disulfides underwent reaction to afford the thioethers **3m** and **3n** in 64 and 63% yields, respectively. The thiolated **3g** gave single crystal whose structure was confirmed by X-ray analysis (Figure 2).

Table 1. Optimization of the Reaction Conditions[a]



Entry	Additive	Oxidant	Ligand	Solvent	Yield (%)[b]
1	$AgSbF_6$	Ag_2CO_3	-	toluene	35
2	**$AgSbF_6$**	**Ag_2CO_3**	**BINOL**	**toluene**	**72**
3	$AgSbF_6$	Ag_2CO_3	PCy_3	toluene	35
4	$AgSbF_6$	Ag_2CO_3	bipyridyl	toluene	27
5	$AgSbF_6$	Ag_2CO_3	Boc-Phe-OH	toluene	25
6	$AgSbF_6$	Ag_2CO_3	BINOL	1,4-dioxane	25
7	$AgSbF_6$	Ag_2CO_3	BINOL	DMF	trace
8	$AgSbF_6$	Ag_2CO_3	BINOL	$(CH_2Cl)_2$	42
9	$AgSbF_6$	Ag_2CO_3	BINOL	*m*-xylene	38
10	$AgSbF_6$	Ag_2CO_3	BINOL	C_6H_5Cl	40
11	$AgSbF_6$	AgOAc	BINOL	toluene	35
12	$AgSbF_6$	$Cu(OAc)_2$	BINOL	toluene	43
13	$AgSbF_6$	$K_2S_2O_8$	BINOL	toluene	trace
14	$AgBF_4$	Ag_2CO_3	BINOL	toluene	trace
15	KPF_6	Ag_2CO_3	BINOL	toluene	20
16	$AgSbF_6$	Ag_2CO_3	BINOL	toluene	63[c]
17	-	Ag_2CO_3	BINOL	toluene	n.r.
18	$AgSbF_6$	Ag_2CO_3	BINOL	toluene	n.r.[d]

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (20 mol %), Ag_2CO_3 (1 equiv), BINOL (20 mol %), toluene (2 mL), air, 100 °C, 15 h.

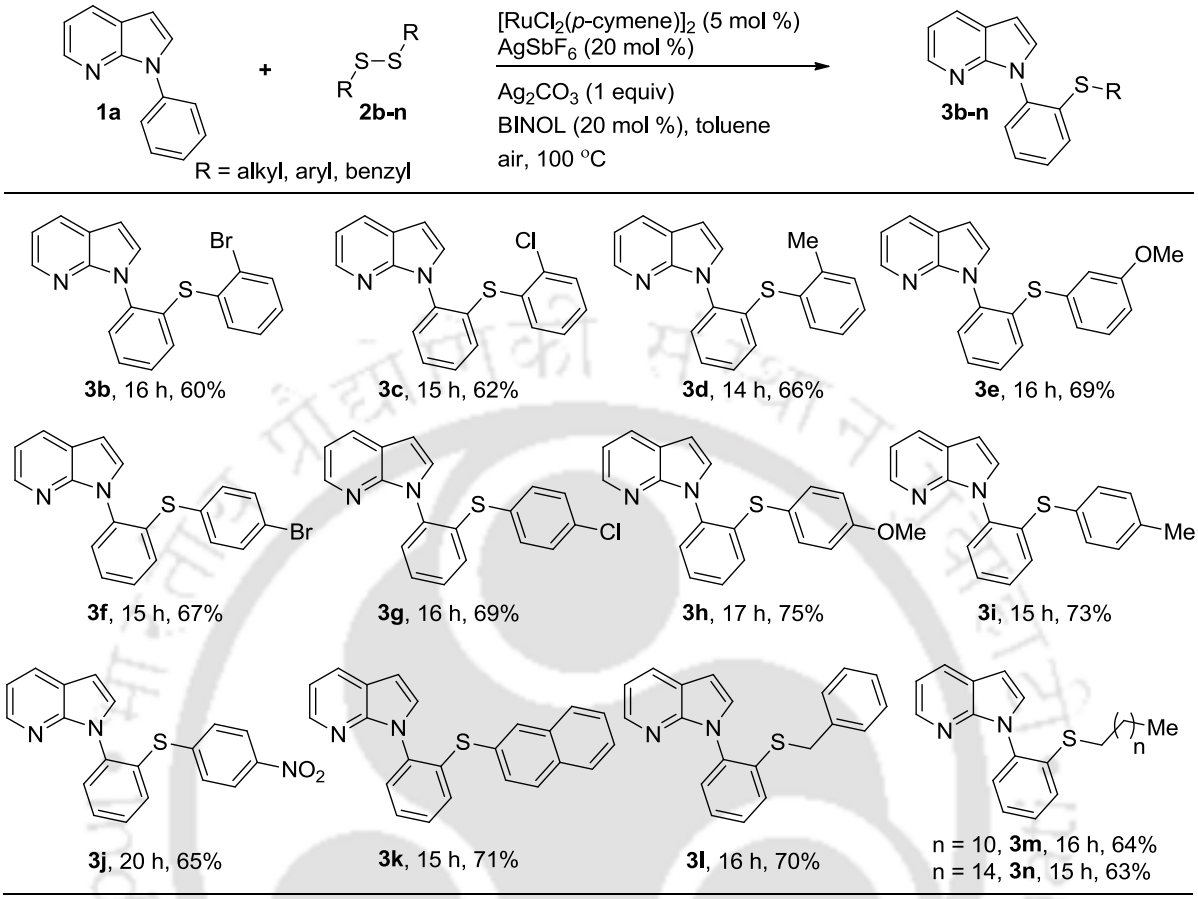
[b] Isolated yield.

[c] 80 °C.

[d] Without Ru-catalyst.

n. r. = no reaction.

Table 2. Reaction of *N*-Phenyl-7-Azaindole **1a** with Different Disulfides **2b-n**.[a,b]



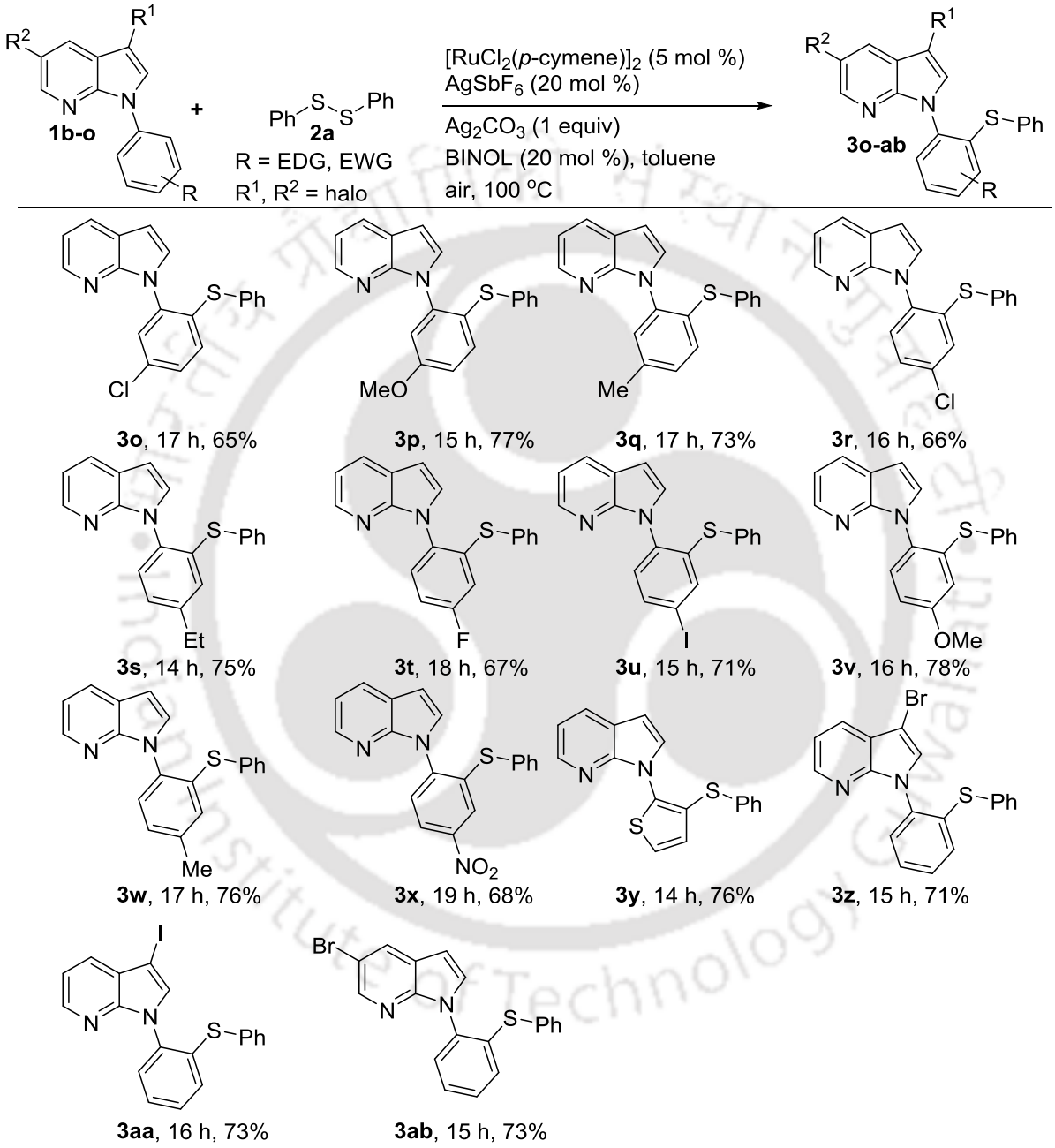
[a] Reaction conditions: **1a** (0.2 mmol), **2b-n** (0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (20 mol %), Ag_2CO_3 (1 equiv), BINOL (20 mol %), toluene (2 mL), air, 100 °C.

[b] Isolated yield.

The scope of the protocol was further elucidated for the reaction of *N*-aryl-7-azaindoles **1b-o** with **2a** as the standard substrate (Table 3). The substrates containing substitution at *meta*-position of the aryl ring with chloro **1b**, methoxy **1c** and methyl **1d** functionalities underwent reaction to deliver the thioethers **3o-q** in 65-77% yields. The reaction of the substrates bearing chloro **1e**, ethyl **1f**, fluoro **1g**, iodo **1h**, methoxy **1i**, methyl **1j** and nitro **1k** substituents at *para*-position delivered the thioethers **3r-x** in 66-78% yields. Furthermore, heterocycle-containing azaindole **1l** underwent reaction to furnish **3y** in 76% yield, whereas the reaction of 7-azaindoles having bromo **1m** and iodo **1n** groups at the 3-position produced

3z and **3aa** in 71 and 73% yields, respectively. In addition, 7-azaindole bearing bromo **1o** substituent at the 5-position underwent thiolation to afford the thioether **3ab** in 73% yield.

Table 3. Reaction of Different *N*-Aryl-7-Azaindoles **1b-o** with Diphenyl Disulfide **2a**.[a,b]



[a] Reaction conditions: **1b-o** (0.2 mmol), **2a** (0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (20 mol %), Ag_2CO_3 (1 equiv), BINOL (20 mol %), toluene (2 mL), air, 100 °C. [b] Isolated yield.

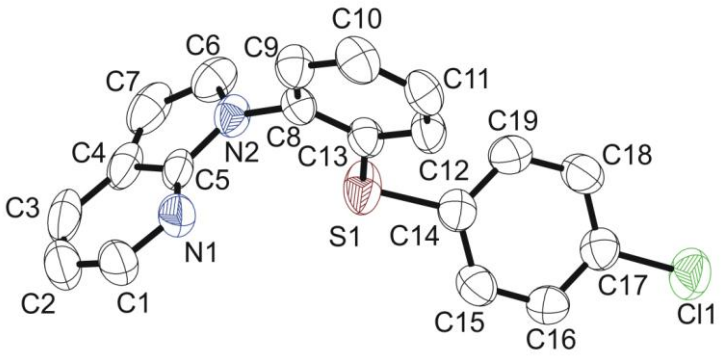
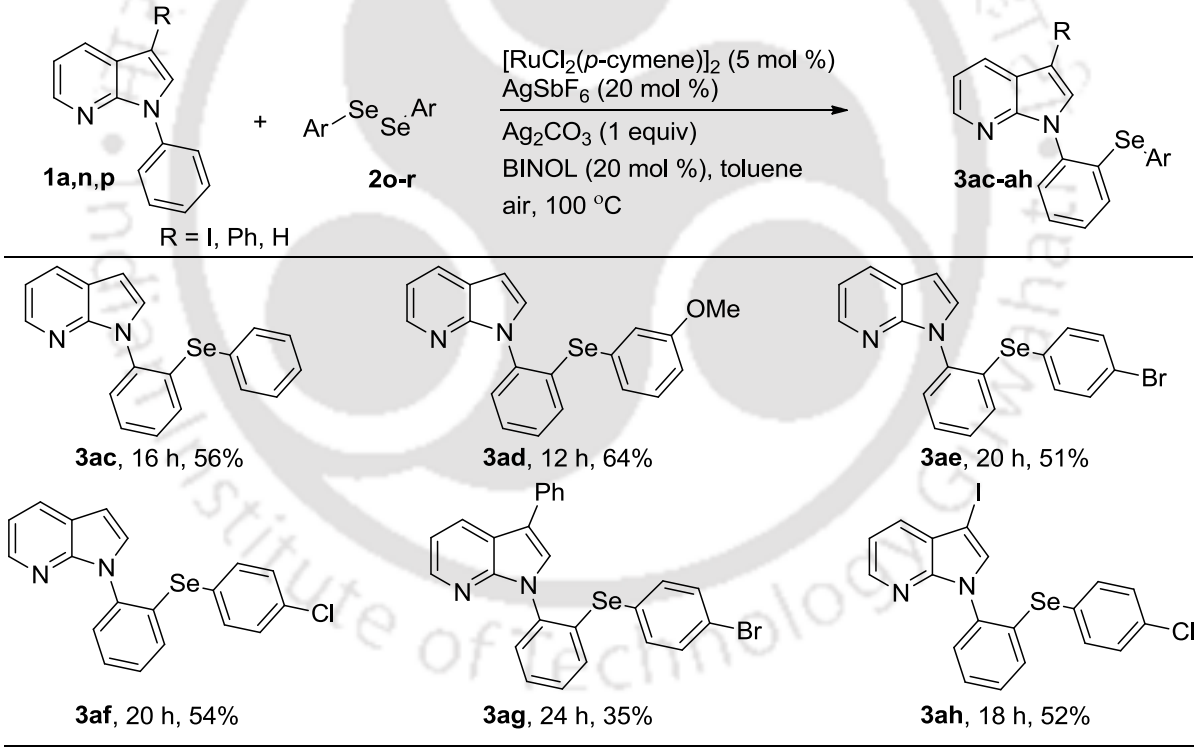


Figure 2. ORTEP diagram of 1-(2-((4-chlorophenyl)thio)phenyl)-1*H*-pyrrolo[2,3-b]pyridine **3g** with 50% ellipsoid. H-Atoms are omitted for clarity (CCDC 1855221).

Table 4. Reaction of *N*-Aryl-7-Azaindoles with Diselenides.[a,b]

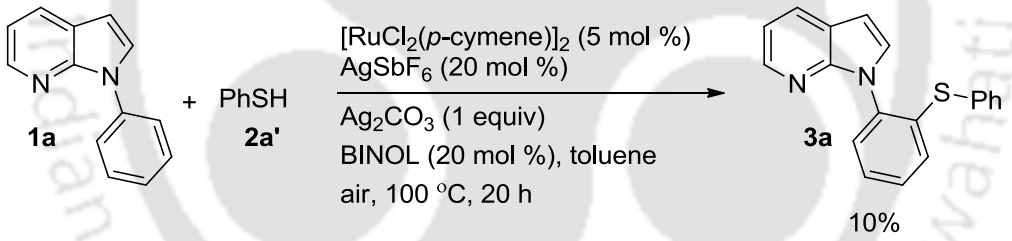


[a] Reaction conditions: *N*-Aryl-7-azaindole **1** (0.2 mmol), **2o-r** (0.2 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $AgSbF_6$ (20 mol %), Ag_2CO_3 (1 equiv), BINOL (20 mol %), toluene (2 mL), air, 100 °C.

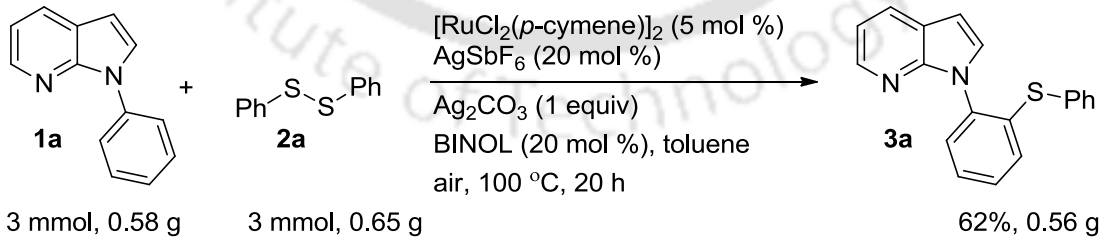
[b] Isolated yield.

We next examined this protocol for the reaction of substituted diselenides with different azaindoles (Table 4). For example, *N*-phenyl-7-azaindole **1a** underwent reaction with diphenyl diselenide **2o** produced **3ac** in 56% yield. Similarly, the reaction of the substrate bearing methoxy **2p** substituent at *meta*-position afforded the *ortho*-selenylated **3ad** in 64% yield. The substrates containing substitution at *para*-position such as bromo **2q** and chloro **2r** groups underwent reaction to deliver **3ae** and **3af** in 51 and 54% yields, respectively. In addition, *N*-aryl-7-azaindole having phenyl **1p** substituent at the 3-position underwent reaction with **2q** to furnish **3ag** in 35% yield, whereas the substrates having iodo **1n** group delivered **3ah** in 52% yield. These results suggest that this protocol can be utilized for the reaction of disulfides and diselenides.

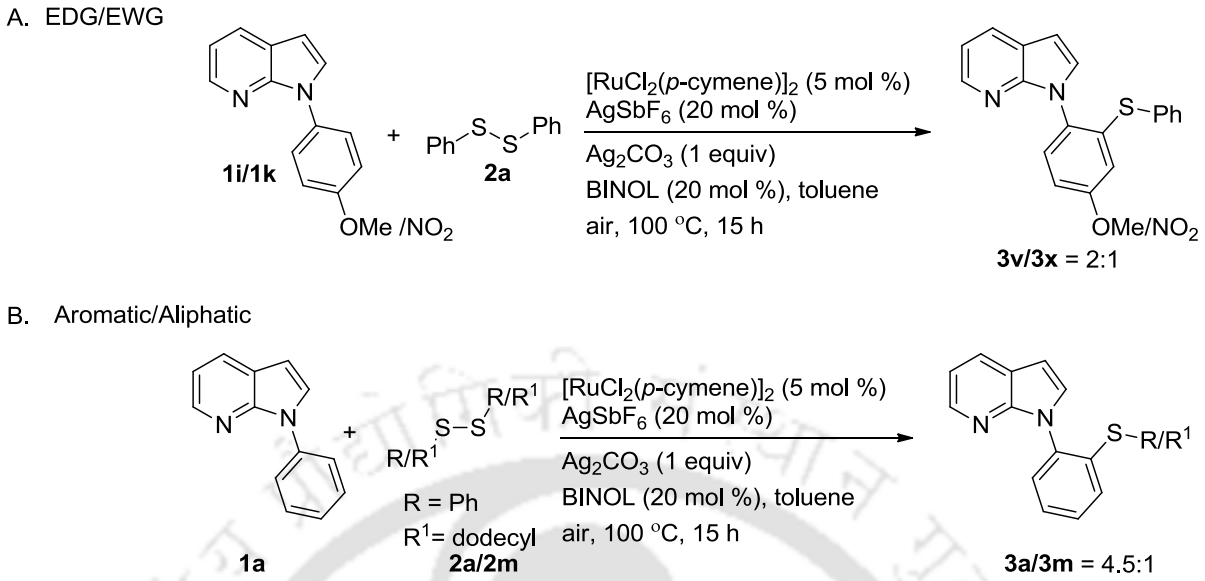
The protocol was further tested for the reaction of thiophenol with *N*-phenyl-7-azaindole **1a** (Scheme 26). However, the reaction was less effective and the thioether was obtained in 10% yield. This result indicates that disulfide is better choice compared to thiol.



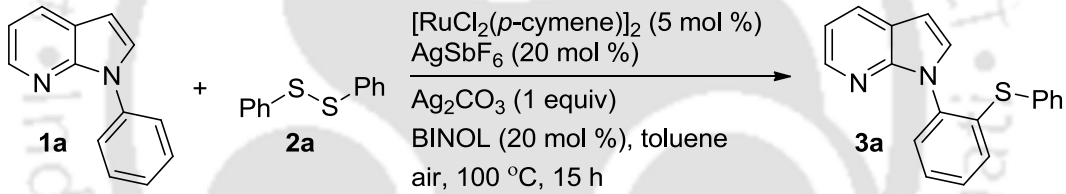
Scheme 26. Reaction of **1a** with Thiophenol



Scheme 27. Scale up Synthesis



Scheme 28. Intermolecular Competitive Experiments

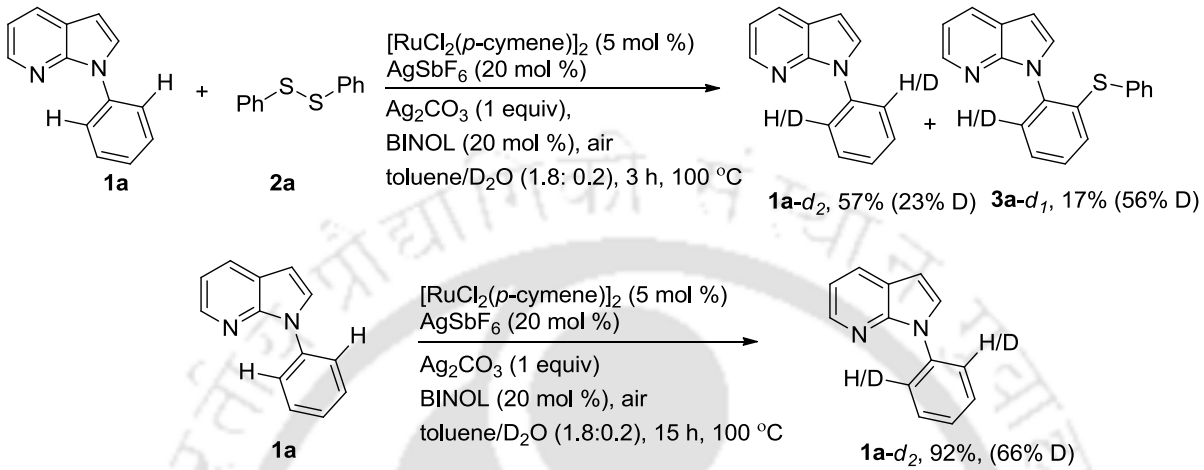


Radical Scavenger (2 equiv)	Yield (%)
TEMPO	55
BHT	63

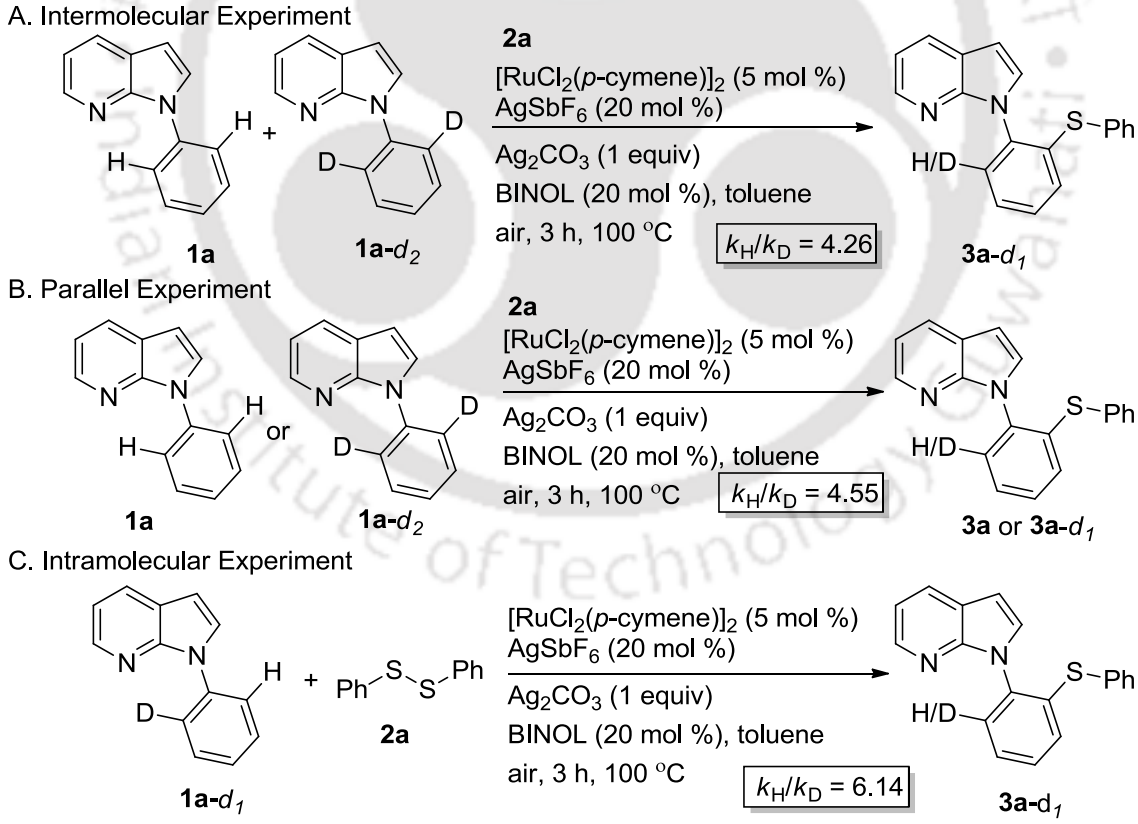
Scheme 29. Radical Scavenger Experiments

To reveal the scale up of the protocol, the reaction of **1a** with **2a** was examined as representative examples (Scheme 27). The reaction occurred to furnish **3a** in 62% yield, which suggests that the scale-up can be performed. To understand the reaction pathway, intermolecular competitive experiments were conducted (Scheme 28). The reaction using electronically different 7-azaindoles such as **1i** and **1k** with **2a** indicated that the substrate bearing electron-donating 4-methoxy group exhibited the greater reactivity compared to that bearing electron deficient 4-nitro group (Scheme 28A). Moreover, the reaction of the diaryl disulfide **2a** and dialkyl disulfide **2m** with **1a** suggested that the former was more reactive compared to the latter (Scheme 28B), which indicate the involvement of an aromatic

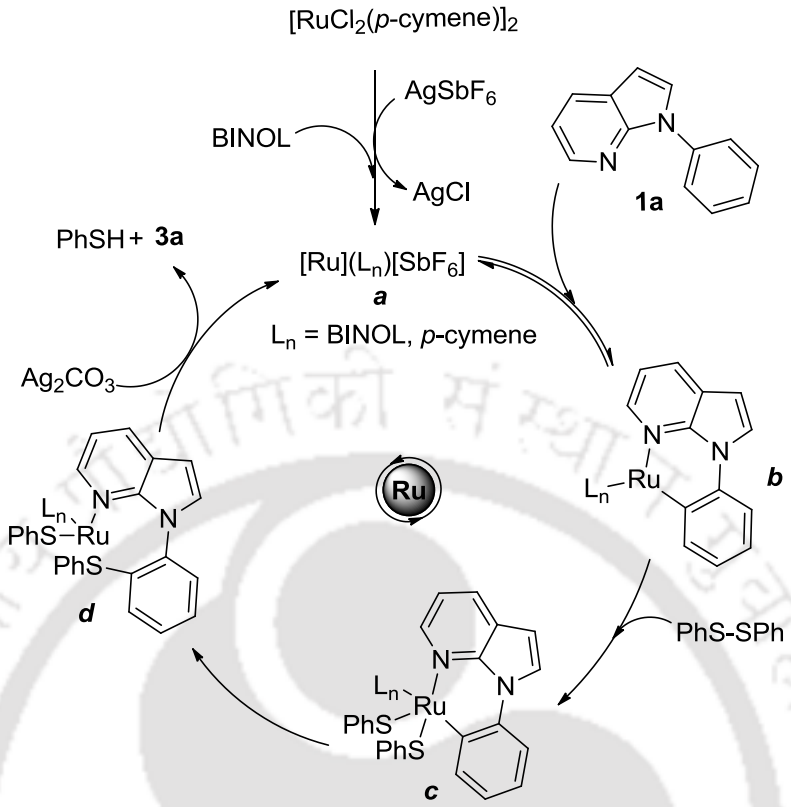
electrophilic type of substitution process. Furthermore, the radical scavenger experiments using TEMPO and BHT produced the thioether **3a** in 55 and 63% yields, respectively, which suggests that the radical process may not be involved (Scheme 29).



Scheme 30. H/D Exchange Experiments



Scheme 31. Kinetic Isotope Studies



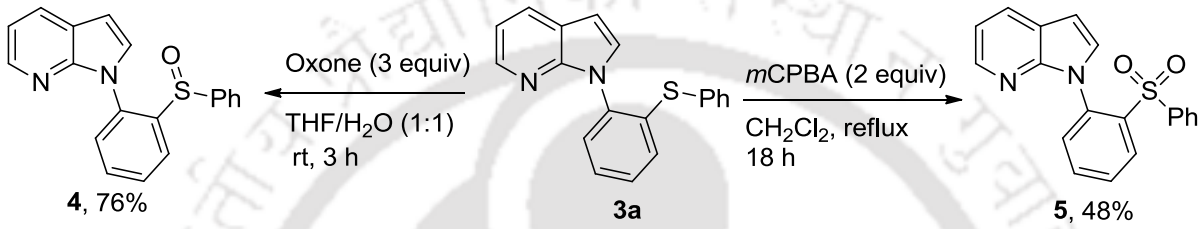
Scheme 32. Proposed Catalytic Cycle

We next performed the kinetic isotope experiments to understand the nature of the C-H activation step. In this regard, the reaction using D_2O as a co-solvent exhibited significant H/D exchange at the *ortho*-position of the reisolated starting material **1a**-d_2 and thioether **3a**-d_1 (Scheme 30). Similarly, the H/D exchange experiment of **1a** in the absence of disulfide **2a** exhibited 66% deuterium incorporation at the *ortho*-position to produce **1a**-d_2 (Scheme 30). These results suggest that C-H bond cleavage step may be reversible. Further, intermolecular kinetic isotope experiment using **1a** and **1a**-d_2 with **2a** revealed k_H/k_D = 4.26 (Scheme 31A) and the parallel kinetic isotope study provided k_H/k_D = 4.55 (Scheme 31B). Similarly, the intramolecular kinetic isotope experiment using **1a**-d_1 with **2a** showed k_H/k_D = 6.14 (Scheme 31C). These results suggest that the C-H bond cleavage may be involved in the rate-determining step.

The proposed catalytic cycle is shown in Scheme 32. Reaction of $[RuCl_2(p\text{-cymene})]_2$ with $AgSbF_6$ in presence of BINOL[17] can give an active Ru-complex ***a***, which may activate the *ortho*-C-H bond of *N*-phenyl-7-azaindole **1a** reversibly to generate a Ru-metallacycle ***b***.[33]

The latter on reaction with disulfide may provide the metallacycle ***c***, which may undergo reductive elimination to provide the Ru-species ***d***, which may deliver the thioether **3a** and Ru(I) species that can be oxidized using Ag_2CO_3 to provide the active Ru species.

Finally, the synthetic efficacy has been demonstrated using the thioether **3a** as representative example (Scheme 33). Treatment of **3a** with oxone in THF/H_2O produced sulfoxide **4** in 76% yield, whereas the reaction using *m*CPBA furnished the sulfone **5** in 48% yield.



Scheme 33. Post Synthetic Application of **3a**

In conclusion, we have developed a Ru-catalyzed directed C-H chalcogenation of arenes tethered with 7-azaindoles using disulfides and diselenides in presence of BINOL under air. The regioselectivity and functional group tolerance are the important features. The mechanistic studies suggest that the reaction may not involve a radical pathway and C-H activation may be the rate-determining step.

4.3 Experimental Section

General Information. $[RuCl_2(p\text{-cymene})]_2$ (97%), $AgSbF_6$ (98%), Ag_2CO_3 (99%), BINOL (99%) of Aldrich and 2,6-di-tert-butyl-4-methylphenol (BHT) (99%) of Merck were utilized as received. *N*-Aryl-7-azaindoles **1a-o**[3a], disulfides **2a-n**[6b,c] and diselenides **2o-r**[5a] were prepared according to literature. Other materials and analyses were investigated as presented in chapters 1.

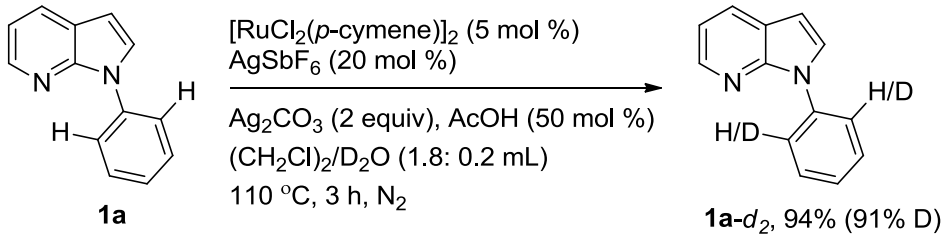
General Procedure for the C-H Chalcogenation of *N*-Aryl-7-Azaindoles. *N*-Aryl-7-azaindole **1** (0.2 mmol), disulfide or diselenide **2** (0.2 mmol), Ag_2CO_3 (0.2 mmol, 55 mg), $AgSbF_6$ (20 mol %, 13.7 mg), BINOL (20 mol %, 11.4 mg) and $[RuCl_2(p\text{-cymene})]_2$ (5 mol %, 6.1 mg) were stirred in toluene (2 mL) at 100 ^oC under air. The progress of the reaction

was monitored by TLC using ethyl acetate and hexane as eluent. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (5 mL). The resultant mixture was passed through a short pad of celite using ethyl acetate (10 mL). The filtrate was concentrated on vacuum and the residue was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

Procedure for the Oxidation of 3a to 4. Thioether **3a** (0.1 mmol, 30.2 mg) and oxone (0.3 mmol, 45.7 mg) were stirred in THF/H_2O (1:1, 2 mL) at room temperature. After completion, THF was evaporated and the aqueous solution was extracted with ethyl acetate (3 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue, which was purified on silica gel column chromatography using ethyl acetate and hexane as eluent.

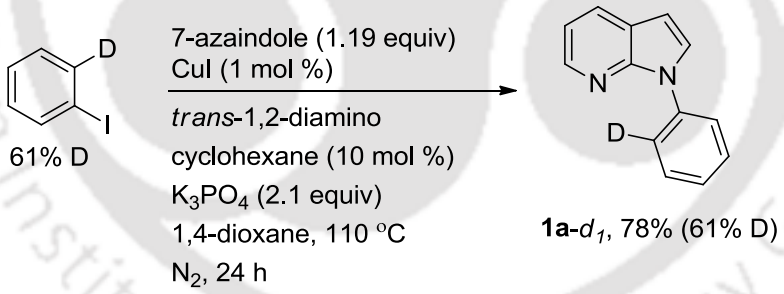
Procedure for the Oxidation of 3a to 5. Thioether **3a** (0.1 mmol, 30.2 mg) and *m*CPBA (0.2 mmol, 34.5 mg) were stirred under reflux in CH_2Cl_2 (2 mL). The progress of the reaction was monitored by TLC using hexane and ethyl acetate as eluent. The reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (3 x 10 mL). The combined organic solution was successively washed with saturated $NaHCO_3$ (1 x 5 mL) and water (1 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent produced a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent.

Preparation of 1a-d_2 (Scheme 34). *N*-Phenyl-7-azaindole **1a** (0.25 mmol, 48.5 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %, 7.6 mg), $AgSbF_6$ (20 mol %, 17.1 mg), AcOH (50 mol %, 7.0 μL) and Ag_2CO_3 (0.5 mmol, 137.5 mg) were stirred at 110 °C for 3 h in $(CH_2Cl)_2/D_2O$ (1.8:0.2) under N_2.[7c] After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2 (15 mL). The resulting solution was passed through a short pad of celite using CH_2Cl_2 (30 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue, which was purified by silica gel column chromatography to yield **1a**-d_2 in 94% yield (46 mg) as a colorless liquid. The deuterium incorporation was determined using 600 MHz ^{1}H NMR, which was found to be 91%.



Scheme 34

Preparation of 1a-d_1 (Scheme 35).[3a] [D]-Iodobenzene (1.85 mmol, 380 mg, 61% D)[34] was added to a stirred solution of 7-azaindole (2.21 mmol, 261 mg), CuI (1 mol %, 3.5 mg), K_3PO_4 (3.86 mmol, 820 mg) and racemic *trans*-1,2-diaminocyclohexane (0.185 mmol, 22 μL) under N_2 in 1,4-dioxane (4 mL). The resulting suspension was heated at 110 °C for 24 h and then cooled to room temperature. The mixture was passed through a short pad of celite using ethyl acetate (30 mL). Evaporation of solvent gave a residue that was purified on silica gel column chromatography using ethyl acetate and hexane as an eluent to give **1a**-d_1 in 78% (282 mg) yield as a colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (dd, J = 4.2, 3.0 Hz, 1H), 7.98 (dd, J = 7.8, 6.0 Hz, 1H), 7.76 (dd, J = 9.0, 7.8 Hz, 1.39H), 7.54-7.51 (m, 3H), 7.34 (t, J = 7.8 Hz, 1H), 7.14-7.12 (m, 1H), 6.64 (d, J = 3.6 Hz, 1H).



Scheme 35

H/D Exchange Experiment with D_2O. *N*-Phenyl-7-azaindole **1a** (0.1 mmol, 19.4 mg), diphenyl disulfide **2a** (0.1 mmol, 21.8 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %, 3 mg), $AgSbF_6$ (20 mol %, 6.8 mg), Ag_2CO_3 (0.1 mmol, 27.5 mg) and BINOL (20 mol %, 5.7 mg) were stirred at 100 °C for 3 h in toluene/D_2O (1.8:0.2 mL) under air. The reaction mixture was cooled to room temperature, diluted with ethyl acetate (10 mL) and passed through a short pad of celite using ethyl acetate (15 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue,

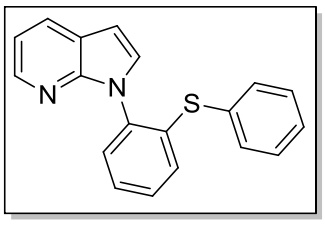
which was purified on silica gel column chromatography to yield **1a**-d_2 in 57% (11 mg) and **3a**-d_1 in 17% (5 mg).

Intermolecular Kinetic Isotope Experiment. Compound **1a** (0.1 mmol, 19.4 mg) and **1a**-d_2 (0.1 mmol, 19.6 mg) were subjected to the standard condition for 3 h. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (10 mL). The resultant solution was passed through a short pad of celite using ethyl acetate (15 mL). The filtrate was evaporated and the residue was purified on silica gel column chromatography using ethyl acetate and hexane as eluent. The k_H/k_D was determined using 600 MHz ^{1}H NMR as 4.26.

Parallel Kinetic Isotope Experiment. Compound **1a** (0.1 mmol, 19.4 mg) and **1a**-d_2 (0.1 mmol, 19.6 mg) were separately subjected to the standard conditions for 3 h. The reaction mixtures were cooled to room temperature and diluted with ethyl acetate (10 mL). Both the reaction mixtures were mixed together and the resultant solution was passed through a short pad of celite using ethyl acetate (15 mL). The filtrate was evaporated and the residue was purified on silica gel column chromatography using ethyl acetate and hexane as eluent. The k_H/k_D was determined using 600 MHz ^{1}H NMR as 4.55.

Intramolecular Kinetic Isotope Experiment. Compound **1a**-d_1 (0.1 mmol, 19.5 mg) was subjected to the standard reaction conditions for 3 h. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (10 mL). The resultant solution was passed through a short pad of celite using ethyl acetate (10 mL). The filtrate was evaporated and the residue was purified on silica gel column chromatography using ethyl acetate and hexane as eluent. The k_H/k_D = 6.14, was determined using 600 MHz ^{1}H NMR.

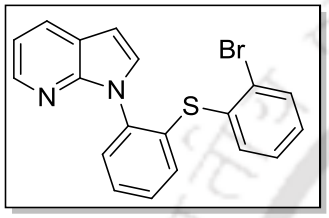
4.4 Characterization Data



1-(2-(Phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3a.

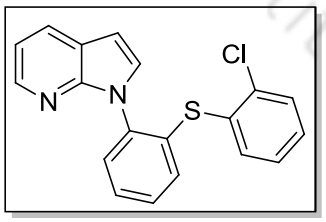
Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.46; colorless liquid; yield 72%

(44 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.93 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.40-7.37 (m, 2H), 7.33-7.32 (m, 2H), 7.26-7.24 (m, 2H), 7.19-7.13 (m, 3H), 7.09-7.07 (m, 1H), 6.60 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.7, 137.4, 135.9, 134.1, 132.4, 132.1, 129.6, 129.3, 129.2, 129.0, 127.8, 127.7, 120.6, 116.6, 101.1; FT-IR (neat) 2923, 2854, 1639, 1583, 1510, 1479, 1440, 1420, 1357, 1321, 1267, 1231, 1149, 959, 893, 796, 742, 692 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{14}N_2S$: 303.0956, found: 303.0955.



1-(2-((2-Bromophenyl)thio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

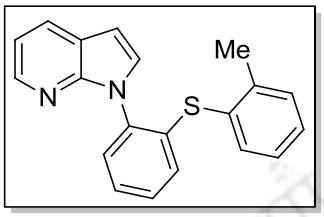
3b. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 60% (46 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.90 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.57 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.44-7.41 (m, 2H), 7.40-7.39 (m, 2H), 7.09-7.06 (m, 2H), 7.02-7.00 (m, 1H), 6.94-6.91 (m, 1H), 6.56 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 143.6, 138.7, 136.4, 134.0, 133.1, 133.0, 132.3, 129.6, 129.5, 129.18, 129.11, 129.0, 128.2, 127.7, 125.0, 120.7, 116.6, 101.2; FT-IR (neat) 2923, 2849, 1638, 1510, 1480, 1420, 1321, 1277, 1229, 1107, 1015, 892, 795, 748, 719 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}BrN_2S$: 381.0061, found: 381.0050.



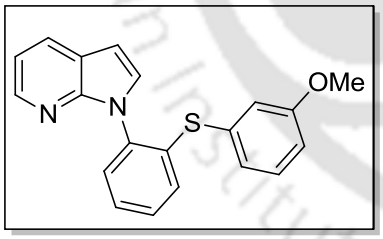
1-(2-((2-Chlorophenyl)thio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

3c. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 62% (42 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.91 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.56 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.49-7.46 (m, 1H), 7.43 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.39-7.37 (m, 2H), 7.25-7.24 (m, 1H), 7.11-7.06 (m, 2H), 7.04-7.01 (m, 1H), 6.98-6.96 (m, 1H), 6.56 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.6, 138.6, 134.9,

134.2, 133.8, 132.9, 132.5, 129.9, 129.6, 129.5, 129.1, 129.06, 129.00, 128.3, 127.1, 120.7, 116.6, 101.2; FT-IR (neat) 2924, 2854, 1639, 1511, 1481, 1448, 1421, 1357, 1321, 1278, 1112, 1032, 892, 797, 773, 749, 719 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}ClN_2S$: 337.0566, found: 337.0565.

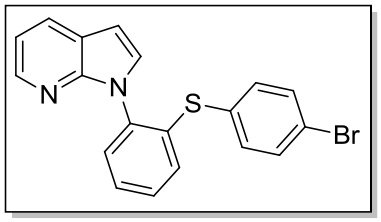


1-(2-(*o*-Tolylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3d. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.46; colorless liquid; yield 66% (42 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.96 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.38 (d, *J* = 3.6 Hz, 1H), 7.35-7.30 (m, 2H), 7.29-7.26 (m, 1H), 7.17 (d, *J* = 4.2 Hz, 2H), 7.12-7.10 (m, 1H), 7.08-7.05 (m, 2H), 6.62 (d, *J* = 3.6 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 143.8, 141.1, 136.6, 136.2, 134.6, 132.2, 130.8, 130.3, 129.5, 129.2, 129.1, 128.6, 127.1, 127.0, 126.8, 120.6, 116.6, 101.1, 20.7; FT-IR (neat) 2924, 2856, 1639, 1511, 1481, 1418, 1384, 1355, 1321, 1265, 1124, 1038, 955, 797, 773, 747 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2S$: 317.1112, found: 317.1120.

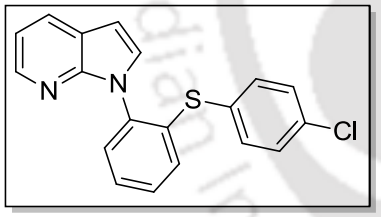


1-(2-((3-Methoxyphenyl)thio)phenyl)-1*H*-pyrrolo[2,3-b]pyridine 3e. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.36; colorless liquid; yield 69% (46 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.94 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.48 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.41-7.33 (m, 4H), 7.11-7.08 (m, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.77-6.76 (m, 1H), 6.69 (dd, *J* = 7.8, 5.4 Hz, 1H), 6.60 (d, *J* = 3.6 Hz, 1H), 3.69 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.9, 148.3, 143.7, 137.5, 135.5, 135.3, 132.4, 130.0, 129.6, 129.4, 129.1, 129.0, 128.0, 124.5, 120.6, 117.1, 116.6, 113.8, 101.1, 55.4; FT-IR (neat) 2923, 2854, 1638, 1511, 1479, 1420, 1384, 1357, 1321, 1265, 1227,

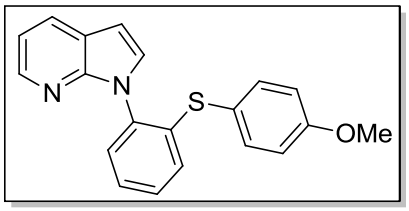
1111, 1033, 896, 795, 773, 739 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2OS$: 333.1062, found: 333.1057.



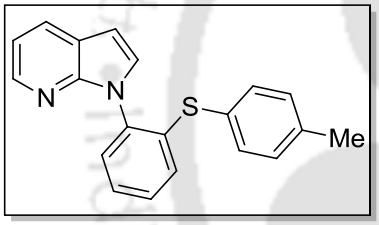
1-(2-((4-Bromophenyl)thio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3f. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 113-114 °C; yield 67% (51 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 4.2, 3.0 Hz, 1H), 7.91 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.44-7.41 (m, 2H), 7.38-7.34 (m, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.09-7.07 (m, 1H), 7.03 (d, *J* = 9.0 Hz, 2H), 6.59 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 143.7, 137.9, 134.8, 133.6, 133.2, 132.9, 132.1, 129.6, 129.4, 129.1, 129.0, 128.6, 121.6, 120.5, 116.6, 101.3; FT-IR (KBr) 2925, 2851, 1639, 1511, 1478, 1420, 1384, 1359, 1321, 1278, 1229, 1110, 1006, 797, 770, 719 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}BrN_2S$: 381.0061, found: 381.0058.



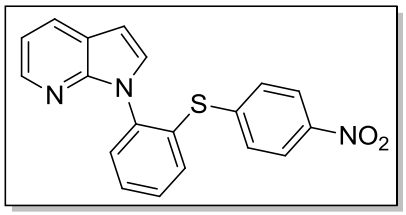
1-(2-((4-Chlorophenyl)thio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3g. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless solid; mp 123-124 °C; yield 69% (46.6 mg); ^1H NMR (600 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 4.2, 3.0 Hz, 1H), 7.92 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.49 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.44-7.39 (m, 2H), 7.38-7.35 (m, 2H). 7.11-7.06 (m, 5H), 6.60 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 143.7, 137.8, 135.1, 133.6, 133.2, 132.9, 132.7, 129.6, 129.4, 129.23, 129.20, 129.1, 128.5, 120.5, 116.6, 101.3; FT-IR (KBr) 2924, 2851, 1638, 1510, 1476, 1418, 1382, 1357, 1321, 1093, 1013, 892, 793, 776, 719 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}ClN_2S$: 337.0566, found: 337.0569.



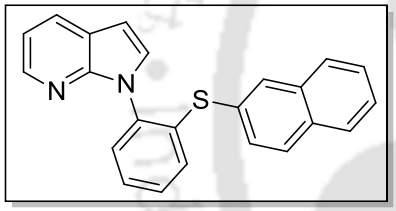
1-(2-((4-Methoxyphenyl)thio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3h. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.36; colorless liquid; yield 75% (50 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.2, 3.0 Hz, 1H), 7.96 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.41-7.40 (m, 2H), 7.31-7.27 (m, 4H), 7.11-7.09 (m, 2H), 6.78 (d, *J* = 8.4 Hz, 2H), 6.64 (d, *J* = 3.6 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.1, 148.3, 143.8, 138.2, 136.0, 135.8, 129.7, 129.6, 129.18, 129.12, 129.0, 126.7, 123.0, 120.6, 116.6, 115.0, 101.1, 55.5; FT-IR (neat) 2925, 2849, 1637, 1593, 1510, 1491, 1442, 1420, 1357, 1321, 1277, 1252, 1174, 1138, 1107, 1029, 952, 893, 827, 797, 751, 721 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2OS$: 333.1062, found: 333.1057.



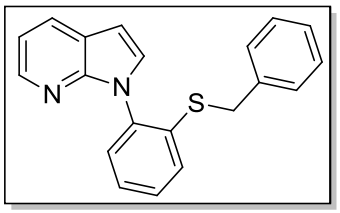
1-(2-(*p*-Tolylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3i. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 73% (46 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.95 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.44 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 1H), 7.35-7.32 (m, 1H), 7.31-7.28 (m, 1H), 7.22-7.19 (m, 3H), 7.11-7.08 (m, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.62 **(**d, *J* = 3.0 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.7, 138.3, 137.1, 136.6, 133.4, 130.9, 130.1, 129.7, 129.6, 129.2, 129.09, 129.04, 127.2, 120.6, 116.5, 101.1, 21.3; FT-IR (neat) 2923, 2851, 1636, 1512, 1483, 1420, 1382, 1321, 1263, 1193, 1106, 1013, 914, 802, 746, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2S$: 317.1112, found: 317.1107.



1-(2-((4-Nitrophenyl)thio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3j. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.33; yellow liquid; yield 65% (45 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.83-7.79 (m, 3H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 4.2 Hz, 2H), 7.52-7.49 (m, 1H), 7.33 (d, *J* = 3.6 Hz, 1H), 7.07 (d, *J* = 9.0 Hz, 2H), 7.03-7.01 (m, 1H), 6.52 **(**d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.0, 145.9, 145.6, 143.6, 140.0, 136.2, 130.84, 130.82, 130.3, 129.5, 129.2, 129.1, 128.3, 123.6, 120.4, 116.8, 101.5; FT-IR (neat) 2923, 2851, 1638, 1578, 1511, 1480, 1421, 1337, 1279, 1232, 1150, 1109, 1088, 957, 893, 850, 798, 773, 722 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}N_3O_2S$: 348.0807, found: 348.0798.

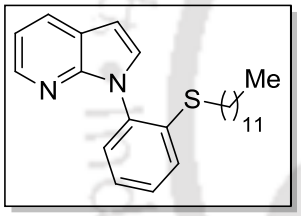


1-(2-(Naphthalen-2-ylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3k. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.46; colorless solid; mp 105-106 ^{o}C; yield 71% (50 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.88 (d, *J* = 7.8, 6.6 Hz, 1H), 7.73-7.72 (m, 2H), 7.66-7.64 (m, 2H), 7.50 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.44-7.41 (m, 2H), 7.40-7.36 (m, 3H), 7.33-7.29 (m, 2H), 7.02-7.00 (m, 1H), 6.59 **(**d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.7, 137.5, 135.8, 133.7, 132.6, 132.3, 131.5, 131.2, 129.67, 129.62, 129.4, 129.1, 129.0, 128.9, 127.9, 127.8, 127.6, 126.6, 126.5, 120.6, 116.6, 101.2; FT-IR (KBr) 2925, 2854, 1638, 1510, 1481, 1420, 1357, 1321, 1278, 1229, 1111, 939, 894, 849, 795, 748, 718 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{16}N_2S$: 353.1112, found: 353.1117.



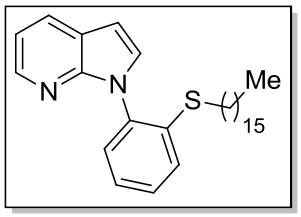
1-(2-(Benzylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3l.

Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 70% (44 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.97 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.50-7.49 (m, 1H), 7.43-7.41 (m, 1H), 7.38-7.35 (m, 2H), 7.26 (d, *J* = 3.6 Hz, 1H), 7.20-7.16 (m, 3H), 7.12-7.10 (m, 3H), 6.61 (d, *J* = 3.6 Hz, 1H), 3.85 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.5, 143.8, 137.6, 136.8, 135.5, 130.9, 129.7, 129.2, 129.1, 129.0, 128.9, 128.5, 127.3, 120.7, 116.6, 100.9, 38.5; FT-IR (neat) 2924, 2851, 1639, 1510, 1480, 1420, 1386, 1355, 1319, 1277, 1260, 1119, 997, 773, 748 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2S$: 317.1112, found: 317.1119.

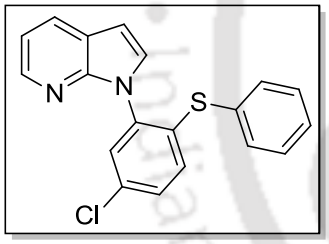


1-(2-(Dodecylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3m.

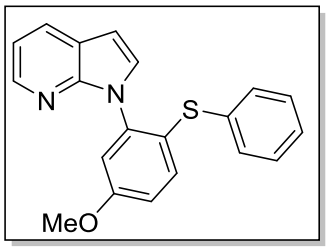
Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.50; colorless liquid; yield 64% (50.4 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.98 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.42-7.39 (m, 2H), 7.37 (d, *J* = 3.6 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.12-7.09 (m, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 2.66 (t, *J* = 7.8 Hz, 2H), 1.48-1.43 (m, 2H), 1.30-1.17 (m, 18H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 143.8, 137.0, 136.4, 129.7, 129.3, 129.2, 129.1, 128.9, 126.4, 120.6, 116.5, 100.9, 33.1, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 28.9, 28.8, 22.9, 14.3; FT-IR (neat) 2924, 2853, 1638, 1558, 1512, 1481, 1420, 1358, 1321, 1279, 1231, 1146, 1109, 1040, 889, 796, 772, 750, 718 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{34}N_2S$: 395.2521, found: 395.2518.



1-(2-(Hexadecylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3n. Analytical TLC on silica gel, 1:5 ethyl acetate/hexane R_f = 0.50; colorless liquid; yield 63% (57 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.98 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.42-7.39 (m, 2H), 7.37 (d, *J* = 3.0 Hz, 1H), 7.34-7.31 (m, 1H), 7.12-7.09 (m, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 2.66 (t, *J* = 7.2 Hz, 2H), 1.48-1.43 (m, 2H), 1.30-1.16 (m, 26H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 143.8, 137.0, 136.4, 129.7, 129.3, 129.2, 129.1, 128.9, 126.4, 120.6, 116.6, 100.9, 33.1, 32.1, 29.9, 29.89, 29.87, 29.83, 29.7, 29.6, 29.5, 29.2, 28.9, 28.8, 22.9, 14.3; FT-IR (neat) 2924, 2853, 1639, 1512, 1480, 1420, 1321, 1264, 1109, 795, 770, 743, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{29}H_{42}N_2S$: 451.3147, found: 451.3156.

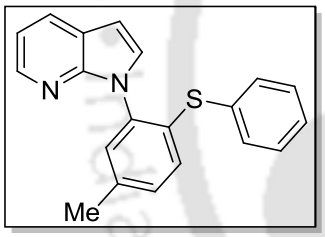


1-(5-Chloro-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3o. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless liquid; yield 65% (43.6 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.94 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.48 (d, *J* = 1.8 Hz, 1H), 7.35 (d, *J* = 3.6 Hz, 1H), 7.30 (dd, *J* = 8.4, 6.6 Hz, 1H), 7.25-7.23 (m, 3H), 7.20-7.17 (m, 3H), 7.12-7.09 (m, 1H), 6.61 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 143.9, 138.1, 134.7, 133.6, 133.2, 132.9, 132.5, 129.4, 129.3, 129.2, 129.1, 128.0, 120.6, 116.9, 101.7; FT-IR (neat) 2923, 2851, 1637, 1579, 1512, 1477, 1431, 1353, 1277, 1148, 1099, 1024, 979, 892, 795, 718 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}ClN_2S$: 337.0566, found: 337.0568.



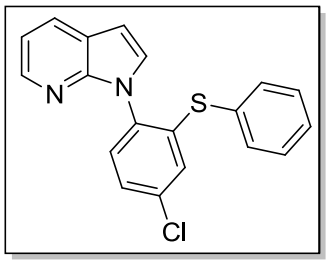
1-(5-Methoxy-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

3p. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.35; colorless solid; mp 124-125 °C; yield 77% (51 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.90 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.53 (d, *J* = 9.0 Hz, 1H), 7.31 (d, *J* = 3.6 Hz, 1H), 7.09-7.04 (m, 6H), 7.02-6.99 (m, 1H), 6.97 (dd, *J* = 9.0, 6.0 Hz, 1H), 6.54 (d, *J* = 3.6 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.4, 148.3, 143.6, 140.6, 136.9, 136.5, 129.7, 129.5, 129.0, 128.8, 126.3, 124.0, 120.6, 116.5, 115.6, 114.8, 100.9, 55.8; FT-IR (KBr) 2924, 2851, 1640, 1591, 1510, 1478, 1433, 1354, 1277, 1215, 1179, 1146, 1054, 1022, 893, 796, 768, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2OS$: 333.1062, found: 333.1058.



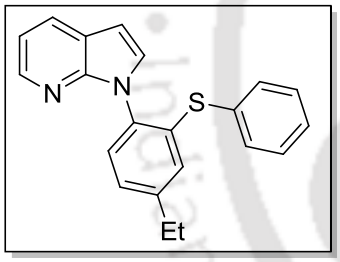
1-(5-Methyl-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

3q. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless solid; mp 83-84 °C; yield 73% (46 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.91 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.35-7.31 (m, 3H), 7.18-7.15 (m, 3H), 7.13-7.11 (m, 2H), 7.09-7.05 (m, 2H), 6.56 (d, *J* = 3.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.6, 138.8, 138.1, 135.3, 133.4, 131.4, 131.2, 130.13, 130.12, 129.7, 129.03, 129.00, 127.0, 120.6, 116.5, 100.9, 21.2; FT-IR (KBr) 2919, 2851, 1638, 1510, 1479, 1435, 1355, 1319, 1280, 1193, 1111, 1022, 894, 796, 769, 741, 719 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2S$: 317.1112, found: 317.1116.



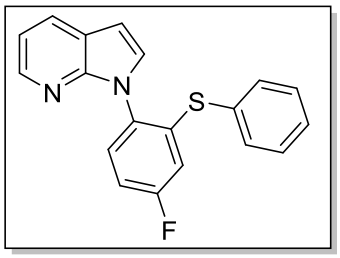
1-(4-Chloro-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

3r. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless liquid; yield 66% (44.3 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.94 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.38-7.35 (m, 2H), 7.31-7.29 (m, 3H), 7.25-7.23 (m, 3H), 7.17 (d, *J* = 2.4 Hz, 1H), 7.11-7.09 (m, 1H), 6.62 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.8, 138.7, 135.0, 134.8, 133.4, 132.2, 130.38, 130.34, 129.6, 129.28, 129.23, 128.6, 127.4, 120.6, 116.8, 101.5; FT-IR (neat) 2924, 2854, 1638, 1511, 1478, 1423, 1354, 1319, 1278, 1102, 1024, 957, 797, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}ClN_2S$: 337.0566, found: 337.0565.

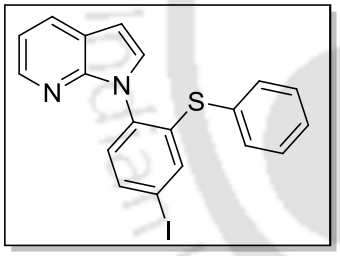


1-(4-Ethyl-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

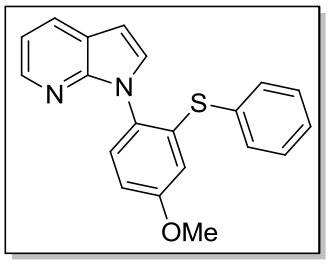
3s. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 75% (49.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.91 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.34 (d, *J* = 3.6 Hz, 1H), 7.24-7.23 (m, 2H), 7.20-7.19 (m, 2H), 7.15-7.09 (m, 3H), 7.07-7.05 (m, 1H), 6.56 (d, *J* = 3.6 Hz, 1H), 2.63 (q, *J* = 7.8 Hz, 2H), 1.21 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 145.3, 143.6, 135.4, 134.8, 134.7, 132.2, 131.6, 129.7, 129.2, 129.0, 128.9, 127.9, 127.3, 120.5, 116.4, 100.8, 28.6, 15.5; FT-IR (neat) 2925, 2849, 1638, 1512, 1489, 1425, 1386, 1355, 1321, 1283, 1263, 1107, 1020, 892, 739 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}N_2S$: 331.1269, found: 331.1274.



1-(4-Fluoro-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3t. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.43; colorless liquid; yield 67% (43 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.96 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.41-7.38 (m, 1H), 7.36-7.35 (m, 3H), 7.28-7.27 (m, 3H), 7.12-7.10 (m, 1H), 7.02-6.99 (m, 1H), 6.83 (dd, *J* = 9.0, 6.0 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3 (d, J_{C-F} = 248.4 Hz), 148.4, 143.9, 140.0, 134.0, 131.9, 130.7 (d, J_{C-F} = 9.15 Hz), 129.7, 129.5, 129.2, 128.9, 120.6, 116.8, 116.78, 116.71, 114.1 (d, J_{C-F} = 22.8 Hz), 101.4; FT-IR (neat) 2923, 2854, 1638, 1597, 1511, 1487, 1425, 1355, 1321, 1254, 1198, 1143, 1022, 961, 890, 797, 770, 719 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}FN_2S$: 321.0862, found: 321.0853.

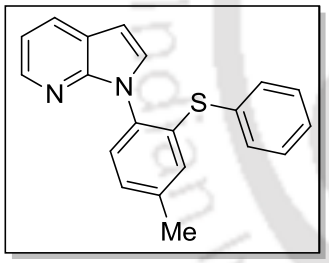


1-(4-Iodo-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3u. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.43; colorless solid; mp 130-131 ^{o}C; yield 71% (61 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.93 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.68 (dd, *J* = 8.4, 6.6 Hz, 1H), 7.58-7.57 (m, 1H), 7.35 (d, *J* = 3.6 Hz, 1H), 7.27-7.25 (m, 2H), 7.22-7.17 (m, 4H), 7.10-7.08 (m, 1H), 6.61 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 143.8, 139.7, 138.6, 136.6, 132.8, 132.7, 130.8, 129.5, 129.2, 129.1, 128.3, 120.6, 116.8, 101.6, 94.3; FT-IR (KBr) 2924, 2851, 1639, 1592, 1573, 1511, 1477, 1422, 1353, 1319, 1279, 1231, 1068, 1023, 953, 893, 796, 771, 718, 690 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}IN_2S$: 428.9922, found: 428.9921.



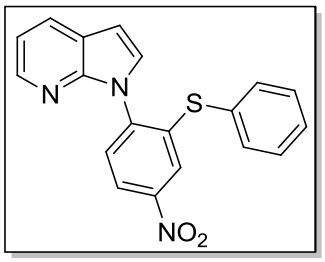
1-(4-Methoxy-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine

3v. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.34; colorless solid; mp 82-83 °C; yield 78% (52 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.93 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 7.33 (d, *J* = 3.6 Hz, 1H), 7.29-7.27 (m, 2H), 7.21-7.17 (m, 3H), 7.08-7.06 (m, 1H), 6.89 (dd, *J* = 9.0, 6.0 Hz, 1H), 6.79 (d, *J* = 2.4 Hz 1H), 6.58 (d, *J* = 3.6 Hz, 1H), 3.74 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.8, 148.6, 143.7, 137.6, 133.4, 132.8, 130.2, 130.0, 129.9, 129.3, 129.0, 128.0, 120.5, 116.7, 116.4, 113.0, 100.8, 55.7; FT-IR (KBr) 2925, 2854, 1639, 1511, 1491, 1424, 1355, 1276, 1219, 1111, 1031, 892, 795, 770, 746, 720 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2OS$: 333.1062, found: 333.1058.

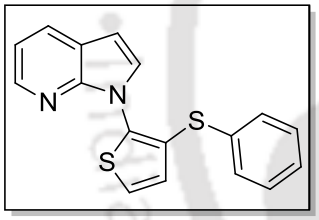


1-(4-Methyl-2-(phenylthio)phenyl)-*1H*-pyrrolo[2,3-*b*]pyridine

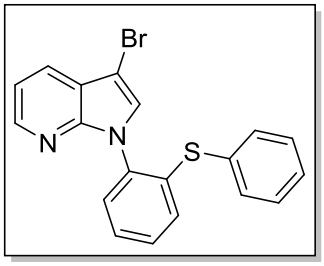
3w. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 76% (48 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.91 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 3.6 Hz, 1H), 7.21-7.19 (m, 4H), 7.17-7.10 (m, 3H), 7.07-7.05 (m, 1H), 6.57 (d, *J* = 3.6 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 143.7, 139.3, 135.2, 135.0, 134.5, 133.1, 131.8, 129.7, 129.18, 129.12, 129.0, 128.9, 127.4, 120.5, 116.4, 100.8, 21.3; FT-IR (neat) 2923, 2854, 1639, 1512, 1489, 1424, 1355, 1319, 1278, 1112, 1024, 894, 797, 744 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2S$: 317.1112, found: 317.1114.



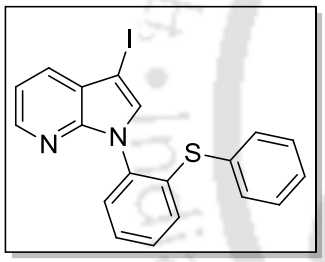
1-(4-Nitro-2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3x. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.32; yellow liquid; yield 68% (47 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 4.8, 3.0 Hz, 1H), 8.16 (dd, *J* = 8.4, 6.0 Hz, 1H), 8.01 (d, *J* = 2.4 Hz, 1H), 7.98 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.67 (d, *J* = 9.0 Hz, 1H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.37-7.36 (m, 2H), 7.31-7.30 (m, 3H), 7.17-7.15 (m, 1H), 6.70 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.1, 147.4, 144.1, 141.2, 139.2, 133.9, 131.1, 130.0, 129.7, 129.5, 129.4, 128.6, 125.3, 121.8, 121.0, 117.4, 102.7; FT-IR (neat) 2925, 2851, 1638, 1517, 1480, 1422, 1342, 1272, 1115, 1018, 876, 795, 741, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}N_3O_2S$: 348.0807, found: 348.0800.



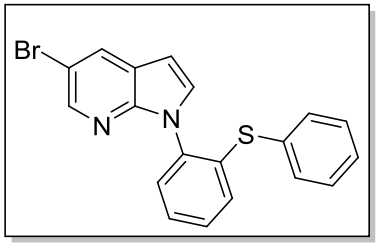
1-(3-(Phenylthio)thiophen-2-yl)-1*H*-pyrrolo[2,3-*b*]pyridine 3y. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.43; colorless liquid; yield 76% (47 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.91 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 1H), 7.33 (d, *J* = 5.4 Hz, 1H), 7.17-7.15 (m, 4H), 7.13-7.08 (m, 2H), 7.01 (d, *J* = 6.0 Hz, 1H), 6.57 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.8, 144.0, 139.1, 136.4, 130.7, 130.1, 129.2, 129.1, 128.8, 126.4, 125.1, 123.5, 121.0, 117.3, 102.3; FT-IR (neat) 2924, 2851, 1638, 1532, 1449, 1409, 1305, 1264, 1227, 1020, 880, 797, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{17}H_{12}N_2S_2$: 309.0520, found: 309.0518.



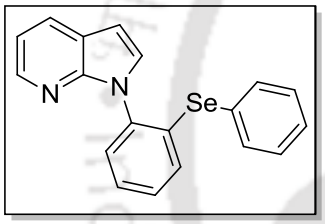
3-Bromo-1-(2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3z. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless liquid; yield 71% (54 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.86 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.44-7.43 (m, 1H), 7.41 (s, 1H), 7.39-7.35 (m, 3H), 7.21-7.20 (m, 2H), 7.16-7.11 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.1, 144.8, 136.5, 135.9, 133.7, 132.4, 132.3, 129.46, 129.42, 129.1, 128.3, 128.0, 127.8, 120.0, 117.2, 90.2; FT-IR (neat) 2924, 2851, 1638, 1516, 1476, 1440, 1413, 1319, 1280, 1218, 1110, 1072, 1022, 988, 928, 793, 750 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}BrN_2S$: 381.0061, found: 381.0059.



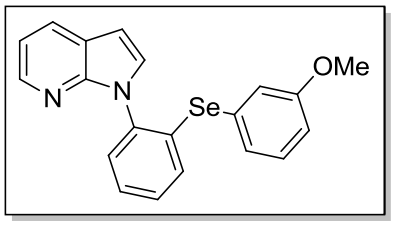
3-Iodo-1-(2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 3aa. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.43; colorless liquid; yield 73% (62.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.8, 3.6 Hz, 1H), 7.71 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.46 (s, 1H), 7.44-7.34 (m, 4H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.16-7.10 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.8, 144.8, 136.6, 135.9, 133.7, 133.3, 132.5, 132.3, 129.5, 129.4, 129.1, 128.0, 127.8, 123.1, 117.4, 55.9; FT-IR (neat) 2923, 2854, 1638, 1584, 1505, 1477, 1440, 1409, 1312, 1278, 1218, 1109, 1069, 1024, 979, 921, 765, 750 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}IN_2S$: 428.9922, found: 428.9919.



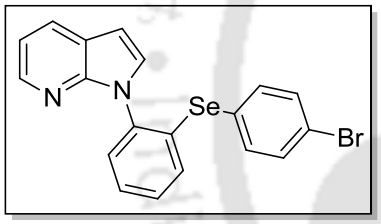
5-Bromo-1-(2-(phenylthio)phenyl)-1*H*-pyrrolo[2,3-b]pyridine 3ab. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless liquid; yield 73% (55.6 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.04 (s, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.41-7.35 (m, 4H), 7.22 (d, *J* = 6.0 Hz, 2H), 7.19-7.16 (m, 3H), 6.54 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.7, 144.2, 136.9, 135.9, 133.8, 132.38, 132.35, 131.1, 131.0, 129.4, 129.2, 129.1, 128.0, 127.8, 122.2, 112.5, 100.6; FT-IR (neat) 2924, 2853, 1637, 1581, 1509, 1477, 1453, 1399, 1307, 1264, 1189, 1114, 957, 885, 746, 721, 689 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}BrN_2S$: 381.0061, found: 381.0057.



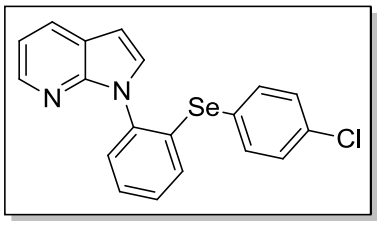
1-(2-(Phenylselanyl)phenyl)-1*H*-pyrrolo[2,3-b]pyridine 3ac. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.46; colorless liquid; yield 56% (39 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.97 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.43-7.42 (m, 3H), 7.39-7.36 (m, 3H), 7.28-7.26 (m, 1H), 7.24-7.19 (m, 3H), 7.12-7.10 (m, 1H), 6.64 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 143.8, 138.0, 134.9, 133.3, 132.9, 129.6, 129.5, 129.3, 129.24, 129.23, 128.9, 128.2, 128.0, 120.6, 116.7, 101.3; FT-IR (neat) 2925, 2851, 1635, 1510, 1476, 1420, 1352, 1320, 1276, 1159, 1022, 894, 795, 773, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{14}N_2Se$: 351.0400, found: 351.0412.



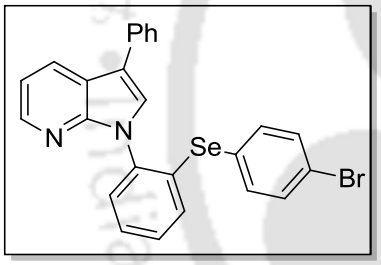
1-(2-((3-Methoxyphenyl)selanyl)phenyl)-1*H*-pyrrolo[2,3-b]pyridine 3ad. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.35; colorless liquid; yield 64% (48.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.97 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.44-7.37 (m, 4H), 7.29-7.26 (m, 1H), 7.14-7.10 (m, 2H), 7.02-7.01 (m, 1H), 6.96 (s, 1H), 6.77 (dd, *J* = 8.4, 6.0 Hz, 1H), 6.63 (d, *J* = 3.6 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.9, 148.4, 143.8, 138.0, 133.4, 132.7, 130.4, 130.2, 129.3, 129.2, 128.9, 128.1, 127.1, 120.6, 119.7, 116.7, 114.3, 101.3, 55.4; FT-IR (neat) 2924, 2854, 1637, 1509, 1473, 1419, 1382, 1355, 1321, 1280, 1228, 1111, 1031, 912, 800, 773, 743 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{16}N_2OSe$: 381.0506, found: 381.0512.



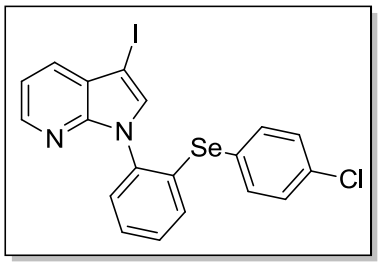
1-(2-((4-Bromophenyl)selanyl)phenyl)-1*H*-pyrrolo[2,3-b]pyridine 3ae. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.45; colorless liquid; yield 51% (43.6 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.2, 3.0 Hz, 1H), 7.95 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.45-7.40 (m, 3H), 7.36 (d, *J* = 3.6 Hz, 1H), 7.31-7.29 (m, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.12-7.10 (m, 1H), 6.62 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.8, 138.4, 136.0, 133.9, 132.4, 132.1, 129.3, 129.27, 129.24, 129.1, 128.8, 128.6, 122.5, 120.5, 116.7, 101.4; FT-IR (neat) 2923, 2851, 1637, 1510, 1478, 1418, 1355, 1321, 1276, 1109, 1005, 797, 773, 752, 716 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}BrN_2Se$: 428.9506, found: 428.9509.



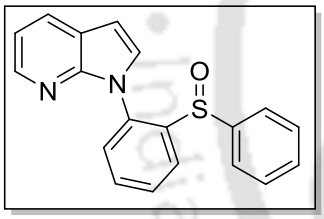
1-(2-((4-Chlorophenyl)selanyl)phenyl)-1*H*-pyrrolo[2,3-b]pyridine 3af. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless liquid; yield 54% (41.4 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.95 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.44-7.39 (m, 3H), 7.36 (d, *J* = 3.0 Hz, 1H), 7.31-7.28 (m, 3H), 7.12-7.10 (m, 3H), 6.63 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.8, 138.3, 135.8, 134.3, 133.8, 132.2, 129.5, 129.3, 129.28, 129.24, 129.1, 128.5, 128.0, 120.6, 116.7, 101.4; FT-IR (neat) 2923, 2854, 1638, 1510, 1475, 1420, 1357, 1320, 1280, 1089, 1010, 892, 795, 773, 750, 718 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{13}ClN_2Se$: 385.0011, found: 385.0024.



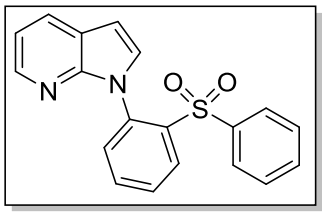
1-(2-((4-Bromophenyl)selanyl)phenyl)-3-phenyl-1*H*-pyrrolo[2,3-b]pyridine 3ag. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.44; colorless liquid; yield 35% (35 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 4.2, 3.0 Hz, 1H), 8.23 (dd, *J* = 8.4, 6.6 Hz, 1H), 7.68 (d, *J* = 6.6 Hz, 2H), 7.56 (s, 1H), 7.54-7.44 (m, 5H), 7.35-7.32 (m, 2H), 7.19-7.15 (m, 5H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.6, 144.1, 138.2, 135.7, 134.6, 134.3, 132.2, 131.7, 129.39, 129.33, 129.2, 128.8, 128.7, 128.4, 127.3, 126.7, 126.3, 122.4, 118.7, 117.1, 116.8 ; FT-IR (neat) 2921, 2854, 1639, 1472, 1420, 1382, 1262, 1106, 1006, 797, 747, 701 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{17}BrN_2Se$: 504.9819, found: 504.9822.



1-(2-((4-Chlorophenyl)selanyl)phenyl)-3-iodo-1*H*-pyrrolo[2,3-b]pyridine 3ah. Analytical TLC on silica gel, 1:10 ethyl acetate/hexane R_f = 0.43; colorless liquid; yield 52% (53 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.73 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.46 (s, 1H), 7.43-7.39 (m, 2H), 7.34-7.31 (m, 1H), 7.22 (d, *J* = 9.0 Hz, 2H), 7.18-7.16 (m, 1H), 7.06 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.7, 144.8, 137.6, 135.6, 134.3, 134.2, 133.0, 132.0, 129.62, 129.60, 129.3, 129.2, 128.7, 127.6, 123.0, 117.5, 56.1; FT-IR (neat) 2921, 2854, 1638, 1504, 1472, 1410, 1312, 1279, 1217, 1088, 1010, 980, 923, 811, 762 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{12}ClIN_2Se$: 510.8977, found: 510.8988.



1-(2-(Phenylsulfinyl)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 4. Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.30; colorless liquid; yield 76% (24 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (dd, *J* = 7.8, 6.6 Hz, 1H), 8.11 (d, *J* = 4.2 Hz, 1H), 7.93 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.70-7.67 (m, 1H), 7.64-7.61 (m, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 6.0 Hz, 1H), 7.18-7.15 (m, 1H), 7.07-7.05 (m, 1H), 7.04 (d, *J* = 4.2 Hz, 4H), 6.65 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.8, 144.0, 143.9, 143.6, 135.1, 132.1, 131.2, 129.6, 129.2, 129.1, 128.9, 128.8, 125.9, 125.6, 120.6, 116.9, 102.1; FT-IR (neat) 2923, 2853, 1638, 1511, 1480, 1420, 1355, 1321, 1276, 1152, 1084, 1037, 957, 892, 797, 746 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{14}N_2OS$: 319.0905, found: 319.0909.



1-(2-(Phenylsulfonyl)phenyl)-1*H*-pyrrolo[2,3-*b*]pyridine 5.

Analytical TLC on silica gel, 1:1 ethyl acetate/hexane R_f = 0.31; colorless liquid; yield 48% (16 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 7.2, 5.4 Hz, 1H), 7.81-7.78 (m, 2H), 7.75-7.70 (m, 2H), 7.52 (d, *J* = 3.6 Hz, 1H), 7.33-7.31 (m, 1H), 7.20 (d, *J* = 6.6 Hz, 2H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.92-6.90 (m, 1H), 6.84 (t, *J* = 7.8 Hz, 2H), 6.61 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.3, 143.2, 140.0, 138.8, 136.4, 134.7, 132.6, 132.2, 132.1, 129.7, 129.4, 128.6, 128.1, 127.1, 120.3, 116.5, 101.0; FT-IR (neat) 2923, 2851, 1638, 1510, 1483, 1442, 1418, 1355, 1316, 1278, 1154, 1089, 797, 746, 712 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{14}N_2O_2S$: 335.0854, found: 335.0855.

Crystal Data of 3g at 293(2) K

Identification code	**3g**
Empirical formula	$C_{19}H_{13}ClN_2S$
Formula weight	336.82
Crystal habit, color	Block / colorless
Crystal size, mm^3	0.33 x 0.21 x 0.11
Temperature, T/K	293(2)
Wavelength, λ/Å	0.71073
Crystal system	monoclinic
Space group	'P 21'
Unit cell dimensions	a = 8.9598(16) Å
	b = 7.6639(13) Å
	c = 11.869(2) Å
	$\alpha = \gamma = 90.00°$
	$\beta = 91.440(2)°$
Volume, V/Å^3	814.8(2)
Z	2

Calculated density, $Mg \cdot m^{-3}$	1.373
Absorption coefficient, μ/mm^{-1}	0.362
F(000)	348
θ range for data collection	3.16 to 25.00°
Limiting indices	$-10 \leq h \leq 10, -9 \leq k \leq 9, -14 \leq l \leq 14$
Reflection collected / unique	19466/ 2648 [R(int) = 0.0268]
Completeness to θ	99.70 % (θ = 25.00°)
Max. and min. transmission	0.961 and 0.913
Refinement method	SHELXL-97 (Sheldrick, 1997)'
Data / restraints / parameters	2858/1/ 209
Goodness–of–fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0271, wR2 = 0.0693
R indices (all data)	R1 = 0.0299, wR2 = 0.0713

4.5 References

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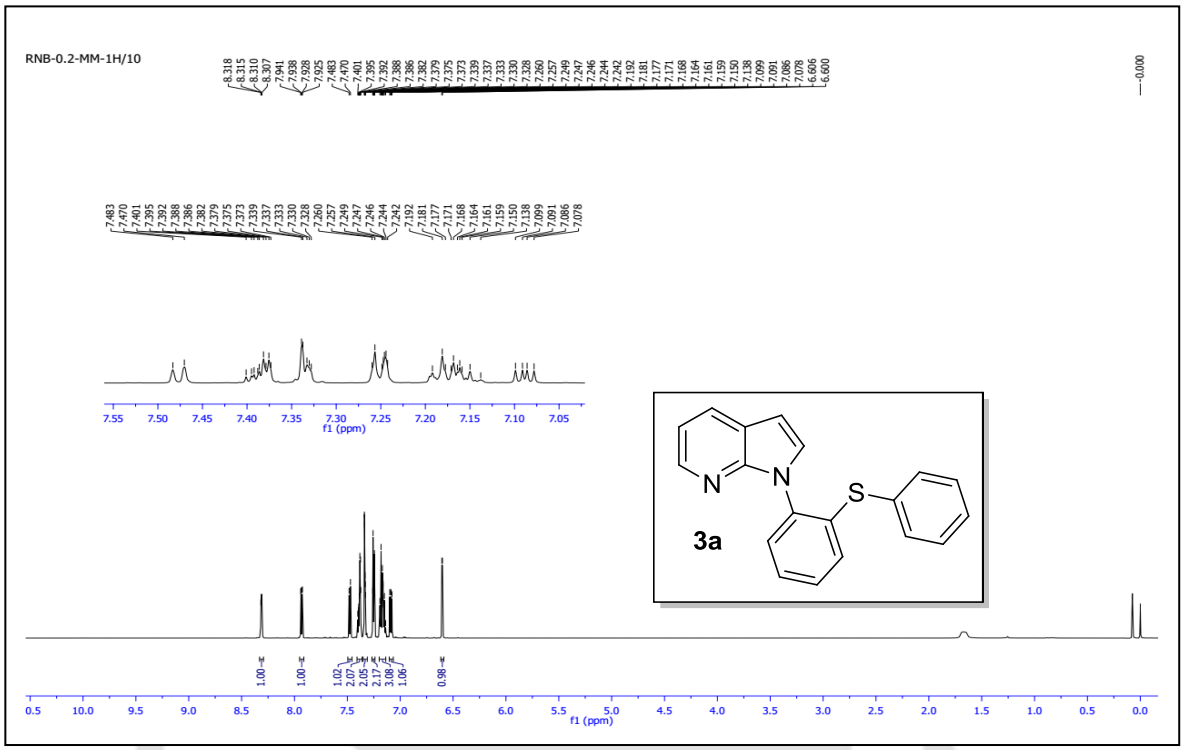
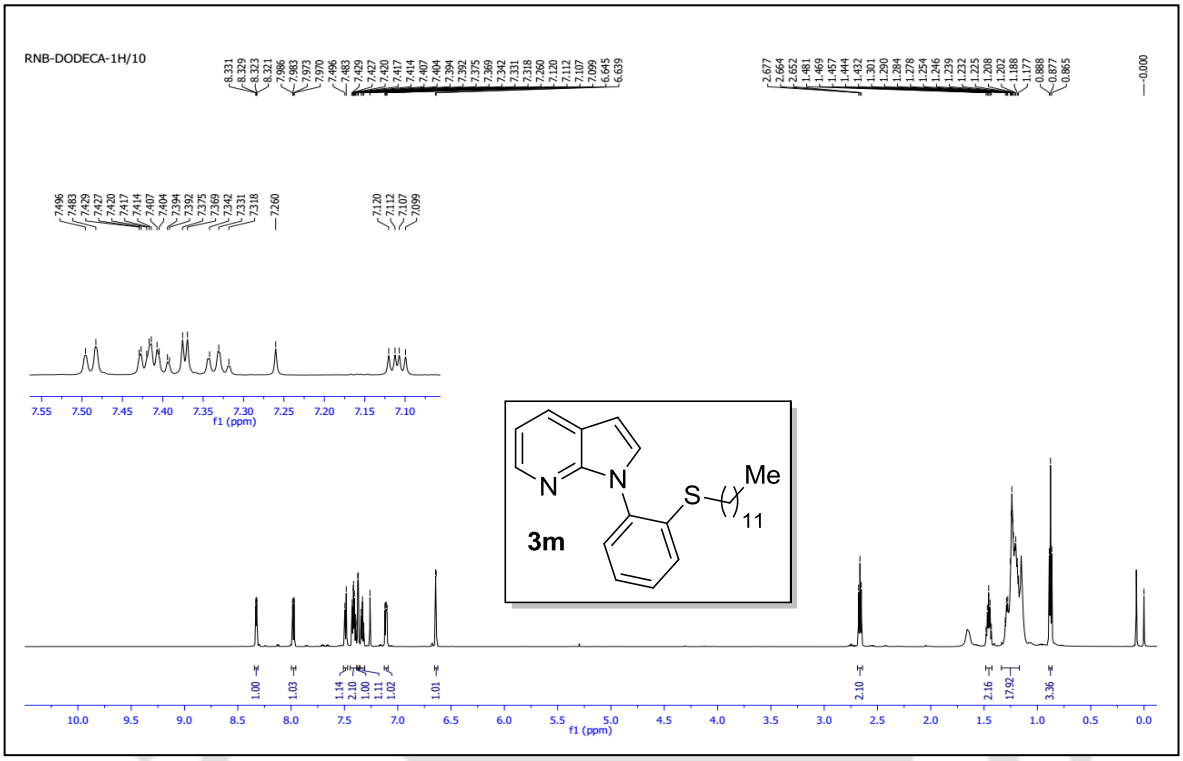
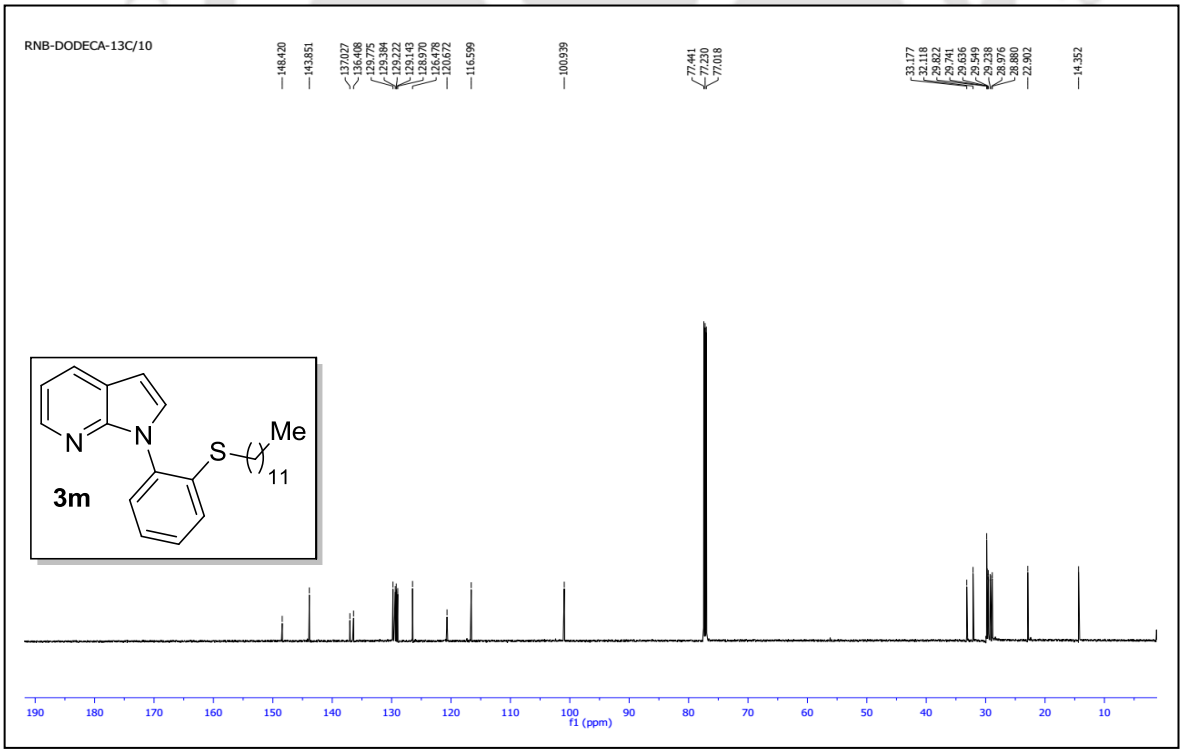
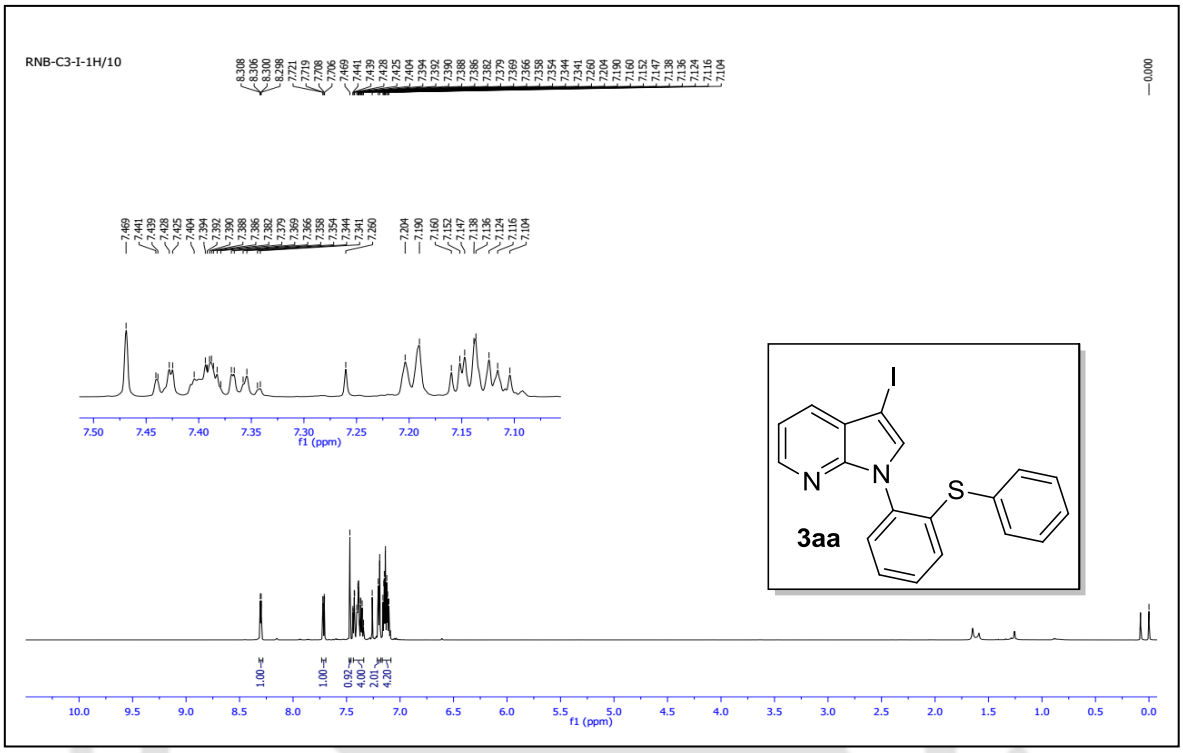
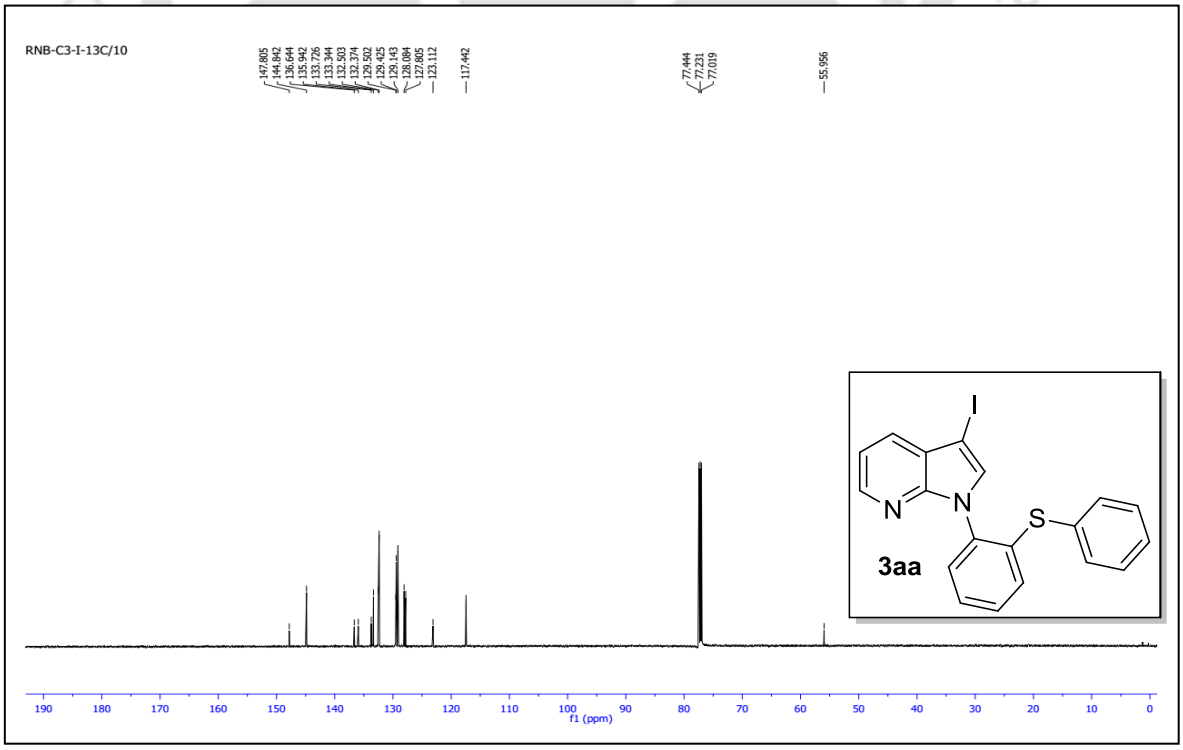
4.6 Selected NMR Spectra

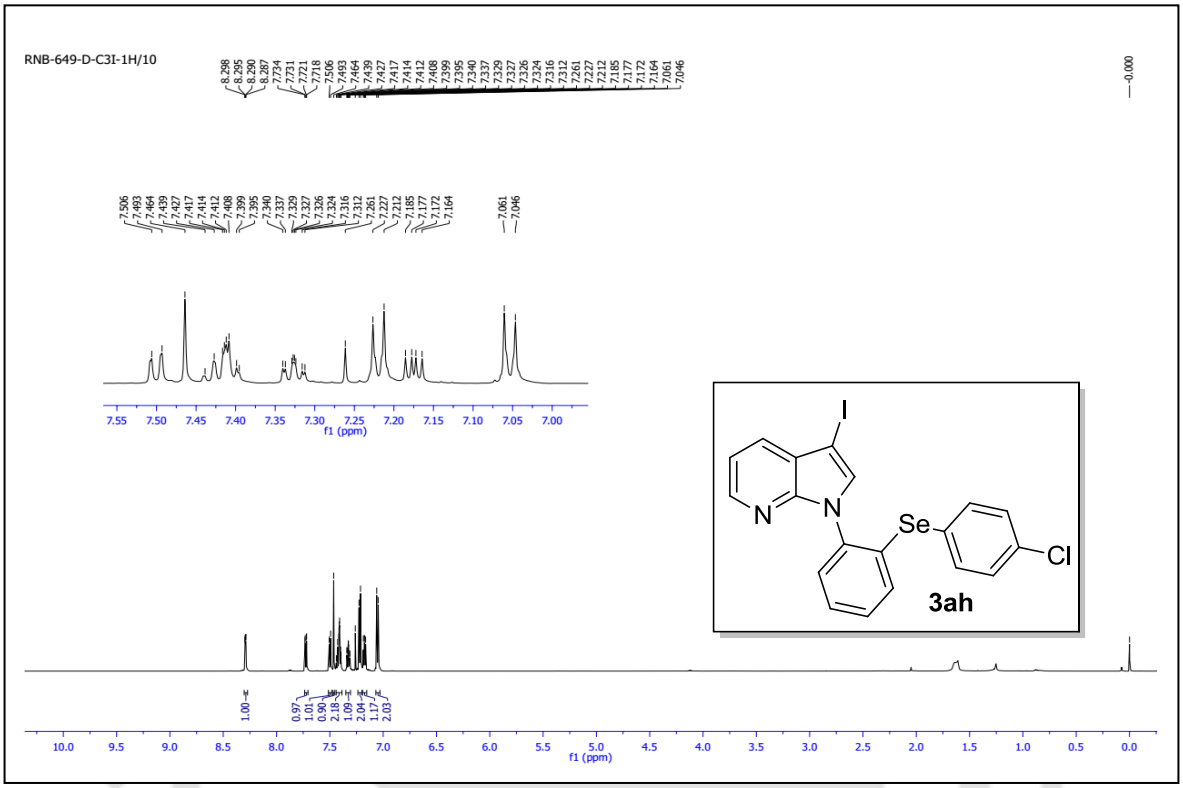


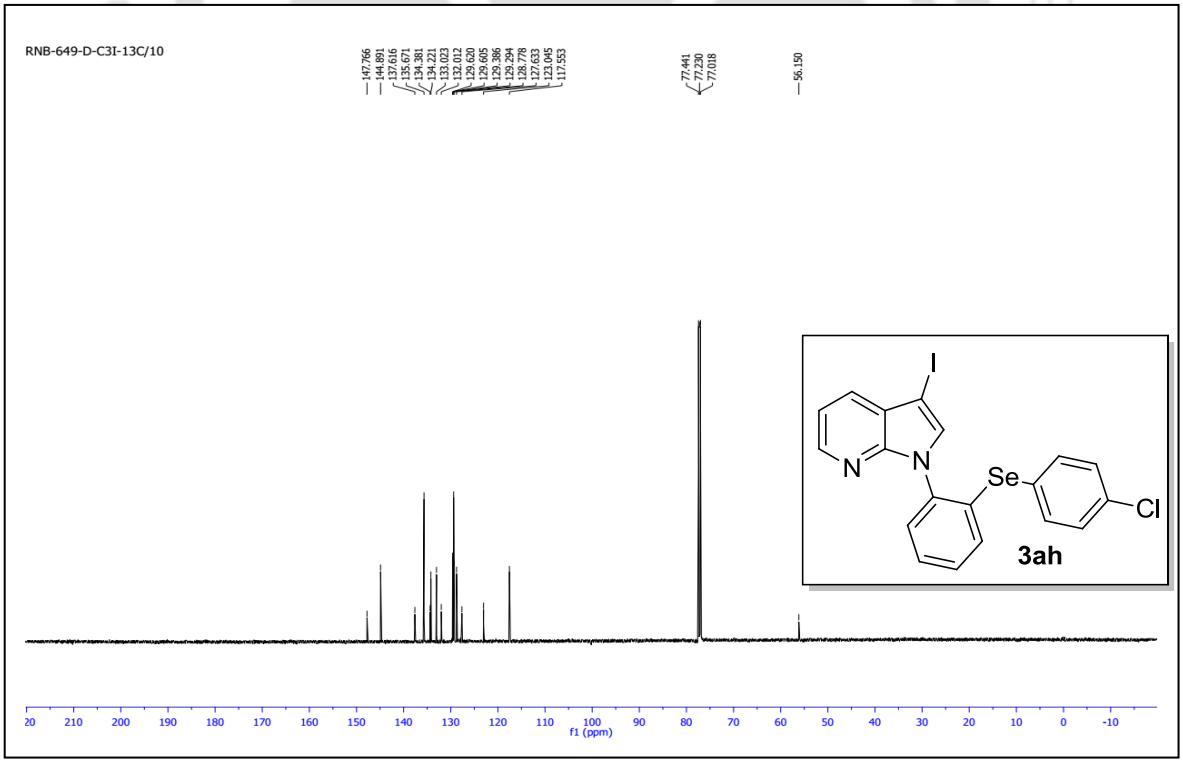


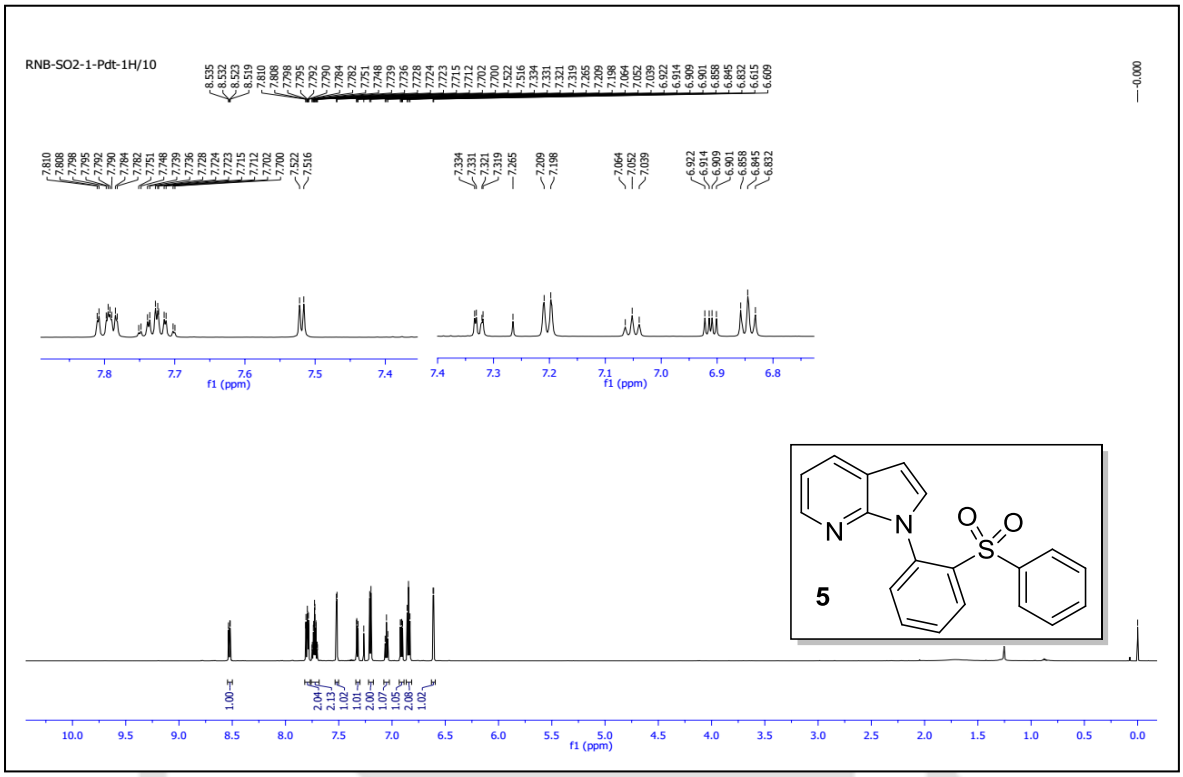


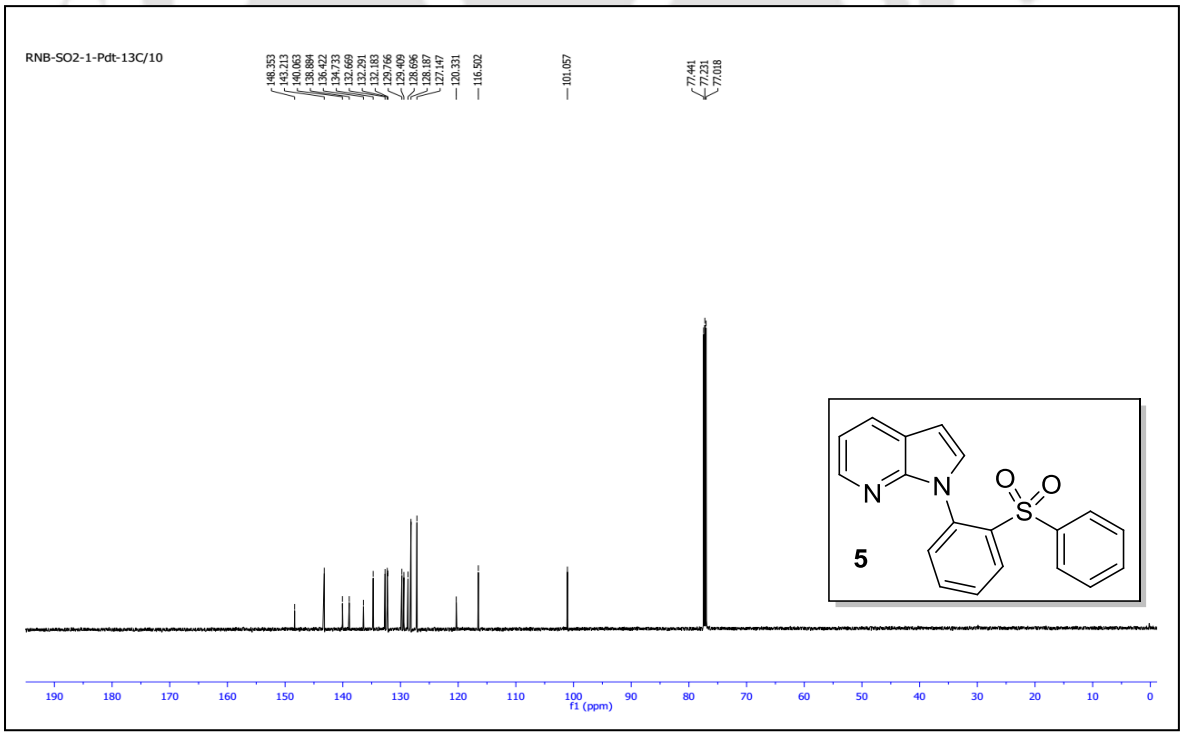












Conclusions

In chapter 1, copper-catalyzed direct dioxygenation of alkenes with NHPI is described to synthesis of *β*-keto-*N*-alkoxyphthalimides employing molecular oxygen from air as the sole oxidant. The reaction is simple and tolerates an array of functionalities with broad substrate scope. Isotope labeling experiment suggests that the source of the ketonic oxygen atom is atmospheric oxygen from air.

In chapter 2, iron-catalyzed dioxygenation of alkenes with NHPI and HOBt is presented to furnish *N*-(*β*-hydroperoxyalkoxy)amines at room temperature. This protocol is applicable for the synthesis of hydroxy compounds and vicinal diols in good yields. The use of molecular oxygen from air as terminal oxidant makes this protocol synthetically potential and attractive.

In chapter 3, a metal-free synthesis of organic nitrate esters from the reaction of alkenes NHPI, NHSI and HOBt with *t*BuONO has been described under air at room temperature. The reaction proceeds through a radical pathway to provide a series of nitrate esters in moderate to good yields. Metal-free condition, greater reactivity, functional group diversity and the use of air as eco-friendly oxidant are the important practical features.

In chapter 4, BINOL enabled ruthenium-catalyzed 7-azaindole directed *ortho*-selective C-H chalcogenation of arenes with disulfides and diselenides has been presented. This reaction provides an effective route for the synthesis of *ortho*-chalcogenated compounds. The mechanistic studies suggest that the reaction may not involve a radical pathway and C-H activation may be the rate-determining step.

List of Publications

1 Copper(II)-Catalyzed Direct Dioxygenation of Alkenes with Air and *N*-Hydroxyphthalimide: Synthesis of *β*-Keto-*N*-Alkoxyphthalimides

Bag, R.; Sar, D.; Punniyamurthy, T. *Org. Lett.* **2015**, *17*, 2010.

2 Iron(III)-Catalyzed Aerobic Dioxygenation of Styrenes using *N*-Hydroxyphthalimide and *N*-Hydroxybenzotriazole

Bag, R.; Sar, D.; Punniyamurthy, T. *Org. Biomol. Chem.* **2016**, *14*, 3246.

3 Recent Advances in Radical Dioxygenation of Olefins

Bag, **R**.; De, P. B.; Pradhan, S.; Punniyamurthy, T. *Eur. J. Org. Chem*. **2017**, 5424.

4 Aerobic Metal-Free Dioxygenation of Alkenes with *tert*-Butyl Nitrite and *N*-Hydroxylamines

Bag, **R**.; Sar, D.; Punniyamurthy, T. *ACS Omega* **2017**, *2*, 6278.

5 $K_2S_2O_8$- Mediated Dioxygenation of Aryl Alkenes using *N*- Hydroxylamines and Air

Bag, R.; Punniyamurthy, T. *ChemistrySelect* **2018**, *3*, 6152.

6 Ruthenium(II)-Catalyzed Regioselective C-H Chalcogenation of 7-Azaindoles with Disulfides and Diselenides

Bag, **R**.; Sarkar, T.; Punniyamurthy, T. (manuscript Submitted).

7 Iron(III)-Mediated Radical Nitration of Bisarylsulfonyl Hydrazones: Synthesis of Bisarylnitromethyl Sulfones

Sar, D.; **Bag**, **R**.; Bhattacharjee, D.; Deka, R. C.; Punniyamurthy, T. *J. Org. Chem*. **2015**, *80*, 6776.

8 Synthesis of Functionalized Pyrazoles *via* Vanadium-Catalyzed C-N Dehydrogenative Cross-Coupling and Fluorescence Switch-On Sensing of BSA Protein

Sar, D.; **Bag, R**.; Yashmeen, A.; Bag, S. S.; Punniyamurthy, T. *Org. Lett*. **2015**, *15*, 5308.

Conferences

1 Copper(II)-Catalyzed Direct Aerobic Dioxygenation of Alkenes with *N*-Hydroxyphthalimide: Synthesis of *β*-Keto-*N*-Alkoxyphthalimides. **Bag, R**.; Sar, D.; Punniyamurthy, T. 11th J-NOST Conference organized by NISER Bhubaneswar, December 14-17, 2015.

2 Direct Aerobic Dioxygenation of Alkenes with *N*-Hydroxyphthalimide (NHPI) and *N*-Hydroxybenzotriazole (HOBt). **Bag, R**.; Sar, D.; Punniyamurthy, T. 21st International Conference on Organic Synthesis held by IIT Bombay, December 11-16, 2016.

3 Aerobic Dioxygenation of Alkenes with *N*-Hydroxyphthalimide (NHPI) and *N*-Hydroxybenzotriazole (HOBt). **Bag, R**.; Sar, D.; Punniyamurthy, T. 20th CRSI National Symposium in Chemistry organized by Guwahati University, February 3-5, 2016.

4 Direct Dioxygenation of Alkenes with *N*-Hydroxyphthalimide (NHPI) and *N*-Hydroxybenzotriazole (HOBt) under Air. **Bag, R**.; Sar, D.; Punniyamurthy, T. Research Conclave'17 held by IIT Guwahati, March 16-19, 2017.

5 Novel Metal-Free Dioxygenation of Alkenes with *tert*-Butyl Nitrite and *N*-Hydroxylamines using Air. **Bag, R**.; Sar, D.; Punniyamurthy, T. International Conference on Chemistry for Human Development (ICCHD-2018) organized by Professor Asima Chatterjee Foundation, January 8-10, 2018.