Carbon–Carbon, Carbon–Oxygen, or Carbon–Nitrogen Bond Formation via 3,3- or 1,3-Rearrangements of *O*-Vinyl

BY

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THESIS

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LIST OF ABBREVIATION

Å	Angstrom
Ac	Acetyl
acac	acetylacetone
AIBN	azobisisobutyronitrile
Alk	alkyl
aq	aqueous
Ar	aryl
atm	atmosphere
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
bipy	2,2'-Bipyridine
Bn	benzyl
Boc	*tert*-butoxycarbonyl
BQ	1,4-benzoquinone
brs	Broad singlet
Bu	butyl
n-Bu	butyl
t-Bu	*tert*-butyl
Bz	benzoyl
Calcd.	calculated
cat.	catalytic amount
Cod	1,5-cyclooctadiene
COSY	correlation spectroscopy
cp	Cyclopentadienyl

LIST OF ABBREVIATION (continued)

Cy	cyclohexyl
d	doublet
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
δ	chemical shifts in parts per million downfield from tetramethylsilane (NMR)
DEPT	distortionless enhancement by polarization transfer
dien	Diethylenetriamine
DMA	dimethylacetamide
DMAP	4-Dimethylaminopyridine
DME	Methyl ether;
dme	1,2-dimethoxyethane
DMF	*N*-*N*-dimethylformamide
DMFDMA	dimethylformamide dimethyl acetal
DMSO	dimethylsulfoxide
dppb	1,1'-bis(diphenylphosphino)butane
dppe	1,1'-bis(diphenylphosphino)ethane
dppf	1,1'- bis(diphenylphosphanyl) ferrocene
dppm	1,1'-bis(diphenylphosphino)methane
EDG	electron-donating group
EI	electron impact ionization (in mass spectrometry)
en	ethylenediamine
enp	*N*,*N'*-bis(α-methylpyrrol)- *N*,*N'*-dimethyl-1,2-ethylenediamine

LIST OF ABBREVIATION (continued)

equiv.	molar equivalent
ESI	Electrospray ionization
Et	ethyl
EWG	electron-withdrawing group
h	hour
Hex	hexyl
hex	hextet (NMR)
HMBC	Heteronuclear multiple-bond correlation spectroscopy
HMPA	Hexamethylphosphoramide
HMQC	heteronuclear multiple-quantum coherence spectroscopy (NMR)
HRMS	high-resolution mass spectrometry
Hz	Hertz
i-	iso
IR	infrared
J	spin-spin coupling constant (NMR)
KIE	kinetic isotope effect
L	ligand
LAH	Lithium aluminium hydride
LDA	lithium diisopropyl amide
m	multiplet (NMR)
m-	meta
μ	micro
[M]	metal

LIST OF ABBREVIATION (continued)

M	molar
mCPBA	*meta*-Chloroperoxybenzoic acid
Me	Methyl
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mmol	millimole
mol	mole
mp	melting point
MS	mass spectrometry
MS	molecular sieves
m/z	mass to charge ratio
n-	normal
nm	nanometer
NMP	*N*-methyl-2-pyrrolidinone
NMR	nuclear magnetic resonance
NOESY	Nuclear Overhauser effect spectroscopy
o-	ortho
p-	para
Ph	phenyl
phen	1,10-Phenanthroline
Phth	phthalyl

LIST OF ABBREVIATION (continued)

Piv	pivaloyl
PMP	*para*-methoxyphenyl
Pr	propyl
i-Pr	isopropyl
n-Pr	propyl
PSI	pounds per square inch
Py	pyridine
q	quartet (NMR)
quant.	quantitative
quint	quintet (NMR)
rt	room temperature
s	singlet (NMR)
S_EAr	electrophilic aromatic substitution
sept	septet (NMR)
S_N2	bimolecular nucleophilic substitution
t	triplet (NMR)
t-	tertiary
terpy	2,2';6',2''-terpyridine
TBS	*tert*-butyldimethylsilyl
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography

LIST OF ABBREVIATION (continued)

TMEDA	Tetramethylethylenediamine
TMS	trimethylsilyl
Tol	tolyl
Ts	*p*-toluenesulfonyl
UV	ultraviolet

SUMMARY

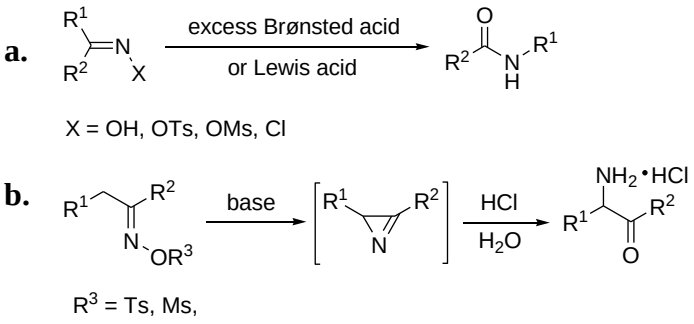
Rearrangements of N–O bonds have been employed in the development of new methods for the preparation highly functionalized molecules. Specifically, [1,3]- and [3,3]-rearrangements of *O*-vinyl oximes and *O*-vinyl hydroxamates have been designed to provide new routes to important synthetic intermediates such as α-oxygenated, α-arylated, and α-aminated ketones as well as privileged medicinally relevant structures such as highly substituted pyrroles and indoles. Two simple routes to *O*-vinyl oximes and *O*-vinyl hydroxamates have been developed through the iridium-catalyzed isomerization of *O*-allyl oxime ethers and the C–O bond coupling of oximes and hydroxamic acids with vinyl boronic acids. These complimentary methods allow for the practical application of the [1,3]- and [3,3]-rearrangements of N–O bonds from simple starting materials. The new processes described in this thesis will promote the development of new retrosynthetic strategies for the preparation of challenging C–C, C–O, and C–N bonds in synthetic targets as well as simplify the preparation of structural derivatives through bypassing the road blocks and limitations of traditional synthetic methods. Mechanistic data has been collected and discussed for all new transformations in order to determine how to further harness and exploit these important new transformations for the relentless demand of new materials and pharmaceutically active compounds.

1 Regioselective Pyrrole Synthesis via Rearrangements of *O*-Vinyl Oximes

1.1 Introduction: Oxime Rearrangements

Oximes are known to undergo a variety of useful synthetic functional group transformations. For example, Beckmann rearrangement allows the transformation from oxime to the amide (Scheme 1a),[1-3] and Neber rearrangement provides the access to the α-amino carbonyl group from the *O*-substituted oxime (Scheme 1b).[1,4] Moreover, the rearrangement of the *O*-substituted oximes also been utilized toward the preparation of heterocyclic products, such as benzofuran and pyrrole.

Scheme 1. Beckmann Rearrangement and Neber Rearrangement



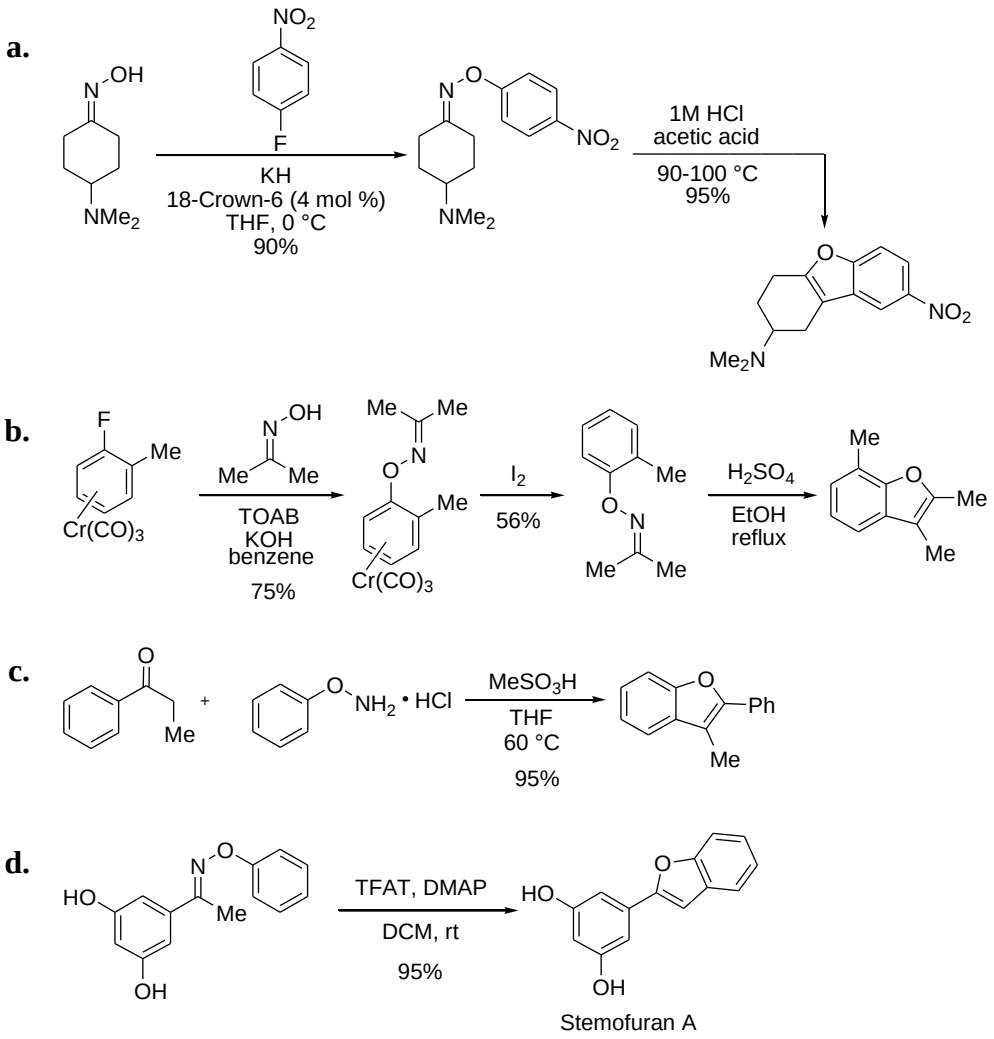
1.1.1 Benzofuran Synthesis via *O*-Aryl Oxime Rearrangements

Benzofurans[5] are crucial motifs in some natural and synthetic heterocyclic products. One of the conventional methods to synthesize benzofurans is through the [3,3]-sigmatropic rearrangement of the *O*-aryl oximes, and these transformation can be promoted by Brønsted or Lewis acids. Generally, the *O*-aryl oximes can be prepared

directly or in situ by the following methods: (1) nucleophilic aromatic substitutions of electron-poor aryl halides with oximes under basic conditions, (2) nucleophilic aromatic substitutions of aryl halides with oximes activated by the tricarbonylchromium complex under basic conditions, or (3) condensation of the corresponding ketones with *O*-aryl hydroxylamines.

Guzzo and coworkers have shown the *O*-aryl oximes can be prepared by the nucleophilic aromatic substitution of oximes to the 1-fluoro-4-nitrobenzene, and which will undergo similar mechanism as the Fischer indole synthesis under acidic condition to give the benzofurans (Scheme 2a).[6] Maiorana and coworkers showed that the *O*-aryl oximes can be synthesized by the nucleophilic aromatic substitution of oximes with aryl halide containing electron-donating group, and which can transform to the benzofuran (Scheme 2b).[7] Tomkinson and coworker show that the in situ preparation of *O*-aryl oximes under the acidic condition gives the formation of benzofuran (Scheme 2c).[8] However, there are some disadvantages of the Brønsted or Lewis acids promoted benzofuran formation. Acid catalysts and high temperature are generally required, and which limit the application of the acid–sensitive substrate. Naito and coworker have shown that the [3,3]-rearrangement can be performed under milder condition using the TFAT and DMAP to trigger the reaction, and it provide an efficient route to the synthesis of the Stemofuran A (Scheme 2d).[9]

Scheme 2. Benzofuran Synthesis via Rearrangement of *O*-Aryl Oximes

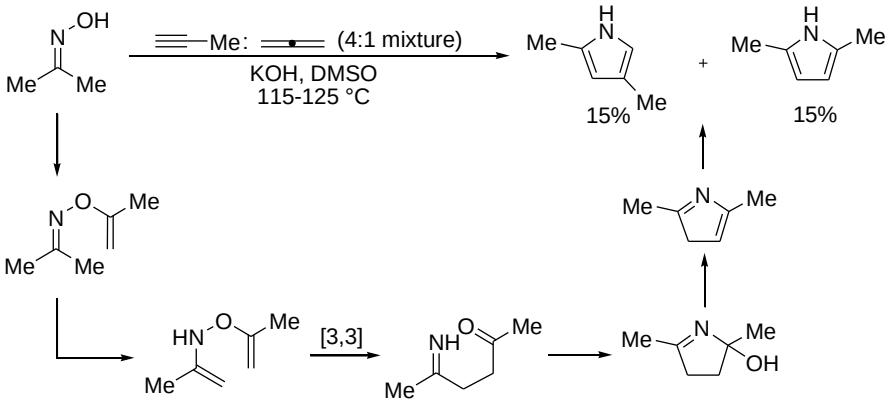


1.1.2 Pyrrole Synthesis via *O*-Vinyl Oxime Rearrangements

Besides the rearrangement of the *O*-aryl oximes to form benzofuran, the rearrangements of *O*-vinyl oximes have also been applied to the synthesis of pyrroles in precedent literatures. Trofimov and coworkers have reported that oximes can be added to acetylenes under strongly basic conditions to form *O*-vinyl oximes which undergo [3,3]-rearrangement to 1,4-imino carbonyl compounds and then participate in

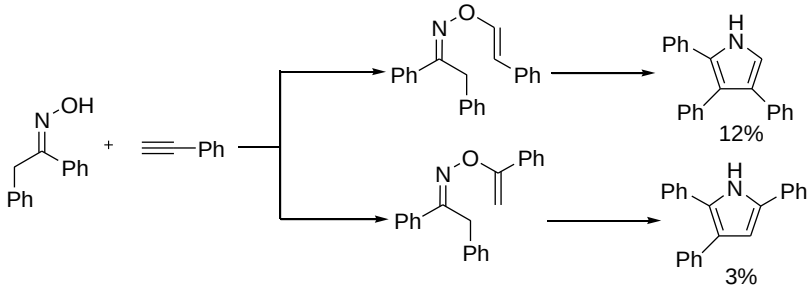
Paal-Knorr cyclization and dehydration sequence to give mixture of pyrrole product (Scheme 3).[10]

Scheme 3. Trofimov Pyrrole Synthesis



However, the Trofimov reaction is limited in scope and efficiency due to the strongly basic conditions and high reaction temperatures which limit the functional group tolerance of this method. Furthermore, the additions of the oximes to the asymmetric acetylenes are not regioselective which lead to mixtures of *O*-vinyl oximes then give mixtures of the pyrroles which lower the yield and the efficiency of this method (Scheme 4).[11]

Scheme 4. Limitations of the Trofimov Reaction

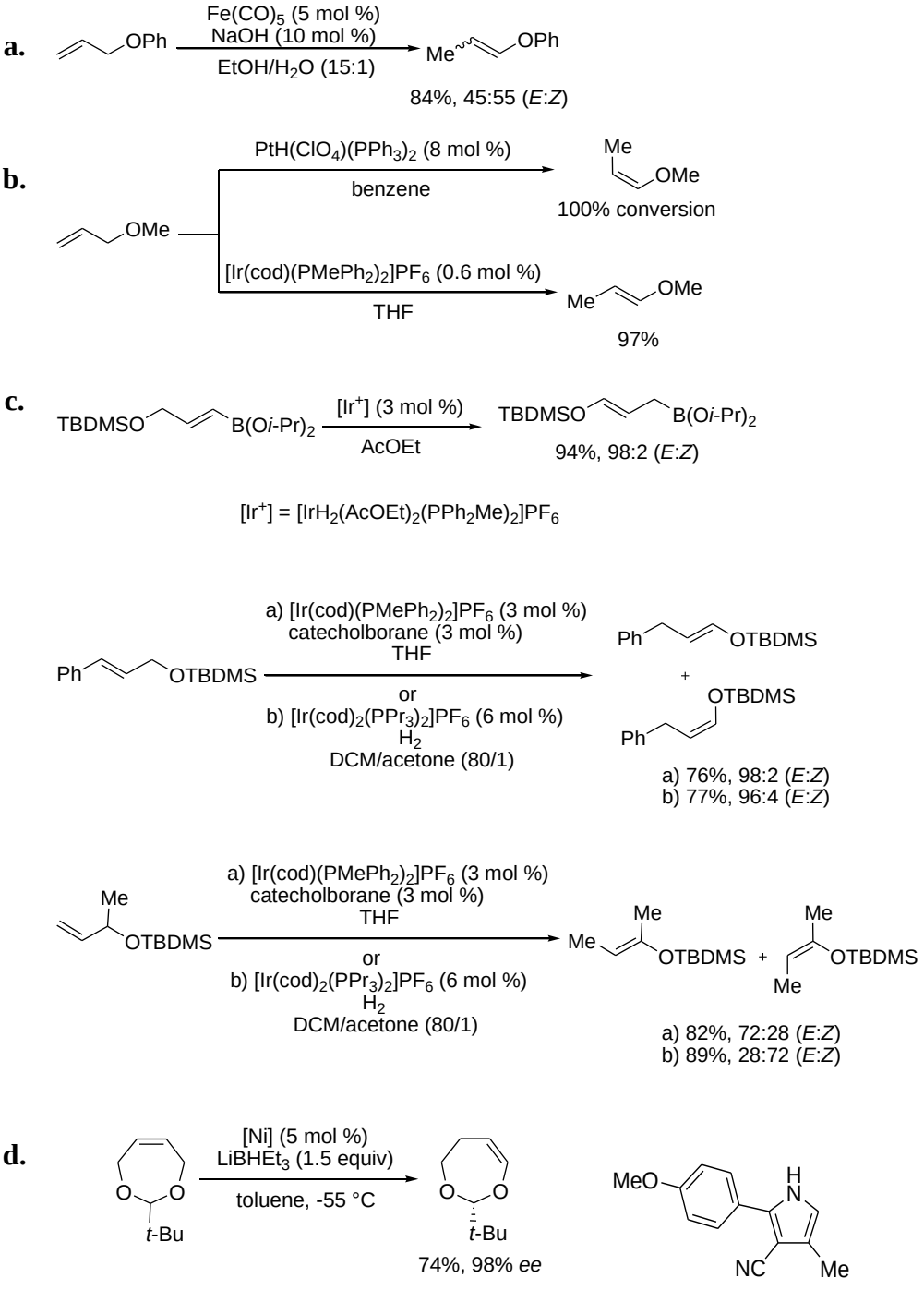


1.2 Preparation of *O*-Vinyl Ethers through Transition Metal-Catalyzed Isomerization of *O*-Allyl Ethers

O-Vinyl ethers have been prepared through the isomerization of *O*-allylic ethers with a variety of transition metal catalysts.

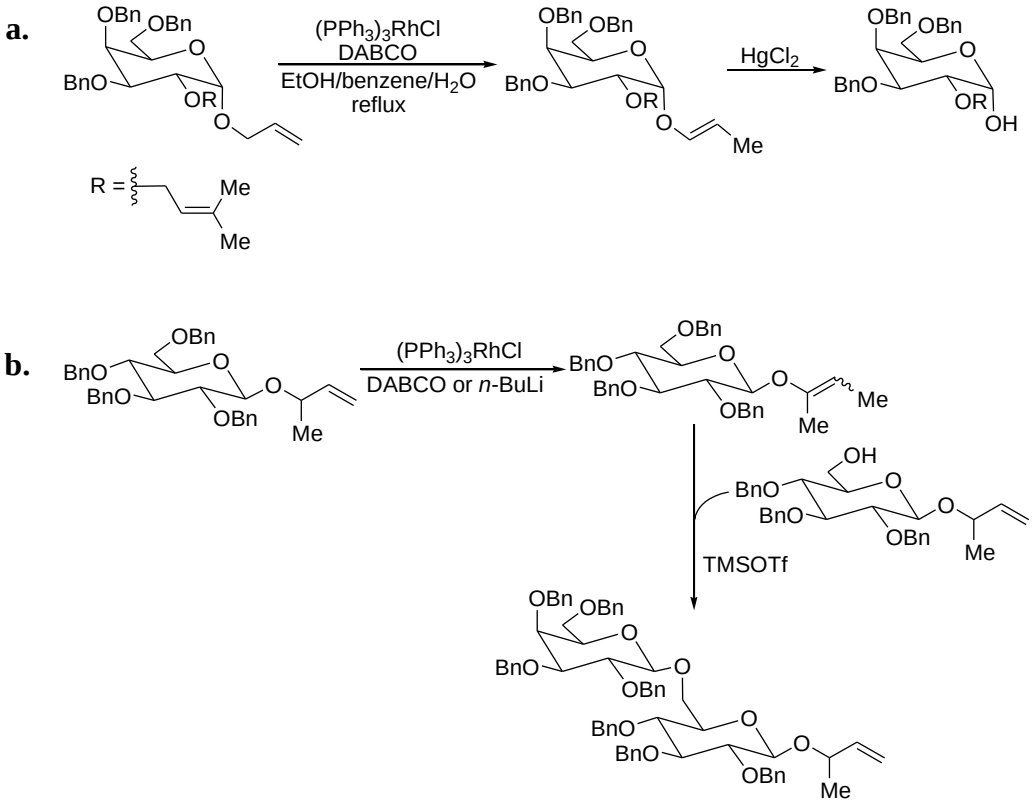
An early example shown by Crivello and coworkers demonstrate that *O*-allyl ethers can be transformed into *O*-vinyl ethers using $Fe(CO)_5$ as catalyst. However, this transformation is not stereoselective and gives 1:1 ratio of *E*:*Z* isomers (Scheme 5a).[12] Clark and Ephritikh have shown the isomerization can be performed in a stereoselective fashion by treating with a platinium-hydride complex or a cationic iridium catalyst to give either the *Z* or *E* isomers, respectively (Scheme 5b).[13] Miyaura and coworkers show several examples of an *O*-allyl silyl ether isomerization by a cationic iridium catalyst. Disubstituted and trisubstituted olefins can be transformed to the corresponding silyl enol ethers efficiently and stereoselectively (Scheme 5c).[14] Frauenrath has shown that transition-metals can also apply to the asymmetric isomerization of acetal species employing the chiral nickel complex as the catalyst (Scheme 5d).[15]

Scheme 5. Transition Metal-Catalyzed Allylic Ether Isomerizations



O-Allylic ethers can sometimes be used as a protecting group for a hydroxyl group. Transition metal-catalyzed isomerization of the *O*-allylic ether to *O*-vinyl ether followed by treating the mercury salt or acid serves as the deprotecting procedure to recover free hydroxyl group. This synthetic strategy was widely used in the carbohydrate synthesis since late 70s (Scheme 6a).[16] Later on, Boons and coworker have shown that the *O*-allyl saccharide can isomerize to *O*-vinyl saccharide by treating with Wilkinson catalyst. The *O*-vinyl saccharide can be an efficient glycosylation acceptor due to it high activity instead of using the common glycosylation acceptor, the *O*-imidate saccharide (Scheme 6b).[17]

Scheme 6. Transition Metal-Catalyzed Isomerizations of Allylic Ether



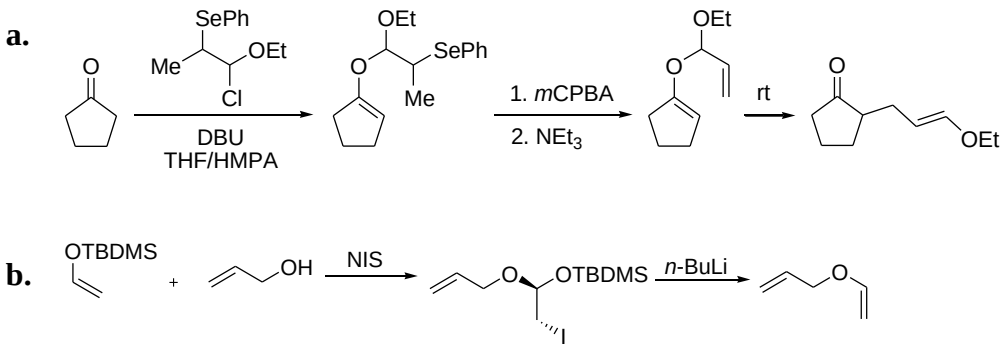
1.2.1 Transformation of *O*-Vinyl Ethers: Claisen Rearrangements and Isomerization Claisen Rearrangements

Claisen rearrangement is a powerful method to form new carbon-carbon bond and introduce complexity to a molecule. It recognizes the structure of allyl *O*-vinyl ether which undergoes stereoselectively [3,3]-sigmatropic rearrangement to give gamma-delta unsaturated carbonyl compounds which contain two potential stereogenic centers (Scheme 7).

Scheme 7. Claisen Rearrangements

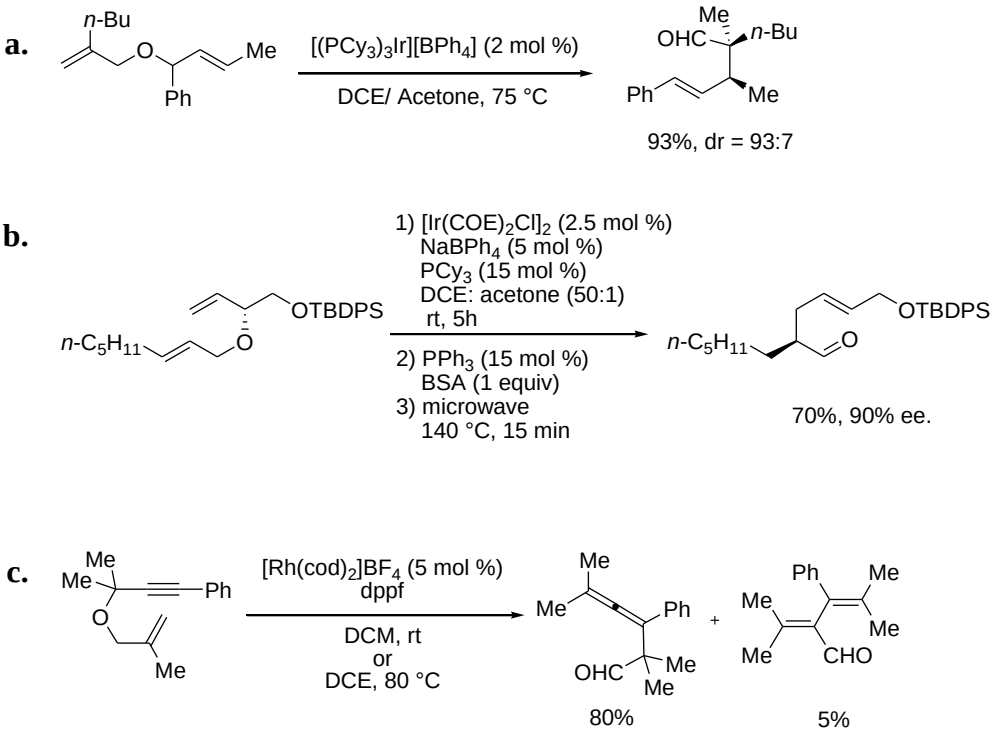
The preparation of allyl *O*-vinyl ether is usually through the elimination reaction. A selenoxide elimination reaction has been demonstrated by Curran to afford allyl *O*-vinyl ether which undergoes Claisen rearrangement at room temperature (Scheme 8a).[18] Nucleophilic attack of allylic alcohol to the silyl iodonium intermediate followed by base mediated elimination has also shown to gives the allyl *O*-vinyl ether motif (Scheme 8b).[19] However, the preparation of the allyl *O*-vinyl can be challenged sometimes due to its high reactivity and time consuming due to the multiple-steps transformation.

Scheme 8. Allylic *O*-Vinyl Ether Preparation through Elimination Reactions



Nelson and coworkers have demonstrated that 1,1-disubstituted olefins isomerize to allyl *O*-vinyl ethers which undergo subsequent Claisen rearrangements to give unsaturated aldehyde by employing a cationic iridium catalyst (Scheme 9a).[20] Trost group has also shown that chemoselective isomerizations of 1,2-disubstituted olefins to *O*-vinyl ethers followed by Claisen rearrangement can be an efficient way to synthesize enantioenriched α-substituted aldehydes by using $[(coe)_2IrCl]_2$ as catalyst (Scheme 9b).[21] A Rhodium catalyzed isomerization/ propargyl Claisen rearrangement reaction has also shown by Tanaka and coworkers to give the transformation of allyl propargyl ethers to allenic aldehydes (Scheme 9c).[22]

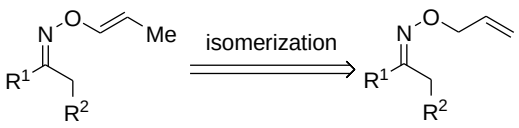
Scheme 9. Isomerization-Claisen Rearrangements



1.3 Preparation of *O*-Vinyl Oximes: Iridium-Catalyzed Isomerization of *O*-Allyl Oximes

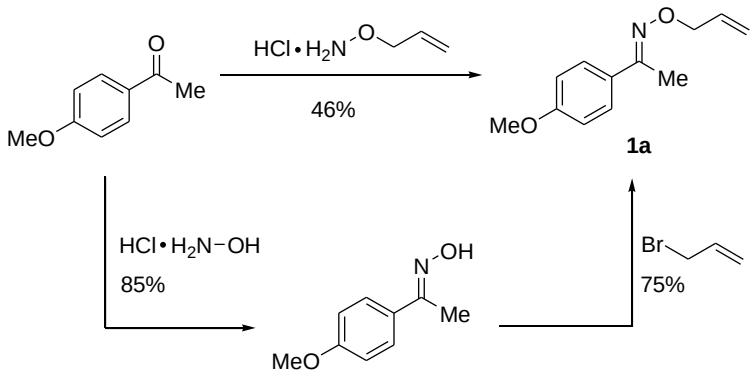
Under the inspiration of the transition metal-catalyzed isomerization reaction shown above, it seems like that the isomerization of the *O*-allyl oximes might be a reasonable pathway to access the *O*-vinyl oximes, the first key intermediate of the Trofimov reaction, and further achieve the intention of pyrrole formation (Scheme 10).

Scheme 10. Proposed Pathway for the Synthesis of *O*-Vinyl Oximes



The *O*-allyl oximes **1a** could be easily prepared by condensation of the *O*-allyl hydroxylamine hydrochloride with the commercial available 4-OMe-acetophenone at room temperature.[23] An alternative pathway to prepare **1a** was through S_N2 reaction of allylbromide and oxime which can be obtained from the condensation of the hydroxylamine hydrochloride with the 4-OMe-acetophenone ketone (Scheme 11).

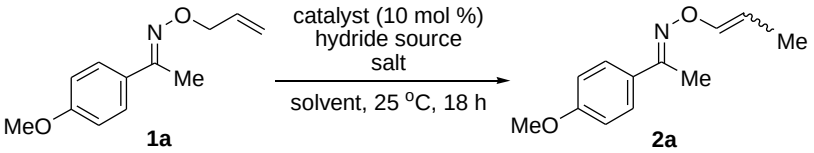
Scheme 11. Preparation of *O*-Allyl Oxime 1a



O-Allyl-4-methoxy acetopheone oxime was chosen as the starting material to perform the isomerization reaction in presence of catalytic amount of Wilkinson catalyst and *n*-BuLi (Table 1, entry 1). However, it gave no formation of the desired *O*-vinyl oximes product. We also obtained no positive result by using $[(coe)_2IrCl]_2$ as the catalyst which shown successful isomerization transformation in the work

demonstrated by Trost and coworkers (Table 1, entries 3,4,6). After trying some common Rh(I) and Ir(I) catalyst and modifying several isomerization reaction condition in literatures by changing the hydride source, salt, and solvent, we found the conversion of the *O*-allyl oxime to the *O*-vinyl oxime was able to be achieved by treating a 1:2:2 mixture of $[(cod)IrCl]_2$,[24,25] $NaBH_4$ or $LiAlH_4$, and AgOTF in THF at 25 ℃ (Table 1, entries 5,9) gave the highest yields of the *O*-vinyl oxime as mixture of *E*/*Z* isomers in 1:2 ratio. A mixture of 5 mol % $[(cod)IrCl]_2$, 10 mol % $LiAlH_4$ or $NaBH_4$, and 10 mol % AgOTF in THF was determined to be the optimal condition. With the optimal conditions in hand, a variety of *O*-vinyl oximes were synthesized from the corresponding *O*-allyl oximes in moderate to excellent yields using the isomerization conditions determined in Table 1. Both electron-poor and electron-rich aryl *O*-allyl oximes were tolerated under the isomerization condition (Table 2, entries 1-7). α-Substituted acetophenone-derived *O*-allyl oximes were also adequate substrates for optimal condition (Table 2, entries 8-11). Heterocyclic *O*-allyl oximes were also tolerated this isomerization condition (Table 2, entries 12-14).

Table 1. Optimization of *O*-Allyl Oxime Isomerization



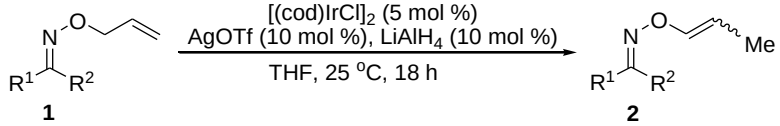
(*E*:*Z* = 1:2.4)

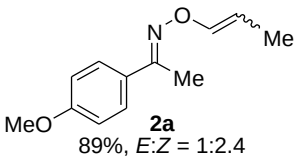
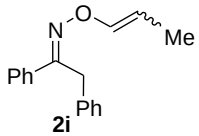
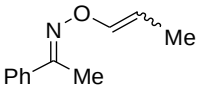
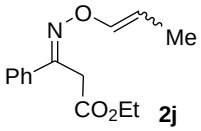
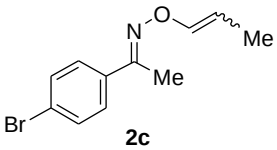
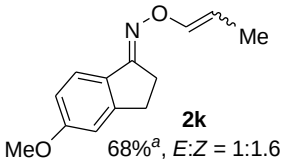
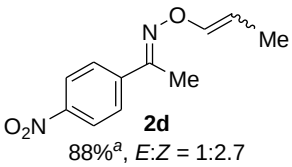
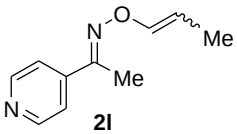
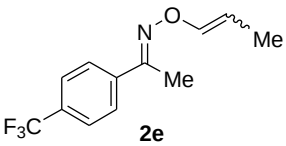
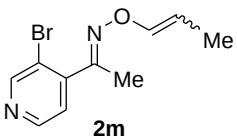
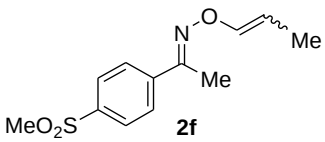
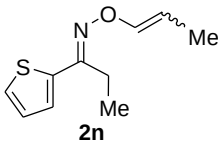
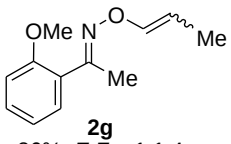
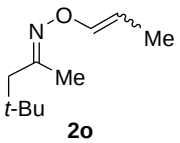
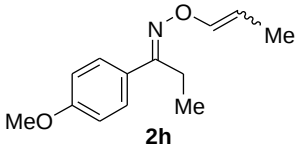
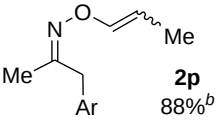
Entry	L_2MX (X equiv)	Hydride Source	Salt	Solvent	Yield[a] (%)
1	$(Ph_3P)_3RhCl$ (1)	*n*-BuLi[b]	none	THF	NR
2	$(Ph_3P)_3RhCl$ (1)	none	none	EtOH	NR
3	$[(coe)_2IrCl]_2$/2PCy_3 (0.5)	none	$AgPF_6$	THF	NR
4	$[(coe)_2IrCl]_2$/2PCy_3 (0.5)	none	$AgPF_6$	DCE/acetone	NR
5	**$[(cod)IrCl]_2$ (0.5)**	**$NaBH_4$**	**AgOTf**	**THF**	**85**
6	$[(coe)_2IrCl]_2$ (0.5)	$NaBH_4$	AgOTf	THF	53
7	$(cod)_2RhBF_4$ (1)	$NaBH_4$	AgOTf	THF	30
8	$[(coe)_2RhCl]_2$ (0.5)	$NaBH_4$	AgOTf	THF	NR
9	**$[(cod)IrCl]_2$ (0.5)**	**$LiAlH_4$**	**AgOTf**	**THF**	**89**
10	$[(cod)IrCl]_2$ (0.5)	DIBAL	AgOTf	THF	71
11	$[(cod)IrCl]_2$ (0.5)	$LiHBEt_3$	AgOTf	THF	64
12	$[(cod)IrCl]_2$ (0.5)	KH	AgOTf	THF	61
13	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	$AgSbF_6$	THF	71
14	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	$AgBF_4$	THF	58
15	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	none	THF	76
16	$[(cod)IrCl]_2$/2 PPh_3 (0.5)	$NaBH_4$	AgOTf	THF	NR
17	$[(cod)IrCl]_2$/dppf (0.5)	$NaBH_4$	AgOTf	THF	NR
18	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	AgOTf	CH_3NC	95
19	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	AgOTf	IPAc	77
20	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	AgOTf	C_6H_6	64
21	$[(cod)IrCl]_2$ (0.5)	$NaBH_4$	AgOTf	DCE	0

[a] Determined by using ^1H NMR spectroscopy with CH_2Br_2 as a reference.

[b] *n*-BuLi was served as an *in situ* hydride source through β-H elimination.

Table 2. Scope of Iridium-Catalyzed *O*-Allyl Oxime Isomerization



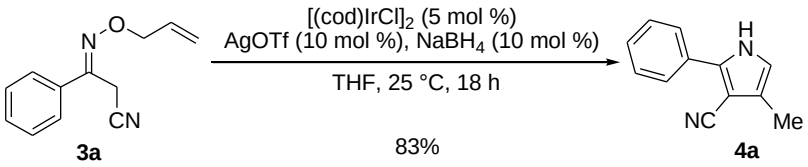
Entry	Product	Entry	Product
1	 **2a** 89%, *E*:*Z* = 1:2.4	9	 **2i** 79%[a], *E*:*Z* = 1:2.3
2	 **2b** 76%, *E*:*Z* = 1:1.7	10	 **2j** 58%[a], *E*:*Z* = 1:2.9
3	 **2c** 77%, *E*:*Z* = 1:2.7	11	 **2k** 68%[a], *E*:*Z* = 1:1.6
4	 **2d** 88%[a], *E*:*Z* = 1:2.7	12	 **2l** 78%[a], *E*:*Z* = 1:1.6
5	 **2e** 78%, *E*:*Z* = 1:3.8	13	 **2m** 79%, *E*:*Z* = 1:2.0
6	 **2f** 82%, *E*:*Z* = 1:2.2	14	 **2n** 77%[a], *E*:*Z* = 1:2.3
7	 **2g** 86%, *E*:*Z* = 1:1.4	15	 **2o** 55%, *E*:*Z* = 1:3.2
8	 **2h** 79%, *E*:*Z* = 1:2.9	16	 **2p** 88%[b] *E*:*Z* = 1:2.7 Ar= *p*-OMEC$_6$H$_4$

[a] $NaBH_4$ was used instead of $LiAlH_4$. [b] DIBAL-H was used instead of $LiAlH_4$.

1.4 Pyrrole Synthesis via the Rearrangement of *O*-Vinyl Oximes

From the result of Table 2, it showed that our iridium isomerization condition was mild, functional group tolerated, and efficient method to prepare *O*-vinyl oximes. While we treating **3a** which containing electron-poor α-substitution under our optimal isomerization condition, it gave the directly formation of the 2,3,4-trisubstituted pyrrole instead of the formation of *O*-vinyl oxime we expected (Scheme 12).

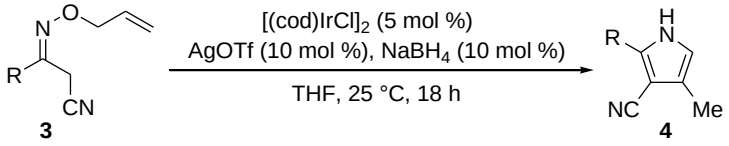
Scheme 12. Observation of 3-Cyano-4-Me-Pyrrole Formation

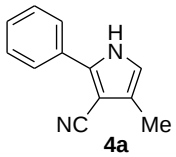
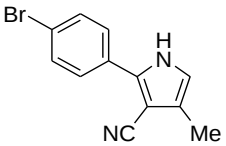
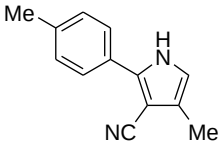
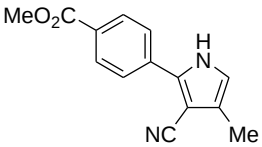
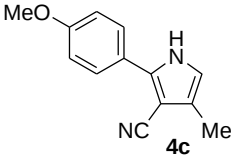
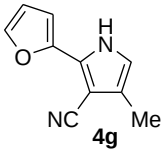
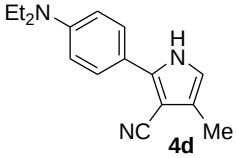
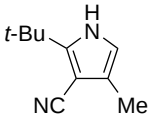


Based on the finding in Scheme 12, we decided to further explore the scope of this transformation, and a variety of analogues of 2,3,4-trisubstituted pyrrole **4a** were synthesized from the corresponding *O*-allyl oximes. Both electron-rich and electron-poor acetophenone cyano-substituted *O*-allyl oximes were tolerated for the Iridium-catalyzed condition to give the corresponding pyrroles (Table 3, entries 2-3,5) but extremely electron-rich or poor give poor transformation of 2,3,4-trisubstituted pyrroles (Table 3, entries 4,6). However, the low yields of entries 4 and 6 in Table 3 might be caused by the coordination of the amine or the ester functional group to the iridium and lower the activity of catalyst but the electronic effect. Heterocyclic

O-allyl oxime was also tolerates the isomerization condition to form the corresponding pyrrole (Table 3, entry 7). Alkyl cyano-substituted *O*-allyl oxime gave poor transformation to the pyrrole, and it might be caused by the electronic destabilized of the *t*-butyl group (Table 3, entry 8).

Table 3. Scope of α-Cyano-*O*-Allyl Oxime Isomerizations

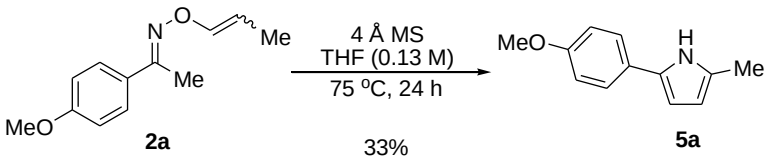


Entry	Product	Entry	Product
1	 **4a** **83%**	5	 **4e** 76%
2	 **4b** 73%	6	 **4f** **30%**
3	 **4c** **74%**	7	 **4g** **64%[a]**
4	 **4d** **48%**	8	 **4h** **24%**

[a] run at 50 ℃. [b] Prepared by Daniel S. Mueller.

O-Vinyl oxime **2a** prepared according to our isomerization condition was tested as precursor to the pyrrole formation by mild heating in the presence of molecular sieves in THF. It gave the conversion of *O*-vinyl oxime to the 2,5-disubstituted pyrrole **5a** in 33% isolated yield (Scheme 13). To be noticed, even though the transformation went well, it, however, gave the different pyrrole regioisomer of the previous one we obtained from the α-CN substituted acetophenone *O*-allyl oxime.

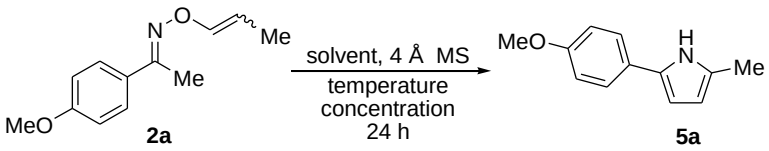
Scheme 13. Obsevation of 5-Me-Pyrrole Formation



Solvent, concentration, and reaction temperature were optimized for the transformation of **2a** to **5a**. Optimization showed polar solvent such as NMP minimized the formation of **5a** (Table 4, entry 6) but *i*-PrOAc and acetonitrile gave moderate transformation (Table 4, entries 3,5). Ethereal solvents gave optimal formation of **5a** (Table 4, entries 4,7). Higher the concentration to 0.27 M or diluted it to 0.07 M gave slightly lower formation of **5a** but the yield dropped dramatically at 0.03 M (Table 4, entries 4,8-10). Higher temperature gave slightly lower yield as well as lower reaction temperature (Table 4, entries 4,11,12). From the results in Table 4, we decided 0.13 M dioxane at 75 ℃ in the presence of molecular sieves was the

optimal condition for the transformation to pyrrole **5a**.

Table 4. Optimization of the Thermal Rearrangement of *O*-Allyl Oximes



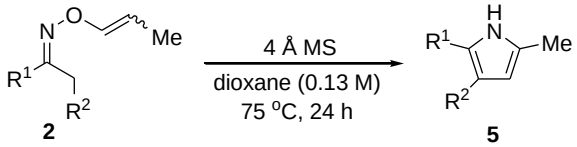
Entry	Solvent	Concentration (M)	Temperature (℃)	Yield (%)[a]
1	THF	0.13	75	33
2	benzene	0.13	75	43
3	acetonitrile	0.13	75	47
4	**dioxane**	**0.13**	**75**	**67**
5	isopropyl acetate	0.13	75	59
6	NMP	0.13	75	17
7	DME	0.13	75	57
8	dioxane	0.27	75	60
9	dioxane	0.07	75	64
10	dioxane	0.03	75	48
11	dioxane	0.13	55	60
12	dioxane	0.13	100	64

[a] Isolate yield

With the optimized condition in hand, a variety of 2,5 or 2,3,5-pyrroles were synthesized from corresponding *O*-vinyl oximes prepared in Table 2. Electron-rich acetophenone *O*-vinyl oximes gave better transformation to the corresponding 2,5-disubstituted pyrroles than the electron-poor *O*-vinyl oximes (Table 5, entries 1-7). It also tolerated the transformation of the α-substituted *O*-vinyl oximes to the corresponding 2,3,5-trisubstituted pyrroles (Table 5, entries 8-11). Heterocyclic *O*-vinyl oximes prepared in Table 2 underwent the conversion to the 2,5-disubstituted

pyrroles as well (Table 5, entries 12-13). However, when the thiophene *O*-vinyl oxime was subjected to the heat, it gave the mixture of the 2,3,5- and 2,3,4-trisubstituted pyrroles in 3 to 1 ratio (Table 5, entry 14). Dialkyl *O*-vinyl oximes **2o** and **2p** were also subjected to this thermal promoted pyrrole formation method. Treating **1o** under the thermal conditions gave **5o** as a single isomer (Table 5, entry 15). Pyrrole **5p** and **5pa** was obtained as a 3 to 1 mixture after treating **2p** under heat (Table 5, entry 16). The formation of the 2,5- and 2,3,5-substituted pyrroles could also be performed using the one-flask conversion from the corresponding *O*-allyl oximes. The *O*-allyl oximes were subjected to the Iridium isomerization condition to transform to *O*-vinyl at room temperature then followed by heating at 75 ℃ (Table 6). These single-flask strategy was particular useful for the preparation of the pyrrole which does not give the full conversion of the *O*-vinyl in the first step of the isomerization (Table 6, entry 6).

Table 5. Scope of *O*-Allyl Oxime Rearrangements under Thermal Condition



2 **5**

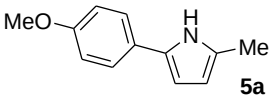
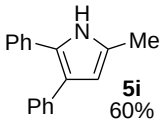
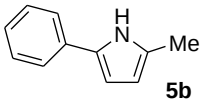
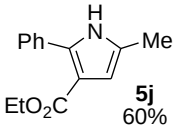
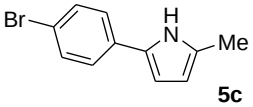
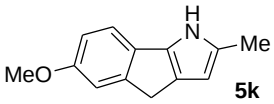
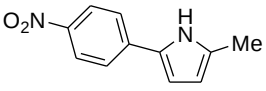
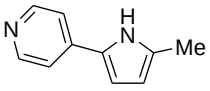
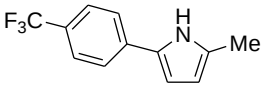
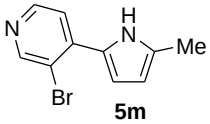
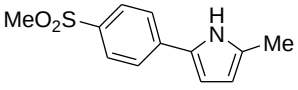
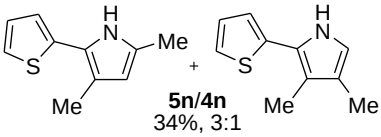
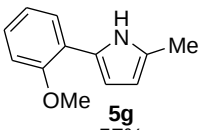
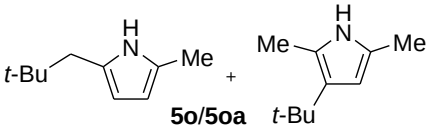
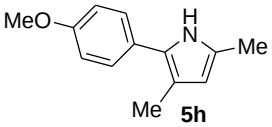
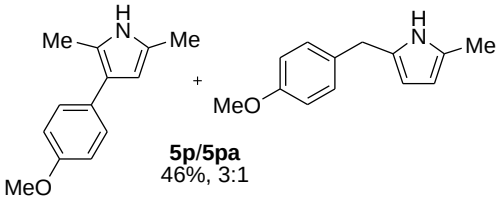
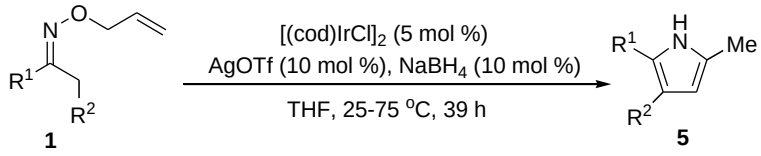
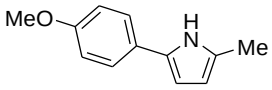
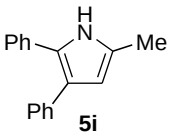
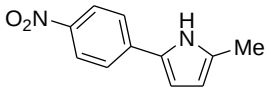
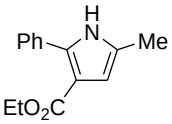
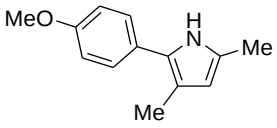
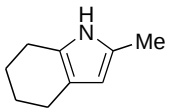
Entry	Product	Entry	Product
1	 **5a** 64%	9	 **5i** 60%
2	 **5b** 58%	10	 **5j** 60%
3	 **5c** 55%	11	 **5k** 32%
4	 **5d** 42%	12	 **5l** 51%
5	 **5e** 46%	13	 **5m** 38%
6	 **5f** **41%**	14	 **5n**/**4n** 34%, 3:1
7	 **5g** 57%	15	 **5o**/**5oa** 73%, >95:5
8	 **5h** 61%	16	 **5p**/**5pa** 46%, 3:1

Table 6. Scope of the Single Flask Conversion of *O*-Allyl Oximes to Pyrroles



1 **5**

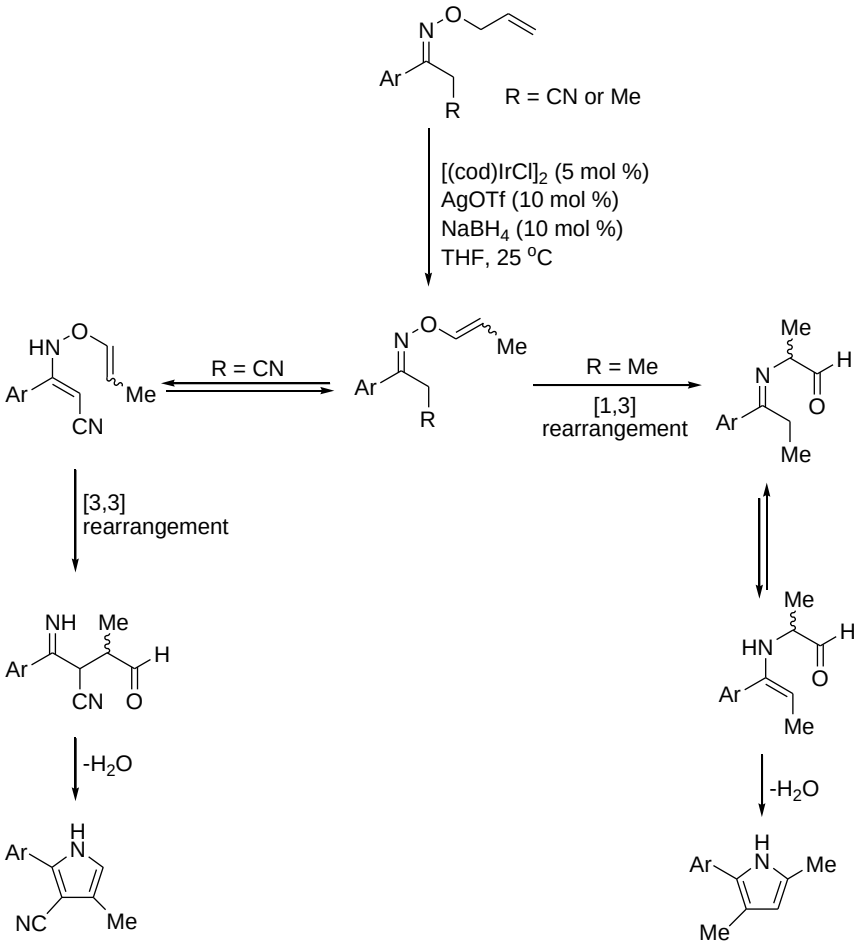
Entry	Product	Entry	Product
1	 **5a** 46%	4	 **5i** 41%
2	 **5d** 46%	5	 **5j** 40%
3	 **5h** 40%	6	 **5q** 42%

1.5 Mechanistic Considerations

From our previous result regarding the formation of two pyrrole regioisomers, we proposed pathway of the formation of the 2,3,4- or the 2,3,5-trisubstituted pyrroles was shown below. The *O*-vinyl oximes intermediate could undergo [3,3]- or [1,3]-rearrangement pathway depending the rate of tautomerization and lead to 2,3,4- or 2,3,5-trisubstituted pyrroles. α-Cyano-*O*-allyl oximes might transform to *O*-vinyl oxime under iridium isomerization condition, and then followed by favorable tautomerization to give the *O*-vinyl enamine intermediate which underwent subsequent [3,3]-rearrangement and dehydration to give the 2,3,4-trisubstituted

pyrrole. On the other hand, acetophenone-like *O*-vinyl oxime underwent irreversible [1,3]-rearrangement due to lack of tendency toward tautomerization (Scheme 14).[26]

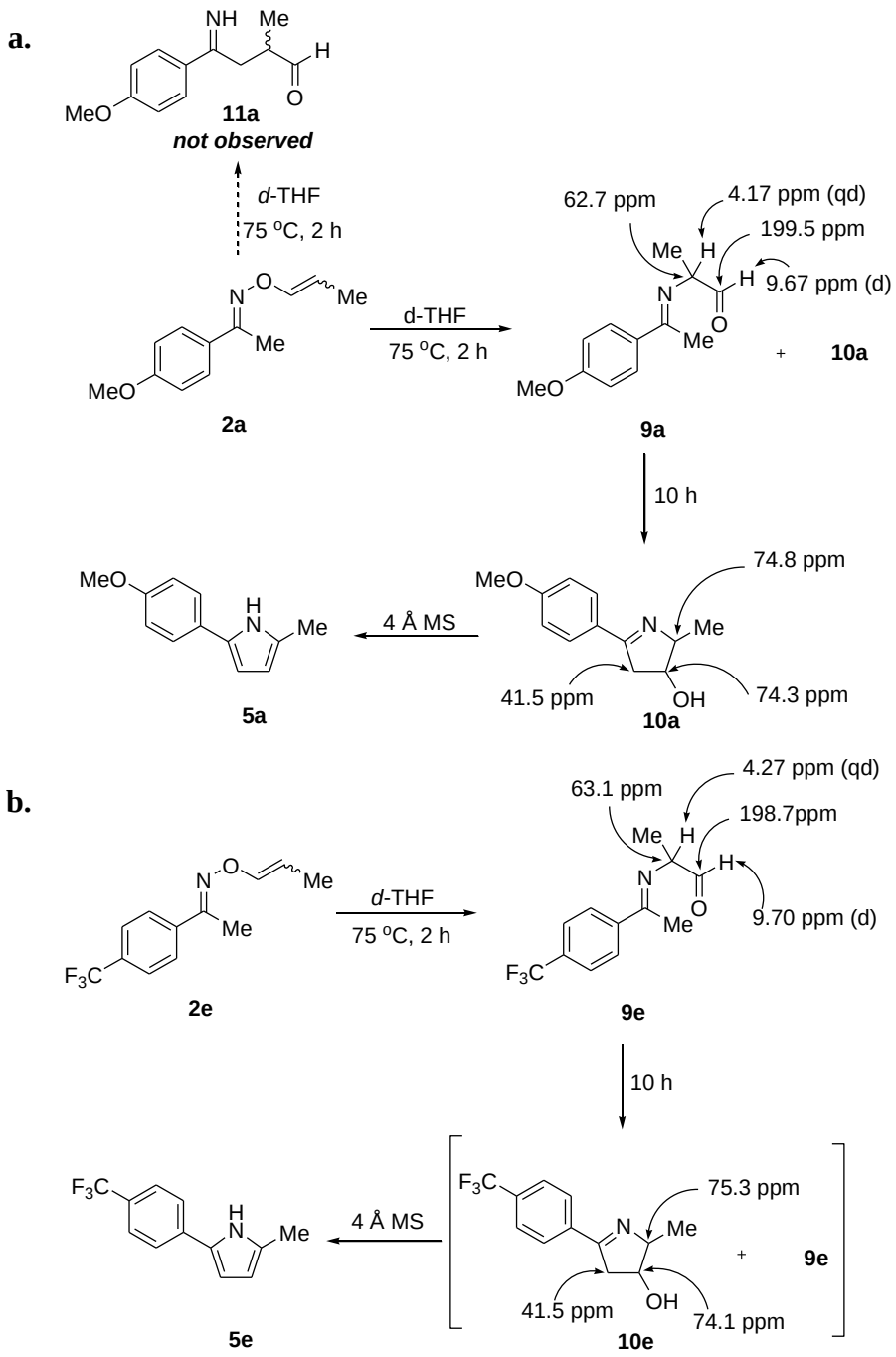
Scheme 14. Proposed Mechanism for Pyrrole Synthesis



In order to gather data to support our proposed pathway for the regioselective pyrroles formation, thermal-promoted [1,3]-rearrangement reactions were monitored by 1H NMR spectroscopy using THF-d_8 as solvent at 75 ℃ (Scheme 15). As shown in the Scheme 15a, the *O*-vinyl oxime **2a** were fully converted to the corresponding intermediate **9a** as the major and **10a** as the minor after 2 hour. α-Imino aldehyde **9a**

was able to be clearly observed and identified by both the ^{1}H and ^{13}C NMR. The NMR spectroscopy of the intermediate mixture after 2 hour showed no formation of intermediate **11a** since the corresponding methylene NMR resonance were not observed in ^{1}H and ^{13}C NMR spectra. Only intermediate **10a** was observed after heating 10 hour further. Hemiaminol **11a** was able to be clearly observed and identified by both the ^{1}H and ^{13}C NMR. Addition of the moleculer seives transformed the intermediate **10a** to pyrrole **5a**. Similar transformation was observed while heating the *O*-vinyl oximes **2e**. α-Imino aldehyde **9e** was the only intermediate after 2 hour heating. After heating 10 hour further, it showed both intermediate **9e** and hemiaminol **10e** in almost 5 to 1 ratio. Addition of the moleculer sieves transformed the intermediate **9e** and **10e** to pyrrole **5e**. From NMR spectroscopy experiment shown in Scheme 15b, it indicated that electron-poor group on aryl slowed down the cyclization and minimize the formation of the hemiaminol intermediate formation which might cause the lower yield of pyrrole formation comparing to the electron-rich aryl substitutent (Table 5, entries 1 and 5).

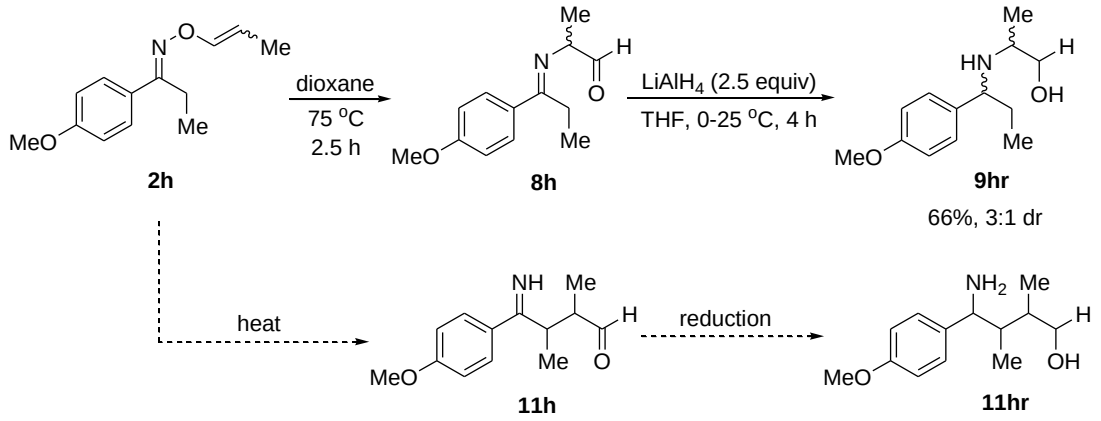
Scheme 15. Observation of Rearrangement Intermediates



Our proposed mechanism regarding the formation of two pyrrole regioisomers and different rearrangement pathway were further backed up by observing then trapping the rearrangement intermediate of **2h**. *O*-vinyl oxime **2h** transformed to the α-imino

aldehyde **8h** after heating for 2.5 hour through [1,3]-rearrangement pathway and then followed by treating with $LiAlH_4$ to give 1,2-aminoalcohol **9hr** (Scheme 16). It was isolated by chromatography and fully characterized by NMR, and the spectral data matched the structure of **9hr** not the structure of **11hr** which would be the reduction product through [3,3]-rearrangement pathway.

Scheme 16. Observation and Trapping of Rearrangement Intermediate of 2h

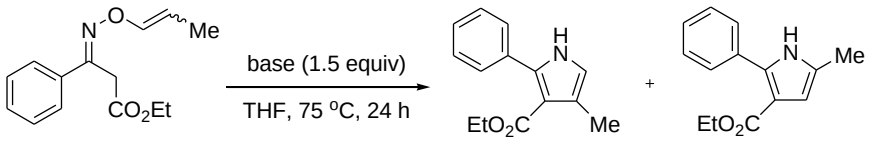


1.6 Use of pKa to Influence Regioselectivity of Pyrrole Formation

Based on our proposed mechanism and experimental data regarding the rearrangement intermediate, tautomerization apparently played an important role in the regioselective pyrrole formation; the tendency of either pathway depended on the relative rate of the tautomerization or the possible [1,3]-rearrangement. α-Cyano substituted substrate bore low pKa on the α-proton which makes tautomerization a facile process and favors subsequent [3,3]-rearrangement pathway instead of the [1,3]-rearrangement. On the other hand, tautomerization was unfavorable to

acetophenone-like substrate due to its high pKa, therefore, the [1,3]-rearrangement was favored. *O*-vinyl oxime **2j** was chosen as our precursor for the regioselective pyrrole formation, since it gave 2,3,5-trisubstituted pyrrole under mild heating condition but also has a lower pKa than the acetophenone-like substrate. Base was incorporated in the heating process in order to facilitate the relative rate of tautomerization. After screening a variety of bases, DBU was found to give excellent conversion of the pyrrole formation as well as great regioslectivity of 2,3,4-trisubstituted pyrrole **4j** (Table 7, entry 2). Other common *N*- or *O*- bases gave moderate or poor conversion and no regioselective control (Table 7, entries 1, 3-9).

Table 7. Evaluation of the Influence of Various Bases on the Regioselectivity of Pyrrole Formation



2j **4j** **5j**

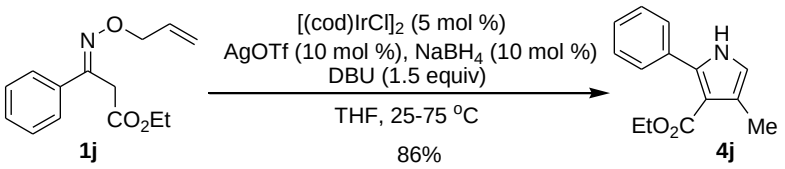
Entry	Base	Yield (%)[a]	**4j**:**5j**[b]
1	NEt_3	58	50:50
2	**DBU**	**88**	**86:14**
3	DABCO	72	84:16
4	imidazole	69	50:50
5	DMAP	64	66:34
6	Cs_2CO_3	62	66:34
7	NaO*t*-Bu	18	50:50
8	KH	14	66:34
9	KHMDS	30	25:75

[a] Determined by ^{1}H NMR spectroscopy with CH_2Br_2 as a reference.

[b] Determined by ^{1}H NMR spectroscopy.

The regioselective formation of pyrrole **4j** was able to be performed using one-flask conversion: *O*-allyloxime **1j** was treated with the optimal iridium isomerization condition and 1.5 equivalent of DBU, and then the reaction mixture was heated to 75 ℃. This one-flask transformation successfully converted **1j** to **4j** in excellent yield (Scheme 17).

Scheme 17. Preliminary Result of One-Flask Regioselective Pyrrole Formation of β-Ester-*O*-Allyl Oxime



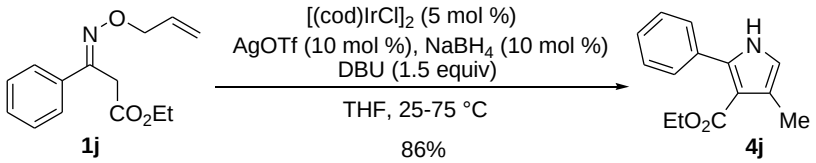
Base on the finding in Scheme 17, we decided to further explore the scope of this transformation, and a variety of analogues of 2,3,4-trisubstituted pyrrole **4j** were synthesized from the corresponding *O*-allyl oximes employing this one-flask isomerization and rearrangement method.

Both electron-rich and poor *para*-substituted aryl substrates were tolerated this transformation (Table 8, entries 1-7). Electron-rich and poor *meta*-substituted substrates also tolerated this transformation (Table 8, entries 8-10). However, when *ortho*-methyl substituted *O*-allyl oxime **1jl** was subjected to the one-flask condition, it gave mixture of **4jk** and **5jk** in a 5 to 3 ratio, and might be due to the steric

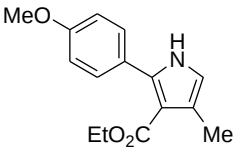
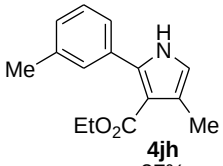
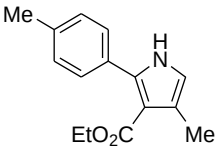
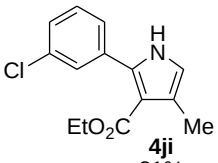
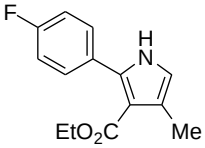
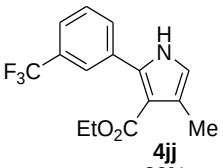
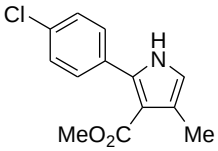
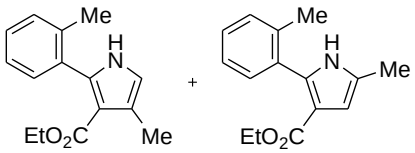
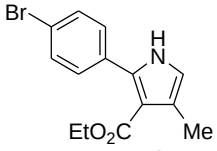
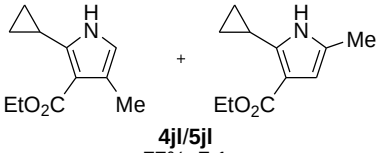
destabilization of the ortho-methyl group (Table 8, entry 11). Alkyl β-ester substrates **1jl** and **1jm** also tolerated this isomerization rearrangement sequence and gave a regioisomeric mixture of pyrroles. **1jl** and **1jm** bore relatively higher pKa than the other acetophenone-like substrates, and that slowed down the rate of tautomerization and increased probability of [1,3]-rearrangement (Table 8, entries 12,13). Substrate **1jn** tolerated this transformation as well but gave mixture of **4jn** and **5jn** in 2 to 3 ratio (Table 8, entry 14). The poor regioselectivity might be caused by the relatively higher pKa and as well as the setric destabilization of *i*-propyl group.

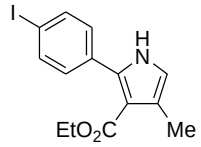
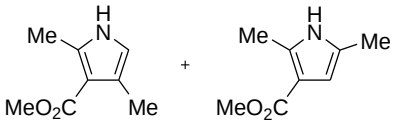
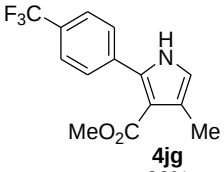
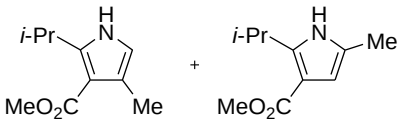
One-flask regioselective pyrrole formation reactions were set up side by side to evaluate the effect of DBU. It showed that the addition of DBU not only gave excellent regio-control of **4j** but also significantly improved the yield of **4j** (Scheme 18).

Table 8. Preparation of 4-Methyl-Pyrroles via the Rearrangement of β-Ester Oxime in Presence of DBU

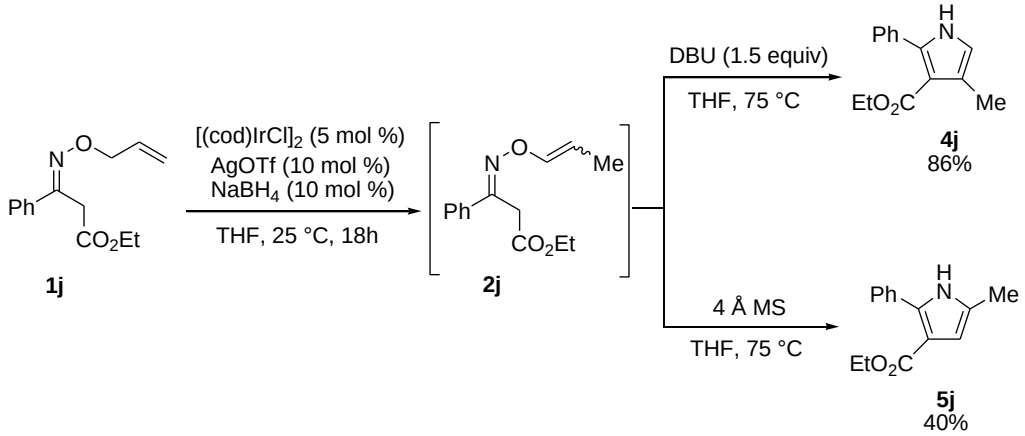


1j **4j**

Entry	Product	Entry	Product
1	 **4ja** 92%	8	 **4jh** 87%
2	 **4jb** 85%	9	 **4ji** 81%
3	 **4jc** 84%	10	 **4jj** 80%
4	 **4jd** 78%	11	 **4jk/5jk** 84%, 5:3
5	 **4je** 78%	12	 **4jl/5jl** 77%, 7:1

6	 **4jf** 76%	13	 **4jm/5jm** 54%, 2:1
7	 **4jg** 82%	14	 **4jn/5jn** 44%, 2:3

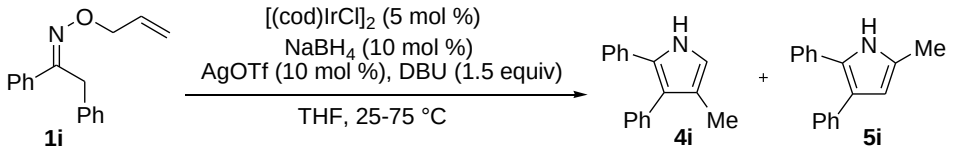
Scheme 18. One-Flask Regioselective Pyrrole Formation of β-Ester-*O*-Allyl Oxime



Besides β-ester *O*-allyl oximes substrate, we also tested this DBU assisted one-flask transformation by using other substrate with lower pKa than the acetophenone oxime. Deoxybenzoin *O*-allyl oxime **1i** was subjected to this one-flask condition, and it gave mixture of the regioisomeric pyrroles **4i** and **5i** (Scheme 19). Even though it gave a regioisomeric mixture of pyrroles, however, treating with DBU allowed us to observe

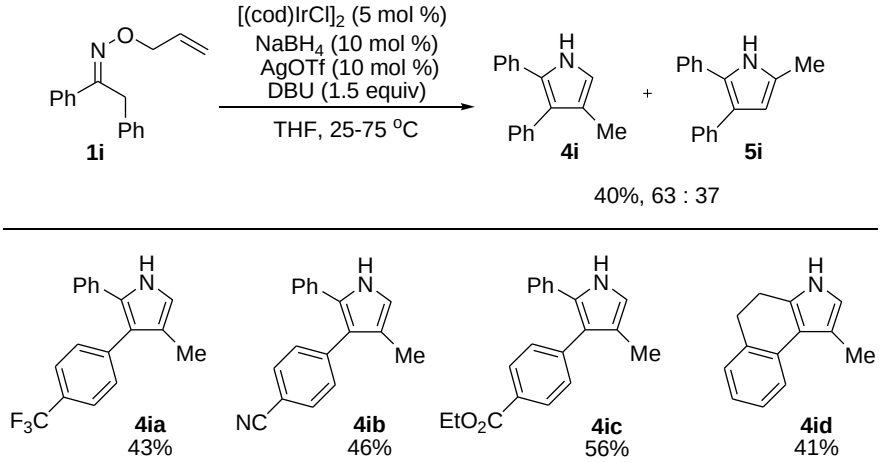
the formation of 2,3,4-trisubstituted pyrrole **4i** which was not observed under the simple thermal condition (Table 6, entry 4).

Scheme 19. Preliminary Result of One-Flask Regioselective Pyrrole Formation of Deoxybenzoin Oxime



Based on the finding in Scheme 19, we decided to further explore the scope of this transformation, and a variety of analogues of 2,3,4-trisubstituted pyrrole **4i** were synthesized from the corresponding *O*-allyl oximes (Scheme 20). Electron-poor *para*-substituted aryl substrates and bicyclic substrate tolerated this transformation and gave moderated yields in one single regioisomer. *O*-allyl oximes **1ja**, **1jb**, and **1jc** were prepared by the condensation of *O*-allyl hydroxamine to the corresponding ketones which were prepared by Daniel S. Mueller using Palladium-catalyzed α-arylation chemistry.[27]

Scheme 20. Effects of DBU to Deoxybenzoin Derived Substrates



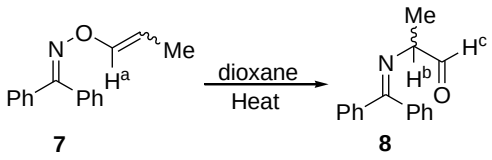
1.7 Mechanistic Studies of [1,3]-Rearrangements of *O*-Vinyl Oximes

In order to have better understanding of the [1,3]-rearrangement mechanism, dynamic NMR spectroscopy were conducted and it allowed us to obtain Eyring plot and afforded information, such as $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, regarding of the [1,3]-rearrangement reaction transition state.

1.7.1 Eyring Analysis of [1,3]-Rearrangement

Substrate **7** and internal standard (ferrocene) were heated at different temperature in dioxane-d_8, and ^{1}H NMR spectroscopy was taken at certain interval. The resonance peaks of H^a, H^b, and H^c were integrated as indication of the consumption of **7** and the formation of **8** (Scheme 21).

Scheme 21. [1,3]-Rearrangement of Benzophenone *O*-Vinyl Oxime 7



7 **8**

The formula of zero order (Eq. 1), first order (Eq. 2), and second order (Eq. 3) rate-law were shown below. The order of the rate-law can be determined by ploting the NMR integration (A), Ln (A), or 1/A versus time and examining the linear correlation of each of the plot.

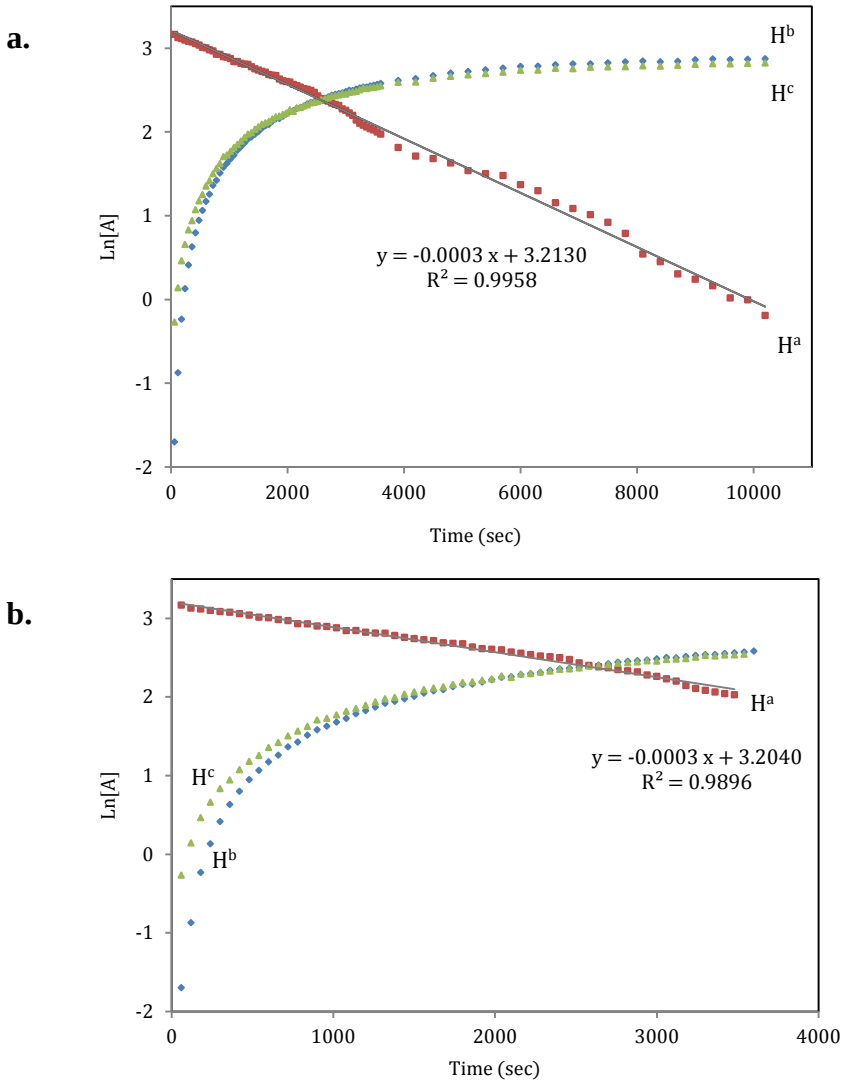
$$[A] = -kt + [A]_0 \qquad (1)$$

$$\ln[A] = -kt + \ln[A]_0 \qquad (2)$$

$$\frac{1}{[A]} = \frac{1}{[A]_0} + kt \qquad (3)$$

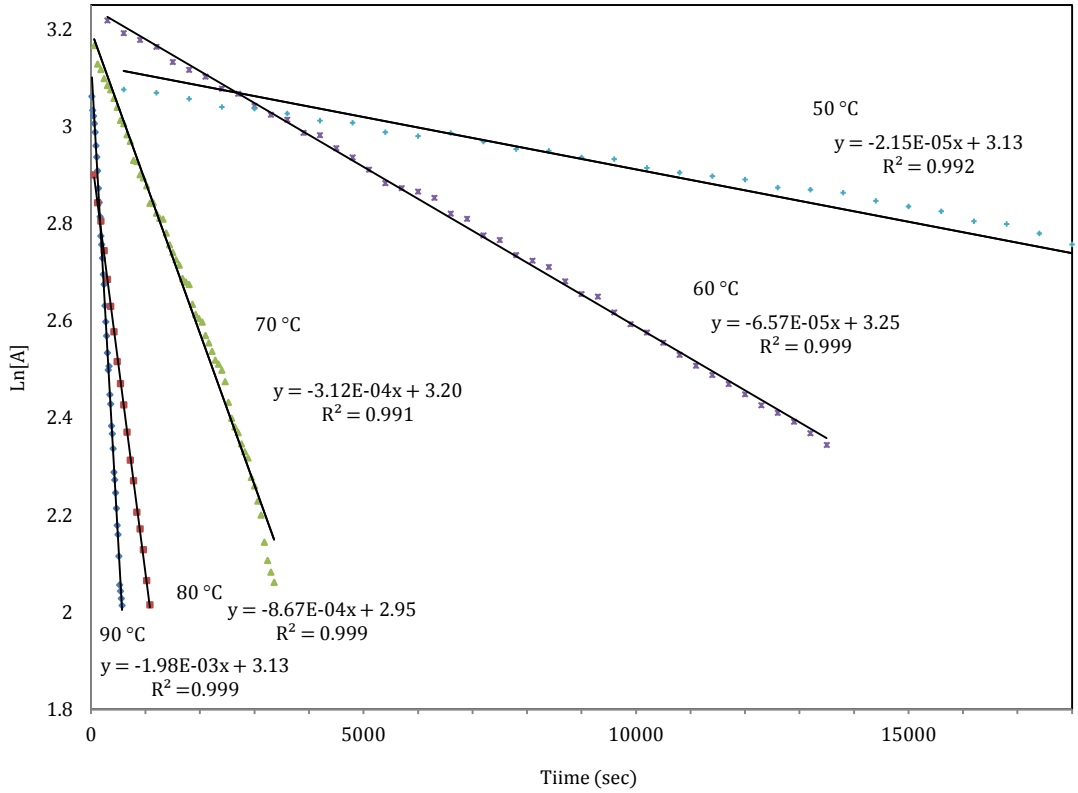
Zero order rate-law plot at 70 ℃ howed moderate linear correlation of the overall data points of H^a to time according to the R^2 value. Second order rate-law plot also showed moderate linear correlation of the overall data points of H^a to time. First order rate-law plot at 70 ℃ was shown below, and it showed excellent linear correlation of the overall data points of H^a to time (Fig. 1a). It also showed excellent linear correlation of the initial data points of H^a to time (Fig. 1b). It seemed like that the [1,3]-rearrangement was likely to obey the first order rate-law but the zero and second order.

Figure 1. First-Order Rate-Law Plot at 70 °C



The rate constant *k* at 70 °C can be determined by the slope of the linear formula in Figure 1. The overall rate constant was found as 0.0003 mol·sec^{-1} from Figure 1a as well as the initial rate constant from Figure 1b. The first order rate-law plot of the initial rate data points H^a versus time in different temperature was shown in Figure 2 below, and the initial rate constant in different temperature were determined by the slope of each linear formula in Figure 2.

Figure 2. First-OrderRate-Law Initial Rate Analysis of the Conversion of *O*-Vinyl Oxime to α-Imino Aldehyde at 50-90 °C

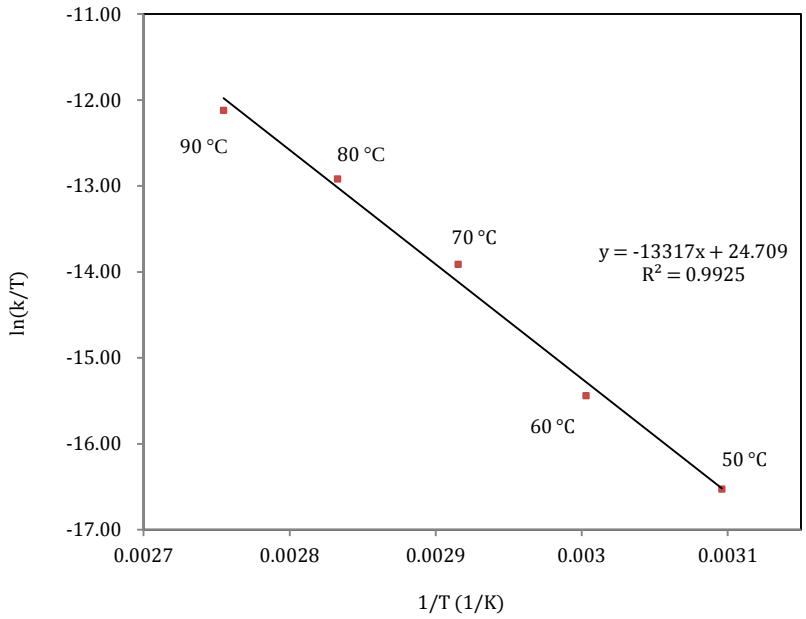


In order to estimate the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ of the [1,3]-rearrangement, Eyring analysis was utilized using the initial rate constant obtained from Figure 2. Eyring equation was shown below (Eq. 4).

$$\ln\frac{k}{T} = \frac{-\Delta H^{\ddagger}}{R} \times \frac{1}{T} + \ln\frac{k_B}{h} + \frac{\Delta S^{\ddagger}}{R} \qquad (4)$$

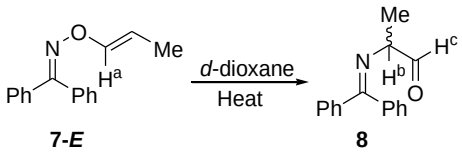
Ploting $ln\frac{k}{T}$ versus $\frac{1}{T}$ gave excellent linear correlation (Fig. 3); $\frac{-\Delta H^{\ddagger}}{R}$ was determined as the slope of the linear formula in Figure3 and intercept were $\ln\frac{k_B}{h} + \frac{\Delta S^{\ddagger}}{R}$. $\Delta H^{\ddagger}$ was found to be 26.446 Kcal·mol^{-1} and $\Delta S^{\ddagger}$ was found to be 1.8846 cal·mol^{-1}.

Figure 3. Eyring Analysis: [1,3]-Rearrangement of 7



E-*O*-vinyl oxime **7-*E*** was synthesized and subjected to dynamic NMR spectroscopy experiments as well. The resonance peaks of H^a, H^b, and H^c were integrated as indication of the consumption of **7-*E*** and the formation of **8** (Scheme 22).

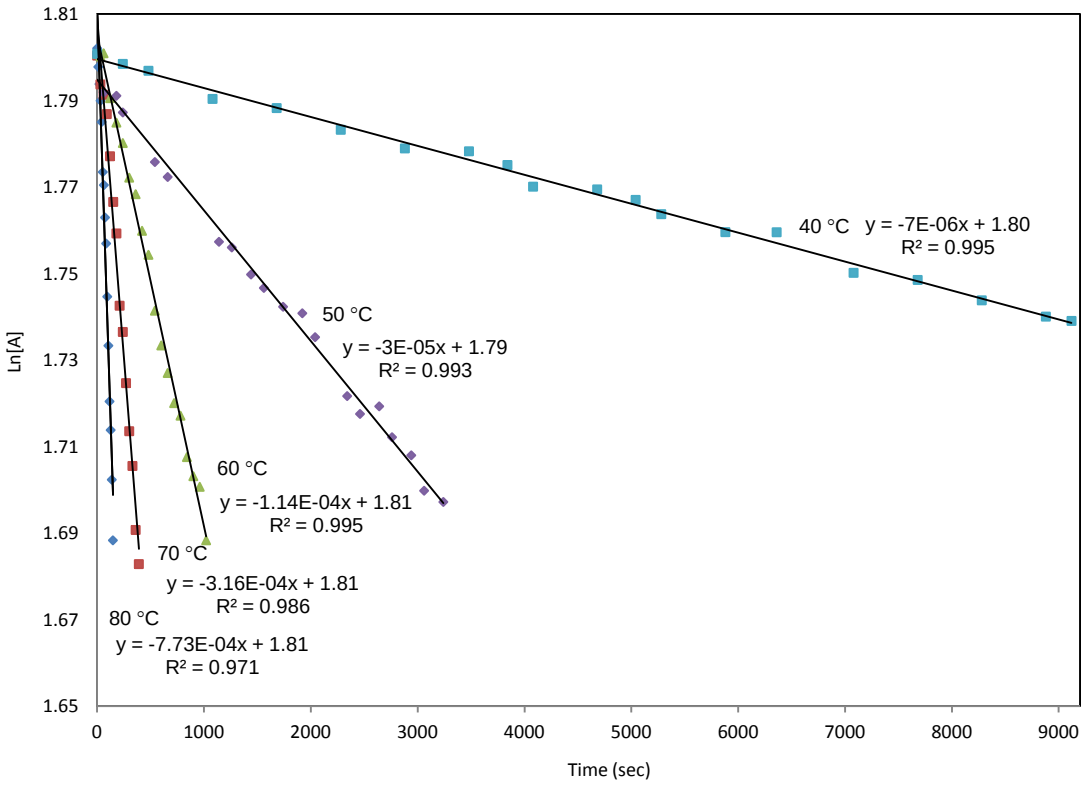
Scheme 22. [1,3]-Rearrangement of Benzophenone *O*-Vinyl Oxime 7-*E*



7-*E* **8**

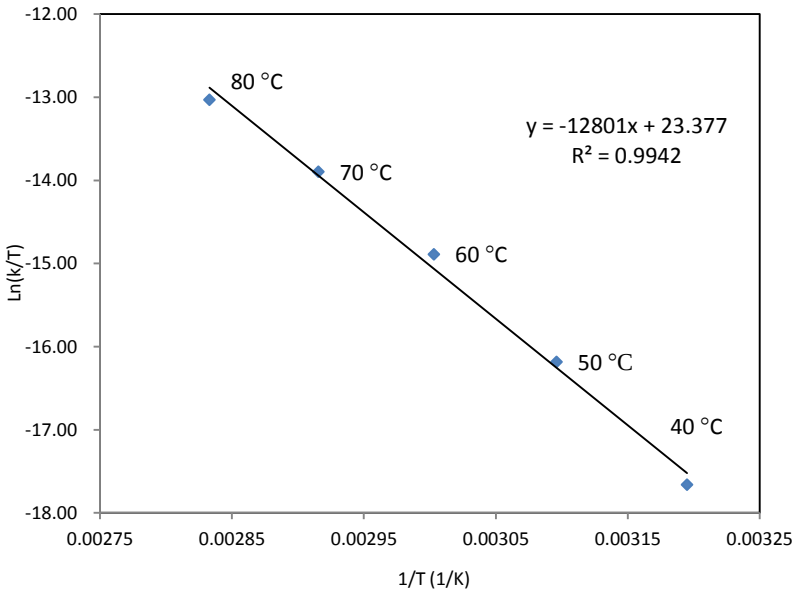
The first order rate-law plot of the initial data points H^a versus time in different temperature was shown below, and the initial rate constant in different temperature were determined by the slope of each linear formula in Figure 4.

Figure 4. First-Order Rate-Law Initial Rate Analysis of the Conversion of *E*-*O*-Vinyl Oxime to α-Imino Aldehyde at 40-80 °C



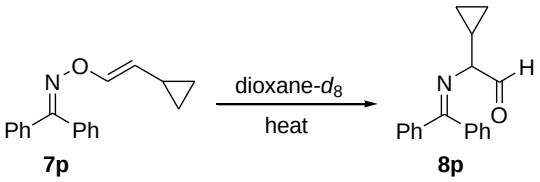
$\Delta H^{\ddagger}$ was found to be 25.421 Kcal·mol^{-1} and $\Delta S^{\ddagger}$ was found to be -0.76055 cal·mol^{-1} according to the slope and intercept in Figure 5. The $\Delta H^{\ddagger}$ we obtained from the Eyring analysis was smaller than the reported enthalpy value regarding of *O*-phenyl benzophenone oxime N–O bond dissociation.[28] It suggested N–O bond was significantly weak during the transition of [1,3]-rearrangement and it also enhanced the possibility that the transformation of *O*-vinyl benzophenone oxime rearrangement might undergo a dissociative mechanism.

Figure 5. Eyring Analysis of [1,3]-Rearrangement of 7-*E*



A radical clock reaction[29] was performed by Daniel S. Mueller to examine the possibility of radical mechanism. No cyclopropyl ring-opening product was oberseved and it suggested that [1,3]-rearrangement might not undergo a radical mechanism.

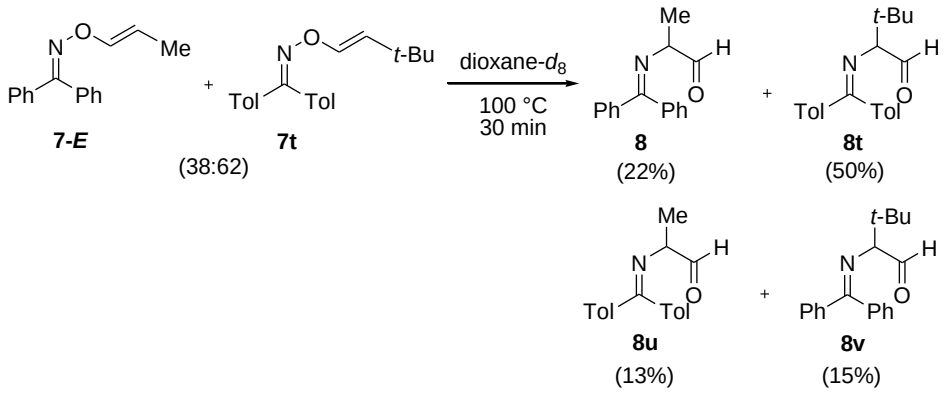
Scheme 23. Radical Clock Reaction



7p **8p**

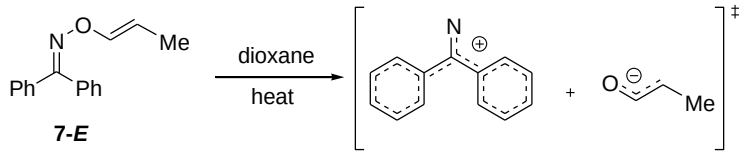
Crossover experiment[29] was conducted to gather more evidence to support about our assumption of dissociative mechanism. By treating a mixture of **7-*E*** and **7t** under 100 ℃, we were able to clearly observe the formation four different α-iminoaldehydes in ^{1}H NMR after 30 min (Scheme 24).

Scheme 24. Crossover Experiment



From the radical clock reaction and crossover experimental data we got,[29] we conclude that solvent separated intermediates might involve in the transition state and the transformation might undergo an ion-pair mechanism (Scheme 25). Heterogenous dissociation of N–O gave oxygen anion fragment and nitrogen cation fragment. Oxygen anion could be stabilized by the resonance and the benzophenone imine cation could be stablilized by the highly conjugation of the biphenyl.

Scheme 25. Proposed Transition State: Intermediate Fragments



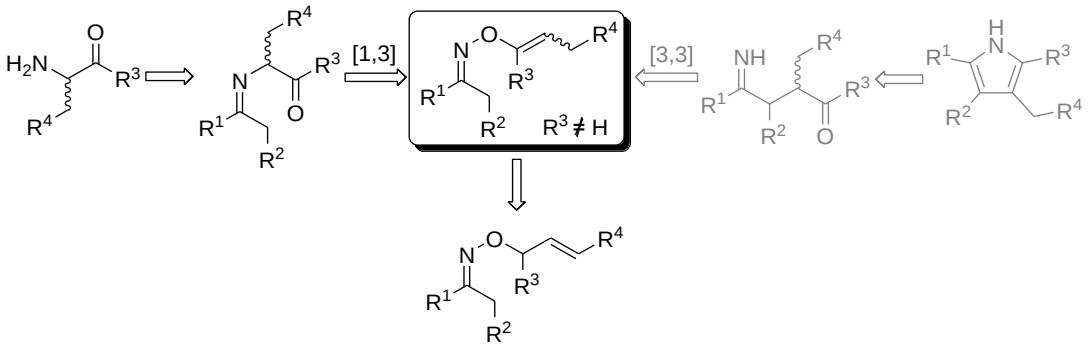
1.8 Extension: Substituted Allylic Ethers

We have learned from our previous results mentioned above that *O*-vinyl oximes can be obtained from the isomerization of *O*-allyl oxime in presence of Iridium and

regioisomeric pyrroles can be prepared through either [3,3]- or [1,3]-rearrangement pathway followed by the sequent cyclization and dehydration process.

Based on those finding, we envision that the cyclization process after [1,3]-rearrangement may be slow down by swapped the intermediate from α-amino aldehyde to the α-amino ketone or shut down by using unenolizable substrate, such as benzophenone. The α-amino ketone can be accessed from the [1,3]-rearrangement of 1,2-disubstituted *O*-vinyl oxime. We also propose the 2,4,5-trisubstituted or 2,3,4,5-tetrasubstituted pyrrole can be prepared from the [3,3]-rearrangement of 1,2-disubstituted *O*-vinyl oxime. 1,2-disubstituted *O*-vinyl oxime can be prepared from the isomerization of α-substituted *O*-allyl oxime (Scheme 26).

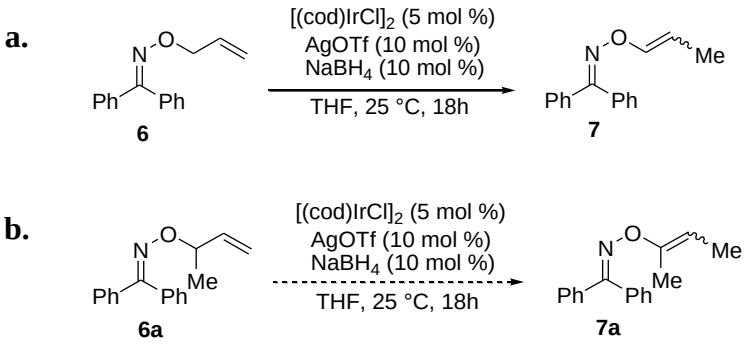
Scheme 26. Preparation of α-Amino Ketones and Tetrasubstituted Pyrroles via Isomerization and Rearrangement of Allylic Oxime Ethers



O-Allyl benzophenone oxime was chosen as the precursor for accessing the α-amino ketone. First, we tested the preparation of *O*-vinyl benzophenone **7** from

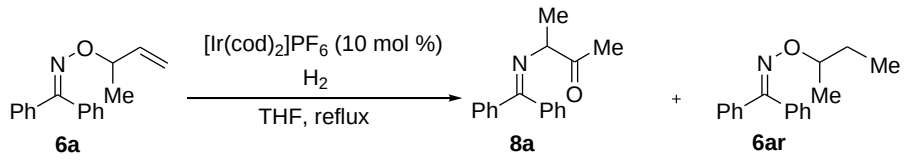
O-allyl benzophenone oxime **6** employing our optimal iridium isomerization condition. It gave excellent transformation to the desired *O*-vinyl oxime 7 (Scheme 27a). However, it gave no reaction by using the *O*-α-methyl allyl oxime **6a**[30] under the same Iridium condition (Scheme 27b).

Scheme 27. Isomerization of *O*-Allyl Oximes and α-Methyl-*O*-Allyl Oximes



Inspired by the *O*-allyl silyl ether isomerization demonstrated by Miyaura and coworkers,[7] we decided to adopt the same condition for our α-methyl-*O*-allyl substrate **6a**. Under the condition of catalytic amount of $[Ir(cod)_2]PF_6$[31, 32] and H_2 in THF, **6a** gave fully conversion to the reduction adduct **6ar** but only observed trace amount of the desired product **8a** (Scheme 28).

Scheme 28. α-Methyl-Allylic Oxime Ethers Isomerization Preliminary Result

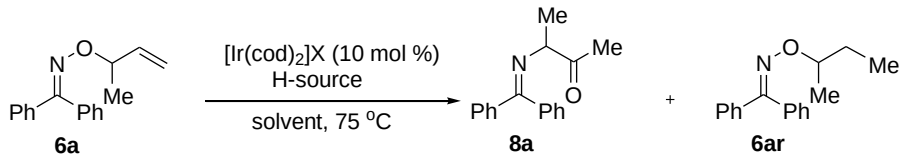


100% conversion, **8a**:**6ar** = 1:9

Counter ion, solvent, and H-source were optimized for the transformation of **6a** to **8a**. It showed moderated conversion and excellent transformation to **8a** employing OTf as the counter ion (Table 9, entry 4). Both conversion and transformation to **8a** were minimized by altering the solvents (Table 9, entries 6-9). A variety of H-source were screened, it was found that bulky H-source, such as 9-BBN, gave exclusive formation of **8a** (Table 9. entries 10-16). Amount of the 9-BBN was also optimized for the **8a** formation, and it was found that decreasing the addition of 9-BBN improved the transformation of **8a** (Table 9, entries 15, 16). It was found that 10 mol % of $[Ir(cod)_2]OTf$[32] without H-source gave the best transformation of **6ar**.

Monodentate and bidentate ligands were also optimized for the transformation of **6a** to **8a**. It was found that most of the bidentate ligands decrese reactivity and gave poor or no formation of **8a** (Table 10, entries 14-20). **8a** was isolated in 44 % yield employing Johnphos as ligand (Table 10, entry 1). A mixture of 10 mol % $[Ir(cod)_2]OTf$ and 10 mol % Johnphos in THF at 75 ℃ was determined as the optimal condition.

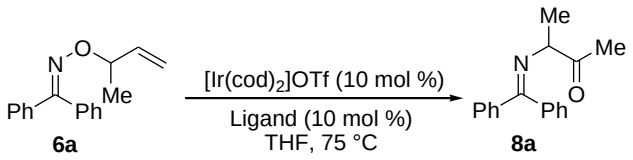
Table 9. Optimization of the Isomerization of α-Methyl-Allylic Oxime Ethers



Entry	$[Ir(cod)_2]X$	H-source	Solvent	Conversion (%)[a]	**8a**:**6ar**[b]
1	$[Ir(cod)_2]SbF_6$	H_2	THF	100	**6ar**
2	$[Ir(cod)_2]PF_6$	H_2	THF	100	10:90
3	$[Ir(cod)_2]BF_4$	H_2	THF	50	50:50
4	$[Ir(cod)_2]OTf$	H_2	THF	53	84:16
5	$[Ir(cod)_2]BArF$	H_2	THF	0	--
6	$[Ir(cod)_2]OTf$	H_2	dioxane	17	**6ar**
7	$[Ir(cod)_2]OTf$	H_2	CH_3CN	0	--
8	$[Ir(cod)_2]OTf$	H_2	DCE	<10	**6ar**
9	$[Ir(cod)_2]OTf$	H_2	IPAc	100	**6ar**
10	$[Ir(cod)_2]OTf$	DIBAL (10 mol %)	THF	<10	6:94
11	$[Ir(cod)_2]OTf$	HBPin (10 mol %)	THF	50	66:34
12	$[Ir(cod)_2]OTf$	9-BBN (10 mol %)	THF	95 (27)[c]	**8a**
13	$[Ir(cod)_2]OTf$	Super-H (10 mol %)	THF	<10	**6ar**
14	$[Ir(cod)_2]OTf$	$NaBH_4$ (10 mol %)	THF	<10	34:66
15	$[Ir(cod)_2]OTf$	$HSiEt_3$ (10 mol %)	THF	<10	62:38
16	$[Ir(cod)_2]OTf$	Catecholborane (10 mol %)	THF	50	**8a**
17	$[Ir(cod)_2]OTf$	9-BBN (5 mol %)	THF	35[c]	**8a**
18	**$[Ir(cod)_2]OTf$**	**none**	**THF**	**34**[c]	**8a**

[a] Determined by ^1H NMR spectroscopy with CH_2Br_2 as a reference. [b] Determined by ^1H NMR spectroscopy. [c] Isolate yield.

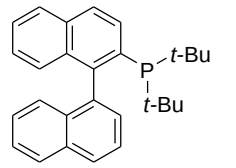
Table 10. Ligand Effects on the Isomerization of α-Methyl-Allylic Oxime Ethers

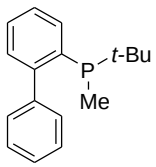


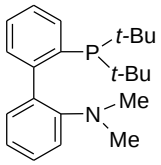
6a **8a**

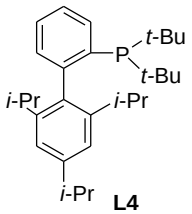
Entry	Ligand	Yield (%)[a]	Entry	Ligand	Yield (%)[a]
1	**Johnphos**	**43(44)[b]**	11	L9	4
2	**L1**	**46**	12	L10	41
3	L2	42	13	$P(Tol)_3$	36
4	L3	38	14	binap	0
5	L4	37	15	xantphos	12
6	L5	19	16	dppe	0
7	monophos	8	17	dppf	15
8	L6	32	18	bipy	0
9	L7	14	19	L11	23
10	L8	0	20	L12	0

[a] Determined by ^{1}H NMR spectroscopy with CH_2Br_2 as a reference. [b] Isolated Yield


L1


L2


L3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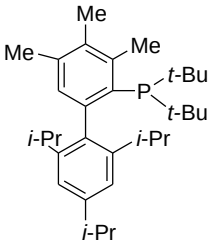
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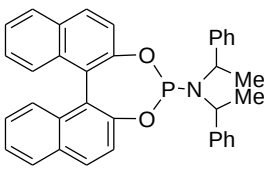
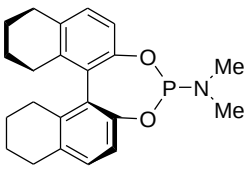
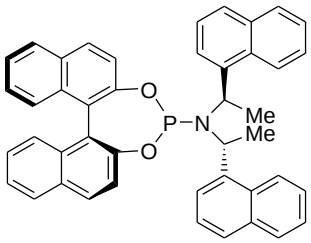
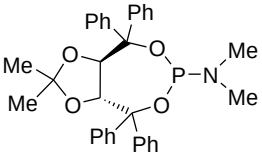
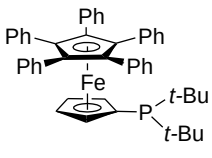

L6


L7


L8


L9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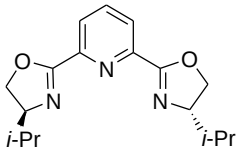
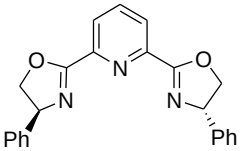
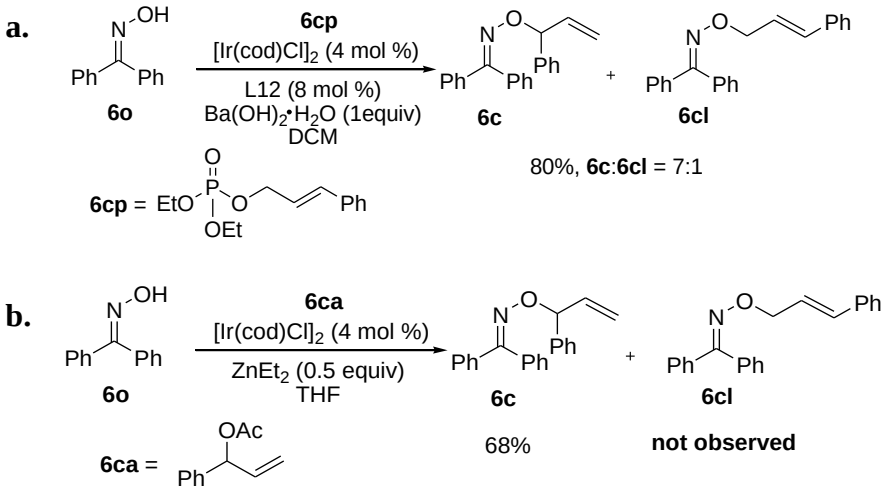

L11


L12

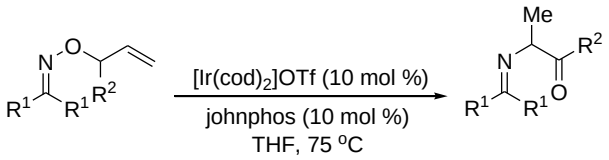
After successfully transforming the α-methyl *O*-allyl oxime to the corresponding α-amino ketone, we decided to extend the scope of this transformation to the α-aryl substituted *O*-allyl oxime. The preparation **6c** was adopted from the Iridium-catalyzed cross-coupling demonstrated by Takemoto and coworkers.[33] However, it gave unseperatable mixture of desired branch product **6c** and linear adduct **6cl** in 7:1 ratio (Scheme 29a). Using alternative coupling partner **6ca** and $ZnEt_2$ gave exclusive formation of **6c** (Scheme 29b).[34]

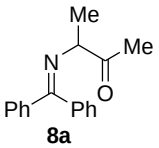
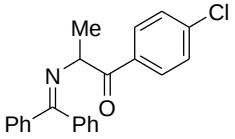
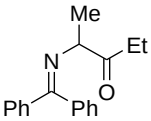
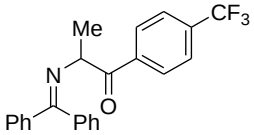
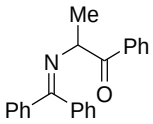
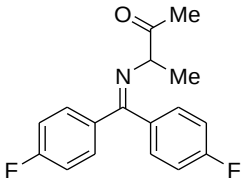
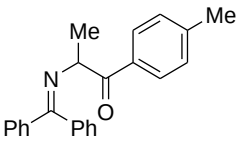
Scheme 29. Preparation of α-Aryl-*O*-Allyl Oxime



With the optimal condition and a variety of α-substituted *O*-allyl oximes in hand, the formations of α-amino ketones were shown in Table 11. However, the reaction was not general and gave low yields.

Table 11. Substrate Scope of Cationic Catalyst and Johnphos Condition



Entry	Product	Entry	Product
1	 **8a** 44%[b]	5	 **8e** 23%[a]
2	 **8b** trace[a]	6	 **8f** 15%[a]
3	 **8c** 35%[b]	7	 **8g** 28%
4	 **8d** 17%[a]		

[a] NMR yield not isolated; yield was determined by ^{1}H NMR spectroscopy with CH_2Br_2 as a reference. [b] Isolated Yield

1.9 Summary

We have demonstrated the efficient preparation of *O*-vinyl oximes can be achieved by the Iridium-catalyzed isomerization of *O*-allyl oximes under mild and functional

group tolerant conditions. However, isomerization To 1,2-disubstituted *O*-vinyl oximes was not a general process. The preparation of 1,2-disubstituted *O*-vinyl oximes may require alternative synthetic route.

We also demonstrated the 2,3,4-trisubstituted pyrroles formation can be achieved by cooperating our Ir-H isomerization condition with α-CN *O*-allyl oximes at room temperature. The 2,3,5-trisubstituted pyrroles can be prepared from the thermal condition of the corresponding *O*-vinyl oximes. The regioselective pyrrole formation can be done by the addition of DBU to the reaction. The 2,3,4-trisubstituted pyrroles from the corresponding β-ester acetophenone *O*-allyl oximes and deoxybenzoin *O*-allyl oximes can be prepared exclusively under the DBU-mediated condition.

Kinetic NMR experiments give us some data regarding of the order of the rate-law and enthalpy and entropy values of transition state. By these information, it allows us to proposed reasonable transition state model of [1,3]-rearrangement.

1.10 Experimental Section

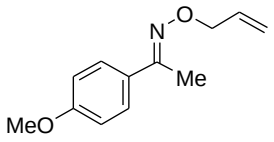
^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using Bruker DRX 500 or Varian DRX 300 spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants

(Hz) and integration. High resolution mass spectra were acquired on a JEOL GCMate II or Thermo Finnigan LTQ FT spectrometer, and were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on Sorbent Technologies 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on Sorbent Technologies 60Å (40– 60 μm) mesh silica gel (SiO_2). All reactions were carried out under an atmosphere of nitrogen in glassware, which had been oven-dried. Unless otherwise noted, all reagents were commercially obtained and, where appropriate, purified prior to use. THF was dried by filtration through alumina according to the procedure of Grubbs.[35] Acetonitrile, isopropyl acetate, benzene, dioxane, dichloroethane, and THF-d_8 were distilled over CaH_2 and degassed prior to use in the glovebox. Metal salts were stored in a Vacuum Atmospheres Omni nitrogen atmosphere dry box.

1.10.1 Preparation of *O*-Allyl Oximes

General Procedure A: A 100 mL rbf was charged with 1 equiv of allylhydroxylamine hydrochloride salt, 1 equiv of NaOAc, and 40 mL of MeOH. The resulting slurry was allowed to stir at 25 ℃ for 30 min. Then 1 equiv of the corresponding ketone was added to the slurry during a 5 min time period. Ketones that were liquids were added neat with

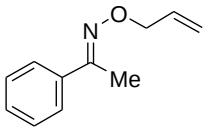
a syringe. Ketones that were solids were mixed with 15 mL of MeOH and added as solutions with a syringe. The reaction mixtures were then allowed to stir at 25 ℃ for 12-24 h. At this time, 30 mL of water were added to the flask and a white precipitate appeared. The mixture was then transferred to a separatory funnel and mixed with an additional 20 mL of water and 40 mL of MTBE or CH_2Cl_2. The water layer was extracted with 3 × 15 mL of MTBE or CH_2Cl_2 and the organic layer was extracted with 2 × 20 mL of water and 1 × 20 mL of brine. The organic layers were then combined and dried over $MgSO_4$, filtered, and concentrated. No further purification was required. The isomeric ratios of *E*:*Z*-oximes present in the product mixtures were determined by comparison of the integration of the allylic methylene resonances in the ^{1}H NMR spectrum. The assignment of the major oxime isomer as the *E*-isomer was made by 1D ^{1}H-^{1}H NOE spectroscopy for compounds **1b** (see below for details). All other oxime isomer assignments were made by comparison to compounds **1b**.



1a

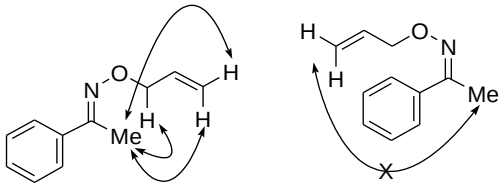
1a was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.635 g, 5.80 mmol) was treated with NaOAc (0.476 g, 5.80 mmol) and 4'-methoxyacetophenone (0.791 g, 5.27 mmol). The reaction mixture was allowed to

stir for 12 h. After workup, **1a** was isolated as a clear, colorless oil (0.501 g, 46%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.60 (m, 2H), 6.90-6.88 (m, 2H), 6.10-6.05 (m, 1H), 5.35 (d, *J* = 19.0 Hz, 1H), 5.24 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 8.5 Hz, 2H), 3.83 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 154.4, 134.6, 129.3, 127.4, 117.2, 113.8, 74.9, 55.3, 12.7; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_2$ $(M+H)^+$ 206.1181, found 206.1177. Only the *E*-oxime isomer was observed.

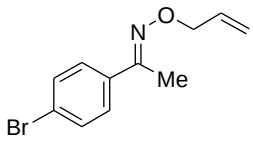


1b

1b was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.792 g, 7.23 mmol) was treated with NaOAc (0.593 g, 7.23 mmol) and acetophenone (0.77 mL, 6.6 mmol). The reaction mixture was allowed to stir for 12 h. After workup, **1b** was isolated as a clear, colorless oil (0.73 g, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.65 (m, 2H), 7.39-7.36 (m, 3H), 6.09-6.06 (m, 1H), 5.36 (d, *J* = 19.0 Hz, 1H), 5.25 (d, *J* = 12.0 Hz, 1H), 4.72 (d, *J* = 8.5 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8, 136.7, 134.5, 129.0, 128.4, 126.1, 117.3, 75.1, 12.8; HRMS (ESI) *m/z* calcd. for $C_{11}H_{14}NO$ $(M+H)^+$ 176.1075, found 176.1078. Only the *E*-oxime isomer was observed.

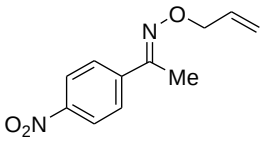


1D ^{1}H-^{1}H NOE spectrum: When the methyl resonance at 2.28 ppm was selected, the vinyl resonances at 5.36, and 5.25 ppm, and the allyl methylene resonance at 4.72 ppm were inverted. These interactions are illustrated in the structure above and indicate that the structure is the *E*-oxime isomer.



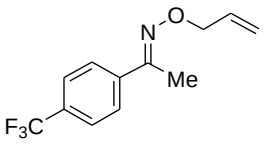
1c

1c was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.604 g, 5.51 mmol) was treated with NaOAc (0.452 g, 5.51 mmol) and 4'-bromoacetophenone (0.998 g, 5.01 mmol). The reaction mixture was allowed to stir for 12 h. After workup, **1c** was isolated as a clear, colorless oil (0.99 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54-7.52 (m, 2H), 7.50-7.48 (m, 2H), 6.07-6.03 (m, 1H), 5.34 (d, *J* = 19.0 Hz, 1H), 5.24 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 8.5 Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.7, 135.6, 134.4, 131.5, 127.6, 123.3, 117.5, 75.2, 12.6; HRMS (ESI) *m/z* calcd. for $C_{11}H_{13}BrNO$ $(M+H)^+$ 254.0181, found 254.0172. Only the *E*-oxime isomer was observed.



1d

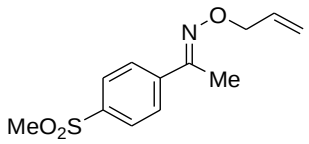
1d was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (1.09 g, 9.99 mmol) was treated with NaOAc (0.820 g, 9.99 mmol) and 4'-nitroacetophenone (1.50 g, 9.08 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1d** was isolated as a light yellow solid (1.53 g, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21-8.19 (m, 2H), 7.83-7.81 (m, 2H), 6.07-6.03 (m, 1H), 5.34 (d, *J* = 19.0 Hz, 1H), 5.25 (d, *J* = 12.0 Hz, 1H), 4.74 (d, *J* = 8.5 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 148.0, 142.6, 134.0, 126.7, 123.6, 117.9, 75.7, 12.5; HRMS (ESI) *m/z* calcd. for $C_{11}H_{13}N_2O_3$ $(M+H)^+$ 221.0926, found 221.0920.; mp 42-44 ℃. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1e

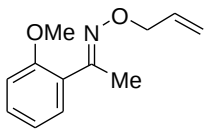
1e was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.641 g, 5.85 mmol) was treated with NaOAc (0.480 g, 5.85 mmol) and 4'-(trifluoromethyl)acetophenone (1.00 g, 5.32 mmol). The reaction mixture was allowed to stir for 12 h. After workup, **1e** was isolated as a clear, colorless oil (1.09 g,

84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.76 (m, 2H), 7.65-7.61 (m, 2H), 6.08-6.04 (m, 1H), 5.35 (d, *J* = 19.0 Hz, 1H), 5.25 (d, *J* = 12 Hz, 1H), 4.73 (d, *J* = 8.5 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 140.0, 134.2, 130.7 (q, $J_{C\text{-}F}$ = 33 Hz), 126.8 (q, $J_{C\text{-}F}$ = 245 Hz), 126.3, 125.3, 117.5, 75.1, 12.6; HRMS (ESI) *m/z* calcd. for $C_{12}H_{13}F_3NO$ $(M+H)^+$ 244.0949, found 244.0937. Less than 20% of the corresponding *Z*-oxime isomer was observed.



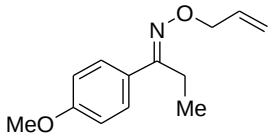
1f

1f was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (2.41 g, 22.0 mmol) was treated with NaOAc (1.81 g, 22.0 mmol) and 4'-(methylsulfonyl)acetophenone (3.96 g, 20.0 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1f** was isolated as a clear, colorless oil (3.34 g, 66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92-7.90 (m, 2H), 7.84-7.82 (m, 2H), 6.04-6.01 (m, 1H), 5.32 (d, *J* = 19.0 Hz, 1H), 5.23 (d, *J* = 12.0 Hz, 1H), 4.72 (d, *J* = 8.5 Hz, 2H), 3.03 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.1, 141.9, 140.5, 134.1, 127.5, 127.3, 117.8, 75.5, 44.5, 12.6; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_3S$ $(M+H)^+$ 254.0859, found 254.0853. Less than 20% of the corresponding *Z*-oxime isomer was observed.



1g

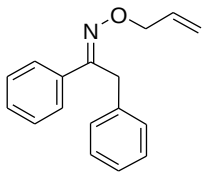
1g was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.606 g, 5.5 mmol) was treated with NaOAc (0.454 g, 5.5 mmol) and 2'-methoxyacetophenone (0.750 g, 5.0 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1g** was isolated as a clear, colorless oil (1.02 g, quant). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 6.92-6.89 (m, 1H), 6.97-6.94 (m, 1H), 6.09-6.06 (m, 1H), 5.36 (d, *J* = 19.0 Hz, 1H), 5.23 (d, *J* = 12.0 Hz, 1H), 4.71 (d, *J* = 8.5 Hz, 2H), 3.83 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 156.9, 134.6, 130.2, 129.6, 127.1, 120.7, 117.2, 111.1, 74.8, 55.5, 16.2; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_2$ $(M+H)^+$ 206.1181, found 206.1174. The Less than 5% of the corresponding *Z*-oxime isomer was observed.



1h

1h was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.548 g, 5.00 mmol) was treated with NaOAc (0.410 g, 5.00 mmol) and 4'-methoxypropiophenone (0.820 g, 5.00 mmol). The reaction mixture was allowed to

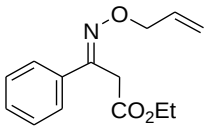
stir for 24 h. After workup, **1h** was isolated as a clear, colorless oil (0.858 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 6.90-6.88 (m, 2H), 6.07-6.04 (m, 1H), 5.34 (d, *J* = 19.0 Hz, 1H), 5.22 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 8.0 Hz, 2H), 2.76 (q, *J* = 7.5 Hz, 2H), 3.82 (s, 3H), 1.14 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 159.5, 134.7, 128.2, 127.6, 117.0, 113.8, 74.8, 55.3, 20.1, 11.2; HRMS (ESI) *m/z* calcd. for $C_{13}H_{18}NO_2$ $(M+H)^+$ 220.1338, found 220.1328. Only the *E*-oxime isomer was observed.



1i

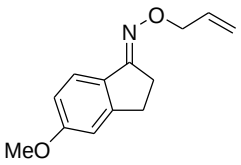
1i was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.513 g, 4.69 mmol) was treated with NaOAc (0.385 g, 4.69 mmol) and 2-phenylacetophenone (0.834 g, 4.26 mmol). The reaction mixture was allowed to stir for 12 h. After workup, **1i** was isolated as a clear, colorless oil (0.830 g, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.34-7.32 (m, 3H), 7.29-7.24 (m, 4H), 7.30-7.18 (m, 1H), 6.11-6.04 (m, 1H), 5.34 (d, *J* = 19.0 Hz, 1H), 5.23 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 8.5 Hz, 2H), 4.20 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 136.8, 135.8, 134.4, 129.1, 128.6, 128.5, 128.4, 126.6, 126.3, 117.4, 75.2, 32.8; HRMS (ESI)

m/z calcd. for $C_{17}H_{18}NO$ $(M+H)^+$ 252.1388, found 252.1381. Only the *E*-oxime isomer was observed.



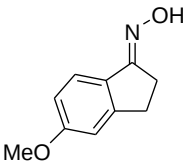
1j

1j was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.606 g, 5.53 mmol) was treated with NaOAc (0.454 g, 5.53 mmol) and ethyl benzoylacetate (0.961 g, 4.90 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1j** was isolated as a clear, colorless liquid (1.19 g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66-7.64 (m, 2H), 7.37-7.36 (m, 3H), 6.06-5.99 (m, 1H), 5.34 (d, *J* = 18.0 Hz, 1H), 5.22 (d, *J* = 12.0 Hz, 1H), 4.73 (d, *J* = 8.5 Hz, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.78 (s, 2H), 1.21(t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 151.6, 135.5, 134.1, 129.4, 128.5, 128.1, 117.3, 75.3, 61.1, 33.4, 14.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{18}NO_3$ $(M+H)^+$ 248.1287, found 248.1278. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1k

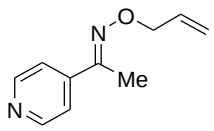
1k was synthesized S_{N2} reaction from the corresponding oxime **1kk** and allyl bromide as a white solid (1.40 g, 43%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.5 Hz, 1H), 6.82 (s, 1H), 6.81 (d, J = 7.5 Hz, 1H), 6.08-6.04 (m, 1H), 5.34 (dd, *J* = 17.0, 1.5 Hz, 1H), 5.22 (dd, *J* = 11.0, 1.5 Hz, 1H), 4.67-4.65 (m, 2H), 3.82 (s, 3H), 3.01-2.98 (m, 2H), 2.93-2.90 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 161.8, 150.4, 134.8, 128.8, 122.6, 117.2, 114.2, 109.6, 74.9, 55.4, 28.7, 26.9; HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}NO_2$ $(M+H)^+$ 218.1181, found 218.1171. Only the *E*-oxime isomer was observed.



1kk

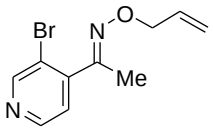
1kk was synthesized according to general procedure **A**. Hydroxylamine hydrochloride (0.350 g, 5.07 mmol) was treated with NaOAc (0.416 g, 5.07 mmol) and 5-methoxy-1-indanone (0.822 g, 5.07 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1kk** was isolated as an off-white solid (0.503 g, 56%). ^{1}H NMR

(500 MHz, $CDCl_3$) δ 8.35 (brs, 1H), 7.57-7.56 (m, 1H), 6.81-6.80 (m, 2H), 3.82 (s, 3H), 3.03-3.00 (m, 2H), 2.97-2.85 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 162.4, 151.0, 129.1, 123.0, 114.8, 110.1, 55.9, 29.1, 26.7; HRMS (ESI) *m/z* calcd. for $C_{10}H_{11}NO_2$ $(M+H)^+$ 178.0868, found 178.0867. Compound **1kk** was then used without further purification to form **1k**.



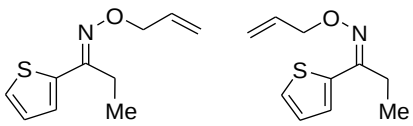
1l

1l was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (2.4 g, 22 mmol) was treated with NaOAc (1.8 g, 22 mmol) and 4-acetylpyridine (2.4 g, 20 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1l** was isolated as a clear, colorless oil (1.9 g, 54%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.60-8.58 (m, 2H), 7.52-7.50 (m, 2H), 6.04-6.01 (m, 1H), 5.32 (d, *J* = 18.0 Hz, 1H), 5.23 (d, *J* = 12.0 Hz, 1H), 4.71 (d, *J* = 7.0 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.5, 150.1, 143.8, 134.0, 120.2, 117.8, 75.6, 12.0; HRMS (ESI) *m/z* calcd. for $C_{10}H_{13}N_2O$ $(M+H)^+$ 177.1028, found 177.1026. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1m

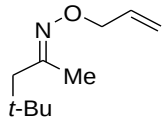
1m was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (1.2 g, 11 mmol) was treated with NaOAc (0.90 g, 11 mmol) and 4-acetyl-3-bromo-pyridine (2.0 g, 10 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1m** was isolated as a clear, colorless oil (1.2 g, 47%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.86-7.84 (m, 1H), 7.47-7.46 (m, 1H), 6.05-6.01 (m, 1H), 5.34 (d, *J* = 18.0 Hz, 1H), 5.25 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 8.0 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 147.6, 142.5, 135.7, 134.0, 131.6, 127.7, 117.8, 75.5, 12.3; HRMS (ESI) *m/z* calcd. for $C_{10}H_{12}N_2OBr$ $(M+H)^+$ 255.0133, found 255.0123. Less than 20% of the corresponding *Z*-oxime isomer was observed.



1n (*E*:*Z* = 3:2)

1n was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.60 g, 5.5 mmol) was treated with NaOAc (0.45 g, 5.5 mmol) and 1-(2-thienyl)-1-propanone (0.70 g, 5.0 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1n** was isolated as a clear, colorless oil (1.0 g, 99%). ^{1}H NMR

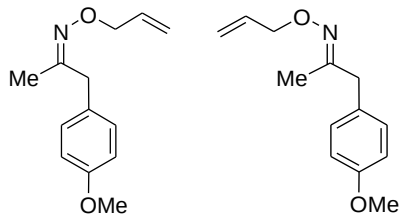
(500 MHz, $CDCl_3$) of *E*-isomer: δ 7.30-7.29 (m, 1H), 7.26-7.25 (m, 1H), 7.05-7.04 (m, 1H), 6.16-6.04 (m, 1H), 5.36 (d, *J* = 17.0 Hz, 1H), 5.25 (d, *J* = 10.5 Hz, 1H), 4.69 (d, *J* = 5.5 Hz, 2H), 2.78 (q, *J* = 7.5 Hz, 2H), 1.23 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 139.6, 134.4, 129.1, 127.0, 125.9, 117.3, 75.1, 20.9, 11.4; ^{1}H NMR (500 MHz, $CDCl_3$) of *Z*-isomer: δ 7.54-7.53 (m, 1H), 7.52-7.51 (m, 1H), 7.13-7.11 (m, 1H), 6.16-6.04 (m, 1H), 5.43 (d, *J* = 17.0 Hz, 1H), 5.28 (d, *J* = 10.5 Hz, 1H), 4.79 (d, *J* = 5.5 Hz, 2H),2.78 (q, *J* = 7.5 Hz, 2H), 1.31 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 131.9, 134.0, 130.3, 126.8, 125.6, 117.5, 75.3, 27.2, 13.0.



1o

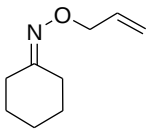
1o was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.794 g, 7.25 mmol) was treated with NaOAc (0.595 g, 7.25 mmol) and 4,4-dimethyl-2-pentanone (1.0 mL, 7.1 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1o** was isolated as a clear, colorless oil (0.725 g, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.03-5.95 (m, 1H), 5.28 (d, *J* = 18.0 Hz, 1H), 5.18 (d, *J* = 12.0 Hz, 1H), 4.55 (d, *J* = 6.0 Hz, 2H), 2.08 (s, 2H), 1.90 (s, 3H). 0.96 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9, 134.8, 116.7, 74.1, 49.2, 31.5, 30.8, 17.1; HRMS (ESI) *m/z* calcd. for $C_{10}H_{19}N_2O$ $(M+H)^+$ 170.1542, found 170.1545. Less than 10% of the

corresponding *Z*-oxime isomer was observed.



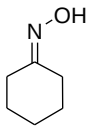
1p (*E*:*Z* = 1:3)

1p was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (1.2 g, 11 mmol) was treated with NaOAc (0.90 g, 11 mmol) and 4-methoxyphenylacetone (1.5 g, 10 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1p** was isolated as a a clear, colorless oil (0.68 g, 32%). ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.14-7.12 (m, 2H), 6.86-6.83 (m, 2H), 6.03-5.99 (m, 1H), 5.32 (d, *J* = 18.0 Hz, 1H), 5.21 (d, *J* = 12.0 Hz, 1H), 4.60 (m, 2H), 3.79 (s, 3H), 3.41 (s, 2H), 1.76 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 157.2, 130.4, 130.0, 129.0, 116.97, 114.0, 74.3, 55.3, 34.7, 19.7. ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 3.80 (s, 3H), 3.64 (s, 2H), 1.78 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 157.0, 130.4, 130.1, 128.8, 117.04, 114.2; HRMS (ESI) *m/z* calcd. for $C_{13}H_{18}NO_2(M+H)^+$ 220.1338, found 220.1333.



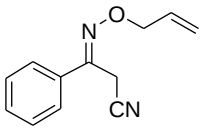
1q

1q was synthesized S_{N2} reaction from the corresponding oxime **1qk** and allyl bromide. as a white solid (280 mg, 59 %). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94-6.02 (m, 1H), 5.27 (d, *J* = 19 Hz, 1H), 5.17 (d, *J* = 11.5 Hz, 1H), 4.51 (d, *J* = 5.5 Hz, 2H), 2.46-2.48 (m, 2H), 2.18-2.20 (m, 2H), 1.58-1.70 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 134.7, 116.9, 74.0, 32.2, 27.0, 25.8, 25.7, 25.4; HRMS (ESI) *m/z* calcd. for $C_9H_{16}NO$ $(M+H)^+$ 154.1232, found 154.1234. Only the *E*-oxime isomer was observed.



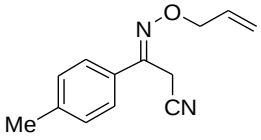
1qk

1qk was synthesized according to general procedure **A**. Hydroxylamine hydrochloride (3.1 g, 44 mmol) was treated with NaOAc (3.6 g, 44 mmol) and cyclohexanone (4.0 g, 40 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **1qk** was isolated as a clear, colorless oil (4.0 g, 89 %). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.55-2.52 (m, 2H), 2.24-2.22 (m, 2H), 1.72-1.60 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 32.1, 26.9, 25.8, 25.6, 24.5. Compound **1qk** was then used without further purification to form **1q**.



3a

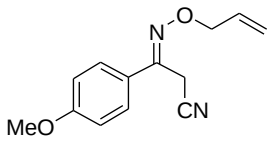
3a was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.60 g, 5.5 mmol) was treated with NaOAc (0.68 g, 8.2 mmol) and benzoylacetonitrile (0.72 g, 4.9 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **3a** was isolated as a clear, colorless oil (0.810 g, 82%). ^{1}H NMR (500 MHz, CDCl3) δ 7.67−7.65 (m, 2H), 7.39-7.36 (m, 3H), 6.09-7.06 (m, 1H), 5.38 (dd, *J* = 17.0 Hz, *J* = 1.0 Hz, 1H), 5.29 (dd, *J* = 10.5 Hz, *J* = 1.0 Hz, 1H), 4.79 (d, *J* = 5.5 Hz, 2H), 3.81 (s, 2H); ^{13}C NMR (125 MHz, CDCl3) δ 146.5, 133.5, 133.3, 130.2, 128.9, 126.2, 118.4, 115.0, 76.0, 15.3; HRMS (ESI) *m/z* calcd. for $C_{12}H_{13}N_2O$ $(M+H)^+$ 201.1028, found 201.1027. Less than 10% of the corresponding *Z*-oxime isomer was observed.



3b

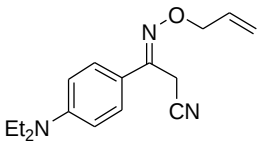
3b was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.76 g, 6.9 mmol) was treated with NaOAc (0.57 g, 6.9 mmol) and 4-toluoylacetonitrile (1.0 g, 6.3 mmol). The reaction mixture was allowed to stir for 24

h. After workup, **3b** was isolated as a clear, colorless oil (1.2 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55-7.53 (m, 2H), 7.23-7.22 (m, 2H), 6.09-6.03 (m, 1H), 5.38 (d, *J* = 18.0 Hz, 1H), 5.27 (d, *J* = 12.0 Hz, 1H), 4.78 (d, *J* = 6.0 Hz, 2H), 3.79 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 140.5, 133.6, 130.4, 129.6, 126.1, 118.3, 115.2, 75.9, 21.4, 15.2; HRMS (ESI) *m/z* calcd. for $C_{13}H_{15}N_2O$ $(M+H)^+$ 215.1184, found 215.1188. Less than 10% of the corresponding *Z*-oxime isomer was observed.



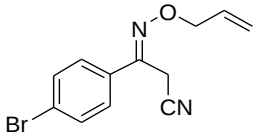
3c

3c was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.606 g, 5.53 mmol) was treated with NaOAc (0.454 g, 5.53 mmol) and 4-methoxybenzoylacetonitrile (0.876 g, 5.01 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **3c** was isolated as a clear, colorless oil (0.997 g, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 6.94-6.92 (m, 2H), 6.06-6.02 (m, 1H), 5.37 (d, *J* = 18.0 Hz, 1H), 5.27 (d, *J* = 12.0 Hz, 1H), 4.76 (d, *J* = 8.0 Hz, 2H), 3.83 (s, 3H), 3.78 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2, 146.1, 133.6, 127.6, 125.7, 118.3, 115.3, 114.2, 75.8, 55.4, 15.2; HRMS (ESI) *m/z* calcd. for $C_{13}H_{15}N_2O_2$ $(M+H)^+$ 231.1134, found 231.1127. Less than 5% of the corresponding *Z*-oxime isomer was observed.



3d

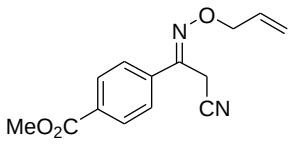
3d: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54-7.52 (m, 2H), 6.68-6.66 (m, 2H), 6.10-6.05 (m, 1H), 5.38 (d, *J* = 18.0 Hz, 1H), 5.28 (d, *J* = 10.5 Hz, 1H), 3.79 (s, 2H), 3.41 (q, *J* = 7.0 Hz, 2H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 146.5, 133.9, 127.4, 119.5, 117.8, 115.6, 111.2, 75.5, 44.4, 14.8, 12.5; HRMS (ESI) *m/z* calcd. for $C_{16}H_{22}N_3O$ $(M+H)^+$ 272.1763, found 272.1760. Less than 10% of the corresponding *Z*-oxime isomer was observed.



3e

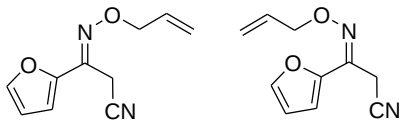
3e was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.606 g, 5.53 mmol) was treated with NaOAc (0.454 g, 5.53 mmol) and (4-bromobenzoyl)acetonitrile (1.12 g, 5.00 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **3e** was isolated as a clear, colorless oil (1.24 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54-7.56 (m, 2H), 7.51-7.53 (m, 2H), 6.01-6.07 (m, 1H), 5.37 (d, *J* = 18.0 Hz, 1H), 5.28 (d, *J* = 12.0 Hz, 1H), 4.78 (d, *J* = 6.0 Hz, 2H), 3.78 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.6, 133.3, 132.1 (2C), 127.7, 124.7, 118.6,

114.9, 76.2, 15.0; HRMS (ESI) *m/z* calcd. for $C_{12}H_{12}N_2OBr$ $(M+H)^+$ 279.0133, found 279.0142. Less than 5% of the corresponding *Z*-oxime isomer was observed.



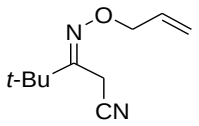
3f

3f was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.606 g, 5.53 mmol) was treated with NaOAc (0.454 g, 5.53 mmol) and methyl 4-(cyanoacetyl)benzoate (1.01 g, 5.0 mmol). The reaction mixture was allowed to stir for 24 h. After workup, **3f** was isolated as a white solid (0.963 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09-8.07 (m, 2H), 7.74-7.72 (m, 2H), 6.06-6.02 (m, 1H), 5.38 (d, *J* = 18.0 Hz, 1H), 5.29 (d, *J* = 12.0 Hz, 1H), 4.81 (d, *J* = 6.0 Hz, 2H), 3.94 (s, 3H), 3.83 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 145.7, 137.2, 133.2, 131.5, 130.0, 126.1, 118.7, 114.7, 76.4, 52.4, 15.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{15}N_2O_3$ $(M+H)^+$ 259.1083, found 259.1086. Less than 5% of the corresponding *Z*-oxime isomer was observed.



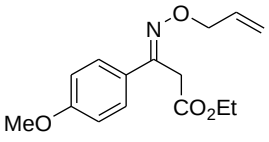
3g (*E*:*Z* = 1:2)

3g was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.41 g, 3.7 mmol) was treated with NaOAc (0.33 g, 4.1 mmol) and 2-furoylacetonitrile (0.50 g, 3.7 mmol). The reaction mixture was allowed to stir at 60 ℃ for 12 h. After workup, **3g** was isolated as a clear, colorless oil (0.530 g, 75%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 7.55−7.54 (m, 1H), 6.84-6.83 (m, 1H), 6.53-6.52 (m, 1H), 6.10-6.04 (m, 1H), 5.40 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.30 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.79 (m, 2H), 3.76 (s, 2H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 147.2, 144.6, 139.2, 133.2, 118.6, 114.7, 112.0, 111.1, 76.3, 14.6; ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 7.54−7.53 (m, 1H), 7.42-7.41 (m, 1H), 6.59-6.58 (m, 1H), 6.10-6.04 (m, 1H), 5.38 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.30 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.79 (m, 2H), 3.73 (s, 2H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 143.8, 143.4, 137.3, 133.5, 119.0, 118.4, 115.8, 112.7, 76.5, 20.9; HRMS (ESI) *m/z* calcd. for $C_{10}H_{11}N_2O_2$ $(M+H)^+$ 191.0822, found 191.0821.



3h

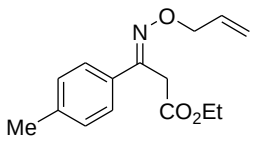
3h was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.24 g, 2.2 mmol) was treated with NaOAc (0.25 g, 3.0 mmol) and 4,4-dimethyl-3-oxopentanenitrile (0.26 g, 2.1 mmol). The reaction mixture was allowed to stir at 60 ℃ for 12 h. After workup, **3h** was isolated as a clear, colorless oil (0.31 g, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.00-5.94 (m, 1H), 5.29 (dd, *J* = 17.0 Hz, *J* = 1.0 Hz, 1H), 5.18 (dd, *J* = 10.5 Hz, *J* = 1.0 Hz, 1H), 4.60 (d, *J* = 6.0 Hz, 2H), 3.25 (s, 2H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 133.8, 117.6, 115.5, 75.1, 37.3, 27.3, 13.4; HRMS (ESI) *m/z* calcd. for $C_{10}H_{17}N_2O$ $(M+H)^+$ 181.1341, found 181.1340. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1ja

1ja was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.526 g, 4.83 mmol) was treated with NaOAc (0.393 g, 4.79 mmol) and ethyl 3-(4-methoxyphenyl)-3-oxopropionate (0.889 g, 4.00 mmol). The reaction mixture was allowed to stir for 24 h at 60 °C. After workup, **1ja** was isolated as a clear

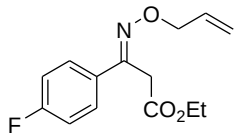
colorless liquid (1.10 g, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60-7.58 (m, 2H), 6.90-6.88 (m, 2H), 6.04-5.98 (m, 1H), 5.31 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.21 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.70 (d, *J* = 5.5 Hz, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 3.75 (s, 2H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 160.6, 151.1, 134.2, 128.0, 127.6, 117.2, 113.9, 75.1, 61.1, 55.3, 33.4, 14.1; HRMS (ESI) *m/z* calcd. for $C_{15}H_{20}NO_4$ $(M+H)^+$ 278.1392, found 278.1395. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1jb

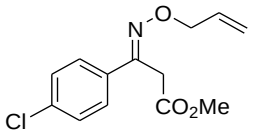
1jb was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.637 g, 5.81 mmol) was treated with NaOAc (0.477 g, 5.81 mmol) and ethyl (4-methylbenzoyl) acetate (1.00 g, 4.85 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jb** was isolated asa clear colorless liquid (1.20 g, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55-7.53 (m, 2H), 7.19-7.17 (m, 2H), 6.05-5.99 (m, 1H), 5.33 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.71 (d, *J* = 5.5 Hz, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.77 (s, 2H), 2.36 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 151.5, 139.4, 134.2,

132.6, 129.2, 126.2, 117.2, 75.2, 61.1, 33.4, 21.3, 14.1; HRMS (ESI) *m/z* calcd. for $C_{15}H_{20}NO_3$ $(M+H)^+$ 262.1443, found 262.1441. Less than 10% of the corresponding *Z*-oxime isomer was observed.



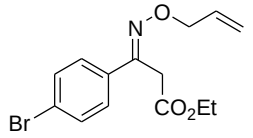
1jc

1jc was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.625 g, 5.70 mmol) was treated with NaOAc (0.468 g, 5.70 mmol) and ethyl (4-fluorobenzoyl) acetate (1.00 g, 4.76 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jc** was isolated as a clear colorless liquid (1.08 g, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64-7.61 (m, 2H), 7.07-7.04 (m, 2H), 6.04-5.98 (m, 1H), 5.32 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.71 (d, *J* = 5.5 Hz, 2H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.76 (s, 2H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 163.5 (d, $J_{C\text{-}F}$ = 247.5 Hz), 150.6, 134.0, 131.6, 128.2, 117.4, 115.6, 75.3, 61.2, 33.4, 14.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{17}NO_3F$ $(M+H)^+$ 266.1192, found 266.1194. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1jd

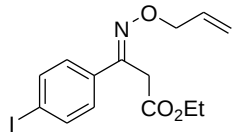
1jd was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.624 g, 5.70 mmol) was treated with NaOAc (0.468 g, 5.70 mmol) and methyl (4-chlorobenzoyl) acetate (1.01 g, 4.46 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jd** was isolated as a clear colorless liquid (1.15 g, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59-7.57 (m, 2H), 7.35-7.33 (m, 2H), 6.03-5.98 (m, 1H), 5.31 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.72 (d, *J* = 5.5 Hz, 2H), 3.77 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 150.3, 135.5, 134.0, 133.7, 128.8, 127.5, 117.6, 75.5, 52.3, 32.8; HRMS (ESI) *m/z* calcd. for $C_{13}H_{15}NO_3Cl$ $(M+H)^+$ 268.0740, found 268.0740. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1je

1je was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.485 g, 4.43 mmol) was treated with NaOAc (0.363 g, 4.42 mmol) and

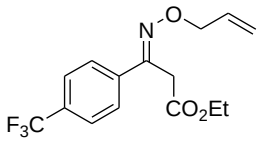
ethyl (4-bromobenzoyl) acetate (1.00 g, 3.69 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1je** was isolated as a clear colorless liquid (0.916 g, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.48 (m, 4H), 6.03-5.98 (m, 1H), 5.32 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.72 (d, *J* = 5.5 Hz, 2H), 4.14 (q, *J* = 7.5 Hz, 2H), 3.75 (s, 2H), 1.21 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 150.6, 134.3, 133.9, 131.7, 127.8, 123.7, 117.5, 75.5, 61.2, 33.1, 14.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{17}NO_3Br$ $(M+H)^+$ 326.0392, found 326.0395. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1jf

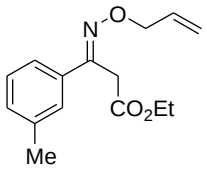
1jf was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.413 g, 3.77 mmol) was treated with NaOAc (0.309 g, 3.77 mmol) and ethyl (4-iodobenzoyl) acetate (1.00 g, 3.14 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jf** was isolated as a clear colorless liquid (0.874 g, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.69 (m, 2H), 7.38-7.37 (m, 2H), 6.04-5.96 (m, 1H), 5.32 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.71 (d, *J* = 5.5 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 3.74 (s, 2H), 1.21 (t, *J* = 7.0 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 150.7, 137.7, 134.9, 133.9, 127.9, 117.5, 95.6, 75.5, 61.2, 33.0, 14.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{17}NO_3I$ $(M+H)^+$ 374.0253, found 374.0257. Less than 10% of the corresponding *Z*-oxime isomer was observed.



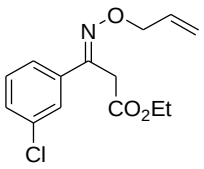
1jg

1jg was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.394 g, 3.60 mmol) was treated with NaOAc (0.295 g, 3.60 mmol) and methyl (4-trifluoromethylbenzoyl) acetate (0.738 g, 3.00 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jg** was isolated asa clear colorless liquid (0.839 g, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77-7.76 (m, 2H), 7.63-7.61 (m, 2H), 6.05-5.98 (m, 1H), 5.33 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.24 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.74 (d, *J* = 5.5 Hz, 2H), 3.81 (s, 2H), 3.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 150.1, 138.7, 133.8, 131.1 (q, J_{C-F} = 32.5 Hz), 126.5, 125.5, 123.9 (d, J_{C-F} = 271.2 Hz), 117.7, 75.7, 52.3, 32.7; HRMS (ESI) *m/z* calcd. For $C_{14}H_{15}NO_3F_3$ $(M+H)^+$ 302.1004, found 302.1001. Less than 10% of the corresponding *Z*-oxime isomer was observed.



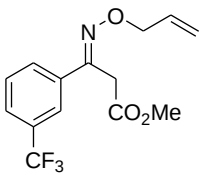
1jh

1jh was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.637 g, 5.81 mmol) was treated with NaOAc (0.477 g, 5.81 mmol) and ethyl (3-methylbenzoyl) acetate (1.00 g, 4.85 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jh** was isolated as a clear colorless liquid (1.01 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.42-7.41 (m, 1H), 7.27-7.25 (m, 1H), 7.19-7.18 (m, 1H), 6.05-5.99 (m, 1H), 5.33 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.72 (d, *J* = 5.5 Hz, 2H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.77 (s, 2H), 2.37 (s, 3H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 151.8, 138.2, 135.4, 134.1, 130.2, 128.4, 126.9, 123.5, 117.3, 75.3, 61.1, 33.6, 21.5, 14.1; HRMS (ESI) *m/z* calcd. for $C_{15}H_{20}NO_3$ $(M+H)^+$ 262.1443, found 262.1444. Less than 10% of the corresponding *Z*-oxime isomer was observed.



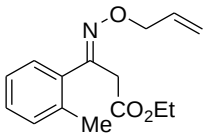
1ji

1ji was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.580 g, 5.29 mmol) was treated with NaOAc (0.434 g, 5.29 mmol) and ethyl (3-chlorobenzoyl) acetate (1.00 g, 4.41 mmol). The reaction mixture was allowed to stir for 24 h at 60 °C. After workup, **1ji** was isolated as a clear colorless liquid (1.13 g, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.51-7.48 (m, 1H), 7.35-7.28 (m, 2H), 6.05-5.98 (m, 1H), 5.33 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.73 (d, *J* = 5.5 Hz, 2H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.75 (s, 2H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 150.4, 137.2, 134.6, 133.9, 129.8, 129.4, 126.4, 124.4, 117.6, 75.5, 61.2, 33.2, 14.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{17}NO_3Cl$ $(M+H)^+$ 282.0897, found 282.0896. Less than 10% of the corresponding *Z*-oxime isomer was observed.



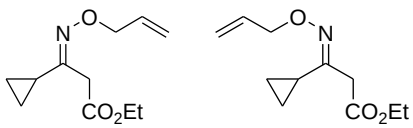
1jj

1jj was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.505 g, 4.61 mmol) was treated with NaOAc (0.378 g, 4.61 mmol) and ethyl (3-trifluoromethylbenzoyl) acetate (1.00 g, 3.84 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jj** was isolated as a clear colorless liquid (1.04 g, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.82-7.81 (m, 1H), 7.63-7.61 (m, 1H), 7.51-7.48 (m, 1H), 6.05-5.99 (m, 1H), 5.33 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.23 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.75 (d, *J* = 5.5 Hz, 2H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.80 (s, 2H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 150.3, 136.2, 133.8, 131.0 (q, $J_{C\text{-}F}$ = 32.5 Hz), 129.5, 129.1, 125.9, 124.0 (d, $J_{C\text{-}F}$ = 271.2 Hz), 123.1, 117.7, 75.6, 61.3, 33.2, 14.0; HRMS (ESI) *m/z* calcd. For $C_{15}H_{17}NO_3F_3$ $(M+H)^+$ 316.1161, found 316.1160. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1jk

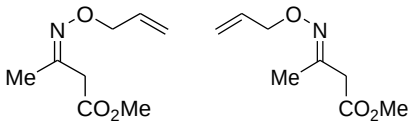
1jk was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.637 g, 5.81 mmol) was treated with NaOAc (0.477 g, 5.81 mmol) and ethyl (2-methylbenzoyl) acetate (1.00 g, 4.85 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jk** was isolated as a clear colorless liquid (1.07 g, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.19 (m, 4H), 6.04-5.98 (m, 1H), 5.33 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.23 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.69 (d, *J* = 5.5 Hz, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 3.67 (s, 2H), 2.41 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 153.1, 136.4, 135.7, 134.2, 130.8, 128.8, 128.6, 125.8, 117.3, 75.0, 61.0, 36.6, 20.2, 14.0; HRMS (ESI) *m/z* calcd. for $C_{15}H_{20}NO_3$ $(M+H)^+$ 262.1443, found 262.1439. Less than 10% of the corresponding *Z*-oxime isomer was observed.



1jl (*E*:*Z* = 5:1)

1jl was synthesized according to general procedure **A**. Allylhydroxylamine

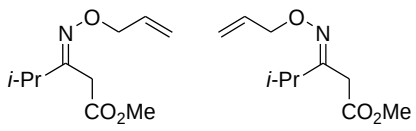
hydrochloride (0.842 g, 7.69 mmol) was treated with NaOAc (0.630 g, 7.68 mmol) and ethyl-3-cyclopropyl-3-oxopropionate (1.00 g, 6.40 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jl** was isolated as a clear colorless liquid (1.22 g, 90%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 5.95-5.89 (m, 1H), 5.23 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.15 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.51 (d, *J* = 5.5 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 3.17 (s, 2H), 1.63-1.58 (m, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 0.75 (d, *J* = 1.0 Hz, 4H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 168.9, 154.6, 134.3, 116.9, 74.5, 60.9, 33.4, 14.6, 14.1, 5.0; ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 6.03-5.96 (m, 1H), 5.29 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.19 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.59 (d, *J* = 5.5 Hz, 2H), 4.13 (q, *J* = 7.0 Hz, 2H), 2.90 (s, 2H), 2.34-2.28 (m, 1H), 1.24 (t, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 1.0 Hz, 2H), 0.70 (d, *J* = 1.0 Hz, 2H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 169.7, 155.4, 134.4, 117.1, 74.7, 61.1, 35.9, 14.1, 9.6, 5.1; HRMS (ESI) *m/z* calcd. for $C_{11}H_{18}NO_3$ $(M+H)^+$ 212.1287, found 212.1286.



1jm (*E*:*Z* = 1:1)

1jm was synthesized according to general procedure **A**. Allylhydroxylamine

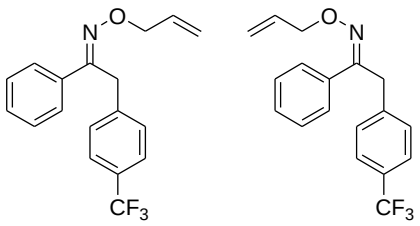
hydrochloride (0.606 g, 5.53 mmol) was treated with NaOAc (0.454 g, 5.53 mmol) and methyl acetoacetate (0.581 g, 5.00 mmol). The reaction mixture was allowed to stir for 24 h at 60 ℃. After workup, **1jm** was isolated as a clear colorless liquid (0.674 g, 79%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 5.99-5.93 (m, 1H), 5.26 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.18 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz,1H), 4.56 (d, *J* = 5.5 Hz, 2H), 3.71 (s, 3H), 3.22 (s, 2H), 1.94 (s, 3H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 170.1, 151.6, 134.3, 117.2, 74.6, 52.1, 41.2, 14.6; ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 5.99-5.93 (m, 1H), 5.28 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.20 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.54 (d, *J* = 5.5 Hz, 2H), 3.70 (s, 3H), 3.36 (s, 2H), 1.97 (s, 3H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 169.3, 150.5, 134.3, 117.0, 74.4, 41.2, 35.2, 20.6; HRMS (ESI) *m/z* calcd. for $C_8H_{14}NO_3$ $(M+H)^+$ 172.0974, found 172.0974.



1jn (*E*:*Z* = 3:1)

1jn was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.526 g, 4.80 mmol) was treated with NaOAc (0.394 g, 4.80 mmol) and methyl 4-methyl-3-oxovalerate (0.736 g, 4.00 mmol). The reaction mixture was

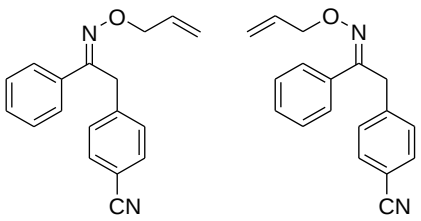
allowed to stir for 24 h at 60 ℃. After workup, **1jn** was isolated as a clear colorless liquid (0.605 g, 76%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 5.96-5.88 (m, 1H), 5.23 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.15 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.51 (d, *J* = 5.5 Hz, 2H), 3.69 (s, 3H), 3.23 (s, 2H), 2.61-2.56 (m, 1H), 1.10 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 169.6, 158.0, 134.3, 116.8, 74.4, 52.0, 33.7, 32.3, 19.6; ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 6.00-5.95 (m, 1H), 5.27 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.20 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.55 (d, *J* = 5.5 Hz, 2H), 3.70 (s, 3H), 3.35-3.30 (m, 1H), 3.17 (s, 2H), 2.61-2.56 (m, 1H), 1.06 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 170.5, 159.2, 134.4, 117.0, 74.6, 52.1, 36.7, 72.4, 18.8; HRMS (ESI) *m/z* calcd. for $C_{10}H_{18}NO_3$ $(M+H)^+$ 200.1287, found 200.1285.



1ia (*E*:*Z* = 3:1)

1ia was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.082 g, 0.75 mmol) was treated with NaOAc (0.092 g, 1.1 mmol) and ketone[36, 37] (0.20 g, 0.75 mmol). The reaction mixture was allowed to stir at 60 ℃ for

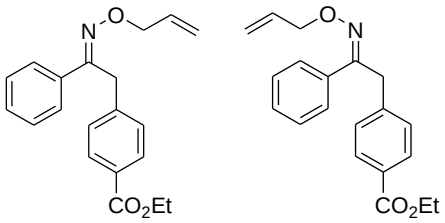
24 h. After workup, **1ia** was isolated as a clear, colorless oil (0.16 g, 68%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 7.98-7.94 (m, 2H), 7.66-7.64 (m, 2H), 7.35-7.28 (m, 5H), 6.08-6.00 (m, 1H), 5.32 (d, *J* = 18.0 Hz, 1H), 5.24 (d, *J* = 10.5 Hz, 1H), 4.76 (d, *J* = 5.5 Hz, 2H), 4.22 (s, 2H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 155.4, 141.0, 135.3, 134.4, 134.2, 129.6, 128.9, 128.8, 128.2, 126.4, 117.8, 75.4, 32.9 (the CF_3 resonance was not observed due to ^{19}F splitting); ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 7.98-7.94 (m, 2H), 7.66-7.64 (m, 2H), 7.35-7.28 (m, 5H), 6.08-6.00 (m, 1H), 5.32 (d, *J* = 18.0 Hz, 1H), 5.24 (d, *J* = 10.5 Hz, 1H), 4.63 (d, *J* = 5.5 Hz, 2H), 3.91 (s, 2H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 155.4, 141.0, 135.3, 134.4, 134.2, 129.6, 128.9, 128.8, 128.2, 125.4, 117.2, 75.0, 41.5 (the CF_3 resonance was not observed due to ^{19}F splitting); HRMS (ESI) *m/z* calcd. for $C_{18}H_{16}F_3NO$ $(M+H)^+$ 320.1262, found 320.1255.



1ib (*E*:*Z* = 3:1)

1ib was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.061 g, 0.57 mmol) was treated with NaOAc (0.062 g, 0.76 mmol) and

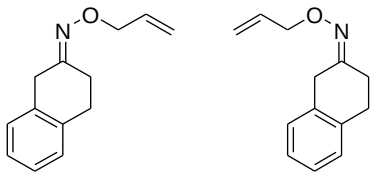
ketone[37, 38] (0.11 g, 0.50 mmol). The reaction mixture was allowed to stir at 60 ℃ for 24 h. After workup, **1ib** was isolated as a clear, colorless oil (0.11 g, 79%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 7.62-7.60 (m, 2H), 7.55-7.52 (m, 2H), 7.35-7.28 (m, 5H), 6.05-5.99 (m, 1H), 5.30 (d, *J* = 16.0 Hz, 1H), 5.23 (d, *J* = 11.5 Hz, 1H), 4.74 (d, *J* = 6.0 Hz, 2H), 4.21 (s, 2H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 117.8, 75.4, 32.9; ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 7.62-7.60 (m, 2H), 7.55-7.52 (m, 2H), 7.35-7.28 (m, 5H), 6.05-5.99 (m, 1H), 5.30 (d, *J* = 16.0 Hz, 1H), 5.23 (d, *J* = 11.5 Hz, 1H), 4.13 (d, *J* = 5.5 Hz, 2H), 3.91 (s, 2H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 117.3, 75.1, 41.8; HRMS (ESI) *m/z* calcd. for $C_{18}H_{16}N_2O$ $(M+H)^+$ 277.1341, found 277.1345.



1ic (*E*:*Z* = 3:1)

1ic was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.128 g, 1.17 mmol) was treated with NaOAc (0.131 g, 1.60 mmol) and ketone[37,39] (0.285 g, 1.06 mmol). The reaction mixture was allowed to stir at 60 ℃ for 24 h. After workup, **1ic** was isolated asa clear, colorless oil (0.271 g, 79%). ^{1}H NMR

of *E*-imine isomer (500 MHz, $CDCl_3$) δ 7.98-7.94 (m, 2H), 7.66-7.64 (m, 1H), 7.35-7.28 (m, 6H), 6.09-6.02 (m, 1H), 5.34 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.25 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.78 (d, *J* = 5.5 Hz, 2H), 4.36 (q, *J* = 7.0 Hz, 2H), 4.24 (s, 2H), 1.38 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 166.5, 155.6, 142.2, 134.3, 133.5, 133.3, 130.2, 128.9, 126.2, 118.4, 115.0, 117.6, 75.3, 60.8, 32.9, 14.4; ^{1}H NMR of *Z*-imine isomer (500 MHz, $CDCl_3$) δ 7.98-7.94 (m, 2H), 7.66-7.64 (m, 1H), 7.35-7.28 (m, 6H), 6.09-6.02 (m, 1H), 5.34 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 5.25 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.65 (d, *J* = 5.5 Hz, 2H), 4.36 (q, *J* = 7 Hz, 2H), 3.92 (s, 2H), 1.38 (t, *J* = 7 Hz, 3H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 166.5, 155.6, 142.2, 134.5, 133.5, 133.3, 130.2, 128.9, 126.2, 118.4, 117.2, 75.0, 60.9, 41.8, 14.4; HRMS (ESI) *m/z* calcd. for $C_{20}H_{21}NO_3$ $(M+H)^+$ 324.1600, found 324.1599.



1id (*E*:*Z* = 1:1)

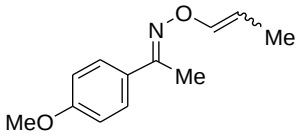
1id was synthesized according to general procedure **A**. Allylhydroxylamine hydrochloride (0.899 g, 8.21 mmol) was treated with NaOAc (0.673 g, 8.21 mmol) and β-Tetralone (1.00 g, 6.84 mmol). The reaction mixture was allowed to stir at 60 ℃ for

24 h. After workup, **1id** was isolated as a light orange liquid (1.25 g, 91%). ^{1}H NMR of *E*-imine isomer (500 MHz, $CDCl_3$) δ 7.22-7.15 (m, 4H), 6.10-5.99 (m, 1H), 5.36 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.22 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.58 (d, *J* = 5.5 Hz, 2H), 3.54 (s, 2H), 2.85 (t, *J* = 7.0 Hz, 2H), 2.72 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR of *E*-imine isomer (125 MHz, $CDCl_3$) δ 158.7, 138.4, 134.6, 133.4, 128.9, 127.6, 126.7, 126.6, 117.3, 74.6, 35.1, 29.1, 27.7; ^{1}H NMR of Z-imine isomer (500 MHz, $CDCl_3$) δ 7.22-7.15 (m, 4H), 6.10-5.99 (m, 1H), 5.32 (dd, *J* = 17.0 Hz, *J* = 1.5 Hz, 1H), 5.26 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.64 (d, *J* = 5.5 Hz, 2H), 3.83 (s, 2H), 2.91 (t, *J* = 7.0 Hz, 2H), 2.59 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR of *Z*-imine isomer (125 MHz, $CDCl_3$) δ 158.1, 137.1, 135.0, 134.7, 128.2, 127.3, 126.6, 126.2, 117.1, 74.5, 35.1, 29.4, 24.9; HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}NO$ $(M+H)^+$ 202.1232, found 202.1230.

1.10.2 Preparation of *O*-Vinyl Oximes

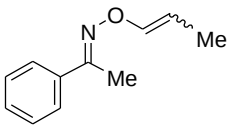
General Procedure B: In an inert atmosphere drybox, a 20 mL scintillation vial was charged with 0.5 equiv of $[(cod)IrCl]_2$, 1 equiv AgOTf, 1 equiv $NaBH_4$ or 1 equiv $LiAlH_4$, and 3 mL of THF. This mixture was then allowed to stir at 25 ℃ for 20 min. *O*-Allyl oxime **1** (10 equiv) was mixed with 2 mL of THF in a small vial. The oxime solution was then transferred to the scintillation vial containing the 10 mol % iridium mixture. The reaction mixture was then allowed to stir at 25 ℃ for 18-36 h. After

stirring, an aliquot of the crude reaction mixture was removed from the scintillation vial and removed from the glovebox. The solvent was removed from the aliquot under vacuum on a high vacuum line and then the crude mixture was checked by ^{1}H NMR spectroscopy to determine if the reaction had gone to completion and to determine the *E*:*Z* ratio of the vinyl group of the *O*-vinyl oxime product by comparison of the integrations of the terminal vinyl protons of the *E*- and *Z*-isomers. This ^{1}H NMR spectrum was used to determined the *E*:*Z* vinyl oxime ratio before purification by chromatography. Once ^{1}H NMR spectroscopy had been used to verify that the isomerization reaction had gone to completion, the reaction mixture was removed from the glovebox and dry-loaded onto ~ 3 mL of silica. The crude product was purified by flash chromatography using a gradient eluent of 2% TEA/hexanes – 2/% TEA/ 2% EtOAc/ hexanes. The fractions containing **2** were combined, the solvent was removed under vacuum using a rotary evaporator, and then the product was transferred to a scintillation vial and all remaining volatiles were removed under high vacuum for a minimum of 10 min. Compounds **2b** was analyzed by 1D ^{1}H-^{1}H NOE spectroscopy to determine which proton resonances corresponded to the *E*- and *Z*-vinyl isomers of the product and which proton resonances corresponded to the *E*- and *Z*-oxime isomers of the product (see details below). All other isomeric assignments were determined by comparison to the data for **2b**.



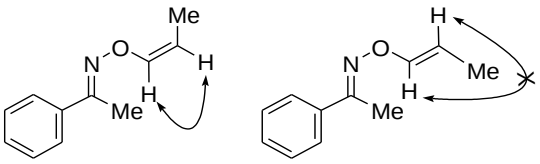
2a (*E*:*Z* = 1:2.4)

2a was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23 mg, 0.034 mmol), AgOTf (18 mg, 0.069 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1a** (131 mg, 0.640 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2a** was isolated as a clear colorless oil (117 mg, 89%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.64-7.61 (m, 2H), 6.91-6.88 (m, 3H), 5.25-5.18 (m, 1H), 3.83 (s, 3H), 2.27 (s, 3H), 1.63 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 156.1, 147.6, 128.5, 128.4, 113.8, 100.4, 55.3, 13.1, 12.3; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.64-7.61 (m, 2H), 6.91-6.88 (m, 3H), 4.52-4.49 (m, 1H), 3.83 (s, 3H), 2.32 (s, 3H), 1.69 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 156.1, 147.1, 128.5, 128.4, 113.8, 99.2, 55.3, 13.1, 9.6; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_2$ $(M+H)^+$ 206.1181, found 206.1175.

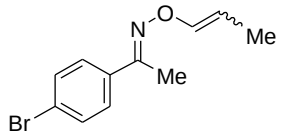


2b (*E*:*Z* = 1:1.7)

2b was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23 mg, 0.034 mmol), AgOTf (18 mg, 0.069 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1b** (125 mg, 0.714 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2b** was isolated as a clear colorless oil (95 mg, 76%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.69-7.66 (m, 2H), 7.54-7.51 (m, 3H), 6.93-6.88 (m, 1H), 5.30-5.21 (m, 1H), 2.35 (s, 3H), 1.69 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 147.6, 135.9, 129.5, 128.5, 126.3, 100.7, 13.2, 12.4; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.69-7.66 (m, 2H), 7.54-7.51 (m, 3H), 6.93-6.88 (m, 1H), 4.55-4.50 (m, 1H), 2.29 (s, 3H), 1.65 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 156.6, 147.0, 135.9, 129.5, 128.5, 126.3, 99.5, 13.3, 9.6; HRMS (ESI) *m/z* calcd. for $C_{11}H_{14}NO$ $(M+H)^+$ 176.1075, found 176.1068.

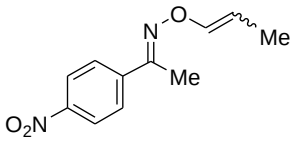


1D ^{1}H-^{1}H NOE spectrum: When the vinyl resonance at 6.90 ppm was selected, the vinyl resonances at 4.53 ppm was inverted. These interactions are illustrated in the structure above and indicate that the structure is the *Z*- configuration for compound **2b**.



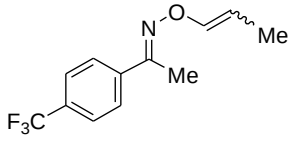
2c (*E*:*Z* = 1:2.7)

2c was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1c** (170 mg, 0.672 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2c** was isolated as a clear colorless oil (131 mg, 77%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.51-7.49 (m, 2H), 6.90-6.88 (m, 1H), 5.26-5.23 (m, 1H), 2.27 (s, 3H), 1.63 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 147.4, 134.8, 131.6, 127.8, 123.8, 101.1, 13.0, 12.3; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.51-7.49 (m, 2H), 6.90-6.88 (m, 1H), 4.55-4.52 (m, 1H), 2.32 (s, 3H), 1.68 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 146.9, 134.8, 131.6, 127.8, 123.8, 99.9, 13.0, 9.6; HRMS (ESI) *m/z* calcd. for $C_{11}H_{13}NOBr$ $(M+H)^+$ 254.0181, found 254.0171.



2d (*E*:*Z* = 1:2.7)

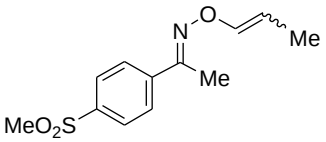
2d was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (45 mg, 0.067 mmol), AgOTf (34 mg, 0.13 mmol), and $NaBH_4$ (5.0 mg, 0.13 mmol) in THF for 15 min. Allyl oxime ether **1d** (290 mg, 1.32 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2d** was isolated as a clear colorless oil (255 mg, 88%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 8.20-8.18 (m, 2H), 7.84-7.82 (m, 2H), 6.91-6.90 (m, 1H), 5.29-5.25 (m, 1H), 2.31 (s, 3H), 1.64 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 148.2, 147.0, 141.8, 127.0, 123.6, 101.8, 12.2, 9.6; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 8.20-8.18 (m, 2H), 7.84-7.82 (m, 2H), 6.91-6.90 (m, 1H), 4.59-4.56 (m, 1H), 2.36 (s, 3H), 1.68 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.4, 147.4, 146.8, 141.8, 127.0, 123.6, 100.6, 12.9, 9.6; HRMS (ESI) *m/z* calcd. for $C_{11}H_{13}N_2O_3$ $(M+H)^+$ 221.0926, found 221.0933.



2e (*E*:*Z* = 1:3.8)

2e was synthesized according to general procedure **B**. The catalyst mixture was

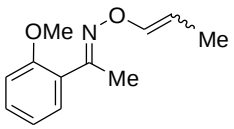
prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1e** (174 mg, 0.716 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2e** was isolated as a clear colorless oil (136 mg, 78%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.80-7.78 (m, 2H), 7.64-7.63 (m, 2H), 6.93-6.91 (m, 1H), 5.26 (m, 1H), 2.32 (s, 3H), 1.64 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 147.7, 139.5, 131.3 (q, $J_{C\text{-}F}$ = 33 Hz), 126.8, 125.3, 125.2 (q, $J_{C\text{-}F}$ = 245 Hz), 101.6, 12.5, 9.8; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.80-7.78 (m, 2H), 7.64-7.63 (m, 2H), 6.93-6.91 (m, 1H), 4.58-4.55 (m, 1H), 2.36 (s, 3H), 1.70 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 147.1, 139.5, 131.3 (q, $J_{C\text{-}F}$ = 33 Hz), 126.8, 125.6, 125.2 (q, $J_{C\text{-}F}$ = 245 Hz), 100.4, 13.3, 9.8; HRMS (ESI) *m/z* calcd. for $C_{12}H_{13}NOF_3$ $(M+H)^+$ 244.0949, found 244.0955.



2f (*E*:*Z* = 1:2.2)

2f was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1f** (168 mg, 0.673 mmol) was then added to the catalyst mixture and the complete reaction

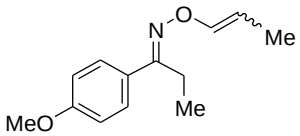
mixture was allowed to stir for 18 h. After column chromatography, **2f** was isolated as a clear colorless oil (139 mg, 82%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.95-7.93 (m, 2H), 7.87-7.85 (m, 2H), 6.92-6.90 (m, 1H), 5.30-5.23 (m, 1H), 3.05 (s, 3H), 2.32 (s, 3H), 1.63 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.7, 147.4, 141.2, 141.0, 127.6, 127.1, 101.7, 44.5, 12.2, 9.6; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.95-7.93 (m, 2H), 7.87-7.85 (m, 2H), 6.92-6.90 (m, 1H), 4.568-4.56 (m, 1H), 3.05 (s, 3H), 2.36 (s, 3H), 1.68 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.6, 146.8, 141.2, 141.0, 127.6, 127.1, 100.5, 44.5, 13.1, 9.6; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_3S(M+H)^+$ 254.0851, found 254.0853.



2g (*E*:*Z* = 1:1.4)

2g was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1g** (147 mg, 0.673 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2g** was isolated as a clear colorless oil (118 mg, 86%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.37-7.32 (m, 2H), 6.98-6.86 (m, 3H), 5.23-5.19 (m, 1H), 3.83 (s, 3H), 2.26 (s, 3H), 1.62 (d, *J* =

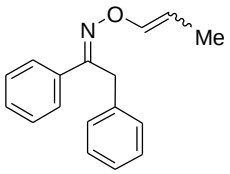
7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 157.5, 147.6, 130.5, 129.5, 126.3, 120.6, 111.1, 100.4, 55.5, 16.5, 9.6; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.37-7.32 (m, 2H), 6.98-6.86 (m, 3H), 4.50-4.48 (m, 1H), 3.83 (s, 3H), 2.31 (s, 3H), 1.70 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 157.5, 147.0, 130.5, 129.5, 126.2, 120.6, 111.1, 99.0, 55.5, 12.3, 9.6; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_2$ $(M+H)^+$ 206.1181, found 206.1183.



2h (*E*:*Z* = 1:2.9)

2h was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1h** (146 mg, 0.673 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2h** was isolated as a clear colorless oil (117 mg, 79%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.63-7.60 (m, 2H), 6.92-6.87 (m, 3H), 5.19-5.23 (m, 1H), 3.83 (s, 3H), 2.84-2.77 (q, *J* = 7.5 Hz , 2H), 1.62 (d, *J* = 8.5 Hz, 3H), 1.15 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 160.7, 147.6, 127.9, 127.3, 113.9, 100.3, 55.3, 20.5, 12.3, 11.2; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.63-7.60 (m, 2H), 6.92-6.87 (m, 3H),

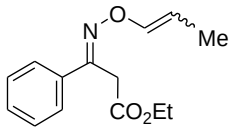
4.51-4.48 (m, 1H), 3.83 (s, 3H), 2.84-2.77 (q, *J* = 7.5 Hz , 2H), 1.68 (d, *J* = 8.5 Hz, 3H), 1.20 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.1, 160.7, 147.1, 127.9, 127.3, 113.9, 99.1, 55.3, 20.7, 11.2, 9.5; HRMS (ESI) *m/z* calcd. for $C_{13}H_{18}NO_2$ $(M+H)^+$ 220.1338, found 220.1328.



2i (*E*:*Z* = 1:2.3)

2i was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1i** (171 mg, 0.673 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2i** was isolated as a clear colorless oil (134 mg, 79%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.70-7.68 (m, 2H), 7.37-7.32 (m, 3H), 7.30-7.19 (m, 5H), 6.97-6.92 (m, 1H), 5.26-5.22 (m, 1H), 4.21 (s, 2H), 1.66-1.63 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.0, 147.4, 146.8, 136.4, 135.0, 129.6, 128.7, 128.5, 126.8, 126.5, 101.2, 33.4, 12.3; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.70-7.68 (m, 2H), 7.37-7.32 (m, 3H), 7.30-7.19 (m, 5H), 6.97-6.92 (m, 1H), 4.57-4.54 (m, 1H), 4.21 (s, 2H), 1.66-1.63 (m, 3H); ^{13}C NMR (125

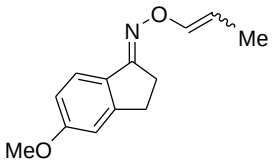
MHz, $CDCl_3$) δ 158.0, 147.4, 146.8, 136.3, 135.0, 129.6, 128.7, 128.5, 126.8, 126.5, 100.0, 33.2, 9.6; HRMS (ESI) *m/z* calcd. for $C_{17}H_{18}NO$ $(M+H)^+$ 252.1388, found 252.1384.



2j (*E*:*Z* = 1:2.9)

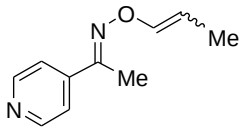
2j was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1j** (132 mg, 0.534 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2j** was isolated as a clear colorless oil (76.8 mg, 58%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.42-7.36 (m, 3H), 6.91-6.85 (m, 1H), 5.28-5.20 (m, 1H), 4.20-4.14 (m, 2H), 3.81 (s, 2H), 1.62 (d, *J* = 7.0 Hz, 3H), 1.24-1.20 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 153.3, 147.1, 134.8, 129.8, 128.6, 128.5, 101.6, 61.3, 34.1, 14.1, 12.2; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.68-7.65 (m, 2H), 7.42-7.36 (m, 3H), 6.91-6.85 (m, 1H), 4.56-4.53 (m, 1H), 4.20-4.14 (m, 2H), 3.81 (s, 2H), 1.62 (d, *J* = 7.0 Hz, 3H), 1.24-1.20 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.5, 153.3, 146.6, 134.8, 129.8, 128.6, 128.5, 100.3, 61.3, 34.1, 14.1, 9.4; HRMS (ESI) *m/z* calcd. for $C_{14}H_{18}NO_3$

$(M+H)^+$ 248.1287, found 248.1282.



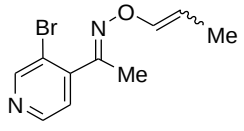
2k (*E*:*Z* = 1:1.6)

2k was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1k** (252 mg, 1.16 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2k** was isolated as a clear colorless oil (172 mg, 68%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.63-7.60 (m, 1H), 6.87-6.80 (m, 3H), 5.23-5.19 (m, 1H), 3.82 (s, 3H), 3.01-2.94 (m, 4H), 1.63 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 164.1, 150.9, 147.7, 128.0, 123.0, 114.5, 109.6, 99.0, 55.5, 28.7, 27.2, 9.7; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.63-7.60 (m, 1H), 6.87-6.80 (m, 3H), 5.23-5.19 (m, 1H), 3.82 (s, 3H), 3.01-2.94 (m, 4H), 1.67 (d, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 164.1, 150.9, 147.3, 128.0, 123.0, 114.5, 109.6, 100.1, 55.5, 28.7, 27.2, 12.4; HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}NO_2$ $(M+H)^+$ 218.1181, found 218.1174.



2l (*E*:*Z* = 1:1.6)

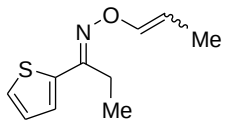
2l was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1l** (133 mg, 0.757 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2l** was isolated as a clear colorless oil (104 mg, 78%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 8.63-8.61 (m, 2H), 7.55-7.53 (m, 2H), 6.91-6.86 (m, 1H), 5.29-5.26 (m, 1H), 2.27 (s, 3H), 1.63 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 150.2, 147.4, 143.1, 120.4, 101.8, 12.3, 9.6; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 8.63-8.61 (m, 2H), 7.55-7.53 (m, 2H), 6.91-6.86 (m, 1H), 4.59-4.55 (m, 1H), 2.32 (s, 3H), 1.68 (d, *J* = 8.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.2, 150.0, 146.8, 122.2, 120.4, 100.6, 13.1, 9.6; HRMS (ESI) *m/z* calcd. for $C_{10}H_{13}N_2O$ $(M+H)^+$ 177.1028, found 177.1025.



2m (*E*:*Z* = 1:2.0)

2m was synthesized according to general procedure **B**. The catalyst mixture was

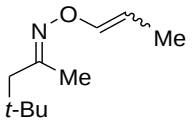
prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1m** (185 mg, 0.728 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2m** was isolated as a clear colorless oil (146 mg, 79%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 8.60-8.59 (m, 1H), 7.87-7.84 (m, 1H), 7.48-7.47 (m, 1H), 6.89-6.83 (m, 1H), 5.27-5.23 (m, 1H), 2.27 (s, 3H), 1.62 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 147.8, 147.3, 146.7, 135.8, 131.0, 127.9, 101.6, 12.2, 9.6; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 8.60-8.59 (m, 1H), 7.87-7.84 (m, 1H), 7.48-7.47 (m, 1H), 6.89-6.83 (m, 1H), 4.57-4.53 (m, 1H), 2.31 (s, 3H), 1.67 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.8, 147.8, 146.7, 143.0, 135.8, 130.9, 127.9, 100.5, 12.7, 9.6; HRMS (ESI) *m/z* calcd. for $C_{10}H_{12}N_2OBr$ $(M+H)^+$ 255.0133, found 255.0125.



2n (*E*:*Z* = 1:2.3)

2n was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1n** (120 mg, 0.616 mmol) was then added to the catalyst mixture and the complete reaction

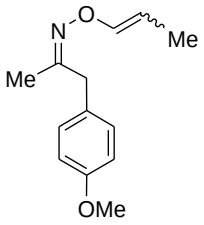
mixture was allowed to stir for 18 h. After column chromatography, **2n** was isolated as a clear colorless oil (66.1 mg, 55%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.07-7.05 (m, 1H), 6.88-6.86 (m, 1H), 5.28-5.22 (m, 1H), 2.79 (q, *J* = 7.5 Hz, 2H), 1.66 (d, *J* = 7.0 Hz, 3H), 1.24 (d, *J* = 7.5 Hz, 3H) ; ^{13}C NMR (125 MHz, C_6D_6) δ 157.4, 147.4, 138.7, 127.5, 127.1, 126.8, 100.8, 21.3, 12.3, 9.5; ^{1}H NMR of *Z*-isomer (500 MHz, C_6D_6) δ 7.34-7.30 (m, 2H), 7.07-7.05 (m, 1H), 6.88-6.86 (m, 1H), 4.57-4.52 (m, 1H), 2.85 (q, *J* = 7.5 Hz, 2H), 1.70 (d, *J* = 7.0 Hz, 3H), 1.28 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 146.9, 138.6, 127.5, 127.1, 126.8, 99.7, 21.5, 11.6, 11.4; HRMS (ESI) *m/z* calcd. for $C_{10}H_{14}NOS$ $(M+H)^+$ 196.0796, found 196.0795.



2o (*E*:*Z* = 1:3.2)

2o was synthesized according to general procedure **B**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $LiAlH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1o** (119.2 mg, 0.705 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2o** was isolated as a clear colorless oil (66.1 mg, 55%). ^{1}H NMR of *E*-isomer (500 MHz,

$CDCl_3$) δ 7.06-7.03 (m, 1H), 5.34-5.30 (m, 1H), 1.94 (s, 2H), 1.74 (s, 3H), 1.49 (d, *J* = 7.0 Hz, 3H), 0.86 (s, 9H); ^{13}C NMR (125 MHz, C_6D_6) δ 157.7, 147.6, 98.9, 48.7, 31.2, 30.1, 17.1, 12.3; ^{1}H NMR of *Z*-isomer (500 MHz, C_6D_6) δ 7.16-7.13 (m, 1H), 4.42-4.36 (m, 1H), 1.93 (s, 2H), 1.74-1.72 (m, 5H), 0.84 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3, 147.6, 97.7, 48.6, 31.2, 30.1, 16.9, 9.6; HRMS (ESI) *m/z* calcd. for $C_{10}H_{19}NO$ $(M+H)^+$ 170.1545, found 170.1537.



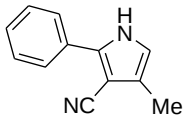
2p (*E*:*Z* = 1:3.6)

2p was synthesized according to general procedure **B**; however, DIBAL was used as a reducing agent instead of $LiBH_4$ or $NaBH_4$. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (10.0 mg, 0.0149 mmol), and a 1 M solution of DIBAL in cyclohexane (30.0 μL, 0.0300 mmol) in THF for 15 min. Allyl oxime ether **1p** (60.7 mg, 0.277 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 18 h. After column chromatography, **2p** was isolated as a clear colorless oil (30.5 mg, 50%). ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.26-7.12 (m, 2H), 6.86-6.80 (m, 3H), 5.18-5.11 (m, 1H), 3.79 (s, 3H), 3.41 (s, 2H), 1.84 (s, 3H), 1.79-1.69 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 147.3, 130.1, 130.0, 128.4,

114.0, 100.1, 75.1, 41.3, 12.3, 9.5; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.26-7.12 (m, 2H), 6.86-6.80 (m, 3H), 4.46-4.43 (m, 1H), 3.79 (s, 3H), 3.44 (s, 2H), 1.74 (s, 3H), 1.65-1.61 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 146.7, 130.0, 129.9, 128.4, 114.0, 98.8, 55.3, 41.0, 14.0, 9.5.

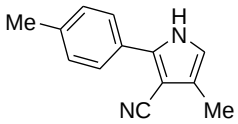
1.10.3 Preparation of 3-CN-4-Me-Pyrroles

General Procedure C: In an inert atmosphere drybox, a 20 mL scintillation vial was charged with 0.5 equiv of $[(cod)IrCl]_2$, 1 equiv AgOTf, 1 equiv $NaBH_4$, and 3 mL of THF. This mixture was then allowed to stir at 25 ℃ for 20 min. *O*-Allyl oxime **3** (10 equiv) was mixed with 2 mL of THF in a small vial. The oxime solution was then transferred to the scintillation vial containing the 10 mol % iridium mixture. The reaction mixture was then allowed to stir at 25 ℃ for 24-48 h. After the indicated reaction time, an aliquot was removed from the reaction mixture and checked by ^{1}H NMR spectroscopy to determine if the transformation had gone to completion. The reaction mixture was then dry-loaded on to silica gel and **4** was purified by flash chromatography (2% TEA/hexanes – 40% EtOAc/ 2% TEA/hexanes).



4a

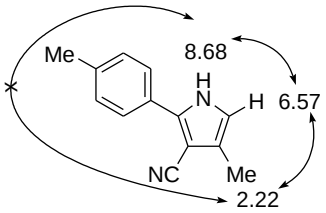
4a[40] was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3a** (122 mg, 0.609 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4a** was isolated as a light yellow solid (0.092 g, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (br s, 1H), 7.69-7.67 (m, 2H), 7.45-7.41 (m, 2H), 7.37-7.33 (m, 1H), 6.60 (m, 1H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 130.1, 129.2, 128.5, 125.5, 124.2, 117.4, 116.8, 91.6, 10.7; IR (thin film) 3214, 3042, 2920, 2218, 1584, 1468, 1098, 763, 694, 623 cm-1; HRMS (ESI) *m/z* calcd. for $C_{12}H_{11}N_2$ $(M+H)^+$ 183.0922, found 183.0920; mp 120-122 ℃.



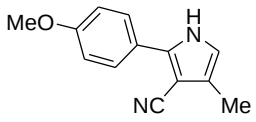
4b

4b was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685

mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3b** (126 mg, 0.587 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4b** was isolated as a light yellow solid (84.7 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (brs, 1H), 7.58-7.56 (m, 2H), 7.23-7.21 (m, 2H), 6.57 (s, 1H), 2.37 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.8, 138.6, 129.9, 127.3, 125.4, 124.0, 117.7, 116.5, 91.0, 21.3, 10.7; IR (thin film) 3429, 3295, 3027, 2941, 2917, 2857, 2206, 1641, 1536, 820, 771 cm^{-1}; HRMS (ESI) *m/z* calcd. For $C_{13}H_{13}N_2$ $(M+H)^+$ 197.1079, found 197.1076.; mp 135-137 ℃.

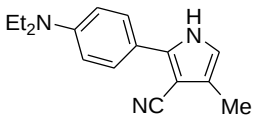


When the methyne resonance at 6.57 ppm was selected for a 1D ^{1}H-^{1}H NOE experiment using a D8 mixing time of 1 s, the amine resonance at 8.68 and the methyl resonance at 2.22 ppm were inverted. When the methyl resonance at 2.22 ppm was selected, the methyne resonance at 6.57 ppm was inverted. When the amine resonance at 8.68 ppm was selected, the methyne resonance at 6.57 ppm was inverted. These interactions indicate that the structure is the 2,3,4-substituted pyrrole.



4c

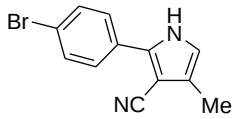
4c was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3c** (147 mg, 0.636 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4c** was isolated as a light yellow solid (101 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (brs, 1H), 7.61-7.59 (m, 2H), 6.93-6.91 (m, 2H), 6.54 (s, 1H), 3.82 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 138.9, 127.0, 123.7, 122.9, 117.9, 116.2, 114.6, 90.4, 55.4, 10.7; IR (thin film) 3288, 3133, 3108, 2917, 2840, 2206, 1613, 1536, 1251, 820, 727 cm^{-1}; HRMS (ESI) *m/z* calcd. For $C_{13}H_{13}N_2O$ $(M+H)^+$ 213.1028, found 213.1026.; mp 114-116 ℃.



4d

4d was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685

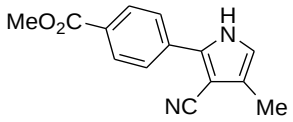
mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3d** (131 mg, 0.484 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4d** was isolated as a light yellow solid (0.059 g, 48%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (brs, 1H), 7.57-7.55 (m, 2H), 6.72-6.70 (m, 2H), 6.51 (s, 1H), 3.40 (q, *J* = 7.0 Hz, 3H), 2.23 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 140.0, 126.7, 123.4, 118.2, 117.0, 115.2, 111.7, 44.4, 12.6, 12.5, 10.7; HRMS (ESI) *m/z* calcd. for $C_{16}H_{20}N_3$ $(M+H)^+$ 254.1657, found 254.1656.



4e

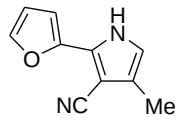
4e was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3e** (168 mg, 0.602 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4e** was isolated as a light yellow solid (120 mg, 76%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.64-7.62 (m, 2H), 7.60-7.58 (m, 2H), 6.68 (s, 1H), 2.18 (s, 3H) the NH peak did not appear in the ^{1}H NMR spectrum; ^{13}C NMR (125 MHz, CD_3OD) δ 136.9, 131.8, 129.6, 126.8, 123.5, 121.5,

117.8, 117.1, 90.3, 9.2; IR (thin film) 3284, 3133, 2921, 2860, 2218, 1523, 824, 771, 706 cm^{-1}; HRMS (ESI) *m/z* calcd. For $C_{12}H_{10}N_2Br$ $(M+H)^+$ 261.0027, found 261.0023.; mp 212-215 ℃.



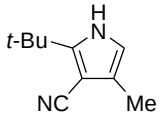
4f

4f was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3f** (164 mg, 0.635 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4f** was isolated as a light yellow solid (91.6 mg, 30%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.98 (brs, 1H), 8.07-8.05 (m, 2H), 7.76-7.74 (m, 2H), 6.67 (s, 1H), 3.93 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 136.8, 134.1, 130.5, 129.6, 125.1, 125.0, 117.9, 117.0, 92.9, 52.3, 10.7; IR (thin film) 3251, 3035, 2954, 2926, 2214, 1714, 1613, 1580, 1271, 857, 727 cm^{-1}; HRMS (ESI) *m/z* calcd. For $C_{14}H_{13}N_2O_2$ $(M+H)^+$ 241.0977, found 241.0969.; mp 198-200 ℃.



4g

4g was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3g** (129 mg, 0.678 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir at 25 ℃ for 18 h then at 50 ℃ for 24 h. After column chromatography, **4g** was isolated as a light-yellow solid (0.0742 g, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (brs, 1H), 7.40 (s, 1H), 6.91-6.90 (m, 1H), 6.54 (s, 1H), 6.50-6.49 (m, 1H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.8, 141.7, 130.2, 123.5, 116.5, 116.2, 112.1, 107.0, 90.0, 10.6; HRMS (ESI) m/z calcd. for $C_{10}H_9N_2O$ $(M+H)^+$ 173.0715, found 173.0715; mp 102-104 ℃.



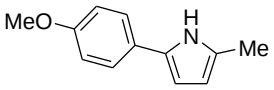
4h

4h was synthesized according to general procedure **C**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685

mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **3h** (114 mg, 0.633 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h. After column chromatography, **4h** was isolated as a light-yellow oil (0.0243 g, 24%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (br s, 1H), 6.35 (s, 1H), 2.13 (s, 3H), 1.41 (s, 9H); ^{13}C NMR of (125 MHz, $CDCl_3$) δ 149.0, 123.1, 117.9, 113.5, 89.3, 32.8, 29.6, 10.6; IR (thin film) 3275, 2968, 2868, 2210, 1594, 1444, 1367, 1267, 804, 756 cm-1; HRMS (ESI) *m/z* calcd. for $C_{10}H_{15}N_2$ $(M+H)^+$ 163.1235, found 163.1234.

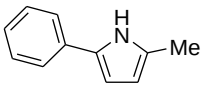
1.10.4 Preparation of 5-Me-Pyrroles

General Procedure D: A 10 mL reaction flask with a Teflon stopper was flushed with N_2 and charged with 1 equiv of **2** dissolved in 4 mL of dioxane and ~15 4Å molecular sieves. The flask was then sealed and heated to 75 °C for 18 h. The reaction mixture was then transferred from the reaction flask and dry-loaded onto ~ 2 mL of silica gel. The crude product was purified by flash chromatography using a solvent gradient of 0-20% EtOAc with 2% TEA/hexanes.



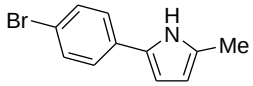
5a

5a[41] was synthesized according to general procedure **D**. Vinyl oxime ether **2a** (117 mg, 0.570 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5a** was isolated as a light yellow solid (68.3 mg, 64%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (brs, 1H), 7.37-7.35 (m, 2H), 6.90-6.89 (m, 2H), 6.28 (s, 1H), 5.93 (s, 1H), 3.82 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 130.9, 128.4, 126.2, 124.8, 114.3, 107.7, 105.0, 55.4, 13.2; HRMS (ESI) *m/z* calcd. for $C_{12}H_{14}NO$ $(M+H)^+$ 188.1075, found 188.1079.; mp 126-129 ℃.



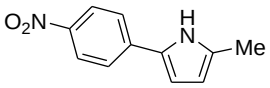
5b

5b[42] was synthesized according to general procedure **D**. Vinyl oxime ether **2b** (143 mg, 0.817 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5b** was isolated as a light yellow solid (75.1 mg, 58%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (brs, 1H), 7.46-7.44 (m, 2H), 7.38-7.34 (m, 2H), 7.21-7.17 (m, 1H), 6.43 (s, 1H), 5.98 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 130.8, 129.1, 128.9, 125.7, 123.4, 108.0, 106.2, 13.2; HRMS (ESI) *m/z* calcd. for $C_{11}H_{12}N$ $(M+H)^+$ 158.0970, found 158.0968.; mp 85-88 ℃.



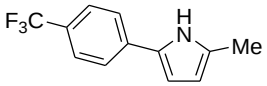
5c

5c[43] was synthesized according to general procedure **D**. Vinyl oxime ether **2c** (227 mg, 0.897 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5c** was isolated as a light yellow solid (117 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (brs, 1H), 7.46-7.44 (m, 2H), 7.30-7.28 (m, 2H), 6.39 (s, 1H), 5.96 (s, 1H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.9, 131.8, 129.7, 124.8, 124.7, 119.0, 108.3, 106.8, 13.2; HRMS (ESI) *m/z* calcd. for $C_{11}H_{11}NBr$ $(M+H)^+$ 236.0075, found 236.0073; mp 102-105 ℃.



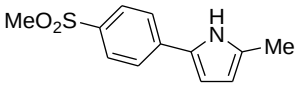
5d

5d was synthesized according to general procedure **D**. Vinyl oxime ether **2d** (132 mg, 0.599 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5d** was isolated as a light yellow solid (51 mg, 42%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (bs, 1H), 7.83 (d, *J* = 9 Hz, 2H), 7.50 (d, *J* = 9 Hz, 2H), 6.63 (s, 1H), 6.04 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 138.9, 132.6, 128.6, 124.8, 122.7, 110.6, 109.7, 13.5; HRMS (ESI) *m/z* calcd. for $C_{11}H_{10}N_2O_2$ $(M+H)^+$ 203.0821, found 203.0822.



5e

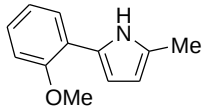
5e[43] was synthesized according to general procedure **D**. Vinyl oxime ether **2e** (130 mg, 0.535 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5e** was isolated as a light yellow solid (55.5 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (brs 1H), 7.58-7.56 (m, 2H), 7.50-7.48 (m, 2H), 6.52 (s, 1H), 6.00 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.1, 130.6, 129.3, 127.1 (q, $J_{C\text{-}F}$ = 33 Hz), 126.6 (q, $J_{C\text{-}F}$ = 270 Hz), 125.9, 123.0, 108.6, 108.1, 13.2; HRMS (ESI) *m/z* calcd. for $C_{12}H_{11}NF_3$ $(M+H)^+$ 226.0844, found 226.0836; mp 130-132 ℃.



5f

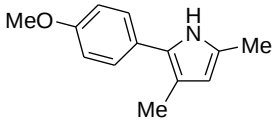
5f was synthesized according to general procedure **D**. Vinyl oxime ether **2f** (149 mg, 0.590 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5f** was isolated as a light yellow solid (57.3 mg, 41%) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (brs, 1H), 7.86-7.85 (m, 2H), 7.58-7.67 (m, 2H), 6.59 (s, 1H), 6.03 (s, 1H), 3.08 (S, 3H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 136.1, 131.8, 128.6, 128.1, 123.2, 109.4, 109.0, 44.7, 13.3; HRMS (ESI) *m/z*

calcd. For $C_{12}H_{14}NO_2S$ $(M+H)^+$ 236.0745, found 236.0737.



5g

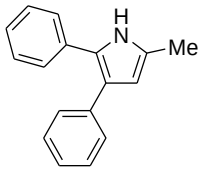
5g was synthesized according to general procedure **D**. Vinyl oxime ether **2g** (95.5 mg, 0.465 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and purification, **5g** was isolated as a light yellow oil (49.3 mg, 57%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.45 (brs, 1H), 7.65-7.64 (m, 1H), 7.15-7.12 (m, 1H), 7.01-6.95 (m, 2H), 6.53 (s, 1H), 5.97 (s, 1H), 3.97 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 128.4, 127.9, 126.2, 126.1, 121.5, 121.4, 111.6, 106.8, 106.5, 55.7, 13.4; HRMS (ESI) *m/z* calcd. For $C_{12}H_{16}NO$ $(M+H)^+$ 188.1075, found 188.1078.



5h

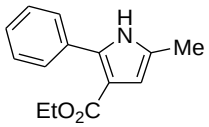
5h[44] was synthesized according to general procedure **D**. Vinyl oxime ether **2h** (141 mg, 0.641 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5h** was isolated as a light yellow

oil (78.2 mg, 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (brs, 1H), 7.33-7.31 (m, 2H), 6.95-6.93 (m, 2H), 5.82 (s, 1H), 3.84 (s, 3H), 2.29 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 127.5, 126.8, 126.7, 126.7, 115.3, 114.1, 109.9, 55.3, 13.0, 12.3; HRMS (ESI) *m/z* calcd. for $C_{13}H_{16}NO$ $(M+H)^+$ 202.1232, found 202.1240.



5i

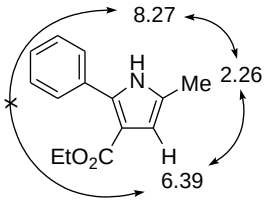
5i[45] was synthesized according to general procedure **D**. Vinyl oxime ether **2i** (145 mg, 0.579 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5i** was isolated as a light yellow amorphous solid (81.4 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (brs, 1H), 7.38-7.18 (m, 10H), 6.12 (s, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.8, 133.6, 128.6, 128.5, 128.4, 128.3, 127.3, 126.9, 126.4, 125.6, 122.3, 109.0, 13.0; HRMS (ESI) *m/z* calcd. for $C_{17}H_{16}N$ $(M+H)^+$ 234.1283, found 234.1272.



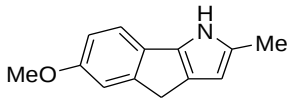
5j

5j[46] was synthesized according to general procedure **D**. Vinyl oxime ether **2j** (130 mg,

0.524 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5j** was isolated as a light yellow amphorous solid (72 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (brs, 1H), 7.56-7.54 (m, 2H), 7.37-7.30 (m, 3H), 6.38 (s, 1H), 4.16 (q, *J* = 7.0 Hz, 2H), 2.24 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 136.1, 132.3, 128.9, 128.0, 127.9, 127.8, 112.0, 109.5, 59.6, 14.3, 12.7; HRMS (ESI) *m/z* calcd. For $C_{14}H_{16}NO_2$ $(M+H)^+$ 230.1181, found 230.1179.

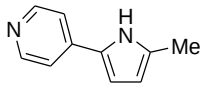


1 D ^{1}H-^{1}H NMR Spectrum: When the methyne resonance at 6.39 ppm was selected for a 1D ^{1}H-^{1}H NOE experiment using a D8 mixing time of 1 s, the methyl resonance at 2.26 was inverted. When the methyl resonance at 2.26 ppm was selected, the methyne resonances at 6.39 ppm and amine resonance at 8.27 ppm were inverted. When the amine resonance at 8.27 ppm was selected, the methyl resonance at 2.26 ppm was inverted. These interactions indicate that the structure is the 2,3,5-substituted pyrrole.



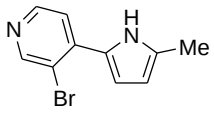
5k

5k was synthesized according to general procedure **D**. Vinyl oxime ether **2k** (144 mg, 0.662 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5k** was isolated as (42 mg, 32%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (brs, 1H), 7.13-7.12 (m, 1H), 7.07 (s, 1H), 6.81-6.79 (m, 1H), 5.98 (s, 1H), 3.85 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 148.6, 136.0, 130.7, 129.3, 128.0, 115.2, 112.5, 111.1, 103.0, 55.6, 31.1, 13.8; HRMS (ESI) *m/z* calcd. For $C_{13}H_{14}NO$ $(M+H)^+$ 200.1075, found 200.1065.



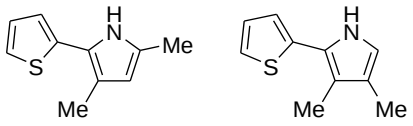
5l

5l[47] was synthesized according to general procedure **D**. Vinyl oxime ether **2l** (197 mg, 1.120 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5l** was isolated as a light yellow solid (90.0 mg, 51%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89-8.74 (brs, 1H), 8.49-8.48 (m, 2H), 7.30-7.29 (m, 2H), 6.64 (s, 1H), 6.01 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.1, 139.6, 131.8, 127.7, 117.2, 109.6, 109.0, 13.3; HRMS (ESI) *m/z* calcd. for $C_{10}H_{11}N_2$ $(M+H)^+$ 159.0922, found 159.0915; mp 210-213 ℃.



5m

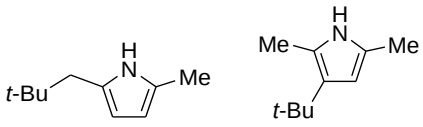
5m was synthesized according to general procedure **D**. Vinyl oxime ether **2m** (192 mg, 0.757 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5m** was isolated as (68.7 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (brs, 1H), 8.44 (s, 1H), 7.60-7.58 (m, 1H), 7.43-7.41 (m, 1H), 6.48 (s, 1H), 6.01 (s, 1H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.4, 137.8, 133.1, 131.2, 128.4, 128.1, 126.0, 108.7, 108.3, 13.2.



5n/**4n** (3:1)

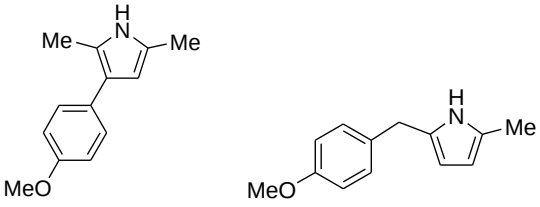
5n/**4n** was synthesized according to general procedure **D**. Vinyl oxime ether **2n** (93.1 mg, 0.477 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5n** was isolated as (29 mg, 34%). ^{1}H NMR of **5n** (500 MHz, $CDCl_3$) δ 7.82 (brs, 1H), 7.20-7.19 (m, 1H), 7.09-7.07 (m, 1H), 6.98-6.97 (m, 1H), 5.84 (s, 1H), 2.31 (s, 3H), 2.27 (s, 3H); ^{13}C NMR of **5n** (125 MHz, $CDCl_3$) δ 136.3, 127.7, 127.4, 122.1, 121.5, 121.1, 117.3, 110.2, 13.0, 12.4; ^{1}H NMR of **4n** (500 MHz, $CDCl_3$) δ 7.92 (brs, 1H), 7.23-7.22 (m, 1H), 7.09-7.07 (m,

1H), 7.03-7.02 (m, 1H), 6.59 (s, 1H), 2.22 (s, 3H), 2.10 (s, 3H); ^{13}C NMR of **4n** (125 MHz, $CDCl_3$) δ 136.3, 127.7, 127.4, 122.7, 121.9, 120.1, 116.4, 115.5, 10.4, 10.1.



5o/**5oa** (>95:5)

5o was synthesized according to general procedure **D**. Vinyl oxime ether **2o** (40.0 mg, 0.236 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃ for 24 h. After workup and column chromatography, **5o** was isolated as a light yellow oil (26 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (brs, 1H), 5.79-5.76 (m, 2H), 2.41 (s, 2H), 2.25 (s, 3H), 0.96 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.9, 125.8, 107.4, 105.7, 42.6, 31.6, 28.2, 13.1; HRMS (ESI) *m/z* calcd. For $C_{10}H_{18}N$ $(M+H)^+$ 152.1439, found 152.1432.



5p/**5pa** (3:1)

5p was synthesized according to general procedure **D**. Vinyl oxime ether **2p** (122 mg, 0.557 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 ℃

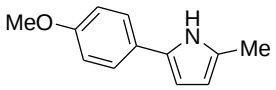
for 24 h. After workup and purification, **5p** was isolated as a light yellow oil (38 mg, 34%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (brs, 1H), 7.36-7.34 (m, 2H), 6.96-6.94 (m, 2H), 5.99 (s, 1H), 3.85 (s, 3H), 2.36 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 130.0, 128.6, 125.7, 121.8, 120.6, 113.8, 106.3, 55.3, 12.9, 12.5; HRMS (ESI) *m/z* calcd. For $C_{13}H_{16}NO$ $(M+H)^+$ 202.1232, found 202.1230.

5pa was synthesized according to general procedure D. Vinyl oxime ether **2p** (122 mg, 0.557 mmol) was dissolved in dioxane with 4Å molecular sieves and heated at 75 °C for 24 h. After workup and purification, **5pa** was isolated as a light yellow oil (13 mg, 12%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (brs 1H), 7.15-7.13 (m, 2H), 6.86-6.85 (m, 2H), 5.83 (s, 1H), 5.78 (s, 1H), 3.87 (s, 2H), 3.80 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2, 131.8, 129.8, 129.7, 126.9, 114.0, 106.3, 105.7, 55.3, 33.3, 13.1; HRMS (EI) *m/z* calcd. For $C_{13}H_{15}NO$ $(M)^+$ 201.1154, found 201.1156.

1.10.5 One-Flask Preparation of 5-Me-Pyrroles

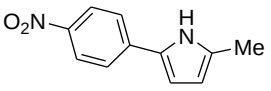
General procedure E: In an inert atmosphere drybox, a 20 mL scintillation vial was charged with 0.5 equiv of $[(cod)IrCl]_2$, 1 equiv AgOTf, 1 equiv $NaBH_4$ or 1 equiv $LiAlH_4$, and 3 mL of THF. This mixture was then allowed to stir at 25 °C for 20 min. *O*-Allyl oxime **1** (10 equiv) was mixed with 2 mL of THF in a small vial. The oxime solution was then transferred to the scintillation vial containing the 10 mol % iridium

mixture. The reaction mixture was then allowed to stir at 25 ℃ for 18 h. After 18 h at 25 ℃, the reaction mixtures were transferred to 10 mL Teflon-sealed reaction flasks, charged with ~15 4Å molecular sieves, and heated to 75 ℃ for 15 h. The crude product was then separated from the reaction mixture by gradient flash chromatography.



5a

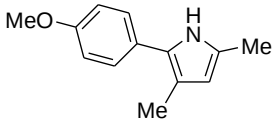
5a was synthesized according to general procedure E. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1a** (133 mg, 0.649 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h and then transferred to a teflon-sealed reaction flask and heated to 75 ℃ for 15 h. After column chromatography, **5a** was isolated as light yellow solid (56.2 mg, 46%).



5d

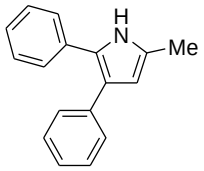
5d was synthesized according to general procedure **E**. The catalyst mixture was

prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1d** (145 mg, 0.660 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h and then transferred to a teflon-sealed reaction flask and heated to 75 ℃ for 15 h. After column chromatography, **5d** was isolated as light yellow solid (62mg, 46%).



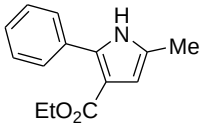
5h

5h was synthesized according to general procedure **E**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1h** (130 mg, 0.594 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h and then transferred to a teflon-sealed reaction flask and heated to 75 ℃ for 15 h. After column chromatography, **5h** was isolated as light yellow oil (47.8 mg, 40%).



5i

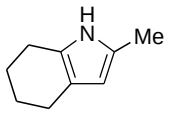
5i was synthesized according to general procedure **E**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1i** (138 mg, 0.550 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h and then transferred to a teflon-sealed reaction flask and heated to 75 ℃ for 15 h. After column chromatography, **5i** was isolated as a light yellow amorphous solid (52 mg, 41%).



5j

5j was synthesized according to general procedure **E**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1j** (128 mg, 0.518 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h and then transferred to a teflon-sealed reaction flask and heated to 75 ℃ for 15 h. After column chromatography, **5j** was isolated as light

yellow oil (47.8 mg, 40%).



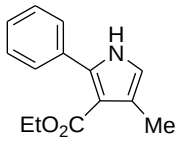
5q

5q[10,48] was synthesized according to general procedure **E**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (23.0 mg, 0.0342 mmol), AgOTf (17.6 mg, 0.0685 mmol), and $NaBH_4$ (2.6 mg, 0.070 mmol) in THF for 15 min. Allyl oxime ether **1q** (120 mg, 0.784 mmol) was then added to the catalyst mixture and the complete reaction mixture was allowed to stir for 24 h and then transferred to a teflon-sealed reaction flask and heated to 75 ℃ for 15 h. After column chromatography, **5q** was isolated as light yellow oil (44 mg, 42%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (vbs, 1H), 5.65 (s, 1H), 2.46-2.54 (m, 4H), 2.24 (s, 3H), 1.73-1.83 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 125.8, 125.4, 117.0, 105.1, 23.9, 23.6, 22.9, 22.7, 13.0; HRMS (EI) *m/z* calcd. for $C_9H_{14}N$ $(M+H)^+$ 136.1, found 136.1.

1.10.6 Reversal of Regioselevtivity with DBU

General procedure F: In an inert atmosphere drybox, a 20 mL scintillation vial was charged with 0.5 equiv of $[(cod)IrCl]_2$, 1 equiv AgOTf, 1 equiv $NaBH_4$, and 3 mL of THF. This mixture was then allowed to stir at 25 ℃ for 20 min. *O*-Allyl oxime **1j** (10

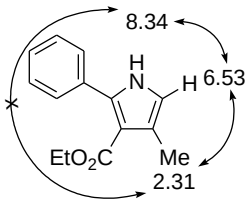
equiv) was mixed with 2 mL of THF in a small vial. The oxime solution was then transferred to the scintillation vial containing the 10 mol % iridium mixture and DBU (10 equiv) was added after the substrate. The reaction mixture was then transferred to a Teflon-sealed, conical vial and allowed to stir at 25 ℃ for 1 h. The vial was then removed from the glovebox and heated to 75 ℃ for 24 h in an aluminum block. The reaction mixture was purified by flash chromatography to give **4j**.



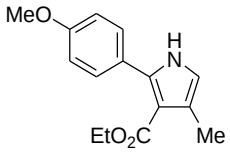
4j

4j[49] was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1j** (165 mg, 0.667 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4j** was isolated as a light yellow oil (132 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (brs, 1H), 7.46-7.44 (m, 2H), 7.37-7.32 (m, 3H), 6.50 (s, 1H), 4.14 (q, *J* = 7.0 Hz, 2H), 2.30 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 137.6, 133.1, 129.1, 128.9, 127.9, 122.5,

116.8, 111.3, 59.4, 14.1, 12.6; HRMS (ESI) *m/z* calcd. For $C_{14}H_{16}NO_2$ $(M+H)^+$ 230.1181, found 230.1183; mp 90-92 °C.



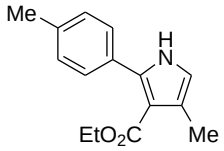
When the methyne resonance at 6.53 ppm was selected for a 1D ^{1}H-^{1}H NOE experiment using a D8 mixing time of 1 s, the amine resonance at 8.34 and the methyl resonance at 2.31 ppm were inverted. When the methyl resonance at 2.31 ppm was selected, the methyne resonance at 6.53 ppm was inverted. When the amine resonance at 8.34 ppm was selected, the methyne resonance at 6.53 ppm was inverted. These interactions indicate that the structure is the 2,3,4-substituted pyrrole.



4ja

4ja was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1ja** (184 mg, 0.664 mmol) was then added to the catalyst mixture followed by DBU (145

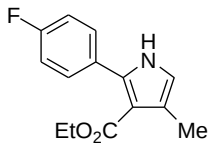
mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4ja** was isolated as light yellow oil (158 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (brs, 1H), 7.39-7.37 (m, 2H), 6.87-6.85 (m, 2H), 6.46 (s, 1H), 4.13 (q, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 2.29 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 159.4, 137.7, 130.3, 125.6, 122.3, 116.4, 113.4, 110.8, 59.4, 55.3, 14.2, 12.7; HRMS (ESI) *m/z* calcd. For $C_{15}H_{18}NO_3$ $(M+H)^+$ 260.1287, found 260.1287; mp 73-76 ℃.



4jb

4jb was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jb** (175 mg, 0.670 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jb** was isolated as: light yellow oil (138 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (brs, 1H), 7.38-7.36 (m,

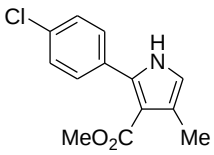
2H), 7.18-7.17 (m, 2H), 6.51 (s, 1H), 4.16 (q, J = 7.0 Hz, 2H), 2.38 (s, 3H), 2.30 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 137.9, 137.8, 130.1, 128.9, 128.7, 122.4, 116.4, 111.1, 59.4, 21.3, 14.2, 12.7; HRMS (ESI) *m/z* calcd. For $C_{15}H_{18}NO_2$ $(M+H)^+$ 244.1338, found 244.1337; mp 85-90 ℃.



4jc

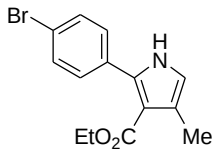
4jc was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jc** (177 mg, 0.668 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jc** was isolated as a light yellow solid (0.139 g, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (brs, 1H), 7.43-7.40 (m, 2H), 7.04-7.01 (m, 2H), 6.51 (s, 1H), 4.14 (q, J = 7.0 Hz, 2H), 2.29 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 162.5 (d, $J_{C\text{-}F}$ = 246.3 Hz), 136.7, 130.9, 129.1, 122.5, 116.7, 114.9, 111.3, 59.5, 14.2, 12.6; HRMS (ESI) *m/z*

calcd. for $C_{14}H_{15}NO_2F$ $(M+H)^+$ 248.1087, found 248.1091; mp 77-82 ℃.



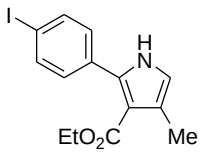
4jd

4jd was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jd** (178 mg, 0.666 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jd** was isolated as: light yellow oil (130 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (brs, 1H), 7.40-7.38 (m, 2H), 7.34-7.32 (m, 2H), 6.55 (s, 1H), 3.69 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 136.4, 134.0, 131.4, 130.2, 128.3, 122.8, 117.0, 111.4, 50.7, 12.6; HRMS (ESI) *m/z* calcd. For $C_{13}H_{13}NO_2Cl$ $(M+H)^+$ 250.0635, found 250.0639; mp 118-122 ℃.



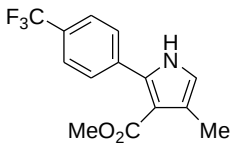
4je

4je was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1je** (217 mg, 0.668 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4je** was isolated as light yellow oil (159 mg, 78%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (brs, 1H), 7.49-7.47 (m, 2H), 7.35-7.32 (m, 2H), 6.55 (s, 1H), 4.16 (q, *J* = 7.0 Hz, 2H), 2.29 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 136.2, 131.9, 131.1, 130.6, 122.8, 122.1, 117.0, 111.7, 59.6, 14.2, 12.6; HRMS (ESI) *m/z* calcd. For $C_{14}H_{15}NO_2Br$ $(M+H)^+$ 308.0286, found 308.0288; mp 111-115 ℃.



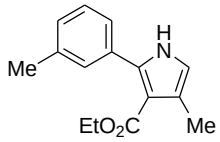
4jf

4jf was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jf** (248 mg, 0.666 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jf** was isolated as a light yellow oil (179 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (brs, 1H), 7.68-7.66 (m, 2H), 7.20-7.19 (m, 2H), 6.53 (s, 1H), 4.16 (q, *J* = 7.0 Hz, 2H), 2.29 (s, 3H), 1.21 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 137.1, 136.3, 132.4, 130.8, 122.8, 117.1, 111.7, 93.8, 59.6, 14.2, 12.7; HRMS (ESI) *m/z* calcd. For $C_{14}H_{15}NO_2I$ $(M+H)^+$ 356.0148, found 356.0148; mp 116-122 ℃.



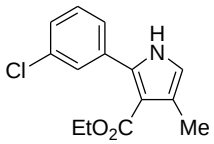
4jg

4jg was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jg** (200 mg, 0.665 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jg** was isolated as light yellow solid (154 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (brs, 1H), 7.60-7.58 (m, 2H), 7.55-7.53 (m, 2H), 6.54 (s, 1H), 3.68 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 136.4, 135.9, 129.5 (d, $J_{C\text{-}F}$ = 32.5 Hz), 129.2, 125.0, 124.1 (q, $J_{C\text{-}F}$ = 270 Hz), 123.0, 117.7, 111.9, 50.8, 12.5; HRMS (ESI) *m/z* calcd. for $C_{14}H_{13}NO_2F_3$ $(M+H)^+$ 284.0898, found 284.0897; mp 134-137 ℃.



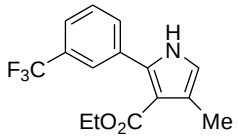
4jh

4jh was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jh** (174 mg, 0.668 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jh** was isolated as light yellow oil (141 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (brs, 1H), 7.26-7.23 (m, 3H), 7.15-7.13 (m, 1H), 6.46 (s, 1H), 4.13 (q, *J* = 7.0 Hz, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 137.8, 137.4, 133.0, 129.7, 128.6, 127.9, 127.8, 126.2, 116.7, 111.1, 59.4, 21.4, 14.1, 12.6; HRMS (ESI) *m/z* calcd. For $C_{15}H_{18}NO_2$ $(M+H)^+$ 244.1338, found 244.1339.



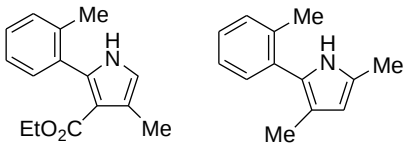
4ji

4ji[50] was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1ji** (189 mg, 0.671 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4ji** was isolated as light yellow solid (144 mg, 81%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (brs, 1H), 7.43 (s, 1H), 7.31-7.24 (m, 3H), 6.49 (s, 1H), 4.12 (q, *J* = 7.0 Hz, 2H), 2.28 (s, 3H), 1.20 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 135.8, 134.7, 133.7, 129.2, 129.1, 127.8, 127.2, 122.8, 117.4, 111.6, 59.6, 14.1, 12.6; HRMS (ESI) *m/z* calcd. for $C_{14}H_{15}NO_2Cl$ $(M+H)^+$ 264.0791, found 264.0791; mp 77-82 ℃.



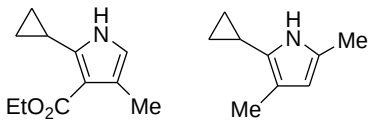
4jj

4jj was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jj** (209 mg, 0.663 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jj** was isolated as light yellow solid (0.157 g, 80%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (brs, 1H), 7.72 (s, 1H), 7.64-7.63 (m, 1H), 7.57-7.56 (m, 1H), 7.47-7.44 (m, 1H), 6.55 (s, 1H), 4.12 (q, J = 7.0 Hz, 2H), 2.29 (s, 3H), 1.15 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 135.6, 133.8, 132.4, 130.3 (d, $J_{C\text{-}F}$ = 32.5 Hz), 128.4, 126.2 (q, $J_{C\text{-}F}$ = 270 Hz), 126.0, 124.5, 123.0, 117.4, 112.0, 59.6, 14.0, 12.5; HRMS (ESI) *m/z* calcd. for $C_{15}H_{15}NO_2F_3$ $(M+H)^+$ 298.1055, found 298.1055; mp 62-65 ℃.



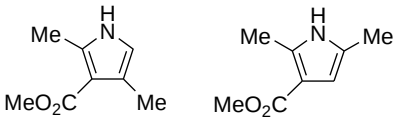
4jk/**5jk** (5:3)

4jk/**5jk** was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jk** (174 mg, 0.666 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jk**/**5jk** was isolated as light yellow oil (136 mg, 84%). ^{1}H NMR of **4jk** (500 MHz, $CDCl_3$) δ 8.21 (brs, 1H), 7.29-7.16 (m, 4H), 6.51 (s, 1H), 4.00 (q, *J* = 7.0 Hz, 2H), 2.32 (s, 3H), 2.16 (s, 3H), 1.00 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR of **4jk** (125 MHz, $CDCl_3$) δ 165.6, 137.8, 133.6, 130.2, 129.7, 128.3, 127.2, 125.1, 121.6, 116.0, 112.4, 59.0, 19.9, 13.9, 12.4; ^{1}H NMR of **5jk** (500 MHz, $CDCl_3$) δ 8.21 (brs, 1H), 7.29-7.16 (m, 4H), 6.35 (s, 1H), 4.00 (q, *J* = 7.0 Hz, 2H), 2.25 (s, 3H), 2.20 (s, 3H), 1.08 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR of **5jk** (125 MHz, $CDCl_3$) δ 165.0, 137.2, 135.5, 132.9, 130.2, 129.7, 128.3, 125.1, 121.6, 113.4, 108.0, 59.3, 19.9, 14.1, 12.7; HRMS (ESI) *m/z* calcd. For $C_{15}H_{18}NO_2$ $(M+H)^+$ 244.1338, found 244.1336.



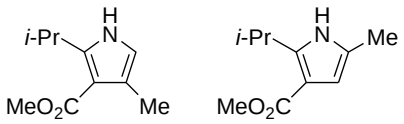
4jl/**5jl** (7:1)

4jl/**5jl** was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jl** (140 mg, 0.664 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jl**/**5jl** was isolated as light yellow oil (99 mg, 77%). ^{1}H NMR of **4jl** (500 MHz, $CDCl_3$) δ 8.03 (brs, 1H), 6.29 (s, 1H), 4.28 (q, *J* = 7.5 Hz, 2H), 2.58-2.51 (m, 1H), 2.22 (s, 3H), 1.35 (t, *J* = 7.0 Hz, 3H), 0.95 (dd, *J* = 8.5 Hz, *J* = 1.5 Hz, 2H), 0.66 (dd, *J* = 5.5 Hz, *J* = 1.5 Hz, 2H); ^{13}C NMR of **4jl** (125 MHz, $CDCl_3$) δ 166.5, 140.7, 121.8, 113.9, 111.8, 59.1, 14.5, 12.7, 9.1, 7.2; ^{1}H NMR of **5jl** (500 MHz, $CDCl_3$) δ 7.94 (brs, 1H), 6.20 (s, 1H), 4.28 (q, *J* = 7.5 Hz, 2H),), 2.58-2.51 (m, 1H), 2.17 (s, 3H), 1.35 (t, *J* = 7.0 Hz, 3H), 0.95 (dd, *J* = 8.5 Hz, *J* = 1.5 Hz, 2H), 0.66 (dd, *J* = 5.5 Hz, *J* = 1.5 Hz, 2H); ^{13}C NMR of **5jl** (125 MHz, $CDCl_3$) δ 165.9, 139.4, 125.2, 112.5, 107.9, 59.3, 14.5, 12.7, 8.5, 7.5; HRMS (ESI) *m/z* calcd. For $C_{11}H_{16}NO_2$ $(M+H)^+$ 194.1179, found 194.1179.



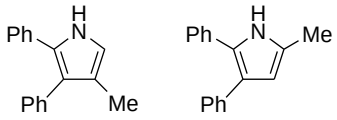
4jm/**5jm** (1.8:1)

4jm[51]/**5jm**[52] was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jm** (108 mg, 0.633 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jm**/**5jm** was isolated as light yellow solid (106 mg, 54%). ^{1}H NMR of **4jm** (500 MHz, $CDCl_3$) δ 8.29 (brs, 1H), 6.35 (s, 1H), 3.81 (s, 3H), 2.47 (s, 3H), 2.23 (s, 3H); ^{13}C NMR of **4jm** (125 MHz, $CDCl_3$) δ 166.9, 136.1, 121.5, 114.4, 110.6, 50.5, 14.1, 12.6; ^{1}H NMR of **5jm** (500 MHz, $CDCl_3$) δ 8.29 (brs, 1H), 6.18 (s, 1H), 3.78 (s, 3H), 2.47 (s, 3H), 2.18 (s, 3H); ^{13}C NMR of **5jm** (125 MHz, $CDCl_3$) δ 166.4, 134.5, 125.8, 111.2, 107.4, 50.7, 13.1, 12.6; HRMS (ESI) *m/z* calcd. For $C_8H_{12}NO_2$ $(M+H)^+$ 154.0868, found 154.0868; mp 68-73 ℃.



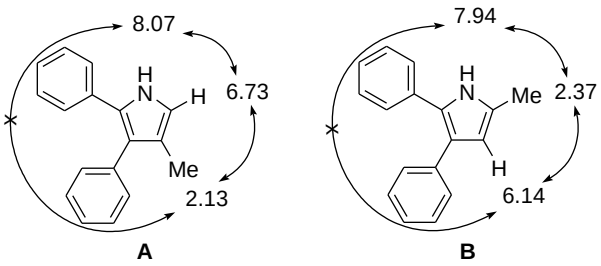
4jn/**5jn** (1:1.7)

4jn/**5jn** was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1jn** (133 mg, 0.667 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4jn**/**5jn** was isolated as light yellow oil (53.2 mg, 44%). ^{1}H NMR of **4jn** (500 MHz, $CDCl_3$) δ 8.18 (brs, 1H), 6.38 (s, 1H), 3.82-3.74 (m, 1H), 3.81 (s, 3H), 2.23 (s, 3H), 1.25 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR of **4jn** (125 MHz, $CDCl_3$) δ 166.6, 145.9, 121.4, 114.3, 109.7, 50.4, 26.3, 22.0, 12.7; ^{1}H NMR of **5jn** (500 MHz, $CDCl_3$) δ 8.09 (brs, 1H), 6.18 (s, 1H), 3.82-3.74 (m, 1H), 3.77 (s, 3H), 2.21 (s, 3H), 1.25 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR of **5jn** (125 MHz, $CDCl_3$) δ 165.9, 144.5, 125.4, 109.7, 107.5, 50.6, 25.9, 22.1, 12.7; HRMS (ESI) *m/z* calcd. For $C_{10}H_{16}NO_2$ $(M+H)^+$ 182.1181, found 182.1183.



4i/**5i** (63:37)

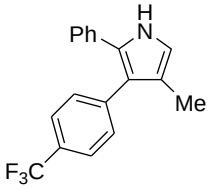
4i/**5i** was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1i** (168 mg, 0.668 mmol) was then added to the catalyst mixture followed by DBU (145 mg, 0.952 mmol). The reaction mixture was allowed to stir for 1 h at 25 ℃ and then heated to 75 ℃ for 20 h. After column chromatography, **4i**/**5i** was isolated as light orange oil (0.062 g, 40%). The ratio of **4i**:**5i** was determined by the relative ^{1}H integrations of the pyrrole methine resonances. ^{1}H NMR of **4i** (500 MHz, $CDCl_3$): δ 8.07 (brs, 1H), 7.40-7.17 (m, 10H), 6.73 (s, 1H), 2.13 (s, 3H); ^{13}C NMR of **4i** (125 MHz, $CDCl_3$) δ 136.4, 133.4, 130.5, 128.6, 128.4, 128.3, 127.4, 126.9, 126.5, 126.3, 126.0, 116.4, 11.1.



A: When the methyne resonance at 6.73 ppm was selected for a 1D ^{1}H-^{1}H NOE experiment using a D8 mixing time of 1 s, the amine resonance at 8.07 ppm and the

methyl resonance at 2.13 ppm were inverted. When the methyl resonance at 2.13 ppm was selected, only the methyne resonance at 6.73 ppm was inverted. When the amine resonance at 8.07 ppm was selected, only the methyne resonance at 6.73 ppm was inverted. These interactions indicate that the methylene resonance at 6.73 ppm, amine resonance at 8.07 ppm and methyl resonance at 2.13 ppm are corresponed to the structure A as the 2,3,4-substituted pyrrole.

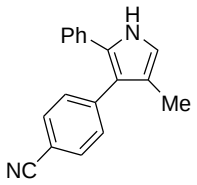
B: When the methyne resonance at 6.14 ppm was selected for a 1D ^{1}H-^{1}H NOE experiment using a D8 mixing time of 1 s, the methyl resonance at 2.37 ppm was inverted. When the methyl resonance at 2.37 ppm was selected, the methyne resonance at 6.14 ppm and the amine resonance at 7.94 ppm were inverted. When the amine resonance at 7.94 ppm was selected, the methyl resonance at 2.37 ppm was inverted. These interactions indicate that the methyne resonance at 6.14 ppm, amine resonance at 7.94 ppm and methyl resonance at 2.37 ppm are corresponed to the structure B as the 2,3,5-substituted pyrrole.



4ia

4ia was synthesized according to general procedure **F**. The catalyst mixture was

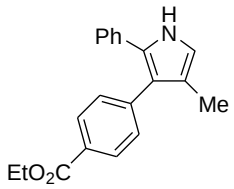
prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1ia** (213 mg, 0.667 mmol) was then added to the catalyst mixture. DBU (132 mg, 0.873 mmole) was added to the complete reaction mixture and the complete reaction mixture was allowed to stir for 1h and then heated to 75 ℃ for 20 h. After column chromatography, **4ia** was isolated as light yellow solid (0.0858 g, 43%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (brs, 1H), 7.60-7.58 (m, 2H), 7.40-7.39 (m, 2H), 7.29-7.27 (m, 2H), 7.25-7.20 (m, 3H), 6.74 (s, 1H), 2.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.2, 132.9, 130.5, 129.5, 128.7, 127.8, 127.1, 126.7, 125.1, 124.6 (q, $J_{C\text{-}F}$ = 270Hz), 120.8, 119.5, 116.7, 11.0; HRMS (ESI) *m/z* calcd. for $C_{18}H_{15}NF_3$ $(M+H)^+$ 302.1157, found 302.1159; mp 72-75 ℃.



4ib

4ib was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (13.5 mg, 0.0201 mmol), AgOTf (10.1 mg, 0.039 mmol), and $NaBH_4$ (1.5 mg, 0.040 mmol) in THF for 15 min. Allyl oxime ether **1ib** (110 mg, 0.398 mmol) was then added to the catalyst mixture. DBU (79 mg, 0.524

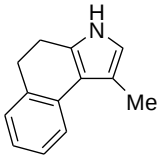
mmole) was added to the complete reaction mixture and the complete reaction mixture was allowed to stir for 1h and then heated to 75 ℃ for 20 h. After column chromatography, **4ib** was isolated as light yellow solid (46.5 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (brs, 1H), 7.58-7.57 (m, 2H), 7.35-7.34 (m, 2H), 7.29-7.26 (m, 2H), 7.24-7.22 (m, 1H), 7.18-7.16 (m, 1H), 6.74 (s, 1H), 2.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.6, 132.6, 132.0, 130.8, 129.9, 128.8, 127.3, 127.0, 120.3, 119.5, 119.3, 117.0, 109.2, 11.1; HRMS (ESI) *m/z* calcd. for $C_{18}H_{15}N_2$ $(M+H)^+$ 259.1235, found 259.1230; mp 185-188 ℃.



4ic

4ic was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (13.5 mg, 0.0201 mmol), AgOTf (10.1 mg, 0.039 mmol), and $NaBH_4$ (1.5 mg, 0.040 mmol) in THF for 15 min. Allyl oxime ether **1ic** (127 mg, 0.390 mmol) was then added to the catalyst mixture. DBU (79 mg, 0.524 mmole) was added to the complete reaction mixture and the complete reaction mixture was allowed to stir for 1h and then heated to 75 ℃ for 20 h. After column chromatography, **4ic** was isolated as light orange oil (68.4 mg, 56%). ^{1}H NMR (500

MHz, $CDCl_3$): δ 8.23 (brs, 1H), 8.01-7.99 (m, 2H), 7.35-7.33 (m, 2H), 7.26-7.23 (m, 2H), 7.20-7.19 (m, 3H), 6.73 (s, 1H), 4.38 (q, *J* = 7.0 Hz, 2H), 2.12 (s, 3H), 1.40 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.0, 141.4, 133.0, 130.2, 129.5, 129.4, 128.7, 127.8, 127.1, 126.6, 121.2, 119.5, 116.7, 60.8, 11.4, 11.1; HRMS (ESI) *m/z* calcd. for $C_{20}H_{20}NO_2$ $(M+H)^+$ 306.1494, found 306.1492.

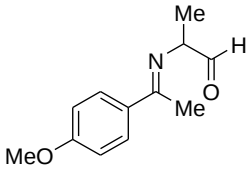


4id

4id was synthesized according to general procedure **F**. The catalyst mixture was prepared by mixing $[(cod)IrCl]_2$ (22.5 mg, 0.0335 mmol), AgOTf (16.8 mg, 0.065 mmol), and $NaBH_4$ (2.5 mg, 0.066 mmol) in THF for 15 min. Allyl oxime ether **1id** (129 mg, 0.642 mmol) was then added to the catalyst mixture. DBU (132 mg, 0.873 mmole) was added to the complete reaction mixture and the complete reaction mixture was allowed to stir for 1 hour and then heated to 75 ℃ for 20 h. After column chromatography, **4id** was isolated as an oil (47.6 mg, 41%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (vbs, 1H), 7.57-7.56 (m, 1H), 7.23-7.18 (m, 2H), 7.05-7.02 (m, 1H), 6.46 (s, 1H), 2.98 (t, *J* = 7.5 Hz, 2H), 2.77 (t, *J* = 7.5 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.6, 133.8, 130.2, 128.1, 126.7, 124.0, 122.1, 116.6, 115.9, 115.1, 30.4,

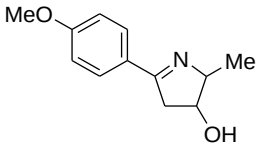
22.1, 13.0; HRMS (ESI) *m/z* calcd. for $C_{13}H_{14}N$ $(M+H)^+$ 184.1126, found 184.1125.

1.10.7 [1,3]-Rearrangement Intermediates Observation and Trapping



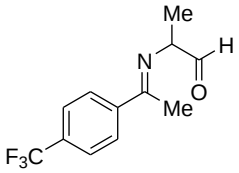
9a

^{1}H NMR of (500 MHz, dioxane-d_8) δ 9.67 (d, *J* = 2.0 Hz, 1H),7.89 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 4.17 (qd, *J* = 7.0 Hz, *J* = 2.0 Hz, 1H), 3.80 (s, 3H), 2.24 (s, 3H), 1.28 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, dioxane-d_8) δ 199.5, 163.3, 126.3, 126.0, 125.0, 111.1, 62.7, 52.6, 13.5, 12.2.



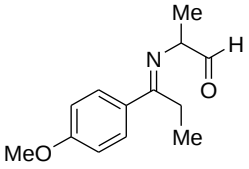
10a

^{1}H NMR of (500 MHz, dioxane-d_8) δ 7.78 (d, *J* = 9.0 Hz, 2H), 6.89 (d, *J* = 9.0 Hz, 2H), 4.12 (brs, 1H), 4.05-4.01(m, 2H), 3.79 (s, 3H), 3.13 (dd, *J* = 17.0 Hz, *J* = 7.5 Hz, 1H), 2.77 (dd, *J* = 17.0 Hz, *J* = 3.0 Hz, 1H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, dioxane-d_8) δ 160.7, 159.5, 127.0, 126.2, 111.3, 74.8, 74.3, 52.6, 41.5, 16.7.



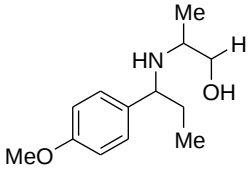
9e

^{1}H NMR of (500 MHz, dioxane-d_8) δ 9.70 (d, *J* = 1.5 Hz, 1H),7.92 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 4.27 (qd, *J* = 7.0 Hz, *J* = 1.5 Hz, 1H), 2.34 (s, 3H), 1.35 (d, *J* = 7.0 Hz, 3H).



9h

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.79 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 2.71 (q, *J* = 7.5 Hz, 2H), 2.62 (q, *J* = 7.5 Hz, 1H), 1.39 (d, *J* = 7.0 Hz, 3H), 1.12 (t, *J* = 7.5 Hz, 3H).

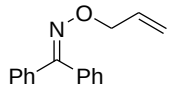


9hr (3:1 dr)

In an inert atmosphere glovebox, a 10 mL Teflon-sealed flask was charged with **2h** (0.1081 g, 0.493 mmol) and 4 mL of dioxane. The flask was then stoppered, removed

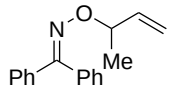
from the glovebox, and heated to 75 °C for 2.5 h to give aldehyde **9h**. The crude solution of **9h** was transferred to a 25 mL round bottom flask containing a slurry of $LiAlH_4$ (0.039 g, 1.03 mmol) in 10 mL THF. The reaction mixture was then allowed to stir for 4 h. At this time, the reaction mixture was diluted with 20 mL of MTBE and slowly quenched with water. The reaction mixture was then extracted with 3 x 20 mL of 1M HCl(aq), neutralized with 1M NaOH(aq), extracted with 3 x 15 mL of MTBE, and volatiles were removed under reduced pressure to give **9hr** as a light yellow oil (0.0728 g, 66%). ^{1}H NMR of major diastereomer (500 MHz, $CDCl_3$): δ 7.19-7.17 (m, 2H), 6.87-6.86 (m, 2H), 3.79 (s, 3H), 3.60 (dd, *J* = 8.0 Hz, *J* = 6.0 Hz, 1H), 3.37 (dd, *J* = 10.5 Hz, *J* = 4.5 Hz, 1H), 3.13 (dd, *J* = 10.5 Hz, *J* = 8.0 Hz, 1H), 2.56-2.53 (m, 1H), 1.69-1.60 (m, 2H), 0.99 (d, *J* = 6.0 Hz, 3H), 0.79 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR of major diasteromer (125 MHz, $CDCl_3$): δ 158.7, 135.9, 128.3, 113.8, 66.6, 61.2, 55.2, 51.3, 31.9, 16.8, 10.9; ^{1}H NMR of minor diastereomer (500 MHz, $CDCl_3$): δ 7.16-7.14 (m, 2H), 6.87-6.86 (m, 2H), 3.80 (s, 3H), 3.57 (dd, *J* = 10.5 Hz, *J* = 4.0 Hz, 1H), 3.48 (dd, *J* = 7.5 Hz, *J* = 6.5 Hz, 1H), 3.16 (dd, *J* = 10.5 Hz, *J* = 5.5 Hz, 1H), 3.17-3.14 (m, 1H), 1.77-1.72 (m, 1H), 1.59-1.53 (m, 1H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.80 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR of minor diasteromer (125 MHz, $CDCl_3$): δ 158.6, 136.7, 127.9, 113.8, 64.6, 61.6, 55.3, 51.4, 30.9, 18.6, 10.9; HRMS (ESI) *m/z* calcd. for $C_{13}H_{23}N_2O$ $(M+H)^+$ 223.1810, found 223.1814.

1.10.8 Preparation of *O*-Allyl Benzophenone Oximes



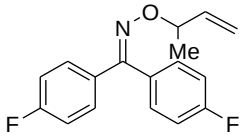
6

6 was prepared according to general procedure **A**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54-7.35 (m, 10 H), 6.12-6.04 (m, 1H), 5.36 (d, *J* = 17.0 Hz, 1H), 5.25 (d, *J* = 10.5 Hz, 1H), 4.72 (d, *J* = 5.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9, 136.6, 134.5, 133.4, 129.3, 129.2, 128.8, 128.2, 128.1, 128.0, 117.3, 75.4.



6a

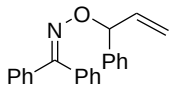
6a was prepared according to procedure reported in reference 36. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52-7.50 (m, 2 H), 7.45-7.40 (m, 5 H), 7.38-7.33 (m, 2 H), 6.02-5.95 (m, 1H), 5.24 (d, *J* = 17.0 Hz, 1H), 5.15 (d, *J* = 11.0 Hz, 1H), 4.88-4.83 (m, 1H), 1.39 (d, *J* = 7.0 Hz, 1H).



6g

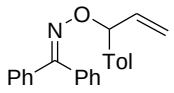
6i was prepared according to procedure reported in reference 36. ^{1}H NMR (500 MHz,

$CDCl_3$): δ 7.48-7.46 (m, 2H), 7.41-7.38 (m, 2H), 7.15-7.11 (m, 2H), 7.06-7.02 (m, 2H), 6.00-5.93 (m, 1H), 5.24 (d, *J* = 17.5 Hz, 1H), 5.16 (d, *J* = 10.5 Hz, 1H), 4.84-4.82 (m, 1H), 1.38 (d, *J* = 7.0 Hz, 3H).



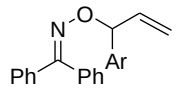
6c

6c was prepared according to procedure reported in reference 33 and 34. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.42 (m, 7H), 7.37-7.28 (m, 8H), 6.15-6.08 (m, 1H), 5.79 (d, *J* = 6.0 Hz, 1H), 5.28 (d, *J* = 17.5 Hz, 1H), 5.24 (d, *J* = 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.1, 140.6, 138.0, 136.6, 133.5, 129.4, 129.2, 128.7, 128.3, 128.1, 128.0, 127.9, 127.5, 127.1, 116.6, 86.4.



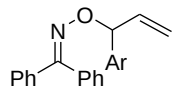
6d

6d was prepared according to procedure reported in reference 33 and 34. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.42 (m, 7H), 7.38-7.31 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.14-6.07 (m, 1H), 5.76 (d, *J* = 6.0 Hz, 1H), 5.27 (d, *J* = 17.5 Hz, 1H), 5.23 (d, *J* = 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.0, 138.2, 137.6, 137.2, 136.7, 133.5, 129.4, 129.2, 129.0, 128.7, 128.1, 128.0, 127.9, 127.1, 116.4, 86.3, 21.2.



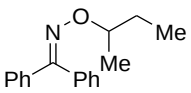
6e, Ar = *p*-Cl-phenyl

6f was prepared according to procedure reported in reference 33 and 34. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47-7.46 (m, 4H), 7.41-7.32 (m, 8H), 7.28-7.25 (m, 2H), 6.10-6.03 (m, 1H), 5.75 (d, *J* = 6.0 Hz, 1H), 5.27 (d, *J* = 3.5 Hz, 1H), 5.24 (s, 1H).



6f, Ar = *p*-CF_3-phenyl

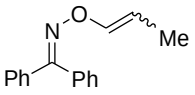
6g was prepared according to procedure reported in reference 33 and 34. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.5 Hz, 2H), 7.48-7.41 (m, 9H), 7.38-7.36 (m, 1H), 7.34-7.31 (m, 2H), 6.10-6.03 (m, 1H), 5.82 (d, *J* = 6.5 Hz, 1H), 5.29 (d, *J* = 4.5 Hz, 1H), 5.26 (s, 1H).



6ar

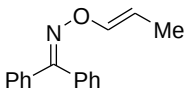
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52-7.50 (m, 2H), 7.44-7.39 (m, 5H), 7.37-7.34 (m, 3H), 4.44-4.27 (m, 1H), 1.78-1.69 (m, 1H), 1.61-1.54 (m, 1H), 1.30 (d, *J* = 6.5 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.5, 137.2, 133.7, 129.5, 128.9, 128.5, 128.1, 127.9, 127.8, 28.5, 26.5, 19.3, 9.9.

1.10.9 Preparation of *O*-Vinyl Benzophenone Oximes



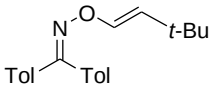
7 (*E*:*Z* = 1:2.1)

7 was synthesized according to general procedure **B**. ^{1}H NMR of *E*-isomer (500 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.50-7.46 (m, 3H), 7.44-7.37 (m, 5H), 6.91-6.87 (m, 1H), 5.24-5.19 (m, 1H), 1.64 (dd, *J* = 7.0, *J* = 1.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 147.5, 135.9, 132.9, 129.7, 129.3, 129.1, 128.3, 128.2, 128.1, 101.1, 12.3; ^{1}H NMR of *Z*-isomer (500 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.50-7.46 (m, 5H), 7.44-7.37 (m, 3H), 6.98-6.96 (m, 1H), 4.54-4.48 (m, 1H), 1.50 (d, *J* = 7.0 Hz, *J* = 2.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 147.0, 135.8, 132.9, 129.7, 129.4, 129.1, 128.3, 128.2, 128.0, 100.0, 9.6.



7-*E*

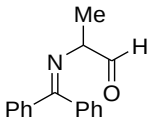
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.5 Hz, 2H), 7.47-7.45 (m, 3H), 7.42-7.35 (m, 5H), 5.20 (dq, *J* = 13.5 Hz, *J* = 6.5 Hz, 1H), 1.64 (dd, *J* = 6.5 Hz, *J* = 1.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 147.4, 135.9, 132.9, 129.7, 129.2, 129.1, 128.3, 128.2, 128.1, 101.1, 12.3.



7t

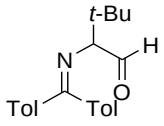
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 13.0 Hz, 1H), 5.23 (d, *J* = 13.0 Hz, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 1.06 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.5, 145.1, 139.8, 139.0, 133.4, 130.1, 129.4, 129.0, 128.7, 128.3, 117.6, 30.9, 30.4, 21.5, 21.4.

1.10.10 Preparation of α-Imino Carbonyl Compounds



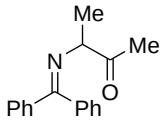
8

^{1}H NMR (500 MHz; dioxane-d_8): δ 9.64 (d, *J* = 1.5 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.50-7.37 (m, 4H), 7.33 (t, *J* = 7.0 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 2H), 3.89 (q, *J* = 6.5 Hz, 1H), 1.30 (d, *J* = 6.5 Hz, 3H).



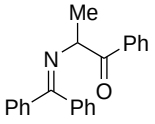
8t

^{1}H NMR (500 MHz; dioxane-d_8): δ 9.70 (d, J = 3.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.0 Hz, 2H), 3.42 (d, J = 3.0 Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H), 1.00 (s, 9H); ^{13}C NMR (125 MHz, dioxane-d_8): δ 201.0, 170.1, 140.3, 138.1, 137.4, 133.7, 129.0, 128.6, 128.5, 127.8, 79.7, 36.0, 26.3, 20.4, 20.3.



8a

^{1}H NMR (500 MHz; $CDCl_3$): δ 7.69 (d, J = 6.5 Hz, 2H), 7.51-7.42 (m, 3H), 7.44 (t, J = 7.5 Hz, 1H), 7.38 (t, J = 7.5 Hz, 2H), 7.16 (d, J = 6.5 Hz, 2H), 4.01 (q, J = 6.5 Hz, 1H), 2.29 (s, 3H), 1.35 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 210.1, 169.0, 139.4, 136.1, 130.4, 128.8, 128.7, 128.6, 128.1, 127.5, 68.1, 26.9, 19.0.

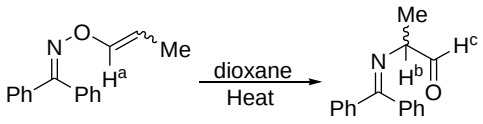


8c

^{1}H NMR (500 MHz; $CDCl_3$): δ 7.88 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H),

7.54-7.48 (m, 4H), 7.43-7.38 (m, 3H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.21-7.19 (m, 2H), 4.91 (q, *J* = 6.5 Hz, 1H), 1.57 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3, 169.2, 139.5, 136.5, 136.2, 132.7, 130.3, 128.9, 128.8, 128.7, 128.6, 128.3, 128.0, 127.7, 64.3, 20.1.

1.10.11 Eyring Analysis and Arrhenius Analysis of [1,3]-Rearrangements



7 **8**

The values for Eyring plot of **7** were shown below (Table 12). Ploting $ln(k)$ versus $\frac{1}{T}$ gave excellent linear correlation shown in Figure 3.

Table 12. Eyring Plot of 7

T	1/T	k	k/T	Ln(k/T)
363	0.002755	1.98E-03	5.45455E-06	-12.12
353	0.002833	8.67E-04	2.45609E-06	-12.92
343	0.002915	3.12E-04	9.09621E-07	-13.91
333	0.003003	6.57E-05	1.97297E-07	-15.44
323	0.003096	2.15E-05	6.65635E-08	-16.53

In order to estimate the *A* and E_a the [1,3]-rearrangement, Arrhenius analysis was utilized using the initial rate constant obtained from Figure 2. Arrhenius equation was shown below (Eq. 5).

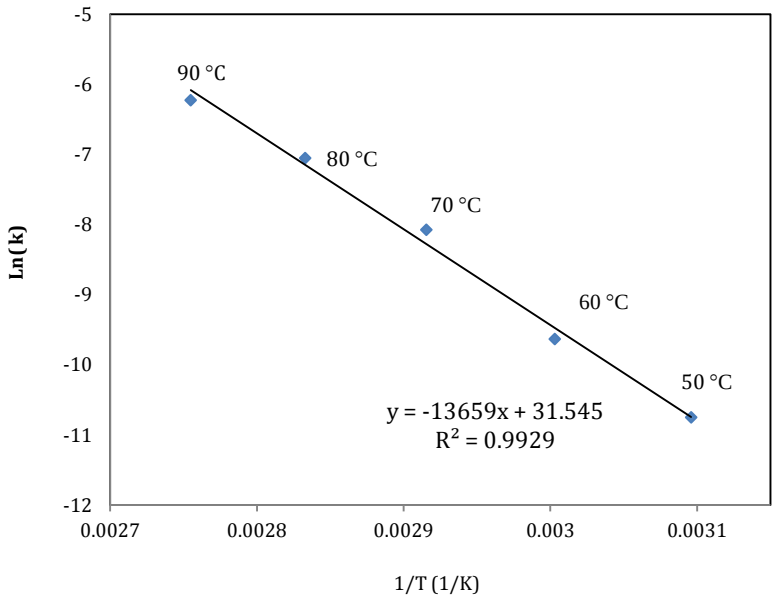
$$\ln(k) = \ln(A) - \frac{E_a}{R}\left(\frac{1}{T}\right) \quad (5)$$

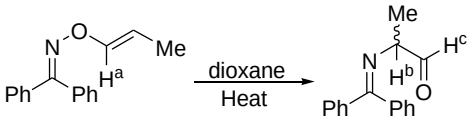
The values for Arrhenius plot of **7** were shown below (Table 13). Ploting $ln(k)$ versus $\frac{1}{T}$ gave excellent linear correlation (Figure 6); -$\frac{E_a}{R}$ was determined as the slope of the linear formula and intercept was $\ln(A)$ in Figure 6. E_a was found to be 27.125 Kcal·mol^{-1} and A was found to be 5.0098E+13 mol·sec^{-1}.

Table 13. Arrhenius Plot of 7

T	1/T	k	Ln k
363	0.002755	1.98E-03	-6.22466
353	0.002833	8.67E-04	-7.05047
343	0.002915	3.12E-04	-8.07251
333	0.003003	6.57E-05	-9.63041
323	0.003096	2.15E-05	-10.7475

Figure 6. Arrhenius Analysis: [1,3]-Rearrangement of 7





7-*E* **8**

The values for Eyring plot of **7-*E*** were shown below (Table 14). Ploting $ln(k)$ versus $\frac{1}{T}$ gave excellent linear correlation shown in Figure 5. The values for Arrhenius plot of **7-*E*** were shown below (Table 15). Ploting $ln(k)$ versus $\frac{1}{T}$ gave excellent linear correlation shown in Figure 7. Using the slope and intercept obtained from Figure 7, E_a was found to be 26.0845 Kcal·mol^{-1} and A was found to be 1.28582E+13 mol·sec^{-1}.

Table 14. Eyring Plot of 7-*E*

T	1/T	k	k/T	Ln(k/T)
353	0.002833	7.73E-04	2.19E-06	-13.03
343	0.002915	3.16E-04	9.22E-07	-13.90
333	0.003003	1.14E-04	3.41E-07	-14.89
323	0.003096	3.02E-05	9.36E-08	-16.18
313	0.003195	6.69E-06	2.14E-08	-17.66

Figure 7. Arrhenius Analysis: [1,3]-Rearrangement of 7-*E*

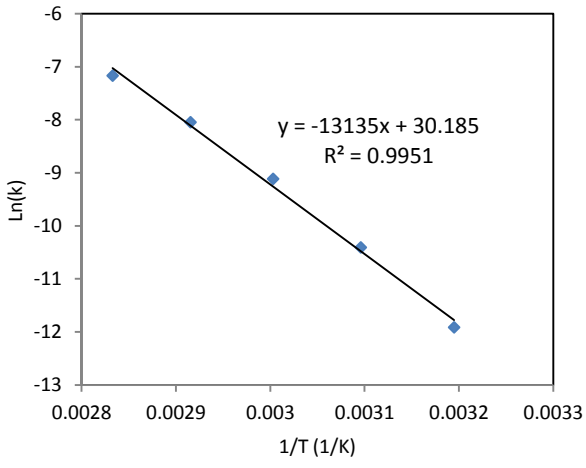


Table 15. Arrhenius Plot of 7-*E*

T	1/T	k	Ln k
353	0.002833	7.70E-04	-7.16912
343	0.002915	3.20E-04	-8.04719
333	0.003003	1.10E-04	-9.11503
323	0.003096	3.02E-05	-10.4077
313	0.003195	6.69E-06	-11.9149

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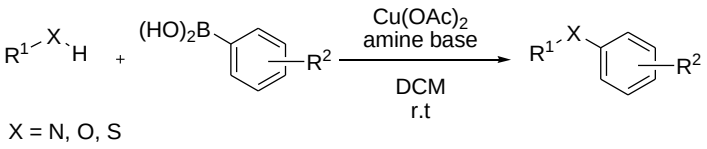
2 Preparation of α-Oxygenated Ketones via Rearrangement of *N*-Enoxyphthalimides

2.1 Chan-Lam-Evans Coupling Reaction

Chan-Lam-Evans coupling reaction was widely used in the formation of C–O, C–N or C–S compounds employing copper salt, amine base, and boronic acid (Scheme 1).[53] Compared to the classic Ullman-Goldberg coupling reaction,[54-58] this transformation required mild reaction conditions, such as weak base, room temperature, and ambient atmosphere.

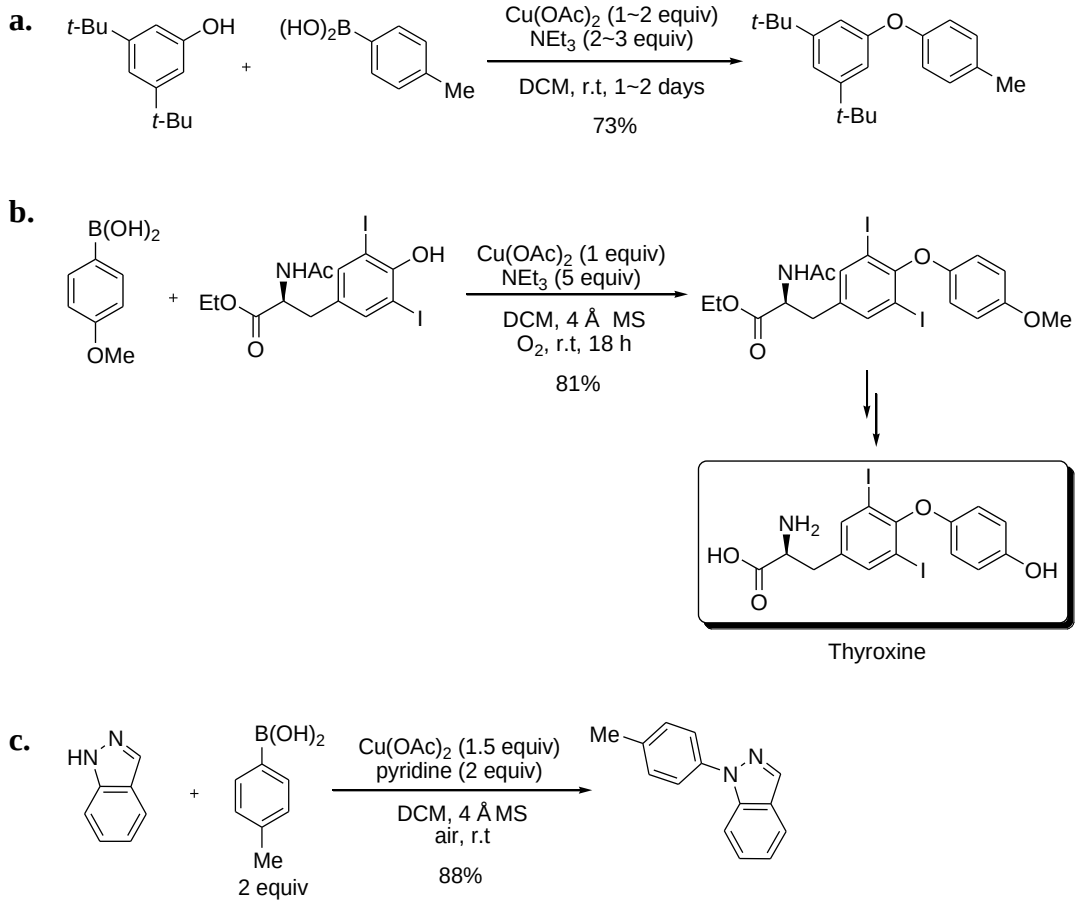
Scheme 1. General Scheme of Chan-Lam-Evans Coupling Reaction



In 1998, Chan reported the original discovery of C(aryl)–O bond formation using copper-mediated arylboronic acid cross coupling and afforded biaryl ether motif (Scheme 2a).[59a] At the same time, Evans and coworkers showed an efficient synthesis of thyroxine employing copper-mediated etherification of phenol and aryl boronic acid (Scheme 2b).[59b] Meanwhile, Lam demonstrated the C–N bond formation[60] under copper-mediated coupling condition using heterocyclic substrate as the nucleophile

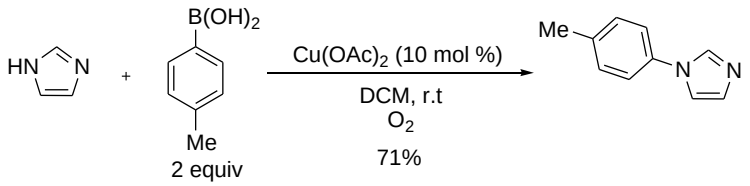
and arylboronic acid (Scheme 2c).[59c]

Scheme 2. Examples of Chan-Lam-Evans Coupling Reaction



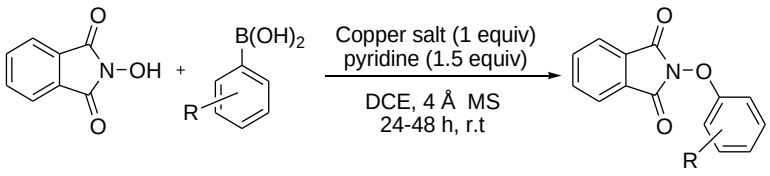
In the synthesis of thyroxine, Evans had shown that a 10 mol % $Cu(OAc)_2$ could be employed to form biaryl ether in 30% yield in presence of oxygen but 9% yield under argon.[59b] It implied these C–heteroatom bonds formation might be possible to perform under catalytic condition. Later on, Collman reported a catalytic cross-coupling condition using 10 mol % $[Cu(OH)\cdot TMEDA]_2Cl_2$, imidazole, and excess arylboronic aicd under an atmosphere of O_2 (Scheme 3).[61]

Scheme 3. Example of Copper-Catalyzed Cross-Coupling



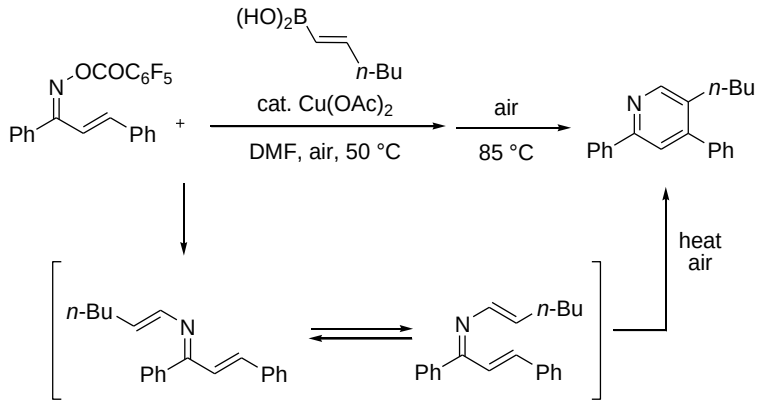
Kelly and Sharpless reported a copper-mediated coupling reaction using phthalimide and arylboronic acid to form new C–O bond (Scheme 4).[62] It showed the diversity of oxygen coupling partner which was not limited to phenol or phenol derivatives.[63,64]

Scheme 4. Copper-Mediated Coupling using Phthalimide as Coupling Partner



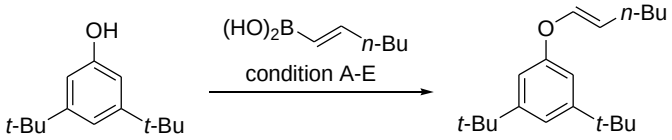
Unlike arylboronic acids, using alkenyl boronic acids as the coupling components were hardly reported. Liebeskind and Liu showed the formation of substituted pyridine through [3,3]-rearrangement of *N*-vinyl chalcone imine which was prepared through copper-catalyzed cross-coupling of α,β-unsaturated ketoxime *O*-pentafluorobenzoate and *trans*-1-hexen-1-yl-boronic acid (Scheme 5).[65]

Scheme 5. Copper-Catalyzed Cross-Coupling using Vinyl Boronic Acid as Coupling Partner



Lam and coworkers also reported a copper-mediated/catalyzed coupling with vinylboronic acid to form a C–N or C–O bond (Scheme 6).[66] Both stoichiometric and catalytic condition were demonstrated the activity toward the formation of new C-heteroatom bonds. However, only stoichiometric condition showed activity for the C-O bond formation; catalytic conditions showed no or poor activity even in presence of O_2 or a variety of external oxidants (Scheme 6).

Scheme 6. Copper-Assisted Coupling using Vinyl Boronic Acid as Coupling Partner



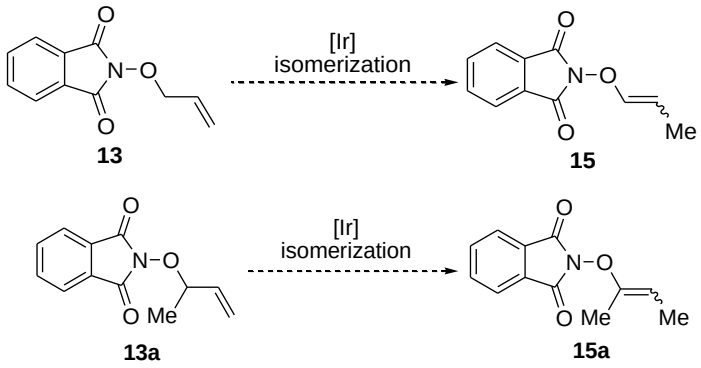
A: $Cu(OAc)_2$ (1.1 equiv), NEt_3, r.t, air 52%
B: $Cu(OAc)_2$ (10 mol %), NEt_3, r.t, O_2 12%
C: $Cu(OAc)_2$ (10 mol %), TEMPO (1.1 equiv), NEt_3, 50 °C, air 12%
D: $Cu(OAc)_2$ (10 mol %), pyridine *N*-oxide (1.1 equiv), NEt_3, 50 °C, air 6%
E: $[Cu(OH)TMEDA]_2Cl_2$ (10 mol %), 50 °C, O_2 NR

2.2 Preparation of *N*-Enoxyphthalimides via Chan-Lam-Evans Reaction

As the result shown in Chapter 1, the iridium-isomerization allowed us to obtain *O*-vinyl oximes through easily prepared substrate *O*-allyl oximes. However, it showed no reactivity or low functional group tolerance to the α-substituted *O*-allyl oximes.

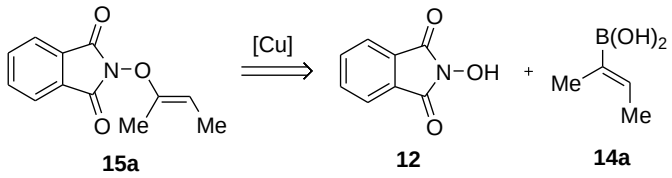
O-allyl phthalimide **13** and **13a** were prepared and subjected to the optimal Ir-isomerization condition described in Chapter 1 to afford *O*-vinyl motif (Scheme 7). However, no formations of **15** or **15a** were observed.

Scheme 7. *O*-Vinyl Phthalimide Formation via Ir-Isomerization



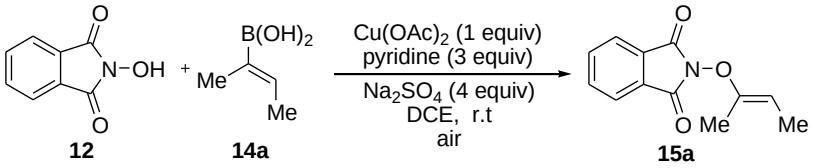
Therefore, an alternative route was proposed to afford **15a**. Inspired by the works done by Kelly and Sharpless regarding of the phthalimide cross-coupling shown in Scheme 4, we envisioned that *E*-conformation *O*-vinyl phthalimide **15a** could be obtained through the cross-coupling of *N*-hydroxyphthalimide **13** and *E*-vinyl boronic acid **14a** under Chan-Lam-Evans condition (Scheme 8).

Scheme 8. Proposed Route for 15a Preparation



The reaction was performed by Dr. Dongliang Mo and Aditi Patil employing conventional copper-mediated Chan-Lam-Evans condition using a mixture of copper salt, pyridine, and Na_2SO_4 under open air, and a variety of copper salts were tested for the transformation of **15a** (Table 1). Copper acetate was found to give the best conversion of **15a** (Table 1, entry 1). Other common copper(II) and copper(I) salts also gave conversion of **15a**.

Table 1. Optimization of Copper Salts

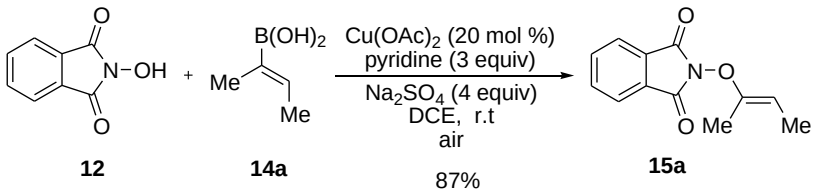


Entry	Cu	yield (%)[a]
1	$Cu(OAc)_2$	96
2	CuCl	84
3	CuI	NR
4	$Cu(O_2CCF_3)_2$	92
5	$Cu(OTf)_2$	60
6	CuTC	88

[a] ^{1}H NMR yields based on the use of 1,3,5-trimethoxybenzene as an internal standard.

A 20 mol % $Cu(OAc)_2$ was also tested by Dr. Dongliang Mo and Aditi Patil for the transformation of **15a** using the same condition in good yield without any addition of external oxidants or under O_2 as the example shown in Scheme 6 (Scheme 9).

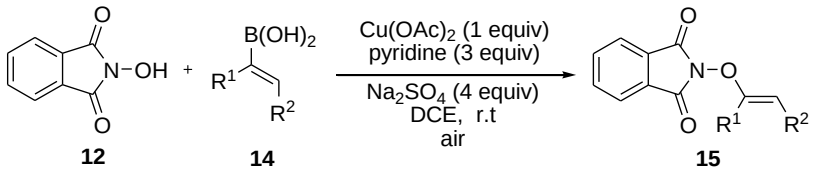
Scheme 9. Preparation of 15a under Catalytic Condition



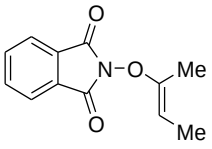
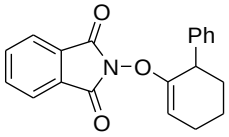
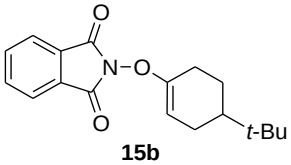
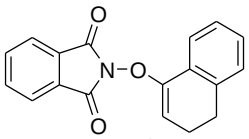
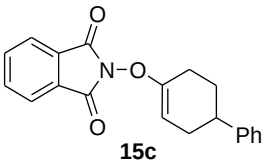
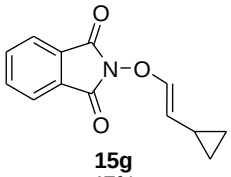
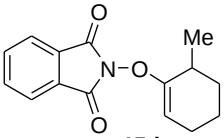
12 **14a** **15a**

With the optimal condition in hand, more than 20 examples of *O*-vinyl phthalimides were prepared employing stoichiometric or catalytic condition. Selected examples of my contribution to the *O*-vinyl phthalimides preparation scope were shown in Table 2. Acyclic vinyl boronic acids were tolerated the transformation. Dialkyl vinyl boronic acid gave excelent yield under both condition (Table 2, entry 1; Scheme 10). Cyclic boronic acids were tolerated the transformation. Both *para*- and *ortho*-substituted cylohexenyl boronic acids gave the formation of corresponding *O*-vinyl phthalimides using stoichiometric condition (Table 2, entries 2-5). Bicyclic boronic acid tolerated the transformation using stoichiometric as well as catalytic condition (Table 2, entry 6; Scheme 10). Mono-substituted boronic acid was also tolerated the transformation using stoichoimetric condition (Table 2, entry 7).

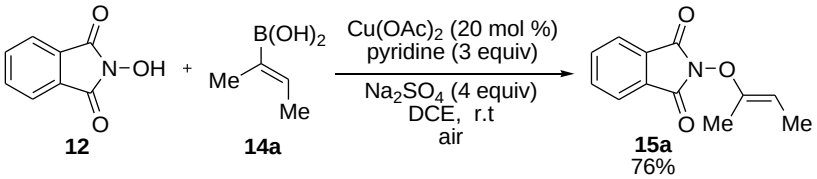
Table 2. Scope under Stoichiometric Cross-Coupling Condition



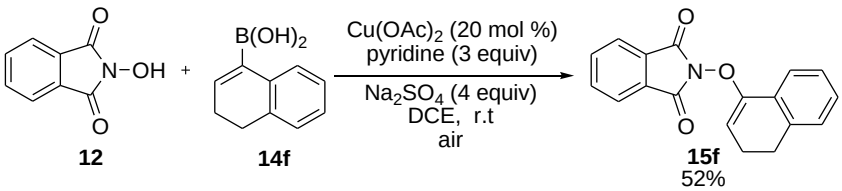
12 **14** **15**

Entry	Product	Entry	Product
1	 **15a** 98%	5	 **15e** 91%
2	 **15b** 83%	6	 **15f** 76%
3	 **15c** 64%	7	 **15g** 47%
4	 **15d** 41%		

Scheme 10. Scope under Catalytic Cross-Coupling Condition



12 **14a** **15a** 76%

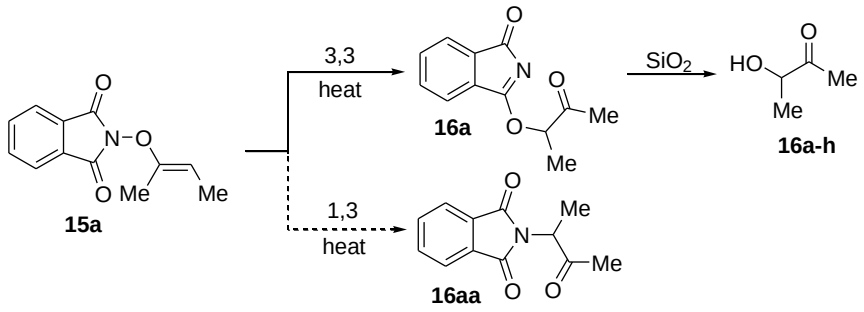


12 **14f** **15f** 52%

2.3 Preparation of α-Oxygenated Ketones via One-Flask Condition

According to the results of pyrrole synthesis shown in Chapter 1, we knew the rearrangement of *O*-vinyl oxime could be triggered by heat. Therefore, we envisioned that 2 possible rearrangement adduct, **16aa** and **16a**, could be formed through [1,3]- or [3,3]-rearrangement pathway respectfully from **15a**. *O*-Vinyl phthalimide **15a** was diluted in benzene-d_6 in a NMR tube and heated to 90 ℃ to test the transformation of rearrangement. However, only **16a** was observed in the NMR and no formation of 1,3-adduct **16aa** when Dr. Dongliang Mo and Aditi Patil performed the rearrangement experiment, and **16a** was hydrolyzed to α-hydroxy ketone **16a-h** during chromatography (Scheme 11).

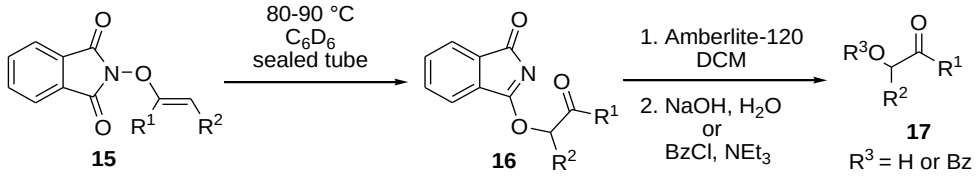
Scheme 11. Possible Rearrangement Pathway of 15a

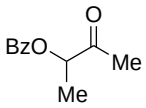
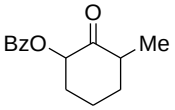
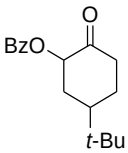
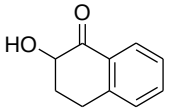
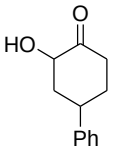


Even though imidate **16a** was hydrolyzed during the chromatography, it occurred to them that the facile formation of α-oxygenated ketones could be achieved using one-flask procedure including [3,3]-rearrangement and hydrolysis. More than 20 examples of α-oxygenated ketones were prepared employing this one-flask method.

Selected examples of my contribution to the α-oxygenated ketones preparation scope were shown in Table 3. Acyclic *O*-vinyl phthalimides, **15a** were tolerated for this one-flask procedure and gave **17a** in good yields (Table 3, entries 1). Cyclic *O*-vinyl phthalimides **15f** tolerated this multiple-steps transformation as well (Table 3, entry 5).

Table 3. Scope under One-Flask Condition

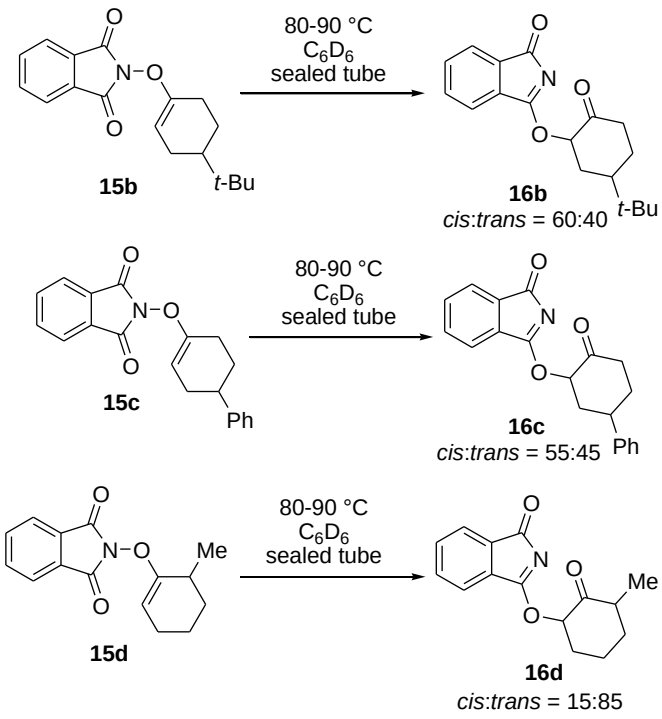


Entry	Product	Entry	Product
1	 **17a** 86%	4	 **17d** 66%, cis: *trans* = 20:80
2	 **17b** 66%, cis: *trans* = 75:25	5	 **17f** 87%
3	 **17c** 82%, cis: *trans* = 60:40		

O-Vinyl phthalimides prepared from the substituted cyclohexenyl boronic acids were subjected to the one-flask method as well and showed different diastereoselectivity due to the position of substitution. The α-oxygenated ketones **17b** and **17c** were prepared in good yields with *cis* isomer as the majority (Table 3, entries 2,

3). However, opposite diastereoselectivity was observed in the preparation of α-oxygenated ketone **17d** (Table 3, entry 4). The same diastereoselectivity were observed in the formation of imidate intermediates **16b**, **16c**, and **16d**. Imidates **16b** and **16c** were observed with *cis* isomer as the major products, and **16d** was observed with *trans* as the major isomer (Scheme 12).

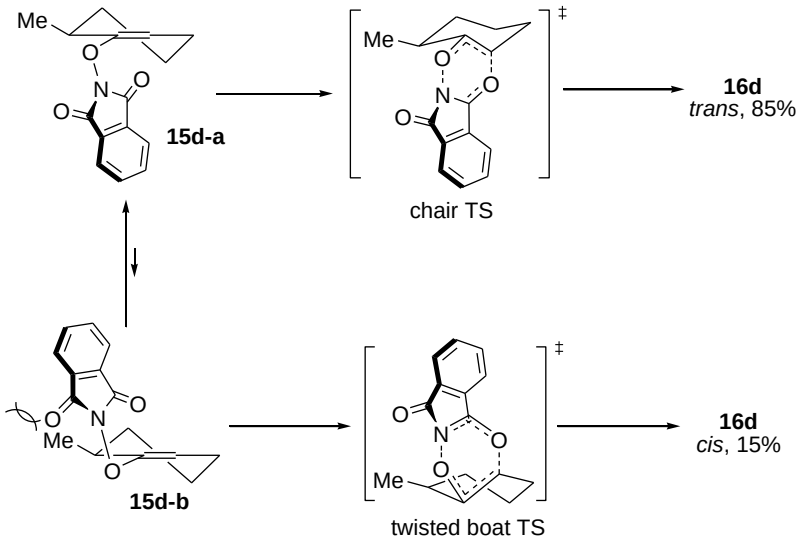
Scheme 12. Observation of Imidates 16b, 16c, and 16d



The diastereoselectivity formation of the imidate **16d** could be explained by the proposed model show in Figure 1. The C–O single bond free rotation was minimized by the methyl substitution at the C-6 position and left the **15d-a** as the major conformation. The ***O*-**vinyl phthalimide **15d-a** underwent chair-like transition state to give *trans* configuration product. In the other hand, the minor conformation **15d-b** underwent

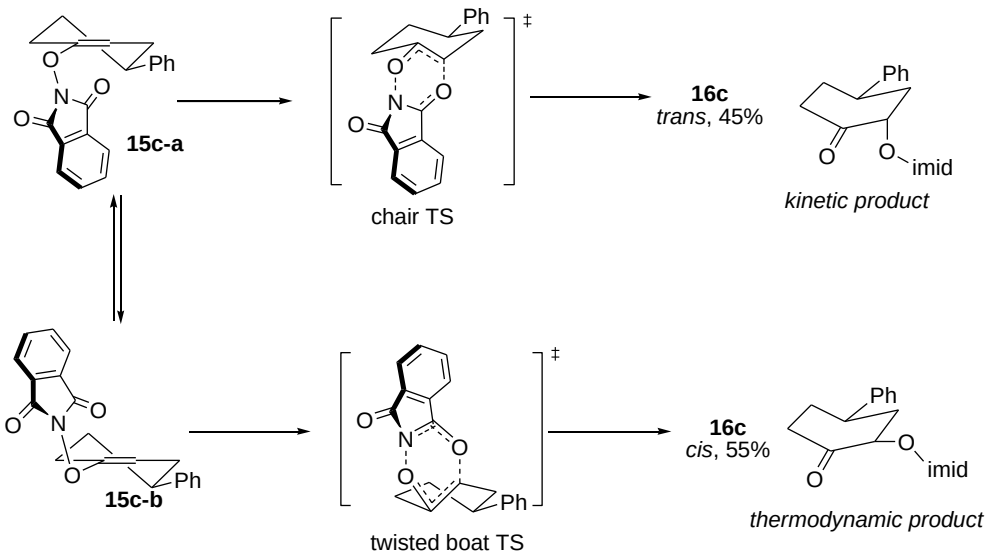
twisted boat-like transition state to give *cis* configuration product.

Figure 1. Diastereoselectivity Formation of Imidate 16d



Likewise, the poor diastereoselectivity formation of imidate **16c** could be explained by the similar model show in Figure 2 as well. The C–O single bond free rotation was not minimized by the substitution at the C-4 position and left the **15c-a** and **15c-b** in equilibrium. The ***O***-vinyl phthalimide **15c-a** underwent chair-like transition state to give *trans* configuration product which was the kinetic product. The ***O***-vinyl phthalimide **15c-b** underwent twisted boat-like transition state to give the thermodynamic *cis* configuration product.

Figure 2. Non-Diastereoselectivity Formation of Imidate 16c



2.4 Summary

The copper-mediated cross-coupling reaction was demonstrated as an adequate alternative route to the formation of *O*-vinyl species. Compared to the *O*-allyl isomerization reaction, this cross-coupling showed more diversity, functional group tolerance, and it allowed us to prepare *O*-vinyl phthalimides with specific olefin geometry. The one-flask reaction provided a facile method to access the α-oxygenated ketones in a simple and mild reaction condition. My contribution to this project lie on the expanding the scope of *N*-enoxyphthalimides and α-oxygenated ketones preparation as well as the optimizations of the boronic acids hydrolysis condition, imidate hydrolysis condition, and benzoylation protection condition.

2.5 Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using 500 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the scale, multiplicity (br = broad, s = singlet, d = doublet, t =triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. High resolution mass spectra were acquired on an LTQ FT spectrometer, and were obtained by peak matching. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Medium pressure liquid chromatography was performed to force flow the indicated solvent system down columns packed with 60Å (40 – 60 μm) mesh silica gel (SiO_2). Unless otherwise noted, all reagents were obtained from commercial sources and, where appropriate, purified prior to use. THF and CH_2Cl_2 were dried by filtration through alumina according to the procedure of Grubbs.[35] TMEDA was distilled over CaH_2 and stored under N_2 prior to use.

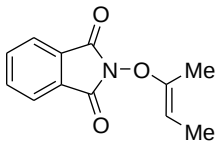
2.5.1 Preparation of *N*-Enoxyphthalimides

N-Enoxyphthalimides **15a-15g**were synthesized according to general procedure **A** or **B**. General procedure **A** and **B** were adopted from reference 62a.

General procedure A:[62a] A scintillation vial was charged with *N*-hydroxyphthalimide

12 (1 equiv), vinyl boronic acid **14** (2 equiv), $Cu(OAc)_2$ (1 equiv), and anhydrous Na_2SO_4 (4-6 equiv). These solids were then diluted with 1,2-dichloroethane to form a 0.1 M solution of *N*-hydroxyphthalimide. Pyridine (3 equiv) was added to the resulting slurry via syringe. The scintillation vial was then capped with a septum pierced with a ventilation needle and the reaction mixture was stirred at 25 ℃ for 12 h. 1,2-Dichloroethane and pyridine were removed under reduced pressure and the crude reaction mixture was purified by medium pressure chromatography to give *N*-enoxyphthalimide **15** as a white solid.

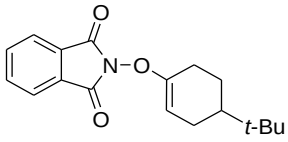
General procedure B:[62a] A scintillation vial was charged with *N*-hydroxyphthalimide **12** (1 equiv), vinyl boronic acid **14** (2 equiv), $Cu(OAc)_2$ (20 mol %), and anhydrous Na_2SO_4 (4-6 equiv). These solids were then diluted with 1,2-dichloroethane to form a 0.1 M solution of *N*-hydroxyphthalimide. Pyridine (3 equiv) was added to the resulting slurry via syringe. The scintillation vial was then capped with a septum pierced with a ventilation needle and the reaction mixture was stirred at 25 ℃ for 12-48 h. 1,2-Dichloroethane and pyridine were removed under reduced pressure and the crude reaction mixture was purified by medium pressure chromatography.



15a

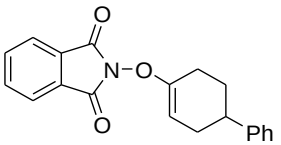
15a was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), *Z*-2-buten-2-yl boronic acid **14a** (0.060 g, 0.60 mmol), $Cu(OAc)_2$ (0.054 g, 0.30 mmol), Na_2SO_4 (0.256 g, 1.80 mmol), and pyridine (72.6 µl, 0.900 mmol). After chromatography (1:4; ethyl acetate: hexanes), **15a** was isolated as a white solid (0.065 g, 98%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.89-7.86 (m, 2H), 7.80-7.76 (m, 2H), 4.85 (q, *J* = 7.0 Hz, 1H), 1.99 (s, 3H), 1.56 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.0, 152.4, 134.6, 128.9, 123.7, 96.4, 13.1, 11.2; HRMS (ESI) *m/z* calcd. for $C_{12}H_{11}NO_3Na$ $(M+Na)^+$ 240.0637, found 240.0636; mp 112-115 ℃.

General procedure **B** was executed using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), *Z*-2-buten-2-yl boronic acid **14a** (0.060 g, 0.60 mmol), $Cu(OAc)_2$ (0.011 g, 0.59 mmol), Na_2SO_4 (0.256 g, 1.80 mmol), and pyridine (72.6 µl, 0.900 mmol). After chromatography, **15a** was isolated as a white solid (0.051 g, 76%).



15b

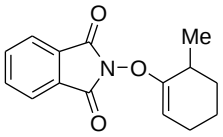
15b was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.040 g; 0.24 mmol), 4-*t*-butyl-1-cyclohexenyl boronic acid **14b** (0.088 g, 0.48 mmol), $Cu(OAc)_2$ (0.044 g, 0.24 mmol), Na_2SO_4 (0.075 g, 1.1 mmol), and pyridine (60 μl, 0.72 mmol). After chromatography (2:8; ethyl acetate: hexanes), **15b** was isolated as a white solid (0.060 g, 83%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.86-7.84 (m, 2H), 7.77-7.75 (m, 2H), 4.94 (d, *J* = 5.5 Hz ,1H), 2.33-2.34 (m, 2H), 2.02-1.99 (m, 1H), 1.92-1.89 (m, 1H), 1.81-1.76 (m, 1H), 1.35-1.23 (m, 2H), 0.84 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.8, 154.6, 134.6, 128.8, 123.7, 98.5, 43.7, 32.1, 27.3, 25.6, 24.1, 23.6; HRMS (ESI) *m/z* calcd. for $C_{18}H_{21}NO_3Na$ $(M+Na)^+$ 322.1419, found 322.1423.



15c

15c was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), 4-phenyl-1-cyclohexenyl boronic acid **14c** (0.120 g, 0.594 mmol), $Cu(OAc)_2$ (0.054 g, 0.30 mmol), Na_2SO_4 (0.256 g,

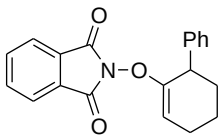
1.80 mmol), and pyridine (72.7 μl, 0.901 mmol). After chromatography (2:8; ethyl acetate: hexanes), **15c** was isolated as a white solid (0.063 g, 64%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.91-7.88 (m, 2H), 7.81-7.77 (m, 2H), 7.32-7.29 (m, 2H), 7.23-7.19 (m, 3H), 5.08 (t, *J* = 2.5 Hz,1H), 2.84 (dddd, *J* = 15.0 Hz, *J* = 8.0 Hz, *J* = 5.0 Hz, *J* = 3.0 Hz, 1H), 2.60-2.53 (m, 1H), 2.47-2.43 (m, 1H), 2.33-2.28 (m, 1H), 2.23-2.17 (m, 1H), 2.09-2.06 (m, 1H), 2.02-1.95 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9, 154.6, 145.8, 134.7, 128.9, 128.5, 126.9, 126.3, 123.8, 98.2, 39.9, 31.0, 29.3, 25.1; HRMS (ESI) *m/z* calcd. for $C_{20}H_{18}NO_3$ $(M+H)^+$ 320.1287, found 320.1296.; mp 127-131 ℃.



15d

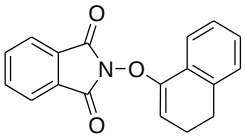
15d was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), 2-methyl-1-cyclohexenyl boronic acid **14d** (0.126 g, 0.900 mmol), $Cu(OAc)_2$ (0.054 g, 0.30 mmol), Na_2SO_4 (0.187 g, 1.32 mmol), and pyridine (72.4 μl, 0.900 mmol). After chromatography (2:8; ethyl acetate: hexanes), **15d** was isolated as a white solid (0.032 g, 41%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.87-7.85 (m, 2H), 7.78-7.76 (m, 2H), 4.86 (t, *J* = 3.0 Hz, 1H), 2.60-2.58 (m, 1H), 2.00-1.98 (m, 2H), 1.88-1.83 (m, 1H), 1.64-1.49 (m, 3H), 1.28 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9, 158.4, 134.6, 128.9, 123.7, 97.4,

31.0, 29.9, 23.3, 19.3, 18.6; HRMS (ESI) *m/z* calcd. for $C_{15}H_{15}NO_3Na$ $(M+Na)^+$ 280.0950, found 280.0944.; mp 78-80 ℃.



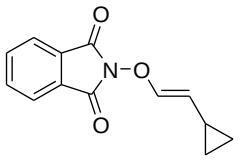
15e

15e was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), 2-phenyl-1-cyclohexenyl boronic acid **14e** (0.131 g, 0.650 mmol), $Cu(OAc)_2$ (0.054 g, 0.30 mmol), Na_2SO_4 (0.187 g, 1.32 mmol), and pyridine (72.4 μl, 0.900 mmol). After chromatography (2:8; ethyl acetate: hexanes), **15e** was isolated as a white solid (0.091 g, 91%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.90-7.88 (m, 2H), 7.80-7.78 (m, 2H), 4.86 (t, *J* = 2.5 Hz, 1H), 2.87-2.81 (m, 1H), 2.60-2.54 (m, 2H), 2.47-2.42 (m, 1H), 2.32-2.29 (m, 1H), 2.22-2.17 (m, 1H), 2.09-2.04 (m, 1H), 2.00-1.92 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.9, 154.6, 145.8, 134.7, 128.8, 128.5, 126.9, 126.3, 123.8, 98.2, 39.8, 31.0, 29.3, 25.1.



15f

15f was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), boronic acid **14f** (0.106 g, 0.609 mmol), $Cu(OAc)_2$ (0.054 g, 0.30 mmol), Na_2SO_4 (0.256 g, 1.80 mmol), and pyridine (72.4 µl, 0.899 mmol). After chromatography (1:2; ethyl acetate: hexanes), **15f** was isolated as alight orange solid (0.068 g, 76%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.92-7.90 (m, 2H), 7.81-7.79 (m, 2H), 7.70 (d, *J* = 7.0 Hz, 1H), 7.28-7.22 (m, 2H), 7.16 (d, *J* = 7.0 Hz, 1H), 5.26 (t, *J* = 4.5, 1H), 2.81 (t, *J* = 8.0, 2H), 2.36-2.32 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7, 152.2, 136.7, 134., 128.9, 128.4, 128.3, 127.3, 126.5, 123.9, 121.7, 99.4, 27.8, 21.4; HRMS (ESI) *m/z* calcd. for $C_{18}H_{13}NO_3Na$ $(M+Na)^+$ 314.0793, found 314.0794.; mp 110-114 ℃.



15g

15g was synthesized according to general procedure **A** using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), *trans*-2-cyclopropylvinyl boronic acid **14g** (0.672 g, 0.601 mmol), $Cu(OAc)_2$ (0.054 g, 0.30 mmol), Na_2SO_4 (0.256 g,

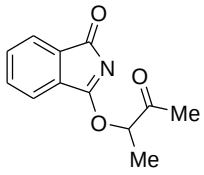
1.80 mmol), and pyridine (72.6 μl, 0.900 mmol). After chromatography (2:8; ethyl acetate: hexanes), **15g** was isolated as a white solid (0.033 g, 47%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.88-7.85 (m, 2H), 7.79-7.77 (m, 2H), 6.57 (d, *J* = 12.0 Hz, 1H), 5.10 (dd, *J* = 12.0 Hz, *J* = 8.5 Hz, 1H), 1.30-1.23 (m, 1H), 0.69-0.66 (m, 2H), 0.34-0.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7, 145.2, 134.7, 128.8, 123.8, 114.8, 8.3, 6.1; HRMS (ESI) *m/z* calcd. for $C_{13}H_{12}NO_3$ $(M+H)^+$ 230.0817, found 230.0823; mp 69-72 ℃.

General procedure **B** was executed using the following reagents: *N*-hydroxyphthalimide **12** (0.050 g; 0.31 mmol), *trans*-2-cyclopropylvinyl boronic acid **14g** (0.0672 g, 0.601 mmol), $Cu(OAc)_2$ (0.011 g, 0.59 mmol), Na_2SO_4 (0.256 g, 1.80 mmol), and pyridine (72.6 μl, 0.901 mmol). After chromatography, **15g** was isolated as a white solid (0.015 g, 21%).

2.5.2 Observation of Imidate Intermediates

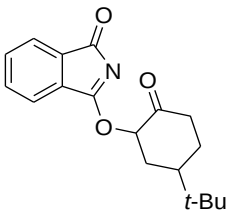
Imidates **16a-16d** were prepared according to general procedure **C**.

General Procedure C: A J-Young tube was charged with a 0.1 M solution of *N*-enoxyphthalimide **15** (1 equiv) in C_6D_6. The reaction mixture was heated to 70-90 ℃ for 10-16 h. Benzene-d_6 was removed from the reaction mixture under vacuum and imidate **16** was isolated as an amorphous solid or oil.



16a

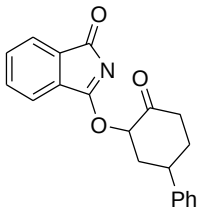
16a was prepared according to general procedure **C** using **15a** (0.0272 g, 0.125 mmol). Heating the reaction mixture to 80 ℃ for 16 h afforded imidate **16a** (0.0272 g, >95% recovery) as a white solid. ^{1}H NMR (500 MHz; C_6D_6): δ 7.49 (d, *J* = 6.0 Hz, 1H), 7.13 (d, *J* = 6.0 Hz, 1H), 6.92-6.86 (m, 2H), 5.35 (q, *J* = 7.0 Hz, 1H), 1.79 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.1, 184.9, 180.1, 135.9, 135.2, 132.5, 132.2, 123.6, 120.1, 80.5, 25.3, 15.6.



16b (*cis*:*trans* = 60:40)

16b was prepared according to general procedure **C** using **15b** (0.0385 g, 0.129 mmol). Heating the reaction mixture to 80 ℃ for 16 h afforded imidate **16b** (0.0383 g, >95% recovery) as amorphous solid. ^{1}H NMR of *cis* diastereomer (500 MHz; $CDCl_3$): δ 7.53-7.47 (m, 1H), 7.35-7.34 (m, 1H), 6.97-6.91 (m, 2H), 5.76 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.38-2.24 (m, 2H), 2.02-1.95 (m, 1H), 1.64-1.59 (m, 1H), 1.56-1.51 (m, 1H), 1.42-1.35 (m, 1H), 1.05-0.96 (m, 1H), 0.73 (s, 9H); ^{13}C NMR of *cis* diastereomer (125

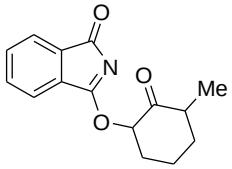
MHz, $CDCl_3$): δ 201.5, 185.2, 180.5, 136.0, 135.5, 132.2, 123.6, 120.6, 82.2, 44.9, 41.0, 39.1, 34.1, 27.5, 27.2, 26.7; ^{1}H NMR of *trans* diastereomer (500 MHz; $CDCl_3$): δ 7.53-7.47 (m, 1H), 7.21-7.20 (m, 1H), 6.97-6.91 (m, 2H), 5.74 (t, *J* = 7.0 Hz, 1H), 2.38-2.24 (m, 1H), 2.11-2.05 (m, 1H), 1.86-1.80 (m, 1H), 1.48-1.45 (m, 1H), 1.31-1.20 (m, 3H), 1.05-0.96 (m, 1H), 0.72 (s, 9H); ^{13}C NMR of *trans* diastereomer (125 MHz, $CDCl_3$): δ 203.8, 184.9, 180.3, 135.8, 135.3, 133.3, 128.1, 122.8, 120.4, 81.2, 42.1, 41.0, 37.6, 30.5, 26.7, 24.1.



16c (*cis*:*trans* = 55:45)

16c was prepared according to general procedure **C** using **15c** (0.0284 g, 0.0890 mmol). Heating the reaction mixture to 90 ºC for 16 h afforded imidate **16c** (0.0275 g, >95% recovery) as an oil. ^{1}H NMR of *cis* diastereomer (500 MHz; $CDCl_3$): δ 7.54-7.47 (m, 1H), 7.34-7.14 (m, 5H), 6.98-6.93 (m, 3H), 5.83 (dd, *J* = 13.0, 6.5 Hz, 1H), 2.73 (tdd, *J* = 13.0 Hz, *J* = 6.5 Hz, *J* = 3.0 Hz, 1H), 2.49-1.97 (m, 3H), 1.85-1.81 (m, 1H), 1.70-1.64 (m, 1H), 1.49-1.46 (m, 1H); ^{13}C NMR of *cis* diastereomer (125 MHz, $CDCl_3$): δ 200.9, 185.2, 180.5, 143.2, 136.0, 135.4, 132.5, 132.3, 128.6, 126.8, 126.7, 123.6, 120.6, 81.5, 41.4, 39.6, 37.3, 33.8; ^{1}H NMR (500 MHz; $CDCl_3$) of *trans* diastereomer:

δ 7.54-7.47 (m, 1H), 7.34-7.14 (m, 5H), 6.98-6.93 (m, 3H), 5.83 (dd, *J* = 9.5 Hz, *J* = 5.5 Hz, 1H), 2.99-2.96 (m, 1H), 2.49-1.97 (m, 5H), 1.70-1.64 (m, 1H); ^{13}C NMR of *trans* diastereomer (125 MHz, $CDCl_3$): δ 202.2, 184.8, 180.2, 142.0, 135.9, 135.5, 132.3, 132.2, 128.8, 126.9, 126.7, 123.6, 120.5, 80.6, 39.4, 37.0, 36.8, 31.8.



16d (*cis*:*trans* = 15:85)

16d was prepared according to general procedure **C** using **15d** (0.030 g, 0.12 mmol). Heating the reaction mixture to 80 ℃ for 12 h afforded imidate **16d** (0.029 g, >95% recovery) as an amorphous solid. ^{1}H NMR of *cis* diastereomer (500 MHz; $CDCl_3$): δ 7.50 (d, *J* = 6.0 Hz, 1H), 7.19 (d, *J* = 6.5 Hz, 1H), 6.94-6.81 (m, 2H), 5.63 (dd, *J* = 13.0, 7.0 Hz, 1H), 2.24-2.20 (m, 1H), 1.94-1.90 (m, 2H), 1.73-1.65 (m, 1H), 1.52-1.45 (m, 1H), 1.40-1.34 (m, 1H), 1.22-1.17 (m, 1H), 0.82 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR of *cis* diastereomer (125 MHz, $CDCl_3$): δ 204.8, 184.9, 180.4, 136.0, 135.4, 132.5, 132.2, 123.5, 120.6, 82.5, 43.8, 35.6, 33.4, 22.6, 13.9; ^{1}H NMR of *trans* diastereomer (500 MHz; $CDCl_3$): δ 7.50 (d, *J* = 6.0 Hz, 1H), 7.19 (d, *J* = 6.5 Hz, 1H), 6.94-6.81 (m, 2H), 5.81 (dd, *J* = 10.0, 5.5 Hz, 1H), 2.69-2.63 (m, 1H), 1.94-1.90 (m, 2H), 1.88-1.83 (m, 1H), 1.52-1.45 (m, 1H), 1.40-1.34 (m, 2H), 1.22-1.17 (m, 1H), 0.96 (d, *J* = 6.0 Hz, 3H);

^{13}C NMR of *trans* diastereomer (125 MHz, $CDCl_3$): δ 204.8, 184.9, 180.4, 136.0, 135.4, 132.5, 132.2, 123.6, 120.4, 80.7, 43.9, 33.5, 32.8, 18.9, 15.1.

2.5.3 Preparation of α-Oxygenated Ketones

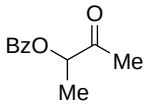
17a-17d and **17f** were synthesized according to general procedure **D** or **E**.

General Procedure D: A J-Young tube or Teflon-sealed reaction flask was charged with *N*-enoxyphthalimide **15** (1 equiv), hexamethylbenzene as an internal standard, and either C_6D_6 or toluene. C_6D_6 was used as the solvent if the reaction was run in a J-Young tube and toluene was used if the solvent if the reaction was run on larger scale in a Teflon-sealed reaction flask. The reaction mixture was heated to 70-90 ℃ for 10-16 h. Reaction mixtures heated in C_6D_6 were analyzed directly by ^{1}H NMR spectroscopy to determine the yield of imidate **16**. Reaction mixtures heated in toluene were first concentrated under reduced pressure, dissolved in C_6D_6, and analyzed by ^{1}H NMR spectroscopy to determine the yield of imidate **16**. The crude solutions of imidate **16** were then transferred to a scintillation vial, C_6D_6 was removed under reduced pressure, and the resulting amorphous solid was dissolved in CH_2Cl_2 to form a 0.1 M solution of **16**. Silica gel (0.200 g/ 0.1 mmol of **16**) or Amberlite-IR120 resin (0.200 g/ 0.1 mmol of **16**) was then added to the CH_2Cl_2 solution and the reaction mixture was stirred at 25 ℃ for 20 min - 1 h if Amberlite-IR120 was used or 16 h if SiO_2 was used. The silica gel or

Amberlite-IR120 resin was then separated from the CH_2Cl_2 solution and washed with CH_2Cl_2 (3 x 4 mL). The filtrate was then concentrated under reduced pressure, dissolved in ethyl acetate (20 mL), and extracted with 1M $NaOH_{(aq)}$ (3 x 2 mL) to remove the phthalimide byproduct. The organic layer was then concentrated under reduced pressure and purified by medium pressure chromatography.

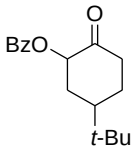
General Procedure E: A J-Young tube or Teflon-sealed reaction flask was charged with *N*-enoxyphthalimide **15** (1 equiv), hexamethylbenzene as an internal standard, and either C_6D_6 or toluene. C_6D_6 was used as the solvent if the reaction was run in a J-Young tube and toluene was used as the solvent if the reaction was run on larger scale in a Teflon-sealed reaction flask. The reaction mixture was heated to 70-90 ℃ for 10-16 h. Reaction mixtures heated in C_6D_6 were analyzed directly by ^{1}H NMR spectroscopy to determine the yield of imidate **16**. Reaction mixtures heated in toluene were first concentrated under reduced pressure, dissolved in C_6D_6, and analyzed by ^{1}H NMR spectroscopy to determine the yield of imidate **16**. The crude solutions of imidate **16** were then transferred to a scintillation vial, C_6D_6 was removed under reduced pressure, and the resulting amorphous solid was dissolved in CH_2Cl_2 to form a 0.1 M solution of **16**. Amberlite-IR120 resin (0.200 g per 0.1 mmol **16**) was then added to the CH_2Cl_2 solution and the reaction mixture was stirred at 25 ℃ until formation of a white precipitate was observed. The Amberlite-IR120 resin was then separated from the CH_2Cl_2

solution and washed with CH_2Cl_2 (3 x 4 mL). The filtrate was then concentrated under reduced pressure to form a 0.05 M solution of **16** which was treated with NEt_3 (5-8 equiv) and benzoyl chloride (2-4 equiv), and allowed to stir for 3 h. At this time, the reaction mixture was concentrated under reduced pressure and purified by medium pressure chromatography.



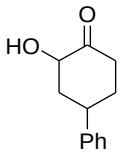
17a

17a[67] was synthesized according to general procedure **E** using the following reagents: **15a** (0.110 g, 0.507 mmol), Amberlite-IR 120, NEt_3 (0.410, 4.05 mmol), and benzol chloride (0.285 g, 2.03 mmol). After chromatography (1:9 ethyl acetate: hexane), **17a** was isolated as an amorphous solid (0.084 g, 86%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.08 (d, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.46-7.43 (m, 2H), 5.31 (q, *J* = 7.0 Hz, 1H), 2.23 (s, 3H), 1.52 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.8, 165.9, 133.4, 129.8, 129.5, 128.5, 75.5, 25.7, 16.2; HRMS (ESI) *m/z* calcd. for $C_{11}H_{12}O_3Na$ $(M+Na)^+$ 215.0684, found 215.0681.



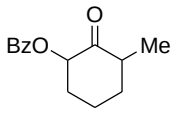
17b (*cis*: *trans* = 75:25)

17b[68] was synthesized according to general procedure **E** using the following reagents: **15b** (0.0385 g, 0.129 mmol), NEt_3 (0.1042 g, 1.030 mmol), and benzoyl chloride (0.0724 g, 0.515 mmol). After chromatography, **17b** was isolated as an amorphous solid (0.0232 g, 66%). ^{1}H NMR of *cis* diastereomer (500 MHz; $CDCl_3$): δ 8.11-8.07 (m, 2H), 7.59-7.53 (m, 1H), 7.47-7.42 (m, 2H), 5.38 (dd, *J* = 12.0, 6.0 Hz, 1H), 2.57-2.43 (m, 3H), 2.18-2.12 (m, 1H), 1.79-1.73 (m, 2H), 1.54-1.46 (m, 1H), 0.97 (s, 9H); ^{13}C NMR of *cis* diastereomer (125 MHz, $CDCl_3$): δ 206.1, 165.6, 133.2, 129.9, 129.7, 128.4, 76.6, 45.9, 39.6, 34.3, 32.3, 28.1, 27.7; ^{1}H NMR of *trans* diastereomer (500 MHz; $CDCl_3$): δ 8.11-8.07 (m, 2H), 7.59-7.53 (m, 1H), 7.47-7.42 (m, 2H), 5.28 (dd, *J* = 10.5, 5.0 Hz, 1H), 2.69-2.63 (m, 1H), 2.57-2.43 (m, 1H), 2.34-2.29 (m, 1H), 1.94-1.83 (m, 1H), 1.68-1.60 (m, 1H), 1.43-1.38 (m, 1H), 0.94 (s, 9H); ^{13}C NMR of *trans* diastereomer (125 MHz, $CDCl_3$): δ 206.1, 165.6, 133.4, 129.8, 129.7, 128.5, 76.2, 41.9, 38.0, 32.3, 32.3, 27.4, 26.6; HRMS (ESI) *m/z* calcd. for $C_{17}H_{23}O_3$ $(M+H)^+$ 275.1647, found 275.1641.



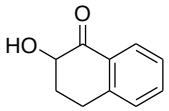
17c (*cis*: *trans* = 60:40)

17c[69] was synthesized according to general procedure **D** using the following reagents: **15c** (0.124 g, 0.388 mmol) and Amberlite-IR 120. After chromatography, **17c** was isolated as an amorphous solid (0.0603 g, 82 %). ^{1}H NMR of *cis* diastereomer (500 MHz; $CDCl_3$) of the major isomer: δ 7.44-7.23 (m, 5H), 4.34 (dd, *J* = 12.0 Hz, *J* = 6.5 Hz, 1H), 3.70 (brs, 1H), 3.18 (ddt, *J* = 12.0 Hz, *J* = 6.0 Hz, *J* = 3.0 Hz, 1H), 2.74-2.50 (m, 3H), 2.27-2.26 (m, 1H), 1.97-1.70 (m, 2H); ^{13}C NMR of *cis* diastereomer (125 MHz, $CDCl_3$): δ 210.8, 143.5, 128.7, 126.7, 126.5, 74.6, 43.2, 41.3, 38.7, 34.9; ^{1}H NMR of *trans* diastereomer (500 MHz; $CDCl_3$): δ 7.44-7.23 (m, 5H), 4.25 (dd, *J* = 10.5 Hz, *J* = 6.0 Hz, 1H), 3.52 (bs, 1H), 3.43-3.41(m, 1H), 2.85-2.82 (m, 1H), 2.74-2.50 (m, 3H), 2.17-2.03 (m, 1H), 1.97-1.70 (m, 1H); ^{13}C NMR of *trans* diastereomer (125 MHz, $CDCl_3$): δ 211.6, 143.5, 128.8, 126.9, 126.6, 72.3, 39.8, 36.3, 36.2, 31.1; HRMS (EI) *m/z* calcd. for $C_{12}H_{15}O_2$ $(M+H)^+$ 190.09938, found 190.09968.



17d (*cis*: *trans* = 20:80)

17d[70] was synthesized according to general procedure **E** using the following reagents: **15d** (0.0468 g, 0.182 mmol), NEt_3 (0.1473 g, 1.456 mmol), and benzoyl chloride (0.1023 g, 0.7281 mmol). After chromatography, **17d** was isolated as a yellow oil (0.028 g, 66%). ^{1}H NMR of *cis* diastereomer (500 MHz; $CDCl_3$): δ 8.12-8.07 (m, 2H), 7.61-7.55 (m, 1H), 7.49-7.42 (m, 2H), 5.39-5.37 (m, 1H), 2.58 (dq, *J* = 13.0 Hz, *J* = 6.0 Hz, 1H), 2.48-2.44 (m, 1H), 2.23-2.09 (m, 2H), 2.07-1.93 (m, 2H), 1.92-1.83 (m, 1H), 1.09 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR of *cis* diastereomer (125 MHz, $CDCl_3$): δ 208.7, 165.5, 133.1, 130.2, 129.8, 128.3, 77.2, 44.4, 36.1, 33.6, 23.2, 13.9;^{1}H NMR of *trans* diastereomer (500 MHz; $CDCl_3$): δ 8.12-8.07 (m, 2H), 7.61-7.55 (m, 1H), 7.49-7.42 (m, 2H), 5.38 (dd, *J* = 8.0, 4.5 Hz, 1H), 2.87 (dq, *J* = 14.0 Hz, *J* = 7.0 Hz, 1H), 2.23-2.09 (m, 2H), 2.07-1.93 (m, 2H), 1.92-1.83 (m, 1H), 1.66-1.59 (m, 1H), 1.18 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR of *trans* diastereomer (125 MHz, $CDCl_3$): δ 208.7, 165.5, 133.3, 129.9, 129.8, 128.5, 76.1, 43.2, 35.2, 33.3, 19.7, 15.2; HRMS (ESI) *m/z* calcd. for $C_{14}H_{16}O_3Na$ $(M+Na)^+$ 255.0997, found 255.1006.



17f

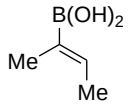
17f[71] was synthesized according to general procedure **D** using the following reagents: **15f** (0.287 g, 0.986 mmol) and Amberlite-IR 120. After chromatography, **17f** was isolated as a yellow oil (0.0139 g, 87%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.04 (d, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.5 Hz, 1H), 4.39 (dd, *J* = 13.5, 5.5 Hz, 1H), 3.91 (bs, 1H), 3.19-3.12 (m, 1H), 3.06-3.02 (m, 1H), 2.54 (dt, *J* = 5.5, 4.5 Hz, 1H), 2.04 (ddd, *J* = 13.5 Hz, *J* = 8.5 Hz, *J* = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.6, 144.4, 134.2, 130.5, 128.9, 127.6, 126.9, 73.9, 31.9, 27.8; HRMS (EI) *m/z* calcd. for $C_{10}H_{10}O_2Na(M+Na)^+$ 185.0578, found 185.0580.

2.5.4 Preparation of Boronic Acids

Boronic acids **14a** were prepared via alkyne hydroboration.[72] Boronic acids **14b-14e** and **14g** were prepared via hydrolysis of the corresponding pinacol esters. Boronic acid **14f** was prepared via Shapiro reaction of the *N*-tosyl hydrazones. Pinacol esters of **14b-14e** were prepared via Shapiro reaction of the *N*-tosyl hydrazones. Pinacol ester of **14g** was prepared according to literature procedure.[73]

2.5.4.1 Preparation of Vinyl Boronic Acids via Alkyne Hydroboration[72]

General procedure F: A round bottom flask was flame-dried under N_2, charged with an alkyne (1 equiv), diluted with CH_2Cl_2 to form a 1 M solution, and cooled to -78 ºC. A 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (1.2 equiv) was slowly added to the alkyne solution and the reaction mixture was allowed to warm up to room temperature and stir for 3 h. The reaction mixture was then treated with 50 mL of a 10:1 mixture of Et_2O:H_2O and allowed to stir for 5 min. The reaction mixture was then diluted with additional Et_2O (50 mL) and extracted with water (3 x 5 mL). The organic layer was then dried with $MgSO_4$ and concentrated under vacuum to give a crude sample of the vinyl boronic acid. This crude sample was used for the copper-coupling reactions without further purification. Any impurities carried on to the copper-coupling reaction were not observed to affect the efficiency of the process when compared to the use of a pure sample of boronic acid.



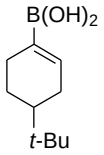
14a

14a[74] was prepared according to general procedure **F** using the following reagents: 2-butyne (5.00 g, 92.4 mmol) and 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (81.0 ml, 81.0 mmol). After work up, **14a** was isolated as an off-white solid (6.61 g, 82 %). ^1H

NMR (500 MHz; $CDCl_3$): δ 6.83 (q, *J* = 6.5, 1H), 1.80 (d, *J* = 6.5 Hz, 3H), 1.75 (s, 3H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.6, 14.8, 12.7, the *C*-B resonance was too broad to be observed.

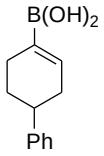
2.5.4.2 Preparation of Boronic Acids from Boronic Acid Pinacol Esters[75]

General procedure G: A scintillation vial was charged with alkenyl boronic acid pinacol ester (1 equiv), $NaIO_4$ (3.6 equiv), and NH_4OAc (3.6 equiv). These reagents were then diluted with a mixture of acetone and water in a 1:1 ratio to form a 0.63 M solution of the alkenyl boronic acid pinacol ester. The resulting slurry was allowed to stir vigorously until the boronic acid pinacol ester was fully consumed. Then the slurry was filtered and acetone was removed from the filtrate under vacuum. The aqueous solution was extracted with diethyl ether (3 x 50 ml). The combined organic layers were washed with water and brine, dried with $MgSO_4$, and concentrated under vacuum to give a crude sample of the vinyl boronic acid.



14b

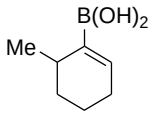
14b was prepared according to general procedure **G** using the following reagents: pinacol ester **14b-s** (0.128 g, 0.485 mmol), $NaIO_4$ (0.340 g, 1.60 mmol), and NH_4OAc (0.149 g, 1.93 mmol). After work up, **14b** was isolated as solid (0.042 g, 48%). ^1H NMR (500 MHz; $CDCl_3$): δ 6.94-6.92 (m, 1H), 2.44-2.40 (m, 1H), 2.22-2.18 (m, 1H), 2.09-2.05 (m, 1H), 1.95-1.90 (m, 1H), 1.87-1.84 (m, 1H), 1.31-1.21 (m, 1H), 1.12-1.06 (m, 1H), 0.88 (s, 9H), the O-H resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.4, 44.1, 32.4, 29.0, 27.3, 24.2, 17.4, the *C*-B resonance was too broad to be observed above the baseline; HRMS (ESI) *m/z* calcd. for $C_{30}H_{51}O_3B_3$ $(M+H)^+$ 492.41175, found 492.41161.



14c

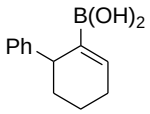
14c was prepared according to general procedure **G** using the following reagents: pinacol ester **14c-s** (0.246 g, 0.897 mmol), $NaIO_4$ (0.603 g, 2.69 mmol), and NH_4OAc (0.353 g, 2.69 mmol). After work up, **14c** was isolated as solid (0.155 g, 86%). ^1H

NMR (500 MHz; $CDCl_3$): δ 7.34-7.30 (m, 2H), 7.25-7.20 (m, 3H), 7.07 (d, *J* = 2.5 Hz, 1H), 2.83-2.81 (m, 1H), 2.52-2.51 (m, 1H), 2.33-2.26 (m, 3H), 2.02-2.00 (m, 1H), 1.75-1.72 (m, 1H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 128.4, 126.9, 126.8, 126.1, 39.9, 35.2, 29.9, 26.2, the *C*-B resonance was too broad to be observed; HRMS (EI) *m/z* calcd. for $C_{36}H_{39}O_3B(M+H)^+$ 552.31785, found 552.31834.



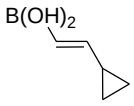
14d

14d was prepared according to general procedure **G** using the following reagents: pinacol ester **14d-s** (0.419 g, 1.89 mmol), $NaIO_4$ (1.30 g, 6.08 mmol), and NH_4OAc (0.589 g, 7.64 mmol). After work up, **14d** was isolated as an amorphous solid (0.080 g, 30%). ^1H NMR (500 MHz; $CDCl_3$): δ 6.93 (t, *J* = 3.5 Hz, 1H), 1.68-1.66 (m, 2H), 1.58-1.56 (m, 1H), 1.47-1.45 (m, 1H), 1.35-1.33 (m, 1H), 1.22-1.18 (m, 1H), 1.09 (t, *J* = 3.5 Hz, 3H), 0.92-0.89 (m, 1H), 0.79 (t, *J* = 7.0 Hz, 1H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.7, 30.3, 29.2, 27.2, 21.4, 18.3, the *C*-B resonance was too broad to be observed.



14e

14e was prepared according to general procedure **G** using the following reagents: pinacol ester **14e-s**, $NaIO_4$, and NH_4OAc. After work up, **14e** was isolated as an amorphous solid. ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.36-7.34 (m, 2H), 7.28-7.24 (m, 3H), 7.09 (s, 1H), 2.86 (s, 1H), 2.55-2.51 (m, 2H), 2.36-2.31 (m, 2H), 2.08-2.03 (m, 1H), 1.81-1.73 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.4, 145.3, 128.5, 127.0, 126.1, 39.9, 31.2, 29.5, 26.3, the *C*-B resonance was too broad to be observed.

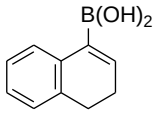


14g[76]

14g: ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.40 (dd, *J* = 17.0 Hz, 9.0 Hz, 1H), 5.58 (d, *J* = 17.0 Hz, 1H), 1.62-1.58 (m, 1H), 0.89 (d, *J* = 6.0 Hz, 2H), 0.62 (d, *J* = 2.0 Hz, 2H), the O-*H* resonances were too broad to be observed.

2.5.4.3 Preparation of Boronic Acid and Boronic Acid Pinacol Ester via Shapiro Reaction [73]

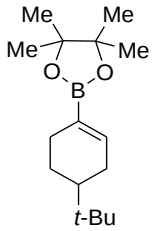
General Procedure H: A 250 mL round bottom flask was flame-dried under N_2 and charged with *N*-tosylhydrazone (1 equiv), hexanes (3 mL/mmol hydrazone), and TMEDA (3 mL/mmol hydrazone). The resulting slurry was cooled to -78 ºC with a dry ice-acetone bath and a 2.5 M *n*-BuLi solution in hexane (4 equiv) was added via syringe. The reaction mixture was allowed to stir at -78 ºC for 1 h and then allowed to warm to 25 ºC. After stirring for an additional 2 h, the reaction mixture was cooled to -78 ºC with a dry ice-acetone bath and BPin(O*i*-Pr) (4 equiv) was added via syringe. After 2 h the reaction mixture was quenched with NH_4Cl (aq). The mixture was extracted with ether. The organic layers were then dried with $MgSO_4$ and concentrated under reduced pressure to give a crude sample of the vinyl boronic acid pinacol ester. The crude sample was then purified by chromatography (2:98; ethyl acetate: hexanes).



14f

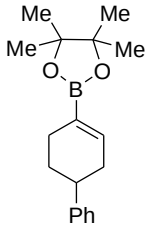
14f[78] was prepared according to general procedure **H** using the following reagents: α-tetralone tosyl hydrazone[79] (2.61 g, 8.30 mmol), 2.5 M *n*-BuLi (13.3 ml, 33.2 mmol), TMDEA (24.9 ml), and $B(OMe)_3$ (3.70 ml, 33.2 mmol). After work up, **14f** was iso-

lated as a solid (0.607 g, 42 %). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.03 (d, *J* = 8 Hz, 1H), 7.54-7.53 (m, 1H), 7.29-7.27 (m, 1H), 7.22-7.18 (m, 2H), 2.82-2.80 (m, 2H), 2.46-2.42 (m, 2H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.8, 136.0, 135.0, 127.6, 127.3, 126.8, 126.5, 27.9, 24.6, the *C*-B resonance was too broad to be observed.



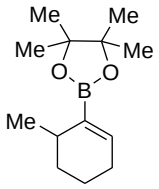
14b-s

14b-s[77] was prepared according to general procedure **H** using the following reagents: *N*-tosyl-4-*t*-butylcyclohexanylhydrazone (2.67 g, 8.30 mmol), 2.5 M *n*-BuLi (13.3 ml, 33.2 mmol), TMDEA (24.9 ml), and BPin(O*i*-Pr) (5.56 g, 29.9 mmol). After work up and chromatography, **14b-s** was isolated as a solid (1.23 g, 56%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.02-6.00 (m, 1H), 2.32-2.29 (m, 1H), 2.20-2.16 (m, 1H), 2.09-2.03 (m, 1H), 1.90-1.82 (m, 3H), 1.28 (s, 12H), 1.14-1.08 (m, 1H), 0.87 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.5, 83.0, 43.7, 32.2, 28.4, 27.8, 27.1, 24.7, 23.9, the *C*-B resonance was too broad to be observed.



14c-s

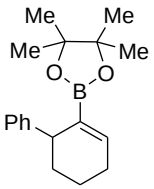
14c-s[77] was prepared according to general procedure **H** using the following reagents: *N*-tosyl-4-phenylcyclohexanylhydrazone (2.84 g, 8.30 mmol), 2.5 M *n*-BuLi (13.3 ml, 33.2 mmol), TMDEA (24.9 ml), and BPin(O*i*-Pr) (5.56 g, 29.9 mmol). After work up and chromatography, **14c-s** was isolated as a solid (1.37 g, 58%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.31-7.28 (m, 2H), 7.22-7.17 (m, 3H), 6.66-6.65 (m, 1H), 2.81-2.75 (m, 1H), 2.43-2.33 (m, 2H), 2.30-2.19 (m, 2H), 1.97-1.94 (m, 1H), 1.74-1.65 (m, 1H), 1.28 (s, 12H).



14d-s

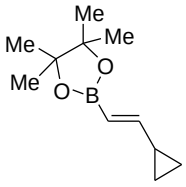
14d-s[80] was prepared according to general procedure **H** using the following reagents: *N*-tosyl-2-methylcyclohexanylhydrazone (1.48 g, 5.28 mmol), 2.5 M *n*-BuLi (3.4 ml, 8.4 mmol), TMDEA (15.8 ml), and BPin(O*i*-Pr) (3.53g, 19.0 mmol). After work up and chromatography, **14d-s** was isolated as a light yellow oil (0.422 g, 36%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.52-6.51 (m, 1H), 2.36 (d, J = 5 Hz, 1H), 2.02 (d, J = 2.5 Hz, 2H),

1.67-1.62 (m, 2H), 1.52-1.50 (m, 1H), 1.36-1.33 (m, 1H), 1.25 (s, 12H), 1.03 (d, *J* = 7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.3, 83.1, 30.6, 30.2, 26.9, 24.6, 21.7, 19.1, the *C*-B resonance was too broad to be observed.



14e-s

14e-s[81] was prepared according to general procedure **H** using the following reagents: *N*-tosyl-2-phenylcyclohexanylhydrazone, 2.5 M *n*-BuLi, TMDEA, and BPin(O*i*-Pr) . After work up and chromatography, **14e-s** was isolated as light yellow oil. ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.35-7.32 (m, 2H), 7.27-7.22 (m, 3H), 6.72-6.71 (m, 1H), 2.86-2.80 (m, 1H), 2.48-2.34 (m, 2H), 2.33-2.24 (m, 2H), 2.02-1.99 (m, 1H), 1.79-1.71 (m, 1H), 1.33 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3, 142.3, 128.4, 126.9, 126.0, 83.1, 39.8, 34.9, 29.8, 27.1, 24.9, the *C*-B resonance was too broad to be observed.



14g-s

A flask was charged with Schwartz's reagent (0.1 equiv, 0.5 mmol). A vial was charged with the alkyne (1 equiv, 5 mmol) and triethylamine (0.1 equiv, 0.5 mmol) under nitrogen. Pinacolborane (2 equiv) was added slowly into the alkyne mixture. Mixture of alkyne and pinacolborane was syringed into the flask, and then the reaction mixture was allowed to stir 18 h at 60 ℃. The crude was purified by column chromatography to give **14g-s** as colorless oil. ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.10 (dd, *J* = 12.0 Hz, *J* = 8.5 Hz, 1H), 5.51 (d, *J* = 12.0 Hz, 1H), 1.57-1.51 (m, 1H), 1.28 (s, 12H), 0.84-0.81 (m, 1H), 0.57-0.54 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.6, 82.9, 24.8, 17.0, 7.88, the *C*-B resonance was too broad to be observed.

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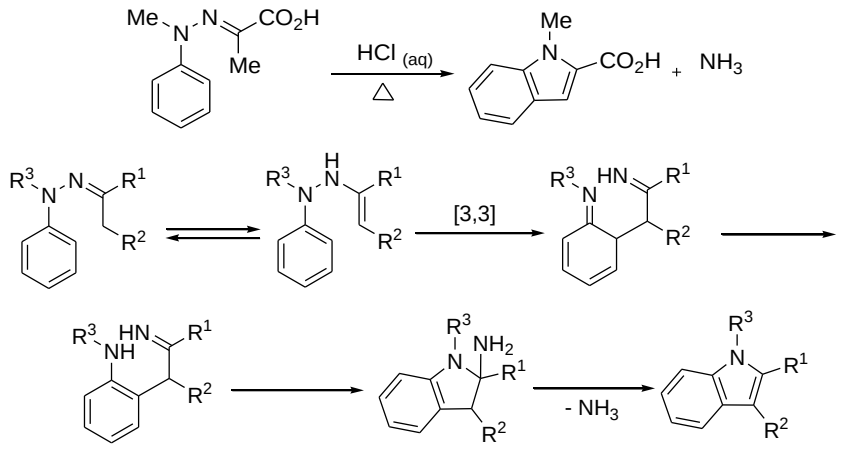
3 α-(*o*-Anilido)Ketones Synthesis via the Rearrangement of *O*-Vinyl Hydroxamates

3.1 Fischer-Indole Synthesis

In 1883, Fischer discovered the preparation of indole by heating pyruvic acid and 1-methylphenylhydrazone in presence of HCl.[82] Since then, the Fischer-Indole reaction has been widely used in the synthesis of natural products containing the indole moiety. The highlights of this reaction included a new C–C bond formation through the [3,3]-rearrangement of aryl hydrazone, a C–N bond formation via the cyclization of aniline to the imine, loss of NH_3, and sequential aromatization to indole (Scheme 1).[82,83] However, under the condition of Fischer-Indole reaction, it was a challenge to halt the process in half way and separate these events from one to another.

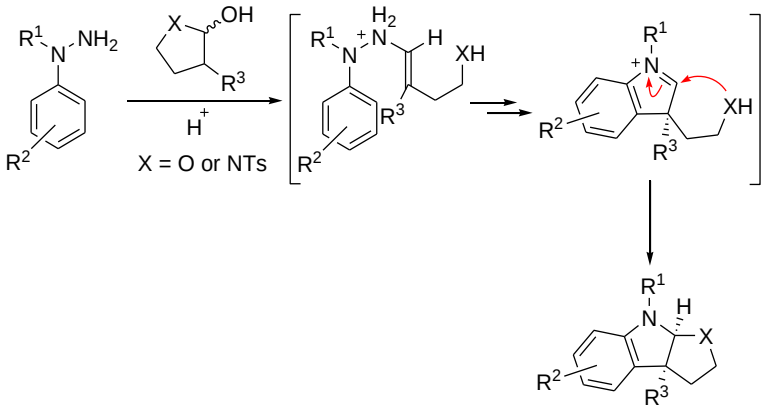
Scheme 1. Fischer-Indole Synthesis



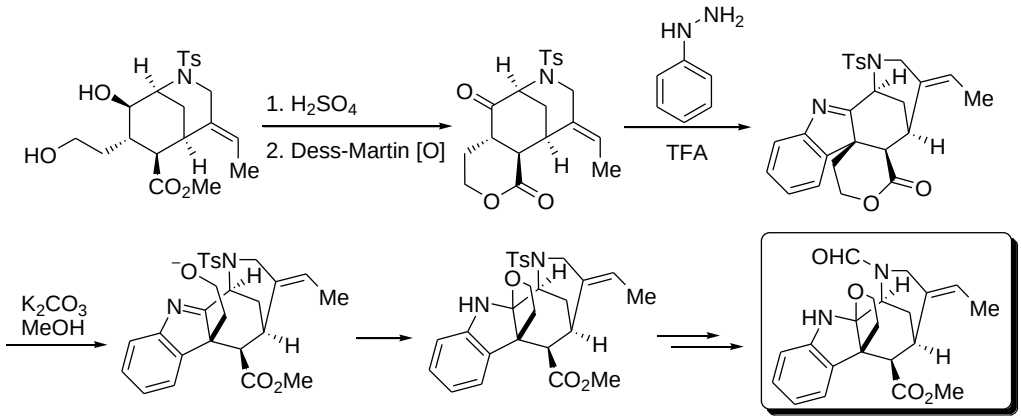
3.1.1 Interrupted-Fischer-Indole Synthesis

Garg and coworkers reported their work of Interrupted Fischer Indolization Cascade as an access to the indoline scaffold by halting the aromatization process to indole after losing the NH_3. Condensation of hydrazine with lactol or hemiaminal gave the structure of hydrazone which underwent sequential [3,3]-rearrangment, cyclization, and loss of NH_3, and then the indolenine underwent intramolecular nucleophilic attack. The process of the aromatization to indole was interrupted by the nucleophilic attack of the heteroatom to give the indoline motif instead of the formation of indole (Scheme 2).[84,85] Moreover, this Interrupted Fischer Indolization Cascade strategy was also used by Garg group as the key step in the total synthesis of Aspidophylline A (Scheme 3).[85]

Scheme 2. Interrupted Fischer Indolization Cascade



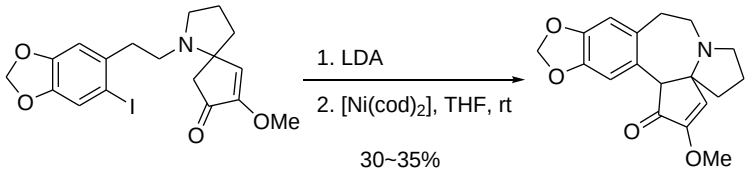
Scheme 3. Synthesis of Aspidophylline A



3.2 Transition Metal-Catalyzed α-Arylation of Ketones

In an early result shown by Semmelhack in 70s, a nickel(0)-mediated α-arylation was employed as the key step in the synthesis of cephalotaxinone (Scheme 4).[86] This nickel-mediated reaction was proposed to undergo oxidative addition of the aryl iodide to give the organonickel complex then subsequent enolate organonickel interaction to close the ring and afford a seven-member ring structure.

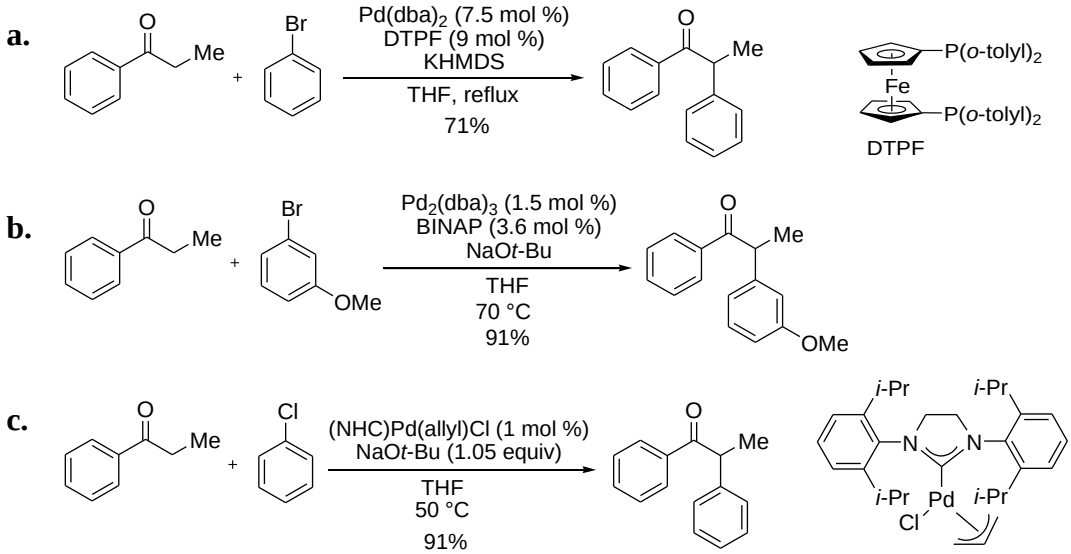
Scheme 4. Synthesis of Cephalotaxinone



After this one of the earliest examples of nickel-mediated α-arylation reaction which did not follow the pattern of conventional aromatic substitution reaction pathway was reported, a number of transition metal-catalyzed methods about this transformation had

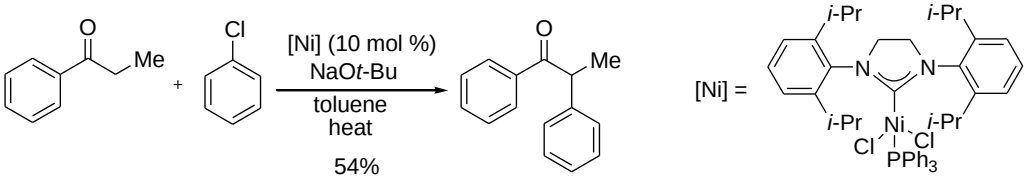
been established. Among of those catalysts, Pd complex was widely used for the direct α-arylation of ketones employing bulky electron-rich phosphine ligands or N-heterocyclic carbine (NHC) ligands.[87] Hartwig and coworkers showed that the direct α-arylation of ketone could be achieved using enolate chemistry, Pd(0), and bulky electron-rich ligand such as DTPF (Scheme 5a).[88] Meanwhile, the Buckwald group demonstrated the same transformation employing Pd(0) and biaryl ligand (Scheme 5b).[89] Nolan and workers had shown that direct α-arylation of ketone was accessible by using the enolate chemistry and cooperating palladium-NHC complex as the catalyst (Scheme 5c).[90,91]

Scheme 5. Examples of Pd-Catalyzed α-Arylation



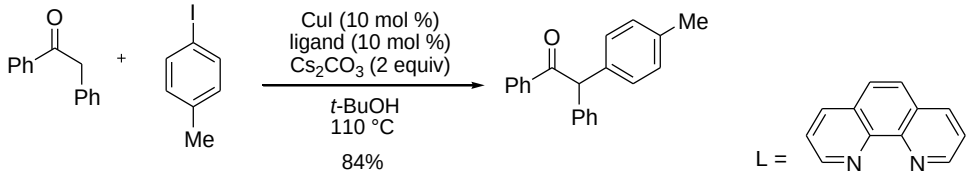
In addition to the Ni-mediated condition, Ni-catalyzed reactions were also developed. Matsubara et al. demonstrated the transformation utilizing Ni-NHC complex as the catalyst which interacted with the enolate to give α-aryl ketone (Scheme 6).[92]

Scheme 6. Ni-Catalyzed α-Arylation



Besides the common catalyst Pd or sometimes Ni, copper had been used for the α-arylation of ketone as well as methylene activated carbonyl compounds.[93] Taillefer showed the direct α-arylation of ketone employing CuI as catalyst (Scheme 7).[94] This example underwent the similar reaction pathway as the conventional palladium–catalyzed chemistry utilizing the interaction of enolate and the copper to afford α-arylated ketones. Meanwhile, it also demonstrated its potential as a surrogate of palladium.

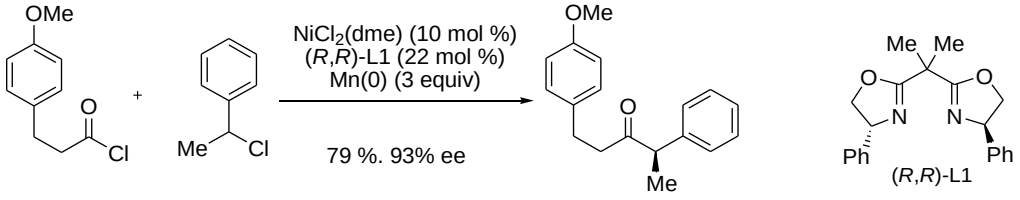
Scheme 7. Cu-Catalyzed α-Arylation



Reisman and coworkers recently published their Ni-catalytic asymmetric reductive acyl cross-coupling chemistry. It relied on different pathway from the enolate chemistry. Oxidative addition of nickel(0) to acyl chloride afforded organonickel(II) species which was reduced to nickel(I) by Mn(0) followed by second oxidative addition of benzyl chloride to give nickel(III) complex. Subsequent reductive elimination gave the

α-arylated ketone (Scheme 8).[94] This chemistry provided an alternative pathway to perform α-arylation instead of using enolate chemistry.

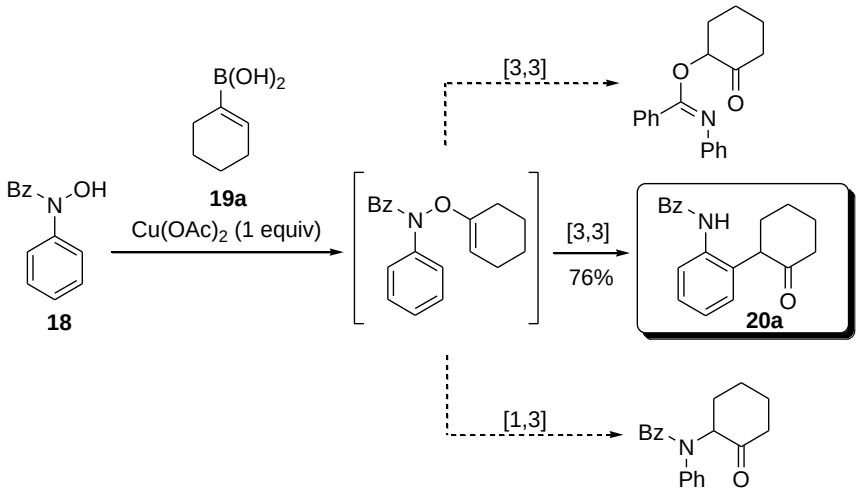
Scheme 8. Ni-Catalytic Asymmetric Reductive Acyl Cross Coupling



3.3 Preparation of α-(*o*-Anilido)Ketones through Vinyl Hydroxamate Rearrangements

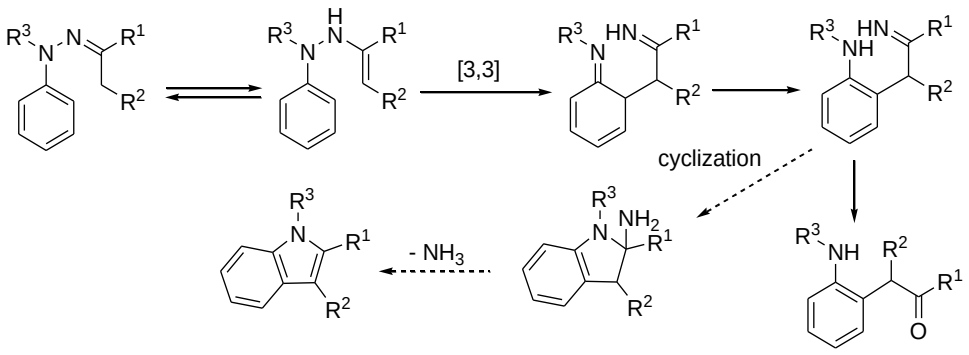
From the previous result demonstrated in Chapter 2, we were interested in the similar transformation with different substrate. *N*-Phenyl-benzoylhydroxamic acid was chosen as our precursor to perform this transformation. We envisioned that the formation of *O*-vinyl hydroxamic acid could be achieved by the cross coupling employing copper as promoter, and then it might undergo rearrangement under the thermal condition to form a new C–O bond via the [3,3]-rearrangement, a new C–C bond through the [3,3]-rearrangement, or a new C–N bond via the [1,3]-rearrangement (Scheme 9). However, the cross coupling reaction between the hydroxamic acid **18** and boronic acid **19a** gave the direct formation of the α-(*o*-anilido)ketone **20a** exclusively **i**nstead of the formation of *O*-vinyl hydroxamate.

Scheme 9. Potential Transformation of *O*-Vinyl Hydroxamic Acid



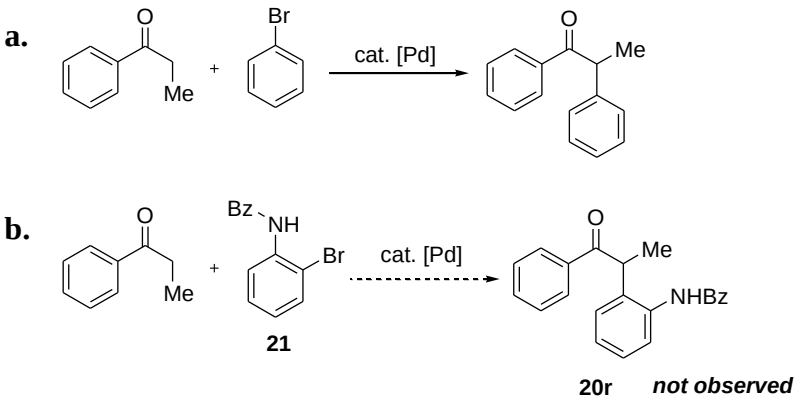
The transformation of **20a** could be considered as an access to the intermediate of Fischer-Indole synthesis. Fischer indolization was interrupted after the [3,3]-rearrangement, and the subsequent cyclization and loss of NH_3 were halted (Scheme 10). Usually, these three events were challenged to separate from one to each another, however, our copper-mediated cross-coupling reaction of hydroxamic acid and boronic acid provided a new perspective of the interrupted Fischer-Indole synthesis.

Scheme 10. Illustration of Fischer-Indole Synthesis Intermediate



The transformation to **20a** could also be considered as α-arylation[87,96-100] of ketones with aniline derivates. Preparation of these compounds had never been reported in an intermolecular fashion employing transition metal-mediated condition even thou there was an intramolecular coupling example reported by Hartwig.[101] Control experiments were conducted using propiophenone an1 employing Buckwald and Hartwig's Pd-catalyzed α-arylation conditions.[102] However, no formation of **20r** was observed in either condition and recovered more than 95 % of both starting materials.

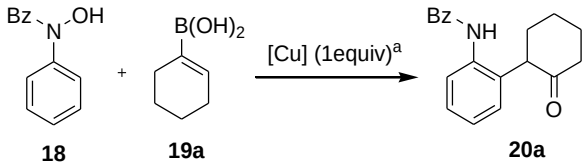
Scheme 11. Control Experiments



Encouraged by the preliminary result and control experiments, we decided to further explore our copper-mediated α-arylation reaction to form α-(*o*-anilido)ketone which apparently was inaccessible through the conventional Pd-catalyzed cross-coupling condition. A variety of copper salts were tested for the optimal condition. Most common copper(II) and copper(I) salts were able to conduct the transformation to **21a**. A mixture of CuBr, boronic acid, and pyridine in a ratio of 1:2:5 in a 0.1 M of DCE with 4Å

molecule sieves under air at 25 ℃ gave the best conversion of **20a** in 84% (Table 1, entry 3).

Table 1. Optimization of Cu-Mediated Condition



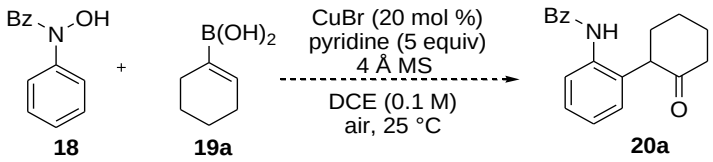
18 **19a** **20a**

Entry	Copper Salt	Yield (%)[b]	Entry	Copper Salt	Yield (%)[b]
1	$Cu(OAc)_2$	76	5	CuI	--
2	$Cu(OTf)_2$	--	6	CuOTf·Tol	69
3	CuBr	84	7	CuCl	77
4	$CuBr \cdot SMe_2$	65	8	CuTc	47

[a] A mixture of [Cu], boronic acid, and pyridine in a ratio of 1:2:5 in a 0.1 M of DCE with 4Å molecule sieves under air at 25 ℃. [b] Determined by using ^1H NMR spectroscopy with CH_2Br_2 as a reference.

With the optimal copper-mediated condition in hand, we wondered if the transformation would proceed with a sub-stoichiometric amount of copper bromide. A reaction was performed with 20 mol % of CuBr to test the formation of **20a** (Scheme 12). However, no desired product was observed under the catalytic condition.

Scheme 12. Preparation of α-(*o*-Anilido)Ketone under Catalytic Condition

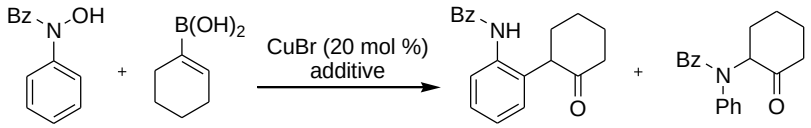


18 **19a** **20a**

In order to prepare **20a** under the catalytic condition, a variety of additives including oxidants, reductants, or Lewis acids were added to the reaction mixture. Common

oxidants, such as benzoquinone, $PhI(OAc)_2$, and Mn, gave no formation of **20a** (Table 2, entries 2-4). Addition of 1 equiv of zinc powder was found to give conversion of **20a** as a mixture of **20a** and **22a** in 2:1 ratio (Table 2, entry 10). Notably, **22a** was not observed in absence of zinc powder, and it was formed via the [1,3]-rearrangement of *O*-vinyl hydroxamate (Scheme 9).[103] Using 50 mol % or 2 equiv of zinc powder gave lower yield of **20a** and **22a** (Table 2, entries 11,12).

Table 2. Optimization: Additive

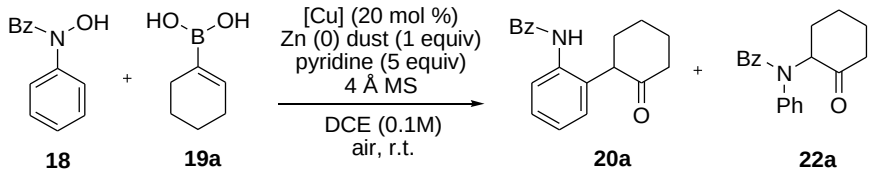


18 **19a** **20a** **22a**

Entry	additive	yield (%)[a]	**20a**:**22a**[b]
1	none	NR	
2	1 equiv BQ	NR	
3	1 equiv $PhI(OAc)_2$	Decom.	
4	1 equiv Mn	NR	
5	1 equiv Al	NR	
6	1 equiv $FeBr_2$	Decom.	
7	2 equiv ascorbate	NR	
8	1 equiv $ZnBr_2$	NR	
9	1 equiv $SnCl_2$	Decom.	
10	**1 equiv Zn**	**60**	**2:1**
11	2 equiv Zn	42	3:1
12	50 mol% Zn	22	2:1

[a] Determined by ^1H NMR spectroscopy with CH_2Br_2 as a reference. [b] Determined by ^1H NMR spectroscopy.

Table 3. Optimization: Copper Salts



18 **19a** **20a** **22a**

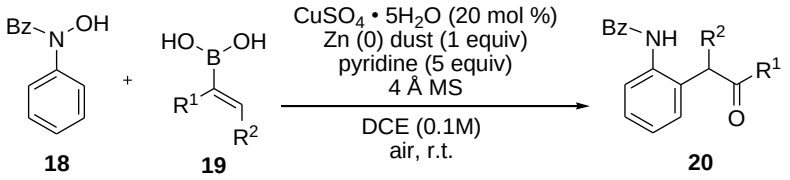
Entry	[Cu]	Yield (%)[a]	**20a**:**22a**[b]
1	CuBr	60	2:1
2	$CuBr \cdot SMe_2$	23	1:1
3	CuCl	33	5:2
4	CuI	41	9:1
5	CuTc	NR	--
6	CuOTf·Tol	NR	--
7	$Cu(OAc)_2$	50	5:1
8	$[Cu(cod)Cl]_2$[c]	NR	--
9	$[(TMEDA)(OH)Cu]_2$[c]	50	3:1
10	$Cu(OTf)_2 \cdot xH_2O$	66	5:2
11	$Cu(OTf)_2$	NR	--
12	Copper(II) hexafluoroacetylacetonate	trace	
13	$CuCl_2$	50	3:1
14	**$CuSO_4 \cdot 5H_2O$**	**75**	**7:1**
15	$Cu(OAc)_2 \cdot 1H_2O$	66	5:1

[a] Determined by ^1H NMR spectroscopy with CH_2Br_2 as a reference. [b] Determined by ^1H NMR spectroscopy. [c] 10 mol %.

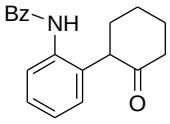
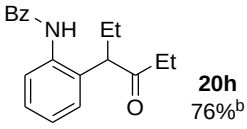
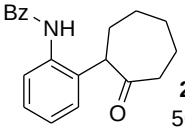
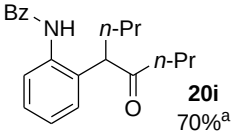
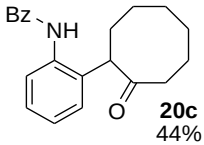
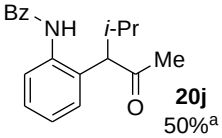
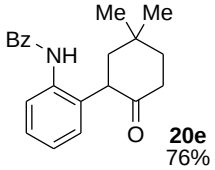
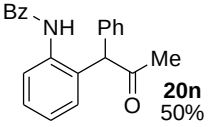
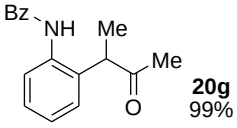
With the optimal copper-mediated and catalyzed condition in hand, a variety of α-(*o*-anilido)ketones were prepared using hydroxamic acid **18** and corresponding boronic acids under either condition. Cyclic boronic acids were tolerated for the transformation (Table 4, entries 1-4; Table 5, entries 1-3). However, the yields decreased as the size of the ring increasing or the number of the carbon increasing. Dialkyl acyclic boronic acids were tolerated for the transformation (Table 4, entries 5-8; Table 5, 5-7).

Heteroatom boronic acid gave moderate yield due to the possible coordination to the copper and decreased its reactivity (Table 5, entry 4). Alkyl-aryl boronic acids were tolerated for the transformation (Table 4, entries 9; Table 5, 9-15).

Table 4. Catalytic Condition Scope: Boronic Acids

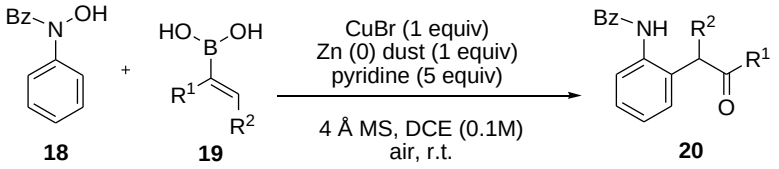


18 **19** **20**

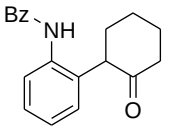
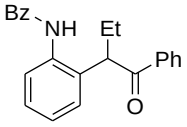
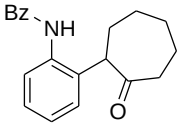
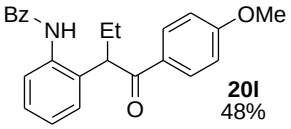
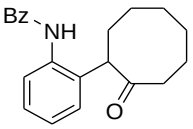
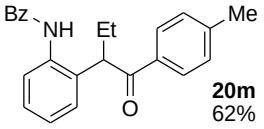
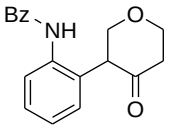
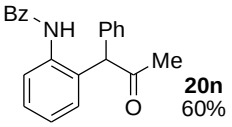
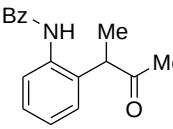
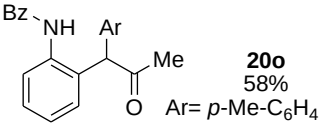
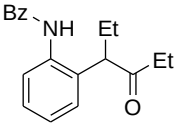
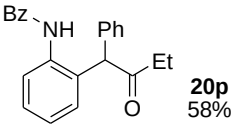
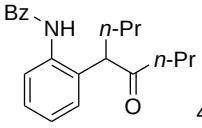
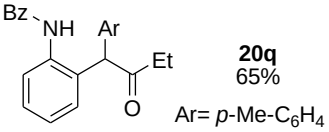
Entry	Product	Entry	Product
1	 **20a** 77%	6	 **20h** 76%[b]
2	 **20b** 56%[a]	7	 **20i** 70%[a]
3	 **20c** 44%	8	 **20j** 50%[a]
4	 **20e** 76%	9	 **20n** 50%
5	 **20g** 99%		

[a] $Cu(OAc)_2$ 20 mol % was used. [b] Regioisomeric boronic acid was used.

Table 5. Stoichiometric Condition Scope: Boronic Acids



18 **19** **20**

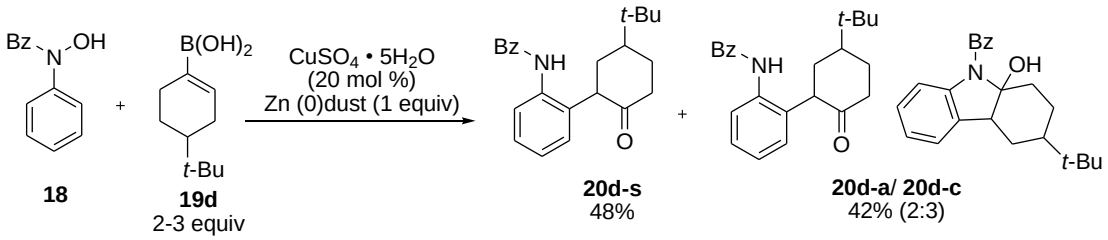
Entry	Product	Entry	Product
1	 **20a** 84%	9	 **20k** 80%
2	 **20b** 85%	10	 **20l** 48%
3	 **20c** 70%	11	 **20m** 62%
4	 **20f** 42%	12	 **20n** 60%
5	 **20g** 94%	13	 **20o** 58% Ar= *p*-Me-C_6H_4
6	 **20h** 59%[b]	14	 **20p** 58%
7	 **20i** 47%[c]	15	 **20q** 65% Ar= *p*-Me-C_6H_4

[a] $Cu(OAc)_2$ 20 mol % was used. [b] Regioisomeric boronic acid was used.

[c] $[Cu(cod)Cl]_2$ 50 mol % was used.

When the reaction was performed under catalytic condition using **18** and boronic acid **19d**, a mixture of *syn* and *anti*-diastereomers as well as the hemiaminol were observed. Thermodynamic stable *syn*-diastereomer **20d-s** was isolated from chromatography, and the isolated yield matched the crude NMR yield. In the other hand, thermodynamic unstable *anti*-diastereomer **20d-a** converted to **20d-c** during purification and gave a 2 to 3 ratio mixture of **20d-a** and **20d-c** (Scheme 13).

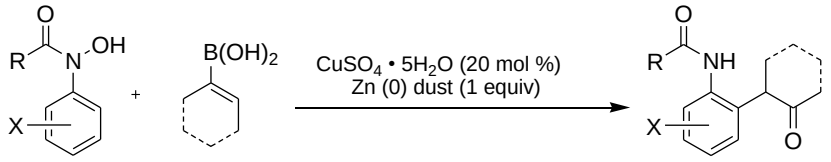
Scheme 13. Disstereoselectivity of α-(*o*-Anilido)Ketones

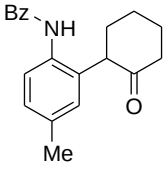
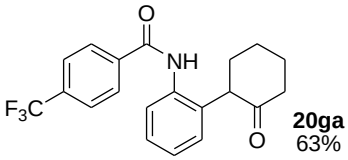
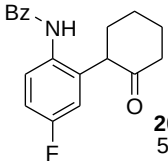
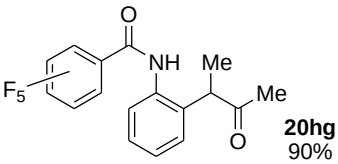
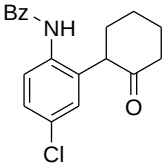
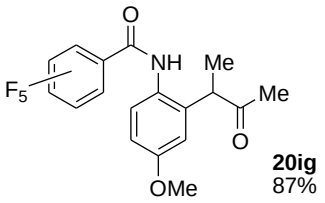
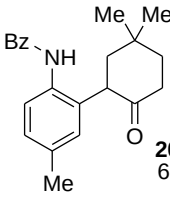
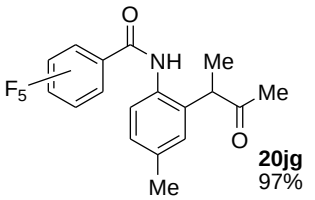
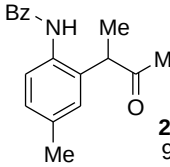
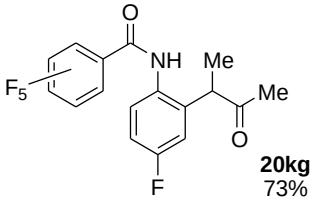
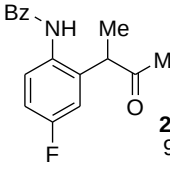
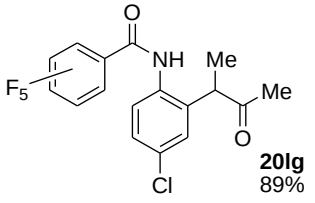


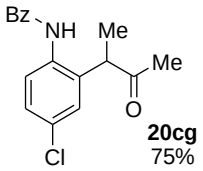
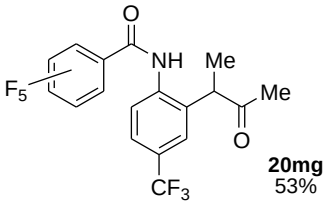
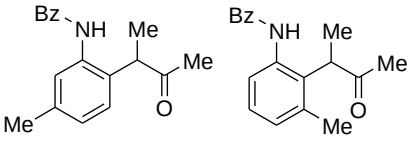
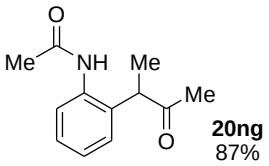
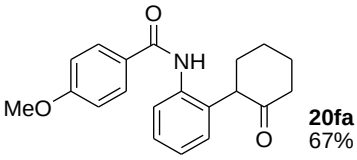
A variety of α-(*o*-anilido)ketones were prepared using corresponding hydroxamic acids and boronic acids using either optimal copper-mediated or catalyzed condition. *para*-Methyl substitution was tolerated under these two method and different boronic acid (Table 6, entries 1,4,5; Table 7, entry 1). Electron-poor *para*-substituted substrates were less tolerated under one or the other condition (Table 6, entries 2,3,6,7; Table 7, entries 2,3). Different substituted benzoyl substrates were tolerated the transformation, and results showed no significant relevant to electronic effect (Table 6, entries 9,10; Table 7, entries 6,7). Extremely electron-poor substituted benzoyl substrates also tolerated the transformation (Table 6, entries 11-16). Acetyl substrate was tolerated the

transformation (Table 6, entry 17).

Table 6. Catalytic Condition Scope: Hydroxamates



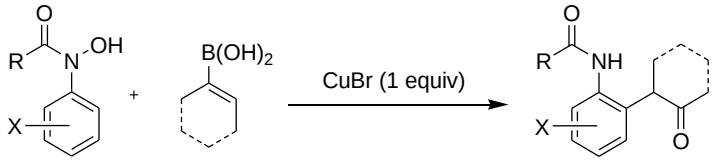
Entry	Product	Entry	Product
1	 **20aa** 88%	10	 **20ga** 63%
2	 **20ba** 50%	11	 **20hg** 90%
3	 **20ca** 25%	12	 **20ig** 87%
4	 **20ae** 68%	13	 **20jg** 97%
5	 **20ag** 95%	14	 **20kg** 73%
6	 **20bg** 99%	15	 **20lg** 89%

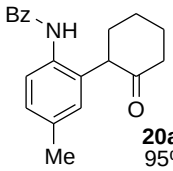
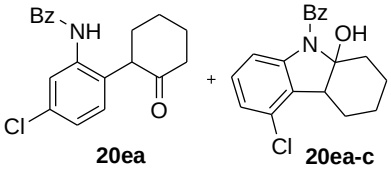
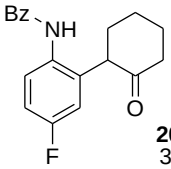
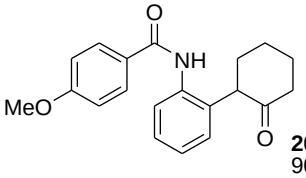
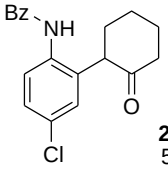
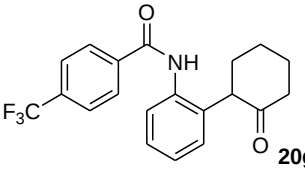
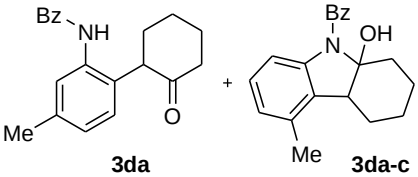
7	 **20cg** 75%	16	 **20mg** 53%
8	 **20dg/ 20dg-m** 75% (1.3:1)	17	 **20ng** 87%
9	 **20fa** 67%		

Reaction mixtures were prepared as 1:2:5 mixtures of **18**:boronic acid:pyridine in DCE (0.1 M) and were run in air.

When the reaction was performed using *meta*-substituted hydroxamic acid **18d** and boronic acid **19a**, a mixture of **20da** and hemiaminol **20da-c** were observed (Table 6, entry 8). It showed approximate 1 to 1 regioselectivity of C2 to C6 during the [3,3]-rearrangement, and the steric hinder α-(*o*-anilido)ketones underwent subsequent cyclization to afford **20da-c**. Similar regioselectivity was observed in the cross-coupling of **18d** and **19g** (Table 7, entry 4), a mixture of 1 to 1 regioisomeric α-(*o*-anilido)ketones were actually observed. Same regioselectivity and pattern were observed using *meta*-Cl substituted substrate **18e** and boronic acid **19a** (Table 7, entry 5).

Table 7. Stoichiometric Condition Scope: Hydroxamates



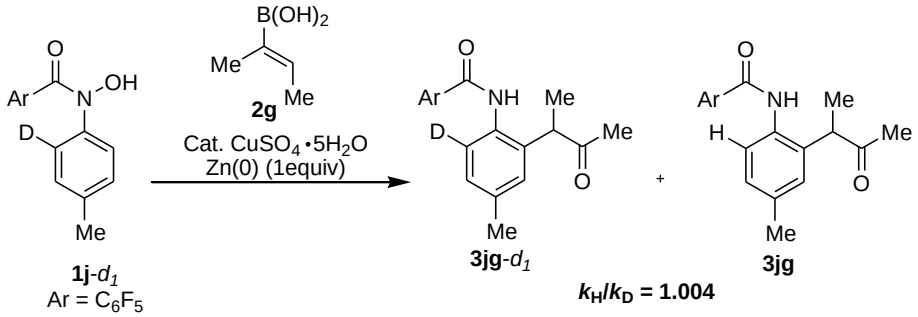
Entry	Product	Entry	Product
1	 **20aa** 95%	5	 **20ea** 32% + **20ea-c** 30%
2	 **20ba** 38%	6	 **20fa** 90%
3	 **20ca** 59%	7	 **20ga** 92%
4	 **3da** 40% + **3da-c** 35%		

Reaction mixtures were prepared as 1:2:5 mixtures of 1:boronic acid:pyridine in DCE (0.1 M) and were run in air.

3.4 Mechanistic Studies

Kinetic isotope effect experiment was conducted to clarify certain mechanistic doubts such as the rate-determining step of the transformation. Deuterium-labeling hydroxamic acid **18o**-d_1 was prepared. Hydroxamic acid **18o**-d_1 was subjected to the Cu-catalyzed

condition; a primary kinetic isotope effect was not observed (Eq. 1).

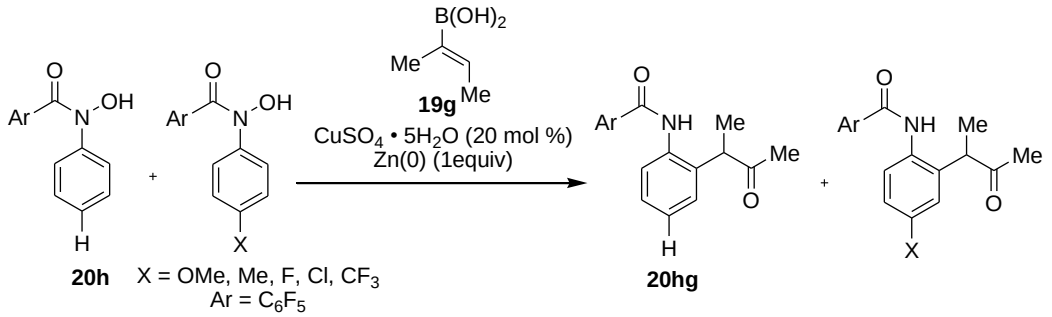


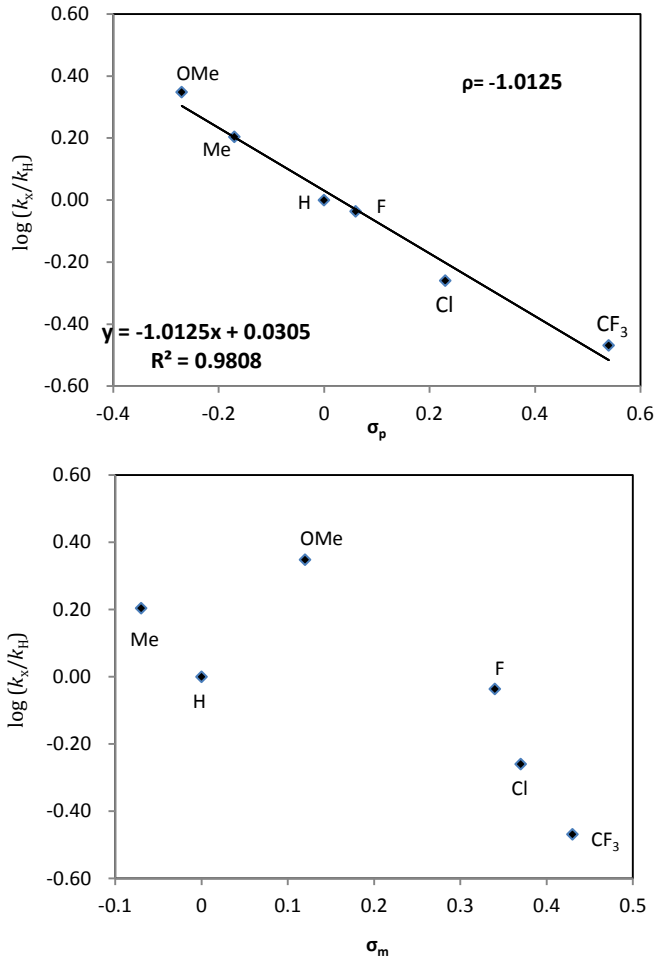
(1)

It indicated that the C-H functionalization was not the rate-determining step and that either the C–O bond formation or [3,3]-rearrangement was the slow step in the transformation.

Hammett study was also conducted to distinguish between the C–O formation and [3,3]-rearrangement. *para*-Substituted substrates were prepared to perform this intermolecular competition reaction. It gave linear correlation with σ_p with a -1.0125 ρ value and non-linear correlation with σ_m (Fig. 1). Based on this data, it suggested that the C–O formation could be the slow step but the [3,3]-rearrangement due to the non-linear correlation with σ_m.

Figure 1. Hammett Plot

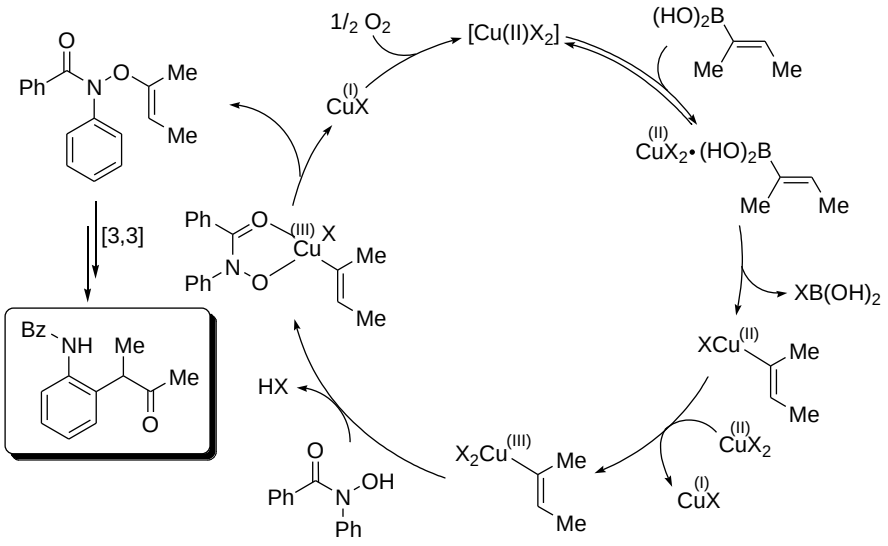




The proposed mechanism of this transformation was shown below. A Chan-Lam-Evans coupling reaction was assumed to be responsible for the formation of *O*-vinyl hydroxmate followed by the subsequent [3,3]-rearrangement and rearomatization to afford α-(*o*-anilido)ketones (Scheme 14). The proposed mechanism of the coupling reaction was adapted from the copper(III) mechanism proposed by Stahl and coworkers.[104] First, active catalyst copper(II) underwent transmetalation followed by oxidation to copper(III) complex. Subsequent hydroxamic acid ligand exchange and reductive elimination afforded *O*-vinyl hydroxamate and released copper(I) which was

oxidized to copper(II) in presence of oxygen. It was not clear what exact the role of zinc powder; however, the best assumption of its role was acting as activator of the boronic acid and facilitated the transmetallation which was believed to be the rate-determining step of the proposed mechanism.

Scheme 14. Proposed Mechanism

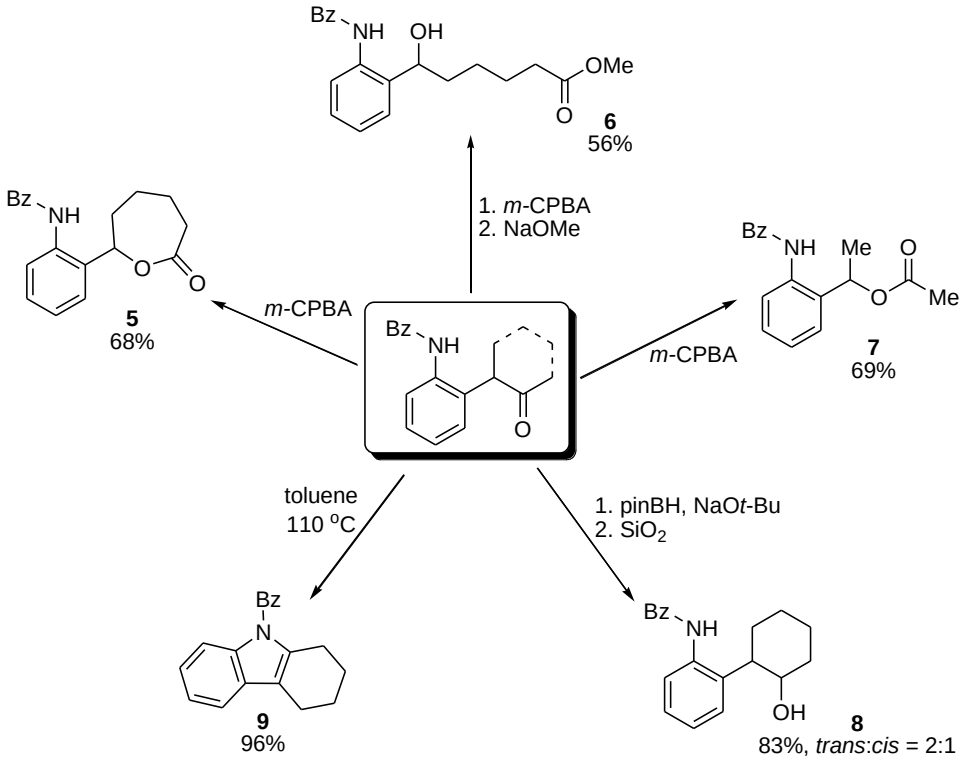


3.5 Functionalization of α-(*o*-Anilido)Ketones

Several common transformations of ketones were chosen to functionalize the α-(*o*-anilido)ketones (Scheme 15). α-(*o*-anilido)ketones **20a** smoothly transformed to lactone **23** exclusively under Baeyer-Villiger oxidation condition.[105] Furthermore, 2-steps oxidation and hydrolysis transformations gave the corresponding anilidol ester **24**. Acyclic α-(*o*-anilido)ketone also tolerated the Baeyer-Villiger oxidation to give anilido ester **25** in good yield. α-(*o*-Anilido)ketone **20a** was tolerated the reduction

condition using pinacolborane as reductant to give the corresponding alcohol **26** in good yield with 2:1 dr.[106] Heating **20a** which was the interrupted Fischer-Indole intermediate provided the corresponding indole **27** as expected in excellent yield.

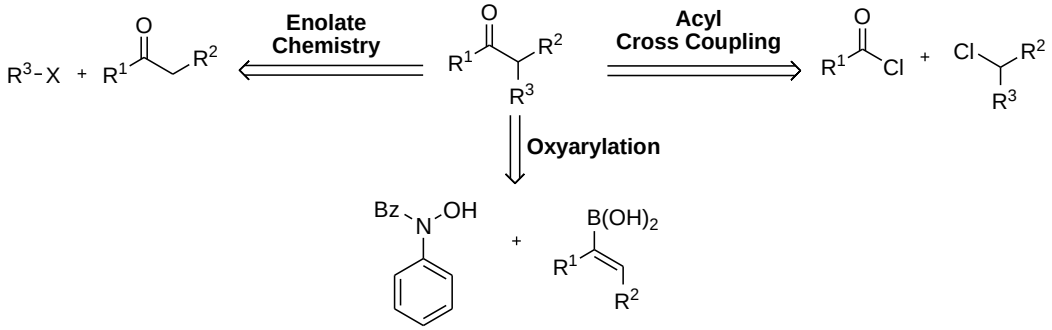
Scheme 15. Functional Group Transformation of α-(*o*-Anilido)Ketones



3.6 Summary

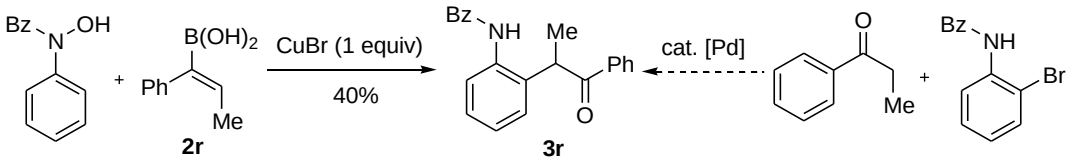
In this chapter, we had demonstrated the access of α-(*o*-anilido)ketones employing our Cu-mediated/catalyzed oxyarylation chemistry of vinyl boronic acids. The preparation of these compounds gave us certain mechanistic insight of the Fischer-Indole synthesis. It also demonstrated a novel pathway to the α-arylation of ketones without participation of enolate or enolate-like species (Scheme 16).

Scheme 16. α-Arylation via Oxyarylation of Vinyl Boronic Acid



We also showed that this oxyarylation chemistry could be applied to certain substrates which were inaccessible through Pd-catalyzed conditions in our control experiment, even though α-arylation of ketones was believed as a solved problem (Scheme 17). However, this oxyarylation chemistry did have its limitation. It gave good to excellent yields when simple cyclic and acyclic boronic acids were employed; boronic acid bearing heteroatom gave low or no transformation.

Scheme 17. Preparation of 20r via Oxyarylation



From the mechanism study, the C–O bond formation was involved in the rate-determining step not the [3,3]-rearrangement or rearomatization. It gave us some thought to improve the transformation such as switching the coupling partner from

boronic acid to boronic acid ester or more efficient coupling condition.

3.7 Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using 500 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the scale, multiplicity (br = broad, s = singlet, d = doublet, t =triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. High resolution mass spectra were acquired on an LTQ FT spectrometer, and were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 60Å (40 – 60 μm) mesh silica gel (SiO_2). Medium pressure liquid chromatography was performed to force flow the indicated solvent system down columns packed with 60Å (40 – 60 μm) mesh silica gel (SiO_2). Unless otherwise noted, all reagents were obtained from commercial sources and, where appropriate, purified prior to use. THF and CH_2Cl_2 were dried by filtration through alumina according to the procedure of Grubbs.[35] TMEDA was distilled over CaH_2 and stored under N_2 prior to use.

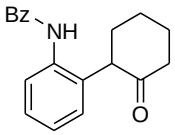
3.7.1 Preparation of α-(*o*-Anilido)Ketones

o-amideketones **3a-3m** were synthesized according to general procedure **A** or **B** described below.

General procedure A: A scintillation vial was charged with *N*-benzoyl-*N*-aryl-hydroxylamine **18** (1 equiv), vinyl boronic acid **19** (2-3 equiv), $CuSO_4 \cdot 5H_2O$ (20 mol %), zinc dust (1 equiv), and 4Å MS (0.050 g per 0.1 mmol **18**). These solids were then diluted with 1,2-dichloroethane to form a 0.1 M solution of *N*-benzoyl-*N*-aryl-hydroxylamine. Pyridine (5 equiv) was added to the resulting slurry via syringe. The scintillation vial was then capped with a septum pierced with a ventilation needle and the reaction mixture was stirred at 25 ℃ for 18 h. 1,2-Dichloroethane and pyridine were removed under reduced pressure and the crude reaction mixture was purified by medium pressure chromatography.

General procedure B: A scintillation vial was charged with *N*-benzoyl-*N*-aryl-hydroxylamine **18** (1 equiv), vinyl boronic acid **19** (2-3 equiv), CuBr (1 equiv), and 4Å MS (0.050 g per 0.1 mmol **18**). These solids were then diluted with 1,2-dichloroethane to form a 0.1 M solution of *N*-benzoyl-*N*-aryl-hydroxylamine. Pyridine (5 equiv) was added to the resulting slurry via syringe. The scintillation vial was then capped with a septum pierced with a ventilation needle and the reaction mixture was stirred at 25 ℃ for 18 h. 1,2-Dichloroethane and pyridine were removed under reduced

pressure and the crude reaction mixture was purified by medium pressure chromatography.

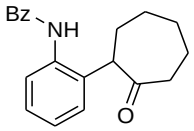


20a

20a was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.085 g, 0.67 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20a** as an amorphous solid (0.068 g, 77%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.51 (bs, 1H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.71 (d, *J* = 7.5 Hz, 1H), 7.56-7.48 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 2H), 3.78 (dd, *J* = 12.5 Hz, *J* = 5.5 Hz, 1H), 2.60-2.55 (m, 1H), 2.51-2.44 (m, 1H), 2.29-2.25 (m, 1H), 2.18-1.99 (m, 3H), 1.86-1.73 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.3, 165.6, 136.0, 134.3, 132.9, 131.6, 128.8, 128.7, 128.0, 127.2, 127.1, 126.4, 54.9, 41.9, 32.9, 27.4, 25.0; HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}NO_2$ $(M+H)^+$ 294.1494, found 294.1492.

General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.082 g, 0.65 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and

pyridine (120 μl, 1.50 mmol). Chromatography afforded **20a** as an amorphous solid (0.074 g, 84%).

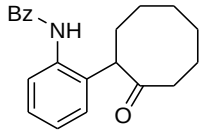


20b

20b was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-cycloheptenyl boronic acid **19b** (0.104 g, 0.742 mmol), $Cu(OAc)_2$ (0.011 g, 0.060 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20b** as a white foam (0.052 g, 56%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 10.1 (bs, 1H), 8.13 (d, *J* = 7.5 Hz, 2H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.58-7.52 (m, 3H), 7.35-7.32 (m, *2*H), 7.17 (t, *J* = 7.5 Hz, 1H), 3.91 (dd, *J* = 12.0 Hz, *J* = 4.0 Hz, 1H), 2.83-2.78 (m, 1H), 2.40-2.36 (m, 1H), 2.26-2.18 (m, 1H), 2.13-1.98 (m, 4H), 1.59-1.48 (m, 2H), 1.36-1.29 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 217.5, 165.6, 137.0, 134.7, 131.9, 130.3, 129.9, 128.8, 128.0, 127.5, 126.6, 125.4, 125.2, 54.7, 41.1, 30.3, 28.8, 28.0, 26.2; HRMS (ESI) *m/z* calcd. for $C_{20}H_{22}NO_2$ $(M+H)^+$ 308.1651, found 308.1648.

General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-cycloheptenyl boronic acid **19b** (0.122 g, 0.871 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and

pyridine (120 µl, 1.50 mmol). Chromatography afforded **20b** as a white foam (0.078 g, 85%).

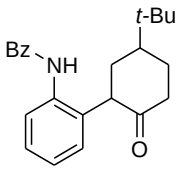


20c

20c was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-cyclooctenyl boronic acid **19c** (0.129 g, 0.837 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20c** as a white foam (0.042 g, 44%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.95 (bs, 1H), 8.19 (d, *J* = 7.5 Hz, 2H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.58-7.53 (m, 3H), 7.37-7.31 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 3.75 (d, *J* = 12.5 Hz, 1H), 2.88-2.82 (m, 1H), 2.73-2.64 (m, 1H), 2.13-2.09 (m, 1H), 1.99-1.96 (m, 1H), 1.91-1.85 (m, 2H), 1.79-1.74 (m, 2H), 1.61-1.57 (m, 1H), 1.45-1.38 (m, 1H), 1.27-1.24 (m, 1H), 1.15-1.12 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 219.5, 165.6, 137.1, 134.6, 131.9, 128.9, 128.8, 128.1, 127.6, 126.7, 125.1, 124.8, 54.8, 37.4, 29.3, 27.9, 27.4, 25.6, 24.7; HRMS (ESI) *m/z* calcd. for $C_{21}H_{24}NO_2$ $(M+H)^+$ 322.1807, found 322.1798.

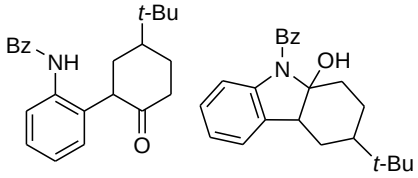
General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-cyclooctenyl boronic acid

19c (0.131 g, 0.850 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography afforded **20c** as a white foam (0.068 g, 70%).



20d-s

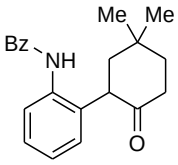
20d-s[107] was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 4-*t*-butyl-1-cyclohexenyl boronic acid **19d** (0.121 g, 0.66 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20d-s** as a white foam (0.050 g, 48%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.27 (bs, 1H), 7.86 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7. 36 (t, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 3.76 (dd, *J* = 13.0 Hz, *J* = 5.0 Hz, 1H), 2.62-2.58 (m, 1H), 2.53-2.46 (m, 1H), 2.28-2.24 (m, 1H), 2.15-2.11 (m, 1H), 1.91 (q, *J* = 13.0 Hz, 1H), 1.71-1.65 (m, 1H), 1.54-1.45 (m, 1H), 0.87 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.5, 165.7, 135.9, 134.3, 133.5, 131.8, 129.0, 128.8, 128.0, 127.6, 127.1, 126.6, 54.8, 46.9, 41.3, 34.0, 32.6, 28.0, 27.5; HRMS (ESI) *m/z* calcd. for $C_{23}H_{28}NO_2$ $(M+H)^+$ 350.2120, found 350.2118



20d-a/**20d-c**

20d-a/**20d-c** was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 4-*t*-butyl-1-cyclohexenyl boronic acid **19d** (0.121 g, 0.66 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20d-a**/**20d-c** as a white foam (0.045 g, 42%) in 2:3 ratio. ^{1}H NMR (500 MHz; $CDCl_3$) of **20d-a**: δ 9.78 (bs, 1H), 8.11 (d, *J* = 7.5 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.56-7.50 (m, 1H), 7.42 (t, *J* = 7.5 Hz, 3H), 7.34 (t, *J* = 7.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 4.01 (d, *J* = 6.5 Hz, 1H), 2.47-2.41 (m, 2H), 2.15-2.12 (m, 1H), 2.04-2.01 (m, 1H), 1.73-1.67 (m, 2H), 1.59-1.56 (m, 1H), 1.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) **20d-a**: δ 215.8, 165.7, 137.2, 134.7, 131.8, 130.5, 128.7, 127.9, 127.5, 126.8, 125.3, 125.1, 49.0, 44.0, 33.0, 30.9, 27.4, 26.3, 22.1; HRMS (ESI) *m/z* calcd. for $C_{23}H_{28}NO_2$ $(M+H)^+$ 350.2120, found 350.2120. ^{1}H NMR (500 MHz; $CDCl_3$) of **20d-c**: δ 7.56 (d, *J* = 7.5 Hz, 2H), 7.56-7.50 (m, 3H), 7.15 (d, *J* = 7.5 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.85 (t, *J* = 7.5 Hz, 1H), 5.97 (d, *J* = 8.0 Hz, 1H), 5.31 (s, 1H), 3.59 (d, *J* = 5.0 Hz, 1H), 2.54-2.51 (m, 1H), 2.47-2.41 (m, 2H), 2.28-2.25 (m, 1H), 2.04-2.01 (m, 1H), 1.59-1.56 (m, 1H), 1.38-1.30 (m, 1H), 0.91 (s, 9H); ^{13}C NMR (125

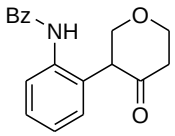
MHz, $CDCl_3$) of **20d-c**: δ 169.8, 140.6, 135.7, 132.7, 131.4, 128.7, 128.1, 126.9, 123.7, 123.1, 115.3, 98.0, 46.6, 42.3, 39.3, 34.3, 32.3, 27.4, 23.9; HRMS (ESI) *m/z* calcd. for $C_{23}H_{28}NO_2$ $(M+H)^+$ 350.2120, found 350.2120.



20e

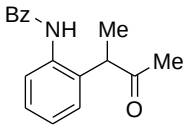
20e was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 4,4-dimethyl-1-cyclohexenyl boronic acid **19e** (0.113 g, 0.733 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20e** as a white foam (0.073 g, 76%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.20 (bs, 1H), 7.86 (d, *J* = 7.0 Hz, 2H), 7.63-7.62 (m, 1H), 7.57-7.54 (m, 1H), 7.50-7.47 (m, 2H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 1H), 3.90 (dd, *J* = 13.5 Hz, *J* = 5.5 Hz, 1H), 2.66-2.59 (m, 1H), 2.48-2.44 (m, 1H), 2.08-2.03 (m, 1H), 1.94-1.90 (m, 1H), 1.79-1.76 (m, 1H), 1.71-1.64 (m, 1H), 1.24 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.3, 165.7, 135.9, 134.3, 133.4, 131.7, 129.1, 128.8, 127.9, 127.5, 127.0, 126.6, 51.0, 45.7, 39.5, 38.5, 31.3, 30.9, 24.3; HRMS (ESI) *m/z* calcd. for $C_{21}H_{24}NO_2$ $(M+H)^+$ 322.1807,

found 322.1812.



20f

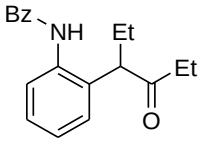
20f was synthesized according general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 3,6-dihydro-2H-pyran-4-boronic acid **19f** (0.091 g, 0.71 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20f** as an amorphous solid (0.037 g, 42%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.19 (bs, 1H), 8.07 (d, *J* = 7.0 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.58-7.50 (m, 3H), 7.36 (t, *J* = 7.0 Hz, 1H), 7.24 (t, *J* = 7.0 Hz, 1H), 4.39 (dd, *J* = 12.0 Hz, *J* = 3.0 Hz, 1H), 4.22-4.18 (m, 1H), 4.13 (dd, *J* = 12.0 Hz, *J* = 5.0 Hz, 1H), 3.96-3.91 (m, 1H), 3.86-3.83 (m, 1H), 2.79-2.72 (m, 1H), 2.48-2.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.1, 165.6, 136.7, 134.3, 132.0, 129.0, 128.8, 128.4, 128.2, 127.4, 126.0, 125.4, 71.3, 67.4, 52.5, 40.2; IR (thin film) 3348, 3017, 2968, 2861, 1704, 1666, 1584, 1527, 1452, 1302 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{18}H_{18}NO_3$ $(M+H)^+$ 296.1287, found 296.1291.



20g

20g was synthesized using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.078 g, 0.78 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20g** as an amorphous solid (0.080 g, 99%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.17 (bs, 1H), 8.05 (d, *J* = 7.5 Hz, 2H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.57-7.48 (m, 3H), 7.34-7.28 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 3.97 (q, *J* = 7.0 Hz, 1H), 2.16 (s, 3H), 1.51 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.1, 165.8, 136.6, 134.4, 131.9, 130.8, 128.8, 128.2, 128.1, 127.4, 125.8, 125.5, 50.4, 27.2, 15.3; HRMS (ESI) *m/z* calcd. for $C_{17}H_{18}NO_2$ $(M+H)^+$ 268.1338, found 268.1344.

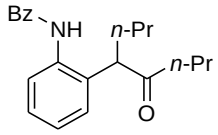
General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **1** (0.064 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **2e** (0.075 g, 0.75 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography afforded **20g** as an amorphous solid (0.075 g, 94%).



20h

20h were synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), *Z*-3-hexen-3-yl boronic acid **19h** (0.105 g, 0.820 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20h** as an amorphous solid (0.067 g, 76%). ^{1}H NMR (500 MHz; $CDCl_3$) of **3h**: δ 9.55 (bs, 1H), 8.14 (d, *J* = 7.0 Hz, 2H), 8.12-8.09 (m, 1H), 7.60-7.52 (m, 3H), 7.36-7.26 (m, 2H), 7.22-7.16 (m, 1H), 3.78 (t, *J* = 7.5 Hz, 1H), 2.67-2.50 (m, 2H), 2.20-2.11 (m, 1H), 1.98-1.89 (m, 1H), 1.03 (t, *J* = 7.5 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) of **3h**: δ 215.0, 165.5, 137.0, 134.5, 131.8, 129.6, 128.8, 128.7, 128.2, 127.5, 125.4, 125.2, 59.0, 34.2, 23.0, 12.5, 7.6; HRMS (ESI) *m/z* calcd. For $C_{19}H_{22}NO_2$ $(M+H)^+$ 296.1651, found 296.1655.

General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), *Z*-3-hexen-3-yl boronic acid **19h** (0.085 g, 0.66 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20h** as an amorphous solid (0.052 g, 59%).



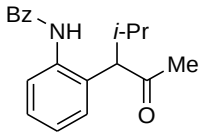
20i

20i was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), *Z*-4-octen-4-yl boronic acid **19i** (0.124 g, 0.794 mmol), $Cu(OAc)_2$ (0.011 g, 0.060 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20i** as an amorphous solid (0.068 g, 70%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.50 (bs, 1H), 8.15-8.12 (m, 3H), 7.60-7.54 (m, 3H), 7.35 (t, *J* = 7.0 Hz, 1H), 7.27 (d, *J* = 7.0 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 3.87 (t, *J* = 7.5 Hz, 1H), 2.54 (t, *J* = 7.5 Hz, 2H), 2.12-2.05 (m, 1H), 1.93-1.85 (m, 1H), 1.61-1.54 (m, 2H), 1.32-1.22 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 214.3, 165.5, 137.0, 134.6, 131.8, 129.6, 128.8, 128.7, 128.2, 127.4, 125.3, 125.1, 57.4, 42.7, 31.8, 21.2, 16.9, 13.9, 13.5; HRMS (ESI) *m/z* calcd. for $C_{21}H_{26}NO_2$ $(M+H)^+$ 324.1964, found 324.1964.

General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), *Z*-4-octen-4-yl boronic acid **19i** (0.121 g, 0.775 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography afforded **20i** as an amorphous solid (0.031 g, 32%).

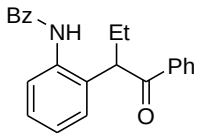
General procedure **B** was executed using the following reagents:

N-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), *Z*-4-octen-4-yl boronic acid **19i** (0.123 g, 0.788 mmol), $[CuCl(COD)]_2$ (0.063 g, 0.15 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography afforded **20i** as an amorphous solid (0.046 g, 47%).



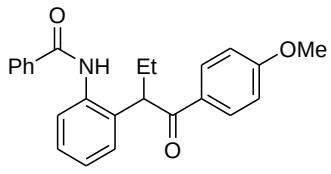
20j

20j was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.043 g; 0.20 mmol), 4-methyl-2-pentynyl boronic acid **19j** (0.071 g, 0.55 mmol), $Cu(OAc)_2$ (0.007 g, 0.04 mmol), zinc dust (0.013 g, 0.20 mmol), 4Å MS (0.100 g), and pyridine (80 µl, 1.0 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20j** as an oil (0.030 g, 50%) ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.54 (bs, 1H), 8.16-8.13 (m, 3H), 7.58-7.53 (m, 3H), 7.36-7.32 (m, 1H), 7.26-7.24 (m, 1H), 7.17-7.14 (m, 1H), 3.47 (d, *J* = 11.5 Hz, 1H), 2.67-2.59 (m, 1H), 2.25 (s, 3H), 1.01 (d, *J* = 6.5 Hz, 1H), 0.73 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.9, 165.3, 137.4, 134.6, 131.9, 128.8, 128.7, 128.4, 127.5, 127.1, 125.2, 125.0, 66.9, 28.0, 27.9, 21.8, 20.6; HRMS (ESI) *m/z* calcd. For $C_{19}H_{22}NO_2$ $(M+H)^+$ 296.1651, found 296.1646.



20k

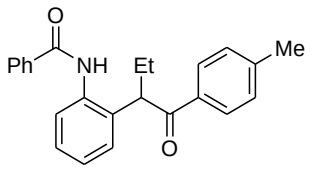
20k was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-phenyl-1-butynyl boronic acid **19k** (0.151 g, 0.857 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20k** as an amorphous solid (0.082 g, 80%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.84 (bs, 1H), 8.16 (d, *J* = 7.0 Hz, 2H), 8.10-8.06 (m, 3H), 7.59-7.53 (m, 4H),7.45 (t, *J* = 8.0 Hz, 2H), 7.34-7.28 (m, 2H), 7.13 (t, *J* = 7.0 Hz, 1H), 4.69 (t, *J* = 7.0 Hz, 1H), 2.28-2.20 (m, 1H), 2.11-2.02 (m, 1H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.7, 165.6, 137.1, 136.6, 134.7, 133.8, 131.8, 131.5, 129.4, 128.9, 128.8, 128.7, 128.3, 127.5, 125.6, 125.4, 55.0, 24.4, 12.8; HRMS (ESI) *m/z* calcd. for $C_{23}H_{22}NO_2$ $(M+H)^+$ 344.1651, found 344.1649.



20l

20l was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol),

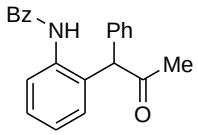
1-(*p*-OMe-phenyl)-1-butynyl boronic acid **19l** (0.165 g, 0.80 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (30:70; ethyl acetate: hexanes) afforded **20l** as an amorphous solid (0.054 g, 48%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 10.18 (bs, 1H), 8.24 (d, *J* = 7.0 Hz, 2H), 8.18 (d, *J* = 8.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 2H), 7.65-7.60 (m, 3H), 7.38-7.36 (m, 2H), 7.18 (t, *J* = 7.0 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 4.70 (t, *J* = 7.5 Hz, 2H), 3.91 (s, 3H), 2.33-2.24 (m, 1H), 2.16-2.08 (m, 1H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.0, 165.7, 164.3, 137.1, 134.7, 131.9, 131.7, 131.4, 129.6, 129.4, 128.8, 128.2, 127.6, 125.5, 125.3, 114.1, 55.6, 54.9, 24.3, 12.8; HRMS (ESI) *m/z* calcd. for $C_{24}H_{24}NO_3$ $(M+H)^+$ 374.1756, found 374.1756.



20m

20m was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 1-(*p*-tolyl)-1-butynyl boronic acid **19m** (0.172 g, 0.905 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20m** as an amorphous solid (0.066 g, 62%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.96 (bs, 1H), 8.17 (d, *J* = 7.0 Hz, 2H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 2H),

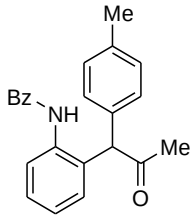
7.60-7.54 (m, 3H), 7.31 (t, *J* = 7.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 8.0 Hz, 1H), 4.66 (t, *J* = 8.0 Hz, 1H), 2.40 (s, 3H), 2.28-2.19 (m, 1H), 2.11-2.02 (m, 1H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.3, 165.5, 144.9, 137.2, 137.1, 134.8, 131.8, 131.7, 131.6, 129.6, 129.1, 128.8, 128.2, 127.6, 125.4, 125.3, 55.0, 24.3, 21.7, 12.8; HRMS (ESI) *m/z* calcd. for $C_{24}H_{24}NO_2$ $(M+H)^+$ 358.1807, found 358.1812.



20n

20n was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 3-phenyl-2-propynyl boronic acid **19n** (0.130 g, 0.803 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20n** as an amorphous solid (0.049 g, 50%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.49 (bs, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.52-7.47 (m, 1H), 7.41-7.36 (m, 3H), 7.29-7.21 (m, 5H), 7.11 (d, *J* = 7.0 Hz, 2H), 5.37 (s, 1H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.0, 165.6, 136.6, 136.3, 134.3, 131.8, 130.9, 130.0, 128.9, 128.8, 128.7, 128.6, 128.5, 127.6, 127.1, 126.0, 62.1, 31.0; HRMS (ESI) *m/z* calcd. for $C_{22}H_{20}NO_2$ $(M+H)^+$ 330.1494, found 330.1505.

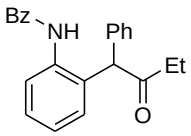
General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 3-phenyl-2-propynyl boronic acid **19n** (0.127 g, 0.784 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography afforded **20n** as an amorphous solid (0.059 g, 60%).



20o

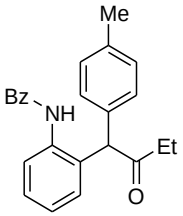
20o was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 3-(*p*-Me-phenyl)-2-propynyl boronic acid **19o** (0.137 g, 0.78 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20o** as a white foam (0.060 g, 58%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.42 (bs, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.43-7.39 (m, 3H), 7.28-7.25 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 2H), 5.34 (s, 1H), 2.36 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.9, 165.6, 137.4, 136.5, 134.3, 133.2, 131.7, 130.7, 130.2, 129.6, 128.7, 128.6, 128.5, 127.1, 125.9, 125.8, 61.8, 30.9, 21.0; HRMS (ESI) *m/z* calcd. for $C_{23}H_{22}NO_2$ $(M+H)^+$ 344.1651,

found 344.1658.



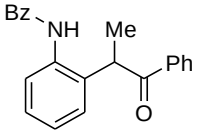
20p

20p was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 4-phenyl-3-butynyl boronic acid **19p** (0.135 g, 0.77 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20p** as an amorphous solid (0.060 g, 58%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.72 (bs, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.42-7.38 (m, 3H), 7.29-7.22 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 5.35 (s, 1H), 2.74 (q, *J* = 7.0 Hz, 2H), 2.27 (s, 3H), 1.11 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.2, 165.5, 136.8, 136.6, 134.4, 131.6, 131.1, 129.5, 128.8, 128.7, 128.5, 128.3, 127.5, 127.1, 125.8, 125.7, 61.6, 317.3, 7.8; HRMS (ESI) *m/z* calcd. for $C_{24}H_{24}NO_2$ $(M+H)^+$ 358.1807, found 358.1811.



20q

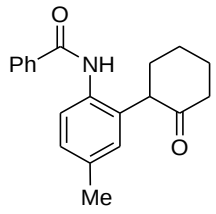
20q was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **18** (0.064 g; 0.30 mmol), 4-(*p*-Me-phenyl)-3-butynyl boronic acid **19q** (0.146 g, 0.768 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20q** as an oil (0.070 g, 65%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.73 (bs, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.42-7.38 (m, 3H), 7.29-7.22 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 5.35 (s, 1H), 2.74 (q, *J* = 7.0 Hz, 2H), 2.27 (s, 3H), 1.11 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.2, 165.6, 137.2, 136.7, 134.4, 133.5, 131.6, 130.9, 129.9, 129.5, 128.7, 128.4, 128.2, 127.1, 125.7, 125.6, 61.2, 37.1, 21.0, 7.9; HRMS (ESI) *m/z* calcd. for $C_{24}H_{24}NO_2$ $(M+H)^+$ 358.1807, found 358.1812.



20r

20r was synthesized according to general procedure **B**. ^{1}H NMR (500 MHz; $CDCl_3$): δ

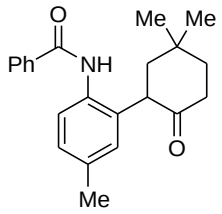
9.37 (bs, 1H), 8.09-8.05 (m, 4H), 7.99-7.95 (m, 1H), 7.60-7.50 (m, 3H),7.45 (t, *J* = 8.0 Hz, 2H), 7.33-7.26 (m, 3H), 7.18 (t, *J* = 7.5 Hz, 1H), 4.94 (q, *J* = 7.0 Hz, 1H), 1.64 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.2, 165.8, 136.4, 136.0, 134.5, 133.7, 132.4, 131.8, 130.3, 128.9, 128.8, 128.7, 128.1, 127.4, 126.0, 125.9, 46.4, 16.9.



20aa

20aa was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-(*p*-tolyl)-hydroxylamine **18a** (0.068 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.085 g, 0.67 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20aa** as an amorphous solid (0.081 g, 88%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.34 (bs, 1H), 7.88 (d, *J* = 7.0 Hz, 2H), 7.54-7.44 (m, 4H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.02 (s, 1H), 3.74 (dd, *J* = 5.5 Hz, *J* = 5.5 Hz, 1H), 2.55-2.52 (m, 1H), 2.47-2.42 (m, 1H), 2.32 (s, 3H), 2.26-2.23 (m, 1H), 2.08-1.95 (m, 3H), 1.79-1.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.1, 165.8, 136.1, 134.3, 133.3, 133.2, 131.8, 129.5, 128.7, 128.5, 127.2, 127.1, 54.7, 42.0, 33.3, 27.5, 25.2, 21.2; HRMS (ESI) *m/z* calcd. for $C_{20}H_{22}NO_2$ $(M+H)^+$ 308.1651, found 308.1649.

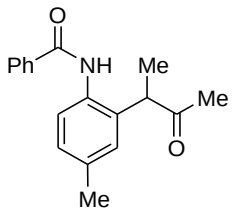
General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-(*p*-tolyl)-hydroxylamine **18a** (0.068 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.087 g, 0.69 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography afforded **20aa** as an amorphous solid (0.088 g, 95%).



20ae

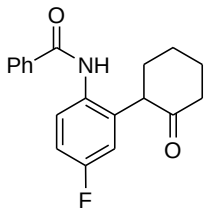
20ae was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-(*p*-Me-phenyl)-hydroxylamine **18a** (0.068 g; 0.30 mmol), 4,4-dimethyl-1-cyclohexenyl boronic acid **19e** (0.109 g, 0.71 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20ae** as an amorphous solid (0.072 g, 68%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.03 (bs, 1H), 7.85 (d, *J* = 7.0 Hz, 2H), 7.56-7.47 (m, 4H), 7.15 (d, *J* = 7.5 Hz, 1H), 6.98 (s, 1H), 3.85 (dd, *J* = 13.5 Hz, *J* = 5.5 Hz, 1H), 2.65-2.58 (m, 1H), 2.47-2.44 (m, 1H), 2.34 (s, 3H), 2.06-2.01 (m, 1H), 1.94-1.91 (m, 1H), 1.79-1.75 (m, 1H), 1.70-1.66 (m, 1H), 1.24 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.3, 165.8, 136.4, 134.4, 133.3, 133.2, 131.7, 129.8, 128.7,

128.6, 127.5, 127.0, 51.1, 45.6, 39.5, 38.5, 31.3, 30.6, 24.3, 21.1; HRMS (ESI) *m/z* calcd. for $C_{22}H_{26}NO_2$ $(M+H)^+$ 336.1964, found 336.1962.



20ag

20ag was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-(*p*-tolyl)-hydroxylamine **18a** (0.068 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.075 g, 0.75 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20ag** as an amorphous solid (0.080 g, 95%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.95 (bs, 1H), 8.04 (d, *J* = 7.0 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.57-7.49 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 3.94 (q, *J* = 7.0 Hz, 1H), 2.36 (s, 3H), 2.18 (s, 3H), 1.51 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.0, 165.7, 135.6, 134.5, 133.9, 131.8, 130.8, 128.9, 128.7, 128.6, 127.4, 125.5, 50.4, 27.3, 21.1, 15.4; HRMS (ESI) *m/z* calcd. for $C_{18}H_{20}NO_2$ $(M+H)^+$ 282.14945, found 282.1501.

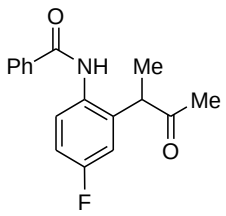


20ba

20ba was synthesized according to general procedures **A** using the following reagents: *N*-benzoyl-*N*-(*p*-F-phenyl)-hydroxylamine **18b** (0.069 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.087 g, 0.69 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20ba** as an amorphous solid (0.047 g, 50%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.25 (bs, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.60-7.54 (m, 2H), 7.48 (t, *J* = 8.0 Hz, 2H), 7.03 (td, *J* = 8.5 Hz, *J* = 3.0 Hz, 1H), 6.95 (dd, *J* = 9.5 Hz, *J* = 3.0 Hz, 1H), 3.74 (dd, *J* = 11.5 Hz, *J* = 5.5 Hz, 1H), 2.59-2.55 (m, 1H), 2.48-2.42 (m, 1H), 2.30-2.26 (m, 1H), 2.12-2.08 (m, 2H), 2.04-1.99 (m, 1H), 1.84-1.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.3, 165.8, 160.9 (d, $J_{C\text{-}F}$ = 244 Hz), 135.8 (d, $J_{C\text{-}F}$ = 7 Hz), 134.0, 132.0, 131.9, 129.0 (d, $J_{C\text{-}F}$ = 8 Hz), 128.8, 127.1, 115.5 (d, $J_{C\text{-}F}$ = 23 Hz), 114.6 (d, $J_{C\text{-}F}$ = 23 Hz), 54.4, 41.9, 32.7, 27.3, 24.9; HRMS (ESI) *m/z* calcd. for $C_{19}H_{19}NO_2F$ $(M+H)^+$ 312.1400, found 312.1405.

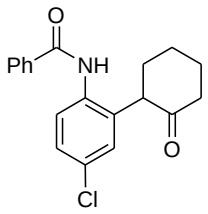
General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-(*p*-F-phenyl)-hydroxylamine **18b** (0.069 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.085 g, 0.67 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and

pyridine (120 µl, 1.50 mmol). Chromatography afforded **20ba** as an amorphous solid (0.035 g, 38%).



20bg

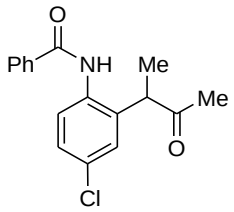
20bg was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-(*p*-F-phenyl)-hydroxylamine **18b** (0.069 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.073 g, 0.73 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20bg** as an amorphous solid (0.085 g, 99%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.02 (bs, 1H), 8.01 (d, J = 7.5 Hz, 2H), 7.86-7.83 (m, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.03-7.00 (m, 2H), 3.94 (q, J = 7.5 Hz, 1H), 2.17 (s, 3H), 1.50 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.2, 165.9, 160.4 (d, $J_{C\text{-}F}$ = 244 Hz), 134.1, 133.7 (d, $J_{C\text{-}F}$ = 7 Hz), 132.5 (d, $J_{C\text{-}F}$ = 2 Hz), 132.1, 128.8, 127.6 (d, $J_{C\text{-}F}$ = 8 Hz), 127.4, 114.9 (d, $J_{C\text{-}F}$ = 22 Hz), 114.6 (d, $J_{C\text{-}F}$ = 23 Hz), 50.0, 27.2, 15.3; HRMS (ESI) *m/z* calcd. for $C_{17}H_{17}NO_2F$ $(M+H)^+$ 286.1243, found 286.1251.



20ca

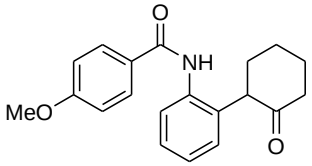
20ca was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-(*p*-chlorophenyl)-hydroxylamine **18c** (0.074 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.085 g, 0.67 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20ca** as an amorphous solid (0.025 g, 25%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.48 (bs, 1H), 7.89 (d, *J* = 8.0 Hz, 2H), 7.61-7.55 (m, 2H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.23 (s, 1H), 3.77 (dd, *J* = 11.0 Hz, *J* = 5.5 Hz, 1H), 2.58-2.55 (m, 1H), 2.50-2.45 (m, 1H), 2.27-2.24 (m, 1H), 2.14-1.99 (m, 3H), 1.82-1.75 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.4, 165.7, 135.0, 134.6, 133.9, 132.0, 131.6, 128.8, 128.4, 128.1, 127.9, 127.2, 54.3, 41.9, 32.9, 27.3, 24.9; HRMS (ESI) *m/z* calcd. for $C_{19}H_{19}NO_2Cl$ $(M+H)^+$ 328.1104, found 328.1106.

General procedure **B** was executed using the following reagents: *N*-benzoyl-*N*-(*p*-chlorophenyl)-hydroxylamine **18c** (0.074 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.087 g, 0.69 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography afforded **20ca** as an amorphous solid (0.058 g, 59%).



20cg

20cg was synthesized according to general procedure **A** using the following reagents: *N*-benzoyl-*N*-(*p*-chlorophenyl)-hydroxylamine **18c** (0.074 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.072 g, 0.72 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20cg** as an amorphous solid (0.068 g, 75%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.18 (bs, 1H), 8.04 (d, *J* = 7.5 Hz, 2H), 7.99 (d, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.32-7.28 (m, 2H), 3.93 (q, *J* = 7.5 Hz, 1H), 2.20 (s, 3H), 1.53 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.7, 165.7, 135.3, 134.1, 132.1, 132.0, 130.8, 128.8, 128.3, 127.9, 127.4, 126.5, 50.3, 27.2, 15.2; HRMS (ESI) *m/z* calcd. for $C_{17}H_{17}NO_2Cl$ $(M+H)^+$ 302.0948, found 302.0956.

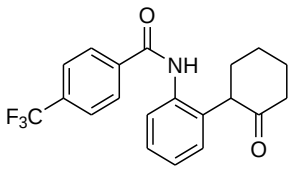


20fa

20fa was synthesized according to general procedure **A** using the following reagents:

N-(*p*-methoxybenzoyl)-*N*-phenylhydroxylamine **18f** (0.073 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.086 g, 0.68 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (30:70; ethyl acetate: hexanes) afforded **20fa** as a white foam (0.065 g, 67%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.51 (bs, 1H), 7.87 (d, *J* = 9.0 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.24-7.18 (m, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H), 3.80 (dd, *J* = 5.5 Hz, *J* = 5.5 Hz, 1H), 2.56-2.53 (m, 1H), 2.48-2.42 (m, 1H), 2.24-2.22 (m, 1H), 2.12-2.10 (m, 2H), 1.98-1.95 (m, 1H), 1.82-1.73 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.3, 165.3, 162.5, 136.2, 133.1, 129.1, 128.8, 127.8, 127.1, 126.5, 126.2, 113.9, 55.5, 54.6, 41.9, 33.2, 27.5, 25.1; HRMS (ESI) *m/z* calcd. for $C_{20}H_{22}NO_3$ $(M+H)^+$ 324.1600, found 324.1602.

General procedure **B** was executed using the following reagents: *N*-(*p*-methoxybenzoyl)-*N*-phenylhydroxylamine **18f** (0.073 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.080 g, 0.63 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography afforded **20fa** as a white foam (0.087 g, 98%).

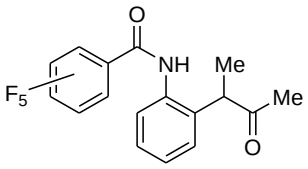


20ga

20ga was synthesized according to general procedure **A** using the following reagents: *N*-(*p*-trifluoromethylbenzoyl)-*N*-phenylhydroxylamine **18g** (0.084 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.081 g, 0.64 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20ga** as an amorphous solid (0.068 g, 63%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.81 (bs, 1H), 8.02 (d, J = 7.5 Hz, 2H), 7.74-7.67 (m, 3H), 7.34-7.21 (m, 3H), 3.80 (dd, J = 10.0 Hz, J = 5.5 Hz, 1H), 2.56-2.53 (m, 1H), 2.49-2.44 (m, 1H), 2.24-2.23 (m, 1H), 2.12-1.99 (m, 3H), 1.85-1.75 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.7, 164.3, 137.6, 135.7, 133.4 (q, J_{C-F} = 32.5 Hz), 132.8, 128.9, 128.0, 127.7, 126.8, 126.6, 125.8, 123.7 (q, J_{C-F} = 271.0 Hz), 56.3, 41.8, 33.1, 27.4, 24.9; HRMS (ESI) *m/z* calcd. for $C_{20}H_{19}NO_2F_3$ $(M+H)^+$ 362.1368, found 362.1371.

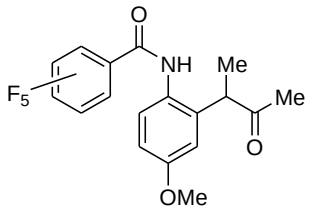
General procedure **B** was executed using the following reagents: *N*-(*p*-trifluoromethylbenzoyl)-*N*-phenylhydroxylamine **18g** (0.084 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.082 g, 0.65 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography afforded **20ga** as an

amorphous solid (0.088 g, 92%).



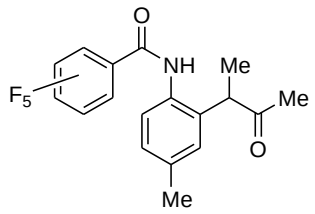
20hg

20hg was synthesized according to general procedure **A** using the following reagents: *N*-(pentafluorobenzoyl)-*N*-phenyl-hydroxylamine **18h** (0.091 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.082 g, 0.82 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (10:90; ethyl acetate: hexanes) afforded **20hg** as an amorphous solid (0.096 g, 90%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.14 (bs, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.32-7.24 (m, 3H), 3.95 (q, *J* = 7.0 Hz, 1H), 2.11 (s, 3H), 1.47 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.6, 156.3, 144.1 (d, *J*C-F =250.0 Hz), 142.4 (d, $J_{C\text{-}F}$ = 256.0 Hz), 137.7 (d, *J*C-F =254.0 Hz), 134.8, 132.2, 128.2, 128.1, 127.2, 125.7, 111.9 (t, $J_{C\text{-}F}$ =18.0 Hz), 49.6, 27.6, 15.7; ^{19}F NMR (300 MHz): -140.7 (ddd, $J_{F\text{-}F}$ = 27.0 Hz, 9.0 Hz, 6.0 Hz), -150.6 (t, $J_{F\text{-}F}$ = 21.0 Hz), -159.9 (ddt, $J_{F\text{-}F}$ = 27.0 Hz, 21.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{17}H_{13}NO_2F_5$ $(M+H)^+$ 358.0866, found 358.0862.



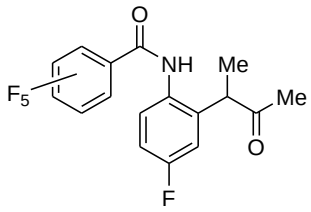
20ig

20ig was synthesized according to general procedure **A** using the following reagents: *N*-(pentafluorobenzoyl)-*N*-(*p*-OMe-phenyl)-hydroxylamine **18i** (0.100 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.085 g, 0.85 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20ig** as an oil (0.101 g, 87%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.75 (bs, 1H), 7.53 (d, J = 8.5 Hz, 1H), 6.80 (dd, J = 8.5 Hz, 2.5 Hz, 1H), 6.74 (d, J = 2.5 Hz, 1H), 3.90 (q, J = 7.5 Hz, 1H), 3.80 (s, 3H), 2.09 (s, 3H), 1.42 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 210.8, 158.6, 165.5, 144.1 (d, $J_{C\text{-}F}$ =251.0 Hz), 142.4 (d, $J_{C\text{-}F}$ =255.0 Hz), 137.7 (d, $J_{C\text{-}F}$ =255.0 Hz), 135.0, 127.6, 127.2, 114.0, 112.6, 111.9 (t, $J_{C\text{-}F}$ =18 Hz), 55.5, 49.3, 27.7, 15.8; ^{19}F NMR (300 MHz; $CDCl_3$): -140.7 (dd, $J_{F\text{-}F}$ = 24.0 Hz, 9.0 Hz), -150.6 (t, $J_{F\text{-}F}$ = 21.0 Hz), -159.9 (ddt, $J_{F\text{-}F}$ = 27.0 Hz, 21.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. For $C_{18}H_{15}NO_3F_5$ $(M+H)^+$ 388.0972, found 388.0962.



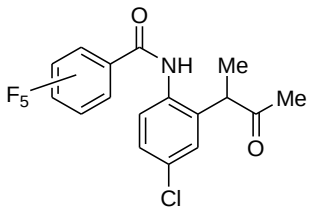
20jg

20jg was synthesized according to general procedure **A** using the following reagents: *N*-(pentafluorobenzoyl)-*N*-(*p*-Me-phenyl)-hydroxylamine **18j** (0.095 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.084 g, 0.84 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (10:90; ethyl acetate: hexanes) afforded **20jg** as an amorphous solid (0.108 g, 97%). ^{1}H NMR (500 MHz; CDCl3): δ 8.93 (bs, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.04 (s, 1H), 3.91 (q, *J* = 7.0 Hz, 1H), 2.34 (s, 3H), 2.11 (s, 3H), 1.45 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.5, 156.3, 144.1 (d, $J_{C\text{-}F}$ =250 Hz), 142.4 (d, $J_{C\text{-}F}$ =256.0 Hz), 137.7 (d, $J_{C\text{-}F}$ =254.0 Hz), 137.2, 132.3, 132.0, 128.8, 128.7, 125.8, 112.0 (t, $J_{C\text{-}F}$ =18.0 Hz), 49.5, 27.7, 21.0, 15.7; ^{19}F NMR (300 MHz; $CDCl_3$): -140.7 (ddd, $J_{F\text{-}F}$ = 21.0 Hz, 6.0 Hz, 3.0 Hz), -150.8 (t, $J_{F\text{-}F}$ = 21.0 Hz), -160.0 (ddt, $J_{F\text{-}F}$ = 21.0 Hz, 15.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. For $C_{18}H_{20}NO_2F_5$ $(M+H)^+$ 372.1023, found 372.1026.



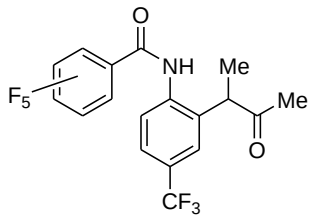
20kg

20kg was synthesized according to general procedure **A** using the following reagents: *N*-(2,3,4,5,6-pentafluorobenzoyl)-*N*-(*p*-F-phenyl)-hydroxylamine **18k** (0.096 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.083 g, 0.83 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20kg** as an amorphous solid (0.054 g, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.87 (bs, 1H), 7.77-7.47 (m, 1H), 7.05-6.98 (m, 2H), 3.93 (q, J = 7.5 Hz, 1H), 2.16 (s, 3H), 1.51 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.0, 161.0 (d, $J_{C\text{-}F}$ =246 Hz), 156.3, 144.2 (d, $J_{C\text{-}F}$ =251 Hz), 142.6 (d, $J_{C\text{-}F}$ =258 Hz), 137.7 (d, $J_{C\text{-}F}$ =254 Hz), 134.7 (d, $J_{C\text{-}F}$ =8 Hz), 130.7 (d, $J_{C\text{-}F}$ =3 Hz), 132.7 (d, $J_{C\text{-}F}$ =8 Hz), 115.0 (d, $J_{C\text{-}F}$ =21 Hz), 114.9 (d, $J_{C\text{-}F}$ =24 Hz), 111.6 (t, $J_{C\text{-}F}$ =21 Hz), 49.5, 27.5, 15.6; ^{19}F NMR (300 MHz; $CDCl_3$): -114.0- -114.1 (m), -140.6- -140.7 (m), -150.2 (t, $J_{F\text{-}F}$ = 21 Hz), -159.6- -159.8 (m); HRMS (ESI) *m/z* calcd. for $C_{17}H_{12}NO_2F_6$ $(M+H)^+$ 376.0772, found 376.0771.



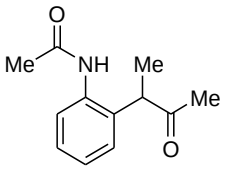
20lg

20lg was synthesized according to general procedure **A** using the following reagents: *N*-(2,3,4,5,6-pentafluorobenzoyl)-*N*-(*p*-Cl-phenyl)-hydroxylamine **18l** (0.101 g; 0.300 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.083 g, 0.83 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (10:90; ethyl acetate: hexanes) afforded **20lg** as a white foam (0.105 g, 89%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.09 (bs, 1H), 7.83 (d, J = 8.5 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 7.25 (s, 1H), 3.91 (q, J = 7.0 Hz, 1H), 2.17 (s, 3H), 1.52 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.4, 156.1, 144.2 (d, $J_{C\text{-}F}$ =251.0 Hz), 142.6 (d, $J_{C\text{-}F}$ =258.0 Hz), 137.7 (d, $J_{C\text{-}F}$ =250.0 Hz), 133.6, 133.2, 132.3, 128.3, 128.2, 126.7, 111.6 (t, $J_{C\text{-}F}$ =20.0 Hz), 49.7, 27.6, 15.5; ^{19}F NMR (300 MHz; $CDCl_3$): -140.5 (dd, $J_{F\text{-}F}$ = 18.0 Hz, 3.0 Hz), -150.0 (t, $J_{F\text{-}F}$ = 21.0 Hz), -160.0 (ddt, $J_{F\text{-}F}$ = 27.0 Hz, 21.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{17}H_{12}NO_2F_5Cl$ $(M+H)^+$ 392.0477, found 392.0480.



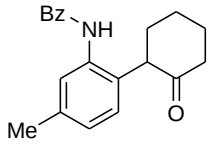
20mg

20mg was synthesized according to general procedure **A** using the following reagents: *N*-(2,3,4,5,6-pentafluorobenzoyl)-*N*-(*p*-CF_3-phenyl)-hydroxylamine **18m** (0.111 g; 0.300 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.083 g, 0.83 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20mg** as an amorphous solid (0.068 g, 53%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.50 (bs, 1H), 8.17 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8.5 Hz, 1H), 7.54 (s, 1H), 4.01 (q, J = 7.5 Hz, 1H), 2.22 (s, 3H), 1.60 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.2, 156.1, 144.2 (d, $J_{C\text{-}F}$ =253.0 Hz), 142.8 (d, $J_{C\text{-}F}$ =258.0 Hz), 138.5, 137.8 (d, $J_{C\text{-}F}$ =255.0 Hz), 131.0, 128.4 (q, $J_{C\text{-}F}$ = 33.0 Hz), 125.5 (d, $J_{C\text{-}F}$ = 3.0 Hz), 125.4 (d, $J_{C\text{-}F}$ = 3.0 Hz), 125.0, 123.7 (q, $J_{C\text{-}F}$ = 270.0 Hz), 111.5 (t, $J_{C\text{-}F}$ =18.0 Hz), 50.3, 27.6, 15.4; ^{19}F NMR (300 MHz; $CDCl_3$): -63.0, -140.5 (d, $J_{F\text{-}F}$ = 18.0 Hz), -149.7 (t, $J_{F\text{-}F}$ = 21.0 Hz), -159.5 (ddt, $J_{F\text{-}F}$ = 30.0 Hz, 21.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{18}H_{12}F_8NO_2$ $(M+H)^+$ 426.0740, found 426.0732.



20ng

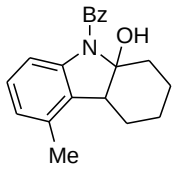
20ng was synthesized according to general procedure **A** using the following reagents: *N*-acetyl-*N*-phenyl-hydroxylamine **18n** (0.045 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.082 g, 0.82 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (50:50; ethyl acetate: hexanes) afforded **20ng** as an oil (0.054 g, 87%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.18 (bs, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 3.88 (q, *J* = 7.0 Hz, 1H), 2.17 (s, 3H), 2.08 (s, 3H), 1.44 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 211.3, 169.1, 136.1, 131.4, 128.1, 128.0, 126.0, 125.5, 50.2, 27.4, 24.2, 15.6; HRMS (ESI) *m/z* calcd. for $C_{12}H_{16}NO_2$ $(M+H)^+$ 206.1181, found 206.1187.



20da

20da was synthesized according to general procedures **B** using the following reagents: *N*-benzoyl-*N*-(*m*-Me-phenyl)-hydroxylamine **18d** (0.068 g; 0.30 mmol), 1-cyclohexenyl boronic acid **19a** (0.084 g, 0.67 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and

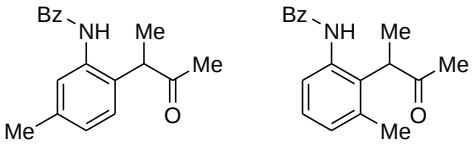
pyridine (120 μl, 1.50 mmol). Chromatography (30:70; ethyl acetate: hexanes) afforded **20da** as an amorphous solid (0.037 g, 40%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.48 (bs, 1H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.54-7.47 (m, 4H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 3.74 (dd, *J* = 10.5 Hz, *J* = 5.5 Hz, 1H), 2.57-2.54 (m, 1H), 2.48-2.43 (m, 1H), 2.35 (s, 3H), 2.25-2.22 (m, 2H), 1.99-1.97 (m, 1H), 1.81-1.73 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.4, 165.6, 137.9, 135.7, 134.3, 131.8, 130.0, 128.8, 128.6, 127.7, 127.3, 127.2, 54.4, 41.9, 33.1, 27.4, 25.1, 21.1.



20da-c

20da-c was synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-(*m*-Me-phenyl)-hydroxylamine **18d** (0.068 g; 0.30 mmol), 1-Cyclohexenyl boronic acid **19a** (0.084 g, 0.67 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (30:70; ethyl acetate: hexanes) afforded **20da-c** as a white foam (0.032 g, 35%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.71 (d, *J* = 7.5 Hz, 2H), 7.60-7.56 (m, 1H), 7.49-7.46 (m, 2H), 6.79-6.75 (m,, 2H), 5.91 (d, *J* = 7.0 Hz, 1H), 4.26 (s, 1H), 3.18-3.15 (m, 1H), 2.86-2.81 (m, 1H), 2.35 (s, 3H), 2.24-2.19 (m, 1H), 2.12-2.10 (m, 2H), 1.80-1.75 (m, 1H), 1.62-1.59 (m, 1H), 1.50-1.47 (m, 2H); ^{13}C NMR

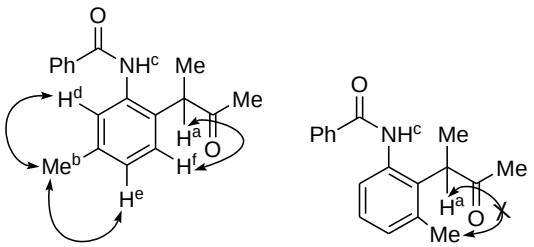
(125 MHz, $CDCl_3$): δ 171.9, 141.4, 135.9, 134.4, 132.9, 132.2, 128.9, 128.8, 127.0, 124.7, 112.7, 95.8, 47.2, 31.9, 28.3, 21.2, 21.1, 18.4.



20dg/20dg-m (1.3:1)

20dg/20dg-m were synthesized according to general procedure **B** using the following reagents: *N*-benzoyl-*N*-(*m*-tolyl)-hydroxylamine **18d** (0.068 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.076 g, 0.76 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (20:80; ethyl acetate: hexanes) afforded **20dg/20dg-m** as an amorphous solid (0.063 g, 75%) in 1.3:1 ratio. ^{1}H NMR (500 MHz; $CDCl_3$) of **20dg**: δ 9.08 (bs, 1H), 8.06 (d, *J* = 7.0 Hz, 2H), 7.87 (s, 1H), 7.56-7.50 (m, 2H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 3.93 (q, *J* = 7.0 Hz, 1H), 2.37 (s, 3H), 2.17 (s, 3H), 1.52 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) of **20dg**: δ 212.4, 165.6, 138.3, 136.4, 134.5, 131.9, 128.8, 127.9, 127.4, 127.3, 126.5, 125.8, 50.3, 27.1, 21.2, 15.3; ^{1}H NMR (500 MHz; $CDCl_3$) of **20dg-m**: δ 8.55 (bs, 1H), 7.98 (d, *J* = 7.0 Hz, 2H), 7.83-7.82 (m, 1H0, 755-7.54 (m, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 4.21 (q, *J* = 7.0 Hz, 1H), 2.45 (s, 3H), 2.15 (s, 3H), 1.42 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) of **20dg-m**: δ 211.7, 165.7, 136.9, 136.5, 134.4, 131.9, 128.2, 128.0, 127.8, 127.7,

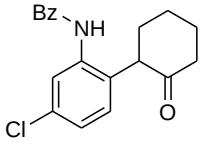
127.3, 124.3, 47.8, 29.2, 21.1, 14.1; HRMS (ESI) *m/z* calcd. for $C_{18}H_{20}NO_2$ $(M+H)^+$ 282.1494, found 282.1494.



1D ^{1}H-^{1}H NOE spectrum of **20dg**: H^a = 3.93 ppm (q, *J* = 7.0 Hz, 1H); Me^b = 2.37 ppm (s, 3H); H^c = 9.08 ppm (bs, 1H); H^d = 7.87 ppm (s, 1H); H^e = 7.02 ppm (d, *J* = 8.0 Hz, 1H); H^f = 7.18 ppm (d, *J* = 8.0 Hz, 1H)

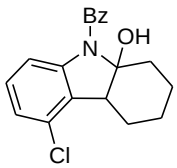
When the methine resonance at 3.93 ppm was irradiated, the resonance at 7.18 ppm was inverted as well as the resonance at 9.08 ppm but no methyl resonance at 2.37 ppm was observed. When the methyl resonance at 2.37 ppm was irradiated, the resonance at 7.87 ppm was inverted as well as the resonance at the 7.02 ppm but no methine resonance at 3.93 ppm was observed.

This confirms that **20dg** has a *para*-orientation of the methyl substituent and the α-position of the ketone.



20ea

20ea was synthesized according to general procedures **B** using the following reagents: *N*-benzoyl-*N*-(*m*-Cl-phenyl)-hydroxylamine **18e** (0.074 g; 0.30 mmol), 1-Cyclohexenyl boronic acid **19a** (0.085 g, 0.67 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol). Chromatography (30:70; ethyl acetate: hexanes) afforded **20ea** as an oil (0.031 g, 32%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.55 (bs, 1H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.80 (s, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.21-7.16 (m, 2H), 3.75 (dd, *J* = 11.0 Hz, *J* = 6.0 Hz, 1H), 2.60-2.55 (m, 1H), 2.51-2.49 (m, 1H), 2.26-2.23 (m, 1H), 2.13-2.09 (m, 2H), 2.02-1.99 (m, 1H), 1.83-1.76 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 213.1, 165.5, 137.2, 133.9, 133.4, 132.1, 131.2, 129.8, 128.9, 127.2, 126.9, 126.3, 54.4, 41.8, 32.9, 27.4, 25.0; HRMS (ESI) *m/z* calcd. for $C_{19}H_{19}NO_2Cl$ $(M+H)^+$ 328.1104, found 328.1106.



20ea-c

20ea-c was synthesized according to general procedures **B** using the following reagents:

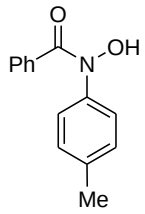
N-benzoyl-*N*-(*m*-Cl-phenyl)-hydroxylamine **18e** (0.074 g; 0.30 mmol), 1-Cyclohexenyl boronic acid **19a** (0.085 g, 0.67 mmol), CuBr (0.043 g, 0.30 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (30:70; ethyl acetate: hexanes) afforded **20ea-c** as an amorphous solid (0.029 g, 30%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.58-7.54 (m, 2H), 7.47-7.44 (m, 2H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 8.0 Hz, 1H), 5.93 (d, *J* = 8.0 Hz, 1H), 4.30 (s, 1H), 3.25-3.24 (m, 1H), 2.76-2.74 (m, 1H), 2.32-2.30(m, 1H), 2.14-2.01 (m, 2H), 1.79-1.74 (m, 2H), 1.5-1.54 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.8, 143.1, 135.4, 132.5, 132.3, 131.0, 128.9, 128.8, 128.0, 127.0, 123.5, 113.3, 96.0, 47.7, 31.7, 27.2, 21.0, 20.8.

3.7.2 Preparation of Hydroxamic Acids

Hydroxamic acids **18a**-**18g** and **18n** were prepared according to general procedure **C**.[108] Hydroxamic acids **18h**-**18m** were prepared according to general procedure **D**.[109]

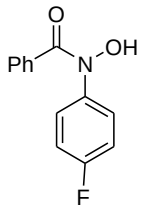
General procedure C: A 250 mL round bottom flask was charged with nitroarene (0.105 mol, 1 equiv), NH_4Cl (0.120 mol, 1.15 equiv), and H_2O (100 mL). While stirring at 25 ℃, zinc dust (0.210 mol, 2 equiv) was added in small portions over the course of 15 min. The reaction mixture was then stirred for 30 min. At this time, the reaction mixture was filtered and the remaining solids were washed with hot water. The filtrate was then extracted with CH_2Cl_2 (3 x 50 mL). The CH_2Cl_2 solution was then dried with

$MgSO_4$ and concentrated to 50 mL under vacuum. The desired benzoyl chloride (0.210, 2 equiv) was then added to the concentrated crude solution of *N*-aryl-hydroxylamine and the mixture was allowed to stir at 25 ºC for 1 h. Volatiles were then removed under vacuum and the crude product was purified by medium pressure chromatography.



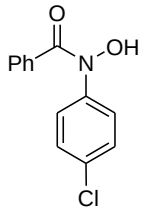
18a

18a[110] was synthesized according to general procedure **C** using the following reagents: 4-nitrotoluene (14.4 g, 0.105 mol), NH_4Cl (6.50 g, 0.120 mol), zinc dust (15.4 g, 0.210 mol), and benzoyl chloride (29.5 g, 0.210 mol). Chromatography afforded **18a** as white solid (2.6 g, 11%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.36 (t, *J* = 7.0 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.10-7.08 (m, 4H), 2.32 (s, 3H), the O-*H* resonance was too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.2, 138.5, 136.9, 132.1, 130.9, 129.8, 128.9, 128.1, 126.2, 21.1; HRMS (ESI) *m/z* calcd. for $C_{14}H_{14}NO_2$ $(M+H)^+$ 228.1025, found 228.1026.



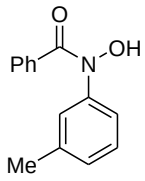
18b

18b: white solid (0.728 g, 3%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.62 (bs, 1H), 7.40-7.34 (m, 3H), 7.27-7.22 (m, 4H), 6.94 (t, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 161.7 (d, $J_{C\text{-}F}$ = 248 Hz), 136.2, 132.3, 131.0, 128.8, 128.3, 116.2, 116.0; HRMS (ESI) *m/z* calcd. for $C_{13}H_{11}NO_2F$ $(M+H)^+$ 232.0774, found 232.0778.



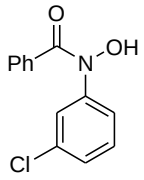
18c

18c[110] was synthesized according to general procedure **C** using the following reagents: 1-chloro-4-nitrobenzene (16.5 g, 0.105 mol), NH_4Cl (6.50 g, 0.120 mol), zinc dust (15.4 g, 0.210 mol), and benzoyl chloride (29.5 g, 0.210 mol). Chromatography afforded **18c** as a white solid (1.56 g, 6%). ^{1}H NMR (500 MHz; DMSO-d_6): δ10.80 (bs, 1H), 7.65-7.61 (m, 4H), 7.49-7.41 (m, 5H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 168.6, 141.4, 135.7, 130.9, 129.6, 128.9, 128.8, 128.3, 123.6; HRMS (ESI) *m/z* calcd. for $C_{13}H_{11}NO_2Cl$ $(M+H)^+$ 248.0478, found 248.0487.



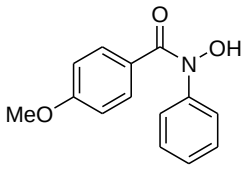
18d

18d[111] was synthesized according to general procedure **C** using the following reagents: 3-nitrotoluene (14.4 g, 0.105 mol), NH_4Cl (6.50 g, 0.120 mol), zinc dust (15.4 g, 0.210 mol), and benzoyl chloride (29.5 g, 0.210 mol). Chromatography afforded **18d** as a white solid (0.715 g, 3%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.45 (bs, 1H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.28-7.26 (m, 2H), 7.16-7.08 (m, 3H), 6.95 (d, *J* = 8.0 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.5, 139.6, 139.2, 132.4, 131.0, 129.0, 128.9, 128.8, 128.1, 126.4, 123.2, 21.2; HRMS (ESI) *m/z* calcd. for $C_{14}H_{14}NO_2$ $(M+H)^+$ 228.1025, found 228.1034.



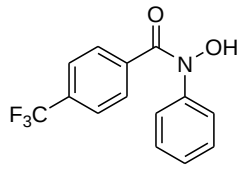
18e

18e: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.25 (bs, 1H), 7.43-7.40 (m, 3H), 7.31-7.29 (m, 3H), 7.22-7.16 (m, 2H), 7.03 (d, *J* = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8, 140.7, 134.7, 131.9, 131.4, 129.8, 128.8, 128.4, 127.9, 125.3, 123.5; HRMS (ESI) *m/z* calcd. for $C_{13}H_{11}NO_2Cl$ $(M+H)^+$ 248.0478, found 248.0484.



18f

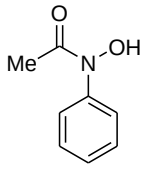
18f[111] was synthesized according to general procedure **C** using the following reagents: nitrobenzene (13.0 g, 0.105 mol), NH_4Cl (6.50 g, 0.120 mol), zinc dust (15.4 g, 0.210 mol), and 4-methoxybenzoyl chloride (22.3 g, 0.210 mol). Chromatography afforded **18f** as a white solid (6.13 g, 24%). ^{1}H NMR (500 MHz; DMSO-d_6): δ 10.63 (bs, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.36 (t, *J* = 8.5 Hz, 2H), 7.17 (t, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.9, 161.4, 143.0, 131.2, 128.9, 127.7, 125.8, 122.7, 113.6, 55.8; HRMS (ESI) *m/z* calcd. for $C_{14}H_{14}NO_3$ $(M+H)^+$ 244.0974, found 244.0977.



18g

18g was synthesized according to general procedure **C** using the following reagents: nitrobenzene (1.3 g, 0.011 mol), NH_4Cl (6.50 g, 0.120 mol), 10 mL of H_2O, zinc dust (1.5 g, 0.021 mol), and 4-(trifluoromethyl)benzoyl chloride (4.38 g, 0.0210 mol). Chromatography afforded **18g** as a white solid (0.531 g, 18%). ^{1}H NMR (500 MHz;

DMSO-d_6): δ 7.86 (d, *J* = 7.5 Hz, 2H), 7.79 (d, *J* = 7.5 Hz, 2H), 7.65-7.64 (m, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, DMSO-d6): δ 167.2, 142.0, 140.2, 130.7 (q, $J_{C\text{-}F}$ = 31.6 Hz), 129.4, 129.0, 126.3, 125.3, 125.2, 124.4 (q, $J_{C\text{-}F}$ = 270.2 Hz); HRMS (ESI) *m/z* calcd. for $C_{14}H_{11}NO_2F_3$ $(M+H)^+$ 282.0742, found 282.0750.

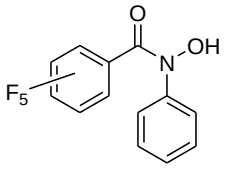


18n

18n[112] was synthesized according to general procedure **C** using the following reagents: nitrobenzene (1.3 g, 0.011 mol), NH_4Cl (6.50 g, 0.120 mol), 10 mL of H_2O, zinc dust (1.5 g, 0.021 mol), and acyl chloride (0.824 g, 0.0105 mol). Chromatography afforded **18n** as a solid (0.283 g, 17%). ^{1}H NMR (500 MHz; DMSO-d_6): δ 10.58 (bs, 1H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 142.1, 128.8 (4*C*), 22.9; HRMS (ESI) *m/z* calcd. for $C_8H_{10}NO_2$ $(M+H)^+$ 152.0712, found 152.0719.

General procedure D: Nitrobenzene (1 equiv) was dissolved in THF (10 mL/g) and cooled to 0 ℃. Rh/C (5 mol %) was then added to form a slurry. Hydrazine

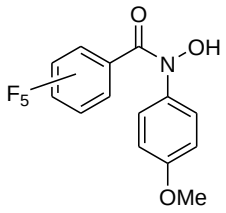
monohydrate (1.2 equiv) was added dropwise to the slurry and then the reaction mixture was allowed to warm up to 25 ℃ and stir for 2.5 h. The reaction mixture was then filtered through celite and washed with THF. The filtrate was concentrated under vacuum to give the crude product, hydroxylamine, as a solid. The crude sample of hydroxylamine was dissolved in DCM to form a 0.5 M solution. Pentafluorobenzoyl chloride (1.6 equiv) was added to the hydroxylamine solution and the mixture was allowed to stir for 1 h. The crude reaction mixture concentrated under vacuum and then purified by medium pressure chromatography.



18h

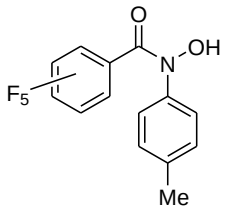
18h was synthesized according to general procedure **D** using the following reagents: nitrobenzene (1.78 g, 14.5 mmol), Rh/C (0.020 g), hydrazine monohydrate (0.84 ml, 17 mmol), and pentafluorobenzoyl chloride (3.3 ml, 23 mmol). After purification by medium pressure chromatography, compound **18h** was isolated as a solid (1.63 g, 37%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.19 (bs, 1H), 7.37-7.36 (m, 3H), 7.30-7.29 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.6, 136.7, 130.2, 129.5, 126.2 (*Ar*-F_5 resonances were too broad to be observed); ^{19}F NMR (300 MHz; $CDCl_3$): -139.1 (d, $J_{F\text{-}F}$ = 18.0 Hz), -149.2 (t, $J_{F\text{-}F}$ = 21.0

Hz), -159.6 (dd, $J_{F\text{-}F}$ = 21.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{13}H_7NO_2F_5(M+H)^+$ 304.0397, found 304.0397.



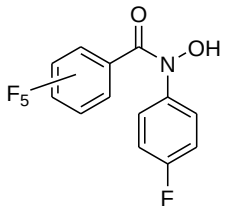
18i

18i was synthesized according to general procedure **D** using the following reagents: 4-nitroanisole (1.0 g, 6.5 mmol), Rh/C (0.010 g), hydrazine monohydrate (0.38 ml, 7.8 mmol), pentafluorobenzoyl chloride (1.5 ml, 10 mmol). After purification by medium pressure chromatography, compound **18i** was isolated as a solid (0.43 g, 20%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.99 (bs, 1H), 7.24 (d, *J* = 9.0 Hz, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.9, 153.8, 129.3, 128.3, 114.7, 55.5 (*Ar*-F_5 resonances were too broad to be observed); ^{19}F NMR (300 MHz; $CDCl_3$): -139.1 (d, $J_{F\text{-}F}$ = 15.0 Hz), -149.9 (t, $J_{F\text{-}F}$ = 21.0 Hz), -159.7 (dd, $J_{F\text{-}F}$ = 21.0 Hz, 15.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{14}H_9NO_3F_5(M+H)^+$ 334.0503, found 334.0501.



18j

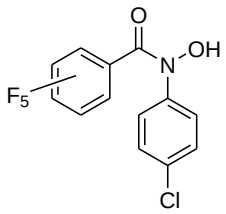
18j was synthesized according to general procedure **D** using the following reagents: nitrotoluene (2.0 g, 14 mmol), Rh/C (0.020 g), hydrazine monohydrate (0.84 ml, 17 mmol), and pentafluorobenzoyl chloride (3.3 ml, 23.2 mmol). After purification by medium pressure chromatography, compound **18j** was isolated as a solid (1.88 g, 41%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.93 (bs, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0, 140.8, 134.0, 130.2, 126.2, 21.3, (*Ar*-F_5 resonances were too broad to be observed); ^{19}F NMR (300 MHz; $CDCl_3$): -139.2 (d, $J_{F\text{-}F}$ = 18.0 Hz), -149.8 (t, $J_{F\text{-}F}$ = 21.0 Hz), -159.7 (dd, $J_{F\text{-}F}$ = 21.0 Hz, 6.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{14}H_9NO_2F_5(M+H)^+$ 318.0553, found 318.0549.



18k

18k was synthesized according to general procedure **D** using the following reagents: 4-fluoronitrobenzene (1.75 g, 12.4 mmol), Rh/C (0.017 g), hydrazine monohydrate (0.72

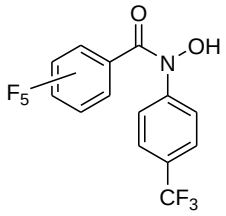
ml, 15 mmol), and pentafluorobenzoyl chloride (2.8 mL, 20 mmol) was added to the solution then the mixture was allow to stir for 1 h. After purification by medium pressure chromatography, compound **18k** was isolated as a solid (1.47 g, 37%). ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.45 (bs, 1H), 7.76-7.73 (m, 2H), 7.33-7.29 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.3 (d, J_{C-F} =243 Hz), 157.2, 142.9 (d, J_{C-F} =246 Hz), 141.8 (d, J_{C-F} =251 Hz), 137.5 (d, J_{C-F} =245 Hz), 136.8, 128.8 (d, J_{C-F} =10 Hz), 123.5 (d, J_{C-F} =9 Hz), 116.1 (d, J_{C-F} =23 Hz); ^{19}F NMR (300 MHz; DMSO-d_6): -110.8, -137.6 (d, J_{F-F} = 18.0 Hz), -148.2 (t, J_{F-F} = 21.0 Hz), -157.0- -157.1 (m); HRMS (ESI) *m/z* calcd. for $C_{13}H_6NO_2F_6$ $(M+H)^+$ 322.0303, found 322.0295.



18l

18l was synthesized according to general procedure **D** using the following reagents: 4-chloronitrobenzene (2.28 g, 14.5 mmol), Rh/C (0.020 g), hydrazine monohydrate (0.84 ml, 17 mmol), and pentafluorobenzoyl chloride (3.3 ml, 23.2 mmol). After purification by medium pressure chromatography, compound **18l** was isolated as a solid (1.85 g, 38%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.40 (bs, 1H), 7.33 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.2, 136.3, 135.5, 129.9,

127.5, (*Ar*-F_5 resonances were too broad to be observed); ^{19}F NMR (300 MHz; $CDCl_3$): -139.1 (m), -148.6 (t, J_{F-F} = 24.0 Hz), -158.9 (m); HRMS (ESI) *m/z* calcd. for $C_{13}H_6NO_2F_5Cl$ $(M+H)^+$ 338.0007, found 338.0004.



18m

18m was synthesized according to general procedure **D** using the following reagents: 4-nitrobenzotrifluoride (1.0 g, 5.2 mmol), Rh/C (0.0072 g), hydrazine monohydrate (0.30 ml, 6.2 mmol), pentafluorobenzoyl chloride (1.2 ml, 8.3 mmol). After purification by medium pressure chromatography, compound **18m** was isolated as a solid (0.66 g, 34%). ^{1}H NMR (500 MHz; acetone-d_6): δ 10.59 (bs, 1H), 8.09 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6): δ 157.9, 143.5, 143.1 (d, J_{C-F} =244.0 Hz), 142.1 (d, J_{C-F} = 253.0 Hz), 137.6 (d, J_{C-F} = 250.0 Hz), 127.1 (q, J_{C-F} = 31.0 Hz), 126.0, 124.2 (q, J_{C-F} = 269.0 Hz), 119.9, 111.8 (t, J_{C-F} =20.0 Hz); ^{19}F NMR (300 MHz; acetone-d_6): -63.5, -143.2 (d, J_{F-F} = 15.0 Hz), -154.7 (t, J_{F-F} = 21.0 Hz), -163.4 (dd, J_{F-F} = 21.0 Hz, 15.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{14}H_6NO_2F_8$ $(M+H)^+$ 372.0271, found 372.0276.

3.7.3 Preparation of Boronic Acids

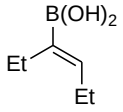
Boronic acids **19g-19i**, **19k-19m**, and **19r** were prepared via alkyne hydroboration.[72] Boronic acids **19a-19f**, **19j**, **19n-19q** were prepared via hydrolysis of the corresponding pinacol esters. The pinacol esters precursors of **19a-19e** were prepared via Shapiro reaction.[77] The pinacol esters precursors of **19j** and **19n-19q** were prepared to literature procedure.[113] The alkyne precursors for **19l**, **19m**, **19o**, and **19q** were prepared according to literature procedures.[114]

3.7.3.1 Preparation of Boronic Acids via Alkyne Hydroboration[72]

Boronic acids **19g-19i**, **19k-19m**, and **19r** were prepared according to the general procedure **E**. Characterization of **2g** was given in section 2.5.4.1. Boronic acid **19r** was prepared as a 1:1 mixture of regioisomeric isomers of **19r** and **19n**.

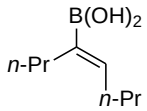
General procedure E: A round bottom flask was flame-dried under N_2, charged with an alkyne (1 equiv), diluted with CH_2Cl_2 to form a 1 M solution, and cooled to -78 ℃ with a dry ice-acetone bath. A 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (1.2 equiv) was slowly added to the alkyne solution and the reaction mixture was allowed to warm up to room temperature and stir for 3 h. The reaction mixture was then treated with 50 mL of a 10:1 mixture of Et_2O:H_2O and allowed to stir for 5 min. The reaction mixture was then diluted with additional Et_2O (50 mL) and extracted with water (3 x 5 mL). The organic layer was

then dried with $MgSO_4$ and concentrated under vacuum to give a crude sample of the vinyl boronic acid. This crude sample was used for the copper-coupling reactions without further purification. Any impurities carried on to the copper-coupling reaction were not observed to affect the efficiency of the process when compared to the use of a pure sample of boronic acid.



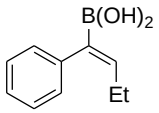
19h

19h[115] was synthesized according to general procedure **E** using the following reagents: 3-hexyne (0.820 g, 10.0 mmol) and a 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (11.0 mL, 11.0 mmol). Hydrolysis and workup gave **19h** as an off-white solid (0.910 g, 71 %). ^1H NMR (500 MHz; $CDCl_3$): δ 6.71-6.68 (m, 1H), 2.26 (q, *J* = 7.5 Hz, 4H), 1.07 (t, *J* = 7.5 Hz, 3H), 1.02 (t, *J* = 7.5 Hz, 3H), the O–*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.2, 21.8, 21.0, 14.9, 13.8, the *C*–B resonance was too broad to be observed.



19i

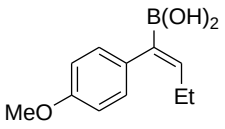
19i[116] was synthesized according to general procedure **E** using the following reagents: 4-octyne (1.10 g, 10.0 mmol) and a 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (11.0 mL, 11.0 mmol). Hydrolysis and workup gave **19i** as colorless oil (1.14 g, 73%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.70 (t, *J* = 7.0 Hz, 1H), 2.21-2.17 (m, 4H), 1.45-1.38 m, 4H), 0.95 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H)), the O–*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.2, 30.9, 30.2, 23.5, 22.4, 14.3, 14.0, the *C*–B resonance was too broad to be observed.



19k

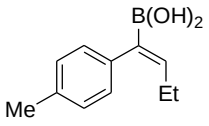
19k was prepared according to general procedure **E** using the following reagents: 1-phenyl-1-butyne (2.8 ml, 20 mmol) and 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (22 ml, 22 mmol). After work up, **19k** was isolated as solid (2.5 g, 71 %). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.41-7.36 (m, 3H), 6.95 (t, *J* = 7.5 Hz, 1H), 2.26-2.17 (m, 2H), 0.88 (t, *J* = 7.0 Hz, 3H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.1, 129.2, 128.3, 127.6, 125.8, 22.7, 14.2, the *C*-B

resonance was too broad to be observed; HRMS (EI) *m/z* calcd. for $C_{11}H_{15}BO_2$ (in MeOH, one of the OH is replaced by MeOH) 190.1165, found 190.1168.



19l

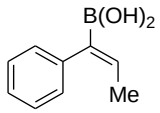
19l was synthesized according to general procedure **E** using the following reagents: 1-(*p*-OMe-phenyl)-1-butyne (1.10 g, 10.0 mmol) and a 1 M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (11.0 mL, 11.0 mmol). Hydrolysis and workup gave **19l** as an amorphous solid (0.95 g, 46%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.97-6.90 (m, 5H), 3.85 (s, 3H), 2.29-2.20 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H), the O–*H* resonances were too broad to be observed.



19m

19m was synthesized according to general procedure **E** using the following reagents: 1-(*p*-Me-phenyl)-1-butyne (1.44 g, 10.0 mmol) and a 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (11.0 mL, 11.0 mmol). Hydrolysis and workup gave **19m** as an amorphous solid (0.97 g, 51%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.32 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 8.0 Hz, 1H), 2.29-2.20 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H), the O–*H*

resonances were too broad to be observed.



19r

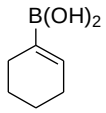
19r was synthesized according to general procedure **E**. ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.41-7.36 (m, 3H), 6.73 (q, *J* = 7.0 Hz, 1H), 1.71 (d, *J* = 7.0 Hz, 3H), the O–*H* resonances were too broad to be observed.

3.7.3.2 Preparation of Boronic Acids from Boronic Acid Pinacol Esters

Boronic acids **19a-19f**, **19j**, **19n-19p** were prepared according to the general procedure **F**.[75] The alkenyl boronic acid pinacol ester precursors for **19a-19e** were prepared using general procedure **G**.[77] The alkenyl boronic acid pinacol ester precursors for **19j** and **19n-19q** were prepared using general procedure **H**.[113] Characterization of **19d** was given in section 2.5.4.2.

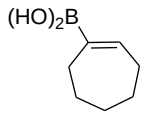
General procedure F: A scintillation vial was charged with alkenyl boronic acid pinacol ester (1 equiv), $NaIO_4$ (3.6 equiv), and NH_4OAc (3.6 equiv). These reagents were then diluted with a mixture of acetone and water in a 1:1 ratio to form a 0.63 M solution of the alkenyl boronic acid pinacol ester. The resulting slurry was allowed to stir vigorously until the boronic acid pinacol ester was fully consumed. Then the slurry was filtered and

acetone was removed from the filtrate under vacuum. The aqueous solution was extracted with diethyl ether (3 x 50 ml). The combined organic layers were washed with water and brine, dried with $MgSO_4$, and concentrated under vacuum to give a crude sample of the vinyl boronic acid. This crude sample was then used for the copper-coupling reaction without further purification. Any impurities carried on to the copper-coupling reaction were not observed to affect the efficiency of the process when compared to the use of a pure sample of boronic acid.



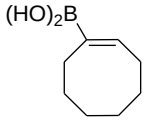
19a

19a was synthesized according to general procedure **F** using the following reagents: 1-cyclohexenyl boronic acid pinacol ester **19a-s** (0.100 g, 0.480 mmol), $NaIO_4$ (0.308 g, 1.40 mmol), and NH_4OAc (0.111 g, 1.40 mmol). After work up, **19a** was isolated as a solid (0.037 g, 61%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.00-6.93 (m, 1H), 2.18-2.09 (m, 4H), 1.63-1.62 (m, 4H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.8, 27.0, 25.4, 22.6, 22.3, the *C*-B resonance was too broad to be observed.



19b

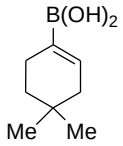
19b was synthesized according to general procedure **F** using the following reagents: 1-cycloheptenyl boronic acid pinacol ester **19b-s** (0.107 g, 0.480 mmol), $NaIO_4$ (0.308 g, 1.40 mmol), and NH_4OAc (0.111 g, 1.40 mmol). After work up, **19b** was isolated as a solid (0.055 g, 82%). ^1H NMR (500 MHz; $CDCl_3$): δ 7.18-7.16 (m, 1H), 2.40-2.38 (m, 2H), 2.30-2.28 (m, 2H), 1.79-1.75 (m, 2H), 1.51-1.48 (m, 4H), the O–*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.6, 32.8, 30.7, 28.3, 27.3, 26.4, the *C*-B resonance was too broad to be observed.



19c

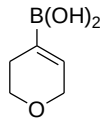
19c was synthesized according to general procedure **F** using the following reagents: 1-cyclooctenyl boronic acid pinacol ester **19c-s** (0.113 g, 0.480 mmol), $NaIO_4$ (0.308 g, 1.40 mmol), and NH_4OAc (0.111 g, 1.40 mmol). After work up, **19c** was isolated as a solid (0.060 g, 81%). ^1H NMR (500 MHz; $CDCl_3$): δ 7.00 (t, J = 8.0 Hz, 1H), 2.42-2.40 (m, 2H), 2.35-2.31 (m, 2H), 1.58-1.56 (m, 4H), 1.50-1.46 (m, 4H), the O–*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.6, 32.8, 30.7, 28.3, 27.3,

26.4, the *C*-B resonance was too broad to be observed.



19e

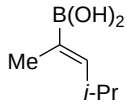
19e was synthesized according to general procedure **F** using the following reagents: 4,4-dimethyl-1-cyclohexenyl boronic acid pinacol ester **19e-s** (0.115 g, 0.485 mmol), $NaIO_4$ (0.340 g, 1.60 mmol), and NH_4OAc (0.149 g, 1.93 mmol). After work up, **19e** was isolated as a solid (0.053 g, 71%). ^1H NMR (500 MHz; $CDCl_3$): δ 6.89-6.87 (m, 1H), 2.24-2.21 (m, 2H), 1.94-1.93 (m, 2H), 1.37-1.35 (m, 2H), 0.90 (s, 6H), the O–*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.0, 40.9, 35.5, 28.5, 28.4, 23.4, the *C*-B resonance was too broad to be observed.



19f

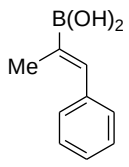
19f was synthesized according to general procedure **F** using the following reagents: 3,6-dihydro-2H-pyran-4-boronic acid pinacol ester **119f-s** (0.060 g, 0.29 mmol), $NaIO_4$ (0.183 g, 0.856 mmol), and NH_4OAc (0.066 g, 0.86 mmol). After work up, **2f** was isolated as a solid (0.018 g, 48%). ^1H NMR (500 MHz; $CDCl_3$): δ 6.90-6.89 (m, 1H), 4.26-4.25 (m,

2H), 3.78-3.75 (m, 2H), 2.30-2.29 (m, 2H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.4, 66.3, 64.3, 25.5, the *C*-B resonance was too broad to be observed.



19j

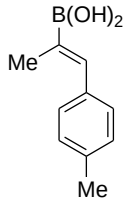
19j was synthesized according to general procedure **F** using the following reagents: 4-Methyl-2-pentynyl boronic acid pinacol ester **19j-s** (0.101 g, 0.480 mmol), $NaIO_4$ (0.308 g, 1.40 mmol), and NH_4OAc (0.111 g, 1.40 mmol). After work up, **19j** was isolated as an oil (0.041 g, 67%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.51 (d, *J* = 8.0 Hz, 1H), 2.80-2.73 (m, 1H), 1.78 (s, 3H), 1.01 (d, *J* = 8.0 Hz, 6H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.2, 27.8, 22.1, 12.9, the *C*-B resonance was too broad to be observed above the baseline.



19n

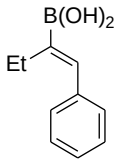
19n was synthesized according to general procedure **F** using the following reagents: 3-phenyl-2-propynyl boronic acid pinacol ester **19n-s** (0.118 g, 0.485 mmol), $NaIO_4$

(0.340 g, 1.60 mmol), and NH_4OAc (0.149 g, 1.93 mmol). After work up, **19n** was isolated as a solid (0.057 g, 73%). ^1H NMR (500 MHz; $CDCl_3$): δ 7.76 (s, 1H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 1H), 2.21 (s, 3H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.1, 137.9, 129.7, 128.2, 127.6, 15.2, the *C*-B resonance was too broad to be observed.



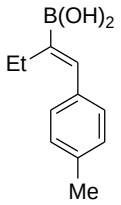
19o

19o was synthesized according to general procedure **F** using the following reagents: 3-(*p*-Me-phenyl)-2-propynyl boronic acid pinacol ester **19o-s** (0.125 g, 0.485 mmol), $NaIO_4$ (0.340 g, 1.60 mmol), and NH_4OAc (0.149 g, 1.93 mmol). After work up, **19o** was isolated as a solid (0.063 g, 74%). ^1H NMR (500 MHz; $CDCl_3$): δ 7.69 (s, 1H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 2.17 (s, 3H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.0, 137.5, 135.1, 129.7, 128.9, 21.3, 15.1, the *C*-B resonance was too broad to be observed.



19p

19p was synthesized according to general procedure **F** using the following reagents: 4-phenyl-3-butynl boronic acid pinacol ester **19p-s** (0.125 g, 0.485 mmol), $NaIO_4$ (0.340 g, 1.60 mmol), and NH_4OAc (0.149 g, 1.93 mmol). After work up, **19p** was isolated as a solid (0.058 g, 68%). ^1H NMR (500 MHz; $CDCl_3$): δ 7.71 (s, 1H), 7.46-7.41 (m, 4H), 7.34-7.32 (m, 1H), 2.58 (q, *J* = 7.0 Hz, 2H), 1.26 (t, *J* = 7.0 Hz, 3H), the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.7, 137.7, 129.1, 128.8, 128.3, 127.6, 22.1, 14.8, the *C*-B resonance was too broad to be observed.



19q

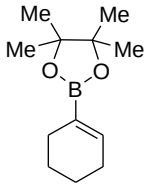
19q was synthesized according to general procedure **F** using the following reagents: 4-(*p*-Me-phenyl)-3-butynl boronic acid pinacol ester **19q-s** (0.132 g, 0.485 mmol), $NaIO_4$ (0.340 g, 1.60 mmol), and NH_4OAc (0.149 g, 1.93 mmol). After work up, **19p** was isolated as a solid (0.063 g, 68%). ^1H NMR (500 MHz; $CDCl_3$): δ 7.67 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 2.58 (q, *J* = 7.5 Hz, 2H), 1.26 (t, *J* = 7.0 Hz, 3H),

the O-*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.5, 137.5, 134.9, 129.2, 129.0, 22.1, 21.3, 14.7, the *C*-B resonance was too broad to be observed.

3.7.3.3 Preparation of Pinacol Esters of Boronic Acids via Shapiro Reaction

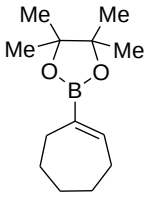
Corresponding pinacol esters of boronic acids **19a-19d** were prepared from *N*-tosyl hydrazones according to the general procedure **G**.[77] Characterization of **19d-s** was given in section 2.5.4.3. Boronic acid pinacol ester of **19f** was purchased from Frontier.

General procedure G: A 250 mL round bottom flask was flame-dried under N_2 and charged with *N*-tosylhydrazone (1 equiv), hexanes (3 mL/mmol hydrazone), and TMEDA (3 mL/mmol hydrazone). The resulting slurry was cooled to -78 ℃ with a dry ice-acetone bath and a 2.5 M *n*-BuLi solution in hexane (4 equiv) was added via syringe. The reaction mixture was allowed to stir at -78 ℃ for 1 h and then allowed to warm to 25 ℃. After stirring for an additional 2 h, the reaction mixture was cooled to -78 ℃ with a dry ice-acetone bath and BPin(O*i*-Pr) (4 equiv) was added via syringe. After 2 h the reaction mixture was quenched with $NH_4Cl_{(aq)}$. The mixture was extracted with ether. The organic layers were then dried with $MgSO_4$ and concentrated under reduced pressure to give a crude sample of the vinyl boronic acid pinacol ester. The crude sample was then purified by chromatography (2:98; ethyl acetate: hexanes).



19a-s

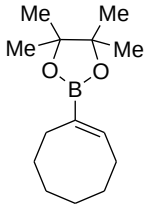
19a-s[77] was synthesized according to general procedure **G** using the following reagents: *N*-tosylcyclohexanylhydrazone (2.00g, 7.48 mmol), hexanes (22 mL), and TMEDA (22 mL), 2.5 M *n*-BuLi solution in hexane (29.9 mmol), and BPin(O*i*-Pr) (5.56 g, 29.9 mmol). After workup and purification by medium pressure chromatography, 1-cyclohexanyl boronic acid pinacol ester **19a-s** was isolated as an oil (0.90 g, 58%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.57-6.55 (m, 1H), 2.09-2.07 (m, 4H), 1.60-1.58 (m, 4H), 1.25 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.0, 83.0, 26.6, 26.1, 24.8, 22.5, 22.2, the *C*-B resonance was too broad to be observed above the baseline.



19b-s

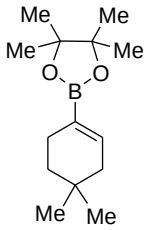
19b-s[77] was synthesized according to general procedure **G** using the following reagents: *N*-tosylcycloheptanylhydrazone (2.10 g, 7.48 mmol), hexanes (22 mL), and TMEDA (22 mL), 2.5 M *n*-BuLi solution in hexane (29.9 mmol), and BPin(O*i*-Pr) (5.56 g, 29.9 mmol). After workup and purification by medium pressure chromatography, 1-cycloheptenyl

boronic acid pinacol ester **19b-s** was isolated as an amorphous solid (0.99 g, 56%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.77 (t, *J* = 6.0 Hz, 1H), 2.27-2.21 (m, 4H), 1.76-1.72 (m, 2H), 1.50-1.45 (m, 4H), 1.25 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.6, 83.1, 32.7, 30.5, 29.5, 27.4, 26.5, 24.8, the *C*-B resonance was too broad to be observed.



19c-s

19c-s was synthesized according to general procedure **G** using the following reagents: *N*-tosylcyclooctanylhydrazone (2.20 g, 7.48 mmol), hexanes (22 mL), and TMEDA (22 mL), 2.5 M *n*-BuLi solution in hexane (29.9 mmol), and BPin(O*i*-Pr) (5.56 g, 29.9 mmol). After workup and purification by medium pressure chromatography, 1-cyclooctenyl boronic acid pinacol ester **19c-s** was isolated as an amorphous solid (0.93 g, 52%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.60 (t, *J* = 8.0 Hz, 1H), 2.31-2.22 (m, 4H), 1.52-1.47 (m, 8H), 1.27 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.1, 83.0, 29.7, 28.8, 27.1, 26.4, 26.2, 25.9, 24.8, the *C*-B resonance was too broad to be observed.

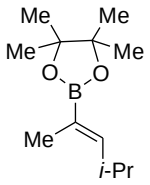


19e-s

19e-s was synthesized according to general procedure **G** using the following reagents: *N*-tosyl-4,4-dimethylcyclohexanylhydrazone (2.20 g, 7.48 mmol), hexanes (22 mL), and TMEDA (22 mL), 2.5 M *n*-BuLi solution in hexane (29.9 mmol), and BPin(O*i*-Pr) (5.56 g, 29.9 mmol). After workup and purification by medium pressure chromatography, 4,4-dimethylcyclohexenyl boronic acid pinacol ester **19e-s** was isolated as an amorphous solid (0.92 g, 52%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 6.49 (t, *J* = 6.0 Hz, 1H), 2.14-2.12 (m, 2H), 1.86-1.85 (m, 2H), 1.33-1.29 (m, 2H), 1.25 (s, 12H), 1.23 (s, 6H).

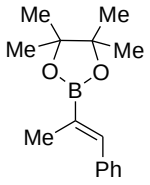
3.7.3.4 Preparation of Pinacol Esters of Boronic Acids via Alkyne Hydroboration

General Procedure H:[113] A conical vial was charged with CuCl (0.005 g, 0.05 mmol), PPh_3 (0.015 g, 0.060 mmol), sodium *tert*-butyloxide (0.020 g, 0.20 mmol) and B_2Pin_2 (0.254 g, 0.100 mmol). A 0.5M solution of alkyne (1.00 mmol) in THF was added to the solids via syringe and the resulting slurry was diluted with MeOH (0.064 g, 2.0 mmol). The mixture was allowed to stir for 18 h at 50 ℃. Volatiles were then removed under vacuum and the crude reaction mixture was purified by medium pressure chromatography to give pinacol ester.



19j-s

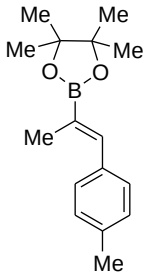
19j-s was synthesized according to general procedure **H** using the following reagents: CuCl (0.005 g, 0.05 mmol), PPh_3 (0.015 g, 0.060 mmol), sodium *tert*-butyloxide (0.020 g, 0.20 mmol), B_2Pin_2 (0.254 g, 0.100 mmol), 0.5M solution of 4-methyl-2-pentyne (0.082 g, 1.00 mmol) in THF, and MeOH (0.064 g, 2.0 mmol). After workup and purification by medium pressure chromatography, boronic acid pinacol ester **19j-s** was isolated as an oil (0.162 g, 77%). ^{1}H NMR (500 MHz; CDCl3): δ 6.10 (d, *J* = 7.5 Hz, 1H), 2.70-2.63 (m, 1H), 1.66 (s, 3H), 1.24 (s, 12H), 0.94 (d, *J* = 7.5 Hz, 6H); ^{13}C NMR (125 MHz, CDCl3): δ 153.3, 83.0, 27.4, 24.8, 22.2, 13.7, the *C*-B resonance was too broad to be observed.



2n-s

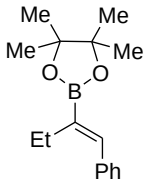
19n-s was synthesized according to general procedure **H** using the following reagents: CuCl (0.005 g, 0.05 mmol), PPh_3 (0.015 g, 0.060 mmol), sodium *tert*-butyloxide (0.020 g, 0.20 mmol), B_2Pin_2 (0.254 g, 0.100 mmol), 0.5M solution of 1-phenyl-1-propyne (0.116 g, 1.00 mmol) in THF, and MeOH (0.064 g, 2.0 mmol). After workup and purification by

medium pressure chromatography, boronic acid pinacol ester **19n-s** was isolated as an oil (0.159 g, 65%). ^{1}H NMR (500 MHz; CDCl3): δ 7.42-7.40 (m, 2H), 7.39-7.35 (m, 2H), 7.29 (s, 1H), 7.26-7.25 (m, 1H), 2.02 (s, 3H), 1.34 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.4, 129.4, 128.1, 128.0, 127.1, 83.5, 24.9, 15.9, the *C*-B resonance was too broad to be observed.



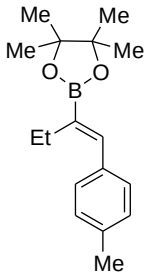
19o-s

19o-s was synthesized according to general procedure **H** using the following reagents: CuCl (0.005 g, 0.05 mmol), PPh_3 (0.015 g, 0.060 mmol), sodium *tert*-butyloxide (0.020 g, 0.20 mmol), B_2Pin_2 (0.254 g, 0.100 mmol), 0.5M solution of 1-(*p*-tolyl)-1-propyne (0.132 g, 1.00 mmol) in THF, and MeOH (0.064 g, 2.0 mmol). After workup and purification by medium pressure chromatography, boronic acid pinacol ester **19o-s** was isolated as an oil (0.163 g, 63%). ^{1}H NMR (500 MHz; CDCl3): δ 7.32 (d, *J* = 8.0 Hz, 2H), 7.23 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H), 2.01 (s, 3H), 1.33 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.3, 137.0, 135.1, 129.4, 128.7, 83.4, 24.9, 21.1, 15.9, the *C*-B resonance was too broad to be observed.



19p-s

19p-s was synthesized according to general procedure **H** using the following reagents: CuCl (0.005 g, 0.05 mmol), PPh_3 (0.015 g, 0.060 mmol), sodium *tert*-butyloxide (0.020 g, 0.20 mmol), B_2Pin_2 (0.254 g, 0.100 mmol), 0.5M solution of 1-(*p*-tolyl)-1-butyne (0.131 g, 1.00 mmol) in THF, and MeOH (0.064 g, 2.0 mmol). After workup and purification by medium pressure chromatography, boronic acid pinacol ester **19p-s** was isolated as an oil (0.201 g, 78%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.37-7.35 (m, 4H), 7.29-7.27 (m, 1H), 7.24 (s, 1H), 2.42 (q, *J* = 7.5 Hz, 2H), 1.35 (s, 12H), 1.13 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.4, 137.9, 128.9, 128.1, 127.0, 83.3, 24.8, 22.7, 14.7, the *C*–B resonance was too broad to be observed.

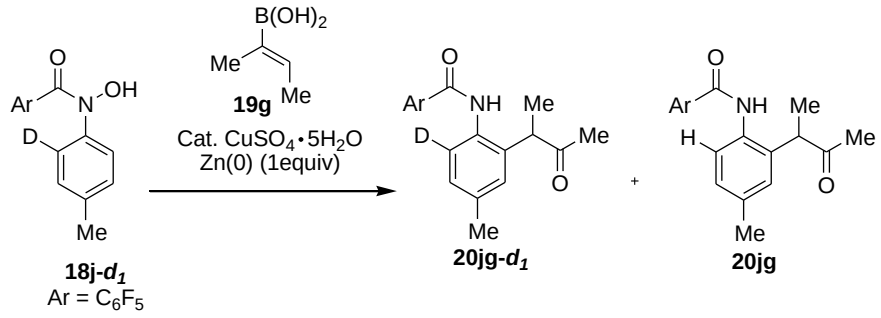


19q-s

19q-s was synthesized according to general procedure **H** using the following reagents: CuCl (0.005 g, 0.05 mmol), PPh_3 (0.015 g, 0.060 mmol), sodium *tert*-butyloxide (0.020 g,

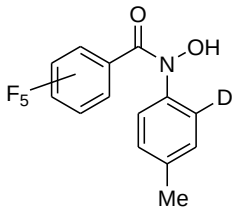
0.20 mmol), B_2Pin_2 (0.254 g, 0.100 mmol), 0.5M solution of 1-(*p*-tolyl)-1-butyne (0.144 g, 1.00 mmol) in THF, and MeOH (0.064 g, 2.0 mmol). After workup and purification by medium pressure chromatography, boronic acid pinacol ester **19q-s** was isolated as an oil (0.21 g, 78%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.29-7.25 (m, 2H), 7.20 (s, 1H), 7.18-7.16 (m, 2H), 2.42 (q, *J* = 7.0 Hz, 2H), 2.37 (s, 3H), 1.34 (s, 12H), 1.13 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.4, 136.8, 135.0, 129.0, 128.8, 83.3, 24.8, 22.7, 21.3, 14.7, the *C*–B resonance was too broad to be observed.

3.7.4 KIE Competition Experiment



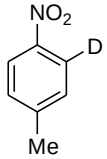
20jg-*d*$_1$/20jg was prepared according to general procedure **A** using the following reagents: *N*-(pentafluorobenzoyl)-*N*-(*o*-deutrio-phenyl)-hydroxylamine **18j-d$_1$** (0.095 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **19g** (0.084 g, 0.84 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 µl, 1.50 mmol). Chromatography (10:90; ethyl acetate: hexanes) afforded **20jg-*d*$_1$/20jg** as an amorphous solid (0.095 g, 85%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.91 (bs, 2H), 7.63 (d, *J* = 8.0 Hz, 1 H), 7.11 (s, 2H), 7.04 (s, 2H), 3.91 (q, *J* = 7.5 Hz, 2H), 2.35 (s, 6H), 2.12 (s,

6H), 1.46 (d, J = 7.5 Hz, 6H).



18j-*d*$_1$

18j-*d*$_1$ was synthesized according to general procedure **D** using the following reagents: 3-deutrio-4-nitrotoluene (1.0 g, 7.2 mmol), Rh/C (0.010 g), hydrazine monohydrate (0.42 ml, 8.7 mmol) and pentafluorobenzoyl chloride (1.7 mL, 11.5 mmol). After purification by medium pressure chromatography, **18j-*d*$_1$** was isolated as a solid (0.41 g, 18 %). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.79 (bs, 1H), 7.16-7.15 (m, 3H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.3, 140.7, 133.9, 130.2, 130.1, 126.2, 125.9 (t, $J_{C\text{-}D}$ = 25.0 Hz), 21.3; ^{19}F NMR (300 MHz; $CDCl_3$): -139.1 (d, $J_{F\text{-}F}$ = 18.0 Hz), -149.8 (t, $J_{F\text{-}F}$ = 21.0 Hz), -159.7 (dd, $J_{F\text{-}F}$ = 24.0 Hz, 15.0 Hz); HRMS (ESI) *m/z* calcd. for $C_{14}H_8DNO_2F_5(M+H)^+$ 319.0616, found 319.0608.



S-18j-*d*$_1$[117]

5-Methyl-2-nitrobenzoic acid (0.91 g, 5.0 mmol) and Ag_2CO_3 (0.14 g, 0.50 mmol) were

dissolved in DMSO (25 mL) to form a 0.2 M solution. D_2O (11.2 ml) was added to the solution via syringe. The mixture was allowed to stir for 16 h at 120 ℃. The crude solution was extracted with ethyl acetate (50 mL) and water (50 mL x 5). The filtrate was dried with $MgSO_4$ and concentrated under vacuum. The crude product was purified by medium pressure chromatography to give **S-18j-*d*$_1$** as an amorphous solid. (0.509 g, 73%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.12 (d, J = 9.0 Hz, 1H), 7.33-7.31 (m, 2H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.1, 145.9, 129.7, 129.6, 123.3, 123.0 (t, $J_{C\text{-}D}$ = 25.0 Hz), 21.2; HRMS (EI) *m/z* calcd. for $C_7H_6DNO_2(M)^+$ 138.0540, found 138.0544.

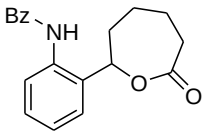
3.7.5 Description of Hammett Study Experiments

Mixtrure of **18h** and **18i** (0.30 mmole, 0.15 mmole each) and *Z*-2-buten-2-yl boronic acid **19g** (0.084 g, 0.84 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), and pyridine (120 μl, 1.50 mmol) was stirred at room temperature for 3.5 hour. The reaction mixture was filter through silica Crude solution was concentrated and dissolved in 25 ml ethyl acetate. Solution was washed with 10 ml 2 M NaOH for 3 times. The ratio of the methine resonances was recorded as in indication of the relative initial rates of the two substrates. The results were then plotted against Hammett parameters[118] as illustrated in Figure 1.

Table 8. Hammett Study

	σ_p	σ_m	k_x/k_H	log (k_x/k_H)
Para-OMe	-0.27	0.12	2.23	0.35
Para-Me	-0.17	-0.07	1.60	0.20
H	0	0	1.00	0.00
Para-Cl	0.23	0.37	0.55	-0.26
Para-CF_3	0.54	0.43	0.34	-0.47
Para-F	0.06	0.34	0.92	-0.04

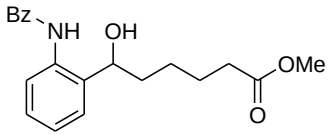
3.7.6 α-(*o*-Anilido)Ketones Functionalized Products



23[105]

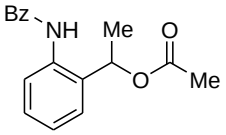
A 10 mL round bottom flask was flame-dried under N_2 and charged with α-(o-anilido)ketone **20a** (0.090 g; 0.31 mmol) and CH_2Cl_2 (3.1 mL). While stirring, *m*-chloroperoxybenzoic acid (77% purity; 0.417 g, 1.55 mmol) and $NaHCO_3$ (0.131 g, 1.55 mmol) were added to the solution of **20a** and the reaction mixture was allowed to stir at 25 ℃ for 3 h. The reaction mixture was then diluted with CH_2Cl_2 (70 mL), washed with saturated aqueous $NaHCO_3$ (7 mL), and dried over $MgSO_4$. Volatiles were removed under vacuum and the crude reaction mixture was then purified by medium pressure chromatography to afford **23** as an amorphous solid (0.065 g, 68%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.05 (bs, 1H), 8.00-7.98 (m, 3H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz,

2H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.28-7.26 (m, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 5.42 (dd, *J* = 6.5 Hz, *J* = 4.5 Hz, 1H), 2.76-2.74 (m, 2H), 2.13-2.11 (m, 2H), 2.11-1.99 (m, 2H), 1.98-1.58 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.2, 165.3, 135.3, 134.1, 132.1, 131.9, 129.2, 128.9, 127.5, 127.2, 125.5, 125.2, 82.9, 35.4, 34.5, 28.5, 22.8; HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}NO_3$ $(M+H)^+$ 310.1443, found 310.1445.



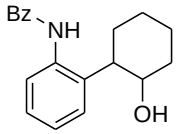
24[105]

A 10 mL round bottom flask was charged with **23** (0.053 g, 0.17 mmol) and diluted with MeOH to form a 0.05 M solution. NaOMe (0.010 g, 0.19 mmol) was then added to the solution and the reaction mixture was allowed to stir at 25 ℃ for 1.5 h. The crude product was purified by medium pressure chromatography to afford **24** as an oil (0.049 g, 83%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 10.20 (d, *J* = 2.0 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.29-7.26 (m, 1H), 7.06-7.01 (m, 2H), 4.78 (td, *J* = 7.0 Hz, *J* = 3.5 Hz, 1H), 3.60 (s, 3H), 3.51 (d, *J* = 3.5 Hz, 1H), 2.23 (t, *J* = 7.5 Hz, 2H), 1.96-1.89 (m, 1H), 1.81-1.74 (m, 1H), 1.62-1.56 (m, 2H), 1.48-1.39 (m, 1H), 1.30-1.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 174.2, 165.2, 137.0, 134.7, 131.7, 128.8, 128.7, 128.5, 127.7, 127.1, 123.9, 122.4, 75.9, 51.5, 35.9, 33.8, 25.6, 24.5; HRMS (ESI) *m/z* calcd. for $C_{20}H_{24}NO_4$ $(M+H)^+$ 342.1705, found 342.1700.



25[105]

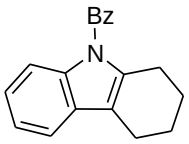
A 10 mL round bottom flask was flame-dried under N_2 and charged with α-(o-anilido)ketone **20g** (0.058 g; 0.21 mmol) and CH_2Cl_2 (2.1 mL). While stirring, *m*-chloroperoxybenzoic acid (77% purity; 0.283 g, 1.05 mmol) and $NaHCO_3$ (0.088 g, 1.1 mmol) were added to the solution of **20g** and the reaction mixture was allowed to stir at 25 ℃ for 3 h. The reaction mixture was then diluted with CH_2Cl_2 (70 mL), washed with saturated aqueous $NaHCO_3$ (7 mL), and dried over $MgSO_4$. The crude reaction mixture was then purified by medium pressure chromatography to afford **25** as an amorphous solid (0.042 g, 69%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.53 (bs, 1H), 8.05 (d, *J* = 7.0 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.57-7.50 (m, 3H), 7.26 (s, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 5.96 (q, *J* = 6.5 Hz, 1H), 2.36 (s, 3H), 2.08 (s, 3H), 1.60 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.9, 165.7, 135.4, 134.6, 132.9, 132.0, 131.8, 130.0, 128.7, 127.6, 127.3, 125.3, 68.7, 21.2, 21.1, 20.5; HRMS (ESI) *m/z* calcd. for $C_{18}H_{20}NO_3$ $(M+H)^+$ 298.1443, found 298.1440.



26[106] (*trans*/*cis* = 2:1)

A 10 mL round bottom flask was flame-dried under N_2 and charged with HBpin (0.128 g, 1.00 mmol), NaO*t*-Bu (0.019 g, 0.20 mmol), and toluene (2 ml). The resulting solution was allowed to stir at 25 ℃ for 45 min. At this time, a solution of **20a** (0.092 g, 0.31 mmol) in toluene (1 ml) was added to the pinBH solution via syringe. The mixture was allowed to stir at 25 ℃ for 18 h. Volatiles were then removed under vacuum and the crude reaction mixture was purified by medium pressure chromatography (30:70-40:60; ethyl acetate: hexanes) to afford **26** as a white solid (0.077 g, 83%) in 2:1 *trans* to *cis* ratio. ^{1}H NMR (500 MHz; $CDCl_3$) of *trans* isomer: δ 9.56 (bs, 1H), 7.94 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.45-7.40 (m, 3H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.23-7.16 (m, 2H), 3.48 (t, *J* = 9.0 Hz, 1H), 3.09 (bs, 1H), 2.78-2.72 (m, 1H), 2.08-2.03 (m, 1H), 1.83-1.76 (m, 3H), 1.73-1.67 (m, 1H), 1.50-1.44 (m, 2H), 1.40-1.31 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) of *trans* isomer: δ 165.6, 137.0, 136.7, 134.6, 131.7, 128.7, 127.3, 126.7, 126.3, 125.8, 125.0, 77.0, 45.3, 36.5, 30.9, 25.9, 25.0; HRMS (ESI) *m/z* calcd. for $C_{19}H_{22}NO_2$ $(M+H)^+$ 296.1651, found 296.1653. ^{1}H NMR (500 MHz; $CDCl_3$) of *cis* isomer: δ 10.28 (bs, 1H), 7.97 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.53-7.48 (m, 3H), 7.23-7.16 (m, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 4.14 (bs, 1H), 3.02 (bs, 1H), 2.78-2.72 (m, 1H), 2.27-2.19 (m, 1H), 1.83-1.76 (m, 3H), 1.73-1.67 (m, 1H), 1.40-1.31 (m, 1H), 1.28-1.23 (m, 2H); ^{13}C

NMR (125 MHz, $CDCl_3$) of *cis* isomer: δ 165.4, 136.8, 136.4, 134.9, 131.5, 130.8, 128.6, 127.4, 127.1, 125.6, 125.3, 71.5, 49.3, 34.3, 26.6, 24.6, 19.8; HRMS (ESI) *m/z* calcd. for $C_{19}H_{22}NO_2$ $(M+H)^+$ 296.1651, found 296.1653.



27

A conical vial was charged with **20a** (0.050 g, 0.17 mmol) and diluted with toluene to form a 0.05 M solution. 4Å MS (0.050 g) were then added to the solution, the vial was capped, and the reaction mixture was heated to 110 ℃ for 18 h. At this time, the volatiles were removed under vacuum and the crude reaction mixture was purified by medium pressure chromatography (10:90; ethyl acetate: hexanes) to afford **27** as light yellow solid (0.045 g, 96%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.08 (t, *J* = 8.0 Hz, 1H), 2.72-2.69 (m, 2H), 2.65-2.62 (m, 2H), 1.89-1.79 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4, 136.6, 136.1, 136.0, 132.3, 130.1, 129.4, 128.7, 128.6, 123.2, 122.6, 117.8, 114.7, 25.6, 23.6, 22.3, 21.1; HRMS (ESI) *m/z* calcd. for $C_{19}H_{18}NO$ $(M+H)^+$ 276.1388, found 276.1397.

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116. Sponholtz, W. R.; Pagni, R. M.; Kabalka, G. W.; Green, J. F.; Tan, L. C. *J. Org. Chem*. **1991**, *56*, 5700.

117. Grainger, R.; Nikmal, A.; Cornella, J.; Larrosa, I. Org. Biomol. Chem. **2012,** *10*, 3172.

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4 Indole Preparation through the Rearrangement of *O*-Vinyl Hydroxmates

4.1 Indole Synthesis

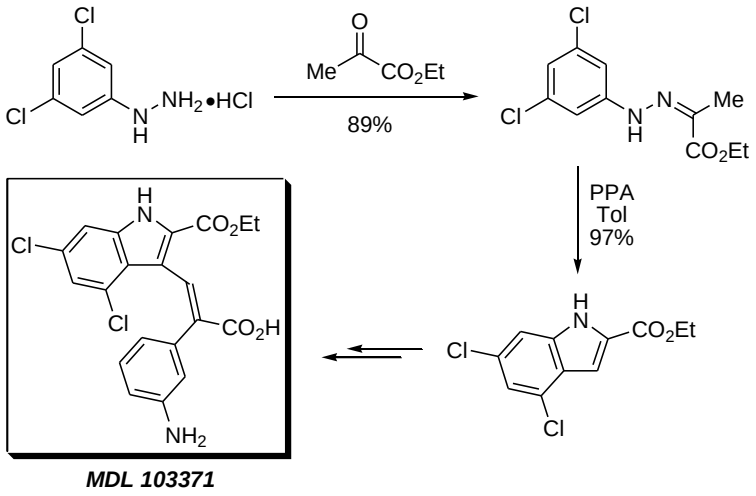
Indole moieties had been found widely among synthetic drugs,[119,120e,120j] natural products,[120] and new materials for dye[121] and fluorophore.[122] Due to the importance of the indoles in many aspects, extensive effort had been made and a variety of methods had been developed for construction of indole core.[123] Fischer indole synthesis was one of the synthetic methods widely applied to the preparation of indoles. Besides Fischer indole synthesis, there were a variety of robust alternative approaches to access indole motifs, such as reductive cyclization, heteroannulation and cyclization of 2-alkynylanilines, heck-type cyclization, Gassman indole synthesis,[124] Bartoli indole synthesis,[125,126] Bischler–Möhlau indole synthesis,[127] Nenitzescu indole synthesis,[128] Madelung indole synthesis,[129] radical cyclization,[130] C-H functionalization of *N*-aryl enamine,[131,132] amination of β-halogen styryl aniline,[133] amination of *o*-halogen styryl amine,[134] azide cyclization,[122a,135-137] and pyrrole modification,[135e,138] etc.

4.1.1 Fischer Indole Synthesis

Fischer indole synthesis[120a,120c,120d,120g,139,140] involved a [3,3]-rearrangement of the *N*-arylhydrazone, and the most common strategy to access the *N*-arylhydrazone was

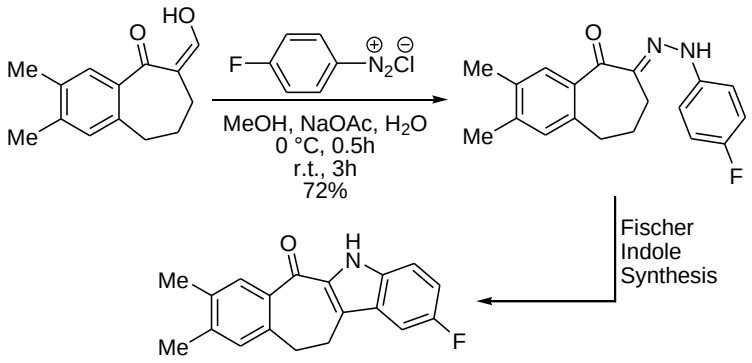
trough the condensation of ketones to the *N*-arylhydrazine. This synthetic method had been applied to natural products and synthetic drug preparation extensively. For example, Watson and coworkers had demonstrated a large scale preparation of MDL 103371, a potential treatment of stroke, using Fischer indole synthesis as the key step to afford indole core followed by further modification to deliver target compound (Scheme 1).[141]

Scheme 1. MDL 10371 Preparation via Fischer Indole Synthesis



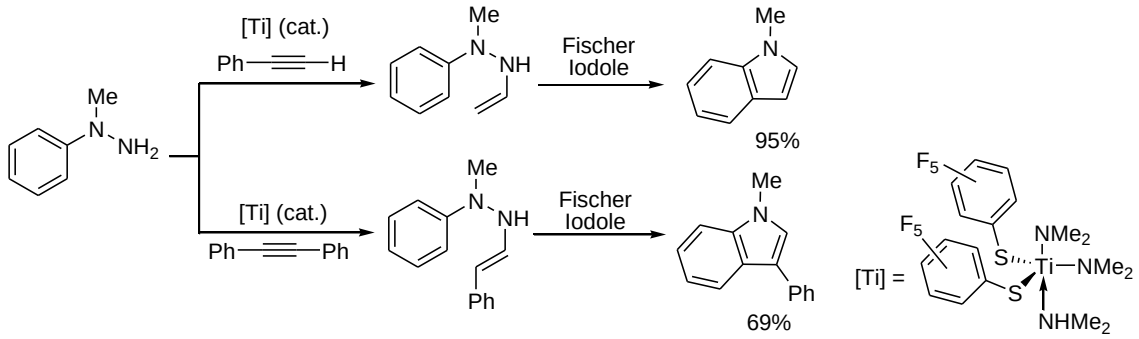
Besides using the condensation *N*-arylhydrazone, Japp-Klingemann reaction[142] was one of the common routes to afford Fischer-Indole precursor employing 1,3-dicarbonyl with benzenediazonium or arenediazonium salts. Primofiore and coworkers has shown a preparation of heterocyclic ring via Japp-Klingemann to afford *N*-arylhydrazone followed by Fischer-Indole Synthesis to give the desired product (Scheme 2).[143]

Scheme 2. Japp-Klingemann Reaction



Metal-catalyzed hydroamination of alkyne was also utilized as a pathway to access *N*-arylhydrazin using *N*-arylhydrazone with terminal or internal alkyne as starting materials. Odom and coworkers had shown the preparation of indoles via hydroamination of both terminal and internal alkynes (Scheme 3).[144]

Scheme 3. Fischer Indole Synthesis via Metal-Catalyzed Hydroamination of Alkyne

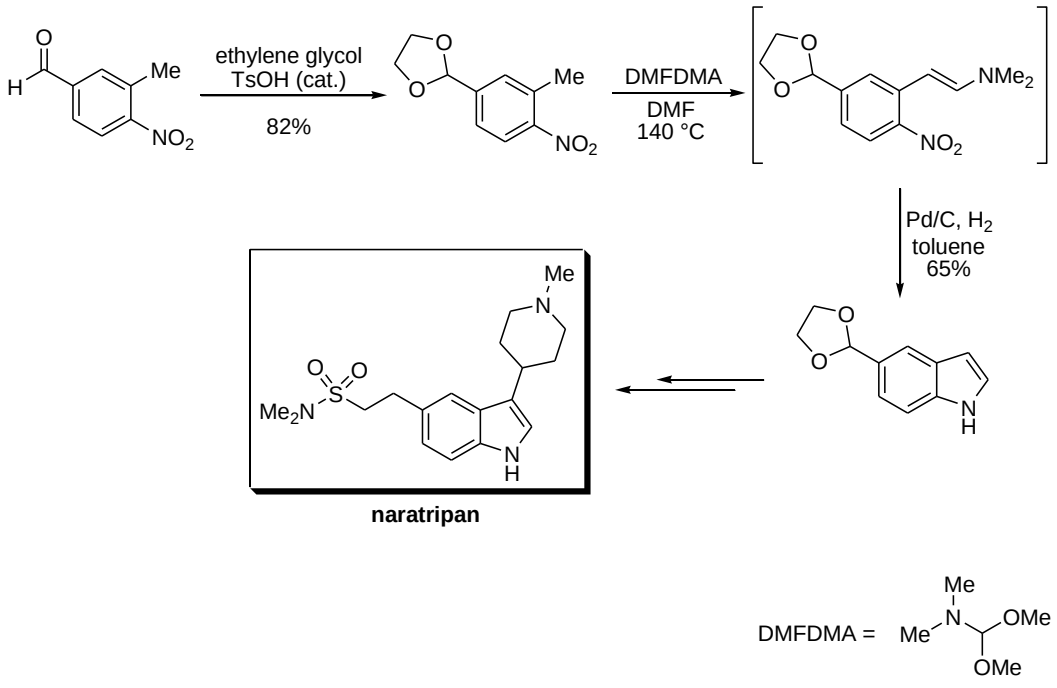


4.1.2 Reductive Cyclization

The reductive cyclization of the nitroaryl species was one of the common strategies for the preparation of indoles, and it was usually performed by suitable reductants, such as

Pd/C, Pt/C, Raney nickel with hydrazine, iron, zinc in acetic acid, $SnCl_2$, $TiCl_2$/HCl, and $TiCl_3$, etc. Leimgruber-Batcho indole synthesis[28] was widely used for the preparation of 2,3-unsubstituted indoles employing the condensation of *o*-nitrotoluene with dimethylformamide dimethyl acetal (DMFDMA) to give β-(dimethylamino)-nitrostyrene intermediate which underwent reductive cyclization to give iodole motifs. Simig and coworkers demonstrated a practical synthesis of antimigraine drug naratriptan using Leimgruber-Batcho indole synthesis as key step to construct indole core with further modification to complete the synthesis of the target compound (Scheme 4).[146]

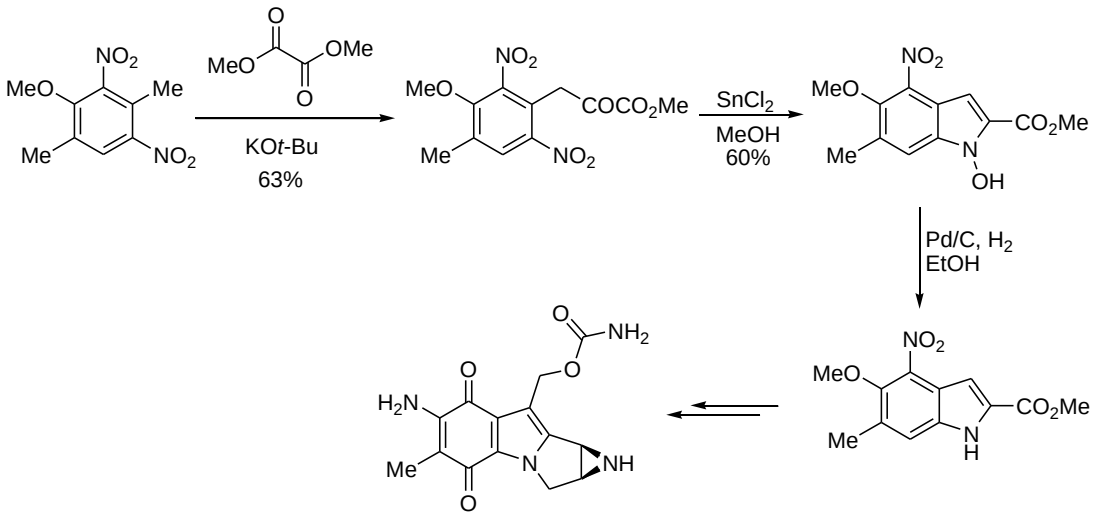
Scheme 4. Preparation of Naratripan



Another common reductive cyclization method, Reissert indole synthesis,[129g,147] was frequently used for the preparation of 2-carboxylic acid derivative indole employing

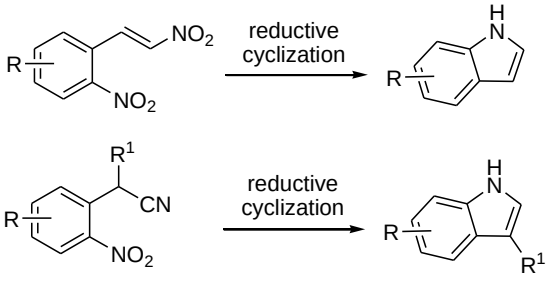
o-nitroarylpyruvate derivative as the precursor for the reductive cyclization. An example of preparation of mitomycin derivative using Reissert indole synthesis as key step was shown by Jimenez and coworkers (Scheme 5).[148]

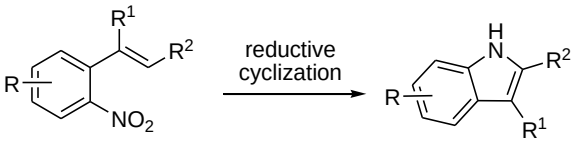
Scheme 5. Preparation of Mitomycin Derivative



Besides Leimgruber-Batcho and Reissert indole synthesis described above, reductive cyclization of dinitrostyrene,[129g] *o*-nitrophenylacetonitrile,[149] and *o*-nitrostyrene[150] were used as facile methods for building up indoles motif in synthesis toward natural products or synthetic drugs (Scheme 6).

Scheme 6. Reductive Cyclization

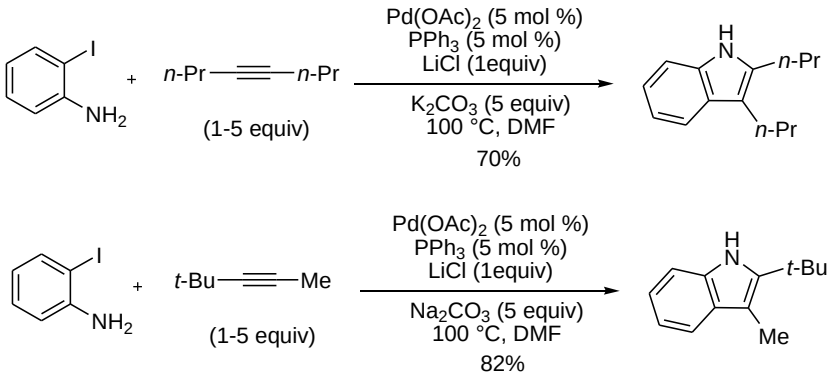




4.1.3 Heteroannulation and Cyclization of 2-Alkynylanilines

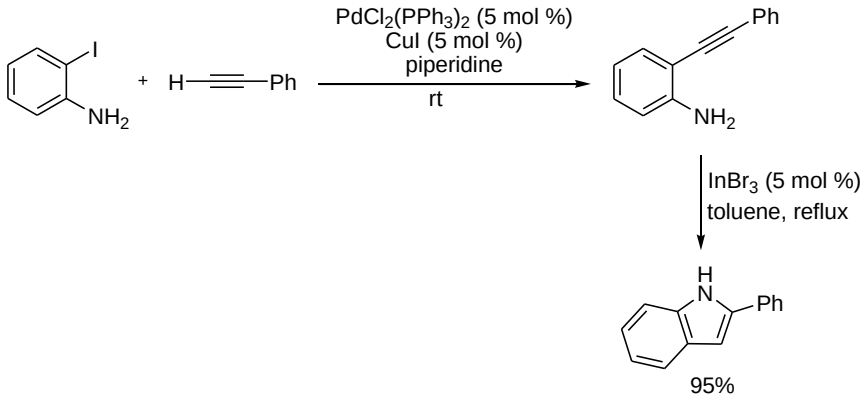
Larock indole synthesis (Larock heteroannulation)[151] was widely used method to prepare 2,3-disubstituted indole employing *o*-iodoanaline with disubstituted alkyne. In 1991, Larock and coworker reported the synthesis of indole using *o*-iodoanaline with symmetry or asymmetry disubstituted alkyne, and regioselectively formed unsymmetry indole (Scheme 7).[152]

Scheme 7. Larock Indole Synthesis



Cyclization of 2-alkynylanilines[153] was often applied to the preparation of indole as well, and 2-alkynylanilines could be preparation through cross-coupling of *o*-iodoanaline with terminal alkyne. Recently, a Lewis acid catalyzed cyclization of 2-alkynylaniline example was demonstrated by Sakai and coworkers (Scheme 8).[154]

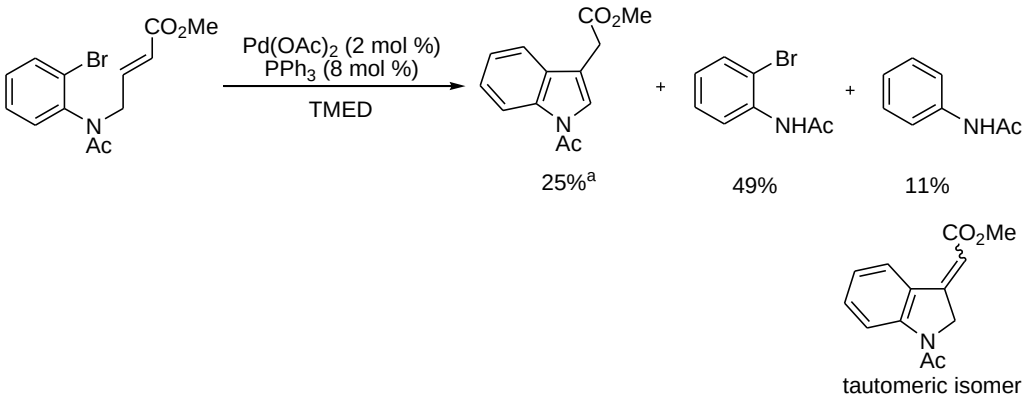
Scheme 8. Lewis-Catalyzed Cyclization of 2-Alkynylaniline



4.1.4 Heck-Type Cyclization[155]

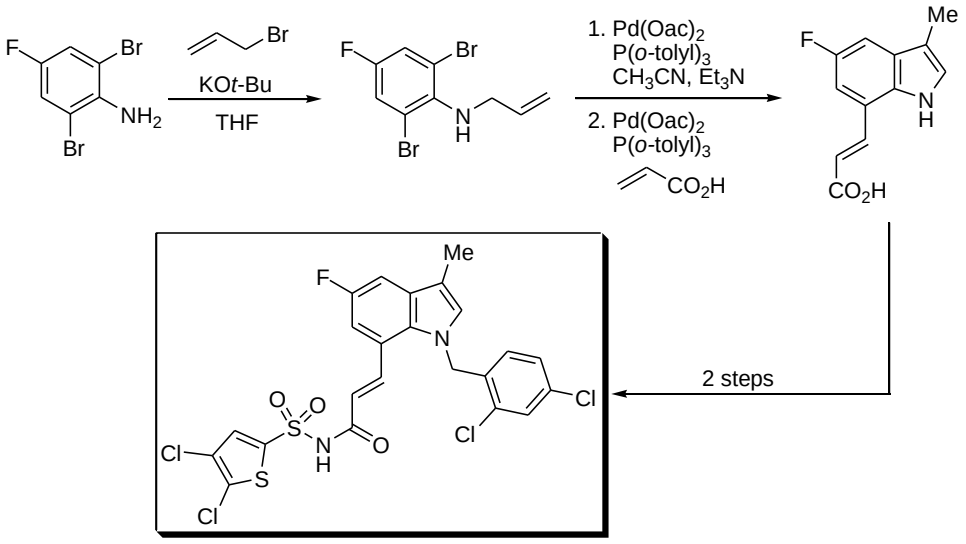
Mori and coworkers reported a palladium catalyzed intramolecular heck-type cyclization to deliver indole along with tautomeric indole, bromo-*N*-acetylaniline, and *N*-acetylaniline (Scheme 9).[156] An example of scalable synthesis of DG-041 for the treatment of peripheral artery disease (PAD) was reported by Zembower and coworkers using heck cyclization as a key to establish indole core (Scheme 10).[157]

Scheme 9. Mori's Indole Preparation via Heck Cyclization



[a] Contained a movable amount of tautomeric isomer

Scheme 10. Preparation of DG-041

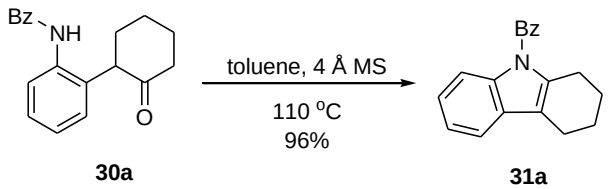


DG-041

4.2 Indole Preparation through Copper-Catalyzed Cross-Coupling and Acid-Promoted Cyclization and Dehydration

From the previous result shown in Chapter 3.6, α-(*o*-anilido)ketone **30a** was smoothly transformed into the corresponding indole **31a** in present of moleculer sieves under thermal condition in excellent yield after 24 hour (Scheme 11).

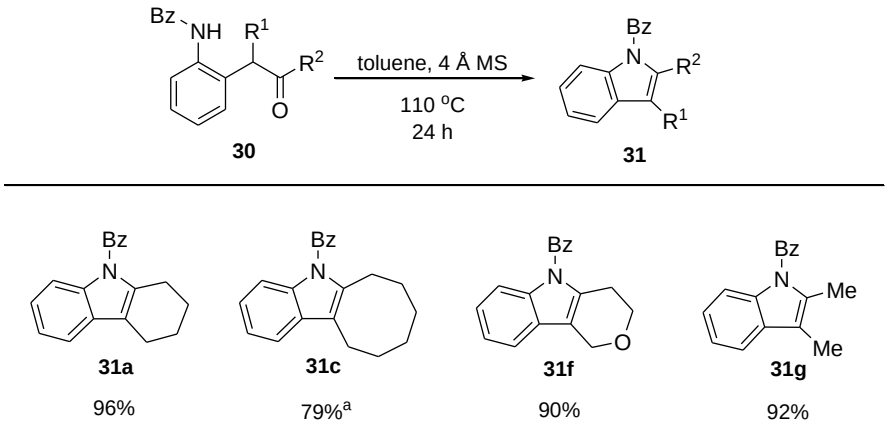
Scheme 11. Preparation of Indole through α-(*o*-Anilido)Ketone under Thermal Condition



30a **31a**

Other α-(*o*-anilido)ketones were subjected to the same thermal condition, in order to investigate their transformation to the corresponding indoles. Acyclic α-(*o*-anilido)ketone **30g** and pyranyl-α-(*o*-anilido)ketone **30f** transformed to the corresponding indoles **31g** and **31f** in good yields. However, the conversion of cyclic α-(*o*-anilido)ketone **30c** was incomplete and gave moderate yield. As the ring size increase from 6-member ring to 8-member ring, the transformation of α-(*o*-anilido)ketone to the corresponding indole became less efficient (Scheme 12).

Scheme 12. Transformation of α-(*o*-Anilido)Ketones

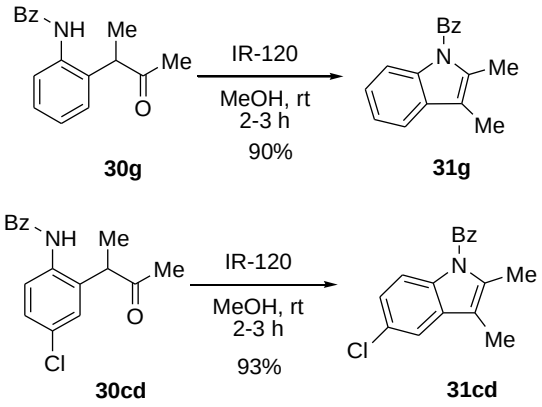


[a] 14% 3**0c** was recovered; crude yield.

In order to prove the efficiency of indole transformation, shorten the reaction, and lower the reaction temperature, mild acid-catalyzed condition were tested using Amberlite IR-120 (H^+) resin and α-(*o*-anilido)ketone **30g** and **30cd** as the precursor (Scheme 13). Under the treatment of IR-120 (H^+) resin, α-(*o*-anilido)ketone **30g** and **30cd** underwent the transformation smoothly and gave corresponding indoles **31g** and **31cg** in good

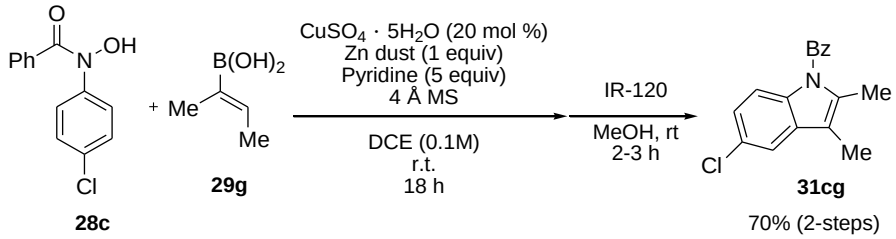
yields, shorter reaction time, and lower reaction temperature.

Scheme 13. Preparation of Indole under IR-120 Condition



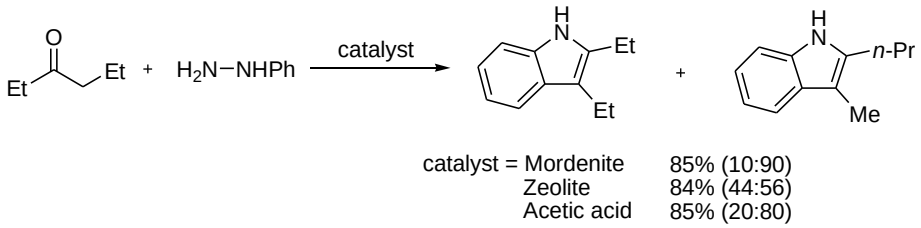
The formation of indole could also be performed using the one-pot conversion from the copper-mediated cross coupling of hydroxamic acids and boronic acid followed by acid-mediated cyclization and dehydration. As shown below, indole **31cg** was prepared in moderate yield using this one-pot method from the corresponding hydroxamic acid **28c** and boronic acid **29g** (Scheme 14). By employing the one-pot method, it allowed us to obtain **31cg** in slightly better yield than the stepwise procedure without purification of intermediate **30cg**.

Scheme 14. Preparation of Indole via One-flask Condition



A variety of indoles were synthesized in moderate to excellent yields using the one-pot method shown in Scheme 14 (Table 1). The transformations were tolerated for cyclic indoles formations (Table 1, entries 1-2) as well as substituted cyclic indole formations (Table 1, entries 3-4). Pyranyl indole was obtained in poor yield due to the inefficiency of pyranyl-α-(*o*-anilido)ketone imtermediate formation (Table 1, entry 5). The transformations were tolerated for acyclic indole formations (Table 1, entries 6-8). Notably, the formation of 1-H analog of **31h** was not favored through the regular Fischer-indole synthesis. As the examples shown in Scheme 15, the transformation were favored for the formation of the **31h-r** analog but disfavored for the **31h** analog.[158]

Scheme 15. Regioselectivity in Fischer-Indole Synthesis



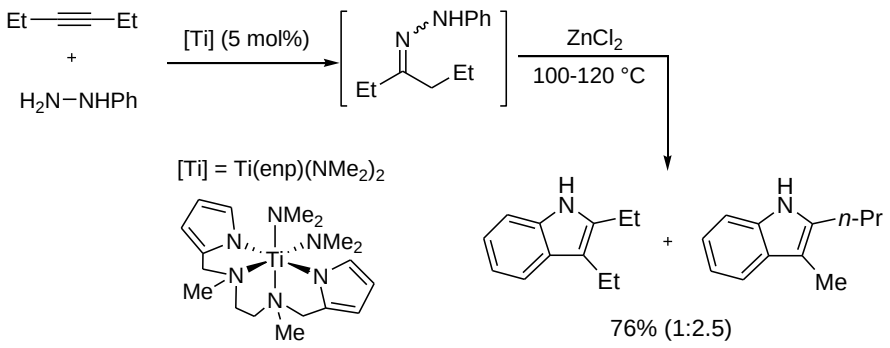
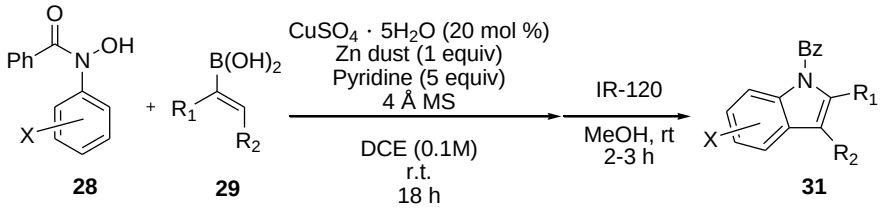
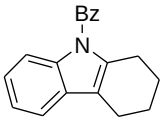
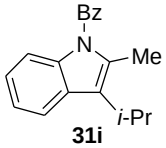
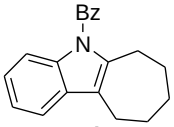
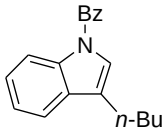
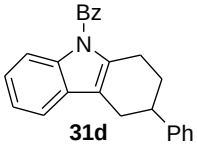
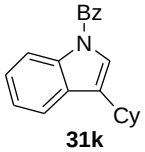
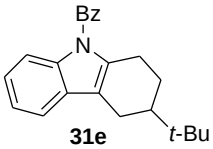
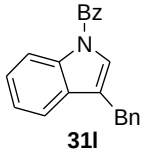
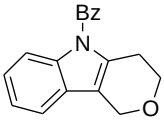
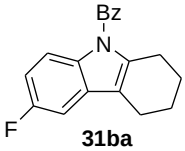
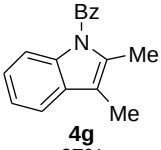
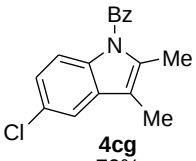
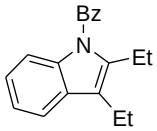
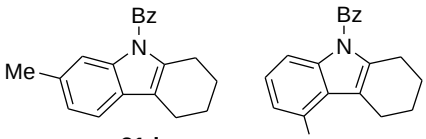


Table 1. Indole Formation via One-Pot Procedure



Entry	Product	Entry	Product
1	 **31a** 82%	8	 **31i** 40%[a]
2	 **31b** 55%	9	 **31j** 73%
3	 **31d** 72%	10	 **31k** 63%
4	 **31e** 71%	11	 **31l** 83%
5	 **31f** 20%	12	 **31ba** 55%
6	 **4g** 67%	13	 **4cg** 70%
7	 **31h** 51%[b]	14	 **31da** **31da-r** 60% (1:1)[c]

[a] Reaction mixture was stirred for 6 h for resin-assisted cyclization and dehydration.

[b] Regiosiomeric boronic acid was used. [c] Ratio was determined by NMR.

3-Substituted indoles were prepared in good yields employing the one-pot procedure (Table 1, entries 9-11). The formation of **31j** and **31k** 1H-analogs were not reported via Fischer indole synthesis in the precedent literature, and preparation were usually through the modification of free *N*-H indole[159] and Larock reaction.[160] Electron-poor aryl were also tolerated the transformation and gave the corresponding indoles in moderate yields (Table 1, entries 12-13). *Meta*-substituted aryl was tolerated this one-pot transformation and gave regioisomeric indole mixture in 1:1 ratio (Table 1, entry 14). Notably, the preparation of deprotected analog of **31da-r** was not reported through Fischer-Indole formation.[161]

4.3 Summary

We have demonstrated the formation of indoles from the corresponding hydroxyamic acids and boronic acids employing one-pot copper-catalyzed cross-coupling followed by mild acid assisted cyclization and dehydration.

This transformation provides an alternative pathway of indole preparation instead of the conventional route, and it also offers a different method for certain indole such as **31j**, **31k**, and **31da-r** which is hard to obtain via Fischer-Indole synthesis.

4.4 Experimental Section

^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using 500 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the scale, multiplicity (br = broad, s = singlet, d = doublet, t =triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. High resolution mass spectra were acquired on an LTQ FT spectrometer, and were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on 60Å (40 – 60 μm) mesh silica gel (SiO_2). Medium pressure liquid chromatography was performed to force flow the indicated solvent system down columns packed with 60Å (40 – 60 μm) mesh silica gel (SiO_2). Unless otherwise noted, all reagents were obtained from commercial sources and, where appropriate, purified prior to use. THF and CH_2Cl_2 were dried by filtration through alumina according to the procedure of Grubbs.[35] TMEDA was distilled over CaH_2 and stored under N_2 prior to use. IR-120(H^+) resin was washed with MeOH and dried under vacuum prior to use.

4.4.1 Preparation of Indoles

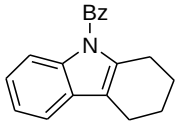
Indoles **31a**, **31b**, **31d-31l**, **31ba**, **31cg**, and **31da/31da-r** were prepared using one-pot procedure employing copper-catalyzed crossing coupling of hydroxamic acids and boronic acids and acid-mediated cyclization and dehydration. Indoles **31a**, **31c**, **31f**, **31g**, **31cg**, **31da**, **31da-r** were prepared using the corresponding α-(*o*-anilido)ketones **30** under thermal or acid-mediated condition.

4.4.1.1 One-Pot Reaction of Copper-Catalyzed Cross-Coupling and Acid-Mediated Cyclization

Indoles **31a**, **31b**, **31d-31l**, **31ba**, **31cg**, and **31da/31da-r** were prepared using one-pot procedure according to general procedure **A**.

General procedure A: A scintillation vial was charged with *N*-benzoyl-*N*-aryl-hydroxylamine **28** (1 equiv), vinyl boronic acid **29** (2-3 equiv), $CuSO_4 \cdot 5H_2O$ (20 mol %), zinc dust (1 equiv), and 4Å MS (0.050 g per 0.1 mmol **28**). These solids were then diluted with 1,2-dichloroethane to form a 0.1 M solution of *N*-benzoyl-*N*-aryl-hydroxylamine. Pyridine (5 equiv) was added to the resulting slurry via syringe. The scintillation vial was then capped with a septum pierced with a ventilation needle and the reaction mixture was stirred at 25 ℃ for 18 h. Crude reaction mixture was filtered and concentrated to give crude α-Arylketone. The crude α-arylketone was diluted

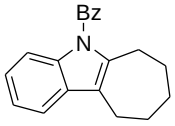
with MeOH to form a 0.05 M solution in a scintillation vial. IR-120 (H^+) (900 mg per 0.1 mmol) was added to the solution. The mixture was allowed to stir at 25 ℃ for 2.5 h. The crude reaction mixture was filtered and washed with EA. The filtrate was concentrated and purified by medium pressure chromatography (5:95; ethyl acetate: hexanes) to give indole **31**.



31a

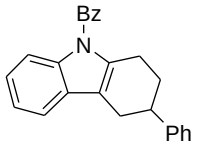
Indole **31a:**[134a] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 1-cyclohexenyl boronic acid **29a** (0.091 g, 0.72 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 µl, 1.50 mmol), and IR-120 (H^+) resin (2.70 g). Chromatography (10:90; ethyl acetate: hexanes) afforded **31a** as an amorphous solid (0.068 g, 82%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.08 (t, *J* = 8.0 Hz, 1H), 2.72-2.69 (m, 2H), 2.65-2.62 (m, 2H), 1.89-1.79 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4, 136.6, 136.1, 136.0, 132.3, 130.1, 129.4, 128.7, 128.6, 123.2, 122.6, 117.8, 114.7, 25.6, 23.6, 22.3, 21.1; IR (thin film) 3054, 2931, 2850, 1677, 1604, 1454, 1353, 1307, 1214, 1153 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{19}H_{18}NO$ $(M+H)^+$

276.1388, found 276.1397.



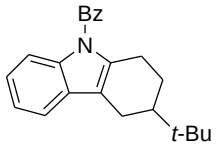
31b

Indole **31b:**[136a] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 1-cycloheptenyl boronic acid **29b** (0.110 g, 0.79 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120 (H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31b** as an oil (0.048 g, 55%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.51-7.47 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 8.0 Hz, 1H), 2.84-2.82 (m, 2H), 2.76-2.74 (m, 2H), 1.88-1.80 (m, 4H), 1.72-1.68 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.8, 139.6, 136.2, 136.1, 132.9, 130.2, 129.9, 128.7, 122.9, 122.3, 122.0, 117.7, 113.9, 31.1, 28.7, 27.1, 26.9, 23.9; IR (thin film) 3056, 2922, 2849, 1676, 1599, 1473, 1350, 1317, 1240, 1176 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{20}NO$ $(M+H)^+$ 290.1545, found 290.1538.



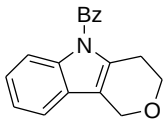
31d

Indole **31d**:[42] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 4-phenyl-1-cyclohexenyl boronic acid **29d** (0.154 g, 0.76 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120 (H^+) resin (3.00 g). Chromatography (10:90; ethyl acetate: hexanes) afforded **31d** as a white foam (0.076 g, 72%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.74 (d, *J* = 7.0 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.40-7.34 (m, 4H), 7.28 (t, *J* = 7.0 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 3.15-3.08 (m, 2H), 2.90-2.76 (m, 3H), 2.19-2.16 (m, 1H), 2.05-1.97 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4, 146.1, 136.9, 136.0, 135.8, 132.5, 129.8, 129.4, 128.7, 128.6, 127.0, 126.5, 123.4, 122.8, 117.8, 117.9, 114.8, 40.1, 30.8, 29.3, 25.8; HRMS (ESI) *m/z* calcd. for $C_{25}H_{22}NO$ $(M+H)^+$ 352.1701, found 352.1704.



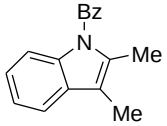
31e

Indole **4e:**[163] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 4-*tert*-butyl-1-cyclohexenyl boronic acid **29e** (0.144 g, 0.79 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120(H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31e** as an amorphous solid (0.071 g, 71%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.69 (d, *J* = 7.0 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 2.83-2.79 (m, 1H), 2.66-2.57 (m, 2H), 2.42-2.37 (m, 1H), 2.03-2.00 (m, 1H), 1.59-1.54 (m, 1H), 1.40-1.31 (m, 1H), 1.00 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.3, 136.9, 136.1, 136.0, 132.3, 130.2, 129.3, 128.6, 123.2, 122.7, 118.4, 117.7, 114.8, 44.4, 32.5, 27.4, 26.6, 25.2, 22.5; IR (thin film) 3051, 2958, 2865, 1678, 1615, 1455, 1353, 1334, 1304, 1243, 1166 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{23}H_{26}NO$ $(M+H)^+$ 332.2014, found 332.2009.



31f

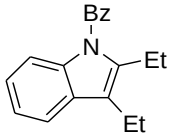
Indole **31f:**[155b] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 3,6-dihydro-2H-pyran-4-boronic acid **29f** (0.100 g, 0.78 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120 (H^+) resin (2.70 g). Chromatography (1:9; ethyl acetate: hexanes) afforded **31f** as an amorphous solid (0.017 g, 20%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.70 (d, *J* = 7.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 8.5 Hz, 1H), 4.89 (s, 2H), 3.81 (t, *J* = 5.5 Hz, 2H), 2.70 (t, *J* = 5.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.0, 136.5, 135.6, 132.8, 132.6, 129.3, 128.9, 127.2, 123.8, 123.1, 117.7, 116.2, 115.2, 64.8, 63.6, 26.7; IR (thin film) 3058, 2962, 2923, 2854, 1712, 1682, 1608, 1450, 1353, 1315 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{18}H_{16}NO_2$ $(M+H)^+$ 278.1181, found 278.1170.



31g

Indole **31g:**[164] General procedure **A** was executed using the following reagents:

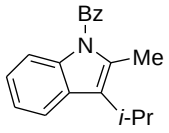
N-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **29g** (0.089 g, 0.89 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120(H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31g** as an oil (0.050 g, 67%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.52-7.46 (m, 3H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.07-7.05 (m, 2H), 2.34 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7, 136.4, 136.0, 133.2, 132.7, 130.9, 129.7, 128.7, 122.9, 122.4, 118.1, 115.1, 114.2, 13.1, 8.7; IR (thin film) 3058, 2973, 2923, 2865, 1677, 1604, 1457, 1342, 1315, 1218 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{17}H_{16}NO$ $(M+H)^+$ 250.1232, found 250.1235.



4h

Indole **4h:**[158] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), *Z*-3-hexen-3-yl boronic acid **29h** (0.10 g, 0.78 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120 (H^+) resin (2.70 g). The mixture was allowed to stir at 25 ℃ for 5 hour. Chromatography (10:90; ethyl acetate: hexanes) afforded **31h** as an oil (0.042 g, 51%) in 4:1 ratio. ^{1}H NMR of **4h** (500

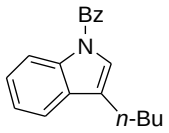
MHz; $CDCl_3$): δ 7.79-7.75 (m, 2H), 7.67-7.63 (m, 1H), 7.54-7.48 (m, 3H), 7.20-7.16 (m, 1H), 7.02-7.97 (m, 1H), 6.75 (q, *J* = 7.5 Hz, 1H), 2.98 (q, *J* = 7.5 Hz, 2H), 2.78 (q, *J* = 7.5 Hz, 2H), 1.31 (t, *J* = 7.5 Hz, 3H), 1.22 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR of **4h** (125 MHz, $CDCl_3$): δ 169.8, 139.4, 136.8, 135.8, 132.9, 129.9, 129.8, 128.8, 122.5, 122.0, 120.7, 118.4, 114.1, 19.1, 17.3, 15.1, 15.0; IR (thin film) 3052, 2966, 2932, 2872, 1680, 1599, 1455, 1353, 1328, 1207 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}NO$ $(M+H)^+$ 278.1545, found 278.1537.



31i

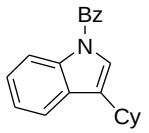
Indole **31i:**[165] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 4-methyl-2-pentynyl boronic acid **29i** (0.100 g, 0.78 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120(H^+) resin (2.70 g). The mixture was allowed to stir at 25 ºC for 6 hour. Chromatography (5:95; ethyl acetate: hexanes) afforded **31i** as an oil (0.033 g, 40%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.74 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 7.04-7.00 (m, 2H), 3.26-3.20 (m, 1H), 2.35 (s, 3H), 1.45 (d, *J* = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.9, 136.9, 136.0, 132.8, 131.7,

129.9, 128.8, 128.7, 124.8, 122.4, 121.9, 119.7, 114.3, 25.8, 22.1, 13.2; IR (thin film) 3050, 2964, 2929, 2871, 1680, 1599, 1456, 1342, 1313, 1264 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{20}NO$ $(M+H)^+$ 290.1545, found 290.1536.



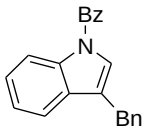
31j

Indole **31j**:[159a,160] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), 1-hexenyl boronic acid **29j** (0.085 g, 0.67 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120 (H^+) resin (2.70 g). Chromatography (10:90; ethyl acetate: hexanes) afforded **31j** as an amorphous solid (0.061 g, 73%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.41 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 2H), 7.63-7.59 (m, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.08 (s, 1H), 2.69 (t, *J* = 7.5 Hz, 2H), 1.71-1.65 (m, 2H), 1.47-1.39 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.4, 136.5, 135.0, 131.6, 131.3, 129.1, 128.6, 124.9, 123.8, 123.6, 123.0, 119.1, 116.6, 31.3, 24.6, 22.6, 13.9; IR (thin film) 3053, 2956, 2929, 2858, 1679, 1601, 1451, 1367, 1331, 1214 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}NO$ $(M+H)^+$ 278.1545, found 278.1544.



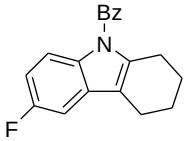
31k

Indole **31k**:[159b,160] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), (*E*)-2-cyclohexylethenylboronic acid **29k** (0.103 g, 0.669 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 μl, 1.50 mmol), and IR-120(H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31k** as an oil (0.057 g, 63%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.37 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 2H), 7.64-7.59 (m, 2H), 7.54 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.03 (s, 1H), 2.79-2.74 (m, 1H), 2.07 (d, *J* = 12.5 Hz, 2H), 1.84 (d, *J* = 12.5 Hz, 2H), 1.79-1.76 (m, 1H), 1.50-1.35 (m, 4H), 1.30-1.25 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.5, 136.6, 135.1, 131.6, 130.6, 129.1, 128.7, 128.6, 124.9, 123.5, 122.3, 119.4, 116.7, 35.1, 33.2, 26.7, 26.3; IR (thin film) 3053, 2923, 2850, 1679, 1601, 1450, 1368, 1342, 1211, 1176 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{21}H_{22}NO$ $(M+H)^+$ 304.1701, found 304.1712.



31l

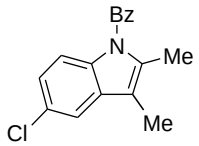
Indole **31l**:[163] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-phenylhydroxylamine **28** (0.064 g; 0.30 mmol), (*E*)-2-phenylethenylboronic acid **29l** (0.109 g, 0.737 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 µl, 1.50 mmol), and IR-120(H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31l** as an amorphous solid (0.077 g, 83%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 8.38 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.31-7.26 (m, 5H), 7.23-7.20 (m, 1H), 7.12 (s, 1H), 4.05 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.4, 139.4, 136.7, 134.8, 131.8, 130.9, 129.1, 128.6, 128.5, 128.4, 126.4, 125.2, 125.1, 123.8, 121.4, 119.5, 116.6, 31.4; IR (thin film) 3027, 2922, 1729, 1681, 1450, 1357, 1263, 1217, 1150 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{22}H_{18}NO$ $(M+H)^+$ 312.1388, found 312.1375.



31ba

Indole **31ba:**[166] General procedure **A** was executed using the following reagents:

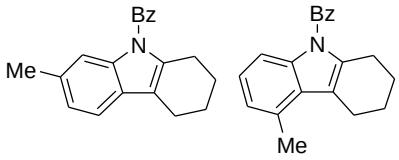
N-benzoyl-*N*-(*p*-F-phenyl)-hydroxylamine **28b** (0.069 g; 0.30 mmol), 1-cyclohexenyl boronic acid **29a** (0.102 g, 0.81 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 µl, 1.50 mmol), and IR-120(H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31ba** as an oil (0.049 g, 55%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.43 (dd, J = 9.0 Hz, J = 4.5 Hz, 1H), 7.19 (d, J = 8.5 Hz, J = 2.5 Hz, 1H), 7.08 (td, J = 9.0 Hz, J = 2.5 Hz, 1H), 2.65-2.63 (m, 2H), 2.58-2.56 (m, 2H), 1.86-1.82 (m, 2H), 1.80-1.77 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.1, 159.4 ($J_{C\text{-}F}$ = 239 Hz), 137.8, 135.9, 132.9, 132.4, 131.2 ($J_{C\text{-}F}$ = 10 Hz), 129.3, 128.7, 117.6 ($J_{C\text{-}F}$ = 3 Hz), 115.6 ($J_{C\text{-}F}$ = 16 Hz), 110.6 ($J_{C\text{-}F}$ = 25 Hz), 103.5 ($J_{C\text{-}F}$ = 24 Hz), 25.8, 23.4, 22.1, 21.0; IR (thin film) 3063, 2953, 2858, 1679, 1600, 1462, 1447, 1358, 1212, 1141 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{19}H_{17}NOF$ $(M+H)^+$ 294.1294, found 294.1285.



31cg

Indole **41cg:** General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-(*p*-chlorophenyl)-hydroxylamine **28c** (0.074 g; 0.30 mmol), *Z*-2-buten-2-yl boronic acid **29g** (0.076 g, 0.76 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust

(0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 µl, 1.50 mmol), and IR-120(H^+) resin (3.00 g). Chromatography (10:90; ethyl acetate: hexanes) afforded **31cg** as an amorphous solid (0.059 g, 70%). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.69 (dd, *J* = 8.0 Hz, *J* = 1.0 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 2.0 Hz, 1H), 6.98 (dd, *J* = 8.5 Hz, *J* = 2.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 2.31 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.5, 135.6, 134.7, 134.6, 132.9, 132.2, 129.7, 128.8, 128.1, 122.9, 117.8, 115.1, 114.5, 13.2, 8.6; IR (thin film) 3066, 2977, 2923, 2857, 1681, 1596, 1454, 1346, 1311, 1265 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{17}H_{15}NOCl$ $(M+H)^+$ 284.0842, found 284.0832.



31da/31da-r (1:1)

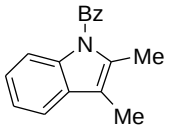
Indole **31da/31da-r:**[161] General procedure **A** was executed using the following reagents: *N*-benzoyl-*N*-(*m*-Me-phenyl)-hydroxylamine **28d** (0.068 g; 0.30 mmol), 1-cyclohexenyl boronic acid **29a** (0.088 g, 0.70 mmol), $CuSO_4 \cdot 5H_2O$ (0.014 g, 0.058 mmol), zinc dust (0.019 g, 0.29 mmol), 4Å MS (0.150 g), pyridine (120 µl, 1.50 mmol), and IR-120 (H^+) resin (2.70 g). Chromatography (5:95; ethyl acetate: hexanes) afforded **31da/31da-r** as an oil (0.052 g, 60%) in 1:1 ratio mixture; ^{1}H NMR of **31da** (500 MHz; $CDCl_3$): δ 7.68 (d, *J*

= 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 2.67-2.66 (m, 2H), 2.52-2.51 (m, 2H), 2.33 (s, 3H), 1.84-1.82 (m, 2H), 1.77-1.75 (m, 2H); ^{13}C NMR of **31da** (125 MHz, $CDCl_3$): δ 169.4, 137.0, 136.3, 135.1, 133.1, 132.2, 129.3, 128.5, 127.9, 124.0, 117.8, 117.3, 115.2, 25.8, 23.6, 22.3, 21.9, 21.2; ^{1}H NMR of **31da-r** (500 MHz; $CDCl_3$): δ 7.69 (d, *J* = 7.0 Hz, 2H), 7.60 (t, *J* = 7.0 Hz, 1H), 7.48 (t, *J* = 7.0 Hz, 2H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.95-6.90 (m, 2H), 3.00-2.99 (m, 2H), 2.65 (s, 3H), 2.59-2.58 (m, 2H),1.85-1.84 (m, 2H), 1.76-1.75 (m, 2H); ^{13}C NMR of **31da-r** (125 MHz, $CDCl_3$): δ 169.4, 136.8, 136.1, 135.5, 132.4, 130.3, 129.6, 128.6, 128.5, 124.3, 122.9, 118.2, 112.4, 25.8, 24.3, 23.0, 22.9, 20.0; IR (thin film) 3055, 3029, 2934, 2858, 1677, 1601, 1490, 1359, 1306, 1264 cm^{-1}; HRMS (ESI) *m/z* calcd. for $C_{20}H_{20}NO$ $(M+H)^+$ 290.1545, found 290.1536.

4.4.1.2 Indole Formation via α-(*o*-Anilido)Ketone under Thermal or Acid-Mediated Condition

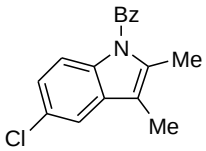
Indoles **31g**, **31cg** were prepared according to general procedure **B** using the corresponding α-(*o*-anilido)ketones. Indoles **31a**, **31c**, **31f**, **31g**, **31da**, and **31da-r** were prepared according to general procedure **C** using the corresponding α-(*o*-anilido)ketones. The preparation and characterizations of the corresponding α-(*o*-anilido)ketones **30a**, **30c**, **30f**, **30g**, **30cg**, **30da** and **30da-c** were given in Chapter 3.8.1.

General procedure B: α-arylketone **30** was diluted with MeOH to form a 0.05 M solution in a scintillation vial. IR-120 (H^+) (900 mg per 0.1 mmol) was added to the solution. The mixture was allowed to stir at 25 ℃ for 2.5 h. The crude reaction mixture was filtered and washed with EA. The filtrate was concentrated and purified by medium pressure chromatography (5:95; ethyl acetate: hexanes) to give indole **31**.



31g

α-Arylketone **30g** (0.116 g, 0.434 mmol) was diluted to a 0.05 M solution in MeOH. IR-120 resin (3.9 g) was added to the solution. The mixture was followed to stir at 25 ℃ for 2 h. The crude reaction mixture was purified by medium pressure chromatography afforded **31 g** (0.097 g, 90%).

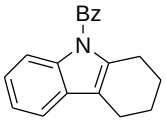


31cg

α-Arylketone **30cg** (0.050 g, 0.17 mmol) was diluted to a 0.05 M solution in MeOH. IR-120 resin (1.5 g) was added to the solution. The mixture was followed to stir at 25 ℃ for 2 h. The crude reaction mixture was purified by medium pressure chromatography

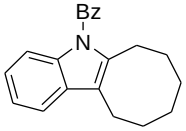
afforded **31cg** (0.044 g, 93%).

General procedure C: α-arylketone **30** was diluted with toluene to form a 0.1 M solution in present of 4Å MS. The mixture was allowed to stir at 110 ℃ for 24 h. The crude reaction mixture was filtered, concentrated and purified by medium pressure chromatography (5:95; ethyl acetate: hexanes) to give indole **31**.



31a

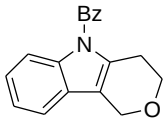
α-Arylketone **30a** (0.050 g, 0.17 mmol) was diluted to a 0.1 M solution in toluene. 4Å MS (0.050 g) was added to the solution. The mixture was heated at 110 ℃ for 24 h. The crude reaction mixture was purified by medium pressure chromatography afforded **31a** (0.045 g, 96%).



31c[166]

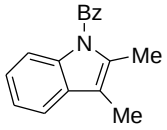
α-Arylketone **30c** (0.042 g, 0.13 mmol) was diluted to a 0.1 M solution in toluene. 4Å MS (0.042 g) was added to the solution. The mixture was heated at 110 ℃ for 24 h. The crude

reaction mixture was concentrated to give indole **31c** (0.032 g, 79%) and **30c** (0.006 g, 14%). ^{1}H NMR of **4c** (500 MHz; $CDCl_3$): δ 7.72 (d, *J* = 7.5 Hz, 2H), 7.63(t, *J* = 7.5 Hz, 1H), 7.50-7.48 (m, 3H), 7.20-7.15 (m, 2H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 3.02-2.99 (m, 2H), 2.87-2.84 (m, 2H), 1.76-1.75 (m, 4H), 1.53-1.52 (m, 2H), 1.39-1.38 (m, 2H).



31f[155b]

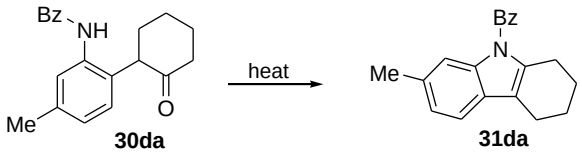
α-Arylketone **30f** (0.059 g, 0.20 mmol) was diluted to a 0.1 M solution in toluene. 4Å MS (0.059 g) was added to the solution. The mixture was heated at 110 °C for 24 h. The crude reaction mixture was purified by medium pressure chromatography afforded **31f** (0.050 g, 90%).



31g

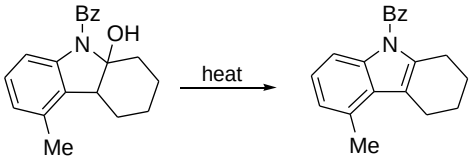
α-Arylketone **30g** (0.132 g, 0.494 mmol) was diluted to a 0.1 M solution in toluene. 4Å MS (0.132 g) was added to the solution. The mixture was heated at 110 °C for 24 h. The crude reaction mixture was purified by medium pressure chromatography afforded **31g**

(0.113 g, 92%).



30da **31da**

α-Arylketone **30da** (0.037 g, 0.12 mmol) was diluted to a 0.1 M solution in toluene. 4Å MS (0.037 g) was added to the solution. The mixture was heated at 110 °C for 24 h. The crude reaction mixture was purified by medium pressure chromatography afforded **31da**.[161a]



30da-c **31da-r**

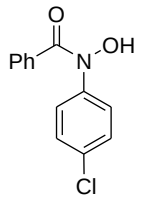
α-Arylketone **30da-c** (0.032 g, 0.11 mmol) was diluted to a 0.1 M solution in toluene. 4Å MS (0.032 g) was added to the solution. The mixture was heated at 110 °C for 24 h. The crude reaction mixture was purified by medium pressure chromatography afforded **31da-r**.[161b]

4.4.2 Preparation of Hydroxamic Acids

Hydroxamic acid **28c** was prepared using general procedure **D**. Preparation of hydroxamic acids **28b** and **28d** were described in Chapter 3.7.2. Characterizations of

28b-28d were given in Chapter 3.7.2.

General procedure D: Nitrobenzene (1 equiv) was dissolved in THF (10 mL/g) and cooled to 0 ℃. Rh/C (5 mol %) was then added to form a slurry. Hydrazine monohydrate (1.2 equiv) was added dropwise to the slurry and then the reaction mixture was allowed to warm up to 25 ℃ and stir for 2.5 h. The reaction mixture was then filtered through celite and washed with THF. The filtrate was concentrated under vacuum to give the crude product, hydroxylamine, as a solid. The crude sample of hydroxylamine was dissolved in DCM to form a 0.5 M solution. Pentafluorobenzoyl chloride (1.6 equiv) was added to the hydroxylamine solution and the mixture was allowed to stir for 1 h. The crude reaction mixture concentrated under vacuum and then purified by medium pressure chromatography.



28c

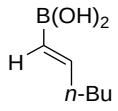
28c was synthesized according to general procedure **D** using the following reagents: nitrobenzene (2.28 g, 14.5 mmol), Rh/C (0.020 g), hydrazine monohydrate (0.84 ml, 17 mmol), and benzoyl chloride (2.0 ml, 14 mmol). After purification by medium pressure chromatography, compound **28c** was isolated as a solid (1.66 g, 46%).

4.4.3 Preparation of Boronic Acids

Boronic acids **29g**, **29h**, and **29j** were prepared via alkyne hydroboration. Boronic acids **29a-29f** and **29i** were prepared via hydrolysis of the corresponding pinacol esters. Boronic acids **29k** and **29l** were purchase from Sigma-Aldrich. The preparation of pinacol esters precursors of **29a-29e** were described in Chapter 3.8.3.3 via Shapiro reaction. The preparatiob of pinacol esters precursors of **29i** was described in Chapter 3.8.3.4.

4.4.3.1 Preparation of Boronic Acids via Alkyne Hydroboration

29g, **29h**, and **29j** were prepared according to general procedure **E** described in Chapter 3. Preparation and characterizations of boronic acids **29g** and **29h** were given in Chapter 2.5.4.1 and 3.8.3.1.



29j

29j was synthesized using the following reagents: 1-hexyne (0.820 g, 10.0 mmol) and a 1M solution of $HBBr_2 \cdot SMe_2$ in CH_2Cl_2 (11.0 mL, 11.0 mmol). Hydrolysis and workup gave **29j** as an off-white solid (0.948 g, 74 %). ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.02-6.96 (m, 1H), 5.56 (d, *J* = 12.5Hz, 1H), 2.27-2.22 (m, 2H), 1.50-1.43 (m, 2H), 1.41-1.33 (m,

2H), 0.94 (t, J = 7.0 Hz, 3H), the O–*H* resonances were too broad to be observed; ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.9, 35.4, 30.4, 22.3, 14.0, the *C*–B resonance was too broad to be observed.

4.4.3.2 Preparation of Boronic Acids from Boronic Acid Pinacol Esters

Boronic acids **29a-29f** and **29i** were prepared via hydrolysis of the corresponding pinacol esters. Preparation and characterizations of boronic acids **29a-29f** and **29i** were described in Chapter 2.5.4.2 and 3.8.3.2.

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EDUCATION

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TEACHING EXPERIENCE

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PUBLICATIONS

1. ‘‘Preparation of Indoles using Vinyl Boronic Acids with *N*-Aryl Hydroxamic Acids via Oxyarylation and Acid-Promoted Cyclization/Dehydration.” Wang, H. -Y.; Anderson, L. L. *In preparation*.

2. ‘‘Preparation of α-Amino Aldehydes by [1,3] Rearrangement of *O*-alkenyl Oximes.” Kontokosta, D.; Mueller, D. S.; Wang, H. -Y.; Anderson, L. L. *Org. Lett. ASAP*.
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REPRESENTIVE PRESENTATIONS

1. "Access to Interrupted Fischer-Indole Intermediates via Oxyarylation of Alkenyl Boronic Acids." Wang, H.-Y.;

Anderson, L. L. 5th Annual Chicago Organic Symposium, Notre Dame, IN, Jul. 2013 (poster)

2. "Access to Interrupted Fischer-Indole Intermediates via Oxyarylation of Alkenyl Boronic Acids." Wang, H.-Y.; Anderson, L. L. 43rd National Organic Chemistry Symposium, Seattle, WA, Jun. 2013 (poster)
3. "Regioselective Pyrrole Formation via [3,3] and [1,3] Sigmatropic Rearrangement of *O*-Vinyl Oxime Ethers." Wang, H.-Y.; Mueller, D. S.; Sachwani, R. M.; Kapadia, R.; Londino, H. N.; Anderson, L. L. 3rd Annual Chicago Organic Symposium, Chicago, IL, Feb. 2012. (poster)
4. "Synthesis of *O*-vinyl oxime ethers by iridium-catalyzed isomerization of *O*-allyl oxime ethers: Reactivity, Control of Stereochemistry, and Application to the Synthesis of Pyrroles." Wang, H.-Y.; Anderson, L. L. 240th America Chemical Society National Meeting, Boston, MA, Aug. 22-26, 2010. (poster)
5. "Carbon-Carbon Bond Formation and Pyrrole Synthesis via the [3,3] sigmatropic Rearrangement of *O*-Vinyl Oxime Ethers." Wang, H.-Y.; Mueller, D. S.; Sachwani, R. M.; Londino, H. N.; Anderson, L. L. 2nd Annual Chicago Organic Symposium, Chicago, IL, Feb. 2010. (poster)

AWARD

2013 UIC Graduate Student Council Travel Award

2010 UIC Graduate Student Council Travel Award

AFFILIATE

2010-present American Chemical Society