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Songbai Liu

Copper-Catalyzed C-N Bond Formation from Ketoxime *O*-Carboxylates and Application to Pyridine Synthesis

By
Songbai Liu
Doctor of Philosophy

Advisor: Dr. Lanny S. Liebeskind
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An Abstract of

A dissertation submitted to the Faculty of the

Graduate School of Emory University in partial fulfillment

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Department of Chemistry

Graduate School of Arts and Sciences

2007

Abstract

Catalytic quantities of copper (I) or copper (II) sources catalyze the *N*-imination of boronic acids and organostannanes through reaction with oxime *O*-carboxylates under non-basic conditions. This method tolerates various functional groups and takes place efficiently using aryl, heteroaryl, and alkenyl boronic acids and stannanes.

A simple, modular synthesis of highly substituted pyridines has been achieved by employing a cascade of cross-coupling, electrocyclization, and oxidation reaction starting with α, β-unsaturated ketoxime *O*-pentafluorobenzoates and alkenylboronic acids with catalytic copper. Readily available starting materials, functionality tolerance, and diverse substitution patterns in the pyridine ring contribute to the power of this method.

A strategy utilizing N-N bond disconnection and reconnection for indole synthesis through a decarboxylation and Fischer indole-like cyclization sequence was proved effective. Further study is required to improve the efficiency of the reaction.

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Finally, thanks to all the beings I can still stand here.

LISTING OF ABBREVIATIONS

Ar	aryl or argon
Bpy	2,2'-bipyridine
Bn	benzyl
bp	boiling point
br	broad
BTMSA	*N*,*O*-bis(trimethylsilyl)acetamide
Bu	butyl
Bz	benzoate
^{o}C	degrees Celsius
C_6F_5	pentafluorophenyl
CuMeSal	copper(I) methyl salicylate
CuTC	copper(I) thiophene carboxylate
cm^{-1}	wavenumber unit
Cy	cyclohexyl
δ	chemical shilft (in ppm for NMR)
d	doublet
dba	dibenzylideneacetone
DMF	dimethylformamide
DMAP	dimethylaminopyridine
equiv	equivalents
Et	ethyl
EtOAc	ethyl acetate
g	gram(s)
Hex	hexane
h	hour(s)
HRMS	high-resolution mass spectrometry
Hz	hertz
IR	infrared spectroscopy
J	coupling constant
L	liter
M	molar
Me	methyl
mg	milligram
MHz	megahertz
mL	milliliter
mmol	millimole
mol%	mole percent

mol	mole
Mp	melting point
NMM	*N*-methylmorpholine
OAc	acetate
Ph	phenyl
ppm	parts per million
pyr	pyridine
q	quartet
R-BINAP	(R)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
r.t. (or rt)	room temperature
s	singlet
t	triplet
TLC	thin layer chromatography
TMEDA	*N*, *N*, *N*, *N*-tetramethylethylenediamine
Tol	toluene
UV	ultraviolet
w	weak
wt%	weight percent

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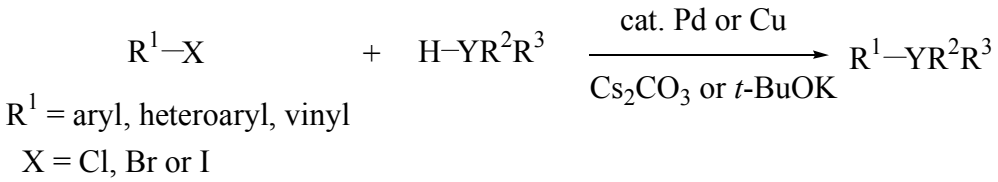
Chapter 1 Copper-Catalyzed *N*-Imination of Boronic Acids and Organostannanes with *O*-Acyl Ketoximes

1.1 Introduction and Background

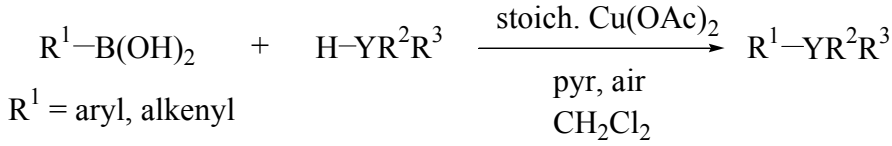
Mild metal-catalyzed methods for the formation of carbon-heteroatom bonds have revolutionized the practice of organic synthesis in both academic and industrial settings.[1] Most noteworthy are the palladium- and copper-catalyzed reactions developed by Buchwald and Hartwig and extended by others.[2] Important complementary reactions that oxidatively couple boronic acids with RYH substrates (Y = N, O, S) have been developed by Chan, Evans, Lam, and others (Scheme 1.1).[3]

Scheme 1.1 Known Cross-Coupling Reactions for C-Y Bond Formation

Buchwald-Hartwig and related couplings
basic conditions



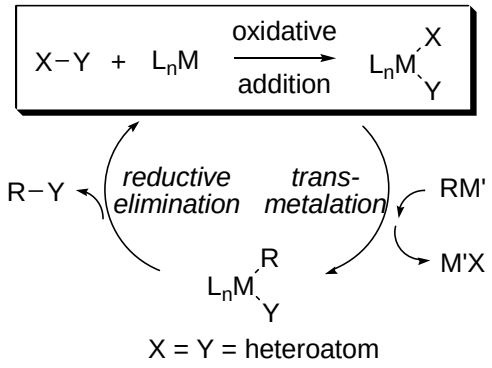
Lam-like couplings
basic, oxidative conditions



Although C-Y bonds can be easily generated under basic conditions through the

Buchwald-Hartwig or oxidative Lam-like conditions, a non-basic and non-oxidative metal-catalyzed protocol could prove useful in complex synthetic settings. The value of an additional method for carbon-heteroatom bond formation becomes apparent if one contemplates hypothetical synthetic challenges such as the easy manipulation of natural product oximes at the O-N bond for structure activity relationship studies, or the generation of transient, reactive imines from oximes for subsequent transformations under mild conditions. Guided by this concept, the Liebeskind laboratory has initiated an exploration of the metal-catalyzed cross-coupling of heteroatom-heteroatom reagents (X-Y, X, Y = O, N, S) seeking carbon-heteroatom bond forming reactions that take place under non-basic and non-oxidizing reaction conditions by using boronic acids and organostannanes as mild, non-basic, and functional group compatible reaction partners.

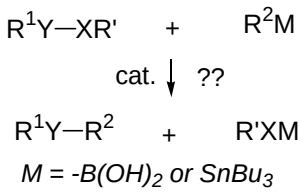
Scheme 1.2 Carbon-Heteroatom Bond Formation from Heteroatom-Heteroatom Bond



The key step in the putative reaction sequence involves oxidative addition of a lower-valent transition metal catalyst L_nM to a heteroatom-heteroatom bond X-Y to generate a species $L_nM(X)Y$ followed by subsequent transmetalation and reductive elimination to provide the desired C-Y bond formation (Scheme 1.2). The putative

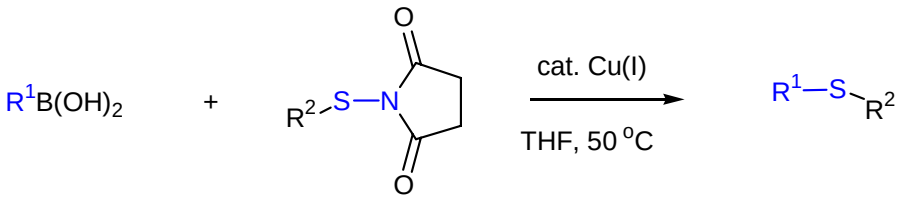
reaction sequence parallels Lam-like reactions, but replaces the requisite oxidant in those transformations (stoichiometric Cu^{II} or air) with the heteroatom-heteroatom bond of the reagent (Scheme 1.3).

Scheme 1.3 Cross-Coupling Concept



This strategy has recently led to the disclosure of a mild and unusual Cu(I)-catalyzed coupling of boronic acids with *N*-thioimides (Scheme 1.4).[4] The reaction takes place in the absence of a base under mild conditions and represents an interesting complement to known methods for thioether synthesis.

Scheme 1.4 Cu(I)-Catalyzed Couplings of Boronic Acids with *N*-Thioimides

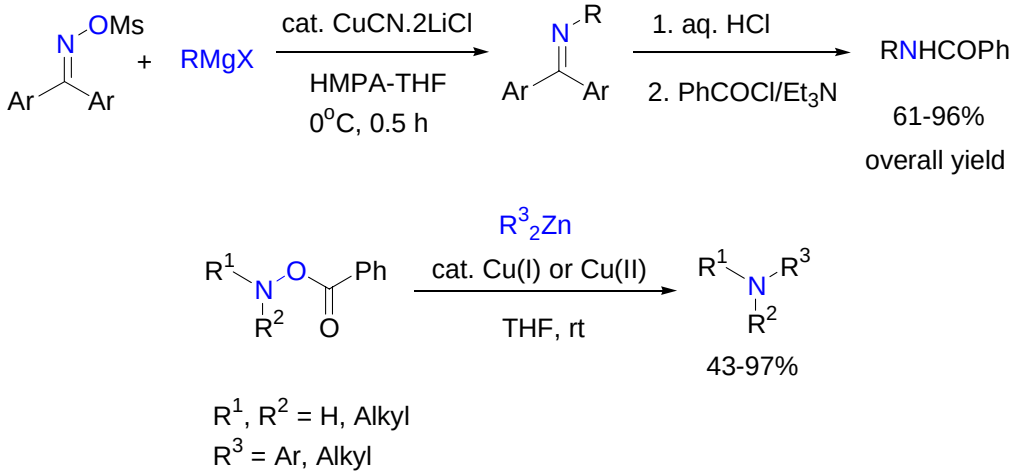


R^1 = aryl, alkenyl ; R^2 = alkyl, aryl, heteroaryl

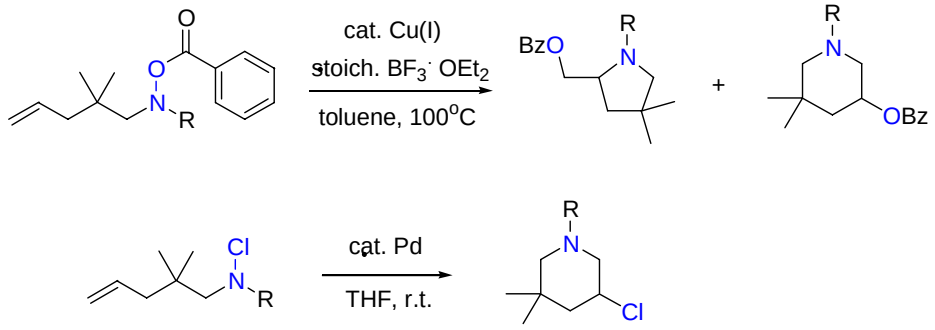
To build up the groundwork for the eventual selective manipulation of biomolecules, the Liebeskind laboratory is exploring metal-tuned transformations of N-O bond based functional groups with boronic acids and organostannanes. Related cross-couplings have also been studied by Narasaka and Johnson and their coworkers but using basic organomagnesium and organozinc reagents, which provide a general process for C-N bond formation (Scheme 1.5). [5] Göttlich and coworkers have explored metal-mediated

reactions of N-halo compounds as well as some hydroxylamine derivatives (Scheme 1.6).[6] However, neither boronic acids nor organostannanes, which are more relevant partners for transformations of sensitive and functionally complex molecules, participate in similar N-O cleavage-based cross-coupling with simple hydroxylamine derivatives.

Scheme 1.5 Narasaka and Johnson's Studies on N-O Bond

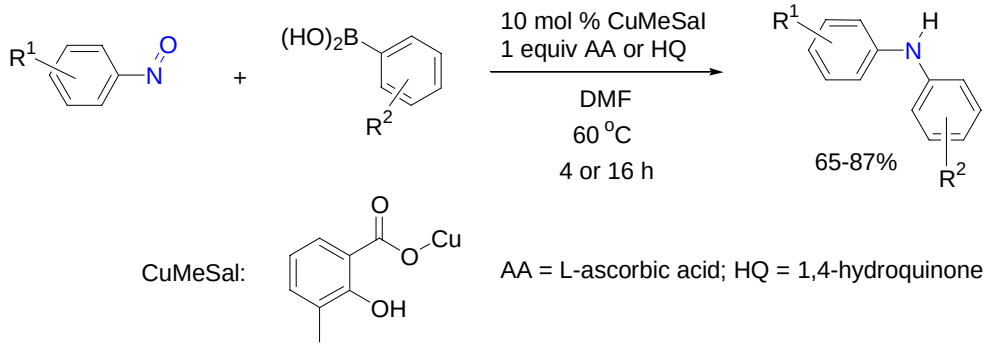


Scheme 1.6 Göttlich's Study on N-O and N-Cl Bonds



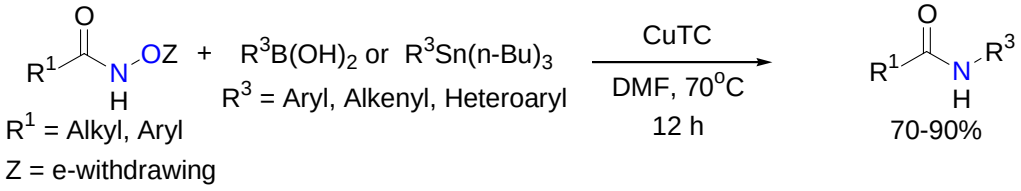
In published work the Liebeskind group has demonstrated a mild and unusual Cu-catalyzed method for the reductive amination of aryl boronic acids with nitroso aromatic compounds (Scheme 1.7).[7] Diarylamines bearing a variety of functional groups can be obtained in good yields.

Scheme 1.7 Cu-Catalyzed Reductive Amination of Aryl Boronic Acids with Nitroso Aromatic Compounds



In unpublished work the Liebeskind group has found that boronic acids and organostannanes couple efficiently with *O*-aryl- and *O*-acylhydroxamic acids in the presence of stoichiometric copper to generate *N*-substituted amides (Scheme 1.8). These reactions complement the Cu-catalyzed Ullmann and Goldberg arylation of amides with aryl halides studied by Buchwald[8] by providing a non-basic protocol that is compatible with the presence of haloaromatics.

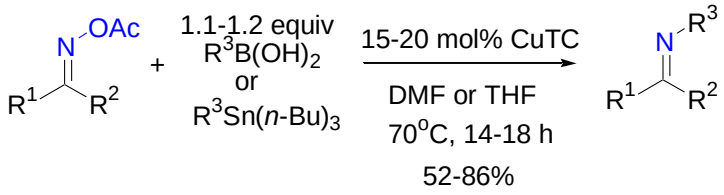
Scheme 1.8 Cu-Mediated *N*-Amidation of Boronic Acids and Organostannanes with *O*-Aryl- and *O*-Acylhydroxamic Acids



As another important category of N-O compounds, oxime derivatives were explored in the metal-catalyzed reaction with boronic acids and organostannanes to fulfill this C-N bond formation protocol. Dr. Ying Yu's preliminary study has demonstrated the

effectiveness of 20 mol% CuTC in DMF at 70 °C for the cross-coupling oxime *O*-acetate with aryl boronic acids and organostannanes (Scheme 1.9). However, to build up a more powerful methodology for C-N bond formation, it is essential to generalize the reaction from simple arylboronic acids and organostannanes to functionalized aryl, alkenyl and heteroaromatic boronic acids and organostannanes and expand the substrate scope from aryl to alkyl and heteroaromatic types. These goals form the substance of the research described in this chapter.

Scheme 1.9 Preliminary Study on Cu-Catalyzed *N*-Imination of Boronic Acids and Organostannanes with *O*-Acyl Ketoximes.

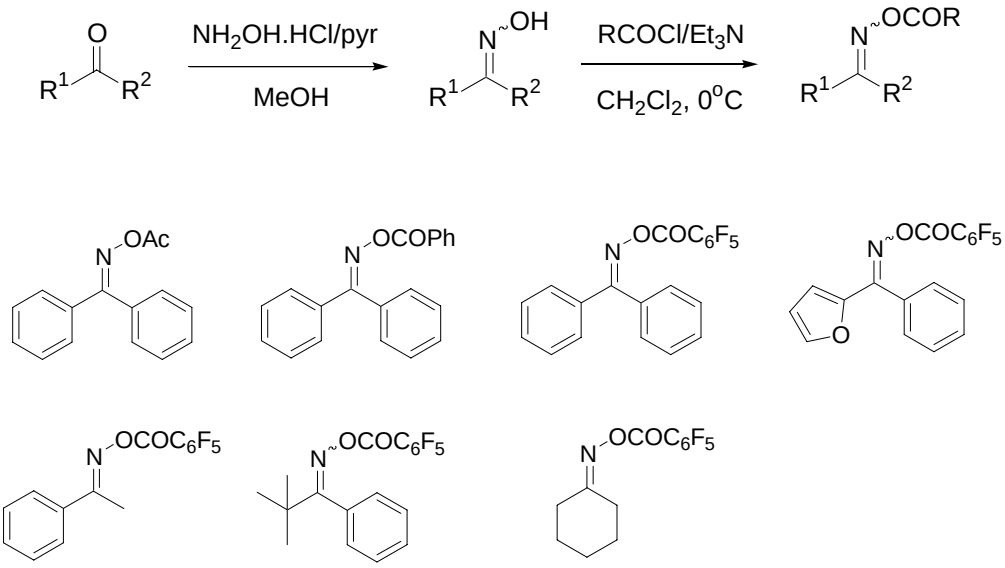


1.2 Results and Discussion

1.2.1 *Preparation of Oxime O-Carboxylates*

The oxime *O*-carboxylates were synthesized starting with the corresponding ketones or aldehydes (Scheme 1.10). The ketone or aldehyde was treated with hydroxylamine hydrochloride and pyridine in methanol. The resulting oxime was then treated with an acyl chloride and triethylamine in dichloromethane at 0 ^{o}C to afford the oxime *O*-carboxylate.

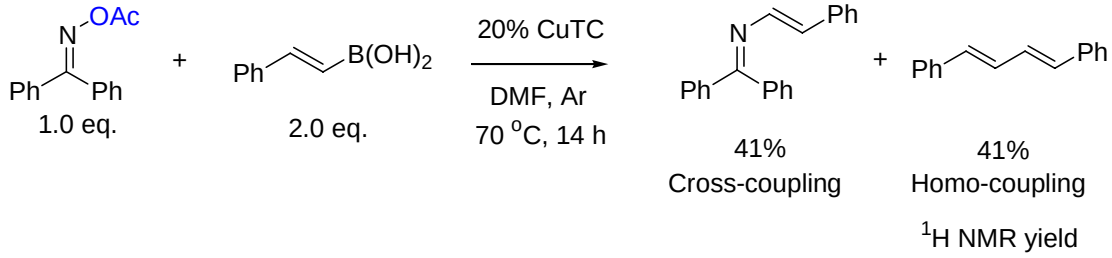
Scheme 1.10 Preparation of Oxime *O*-Carboxylates from Ketones



1.2.2 *N-Imination of Boronic Acids with Ketoxime O-Carboxylates*

Upon extending the reaction conditions developed by Dr. Ying Yu [9] to the cross-coupling of alkenyl boronic acids with oxime acetates, the boronic acid homo-coupling side-product was observed in significant quantities. For example when benzophenone *O*-acetyloxime and *E*-β-styrylboronic acid were treated with 20 % CuTC in DMF at 70 °C for 14 h under argon, a mixture of cross-coupling product and homo-coupling product was obtained (Scheme 1.11).

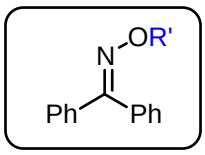
Scheme 1.11 Homo-Coupling Issue as Alkenylboronic Acid Employed



It was hypothesized that a *O*-substituent more reactive than *O*-acetyl for the oxime derivatives could enhance the desired cross-coupling reaction and minimize the

competitive homo-coupling reaction accordingly. To obtain appropriate N-O bond reactivity, various substituents were probed (Figure 1.1). The reactive mesyl oxime spontaneously underwent Beckmann rearrangement at room temperature and the less reactive sulfamoyl oxime also suffered Beckmann rearrangement under the reaction conditions. Trifluoroacetyl and trichloroacetyl oximes were unstable during isolation. They were easily hydrolyzed and were unsuitable as efficient substrates. Upon switching to the more stable benzoyl oxime, the homo-coupling side reaction was still problematic. Fortunately, when the pentafluorobenzoyl oxime was applied,[10] the homo-coupling side reaction was completely suppressed. The greater reactivity of the *O*-pentafluorobenzoyl oximes allowed efficient coupling to be carried out with lower catalyst loadings (10 mol% rather than 20 mol% Cu), at lower temperature (50 °C rather than 70 °C), and within 3 h.

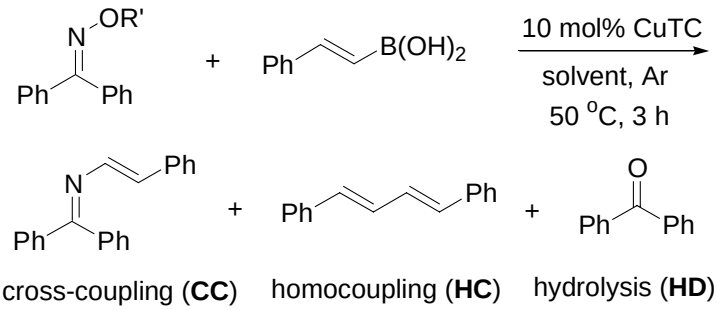
Figure 1.1 Investigations of *O*-Substituents



R' =		
	Ms	Beckmann Rearrangement
	SO_2NMe_2	Beckmann Rearrangement
	$COCF_3$	Unstable
	$COCCl_3$	Unstable
	COPh	Homo-coupling
	COC_6F_5	✓ ✓ ✓

The effect of solvent was explored (Table 1.1) and DMF proved to be the best solvent studied. Other solvents such as THF, toluene, and dioxane gave competitive hydrolysis of the imine product caused by water generated *in situ* from the boronic acid – boroxine equilibrium.

Table 1.1 Optimization of Solvents



Entry	R'	solvents	yield (%)[a]		
			CC	HC	HD
1	Ac	DMF	41	12	9
2	COPh	DMF	63	9	12
3	COC_6F_5	DMF	86	0	5
4	COC_6F_5	THF	81	0	12
5	COC_6F_5	toluene	41	0	38
6	COC_6F_5	dioxane	39	0	38

[a] ^{1}H NMR yield, *para*-dimethoxybenzene as internal standard.

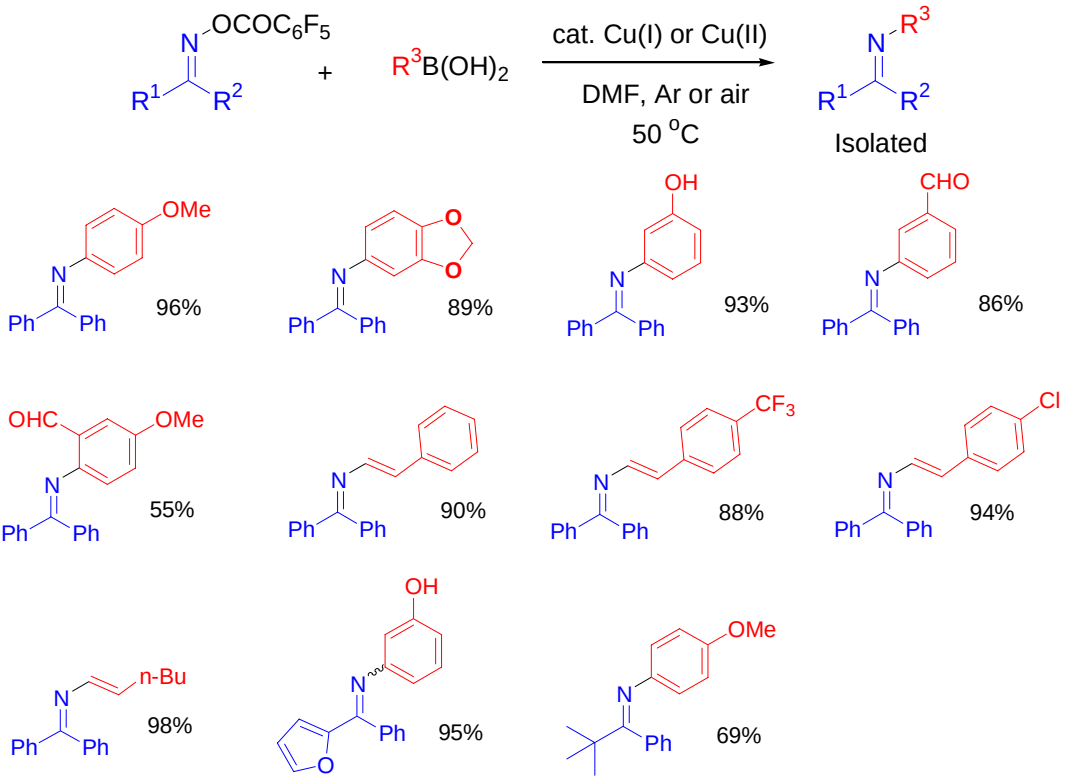
Many different copper sources including both copper (I) (like CuCl, CuBr, CuI) and copper (II) (like $CuBr_2$, $Cu(OAc)_2$) were effective catalysts for the cross-coupling (Table 1.2).No reaction occurred in the absence of the catalyst. Interestingly, the reaction can be carried out in the presence of air. Palladium was not an effective catalyst for this coupling.

Table 1.2 Survey of Copper Sources

catalyst	^{1}H NMR yield (%)	
	CC	HD
none	0	0
CuTC	86	5
CuCl	70	4
CuBr	91	3
CuI	76	2
$CuBr_2$	82	4
$Cu(OAc)_2$	87	3
$Cu(OAc)_2$, air	88	2
$Pd(PPh_3)_4$	0	1

Using the optimized conditions, the scope of this new methodology was examined as shown in Scheme 1.12. Electron-rich and electron-deficient arylboronic acids participated efficiently in the reaction. 4-Methoxy-2-formylphenyl boronic acid, the *ortho*-substituted arylboronic acid investigated in this study, gave acceptable yields of the product under the conditions investigated. Unprotected phenolic and aldehydic functional groups were well-tolerated using this method suggesting that interesting functionalized imine intermediates could be prepared by this mild synthetic method. Synthetically useful 2-azadienes[11] were easily and efficiently produced when alkenylboronic acids were the reactants.

Scheme 1.12 Cu-Catalyzed *N*-Imination of Boronic Acids



The scope of the substrate oxime was also probed. The aryl-aryl type, heteroaryl-aryl and *tert*-butyl-aryl types are suitable substrates. Unfortunately, aldoxime *O*-carboxylates did not produce the desired aldimines; rather, they suffered β-elimination to give the corresponding nitrile products under the reaction conditions (Scheme 1.13). Although extensive conditions were explored, including different catalysts, solvents, and ligands, the β-elimination could not be prevented (Table 1.3).

Scheme 1.13 β-Elimination of Aldoxime *O*-Carboxylates

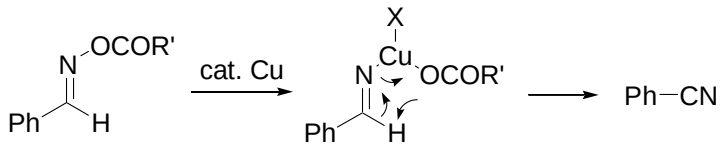
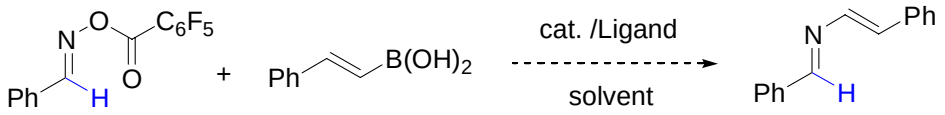


Table 1.3 Attempts to Suppress β-Elimination

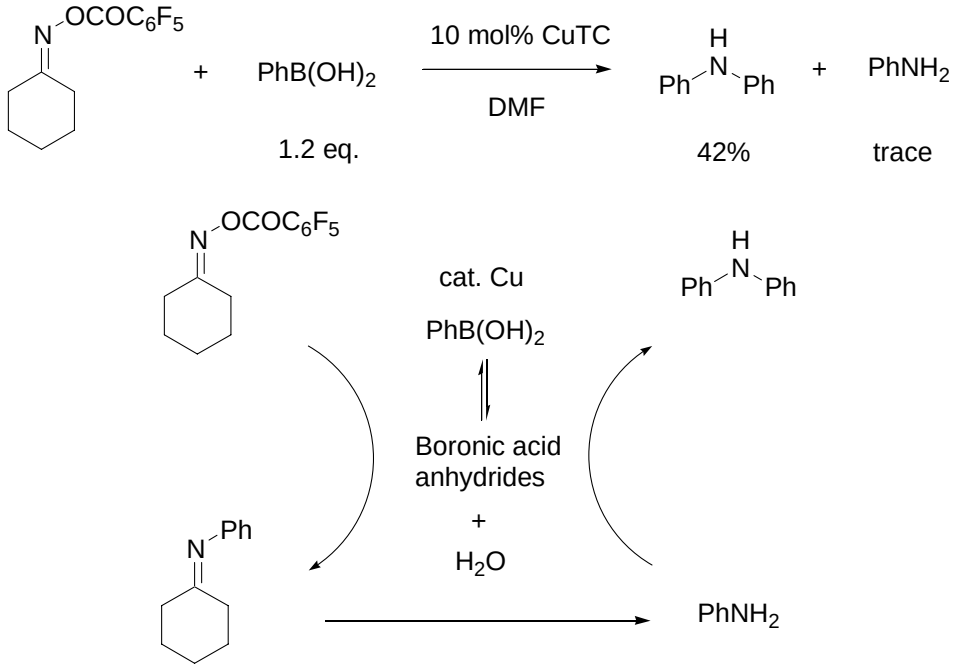


Cat.	Ligand	Solvent/T/time	Results
10mol% CuTC	NONE	THF/r.t./24 h	PhCN
10mol% CuTC	20mol% TMEDA	THF/r.t./24 h	PhCN
10mol% CuTC	20mol% NMM	THF/r.t./24 h	PhCN
10mol% CuTC	20mol% pyridine	THF/r.t./24 h	PhCN
10mol% CuTC	20mol% R-BINAP	THF/r.t./24 h	SM
10mol% CuTC	5mol% R-BINAP	THF/r.t./20 h	SM
10mol% CuTC	5mol% R-BINAP	THF/50 ^{o}C /1 h	PhCN
10mol% CuTC	10mol% R-BINAP	THF/50 ^{o}C /1 h	SM
10mol% CuTC	40mol% $P(OEt)_3$	THF/r.t./24 h	SM
10mol% CuTC	10mol% $P(OEt)_3$	THF/50 ^{o}C/2 h	PhCN
10mol% CuTC	20mol% $P(OEt)_3$	THF/50 ^{o}C/2 h	PhCN
10mol% CuTC	30mol% $P(OEt)_3$	THF/50 ^{o}C/2 h	SM
10mol% $Pd_2(dba)_3$	20mol% R-BINAP	Toluene/70^{o}C/18 h	PhCN + HC
10mol% $Pd_2(dba)_3$	20mol% R-BINAP	THF/70^{o}C/18 h	PhCN + HC
10mol% $Pd_2(dba)_3$	20mol% R-BINAP	DMF/70^{o}C/18 h	PhCN + HC
2.5mol% $Pd_2(dba)_3$	20mol% $P(OEt)_3$	THF/50^{o}C/12 h	SM + HC

Upon extending the substrate to the alkyl substituted oxime *O*-carboxylates, like the cyclohexanone oxime *O*-pentafluorobenzoate, the cross-coupling with phenylboronic

acid gave only diphenyl amine and a trace amount of aniline instead of the desired imine product (Scheme 1.14). This suggested that the cross-coupling reaction did work, but the imine product was very sensitive to the trace amount of water generated *in situ* from the boronic acid – boroxine equilibrium and hydrolyzed to aniline. Subsequent oxidative coupling with phenylboronic acid in the presence of catalytic amount of copper afforded diphenyl amine.

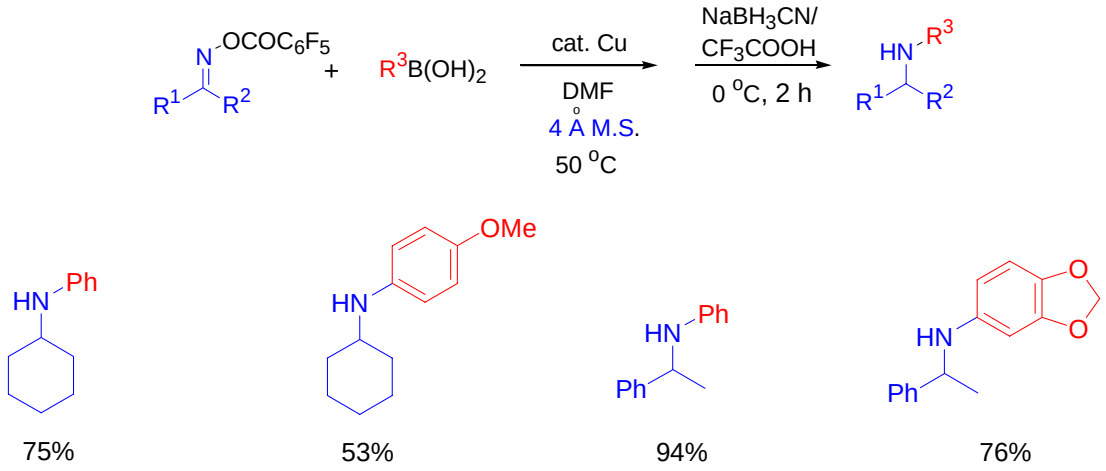
Scheme 1.14 Hydrolysis Issue on Alkyl Substituted Ketoxime *O*-carboxylates



Guided by this knowledge, molecular sieves were applied for the alkyl substituted oxime *O*-pentafluorobenzoates to prevent hydrolysis of the imine product. Because imines were typically unstable to workup and isolation, rather than carrying out direct isolation of these imines, a reductive workup using $NaCNBH_3$ and trifluoroacetic acid allowed a more convenient isolation of the corresponding amines (Scheme 1.15). Thus

the aryl-alkyl and alkyl-alkyl type oxime *O*-pentafluorobenzoates are suitable substrates for this chemistry.

Scheme 1.15 Coupling with Alkyl Substituted Ketoxime *O*-Pentafluorobenzoates

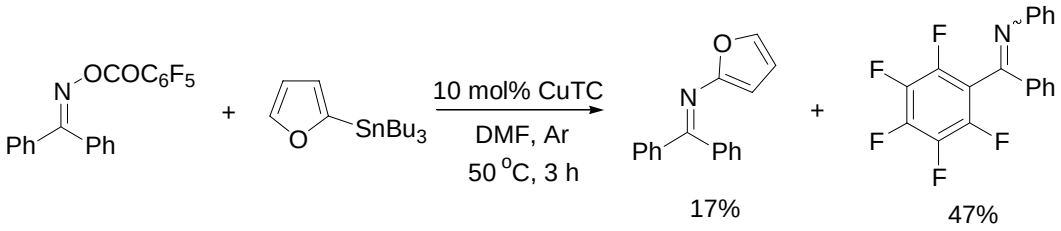


1.2.3 *N-Imination of Organostannanes with Ketoxime O-Carboxylates*

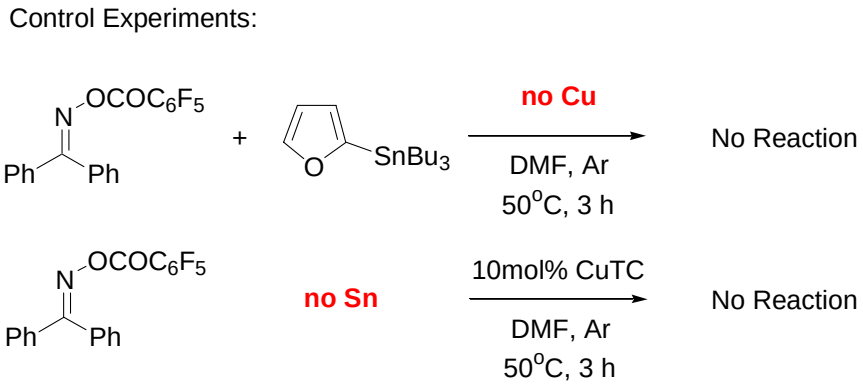
As demonstrated above using boronic acids as reaction partners the pentafluorobenzoyl oximes generally gave better results than acetyl oximes, probably due to the milder conditions using the former reactants (lower temperature and shorter reaction time). Interestingly, when organostannanes were employed as reaction partners, the acetyl oximes performed better than pentafluorobenzoyl oximes. As shown in Scheme 1.16, the pentafluorobenzoyl oxime when coupling with 2-furyl-tri-*n*-butylstannane suffered a competitive side reaction. This side product was deduced to result from the Beckmann rearrangement of the pentafluorobenzoyl oxime. Control experiments demonstrated that the Beckmann rearrangement did not occur in the absence of either the copper catalyst or 2-furyl-tri-*n*-butylstannane. These results suggested that the Beckmann

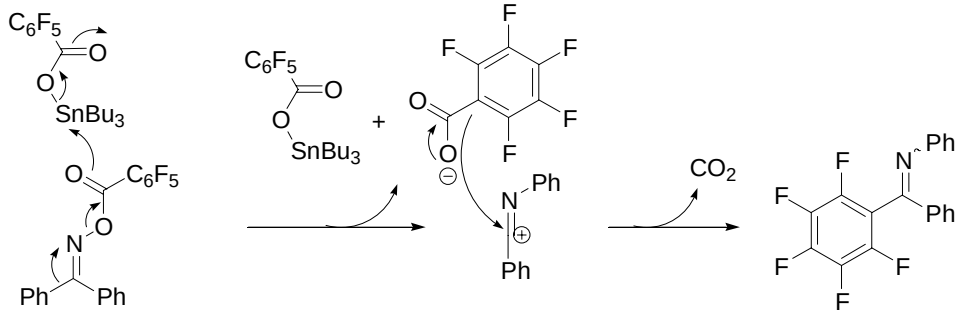
rearrangement is induced by the pentafluorobenzoyl-tri-*n*-butylstannane generated from the coupling reaction (Scheme 1.17). In our earlier study, the $Ph_2P(O)O^-$ counterion was identified as an effective scavenger of the tri-*n*-butyl tin moiety by the formation of *n*-$Bu_3SnOP(O)Ph_2$. [12] Addition of stoichiometric tetrabutylammonium diphenylphosphinate did completely suppress the Beckmann rearrangement regardless of decomposition caused by it (Scheme 1.18).

Scheme 1.16 Beckmann Rearrangment Issue as Organostannanes applied



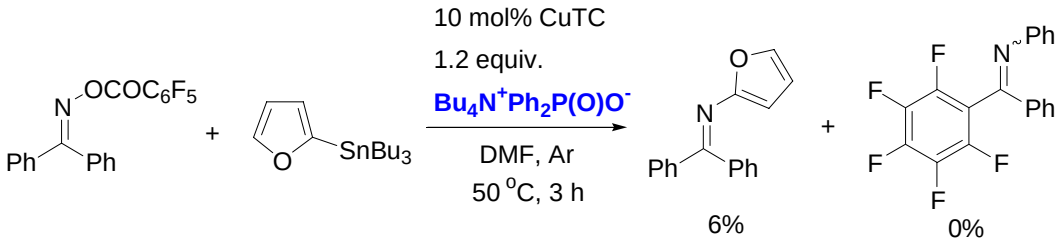
Scheme 1.17 Plausible Origin of the Beckmann Rearrangement





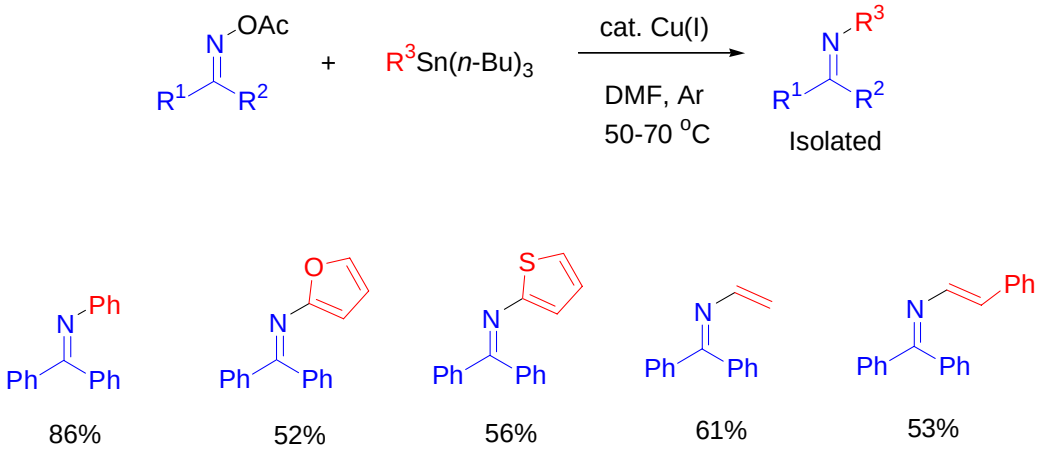
Scheme 1.18 Beckmann Rearrangement Suppressed by Tetrabutylammonium

Diphenylphosphinate



Thus, the less reactive acetyl oximes were used when organostannanes were applied as reaction partners. Although providing somewhat lower yields of *N*-substituted imine products, aryl, heteroaryl, such as furan and thiophene, and alkenyl stannanes were suitable reaction partners in this chemistry (Scheme 1.19). It was revealed that an inert atmosphere was required when organostannanes were employed.

Scheme 1.19 Cu-Catalyzed *N*-Imination of Organostannanes

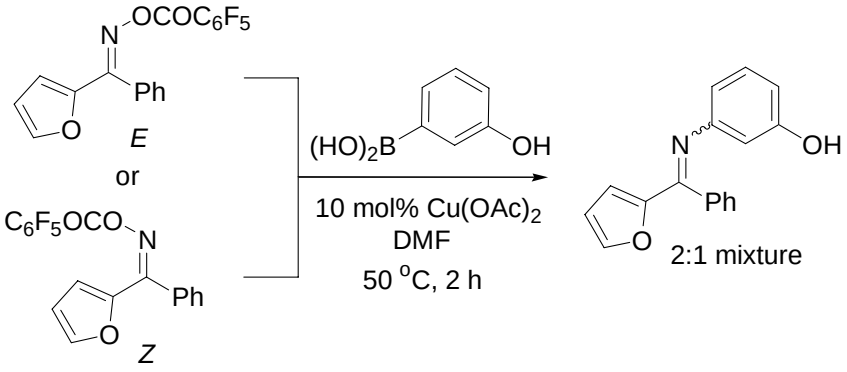


1.2.4 *Stereochemistry Study for the Cross-Coupling Reaction*

After establishment of the chemistry, the stereochemistry of this new reaction was explored. Unfortunately, under the conditions studied thus far, this new reaction was not appropriate for the stereodefined synthesis of imines (Scheme 1.20). Separate treatment

of each stereoisomeric *E*- and *Z*-oxime *O*-pentafluorobenzoate derived from phenyl-2-furyl ketone with 3-hydroxyphenylboronic acid produced the same 2:1 mixture of product imines.

Scheme 1.20 Stereochemistry of the Cross-Coupling

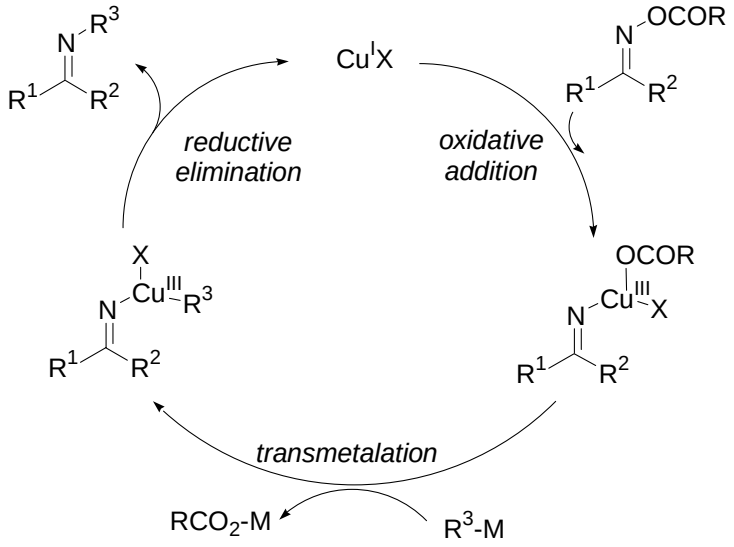


1.2.5 *Mechanistic Speculation*

A reasonable mechanistic pathway for the copper catalyzed coupling of ketoxime O-carboxylates with boronic acids or organostannanes is shown in Scheme 1.21. Oxidative additions to N–O bonded species are precedented.[13] In the current study strong support for oxidative addition of the oxime O-carboxylate to Cu(I) comes from the formation of benzophenone imine in 90% yield after a mixture of benzophenone oxime O-acetate and 1 equiv of CuTC in DMF was subjected to workup after 30 min. Transmetallation of either the boronic acid or the organostannane to the putative Cu(III) intermediate followed by reductive elimination would produce the desired C-N bond and regenerate a catalytically active Cu(I). The requisite Cu(I) catalyst is either added to the reaction system or generated *in situ* through reduction of a Cu(II) precatalyst by the

coupling agent.

Scheme 1.21 Plausible Mechanism



1.3 Conclusion

In summary, a general copper-catalyzed *N*-imination of boronic acids and organostannanes has been developed. The reaction uses oxime *O*-carboxylates as iminating agents and proceeds under non-basic and non-oxidizing conditions thus complementing existing C-N bond forming reactions.

1.4 References

[1] (a) Beletskaya, I. P. *Pure Appl. Chem.* **2005**, *77*, 2021. (b) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337. (c) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400.

[2] (a) Buchwald, S. L.; Mauger, C.; Mignani, G.; Scholz, U. *Adv. Synth. Catal.* **2006,** *348*, 23. (b) Hartwig, J. F. *Synlett.* **2006,** *9*, 1283. (c) Muci, A. R.; Buchwald, S. L. In *Topics*

in Current Chemistry, 2002; Vol. 219, pp 131. (d) Hartwig, J. F. *Comprehensive Coordination Chemistry II* **2004**, *9*, 369. (e) Schlummer, B.; Scholz, U. *Adv. Synth. Catal.* **2004,** *346*, 1599. (f) Zhang, H.; Cai, Q.; Ma, D. *J. Org. Chem.* **2005**, *70*, 5164.

[3] (a) Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C. G. *Tetrahedron Lett.* **2003,** *44*, 4927. (b) Lam, P. Y. S.; Bonne, D.; Vincent, G.; Clark, C. G.; Combs, A. P. *Tetrahedron Lett.* **2003,** *44*, 1691. (c) Chan, D. M. T.; Monaco, K. L.; Li, R.; Bonne, D.; Clark, C. G.; Lam, P. Y. S. *Tetrahedron Lett.* **2003,** *44*, 3863. (d) Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C. G. *Tetrahedron Lett.* **2002,** *43*, 3091. (e) Lam, P. Y. S.; Vicent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. *Tetrahedron Lett.* **2001,** *42*, 3415. (f) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Averill, K. M.; Chan, D. M. T.; Combs, A. *Synlett* **2000**, *5*, 674. (g) Antilla, J. C.; Buchwald, S. L. *Org. Lett.* **2001,** *3*, 2077. (h) Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000,** *2*, 2019. (i) Collman, J. P.; Zhong, M. *Org. Lett.* **2000,** *2*, 1233. (j) Chan, D. M. T.; Monaco, K. L.; Wang, R. -P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933. (k) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937. (l) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941.

[4] Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2002**, *4*, 4309.

[5] (a) Kitamura, M.; Suga, T.; Chiba, S.; Narasaka, K. *Org. Lett.* **2004,** *6*, 4619. (b) Narasaka, K. *Pure Appl. Chem.* **2002,** *74*, 143. (c) Berman, A. M.; Johnson, J. S. *J. Org. Chem.* **2006,** *71*, 219. (d) Berman, A. M.; Johnson, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 5680.

[6] (a) Noack, M.; Göttlich, R. *Chem. Commun*. **2002**, 536-537. (b) Helaja, J.; Göttlich, R. *Chem. Commun.* **2002**, 720. (c) Heuger, G.; Kalsow, S.; Göttlich, R. *Eur. J. Org. Chem.*

2002, 1848. (d) Noack, M.; Göttlich, R. *Eur. J. Org. Chem.* **2002**, 3171.

[7] Yu, Y.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2004**, *6*, 2631.

[8] Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem.Soc.* **2005,** *127*, 4120.

[9] Yu, Y. Liebeskind, L. S. *Ph.D. Dissertation*, Emory University, **2004**.

[10] Tsutsui, H.; Narasaka, K. *Chem. Lett.* **1999**, 45.

[11] (a) Jayakumar, S.; Ishar, M. P. S.; Mahajan, M. P. *Tetrahedron* **2002**, *58*, 379. (b) Boger, D. L. *J. Heterocycl. Chem.* **1996**, *33*, 1519. (c) Gilchrist, T. L.; Rocha Gonsalves, A. M. d'A.; Pinho e Melo, T. M. V. D. *Pure Appl. Chem.* **1996**, *68*, 859.

[12] Wittenberg, R.; Srogl, J.; Egi, M.; Liebeskind, L. S. *Org. Lett.* **2003**, *5*, 3033.

[13] For oxidative addition of oxime derivatives to various transition metals such as Re, Pd and Cu, see: (a) Kusama, H.; Yamashita, Y.; Uchiyama, K.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 965. (b) Ferreira, C. M. P.; Guedes da Silva, M. F. C.; Kukushkin, V. Y.; Fraústo da Silva, J. J. R.; Pombeiro, A. J. L. *J. Chem. Soc., Dalton Trans.* **1998**, 325. (c) Tsutsui, H.; Narasaka, K. *Chem. Lett.* **1999**, 45. (d) Tsutsui, H.; Narasaka, K. *Chem. Lett.* **2001**, 526. (e) Kitamura, M.; Zaman, S.; Narasaka, K. *Synlett* **2001**, 974. (f) Kitamura, M; Narasaka, K. *Chem. Rec.* **2002**, *2*, 268. (g) Chiba, S.; Kitamura, M.; Saku, O.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 785. (h) Tsutsui, H.; Hayashi, Y.; Narasaka, K. *Chem. Lett.* **1997**, 317. (i) Narasaka, K. *Pure Appl. Chem.* **2002**, *74*, 19.

1.5 Experimental

General Methods

All reactions were performed under an atmosphere of dry Ar in oven-dried glassware unless otherwise specified. Solvents (THF, dioxane, DMF, MeOH, CH_2Cl_2 and toluene)

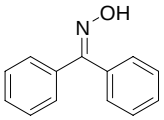
were ACS reagent grade and purchased from Aldrich. Solvents were dried over 4 Å molecular sieves and titrated for water level with a Fisher Coulomatic K-F titrator before use. All solvents were purged with Ar before using unless otherwise noted. Hexanes, ethyl acetate (EtOAc), and ethyl ether (Et_2O) used for extraction and chromatography were obtained from EM Science and were used as purchased. Solutions of NH_4OH refers to aqueous solution. Brine refers to a saturated aqueous solution of NaCl. Purification by preparative plate chromatography was performed on EM Science Kieselgel 0.5 mm/1 mm 60 F_{254} plates. Analytical thin-layer chromatography (TLC) was carried out using Merck Kieselgel 0.25 mm 60 F_{254} plates with visualization by UV or phosphomolybdic acid. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 600 MHz or 400 MHz NMR spectrometer at room temperature in $CDCl_3$ or acetone-d_6 with the solvent residual peak as internal reference ($CDCl_3$: ^{1}H = 7.24 ppm, ^{13}C = 77.0 ppm; acetone-d_6: ^{1}H = 2.05 ppm, ^{13}C = 29.5 ppm) unless otherwise stated. ^{19}F NMR spectra were recorded on a Varian Inova 376 MHz NMR spectrometer at room temperature in $CDCl_3$ without a reference. Data are reported in the following order: chemical shifts (δ); multiplicities (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet)); coupling constants, *J* (Hz); integration. Infrared (IR) spectroscopy was performed on a Nicolet 380 FT-IR or ASI ReactIR 1000 spectrometer. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak 20-40%), and br (broad). Melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes and are uncalibrated. High resolution

mass spectra were obtained on a JEOL JMS-SX102/SX102A/E instrument.

Starting Materials

Acetyl chloride, benzoyl chloride, benzophenone, hydroxylamine hydrochloride, cyclohexanone oxime, *trans*-2-phenylvinylboronic acid, *trans*-1-hexen-1-ylboronic acid, *trans*-2-[4-(trifluoromethyl) phenyl]vinylboronic acid, *trans*-2-(4-chlorophenyl)vinylboronic acid, CuOAc, $Cu(OAc)_2$, CuCl, CuBr, $CuBr_2$, CuI, $Pd(PPh_3)_4$, phenyl-tri-*n*-butylstannane, 2-furyl-tri-*n*-butylstannane, 2-thienyl-tri-*n*-butylstannane and $NaBH_3CN$ (1.0 M in THF) were purchased from Aldrich and used as obtained. Other boronic acids were obtained from Frontier Scientific, Inc. and used as received. (*E*)-Acetophenone oxime was obtained from Acros Organics.[1] 9-Fluorenone oxime was purchased from TCI America Inc. Pentafluorobenzoyl chloride was purchased from Alfa/Aesar. CuTC[2] was prepared according to the literature procedure.

Benzophenone oxime.[3]

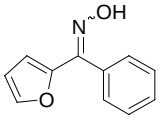


Benzophenone (3.644 g, 20 mmol) and hydroxylamine hydrochloride (6.682 g, 80 mmol) were dissolved in 80 mL MeOH. Pyridine (7.91 g, 100 mmol) was added *via* syringe and after stirring at room temperature overnight the solvent was evaporated. The

[1] The configuration was determined by ^{1}H NMR, see: Moehrle, H.; Wehefritz, B.; Steigel, A. *Tetrahedron Lett.* **1987**, *43*, 2255.
[2] Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312.
[3] Jain, N.; Kumar, A.; Chauhan, S. M. S. *Tetrahedron Lett.* **2005**, *46*, 2599.

product was extracted into a mixture of hexanes/EtOAc (20 mL/20 mL) and the organic phase was washed with 1 M HCl (20 mL), water and brine. After drying over $MgSO_4$ the solvent was evaporated. Purification by flash chromatography (silica gel, 2:1 hexanes:EtOAc) afforded 3.68 g of the title compound as a white solid. Yield: 93%. TLC (R_f = 0.64, silica gel, 2:1 hexanes:EtOAc). Mp = 143-145 °C (EtOAc/hexanes, lit. {143-144 °C}[3]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1 H), 7.43-7.50 (m, 7 H), 7.30-7.37 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 136.1, 132.6, 129.5, 129.2, 129.1, 128.3, 128.2, 127.8. IR (neat, cm^{-1}) 3235 (br, s), 1494 (m), 1444 (s), 1328 (s), 1162 (m).

2-Furanylphenyl-methanone oxime.[4]

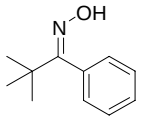


2-Furanylphenyl-methanone (3.0 g, 17.4 mmol) and hydroxylamine hydrochloride (1.816 g, 26.1 mmol) were dissolved in 30 mL MeOH. Pyridine (3.52 mL, 43.5 mmol) was added *via* syringe and the reaction mixture was stirred under reflux for 12 h before the solvent was evaporated. EtOAc (50 mL) was added to extract the product. The organic layer was sequentially washed with 1 M HCl (20 mL) and brine (3 × 50 mL). After drying over $MgSO_4$ the solvent was evaporated. Purification by flash chromatography (silica gel, 5:1 hexanes:EtOAc) afforded 2.85 g of an E/Z mixture of isomers of the title compound as a yellow solid. Yield: 87%. TLC (R_f = 0.45, silica gel,

[4] Demir, A.; Sesenoglu, O.; Ulku, D.; Arici, C. *Helv. Chim. Acta* **2003**, *86*, 91.

5:1 hexanes:EtOAc). Mp = 132-135 °C (of the mixture, EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) The integration of 1 H of the minor isomer was set as 1, so that 1 H of the major isomer exhibited 2 H accordingly. δ 9.98 (br, 2 H), 7.42 -7.58 (m, 20 H), 6.57-6.59 (m, 2 H), 6.40-6.41 (m, 1 H), 6.29-6.30 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 149.0, 147.8, 144.6, 144.2, 143.1, 134.3, 130.7, 129.5, 129.3, 128.97, 128.93, 128.2, 119.2, 113.6, 111.9, 111.3. IR (neat, cm^{-1}) 3150 (br, s), 1629 (m), 1563(s), 1494 (s), 1444 (s), 1393 (s), 1185 (s).

(*Z*)-2,2-Dimethyl-1-phenyl-1-propanone oxime.[3,5]

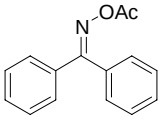


A 3.0 M solution in Et_2O of phenylmagnesium bromide (1.67 mL, 5 mmol) was added dropwise under Ar to a stirred solution of pivaloyl chloride (0.62 mL, 5 mmol) and $Fe(acac)_3$ (0.053 g, 0.15 mmol) in 20 mL of dry THF at 0 °C. After addition was complete, stirring was continued for 2 h at the same temperature. The reaction mixture was poured into dilute hydrochloric acid and extracted with several portions of ether. The combined ether extracts were washed with sat'd aqueous $NaHCO_3$, water, and dried over $MgSO_4$. After evaporation of the solvent the crude product and hydroxylamine hydrochloride (0.42 g, 6 mmol) were dissolved in 20 mL MeOH. Pyridine (0.88 mL, 11 mmol) was added *via* syringe and the reaction mixture was stirred at reflux overnight. After evaporation of the solvent the product was extracted into EtOAc (50 mL). The

[5] Fiandanese, V.; Marchese, G.; Martina, V.; Ronzini, L. *Tetrahedron Lett.* **1984**, *25*, 4805.

organic layer was sequentially washed with 1 M HCl (20 mL) and brine (3 × 50 mL). After drying over $MgSO_4$ the solvent was evaporated. The crude product was purified by flash chromatography (silica gel, 5:1 hexanes:EtOAc) to afford 0.32 g of the title compound as a white solid. Yield: 52% (over two steps). TLC (R_f = 0.56, silica gel, 5:1 hexanes:EtOAc). Mp = 164-165 °C (EtOAc/hexanes, lit. {167-168 °C (EtOH/H_2O)}[6]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1 H), 7.34-7.43 (m, 3 H), 7.09-7.11 (m, 2 H), 1.14 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 133.6, 128.0, 127.9, 127.6, 37.3, 28.2. IR (neat, cm^{-1}) 3254 (br, m), 2968 (s), 1463 (s), 1011 (s). The *Z*-configuration was verified by NOE irradiation experiments.

Benzophenone *O*-acetyloxime.[7]

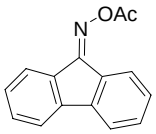


Benzophenone (3.644 g, 20 mmol) and hydroxylamine hydrochloride (6.682 g, 80 mmol) were dissolved in 80 mL EtOH. Pyridine (7.91 g, 100 mmol) was added *via* syringe and the mixture was stirred at room temperature overnight. The solvent was evaporated and the product was extracted into a mixture of hexanes/EtOAc (20 mL/20 mL). The organic solution was washed with 1 M HCl (20 mL), water, and brine. After drying over $MgSO_4$ the solvent was evaporated to give 3.859 g of the title oxime as a white solid. The white solid was dissolved in 50 mL CH_2Cl_2 and AcCl (1.727 g, 22 mmol) was added followed by Et_3N (2.226 g, 22 mmol). After stirring at room temperature for 5 h, the

[6] Brunner, H.; Becker, R.; Gauder, S. *Organometallics* **1986**, *5*, 739.
[7] Kawase, M.; Kikugawa, Y. *J. Chem. Soc., Perkin Trans. 1* **1979**, 643.

white precipitate was removed by filtration. The filtrate was washed with water then brine and then dried over $MgSO_4$. The solvent was evaporated to give a crude product that was recrystallized from hexane/Et_2O to give 4.445 g (93%) of the product as a white solid. TLC (R_f = 0.52, 1:1 hexanes: Et_2O). Mp = 72-73 °C (ethyl ether/hexane, lit. {73 °C (hexane)}[7]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.57 (m, 2 H), 7.41-7.46 (m, 4 H), 7.29-7.36 (m, 4 H), 2.09 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 164.7, 134.8, 132.6, 130.9, 129.6, 129.0, 128.8, 128.4, 128.2, 19.7. IR (neat, cm^{-1}) 3061 (w), 1768 (s), 1197 (s).

Fluoren-9-one *O*-acetyloxime.[7]



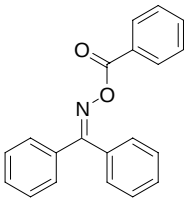
9-Fluorenone oxime (0.976 g, 5 mmol) was dissolved in 20 mL THF. AcCl (0.416 g, 5.3 mmol) was added followed by Et_3N (0.536 g, 5.3 mmol). After stirring at room temperature for 5 h, the white precipitate was removed by filtration. The filtrate was evaporated and EtOAc (20 mL) was added to dissolve the residue. The organic phase was washed with 1 M HCl (10 mL), water, and then brine. After drying over $MgSO_4$ the solvent was evaporated to give a solid yellow residue. Recrystallization from hexane/Et_2O gave the product as a yellow solid (1.090 g, 92%). TLC (R_f = 0.50 1:1 hexanes:Et_2O). Mp = 77-78 °C (ethyl ether/hexane, lit. {76-78 °C (hexane)}[7]). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, J = 7.5 Hz, 1 H), 7.89 (d, J = 7.5 Hz, 1 H), 7.24-7.61 (m, 6 H), 2.39 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 157.8, 142.5, 141.1, 134.3, 132.5,

131.6, 130.1, 130.0, 128.4, 128.3, 123.2, 120.2, 120.0, 19.6. IR (neat, cm^{-1}) 3061 (w), 2937 (w), 1772 (s), 1598 (m), 1189 (s).

General Procedure for Preparation of other Oxime *O*-carboxylates

To the oxime (1.0 equiv) in CH_2Cl_2 at 0 °C was added dropwise Et_3N (2.0 equiv) followed by the acyl chloride (1.2 equiv). After stirring for 0.5 h at 0 °C the reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The reaction mixture was extracted with EtOAc and the organic phase was sequentially washed with saturated aqueous $NaHCO_3$ and brine and then dried over $MgSO_4$. After evaporation of the solvent the residue was subjected to flash chromatography giving the corresponding oxime *O*-carboxylate.

Benzophenone *O*-benzoyloxime.[8]

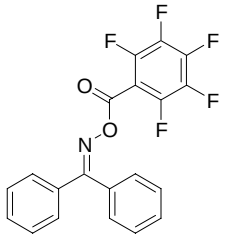


Benzoyl chloride (0.17 mL, 1.5 mmol) was added dropwise to a mixture of benzophenone oxime (0.197 g, 1 mmol) and sodium hydride (0.048 g, 2 mmol) in 5 mL THF at 0 °C. After stirring at 0 °C for 1 h, the reaction mixture was stirred further at room temperature for 1 h. The reaction mixture was extracted with EtOAc and the organic phase was sequentially washed with saturated aqueous $NaHCO_3$ and brine and then dried over $MgSO_4$. After evaporation of the solvent, purification by flash

[8] Wylie, B. B.; Isaacson, E. I.; Delgado, J. N. *J. Pharm. Sci.* **1965**, *54*, 1373.

chromatography (silica gel, 4:1 hexanes:EtOAc) afforded the title compound as a white solid (0.231 g, 76%). TLC (R_f = 0.62, silica gel, 3:1 hexanes:EtOAc). Mp = 98-100 °C (CH_2Cl_2/hexanes, lit. {98-99}[8]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.80 (m, 2 H), 7.65-7.67 (m, 2 H), 7.44-7.53 (m, 5 H), 7.33-7.41 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.8, 134.6, 133.2, 132.8, 131.0, 129.7, 129.6, 129.1, 128.8, 128.7, 128.43, 128.41, 128.2. IR (neat, cm^{-1}) 3061 (m), 1749 (s), 1602 (m), 1328 (s), 1243 (s), 1061 (s).

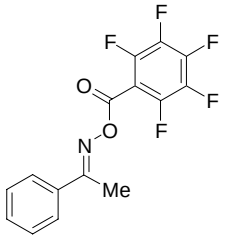
Benzophenone *O*-pentafluorobenzoyloxime.



Following the general procedure, benzophenone oxime (0.394 g, 2.0 mmol), pentafluorobenzoyl chloride (0.33 mL, 2.4 mmol) and Et_3N (0.56 mL, 4.0 mmol) were reacted in 5 mL CH_2Cl_2. Purification by flash chromatography (silica gel, 4:1 hexanes:EtOAc) afforded the title compound as a white solid (0.760 g, 97%). TLC (R_f = 0.62, silica gel, buffered by Et_3N, 4:1 hexanes:EtOAc). Mp = 124-125 °C (CH_2Cl_2/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.61 (m, 2 H), 7.43-7.49 (m, 4 H), 7.36-7.40 (m, 2 H), 7.32-7.34 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 156.7, 134.0, 131.9, 131.5, 130.0, 129.2, 128.6, 128.5, 128.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.58 (m, 2 F), -148.23 (m, 1 F), -160.38 (m, 2 F). IR (neat, cm^{-1}) 3065 (w), 2922 (m), 1760 (s), 1498 (s), 1328 (s), 1193 (s), 1004 (s). HRMS (FAB) Calcd. for $C_{20}H_{11}O_2NF_5$

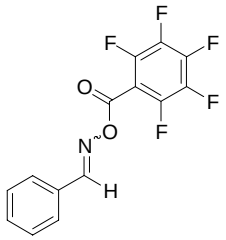
([M+H]$^+$): 392.0704. Found: 392.0697.

(*E*)-1-Phenyl-ethanone *O*-pentafluorobenzoyloxime.[9]



Following the general procedure, (*E*)-acetophenone oxime (0.270 g, 2.0 mmol), pentafluorobenzoyl chloride (0.33 mL, 2.4 mmol) and Et_3N (0.56 mL, 4.0 mmol) were reacted in 5 mL CH_2Cl_2. Purification by flash chromatography (silica gel, 5:1 hexanes:EtOAc) afforded the title compound as a white solid (0.633 g, 96%). TLC (R_f = 0.58, silica gel, 5:1 hexanes:EtOAc). Mp = 146-149 °C (CH_2Cl_2/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.78 (m, 2 H), 7.40-7.47 (m, 3 H), 2.44 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 134.0, 131.1, 128.7, 127.2, 15.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.45 (m, 2 F), -148.00 (m, 1 F), -160.24 (m, 2 F). IR (neat, cm^{-1}) 1768 (s), 1652 (m), 1498 (s), 1332 (s), 1200 (s).

1-Phenyl-methanone *O*-pentafluorobenzoyloxime.

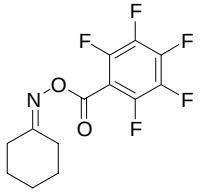


Following the general procedure, benzaldehyde oxime (0.121 g, 1.0 mmol), pentafluorobenzoyl chloride (0.166 mL, 1.2 mmol) and Et_3N (0.28 mL, 2.0 mmol) were

[9] Tsutsui, H.; Kitamura, M.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **2002**, *5*, 51.

reacted in 5 mL CH_2Cl_2. Purification by flash chromatography (silica gel, 5:1 hexanes:EtOAc) afforded the title compound as a white solid (0.633 g, 80%). TLC (R_f = 0.67, silica gel, 5:1 hexanes:EtOAc). Mp = 145-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1 H), 7.74-7.77 (m, 2 H), 7.42-7.53 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 132.4, 129.2, 129.0, 128.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.36 to -137.25 (m, 2 F), -147.81 to -147.68 (m, 1 F), -160.21 to -160.06 (m, 2 F). IR (neat, cm^{-1}) 1752 (s), 1652 (m), 1494 (s), 1332 (m), 1204 (s). HRMS (ESI) Calcd. for $C_{14}H_7O_2NF_5$ ($[M+H]^+$): 316.0392. Found: 316.0387.

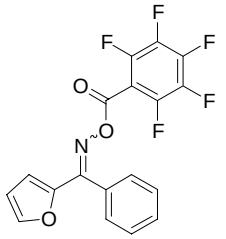
Cyclohexanone *O*-pentafluorobenzoyloxime.



Following the general procedure, cyclohexanone oxime (0.566 g, 5.0 mmol), pentafluorobenzoyl chloride (0.83 mL, 6.0 mmol) and Et_3N (1.4 mL, 10.0 mmol) were reacted in 20 mL CH_2Cl_2. Purification by flash chromatography (silica gel, 5:1 hexanes:EtOAc) afforded the title compound as a white solid (1.433 g, 93%). TLC (R_f = 0.52, silica gel, 5:1 hexanes:EtOAc). Mp = 38-39 °C (EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (t, J = 6.4 Hz, 2 H), 2.41 (t, J = 6.4 Hz, 2 H), 1.74-1.81 (m, 2 H), 1.61-1.71 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 31.9, 27.4, 26.7, 25.8, 25.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.79 (m, 2 F), -148.54 (m, 1 F), -160.48 (m, 2 F) IR (neat, cm^{-1}) 2941 (s), 2864 (m), 1760 (s), 1652 (s), 1498 (s), 1328 (s), 1193 (s), 1096 (s).

HRMS (FAB) Calcd. for $C_{13}H_{11}O_2NF_5$ ($[M+H]^+$): 308.0704. Found: 308.0698.

2-Furanylphenyl-methanone *O*-pentafluorobenzoyloxime.

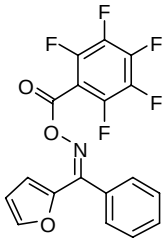


Following the general procedure, 2-furanylphenyl-methanone oxime (0.374 g, 2.0 mmol), pentafluorobenzoyl chloride (0.33 mL, 2.4 mmol) and Et_3N (0.42 mL, 3.0 mmol) were reacted in 10 mL CH_2Cl_2. Purification by flash chromatography (silica gel, 5:1 hexanes:EtOAc) afforded the title compound as a light yellow solid (a mixture of *E/Z* isomers, *E*:*Z* = 1:1.8, 0.712 g, 93%). TLC (R_f = 0.52, silica gel, 5:1 hexanes:EtOAc). Mp = 107-110 °C (of the mixture, EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$. The integration of 1 H of the minor *E*-isomer was set as 1, so that 1 H of the major *Z*-isomer exhibited 1.8 H accordingly.) δ 7.39-7.63 (m, 17 H), 7.26 (d, *J* = 3.2 Hz, 1.9 H), 6.60 (dd, *J* = 3.6, 1.4 Hz, 1.8 H), 6.56 (d, *J* = 3.2 Hz, 1 H), 6.48 (dd, *J* = 3.2, 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 155.1, 147.4, 146.4, 145.6, 143.7, 132.2, 130.8, 130.3, 130.1, 129.7, 128.4, 128.36, 128.2, 121.6, 119.0, 112.4, 112.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.46 (m, 6 F), -147.82 (m, 2 F), -148.06 (m, 1 F), -159.90 (m, 4 F), -160.35 (m, 2 F). IR (neat, cm^{-1}) 3154 (w), 1764 (s), 1652 (s), 1498 (s), 1328 (s), 1189 (s), 1089 (s). HRMS (FAB) Calcd. for $C_{18}H_9O_3NF_5$ ($[M+H]^+$): 382.0497. Found: 382.0490.

The *E*/*Z* isomers can be separated by careful chromatography on silica gel eluting with

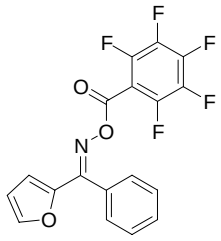
5:1 hexanes:EtOAc. The *E*-isomer is slightly more polar than the *Z*-isomer. The *E* and *Z* configurations can be differentiated by their different ^{1}H NMR signal patterns of the furan ring as exhibited in the corresponding oxime isomers.[10]

(*Z*)-2-Furanylphenyl-methanone *O*-pentafluorobenzoyloxime.[10]



Light yellow solid. Mp = 113-114 °C (EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.63 (m, 2 H), 7.57 (d, *J* = 1.6 Hz, 1 H), 7.49-7.53 (m, 1 H), 7.43-7.47 (m, 2 H), 7.26 (d, *J* = 3.6 Hz, 1 H), 6.60 (dd, *J* = 3.6, 1.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 145.6, 143.7, 132.2, 130.8, 129.7, 128.4, 121.6, 112.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.44 (m, 2 F), -147.80 (m, 1 F), -159.90 (m, 2 F). IR (neat, cm^{-1}) 1764 (s), 1652 (s), 1498 (s), 1328 (s), 1185 (s), 1089 (s). HRMS (FAB) Calcd. for $C_{18}H_9O_3NF_5$ ($[M+H]^+$): 382.0497. Found: 382.0490.

(*E*)-2-Furanylphenyl-methanone *O*-pentafluorobenzoyloxime.[10]

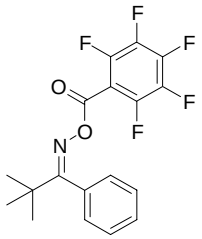


Light yellow solid. Mp = 147-149 °C (EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 1.2 Hz, 1 H), 7.38-7.48 (m, 5 H), 6.56 (d, *J* = 3.6 Hz, 1 H), 6.48 (dd, *J* = 3.6,

[10] Demir, A. S.; Sesenoglu, O. *Helv. Chim. Acta* **2003**, *86*, 91.

1.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 147.4, 146.4, 130.3, 130.1, 128.4, 128.2, 119.0, 112.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.43 (m, 2 F), -148.04 (m, 1 F), -160.35 (m, 2 F). IR (neat, cm^{-1}) 3115 (m), 1752 (s), 1652 (m), 1494 (s), 1320 (s), 1204 (s). HRMS (FAB) Calcd. for $C_{18}H_9O_3NF_5$ ($[M+H]^+$): 382.0497. Found: 382.0490.

(*Z*)-2,2-Dimethyl-1-phenyl-1-propanone *O*-pentafluorobenzoyloxime.



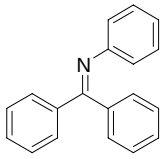
Following the general procedure, (*Z*)-2,2-dimethyl-1-phenyl-1-propanone oxime (0.177 g, 1.0 mmol), pentafluorobenzoyl chloride (0.166 mL, 1.2 mmol) and Et_3N (0.28 mL,2.0 mmol) were reacted in 10 mL CH_2Cl_2. Purification by flash chromatography (silica gel, 10:1 hexanes:EtOAc) afforded the title compound as a light yellow solid (0.311 g, 84%). TLC (R_f = 0.47, silica gel, 5:1 hexanes:EtOAc). Mp = 82-84 °C (EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.37 (m, 3 H), 7.03-7.06 (m, 2 H), 1.27 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 132.5, 128.5, 127.9, 126.4, 38.8, 27.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -138.00 (m, 2 F), -148.93 (m, 1 F), -160.77 (m, 2 F). IR (neat, cm^{-1}) 2976(m), 1756 (s), 1652 (s), 1498 (s), 1328 (s), 1193 (s), 1096 (s). HRMS (FAB) Calcd. for $C_{18}H_{15}O_2NF_5$ ($[M+H]^+$): 372.1018. Found: 372.1012.

General Procedure for Cu-catalyzed *N*-Imination of Boronic Acids or Organostannanes with Oxime *O*-Acetates

A Schlenk tube containing the *O*-substituted oxime (0.3 mmol), the boronic acid or

organostannane (0.36 mmol) and CuTC (12 mg, 0.06 mmol) was flushed with argon. DMF (8 mL) was added and the mixture was stirred at 70 °C for 14 h, cooled, and partitioned between Et_2O (20 mL) and H_2O (20 mL). The aqueous layer was extracted with Et_2O (10 mL) and the combined ether layers were dried with $MgSO_4$. The residue after evaporation was subjected to GC/MS analysis or preparative plate silica chromatography using a mixture of hexanes and Et_2O as the eluent.

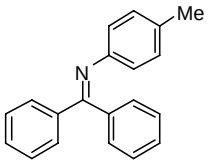
_N_-Benzhydrylidenaniline.[11]



Following the general procedure, (72 mg, 0.3 mmol) benzophenone *O*-acetyloxime, phenylboronic acid (45 mg, 0.36 mmol) and CuTC (9 mg, 0.045 mmol) were reacted in 8 mL DMF. The product was obtained as a light yellow solid: 63 mg (82%). TLC (R_f = 0.76, 2:1 hexanes: EtOAc). Mp = 115-116 °C (ethyl ether/hexane, lit. {113-115 °C}[11]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.74 (m, 2 H), 7.37-7.48 (m, 3 H), 7.21-7.26 (m, 3 H), 7.09 -7.15 (m, 4 H), 6.88-6.92 (m, 1 H), 6.71 (d, J = 7.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 151.2, 139.6, 136.2, 130.7, 129.5, 129.3, 128.6, 128.5, 128.2, 127.9, 123.1, 120.9. IR (neat, cm^{-1}) 3053 (m), 1610 (s), 1590 (s), 1482 (s), 1444 (s).

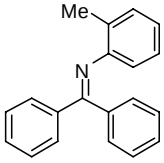
_N_-(Diphenylmethylene)-_p_-toluidine.[12]

[11] Paventi, M.; Hay, A. S. *J. Org. Chem.* **1991**, *56*, 5875.
[12] Nongkunsarn, P.; Ramsden, C. A. *Tetrahedron* **1997**, *53*, 3805.



Following the general procedure, benzophenone *O*-acetyloxime (72 mg, 0.3 mmol), *p*-tolylboronic acid (48 mg, 0.36 mmol) and CuTC (12 mg, 0.06 mmol) were reacted in 8 mL DMF. The product was obtained as a brown solid: 66 mg (81%). TLC (R_f = 0.80, 2:1 hexanes: EtOAc). Mp = 45-46 °C (ethyl ether/hexane, lit. {47-48 °C (ethanol)}[12]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.73 (m, 2 H), 7.35-7.46 (m, 3 H), 7.22-7.27 (m, 3 H), 7.09-7.12 (m, 2 H), 6.92 (d, *J* = 8.0 Hz, 2 H), 6.61 (d, *J* = 8.0 Hz, 2 H), 2.21 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 148.5, 139.9, 136.4, 132.6, 130.6, 129.5, 129.3, 129.1, 128.5, 128.2, 127.9, 121.0, 20.8. IR (neat, cm^{-1}) 3057 (m), 2922 (w), 1617 (s), 1502 (s).

***N*-(Diphenylmethylene)-2-methylbenzenamine.[13]**

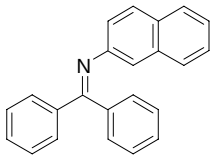


Following the general procedure, benzophenone *O*-acetyloxime (72 mg, 0.3 mmol), *o*-tolylboronic acid (48 mg, 0.36 mmol) and CuTC (12 mg, 0.06 mmol) were reacted in 8 mL DMF. The product was obtained as a brown solid: 48 mg (59%). TLC (R_f = 0.81, 2:1 hexanes: EtOAc). Mp = 51-52 °C (ethyl ether/hexane, lit. {50-51 °C}[13]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.2 Hz, 2 H), 7.38-7.48 (m, 3 H), 7.20-7.26 (m, 3 H), 7.04-7.10 (m, 3 H), 6.81-6.92 (m, 2 H), 6.43 (d, *J* = 7.6 Hz, 1 H), 2.17 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 150.0, 139.4, 136.2, 130.5, 129.6, 129.1, 128.7, 128.4, 128.0,

[13] Love, B. E.; Ren, J. *J. Org. Chem.* **1993**, *58*, 5556.

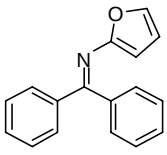
127.7, 125.6, 122.8, 119.2, 17.9. IR (neat, cm^{-1}) 3061 (m), 2926 (m), 1621 (s), 1594 (s), 1575 (s).

_N_-(Diphenylmethylene)-2-naphthalenamine.[14]



Following the general procedure, benzophenone *O*-acetyloxime (72 mg, 0.3 mmol), 2-naphthylboronic acid (62 mg, 0.36 mmol) and CuTC (12 mg, 0.06 mmol) were reacted in 8 mL DMF. The product was obtained as a brown solid: 66 mg (72%). TLC (R_f = 0.82, 2:1 hexanes: EtOAc). Mp = 91-92.5 °C (ethyl ether/hexane, lit. {96.5 °C}[14]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.81 (m, 2 H), 7.69 (d, *J* = 8.0 Hz, 1 H), 7.56-7.63 (m, 2 H), 7.14-7.52 (m, 11 H), 6.91 (dd, *J* = 8.6, 1.8 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 136.0, 133.9, 132.4, 130.9, 130.3, 130.1, 129.6, 129.5, 128.8, 128.3, 128.2, 128.0, 127.6, 127.4, 126.0, 124.5, 121.8, 117.7. IR (neat, cm^{-1}) 3057 (m), 1613 (s), 1575 (s), 1316 (s), 1289 (s).

_N_-(Diphenylmethylene)- 2-furanamine.[15]

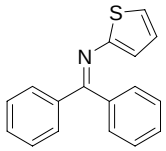


Following the general procedure, benzophenone *O*-acetyloxime (72 mg, 0.3 mmol), 2-furyl-tri-*n*-butylstannane (129 mg, 0.36 mmol) and CuTC (12 mg, 0.06 mmol) were

[14] Reddelien, G. *Chem. Ber.* **1921**, *54*, 3130.
[15] Kim, S.; Do, J. Y. *J. Chem. Soc., Chem. Commun.* **1995**, 1607.

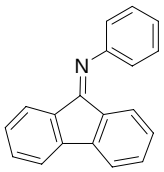
reacted in 8 mL DMF. The product was obtained as a dark-yellow solid: 38 mg (52%). TLC (R_f= 0.74, 1:1 hexanes: Et_2O). Mp = 38-39 °C (ethyl ether/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) . 7.76 (d, *J* = 8.0 Hz, 2 H), 7.47-7.51 (m, 3 H), 7.32-7.42 (m, 3 H), 7.22-7.24 (m, 3 H), 6.19 (dd, *J* = 1.6, 1.6 Hz, 1 H), 4.99 (d, *J* = 3.6 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 156.2, 139.5, 139.2, 138.2, 130.6, 129.2, 128.9, 128.8, 128.2, 127.4, 112.0, 101.0. IR (neat, cm^{-1}) 3061 (w), 1602 (m), 1571 (s), 1459 (s).

***N*-(Diphenylmethylene)-2-thiophenamine.[15]**



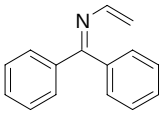
Following the general procedure, benzophenone *O*-acetyloxime (48 mg, 0.2 mmol), 2-thienyl-tri-*n*-butylstannane (112 mg, 0.3 mmol) and CuTC (8 mg, 0.04 mmol) were reacted in 1 mL DMF. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow oil (15 mg, 56%). TLC (R_f = 0.65, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.73-7.75 (m, 2 H), 7.58-7.61 (m, 3 H), 7.39-7.48 (m, 3 H), 7.27-7.30 (m, 2 H), 7.13 (dd, *J* = 5.6, 1.2 Hz, 1 H), 7.06 (dd, *J* = 4.0, 1.2 Hz, 1 H), 6.88 (dd, *J* =5.6, 4.0 Hz, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 162.4, 151.9, 139.9, 136.8, 130.9, 130.1, 130.0, 129.1, 128.9, 128.7, 127.2, 125.5, 125.3. IR (neat, cm^{-1}) 3061 (m), 2922 (m), 1567 (s), 1444 (s), 1289 (s), 1189 (s). HRMS (FAB) Calcd. for $C_{17}H_{14}N^{32}S$ ($[M+H]^+$): 264.0842. Found: 264.0834.

***N*-Phenylfluorenimine.**[16]



Following the general procedure, fluoren-9-one *O*-acetyloxime (72 mg, 0.3 mmol), phenylboronic acid (45 mg, 0.36 mmol) and CuTC (9 mg, 0.045 mmol) were reacted in 8 mL DMF. The product was obtained as a yellow solid: 66 mg (86%). TLC (R_f = 0.58, 4:1 hexanes: EtOAc). Mp = 83-84 °C (ethyl ether/hexane, lit. {83-84 °C}[16]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 1 H), 7.57-7.59 (m, 2 H), 7.29-7.48 (m, 5 H), 7.20 (t, *J* = 7.6 Hz, 1 H), 6.99 (d, *J* = 7.6 Hz, 2 H), 6.90 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.54 (d, *J* = 8.0 Hz, 1 H). IR (neat, cm^{-1}): 3061 (w), 1731 (m), 1648 (s), 1594 (s), 1486 (s), 1447 (s).

***N*-(Diphenylmethylene)-ethenamine.**[17]

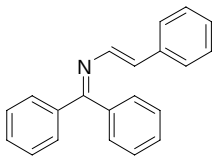


Following the general procedure, (24 mg, 0.1 mmol) benzophenone *O*-acetyloxime, vinyl-tri-*n*-butylstannane (0.035 mL, 0.12 mmol) and CuTC (4 mg, 0.02 mmol) were reacted in 2 mL DMF at 50 °C for 18 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a colorless oil: 13 mg (61%). TLC (R_f = 0.75, silica gel, buffered by Et_3N, 20:1 hexanes: EtOAc). ^{1}H

[16] Dai, W.; Srinivasan, R.; Katzenellenbogen, J. A**.** *J. Org. Chem.* **1989**, *54*, 2204.
[17] Boehme, H.; Ingendoh, A. *Chem. Ber.* **1979**, *112*, 1297.

NMR (400 MHz, acetone-d_6) δ 7.68-7.70 (m, 2 H), 7.50-7.58 (m, 3 H), 7.38-7.48 (m, 3 H), 7.20-7.23 (m, 2 H), 6.87 (dd, *J* = 14.4, 11.2 Hz, 1 H), 5.51 (dd, *J* = 14.4, 1.6 Hz, 1 H), 5.00 (dd, *J* = 11.2, 1.6 Hz, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 167.6, 143.8, 139.8, 136.8, 131.0, 129.4, 129.2, 129.16, 128.9, 128.6, 114.6. IR (neat, cm^{-1}): 3084 (m), 1633 (m), 1556 (s), 1444 (s).

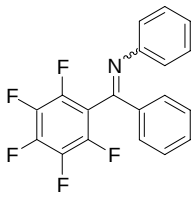
***N*-(Diphenylmethylene)-2-phenyl-ethenamine.** [18]



Following the general procedure, benzophenone *O*-acetyloxime (24 mg, 0.1 mmol), *trans*-2-phenylvinyl-tri-*n*-butylstannane (47 mg, 0.12 mmol) and CuTC (4 mg, 0.02 mmol) were reacted in 2 mL DMF at 50 °C for 18 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow oil: 10 mg (53%). TLC (R_f = 0.58, silica gel, buffered by Et_3N, 20:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.72-7.75 (m, 2 H), 7.56-7.63 (m, 3 H), 7.50 (d, *J* = 13.2 Hz, 1 H), 7.39-7.46 (m, 3 H), 7.27-7.35 (m, 6 H), 7.21 (tt, *J* = 6.8, 1.6 Hz, 1 H), 7.02 (d, *J* = 13.2 Hz, 1 H). ^{13}C NMR (150 MHz, acetone-d_6) δ 167.0, 140.0, 137.6, 137.2, 136.8, 132.0, 130.9, 129.5, 129.3, 129.23, 129.19, 128.7, 128.2, 127.1. IR (neat, cm^{-1}) 3057 (w), 3026 (w), 1540 (m), 942 (s), 691 (s). HRMS (FAB) Calcd. for $C_{21}H_{18}N$ ($[M+H]^+$): 284.1434. Found: 284.1430.

***N*-[(Pentafluorophenyl)phenylmethylene]-benzenamine.**

[18] Balsamini, C.; Bedini, A.; Spadoni, G.; Burdisso, M.; Capelli, A. M. *Tetrahedron* **1994**, *50*, 3773.



Dry DMF (2 mL) was added to a Schlenk tube that was flushed with argon containing benzophenone oxime *O*-pentafluorobenzoate (39.1 mg, 0.1 mmol), 2-furyl-tri-*n*-butylstannane (0.038 mL, 0.12 mmol) and CuTC (1.9 mg, 0.01 mmol). The reaction mixture was stirred at 50 °C for 3 h and then diluted with EtOAc (30 mL). Purification by flash chromatography (10:1, hexanes:EtOAc) afforded the title compound as a white solid (16.4 mg, 47%). TLC (R_f = 0.67, 5:1 hexanes:EtOAc). Mp = 128-129 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.77 (m, 2 H), 7.50-7.55 (m, 1 H), 7.31-7.44 (m, 5 H), 7.15 (d, *J* = 6.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 137.5, 135.9, 132.2, 129.9, 129.8, 128.39, 128.37, 127.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -151.81 (m, 2 F), -163.84 (m, 1 F), -164.13 (m, 2 F). IR (neat, cm^{-1}) 1625 (s), 1598 (w), 1579 (w), 1502 (s), 1316 (m), 1293 (m). HRMS (ESI) Calcd. for $C_{19}H_{11}N_1F_5$ ($[M+H]^+$): 348.0806. Found: 348.0802.

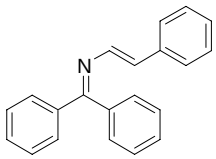
General Procedure for Cu-catalyzed *N*-Imination of Boronic Acids with Oxime *O*-pentafluorobenzoates

Under Argon. Dry DMF (2 mL) was added to a Schlenk tube that was flushed with argon containing the oxime *O*-pentafluorobenzoate (0.1 mmol), the boronic acid (0.12 mmol) and CuTC (2 mg, 0.01 mmol). The reaction mixture was stirred at 50 °C for 3 h and then diluted with EtOAc (30 mL).

Open to Air. Dry DMF (2 mL) was added to a Schlenk tube containing the oxime *O*-pentafluorobenzoate (0.1 mmol), the boronic acid (0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol). The reaction mixture was stirred under an atmosphere of air at 50 °C for 3 h and diluted with EtOAc (30 mL).

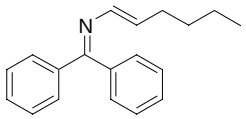
The copper catalyst was removed by passing through a short pad of silica gel which was buffered by triethylamine. After evaporation of the solvent, the residue was subjected to a flash chromatography giving the desired product.

***N*-(Diphenylmethylene)-2-phenyl-ethenamine.[18]**



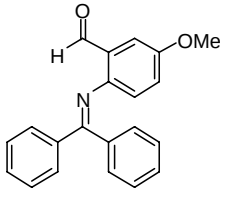
Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), *trans*-2-phenylvinylboronic acid (18 mg, 0.12 mmol) and CuTC (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 3 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow oil (26 mg, 90%). TLC (R_f = 0.58, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^1H NMR (400 MHz, acetone-d_6) δ 7.72-7.75 (m, 2 H), 7.56-7.63 (m, 3 H), 7.50 (d, *J* = 13.2 Hz, 1 H), 7.39-7.46 (m, 3 H), 7.27-7.35 (m, 6 H), 7.21 (tt, *J* = 6.8, 1.6 Hz, 1 H), 7.02 (d, *J* = 13.2 Hz, 1 H). ^{13}C NMR (150 MHz, acetone-d_6) δ 167.0, 140.0, 137.6, 137.2, 136.8, 132.0, 130.9, 129.5, 129.3, 129.23, 129.19, 128.7, 128.2, 127.1. IR (neat, cm^{-1}) 3057 (w), 3026 (w), 1540 (m), 942 (s), 691 (s). HRMS (FAB) Calcd. for $C_{21}H_{18}N$ ($[M+H]^+$): 284.1434. Found: 284.1430.

***N*-(Diphenylmethylene)-1-hexen-1-amine.**



Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15 mg, 0.12 mmol) and CuTC (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2.5 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a colorless oil (26 mg, 98%). TLC (R_f = 0.66, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.63-7.66 (m, 2 H), 7.49-7.56 (m, 3 H), 7.33-7.40 (m, 3 H), 7.18-7.20 (m, 2 H), 6.70 (dt, *J* = 12.8, 1.2 Hz, 1 H), 6.13 (dt, *J* = 12.8, 7.2 Hz, 1 H), 2.02-2.08 (m, 2 H), 1.26-1.38 (m, 4 H), 0.85 (t, *J* = 7.0 Hz, 3 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 164.3, 140.2, 138.4, 137.1, 134.3, 130.5, 129.2, 129.1, 128.9, 128.86, 128.6, 32.1, 30.4, 22.5, 13.8. IR (neat, cm^{-1}) 3084 (w), 2926 (s), 1637 (w), 1556 (s), 1320 (s), 946 (s), 695 (s). HRMS (FAB) Calcd. for $C_{19}H_{22}N$ ($[M+H]^+$): 264.1747. Found: 264.1744.

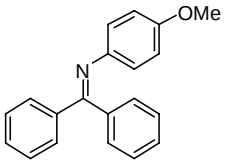
2-(Benzhydrylidene-amino)-5-methoxy-benzaldehyde.



Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), 2-formyl-4-methoxyphenylboronic acid (36 mg, 0.2 mmol) and CuTC (4 mg, 0.02 mmol) were reacted in 2 mL DMF at 50 °C for 2 h. Purification by flash

chromatography (silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc) afforded the title compound as a yellow oil (17 mg, 55%). TLC (R_f = 0.47, silica gel, buffered by Et_3N, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, acetone-d_6) δ 10.30 (s, 1 H), 7.77-7.80 (m, 2 H), 7.56 (t, *J* = 7.6 Hz, 1 H), 7.48 (t, *J* = 7.6 Hz, 2 H), 7.34-7.36 (m, 3 H), 7.18-7.22 (m, 3 H), 6.96 (dd, *J* = 8.8, 3.2 Hz, 1 H), 6.62 (d, J = 8.8 Hz, 1 H), 3.77 (s, 3 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 190.5, 170.2, 156.5, 148.4, 139.5, 136.8, 131.7, 129.7, 129.4, 129.35, 128.8, 128.7, 127.6, 123.4, 122.3, 109.9, 55.4. IR (neat, cm^{-1}) 3061 (w), 2930 (m), 2849 (m), 1687 (s), 1606 (s), 1482 (s), 1316 (s), 1274 (s). HRMS (FAB) Calcd. for $C_{21}H_{18}O_2N$ ($[M+H]^+$): 316.1332. Found: 316.1326.

***N*-(Diphenylmethylene)-4-methoxy-benzenamine.[19]**

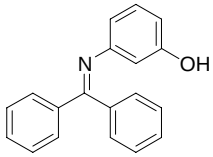


Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), (18 mg, 0.12 mmol) 4-methoxyphenylboronic acid and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow oil (28 mg, 96%). TLC (R_f = 0.47, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.71-7.73 (m, 2 H), 7.47-7.51 (m, 1 H), 7.41-7.45 (m, 2 H), 7.32-7.36 (m, 3 H), 7.14-7.17 (m, 2 H), 6.69-6.72 (m, 2 H), 6.64-6.67 (m, 2H), 3.68 (s, 3 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 167.6, 156.5, 145.1,

[19] Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729.

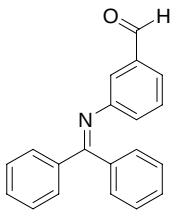
140.4, 137.4, 131.0, 129.7, 129.4, 128.9, 128.62, 128.6, 122.7, 114.1, 55.1. IR (neat, cm^{-1}) 3057 (m), 2930 (m), 1610 (s), 1502 (s), 1243 (s), 1034 (s).

3-[(Diphenylmethylene)amino]-phenol.[20]



Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), 3-hydroxyphenylboronic acid (17 mg, 0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 10:1 hexanes:EtOAc) afforded the title compound as a yellow oil (25 mg, 93%). TLC (R_f = 0.46, silica gel, buffered by Et_3N, 1:2 hexanes:EtOAc). ^1H NMR (400 MHz, acetone-d_6) δ 8.23 (br, 1 H), 7.70-7.73 (m, 2 H), 7.48-7.53 (m, 1 H), 7.42-7.46 (m, 2 H), 7.31-7.34 (m, 3 H), 7.16-7.20 (m, 2 H), 6.93 (t, *J* = 8.0 Hz, 1 H), 6.37-6.40 (m, 1 H), 6.24 (t, *J* = 2.4 Hz, 1 H), 6.15-6.18 (m, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 167.8, 158.2, 153.5, 140.1, 137.0, 131.2, 129.7, 129.6, 129.5, 129.0, 128.7, 128.4, 112.2, 110.4, 108.1. IR (neat, cm^{-1}) 3343 (br, s), 1691 (s), 1590 (s), 1270 (s).

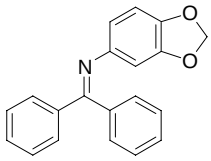
3-(Benzhydrylidene-amino)-benzaldehyde.



[20] Cantarel, R.; Souil, F. *Compt. Rend.* **1958**, *246*, 1436.

Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), 3-formylphenylboronic acid(18 mg, 0.12 mmol) and $Cu(OAc)_2$ (4 mg, 0.02 mmol) were reacted in 2 mL DMF at 50 °C for 1 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 5:1 hexanes:EtOAc) afforded the title compound as a yellow oil (25 mg, 86%). TLC (R_f = 0.28, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^1H NMR (400 MHz, acetone-d_6) δ 9.90 (s, 1 H), 7.76-7.77 (m, 2 H), 7.53-7.57(m, 1 H), 7.46-7.49 (m, 3 H), 7.30-7.39 (m, 4 H), 7.26 (t, *J* = 1.6 Hz, 1 H), 7.19-7.22 (m, 2 H), 7.02-7.05 (m, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 192.4, 169.6, 153.0, 139.6, 137.7, 136.4, 131.6, 129.75, 129.7, 129.6, 129.2, 128.8, 128.6, 127.0, 124.7, 121.5. IR (neat, cm^{-1}) 3061 (m), 2926 (m), 2725 (m), 1695 (s), 1617 (s), 1594 (s), 1293 (s), 1247 (s), 1170 (s). HRMS (FAB) Calcd. for $C_{20}H_{16}ON$ ($[M+H]^+$): 286.1226. Found: 286.1220.

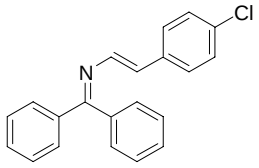
Benzhydrylidene-benzo[1,3]dioxol-5-yl-amine.



Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), 3,4-methylenedioxyphenylboronic acid (20 mg, 0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow solid (27 mg, 89%). TLC (R_f = 0.43, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). Mp = 108-110 °C (ether/hexanes). ^1H NMR (400 MHz, acetone-d_6) δ 7.69-7.71 (m, 2 H), 7.35-7.52 (m, 6 H), 7.18-7.20 (m, 2 H), 6.62 (d, *J* = 8.0 Hz, 1 H),

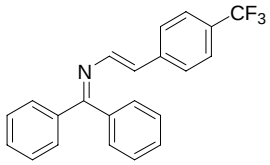
6.28 (d, J = 2.0 Hz, 1 H), 6.18 (dd, J = 8.0, 2.0 Hz, 1 H), 5.87 (s, 2 H). ^{13}C NMR (150 MHz, acetone-d_6) δ 168.2, 148.2, 146.7, 144.0, 140.2, 137.2, 131.1, 129.6, 129.5, 129.0, 128.65, 128.64, 114.1, 108.2, 103.0, 101.5. IR (neat, cm^{-1}) 3061 (w), 2891 (w), 1702 (w), 1613 (s), 1478 (s), 1239 (s), 1038 (s). HRMS (FAB) Calcd. for $C_{20}H_{16}O_2N$ ([M+H]$^+$): 302.1176. Found: 302.1167.

***N*-(Diphenylmethylene)-2-(4-chlorophenyl)-ethenamine.**



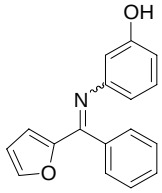
Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), *trans*-2-(4-chlorophenyl)]vinylboronic acid (22 mg, 0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2.5 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow solid (30 mg, 94%). TLC (R_f = 0.69, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). Mp = 137-139 °C (ether/hexanes). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.72-7.74 (m, 2 H), 7.56-7.61 (m, 3 H), 7.50 (d, J = 13.6 Hz, 1 H), 7.39-7.47 (m, 3 H), 7.28-7.36 (m, 6 H), 7.01 (d, J = 13.6 Hz, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 167.6, 139.9, 138.2, 136.7, 136.1, 133.2, 131.0, 130.5, 129.6, 129.27, 129.26, 129.25, 129.2, 128.7, 128.6. IR (neat, cm^{-1}) 3061 (w), 1702 (m), 1540 (s), 1490 (s), 1320 (s), 1096 (s), 695 (s). HRMS (FAB) Calcd. for $C_{21}H_{17}N^{35}Cl$ ([M+H]$^+$): 318.1044. Found: 318.1053.

***N*-(Diphenylmethylene)-2-(4-(trifluoromethyl)phenyl)-ethenamine.**



Following the general procedure, benzophenone *O*-pentafluorobenzoyloxime (39 mg, 0.1 mmol), *trans*-2-[4-(trifluoromethyl)phenyl]vinylboronic acid (26 mg, 0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2.5 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a yellow oil (31 mg, 88%). TLC (R_f = 0.69, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^1H NMR (400 MHz, acetone-d_6) δ 7.74-7.76 (m, 2 H), 7.54-7.63 (m, 8 H), 7.41-7.51 (m, 3 H), 7.30-7.33 (m, 2 H), 7.08 (d, *J* = 13.2 Hz, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 168.8, 141.3, 139.9, 139.8, 136.6, 131.3, 129.9, 129.8, 129.4, 129.3, 129.28, 128.8, 127.5, 126.1 (q, *J* = 3.8 Hz). IR (neat, cm^{-1}) 3061 (w), 1613 (m), 1544 (m), 1324(s), 1119(s), 695(s). HRMS (FAB) Calcd. for $C_{22}H_{17}NF_3$ ($[M+H]^+$): 352.1308. Found: 352.1317.

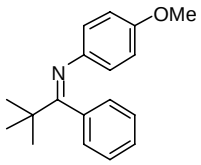
3-[(2-Furanylphenyl-methylene)amino]-phenol.



Following the general procedure, 2-furanylphenyl-methanone *O*-pentafluorobenzoyl oxime (38 mg, 0.1 mmol), 3-hydroxyphenylboronic acid (17 mg, 0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 2:1 hexanes:EtOAc) afforded the

title compound as a yellow oil (a mixture of *E/Z* isomers, 25 mg, 95%). TLC (R_f = 0.31, silica gel, buffered by Et_3N, 1:2 hexanes:EtOAc). ^1H NMR (400 MHz, acetone-d_6) δ 8.31 (br, 0.7 H), 8.17 (br, 1.4 H), 7.74-7.78 (m, 3.4 H), 7.47-7.58 (m, 3.5 H), 7.31-7.34 (m, 5.2 H), 7.25-7.27 (m, 3.5 H), 7.12 (t, *J* = 7.6 Hz, 1 H), 6.92 (t, *J* = 8.0 Hz, 1.7 H), 6.60-6.62 (m, 3.4 H), 6.54-6.57 (m, 1 H), 6.47-6.49 (m, 1 H), 6.37-6.40 (m, 1.8 H), 6.28-6.30 (m, 1.7 H), 6.22-6.25 (m, 2.5 H), 6.14-6.16 (m, 1.8 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 158.7, 158.1, 157.7, 156.5, 154.5, 154.3, 152.6, 148.2, 146.2, 144.4, 139.4, 135.7, 130.9, 130.3, 129.65, 129.64, 129.6, 129.4, 128.5, 128.4, 117.2, 116.9, 112.6, 112.4, 111.8, 110.7, 110.6, 110.2, 108.4, 106.1. IR (neat, cm^{-1}) 3142 (br, s), 1695 (s), 1586 (s), 1471 (s). HRMS (FAB) Calcd. for $C_{17}H_{14}O_2N$ ($[M+H]^+$): 264.1019. Found: 264.1011.

(*Z*)-N-α-*tert*-Butylbenzal-*p*-anisidine.[21]



Following the general procedure, (*Z*)-2,2-dimethyl-1-phenyl-1-propanone *O*-pentafluorobenzoyloxime (37 mg, 0.1 mmol), 4-methoxyphenylboronic acid (18 mg, 0.12 mmol) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 °C for 2 h. Purification by flash chromatography (silica gel, buffered by Et_3N, 40:1 hexanes:EtOAc) afforded the title compound as a colorless oil (18 mg, 69%). TLC (R_f = 0.52, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^1H NMR (400 MHz, acetone-d_6) δ 7.20-7.24 (m, 2 H), 7.14-7.18 (m, 1 H), 7.01-7.04 (m, 2 H), 6.58-6.61 (m, 2 H),

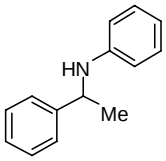
[21] Ramart-Lucas, P.; Hoch, J. *Bull. Soc. Chim.* **1936**, 3, 918.

6.46-6.50 (m, 2 H), 3.62 (s, 3 H), 1.24 (s, 9 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 179.7, 155.7, 145.4, 138.0, 128.6, 127.8, 127.6, 121.6, 113.8, 55.0, 40.6, 28.5. IR (neat, cm^{-1}) 2968 (s), 1637 (s), 1505 (s), 1239 (s). The *Z*-configuration was verified by NOE irradiation experiments.

General Procedure for Cu-catalyzed *N*-Imination of Boronic Acids with Oxime *O*-pentafluorobenzoates followed by *in situ* Reduction

Dry DMF (2 mL) was added to an argon flushed Schlenk tube containing oxime *O*-pentafluorobenzoate (0.1 mmol), boronic acid (0.12 mmol) and CuTC (2 mg, 0.01 mmol) [100 mg freshly-dried 4 Å M.S. powder is required for the alkyl-alkyl type of oxime *O*-pentafluorobenzoates]. The reaction mixture was stirred at 50 °C for 2 h. $NaBH_3CN$ (1.0 M in THF, 0.3 mmol) was then added *via* syringe followed by CF_3COOH (0.2 mmol) at 0 °C. The mixture was stirred for another 2 h at room temperature, basified with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The combined organic phase was sequentially washed with saturated aqueous solution of $NaHCO_3$ and brine, and then dried over $MgSO_4$. After evaporation of the solvent, the residue was subjected to flash chromatography giving the desired product.

α-Methyl-*N*-phenyl-benzenemethanamine.[22]

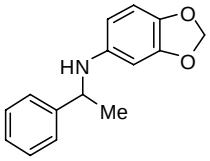


Following the general procedure, (*E*)-1-phenyl-ethanone *O*-pentafluorobenzoyloxime (33

[22] Khedkar, V.; Tillack, A.; Beller, M. *Org. Lett.* **2003**, *5*, 4767.

mg, 0.1 mmol), phenylboronic acid (18 mg, 0.15 mmol) and CuTC (2 mgm 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (silica gel, 15:1 hexanes:EtOAc) afforded the title compound as a light yellow oil (18 mg, 94%). TLC (R_f = 0.40, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.37 (m, 4 H), 7.20-7.24 (m, 1 H), 7.06-7.10 (m, 2 H), 6.61-6.65 (m, 1 H), 6.49-6.51 (m, 2 H), 4.48 (q, *J* = 6.4 Hz, 1 H), 4.02 (br, 1 H), 1.51 (d, *J* = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 145.0, 129.1, 128.6, 126.9, 125.8, 117.3, 113.4, 53.6, 25.0. IR (neat, cm^{-1}) 3408 (m), 1602 (s), 1505 (s).

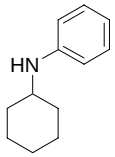
Benzo[1,3]dioxol-5-yl-(1-phenyl-ethyl)-amine.



Following the general procedure, (*E*)-1-phenyl-ethanone *O*-pentafluorobenzoyloxime (33 mg, 0.1 mmol), 3, 4-methylenedioxyphenylboronic acid (20 mg, 0.12 mmol) and CuTC (2 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (silica gel, 15:1 hexanes:EtOAc) afforded the title compound as a light yellow oil (18 mg, 76%). TLC (R_f = 0.11, silica gel, buffered by Et_3N, 20:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.34 (m, 4 H), 7.18-7.22 (m, 1 H), 6.54 (d, *J* = 8.0 Hz, 1 H), 6.12 (d, *J* = 2.0 Hz, 1 H), 5.91 (dd, *J* = 8.0, 2.0 Hz, 1 H), 5.78 (q, *J* = 1.2 Hz, 2 H), 4.37 (q, *J* = 6.8 Hz, 1 H), 3.82 (br, 1 H), 1.47 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 145.2, 143.0, 139.3, 128.6, 126.9, 125.8, 108.5, 105.0, 100.4, 96.3, 54.3, 25.1. IR (neat, cm^{-1}) 3412 (w), 3026 (w), 2876 (w), 1505 (s), 1208 (s), 1038 (s). HRMS (FAB) Calcd.

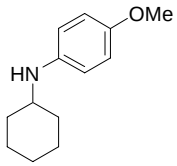
for $C_{15}H_{16}O_2N$ ($[M+H]^+$): 242.1176. Found: 242.1171.

_N_-Cyclohexyl-benzenamine.[23]



Following the general procedure, cyclohexanone *O*-pentafluorobenzoyloxime (31 mg, 0.1 mmol), phenylboronic acid (15 mg, 0.12 mmol) and CuTC (2 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (silica gel, 5:1 hexanes:EtOAc) afforded the title compound as a light yellow oil (13 mg, 75%). TLC (R_f = 0.70, silica gel, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11-7.15 (m, 2 H), 6.61-6.66 (m, 1 H), 6.56-6.58 (m, 2 H), 3.49 (br, 1 H), 3.19-3.25 (m, 1 H), 2.02-2.05 (m, 2 H), 1.71-1.77 (m, 2 H), 1.61-1.66 (m, 1 H), 1.08-1.40 (m, 5 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.4, 129.2, 116.8, 113.1, 51.6, 33.5, 25.9, 25.0. IR (neat, cm^{-1}) 3401 (w), 3053 (w), 2930 (s), 2853 (s), 1602 (s), 1505 (s), 1320 (s).

_N_-Cyclohexyl-4-methoxy-benzenamine.[24]



Following the general procedure, cyclohexanone *O*-pentafluorobenzoyloxime (31 mg, 0.1 mmol), 4-methoxyphenylboronic acid (18 mg, 0.12 mmol) and CuTC (2 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (silica gel, 5:1

[23] Rao, H.; Jin, Y.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem. Eur. J.* **2006**, *12*, 3636.
[24] Sato, S.; Sakamoto, T.; Miyazawa, E.; Kikugawa, Y. *Tetrahedron* **2004**, *60*, 7899.

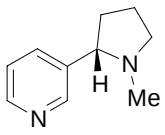
hexanes:EtOAc) afforded the title compound as a light yellow oil (11 mg, 53%). TLC (R_f = 0.52, silica gel, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.74 (dd, *J* = 6.8, 2.4 Hz, 2 H), 6.54 (dd, *J* = 6.8, 2.4 Hz, 2 H), 3.72 (s, 3 H), 3.18 (br, 1 H), 3.14 (m, 1 H), 2.00-2.04 (m, 2 H), 1.70-1.76 (m, 2 H), 1.60-1.65 (m, 1 H), 1.08-1.38 (m, 5 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 141.6, 114.9, 114.8, 55.8, 52.8, 33.6, 26.0, 25.1. IR (neat, cm^{-1}) 3389 (w), 2926 (s), 2853 (s), 1513 (s), 1239 (s).

Chapter 2 Pyridine Synthesis through a Cross-coupling, Electrocyclization, and Oxidation Cascade Reaction

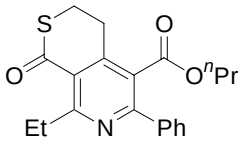
2.1 Introduction and Background

The first pyridine base, picoline, was isolated from the pyrolysis oil of bone by Anderson in 1846. During the following 161 years, pyridine has taken an important role in pharmaceutical industry, synthetic chemistry, biological chemistry and material science.[1] For example, pyridine and 4-dimethylaminopyridine (DMAP) are among the most commonly utilized reagents. The pyridine nucleus is ubiquitous in natural products, drugs, and functional ligands as shown in Figure 2.1.

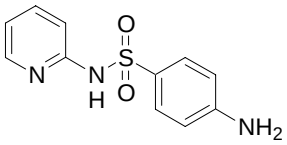
Figure 2.1 Pyridine Nucleus Examples



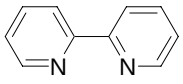
nicotine



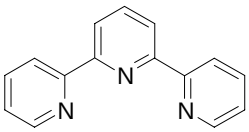
A3 adenosine receptor antagonist (antiflammatory, antiasthmatic)



sulfapyridine (antibacterial)



bipyridine



terpyridine

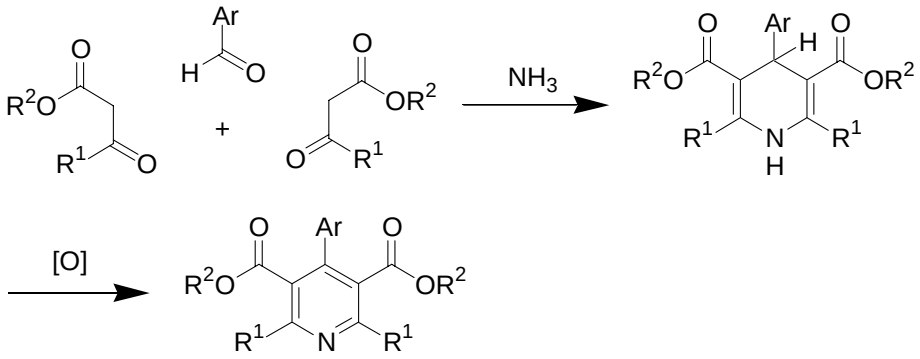
Although many methods of pyridine syntheses have been developed for more than one hundred years, the basic types of pyridine synthesis are limited. Most approaches are based on the condensation of carbonyl compounds or cycloaddition reactions.

For the condensation of carbonyl compounds to pyridines, representative methods

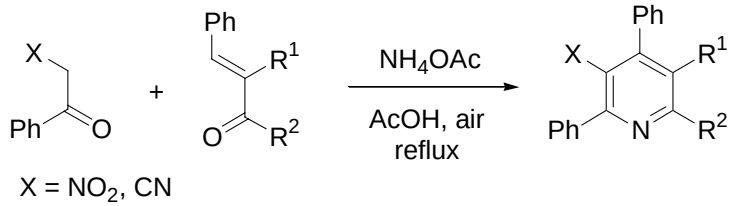
are Hantzsch synthesis,[2] Kröhnke annulation[3] and Bohlmann-Rahtz synthesis.[4]

Hantzsch synthesis is of great synthetic significance for the preparation of highly-substituted pyridines despite its serious limitation to carboxyl substituents at the 3- and 5-positions and an aryl substituent at the 4-position of the resulting pyridine nucleus. The initial product in the reaction is a dihydropyridine which can be oxidized to a pyridine in a subsequent step (Scheme 2.1). A modern variation allows for the synthesis of unsymmetrical pyridines with full regiochemical control of substituents by pre-forming the enone intermediate (Scheme 2.2).[5]

Scheme 2.1 Hantzsch Synthesis



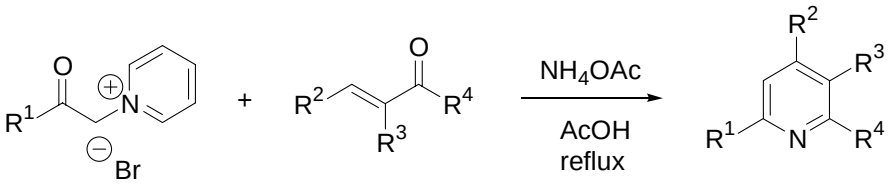
Scheme 2.2 Modern Modification of Hantzsch Synthesis



X = NO_2, CN

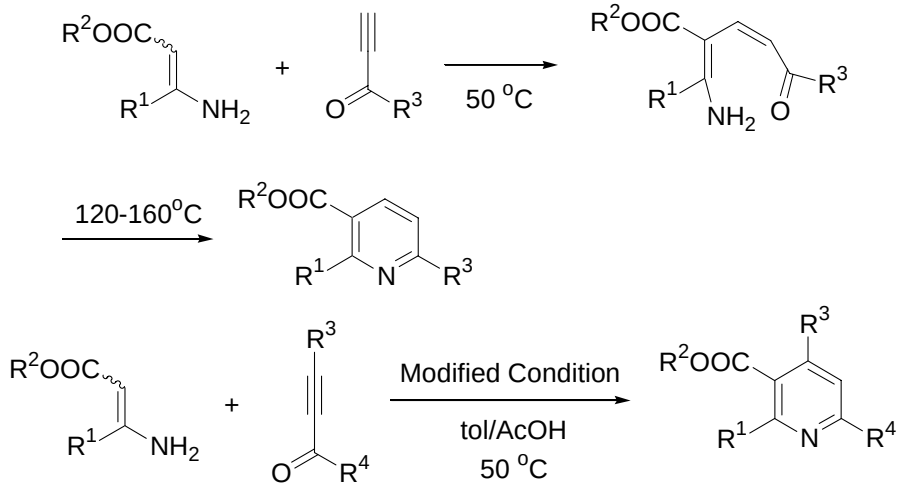
In the Kröhnke annulation, the aromatization of the pyridine ring proceeds through the elimination of the α-substituent instead of dehydrogenation (Scheme 2.3). The reaction is especially useful for the synthesis of 2, 4, 6-trisubstitued pyridines. However, the substitution at the 5-position is limited due to the instability of pyridinium salts with an extra α-substituent under the reaction conditions.

Scheme 2.3 Kröhnke Annulation



Bohlmann-Rahtz synthesis usually requires high temperature in the dehydration step which can be overcome by conducting the reaction under acidic conditions (Scheme 2.4).[6] This reaction efficiently yields 2, 3, 6-trisubstituted pyridines, although substituents at the 2-position are limited to carboxyl and no substituents can be introduced at the 5-position.

Scheme 2.4 Bohlmann-Rahtz Synthesis



For the cycoaddition reactions to pyridines, representative approaches are aza Diels-Alder reactions,[7] metal-catalyzed [2+2+2] cycloadditions[8] and electrocyclization of azatrienes.

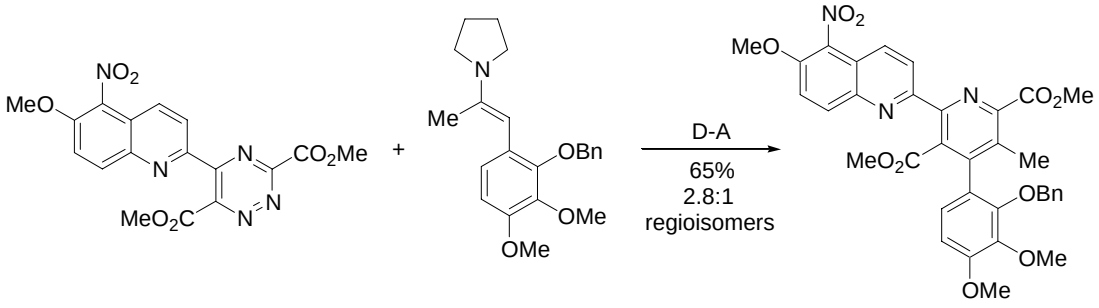
Diels-Alder reactions of azadienes, especially inverse electron demand reactions of heterocylic azadienes, are powerful for pyridine ring construction (Scheme 2.5).[9] However, activation of azadienes with additional substituents is usually required to achieve productive yields and special efforts are also needed to control the

regioselectivity.

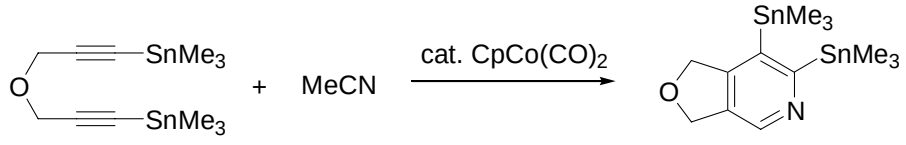
Cycloadditions of a wide variety of alkynes and nitriles catalyzed by transition metals afford highly functionalized pyridines under mild reaction conditions despite problems of regioselectivity in intermolecular reactions (Scheme 2.6).[10]

The strategy involving electrocyclization of azatrienes is intriguing. However, the application is limited due to the difficulty to access azatrienes. A few examples employing 1-azatrienes and 2-azatrienes have demonstrated the efficiency of this strategy (Scheme 2.7).[11] Most recently, Movassaghi and co-workers discovered a ruthenium-catalyzed cycloisomerization of 3-azadienynes that constructs 2, 3, 6-trisubstituted pyridines under mild conditions (Scheme 2.8a).[12] After that, a more general and powerful synthesis of highly substituted pyridines was also disclosed by the Movassaghi group, although strong acid (TfOH) was generated in the reaction (Scheme 2.8b).[13]

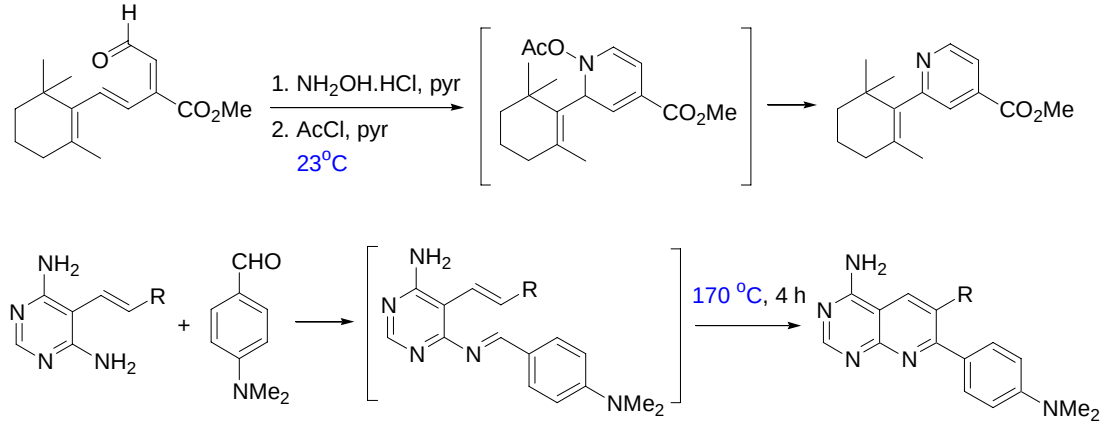
Scheme 2.5 Aza Diels-Alder Reaction



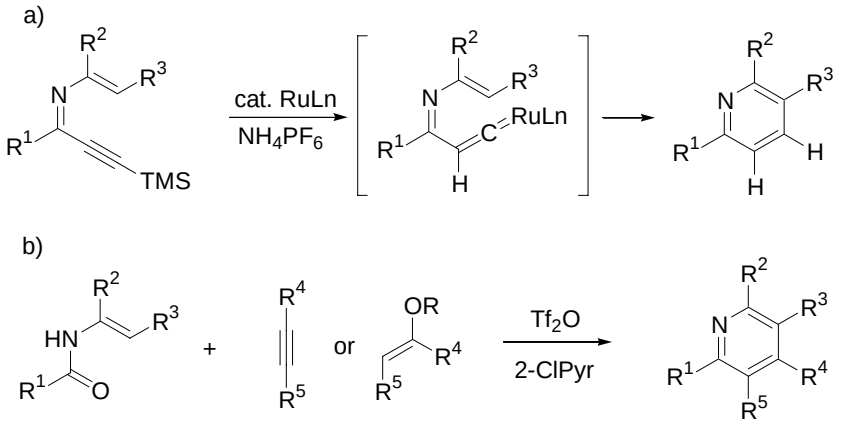
Scheme 2.6 Cobalt Catalyzed Cyclocaddition



Scheme 2.7 Electrocyclization of Azadienes



Scheme 2.8 Movassaghi Synthesis

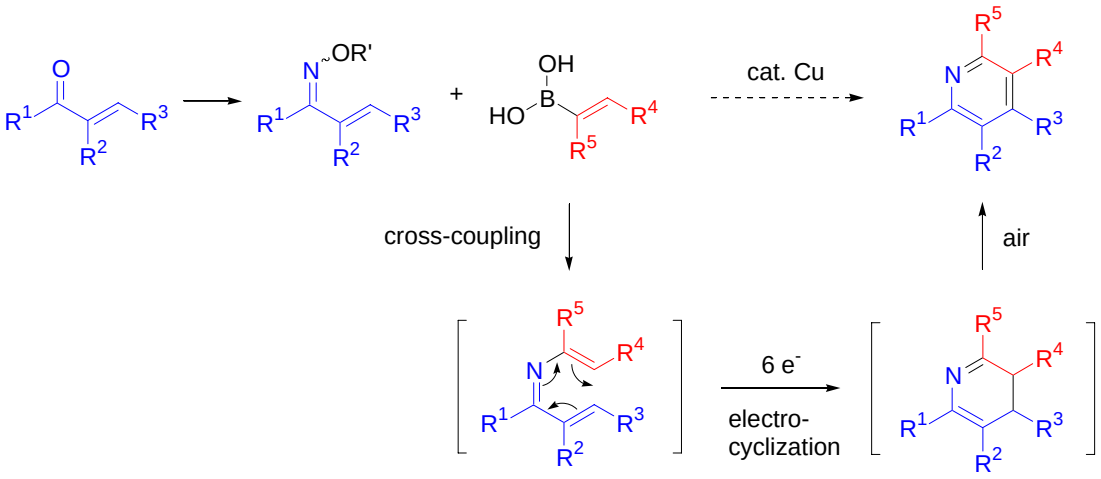


As discussed above, there still is a continuing demand to develop improved methods for pyridine synthesis because each synthesis available thus far is incompatible with certain functional groups or substitution patterns.

Inspired by the efficiency of electrocyclization of azatrienes for pyridine formation, we reasoned the pyridine ring could be derived from 3-azatrienes *via* a sequence of electrocyclization and oxidation (Scheme 2.9). Our newly-discovered C-N bond formation methodology allows for easy access to the requisite 3-azatrienes *via* the cross-coupling of α, β-unsaturated ketoxime *O*-pentafluorobenzoates and

alkenylboronic acids.[14] This cascade reaction would be compatible with a wide range of functionalities and realize various substitution patterns due to the efficient and mild method for C-N bond formation.

Scheme 2.9 Pyridine Synthesis Design through a Cascade of Cross-Coupling, Electrocyclization, and Oxidation

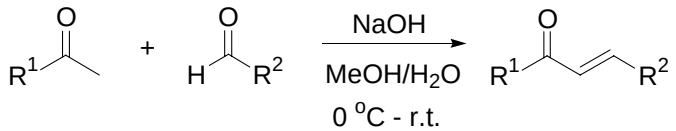


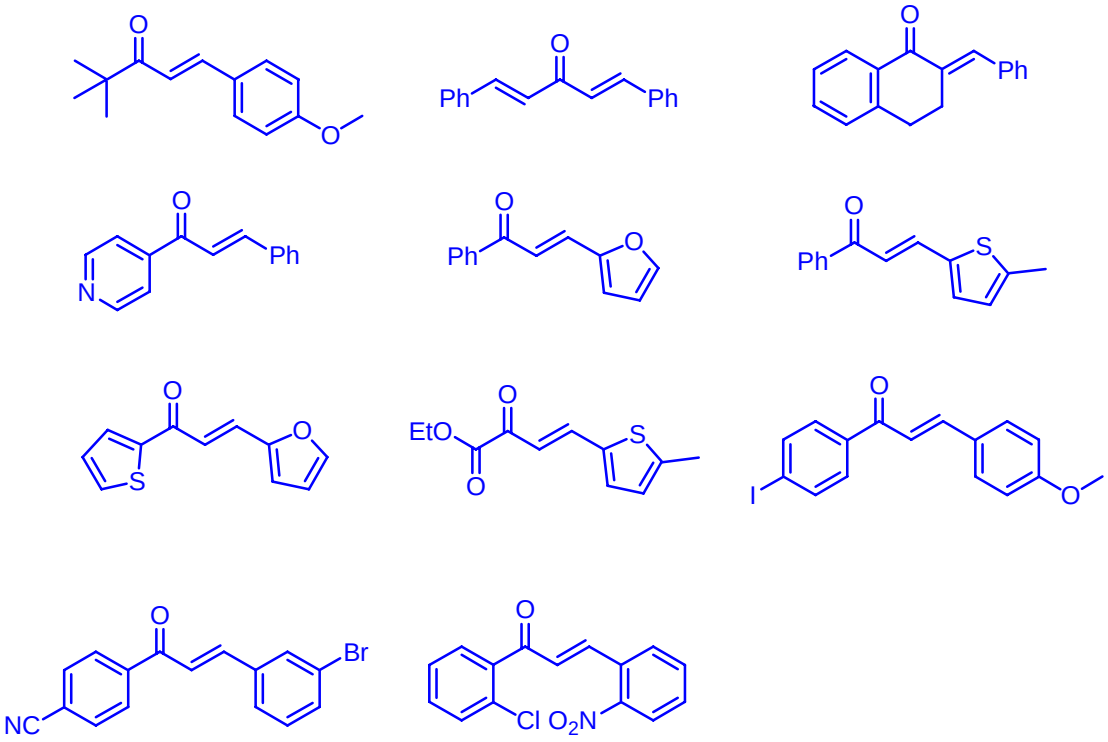
2.2 Results and Discussion

2.2.1 Preparation of α, β-Unsaturated Ketoxime O-Pentafluorobenzoates

The α, β-unsaturated ketoxime *O*-pentafluorobenzoates were synthesized starting with the corresponding α, β-unsaturated ketones. Generally, α, β-unsaturated ketones were readily prepared by the Claisen-Schmidt condensation of the corresponding ketone and aldehyde (Scheme 2.10).[15]

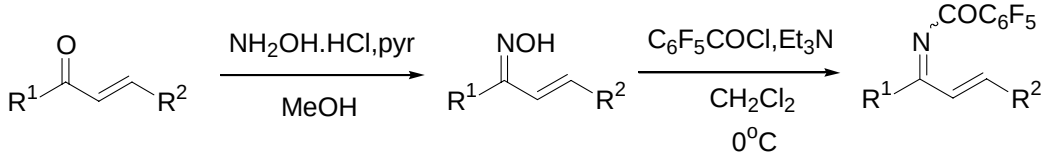
Scheme 2.10 Preparation of α, β-Unsaturated Ketones by Claisen-Schmidt Condensation

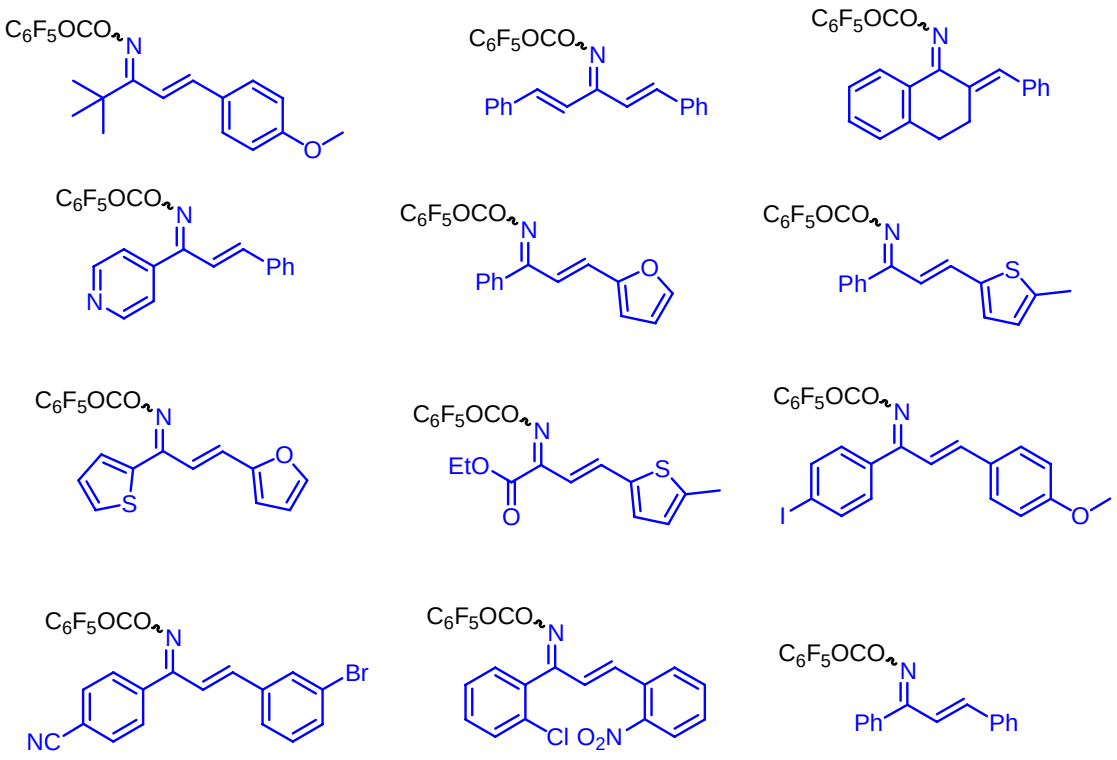




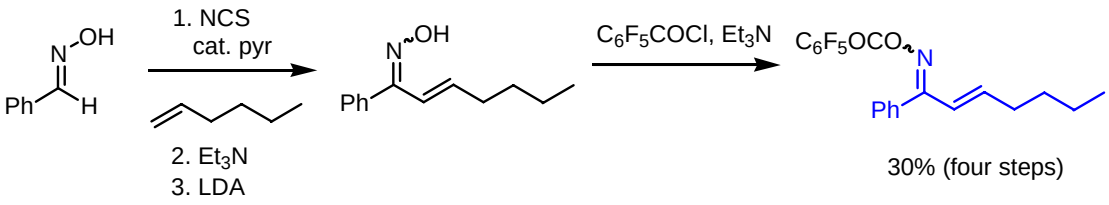
Condensation of the α, β-unsaturated ketones with hydroxylamine in methanol gave the oximes. After simple acylation by treatment with pentafluorobenzoyl chloride and triethylamine in dichloromethane at 0 ^{o}C, the desired α, β-unsaturated ketoxime *O*-pentafluorobenzoates were obtained (Scheme 2.11). 1-Phenyl-2-hepten-1-one oxime *O*-pentafluorobenzoate was prepared by a sequence of 1, 3-dipolar cycloaddition, base-induced elimination, and acylation in 30% yield (Scheme 2.12).

Scheme 2.11 Preparation of α, β-Unsaturated Ketoxime *O*-pentafluorobenzoates





Scheme 2.12 Preparation of 1-Phenyl-2-hepten-1-one Oxime *O*-Pentafluorobenzoate

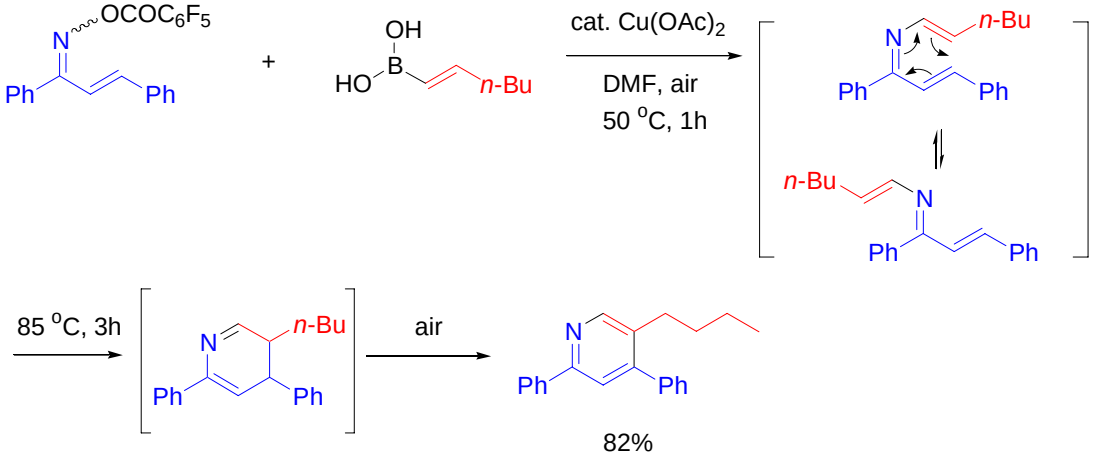


2.2.2 *Pyridine Synthesis from Alkenylboronic Acids*

Once α, β-unsaturated ketoxime *O*-pentafluorobenzoates were in hand, they were exposed to the *N*-imination reaction conditions. A mixture of 2-benzylideneacetophenone oxime *O*-pentafluorobenzoate and *trans*-1-hexen-1-ylboronic acid with 10 mol% $Cu(OAc)_2$ in DMF was heated at 50 ^{o}C (Scheme 13). After 1 hour, starting materials were completely transformed to a new

spot (as monitored by TLC) which was assumed to be the 3-azatriene intermediate. Then, the temperature was increased to 85 °C to enforce the electrocyclization. Heating at 85 °C for 3 hours under air afforded the desired pyridine product in 82% yield. As expected, both geometric isomers of the α, β-unsaturated ketoxime *O*-pentafluorobenzoate participated in the reaction.

Scheme 13 First Attempt to Pyridine Synthesis

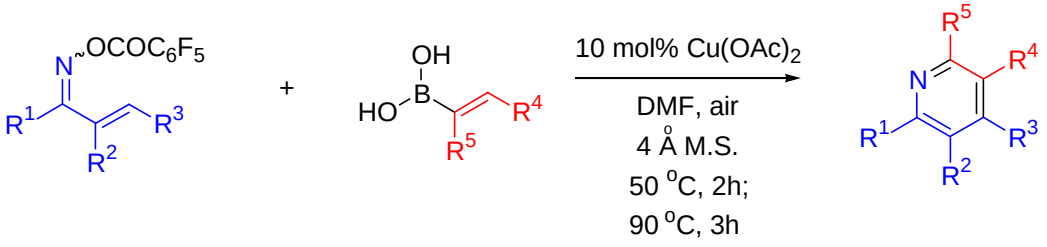


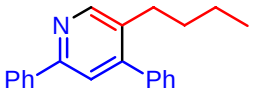
Encouraged by the initial success, the conditions for this new method were optimized. It was found that the addition of 4 Å molecular sieves gave better yields by minimizing competitive hydrolysis of the 3-azatrienes at the higher temperature needed for electrocyclization owing to water generated *in situ* from boronic acid – boroxine equilibrium. A reaction temperature of 90 °C was effective for most substrates to enforce the electrocyclization, although higher temperature was required in a few cases. Finally, the optimal conditions were revealed to be 50 °C for 2 hours for the cross-coupling followed by 90 °C for 3 hours for the electrocyclization.

Using the optimized conditions, the scope of this new methodology was examined. The scope of this new methodology was demonstrated to be quite general as shown in Scheme 14. R^1 can be aryl, heteroaryl (electron-rich and

electron-deficient), alkenyl, alkyloxycarbonyl and *tert*-butyl. R^2 can be H and alkyl. R^3 can be aryl, heteroaryl and alkyl. R^4 can be aryl, heteroaryl and alkyl. R^5 can be H and alkyl. In principle this method has the potential to realize every kind of substitution pattern about the pyridine ring. This cascade reaction exhibits great efficiency by affording highly substituted pyridines in moderate to excellent yield (43-91%) starting from simple α, β-unsaturated ketoxime *O*-pentafluorobenzoates, alkenylboronic acids, and a cheap catalyst, $Cu(OAc)_2$. Most noteworthy is that a desired substituent can be selectively incorporated to the pyridine ring that would be fairly difficult to introduce *via* many other methods. The new method tolerates many functional groups, like chloride, bromide, ester, nitrile, and nitro. Particularly, iodide, which is sensitive to various reactions such as Suzuki, Stille coupling and Ullmann reaction, is compatible with the reaction conditions. Hence functionalization complementary to the classic cross-coupling methods can be achieved in this method and provide substrates for further elaboration. Amides are certainly tolerated since the reaction is conducted in DMF. As disclosed in our previous study, hydroxyl and aldedyde should also be compatible with the reaction conditions. These attributes would render this method very useful for the synthesis of highly functionalized molecules.

Scheme 14 A New Pyridine Synthesis Method from Alkenylboronic Acids





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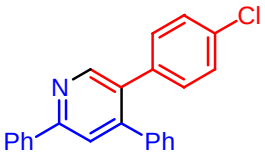
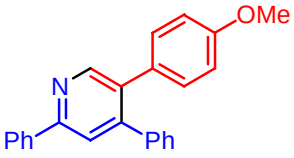


91%



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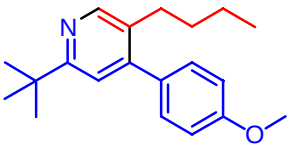

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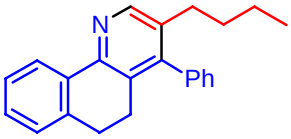

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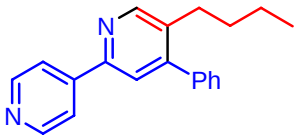

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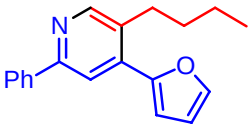

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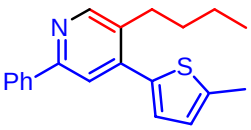

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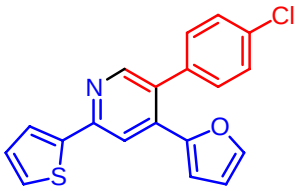

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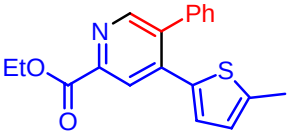

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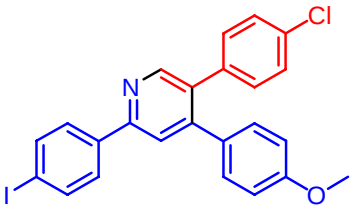

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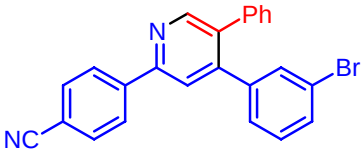

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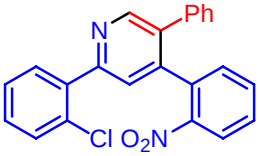
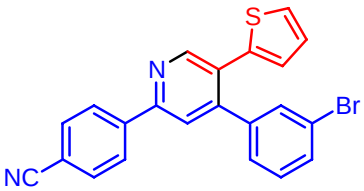


70%
(MW, 150°C, 0.5 h
for electrocyclization)



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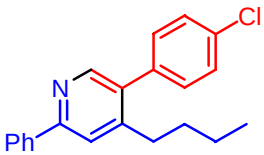

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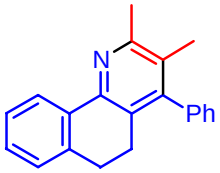

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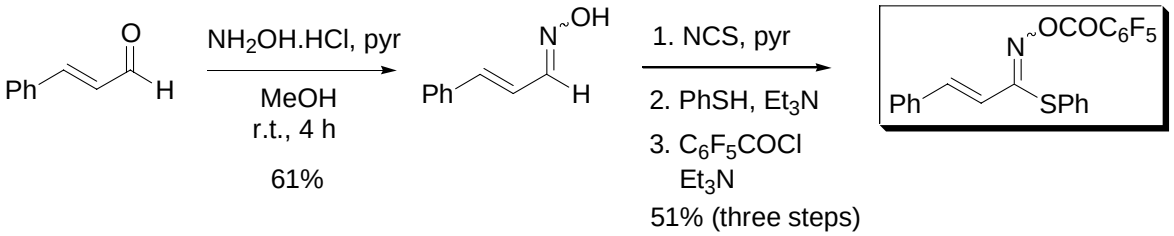
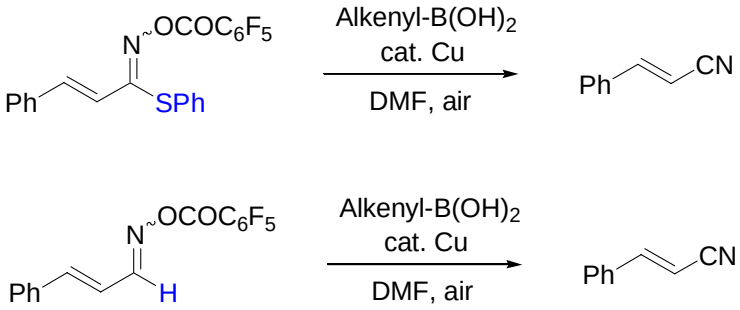
When R^1 is H or SPh, the reaction suffered β-elimination as uncovered in previous study (Scheme 15). One solution to circumvent this issue may employ a

hydrogen surrogate, like TMS. After pyridine formation, TMS could be either deprotected or functionalized.

Scheme 15 β-Elimination Issue

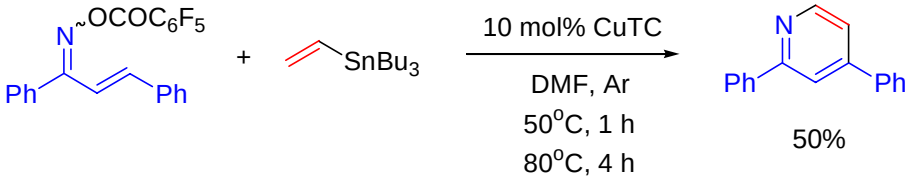




2.2.3 *Pyridine Synthesis from Alkenyl Stannanes*

Alkenyl stannanes are also suitable for pyridine synthesis as exemplified in Scheme 16. The yield is lower than alkenylboronic acids owing to the decreased efficiency in coupling between α, β-unsaturated ketoxime *O*-pentafluorobenzoates and alkenyl stannanes as revealed in the previous study.

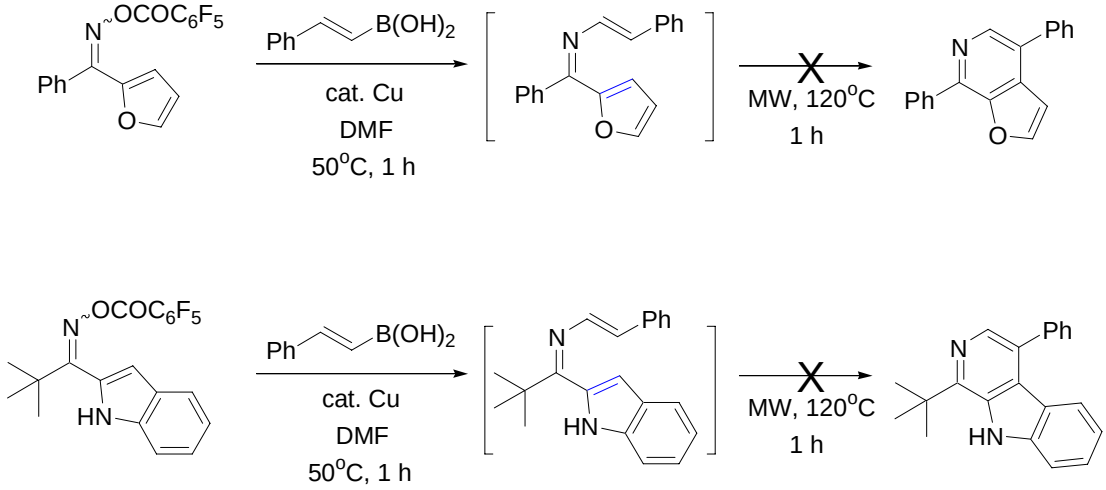
Scheme 16 Pyridine Synthesis from Alkenylstannanes



2.2.4 *Investigation of Electrocyclization Participation of 3-Azatrienes of Which One Double Bond is part of Aromatic Ring*

As an extension of this chemistry, it is interesting to explore whether the electrocyclization will happen when double bonds of the 3-azatrienes are part of aromatic systems. It was proved that furan and indole were not suitable as part of α, β-unsaturated ketoxime *O*-pentafluorobenzoates: the electrocyclization did not happen at 120 ^{o}C (Scheme 17).

Scheme 17 Extensional Study

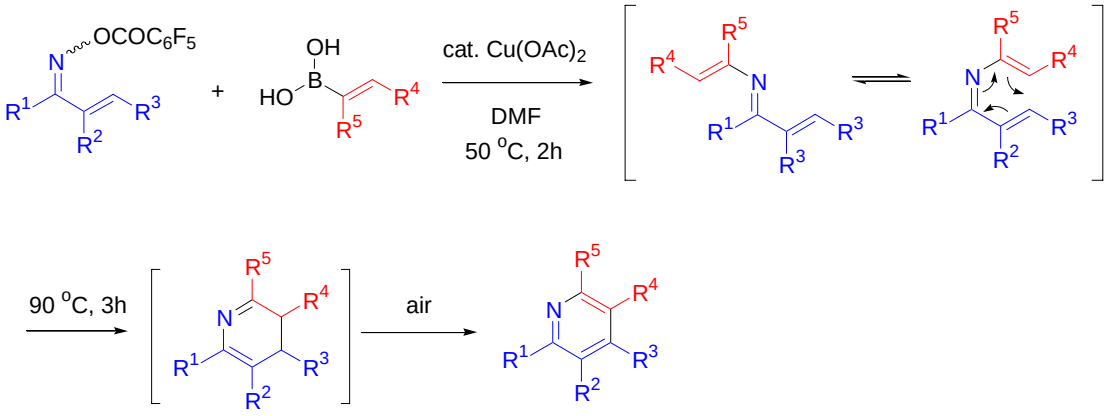


2.3 Mechanistic Speculation

The mechanism of this methodology is fairly obvious (Scheme 18). At first the coupling of α, β-unsaturated ketoxime *O*-pentafluorobenzoates and alkenylboronic acids with catalytic copper produces the 3-azadiene intermediate. The two geometric isomers equilibrate under the reaction conditions and the *cis*-isomer undergoes electrocyclization at high temperature to afford dihydropyridine which is oxidized to the pyridine upon exposure to air. Presumably, the inefficiency of this reaction when R^1 is methyl results from the low population of the *cis*-isomer in the equilibrium due to its small volume so that a competitive pathway ene-cyclization probably

predominates. Usually 90 °C is sufficient to induce electrocyclization, however, sterically congested di-orthosubstituted substrates need 150 °C.

Scheme 18 Plausible Mechanism



2.4 Conclusion

In summary, a convergent method to prepare highly substituted pyridines has been disclosed by employing a cross-coupling, electrocyclization, and oxidation cascade reaction. Readily available starting materials, functionality tolerance, and diverse substitution patterns in the pyridine ring contribute to the power of this method. This method will especially enrich diversity-oriented synthetic tools for drug discovery.

2.5 References

[1] Henry, G. D. *Tetrahedron*. **2004**, *60*, 6043.

[2] Hantzsch, A. *Chem. Ber.* **1881**, *14*, 1637.

[3] Kroehnke, F. *Synthesis* **1976**, 1.

[4] Bohlmann, F.; Rahtz, D. *Chem. Ber.* **1957**, *90*, 2265.

[5] Robinson, J. M.; Ahmed, M.; Alaniz, N. J.; Boyles, T. P.; Brasher, C. D.; Floyd, K. A.; Holland, P. L.; Maruffo, L. D.; McMahan, T. L.; Middleton, S.; O'Hara, K. D.;

Pack, M. J.; Reynolds, B. D.; Rodriquez, R. R.; Sawyer, D. E.; Sharp, E.; Simpson, S. L.; Vanlandingham, C. L.; Velasquez, R. S.; Welch, B. M.; Wright, C. D. *J. Heterocycl. Chem.* **1998**, *35*, 65.

[6] Bagley, M. C.; Dale, J. W.; Bower, J. *Synlett* **2001**, 1149.

[7] (a) Boger, D. L. *Chem. Rev.* **1986**, *86,* 781. (b) Boger, D. L.; Panek, J. S. *J. Org. Chem.* **1981**, *46*, 2179. (c) Boger, D. L.; Panek, J. S.; Meier, Michael M. *J. Org. Chem.* **1982**, *47*, 895.

[8] Heller, B.; Hapke, M. *Chem. Soc. Rev.* **2007**, 36, 1085.

[9] Boger, D. L.; Panek, J. S.; Duff, S. R. *J. Am. Chem. Soc.* **1985, *107,*** 5745.

[10] Parnell, C. A.; Peter, K.; Vollhardt, C. *Tetrahedron* **1985**, *41*, 5791.

[11] (a) Tanaka, K.; Mori, H.; Yamamoto, M.; Katsumura, S. *J. Org. Chem.* **2001**, *66*, 3099. (b) Lee, C.; Jiang, M.; Cowart, M.; Gfesser, G.; Perner, R.; Kim, K. H.; Gu, Y. G.; Williams, M.; Jarvis, M. F.; Kowaluk, E. A.; Stewart, A. O.; Bhagwat, S. S. *J. Med. Chem.* **2001**, *44*, 2133.

[12] Movassaghi, M. Hill, M.D. *J. Am. Chem. Soc.* **2006**, *128*, 4592.

[13] Movassaghi, M.; Hill, M. D.; Ahmad, O. K. *J. Am. Chem. Soc.* **2007**, *129*, 10096.

[14] Liu, S.; Yu, Y.; Liebeskind, L.S. *Org. Lett.* **2007**, *9*, 1947.

[15] (a)Claisen, L.; Claparede, A. *Ber.* **1881**, *14*, 2460. (b) Schmidt, J. G. *Ber.* **1881**, *14*, 1459.

2.6 Experimental

General Methods

All reactions were performed under an atmosphere of dry argon in oven-dried glassware unless otherwise noted. Solvents (THF, DMF, MeOH, CH_2Cl_2 and toluene) for reaction media were ACS reagent grade and purchased from Aldrich. Solvents

were dried over 4 Å molecular sieves and titrated for water level with a Fisher Coulomatic K-F titrator before using. All solvents were purged with Ar before using unless otherwise noted. Hexanes, ethyl acetate (EtOAc), and ethyl ether (Et_2O) used for extraction and chromatography were obtained from EM Science and used as purchased. Solutions of $NH_3 \cdot H_2O$ refers to aqueous solution. Brine refers to a saturated aqueous solution of NaCl. Purification by preparative plate chromatography was performed on EM Science Kieselgel 0.5 mm/1 mm 60 F_{254} plates. Analytical thin-layer chromatography (TLC) was carried out using Merck Kieselgel 0.25 mm 60 F_{254} plates with visualization by UV or phosphomolybdic acid. ^1H NMR and ^{13}C NMR spectra were recorded on a Varian Inova 600 MHz or 400 MHz NMR spectrometer at room temperature in $CDCl_3$ or acetone-d_6 with the solvent residual peak as internal reference ($CDCl_3$: ^1H = 7.24 ppm, ^{13}C = 77.0 ppm; acetone-d_6: ^1H = 2.05 ppm, ^{13}C = 29.5 ppm) unless otherwise stated. ^{19}F NMR spectra were recorded on a Varian Inova 376 MHz NMR spectrometer at room temperature in $CDCl_3$ without a reference. Data are reported in the following order: chemical shifts (δ); multiplicities (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet)); coupling constants, *J* (Hz); integration. Infrared (IR) spectroscopy was performed on a Nicolet 380 FT-IR or ASI ReactIR 1000 spectrometer. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak 20-40%), and br (broad). Uncalibrated melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes. High resolution mass spectra were obtained on a JEOL JMS-SX102/SX102A/E

instrument.

Starting Materials

Et_2AlCl, LiHMDS, *n*-butyl lithium, *N*-chlorosuccinimide, 1-hexene, 2-butyne, benzenethiol, catecholborane, $HBBr_2{\cdot}SMe_2$, methanesulfonyl chloride, ethyl chloroformate, trimethylacetyl chloride, hydroxylamine hydrochloride, 1-tetralone, benzaldehyde, 2-furaldehyde, 5-methyl-2-thiophenecarboxaldehyde, 2-nitrobenzaldehyde, 4-methoxybenzaldehyde, 3-bromobenzaldehyde, *trans*-cinnamaldehyde, 2-acetylthiophene, 4-acetylbenzonitrile, 4'-iodoacetophenone, 4-acetylpyridine, 2'-chloroacetophenone, acetophenone, indole, pyruvic acid, 4-phenyl-3-buten-2-one, *trans*-chalcone, *trans*-2-phenylvinylboronic acid, *trans*-1-hexen-1-ylboronic acid, *trans*-2-(4-chlorophenyl)vinylboronic acid, *trans*-2-(4-methoxyphenyl)vinylboronic acid, $Cu(OAc)_2$, vinyl-tri-*n*-butylstannane, potassium hydroxide, sodium hydroxide, potassium carbonate were purchased from Aldrich and used as obtained. Palladium catalysts, CuI, Cu_2O were purchased from Strem Chemicals. (Trimethylsilyl)acetylene was purchased from GFS Chemicals and used as received. Pentafluorobenzoyl chloride was purchased from Alfa/Aesar. CuTC[1] and (2*Z*)-2-buten-2-ylboronic acid[2] were prepared according to the literature procedure.

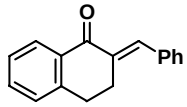
General Procedure for Preparation of α, β-Unsaturated Ketones by Claisen-Schmidt Condensation[3]

To a solution of the aldehyde (5 mmol) in 10 mL methanol (or ethanol) at 0 ^{o}C was

[1] Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312.
[2] Gamsey, S.; DeLaTorre, K.; Singaram, B. *Tetrahedron*: Asymmetry **2005**, *16*, 711.
[3] Agarwal, A.; Srivastava, K.; Puri, S. K.; Chauhan, P. M. S. *Bioorg. & Med. Chem.* **2005**, *13*, 4645.

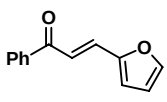
added slowly aqueous NaOH solution (10 wt %, 5 mL), followed by slow addition of the ketone (5 mmol) (slow addition of the ketone is essential to minimize side reactions). The reaction mixture was stirred at 0 ^{o}C to room temperature and monitored by TLC. The reaction was usually completed in 4 h and diluted with water. The precipitate was washed by water and minimal ethyl ether to afford pure product.

3,4-Dihydro-2-(phenylmethylene)-1(2*H*)-naphthalenone.[4]



Following the general procedure, 0.66 mL (5 mmol) 1-tetralone and 0.50 mL (5 mmol) benzaldehyde were reacted in ethanol. The product was obtained as an off-white solid in 1.01 g (Yield: 86%). TLC (R_f = 0.72, 5:1 hexanes: EtOAc). Mp = 104-105 °C (lit. {107 °C}). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 1 H), 7.86 (s, 1 H), 7.46-7.49 (m, 1 H), 7.39-7.44 (m, 4 H), 7.33-7.36 (m, 2 H), 7.23 (d, *J* = 5.4 Hz, 1 H), 3.11-3.13 (m, 2 H), 2.94 (t, *J* = 7.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9, 143.2, 136.6, 135.8, 135.4, 133.4, 133.3, 129.9, 128.5, 128.4, 128.20, 128.16, 127.0, 28.8, 27.2. IR (neat, cm^{-1}) 1668 (s), 1602 (s), 1297 (s).

3-(2-Furanyl)-1-phenyl-2-propen-1-one.[5]

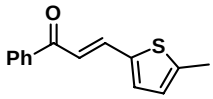


Following the general procedure, 0.58 mL (5 mmol) acetophenone and 0.41mL (5 mmol) 2-furaldehyde were reacted. The product was extracted with dichloromethane,

[4] Mitsui, S.; Senda, Y.; Saito, H. *Bull. Chem. Soc. Jp.* **1966**, *39*, 694.
[5] Drake, N. L.; Gilbert, H. W. *J. Am. Chem. Soc.* **1930**, *52*, 4965.

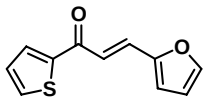
subject to chromatography (10:1 to 5:1, hexanes: EtOAc) and obtained as a yellow oil in 0.971 g (Yield: 98%). TLC (R_f = 0.55, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-8.02 (m, 2 H), 7.42-7.60 (m, 6 H), 6.70 (d, *J* = 3.2 Hz, 1 H), 6.49-6.50 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.8, 151.6, 144.9, 138.1, 132.7, 130.6, 128.6, 128.4, 119.2, 116.3, 112.7. IR (neat, cm^{-1}) 1664 (s), 1602 (s), 1552 (s), 1478 (s).

3-(5-Methyl-2-thienyl)-1-phenyl-2-propen-1-one.[6]



Following the general procedure, 0.58 mL (5 mmol) acetophenone and 0.54 mL (5 mmol) 5-methyl-2-thiophenecarboxaldehyde were reacted. The product was obtained as a yellow solid in 1.034 g (Yield: 91%). TLC (R_f = 0.61, 5:1 hexanes: EtOAc). Mp = 51-52 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.98 (m, 2 H), 7.85 (d, *J* = 15.2 Hz, 1 H), 7.53-7.57 (m, 1 H), 7.47 (t, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 15.2 Hz, 1 H), 7.14 (d, *J* = 4.0 Hz, 1 H), 6.72-6.73 (m, 1 H), 2.50 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9, 144.6, 138.4, 138.2, 137.7, 133.0, 132.6, 128.5, 128.3, 126.8, 119.4, 15.9. IR (neat, cm^{-1}) 3061 (m), 1652 (s), 1586 (s), 1532 (s), 1467 (s), 1355 (s).

3-(2-Furanyl)-1-(2-thienyl)-2-propen-1-one.[7]

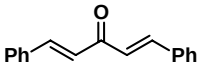


Following the general procedure, 0.54 mL (5 mmol) 2-acetylthiophene and 0.41 mL (5 mmol) 2-furaldehyde were reacted. The product was obtained as a yellow solid in

[6] Musumarra, G.; Ballistreri, F. P. *Org. Magn. Reson.* **1980**, *14*, 384.
[7] Shibata, K.; Katsuyama, I.; Matsui, M.; Muramatsu, H. *J. Heterocycl. Chem.* **1991**, *28*, 161.

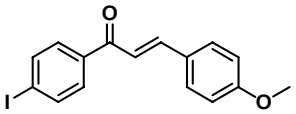
0.887 g (Yield: 87%). TLC (R_f = 0.48, 5:1 hexanes: EtOAc). Mp = 69-70 °C (lit. {71-72°C}). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 3.6, 1.2 Hz, 1 H), 7.65 (dd, *J* = 5.2, 1.2 Hz, 1 H), 7.59 (d, *J* =15.2 Hz, 1 H), 7.52 (d, *J* = 2.0 Hz, 1 H), 7.31 (d, *J* = 15.2 Hz, 1 H), 7.16 (dd, *J* = 5.2, 3.6 Hz, 1 H), 6.71 (d, *J* = 3.6 Hz, 1 H), 6.50 (dd, *J* = 3.6, 2.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.7, 151.4, 145.6, 145.0, 133.8, 131.7, 129.9, 128.2, 119.0, 116.4, 112.7. IR (neat, cm^{-1}) 3103 (m), 1648 (s), 1590 (s), 1552 (s), 1517 (s), 1478 (s), 1413 (s), 1231 (s).

1,5-Diphenyl-1,4-pentadien-3-one.[8]



Following the general procedure, 0.37 mL (5 mmol) acetone and 1.02 mL (10 mmol) benzaldehyde were reacted. The product was obtained as a yellow solid in 1.02 g (Yield: 87%). TLC (R_f = 0.53, 5:1 hexanes: EtOAc). Mp = 105-106 °C (lit. {110-112 °C}). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.0 Hz, 2 H), 7.60-7.62 (m, 4 H), 7.39-7.41 (m, 6 H), 7.08 (d, *J* = 15.6 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9, 143.3, 134.7, 130.5, 128.9, 128.4, 125.3. IR (neat, cm^{-1}) 3057 (m), 3030 (m), 1652 (s), 1625 (s), 1590 (s), 1494 (s), 1447 (s), 1339 (s), 1193 (s).

4'-Iodo-4-methoxy-chalcone.[9]

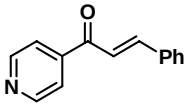


Following the general procedure, 1.230 g (5 mmol) 4'-iodoacetophenone and 0.61 mL (5 mmol) 4-methoxybenzaldehyde were reacted. The product was obtained as an

[8] Weber, W. M.; Hunsaker, L. A.; Abcouwer, S. F.; Deck, L. M.; Vander Jagt, D. L. *Bioorg. & Med. Chem.* **2005**, *13*, 3811.
[9] Sherif, S. *Can. J. Chem.* **1961**, *39*, 2563.

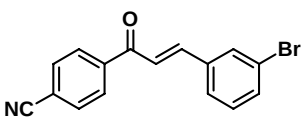
off-white solid in 1.662 g (Yield: 91%). TLC (R_f = 0.42, 5:1 hexanes: EtOAc). Mp = 163-164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.8 Hz, 2 H), 7.77 (d, *J* = 15.6 Hz, 1 H), 7.70 (d, *J* = 8.8 Hz, 2 H), 7.58 (d, *J* = 8.4 Hz, 2 H), 7.32 (d, *J* = 15.6 Hz, 1 H), 6.92 (d, *J* = 9.2 Hz, 2 H), 3.84 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.7, 161.8, 145.3, 137.8, 137.7, 130.3, 129.9, 127.4, 119.0, 114.4, 100.3, 55.4. IR (neat, cm^{-1}) 1660 (s), 1598 (s), 1579 (s), 1509 (s).

3-Phenyl-1-(4-pyridinyl)-2-propen-1-one.[10]



Following the general procedure, 0.55 mL (5 mmol) 4-acetylpyridine and 0.50 mL (5 mmol) benzaldehyde were reacted in 5 mL 10% aqueous NaOH solution without methanol. The product was extracted with dichloromethane, subject to chromatography (2:1, hexanes: EtOAc) and obtained as a yellow solid in 0.42 g (Yield: 40%). TLC (R_f = 0.18, 5:1 hexanes: EtOAc). Mp = 86-87 °C (lit. {89.5-90.0 °C}). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 4.4, 2.0 Hz, 2 H), 7.82 (d, *J* = 15.6 Hz, 1 H), 7.75 (dd, *J* = 4.4, 2.0 Hz, 2 H), 7.62-7.65 (m, 2 H), 7.39-7.44 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9, 150.8, 146.9, 144.3, 134.2, 131.2, 129.1, 128.7, 121.5, 121.1. IR (neat, cm^{-1}) 3061 (m), 3030 (m), 1668 (s), 1644 (s), 1606 (s), 1575 (s), 1339 (s), 1220 (s).

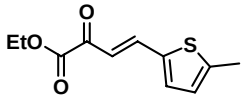
4-[3-(3-Bromophenyl)-1-oxo-2-propenyl]-benzonitrile.



[10] Mubofu, E. B.; Engberts, J. B. F. N. *J. Phys. Org. Chem.* **2004**, *17*, 180.

Following the general procedure, 1.452 g (10 mmol) 4-acetylbenzonitrile and 1.2 mL (10 mmol) 3-bromobenzaldehyde were reacted in 20 mL methanol. The product was obtained as a yellow solid in 3.1 g (Yield: 99%). TLC (R_f=0.36, 5:1 hexanes: EtOAc). Mp = 162-164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.09 (m, 2 H), 7.78-7.82 (m, 3 H), 7.74 (d, *J* =15.6 Hz, 1 H), 7.52-7.56 (m, 2 H), 7.44 (d, *J* = 15.6 Hz, 1 H), 7.30 (t, *J* = 8.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.7, 144.7, 141.0, 136.4, 133.8, 132.6, 131.0, 130.6, 128.9, 127.5, 123.2, 122.2, 118.0, 116.2. IR (neat, cm^{-1}) 3065 (w), 2227 (m), 1671 (s), 1610 (s), 1556 (s), 1312 (s), 1212 (s). HRMS (ESI) Calcd. for $C_{16}H_{11}O_1N_1Br_1$ ($[M+H]^+$): 312.0019. Found: 312.0014.

4-(5-Methyl-2-thienyl)-2-oxo-3-butenoic acid ethyl ester.[11,12]

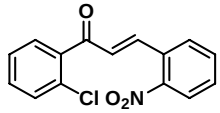


To a solution of potassium hydroxide (0.168 g, 85%, 3 mmol) in 2 mL methanol at 0 ^{o}C was added 5-methyl-2-thiophenecarboxaldehyde (0.216 mL, 2 mmol), followed by pyruvic acid (0.102 mL, 2 mmol). The reaction mixture was stirred at 0 ^{o}C to r.t. for 12 h. The brown solid was washed by a mixture of diethtyl ether and methanol. The following reaction was carried out without further purification. To a suspension of the brown solid in 10 mL CH_2Cl_2 at 0 ^{o}C was added dropwise ethyl chloroformate (0.21 mL, 2.2 mmol) and triethylamine (0.28 mL, 2.2 mmol). The reaction was allowed to be stirred at 0 ^{o}C to r.t. for 2 h. The reaction was quenched by brine. Extraction with CH_2Cl_2 afforded a dark brown residue which was subjected to chromatography purification (5:1, hexanes: EtOAc). The product was obtained as an orange oil in

[11] Slavinska, V.; Sile, Dz.; Korchagova, E.; Katkevich, M.; Lukevics, E. *Synth. Commun.* **1996**, *26*, 2229.
[12] Domagala, J. M. *Tetrahedron Lett.* **1980**, *21*, 4997.

0.251 g (Yield: 56%). TLC (R_f = 0.50, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 15.6 Hz, 1 H), 7.20 (d, *J* = 3.6 Hz, 1 H), 6.99 (d, *J* = 15.6 Hz, 1 H), 6.75 (dd, *J* =3.6, 1.2 Hz, 1 H), 4.35 (q, *J* = 7.2 Hz, 2 H), 2.51 (s, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.1, 162.2, 147.2, 141.0, 137.8, 134.9, 127.4, 117.9, 62.4, 16.1, 14.0. IR (neat, cm^{-1}) 1729 (s), 1683 (m), 1656 (m), 1583 (s), 1459 (s), 1254 (s).

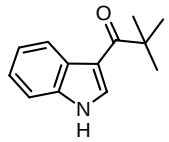
1-(2-Chlorophenyl)-3-(2-nitrophenyl)-2-propen-1-one.[13]



To a vigorously stirred suspension of 1.511 g (10 mmol) 2-nitrobenzaldehyde with 0.04 g (1 mmol) sodium hydroxide and 0.138 g (1 mmol) potassium carbonate at room temperature was added dropwise 1.3 mL (10 mmol) 2'-chloroacetophenone. The reaction was completed in 5 min. The precipitate was washed by water and minimal ethyl ether to afford the product as a yellow solid in 2.37 g (Yield: 82%). TLC (R_f = 0.33, 5:1 hexanes: EtOAc). Mp = 87-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.84 (d, *J* = 16.0 Hz, 1 H), 7.64-7.71 (m, 2 H), 7.50-7.57 (m, 2 H), 7.34-7.45 (m, 3 H), 6.98 (d, *J* = 16.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 148.2, 141.7, 138.0, 133.7, 131.8, 131.3, 130.7, 130.65, 130.63, 130.3, 129.5, 129.2, 126.9, 125.0. IR (neat, cm^{-1}) 3073 (m), 1660 (s), 1606 (s), 1571 (s), 1521 (s), 1343 (s), 1293 (s).

1-(1H-Indol-3-yl)-2,2-dimethyl-1-propanone.[14]

[13] Han, R.; Chen, S.; Wu, X. *Huaxue Shiji* **2006**, *28*, 243.
[14] Okauchi, T.; Itonaga, M.; Minami, T.; Owa, T.; Kitoh, K.; Yoshino, H. *Org. Lett.* **2000**, *2*, 1485.



To a solution of indole (0.586 g, 5 mmol) in 10 mL CH_2Cl_2 was added 10 mL Et_2AlCl (1.0 M in hexane, 10 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. To this solution was added dropwise trimethylacetyl chloride (0.92 mL, 7.5 mmol) at 0 °C. The resulting solution was stirred at 0 °C for 2 h and quenched by aqueous $NaHCO_3$. After extraction by EtOAc, the residue was purified by chromatography (2:1, hexanes : EtOAc) to give the product as a yellow solid in 1.03 g (Yield: 100%). TLC (R_f = 0.22, 5:1 hexanes: EtOAc). Mp = 158-160 °C (lit. {160-162 °C}[15]). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (br, 1 H), 8.49-8.51 (m, 1 H), 7.89 (d, *J* = 3.2 Hz, 1 H), 7.23-7.39 (m, 3 H), 1.40 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 135.4, 130.5, 127.2, 123.5, 122.9, 122.5, 114.0, 111.2, 44.1, 28.9. IR (neat, cm^{-1}) 3235 (br, s), 1610 (s), 1579 (s), 1521 (s), 1424 (s), 1243 (s), 1127 (s).

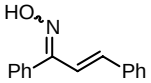
General Procedure for Preparation of α, β-Unsaturated Ketoximes

To a mixture of the α, β-unsaturated ketone (1 equiv) and hydroxylamine hydrochloride (2 equiv.) was added methanol and pyridine (3 equiv). The reaction mixture was stirred at room temperature (occasionally higher temperature required) and monitored by TLC. The reaction was usually completed in 24 h. The reaction mixture was extracted with CH_2Cl_2. Then the combined organic phase was sequentially washed by 1 N HCl, saturated aqueous solution of $NaHCO_3$ and brine, dried over $MgSO_4$. After evaporation of the solvent, the residue was subjected to a

[15] Wynne, J. H.; Lloyd, C. T.; Jensen, S. D.; Boson, S.; Stalick, W. M. *Synthesis* **2004**, 2277.

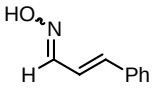
flash chromatography giving the corresponding α, β-unsaturated ketoxime.

1,3-Diphenyl-2-propen-1-one oxime.[16]



Following the general procedure, 0.208 g (1 mmol) *trans*-chalcone and 0.083 g (1.2 mmol) hydroxylamine hydrochloride with 0.18 mL (2.2 mmol) pyridine were reacted in 5 mL methanol at r.t. for 16 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as an off-white solid in 0.155 g (Yield: 70%). TLC (R_f =0.77, 2:1 hexanes: EtOAc). Mp = 85-88 °C (lit. {113-115 ^{o}C}). ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.49 ppm was set as 1. δ 9.52 (br, 1.6 H), 7.71 (d, *J* = 16.4 Hz, 1 H), 7.26-7.53 (m, 18.9 H), 7.08 (d, *J* = 16.4 Hz, 1.1 H), 6.82 (d, *J* = 16.4 Hz, 0.9 H), 6.49 (d, *J* = 16.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 157.8, 139.7, 137.0, 136.1, 134.7, 131.4, 129.2, 128.9, 128.72, 128.68, 128.59, 128.56, 128.4, 128.3, 127.5, 126.9, 125.6, 117.0. IR (neat, cm^{-1}) 3246 (br, s), 1621 (s), 1575 (m), 1494 (s), 1447 (s), 1336 (s), 1266 (s).

3-Phenyl-2-propenal oxime.[17]

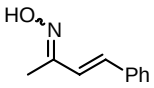


Following the general procedure, 1.26 mL (10.0 mmol) *trans*-cinnamaldehyde and 0.834 g (12.0 mmol) hydroxylamine hydrochloride with 1.78 mL (22.0 mmol) pyridine were reacted in 20 mL methanol at r.t. for 4 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow solid in 0.9 g (Yield: 61%). TLC (R_f = 0.51, 3:1 hexanes: EtOAc). Mp = 85-86 °C. ^{1}H NMR (400

[16] Unterhalt, B. *Arch. Pharm.* **1966**, *299*, 274.
[17] Narsaiah, A. V.; Nagaiah, K. *Adv. Synth. Catal.* **2004**, *346*, 1271.

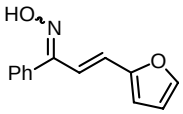
MHz, $CDCl_3$) δ 9.26 (br, 1 H), 7.94-7.96 (m, 1 H), 7.44-7.46 (m, 2 H), 7.28-7.37 (m, 3 H), 6.83-6.85 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 139.0, 135.7, 128.9, 128.8, 127.0, 121.6. IR (neat, cm^{-1}) 3281 (br, s), 1629 (m), 1444 (m).

4-Phenyl-3-buten-2-one oxime.[18]



Following the general procedure, 2.924 g (20.0 mmol) 4-phenyl-3-buten-2-one and 2.085 g (30.0 mmol) hydroxylamine hydrochloride with 4.0 mL (50.0 mmol) pyridine were reacted in 20 mL methanol at r.t. for 12 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow solid in 3.038 g (Yield: 94%). TLC (R_f = 0.32, 5:1 hexanes: EtOAc). Mp = 112-113 °C (lit. {116 °C}). ^1H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 7.62 ppm was set as 1. δ 9.66 (br, 4 H), 7.62 (d, *J* = 16.4 Hz, 1 H), 7.26-7.55 (m, 28 H), 6.83-6.97 (m, 10.5 H), 2.153 (s, 13.9 H), 2.149 (s, 3.4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 153.3, 136.6, 136.2, 136.1, 133.4, 129.1, 128.7, 128.4, 127.5, 126.8, 125.7, 116.8, 16.9, 9.7. IR (neat, cm^{-1}) 3246 (br, s), 1625 (s), 1494 (s), 1447 (s), 1374 (s), 1309 (s).

3-(2-Furanyl)-1-phenyl-2-propen-1-one oxime.[19]

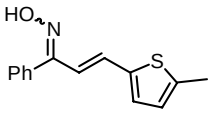


Following the general procedure, 0.991 g (5.0 mmol) 3-(2-furanyl)-1-phenyl-2-propen-1-one and 0.521 g (7.5 mmol) hydroxylamine hydrochloride with 1.01 mL (12.5 mmol) pyridine were reacted in 10 mL methanol at r.t. for 24 h.

[18] Talapatra, S. K.; Chaudhuri, P.; Talapatra, B. *Heterocycles* **1980**, *14*, 1279.
[19] Alberola, A.; Banez, J. M.; Calvo, L.; Rodriguez, M. T.; Sanudo, M. C. *J. Heterocycl. Chem.* **1993**, *30*, 467.

Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow oil in 0.835 g (Yield: 78%). TLC (R_f = 0.37, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.97 ppm was set as 1. δ 9.25 (br, 2.6 H), 7.54 (d, *J* = 16.4 Hz, 1.6 H), 7.39-7.49 (m, 13.1 H), 7.30-7.32 (m, 2 H), 6.97 (d, *J* = 16.0 Hz, 1 H), 6.57 (d, *J* = 16.4 Hz, 1.5 H), 6.41 (d, *J* = 1.6 Hz, 3 H), 6.37 (dd, *J* = 3.2, 1.6 Hz, 1.1 H), 6.28 (d, *J* = 3.2 Hz, 1 H), 6.24 (d, *J* = 16.0 Hz, 1.1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 157.4, 152.2, 143.8, 143.1, 134.5, 131.3, 129.2, 129.1, 128.9, 128.5, 128.44, 128.39, 126.5, 124.2, 123.9, 114.9, 112.4, 112.0, 111.8, 110.8. IR (neat, cm^{-1}) 3246 (br, s), 1671(s), 1625 (s).

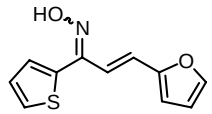
3-(5-Methyl-2-thienyl)-1-phenyl-2-propen-1-one oxime.



Following the general procedure, 1.142 g (5.0 mmol) 3-(5-methyl-2-thienyl)-1-phenyl-2-propen-1-one and 0.695 g (10.0 mmol) hydroxylamine hydrochloride with 1.21 mL (15.0 mmol) pyridine were reacted in 20 mL methanol at r.t. for 24 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow oil in 0.77 g (Yield: 67%). TLC (R_f = 0.41, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.47 ppm was set as 1. δ 8.82 (br, 1.7 H), 7.40-7.49 (m, 9.9 H), 7.29-7.33 (m, 3.4 H), 6.83-6.84 (m, 2.2 H), 6.77 (d, *J* = 14.8 Hz, 1.1 H), 6.58-6.72 (m, 3.8 H), 6.47 (d, *J* = 16.0 Hz, 1 H), 2.47 (s, 4.3 H), 2.45 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 157.7, 142.4, 141.2, 139.6, 139.5, 134.7, 132.7, 131.4, 130.2, 129.6, 129.2, 129.1, 128.9, 128.5, 128.41, 128.37, 128.2, 126.1, 126.0, 123.7, 114.8, 15.8, 15.7. IR (neat, cm^{-1}) 3227 (br, s), 1610 (s), 1471 (s),

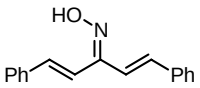
1444 (s), 1343 (s), 1100 (s). HRMS (ESI) Calcd. for $C_{14}H_{14}O_1N_1S_1$ ($[M+H]^+$): 244.0791. Found: 244.0788.

3-(2-Furanyl)-1- (2-thienyl)-2-propen-1-one oxime.



Following the general procedure, 0.613 g (3.0 mmol) 3-(2-furanyl)-1-(2-thienyl)-2-propen-1-one and 0.417 g (6.0 mmol) hydroxylamine hydrochloride with 0.73 mL (9.0 mmol) pyridine were reacted in 10 mL methanol at 50 ^oC for 24 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow oil in 0.301 g (Yield: 46%). TLC (R_f = 0.50, 5:1 hexanes: EtOAc). ^1H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.89 ppm was set as 1. δ 9.66 (br, 3.1 H), 7.52-7.57 (m, 2.2 H), 7.40-7.46 (m, 6 H), 7.36 (dd, *J* = 4.8, 1.2 Hz, 2.5 H), 7.30 (dd, *J* = 3.6, 1.2 Hz, 2.5 H), 6.97-7.14 (m, 7 H), 6.89 (d, *J* = 15.6 Hz, 1 H), 6.40-6.49 (m, 6.9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 152.07, 151.4, 149.3, 143.9, 143.1, 136.8, 130.8, 130.2, 130.0, 128.1, 127.3, 126.9, 126.3, 126.0, 122.8, 121.2, 114.6, 112.6, 112.1, 111.8, 111.1. IR (neat, cm^{-1}) 3239 (br, s), 1671 (m), 1625 (s). HRMS (ESI) Calcd. for $C_{11}H_{10}O_2N_1S_1$ ($[M+H]^+$): 220.0427. Found: 220.0425.

1,5-Diphenyl-1,4- pentadien-3-one oxime.[20]

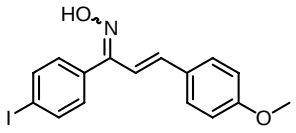


Following the general procedure, 0.469 g (2.0 mmol) 1,5-diphenyl-1,4-pentadien-3-one and 0.278 g (4.0 mmol) hydroxylamine hydrochloride with 0.485 mL

[20] Unterhalt, B. *Arch. Pharm.* **1966**, *299*, 274.

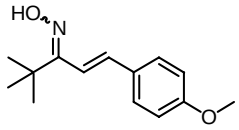
(6.0 mmol) pyridine were reacted in 5 mL methanol at r.t. for 18 h. Purification by flash chromatography (3:1, hexanes: EtOAc) afforded the product as a yellow solid in 0.3 g (Yield: 60%). TLC (R_f = 0.42, 5:1 hexanes: EtOAc). Mp = 137-139 °C (lit. {143-144 °C}). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (br, 1 H), 7.50-7.56 (m, 4 H), 7.28-7.41 (m, 7 H), 7.12 (dd, *J* = 16.0, 11.2 Hz, 2 H), 6.90 (d, *J* =16.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 137.6, 136.4, 136.1, 135.2, 129.1, 128.78, 128.74, 128.6, 127.4, 127.0, 122.1, 116.7. IR (neat, cm^{-1}). 3246 (br, s), 1698 (m), 1629 (s), 1602 (s), 1579 (s).

4'-Iodo-4-methoxy-chalcone oxime.



Following the general procedure, 0.728 g (2.0 mmol) 4'-iodo-4-methoxy-chalcone and 0.278 g (4.0 mmol) hydroxylamine hydrochloride with 0.485 mL (6.0 mmol) pyridine were reacted in 5 mL methanol at 50 ^{o}C for 24 h. Washing the solid by minial ether afforded the product as a white solid in 0.54 g (Yield: 71%). TLC (R_f =0.32, 5:1 hexanes: EtOAc). Mp = 158-160 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (br, 1 H), 7.75 (d, *J* = 8.4 Hz, 2 H), 7.48 (d, *J* = 16.4 Hz, 1 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 6.86 (d, *J* = 9.2 Hz, 2 H), 6.68 (d, *J* = 16.8, 1 H), 3.81 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 157.6, 139.2, 137.6, 134.5, 131.0, 129.0, 128.6, 114.3, 114.2, 95.3, 55.3. IR (neat, cm^{-1}) 3231 (br, m), 1602 (s), 1509 (s), 1247 (s), 1173 (s). HRMS (ESI) Calcd. for $C_{16}H_{15}O_2N_1I_1$ ($[M+H]^+$): 380.0142. Found: 380.0138.

1-(4-Methoxyphenyl)-4,4-dimethyl-1-penten-3-one oxime.[21]



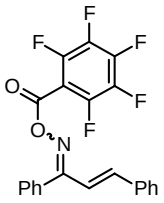
To a solution of pinacolone (0.693 mL, 5.0 mmol) in 10 mL THF at -78 ^{o}C was added dropwise LiHMDS (5 mL, 1.0 M in THF, 5.0 mmol). After stirring at -78 ^{o}C for 0.5 h, 4-methoxybenzaldehyde (0.61 mL, 5.0 mmol) was added to the reaction mixture. After stirring at -78 ^{o}C for 1 h, MsCl (0.466 mL, 6.0 mmol) was added. The reaction mixture was stirred at -78 ^{o}C to r.t. for 1 h. Aqueous potassium hydroxide (5 mL, 40 wt%) was added. The reaction mixture was stirred further for 1 h at r.t. The residue obtained from extraction by dichloromethane was subjected to the next step. To a solution of the residue in 10 mL methanol was added hydroxylamine hydrochloride (0.42 g, 6.0 mmol) and pyridine (0.81 mL, 10.0 mmol). The reaction was stirred at r.t. for 24 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a colorless oil in 0.382 g (Yield: 33%). TLC (R_f = 0.49, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (br, 1 H), 7.51 (d, J =16.8 Hz, 1 H), 7.43 (d, J = 9.2 Hz, 2 H), 6.87 (d, J = 8.8 Hz, 2 H), 6.59 (d, J =16.8 Hz, 1 H), 3.81 (s, 3 H), 1.25 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 160.0, 138.8, 138.7, 129.7, 128.3, 128.2, 114.2, 114.1, 114.0, 55.33, 55.29, 37.5, 28.8. IR (neat, cm^{-1}) 3250 (br, s), 2968 (s), 1679 (m), 1606 (s), 1513 (s).

General Procedure for Preparation of α, β-Unsaturated Ketoxime *O*-pentafluorobenzoates

[21] Unterhalt, B.; Koehler, H.; Reinhold, H. J. *Arch. Pharm.* **1978**, *311*, 604.

To the α, β-unsaturated ketoxime (1.0 equiv) in CH_2Cl_2 at 0 °C was added dropwise pentafluorobenzoyl chloride (1.2 equiv) followed by Et_3N (2.0 equiv). After stirring for 0.5 h at 0 °C the reaction was quenched with a saturated aqueous solution of $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 and the organic phase was sequentially washed with saturated aqueous $NaHCO_3$ and brine and then dried over $MgSO_4$. After evaporation of the solvent the residue was subjected to flash chromatography giving the corresponding α, β-unsaturated ketoxime *O*-pentafluorobenzoate.

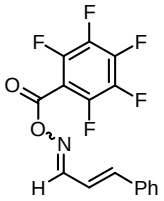
1,3-Diphenyl-2-propen-1-one oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.155 g (0.7 mmol) 1,3-diphenyl-2-propen-1-one oxime and 0.20 mL (1.4 mmol) triethylamine with 0.114 mL (0.83 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as an off-white solid in 0.207 g (Yield: 72%). TLC (R_f = 0.61, 3:1 hexanes: EtOAc). Mp = 124-126 °C. ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.68 ppm was set as 1. δ 7.25-7.61 (m, 26.6 H), 6.89 (d, *J* = 16.4 Hz, 1.4 H), 6.68 (d, *J* = 16.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 165.7, 144.8, 143.3, 135.2, 135.0, 132.3, 130.6, 130.4, 129.9, 129.8, 129.7, 129.0, 128.9, 128.6, 128.4, 128.0, 127.5, 123.5, 116.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.44 to -137.32 (m, 2 F), -148.05 to -147.78 (m, 1 F), -160.46 to -159.96 (m, 2 F). IR (neat, cm^{-1}) 3061 (w), 1760 (s), 1652 (m), 1625 (m), 1525 (s), 1498 (s), 1328 (s),

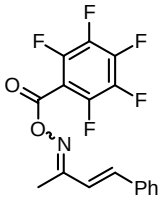
1193 (s). HRMS (ESI) Calcd. for $C_{22}H_{13}O_2N_1F_5$ ($[M+H]^+$): 418.0861. Found: 418.0859.

3-Phenyl-2-propenal oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.147 g (1.0 mmol) 3-phenyl-2-propenal oxime and 0.28 mL (2.0 mmol) triethylamine with 0.166 mL (1.2 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as an off-white solid in 0.291 g (Yield: 85%). TLC (R_f = 0.49, 5:1 hexanes: EtOAc). Mp = 141-143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 9.6 Hz, 1 H), 7.48-7.50 (m, 2 H), 7.37-7.41 (m, 3 H), 7.09 (d, *J* = 16.0 Hz, 1 H), 7.00 (dd, *J* = 16.0, 10.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 145.4, 130.3, 129.0, 127.6, 119.2. ^{19}F NMR (376 MHz, CDCl3) δ -137.28 to -137.17 (m, 2 F), -147.72 to -147.59 (m, 1 F), -160.21 to -160.05 (m, 2 F). IR (neat, cm^{-1}) 1749 (s), 1652 (m), 1633 (m), 1490 (s), 1204 (s). HRMS (ESI) Calcd. for $C_{16}H_9O_2N_1F_5$ ($[M+H]^+$): 342.0548. Found: 342.0542.

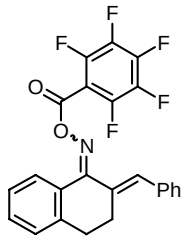
4-Phenyl-3-buten-2-one oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.806 g (5.0 mmol) 4-phenyl-3-buten-2-one oxime and 1.4 mL (10.0 mmol) triethylamine with 0.83 mL (6.0 mmol) pentafluorobenzoyl

chloride were reacted. Purification by flash chromatography (5:1 hexanes: EtOAc) afforded the product as a white solid in 1.6 g (Yield: 90%). TLC (R_f = 0.65, 5:1 hexanes: EtOAc). Mp = 177-179 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.51 (m, 2 H), 7.34 -7.40 (m, 3 H), 7.15 (d, *J* = 16.8 Hz, 1 H), 7.02 (d, *J* = 16.4 Hz, 1 H), 2.29 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 138.9, 135.2, 129.6, 129.0, 127.4, 123.2, 12.1. ^{19}F NMR (376 MHz, CDCl3) δ -137.31 to -137.20 (m, 2 F), -147.78 to -147.64 (m, 1 F), -160.24 to -160.08 (m, 2 F). IR (neat, cm^{-1}) 1760 (s), 1652 (m), 1633 (w), 1494 (s), 1324 (s), 1189 (s). HRMS (ESI) Calcd. for $C_{17}H_{11}O_2N_1F_5$ ($[M+H]^+$): 356.0705. Found: 356.0697.

3,4-Dihydro-2-(phenylmethylene)-1(2*H*)-naphthalenone oxime *O*-pentafluorobenzoate.[22]

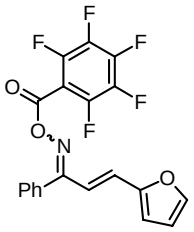


To a mixture of 3,4-dihydro-2-(phenylmethylene)-1(2*H*)-naphthalenone (2.343 g, 10.0 mmol) and benzylamine (3.3 mL, 30.0 mmol) in 25 mL toluene at 0 ^{o}C was added dropwise $TiCl_4$ (5 mL, 1.0 M in toluene, 5.0 mmol). The reaction was stirred for 24 h at 0 ^{o}C to r.t. After evaporation of the solvent, hydroxylamine hydrochloride (2.8 g, 40.0 mmol) and 10 mL pyridine was added. The reaction was stirred at r.t. for 24 h. The reaction mixture was washed by 1 N HCl and dried over $MgSO_4$. The afforded yellow oil was treated with pentafluorobenzoyl chloride (0.66 mL, 4.74 mmol) and

[22] Bouquillon, S.; Henin, F.; Muzart, J. *Synth. Commun.* **2001**, *31*, 39.

triethylamine (1.1 mL, 8.0 mmol) at 0 °C. The reaction was stirred at 0 °C to r.t. for 0.5 h. Purification by flash chromatography (10:1, hexanes: EtOAc) afforded the product as a yellow solid in 1.33 g (Yield: 30%). TLC (R_f = 0.57, 5:1 hexanes: EtOAc). Mp = 111-114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 8.47 ppm was set as 1. δ 8.47 (s, 1 H), 8.16 (dd, *J* = 8.0, 1.2 Hz, 5 H), 7.85 (d, *J* = 7.6 Hz, 3 H), 7.75-7.77 (m, 2.1 H), 7.26-7.55 (m, 70.5 H), 7.16-7.18 (m, 5.5 H), 2.81-2.97 (m, 33.4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 161.1, 158.0, 140.5, 139.8, 136.3, 136.0, 135.8, 132.4, 132.2, 131.2, 131.0, 130.9, 130.0, 129.5, 129.4, 129.1, 128.9, 128.70, 128.68, 128.5, 128.4, 128.3, 127.9, 127.6, 126.9, 126.2, 125.8, 30.5, 28.8, 26.9, 26.2. ^{19}F NMR (376 MHz, CDCl3) δ -137.57 to -137.26 (m, 2 F), -148.14 to -147.67 (m, 1 F), -160.33 to -160.06 (m, 2 F). IR (neat, cm^{-1}) 3061 (m), 1764 (s), 1652 (s), 1610 (m), 1525 (s), 1498 (s), 1324 (s), 1193 (s). HRMS (ESI) Calcd. for $C_{24}H_{15}O_2N_1F_5$ ($[M+H]^+$): 444.1018. Found: 444.1014.

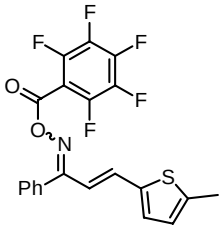
3-(2-Furanyl)-1- phenyl-2-propen-1-one oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.306 g (1.43 mmol) 3-(2-furanyl)-1-phenyl-2-propen-1-one oxime and 0.42 mL (3.0 mmol) triethylamine with 0.3 mL (2.2 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow oil in 0.598 g (Yield: 100%). TLC (R_f = 0.53, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$)

The integration of the signal at δ 7.15 ppm was set as 1. δ 7.39-7.57 (m, 15 H), 7.26-7.28 (m, 1.9 H), 7.15 (d, *J* = 16.4 Hz, 1 H), 6.63 (d, *J* = 16.0 Hz, 1.5 H), 6.41-6.52 (m, 5.9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 165.5, 156.6, 151.6, 151.3, 145.1, 144.4, 132.1, 130.9, 130.5, 129.8, 129.7, 129.6, 128.6, 128.4, 127.9, 121.4, 115.2, 114.5, 113.3, 112.5, 112.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.48 to -137.24 (m, 2 F), -148.17 to -148.05 (m, 1 F), -160.51 to -160.13 (m, 2 F). IR (neat, cm^{-1}) 1764 (s), 1652 (s), 1625 (s). HRMS (ESI) Calcd. for $C_{20}H_{11}O_3N_1F_5$ ($[M+H]^+$): 408.0654. Found: 408.0652.

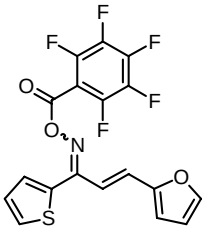
3-(5-Methyl-2-thienyl)-1- phenyl-2-propen-1-one oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.228 g (1.0 mmol) 3-(5-methyl-2-thienyl)-1-phenyl-2-propen-1-one oxime and 0.28 mL (2.0 mmol) triethylamine with 0.21 mL (1.5 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1 hexanes: EtOAc) afforded the product as a yellow solid in 0.450 g (Yield: 100%). TLC (R_f = 0.51, 5:1 hexanes: EtOAc). Mp = 104-105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 7.19 ppm was set as 1. δ 7.43-7.57 (m, 6.2 H), 7.26-7.29 (m, 1 H), 7.19 (d, *J* = 15.6 Hz, 1 H), 6.81-6.96 (m, 2.9 H), 6.63-6.70 (m, 2 H), 2.50 (d, *J*= 0.8 Hz, 2.9 H), 2.47 (s, 1.5 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 165.6, 156.5, 144.7, 143.5, 138.8, 138.4, 137.6, 136.1, 132.2, 131.8, 130.6, 130.4, 130.3, 129.8, 129.6, 128.6, 128.3, 127.9, 126.7, 126.4, 121.2,

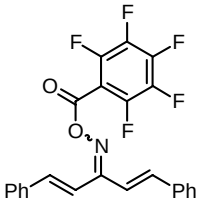
114.4, 15.9, 15.8. ^{19}F NMR (376 MHz, CDCl3) δ -137.51 to -137.29 (m, 2 F), -148.21 to -147.99 (m, 1 F), -160.53 to -160.11 (m, 2 F). IR (neat, cm^{-1}) 3065 (w), 1760 (s), 1652 (s), 1610 (s), 1498 (s), 1328 (s), 1193 (s). HRMS (ESI) Calcd. for $C_{21}H_{13}O_2N_1F_5S_1$ ([M+H]$^+$): 438.0582. Found: 438.0578.

3-(2-Furanyl)-1- (2-thienyl) -2-propen-1-one oxime *O*-pentafluorobenzoate.



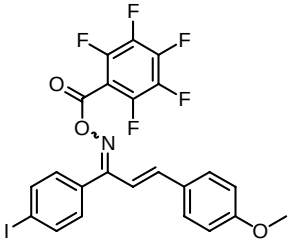
Following the general procedure, 0.2 g (0.9 mmol) 3-(2-furanyl)-1-(2-thienyl) -2-propen-1-one oxime and 0.25 mL (1.8 mmol) triethylamine with 0.19 mL (1.35 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow oil in 0.392 g (Yield: 100%). TLC (R_f = 0.37, 5:1 hexanes: EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 7.07 ppm was set as 1. δ 7.61 (dd, *J* = 4.8, 1.2 Hz, 0.6 H), 7.45-7.53 (m, 5.2 H), 7.31 (d, *J* = 16.0 Hz, 1.5 H), 7.12-7.16 (m, 2 H), 7.07 (d, *J* = 12.0 Hz, 1 H), 7.02 (d, *J* = 15.6 Hz, 1.5 H), 6.58 (d, *J* = 3.2 Hz, 1.4 H), 6.44-6.51 (m, 2.6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 157.3, 156.3, 151.6, 151.2, 145.0, 144.2, 133.7, 132.4, 131.6, 131.1, 129.9, 129.6, 127.6, 127.3, 126.8, 119.3, 115.0, 114.4, 113.2, 112.5, 112.2. ^{19}F NMR (376 MHz, CDCl3) δ -137.27 to -137.14 (m, 2 F), -148.05 to -147.84 (m, 1 F), -160.25 to -159.96 (m, 2 F). IR (neat, cm^{-1}) 1760 (s), 1652 (s), 1625 (s). HRMS (ESI) Calcd. for $C_{18}H_9O_3N_1F_5S_1$ ([M+H]$^+$): 414.0218. Found: 414.0214.

1,5-Diphenyl-1,4- pentadien-3-one oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.17 g (0.68 mmol) 1,5-diphenyl-1,4-pentadien-3-one oxime and 0.28 mL (2.0 mmol) triethylamine with 0.12 mL (0.82 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a white solid in 0.201 g (Yield: 67%). TLC (R_f = 0.55, 5:1 hexanes: EtOAc). Mp = 133-134 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.55 (m, 10 H), 7.16-7.30 (m, 3 H), 7.01 (d, J = 16.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 141.3, 140.2, 135.5, 135.0, 130.1, 129.6, 129.0, 128.9, 127.7, 127.5, 119.5, 116.5. ^{19}F NMR (376 MHz, CDCl3) δ -137.39 to -137.27 (m, 2 F), -147.79 to -147.65 (m, 1 F), -160.11 to -159.95 (m, 2 F). IR (neat, cm^{-1}) 1756 (s), 1637 (s). HRMS (ESI) Calcd. for $C_{24}H_{15}O_2N_1F_5$([M+H]$^+$): 444.1018. Found: 444.1013.

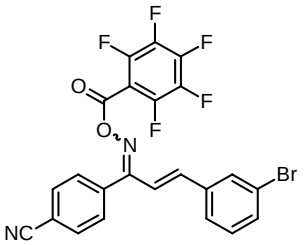
4'-Iodo-4-methoxy-chalcone oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.379 g (1.0 mmol) 4'-iodo-4-methoxy-chalcone oxime and 0.28 mL (2.0 mmol) triethylamine with 0.166 mL (1.2 mmol) pentafluorobenzoyl chloride were reacted. The solid was washed by ether and afforded the product as a white solid in 0.54 g (Yield: 95%). TLC (R_f = 0.55, 5:1

hexanes: EtOAc). Mp = 172-175 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.82 (m, 2 H), 7.31-7.43 (m, 5 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 6.80 (d, *J* = 16.4 Hz, 1 H), 3.83 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 161.6, 144.5, 137.8, 132.0, 131.5, 129.7, 127.5, 114.5, 114.1, 97.1, 55.4. ^{19}F NMR (376 MHz, CDCl3) δ -137.42 to -137.31 (m, 2 F), -147.83 to -147.69 (m, 1 F), -160.08 to -159.92 (m, 2 F). IR (neat, cm^{-1}) 1752 (s), 1652 (s), 1621 (s), 1602 (s). HRMS (ESI) Calcd. for $C_{23}H_{14}O_3N_1F_5I_1$ ($[M+H]^+$): 573.9933. Found: 573.9930.

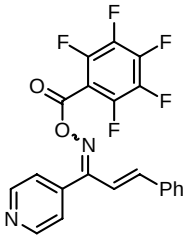
4-[3-(3-Bromophenyl)-1-oxo-2-propenyl]-benzonitrile oxime *O*-pentafluorobenzoate.



To a suspension of 4-[3-(3-bromophenyl)-1-oxo-2-propenyl]-benzonitrile (0.624 g, 2.0 mmol) and hydroxylamine hydrochloride (0.278 g, 4.0 mmol) in 5 mL methanol was added pyridine (0.485 mL, 6.0 mmol). The reaction was stirred at 60 ^{o}C for 18 h. After removal of solvent, the residue was washed by 1 N HCl and dried over $MgSO_4$. Then the residue was treated with 0.33 mL (2.4 mmol) pentafluorobenzoyl chloride and 0.42 mL (3.0 mmol) triethylamine at 0 ^{o}C for 0.5 h in dichloromethane. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a white solid in 0.365 g (Yield: 35%). TLC (R_f = 0.48, 5:1 hexanes: EtOAc). Mp = 185-189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.73 ppm was set as 1. δ 7.78-7.81 (m, 4.4 H), 7.71-7.73 (m, 2 H), 7.61 (t, *J* = 1.6 Hz, 1 H),

7.22-7.54 (m, 12.4 H), 6.73 (d, J = 16.8 Hz, 1 H), 6.50 (d, J = 16.4 Hz, 1.3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 163.6, 143.1, 141.8, 136.7, 136.6, 136.5, 135.0, 133.6, 133.0, 132.5, 132.4, 130.9, 130.7, 130.6, 130.5, 128.7, 126.4, 125.8, 124.1, 123.2, 123.1, 118.0, 117.9, 117.5, 114.6, 113.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.34 to -137.07 (m, 2 F), -146.88 to -146.59 (m, 1 F), -159.77 to -159.52 (m, 2 F). IR (neat, cm^{-1}) 2231 (m), 1760 (s), 1648 (s), 1625 (m). HRMS (ESI) Calcd. for $C_{23}H_{11}O_2N_2Br_1F_5$ ($[M+H]^+$): 520.9930. Found: 520.9930.

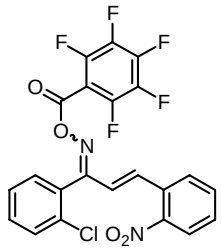
3-Phenyl-1-(4-pyridinyl)-2-propen-1-one oxime *O*-pentafluorobenzoate.



To a suspension of 3-phenyl-1-(4-pyridinyl)-2-propen-1-one (0.4 g, 1.9 mmol) and hydroxylamine hydrochloride (0.278 g, 4.0 mmol) in 5 mL methanol was added pyridine (0.485 mL, 6.0 mmol). The reaction was stirred at r.t. for 18 h. After removal of solvent, the residue was washed by 1 N HCl and dried over $MgSO_4$. Then the residue was treated with 0.33 mL (2.4 mmol) pentafluorobenzoyl chloride and 0.42 mL (3.0 mmol) triethylamine at 0 ^{o}C for 0.5 h in dichloromethane. Purification by flash chromatography (3:1, hexanes: EtOAc) afforded the product as a yellow solid in 0.437g (Yield: 55%). TLC (R_f = 0.20, 5:1 hexanes: EtOAc). Mp = 148-151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 6.59 ppm was set as 1. δ 8.86 (br, 2.8 H), 7.24-7.58 (m, 15.9 H), 6.84 (d, J = 16.4 Hz, 1 H), 6.59 (d, J = 16.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 163.5, 149.9, 145.1, 143.8, 134.7,

134.4, 130.9, 130.3, 129.1, 129.0, 128.1, 127.6, 122.1, 115.6. ^{19}F NMR (376 MHz, CDCl3) δ -137.36 to -137.02 (m, 2 F), -147.07 to -146.89 (m, 1 F), -159.92 to -159.64 (m, 2 F). IR (neat, cm^{-1}) 3061 (w), 1764 (s), 1652 (s), 1621 (s), 1525 (s), 1498 (s), 1324 (s), 1189 (s). HRMS (ESI) Calcd. for $C_{21}H_{12}O_2N_2F_5$ ($[M+H]^+$): 419.0814. Found: 419.0810.

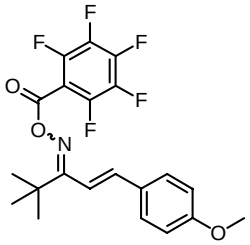
1-(2-Chlorophenyl)-3-(2-nitrophenyl)-2-propen-1-one oxime *O*-pentafluorobenzoate.



To a suspension of 1-(2-chlorophenyl)-3-(2-nitrophenyl)-2-propen-1-one (0.575 g, 2.0 mmol) and hydroxylamine hydrochloride (0.278 g, 4.0 mmol) in 5 mL methanol was added pyridine (0.485 mL, 6.0 mmol). The reaction was stirred at 60 ^{o}C for 18 h. After removal of solvent, the residue was washed by 1 N HCl and dried over $MgSO_4$. Then the residue was treated with 0.33 mL (2.4 mmol) pentafluorobenzoyl chloride and 0.42 mL (3.0 mmol) triethylamine at 0 ^{o}C for 0.5 h in dichloromethane. Purification by flash chromatography (3:1, hexanes: EtOAc) afforded the product as a light yellow solid in 0.328 g (Yield: 33%). TLC (R_f = 0.43, 5:1 hexanes: EtOAc). Mp= 149-151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 7.12 ppm was set as 1. δ 7.98-8.03 (m, 2.4 H), 7.64-7.73 (m, 4.9 H), 7.38-7.55 (m, 11.7 H), 7.25-7.27 (m, 1.5 H), 7.20 (d, *J* = 16.0 Hz, 1.5 H), 7.12 (d, *J* = 16.0 Hz, 1 H), 7.07 (d, *J* = 16.0 Hz, 1.5 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 163.3, 147.9, 147.7, 140.3,

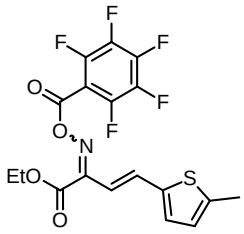
138.4, 133.9, 133.8, 131.7, 131.6, 131.3, 131.2, 131.1, 130.7, 130.4, 130.1, 130.0, 129.9, 129.8, 129.2, 128.79, 128.81, 127.1, 126.92, 126.90, 125.1, 125.0, 120.4. ^{19}F NMR (376 MHz, CDCl3) δ -136.99 to -136.82 (m, 2 F), -147.43 to -147.18 (m, 1 F), -160.32 to -159.83 (m, 2 F). IR (neat, cm^{-1}) 1764 (s), 1652 (s), 1625 (m). HRMS (ESI) Calcd. for $C_{22}H_{11}O_4N_2Cl_1F_5$ ([M+H]$^+$): 497.0322. Found: 497.0325.

1-(4-Methoxyphenyl)-4,4-dimethyl-1-penten-3-one oxime *O*-pentafluorobenzoate.



Following the general procedure, 0.233 g (1.0 mmol) 1-(4-methoxyphenyl)-4,4-dimethyl-1-penten-3-one oxime and 0.28 mL (2.0 mmol) triethylamine with 0.166 mL (1.2 mmol) pentafluorobenzoyl chloride were reacted. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow solid in 0.4 g (Yield: 94%). TLC (R_f = 0.56, 5:1 hexanes: EtOAc). Mp = 75-76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.8 Hz, 2 H), 7.11 (d, *J* = 16.8 Hz, 1 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.46 (d, *J* =16.8 Hz, 1 H), 3.82 (s, 3 H), 1.31 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 160.6, 139.9, 128.5, 128.3, 114.3, 113.4, 55.4, 38.8, 28.5. ^{19}F NMR (376 MHz, CDCl3) δ -137.99 to -137.88 (m, 2 F), -148.85 to -148.74 (m, 1 F), -160.55 to -160.40 (m, 2 F). IR (neat, cm^{-1}) 2972 (s), 1756 (s), 1652 (s), 1633 (s), 1606 (s). HRMS (ESI) Calcd. for $C_{21}H_{19}O_3N_1F_5$ ([M+H]$^+$): 428.1280. Found: 428.1275.

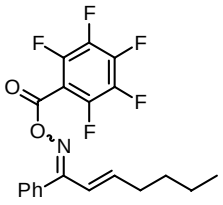
4-(5-Methyl-2-thienyl)-2-oxo-3-butenoic acid ethyl ester oxime *O*-pentafluorobenzoate.



To a suspension of 4-(5-methyl-2-thienyl)-2-oxo-3-butenoic acid ethyl ester (0.25 g, 1.1 mmol) and hydroxylamine hydrochloride (0.153 g, 2.2 mmol) in 5 mL methanol was added pyridine (0.27 mL, 3.3 mmol). The reaction was stirred at r.t. for 20 h. After removal of solvent, the residue was washed by 1 N HCl and dried over $MgSO_4$. Then the residue was treated with 0.17 mL (1.2 mmol) pentafluorobenzoyl chloride and 0.28 mL (2.0 mmol) triethylamine at 0 ^oC for 0.5 h in dichloromethane. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a light yellow oil in 0.315 g (Yield: 66%). TLC (R_f = 0.85, 1:1 hexanes: EtOAc). ^1H NMR (400 MHz, $CDCl_3$) The integration of the signal at δ 7.55 ppm was set as 1. δ 7.55 (d, *J* = 16.0 Hz, 1 H), 6.98-7.08 (m, 7.2 H), 6.87 (d, *J* = 16.4 Hz, 1.1 H), 6.69-6.73 (m, 4.1 H), 6.62 (d, *J* = 16.4 Hz, 3 H), 4.39-4.45 (m, 8.5 H), 2.50 (s, 3.9 H), 2.49 (s, 9 H), 1.35-1.57 (m, 12.9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 161.3, 159.8, 156.4, 155.5, 145.8, 144.8, 138.4, 138.0, 137.7, 135.9, 133.0, 131.4, 127.0, 126.7, 114.8, 109.9, 63.0, 62.8, 16.0, 15.9, 14.0, 13.9. ^{19}F NMR (376 MHz, CDCl3) δ -136.79 to -136.57 (m, 2 F), -146.95 to -146.60 (m, 1 F), -160.08 to -159.74 (m, 2 F). IR (neat, cm^{-1}) 1768 (s), 1741 (s), 1652 (s), 1610 (s), 1525 (s), 1498 (s), 1324 (s), 1200 (s). HRMS (ESI) Calcd. for $C_{18}H_{13}O_4N_1F_5S_1([M+H]^+)$: 434.0480. Found:

434.0469.

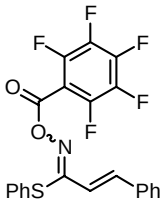
1-Phenyl-2-hepten-1-one oxime *O*-pentafluorobenzoate.



To a solution of benzaldehyde oxime (1.211 g, 10.0 mmol) in 10 mL dichloromethane at 0 °C was treated with *N*-chlorosuccinimide (1.335 g, 10.0 mmol) and one drop of pyridine. The reaction was stirred at 0 °C to r.t. for 2 h. Then 1-hexene (1.4 mL, 11.0 mmol) was added dropwise, followed by triethylamine (1.55 mL, 11.0 mmol) at 0 °C. After 2 h at 0 °C to r.t., the reaction was quenched by brine and extracted with dichloromethane. The residue was dissolved in 15 mL THF, cooled to -78 °C and treated with LDA [15.0 mmol, freshly prepared from BuLi (6.0 mL, 2.5 M in hexanes, 15.0 mmol) and diisopropylamine (2.8 mL, 20.0 mmol)]. After 10 min at -78 °C and 20 min at 0 °C, the reaction was quenched by saturated aqueous NH_4Cl and extracted with dichloromethane. The residue was treated with 1.66 mL (12.0 mmol) pentafluorobenzoyl chloride and 2.09 mL (15.0 mmol) triethylamine at 0 °C for 0.5 h. Purification by flash chromatography (15:1, hexanes: EtOAc) afforded the product as a white solid in 1.192 g (Yield: 30%). TLC (R_f = 0.87, 5:1 hexanes: EtOAc). Mp = 76-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.52 (m, 5 H), 6.86 (dt, *J* = 16.0, 1.6 Hz, 1 H), 6.17 (dt, *J* = 16.0, 6.8 Hz, 1 H), 2.23-2.29 (m, 2 H), 1.29-1.43 (m, 4 H), 0.89 (t, *J* = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 150.1, 132.5, 130.4, 129.7, 128.4, 119.9, 33.2, 30.3, 22.2, 13.8. ^{19}F NMR (376 MHz, CDCl3) δ -137.53 to -137.42 (m, 2 F), -148.27 to -148.13 (m, 1 F), -160.36 to -160.20 (m, 2 F). IR (neat,

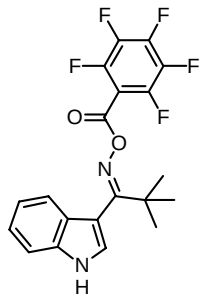
cm^{-1}) 2934 (m), 1760 (s), 1652 (s). HRMS (ESI) Calcd. for $C_{20}H_{17}O_2N_1F_5$ ($[M+H]^+$): 398.1174. Found: 398.1171.

***N*-Pentafluorobenzoyloxy-3-phenyl-2-propenimidothioic acid phenyl ester.**



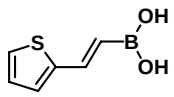
3-Phenyl-2-propenal oxime (0.147 g, 1.0 mmol) in 2 mL $CHCl_3$ at r.t. was treated with *N*-chlorosuccinimide (0.147 g, 1.1 mmol) and pyridine (0.016 mL, 0.2 mmol). The reaction was stirred at r.t. for 1 h, washed by brine and dried over $MgSO_4$. The residue in 5 mL CH_2Cl_2 at r.t. was treated with benzenethiol (0.1 mL, 1.0 mmol) and triethylamine (0.28 mL, 2.0 mmol). The reaction mixture was washed by aqueous $NaHCO_3$ and dried over $MgSO_4$. The residue was treated with 0.166 mL (1.2 mmol) pentafluorobenzoyl chloride and 0.28 mL (2.0 mmol) triethylamine at 0 ^oC for 0.5 h. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as an off-white solid in 0.229 g (Yield: 51%). TLC (R_f = 0.51, 5:1 hexanes: EtOAc). Mp = 159-161 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.54 (m, 2 H), 7.35-7.44 (m, 4 H), 7.25-7.27 (m, 3 H), 7.14-7.16 (m, 2 H), 6.06 (d, *J* = 16.0 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 138.1, 135.6, 134.9, 130.1, 129.6, 129.5, 128.8, 127.6, 127.5, 117.9. ^{19}F NMR (376 MHz, CDCl3) δ -136.72 to -136.60 (m, 2 F), -147.69 to -147.56 (m, 1 F), -160.25 to -160.09 (m, 2 F). IR (neat, cm^{-1}) 1752 (s), 1652 (m), 1629 (s), 1525 (s), 1498 (s), 1324 (s), 1200 (s). HRMS (ESI) Calcd. for $C_{22}H_{13}O_2N_1F_5S_1$ ($[M+H]^+$): 450.0582. Found: 450.0574.

1-(1*H*-Indol-3-yl)-2,2-dimethyl-1-propanone oxime *O*-pentafluorobenzoate.



To a suspension of 1-(1H-indol-3-yl)-2,2-dimethyl-1-propanone (0.201 g, 1.0 mmol) and hydroxylamine hydrochloride (0.14 g, 2.0 mmol) in 10 mL methanol was added pyridine (0.24 mL, 3.0 mmol). The reaction was stirred at 50 ^{o}C for 30 h. After removal of solvent, the residue was washed by 1 N HCl and dried over $MgSO_4$. Then the residue was treated with 0.15 mL (1.1 mmol) pentafluorobenzoyl chloride and 0.28 mL (2.0 mmol) triethylamine at 0 ^{o}C for 0.5 h in 2 mL dichloromethane. Purification by flash chromatography (5:1, hexanes: EtOAc) afforded the product as a yellow solid in 0.272 g (Yield: 66%). TLC (R_f = 0.23, 5:1 hexanes: EtOAc). Mp = 123-125 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (br, 1 H), 7.33-7.38 (m, 2 H), 7.07-7.19 (m, 3 H), 1.32 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 135.1, 126.2, 122.6, 121.9, 120.4, 119.9, 111.2, 107.6, 39.5, 27.7. ^{19}F NMR (376 MHz, CDCl3) δ -138.21 to -138.10 (m, 2 F), -149.36 to -149.23 (m, 1 F), -161.01 to -160.86 (m, 2 F). IR (neat, cm^{-1}) 3401 (br, m), 2976 (m), 1745 (s), 1652 (s), 1621 (m), 1525 (s), 1505 (s), 1328 (s), 1204 (s). HRMS (ESI) Calcd. for $C_{20}H_{16}O_2N_2F_5$ ($[M+H]^+$): 411.1127. Found: 411.1129.

[2-(2-Thienyl)ethenyl]-boronic acid.



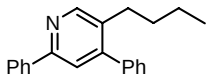
A mixture of 2-bromothiophene (0.19 mL, 2.0 mmol), (trimethylsilyl)acetylene (0.216

g, 2.2 mmol), disopropylamine (0.8 mL), $PdCl_2$ (0.0177 g, 0.1 mmol), PPh_3 (0.0528 g, 0.2 mmol) and CuI (0.0228 g, 0.12 mmol) was reacted under argon at 50 ^oC for 6 h in 15 mL degassed THF. Then the reaction mixture was treated with TBAF (2.5 mL, 1.0 M in THF, 2.5 mmol) at r.t. for 0.5 h. The yellow oil afforded by chromatography purification (5:1, hexanes:EtOAc) was exposed to catecholborane (0.234 mL, 2.2 mmol) in 2 mL THF at 70 ^oC for 2 h. Then the reaction mixture was added 2mL water and stirred at r.t. for 10 h. Purification by chromatography (2:1, hexanes:EtOAc) gave the product as a white solid in 0.182 g (Yield: 59%). TLC (R_f = 0.44, 1:1 hexanes: EtOAc). Mp = 156-158 °C. ^1H NMR (400 MHz, acetone-d_6) δ 7.47 (d, *J* = 18.0 Hz, 1 H), 7.39 (d, *J* = 5.2 Hz, 1 H), 7.12 (d, *J* = 3.6 Hz, 1 H), 7.03 (dd, *J* = 5.2, 3.6 Hz, 1 H), 5.92 (d, *J* = 18.0 Hz, 1 H). ^{13}C NMR (100 MHz, acetone-d_6) δ 144.8, 139.8, 128.2, 127.9, 126.3. IR (neat, cm^{-1}) 3227 (br, s), 1610 (s), 1359 (s), 1305 (s), 1185 (s). HRMS (ESI) Calcd. for $C_6H_6O_2B_1S_1$ ($[M-H]^-$): 153.0176. Found: 153.0188.

General Procedure for Cu-Catalyzed Pyridine Synthesis from Boronic Acids and α, β-Unsaturated Ketoxime *O*-Pentafluorobenzoates

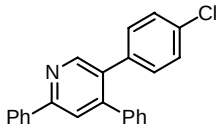
Dry DMF (2 mL) was added to a Schlenk tube containing the α, β-unsaturated ketoxime *O*-pentafluorobenzoate (0.1 mmol), the boronic acid (0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol). The reaction mixture was stirred under air at 50 °C for 2 h and then at 90 °C for 3 h. The reaction mixture was extracted with ether and the organic phase was washed with brine and then dried over $MgSO_4$. After evaporation of the solvent the residue was subjected to flash chromatography giving the corresponding pyridine.

5-Butyl-2,4-diphenyl-pyridine.



Following the general procedure, 1,3-diphenyl-2-propen-1-one oxime *O*-pentafluorobenzoate (41.7 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (20:1, hexanes:EtOAc) afforded the title compound as a colorless oil (25.1 mg, Yield: 87%). TLC (R_f = 0.67, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1 H), 7.97-7.80 (m, 2 H), 7.55 (s, 1 H), 7.33-7.47 (m, 8 H), 2.63 (t, *J* = 8.0 Hz, 2 H), 1.41-1.48 (m, 2 H), 1.18-1.28 (m, 2 H), 0.79 (t, *J* = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 150.7, 149.9, 139.5, 139.2, 134.0, 128.7, 128.6, 128.5, 128.4, 127.8, 126.7, 121.3, 33.1, 29.7, 22.3, 13.7. IR (neat, cm-1) 3061 (m), 2957 (s), 1594 (s), 1475 (s). HRMS (ESI) Calcd. for $C_{21}H_{22}N_1$ ($[M+H]^+$): 288.1747. Found: 288.1755.

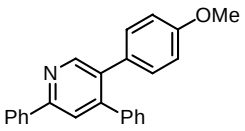
5-(4-Chlorophenyl)-2,4-diphenyl-pyridine.



Following the general procedure, 1,3-diphenyl-2-propen-1-one oxime *O*-pentafluorobenzoate (41.7 mg, 0.1 mmol), *trans*-2-(4-chlorophenyl)vinylboronic acid (21.9 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (20:1, hexanes:EtOAc) afforded the title compound as a colorless oil (31.2 mg, Yield: 91%). TLC (R_f = 0.62, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1 H),

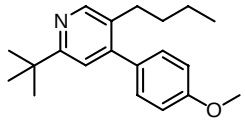
8.04-8.06 (m, 2 H), 7.76 (s, 1 H), 7.41-7.51 (m, 3 H), 7.18-7.32 (m, 7 H), 7.10 (d, J = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 150.7, 148.5, 138.8, 138.7, 136.1, 133.5, 133.1, 131.0, 129.3, 129.2, 128.8, 128.6, 128.5, 128.1, 126.9, 121.6. IR (neat, cm-1) 3061 (m), 1590 (s), 1471 (s). HRMS (ESI) Calcd. for $C_{23}H_{17}N_1Cl_1$ ($[M+H]^+$): 342.1044. Found: 342.1053.

5-(4-Methoxyphenyl)-2,4-diphenyl-pyridine.



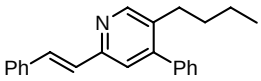
Following the general procedure, 1,3-diphenyl-2-propen-1-one oxime *O*-pentafluorobenzoate (41.7 mg, 0.1 mmol), *trans*-2-(4-methoxyphenyl) vinylboronic acid (21.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (20:1, hexanes:EtOAc) afforded the title compound as a colorless oil (26.0 mg, Yield: 77%). TLC (R_f = 0.46, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 0.4 Hz, 1 H), 8.03-8.05 (m, 2 H), 7.73 (s, 1 H), 7.39-7.50 (m, 3 H), 7.28-7.30 (m, 3 H), 7.20-7.23 (m, 2 H), 7.07-7.10 (m, 2 H), 6.79-6.82 (m, 2 H), 3.78 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 156.1, 150.9, 148.3, 139.2, 139.1, 133.9, 130.9, 129.8, 129.3, 128.9, 128.8, 128.3, 127.8, 126.9, 121.6, 113.8, 55.2. IR (neat, cm-1) 3034 (m), 1610 (s), 1590 (s), 1513 (s), 1471 (s), 1251 (s). HRMS (ESI) Calcd. for $C_{24}H_{20}O_1N_1$ ($[M+H]^+$): 338.1539. Found: 338.1549.

5-Butyl-4-(4-methoxyphenyl)-2-(*tert*-butyl)-pyridine.



Following the general procedure, 1-(4-methoxyphenyl)-4,4- dimethyl-1-penten-3-one oxime *O*-pentafluorobenzoate (42.7 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (25.7 mg, Yield: 86%). TLC (R_f = 0.71, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1 H), 7.21-7.23 (m, 2 H), 7.11 (s, 1 H), 6.94-6.96 (m, 2 H), 3.85 (s, 3 H), 2.56 (t, *J* = 8.0 Hz, 2 H), 1.39-1.43 (m, 2 H), 1.35 (s, 9 H), 1.18-1.30 (m, 2 H), 0.78 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 159.1, 149.6, 148.8, 132.4, 132.3, 129.8, 119.9, 113.7, 55.3, 36.9, 33.2, 30.3, 29.6, 22.4, 13.8. IR (neat, cm-1) 2957 (s), 1610 (m), 1513 (s). HRMS (ESI) Calcd. for $C_{20}H_{28}O_1N_1$ ($[M+H]^+$): 298.2165. Found: 298.2163.

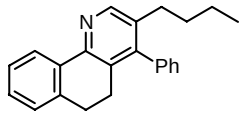
5-Butyl-4-phenyl-2-(2-phenylethenyl)-pyridine.



Following the general procedure, 1,5-diphenyl-1,4-pentadien-3-one oxime *O*-pentafluorobenzoate (44.3 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (19.1 mg, Yield: 74%). TLC (R_f = 0.64, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1 H), 7.54-7.61 (m, 3 H), 7.25-7.47 (m, 8 H), 7.23 (s, 1 H), 7.16 (d, *J* = 15.6 Hz, 1 H), 2.60 (t, *J* = 8.0 Hz, 2 H), 1.38-1.45 (m, 2 H), 1.18-1.24 (m, 2 H), 0.78 (t, *J* = 7.2 Hz, 3 H).

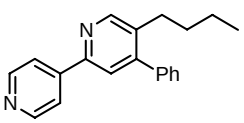
^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 150.8, 149.7, 139.3, 136.8, 134.2, 131.9, 128.7, 128.5, 128.4, 128.1, 127.8, 127.0, 122.8, 33.2, 29.8, 22.3, 13.7. IR (neat, cm-1) 3061 (m), 2957 (s), 1590 (s), 1494 (s). HRMS (ESI) Calcd. for $C_{23}H_{24}N_1$ ($[M+H]^+$): 314.1903. Found: 314.1901.

5,6-Dihydro-4-phenyl-3-butyl-benzo[h]quinoline.



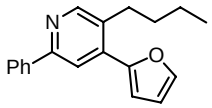
Following the general procedure, 3,4-dihydro-2-(phenylmethylene)-1(2*H*)-naphthalenone oxime *O*-pentafluorobenzoate (44.3 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (10:1, hexanes:EtOAc) afforded the title compound as a yellow oil (23.5 mg, Yield: 75%). TLC (R_f = 0.73, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1 H), 8.29 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.25-7.47 (m, 5 H), 7.14-7.17 (m, 3 H), 2.76 (t, *J* = 8.0 Hz, 2 H), 2.55 (t, *J* = 8.0 Hz, 2 H), 2.38 (t, *J* = 8.0 Hz, 2 H), 1.33-1.39 (m, 2 H), 1.15-1.20 (m, 2 H), 0.74 (t, *J* = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 148.2, 148.1, 137.7, 135.0, 134.7, 129.7, 128.6, 128.5, 127.5, 127.0, 124.9, 33.1, 30.5, 28.0, 25.6, 22.3, 13.7. IR (neat, cm-1) 3061 (m), 2957 (s), 1606 (m), 1567 (m), 1455 (s), 1390 (s). HRMS (ESI) Calcd. for $C_{23}H_{24}N_1$ ($[M+H]^+$): 314.1903. Found: 314.1896.

5-Butyl-4-phenyl-2,4'-bipyridine.



Following the general procedure, 3-phenyl-1-(4-pyridinyl)-2-propen-1-one oxime *O*-pentafluorobenzoate (41.8 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (2:1, hexanes:EtOAc) afforded the title compound as a yellow oil (17.8 mg, Yield: 62%). TLC (R_f =0.17, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 2 H), 8.61 (s, 1 H), 7.87-7.89 (m, 2 H), 7.62 (s, 1 H), 7.42-7.48 (m, 3 H), 7.31-7.34 (m, 2 H), 2.65 (t, *J* = 8.0 Hz, 2 H), 1.43-1.46 (m, 2 H), 1.20-1.25 (m, 2 H), 0.78 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 151.2, 150.3, 150.2, 146.3, 138.9, 136.1, 128.5, 128.4, 128.1, 121.6, 120.9, 33.1, 29.8, 22.3, 13.7. IR (neat, cm-1) 3030 (m), 2957 (s), 1590 (s), 1471 (s). HRMS (ESI) Calcd. for $C_{20}H_{21}N_2$ ($[M+H]^+$): 289.1699. Found: 289.1697.

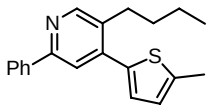
5-Butyl-4-(2-furanyl)-2-phenyl-pyridine.



Following the general procedure, 3-(2-furanyl)-1-phenyl-2-propen-1-one oxime *O*-pentafluorobenzoate (40.7mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (10:1, hexanes:EtOAc) afforded the title compound as a yellow oil (21.7 mg, Yield: 78%). TLC (R_f = 0.68, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1 H), 7.98-8.01 (m, 3 H), 7.58 (d, *J* = 1.6 Hz, 1 H), 7.37-7.48 (m, 3 H), 6.78 (d, *J* = 3.2 Hz, 1 H), 6.55-6.57 (m, 1 H), 2.87 (t, *J* = 8.0 Hz, 2 H), 1.58-1.63 (m, 2 H), 1.41-1.49 (m, 2

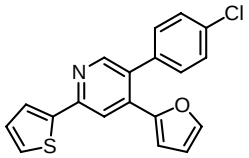
H), 0.95 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 151.7, 151.2, 143.1, 139.3, 136.9, 131.7, 128.7, 126.7, 117.4, 111.9, 111.0, 32.3, 31.2, 22.7, 13.9. IR (neat, cm-1) 3069 (w), 2957 (s), 1598 (s), 1471 (s). HRMS (ESI) Calcd. for $C_{19}H_{20}O_1N_1$ ($[M+H]^+$): 278.1539. Found: 278.1538.

5-Butyl-4-(5-methyl-2-thienyl)-2-phenyl-pyridine.



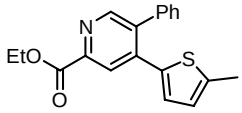
Following the general procedure, 3-(5-methyl-2-thienyl)-1-phenyl-2-propen-1-one oxime *O*-pentafluorobenzoate (43.7 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (2 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (25.0 mg, Yield: 81%). TLC (R_f = 0.63, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1 H), 7.97 (d, J = 7.2 Hz, 2 H), 7.68 (s, 1 H), 7.45 (t, J = 7.2 Hz, 2 H), 7.38 (t, J = 7.6 Hz, 1 H), 7.01 (d, J = 3.2 Hz, 1 H), 6.78 (dd, J = 7.6, 0.8 Hz, 1 H), 2.82 (t, J = 8.0 Hz, 2 H), 2.54 (s, 3 H), 1.53-1.59 (m, 2 H), 1.35-1.40 (m, 2 H), 0.90 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 151.3, 142.2, 141.6, 139.2, 137.8, 133.7, 128.7, 127.3, 126.7, 125.8, 121.2, 33.2, 30.5, 22.5, 15.3, 13.9. IR (neat, cm-1) 3065 (w), 2957 (s), 1594 (s), 1471 (s). HRMS (ESI) Calcd. for $C_{20}H_{22}N_1S_1$ ($[M+H]^+$): 308.1468. Found: 308.1466.

5-(4-Chlorophenyl)-4-(2-furanyl)-2-(2-thienyl)-pyridine.



Following the general procedure, 3-(2-furanyl)-1- (2-thienyl) -2-propen-1-one oxime *O*-pentafluorobenzoate (50.0 mg, 0.12 mmol), *trans*-2-(4-chlorophenyl)vinylboronic acid (26.3 mg, 0.144 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (2.2 mg, 0.012 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (10:1, hexanes:EtOAc) afforded the title compound as a yellow oil (25.1 mg, Yield: 74%). TLC (R_f =0.72, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1 H), 8.06 (s, 1 H), 7.69 (d, *J* = 3.6 Hz, 1 H), 7.41-7.46 (m, 4 H), 7.24-7.26 (m, 2 H), 7.14 (t, *J* = 4.8 Hz, 1 H), 6.31 (d, *J* = 1.6 Hz, 1 H), 5.83 (d, *J* =3.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 150.8, 149.8, 144.4, 143.2, 136.7, 136.5, 134.2, 130.7, 130.4, 129.0, 128.1, 127.8, 124.9, 114.7, 112.6, 112.0. IR (neat, cm-1) 1594 (s), 1567 (m), 1467 (s). HRMS (ESI) Calcd. for $C_{19}H_{13}O_1N_1Cl_1S_1$ ($[M+H]^+$): 338.0401. Found: 338.0400.

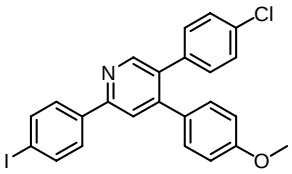
5-Phenyl-4-(5-methyl-2-thienyl)-2-pyridinecarboxylic acid ethyl ester.



Following the general procedure, 4-(5-methyl-2-thienyl)-2-oxo-3-butenoic acid ethyl ester oxime *O*-pentafluorobenzoate (43.3 mg, 0.1 mmol), *trans*-2-phenylvinylboronic acid (17.8 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (14.0 mg, Yield: 43%). TLC (R_f = 0.31, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1 H),

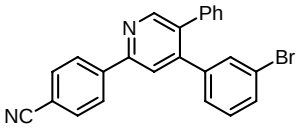
8.26 (s, 1 H), 7.39-7.41 (m, 3 H), 7.27-7.30 (m, 2 H), 6.73 (d, J = 3.6 Hz, 1 H), 6.56 (dd, *J* = 2.4, 1.2 Hz, 1 H), 4.50 (q, *J* = 7.2 Hz, 2 H), 2.39 (d, *J* = 0.8 Hz, 3 H), 1.45 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 151.6, 147.2, 143.3, 141.5, 137.5, 137.2, 136.6, 129.5, 129.0, 128.7, 128.4, 125.9, 124.5, 62.0, 15.3, 14.4. IR (neat, cm^{-1}) 3030 (m), 1718 (s), 1586 (s), 1463 (s), 1378 (s), 1301 (s), 1247 (s). HRMS (ESI) Calcd. for $C_{19}H_{18}O_2N_1S_1$ ($[M+H]^+$): 324.1053. Found: 324.1052.

5-(4-Chlorophenyl)-4-(4-methoxyphenyl)-2-(4-iodophenyl)-pyridine.



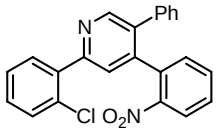
Following the general procedure, 4'-iodo-4-methoxy-chalcone oxime *O*-pentafluorobenzoate (57.3 mg, 0.1 mmol), *trans*-2-(4-chlorophenyl)vinylboronic acid (21.9 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (32.0 mg, Yield: 64%). TLC (R_f = 0.54, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1 H), 7.77-7.82 (m, 4 H), 7.69 (s, 1 H), 7.24-7.27 (m, 2 H), 7.09-7.11 (m, 4 H), 6.82 (d, *J* = 8.4 Hz, 2 H), 3.80 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 155.6, 150.8, 148.3, 138.4, 137.9, 136.1, 133.5, 133.3, 131.0, 130.6, 130.5, 128.63, 128.57, 121.2, 113.9, 95.5, 55.3. IR (neat, cm^{-1}) 3003 (w), 1610 (s), 1590 (s), 1509 (s), 1467 (s), 1251 (s). HRMS (ESI) Calcd. for $C_{24}H_{18}O_1N_1Cl_1I_1$ ($[M+H]^+$): 498.0116. Found: 498.0112.

5-Phenyl-4-(3-bromophenyl)-2-(4-cyanophenyl)-pyridine.



Following the general procedure, 4-[3-(3-bromophenyl)-1-oxo-2-propenyl]-benzonitrile oxime *O*-pentafluorobenzoate (20.0 mg, 0.038 mmol), *trans*-2-phenylvinylboronic acid (6.8 mg, 0.046 mmol), 4 Å molecular sieves (50 mg) and $Cu(OAc)_2$ (0.7 mg, 0.004 mmol) were reacted in 1 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (10.6 mg, Yield: 68%). TLC (R_f = 0.43, hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1 H), 8.18-8.20 (m, 2 H), 7.76-7.79 (m, 3 H), 7.43-7.45 (m, 2 H), 7.30-7.32 (m, 3 H), 7.02-7.18 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 151.4, 147.2, 142.9, 140.6, 136.5, 135.4, 132.6, 132.0, 131.2, 129.8, 129.7, 128.5, 128.1, 127.9, 127.4, 122.5, 121.7, 118.8, 112.6. IR (neat, cm^{-1}) 3061 (w), 2227 (s), 1586 (s), 1467 (s). HRMS (ESI) Calcd. for $C_{24}H_{16}N_2Br_1$ ($[M+H]^+$): 411.0491. Found: 411.0491.

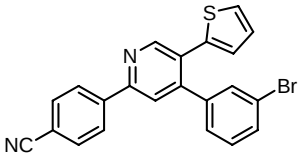
5-Phenyl-4-(2-nitrophenyl)-2-(2-chlorophenyl)-pyridine.



1-(2-Chlorophenyl)-3-(2-nitrophenyl)- 2-propen-1-one oxime *O*-pentafluorobenzoate (20.0 mg, 0.04 mmol), *trans*-2-phenylvinylboronic acid (7.1 mg, 0.048 mmol), 4 Å molecular sieves (50 mg) and $Cu(OAc)_2$ (0.7 mg, 0.004 mmol) were reacted in 1 mL DMF at 50 ^{o}C for 1.5 h under air. Then the reaction mixture was heated at 150 ^{o}C for 0.5 h in microwave reactor under air. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (10.8 mg, Yield: 70%).

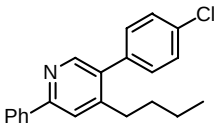
TLC (R_f = 0.73, 1:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1 H), 7.89 (dd, *J* = 8.4, 1.2 Hz, 1 H), 7.72 (dd, *J* = 7.2, 1.6 Hz, 1 H), 7.62 (s, 1 H), 7.23-7.58 (m, 9 H), 7.13-7.16 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 150.2, 148.5, 144.4, 138.3, 136.2, 134.4, 134.2, 133.0, 132.4, 132.2, 131.7, 130.2, 129.8, 129.5, 129.1, 128.4, 127.8, 127.1, 124.6, 124.5. IR (neat, cm^{-1}) 1590 (w), 1525 (s), 1351 (m). HRMS (ESI) Calcd. for $C_{23}H_{16}O_2N_2Cl_1$ ($[M+H]^+$): 387.0895. Found: 387.0890.

5-(2-Thienyl)-4-(3-bromophenyl)-2-(4-cyanophenyl)-pyridine.



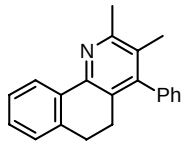
Following the general procedure, 4-[3-(3-bromophenyl)-1-oxo-2-propenyl]-benzonitrile oxime *O*-pentafluorobenzoate (26.1 mg, 0.05 mmol), [2-(2-thienyl)ethenyl]-boronic acid (9.3 mg, 0.06 mmol), 4 Å molecular sieves (50 mg) and $Cu(OAc)_2$ (0.9 mg, 0.005 mmol) were reacted in 2 mL DMF. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow solid (15.2 mg, Yield: 73%). TLC (R_f = 0.53, 5:1 hexanes:EtOAc). Mp = 188-190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1 H), 8.17 (d, *J* = 7.6 Hz, 2 H), 7.77 (d, *J* = 7.6 Hz, 2 H), 7.70 (s, 1 H), 7.48-7.54 (m, 2 H), 7.31 (dd, *J* = 4.8, 1.2 Hz, 1 H), 7.17-7.25 (m, 2 H), 6.97-6.99 (m, 1 H), 6.89 (dd, *J* = 3.6, 1.2 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 150.9, 147.2, 142.6, 140.5, 137.8, 132.6, 131.8, 131.6, 130.0, 128.7, 128.0, 127.7, 127.5, 127.4, 127.3, 122.6, 121.8, 118.8, 112.7. IR (neat, cm^{-1}) 2227 (s), 1583 (s), 1467 (s). HRMS (ESI) Calcd. for $C_{22}H_{14}N_2Br_1S_1$ ($[M+H]^+$): 417.0056. Found: 417.0054.

5-(4-Chlorophenyl)-4-butyl-2-phenyl-pyridine.



1-Phenyl-2-hepten-1-one oxime *O*-pentafluorobenzoate (39.7 mg, 0.1 mmol), *trans*-2-(4-chlorophenyl)vinylboronic acid (21.9 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF at 50 ^oC for 2 h and at 90 ^oC for 5 h under air. Purification by flash chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (18.6 mg, Yield: 58%). TLC (R_f = 0.70, 5:1 hexanes:EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1 H), 7.98-8.01 (m, 2 H), 7.62 (s, 1 H), 7.41-7.50 (m, 5 H), 7.26-7.28 (m, 2 H), 2.62 (t, *J* = 7.6 Hz, 2 H), 1.46-1.52 (m, 2 H), 1.22-1.28 (m, 2 H), 0.82 (t, *J* = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 150.0, 149.8, 139.2, 136.4, 134.9, 133.7, 130.7, 128.9, 128.7, 128.6, 126.9, 120.8, 32.6, 32.3, 22.4, 13.8. IR (neat, cm^{-1}) 2957 (m), 1594 (s), 1475 (s). HRMS (ESI) Calcd. for $C_{21}H_{21}N_1Cl_1$ ($[M+H]^+$): 322.1357. Found: 322.1355.

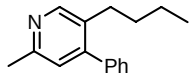
5,6-Dihydro-4-phenyl-2,3-dimethyl-benzo[h]quinoline.



Following the general procedure, 3,4-dihydro-2-(phenylmethylene)-1(2H)-naphthalenone oxime *O*-pentafluorobenzoate (44.3 mg, 0.1 mmol), (2*Z*)-2-buten-2-ylboronic acid (12.0 mg, 0.12 mmol), 4 Å molecular sieves (100 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF. Purification by flash

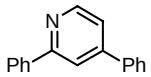
chromatography (5:1, hexanes:EtOAc) afforded the title compound as a yellow oil (21.1 mg, Yield: 74%). TLC (R_f = 0.66, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.31-7.47 (m, 4 H), 7.23-7.27 (m, 1 H), 7.11-7.16 (m, 3 H), 2.74 (t, *J* = 8.0 Hz, 2 H), 2.60 (s, 3 H), 2.50 (t, *J* = 8.0 Hz, 2 H), 1.99 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 148.9, 148.4, 138.8, 137.6, 135.1, 128.5, 128.3, 128.1, 127.4, 127.3, 127.0, 124.8, 28.2, 25.7, 23.5, 16.6. IR (neat, cm^{-1}) 3061 (m), 2934 (m), 1556 (s), 1444 (s), 1401 (s). HRMS (ESI) Calcd. for $C_{21}H_{20}N_1$ ($[M+H]^+$): 286.1590. Found: 286.1588.

5-Butyl-4-phenyl-2-methyl-pyridine.



4-Phenyl-3-buten-2-one oxime *O*-pentafluorobenzoate (35.5 mg, 0.1 mmol), *trans*-1-hexen-1-ylboronic acid (15.4 mg, 0.12 mmol), 4 Å molecular sieves (200 mg) and $Cu(OAc)_2$ (1.8 mg, 0.01 mmol) were reacted in 2 mL DMF for 2 h at 50 ^{o}C. Then the reaction mixture was heated at 120 ^{o}C for 0.5 h in the microwave reactor. Purification by flash chromatography (5:1, hexanes : EtOAc) afforded the title compound as a yellow oil (4.5 mg, Yield: 20%). TLC (R_f = 0.23, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1 H), 7.37-7.43 (m, 3 H), 7.25-7.28 (m, 2 H), 6.97 (s, 1 H), 2.52-2.57 (m, 5 H), 1.35-1.39 (m, 2 H), 1.15-1.23 (m, 2 H), 0.76 (t, J = 7.6 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 150.1, 149.5, 139.5, 132.3, 128.5, 128.3, 127.7, 123.9, 33.3, 29.5, 23.9, 22.3, 13.7. IR (neat, cm-1) 2957 (s), 1598 (s), 1544 (m), 1482 (s), 1459 (s), 1382 (s). HRMS (ESI) Calcd. for $C_{16}H_{20}N_1$ ($[M+H]^+$): 226.1590. Found: 226.1586.

2, 4-Diphenyl-pyridine.[23]



1,3-Diphenyl-2-propen-1-one oxime *O*-pentafluorobenzoate (41.7 mg, 0.1 mmol), vinyl-tri-*n*-butylstannane (0.035 mL, 0.12 mmol) and CuTC (1.9 mg, 0.01 mmol) were reacted in 2 mL DMF under Ar at 50 ^{o}C for 1 h and then heated under air at 80 ^{o}C for 4 h. Purification by flash chromatography (20:1, hexanes:EtOAc) afforded the title compound as a colorless oil (11.5 mg, Yield: 50%). TLC (R_f = 0.51, 5:1 hexanes:EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (dd, *J* = 4.8, 0.8 Hz, 1 H), 8.02-8.04 (m, 2 H), 7.915-7.921 (m, 1 H), 7.67-7.70 (m, 2 H), 7.40-7.52 (m, 7 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 150.1, 149.3, 139.5, 138.5, 129.1, 129.03, 129.01, 128.8, 127.1, 127.0, 120.3, 118.8. IR (neat, cm^{-1}) 3061 (m), 1594 (s), 1544 (s), 1471 (s), 1390 (s).

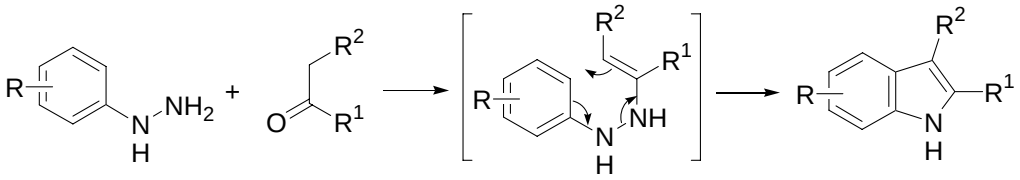
[23] Andersson, H.; Almqvist, F.; Olsson, R. *Org. Lett.* **2007**, *9*, 1335.

Chapter 3 Indole Synthesis through a Decarboxylation and Fischer Indole-like Cyclization Sequence

3.1 Introduction and Background

Indoles are probably the most prevalent heterocycles in nature. Their biological activity and structural diversity have stimulated the imagination in both academic and industrial settings. For over a century, the synthesis and elaboration of indoles has been one of the hottest areas for synthetic organic chemists.[1] A large number of methods have been developed to construct the indole ring. According to the classification adopted by Gribble,[2] the key step for the indole ring formation involves a wide range of reactions, such as sigmatropic rearrangements, nucleophilic cyclization, electrophilic cyclization, reductive cyclization, oxidative cyclization, metal-catalyzed reactions, cycloaddition and electrocyclization.

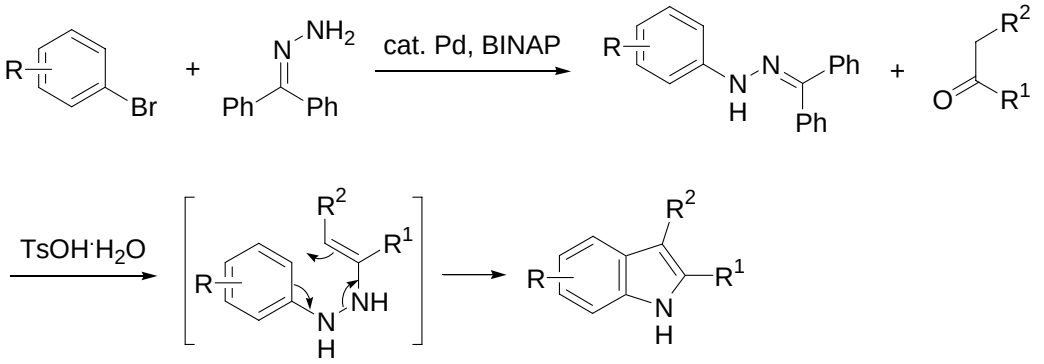
Scheme 3.1 Fischer Indole Synthesis



Among all the established approaches, the Fischer indole synthesis has provided an extremely important access to indoles with good tolerance of functionalities regardless of its long history and complications.[3] The Fischer indole synthesis smoothly transforms an enolizable *N*-arylhydrazone to the indole *via* a [3,3]-sigmatropic rearrangement with simultaneous formation of C-C and C-N bonds (Scheme 3.1). One drawback of the Fischer indolization is the availability of

N-arylhydrazines, which are usually prepared from reduction of aryl diazonium salts. To address this issue, Buchwald and co-workers disclosed a palladium-catalyzed cross-coupling reaction that affords stable *N*-aryl benzophenone hydrazones from aryl bromides and inexpensive benzophenone hydrazone (Scheme 3.2).[4] When *N*-aryl benzophenone hydrazones are treated with acid in the presence of various ketones, enolizable hydrazones are generated which undergo efficient Fischer indolization.

Scheme 3.2 Buchwald Modification

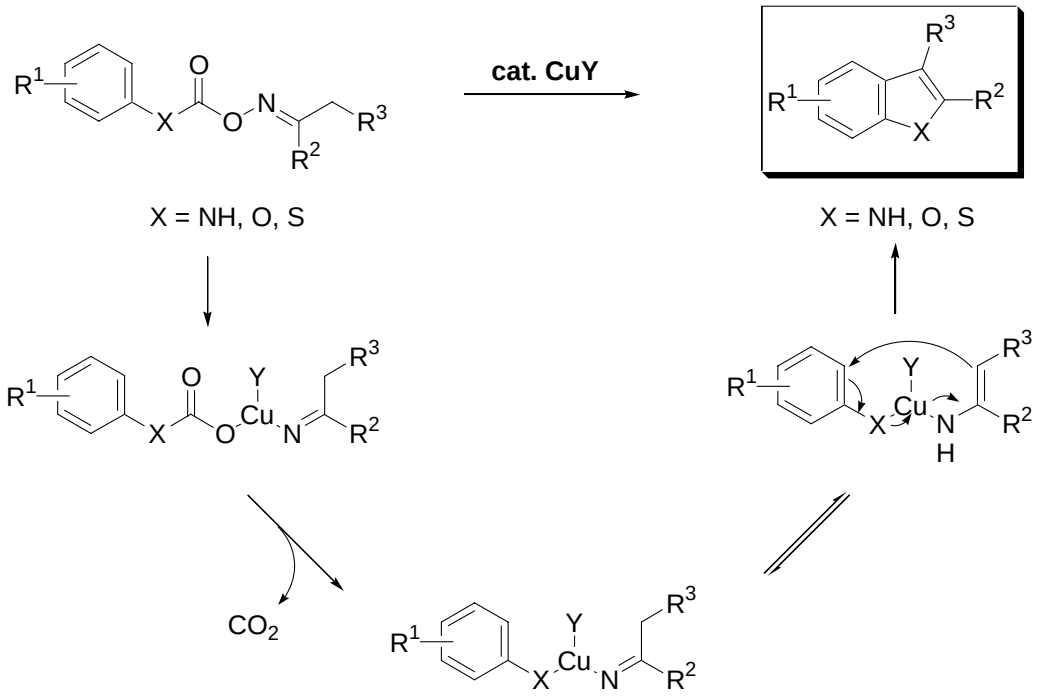


Inspired by the great efficiency of Fischer indole synthesis, we planned to utilize cleavage of the N-O bond to drive Fischer-like indolization. To realize this goal, a molecule such as that shown in Scheme 3.3 was designed to incorporate both the N-O bond and the equivalent of hydrazone functionality. Following the devised pathway, the intermediate generated from oxidative addition of the N-O bond to the copper (I) catalyst should readily undergo decarboxylation which would result in a copper (III) templated hydrazone-like complex but with scission of the N-N bond. This complex might undergo a copper-mediated [3,3]-sigmatropic rearrangement to afford the desired indole.

Disconnection of the N-N bond of the hydrazone by the carboxyl and reconnection by the copper catalyst would allow for great freedom to switch both the

arylamine and the oxime. In this way, the issue of preparation of the hydrazones would be reduced to finding easily accessible fragments, arylamines and oximes. Furthermore, this strategy could be extended to O-N or S-N bonds to construct benzofurans or benzothiophenes.

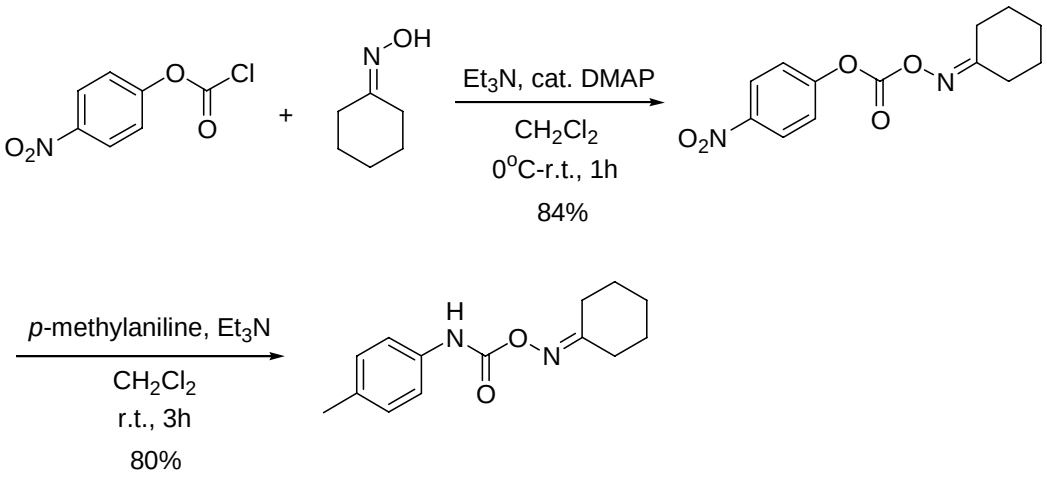
Scheme 3.3 Disconnection and Reconnection of X-N Bond Strategy for Synthesis of Indole and Related Compounds



3.2 Results and Discussion

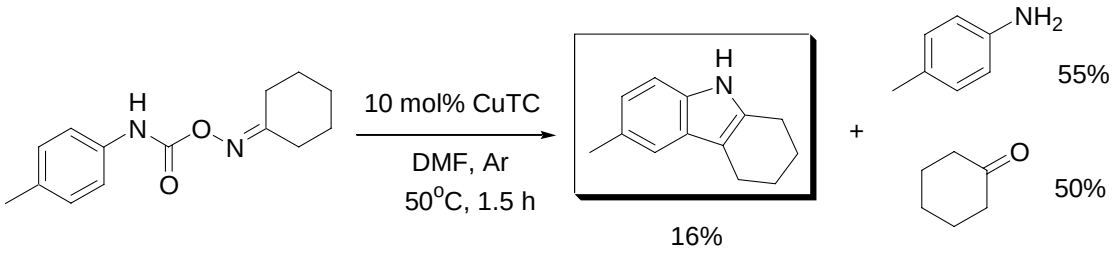
The starting material was synthesized starting with the oxime (Scheme 3.4). Commercially available cyclohexanone oxime was treated with 4-nitrophenylchloroformate and triethylamine in dichloromethane. The resultant product which was obtained in 84% yield was treated with *para*-methylaniline and triethylamine in dichloromethane at room temperature for 3 h to afford the desired product in 80% yield.

Scheme 3.4 Preparation of Starting Material



When the starting material was treated with 10 mol% CuTC in DMF at 50 °C under argon for 1.5 h, the desired indole was formed in 16% yield accompanied by significant amounts of decomposed products: *para*-toluidine (55%) and cyclohexanone (50%) (Scheme 3.5). The inefficiency of this reaction was attributed to a reluctant imine-enamine tautomerization.

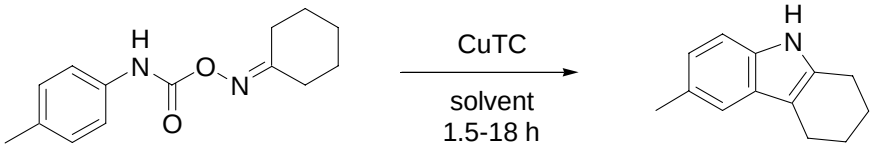
Scheme 3.5 Indole Synthesis by Decarboxylation



Although various conditions were investigated including solvents, catalyst loading and additives, no improvement was achieved (Table 3.1). Control experiments revealed that copper catalyst and inert atmosphere were required for the reaction. The reaction did not take place at room temperature and DMF was the best solvent among the screened solvents. In THF and toluene, the reaction was slow. In ethanol, the

reaction only led to decomposed products: *para*-toluidine and cyclohexanone. Lewis acids such as BF_3·OEt, $ZnCl_2$, and $AlCl_3$were applied to facilitate the imine-enamine tautomerization but they induced the rapid decomposition of starting material. The weak Lewis acid, $Zn(OAc)_2$, retarded the reaction and *N*,*O*-bis(trimethylsilyl) acetamide (BTMSA) did not improve the reaction.

Table 3.1 Searching for Optimal Condition



Cu (mol%)	Additive	solvent	Temp (^oC)	atmosphere	Yield (%)
10	NONE	DMF	50	Ar	16
10	NONE	DMF	r.t.	Ar	Recvry SM
0	NONE	DMF	50	Ar	Recvry SM
10	NONE	DMF	50	air	Recvry SM
100	NONE	DMF	50	Ar	0
10	BTMSA	DMF	50	Ar	15
10	$Zn(OAc)_2$	DMF	50	Ar	0
10	BF_3·OEt	THF	50	Ar	0
10	$ZnCl_2$	THF	50	Ar	0
10	$AlCl_3$	DMF	50	Ar	0
10	NONE	THF	50	Ar	<5
10	NONE	Toluene	50	Ar	<5
10	NONE	EtOH	50	Ar	0

3.3 Conclusion

In summary, the strategy employing N-N bond disconnection and reconnection for indole synthesis was reduced to practice, albeit in nonproductive yields. Further study is needed to improve the efficiency of the reaction.

3.4 References

[1] (a) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006,** 106, 2875. (b) Gribble, G. W. *J. Chem. Soc*., *Perkin Trans. 1,* **2000**, 1045. (c) Gilchrist, T. L. *J. Chem. Soc.*, *Perkin Trans. 1*, **1999**, 2848. (d) Sundberg, R. J. *Indoles* Academic Press, San Diego,CA, **1996** (e) Moody, C. J. *Synlett* **1994**, 681. (f) Pindur, U.; Adam, R. *J. Heterocycl. Chem.* **1988**, *25*, 1.

[2] Gribble, G. W. *Contemp. Org. Synth.* **1994**, 145.

[3] (a) Robinson, B. *Chem. Rev.* **1969**, *69*, 227. (b) Robinson, B. *Chem. Rev.* **1963**, *63*, 373. (c) Van Orden, R. B.; Lindwell, H. G. *Chem. Rev.* **1942**, *30*, 69. (d) Fischer, E.; Hess, O. *Ber.* **1884**, *17*, 559. (e) Fischer, E.; Jourdan, F. *Ber.* **1883**, *16*, 2241.

[4] Wagaw, S.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 6621.

3.5 Experimental

General Methods

All reactions were performed under an atmosphere of dry Ar in oven-dried glassware unless otherwise noted. Solvents (THF, Dioxane, DMF, MeOH, CH_2Cl_2 and toluene) for reaction media were ACS reagent grade and purchased from Aldrich. They were dried over 4 Å molecular sieves and titrated for water level with a Fisher Coulomatic K-F titrator before using. All solvents were purged with Ar before using

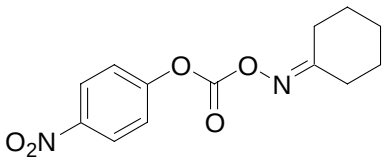
unless otherwise noted. Hexanes, ethyl acetate (EtOAc), and ethyl ether (Et_2O) used for extraction and chromatography were obtained from EM Science and used as purchased. Solutions of $NH_3 \cdot H_2O$ refers to aqueous solution. Brine refers to a saturated aqueous solution of NaCl. Purification by preparative plate chromatography was performed on EM Science Kieselgel 0.5 mm/1 mm 60 F_{254} plates. Analytical thin-layer chromatography (TLC) was carried out using Merck Kieselgel 0.25 mm 60 F_{254} plates with visualization by UV or phosphomolybdic acid. ^1H NMR and ^{13}C NMR spectra were recorded on a Varian Inova 600 MHz or 400 MHz NMR spectrometer at room temperature in $CDCl_3$ or acetone-d_6 with the solvent residual peak as internal reference ($CDCl_3$: ^1H = 7.24 ppm, ^{13}C = 77.0 ppm) unless otherwise stated. ^{19}F NMR spectra were recorded on a Varian Inova 376 MHz NMR spectrometer at room temperature in $CDCl_3$ without a reference. Data are reported in the following order: chemical shifts (δ); multiplicities (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet)); coupling constants, *J* (Hz); integration. Infrared (IR) spectroscopy was performed on a Nicolet 380 FT-IR or ASI ReactIR 1000 spectrometer. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak 20-40%), and br (broad). Uncalibrated melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes. High resolution mass spectra were obtained on a JEOL JMS-SX102/SX102A/E instrument.

Starting Materials

4-Nitrophenylchloroformate, cyclohexanone oxime, *para*-toluidine were purchased

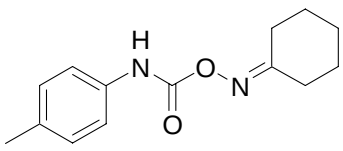
from Aldrich. CuTC was prepared according to the literature procedure.[1]

Cyclohexanone *O*-[(4-nitrophenoxy)carbonyl]oxime.



To mixture of 4-nitrophenylchloroformate (0.403 g, 2.0 mmol) and cyclohexanone oxime (0.226 g, 2.0 mmol) in 2 mL CH_2Cl_2 at 0 ^oC was added dropwise triethylamine (0.56 mL, 4.0 mmol) and catalytic amount of DMAP. The reaction was stirred for 1 h at 0 ^oC to r.t. After extraction with CH_2Cl_2, the residue was subjected to chromatography purification (5:1, hexanes:EtOAc) to afford the titled product as a yellow solid (0.466 g, Yield: 84%). Mp = 147-149 ^oC. TLC (R_f = 0.31, 5:1 hexanes:EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 8.26-8.28 (m, 2 H), 7.39-7.42 (m, 2 H), 2.60 (t, J = 6.4 Hz, 2 H), 2.39 (t, J = 6.4, 2 H), 1.62-1.78 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 155.3, 151.5, 145.4, 125.3, 121.7, 31.8, 26.9, 26.7, 25.8, 25.2. IR (neat, cm^{-1}) 2949 (m), 2864 (m), 1779 (s), 1640 (m), 1617 (m), 1594 (s), 1525 (s), 1347 (s), 1224 (s). HRMS (ESI) Calcd. for $C_{13}H_{15}O_5N_2$ ($[M+H]^+$): 279.0976. Found: 279.0975.

Cyclohexanone *O*-[[(4-methylphenyl)amino]carbonyl]oxime.

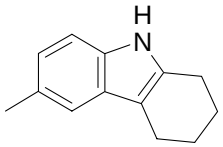


To mixture of cyclohexanone *O*-[(4-nitrophenoxy)carbonyl]oxime (0.466 g, 1.67 mmol) and *para*-toluidine (0.179 g, 1.67 mmol) in 5 mL CH_2Cl_2 at r.t. was added

[1] Zhang, S.; Zhang, D.; Liebeskind, L. S. *J. Org. Chem.* **1997**, *62*, 2312.

dropwise triethylamine (0.47 mL, 3.35 mmol). The reaction was stirred for 3 h at r.t. After extraction with CH_2Cl_2, the residue was subjected to chromatography purification (5:1, hexanes:EtOAc) to afford the titled product as a white solid (0.33 g, Yield: 80%). Mp = 138-139 ^oC. TLC (R_f = 0.33, 5:1 hexanes:EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (br, 1 H), 7.36 (d, J = 8.0 Hz, 2 H), 7.12 (d, J = 8.0 Hz, 2 H), 2.63 (t, J = 6.8 Hz, 2 H), 2.33 (t, J =6.4 Hz, 2 H), 2.30 (s, 3 H), 1.61-1.78 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 134.6, 133.6, 129.5, 119.7, 32.2, 26.92, 26.86, 25.8, 25.4, 20.8. IR (neat, cm^{-1}) 3277 (br, m), 2937 (s), 1725 (s), 1644 (m), 1602 (s), 1521 (s), 1447 (s), 1409 (s), 1316 (s), 1231 (s), 1193 (s). HRMS (ESI) Calcd. for $C_{14}H_{19}O_2N_2$ ($[M+H]^+$): 247.1441. Found: 247.1436.

2,3,4,9-Tetrahydro-6-methyl-1*H*-carbazole.[2]



A mixture of cyclohexanone *O*-[[(4-methylphenyl)amino]carbonyl]oxime (24.6 mg, 0.1 mmol) and CuTC (1.9 mg, 0.01 mmol) was flushed with argon and added 2 mL degassed DMF. The reaction was stirred under argon at 50 ^oC for 1.5 h. Purification by chromatography (10:1, hexanes : EtOAc) gave the titled compound as a white solid with matching known spectra (3 mg, Yield: 16%). Mp = 125-126 ^oC (lit. {135 ^oC}). TLC (R_f = 0.65, 5:1 hexanes : EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (br, 1 H), 7.22 (s, 1 H), 7.14 (d, *J* = 8.4 Hz, 1 H), 6.91 (dd, *J* = 8.4, 1.2 Hz, 1 H), 2.64-2.71 (m, 4 H), 2.41 (s, 3 H), 1.83-1.89 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.2, 133.8,

[2] Caubere, C.; Caubere, P.; Ianelli, S.; Nardelli, M.; Jamart-Gregoire, B. *Tetrahedron* **1994**, *50*, 11903.

128.2, 128.0, 122.4, 117.5, 109.9, 109.7, 23.29, 23.27, 23.2, 21.5, 20.9. IR (neat, cm^{-1}) 3397 (s), 2930 (s), 1594 (w).