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Debra D. Dolliver,* Bijay T. Bhattarai, Arjun Pandey, Megan L. Lanier, Amber S. Bordelon, Sarju Adhikari, Jordan A. Dinser, Patrick F. Flowers, Veronica S. Wills, Caroline L. Schneider

Department of Chemistry and Physics, Southeastern Louisiana University, SLU 10878
Hammond, LA 70402, USA
ddolliver@selu.edu

Kevin H. Shaughnessy, Jane N. Moore, Steven M. Raders, Timothy S. Snowden

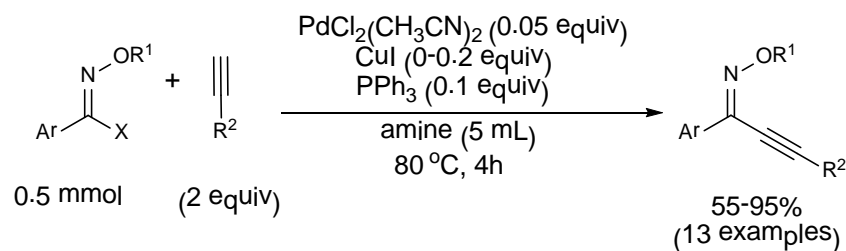
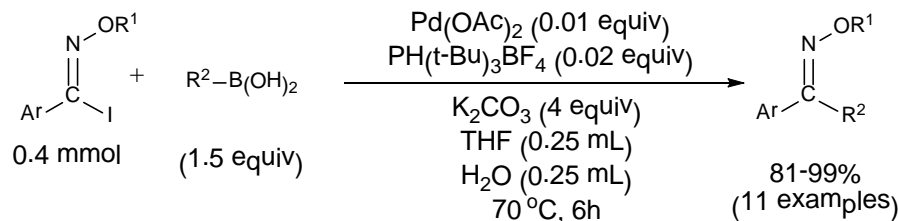
Department of Chemistry, The University of Alabama, Box 870336, Tuscaloosa, AL 35487-0336

Artie S. McKim

Gaylord Chemical Company, 106 Galaria Blvd., Slidell, LA, 70459-1209

Frank R. Fronczek

Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803



Abstract: A high-yielding stereospecific route to the synthesis of single geometric isomers of diaryl oxime ethers through Suzuki coupling of *N*-alkoxyimidoyl iodides is described. This reaction occurs with complete retention of the imidoyl halide geometry to give single *E* or *Z* isomers of diaryl oxime ethers. The Sonogashira coupling of *N*-alkoxyimidoyl iodides and bromides with a wide variety of terminal alkynes to afford single geometric isomers of aryl alkynyl oxime ethers has also been developed. Several of these reactions proceed through copper-free conditions. The Negishi coupling of *N*-alkoxyimidoyl halides is introduced. The

E and Z configurations of nine Suzuki-coupling products and two Sonogashira-coupling products were confirmed by X-ray crystallography.

Introduction:

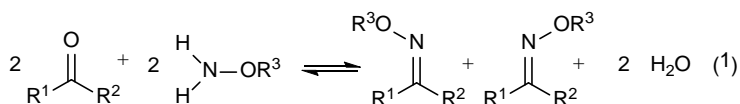
Palladium-catalyzed coupling reactions are widely used to make new carbon-carbon bonds under relatively mild conditions with good functional group tolerance. The vast majority of these coupling reactions occur at the sp^2 hybridized carbon atom of vinyl or aryl halides. Coupling reactions of sp^2 centers where the carbon is π -bonded to a heteroatom, such as acid chlorides and imidoyl halides, have received less attention, however. Cross-coupling of acyl halides with alkynes, organoboron, organotin, and other organometallic reagents to provide ketones are well precedented.¹⁻¹¹ In contrast, there are few examples of palladium-catalyzed coupling of imidoyl halides $[RC(X)=N-Y]$ to give imines.

There are a few examples of successful palladium-catalyzed coupling reactions between imidoyl halides/pseudohalides having either an alkyl or aryl group attached to nitrogen $[R'C(X)=NR''$ or $R'C(X)=NAr]$ and a nucleophilic coupling partner. Most of these reactions involve Sonogashira coupling where an imidoyl halide is coupled to a terminal alkyne.¹²⁻²² The rest are divided between Suzuki,²³ Hiyama,²⁴ Stille,^{25,26} and Negishi²⁷ coupling reactions. These reactions have provided routes to pharmacologically important compounds, including quinolines,^{14,22} lactams,²⁵ and subunits of peptides.²⁴ There are even fewer reports in which an imidoyl halide/pseudohalide containing a heteroatom attached to the nitrogen of the $C=N$ bond is used in palladium-catalyzed coupling schemes. Only two of these report coupling where the heteroatom attached to the nitrogen of the $C=N$ bond is sulfur or nitrogen. In 2008, Deng and Qian reported the palladium-catalyzed coupling of an *N*-tosyl imidoyl chloride with a boronic acid.²⁸ In 2009, Grimm described the palladium-catalyzed coupling of cyclic hydrazonyl nonaflates with boronate esters and trifluoroborate

salts.²⁹ The reports of coupling reaction where the heteroatom attached to the nitrogen of the C=N bond is oxygen will be discussed below.

The barrier to E/Z isomerization is relatively low (usually <25 kcal/mole) in most imines that have either an alkyl or aryl group attached to the nitrogen of the C=N bond.³⁰⁻³⁴ In these cases, the E/Z isomers generally interconvert readily at room temperature. This is not the case with most oxime ethers [R¹C(R²)=N-OR³], however. In these cases, the barrier to geometric isomerization is high, and they do not readily thermally isomerize.³²

The common way to make oxime ethers involves a condensation reaction between a ketone and an *N*-alkoxyamine, which generally results in a mixture of E and Z isomers (eq 1).³⁵⁻⁴² When R¹ and R² are similarly sized, such as two aryl groups, the product ratio is typically close to 50:50. These mixtures of geometric isomers, depending on the nature of R¹ and R², can be very difficult to separate. This paper explores palladium-catalyzed routes using diastereomerically pure (*Z*)-*N*-alkoxybenzimidoyl halides to stereospecifically synthesize single geometric isomers of diaryl and aryl alkynyl oxime ethers.



There have been three groups to report instances where *N*-alkoxyimidoyl halides [R¹C(X)=N-OR², X = halogen] have been used in palladium-catalyzed coupling reactions with an organometallic species [Met-R³] to make oxime ethers [R¹C(R³)=N-OR²]. The first reported example involved the Stille-type coupling of an *N*-alkoxyimidoyl bromide with an organostannane.⁴³ This reaction gave excellent yields and was thought to proceed with retained stereochemistry, but no evidence was given to support this conclusion. Our group provided the first report of Sonogashira and Suzuki coupling reactions of *N*-alkoxybenzimidoyl iodides [ArC(I)=N-OR], which demonstrated the ability to target a single geometric isomer of the oxime ether product.⁴⁴⁻⁴⁸ Subsequently Miyata, *et. al.*, wrote a communication reporting the Sonogashira and Suzuki coupling of *N*-alkoxybenzimidoyl

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2
3 bromides.⁴⁹ Their report indicated that the Sonogashira coupling generally gave good yields
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5 (67-91%) of the coupling product, but the study was somewhat limited in scope. The Suzuki
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7 coupling reaction required high catalyst (10 mol%) and ligand (20 mol%) loadings. It gave
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9 good yields when the substituent on the aromatic ring of the boronic acid was electron
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11 donating, but poor yields were seen with electron-deficient or sterically-demanding aryl
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13 boronic acids. Whereas they reported generation of a single geometric isomer for the
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15 Suzuki reaction, they failed to demonstrate that either the *E* or *Z* isomer could be made by
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17 this technique.
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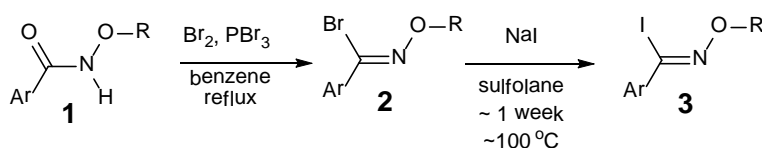
20
21 This paper reports high-yielding, stereospecific Suzuki and Sonogashira coupling
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23 reactions of (*Z*)-*N*-alkoxybenzimidoyl halides [ArC(X)=N-OR] with a variety of coupling
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25 partners to give diastereomerically pure oxime ether derivatives. The reported methodology
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27 provides high-yielding Sonogashira couplings with a wide range of alkyne coupling partners
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29 and Suzuki coupling of *N*-alkoxyimidoyl iodides using low catalyst/ligand loads while still
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31 attaining excellent yields when coupled with a wide variety of boronic acids or boronic acid
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33 derivatives. The ability of this Suzuki coupling reaction to stereospecifically produce the *E*
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35 or *Z* isomer of the oxime ether as single diastereomers is shown. In addition, the first study
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37 of an alternate pathway to the diaryl oxime ether product through Negishi coupling of an *N*-
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39 alkoxyimidoyl halide with an organozinc coupling partner is reported.
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45 Results and Discussion:

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47 Our group has previously reported the first synthesis of *N*-alkoxyimidoyl iodides⁵⁰ by
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49 the route given in Scheme 1. Although this route is high yielding, it suffers from long
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51 reaction times (up to a week), and it is difficult to remove unreacted *N*-alkoxyimidoyl bromide
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53 starting material **2** from the product. This reaction was shown to result in only the *Z*-isomer
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55 of the imidoyl iodide **3**. An improved method to synthesize the iodides (Scheme 2), which
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57 proceeds through the *N*-alkoxyimidoyl tosylates **4a-i**, was developed. The tosylates
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59
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themselves were synthesized by a method similar to that reported in the literature.⁵¹⁻⁵³ This route requires shorter reaction times and lower temperatures. The reaction mixture is easier to purify in comparison to the reaction shown in Scheme 1 as the unreacted tosylate (**4**) is easier to separate from the iodide product than bromide **2**. This reaction also results in only the Z-isomer of compound **3**. It gives good yields in all cases except in the conversion of *N*-methoxy-4-nitrobenzimidoyl tosylate **4e** to the iodide **3e**, where the reaction is very slow.

Scheme 1: Previously reported route to synthesize *N*-alkoxybenzimidoyl iodides⁵⁰



Scheme 2: Alternate route to the synthesis of *N*-alkoxybenzimidoyl iodides

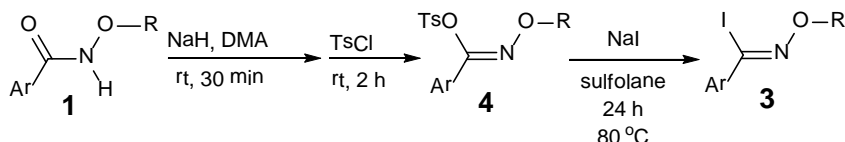


Table 1: Isolated yields of *N*-alkoxybenzimidoyl tosylates and iodides from route shown in Scheme 2

entry	Ar	R	4	yield 4 (%)	3	yield 3 (%)
1	Ph	CH ₃	4a	88	3a	87
2	4-CH ₃ Ph	CH ₃	4b	86	3b	97
3	4-ClPh	CH ₃	4c	87	3c	86
4	4-CH ₃ OPh	CH ₃	4d	72	3d	80
5	4-NO ₂ Ph	CH ₃	4e	69	3e	<20
6	3-NO ₂ Ph	CH ₃	4f	84	3f	62
7	Ph	<i>i</i> -Pr	4g	76	3g	93
8	4-CH ₃ Ph	<i>i</i> -Pr	4h	77	3h	82
9	4-ClPh	<i>i</i> -Pr	4i	78	3i	93

Suzuki Coupling: Initial studies of the Suzuki coupling utilized *N*-alkoxyimidoyl iodides **3** with trifluoroborate salts **5'**, Pd(OAc)₂, and K₂CO₃ in methanol following a procedure in the literature (eq 2).^{54,55} These conditions gave moderate to good isolated yields when using *N*-alkoxybenzimidoyl iodides **3** containing electron-withdrawing groups on the aromatic ring

and/or electron-donating groups on the trifluoroborate salt **5'**. However, under these conditions, yields were poor when there were electron-donating groups on the aromatic ring of **3** or electron-withdrawing groups on **5'** (Table 2). Of note, reactions run under these conditions produced a significant amount of the benzonitrile ($Y-C_6H_4C\equiv N$) side product and were therefore difficult to purify due to coelution of **6** and the benzonitrile side product.

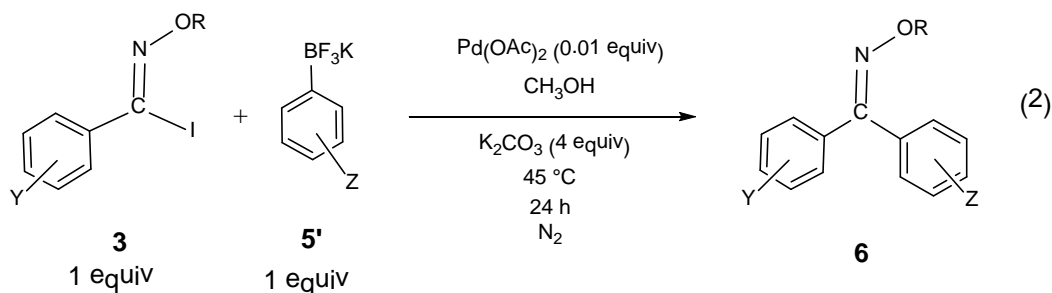
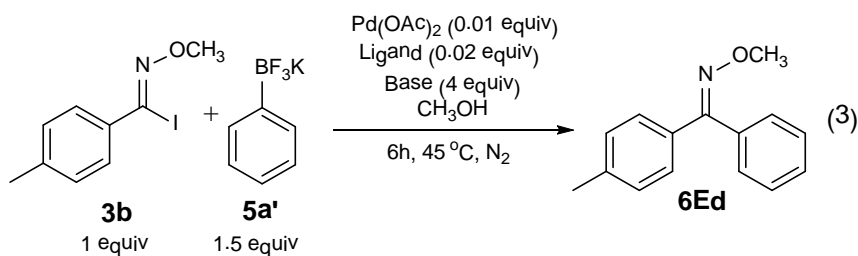


Table 2: Isolated yields for unoptimized Suzuki coupling of 3

entry	Y	Z	6	6 (% yield)
1	4-NO ₂	H	6Ee	73
2	3-NO ₂	H	6Ef	57
3	4-Cl	H	6Eb	49
4	4-CH ₃	H	6Ed	42
5	4-OCH ₃	H	6Ea	25
6	H	4-NO ₂	6Ze	0
7	H	3-NO ₂	6Zf	0
8	H	4-Cl	6Zb	35
9	H	4-CH ₃	6Zd	41
10	H	4-OCH ₃	6Za	64

The effects of added ligand [PPh_3 , $P(t-Bu)_3HBF_4$, dppf, SPhos] and different bases [Cs_2CO_3 , K_2CO_3 , KOH, KF] were then assessed using the conditions shown in equation 3. The phosphonium salt of tri-*t*-butylphosphine with potassium carbonate gave the best yields (Table 3). Although the reaction using SPhos and potassium carbonate gave a similar yield of the coupling product **6Ed**, $P(t-Bu)_3HBF_4$ was thought to be a better choice as it gave less of the 3-methylbenzonitrile byproduct.

Table 3: Optimization of Conditions for the Suzuki Coupling of **3b**

ligand	base	3b (%) ^a	6Ed (%) ^{a,b}
PPh_3	KOH	0	29
PPh_3	Cs_2CO_3	8	42
PPh_3	K_2CO_3	73	17
SPhos	KOH	0	18
SPhos	Cs_2CO_3	5	52
SPhos	K_2CO_3	3	70
$\text{P}(t\text{-Bu})_3\text{HBF}_4$	KOH	0	1
$\text{P}(t\text{-Bu})_3\text{HBF}_4$	Cs_2CO_3	65	2
$\text{P}(t\text{-Bu})_3\text{HBF}_4$	K_2CO_3	6	73
Dppf	KOH	74	0
Dppf	Cs_2CO_3	72	4
Dppf	K_2CO_3	79	2
None	KOH	1	31
None	Cs_2CO_3	6	35
None	K_2CO_3	6	32

^aAverage GC yield of four trials using tridecane as internal standard. ^bRemaining mass balance composed of benzonitrile and uncharacterized side products.

The reaction was also tried in THF and THF/H₂O, and the latter was found to increase the product yield, while decreasing formation of benzonitrile and other unidentified byproducts. Further optimization of temperature, concentration and reaction time (using the 4-methyl-substituted imidoyl iodide **3b**, and the unsubstituted trifluoroborate salt **5a'**) showed that the reaction conditions given in equation 4 gave a quantitative yield by GC analysis of the reaction mixture at 6 hours. Of note, this reaction requires low metal (1 mol%) and ligand (2 mol%) loading. Under the optimized conditions, boronic acid **5** afforded the same or higher yields as trifluoroborate salt **5'**. Therefore, the more widely available boronic acids can be used in this methodology.

Under the optimized conditions given in equation 4, good to excellent (70-99%) isolated yields of oxime ether products were obtained (Table 4). Good yields were obtained with challenging substrates, such as when strong electron-withdrawing groups were attached to the boron coupling partner (entries 13 and 15), when strong electron-donating groups were attached to the *N*-alkoxybenzimidoyl iodide (entry 3), when the more sterically demanding *N*-isopropoxyimidoyl iodide substrate was used (entries 18 and 19), or when there was a single *ortho*-substituent on the boron coupling partner (entry 7). This reaction also gave high product yield using the vinylboronic acid *trans*- β -styrylboronic acid (**5h**, entry 20), which resulted in no isomerization of the C=C or C=N bond. Coupling with 4-styrylboronic (**5i**) acid gave selective Suzuki coupling without competitive Heck reaction (entry 21). The more sterically hindered mesitylboronic acid (**5j**, entry 17) led to recovery of unreacted starting material. The reaction of 4-pyridinylboronic acid **5k** (entry 22) also gave no coupling product and showed only unreacted starting material by GC at the end of 6 hours. Using *N*-methoxyimidoyl bromide **2a** instead of the iodide **3a** (entry 9 vs. 8, 43% yield vs. 99% yield) significantly diminished the yield, suggesting that in these Suzuki coupling reactions the *N*-alkoxyimidoyl iodide is a better coupling partner

A benefit of this method is its ability to predictably synthesize exclusively the *E*- or the *Z*-oxime ether product (examples include entries 1 and 2 vs. 3, 4 and 5 vs. 6, 8 and 10 vs. 11 and 12, 13 vs. 14, 15 vs. 16, 18 vs. 19). A single diastereomer was obtained in each case where unsymmetrical oxime ethers were synthesized as determined by GC analysis and ^1H and ^{13}C NMR spectroscopy. In cases where both isomers were synthesized, such as **6Za** and **6Ea** (entries 1 and 3), the isolated products could be distinguished by both GC and ^1H and ^{13}C NMR spectroscopy.

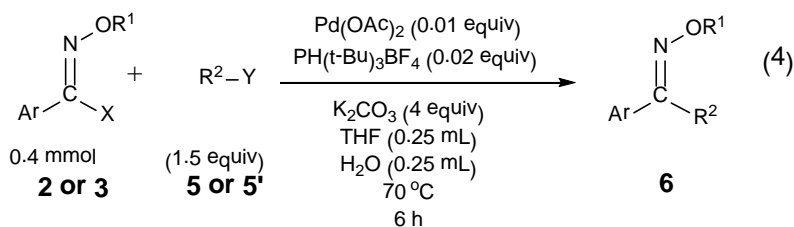


Table 4: Isolated yields for optimized Suzuki coupling reactions of *N*-alkoxybenzimidoyl halides

entry	3	5	6	yield ^a	entry	3	5	6	yield ^a
1	3a			88%	12	3b	PhB(OH) ₂		85%
		5d'	6Za				5a	6Ed	
2	3a		6Za	99%	13	3a			72%
		5d					5e	6Ze	
3	3d	PhBF ₃ K		79%	14	3e	5a		97%
		5a'	6Ea					6Ee	
4	3a			75%	15	3a			70%
		5c'	6Zb				5f	6Zf	
5	3a		6Zb	81%	16	3f	5a		96%
		5c						6Ef	
6	3c	5a'		93%	17	3a			0%
			6Eb				5j	6Zg	
7	3a			84%	18	3g	5b'		98%
		5g'	6Zc					6Zh	
8	3a			99%	19	3g	5a'		99%
		5b'	6Zd					6Eh	
9	2a	5b'	6Zd	43%	20	3a			89%
							5h	6Ei	
10	3a		6Zd	93%	21	3a			82%
		5b					5i	6Zj	
11	3c	5a'		85%	22	3a			0%
			6Eb				5k	6Zb	

^a Isolated yield carried out under the conditions in Equation 4.

The oxidative addition, transmetalation, and reductive elimination steps of the Suzuki coupling are known to occur with retention of configuration in most cases.⁵⁶ Based on this precedent, the formation of the oxime ethers would be expected to occur with retention of configuration at the imine. Several of the oxime ether products were crystalline, so X-ray crystallography was used to confirm the *E*- or *Z*-configuration of these compounds. X-ray crystallography was performed on nine of the compounds synthesized through the Suzuki coupling reaction (see Supporting Information). The X-ray crystal structures of two of the coupling reaction products run under the conditions in equation 4 are shown in Figures 1 and 2. As can be seen, the aryl group from the boron coupling partner substitutes the iodide with retention of the geometry of the C=N bond. All other compounds that were structurally characterized showed retention independent of the nature or position of the substituent on the aromatic rings on either the *N*-alkoxybenzimidoyl iodide or the boron coupling partner. Additionally, the nature of the R group attached to oxygen (methyl vs. isopropyl) does not change this trend. Based on these findings, it appears that the reaction proceeds with retention of geometric configuration, and the oxime ether moiety does not undergo isomerization under these reaction conditions.

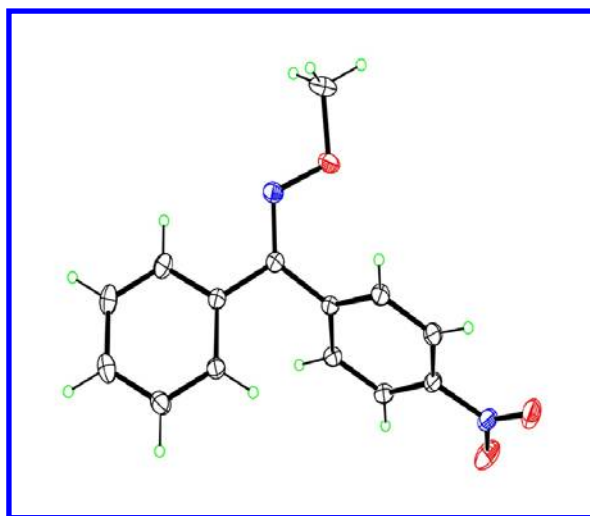


Figure 1. Thermal ellipsoid plot (50% level) of the molecular structure of **6Ze** formed from **3a** and **5e**.

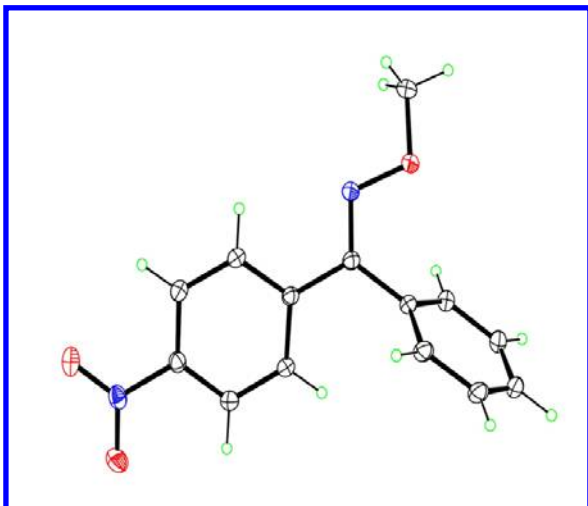


Figure 2. Thermal ellipsoid plot (50% level) of the molecular structure of **6Ee** formed from **3e** and **5a**.

The structure of one of the five *Z* Suzuki-coupled isomers determined by X-ray crystallography is illustrated in Fig.1, and one of the four *E* isomers in Fig. 2. There is little variation of the oxime ether C=N and N-O distances over all nine compounds studied. C=N distances fall in the range 1.2857(17) - 1.2949(8) Å, with mean value 1.290 Å. N-O distances fall in the range 1.4004(6) - 1.411(2) Å, with mean value 1.406 Å.

Sonogashira Coupling:

The study of the Sonogashira coupling of *N*-alkoxyimidoyl halides began using conditions similar to those given in the literature for the Sonogashira reaction of *N*-arylimidoyl chlorides.^{12,14} Initially, dichlorobis(chlorodi-*tert*-butylphosphine)palladium(II) {PdCl₂[(*t*-Bu)₂PCl]₂} was used as the precatalyst. This reaction was performed using *N*-isopropylbenzimidoyl iodide **3g** with phenylacetylene **7a** in the presence of catalytic amounts of PdCl₂[(*t*-Bu)₂PCl]₂ (5 mol%) and CuI (7 mol%) in triethylamine to produce **8Zf** in a 45% yield as measured by GC using tridecane as an internal standard. The effect of added ligands on the reaction was then examined by testing the ability of catalysts derived from a triarylphosphine (PPh₃), a sterically-hindered trialkylphosphine in its salt form [P(*t*-

Bu₃)HBF₄], a ferrocenyl diphosphine (dppf), and a Buchwald-type phosphine (SPhos) using PdCl₂(CH₃CN)₂ as the metal source for the coupling of **3g** and **7a** (eq 5). All of these ligands improved the yield of product over the ligand-free reaction, and triphenylphosphine gave the best yield of coupling product (Table 5).

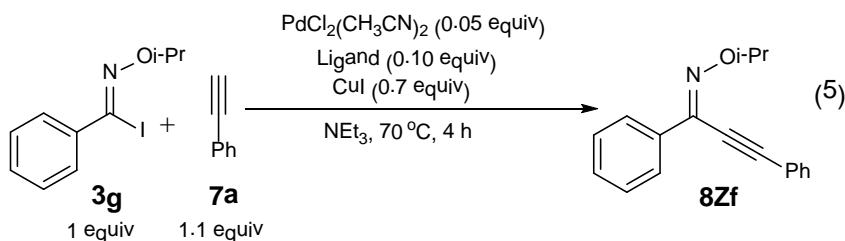
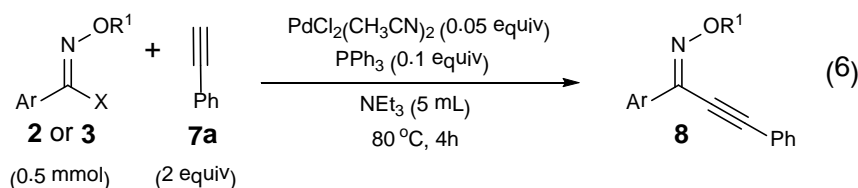


Table 5: Optimization of Conditions for the Sonogashira Coupling of 3g

ligand	3g (%) ^a	8zf (%) ^a	% other ^{a,b}
PPh ₃	13	80	7
SPhos	56	19	25
P(<i>t</i> -Bu) ₃ HBF ₄	61	23	16
dppf	59	35	6
None	77	17	6

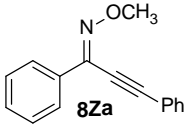
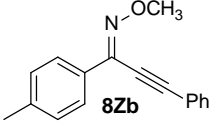
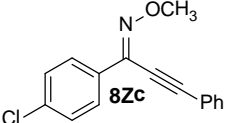
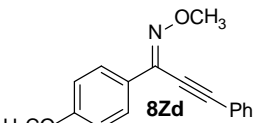
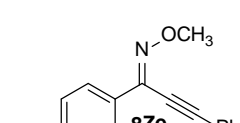
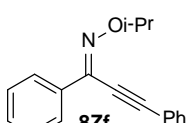
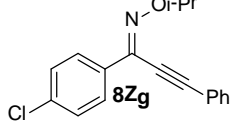
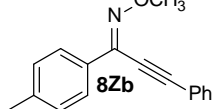
^aAverage of three GC runs using tridecane as an internal standard. ^bRemaining mass balance composed of uncharacterized side products.

The concentrations of catalyst/reagents and temperature were then adjusted using bis(acetonitrile)dichloropalladium (II) [PdCl₂(CH₃CN)₂] and triphenylphosphine ligand to give optimal yields. The optimized conditions are given in equation 6.



Using these optimized conditions, the effect of the substituent on the aryl ring of the *N*-alkoxybenzimidoyl halide was tested in the reaction with phenylacetylene (entries 1-5, Table 6). While conducting this study, it was discovered that the reaction yield was actually better in the absence of the copper co-catalyst, so all the reactions with phenylacetylene were run under copper-free conditions. It was found that the reaction worked well for all substituents (electron-donating to electron-withdrawing). Additionally, the effect of the halogen of the *N*-alkoxyimidoyl halide was tested by comparing the reaction with 4-methyl-*N*-methoxybenzimidoyl iodide **3b** vs. 4-methyl-*N*-methoxybenzimidoyl bromide **2b** (entry 2 vs. 8, 92% yield vs. 81% yield). For these reactions with phenylacetylene, it appeared that the halogen did not make a tremendous difference with the imidoyl bromide still giving a good yield. In addition, the effect of the alkoxy group attached to nitrogen (entries 6 & 7, Table 6) was examined, and it was found that this too had little effect on the reaction with the *N*-isopropoxyimidoyl iodides **3g** and **3i** also affording high yields. In all cases, products were formed as a single diastereomer as determined by GC and NMR analysis. As with the Suzuki coupling reactions, the geometry is retained in the Sonogashira reaction (Figure 3 and Supporting Information).

Table 6: Isolated yields for the optimized Sonogashira coupling reactions of *N*-alkoxyimidoyl halides (2 or 3) with phenylacetylene (7a).

entry	imidoyl halide	8	yield ^a
1	3a	 8Za	92%
2	3b	 8Zb	92%
3	3c	 8Zc	89%
4	3d	 8Zd	94%
5	2e	 8Ze	92%
6	3g	 8Zf	93%
7	3i	 8Zg	88%
8	2b	 8Zb	81%

^a Isolated yield carried out under the conditions in Equation 6.

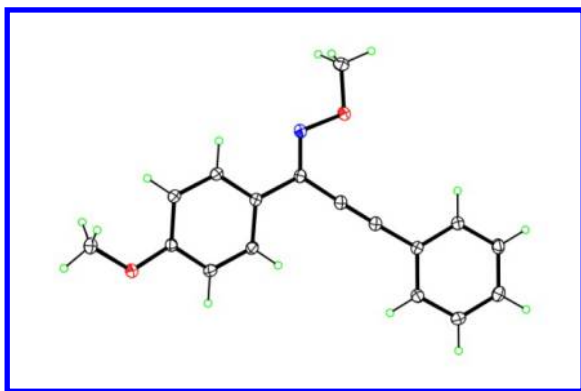


Figure 3. Thermal ellipsoid plot (50% level) of the molecular structure of **8Zd** formed from **3d** and phenylacetylene.

The structure the Sonogashira-coupled **8Zd** is illustrated in Fig. 3. The structure of **8Zi** was also determined, containing three independent molecules. Over the two structures, the oxime ether C=N distances fall in the range 1.293(4) - 1.299(4) Å, with mean value 1.297 Å. N-O distances fall in the range 1.392(4) - 1.401(3) Å, with mean value 1.396 Å.

The utility of this reaction was expanded using a straight-chain aliphatic alkyne, 1-hexyne **7b**, in the place of phenylacetylene **7a** (eq 7). It was found that this reaction did not work well without the copper co-catalyst (entry 1, Table 7). However, when copper(I) iodide was included, the reaction provided a good yield of the coupling product **8Zh** (entry 2, Table 7). As yields for this reaction were not quite as high as those for the coupling with phenylacetylene, the reaction was run with a more basic amine solvent (diisopropylamine) (entry 3, Table 7) to see if this improved the situation, but this did not significantly affect the yield. Since the Sonogashira reaction of 4-methyl-*N*-methoxybenzimidoyl bromide **2b** with phenylacetylene looked to give approximately the same yield as that between 4-methyl-*N*-methoxybenzimidoyl iodide **3b** and phenylacetylene, the effect of the halogen on the imidoyl halide was also examined when coupling with the more difficult hexyne substrate. In this more difficult reaction, it can be seen that the *N*-methoxybenzimidoyl iodide **3a** (74% yield) outperforms the *N*-methoxybenzimidoyl bromide **2a** (45% yield) (entries 3 & 4, Table 7)

under identical conditions. It appears that in this more challenging Sonogashira coupling reaction, the *N*-alkoxyimidoyl iodide **3** would be a better starting material than the bromide **2**.

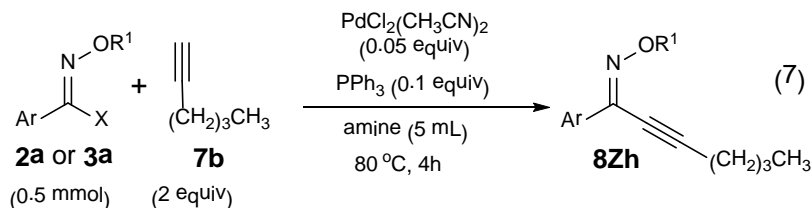


Table 7: Isolated yields of 8Zh from the Sonogashira coupling with 1-hexyne (7b)

entry	imidoyl halide	amine	CuI	8Zh (% yield)
1	3a	NEt ₃	none	11
2	3a	NEt ₃	0.15 equiv	81
3	3a	NH(<i>i</i> -Pr) ₂	0.15 equiv	74
4	2a	NH(<i>i</i> -Pr) ₂	0.15 equiv	45

The reaction was subsequently tested with a variety of functional groups on the alkyne (eq 8), and it was found that the reaction worked well in most cases if copper(I) iodide was included (Table 8) even when using the *N*-alkoxyimidoyl bromide **2a**. The one exception was 1-amino-2-propyne **7g**, which failed to give any product under these conditions (entries 3 & 4).

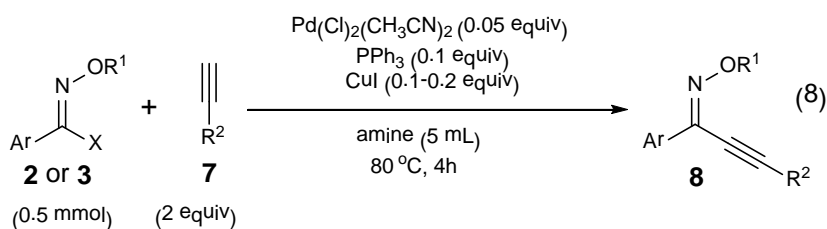
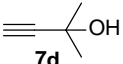
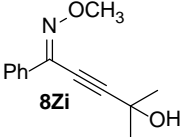

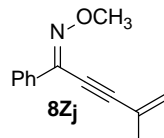
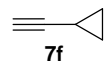
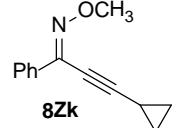
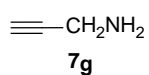
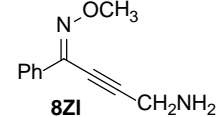
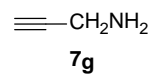
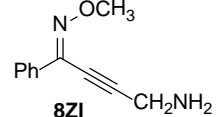
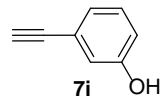
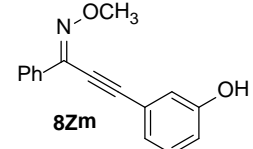


Table 8: Conditions and isolated yields of Sonogashira reaction with functionalized alkynes

entry	imidoyl halide	7	amine	CuI	8	yield ^a
1	2a		NH(<i>i</i> -Pr) ₂	(0.1 equiv)		85%
1	2a		NEt ₃	(0.2 equiv)		55%
2	2a		NH(<i>i</i> -Pr) ₂	(0.1 equiv)		95%
3	2a		NEt ₃	(0.1 equiv)		0%
4	2a		NH(<i>i</i> -Pr) ₂	(0.1 equiv)		0%
5	2a		NEt ₃	(0.1 equiv)		90%

^aIsolated yield carried out under the conditions in Equation 8

Negishi Coupling Screening:

To extend the coupling reaction to other metal species, an investigation of the coupling of *N*-alkoxyimidoyl halides with an organozinc reagent was undertaken (eq 9, Table 9). In this initial work, imidoyl iodide **3b** and phenylzinc bromide were used as model substrates. For these reactions, Pd₂(dba)₃ (5 mol %) was initially used as the palladium source along with the ligands (5 mol %) indicated in entries 1-5 in Table 9, and the reaction was run at room temperature for 1 hour. Triphenylphosphine allowed the reaction to go to completion and provided the best product **6Eb**/nitrile **9b** ratio (entry 5). On switching to PdCl₂(CH₃CN)₂ (5 mol%) as the metal source with triphenylphosphine (5 mol %) the **6Eb**/**9b** ratio further improved (entry 6).

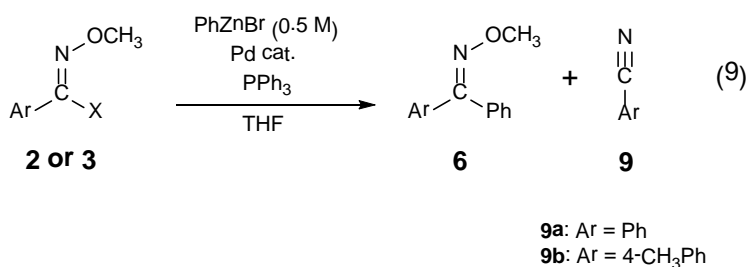


Table 9: Initial screening of palladium source and ligand in the Negishi reaction^a

entry	imidoyl halide	palladium source	ligand	6 / 9 / 3 ^b
1	3b	Pd ₂ (dba) ₃	no ligand	6.0% / 94% / 0%
2	3b	Pd ₂ (dba) ₃	SPhos	7.0% / 93% / 0%
3	3b	Pd ₂ (dba) ₃	dppf	12% / 88% / 0%
4	3b	Pd ₂ (dba) ₃	P(<i>t</i> -Bu) ₃ HBF ₄	25% / 75% / 0%
5	3b	Pd ₂ (dba) ₃	PPh ₃	26% / 74% / 0%
6	3b	PdCl ₂ (CH ₃ CN) ₂	PPh ₃	66% / 34% / 0%
7	2a	PdCl ₂ (CH ₃ CN) ₂	PPh ₃	68% / 21% / 11%

^aReaction conditions are described in equation 9. ^bDetermined by FID-GC.

Thinking that the temperature of the reaction might affect the amount of benzonitrile formation, the reaction was run at 0 °C, but the ratio of coupling product to benzonitrile remained essentially unchanged. Increasing the catalyst loading to 10 mol% Pd and 20 mol% triphenylphosphine worsened the **6Eb/9b** ratio to 52:48. Addition of TMEDA to Negishi reactions has been shown to affect coupling of alkenyl halides,⁵⁷ so the effect of this additive was investigated in this reaction. Addition of TMEDA led to mostly unreacted starting material and a lower **6Eb/9b** ratio (**6Eb/9b/3b** = 13:10:77).

The effect of the halogen on the *N*-alkoxybenzimidoyl halide was also examined, using *N*-alkoxybenzimidoyl bromide **2a** with PdCl₂(CH₃CN)₂ (5 mol %)/PPh₃ (5 mol %) at room temperature for 1 hour. The less reactive bromide **2a** gave only 89% conversion after one hour, but the **6** : **9a** ratio improved giving a **6/9a/2a** ratio of 68:21:11. This improvement in selectivity could indicate that the ease of dissociation of the halogen plays a role in the rate of formation of the benzonitrile. Addition of halide salts [N(Bu)₄Br and LiBr] in an attempt to dampen dissociation of the halide from the *N*-alkoxyimidoyl halide had no effect on the product selectivity. Future work with this reaction will focus on optimizing conditions for the Negishi coupling using the *N*-alkoxyimidoyl bromide or chloride as the coupling partner.

Conclusions:

A high yielding, stereospecific Suzuki coupling reaction of *N*-alkoxyimidoyl iodides with boronic acids or trifluoroborate salts has been established. This reaction occurs with complete retention of the imidoyl halide geometry to give single *E*- or *Z*-isomers of diaryl oxime ethers. The *N*-alkoxyimidoyl iodides and bromides also are successful substrates in the Sonogashira coupling with terminal alkynes. High yields are achieved under copper-free conditions in the coupling of phenylacetylene, whereas alkyl-substituted alkynes required copper to achieve high yields. The first attempts at Negishi coupling of *N*-alkoxyimidoyl

iodides and bromides have shown good product formation but suffer from a competing elimination reaction that forms benzonitrile. Work is currently underway to slow the elimination process responsible for the undesirable formation of benzonitrile.

Experimental:

General Procedures. All reagents were purchased from commercial sources except for $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ which was prepared by a literature procedure.⁵⁸ Phenylzinc bromide was purchased as a 1M solution in THF and stored in a glovebox. All reaction vessels were either loaded in a nitrogen atmosphere or were purged with nitrogen prior to heating. All solvents were sparged with nitrogen. ^1H and ^{13}C NMR spectra were recorded either on a 360 or 500 MHz NMR spectrometer. High resolution mass spectra were acquired in positive mode using electron impact ionization and a magnetic sector mass analyzer.

Typical procedure for the synthesis of N-alkoxybenzimidoyl tosylates (4). O-Alkyarylhydroxamate **1** (10 mmol) was placed in an oven-dried 100 mL round-bottomed flask. Anhydrous DMA (20 mL) was transferred to the flask with a syringe. Sodium hydride (60% dispersion in mineral oil) (13 mmol) was added, and the solution stirred at room temperature for approximately 30 minutes. After vigorous gas evolution had ceased, a septum was placed on the flask. The *p*-toluenesulfonyl chloride (13 mmol) was added in one portion, and the resulting solution stirred for 1 hour at room temperature. Water (25 mL) was added, and the solution was cooled on ice. The resulting precipitate was collected by suction filtration. This residue was purified by recrystallization in hexane:EtOAc or by flash chromatography (hexane:EtOAc, gradient elution).

(Z)-N-Methoxybenzimidic 4-methylbenzenesulfonic anhydride (4a). Starting from hydroxamate **1a** (1.51 g, 10 mmol), **4a** was obtained as a white crystalline solid (2.69 g, 88%, recrystallized in hexane:EtOAc). m.p 74.5-75.6 °C; IR (Nujol mull ν cm^{-1}) 1606, 1596,

1463, 1372, 1291, 1179, 1054, 1034, 1014, 934; ^1H NMR (500 MHz, CDCl_3) δ 7.85 (d, J = 8.3 Hz, 2H), 7.70-7.68 (m, 2H), 7.42-7.32 (m, 5H), 3.85 (s, 3H), 2.46 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.3, 144.9, 134.1, 130.7, 129.4, 129.2, 128.4, 128.3, 126.6, 62.8, 21.6; Anal. calcd. for $\text{C}_{15}\text{H}_{15}\text{NO}_4\text{S}$: C, 59.00; H, 4.95; N, 4.59; S, 10.50. found: C, 59.05; H, 4.99; N, 4.67; S, 10.35.

(Z)-N-Methoxy-4-methylbenzimidic 4-methylbenzenesulfonic anhydride (4b).

Starting from hydroxamate **1b** (1.65 g, 10 mmol), **4b** was obtained as a white crystalline solid (2.75 g, 86%, recrystallized in hexane:EtOAc). mp 94.8-95.9 °C; IR (Nujol mull ν cm^{-1}) 1596, 1462, 1376, 12919, 1187, 1170, 1054, 1028, 1010, 935; ^1H NMR (300 MHz, CDCl_3) δ 7.86 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 3.83 (s, 3H), 2.47 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.2, 145.1, 141.1, 134.3, 129.4, 129.2, 128.3, 126.6, 126.4, 62.7, 21.7, 21.4; Anal. calcd. for $\text{C}_{16}\text{H}_{17}\text{NO}_4\text{S}$: C, 60.17; H, 5.37; N, 4.39; S, 10.04. found: C, 60.47; H, 5.49; N, 4.50; S, 9.92.

(Z)-4-Chloro-N-methoxybenzimidic 4-methylbenzenesulfonic anhydride (4c).

Starting from hydroxamate **1c** (1.86 g, 10 mmol), **4c** was obtained as a white crystalline solid (2.96 g, 87%, recrystallized in hexane:EtOAc); mp 94.5-95.3 °C; IR (Nujol mull ν cm^{-1}) 1603, 1594, 1456, 1381, 1306, 1180, 1061, 1036, 1010, 940; ^1H NMR (360 MHz, CDCl_3) δ 7.85 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.7 Hz, 2H), 7.36-7.26 (m, 4H), 3.84 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.5, 144.1, 136.9, 134.0, 129.5, 128.8, 128.3, 127.9, 127.9, 62.9, 21.7; Anal. calcd for $\text{C}_{15}\text{H}_{14}\text{ClNO}_4\text{S}$: C, 53.02; H, 4.15; N, 4.12; S, 9.44; Cl, 10.43. found: C, 52.93; H, 4.21; N, 4.16; S, 9.16; Cl, 10.23.

(Z)-N,4-Dimethoxybenzimidic 4-methylbenzenesulfonic anhydride (4d). Starting from hydroxamate **1d** (1.81 g, 10 mmol), **4d** was obtained as a white crystalline solid (2.41 g, 72%, recrystallized in hexane:EtOAc). mp 105.9-107.0 °C; IR (Nujol mull ν cm^{-1}) 1605,

1511, 1464, 1369, 1302, 1259, 1189, 1179, 1061, 1034, 931; ^1H NMR (360 MHz, CDCl_3) δ 7.86 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 9.1 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 161.6, 145.2, 144.8, 134.2, 129.4, 128.3, 128.3, 121.6, 113.9, 62.6, 55.3, 21.6; Anal. calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_5\text{S}$: C, 57.30; H, 5.11; N, 4.18; S, 9.56. found: C, 57.37; H, 5.37; N, 4.19; S, 9.39.

(Z)-N-Methoxy-4-nitrobenzimidic 4-methylbenzenesulfonic anhydride (4e). Starting from hydroxamate **1e** (1.96 g, 10 mmol), **4e** was obtained as a yellowish crystalline solid (2.42 g, 69%, recrystallized in hexane:EtOAc). mp 103.0-104.0 $^\circ\text{C}$; IR (Nujol mull ν cm^{-1}) 1589, 1519, 1454, 1364, 1343, 1297, 1172, 1031, 944; ^1H NMR (500 MHz, CDCl_3) δ 7.85 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.8 Hz, 2H), 3.84 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.5, 144.1, 136.9, 134.0, 129.5, 128.8, 128.3, 127.9, 127.9, 62.9, 21.7; Anal. calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_6\text{S}$: C, 51.42; H, 4.03; N, 8.00; S, 9.15. found: C, 51.23; H, 3.99; N, 7.98; S, 9.08.

(Z)-N-Methoxy-3-nitrobenzimidic 4-methylbenzenesulfonic anhydride (4f). Starting from hydroxamate **1f** (1.96 g, 10 mmol), **4f** was obtained as a yellowish crystalline solid (2.94 g, 84%, recrystallized in hexane:EtOAc). mp 108.2-109.0 $^\circ\text{C}$; IR (Nujol mull ν cm^{-1}) 1526, 1463, 1377, 1351, 1308, 1192, 1180, 1057, 1028, 946; ^1H NMR (CDCl_3 , 500 MHz) δ 8.44 (t, J = 1.0 Hz, 1H), 8.25 (d, J = 4.8 Hz, 1H), 8.07 (d, J = 5.1 Hz, 1H), 7.87 (d, J = 5.1 Hz, 2H), 7.56 (t, J = 4.8 Hz, 1H), 7.38 (d, J = 4.8 Hz, 2H), 3.92 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 148.3, 146.0, 143.0, 133.7, 132.1, 131.3, 129.7, 129.7, 128.3, 125.0, 121.5, 63.4, 21.7; HRMS m/z calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_6\text{S}$, 350.0573; found 350.0573.

(Z)-N-Isopropoxybenzimidic 4-methylbenzenesulfonic anhydride (4g). Starting from hydroxamate **1g** (1.79 g, 10 mmol), **4g** was obtained as a white crystalline solid (2.53 g, 76%, recrystallized in hexane:EtOAc). mp 82.5-82.7 $^\circ\text{C}$; IR (Nujol mull ν cm^{-1}) 1594, 1463,

1366, 1287, 1190, 1014, 991; ^1H NMR (CDCl_3 , 300 MHz) δ 7.89 (d, J = 8.4 Hz, 2H), 7.75-7.72 (m, 2H), 7.41-7.32 (m, 5 H), 4.33 (m, J = 6.3 Hz, 1H), 2.47 (s, 3H), 1.16 (d, J = 6.3 Hz, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 145.1, 144.0, 134.6, 130.4, 129.9, 129.4, 128.4, 128.3, 126.6, 77.4, 21.7, 21.1; HRMS m/z calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_4\text{S}$, 333.1035; found, 333.1042.

(Z)-N-Isopropoxy-4-methylbenzimidic 4-methylbenzenesulfonic anhydride (4h).

Starting from hydroxamate **1h** (1.92 g, 10 mmol), **4h** was obtained as a whitish crystalline solid (2.68 g, 77%, recrystallized in hexane:EtOAc). mp 102.0-103.1 $^\circ\text{C}$; IR (KBr pellet ν cm^{-1}) 1612, 1595, 989; ^1H NMR (CDCl_3 , 360 MHz) δ 7.88 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 4.31 (m, J = 6.3 Hz, 1H), 2.46 (s, 3H), 2.36 (s, 3H), 1.14 (d, J = 6.3 Hz, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 145.0, 144.2, 140.7, 134.6, 129.4, 129.2, 128.3, 127.1, 126.5, 21.6, 21.4, 21.2 (OCH peak did not resolve in CDCl_3); ^{13}C NMR (d_6 -DMSO, 125 MHz) δ 145.6, 143.5, 140.9, 133.4, 129.9, 129.4, 127.9, 126.4, 126.0, 76.8, 21.1, 20.9, 20.8. HRMS m/z calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{S}$, 347.1191; found 347.1198.

(Z)-4-Chloro-N-isopropoxybenzimidic 4-methylbenzenesulfonic anhydride (4i).

Starting from hydroxamate **1i** (2.13 g, 10 mmol), **4i** was obtained as a yellowish crystalline solid (2.87 g, 78%, recrystallized in hexane:EtOAc). mp 126.7-127.6 $^\circ\text{C}$; IR (Nujol mull ν cm^{-1}) 1594, 1461, 1365, 1292, 1191, 1090, 1029, 988; ^1H NMR (CDCl_3 , 3500 MHz) δ 7.88 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.7 Hz, 2 H), 7.34-7.31 (m, 4H), 4.32 (m, J = 6.3 Hz, 1 H), 2.46 (s, 3H), 1.14 (d, J = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.3, 143.2, 136.5, 134.3, 129.5, 128.7, 128.5, 128.3, 127.8, 77.6, 21.6, 21.1; GC/MS: 305 (4.1), 303 (11.5), 198 (1.6), 196 (4.8), 155 (30.9), 141 (27.6), 139 (100), 113 (3.3), 111 (10.2), 91 (26.4); Anal. calcd. for $\text{C}_{17}\text{H}_{18}\text{ClNO}_4\text{S}$: C, 55.51; H, 4.93; Cl, 9.64, N, 3.81; S, 8.72. found: C, 55.45; H, 4.99; Cl, 9.62; N, 3.82; S, 8.52.

Typical procedure for the synthesis of *N*-alkoxybenzimidoyl iodides (3) from tosylates (4). *N*-Alkoxybenzimidoyl tosylate **4** (3.5 mmol), NaI (35 mmol) and sulfolane (20 mL) were placed in a septum-sealed vial. The mixture was stirred in an 80 °C oil bath for 24 hours. The reaction mixture was poured into 100 mL of distilled water and extracted with hexanes (3 × 100 mL). The extract was then washed with saturated aqueous NaHCO₃ solution (100 mL). The organic layer was dried with MgSO₄, and the solvent was removed under reduced pressure. The product was purified by flash silica gel chromatography using hexane:EtOA (gradient elution).

(*Z*)-*N*-Methoxy-3-nitrobenzimidoyl iodide (3f). Starting from tosylate **4f** (1.23 g, 3.5 mmol), compound **3f** was isolated as a yellow crystalline solid (664 mg, 62%). mp 67.7-68.7 °C; ¹H NMR (CDCl₃, 360 MHz) δ 8.64 (t, *J* = 1.9 Hz, 1H), 8.27-8.24 (m, 1H), 8.13-8.10 (m, 1H), 7.57 (t, *J* = 7.9 Hz, 1H); ¹³C NMR (CDCl₃, 125 MHz) δ 148.0, 137.7, 134.9, 129.3, 124.6, 124.1, 113.4, 63.0; HRMS *m/z* calcd for C₈H₇IN₂O₃, 305.9501; found 305.9502.

(*Z*)-*N*-Isopropoxy-4-methylbenzimidoyl iodide (3h). Starting from tosylate **4h** (1.22 g, 3.5 mmol), compound **3h** was isolated as a low-melting yellow crystalline solid (870 mg, 82%). mp 30.9-32.1 °C; ¹H NMR (CDCl₃, 360 MHz) δ 7.65 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 4.66 (m, *J* = 6.3 Hz, 1H), 2.35 (s, 3H), 1.39 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 140.4, 134.1, 129.4, 129.0, 116.2, 77.3, 21.8, 21.2; HRMS *m/z* calcd for C₁₁H₁₄INO, 303.0120; found 303.0123.

General Procedure for Suzuki Coupling Reactions. Tri-*t*-butylphosphonium tetrafluoroborate (2.3 mg, 0.008 mmol), anhydrous potassium carbonate (221 mg, 1.6 mmol), and either trifluoroborate salt **5'** (0.6 mmol) or boronic acid **5** (0.6 mmol) were weighed into a 3 mL vial in a glovebox and sealed with a septum. *N*-alkoxyimidoyl iodide **3** (0.4 mmol) and a solution of palladium acetate in anhydrous THF (0.016 M, 0.25 mL) were added sequentially by syringe. Nitrogen-sparged deionized water (0.25 mL) was added with

a syringe. The mixture was stirred in a 70 °C oil bath for 6 hours. The reaction mixture was poured into 50 mL of ethyl acetate, dried with MgSO₄, and the solvent was removed under reduced pressure. The product was purified by flash silica gel chromatography using hexane:EtOAc (gradient elution).

(Z)-4-Methoxybenzophenone O-methyl oxime (6Za). Starting with compound **3a** (107 mg, 0.410 mmol) and compound **5d'** (128 mg, 0.598 mmol), compound **6Za** was obtained as a colorless oil (87 mg, 88%). ¹H NMR (CDCl₃, 360 MHz) δ 7.49-7.46 (m, 2H), 7.35-7.31 (m, 5H), 6.93 (d, *J* = 8.9, 2H), 3.98 (s, 3H), 3.82 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 159.9, 156.4, 136.9, 131.1, 129.2, 128.2, 128.1, 125.4, 113.4, 62.3, 55.2; GC/MS: 241 (M, 100.0%), 210 (77.1), 167 (9.7), 77 (36.5); HRMS *m/z* calcd for C₁₅H₁₅NO₂, 241.1103; found 241.1094.

Alternatively, compound **3a** (116 mg, 0.445 mmol) and **5d** (94.3 mg, 0.621 mmol) were coupled to provide compound **6Za** as a colorless oil (106 mg, 99 %).

(E)-4-Methoxybenzophenone O-methyl oxime (6Ea). Starting with compound **3d** (119 mg, 0.409 mmol) and compound **5a'** (115 mg, 0.625 mmol), compound **6Ea** was obtained as a reddish oil that slowly crystallized (78 mg, 79%). mp 75.8-76.6 °C; ¹H NMR (CDCl₃, 360 MHz) δ 7.45-7.31 (m, 7H), 6.84 (d, *J* = 9.0, 2H), 3.94 (s, 3H), 3.79 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 160.6, 156.4, 133.6, 129.1, 129.1, 129.0, 128.6, 128.0, 113.6, 62.2, 55.2; GC/MS: 241 (M, 100.0%), 210 (74.5), 167 (10.1), 77 (34.4); HRMS *m/z* calcd for C₁₅H₁₅NO₂, 241.1103; found 241.1102.

(Z)-4-Chlorobenzophenone O-methyl oxime (6Zb). Starting with compound **3a** (111 mg, 0.425 mmol) and compound **5c'** (133 mg, 0.607 mmol), compound **6Zb** was obtained as a white crystal solid (78 mg, 75%). m.p 62.8-63.8 °C; ¹H NMR (CDCl₃, 360 MHz) δ 7.47-7.28 (m, 9H), 3.98 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 155.6, 136.0, 134.8, 131.6, 130.7,

129.4, 128.4, 128.3, 127.8, 62.4; GC/MS: 245 (M, 100.0%), 214 (67.3), 111 (14.4), 77 (55.7); HRMS m/z calcd for $C_{14}H_{12}ClNO$, 245.0607; found 245.0615.

Alternatively, compound **3a** (107 mg, 0.410 mmol) and **5c** (94.2 mg, 0.602 mmol) were coupled to provide compound **6Zb** as a white crystalline solid (82 mg, 81%).

(E)-4-Chlorobenzophenone O-methyl oxime (6Eb). Starting with compound **3c** (123 mg, 0.417 mmol) and compound **5a'** (112 mg, 0.609 mmol), compound **6Eb** was obtained as a light yellow oil (95 mg, 93%). 1H NMR ($CDCl_3$, 360 MHz) δ 7.46-7.40 (m, 5H), 7.33-7.27 (m, 4H), 3.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.6, 135.3, 134.9, 132.8, 129.1, 129.0, 129.0, 128.4, 128.2, 62.5; GC/MS: 245 (M, 100.0%), 214 (52.5), 111 (7.2), 77 (22.1); HRMS m/z calcd for $C_{14}H_{12}ClNO$, 245.0607; found 245.0610.

(Z)-2-Methylbenzophenone O-methyl oxime (6Zc). Starting with compound **3a** (106 mg, 0.406 mmol) and compound **5g'** (119 mg, 0.601 mmol) compound **6Zc** was obtained as white crystals (76 mg, 84%). mp 111.5-112.6 °C; 1H NMR ($CDCl_3$, 360 MHz) δ 7.48-7.45 (m, 2H), 7.35-7.22 (m, 6H), 7.07 (bd, J = 7.4 Hz, 1H), 3.96 (s, 3H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.6, 135.9, 135.6, 133.9, 129.9, 129.3, 128.5, 128.3, 127.9, 126.9, 125.6, 62.4, 19.6; GC/MS: 225 (M, 41.5%), 194 (100.0), 116 (16.0); HRMS m/z calcd for $C_{15}H_{15}NO$, 225.1154; found 225.1154.

(Z)-4-Methylbenzophenone O-methyl oxime (6Zd). Starting with compound **3a** (108 mg, 0.414 mmol) and compound **5b'** (120 mg, 0.606 mmol), compound **6Zd** was obtained as white crystals (92 mg, 99%). mp 69.9-70.8 °C; 1H NMR ($CDCl_3$, 360 MHz) δ 7.49-7.47 (m, 2H), 7.33-7.21 (m, 7H), 3.97 (s, 3H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.7, 138.8, 136.6, 130.3, 129.2, 129.1, 128.8, 128.1, 127.9, 62.3, 21.4; GC/MS: 225 (M, 100.0%), 194 (69.2), 91 (24.6), 77 (23.2); HRMS m/z calcd for $C_{15}H_{15}NO$, 225.1154; found 225.1161.

Alternatively, compound **3a** (109 mg, 0.418 mmol) and **5b** (81.6 mg, 0.600 mmol) were coupled to provide compound **6Zd** as a white crystals (88 mg, 93 %).

(E)-4-Methylbenzophenone O-methyl oxime (6Ed). Starting with compound **3b** (119 mg, 0.433 mmol) and compound **5a'** (112 mg, 0.609 mmol), compound **6Ed** was obtained as a colorless oil (83 mg, 85%). ^1H NMR (CDCl_3 , 360 MHz) δ 7.42-7.32 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 3.96 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 156.7, 139.3, 133.6, 133.5, 129.2, 128.9, 128.7, 128.0, 127.7, 62.3, 21.3; GC/MS: 225 (M, 100.0%), 194 (67.4), 91 (30.0), 77 (25.1); HRMS m/z calcd for $\text{C}_{15}\text{H}_{15}\text{NO}$, 225.1154; found 225.1151.

Alternatively, compound **3b** (103 mg, 0.420 mmol) and **5a** (7302 mg, 0.600 mmol) were coupled to provide compound **6Ed** as a colorless oil (80 mg, 85 %).

(Z)-4-Nitrobenzophenone O-methyl oxime (6Ze). Starting with compound **3a** (116 mg, 0.444 mmol) and compound **5e** (73.2 mg, 0.600 mmol), compound **6Ze** was obtained as reddish crystals (82 mg, 72%). mp 92.2-93.0 °C; ^1H NMR (CDCl_3 , 500 MHz) δ 8.29 (d, J = 8.9 Hz, 2H), 7.52 (d, J = 8.9 Hz, 2H), 7.45-7.33 (m, 5H), 3.99 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 154.7, 147.8, 139.9, 135.1, 130.3, 129.8, 128.5, 127.5, 123.4, 62.7; GC/MS: 256 (M, 100.0%), 225 (37.7), 179 (59.0), 77 (32.8); HRMS m/z calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_3$, 256.0848; found 256.0840.

(E)-4-Nitrobenzophenone O-methyl oxime (6Ee). Starting with compound **3e** (127 mg, 0.415 mmol) and compound **5a** (75 mg, 0.615 mmol), compound **6Ee** was obtained as a tan solid (102 mg, 97%). mp 96.6-97.6 °C; ^1H NMR (CDCl_3 , 360 MHz) δ 8.16 (d, J = 9.0 Hz, 2H), 7.66 (d, J = 9.0 Hz, 2H), 7.47-7.44 (m, 3H), 7.33-7.30 (m, 2H), 4.02 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 154.7, 148.1, 142.4, 132.0, 129.3, 128.9, 128.4, 128.4, 123.4, 62.9; GC/MS: 256 (M, 100.0%), 225 (45.8), 179 (66.0), 77 (36.8); HRMS m/z calcd for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_3$, 256.0848; found 256.0848.

(Z)-3-Nitrobenzophenone O-methyl oxime (6Zf). Starting with compound **3a** (117 mg, 0.448 mmol) and compound **5f** (137 mg, 0.598 mmol), compound **6Zf** was obtained as a tan solid (80 mg, 70%). mp 78.7-79.8 °C; ¹H NMR (CDCl₃, 360 MHz) δ 8.29-8.24 (m, 2H), 7.69-7.59 (m, 2H), 7.46-7.32 (m, 5H), 3.99 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 154.3, 148.1, 135.3, 135.2, 134.8, 129.8, 129.1, 128.5, 127.6, 124.4, 123.6, 62.6; GC/MS: 256 (M, 100.0%), 225 (51.4), 179 (71.0), 77 (39.2); HRMS *m/z* calcd for C₁₄H₁₂N₂O₃, 256.0848; found 256.0844.

(E)-3-Nitrobenzophenone O-methyl oxime (6Ef). Starting with compound **3f** (133 mg, 0.435 mmol) and compound **5a** (78 mg, 0.640 mmol), compound **6Ef** was obtained as a tan solid (107 mg, 96%). mp 71.5-72.3 °C; ¹H NMR (CDCl₃, 500 MHz) δ 8.38 (t, *J* = 1.9 Hz, 1H), 8.20-8.17 (m, 1H), 7.78 (dt, *J* = 7.8, *J* = 1.1 Hz, 1H), 7.49-7.43 (m, 4H), 7.34-7.32 (m, 2H), 4.01 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 154.4, 148.3, 138.2, 133.4, 131.9, 129.4, 129.1, 128.9, 128.4, 123.7, 122.4, 62.7; GC/MS: 256 (M, 100.0%), 225 (45.2), 179 (55.5), 77 (27.6); HRMS *m/z* calcd for C₁₄H₁₂N₂O₃, 256.0848; found 256.0846.

(Z)-4-Methylbenzophenone O-isopropyl oxime (6Zh). Starting with compound **3g** (129 mg, 0.426 mmol) and compound **5b'** (119 mg, 0.601 mmol), compound **6Zh** was obtained as white crystals (106 mg, 98%). mp 50.8-51.4 °C; ¹H NMR (CDCl₃, 360 MHz) δ 7.49-7.46 (m, 2H), 7.36-7.28 (m, 5H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.49 (m, *J* = 6.2 Hz, 1H), 2.39 (s, 3H), 1.28 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 155.6, 138.5, 137.5, 130.6, 129.7, 128.8, 128.5, 128.1, 128.1, 76.1, 21.6, 21.4; GC/MS: 253 (M, 100.0%), 211 (51.9), 194 (81.6), 165 (16.6), 91 (20.0), 77 (21.7); HRMS *m/z* calcd for C₁₇H₁₉NO, 253.1467; found 253.1465.

(E)-4-Methylbenzophenone O-isopropyl oxime (6Eh). Starting with compound **3h** (129 mg, 0.426 mmol) and compound **5a'** (110 mg, 0.598 mmol), compound **6Eh** was obtained as tan crystals (107 mg, 99%). mp 55.0-55.9 °C; ¹H NMR (CDCl₃, 360 MHz) δ

7.42-7.34 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 4.47 (m, J = 6.3 Hz, 1H), 2.34 (s, 3H), 1.27 (d, J = 6.3 Hz, 6H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 155.6, 138.9, 134.4, 133.8, 129.6, 128.8, 128.4, 127.8, 127.8, 75.9, 21.6, 21.2; GC/MS: 253 (M, 100.0%), 211 (45.0), 195 (78.8), 165 (17.8), 91 (19.6), 77 (17.8); HRMS m/z calcd for $\text{C}_{17}\text{H}_{19}\text{NO}$, 253.1467; found 253.1475.

(1E,2E)-Chalcone O-methyl oxime (6Ei). Starting with compound **3a** (112 mg, 0.428 mmol) and compound **5h** (88.7 mg, 0.599 mmol), compound **6Ei** was obtained as light orange crystal (90 mg, 89%). mp 41.6-42.8 °C; ^1H NMR (CDCl_3 , 500 MHz) δ 7.58 (d, J = 16.6 Hz, 1H), 7.53-7.49 (m, 2H), 7.46-7.39 (m, 5H), 7.33-7.26 (m, 3H), 6.75 (d, J = 16.6 Hz, 1H), 4.04 (s, 1H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 156.9, 139.1, 136.2, 134.9, 129.2, 129.0, 128.6, 128.3, 127.4, 117.7, 62.2; GC/MS: 237 (M, 28.9%), 236 (100), 206 (71.6), 128 (26.4), 102 (22.2), 91 (10.0), 77 (48.5); HRMS m/z calcd for $\text{C}_{16}\text{H}_{15}\text{NO}$, 237.1154; found 237.1151.

(Z)-4-Vinylbenzophenone O-methyl oxime (6Zj). Starting with compound **3a** (107 mg, 0.410 mmol) and compound **5i** (89.2 mg, 0.603 mmol), compound **6Zj** was obtained as a reddish oil (80 mg, 82%). ^1H NMR (CDCl_3 , 360 MHz) δ 7.50-7.44 (m, 4H), 7.36-7.28 (m, 5H), 6.73 (dd, J = 17.6 Hz, J = 10.9 Hz, 1H), 5.79 (dd, J = 17.6, J = 0.8 Hz, 1H), 5.29 (dd, J = 10.9, J = 0.7 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 156.4, 138.0, 136.4, 136.3, 132.6, 129.5, 129.2, 128.2, 127.9, 125.8, 114.8, 62.3; GC/MS: 237 (M, 100%), 206 (64.7), 103 (17.6), 77 (45.5); HRMS m/z calcd for $\text{C}_{16}\text{H}_{15}\text{NO}$, 237.1154; found 237.1147.

General procedure for Sonogashira coupling reactions. All the reactions were performed under an N_2 atmosphere. $\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (6.5 mg, 0.025 mmol), PPh_3 (13 mg, 0.05 mmol) and, if applicable, CuI (10-20 mol%) were weighed into a 8 mL reaction vial inside a glovebox. The vial was sealed with a septum, removed from the glovebox, and *N*-alkoxybenzimidoyl halide **2** or **3** (0.5 mmol), terminal alkyne **7** (2 equiv.), and amine solvent (5 mL) were added to the reaction vial with syringes. If compound **2** or **3** was solid, it was

also weighed in the glove box along with catalysts and ligands. The reaction vial was placed in an oil bath at 80 °C with stirring for 4 hours. Subsequently, distilled water (10 mL) was added to the reaction mixture, and the resulting mixture was extracted with ethyl acetate (3 X 10 mL). The organic layer was dried with anhydrous MgSO₄, and the solvent was removed under reduced pressure. The crude product was further purified by flash silica chromatography using hexane and ethyl acetate (gradient elution).

(Z)-1,3-Diphenylprop-2-yn-1-one O-methyl oxime (8Za). Starting with compound **3a** (131 mg, 0.50 mmol) and **7a** (105 mg, 1.03 mmol) in triethylamine, compound **8Za** was obtained as a reddish oil (109 mg, 92%). ¹H NMR (CDCl₃, 360 MHz) δ 7.93-7.90 (m, 2H), 7.62-7.59 (m, 2H), 7.41-7.34 (m, 6H), 4.13 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 139.9, 133.6, 132.1, 129.6, 129.5, 128.4, 128.4, 126.5, 121.8, 101.1, 79.5, 63.1; HRMS *m/z* calcd for C₁₆H₁₃NO, 235.0997; found 235.1008. ¹H NMR data are in good agreement with the literature data.⁵⁹

(Z)-3-Phenyl-1-*p*-tolylprop-2-yn-1-one O-methyl oxime (8Zb). Starting with compound **3b** (136 mg, 0.49 mmol) and **7a** (105 mg, 1.03 mmol) in triethylamine, compound **8Zb** was obtained as a reddish oil (113mg, 92%). ¹H NMR (CDCl₃, 360 MHz) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.62-7.59 (m, 2H), 7.38-7.34 (m, 3H), 7.20 (d, *J* = 8.2 Hz, 2H), 4.12 (s, 3H), 2.37 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 139.9, 139.8, 132.1, 130.9, 129.4, 129.1, 128.4, 126.4, 121.9, 100.9, 79.6, 63.0, 21.3; HRMS *m/z* calcd for C₁₇H₁₅NO, 249.1154; found 249.1158.

(Z)-1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-one O-methyl oxime (8Zc). Starting with **3c** (151 mg, 0.51 mmol) and **7a** (102 mg, 1.00 mmol) in triethylamine, compound **8Zc** was obtained as a light brown solid (123 mg, 89%). mp 48.7 – 49.6 °C; ¹H NMR (CDCl₃, 360 MHz) δ 7.84 (d, *J* = 8.8 Hz, 2H), 7.61-7.58 (m, 2H), 7.39-7.33 (m, 5H), 4.12 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 138.8, 135.6, 132.1, 132.1, 129.6, 128.6, 128.4, 127.7, 121.6, 101.5, 79.0, 63.2; HRMS *m/z* calcd for C₁₆H₁₂ClNO, 269.0607; found 269.0601.

(Z)-1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-one O-methyl oxime (8Zd). Starting with **3d** (146 mg, 0.50 mmol) and **7a** (108 mg, 1.06 mmol) in triethylamine, compound **8Zd** was obtained as a reddish-brown oil that slowly crystallized to form a light yellow solid (124 mg, 94%). mp 60.8 – 61.7 °C; ¹H NMR (CDCl₃, 360 MHz) δ 7.85 (d, *J* = 9.0 Hz, 2H), 7.61-7.59 (m, 2H), 7.38-7.34 (m, 3H), 6.91 (d, *J* = 9.0 Hz, 2H), 4.10 (s, 3H), 3.80 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 160.9, 139.5, 132.1, 129.4, 128.4, 127.9, 126.3, 121.9, 113.8, 100.8, 79.6, 62.9, 55.3; HRMS *m/z* calcd for C₁₇H₁₅NO₂, 265.1103; found 265.1105.

(Z)-1-(4-Nitrophenyl)-3-phenylprop-2-yn-1-one O-methyl oxime (8Ze). Starting with **2e** (154 mg, 0.50 mmol) and **7a** (110 mg, 1.07 mmol) in triethylamine, compound **8Ze** was obtained as yellow crystals (129 mg, 92%). m. p. 131.5 – 132.8 °C; ¹H NMR (CDCl₃, 360 MHz) δ 8.24 (d, *J* = 9.1 Hz, 2H), 8.07 (d, *J* = 9.1 Hz, 2H), 7.63-7.61 (m, 2H), 7.46-7.37 (m, 2H), 4.18 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 148.3, 139.5, 138.0, 132.1, 129.9, 128.5, 127.1, 123.6, 121.2, 102.5, 78.5, 63.6; HRMS *m/z* calcd for C₁₆H₁₂N₂O₃, 280.0848; found 280.0854. ¹H NMR data are in good agreement with the literature data.⁵⁹

(Z)-1,3-Diphenylprop-2-yn-1-one O-isopropyl oxime (8Zf). Starting with **3g** (144 mg, 0.50 mmol) and **7a** (111 mg, 1.08 mmol) in triethylamine, compound **8Zf** was obtained as a brownish oil (122 mg, 93%). ¹H NMR (CDCl₃, 360 MHz) δ 7.94-7.91 (m, 2H), 7.61-7.58 (m, 2H), 7.41-7.34 (m, 6H), 4.58 (m, *J* = 6.3 Hz, 1H), 1.39 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 139.0, 134.1, 132.1, 129.3, 129.3, 128.4, 128.3, 126.4, 122.2, 100.6, 80.0, 77.1, 21.6; HRMS *m/z* calcd for C₁₈H₁₇NO, 263.1310; found 263.1309.

(Z)-1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-one O-isopropyl oxime (8Zg). Starting with **3i** (163 mg, 0.50 mmol) and **7a** (105 mg, 1.03 mmol) in triethylamine, compound **8Zg** was obtained as a reddish-brown oil (133 mg, 88%). ¹H NMR (CDCl₃, 360 MHz) δ 7.85 (d, *J* = 8.8, 2H), 7.60-7.57 (m, 2H), 7.40-7.34 (m, 5H), 4.57 (m, *J* = 6.3 Hz, 1H), 1.39 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 138.0, 135.3, 132.7, 132.1, 129.4, 128.5, 128.4,

127.6, 122.0, 100.9, 79.6, 77.3, 21.6; HRMS m/z calcd for $C_{18}H_{16}ClNO$, 297.0920; found 297.0928.

(Z)-1-Phenylhept-2-yn-1-one O-methyl oxime (8Zh). Starting with **3a** (119 mg, 0.45 mmol), CuI (13.6 mg, 0.07 mmol) and **7b** (88 mg, 1.08 mmol) in triethylamine, compound **8Zh** was obtained as a reddish-brown oil (99 mg, 81%). 1H NMR ($CDCl_3$, 360 MHz) δ 7.85-7.82 (m, 2H), 7.37-7.35 (m, 3H), 4.08 (s, 3H), 2.54 (t, $J = 7.2$, 2H), 1.67-1.61 (m, 2H), 1.53-1.46 (m, 2H), 0.95 (t, $J = 7.3$, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 140.2, 133.9, 129.4, 128.2, 126.4, 103.8, 71.5, 62.8, 30.3, 22.0, 19.4, 13.5; HRMS m/z calcd for $C_{14}H_{17}NO$, 215.1310; found 215.1302.

(Z)-4-Hydroxy-4-methyl-1-phenylpent-2-yn-1-one O-methyl oxime (8Zi). Starting with **3a** (108 mg, 0.50 mmol), CuI (21 mg, 0.11 mmol) and **7c** (94 mg, 1.12 mmol) in diisopropylamine, compound **8Zi** was obtained as a whitish solid (93 mg, 85%). mp 64.3-65.1 °C; 1H NMR ($CDCl_3$, 360 MHz) δ 7.82-7.79 (m, 2H), 7.38-7.34 (m, 3H), 4.08 (s, 3H), 2.95 (s, 1H), 1.65 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.5, 133.3, 129.6, 128.3, 126.3, 106.3, 72.5, 65.5, 62.9, 31.1; HRMS m/z calcd for $C_{13}H_{15}NO_2$, 217.1103; found 217.1097.

(Z)-4-Methyl-1-phenylpent-4-en-2-yn-1-one O-methyl oxime (8Zj). Starting with **2a** (108 mg, 0.50 mmol), **7d** (64 mg, 0.97 mmol), and CuI (15 mg, 0.08 mmol) in NEt_3 , compound **8Zj** was obtained as a light yellow liquid (55 mg, 55%). 1H NMR ($CDCl_3$, 360 MHz) δ 7.85-7.82 (m, 2H), 7.38-7.36 (m, 3H), 5.57-5.55 (m, 1H), 5.44 (m, $J = 1.6$, 1H), 4.10 (s, 3H), 2.03 (dd, $J = 1.6$, $J = 1.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 139.8, 133.6, 129.6, 128.3, 126.4, 125.9, 124.7, 102.2, 78.3, 63.0, 23.0; HRMS m/z calcd for $C_{13}H_{13}NO$, 199.0997; found 199.1005.

(Z)-3-Cyclopropyl-1-phenylprop-2-yn-1-one O-methyl oxime (8Zk). Starting with **2a** (117 mg, 0.55 mmol), **7e** (67 mg, 1.01 mmol), CuI (10.3 mg, 0.05 mmol) in diisopropylamine, compound **8Zk** was obtained as a light yellow liquid (104 mg, 95%). 1H NMR ($CDCl_3$, 500

MHz) δ 7.80-7.78 (m, 2H), 7.35-7.34 (m, 3H), 4.07 (s, 3H), 1.60-1.54 (m, 1H), 0.99-0.92 (m, 4H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 140.0, 133.9, 129.4, 128.2, 126.4, 107.1, 66.7, 62.8, 9.4, 0.5; HRMS m/z calcd for $\text{C}_{13}\text{H}_{13}\text{NO}$, 199.0997; found 199.1002.

(Z)-3-(3-Hydroxyphenyl)-1-phenylprop-2-yn-1-one O-methyl oxime (8Zm). Starting with **2a** (109 mg, 0.51 mmol), **7h** (122 mg, 1.03 mmol), CuI (12 mg, 0.06 mmol) in NEt_3 , compound **8Zn** was obtained as a brown oil (115 mg, 90%). ^1H NMR (CDCl_3 , 360 MHz) δ 7.91-7.88 (m, 2H), 7.42-7.38 (m, 3H), 7.26-7.17 (m, 3H), 7.08-7.07 (m, 1H), 6.90-6.87 (m, 1H), 4.14 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 155.4, 140.0, 133.5, 129.8, 129.7, 128.4, 126.5, 124.8, 122.9, 118.7, 117.1, 101.8, 79.4, 63.1; HRMS m/z calcd for $\text{C}_{16}\text{H}_{13}\text{NO}_2$, 251.0946; found 251.0950.

General Procedure for monitoring Negishi Cross-Coupling Reactions.

$\text{PdCl}_2(\text{CH}_3\text{CN})_2$ (0.005 mmol) and PPh_3 (0.005 mmol) were added to a solution of *N*-alkoxybenzimidoyl halide **2** or **3** (1.0 mmol) and 1 mL of a 0.5 M solution of phenylzinc bromide (2.5 mmol) in THF. The reaction mixture was stirred in an oil bath at a set temperature. GC analysis was performed at intervals to determine product/nitrile/unreacted starting material ratio.

X-ray Experimental

Diffraction data for **6Zb**, **6Zc**, **6Zd**, **6Ze**, **6Zf**, **6Ea**, **6Ee**, **6Eh** and **8Zd** were collected at $T=90\text{K}$ using $\text{MoK}\alpha$ radiation, as were data for **6Ef** at $T=180\text{K}$. Data for **8Zi** were collected at $T=90\text{K}$ using $\text{CuK}\alpha$ radiation. All structures were solved by direct methods and refined using SHELXL⁶⁰, with H atoms in calculated positions. The 2-tolyl group of **6Zc** exhibited disorder. **6Zb**, **6Zd**, and **6Ef** have $Z'=2$, and **8Zi** has $Z'=3$. The 11 CIFs have been deposited at the Cambridge Crystallographic Data Centre, CCDC 906045-906055.

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Supporting Information: ^1H and ^{13}C NMR spectra of the products in Tables 3, 5, and 7 and X-ray results in CIF format for compounds **6Zb**, **6Zc**, **6Zd**, **6Ze**, **6Zf**, **6Ea**, **6Ee**, **6Ef**, **6Eh**, **8Zd**, and **8Zi**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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