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Palladium-Catalyzed Suzuki–Miyaura Cross-Coupling of α-Halomethyl Oxime Ethers and Site-Selective Cross-Coupling of Dihalo Derivatives

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Dedicated to Prof. Dr. M. A. Miranda on the occasion of his 60th birthday.

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Abstract: The cross-coupling reaction of chloro- and bromomethyl oxime ethers with a wide range of aryl-, heteroaryl- and vinylboronic acids in the presence of catalytic palladium complexes with different phosphines has been carried out with good yields (60–98%, 40 examples). Regioselective cross-coupling reactions differentiating between an alkyl or aryl position are achieved from dihalo oxime ethers containing Csp^2- and Csp^3-halogen bonds using mono- or dicoordinated palladium catalysts such as $Pd(dba)_2$/P(*o*-tolyl)$_3$ or $Pd(PPh_3)_4$. The selective orthogonal functionalization of dihalo oxime ethers is also described. Site-selective transformations allow the introduction of the biaryl motif into dihalo oxime ethers preserving the highly activated alkyl halide moiety vicinal to the oxime group for further transformations. In this context, *Z*- and *E*-oxime ethers could be considered as synthetic equivalents of ketones in palladium-catalyzed Suzuki reactions.

Keywords: cross-coupling; ketones; palladium; oximes; Suzuki–Miyaura reaction

Introduction

The preparation of α-arylated carbonyl compounds, a common motif in many natural and pharmaceuticals products, is a widespread topic in synthetic organic chemistry.[1] Different protocols have been established for these compounds in an attempt to avoid the use of stoichiometric strong bases and harsh reaction conditions that prevent the scale-up of the most common procedures.[2] Synthetic strategies based on metal-catalyzed[3] cross-coupling reactions have arisen with this objective in mind. In this context, the Suzuki and Buchwald–Hartwig cross-coupling approaches emerge as the most representative for these compounds using Ni or Pd catalysts. Palladium-catalyzed cross-coupling reactions offer important handling advantages,[4] but palladium shows disadvantages with substrates having β-hydrogen atoms due to the easy β-elimination reaction,[5] that can be suppressed only with the use of very basic or hindered phosphine ligands.[6] Use of Ni catalysts gives good results in these instances with the usual ligands.[7,8] The Buchwald–Hartwig palladium-catalyzed cross-coupling approach, i.e., with the carbonyl compound (functionalized substrate) acting as nucleophilic partner, has been thoroughly developed. The α-arylation of many carbonyl compounds or derivatives, such as ketones, aldehydes, esters, amides, nitriles and nitroalkanes, sulfones or sulfoximides, has been carried out successfully by this approach.[9] Electron-rich ligands capable of stabilizing the intermediate Pd(II) species are needed to catalyze these reactions. Alternatively, ligands with high steric demand are also used to favor the reductive elimination step. Consequently, biphosphines, such as BINAP,[10] 1,1′-(di-*tert*-butylphosphino)ferrocene (D*t*BPF)[11] and hindered monodentate phosphines[12] or N-heterocyclic carbenes,[13] have been reported as effective palladium ligands in these coupling reactions. One major drawback that limits the scope of this approach is the use of strong bases precluding the presence of many functional groups in the substrate.

Suzuki cross-coupling takes place under milder conditions and has been successfully applied to a variety of α-halomethyl esters,[14] amides,[15] nitriles and secondary α-cyano triflates with which the β-elimination reaction does not occur.[16] Nevertheless, only one successful example is found in the literature[14a] which employs α-halomethyl ketones in Suzuki cross-coupling; all the other attempts failed.[17]

Hence in this area, the main drawback has been the reluctance of α-halo ketones to undergo palladium-catalyzed coupling processes with arylboronic acids, apparently the simplest and most straightforward approach to α-aryl-substituted ketones.

Conversely, the palladium-catalyzed Suzuki α-arylation of oxime ethers has not been addressed to date. Many uses of these carbonyl derivatives have been found in recent years as non-steroidal anti-inflammatory drugs, mild inhibitory active compounds in poultry science, anti-protozoan, insect growth regulators, herbicides, and as various materials with steroidal effects.[18]

The Buchwald–Hartwig approach is not suitable for the α-arylation of oxime ethers as they are approximately 10 powers of 10 less acidic than the corresponding ketones.[19] The reverse approach, i.e., formation of an oxime ether by condensation of the previously α-arylated ketone obtained by cross-coupling, is unlikely due to the reluctance of α-halo ketones to participate efficiently in this type of reaction.[17] Oxime ethers and esters are efficient directing groups applied in palladium C–H activation reactions. In this way, new Csp^2–Csp^2,[20] and Csp^2–N[21] bonds at position *ortho* and new Csp^3–O[22] bonds at position β to the oxime ether function are formed (Figure 1). Furthermore, the fairly configurationally stable α-halo oxime ethers are able to avoid the direct addition of arylboronic acids to the C=N group in the presence of Pd(II) species,[23] are stable toward hydrolysis and the coupled products might have an additional value as suitable precursors for chiral primary amines[24] or may be converted into α-arylated carbonyls.[25] In spite of the preceding work, the palladium-catalyzed α-arylation reaction of oxime ethers has not yet been described and we envisaged that α-halo oxime ethers might be suitable electrophilic components in the Csp^3–Csp^2 palladium-catalyzed cross-coupling reaction. Now we describe our study on the α-arylation of halomethyl oxime ethers and the chemoselective and site-selective cross-coupling of dihalo oxime ether derivatives bearing Csp^3–X and Csp^2–X (X = Cl, Br) reactive centers with arylboronic acids which complements previous works in this field.[26,27,28,29,30,31]

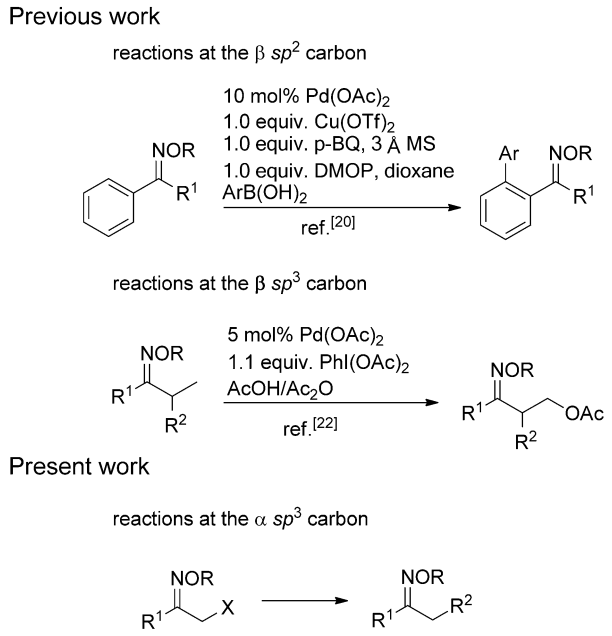


Figure 1. Palladium-catalyzed transformations with oxime ethers.

Results and Discussion

α-Bromomethyl (*Z*)-**1a** and α-chloromethyl (*Z*)-**1b** oxime ethers (Figure 2) react with aryl-, heteroaryl- and alkenylboronic acids **2** (Figure 3) in the presence of a Pd(0) catalyst to efficiently afford the corresponding α-arylated derivatives **3** with good yields (Table 1, runs 1–4, 8, 12 and Table 2). Both compounds **1a** and **1b** gave similar yields with the parent phenylboronic acid **2a** or electron-rich substituted boronic acids. Bromo oxime ether (*Z*)-**1a** reacted with the electron-deficient boronic acid **2c** to give (*E*)-**3c** contaminated with dehalogenation (*E*)-**4a** and reductive homocoupling **5a** products. Reactions with the chloro derivative **1b** were slower recovering unreacted about 20% of the starting material after 3 h. However, the readily available oxime ether (*Z*)-**1b** was selected to assay the optimal reaction conditions for the cross-coupling due to its greater stability (see the Supporting Information) and given the absence of secondary reactions.

Monophosphines (PPh_3) and diphosphines (Xantphos and BINAP) were tested as ligands in the reaction of (*Z*)-**1b** with three representative boronic acids with different electronic characters (Table 1).

PPh_3 gave the best results with the parent boronic acid **2a** (runs 4, 6 and 7), but Xantphos gave the best yield with the electron-poor boronic acid **2c** (runs 12, 14 and 15). Conversely, no differences were found in the catalytic behavior of these three ligands in reactions with the electron-rich boronic acid **2b** (runs 8, 10 and 11).

Cesium fluoride in THF, which is inert towards **1** (see the Supporting Information), is very effective in promoting the transmetallation of boronic acids in

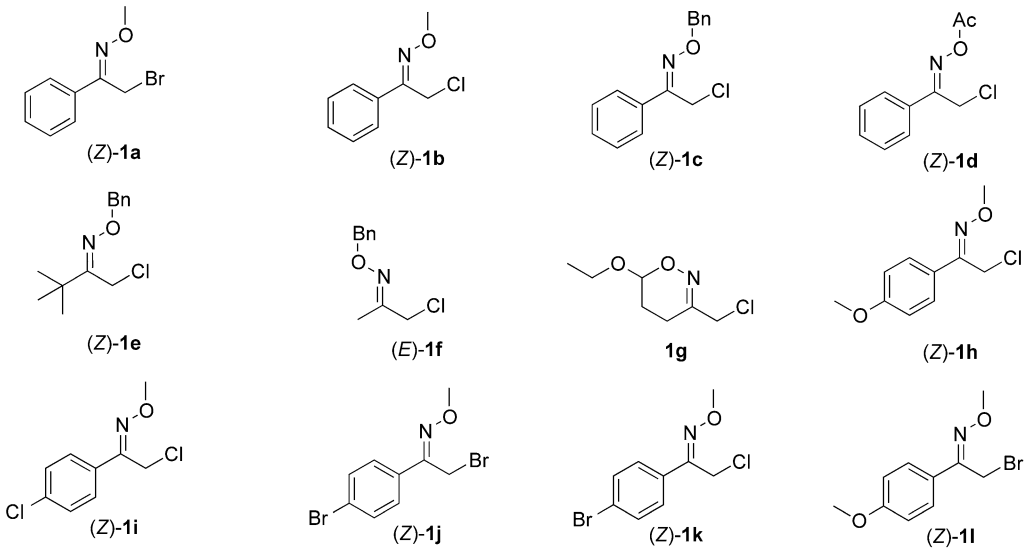


Figure 2. Halomethyl oxime ethers **1**.

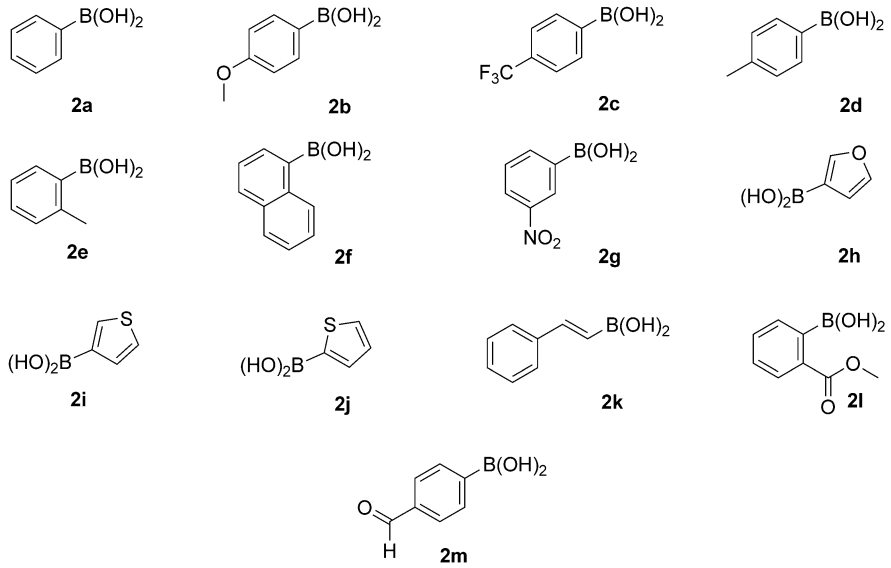
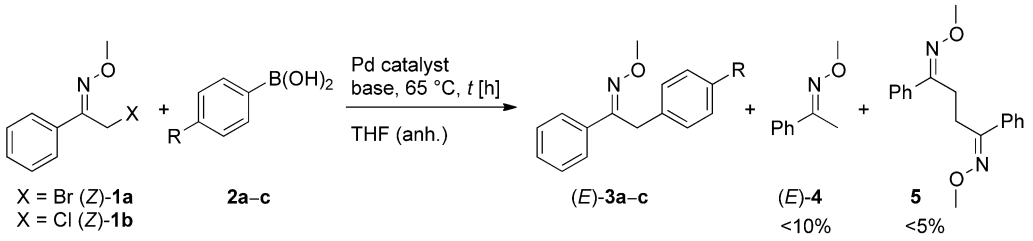


Figure 3. Boronic acids **2**.

the oxime coupling process. However, the reactions promoted by Cs_2CO_3 were very slow, probably due to the low solubility of this salt, and led to a 90% conversion after 16 h thus favoring the formation of secondary products (*E*)-**4** (10%) and **5** (8%) (see Table S1 in the Supporting Information). The total conversion of **1a** was achieved in 2 h improving the solubility of Cs_2CO_3 by using a 4:1 THF/water mixture as the solvent, but a 40% yield of dehalogenation product (*Z*)-**4** resulted under these conditions (see Table S1 in the Supporting Information). It is worthy of note that despite the basic character of the oxime group, no reaction took place in the absence of base, thus suggesting that this group is unable to promote the transmetallation with boronic acid (see the Supporting Information).

Optimization of the concentration of all the reagents was also carried out (Table 1). Electron-poor boronic acid **2c** was sensitive to the concentration leading to the best yield in 6×10^{-2} M solution (runs 12 and 13). In contrast, the parent and the electron-rich boronic acids **2a** and **2b** gave similar results in either 6×10^{-2} M or 3×10^{-2} M solution (runs 4/5, 8/9). Increasing the concentration with Xantphos as the ligand favored the formation of the inactive complex[32] $Pd(Xantphos)_2$ and yield decreased (see Table S1 in the Supporting Information).

Table 1. Optimization of the catalytic system[a] for palladium-catalyzed Suzuki cross-coupling reactions with α-halomethyl oxime ethers.



Run	1	2	Pd catalyst	(n×10^{-2}) [M]	Base [equiv.]	*t* [h]	3 Yield [%]
1	**a**	**a**	$Pd(PPh_3)_4$ 10 mol%	3	4 CsF	0.5	(*E*)-**3a** 94
2	**a**	**b**	$Pd(PPh_3)_4$ 10 mol%	3	4 CsF	0.5	(*E*)-**3b** 90
3	**a**	**c**	$Pd(PPh_3)_4$ 10 mol%	3	4 CsF	0.5	(*E*)-**3c** 83
4	**b**	**a**	$Pd(PPh_3)_4$ 10 mol%	3	4 CsF	1	(*E*)-**3a** 99
5	**b**	**a**	$Pd(PPh_3)_4$ 10 mol%	6	3 CsF	0.75	(*E*)-**3a** 98
6	**b**	**a**	$Pd(OAc)_2$ 10 mol%/Xantphos 7 mol%	3	4 CsF	3	(*E*)-**3a** 91
7	**b**	**a**	$Pd(OAc)_2$ BINAP 10 mol%	3	4 CsF	1	(*E*)-**3a** 85
8	**b**	**b**	$Pd(PPh_3)_4$ 10 mol%	3	4 CsF	1	(*E*)-**3b** 92
9	**b**	**b**	$Pd(PPh_3)_4$ 10 mol%	6	4 CsF	1	(*E*)-**3b** 86
10	**b**	**b**	$Pd(OAc)_2$ 10 mol%/Xantphos 7 mol%	3	4 CsF	1	(*E*)-**3b** 99
11	**b**	**b**	$Pd(OAc)_2$ BINAP 10 mol%	3	4 CsF	3	(*E*)-**3b** 92
12	**b**	**c**	$Pd(PPh_3)_4$ 10 mol%	3	4 CsF	3	(*E*)-**3c** 65
13	**b**	**c**	$Pd(PPh_3)_4$ 10 mol%	6	3 CsF	1	(*E*)-**3c** 87
14	**b**	**c**	$Pd(OAc)_2$ 10 mol%/Xantphos 7 mol%	3	4 CsF	4	(*E*)-**3c** 75
15	**b**	**c**	$Pd(OAc)_2$ BINAP 10 mol%	6	4 CsF	3	(*E*)-**3c** 48

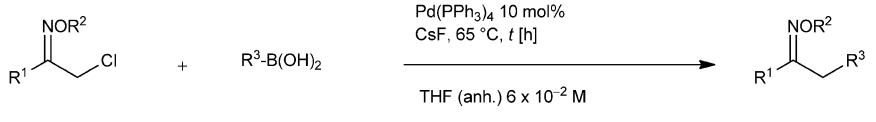
[a] *Reaction conditions:* 0.3 mmol **1a** or **1b**, 0.6 mmol **2a–c**, Pd source, phosphine ligand, CsF, degassed dry THF, *t* [h]. Yields were determined by ^{1}H NMR analysis, with acetophenone as internal standard.

With the optimized conditions in hand, we next tested a wide range of boronic acids **2a–m** with aryl halomethyl oxime ether (*Z*)-**1b** affording the expected cross-coupling products with good yields (Table 2). The best results were obtained with the parent boronic acid **2a** and substituted boronic acids containing electron donor groups **2b** and **2d**, even at the *ortho*-position **2e**. Heteroarylboronic acids (**2h**, **2i**, **2j**) also gave satisfactory results in the cross-coupling. In general, all the reactions took place with moderate to good yields, including the strong electron-deficient boronic acids **2c** and **2g**. Moreover, the reaction allowed other substituents such as esters **2l** or aldehydes **2m**.

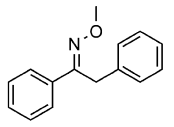
To determine the scope of the electrophilic partner in this new coupling, we also tested the behavior of different oxime ethers **1c–i** and the oxime ester **1d** with representative boronic acids. All the reactions took place under the same conditions as described above for aryl oximes (*Z*)-**1b**, and also gave comparable yields (Table 2). The reactions with alkyl (CH_3 or *t*-Bu) oxime ethers worked nicely with acids **2a** and **2c**, but the coupling with **2b** proved less efficient with a lower conversion, giving the corresponding product **3**, contaminated by the oxidative homocoupling derivative from **2b**. Cyclic oxime **1g** gave the coupled products with only a moderate yield but, in this case, with total conversion and formation of the corresponding dehalogenated product **4** to some extent. The electronic character of the aryl group in aryl oxime ethers did not significantly affect the course of the coupling reaction. Substitution of the oxime OCH_3 for the bulkier OCH_2Ph group in (*Z*)-**1c** did not influence the course of the reactions [Table 2, products (*E*)-**3n–p**]. However, oxime (*Z*)-**1d**, in which the oxime ether group had been replaced by an ester, reacted with the electron-rich boronic acid **2b** to give coupled product (*E*)-**3q** in only 18% yield, as well as other products from the nucleophilic attack of the palladium enolate to the oxime ester. Acyclic starting oxime ethers **1** showed *Z* stereochemistry and were prepared from the corresponding commercially available α-halo ketones as a single diastereosisomer after column chromatography (determined by GC analysis), except for **1f** and **1d**. All the cross-coupling products showed *E* stereochemistry;[33] i.e., the same geometry as the starting oxime. Minor isomerization (2–8%) was observed only in the case of (*Z*)-**1e**, suggesting that the coordination between the C=N double bond and the metal promotes the isomerization to give the product with the thermodynamic equilibrium mixture composition.

Conversely, methyl oxime ether (*E*)-**1f** was obtained as a 90:10 *E*/*Z* diastereomeric mixture. The

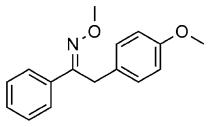
Table 2. Palladium-catalyzed cross-coupling reactions of α-halomethyl oxime ethers **1** with boronic acids **2**.[a]



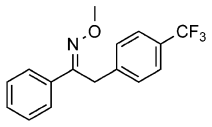
1b–i **2a–m** **3a–af**



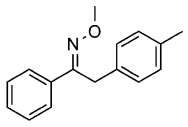
(*E*)-**3a** (90%, 1 h, B)



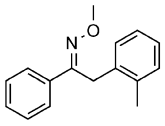
(*E*)-**3b** (83%, 1 h, A)



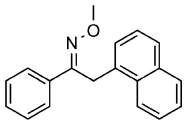
(*E*)-**3c** (98%, 0.5 h, B)



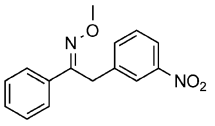
(*E*)-**3d** (70%, 2 h, A)



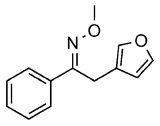
(*E*)-**3e** (84%, 2 h, A)



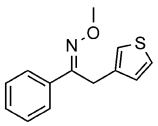
(*E*)-**3f** (60%, 3.5 h, B)



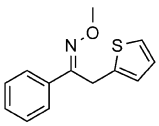
(*E*)-**3g** (63%, 5 h, B)



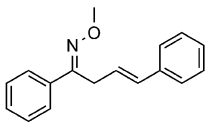
(*E*)-**3h** (85%, 2 h, B)



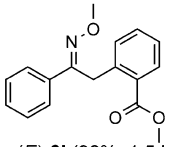
(*E*)-**3i** (79%, 1 h, B)



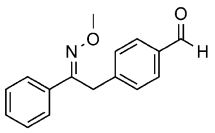
(*E*)-**3j** (67%, 1 h, B)



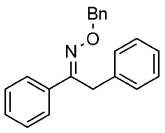
(*E*)-**3k** (81%, 1.5 h, A)



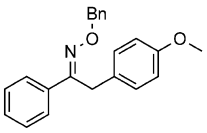
(*E*)-**3l** (98%, 1.5 h, A)



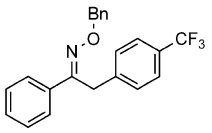
(*E*)-**3m** (40%, 1 h, B)



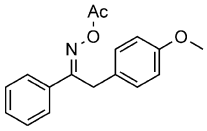
(*E*)-**3n** (88%, 1 h, B)



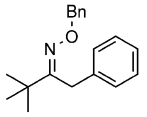
(*E*)-**3o** (75%, 1 h, A)



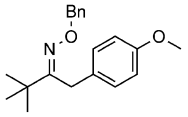
(*E*)-**3p** (85%, 1 h, B)



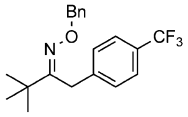
(*E*)-**3q** (18%, 12 h, A)



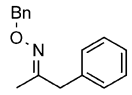
(*E*)-**3r** (98%, 1 h, B)
(*E*/*Z*) 92:8



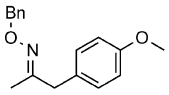
(*E*)-**3s** (65%, 1 h, A)
(*E*/*Z*) 94:6



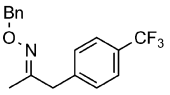
(*E*)-**3t** (80%, 1 h, A)
(*E*/*Z*) 98:2



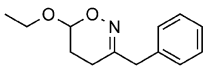
(*E*)-**3u** (88%, 1 h, B)
(*E*/*Z*) 94:6



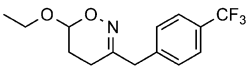
(*E*)-**3v** (62%, 2.5 h, A)
(*E*/*Z*) 91:9



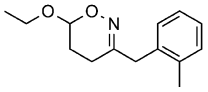
(*E*)-**3w** (90%, 1 h, B)
(*E*/*Z*) 94:6



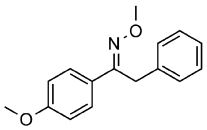
(*E*)-**3x** (52%,[b] 2 h, B)



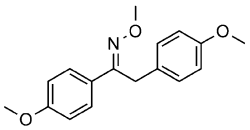
(*E*)-**3y** (59%, 2 h, B)



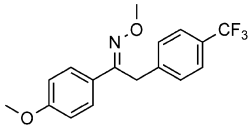
(*E*)-**3z** (65%, 2 h, A)



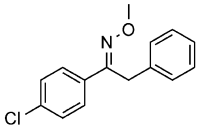
(*E*)-**3aa** (93%, 1 h, B)



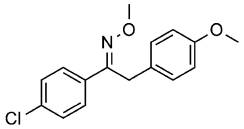
(*E*)-**3ab** (78%, 1 h, A)



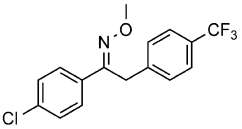
(*E*)-**3ac** (68%, 2 h, B)



(*E*)-**3ad** (97%, 1 h, B)



(*E*)-**ae** (87%, 1 h, A)

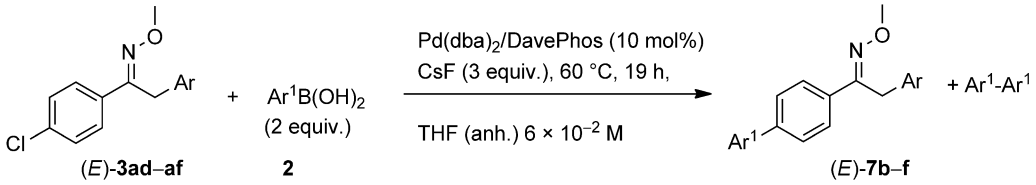


(*E*)-**3af** (96%, 1 h, B)

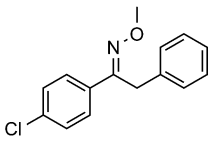
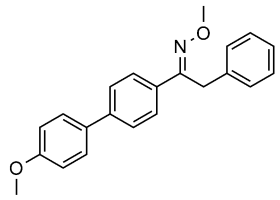
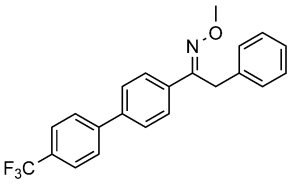
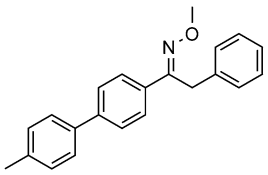
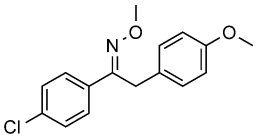
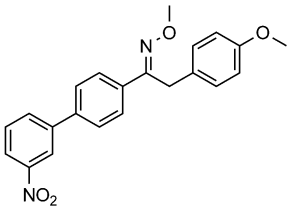
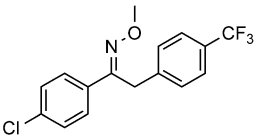
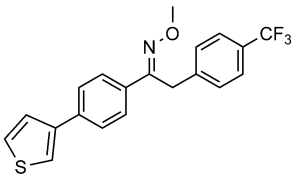
[a] *Reaction conditions:* A = 0.3 mmol **1a–f**, 0.6 mmol **2a–j**, 0.03 mmol $Pd(PPh_3)_4$, 1.2 mmol CsF, 5 mL degassed dry THF, 65 °C, *t*; B = 0.9 mmol CsF. Isolated yields.

[b] 64%, 20 h when $Pd(OAc)_2$/BINAP 10 mol% was used.

Table 3. Palladium-catalyzed orthogonal functionalization of (*Z*)-**1i**.



(*E*)-**3ad**–**af** **2** (*E*)-**7b**–**f**

Run	(*E*)-**3**	**2**	(*E*)-**7**	Yield[a] [%]
1		**b**		-
2	(*E*)-**3ad**	**c**		72
3	(*E*)-**3ad**	**d**		15
4		**g**		56
5		**i**		56

[a] Isolated yields.

isomers ratio was determined by ^{1}H NMR and the stereochemistry was assigned according to the ^{13}C NMR data. When a 97:3 *E/Z* mixture of **1f** was used in the cross-coupling with different boronic acids under similar conditions, the same (±3–6%) isomer composition ratio was determined for the *E*/*Z* alkyl, aryl oxime ether mixtures after coupling.

(*Z/E*)-2-Chloro-1-phenylethanone *O*-acetyloxime **1d** was obtained after purification as a 96:4 *Z*/*E* diastereoisomeric mixture. A similar *E/Z* isomer ratio was observed after reaction with **2d**.

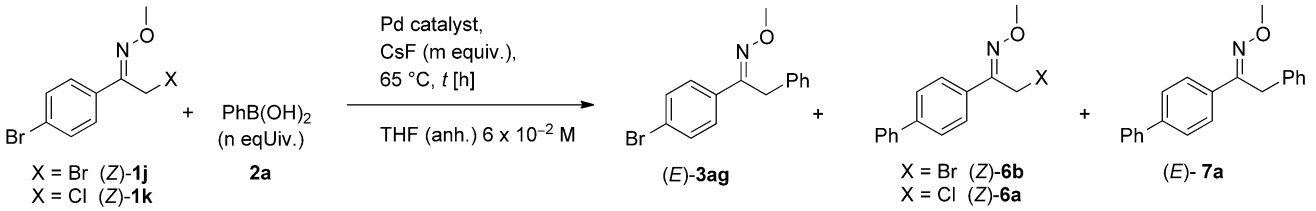
Oxime (*Z*)-**1i** is a bifunctional alkyl and aryl halide bearing two alternative Csp^3–Cl and Csp^2–Cl positions for the cross-coupling reaction. A high regioselectivity was exhibited by (*Z*)-**1i** to the reaction of the Csp^3–Cl bond with arylboronic acids of any electronic character to give compounds (*E*)-**3ad**, (*E*)-**3ae**, and (*E*)-**3af** (see Table 2). In the absence of activating groups, the high reactivity of aryl and vinyl halides and the low reactivity of alkyl halides in palladium-catalyzed cross-coupling reactions are well-established. Our results clearly show a strong activation of the (oxime) Csp^3–Cl bond as compared to the (aryl) Csp^2–Cl bond present in the molecule. The presence of a sulfoxide group[34] at the α-position in relation to the sp^3 carbon or a benzyl halide[35] also gives rise to highly reactive alkyl halides as previously reported.

The enhanced reactivity shown by α-chloro oximes at the Csp^3–Cl bond suggests an S_N2 oxidative addition mechanism similar to that observed in the cross-coupling reactions with α-bromo sulfoxides.[36] This prompted us to study the regioselective cross-coupling reaction of either the alkyl or aryl halide in a series of difunctional dihalo oxime ethers **1i–k** to determine the scope and limits of this challenging reaction (see Table 4 and Table S2 in the Supporting Information). The reaction at the sp^3 hybridized C–Cl bond was always faster if compared to the sp^2 carbon, despite the ligand in the Pd-catalyst, thus showing the difficulty in carrying out the selective oxidative addition at the Csp^2–Cl bond (see Table S2 in the Supporting Information). On the other hand, Buchwald's phosphine 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl (DavePhos) or $P(Cy)_3$ increased the reactivity of the catalyst at the Csp^2–Cl bond, but doubly coupled products were obtained. However, the high discrimination caused by the $Pd(PPh_3)_4$ catalyst presented an opportunity for the orthogonal functionalization of (*Z*)-**1i**. Consecutive cross-coupling reactions catalyzed first with Pd-PPh_3 and then with Pd-DavePhos enabled the incorporation of two different aryl groups into the molecule with moderate yields (Table 3). Similar results in this double functionalization were obtained in a *one-pot* reaction (see the Supporting Information for details). Only moderate conversions were accomplished in the second coupling at the sp^2 carbon. Besides products **7**, compounds **3** were recovered partially unchanged after 19 h at 60 °C. The slow oxidative addition step at the Csp^2–Cl bond allowed the undesired homocoupling reaction of electron-rich[37] boronic acids **2b** and **2d** in the reaction with *(E)*-**3ad**.

Next we explored the site-selective palladium-catalyzed cross-coupling reaction just at the sp^2 carbon using (*Z*)-**1j** as the model compound. This bromo oxime ether holds two C–Br electrophilic carbons with sp^3 and sp^2 hybridization, respectively. Our previous findings in regioselective palladium-catalyzed reactions of bromomethyl *p*-bromophenyl sulfoxide showed that the oxidative addition to Csp^3– and Csp^2–Hal bonds follows two different reaction mechanisms.[36] The first, identified as an S_N2 substitution, occurs at the Csp^3–Hal bonds and involves Pd(0) dicoordinated species. The second, a concerted mechanism, takes place with Csp^2–Hal bonds and involves monocoordinated Pd(0). In this way, encumbered triaryl monophosphines as palladium ligands, give efficient catalysts in the cross-coupling at Csp^2 for biaryls. Thus, we assayed the reaction with hindered [P(*o*-tolyl)$_3$] and unhindered PPh_3 as metal ligands (Table 4, runs 1 and 2). The reaction at the Csp^3–Br bond was very fast and, as expected, the catalytic system Pd-PPh_3 showed a high preference to couple at the Csp^3 site. Hence monoarylated regioisomer **3ag** prevailed over **6b** and the double-coupled product **7a**. In contrast, reactions catalyzed with the hindered Pd-P(*o*-tolyl)$_3$ preferentially gave the monoarylated product **6b** with moderate regioselectivity as compared to Csp^3 coupled product **3ag**, but poor given the amount of diarylated product **7a** obtained. The reactivity of the Csp^3–Br bond in position α to the activating oxime ether group appears to be exceedingly high to be tuned by the ligand in the palladium catalyst.

At this point, in order to tune up the regioselective coupling with the ligand, we designed the readily available oxime ether (*Z*)-**1k** as a difunctional model. It combines, on the one hand, the less reactive C–Cl bond at the Csp^3 site to slow down the oxidative addition rate and, on the other hand, the more reactive C–Br bond at the Csp^2 position to enhance the reactivity at this site. In this context, we assayed a series of palladium catalysts containing phosphines with different properties (Table 4, runs 3 and 4). Oxime (*Z*)-**1k** reacted with one equivalent of boronic acid **2a** in the presence of 10 mol% $Pd(PPh_3)_4$ to afford the monoarylated cross-coupling product **3ag** at the sp^3 carbon with good conversion and high regioselectivity (Table 4, run 3). Only minor amounts of monoarylated derivative **6a** (1%) and diarylated product **7a** (3%) were formed under these conditions. However, use of **2a** in excess led to increasing amounts of diarylated **7a**, revealing that the oxidative addition is faster at the Csp^3–Cl than at the Csp^2–Br bond with diphosphine complexes (see Table S3 in the Supporting In-

Table 4. Effect of the ligand on the regioselectivity of a Suzuki reaction.[a]



Run	**1**	*n* [equiv.]	*m* [equiv.]	Time [h]	Pd catalyst[b]	Conv. [%]	(*E*)-**3** [%]	(*Z*)-**6** [%]	(*E*)-**7** [%]
1	**j**	1	2	1	C	**93**	**85**	0	7
2	**j**	1	2	3	D	54	2	24	24
3	**k**	1	2	1	C	77	71	1	3
4	**k**	1.5	3	1	E	**100**	0	**91**	9

[a] Yields were determined by the ^{1}H NMR analysis, with acetophenone as an internal standard.
[b] C = $Pd(PPh_3)_4$ 10 mol%; D = $Pd(OAc)_2$ 10 mol%/P(*o*-tolyl)$_3$ 20 mol%, E = $Pd(dba)_2$ 10 mol%/P(*o*-tolyl)$_3$ 20 mol%.

formation,). On the other hand, the Pd-P(*o*-tolyl)$_3$ catalyst led to monocoupled product **6a** at the sp^2 carbon with high conversion and regioselectivity (Table 4, run 4). The (*Z*)-**1k**/**2a** ratio modified only the conversion, but the regioselectivity remained unchanged. Conversely, selectivity decreased from 91% to 79% when $Pd(dba)_2$ was substituted for $Pd(OAc)_2$ as the Pd source in the catalyst (see Table S3 in the Supporting Information,). With the optimized conditions in hand, we next tested different boronic acids and (*Z*)-**1k** in the cross-coupling with $Pd(PPh_3)_4$ and $Pd(dba)_2$/P(*o*-tolyl)$_3$ as catalysts (Table 5).

Regioselectivity did not depend on the electronic character of the substituents in the boronic acid and compounds **2a–d** gave similar results in the coupling (Table 5).

Mechanism

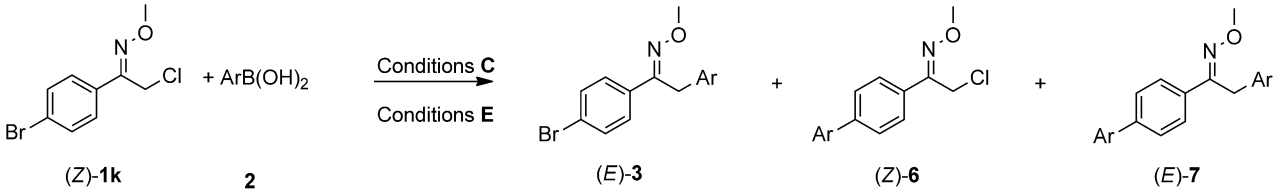
Palladium-catalyzed cross-coupling reactions involving carbonyl compounds playing the role of either the electrophilic or the nucleophilic partner require the use of hindered and/or electron-rich phosphine ligands to stabilize the intermediate Pd(II) oxidative addition species and/or to facilitate the reductive elimination step. Surprisingly, triphenylphosphine, a ligand lacking the above-mentioned characteristics, has been revealed as the ligand of choice to couple carbonyl derivatives such as α-halomethyl oxime ethers with boronic acids. This fact prompted us to examine whether the oxime ether group itself shows some inherent coordinating ability to stabilize the intermediate Pd(II) species. This could be related to the presence of an oxygen atom in the oxime ether placed at four bonds from the Pd(II) center. A similar interaction model has been discussed in the formation of palladacycles from *N,N*-dimethylhydrazones.[38] This O–Pd coordination would be present in the reactions of compounds **1** shown in Figure 2 with the only exception being cyclic oxime **1g**, from which an increased amount of dehalogenation and a slower overall coupling reaction time were observed if compared to its linear counterparts. The variable temperature ^{1}H, ^{13}C and ^{31}P NMR behavior of the oxidative addition product **8**, generated in $CDCl_3$ in a sealed tube under an Ar atmosphere, was registered to verify the suggested O···Pd interaction. The broad signals corresponding to the oxime methylene and methyl protons (2.39 and 3.57 ppm, respectively) in the ^{1}H (400 MHz) and the broad signal (9.4 ppm) in the proton-decoupled ^{31}P (162 MHz) NMR spectra suggest the existence of a fast ligand coordination–decoordination process taking place at room temperature.[39]

The ^{31}P NMR spectrum at 0 °C shows the presence of a minor amount of the square-planar complex *cis*-**8** [δ = 38.31 ppm (d, J = 37.9 Hz, 1 P) and δ = 16.91 ppm (d, J = 37.9 Hz, 1 P)] together with a broad band assigned to a major mixture of phosphorus containing species in equilibrium with free PPh_3.This equilibrium was slower at −20 °C and finally collapsed at −60 °C, giving two sharp phosphorus signals at δ = 25.61 and −7.3 ppm assigned to the square-planar complex *trans*-**8** and free PPh_3, respectively. However, the methyl ether and the α-methylene groups appeared in the ^{1}H NMR spectrum as broad coupled signals, even at this low temperature (see the Supporting Information).

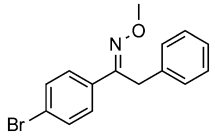
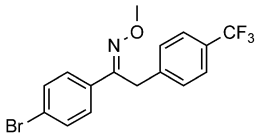
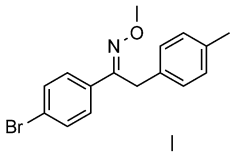
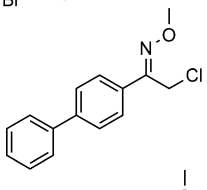
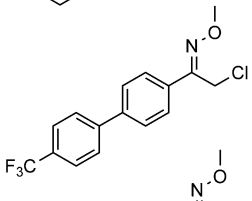
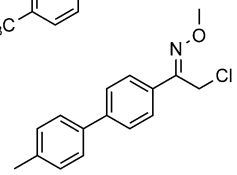
These results evidenced the existence of a slow *cis*-*trans* equilibrium between two palladium species **8**, and an unusually fast PPh_3 exchange which is frozen at −60 °C. However, this later exchange was slow for the oxidative addition complex **9**, even at 0 °C (see the Supporting Information).

The ether oxygen at the oxime moiety appeared to behave as an intramolecular labile ligand, occupying a coordination vacancy in the Pd(II) complex[40] and allowing the fast phosphine exchange in intermediate

Table 5. Regioselective arylation of (*Z*)-**1k**.



(*Z*)-**1k** **2** (*E*)-**3** (*Z*)-**6** (*E*)-**7**

Run	Conditions[a]	2	Product		Yield [%][b]	Conv. [%]	3:6:7
1	C	**a**		(*E*)-**3ag**	68	77	95:1:4
2	C	**c**		(*E*)-**3ah**	58	65	100:0:0
3	C	**d**		(*E*)-**3ai**	60	64	100:0:0
4	E	**a**		(*E*)-**6a**	88	100	0:91:9
5	E	**c**		(*E*)-**6c**	71	73	0:100:0
6	E	**d**		(*E*)-**6d**	87	100	0:92:8

[a] C = $Pd(PPh_3)_4$ (0.03 mmol, 10 mol%), **1k** (0.3 mmol, 1 equiv.), **2** (0.3 mmol, 1 equiv.), CsF (0.6 mmol, 2 equiv.), degassed dry THF 5 mL, 65 °C, 1 h; E = $Pd(dba)_2$ (0.03 mmol, 10 mol%), P(*o*-tolyl)$_3$ (0.03 mmol, 10 mol%), **1k** (0.3 mmol, 1 equiv.), **2** (0.45 mmol, 1.5 equiv.), CsF (0.9 mmol, 3 equiv.), degassed dry THF 5 mL, 65 °C, 1 h.
[b] Isolated yield.
[c] Reaction time 5 h.

8. In this way, the ether group in the catalytic cycle would play a similar role to that usually played by oxygenated solvents,[41] which are coordinated at the axial position in the usual catalytic processes (see Figure 4). In this way, the coordination of the oxime ether would play a double role to favor the coupling reaction by fixing, on the one hand, the Pd position at the C-terminus in the azaenolate system and facilitating, on the other hand, the *cis-trans* isomerization[42,43] and ligand dissociation processes[44] in the catalytic cycle.

Conclusions

In short, (*Z*)-α-halomethyl oxime ethers are suitable substrates for palladium-catalyzed Suzuki cross-coupling reactions with a wide variety of aryl-, heteroaryl- and vinylboronic acids to afford the corresponding

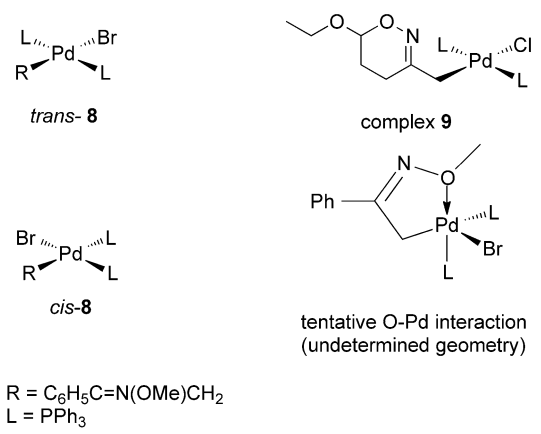


Figure 4. Oxidative addition complexes.

α-methyl-substituted oxime ethers with good yields. The behavior of halo oxime ethers in palladium-catalyzed reactions is substantially different if compared with the parent α-halo ketones that hardly give the expected α-coupled products in palladium-catalyzed Suzuki reactions. This different behavior strongly suggests that the nature of the functional group adjacent to the reactive C–Hal bond plays a key role in the outcome of the reaction. This role, in the case of oxime ethers, becomes particularly significant when the relative orientation of the oxime ether group and the α-halogen is *syn*. This *syn*-orientation allows the O–Pd interaction between the oxygen ether and palladium in the intermediate oxidative addition complex, and (*Z*)-α-halomethyl oxime ethers become privileged substrates for the α-coupled products. Accordingly, cyclic oximes with *anti*-orientation of oxygen and palladium give the coupled products, but only with a moderate yield. In this context, *Z*- and *E*-oxime ethers can be considered as synthetic equivalents of ketones in palladium-catalyzed Suzuki reactions. This approach nicely complements previous existing methods for the transition metal-catalyzed arylation of ketones, most of them under basic conditions, and could be advantageous due to the use of air-stable chemicals, easy-to-handle catalysts, simple phosphine ligands and non-basic mild conditions.

In addition, chemo- and site-selective cross-coupling reactions have been developed by differentiating between the alkyl or aryl position in dihalo oxime ethers containing Csp^2– and Csp^3–Hal bonds and by taking advantage of the different mechanism of the oxidative addition step with mono- or dicoordinated palladium catalysts. The synthesis of monoarylated products at either the sp^3 or sp^2 carbons, and the selective orthogonal functionalization of dihalo oxime ethers, has been achieved with good yields and high selectivity.

Experimental Section

General Methods

Reactions were carried out under an argon atmosphere. All reagents were used as received from the commercial supplier. THF was distilled from sodium/benzophenone. Cross-coupling reactions were monitored by analytical thin layer chromatography using commercial aluminum sheets precoated (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck). Visualization was carried out with UV light. Selective cross-coupling reactions were monitored by gas chromatography. GC analyses were performed with a Finnigan Focus GC instrument equipped with a glass capillary column SGE PBX5 (30 m length, 0.25 mm inner diameter, 0.25 μm film thickness) and flame ionization detection under a constant flow of 1 mL min^{-1} helium carrier gas. GC-MS analyses were performed with a GC Agilent 6890N system equipped with a glass capillary column HP-5 MS UI (30 m length, 0.25 mm inner diameter, 0.25 μm film thickness) and a low resolution quadrupole analyzer detector with helium carrier gas at a constant flow of 1 mL min^{-1}. Product purification by flash chromatography was performed using E. Merck Silica Gel (230–400 mesh). Proton and carbon magnetic nuclear resonance spectra were recorded at 300 MHz and 75 MHz, respectively, with a Bruker AC-300 or at 400 MHz and 101 MHz with a Bruker AV-400. Chemical shifts are reported in ppm relative to the TMS peak at 0.000 ppm (^{1}H) and the $CHCl_3$ peak at 77.16 ppm (^{13}C). Coupling constants (*J*) are given in Hertz (Hz). The letters m, s, d, t, q and sept stand for multiplet, singlet, doublet, triplet, quartet and septuplet, respectively. The letters br indicate broad signal. High-resolution mass spectra were determined in a Fisons VG Autospec instrument. All melting points are uncorrected and were recorded in a Cambridge Instruments apparatus.

Preparation and Characterization of Starting Materials (1)

For synthesis and characterization of halomethyl oxime ethers (**1a–1l**), see the Supporting Information.

Palladium-Catalyzed Suzuki–Miyaura Cross-Coupling Reaction with α-Halomethyl Oxime Ethers (1a–1i); General Procedure

To an oven-dried 15-mL flask, previously evacuated and flushed with argon for three times, the appropriate boronic acid **2a–m** (0.6 mmol), CsF (1.2 mmol for conditions A or 0.9 mmol for conditions B), $Pd(PPh_3)_4$ (0.03 mmol), α-halo oxime **1a–i** (0.3 mmol) and dry degassed THF (5 mL) were added. The resulting mixture was stirred at 65 °C for the appropriate time, and then cooled to room temperature, filtered through a Celite pad and washed with CH_2Cl_2 (20 mL). Solvents were removed under reduced pressure and the residue was purified by column chromatography yielding the corresponding products **3a–3af**.

For details on the procedure for palladium-catalyzed Suzuki–Miyaura cross-coupling reactions with (*E*)-**3ad**, (*E*)-**3ae** and (*E*)-**3af** and palladium-catalyzed regioselective Suzuki–Miyaura cross-coupling reactions with dihalo oxime ethers (**1j** and **1k**), see the Supporting Information.

Reaction of (*Z*)-2-Bromo-1-phenylethanone *O*-Methyloxime (1a) with $Pd(PPh_3)_4$: Oxidative Addition Complexes 8 and 9

For details on the synthesis and detection of compounds **8** and **9**, see the Supporting Information.

Spectral Data for Compounds 3

***(E)*-1,2-Diphenylethanone *O*-methyloxime[45] (3a) [CAS: 163586-90-1]:** Yield: 90%; white solid; mp 52–56 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.60–7.52 (m, 2H), 7.26–7.19 (m, 3H), 7.19–7.04 (m, 5H), 4.06 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.2, 136.8, 135.8, 129.2, 128.7, 128.6 (2), 126.6, 126.4, 62.2, 32.8; HR-MS (EI): m/z = 225.1152 (M^+), calcd. for $C_{15}H_{15}NO$: 225.1154.

***(E)*-2-(4-Methoxyphenyl)-1-phenylethanone *O*-methyloxime (3b) [CAS: 146364-41-2]:** Yield: 80%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.61–7.51 (m, 2H), 7.28–7.21 (m, 3H), 7.06 (dm, J = 8.7 Hz, 2H), 6.72 (dm, J = 8.7 Hz, 2H), 4.00 (s, 2H), 3.95 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.2, 156.6, 135.9, 129.6, 129.2, 128.6, 127.9, 126.6, 114.1, 62.2, 55.4, 31.9; HR-MS (EI): m/z = 255.1251 (M^+), calcd. for $C_{16}H_{17}NO_2$: 255.1259.

***(E)*-1-Phenyl-2-[4-(trifluoromethyl)phenyl]ethanone *O*-methyloxime (3c):** Yield: 680%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.57–7.51 (m, 2H), 7.42 (dm, J = 8.0 Hz, 2H), 7.28–7.20 (m, 5H), 4.10 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.3, 141.0, 135.4, 129.5, 128.9, 128.7, 126.5, 125.6, 125.6 (q, J = 3.8 Hz), 124.4 (q, J = 271.7 Hz), 62.3, 32.6; HR-MS (EI): m/z = found 293.1035 (M^+), calcd. for $C_{16}H_{14}F_3NO$: 293.1027.

***(E)*-1-Phenyl-2-*p*-tolylethanone *O*-methyloxime (3d) [CAS: 113694-72-7]:** Yield: 70%; white solid; mp 29–31 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.60–7.52 (m, 2H), 7.27–7.19 (m, 3H), 7.03 (dm, J = 8.2 Hz, 2H), 6.98 (dm, J = 8.2 Hz, 2H), 4.02 (s, 2H), 3.94 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.4, 135.9, 133.7, 129.6, 129.4, 129.2, 128.5, 128.4, 126.6, 62.2, 32.3, 21.1; HR-MS (EI): m/z = 240.1391 ($M+H^+$), calcd. for $C_{16}H_{18}NO$: 240.1383.

***(E)*-1-Phenyl-2-*o*-tolylethanone *O*-methyloxime (3e):** Yield: 84%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.53–7.45 (m, 2H), 7.25–7.17 (m, 3H), 7.10–6.88 (m, 4H), 3.96 (s, 2H), 3.91 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.3, 136.2, 136.0, 134.8, 130.2, 129.2, 128.5, 127.7, 126.5, 126.5, 126.3, 62.2, 30.6, 19.9; HR-MS (EI): m/z = 239.1304 (M^+), calcd. for $C_{16}H_{17}NO$: 239.1310.

***(E)*-2-(Naphthalen-1-yl)-1-phenylethanone *O*-methyloxime (3f):** Yield: 60%; white solid; mp 105–107 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.03 (dd, J = 8.3, 0.8 Hz, 1H), 7.79 (dd, J = 7.9, 1.6 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.58–7.38 (m, 4H), 7.29–7.07 (m, 5H), 4.47 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.2, 135.9, 133.9, 132.2, 132.0, 129.2, 129.0, 128.5, 127.2, 126.5, 126.3, 125.8 (2), 125.3, 123.5, 62.3, 30.1; HR-MS (EI): m/z = 276.1375 ($M+H^+$), calcd. for $C_{19}H_{18}NO$: 276.1383.

***(E)*-2-(3-Nitrophenyl)-1-phenylethanone *O*-methyloxime (3g):** Yield: 63%; white solid; mp 68–72 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 8.03 (ddd, J = 2.2, 1.7, 0.5 Hz, 1H), 7.97 (dm, J = 8.1 Hz, 1H), 7.59–7.52 (m, 2H), 7.45 (dtd, J = 7.6, 1.7, 0.6 Hz, 1H), 7.34 (t, J = 7.9 Hz, 1H), 7.31–7.22 (m, 3H), 4.15 (s, 2H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.9, 148.6, 139.0, 135.0, 134.8, 129.6, 129.6, 128.8, 126.4, 123.7, 121.7, 62.4, 32.4; HR-MS (EI): m/z = 270.1005 (M^+), calcd. for $C_{15}H_{14}N_2O_3$: 270.1004.

***(E)*-2-(Furan-3-yl)-1-phenylethanone *O*-methyloxime (3h):** Yield: 85%; white solid; mp 28–30 °*C*; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.61–7.53 (m, 2H), 7.30–7.24 (m, 3H), 7.22 (t, J = 1.7 Hz, 1H), 7.15 (dd, J = 2.3, 1.4 Hz, 1H), 6.19 (d, J = 0.9 Hz, 1H), 3.94 (s, 3H), 3.79 (d, J = 0.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 142.9, 140.1, 135.6, 129.3, 128.6, 126.4, 120.0, 111.4, 62.2, 22.7; HR-MS (EI): m/z = 216.1015 ($M+H^+$), calcd. for $C_{13}H_{14}NO_2$: 216.1019.

***(E)*-1-Phenyl-2-(thiophen-3-yl)ethanone *O*-methyloxime (3i):** Yield: 79%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.62–7.51 (m, 2H), 7.29–7.19 (m, 3H), 7.12 (dd, J = 6.4, 3.4 Hz, 1H), 6.90–6.88 (m, 1H), 6.87 (dd, J = 4.9, 1.3 Hz, 1H), 4.01 (d, J = 0.9 Hz, 2H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.0, 136.5, 135.7, 129.3, 128.6, 128.4, 126.5, 125.6, 121.7, 62.2, 27.8; HR-MS (EI): m/z = 231.0710 (M^+), calcd. for $C_{13}H_{13}NOS$: 231.0718.

***(E)*-1-Phenyl-2-(thiophen-2-yl)ethanone *O*-methyloxime (3j):** Yield: 67%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.65–7.56 (m, 2H), 7.31–7.23 (m, 3H), 7.03 (dd, J = 5.1, 1.3 Hz, 1H), 6.83–6.74 (m, 2H), 4.19 (d, J = 0.8 Hz, 2H), 3.98 (s, 3H); ^{3}C NMR (75 MHz, $CDCl_3$): δ = 155.5, 138.7, 135.3, 129.4, 128.6, 126.8, 126.5, 125.9, 124.2, 62.2, 27.4; HR-MS (EI): m/z = 231.0714 (M^+), calcd. for $C_{13}H_{13}NOS$: 231.0718.

(1*E*,3*E*)-1,4-Diphenylbut-3-en-1-one *O*-methyloxime (3k): Yield: 81%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.65–7.57 (m, 2H), 7.33–7.06 (m, 8H), 6.40 (dt, J = 15.9, 1.6 Hz, 1H), 6.18 (dt, J = 15.9, 6.4 Hz, 1H), 3.95 (s, 3H), 3.58 (dd, J = 6.4, 1.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.7, 137.4, 135.8, 132.1, 129.3, 128.6 (2), 127.4, 126.5, 126.3, 124.3, 62.2, 30.8; HR-MS (EI): m/z = 252.1391 ($M+H^+$), calcd. for $C_{17}H_{18}NO$: 252.1388.

***(E)*-Methyl 2-[2-(methoxyimino)-2-phenylethyl]benzoate (3l):** Yield: 98%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.83 (dd, J = 7.8, 1.5 Hz, 1H), 7.57–7.48 (m, 2H), 7.31–7.10 (m, 5H), 7.07 (dm, J = 7.7 Hz, 1H), 4.49 (s, 2H), 3.90 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.1, 156.4, 138.1, 135.7, 132.4, 130.9, 129.5, 129.2, 129.2, 128.5, 126.6, 126.3, 62.2, 52.1, 31.0; HR-MS (EI): m/z = 284.1289 ($M+H^+$), calcd. for $C_{17}H_{18}NO_3$: 284.01281.

***(E)*-4-[2-(Methoxyimino)-2-phenylethyl)benzaldehyde (3m):** Yield: 40%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 9.88 (s, 1H), 7.71 (d, J = 8.1 Hz, 2H), 7.55 (dd, J = 6.7, 2.9 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.28–7.24 (m, 3H), 4.15 (s, 2H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.0, 155.2, 144.3, 134.9, 130.3, 129.5, 129.3, 128.7, 126.5, 62.4, 33.0; HR-MS (EI): m/z = 253.1101 (M^+), calcd. for $C_{16}H_{15}NO_2$: 253.1103.

***(E)*-1,2-Diphenylethanone *O*-benzyloxime (3n):** Yield: 88%; white solid; mp 35–37 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.63–7.50 (m, 2H), 7.34–7.18 (m, 8H), 7.17–7.03 (m, 5H), 5.19 (s, 2H), 4.09 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.6, 138.0, 136.8, 135.8, 129.2, 128.6, 128.5, 128.4, 128.3, 127.9, 126.7, 126.3, 76.5, 32.9; HR-MS (EI): m/z = 302.1543 ($M+H^+$), calcd. for $C_{21}H_{20}NO$: 302.1539.

***(E)*-2-(4-Methoxyphenyl)-1-phenylethanone *O*-benzyloxime (3o):** Yield: 75%; white solid; mp 68–70 °C; ^{1}H NMR

(300 MHz, $CDCl_3$, TMS): $\delta = 7.59–7.51$ (m, 2H), 7.34–7.18 (m, 8H), 7.02 (dm, $J = 8.8$ Hz, 2H), 6.68 (dm, $J = 8.8$ Hz, 2H), 5.20 (s, 2H), 4.02 (s, 2H), 3.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 158.1$, 156.9, 138.1, 135.8, 129.6, 129.2, 128.8, 128.5, 128.5, 128.4, 127.9, 126.7, 114.0, 76.4, 55.3, 32.0; HR-MS (EI): $m/z = 332.1650$ (M^+), calcd. for $C_{22}H_{22}NO_2$: 332.1645.

(*E*)-1-Phenyl-2-[4-(trifluoromethyl)phenyl]ethanone *O*-benzyloxime (3p): Yield: 85%; white solid; mp 56–58 °C; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.58–7.52$ (m, 2H), 7.39 (d, $J = 8.2$ Hz, 2H), 7.30–7.23 (m, 8H), 7.23–7.17 (m, 2H), 5.19 (s, 2H), 4.13 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 155.7$, 141.1, 137.7, 135.4, 129.5, 128.9, 128.7, 128.5, 128.4, 128.1, 126.5, 125.6 (q, $J = 3.8$ Hz), 124.4 (q, $J = 271.8$ Hz), 76.7, 32.8; HR-MS (EI): $m/z = 370.1414$ (M^+), calcd. for $C_{22}H_{19}F_3NO$: 370.1413.

(*E*)-2-(4-Methoxyphenyl)-1-phenylethanone *O*-acetyloxime (3q): Yield: 18%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.65$ (dd, $J = 7.9$, 1.5 Hz, 2H), 7.37–7.23 (m, 3H), 7.03 (d, $J = 8.4$ Hz, 2H), 6.78–6.65 (m, 2H), 4.10 (s, 2H), 3.69 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 169.0$, 164.2, 134.2, 130.7, 129.6, 128.8, 127.7, 127.3, 114.4, 55.4, 33.6, 20.0; HR-MS (EI): $m/z = 283.1235$ (M^+), calcd. for $C_{17}H_{17}NO_3$: 283.1208.

(*E/Z*)-3,3-Dimethyl-1-phenylbutan-2-one *O*-benzyloxime (3r): Isomeric ratio (92:8); yield: 98%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.27–6.99$ (m, 10H), 5.00 (s, 2H), 3.66 (s, 2H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.7$, 138.3, 137.7, 128.5, 128.4, 128.3, 128.2, 127.6, 125.9, 75.7, 37.8, 31.8, 28.5; HR-MS (EI): $m/z = 281.1783$ (M^+), calcd. for $C_{19}H_{23}NO$: 281.1780.

(*E/Z*)-1-(4-Methoxyphenyl)-3,3-dimethylbutan-2-one *O*-benzyloxime (3s): Isomeric ratio (94:6); yield: 65%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.26–7.16$ (m, 5H), 6.98–6.91 (m, 2H), 6.70–6.62 (m, 2H), 5.01 (s, 2H), 3.68 (s, 3H), 3.59 (s, 2H), 1.00 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.0$, 157.8, 138.4, 129.6, 129.5, 128.5, 128.3, 127.6, 113.7, 75.6, 55.3, 37.8, 30.8, 28.5; HR-MS (EI): $m/z = 311.1850$ (M^+), calcd. for $C_{20}H_{25}NO_2$: 311.1885.

(*E/Z*)-3,3-Dimethyl-1-[4-(trifluoromethyl)phenyl]butan-2-one *O*-benzyloxime (3t): Isomeric ratio (98:2); yield: 80%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.34$ (d, $J = 8.1$ Hz, 2H), 7.23–7.05 (m, 7H), 4.97 (s, 2H), 3.67 (s, 2H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 163.9$, 141.9, 138.0, 128.8, 128.6, 128.3, 128.0, 127.8, 125.2 (q, $J = 3.8$ Hz), 124.5 (q, $J = 271.9$ Hz), 75.9, 37.8, 31.7, 28.3; HR-MS (EI): $m/z = 350.1723$ ($M+H^+$), calcd. for $C_{20}H_{23}F_3NO$: 350.1726.

(*E/Z*)-1-Phenylpropan-2-one *O*-benzyloxime (3u): Isomeric ratio (93:7); yield: 88%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.40–7.03$ (m, 10H), 5.06 (s, 2H), 3.37 (s, 2H), 1.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 157.3$, 138.4, 137.1, 129.1, 128.6, 128.4, 128.0, 127.7, 126.8, 75.5, 42.2, 14.1; HR-MS (EI): $m/z = 239.1333$ (M^+), calcd. for $C_{16}H_{17}NO$: 239.1310.

(*E/Z*)-1-(4-Methoxyphenyl)propan-2-one *O*-benzyloxime (3v): Isolated as a mixture (91:9) after column purification; yield: 62%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.34–7.19$ (m, 5H), 7.05–6.98 (m, 2H), 6.78–6.72 (m, 2H), 5.06 (s, 2H), 3.71 (s, 3H), 3.32 (s, 2H), 1.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 158.6$, 157.6, 138.5, 130.1, 129.1, 128.4, 128.0, 127.7, 114.1, 75.5, 55.4, 41.4, 14.0; HR-MS (EI): $m/z = 269.1410$ (M^+), calcd. for $C_{17}H_{19}NO_2$: 269.1416.

(*E/Z*)-1-[4-(Trifluoromethyl)phenyl]propan-2-one *O*-benzyloxime (3w): Isolated as a mixture (94:6) after column purification; yield: 90%; oil; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.45$ (d, $J = 8.0$ Hz, 2H), 7.37–7.23 (m, 5H), 7.19 (d, $J = 8.0$ Hz, 2H), 5.06 (s, 2H), 3.43 (s, 2H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 156.3$, 141.3 (q, $J = 1.1$ Hz), 138.3, 134.7 (q, $J = 6.3$ Hz), 129.4, 128.5, 128.1, 127.8, 125.6 (q, $J = 3.8$ Hz), 124.3 (q, $J = 272.1$ Hz), 75.7, 42.1, 14.2; HR-MS (EI): $m/z = 307.1180$ (M^+), calcd. for $C_{17}H_{16}F_3NO$: 307.1184.

3-Benzyl-6-ethoxy-5,6-dihydro-4*H*-1,2-oxazine (3x): Yield: 52%; colorless liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.29–7.13$ (m, 5H), 4.97 (t, $J = 2.6$ Hz, 1H), 3.81 (dq, $J = 9.7$, 7.1 Hz, 1H), 3.52 (dq, $J = 9.7$, 7.1 Hz, 1H), 3.46 (s, 2H), 2.17–2.01 (m, 1H), 1.88–1.73 (m, 3H), 1.13 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 159.3$, 136.9, 129.0, 128.8, 127.0, 94.6, 63.4, 42.8, 23.2, 18.0, 15.2; HR-MS (EI): $m/z = 220.1337$ ($M+H^+$), calcd. for $C_{13}H_{17}NO_2$: 220.1332.

6-Ethoxy-3-[4-(trifluoromethyl)benzyl]-5,6-dihydro-4*H*-1,2-oxazine (3y): Yield: 59%; pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.50$ (d, $J = 8.1$ Hz, 2H), 7.30 (d, $J = 8.1$ Hz, 2H), 4.99 (t, $J = 2.6$ Hz, 1H), 3.80 (dq, $J = 9.7$, 7.1 Hz, 1H), 3.69–3.46 (m, 1H), 3.53 (d, $J = 2.8$ Hz, 1H), 3.51 (d, $J = 2.8$ Hz, 1H), 2.22–1.98 (m, 1H), 1.94–1.70 (m, 3H), 1.13 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 158.5$, 141.1, 129.3, 125.7 (q, $J = 3.8$ Hz), 94.6, 63.5, 42.6, 23.1, 18.2, 15.2; HR-MS (EI): $m/z = 288.1205$ ($M+H^+$), calcd. for $C_{14}H_{17}F_3NO_2$: 288.1206.

6-Ethoxy-3-(2-methylbenzyl)-5,6-dihydro-4*H*-1,2-oxazine (3z): Yield: 65%; colorless liquid; ^1H NMR (400 MHz, $CDCl_3$, TMS): $\delta = 7.14–6.99$ (m, 4H), 4.97 (t, $J = 2.7$ Hz, 1H), 3.79 (dq, $J = 9.7$, 7.1 Hz, 1H), 3.57–3.41 (m, 3H), 2.25 (s, 3H), 2.12–1.95 (m, 1H), 1.85–1.72 (m, 3H), 1.12 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 158.9$, 137.3, 134.9, 130.6, 129.9, 127.1, 126.2, 94.5, 63.4, 40.6, 23.2, 19.6, 18.1, 15.2; HR-MS (EI): $m/z = 234.1491$ ($M+H^+$), calcd. for $C_{14}H_{20}NO_2$: 234.1489.

(*E*)-1-(4-Methoxyphenyl)-2-phenylethanone *O*-methyloxime (3aa) [CAS: 146364-30-9]: Yield: 93%; white solid; mp 35–37 °C; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.56–7.47$ (m, 2H), 7.21–7.04 (m, 5H), 6.78–6.71 (m, 2H), 4.03 (s, 2H), 3.92 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.5$, 155.7, 137.0, 128.7, 128.5, 128.3, 127.9, 126.3, 113.9, 62.0, 55.4, 32.6; HR-MS (EI): $m/z = 225.1245$ (M^+), calcd. for $C_{16}H_{17}NO_2$: 225.1259.

(*E*)-1,2-Bis(4-methoxyphenyl)ethanone *O*-methyloxime (3ab) [CAS: 144889-01-0]: Yield: 78%; white solid; mp 39–41 °C; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.54–7.46$ (m, 2H), 7.08–7.01 (m, 2H), 6.80–6.67 (m, 4H), 3.97 (s, 2H), 3.92 (s, 3H), 3.70 (s, 3H), 3.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.4$, 158.1, 156.1, 129.6, 128.9, 128.3, 128.0, 114.1, 113.9, 62.0, 55.4, 55.3, 31.7; HR-MS (EI): $m/z = 285.1361$ (M^+), calcd. for $C_{17}H_{19}NO_3$: 285.1365.

(*E*)-2-[4-(Trifluoromethyl)phenyl]-1-(4-methoxyphenyl)-ethanone *O*-methyloxime (3ac): Yield: 68%; white solid; mp 36–38 °C; ^1H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 7.54–7.47$ (m, 2H), 7.43 (d, $J = 8.1$ Hz, 2H), 7.24 (d, $J = 8.0$ Hz, 2H), 6.83–6.73 (m, 2H), 4.09 (s, 2H), 3.93 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 160.7$, 154.9, 141.2, 128.9, 127.9, 127.8, 127.5, 125.6 (q, $J = 3.7$ Hz), 124.4 (q, $J =$

271.8 Hz), 114.1, 62.2, 55.4, 32.4; HR-MS (EI): m/z = 323.1100 (M^+), calcd. for $C_{17}H_{16}F_3NO$: 323.1133.

(*E*)-1-(4-Chlorophenyl)-2-phenylethanone *O*-methyloxime (3ad) [CAS: 146364-38-7]: Yield: 97%; white solid; mp 42–46 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.52–7.45 (m, 2H), 7.22–7.03 (m, 7H), 4.02 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.1, 136.5, 135.2, 134.2, 128.8, 128.7, 128.5, 127.9, 126.5, 62.3, 32.5; HR-MS (EI): m/z = 259.0732 (M^+), calcd. for $C_{15}H_{14}ClNO$: 259.0764.

(*E*)-1-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethanone *O*-methyloxime (3ae): Yield: 87%; white solid; mp 45–50 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.46 (m, 2H), 7.25–7.16 (m, 2H), 7.05–6.99 (m, 2H), 6.76–6.68 (m, 2H), 3.96 (s, 2H), 3.95 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3, 155.5, 135.1, 134.2, 129.5, 128.7, 128.4, 127.9, 114.2, 62.3, 55.3, 31.6; HR-MS (EI): m/z = 289.0883 (M^+), calcd. for $C_{16}H_{16}ClNO_2$: 289.0870.

(*E*)-1-(4-Chlorophenyl)-2-[4-(trifluoromethyl)phenyl]ethanone *O*-methyloxime (3af): Yield: 96%; white solid; mp 81–83 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.51–7.45 (m, 2H), 7.43 (d, J = 8.0 Hz, 2H), 7.24–7.17 (m, 4H), 4.07 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.2, 140.7 (q, J = 1.0 Hz), 135.5, 133.8, 128.9, 128.8,128.3, 127.7, 125.7 (q, J = 3.8 Hz), 124.3 (q, J = 271.9 Hz), 62.4, 32.3; HR-MS (EI): m/z = 327.0624 (M^+), calcd. for $C_{16}H_{13}ClF_3NO$: 327.0638.

(*E*)-1-(4-Bromophenyl)-2-phenylethanone *O*-methyloxime (3ag): Yield: 68%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.45–7.32 (m, 4H), 7.26–6.97 (m, 5H), 4.03 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.1, 136.4, 134.6, 131.7, 128.8, 128.5, 128.1, 126.5, 123.5, 62.3, 32.4; HR-MS (EI): m/z = 304.0343 ($M+H^+$), calcd. for $C_{15}H_{15}BrNO$: 304.0337.

(*E*)-1-(4-Bromophenyl)-2-[4-(trifluoromethyl)phenyl]-ethanone *O*-methyloxime (3ah): Yield: 58%; white solid; mp 83–85 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.51–7.33 (m, 6H), 7.26–7.15 (m, 2H), 4.08 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3, 140.6, 134.2, 131.9, 128.8, 128.0, 127.8, 125.7 (q, J = 3.7 Hz), 124.3 (q, J = 272.1 Hz), 123.8, 62.5, 32.2; HR-MS (EI): m/z = 372.0204 ($M+H^+$), calcd. for $C_{16}H_{14}BrF_3NO$: 372.0205.

(*E*)-1-(4-Bromophenyl)-2-*p*-tolylethanone *O*-methyloxime (3ai): Yield: 60%; white solid; mp 53–55 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.47–7.31 (m, 4H), 6.98 (s, 4H), 3.99 (s, 2H), 3.94 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.4, 136.1, 134.7, 133.3, 131.7, 129.5, 128.4, 128.2, 123.5, 62.3, 32.0, 21.1; HR-MS (EI): m/z = 318.0482 ($M+H^+$), calcd. for $C_{16}H_{17}BrNO$: 318.0488.

Spectral Data for Compounds 6

(*Z*)-1-(Biphenyl-4-yl)-2-chloroethanone *O*-methyloxime (6a) [CAS: 77561-96-7]: Yield: 88%; white solid; mp 59–61 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.76–7.66 (m, 2H), 7.58–7.49 (m, 4H), 7.42–7.24 (m, 3H), 4.48 (s, 2H), 4.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.4, 142.5, 140.4, 132.3, 129.0, 127.8, 127.4, 127.2, 126.7, 62.9, 32.6; HR-MS (EI): m/z = 260.0836 ($M+H^+$), calcd. for $C_{15}H_{15}ClNO$: 260.0837.

(*Z*)-1-(Biphenyl-4-yl)-2-bromoethanone *O*-methyloxime (6b) [CAS: 930600-75-2]: Yield: 40%; white solid; mp 68–70 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.75–7.69 (m, 2H), 7.59–7.51 (m, 4H), 7.42–7.34 (m, 2H), 7.33–7.26 (m, 1H), 4.32 (s, 2H), 4.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.4, 142.6, 140.4, 132.4, 129.0, 127.8, 127.5, 127.2, 126.6, 63.0, 18.1; HR-MS (EI): m/z = 304.0317 ($M+H^+$), calcd. for $C_{15}H_{15}BrNO$: 304.0332.

(*Z*)-2-Chloro-1-[4′-(trifluoromethyl)biphenyl-4-yl]ethanone *O*-methyloxime (6c): Yield: 91%; white solid; mp 83–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 7.78–7.71 (m, 2H), 7.63 (s, 4H), 7.58–7.52 (m, 2H), 4.50 (s, 2H), 4.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 152.1, 144.0, 141.0, 133.4, 130.1, 127.6, 127.5, 126.9, 126.0 (q, J = 3.7 Hz), 124.4 (q, J = 272.1 Hz), 63.0, 32.5; HR-MS (EI): m/z = 328.0706 ($M+H^+$), calcd. for $C_{16}H_{14}ClF_3NO$: 328.0711.

(*Z*)-2-Chloro-1-(4′-methylbiphenyl-4-yl)ethanone *O*-methyloxime (6d): Yield: 87%; white solid; mp 90–92 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.73–7.66 (m, 2H), 7.57–7.50 (m, 2H), 7.46–7.40 (m, 2H), 7.22–7.14 (m, 2H), 4.48 (s, 2H), 4.01 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.4, 142.5, 137.7, 137.5, 132.1, 129.7, 127.2, 127.0, 126.6, 62.9, 32.6, 21.3; HR-MS (EI): m/z = 274.0992 ($M+H^+$), calcd. for $C_{16}H_{17}ClNO$: 274.0993.

Spectral Data for Compounds 7

(*E*)-1-(Biphenyl-4-yl)-2-phenylethanone *O*-methyloxime (7a): White solid; mp 110–112 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.68–7.62 (m, 2H), 7.53–7.44 (m, 4H), 7.35 (tt, J = 8.3, 1.8 Hz, 2H), 7.30–7.07 (m, 6H), 4.11 (s, 2H), 3.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 141.9, 140.6, 136.8, 134.7, 128.9, 128.8, 128.6, 127.7, 127.3, 127.2, 127.0, 126.4, 62.3, 32.7; HR-MS (EI): m/z = 302.1542 ($M+H^+$), calcd. for $C_{21}H_{20}NO$: 302.1539.

(*E*)-2-Phenyl-1-[4′-(trifluoromethyl)biphenyl-4-yl]ethanone *O*-methyloxime (7c): Yield: 72%; white solid; mp 67–69 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.73–7.64 (m, 2H), 7.62–7.54 (m, 4H), 7.52–7.42 (m, 2H), 7.25–7.06 (m, 5H), 4.10 (s, 2H), 3.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.6, 144.1, 140.4, 136.7, 135.6, 129.9, 129.4, 128.8, 128.6, 127.4, 127.2, 126.5, 125.9 (q, J = 3.7 Hz), 124.4 (q, J = 271.9 Hz), 62.3, 32.6; HR-MS (EI): m/z = 370.1412 ($M+H^+$), calcd. for $C_{22}H_{19}F_3NO$: 370.1413.

(*E*)-1-(4′-Methylbiphenyl-4-yl)-2-phenylethanone *O*-methyloxime (7d): Yield: 15%; white solid; mp 110–112 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.67–7.60 (m, 2H), 7.49–7.36 (m, 4H), 7.21–7.10 (m, 7H), 4.10 (s, 2H), 3.97 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.9, 141.9, 137.7, 137.5, 136.9, 134.4, 129.7, 128.7, 128.6, 127.0, 127.0, 127.0, 126.4, 62.2, 32.6, 21.3; HR-MS (EI): m/z = 316.1699 ($M+H^+$), calcd. for $C_{22}H_{22}NO$: 316.1696.

(*E*)-2-(4-Methoxyphenyl)-1-(3′-nitrobiphenyl-4-yl)ethanone *O*-methyloxime (7e): Yield: 56%; colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 8.35 (t, J = 1.9 Hz, 1H), 8.12 (ddd, J = 8.2, 2.2, 1.0 Hz, 1H), 7.81 (ddd, J = 7.8, 1.7, 1.1 Hz, 1H), 7.75–7.66 (m, 2H), 7.59–7.46 (m, 3H), 7.13–7.04 (m, 2H), 6.78–6.69 (m, 2H), 4.04 (s, 2H), 3.99 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.6, 144.1, 140.4, 136.7, 135.6, 130.3, 129.9, 129.4, 128.8, 128.6, 127.4, 127.2, 126.5, 126.2, 126.0, 125.9, 125.8, 125.8, 122.6,

119.0, 62.3, 32.6; HR-MS (EI): $m/z = 377.1492$ ($M+H^+$), calcd. for $C_{22}H_{21}N_2O_4$: 377.1496.

(*E*)-1-[4-(Thiophen-3-yl)phenyl]-2-[4-(trifluoromethyl)-phenyl]ethanone *O*-methyloxime (7f): Yield: 56%; white solid; mp 86–88 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta =$ 7.62–7.56 (m, 2H), 7.52–7.46 (m, 2H), 7.44 (d, $J = 8.1$ Hz, 2H), 7.39 (dd, $J = 2.4$, 1.9 Hz, 1H), 7.31–7.29 (m, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 4.12 (s, 2H), 3.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 154.9$, 141.6, 141.1, 136.8, 133.9, 128.9, 128.6, 126.9, 126.6, 126.6, 126.3, 126.2, 125.7 (q, $J = 3.7$ Hz), 124.3 (q, $J = 271.9$ Hz), 121.0, 62.3, 32.4; HR-MS (EI): $m/z =$ 376.0970 ($M+H^+$), calcd. for $C_{20}H_{17}F_3NOS$: 376.0977.

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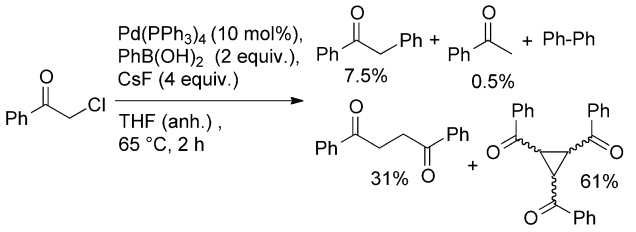

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