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Synthesis of 2-Aminobenzoxazoles and 3-Aminobenzoxazines via Palladium-Catalyzed Aerobic Oxidation of *o*-Aminophenols with Isocyanides

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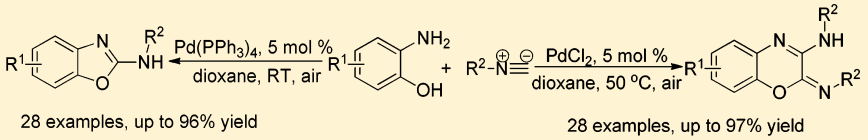
Supporting Information



28 examples, up to 96% yield

28 examples, up to 97% yield

ABSTRACT: A Pd-catalyzed aerobic oxidation of *o*-aminophenols and isocyanides for the synthesis of 2-aminobenzoxazoles and 3-aminobenzoxazines has been achieved in an air atmosphere. The procedure constructs 2-aminobenzoxazoles and 3-aminobenzoxazines with moderate to excellent yields and a broad substrate scope. Apart from experimental simplicity, this methodology has the advantages of mild reaction conditions and easily accessible starting materials. Furthermore, the utility of this method has also been successfully applied to the synthesis of other types of useful nitrogen heterocycles.

INTRODUCTION

Benzoxazoles and benzoxazines are ubiquitous heterocyclic scaffolds found in many bioactive natural products, pharmaceuticals, and agrochemicals.[1] Among them, 2-aminobenzoxazoles and 3-aminobenzoxazines have been extensively studied for their biological and therapeutic activities (Figure 1). They have been used as tyrosine kinase inhibitors for the treatment of cancers (VEGFR-2),[2] 5-HT receptor antagonists for the treatment of Alzheimer's disease and schizophrenia,[3] dual orexin receptor antagonists for the treatment of insomnia (MK-4305),[4] and GABA receptor inhibitors for anxiolytics and anticonvulsants (etifoxine).[5]

Consequently, considerable efforts have been made to develop efficient methods for their synthesis (Scheme 1). The classical approach is the nucleophilic substitution of appropriately 2-substituted benzoxazoles with amines. However, this method always needs inconvenient multiple steps and harsh reagents and conditions or produces undesirable byproducts during the preparation of the 2-substituted benzoxazoles.[6] A more general method is the cyclodesulfurization of an intermediary thiourea, which usually involves toxic heavy-metal oxide or a potentially explosive oxidant for this transformation.[7] Over the past decade, directly oxidative C−H amination of benzoxazoles to construct 2-aminobenzoxazoles has been extensively investigated.[8] However, such transformations typically require initial chlorination of the amine or harsh conditions and the use of expensive 2-unsubstituted benzoxazoles.[9] Previously reported synthetic approaches to generate 2-aminobenzoxazoles directly from 2-aminophenols may need multiple steps for the preparation of proper amine surrogates prior to cyclization.[10] Therefore, exploring atom and/or step efficiency and environmentally friendly processes is highly desirable.

Isocyanides, types of unsaturated molecules similar to carbon monoxide, are the best known amphoteric reagents. Despite the extremely unpleasant odor and toxicity of isocyanides (especially for cyclohexyl isocyanide), isocyanides have played an irreplaceable role in modern organic chemistry. Since the pioneering work of Ugi and Passerini,[11] isocyanides have been widely applied to construct various nitrogen-containing heterocycles due to their superior capability to rapidly create molecular diversity.[12] However, palladium-catalyzed processes that involve isocyanide insertion to assemble *N*-containing heterocycles have been relatively undervalued and have drawn great attention only in very recent years.[13] Recently, we reported a palladium-catalyzed tandem reaction of *o*-aminophenols, bromoalkynes, and isocyanides to give 4-aminobenzo[*b*][1,4]oxazepines.[14] During the course of the study, we occasionally observed a small amount of 2-(*tert*-butylamino)-benzoxazole along with the major product. This intriguing result suggested that *o*-aminophenols and isocyanides might have a distinct reactivity difference from the three-component tandem reaction, which prompted us to investigate this unique transformation in detail. As part of our ongoing programs on palladium-catalyzed cascade reactions involving isocyanide insertion,[15] herein we report a convenient and convergent method for the synthesis of 2-aminobenzoxazoles and 3-aminobenzooxazines via palladium-catalyzed aerobic oxidation of *o*-aminophenols and isocyanides.

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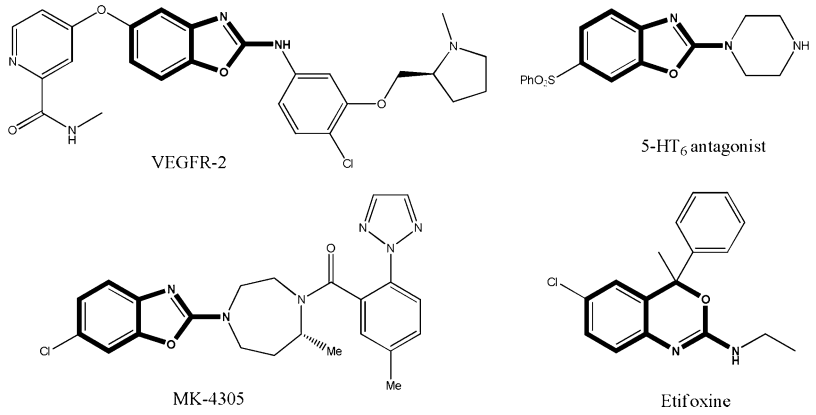
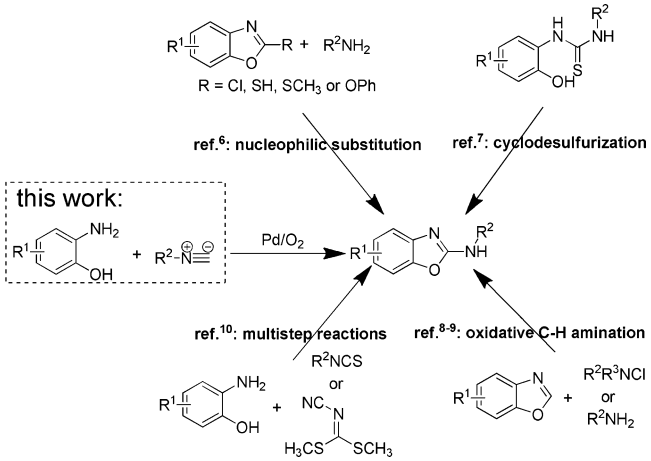


Figure 1. Aminobenzoxazole and aminobenzoxazine moieties in drugs.

Scheme 1. Typical Methods for Synthesis of 2-Aminobenzoxazoles



RESULTS AND DISCUSSION

To explore this approach, we selected *o*-aminophenol (**1a**) and *tert*-butyl isocyanide (**2a**) as the model substrates for reaction development and screened several transition-metal catalysts in common solvents for their catalytic activities (Table 1). Initially, we preformed this palladium-catalyzed aerobic oxidation of **1a** with **2a** under the optimized conditions of our previous work.[14] To our delight, the reaction gave the expected 2-(*tert*-butylamino)benzoxazole (**4aa**) in 56% yield and the unexpected unsubstituted benzoxazole **3aa** in 15% yield in the presence of $Pd(PPh_3)_2Cl_2$ (5 mol %) and PPh_3 (10 mol %) in dioxane at 80 °C for 2 h (entry 1). However, the yield of **4aa** slightly decreased to 43% in the absence of PPh_3 (entry 2) and further optimization revealed that base was unnecessary for this reaction (entry 3). To our surprise, when the reaction was catalyzed by $Pd(PPh_3)_2Cl_2$ with no bases or phosphines, no **4aa** but a 40% yield of *N*-(*tert*-butyl)-2-(*tert*-butylimino)-2*H*-benzo[*b*][1,4]oxazin-3-amine (**5aa**) was detected (entry 4). Among the Pd(0) catalysts tested, $Pd(PPh_3)_4$ was the best choice for the formation of **4aa** (entries 5 and 6). Further screening of the catalytic reaction conditions indicated that the cyclization product **4aa** could not be formed without a palladium catalyst (entries 7–9). The yield of **4aa** was increased and the side product **3aa** was reduced by decreasing the reaction temperature to room temperature (entries 10 and 11). The screening of solvents showed that dioxane was the optimal solvent (entries 12–15). The reaction proceeded well in air, but only 9% of **4aa** was obtained under an argon atmosphere (entry 16). As expected, a higher yield (in comparison with entry 4) of **5aa** was formed when the substrates were combined in a 1:2.4 ratio on treatment with $Pd(PPh_3)_2Cl_2$ (entry 17). Further investigation revealed that 50 °C was the most suitable reaction temperature for the formation of **5aa** (entries 18 and 19). On the basis of screening of various palladium(II) salts, the highest yield for the formation of **5aa** was achieved when $PdCl_2$ was used (entries 20–23). Surprisingly, **4aa** was obtained in 87% yield while no **5aa** was detected with $Pd(OAc)_2$ as the catalyst (entry 23). Notably, the reaction did not perform well for the formation of **5aa** under an argon atmosphere (entry 24).

Substrate Scope for the Synthesis of 2-Aminobenzoxazoles. With the optimum reaction conditions in hand (Table 1, entry 11), we turned our attention to the scope of the palladium-catalyzed aerobic oxidative synthesis of 2-aminobenzoxazoles by using various *o*-aminophenols as the substrates (Table 2). Generally, *o*-aminophenols with electron-donating groups (Me, OMe, *t*-Bu) and weakly or moderately electron-withdrawing groups (F, Cl, Br) afforded the corresponding 2-aminobenzoxazoles **4ba**–**4ha** in excellent yields within 2 h (entries 2–8). Importantly, the successful preparation of **4ga** and **4ha** with intact chlorine or bromine provided good opportunities for further formation of C–C or C–heteroatom bonds by transition-metal-catalyzed coupling reactions. The treatment of acetyl-, ester-, and 4,6-dichloro-substituted *o*-aminophenols could also generate the corresponding products **4ia**–**4ka** in good yields but required higher temperatures and longer reaction times (entries 9 and 11). However, the reaction activity of the *o*-aminophenols with strong electron-withdrawing groups (NO_2 and CN) was much lower than that with electron-donating groups (Me, OMe, *t*-Bu) and moderately electron-withdrawing groups (F, Cl, Br). Importantly, the methylsulfonyl and sulfonamide groups on *o*-aminophenols were also tolerated in this transformation and gave the desired products **4pa** and **4qa** in good yields (entries 16 and 17). Importantly, we were pleased to find that 3-amino-2-naphthol (**1r**) and 3,3′-dihydroxybenzidine (**1s**) were also compatible with this reaction system, generating the corresponding products in 96% and 83% yields, respectively (entries 18 and 19). The reaction with heterocyclic substrates such as 3-aminopyridin-2-ol (**1t**) was slower than *o*-aminophenols and gave the corresponding product **4ta** in moderate yield (entry 20). However, under the present reaction conditions, only a trace amount of **4ua** was detected when 2-amino-3-pyridinol

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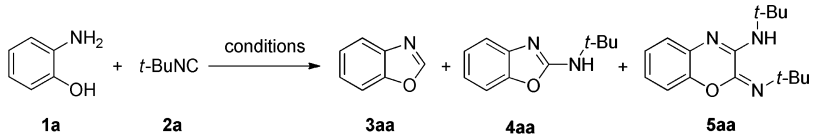
Table 1. Optimization of Reaction Conditions[a]



1a 2a 3aa 4aa 5aa

entry	catalyst/ligand	base	solvent	temp (°C)	yield of **3a** (%)	yield of **4a** (%)[b]	yield of **5a** (%)
1	$Pd(PPh_3)_2Cl_2/PPh_3$	Cs_2CO_3	dioxane	80	15	56	
2	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	dioxane	80	12	43	
3	$Pd(PPh_3)_2Cl_2/PPh_3$		dioxane	80	5	60	
4	$Pd(PPh_3)_2Cl_2$		dioxane	80	7		40
5	$Pd_2(dba)_3$		dioxane	80	10	78	
6	$Pd(PPh_3)_4$		dioxane	80		87	9
7			dioxane	80			
8	CuI		dioxane	80			
9	$Cu(OAc)_2$		dioxane	80			
10	$Pd(PPh_3)_4$		dioxane	50		92	5
11	$Pd(PPh_3)_4$		dioxane	room temp		99 (95)	
12	$Pd(PPh_3)_4$		toulene	room temp		15	
13	$Pd(PPh_3)_4$		DMSO	room temp		78	7
14	$Pd(PPh_3)_4$		DMF	room temp		91	6
15	$Pd(PPh_3)_4$		CH_3CN	room temp		83	11
16[c]	$Pd(PPh_3)_4$		dioxane	room temp		9	
17	$Pd(PPh_3)_2Cl_2$		dioxane	80	9		79
18	$Pd(PPh_3)_2Cl_2$		dioxane	50	4		90
19	$Pd(PPh_3)_2Cl_2$		dioxane	room temp			85
20	$PdCl_2$		dioxane	50	2		98 (92)
21	$PdBr_2$		dioxane	50	4		79
22	PdI_2		dioxane	50	8		61
23	$Pd(OAc)_2$		dioxane	50	3	87	
24[c]	$PdCl_2$		dioxane	50	12	4	38

[a]Reaction conditions: all reactions were performed with **1a** (0.5 mmol), **2a** (0.6 mmol, entries 1−16) or **2a** (1.2 mmol, entries 17−24), catalyst (5 mol %), ligand (10 mol %), base (1.0 mmol), and 2.0 mL of solvent in an air atmosphere for 2 h unless otherwise noted. [b]Yields and conversions analyzed by GC/MS are based on **1a**. Values in parentheses are isolated yields. [c]Reaction performed under an N_2 atmosphere.

(**1u**) was employed as the coupling partner (entry 21). The observed lower reactivity for this type of substrate might stem from the low nucleophilicity of the aminopyridinols.

Moreover, various isocyanides were also applied to probe the scope of the reaction substrates (Table 3). Fortunately, almost all the isocyanides were found to be suitable for this transformation, affording the corresponding 2-aminobenzoxazoles in good to excellent yields. Even if sterically bulky isocyanides such as 1,1,3,3-tetramethylbutyl isocyanide (**2b**) and 2,6-dimethylphenyl isocyanide (**2h**) were used, the corresponding **4ab** and **4ah** were obtained in 89% and 85% yields, respectively (entries 1 and 7). However, **4ag** was obtained in 75% yield when 1-isocyano-4-methoxybenzene (**2g**) was used (entry 6). In addition to the secondary (**2d** and **2f**), tertiary (**2a** and **2b**), and aromatic isocyanides (**2g** and **2h**), primary isocyanides (**2c** and **2e**) were also effective in affording the corresponding 2-aminobenzoxazoles in good yields (entries 2 and 4). Nevertheless, ethyl isocyanoacetate was not effective under this set of conditions (entry 8).

Substrate Scope for the Synthesis of 3-Amino-2*H*-benzoxazines. The efficiency of the expeditious palladium-catalyzed aerobic oxidative cyclization process for 2-aminobenzoxazoles prompted us to examine the synthesis of 3-amino-2*H*-benzoxazines from *o*-aminophenols and two molecular isocyanides. As shown in Table 4, the scope of *o*-aminophenols **1** for the aerobic oxidative cyclization reaction was explored under the standard reaction conditions (Table 1, entry 20). The method tolerated a wide range of substituents on *o*-aminophenols, including halogen, acetyl, cyano, ester, nitro, and sulfonyl groups (Table 4). The results demonstrated that the electronic effect on *o*-aminophenols had only a slight influence on the formation of the desired 3-amino-2*H*-benzoxazines. In general, aryl rings substituted with electron-rich functional groups (entries 2−5) and weakly or moderately electron-withdrawing groups (entries 6−8) fared better than those with electron-withdrawing groups (entries 9−15). Reactions of substrates bearing sulfonyl groups led to excellent yields (entries 16 and 17), and most impressively even aminopyridinols with low nucleophilicity could also undergo the oxidative cyclization efficiently and gave the corresponding products in good yields (entries 20 and 21).

Moreover, we were pleased to find that various isocyanides could be successfully extended to the corresponding 3-amino-2*H*-benzoxazines in good to excellent yields (Table 5, entries 1−7). Unfortunately, when ethyl isocyanoacetate was applied to this process under the optimized reaction conditions, the desired product was detected by GC-MS, but the reaction system was very complicated and failed to give the pure product (entry 8). Furthermore, we were able to access 3-amino-2*H*-benzo[*b*][1,4]oxazin-2-ones by a one-pot simple acid hydrolysis sequence. Addition of HOAc to the reaction mixture (after the formation of **5aa** was complete) and subsequent heating at 80 °C for 12 h generated 3-(*tert*-butylamino)-2*H*-benzo[*b*][1,4]-oxazin-2-one (**6aa**) in an excellent 88% yield (Table 5, entry 9).

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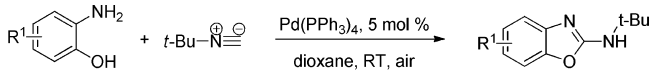
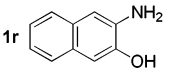
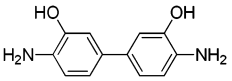
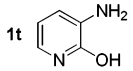
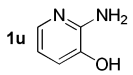
Table 2. Scope of *o*-Aminophenols for the Synthesis of 2-Aminobenzoxazoles[a]



1 2a 4

entry	*o*-aminophenols (R^1)	*tert*-butyl isocyanide (**2a**)	products	yield (%) [b]
1	**1a (R^1 = H)**	**2a**	**4aa**	95
2	**1b (R^1 = 4-Me)**	**2a**	**4ba**	93
3	**1c (R^1 = 5-Me)**	**2a**	**4ca**	91
4	**1d (R^1 = 4-OMe)**	**2a**	**4da**	96
5	**1e (R^1 =4-*t*-Bu)**	**2a**	**4ea**	93
6	**1f (R^1 = 5-F)**	**2a**	**4fa**	92
7	**1g (R^1 = 4-Cl)**	**2a**	**4ga**	94
8	**1h (R^1 = 4-Br)**	**2a**	**4ha**	93
9 [c]	**1i (R^1 = 4-COOMe)**	**2a**	**4ia**	87
10 [c]	**1j (R^1 = 3-COMe)**	**2a**	**4ja**	84
11 [c]	**1k (R^1 = 4,6-dichloro)**	**2a**	**4ka**	85
12 [d]	**1l (R^1 = 3-NO_2)**	**2a**	**4la**	84
13 [d]	**1m (R^1 = 4-NO_2)**	**2a**	**4ma**	75
14 [d]	**1n (R^1 = 5-NO_2)**	**2a**	**4na**	88
15 [d]	**1o (R^1 = 4-CN)**	**2a**	**4oa**	78
16 [c]	**1p (R^1 = 4-methylsulfonyl)**	**2a**	**4pa**	88
17 [c]	**1q (R^1 = 4-sulfonamide)**	**2a**	**4qa**	85
18	 **1r**	**2a**	**4ra**	96
19 [e]	 **1s**	**2a**	**4sa**	83
20 [d, f]	 **1t**	**2a**	**4ta**	67
21 [d, f, g]	 **1u**	**2a**	**4ua**	trace

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), dioxane (2.0 mL), at room temperature, in an air atmosphere for 2 h unless otherwise noted. [b]Isolated yield. [c]50 °C for 8 h. [d]80 °C for 12 h. [e]1.2 mmol of **1a** was added. [f]2.0 mL of DMSO was added instead of dioxane. [g]**1u** was recovered.

This process, providing one of the simplest methods for the synthesis of this class of valuable 3-aminobenzoxazin-2-ones, involved two steps, including a cyclization reaction and simple acid hydrolysis.

Application to the Synthesis of Various Other Important *N*-Heterocycles. With the above results in hand, we envisioned that other bis-nucleophiles could be also extended to the synthesis of other types of useful nitrogen heterocycles (Table 6). Not surprisingly, the corresponding 6-amino-dibenzo[d_f][1,3]oxazepines (**8aa**–**8ca**) were obtained in good yields when 2′-amino-[1,1′-biphenyl]-2-ols were applied to the reaction system (entries 1–3). Importantly, the oxidative cyclization could proceed smoothly by the use of aliphatic alcohols (**7d**) or aliphatic amines (**7e**), giving the desired 2-amino-4*H*-benzo[*d*][1,3]oxazines (**8da** and **8db**) and 2-amino-4*H*-benzo[*e*][1,3]oxazines (**8ea** and **8eb**), respectively. Unfortunately, when salicylamide and 2-hydroxybenzothioamide (**7f**) were employed in this process, only trace amounts of the desired products (**8fa**) were detected even at raised reaction temperatures. Fortunately, 2-aminothiophenol (**7g**) transferred to 2-(*tert*-butylamino)benzothiazole (**8ga**) in 91% yield. Interestingly, **8ha** was obtained in 88% yield when 2-amino-4-(trifluoromethyl)thiophenol hydrochloride (**7h**) was used, which was caused by the cleavage of the *tert*-butylamino group. As expected, when 2-(methylamino)phenol (**7i**) was examined in the $Pd(PPh_3)_4$ catalyst system, a 90% yield of the desired product **8ia** was obtained. However, no desired product **9** was detected when **7i** was used in the $PdCl_2$ catalyst system. These results suggested that the primary amino group was essential for the double insertions of isocyanides.

Mechanistic Studies of the Synthesis of 2-Aminobenzoxazoles and 3-Aminobenzoxazines. On the basis of some related work[13e,16] and the control experiments (see the Supporting Information) we propose the mechanism shown in Scheme 2. For the formation of 2-aminobenzoxazoles (**4**), two alternative paths (a and b) are presented. Initial oxidation of

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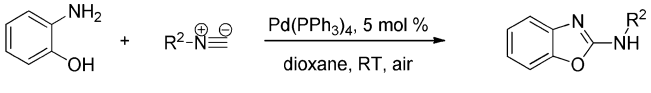
Table 3. Scope of Isocyanides for the Synthesis of 2-Aminobenzoxazoles[a]



1a 2 4

entry	isocyanides (R^2)	product	yield (%)[b]
1	**2b** (R^2 = 1,1,3,3- tetramethylbutyl)	**4ab**	89
2	**2c** (R^2 = 2-morpholinoethyl)	**4ac**	81
3[c]	**2d** (R^2 = *c*-Hex)	**4ad**	93
4	**2e** (R^2 = *n*-Bu)	**4ae**	96
5	**2f** (R^2 = Bn)	**4af**	95
6	**2g** (R^2 = 4-OMe-Ph)	**4ag**	75
7	**2h** (R^2 = 2,6-dimethylbenzyl)	**4ah**	85
8	**2i** (R^2 = $CH_2COOC_2H_5$)	**4ai**	trace

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), dioxane (2.0 mL), at room temperature, in an air atmosphere for 2 h unless otherwise noted. [b]Isolated yield. [c]**1a** was recovered.

$[Pd(PPh_3)_4]$ by molecular oxygen affords the $[(\eta\text{-}O_2)Pd(PPh_3)_2]$ complex.[17] In path a, nucleophilic addition of *o*-aminophenols (**2**) to isocyanide (**3**) gives the carbene intermediate **A**, which undergoes coordination with Pd(II) species to generate the palladium complex **B**. Subsequent ligand dissociation results in the formation of intermediate **C** and regenerates the Pd(II) species. Finally, aerobic oxidation of **C** provides the final product **4**.[18] In addition, deamination of the intermediate **C** leads to the formation of the side product **3**. In path b, $[(\eta\text{-}O_2)Pd(PPh_3)_2]$ reacts with **1** to form intermediate **D** and H_2O_2. Subsequent migratory insertion of **2** leads to the formation of intermediate **E** and subsequent reductive elimination to afford **4**. Finally, the palladium(0) species is reoxidized to palladium(II) by air in the system to complete the cycle. On the other hand, compound **3** could not be generated from **4** under the standard conditions (see the Supporting Information). Thus, the formation of 2-aminobenzoxazoles through path b is predicted. For the formation of 3-aminobenzoxazines (path c), $PdCl_2$ reacts with **1** to provide intermediate **G**. The subsequent double insertion reaction with **2** leads to the formation of the seven-membered azapalladacyclic intermediate **H**, which undergoes reductive elimination to generate the intermediate **I**. Immediately, isomerization of unstable intermediate **I** gives the final product 3-aminobenzoxazines (**5**).

CONCLUSION

In conclusion, a practical and general protocol for the Pd-catalyzed aerobic oxidation of *o*-aminophenols with isocyanides to the synthesis of 2-aminobenzoxazoles and 3-aminobenzoxazines has been exploited under aerobic conditions. This method was applicable to a large synthetic scope with wide functional group compatibility for *o*-aminophenols and isocyanides and gave the corresponding products in good to excellent yields. Further, this transformation was successfully applied to the synthesis of other types of important *N*-heterocyclic systems. The readily available starting reagents and mild conditions were some of the additional features of this protocol.

EXPERIMENTAL SECTION

General Procedures. All reactions were carried out in 10 mL tubes in an air atmosphere. TLC was performed by using commercially prepared 100−400 mesh silica gel plates (GF_{254}) and visualization was effected at 254 nm. All reagents were purchased as reagent grade and used without further purification. Melting points were measured with a micro melting point apparatus. ^1H NMR spectra were recorded at 400 MHz using TMS as an internal standard and ^{13}C NMR spectra at 100 MHz, using $CDCl_3$. The chemical shifts are referenced to signals at 7.24 and 77.0 ppm, respectively. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with an infrared Fourier spectrometer. High-resolution mass spectra (ESI) were obtained with a LCMS-IT-TOF mass spectrometer.

General Procedure for the Synthesis of 2-Aminobenzoxazoles. *o*-Aminophenols **1a−u** (0.5 mmol), isocyanides **2a−i** (0.6 mmol), and $Pd(PPh_3)_4$ (5 mol %, 29.0 mg) were stirred at room temperature in dioxane (2 mL) in air. After it was stirred for the appropriate time, the reaction mixture was cooled to room temperature and passed through a short pad of silica gel using a mixture of ethyl acetate and petroleum ether (5/1) as eluent to give the target 2-aminobenzoxazoles **4** in analytically pure form.

General Procedure for the Synthesis of 3-Aminobenzoxazines. *o*-Aminophenols **1a−u** (0.5 mmol), isocyanides **2a−i** (1.2 mmol), and $PdCl_2$ (5 mol %, 4.4 mg) were stirred at 50 °C in dioxane (2 mL) in air. After it was stirred for the appropriate time, the reaction mixture was cooled to room temperature and passed through a short pad of silica gel using a mixture of ethyl acetate and petroleum ether (10/1) as eluent to give the target 3-aminobenzoxazines **5** in analytically pure form.

*N-(tert-Butyl)benzo[d]oxazol-2-amine (**4aa**) (known compound).*[8e,10b] Light yellow solid (90 mg, 95%), mp 100−102 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.35 (d, J = 8.0 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 5.77 (br s, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.1, 148.1, 143.0, 123.6, 120.4, 116.1, 108.5, 52.0, 29.2.

*N-(tert-Butyl)-5-methylbenzo[d]oxazol-2-amine (**4ba**).* Light yellow solid (95 mg, 93%), mp 93−95 °C. IR (KBr): 2975, 1765, 1647, 1588, 1243 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.16 (s, 1H), 7.10 (d, J = 8.0 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 5.60 (br s, 1H), 2.37 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.3, 146.3, 143.1, 133.2, 121.1, 116.6, 107.8, 51.9, 29.2, 21.4. HRMS (ESI): m/z calcd for $C_{12}H_{17}N_2O^+$ 205.1335, found 205.1339.

*N-(tert-Butyl)-6-methylbenzo[d]oxazol-2-amine (**4ca**).* Yellow solid (93 mg, 91%), mp 104−106 °C. IR (KBr): 2972, 1764, 1642, 1579, 1244 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.23 (d, J = 8.0 Hz, 1H), 7.05 (s, 1H), 6.94 (d, J = 8.0 Hz, 1H), 5.29 (br s, 1H), 2.38 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 160.6, 148.3, 140.7, 130.5, 124.3, 115.7, 109.1, 51.9, 29.2, 21.4. HRMS (ESI): m/z calcd for $C_{12}H_{17}N_2O^+$ 205.1335, found 205.1340.

*N-(tert-Butyl)-5-methoxybenzo[d]oxazol-2-amine (**4da**).* Brown solid (106 mg, 96%), mp 111−113 °C. IR (KBr): 3346, 2966, 1639, 1584, 1154 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.07 (d, J = 8.8 Hz, 1H), 6.90 (d, J = 2.8 Hz, 1H), 6.53 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 5.91 (br s, 1H), 3.75 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.9, 156.7, 143.8, 142.6, 108.2, 106.7, 101.3, 55.7, 51.8, 29.1. HRMS (ESI): m/z calcd for $C_{12}H_{17}N_2O_2^+$ 221.1285, found 221.1274.

*N,5-Di-tert-butylbenzo[d]oxazol-2-amine (**4ea**).* Brown solid (121 mg, 93%), mp 113−115 °C. IR (KBr): 2963, 1647, 1585, 1429, 1220 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (d, J = 1.6 Hz, 1H), 7.13 (d, J = 8.4 Hz, 1H), 7.05 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H), 5.20 (br s, 1H), 1.48 (s, 9H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.0, 147.1, 146.0, 142.9, 117.7, 113.4, 107.5, 51.9, 34.8, 31.8, 29.1. HRMS (ESI): m/z calcd for $C_{15}H_{23}N_2O^+$ 247.1805, found 247.1807.

*N-(tert-Butyl)-6-fluorobenzo[d]oxazol-2-amine (**4fa**).* Yellow solid (96 mg, 92%), mp 85−87 °C. IR (KBr): 2973, 1651, 1593, 1480, 1124 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26−7.23 (m, 1H), 6.99 (dd, J_1 = 2.4 Hz, J_2 = 8.0 Hz, 1H), 6.90−6.85 (m, 1H), 5.29 (br s, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.1, 157.9 (J = 236.8 Hz), 147.7 (J = 14.4 Hz), 139.2, 115.8 (J = 9.5 Hz),

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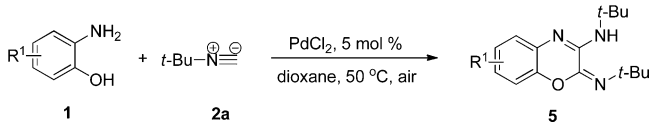
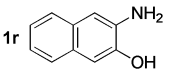
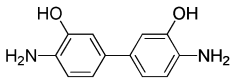
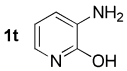
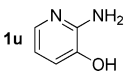
Table 4. Scope of *o*-Aminophenols for the Synthesis of 3-Amino-2*H*-benzoxazines[a]



1 2a 5

entry	*o*-aminophenols (R^1)	*tert*-butyl isocyanide (**2a**)	products	yield (%) [b]
1	**1a (R^1 = H)**	**2a**	**5aa**	92
2	**1b (R^1 = 4-Me)**	**2a**	**5ba**	96
3	**1c (R^1 = 5-Me)**	**2a**	**5ca**	90
4	**1d (R^1 = 4-OMe)**	**2a**	**5da**	97
5	**1e (R^1 =4-*t*-Bu)**	**2a**	**5ea**	95
6	**1f (R^1 = 5-F)**	**2a**	**5fa**	93
7	**1g (R^1 = 4-Cl)**	**2a**	**5ga**	89
8	**1h (R^1 = 4-Br)**	**2a**	**5ha**	87
9 [c]	**1i (R^1 = 4-COOMe)**	**2a**	**5ia**	78
10 [c]	**1j (R^1 = 3-COMe)**	**2a**	**5ja**	77
11 [c]	**1k (R^1 = 4,6-dichloro)**	**2a**	**5ka**	82
12 [d]	**1l (R^1 = 3-NO_2)**	**2a**	**5la**	86
13 [d]	**1m (R^1 = 4-NO_2)**	**2a**	**5ma**	83
14 [d]	**1n (R^1 = 5-NO_2)**	**2a**	**5na**	85
15 [d]	**1o (R^1 = 4-CN)**	**2a**	**5oa**	87
16 [d]	**1p (R^1 = 4-methylsulfonyl)**	**2a**	**5pa**	89
17 [d]	**1q (R^1 = 4-sulfonamide)**	**2a**	**5qa**	86
18	 **1r**	**2a**	**5ra**	97
19 [e]	 **1s**	**2a**	**5sa**	89
20 [d,f]	 **1t**	**2a**	**5ta**	83
21 [d,f]	 **1u**	**2a**	**5ua**	76

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1.2 mmol), dioxane (2.0 mL), 50 °C, in an air atmosphere for 2 h unless otherwise noted. [b]Isolated yield. [c]4 h. [d]8 h. [e]2.4 mmol of **1a** was added. [f]2.0 mL of DMSO was added instead of dioxane.

110.4 (J = 23.5 Hz), 97.3 (J = 28.5 Hz), 52.1, 29.1. HRMS (ESI): m/z calcd for $C_{11}H_{14}FN_2O^+$ 209.1085, found 209.1088.

*N-(tert-Butyl)-5-chlorobenzo[d]oxazol-2-amine (**4ga**).* Yellow solid (105 mg, 94%), mp 84−96 °C. IR (KBr): 2961, 1654, 1573, 1453, 1213 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29 (d, J = 1.6 Hz, 1H), 7.10 (d, J = 8.4 Hz, 1H), 6.94 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H), 5.68 (br s, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.9, 146.8, 144.4, 129.0, 120.3, 116.2, 109.0, 52.2, 29.1. HRMS (ESI): m/z calcd for $C_{11}H_{14}ClN_2O^+$ 225.0789, found 225.0786 (100.0%), 227.0776 (32.0%).

*5-Bromo-N-(tert-butyl)benzo[d]oxazol-2-amine (**4ha**).* Brown solid (125 mg, 93%), mp 102−104 °C. IR (KBr): 3148, 2962, 1659, 1570, 1453, 1218 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 (s, 1H), 7.09−7.04 (m, 2H), 6.02 (br s, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.8, 147.1, 144.7, 123.0, 119.0, 116.3, 109.5, 52.2, 29.1. HRMS (ESI): m/z calcd for $C_{11}H_{14}BrN_2O^+$ 269.0284, found 269.0287 (100.0%), 271.0267 (98.2%).

*Methyl 2-(tert-Butylamino)benzo[d]oxazole-5-carboxylate (**4ia**).* Yellow solid (108 mg, 87%), mp 184−186 °C. IR (KBr): 3347, 1705, 1642, 1580, 1442, 1289 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.00 (s, 1H), 7.75 (d, J = 8.8 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 5.71 (br s, 1H), 3.87 (s, 3H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 167.2, 161.6, 151.3, 143.3, 126.0, 123.0, 117.6, 108.1, 52.2, 52.0, 29.0. HRMS (ESI): m/z calcd for $C_{13}H_{17}N_2O_3^+$, 249.1234, found 249.1230.

*1-(2-(tert-Butylamino)benzo[d]oxazol-7-yl)ethanone (**4ja**).* Brown solid (97 mg, 84%), mp 116−118 °C. IR (KBr): 3320, 2973, 1639, 1569, 1430, 1212 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.74 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 7.6 Hz, 1H), 6.97 (t, J = 8.0 Hz, 1H), 5.42 (br s, 1H), 2.88 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 198.1, 160.8, 149.0, 144.3, 125.4, 123.4, 119.5, 112.2, 52.2, 30.9, 28.7. HRMS (ESI): m/z calcd for $C_{13}H_{17}N_2O_2^+$ 233.1285, found 233.1289.

*N-(tert-Butyl)-5,7-dichlorobenzo[d]oxazol-2-amine (**4ka**).* Brown solid (110 mg, 85%), mp 143−145 °C. IR (KBr): 3153, 2969, 1765, 1662, 1571, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.18 (s, 1H), 6.97 (s, 1H), 5.59 (br s, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.4, 145.2, 143.3, 129.3, 120.7, 115.0, 114.0, 52.5, 29.0. HRMS (ESI): m/z calcd for $C_{11}H_{13}Cl_2N_2O^+$ 259.0399, found 259.0399 (100.0%), 261.0371 (63.9%), 263.0345 (10.2%).

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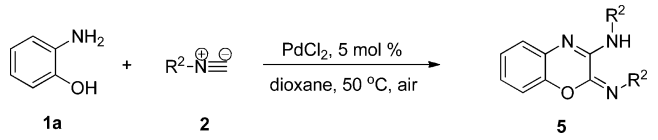
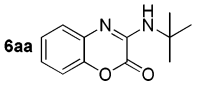
Table 5. Scope of Isocyanides for the Synthesis of 3-Amino-2*H*-benzoxazines[a]



1a 2 5

entry	*o*-aminophenol (**1a**)	isocyanides (R^2)	products	yield (%)[b]
1	**1a**	**2b (R^2 = 1,1,3,3-tetramethylbutyl)**	**5ab**	94
2	**1a**	**2c (R^2 = 2-Morpholinoethyl)**	**5ac**	82
3	**1a**	**2d (R^2 = *c*-Hex)**	**5ad**	95
4	**1a**	**2e (R^2 = *n*-Bu)**	**5ae**	89
5	**1a**	**2f (R^2 = Bn)**	**5af**	94
6	**1a**	**2g (R^2 = 4-OMe-Ph)**	**5ag**	87
7	**1a**	**2h (R^2 = 2,6-dimethylbenzyl)**	**5ah**	92
8	**1a**	**2i (R^2 = $CH_2COOC_2H_5$)**	**5ai**	complicated
9[c]	**1a**	**2a (R^2 = *t*-Bu)**	**6aa** 	88

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (1.2 mmol), dioxane (2.0 mL), 50 °C, in an air atmosphere for 2 h unless otherwise noted. [b]Isolated yield. [c]HOAc (5.0 equiv) was added after 2 h and then 12 h at 80 °C.

N-(tert-Butyl)-4-nitrobenzo[d]oxazol-2-amine (***4la***). Brown solid (99 mg, 84%), mp 131−133 °C. IR (KBr): 2975, 1764, 1645, 1576, 1207 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94 (d, J = 8.8 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.00 (t, J = 8.2 Hz, 1H), 6.21 (br s, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 164.1, 150.6, 139.4, 135.7, 119.9, 118.9, 113.6, 53.0, 29.2. HRMS (ESI): m/z calcd for $C_{11}H_{14}N_3O_3^+$ 236.1030, found 236.1031.

N-(tert-Butyl)-5-nitrobenzo[d]oxazol-2-amine (***4ma***). Brown solid (88 mg, 75%), mp 168−170 °C. IR (KBr): 3349, 3205, 2968, 1665, 1218 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.19 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 5.84 (br s, 1H), 1.53 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.4, 152.1, 144.9, 144.1, 117.1, 111.6, 108.0, 52.5, 28.9. HRMS (ESI): m/z calcd for $C_{11}H_{14}N_3O_3^+$ 236.1030, found 236.1033.

N-(tert-Butyl)-6-nitrobenzo[d]oxazol-2-amine (***4na***). Brown solid (103 mg, 88%), mp 139−141 °C. IR (KBr): 3350, 2965, 1667, 1588, 1322, 1281, 1210 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.12 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 8.08 (s, 1H), 7.30 (d, J = 8.4 Hz, 1H), 5.92 (br s, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 163.7, 157.1, 147.2, 141.4, 121.1, 114.9, 104.8, 52.8, 29.0. HRMS (ESI): m/z calcd for $C_{11}H_{14}N_3O_3^+$ 236.1030, found 236.1032.

2-(tert-Butylamino)benzo[d]oxazole-5-carbonitrile (***4oa***). Yellow solid (84 mg, 78%), mp 91−93 °C. IR (KBr): 3366, 2970, 2226, 1651, 1584, 1169 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.27 (s, 1H), 7.71−7.67 (m, 2H), 5.89 (br s, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.7, 154.3, 129.5, 125.2, 125.1, 119.4, 112.3, 109.1, 52.3, 28.7. HRMS (ESI): m/z calcd for $C_{12}H_{12}N_3O^-$ 214.0986, found 214.0989.

N-(tert-Butyl)-5-(methylsulfonyl)benzo[d]oxazol-2-amine (***4pa***). Brown solid (118 mg, 88%), mp 134−136 °C. IR (KBr): 3340, 2926, 1646, 1576, 1254, 1140 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.87 (s, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 5.48 (br s, 1H), 3.02 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.9, 151.3, 144.3, 136.1, 120.5, 115.4, 108.8, 52.5, 44.9, 28.9. HRMS (ESI): m/z calcd for $C_{12}H_{17}N_2O_3S^+$ 269.0954, found 269.0966.

2-(tert-Butylamino)benzo[d]oxazole-5-sulfonamide (***4qa***). Brown solid (114 mg, 85%), mp 139−141 °C. IR (KBr): 3342, 2976, 1725, 1646, 1577, 1154 cm^{-1}. ^1H NMR (400 MHz, *d*-acetone): δ (ppm) 7.81 (d, J = 1.2 Hz, 1H), 7.61 (dd, J_1 = 1.6 Hz, J_2 = 8.4 Hz, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.01 (br s, 1H), 6.56 (br s, 2H), 1.51 (s, 9H). ^{13}C NMR (100 MHz, *d*-acetone): δ (ppm) 163.1, 150.9, 145.1, 140.7, 119.9, 114.6, 109.1, 52.7, 29.0. HRMS (ESI): m/z calcd for $C_{11}H_{16}N_3O_3S^+$ 270.0907, found 270.0899.

N-(tert-Butyl)naphtho[2,3-d]oxazol-2-amine (***4ra***). Brown solid (115 mg, 96%), mp 112−114 °C. IR (KBr): 3399, 2970, 1642, 1585, 1444, 1220 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.85−7.81 (m, 2H), 7.70 (s, 1H), 7.58 (s, 1H), 7.40−7.34 (m, 2H), 5.66 (br s, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 162.0, 148.2, 143.5, 131.7, 129.4, 127.5, 127.5, 124.2, 123.7, 111.9, 104.2, 52.3, 29.2. HRMS (ESI): m/z calcd for $C_{15}H_{17}N_2O^+$ 241.1335, found 241.1332.

N_2,$N_{2'}$-Di-tert-butyl[6,6′-bibenzo[d]oxazole]-2,2′-diamine (***4sa***). Brown solid (157 mg, 83%), mp 125−127 °C. IR (KBr): 3188, 2964, 1766, 1649, 1463, 1235 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.44 (s, 2H), 7.42−7.34 (m, 4H), 5.11 (br s, 2H), 1.50 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.0, 148.8, 142.3, 134.8, 123.0, 116.2, 107.3, 52.1, 29.2. HRMS (ESI): m/z calcd for $C_{22}H_{27}N_4O_2^+$ 379.2129, found 379.2128.

N-(tert-Butyl)oxazolo[4,5-b]pyridin-2-amine (***4ta***). Brown solid (64 mg, 67%), mp 117−119 °C. IR (KBr): 3239, 2971, 1765, 1646, 1579, 1402, 1203 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.88 (d, J = 4.0 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.07 (dd, J_1 = 4.8 Hz, J_2 = 7.6 Hz, 1H), 5.77 (br s, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 160.2, 157.7, 138.8, 135.5, 122.9, 120.2, 52.4, 29.1. HRMS (ESI): m/z calcd for $C_{10}H_{14}N_3O^+$ 192.1131, found 192.1128.

N-(2,4,4-Trimethylpentan-2-yl)benzo[d]oxazol-2-amine (***4ab***). Brown solid (109 mg, 89%), mp 95−97 °C. IR (KBr): 2954, 1766, 1651, 1581, 1461, 1244 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm)

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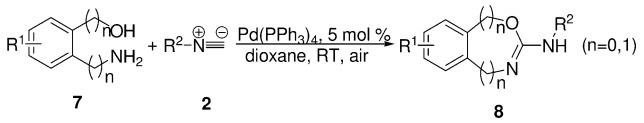
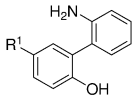
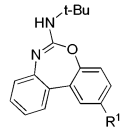
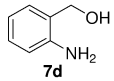
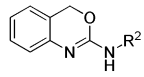
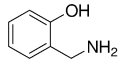
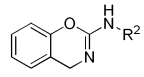
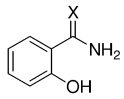
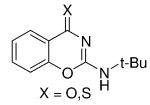
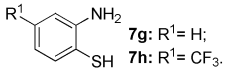
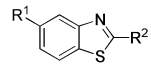
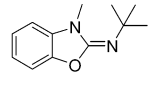
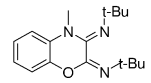
Table 6. Substrate Scope of the Aerobic Oxidative Coupling of Various Bisnucleophiles and Isocyanides[a]



7 2 8

entry	bisnucleophiles (**7**)	isocyanides (**2**)	products (**8**)	yield (%) [b]
1	 **7a:** R^1= H; **7b:** R^1= F; **7c:** R^1= Cl;	**2a**		(**8aa**) 94
2				(**8ba**) 85
3				(**8ca**) 89
4	 **7d**	**2a**		(**8da**) 95
		2b		(**8db**) 91
5	 **7e**	**2a**		(**8ea**) 93
		2b		(**8eb**) 95
6 [c]	 **7f**	**2a**		(**8fa**) n.r
7	 **7g:** R^1= H; **7h:** R^1= CF_3.	**2a**		(**8ga:** R^2 = *t*-BuNH)
8				91
				(**8ha:** R^2 = H) 88
9	 **7i**	**2a**		(**8ia**) 90
10 [d]	**7i**	**2a**		(**9**) n.d

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), dioxane (2.0 mL), at room temperature, in an air atmosphere for 2 h unless otherwise noted. n.r = no reaction; n.d = not detected. [b]Isolated yield. [c]80 °C for 12 h. [d]1.2 mmol of **2a** was added, $Pd(PPh_3)_4$ was replaced by $PdCl_2$ (5 mol %), 50 °C for 10 h.

7.35 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.15−7.11 (m, 1H), 7.01−6.97 (m, 1H), 5.70 (br s, 1H), 1.84 (s, 2H), 1.53 (s, 6H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 160.8, 148.1, 143.1, 123.6, 120.3, 116.1, 108.4, 55.7, 51.8, 31.4, 29.7. HRMS (ESI): *m*/*z* calcd for $C_{15}H_{23}N_2O^+$ 247.1805, found 247.1807.

*N-(2-Morpholinoethyl)benzo[d]oxazol-2-amine (**4ac**).* Yellow oil (100 mg, 81%). IR (KBr): 3856, 3745, 2926, 1765, 1649, 1398, 1243, 1115 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* (ppm) 7.33 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 5.73 (br s, 1H), 3.69 (t, *J* = 4.2 Hz, 4H), 3.54 (t, *J* = 5.6 Hz, 2H), 2.62 (t, *J* = 5.8 Hz, 2H), 2.48 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 162.0, 148.5, 142.9, 123.8, 120.8, 116.3, 108.6, 66.8, 56.8, 53.2, 39.0. HRMS (ESI): *m*/*z* calcd for $C_{13}H_{18}N_3O_2^+$ 248.1394, found 248.1396.

*N-Cyclohexylbenzo[d]oxazol-2-amine (**4ad**) (Known Compound)..*[8e,10b] Yellow solid (100 mg, 93%), mp 109−111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.33 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 5.41 (br s, 1H), 3.80−3.67 (m, 1H), 2.12−2.05 (m, 2H), 1.77−1.74 (m, 2H), 1.65−1.61 (m, 1H), 1.46−1.37 (m, 2H), 1.33−1.19 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 161.5, 148.3, 143.0, 123.8, 120.5, 116.0, 108.6, 52.0, 33.4, 25.4, 24.7.

*N-Butylbenzo[d]oxazol-2-amine (**4ae**) (Known Compound)..*[8d,e] White solid (91 mg, 96%), mp 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.31 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.15−7.11 (m, 1H), 7.00−6.96 (m, 1H), 6.15 (br s, 1H), 3.45 (t, *J* = 7.2 Hz, 2H), 1.68−1.60 (m, 2H), 1.45−1.38 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 162.4, 148.3, 142.9, 123.7, 120.4, 115.8, 108.6, 42.7, 31.7, 19.8, 13.6.

*N-Benzylbenzo[d]oxazol-2-amine (**4af**) (Known Compound)..*[8e,10b] White solid (106 mg, 95%), mp 110−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.36−7.25 (m, 5H), 7.21−7.19 (m, 2H), 7.13−7.09 (m, 1H), 7.00−6.97 (m, 1H), 6.41 (br s, 1H), 4.63 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 162.1, 148.4, 142.7, 137.7, 128.7, 127.7, 127.5, 123.9, 120.8, 116.2, 108.7, 46.9.

*N-(4-Methoxyphenyl)benzo[d]oxazol-2-amine (**4ag**) (Known Compound).*[19] Brown solid (90 mg, 75%), mp 137−139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.50−7.45 (m, 2H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.21−7.18 (m, 1H), 7.10−7.06 (m, 1H), 6.94−6.91 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* (ppm) 159.4, 156.1, 147.9, 142.1, 131.0, 124.2, 121.4, 121.0, 116.5, 114.5, 109.0, 55.5.

*N-(2,6-Dimethylphenyl)benzo[d]oxazol-2-amine (**4ah**).* Yellow solid (101 mg, 85%), mp 195−197 °C. IR (KBr): 2920, 1662, 1581, 1461, 1214, 746 cm^{-1}. ^{1}H NMR (400 MHz, d-DMSO) *δ* 9.53 (br s, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.15−7.11 (m, 4H), 7.02 (t, *J* = 7.6 Hz, 1H), 2.22 (s, 6H). ^{13}C NMR (100 MHz, *d*-DMSO): *δ* (ppm) 160.3, 148.1, 143.1, 135.6, 135.0, 128.1, 126.8,

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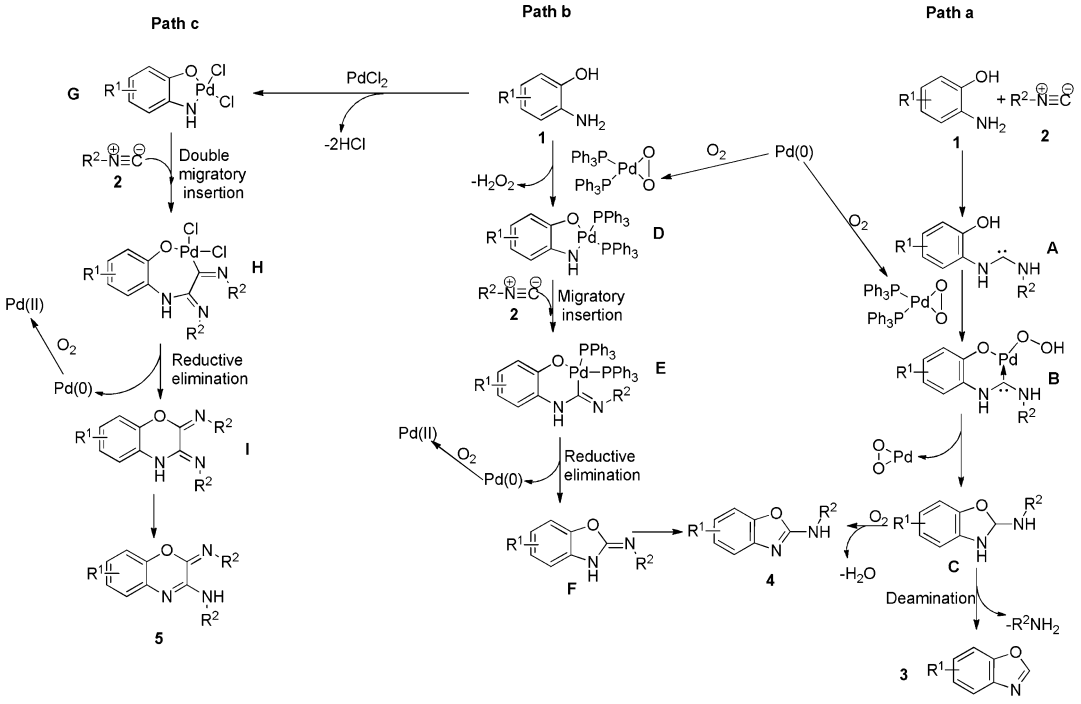
Scheme 2. Proposed Mechanism



123.7, 120.5, 115.8, 108.7, 17.9. HRMS (ESI): m/z calcd for $C_{15}H_{15}N_2O^+$ 239.1179, found 239.1182.

*N-(tert-Butyl)-2-(tert-butylimino)-2H-benzo[b][1,4]oxazin-3-amine (**5aa**).* White solid (126 mg, 92%), mp 128−130 °C. IR (KBr): 3748, 3375, 2960, 1659, 1613, 1514, 1222, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33 (d, J = 8.0 Hz, 1H), 7.12−6.99 (m, 3H), 6.55 (br s, 1H), 1.55 (s, 9H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 146.8, 143.5, 138.3, 132.7, 125.4, 123.8, 122.8, 114.6, 53.7, 51.4, 29.6, 28.5. HRMS (ESI): m/z calcd for $C_{16}H_{24}N_3O^+$ 274.1914, found 274.1916.

*N-(tert-Butyl)-2-(tert-butylimino)-6-methyl-2H-benzo[b][1,4]-oxazin-3-amine (**5ba**).* Light yellow solid (138 mg, 96%), mp 100−102 °C. IR (KBr): 3368, 2966, 1669, 1620, 1579, 1524, 1223, 801 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.12 (s, 1H), 6.89 (d, J = 8.4 Hz, 1H), 6.79−6.77 (m, 1H), 6.50 (br s, 1H), 2.32 (s, 3H), 1.50 (s, 9H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.0, 141.4, 138.6, 133.3, 132.3, 125.7, 123.4, 114.2, 53.7, 51.4, 29.6, 28.5, 20.8. HRMS (ESI): m/z calcd for $C_{17}H_{26}N_3O^+$ 288.2070, found 288.2073.

*N-(tert-Butyl)-2-(tert-butylimino)-7-methyl-2H-benzo[b][1,4]-oxazin-3-amine (**5ca**).* Light yellow solid (129 mg, 90%), mp 110−112 °C. IR (KBr): 3371, 2967, 1670, 1620, 1588, 1516, 1232, 1164 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.17 (d, J = 7.6 Hz, 1H), 6.87 (d, J = 8.0 Hz, 1H), 6.84 (s, 1H), 6.42 (br s, 1H), 2.33 (s, 3H), 1.50 (s, 9H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$):: δ (ppm) (ppm) 146.4, 143.2, 138.5, 132.9, 130.2, 125.1, 124.5, 115.0, 53.7, 51.3, 29.6, 28.6, 20.9. HRMS (ESI): m/z calcd for $C_{17}H_{26}N_3O^+$ 288.2070, found 288.2075.

*N-(tert-Butyl)-2-(tert-butylimino)-6-methoxy-2H-benzo[b][1,4]-oxazin-3-amine (**5da**).* Brown solid (147 mg, 97%), mp 105−107 °C. IR (KBr): 3365, 2968, 1764, 1669, 1580, 1242, 1143, 1045 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 6.92 (d, J = 8.8 Hz, 1H), 6.83 (d, J = 3.2 Hz, 1H), 6.57−6.55 (m, 2H), 3.81 (s, 3H), 1.51 (s, 9H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 156.2, 147.2, 138.6, 137.9, 133.3, 114.9, 109.5, 109.2, 55.7, 53.7, 51.5, 29.7, 28.6. HRMS (ESI): m/z calcd for $C_{17}H_{26}N_3O_2^+$, 304.2020, found 304.2021.

*N,6-Di-tert-butyl-2-(tert-butylimino)-2H-benzo[b][1,4]oxazin-3-amine (**5ea**).* White solid (156 mg, 95%), mp 135−137 °C. IR (KBr): 3369, 2965, 2361, 1765, 1579, 1240, 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.33 (d, J = 2.0 Hz, 1H), 7.06−7.03 (m, 1H), 6.97 (d, J = 8.4 Hz, 1H), 6.53 (br s, 1H), 1.54 (s, 9H), 1.41 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.0, 147.0, 141.3, 138.6, 132.0, 122.3, 120.0, 114.0, 53.7, 51.4, 34.3, 31.6, 29.6, 28.6. HRMS (ESI): m/z calcd for $C_{20}H_{32}N_3O^+$ 330.2540, found 330.2551.

*N-(tert-Butyl)-2-(tert-butylimino)-7-fluoro-2H-benzo[b][1,4]-oxazin-3-amine (**5fa**).* Brown solid (135 mg, 93%), mp 102−104 °C. IR (KBr): 3374, 2964, 2361, 1764, 1616, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.21−7.18 (m, 1H), 6.80−6.72 (m, 2H), 6.40 (br s, 1H), 1.48 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.5 (J = 240.7 Hz), 146.1, 143.5 (J = 12.3 Hz), 137.4, 129.1, 125.8 (J = 9.2 Hz), 110.6 (J = 22.1 Hz), 102.3 (J = 26.4 Hz), 53.9, 51.4, 29.6, 28.5. HRMS (ESI): m/z calcd for $C_{16}H_{23}FN_3O^+$ 292.1820, found 292.1818 .

*N-(tert-Butyl)-2-(tert-butylimino)-6-chloro-2H-benzo[b][1,4]-oxazin-3-amine (**5ga**).* Light yellow solid (137 mg, 89%), mp 162−164 °C. IR (KBr): 3373, 2963, 2362, 1667, 1611, 1573, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26 (s, 1H), 6.92−6.88 (m, 2H), 6.57 (br s, 1H), 1.48 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.2, 142.1, 137.6, 133.8, 128.6, 124.9, 122.4, 115.4, 53.9, 51.7, 29.6, 28.5. HRMS (ESI): m/z calcd for $C_{16}H_{23}ClN_3O^+$ 308.1524, found 308.1522 (100.0%), 310.1518 (32.0%).

*6-Bromo-N-(tert-butyl)-2-(tert-butylimino)-2H-benzo[b][1,4]-oxazin-3-amine (**5ha**).* Yellow solid (153 mg, 87%), mp 180−182 °C. IR (KBr): 3369, 2961, 2361, 1764, 1569, 1242, 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 (d, J = 2.0 Hz, 1H), 7.04 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.57 (br s, 1H), 1.48 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.2, 142.5, 137.6, 134.2, 127.9, 125.2, 116.0, 115.8, 54.0, 51.7, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{16}H_{23}BrN_3O^+$, 352.1019, found 352.1025 (100.0%), 354.1012 (98.2%).

*Methyl 3-(tert-Butylamino)-2-(tert-butylimino)-2H-benzo[b][1,4]-oxazine-6-carboxylate (**5ia**).* Light yellow solid (129 mg, 78%), mp 128−130 °C. IR (KBr): 3367, 2967, 2360, 1724, 1617, 1578, 1237 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94 (d, J = 2.0 Hz, 1H), 7.65 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.49 (br s, 1H), 3.88 (s, 3H), 1.48 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 166.7, 146.9, 146.8, 137.2, 132.5, 127.0, 125.9, 124.4, 114.5, 54.0, 51.9, 51.6, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{18}H_{26}N_3O_3^+$ 332.1969, found 332.1977.

*1-(3-(tert-Butylamino)-2-(tert-butylimino)-2H-benzo[b][1,4]-oxazin-5-yl)ethanone (**5ja**).* Brown solid (121 mg, 77%), mp 125−

dx.doi.org/10.1021/jo400002f | J. Org. Chem. 2013, 78, 3009−3020

127 °C. IR (KBr): 3353, 2969, 1765, 1678, 1602, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31−7.29 (m, 1H), 7.08 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 6.75 (br s, 1H), 2.77 (s, 3H), 1.47 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 202.8, 146.3, 143.5, 137.4, 135.6, 131.5, 123.7, 122.2, 117.6, 53.9, 51.4, 32.4, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{18}H_{26}N_3O_2^+$ 316.2020, found 316.2024.

*N-(tert-Butyl)-2-(tert-butylimino)-6,8-dichloro-2H-benzo[b][1,4]-oxazin-3-amine (**5ka**).* White solid (140 mg, 82%), mp 183−185 °C. IR (KBr): 3369, 2991, 1764, 1608, 1564, 1241 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.15 (d, J = 2.4 Hz, 1H), 7.00 (d, J = 2.4 Hz, 1H), 6.60 (br s, 1H), 1.47 (s, 9H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.3, 138.6, 136.5, 134.6, 128.3, 123.5, 122.7, 119.9, 54.3, 51.9, 29.3, 28.4. HRMS (ESI): m/z calcd for $C_{16}H_{22}Cl_2N_3O^+$ 342.1134, found 342.1132 (100.0%), 344.1114 (63.9%), 346.1080 (10.2%).

*N-(tert-Butyl)-2-(tert-butylimino)-5-nitro-2H-benzo[b][1,4]-oxazin-3-amine (**5la**).* Yellow solid (137 mg, 86%), mp 169−171 °C. IR (KBr): 3380, 2989, 1765, 1577, 1242, 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 (dd, J_1 = 1.2 Hz, J_2 = 8.0 Hz, 1H), 7.15−7.12 (m, 1H), 6.96 (t, J = 8.0 Hz, 1H), 6.74 (br s, 1H), 1.47 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.6, 144.6, 144.1, 136.3, 127.5, 121.2, 118.7, 117.8, 54.3, 52.3, 29.6, 28.3. HRMS (ESI): m/z calcd for $C_{16}H_{23}N_4O_3^+$ 319.1765, found 319.1770.

*N-(tert-Butyl)-2-(tert-butylimino)-6-nitro-2H-benzo[b][1,4]-oxazin-3-amine (**5ma**).* Yellow solid (132 mg, 83%), mp 171−173 °C. IR (KBr): 3368, 2991, 1765, 1242, 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.11 (d, J = 2.8 Hz, 1H), 7.84 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H), 7.04 (d, J = 8.8 Hz, 1H), 6.61 (br s, 1H), 1.49 (s, 9H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.8, 147.4, 144.2, 136.2, 133.2, 120.8, 118.2, 114.9, 54.4, 52.0, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{16}H_{23}N_4O_3^+$ 319.1765, found 319.1767.

*N-(tert-Butyl)-2-(tert-butylimino)-7-nitro-2H-benzo[b][1,4]-oxazin-3-amine (**5na**).* Yellow solid (135 mg, 85%), mp 171−173 °C. IR (KBr): 3359, 2970, 1617, 1555, 1333, 1224 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.96−7.93 (m, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 6.85 (br s, 1H), 1.50 (s, 9H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 148.3, 142.5, 142.2, 139.3, 136.4, 124.9, 119.9, 110.7, 54.4, 52.3, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{16}H_{23}N_4O_3^+$ 319.1765, found 319.1755.

*3-(tert-Butylamino)-2-(tert-butylimino)-2H-benzo[b][1,4]oxazine-6-carbonitrile (**5oa**).* White solid (130 mg, 87%), mp 153−155 °C. IR (KBr): 3362, 2967, 2221, 1765, 1678, 1611, 1568, 1228, 807 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.53 (d, J = 1.6 Hz, 1H), 7.22 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 1H), 6.59 (br s, 1H), 1.47 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.3, 146.5, 136.4, 133.5, 129.1, 126.4, 118.8, 115.6, 107.4, 54.2, 51.9, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{17}H_{23}N_4O^+$ 299.1866, found 299.1877.

*N-(tert-Butyl)-2-(tert-butylimino)-6-(methylsulfonyl)-2H-benzo-[b][1,4]oxazin-3-amine (**5pa**).* White solid (156 mg, 89%), mp 154−156 °C. IR (KBr): 3363, 2969, 1760, 1679, 1614, 1573, 1311, 1228, 1150 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.81 (d, J = 2.0 Hz, 1H), 7.52−7.50 (m, 1H), 7.10 (d, J = 8.4 Hz, 1H), 6.59 (br s, 1H), 3.03 (s, 3H), 1.47 (s, 9H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.4, 147.0, 136.5, 135.8, 133.5, 124.6, 121.6, 115.4, 54.3, 51.9, 44.7, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{17}H_{26}N_3O_3S^+$ 352.1689, found 352.1676.

*3-(tert-Butylamino)-2-(tert-butylimino)-2H-benzo[b][1,4]oxazine-6-sulfonamide (**5qa**).* White solid (151 mg, 86%), mp 200−202 °C. IR (KBr): 3365, 2969, 1678, 1615, 1226, 1160 cm^{-1}. ^1H NMR (400 MHz, *d*-acetone): δ (ppm) 7.75 (d, J = 1.6 Hz, 1H), 7.55 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 6.75 (br s, 1H), 6.54 (br s, 2H), 1.51 (s, 9H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, *d*-acetone): δ (ppm) 148.3, 146.5, 140.9, 137.9, 133.6, 124.0, 121.8, 116.0, 54.8, 52.4, 30.5. HRMS (ESI): m/z calcd for $C_{16}H_{23}N_4O_3S^-$ 351.1496, found 351.1488.

*N-(tert-Butyl)-2-(tert-butylimino)-2H-naphtho[2,3-b][1,4]oxazin-3-amine (**5ra**).* Light yellow solid (157 mg, 97%), mp 158−160 °C. IR (KBr): 3374, 2967, 1764, 1592, 1237 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.62−7.54 (m, 3H), 7.21−7.16 (m, 2H), 6.43 (br s, 1H), 1.40 (s, 9H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 146.9, 143.3, 138.0, 132.6, 131.3, 130.2, 127.1, 126.7, 124.7, 124.6, 121.9, 110.3, 54.0, 51.6, 29.7, 29.6, 28.6. HRMS (ESI): m/z calcd for $C_{20}H_{26}N_3O^+$ 324.2070, found 324.2068.

*N^3,$N^{3'}$-Di-tert-butyl-2,2′-bis(tert-butylimino)-2H,2′H-[7,7′-bibenzo[b][1,4]oxazine]-3,3′-diamine (**5sa**).* Yellow solid (242 mg, 89%), mp 211−213 °C. IR (KBr): 3368, 2966, 1764, 1672, 1617, 1581, 1237 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26−7.22 (m, 4H), 7.16 (s, 2H), 6.45 (br s, 2H), 1.43 (s, 18H), 1.34 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 146.8, 143.7, 138.2, 135.2, 131.9, 125.6, 122.2, 112.5, 53.9, 51.5, 29.7, 28.6. HRMS (ESI): m/z calcd for $C_{32}H_{45}N_6O_2^+$ 545.3599, found 545.3597.

*N-(tert-Butyl)-3-(tert-butylimino)-3H-pyrido[2,3-b][1,4]oxazin-2-amine (**5ta**).* Light yellow solid (114 mg, 83%), mp 115−117 °C. IR (KBr): 3364, 2922, 1764, 1662, 1603, 1239 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.89 (d, J = 3.6 Hz, 1H), 7.55 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H), 7.05−7.02 (m, 1H), 6.58 (br s, 1H), 1.48 (s, 9H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 150.0, 147.0, 140.6, 138.4, 132.9, 128.3, 120.9, 54.3, 51.7, 29.6, 28.5. HRMS (ESI): m/z calcd for $C_{15}H_{23}N_4O^+$ 275.1866, found 275.1869.

*N-(tert-Butyl)-2-(tert-butylimino)-2H-pyrido[3,2-b][1,4]oxazin-3-amine (**5ua**).* Light yellow solid (104 mg, 76%), mp 167−169 °C. IR (KBr): 3750, 3368, 2963, 1765, 1662, 1609, 1240 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.18 (d, J = 4.4 Hz, 1H), 7.22 (s, 1H), 6.89−6.86 (m, 1H), 6.76 (br s, 1H), 1.50 (s, 9H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 149.3, 145.9, 144.3, 139.1, 136.9, 121.9, 118.1, 54.1, 52.1, 29.6, 28.4. HRMS (ESI): m/z calcd for $C_{15}H_{23}N_4O^+$ 275.1866, found 275.1867.

*N-(2,4,4-Trimethylpentan-2-yl)-2-((2,4,4-trimethylpentan-2-yl)-imino)-2H-benzo[b][1,4]oxazin-3-amine (**5ab**).* Yellow oil (181 mg, 94%). IR (KBr): 3371, 2955, 1673, 1616, 1523, 1224, 748 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29 (dd, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H), 7.09−7.04 (m, 1H), 7.02−6.95 (m, 2H), 6.68 (br s, 1H), 1.91 (s, 2H), 1.73 (s, 2H), 1.55 (s, 6H), 1.44 (s, 6H), 1.03 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 146.9, 143.5, 137.4, 132.9, 125.4, 123.8, 122.6, 114.6, 57.4, 55.5, 55.2, 51.4, 32.0, 31.9, 31.7, 31.5, 29.7, 29.0. HRMS (ESI): m/z calcd for $C_{24}H_{40}N_3O^+$ 386.3166, found 386.3171.

*N-(2-Morpholinoethyl)-2-((2-morpholinoethyl)imino)-2H-benzo-[b][1,4]oxazin-3-amine (**5ac**).* Reddish brown oil (159 mg, 82%). IR (KBr): 2955, 2856, 1670, 1614, 1116, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.26 (d, J = 7.6 Hz, 1H), 7.07−7.03 (m, 1H), 7.00−6.96 (m, 2H), 6.84 (br s, 1H), 3.71−3.63 (m, 10H), 3.57−3.53 (m, 2H), 2.65 (t, J = 7.0 Hz, 2H), 2.60 (t, J = 6.2 Hz, 2H), 2.55−2.43 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.4, 143.6, 141.3, 132.6, 125.1, 124.2, 123.4, 114.6, 66.9, 66.8, 59.0, 56.6, 53.9, 53.3, 43.4, 37.1. HRMS (ESI): m/z calcd for $C_{20}H_{30}N_5O_3^+$ 388.2343, found 388.2348.

*N-Cyclohexyl-2-(cyclohexylimino)-2H-benzo[b][1,4]oxazin-3-amine (**5ad**).* Light yellow oil (154 mg, 95%). IR (KBr): 3386, 2929, 2854, 1759, 1668, 1613, 1520, 1215 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 7.6 Hz, 1H), 7.07−6.95 (m, 3H), 6.39 (br s, 1H), 4.01−3.79 (m, 2H), 2.08−2.05 (m, 2H), 1.79−1.73 (m, 6H), 1.66−1.63 (m, 2H), 1.49−1.36 (m, 6H), 1.33−1.18 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 146.9, 143.6, 139.3, 132.9, 124.9, 123.8, 122.9, 114.5, 53.9, 48.9, 33.3, 32.8, 25.8, 25.7, 24.8, 24.7. HRMS (ESI): m/z calcd for $C_{20}H_{28}N_3O^+$ 326.2227, found 326.2225.

*N-Butyl-2-(butylimino)-2H-benzo[b][1,4]oxazin-3-amine (**5ae**).* Brown oil (121 mg, 89%). IR (KBr): 3399, 2929, 2867, 1671, 1614, 1215 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.30−7.28 (m, 1H), 7.08−6.96 (m, 3H), 6.40 (br s, 1H), 3.50−3.44 (m, 4H), 1.67−1.57 (m, 4H), 1.47−1.37 (m, 4H), 0.98−0.93 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.6, 143.7, 140.8, 132.9, 125.1, 124.0, 123.2, 114.6, 45.5, 40.5, 32.5, 31.3, 20.6, 20.2, 13.9, 13.8. HRMS (ESI): m/z calcd for $C_{16}H_{24}N_3O^+$ 274.1914, found 274.1910.

*N-Benzyl-2-(benzylimino)-2H-benzo[b][1,4]oxazin-3-amine (**5af**).* White solid (160 mg, 94%), mp 86−88 °C. IR (KBr): 3396, 1747, 1669, 1612, 1240, 748 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41−7.25 (m, 11H), 7.16−7.12 (m, 2H), 7.09−7.05 (m, 1H), 6.80 (br s, 1H), 4.74 (s, 2H), 4.71 (d, J = 6.0 Hz, 2H). ^{13}C NMR (100

MHz, $CDCl_3$): δ (ppm) 147.3, 143.7, 141.3, 139.6, 138.3, 132.6, 128.6, 128.4, 127.9, 127.8, 127.4, 126.8, 125.4, 124.4, 123.7, 114.7, 49.8, 44.7. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{20}N_3O^+$, 342.1601, found 342.1608.

N-(4-Methoxyphenyl)-2-((4-methoxyphenyl)imino)-2H-benzo[b][1,4]oxazin-3-amine (**5ag**). Brown solid (162 mg, 87%), mp 177−179 °C. IR (KBr): 3748, 1767, 1612, 1243 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.60 (br s, 1H), 7.81 (d, *J* = 9.2 Hz, 2H), 7.47 (d, *J* = 9.2 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.16−7.12 (m, 1H), 7.07 (d, *J* = 4.0 Hz, 2H), 6.96−6.92 (m, 4H), 3.84 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 157.5, 155.7, 144.7, 143.3, 138.3, 136.4, 132.2, 132.1, 126.0, 125.9, 124.6, 124.5, 121.3, 115.0, 114.2, 114.0, 55.5, 55.4. HRMS (ESI): *m*/*z* calcd for $C_{22}H_{20}N_3O_3^+$ 374.1499, found 374.1489.

N-(2,6-Dimethylphenyl)-2-((2,6-dimethylphenyl)imino)-2H-benzo[b][1,4]oxazin-3-amine (**5ah**). Light yellow solid (170 mg, 92%), mp 139−141 °C. IR (KBr): 3346, 2920, 1766, 1672, 1615, 1577, 1509, 1229, 760 cm^{-1}. ^1H NMR (400 MHz, *d*-DMSO): δ (ppm) 7.94 (br s, 1H), 7.21−7.19 (m, 1H), 7.06−7.01 (m, 5H), 6.98−6.83 (m, 4H), 2.26 (s, 6H), 2.09 (s, 6H). ^{13}C NMR (100 MHz, d-DMSO): δ (ppm) 145.1, 143.6, 142.8, 139.0, 135.5, 134.7, 132.4, 128.2, 128.0, 127.8, 127.1, 126.0, 124.5, 124.4, 123.9, 115.1, 18.7, 18.3. HRMS (ESI): *m*/*z* calcd for $C_{24}H_{24}N_3O^+$ 370.1914, found 370.1919.

3-(tert-Butylamino)-2H-benzo[b][1,4]oxazin-2-one (**6aa**). White solid (96 mg, 88%), mp 85−87 °C. IR (KBr): 3374, 2972, 1730, 1615, 1577, 1520, 1225, 754, 495 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 (d, *J* = 8.0 Hz, 1H), 7.22−7.08 (m, 3H), 6.09 (br s, 1H), 1.51 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 152.4, 144.3, 143.3, 132.5, 125.8, 125.4, 124.2, 115.8, 52.2, 28.1. HRMS (ESI): *m*/*z* calcd for $C_{12}H_{15}N_2O_2^+$ 219.1128, found 219.1125.

N-(tert-Butyl)dibenzo[d,f][1,3]oxazepin-6-amine (**8aa**). Yellow solid (125 mg, 94%), mp 94−96 °C. IR (KBr): 3423, 2969, 1765, 1668, 1487, 1242, 1177, 766 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.54 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.29−7.20 (m, 3H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 4.52 (br s, 1H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 155.8, 149.8, 145.5, 131.5, 130.1, 128.8, 128.6, 128.4, 128.4, 126.5, 125.8, 122.7, 120.2, 51.1, 28.5. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{19}N_2O^+$ 267.1492, found 267.1493.

N-(tert-Butyl)-2-fluorodibenzo[d,f][1,3]oxazepin-6-amine (**8ba**). Brown solid (121 mg, 85%), mp 127−129 °C. IR (KBr): 2977, 2226, 1765, 1648, 1583, 1242 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.40−7.38 (m, 1H), 7.28−7.15 (m, 3H), 7.03−6.99 (m, 1H), 6.93−6.87 (m, 2H), 4.55 (br s, 1H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 160.2 (d, *J* = 241.5 Hz), 151.6 (d, *J* = 2.3 Hz), 149.7, 145.5, 133.2 (d, *J* = 8.2 Hz), 128.9 (d, *J* = 1.7 Hz), 128.9, 128.2, 126.6, 122.7, 121.4 (d, *J* = 8.9 Hz), 114.9 (d, *J* = 23.5 Hz), 114.6 (d, *J* = 23.8 Hz), 51.0, 28.3. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{18}FN_2O^+$ 285.1398, found 285.1393.

N-(tert-Butyl)-2-chlorodibenzo[d,f][1,3]oxazepin-6-amine (**8ca**). Light yellow solid (134 mg, 89%), mp 103−105 °C. IR (KBr): 3430, 2972, 1765, 1669, 1482, 1243, 1175, 759 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.51 (d, *J* = 2.4 Hz, 1H), 7.44−7.42 (m, 1H), 7.30−7.22 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.09−7.05 (m, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 4.52 (br s, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 154.2, 149.7, 145.4, 133.2, 131.1, 129.1, 128.8, 128.5, 128.4, 128.4, 126.6, 122.9, 121.5, 51.3, 28.5. HRMS (ESI): *m*/*z* calcd for $C_{17}H_{18}ClN_2O^+$ 301.1102, found 301.1114 (100.0%), 303.1105 (32.0%).

N-(tert-Butyl)-4H-benzo[d][1,3]oxazin-2-amine (**8da**). Brown oil (97 mg, 95%). IR (KBr): 2988, 1765, 1692, 1376, 1242, 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.15−7.11 (m, 1H), 7.00 (d, *J* = 4.4 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 4.44 (br s, 1H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 150.1, 148.0, 127.5, 125.8, 123.7, 121.7, 114.9, 50.6, 44.2, 29.2. HRMS (ESI): *m*/*z* calcd for $C_{12}H_{17}N_2O^+$ 205.1335, found 205.1333.

N-(2,4,4-Trimethylpentan-2-yl)-4H-benzo[d][1,3]oxazin-2-amine (**8db**). Brown oil (118 mg, 91%). IR (KBr): 2954, 1765, 1693, 1479, 1374, 1239, 1068, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.16−7.11 (m, 1H), 7.00 (d, *J* = 4.4 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 1H), 4.44 (br s, 1H), 1.74 (s, 2H), 1.40 (s, 6H), 1.00 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 150.0, 147.8, 127.4, 125.8, 123.7, 121.7, 114.9, 54.4, 51.6, 44.0, 31.6, 31.5, 29.8. HRMS (ESI): *m*/*z* calcd for $C_{16}H_{25}N_2O^+$ 261.1961, found 261.1965.

N-(tert-Butyl)-4H-benzo[e][1,3]oxazin-2-amine (**8ea**). White solid (95 mg, 93%), mp 126−128 °C. IR (KBr): 3409, 2970, 1765, 1625, 1559, 1238, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.16 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.77 (t, *J* = 7.4 Hz, 1H), 4.17 (br s, 1H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.3, 155.8, 130.6, 129.6, 125.8, 119.6, 117.4, 50.8, 40.8, 29.3. HRMS (ESI): *m*/*z* calcd for $C_{12}H_{17}N_2O^+$ 205.1335, found 205.1336.

N-(2,4,4-Trimethylpentan-2-yl)-4H-benzo[e][1,3]oxazin-2-amine (**8eb**). Yellow solid (124 mg, 95%), mp 116−118 °C. IR (KBr): 3366, 2954, 1765, 1560, 1240, 753 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.17−7.13 (m, 1H), 7.00−6.98 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.77−6.74 (m, 1H), 5.26 (br s, 1H), 4.19 (s, 2H), 1.68 (s, 2H), 1.32 (s, 6H), 0.93 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 159.1, 155.9, 130.5, 129.5, 126.0, 119.5, 117.5, 54.7, 51.9, 40.8, 31.5, 31.4, 29.9. HRMS (ESI): *m*/*z* calcd for $C_{16}H_{25}N_2O^+$ 261.1961, found 261.1967.

N-(tert-Butyl)benzo[d]thiazol-2-amine (**8ga**) *(Known Compound).*[20] White solid (94 mg, 91%), mp 92−94 °C. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.55 (d, *J* = 6.8 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.6 Hz, 1H), 5.35 (br s, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 164.6, 152.3, 130.7, 125.6, 121.4, 120.4, 118.9, 53.2, 29.0.

5-(Trifluoromethyl)benzo[d]thiazole (**8ha**). Yellow solid (89 mg, 88%), mp 65−67 °C. IR (KBr): 2991, 1765, 1243, 1056 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.05 (s, 1H), 8.36 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 155.8, 152.8, 137.1, 128.8 (*J* = 32.6 Hz), 124.1 (*J* = 270.7 Hz), 122.5, 121.8 (*J* = 3.4 Hz), 120.8 (*J* = 4.2 Hz). HRMS (ESI): *m*/*z* calcd for $C_8H_5F_3NS^+$ 204.0089, found 204.0093.

2-Methyl-N-(3-methylbenzo[d]oxazol-2(3H)-ylidene)propan-2-amine (**8ia**). Light yellow solid (92 mg, 90%), mp 61−63 °C. IR (KBr): 2966, 1711, 1496, 1357, 1219, 734 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.04−7.00 (m, 2H), 6.89−6.85 (m, 1H), 7.04−7.00 (m, 1H), 6.70−6.68 (m, 1H), 3.22 (s, 1H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 147.2, 145.0, 133.7, 122.9, 119.5, 108.1, 105.8, 52.2, 30.6, 28.6. HRMS (ESI): *m*/*z* calcd for $C_{12}H_{17}N_2O^+$ 205.1335, found 205.1338.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^1H and ^{13}C NMR spectra for all products and text giving details of the control experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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