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Synthesis of Benzoxazoles from 2-Aminophenols and β-Diketones Using a Combined Catalyst of Brønsted Acid and Copper Iodide

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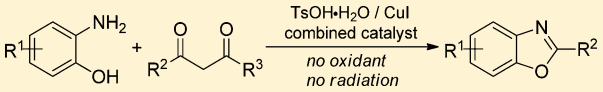
Supporting Information

ABSTRACT: Cyclization reactions of 2-aminophenols with β-diketones catalyzed by a combination of Brønsted acid and CuI are presented. Various 2-substituted benzoxazoles were obtained through these reactions. Different substituents such as methyl, chloro, bromo, nitro, and methoxy on 2-aminophenol are tolerated under the optimized reaction conditions.

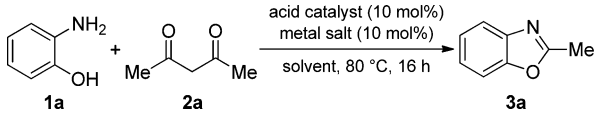


The development of convenient and efficient methods for the synthesis of benzoxazoles is attracting considerable attention. Benzoxazoles are used as versatile and key synthetic intermediates for the preparation of several natural products[1] and bioactive compounds.[2] Regarding the synthesis of these compounds, different approaches have been reported in past years, which include the condensation reactions of 2-aminophenols with either carboxylic acids/derivatives[3] or aldehydes[4] under strong oxidative conditions, the intramolecular cyclization of 2-haloanilides/analogues[5] or 2-hydroxyanilides,[6] and others.[7] These methods are undoubtedly effective but suffer from drawbacks such as requiring microwave radiation, high-temperature conditions, special catalysts, use of a molar equivalent or excess amount of an additive, or expensive and/or noncommercially available starting materials. Thus, the development of novel methods under mild reaction conditions is necessary.

Recently, the cyclization reactions of β-diketones with 2-aminothiophenols/2-aminoanilines to furnish benzothiazoles and benzimidazoles have been reported by our group.[8] This reaction smoothly proceeds in the presence of Brønsted acid under solvent-free conditions or in acetonitrile (CH_3CN) under oxidant-, transition-metal-, and radiation-free conditions. This success in achieving cyclization reactions of 2-aminothiophenols/2-aminoanilines with β-diketones encouraged us to examine the cyclization reactions of 2-aminophenols with β-diketones under similar reaction conditions. This paper reports the cyclization reactions of 2-aminophenols with β-diketones occurring in the presence of *p*-toluene sulfonic acid (TsOH·H_2O) and copper iodide (CuI) to produce benzoxazoles.

The reaction conditions were screened by using 2-aminophenol (**1a**) and 2,4-pentanedione (**2a**) as starting materials, and the results are summarized in Table 1. The reaction of **1a** with **2a** was initially performed under the same reaction conditions as those in the reactions of 2-aminothiophenols/2-aminoanilines with **2a** (in CH_3CN in the presence of TsOH·H_2O at 80 °C for 16 h).[8] The desired product, 2-methylbenzoxazole (**3a**), was produced with only 45% yield (entry 1). This yield of **3a** cannot be significantly increased even after increasing the acid catalyst loading 2-fold (entry 2, 47% yield). We then tried different salts of copper, iron, and

Table 1. Screening of Reaction Conditions[a]



1a 2a 3a

entry	Acid catalyst	Cu catalyst	solvent	yield (%)[b]
1	TsOH·H_2O	none	CH_3CN	45
2	TsOH·H_2O	none	CH_3CN	47[c]
3	TsOH·H_2O	CuCl	CH_3CN	63
4	TsOH·H_2O	CuBr	CH_3CN	77
5	TsOH·H_2O	CuI	CH_3CN	82
6	TsOH·H_2O	$Cu(OAc)_2$	CH_3CN	trace
7	TsOH·H_2O	$Cu(OTf)_2$	CH_3CN	61
8	TsOH·H_2O	$FeCl_3·6H_2O$	CH_3CN	52
9	TsOH·H_2O	$Fe(NO_3)_3·9H_2O$	CH_3CN	50
10	TsOH·H_2O	$NiCl_2·6H_2O$	CH_3CN	60
11	PhCOOH	CuI	CH_3CN	trace
12	CH_3COOH	CuI	CH_3CN	trace
13	DCSA	CuI	CH_3CN	53
14	HCl	CuI	CH_3CN	trace
15	TsOH·H_2O	CuI	EtOH	trace
16	TsOH·H_2O	CuI	dioxane	trace
17	TsOH·H_2O	CuI	THF	trace
18	TsOH·H_2O	CuI	DCE	74
19	none	CuI	CH_3CN	NR[d]

[a]Reaction conditions: 2-aminophenol (**1a**, 0.5 mmol), 2,4-pentanedione (**2a**, 0.75 mmol), acid catalyst (10 mol %), metal salt (10 mol %) in a solvent (4.0 mL) at 80 °C for 16 h in a sealed reactor. [b]Isolated yield. [c]With 20 mol % of acid catalyst TsOH·H_2O. [d]No reaction.

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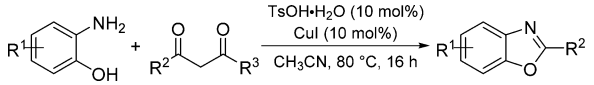
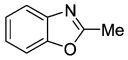
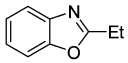
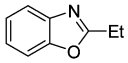
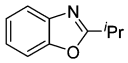
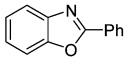
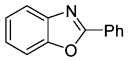
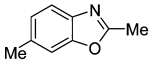
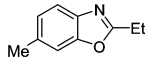
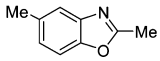
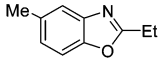
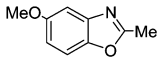
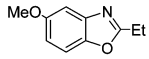
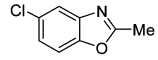
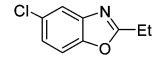
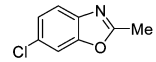
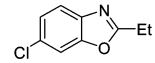
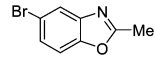
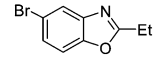
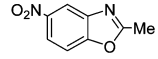
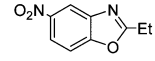
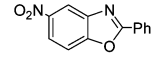
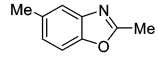
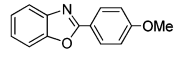
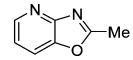
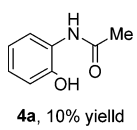
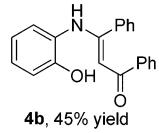
Table 2. Synthesis of Benzoxazoles from 2-Aminophenols and β-Diketones[a]

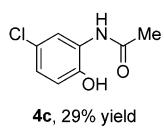


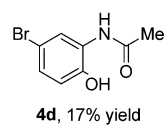
entry	substrate 1	substrate 2	product 3		yield (%)[b]
1	**1a** R^1 = H	**2a** $R^2 = R^3$ = Me		**3a**	82[c]
2	**1a**	**2b** $R^2 = R^3$ = Et		**3b**	56
3	**1a**	**2b**		**3b**	76[d]
4	**1a**	**2c** $R^2 = R^3$ = ^{i}Pr		**3c**	25[d]
5	**1a**	**2d** $R^2 = R^3$ = Ph		**3d**	0[e]
6	**1a**	**2d**		**3d**	49[f]
7	**1b** R^1 = 5-Me	**2a**		**3e**	74
8	**1b**	**2b**		**3f**	70[d]
9	**1c** R^1 = 4-Me	**2a**		**3g**	78
10	**1c**	**2b**		**3h**	72[d]
11	**1d** R^1 = 4-OMe	**2a**		**3i**	75
12	**1d**	**2b**		**3j**	73
13	**1e** R^1 = 4-Cl	**2a**		**3k**	67[g]
14	**1e**	**2b**		**3l**	69[d]
15	**1f** R^1 = 5-Cl	**2a**		**3m**	89
16	**1f**	**2b**		**3n**	66[d]
17	**1g** R^1 = 4-Br	**2a**		**3o**	80[h]
18	**1g**	**2b**		**3p**	73[d]
19	**1h** R^1 = 4-NO_2	**2a**		**3q**	65
20	**1h**	**2b**		**3r**	64[d]
21	**1h**	**2d** $R^2 = R^3$ = Ph		**3s**	40[f]
22	**1c**	**2e** R^2 = Me R^3 = Ph		**3g**	70
23	**1a**	**2f** R^2= 4-OMeC$_6$H$_4$ R^3 = Ph		**3t**	15[f,i]
24	**1i**	**2a**		**3u**	59[f]

[a]Reaction conditions: 2-aminophenols (**1**, 0.5 mmol), β-diketone (**2**, 0.75 mmol), TsOH·H_2O (10 mol %, 9.51 mg), and CuI (10 mol %, 9.50 mg) in CH_3CN (4 mL) at 80 °C for 16 h. [b]Isolated yield. [c]Byproduct **4a** was also separated. [d]The reaction was carried out in a sealed reactor at 100 °C. [e]Only intermediate **4b** was isolated. [f]Toluene was used as a solvent instead of acetonitrile; the reaction was carried out in a sealed reactor at 130 °C. [g]Byproduct **4c** was also separated. [h]Byproduct **4d** was also separated. [i]Benzoxazole **3d** was also separated in 31% yield as a major product.


4a, 10% yielld


4b, 45% yield


4c, 29% yield


4d, 17% yield

nickel as a cocatalyst in the presence of TsOH·H_2O to increase the product yield (entries 3−10). Among the salts tested, CuI was found to be the most suitable cocatalyst (entry 5, 82% yield). Different acids such as benzoic acid (PhCOOH), acetic acid (CH_3COOH), D-camphor-10-sulfonic acid (DCSA), and hydrochloric acid (HCl) with CuI did not further improve the product yield (entries 11−14). Finally, we screened different solvents using TsOH·H_2O and CuI as catalysts (entries 15−18). Results showed that the use of ethanol (EtOH), 1,4-dioxane, and tetrahydrofuran (THF) as solvent failed to produce the desired product **3a**. However, **3a** was obtained in 74% yield when 1,2-dichloroethane (DCE) was used as solvent. No reaction was observed in the absence of the acid catalyst TsOH·H_2O (entry 19). Therefore, under the optimum conditions (TsOH·H_2O and CuI as catalysts in CH_3CN at 80 °C for 16 h), the scope of the reaction was explored using various 2-aminophenols and β-diketones. The results are summarized in Table 2.

A relatively low yield (56%) was obtained when the reaction of **1a** with 3,5-heptanedione (**2b**) was carried out under

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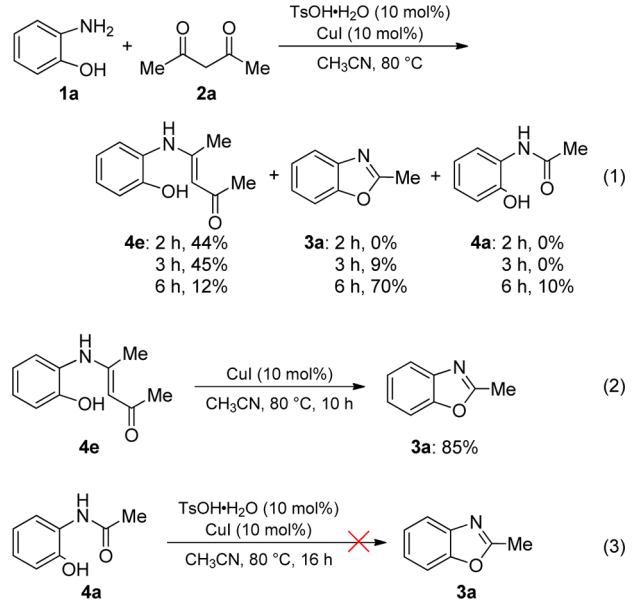
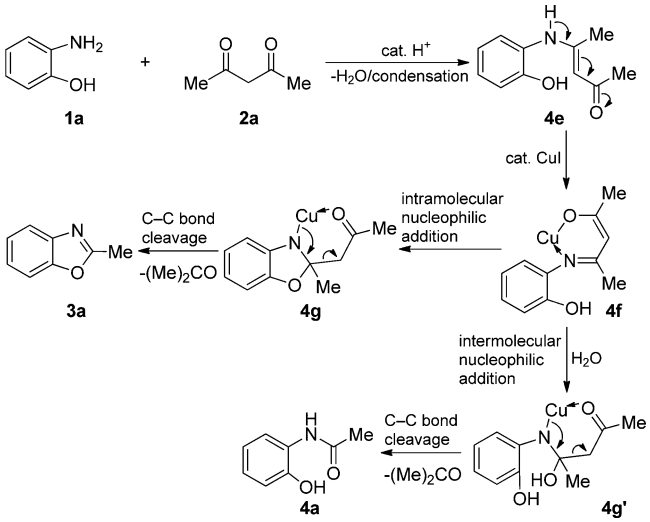
optimized conditions (Table 2, entry 2). However, a good yield similar to that of **3a** was obtained when the reaction was performed at 100 °C in a sealed reactor (entry 1 vs 3; **3a**, 82%; **3b**, 76%). The treatment of **1a** with 2,6-dimethylheptane-3,5-dione (**2c**) furnished the desired product 2-isopropylbenzo-[*d*]oxazole (**3c**) in low yield even at 100 °C, which may potentially be due to steric hindrance of bulky **2c** (entry 4, 25% yield). When **1a** was treated with 1,3-diphenylpropane-1,3-dione (**2d**) in CH_3CN at 80 °C, an intermediate (*E*)-3-(2-hydroxyphenylamino)-1,3-diphenylprop-2-en-1-one (**4b**) was separated in 45% yield as a sole product (entry 5). However, the desired product 2-phenylbenzoxazole (**3d**) was finally produced in relatively low yield when the reaction was performed at high temperature (130 °C) using toluene as a solvent (entry 6, 49% yield). The reactions of 5-methyl-2-aminophenol (**1b**), 4-methyl-2-aminophenol (**1c**), 4-methoxy-2-aminophenol (**1d**), 4-chloro-2-aminophenol (**1e**), 5-chloro-2-aminophenol (**1f**), 4-bromo-2-aminophenol (**1g**), and 4-nitro-2-aminophenol (**1h**) with *β*-diketones **2a** and **2b** smoothly proceeded to give benzoxazole products **3e**−**3r** in 64 to 89% yields (entries 7−20). From these results, it is concluded that the different substituent (either electron-donating group or electron-withdrawing group) on 2-aminophenol has almost insignificant effect on the reaction yield. The low yield of product 5-nitro-2-phenylbenzo[*d*]oxazole (**3s**) demonstrated again that **2d** is less reactive (entry 21). To evaluate the reactivity of acetyl and benzoyl groups, an asymmetric *β*-diketone, 1-methyl-3-phenyl-1,3-dione (**2e**), was examined with **1c**. The benzoxazole product **3g** was produced in 70% yield (entry 22). This result reinforced our previous evaluation that the reactivity of acetyl group is better than that of the benzoyl group.[8] We also tried the reaction of asymmetric diaryl *β*-diketone, 1-(4-methoxyphenyl)-3-phenylpropane-1,3-dione (**2f**), with **1a** (entry 23). Two products, 2-(4-methoxyphenyl)-benzo[*d*]oxazole (**3t**) and **3d**, were separated in 15 and 31% yields, respectively. Finally, we tried the reaction of 2-aminopyridin-3-ol (**1i**) with **2a** but failed to produce the desired product 2-methyloxazolo[4,5-*b*]pyridine (**3t**) under optimized reaction conditions. However, **3t** was produced in 59% yield at a high temperature (entry 24, 130 °C). During the course of our experiments, we also observed the byproducts *N*-(2-hydroxyphenyl)acetamide (**4a**, 10% yield), *N*-(5-chloro-2-hydroxyphenyl)acetamide (**4c**, 29% yield), and *N*-(5-bromo-2-hydroxyphenyl)acetamide (**4d**, 17% yield) when **1a**, **1e**, and **1g** were treated with **2a**, respectively.

To explore the reaction mechanism, we conducted controlled experiments under the optimized reaction conditions (Scheme 1). Reaction of **1a** with **2a** over a period of 2 h generated intermediate **4e** nearly exclusively (44% isolated yield); however, desired product **3a**, along with byproduct **4a** and intermediate **4e**, could be obtained after 6 h of heating (70, 10, and 12%, respectively, Scheme 1). The intermediate **4e** could be transformed to final product **3a** under optimized conditions in the absence of acid catalyst $TsOH{\cdot}H_2O$ (eq 2). With the findings presented in Table 1 (entry 19), we found that the Lewis acid catalyst CuI worked in the cyclization step. Finally, we tried to convert **4a** into **3a** under optimized conditions, but no reaction was observed (eq 3). Based on these observations, a possible mechanism is illustrated in Scheme 2. The condensation reaction of **1a** with **2a** in the presence of Brønsted acid would occur to generate an intermediate **4e**. Intermediate **4f** would be generated in the presence of CuI, and then the intramolecular nucleophilic addition of **4f** would take

Scheme 1. Control Experiments



Scheme 2. Possible Reaction Mechanism



place to produce adduct **4g**. Finally, C−C bond cleavage would occur to generate the product **3a**. In addition, the intermolecular nucleophilic addition of **4f** with H_2O generated in the condensation reaction step would produce an adduct **4g′**. Byproduct **4a** would finally generate through C−C bond cleavage.

In summary, a novel and general method for the synthesis of benzoxazoles was developed using simple and readily available starting materials as well as a combined catalyst of Brønsted acid and copper iodide. The wide availability of the starting materials, mild reaction conditions, and experimental simplicity should make the present methodology useful in organic synthesis.

EXPERIMENTAL SECTION

General Methods. Solvents were dried and degassed before use by standard procedures. NMR spectra were run in $CDCl_3$ or DMSO-d_6 on a 400 MHz instrument and recorded at the following frequencies: proton (^{1}H, 400 MHz), carbon (^{13}C, 100 MHz). The starting materials **1a**−**1i** and **2a**−**2f** are commercially available.

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Representative Procedure for the Synthesis of Benzoxazoles. An oven-dried reaction tube (25 mL) with a magnetic stir bar was charged with $Ts(OH)\cdot H_2O$ (9.51 mg, 0.1 mmol), CuI (9.50 mg, 0.1 mmol), 2-aminophenol (**1a**, 54.53 mg, 0.5 mmol), 2,4-pentanedione (**2a**, 75.0 mg, 0.75 mmol), and CH_3CN (4 mL). The reaction mixture was sealed and stirred at 80 °C for 16 h. The solvent was removed under reduced pressure, and the residue obtained was purified via silica gel chromatography (eluent: ethyl acetate/petroleum ether = 1:5) to afford 2-methylbenzo[*d*]oxazole (**3a**) as a colorless oil (54.7 mg, 82% yield).

2-Methylbenzo[*d*]oxazole (3a):[5b] Yield 82%, 54.7 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.27−7.29 (m, 2H), 7.45−7.47 (m, 1H), 7.64−7.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 110.4, 119.6, 124.3, 124.6, 141.7, 151.2, 164.0.

2-Ethylbenzo[*d*]oxazole (3b):[5b] Yield 76%, 56.0 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (t, J = 7.6 Hz, 3H), 2.97 (q, J = 7.6 Hz, 2H), 7.29−7.31 (m, 2H), 7.47−7.50 (m, 1H), 7.68−7.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 22.2, 110.2, 119.5, 124.0, 124.4, 141.4, 150.8, 168.1.

2-Isopropylbenzo[*d*]oxazole (3c):[5b] Yield 25%, 20.0 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 7.0 Hz, 6H) 3.22−3.29 (m, 1H), 7.29−7.31 (m, 2H), 7.47−7.50 (m, 1H), 7.68−7.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 29.2, 110.2, 119.9, 124.3, 124.7, 141.5, 151.0, 171.6.

2-Phenylbenzo[*d*]oxazole (3d):[9] Yield 49%, 48.0 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.38 (m, 2H), 7.52−7.60 (m, 4H), 7.77−7.79 (m, 1H), 8.25−8.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 110.8, 120.1, 124.7, 125.3, 127.3, 127.7, 129.1, 131.7, 142.2, 150.9, 163.2.

2,6-Dimethylbenzo[*d*]oxazole (3e):[9] Yield 74%, 54.7 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 2.62 (s, 3H), 7.11 (d, J = 8.0 Hz, 1H), 7.27 (s, 1H), 7.52 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 21.6, 110.3, 118.6, 125.1, 134.6, 139.2, 151.2, 163.2.

2-Ethyl-6-methylbenzo[*d*]oxazole (3f): Yield 70%, 56.4 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, J = 7.6 Hz, 3H), 2.45 (s, 3H), 2.92 (q, J = 7.6 Hz, 2H), 7.09 (d, J = 8.0 Hz, 1H), 7.26 (s, 1H) 7.52 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.2, 21.9, 22.4, 110.7, 119.1, 125.4, 134.9, 139.4, 151.3, 167.8; IR (neat) 3384, 2959, 2924, 1730, 1575, 1454, 1259, 1117, 1072, 1037, 923, 811 cm^{-1}; HRMS (ES) calcd for $C_{10}H_{11}NONa$ 184.0738 $[M + Na]^+$; found 184.0734.

2,5-Dimethylbenzo[*d*]oxazole (3g):[9] Yield 78%, 57.5 mg, light yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.62 (s, 3H), 7.09 (d, J = 8.3 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.2, 16.1, 104.2, 114.0, 120.1, 128.5, 136.4, 143.9, 158.6.

2-Ethyl-5-methylbenzo[*d*]oxazole (3h):[10] Yield 72%, 58.1 mg, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, J = 7.6 Hz, 3H), 2.44 (s, 3H), 2.93 (q, J = 7.6 Hz, 2H), 7.08 (d, J = 8.2 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 7.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 21.5, 22.2, 109.6, 119.5, 125.4, 133.8, 141.6, 149.1, 168.2.

5-Methoxy-2-methylbenzo[*d*]oxazole (3i):[9] Yield 75%, 61.3 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.59 (s, 3H), 3.82 (s, 3H), 6.86 (dd, J = 8.8, 2.3 Hz, 1H), 7.13 (d, J = 2.3 Hz, 1H), 7.32 (dd, J = 8.8, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 55.9, 102.7, 110.2, 112.6, 142.4, 145.6, 157.0, 164.6.

2-Ethyl-5-methoxybenzo[*d*]oxazole (3j): Yield 73%, 64.4 mg, yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, J = 7.6 Hz, 3H), 2.92 (q, J = 7.6 Hz, 2H), 3.83 (s, 3H), 6.87 (dd, J = 8.8, 2.4 Hz, 1H), 7.17 (d, J = 2.2 Hz, 1H), 7.33 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 22.2, 55.9, 102.8, 110.3, 112.6, 142.2, 145.5, 157.0, 169.0; IR (neat) 2941, 1573, 1483, 1441, 1285, 1196, 1152, 1028, 839, 804 cm^{-1}; HRMS (ES) calcd for $C_{10}H_{12}NO_2$ 178.0868 $[M + H]^+$; found 178.0865.

5-Chloro-2-methylbenzo[*d*]oxazole (3k):[9] Yield 67%, 56.3 mg, off white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.25 (d, J = 8.6 Hz, 1H), 7.37 (d, J = 8.6 Hz, 1H), 7.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 111.0, 119.5, 124.8, 129.6, 142.7, 149.6, 165.4.

5-Chloro-2-ethylbenzo[*d*]oxazole (3l):[10] Yield 69%, 62.6 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, J = 7.5 Hz, 3H), 2.95 (q, J = 7.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 7.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 22.3, 111.1, 119.7, 124.8, 129.6, 142.6, 149.5, 169.7.

6-Chloro-2-methylbenzo[*d*]oxazole (3m):[11] Yield 89%, 74.4 mg, off white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.27 (d, J = 8.4 Hz, 1H), 7.47 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 111.0, 120.0, 124.9, 130.2, 140.4, 151.3, 164.7.

6-Chloro-2-ethylbenzo[*d*]oxazole (3n): Yield 66%, 59.5 mg, off white solid, mp 40−42 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (t, J = 7.5 Hz, 3H), 2.94 (q, J = 7.5 Hz, 2H), 7.28 (dd, J = 7.8, 1.4 Hz, 1H), 7.50 (s, 1H), 7.58 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 22.3, 111.1, 120.2, 124.8, 130.2, 140.4, 151.4, 169.8; IR (KBr) 3104, 2983, 1618, 1576, 1451, 1226, 1153, 924, 859, 828, 733 cm^{-1}; HRMS (EI) calcd for C_9H_8NOCl 181.0294 $[M]^+$; found 181.0288.

5-Bromo-2-methylbenzo[*d*]oxazole (3o):[9] Yield 80%, 84.0 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.33(d, J = 8.6 Hz, 1H), 7.39 (d, J = 8.6 Hz, 1H), 7.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 111.5, 116.9, 122.5, 127.5, 143.2, 150.0, 165.2.

5-Bromo-2-ethylbenzo[*d*]oxazole (3p): Yield 73%, 82.2 mg, off white solid, mp 52−54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, J = 7.6 Hz, 3H), 2.95 (q, J = 7.6 Hz, 2H), 7.33 (d, J = 8.6 Hz, 1H), 7.39 (d, J = 8.5 Hz, 1H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.9, 22.2, 111.5, 116.8, 122.6, 127.5, 143.1, 149.9, 169.4; IR (KBr) 3097, 2984, 1731, 1610, 1567, 1463, 1365, 1223, 1152, 929, 810 cm^{-1}; HRMS (EI) calcd for C_9H_8NOBr 224.9789, 226.9769; found 224.9795, 226.9770.

2-Methyl-5-nitrobenzo[*d*]oxazole (3q):[10] Yield 65%, 58.0 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 (s, 3H), 7.58 (d, J = 8.9 Hz, 1H), 8.27 (dd, J = 8.9, 2.2 Hz, 1H), 8.54 (d, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 110.6, 116.0, 120.9, 142.1, 145.3, 154.7, 167.3.

2-Ethyl-5-nitrobenzo[*d*]oxazole (3r):[10] Yield 64%, 61.1 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (t, J = 7.6 Hz, 3H), 3.03 (q, J = 7.6 Hz, 2H), 7.58 (d, J = 8.9 Hz, 1H), 8.27 (dd, J = 8.9, 2.2 Hz, 1H), 8.55 (d, J = 2.1 Hz, 1H).

5-Nitro-2-phenylbenzo[*d*]oxazole (3s):[5c] Yield 40%, 48.3 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.62 (m, 3H), 7.66 (d, J = 8.9 Hz, 1H), 8.25 (d, J = 7.8 Hz, 2H), 8.30 (d, J = 8.9 Hz, 1H), 8.62 (s, 1H).

2-(4-Methoxyphenyl)benzo[*d*]oxazole (3t):[5b] Yield 15%, 17 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (s, 3H), 7.03 (dd, J = 8.9, 2.7 Hz, 2H), 7.31−7.34 (m, 2H), 7.53−7.57 (m, 1H), 7.73−7.75 (m, 1H), 8.20 (dd, J = 8.9, 2.7 Hz, 2H).

2-Methyloxazolo[4,5-*b*]pyridine (3u):[12] Yield 59%, 39.4 mg, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 (s, 3H), 7.28 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 8.54 (s, 1H).

***N*-(2-Hydroxyphenyl)acetamide (4a):**[6a] Yield 10%, 7.6 mg, off white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.10 (s, 3H), 6.76 (dd, J = 7.5, 7.4 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 6.94 (dd, J = 7.6, 7.4 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 9.32 (s, 1H), 9.76 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.7, 115.9, 119.0, 122.4, 124.7, 126.5, 147.9, 169.0.

(*E*)-3-(2-Hydroxyphenylamino)-1,3-diphenylprop-2-en-1-one (4b): Yellowish solid, mp 146−148 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.14 (s, 1H), 6.31 (d, J = 8.0 Hz, 1H), 6.46 (dd, J = 7.2, 7.2 Hz, 1H), 6.86 (dd, J = 7.6, 7.2 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 7.42−7.55 (m, 8H), 8.01 (d, J = 7.2 Hz, 2H), 10.09 (s, 1H), 12.66 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 97.2, 116.5, 120.0, 125.3, 125.8, 128.0, 129.0, 129.1, 129.3, 130.4, 132.0, 137.1, 150.4, 162.3, 189.4. IR (KBr) 3376, 3154, 1587, 1479, 1343, 1285, 1222, 1096, 942, 851, 753, 695 cm-^{1}; HRMS (ES) calcd for $C_{21}H_{18}NO_2$ 316.1338 $[M + H]^+$; found 316.1337; for $C_{21}H_{17}NO_2Na$ 338.1157 $[M + Na]^+$; found 338.1153.

***N*-(5-Chloro-2-hydroxyphenyl)acetamide (4c):**[6a] Yield 29%, 26.9 mg, off white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.11 (s, 3H), 6.86 (d, J = 8.6 Hz, 1H), 6.96 (dd, J = 2.2, 8.6 Hz, 1H), 7.96 (d, J

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= 2.1 Hz, 1H), 9.30 (s, 1H), 10.17 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.8, 116.3, 121.0, 122.1, 123.5, 127.8, 146.3, 169.1.

***N*-(5-Bromo-2-hydroxyphenyl)acetamide (4d):**[13] Yield 17%, 19.4 mg, off white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.11 (s, 3H), 6.82 (d, J = 8.6 Hz, 1H), 7.07 (dd, J = 8.6, 2.3 Hz, 1H), 8.08 (d, J = 2.1 Hz, 1H), 9.29 (s, 1H), 10.19 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 23.8, 109.6, 116.9, 123.8, 126.4, 128.2, 146.7, 169.1.

(*E*)-4-((2-Hydroxyphenyl)amino)pent-3-en-2-one (4e): Yellowish solid, mp 188−190 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.961 (s, 3H), 1.964 (s, 3H), 5.20 (s, 1H), 6.78 (dd, J = 7.4, 7.8 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 7.01 (dd, J = 7.4, 7.7 Hz, 1H), 7.16 (d, J = 7.8 Hz, 1H), 9.92 (s, 1H), 12.14 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.6, 29.0, 97.3, 115.8, 119.1, 125.0, 126.1, 150.3, 160.0, 194.3. IR (KBr) 3433, 2724, 2602, 1606, 1551, 1459, 1315, 1240, 1175, 1027, 929, 837, 750 cm^{-1}; HRMS (ES) calcd for $C_{11}H_{14}NO_2$ 192.1025 $[M + H]^+$; found 192.1024l for $C_{11}H_{13}NO_2Na$ 214.0844 $[M + Na]^+$; found 214.0840. The structure of **4e** was also confirmed through NOE determination (see Supporting Information).

■ ASSOCIATED CONTENT

Supporting Information

Characterization of compounds, including copies of ^{1}H and ^{13}C NMR spectra. 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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