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Palladium-Catalyzed Oxidative O−H/N−H Carbonylation of Hydrazides: Access to Substituted 1,3,4-Oxadiazole-2(3*H*)-ones

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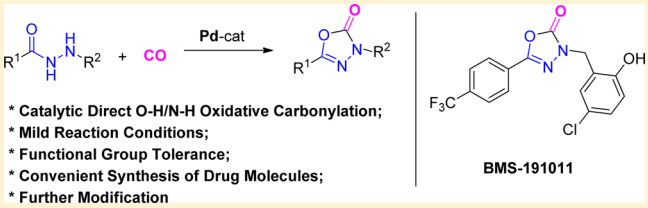
Supporting Information

ABSTRACT: A novel palladium-catalyzed oxidative annulation reaction for the C−O, C−N bond formations is developed. The intramolecular cyclocarbonylation provides an efficient and direct approach for the construction of valuable 1,3,4-oxadiazole-2(3*H*)-ones and their derivatives. The reaction also facilitated the convenient synthesis of BMS-191011, an opener of the cloned large-conductance Ca^{2+}-activated potassium channel, providing an attractive method for medicinal chemistry.



INTRODUCTION

1,3,4-Oxadiazole core is a popular bioisostere for improving the pharmacological profile of biologically active amides, esters, and ureas.[1] Compounds bearing 1,3,4-oxadiazole skeleton have been found to exhibit a wide spectrum of biological activities such as anti-HCV and antitumor agents (**1**),[2] $GABA_A$ receptor agonists (**2**),[3] BMS-191011: opener of large-conductance Ca^{2+}-activated potassium (Maxi-K) channels (**3**),[4] and fungicides (**4**)[5] (Figure 1). This heterocycle is a privileged scaffold in

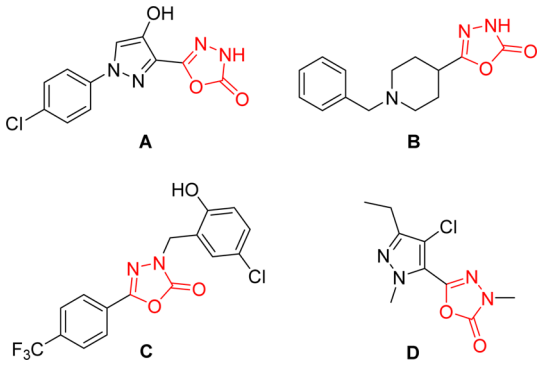
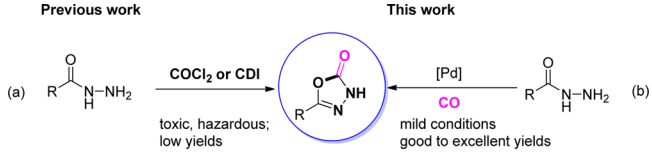


Figure 1. Structures of pharmacologically important substituted 1,3,4-oxadiazole-2(3*H*)-ones.

medicinal chemistry. The representative methods for the synthesis of substituted 1,3,4-oxadiazole-2(3*H*)-ones have been reported in the literature.[6] Although these procedures are useful for the construction of 1,3,4-oxadiazole cores, most of them still suffer from some limitations such as the use of toxic and hazardous reagents,[6c] harmful organic solvents, and laborious reaction procedures with unsatisfactory yields (Scheme 1a).[6b,d] Therefore, the development of a simple, efficient, and atom-economical method to access structurally diverse 1,3,4-oxadiazoles remains highly desirable.

Scheme 1. Selected Synthetic Methods for 1,3,4-Oxadiazole Cores



Oxidative carbonylation reactions have continued to be an important strategy for the construction of carbocyclic and heterocyclic compounds.[7] Enormous efforts have gone into the synthesis of heterocyclic framework through the oxidative carbonylation. Carbon monoxide (CO) as carbon-atom source holds the synthetic advantages of inexpensive and readily available nature.[8] Heterocyclic compounds are highly important in different research fields such as pharmaceutical chemistry and electroactive materials.[9] Considering the importance of both topics, herein, we report our recent effort on palladium-catalyzed oxidative carbonylation of hydrazines, whereby a sequential CO insertion into the N−H and O−H bonds occurs to form substituted 1,3,4-oxadiazole-2(3*H*)-ones (Scheme 1b).

RESULTS AND DISCUSSION

To explore this approach, initial studies were focused on using benzohydrazide (**1a**) as a model substrate (Table 1). Treatment of **1a** using 5 mol % of $Pd(OAc)_2$ as catalyst in DMSO under CO/O_2 atmosphere and TFA as an additive at 60 °C afforded the desired product 5-phenyl-1,3,4-oxadiazol-2(3*H*)-one (**2a**) in only 36% yield (Table 1, entry 1). Intriguingly, the use of $Pd(TFA)_2$ as a catalyst gave a further improvement in the yield of **2a**, while other catalysts were ineffective for this transformation (entries 2, 3, and 5).

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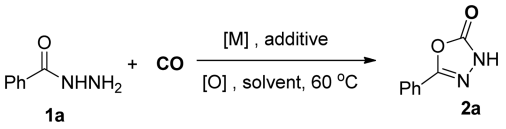
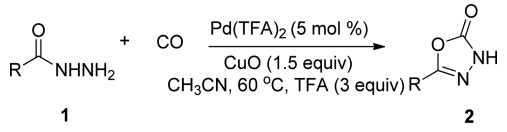
Table 1. Optimization of the Reaction Conditions[a]

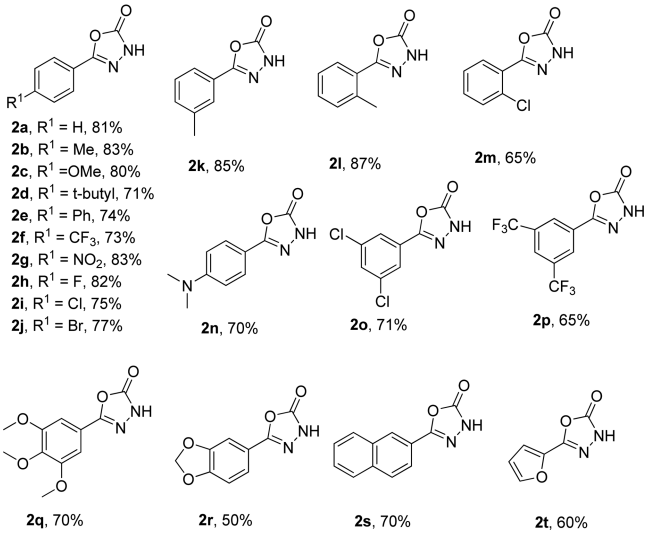


entry	[M]	[O]	additive	solvent	yield (%)[b]
1	$Pd(OAc)_2$	O_2	TFA	DMSO	36
2	$PdCl_2$	O_2	TFA	DMSO	trace
3	PdI_2	O_2	TFA	DMSO	trace
4	$Pd(TFA)_2$	O_2	TFA	DMSO	41
5	$PdBr_2$	O_2	TFA	DMSO	trace
6	$Pd(TFA)_2$	O_2	_	DMSO	23
7	$Pd(TFA)_2$	O_2	LiBr	DMSO	5
8	$Pd(TFA)_2$	O_2	PivOH	DMSO	11
9	$Pd(TFA)_2$	BQ	TFA	DMSO	trace
10	$Pd(TFA)_2$	MnO_2	TFA	DMSO	27
11	$Pd(TFA)_2$	$Cu(OAc)_2$	TFA	DMSO	trace
12	$Pd(TFA)_2$	Ag_2CO_3	TFA	DMSO	trace
13	$Pd(TFA)_2$	$K_2S_2O_8$	TFA	DMSO	trace
14	$Pd(TFA)_2$	CuO	TFA	DMSO	75
15	$Pd(TFA)_2$	CuO	TFA	toluene	n.d.
16	$Pd(TFA)_2$	CuO	TFA	THF	trace
17	$Pd(TFA)_2$	CuO	TFA	DMF	59
18	$Pd(TFA)_2$	CuO	TFA	CH_3CN	81
19	_	CuO	TFA	CH_3CN	n.d.

[a]Reaction conditions: unless otherwise noted, all reactions were performed with **1** (0.2 mmol), catalyst (5 mol %), oxidant (1.5 equiv), additive (0.6 mmol) at 60 °C for 12 h, CO (1 balloon). [b]Isolated yield.

Table 2. Pd-Catalyzed Synthesis of Substitued 1,3,4-Oxadiazole-2(3*H*)-ones[a]





[a]The reactions were carried out at 60 °C, using **1** (0.2 mmol), CuO (0.3 mmol), TFA (0.6 mmol), CO (1 balloon), $Pd(TFA)_2$ (5 mol %) in CH_3CN (2 mL) at 60 °C for 12 h. Yields refer to isolated yield.

Furthermore, the additive was found to be vital to the catalytic system, and the yield was decreased to 23% without the use of TFA (entry 6). Other additives such as LiBr or PivOH just gave low yield (entries 7 and 8). By switching different oxidants, CuO resulted in a decent boost in the yield of **2a** (entry 14); other oxidants such as BQ, $Cu(OAc)_2$, Ag_2CO_3, and $K_2S_2O_8$ turned out to be unfavorable in the system (entries 9−13). When CH_3CN was used as the reaction solvent, the yield was slightly increased (entry 18), while toluene, THF, and DMF all gave disappointing results (entries 15−17). In addition, no reaction could be observed in the absence of the Pd catalyst (entry 19).

Having identified our optimized reaction conditions, we next investigated the scope of the reaction, as illustrated in Table 2. The intramolecular cyclocarbonylation reaction displayed a good functional-group tolerance. Benzohydrazides bearing various substituents all gave the desired products in moderate to good yields regardless of their electronic properties (**2a−2g**). It is worth noting that the substrates with sensitive functional groups such as fluoro, chloro, and bromo groups all gave the corresponding products in high to excellent yields, which could be subjected to further functionalization (**2h−2j**). Treatment of substrates bearing different substitution positions also afforded the desired products in good yields (**2k−2m**). Di/trisubstituted-hydrazides all gave the targeted products in moderate yields (**2o−2q**). To our delight, substrates with naphthalene or heterocyclic ring were also tolerated in the system, which expanded the scope of this kind of reactions significantly (**2r−2t**). However, aliphatic hydrazide did not work in this reaction system.

To further demonstrate the efficiency and generality of this reaction system, we then explored the transformation of *N*-aryl substituted derivatives (Table 3). However, when *N*′-phenylbenzohydrazide (**3a**) was subjected to the standard reaction conditions, the corresponding product 3,5-diphenyl-1,3,4-oxadiazol-2(3*H*)-one (**4a**) was obtained in only 15% yield. After careful modification of the reaction conditions, we found that only the employment of Ag_2CO_3 as the oxidant at 60 °C for 6 h could provide the desired product **4a** in 62% yield, while other oxidants were inactive (see the Supporting Information for details). Under the optimized conditions, the carbonylation reaction proceeded smoothly to give the corresponding *N*-substituted 1,3,4-oxadiazoles in good yields (**4a−4h**). Various substituents at the aryl, such as methyl, methoxyl, and trimethyl were tolerated well, affording the corresponding products in good to excellent yields (**4a−4e**). It is noteworthy that halide substituents (**4f−4h**) could survive in the reaction system, which allowed further functionalization such as metal-catalyzed cross-coupling reactions.

The ready access to the N-substituted 1,3,4-oxadiazole-2(3*H*)-ones through this chemistry offers a novel strategy for many biologically active compounds. Noteworthy, it is found that the well-known maxi-K opener could be synthesized from the newly formed **2f**. After methylation, Mitsunobu reaction, and deprotection, compound **2f** was successfully converted to the corresponding BMS-191011 in 78% yield (Scheme 2). Therefore, this reaction system could be potentially used in drug discovery for the preparation of BMS-191011.[4,10]

A plausible reaction mechanism is proposed for the construction of substituted-1,3,4-oxadiazole-2(3*H*)-ones as shown in Scheme 3.[11] The intermediate **A** is first formed by N−H activation of **1**. Subsequently, the coordination of carbonyl group with Pd complex affords a five-membered palladacycle **B**, which further reacts with CO to form intermediate **C**. Finally, reductive elimination of **C** gives the

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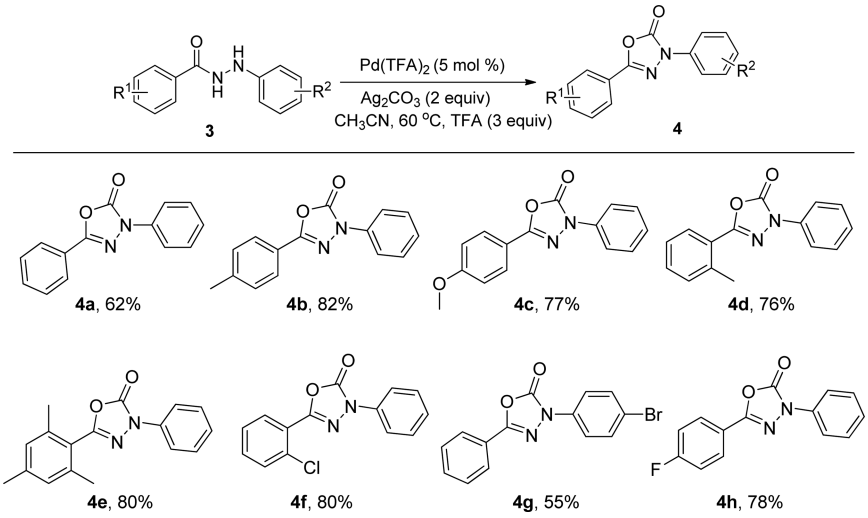
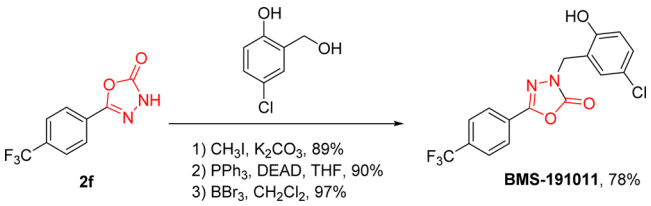
Table 3. Synthesis of *N*-Substituted 1,3,4-Oxadiazoles.[a]

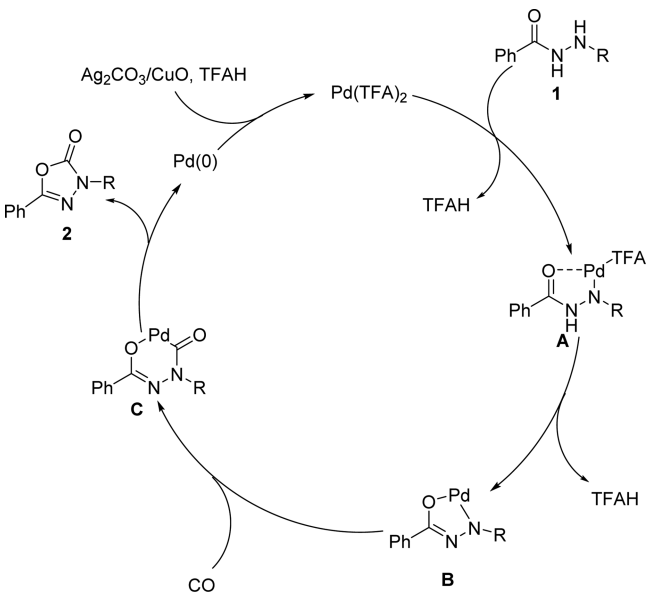


[a]The reactions were carried out at 60 °C, using **1** (0.2 mmol), Ag_2CO_3 (0.3 mmol), TFA (0.6 mmol), CO (1 balloon), $Pd(TFA)_2$ (5 mol %) in CH_3CN (2 mL) at 60 °C for 12 h. Yields refer to isolated yield.

Scheme 2. Preparation for BMS-191011



Scheme 3. Proposed Mechanism



desired carbonylation product **2** and Pd(0) is then reoxidized by CuO or Ag_2CO_3 to regenerate the Pd(II) species.

CONCLUSION

In conclusion, we have developed the first palladium-catalyzed O−H/N−H carbonylation for the synthesis of various 1,3,4-oxadiazoles. The reaction starts from commercially available hydrazides and proceeds under mild reaction conditions. This novel palladium-catalyzed carbonylation reaction features a broad substrates scope and excellent functional-group tolerance. Notably, this protocol provides a useful tool for the convenient synthesis of BMS-191011.

EXPERIMENTAL SECTION

General Information. Melting points were measured with a melting point instrument and were uncorrected. ^1H and ^{13}C NMR spectra were recorded using a 400 MHz NMR spectrometer. The chemical shifts are referenced to signals at 7.24 and 77.0 ppm, respectively, and chloroform is solvent with TMS as the internal standard. IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a spectrometer. GC−MS was obtained using electron ionization. HRMS was obtained with a LCMS-IT-TOF mass spectrometer. TLC was performed by using commercially prepared 100−400 mesh silica gel plates and visualization was effected at 254 nm.

Typical Experimental Procedure for Synthesis of 2a−2t. The mixture of **1** (0.2 mmol), CuO (0.3 mmol), $Pd(TFA)_2$ (5 mol %), and TFA (0.6 mmol) was stirred in CH_3CN (2.0 mL) at 60 °C, in a 20 mL tube with a balloon CO for 12 h. When the reaction was complete (detected by TLC), the mixture was cooled to room temperature. The residue was purified by column chromatography on silica gel to afford the corresponding products **2** with petroleum ether/ethyl acetate as the eluent.

Typical Experimental Procedure for Synthesis of 4a−4h. The mixture of **1** (0.2 mmol), Ag_2CO_3 (0.3 mmol), $Pd(TFA)_2$ (5 mol %), and TFA (0.6 mmol) was stirred in CH_3CN (2.0 mL) at 60 °C, in a 20 mL tube with a balloon CO for 12 h. When the reaction was complete (detected by TLC), the mixture was cooled to room temperature. The residue was purified by column chromatography on silica gel to afford the corresponding products **4** with petroleum ether/ethyl acetate as the eluent.

*5-Phenyl-1,3,4-oxadiazol-2(3H)-one (**2a**).* White solid (26 mg, 81%); mp: 137.2−138.6. IR (KBr): 3216, 1739, 1569, 1413, 687. ^1H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 7.86 (d, J = 7.6 Hz, 2H), 7.61−7.38 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 155.0, 131.8, 129.0, 125.8, 123.8; HRMS (ESI) m/z: calcd for $C_8H_6N_2NaO_2$ $[M + Na]^+$, 185.0321; found, 185.0322

5-(*p*-Tolyl)-1,3,4-oxadiazol-2(3*H*)-one (2b). White solid (29 mg, 83%); mp: 167.2−168.7. IR (KBr): 3207, 1791, 1613, 1568, 1412, 731. ^1H NMR (400 MHz, DMSO) δ 7.68 (d, J = 7.6 Hz, 2H), 7.35 (d, J = 7.6 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 154.5,

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153.9, 141.5, 129.7, 125.2, 121.2, 21.0; HRMS (ESI) m/z: calcd for $C_9H_8N_2NaO_2$ $[M + Na]^+$, 199.0478; found, 199.0481.

5-(4-Methoxyphenyl)-1,3,4-oxadiazol-2(3H)-one (**2c**). White solid (31 mg, 80%); mp: 192.1−193.6. IR (KBr): 3359, 1769, 1568, 1415, 1021, 757. ^{1}H NMR (400 MHz, DMSO) δ 12.41 (s, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 161.6, 154.5, 153.8, 127.0, 116.3, 114.7, 55.4; HRMS (ESI) m/z: calcd for $C_9H_8N_2NaO_3$ $[M + Na]^+$, 215.0427; found, 215.0429.

5-(4-(tert-Butyl)phenyl)-1,3,4-oxadiazol-2(3H)-one (**2d**). White solid (31 mg, 71%); mp: 134.2−135.8. IR (KBr): 3270, 2964, 1783, 1619, 1346, 923. ^{1}H NMR (400 MHz, DMSO) δ 7.72 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 7.8 Hz, 2H), 1.30 (s, 9H); ^{13}C NMR (101 MHz, DMSO) δ 154.5, 154.3, 153.9, 126.0, 125.1, 121.2, 34.7, 30.8; HRMS (ESI) m/z: calcd for $C_{12}H_{15}N_2O_2$ $[M + H]^+$, 219.1128; found, 219.1128.

5-([1,1′-Biphenyl]-4-yl)-1,3,4-oxadiazol-2(3H)-one (**2e**). White solid (35 mg, 74%); mp: 254.2−255.8. IR (KBr): 2922, 1572, 1410, 957, 768. ^{1}H NMR (400 MHz, DMSO) δ 8.08−7.82 (m, 4H), 7.75 (t, J = 7.4 Hz, 2H), 7.51 (t, J = 7.0 Hz, 2H), 7.43 (t, J = 7.0 Hz, 1H); ^{13}C NMR (101 MHz, DMSO) δ 154.5, 153.6, 142.8, 138.8, 129.1, 128.2, 127.4, 126.8, 125.8, 122.9;HRMS (ESI) m/z: calcd for $C_{14}H_{11}N_2O_2$ $[M + H]^+$, 239.0815; found, 239.0813.

5-(4-(Trifluoromethyl)phenyl)-1,3,4-oxadiazol-2(3H)-one (**2f**). White solid (34 mg, 73%); mp: 213.7−215.0. IR (KBr): 3420, 1571, 1415, 1322, 1128, 709. ^{1}H NMR (400 MHz, DMSO) δ 12.81 (s, 1H), 8.00 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.0 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.74, 153.14, 131.97, 131.65, 131.33, 131.01, 128.22, 128.02, 127.63, 127.45, 126.69, 126.66, 126.62, 126.58, 126.52, 125.57, 122.86; HRMS (ESI) m/z: calcd for $C_9H_5F_3N_2NaO_2$ $[M + Na]^+$, 253.0195; found, 253.0201.

5-(4-Nitrophenyl)-1,3,4-oxadiazol-2(3H)-one (**2g**).[12] White solid (34 mg, 83%); mp: 250.1−251.6. IR (KBr): 3441, 2923, 2384, 1647, 1516, 1338, 1268, 753. ^{1}H NMR (400 MHz, DMSO) δ 12.91 (s, 1H), 8.35 (d, J = 8.4 Hz, 2H), 8.02 (d, J = 8.4 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.2, 152.3, 148.7, 129.5, 126.5, 124.4; MS (EI) m/z 104.10, 133.13, 163.10, 177.09, 207.09.

5-(4-Fluorophenyl)-1,3,4-oxadiazol-2(3H)-one (**2h**). White solid (30 mg, 82%); mp: 169.9−171.7. IR (KBr): 3072, 1774, 1616, 1510, 1235, 1026, 841, 730, 698, 513. ^{1}H NMR (400 MHz, DMSO) δ 7.85 (dd, J = 7.2, 6.0 Hz, 2H), 7.39 (t, J = 8.6 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 164.9, 162.5, 154.4, 153.1, 127.9, 127.8, 120.6, 120.6, 116.5, 116.3; HRMS (ESI) m/z: calcd for $C_8H_5FN_2NaO_2$ $[M + Na]^+$, 203.0227; found, 203.0225

5-(4-Chlorophenyl)-1,3,4-oxadiazol-2(3H)-one (**2i**). White solid (29 mg, 75%); mp: 226.4−227.6. IR (KBr): 3449, 1840, 1652, 1563, 1411, 725. ^{1}H NMR (400 MHz, DMSO) δ 12.63 (s, 1H), 7.80 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.3, 153.0, 136.1, 129.4, 127.0, 122.8; HRMS (ESI) m/z: calcd for $C_8H_5ClN_2NaO_2$ $[M + Na]^+$, 218.9932; found, 218.9933.

5-(4-Bromophenyl)-1,3,4-oxadiazol-2(3H)-one (**2j**). White solid (37 mg, 77%); mp: 238.3−239.9. IR (KBr): 3449, 1568, 1412, 1018, 752. ^{1}H NMR (400 MHz, DMSO) δ 12.68 (s, 1H), 7.74 (q, J = 8.4 Hz, 4H); ^{13}C NMR (101 MHz, DMSO) δ 154.3, 153.1, 132.3, 127.2, 124.9, 123.2; HRMS (ESI) m/z: calcd for $C_8H_5BrN_2NaO_2$ $[M + Na]^+$, 262.9427; found, 262.9429.

5-(m-Tolyl)-1,3,4-oxadiazol-2(3H)-one (**2k**). White solid (30 mg, 85%); mp: 112.3−113.7. IR (KBr): 3219, 1762, 1583, 1326, 966, 708. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 7.65 (d, J = 9.6 Hz, 2H), 7.36−7.30 (m, 2H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 155.4, 138.9, 132.6, 128.9, 126.3, 123.7, 123.0, 21.3; HRMS (ESI) m/z: calcd for $C_9H_8N_2NaO_2$ $[M + Na]^+$, 199.0478; found, 199.0479.

5-(o-Tolyl)-1,3,4-oxadiazol-2(3H)-one (**2l**). White solid (31 mg, 87%); mp: 87.7−89.6. IR (KBr): 3115, 1775, 1733, 974, 727;.^{1}H NMR (400 MHz, DMSO) δ 7.71 (d, J = 7.6 Hz, 1H), 7.45 (t, J = 7.2 Hz, 1H), 7.42−7.26 (m, 2H), 2.53 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 154.3, 154.1, 136.8, 131.6, 130.9, 127.7, 126.3, 122.8, 21.3; HRMS (ESI) m/z: calcd for $C_9H_8N_2NaO_2$ $[M + Na]^+$, 199.0478; found, 199.0479

5-(2-Chlorophenyl)-1,3,4-oxadiazol-2(3H)-one (**2m**). White solid (25 mg, 65%); mp: 156.9−158.6. IR (KBr): 3746, 2926, 2381, 1645, 1270, 752. ^{1}H NMR (400 MHz, DMSO) δ 7.83 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H); ^{13}C NMR (101 MHz, DMSO) δ 154.3, 151.9, 132.7, 131.1, 131.1, 130.3, 127.7, 122.8; HRMS (ESI) m/z: calcd for $C_8H_5ClN_2NaO_2$ $[M + Na]^+$, 218.9932; found, 218.9932.

5-(4-(Dimethylamino)phenyl)-1,3,4-oxadiazol-2(3H)-one (**2n**). White solid (29 mg, 70%); mp: 231.4−233.3. IR (KBr): 2922, 1773, 1670, 1608, 1413, 1189, 1025, 826, 772. ^{1}H NMR (400 MHz, DMSO) δ 12.09 (s, 1H), 7.76 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.4 Hz, 2H), 2.99 (s, 6H); ^{13}C NMR (101 MHz, DMSO) δ 167.5, 153.4, 153.0, 130.9, 116.9, 110.7, 29.2; HRMS (ESI) m/z: calcd for $C_{10}H_{12}N_3O_2$ $[M + H]^+$, 206.0924; found, 206.0926.

5-(3,5-Dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one (**2o**).[13] White solid (33 mg, 71%); mp: 99.0−101.9. IR (KBr): 3076, 1807, 1590, 1340, 1102, 931, 717. ^{1}H NMR (400 MHz, DMSO) δ 7.84 (s, 1H), 7.75 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.1, 151.6, 135.07, 130.7, 127.2, 123.7; MS (EI) m/z 109.05, 145.01, 173.05, 186.06, 188.04, 230.04.

5-(3,5-Bis(trifluoromethyl)phenyl)-1,3,4-oxadiazol-2(3H)-one (**2p**).[4] White solid (39 mg, 65%); mp: 73.0−74.1. IR (KBr): 3082, 1772, 1397, 1281, 1137, 933, 701. ^{1}H NMR (400 MHz, DMSO) δ 8.32 (s, 1H), 8.29 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.5, 152.0, 132.3, 132.0, 131.6, 131.3, 127.3, 127.1, 126.1, 126.0, 125.1, 124.6, 121.9, 119.1; MS (EI) m/z 163.09, 213.07, 241.05, 254.07, 279.08, 298.07.

5-(3,4,5-Trimethoxyphenyl)-1,3,4-oxadiazol-2(3H)-one (**2q**). White solid (35 mg, 70%); mp: 189.3−191.7. IR (KBr): 3744, 2923, 1800, 1274, 754. ^{1}H NMR (400 MHz, DMSO) δ 12.58 (s, 1H), 7.05 (s, 2H), 3.86 (s, 6H), 3.73 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 154.4, 153.6, 153.3, 140.1, 119.1, 102.6, 60.2, 56.1; HRMS (ESI) m/z: calcd for $C_{11}H_{13}N_2O_5$ $[M + H]^+$, 253.0819; found, 253.0826.

5-(Benzo[d][1,3]dioxol-5-yl)-1,3,4-oxadiazol-2(3H)-one (**2r**). White solid (21 mg, 50%); mp: 219.1−220.5. IR (KBr): 3302, 2923, 1570, 1411, 1029, 882. ^{1}H NMR (400 MHz, DMSO) δ 12.48 (s, 1H), 7.32 (d, J = 8.2 Hz, 1H), 7.27 (s, 1H), 7.07 (d, J = 8.2 Hz, 1H), 6.14 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.4, 153.6, 150.0, 148.0, 120.4, 117.7, 108.9, 105.0, 102.0; HRMS (ESI) m/z: calcd for $C_9H_6N_2NaO_4$ $[M + Na]^+$, 229.0220; found, 229.0223.

5-(Naphthalen-2-yl)-1,3,4-oxadiazol-2(3H)-one (**2s**). White solid (30 mg, 70%); mp: 189.5−190.7. IR (KBr): 2923, 1685, 1305, 897, 745. ^{1}H NMR (400 MHz, DMSO) δ 12.65 (s, 1H), 8.39 (s, 1H), 8.11 (d, J = 7.6 Hz, 1H), 8.06 (d, J = 8.6 Hz, 1H), 7.98 (d, J = 7.6 Hz, 1H), 7.88 (d, J = 8.6 Hz, 1H), 7.66−7.60 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.5, 153.9, 133.9, 132.4, 129.0, 128.7, 127.9, 127.8, 127.2, 125.7, 121.5, 121.2; HRMS (ESI) m/z: calcd for $C_{12}H_8N_2NaO_2$ $[M + Na]^+$, 235.0478; found, 235.0481.

5-(Furan-2-yl)-1,3,4-oxadiazol-2(3H)-one (**2t**). White solid (18 mg, 60%); mp: 110.4−111.7. IR (KBr): 3132, 1777, 1650, 1335, 1097, 920, 706. ^{1}H NMR (400 MHz, DMSO) δ 12.63 (s, 1H), 7.97 (s, 1H), 7.15 (d, J = 2.8 Hz, 1H), 6.74 (d, J = 1.6 Hz, 1H); ^{13}C NMR (101 MHz, DMSO) δ 153.8, 147.3, 146.3, 138.7, 113.2, 112.2; HRMS (ESI) m/z: calcd for $C_6H_4N_2NaO_3$ $[M + Na]^+$, 175.0114; found, 175.0116.

3,5-Diphenyl-1,3,4-oxadiazol-2(3H)-one (**4a**). White solid (30 mg, 62%); mp: 136.7−137.9. IR (KBr): 3432, 1624, 1331, 1114, 748. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.85−7.80 (m, 3H), 7.61 (dd, J = 15.6, 7.6 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.24−7.15 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 160.6, 147.9, 135.3, 133.0, 131.8, 129.9, 127.9, 125.7, 122.9, 117.9, 112.4. HRMS (ESI) m/z: calcd for $C_{14}H_{10}N_2NaO_2$ $[M + Na]^+$, 261.0634; found, 261.0637.

3-Phenyl-5-(p-tolyl)-1,3,4-oxadiazol-2(3H)-one (**4b**). White solid (41 mg, 82%); mp: 156.6−157.9. IR (KBr): 3290, 1725, 1658, 1339, 742. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 1H), 7.77 (d, J = 7.6 Hz, 2H), 7.61 (t, J = 7.8 Hz, 1H), 7.28−7.26 (m, 3H), 7.23−7.14 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 160.7, 147.8, 144.0, 135.1, 130.1, 128.9, 128.6, 125.6, 122.8, 118.0, 112.4, 21.8. HRMS (ESI) m/z: calcd for $C_{15}H_{12}N_2NaO_2$ $[M + Na]^+$, 275.0791; found, 275.0795.

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*5-(4-Methoxyphenyl)-3-phenyl-1,3,4-oxadiazol-2(3H)-one (**4c**).* White solid (41 mg, 77%); mp: 137.1−138.4. IR (KBr): 3419, 1569, 1412, 1257, 1022, 750. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.82 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 6.97 (d, J = 8.4 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 163.8, 160.8, 147.8, 135.0, 132.7, 125.6, 123.6, 122.8, 118.1, 113.3, 112.4, 55.5. HRMS (ESI) m/z: calcd for $C_{15}H_{12}N_2NaO_3$ $[M + Na]^+$, 291.0740; found, 291.0739.

*3-Phenyl-5-(o-tolyl)-1,3,4-oxadiazol-2(3H)-one (**4d**).* White solid (38 mg, 76%); mp: 82.7−84.4. IR (KBr): 2924, 1681, 1411, 1303, 978, 740, 654. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.42 (t, J = 7.0 Hz, 2H), 7.30 (d, J = 6.8 Hz, 2H), 7.23 (d, J = 8.4 Hz, 1H), 7.17 (t, J = 7.4 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 160.0, 147.6, 136.2, 135.4, 133.0, 131.0, 130.6, 127.9, 125.7, 125.6, 122.9, 117.8, 112.3, 19.4. HRMS (ESI) m/z: calcd for $C_{15}H_{12}N_2NaO_2$ $[M + Na]^+$, 275.0791; found, 275.0790.

*5-Mesityl-3-phenyl-1,3,4-oxadiazol-2(3H)-one (**4e**).* White solid (45 mg, 80%); mp: 60.2−61.8. IR (KBr): 3212, 1683, 1618, 1339, 1301, 893, 752. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 6.90 (s, 2H), 2.31 (s, 3H), 2.23 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 159.5, 147.5, 139.7, 135.3, 134.3, 131.3, 128.4, 125.6, 122.7, 117.5, 112.3, 21.3, 19.1. HRMS (ESI) m/z: calcd for $C_{17}H_{16}N_2NaO_2$ $[M + Na]^+$, 303.1104; found, 303.1103.

*5-(2-Chlorophenyl)-3-phenyloxazol-2(3H)-one (**4f**).* White solid (44 mg, 80%); mp: 145.0−146.1. IR (KBr): 2923, 1670, 1413, 1189, 998, 772, 653. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.54−7.42 (m, 3H), 7.42−7.36 (m, 1H), 7.23 (s, 1H), 7.18 (t, J = 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 160.0, 147. 8, 135.6, 133.4, 131.8, 131.5, 129.7, 128.6, 126.9, 125.7, 123.1, 117.5, 112.5. HRMS (ESI) m/z: calcd for $C_{14}H_9ClN_2NaO_2$ $[M + Na]^+$, 295.0245; found, 295.0241.

*3-(4-Bromophenyl)-5-phenyl-1,3,4-oxadiazol-2(3H)-one (**4g**).* White solid (35 mg, 55%); mp: 146.0−147.9. IR (KBr): 2924, 1748, 1570, 1413, 1255, 1054, 751. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.93 (s, 1H), 7.82 (d, J = 7.6 Hz, 2H), 7.71 (d, J = 8.4 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.14 (d, J = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 159.1, 146.3, 138.2, 133.3, 131.4, 129.9, 128.2, 128.0, 119.6, 115.5, 114.0. HRMS (ESI) m/z: calcd for $C_{14}H_9BrN_2NaO_2$ $[M + Na]^+$, 338.9740; found, 338.9735.

*5-(4-Fluorophenyl)-3-phenyl-1,3,4-oxadiazol-2(3H)-one (**4h**).* White solid (40 mg, 78%); mp: 124.5−126.0. IR (KBr): 3074, 1747, 1623, 1506, 1242, 1153, 748. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 8.4, 5.6 Hz, 2H), 7.81 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.29−7.07 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 164.8, 164.4, 160.8, 147.9, 135.4, 132.8, 132.7, 127.8, 125.6, 122.9, 117.6, 115.3, 115.1, 112.4. HRMS (ESI) m/z: calcd for $C_{14}H_9FN_2NaO_2$ $[M + Na]^+$, 279.0540; found, 279.0537.

BMS-191011. White solid (90 mg, 83%); mp: 216.7−217.8. IR (KBr): 2929, 2382, 1782, 1324, 1134, 1011, 848, 747. ^{1}H NMR (400 MHz, DMSO) δ 10.12 (s, 1H), 7.95 (d, J = 8.0 Hz, 2H), 7.92 (d, J = 8.0 Hz, 2H), 7.29 (s, 1H), 7.20(dd, J = 8.7, 2.6 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 4.91 (s, 2H); ^{13}C NMR (101 MHz, DMSO) δ 154.1, 152.7, 151.3, 131.3, 131.0, 128.8, 128.8, 127.2, 126.1, 125.0, 123.2, 122.4, 122.3, 116.7, 44.3. HRMS (ESI) m/z: calcd for $C_{16}H_{10}ClF_3N_2NaO_3$ $[M + Na]^+$, 393.0224; found, 393.0222.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all synthesized compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00664.

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Notes

The authors declare no competing financial interest.

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