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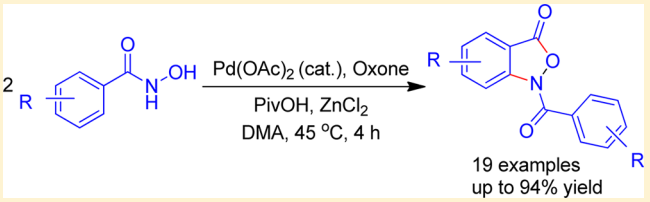
Pd(II)-Catalyzed Synthesis of Benzisoxazolones from Benzohydroxamic Acids via C−H Activation

Xi-Ai Gao, Ru-Long Yan,* Xian-Xue Wang, Hao Yan, Jian Li, Han Guo, and Guo-Sheng Huang*

State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Key Laboratory of Nonferrous Metal Chemistry and Resources Utilization of Gansu Province, Lanzhou 730000, People's Republic of China

Supporting Information

ABSTRACT: A Pd-catalyzed method for the synthesis of benzisoxazolones from benzohydroxamic acids using Oxone as an oxidant in a one-pot procedure has been developed. In this process, the reaction appears to be suitable for construction of various benzisoxazolones.



The ubiquity of heterocycles in biologically active molecules has provided a driving force for chemists to develop increasingly efficient methods toward their preparation.[1] Among the many ring-forming reactions in heterocycle synthesis, transition-metal-catalyzed C−H activation,[2] particularly, Pd-catalyzed C−H activation, has become one of the important methods to construct many heterocyclic molecules in recent years.[3]

Isoxazolones are important heterocycles, not only because of the significant pharmaceutical and therapeutic properties, such as hypoglycemic, immunosuppressive, anti-inflammatory, and antibacterial activities,[4] but because they can also serve as versatile building blocks in organic synthesis.[5] Consequently, isoxazolones have attracted considerable interests from chemists and stimulated the development of numerous methods for their synthesis.[6] Recently, several new approaches have been reported for the construction of benzisoxazolones using nitrobenzoates[7] and 2-nitrophenylacetylene.[8] However, there are very few general methods that convert easily available materials in one step to substituted benzisoxazolones. Herein, we wish to report a suitable and efficient method for the preparation of functionalized benzisoxazolones from a variety of benzohydroxamic acids by Pd-catalyzed reaction using Oxone as oxidant.

Initially, we examined the reaction of *N*-hydroxybenzamide (**1a**) with Oxone in *N*,*N*-dimethylacetamide (DMA) catalyzed by $Pd(OAc)_2$ at 45 °C (Table 1, entry 1). Gratifyingly, the desired 1-benzoylbenzo[*c*]isoxazol-3(1*H*)-one (**2a**) was obtained in 42% yield after 4 h. Several additional oxidants were then evaluated, and results showed that Oxone was superior to $K_2S_2O_8$, *tert*-butyl hydroperoxide (TBHP), 1,4-benzoquinone (BQ), and iodobenzene diacetate (PIDA) (Table 1, entries 2−5). Thus, Oxone was chosen as the oxidant for further optimization. Among the Pd sources we examined, $Pd(OAc)_2$ showed the highest activity for this reaction (Table 1, entries 6−8). Moreover, the use of DMF, DMSO, and *N*-methyl-2-pyrrolidone (NMP) did not improve the yield of the product relative to DMA (Table 1, entries 9−11). To our delight, when Lewis acids such as $ZnCl_2$, $AlCl_3$, and $NiCl_2$ and organic acid pivalic acid (PivOH) were employed as additives, the combination of $ZnCl_2$ and PivOH was proven to be highly effective and resulted in 89% yield (Table 1, entry 16). Yield decreased when temperature changed to 80 or 25 °C (Table 1, entries 17 and 18). In addition, in the absence of palladium, no target product was obtained (Table 1, entry 19). Furthermore, changing the loading of Oxone and PivOH/$ZnCl_2$ did not improve the yield (Table 1, entries 20−23). As a result, optimized conditions were identified, which provided **2a** in good yield (Table 1, entry 16).

Using the optimized conditions, we extended the scope of the reaction, and the results are summarized in Table 2. Generally, the reaction of benzohydroxamic acids proceeded smoothly and afforded the corresponding benzisoxazolones **2** in moderate to good yields. Satisfactorily, a variety of substituted benzohydroxamic acids gave corresponding products **2a−2r**. The electron-rich benzohydroxamic acids showed better reactivity and achieved higher yields than electron-deficient ones (52−94% for **2b−2k** vs 35−71% for **2m−2r**). Further investigations demonstrated that *N*-hydroxy-3,5-dimethylbenzamide (**1l**) gave much lower yield than *N*-hydroxy-3-methylbenzamide (**1c**) due to steric hindrance.

Additionally, the desired 3-(1-naphthoyl)naphtho[2,1-*c*]-isoxazol-1(3*H*)-one (**2s**) from *N*-hydroxy-1-naphthamide (**1s**) was obtained in 55% yield (eq 1).

It is worth mentioning that the reaction of *N*-hydroxy-1-methyl-1*H*-indole-3- carboxamide (**1t**) gave unexpected product 1-methylindoline-2,3-dione (**2t**) under the optimal condition in 75% yield (eq 2). The structure of **2t** was unambiguously confirmed through single-crystal X-ray analysis.[9]

In order to gain insight into the reaction mechanism, an additional experiment was performed. *N*-(Benzoyloxy)-benzamide (**3**) as substrate under the optimal condition

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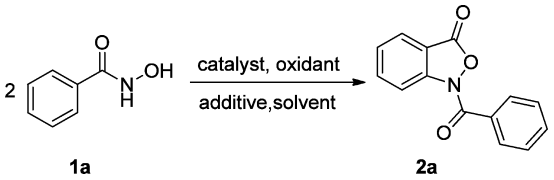
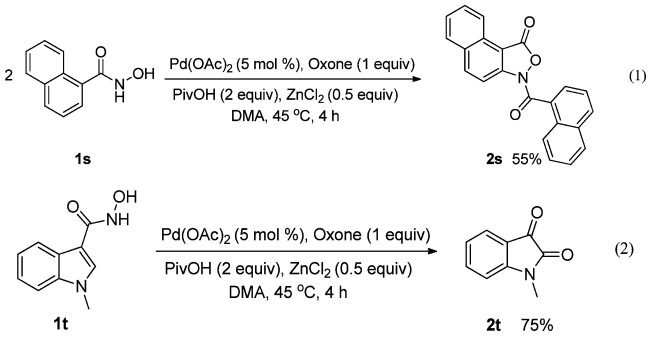
Table 1. Optimization of the Reaction Condition[a]



1a 2a

entry	catalyst	oxidant	additive	solvent	temp (°C)	yield (%)
1	$Pd(OAc)_2$	Oxone		DMA	45	42
2	$Pd(OAc)_2$	$K_2S_2O_8$		DMA	45	20
3	$Pd(OAc)_2$	TBHP		DMA	45	trace
4	$Pd(OAc)_2$	BQ		DMA	45	0
5	$Pd(OAc)_2$	PIDA		DMA	45	0
6	$PdCl_2$	Oxone		DMA	45	28
7	$Pd(dba)_2$	Oxone		DMA	45	10
8	$Pd(PPh_3)_2Cl_2$	Oxone		DMA	45	0
9	$Pd(OAc)_2$	Oxone		DMF	45	22
10	$Pd(OAc)_2$	Oxone		DMSO	45	0
11	$Pd(OAc)_2$	Oxone		NMP	45	30
12	$Pd(OAc)_2$	Oxone	$ZnCl_2$	DMA	45	45
13	$Pd(OAc)_2$	Oxone	$AlCl_3$	DMA	45	0
14	$Pd(OAc)_2$	Oxone	$NiCl_2$	DMA	45	0
15	$Pd(OAc)_2$	Oxone	PivOH	DMA	45	10
16	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	45	89
17	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	80	70
18[f]	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	25	40
19		Oxone	PivOH/ $ZnCl_2$	DMA	45	0
20[b]	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	45	87
21[c]	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	45	61
22[d]	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	45	53
23[e]	$Pd(OAc)_2$	Oxone	PivOH/ $ZnCl_2$	DMA	45	65

[a]Unless otherwise specified, all reactions were carried out with **1a** (0.3 mmol), catalyst (0.015 mmol), oxidant (0.3 mmol), PivOH (0.6 mmol)/$ZnCl_2$ (0.15 mmol), solvent (1.5 mL), 4 h. [b]PivOH (0.9 mmol)/$ZnCl_2$ (0.15 mmol). [c]PivOH (0.3 mmol)/$ZnCl_2$ (0.15 mmol). [d]Oxone (0.15 mmol). [e]Oxone (0.45 mmol). [f]For 10 h.



could not cyclize to **2a**, thus ruling out the intermediacy of **3** in the formation of **2a** (Scheme 1).

On the basis of the results obtained above, a plausible reaction mechanism has been proposed (Scheme 2). Palladation of benzohydroxamic acid **1** with $Pd(OAc)_2$ produces five-membered palladacycle **4**,[10] which could be promoted by PivOH and $ZnCl_2$,[2h,11] followed by oxidation of the Pd(II) intermediate **4** to the Pd(IV) intermediate **5**. Subsequently, benzohydroxamic acid **1** attacks intermediate **5** to give the intermediate **6**. Then carbon−heteroatom bond formation via reductive elimination affords compound **7**. Meanwhile, Pd(II) oxidized to Pd(IV) enters the next catalytic cycle. In the final step, intermediate **7** undergoes intramolecular nucleophilic addition and subsequent elimination to afford product **2**.

In conclusion, we have developed a direct Pd-catalyzed method for the synthesis of benzisoxazolones from benzohydroxamic acids using Oxone as oxidation agent in a one-pot manner, involving the cleavage of a C−H bond and the formation of a C−N bond. A variety of substituents are tolerated in this reaction, which proceeds smoothly in moderate to good yields.

EXPERIMENTAL SECTION

General Methods. All reactions were performed in a test tube under air. Column chromatography was performed using silica gel (200−400 mesh). ^1H NMR and ^{13}C NMR spectra were recorded on 400 MHz in DMSO-d_6 and $CDCl_3$ using TMS as the internal standard. IR spectra were recorded on a FT-IR spectrometer, and only major peaks are reported in cm^{-1}. All new compounds were further characterized by HRMS (ESI), and the mass analyzer type used for the HRMS was FT; copies of all ^1H NMR and ^{13}C NMR spectra are provided in the Supporting Information. All melting points were determined without correction. Commercially available reagents and solvents were used without further purification.

Typical Procedure for the Preparation of Benzisoxazolones 2. A test tube was charged with **1** (0.3 mmol), $Pd(OAc)_2$ (0.015 mmol), Oxone (0.3 mmol), and PivOH (0.6 mmol)/$ZnCl_2$ (0.15 mmol). Then 1.5 mL of DMA was added to the reaction system. The reaction was stirred at 45 °C for 4 h under air. After being cooled to room temperature, the solvent was diluted with 10 mL of ethyl acetate, washed with 5 mL of brine, and dried over anhydrous Na_2SO_4. After the solvent was evaporated in vacuo, the residues were purified by column chromatography (SiO_2), eluting with petroleum ether/EtOAc to afford pure **2**.

1-Benzoylbenzo[*c*]isoxazol-3(1*H*)-one 2a: White solid (31.9 mg, 89%); mp 140−142 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26−8.24 (d, J = 8.4 Hz, 1H), 8.00−7.98 (d, J = 7.6 Hz, 2H), 7.95−7.93 (d, J = 7.6 Hz, 1H), 7.86−7.82 (m, 1H), 7.64−7.60 (t, J = 7.2 Hz, 1H), 7.55−7.51 (m, 2H), 7.47−7.43 (t, J = 7.6 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.0, 163.7, 145.8, 136.5, 132.9, 131.1, 129.7, 128.4, 126.0, 125.6, 115.8, 111.7; IR (neat, cm^{-1}) 1785, 1679, 1465, 1366, 1331, 1252, 1069, 973, 752, 698, 674; HRMS (ESI) calcd for $C_{14}H_{10}NO_3$ $[M + H]^+$ 240.0661, found 240.0656.

6-Methyl-1-(4-methylbenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2b: White solid (36.8 mg, 92%); mp 162−164 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.92−7.90 (d, J = 8.0 Hz, 2H), 7.81−7.79 (d, J = 8.0 Hz, 1H), 7.33−7.31 (d, J = 8.0 Hz, 2H), 7.25−7.23 (d, J = 8.0 Hz, 1H), 2.57 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.0, 163.8, 148.5, 146.4, 143.8, 129.8, 129.1, 128.3, 127.5, 125.1, 115.6, 109.2, 22.5, 21.6; IR (neat, cm^{-1}) 1787, 1770, 1684, 1607, 1437, 1354, 1326, 1263, 1183, 1065, 1028, 977, 915, 823, 765, 730, 671; HRMS (ESI) calcd for $C_{16}H_{14}NO_3$ $[M + H]^+$ 268.0974, found 268.0976.

5-Methyl-1-(3-methylbenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2c: White solid (36.4 mg, 91%); mp 126−128 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12−8.10 (d, J = 8.4 Hz, 1H), 7.78−7.74 (m, 2H), 7.71−7.70 (d, J = 0.8 Hz, 1H), 7.65−7.63 (dd, J = 1.2 Hz, J = 8.4 Hz, 1H), 7.43−7.38 (m, 2H), 2.49 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.1, 163.9, 144.1, 138.2, 137.8, 136.3, 133.6, 131.2, 130.0, 128.2, 126.8, 124.8, 115.5, 111.8, 21.3, 21.0; IR (neat, cm^{-1}) 1798, 1676, 1490, 1365, 1326, 1266, 1150, 1046, 975, 873, 822, 715; HRMS (ESI) calcd for $C_{16}H_{14}NO_3$ $[M + H]^+$ 268.0974, found 268.0978.

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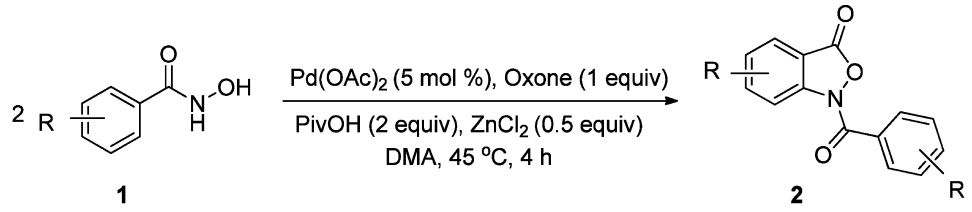
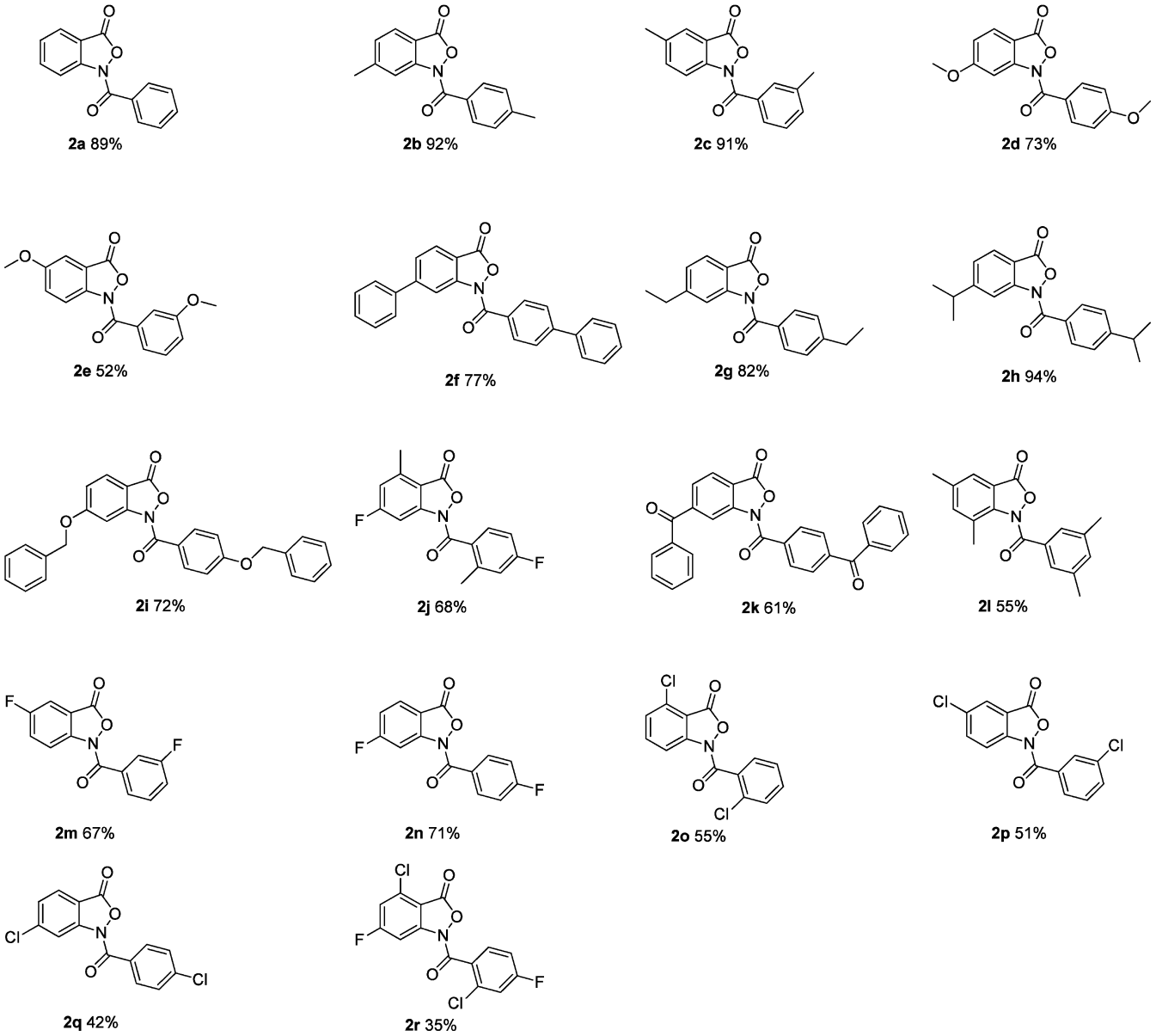
Table 2. Synthesis of Benzisoxazolones from Benzohydroxamic Acids[a]

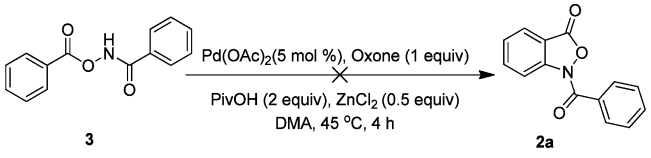


1 2



[a]Reaction conditions: **1** (0.3 mmol), $Pd(OAc)_2$ (0.015 mmol), Oxone (0.3 mmol), PivOH (0.6 mmol)/$ZnCl_2$ (0.15 mmol), 1.5 mL of DMA, in an open tube, 45 °C, 4 h.

Scheme 1. Attempted Pd-Catalyzed Cyclization of 3



3 2a

6-Methoxy-1-(4-methoxybenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2d: White solid (32.7 mg, 73%); mp 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–8.02 (m, 2H), 7.78–7.76 (d, J = 8.8 Hz, 1H), 7.70–7.69 (d, J = 2.4 Hz, 1H), 7.02–6.98 (m, 2H), 6.96–6.93 (dd, J = 2.0 Hz, J = 8.8 Hz, 1H), 3.97 (s, 3H), 3.90 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 166.7, 163.6, 163.4, 148.5, 132.2, 126.5, 123.1, 115.9, 113.8, 103.9, 98.2, 56.2, 55.5; IR (neat, cm^{-1}) 1765, 1678, 1619, 1601, 1489, 1453, 1289, 1263, 1174, 1101, 1023, 981, 911, 845, 830, 748, 676, 622; HRMS (ESI) calcd for $C_{16}H_{14}NO_5$ $[M + H]^+$ 300.0872, found 300.0875.

5-Methoxy-1-(3-methoxybenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2e: White solid (23.3 mg, 52%); mp 124–126 °C; ^{1}H NMR (400

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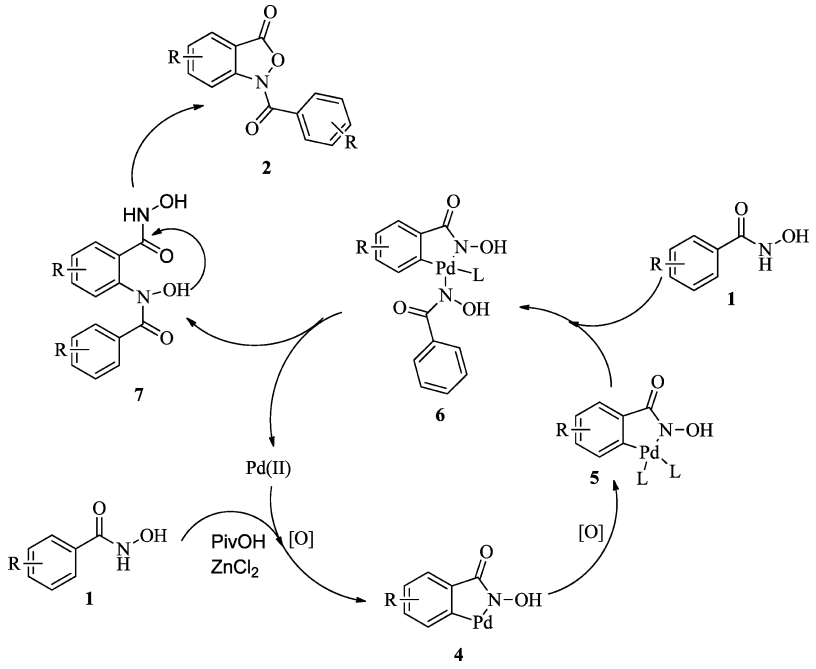
Scheme 2. Proposed Reaction Mechanism



MHz, $CDCl_3$) δ 8.14−8.12 (d, J = 9.2 Hz, 1H), 7.58−7.56 (d, J = 7.6 Hz, 1H), 7.46 (s, 1H), 7.44−7.40 (m, 2H), 7.29−7.28 (d, J = 2.4 Hz, 1H), 7.16−7.13 (dd, J = 2.4 Hz, J = 8.4 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 163.8, 163.5, 159.4, 158.1, 140.6, 132.3, 129.4, 126.3, 122.0, 119.1, 117.1, 114.5, 112.6, 105.6, 55.9, 55.4; IR (neat, cm^{-1}) 1784, 1667, 1594, 1491, 1344, 1277, 1254, 1140, 1061, 1021, 992, 911, 874, 824, 791, 740, 683; HRMS (ESI) calcd for $C_{16}H_{14}NO_5$ $[M + H]^+$ 300.0872, found 300.0877.

1-([1,1′-Biphenyl]-4-carbonyl)-6-phenylbenzo[*c*]isoxazol-3(1*H*)-one 2f: White solid (45.1 mg, 77%); mp 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.11−8.09 (d, J = 8.4 Hz, 2H), 7.98−7.96 (d, J = 8.0 Hz, 1H), 7.75−7.64 (m, 7H), 7.53−7.40 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 163.8, 163.6, 150.1, 146.5, 145.8, 139.7, 139.1, 130.4, 129.7, 129.13, 129.10, 128.9, 128.3, 127.7, 127.3, 127.0, 125.8, 125.6, 113.9, 110.3; IR (neat, cm^{-1}) 1780, 1672, 1608, 1423, 1363, 1264, 1072, 973, 898, 738, 695; HRMS (ESI) calcd for $C_{26}H_{18}NO_3$ $[M + H]^+$ 392.1287, found 392.1289.

6-Ethyl-1-(4-ethylbenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2g: Colorless liquid (36.3 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.93−7.91 (d, J = 8.4 Hz, 2H), 7.83−7.81 (d, J = 8.0 Hz, 1H), 7.35−7.33 (d, J = 8.4 Hz, 2H), 7.28 (s, 1H), 2.87−2.82 (q, J = 7.6 Hz, 2H), 2.77−2.71 (m, 2H), 1.35−1.31 (t, J = 7.6 Hz, 3H), 1.30−1.26 (t, J = 7.6 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.0, 163.8, 154.7, 149.9, 146.5, 129.9, 128.6, 127.9, 126.4, 125.2, 114.6, 109.4, 29.8, 28.9, 15.2, 15.1; IR (neat, cm^{-1}) 1783, 1674, 1610, 1441, 1416, 1362, 1334, 1260, 1187, 1073, 984, 967, 907, 842, 748, 681; HRMS (ESI) calcd for $C_{18}H_{18}NO_3$ $[M + H]^+$ 296.1287, found 296.1283.

6-Isopropyl-1-(4-isopropylbenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2h: Colorless liquid (45.5 mg, 94%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.94−7.92 (dd, J = 1.6 Hz, J = 6.8 Hz, 2H), 7.84−7.82 (d, J = 8.0 Hz, 1H), 7.38−7.36 (d, J = 8.4 Hz, 2H), 7.32−7.29 (dd, J = 1.2 Hz, J = 8.0 Hz, 1H), 3.17−3.06 (m, 1H), 3.05−2.95 (m, 1H), 1.35 (s, 3H), 1.33 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 164.0, 163.8, 159.3, 154.4, 146.6, 129.9, 128.8, 126.5, 125.3, 125.1, 113.3, 109.5, 35.2, 34.3, 23.6; IR (neat, cm^{-1}) 1783, 1675, 1610, 1440, 1416, 1346, 1261, 1189, 1055, 978, 918, 878, 842, 741, 689; HRMS (ESI) calcd for $C_{20}H_{22}NO_3$ $[M + H]^+$ 324.1600, found 324.1605.

6-(Benzyloxy)-1-(4-(benzyloxy)benzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2i: White solid (49.1 mg, 72%); mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−8.01 (d, J = 8.8 Hz, 2H), 7.80−7.76 (m, 2H), 7.47−7.33 (m, 10H), 7.08−7.06 (d, J = 8.8 Hz, 2H), 7.02−7.00 (dd, J = 2.0 Hz, J = 8.8 Hz, 1H), 5.21 (s, 2H), 5.16 (s, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 165.8, 163.6, 163.5, 162.7, 148.5, 136.1, 135.4, 132.3, 128.8, 128.8, 128.6, 128.3, 127.8, 127.5, 126.7, 123.5, 116.3, 114.7, 104.2, 99.4, 71.0, 70.3; IR (neat, cm^{-1}) 1776, 1667, 1604, 1490, 1449, 1378, 1335, 1284, 1258, 1177, 1091, 1071, 981, 912, 839, 737, 697, 654; HRMS (ESI) calcd for $C_{28}H_{22}NO_5$ $[M + H]^+$ 452.1498, found 452.1493.

6-Fluoro-1-(4-fluoro-2-methylbenzoyl)-4-methylbenzo[*c*]-isoxazol-3(1*H*)-one 2j: White solid (31.2 mg, 68%); mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.70 (m, 1H), 7.54−7.50 (m, 1H), 7.02−6.98 (m, 2H), 6.93−6.91 (dd, J = 1.6 Hz, J = 9.6 Hz, 1H), 2.68 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 168.9, 165.9 (d, J_{C-F} = 324 Hz), 163.8, 163.0 (d, J_{C-F} = 132 Hz), 146.8 (d, J_{C-F} = 64 Hz), 143.2 (d, J_{C-F} = 44 Hz), 140.6 (d, J_{C-F} = 36 Hz), 130.8 (d, J_{C-F} = 36 Hz), 127.6, 118.1 (d, J_{C-F} = 84 Hz), 115.8 (d, J_{C-F} = 100 Hz), 113.1 (d, J_{C-F} = 88 Hz), 106.5, 100.5 (d, J_{C-F} = 116 Hz), 19.9, 17.6; IR (neat, cm^{-1}) 1779, 1689, 1606, 1588, 1539, 1493, 1444, 1423, 1367, 1339, 1306, 1281, 1235, 1180, 1134, 1101, 1032, 991, 961, 923, 863, 813, 751, 669, 621; HRMS (ESI) calcd for $C_{16}H_{12}F_2NO_3$ $[M + H]^+$ 304.0785, found 304.0788.

6-Benzoyl-1-(4-benzoylbenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2k: White solid (41.3 mg, 61%); mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.10−8.07 (m, 3H), 7.94−7.92 (d, J = 8.4 Hz, 2H), 7.88−7.83 (m, 5H), 7.69−7.62 (m, 2H), 7.57−7.51 (dd, J = 7.6 Hz, J = 15.6 Hz, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 195.5, 194.7, 163.2, 162.7, 145.6, 145.3, 141.5, 136.7, 136.0, 133.8, 133.7, 133.1, 130.2, 130.1, 129.7, 129.6, 128.7, 128.5, 127.1, 125.9, 116.9, 113.9; IR (neat, cm^{-1}) 1788, 1664, 1613, 1596, 1502, 1431, 1404, 1361, 1321, 1274, 1234, 1181, 1072, 989, 923, 857, 798, 729, 703, 663; HRMS (ESI) calcd for $C_{28}H_{18}NO_5$ $[M + H]^+$ 448.1185, found 448.1183.

1-(3,5-Dimethylbenzoyl)-5,7-dimethylbenzo[*c*]isoxazol-3(1*H*)-one 2l: White solid (24.3 mg, 55%); mp 120−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 2H), 7.52 (s, 1H), 7.45 (s, 1H), 7.26 (s, 1H), 2.45 (s, 3H), 2.44 (s, 3H), 2.40 (s, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 168.4, 165.6, 146.1, 139.4, 138.2, 137.3, 135.3, 131.6, 128.2, 127.5, 122.5, 114.5, 21.3, 20.9, 19.9; IR (neat, cm^{-1}) 1786, 1698, 1603, 1492, 1307, 1266, 1193, 1093, 1024, 885, 863, 763, 733, 679; HRMS (ESI) calcd for $C_{18}H_{18}NO_3$ $[M + H]^+$ 296.1287, found 296.1285.

5-Fluoro-1-(3-fluorobenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2m: White solid (27.6 mg, 67%); mp 160−162 °C; ^{1}H NMR (400

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MHz, $CDCl_3$) δ 8.04−8.02 (d, J = 8.4 Hz, 1H), 7.85−7.80 (m, 1H), 7.65−7.56 (m, 2H), 7.32−7.28 (m, 1H), 7.24−7.20 (t, J = 9.2 Hz, 1H), 7.11−7.07 (t, J = 8.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 160.7 (d, J_{C-F} = 172 Hz), 159.5, 157.6, 156.2, 146.0, 139.0 (d, J_{C-F} = 32 Hz), 134.2 (d, J_{C-F} = 36 Hz), 130.0, 124.4 (d, J_{C-F} = 12 Hz), 120.4 (d, J_{C-F} = 56 Hz), 116.6 (d, J_{C-F} = 84 Hz), 112.5 (d, J_{C-F} = 72 Hz), 111.2 (d, J_{C-F} = 20 Hz), 101.4; IR (neat, cm^{-1}) 1787, 1685, 1627, 1610, 1493, 1453, 1369, 1330, 1299, 1258, 1185, 1148, 1005, 970, 797, 774, 668; HRMS (ESI) calcd for $C_{14}H_8F_2NO_3$ $[M + H]^+$ 276.0472, found 276.0475.

6-Fluoro-1-(4-fluorobenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2n: White solid (29.3 mg, 71%); mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−8.03 (m, 2H), 7.96−7.92 (m, 2H), 7.24−7.14 (m, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 169.2, 166.9 (d, J_{C-F} = 124 Hz), 164.4, 162.7 (d, J_{C-F} = 48 Hz), 147.3 (d, J_{C-F} = 60 Hz), 132.7 (d, J_{C-F} = 40 Hz), 127.9 (d, J_{C-F} = 44 Hz), 126.7, 115.9 (d, J_{C-F} = 88 Hz), 115.1 (d, J_{C-F} = 100 Hz), 107.8, 103.5 (d, J_{C-F} = 120 Hz); IR (neat, cm^{-1}) 1791, 1684, 1602, 1506, 1483, 1450, 1412, 1367, 1335, 1279, 1249, 1162, 1065, 984, 927, 842, 760, 668, 618; HRMS (ESI) calcd for $C_{14}H_8F_2NO_3$ $[M + H]^+$ 276.0472, found 276.0478.

4-Chloro-1-(2-chlorobenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2o: White solid (25.2 mg, 55%); mp 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.14 (d, J = 8.0 Hz, 1H), 7.78−7.74 (t, J = 8.0 Hz, 1H), 7.54−7.50 (m, 3H), 7.43−7.39 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 161.7, 160.5, 145.8, 137.5, 133.3, 132.4, 131.9, 131.6, 130.1, 129.0, 127.1, 126.9, 113.3, 109.5; IR (neat, cm^{-1}) 1794, 1694, 1596, 1475, 1436, 1360, 1321, 1228, 1060, 970, 792, 765, 736, 663, 641; HRMS (ESI) calcd for $C_{14}H_8Cl_2NO_3$ $[M + H]^+$ 307.9881, found 307.9885.

5-Chloro-1-(3-chlorobenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2p: White solid (23.4 mg, 51%); mp 115−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21−8.19 (d, J = 8.8 Hz, 1H), 7.94 (s, 1H), 7.91−7.90 (d, J = 1.6 Hz, 1H), 7.88−7.86 (d, J = 8.0 Hz, 1H), 7.81−7.78 (dd, J = 2.0 Hz, J = 8.8 Hz, 1H), 7.61−7.59 (d, J = 8.4 Hz, 1H), 7.49−7.45 (t, J = 8.0 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 162.4, 162.1, 144.0, 137.0, 134.7, 133.2, 132.3, 132.1, 129.8, 129.7, 127.8, 125.1, 117.1, 113.1; IR (neat, cm^{-1}) 1789, 1669, 1463, 1362, 1315, 973, 909, 829, 736, 674, 651; HRMS (ESI) calcd for $C_{14}H_8Cl_2NO_3$ $[M + H]^+$ 307.9881, found 307.9883.

6-Chloro-1-(4-chlorobenzoyl)benzo[*c*]isoxazol-3(1*H*)-one 2q: White solid (19.3 mg, 42%); mp 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.96−7.94 (d, J = 8.4 Hz, 2H), 7.87−7.85 (d, J = 8.4 Hz, 1H), 7.52−7.50 (d, J = 8.4 Hz, 2H), 7.44−7.42 (d, J = 8.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 162.8, 162.5, 146.2, 143.5, 139.9, 131.2, 128.9, 127.1, 126.6, 116.0, 110.0; IR (neat, cm^{-1}) 1792, 1742, 1679, 1606, 1590, 1462, 1434, 1404, 1364, 1317, 1260, 1183, 1092, 1066, 1017, 978, 900, 863, 833, 804, 732, 665; HRMS (ESI) calcd for $C_{14}H_8Cl_2NO_3$ $[M + H]^+$ 307.9881, found 307.9887.

4-Chloro-1-(2-chloro-4-fluorobenzoyl)-6-fluorobenzo[*c*]-isoxazol-3(1*H*)-one 2r: White solid (18.2 mg, 35%); mp 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.87 (m, 1H), 7.56−7.53 (dd, J = 5.6 Hz, J = 8.4 Hz, 1H), 7.27−7.25 (m, 1H), 7.19−7.12 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 168.8, 165.8 (d, J_{C-F} = 332 Hz), 162.8, 160.3 (d, J_{C-F} = 592 Hz), 146.7 (d, J_{C-F} = 64 Hz), 135.3 (d, J_{C-F} = 56 Hz), 133.6 (d, J_{C-F} = 40 Hz), 131.0 (d, J_{C-F} = 40 Hz), 127.7 (d, J_{C-F} = 16 Hz), 118.1 (d, J_{C-F} = 100 Hz), 116.3 (d, J_{C-F} = 112 Hz), 114.7 (d, J_{C-F} = 88 Hz), 106.0, 101.4 (d, J_{C-F} = 116 Hz); IR (neat, cm^{-1}) 1802, 1703, 1601, 1538, 1483, 1425, 1363, 1335, 1290, 1264, 1215, 1176, 1110, 1077, 1046, 995, 952, 913, 857, 800, 735, 659, 620; HRMS (ESI) calcd for $C_{14}H_6Cl_2F_2NO_3$ $[M + H]^+$ 343.9693, found 343.9697.

3-(1-Naphthoyl)naphtho[2,1-*c*]isoxazol-1(3*H*)-one 2s: Lilac solid (27.9 mg, 55%); mp 200−202 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61−8.59 (d, J = 8.0 Hz, 1H), 8.55−8.53 (d, J = 8.8 Hz, 1H), 8.25−8.18 (m, 3H), 8.12−8.07 (m, 2H), 8.03−8.01 (d, J = 7.2 Hz, 1H), 7.89−7.85 (m, 1H), 7.74−7.70 (m, 2H), 7.66−7.60 (m, 2H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 163.16, 163.13, 146.0, 138.6, 132.9, 131.9, 130.5, 130.3, 129.4, 129.2, 128.5, 127.7, 127.6, 127.5, 126.9, 126.7, 124.9, 124.6, 121.7, 113.3, 103.7; IR (neat, cm^{-1}) 1783, 1658, 1447, 1335, 1229, 1052, 1026, 1005, 824, 762, 624; HRMS (ESI) calcd for $C_{22}H_{14}NO_3$ $[M + H]^+$ 340.0974, found 340.0978.

1-Methylindoline-2,3-dione 2t: Yellow solid (36.2 mg, 75%); mp 120−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.59 (m, 2H), 7.15−7.11 (m, 1H), 6.91−6.89 (d, J = 8.0 Hz, 1H), 3.26 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 183.3, 158.2, 151.4, 138.3, 125.2, 123.8, 117.4, 109.8, 26.2; IR (neat, cm^{-1}) 1743, 1726, 1606, 1467, 1366, 1325, 1253, 1190, 1157, 1112, 1089, 1035, 954, 862, 814, 754, 700; HRMS (ESI) calcd for $C_9H_8NO_2$ $[M + H]^+$ 162.0555, found 162.0557.

***N*-(Benzoyloxy)benzamide 3:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.17−8.14 (m, 2H), 7.88−7.86 (m, 2H), 7.67−7.63 (m, 1H), 7.60−7.57 (m, 1H), 7.52−7.46 (m, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 166.5, 165.2, 134.3, 132.8, 130.8, 130.0, 128.8, 128.7, 127.5, 126.5.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectral data for all new compounds, and X-ray data for **2t**, in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hgs@lzu.edu.cn. yanrl@lzu.edu.cn.

Notes

The authors declare no competing financial interest.

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