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Hypervalent Iodine(III)-Promoted Radical Oxidative C−H Annulation of Arylamines with α-Keto Acids

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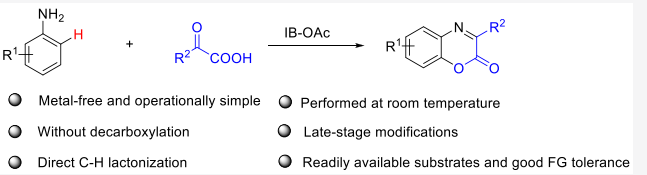
ABSTRACT: A novel catalyst-free radical oxidative C−H annulation reaction of arylamines with α-keto acids toward benzoxazin-2-ones synthesis under mild conditions was developed. This hypervalent iodine(III)-promoted process eliminated the use of a metal catalyst or additive with high levels of functional group tolerance. Hypervalent iodine(III) was both an oxidant and a radical initiator for this reaction. The synthetic utility of this method was confirmed by the synthesis of the natural product cephalandole A.



INTRODUCTION

The benzoxazin-2-one nucleus represents a significant class of lactone compounds[1] that exhibits a broad spectrum of biological and pharmacological activity.[2] As a consequence, it has received considerable attention to developing efficient synthetic methods for their preparation. The current methods toward benzoxazin-2-ones involve the use of *o*-aminophenols[3] or its precursor[4] in the presence of strong acids or bases at elevated temperatures. However, the modern approaches from the nonfunctionalized and more accessible anilines toward 2*H*-benzoxazin-2-ones were still barely developed. Recently, transition-metal-catalyzed oxidative C−H bond functionalization proved to be a powerful tool to construct lactone compounds.[5] This strategy avoided the preinstallation of functional groups with step and atom economy. Despite the obvious advantages, some transition-metal catalysts still have some shortcomings, such as high price, residual metallic impurities, and generation of toxic waste. In the interest of green and sustainable chemistry, further research into mild and metal-free methods to access diverse benzoxazin-2-ones from readily accessible precursors remains a great challenge.

On the other hand, C−H direct functionalization via a radical process has been considered as one of the most effective and straightforward method to form carbon−carbon and carbon−heteroatom bonds from readily available starting materials.[6] The addition of oxygen-centered radicals to aromatic rings is an efficient method for the construction of complex molecules.[7] The direct generation of oxygen-centered radicals by the use of hypervalent iodine reagents (HIR)[8] is easy to handle and nontoxic under mild photoredox conditions.[9] α-Keto acids are cheap, readily available, stable, and nontoxic, making them ideal precursors for the synthesis of important compounds.[10] In the past few years, they have played an important role in the development of photoredox-catalyzed,[11] transition-metal-catalyzed,[12] and hypervalent iodine-facilitated decarboxylative radical acylation reactions,[13] where the new C−C, C−N, and C−S bonds were formed. Very recently, tandem condensation and decarboxylative amination reactions between amines and α-keto acids have attracted great attention. For example, Xu's group described a catalyst-free photocatalytic α-imino acids oxidative decarboxylation followed by the hydrolysis approach to produce amides[14] (Scheme 1a). Takemoto's group presented a decarboxylative synthesis of amides via the nucleophilic addition of *tert*-butyl hydroperoxide (TBHP) to imine intermediate (Scheme 1b).[15] They also reported using nucleophilic sulfurizing species instead of the TBHP method to afford thioamides (Scheme 1c).[16] Although the decarboxylative coupling of ketoacids as acyl radicals has achieved great success, their binding as the ketoacid radicals has been less explored.[17] Herein we described the first metal-free hypervalent iodine(III)-promoted tandem condensation/radical oxidative C−H annulation of arylamines with α-keto acids for the synthesis of 2*H*-benzo[*b*][1,4]oxazin-2-ones (Scheme 1d).

RESULTS AND DISCUSSION

We commenced our investigation with the reaction of 4-methoxyaniline **1a** and phenylglyoxylic acid **2a** at room temperature. As shown in Table 1, a variety of hypervalent iodines including 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (IB−

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Scheme 1. Different Transformations of Amines and α-Keto Acids

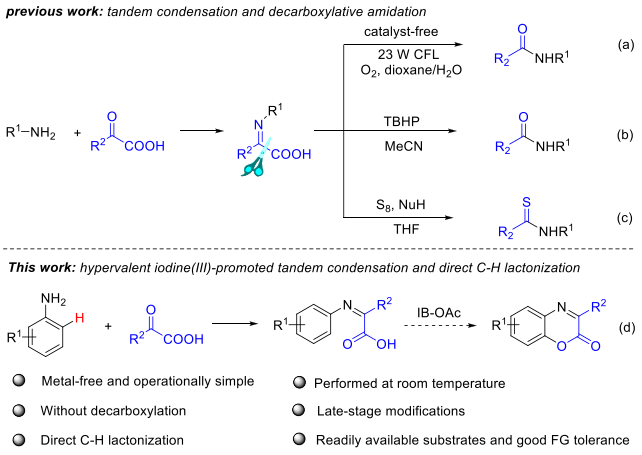
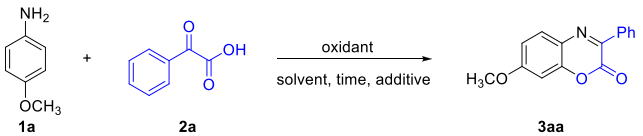


Table 1. Optimization of the Reaction Parameters[a]



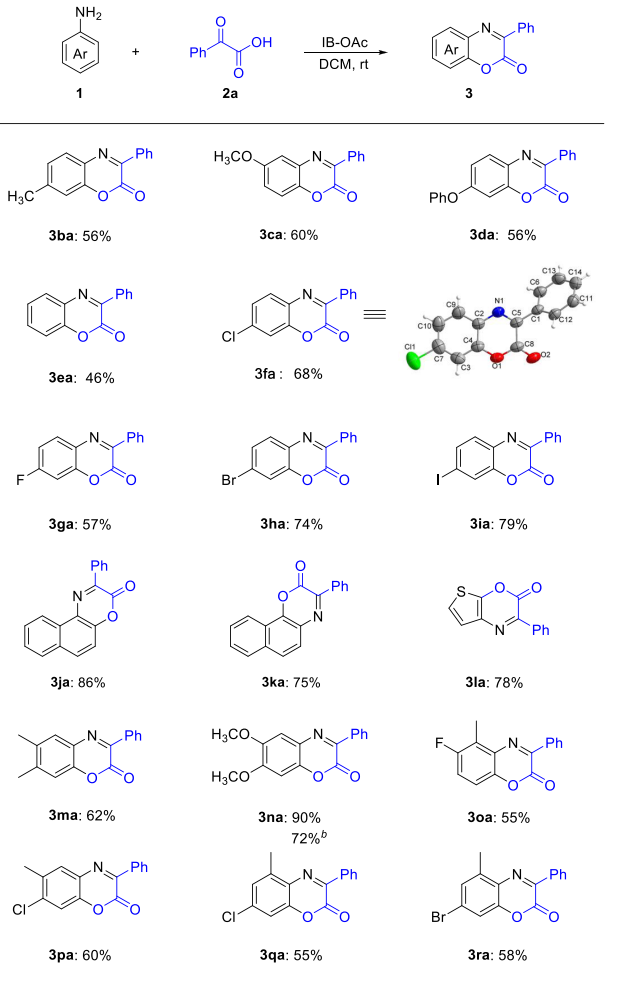
entry	oxidant	solvent	additive	yield (%)
1	IB−OH	CH_2Cl_2		52
2	IB-OAc	CH_2Cl_2		80
3	IB-CF_3	CH_2Cl_2		35
4	$PhI(OAc)_2$	CH_2Cl_2		40
5	$PhI(OOCCF_3)_2$	CH_2Cl_2		10
6		CH_2Cl_2		nr
7	IB-OAc	$CHCl_3$		40
8	IB-OAc	DCE		35
9	IBOAc	CH_3CN		20
10	IB-OAc	CH_2Cl_2	Et_3N[b]	5
11	IB-OAc	CH_2Cl_2	NaOAc[b]	53
12	IB-OAc	CH_2Cl_2	HOAc[b]	73
13[c]	IB-OAc	CH_2Cl_2		66
14[d]	IB-OAc	CH_2Cl_2		80
15[e]	IB-OAc	CH_2Cl_2		65
16[f]	IB-OAc	CH_2Cl_2		62
17[g]	IB-OAc	CH_2Cl_2		38
18[h]	IB-OAc	CH_2Cl_2		58
19[i]	IB-OAc	CH_2Cl_2		76

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), oxidant (0.1 mmol) in solvent (1.0 mL) for 8 h under air in an oil bath at room temperature. [b]The amount of additive was 0.10 mmol (1 equiv). [c]6 h. [d]10 h. [e]In a preheated oil bath at 40 °C. [f]The ratio of **1a** to **2a** is 1:1. [g]The ratio of **1a** to **2a** is 1.5:1. [h]40 W blue LEDs (410−490 nm). [i]Light-shielded. nr = no reaction.

OH), 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (IB-OAc), 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (IB-CF_3), diacetoxyiodo benzene ($PhI(OAc)_2$), and [bis(trifluoroacetoxy)-iodo]benzene ($PhI(OOCCF_3)_2$) were examined in the reaction, among which IB-OAc was the most efficient with a yield of 80% (Table 1, entries 1−5). Notably, the reaction could not occur without an oxidant (Table 1, entry 6). The screening of solvents showed that CH_2Cl_2 was an optimal solvent (Table 1, entries 7−9). The addition of a base or an acid would decrease the yield of **3aa** (Table 1, entries 10−12). It was unfavorable when the reaction time was shortened to 6 h (Table 1, entries 13 and 14). When the reaction was performed at 40 °C, the yield of **3aa** was slightly decreased (Table 1, entry 15). In addition, the ratios of **1a** to **2a** were tested, and it was found an excess of α-keto acid was beneficial to the reaction (Table 1, entries 16 and 17). Furthermore, blue LED irradition reduced the yield of **3aa**, and shielded light did not affect the yield (Table 1, entries 18 and 19). The optimal conditions for **3aa** are **1a**/**2a** (1:1.5) with IB-OAc in CH_2Cl_2 solvent.

With the optimized conditions in hand, the substrate scope was evaluated. As illustrated in Scheme 2, a variety of

Scheme 2. Scope of Arylamines[a]



[a]Reaction conditions: **1** (0.1 mmol), **2a** (0.15 mmol), IB-OAc (0.1 mmol) in DCM (1.0 mL) for 8 h under air in an oil bath at room temperature. [b]Two mmol scale.

arylamines were tolerated with 2-oxo-2-phenylacetic acid **2a** to generate the benzoxazin-2-one products in moderate to excellent yields (**3ba**−**3ra**). Various aniline-bearing electron-donating (**3ba**−**3da**) or electron-deficient groups (**3fa**−**3ia**) were all suitable substrates for this transformation. It was found that *m*-anisidine only produced *para*-cyclized product **3ca**, probably due to the steric hindrance. It is noteworthy that aryl bromide and iodide could be further functionalized in metal-catalyzed cross-coupling reactions (**3ha**−**3ia**). Strangely, aniline was carried out to give the desired product **3ea** in a

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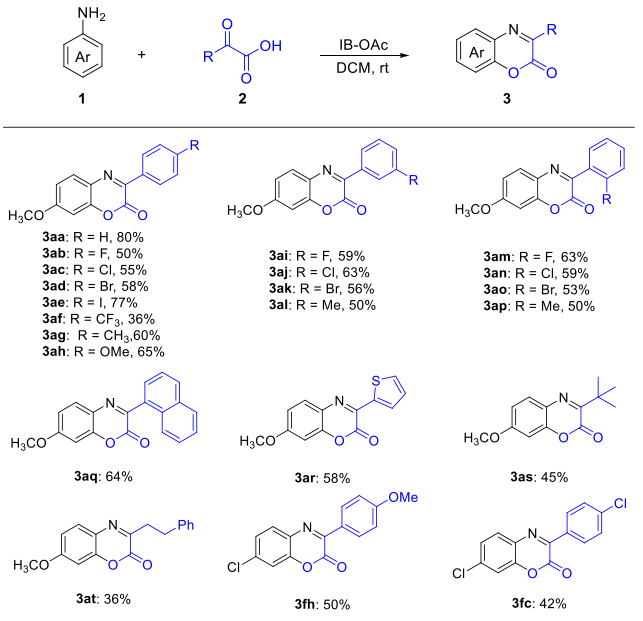
moderate yield. 1-Naphthylamine and 2-naphthylamine also worked well to render the corresponding products **3ja** and **3ka** in 86% and 75% yields, respectively. When 2-naphthylamine was employed in this reaction, regioselective product **3ka** was obtained in a good yield. Fortunately, heteroaryl-substituted 2-thienylamine was also compatible with this reaction (**3la**). Moreover, disubstituted arylamines proved to be compatible with the tandem annulation reaction, providing the corresponding products in good to excellent yields (**3ma**–**3ra**). Note that 3,4-dimethoxylbenzenamine delivered the product **3na** in 90% yield, thus indicating the electronic effect was essential for the reaction. The structure of **3fa** was unambiguously confirmed by X-ray crystal analysis.[18] Luckily, the reaction could be performed by large-scale synthesis and yielded the product **3na** in 72% yield.

The scope of α-oxocarboxylic acids was then tested in the reaction with 4-methoxyaniline or 4-chloroaniline, as shown in Scheme 3. This reaction proceeded smoothly with electron-

Scheme 3. Scope of Arylamines and α-Keto Acids[a]

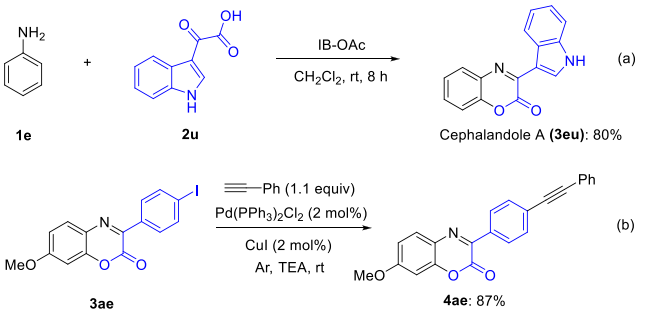


[a]Reaction conditions: **1** (0.1 mmol), **2** (0.15 mmol), IB-OAc (0.1 mmol) in DCM (1.0 mL) for 8 h under air in an oil bath at room temperature.

deficient groups such as fluoro, chloro, bromo, iodo, and trifluoromethyl groups (**3ab**–**3af**, **3ai**–**3ak**, **3am**–**3ao**), likewise electron-rich groups (**3ag**, **3ah**, **3al**, **3ap**). The reaction was tolerable with various functional groups, whether *p*-substituted phenylglyoxylic acids (**3ab**–**3ah**), *m*-substituted phenylglyoxylic acids (**3ai**–**3al**), or *o*-substituted phenylglyoxylic acids (**3am**–**3ap**), providing the corresponding benzoxazin-2-ones in moderate to good yields. It indicated that the steric hindrances of the substituents on the ketoacids were negligible in the reaction. When α-naphthyloxoacetic acid was employed in this reaction, the desired product **3aq** was achieved in 64% yield. While, in Duan's work,[4b] only a trace amount of product was detected. To our delight, the heterocylic substituted 2-thienylglyoxylic acid was also compatible in the reaction, albeit in a relatively low yield (**3ar**). Apart from aryl groups, this reaction was also applicable for alkyl-substituted substrates and yielded the corresponding **3as** and **3at** in moderate yields. In addition, 4-chloroaniline reacted successfully with phenylglyoxylic acid bearing am electron-donating (**3fh**) or electron-withdrawing group (**3fc**). These results implied that this annulation reaction can be effective in elaborating the benzoxazin-2-one library.

Cephalandole A is known to be an important natural product.[4a,c] The target molecule **3eu** can be easily synthesized in 80% yield from aniline **1e** and 3-indolyloxoacetic acid **2u** via an HIR-promoted radical oxidative C–H annulation reaction (Scheme 4a). Furthermore, the synthetic utility of the product

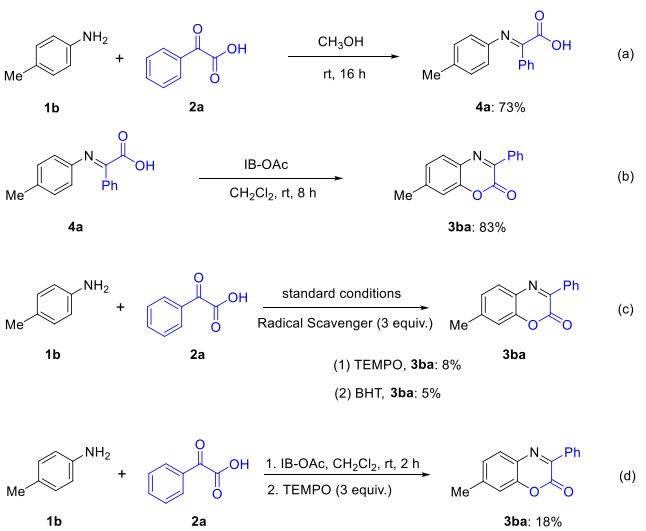
Scheme 4. Synthesis of Natural Product Cephalandole A and Late-Stage Modifications of Benzoxazin-2-one



was demonstrated for the construction of more highly functionalized benzoxazin-2-one. The **4ae** product was prepared through the classic Sonogashira reaction with a terminal alkyne in 87% yield (Scheme 4b).

Several control experiments were carried out to gain insight into the reaction mechanism (Scheme 5). The control

Scheme 5. Control Experiments



experiment indicated that HIR was necessary for this reaction (Table 1, entry 6). When *p*-toluidine **1b** was subjected to the reaction with phenylglyoxylic acid **2a** without IB-OAc in methanol, imino intermediate **4a** was obtained in 73% yield (Scheme 5a). To our delight, **4a** could be transformed into **3ba** product under the optimal conditions (Scheme 5b). These results suggested that imino acetic acid was involved in the reaction. Under the standard conditions, the formation of

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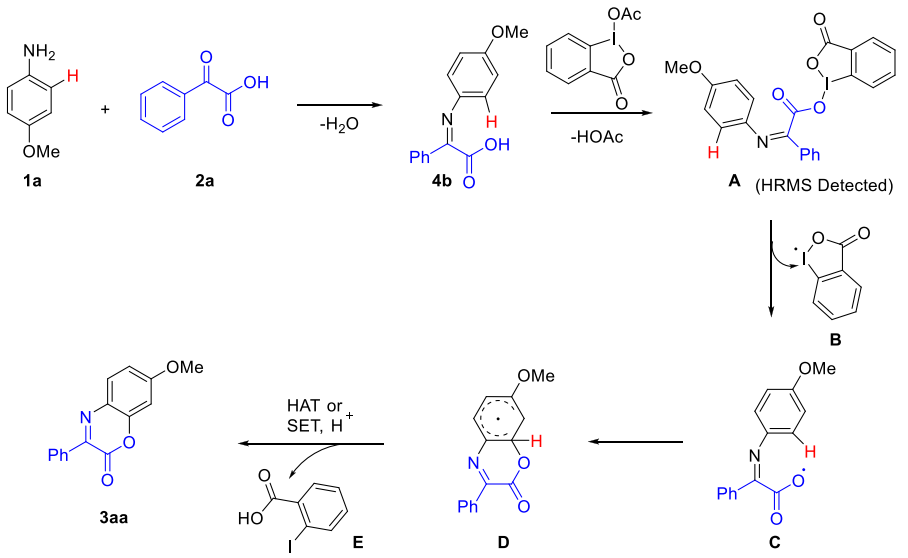
Scheme 6. Possible Reaction Mechanism



product **3ba** was largely suppressed in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or butylated hydroxytoluene (BHT) as a radical scavenger (Scheme 5c). Additionally, the yield of **3ba** was still reduced to 18%, when the free radical inhibitor TEMPO was added after the reaction had proceeded for 2 h, as shown in Scheme 5d. These experiments inferred that this transformation undergoes a radical process.

Based on the mechanistic investigations above, a possible reaction pathway for this radical oxidative C−H annulation process was depicted in Scheme 6. Initially, the condensation of primary amine **1a** with α-keto acid **2a** afforded the intermediate α-iminoacid **4b**.[14] Next, transesterification of BI-OAc with α-iminoacids **4b** generated intermediate **A** with the release of HOAc, and homolytic cleavage of **A** achieved iodanyl radical **B**[19] and carboxyl radical **C**.[17] Subsequently, intermediate **D** was afforded through the intramolecular free radical addition of a carboxyl radical to a phenyl ring. Finally, intermediate **D** oxidized to product **3aa** via a hydrogen atom abstraction (HAT) or SET/deprotonation processes, along with the formation of *o*-iodobenzoic acid. It is important to note that intermediate **A** was detected by HRMS.

In summary, we have explored an efficient tandem condensation and C(sp^2)−H lactonization reaction for the synthesis of benzoxazin-2-ones from arylamines and α-keto acids. A wide range of lactone compounds was constructed in moderate to excellent yields via hypervalent iodine(III) as the oxidant and radical initiator under room temperature. The advantages of this transformation include catalyst and additive-free, direct C(sp^2)−H lactonization without decarboxylation, readily accessible substrates, good functional group tolerance, operational simplicity, etc. Further studies on the detailed reaction mechanism and the application of HIRs are currently ongoing in our laboratory.

EXPERIMENTAL SECTION

General Information. Melting points were investigated using a melting point instrument and are uncorrected. ^{1}H and ^{13}C{^{1}H} NMR spectra were obtained on a 400 or 500 MHz for ^{1}H NMR and 100 or 125 MHz for ^{13}C{^{1}H} NMR. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively, chloroform is solvent with TMS as the internal standard unless otherwise noted. Mass spectra were recorded on a GC−MS spectrometer at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter: 0.25 mm, length: 30 m). High-resolution mass spectra (HRMS) (TOF) were measured using electrospray ionization (ESI) mass spectrometry. Silica gel (300−400 mesh) was used for flash column chromatography, eluting (unless otherwise stated) with an ethyl acetate/petroleum ether (PE) (60−90 °C) mixture.

The arylamines **1a−1r** and α-ketoacids **2s** and **2t** were commercially available from Sigma-Aldrich China. Substituted α-ketoacids **2a−2r** and **2u** were prepared using the literature procedure.[20,11a] The typical experimental procedures for the preparation of starting materials and the characterization data for new compounds are given below.

*General Procedure for the Preparation of Substituted α-Keto Acids (**2a−2r** and **2u**)..*[20,11a] Methyl ketones (5 mmol), SeO_2 (6 mmol), and 20 mL of pyridine were added to a 50 mL round-bottom flask. The reaction mixture was stirred at 110 °C for 1 h in an oil bath, and then the temperature was reduce to 90 °C for 4 h. The desired products were isolated by flash chromatography on silica gel to give α-ketoacids **2** in 65−90% yields.

General Procedure for the Synthesis of Hypervalent Iodine.[21] *Synthesis of 1-Hydroxy-1,2-benziodoxol-3-(1H)-one.* $NaIO_4$ (7.24 g, 33.8 mmol), 2-iodobenzene (I) (8 g, 32.2 mmol), and 50 mL of 30% (v/v) AcOH were added to a 100 mL round-bottom flask. The reaction mixture was refluxed for 4 h in a preheated oil bath with vigorous stirring. The reaction mixture was then diluted with 180 mL of cold water and cooled to room temperature, and the crude was collected via suction filtration. The crude white solid was washed with cold water (×3) and acetone (×3) and air-dried in the dark overnight to afford 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (7.6 g, 90% yield).

Synthesis of 1-Acetoxy-1,2-benziodoxol-3-(1H)-one. 1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (5.00 g, 18.9 mmol) and Ac_2O were refluxed in a preheated oil bath until the solution became clear. The reaction mixture was then cooled slowly to −20 °C for 4 h using a dry ice/ethylene glycol/ethanol (9:1) bath. The solution was decanted, and the white solid (III) was dried under a vacuum with stirring for 24 h to afford 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (3.9 g, 67% yield).

Synthesis of 1-Trifluoromethyl-1,2-benziodoxol-3-(1H)-one. 1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one(5.0 g, 16.3 mmol) was dissolved in 50 mL of dry MeCN (under Ar). To the mixture were added trimethyl(trifluoromethyl)silane (3.6 mL, 24.4 mmol) and cesium fluoride (0.04 g, 0.26 mmol) under argon. The reaction mixture was then stirred vigorously at room temperature for 22 h. The solvent was removed using a rotovap, and the mixture was purified by column chromatography (CH_2Cl_2/MeOH (15:1)) to afford 1-

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trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one as a pure white solid (3.6 g, 70% yield).

General Procedure for the Synthesis of 2H-Benzo[b][1,4]oxazin-2-ones. A mixture of arylamine (0.1 mmol), α-keto acid (0.15 mmol), and IB-OAc (30.6 mg, 1 equiv) in DCM (1.0 mL) was stirred in the air in an oil bath at room temperature for 8 h. After the reaction was finished, water (5 mL) was added, and the solution was extracted with ethyl acetate (3 × 5 mL), and the combined extract was dried with anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography to give the pure sample.

Large-Scale Synthesis. A mixture of 3,4-dimethoxyaniline (306 mg, 2 mmol), 2-oxo-2-phenylacetic acid (450 mg, 3 mmol), and IB-OAc (612 mg, 1 equiv) in DCM (5.0 mL) was stirred in the air in an oil bath at room temperature for 8 h. After the reaction was finished, water (10 mL) was added, the solution was extracted with ethyl acetate (3 × 10 mL), and the combined extract was dried with anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography to give **3na** (408 mg, 72%).

7-Methoxy-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3aa***): yellow solid, 20.2 mg, 80% yield; mp 129−130 °C; R_f = 0.21 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32−8.24 (m, 2H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.47 (dd, *J* = 10.0, 5.0 Hz, 3H), 6.94 (dd, *J* = 8.9, 2.6 Hz, 1H), 6.79 (d, *J* = 2.5 Hz, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.2, 152.5, 148.1, 147.2, 134.4, 130.8, 130.4, 129.1, 128.3, 126.3, 113.3, 100.1, 56.00; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{12}NO_3$ [M + H]$^+$ 254.0812, found 254.0824.

7-Methyl-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ba***):[4b] yellow solid, 13.3 mg, 56% yield; mp 117−118 °C; R_f = 0.38 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34−8.29 (m, 2H), 7.71 (d, *J* = 8.1 Hz, 1H), 7.54−7.46 (m, 3H), 7.19 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.12 (s, 1H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.5, 149.6, 146.4, 142.6, 134.3, 131.2, 129.8, 129.3, 129.0, 128.3, 126.7, 116.2, 21.8.

6-Methoxy-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ca***): yellow solid, 15.2 mg, 60% yield; mp 121−122 °C; R_f = 0.25 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36−8.29 (m, 2H), 7.56−7.47 (m, 3H), 7.31 (d, *J* = 2.9 Hz, 1H), 7.26 (d, *J* = 1.9 Hz, 1H), 7.10 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.1, 152.5, 151.1, 140.8, 134.2, 132.1, 131.4, 129.5, 128.4, 119.4, 116.8, 111.2, 55.9; HRMS (ESI) *m*/*z* calcd for $C_{15}H_{12}NO_3$ [M + H]$^+$ 254.0812, found 254.0813.

7-Phenoxy-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3da***): yellow solid, 17.6 mg, 56% yield; mp 121−122 °C; R_f = 0.30 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35−8.27 (m, 2H), 7.78 (dd, *J* = 9.5, 5.1 Hz, 1H), 7.55−7.40 (m, 5H), 7.23 (dd, *J* = 4.8, 3.7 Hz, 1H), 7.14−7.09 (m, 2H), 7.01 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.84 (d, *J* = 2.6 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 160.6, 155.2, 152.2, 148.2, 147.8, 134.3, 131.1, 130.6, 130.2, 129.2, 128.4, 127.4, 125.2, 120.4, 115.4, 104.3; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{14}NO_3$ [M + H]$^+$ 316.0968, found 316.0981.

3-Phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ea***):[4b] white solid, 10.3 mg, 46% yield; mp 109−110 °C; R_f = 0.30 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.83 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.57−7.44 (m, 4H), 7.37 (td, *J* = 7.8, 1.2 Hz, 1H), 7.31 (dd, *J* = 8.2, 1.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.2, 150.8, 146.5, 134.1, 131.7, 131.4, 131.1, 129.5, 129.4, 128.4, 125.6, 116.2.

7-Chloro-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3fa***): yellow solid, 17.5 mg, 68% yield; mp 103−104 °C; R_f = 0.51 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34−8.29 (m, 2H), 7.77−7.72 (m, 1H), 7.56−7.51 (m, 1H), 7.48 (tt, *J* = 8.4, 1.5 Hz, 2H), 7.36−7.29 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.4, 150.5, 146.7, 136.7, 133.8, 131.6, 130.2, 130.1, 129.4, 128.4, 126.1, 116.4; HRMS (ESI) *m*/*z* calcd for $C_{14}H_9ClNO_2$ [M + H]$^+$ 258.0316, found 258.0325.

7-Fluoro-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ga***): yellow solid, 13.7 mg, 57% yield; mp =142−143 °C; R_f = 0.65 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34−8.28 (m, 2H), 7.83 (dd, *J* = 8.9, 5.8 Hz, 1H), 7.57−7.46 (m, 3H), 7.12 (ddd, *J* = 8.8, 8.2, 2.7 Hz, 1H), 7.05 (dd, *J* = 8.4, 2.7 Hz, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 163.6 (d, *J* = 252.5 Hz), 151.6, 149.5 (d, *J* = 3.7 Hz), 147.5 (d, *J* = 12.5 Hz), 133.9, 131.5, 130.9 (d, *J* = 10.5 Hz), 129.4, 128.6 (d, *J* = 2.9 Hz), 128.4, 113.5 (d, *J* = 23.3 Hz), 103.7(d, *J* = 26.3 Hz); HRMS (ESI) *m*/*z* calcd for $C_{14}H_9FNO_2$ [M + H]$^+$ 242.0612, found 242.0623.

7-Bromo-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ha***): brown solid, 22.3 mg, 74% yield; mp 121−122 °C; R_f = 0.52 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32−8.27 (m, 2H), 7.63 (td, *J* = 8.1, 2.1 Hz, 1H), 7.54−7.49 (m, 1H), 7.48−7.39 (m, 4H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 151.3, 150.7, 146.7, 133.8, 131.7, 130.6, 130.4, 129.5, 129.0(d, *J* = 1.9 Hz), 128.4, 124.6, 119.4; HRMS (ESI) *m*/*z* calcd for $C_{14}H_9BrNO_2$ [M + H]$^+$ 301.9811, found 301.9823.

7-Iodo-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ia***): yellow solid, 27.6 mg, 79% yield; mp 136−137 °C; R_f = 0.43 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dt, *J* = 8.6, 2.0 Hz, 2H), 7.70 (dt, *J* = 4.8, 1.7 Hz, 2H), 7.56−7.46 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.4, 151.1, 146.5, 135.0, 133.9, 131.8, 131.2, 130.5, 129.5, 128.5, 125.3, 96.1; HRMS (ESI) *m*/*z* calcd for $C_{14}H_9INO_2$ [M + H]$^+$ 349.9672, found 349.9678.

2-Phenyl-3H-naphtho[2,1-b][1,4]oxazin-3-one (***3ja***):[22] yellow solid, 23.5 mg, 86% yield; mp 168−169 °C; R_f = 0.39 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (d, *J* = 8.4 Hz, 1H), 8.53 (dd, *J* = 7.6, 1.9 Hz, 2H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.64−7.50 (m, 4H), 7.47−7.38 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.7, 148.4, 144.8, 134.5, 132.4, 131.4, 131.1, 130.5, 129.5, 128.4, 128.3, 128.1, 126.7, 126.4, 122.9, 115.7.

3-Phenyl-2H-naphtho[1,2-b][1,4]oxazin-2-one (***3ka***):[22] yellow solid, 20.5 mg, 75% yield; mp 157−158 °C; R_f = 0.53 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53−8.46 (m, 1H), 8.43 (ddd, *J* = 5.5, 4.3, 2.6 Hz, 2H), 7.93−7.87 (m, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.70−7.62 (m, 2H), 7.60−7.49 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.3, 149.8, 142.5, 134.2, 131.3, 129.4, 128.7, 128.4, 127.9, 127.8, 127.2, 125.6, 125.4, 122.4, 122.0; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{12}NO_2$ [M + H]$^+$ 274.0863, found 274.0866.

2-Phenyl-3H-thieno[2,3-b][1,4]oxazin-3-one (***3la***): yellow solid, 17.9 mg, 78% yield; mp 127−128 °C; R_f = 0.37 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29−8.21 (m, 2H), 7.53−7.45 (m, 3H), 7.22 (d, *J* = 6.0 Hz, 1H), 7.01 (d, *J* = 5.9 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.3, 151.4, 146.3, 134.2, 132.1, 131.0, 128.9, 128.4, 122.6, 116.6; HRMS (ESI) *m*/*z* calcd for $C_{12}H_8NO_2S$ [M + H]$^+$ 230.0270, found 230.0279.

6,7-Dimethyl-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3ma***): yellow solid, 15.6 mg, 62% yield; mp 136−137 °C; R_f = 0.39 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36−8.25 (m, 2H), 7.59 (s, 1H), 7.49 (d, *J* = 6.9 Hz, 3H), 7.09 (s, 1H), 2.37 (s, 3H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 152.8, 149.6, 144.6, 141.4, 134.5, 134.4, 131.0, 129.9, 129.4, 129.3 128.3, 116.5, 20.3, 19.3; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{14}NO_2$ [M + H]$^+$ 252.1019, found 252.1021.

6,7-Dimethoxy-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3na***): yellow solid, 25.5 mg, 90% yield; m.p 155−156 °C; R_f = 0.29 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (t, *J* = 2.7 Hz, 2H), 7.49 (dd, *J* = 6.0, 4.6 Hz, 3H), 7.26 (d, *J* = 1.3 Hz, 1H), 6.81 (s, 1H), 3.97 (s, 3H), 3.96 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 152.8, 152.3, 147.5, 147.2, 142.0, 134.5, 130.8, 129.1, 128.3, 125.7, 109.8, 98.6, 56.6, 56.4; HRMS (ESI) *m*/*z* calcd for $C_{16}H_{14}NO_4$ [M + H]$^+$ 284.0917, found 284.0929.

6-Fluoro-5-methyl-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (***3oa***): yellow solid, 14.0 mg, 55% yield; mp 140−141 °C; R_f = 0.51 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44−8.36 (m, 2H), 7.56−7.48 (m, 3H), 7.21 (t, *J* = 8.8 Hz, 1H), 7.14 (d, *J* = 4.8 Hz, 1H), 2.62 (d, *J* = 2.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.0 (d, *J* = 240.1 Hz), 152.0, 149.7, 143.1, 134.2, 131.6, 130.7 (d, *J* = 9.2 Hz), 129.6, 128.4, 124.7 (d, *J* = 19.2 Hz), 117.9 (d, *J* = 26.0 Hz), 113.6 (d, *J* = 9.3 Hz), 9.2 (d, *J* = 3.5 Hz); HRMS (ESI) *m*/*z* calcd for $C_{15}H_{11}FNO_2$ [M + H]$^+$ 256.0768, found 256.0771.

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*7-Chloro-6-methyl-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (**3pa**):* yellow solid, 16.3 mg, 60% yield; mp 181−182 °C; R_f = 0.43 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35−8.28 (m, 2H), 7.83 (s, 1H), 7.57−7.45 (m, 3H), 7.19 (s, 1H), 2.49 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 152.0, 150.7, 144.9, 140.1, 133.9, 131.6, 131.1, 130.5, 129.5, 128.9, 128.4, 117.7, 20.6; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_2$ $[M + H]^+$ 272.0473, found 272.0482.

*7-Chloro-5-methyl-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (**3qa**):* white solid, 14.9 mg, 55% yield; m.p 160−161 °C; R_f = 0.53 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41−8.33 (m, 2H), 7.57−7.45 (m, 3H), 7.22 (d, J = 1.3 Hz, 1H), 7.16 (d, J = 1.9 Hz, 1H), 2.67 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.7, 148.5, 147.0, 140.1, 136.4, 134.2, 131.5, 129.5, 128.9, 128.4, 127.0, 114.0, 16.9; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_2$ $[M + H]^+$ 272.0473, found 272.0478.

*7-Bromo-5-methyl-3-phenyl-2H-benzo[b][1,4]oxazin-2-one (**3ra**):* brown solid, 18.3 mg, 58% yield; mp 170−171 °C; R_f = 0.51 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40−8.34 (m, 2H), 7.54−7.45 (m, 3H), 7.36 (dd, J = 1.9, 0.7 Hz, 1H), 7.30 (d, J = 1.6 Hz, 1H), 2.66 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.6, 148.7, 146.9, 140.3, 134.2, 131.5, 129.8, 129.5, 129.2, 128.4, 124.4, 117.0, 16.8; HRMS (ESI) m/z calcd for $C_{15}H_{11}BrNO_2$ $[M + H]^+$ 315.9968, found 315.9971.

*3-(4-Fluorophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ab**):* yellow solid, 13.6 mg, 50% yield; mp 149−150 °C; R_f = 0.20 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (ddd, J = 7.1, 5.3, 2.5 Hz, 2H), 7.71 (d, J = 8.9 Hz, 1H), 7.18−7.11 (m, 2H), 6.94 (dd, J = 8.9, 2.7 Hz, 1H), 6.78 (d, J = 2.6 Hz, 1H), 3.89 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 164.5 (d, J = 250.8 Hz), 162.2, 152.5, 148.0, 145.8, 131.4 (d, J = 8.7 Hz), 130.6 (d, J = 3.0 Hz), 130.3, 126.2, 115.4(d, J = 21.4 Hz), 113.4, 100.1, 56.0; HRMS (ESI) m/z calcd for $C_{15}H_{11}FNO_3$ $[M + H]^+$ 272.0718, found 272.0728.

*3-(4-Chlorophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ac**):* yellow solid, 15.8 mg, 55% yield; mp 178−179 °C; R_f = 0.25 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 7.7 Hz, 2H), 7.69 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 7.7 Hz, 2H), 6.93 (d, J = 8.1 Hz, 1H), 6.76 (s, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.4, 152.3, 148.1, 145.6, 137.0, 132.8, 130.4, 130.3, 128.5, 126.1, 113.5, 100.0, 56.0; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_3$ $[M + H]^+$ 288.0422, found 288.0434.

*3-(4-Bromophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ad**):* yellow solid, 19.2 mg, 58% yield; mp 141−142 °C; R_f = 0.40 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26−8.19 (m, 2H), 7.73 (d, J = 8.9 Hz, 1H), 7.64−7.57 (m, 2H), 6.96 (dd, J = 8.9, 2.7 Hz, 1H), 6.80 (d, J = 2.7 Hz, 1H), 3.91 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.4, 152.4, 148.2, 145.8, 133.3, 131.6, 130.6, 130.4, 126.2, 125.7, 113.5, 100.1, 56.0; HRMS (ESI) m/z calcd for $C_{15}H_{11}BrNO_3$ $[M + H]^+$ 331.9917, found 331.9930.

*3-(4-Iodophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ae**):* yellow solid, 29.2 mg, 77% yield; mp 170−171 °C; R_f = 0.25 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−8.01 (m, 2H), 7.82−7.77 (m, 2H), 7.70 (d, J = 8.9 Hz, 1H), 6.93 (dd, J = 8.9, 2.7 Hz, 1H), 6.76 (d, J = 2.6 Hz, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.4, 152.3, 148.1, 145.9, 137.5, 133.8, 130.6, 130.4, 126.2, 113.5, 100.0, 98.1, 56.1; HRMS (ESI) m/z calcd for $C_{15}H_{11}INO_3$ $[M + H]^+$ 379.9778, found 379.9782.

*7-Methoxy-3-(4-(trifluoromethyl)phenyl)-2H-benzo[b][1,4]-oxazin-2-one (**3af**):* yellow solid, 11.6 mg, 36% yield; mp 140−141 °C; R_f = 0.38 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 8.2 Hz, 2H), 7.74 (dd, J = 12.3, 8.6 Hz, 3H), 6.97 (dd, J = 8.9, 2.7 Hz, 1H), 6.80 (d, J = 2.6 Hz, 1H), 3.91 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.8, 152.3, 148.3, 145.4, 137.6, 132.2 (q, J = 32.0 Hz), 130.7, 129.4, 126.2, 125.2 (q, J = 4.0 Hz), 123.9 (q, J = 271.0 Hz), 113.7, 100.1, 56.1; HRMS (ESI) m/z calcd for $C_{16}H_{11}F_3NO_3$ $[M + H]^+$ 322.0686, found 322.0690.

*7-Methoxy-3-(p-tolyl)-2H-benzo[b][1,4]oxazin-2-one (**3ag**):* yellow solid, 16.0 mg, 60% yield; mp 138−139 °C; R_f = 0.25 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 8.9 Hz, 1H), 7.28 (d, J = 8.1 Hz, 2H), 6.92 (dd, J = 8.9, 2.6 Hz, 1H), 6.77 (d, J = 2.4 Hz, 1H), 3.88 (s, 3H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.9, 152.6, 148.0, 147.1, 141.3, 131.7, 130.2, 129.1, 126.3, 113.2, 100.0, 56.0, 21.5; HRMS (ESI) m/z calcd for $C_{16}H_{14}NO_3$ $[M + H]^+$ 268.0968, found 268.0971.

*7-Methoxy-3-(4-methoxyphenyl)-2H-benzo[b][1,4]oxazin-2-one (**3ah**):* yellow solid, 18.4 mg, 65% yield; m.p 137−138 °C; R_f = 0.30 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35−8.32 (m, 2H), 7.70 (d, J = 8.9 Hz, 1H), 7.00−6.97 (m, 2H), 6.93 (dd, J = 8.9, 2.7 Hz, 1H), 6.78 (d, J = 2.6 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 161.9, 161.7, 152.7, 147.8, 146.5, 130.9, 130.0, 127.1, 126.4, 113.8, 113.2, 100.0, 56.0, 55.4; HRMS (ESI) m/z calcd for $C_{16}H_{14}NO_4$ $[M + H]^+$ 284.0917, found 284.0929.

*3-(3-Fluorophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ai**):* yellow solid, 16.0 mg, 59% yield; mp 126−127 °C; R_f = 0.39 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 7.9 Hz, 1H), 8.05 (dd, J = 10.5, 1.8 Hz, 1H), 7.70 (d, J = 8.9 Hz, 1H), 7.51−7.35 (m, 1H), 7.17 (td, J = 8.2, 2.5 Hz, 1H), 6.93 (dd, J = 8.9, 2.6 Hz, 1H), 6.76 (d, J = 2.6 Hz, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.6 (d, J = 243.8 Hz), 162.5, 152.2, 148.2, 145.4 (d, J = 3.8 Hz), 136.4 (d, J = 7.5 Hz), 130.5, 129.8 (d, J = 7.5 Hz), 126.08, 124.8 (d, J = 3.8 Hz), 117.7 (d, J = 21.3 Hz), 116.0 (d, J = 23.8 Hz), 113.5, 100.0, 56.0; HRMS (ESI) m/z calcd for $C_{15}H_{11}FNO_3$ $[M + H]^+$ 272.0718, found 272.0729.

*3-(3-Chlorophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3aj**):* yellow solid, 18.1 mg, 63% yield; mp 137−138 °C; R_f = 0.40 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (t, J = 1.7 Hz, 1H), 8.26−8.21 (m, 1H), 7.72 (d, J = 8.9 Hz, 1H), 7.49−7.36 (m, 2H), 6.94 (dd, J = 8.9, 2.6 Hz, 1H), 6.78 (d, J = 2.6 Hz, 1H), 3.89 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.6, 152.2, 148.2, 145.4, 136.0, 134.4, 130.8, 130.5, 129.5, 129.0, 127.3, 126.1, 113.5, 100.1, 56.0; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_3$ $[M + H]^+$ 288.0422, found 288.0433.

*3-(3-Bromophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ak**):* yellow solid, 18.5 mg, 56% yield; mp 81−82 °C; R_f = 0.39 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (t, J = 1.8 Hz, 1H), 8.33−8.26 (m, 1H), 7.74 (d, J = 8.9 Hz, 1H), 7.61 (ddd, J = 7.9, 1.8, 0.9 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 6.96 (dd, J = 8.9, 2.7 Hz, 1H), 6.79 (d, J = 2.6 Hz, 1H), 3.90 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 162.6, 152.2, 148.2, 145.3, 136.3, 133.7, 131.8, 130.6, 129.8, 127.8, 126.2, 122.5, 113.6, 100.1, 56.1; HRMS (ESI) m/z calcd for $C_{15}H_{11}BrNO_3$ $[M + H]^+$ 331.9917, found 331.9930.

*7-Methoxy-3-(m-tolyl)-2H-benzo[b][1,4]oxazin-2-one (**3al**):* yellow oil, 13.4 mg, 50% yield; mp 152−153 °C; R_f = 0.27 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 6.8 Hz, 2H), 7.74 (d, J = 8.9 Hz, 1H), 7.33 (dd, J = 19.9, 7.9 Hz, 2H), 6.94 (dd, J = 8.9, 2.6 Hz, 1H), 6.79 (d, J = 2.6 Hz, 1H), 3.89 (s, 3H), 2.44 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.1, 152.5, 148.1, 147.4, 138.0, 134.4, 131.7, 130.3, 129.5, 128.2, 126.4, 126.3, 113.3, 100.1, 56.0, 21.5; HRMS (ESI) m/z calcd for $C_{16}H_{14}NO_3$ $[M + H]^+$ 268.0968, found 268.0976.

*3-(2-Fluorophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3am**):* white solid, 17.1 mg, 63% yield; mp 174−175 °C; R_f = 0.59 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.9 Hz, 1H), 7.68 (td, J = 7.4, 1.7 Hz, 1H), 7.49 (tdd, J = 8.2, 5.1, 1.8 Hz, 1H), 7.28 (dd, J = 5.8, 4.8 Hz, 1H), 7.23−7.16 (m, 1H), 6.96 (dd, J = 8.9, 2.7 Hz, 1H), 6.83 (d, J = 2.6 Hz, 1H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.7, 160.7 (d, J = 252.9 Hz), 152.0, 148.4, 146.7, 132.1 (d, J = 8.4 Hz), 131.0 (d, J = 2.5 Hz), 130.6, 126.2, 124.2 (d, J = 3.6 Hz), 123.2 (d, J = 13.6 Hz), 116.3(d, J = 21.6 Hz), 113.4, 100.3, 56.1; HRMS (ESI) m/z calcd for $C_{15}H_{11}FNO_3$ $[M + H]^+$ 272.0718, found 272.0725.

*3-(2-Chlorophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3an**):* yellow solid, 16.9 mg, 59% yield; mp 151−152 °C; R_f = 0.58

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(petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 8.9 Hz, 1H), 7.54 (dd, J = 7.3, 1.8 Hz, 1H), 7.49 (dd, J = 7.9, 1.0 Hz, 1H), 7.41 (dtd, J = 16.2, 7.4, 1.5 Hz, 2H), 6.96 (dd, J = 8.9, 2.6 Hz, 1H), 6.84 (d, J = 2.6 Hz, 1H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.7, 152.0, 149.3, 148.6, 134.2, 133.4, 131.1, 130.8, 130.6, 130.0, 126.9, 125.9, 113.4, 100.5, 56.1; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_3$ [M + H]$^+$ 288.0422, found 288.0434.

*3-(2-Bromophenyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3ao**):* white solid, 17.5 mg, 53% yield; mp 141−142 °C; R_f = 0.55 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.9 Hz, 1H), 7.68 (dd, J = 8.0, 0.9 Hz, 1H), 7.51 (dd, J = 7.6, 1.7 Hz, 1H), 7.44 (d, J = 1.0 Hz, 1H), 7.34 (td, J = 7.8, 1.8 Hz, 1H), 6.96 (dd, J = 8.9, 2.7 Hz, 1H), 6.84 (d, J = 2.6 Hz, 1H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.7, 151.9, 150.4, 148.6, 136.0, 133.1, 131.2, 130.8, 130.6, 127.5, 125.8, 122.5, 113.4, 100.5, 56.1; HRMS (ESI) m/z calcd for $C_{15}H_{11}BrNO_3$ [M + H]$^+$ 331.9917, found 331.9930.

*7-Methoxy-3-(o-tolyl)-2H-benzo[b][1,4]oxazin-2-one (**3ap**):* white solid, 13.4 mg, 50% yield; mp 147−148 °C; R_f = 0.34 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.9 Hz, 1H), 7.52−7.48 (m, 1H), 7.37 (dd, J = 10.8, 4.1 Hz, 1H), 7.32−7.27 (m, 2H), 6.96 (dd, J = 8.9, 2.6 Hz, 1H), 6.83 (d, J = 2.6 Hz, 1H), 3.91 (s, 3H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.3, 152.7, 151.2, 148.3, 137.1, 134.3, 130.9, 130.4, 129.9, 129.5, 126.1, 125.8, 113.2, 100.4, 56.1, 20.1; HRMS (ESI) m/z calcd for $C_{16}H_{14}NO_3$ [M + H]$^+$ 268.0968, found 268.0971.

*7-Methoxy-3-(naphthalen-1-yl)-2H-benzo[b][1,4]oxazin-2-one (**3aq**):* yellow solid, 19.4 mg, 64% yield; mp 193−194 °C; R_f = 0.58 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08−8.01 (m, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.96−7.88 (m, 1H), 7.80 (dd, J = 21.1, 7.9 Hz, 2H), 7.64−7.47 (m, 3H), 7.01−6.95 (m, 1H), 6.87 (s, 1H), 3.92 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 162.5, 153.1, 150.0, 148.4, 133.9, 131.7, 131.2, 130.8, 130.5, 128.7, 128.3, 126.9, 126.2, 124.9 (d, J = 10 Hz), 113.3, 100.4, 56.1; HRMS (ESI) m/z calcd for $C_{19}H_{14}NO_3$ [M + H]$^+$ 304.0968, found 304.0982.

*7-Methoxy-3-(thiophen-2-yl)-2H-benzo[b][1,4]oxazin-2-one (**3ar**):* green solid, 15.0 mg, 58% yield; mp 167−168 °C; R_f = 0.25 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (dd, J = 3.8, 1.0 Hz, 1H), 7.69 (d, J = 8.9 Hz, 1H), 7.55 (dd, J = 5.0, 1.0 Hz, 1H), 7.16 (dd, J = 5.0, 3.9 Hz, 1H), 6.94 (dd, J = 8.9, 2.7 Hz, 1H), 6.80 (d, J = 2.6 Hz, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.7, 151.7, 147.6, 142.3, 138.9, 132.1, 131.3, 129.8, 128.4, 126.1, 113.4, 100.2, 56.0; HRMS (ESI) m/z calcd for $C_{13}H_{10}NO_3S$ [M + H]$^+$ 260.0376, found 260.0388.

*3-(tert-Butyl)-7-methoxy-2H-benzo[b][1,4]oxazin-2-one (**3as**):* yellow solid, 10.5 mg, 45% yield; mp 87−88 °C; R_f = 0.38 (petroleum ether/ethyl acetate = 20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.8 Hz, 1H), 6.88 (dd, J = 8.8, 2.5 Hz, 1H), 6.72 (d, J = 2.5 Hz, 1H), 3.86 (s, 3H), 1.43 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 161.4, 159.0, 151.1, 148.1, 130.0, 125.4, 112.6, 99.9, 55.9, 39.0, 27.7; HRMS (ESI) m/z calcd for $C_{13}H_{16}NO_3$ [M + H]$^+$ 234.1125, found 234.1136.

*7-Methoxy-3-phenethyl-2H-benzo[b][1,4]oxazin-2-one (**3at**):* yellow solid, 10.1 mg, 36% yield; mp 106−107 °C; R_f = 0.33 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, CDCl3) δ 7.64 (d, J = 8.9 Hz, 1H), 7.30 (d, J = 4.6 Hz, 4H), 7.21 (d, J = 4.2 Hz, 1H), 6.91 (dd, J = 8.9, 2.7 Hz, 1H), 6.75 (d, J = 2.7 Hz, 1H), 3.88 (s, 3H), 3.17 (ddd, J = 5.9, 5.3, 2.0 Hz, 2H), 3.10 (ddd, J = 9.0, 5.2, 1.9 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.6, 153.2, 153.1, 147.9, 141.0, 129.7, 128.6, 128.5, 126.2, 125.7, 112.9, 100.4, 56.0, 35.6, 32.3; HRMS (ESI) m/z calcd for $C_{17}H_{16}NO_3$ [M + H]$^+$ 282.1125, found 282.1130.

*8-Chloro-3-(4-methoxyphenyl)-2H-benzo[b][1,4]oxazin-2-one (**3fh**):* yellow solid, 14.4 mg, 50% yield; mp 156−157 °C; R_f = 0.55 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40−8.34 (m, 2H), 7.71 (d, J = 8.5 Hz, 1H), 7.35−7.28 (m, 2H), 7.00−6.95 (m, 2H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 151.7, 149.5, 146.5, 136.0, 131.4, 130.4, 129.8, 126.5, 126.0, 116.3, 113.9, 55.5; HRMS (ESI) m/z calcd for $C_{15}H_{11}ClNO_3$ [M + H]$^+$ 288.0422, found 288.0424.

*7-Chloro-3-(4-chlorophenyl)-2H-benzo[b][1,4]oxazin-2-one (**3fc**):* yellow solid, 12.2 mg, 42% yield; mp 173−174 °C; R_f = 0.73 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.6 Hz, 2H), 7.74 (d, J = 8.5 Hz, 1H), 7.44 (d, J = 8.6 Hz, 2H), 7.40−7.28 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 151.3, 149.1, 146.7, 138.2, 137.1, 132.1, 130.8, 130.2, 130.1, 128.7, 126.3, 116.5; HRMS (ESI) m/z calcd for $C_{14}H_8Cl_2NO_2$ [M + H]$^+$ 291.9927, found 291.9938.

*3-(1H-indol-3-yl)-2H-benzo[b][1,4]oxazin-2-one (**3eu**):*[4a] yellow solid, 21.0 mg, 80% yield; mp 248−249 °C; R_f = 0.38 (petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, DMSO) δ 11.98 (s, 1H), 8.75 (dt, J = 6.3, 2.7 Hz, 1H), 8.70 (s, 1H), 7.89−7.79 (m, 1H), 7.57−7.50 (m, 1H), 7.49−7.38 (m, 3H), 7.30−7.23 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO) δ 152.5, 148.4, 145.3 137.1, 134.2, 132.4, 129.1, 128.2, 126.4, 125.8, 123.5, 123.3, 122.0, 116.4, 112.7, 111.1; HRMS (ESI) m/z calcd for $C_{16}H_{11}N_2O_2$ [M + H]$^+$ 263.0815, found 263.0821.

*7-Methoxy-3-(4-(phenylethynyl)phenyl)-2H-benzo[b][1,4]-oxazin-2-one (**4ae**):* yellow solid, 30.7 mg, 87% yield; mp 168−169 °C; R_f = 0.33 (petroleum ether/ethyl acetate = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38−8.33 (m, 2H), 7.74 (d, J = 8.9 Hz, 1H), 7.64−7.60 (m, 2H), 7.56 (dd, J = 6.5, 3.2 Hz, 2H), 7.39−7.34 (m, 3H), 6.95 (dd, J = 8.9, 2.7 Hz, 1H), 6.80 (d, J = 2.6 Hz, 1H), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.3, 152.5, 148.1, 146.0, 134.0, 131.7, 131.5, 130.4, 129.0, 128.6, 128.4, 126.3, 125.8, 123.0, 113.5, 100.0, 91.9, 89.2, 56.1; HRMS (ESI) m/z calcd for $C_{23}H_{16}NO_3$ [M + H]$^+$ 354.1125, found 354.1127.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01424.

^{1}H and ^{13}C NMR spectra, crystal data, and preparation of starting materials (PDF)

Accession Codes

CCDC 2076545 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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