JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

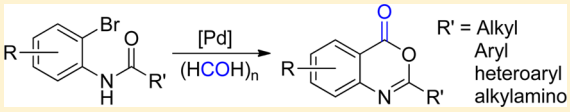
Palladium-Catalyzed Carbonylative Synthesis of Benzoxazinones from *N*-(*o*-Bromoaryl)amides Using Paraformaldehyde as the Carbonyl Source

Wanfang Li and Xiao-Feng Wu*

Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Strasse 29a, 18059 Rostock, Germany

Supporting Information

ABSTRACT: Carbonylation reactions have been widely used in organic synthesis. However, the manipulation of toxic and pressurized carbon monoxide limited their applications in organic laboratories. The search for alternative carbonyl sources as an important method for carbonylative organic synthesis is spreading. Herein, a series of substituted benzoxazinones were synthesized from *N*-(*o*-bromoaryl)amides by palladium-catalyzed carbonylation with paraformaldehyde as the carbonyl source, which is inexpensive, stable, and easy to use. Notably, this is the first example of using paraformaldehyde as the CO source in palladium-catalyzed carbonylative synthesis of heterocycles.

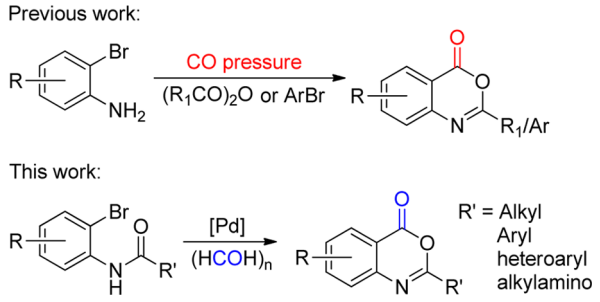


INTRODUCTION

Benzoxazinone derivatives are important skeletons for many physiologically and pharmaceutically active molecules,[1] and their synthesis has attracted much interest from both organic and pharmaceutical chemists.[2] Until now, the cyclizations from anthranilic acids,[3] *N*-acylanthranilic acids,[4] and isocyanate derivatives[5] are the most traditional methods for their synthesis. Several other methods have also been reported; however, they are still lacking in simplicity and generality.[6]

Palladium-catalyzed carbonylation facilitated the transformation of (hetero)aryl halides to various benzoic acid derivatives,[7] which may combine with the subsequent intramolecular condensation reactions to form many heterocyclic compounds.[8] This strategy has been used in the synthesis of benzoxazinones by several groups.[9] Our group also reported the synthesis of 2-alkyl- and aryl-substituted benzoxazinones from 2-bromoanilines by palladium-catalyzed carbonylations using CO gas.[10] Although carbon monoxide (CO) is one of the most cheap and readily available C1 sources, its toxicity and the need for high-pressure equipment limited the synthetic applications. Therefore, the search for some alternative sources of CO is an effective supplement to the carbonylation reactions.[11] For example, Skrydstrup et al. reported a series of CO-free carbonylation reactions using *ex*-generated carbon monoxide.[12] We had recently made some progress in the utilization of CO surrogates like aryl formates in carbonylation reactions.[13] In 2013, we succeeded in obtaining the 2-aminobenzoxazinones using $[Mo(CO)_6]$ as the solid carbonyl source; however, large amounts of metal waste will be generated.[14] Compared to many other CO surrogates, paraformaldehyde is more desirable because it is cheap and stable and exhibits low toxicity. The employment of paraformaldehyde had been explored in several Rh-catalyzed CO-free carbonylation reactions of alkynes,[15] but little success in palladium-catalyzed carbonylation of aryl halides has been reported.[16] Herein, we report the first example of palladium-catalyzed carbonylation of *N*-(*o*-bromoaryl)amides to form various benzoxazinone derivatives using paraformaldehyde as the CO source (Scheme 1).

Scheme 1. Synthesis of Benzoxazinones by Palladium-Catalyzed Carbonylative Transformations



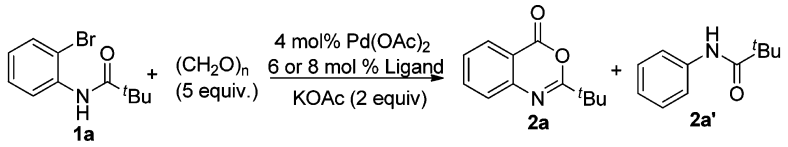
RESULTS AND DISCUSSION

Initially, we tested the model reaction between *N*-(2-bromophenyl)pivalamide (**1a**) and paraformaldehyde catalyzed by $Pd(OAc)_2$ and XantPhos. At 100 °C, with 1.5 equiv of paraformaldehyde, only 11% conversion was detected (Table 1, entry 1). Using 3 equiv of paraformaldehyde, the conversion of **1a** was increased to 83% and the yield of **2a** to 51% (Table 1, entry 2). To further improve the conversion, the temperature was increased to 110 °C and the yield was still moderate (Table 1, entry 3). In each case, the major side product was debromination of starting material **1a**, which was increased when the temperature was elevated (Table 1, entry 4). To our delight, the yield of **2a** was increased to 91% when 5 equiv of paraformaldehyde was used (Table 1, entry 5). The screening of the ligands (see Table S2 of the Supporting Information for

Received: September 1, 2014
Published: October 3, 2014

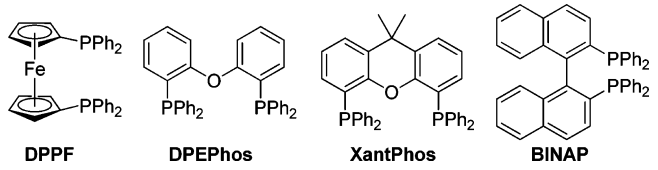
   dx.doi.org/10.1021/jo5020118 | J. Org. Chem. 2014, 79, 10410−10416

Table 1. Optimization of the Reaction Conditions[a]



entry	ligand	base	T (°C)	conversion[b] (%)	yield[b] (%) 2a	yield[b] (%) 2a′
1[c]	XantPhos	KOAc	100	11	2	–
2[d]	XantPhos	KOAc	100	83	51	30
3[d]	XantPhos	KOAc	110	100	66	28
4	XantPhos	KOAc	120	100	32	59
5	XantPhos	KOAc	110	100	91[e]	5
6	PPh_3	KOAc	110	99	45	47
7	DPPP	KOAc	110	99	47	63
8	BINAP	KOAc	110	11	7	–
9	DPPF	KOAc	110	18	<1	–
10	DPEPhos	KOAc	110	38	6	–
11	XantPhos	NaOAc	110	8	3	–
12	XantPhos	K_2CO_3	110	100	39	51
13	XantPhos	Cs_2CO_3	110	100	8	65
14	XantPhos	Na_2CO_3	110	29	12	11
15	XantPhos	K_3PO_4	110	100	39	48
16	XantPhos	DABCO	110	15	2	–
17	XantPhos	Et_3N	110	14	<1	–
18[f]	XantPhos	KOAc	110	100	91	2

[a]Unless otherwise specified, all reactions were conducted with 0.25 mmol of substrates (64 mg) and 1.25 mmol (37.5 mg) of $(CH_2O)_n$ in 2 mL of toluene. [b]Determined by GC using *n*-hexadecane as the internal standard. [c]With 1.5 equiv of $(CH_2O)_n$. [d]With 3 equiv of $(CH_2O)_n$. [e]Corresponding to an isolated yield of 86%. [f]*o*-Xylene as the solvent.

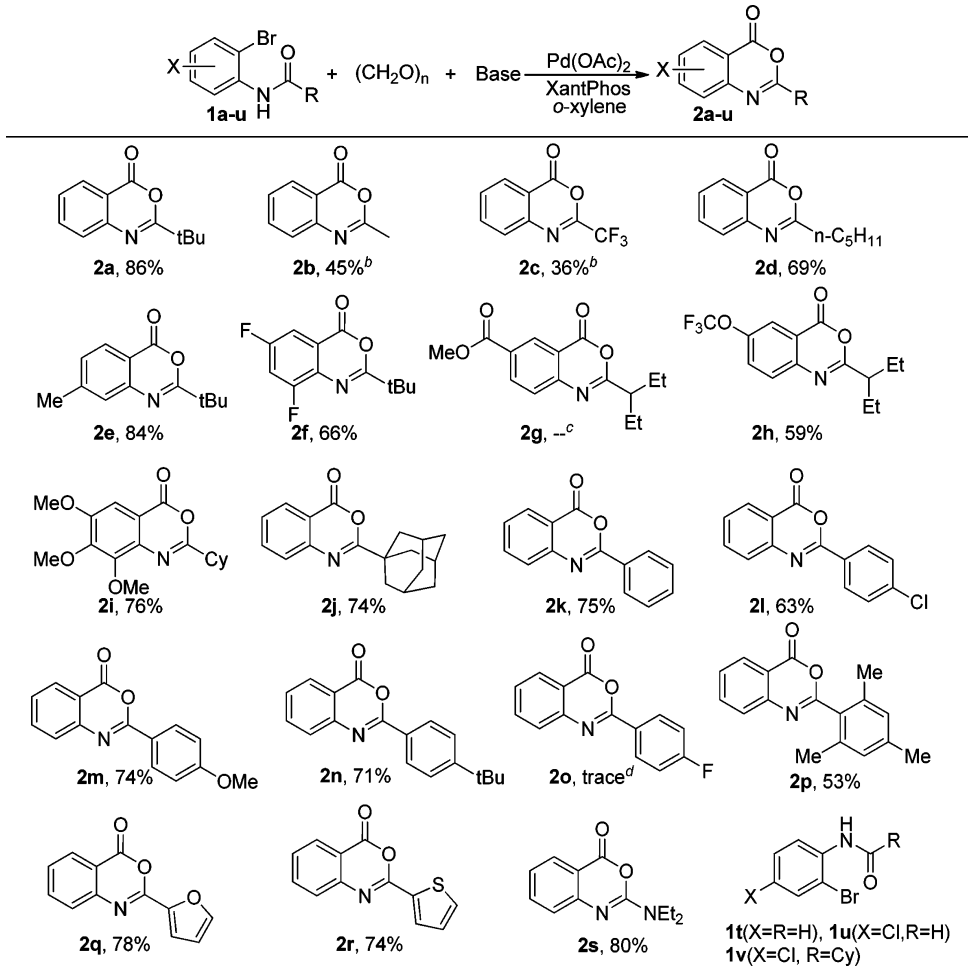


details) showed XantPhos was the best ligand for this carbonylative cyclization (Table 1, entries 5−10). Notably, bases played an important role in these reactions (Table 1, entries 10−17, and Table S1 of the Supporting Information). For example, when KOAc was replaced with NaOAc, the yield of **2a** decreased drastically from 91 to 3% (Table 1, entry 5 vs entry 11). Organic bases were rather inefficient for this reaction. After screening different solvents (Table S2 of the Supporting Information, entries 8−13), we found that the yield of **2a** was better in *o*-xylene and the amount of debromination product was lower than those with other solvents like 1,2-dichloroethane, *N*,*N*-dimethylformamide, and 1,4-dioxane. When using other palladium precursors like $PdCl_2$, $Pd(OCOCF_3)_2$, $Pd(MeCN)_2Cl_2$, and $Pd(dba)_2$, somewhat lower yields were obtained (Table S3 of the Supporting Information, entries 1−7). To illustrate the uniqueness of paraformaldehyde, trioxin and formalin (37% aqueous solution) were also tested as carbonyl sources, but the conversions of **1a** were only 11 and 31%, respectively (Table S3 of the Supporting Information, entries 8 and 9, respectively). On the basis of these results, the optimized reaction conditions were specified as follows: $Pd(OAc)_2$ as the palladium source, XantPhos as the ligand, KOAc as the base, and *o*-xylene as the solvent.

With the optimized reaction conditions in hand, we next extended the reaction to other *N*-(*o*-bromoaryl)amides to examine the scope of this method (Table 2). The acyl groups had an obvious effect on the selectivity of the reaction. When the R group was changed from *tert*-butyl (**2a**) to methyl (**2b**), the yield decreased from 86 to 45%. The major side product was the debrominated starting material, *N*-phenylacetamide, which was obtained in 50% yield. For the trifluoromethyl group-substituted substrate, debromination of the starting material (**1c**) also dominated the reaction and the yield of **2c** was only 36%. However, in the case of **1d** with a longer alkyl chain, the yield was much higher (**2d**, 69%). A substrate with a bulkier 1-adamantyl group (**1j**) could be cyclized to the product (**2j**) in 76% yield. To our surprise, *N*-(2-bromophenyl)-formamides (**1t** and **1u**) are not suitable for this reaction. For example, no conversion of **1t** was observed at 110 °C. At 120 °C, the reaction became very unselective. The substituents on the phenyl rings also influenced the reaction. On the whole, the electron withdrawing groups increase the level of debromination of the starting materials and thus led to lower yields of the target products (comparing **2a**, **2e**, and **2f**). Under the same conditions, **1h** was converted to the benzoxazinone product in 59% yield (**2h**), while with its counterpart **1g**, with an electron-withdrawing ester group on the phenyl ring, no **2g** was obtained. Similarly, **1i** with three electron-donating methoxy groups gave **2i** in 76% yield, while chloroaryl **1v** led to complete debromination product *N*-(4-chlorophenyl)-cyclohexanecarboxamide (**2v′**).

dx.doi.org/10.1021/jo5020118 | J. Org. Chem. 2014, 79, 10410−10416

Table 2. Substrate Scope[a]

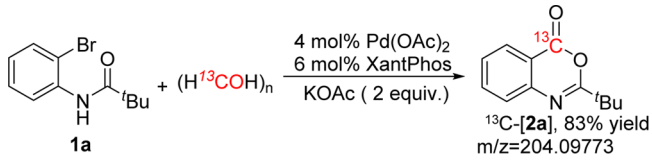


[a]All reactions were conducted with 0.25 mmol of substrates in 2 mL of *o*-xylene. For substrates in which R = alkyl (**1a**–**i**), the reactions were conducted at 110 °C; for other substrates, the reactions were conducted at 120 °C. [b]The lower yields were due to the debromination of the starting material. [c]No **2g** was detected by GC–MS. [d]Only 4-fluoro-*N*-phenylbenzamide was isolated.

On the basis of the success in preparing various 2-alkyl-substituted benzoxazinones described above, we tried the reaction of arylacyl-protected *o*-bromoanilines under the same conditions. The reactions became more difficult, and a higher temperature (120 °C) was necessary for the full conversion of the starting materials. The nature of the substituents on the amidoaryl moiety had obvious effect on the yields of the product. Specifically, the electron-withdrawing group depleted the yield to a large extent (**2l** and **2m**). For example, *p*-fluorophenylamide **1o** afforded only trace amounts of **2o** as the debromination product became dominant [4-fluoro-*N*-phenylbenzamide (**2o′**)]. Heteroaryl groups such as 2-furanoyl and thienyl were also tolerated, and the yields of **2q** and **2r** were 78 and 74%, respectively. With 3-(2-bromophenyl)-1,1-diethylurea (**1s**) as the starting product, 2-amino-substituted benzoxazinone could be obtained in 80% yield. On the whole, this method showed good generality for many substrates.

To make it more convenient for practical use, we tried the reaction with 2-bromoaniline, pivalic anhydride, and paraformaldehyde in one pot, but only **1a** (6–20% yield) was detected by GC. Additionally, using ^{13}C-labeled paraformaldehyde as the carbonyl source, a 4-^{13}C-labeled benzoxazinone derivative can also been prepared by this method (Scheme 2), which has many important pharmaceutical and biological applications.[17]

Scheme 2. Synthesis of ^{13}C-Labeled Benzoxazinone

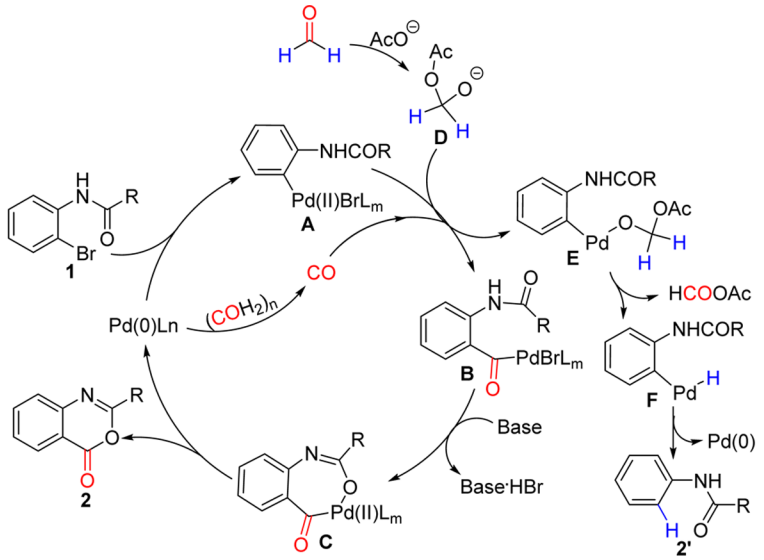


Finally, a reaction pathway was proposed (Scheme 3) on the basis of our observation that paraformaldehyde could be decomposed to carbon monoxide (CO, by GC–MS) catalyzed by a palladium catalyst.[16] In the presence of *in situ*-generated CO, the substrates **1** could be smoothly converted to product **2** through the same intermediates that we reported previously.[10] Meanwhile, the side reaction could also been explained by this process. If the hemiacetal anion **D**, which resulted from the attack of the acetate anion on formaldehyde, undergoes ligand exchange with **A**, then intermediate **E** will form. Elimination of the *β*-hydride from **E** would lead to the hydroaryl palladium complex **F**, which is unstable and easily eliminated to the hydrodebromination product **2′**. **F** is unstable and easily eliminated to form hydrodebromination product **2′**.[18]

In conclusion, a simple and general method for the synthesis of benzoxazinone derivatives has been developed. The starting

dx.doi.org/10.1021/jo5020118 | J. Org. Chem. 2014, 79, 10410–10416

Scheme 3. Proposed Reaction Mechanism



materials can been easily prepared from the 2-bromoanilines and acid chlorides or anhydrides. Most importantly, paraformaldehyde was used as a solid, cheap, and easy-to-handle carbonyl source. Therefore, this method provided a practical pathway for the carbonylative synthesis of benzoxazinone heterocycles.

EXPERIMENTAL SECTION

General Considerations. NMR spectra were recorded on a 300 MHz spectrometer at 295 K in $CDCl_3$ or DMSO. Chemical shifts (parts per million) are given relative to solvent. References for $CDCl_3$ were 7.26 ppm (^{1}H NMR) and 77.00 ppm (^{13}C NMR); references for d_6-DMSO were 2.50 ppm (^{1}H NMR) and 40.00 ppm (^{13}C NMR). High-resolution mass spectrometry (HRMS) was performed using an ESI-TOF/MS instrument. The products were isolated from the reaction mixture by column chromatography on silica gel 60 (0.063−0.2 mm, 70−230 mesh).

General Procedure for the Synthesis and Characterization of the Starting *N*-(*o*-Bromoaryl)amides. 2-Bromoarylamine (10 mmol) and triethylamine (13 mmol) were dissolved in CH_2Cl_2 (25 mL) at 0 °C. Then the corresponding acyl chloride (11 mmol) was added dropwise. After addition, the mixture was warmed to room temperature and stirred for a certain amount of time until the 2-bromoarylamine was consumed by TLC. Thirty milliliters of water was added to the reaction mixture, and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic phase was washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the *N*-(*o*-bromoaryl)amides were obtained as the crude products. Purifications were conducted by the reported procedure through recrystallization or column chromatography using a pentane (PE)/ethyl acetate (EA) eluent.

*N-(2-Bromophenyl)pivalamide (**1a**).*[19] Yellow solid, used directly without further purification, 98% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (dd, J = 8.3, 1.6 Hz, 1H), 8.00 (s, 1H), 7.52 (dd, J = 8.0, 1.5 Hz, 1H), 7.30 (dd, J = 8.6, 7.3, 1.5 Hz, 1H), 6.95 (dd, J = 8.0, 7.4, 1.6 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 135.8, 132.0, 128.3, 124.8, 121.6, 113.6, 40.2, 27.6.

*N-(2-Bromophenyl)acetamide (**1b**).*[19] White solid, purified by recrystallization from ethanol, 65% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, J = 8.3 Hz, 1H), 7.51 (d, J = 23.4 Hz, 1H), 7.49−7.41 (m, 1H), 7.28−7.20 (m, 1H), 6.90 (t, J = 7.7, 1.6 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 135.6, 132.2, 128.3, 125.1, 121.9, 113.2, 24.8.

*N-(2-Bromophenyl)-2,2,2-trifluoroacetamide (**1c**).*[20] Yellow solid, purified by sublimation, 55% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.31 (dd, J = 8.3, 1.6 Hz, 1H), 7.61 (dd, J = 8.1, 1.5 Hz, 1H), 7.46−7.33 (m, 1H), 7.19−7.05 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.2, 132.6, 128.7, 127.2, 122.0, 117.5, 114.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ −75.5.

*N-(2-Bromophenyl)hexanamide (**1d**).*[21] White solid, recrystallized from ethanol and pentane, 77% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, J = 8.3 Hz, 1H), 7.62 (s, 1H), 7.53 (dd, J = 8.0, 1.5 Hz, 1H), 7.34−7.27 (m, 1H), 7.01−6.91 (m, 1H), 2.42 (t, J = 7.5 Hz, 2H), 1.81−1.68 (m, 2H), 1.47−1.26 (m, 4H), 0.98−0.84 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 135.7, 132.1, 128.4, 125.0, 121.9, 113.2, 38.0, 31.3, 25.2, 22.4, 13.9.

*N-(2-Bromo-5-methylphenyl)pivalamide (**1e**).*[22] Yellow solid, used directly without further purification, 91% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (dd, J = 2.1, 0.9 Hz, 1H), 7.96 (s, 1H), 7.36 (d, J = 8.1 Hz, 1H), 6.80−6.72 (m, 1H), 2.30 (s, 3H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.6, 138.5, 135.3, 131.5, 125.7, 122.1, 110.2, 40.1, 27.5, 21.2.

*N-(2-Bromo-4,6-difluorophenyl)pivalamide (**1f**).*[23] Yellow solid, further purified by column chromatography (PE:EA ratio of 15), 88% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (s, 1H), 7.11 (ddd, J = 7.8, 2.8, 1.9 Hz, 1H), 6.82 (ddd, J = 9.4, 8.4, 2.8 Hz, 1H), 1.29 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.89, 162.23, 160.08, 159.90, 159.06, 158.89, 156.69, 156.51, 123.05, 123.00, 122.88, 122.84, 121.47, 121.41, 121.26, 121.20, 115.56, 115.51, 115.23, 115.17, 104.07, 103.73, 39.23, 27.37; ^{19}F NMR (282 MHz, $CDCl_3$) δ −109.8, −110.0.

*Methyl 4-Bromo-3-(2-ethylbutanamido)benzoate (**1g**).* **1g** was prepared from 2-methyl 4-amino-3-bromobenzoate (prepared by the bromination of methyl 4-aminobenzoate with NBS[24] in chloroform, 98% yield) and 2-ethylbutanoyl chloride by the general procedure. Purified by column chromatography (PE:EA ratio of 5) as a light yellow solid, in 86% yield for two steps: mp 99−101 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J = 8.7 Hz, 1H), 8.21 (d, J = 1.9 Hz, 1H), 7.96 (dd, J = 8.6, 1.9 Hz, 1H), 7.82 (s, 1H), 3.89 (s, 3H), 2.22−2.09 (m, 1H), 1.81−1.53 (m, 5H), 0.97 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 165.3, 139.5, 133.5, 129.9, 126.3, 120.5, 112.4, 52.6, 52.2, 25.7, 11.9; HRMS (ESI) calcd for $C_{14}H_{19}BrO_3N$ $(M + H)^+$ 328.05428 (^{79}Br) and 330.05328 (^{81}Br), found 328.05456 and 330.05267, respectively.

*N-[2-Bromo-5-(trifluoromethoxy)phenyl]-2-ethylbutanamide (**1h**).* White solid, purified by column chromatography (PE:EA ratio of 20), 68% yield: mp 109−110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 9.1 Hz, 1H), 7.64−7.52 (m, 1H), 7.46−7.42 (m, 1H), 7.24−7.17 (m, 1H), 2.23−2.01 (m, 1H), 1.77−1.54 (m, 4H), 0.98 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 134.6, 125.0, 122.5,

dx.doi.org/10.1021/jo5020118 | J. Org. Chem. 2014, 79, 10410−10416

121.1, 118.6, 113.1, 52.6, 25.8, 12.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ −57.3; HRMS (ESI) calcd for $C_{13}H_{16}BrF_3O_2N$ $(M + H)^+$ 354.03110 (^{79}Br) and 356.02917 (^{81}Br), found 354.03129 and 356.02938, respectively.

*N-(2-Bromo-3,4,5-trimethoxyphenyl)cyclohexanecarboxamide (**1i**).* White solid, purified by column chromatography (PE:EA ratio of 6), 70% yield: mp 131−134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.70 (s, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.81 (s, 3H), 2.34−2.21 (m, 1H), 2.04−1.92 (m, 2H), 1.88−1.76 (m, 2H), 1.69−1.16 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 152.8, 150.4, 139.0, 132.0, 101.0, 99.5, 77.0, 61.1, 61.0, 56.0, 46.6, 29.6, 25.6, 25.5; HRMS (ESI) calcd for $C_{16}H_{23}BrO_4N$ $(M + H)^+$ 372.08050 (^{79}Br) and 374.07864 (^{81}Br), found 372.08065 and 374.07865, respectively.

*N-(2-Bromophenyl)adamantane-1-carboxamide (**1j**).*[25] White solid, purified by column chromatography (PE:EA ratio of 15), 83% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (dd, J = 8.3, 1.6 Hz, 1H), 7.91 (s, 1H), 7.43 (dd, J = 8.0, 1.5 Hz, 1H), 7.25−7.15 (m, 1H), 6.92−6.81 (m, 1H), 2.02 (d, J = 3.2 Hz, 3H), 1.92 (d, J = 2.9 Hz, 6H), 1.68 (t, J = 2.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 135.7, 132.0, 128.3, 124.7, 121.6, 113.6, 42.0, 39.2, 36.3, 28.0.

*N-(2-Bromophenyl)benzamide (**1k**).*[26] White solid, further purified by column chromatography (PE:EA ratio of 20), 85% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, J = 8.3, 1.6 Hz, 1H), 8.47 (s, 1H), 8.02−7.85 (m, 2H), 7.62−7.47 (m, 4H), 7.42−7.32 (m, 1H), 7.09−6.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 147.5, 144.6, 135.3, 132.2, 128.3, 125.1, 121.5, 115.6, 113.3, 112.6.

*N-(2-Bromophenyl)-4-chlorobenzamide (**1l**).*[26] White solid, without further purification, 86% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (dd, J = 8.1, 1.6 Hz, 1H), 8.39 (s, 1H), 7.92−7.72 (m, 2H), 7.63−7.28 (m, 4H), 7.09−6.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1, 138.5, 135.5, 132.8, 132.2, 129.2, 128.5, 128.5, 125.5, 121.8, 113.8.

*N-(2-Bromophenyl)-4-methoxybenzamide (**1m**).*[26] White solid, without further purification, 87% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, J = 8.3, 1.6 Hz, 1H), 8.39 (s, 1H), 7.94−7.86 (m, 2H), 7.57 (dd, J = 8.0, 1.5 Hz, 1H), 7.41−7.32 (m, 1H), 7.04−6.95 (m, 3H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.7, 162.7, 136.0, 132.2, 129.0, 128.5, 126.8, 125.0, 121.6, 114.1, 113.6, 55.5.

*N-(2-Bromophenyl)-4-(tert-butyl)benzamide (**1n**).*[27] White solid, further purified by column chromatography (PE:EA ratio of 15), 80% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60−8.52 (m, 1H), 8.47 (s, 1H), 7.92−7.84 (m, 2H), 7.61−7.50 (m, 3H), 7.41−7.31 (m, 1H), 7.05−6.96 (m, 1H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 155.8, 135.9, 132.2, 131.7, 128.5, 126.9, 125.9, 125.0, 121.6, 113.6, 35.0, 31.1.

*N-(2-Bromophenyl)-4-fluorobenzamide (**1o**).*[26] White solid, further purified by column chromatography (PE:EA ratio of 20), 78% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (dd, J = 8.2, 1.6 Hz, 1H), 8.39 (s, 1H), 8.03−7.86 (m, 2H), 7.57 (dd, J = 8.0, 1.5 Hz, 1H), 7.43−7.30 (m, 1H), 7.25−7.11 (m, 2H), 7.08−6.95 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 164.1, 163.4, 135.6, 132.2, 130.7 (d, J = 3.3 Hz), 129.5 (d, J = 9.0 Hz), 128.5, 125.4, 121.8, 116.1, 115.9, 113.8. 130.7.

*N-(2-Bromophenyl)-2,4,6-trimethylbenzamide (**1p**).* White solid, purified by column chromatography (PE:EA ratio of 20), 85% yield: mp 107−109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (dd, J = 8.2, 1.6 Hz, 1H), 7.76 (s, 1H), 7.57 (dd, J = 8.0, 1.5 Hz, 1H), 7.44−7.34 (m, 1H), 7.08−7.00 (m, 1H), 6.95−6.88 (m, 2H), 2.40 (s, 6H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 139.0, 135.5, 134.6, 134.3, 132.3, 128.4, 128.4, 125.5, 122.4, 113.7, 21.1,19.2; HRMS (ESI) calcd for $C_{16}H_{17}BrON$ $(M + Na)^+$ 340.03075 (^{79}Br) and 342.02884 (^{81}Br), found 340.03083 and 340.02890, respectively.

*N-(2-Bromophenyl)furan-2-carboxamide (**1q**).*[28] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (s, 1H), 8.41 (dd, J = 8.3, 1.6 Hz, 1H), 7.51−7.38 (m, 2H), 7.24 (t, J = 8.9, 1H), 7.16 (dd, J = 3.6, 0.8 Hz, 1H), 6.89 (ddd, J = 8.0, 7.4, 1.6 Hz, 1H), 6.47 (dd, J = 3.5, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 147.5, 144.6, 135.3, 132.2, 128.3, 125.1, 121.5, 115.6, 113.3, 112.6.

*N-(2-Bromophenyl)thiophene-2-carboxamide (**1r**).*[29] White solid, further purified by column chromatography (PE:EA ratio of 15), 84% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76−7.64 (m, 1H), 7.64−7.48 (m, 4H), 7.38−7.22 (m, 3H), 7.01 (dd, J = 5.0, 3.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 139.2, 137.8, 133.9, 133.8, 133.4, 131.0, 130.2, 128.7, 127.7, 123.3.

*3-(2-Bromophenyl)-1,1-diethylurea (**1s**).* Prepared by the reaction with 2-bromophenyl isocynate (1 g, 5 mmol) and diethylamine (0.58 mL, 5.6 mmol) in toluene at 80 °C for 6 h; purified by column chromatography (PE:EA ratio of 8) that gave the product in 94% yield as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.2 (dd, J = 8.3, 1.6 Hz, 1H), 7.4 (dd, J = 8.0, 1.5 Hz, 1H), 7.3−7.1 (m, 1H), 7.0 (s, 1H), 6.9−6.7 (m, 1H), 3.3 (q, J = 7.2 Hz, 4H), 1.2 (t, J = 7.6, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 136.9, 131.5, 127.9, 122.9, 120.6, 112.6, 112.6, 41.5, 13.6.

*N-(2-Bromo-4-chlorophenyl)cyclohexanecarboxamide (**1v**).* Yellow solid, further purified by column chromatography (PE:EA ratio of 10), 76% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 8.9 Hz, 1H), 7.59 (s, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.24−7.16 (m, 1H), 2.30−2.17 (m, 1H), 2.00−1.87 (m, 2H), 1.84−1.72 (m, 2H), 1.70−1.60 (m, 1H), 1.54−1.37 (m, 2H), 1.34−1.14 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 134.5, 131.5, 129.1, 128.4, 122.4, 113.4, 46.5, 29.6, 25.6; HRMS (ESI) calcd for $C_{13}H_{16}BrClON$ $(M + H)^+$ 316.00983 (^{79}Br) and 318.00764 (^{81}Br), found 316.0099 and 318.00781, respectively.

General Procedure (GP) for the Carbonylative Cyclization of 1 To Form 2. To an oven-dried Schlenk (10 mL) tube were added **1** (0.25 mmol), $Pd(OAc)_2$ (2.24 mg, 10 μmol), XantPhos (8.67 mg, 15 μmol), paraformaldehyde (37.5 mg, 1.25 mmol), and KOAc (49 mg, 0.5 mmol). Then the Schlenk tube was vacuumed and purged with argon three times before 1 mL of toluene was added. After being stirred at 110 or 120 °C for 18 h, the mixture was cooled to room temperature.

*2-(tert-Butyl)-4H-benzo[d][1,3]oxazin-4-one (**2a**).*[10b] Prepared according to the GP and purified as a white solid in 86% yield (43.6 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19−8.11 (m, 1H), 7.79−7.71 (m, 1H), 7.59−7.53 (m, 1H), 7.50−7.42 (m, 1H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 160.0, 146.5, 136.2, 128.2, 127.9, 126.8, 116.7, 37.9, 27.6.

*2-Methyl-4H-benzo[d][1,3]oxazin-4-one (**2b**).*[10b] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 30) as a colorless thick oil in 45% yield (18.2 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (dd, J = 7.9, 1.6 Hz, 1H), 7.79 (dd, J = 8.1, 7.3, 1.6 Hz, 1H), 7.57−7.45 (m, 2H), 2.47 (s, 3H).

*2-(Trifluoromethyl)-4H-benzo[d][1,3]oxazin-4-one (**2c**).*[10b] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 40) as a colorless thick oil in 36% yield (19.6 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (dd, J = 7.9, 1.5, 0.6 Hz, 1H), 7.94 (dd, J = 8.1, 1.5 Hz, 1H), 7.79 (d, J = 8.1, 0.8 Hz, 1H), 7.74−7.65 (m, 1H).

*2-Pentyl-4H-benzo[d][1,3]oxazin-4-one (**2d**).*[10b] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 40) as a colorless oil in 69% yield (37.6 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22−8.13 (m, 1H), 7.83−7.72 (m, 1H), 7.60−7.43 (m, 2H), 2.74−2.59 (m, 2H), 1.83 (t, J = 7.6 Hz, 2H), 1.48−1.26 (m, 4H), 0.98−0.79 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 159.9, 146.5, 136.4, 128.4, 128.1, 126.5, 116.8, 34.8, 31.2, 25.8, 22.3, 13.9.

*2-(tert-Butyl)-7-methyl-4H-benzo[d][1,3]oxazin-4-one (**2e**).* Prepared according to the GP and purified by column chromatography (PE:EA ratio of 30) as a white solid in 84% yield (45.6 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 8.1 Hz, 1H), 7.39 (dt, J = 1.6, 0.8 Hz, 1H), 7.29 (dd, J = 8.1, 1.8, 0.7 Hz, 1H), 2.48 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 160.2, 147.8, 146.6, 129.3, 128.1, 126.9, 126.9, 114.2, 37.9, 27.7, 22.0; HRMS (ESI) calcd for $C_{13}H_{16}O_2N$ $(M + H)^+$ 218.11756, found 218.11758.

*2-(tert-Butyl)-6,8-difluoro-4H-benzo[d][1,3]oxazin-4-one (**2f**).* Yellowish white solid, prepared according to the GP and purified by column chromatography (PE:/EA ratio of 20) in 66% yield (39.5 mg): mp 81−82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (ddd, J = 7.6, 2.8, 1.6 Hz, 1H), 7.27−7.18 (m, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4 (d, J = 2.5 Hz), 162.2 (d, J = 10.8 Hz), 158.8 (dd, J = 11.2, 3.4 Hz), 155.3 (d, J = 11.8 Hz), 111.7 (q, J = 27.0, 22.6 Hz),

109.4 (dd, J = 23.8, 4.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ −106.6 (q, J = 15.5, 8.1 Hz), −117.7 (t, J = 16.6, 9.5 Hz); HRMS (ESI) calcd for $C_{12}H_{12}O_2NF_2$ $(M + H)^+$ 239.07524, found 239.07525.

*Methyl 4-(2-Ethylbutanamido)benzoate (**2g′**).* White solid, prepared according to the GP and isolated as a byproduct by column chromatography (PE:EA ratio of 5) in 67% yield (41.7 mg): mp 139−140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 8.6 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 7.60 (s, 1H), 3.89 (s, 3H), 2.15−2.02 (m, 1H), 1.82−1.48 (m, 4H), 0.94 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 166.6, 142.2, 130.7, 125.4, 118.9, 52.3, 52.0, 52.0, 25.7, 12.0; HRMS (ESI) calcd for $C_{14}H_{20}O_3N$ $(M + H)^+$ 250.14377, found 250.14403.

*2-(Pentan-3-yl)-6-(trifluoromethoxy)-4H-benzo[d][1,3]oxazin-4-one (**2h**).* Prepared according to the GP and purified by column chromatography (PE:EA ratio of 20) as a yellowish oil in 66% yield (49.7 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04−7.98 (m, 1H), 7.66−7.58 (m, 2H), 2.61−2.39 (m, 1H), 1.91−1.66 (m, 4H), 0.94 (t, J = 7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 159.0, 148.0, 144.9, 129.4 (d, J_{F-C} = 1.6 Hz), 128.8, 119.7, 119.6, 118.0, 48.9, 25.5, 11.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ −57.7; HRMS (ESI) calcd for $C_{14}H_{15}O_3NF_3$ $(M + H)^+$ 301.09203, found 301.09186.

*2-Cyclohexyl-5,6,7-trimethoxy-4H-benzo[d][1,3]oxazin-4-one (**2i**).* Prepared according to the GP and purified by column chromatography (PE:EA ratio of 5) as a white solid in 76% yield (66.1 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.80 (s, 1H), 3.97 (s, 3H), 3.94 (s, 3H), 3.87 (s, 3H), 2.60−2.47 (m, 1H), 2.08−1.96 (m, 2H), 1.88−1.77 (m, 2H), 1.71−1.49 (m, 3H), 1.39−1.20 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 160.1, 156.2, 154.2, 145.1, 142.2, 104.5, 104.3, 61.9, 61.3, 56.3, 43.2, 29.7, 25.6, 25.5; HRMS (ESI) calcd for $C_{17}H_{22}O_5N$ $(M + H)^+$ 320.14925, found 320.14918.

*2-(1-Adamantyl)-4H-benzo[d][1,3]oxazin-4-one (**2j**).*[4e] White solid, prepared according to the GP and purified by column chromatography (PE:EA ratio of 50) as a white solid in 74% yield (52.1 mg): mp 161−163 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (dd, J = 7.9, 1.5 Hz, 1H), 7.82−7.70 (m, 1H), 7.62−7.52 (m, 1H), 7.52−7.40 (m, 1H), 2.09 (d, J = 2.9 Hz, 2H), 2.07 (d, J = 2.8 Hz, 6H), 1.77 (d, J = 3.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 160.2, 146.7, 136.2, 128.2, 127.9, 126.8, 116.9, 39.6, 39.2, 39.2, 36.4, 27.9.

*2-(4-Phenyl)-4H-benzo[d][1,3]oxazin-4-one (**2k**).*[30] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 15) as a white solid in 75% yield (42.1 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27−8.09 (m, 3H), 7.78−7.66 (m, 1H), 7.64−7.55 (m, 1H), 7.52−7.34 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.5, 157.0, 146.9, 136.5, 132.6, 130.2, 128.7, 128.5, 128.3, 128.2, 127.2, 117.0.

*2-(4-Chlorophenyl)-4H-benzo[d][1,3]oxazin-4-one (**2l**).*[10a] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 10) as a white solid in 63% yield (40.6 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34−8.14 (m, 3H), 7.89−7.74 (m, 1H), 7.73−7.61 (m, 1H), 7.58−7.41 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 156.2, 146.7, 139.0, 136.6, 129.6, 129.1, 128.7, 128.6, 128.4, 127.2, 116.9.

*2-(4-Methoxyphenyl)-4H-benzo[d][1,3]oxazin-4-one (**2m**).*[10a] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 8) as a white solid in 74% yield (46.8 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27−8.14 (m, 3H), 7.77 (dd, J = 8.6, 7.3 Hz, 1H), 7.66−7.57 (m, 1H), 7.50−7.39 (m, 1H), 7.03−6.91 (m, 2H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 159.7, 157.0, 147.3, 136.4, 130.2, 128.5, 127.6, 126.8, 122.5, 116.6, 114.1, 55.4.

*2-[4-(tert-Butyl)phenyl]-4H-benzo[d][1,3]oxazin-4-one (**2n**).*[10a] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 20) as a white solid in 71% yield (49.6 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26−8.18 (m, 3H), 7.84−7.76 (m, 1H), 7.71−7.64 (m, 1H), 7.56−7.44 (m, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 157.2, 156.4, 147.1, 136.4, 128.5, 128.1, 127.9, 127.4, 127.1, 125.7, 116.9, 35.1, 31.1.

*2-Mesityl-4H-benzo[d][1,3]oxazin-4-one (**2p**).*[31] White solid, prepared according to the GP and purified by column chromatography (PE:EA ratio of 10) in 53% yield (35.1 mg): mp 139−141 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (dd, J = 7.8, 1.5 Hz, 1H), 7.89−7.81 (m, 1H), 7.71−7.66 (m, 1H), 7.62−7.54 (m, 1H), 6.94 (s, 2H), 2.33 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 159.4, 146.4, 140.1, 136.6, 129.0, 128.7, 128.6, 128.5, 127.1, 116.8, 21.2, 19.8.

*2-(Furan-2-yl)-4H-benzo[d][1,3]oxazin-4-one (**2q**).*[4e] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 15) as a white solid in 78% yield (41.7 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 7.2, 1.4 Hz, 1H), 7.75−7.62 (m, 2H), 7.55−7.43 (m, 1H), 7.39−7.30 (m, 1H), 6.66−6.56 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 149.7, 147.1, 147.0, 146.6, 144.4, 136.8, 128.7, 128.2, 127.1, 117.2, 116.9, 112.5.

*2-(Thiophen-2-yl)-4H-benzo[d][1,3]oxazin-4-one (**2r**).*[4e] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 15) as a white solid in 74% yield (42.5 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (dd, J = 7.9, 1.6, 0.6 Hz, 1H), 7.95 (dd, J = 3.8, 1.3 Hz, 1H), 7.79 (dd, J = 8.1, 7.3, 1.6 Hz, 1H), 7.67−7.56 (m, 2H), 7.47 (dd, J = 7.8, 7.3, 1.2 Hz, 1H), 7.16 (dd, J = 5.0, 3.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 153.6, 147.0, 136.6, 134.1, 132.3, 131.7, 128.7, 128.3, 127.9, 126.8, 116.7.

*2-(Diethylamino)-4H-benzo[d][1,3]oxazin-4-one (**2s**).*[32] Prepared according to the GP and purified by column chromatography (PE:EA ratio of 8) as a yellow thick oil in 80% yield (43.7 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (dd, J = 8.0, 1.6 Hz, 1H), 7.63−7.53 (m, 1H), 7.24−7.18 (m, 1H), 7.14−7.04 (m, 1H), 3.56 (q, J = 7.1 Hz, 4H), 1.25 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.3, 153.5, 151.4, 136.5, 128.6, 124.1, 122.7, 112.1, 42.2, 13.4.

*N-(4-Chlorophenyl)cyclohexanecarboxamide (**2v′**).* Prepared according to the GP and purified by column chromatography (PE:EA ratio of 20) as a white solid in 51% yield (30.3 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, J = 8.8 Hz, 2H), 7.28 (dd, J = 4.2, 2.5 Hz, 2H), 2.30−2.14 (m, 1H), 2.02−1.79 (m, 4H), 1.65−1.50 (m, 2H), 1.42−1.15 (m, 4H); ^{13}C NMR (75 MHz, DMSO) δ 174.9, 138.9, 129.0, 126.8, 121.0, 45.3, 29.6, 25.9, 25.7; HRMS (ESI) calcd for $C_{13}H_{17}ClON$ $(M + H)^+$ 238.09932, found 238.09913.

■ ASSOCIATED CONTENT

Supporting Information

Detailed screening conditions (Tables S1−S3) and ^{1}H, ^{13}C, and ^{19}F NMR spectra for the substrates and products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: xiao-feng.wu@catalysis.de.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the State of Mecklenburg-Vorpommern, the Bundesministerium für Bildung und Forschung (BMBF), and the Deutsche Forschungsgemeinschaft for financial support. We also appreciate the general support from Prof. Matthias Beller of LIKAT.

■ REFERENCES

(1) (a) Sicker, D.; Schulz, M. In *Studies of Natural Product Chemistry*; Attaur, R., Ed.; Elsevier: Amsterdam, 2002; Vol. *27*, Part H, pp 185−232. (b) Grover, G.; Kini, S. G. *Eur. J. Med. Chem.* **2006**, *41*, 256−262.

(2) (a) Coppola, G. M. *J. Heterocycl. Chem.* **2000**, *37*, 1369−1388. (b) El-Mekabaty, A. *International Journal of Modern Organic Chemistry* **2013**, *2*, 81−121.

(3) (a) Mitsos, C. P.; Markopoulos, J.; Igglessi-Markopoulou, O. *J. Heterocycl. Chem.* **1999**, *36*, 881. (b) Kumar, A.; Sharma, S.; Archana; Bajaj, K.; Sharma, S.; Panwar, H.; Singh, T.; Srivastava, V. K. *Bioorg. Med. Chem.* **2003**, *11*, 5293−5299. (c) Madkour, H. M. F. *Arkivoc*

2004, 36−54. (d) Habib, O. O.; Hassan, H.; El-Mekabaty, A. *Med. Chem. Res.* **2013**, *22*, 507−519.
(4) (a) Pavlidis, V. H.; Perry, P. J. *Synth. Commun.* **1994**, *24*, 533−548. (b) Kato, S.; Morie, T.; Ohno, K.; Yoshida, N.; Yoshida, T.; Naruto, S. *Chem. Pharm. Bull.* **1995**, *43*, 582−587. (c) Gilmore, J. L.; Hays, S. J.; Caprathe, B. W.; Lee, C.; Emmerling, M. R.; Michael, W.; Jaen, J. C. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 679−682. (d) Shariat, M.; Abdollahi, S. *Molecules* **2004**, *9*, 705−712. (e) Ge, Z.-Y.; Xu, Q.-M.; Fei, X.-D.; Tang, T.; Zhu, Y.-M.; Ji, S.-J. *J. Org. Chem.* **2013**, *78*, 4524−4529.
(5) (a) Kurihara, M.; Yoda, N. *Tetrahedron Lett.* **1965**, 2597−2606. (b) Kurihara, M.; Yoda, N. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1942−1948. (c) Papadopoulos, E. P. *J. Heterocycl. Chem.* **1984**, *21*, 1411. (d) Jarvest, R. L.; Parratt, M. J.; Debouck, C. M.; Gorniak, J. G.; John Jennings, L.; Serafinowska, H. T.; Strickler, J. E. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2463−2466.
(6) (a) Rabilloud, G.; Sillion, B. *J. Heterocycl. Chem.* **1980**, *17*, 1065−1068. (b) Minami, T.; Ogata, M.; Hirao, I.; Tanaka, M.; Agawa, T. *Synthesis* **1982**, *1982*, 231−233. (c) Balsubramaniyan, V.; Argade, N. P. *Tetrahedron Lett.* **1986**, *27*, 2487−2488. (d) Khajavi, M. S.; Shariat, S. M. *Heterocycles* **2005**, *65*, 1159−1165.
(7) (a) Brennfuehrer, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4114−4133. (b) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 4986−5009.
(8) Wu, X.-F.; Neumann, H.; Beller, M. *Chem. Rev.* **2013**, *113*, 1−35.
(9) (a) Larock, R. C.; Fellows, C. A. *J. Org. Chem.* **1980**, *45*, 363−365. (b) Cacchi, S.; Fabrizi, G.; Marinelli, F. *Synlett* **1996**, 997. (c) Salvadori, J.; Balducci, E.; Zaza, S.; Petricci, E.; Taddei, M. *J. Org. Chem.* **2010**, *75*, 1841−1847.
(10) (a) Wu, X.-F.; Schranck, J.; Neumann, H.; Beller, M. *Chem.—Eur. J.* **2011**, *17*, 12246−12249. (b) Wu, X.-F.; Neumann, H.; Beller, M. *Chem.—Eur. J.* **2012**, *18*, 12599−12602.
(11) (a) Morimoto, T.; Kakiuchi, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 5580−5588. (b) Wu, L.; Liu, Q.; Jackstell, R.; Beller, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 6310−6320.
(12) (a) Friis, S. D.; Taaning, R. H.; Lindhardt, A. T.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 18114−18117. (b) Hermange, P.; Gøgsig, T. M.; Lindhardt, A. T.; Taaning, R. H.; Skrydstrup, T. *Org. Lett.* **2011**, *13*, 2444−2447. (c) Gøgsig, T. M.; Nielsen, D. U.; Lindhardt, A. T.; Skrydstrup, T. *Org. Lett.* **2012**, *14*, 2536−2539. (d) Nielsen, D. U.; Neumann, K.; Taaning, R. H.; Lindhardt, A. T.; Modvig, A.; Skrydstrup, T. *J. Org. Chem.* **2012**, *77*, 6155−6165. (e) Brancour, C.; Fukuyama, T.; Mukai, Y.; Skrydstrup, T.; Ryu, I. *Org. Lett.* **2013**, *15*, 2794−2797. (f) Burhardt, M. N.; Taaning, R. H.; Skrydstrup, T. *Org. Lett.* **2013**, *15*, 948−951. (g) Korsager, S.; Taaning, R. H.; Lindhardt, A. T.; Skrydstrup, T. *J. Org. Chem.* **2013**, *78*, 6112−6120.
(13) Li, H.; Neumann, H.; Beller, M.; Wu, X.-F. *Angew. Chem., Int. Ed.* **2014**, *53*, 3183−3186.
(14) Wu, X.-F.; Sharif, M.; Shoaib, K.; Neumann, H.; Pews-Davtyan, A.; Langer, P.; Beller, M. *Chem.—Eur. J.* **2013**, *19*, 6230−6233.
(15) (a) Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. *Chem. Commun.* **2005**, 3295−3297. (b) Morimoto, T.; Fujioka, M.; Fuji, K.; Tsutsumi, K.; Kakiuchi, K. *J. Organomet. Chem.* **2007**, *692*, 625−634.
(16) Natte, K.; Dumrath, A.; Neumann, H.; Beller, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 10090−10094.
(17) (a) Persson, A.; Dargy, R.; Gillberg, P. G.; Halldin, C.; Litton, J. E.; Swahn, C. G.; Sedvall, G. *J. Neurosci. Methods* **1991**, *36*, 53−61. (b) Schou, M.; Pike, V. W.; Sovago, J.; Gulyas, B.; Gallagher, P. T.; Dobson, D. R.; Walter, M. W.; Rudyk, H.; Farde, L.; Halldin, C. *Bioorg. Med. Chem.* **2007**, *15*, 616−625. (c) Cai, L.; Liow, J.-S.; Zoghbi, S. S.; Cuevas, J.; Baetas, C.; Hong, J.; Shetty, H. U.; Seneca, N. M.; Brown, A. K.; Gladding, R.; Temme, S. S.; Herman, M. M.; Innis, R. B.; Pike, V. W. *J. Med. Chem.* **2008**, *51*, 148−158. (d) Khdour, O.; Skibo, E. B. *Org. Biomol. Chem.* **2009**, *7*, 2140−2154. (e) De Bruyne, S.; La Regina, G.; Staelens, S.; Wyffels, L.; Deleye, S.; Silvestri, R.; De Vos, F. *Nucl. Med. Biol.* **2010**, *37*, 459−467. (f) Funke, U.; Vugts, D. J.; Janssen, B.; Spaans, A.; Kruijer, P. S.; Lammertsma, A. A.; Perk, L. R.; Windhorst, A. D. *J. Labelled Compd. Radiopharm.* **2013**, *56*, 120−129. (g) Mason, N. S.; Mathis, C. A.; Klunk, W. E. *J. Labelled Compd. Radiopharm.* **2013**, *56*, 89−95. (h) Zanotti-Fregonara, P.; Barth, V. N.; Liow, J.-S.; Zoghbi, S. S.; Clark, D. T.; Rhoads, E.; Siuda, E.; Heinz, B. A.; Nisenbaum, E.; Dressman, B.; Joshi, E.; Luffer-Atlas, D.; Fisher, M. J.; Masters, J. J.; Goebl, N.; Kuklish, S. L.; Morse, C.; Tauscher, J.; Pike, V. W.; Innis, R. B. *Eur. J. Nucl. Med. Mol. Imaging* **2013**, *40*, 245−253.
(18) Pyo, A.; Kim, S.; Kumar, M. R.; Byeun, A.; Eom, M. S.; Han, M. S.; Lee, S. *Tetrahedron Lett.* **2013**, *54*, 5207−5210.
(19) Benedí, C.; Bravo, F.; Uriz, P.; Fernández, E.; Claver, C.; Castillón, S. *Tetrahedron Lett.* **2003**, *44*, 6073−6077.
(20) Wender, P. A.; White, A. W. *Tetrahedron* **1983**, *39*, 3767−3776.
(21) Saha, P.; Ramana, T.; Purkait, N.; Ali, M. A.; Paul, R.; Punniyamurthy, T. *J. Org. Chem.* **2009**, *74*, 8719−8725.
(22) Heinicke, J.; Gupta, N.; Surana, A.; Peulecke, N.; Witt, B.; Steinhauser, K.; Bansal, R. K.; Jones, P. G. *Tetrahedron* **2001**, *57*, 9963−9972.
(23) Kyba, E. P.; Liu, S. T.; Chockalingam, K.; Reddy, B. R. *J. Org. Chem.* **1988**, *53*, 3513−3521.
(24) Tobe, Y.; Utsumi, N.; Kawabata, K.; Nagano, A.; Adachi, K.; Araki, S.; Sonoda, M.; Hirose, K.; Naemura, K. *J. Am. Chem. Soc.* **2002**, *124*, 5350−5364.
(25) Ilies, M. A.; Masereel, B.; Rolin, S.; Scozzafava, A.; Câmpeanu, G.; Cîmpeanu, V.; Supuran, C. T. *Bioorg. Med. Chem.* **2004**, *12*, 2717−2726.
(26) Evindar, G.; Batey, R. A. *J. Org. Chem.* **2006**, *71*, 1802−1808.
(27) Saal, W. v. d.; Martens, A.; Zilch, H.; Boehm, E. U.S. Patent 5135949A1, 1992; *Chem. Abstr.* **1992**, *113*, 152047.
(28) Aluri, B. R.; Niaz, B.; Kindermann, M. K.; Jones, P. G.; Heinicke, J. *Dalton Trans.* **2011**, *40*, 211−224.
(29) Barbero, N.; Carril, M.; SanMartin, R.; Domínguez, E. *Tetrahedron* **2007**, *63*, 10425−10432.
(30) Larksarp, C.; Alper, H. *Org. Lett.* **1999**, *1*, 1619−1622.
(31) Arcus, C. L.; Marks, R. E. *J. Chem. Soc. (Resumed)* **1956**, 1627−1633.
(32) Gütschow, M. *J. Org. Chem.* **1999**, *64*, 5109−5115.