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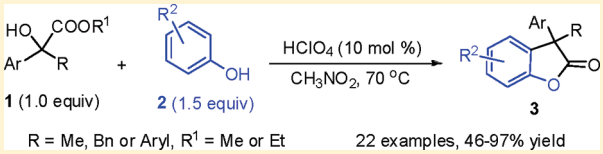
Metal-Free Tandem Friedel–Crafts/Lactonization Reaction to Benzofuranones Bearing a Quaternary Center at C3 Position

Long Chen, Feng Zhou, Tao-Da Shi, and Jian Zhou*

Shanghai Key Laboratory of Green Chemistry and Chemical Processes, Department of Chemistry, East China Normal University, 3663 N. Zhongshan Road, Shanghai, 200062, P. R. China

Supporting Information

ABSTRACT: A metal-free tandem Friedel–Crafts/lactonization reaction to 3,3-diaryl or 3-alkyl-3-aryl benzofuranones catalyzed by $HClO_4$ was reported. A variety of tertiary α-hydroxy acid esters could readily react with substituted phenols to afford the desired products in rich diversity. The synthetic utility of the products was demonstrated by the synthesis of polycyclic compounds. ^1H NMR studies supported that this tandem reaction proceeded via tandem Friedel–Crafts/lactonization sequence.



INTRODUCTION

The 3,3-disubstituted benzofuranone is a prominent structural motif in many natural bioactive products, such as yuccaol A, hopeahainol A, radulifoline, and rosmadial.[1] It also serves as a synthon for the synthesis of bioactive natural products such as aplysin, isolaurinterol, and isoaplysin (Figure 1).[2]

While several methods had been developed, including the condensation of benzil with phenols to symmetrical 3,3-diaryl benzofuranones,[3] transition metal catalyzed coupling reactions, and the functionalization of 3-substituted benzofuranones,[4] these methods suffered from narrow substrate scope or the difficulty in the synthesis of starting materials. In addition, methods to unsymmetrical 3,3-diaryl benzofuranones were very limited. Accordingly, it is valuable to develop new catalytic cost-effective methods to enable the synthesis of this framework in rich structural diversity from simple starting materials to facilitate structure–activity relationship studies for drug discovery.

The tandem reaction[5] from α-hydroxy acid esters **1** and phenols **2**, possibly through Friedel–Crafts/lactonization sequence (path a in Scheme 1) or ester exchange/Friedel–Crafts reaction cascade (path b), was an efficient method to prepare unsymmetric 3,3-disubstituted benzofuranones. The major advantages of this tandem reaction include the ready access of starting materials and the rich diversity of the desired product **3** by varying the substituents of R, R^1, and R^2. This reaction was discovered in 2010 by Nicolaou et al. during the total synthesis of hopeahainol A.[6] They found that the use of 3.0 equiv of *p*-tolunesulfonic acid could promote the reaction of 3.0 equiv of resorcinol with 1.0 equiv of an ester **1** to form the corresponding product **3**, which they proposed to proceed through path a.[6] However, the substrate scope remained unexplored. To date, no catalytic version of this reaction and no systematic studies into this efficient reaction have been reported. To develop a catalytic version, the main challenge is to overcome the difficulty in the formation of the carbocationic intermediate **i** or **iv** for the Friedel–Crafts reaction step, which resulted from the net destabilizing effect of the electron-withdrawing ester group. Despite achievements in the catalytic arylation of tertiary alcohols,[7] the use of tertiary alcohols with an α-electron-withdrawing-substitutent for reaction development is limited to alcohols that could form reactive vinylogous iminium or oxonium intermediates.[7e,8]

RESULTS AND DISCUSSION

Most recently, we have reported that $Hg(ClO_4)_2{\cdot}3H_2O$ could catalyze a highly efficient Friedel–Crafts arylation of 3-alkyl or 3-arylhydroxyoxindoles.[9] On the basis of this result, we tried to develop an efficient catalytic version of this tandem reaction to 3,3-disubstituted benzofuranones. The reaction of α-hydroxy ester **1a** and phenol **2a** was undertaken for condition optimization, and typical results were shown in Table 1.

We first screened a variety of cheap and easy to handle metal perchlorate hydrates,[10] known powerful Lewis acids. When reaction was run in CH_3NO_2 at 60 °C using 1.5 equiv of phenol **2a**, only perchlorate hydrates of Hg(II), In(III), Fe(III), and Zr(III) could work, and $Zr(ClO_4)_2{\cdot}8H_2O$ seemed to be the most reactive, affording **3a** in 43% yield (Table 1, entries 1–4). Brønsted acids were also tried, and only HOTf and $HClO_4$ could give product **3a** in moderate yield (Table 1, entries 5–6). Next, $Zr(ClO_4)_2{\cdot}8H_2O$ and $HClO_4$ were used for further optimization. Interestingly, when increasing the temperature from 60 to 70 °C, the reaction catalyzed by $HClO_4$ could finish within 24 h, giving product **3a** in 85% yield (Table 1, entry 8), superior to that catalyzed by $Zr(ClO_4)_2{\cdot}8H_2O$ (Table 1, entry 7). Reaction at 80 °C resulted in the formation of side products and lower yield of **3a** (Table 1, entry 9). The use of 1.2 equiv of **2a** gave **3a** in lower yield (Table 1, entry 10). The solvent effects were also evaluated, and CH_3NO_2 turned out to be the best. For example, no reaction took place in toluene or ^{t}BuOMe, and reaction in CH_3CN or ethyl acetate afforded

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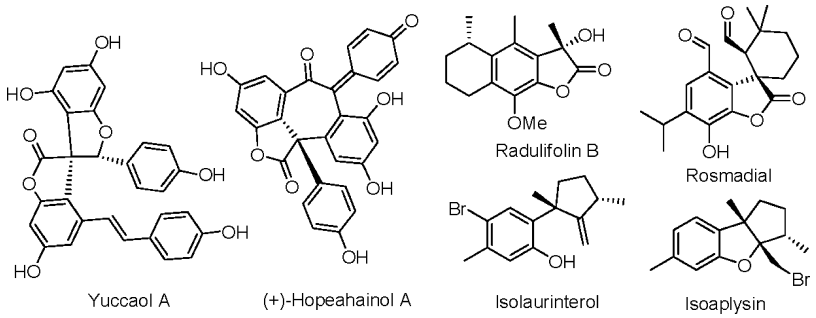


Figure 1. Representative natural products.

Scheme 1. Tandem Reaction to 3,3-Disubstituted Benzofuranones

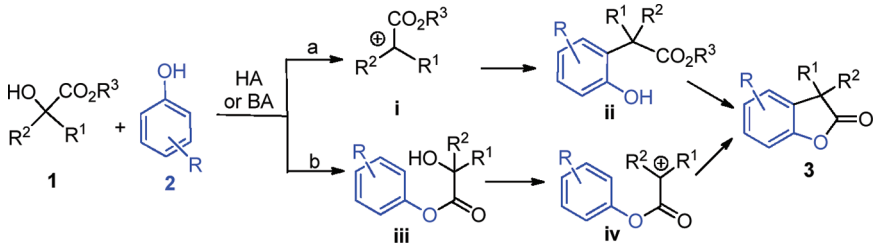
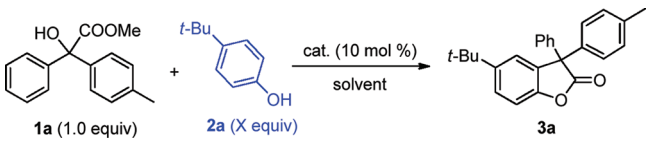


Table 1. Condition Optimization



entry[a]	catalyst	solvent	X	temp (°C)	time (h)	yield (%)[b]
1	$Hg(ClO_4)_2·3H_2O$	CH_3NO_2	1.5	60	36	31
2	$In(ClO_4)_3·8H_2O$	CH_3NO_2	1.5	60	36	20
3	$Fe(ClO_4)_3·xH_2O$	CH_3NO_2	1.5	60	36	23
4	$Zr(ClO_4)_2·8H_2O$	CH_3NO_2	1.5	60	36	43
5	HOTf	CH_3NO_2	1.5	60	36	28
6	$HClO_4$	CH_3NO_2	1.5	60	36	34
7	$Zr(ClO_4)_2·8H_2O$	CH_3NO_2	1.5	70	24	48
8	$HClO_4$	CH_3NO_2	1.5	70	24	85
9	$HClO_4$	CH_3NO_2	1.5	80	24	79
10	$HClO_4$	CH_3NO_2	1.2	70	24	56
11	$HClO_4$	CH_3CN	1.5	70	24	57
12	$HClO_4$	EtOAc	1.5	70	24	44

[a]On a 0.10 mmol scale. [b]Isolated yield.

product **3a** in lower yield (Table 1, entries 11−12). The evaluation of substrate scope was then carried out in CH_3NO_2 at 70 °C, using 10 mol % of $HClO_4$ as the catalyst.

Different substituted phenols were first examined (Table 2). Generally, electron-rich phenols such as **2c** and **2e−f** worked well to give the desired products in excellent yield (Table 2, entries 1, 3, 5 and 6). Bromo-substituted phenols **2b** and **2d** could also afford products **3b** and **3d** in good yield (Table 2, entries 2 and 4), but the reaction time was much longer. Phenols **2g−j** with a methyl group on different positions were also tried, and the corresponding products **3g−j** were obtained in good yield (Table 2, entries 7−10).

Then different substituted α-hydroxy acid esters **1a−l** were tried (Table 3), and the electronic effects of substituents on reaction rate were obvious. In the case of α,α-diaryl esters **1a**, **1b**, and **1d** with electron-rich substituent on the *ortho or para* position of phenyl ring, the reaction proceeded smoothly to afford the product in high yield (Table 3, entries 1, 2 and 4). With only one electron-withdrawing group, esters **1e** and **1f** worked well to afford the desired products **3n** and **3o** in good yield. However, with two CF_3 groups, ester **1g** reacted very slowly to give product **3p** in 46% yield after 120 h (Table 3, entries 5−7). To our delight, this protocol could be extended to α-alkyl α-aryl hydroxy acid esters **1i−l**, which provided the corresponding 3-alkyl-3-aryl benzofuranones **3r−u** in good yield (Table 3, entries 9−12).

We also tried to synthesize 3,3-dialkyl benzofuranones by this protocol. Unfortunately, even in the presence of 100 mol % of $HClO_4$, α,α-dialkyl hydroxy acid ester **1m** failed to react with phenols to give the desired product, possibly because **1m** underwent elimination reaction under this condition.

In addition to being interesting targets for medicinal chemistry, the thus obtained 3,3-disubstituted benzofuranones with a phenol or bromo substituent were versatile for further elaboration (Scheme 2). For example, product **4**, obtained from **3e** in 82% yield, could be readily converted to compound **5** and **6** via Pd-catalyzed coupling reactions. After protecting the phenol hydroxy group of product **3v** with suitable functional groups, the resulting products **7** and **8** could be readily transformed into interesting polycyclic compounds **9−11** in reasonable yields.

Since the reaction of **1d** and **2e** proceeded rapidly at 25 °C to give product **3m** in 78% yield after 24 h (Table 3, entry 4), it offered the premise to investigate the reaction mechanism by NMR studies. Accordingly, the reaction of **1d** and **2e** was subjected to NMR studies using CD_3NO_2 as the solvent at 25 °C, in the presence of 10 mol % $HClO_4$. As shown in Figure 2, no obvious change happened after mixing **1d** and **2e**, except the peak of OH group of **1d** shifted from 4.53 to 4.63 (Figure 2c).

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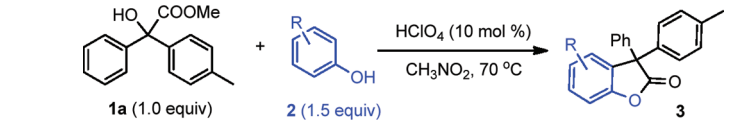
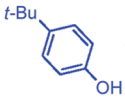
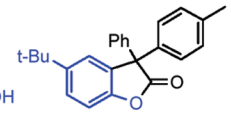
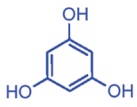
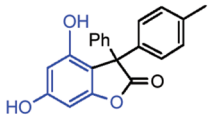
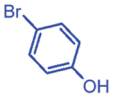
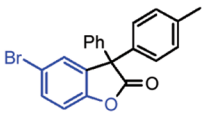
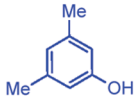
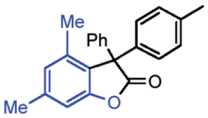
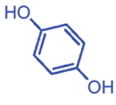
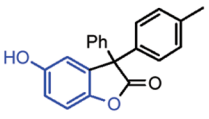
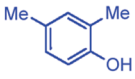
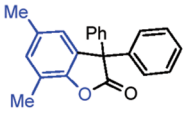
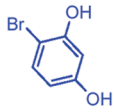
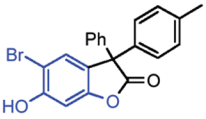
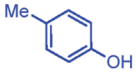
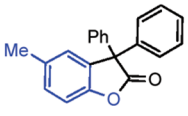
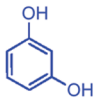
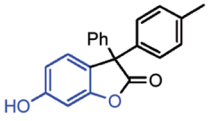
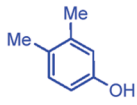
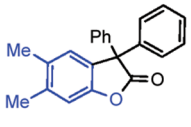
Table 2. Substrate Scope of Different Phenols



Entry[a]	2	Product 3	Entry	2	Product 3[b]
1			6		
	2a	**3a** (28 h, 85%)		2f	**3f** (5 h, 97%)
2			7		
	2b	**3b** (72 h, 60%)		2g	**3g** (45 h, 61%)
3			8		
	2c	**3c** (3 h, 86%)		2h	**3h** (25 h, 56%)
4			9		
	2d	**3d** (17 h, 68%)		2i	**3i** (25 h, 70%)
5			10		
	2e	**3e** (2 h, 94%)		2j	**3j** (45 h, 80%)

[a]On a 0.3 mmol scale. [b]Isolated yield.

In contrast, two new peaks at 3.88 and 3.76 appeared with 1:1 ratio after adding 10 mol % of $HClO_4$ for 10 min (Figure 2d), which possibly correlated to the methyl ester and methoxy group of the Friedel–Crafts adduct **v**, which we tried in vain to isolate from the reaction mixture. This observation, together with the fact that only trace amount of MeOH could be detected at the first 10 min (Figure 2d) and the characteristic peak of MeOH at 3.45 is much weaker than the two peaks at 3.88 and 3.76 even after one hour (Figure 2e), suggested that this reaction began with an intermolecular Friedel–Crafts reaction, followed by lactone formation (for the full NMR spectra, see the Supporting Information). A weak new peak at 3.66 correlated to methoxy group of **3m** was also observed at the first 10 min, which gradually developed. For comparison, the NMR changes of the individual starting materials **2e** and **1d** when independently mixed with 10 mol % of $HClO_4$ in CD_3NO_2 at 25 °C were also examined, and the results are provided in the Supporting Information.

CONCLUSION

A simple and highly efficient tandem reaction from easily available α-hydroxy acid esters and substituted phenols has been developed, allowing ready synthesis of both 3,3-diaryl and 3-alkyl-3-aryl benzofuranones with hindered all-carbon quaternary centers, in high structural diversity for biological evaluation and studies on the structure–activity relationship. The usefulness of the products has been demonstrated by the facile transformation to interesting polycyclic compounds. The NMR studies supported that the reaction proceeded via the sequential Friedel–Crafts/lactonization reaction. The use of simple and inexpensive catalyst and starting materials, together with the usefulness of the products, made our method potentially useful.

EXPERIMENTAL SECTION

General Information. Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products were carried out by flash chromatography on silica gel. Chemical yields refer to pure isolated substances. All reactions were run in air except noted. Anhydrous CH_3NO_2 was prepared by drying over anhydrous Na_2SO_4 and then distilling under reduced pressure. Commercially available $HClO_4$ (70%, aq) was used as received. α-Hydroxy acid esters **1**[6,11] and 4-bromobenzene-1,2-diol[12] were prepared using literature procedures.

Caution! Although the use of $HClO_4$ (70%, aq) as the catalyst could reduce the potential danger associated with $HClO_4$, special care should still be taken during the reaction course when heating the nitromethane solution containing $HClO_4$.

General Procedure for the Tandem Friedel–Crafts/Lactonization Reaction. Unless mentioned, the reaction was carried out in air. To a 5-mL vial were added α-hydroxy acid esters **1** (0.3 mmol), phenols **2** (0.45 mmol, 1.5 equiv.), and 0.5 mL of anhydrous CH_3NO_2.

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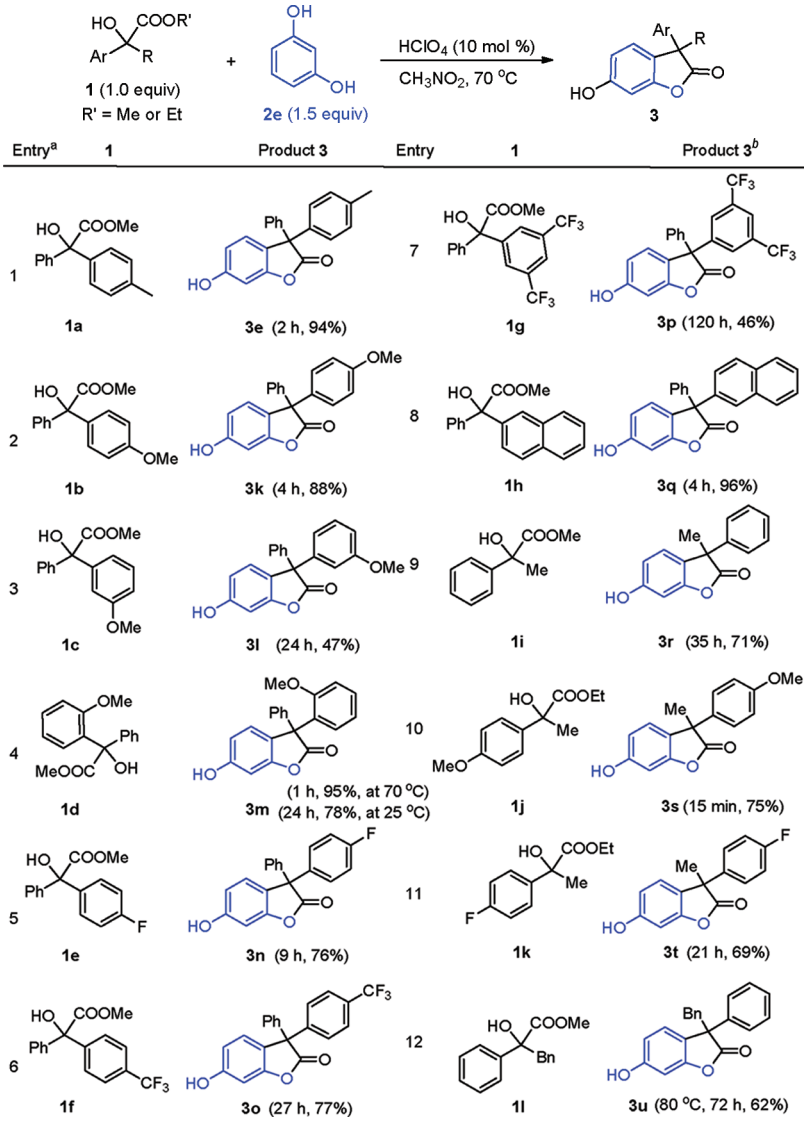
Table 3. Substrate Scope of Different α-Hydroxy Acid Esters



[a]On a 0.3 mmol scale. [b]Isolated yield.

After adding $HClO_4$ (solution in CH_3NO_2), the reaction mixture was stirred at 70 °C until almost full conversion of **1**, confirmed by TLC analysis. The reaction mixture was directly subjected to column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to afford the desired product **3**.

*5-tert-Butyl-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3a**).* Reaction was run under N_2 atmosphere. White solid: 91.2 mg, isolated yield 85%; mp 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.16 (m, 7H), 7.08−7.02 (m, 5H), 2.24 (s, 3H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 150.4, 147.7, 141.0, 137.9, 137.6, 130.7, 129.4, 128.6, 128.1, 128.0, 127.7, 126.0, 122.91, 110.3, 61.4, 34.7, 31.5, 21.0; IR (neat) 2954, 1800, 1613, 1486, 1140, 1056, 746, 698 cm^{-1}; GC−MS (EI) 356 (M^+, 21), 313 (100). HRMS (EI) Exact mass calcd for $C_{25}H_{24}O_2$ $[M]^+$: 356.1776. Found: 356.1771.

*5-Bromo-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3b**).* Yellow oil: 68.0 mg, isolated yield 60%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.38 (m, 1H), 7.30−7.25 (m, 4H), 7.18−7.15 (m, 2H), 7.09−7.01 (m, 5H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 151.5, 140.0, 138.1, 137.0, 133.4, 132.2, 129.6, 129.1, 128.9, 128.1, 128.0, 127.9, 117.1, 112.8, 61.2, 21.0; IR (neat) 2963, 1806, 1699, 1486, 1261, 1057, 928, 696, 623 cm^{-1}; GC−MS (EI) 378, 380 (M^+, 22, 21), 335 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{15}O_2{}^{79}Br$ $[M]^+$: 378.0255. Found: 378.0253.

*5-Hydroxy-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3c**).* White solid: 80.0 mg, isolated yield 86%; mp 149−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.26 (m, 5H), 7.13 (m, 4H), 7.06−7.04 (m, 1H), 6.79−6.75 (m, 2H), 4.91 (s, br, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 152.6, 146.4, 140.6, 137.8, 137.5, 132.4, 129.4, 128.7, 128.1, 128.0, 127.9, 115.8, 113.3, 111.8, 61.7, 21.0; IR (neat) 3430, 2961, 1762, 1609, 1490, 1337, 1072, 801, 698 cm^{-1}; GC−MS (EI) 316 (M^+, 20), 273 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_3$ $[M]^+$: 316.1099. Found: 316.1100.

*5-Bromo-6-hydroxy-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3d**).* Yellow solid: 79.4 mg, isolated yield 68%; mp 174−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.21 (m, 4H), 7.15−7.13 (m, 2H), 7.03 (s, 4H), 6.80 (s, 1H), 5.77 (s, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 153.1, 152.9, 140.4, 137.9, 137.3, 129.5, 128.8, 128.0, 127.9, 127.8, 127.2, 124.8, 105.3, 99.8, 60.8, 21.0; IR (neat) 3386, 3031, 2923, 1778, 1632, 1491, 1290, 1090, 960, 761, 696 cm^{-1}; GC−MS (EI) 394, 396 (M^+, 34, 36), 353 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{15}O_3{}^{79}Br$ $[M]^+$: 394.0205. Found: 394.0215.

*6-Hydroxy-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3e**).* White solid: 89.0 mg, isolated yield 94%; mp 195−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, br, 1H), 7.30−7.24 (m, 5H), 7.14−7.10 (m, 4H), 7.07 (ABd, J = 8.0 Hz, 1H), 6.73 (s, 1H), 6.67 (ABd, J = 8.0 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 157.4,

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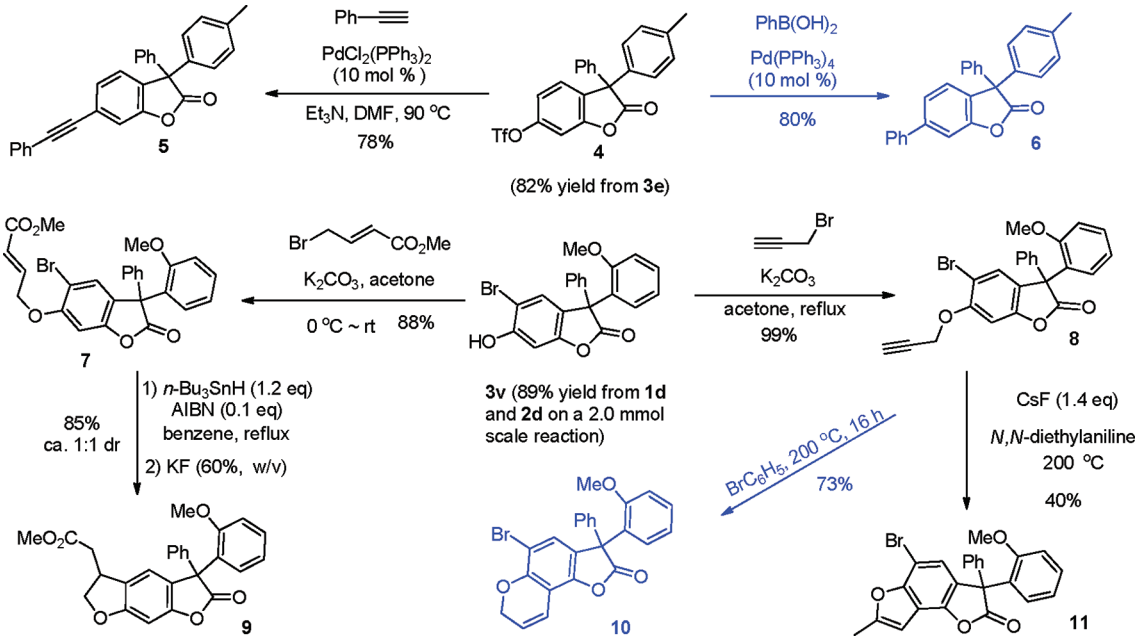
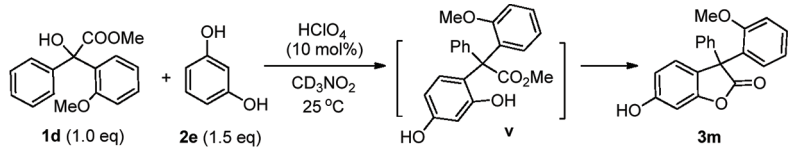
Scheme 2. Product Elaboration





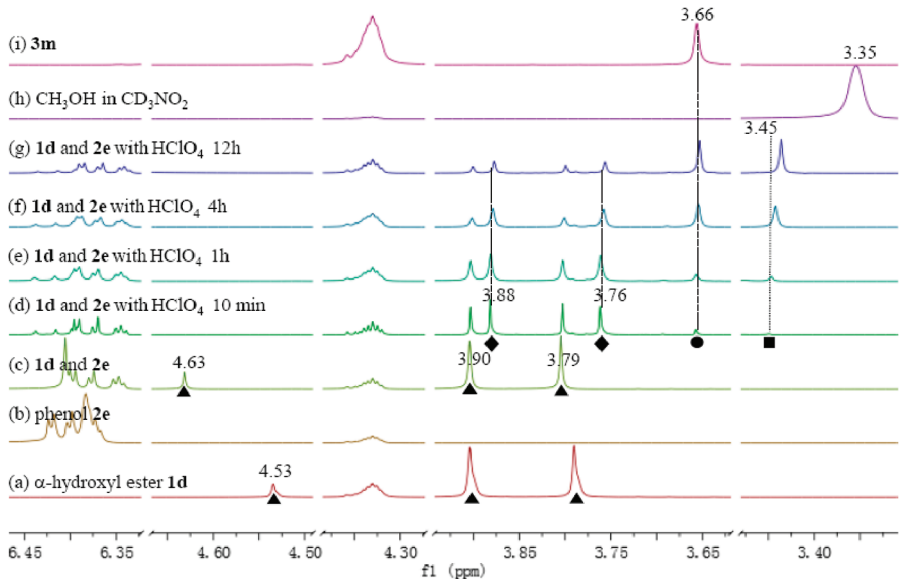


Figure 2. ^{1}H NMR analysis of the reaction of **1d** and **2e** in CD_3NO_2 at 25 °C.

153.3, 141,1, 138.0, 137.5, 129.3, 128.6, 128.0, 127.9, 127.6, 126.6, 122.3, 111.8, 99.1, 60.7, 21.0; IR (neat) 3430, 3056, 1783, 1621,1452, 1133, 1064, 970, 794, 635 cm^{-1}; GC−MS (EI) 316 (M^+, 6), 273 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_3$ $[M]^+$: 316.1099. Found: 316.1096.

4,6-Dihydroxy-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (***3f***). White solid: 96.9 mg, isolated yield 97%; mp 110−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 5H), 7.21−7.14 (m, 4H), 6.36 (d, J = 2.0 Hz, 1H), 6.12 (d, J = 2.0 Hz, 1H), 5.40 (s, br, 1H), 4.91 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 157.9, 153.7, 153.1, 138.7, 138.0, 135.6, 129.5, 128.7, 128.4, 128.2, 128.1, 109.3, 99.9, 92.5, 60.7, 21.0; IR (neat) 3333, 1777, 1626, 1460, 1130, 995, 928, 811, 696 cm^{-1}; GC−MS (EI) 332 (M^+, 4), 149 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_4$.$[M]^+$:332.1049. Found: 332.1050.

4,6-Dimethyl-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (***3g***). White solid: 60.0 mg, isolated yield 61%; mp 137−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.15 (m, 5H), 7.09−7.03 (m, 4H), 6.81 (s, 1H), 6.67 (s, 1H), 2.28 (s, 3H), 2.24 (s, 3H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 152.8, 139.6, 138.2, 137.7, 136.2, 134.8, 129.1, 129.0, 128.9, 128.4, 127.8, 127,5, 126.8, 109.3, 61.5, 21.5, 21.0, 18.6; IR (neat) 2961, 1791, 1631, 1494, 1262, 1026, 869, 636 cm^{-1}; GC−MS (EI) 328 (M^+, 16), 285 (100). HRMS (EI) Exact mass calcd for $C_{23}H_{20}O_2$ $[M]^+$: 328.1463. Found: 328.1464.

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5,7-Dimethyl-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3h**). Reaction was run under N_2 atmosphere. White solid: 54.2 mg, isolated yield 56%; mp 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.22−7.18 (m, 5H), 7.08−7.03 (m, 4H), 6.87 (s, 1H), 6.79 (s, 1H), 2.25 (s, 6H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 177.5, 149.0, 141.0, 138.0, 137.5, 133.8, 131.1, 130.7, 129.3, 128.6, 128.2, 128.1, 127.7, 123.7, 120.9, 61.6, 21.2, 21.0, 15.1; IR (neat) 2924, 1794, 1673, 1486, 1381, 1254, 1099, 936, 736, 699 cm^{-1}; GC−MS (EI) 328 (M^+, 29), 285 (100). HRMS (EI) Exact mass calcd for $C_{23}H_{20}O_2$ $[M]^+$: 328.1463. Found: 328.1465.

5-Methyl-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3i**). Reaction was run under N_2 atmosphere. White solid: 66 mg, isolated yield 70%; mp 154−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.19 (m, 5H), 7.08−7.03 (m, 5H), 7.00−6.97 (m, 2H), 2.24 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 150.5, 140.9, 137.8, 137.6, 134.2, 131.2, 129.6, 129.4, 128.6, 128.2, 128.0, 127.7, 126.4, 110.70, 61.2, 21.2, 21.0; IR (neat) 3028, 2951, 1797, 1602, 1487, 1139, 1064, 936, 697, 632 cm^{-1}; GC−MS (EI) 314 (M^+, 34), 271 (100). HRMS (EI) Exact mass calcd for $C_{22}H_{18}O_2$ $[M]^+$: 314.1307. Found: 314.1306.

5,6-Dimethyl-3-phenyl-3-p-tolylbenzofuran-2(3H)-one (**3j**). White solid: 78.0 mg, isolated yield 80%; mp 170−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.14 (m, 5H), 7.07−7.02 (m, 4H), 6.92−6.89 (m, 2H), 2.22 (s, 3H), 2.19 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 150.8, 141.1, 138.0, 137.9, 137.5, 132.7, 129.3, 128.6, 128.4, 128.1, 128.0, 127.6, 126.7, 111.9, 61.1, 21.0, 20.2, 19.6; IR (neat) 2922, 2853, 1459, 1799, 1628, 1459, 1057, 959, 760, 696 cm^{-1}; GC−MS (EI) 328 (M^+, 26), 285 (100). HRMS (EI) Exact mass calcd for $C_{23}H_{20}O_2$ $[M]^+$: 328.1463. Found: 328.1461.

6-Hydroxy-3-(4-methoxyphenyl)-3-phenylbenzofuran-2(3H)-one (**3k**). White solid: 87.2 mg, isolated yield 88%; mp 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, br, 1H), 7.30−7.23 (m, 5H), 7.17 (ABd, J = 7.6 Hz, 2H), 7.05 (ABd, J = 8.4 Hz, 1H), 6.83 (ABd, J = 8.4 Hz, 2H), 6.73 (s, 1H), 6.67 (ABd, J = 8.4 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 159.0, 157.7, 153.2, 141.4, 132.9, 129.3, 128.6, 127.9, 127.6, 126.5, 122.2, 113.9, 111.8, 99.1, 60.3, 55.2; IR (neat) 3434, 2950, 2833, 1781, 1621, 1453, 1253, 1064, 970, 832, 635 cm^{-1}; GC−MS (EI) 332 (M^+, 46), 303 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_4$ $[M]^+$: 332.1049. Found: 332.1048.

6-Hydroxy-3-(3-methoxyphenyl)-3-phenylbenzofuran-2(3H)-one (**3l**). Colorless oil: 47.0 mg, isolated yield 47%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.21 (m, 6H), 7.10−7.08 (m, 1H), 6.84−6.80 (m, 3H), 6.70 (s, 1H), 6.65−6.62 (m, 1H), 5.76 (s, 1H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 177.5, 159.6, 156.8, 153.3, 142.2, 140.6, 129.7, 128.7, 128.0, 127.8, 126.8, 122.7, 120.5, 114.4, 112.9, 111.8, 99.2, 61.0, 55.2; IR (neat) 3391, 2837, 1802, 1628, 1489, 1256, 1056, 965, 735, 695 cm^{-1}; GC−MS (EI) 332 (M^+, 63), 273 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_4$ $[M]^+$: 332.1049. Found: 332.1048.

6-Hydroxy-3-(2-methoxyphenyl)-3-phenylbenzofuran-2(3H)-one (**3m**). White solid: 95.0 mg, isolated yield 95%; mp 213-214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.46−7.45 (m, 2H), 7.36−7.33 (m, 3H), 7.26−7.23 (m, 1H), 7.08 (s, 1H), 6.88−6.81 (m, 4H), 6.71−6.70 (m, 1H), 6.62−6.60 (m, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 178.1, 158.3, 156.7, 154.2, 137.9, 131.8, 129.4, 129.2, 129.0, 128.3, 128.2, 126.2, 120.8, 120.4, 112.2, 111.0, 98.5, 57.4, 55.8; IR (neat) 3382, 3055, 1777, 1619, 1456, 1066, 967, 766, 695 cm^{-1}; GC−MS (EI) 332 (M^+, 46), 303 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_4$ $[M]^+$: 332.1049. Found: 332.1048.

3-(4-Fluorophenyl)-6-hydroxy-3-phenylbenzofuran-2(3H)-one (**3n**). White solid: 73.1 mg, isolated yield 76%; mp 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.23 (m, 7H), 7.08−7.00 (m, 3H), 6.73 (s, 1H), 6.68−6.66 (m, 1H), 6.00 (s, br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 163.5, 161.0, 156.90, 153.2, 140.8, 136.4 (d, J = 3.0 Hz), 129.9, (d, J = 8.0 Hz), 128.8, 127.9 (d, J = 13.0 Hz), 126.7, 126.6, 115.6 (d, J = 21.0 Hz), 112.0, 99.3, 60.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.2; IR (neat) 3419, 3066, 2962, 1776, 1625, 1457, 1298, 1070, 973, 696 cm^{-1}; GC−MS (EI) 320 (M^+, 4), 291(100). HRMS (EI) Exact mass calcd for $C_{20}H_{13}O_3F$ $[M]^+$: 320.0849. Found: 320.0850.

6-Hydroxy-3-phenyl-3-(4(trifluoromethyl)phenyl)benzofuran-2(3H)-one (**3o**). White solid: 85.0 mg, isolated yield 77%; mp 184−186 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (ABd, J = 8.4 Hz, 2H), 7.39 (ABd, J = 8.0 Hz, 2H), 7.35−7.32 (m, 3H), 7.24−7.22 (m, 2H), 7.12−7.10 (m, 1H), 6.75−6.74 (m, 1H), 6.70−6.67 (m, 1H), 5.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 176.8, 159.0, 153.2, 145.2, 140.5, 129.2 (q, J = 73.0 Hz), 128.0, 127.9, 126.4, 125.52, 125.48, 125.3, 122.5, 120.1, 112.3, 99.2, 60.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.7; IR (neat) 3444, 2925, 2854, 1787, 1620, 1064, 959, 834, 633 cm^{-1}; GC−MS (EI) 370 (M^+, 45), 341 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{13}O_3F_3$ $[M]^+$: 370.0817. Found: 370.0818.

3-(3,5-Bis(trifluoromethyl)phenyl)-6-hydroxy-3-phenylbenzofuran-2(3H)-one (**3p**). White solid: 61.0 mg, isolated yield 46%; mp 144−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.74 (m, 2H), 7.35 (m, 3H), 7.19−7.18 (m, 2H), 7.11 (ABd, J = 8.0 Hz, 1H), 6.78 (s, 1H), 6.72 (ABd, J = 8.0 Hz, 1H), 5.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 176.2, 157.5, 153.4, 143.3, 139.7, 132.1 (q, J = 34.0 Hz), 129.3, 128.6, 128.4, 127.6, 126.6, 122.9 (q, J = 271.0 Hz), 122.1, 121.1, 112.4, 99.8, 60.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.8; IR (neat) 3452, 2925, 1785, 1626, 1276, 1071, 681 cm^{-1}; GC−MS (EI) 438 (M^+, 39), 409 (100). HRMS (EI) Exact mass calcd for $C_{22}H_{12}O_3F_6$ $[M]^+$: 438.0691. Found: 438.0693.

6-Hydroxy-3-(naphthalen-2-yl)-3-phenylbenzofuran-2(3H)-one (**3q**). White solid: 101.0 mg, isolated yield 96%; mp 174−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.79 (m, 2H), 7.75−7.74 (m, 1H), 7.68 (s, 1H), 7.57 (s, 1H), 7.48−7.46 (m, 2H), 7.41−7.39 (m, 1H), 7.31−7.26 (m, 5H), 7.15 (ABd, J = 8.4 Hz, 1H), 6.78 (s, 1H), 6.70 (ABd, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 157.7, 153.4, 140.9, 138.2, 132.9, 132.6, 128.71, 128.66, 128.2, 128.1, 127.8, 127.5, 126.8, 126.7, 126.5, 126.4, 126.0, 122.0, 111.9, 99.3, 61.1; IR (neat) 3067, 1783, 1623, 1451, 1294, 1054, 963, 857, 698 cm^{-1}; GC−MS (EI) 352 (M^+, 48), 289 (100). HRMS (EI) Exact mass calcd for $C_{24}H_{16}O_3$ $[M]^+$: 352.1099. Found: 352.1098.

6-Hydroxy-3-methyl-3-phenylbenzofuran-2(3H)-one (**3r**). Brown solid: 48.0 mg, isolated yield 71%; mp 94−96 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.17 (m, 5H), 6.96 (ABd, J = 8.0 Hz, 1H), 6.64 (s, 1H), 6.59 (ABd, J = 8.0 Hz, 1H), 6.03 (s, br, 1H), 1.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.9, 156.7, 153.4, 139.6, 128.8, 127.8, 126.4, 125.1, 124.1 111.7, 99.2, 50.7, 24.9; IR (neat) 3393, 2978, 1780, 1629, 1281, 1025, 959, 731, 632 cm^{-1}; GC−MS (EI) 240 (M^+, 14), 211 (100). HRMS (EI) Exact mass calcd for $C_{15}H_{12}O_3$ $[M]^+$:240.0786. Found: 240.0785.

6-Hydroxy-3-(4-methoxyphenyl)-3-methylbenzofuran-2(3H)-one (**3s**). Colorless oil: 60.0 mg, isolated yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.22 (m, 2H), 7.04 (ABd, J = 8.0 Hz, 1H), 6.86−6.84 (m, 2H), 6.70 (s, 1H), 6.67 (ABd, J = 8.0 Hz, 1H), 6.17 (s, br, 1H), 3.77 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0, 159.1, 156.7, 153.5, 131.8, 127.7, 125.1, 124.3, 114.1, 111.6, 99.2, 55.3, 50.0, 25.0; IR (neat) 3394, 2976, 2838, 1781, 1629, 1252, 1026, 959, 727, 621 cm^{-1}; GC−MS (EI) 270 (M^+, 68), 241 (100). HRMS (EI) Exact mass calcd for $C_{16}H_{14}O_4$ $[M]^+$: 270.0892. Found: 270.0893.

3-(4-Fluorophenyl)-6-hydroxy-3-methylbenzofuran-2(3H)-one (**3t**). Yellow oil: 51.3 mg, isolated yield 69%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.28 (m, 2H), 7.06−6.98 (m, 3H), 6.73 (s, 1H), 6.70−6.68 (m, 1H), 6.14 (s, 1H), 1.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 163.5, 161.0, 156.8, 153.4, 135.4 (d, J = 3.0 Hz), 128.3 (d, J = 8.0 Hz), 125.1, 123.8, 115.7 (d, J = 2.0 Hz), 111.8, 99.3, 50.1, 25.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −114.4; IR (neat) 3409, 2981, 1781, 1630, 1456, 1142, 960, 830, 627 cm^{-1}; GC−MS (EI) 258 (M^+, 47), 229 (100). HRMS (EI) Exact mass calcd for $C_{15}H_{11}O_3F$ $[M]^+$: 258.0692. Found: 258.0693.

3-Benzyl-6-hydroxy-3-phenylbenzofuran-2(3H)-one (**3u**). Yellow solid: 58.0 mg, isolated yield 62%; mp 183−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) 8.66 (s, br, 1H), 7.45−7.43 (m, 2H), 7.30−7.20 (m, 3H), 7.01−7.00 (m, 3H), 6.92−6.90 (m, 1H), 6.80−6.78 (m, 2H), 6.60−6.58 (m, 1H), 6.40 (s, 1H), 3.58 (AB, J = 13.2 Hz, 1H), 3.38 (AB, J = 13.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 178.3, 158.4, 153.9, 139.3, 135.3, 130.2, 128.8, 128.0, 127.9, 127.1, 127.0, 126.5, 119.1, 111.4, 98.9, 57.1, 45.1; IR (neat) 3444, 3032, 2923, 1798, 1624, 1290, 1057, 961, 698 cm^{-1}; GC−MS (EI) 316 (M^+, 6), 225 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{16}O_3$ $[M]^+$: 316.1099. Found: 316.1100.

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*5-Bromo-6-hydroxy-3-(2-methoxyphenyl)-3-phenylbenzofuran-2(3H)-one (**3v**).* Prepared from **2d** and **1d** on a 2.0 mmol scale. White solid: 732 mg, isolated yield 89%; mp 236−238 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.35 (m, 5H), 7.30−7.24 (m, 1H), 7.11 (s, 1H), 6.89−6.80 (m, 4H), 5.85 (s, 1H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 156.5, 153.9, 152.8, 136.8, 130.8, 129.44, 129.4, 129.1, 128.5, 128.40, 128.35, 123.8, 120.9, 112.0, 104.3, 99.3, 57.4, 55.7; IR (neat) 3339, 2974, 1779, 1618, 1287, 1048, 761, 695 cm^{-1}; MS (EI) 410, 412 (M^+, 21, 22), 351 (100). HRMS (EI) Exact mass calcd for $C_{21}H_{15}O_4{}^{79}Br$ $[M]^+$: 410.0154. Found: 410.0155.

Procedure for the Preparation of 4 from 3e.[13] A solution of Tf_2O (169.2 mg, 0.6 mmol) in CH_2Cl_2 was added dropwise to a solution of pyridine (79 mg, 1.0 mmol) and **3e** (197 mg, 0.5 mmol) in anhydrous CH_2Cl_2 at 0 °C. The mixture was warmed to room temperature naturally and allowed to stir until almost full conversion of **3e**, confirmed by TLC analysis. The mixture was then diluted with Et_2O, quenched with saturated NH_4Cl, and washed with saturated $NaHCO_3$ and brine. After drying with anhydrous Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified by column chromatography to give **4** (184.0 mg, 82% yield) as a white solid: mp 99−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.24 (m, 4H), 7.23−7.21 (m, 2H), 7.17−7.09 (m, 6H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 153.0, 149.1, 139.8, 138.3, 136.7, 131.7, 129.7, 128.9, 128.2, 128.0, 127.8, 127.4, 118.7 (q, J = 319.0 Hz), 117.5, 105.5, 60.8, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −72.7; IR (neat) 3331, 2975, 1811, 1422, 1055, 959, 696 cm^{-1}; GC−MS(EI) 448 (M^+, 45), 405 (100). HRMS (EI) Exact mass calcd for $C_{22}H_{15}O_5SF_3[M]^+$: 448.0592. Found: 448.0589.

Procedure for the Preparation of 5 from 4. The compound **5** was prepared according to the literature procedure.[14] A mixture of **4** (67.2 mg, 0.15 mmol), phenylacetylene (30.6 mg, 0.3 mmol), Et_3N (0.2 mL), and $Pd(PPh_3)_2Cl_2$ (11 mg, 0.015 mmol) in 0.5 mL of anhydrous DMF was stirred at 90 °C under N_2 atmosphere until full conversion of **4**, confirmed by TLC analysis. The reaction mixture was then diluted with water, extracted with Et_2O (3 × 10 mL), washed with water (3 × 10 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Column chromatography of the residue on silica gel to afford the desired product **5** (47 mg, 78% yield) as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.43 (m, 2H), 7.28−7.14 (m, 11H), 7.13−7.05 (m, 4H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 152.4, 140.3, 137.9, 137.2, 131.7, 131.4, 129.5, 128.8, 128.64, 128.56, 128.4, 128.1, 128.0, 127.95, 126.0, 124.3, 122.7, 113.9, 90.5, 88.3, 61.0, 21.0; IR (neat) 2962, 1806, 1619, 1573, 1494, 1260, 1055, 961, 690 cm^{-1}; MS (EI) 400 (M^+, 24). HRMS (EI) Exact mass calcd for $C_{29}H_{20}O_2$ $[M]^+$: 400.1463. Found: 400.1461.

Procedure for the Preparation of 6 from 4. The compound **6** was prepared according to the literature procedure.[15] A solution of **4** (44.8 mg, 0.1 mmol), phenylboronic acid (24.4 mg, 0.2 mmol), K_2CO_3 (2M, 1.0 mL), and $Pd(PPh_3)_4$ (12.4 mg, 0.01 mmol) in 1.0 mL of 1,4-dioxane was stirred at 130 °C for 5 h under N_2 atmosphere. To the reaction mixture was then added 10 mL of H_2O, which was then extracted with CH_2Cl_2 (3 × 20 mL), washed with water (2 × 10 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Column chromatography of the residue on silica gel affordeed the desired product **6** (30 mg, 80% yield) as white solid: mp 216−218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.56 (m, 2H), 7.47−7.30 (m, 5H), 7.37−7.34 (m, 6H), 7.19 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 153.0, 142.8, 140.7, 140.0, 137.8, 137.6, 130.1, 129.4, 128.9, 128.7, 128.1, 128.0, 127.9, 127.8, 127.2, 126.2, 123.5, 109.8, 61.0, 21.0; IR (neat) 2926, 1798, 1417, 1259, 1083, 953, 808, 764, 697 cm^{-1}; MS (EI) 376 (M^+, 37), 43 (100). HRMS (EI) Exact mass calcd for $C_{27}H_{20}O_2$ $[M]^+$: 376.1463. Found: 376.1465.

Procedure for the Preparation of 7 from 3v.[16] A mixture of **3v** (123 mg, 0.3 mmol) and anhydrous potassium carbonate (41.4 mg, 0.3 mmol) in dry acetone (3 mL) was stirred at 0 °C for 15 min. To this mixture was added a solution of methyl 4-bromocrotonate (82 mg, 0.36 mmol) in acetone (6 mL) drop by drop over a period of about 1 h; the mixture was maintained at 0 °C during the addition. After the addition was over, the reaction mixture was stirred overnight at room temperature. After this time, the inorganic salts were filtered, and the solvent was evaporated under reduced pressure. The residue was taken up in ether, washed with 2 N NaOH and water, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 10/1) to afford the product **7** (135 mg, 88% yield) as white solid: mp 194−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.36 (m, 5H), 7.30−7.26 (m, 1H), 7.22 (s, 1H), 7.08 (dt, J = 15.6 Hz, 3.6 Hz, 1H), 6.90−6.86 (m, 2H), 6.82−6.81 (m, 1H), 6.75 (s, 1H), 6.37 (d, J = 15.6 Hz, 1H), 4.79−4.78 (d, J = 1.6 HZ, 2H), 3.78 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 166.3, 156.4, 154.7, 153.5, 141.1, 136.8, 130.6, 129.9, 129.5, 129.4, 129.0, 128.5, 128.4, 123.7, 122.1, 120.9, 112.0, 106.1, 96.8, 67.6, 57.5, 55. 7, 51.7; IR (neat) 3001, 2949, 2836, 1816, 1727, 1484, 1177, 975, 755 cm^{-1}; MS (EI) 508, 510 (M^+, 33, 37), 451 (100). HRMS (EI) Exact mass calcd for $C_{26}H_{21}O_6{}^{79}Br$ $[M]^+$: 508.0521. Found: 508.0525.

Procedure for the Preparation of 9 from 7.[17] To a stirred solution of compound **7** (76 mg, 0.15 mmol) in anhydrous benzene (2 mL) at reflux was added AIBN (3 mg, 0.015 mmol). A solution of Bu_3SnH (52 mg, 0.18 mmol) in anhydrous benzene (4 mL) was added over 1.5 h. The reaction was maintained at reflux until full conversion of **7**, confirmed by TLC analysis. The solvent was removed by rotary evaporation, and the residue was dissolved in 1 mL of Et_2O and an aqueous solution of potassium fluoride (60%, w/v). The mixture was stirred vigorously overnight. The precipitate that formed was removed by vacuum filtration, and the two layers of the filtrate were separated. The aqueous layer was extracted with ether. The filtrate was evaporated and subjected to flash chromatography (petroleum ether/ethyl acetate = 10/1 to 6/1) to give the desired product **9** with 1:1 dr (55 mg, 85% yield) as white solid: mp 84−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.42−7.33 (m, 5H), 7.27−7.22 (m, 1H), 6.88−6.82 (m, 3H), 6.77−6.75 (m, 1H), 6.64 (s, 1H), 4.83−4.74 (m, 1H), 4.35−4.29 (m, 1H), 3.91−3.72 (m, 1H), 3.69 (s, 1.5 H), 3.66 (s, 1.5 H), 3.64 (s, 1.5 H), 3.49 (s, 1.5 H), 2.73 (ABd, J = 16.8 Hz, 5.6 Hz, 1H), 2.54 (ABd, J = 16.2 Hz, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 177.7, 172.0, 160.2, 156.7, 156.6, 153.8, 137.8, 137.7, 131.7, 131.6, 129.4, 129.3, 129.14, 129.08, 129.0, 128.3, 128.1, 124.3, 124.2, 121.9, 121.7, 121.13, 120.99, 120.8, 112.3, 112.1, 93.85, 93.82, 77.6, 57.5, 55.8, 55.7, 51.8, 51.6, 39.5, 39.2, 38.0, 37.9; IR (neat) 2951, 1802, 1733, 1619, 1481, 1253, 1140, 952, 792, 698 cm^{-1}; MS (EI) 430 (M^+, 36), 371 (100). HRMS (EI) Exact mass calcd for $C_{26}H_{22}O_6$ $[M]^+$: 430.1416. Found: 430.1417.

Procedure for the Preparation of 8 from 3v.[18] To a solution of **3v** (187 mg, 0.45 mmol) and potassium carbonate (124 mg, 0.9 mmol) in anhydrous acetone (3 mL) was added propargyl bromide (64 mg, 0.54 mmol). The mixture was then stirred at reflux until full conversion of **3u**, confirmed by TLC analysis. After filtration through Celite and washing with Et_2O, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (petroleum ether/ethyl acetate = 20/1) to afford the product **8** (199 mg, 99% yield) as white solid: mp 244−246 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.30 (m, 5H), 7.28−7.25 (m, 1H), 7.22 (s, 1H), 6.98 (s, 1H), 6.90−6.85 (m, 2H), 6.82−6.80 (m, 1H), 4.82−4.81 (d, J = 2.0 Hz, 2H), 3.65 (s, 3H), 2.59 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 156.5, 154.4, 153.4, 136.8, 130.7, 129.9, 129.5, 129.0, 128.6, 128.3, 124.1, 120.9, 112.0, 106.2, 97.8, 77.2, 76.8, 57.5, 57.3, 55.7; IR (neat) 3282, 2923, 1621, 1476, 1287, 1066, 954, 754, 631 cm^{-1}; GC−MS (EI) 448 (M^+, 45), 405 (100). HRMS (EI) Exact mass calcd for $C_{24}H_{17}O_4{}^{79}Br$ $[M]^+$: 448.0310. Found: 448.0313.

Procedure for the Preparation of 10 from 8.[19] A mixture of **8** (89.6 mg, 0.2 mmol) in bromobenzene (1 mL) was heated at 200 °C for 16 h in a sealed tube. After cooling to room temperature, the reaction mixture was directly subjected to column chromatography using petroleum ether/ethyl acetate (40/1 to 30/1) as the eluent to afford the desired product **10** (65 mg, 73% yield) as white solid: mp 225−227 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.30 (m, 5H), 7.28−7.25 (m, 1H), 6.97 (s, 1H), 6.89−6.88 (m, 2H), 6.80−6.79 (m, 1H), 6.68 (d, J = 10.0 Hz, 1H), 5.88 (dt, J = 10.0 Hz, 3.6 Hz, 1H), 5.04−4.96 (m, 2H), 3.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

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176.9, 156.5, 150.6, 148.2, 136.8, 130.6, 129.4, 129.1, 128.5, 128.4, 123.8, 122.8, 120.9, 117.8, 112.0, 108.2, 103.7, 66.5, 57.6, 55.7; IR (neat) 3007, 2838, 1809, 1645, 1488, 1375, 1070, 944, 754, 699 cm^{-1}; MS (EI) 448, 450 (M^+, 16, 16), 391 (100). HRMS (EI) Exact mass calcd for $C_{24}H_{17}O_4{}^{79}Br$ $[M]^+$: 448.0310. Found: 448.0307.

Procedure for the Preparation of 11 from 8.[20] A suspension of **8** (67.2 mg, 0.15 mmol) and CsF (32 mg, 0.21 mmol) in *N*,*N*-diethylaniline (0.5 mL) was heated at 200 °C for 5 h under N_2 atmosphere with stirring. The mixture was directly subjected to column chromatography using petroleum ether/ethyl acetate (100/1 to 40/1) as the eluent to afford the desired product **11** (27 mg, 40% yield) as white solid: mp 214−216 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44−7.35 (m, 5 H), 7.35−7.26 (m, 1H), 7.01 (s, 1H), 6.93−6.85 (m, 3H), 6.59 (s, 1H), 3.61 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 157.4, 156.6, 153.0, 144.5, 137.4, 131.1, 129.5, 129.4, 129.2, 128.5, 128.3, 124.4, 122.5, 121.0, 115.2, 112.1, 100.1, 97.7, 57.9, 55.7, 14.2; IR (neat) 2935, 1812, 1589, 1487, 1250, 1044, 943, 793, 698 cm^{-1}; MS (EI) 448, 450 (M^+, 14, 13), 391 (100). HRMS (EI) Exact mass calcd for $C_{24}H_{17}O_4{}^{79}Br$ $[M]^+$: 448.0310. Found: 448.0309.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterizations, copies of ^1H NMR and ^{13}C NMR of new compounds, and details about the NMR analysis of the reaction mechanism. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: jzhou@chem.ecnu.edu.cn.

Notes

The authors declare no competing financial interest.

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