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Nickel-Catalyzed Decarbonyloxidation of 3-Aryl Benzofuran-2(*3H*)ones to 2-Hydroxybenzophenones

Zhou Tong,[†] Zhi Tang,[†] Chak-Tong Au, [‡] Renhua Qiu^{*,†}

[†]State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha, 410082, P. R. China

[‡]College of Chemistry and Chemical Engineering, Hunan Institute of Engineering, Xiangtan, 411100, P.R. China

Supporting Information Placeholder



ABSTRACT: We have developed a protocol to facilitate the nickel-catalyzed decarbonyloxidation of 3-aryl benzofuran-2(3H)ones to 2-hydroxybenzophenones under mild conditions, which is an efficient approach for the decarbonyloxidation of lactones in
organic synthesis. A diverse range of substrates can undergo C(O)–O/C(O)–C bond cleavage to generate the target products in
good yields. These 2-hydroxybenzophenones can be converted into a variety of compounds via reactions such as esterification,
cyclization, and reduction.

INTRODUCTION

Owing to their high reactivity, 2-hydroxybenzophenones are important building blocks in organic synthesis for medicinal chemicals.¹ The derivatives with 2-hydroxybenzophenone skeleton exhibit a variety of biological activities. For example, 4-phenylchromenone is a building block for calcium channel blockers (a),^{1c} anti-influenza drug (b),^{1d} anti-HAV drug (c),^{1e} and antispasmodic agents (d) (Figure 1).^{1f}



Figure 1. Bioactive 2-hydroxybenzophenone derivatives

To fulfill the increasing requirement of 2-hydroxybenzophenones in organic synthesis and biological research, a number of valuable synthetic routes were developed (Scheme S1). The classical, efficient and reliable approach for the synthesis of 2-hydroxybenzophenones relies on the Fries rearrangement of phenyl ester.² Transition-metal-catalyzed synthesis of 2-hydroxybenzophenones is also disclosed with a few examples. For instance, the Pd-catalyzed *ortho*-C-H hydroxylation of benzophenones is an efficient method.³ However, the yield was moderate and bromide substrates was not compatible in this systems. Another route is the Rh-catalyzed oxidative coupling of salicylaldehyde with arylboronic acid,^{4a,4b} but a noble metal catalyst was required. The third route is Rh–Cu catalyzed C \equiv C bond cleavage reaction of alkynes with N-phenoxyacetamides,^{4c} but only limited examples are available for the synthesis of 2-hydroxybenzophenones with electron-withdrawing groups. Therefore, developing a new protocol to afford 2-hydroxybenzophenones is still valuable.

The cleavage of carbon–carbon (C-C) bond reaction is one of the most important bond transformations in organic synthesis,⁵ especially the decarbonylation, which has been recognized as a reliable synthetic method to diversified organic products. The decarbonylation is known as the

Tsuji-Wilkinson reaction that first disclosed as a rhodium-mediated reaction of aldehyde conversion to its parent alkane (Scheme 1a).⁶ The extension of this decarbonylation reaction to carboxyl and ketone substrates has attracted much attention.7-11 The decarboxylation of aromatic acid under harsh conditions (Scheme 1b) was developed by the Shepard,¹² Nilsson,¹³ Cohen,14,15 Sheppard,16 and Schleyer17 groups. In 1982, Schleyer successfully achieved decarboxylation with a nickel (180 °C) and palladium (330 °C) catalyst under a H₂ atmosphere.¹⁷ As for the decarbonylation of ketones (Scheme 1c), Murakami et al. first reported such work in 1994 on strained and unstrained cyclic aliphatic ketones using RhCl(PPh₃)₃ as catalyst.¹⁸ Afterward, many decarboxylation coupling reactions were reported.¹⁹ For example, Lundgren conducted decarboxylative carbonyl aarylation by coupling arylboron nucleophiles with malonic acid derivatives. As for the catalytic decarbonylation of unstrained ketones, such as 1,2- and 1,3-diketones,20 alkynyl ketones21 and ketones bearing a directing group, it was achieved with Rh catalysts. In 2017, Chatani et al. reported the first nickel system capable of mediating the decarbonylation of simple diaryl ketone.22

Scheme 1. Decarbonylation of carbonyl compounds



S especially the synthetic method s known as the ACS Paragon Plus Environment Unlike the decarboxylation of aldehydes, carboxylic acids, and ketones, there are only two examples till now for the decarboxylation of lactones (Scheme 1d). In 1969, Richard reported the first decarboxylation reaction

of α , γ -butyrolactone through photocatalysis.²³ Unfortunately, the yield of this method is very low (<11%). In 1971, Richard reported the decarboxylation reaction of a different γ -butyrolactone, but the yield is still not high (<51%).²⁴ Therefore, despite the great progresses of extending the decarbonylation reaction to carboxyl substrates, the decarbonylation of lactones remains a big challenge.

Recently, we developed an efficient method for the synthesis of 3-aryl benzofuran-2(3H)-ones.^{25a} Herein, we demonstrate the use of these compounds as useful precursors for efficient synthesis of 2-hydroxybenzophenones via nickel-catalyzed decarbonyloxidation of lactones (Scheme 1e). The method uses cheap nickel as catalyst and the reaction condition is mild. The protocol shows a broad substrate scope and gram-scalable ability. It is noted that the target products can be converted into a variety of compounds via esterification, cyclization, and reduction, etc., which are bioactive skeletons. Finally, a possible mechanism is proposed based on the control experiment.

RESULTS AND DISCUSSION

Initially, we explored the nickel catalyzed reactions using 4methylbenzofuranone 1a as substrate under different reaction conditions (Table 1). Four oxidants, AgBr, K₂S₂O₈, PhI(OAc)₂ and *t*butylhydroperoxide (TBHP, 70wt.% in H₂O) were screened at the conditions of 10 mol% of NiCl₂, 2.0 eq. of base Na₂CO₃ in toluene solution at 80 °C (entries 1–4). Among them, only TBHP gives the target product 2hydroxybenzophenone (**2a**) in over 99% yield (entry 4). The adoption of other temperatures, solvents, bases and Ni catalysts would result in lower yields (entries 5–14). It should be noted that the yield of 2a at 25 °C is 74%, and the use of Ni(cod)₂ instead can also give 2a in 91% yield. Also, it was observed that the presence of NiCl₂, base and TBHP is important in the reaction system (entries 15–19).

Table 1. Survey on condition for 2a formation^a

Ni Cat. (10mol%) Base, oxidant solvent temp., Time 1a 2a yield^b temp oxidant base Ni (°C) Entry solvent (mol%) (2.0 eq.) (2.0 eq.) (%) NiCl₂ (10) 1 Na₂CO₃ AgBr toluene 80 0 2 $NiCl_2(10)$ Na₂CO₃ K₂S₂O₈ toluene 80 0 3 NiCl₂ (10) Na₂CO₃ PhI(OAc)₂ toluene 80 0 NiCl₂ (10) >99% Na₂CO₃ TBHP toluene 4 80 5 $NiCl_2(10)$ Na₂CO₂ TBHP toluene 70 89% 6 NiCl₂ (10) Na₂CO₃ TBHP toluene 60 86% 7 NiCl₂ (10) Na₂CO₃ TBHP toluene 25 74% 8 NiCl₂ (10) Na₂CO₃ TBHP DMF 80 46% 9 NiCl₂ (10) Na₂CO₃ TBHP THE 80 98% 10 NiCl₂ (10) K₂CO₃ TBHP toluene 80 99% Cs₂CO₃ 97% 11 NiCl₂ (10) TBHP toluene 80 12 Ni(OTf)₂ (10) Na₂CO₃ TBHP 80 88% toluene 13 Ni(acac)₂ (10) Na₂CO₂ TBHP toluene 80 89% 14 Ni(cod)₂(10) Na₂CO₃ TBHP toluene 80 91% 15 NiCl₂ (10) Na₂CO₃ toluene 80 0 NiCl₂ (10) 16 TBHP 68% toluene 80 17 Na₂CO₃ TBHP toluene 80 10% 18 Na₂CO₃ TBHP toluene 120 24% TRHP 19 Na₂CO₃ toluene 140 30%

^aReaction conditions: Benzofuranone **1a** (0.2 mmol), Ni source (mol% as indicated), base (0.4 mmol), oxidant (0.4 mmol), and solvent (1.0 mL) were stirred at a specified reaction temperature for 12 h under air. ^bIsolated yield.

Having optimized the reaction conditions, we proceeded to explore the scope of this nickel-catalyzed decarbonyloxidation protocol using benzofuranones with different functional groups in the phenyl ring. As displayed in Scheme 2, a variety of benzofuranones were smoothly transformed into the corresponding phenol products with moderate to excellent yields. The results revealed that electron-donating substituents such as 4-ethyl (2c), 2,4-dimethyl (2d), 3,5-dimethyl (2e), 4-isopropyl(2f), 4-tertbutyl (2g), 3-tertbutyl(2h), 2-tertbutyl(2i), 4-phenyl group (2j) and 4-methoxy (2k) are well tolerated. The reason for the low yield of 2e (30%) is that 1e produces a by-product 2e' (35%, see SI) through the condensation of benzofuranone with tert-butyl peroxide. Substrates with chlorine (2I, 73%) and fluorine (2m, 83%) at the *para*-position of phenyl ring were explored and found to furnish the desired products in good yields. It should

Scheme 2. Investigation of benzo-ring scope^a



^a3-Aryl benzofuran-2(3H)-ones 1 (0.2 mmol), NiCl₂ (10 mol%), Na₂CO₃ (2.0 eq.), TBHP (2.0 eq.), toluene (1.0 mL), under air condition, sealed tube, isolated yield of 2.

The protocol also exhibits a high level of tolerance toward substrates bearing para-position and ortho-position substituent on the 4-phenyl ring (Scheme 3). First, the decarbonyloxidation was carried out using orthochlrine (2n) and para-chlorine (2o) substrates, which resulted in satisfactory yields. Then we used para-bromo substrate in the 4-phenyl ring and the yield was up to 98%. We screened substrates with different groups on the benzene ring as well as those with halogen-containing 4-benzene ring, and found that the yields of the corresponding products (2q-2s) were 90-99%. As for 2t with ortho-methyl group, the yield was low, possibly due to steric effect. The substrates with electron-withdrawing groups (-CF₃, -CN) were also accommodated (2u-2v). The lower yield of cyano substrate can be attributed to the effect of cyano group on nickel coordination. Overall, the adaptability of the reaction system to functional groups is good, and electron-withdrawing groups do not have significant inhibitory effect on the reaction. It should be noted that 5,7-di-tert-butyl-3-(3,4-dimethylphenyl)benzofuran-2(3H)-one (1w, Antioxidant HP-136) with various groups on the benzene ring successfully undergoes decarbonyloxidation, illustrating that the method is suitable for multi-functionalized steric substrates. And 7-Cyclohexyl-[1,3]dioxolo[4,5-f]benzofuran-6(7H)-one (1x) can get the corresponding product (2x) in lower to 22% yield, due to the in-stable alkyl intermediate.

Scheme 3. Investigation of 4-Substituents scope^a



^a3-Aryl benzofuran-2(*3H*)-ones **1** (0.2 mmol), NiCl₂ (10 mol%), Na₂CO₃ (2.0 eq.), TBHP (2.0 eq.), toluene (1.0 mL), under air condition, sealed tube, isolated yield of **2**.

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To demonstrate the synthetic utility of this decarbonyl oxidation reaction, a variety of biologically important oxygen-containing heterocyclic compounds were prepared from 2-hydroxylated aryl ketone products. As shown in Scheme 4, the ring-closing reaction can be carried out between 2hydroxybenzophenone and 2-bromo-acetophenone (3 in 99% yield, Scheme 4a) or methyl bromoacetate (4 in 99% yield, Scheme 4b).^{26a} Also 2a can be esterified with acetic anhydride (5 in 98% yield, Scheme 4c)^{26b} or trifluoroacetic anhydride (9 in 85% yield, Scheme 4g). The obtained 2benzoylphenyl 2,2,2-trifluoroacetate (9) can react with phenylboronic acid to give coupling product (11 in 70% yield, Scheme 4h) or with the removal of trifluoroacetate to give benzophenone 10 (94% yield, Scheme 4i) 26d. Also, 2a can be used for ring-closing reaction with acetic anhydride to obtain 4-phenylchromenone compound (6 in 91% yield, Scheme 4d)^{26b} or react with chlorosulfonyl isocyanate to obtain 4-phenylbenzo[e][1,2,3] oxathiazine 2,2-dioxide (7 in 76% yield) (Scheme 4e)^{26b}. In the presence of sodium hydroxide, 20 with chloride can be easily transformed to 9Hxanthen-9-one 8 in 89% yield (Scheme 4f).26c

Scheme 4. Divergent transformations of 2a.^a



^aReaction conditions: (a) methyl bomoacetate, K_2CO_3 , acetone, reflux, 2 h, 99%; (b) 2-bromoacetophenone, K_2CO_3 , MeCN, 120 °C, 4 h, 99%; (c) acetic anhydride, KOAc, MeCN, 150 °C, 4 h, 99%; (d) acetic anhydride, DBU, MeCN, reflux, 8 h, 91%; (e) ClSO₂NCO, toluene, reflux, 10 h, 76%; (f) NaOH, H₂O, 100 °C, 16 h, 89%; (g) trifluoromethanesulfonic anhydride, Et₃N, 80 °C, 12 h, 85 %; (h) Pd(PPh₃)₄, Na₂CO₃, toluene, H₂O, 140 °C, 12 h, 70 %; (i) Pd(OAc)₂, dppf, HCOOH, Et₃N, DMSO, 25 °C, 12 h, 94%.

It is known that systems containing peroxides are difficult to scale up, because at elevated temperatures the reactions of peroxides could lead to violent explosion. Furthermore, peroxides are highly active and the production of by-products is common. Nonetheless, in this study, a gram scale experiment was performed, and the yield is up to 77 % (Scheme 5). Also, we observed the release of CO_2 by GC analysis without any detection of CO.

Scheme 5. Gram-scale experiment



To gain insights into the reaction mechanism, several control experiments were conducted. First, TEMPO and BHT affect the yield significantly, indicating the involvement of free radicals (Scheme 6a). In the case of catalyst absence, the product yield is extremely low (2a, 11%), while the yield of by-product 2a' is 88% (Scheme 6b). It was observed that

2e' cannot be converted to 2e in the presence of NiCl₂ and/or TBHP, the involvement of 2a' as an intermediate can be discarded in the mechanism (Scheme 6c). With a proper nickel catalyst, the yield of 2a could be up to 99%, indicating the importance of a nickel catalyst. To exclude the possibility that CO2 might be generated from the base Na2CO3, we changed the base to NaOAc and CO₂ was still observed by GC analysis (Scheme 6d); the phenomenon indicates the action of decarbonyloxidation in the reaction mechanism. To clarify whether the reaction process is first hydrolyzed or not, 1a was hydrolyzed with NaOH (Scheme 6e) to 1aa in 55% yield (Scheme 6e),^{26e} but **1aa** cannot be converted to **2a** in the absence of NiCl₂ and TBHP. With NiCl₂, 1aa is esterified to starting material 1a in 58% yield, while with TBHP, the yield of 2a is only 21%. When adding NiCl₂ and TBHP together to 1aa, the yields of 1a and 2a are 30%, 32%, respectively. It is significantly lower than that starting from 1a directly (Table 1, entry 4, 2a, >99%). These results indicate that 1aa maybe not a possible intermediate in the possible mechanism.

Scheme 6. Control experiments

a) Radical Trapping Experiments



Scheme 7. Plausible mechanism



Although the exact mechanism is still unknown, based on the above results and those reported in the literature,^{22,27} a possible pathway for the decarbonyloxidation of 3-aryl benzofuran-2(*3H*)-ones is proposed (Scheme 7). At first, intermediate **A** is generated from benzofuranones (**1a**) in the presence of a base. ^{27a} Then **A** reacts with TBHP to form **B** with the generation of radical tBuO[•], while **B** can isomerizes to carbon radical **B**[•]. Then **B** or **B**[•] can follow two pathways in the absence of a nickel catalyst. The fast path is trapped by tBuO[•] to form byproduct **2a**[•]; the other is a slow one that **B** or **B**[•] reacts with TBHP and tBuO[•] to form intermediate **D**. In the presence of a nickel catalyst and with CO migration, radical **B** or **B**[•] directly reacts with radical tBuO[•] to intermediate **C**.^{22a,22b} Then with another

equiv. of THBP, the reductive elimination of nickel leads to the formation of intermediate **D**. Finally, **D** decomposes with the release of one CO₂ and two tBuOH molecules to give the target product **2a** in the presence of water.^{27b}

CONCLUSIONS

In summary, we developed an efficient and convenient method for the synthesis of 2-hydroxybenzophenone from benzofuranone using inexpensive NiCl₂ as catalyst, Na₂CO₃ as base, and TBHP as oxidant under mild conditions. The reaction involves the decarbonyloxidation of lactone. The catalytic system shows tolerance toward numerous substituted benzofuranones, giving the corresponding products in good to excellent yield. This protocol can be easily enlarged and applied.

EXPERIMENTAL SECTION

General Information. All commercially available regents were used without further purification. Nuclear magnetic resonance (NMR) spectra was acquired at 298 K on a 400 MHz Bruker NMR spectrometer with the sample dissolved in CDCl₃. All values of chemical shift were reported in parts per million (ppm) relative to the solvent signal with the coupling constant (*J*) reported in hertz. All compounds were characterized by ¹H NMR, ¹³C NMR and EI (or HRMS (double focusing mass analyzer). For substrates and products that contained F, selected ones were also characterized by ¹⁹F NMR. Column chromatography was performed on silica gel (300–400 mesh) using petroleum ether (PE)/ethyl acetate (EA) as developing solvent.

General Procedure for Synthesis of 1a-1t. The starting materials was synthesized according to reported procedure.^{25a} To a flask was added Mandelic acid (3.04 g, 20 mmol), phenol (1.9 mL, 20 mmol) and Ni(OTf)₂ (712 mg, 2 mmol). Then put the flask in the reaction system at 160 °C (oil bath) and stirred for 12 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to obtain the product. 1a-1n, 1p, 1r, 1w have been reported in the published article of this group.²⁵

3-(2-Chlorophenyl)-7-methylbenzofuran-2(3H)-one (10). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 20/1) yielded the title compound **1**o in 68% (3.5 g) as a white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.50 (d, J = 7.9 Hz, 1H), 7.37 – 7.26 (m, 2H), 7.18 (t, J = 13.9 Hz, 2H), 7.07 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H), 5.41 (s, 1H), 2.42 (s, 3H). ¹³C ¹H NMR (101 MHz, CDCl₃) δ 174.5, 152.3, 134.3, 133.8, 130.7, 130.2, 129.6, 127.4, 126.5, 124.3, 121.9, 121.1, 15.1. HRMS (EI) *m/z*: [M⁺] calcd for C₁₅H₁₁ClO₂ 258.0448, Found 258.0438.

6-(Tert-butyl)-3-(4-chlorophenyl)benzofuran-2(3H)-one (1q). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 20/1) yielded the title compound **1q** in 77% (4.6 g) as a white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.41–7.38 (m, 2H), 7.28 (m, 2H), 7.24 (d, *J* = 1.6 Hz, 1H), 7.18 (m, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 4.90 (s, 1H), 1.41 (d, *J* = 1.3 Hz, 9H). ¹³C {¹H</sup> NMR (101 MHz, CDCl₃) δ 175.5, 151.8, 147.8, 135.3, 129.1, 128.3, 128.1, 126.4, 126.2, 122.2, 110.1, 50.1, 34.7, 31.5. HRMS (EI) *m/z*: [M⁺] caled for C₁₈H₁₇ClO₂ 300.0917, Found 300.0916.

3-(4-Bromophenyl)-7-methylbenzofuran-2(3H)-one (1s). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 1s in 62% (3.7 g) as a white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.47 (d, *J* = 7.8 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 4.86 (s, 1H), 2.38 (s, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 174.4, 152.2, 134.1, 131.9, 130.8, 129.8, 125.7, 124.2, 122.3, 122.0, 121.0, 49.2, 14.9. HRMS (EI) *m/z*: [M⁺] calcd for C₁₅H₁₁BrO₂ 301.9942, Found 301.9939.

3-(4-Bromophenyl)-4,6-dimethylbenzofuran-2(3H)-one (1t). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **1t** in 60% (3.8 g) as a white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.3 Hz, 2H), 7.00 (s, 1H), 6.81 (s, 1H), 4.81 (s, 1H), 2.32 (d, *J* = 13.7 Hz, 6H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 174.9, 150.3, 134.4, 134.0, 132.1, 131.4, 129.9, 125.8, 122.8, 122.1, 120.7, 49.6, 20.9, 15.0. HRMS (EI) *m/z*: [M⁺] calcd for C₁₆H₁₃BrO₂ 316.0099, Found 316.0089.

(4-cyanopheny)boronic acid (119.0 mg, 0.8 mmol), $Pd(PPh_{3})_{4}$ (40.0 mg, 0.04 mmol), K_2CO_3 (110.4 mg, 0.8 mmol), toluene (1.0 mL) and H_2O (1.0 mL). Then put the flask in the reaction system at 140 °C (oil bath) and stirred for 12 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to obtain the product.

5-Methyl-3-(4'-(Trifluoromethyl)-[1,1'-biphenyl]-4-yl)benzofuran-

2(3H)-one (1u). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **1u** in 40% (58.8 mg) as a white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.72–7.65 (m, 4H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.19 (m, 1H), 7.10 (d, *J* = 8.2 Hz, 1H), 7.05 (s, 1H), 4.92 (s, 1H), 2.35 (s, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 175.2, 151.9, 144.0, 139.7, 135.4, 134.4, 130.0, 129.6 (q, *J* = 32.3 Hz), 129.1, 129.0, 127.4, 126.7, 125.8 (q, *J* = 3.8 Hz), 125.7, 124.2 (q, *J* = 270.5 Hz), 110.6, 21.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.44. HRMS (EI) *m/z*: [M⁺] calcd for C₂₂H₁₅F₃O₂ 368.1024, Found 368.1018.

4'-(5-Methyl-2-oxo-2,3-dihydrobenzofuran-3-yl)-[1,1'-biphenyl]-4carbonitrile (1v). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 1v in 57% (74.0 mg) as a white solid; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, J = 8.4 Hz, 2H), 7.66 (d, J =8.3 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H), 7.38–7.32 (m, 2H), 7.19 (m, 1H), 7.09 (d, J = 8.2 Hz, 1H), 7.04 (s, 1H), 4.92 (s, 1H), 2.35 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 175.1, 151.9, 144.8, 139.1, 135.8, 134.4, 132.7, 130.0, 129.1, 128.0, 127.7, 126.6, 125.7, 118.8, 111.2, 110.6, 49.6, 21.1. HRMS (EI) *m/z*: [M⁺] calcd for C₂₂H₁₅NO₂ 325.1103, Found 325.1093.

Synthesis of 7-Cyclohexyl-[1,3]dioxolo[4,5-f]benzofuran-6(7H)-one (1x).^{25b} A 10 mL oven-dried Schlenk tube equipped with a magnetic stirring bar was added Pd(PPh₃)₄ (5 mol %, 57.8 mg), P(o-tolyl)₃ (20 mol %, 60.8 mg) and sesamol (1.0 mmol, 138 mg) were transferred into an oven-dried tube which was filled with nitrogen. Chlorobenzene (2.0 mL), benzaldehyde (2 mmol, 224 uL), TFA (15 mol %, 11 uL) were added into the reaction tube. Then a mixture of formic acid (3.0 mmol, 113.1 uL) and acetic anhydride (3.0 mmol, 306.2 uL) which was stirred for 1.5 h at 30 °C, added to the reaction tube. The mixture was stirred for 18h at 130 °C. After the reaction was complete, the reaction mixture was filtered and concentrated, column chromatography on silica gel (petroleum ether/ethyl acetate 50:1), yielded in 60% (156.8 mg) as a white solid; ¹H NMR (400 MHz, CDCl₃) & 6.74 (s, 1H), 6.64 (s, 1H), 5.96 (s, 2H), 3.53 (s, 1H), 2.04 (m, 1H), 1.70 (m, 4H), 1.56 (d, J = 10.9 Hz, 1H), 1.25 (m, 4H), 1.12 (m, 1H). ¹³C{¹H} (101 MHz, CDCl₃) δ 177.1, 148.2, 147.4, 144.0, 117.5, 104.8, 101.4, 94.2, 50.0, 41.3, 29.8, 28.7, 26.4, 26.1, 25.8. HRMS (EI) m/z: [M+] calcd for C15H16O4 260.1049, Found 260.1044.

General Procedure for Synthesis of Products. A 10 mL oven-dried Schlenk tube equipped with a magnetic stirring bar was added benzofuran-2(3H)-ones 1 (0.24 mmol, 1.0 equiv.), NiCl₂ (0.02 mmol, 10 mol%, 2.6 mg), Na₂CO₃ (0.4 mmol, 2 equiv., 42.4 mg), TBHP (0.4 mmol, 2.0 equiv., 39 μ L), and toluene (1.0 mL) and was vigorously stirred at 80 °C (oil bath) for 12 h under air. Then the mixture was cooled to room temperature, filtered and concentrated in vacuo. Further purification by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate) provided the desired product.

(2-Hydroxy-5-methylphenyl)(phenyl)methanone (2a)²⁸. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2a in 99% (42.0 mg) as a yellow solid; mp: 70–73 °C; Reported mp: 81 °C; $R_f = 0.35$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl3) δ 11.85 (s, 1H), 7.67 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.3 Hz, 1H), 7.51 (t, J = 7.4 Hz, 2H), 7.38 – 7.29 (m, 2H), 6.98 (d, J = 8.4 Hz, 1H), 2.25 (s, 3H). ¹³C {¹H} NMR (100 MHz, CDCl3) δ 201.6, 161.1, 138.0, 137.4, 133.2, 131.8, 129.1, 128.3, 127.8, 118.8, 118.1, 20.4. GC-MS (EI) m/z: [M⁺] Calcd for C₁₄H₁₂O₂ 212, Found 212.

(2-Hydroxyphenyl)(phenyl)methanone (2b)²⁹. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2b in 99% (39.2 mg) as a yellow liquid; $R_f = 0.36$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCI3) δ 12.03 (s, 1H), 7.68 (d, J = 7.6 Hz, 2H), 7.60 (m, 2H), 7.51 (t, J = 7.5 Hz, 3H), 7.08 (d, J = 8.4 Hz, 1H), 6.88 (t, J = 7.5 Hz, 1H). ¹³C {¹H} NMR (100 MHz, CDCI3) δ 201.6, 163.2, 137.9, 136.3, 133.6, 131.9, 129.2, 128.3, 119.1, 118.6, 118.4. GC-MS (EI) m/z: [M⁺] Calcd for C₁₃H₁₀O₂ 198, Found 198.

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(5-Ethyl-2-hydroxyphenyl)(phenyl)methanone (2c)³⁰. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2c in 94% (42.5 mg) as a yellow solid; mp: 56–59 °C; Reported mp: 40–41 °C; Reported melting point: 69–72 °C; $R_f = 0.35$ (petroleum ether/ethyl acetate = 200/1); 'H NMR (400 MHz, CDCI3) δ 11.86 (s, 1H), 7.68 (d, J = 7.4 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.52 (t, J = 7.4 Hz, 2H), 7.37 (d, J = 10.3 Hz, 2H), 7.01 (d, J = 8.3 Hz, 1H), 2.55 (q, J = 7.5 Hz, 2H), 1.17 (t, J = 7.5 Hz, 3H). '³C {¹H} NMR (100 MHz, CDCI3) δ 201.6, 161.3, 138.1, 136.3, 134.3, 132.1, 131.8, 129.1, 128.3, 118.8, 118.2, 27.9, 15.7. GC-MS (EI) m/z: [M⁺] Calcd for C₁₅H₁₄O₂ 226, Found 226.

(2-Hydroxy-4,6-dimethylphenyl)(phenyl)methanone (2d)³¹. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2d in 74% (33.4 mg) as a yellow liquid; R_f = 0.33 (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl3) δ 12.15 (s, 1H), 7.66 (d, J = 7.6 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.3 Hz, 2H), 7.20 (d, J = 5.1 Hz, 2H), 2.29 (s, 3H), 2.22 (s, 3H). ¹³C {¹H} (100 MHz, CDCl3) δ 201.9, 159.6, 138.4, 138.4, 131.6, 130.8, 129.1, 128.2, 127.1, 126.9, 118.1, 20.4, 15.5. GC-MS (EI) m/z: [M⁺] Calcd for C₁₅H₁₄O₂ 226, Found 226.

(2-Hydroxy-4,6-dimethylphenyl)(phenyl)methanone (2e)³². The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 10/1) yielded the title compound 2e in 42% (19.0 mg) as a yellow solid; mp: 100–102 °C; Reported mp: 143 °C; $R_f = 0.31$ (petroleum ether/ethyl acetate = 10/1); 'H NMR (400 MHz, CDCI3) δ 9.38 (s, 1H), 7.66 (d, J = 7.7 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.4 Hz, 1H), 6.70 (s, 1H), 6.57 (s, 1H), 2.32 (s, 2H), 1.93 (s, 2H). ¹³C {¹H} NMR (100 MHz, CDCI3) δ 201.32, 159.3, 144.6, 140.4, 138.8, 132.6, 128.8, 128.6, 124.0, 120.3, 115.4, 22.5, 21.6. GC-MS (EI) m/z: [M⁺] Calcd for C₁₅H₁₄O₂ 226, Found 226.

(2-Hydroxy-5-isopropylphenyl)(phenyl)methanone (2f)³³. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2f in 99% (47.5 mg) as a yellow solid; mp: 76–77 °C; Reported mp: 70–73 °C; R_f = 0.41 (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCI3) δ 11.87 (s, 1H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 7.1 Hz, 2H), 7.02 (d, *J* = 9.2 Hz, 1H), 2.82 (m, 1H), 1.18 (d, *J* = 6.9 Hz, 6H) ¹³C {¹H} NMR (100 MHz, CDCI3) δ 201.5, 161.4, 139.0, 138.1, 134.8, 131.8, 130.8, 129.2, 128.3, 118.8, 118.2, 33.2, 24.0. GC-MS (EI) m/z: [M⁺] Calcd for C₁₆H₁₆O₂ 240, Found 240.

(5-(Tert-butyl)-2-hydroxyphenyl)(phenyl)methanone (2g)³⁴. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2g in 99% (50.2 mg) as a yellow solid; mp:57–60 °C; Reported mp: 67–68 °C; R_f = 0.41 (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.86 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.58 (t, *J* = 8.2 Hz, 3H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 9.5 Hz, 1H), 1.25 (s, 9H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 201.6, 161.0, 141.3, 138.1, 133.9, 131.9, 129.8, 129.2, 128.3, 118.4, 117.9, 34.1, 31.2. GC-MS (EI) *m/z*: [M⁺] Calcd for C₁₇H₁₈O₂ 254, Found 254.

(4-(Tert-butyl)-2-hydroxyphenyl)(phenyl)methanone (2h). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2h in 92% (46.7 mg) as a yellow solid; mp: 68–69 °C; $R_f = 0.42$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 12.10 (s, 1H), 7.67 (d, J = 7.4 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.50 (m, 3H), 7.09 (s, 1H), 6.91 (d, J = 8.4 Hz, 1H), 1.33 (s, 9H). ¹³C{¹H} MR (100 MHz, CDCl₃) δ 201.0, 163.3, 161.0, 138.1, 133.3, 131.7, 129.0, 128.3, 116.8, 116.4, 115.1, 35.4, 30.8. HRMS (ESI) m/z: [M+Na]⁺ calcd for C₁₇H₁₈O₂Na⁺ 277.1199, Found 277.1203.

(3-(Tert-butyl)-2-hydroxyphenyl)(phenyl)methanone (2i)³⁵. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2i in 78% (39.6 mg) as a yellow solid; mp: 65–67 °C; Reported mp: 53 °C; $R_f = 0.42$ (petroleum ether/ethyl acetate = 200/1); 'H NMR (400 MHz, CDCl₃) δ 11.84 (s, 1H), 7.69 (d, J = 7.8 Hz, 2H), 7.62 – 7.55 (m, 3H), 7.52 (t, J = 7.4 Hz, 2H), 7.02 (d, J = 8.3 Hz, 1H), 1.25 (s, 9H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 201.6, 161.0, 141.3, 138.1, 133.9, 131.9, 129.8, 129.2, 128.3, 118.4, 117.9, 34.1, 31.2. GC-MS (EI) *m/z*: [M⁺] Calcd for C₁₇H₁₈O₂ 254, Found 254.

(4-Hydroxy-[1,1'-biphenyl]-3-yl)(phenyl)methanone (2j)²⁹. The representative general procedure mentioned above was followed.

Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **2j** in 99% (54.1 mg) as a yellow solid; mp:73–76 °C; Reported mp: 89–91 °C; $R_f = 0.43$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 12.02 (s, 1H), 7.82 (s, 1H), 7.76 (t, *J* = 9.1 Hz, 3H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.1 Hz, 1H), 7.18 (d, *J* = 8.6 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 201.6, 162.6, 139.8, 137.8, 135.1, 132.1, 132.0, 131.7, 129.2, 128.9, 128.4, 127.1, 126.6, 119.2, 118.9, GC-MS (EI) *m/z*: [M⁺] Calcd for C₁₉H₁₄O₂ 274, Found 274.

(2-Hydroxy-5-methoxyphenyl)(phenyl)methanone (2k)³³. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 100/1) yielded the title compound **2k** in 82% (37.5 mg) as a yellow solid; mp: 68–71 °C; Reported mp: 82–84 °C; $R_f = 0.42$ (petroleum ether/ethyl acetate = 100/1); ¹H NMR (400 MHz, CDCl₃) δ 11.59 (s, 1H), 7.70 (d, J = 8.2 Hz, 2H), 7.60 (t, J = 6.9 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.15 (m, 1H), 7.04 (m, 2H), 3.70 (s, 3H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 201.2, 157.5, 151.4, 137.9, 132.0, 129.1, 128.4, 124.1, 119.2, 118.7, 116.4, 56.0. GC-MS (EI) *m/z*: [M⁺] Calcd for C1₄H₁₂O₃ 228, Found 228.

(5-Chloro-2-hydroxyphenyl)(phenyl)methanone (21)³⁶. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 21 in 73% (33.8 mg) as a yellow solid; mp:85–89 °C; Reported mp: 90–95 °C; $R_f = 0.39$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.82 (s, 1H), 7.58 (d, J = 6.6 Hz, 2H), 7.52 (d, J = 6.9 Hz, 1H), 7.45 (m, 3H), 7.36 (d, J = 8.5 Hz, 1H), 6.94 (d, J = 8.6 Hz, 1H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 200.5, 161.6, 137.2, 136.1, 132.4, 129.1, 128.5, 123.3, 120.0, 119.7. GC-MS (EI) m/z: [M⁺] Calcd for C₁₃H₉ClO₂ 232, Found 232.

(5-Fluoro-2-hydroxyphenyl)(phenyl)methanone (2m)³⁷. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **2m** in 83% (35.8 mg) as a yellow solid; mp:73–76 °C; Reported mp: 77 °C; $R_f = 0.38$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.76 (s, 1H), 7.71 (d, J = 7.5 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 7.55 (t, J = 7.4 Hz, 2H), 7.34 – 7.27 (m, 2H), 7.07 (m, 1H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 200.6 (d, J = 2 Hz), 159.4, 155.7, 153.3, 137.3, 132.3, 128.8 (d, J = 53.5 Hz), 123.9 (d, J = 23.5 Hz), 118.7 (d, J = 6.4 Hz), 118.3 (d, J = 23.6 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ -124.0 (q, J = 8.2 Hz). GC-MS (EI) m/z: [M⁺] Calcd for C₁₃H₉FO₂ 216, Found 216.

(2-Chlorophenyl)(2-hydroxy-5-methylphenyl)methanone (2n)³⁸. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2n in 99% (48.6 mg) as a yellow solid; mp:74–78 °C; Reported mp:76–77 °C; $R_f = 0.36$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.84 (s, 1H), 7.58–7.48 (m, 2H), 7.44 (m, 1H), 7.41–7.35 (m, 2H), 7.03 (t, J = 5.8 Hz, 2H), 2.24 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 200.5, 161.2, 138.4, 137.5, 132.9, 131.1, 130.8, 130.1, 128.5, 128.3, 126.7, 119.0, 118.1, 20.4. GC-MS (EI) *m/z*: [M⁺] Calcd for C₁₄H₁₁ClO₂ 246, Found 246.

(2-Chlorophenyl)(2-hydroxy-3-methylphenyl)methanone (20). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **20** in 71% (35.0 mg) as a yellow solid; mp:86–89 °C; $R_f = 0.38$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.82 (s, 1H), 7.48 (q, J = 8.0 Hz, 2H), 7.40 (t, J = 7.2 Hz, 1H), 7.36–7.31 (m, 2H), 7.02–6.95 (m, 2H), 2.20 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 200.8, 161.7, 137.9, 137.6, 131.1, 130.8, 130.0, 128.5, 127.4, 126.6, 118.7, 118.4, 15.4. HRMS (ESI) m/z: [M+H] ⁺ calcd for C₁₄H₁₂ClO₂ 247.0520, Found 247.0526.

(4-Chlorophenyl)(2-hydroxy-5-methylphenyl)methanone (2p)³⁹. The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **2p** in 80% (39.3 mg) as a yellow solid; mp:66–69 °C; Reported mp:85–87 °C; $R_f = 0.36$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.74 (s, 1H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.42–7.33 (m, 2H), 7.03 (d, *J* = 8.4 Hz, 1H), 2.30 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 200.2, 161.2, 138.3, 137.6, 136.4, 132.8, 130.6, 128.7, 128.0, 118.6, 118.3, 20.5. GC-MS (EI) *m/z*: [M⁺] Calcd for C₁₄H₁₁ClO₂ 246, Found 246.

(4-(Tert-butyl)-2-hydroxyphenyl)(4-chlorophenyl)methanone (2q). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1)

yielded the title compound **2q** in 90% (51.8 mg) as a yellow liquid; $R_f = 0.34$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.97 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 2H), 7.48 (m, 3H), 7.09 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 1.33 (s, 9H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 199.5, 163.3, 161.3, 138.1, 136.4, 132.9, 130.5, 128.6, 116.5, 115.2, 35.4, 30.8. HRMS (ESI) *m/z*: [M+Na] ⁺ calcd for C₁₇H₁₇ClO₂Na⁺ 311.0809, Found 311.0814.

(4-Bromophenyl)(2-hydroxy-5-methylphenyl)methanone (2r). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2r in 98% (56.8 mg) as a yellow liquid; $R_f = 0.37$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 11.69 (s, 1H), 7.66 (d, J = 7.1 Hz, 2H), 7.55 (d, J = 7.2 Hz, 2H), 7.36 – 7.29 (m, 2H), 6.98 (d, J = 8.4 Hz, 1H), 2.26 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 200.3, 161.1, 137.7, 136.7, 132.8, 131.6, 130.6, 128.0, 126.7, 118.6, 118.30, 20.5. HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₄H₁₂BrO₂ 291.0012, Found 291.0013.

(4-Bromophenyl)(2-hydroxy-3-methylphenyl)methanone (2s). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound 2s in 99% (57.4 mg) as a yellow liquid; R_f = 0.36 (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 12.19 (s, 1H), 7.72–7.59 (m, 2H), 7.55 (d, J = 7.1 Hz, 2H), 7.38 (t, J = 6.4 Hz, 2H), 6.78 (t, J = 7.7 Hz, 1H), 2.32 (s, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 200.6, 161.6, 137.4, 136.9, 131.6, 130.8, 130.7, 127.6, 126.7, 118.1, 118.1, 15.6. HRMS (ESI) m/z: [M+H] ⁺ calcd for C₁₄H₁₂BrO₂ 291.0011, Found 291.0012.

(4-Bromophenyl)(2-hydroxy-4,6-dimethylphenyl)methanone (2t). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 10/1) yielded the title compound 2t in 30% (18.2 mg) as a yellow liquid; $R_f = 0.39$ (petroleum ether/ethyl acetate = 10/1); ¹H NMR (400 MHz, CDCl₃) δ 12.01 (s, 1H), 7.65 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.5 Hz, 2H), 7.22 (s, 1H), 7.13 (s, 1H), 2.29 (s, 3H), 2.22 (s, 3H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 200.6, 159.6, 138.7, 137.1, 131.6, 130.6, 130.4, 127.3, 127.1, 126.5, 117.9, 20.5, 15.5. HRMS (ESI) *m/z*: [M+H] ⁺ calcd for C₁₅H₁₄BrO₂ 305.0169, Found 308.0170.

(2-Hydroxy-5-methylphenyl)(4'-(trifluoromethyl)-[1,1'-biphenyl]-4yl)methanone (2u). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 50/1) yielded the title compound 2u in 82% (58.3 mg) as a yellow solid; mp:171–172 °C; R_f = 0.51 (petroleum ether/ethyl acetate = 50/1); ¹H NMR (400 MHz, CDCl₃) δ 11.83 (s, 1H), 7.82–7.73 (m, 8H), 7.41 (s, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.01 (d, *J* = 8.5 Hz, 1H), 2.28 (s, 3H). 13C {1H} NMR (101 MHz, CDCl₃) δ 200.87, 161.2, 143.4, 143.1, 137.6, 137.5, 133.0,130.2 (d, *J* = 32.9 Hz), 127.9, 127.6, 127.2, 125.9 (q, *J* = 3.7 Hz), 124.1 (q, *J* = 273.1 Hz), 118.8, 118.3, 20.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.53. HRMS (ESI) *m/z*: [M+H] + calcd for C₂₁H₁₆F₃O₂ 357.1070, Found 357.1080.

4'-(2-Hydroxy-5-methylbenzoyl)-[1,1'-biphenyl]-4-carbonitrile (2v). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 20/1) yielded the title compound **2v** in 50% (31.6 mg) as a whitle solid; mp:183–185 °C; $R_f = 0.67$ (petroleum ether/ethyl acetate = 20/1); ¹H NMR (400 MHz, CDCl₃) δ 11.80 (s, 1H), 7.83–7.76 (m, 6H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.42–7.32 (m, 2H), 7.00 (d, *J* = 8.4 Hz, 1H), 2.27 (s, 3H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 200.7, 161.2, 144.3, 142.4, 138.0, 137.6, 132.9, 132.8, 129.9, 127.9, 127.2, 118.7, 118.6, 118.3, 111.9, 20.5. HRMS (ESI) *m/z*: [M+H]⁺ calcd for C₂₁H₁₆NO₂ 314.1161, Found 314.1166.

(3,5-Di-tert-butyl-2-hydroxyphenyl)(3,4-dimethylphenyl)-

methanone (2w). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 200/1) yielded the title compound **2x** in 80% (54.0 mg) as a yellow solid; mp:161–163 °C; $R_f = 0.35$ (petroleum ether/ethyl acetate = 200/1); ¹H NMR (400 MHz, CDCl₃) δ 12.71 (s, 1H), 7.57 (s, 1H), 7.49 (s, 2H), 7.42 (d, J = 7.7 Hz, 1H), 7.24 (d, J = 7.1 Hz, 1H), 2.34 (d, J = 8.6 Hz, 6H), 1.47 (s, 9H), 1.25 (s, 9H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 202.3, 160.4, 141.1, 139.5, 137.7, 136.6, 136.2, 130.8, 130.7, 129.2, 128.0, 127.2, 118.4, 35.2, 34.2, 31.3, 29.4, 19.9, 19.7. HRMS (ESI) *m/z*: [M+H] ⁺ calcd for C₂₃H₃₁O₂ 339.2319, Found 339.2316.

Cyclohexyl(6-hydroxybenzo[d][1,3]dioxol-5-yl)methanone (2x). The representative general procedure mentioned above was followed. Purification by PTLC on silica gel (petroleum ether/ethyl acetate = 50/1) yielded the title compound **2x** in 22% (10.8 mg) as a white solid; mp:120–

122 °C; $R_f = 0.57$ (petroleum ether/ethyl acetate = 50/1); ¹H NMR (400 MHz, CDCl₃) δ 13.39 (s, 1H), 7.11 (s, 1H), 6.46 (d, J = 1.1 Hz, 1H), 5.98 (d, J = 1.1 Hz, 2H), 3.15 – 3.00 (m, 1H), 1.89 – 1.83 (m, 4H), 1.52 (m, 2H), 1.41 – 1.32 (m, 2H), 1.29 – 1.20 (m, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 207.6, 162.8, 154.1, 140.4, 110.8, 106.4, 101.8, 99.0, 45.2, 29.6, 25.8, 25.8. HRMS (EI) *m/z*: [M⁺] calcd for C₁₄H₁₆O₄ 248.1049, Found 248.1044.

Synthesis of 3-(tert-butoxy)-4,6-dimethyl-3-phenylbenzofuran-2(*3H*)-one (2e'). A 10 mL oven-dried Schlenk tube equipped with a magnetic stirring bar was added 4,6-dimethyl-3-phenylbenzofuran-2(*3H*)-one 1e (0.24 mmol, 1.0 equiv.), NiCl₂ (0.02 mmol, 10 mol%, 2.6 mg), Na₂CO₃ (0.4 mmol, 2 equiv., 42.4 mg), TBHP (0.4 mmol, 2.0 equiv., 39 μ L), and toluene (1.0 mL) and was vigorously stirred at 80 °C (oil bath) for 12 h under air. Then the mixture was cooled to room temperature, filtered and concentrated in vacuo. Further purification by flash column chromatography on silica gel (eluting with petroleum ether/ethyl acetate) provided the byproduct 2e'. ¹H NMR (400 MHz, CDCl₃) δ 7.35 (s, 5H), 6.82 (d, *J* = 11.1 Hz, 2H), 2.40 (s, 3H), 2.11 (s, 3H), 1.26 (s, 9H). ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 173.7, 154.3, 141.2, 137.8, 134.3, 129.3, 128.7, 127.0, 126.7, 121.1, 109.0, 81.4, 26.5, 21.9, 17.4, 1.0.

Synthesis of 2-(2-hydroxy-5-methylphenyl)-2-phenylacetic acid (1aa). To a flask was added 1a (1.12 g, 5 mmol), NaOH (0.39 g, 10 mmol) and solvent (MeOH : $H_2O = 3 : 1$) 40 mL. Then put the flask in the reaction system at 80 °C and stirred for 12 h. Acidified of cool reaction mixture. With HCl to pH = 2, and extracted with ethyl acetate (3x30 mL). The organic layer was washed with brine, dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. ¹H NMR (400 MHz, DMSO) δ 9.47 (s, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 6.5 Hz, 3H), 7.24 (t, *J* = 7.1 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.81 – 6.72 (m, 2H), 2.12 (s, 3H). ¹³C{¹H} NMR (101 MHz, DMSO) δ 174.2, 152.9, 139.4, 129.6, 129.3, 128.7, 128.6, 127.4, 127.1, 126.4, 115.3, 50.8, 20.8. HRMS (EI) *m/z*: [M⁺] calcd for C₁₅H₁₄O₃ 242.0943, Found 242.0942.

Synthesis of methyl 2-(3-phenylbenzofuran-2-yl)acetate (3).⁴⁰ To a flask was added 2b (100 mg, 0.5 mmol), 3a (57 µL, 0.6 mmol), K₂CO₃ (103.5 mg, 0.75 mmol) and toluene (10 mL). Then put the flask in the reaction system at 80 °C and reflux for 10 h.The reaction mixture was dissolved in 2.0 mL ethyl acetate . Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 5/1) to obtain the product 3 in 99 % (159.0 mg) as a colorless liquid. R_{*J*} = 0.45 (petroleum ether/ethyl acetate = 5/1); ¹H NMR (400 MHz, CDCl₃) δ 7.88–7.83 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (m, 4H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 4.56 (s, 2H), 3.69 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 196.1, 168.9, 155.6, 137.7, 133.0, 131.8, 123.0, 129.6, 128.2, 121.9, 112.7, 65.8, 52.2.

Synthesis of phenyl(3-phenylbenzofuran-2-yl)methanone (4).⁴⁰ To a flask was added 2b (100 mg, 0.5 mmol), 3b (110.0 μ L, 0.6 mmol), K₂CO₃ (138 mg, 1.0 mmol) and acetonitrile (1.0 mL). Then put the flask in the reaction system at 120 °C and stirred for 4 h. The reaction mixture was dissolved in 2 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 40/1) to obtain the product 4 in 99 % (151.5 mg) as a colorless liquid; R_f = 0.51 (petroleum ether/ethyl acetate = 40/1); ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 7.3 Hz, 2H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.57–7.46 (m, 4H), 7.41–7.33 (m, 6H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 185.8, 154.6, 147.2, 137.3, 132.7, 131.0, 130.0, 129.9, 129.4, 128.4,

Synthesis of 2-benzoylphenyl acetate (5).⁴¹ To a flask was added 2b (40.0 mg, 0.2 mmol), 3c (110.0 μ L, 0.6 mmol), NaOAc (54.4 mg, 0.4 mmol) and acetonitrile (1.0 mL). Then put the flask in the reaction system at 150 °C and stirred for 4 h.The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to obtain the product 5 in 98 % (47.2 mg) as a colorless liquid. $R_f = 0.42$ (petroleum ether/ethyl acetate =10/1); ¹H NMR (400 MHz, CDCl₃) δ 7.86–7.79 (m, 2H), 7.66–7.56 (m, 3H), 7.50 (t, J = 7.7 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.24 (d, J = 8.1 Hz, 1H), 1.98 (s, 3H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 194.8, 169.1, 148.8, 137.1, 133.0, 132.3, 131.6, 130.5, 129.8, 128.4, 125.7, 123.2, 20.5.

Synthesis of 4-phenyl-2H-chromen-2-one (6).⁴¹ To a flask was added 2b (100 mg, 0.5 mmol), 3d (153 μ L, 1.5 mmol), DBU (228 μ L, 1.5 mmol) and acetonitrile (1.0 mL). Then put the flask in the reaction system at 80 °C and reflux for 8 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate . Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 10/1) to obtain the product 6 in 91 % (101.2 mg) as a white solid. $R_f = 0.42$ (petroleum ether/ethyl acetate =10/1); ¹H NMR (400 MHz, CDCl₃) δ 7.50–7.41 (m, 5H), 7.37 (m, 2H), 7.29 (d, J = 8.3 Hz, 1H), 7.18–7.13 (m, 1H), 6.27 (s, 1H). ¹³C {¹H}

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NMR (100 MHz, CDCl₃) δ 160.6, 155.6, 154.1, 135.1, 131.9, 129.7, 128.9, 128.4, 127.0, 124.2, 118.9, 117.2, 115.1.

Synthesis of 4-phenylbenzo[e][1,2,3]oxathiazine 2,2-dioxide (7).⁴¹ To a flask was added **2b** (100 mg, 0.5 mmol), **3e** (44 μ L, 0.5 mmol), and toluene 10 mL. Then put the flask in the reaction system at 80 °C and reflux for 10 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 5/1) to obtain the product 7 in 76 % (99.2 mg) as a colorless liquid. $R_f = 0.52$ (petroleum ether/ethyl acetate = 10/1); ¹H NMR (400 MHz, CDCl₃) δ 7.79–7.72 (m, 3H), 7.69–7.62 (m, 2H), 7.55 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 8.3 Hz, 2H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 176.5, 154.5, 137.1, 133.6, 133.3, 131.9, 130.6, 128.9, 125.9, 119.4, 116.5.

Synthesis of 2-methyl-9H-xanthen-9-one (8).⁴² To a flask was added 2p (49.2 mg, 0.2 mmol), NaOH (8.0 mg, 0.4 mmol), and H₂O 1.0 mL. Then put the flask in the reaction system at 100 °C and reflux for 16 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to obtain the product 8 in 89 % (37.2 mg) as a colorless liquid. $R_f = 0.68$ (petroleum ether/ethyl acetate = 20/1); ¹H NMR (400 MHz, CDCl₃) δ 8.32 (d, J = 8.0 Hz, 1H), 8.09 (s, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.47 (m, 2H), 7.35 (t, J = 8.6 Hz, 2H), 2.44 (s, 3H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 177.2, 156.1, 154.3, 1356.0, 134.6, 133.6, 126.6, 125.9, 123.6, 121.7, 121.4, 117.9, 117.7, 20.8.

Synthesis of 2-benzoylphenyl trifluoromethanesulfonate (9).⁴³ To a flask was added 2b (0.99 g, 5 mmol), 3f (0.84 mL, 6 mmol), Et₃N (1.4 mL, 10 mmol), and DCM 0.5 mL. Then put the flask in the reaction system at 80 °C and stirred for 12 h.The reaction mixture was dissolved in 2.0 mL ethyl acetate . Dried by Rotary Evaporator, the residue was purified by column chr-omatography (petroleum ether/ethyl acetate = 20/1) to obtain the product 9 in 85 % (1.25 mg) as a colorless liquid. R_f = 0.36 (petroleum ether/ethyl acetate = 20/1); ¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.60 (m, 3H), 7.46 (m, 3H), 7.41 (d, *J* = 8.3 Hz, 1H). ¹³C {¹H} NMR (100 MHz, CDCl₃) δ 192.7, 146.8, 136.5, 133.8, 132.8, 132.4, 131.3, 130.1, 128.6, 128.1, 122.4, 118.5 (q, *J* = 318.6 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ -73.6.

Synthesis of benzophenone (10).⁴⁴To a flask was added 9 (58.8 mg, 0.2 mmol), Pd(OAc)₂ (2.2 mg, 0.01 mmol), DPPF (5.5 mg, 0.01 mmol), HCOOH (15 μ L, 0.4 mmol), Et₃N (56 μ L, 0.4 mmol), and DMSO (1.0 mL). Then put the flask in the reaction system at 25 °C and stirred for 12 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to obtain the product 10 in 94 % (34.6 mg) as a white solid. R_f = 0.52 (petroleum ether/ethyl acetate =20/1); 1H NMR (400 MHz, CDCl₃) δ 7.81 (d, *J* = 7.8 Hz, 4H), 7.59 (t, *J* = 7.4 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 4H). ¹³C{¹¹H} NMR (100 MHz, CDCl₃) δ 196.7, 137.6, 132.4, 130.0, 128.2.

phenyl(4'-(trifluoromethyl)-[1,1'-biphenyl]-2-Synthesis of yl)methanone (11).⁴⁵ To a flask was added 9 (58.8 mg, 0.2 mmol), 4trifluoromethylphenylboronic acid (76 mg, 0.4mmol), Pd(PPh₃)₄ (23.0 mg, 0.02 mmol), Na₂CO₃ (42.4 mg, 0.4 mmol), toluene (1.0 mL) and H₂O (1.0 mL). Then put the flask in the reaction system at 140 °C and stirred for 12 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate . Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 20/1) to obtain the product 11 in 70 % (45.4 mg) as a white solid. $R_f = 0.52$ (petroleum ether/ethyl acetate =20/1); ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, J = 7.7 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.57 - 7.43 (m, 6H), 7.38 (d, J = 8.1 Hz, 2H), 7.32 (t, J = 7.7 Hz, 2H). ¹³C{¹H} (100 MHz, CDCl₃) δ 198.1, 143.9, 139.9, 139.0, 137.3, 133.2, 130.6, 130.2, 129.9, 129.4 (q, J = 32.3 Hz), 129.3, 129.0, 128.3, 127.7, 125.2 (q, J = 3.8 Hz), 124.1 (q, J = 270.3 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ-62.6

Procedure for gram scale experiment. To a flask was added 1a (1.12 g, 5 mmol), NiCl₂ (65 mg, 0.5 mmol), Na₂CO₃ (4.24 g, 10 mmol), TBHP (975 μ L, 5 mmol) and toluene (1.0 mL). Then put the flask in the reaction system at 80 °C and stirred for 36 h. The reaction mixture was dissolved in 2.0 mL ethyl acetate. Dried by Rotary Evaporator, the residue was purified by column chromatography (petroleum ether/ethyl acetate = 100/1) to obtain the product.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures, characterization data, spectra copies of the ¹H, ¹⁹F, ¹³C NMR.

AUTHOR INFORMATION

Corresponding Author

*E-mail: renhuaqiu1@hnu.edu.cn (R.Q.).

Author Contributions

The authors declare no competing financial interest.

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