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Silver-Catalyzed C(sp^2)−H Functionalization/C−O Cyclization Reaction at Room Temperature

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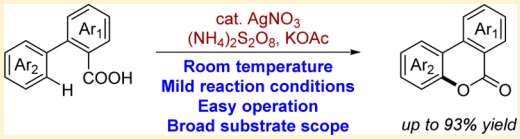
Supporting Information

ABSTRACT: Silver-catalyzed C(sp^2)−H functionalization/C−O cyclization has been developed. The scalable reaction proceeds at room temperature in an open flask. The present method exhibits good functional-group compatibility because of the mild reaction conditions. Using a $AgNO_3$ catalyst and a $(NH_4)_2S_2O_8$ oxidant in CH_2Cl_2/H_2O solvent, various lactones are obtained in good to excellent yields. A kinetic isotope effect (KIE) study indicates that the reaction may occur via a radical process.



INTRODUCTION

In recent years, transition-metal-catalyzed C−H functionalization has emerged as a useful and popular strategy for the formation of complex molecules from simple substrates.[1] Among them, C−H functionalization/C−O cyclization reactions have been successfully applied for rapid access to oxygen-containing heterocycles with atom economy.[2] For example, in 2010 Yu et al. reported palladium-catalyzed C−H activation/C−O cyclization directed by aliphatic alcohol for the synthesis of dihydrobenzofurans [Scheme 1a, eq 1].[2a] In 2011, Liu et al. and Yoshikai et al. independently described palladium-catalyzed C−H activation/C−O cyclization of 2-aryl phenols to prepare dibenzofurans [Scheme 1a, eqs 2 and 3].[2b,m] Recently, Wang et al. further extended the palladium-catalyzed system to carboxyl-directed C−H activation/C−O cyclization with the use of acetyl-protected glycine as the ligand [Scheme 1a, eqs 4 and 5].[2c,d] In comparison to the palladium, copper recently has been shown to catalyze the C−H functionalization/C−O cyclization of 2-aryl acids. For instance, Martin et al. and Gevorgyan et al. recently showed copper-catalyzed radical-based C−H functionalization/C−O cyclization reactions of 2-aryl acids, respectively (Scheme 1b).[2e,f] Such radical-based reactions could be more practical than palladium-catalyzed C−H activation/C−O cyclization for the synthesis of lactones[3,4] because these copper catalysts are much less expensive and no ligands are needed. Despite these notable advances, developing milder and more efficient transition metal catalyzed radical-based C−H functionalization/C−O cyclization reactions remains an important challenge task.

Herein, we report a novel silver-catalyzed C(sp^2)−H functionalization/C−O cyclization of 2-aryl acids to form lactones under mild conditions at room temperature (rt) (Scheme 1c).[5] The present work was inspired by classic Minsci reaction and the recent work of Baran et al. on silver-catalyzed radical-based C−H functionalization of heteroarenes.[6,7] This study not only provides a convenient, easy-to-handle protocol into the lactones scaffolds but also further confirms the value of radical-based C−H functionalization for synthetic applications.[8]

RESULTS AND DISSCUSION

We began our study with 2-phenylbenzoic acid **1a** as the probe substrate in the presence of the $AgNO_3$ catalyst and $(NH_4)S_2O_8$ oxidant at rt (Table 1). Different solvents were tested first (Table 1, entries 1−5). To our delight, the use of CH_2Cl_2/H_2O (1:1, v:v) afforded the desired product **2a** in 86% yield (Table 1, entry 1). Note that low yield was obtained without the use of water as cosolvent (see Supporting Information (SI) for more details). When 10 mol % $AgNO_3$ and 1.5 equiv of $(NH_4)_2S_2O_8$ were employed the yields of **2a** were diminished to 76% and 62%, respectively (Table 1, entries 6 and 7). Reactions catalyzed by silver salts, such as AgOAc, $AgBF_4$, and $AgSbF_6$, afforded moderate yields of the desired product. To further improve the conversion of **1a**, several additives including acids and bases were investigated (Table 1, entries 14−17). It was found that the use of KOAc as the additive afforded the desired product **2a** in 93% yield with full conversion of **1a**. Finally, it is important to mention that the control experiment conducted in the absence of the Ag(I) catalyst gave only a trace amount of **2a** (Table 1, entry 18).

With the optimized reaction conditions in hand, we next studied the scope of 2-aryl carboxylic acids that undergo these cyclizations, and the results are summarized in Scheme 2. It was found that a variety of 2-aryl carboxylic acids can be converted to the desired product in modest to good yields. The present reaction can tolerate well electron-donating groups such as methyl (**2b**, **2q**, **2s**), ether (**2h**, **2j**, **2k**, **2l**, **2r**, **2w**), and electron-withdrawing groups such as ketone (**2f**). The structure of **2j** was also confirmed by X-ray diffraction (see SI). Notably, this reaction can even tolerate an unprotected OH group (**2n**). Remarkably, a terminal alkene (**2l**) was found to be compatible

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Scheme 1. Examples of Transition-Metal-Catalyzed C(sp^2)–H Functionalization/C–O Cyclization

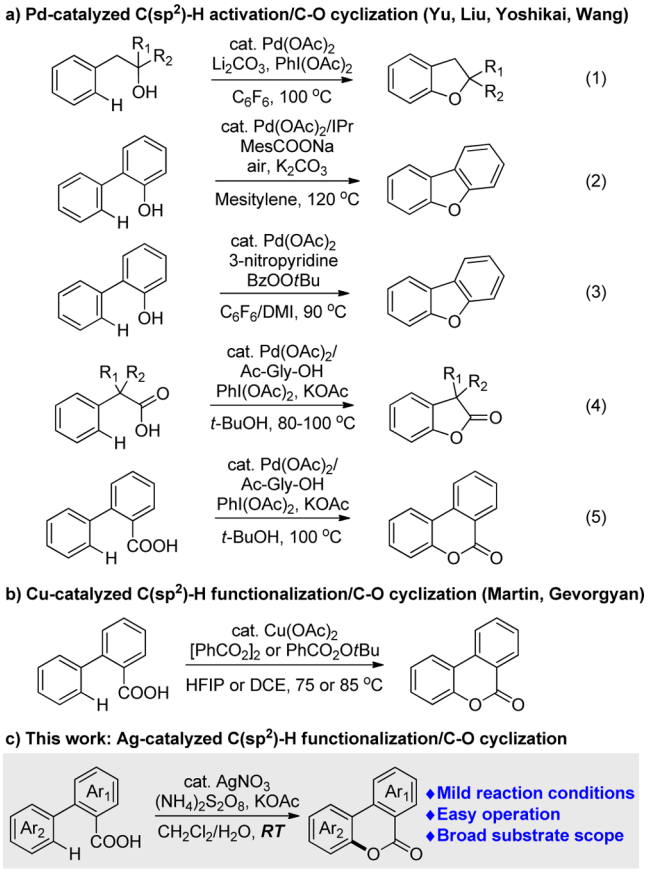
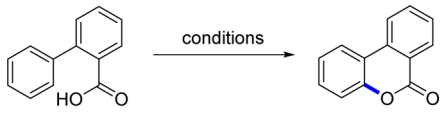


Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	oxidant	additive	solvent[b]	yield/%[c]
1	$AgNO_3$	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	86
2	$AgNO_3$	$(NH_4)_2S_2O_8$	–	$EtOAc/H_2O$	53
3[d]	$AgNO_3$	$(NH_4)_2S_2O_8$	–	$HFIP/H_2O$	35
4	$AgNO_3$	$(NH_4)_2S_2O_8$	–	$acetone/H_2O$	68
5	$AgNO_3$	$(NH_4)_2S_2O_8$	–	CH_3CN/H_2O	14
6[e]	$AgNO_3$	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	72
7[f]	$AgNO_3$	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	61
8	AgOAc	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	70
9	$AgBF_4$	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	71
10	$AgSbF_6$	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	73
11	$AgNO_3$	$K_2S_2O_8$	–	CH_2Cl_2/H_2O	82
12	$AgNO_3$	$Na_2S_2O_8$	–	CH_2Cl_2/H_2O	78
13	$AgNO_3$	$(NH_4)_2S_2O_8$	HOAc	CH_2Cl_2/H_2O	74
14	$AgNO_3$	$(NH_4)_2S_2O_8$	K_2HPO_4	CH_2Cl_2/H_2O	64
15	**$AgNO_3$**	**$(NH_4)_2S_2O_8$**	**KOAc**	**CH_2Cl_2/H_2O**	**96(93)**
16	$AgNO_3$	$(NH_4)_2S_2O_8$	NaOAc	CH_2Cl_2/H_2O	88
17	$AgNO_3$	$(NH_4)_2S_2O_8$	KH_2PO_4	CH_2Cl_2/H_2O	75
18	——	$(NH_4)_2S_2O_8$	–	CH_2Cl_2/H_2O	trace

[a]Reaction conditions: **1a** (0.3 mmol), additive (0.9 mmol, 3.0 equiv), Ag catalyst (20 mol %), and oxidant (0.9 mmol, 3 equiv) in the solvent (6 mL) at room temperature for 24 h under an air atmosphere, unless otherwise noted. [b]The ratio is 1:1 (v:v). [c]GC yields with benzophenone as an internal standard added after the reaction. Yield of isolated products given in parentheses. [d]HFIP = Hexafluoroisopropanol. [e]10 mol % $AgNO_3$ was used. [f]1.5 equiv $(NH_4)_2S_2O_8$ was used.

to some extent and gave the product in a modest yield. Furthermore, aryl halide groups such as F (**2c**, **2y**), Cl (**2d**, **2t**), and Br (**2e**) were also well compatible with the reaction, enabling additional functionalization at these positions via transition-metal-catalyzed cross-coupling reactions.[9] Interestingly, when a *meta*-OMe substituted substrate (**1r**) was subjected to this reaction, a major isomer (**2r**) was obtained. However, the use of a *meta*-Me substituted substrate (**1s**) afforded a mixture of regioisomers (**2s** and **2s′**) in a 1:1 ratio. Moreover, the 2-naphthyl substituted substrate (**1p**) also gave a single isomer (**2p**) at the more electron-rich 1-position. This result also demonstrates the complementarity of this method to Wang's previous Pd-catalyzed C–H activation/C–O cyclization protocol.[2b] A sterically hindered substrate could also undergo this transformation. For example, the reaction of 2,6-diphenylbenzoic acid (**1x**) gave the desired product (**2x**) in a modest yield. Finally, a heteroaromatic substrate (e.g., 3-phenylthiophene-2-carboxylic acid (**1z**)) can be converted to the corresponding product (**2z**) in a modest yield.

To further probe the utility of this silver-catalyzed C–H functionalization/C–O cyclization in preparative organic synthesis, a gram-scale reaction was conducted. As depicted in Scheme 3, a 3.96 g (20 mmol) scale of **1a** can be converted to **2a** in 89% yield at a lowered (10 mol %) catalyst loading. Moreover, the present reaction was conducted in an open flask. Next, treatment of **2a** with LiOH[2e,10] and $NaBH_4$[11] gave the corresponding hydroxylation of benzoic acids (**3**) and chromene (**4**) in 86% and 78% yields, respectively. Notably, the present study provides an alternative route for the achievement remote hydroxylated arenes.[12]

Note that the present reaction permits a compatible reaction profile. Under the reaction conditions described in this study, a chemoselective C–O cyclization of a carboxyl group in the presence of an unprotected hydroxyl group could be accomplished in 72% yield. Considering that Yu's group[2a] reported a hydroxyl group as a partner for Pd-catalyzed C–H activation/C–O cyclization reactions formed dihydrobenzofurans, subsequent treatment of the resulting aliphatic alcohol (**6**) under Yu's conditions delivered the final product in 64% yield (Scheme 4).

Next, we carried out a kinetic isotope effect (KIE) experiment to gain more insights into the mechanism. When a 1:1 mixture of **1a** and [**D5**]**1a** was subjected to the silver-catalyzed reaction conditions, we obtained the products **2a** and [**D4**]**2a** in a ratio of 1.27:1 (Scheme 5). This KIE value of 1.27 suggests that C–H cleavage is not the first irreversible step in the catalytic cycle.

Based on the mechanistic investigation above and previous reports,[13] we propose a plausible mechanism shown in Scheme 6. First, the Ag(I) is oxidized to Ag(II), which then reacts with 2-aryl acids (**1**) to give the carboxyl radical (**8**). Second, the carboxyl radical (**8**) cyclizes onto the aromatic ring to afford the intermediate (**9**), which further proceeds to one-electron oxidation and proton loss to furnish the final product (**2**). It is worth noting that the regioselectivities of the present reaction shown in Scheme 2 also indicate a radical-based mechanism.

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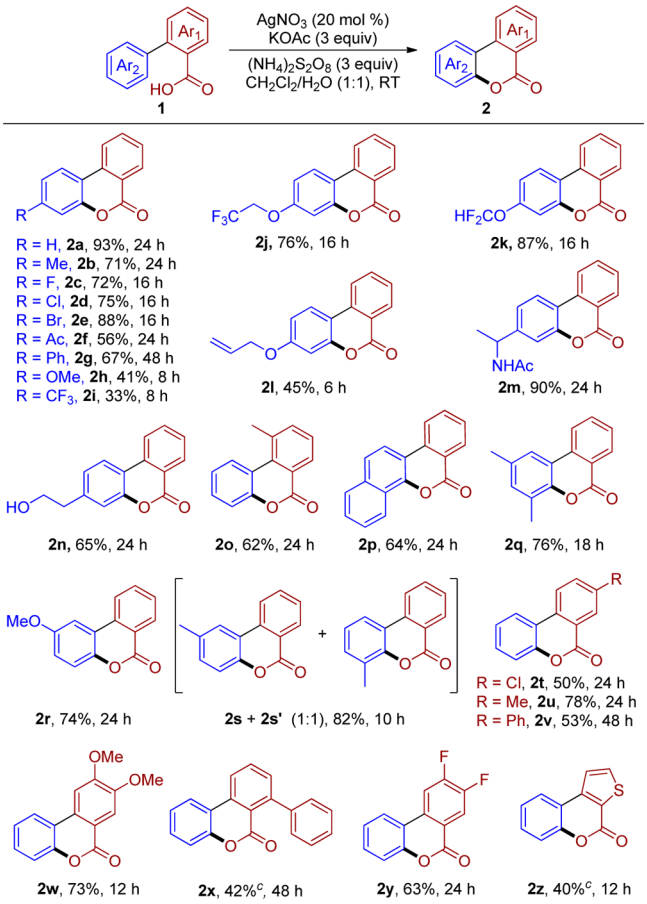
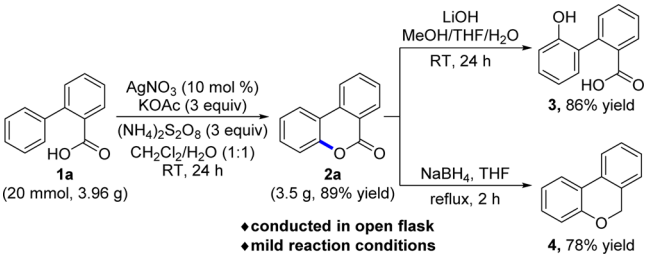
Scheme 2. Substrate Scope of 2-Aryl Carboxylic Acids[a,b]



[a]Reaction conditions: **1** (0.3 mmol), $AgNO_3$ (20 mol %), KOAc (0.9 mmol, 3 equiv), and $(NH_4)S_2O_8$ (0.9 mmol, 3 equiv), rt, CH_2Cl_2/H_2O. [b] Yields of isolated products are shown. [c] 0.2 mmol scale.

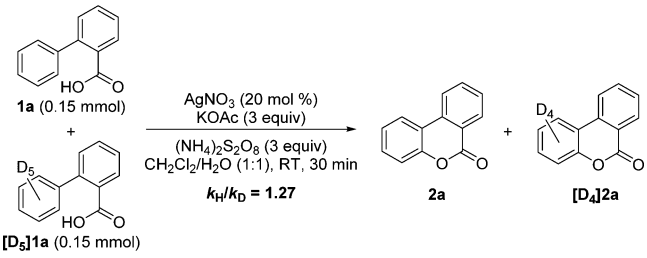
Scheme 3. Gram-Scale Reaction and Further Conversion



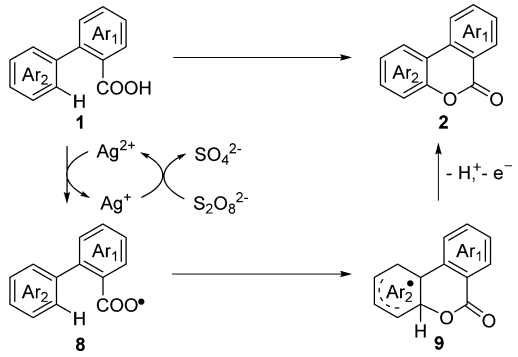
CONCLUSIONS

In summary, we have successfully achieved C−H functionalization/C−O cyclization by employing inexpensive $AgNO_3$ as the catalyst and environmentally friendly $(NH_4)_2S_2O_8$ as the oxidant. This new reaction is operationally simple and can be conducted under mild conditions at room temperature. A wide variety of synthetically useful yet sensitive functional groups are well-tolerated. Furthermore, chemoselectivity C−H functionalization/C−O cyclization has also been achieved. Further studies are currently underway to investigate the detail mechanism and the application of this transformation.

Scheme 5. Intermolecular Kinetic Isotope Effect (KIE)



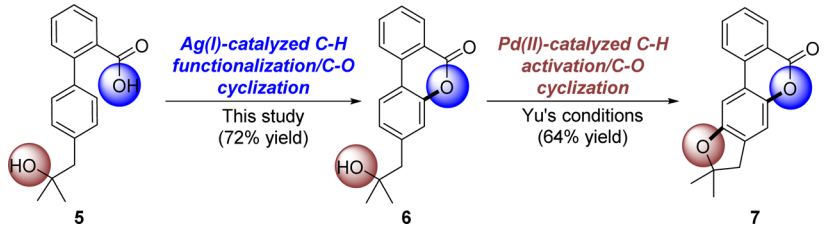
Scheme 6. Proposed Reaction Mechanism



EXPERIMENTAL SECTION

General Information. Chemicals and solvents (CH_3CN, HFIP, EtOAc, acetone, and CH_2Cl_2) were used as received. ^1H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a 400 MHz spectrometer at ambient temperature, using TMS as an internal standard (chemical shifts in δ). Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, etc.), coupling constant (Hz), and integration. Gas chromatographic (GC) analyses were performed on a GC equipped with a flame-ionization detector and an Rtx@-65 (30 m × 0.32 mm ID × 0.25 μm df) column using benzophenone as an internal standard, added during reaction workup. GC-MS analyses were performed on a GC-MS with an EI mode. High resolution mass spectra were obtained on an HRMS-TOF spectrometer. Analytical thin layer chromatography (TLC) was performed on precoated silica gel plates. After elution, the plate was visualized under UV illumination at 254 nm for UV active materials. Organic solutions were concentrated under reduced pressure on a rotary evaporator. Column chromatography was

Scheme 4. Chemoselectivity Profile in C−H Functionalization/C−O Cyclization



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performed on silica gel (200−300 mesh) by standard techniques eluting with solvents as indicated.

Preparation of Starting Materials.[14] General Procedure for Preparation of 1b−1i, 1o−1z. To a 100 mL Schlenk tube methyl 2-iodobenzoate (1 mL, 6.8 mmol, 1 equiv), $Pd(PPh_3)_2Cl_2$ (381 mg, 0.544 mmol, 8 mol %), and arylboronic acid (8.8 mmol, 1.3 equiv) were added, followed by a solution of Na_2CO_3 (1.44 g, 13.6 mmol, 2 equiv in 15 mL of H_2O) and THF (30 mL). The reaction mixture was heated at 60 °C overnight. The resulting reaction mixture was cooled to room temperature and added to water, and the product was extracted with EtOAc three times. The combined organic extract were dried over Na_2SO_4, evaporated, and purified by column chromatography. The purified product was dissolved in a solution of NaOH (1 g) in H_2O (25 mL) and MeOH (25 mL) and stirred at 50 °C for 6 h. MeOH was removed under vacuum, and the reaction mixture was diluted with H_2O and washed with Et_2O. The aqueous phase was acidified with 3 N HCl and then extracted with Et_2O three times. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, and filtered, and the filtration was evaporated under reduced pressure to give the desired product as a solid.

General Procedure for Preparation of 1j−1n, 5. To a 100 mL Schlenk tube methyl 2-iodobenzoate (1 mL, 6.8 mmol, 1 equiv), $Pd(PPh_3)_2Cl_2$ (381 mg, 0.544 mmol, 8 mol %), and arylboronic acid (8.8 mmol, 1.3 equiv) were added, followed by a solution of Na_2CO_3 (1.44 g, 13.6 mmol, 2 equiv in 15 mL H_2O) and THF (30 mL). The reaction mixture was heated at 60 °C overnight. The resulting reaction mixture was cooled to room temperature and added to water, and the product was extracted with EtOAc three times. The combined organic extract were dried over Na_2SO_4, evaporated, and purified by column chromatography. The purified product was dissolved in a solution of NaOH (1 g) in H_2O (25 mL) and MeOH (25 mL) and stirred at 50 °C for 6 h. MeOH was removed under vacuum, and the reaction mixture was diluted with H_2O and washed with Et_2O. The aqueous phase was acidified with 3 N HCl and then extracted with Et_2O three times. The combined organic phase was washed with H_2O and brine, dried over Na_2SO_4, and filtered, and the filtration was evaporated under reduced pressure to give the desired product as a solid.

*4′-Methyl-[1,1′-biphenyl]-2-carboxylic Acid (**1b**).*[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 7.8, 1.1 Hz, 1H), 7.54 (td, J = 7.6, 1.4 Hz, 1H), 7.44−7.32 (m, 2H), 7.27−7.15 (m, 4H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 143.3, 138.0, 137.1, 132.1, 131.2, 130.7, 129.3, 128.9, 128.4, 127.0, 21.2.

*4′-Fluoro-[1,1′-biphenyl]-2-carboxylic Acid (**1c**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, J = 7.8, 1.1 Hz, 1H), 7.56 (td, J = 7.6, 1.3 Hz, 1H), 7.43 (td, J = 7.7, 1.1 Hz, 1H), 7.35−7.31 (m, 1H), 7.31−7.26 (m, 2H), 7.14−6.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 162.4 (d, J = 246.3 Hz), 142.5, 137.03 (d, J = 3.4 Hz), 132.3, 131.3, 130.9, 130.1 (d, J = 8.1 Hz), 129.1, 127.4, 115.0 (d, J = 21.6 Hz).

*4′-Chloro-[1,1′-biphenyl]-2-carboxylic Acid (**1d**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.8, 1.1 Hz, 1H), 7.57 (td, J = 7.6, 1.3 Hz, 1H), 7.44 (td, J = 7.7, 1.2 Hz, 1H), 7.38−7.34 (m, 2H), 7.32 (dd, J = 7.7, 0.8 Hz, 1H), 7.27−7.21 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 142.4, 139.6, 133.5, 132.4, 131.2, 131.0, 129.8, 129.0, 128.2, 127.6.

*4′-Bromo-[1,1′-biphenyl]-2-carboxylic Acid (**1e**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.8, 1.1 Hz, 1H), 7.57 (td, J = 7.5, 1.3 Hz, 1H), 7.53−7.49 (m, 2H), 7.44 (td, J = 7.7, 1.2 Hz, 1H), 7.32 (dd, J = 7.6, 0.9 Hz, 1H), 7.23−7.15 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 142.4, 140.0, 132.4, 131.2, 131.1, 131.0, 130.2, 128.9, 127.6, 121.7.

*4′-Acetyl-[1,1′-biphenyl]-2-carboxylic Acid (**1f**).*[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, J = 7.9, 1.1 Hz, 1H), 7.98 (d, J = 8.4 Hz, 2H), 7.60 (td, J = 7.6, 1.3 Hz, 1H), 7.47 (td, J = 7.7, 1.2 Hz, 1H), 7.42 (d, J = 8.3 Hz, 2H), 7.34 (dd, J = 7.6, 0.8 Hz, 1H), 2.64 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 172.5, 146.2, 142.5, 135.9, 132.4, 131.1, 131.0, 128.9, 128.8, 128.2, 127.9, 26.7.

*[1,1′:4′,1″-Terphenyl]-2-carboxylic Acid (**1g**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, J = 7.7, 0.9 Hz, 1H), 7.68−7.52 (m, 5H), 7.49−7.38 (m, 6H), 7.38−7.31 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 143.0, 140.7, 140.2, 140.0, 132.2, 131.2, 130.8, 129.2, 128.9, 128.8, 127.3, 127.3, 127.1, 126.8. HRMS (EI) calcd for $C_{19}H_{14}O_2$ [M^+] 274.0994, found 274.1000.

*4′-Methoxy-[1,1′-biphenyl]-2-carboxylic Acid (**1h**).*[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 7.8, 1.1 Hz, 1H), 7.53 (td, J = 7.6, 1.4 Hz, 1H), 7.44−7.32 (m, 2H), 7.32−7.18 (m, 2H), 7.01−6.83 (m, 2H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 159.1, 142.9, 133.3, 132.1, 131.2, 130.7, 129.6, 129.3, 126.8, 113.6, 55.2.

*4′-(Trifluoromethyl)-[1,1′-biphenyl]-2-carboxylic Acid (**1i**).*[2f] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.8, 1.1 Hz, 1H), 7.63 (d, J = 8.2 Hz, 2H), 7.59 (dd, J = 7.6, 1.3 Hz, 1H), 7.48 (td, J = 7.7, 1.2 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.32 (dd, J = 7.6, 0.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 144.9, 142.3, 132.5, 131.2, 131.2, 129.5 (q, J = 32.4 Hz), 128.9, 128.8, 128.0, 124.9 (q, J = 3.7 Hz), 124.3 (q, J = 272.0 Hz).

*4′-(2,2,2-Trifluoroethoxy)-[1,1′-biphenyl]-2-carboxylic Acid (**1j**).* ^{1}H NMR (400 MHz, CDCl3) δ 7.95 (dd, J = 7.7, 0.9 Hz, 1H), 7.56 (td, J = 7.6, 1.2 Hz, 1H), 7.47−7.39 (m, 1H), 7.34 (d, J = 7.6 Hz, 1H), 7.29 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 4.38 (q, J = 8.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 156.8, 142.6, 135.3, 132.2, 131.3, 130.8, 129.9, 129.1, 127.2, 123.4 (q, J = 278.7 Hz), 114.5, 65.8 (q, J = 35.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.93 (s). HRMS (EI) calcd for $C_{15}H_{11}F_3O_3$ [M^+] 296.0660, found 296.0664.

*4′-(Difluoromethoxy)-[1,1′-biphenyl]-2-carboxylic Acid (**1k**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.8, 1.1 Hz, 1H), 7.57 (td, J = 7.6, 1.3 Hz, 1H), 7.44 (td, J = 7.7, 1.1 Hz, 1H), 7.37−7.28 (m, 3H), 7.13 (d, J = 8.5 Hz, 2H), 6.56 (t, J = 74.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 150.7 (t, J = 2.8 Hz), 142.4, 138.3, 132.4, 131.3, 131.0, 130.0, 129.0, 127.5, 118.9, 116.0 (t, J = 259.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.62 (s). HRMS (EI) calcd for $C_{14}H_{10}F_2O_3$ [M^+] 264.0598, found 264.0592.

*4′-(Allyloxy)-[1,1′-biphenyl]-2-carboxylic Acid (**1l**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.8 Hz, 1H), 7.53 (td, J = 7.5, 1.0 Hz, 1H), 7.37 (dd, J = 16.0, 7.9 Hz, 2H), 7.26 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.6 Hz, 2H), 6.08 (ddd, J = 22.5, 10.6, 5.3 Hz, 1H), 5.43 (dd, J = 17.3, 1.4 Hz, 1H), 5.30 (dd, J = 10.5, 1.1 Hz, 1H), 4.56 (d, J = 5.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 158.1, 142.9, 133.5, 133.3, 132.1, 131.2, 130.7, 129.6, 129.3, 126.8, 117.8, 114.4, 68.8. HRMS (EI) calcd for $C_{16}H_{14}O_3$ [M^+] 254.0943, found 254.0948.

*4′-(1-Acetamidoethyl)-[1,1′-biphenyl]-2-carboxylic Acid (**1m**).* ^{1}H NMR (400 MHz, DMSO) δ 12.78 (s, 1H), 8.35 (d, J = 8.2 Hz, 1H), 7.69 (d, J = 7.6 Hz, 1H), 7.56 (td, J = 7.5, 1.1 Hz, 1H), 7.43 (dd, J = 10.8, 4.2 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 4.96 (p, J = 7.1 Hz, 1H), 1.86 (s, 3H), 1.36 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 170.2, 168.7, 144.1, 141.0, 139.5, 132.9, 131.2, 130.9, 129.4, 128.7, 127.6, 126.3, 47.9, 23.2, 22.9. HRMS (EI) calcd for $C_{17}H_{17}NO_3$ [M^+] 283.1208, found 283.1210.

*4′-(2-Hydroxyethyl)-[1,1′-biphenyl]-2-carboxylic Acid (**2n**).* ^{1}H NMR (400 MHz, DMSO) δ 12.75 (s, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.55 (t, J = 7.3 Hz, 1H), 7.43 (t, J = 7.4 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.25 (s, 4H), 4.70 (s, 1H), 3.65 (t, J = 6.9 Hz, 2H), 2.77 (t, J = 7.0 Hz, 2H). ^{13}C NMR (101 MHz, DMSO) δ 170.3, 141.2, 139.0, 138.8, 132.9, 131.2, 130.9, 129.4, 129.2, 128.6, 127.5, 62.5, 39.1. HRMS (EI) calcd for $C_{15}H_{14}O_3$ [M^+] 242.0943, found 242.0948.

*6-Methyl-[1,1′-biphenyl]-2-carboxylic Acid (**1o**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.3 Hz, 1H), 7.43 (d, J = 7.2 Hz, 1H), 7.41−7.28 (m, 4H), 7.18−7.10 (m, 2H), 2.07 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 142.5, 139.9, 137.5, 133.9, 130.0, 128.5, 128.0, 127.9, 127.1, 127.0, 20.8.

*2-(Naphthalen-2-yl)benzoic Acid (**1p**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.4 Hz, 1H), 7.87−7.81 (m, 2H), 7.81−7.75 (m, 2H), 7.64−7.56 (m, 1H), 7.52−7.47 (m, 2H), 7.46−7.39 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 143.4, 138.7, 133.2, 132.5, 132.2, 131.5, 130.8, 129.2, 128.1, 127.7, 127.4, 127.3, 127.1, 126.9, 126.2, 126.0.

*3′,5′-Dimethyl-[1,1′-biphenyl]-2-carboxylic Acid (**1q**).*[2f] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, J = 7.8, 1.0 Hz, 1H), 7.52 (td, J = 7.6, 1.3 Hz, 1H), 7.42−7.32 (m, 2H), 6.98 (s, 1H), 6.95 (s, 2H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 143.4, 140.8, 137.5, 131.9, 131.2, 130.5, 129.4, 129.1, 127.0, 126.3, 21.3.

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*3′-Methoxy-[1,1′-biphenyl]-2-carboxylic Acid (**1r**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, J = 7.8, 1.0 Hz, 1H), 7.55 (td, J = 7.6, 1.3 Hz, 1H), 7.42 (td, J = 7.6, 1.1 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.33−7.25 (m, 1H), 6.95−6.88 (m, 2H), 6.88 (s, 1H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 159.3, 143.1, 142.4, 132.0, 131.1, 130.6, 129.4, 129.1, 127.3, 121.1, 114.1, 113.0, 55.2.

*3′-Methyl-[1,1′-biphenyl]-2-carboxylic Acid (**1s**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−7.83 (m, 1H), 7.54 (td, J = 7.6, 1.3 Hz, 1H), 7.40 (td, J = 7.6, 1.1 Hz, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.30−7.25 (m, 1H), 7.20−7.04 (m, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 143.4, 140.9, 137.7, 132.0, 131.2, 130.6, 129.3, 129.1, 128.2, 128.0, 127.1, 125.7, 21.5.

*4-Chloro-[1,1′-biphenyl]-2-carboxylic Acid (**1t**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 2.2 Hz, 1H), 7.53 (dd, J = 8.3, 2.3 Hz, 1H), 7.43−7.34 (m, 3H), 7.33−7.27 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 141.8, 139.8, 133.3, 132.6, 132.1, 130.6, 130.5, 128.4, 128.2, 127.7.

*4-Methyl-[1,1′-biphenyl]-2-carboxylic Acid (**1u**).*[2d] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.40−7.28 (m, 6H), 7.25 (d, J = 6.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 141.0, 140.5, 137.1, 132.8, 132.1, 131.1, 129.1, 128.5, 128.0, 127.1, 20.9.

*[1,1′:4′,1″-Terphenyl]-2′-carboxylic Acid (**1v**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 7.5 Hz, 2H), 7.54−7.42 (m, 3H), 7.42−7.32 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 142.1, 140.7, 140.2, 139.5, 131.8, 130.5, 129.7, 129.3, 129.0, 128.5, 128.1, 127.9, 127.4, 127.1. HRMS (EI) calcd for $C_{19}H_{14}O_2$ [M^+] 274.0994, found 274.0998.

*4,5-Dimethoxy-[1,1′-biphenyl]-2-carboxylic Acid (**1w**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.42−7.33 (m, 3H), 7.33−7.28 (m, 2H), 6.77 (s, 1H), 3.94 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 151.9, 147.7, 141.4, 138.7, 128.6, 127.9, 127.1, 120.3, 114.0, 113.6, 56.1, 56.1. HRMS (EI) calcd for $C_{15}H_{14}O_4$ [M^+] 258.0892, found 258.0888.

*[1,1′:3′,1″-Terphenyl]-2′-carboxylic Acid (**1x**).*[17] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.47 (m, 1H), 7.44−7.32 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 140.3, 140.2, 131.6, 129.6, 129.0, 128.4, 128.4, 127.6.

*4,5-Difluoro-[1,1′-biphenyl]-2-carboxylic Acid (**1y**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 10.7, 8.1 Hz, 1H), 7.41−7.33 (m, 3H), 7.30−7.23 (m, 2H), 7.16 (dd, J = 10.7, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 152.2 (dd, J = 257.1, 12.6 Hz), 149.0 (dd, J = 250.5, 12.8 Hz), 141.7 (dd, J = 6.9, 3.9 Hz), 139.1, 128.3, 128.2, 128.0, 125.3 (dd, J = 5.2, 3.5 Hz), 120.4 (d, J = 17.7 Hz), 120.3 (dd, J = 19.1, 1.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −130.43 (d, J = 21.8 Hz), −138.47 (d, J = 21.8 Hz). HRMS (EI) calcd for $C_{13}H_8F_2O_2$ [M^+] 234.0492, found 234.0496.

*3-Phenylthiophene-2-carboxylic Acid (**1z**).* ^{1}H NMR (400 MHz, DMSO) δ 12.90 (s, 1H), 7.86 (d, J = 5.1 Hz, 1H), 7.46 (d, J = 6.6 Hz, 2H), 7.43−7.32 (m, 3H), 7.18 (d, J = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 163.3, 147.6, 136.0, 132.2, 131.5, 129.7, 128.5, 128.2, 128.1.

General Procedure for Silver-Catalyzed C(sp^2)−H Functionalization/C−O Cyclization Reaction. To a 15 mL tube were sequentially added **1** (0.3 mmol, 1 equiv), $AgNO_3$ (10.2 mg, 0.06 mmol, 0.02 equiv), $(NH_4)_2S_2O_8$ (205 mg, 0.9 mmol, 3 equiv), KOAc (88.3 mg, 0.9 mmol, 3 equiv), 3 mL of CH_2Cl_2, and 3 mL of H_2O. The reaction mixture was then stirred at room temperature for the appointed time. After completion, the reaction mixture was diluted with H_2O and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

*6H-Benzo[c]chromen-6-one (**2a**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (55 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (dd, J = 7.9, 0.5 Hz, 1H), 8.10 (d, J = 8.1 Hz, 1H), 8.04 (d, J = 7.9 Hz, 1H), 7.81 (td, J = 7.9, 1.1 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.51−7.42 (m, 1H), 7.40−7.29 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 151.2, 134.8, 134.7, 130.5, 130.4, 128.9, 124.5, 122.7, 121.7, 121.2, 118.0, 117.7. GCMS (EI) m/z 196 $(M)^+$.

*3-Methyl-6H-benzo[c]chromen-6-one (**2b**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (45 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, J = 8.0, 1.0 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.86−7.73 (m, 1H), 7.64−7.43 (m, 1H), 7.14 (d, J = 8.7 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 151.2, 141.3, 134.9, 134.8, 130.5, 128.4, 125.7, 122.5, 121.4, 120.8, 117.9, 115.4, 21.4. GCMS (EI) m/z 210 $(M)^+$.

*3-Fluoro-6H-benzo[c]chromen-6-one (**2c**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 16 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (45 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 8.0, 1.0 Hz, 1H), 8.00 (dd, J = 8.3, 5.6 Hz, 2H), 7.86−7.74 (m, 1H), 7.61−7.48 (m, 1H), 7.12−6.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4 (d, J = 251.3 Hz), 160.8, 152.1 (d, J = 12.3 Hz), 135.1, 134.2, 130.6, 128.7, 124.3 (d, J = 9.9 Hz), 121.5, 120.4, 114.6 (d, J = 3.2 Hz), 112.4 (d, J = 22.4 Hz), 105.0 (d, J = 25.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.36 (s). GCMS (EI) m/z 214 $(M)^+$.

*3-Chloro-6H-benzo[c]chromen-6-one (**2d**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 16 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (52 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 7.9, 1.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.3 Hz, 1H), 7.87−7.72 (m, 1H), 7.64−7.46 (m, 1H), 7.32−7.24 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 151.4, 135.8, 135.0, 133.8, 130.6, 129.1, 124.8, 123.7, 121.6, 120.7, 117.8, 116.6. GCMS (EI) m/z 230 ($^{35}M)^+$, 232 ($^{37}M)^+$.

*3-Bromo-6H-benzo[c]chromen-6-one (**2e**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 16 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (73 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dd, J = 7.9, 0.7 Hz, 1H), 8.04 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.85−7.78 (m, 1H), 7.63−7.56 (m, 1H), 7.48 (d, J = 1.9 Hz, 1H), 7.44 (dd, J = 8.5, 1.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 151.4, 135.1, 133.9, 130.7, 129.3, 127.8, 123.9, 123.7, 121.6, 120.9, 120.8, 117.0. GCMS (EI) m/z 274 ($^{79}M)^+$, 276 ($^{81}M)^+$.

*3-Acetyl-6H-benzo[c]chromen-6-one (**2f**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 10:1, R_f = 0.3) as a white solid (40 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (dd, J = 8.0, 1.0 Hz, 1H), 8.16 (t, J = 8.8 Hz, 2H), 7.97−7.81 (m, 3H), 7.73−7.57 (m, 1H), 2.67 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.5, 160.6, 151.1, 138.3, 135.1, 133.6, 130.8, 130.1, 123.9, 123.2, 122.4, 122.0, 121.7, 117.9, 26.8. GCMS (EI) m/z 238 $(M)^+$.

*3-Phenyl-6H-benzo[c]chromen-6-one (**2g**).* According to the general procedure, the reaction mixture was stirred at room temperature for 48 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.5) as a white solid (54 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 7.9, 1.0 Hz, 1H), 8.06 (dd, J = 11.3, 8.1 Hz, 2H), 7.79 (td, J = 7.8, 1.4 Hz, 1H), 7.62 (dd, J = 5.2, 3.3 Hz, 2H), 7.56−7.50 (m, 3H), 7.50−7.43 (m, 2H), 7.43−7.35 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 151.5, 143.4, 139.1, 134.8, 134.5, 130.5, 129.0, 128.7, 128.3, 127.0, 123.2, 123.1, 121.6, 121.0, 116.8, 115.7. HRMS (EI) calcd for $C_{19}H_{12}O_2$ [M^+] 272.0837, found 272.0832.

*3-Methoxy-6H-benzo[c]chromen-6-one (**2h**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 8 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (28 mg, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, J = 8.0, 1.0 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 8.8 Hz, 1H), 7.82−7.71 (m, 1H), 7.55−7.41 (m, 1H), 6.89 (dd, J = 8.8, 2.5 Hz, 1H), 6.82 (d, J = 2.5 Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 161.5, 152.5, 135.1,

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134.8, 130.5, 127.7, 123.7, 121.0, 119.9, 112.4, 111.1, 101.6, 55.7. GCMS (EI) m/z 226 $(M)^+$.

*3-(Trifluoromethyl)-6H-benzo[c]chromen-6-one (**2i**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 8 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.5) as a white solid (26 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, J = 7.9, 1.0 Hz, 1H), 8.17 (t, J = 7.8 Hz, 2H), 7.89 (td, J = 7.8, 1.4 Hz, 1H), 7.74−7.63 (m, 1H), 7.63−7.53 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 150.9, 135.2, 133.3, 132.2 (q, J = 33.5 Hz), 130.8, 130.2, 123.6, 123.3 (q, J = 272.5 Hz), 122.2, 121.6, 121.1 (q, J = 3.6 Hz), 121.1, 115.2 (q, J = 4.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.79.

*3-(2,2,2-Trifluoroethoxy)-6H-benzo[c]chromen-6-one (**2j**).* According to the general procedure, the reaction mixture was stirred at room temperature for 16 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.5) as a white solid (67 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (dd, J = 8.0, 1.0 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.93 (d, J = 8.9 Hz, 1H), 7.83−7.72 (m, 1H), 7.55−7.47 (m, 1H), 6.93 (dd, J = 8.8, 2.6 Hz, 1H), 6.83 (d, J = 2.6 Hz, 1H), 4.42 (q, J = 8.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 158.7, 152.3, 135.0, 134.5, 130.6, 128.3, 124.2, 123.1 (q, J = 278.0 Hz), 121.3, 112.8, 112.5, 102.9, 65.8 (q, J = 36.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.70 (s). HRMS (EI) calcd for $C_{15}H_9F_3O_3$ $[M^+]$ 294.0504, found 294.0501.

*3-(Difluoromethoxy)-6H-benzo[c]chromen-6-one (**2k**).* According to the general procedure, the reaction mixture was then stirred at room temperature for 16 h. The product was isolated by flash chromatography (PE/EA = 10:1, R_f = 0.3) as a white solid (68 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 7.9 Hz, 1H), 8.17−7.92 (m, 2H), 7.82 (t, J = 7.7 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.10 (dd, J = 6.6, 2.2 Hz, 2H), 6.62 (t, J = 73.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.7, 152.2 (t, J = 2.9 Hz), 151.9, 135.1, 134.0, 130.7, 128.9, 124.2, 121.6, 120.6, 115.8, 115.4 (t, J = 262.0 Hz), 115.3, 108.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.76 (s). HRMS (EI) calcd for $C_{14}H_8F_2O_3$ $[M^+]$ 262.0442, found 262.0448.

*3-(Allyloxy)-6H-benzo[c]chromen-6-one (**2l**).* According to the general procedure, the reaction mixture was stirred at room temperature for 6 h. The product was isolated by flash chromatography (PE/EA = 50:1, R_f = 0.4) as a white solid (34 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, J = 8.0, 1.5 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.84 (dd, J = 8.8, 2.1 Hz, 1H), 7.70 (dd, J = 10.8, 4.6 Hz, 1H), 7.41 (t, J = 7.6 Hz, 1H), 6.89−6.80 (m, 1H), 6.78 (t, J = 2.3 Hz, 1H), 5.99 (dtd, J = 15.8, 10.6, 5.3 Hz, 1H), 5.38 (dd, J = 17.3, 1.1 Hz, 1H), 5.27 (dd, J = 10.5, 1.0 Hz, 1H), 4.63−4.28 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 160.4, 152.5, 135.1, 134.9, 132.4, 130.5, 127.7, 123.8, 121.1, 120.0, 118.4, 113.0, 111.3, 102.5, 69.2. HRMS (EI) calcd for $C_{16}H_{12}O_3$ $[M^+]$ 252.0786, found 252.0782.

*N-(1-(6-Oxo-6H-benzo[c]chromen-3-yl)ethyl)acetamide (**2m**).* According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 2:1, R_f = 0.5) as a white solid (76 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 23.5, 7.8 Hz, 1H), 8.00 (t, J = 12.6 Hz, 1H), 7.86 (t, J = 12.9 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.32−7.23 (m, 2H), 6.82 (d, J = 6.8 Hz, 1H), 5.18 (p, J = 6.8 Hz, 1H), 2.09 (s, 3H), 1.54 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 161.3, 151.3, 146.6, 134.9, 134.5, 130.4, 128.8, 123.1, 123.0, 121.7, 120.8, 116.8, 114.8, 48.6, 23.2, 21.7. HRMS (EI) calcd for $C_{17}H_{15}NO_3$ $[M^+]$ 281.1052, found 281.1056.

*3-(2-Hydroxyethyl)-6H-benzo[c]chromen-6-one (**2n**).* According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 4:1, R_f = 0.6) as a white solid (47 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, J = 7.9 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.90 (d, J = 8.5 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.21−7.19 (m, 2H), 3.95 (t, J = 6.4 Hz, 2H), 2.96 (t, J = 6.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 151.3, 142.2, 134.8, 134.7, 130.5, 128.6, 125.5, 122.8, 121.5, 120.8, 117.9, 116.3, 63.2, 38.9. HRMS (EI) calcd for $C_{15}H_{12}O_3$ $[M^+]$ 240.0786, found 240.0783.

*10-Methyl-6H-benzo[c]chromen-6-one (**2o**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (39 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 7.7 Hz, 1H), 8.25 (d, J = 8.2 Hz, 1H), 7.61 (d, J = 7.4 Hz, 1H), 7.44 (ddd, J = 7.6, 5.7, 2.8 Hz, 2H), 7.39−7.33 (m, 1H), 7.33−7.27 (m, 1H), 2.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 151.1, 139.0, 135.0, 133.4, 129.6, 129.0, 128.2, 127.1, 124.0, 122.6, 119.5, 117.8, 25.3. GCMS (EI) m/z 210 $(M)^+$.

*6H-Dibenzo[c,h]chromen-6-one (**2p**).*[2f] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.5) as a light yellow solid (47 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51−8.41 (m, 1H), 8.35 (dd, J = 7.9, 1.0 Hz, 1H), 8.03 (d, J = 8.1 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.82−7.73 (m, 2H), 7.63 (d, J = 8.7 Hz, 1H), 7.58−7.48 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.1, 147.0, 135.1, 134.8, 134.1, 130.4, 128.4, 127.7, 127.5, 126.9, 124.4, 123.6, 122.1, 121.9, 120.9, 119.0, 112.8. GCMS (EI) m/z 246 $(M)^+$.

*2,4-Dimethyl-6H-benzo[c]chromen-6-one (**2q**).*[2f] According to the general procedure, the reaction mixture was stirred at room temperature for 18 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.5) as a white solid (51 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 7.9 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.80−7.56 (m, 1H), 7.54 (s, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.05 (s, 1H), 2.38 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 147.5, 135.0, 134.5, 133.3, 132.7, 130.3, 128.3, 126.4, 121.7, 120.9, 120.2, 117.1, 21.0, 15.8. GCMS (EI) m/z 224 $(M)^+$.

*2-Methoxy-6H-benzo[c]chromen-6-one (**2r**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 50:1, R_f = 0.3) as a white solid (50 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, J = 7.9, 1.1 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.79 (td, J = 7.9, 1.4 Hz, 1H), 7.60−7.51 (m, 1H), 7.42 (d, J = 2.9 Hz, 1H), 7.29−7.20 (m, 1H), 7.01 (dd, J = 9.0, 2.9 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 156.3, 145.5, 134.7, 134.5, 130.6, 128.9, 121.7, 121.2, 118.6, 118.4, 117.1, 106.2, 55.8. GCMS (EI) m/z 226 $(M)^+$.

*Mixture Isomers of **2s** and **2s′**.* According to the general procedure, the reaction mixture was stirred at room temperature for 10 h. The mixture product were isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (52 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40−8.25 (m, two isomers, 2H), 8.10−7.95 (m, two isomers, 2H), 7.82 (d, J = 7.9 Hz, 1H), 7.77 (dd, J = 11.8, 4.6 Hz, two isomers, 3H), 7.52 (t, J = 7.6 Hz, two isomers, 2H), 7.33−7.09 (m, two isomers, 4H), 2.45 (s, one isomer, 3H), 2.42 (s, the other isomer, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 161.2, 149.5, 149.2, 135.0, 134.7, 134.7, 134.0, 131.7, 131.3, 130.4, 130.3, 128.6, 128.6, 126.9, 123.9, 122.7, 121.8, 121.5, 121.1, 120.9, 120.3, 117.7, 117.5, 117.4, 21.1, 15.9. GCMS (EI) m/z 210 $(M)^+$.

*8-Chloro-6H-benzo[c]chromen-6-one (**2t**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (34 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 2.3 Hz, 1H), 8.02 (d, J = 8.6 Hz, 1H), 8.00−7.92 (m, 1H), 7.74 (dd, J = 8.6, 2.3 Hz, 1H), 7.54−7.43 (m, 1H), 7.34 (dd, J = 12.0, 4.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 151.0, 135.1, 134.9, 133.1, 130.8, 129.9, 124.8, 123.4, 122.7, 122.4, 117.8, 117.2. GCMS (EI) m/z 230 (^{35} $M)^+$, 232 (^{37} $M)^+$.

*8-Methyl-6H-benzo[c]chromen-6-one (**2u**).*[2d] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.5) as a white solid (49 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.98−7.93 (m, 1H), 7.91 (d, J = 8.2 Hz, 1H), 7.56 (dd, J = 8.2, 1.5 Hz, 1H), 7.47−7.35 (m, 1H), 7.34−7.22 (m, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz,

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$CDCl_3$) δ 161.3, 150.9, 139.1, 136.0, 132.1, 130.2, 129.8, 124.4, 122.5, 121.6, 120.9, 118.1, 117.5, 21.2. GCMS (EI) m/z 210 $(M)^+$.

*8-Phenyl-6H-benzo[c]chromen-6-one (**2v**).* According to the general procedure, the reaction mixture was stirred at room temperature for 48 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (43 mg, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 2.0 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.10−7.99 (m, 2H), 7.75−7.64 (m, 2H), 7.57−7.45 (m, 3H), 7.45−7.29 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 151.2, 141.7, 138.9, 133.5, 133.4, 130.4, 129.1, 128.5, 128.3, 127.0, 124.6, 122.8, 122.4, 121.6, 117.9, 117.8. GCMS (EI) m/z 272 $(M)^+$. HRMS (EI) calcd for $C_{19}H_{12}O_2$ $[M^+]$ 272.0837, found 272.0832.

*8,9-Dimethoxy-6H-benzo[c]chromen-6-one (**2w**).*[18] According to the general procedure, the reaction mixture was stirred at room temperature for 12 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.3) as a white solid (56 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.38 (td, J = 7.9, 1.4 Hz, 1H), 7.32 (s, 1H), 7.31−7.21 (m, 2H), 4.07 (s, 3H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 154.9, 150.8, 149.9, 129.7, 129.5, 124.3, 122.1, 117.9, 117.5, 114.3, 110.2, 102.5, 56.3, 56.2. GCMS (EI) m/z 256 $(M)^+$.

*7-Phenyl-6H-benzo[c]chromen-6-one (**2x**).*[19] According to the general procedure, the reaction mixture was stirred at room temperature for 48 h. The product was isolated by flash chromatography (PE/EA = 50:1, R_f = 0.4) as a white solid (0.2 mmol scale, 22 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.1 Hz, 1H), 8.11 (dd, J = 8.2, 1.1 Hz, 1H), 7.81 (t, J = 7.8 Hz, 1H), 7.53−7.39 (m, 5H), 7.39−7.29 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 151.5, 146.9, 141.9, 136.2, 133.6, 132.4, 130.5, 128.2, 127.8, 127.3, 124.3, 123.1, 121.2, 118.7, 118.1, 117.5. GCMS (EI) m/z 271 $(M)^+$.

*8,9-Difluoro-6H-benzo[c]chromen-6-one (**2y**).*[20] According to the general procedure, the reaction mixture was stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 50:1, R_f = 0.4) as a white solid (43 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (dd, J = 9.9, 8.0 Hz, 1H), 7.97−7.80 (m, 2H), 7.53 (td, J = 7.6, 1.4 Hz, 1H), 7.37 (ddd, J = 6.1, 3.6, 1.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (d, J = 1.8 Hz), 155.4 (dd, J = 259.7, 13.8 Hz), 151.3, 150.6 (dd, J = 254.2, 13.7 Hz), 133.1 (dd, J = 8.2, 3.4 Hz), 131.2, 125.0, 122.8, 119.2 (dd, J = 18.9, 2.4 Hz), 118.4 (dd, J = 6.2, 2.9 Hz), 118.0, 116.7 (dd, J = 2.2, 1.7 Hz), 110.7 (d, J = 19.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ −124.86 (d, J = 21.5 Hz), −133.84 (d, J = 21.4 Hz). GCMS (EI) m/z 232 $(M)^+$.

*4H-Thieno[2,3-c]chromen-4-one (**2z**).*[3o] According to the general procedure, the reaction mixture was stirred at room temperature for 12 h. The product was isolated by flash chromatography (PE/EA = 10:1, R_f = 0.3) as a yellow solid (0.2 mmol scale, 16 mg, 40%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 5.2 Hz, 1H), 7.84 (dd, J = 7.8, 1.4 Hz, 1H), 7.65 (d, J = 5.2 Hz, 1H), 7.54−7.47 (m, 1H), 7.44 (dd, J = 8.3, 1.0 Hz, 1H), 7.38−7.32 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 152.6, 145.0 136.9, 130.2, 124.6, 124.4, 123.8, 122.4, 117.5, 117.4.

Gram Scale Reaction and Further Conversion of Lactone. To a 500 mL flask were sequentially added **1a** (3.96 g, 20 mmol), $AgNO_3$ (338 mg, 2 mmol, 0.1 equiv), $(NH_4)_2S_2O_8$ (13.6 g, 60 mmol, 3 equiv), KOAc (5.88 g, 60 mmol, 3 equiv), CH_2Cl_2 (200 mL), and H_2O (200 mL). The reaction mixture was then stirred at room temperature for 24 h. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.4) as a white solid (3.5 g, 89% yield).

To a 25 mL flask were added the lactone **2a** (196.2 mg, 0.25 mmol) and $LiOH{\cdot}H_2O$ (1.0 g, 24 mmol, 24 equiv). To this mixture was then added MeOH (16 mL), THF (8 mL), and H_2O (4 mL). The reaction mixture was then stirred for 24 h at room temperature, and the course of the reaction was followed by TLC until completion. The MeOH and THF were then removed in vacuo, and the resulting residue was diluted with H_2O (15 mL), ice, and EtOAc (20 mL). After acidification with 2 M HCl (pH 4−5), the solution was extracted with EtOAc three times. The combined organic extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude was washed with EtOAc furnishing the final hydroxyacids **3** as a white solid (184 mg, 86% yield).

*2′-Hydroxy-[1,1′-biphenyl]-2-carboxylic Acid (**3**).*[2e] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, J = 7.9, 0.9 Hz, 1H), 8.14 (d, J = 8.1 Hz, 1H), 8.08 (dd, J = 7.9, 1.3 Hz, 1H), 7.89−7.78 (m, 1H), 7.66−7.56 (m, 1H), 7.55−7.44 (m, 1H), 7.41−7.32 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2, 151.3, 134.9, 134.8, 130.6, 130.5, 128.9, 124.6, 122.8, 121.7, 121.3, 118.1, 117.8.

A cooled solution of lactone **2a** (392.4 mg, 2 mmol) in a mixture of $BF_3{\cdot}Et_2O$ (5 mL) and THF (10 mL) was added over 15 min to a suspension of $NaBH_4$ (250 mg, 6.6 mmol) in THF (5 mL) under nitrogen while maintaining the reaction temperature below 10 °C. The reaction mixture was then raised within 30 min to the reflux temperature, kept under reflux for 1 h, and then cooled to −3 °C. Cold HCl aq. (2 N, 8 mL) was then cautiously added, and the temperature was allowed to increase to 25 °C. Water (40 mL) was added, and the reaction mixture was extracted with $CHCl_3$ (3 × 50 mL). The combined extracts were evaporated, and the oily residue was heated at 80 °C with 2 N NaOH aq. (80 mL) for 20 min. The resulting mixture was cooled and extracted with ether (4 × 30 mL). The ether extracts were combined, dried over Na_2SO_4, and concentrated in vacuo. The product was isolated by flash chromatography (PE/EA = 20:1, R_f = 0.6) as a colorless liquid (284 mg, 78% yield).

*6H-Benzo[c]chromene (**4**).*[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 7.7, 1.5 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.34 (dd, J = 11.1, 4.0 Hz, 1H), 7.30−7.18 (m, 2H), 7.11 (d, J = 7.5 Hz, 1H), 7.03 (td, J = 7.6, 1.2 Hz, 1H), 6.98 (dd, J = 8.1, 1.0 Hz, 1H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 131.4, 130.1, 129.4, 128.4, 127.6, 124.6, 123.3, 122.9, 122.1, 122.0, 117.4, 68.4.

Chemoselectivity Profile in C−H Functionalization/C−O Cyclization. To a 15 mL tube were sequentially added **5** (70.2 mg, 0.3 mmol), $AgNO_3$ (10.2 mg, 0.06 mmol, 0.2 equiv), $(NH_4)_2S_2O_8$ (205 mg, 0.9 mmol, 3 equiv), KOAc (88.3 mg, 0.9 mmol, 3 equiv), 3 mL of CH_2Cl_2, and 3 mL of H_2O. The reaction mixture was then stirred at room temperature for 3 h. The product was isolated by flash chromatography (PE/EA = 5:1, R_f = 0.5) as a white solid (43 mg, 72%).

*3-(2-Hydroxy-2-methylpropyl)-6H-benzo[c]chromen-6-one (**6**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J = 7.9 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.85−7.70 (m, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.26−7.18 (m, 2H), 2.86 (s, 2H), 1.28 (s, 11H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 151.0, 141.3, 134.9, 134.8, 130.6, 128.6, 127.0, 122.4, 121.5, 121.0, 119.3, 116.3, 70.9, 49.4, 29.4. HRMS (EI) calcd for $C_{17}H_{16}O_3[M^+]$ 268.1099, found 268.1095.

In a 15 mL sealed tube, 2.0 mL of hexafluorobenzene were added to a mixture of alcohol substrate **6** (53.6 mg, 0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (2.3 mg, 0.01 mmol, 0.05 equiv, 5 mol %), Li_2CO_3 (22.2 mg, 0.3 mmol, 1.5 equiv), and iodobenzene diacetate (96.6 mg, 0.3 mmol, 1.5 equiv) under air. The tube was sealed with a Teflon lined cap, and the reaction mixture was stirred at 100 °C for 48 h. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (15 mL), filtered through Celite, washed with diethyl ether (10 mL × 2), and concentrated under vacuum carefully, and the residue was purified by flash chromatography (PE/EA = 50:1, R_f = 0.6), giving the corresponding product **7** as a white solid (34 mg, 64%).

*9,9-Dimethyl-8,9-dihydro-5H-benzo[c]furo[2,3-g]chromen-5-one (**7**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (dd, J = 7.9, 0.9 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.83−7.71 (m, 1H), 7.62−7.48 (m, 1H), 7.29 (s, 1H), 7.15 (s, 1H), 3.10 (s, 2H), 1.52 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6, 156.0, 145.8, 135.1, 134.7, 131.3, 130.5, 128.5, 121.6, 120.7, 117.4, 114.6, 101.5, 87.8, 43.0, 28.1. HRMS (EI) calcd for $C_{17}H_{14}O_3[M^+]$ 266.0943, found 266.0945.

Intermolecular Kinetic Isotope Effect (KIE). A 15 mL tube equipped with a magnetic stirrer was charged with **1a** (0.15 mmol), [**D5**]**1a** (0.15 mmol), $AgNO_3$ (20 mol %), KOAc (3 equiv), $(NH_4)_2S_2O_8$ (3 equiv), and CH_2Cl_2 (3 mL), H_2O (3 mL). The mixture was stirred at room temperature for 30 min. The reaction mixture was purified by flash chromatography to give the desired

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product. This KIE value was determined by ^{1}H NMR analysis (KIE ≈ 1.27).

■ ASSOCIATED CONTENT

Supporting Information

The supplementary crystallographic data and (CIF File) for the compound has been provided in the Supporting Information. CCDC 1038197 contains supplementary crystallographic data for the structure **2j**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Optimization data, ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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