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Rh(III)-catalyzed aldehyde C–H bond functionalization of salicylaldehydes with arylboronic acids

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ABSTRACT

A Rh(III)-catalyzed aldehyde C–H bond functionalization of salicylaldehydes with arylboronic acids has been developed, with features of mild reaction condition and high efficiency. Furthermore, the functionalized 2-hydroxybenzophenone could be subject to divergent synthesis of heterocycles.

1. Introduction

2-Hydroxybenzophenones are important building blocks in synthetic chemistry owing to their high reactivity, particular in the fields of medicinal chemistry. Due to its prevalence in biologically active products and synthetic molecules, great efforts have been devoted to the synthesis of molecules with the 2-hydroxybenzophenone skeleton, and representative examples are shown in Fig. 1. These molecules exhibiting a variety of biological activities, and acted as selective inhibitors of human immunodeficiency virus type 1 reverse transcriptase,[1] antispasmodic agents,[2] inhibitors of transforming growth factor-kinase.[3] Therefore, there are many methods reported toward construction of these molecules. The classical approach relies on Fries rearrangement of phenyl ester which is derived from phenol.[4] There also are transition-metal-catalyzed transformations for access to these compounds. For example, Chen reported a Pd-catalyzed cross coupling of salicylaldehyde and diaryliodonium salts for synthesis of 2-hydroxybenzophenones.[5] Meanwhile, Xu also developed a Pd-catalyzed oxidative coupling of salicylaldehyde with arylboronic acids.[6] Recently, Li reported a Rh-catalyzed rearrangement of 2-aryloxybenzaldehyde for transforming to 2-hydroxybenzophenones.[7] Interestingly, Rao and Dong independently reported the Pd-catalyzed ketone-directed hydroxylation of arenes for synthesis of 2-acylphenols.[8]

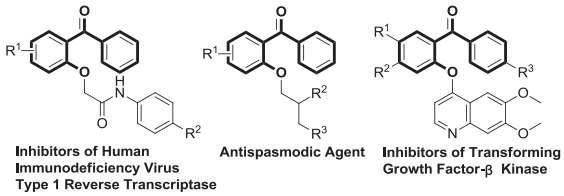

Fig. 1. Biologically active products containing 2-hydroxybenzophenone skeleton.

Recently, Rh(III)-catalyzed functionalization of aryl C–H bond has enjoyed tremendous advance owing to their wide applications to the rapid assembly of various complex molecular structures, particular in the fields of medicinal chemistry.[9] In particular, the Rh(III)-catalyzed C–H functionalization of aldehyde has been paid attention. For example, Miura explored the Rh(III)-catalyzed oxidative coupling between salicylaldehydes and internal alkynes, demonstrating the flexible reactivity of aldehyde in C–H functionalization.[10] Inspired by this, Glorius,[11] Radhakrishnan[12] and Li[13] reported that Rh(III)-catalyzed oxidative coupling of salicylaldehydes with electron deficient olefins, diazabicyclic olefins and TIPS-EBX, respectively. In continuation of our interest in Rh(III)-catalyzed C–H functionalization for biologically interesting small molecule synthesis,[14] herein we report a Rh(III)-catalyzed aldehyde C–H bond functionalization of salicylaldehydes with arylboronic acids. Moreover, the functionalized 2-hydroxybenzophenones

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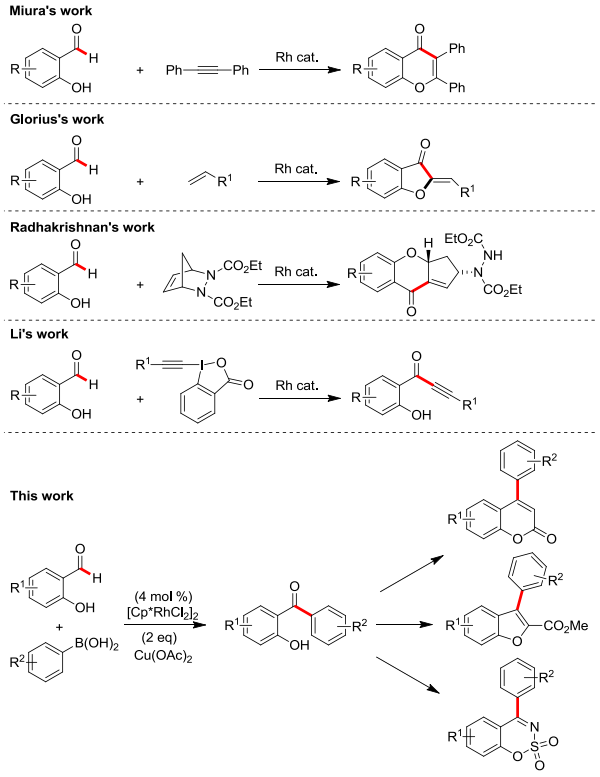
could be subject to various transformations to access divergent compounds (Scheme 1).



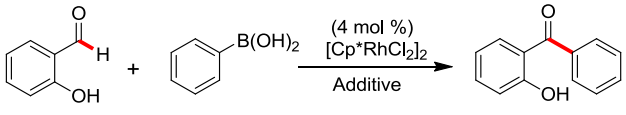
Scheme 1. Rh(III)-catalyzed aldehyde C–H functionalization of salicylaldehydes.

2. Results and discussions

We commenced our study by investigating the coupling of salicylaldehyde **1a** and phenylboronic acid **2a** using $[Cp^*RhCl_2]_2$ as catalyst. When the reaction was conducted in DMF at 80 °C without additives, the Rh(III) catalyzed C–H functionalized product was not observed (Table 1, entry 1). Gratifyingly, equivalent addition of $Cu(OAc)_2$ led to the formation of 2-hydroxybenzophenone **3a** in 98% yield (Table 1, entry 2). This encouraged us to screen the additives, and we found other additives, such as AgOAc, Ag_2O and $K_2S_2O_8$ were inferior (Table 1, entries 3–5). When the solvent was changed to CH_3CN, the reaction afforded trace product when $Cu(OAc)_2$ was used as additive (entry 6). Surprisingly, the combination of CH_3CN and Ag_2O gave the product in 85% yield (entry 7). Further survey of solvents revealed that MeOH, t-amyl alcohol, trifluoroethanol (TFE) and dioxane were not optimal to produce trace products (entries 8–11). Moreover, when the temperature was decreased to 40 °C, the reaction would give the product in a slightly lower yield (entry 12, 76%).

With the optimized reaction condition in hand, we next expanded the scope of this Rh(III)-catalyzed aldehyde functionalization using a variety of salicylaldehydes and arylboronic acids. As depicted in Table 2, various *para*-substituted arylboronic acids with valuable functional groups like bromo, chloro, methoxy, methyl, cyano, hydroxy, phenyl, could react smoothly with **1a** in this process to furnish the products (**3b**–**3h**) in excellent yields, thus offering ample opportunity for further derivatization. The

Table 1
Optimization of reaction conditions[a]

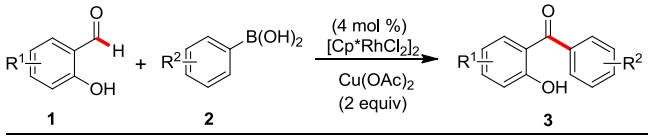


1a 2a 3a

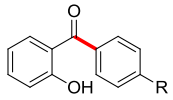
Entry	Additive	Solvent	T [°C]	Yield [%][b]
1	None	DMF	80	0
2	$Cu(OAc)_2$	DMF	80	98
3	AgOAc	DMF	80	Trace
4	Ag_2O	DMF	80	Trace
5	$K_2S_2O_8$	DMF	80	Trace
6	$Cu(OAc)_2$	CH_3CN	60	Trace
7	Ag_2O	CH_3CN	60	85
8	$Cu(OAc)_2$	MeOH	60	Trace
9	$Cu(OAc)_2$	*t*-Amyl alcohol	80	Trace
10	$Cu(OAc)_2$	TFE	60	Trace
11	$Cu(OAc)_2$	Dioxane	80	Trace
12	$Cu(OAc)_2$	DMF	40	76

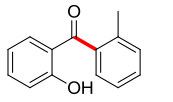
[a] Reaction conditions: 1a (0.2 mmol), 2a (0.4 mmol), $[Cp^*RhCl_2]_2$ (4 mol %), additives (2 equiv), solvent (2 mL).
[b] Yields of isolated products.

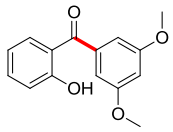
Table 2
Rh(III)-catalyzed aldehyde functionalization of salicylaldehydes[a]

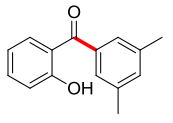


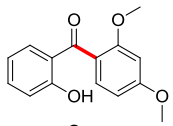
1 2 3

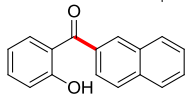

3a, R = H, 98%
3b, R = Br, 93%
3c, R = Cl, 98%
3d, R = OCH_3, 70%
3e, R = Me, 76%
3f, R=CN, 84%
3g, R=OH, 45%
3h, R=Ph, 43%

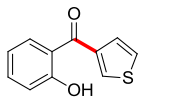

3i, 84%

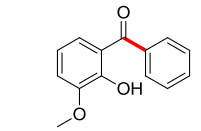

3j, 61%

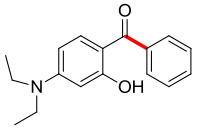

3k, 98%

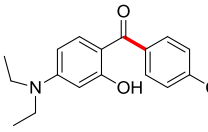

3l, 44%

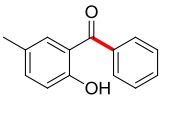

3m, 98%

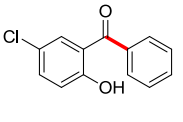

3n, 38%

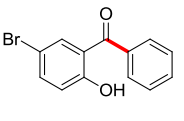

3o, 86%

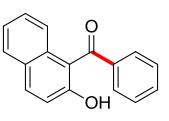

3p, 70%

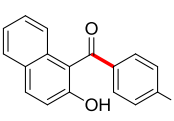

3q, 62%


3r, 98%


3s, 98%


3t, 91%

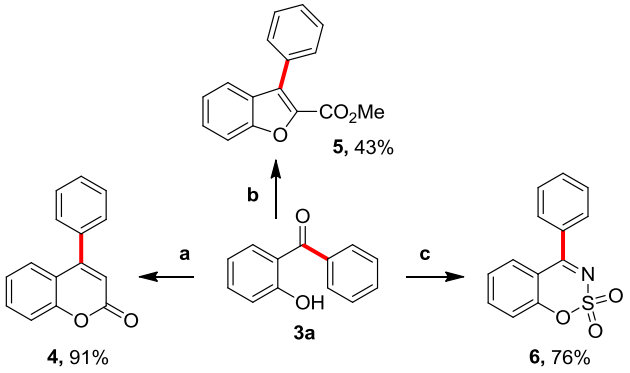

3u, 94%


3v, 81%

[a] Reaction Conditions: **1** (0.2 mmol), **2** (0.4 mmol), $[Cp^*RhCl_2]_2$ (4 mol %), $Cu(OAc)_2$ (2 equiv), DMF (2 mL), 80 °C, 8 h.

ortho-substituted and polysubstituted arylboronic acids were also applicable to furnish the product in moderate to excellent yields (**3i**–**3l**). Additionally, naphthalen-2-ylboronic acid and thiophen-3-ylboronic acid were amenable to afford the products in moderate to excellent yields (**3m**–**3n**). Next, various functionalized salicylaldehydes were employed and found suitable in this oxidative coupling to afford the structural differential 2-hydroxybenzophenones, with diethylamino, chloro and bromo substitution in the aromatic ring (**3o**–**3t**). Furthermore, 2-hydroxy-1-naphthaldehyde was also applicable to access the corresponding products in good yields (**3u**, **3v**).

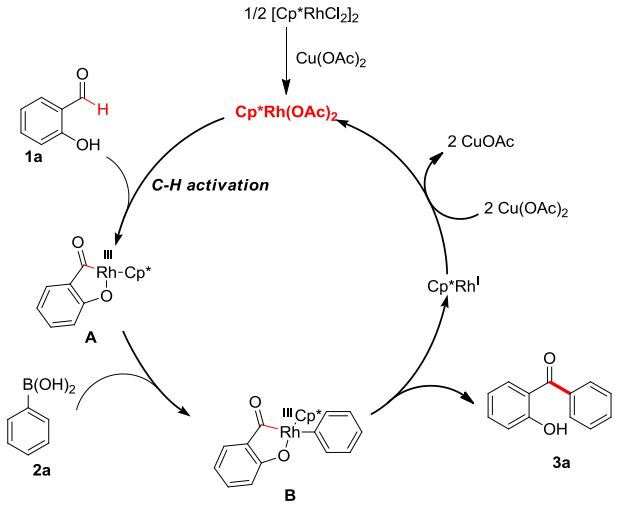
As mentioned before, 2-hydroxybenzophenones were versatile building block and could be subject to divergent transformations. The unique features were then studied using **3a** as model compound. As shown in Scheme 2, when **3a** was treated with ethyl-2-(triphenylphosphoranylidene)acetate in the presence of catalytic DMAP, the Wittig reaction occurred to form coumarin derivative **4**



Scheme 2. Divergent transformations of **3a**. Reaction conditions: (a) Ethyl-2-(triphenylphosphoranylidene)acetate (1.07 equiv), DMAP (5.4% mmol), toluene, reflux, Argon, 10 h; (b) (i) Methyl bromoacetate (1.2 equiv), K_2CO_3 (1.5 equiv), acetone, reflux, 2 h; (ii) sodium methanolate (3 equiv), MeOH, reflux, 10 h; (c) $ClSO_2NCO$ (1 equiv), toluene, reflux, 10 h.

in 91% yield. **3a** could also be transformed into a benzofuran derivative **5** in 43% yield, when treated with methyl bromoacetate, K_2CO_3 and sodium methanolate. Furthermore, 2-hydroxybenzophenones can be converted to 4-phenylbenzo[*e*][1,2,3]oxathiazine 2,2-dioxide **6** upon cyclization with $ClSO_2NCO$.

Based on the results and precedents, a plausible mechanism was depicted in Scheme 3. The initial rhodium diacetate was generated from $[Cp^*RhCl_2]_2$ and $Cu(OAc)_2$, and a carboxylate-assisted C–H activation of aldehyde occurred to form intermediate **A**. The transmetalation of **A** with arylboronic acid **2a** would lead to **B**, and reductive elimination furnished the C–C coupling product **3a** and a Rh(I) species. Reoxidation of Rh(I) to $Cp^*Rh(OAc)_2$ by $Cu(OAc)_2$ would enable the catalytic cycle to proceed. Indeed, when benzaldehyde was subjected to this reaction condition, the oxidative coupling was not observed while benzaldehyde was recovered, thus demonstrating this reaction triggered by the *ortho*-hydroxy directed C–H activation.



Scheme 3. Proposed mechanism.

3. Conclusions

In conclusion, we have developed a Rh(III)-catalyzed aldehyde C–H bond functionalization of salicylaldehydes with arylboronic acids under mild reaction condition. Furthermore, the functionalized 2-hydroxybenzophenones could take divergent transformations to access a variety of heterocycles.

4. Experimental section

4.1. General

All commercially available reagents were used without purification unless otherwise noted. Column chromatography was performed using silica gel (200–300 mesh). Visualization of the compounds was accomplished with UV light (254 nm) and iodine. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ operating at 400 MHz and 100 MHz, respectively. Proton chemical shifts are reported relative to the residual proton signals of the deuterated solvent $CDCl_3$ (7.26 ppm) or TMS. Carbon chemical shifts were internally referenced to the deuterated solvent signals in $CDCl_3$ (77.160 ppm). Chemical shifts are reported in δ (parts per million) values. Coupling constants *J* are reported in Hertz. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), and multiple (m). Mass spectra were measured with a low-resolution MS instrument using ESI ionization.

General procedure for the synthesis of compounds **3a**–**3v**. A mixture of salicylaldehyde (0.2 mmol) and arylboronic acid (0.4 mmol) was dissolved in DMF (2 mL) and $[Cp^*RhCl_2]_2$ (4.9 mg, 4 mol %) and $Cu(OAc)_2$ (72.8 mg, 0.4 mmol) was added. Then the reaction was conducted in a sealed tube at a temperature of 80 °C for 8 h. The reaction mixture was diluted with ethylacetate (20 mL), washed with H_2O (3×10 mL). The organic layer was then dried over anhydrous Na_2SO_4, filtered and concentrate. The crude product was loaded on a silica gel column and flashed with 5–10% ethyl acetate in petroleum ether to afford the desired products **3** as solid or liquid.

4.2. Compound (3a)

(2-Hydroxyphenyl)(phenyl)methanone **3a**. Pale yellow liquid (38.8 mg, 98%); ^1H NMR ($CDCl_3$, 400 MHz), δ: 12.05 (s, 1H), 7.69–7.67 (m, 2H), 7.62–7.58 (m, 2H), 7.53–7.49 (m, 3H), 7.08 (dd, J_1=8.4 Hz, J_2=1.2 Hz, 1H), 6.90–6.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 201.6, 163.3, 137.9, 136.4, 133.6, 132.0, 129.2, 128.4, 119.1, 118.7, 118.4; IR (KBr) v: 3061, 2340, 1626, 1479, 1323, 1238, 935, 819, 695, 641 cm^{-1}; ESI-MS *m*/*z* positive 199.3 $(M+H)^+$, negative *m*/*z* 197.3 $(M-H)^-$.

4.3. Compound (3b)

(4-Bromophenyl)(2-hydroxyphenyl)methanone **3b**. Yellow solid (51.5 mg, 93%); Mp 85–89 °C; ^1H NMR ($CDCl_3$, 400 MHz), δ: 11.89 (s, 1H), 7.66–7.63 (m, 2H), 7.57–7.50 (m, 4H), 7.07 (d, J=8.4 Hz, 1H), 6.90–6.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 200.4, 163.3, 136.72, 136.68, 133.3, 131.8, 130.9, 127.0, 119.0, 118.9, 118.7; IR (KBr)

v: 3480, 2340, 1944, 1804, 1603, 1494, 1214, 912, 811, 749 cm^{-1}; ESI-MS *m*/*z* positive 277.2/279.3 $(M+H)^+$, negative *m*/*z* 275.3/277.3 $(M-H)^-$.

4.4. Compound (3c)

(4-Chlorophenyl)(2-hydroxyphenyl)methanone **3c**. Yellow solid (45.6 mg, 98%); Mp 68–72 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 11.89 (s, 1H), 7.65–7.62 (m, 2H), 7.55–7.47 (m, 4H), 7.08 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.91–6.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 200.3, 163.3, 138.5, 136.7, 136.2, 133.3, 130.7, 128.8, 119.0, 118.9, 118.6; IR (KBr) *v*: 3403, 2937, 2332, 1952, 1843, 1618, 1486, 912, 765, 664 cm^{-1}; ESI-MS *m*/*z* positive 233.3/235.3 $(M+H)^+$, negative *m*/*z* 231.3/233.3 $(M-H)^-$.

4.5. Compound (3d)

(2-Hydroxyphenyl)(4-methoxyphenyl)methanone **3d**. Pale yellow liquid (31.9 mg, 70%); ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 11.98 (s, 1H), 7.73–7.70 (m, 2H), 7.63 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.51–7.47 (m, 1H), 7.06 (dd, J_1=8.0 Hz, J_2=0.8 Hz, 1H), 7.01–6.98 (m, 2H), 6.90–6.86 (m, 1H), 3.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 200.2, 163.02, 163.01, 135.9, 133.4, 132.0, 130.4, 119.5, 118.6, 118.4, 113.8, 55.6; IR (KBr) *v*: 2968, 2844, 2355, 1595, 1486, 1339, 1246, 1160, 935, 765, 602 cm^{-1}; ESI-MS *m*/*z* positive 229.4 $(M+H)^+$, negative *m*/*z* 227.4 $(M-H)^-$.

4.6. Compound (3e)

(2-Hydroxyphenyl)(*p*-tolyl)methanone **3e**. Pale yellow liquid (32.2 mg, 76%); ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 12.06 (s, 1H), 7.63–7.59 (m, 3H), 7.52–7.48 (m, 1H), 7.31 (d, *J*=8.0 Hz, 2H), 7.07 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.90–6.85 (m, 1H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 201.5, 163.2, 142.9, 136.2, 135.3, 133.7, 129.6, 129.1, 119.4, 118.7, 118.5, 21.7; IR (KBr) *v*: 3030, 2355, 1610, 1486, 1331, 1246, 935, 765, 609 cm^{-1}; ESI-MS *m*/*z* positive 213.3 $(M+H)^+$, negative *m*/*z* 211.3 $(M-H)^-$.

4.7. Compound (3f)

4-(2-Hydroxybenzoyl)benzonitrile **3f**. Yellow solid (37.5 mg, 84%); Mp 117–119 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 11.78 (s, 1H), 7.82–7.80 (m, 2H), 7.77–7.75 (m, 2H), 7.57–7.53 (m, 1H), 7.45 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.09 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.92–6.87 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 199.9, 163.5, 141.6, 137.3, 133.2, 132.3, 129.5, 119.2, 118.9, 118.6, 118.0, 115.4; IR (KBr) *v*: 3480, 2363, 2231, 1626, 1470, 1331, 1230, 920, 842, 772, 687 cm^{-1}; ESI-MS *m*/*z* negative *m*/*z* 222.3 $(M-H)^-$.

4.8. Compound (3g)

(2-Hydroxyphenyl)(4-hydroxyphenyl)methanone **3g**. Yellow solid (19.3 mg, 45%); Mp 144–147 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 11.98 (s, 1H), 7.68–7.62 (m, 3H), 7.52–7.48 (m, 1H), 7.07 (d, *J*=8.0 Hz, 1H), 6.94–6.88 (m, 3H), 6.06 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 200.3, 163.0, 159.7, 136.1, 133.5, 132.3, 130.5, 119.5, 118.8, 118.5, 115.4; IR (KBr) *v*: 3434, 2363, 1579, 1494, 1432, 1323, 1207, 912, 765, 609 cm^{-1}; ESI-MS *m*/*z* positive 215.4 $(M+H)^+$, negative *m*/*z* 213.3 $(M-H)^-$.

4.9. Compound (3h)

[1,1′-Biphenyl]-4-yl(2-hydroxyphenyl)methanone **3h**. Yellow solid (23.6 mg, 43%); Mp 87–90 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 12.07 (s, 1H), 7.76 (m, 4H), 7.70–7.66 (m, 3H), 7.56–7.49 (m, 3H), 7.45–7.41 (m, 1H), 7.11 (d, *J*=8.0 Hz, 1H), 6.94–6.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 201.3, 163.3, 145.0, 140.0, 136.7, 136.5, 133.6, 130.0, 129.1, 128.4, 127.4, 127.2, 119.4, 118.8, 118.6; IR (KBr) *v*: 3418, 2332, 1967, 1610, 1432, 1308, 935, 734, 648 cm^{-1}; ESI-MS *m*/*z* positive 275.4 $(M+H)^+$, negative *m*/*z* 273.4 $(M-H)^-$.

4.10. Compound (3i)

(2-Hydroxyphenyl)(*o*-tolyl)methanone **3i**. Yellow solid (35.6 mg, 84%); Mp 62–67 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 12.26 (s, 1H), 7.52–7.47 (m, 1H), 7.42–7.38 (m, 1H), 7.31–7.25 (m, 4H), 7.06 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.83–6.79 (m, 1H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 204.6, 163.4, 138.0, 136.9, 135.6, 133.8, 131.0, 130.3, 127.6, 125.5, 120.0, 119.0, 118.4, 19.7; IR (KBr) *v*: 3387, 2945, 2340, 1998, 1828, 1564, 928, 780, 687 cm^{-1}; ESI-MS *m*/*z* positive 213.3 $(M+H)^+$, negative *m*/*z* 211.4 $(M-H)^-$.

4.11. Compound (3j)

(3,5-Dimethoxyphenyl)(2-hydroxyphenyl)methanone **3j**. Yellow solid (31.5 mg, 61%); Mp 62–65 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 11.97 (s, 1H), 7.64 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.52–7.48 (m, 1H), 7.06 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.89–6.85 (m, 1H), 6.78 (d, *J*=2.4 Hz, 2H), 6.66 (t, *J*=2.4 Hz, 1H), 3.83 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 201.5, 163.3, 160.7, 139.8, 136.6, 133.7, 119.2, 118.8, 118.5, 107.1, 104.1, 55.7; IR (KBr) *v*: 3464, 2968, 2836, 1603, 1455, 1362, 1168, 1044, 912, 734, 656 cm^{-1}; ESI-MS *m*/*z* positive 259.3 $(M+H)^+$, negative *m*/*z* 257.3 $(M-H)^-$.

4.12. Compound (3k)

(3,5-Dimethylphenyl)(2-hydroxyphenyl)methanone **3k**. Pale yellow liquid (44.3 mg, 98%); ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 12.10 (s, 1H), 7.61 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.52–7.48 (m, 1H), 7.27 (s, 2H), 7.22 (s, 1H), 7.07 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.90–6.86 (m, 1H), 2.39 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 202.2, 163.3, 138.2, 138.1, 136.3, 133.8, 133.7, 126.9, 119.4, 118.7, 118.4, 21.4; IR (KBr) *v*: 3046, 2914, 1618, 1486, 1339, 1214, 1153, 858, 788, 710 cm^{-1}; ESI-MS *m*/*z* positive 227.3 $(M+H)^+$, negative *m*/*z* 225.3 $(M-H)^-$.

4.13. Compound (3l)

(2,4-Dimethoxyphenyl)(2-hydroxyphenyl)methanone **3l**. Pale yellow liquid (22.7 mg, 44%); ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 12.23 (s, 1H), 7.47–7.39 (m, 2H), 7.28 (d, *J*=8.4 Hz, 1H), 7.01 (dd, J_1=8.0 Hz, J_2=0.8 Hz, 1H), 6.82–6.78 (m, 1H), 6.58–6.54 (m, 2H), 3.87 (s, 3H), 3.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz), *δ*: 201.4, 163.3, 163.0, 158.7, 136.2, 133.9, 131.1, 120.8, 120.6, 118.6, 118.1, 104.7, 99.0, 55.8, 55.7; IR (KBr) *v*: 2937, 2844, 2363, 1610, 1463, 1214, 1145, 1021, 935, 757, 609 cm^{-1}; ESI-MS *m*/*z* positive 259.3 $(M+H)^+$, negative *m*/*z* 257.2 $(M-H)^-$.

4.14. Compound (3m)

(2-Hydroxyphenyl)(naphthalen-2-yl)methanone **3m**. Yellow solid (48.6 mg, 98%); Mp 77–81 °C; ^1H NMR ($CDCl_3$, 400 MHz), *δ*: 12.09 (s, 1H), 8.18 (s, 1H), 7.98–7.92 (m, 3H), 7.79 (dd, J_1=8.4 Hz, J_2=1.6 Hz, 1H), 7.68 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.65–7.52 (m, 3H), 7.13 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.92–6.88 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), *δ*: 201.6, 163.3, 136.4, 135.2, 134.9, 133.8, 132.3, 130.6, 129.3, 128.5, 128.3, 128.0, 127.1, 125.4, 119.4, 118.8, 118.5; IR (KBr) *v*: 3472, 2355, 1633, 1595, 1486, 1308, 1191, 795, 718 cm^{-1}; ESI-MS *m*/*z* positive 249.4 $(M+H)^+$, negative *m*/*z* 247.4 $(M-H)^-$.

4.15. Compound (3n)

(2-Hydroxyphenyl)(thiophen-3-yl)methanone **3n**. Pale yellow liquid (15.5 mg, 38%); ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 11.62 (s, 1H), 7.96 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 7.75 (d, J_1=4.4 Hz, 2H), 7.54–7.50 (m, 1H), 7.20 (t, J_1=4.4 Hz, 1H), 7.07 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 6.98–6.93 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 191.3, 162.7, 142.4, 136.1, 134.7, 134.1, 132.0, 128.1, 119.6, 119.1, 118.6; IR (KBr) ν: 2967, 2929, 2355, 1579, 1409, 1246, 757, 648 cm^{-1}; ESI-MS m/z positive 205.3 $(M+H)^+$, negative m/z 203.3 $(M-H)^-$.

4.16. Compound (3o)

2-Hydroxy-3-methoxyphenyl)(phenyl)methanone **3o**. Yellow liquid (39.2 mg, 86%); ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 12.24 (s, 1H), 7.69–7.66 (m, 2H), 7.60–7.56 (m, 1H), 7.50–7.46 (m, 2H), 7.18 (dd, J_1=8.0 Hz, J_2=1.2 Hz, 1H), 7.09 (d, J=7.6 Hz, 1H), 6.81 (t, J=8.0 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 201.9, 153.5, 149.1, 138.1, 132.1, 129.3, 128.4, 124.9, 119.4, 118.1, 117.1, 56.4; IR (KBr) ν: 2929, 2363, 1595, 1447, 1347, 1254, 982, 741, 695 cm^{-1}; ESI-MS m/z positive 228.9 $(M+H)^+$, negative m/z 226.8 $(M-H)^-$.

4.17. Compound (3p)

(4-(Diethylamino)-2-hydroxyphenyl)(phenyl)methanone **3p**. Yellow gel (37.7 mg, 70%); ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 12.99 (s, 1H), 7.62–7.60 (m, 2H), 7.53–7.44 (m, 3H), 7.37 (d, J=9.2 Hz, 1H), 6.17–6.13 (m, 2H), 3.41 (q, J=7.2 Hz, 4H), 1.21 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 198.1, 166.4, 154.0, 139.1, 135.7, 130.8, 128.8, 128.2, 109.1, 103.7, 97.4, 44.8, 12.8; IR (KBr) ν: 2967, 2921, 1618, 1525, 1339, 1230, 1129, 795, 694 cm^{-1}; ESI-MS m/z positive 270.4 $(M+H)^+$, negative m/z 268.4 $(M-H)^-$.

4.18. Compound (3q)

(4-Chlorophenyl)(4-(diethylamino)-2-hydroxyphenyl) methanone **3q**. Yellow solid (37.6 mg, 62%); Mp 104–108 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 12.86 (s, 1H), 7.56–7.54 (m, 2H), 7.44–7.42 (m, 2H), 7.31 (d, J=9.6 Hz, 1H), 6.15–6.13 (m, 2H), 3.43 (q, J=6.8 Hz, 4H), 1.20 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 196.5, 166.4, 154.1, 137.4, 137.0, 135.3, 130.2, 128.5, 108.9, 103.8, 97.4, 44.8, 12.7; IR (KBr) ν: 3472, 2960, 2929, 2347, 2347, 1610, 1432, 1067, 835, 672 cm^{-1}; ESI-MS m/z positive 304.4/306.4 $(M+H)^+$, negative m/z 302.4/304.4 $(M-H)^-$.

4.19. Compound (3r)

(2-Hydroxy-5-methylphenyl)(phenyl)methanone **3r**. Yellow solid (41.6 mg, 98%); Mp 78–80 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 11.88 (s, 1H), 7.69–7.66 (m, 2H), 7.62–7.58 (m, 1H), 7.53–7.49 (m, 2H), 7.37–7.31 (m, 2H), 6.99 (d, J=8.4 Hz, 1H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 201.7, 161.3, 138.2, 137.5, 133.3, 131.9, 129.2, 128.5, 127.9, 118.9, 118.3, 20.6; IR (KBr) ν: 3449, 2363, 1626, 1595, 1479, 1331, 1223, 951, 749, 710 cm^{-1}; ESI-MS m/z positive 213.3 $(M+H)^+$, negative m/z 211.4 $(M-H)^-$.

4.20. Compound (3s)

(5-Chloro-2-hydroxyphenyl)(phenyl)methanone **3s**. Yellow solid (45.6 mg, 98%); Mp 89–92 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 11.92 (s, 1H), 7.69–7.66 (m, 2H), 7.65–7.60 (m, 1H), 7.56–7.51 (m, 3H), 7.45 (dd, J_1=8.8 Hz, J_2=2.8 Hz, 1H), 7.04 (d, J=8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 200.7, 161.8, 137.3, 136.3, 132.5, 129.3, 128.7, 123.5, 120.2, 119.9; IR (KBr) ν: 3434, 3085, 2378, 1905, 1820, 1572, 1470, 1339, 928, 827, 741 cm^{-1}; ESI-MS m/z positive 233.4 $(M+H)^+$, negative m/z 231.3/233.3 $(M-H)^-$.

4.21. Compound (3t)

(5-Bromo-2-hydroxyphenyl)(phenyl)methanone **3t**. Yellow solid (50.4 mg, 91%); Mp 105–107 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 11.93 (s, 1H), 7.70–7.66 (m, 3H), 7.64–7.57 (m, 2H), 7.55–7.52 (m, 2H), 6.99 (d, J=9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 200.6, 162.2, 139.1, 137.3, 135.5, 132.5, 129.3, 128.7, 120.6, 120.5, 110.4; IR (KBr) ν: 3449, 2922, 2355, 1595, 1479, 1331, 935, 780, 664 cm^{-1}; ESI-MS negative m/z 275.3/277.3 $(M-H)^-$.

4.22. Compound (3u)

(2-Hydroxynaphthalen-1-yl)(phenyl)methanone **3u**. Yellow solid (46.6 mg, 94%); Mp 136–139 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 11.20 (s, 1H), 7.91 (d, J=8.8 Hz, 1H), 7.73 (d, J=8.0 Hz, 1H), 7.63–7.61 (m, 2H), 7.56–7.52 (m, 1H), 7.38 (t, J=8.0 Hz, 2H), 7.30–7.22 (m, 3H), 7.16–7.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 200.5, 161.4, 140.4, 136.4, 132.8, 132.5, 129.5, 128.7, 128.5, 126.8, 126.4, 123.8, 119.3, 114.5; IR (KBr) ν: 3387, 2347, 1642, 1564, 1424, 1238, 966, 819, 702 cm^{-1}; ESI-MS m/z positive 249.4 $(M+H)^+$, negative m/z 247.4 $(M-H)^-$.

4.23. Compound (3v)

(4-Bromophenyl)(2-hydroxynaphthalen-1-yl)methanone **3v**. Yellow solid (53.0 mg, 81%); Mp 151–155 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 11.08 (s, 1H), 7.92 (d, J=8.8 Hz, 1H), 7.75–7.73 (m, 1H), 7.53–7.47 (m, 4H), 7.29–7.26 (m, 2H), 7.24–7.17 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 199.1, 161.5, 139.0, 136.6, 132.2, 132.0, 131.1, 128.8, 128.5, 127.9, 127.1, 126.2, 124.0, 119.3, 114.2; IR (KBr) ν: 3364, 1642, 1579, 1517, 1424, 1277, 1075, 904, 811, 749, 609 cm^{-1}; ESI-MS m/z positive 327.4/329.4 $(M+H)^+$, negative m/z 325.4/327.3 $(M-H)^-$.

Procedure for the synthesis of compounds **4**. A mixture of **3a** (20 mg, 0.1 mmol) was dissolved in toluene (2 mL), ethyl-2-(triphenylphosphoranylidene)acetate (37 mg, 0.107 mmol) DMAP (0.7 mg, 5.4% mmol) was added. Then the reaction mixture was heated at reflux under Argon for 10 h. The resulting reaction mixture was loaded on a silica gel column and flashed with 10% ethyl acetate in petroleum ether to afford the desired products **4** as solid.

4.24. Compound (4)

4-Phenyl-2*H*-chromen-2-one **4**. Pale yellow solid (20.2 mg, 91%); Mp 83–86 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.58–7.40 (m, 8H), 7.25–7.21 (m, 1H), 6.38 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz), δ: 160.9, 155.8, 154.3, 135.3, 132.1, 129.8, 129.0, 128.6, 127.1, 124.3, 119.1, 117.5, 115.3; IR (KBr) ν: 3069, 2914, 2852, 1735, 1603, 1432, 1261, 1036, 935, 873, 749 cm^{-1}; ESI-MS m/z positive 222.9 $(M+H)^+$.

Procedure for the synthesis of compounds **5**. A mixture of **3a** (100 mg, 0.5 mmol) was dissolved in acetone (10 mL), K_2CO_3 (104 mg, 0.75 mmol) and methyl bromoacetate (91.8 mg, 56.7 μL, 0.6 mmol) was then added. The reaction mixture was heated under reflux for 2 h. The reaction mixture was then diluted with ethylacetate (20 ml), washed with H_2O (3×10 mL). The organic layer was then dried over anhydrous Na_2SO_4, filtered and concentrated to afford the crude product.

The crude product was dissolved in MeOH (5 mL), sodium methanolate (81 mg, 1.5 mmol) was added. Then the reaction mixture was stirred for 10 h at 60 °C. The reaction mixture was diluted with ethylacetate (20 ml), washed with H_2O (3×10 mL). The organic layer was then dried over anhydrous Na_2SO_4, filtered and concentrate. The crude product was loaded on a silica gel column and flashed with 10% ethyl acetate in petroleum ether to afford the desired products **5** as solid.

4.25. Compound (5)

Methyl 3-phenylbenzofuran-2-carboxylate **5**. White solid (54.2 mg, 43%); Mp 88–92 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.65–7.58 (m, 4H), 7.53–7.44 (m, 4H), 7.34–7.30 (m, 1H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 160.3, 154.6, 139.8, 130.5, 130.0, 129.7, 128.6, 128.31, 128.29, 128.2, 123.9, 122.2, 112.4, 52.2; IR (KBr) ν: 3434, 2922, 2852, 2347, 1719, 1572, 1277, 1137, 990, 749, 702 cm^{-1}; ESI-MS m/z positive 253.4 $(M+H)^+$.

Procedure for the synthesis of compounds **6**. A mixture of **3a** (100 mg, 0.5 mmol) was dissolved in toluene (10 mL), $ClSO_2NCO$ (70.8 mg, 43.4 μL, 0.5 mmol) was added. Then the reaction mixture was heated at reflux for 10 h. The reaction mixture was washed with H_2O (10 mL). The organic layer was then dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was loaded on a silica gel column and flashed with 20% ethyl acetate in petroleum ether to afford the desired products **6** as solid.

4.26. Compound (6)

4-Phenylbenzo[*e*][*1,2,3*]oxathiazine 2,2-dioxide **6**. White solid (98.4 mg, 76%); Mp 105–110 °C; ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.78–7.74 (m, 3H), 7.69–7.64 (m, 2H), 7.56 (t, J=7.6 Hz, 2H), 7.41–7.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 176.5, 154.6, 137.1, 133.6, 133.3, 131.9, 130.6, 128.9, 125.9, 119.4, 116.5; IR (KBr) ν: 3441, 2340, 1991, 1595, 1517, 1393, 1184, 935, 819, 734 cm^{-1}; ESI-MS m/z positive 260.4 $(M+H)^+$, negative m/z 258.4 $(M-H)^-$.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.09.053.

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