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A One-pot Approach to 2,3-Diarylbenzo[*b*]furans through *N*-Heterocyclic Carbene Catalyzed 1,6-Conjugate Addition Followed by Acid Mediated Dehydrative Annulation

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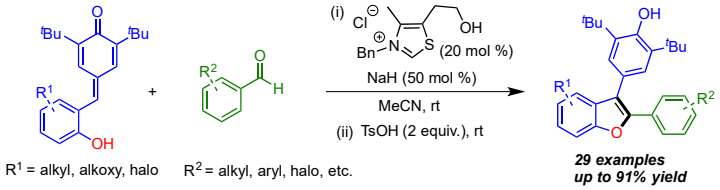


ABSTRACT: A one-pot protocol for the synthesis of 2,3-diarylbenzo[*b*]furan derivatives through an *N*-heterocyclic carbene (NHC) catalyzed 1,6-conjugate addition of aromatic aldehydes to 2-hydroxyphenyl-substituted *para*-quinone methides followed by acid-mediated dehydrative annulation has been developed. This protocol allowed us to access a wide range of 2,3-diarylbenzo[*b*]furan derivatives in moderate to good yields.

The 2,3-diarylbenzo[*b*]furan scaffold is widely found in many natural products[1] (Fig. 1) and several of them, including a few unnatural molecules,[2] display a variety of pharmacological activities. Apart from therapeutic applications, some of the 2,3-diarylbenzo[*b*]furan derivatives have found remarkable applications in the area of materials chemistry as electroluminescence molecules.[3]

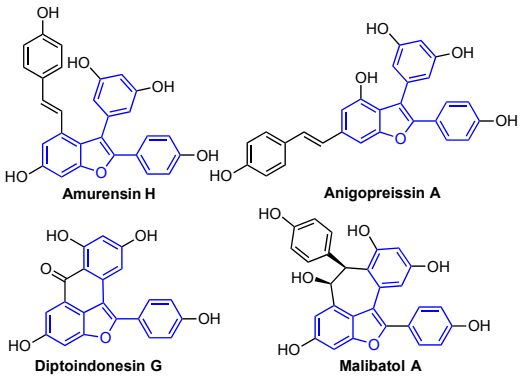
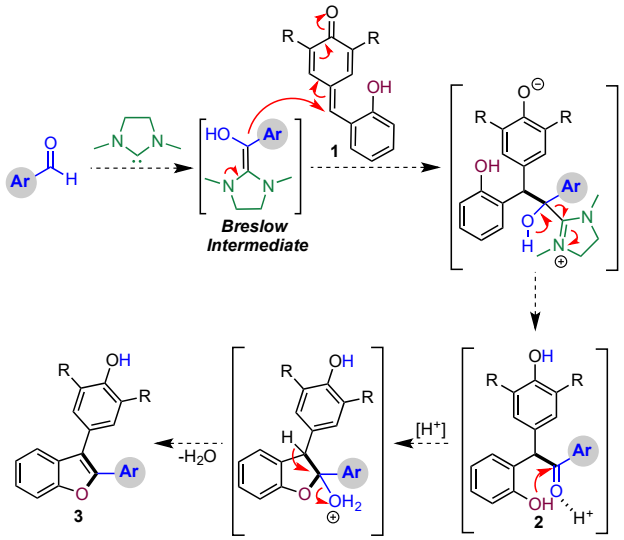


Figure 1. Biologically active 2,3-diarylbenzo[*b*]furan based natural products

Due to their diverse range of applications, numerous synthetic approaches to construct the 2,3-diarylbenzo[*b*]furan core have been developed.[4] Among those methods, the metal-catalyzed cyclization of 2-alkynyl phenols followed by coupling with suitable aryl coupling partners is widely explored for the synthesis of 2,3-diarylbenzo[*b*]furan derivatives.[5] A few other protocols based on metal-catalyzed direct C-3 arylation of 2-arylbenzo[*b*]furan derivatives with aryl halides have been reported.[6] In addition, other metal-catalyzed approaches such as, dehydrative C-H alkenylation and cyclization of phenols,[7] dehydrative cyclization of aryloxyketones followed by arylation,[8] oxidative annulation of phenols or their derivatives with internal alkynes,[9] Heck oxyarylation of *o*-hydroxystyrenes,[10] one-pot decarbonylative diarylation of coumarins,[11] and intramolecular aryl-etherification of alkoxy alkynes[12] have also been developed to access 2,3-diarylbenzo[*b*]furans. Very recently, Rh-catalyzed carboacylation/aromatization of benzo-cyclobutenones was also demonstrated.[13]

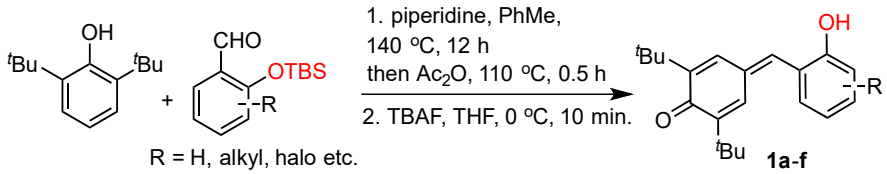
Apart from the metal-catalyzed reactions, a few metal-free approaches have also been established for the synthesis of 2,3-diarylbenzo[*b*]furans.[14] Although all the above-mentioned approaches are elegant, most of them involve either the use of expensive metal catalysts or harsh reaction conditions, which make those processes practically less attractive. Therefore, developing a practical method, especially, under organocatalytic conditions would be highly desirable.

Recently, our group developed a bis(amino)-cyclopropenylidene (BAC) catalyzed 1,6-conjugate addition of aromatic aldehydes to *p*-quinone methides (*p*-QMs) to access α,α'-diaryl acetophenone derivatives.[15a] Later, Zhang, Jiang and co-workers reported the same methodology, where NHC was as a catalyst.[15b] While working in this particular transformation, we envisioned that if a hydroxyl group is introduced at the 2-position of the aryl group of *p*-QM **1**, then it is possible to elaborate the 1,6-adduct **2** to the corresponding 2,3-diarylbenzo[*b*]furan derivative **3** in a one-pot manner through acid mediated dehydrative annulation reaction (Scheme 1). Based on this concept, we have developed a one-pot approach to access 2,3-diarylbenzo[*b*]furan derivatives through *N*-heterocyclic carbene (NHC) catalyzed 1,6-conjugate addition of aromatic aldehydes to 2-hydroxyphenyl-substituted *p*-quinone methides followed by acid mediated dehydrative annulation reaction, and the results are exemplified herein. Although 2-hydroxyphenyl-substituted *p*-quinone methides[16] have already been utilized as electrophiles in few other synthetic transformations, to the best of our knowledge, these synthons have not been utilized in combination with NHC catalysis[17] for the synthesis of 2,3-diarylbenzo[*b*]furan derivatives so far. Thus, we have decided to explore this transformation in detail.



Scheme 1. Our hypothesis for the one-pot synthesis of 2,3-diarylbenzo[*b*]furans

The 2-hydroxyphenyl-substituted *p*-QMs (**1a-f**) used in this study were prepared according to the literature procedure (Scheme 2).[16a]



Scheme 2. Synthesis of 2-hydroxyphenyl-substituted *p*-QMs (**1a-f**)

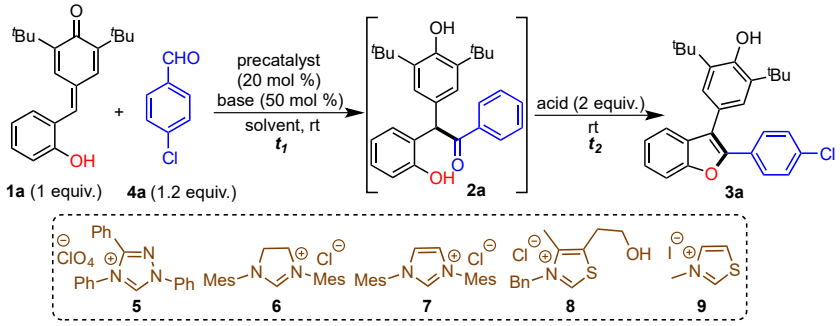
The optimization studies were carried out with **1a** and 4-chloro benzaldehyde (**4a**) in the presence of a wide range of carbene precursors (**5-9**) under different conditions, and the results are summarized in Table 1. Our initial attempts were highly disappointing, by using carbene precursors **5-7** and K_2CO_3 as a base in THF, as even the formation of intermediate **2a** did not take place under these reaction conditions (entries 1-3). However, delightfully, in the presence of thiazolium based carbene precursor **8** and 50 mol% K_2CO_3, complete conversion of **1a** to **2a** was observed within 12 h, and the expected diarylbenzo[*b*]furan **3a** was obtained in 50% yield in 12 h, after treating the reaction mixture with 2 equivalents of TsOH at rt (entry 4).

When the reaction was carried out with another thiazolium precatalyst **9**, the product **3a** was obtained only in 10% yield (entry 5). Unfortunately, when Cs_2CO_3 was used as a base, the 1,6-addition reaction did not take place even after 24 h (entry 6). However, the reaction worked well when KO^{t}Bu was used as a base, and **3a** was obtained in 72% yield in that case (entry 7). Interestingly, when NaH was used as a base and **8** was used as a precatalyst in THF, the diarylbenzo[*b*]furan **3a** was obtained in 78% isolated yield.

Encouraged by this result, the optimization studies were elaborated with other solvents such as, CH_2Cl_2 and acetonitrile (entries 9 & 10). Although both the solvents were found to be

very effective to drive this transformation with a considerable reduction in the reaction times, acetonitrile was found to be a bit superior than CH_2Cl_2 in driving the TsOH mediated annulation step and, as a result, the product **3a** was obtained in 91% yield in that case (entry 10). Other acids such as, camphorsulfonic acid (CSA), methanesulfonic acid and trifluoroacetic acid (TFA) were found to be less effective or ineffective for the annulation step (entries 11-13).

Table 1. Catalyst screen and optimization[a]



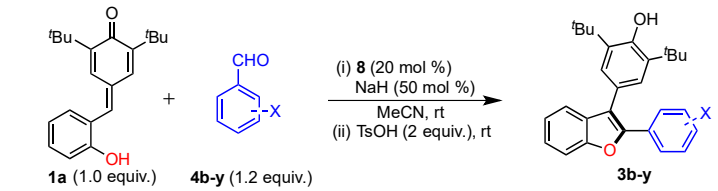
entry	precatalyst	base	acid	solvent	time (t_1+t_2) [h]	Yield of **3a** [%]
1	**5**	K_2CO_3	-	THF	24+0	nr
2	**6**	K_2CO_3	-	THF	24+0	nr
3	**7**	K_2CO_3	-	THF	24+0	nr
4	**8**	K_2CO_3	TsOH	THF	12+12	50
5	**9**	K_2CO_3	TsOH	THF	12+12	10
6	**8**	Cs_2CO_3	TsOH	THF	24+0	nr
7	**8**	KO^{t}Bu	TsOH	THF	12+12	72
8	**8**	NaH	TsOH	THF	12+12	78
9	**8**	NaH	TsOH	CH_2Cl_2	4+2	85
10	**8**	**NaH**	TsOH	**MeCN**	**4+1**	**91**
11	**8**	NaH	CSA	MeCN	4+6	80
12	**8**	NaH	MsOH	MeCN	4+20	60
13	**8**	NaH	TFA	MeCN	4+20	nr
14[b]	**8**	NaH	TsOH	MeCN	24+1	65
15[c]	**8**	NaH	TsOH	MeCN	4+10	60
16[d]	**8**	NaH	TsOH	MeCN	6+1	86

[a] All reactions were carried out with 30 mg of **1a** in 1.5 mL of solvent. [b] 20 mol% of sodium hydride was used. [c] 1 equiv. of TsOH was used. [d] Reaction was carried out with 3.22 mmol (1.0 g) of **1a** and 3.87 mmol of **4a**. nr = No reaction. Yields reported are isolated yields.

When the amount of NaH was reduced to 20 mol%, the 1,6-conjugate addition step was found to be very slow and, in fact, the reaction was not complete even after 24 h; so **3a** was obtained only in 65% yield (entry 14). Similarly, when one equivalent of TsOH was used instead of two equivalents, the annulation reaction was not complete even after 10 h, and the yield of **3a** was considerably reduced to 60% (entry 15). To show the practical applicability of this one-pot transformation, an experiment was carried out in gram scale, in which 1.0 g (3.22 mmol) of **1a** was treated with **4a** (3.87 mmol) under the best conditions (entry 10), and in this case, **3a** was obtained in 1.20 g (86% yield) [entry 16].

With the optimized conditions (entry 10, Table 1) in hand, the scope and limitation of this transformation were examined (Table 2). This one-pot protocol worked well with electron-poor aromatic aldehydes (**4b**-**e**), and in those cases, the respective 2,3-diarylbenzo[*b*]furans **3b**-**e** were obtained in moderate to good yields (66-75%). This protocol was found to be very effective in the cases of benzaldehyde (**4f**) and methoxy- or trifluoromethoxy benzaldehydes (**4g** & **4h**) as the desired products (**3f-h**) were obtained in very good yields (75-84%). However, surprisingly in the cases of alkyl substituted aldehydes (**4i-k**), the reaction was found to be very sluggish, and the respective products **3i-k** were isolated in poor yields (23-28%); because in those cases, the 1,6-conjugate addition step was found to be very slow, and also the complete conversion of **1a** to the respective 1,6-adducts were not realized even after stirring the reaction mixture for a prolonged period (24 h). The halo-substituted aromatic aldehydes (**4l-t**) reacted efficiently with **1a** to afford the desired annulated products **3l-t** in moderate to good yields (35-85%). Sterically hindered aldehydes such as, biphenyl-4-carboxaldehyde (**4u**) and 1-naphthaldehyde (**4v**) also underwent smooth conversion to the desired 2,3-diarylbenzo[*b*]furans (**3u-v**) in 72% and 69% yields, respectively. Under the standard conditions, heteroaromatic aldehydes (**4w-y**) provided the corresponding 2,3-diarylbenzo[*b*]furans **3w-y** in good yields (72-75%).

Table 2. Substrate scope with different aromatic aldehydes[a]



1a (1.0 equiv.) **4b-y** (1.2 equiv.) **3b-y**

3b, X = 4-CN, (4+1) h, 70%
3c, X = 3-NO_2, (5+1) h, 75%
3d, X = 4-CF_3, (6+1) h, 72%
3e, X = 3-CF_3, (6+1) h, 66%

3f, X = H, (5+1) h, 78%
3g, X = 3,5-dimethoxy, (7+1) h, 75%
3h, X = 4-OCF_3, (5+1) h, 84%

3i, X = ^{t}Bu, (11+1) h, 28%
3j, X = Et, (11+1) h, 23%
3k, X = Me, (11+1) h, 25%

3l, X = 4-Br, (7+1.5) h, 81%[b]
3m, X = 2-Cl, (4+1) h, 81%
3n, X = 2-Br, (4+1) h, 82%
3o, X = 2-F, (4+1) h, 85%

3p, X = 2,4-dichloro, (4+1) h, 70%
3q, X = 2,4-difluoro, (4+1) h, 78%

3r, X = 5-F, (4+1) h, 58%
3s, X = 5-OMe, (7+1) h, 51%
3t, X = 4-Me, (11+1) h, 35%

3u, (7+1) h, 72%

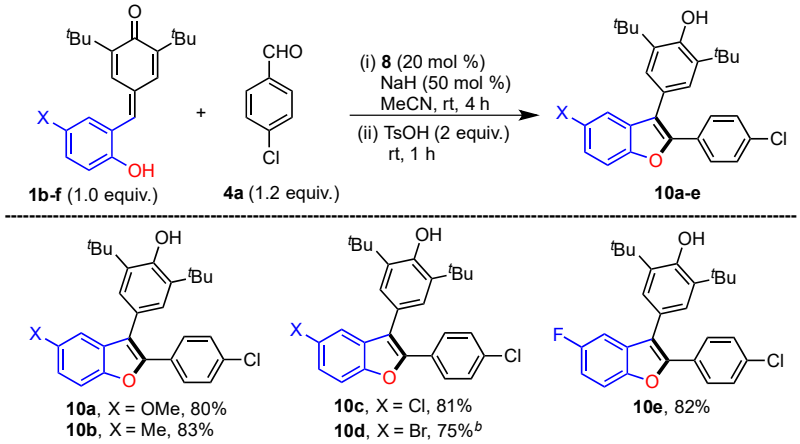
3v, (7+1) h, 69%

3w, X = S, R^1 = H, (9+1) h, 72%
3x, X = S, R^1 = Br, (9+1) h, 75%
3y, X = O, R^1 = H, (9+1) h, 75%

[a]All reactions were carried out in 30 mg (0.097 mmol) scale of **1a** in 1.5 mL of MeCN. [b] Reaction was carried out with 2.0 g (6.45 mmol) of **1a** in 30 mL of MeCN. Yields reported are isolated yields.

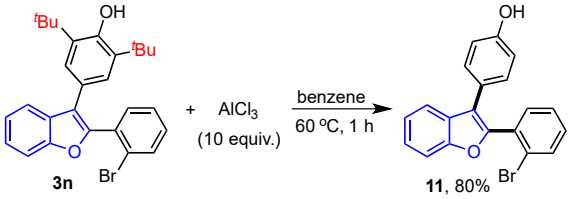
After exploring the substrate scope with different aromatic aldehydes, we investigated the generality of this protocol using different 2-hydroxyphenyl-substituted *para*-quinone methides (**1b-f**) and 4-chlorobenzaldehyde (**4a**) under optimized reaction conditions, and the results are summarized in Table 3. To our delight, this method worked very well with 2-hydroxy substituted *para*-quinone methides (**1b** & **1c**), derived from electron-rich salicylaldehydes, and the desired products **10a** & **10b** were obtained in 80% and 83% isolated yields, respectively. Similarly, when **4a** was treated with halo-substituted 2-hydroxyphenyl-substituted *para*-quinone methides (**1d-f**), the desired 2,3-diarylbenzo[*b*]furans **10c-e** were obtained in the range of 75-82% yields.

Table 3. Substrate scope with different 2-hydroxy *para*-quinone methides[a]



[a]All reactions were carried out with 30 mg scale of **1b-f** in 1.5 mL of MeCN. [b] Reaction was carried out with 2.0 g (5.11 mmol) of **1e** in 30 mL of MeCN. Yields reported are isolated yields.

Toward the further expansion of the substrate scope, we attempted the de-*tert*-butylation reaction of one of the diarylbenzo[*b*]furans. In this context, **3n** was treated with excess of $AlCl_3$ in benzene at 60 °C and, as expected, the corresponding de-*tert*-butylated 2,3-diarylbenzo[*b*]furan **11** was obtained in 80% yield within 1 h (Scheme 3).



Scheme 3. De-*tert*-butylation of **3n**

In summary, we have successfully demonstrated a one-pot approach for the synthesis of 2,3-diarylbenzo[*b*]furans through *N*-heterocyclic carbene catalyzed 1,6-conjugate addition of aromatic aldehydes to 2-hydroxyphenyl-substituted *para*-quinone methides followed by TsOH mediated dehydrative aromatic annulation. This transformation occurs at mild conditions and is tolerant to a variety of functional groups. Moreover, this protocol provides an easy and straight-forward access to a new set of 2,3-diarylbenzo[*b*]furans in moderate to good yields.

Experimental Section

General Information. All reactions were carried out under an argon atmosphere in an oven dried round bottom flask. All the solvents were distilled before use and stored under argon atmosphere. Most of the reagents and starting materials and NHC precursors (**6** to **9**) were purchased from commercial sources and used as such. All 2-hydroxyphenyl-substituted *p*-quinone methides were prepared by following a literature procedure.[16a] NHC precursor **5** was prepared according to the literature procedure.[18] Melting points were recorded on SMP20 melting point apparatus and are uncorrected. ^{1}H, ^{13}C and ^{19}F spectra were recorded in $CDCl_3$ (400, 100 and 376 MHz respectively) on Bruker FT–NMR spectrometer. Chemical shift (δ) values are reported in parts per million relative to TMS and the coupling constants (J) are reported in Hz. High resolution mass spectra were recorded on Waters Q–TOF Premier–HAB213 spectrometer. FT-IR spectra were recorded on a Perkin-Elmer FTIR spectrometer. Thin layer chromatography was performed on Merck silica gel 60 F_{254} TLC pellets and visualized by UV irradiation and $KMnO_4$ stain. Column chromatography was carried out through silica gel (100–200 mesh) using EtOAc/hexane as an eluent.

General procedure for the synthesis of 2,3-diarylbenzo[b]furans:

A mixture of 2-hydroxyphenyl-substituted *p*-quinone methide (0.097 mmol), aromatic aldehyde (0.116 mmol), precatalyst **8** (0.0194 mmol) and NaH (0.0485 mmol) in anhydrous MeCN (1.5 mL) was stirred at room temperature under Ar atmosphere. After the reaction was complete (based on TLC analysis), TsOH (0.194 mmol) was added to the reaction mixture and the resultant mixture was further stirred at room temperature until most of the intermediate (1,6-adduct) was completely consumed (based on TLC analysis). The reaction mixture was concentrated under reduced pressure and the crude was directly loaded on to a silica gel column and purified using EtOAc/Hexane mixture as an eluent to get the pure product.

*2,6-di-tert-butyl-4-(2-(4-chlorophenyl)benzofuran-3-yl)phenol (**3a**)*: The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (37.7 mg, 91% yield); m. p. = 209–211 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.6 Hz, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.36 (dd, J = 7.4, 1.2 Hz, 1H), 7.33 (s, 2H), 7.31 (d, J = 8.7 Hz, 2H), 7.27 – 7.25 (m, 1H), 5.34 (s, 1H), 1.46 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 153.7, 148.9, 136.6, 133.9, 130.3, 129.7, 128.6, 128.2, 126.4, 124.9, 123.1, 123.05, 120.5, 118.9, 111.2, 34.6, 30.5; FT-IR (thin film, neat): 3633, 2659, 750 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{28}ClO_2$ $[M–H]^–$: 431.1778; found : 431.1759.

*4-(3-(3,5-di-tert-butyl-4-hydroxyphenyl)benzofuran-2-yl)benzonitrile (**3b**)*: The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.4 (5% EtOAc in hexane); white solid (28.7 mg, 70% yield); m. p. = 235–237 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2H), 7.60 – 7.55 (m, 4H), 7.41 – 7.36 (m, 1H), 7.29 (s, 2H), 7.26 (s, 1H), 5.38 (s, 1H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 154.1, 147.7, 136.8, 135.5, 132.1, 130.1, 127.1, 126.3, 125.8, 123.4, 122.6, 121.7, 121.0, 119.1, 111.4, 111.0, 34.7, 30.5; FT-IR (thin film, neat): 3615, 2960, 2856, 2220, 751 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{28}NO_2$ $[M–H]^–$: 422.2120; found : 422.2105.

*2,6-di-tert-butyl-4-(2-(3-nitrophenyl)benzofuran-3-yl)phenol (**3c**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.4 (5% EtOAc in hexane); pale yellow solid (32.2 mg, 75% yield); m. p. = 197–199 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (t, J = 1.9 Hz, 1H), 8.14 (ddd, J = 3.2, 2.2, 0.9 Hz, 1H), 8.07 – 8.04 (m, 1H), 7.59 – 7.57 (m, 2H), 7.48 (t, J = 8.0 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.32 (s, 2H), 7.31 – 7.27 (m, 1H), 5.39 (s, 1H),1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 154.1, 148.5, 147.2, 136.9, 132.9, 132.2, 130.2, 129.3, 126.3, 125.7, 123.4, 122.5, 122.4, 121.4, 121.0, 120.9, 111.4, 34.6, 30.5; FT-IR (thin film, neat): 3630, 2961, 1531, 1265, 753 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{28}NO_4$ $[M–H]^–$: 442.2018; found : 442.2001.

*2,6-di-tert-butyl-4-(2-(4-(trifluoromethyl)phenyl)benzofuran-3-yl)phenol (**3d**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (32.5 mg, 72% yield); m. p. = 205–207 ºC; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.85 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.2 Hz, 4H), 7.37 (t, J = 7.4 Hz, 1H), 7.31 (s, 2H), 7.29 (d, J = 7.8 Hz, 1H), 5.36 (s, 1H), 1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 153.9, 148.4, 136.7, 134.6 (q, $J_{C\text{-}F}$ = 1.2 Hz), 130.3, 129.7 (q, $J_{C\text{-}F}$ = 32.4 Hz), 127.0, 126.4, 125.4, 125.3 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.2 (q, $J_{C\text{-}F}$ = 270.5 Hz), 123.2, 122.9, 120.8, 120.5, 111.4, 34.6, 30.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ –62.65; FT-IR (thin film, neat): 3631, 2960, 743 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{28}F_3O_2$ $[M–H]^–$: 465.2041; found : 465.2029.

*2,6-di-tert-butyl-4-(2-(3-(trifluoromethyl)phenyl)benzofuran-3-yl)phenol (**3e**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (29.8 mg, 66% yield); m. p. = 138–140 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.93 (m, 2H), 7.58 – 7.55 (m, 2H), 7.52 (d, J = 7.8 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 7.36 (t, J = 7.3 Hz, 1H), 7.30 (s, 2H), 7.26 (s, 1H), 5.34 (s, 1H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.9, 148.3, 136.8, 132.0, 130.9 (q, $J_{C\text{-}F}$ = 32.0 Hz), 130.3, 129.8, 128.9, 126.3, 125.3, 124.6 (q, $J_{C\text{-}F}$ = 3.7 Hz), 124.1 (q, $J_{C\text{-}F}$ = 270.9 Hz), 123.6 (q, $J_{C\text{-}F}$ = 4.0 Hz), 123.2, 122.8, 120.8, 120.0, 111.3, 34.6, 30.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ –62.85; FT-IR (thin film, neat): 3642, 2965, 751 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{28}F_3O_2$ $[M–H]^–$: 465.2041; found : 465.2026.

*2,6-di-tert-butyl-4-(2-phenylbenzofuran-3-yl)phenol (**3f**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (30.0 mg, 78% yield); m. p. = 151–153 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.1 Hz, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.33 (s, 3H), 7.31 – 7.25 (m, 4H), 5.29 (s, 1H), 1.43 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.5, 150.2, 136.4, 131.2, 130.4, 128.33, 128.27, 127.2, 126.5, 124.6, 123.4, 122.9, 120.4, 118.4, 111.2, 34.6, 30.5; FT-IR (thin film, neat): 3642, 2966, 762 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{29}O_2$ $[M–H]^–$: 397.2168; found : 397.2152.

*2,6-di-tert-butyl-4-(2-(3,5-dimethoxyphenyl)benzofuran-3-yl)phenol (**3g**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.3 (5% EtOAc in hexane); white solid (34.2 mg, 77% yield); m. p. = 174–176 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.53 (m, 2H), 7.36 – 7.34 (m, 1H), 7.32 (s, 2H), 7.27 – 7.24 (m, 1H), 6.88 (d, J = 2.3 Hz, 2H), 6.41 (t, J = 2.3 Hz, 1H), 5.31 (s, 1H), 3.69 (s, 6H), 1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 153.9, 153.5, 150.0, 136.5, 132.7, 130.7, 126.6, 124.8, 123.6, 122.9, 120.4, 119.0, 111.2, 104.7, 101.3, 55.3, 34.6, 30.5; FT-IR (thin film, neat): 3631, 2958, 749 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{30}H_{33}O_4$ $[M–H]^–$: 457.2379; found : 457.2391.

*2,6-di-tert-butyl-4-(2-(4-(trifluoromethoxy)phenyl)benzofuran-3-yl)phenol (**3h**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.4 (5% EtOAc in hexane); white solid (38.8 mg, 83% yield); m. p. = 174–176 ºC; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.75 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 7.7, Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.31 (s, 2H), 7.29 (d, J = 7.5 Hz, 1H), 7.18 (d, J = 8.5 Hz, 2H), 5.34 (s, 1H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.7, 148.9 (q, $J_{C\text{-}F}$ = 1.7 Hz), 148.8, 136.6, 130.2, 130.0, 128.6, 126.4, 125.0, 123.1, 123.0, 120.8, 120.59 (q, $J_{C\text{-}F}$ = 255.7 Hz), 120.57, 119.1, 111.3, 34.6, 30.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ –57.80; FT-IR (thin film, neat): 3631, 2961, 746 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{28}F_3O_3$ $[M–H]^–$: 481.1991; found : 481.2009.

*2,6-di-tert-butyl-4-(2-(4-(tert-butyl)phenyl)benzofuran-3-yl)phenol (**3i**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid; (12.3 mg, 28% yield); m. p. = 178–180 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.6 Hz, 2H), 7.58 – 7.56 (m, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.35 (d, J = 8.7 Hz, 2H), 7.31 (s, 2H), 7.30 – 7.29 (m, 1H), 7.26 – 7.23 (m, 1H), 5.28 (s, 1H), 1.43 (s, 18H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 153.4, 151.4, 150.6, 136.2, 130.5, 128.3, 126.9, 126.5, 125.3, 124.4, 123.6, 122.8, 120.3, 117.8, 111.2, 34.8, 34.6, 31.4, 30.5; FT-IR (thin film, neat): 3636, 2959, 748 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{32}H_{37}O_2$ $[M–H]^–$: 453.2794; found : 453.2813.

*2,6-di-tert-butyl-4-(2-(4-ethylphenyl)benzofuran-3-yl)phenol (**3j**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow gummy solid; (9.5 mg, 23% yield); ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.64 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.32 (s, 2H), 7.30 (dd, J = 8.1, 1.1 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.15 (d, J = 8.2 Hz, 2H), 5.28 (s, 1H), 2.65 (q, J = 7.6 Hz, 2H), 1.43 (s, 18H), 1.24 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 153.4, 150.5, 144.6, 136.3, 130.5, 128.6, 127.8, 127.1, 126.5, 124.4, 123.6, 122.8, 120.3, 117.7, 111.2, 34.6, 30.5, 28.9, 15.7; FT-IR (thin film, neat): 3637, 2960, 748 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{30}H_{33}O_2$ $[M–H]^–$: 425.2481; found : 425.2477.

*2,6-di-tert-butyl-4-(2-(p-tolyl)benzofuran-3-yl)phenol (**3k**):* The reaction was performed at 0.082 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (10.0 mg, 25% yield); m. p. = 182–184 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.32 (s, 2H), 7.30 (d, J = 7.8 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.13 (d, J = 7.9 Hz, 2H), 5.28 (s, 1H), 2.36 (s, 3H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 153.4, 150.4, 138.2, 136.3, 130.6, 129.0, 128.3, 127.0, 126.5, 124.4, 123.6, 122.8, 120.3, 117.7, 111.1, 34.6, 30.6, 21.5; FT-IR (thin film, neat): 3637, 2961, 759 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{31}O_2$ $[M–H]^–$: 411.2324; found : 411.2307.

*4-(2-(4-bromophenyl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3l**):* The reaction was performed at 6.45 mmol scale of **1a** in 30 mL of MeCN; R_f = 0.5 (5% EtOAc in hexane); white solid (2.50 g, 81% yield); m. p. = 229–231 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.7 Hz, 2H), 7.58 – 7.53 (m, 2H) 7.45 (d, J = 8.7 Hz, 2H), 7.36 – 7.32 (m, 1H), 7.32 (s, 2H), 7.28 – 7.24 (m, 1H), 5.33 (s, 1H) 1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 153.7, 148.9, 136.6, 131.5, 130.4, 130.1, 128.4, 126.4, 125.0, 123.08, 123.06, 122.2, 120.5, 119.1, 111.2, 34.6, 30.5; FT IR (thin film, neat): 3632, 2965, 752 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{28}BrO_2$ $[M–H]^–$: 475.1273; found : 475.1252.

*2,6-di-tert-butyl-4-(2-(2-chlorophenyl)benzofuran-3-yl)phenol (**3m**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (33.9 mg, 81% yield); m. p. = 177–179 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.81 (m, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.49 (dd, J = 8.0, 1.2 Hz, 1H), 7.44 (dd, J = 7.6, 1.7 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.36 – 7.32 (m, 2H), 7.31 – 7.28 (m, 1H), 7.22 (s, 2H), 5.20 (s, 1H), 1.35 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 153.1, 148.6, 136.1, 135.0, 132.9, 131.0, 130.4, 130.1, 128.3, 126.7, 125.6, 124.7, 123.1, 123.0, 120.7, 120.4, 111.6, 34.5, 30.4; FT-IR (thin film, neat): 3633, 2958, 753 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{28}ClO_2$ $[M–H]^–$: 431.1778; found : 431.1767.

*4-(2-(2-bromophenyl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3n**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (37.9 mg, 82% yield); m. p. = 204–206 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.83 (m, 1H), 7.70 (dd, J = 7.7, 1.2 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.44 – 7.41(m, 1H), 7.39 (dd, J = 7.3, 1.4 Hz, 1H), 7.36 (dd, J = 4.2, 1.6 Hz 1H), 7.34 – 7.31 (m, 1H), 7.309 – 7.27 (m, 1H), 7.23 (s, 2H); 5.20 (s, 1H) 1.36 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 153.1, 150.0, 136.0, 133.2, 133.1, 130.7, 128.2, 127.3, 125.6 (2C), 124.9, 124.7, 123.05, 123.02, 120.8, 120.0, 111.7, 34.5, 30.4; FT-IR (thin film, neat): 3633, 2958, 752 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{28}BrO_2$ $[M–H]^–$: 475.1273; found : 475.1251.

*2,6-di-tert-butyl-4-(2-(2-fluorophenyl)benzofuran-3-yl)phenol (**3o**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (33.8 mg, 84% yield); m. p. = 155–157 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.75 (m, 1H), 7.58 – 7.56 (m, 1H), 7.52 (td, J = 7.3, 1.7 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.30 (td, J = 7.7, 1.2 Hz, 1H), 7.26 (s, 2H), 7.17 – 7.15 (m, 1H), 7.14 – 7.10 (m, 1H), 5.24 (s, 1H), 1.38 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2 (d, $J_{C\text{-}F}$ = 251.2 Hz), 154.9, 153.3, 145.9 (d, $J_{C\text{-}F}$ = 1.5 Hz), 136.1, 131.7 (d, $J_{C\text{-}F}$ = 2.8 Hz), 130.7 (d, $J_{C\text{-}F}$ = 8.1 Hz), 128.8, 125.6, 124.8, 124.0 (d, $J_{C\text{-}F}$ = 3.6 Hz), 123.3 (d, $J_{C\text{-}F}$ = 0.7 Hz), 123.0, 120.6, 119.6, 119.5, 116.3 (d, $J_{C\text{-}F}$ = 21.4 Hz), 111.5, 34.5, 30.4;

^{19}F NMR (376 MHz, $CDCl_3$) δ –111.04; FT-IR (thin film, neat): 3634, 2958, 753 cm^{-1} HRMS (ESI): *m/z* calcd for $C_{28}H_{28}FO_2$ $[M–H]^-$: 415.2073; found : 415.2054.

*2,6-di-tert-butyl-4-(2-(2,4-dichlorophenyl)benzofuran-3-yl)phenol (**3p**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (31.6 mg, 70% yield); m. p. = 147–149 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.79 (m, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.51 (d, J = 2.0 Hz, 1H), 7.40 – 7.38 (m, 2H), 7.34 (ddd, J = 8.8, 7.6, 1.5 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.19 (s, 2H), 5.24 (s, 1H), 1.37 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 153.3, 147.4, 136.2, 135.7, 135.6, 133.7, 130.0, 129.6, 128.3, 127.1, 125.6, 125.0, 123.1, 122.9, 121.0, 120.8, 111.6, 34.5, 30.4; FT-IR (thin film, neat): 3635, 2959, 750 cm^{-1} HRMS (ESI): *m/z* calcd for $C_{28}H_{27}Cl_2O_2$ $[M–H]^-$: 465.1388; found : 465.1374.

*2,6-di-tert-butyl-4-(2-(2,4-difluorophenyl)benzofuran-3-yl)phenol (**3q**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (33.2 mg, 79% yield); m. p. = 144–146 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.73 (m, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.37 (td, J = 7.3, 1.3 Hz, 1H), 7.30 (td, J = 7.7, 1.1 Hz, 1H), 7.24 (s, 2H), 6.93 – 6.90 (m, 1H), 6.89 – 6.86 (m, 1H), 5.25 (s, 1H), 1.39 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6 (d, $J_{C\text{-}F}$ = 254.2 Hz), 160.5 (d, $J_{C\text{-}F}$ = 253.9 Hz), 154.9, 153.4, 145.0 (d, $J_{C\text{-}F}$ = 1.7 Hz), 136.2, 132.7 (dd, $J_{C\text{-}F}$ = 9.6, 4.3 Hz), 128.7, 125.6, 124.9, 123.1, 120.7, 120.6, 116.0 (dd, $J_{C\text{-}F}$ = 141.0, 3.8 Hz), 111.53, 111.50 (dd, $J_{C\text{-}F}$ = 21.2, 3.6 Hz), 104.7 (t, $J_{C\text{-}F}$ = 25.4 Hz), 104.5, 34.5, 30.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ –106.38 (d, J = 8.7 Hz), –108.24 (d, J = 8.8 Hz); FT-IR (thin film, neat): 3636, 2959, 2877, 1451, 1267, 1147, 753 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{27}F_2O_2$ $[M–H]^-$: 433.1979; found : 433.1958.

*4-(2-(2-bromo-5-fluorophenyl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3r**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); white solid (28.3 mg, 59% yield); m. p. = 193–195 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.82 (m, 1H), 7.64 (dd, J = 8.8, 5.2 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.40 (td, J = 7.3, 1.3 Hz, 1H), 7.35 (td, J = 7.6,

1.2 Hz, 1H), 7.23 (s, 2H), 7.17 (dd, J = 8.8, 3.0 Hz, 1H), 7.03 (ddd, J = 8.8, 7.9, 3.1 Hz, 1H), 5.24(s, 1H), 1.38 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (d, $J_{C\text{-}F}$ = 246.7 Hz), 154.8, 153.4, 148.4 (d, $J_{C\text{-}F}$ = 1.8 Hz), 136.2, 134.8 (d, $J_{C\text{-}F}$ = 8.5 Hz), 134.6 (d, $J_{C\text{-}F}$ = 8.1 Hz), 128.1, 125.6, 125.1, 123.2, 122.7, 120.9, 120.7, 120.1 (d, $J_{C\text{-}F}$ = 23.0 Hz), 119.2 (d, $J_{C\text{-}F}$ = 3.3 Hz), 117.9 (d, $J_{C\text{-}F}$ = 22.3 Hz), 111.7, 34.5, 30.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.82; FT-IR (thin film, neat): 3635, 2957, 752 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{27}BrFO_2$ $[M–H]^-$: 493.1178; found : 493.1159.

*4-(2-(2-bromo-5-methoxyphenyl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3s**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.3 (5% EtOAc in hexane); pale yellow gummy solid (25.0 mg, 51% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.40 – 7.31 (m, 2H), 7.24 (s, 2H), 6.93 (d, J = 2.6 Hz, 1H), 6.85 (dd, J = 8.8, 2.8 Hz, 1H), 5.21 (s, 1H), 3.70 (s, 3H), 1.36 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 154.7, 153.2, 149.8, 136.1, 133.9, 133.7, 128.3, 125.7, 124.8, 123.1, 123.0, 120.8, 120.1, 118.0, 117.1, 115.2, 111.7, 55.7, 34.5, 30.4; FT-IR (thin film, neat): 3642, 2970, 753 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{30}BrO_3$ $[M+Na]^+$: 505.1378; found : 505.1394.

*4-(2-(2-bromo-4-methylphenyl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3t**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (10% EtOAc in hexane); pale solid (16.6mg, 35% yield); m. p. = 145–147 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.81 (m, 1H), 7.58 – 7.56 (m, 1H), 7.53 – 7.52 (m, 1H), 7.37 (td, J = 7.2, 1.4 Hz, 1H), 7.33 (dd, J = 7.6, 1.4 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 7.23 (s, 2H), 7.14 – 7.12 (m, 1H), 5.19 (s, 1H), 2.39 (s, 3H), 1.36 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 153.0, 150.1, 141.1, 136.0, 133.6, 132.8, 130.1, 128.3, 128.1, 125.6, 124.7, 124.6, 123.2, 122.9, 120.7, 119.8, 111.6, 34.5, 30.4, 21.2; FT-IR (thin film, neat): 3633, 2958, 753 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{30}BrO_2$ $[M–H]^-$: 489.1429; found : 489.1443.

*4-(2-([1,1'-biphenyl]-4-yl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3u**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.3 (5% EtOAc in hexane); pale yellow solid (33.0 mg, 72% yield); m. p. = 207–209 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.1 Hz, 2H), 7.62 (d, J = 7.8 Hz, 2H), 7.59 – 7.55 (m, 4H), 7.45 (t, J = 7.6 Hz, 2H), 7.36 (s, 2H), 7.33 (d, J = 8.0 Hz 1H), 7.28 – 7.24 (m, 2H), 5.31 (s, 1H), 1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.6, 149.9, 140.8, 140.7, 136.5, 130.5, 130.2, 129.0, 127.6, 127.4, 127.1, 127.0, 126.5, 124.7, 123.5, 122.9, 120.4, 118.6, 111.2, 34.6, 30.6; FT-IR (thin film, neat): 3632, 2965, 744 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{34}H_{33}O_2$ $[M–H]^–$: 473.2481; found : 473.2461.

*2,6-di-tert-butyl-4-(2-(naphthalen-1-yl)benzofuran-3-yl)phenol (**3v**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.4 (20% EtOAc in hexane); pale yellow gummy solid (30.0 mg, 69 % yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.2 Hz, 1H), 7.89 – 7.87 (m, 2H), 7.80 (d, J = 8.4 Hz, 1H), 7.68 (dd, J = 7.1, 1.0 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.53 – 7.49 (m, 1H), 7.47 – 7.42 (m, 1H), 7.38 (td, J = 7.8, 1.5 Hz, 2H), 7.35 – 7.28 (m, 1H), 7.16 (s, 2H), 5.11 (s, 1H), 1.21 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 152.9, 150.5, 136.0, 133.9, 131.8, 129.7, 129.4, 129.0, 128.7, 128.2, 126.4, 126.1, 125.7 (2C), 125.3, 124.5, 123.3, 123.0, 120.6, 120.1, 111.6, 34.3, 30.2; FT-IR (thin film, neat): 3633, 2957, 750 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{32}H_{31}O_2$ $[M–H]^–$: 447.2324; found : 447.2311.

*2,6-di-tert-butyl-4-(2-(thiophen-2-yl)benzofuran-3-yl)phenol (**3w**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (28.2 mg, 72 % yield); m. p. = 188–190 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, J = 7.7 Hz, 2H), 7.44 – 7.43 (m, 1H), 7.37 (s, 2H), 7.31 (t, J = 7.9 Hz, 1H), 7.26 – 7.21 (m, 2H), 7.02 – 7.00 (m, 1H), 5.33 (s, 1H), 1.47 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.93, 153.87, 146.4, 136.4, 133.2, 130.5, 127.3, 126.7, 125.8, 125.5, 124.7, 123.1, 122.6, 120.3, 117.8, 111.1, 34.6, 30.5; FT-IR (thin film, neat): 3642, 2961, 762 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{26}H_{27}O_2S$ $[M–H]^–$: 403.1732; found : 403.1746.

*4-(2-(3-bromothiophen-2-yl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**3x**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.5 (5% EtOAc in hexane); pale yellow solid (35.0 mg, 75 % yield); m. p. = 180–182 ºC; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.75 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.31 (d, J = 7.5 Hz, 1H), 7.28 (s, 2H), 7.04 (d, J = 5.3 Hz, 1H), 5.25 (s, 1H), 1.40 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 154.9, 153.5, 136.2, 131.1, 128.6, 128.5, 128.1, 125.9, 125.3, 123.2, 122.8, 122.2, 120.8, 112.6, 111.6, 34.5, 30.4; FT-IR (thin film, neat): 3632, 2958, 749 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{26}H_{26}BrO_2S$ $[M–H]^–$: 481.0837; found : 481.0827.

*2,6-di-tert-butyl-4-(2-(furan-2-yl)benzofuran-3-yl)phenol (**3y**):* The reaction was performed at 0.097 mmol scale of **1a**; R_f = 0.4 (5% EtOAc in hexane); pale yellow solid (27.8 mg, 74 % yield); m. p. = 165–167 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.7 Hz, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.46 (d, J = 1.0 Hz, 1H), 7.45 (s, 2H), 7.35 –7.31 (m, 1H), 7.28 – 7.24 (m, 2H), 6.71 (d, J = 3.4 Hz, 1H), 5.33 (s, 1H), 1.49 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 153.6, 146.4, 142.7, 142.4, 136.0, 129.7, 126.5, 124.9, 123.2, 122.4, 120.5, 118.0, 111.6, 111.3, 108.9, 34.6, 30.6; FT-IR (thin film, neat): 3628, 2961, 739 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{26}H_{27}O_3$ $[M–H]^–$: 387.1960; found : 387.1977.

*2,6-di-tert-butyl-4-(2-(4-chlorophenyl)-5-methoxybenzofuran-3-yl)phenol (**10a**):* The reaction was performed at 0.088 mmol scale of **1b**; R_f = 0.3 (5% EtOAc in hexane); orange solid (32.6 mg, 80% yield); m. p. = 189–191 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.7 Hz, 2H), 7.42 (d, J = 8.8 Hz, 1H), 7.30 (s, 2H), 7.27 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 2.5 Hz, 1H), 6.94 (dd, J = 8.9, 2.6 Hz, 1H), 5.33 (s, 1H), 3.83 (s, 3H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 153.7, 149.8, 149.1, 136.6, 133.9, 130.8, 129.7, 128.5, 128.2, 126.3, 123.2, 119.1, 113.8, 111.7, 102.7, 56.0, 34.6, 30.6; FT-IR (thin film, neat): 3637, 2965, 754 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{30}ClO_3$ $[M–H]^–$: 461.1883; found : 461.1866.

*2,6-di-tert-butyl-4-(2-(4-chlorophenyl)-5-methylbenzofuran-3-yl)phenol (**10b**):* The reaction was performed at 0.092 mmol scale of **1c**; R_f = 0.5 (5% EtOAc in hexane); white solid (34.3 mg, 83% yield); m. p. = 222–224 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 8.4 Hz, 1H), 7.36 – 7.35 (m, 1H) 7.32 (s, 2H), 7.29 (d, J = 8.8 Hz, 2H), 7.16 (dd, J = 8.4, 1.3 Hz, 1H), 5.34 (s, 1H), 2.46 (s, 3H), 1.47 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 152.5, 149.1, 136.6, 133.8, 132.5, 130.4, 129.8, 128.5, 128.1, 126.4, 126.2, 123.3, 120.2, 118.8, 110.7, 34.6, 30.5, 21.6; FT-IR (thin film, neat): 3633, 2957, 757 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{30}ClO_2$ $[M–H]^–$: 445.1934; found : 445.1915.

*2,6-di-tert-butyl-4-(5-chloro-2-(4-chlorophenyl)benzofuran-3-yl)phenol (**10c**):* The reaction was performed at 0.087 mmol scale of **1d**; R_f = 0.5 (5% EtOAc in hexane); white solid (33.0 mg, 81% yield); m. p. = 226–228 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 2.0 Hz, 1H), 7.44 (d, J = 8.7 Hz, 1H), 7.31 – 7.30 (m, 1H), 7.29 – 7.27 (m, 2H), 7.26 (s, 2H), 5.36 (s, 1H), 1.45 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.5, 150.3, 136.8, 134.4, 131.8, 129.2, 128.7, 128.6, 128.2, 126.3, 125.1, 122.5, 120.1, 118.6, 112.2, 34.6, 30.5; FT-IR (thin film, neat): 3632, 2961, 754 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{27}Cl_2O_2$ $[M–H]^–$: 465.1388; found : 465.1378.

*4-(5-bromo-2-(4-chlorophenyl)benzofuran-3-yl)-2,6-di-tert-butylphenol (**10d**):* The reaction was performed at 5.11 mmol scale of **1e** in 30 mL MeCN; R_f = 0.5 (5% EtOAc in hexane); orange solid (1.96 g, 75% yield); m. p. = 211–213 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.63 (m, 2H), 7.62 – 7.61 (m, 1H), 7.41 – 7.40 (m, 2H), 7.29 (d, J = 8.8 Hz, 2H), 7.24 (s, 2H), 5.36 (s, 1H), 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.8, 150.2, 136.8, 134.4, 132.5, 129.1, 128.7, 128.2, 127.8, 126.3, 123.2, 122.4, 118.5, 116.2, 112.7, 34.6, 30.5; FT-IR (thin film, neat): 3633, 2959, 754 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{27}BrClO_2$ $[M–H]^–$: 509.0883; found : 509.0905.

*2,6-di-tert-butyl-4-(2-(4-chlorophenyl)-5-fluorobenzofuran-3-yl)phenol (**10e**):* The reaction was performed at 0.091 mmol scale of **1f**; R_f = 0.5 (5% EtOAc in hexane); white solid (33.6 mg, 82% yield); m. p. = 234–236 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.5 Hz, 2H), 7.45 (dd, J = 8.8, 4.0 Hz, 1H), 7.29 (d, J = 8.6 Hz, 2H), 7.26 (s, 2H), 7.19 (dd, J = 8.6, 2.4 Hz, 1H), 7.04 (td, J = 9.0, 2.4 Hz, 1H), 5.34 (s, 1H) 1.44 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6 (d, $J_{C\text{-}F}$ = 236.9 Hz), 153.8, 150.5 (d, $J_{C\text{-}F}$ = 37.8 Hz), 136.7, 134.3, 131.3 (d, $J_{C\text{-}F}$ = 10.3 Hz), 129.3, 128.6, 128.3, 126.2, 122.6, 119.2 (d, $J_{C\text{-}F}$ = 4.0 Hz), 112.6 (d, $J_{C\text{-}F}$ = 26.3 Hz), 111.9 (d, $J_{C\text{-}F}$ = 9.5 Hz) 106.1, 105.9, 34.6, 30.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ –120.54; FT-IR (thin film, neat): 3637, 2956, 795 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{27}ClFO_2$ $[M–H]^-$: 449.1684; found : 449.1698.

Procedure for the de-tert-butylation of 3n

$AlCl_3$ (84 mg, 0.63 mmol) was added to a solution of **3n** (30 mg, 0.063 mmol) in dry benzene (3 mL) under argon atmosphere and the resulting mixture was stirred at 60 ºC for 1 h. The reaction mixture was then quenched with 10 mL of cold ice water. It was extracted with EtOAc (3 x 10 mL) and the combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue was then purified through a silica gel column using EtOAc/Hexane mixture as an eluent to get the pure product **11** (18.4 mg, 80%) as pale yellow gummy solid; R_f = 0.3 (15% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 7.7, 0.5 Hz, 1H), 7.67 (dd, J = 7.7, 1.4 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.41 – 7.38 (m, 2H), 7.36 – 7.33 (m, 1H), 7.31 (s, 1H), 7.30 – 7.29 (m, 1H), 7.273 – 7.268 (m, 1H), 7.26 – 7.25 (m, 1H), 6.83 (d, J = 8.5 Hz, 2H), 4.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 154.7, 150.1, 133.5, 133.0, 132.5, 130.8, 130.4, 128.5, 127.4, 124.93, 124.89, 124.3, 123.1, 120.5, 119.2, 115.8, 111.6; FT-IR (thin film, neat): 3394, 2923, 753 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{20}H_{12}BrO_2$ $[M–H]^-$: 363.0021; found : 363.0039.

General procedure for the gram scale synthesis of 3a

A mixture of 2-hydroxy *p*-quinone methide **1a** (1.0 g, 3.22 mmol), 4-chlorobenzaldehyde **4a** (544 mg, 3.87 mmol), precatalyst **8** (17.8 mg, 0.066 mmol) and NaH (64.4 mg, 1.61 mmol) in anhydrous MeCN (40 mL) was stirred under argon atmosphere at room temperature. After the reaction was complete (based on TLC analysis), TsOH (1.11 g, 6.44 mmol) was added to the reaction mixture and the resultant mixture was stirred at room temperature until the intermediate (1,6-adduct) was completely consumed (based on TLC analysis). The residue was then concentrated under reduced pressure and the residue was then purified through a silica gel column using EtOAc/Hexane mixture as an eluent to get the pure product **3a** (1.2 g, 86%).

Supporting Information

^{1}H, ^{13}C and ^{19}F spectra of all new compounds

Notes

The authors declare no competing financial interest.

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