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Synthesis of Functionalized Benzo[b]furans *via* Oxidative Cyclization of *o*-Cinnamyl Phenols

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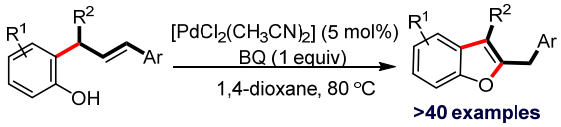


ABSTRACT: Disclosed herein an efficient synthetic route for the synthesis of functionalized 2-benzyl benzo[b]furans via a regioselective *5-exo-trig* intramolecular oxidative cyclization of *ortho*-cinnamyl phenols using $[PdCl_2(CH_3CN)_2]$ as catalyst and benzoquinone as an oxidant. Further, a sequential *ortho*-cinnamyaltion of phenols using cinnamyl alcohols catalyzed by Re_2O_7 followed by an oxidative cyclization using the above Pd-catalyst is performed. The reaction showed broad substrate scope with good to excellent yields.

INTRODUCTION

Benzo[b]furan is a common structural motif found in natural products, pharmaceuticals and agrochemicals.[1] Derivatives of benzo[b]furans are acting, for examples, as antitumor[2]/anticancer-agents,[3] 5-lipoxygenase[4]/mTOR signaling[5a]/angiotensin-inhibitors,[5b] and immunosuppressive activitors.[6] The intriguing biological properties, medicinal applications and molecular architecture of benzo[b]furan based natural products continue to draw a challenge and motivation for their synthesis. Various efficient synthetic method has been developed;[7] the traditional strategies for accessing the functionalized benzofurans relied mainly on the transition-metal catalyzed inter- or intra-molecular heteroannulation of pre-functionalized substrates (such as *ortho*-halo[8] or *ortho*-alkynyl[9] phenols). Recently, efforts have been directed towards the synthesis of benzo[b]furans via *ortho* C–H activation/functionalization of phenols (Scheme 1).[10-15] Notably, highly substituted benzo[b]furan motifs are also present in various leading drugs and organic materials. In particular, a significant number of natural products and synthetic compounds contain the 2-benzyl 3-aryl/alkyl benzo[b]furan core (see Figure 1).[16] Despite the significant advances in the synthesis of benzo[b]furans, selective synthesis of 2-benzyl 3-aryl/alkyl benzo[b]furan motifs from readily accessible phenols still remains a daunting challenge. Notably, among the above mentioned methods, only the *ortho*-propargylation/annulation strategy successfully provided such moiety, albeit with limited substrate scope.[13,17] Therefore, the development of a method to synthesize the

above mentioned benzo[b]furans from readily available substrates with broad substrate scope would be significantly rewarding.

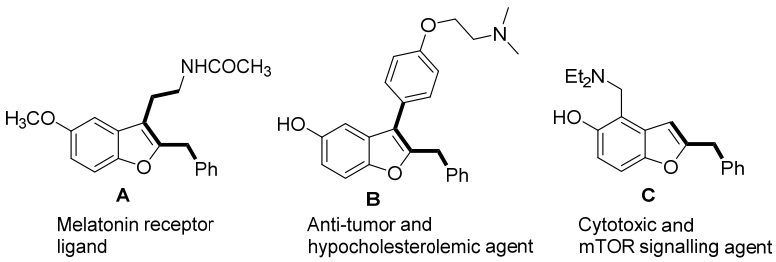
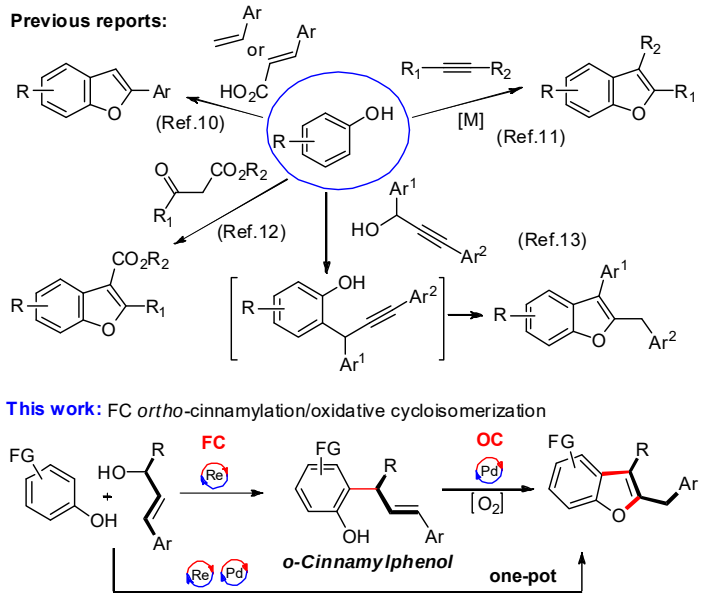


Figure 1. **Bioactive 2-benzyl benzo[b]furans**

Inspired by the oxidative-annulation strategy,[18] our group has a long-standing interest in the Pd-catalysed oxidative cycloannulation of various cinnamyl-substituted building blocks, which has been proven to be an important strategy for the synthesis of many hetrocycles.[19] For instances, *o*-cinnamylanilines have been utilized for the synthesis of 2-benzyl indoles[19a] and 2-aryl quinolines[19b]. More recently, the synthesis of 2-benzyl furans also have been developed from 2-cinnamyl-1,3-dicarbonyls.[19c] Here, we sought for the synthesis of functionalized 2-benzyl 3-aryl/alkyl benzo[b]furan *via* an intramolecular oxidative cyclization of *o*-cinnamylphenols.[20]



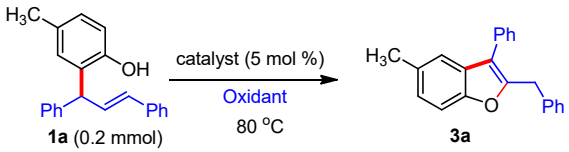
Scheme 1. Synthesis of Functionalized Benzo[b]furans from Phenol

Further, a simple and effecient one-pot protocol for the synthesis of functionalized 2-benzyl benzo[b]furan *via* a sequential *o*-cinnamylation of phenol followed by oxidative cyclization has also been demonstrated. An easy avaiablility of the cinnamyl alcohols compared to the propargyl alcohol might provide a broader synthetic utility of the current methodology.

RESULTS AND DISCUSSION

The reaction optimization studies for the oxidative cyclization of the model substrate *o*-cinnamylphenol (**1a**), which was prepared via a Friedel-Crafts alkylation of cinnamylalcohol with phenols using Re_2O_7 catalyst in acetonitrile as solvent (for details, see Supporting Information), is summarised in **Table 1**. When **1a** was stirred in 1,4-dioxane at 80 °C in the presence of a 5 mol% of various palladium catlysts (such as $Pd(OAc)_2$, $[Pd(PPh_3)_2Cl_2]$, $Pd(OTFA)_2$, $PdCl_2$ and $[PdCl_2(CH_3CN)_2]$, entries 1-5, respectively), it was observed that $[PdCl_2(CH_3CN)_2]$ provided the desired 2-benzyl-5-methyl-3-phenyl benzo[b]furan **3a** (entry 5) in 38% isolated yield in the presence of O_2 ballon as an oxidant.

Table 1. Catalyst optimization[a]



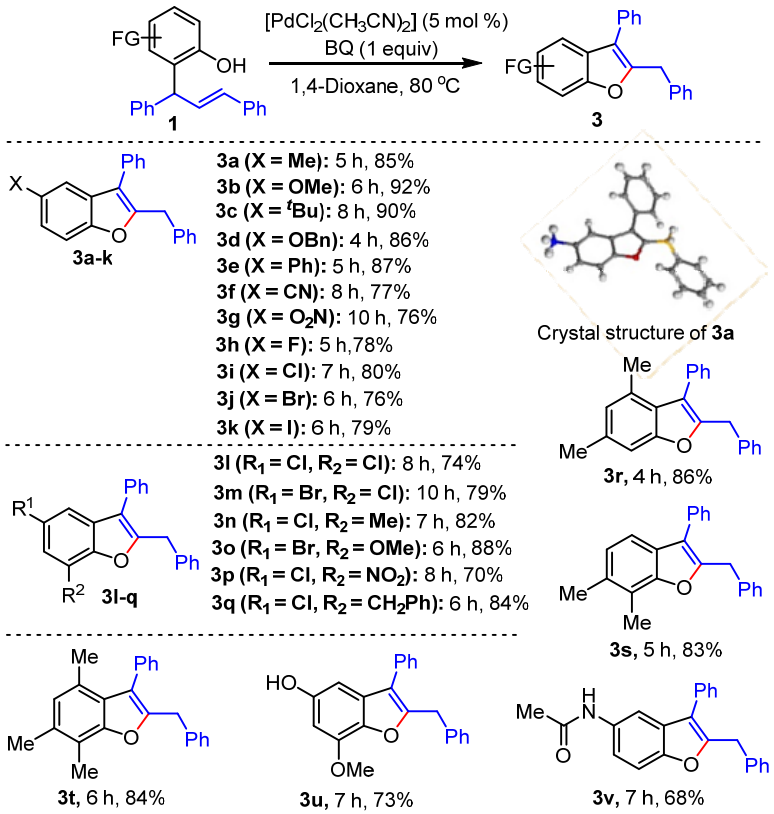
entry	Catalyst	Oxidant	Solvent	Yield (%)[b]
1	$Pd(OAc)_2$	O_2	toluene	28
2	$Pd(PPh_3)_2Cl_2$	O_2	toluene	trace
3	$Pd(OTFA)_2$	O_2	toluene	17
4	$PdCl_2$	O_2	toluene	23
5	$PdCl_2(CH_3CN)_2$	O_2	toluene	38
6	$PdCl_2(CH_3CN)_2$	BQ	toluene	66
7	$PdCl_2(CH_3CN)_2$	BQ	1,4-dioxane	85
8	$PdCl_2(CH_3CN)_2$	BQ	Other solvents[c]	<47

[a]Reaction conditions: *o*-Cinnamylphenol **1** (0.20 mmol), $PdCl_2(CH_3CN)_2$ (5 mol %), BQ (1 equiv), 1,4-dioxane (1.0 mL), 5 h. [b]Isolated yields after column chromatography. [c]Other solvents such as DCE, MeCN, THF and Et_2O.

When the same reaction was carried out in presence of benzoquinone (BQ) as oxidant instead of oxygen, the yield of the product was substantially increased (entry 6). Screening of the solvents such as THF, DCE, CH_3CN, 1,4-dioxane, toluene and diethyl ether, the reactivity in 1,4-dioxane was found to be the best using $[PdCl_2(CH_3CN)_2]$ as catalyst and BQ as oxidant (entry 7). This reactivity could be because of the better solubility of all the reaction components.

After establishing the efficient reaction conditions for the intramolecular catalytic oxidative cyclization reaction, the substrate scope was studied (Scheme 2). The overall process was shown to be effective in the presence of various substituted *o*-cinnamylphenols (**1a-q**). Substrates with electron-donating substitutents, such as Me- (**3a**), MeO- (**3b**), *tert*-butyl- (**3c**), BnO- (**3d**) and Ph- (**3e**), groups on the phenol moiety, reacted nicely to provide the desired 2-benzyl benzo[b]furans in good to excellent yields. Similarly, substrates with electron-withdrawing substituents, including, NC- (**3f**), O_2N- (**3g**), F- (**3h**), Cl- (**3i, 3l-n** and **3q**), Br- (**3j**, **3m** and **3o**) and I- (**3k**) yielded the corresponding 2-benzyl benzo[b]furans smoothly. Remarkably, halogen substitutions on phenol substrate such as iodo, bromo and chloro, which

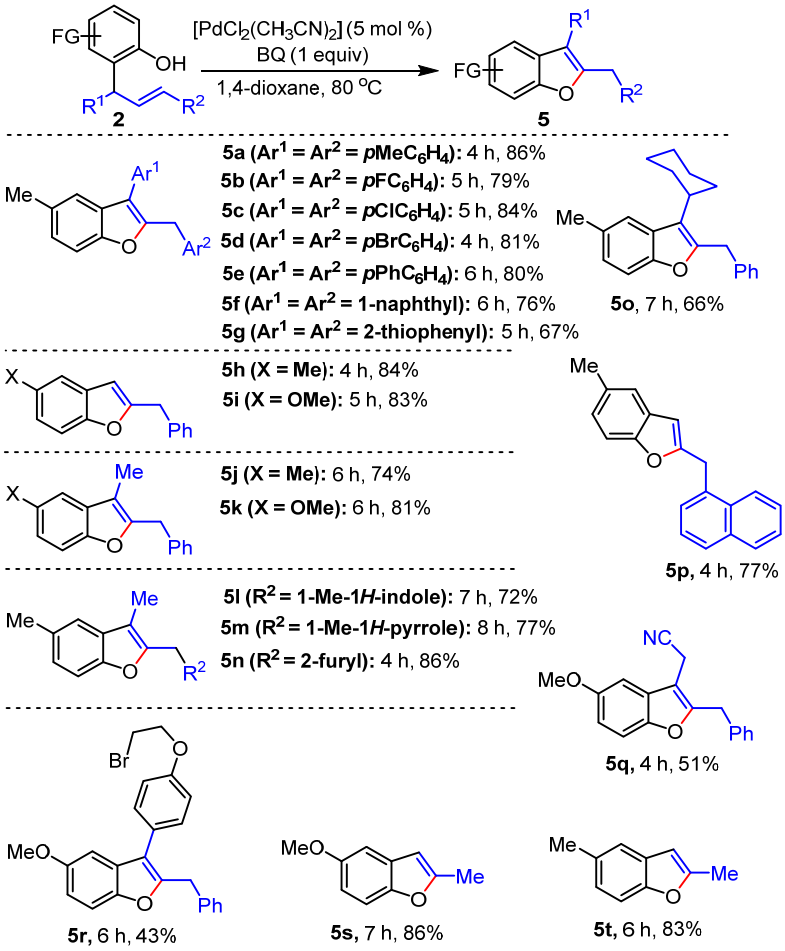
Scheme 2. Variation of aryl phenol[a]



[a]Reaction conditions: *o*-Cinnamylphenol **1** (0.20 mmol), $PdCl_2(CH_3CN)_2$ (5 mol %), BQ (1 equiv), 1,4-dioxane (1 mL). [b]Isolated yields after column chromatography.

are sensitive to palladium-catalysed reactions, were also successfully converted to the desired functionalized benzo[b]furans without any complication. Notably, di- (**3l-s**) and tri-(**3t**)-substituted *o*-cinnamylphenols were also tolerated well in the current reaction conditions. Di-substituted functional groups such as hydroxyl (**3u**) and amide (**3v**) were also tolerated under these reaction conditions. The structure of the compound **3a** was confirmed by X-ray crystallographic analysis.

Scheme 3. Variation of allyl counterpart[a,b]

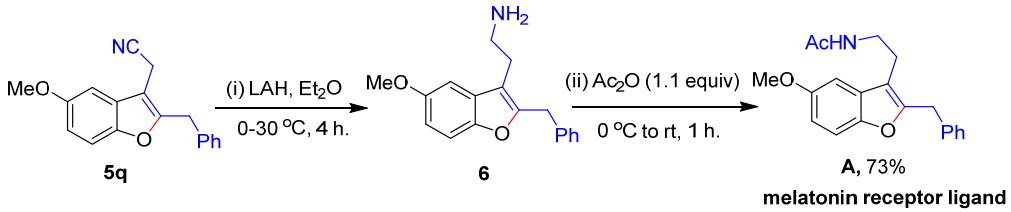


[a]Reaction conditions: *o*-Cinnamylphenol **2** (0.20 mmol), $PdCl_2(CH_3CN)_2$ (5 mol %), BQ (1 equiv), 1,4-dioxane (1 mL). [b]Isolated yields.

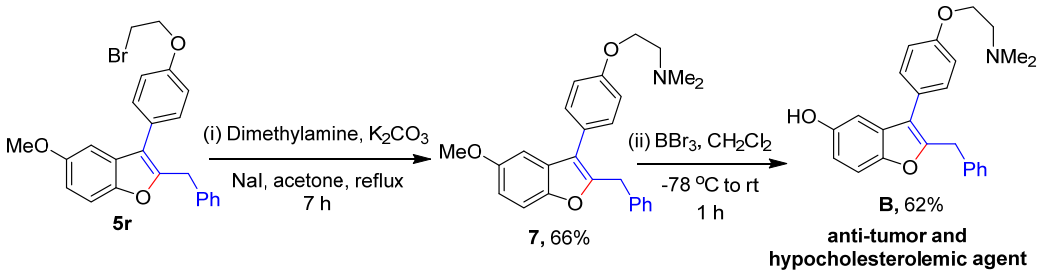
To further expand the substrate scope, a variety of *o*-cinnamylphenols were examined under the current oxidative cyclisation reaction conditions, which are summerized in Scheme 3. Various symmetrical substitutions were tolerated on 1′,3′-diarylallyls attached to phenols at the *ortho*-position to provide good yields of the corresponding benzo[b]furans. Substituents such as *p*-methyl (**5a**), *p*-fluoro (**5b**), *p*-

chloro (**5c**), *p*-bromo (**5d**) and *p*-biphenyl (**5e**) worked smoothly to provide the desired benzo[b]furan. A similar reactivity was observed with *o*-cinnamylphenol having α-naphthyl (**5f**) and 2-thiophenyl- (**5g**) as the aryl counterpart on the cinnamyl moiety. The unsymmetrically substituted *o*-cinnamylphenols were also easily underwent cycloannulation to afford the benzo[b]furans (**5h-r**) with good yields. 3-Unsubstituted (**5h-i, 5p**) as well as alkyl substitutions at 3-position such as methyl (**5j-n, 5q**) and cyclohexyl (**5o**) groups on 2-benzyl benzo[b]furans were also synthesized using this methodology. Even, heteroaromatic rings, such as 2-thiophenyl (**5g**), 2-furyl (**5l**), pyrole (**5m**) and indole (**5n**) remained effective under these conditions. 2-allyl substituted phenols were also tolerated under the same reaction conditions and provided the corresponding **(5s)** and **(5t)** benzo[b]furan with good yields.

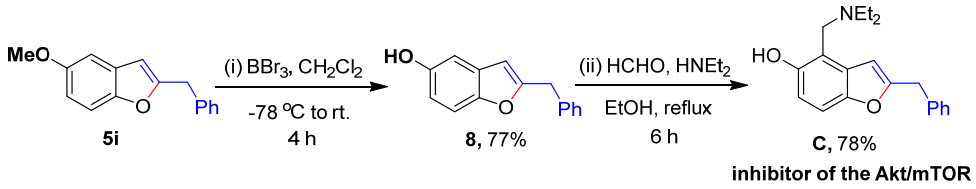
Scheme 4. Synthesis of Melatonin Receptor Ligand



Scheme 5. Synthesis of Anti-tumor and Hypocholesterolemic Agent



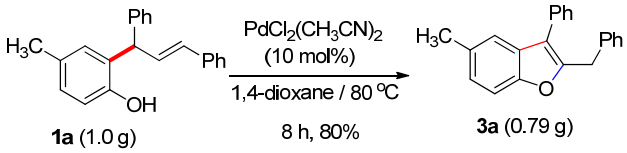
Scheme 6. Synthesis of Inhibitor of the Akt/mTOR



To illustrate the practical synthetic utility of our methodology, the synthesis of the melatonin receptor ligand **A**[16a] (Scheme 4), the anti-tumor/hypocholesterolemic agent **B** (Scheme 5) and the Akt/mtor signaling inhibitor **C** (Scheme 6), has been realized from correponding 2-benzyl benzo[b]furans **5q**, **5r** and **5i**, respectively.

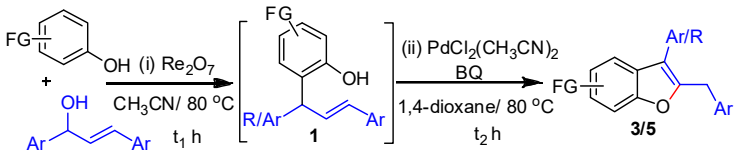
To showcase the scalability and the practicality of the process, we performed a gram-scale reaction of **1a** to provide the desired benzo[b]furan **3a** as shown in Scheme 7.

Scheme 7. Gram Scale Synthesis

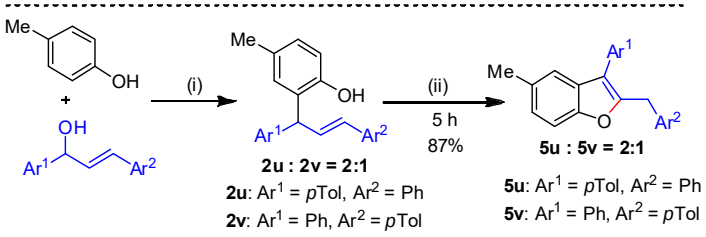


Further, a simple sequential reaction protocol has been developed for the synthesis of functionalized 2-benzyl benzo[b]furans via Friedel-Crafts alkylation of phenols with cinnamyl alcohols in the presence of Re_2O_7-catalyst followed by Pd(II)-catalysed oxidative annulation of *insitu* generated *o*-cinnamylphenols (Table 2). Synthesis of 2-benzyl benzo[b]furans were achieved in good yields. However, an unsymmetrical diaryl cinnamyl alcohol provides a mixture of *o*-cinnamylphenols (e.g., **2u** and **2v,** ratio: 2:1). This reflects their cationic stability under cyclization conditions which gave a mixture of benzo[b]furans (**5u** and **5v**) maintaining the same ratio.

Table 2. Sequential Protocol: Co-operative Catalysis[a]

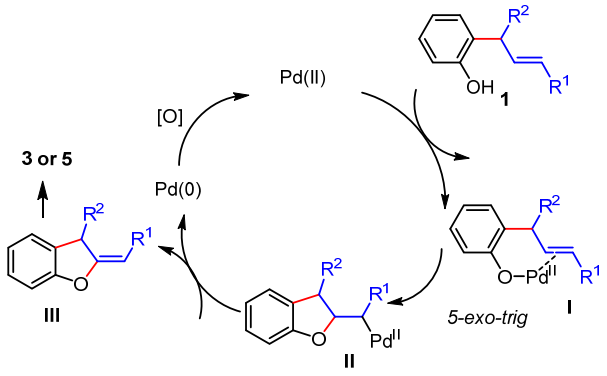


entry	3/5	t_1 (h)	t_2 (h)	yield (%)[b]
1	**3a**	7	6	52
2	**3b**	8	5	50
3	**3q**	12	6	58
4	**3r**	8	6	62
5	**3s**	10	4	63
6	**3t**	12	6	65
7	**5a**	9	4	53
8	**5b**	10	6	48
9	**5c**	10	6	47
10	**5h**	9	5	64
11	**5i**	10	7	63



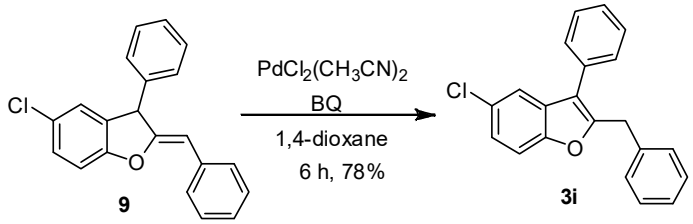
[a]Reaction conditions: (i) Alcohol (0.50 mmol), phenol (0.5 mmol), Re_2O_7 (5 mol %), CH_3CN (2 mL) refluxed at 80 °C. (ii) $PdCl_2(CH_3CN)_2$ (5 mol %), BQ (1 equiv), 1,4-dioxane (1 mL) refluxed at 80 °C. [b]Isolated yields.

Scheme 8. Proposed mechanism for current oxidative cyclization



On the basis of the reported literature[8b,c,11b,c,g] and the above results, a proposed mechanism was demonstrated in Scheme 8. The initial step involves oxa-palladation of the *o*-cinnamylphenol (**1**) to give an intermediate **I**, which undergoes intramolecular *5-exo-trig* cyclization to gives an intermediate **II**. Followed by a β-hydride elimination of intermediate **II** affords an intermediate **III**, which undergoes subsequent isomerization to form desired cyclisation product **3** or **5**. Further, the Pd(0) was assumed to be oxidized by benzoquinone (BQ) to regenerate the active Pd(II)-catalyst.

Scheme 9. Control Experiment[a,b]



[a]Reaction conditions: **9** (0.05 mmol), $PdCl_2(CH_3CN)_2$ (5 mol %), BQ (1 equiv), 1,4-dioxane (0.5 mL) refluxed at 80 °C. [b]Isolated yields.

A control experiment was carried out to forsee wheather the reaction was really procceding through the intermediate **III** as shown in Scheme 8. The compound **9** was independently synthesized and was

further applied to the standard reaction conditions (Scheme 9).[31] As expected, the desire product **3i** was obtained in good yield.

CONCLUSIONS

In conclusion, we have developed an efficient synthetic route for the synthesis of highly functionalized 2-benzyl benzo[b]furans *via* palladium catalyzed oxidative cyclization of *o*-cinnmaylphenols. It is noteworthy that this protocol provides an attractive synthetic strategy for the creation of 2-benzyl benzo[b]furan derivatives in good yield and with broad substrate scope. Further, a one-pot, sequential synthesis of *o*-cinnamylphenols, starting from readily available cinnmayl alcohols and phenols, followed by Pd(II)-catalysed oxidative annulation has also been developed. Considering the easy availability of cinnamyl alcohols and the water is the only by product for *o*-cinnamylphenols synthesis, the current strategy might have superior synthetic utility compared to many methods given in Scheme 1.

EXPERIMENTAL SECTION

General Remarks: All reagents and solvents were used as supplied commercially. Commercial $PdCl_2(CH_3CN)_2$ (99.99%) were stored in a desiccator over $CaCl_2$. Analytical thin-layer chromatography (TLC) were performed on 0.2 mm coated Science silica gel (EM 60-F254) plates. Visualization was accomplished with UV light (254 nm) and exposure to either ethanolic phosphomolybdic acid (PMA), anisaldehyde or $KMnO_4$, $CeSO_4$ + ammonium phosphomolybdate + 10% H_2SO_4, ninhydrine solution followed by heating. Melting points are uncorrected. ^{1}H NMR spectra were acquired on a 400 MHz spectrometer and chemical shifts are reported relative to the residual solvent peak. ^{13}C NMR spectra were acquired on a 100 MHz spectrometer and chemical shifts are reported in ppm relative to the residual solvent peak. Unless noted, NMR spectra were acquired in $CDCl_3$; individual peaks are reported as: multiplicity, integration, coupling constant in Hz. All IR spectra were obtained as neat films and selected absorbance's are reported in cm^{-1}.

General Procedure A: For the preparation of *ortho*-cinnamyl-phenols (1a-e), (1h-o), (1q-t) and (2a-e), (2h-i), (2k-r): To a stirred solution of cinnamyl alcohol (0.5 mmol) and phenol (0.6 mmol) in CH_3CN (2.0 ml), taken in a round-bottom flask attached to a refluxed condenser, Re_2O_7 (5 mol %) was added. Unless otherwise noted, the reaction was stirred at 80 ^oC for the given time. The reaction was quenched with the addition of brine solution (2 ml), followed by extraction with EtOAc (3 × 10 ml). The combined organic layer was dried over anhydrous $MgSO_4$. The solvent was removed under vacuum and the crude residue was purified by flash column chromatography (EtOAc/n-Hexane) on silica gel.

Characterization of the *ortho*-cinnamyl-phenols for 1a-e, 1h-o, 1q-t:

(*E*)-2-(1,3-Diphenylallyl)-4-methylphenol (1a):[21] The title compound was prepared using the general procedure A; Yield: 120 mg, 80% ; R_f = 0.40 (10:90 = EtOAc/n-Hexane); Light brown liquid ; IR (neat): 3365, 2963, 1612, 1465, 1265, 1208, 1124, 967, 825, 763 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38 (m, 3H), 7.33 – 7.29 (4H), 7.26 (m, 3H), 6.95 (d, J = 8.0 Hz, 2H), 6.72 – 6.65 (m, 2H), 6.35 (d, J = 16.0 Hz, 1H), 5.08 (d, J = 8.0 Hz, 1H), 4.63 (bs, 1H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.2, 142.1, 137.1, 131.7, 131.3, 130.2, 130.2, 129.1, 128.7, 128.6, 128.5, 128.5, 127.4, 126.8, 126.4, 116.2, 48.6, 20.7; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{22}H_{20}O$: 300.1; found: 300.1.

(*E*)-2-(1,3-Diphenylallyl)-4-methoxyphenol (1b):[21] The title compound was prepared using the general procedure A; Yield: 114 mg (72%); R_f = 0.38 (10:90 = EtOAc/n-Hexane); Light Yellow liquid; IR (neat): 3345, 2954, 1623, 1458, 1262, 1214, 1135, 958, 841, 760 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ, 7.38 (d, *J* = 7.3 Hz, 2H), 7.34-7.27 (m, 6H), 7.25-7.20 (m, 2H), 6.78-6.64 (m, 4H), 6.37 (d, *J* = 15.9 Hz, 1H), 5.12 (d, *J* = 7.1 Hz, 1H), 4.90-4.20 (bs, 1H), 3.73 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 153.8, 147.4, 141.9, 137.0, 131.9, 131.0, 130.8, 128.7, 128.6, 128.5, 127.5, 126.8, 126.4, 117.0, 115.9, 112.3, 55.7, 48.6; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{22}H_{20}O_2$: 316.1; found: 316.1.

(*E*)-4-(*tert*-Butyl)-2-(1,3-diphenylallyl)phenol (1c):[21] The title compound was prepared using the general procedure A; Yield: 139 mg, 81% ; R_f = 0.40 (10:90 = EtOAc/n-Hexane); Light brown liquid ; IR (neat): 3365, 2963, 1612, 1465, 1265, 1208, 1124, 967, 825, 763 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.30 (6H), 7.27 – 7.26 (m, 2H), 7.21 – 7.19 (2H), 6.78 – 6.73 (m, 2H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.14 (d, *J* = 4.0Hz, 1H), 4.76 (bs, 1H), 1.30 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.2, 143.7, 142.2, 137.2, 131.9, 131.4, 128.8, 128.6, 128.60, 128.5, 127.5, 126.8, 126.8, 126.4, 124.8, 115.9, 49.2, 34.2, 31.6; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{25}H_{26}O$: 342.1; found: 342.1.

(*E*)-4-(Benzyloxy)-2-(1,3-diphenylallyl)phenol (1d): The title compound was prepared using the general procedure A; Yield: 152 mg (77%); R_f = 0.32 (10:90 = EtOAc/n-Hexane); Brown liquid; IR (neat): 3425, 3029, 2653, 1624, 1542, 1475, 1426, 1013, 956, 845, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ, 7.45-7.26 (m, 15H), 6.89-6.62 (m, 4H), 6.39 (d, *J* = 15.9 Hz, 1H), 5.15 (d, *J* = 7.1 Hz, 1H), 5.00 (s, 2H), 4.77 (s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 153.0, 147.6, 141.9, 137.2, 137.1, 131.9, 131.1, 130.9,

128.7, 128.7, 128.6, 127.9, 127.7, 127.5, 126.9, 126.5, 117.0, 116.9, 113.7, 70.7, 48.4; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{28}H_{23}O_2$: 391.1693; found: 391.1711.

(*E*)-3-(1,3-Diphenylallyl)-[1,1'-biphenyl]-4-ol (1e): The title compound was prepared using the general procedure A; Yield: 137 mg (76%); R_f = 0.37(10:90 = EtOAc/n-Hexane); Yellow liquid; IR (neat): 3024, 2665, 1631, 1542, 1456, 1437, 1021, 963, 804, 751 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ, 7.59 (d, *J* = 7.2 Hz, 2H), 7.50-7.43 (m, 6H), 7.41-7.28 (9H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.83 (dd, *J* = 15.9, 7.2 Hz, 1H), 6.49 (d, *J* = 15.9 Hz, 1H), 5.28 (d, *J* = 7.1 Hz, 1H), 5.23-4.5 (bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 153.1, 142.1, 141.0, 137.1, 134.2, 132.1, 131.2, 129.9, 128.86, 128.84, 128.7, 128.68, 128.64, 127.6, 126.98, 126.90, 126.83, 126.82, 126.5, 116.8, 48.7; **HR-MS (APCI, m/z)**: $[M-H]^+$ calculated for $C_{27}H_{21}O$: 361.1587; found: 361.1615.

(*E*)-2-(1,3-Diphenylallyl)-4-fluorophenol (1h): The title compound was prepared using the general procedure A; Yield: 101 mg (66%); **R_f** = 0.32 (10:90 = EtOAc/n-Hexane); Light Yellow liquid; **IR (neat):** 3428, 2924, 1476, 1284, 1193, 1156, 1068, 984, 875, 762 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.04-8.01 (m, 1H), 7.65-7.63 (m, 1H), 7.56-7.51 (1H), 7.43-7.41 (m, 1H), 7.39-7.31 (3H), 7.28-7.25 (3H), 6.88-6.84 (m, 2H), 6.78-6.75 (m, 1H), 6.64 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.12 (d, *J* = 8.0 Hz, 1H), 4.98 (bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 157.31 (d, *J* = 238.3 Hz, 1C), 149.5 (d, *J* = 2.2 Hz, 1C), 145.2, 141.5, 132.3, 131.3 (d, *J* = 6.7 Hz, 1C), 130.5, 128.8 (2C), 128.62 (2C), 128.61 (2C), 127.6, 127.0, 126.4 (2C), 122.1, 117.2 (d, *J* = 8.1 Hz, 1C), 116.20 (d, *J* = 23.8 Hz, 1C), 114.2 (d, *J* = 23.1 Hz), 48.2; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{21}H_{16}FO$: 303.1180; found: 303.1187.

(*E*)-4-Chloro-2-(1,3-diphenylallyl)phenol (1i): The title compound was prepared using the general procedure A; Yield: 107 mg (67%); R_f = 0.37 (10:90 = EtOAc/n-Hexane); Brown Liquid; IR (neat): 3463, 2921, 1508, 1476, 1317, 1189, 1048, 987, 765 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.65 – 7.60 (1H), 7.53 – 7.43 (1H), 7.36 (m, 4H), 7.28 (m, 4H), 7.13 – 7.10 (2H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.64 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.11 (s, 1H), 5.09 (bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 152.1, 141.3, 136.8, 132.3, 131.4, 130.4, 129.5, 129.0, 128.8, 128.6, 128.6, 127.8, 127.7, 127.1, 126.5, 125.8, 48.3; **HR-MS** (**APCI**, **m/z**): $[M-H]^+$ calculated for $C_{21}H_{16}ClO$: 319.0884; found: 319.0911.

(*E*)-4-Bromo-2-(1,3-diphenylallyl)phenol (1j): The title compound was prepared using the general procedure A; Yield: 107 mg (63%); R_f = 0.35 (10:90 = EtOAc/n-Hexane); Brown Liquid; IR (neat): 3386, 3022, 1535, 1442, 1252, 1135, 1051, 924, 821, 752, cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.65 – 7.60 (1H), 7.53 – 7.43 (1H), 7.36 (m, 4H), 7.28 (m, 4H), 7.13 – 7.10 (2H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.64 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.11 (s, 1H), 5.09 (bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.1, 141.3, 136.8, 132.3, 131.4, 130.4, 129.5, 129.0, 128.8, 128.6, 128.5, 127.8, 127.7, 127.1, 126.5, 125.8, 48.3; **HR-MS** (**APCI, m/z**): $[M-H]^+$ calculated for $C_{21}H_{16}BrO$: 363.0379; found: 363.0385.

(*E*)-2-(1,3-Diphenylallyl)-4-iodophenol (1k): The title compound was prepared using the general procedure A; Yield: 134 mg (66%); R_f = 0.36 (10:90 = EtOAc/n-Hexane); Brown Liquid; IR (neat): 3341, 1475, 1410, 1084, 1018, 947, 814, 738 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.52 (m, 1H), 7.42 – 7.38 (5H), 7.31 (m, 2H), 7.26 (m, 2H), 7.13 (s, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.64 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.11 (s, 1H), 5.09 (bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.1, 145.4, 141.4, 136.7, 132.4, 131.3, 130.4, 128.7, 128.6, 128.5, 127.7, 127.6, 126.5, 125.7, 122.0, 117.5, 48.2; **HR-MS** (**APCI**, **m/z**): $[M-H]^+$ calculated for $C_{21}H_{16}IO$: 411.0240; found: 411.0238.

(*E*)-2,4-Dichloro-6-(1,3-diphenylallyl)phenol (1l): The title compound was prepared using the general procedure A; Yield: 42 mg (58%); R_f = 0.33 (10:90 = EtOAc/n-Hexane); Light brown Liquid; IR (neat): 3427, 3375, 3031, 2905, 1521, 1042, 957, 719cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.60 – 7.58 (m, 2H), 7.50 – 7.46 (2H), 7.45 – 7.41(3H), 7.38 – 7.30 (4H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.83 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 5.28 (d, *J* = 8.0 Hz, 1H), 5.11 (bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.1, 142.1, 141.0, 137.1, 134.2, 132.1, 131.2, 129.9, 128.9, 128.8, 128.6, 127.6, 126.9, 126.8, 126.5, 116.8, 48.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{21}H_{15}Cl_2O$: 353.0494; found: 353.0485.

(*E*)-2-Bromo-4-chloro-6-(1,3-diphenylallyl)phenol (1m): The title compound was prepared using the general procedure A; Yield: 107 mg (55%); R_f = 0.34 (10:90 = EtOAc/n-Hexane); Yellow Liquid; IR (neat):3422, 2931, 2845, 15847, 1486, 1452, 1346, 1261, 1107, 968, 819, 745cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.83 (2H), 7.41 – 7.33 (4H), 7.31 – 7.26 (3H), 6.86 – 6.74 (m, 2H), 6.63 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.12 (d, *J* = 8.0 Hz, 1H), 4.98

(bs, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 154.9, 149.1, 137.1, 131.1, 131.0, 129.0, 128.7, 128.6, 128.6, 127.5, 126.7, 126.5, 117.1, 115.9, 112.4, 55.7, 48.6; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{21}H_{15}BrClO$: 398.9989; found: 398.9980.

(*E*)-4-Chloro-2-(1,3-diphenylallyl)-6-methylphenol (1n): The title compound was prepared using the general procedure A; Yield: 102 mg (60%); R_f = 0.29 (10:90 = EtOAc/n-Hexane); Yellow Liquid; IR (neat): 3421, 2934, 1467, 1258, 1196, 1142, 1019, 970, 843, 736 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 – 7.35 (4H), 7.29 – 7.21 (5H), 6.95 (m, 2H), 6.72 (s, 1H), 6.68 (m, 1H), 6.35 (d, *J* = 16.0 Hz, 1H), 5.08 (d, *J* = 8.0 Hz, 1H), 4.63 (bs, 1H), 2.25 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.3, 142.2, 137.2, 131.7, 131.4, 130.2, 130.2, 129.1, 128.7, 128.6, 128.5, 128.4, 127.4, 126.7, 126.4, 116.2, 48.5, 20.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{18}ClO$: 333.1040; found: 333.1035.

(*E*)-2-Benzyl-4-chloro-6-(1,3-diphenylallyl)phenol (1o): The title compound was prepared using the general procedure A; Yield: 130 mg (62%); R_f = 0.32 (10:90 = EtOAc/n-Hexane); Yellow Liquid; IR (neat): 3326, 2937, 1483,1257, 1194, 1148, 1052, 953, 754cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.3 (m, 3H), 7.33 –7.28(6H), 7.26 – 7.25(4H), 7.20 (m, 2H), 7.02 (dd, *J* = 8.0, 4.0 Hz, 2H), 6.62 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.34 (d, *J* = 16.0 Hz, 1H), 5.03 (d, *J* = 8.0 Hz, 1H), 4.80 (s, 1H), 3.94 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 150.4, 141.0, 139.0, 136.7, 132.5, 131.4, 130.2, 129.8, 129.1, 128.9, 128.8, 128.7, 128.6, 128.6, 127.7, 127.6, 127.3, 126.6, 126.5, 125.6, 48.7, 36.4; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{28}H_{22}ClO$: 409.1354; found: 409.1355.

(*E*)-4-Bromo-2-(1,3-diphenylallyl)-6-methoxyphenol (1q): The title compound was prepared using the general procedure A; Yield: 132 mg (67%); R_f = 0.26 (10:90 = EtOAc/n-Hexane); Yellow Liquid; IR (neat): 3362, 3024, 2956, 1478, 1465, 1236, 1145, 1014, 925, 845, 763 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.37 – 7.30 (3H), 7.30 – 7.26 (4H), 7.23 (m, 2H), 6.75 (m, 2H), 6.69 – 6.65(2H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.12 (d, *J* = 4.0 Hz, 1H), 4.57 (bs, 1H), 3.73 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.8, 147.5, 141.9, 137.0, 131.9, 131.1, 130.7, 128.7, 128.6, 128.5, 127.3, 126.8, 126.3, 117.0, 115.9, 112.3, 55.7, 48.6; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{18}BrO_2$: 393.0484; found: 393.0476.

(*E*)-2-(1,3-Diphenylallyl)-3,5-dimethylphenol (1r): The title compound was prepared using the general procedure A; Yield: 124 mg (78%); R_f = 0.32 (40:60 = Dichloromethane/n-Hexane); Yellow

Liquid; IR (neat): 3358, 3021, 2966, 1468, 1314, 1240, 1142, 1012, 933, 856, 756cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.43 – 7.42 (2H), 7.36 – 7.33 (5H), 7.31 – 7.25 (3H), 6.87 (dd, *J* = 16.0, 4.0 Hz, 1H), 6.69 (s, 1H), 6.56 (s, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.29 (d, *J* = 8.0 Hz, 1H), 5.00 (s, 1H), 2.37 (s, 3H), 2.30 (s, 3H).**^{13}C NMR (100 MHz, $CDCl_3$):** δ 154.5, 141.8, 137.9, 137.6, 137.1, 132.5, 129.9, 128.8, 128.6, 127.8, 127.6, 126.8, 126.5, 124.3, 124.1, 115.9, 46.5, 20.9, 20.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{23}H_{22}O$: 313.1593; found: 313.1571.

(*E*)-6-(1,3-Diphenylallyl)-2,3-dimethylphenol (1s): The title compound was prepared using the general procedure A; Yield: 121 mg (77%); R_f = 0.33 (40:60 = Dichloromethane/n-Hexane); Light Yellow Liquid; IR (neat): 3362, 3024, 2956, 1478, 1465, 1236, 1145, 1014, 925, 845, 763 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.45 – 7.43 (3H), 7.40 – 7.32 (5H), 7.30 – 7.26 (2H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.77 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 5.12 (d, J = 8.0 Hz, 1H), 4.90 (s, 1H), 2.34 (s, 3H), 2.22 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.7, 142.1, 137.1, 136.7, 131.9, 131.4, 128.9, 128.7, 128.6, 127.6, 127.0, 126.6, 126.5, 126.5, 123.5, 122.2, 49.2, 20.2, 11.9; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{23}H_{21}O$: 313.1587; found: 313.1567.

(*E*)-2-(1,3-Diphenylallyl)-3,5,6-trimethylphenol (1t): The title compound was prepared using the general procedure A; Yield: 132 mg (80%); R_f = 0.35 (40:60 = Dichloromethane/n-Hexane); Light Yellow Liquid; IR (neat): 3348, 3014, 2956, 1453, 1435, 1232, 1134, 1012, 933, 856, 758cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.44 – 7.42 (3H), 7.37 – 7.35 (4H), 7.33 – 7.25 (3H), 6.86 (dd, J = 16.0, 8.0 Hz, 1H), 6.70 (s, 1H), 6.50 (d, J = 16.0 Hz, 1H), 5.29 (d, J = 8.0 Hz, 1H), 5.08 (s, 1H), 2.36 (s, 3H), 2.27 (s, 3H), 2.13 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.6, 141.6, 137.0, 136.4, 134.1, 132.7, 129.8, 128.9, 128.6, 127.9, 127.6, 126.9, 126.5, 124.5, 124.1, 122.1, 46.9, 20.5, 19.9, 11.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{24}H_{24}O$: 327.1749; found: 327.1756.

Compound **1f-h**, **1p** and **1u-v** were not separable in column chromatography (it was having the same Rf value with their corresponding phenol counterpart).

Characterization of the *ortho*-cinnamyl phenol 2a-e, 2h-o and 2s-t: The title compound was prepared using the general procedure A:

(*E*)-2-(1,3-Di-p-tolylallyl)-4-methylphenol (2a): The title compound was prepared using the general procedure A: Yield: 126 mg (77%); R_f = 0.31 (10:90 = EtOAc/n-Hexane); Yellow Liquid; IR (neat): 3433,2936, 1578, 1523, 1235, 1199, 1035, 956, 801, 765cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.32 (d,

J = 8.0 Hz, 2H), 7.20 – 7.18 (3H), 7.15 – 7.10 (3H), 6.99 (m,2H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.67 (dd, *J* = 12.0, 4.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.06 (d, *J* = 8.0 Hz, 1H), 4.80 (bs, 1H), 2.37 (s, 3H), 2.36 (s, 3H), 2.29 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):**δ 151.3, 139.1, 137.2, 136.4, 134.4, 131.5, 130.5, 130.2, 130.1, 129.5, 129.4, 129.3, 128.5, 128.4, 126.4, 116.3, 48.4, 21.2, 21.1, 20.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{24}H_{23}O$: 327.1743; found: 327.1738.

(*E*)-2-(1,3-Bis(4-fluorophenyl)allyl)-4-methylphenol (2b): The title compound was prepared using the general procedure A; Yield: 110 mg (65%); R_f = 0.30 (10:90 = EtOAc/n-Hexane); Yellow Liquid; IR (neat): 3421, 2944, 1489, 1457, 1281, 1047, 935, 754cm^{-1};**^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.35 – 7.31 (2H), 7.23 – 7.19 (2H), 7.02 – 6.91 (6H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.57 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 5.08 (d, *J* = 8.0 Hz, 1H), 4.65 (s, 1H), 2.26 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 150.9, (d, *J* = 238.3 Hz, 1C), 137.9, 137.9,(d, *J* = 3.3 Hz, 1C) 133.2, 133.1 (2C), 131.0, 130.6, 130.3, 130.1 (2C), 129.0, 128.5, 127.9, 127.8, (d, *J* = 8.0 Hz, 1C), 116.1 (2C),115.5 (d, *J* = 4.5 Hz, 1C), 115.3,(d, *J* = 4.2 Hz, 1C), 47.5, 20.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{17}F_2O$: 335.1242; found: 335.1237.

(*E*)-2-(1,3-Bis(4-Chlorophenyl)allyl)-4-methylphenol (2c): The title compound was prepared using the general procedure A: Yield: 116 mg (63%); R_f = 0.33 (10:90 = EtOAc/n-Hexane); Light Yellow Liquid; IR (neat): 3254, 3104, 1478, 1424, 1275, 1204, 1112, 1042, 957, 754cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.31 – 7.25 (6H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.97 – 6.93(2H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.64 (dd, *J* = 16.0, 8.0 Hz, 1H), 6.28 (dd, *J* = 16.0, 4.0 Hz, 1H), 5.11 (d, *J* = 8.0 Hz, 1H), 4.74 (s, 1H), 2.27 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 150.9, 140.8, 135.5, 133.1, 132.4, 131.8, 130.7, 130.4, 130.1, 129.9, 128.8, 128.7, 128.6, 128.5, 127.6, 116.1, 47.5, 20.7; **HR-MS (APCI, m/z):**$[M-H]^+$ calculated for $C_{22}H_{17}Cl_2O$: 367.0651; found: 367.0653.

(*E*)-2-(1,3-Bis(4-Bromophenyl)allyl)-4-methylphenol (2d):[22] The title compound was prepared using the general procedure A; Yield: 136 mg (61%); R_f = 0.35 (10:90 = EtOAc/n-Hexane); Light Yellow Liquid; IR (neat): 3356, 3026, 1494, 1487, 1325, 1245, 1104, 1008, 956, 824, 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44– 7.41 (4H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 6.96 – 6.91 (2H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.63(t, *J* = 8.0 Hz, 1H), 6.26 (d, *J* = 16.0 Hz, 1H), 5.08 (d, *J* = 8.0 Hz, 1H), 4.65 (bs, 1H), 2.26 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 150.9, 141.3, 135.9, 131.9, 131.6, 131.6,

130.8, 130.4, 130.4, 130.1, 128.7, 128.6, 127.9, 121.3, 120.6, 116.1, 47.6, 20.7; **GCLR-MS (EI, m/z):**$[M]^+$ calculated for $C_{22}H_{18}Br_2O$: 455.9; found: 455.9.

(*E*)-2-(1,3-Di([1,1'-Biphenyl]-4-yl)allyl)-4-methylphenol (2e): The title compound was prepared using the general procedure A; Yield: 172 mg (78%); R_f = 0.36 (10:90 = EtOAc/n-Hexane); Light Yellow Liquid; IR (neat): 3324, 3048, 1463, 1410, 1281, 1232, 1108, 1072, 947, 764 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.64 – 7.58 (8H), 7.52 – 7.49 (4H), 7.47– 7.45 (m, 2H), 7.39 – 7.35 (m, 4H), 7.05 (m, 1H), 7.02 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.82 (d, *J* = 16.0, 8.0 Hz, 1H), 6.77 (d, *J* = 8.0, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 5.22 (d, *J* = 8.0 Hz, 1H), 4.85 (s, 1H), 2.33 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.2, 141.4, 140.9, 140.8, 140.3, 139.6, 136.2, 131.6, 131.4, 130.3, 130.3, 130.1, 129.2, 129.1, 128.8, 128.8, 128.6, 127.4, 127.3, 127.3, 127.1, 127.0, 126.9, 116.3, 48.3, 20.8; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{34}H_{27}O$: 451.2056; found: 451.2064.

2-Cinnamyl-4-methylphenol (2h):[23] The title compound was prepared using the general procedure A; Yield: 85 mg (76%); R_f = 0.36 (10:90 = EtOAc/n-Hexane); Light yellow liquid; IR (neat): 3368, 2967, 1603, 1485, 1271, 1235, 1206, 1147, 966, 834, 766cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.38 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.00 (s, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.41 (m, 1H), 4.92 (s, 1H), 3.56 (d, *J* = 6.3 Hz, 2H), 2.30 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 151.7, 137.2, 131.4, 131.0, 130.2, 128.5, 128.3, 128.1, 127.3, 126.2, 125.5, 115.6, 34.1, 20.5; **GCLR-MS (ESI, m/z):** $[M]^+$ calculated for $C_{16}H_{16}O$: 224.1; found: 224.1.

2-Cinnamyl-4-methoxyphenol (2i):[24] The title compound was prepared using the general procedure A; Yield: 89 mg (74%); R_f = 0.34 (10:90 = EtOAc/n-Hexane); Light brown liquid ; IR (neat): 3358, 2947, 1613, 1465, 1251, 1235, 1210, 1137, 948, 832, 760cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.35 – 7.33 (2H), 7.30 – 7.26 (2H), 7.21 – 7.18 (m, 1H), 6.76 – 6.73 (2H), 6.68 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 6.39 – 6.32 (1H), 4.58 (s, 1H), 3.75 (s, 3H), 3.52 (d, *J* = 4.0 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 151.7, 137.2, 131.4, 131.0, 130.2, 128.5, 128.3, 128.1, 127.3, 126.2, 125.5, 115.6, 34.1, 20.5; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{16}H_{16}O_2$: 240.1; found: 240.1.

(*E*)-4-Methyl-2-(4-phenylbut-3-en-2-yl)phenol (2j):[25] The title compound was prepared using the general procedure A; Yield: 72 mg (60%); R_f = 0.34 (10:90 = EtOAc/n-Hexane); Light brown liquid; IR

(neat): 2954, 1684, 1475, 1249, 1263, 1208, 1147, 1023, 949, 850, 760 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.38 – 7.36 (2H), 7.31 – 7.27 (2H), 7.23(m, 1H), 7.0 – 6.91 (2H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.53 – 6.40 (2H), 4.83 (s, 1H), 3.86 (q, *J* = 16.0, 8.0 Hz, 1H), 2.28 (s, 3H), 1.48 (d, *J* = 8.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.2, 137.2, 134.1, 130.5, 130.2, 129.2, 128.6, 128.5, 127.9, 127.3, 126.3, 115.9, 36.8, 20.7, 19.5; **GCLR-MS (EI, m/z):**$[M]^+$ calculated for $C_{17}H_{18}O$: 238.1; found: 238.1.

(*E*)-4-Methoxy-2-(4-phenylbut-3-en-2-yl)phenol (2k):[25] The title compound was prepared using the general procedure A; Yield: 93 mg (73 %); R_f = 0.34 (10:90 = EtOAc/n-Hexane); Light brown liquid; IR (neat): 2956, 1680, 1465, 1253, 1260, 1218, 1152, 1026, 952, 847, 753cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37-7.35 (2H), 7.31-7.27 (2H), 7.22-7.29 (m, 1H), 6.79 (d, *J* = 4.0 Hz, 1H), 6.74 (d, *J* = 4.0 Hz, 1H), 6.67 (dd, *J* =12.0, 8.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 6.41 (dd, *J* = 16.0, 8.0 Hz, 1H), 4.87 (s, 1H), 3.88 (m, 1H), 3.77 (s, 3H), 1.47 (d, *J* = 8.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.9, 147.5, 137.2, 133.8, 132.2, 129.42, 128.5, 127.3, 126.3, 116.7, 114.0, 111.9, 55.8, 55.7, 36.8, 36.8, 19.5; **HR-MS (APCI, m/z):** $[M]^+$ calculated for $C_{17}H_{18}O_2$: 254.1307; found: 254.1293.

(*E*)-4-Methyl-2-(4-(1-methyl-1H-indol-3-yl)but-3-en-2-yl)phenol (2l): The title compound was prepared using the general procedure A; Yield: 82 mg (56%); R_f = 0.35 (40:60 = Dicholoromethane/n-Hexane); Yellow liquid ; IR (neat): 2964, 2132, 1845, 1712, 1613, 1472, 1329, 1243, 1234, 1145, 967, 863, 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 8.33 – 8.31 (m, 1H), 7.58 (s, 1H), 7.36 – 7.27 (3H), 7.22 – 7.18 (1H), 7.02 (d, J = 4.0 Hz, 1H), 6.92 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.49 (d, *J* = 3.4 Hz, 1H), 4.01 – 3.98 (1H), 3.78 (s, 3H), 2.29 (s, 3H), 1.49 (d, *J* = 4.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 151.6, 139.7, 137.9, 137.5, 134.6, 131.2, 129.7, 128.5, 126.2, 125.3, 124.1, 123.0, 122.0, 117.9, 115.8, 109.9, 36.3, 33.6, 20.7, 19.8; **HR-MS (APCI, m/z)**: $[M+H]^+$ calculated for $C_{20}H_{22}NO$: 292.1701; found: 292.1723.

(*E*)-4-Methyl-2-(4-(1-methyl-1H-pyrrol-2-yl)but-3-en-2-yl)phenol (2m): The title compound was prepared using the general procedure A; Yield: 63 mg (52%); R_f = 0.32 (40:60 = Dicholoromethane/n-Hexane); Yellow liquid; IR (neat): 2964, 2132, 1845, 1712, 1613, 1472, 1329, 1243, 1234, 1145, 967, 863, 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.41– 7.40 (m, 1H), 7.34 – 7.31 (1H), 7.25 (m, 1H), 7.03 (s, 1H), 6.94 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.51 (m, 1H), 4.01 – 3.96 (1H), 3.91 (s, 3H), 2.31 (s, 3H), 1.52 (d, *J* = 4.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)**: δ 164.7, 151.4, 137.4, 134.4, 132.1, 131.0, 129.9, 128.5, 127.8, 127.1, 126.2, 115.8, 114.4,

55.6, 36.3, 20.7, 19.7; **HR-MS (APCI, m/z)**: $[M+H]^+$ calculated for $C_{16}H_{20}NO$: 242.1545; found: 242.1536.

(*E*)-2-(4-(Furan-2-yl)but-3-en-2-yl)-4-methylphenol (2n):[25] The title compound was prepared using the general procedure A; Yield: 60 mg (53%); R_f = 0.35 (40:60 = Dichloromethane/n-Hexane); Light brown liquid; IR (neat): 2834, 1724, 1652, 1421, 1253, 1241, 1150, 1027, 956, 875, 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.38 – 7.36 (d, *J* = 8.0 Hz, 1H), 7.28 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.00 (s, 1H), 6.93 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.43 (dd, *J* = 16.0, 8.0 Hz, 1H), 4.83 (bs, 1H), 3.86 (m, 1H), 2.28 (s, 3H), 1.48 (d, *J* = 8.0 Hz, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.3, 151.2, 137.2, 134.1, 130.5, 130.2, 129.2, 128.5, 127.9, 127.3, 126.2, 115.9, 36.8, 20.7, 19.5; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{15}H_{15}O_2$: 227.1072; found: 227.1069.

(*E*)-2-(1-Cyclohexyl-3-phenylallyl)-4-methylphenol (2o): The title compound was prepared using the general procedure A; Yield: 72 mg (62%); R_f = 0.35 (10:90 = EtOAc/n-Hexane); Light brown liquid; IR (neat): 2956, 1663, 1524, 1455, 1245, 1239, 1205, 1124, 957, 862, 752cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.35 – 7.33 (2H), 7.29 – 7.26 (2H), 7.21 – 7.25 (m, 1H), 6.96 (d, *J* = 2.0 Hz, 1H), 6.85 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 6.43 – 6.41 (m, 2H), 4.58 (s, 1H), 3.39 (m, 1H), 2.27 (s, 3H), 1.96 (d, *J* = 12.0 Hz, 1H), 1.80 – 1.72 (2H), 1.62 (2H), 1.26 – 1.12 (4H), 1.02 – 0.82 (2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 150.9, 137.6, 132.3, 130.4, 130.1, 129.6, 129.5, 128.4, 127.4, 126.9, 126.1, 115.7, 50.0, 41.2, 31.8, 31.4, 26.6, 26.4, 26.4, 20.7; **HR-MS (APCI, m/z):**$[M+H]^+$ calculated for $C_{22}H_{26}O$: 307.2068; found: 307.2057.

Compound **2f-g** and **2p-r** was not separable in column chromatography (it was having the same Rf value with their corresponding phenol counterpart).

Preparation of 2s & **2t: 2s** and **2t** were synthesized by a previously reported method and the characterization data for these compound were matched with the previously reported data.[30]

2-Allyl-4-methoxyphenol (2s): R_f = 0.35 (10:90 = EtOAc/n-Hexane); Light Yellow Liquid; IR (neat): 3326, 2989, 2931, 1446, 1405, 1182, 1034, 965, 846, 739 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ, 6.77 (d, *J* = 8.0 Hz, 1H), 6.72 – 6.69 (2H), 6.08 – 6.0 (1H), 5.20 – 5.16 (2H), 4.88 – 4.84 (m, 1H), 3.79 (s, 3H), 3.41 (d, *J* = 8.0 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 153.7, 148.0, 136.2, 126.6, 116.5, 116.5, 115.9, 112.6, 55.7, 35.3; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{10}H_{12}O_2$: 164.0; found: 164.0.

2-Allyl-4-methylphenol (2t): R_f = 0.35 (05:95 = EtOAc/n-Hexane); Light Yellow Liquid; IR (neat): 3348, 3014, 2956, 1453, 1435, 1232, 1134, 1012, 933, 856, 758 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ, 6.94 – 9.92 (2H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.07 – 5.97 (1H), 5.17 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.14 (t, *J* = 4.0 Hz, 1H), 4.86 (s, 1H), 3.38 (d, *J* = 8.0 Hz, 2H), 2.27 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 151.8, 136.6, 130.9, 130.1, 128.3, 125.1, 116.4, 115.7, 35.1, 20.5; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{10}H_{12}O$: 148.08; found: 148.1.

General Procedure B: Synthesis of 2-benzyl benzo[b]furan *via* palladium catalyzed oxidative cyclization of *o*-cinnamylphenols: *o*-Cinnamylphenols **1** or **2** (0.20 mmol) in 1,4-dioxane (1 mL) was taken in a 5 mL round bottom flask, $PdCl_2(CH_3CN)_2$ (5 mol %) and benzoquinone (1 equiv) was added. The reaction mixture containing RB flask was fitted with a reflux condenser, placed into a preheated oil bath at 80 ºC. After consumption of starting material (followed by TLC analysis), the mixture was cooled to room temperature and filtered through celite. The filtrate was diluted with H_2O (10 mL) followed by washing with ethylacetate (3 x 10 mL). The organic extract was dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure to provide the crude product **3** or **5**, respectively, which was purified by flash chromatography on silica-gel using n-hexane/ethylacetate as eluent.

Characterization of benzo[b]furan products (3a-v) & (5a-v): 2-Benzyl-5-methyl-3-phenylbenzofuran (3a):[26a] The title compound was prepared using the general procedure B; Yield: 50 mg (85%); R_f = 0.41 (02:98 = EtOAc/n-Hexane); **mp:**148-150 ^{o}C; IR (neat): 3065, 2920, 1614, 1462, 1448, 1321, 1263, 1223, 1056, 1018, 965, 820, 765 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.56 – 7.49 (4H), 7.41 (m, 2H), 7.36 – 7.25 (6H), 7.12 (d, *J* = 8.0Hz, 1H), 4.23 (s, 2H), 2.46 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 152.8, 152.7, 138.1, 132.7, 132.2, 129.1, 128.9, 128.8, 128.7, 128.5, 127.3, 126.6, 125.2, 119.6, 118.2, 110.7, 32.9, 21.4; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{22}H_{18}O$: 298.1; found: 298.1.

2-Benzyl-5-methoxy-3-phenylbenzofuran (3b):[26a] The title compound was prepared using the general procedure B; Yield: 58 mg (92%); R_f = 0.36 (05:95 = EtOAc/n-Hexane); White solid; **mp:**165-168 ^{o}C; IR (neat): 3057, 2926, 1548, 1484, 1460, 1444, 1278, 1131, 1065, 1051, 912, 885, 823, 748, cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.51-7.47 (m, 4H), 7.41-7.34 (m, 2H), 7.30 (d, *J* = 7.2 Hz, 2H), 7.27-7.22 (m, 3H), 7.06 (d, *J* = 2.5 Hz, 1H), 6.89 (dd, *J* = 8.9, 2.6 Hz, 1H), 4.20 (s, 2H), 3.82 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 156.1, 153.5, 149.3, 137.9, 132.6, 129.2, 129.0, 128.9, 128.6, 128.5, 127.3,

126.6, 118.5, 112.5, 111.6, 102.4, 56.0, 33.0; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{22}H_{18}O_2$: 314.1; found: 314.1.

2-Benzyl-5-(tert-butyl)-3-phenylbenzofuran (3c):[26a] The title compound was prepared using the general procedure B; Yield: 61 mg (90%); R_f = 0.38 (05:95 = EtOAc/n-Hexane); White solid ; **mp:**175-176 ^oC; IR (neat): 3086, 2932, 1628, 1468, 1436, 1327, 1243, 1125, 1056, 1016, 958, 829, 760 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.56 (d, *J* = 1.5 Hz, 1H), 7.52-7.48 (m, 4H), 7.40-7.33 (m, 3H), 7.25 (5H), 4.18 (s, 2H), 1.35 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 152.7, 152.5, 145.9, 138.0, 132.7, 129.1, 128.8, 128.5, 128.4, 128.2, 127.2, 126.5, 121.8, 118.4, 115.7, 110.4, 34.8, 32.9, 31.9; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{25}H_{24}O$: 340.1; found: 340.1.

2-Benzyl-5-(benzyloxy)-3-phenylbenzofuran (3d): The title compound was prepared using the general procedure B; Yield: 67 mg (86%); R_f = 0.35 (0.5:95 = EtOAc/n-Hexane); White solid; **mp:**182-184 ^oC; IR (neat): 2985, 2956, 1624, 1512, 1448, 1381, 1332, 1310, 1258, 1175, 1042, 948, 879, 852, 825, 745 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.53-7.45 (m, 6H), 7.41 (3H), 7.36-7.31 (4H), 7.28 (d, *J* = 7.0 Hz, 3H), 7.18 (d, *J* = 2.5 Hz, 1H), 6.99 (dd, *J* = 8.9, 2.5 Hz, 1H), 5.08 (s, 2H), 4.22 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 155.3, 153.5, 149.5, 137.9, 137.3, 132.5, 129.2, 129.0, 128.9, 128.6, 128.59, 128.54, 127.9, 127.6, 127.3, 126.6, 118.5, 113.2, 111.6, 104.2, 71.0, 33.0; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{28}H_{23}O_2$: 391.1698; found: 391.1704.

2-Benzyl-3,5-diphenylbenzofuran (3e):[26a] The title compound was prepared using the general procedure B; Yield: 63 mg (87%); R_f = 0.43 (05:90= EtOAc/n-Hexane); White solid; **mp:**174-176 ^oC; IR (neat): 2986, 1621, 1578, 1514, 1451, 1272, 1158, 1062, 1015, 938, 865, 819, 740, cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.76 (s, 1H), 7.59 (d, J = 7.2 Hz, 2H)), 7.55 (d, *J* = 7.0 Hz, 2H), 7.50 (d, *J* = 7.3 Hz, 4H), 7.42 (t, *J* = 7.6 Hz, 3H), 7.34-7.28 (m, 6H), 4.23 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 154.0, 153.3, 141.8, 137.8, 136.6, 132.3, 129.2, 129.1, 128.9, 128.7, 128.6, 128.5, 127.5, 127.4, 126.8, 126.6, 123.6, 118.3, 118.5, 111.2, 32.9; **GCLR-MS (ESI, m/z):** $[M]^+$ calculated for $C_{27}H_{20}O$: 360.1; found: 360.1.

2-Benzyl-3-phenylbenzofuran-5-carbonitrile (3f): The title compound was prepared using the general procedure B; Yield: 49 mg (77%); R_f = 0.23 (05:10 = EtOAc/n-Hexane); White solid ; **mp:**168-170 ^oC; IR (neat)**:** 2942, 1615, 1532, 1441, 1229, 1167, 1120, 1035, 1020, 965, 826, 780, 746 cm^{-1}; **^{1}H NMR**

(400 MHz, $CDCl_3$): δ, 7.76 (s, 1H), 7.57-7.53 (m, 3H), 7.49 (2H), 7.49 (1H), 7.42-7.38 (m, 2H), 7.32 (dd, *J* = 7.6, 1.2 Hz, 2H), 7.29 (d, *J* = 6.3 Hz, 2H), 4.23 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 154.0, 153.3, 141.8, 137.8, 136.6, 132.3, 129.1, 128.9, 128.7, 128.67, 128.5, 127.5, 126.8, 126.6, 123.6, 118.3, 111.2, 32.9; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{22}H_{16}NO$: 310.1232;found: 310.1229.

2-Benzyl-5-nitro-3-phenylbenzofuran (3g): The title compound was prepared using the general procedure B; Yield: 50 mg (76%); R_f = 0.31(05:90 = EtOAc/n-Hexane); Yellow Solid; **mp:**170-172 ^oC; IR (neat): 2965, 2775, 2082, 1542, 1456, 1420, 1136, 1123, 1013, 982, 878, 816, 736 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.69 (d, *J* = 1.8 Hz, 1H), 7.51–7.47 (4H), 7.43-7.39 (m, 1H), 7.36 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.31-7.29 (3H), 7.25-7.21 (3H), 4.20 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.9, 153.1, 137.5, 131.7, 130.7, 129.03, 129.02, 128.7, 128.5, 127.6, 126.8, 126.7, 122.4, 117.9, 115.9, 112.6, 32.9; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{21}H_{16}NO_3$: 330.1130; found: 330.1132.

2-Benzyl-5-fluoro-3-phenylbenzofuran (3h): The title compound was prepared using the general procedure B; Yield: 47 mg (78%); R_f = 0.42(05:90 = EtOAc/n-Hexane); White Solid; **mp:**168-170 ^oC; IR (neat): 2985, 1686, 1542, 1512, 1458, 1345, 1238, 1164, 1087, 1042, 1013, 934, 878, 841, 797, 739 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.48 (d, *J* = 4.4 Hz, 4H), 7.38 (m, 2H), 7.30 (d, *J* = 7.2 Hz, 2H), 7.26-7.20 (m, 4H), 6.98 (td, *J* = 9.0, 2.6 Hz, 1H), 4.19 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 160.6, 158.2, 154.4, 150.5, 137.6, 131.9, 129.5 (d, *J* = 10.3 Hz), 128.9 (d, *J* = 4.9 Hz), 128.6 (d, *J* = 19.1 Hz), 127.5, 126.7, 118.5 (d, *J* = 3.8 Hz), 111.7, 111.6, 111.4, 105.45 (d, *J* = 25.4 Hz), 33.0; **HR-MS (APCI, m/z):** $[M]^+$ calculated for $C_{21}H_{15}FO$: 302.1101; found: 302.1126.

2-Benzyl-5-chloro-3-phenylbenzofuran (3i):[26a] The title compound was prepared using the general procedure B; Yield: 51 mg (80%); R_f = 0.45 (05:95= EtOAc/n-Hexane); White Solid; **mp:**175-178 ^oC; IR (neat): 2931, 1599, 1545, 1476, 1439, 1412, 1328, 1259, 1232, 1112, 1084, 1060, 1031, 905, 874, 746 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.53 (d, *J* = 2.0 Hz, 1H), 7.48 (d, *J* = 1.7 Hz, 1H), 7.47 (2H), 7.41-7.34 (m, 3H), 7.29 (d, *J* = 6.4 Hz, 2H), 7.24-7.20 (m, 4H), 4.19 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 154.1, 152.7, 137.5, 131.7, 130.1, 129.0, 128.9, 128.7, 128.49, 128.45, 127.6, 126.7, 124.1, 119.4, 118.0, 112.1, 32.9; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{21}H_{15}ClO$: 318.1; found: 318.1.

2-Benzyl-5-bromo-3-phenylbenzofuran (3j):[26a] The title compound was prepared using the general procedure B; Yield: 55 mg (76%); R_f = 0.43(05:95 = EtOAc/n-Hexane); White Solid; **mp:**169-171 ^oC;

IR (neat): 2923, 2093, 1856, 1756, 1486, 1356, 1092, 954, 826, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ, 7.69 (d, *J*= 1.8 Hz, 1H), 7.50 -7.46 (m, 4H), 7.42-7.40 (m, 1H), 7.36 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.34-7.28 (m, 3H), 7.27-7.22 (m, 3H), 4.20 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ, 153.9, 153.1, 137.5, 131.7, 130.7, 129.03, 129.02, 128.7, 128.5, 127.6, 126.8, 126.7, 122.4, 117.9, 115.9, 112.6, 32.9; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{21}H_{15}BrO$: 362.0; found: 362.0.

2-Benzyl-5-iodo-3-phenylbenzofuran (3k):[26a] The title compound was prepared using the general procedure B; Yield: 65 mg (79%); R_f = 0.38 (05:90 = EtOAc/n-Hexane); White Solid; **mp:**182-184 ˚C; IR (neat): 2945, 1924, 1826, 1584, 1456, 1258, 1142, 1035, 924, 846, 743 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.89 (d, *J* = 1.6 Hz, 1H), 7.54 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.48 (d, *J*= 2.3 Hz, 4H), 7.41-7.38 (m, 1H), 7.30 (2H), 7.24–7.20 (4H), 4.19 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.7, 153.5, 137.50 132.5, 131.7, 131.4, 129.07, 129.02, 128.7, 128.6, 128.5, 127.6, 126.7, 117.6, 113.1, 86.3, 32.8; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{21}H_{15}IO$: 410.0; found: 410.1.

2-Benzyl-5,7-dichloro-3-phenylbenzofuran (3l): The title compound was prepared using the general procedure B; Yield: 52 mg (74%); R_f = 0.37 (02:98 = EtOAc/n-Hexane); White Solid; **mp:**165-167 ^oC; IR (neat): 2926, 1612, 1547, 1520, 1448, 1284, 1032, 867, 801, 792, 759 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.57–7.39 (m, 6H), 7.39–7.17 (m, 6H), 4.24 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 155.1, 148.8, 137.1, 131.18, 131.17, 129.07, 129.00, 128.7, 128.6, 128.4, 127.9, 126.8, 124.1, 118.6, 118.1, 117.1, 32.8; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{21}H_{15}Cl_2O$: 353.0494; found: 353.0482.

2-Benzyl-5-bromo-7-chloro-3-phenylbenzofuran (3m): The title compound was prepared using the general procedure B; Yield: 62 mg (79%); R_f = 0.31 (02:98 = EtOAc/n-Hexane); White Solid; **mp:**186-188 ^oC; IR (neat): 2965, 1612, 1574, 1521, 1450, 1381, 1330, 1257, 1214, 1108, 1048, 1015, 932, 875, 759 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.56 (d, *J* = 1.7 Hz, 1H), 7.51-7.45 (2H), 7.42 (dd, *J* = 7.2, 4.3 Hz, 3H), 7.35-7.28 (m, 3H), 7.26-7.23 (m, 3H), 4.20 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 154.9, 149.1, 137.1, 131.7, 131.1, 129.08, 129.02, 128.7, 128.4, 127.9, 126.8, 126.7, 121.1, 118.5, 117.5, 115.6, 32.8; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{21}H_{15}BrClO$: 396.9989; found: 397.0000.

2-Benzyl-5-chloro-7-methyl-3-phenylbenzofuran (3n): The title compound was prepared using the general procedure B; Yield: 56 mg (82%); R_f = 0.31(05:95 = EtOAc/n-Hexane); Yellow Solid; **mp:**185-

187 °C; IR (neat): 2920, 1625, 1580, 1522, 1451, 1272, 1159, 1049, 1022, 940, 876, 746 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.47 (4H), 7.41-7.36 (m, 2H), 7.30 (d, *J* = 7.2 Hz, 2H), 7.25 (d, *J* = 6.6 Hz, 3H), 7.06 (d, *J* = 1.0 Hz, 1H), 4.20 (s, 2H), 2.48 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.6, 151.7, 137.7, 132.0, 129.4, 129.0, 128.9, 128.6, 128.4, 128.2, 127.5, 126.6, 124.9, 122.7, 118.2, 116.8, 32.9, 14.9; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{22}H_{17}ClO$: 333.1041; found: 333.1049.

2,7-Dibenzyl-5-chloro-3-phenylbenzofuran (3o): The title compound was prepared using the general procedure B; Yield: 68 mg (84%); R_f = 0.38 (0.2:98 = EtOAc/n-Hexane); White Solid; **mp:**188-190 °C; IR (neat): 2975, 2929, 1642, 1526, 1429, 1398, 1225, 1109, 956, 847, 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 (m, 4H), 7.37 (d, *J* = 1.9 Hz, 2H), 7.28 (d, *J* = 7.4 Hz, 2H), 7.26-7.19 (m, 8H), 7.02 (d, *J* = 1.8 Hz, 1H), 4.18 (s, 2H), 4.16 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.8, 151.1, 139.3, 137.6, 131.9, 129.8, 129.01, 129.00, 128.9, 128.6, 128.56, 128.55, 128.50, 127.5, 126.6, 126.3, 126.1, 124.3, 118.1, 117.5, 35.7, 32.9; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{28}H_{22}ClO$: 409.1359; found: 409.1329.

2-Benzyl-5-chloro-7-nitro-3-phenylbenzofuran (3p): The title compound was prepared using the general procedure B; Yield: 51 mg (70%); R_f = 0.31 (05:95 = EtOAc/n-Hexane); Light Yellow Solid; **mp:** 177-180 °C; IR (neat): 2921, 2053, 1531, 1461, 1424, 1128, 1110, 1031, 996, 884, 864,746 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.56 – 7.50 (3H), 7.48 – 7.46 (m, 2H), 7.45 – 7.43 (3H), 7.34 (m, 2H), 7.30 – 7.26 (m, 2H), 4.24 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 155.1, 148.8, 137.1, 131.18, 131.17, 129.07, 129.00, 128.7, 128.6, 128.4, 127.9, 126.8, 124.1, 118.6, 118.1, 117.1, 32.8; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{21}H_{15}ClNO_3$: 364.0740; found: 364.0735.

2-Benzyl-5-bromo-7-methoxy-3-phenylbenzofuran (3q): The title compound was prepared using the general procedure B; Yield: 63 mg (88%); R_f = 0.39 (05:90 = EtOAc/n-Hexane); White Solid; **mp:**163-164 °C; IR (neat): 2923, 1617, 1585, 1442, 1340, 1257, 1218, 1166, 1120, 1070, 1028, 924, 870, 841, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.46-7.44 (3H), 7.38 (m, 1H), 7.31-7.24 (m, 4H), 7.21 (d, *J* = 7.5 Hz, 3H), 6.90 (d, *J* = 1.6 Hz, 1H), 4.19 (s, 2H), 3.97 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.8, 145.5, 142.5, 137.5, 131.7, 131.6, 129.0, 128.9, 128.6, 128.4, 127.6, 126.6, 118.3, 115.9, 114.9, 110.0, 56.3, 32.8; **HR-MS (APCI, m/z):** $[M+Na]^+$ calculated for $C_{22}H_{17}BrNaO_2$: 415.0310; found: 415.0283.

2-Benzyl-4,6-dimethyl-3-phenylbenzofuran (3r): The title compound was prepared using the general procedure B; Yield: 135 mg (86%); R_f = 0.39 (05:90 = EtOAc/n-Hexane); White Solid; **mp:** 180-182

°C; IR (neat): 2930, 1612, 1573, 1432, 1338, 1280, 1221, 1148, 1124, 1067, 1015, 932, 853, 812, 751 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 – 7.38 (5H), 7.28 – 7.26 (m, 2H), 7.20 – 7.18 (3H), 7.11 (s, 1H), 3.96 (s, 2H), 2.41 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 154.6, 152.3, 138.2, 133.9, 133.8, 130.9, 130.8, 128.5, 128.5, 128.1, 127.4, 126.4, 125.6, 124.9, 118.7, 109.0, 32.6, 21.4, 19.3; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{23}H_{19}O$: 311.1436; found: 311.1415.

2-Benzyl-6,7-dimethyl-3-phenylbenzofuran (3s): The title compound was prepared using the general procedure B; Yield: 130 mg (83%); R_f = 0.37 (05:90 = EtOAc/n-Hexane); White Solid; **mp:** 176-178 °C; IR (neat): 2930, 1612, 1573, 1432, 1338, 1280, 1221, 1148, 1124, 1067, 1015, 932, 853, 812, 751 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.55 – 7.53 (2H), 7.49 (m, 2H), 7.41 – 7.30 (6H), 7.27 – 7.25 (m, 1H), 7.09 (d, *J* = 7.9 Hz, 1H), 4.25 (s, 2H), 2.46 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.9, 151.7, 138.3, 132.9, 132.4, 129.0, 128.8, 128.6, 128.5, 127.1, 126.5, 126.0, 124.7, 119.7, 118.5, 116.4, 32.9, 19.2, 11.7; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{23}H_{19}O$: 311.1436; found: 311.1424.

2-Benzyl-4,6,7-trimethyl-3-phenylbenzofuran (3t): The title compound was prepared using the general procedure B; Yield: 136 mg (84%); R_f = 0.40 (05:90 = EtOAc/n-Hexane); White Solid; **mp:** 177-180 °C; IR (neat): 2930, 1627, 1573, 1432, 1338, 1280, 1221, 1148, 1124, 1067, 1015, 932, 853, 812, 751 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 – 7.38 (5H), 7.28 – 7.26 (m, 2H), 7.20 – 7.18 (3H), 7.11 (s, 1H), 3.96 (s, 2H), 2.41 (s, 3H), 2.34 (s, 3H), 2.08 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.5, 152.1, 138.4, 134.1, 131.9, 130.8, 128.53, 128.4, 128.0, 127.6, 127.3, 126.3, 126.2, 124.7, 119.1, 117.0, 32.6, 18.9, 11.4 ; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{24}H_{23}O$: 327.1749; found: 327.1753.

2-Benzyl-7-methoxy-3-phenylbenzofuran-5-ol (3u): The title compound was prepared using the general procedure B; Yield: 49 mg (73%); R_f = 0.35 (20:80 = EtOAc/n-Hexane); Yellow solid; **mp:**164-166 °C; IR (neat): 2835, 2079, 1644, 1576, 1423, 1266, 1210, 1109, 962, 854, 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.53 – 7.4 (4H), 7.39 – 7.37 (1H), 7.31 – 7.22 (5H), 7.14 (s, 1H), 7.01 (s, 1H), 5.54 (s, 1H), 4.19 (s, 2H), 3.91 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.6, 148.4, 144.9, 142.7, 138.3, 136.5, 132.7, 128.9, 128.8, 128.6, 128.5, 127.2, 126.5, 121.3, 118.3, 103.8, 94.7, 56.4, 32.9. **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{22}H_{19}O_3$: 331.1329; found: 331.1352.

N-(2-Benzyl-3-phenylbenzofuran-5-yl)acetamide (3v):[26c] The title compound was prepared using the general procedure B; Yield: 47 mg (68%); R_f = 0.30 (50:50 = EtOAc/n-Hexane); Brown solid; **mp:**176-

178 °C; IR (neat): 3326, 2935, 2841, 1426, 1136, 1048, 959, 847, 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.72 (d, *J* = 4.0 Hz, 1H), 7.48 – 7.42 (4H), 7.37 – 7.27 (6H), 7.25 – 7.23(2H), 4.18 (s,2H), 2.13 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 168.4, 151.5, 137.8, 133.1, 132.2, 129.1, 129.1, 128.9, 128.7, 128.5, 127.4, 126.6, 118.9, 118.5, 117.7, 112.1, 111.2, 32.9, 24.4; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{23}H_{19}NO_2$: 341.1; found: 341.1.

5-Methyl-2-(4-methylbenzyl)-3-(p-tolyl)benzofuran (5a): The title compound was prepared using the general procedure B; Yield: 56 mg (86%); R_f = 0.42(02:98 = EtOAc/n-Hexane); White Solid; **mp:**184-186 °C; IR (neat): 2920, 2092, 1637, 1421, 1353, 1223, 1114, 1024, 954, 882, 823, 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 (d, *J* = 8.0 Hz, 2H), 7.39 (s, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.14-7.07 (m, 3H), 4.17 (s, 2H), 2.45 (s, 6H), 2.34 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.7, 136.9, 136.0, 135.0, 132.0, 129.7, 129.5, 129.3, 129.0, 128.9, 128.4, 125.0, 119.6, 118.4, 117.8, 110.6, 32.5, 21.4, 21.3, 21.0; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{24}H_{21}O$: 325.1587; found: 325.1580.

2-(4-Fluorobenzyl)-3-(4-fluorophenyl)-5-methylbenzofuran (5b): The title compound was prepared using the general procedure B; Yield: 53 mg (79%); R_f = 0.45 (02:98 = EtOAc/n-Hexane); White Solid; **mp:**175-177 °C; IR (neat): 2923, 2092, 1646, 1484, 1353, 1256, 1124, 1088, 1009, 826, 742cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.42 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 1H), 7.16 (dd, *J* = 11.2, 6.2 Hz, 4H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.96 (t, *J* = 8.7 Hz, 2H), 4.11 (s, 2), 2.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 163.1 (d, *J* = 46.4 Hz), 160.7 (d, *J* = 44.5 Hz), 152.6, 152.4, 133.4 (d, *J* = 3.4 Hz), 132.4, 130.6 (d, *J* = 8.0 Hz), 129.9 (d, *J* = 8.0 Hz), 128.6, 128.4 (d, *J* = 3.4 Hz), 125.3, 119.3, 117.1, 115.8 (d, *J* = 21.5 Hz), 115.5 (d, *J* = 21.4 Hz), 110.6, 32.0, 21.3; **HR-MS (ESI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{15}F_2O$: 333.1085; found: 333.1081.

2-(4-Chlorobenzyl)-3-(4-chlorophenyl)-5-methylbenzofuran (5c): The title compound was prepared using the general procedure B; Yield: 62 mg (84%); R_f = 0.43 (02:98 = EtOAc/n-Hexane); White Solid; **mp:** 178-180 °C; IR (neat): 2956, 1629, 1569, 1512, 1439, 1328, 1238, 1112, 1051, 1031, 1121, 926, 875, 843, 797,cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.44 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 1H), 7.24 (2H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.09 (dd, *J* = 8.4, 1.2 Hz, 1H), 4.11 (s, 2H), 2.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.7, 152.2, 136.1, 133.3, 132.5, 130.9, 130.3, 130.2, 129.7, 129.1, 128.7, 128.3, 125.5, 119.3, 117.2, 110.7, 32.2, 21.3; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{15}Cl_2O$: 365.0494; found: 365.0486.

2-(4-Bromobenzyl)-3-(4-bromophenyl)-5-methylbenzofuran (5d): The title compound was prepared using the general procedure B; Yield: 73 mg (81%); R_f = 0.44 (02:98 = EtOAc/n-Hexane); White Solid; **mp:** 188-190 °C; IR (neat): 2923, 2082, 1634, 1527, 1479, 1385, 1260, 1128, 1065, 1034, 1019, 986, 826, 745 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.34–7.28 (4H), 7.09 (dd, *J* = 10.0, 4.7 Hz, 3H), 4.09 (s, 2H), 2.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.7, 152.0, 136.6, 132.5, 132.0, 131.7, 131.3, 130.6, 130.1, 128.2, 125.5, 121.4, 120.5, 119.3, 117.2, 110.7, 32.3, 21.3; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{15}Br_2O$: 452.9484; found: 452.9474.

3-([1,1'-Biphenyl]-4-yl)-2-([1,1'-biphenyl]-4-ylmethyl)-5-methylbenzofuran (5e): The title compound was prepared using the general procedure B; Yield: 72 mg (80%); R_f = 0.4 (05:95 = EtOAc/n-Hexane); White solid; **mp:**198-200°C; IR (neat): 2938, 1982, 1645, 1532, 1465, 1383, 1274, 1108, 1049, 1014, 986, 843, 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.67 (m, 2H), 7.62 – 7.53 (6H), 7.50 – 7.53 (10H), 7.12 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.29 (s, 2H), 2.46 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.8, 152.7, 140.9, 140.7, 140.1, 139.6, 137.0, 132.3, 131.6, 129.5, 128.9, 128.9, 128.8, 128.7, 128.6, 127.5, 127.4, 127.2, 127.1, 127.0, 125.3, 119.6, 117.8, 110.7, 32.7, 21.4; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{34}H_{25}O$: 449.1900; found: 449.1903.

5-Methyl-3-(naphthalen-1-yl)-2-(naphthalen-1-ylmethyl)benzofuran (5f): The title compound was prepared using the general procedure B; Yield: 60 mg (76%); R_f = 0.42 (02:98 = EtOAc/n-Hexane); White solid; **mp** 186-188 °C; IR (neat): 2907, 1974, 1651, 1524, 1452, 1387, 1265, 1098, 1053, 1031, 965, 850, 746 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.05 – 8.03 (m, 2H), 7.88 – 7.86 (m, 2H), 7.79 (d, *J* = 8.0 Hz, 2H), 7.49 – 7.46 (4H), 7.43 – 7.40(3H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.17 (s, 1H), 7.00 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.15 (d, *J* = 4.0 Hz, 1H), 4.53 (s, 2H), 2.38 (s, 3H) ; **^{13}C NMR (100 MHz, $CDCl_3$):** δ 157.6, 153.2, 133.9, 133.2, 131.9, 131.7, 131.1, 128.9, 128.7, 128.5, 127.7, 127.5, 127.3, 127.1, 126.4, 126.1, 125.9, 125.9, 125.7, 125.3, 125.1, 124.5, 124.1, 123.9, 121.0, 120.3, 110.3, 103.5, 32.5, 21.3; **HR-MS (APCI, m/z):** $[M]^+$ calculated for $C_{30}H_{22}O$: 398.1665; found: 398.1663.

5-Methyl-3-(thiophen-2-yl)-2-(thiophen-3-yl)benzofuran (5g): The title compound was prepared using the general procedure B; Yield: 40 mg (67%); R_f = 0.45 (05:95 = EtOAc/n-Hexane); Yellow white solid; **mp:** 156-158 °C; IR (neat):2965, 1584, 1513, 1450, 1375, 1322, 1020, 934, 831, 802, 781, 767,

748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.54 (m, 2H), 7.51 – 7.47 (2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.27 (1H), 7.12 (d, *J* = 8.0 Hz, 1H), 4.23 (s, 2H), 2.46 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.8, 152.6, 132.7, 132.2, 129.2, 128.9, 128.8, 128.8, 128.6, 128.5, 127.3, 126.7, 125.2, 119.6, 118.1, 110.8, 32.9, 21.4; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{18}H_{13}OS_2$: 309.0402; found: 309.0405.

2-Benzyl-5-methylbenzofuran (5h): The title compound was prepared using the general procedure B; Yield: 38 mg (84%); R_f = 0.45 (02:98 = EtOAc/n-Hexane); Light Yellow liquid; IR (neat): 2935, 1642, 1536, 1503, 1449, 1325, 1281, 1123, 972, 856, 741 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.37-7.22 (m, 7H), 7.02 (d, *J* = 8.2 Hz, 1H), 6.30 (s, 1H), 4.09 (s, 2H), 2.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 157.8, 153.4, 137.3, 131.9, 128.9, 128.9, 128.6, 126.7, 124.6, 120.3, 110.4, 103.1, 35.0, 21.3; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{16}H_{14}O$: 222.1; found: 222.1.

2-Benzyl-5-methoxybenzofuran (5i):[27] The title compound was prepared using the general procedure B; Yield: 39 mg (83%); R_f = 0.35 (10:90 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 2962, 1628, 1537, 1497, 1436, 1357, 1242, 1132, 1083, 949, 845, 752 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.34 – 7.26 (6H), 6.94 (d, *J* = 4.0 Hz, 1H), 6.81 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.31 (s, 1H), 4.08 (s, 2H), 3.81 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.7, 155.8, 149.9, 137.3, 129.4, 128.9, 128.6, 126.7, 111.8, 111.3, 103.5, 103.3, 55.9, 35.1; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{16}H_{14}O_2$: 238.0; found: 238.0.

2-Benzyl-3,5-dimethylbenzofuran (5j): The title compound was prepared using the general procedure B; Yield: 35 mg (74%); R_f = 0.38 (5:95 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 3025, 2965, 1623, 1510, 1450, 1285, 1125, 1042, 972, 856, 745 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.29 (7H), 7.11 (dd, J = 8.0, 4.0 Hz, 1H), 4.15 (s, 2H), 2.53 (s, 2H), 2.28 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.6, 152.3, 138.2, 131.5, 130.4, 128.6, 128.6, 126.5, 124.7, 118.9, 110.6, 110.4, 32.7, 21.5, 8.1; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{17}H_{17}O$: 237.1274; found: 237.1258.

2-Benzyl-5-methoxy-3-methylbenzofuran (5k): The title compound was prepared using the general procedure B; Yield: 41 mg (81%); R_f = 0.37 (5:95 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 2975, 1628, 1512, 1465, 1279, 1134, 1027, 976, 848, 760cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.28 (6H), 7.02 (d, *J* = 4.0 Hz, 1H), 6.92 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.15 (s, 2H), 3.92 (s, 3H), 2.29 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 155.8, 153.2, 149.1, 138.1, 130.9, 128.7, 128.6, 126.6, 111.8,

111.3, 111.0, 102.0, 56.0, 32.8, 8.2; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{17}H_{17}O_2$: 253.1229; found: 253.1209.

2-(Furan-2-ylmethyl)-3,5-dimethylbenzofuran (5l): The title compound was prepared using the general procedure B; Yield: 97 mg (86%); R_f = 0.36 (5:95 = EtOAc/n-Hexane) ; Light red liquid; IR (neat): 3025, 2965, 1623, 1510, 1450, 1285, 1125, 1042, 972, 856, 745 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.37 (1H), 7.35 (m, 1H), 7.33 – 7.27 (m, 3H), 7.11 (d, *J* = 8.0 Hz, 1H), 4.15 (s, 2H), 2.53 (s, 3H), 2.28 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.5, 152.4, 139.2, 131.5, 130.8, 129.7, 128.5, 126.5, 124.7, 118.9, 110.6, 110.4, 32.7, 21.5, 8.2; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{15}H_{13}O_2$: 225.0916; found: 225.0923.

2-((3,5-Dimethylbenzofuran-2-yl)methyl)-1-methyl-1H-pyrrole (5m): The title compound was prepared using the general procedure B; Yield: 92 mg (77%); R_f = 0.33 (10:90 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 2872, 2532, 1986, 1854, 1723, 1458, 1238, 1132, 960, 852, 752, cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.37 – 8.35 (m, 1H), 7.44 (1H), 7.35 – 7.31 (3H), 7.28 – 7.26 (1H), 7.05 (m, 1H), 4.08 (s, 2H), 3.64 (s, 3H), 2.48 (s, 36H), 2.22 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.3, 128.6, 128.4, 126.5, 124.8, 124.1, 122.9, 121.8, 119.1, 117.9, 110., 110.0, 33.4, 32.6, 21.4, 8.7; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{16}H_{18}NO$: 240.1388; found: 240.1392.

3-((3,5-Dimethylbenzofuran-2-yl)methyl)-1-methyl-1H-indole (5n): The title compound was prepared using the general procedure B; Yield: 103 mg (72%); R_f = 0.38 (10:90 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 2995, 2612, 2076, 1846, 1735, 1484, 1238, 1036, 954, 835, 760, cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.37 – 8.35 (m, 1H), 7.43 (s, 1H), 7.35 – 7.33 (m, 2H), 7.32 – 7.29 (m, 1H), 7.27 – 7.25 (2H), 7.06 (s, 1H), 4.08 (s, 2H), 3.65 (s, 3H), 2.48 (s, 3H), 2.22 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.5, 152.4, 139.6, 138.2, 137.9, 131.5, 130.4, 128.6, 128.6, 126.5, 125.2, 124.7, 124.0, 122.9, 121.9, 119.0, 117.9, 33.4, 32.6, 21.4, 8.1; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{20}H_{20}NO$: 290.1545; found: 290.1537.

2-Benzyl-3-cyclohexyl-5-methylbenzofuran (5o): The title compound was prepared using the general procedure B; Yield: 35 mg (66%); R_f = 0.30 (5:95 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 2965, 2512, 2084, 1641, 1456, 1130, 1032, 910, 835, 758, 744 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.43 (s, 1H), 7.29 – 7.25 (3H), 7.21 (m, 3H), 6.99 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.10 (s, 2H), 2.72 (m, 1H),

2.44 (s, 3H), 1.88 – 1.78 (7H), 1.40 – 1.35 (3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.8, 151.1, 138.3, 131.1, 129.4, 128.5, 128.4, 126.4, 124.2, 120.4, 120.3, 110.6, 36.0, 32.9, 32.6, 26.9, 26.2, 21.5; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{22}H_{23}O$: 303.1743; found: 303.1755.

5-Methyl-2-(naphthalen-1-ylmethyl)benzofuran (5p): The title compound was prepared using the general procedure B; Yield: 42 mg (77%); R_f = 0.35 (10:90 = EtOAc/n-Hexane) ; Light Yellow liquid; IR (neat): 2969, 1633, 1579, 1563, 1457, 1341, 1262, 1113, 1077, 1027, 938, 851, 762 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.82– 7.78 (3H), 7.73 (s, 1H), 7.47 – 7.44 (m, 2H), 7.42 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.27 (m, 2H), 7.01 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.33 (d, *J* = 4.0 Hz, 1H), 4.25 (s, 2H), 2.41 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 157.7, 153.4, 134.8, 133.6, 132.4, 131.9, 128.9, 128.2, 127.7, 127.6, 127.3, 127.3, 126.1, 125.6, 124.65 120.3, 110.4, 103.4, 35.2, 21.3; **HR-MS (APCI, m/z):** $[M-H]^+$ calculated for $C_{20}H_{15}O$: 271.1117; found: 271.1121.

3-(2-Benzyl-5-methoxybenzofuran-3-yl)propanenitrile (5q): The title compound was prepared using the general procedure B; Yield: 70 mg (51%); R_f = 0.20 (20:80 = EtOAc/n-Hexane) ; Yellow solid; **mp:** 110-112 ^oC; IR (neat): 2894, 1754, 1632, 1557, 1465, 1421, 1235, 1145, 1028, 926, 848, 776 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.33-7.29 (3H), 7.26-7.23 (3H), 6.99 (d, *J* = 4.0 Hz, 1H), 6.87 (dd, *J* = 8.0, 4.0 Hz, 1H), 4.13 (s, 2H), 3.84 (s, 3H), 3.60 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 156.8, 154.9, 148.9, 136.3, 128.9, 128.5, 128.1, 127.0, 116.6, 113.2, 111.8, 104.9, 101.2, 56.0, 33.0, 12.6; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{18}H_{15}NO_2$: 278.1181; found: 278.1164.

2-Benzyl-3-(4-(2-bromoethoxy)phenyl)-5-methoxybenzofuran (5r): The title compound was prepared using the general procedure B; Yield: 102 mg (43%); R_f = 0.35 (10:90 = EtOAc/n-Hexane) ; Brown solid; **mp**: 146-148 ^oC; IR (neat)**:** 2975, 2835, 1814, 1630, 1560, 1423, 1356, 1225, 1142, 1009, 938, 878, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 (d, *J* = 4.0 Hz, 2H), 7.35-7.33 (m, 1H), 7.32-7.30 (5H), 7.29-7.28 (1H), 7.20-7.18 (2H), 6.88 (d, *J* = 4.0 Hz, 1H), 4.33 (t, *J* = 4.0 Hz, 2H), 4.11 (s, 2H), 3.84 (s, 3H), 3.68 (t, *J* = 4.0 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 164.8, 156.2, 151.8, 145.7, 137.1, 131.8, 128.9, 128.8, 128.5, 113.6, 112.7, 105.6, 68.3, 55.6, 33.3, 29.3; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{24}H_{22}BrO_3$: 437.0752; found: 437.0746.

5-Methoxy-2-methylbenzofuran (5s):[26b] The title compound was prepared using the general procedure B; Yield: 28 mg (86%); R_f = 0.42 (05:90 = EtOAc/n-Hexane); Light Yellow liquid; IR (neat): 2856,

1627, 1573, 1252, 1208, 1112, 954, 842, 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.27 (d, *J* = 8.0 Hz, 1H), 6.93 (d, *J* = 4.0 Hz, 1H), 6.79 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.29 (s, 1H), 3.82 (s, 3H), 2.42 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 156.4, 152.8, 132.1, 129.4, 124.7, 119.7, 110.3, 107.3, 55.9, 13.1; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{10}H_{10}O_2$: 162.06; found: 162.1.

2,5-Dimethylbenzofuran (5t):[26b] The title compound was prepared using the general procedure B; Yield: 24 mg (83%); R_f = 0.42 (05:90 = EtOAc/n-Hexane); Light Yellow liquid; IR (neat): 2796, 16234, 1588, 1246, 1210, 1109, 957, 834, 751 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.46 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 4.0 Hz, 1H), 6.81 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.32 (s, 1H), 2.38 (s, 3H), 2.37 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.7, 152.6, 132.0, 129.4, 124.6, 119.7, 110.3, 107.3, 21.4, 13.1; **GCLR-MS (EI, m/z):** $[M]^+$ calculated for $C_{10}H_{10}O_2$: 162.06; found: 162.1.

General procedure C: Synthesis of 2-benzyl benzo[b]furan via sequential protocol: To a stirred solution of cinnamyl alcohol (0.5 mmol) and phenol (0.5 mmol) in CH_3CN (2.0 ml), taken in a round-bottom flask attached to a refluxed condenser, Re_2O_7 (5 mol %) was added. The reaction was stirred at 80 ^oC. After consumption of starting material (followed by TLC analysis), the solvent was removed under reduced pressure. To this reaction mixture, 1,4-dioxane (2 mL) was added. Then $PdCl_2(CH_3CN)_2$ (5 mol %) / benzoquinone (1 equiv) was added. The reaction mixture containing RB flask was fitted with a reflux condenser was placed into a preheated oil bath at 80 ºC. After consumption of starting material (monitored by TLC analysis), the mixture was cooled to room temperature and filtered through celite. The filtrate was diluted with H_2O (10 mL) followed by washing with ethyl acetate (3 x 10 mL). The organic extract was dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure to provide the crude product which was purified by flash chromatography on silica-gel using n-hexane / ethyl acetate as eluent.

Reaction performed with non-symmetric diarylcinnamyl alcohol:

2-Benzyl-5-methyl-3-(p-tolyl)benzofuran & 5-methyl-2-(4-methylbenzyl)-3-phenylbenzofuran (5u:5v): The title compound was prepared using the general procedure B; Yield: 137 mg (87%); R_f = 0.38 (10:90 = EtOAc/n-Hexane) ; White solid ; **mp:** 178-180 ^oC; IR (neat): 2995, 2612, 2076, 1846, 1735, 1484, 1238, 1036, 954, 835, 760, cm^{-1}; Major isomer **5u: ^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.60 – 7.58 (m, 1H), 7.49 – 7.45 (4H), 7.36 – 7.33 (5H), 7.15 – 7.13 (m, 2H), 4.25 (s, 2H), 2.49 (s, 6H); Minor isomer **5v**: **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.56 – 7.52 (m, 2H), 7.45 – 7.39 (6H), 7.30 – 7.23 (4H), 4.23 (s, 2H), 2.48 (s, 6H); Major isomer **5u: ^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.8, 152.5, 138.1, 137.0, 132.1, 129.6, 129.3, 129.1, 129.0, 128.8, 128.6, 128.5, 126.5, 125.1, 119.6, 110.6, 32.9, 21.4,

21.3; Minor isomer **5v**: **^{13}C NMR (100 MHz, $CDCl_3$):** δ 152.9, 136.1, 134.9, 132.7, 132.2, 129.6, 129.4, 129.3, 129.1, 128.9, 128.8, 127.2, 119.6, 118.0, 117.9, 110.7, 32.5, 21.4, 21.0; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{23}H_{21}O$: 313.1592; found: 313.1605.

Typical procedure for the synthesis of the Melatonin receptor ligand A (see the reaction Scheme S2.1 in Supporting Information):

General procedure D; Synthesis of ethyl cinnamate S_3: A solution of cinnamic acid (500 mg, 3.38 mmol) in 10 mL ethanol, H_2SO_4 was added in catalytic amount into the reaction mixture. The reaction mixture was refluxed at 70 ^oC temperature (8 h). After consumption of starting material (followed by TLC analysis), the reaction mixture was kept at room temperature and $NaHCO_3$ (5 mL) was added slowly into the reaction mixture until the complete absence of effervescence was observed. The organic layer was washed with H_2O (10 mL). The aqueous layers were combined and washed with ethyl acetate (3x10 mL). The organic layers were combined, dried ($MgSO_4$) and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using EtOAc /n-hexane as a solvent to obtain 88 % of **S_3**.

Ethylcinnamate (S_3): The title compound was prepared using the general procedure D; Yield: 137 mg (87%); R_f = 0.40 (05:95 = EtOAc/n-Hexane); White solid; **mp:** 78-80 ^oC; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 16.0 Hz, 1H), 7.51-7.49 (2H), 7.36 – 7.35 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 4.25 (q, *J* = 8.0, 4.0 Hz, 2H), 1.32 (t, *J* = 8.0 Hz, 3H)**; ^{13}C NMR (100 MHz, $CDCl_3$):** δ 166.9, 144.6, 134.5, 130.2, 128.9, 128.1, 118.3, 60.5, 14.3.

General procedure E: Synthesis of (*E*)-3-oxo-5-phenylpent-4-enenitrile (S_4): A solution of **S_3** (400 mg, 2.27 mmol) in 10 mL THF, CH_3CN (0.13 mL, 2.72 mmol) was added followed by NaH (64.8 mg, 2.7 mmol) into the reaction mixture. The reaction mixture was refluxed at 80 ^oC temperature (8 h). After consumption of starting material (followed by TLC analysis), the reaction mixture was kept at room temperature and brine (5 mL) was added slowly into the reaction mixture until the complete absence of effervescence was observed. The organic layer was washed with H_2O (10 mL). The aqueous layers were combined and washed with ethyl acetate (3x10 mL) and dried over $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using EtOAc /n-hexane as a solvent to obtain 65 % of **S_4**.

(*E*)-3-Oxo-5-phenylpent-4-enenitrile (S_4): The title compound was prepared using the general procedure E; Yield: 112 mg (65%); R_f = 0.22 (20:80 = EtOAc/n-Hexane); Yellow solid; **mp:** 125-127 ^oC; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.67 (d, *J* = 16.0 Hz, 1H), 7.58 – 7.56 (2H), 7.45 – 7.40 (3H), 6.86 (d, *J* = 16.0 Hz, 1H), 3.69 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 186.3, 146.6, 133.4, 131.7, 129.2, 128.8, 122.4, 113.9, 30.8.

(*E*)-3-(2-Hydroxy-5-methoxyphenyl)-5-phenylpent-3-enenitrile & (*E*)-5-(2-hydroxy-5-methoxy phenyl)-5-phenylpent-3-enenitrile (2w:2x): The title compound was prepared using the general procedure A; Yield: 107 mg (78%); R_f = 0.38 (20:80 = EtOAc/n-Hexane) ; brown liquid; IR (neat): 2995, 2612, 2076, 1846, 1735, 1484, 1238, 1036, 954, 835, 760 cm^{-1}; Major isomer **2w**: **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37-7.36 (2H), 7.32 – 7.29 (m, 2H), 7.23 (m, 1H), 6.77 (d, *J* = 4.0 Hz, 1H), 6.70-6.68 (1H), 6.64 (m, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 6.48-6.42 (dd, *J* = 16.0, 8.0 Hz, 1H), 5.02 (s, 1H), 4.14 (q, *J* = 12.0, 4.0 Hz, 1H), 3.73(s, 3H), 2.89 – 2.87 (m, 2H); Minor isomer **2x**: **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.28-7.27 (m, 1H), 7.20 – 7.18 (2H), 6.77 (d, *J* = 4.0 Hz, 1H), 6.72-6.70 (1H), 6.67 (m, 1H), 6.64 (s, 1H), 6.34-6.28 (1H), 5.31-5.27 (1H), 5.01 (s, 1H), 4.14 (q, *J* = 8.0, 4.0 Hz, 1H), 3.72 (s, 3H), 3.11 (d, *J* = 4.0 Hz, 2H); Major isomer **2w: ^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.8, 147.1, 136.6, 132.2, 130.1, 128.7, 128.6, 128.3, 128.2, 127.8, 126.5, 119.6, 116.7, 115.7, 112.4, 55.8, 47.4, 22.7; Minor isomer **2x**: **^{13}C NMR (100 MHz, $CDCl_3$):** δ 153.7, 147.2, 141.3, 137.0, 130.1, 128.4, 128.2, 126.9, 118.7, 117.5, 116.8, 114.6, 113.2, 55.7, 47.4, 22.7; **HR-MS (APCI, m/z):** $[M]^+$ calculated for $C_{18}H_{17}NO_2$: 279.1259; found: 279.1245.

3-(5-Methoxy-3-phenylbenzofuran-2-yl)propanenitrile (5x): The title compound was prepared using the general procedure B; Yield: 29 mg (23%); R_f = 0.23 (20:80 = EtOAc/n-Hexane); yellow solid; **mp**: 123-125 ^oC; IR (neat): 2954, 1635, 1548, 1524, 1457, 1385, 1256, 1135, 1052, 934, 821, 732 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.53 – 7.47 (4H), 7.43-7.39 (1H), 7.36 (d, *J* = 8.0Hz, 1H), 7.00 (d, *J* = 4.0 Hz, 1H), 6.92 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.80 (s, 3H), 3.19 (t, *J* = 8.0 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 156.3, 150.4, 149.1, 131.7, 129.1, 129.0, 128.9, 128.1, 127.7, 119.4, 118.6, 113.3, 111.6, 102.5, 56.0, 23.3, 16.2; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{18}H_{16}NO_2$: 278.1181; found: 278.1165.

General procedure F; Synthesis of N-(2-(2-benzyl-5-methoxybenzofuran-3-yl) ethyl) acetamide (A): From a reported procedure[29a]: A solution of compound **5q** (138.5 mg, 0.5mmol) was dissolved in

diethyl ether (2 mL), and reaction mixture was added to a slurry of LAH (76 mg, 2.0mmol) in diethyl ether (5 mL) at 0 °C. The reaction mixture was then heated slowly to 30 °C for 4 h. After completion of the reaction, the reaction mixture was cooled to 0 °C, and the reaction was quenched by the dropwise addition of water (1 mL). The reaction mixture was filtered, and the filtrate was dried over $MgSO_4$ and concentrated in vacuum to afford a yellow oil compound **6**, which was diluted with DCM (1 mL); Ac_2O (56 µL, 0.55mmol) was added dropwise at 0 °C, and the reaction mixture warmed at room temperature and again stirred for 1 h. The reaction mixture was extracted with DCM and water, and the DCM layer was separated, dried with anhydrous $MgSO_4$, and concentrated under vacuum to give the crude product, which was furthered purified by column chromatography with DCM/MeOH as eluent to yield the desired product **A**.

N-(2-(2-Benzyl-5-methoxybenzofuran-3-yl)ethyl)acetamide (A):[29a] The title compound was prepared using the general procedure F; Yield: 102 mg (73%); R_f = 0.28 (30:70 = EtOAc/n-Hexane) ; Brown solid; **mp**: 120-122 °C; IR (neat): 2895, 1628, 1559, 1521, 1434, 1386, 1245, 1142, 1012, 932, 874, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38 (m, 2H), 7.33-7.31 (4H), 7.15 (d, *J* = 4.0 Hz, 1H), 6.80 (d, *J* = 8.0, 4.0 Hz, 1H), 6.34 (s, 1H), 4.13 (t, *J* = 4.0 Hz, 2H), (4.10 (s, 2H), 3.84 (s, 3H), 2.82 (t, *J* = 4.0 Hz, 2H), 2.39 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.8, 156.2, 151.8, 145.7, 137.1, 131.8, 128.9, 128.8, 128.5, 113.6, 112.7, 105.6, 55.8, 41.5, 33.8, 23.3, 21.0; **GCLR-MS (ESI, m/z):** $[M]^+$ calculated for $C_{20}H_{21}NO_3$: 323.1; found: 323.1.

Procedure for the synthesis of the anti-tumor and hypocholesterolemic agent B (see the reaction scheme S2.2 in Supporting Information):

General procedure G; For the preparation of S_6:[29b] To a solution of chalcone ((*E*)-1-(4-hydroxyphenyl)-3-phenylprop-2-en-1-one) (1.12 g, 5 mmol) and K_2CO_3 (2.07 g, 15 mmol) in DMF (15 mL), an appropriate amount of 1,2-dibromoethane (940 mg, 5mmol) was added. After stirring at 80 °C for 10 h until the chalcone disappeared, the solvent was poured into ice water (100 mL), extracted with EtOAc (3x30 mL) and washed with saturated aqueous NaCl solution (2x10 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuum. Then the residue was purified by a silica-gel column chromatography to afford product 63 % of **S_6**.

(*E*)-1-(4-(2-Bromoethoxy)phenyl)-3-phenylprop-2-en-1-one (S_6):[29b] The title compound was prepared using the general procedure G; Yield: 820 mg (63%); R_f = 0.32 (05:95 = EtOAc/n-Hexane) ; White sol-

id; **mp**: 90-92 ^{o}C ; IR (neat): 3012, 2948, 2854, 1658, 1612, 1568, 1521, 1420, 1320, 1242, 1122, 932, 874, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 16.0 Hz, 1H), 7.65-7.63 (1H), 7.56-7.52 (d, *J* = 16.0 Hz, 1H), 7.42-7.41 (2H), 6.99 (d, *J* = 8.0Hz, 1H), 4.35 (t, *J* = 8.0 Hz, 2H), 3.66 (t, *J* = 8.0 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 188.6, 161.9, 144.2, 135.1, 131.7, 130.9, 130.7, 130.4, 128.9, 128.4, 121.8, 114.5, 67.9, 28.8.

Procedure for the preparation of S_7:[29c] To a stirred solution of $CeCl_3.7H_2O$ (0.670 g, 1.8 mmol) and **S_6** (0.312 g, 1.5 mmol) in MeOH (10 mL) at 0 °C added sodium borohydride (45 mg, 1.8 mmol) was added portion wise and the reaction mixture was further stirred for 15 min at rt. Then, the reaction mixture was adjusted to pH 7 using a 10% HCl solution and extracted three times with Et_2O. The combined organic layers were washed with brine and dried over anhydrous MgSO4. Then the solvent was removed under reduced pressure and the crude residue was purified by column chromatography on silica-gel using ethyl acetate/n-hexane as eluent to obtain the product **S_7**. The compounds were reported in literature.[29c] The experimental data were completely matched with the reported value.

The synthesis of compound **5r** was achieved using the general procedure **A** and **B**.

Procedure for the synthesis of 2-(4-(2-Benzyl-5-methoxybenzofuran-3-yl)phenoxy)-N,N-dimethylethanamine (7): Then, a mixture of compounds **5r** (218 mg, 0.5 mmol), secondary amines dimethylamine (0.1 ml, 2 mmol), K_2CO_3 (207mg, 1.5 mmol), NaI (3.75 mg, 0.05 mmol), acetone (10 mL) was heated under reflux for 8 h. The solvent was removed and the residue was dissolved with EtOAc (30 mL). Then the organic extracts were washed with saturated aqueous NaCl solution (10 mL), dried over anhydrous Na_2SO_4 and evaporated in vacuum, giving a crude product which was chromatographed on silica gel with different ratio of (05:95 = methanol/dichloromethane) as elution to afford the compounds **7**.

2-(4-(2-Benzyl-5-methoxybenzofuran-3-yl)phenoxy)-N,N-dimethylethanamine (7): Yield: 67 mg (66%); R_f = 0.24 (10:90 = MeOH/dichloromethane); Brown solid; **mp**: 130-132 ^{o}C; IR (neat): 2895, 1628, 1559, 1521, 1434, 1386, 1245, 1142, 1012, 932, 874, 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38-7.33 (2H), 7.31-7.27 (6H), 7.14 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.93 (d, *J* = 4.0 Hz, 1H), 6.86-6.79 (2H), 4.09 (t, *J* = 4.0 Hz, 2H), 4.07 (s, 2H), 3.80 (s, 3H), 2.78 (t, *J* = 4.0 Hz, 2H), 2.36 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.6, 155.8, 153.3, 149.9, 137.2, 130.0, 129.4, 128.6, 127.5, 126.7, 125.8, 123.8, 114.2, 111.8, 111.3, 103.5, 68.1, 57.8, 55.9, 46.1, 35.1; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{26}H_{28}NO_3$: 402.2069; found: 402.2048.

Prosedure for the synthesis of 2-Benzyl-3-(4-(2-(dimethylamino)ethoxy)phenyl)benzofuran-5-ol (B): From a reported general procedure: [28] A 1 M CH_2Cl_2 solution of BBr_3 (47 µL, 0.05 mmol) was added, at -78 °C, to an anhydrous CH_2Cl_2 (3 mL) mixture of compound **7** (80 mg, 0.2 mmol). The reaction mixture was stirred at room temperature (2 h). After consumption of starting material (followed by TLC analysis), the reaction mixture was kept in ice bath and H_2O (5 mL) was added slowly into the reaction mixture until the complete absence of effervescence was observed. The organic layer was washed with H_2O (5 mL). The aqueous layers were combined and washed with CH_2Cl_2 (3x10 mL). The organic layers were combined, dried (MgSO4) and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using (05:95=Methanol /dichloromethane) as a solvent to obtain **B**.

2-Benzyl-3-(4-(2-(dimethylamino)ethoxy)phenyl)benzofuran-5-ol (B): Yield: 57 mg (62%); R_f = 0.23 (10:90 = MeOH/dicholoromethane) ; Light yellow semi solid; IR (neat): 2985, 2922, 2865, 1812, 1732, 1621, 1478, 1423, 1218, 1186, 1140, 948, 795, 765 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38-7.37 (3H), 7.34 – 7.28 (4H), 7.22 (d, *J* = 4.0 Hz, 1H), 7.16 (dd, *J* = 8.0, 4.0 Hz, 2H), 6.85 (m, 1H), 6.84-6.82 (1H), 6.24 (s, 1H), 4.14 (t, *J* = 4.0 Hz, 1H), 4.09 (s, 2H), 2.86 (t, *J* = 4.0 Hz, 2H), 2.43 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.6, 153.1, 152.3, 149.6, 137.2, 129.9, 128.9, 128.6, 127.5, 125.9, 123.7, 114.1, 112.3, 111.1, 105.8, 103.3, 67.9, 57.7, 46.0, 35.1; **GCLR-MS (ESI, m/z):** $[M]^+$ calculated for $C_{25}H_{25}NO_3$: 387.1; found: 387.1.

Procedure for the synthesis of the Akt/mTOR (C):[28]

Procedure for the synthesis of 2-benzylbenzofuran-5-ol (8): A 1 M CH_2Cl_2 solution of BBr_3 (2.7 mL, 1.05mmol) was added, at -78 °C, to an anhydrous CH_2Cl_2 (3 mL) mixture of **5i** (100 mg, 0.42mmol). The reaction mixture was stirred at room temperature (8 h). After consumption of starting material (followed by TLC analysis), the reaction mixture was kept in ice bath and H_2O (5 mL) was added slowly into the reaction mixture until the complete absence of effervescence was observed. The organic layer was washed with H_2O (10 mL). The aqueous layers were combined and washed with CH_2Cl_2 (3x10 mL). The organic layers were combined, dried (MgSO4) and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using EtOAc /n-hexane as a solvent to obtain **8**.

2-Benzylbenzofuran-5-ol (8):[28] Yield: 86 mg (77%); R_f = 0.2 (20:80 = EtOAc/n-Hexane) ; White solid; **mp**: 189-190 °C; IR (neat): 2968, 1617, 1521, 1434, 1372, 1245, 1122, 1034, 928, 865, 784 cm^{-1}; **^{1}H**

NMR (400 MHz, $CDCl_3$): δ 7.35 – 7.23 (6H), 6.88 (d, *J* = 4.0 Hz, 1H), 6.71 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.27 (s, 1H), 4.76 (bs, 1H), 4.07 (s, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.9, 151.3, 150.1, 137.2, 129.7, 128.9, 128.6, 126.8, 111.8, 111.3, 105.6, 103.3, 35.1; **GCLR-MS (ESI, m/z):** $[M]^+$ calculated for $C_{15}H_{12}O_2$: 224.0; found: 224.0.

Procedure for the synthesis of 2-benzyl-4-((diethylamino)methyl)benzofuran-5-ol (C): The diethylamine amine (38 mg, 0.52 mmol) and formaldehyde (37% in water) (17 µL, 0.52 mmol), was added to an EtOH (1.5 mL) solution of compound **8** (60 mg, 0.26 mmol) and formaldehyde (37% in water, 0.52 mmol). The reaction mixture was stirred at reflux for 8 h. After consumption of starting material (followed by TLC analysis), the solution concentrated under vacuum. The aqueous layers were combined and washed with EtOAc (3x10 mL). The organic layers were combined, dried (MgSO4) and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using EtOAc /n-hexane as a solvent to obtain **C**.

2-Benzyl-4-((diethylamino)methyl)benzofuran-5-ol (C):[28] Yield: 57 mg (71%); R_f = 0.2 (30:70 = EtOAc/n-Hexane); light yellow liquid; IR (neat): 2965, 2928, 2845, 1618, 1488, 1443, 1229, 1197, 1135, 947, 790, 760 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.33 – 7.26 (5H), 7.20 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.23 (s, 1H), 4.06 (s, 2H), 3.92 (s, 2H), 2.70 (q, *J* = 8.0 Hz, 4H), 1.14 (t, *J* = 8.0, 4.0 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 158.5, 153.7, 148.9, 137.3, 128.9, 128.7, 128.3, 126.8, 113.1, 111.3, 110.5, 101.0, 53.0, 46.8, 35.2, 11.0; **GCLR-MS (ESI, m/z):** $[M]^+$ calculated for $C_{20}H_{23}NO_2$: 309.1; found: 309.1.

Reaction performed with non-symmetric diarylcinnamyl alcohol:

(*E*)-4-Methyl-2-(3-phenyl-1-(p-tolyl)allyl)phenol (2u & 2v): The title compound was prepared using the general procedure A; Yield: 120 mg (73%); R_f = 0.35 (40:90 = Dichloromethane/n-Hexane) ; Light yellow loquid; IR (neat): 3012, 2986, 2701, 2632, 2057, 1924, 1735, 1471, 1252, 1042, 963, 838, 750 cm^{-1}; Major isomer **2u** : **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.41 – 7.39 (d, *J* = 8.0 Hz, 2H), 7.33– 7.30 (2H), 7.29 – 7.26 (2H), 7.18 (3H), 6.98 – 6.96 (s, 2H), 6.72 (d, *J* = 8.0 Hz, 2H), 6.38 (d, *J* = 12.0 Hz, 1H), 5.06 (d, *J* = 4.0 Hz, 1H), 4.71 (s, 1H), 2.35 (s, 3H), 2.28 (s, 3H); Minor isomer **2v**: **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.36 – 7.33 (3H), 7.26 – 7.23 (3H), 7.14 – 7.13 (3H), 6.96 (s, 2H), 6.69 – 6.63 (2H), 6.34 (d, *J* = 12.0Hz, 1H), 5.09 (d, *J* = 8.0 Hz, 1H), 4.72 (s, 1H), 2.34 (s, 3H), 2.27(s, 3H); Major isomer **2u: ^{13}C NMR (100 MHz, $CDCl_3$):** δ 151.3, 138.9, 137.2, 136.4, 131.6, 131.5, 130.2, 129.5, 129.3,

128.7, 128.6, 128.5, 128.5, 127.4, 126.4, 116.3, 48.4, 21.1, 20.7; Minor isomer **2v**: **^{13}C NMR (100 MHz, $CDCl_3$):** δ 142.2, 137.3, 134.3, 131.7, 131.5, 130.3, 130.2, 130.2, 129.3, 129.0, 128.7, 128.6, 126.8, 126.3, 116.3, 48.6, 21.2, 20.8; **HR-MS (APCI, m/z):** $[M+H]^+$ calculated for $C_{23}H_{23}O$: 315.1749; found: 315.1756.

(Z)-2-Benzylidene-5-chloro-3-phenyl-2,3-dihydrobenzofuran (**9**)**:** It was synthesized with the modified reported procedure.[31] Yield: (78%); R_f = 0.20 (20:80 = EtOAc/n-Hexane); brown liquid; IR (neat): 2967, 2355, 2074, 1640, 1476, 1335, 1267, 1123, 972, 805 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ, 7.52 – 7.42 (6H), 7.41 – 7.32 (2H), 7.27 (d, J = 8.0, 2H), 7.18 – 7.17 (4H), 5.08 (s, 1H), 4.22 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 153.2, 142.1, 141.0, 137.2, 134.3, 132.1, 131.2, 129.9, 128.8, 128.8, 128.7, 128.7, 128.6, 127.6, 126.9, 116.8, 48.7; **HR-MS (m/z):** $[M-H]^+$ calculated for $C_{21}H_{14}ClO$: 317.0739; found: 317.0742.

ASSOCIATED CONTENT

Supporting Information

The copies of ^{1}H and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

Crystallography data of product **3a** (CCDC-1475310) (CIF)

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