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Synthesis of 5,5′-bis-benzofurans and 5-arylbenzofurans

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ABSTRACT

A facile synthetic route of the tandem Claisen rearrangement/aerobic Wacker-type oxidative cyclization toward 5,5′-bis-benzofurans **2** and 5-arylbenzofurans **3** starting with bis-allyl aryl ethers **4** or allyl aryl ethers **5** with good yields is described. Skeletons **4** or **5** was prepared from 4,4′-biphenol (**1**) in moderate total yields via the known protocol.

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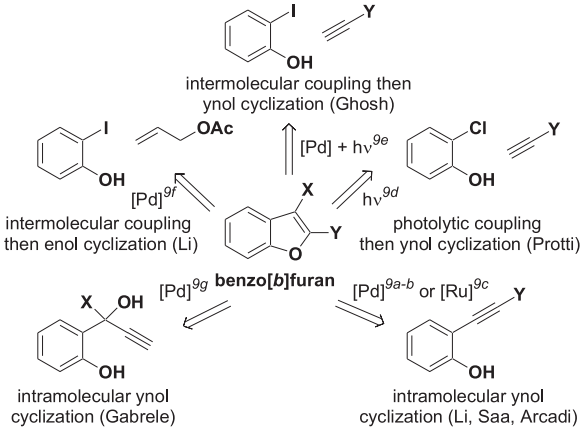
1. Introduction

During the last decade, the development of effective routes for the synthesis of large structural libraries of different benzannulated heterocycles has been an important course for modern organic synthesis.[1] Among these transformations, the palladium-catalyzed one-pot reaction has become a powerful and efficient tool to access a versatile class of functionalized cycloadducts that have been useful in the discovery of new drugs. A number of review articles have highlighted fascinating researches based on the Wacker-type reaction.[2–6] In continuation of our recent investigation of 4,4′-biphenol (**1**) for preparing several benzannulated molecules,[7] substituted 5,5′-bis-benzofurans **2** or 5-arylbenzofurans **3** are prepared by one-pot Pd^{II}/Cu^{II}-mediated tandem annulation of bis-allyl aryl ethers **4** or allyl aryl ethers **5** via an easy synthetic procedure of Claisen rearrangement and Wacker-type oxidative cyclization.

Substituted benzofurans have played an important role in organic synthesis due to their high reactivity and suitability.[8–10] Most of the relevant literature on one-pot synthesis of substituted benzofurans is focused on transition metal-catalyzed oxidative cyclization. Common transition metal-catalyzed one-pot synthetic routes for making the skeleton of benzofuran include intermolecular, intramolecular ynol or enol cyclization,[9] as shown in Scheme 1.



Scheme 1. Metal ion-catalyzed synthetic routes of benzofurans.

After a further comparison of literature reports on the synthesis of benzofurans,[9] we find that this Pd^{II}/Cu^{II} system catalyzing intramolecular aerobic Wacker-type oxidative cyclization of allylphenols has been mentioned in a few reports,[10] and is becoming an attractive candidate for the construction of substituted 5,5′-bis-benzofurans **2** or 5-arylbenzofurans **3** with molecular oxygen (O_2) as the co-oxidant. From information gleaned in literature reports, we speculate that molecular oxygen may control this reaction to generate different kinds of products; it should provide different results in the assumed catalytic cycles under the Wacker-type oxidative reaction. There have been extensive studies on the preparation of functionalized benzofurans, owing to their prevalence in a variety of derivatives possessing important physical and biological properties.[11]

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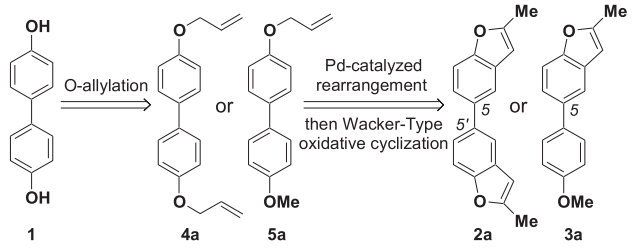
However, as yet, there have been very few efficient syntheses of skeletons of 5,5′-bis-benzofurans **2** or 5-aryl-benzofurans **3** bearing the appropriate groups.[12,13] The retrosynthetic synthesis of skeletons **2** or **3** is shown in Scheme 2.



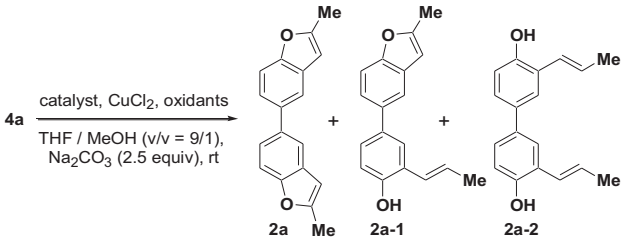
Scheme 2. Representative example for synthesis of compound **2a** or **3a** from 4,4′-biphenol (**1**).

2. Results and discussion

With our experience in using the *O*-allyl group for employing 4,4′-biphenol (**1**) for the synthesis of molecules, we believe that it may be possible to develop this one-pot methodology for preparing the skeletons of 5,5′-bis-benzofurans **2** or 5-aryl-allylbenzofurans **3**. As shown in Scheme 3, a facile route was employed to create skeletons **2** and **3**, starting with 4,4′-biphenol (**1**) or 4′-methoxy-biphenyl-4-ol (**1a**) via (1) O-allylation of compound **1** or **1a** with allyl or crotyl bromide (R_1=H/Me) in the boiling acetone, (2) Claisen rearrangement of compounds **4a**–**4b** or **5a**–**5b** with the refluxing decalin (for **6a**–**6b**, 3–4 h; for **7a**–**7b** 8–10 h), (3) hydrogenation of compounds **6a**–**6b** or **7a**–**7b** with H_2 and 10% Pd/C in EtOAc at rt, and (4) O-allylation of compounds **8a**–**8b** or **9a**–**9b** with allyl or crotyl bromide (R_2=H/Me) in boiling acetone. Under the above four-step reaction conditions, compounds **4a**–**4f** and **5a**–**5f** were isolated from compounds **1** and **1a** with acceptable total yields.

As shown in Table 1, the Pd^{II}/Cu^{II} system mediated one-pot Claisen rearrangement/Wacker-type oxidative cyclization of model compound **4a** was further studied; it created three structural skeletons of bis-benzofuran **2a** (35%), benzofuran with a styrenyl motif **2a-1** (29%), and biphenol with two styrenyl groups **2a-2** (30%)

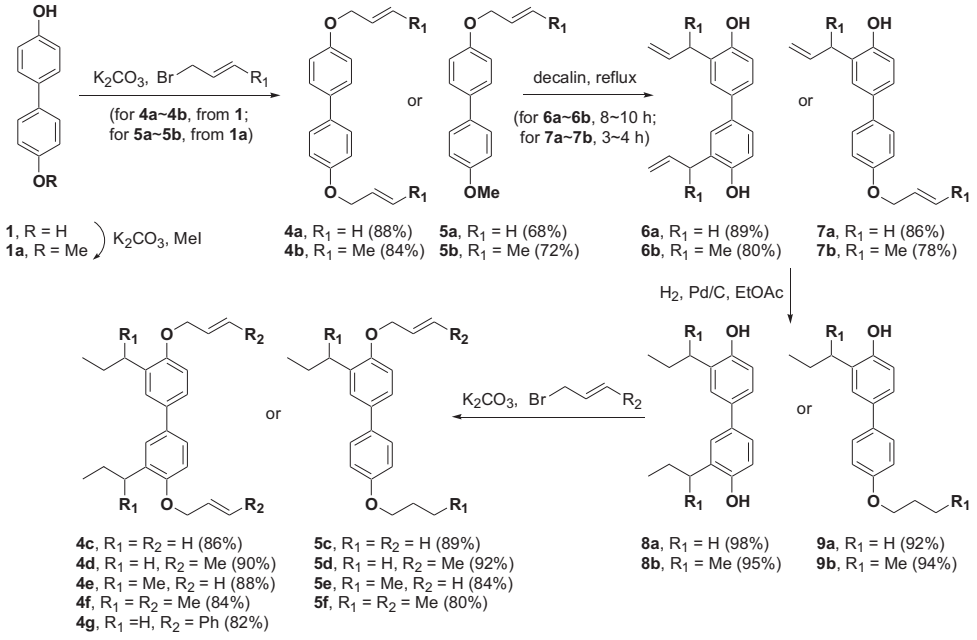
Table 1
One-pot Wacker-type cyclization of bis-allyl aryl ether **4a**[a,b]



Entry	Catalyst (mol %), $CuCl_2$, oxidants (equiv)	Yield (%) **2a**/**2a-1**/**2a-2**
1	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), air	35/29/30[c]
2	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), *t*-BuO_2H (1.0)	—/<10/80[d]
3	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), DDQ (1.0)	—/<10/42[c,d]
4	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), CAN (1.0)	—/<10/56[c,d]
5	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), Oxone® (1)	—/—/85[d]
6	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), $PhI(OAc)_2$ (1)	—/—/81[d]
7	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (1.5), O_2	80/—/—[d]
8	$PdCl_2(MeCN)_2$ (20), $CuCl_2$ (1.5), O_2	75/—/—[d]
9	$PdCl_2(MeCN)_2$ (5), $CuCl_2$ (1.5), O_2	72/—/—[d]
10	$PdCl_2(MeCN)_2$ (10), $CuCl_2$ (0), O_2	25/30/33[d]
11	$RuCl_2(PPh_3)_3$ (10), $CuCl_2$ (1.5), O_2	71/15/—[d]
12	$Pd(OAc)_2$ (10), $CuCl_2$ (1.5), O_2	65/22/—[d]
13	$PdCl_2$ (10), $CuCl_2$ (1.5), O_2	75/10/—[d]

[a] The reactions were run on a 1.0 mmol scale with starting material **4a**.
[b] The products **2a**, **2a-1**, and **2a-2** were >95% pure as determined by ^1H NMR analysis.
[c] The unknown products (for entry 3, 30%; entry 4, 24%) were obtained.
[d] The starting material **4a** (for entries 2–6, 5–10%; for entries 7–13, <5%) was recovered.

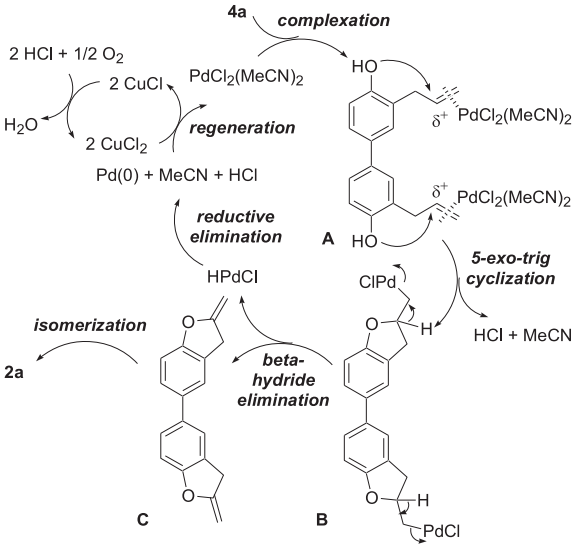
at rt for 8 h under the co-solvent (THF/MeOH=9/1) condition (entry 1). After screening different conditions, we found that the Pd^{II}/Cu^{II} system mediated Wacker-type oxidation of substrate **4a** with five different oxidants (*t*-BuO_2H, DDQ, CAN, Oxone® and $PhI(OAc)_2$), provided these major migrated olefins. As shown in entries 2–6, compound **2a** was not isolated in the product mixture; starting material **4a**, products **2a-1** or **2a-2**, and an unknown mixture, were isolated at different ratios.



Scheme 3. Synthesis of bis-allyl aryl ethers **4** and allyl aryl ethers **5**.

From the above results, we found that molecular oxygen should be an important oxidant for synthesizing the skeleton of benzofuran. To our delight, by adjusting the molecular oxygen (by the bubbled method) as the oxidant, the isolated yield of product **2a** (80%) was noticeably enhanced (entry 7). After the amount of $PdCl_2(MeCN)_2$ was increased two-fold or half-fold, product **2a** provided similar yields (for entry 8, 75%; for entry 9, 72%). Without the addition of $CuCl_2$, a mixture of products **2a**, **2a-1**, and **2a-2** was isolated in similar ratios (entry 10). When changing the catalyst from $PdCl_2(MeCN)_2$ to $RuCl_2(PPh_3)_3$, $Pd(OAc)_2$ or $PdCl_2$, product **2a** provided a poorer yield (entries 11–13) along with trace amounts of product **2a-1**. We inferred that the optimized one-pot process for synthesizing bis-benzofuran **2a** would involve the $PdCl_2(MeCN)_2$/$CuCl_2/O_2$ system.

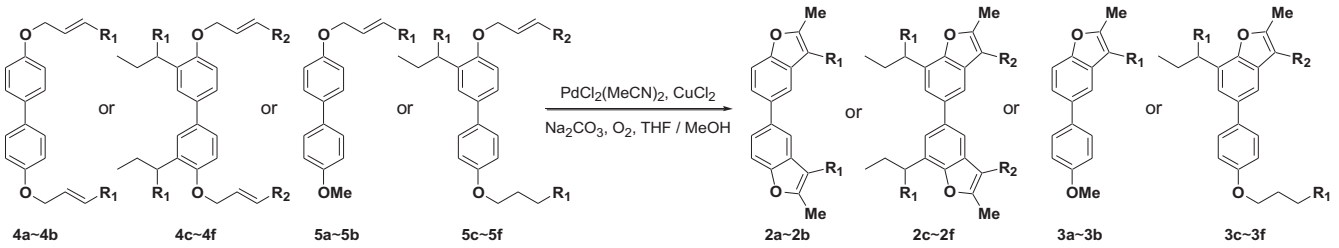
Based on the experimental results, a possible reaction mechanism is shown in Scheme 4. How is product **2a** produced? Initially, complexation of $PdCl_2(MeCN)_2$ with terminal olefin of substrate **4a** yields intermediate **A**. Intermediate **B** should be afforded via intramolecular 5-*exo-trig* cyclization. This is followed by a β-hydride elimination on the skeleton of intermediate **B**, generating intermediate **C** is generated. After isomerization of intermediate **C**, olefinic migration affords product **2a**. Subsequently, Pd(0) is recycled into $PdCl_2(MeCN)_2$ by using $CuCl_2$ and O_2, which is regenerated by forming CuCl and HCl in situ.[14]

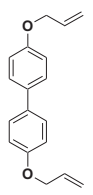
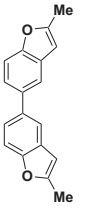
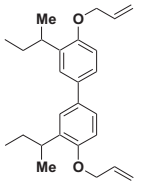
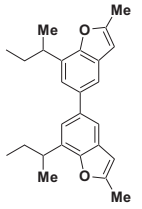
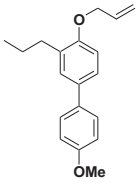
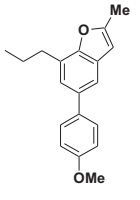
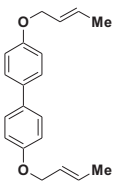
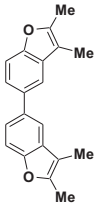
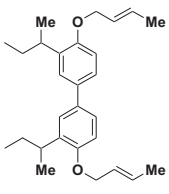
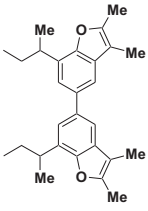
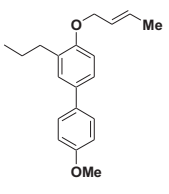
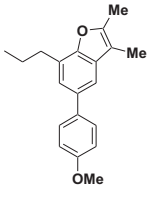


Scheme 4. A possible mechanism for synthesizing product **2a**.

Changing the substituents (R_1 and R_2) of skeletons **4** and **5**, six 5,5′-bis-benzofurans **2a**–**2f** and six 5-arylbenzofurans **3a**–**3f** were isolated with 40%–80% and 82%–49% yields via the above-mentioned one-pot oxidative protocol as shown in Table 2. In comparison with the isolated yields of products with different substituents, it was found that the yields of products **2e**–**2f** and **3e**–**3f** (R_1=Me, entries 5–6 and 11–12) were slightly poorer than those for the other analogues **2a**–**2d** and **3a**–**3d** (entries 1–4 and 7–10). For the one-pot reaction of compound **4g**, however, attempts to obtain the skeleton of benzofuran were unsuccessful (see equation 1). The structural frameworks of compounds **2b** and **3b** were constructed using single-crystal X-ray analysis (Fig. 1).[15] Single-crystal X-ray diffraction analysis was employed to determine the constitution and relative configuration of the isolated product. According to the above procedure, skeletons **4** and **5** were constructed by $PdCl_2(MeCN)_2/CuCl_2/O_2$ system mediated annulation of skeletons **2** and **3** with different substituents.

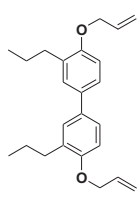
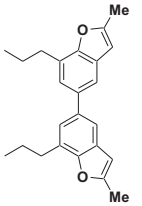
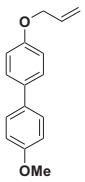
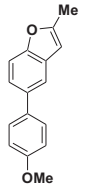
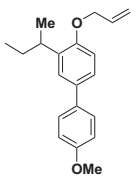
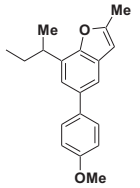
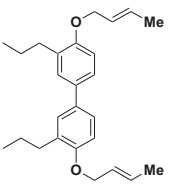
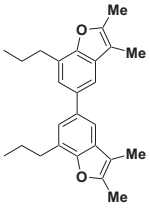
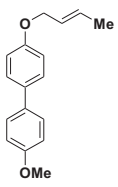
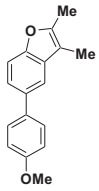
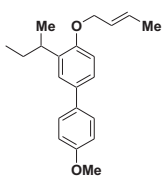
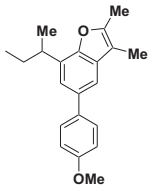
Table 2
One-pot synthetic route toward 5,5′-bis-benzofurans **2** and 5-arylbenzofurans **3**[a,b]



Entry	Reactants **4**/**5**	Products **2**/**3**	Entry	Reactants **4**/**5**	Products **2**/**3**	Entry	Reactants **4**/**5**	Products **2**/**3**
1			5			9		
	4a	**2a**/80%		**4e**	**2e**/52%		**5c**	**3c**/74%
2			6			10		
	4b	**2b**/75%		**4f**	**2f**/40%		**5d**	**3d**/62%

(*continued on next page*)

Table 2 (*continued*)

Entry	Reactants **4**/**5**	Products **2**/**3**	Entry	Reactants **4**/**5**	Products **2**/**3**	Entry	Reactants **4**/**5**	Products **2**/**3**
3	 **4c**	 **2c**/78%	7	 **5a**	 **3a**/82%	11	 **5e**	 **3e**/58%
4	 **4d**	 **2d**/70%	8	 **5b**	 **3b**/74%	12	 **5f**	 **3f**/49%

[a] For the optimal reaction conditions: (i) skeleton 4 or 5 (1.0 mmol), $PdCl_2(MeCN)_2$ (26 mg, 10 mol %), $CuCl_2$ (200 mg, 1.5 mmol), Na_2CO_3 (265 mg, 2.5 mmol), O_2 (bubbled), THF/MeOH (*v*/*v*=9/1, 10 mL), rt, 10 h.

[b] The isolated products were>95% pure as determined by ^1H NMR analysis.

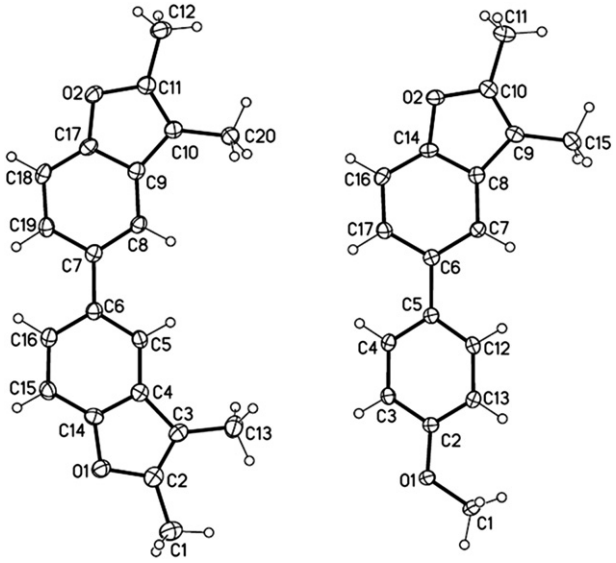
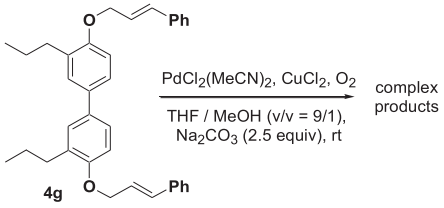
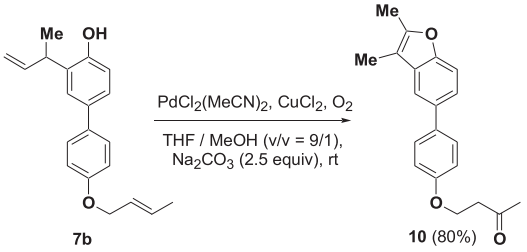


Fig. 1. X-ray structures of compounds **2b** and **3b**.



Equation 1. One-pot reaction of compound **4g**.

To further examine the reaction of compound **6a** with the $PdCl_2(MeCN)_2/CuCl_2/O_2$ system, we found that product **2a** provided with 92% yield. In comparison with two routes, the two-step transformation of Claisen rearrangement and aerobic Wacker-type oxidative cyclization (**4a**→**6a**→**2a**) provided a similar yield (82% for two-steps) to that of a one-pot conversion process (**4a**→**2a**, 80%). Under the above conditions, the reaction for compound **7b** was further studied, as shown in Scheme 5. Compound **10** was prepared in 80% yield from the Pd^{II}/Cu^{II} system mediated one-pot combination of compound **7b**.



Scheme 5. Synthesis of compound **10**.

3. Conclusion

A synthetic methodology for producing functionalized 5,5′-bis-benzofurans 2 and 5-arylbenzofurans 3 has been successfully presented from the one-pot facile $PdCl_2/CuCl_2$-mediated reaction of substituted bis-allylphenols 4 or 5-aryl-allylphenols 5 with the involvement of molecular oxygen. This resulted in acceptable to good yields via a tandem process of Claisen rearrangement and Wacker-type oxidative cyclization. The overall preparation procedures for synthesizing the functionalized skeletons of benzofurans are simple.

4. Experimental section

4.1. General

All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous $MgSO_4$ before concentration in vacuo. Melting points were determined with a SMP3 melting apparatus. ^1H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer operating at 200/400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants

(*J*) are given in Hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer Finnigan/Thermo Quest MAT 95XL. X-ray crystal structures were obtained with an Enraf-Nonius FR-590 diffractometer (CAD4, Kappa CCD). Elemental analyses were carried out with Heraeus Vario III-NCSH, Heraeus CHN-OS-Rapid Analyzer or Elementar Vario EL III.

4.2. A representative procedure of skeleton 2 or 3 is as follows

$PdCl_2(MeCN)_2$ (26 mg, 10 mol %), $CuCl_2$ (200 mg, 1.5 mmol), and Na_2CO_3 (265 mg, 2.5 mmol) were added to a solution of skeleton **4** or **5** (1.0 mmol) in the co-solvent of THF and MeOH (20 mL, *v*/*v*=9/1) at rt. Then oxygen was bubbled into the mixture for 2 h, and stirring occurred at rt for 8 h. The residue was diluted with water (2 mL) and the mixture was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc=10/1–6/1) afforded skeleton **2** or **3**.

*4.2.1. 2,2′-Dimethyl[5,5′]bibenzofuranyl (**2a**).* Yield=80% (210 mg); mp=141–143 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2935, 1493, 1270, 1120, 958 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{18}H_{15}O_2$ 263.1072, found 263.1077; ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (t, *J*=1.2 Hz, 2H), 7.45 (br s, 4H), 6.42 (s, 2H), 2.49 (d, *J*=1.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.03 (2×), 154.10 (2×), 136.76 (2×), 129.65 (2×), 123.01 (2×), 118.84 (2×), 110.55 (2×), 102.76 (2×), 14.12 (2×).

*4.2.2. 2,3,2′,3′-Tetramethyl[5,5′]bibenzofuranyl (**2b**).* Yield=75% (217 mg); mp=157–158 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2939, 1501, 1274, 1122, 961 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{20}H_{19}O_2$ 291.1385, found 291.1389; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (s, 2H), 7.47 (dd, *J*=1.2, 8.4 Hz, 2H), 7.42 (d, *J*=8.0 Hz, 2H), 2.42 (s, 6H), 2.21 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.17 (2×), 151.10 (2×), 136.52 (2×), 130.91 (2×), 122.98 (2×), 117.32 (2×), 110.34 (2×), 109.92 (2×), 11.87 (2×), 7.97 (2×); Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.98; H, 6.45. Single-crystal X-ray diagram: crystal of **2b** was grown by slow diffusion of EtOAc into a solution of **2b** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 1 21/c 1, *a*=17.2542(17) Å, *b*=6.7387(7) Å, *c*=13.1842(12) Å, *V*=1499.1(3) $Å^3$, *Z*=4, d_{calcd}=1.286 g/cm^3, *F*(000)=616, 2θ range 1.21–26.37°, *R* indices (all data) *R*1=0.0617, w*R*2=0.1398.

*4.2.3. 2,2′-Dimethyl-7,7′-dipropyl[5,5′]bibenzofuranyl (**2c**).* Yield=78% (270 mg); mp=63–64 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2933, 1494, 1272, 1122, 960 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{24}H_{27}O_2$ 347.2011, found 347.2015; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J*=1.6 Hz, 2H), 7.30 (d, *J*=1.6 Hz, 2H), 6.42 (d, *J*=1.2 Hz, 2H), 2.95 (t, *J*=7.6 Hz, 4H), 2.51 (d, *J*=0.8 Hz, 6H), 1.92–1.82 (m, 4H), 1.08 (t, *J*=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.47 (2×), 152.86 (2×), 137.01 (2×), 129.01 (2×), 125.43 (2×), 123.29 (2×), 116.37 (2×), 102.93 (2×), 32.07 (2×), 23.17 (2×), 14.20 (2×), 14.14 (2×).

*4.2.4. 2,3,2′,3′-Tetramethyl-7,7′-dipropyl[5,5′]bibenzofuranyl (**2d**).* Yield=70% (262 mg); mp=70–71 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2938, 1493, 1271, 1121, 956 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{26}H_{31}O_2$ 375.2324, found 375.2328; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J*=2.0 Hz, 2H), 7.27 (d, *J*=2.0 Hz, 2H), 2.90 (t, *J*=7.6 Hz, 4H), 2.41 (s, 6H), 2.20 (s, 6H), 1.86–1.80 (m, 4H), 1.03 (t, *J*=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.83 (2×), 150.57 (2×), 136.82 (2×), 130.50 (2×), 125.26 (2×), 123.32 (2×), 114.86 (2×), 110.03 (2×), 32.02 (2×), 23.24 (2×), 14.16 (2×), 11.94 (2×), 8.12 (2×).

*4.2.5. 7,7′-Di-sec-butyl-2,2′-dimethyl[5,5′]bibenzofuranyl (**2e**).* Yield =52% (195 mg); Colorless viscous gum; IR ($CHCl_3$) 2942, 1488, 1273, 1116, 955 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{26}H_{31}O_2$ 375.2324, found 375.2326; ^1H NMR (200 MHz, $CDCl_3$): δ 7.54 (s, 2H), 7.29 (s, 2H), 6.44 (s, 2H), 3.22–3.17 (m, 2H), 2.45 (s, 6H), 1.86–1.78 (m, 4H), 1.43 (d, *J*=7.2 Hz, 6H), 0.93 (t, *J*=7.2 Hz, 6H).

*4.2.6. 7,7′-Di-sec-butyl-2,3,2′,3′-tetramethyl[5,5′]bibenzofuranyl (**2f**).* Yield=40% (160 mg); Colorless gum; IR ($CHCl_3$) 2940, 1482, 1273, 1113, 952 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{28}H_{35}O_2$ 403.2637, found 403.2636; ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J*=1.6 Hz, 2H), 7.28 (d, *J*=1.6 Hz, 2H), 3.23–3.18 (m, 2H), 2.43 (d, *J*=0.4 Hz, 6H), 2.22 (d, *J*=0.8 Hz, 6H), 1.84–1.75 (m, 4H), 1.43 (d, *J*=6.8 Hz, 6H), 0.93 (t, *J*=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.39 (2×), 150.45 (2×), 137.10 (2×), 130.64 (2×), 130.31 (2×), 121.11 (2×), 114.77 (2×), 109.95 (2×), 36.30 (2×), 29.81 (2×), 20.56 (2×), 12.46 (2×), 11.95 (2×), 8.10 (2×).

*4.2.7. 5-(4-Methoxyphenyl)-2-methylbenzofuran (**3a**).* Yield=82% (195 mg); mp=128–129 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2939, 1466, 1243, 1147, 966 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{16}H_{15}O_2$ 239.1072, found 239.1074; ^1H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, *J*=0.4, 1.6 Hz, 1H), 7.55 (d, *J*=9.2 Hz, 2H), 7.44 (dt, *J*=0.8, 8.4 Hz, 1H), 7.39 (dd, *J*=1.6, 8.4 Hz, 1H), 6.99 (d, *J*=9.2 Hz, 2H), 6.41 (t, *J*=1.2 Hz, 1H), 3.86 (s, 3H), 2.48 (d, *J*=1.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.74, 156.03, 154.05, 135.74, 134.47, 129.68, 128.34 (2×), 122.38, 118.17, 114.11 (2×), 110.60, 102.74, 55.31, 14.11; Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.88; H, 6.12.

*4.2.8. 5-(4-Methoxyphenyl)-2,3-dimethylbenzofuran (**3b**).* Yield=74% (186 mg); mp=132–133 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2938, 1469, 1245, 1143, 966 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{17}H_{17}O_2$ 253.1229, found 253.1230; ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J*=9.2 Hz, 2H), 7.58–7.55 (m, 1H), 7.40–7.38 (m, 2H), 7.00 (d, *J*=9.2 Hz, 2H), 3.87 (s, 3H), 2.41 (d, *J*=0.8 Hz, 3H), 2.20 (d, *J*=0.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.72, 153.13, 151.11, 135.35, 134.64, 130.93, 128.35 (2×), 122.31, 116.66, 114.11 (2×), 110.39, 109.87, 55.32, 11.83, 7.91; Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.23; H, 6.62. Single-crystal X-ray diagram: crystal of **3b** was grown by slow diffusion of EtOAc into a solution of **3b** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 1 21/n 1, *a*=7.0591(4) Å, *b*=7.2045(4) Å, *c*=25.9203(15) Å, *V*=1312.44(13) $Å^3$, *Z*=4, d_{calcd}=1.277 g/cm^3, *F*(000)=536, 2θ range 1.58–26.52°, *R* indices (all data) *R*1=0.0506, w*R*2=0.1039.

*4.2.9. 2-Methyl-5-(4-propoxyphenyl)-7-propylbenzofuran (**3c**).* Yield =74% (228 mg); mp=81–83 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2935, 1462, 1240, 1143, 964 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{21}H_{25}O_2$ 309.1855, found 309.1856; ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J*=8.8 Hz, 2H), 7.44 (d, *J*=2.0 Hz, 1H), 7.20 (d, *J*=1.6 Hz, 1H), 6.97 (d, *J*=8.8 Hz, 2H), 6.38 (d, *J*=1.2 Hz, 1H), 3.97 (t, *J*=6.4 Hz, 2H), 2.89 (t, *J*=7.6 Hz, 2H), 2.47 (d, *J*=0.8 Hz, 3H), 1.87–1.79 (m, 4H), 1.07 (t, *J*=6.8 Hz, 3H), 1.02 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.21, 155.54, 152.83, 135.77, 134.59, 129.28, 128.31 (2×), 125.53, 122.63, 115.71, 114.66 (2×), 102.90, 69.59, 32.03, 23.11, 22.63, 14.21, 14.11, 10.54.

*4.2.10. 2,3-Dimethyl-5-(4-propoxyphenyl)-7-propylbenzofuran (**3d**).* Yield=62% (200 mg); Viscous gum; IR ($CHCl_3$) 2934, 1467, 1243, 1152, 958 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{22}H_{27}O_2$ 323.2011, found 323.2013; ^1H NMR (200 MHz, $CDCl_3$): δ 7.57 (d, *J*=9.2 Hz, 2H), 7.42 (s, 1H), 7.22 (s, 1H), 6.99 (d, *J*=9.2 Hz, 2H), 3.99 (t, *J*=6.8 Hz, 2H), 2.91 (t, *J*=7.2 Hz, 2H), 2.47 (s, 3H), 2.22 (s, 3H), 1.88–1.75 (m, 4H), 1.10 (t, *J*=7.2 Hz, 3H), 1.00 (t, *J*=7.2 Hz, 3H).

*4.2.11. 5-(4-Butoxyphenyl)-7-sec-butyl-2-methylbenzofuran (**3e**).* Yield=58% (195 mg); Viscous gum; IR ($CHCl_3$) 2941, 1462, 1240, 1142, 956 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{23}H_{29}O_2$ 337.2168,

found 337.2170; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J=8.8 Hz, 2H), 7.43 (d, J=1.6 Hz, 1H), 7.19 (d, J=2.0 Hz, 1H), 6.87 (d, J=8.8 Hz, 2H), 6.37 (d, J=0.8 Hz, 1H), 4.01 (t, J=6.4 Hz, 2H), 3.20–3.15 (m, 1H), 2.46 (d, J=1.2 Hz, 3H), 1.88–1.70 (m, 4H), 1.56–1.45 (m, 2H), 1.39 (d, J=7.2 Hz, 3H), 1.39 (t, J=7.2 Hz, 3H), 0.91 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.22, 155.41, 152.41, 144.88, 135.86, 134.76, 130.56, 128.34 (2×), 120.33, 115.57, 114.66 (2×), 102.86, 67.78, 36.15, 31.38, 29.78, 20.50, 19.27, 14.23, 13.86, 12.36.

*4.2.12. 5-(4-Butoxyphenyl)-7-sec-butyl-2,3-dimethylbenzofuran (**3f**).* Yield=49% (172 mg); Viscous gum; IR ($CHCl_3$) 2940, 1459, 1239, 1139, 960 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{24}H_{31}O_2$ 351.2324, found 351.2328; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.57 (d, J=9.2 Hz, 2H), 7.42 (s, 1H), 7.22 (s, 1H), 6.99 (d, J=9.2 Hz, 2H), 4.04 (t, J=6.8 Hz, 2H), 3.22–3.17 (m, 1H), 2.46 (s, 3H), 2.22 (s, 3H), 1.91–1.74 (m, 4H), 1.60–1.51 (m, 2H), 1.38 (d, J=7.2 Hz, 3H), 1.35 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H).

4.3. A representative procedure of skeleton 6 or 7 is as follows

Decalin (8 mL) was added to a solution of compounds **4a**–**4b** or **5a**–**5b** (0.7 mmol) at rt. The reaction mixture was stirred at reflux for 3–4 h (for **5a**–**5b** → **7a**–**7b**) or 8–10 h (for **4a**–**4b** → **6a**–**6b**). The reaction was traced by TLC until compounds **4a**–**4b** or **5a**–**5b** was consumed. The reaction mixture was cooled to rt. Decalin was evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc=8/1–4/1) afforded compounds **6a**–**6b** or **7a**–**7b**.

*4.3.1. 3,3′-Diallyl-biphenyl-4,4′-diol (**6a**).* Yield=89% (166 mg); mp=81–82 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 3310, 2957, 2877, 1636, 1461, 1240, 1141, 911 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{18}H_{19}O_2$ 267.1385, found 267.1391; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.28 (m, 4H), 6.85 (d, J=8.0 Hz, 2H), 6.10–6.00 (m, 2H), 5.23–5.16 (m, 4H), 5.05 (br s, 2H), 3.46 (d, J=6.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.20 (2×), 136.32 (2×), 133.87 (2×), 128.80 (2×), 126.14 (2×), 125.47 (2×), 116.62 (2×), 116.11 (2×), 35.29 (2×); Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.30; H, 6.62.

*4.3.2. 3,3′-Bis-(1-methylallyl)biphenyl-4,4′-diol (**6b**).* Yield=80% (165 mg); Colorless gum; IR ($CHCl_3$) 3318, 2967, 2870, 1646, 1458, 1239, 1140, 918 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{20}H_{23}O_2$ 295.1698, found 295.1710; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (s, 2H), 7.31–7.29 (m, 2H), 6.89–6.85 (m, 2H), 6.19–6.11 (m, 2H), 5.30 (br s, 2H), 5.27–5.19 (m, 4H), 3.80–3.74 (m, 2H), 1.45 (d, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.79 (2×), 142.27 (2×), 134.10 (2×), 130.57 (2×), 126.55 (2×), 125.91 (2×), 116.45 (2×), 114.41 (2×), 37.85 (2×), 18.78 (2×).

*4.3.3. 3-Allyl-4′-allyloxybiphenyl-4-ol (**7a**).* Compound **7a** is a known compound and the analytical data are consistent with those in the literature.[7c] Yield=86% (160 mg).

*4.3.4. 4′-But-2-enyloxy-3-(1-methylallyl)biphenyl-4-ol (**7b**).* Compound **7b** is a known compound and the analytical data are consistent with those in the literature.[7c] Yield=78% (161 mg).

4.4. A representative procedure of skeleton 4 or 5 is as follows

K_2CO_3 (for **1** or **1a**, 2.8 g, 20.0 mmol; for **8a**–**8b** or **9a**–**9b**, 280 mg, 2.0 mmol) was added to a solution of compound **1** or **1a** (5.0 mmol) or compounds **8a**–**8b** or **9a**–**9b** (0.5 mmol) in acetone (for **1** or **1a**, 100 mL; for **8a**–**8b** or **9a**–**9b**, 10 mL) at rt. The reaction mixture was stirred at rt for 10 min. Allyl bromide (for **1** or **8a**–**8b**, 3.0 mmol; for **1a** or **9a**–**9b**, 1.5 mmol), crotyl bromide (for **1** or **8a**–**8b**, 3.0 mmol; for **1a** or **9a**–**9b**, 1.5 mmol) or cinnamyl chloride (for **8a**, 3.0 mmol) was added to the reaction mixture at rt. The reaction mixture was stirred at reflux for 10 h. The reaction was traced by TLC until compound **1** or **1a** and compounds **8a**–**8b** or **9a**–**9b** was consumed. The reaction mixture was cooled to rt, concentrated, and extracted with EtOAc (3×60 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc=15/1–10/1) afforded skeleton **4** or **5**.

*4.4.1. 4,4′-Bis-allyloxybiphenyl (**4a**).* Compound **4a** is a known compound and the analytical data are consistent with those in the literature.[7c] Yield=88% (1.17 g).

*4.4.2. 4,4′-Bis-but-2-enyloxybiphenyl (**4b**).* Compound **4b** is a known compound and the analytical data are consistent with those in the literature.[7c] Yield=84% (1.23 g).

*4.4.3. 4,4′-Bis-allyloxy-3,3′-dipropyl-biphenyl (**4c**).* Yield=86% (151 mg); mp=102–103 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2968, 2870, 1642, 1460, 1232, 1132, 926 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{24}H_{31}O_2$ 351.2324, found 351.2339; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (s, 2H), 7.33–7.30 (m, 2H), 6.86 (dd, J=1.2, 8.8 Hz, 2H), 6.13–6.04 (m, 2H), 5.47–5.42 (m, 2H), 5.30–5.26 (m, 2H), 4.57 (dt, J=1.6, 4.8 Hz, 4H), 2.69–2.65 (m, 4H), 1.72–1.62 (m, 4H), 0.98 (t, J=6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.55 (2×), 133.67 (2×), 133.48 (2×), 131.58 (2×), 128.52 (2×), 124.88 (2×), 116.67 (2×), 111.74 (2×), 68.73 (2×), 32.60 (2×), 23.13 (2×), 14.17 (2×).

*4.4.4. 4,4′-Bis-but-2-enyloxy-3,3′-dipropylbiphenyl (**4d**).* Yield=90% (170 mg); mp=85–86 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2978, 2872, 1640, 1462, 1235, 1128, 933 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{26}H_{35}O_2$ 379.2637, found 379.2643; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (s, 2H), 7.32–7.30 (m, 2H), 6.87 (dd, J=1.2, 8.8 Hz, 2H), 5.90–5.82 (m, 2H), 5.77–5.70 (m, 2H), 4.50 (d, J=5.6 Hz, 4H), 2.67–2.64 (m, 4H), 1.77 (dd, J=1.2, 5.6 Hz, 6H), 1.71–1.62 (m, 4H), 0.98 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.76 (2×), 133.42 (2×), 131.59 (2×), 129.15 (2×), 128.43 (2×), 126.63 (2×), 124.84 (2×), 111.92 (2×), 68.87 (2×), 32.50 (2×), 23.09 (2×), 17.86 (2×), 14.15 (2×); Anal. Calcd for $C_{26}H_{34}O_2$: C, 82.49; H, 9.05. Found: C, 82.80; H, 9.32.

*4.4.5. 4,4′-Bis-allyloxy-3,3′-di-sec-butylbiphenyl (**4e**).* Yield=88% (166 mg); Viscous gum; IR ($CHCl_3$) 2972, 2861, 1639, 1470, 1242, 1133, 932 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{26}H_{35}O_2$ 379.2637, found 379.2638; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.35–7.22 (m, 4H), 6.89 (d, J=7.8 Hz, 2H), 6.16–6.03 (m, 2H), 5.46–5.42 (m, 2H), 5.30–5.24 (m, 2H), 4.57 (d, J=4.8 Hz, 4H), 3.22–3.16 (m, 2H), 1.75–1.60 (m, 4H), 1.20 (d, J=7.2 Hz, 6H), 0.92 (t, J=7.2 Hz, 6H).

*4.4.6. 4,4′-Bis-but-2-enyloxy-3,3′-di-sec-butylbiphenyl (**4f**).* Yield=84% (171 mg); Viscous gum; IR ($CHCl_3$) 2977, 2872, 1644, 1461, 1233, 1132, 924 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{28}H_{39}O_2$ 407.2950, found 407.2953; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.28 (m, 4H), 6.88 (d, J=8.4 Hz, 2H), 5.89–5.81 (m, 2H), 5.77–5.70 (m, 2H), 4.48 (dd, J=1.2, 5.6 Hz, 4H), 3.21–3.13 (m, 2H), 1.76 (dd, J=1.2, 6.4 Hz, 6H), 1.73–1.54 (m, 4H), 1.25 (d, J=7.2 Hz, 6H), 0.88 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.40 (2×), 136.38 (2×), 133.92 (2×), 129.12 (2×), 126.65 (2×), 125.48 (2×), 124.62 (2×), 112.20 (2×), 69.09 (2×), 33.85 (2×), 29.87 (2×), 20.49 (2×), 17.85 (2×), 12.27 (2×).

*4.4.7. 4′-But-2-enyloxy-3-(1-methylallyl)biphenyl-4-ol (**4g**).* Compound **4g** is a known compound and the analytical data are consistent with those in the literature.[7c] Yield=82% (206 mg).

*4.4.8. 4-Allyloxy-4′-methoxybiphenyl (**5a**).* Yield=68% (816 mg); mp=136–137 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2975, 2871, 1640, 1451, 1222, 1125, 912 cm^{-1}; HRMS (ESI,

M^++1) calcd for $C_{16}H_{17}O_2$ 241.1229, found 241.1236; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.44 (m, 4H), 6.97 (m, 4H), 6.12–6.03 (m, 1H), 5.43 (dq, J=1.6, 17.2 Hz, 1H), 5.30 (dq, J=1.6, 10.4 Hz, 1H), 4.56 (dt, J=1.2, 6.4 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.68, 157.69, 133.60, 133.41, 133.31, 127.69 (2×), 127.66 (2×), 117.65, 114.97 (2×), 114.13 (2×), 68.87, 55.30.

*4.4.9. 4-But-2-enyloxy-4′-methoxybiphenyl (**5b**).* Yield=92% (1.17 g); mp=129–131 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2970, 2872, 1633, 1446, 1218, 1135, 931 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{17}H_{19}O_2$ 255.1385, found 255.1388; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.42 (m, 4H), 6.98–6.92 (m, 4H), 5.90–5.83 (m, 1H), 5.78–5.71 (m, 1H), 4.48 (dt, J=1.2, 6.0 Hz, 2H), 3.82 (s, 3H), 1.76 (dd, J=0.8, 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.65, 157.81, 133.41, 130.56, 127.67 (2×), 127.64 (2×), 126.08, 114.92 (2×), 114.22, 114.11 (2×), 68.75, 55.28, 17.84.

*4.4.10. 4-Allyloxy-4′-propoxy-3-propylbiphenyl (**5c**).* Yield=89% (138 mg); Colorless gum; IR ($CHCl_3$) 2965, 2882, 1634, 1450, 1224, 1130, 923 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{21}H_{27}O_2$ 311.2011, found 311.2021; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.45 (m, 2H), 7.34–7.31 (m, 2H), 6.97–6.93 (m, 2H), 6.87 (d, J=8.0 Hz, 1H), 6.14–6.04 (m, 1H), 5.48–5.42 (m, 1H), 5.31–5.27 (m, 1H), 4.58 (dt, J=1.6, 4.8 Hz, 2H), 3.96 (t, J=6.4 Hz, 2H), 2.70–2.66 (m, 2H), 1.88–1.79 (m, 2H), 1.72–1.63 (m, 2H), 1.06 (t, J=7.6 Hz, 3H), 0.99 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.14, 155.60, 133.64, 133.55, 133.23, 131.61, 128.47, 127.70 (2×), 124.82, 116.69, 114.67 (2×), 111.76, 69.56, 68.73, 32.57, 23.10, 22.62, 14.16, 10.54.

*4.4.11. 4-But-2-enyloxy-4′-propoxy-3-propylbiphenyl (**5d**).* Yield=92% (149 mg); mp=83–84 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2974, 2878, 1632, 1440, 1228, 1141, 931 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{22}H_{29}O_2$ 325.2168, found 325.2170; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–7.46 (m, 2H), 7.34–7.29 (m, 2H), 6.99–6.94 (m, 2H), 6.88 (d, J=8.0 Hz, 1H), 5.91–5.83 (m, 1H), 5.79–5.72 (m, 1H), 4.51 (dt, J=1.2, 5.6 Hz, 2H), 3.96 (t, J=6.4 Hz, 2H), 2.69–2.64 (m, 2H), 1.89–1.81 (m, 2H), 1.78 (dd, J=1.2, 6.0 Hz, 3H), 1.73–1.63 (m, 2H), 1.07 (t, J=7.6 Hz, 3H), 0.99 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.12, 155.81, 133.63, 133.07, 131.63, 129.17, 128.36, 127.67 (2×), 126.57, 124.78, 114.67 (2×), 111.91, 69.56, 68.84, 32.47, 23.05, 22.61, 17.86, 14.13, 10.53.

*4.4.12. 4-Allyloxy-4′-butoxy-3-sec-butylbiphenyl (**5e**).* Yield=84% (142 mg); Viscous gum; IR ($CHCl_3$) 2963, 2863, 1641, 1449, 1223, 1145, 940 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{23}H_{31}O_2$ 339.2324, found 339.2325; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J=8.8 Hz, 2H), 7.35 (d, J=2.4 Hz, 1H), 7.30 (dd, J=2.4, 8.4 Hz, 1H), 6.94 (d, J=9.2 Hz, 2H), 6.87 (d, J=8.4 Hz, 1H), 6.13–6.04 (m, 1H), 5.45 (dq, J=1.6, 17.2 Hz, 1H), 5.28 (dq, J=1.6, 10.8 Hz, 1H), 4.56 (dt, J=1.6, 4.8 Hz, 2H), 3.99 (t, J=6.4 Hz, 2H), 3.21–3.16 (m, 1H), 1.82–1.46 (m, 6H), 1.25 (d, J=7.2 Hz, 3H), 0.99 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.18, 155.25, 136.39, 133.81, 133.71, 133.50, 127.74 (2×), 125.46, 124.54, 116.73, 114.68 (2×), 112.05, 58.98, 67.76, 33.88, 31.37, 29.87, 20.46, 19.26, 13.86, 12.26.

*4.4.13. 4-But-2-enyloxy-4′-butoxy-3-sec-butylbiphenyl (**5f**).* Yield=84% (148 mg); Viscous gum; IR ($CHCl_3$) 2965, 2871, 1635, 1452, 1221, 1144, 935 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{24}H_{33}O_2$ 353.2481, found 353.2484; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J=8.8 Hz, 2H), 7.34 (d, J=2.4 Hz, 1H), 7.30 (dd, J=2.4, 8.4 Hz, 1H), 6.95 (d, J=8.8 Hz, 2H), 6.89 (d, J=8.4 Hz, 1H), 5.91–5.82 (m, 1H), 5.78–5.71 (m, 1H), 4.50 (dt, J=1.6, 5.6 Hz, 2H), 4.00 (t, J=6.4 Hz, 2H), 3.22–3.14 (m, 1H), 1.83–1.47 (m, 9H), 1.25 (d, J=6.8 Hz, 3H), 1.00 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.13, 155.45, 136.44, 133.86, 133.33, 129.20, 127.73 (2×), 126.60, 125.36, 124.50, 114.65 (2×), 112.22, 69.09, 67.75, 33.72, 31.36, 29.87, 20.53, 19.26, 17.88, 13.86, 12.25.

4.5. A representative procedure of skeleton 8 or 9 is as follows

Palladium on activated carbon (10%, 5 mg) was added to a solution of skeleton **6** or **7** (1.0 mmol) in EtOAc (20 mL) at rt. Then hydrogen was bubbled into the mixture for 10 min, and stirring occurred at rt for 20 h. The reaction mixture was filtered and evaporated to yield crude product. Purification on silica gel (hexanes/EtOAc=6/1–3/1) afforded skeleton **8** or **9**.

*4.5.1. 3,3′-Dipropylbiphenyl-4,4′-diol (**8a**).* Yield=98% (265 mg); mp=115–116 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 3323, 2973, 2867, 1655, 1450, 1231, 1143, 963 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{18}H_{23}O_2$ 271.1698, found 271.1703; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J=2.4 Hz, 2H), 7.26 (dd, J=2.4, 8.0 Hz, 2H), 6.81 (d, J=8.0 Hz, 2H), 4.80 (s, 2H), 2.64 (t, J=7.6 Hz, 4H), 1.75–1.66 (m, 4H), 1.02 (t, J=7.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.52 (2×), 133.85 (2×), 128.68 (2×), 128.55 (2×), 125.31 (2×), 115.46 (2×), 32.20 (2×), 23.02 (2×), 14.05 (2×).

*4.5.2. 3,3′-Di-sec-butylbiphenyl-4,4′-diol (**8b**).* Yield=95% (283 mg); mp=113–114 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 3329, 2968, 2863, 1651, 1442, 1238, 1146, 958 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{20}H_{27}O_2$ 299.2011, found 299.2012; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J=2.4 Hz, 2H), 7.23 (dd, J=2.4, 8.4 Hz, 2H), 6.79 (d, J=8.4 Hz, 2H), 4.74 (s, 2H), 3.04–2.95 (m, 2H), 1.78–1.58 (m, 4H), 1.29 (d, J=7.2 Hz, 6H), 0.91 (t, J=7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.09 (2×), 134.28 (2×), 133.38 (2×), 125.70 (2×), 124.96 (2×), 115.55 (2×), 34.26 (2×), 29.83 (2×), 20.44 (2×), 12.24 (2×).

*4.5.3. 4′-Propoxy-3-propylbiphenyl-4-ol (**9a**).* Yield=92% (248 mg); Colorless gum; IR ($CHCl_3$) 3315, 2983, 2877, 1668, 1452, 1239, 1154, 958 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{18}H_{23}O_2$ 271.1698, found 271.1702; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.45 (m, 2H), 7.32 (d, J=2.4 Hz, 1H), 7.27 (dd, J=2.4, 8.4 Hz, 1H), 6.98–6.94 (m, 2H), 6.81 (d, J=8.4 Hz, 1H), 4.80 (br s, 1H), 3.97 (t, J=6.4 Hz, 2H), 2.67–2.63 (m, 2H), 1.89–1.80 (m, 2H), 1.75–1.66 (m, 2H), 1.07 (t, J=7.2 Hz, 3H), 1.02 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.12, 152.57, 133.60, 133.51, 128.65, 128.57, 127.67 (2×), 125.24, 115.47, 114.69 (2×), 69.60, 32.18, 22.98, 22.59, 14.05, 10.52.

*4.5.4. 4′-Butoxy-3-sec-butylbiphenyl-4-ol (**9b**).* Yield=94% (280 mg); mp=92–93 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 3322, 2979, 2876, 1659, 1450, 1241, 1156, 957 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{20}H_{27}O_2$ 299.2011, found 299.2013; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J=8.8 Hz, 2H), 7.36 (d, J=2.4 Hz, 1H), 7.26 (dd, J=2.4, 8.4 Hz, 1H), 6.98 (d, J=8.8 Hz, 2H), 6.81 (d, J=8.4 Hz, 1H), 4.97 (br s, 1H), 4.03 (t, J=6.4 Hz, 2H), 3.06–3.01 (m, 1H), 1.85–1.63 (m, 4H), 1.59–1.49 (m, 2H), 1.31 (d, J=7.2 Hz, 3H), 1.02 (t, J=7.2 Hz, 3H), 0.93 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.11, 152.17, 133.80, 133.75, 133.47, 127.71 (2×), 125.61, 124.82, 115.58, 114.71 (2×), 67.81, 34.11, 31.32, 29.81, 20.46, 19.23, 13.83, 12.20.

4.6. In Table 1 and entry 1 (no involvement of oxygen)

$Pd(MeCN)_2Cl_2$ (26 mg, 10 mol %), $CuCl_2$ (200 mg, 1.5 mmol) and Na_2CO_3 (265 mg, 2.5 mmol) were added to a solution of compound **4a** or **7b** (1.0 mmol) in the co-solvent of THF and MeOH (20 mL, v/v=9/1) at rt. The residue was diluted with water (2 mL) and the mixture was extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc=10/1–6/1) afforded compounds **2a**, **2a-1**, and **2a-2** or **10**.

*4.6.1. 4-(2-Methylbenzofuran-5-yl)-2-propenylphenol (**2a-1**).* Yield=29% (77 mg); Colorless viscous gum; IR ($CHCl_3$) 3328, 2978, 2874, 1677, 1454, 1242, 1148, 920 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{18}H_{17}O_2$ 265.1229, found 265.1232; ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J=1.6 Hz, 1H), 7.53 (d, J=2.4 Hz, 1H), 7.42 (d, J=8.4 Hz, 1H), 7.37 (dd, J=2.0, 8.4 Hz, 1H), 7.33 (dd, J=2.0, 8.4 Hz, 1H), 6.86 (d, J=8.0 Hz, 1H), 6.64 (dq, J=2.0, 15.6 Hz, 1H), 6.39 (t, J=0.8 Hz, 1H), 6.29 (dq, J=6.4, 15.6 Hz, 1H), 6.06 (s, 1H), 2.47 (d, J=1.2 Hz, 3H), 1.95 (dd, J=1.6, 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.05, 154.07, 151.58, 135.82, 134.75, 129.65, 128.64, 126.92, 126.39, 125.39, 125.17, 122.40, 118.19, 115.93, 110.57, 102.73, 18.94, 14.12.

*4.6.2. 3,3′-Dipropenylbiphenyl-4,4′-diol (**2a-2**).* Yield=30% (80 mg); mp=94–95 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 3328, 2972, 2878, 1655, 1438, 1241, 1143, 947 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{18}H_{19}O_2$ 267.1385, found 267.1388; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J=2.4 Hz, 2H), 7.27 (dd, J=2.4, 8.0 Hz, 2H), 6.83 (d, J=8.4 Hz, 2H), 6.62 (dq, J=2.0, 15.6 Hz, 2H), 6.27 (dq, J=6.4, 15.6 Hz, 2H), 5.09 (br s, 2H), 1.94 (dd, J=1.6, 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.55 (2×), 133.81 (2×), 128.66 (2×), 126.32 (2×), 125.75 (2×), 125.37 (2×), 125.19 (2×), 115.93 (2×), 18.93 (2×).

*4.6.3. 4-[4-(2,3-Dimethylbenzofuran-5-yl)phenoxy]butan-2-one (**10**).* Yield=80% (246 mg); mp=103–104 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$) 2948, 1760, 1672, 1518, 1277, 1142, 973 cm^{-1}; HRMS (ESI, M^++1) calcd for $C_{20}H_{21}O_3$ 309.1491, found 309.1493; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J=8.4 Hz, 2H), 7.54–7.52 (m, 1H), 7.38–7.37 (m, 2H), 6.97 (d, J=8.8 Hz, 2H), 4.28 (t, J=6.4 Hz, 2H), 2.93 (t, J=6.4 Hz, 2H), 2.39 (d, J=0.4 Hz, 3H), 2.26 (s, 3H), 2.17 (d, J=0.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.41, 157.66, 153.14, 151.14, 135.26, 134.95, 130.92, 128.36 (2×), 122.29, 116.67, 114.75 (2×), 110.38, 109.87, 62.99, 43.02, 30.52, 11.84, 7.93.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.02.031. Scanned photocopies of spectral data and crystallographic data of compounds **2b** and **3b** (CIF) were supported.

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15. CCDC 913059 (3b) and 913060 (2b) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: 44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).