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Total Synthesis of Ailanthoidol and Precursor XH14 by Stille Coupling

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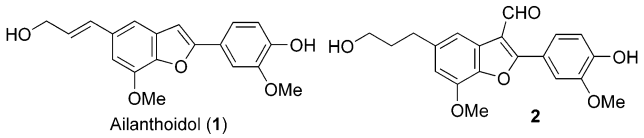
Abstract: Ailanthoidol **1**, which can be isolated from Chinese herbal medicine, is achieved in which the longest linear sequence is only six steps in 48% overall yield from commercially available 5-bromo-2-hydroxy-3-methoxybenzaldehyde. The key transformations in the synthesis are the Stille coupling reactions of benzofuranyl bromide with stannanyl compounds. This synthetic strategy can be modified to give access to a variety of different ailanthoidol and XH14 analogues.

Studies on the constituents of plants of *Zanthoxylum ailanthoidos*[1] and *Salvia miltiorrhiza* Bunge (Danshen),[2] which are used in Chinese traditional herbal medicines, showed a number of them with pharmacological interest.[3] Ailanthoidol (**1**) and XH14 (**2**) were isolated from the chloroform-soluble fraction of stem woods of *Zanthoxylum ailanthoidos* and the aqueous extracts of Danshen, respectively. Recently, during a synthesis of the phytotoxin, Garcifuran B,[4] we became aware of the facile conversion of *o*-hydroxybenzaldehydes to benzofurans and the proceeding of Stille[5] coupling of bromobenzofurans and stannanes to arylbenzofuran skeleton. Therefore, ailanthoidol (**1**) and XH14 (**2**) are ideal targets for the application of these reactions. Although **1** and **2** have



been synthesized by several groups,[6] they were achieved with very time-consuming and complicated synthetic approaches. To overcome these technical difficulties, we report our studies on the synthesis of ailanthoidol analogues from the readily available 5-bromo-7-methoxy-2-bromobenzofuran (**5**) by Stille coupling.

The Pd-catalyzed cross-coupling reaction is well-known in a wide variety of transmetalation reagents including Sn, Mg, Zn, B, Al, Zr, and Cu.[7] Perhaps the easiest route to **1** would have been to couple dibromobenzofuran, bromophenol, and bromopropenol by Pd-catalyzed reaction. In previous projects[8] we have achieved such couplings by treating a mixture of two aryl bromides with a bis-(trialkyltin) in the presence of a palladium catalyst. The reaction proceeds via in situ conversion of one aryl bromide to the corresponding stannane followed by coupling of the latter with the other benzofuranyl bromide. In the beginning of our synthesis, the commercial availability of 5-bromo-2-hydroxy-3-methoxybenzaldehyde prompted us to prepare dibromobenzofuran **5** from this compound. It was anticipated that **5** was smoothly prepared as shown in Scheme 1. In the case of **5** and the known 1-benzyloxy-4-bromo-2-methoxybenzene,[9] however, the palladium-catalyzed reaction with $(Me_3Sn)_2$ to give 2-arylbenzofuran **7** was unsuccessful. The major product was biphenyl, the product from the homocoupling of 4-bromomethoxylbenzoxylbenzene. Consequently we sought to first convert bromobenzene into a stannane in a separate step, which proceeded smoothly to provide arylstannane **6**. Although we did not know yet the chemoselectivity of the two different bromo substituents in **5**, we did run the Sonogashira reactions with tetrahydropyranoxypropyne and **5** to give only 2-acetylenebenzofuran. Similarly, we would anticipate that the reactivity of the furan ring in **5** could also undergo the Stille coupling faster than that of the benzene ring. Fortunately, with dibromide **5** and stannane **6** in hand, palladium-catalyzed cross coupling gave the regioselective 2-arylbenzofuran **7** in excellent yield (96%). The resultant benzofuran **7** was then transformed into ailanthoidol in two steps. Briefly, this involved Stille coupling of stannylpropenol and **7**, followed by removal of the benzyl protecting group with $TiCl_4$, but in low yield (5% yield over two steps). The low isolated yield might be caused because the free hydroxy group of stannylpropenol made this compound more hydrophilic than that of the protected stannyl alcohol. Also, the allyl alcohol **8** was very unstable under acid and neutral conditions during isolation.

With the aim of developing a successful route to **1**, an alternative method of construction was examined (Scheme 1). Coupling of the benzofuranyl bromide **7** with stannanyl ester proceeded readily in dioxane by Pd(0)-catalysis to give the known[6e] **9** in excellent 92% yield. According to the procedure of Lutjens and Scammells, it involved removal of the benzyl protecting group with $TiCl_4$ followed by DIBAL or $LiAlH_4$ reduction of the ester to afford **1** in the highest 95% yield (over two steps). Melting point and ^1H and ^{13}C NMR spectra of the synthetic product

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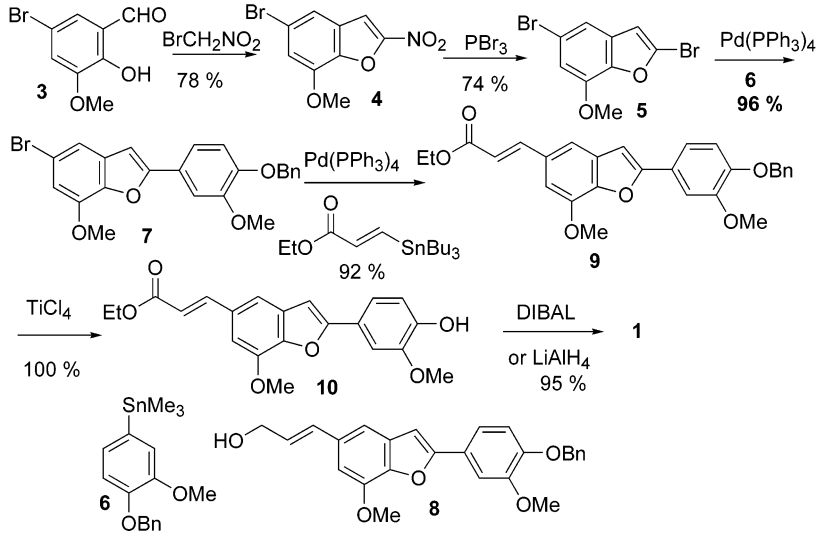
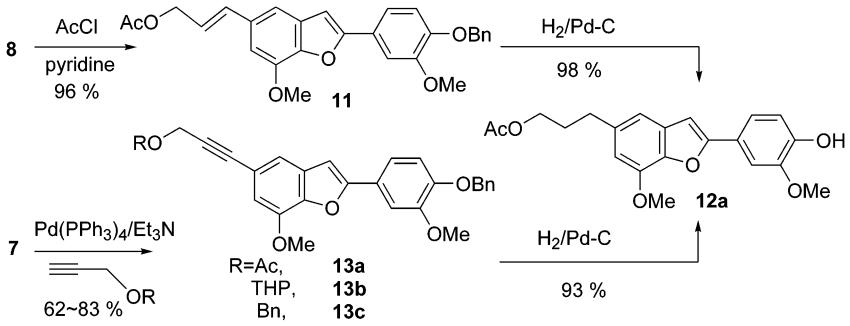
SCHEME 1. Synthesis of Ailanthoidol (1)



SCHEME 2. Synthesis of Precursor XH14



are in agreement with those reported for the naturally derived material.[1,2b]

It is worth noting that our synthetic strategy can be employed in the formal synthesis of XH14. The synthesis of precusor XH14 **12a** was achieved by using a closely related strategy that utilized the Stille coupling conditions described above. Alcohol **8** was converted to acetoxy compound **11**. Subsequent catalytic hydrogenation effected simultaneous debenzylation and reduction of the alkene in 98% yield (Scheme 2). On the other hand, the Sonogashira reaction can be employed to couple the key bromobenzofuran **7** and protected propargyl alcohol, especially acetoxy, to provide **13** in 62∼83% yield, respectively. The precursor **13a** was smoothly carried out with Pd on carbon under 1 atm of H_2 to generate **12a** in 93% yield. Finally, it suggests that the key precursor **12a** can undergo the regioselective 3-position formylation by using a Gatterman−Adams reaction[3c,6c] to achieve XH14.

In conclusion, a concise route to ailanthoidol **1** has been achieved in which the longest linear sequence is only six steps from commercially available materials in 48% overall yield. This synthesis is high yielding and easily modified to give access to a variety of different ailanthoidol and XH14 analogues. In addition, it demonstrated the usefulness of the Stille coupling reaction for 2-arylbenzofuran synthesis. The preparation of theses compounds is currently underway and their biological activities will be investigated to evaluate the efficacy of these compounds as antitumor agents.

Experimental Section[10]

5-Bromo-7-methoxy-2-bromobenzofuran (5). Nitrobenzofuran **4** (0.80 g, 3.0 mmol) was placed together with PBr_3 (5 mL) into a 25-mL round-bottomed flask under a nitrogen atmosphere. The mixture was then heated to 175 °C (oil bath temperature) with stirring under nitrogen flux and maintained at that temperature for 5 h. The flask was removed from the oil bath and allowed to cool to ambient temperature. The a dark-brown suspension was neutralized with $NaHCO_3$ until pH 8, followed by extraction with CH_2Cl_2 (3 × 100 mL). The organic layer was concentrated and the crude product was subjected to column chromatography (SiO_2, CH_2Cl_2/ether 1/1) to yield dibromide **5** (0.66 g, 74%) as white solid: mp 82−84 °C; ^{1}H NMR ($CDCl_3$) δ 3.93 (s, 3H), 6.58 (s, 1H), 6.81 and 7.14 (d, J = 1.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 56.2, 108.0, 109.9, 114.8, 116.5, 129.1, 131.1, 143.8, 144.7; HRMS (FAB) calcd for $C_9H_6O_2Br_2$ (M^+) 303.8735, found 303.8730. Anal. Calcd for $C_9H_6O_2Br_2$: C, 35.33; H, 1.98; O, 10.46. Found: C, 35.17; H, 1.68; O, 10.76.

(4-Benzyloxy-3-methoxyphenyl)trimethylstannane (6). A mixture of the known 1-benzyloxy-4-bromo-2-methoxybenzene[9] (0.60 g, 2.1 mmol), hexamethyl ditin (0.60 mL, 3.1 mmol), and freshly prepared tetrakis(triphenylphosphine)palladium(0)[4] (0.12 g, 5 mol %) in 5 mL of dioxane was placed into a sealable tube equipped with a small magnetic stir bar. The tube was degassed by three cycles of evacuation and refilling with N_2 and sealed under vacuum. The vertical tube was partly immersed in an oil bath heated to 105 °C. The solution was heated under reflux for 2 h. After cooling, the reaction mixture was filtered and the

(10) For general experimental procedures, see: Lee, J. M.; Tseng, T. H.; Lee, Y. J. *Synthesis* **2001**, *15*, 2247. Elemental analyses were performed on a Heracus CHN-OS Rapid spectrometer in the Taichung Instrumentation Center, National Science Council, Taiwan.

filtrate evaporated. The residue was subjected to flash column chromatography (Al_2O_3, cyclohexane) to give **6** (0.77 g, 100%) as a colorless oil:^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 3.93 (s, 3H), 5.17 (s, 2H), 6.89−7.47 (m, 8H); ^{13}C NMR ($CDCl_3$) δ −9.4, 56.1, 70.8, 113.9, 118.8, 127.2, 127.7, 128.5, 133.7, 137.3, 148.6, 149.4; HRMS (EI) calcd for $C_{17}H_{22}O_2Sn$ (M^+) 378.0642, found 378.0637.

2-(4-Benzyloxy-3-methoxyphenyl)-5-bromo-7-methoxybenzofuran (7). Dibromide **5** (2.50 g, 8.2 mmol), tetrakis(triphenylphosphine)palladium(0) (0.95 g, 10 mol %), and stannane **6** (3.41 g, 9.0 mmol) were introduced to a sealable tube containing anhydrous dioxane (10 mL) and the reaction mixture was degassed. The tube was sealed and heated for 5 h at 145 °C, and after cooling the solution was filtered and evaporated in vacuo. The filtrate residue was subjected to flash chromatography (SiO_2, CH_2Cl_2/ether 1/3) to provide the desired **7** (3.47 g, 96%) as a white solid: mp 156−158 °C; ^{1}H NMR ($CDCl_3$) δ 3.98 and 4.01 (s, 6H), 5.20 (s, 2H), 6.79 (s, 1H), 6.88 (d, J = 1.6 Hz, 1H), 6.92 (d, J = 8.9 Hz, 1H), 7.28 (d, J = 1.6 Hz, 1H), 7.33−7.47 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 56.1, 56.2, 70.9, 99.8, 108.6, 109.9, 113.8, 115.6, 115.9, 118.2, 123.2, 127.2, 127.9, 128.6, 132.2, 136.7, 142.7, 145.4, 149.0, 149.7, 157.1; HRMS (FAB) calcd for $C_{23}H_{19}O_4Br$ (M^+) 438.0467, found 438.0464.

(*E*)-2-(4-Benzyloxy-3-methoxyphenyl)-5-(3-hydroxypropenyl)-7-methoxybenzofuran (8). This allyl alcohol **8** was prepared, using the above procedure, from **7** (0.50 g, 1.1 mmol) and (*E*)-2-(tri-*n*-butylstannyl)propenol[5] (0.48 g, 1.4 mmol) with catalyst Pd(0) (0.13 g, 10 mol %) in dioxane (5 mL) under reflux for 4 h at 145 °C. The product was isolated in 36% yield (0.17 g, 0.4 mmol) after flash chromatography (SiO_2, CH_2Cl_2/cyclohexane 1/1) as a white solid: mp 159−160 °C; ^{1}H NMR ($CDCl_3$) δ 1.72 (br s, 1H), 3.89 and 3.95 (s, 6H), 4.24 (d, J = 5.4 Hz, 2H), 5.10 (s, 2H), 6.21 (dt, J = 15.7, 5.4 Hz, 1H), 6.57 (d, J = 15.7 Hz, 1H), 6.74 (s, 1H), 6.75 (s, 1H), 6.83 (d, J = 8.2 Hz, 1H), 7.03 (s, 1H), 7.22−7.38 (m, 7H); ^{1}H NMR [$(CD_3)_2CO$] δ 3.83 (t, J = 5.4 Hz, 1H), 3.92 and 4.03 (s, 6H), 4.23 (t, J = 5.3 Hz, 2H), 5.17 (s, 2H), 6.37 (dt, J = 15.8, 5.3 Hz, 1H), 6.65 (d, J = 15.8 Hz, 1H), 7.01 (d, J = 1.4 Hz, 1H), 7.11 (s, 1H), 7.13 (d, J = 8.2 Hz, 1H), 7.17 (d, J = 1.2 Hz, 1H), 7.35−7.49 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 56.0, 56.1, 63.8, 70.9, 100.5, 104.5, 108.6, 111.7, 113.8, 118.0, 123.6, 127.3, 127.3, 127.9, 128.5, 131.2, 131.7, 132.7, 136.8, 143.7, 145.0, 148.7, 149.7, 156.6; HRMS (EI) calcd for $C_{26}H_{24}O_5$ (M^+) 416.1624, found 416.1615.

(*E*)-2-(4-Benzyloxy-3-methoxyphenyl)-5-(carbethoxyethylene)-7-methoxybenzofuran (9). Into a sealable tube were introduced bromide **7** (1.80 g, 4.1 mmol), (*E*)-3-(tri-*n*-butylstannyl)propenoic acid ethyl ester[5] (1.91 g, 4.9 mmol), freshly prepared tetrakis(triphenylphosphine)palladium(0) (0.47 g, 10 mol %), and anhydrous dioxane (10 mL). The tube was sealed and heated at 140 °C for 5 h. After cooling, the solution was filtered, the filtrate was evaporated in vacuo, and the residue was subjected to flash chromatography (SiO_2, CH_2Cl_2/cyclohexane 1/1). The known[6e] ester **9** (1.73 g, 92%) was isolated as a white solid: mp 142−144 °C; ^{1}H NMR [$(CD_3)_2CO$] δ 1.28 (t, J = 7.1 Hz, 3H), 3.92 and 4.07 (s, 6H), 4.20 (q, J = 7.1 Hz, 2H), 5.15 (s, 2H), 6.52 (d, J = 16.0 Hz, 1H), 7.12 (d, J = 8.3 Hz, 1H), 7.15 (s, 1H), 7.26 (d, J = 1.4 Hz, 1H), 7.31−7.52 (m, 8H), 7.72 (d, J = 16.0 Hz, 1H); ^{13}C NMR [$(CD_3)_2CO$] δ 14.8, 56.5, 56.7, 60.8, 71.5, 101.7, 106.5, 109.8, 115.1, 115.6, 118.1, 118.8, 124.3, 128.7, 128.9, 129.4, 131.9, 132.5, 138.4, 146.1, 146.1, 146.6, 150.5, 151.3, 158.1, 167.4; HRMS (EI) calcd for $C_{28}H_{26}O_6$ (M^+) 458.1729, found 458.1731. Anal. Calcd for $C_{28}H_{26}O_6$: C, 73.35; H, 5.72; O, 20.94. Found: C, 73.16; H, 5.52; O, 20.75.

(*E*)-2-(4-Hydroxy-3-methoxyphenyl)-5-(carbethoxyethylene)-7-methoxybenzofuran (10). To a solution of **9** (1.25 g, 2.7 mmol) in CH_2Cl_2 (25 mL) was added $TiCl_4$ (0.33 mL, 3.0 mmol) dropwise at ambient temperature. The reaction was monitored by TLC and quenched by treatment with MeOH. The solvent was removed and the residue was subjected to flash chromatography (SiO_2, CH_2Cl_2) to give **10** (1.00 g, 100%) as a white solid: mp 149−151 °C (lit.[3a,b] mp 149−151 °C); ^{1}H NMR [$(CD_3)_2CO$] δ 1.27 (t, J = 7.1 Hz, 3H), 3.93 and 4.07 (s, 6H), 4.20 (q, J = 7.1 Hz, 2H), 6.52 (d, J = 16.0 Hz, 1H), 6.94 (d, J = 8.2 Hz, 1H), 7.07 (s, 1H), 7.24 (d, J = 1.4 Hz, 1H), 7.41 (dd, J = 8.2, 2.0 Hz, 1H), 7.43 (d, J = 1.4 Hz, 1H), 7.47 (d, J = 2.0 Hz, 1H), 7.70 (d, J = 16.0 Hz, 1H), 8.07 (s, 1H); ^{13}C NMR [$(CD_3)_2CO$] δ 14.8, 56.6, 56.6, 60.9, 100.1, 106.5, 109.4, 115.5, 116.6, 118.0, 119.5, 123.0, 129.5, 131.9, 132.6, 146.1, 146.6, 148.9, 148.9, 158.4, 167.5.

(*E*)-2-(4-Hydroxy-3-methoxyphenyl)-5-(3-hydroxypropenyl)-7-methoxybenzofuran (1). DIBAL (8.2 mL of a 1 M solution in hexane, 8.2 mmol) was added to a solution of **10** (0.76 g, 2.1 mmol) in THF (50 mL) at −78 °C. The mixture was stirred for 2 h, then quenched with saturated aqueous $Na_2SO_4 \cdot 10H_2O$ (5 mL) and allowed to warm to room temperature. When a gelatinous mixture formed it was diluted with CH_2Cl_2 and MeOH. The mixture was filtered, washing with ethyl acetate and MeOH. The solvent was evaporated and the residue was subjected to flash chromatography (SiO_2, CH_2Cl_2) to afford **1** (0.64 g, 95%) as a white solid: mp 199−201 °C (lit.[1] mp 199−201 °C); ^{1}H NMR (DMSO) δ 3.87 and 3.97 (s, 6H), 4.13 (d, J = 4.7 Hz, 2H), 5.59 (s, 1H), 6.31 (dt, J = 15.8, 5.0 Hz, 1H), 6.57 (d, J = 15.8 Hz, 1H), 6.86 (d, J = 8.2 Hz, 1H), 6.90 (s, 1H), 7.03 (d, J = 1.4 Hz, 1H), 7.10 (s, 1H), 7.29 (dd, J = 8.2, 1.4 Hz, 1H), 7.33 (s, 1H); ^{13}C NMR ($CDCl_3$ + DMSO) δ 55.8, 55.8, 61.8, 100.3, 104.4, 108.6, 111.0, 115.9, 118.1, 121.3, 129.4, 129.4, 131.0, 133.2, 142.7, 144.7, 147.7, 148.0, 156.4.

(*E*)-2-(4-Benzyloxy-3-methoxyphenyl)-5-(3-acetoxypropenyl)-7-methoxybenzofuran (11). A mixture of **8** (0.50 g, 1.2 mmol) and pyridine (0.15 mL, 1.8 mmol) in CH_2Cl_2 (25 mL) was added to acetyl chloride (0.13 mL, 1.8 mmol), and the solution was stirred at ambient temperature for 20 min. The solvent was removed in vacuo, and the residue was chromatographed on a silica gel column (CH_2Cl_2) to give **11** (0.53 g, 96%) as a white solid: mp 160−161.5 °C; ^{1}H NMR ($CDCl_3$) δ 2.13 (s, 3H), 4.00 and 4.06 (s, 6H), 4.76 (dd, J = 6.6, 0.8 Hz, 2H), 5.20 (s, 2H), 6.28 (dt, J = 15.8, 6.6 Hz, 1H), 6.73 (d, J = 15.8 Hz, 1H), 6.85 (s, 1H), 6.90 (dd, J = 8.1, 1.5 Hz, 1H), 6.96 (d, J = 1.5 Hz, 1H), 7.16 (d, J = 1.3 Hz, 1H), 7.29−7.50 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 20.8, 55.7, 55.8, 64.9, 70.6, 100.3, 104.2, 108.3, 111.8, 113.5, 117.7, 121.7, 123.3, 127.1, 127.7, 128.3, 130.9, 132.0, 134.6, 136.5, 143.6, 144.8, 148.5, 149.4, 156.3, 170.6. MS (EI$^+$) *m*/*z* (%) 458 (M^+, 30), 459 (M + 1, 8), 368 (22), 367 (100), 91 (18); HRMS (EI) calcd for $C_{28}H_{26}O_6$ (M^+) 458.1729, found 458.1732.

2-(4-Hydroxy-3-methoxyphenyl)-5-(3-acetoxypropyl)-7-methoxybenzofuran (12a). Compound **11** (0.28 g, 0.6 mmol) was dissolved in THF (15 mL). Acetic acid (glacial, 2.0 mL) and palladium on carbon (10%, 0.13 g) were added and the reaction was placed with shaking in Parr-Shaker equipment under 1 atm of H_2. After stirring for 8 h at ambient temperature, the reaction mixture was filtered and evaporated to provide a colorless oil. Column chromatography with CH_2Cl_2/ether/hexane (1/1/1) as an eluent gave pure **12a** (0.22 g, 98%) as a white solid: mp 79−80 °C (lit.[3c] mp 80−80.5 °C); ^{1}H NMR [$(CD_3)_2CO$] δ 1.97 (m, 2H), 2.01 (s, 3H), 2.73 (t, J = 6.4 Hz, 2H), 3.94 and 4.00 (s, 6H), 4.06 (t, J = 6.6 Hz, 2H), 6.76 (d, J = 1.3 Hz, 1H), 6.95 (d, J = 8.2 Hz, 1H), 6.98 (d, J = 1.3 Hz, 1H), 7.02 (s, 1H), 7.41 (dd, J = 8.2, 2.0 Hz, 1H), 7.47 (d, J = 2.0 Hz, 1H), 8.05 (s, 1H); ^{13}C NMR [$(CD_3)_2CO$] δ 21.0, 31.7, 33.1, 56.4, 56.5, 64.3, 100.9, 108.3, 109.2, 113.1, 116.5, 119.2, 123.4, 132.3, 138.3, 142.3, 146.0, 148.6, 148.9, 157.5, 171.2; HRMS (EI) calcd for $C_{21}H_{22}O_6$ (M^+) 370.1416, found 370.1422.

General Conditions for the Sonogashira Reaction. 2-(4-Benzyloxy-3-methoxyphenyl)-5-(3-acetoxypropynyl)-7-methoxybenzofuran (13a). A mixture of bromobenzofuran **7** (0.40 g, 0.9 mmol), tetrakis(triphenylphosphine)palladium(0) (0.11 g, 10 mol %), CuI (0.33 g, 20 mol %), and acetoxy propyne (0.13 g, 1.4 mmol) was introduced to a sealable tube containing anhydrous Et_3N (5 mL) and the reaction mixture was degassed. The tube was sealed and heated for 5 h at 90 °C, and after cooling, the solution was filtered and evaporated in vacuo. The filtrate residue was subjected to flash chromatography (SiO_2, CH_2Cl_2/ether 1/3) to provide the desired **13a** (0.27 g, 66%) as a white solid: mp 149−151 °C; ^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3H), 3.99 and 4.01 (s, 6H), 4.93 (s, 2H), 5.19 (s, 2H), 6.83 and 6.87 (s, 2H), 6.93 (d, J = 8.8 Hz, 1H), 7.30−7.47 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 20.8, 52.9, 56.1, 56.2, 71.0, 81.2, 87.0, 100.2, 108.7, 109.9, 113.9, 117.1, 117.4, 118.1, 123.3, 127.3, 127.9, 128.6, 130.9,

136.7, 144.0, 144.7, 148.9, 149.8, 157.1, 170.3; HRMS (EI) calcd for $C_{28}H_{24}O_6$ (M^+) 456.1573, found 456.1577.

2-(4-Benzyloxy-3-methoxyphenyl)-5-(3-tetrahydropyranoxypropynyl)-7-methoxybenzofuran (13b). The **13b** was prepared, using the general procedure, from **7** (0.62 g, 1.4 mmol) and tetrahydropyranoxypropyne (0.30 g, 2.1 mmol). The product **13b** was isolated in 82**%** yield (0.58 g, 1.2 mmol) as a white solid: mp 169−171 °C; ^{1}H NMR ($CDCl_3$) δ 1.54−1.85 (m, 6H), 3.61 and 3.90 (m, 2H), 3.99 and 4.02 (s, 6H), 4.52 (ABq, J = 15.8, 4.7 Hz, 2H), 4.93 (t, J = 3.3 Hz, 1H), 5.20 (s, 2H), 6.84 (s, 1H), 6.86 (d, J = 1.3 Hz, 1H), 6.93 (d, J = 8.9 Hz, 1H), 7.27−7.47 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 19.1, 25.4, 30.3, 54.8, 56.1, 56.2, 62.0, 71.0, 83.4, 86.4, 96.8, 100.2, 108.7, 109.9, 113.9, 117.3, 118.1, 123.4, 127.3, 128.0, 130.9, 136.8, 144.0, 144.7, 148.9, 149.8, 157.0.

2-(4-Benzyloxy-3-methoxyphenyl)-5-(3-benzyloxypropynyl)-7-methoxybenzofuran (13c). From **7** (0.25 g, 5.7×10^{-1} mmol) and benzyloxypropyne (0.12 g, 8.5×10^{-1} mmol), **13c** was obtained in 62% (0.18 g, 3.5×10^{-1} mmol) yield as a white solid: mp 122−125 °C; ^{1}H NMR ($CDCl_3$) δ 3.99 and 4.03 (s, 6H), 4.43 and 4.71 (s, 4H), 5.20 (s, 2H), 6.85 (s, 2H), 6.88 (d, J = 1.2 Hz, 1H), 6.94 (d, J = 8.9 Hz, 1H), 7.30−7.48 (m, 13H); ^{13}C NMR ($CDCl_3$) δ 56.1, 56.2, 58.0, 62.0, 71.0, 71.7, 83.3, 87.0, 100.2, 108.7, 109.8, 113.9, 117.2, 117.7, 118.1, 123.4, 127.3, 127.8, 127.9, 128.1, 128.4, 128.6, 130.9, 136.8, 137.5, 144.0, 144.7, 148.9, 149.8, 157.0; HRMS (EI) calcd for $C_{33}H_{28}O_5$ (M^+) 504.1937, found 504.1934.

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Supporting Information Available: Spectroscopic characterization and ^{1}H and ^{13}C NMR spectra of the compounds described in the text. This material is available free of charge via the Internet at http://pubs.acs.org.

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