General Synthesis of Polysubstituted Benzo[*b*]furans

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2-(Benzotriazol-1-ylmethyl)furans **4a**−**c**, on treatment with *n*-BuLi followed by various α,*β*-unsaturated ketones and aldehydes, gave the adducts **6a**−**f** which underwent intramolecular cyclization to form substituted benzo[*b*]furans **10a**−**f**. Lithiation and subsequent alkylation of **4a**−**c** afforded intermediates **8a**−**c**, which underwent similar transformations with α,*β*-unsaturated ketones or aldehydes to give the corresponding polysubstituted benzo[*b*]furans **7a**−**c**. *o*-Iodophenol (**11**) with 1-propargylbenzotriazole (**1**) in the presence of $(PPh_3)_2PdCl_2$, CuI, and Et_3N gave 2-(benzotriazol-1-ylmethyl)benzo[*b*]furan (**12**). The benzotriazolyl-CH_2 side chain of **12** was further elaborated by (i) alkylation with *trans*-cinnamaldehyde to give the adduct **14**, followed by intramolecular cyclization to give dibenzofuran **17**; (ii) alkylation with benzyl bromide followed by elimination or nucleophilic displacement of the benzotriazolyl moiety with Grignard reagent and subsequent dehydrogenation to give 2-alkenylbenzofurans **15** or **20**, respectively; (iii) alkylation with $(CH_3)_3CCHO$ followed by low-valent titanium-promoted olefination to give olefin **19**; and (iv) alkylation with benzaldehyde followed by Lewis acid catalyzed pinacol type reaction to give **18**.

Introduction

Benzo[*b*]furan derivatives are important because of their occurrence in nature and their physiological properties.[1] Recently there has been a growing interest in developing general and versatile synthetic methods for the synthesis of benzo[*b*]furan derivatives due to their activity as modulators of androgen biosynthesis (furanosteroids),[2] as inhibitors of 5-lipoxygenase,[3] as antagonists of the angiotensin II receptor,[4] as blood coagulation factor Xa inhibitors,[5] and as ligands of adenosine A_1 receptor.[6] 1-[[4-(Aminoalkoxy)phenyl]sulfonyl]benzo[*b*]furan derivatives have been synthesized and tested as a potent class of calcium blockers.[7]

Various methods exist for the synthesis of benzo[*b*]-furans[1,8] of which the intramolecular cyclization of a suitably substituted benzene is the most often employed.[8a] However, recent efforts have centered around the construction of benzo[*b*]furan structures by C−C bond formation using transition metal reagents including copper and especially palladium catalysts.[9] Alkyne-based palladium-catalyzed reactions provide some of the most versatile and efficient routes to heterocyclic derivatives.[10]

In previous reports, we demonstrated the use of 2-(benzotriazol-1-ylmethyl)-pyrroles[11] and -indoles[12] as versatile building blocks for the synthesis of functionalized heterocycles. We also reported the synthesis of indoles via [3 + 3] annulation of 2-(benzotriazole-1-ylmethyl)pyrroles with α,*β*-unsaturated aldehydes and ketones.[13] The anion stabilizing and good leaving abilities of benzotriazolyl moieties in the above ring systems motivated us to extend these methodologies to elaborate furans. We now report investigations on the use of 2-(benzotriazol-1-ylmethyl)furans **4a**−**c** and 2-(benzotriazol-1-ylmethyl)benzofuran (**12**) for the synthesis of polysubstituted benzo[*b*]furans **7a**−**c**, **10a**−**f**, **16a**,**b**, **15**, and **17**−**20** (Schemes 1 and 2).

Results and Discussion

Synthesis of 3,4,5,6-Substituted Benzo[*b*]furans 10a−f and 2,3,4,5,6-Substituted Benzo[*b*]furans 7a−c. 2-(Benzotriazol-1-ylmethyl)furans **4a**−**c** are readily available from alkynyloxiranes **3a**−**c**, themselves derived from 1-propargylbenzotriazole (**1**) and α-bromo ketones **2a**−**c**.[14] Treatment of **4a**−**c** with 1 equiv of *n*-BuLi at −78 °C, followed by 1 equiv of α,*β*-unsaturated ketones or aldehydes **5a**−**e**, gave 1,4-addition intermediates **6a**−**f**. The intermediates **6a**−**f** (obtained as mixtures of diastereomers), without further purification, were treated with *p*-toluenesulfonic acid in 1,4-dioxane under reflux to undergo intramolecular cyclization to intermediates

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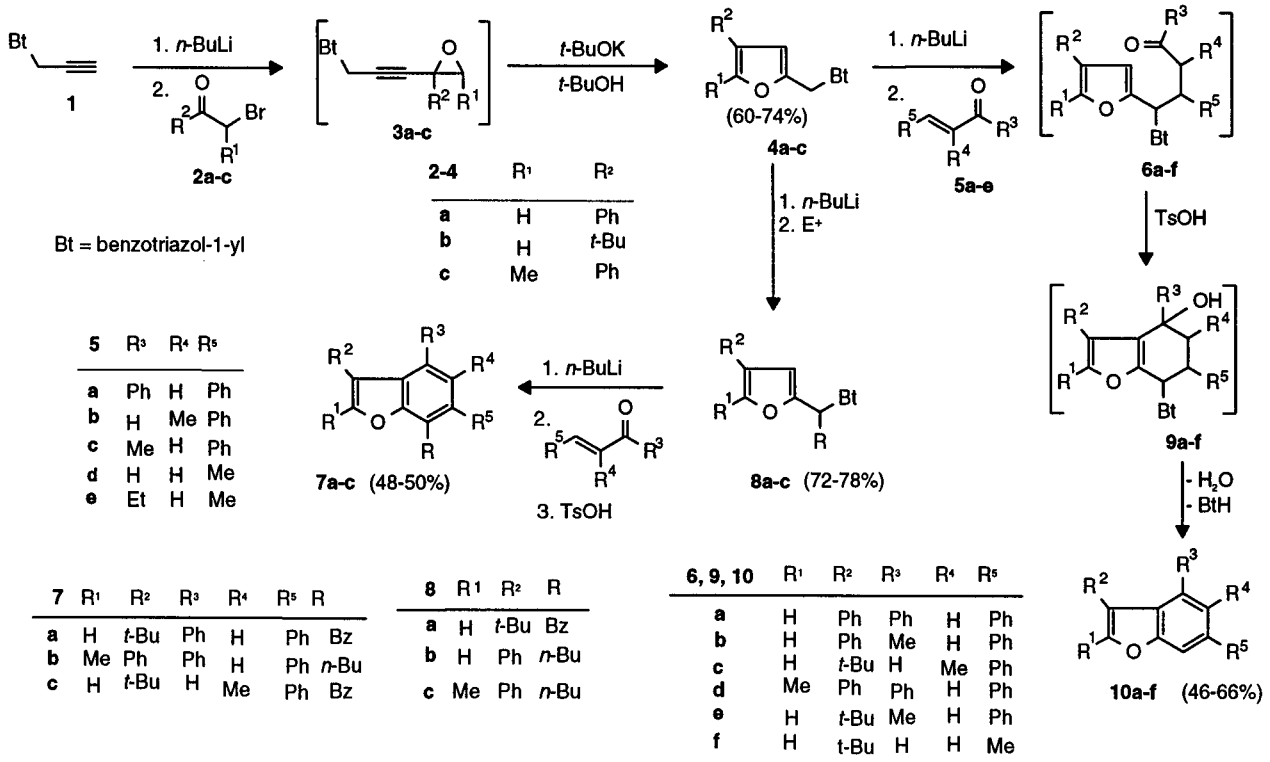
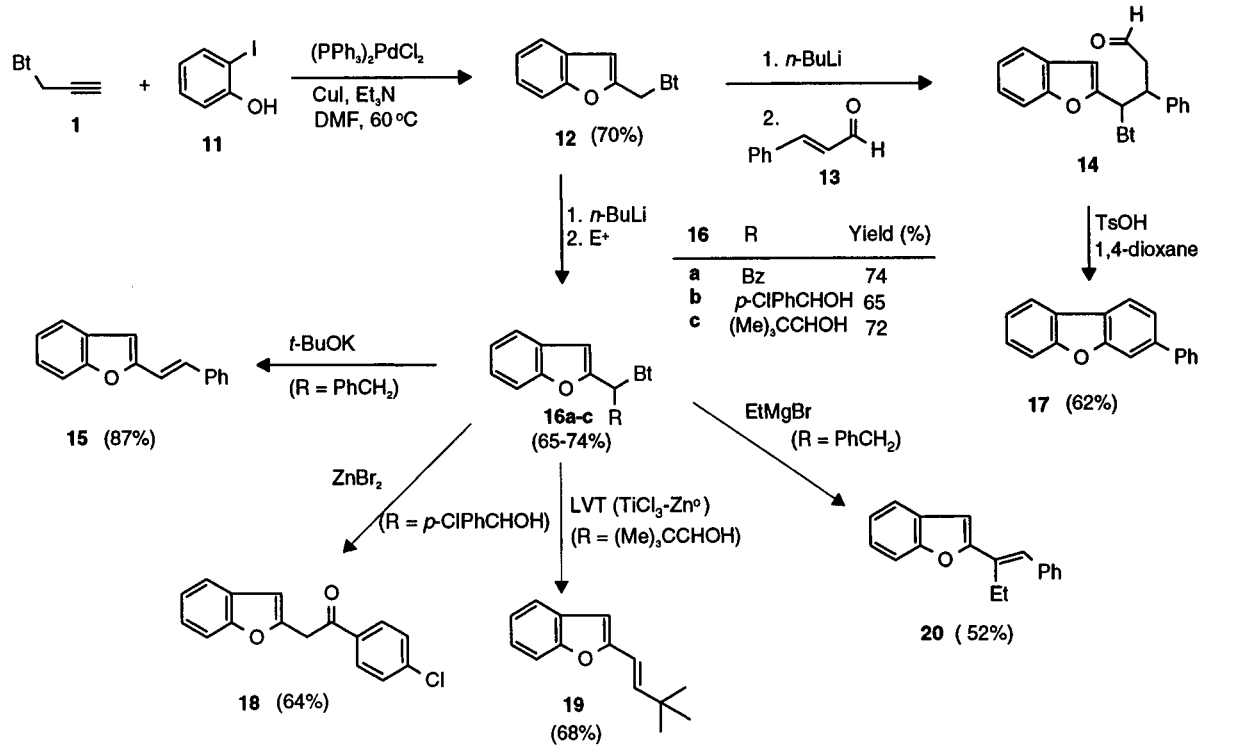
Scheme 1



Scheme 2



9a−**f**, followed by spontaneous elimination of benzotriazole and water to give the benzo[*b*]furans **10a**−**f**. We found that the best solvent was 1,4-dioxane; initial attempts to carry out these cyclization reactions in THF failed, probably due to the lower boiling temperature of THF.

Alternatively, the 2-(benzotriazol-1-yl)methyl moiety can be alkylated by lithiation of **4a**−**c** with 1 equiv of *n*-BuLi at −78 °C for 30 min, followed by reactions with *n*-butyl iodide or benzyl bromide as electrophiles for 12 h, to give **8a**−**c** in good yields. Reactions of **8a**−**c** with α,β-unsaturated ketones followed by cyclization gave polysubstituted benzo[*b*]furans **7a**−**c**.

Synthesis of 2-(Benzotriazol-1-ylmethy)lbenzo[*b*]-furan (12) and Synthetic Manipulation of the Benzotriazol-1-ylmethyl-Attached Side Chain. The synthesis of 2-substituted benzo[*b*]furans *via* palladium-catalyzed heteroannulation of acetylenic compounds has been reported.[10a] The presence of a benzotriazolyl group at the 2-position of the benzo[*b*]furan ring should allow

further elaboration to generate various products by sequential lithiation, alkylation, and elimination or substitution of the benzotriazolyl group.

The reaction of *o*-iodophenol (**11**) with 1-propargylbenzotriazole (**1**) in the presence of $(PPh_3)_2PdCl_2$, CuI, and Et_3N, at 60 °C using DMF as solvent, gave 2-(benzotriazol-1-ylmethyl)benzofuran (**12**) in 70% yield after 12 h. Lithiation of **12** with 1 equiv of *n*-BuLi, followed by addition of α,*β*-unsaturated aldehyde **13**, gave the 1,4-addition product **14**, which without further purification was refluxed in 1,4-dioxane in the presence of *p*-toluenesulfonic acid to give dibenzofuran **17** in good yield. Lithiation of **12** with 1 equiv of *n*-BuLi followed by alkylation with electrophiles gave **16a**−**c** in good yields. Refluxing **16a** in a 1:1 mixture of *t*-BuOH/THF in the presence of *t*-BuOK for 24 h gave exclusively 2-(*trans*-2-phenylethenyl)benzofuran (**15**) in excellent yield. No formation of the *cis* isomer was observed by NMR or GCMS. Surprisingly, nucleophilic substitution of the benzotriazole group in **16a** with Grignard reagent was followed by dehydrogenation to give the alkene **20**. Intermediate **16b**, when treated with zinc bromide and heated at 150 °C (neat) for 12 h, underwent a pinacol type reaction with elimination of benzotriazole to give the ketone **18**.[15]

Recently, we found that stereoselective olefination of aldehydes and ketones with *N*-benzyl- and *N*-allylbenzotriazoles was promoted by low-valent titanium.[16] In the present study, this method was applied to 2-(benzotriazol-1-ylmethyl)benzofuran (**12**). Thus, compound **12** was treated with 1 equiv of *n*-BuLi followed by the reaction with trimethylacetaldehyde to give a mixture of distereomers **16c**, which upon treatment with low-valent titanium underwent dehydroxybenzotriazolation stereospecifically to give *trans*-1-(benzofuran-2-yl)-2-*tert*-butylethylene (**19**) exclusively. The *trans* structure was confirmed by the large coupling constant (16.2 Hz) of the double-bond protons.

Conclusions

In conclusion, general syntheses of polysubstituted benzo[*b*]furans have been described. These approaches utilize readily available starting materials and involve sequential lithiation and alkylation of the 2-(benzotriazol-1-yl)methyl side chain of furans **4a**−**c** and **8a**−**c** and benzo[*b*]furan **12** with α,*β*-unsaturated ketones or aldehydes, followed by intramolecular cyclization with elimination of benzotriazole and water to give **7a**−**c**, **10a**−**g**, and **17**, base-assisted elimination to give **15**, Lewis acid assisted elimination of benzotriazole to give **18**, and low-valent titanium-promoted olefination to give **19**.

Experimental Section

General Comments. Melting points were determined on a hot-stage microscope and are uncorrected. ^{1}H NMR spectra were recorded on a 300 MHz spectrometer using TMS as the internal standard and $CDCl_3$ as the solvent. ^{13}C NMR spectra were recorded at 75 MHz on the same instrument with the solvent peak ($CDCl_3$) as the reference. HRMS and elemental analyses (C,H,N) were carried out within the department. Dichlorobis(triphenylphosphine)palladium(II) was freshly prepared according to literature procedure.[17] 1-Propargylbenzotriazole (**1**)[18] and 2-(benzotriazol-1-ylmethyl)furan (**4a**) were prepared according to previously reported procedures and compounds **4b**,**c** were prepared using the same procedure.[14]

2-(Benzotriazol-1-ylmethyl)-4-*tert*-butylfuran (4b): white microcrystals, yield 74%; mp 63−65 °C; ^{1}H NMR δ 8.06 (d, J = 8.1 Hz, 1 H), 7.59 (d, J = 8.4 Hz, 1 H), 7.48 (t, J = 7.7 Hz, 1 H), 7.37 (t, J = 7.7 Hz, 1 H), 7.12 (s, 1 H), 6.39 (s, 1 H), 5.77 (s, 2 H), 1.54 (s, 9 H); ^{13}C NMR δ 147.8, 146.1, 137.3, 137.2, 132.8, 127.4, 123.8, 119.8, 109.8, 109.2, 45.2, 30.6, 29.8. Anal. Calcd for $C_{15}H_{17}N_3O$: C, 70.56; H, 6.71; N, 16.46. Found: C, 70.62; H, 7.07; N, 16.58.

2-(Benzotriazol-1-ylmethyl)-4-phenyl-5-methylfuran (4c): yellow microcrystals, yield 60%; mp 109−110 °C; ^{1}H NMR δ 8.04 (d, J = 8.4 Hz, 1 H), 7.62 (d, J = 8.2 Hz, 1 H), 7.45 (t, J = 7.3 Hz, 1 H), 7.38−7.21 (m, 6 H), 6.56 (s, 1 H), 5.78 (s, 2 H), 2.36 (s, 3 H); ^{13}C NMR δ 148.7, 146.3, 145.5, 133.4, 132.9, 128.6, 127.4, 126.6, 123.8, 123.9, 122.1, 120.0, 111.2, 109.8, 45.2, 13.0. Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.94; H, 5.27; N, 14.67.

Preparation of 2-(Benzotriazol-1-ylmethyl)benzo[*b*]furan (12). A mixture of *o*-iodophenol (5.5 g, 25 mmol), $(PPh_3)_2PdCl_2$ (0.61 g, 0.88 mmol), CuI (0.62 g, 3.3 mmol), and triethylamine (5.1 g, 50 mmol) was stirred in DMF (60 mL) under nitrogen for 1 h. 1-Propargylbenzotriazole (**1**) (7.9 g, 50 mmol) was added, and the mixture was stirred at room temperature for an additional 1 h and heated at 60 °C for 16 h. The mixture was then cooled, poured into water (150 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were washed with NaOH (5 N, 3 × 100 mL) followed by water (3 × 100 mL) and dried ($MgSO_4$). After evaporation of the solvent, the residue was purified by column chromatography using EtOAc/hexane (1:3) to give the product **12** as brown needles, yield 70%: mp 160−162 °C; ^{1}H NMR δ 8.03 (d, J = 8.5 Hz, 1 H), 7.91 (d, J = 8.5 Hz, 1 H), 7.62−7.52 (m, 2 H), 7.49−7.37 (m, 2 H), 7.30−7.18 (m, 2 H), 7.05 (s, 1 H), 6.20 (s, 2 H); ^{13}C NMR δ 154.4, 151.0, 145.2, 132.6, 127.4, 127.3, 124.5, 123.8, 122.8, 121.1, 119.1, 110.9, 110.3, 106.1, 44.6. Anal. Calcd for $C_{15}H_{11}N_3O$: C, 72.28; H, 4.45; N, 16.86. Found: C, 72.12; H, 4.42; N, 16.70.

General Procedure for the Preparation of 8a−c and 16a−c *via* the Alkylation of 2-(Benzotriazol-1-ylmethyl)-furans 4a−c and -benzofuran (12). To a solution of 2-(benzotriazol-1-ylmethyl)furan **4a**−**c** or -benzofuran (**12**) (16 mmol) in THF (100 mL) was added a solution of *n*-BuLi (16 mmol, 9.8 mL, 1.6 M in hexane) at −78 °C. After 30 min, a solution of the electrophile (benzyl bromide, *n*-butyl iodide, benzaldehyde, or trimethylacetaldehyde (16 mmol) in THF (10 mL) was added. The reaction mixture was stirred at this temperature for 4 h and allowed to warm to room temperature overnight. The reaction was quenched with a saturated NH_4-Cl solution (50 mL), extracted with EtOAc, washed with brine (3 × 50 mL), and dried ($MgSO_4$). The solvent was removed to give the crude product which was purified by column chromatography to give the corresponding compounds **8a**−**c** or **16a**. The crude products **16b**,**c** were used directly for the synthesis of compounds **18** and **19** without further purification, and the yields were determined by GCMS.

2-(1-Benzotriazol-1-yl-2-phenyl)ethyl-4-*tert*-butylfuran (8a): purified by column chromatography using EtOAc/hexane (1:1), white powder, yield 78%; mp 104−105 °C; ^{1}H NMR δ 8.01 (d, J = 8.1 Hz, 1 H), 7.45−7.26 (m, 3 H), 7.12 (d, J = 6.0 Hz, 4 H), 6.99−6.93 (m, 2 H), 6.35 (s, 1 H), 6.13 (t, J = 7.3 Hz, 1 H), 3.90−3.70 (m, 2 H), 1.18 (s, 9 H); ^{13}C NMR δ 150.6, 146.1, 137.2, 136.8, 136.3, 132.6, 128.8, 128.5, 127.1, 126.9, 123.7, 119.9, 109.9, 108.3, 59.2, 38.8, 30.7, 29.8. Anal. Calcd for $C_{22}H_{23}N_3O$: C, 76.49; H, 6.71; N, 12.16. Found: C, 76.65; H, 6.93; N, 12.27.

2-(1-Benzotriazol-1-ylpentyl)-4-phenylfuran (8b): purified by column chromatography using EtOAc/hexane (1:1), white powder, yield 76%; mp 113−115 °C; ^{1}H NMR δ 8.08 (d, J = 8.1 Hz, 1 H), 7.64 (s, 1 H), 7.55 (d, J = 8.1 Hz, 1 H), 7.45−7.23 (m, 7 H), 6.72 (s, 1 H), 6.07 (t, J = 7.5 Hz, 1 H), 2.61−

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2.52 (m, 2 H), 1.44−1.17 (m, 4 H), 0.87 (t, J = 7.1 Hz, 3 H); ^{13}C NMR δ 152.5, 146.4, 138.2, 132.2, 131.7, 128.8, 128.7, 127.3, 127.2, 125.7, 123.8, 120.1, 110.1, 107.5, 57.7, 31.9, 28.1, 22.0, 13.7. Anal. Calcd for $C_{21}H_{21}N_3O$: C, 76.11; H, 6.39; N, 12.68. Found: C, 75.80; H, 6.55; N, 12.54.

2-(1-Benzotriazol-1-ylpentyl)-4-phenyl-5-methylfuran (8c): purified by column chromatography using EtOAc/hexane (1:1), white powder, yield 72%; mp 110−111 °C; ^{1}H NMR δ 8.08 (d, J = 8.1 Hz, 1 H), 7.59 (d, J = 8.1 Hz, 1 H), 7.46−7.23 (m, 7 H), 6.54 (s, 1 H), 6.03 (t, J = 7.8 Hz, 1 H), 2.59−2.52 (m, 2 H), 2.37 (s, 3 H), 1.43−1.17 (m, 4 H), 0.87 (t, J = 6.9 Hz, 3 H); ^{13}C NMR δ 149.0, 148.1, 146.4, 133.5, 132.2, 128.6, 127.4, 127.1, 126.6, 123.8, 121.7, 120.1, 110.3, 109.7, 57.8, 31.8, 28.3, 22.1, 13.8, 13.1. Anal. Calcd for $C_{22}H_{23}N_3O$: C, 76.49; H, 6.71; N, 12.16. Found: C, 76.57; H, 6.85; N, 12.19.

2-(1-Benzotriazol-1-yl-2-phenyl)ethylbenzo[*b*]furan (16a): purified by column chromatography using EtOAc/hexane (1:1), white powder, yield 74%; mp 134−135 °C; ^{1}H NMR δ 8.03 (d, J = 8.0 Hz, 1 H), 7.53−7.21 (m, 8 H), 7.18−7.04 (m, 4 H), 6.74 (s, 1 H), 6.33 (t, J = 7.7 Hz, 1 H), 3.95 (d, J = 7.7 Hz, 2 H); ^{13}C NMR δ 153.3, 146.2, 144.8, 136.1, 132.7, 128.8, 128.6, 127.7, 127.4, 127.1, 124.9, 123.9, 123.2, 121.3, 120.1, 111.4, 109.8, 105.5, 59.4, 38.7. Anal. Calcd for $C_{22}H_{17}N_3O$: C, 77.86; H, 5.05; N, 12.38. Found: C, 77.86; H, 5.07; N, 12.43.

General Procedure for the Preparation of Polysubstituted Benzo[*b*]furans 10a−g and 7a−c and 3-Phenyldibenzo[*b*]furan (17). To a solution of compound **4** or **8** or **12** (7.3 mmol) in THF (100 mL) was added a solution of *n*-BuLi (7.3 mmol, 4.6 mL, 1.6 M in hexane) at −78 °C, and the solution was stirred at this temperature for 30 min. A solution of an appropriate α,β-unsaturated ketone or aldehyde (**5** or **13**) (7.3 mmol) in THF (10 mL) was added, and the reaction mixture was stirred at −78 °C for 20 h. A saturated NH_4Cl solution (100 mL) was added, and the solution was extracted with EtOAc (100 mL). The organic phase was separated, washed with saturated NH_4Cl solution (3 × 100 mL), and dried ($MgSO_4$). After removal of the solvent, the residue was dissolved in 1,4-dioxane (50 mL), *p*-toluenesulfonic acid (2.8 g, 15 mmol) added, and the solution was refluxed for 24 h. The mixture was cooled, diluted with water (50 mL), and extracted with Et_2O (3 × 50 mL). The combined extracts were washed with water (3 × 50 mL) and dried ($MgSO_4$). The solvent was removed and the residue was subjected to column chromatography or recrystallization to afford the corresponding product **10a**−**f** or **7a**−**c** or **17**.

3,4,6-Triphenylbenzo[*b*]furan (10a): purified by recrystallization from pentane, white microcrystals, yield 53%; mp 108−109 °C; ^{1}H NMR δ 7.75 (s, 1 H), 7.69 (d, J = 7.4 Hz, 2 H), 7.46−7.32 (m, 5 H), 7.07−6.91 (m, 10 H); ^{13}C NMR δ 156.8, 143.1, 141.0, 139.3, 138.2, 136.8, 132.0, 129.4, 129.1, 128.9, 127.5, 127.4, 127.3, 126.8, 126.6, 124.0, 123.3, 109.0. Anal. Calcd for $C_{26}H_{18}O$: C, 90.14; H, 5.24. Found: C, 90.09; H, 5.48.

4-Methyl-3,6-diphenylbenzo[*b*]furan (10b): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, white crystals, yield 50%; mp 119−121 °C; ^{1}H NMR δ 7.62−7.48 (m, 3 H), 7.54 (s, 1 H), 7.46−7.26 (m, 9 H), 2.30 (s, 3 H); ^{13}C NMR δ 142.4, 141.2, 138.1, 132.8, 132.1, 130.1, 128.8, 128.0, 127.6, 127.4, 127.3, 127.1, 125.1, 124.0, 123.3, 107.8, 19.9. Anal. Calcd for $C_{21}H_{16}O$: C, 88.70; H, 5.67. Found: C, 88.37; H, 5.94.

3-*tert*-Butyl-5-methyl-6-phenylbenzo[*b*]furan (10c): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, yellow crystals, yield 52%; mp 54−55 °C; ^{1}H NMR δ 7.63 (d, J = 7.2 Hz, 2 H), 7.54 (s, 1 H), 7.45−7.40 (m, 3 H), 7.35−7.30 (m, 2 H), 2.84 (s, 3 H), 1.47 (s, 9 H); ^{13}C NMR δ 157.8, 141.0, 140.9, 137.3, 131.0, 130.8, 128.7, 127.2, 127.1, 125.4, 124.7, 107.9, 31.5, 30.4, 24.2. Anal. Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.60; H, 7.94.

2-Methyl-3,4,6-triphenylbenzo[*b*]furan (10d): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, white crystals, yield 46%; mp 102−103 °C: ^{1}H NMR δ 7.69−7.66 (m, 3 H), 7.45−7.40 (m, 3 H), 7.32 (t, J = 7.2 Hz, 1 H), 7.07−6.88 (m, 8 H), 6.87 (d, J = 7.8 Hz, 2 H), 2.42 (s, 3 H); ^{13}C NMR δ 155.1, 152.8, 141.2, 139.1, 136.9, 135.8, 133.1, 129.8, 129.2, 128.8, 127.4, 127.3, 127.2, 127.1, 126.4, 126.2, 125.2, 123.7, 117.6, 108.1, 12.6. Anal. Calcd for $C_{27}H_{20}O$: C, 89.97; H, 5.59. Found: C, 89.69; H, 5.70.

3-*tert*-Butyl-4-methyl-6-phenylbenzo[*b*]furan (10e): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, yellow crystals, yield 48%; mp 55−57 °C; ^{1}H NMR δ 7.56 (d, J = 7.5 Hz, 2 H), 7.46 (s, 1 H), 7.36−7.33 (m, 3 H), 7.27−7.23 (m, 2 H), 2.77 (s, 3 H), 1.41 (s, 9 H); ^{13}C NMR δ 157.8, 141.0, 140.9, 137.3, 131.0, 130.8, 128.7, 127.2, 127.1, 125.4, 124.8, 107.9, 31.6, 30.5, 24.2. Anal. Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.60; H, 7.94.

3-*tert*-Butyl-6-methylbenzo[*b*]furan (10f): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, yellow oil, yield 46%; ^{1}H NMR δ 7.50 (d, J = 8.0 Hz, 1 H), 7.17 (s, 2 H), 6.95 (d, J = 8.0 Hz, 1 H), 2.36 (s, 3 H), 1.31 (s, 9 H); ^{13}C NMR δ 156.5, 138.7, 133.9, 130.2, 124.4, 123.3, 121.1, 111.9, 30.0, 29.7, 29.4. HRMS calcd for $C_{13}H_{16}$ 188.1201, found 188.1203. Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.94; H, 8.85.

3-*tert*-Butyl-4,6-diphenyl-7-benzylbenzo[*b*]furan (7a): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, white crystals, yield 50%; mp 148−149 °C; ^{1}H NMR δ 7.43 (s, 3 H), 7.35−7.30 (m, 8 H), 7.20−7.05 (m, 5 H), 6.98 (s, 1 H), 4.31 (s, 2 H), 1.05 (s, 9 H); ^{13}C NMR δ 155.7, 143.8, 141.5, 141.0, 140.7, 137.1, 134.7, 131.2, 130.5, 129.7, 128.4, 128.1, 128.0, 127.9, 127.4, 127.3, 126.9, 125.7, 124.4, 121.0, 32.7, 31.0, 30.5. Anal. Calcd for $C_{31}H_{28}O$: C, 89.38; H, 6.78. Found: C, 89.37; H, 6.96.

2-Methyl-3,4,6-triphenyl-7-butylbenzo[*b*]furan (7b): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, white crystals, yield 66%; mp 95−96 °C; ^{1}H NMR δ 7.44−7.33 (m, 5 H), 7.12−6.92 (m, 11 H), 2.96 (t, J = 8.0 Hz, 2 H), 2.48 (s, 3 H), 1.72−1.64 (m, 2 H), 1.39−1.30 (m, 2 H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 153.6, 152.2, 141.7, 139.2, 137.2, 133.4, 132.6, 129.9, 129.7, 129.3, 128.0, 127.4, 127.1, 126.9, 126.7, 126.5, 126.1, 124.6, 122.9, 117.8, 32.4, 26.7, 22.9, 13.8, 12.7. Anal. Calcd for $C_{31}H_{28}O$: C, 89.38; H, 6.78. Found: C, 89.06; H, 7.18.

3-*tert*-Butyl-5-methyl-6-phenyl-7-benzylbenzo[*b*]furan (7c): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, yellow oil, yield 48%; ^{1}H NMR δ 7.41 (s, 1 H), 7.26−7.22 (m, 4 H), 6.99−6.94 (m, 5 H), 6.80 (d, J = 6.0 Hz, 2 H), 3.92 (s, 2 H), 2.01 (s, 3 H), 1.34 (s, 9 H); ^{13}C NMR δ 153.8, 140.7, 140.1, 139.5, 137.9, 130.3, 130.1, 129.9, 128.6, 128.1, 127.9, 126.8, 125.6, 125.5, 122.7, 120.2, 33.2, 31.0, 30.0, 21.7. Anal. Calcd for $C_{26}H_{26}O$: C, 88.09; H, 7.39. Found: C, 87.67; H, 7.56.

3-Phenyldibenzo[*b*]furan (17): purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent, white crystals, yield 62%; mp 128−130 °C; ^{1}H NMR δ 7.93−7.89 (m, 2 H), 7.74 (s, 1 H), 7.64 (d, J = 7.4 Hz, 2 H), 7.54 (d, J = 7.7 Hz, 2 H), 7.46−7.28 (m, 5 H); ^{13}C NMR δ 156.9, 156.7, 141.1, 140.8, 128.9, 127.5, 127.4, 127.1, 124.1, 123.3, 122.8, 122.1, 120.7, 120.6, 111.7, 110.1. Anal. Calcd for $C_{18}H_{12}O$: C, 88.50; H, 4.95. Found: C, 88.31; H, 4.94.

Preparation of 2-(*trans*-2-Phenylethenyl)benzo[*b*]furan (15). 2-(1-Benzotriazol-1-yl-2-phenyl)ethylbenzo[*b*]furan (**16a**) (1.0 g, 3.0 mmol) and *t*-BuOK (0.66 g, 5.9 mmol) were dissolved in a mixture of dry THF (20 mL) and *t*-BuOH (30 mL). The mixture was refluxed for 24 h. After cooling, the reaction was quenched with water (100 mL) and extracted with Et_2O (3 × 100 mL). The combined extracts were washed with water (3 × 100 mL) and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography, using CH_2Cl_2/hexane (1:4) as the eluent, gave the product as white crystals: yield 87%; mp 125−126 °C; ^{1}H NMR δ 7.47 (t, J = 8.9 Hz, 4 H), 7.35−7.17 (m, 6 H), 6.95 (d, J = 16.2 Hz, 1 H), 6.61 (s, 1 H); ^{13}C NMR δ 155.1, 154.9, 136.6, 130.3, 129.1, 128.7, 128.1, 126.7, 124.6, 122.8, 120.8, 116.4, 110.9, 105.1. Anal. Calcd for $C_{16}H_{12}O$: C, 87.25; H, 5.49. Found: C, 87.11; H, 5.57.

Preparation of 2-(*trans*-2-*tert*-Butylethenyl)benzo[*b*]-furan (19). To a solution of 2-(benzotriazol-1-ylmethyl)benzo-[*b*]furan (**12**) (2.0 g, 8.0 mmol) in THF (80 mL) under argon was added a solution of *n*-BuLi (5.0 mL, 8.0 mmol, 1.6 M in hexane) at −78 °C. The mixture was stirred at −78 °C for 1 h, and a solution of trimethylacetaldehyde (0.7 g, 8.1 mmol) in THF (10 mL) was added. After being stirred for 2 h at −78

°C, the reaction was quenched with saturated NH_4Cl solution (100 mL) and extracted with diethyl ether (100 mL). The organic phase was separated, washed with brine (3 × 100 mL), and dried ($MgSO_4$). The solvent was removed under reduced pressure to give the crude product **16c** which was used in the following reaction without further purification.

A mixture of $TiCl_3$ (3.9 g, 25 mmol) and zinc dust (5.4 g, 83 mmol) in dry DME (100 mL) was refluxed for 1 h under argon. After cooling, the above crude compound **16c** in dry DME (10 mL) was added and refluxed for 12 h. The reaction mixture was cooled, diluted with diethyl ether (100 mL), and filtered. The filtrate was washed with NaOH (5%, 3 × 100 mL) and brine (3 × 100 mL) and dried ($MgSO_4$). After removal of the solvent, the residue was purified by short column chromatography using hexane as the eluent to give the product as an oil, yield 68%; ^{1}H NMR δ 7.47−7.39 (m, 2 H), 7.20−7.14 (m, 2 H), 6.53 (d, J = 16.2 Hz, 1 H), 6.44 (s, 1 H), 6.23 (d, J = 16.2 Hz, 1 H), 1.13 (s, 9 H); ^{13}C NMR δ 155.5, 154.6, 144.2, 129.2, 123.9, 122.6, 120.5, 114.0, 110.7, 102.9, 33.5, 29.4. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.07; H, 8.38.

Preparation of 1-(4-Chlorophenyl)-2-(benzofuran-2-yl)ethanone (18). To a solution of 2-(benzotriazol-1-ylmethyl)benzo[*b*]furan (**12**) (1.0 g, 4 mmol) in THF (50 mL) at −78 °C under argon was added *n*-BuLi (1.6 M, 2.74 mL, 4.4 mmol). After 30 min, a solution of 4-chlorobenzaldehyde (0.62 g, 4.4 mmol) in THF (10 mL) was added. The mixture was stirred at −78 °C for 4 h and allowed to warm to room temperature overnight. A solution of zinc bromide (15 mmol) in THF (15 mL) was added. THF was removed, and the residue was heated at 150 °C for 12 h. Ethyl acetate (100 mL) and diethyl ether (100 mL) were added, and the mixture was stirred for 1 h at room temperature. The solid was filtered off, and the solution was washed with water (2 × 100 mL) and dried ($MgSO_4$). The solvent was removed, and the residue was subjected to column chromatography (EtOAc/hexane, 1:7) to give the product as yellow crystals, yield 64%: ; mp 105−106 °C; ^{1}H NMR δ 7.96 (d, J = 8.3 Hz, 2 H), 7.50 (d, J = 8.2 Hz, 1 H), 7.42 (d, J = 8.4 Hz, 3 H), 7.23−7.18 (m, 2 H), 6.62 (s, 1 H), 4.39 (s, 2 H); ^{13}C NMR δ 193.1, 154.9, 151.0, 140.0, 134.5, 130.0, 129.1, 129.0, 123.9, 122.8, 120.7, 111.0, 105.5, 38.8. Anal. Calcd for $C_{16}H_{11}O_2Cl$: C, 70.99; H, 4.10. Found: C, 70.93; H, 4.00.

Preparation of 2-(1-Ethyl-2-phenylethenyl)benzofuran (20). To a solution of compound **16a** (2 mmol) in toluene (30 mL) under argon was added a solution of ethyl magnesium-bromide (4 mmol) in Et_2O, and the reaction mixture was refluxed for 3 h. The solvent was removed under reduced pressure, and the residue was extracted with Et_2O (2 × 50 mL). The combined diethyl ether solution was washed with water (2 × 50 mL) and dried ($MgSO_4$). After removal of the solvent, the residue was purified by column chromatography using CH_2Cl_2/hexane (1:4) as the eluent to give the product as a yellow powder, 52% yield: mp 63−64 °C; ^{1}H NMR δ 7.79 (d, J = 7.4 Hz, 2 H), 7.36 (t, J = 7.8 Hz, 2 H), 7.18 (t, J = 7.2 Hz, 2 H), 7.09−7.05 (m, 2 H), 6.97 (t, J = 7.4 Hz, 1 H), 6.44 (s, 1 H), 5.59 (s, 1 H), 2.40 (q, J = 7.1 Hz, 2 H), 1.28 (t, J = 7.4 Hz, 3 H); ^{13}C NMR δ 152.3, 149.7, 136.1, 134.7, 128.7, 128.3, 128.2, 125.9, 125.6, 122.5, 121.6, 121.4, 114.7, 101.6, 24.7, 12.2. Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49. Found: C, 87.24; H, 6.60.

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