β-H dd splitting pattern for both stereoisomers (16 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

A Short, Efficient Synthesis of *tert*-Butyl-Hydroxylated Di-*tert*-butylphenols

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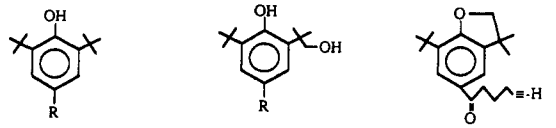
The enzymatic hydroxylation of a *tert*-butyl group in the food antioxidant BHT (butylated hydroxytoluene, **1**) to produce the diol **2** occurs in hepatic and pulmonary microsomes of rats and mice and has been found to be an important step both in BHT bioactivation and the resulting toxicity in these species.[2] Not surprisingly, a similar hydroxylation reaction has also been found to be a significant biliary metabolic pathway in rats for the new di-*tert*-butylphenolic antiinflammatory drug tebufelone **3**. Upon requiring samples of the two tebufelone derivatives **4** and **5** derived from hydroxylation of a *tert*-butyl group, we realized that synthetic methods to allow construction of this functionality had not been previously reported.[3] This paper describes an expedient method for the synthesis of the hydroxylated di-*tert*-butylphenol building block **6**, and its elaboration into both tebufelone derivatives **4** and **5**.



1: R = Me
3: R = -C(=O)(CH$_2$)$_3$C≡CH

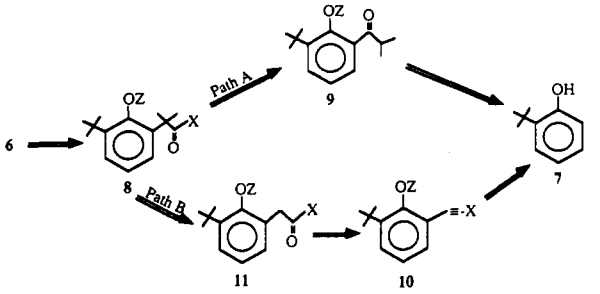
2: R = Me
4: R = -C(=O)(CH$_2$)$_3$C≡CH

5

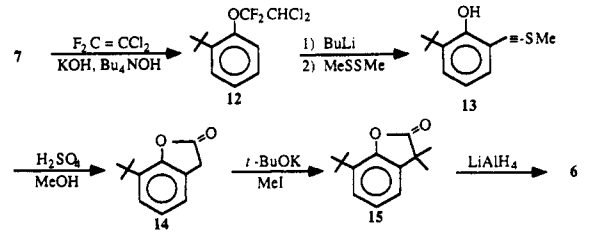
6: R = H

Two approaches were considered initially for the conversion of the commercially available 2-*tert*-butylphenol (**7**) into **6**, with both routes proceeding through the dimethylated arylacetyl derivative **8** (Scheme I). The more direct pathway (A) utilized the Tl-mediated rearrangement[4] of the aryl ketone **9** into the corresponding geminal dimethylated methyl ester **8** (X = OMe). Although the conversion of the model system isobutyrophenone → methyl α,α-dimethylphenylacetate[5] was straightforward [Tl(NO$_3$)$_3$, CH(OMe)$_3$–MeOH, 50 °C, 4 h; 74% yield], the application of this chemistry to the *tert*-butylphenolic system **9**[6] led to the formation of complex product mixtures under a variety of reaction conditions. The feasibility of the alternate pathway (B) hinged on two steps: introduction of the ortho acetylenic group, followed by its conversion into the corresponding arylacetyl derivative. Whereas the ortho acetylenic moiety in **10** (X = TMS, Z = H) could indeed be successfully introduced via Pd-catalyzed coupling[8] of (trimethylsilyl)ethynylzinc chloride with the corresponding aryl iodide, the overall sequence from **7** contained several steps and produced **10** in a low combined yield.[9] As an attractive alternative, Johnson has recently described a procedure whereby haloethyl aryl ethers are converted in a single step into (2-hydroxyaryl)acetylenes by means of BuLi.[11] Furthermore, since this reaction affords the respective lithium acetylide prior to hydrolysis, addition of an electrophile other than water can directly provide the corresponding derivatized alkyne. Using this approach, **7** was first converted into the requisite phenolic 1,1-difluoro-2,2-dichloroethyl ether **12** (93%; Scheme II) via reaction with 1,1-dichloro-2,2-difluoroethylene under phase-transfer conditions.[11] The ether **12** was then transformed into the corresponding *o*-silyloxy silylacetylene **10** (X, Z = TMS) by treatment with BuLi and subsequent silylation. Interestingly, hydroboration–oxidation of this silylated alkyne did not afford the desired substituted acetic acid analogue **11** (Z = H, X = OH) cleanly.[12]

Scheme I



Scheme II



(1) Present address: Exxon Chemical Co., Basic Chemicals Technology, P.O. Box 4900, Baytown, TX 77522-4900.

(2) Thompson, J. A.; Malkinson, A. M.; Wand, M. D.; Mastovich, S. L.; Mead, E. W.; Schullek, K. M.; Laudenschlager, W. G. *Drug Metab. Dispos.* **1987**, *15*, 833 and references cited therein. Thompson, J. A.; Schullek, K. M.; Fernandez, C. A.; Malkinson, A. M. *Carcinogenesis* **1989**, *10*, 773. Malkinson, A. M.; Thaete, L. G.; Blumenthal, E. J.; Thompson, J. A. *Toxicol. Appl. Pharmacol.* **1989**, *101*, 196. Bolton, J. L.; Sevestre, H.; Ibe, B. O.; Thompson, J. A. *Chem. Res. Toxicol.* **1990**, *3*, 65. Bolton, J. L.; Thompson, J. A. *Drug Metab. Dispos.* **1991**, *19*, 467.

(3) Two other studies appeared after completion of this work that also describe the synthesis of phenolic compounds containing a hydroxylated *tert*-butyl group: Ikuta, H.; Yamagishi, Y.; Akasaka, K.; Yamaysu, I.; Kobayashi, S.; Shirota, H.; Katayama, K. *Japanese Patent* JP 63115860 (1988). Goto, K.; Hashimoto, K.; Kanai, K. *World Patent* WO 9009985 (1990).

(4) McKillop, A.; Swann, B. P.; Taylor, E. C. *J. Am. Chem. Soc.* **1973**, *95*, 3340. Taylor, E. C.; Robey, R. L.; Liu, K.-T.; Favre, B.; Bozimo, H. T.; Conley, R. A.; Chiang, C.-S.; McKillop, A.; Ford, M. E. *J. Am. Chem. Soc.* **1976**, *98*, 3037. Taylor, E. C.; Chaing, C.-S.; McKillop, A.; White, J. F. *J. Am. Chem. Soc.* **1976**, *98*, 6750.

(5) The conversion of isobutyrophenone → methyl α,α-dimethylphenylacetate has been accomplished in low yield (17%) previously using I$_2$/AgNO$_3$: Higgins, S. D.; Thomas, C. B. *J. Chem. Soc., Perkin Trans. 1* **1982**, 235.

(6) Compound **9** (Z = H) was prepared (59% yield) via metal-promoted Fries rearrangement[7] of the corresponding *o*-bromoaryl isobutyrate.

(7) Miller, J. A. *J. Org. Chem.* **1987**, *52*, 322.

(8) King, A. O.; Negishi, E.; Villani, Jr., F. J.; Silveira, A., Jr. *J. Org. Chem.* **1978**, *43*, 358.

(9) For example, the reaction of 2-iodo-6-*tert*-butylphenol with (trimethylsilyl)ethynylzinc chloride [2.2 equiv, 5 mol % Pd(Ph$_3$P)$_4$, THF, 25 °C] afforded the arylalkyne **11** (Z = H, X = TMS) in 80% yield. The starting aryl iodide was prepared in two steps from **7** via ortho bromination[10] (Br$_2$; Zn/NaOH, 100 °C; 50% yield) and then lithiation/iodination of the resulting bromide (*t*-BuLi, THF, −78 °C; I$_2$, −78 → 0 °C; 31% yield).

(10) Tashiro, M.; Fukata, G. *J. Org. Chem.* **1977**, *42*, 835.

(11) Subramanian, R.; Johnson, F. *J. Org. Chem.* **1985**, *50*, 5430.

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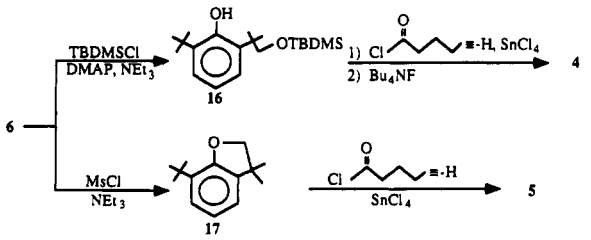
Scheme III



After examining several other methods for the conversion of the terminal acetylene group into a substituted acetic acid moiety, we found the corresponding acetylenic methyl thioether **13** to be a very effective precursor for this transformation.[13] Thus, as shown in Scheme II, the halo ether **12** was treated with BuLi to form the respective *o*-phenoxyaryl acetylide anion, and this intermediate was trapped as its methyl thioether **13** by adding methyl disulfide (68%).[14,15] Hydrolysis of the thioether **13** in acidic methanol then directly afforded the lactone **14** (69%), with none of the corresponding open-chain phenolic acid **11** (Z = H, X = OH) being present. Geminal dimethylation of **14** was cleanly accomplished in a single step using excess *t*-BuOK/MeI to provide **15** (78%). No trace of the monomethylated lactone was detected in the reaction mixture. Finally, reduction of the lactone **15** with $LiAlH_4$ produced the *tert*-butyl-hydroxylated phenol **6** quantitatively, with an overall yield of 34% for the entire five-step process shown in Scheme II.

As noted above, we also required samples of the *tert*-butyl-hydroxylated tebufelone derivative **4** and the corresponding dihydrobenzofuran **5**. Having devised an efficient route to the diol substrate **6**, these latter syntheses were readily accomplished via the short reaction sequences shown in Scheme III. In the first, the alcoholic moiety in **6** was selectively protected as its *tert*-butyldimethylsilyl (TBDMS) ether **16** (95%), and the latter was acylated in a modified Friedel–Crafts reaction with 5-hexynoyl chloride/$SnCl_4$ at −78 °C.[16] Desilylation then gave the free dihydroxy ketone **4** (78%). Failure to silylate the aliphatic hydroxyl group rendered the aromatic substrate less reactive toward Friedel–Crafts acylation, and, as a result of warming the reaction mixture to 0 °C, Lewis acid-promoted cyclization of the acid chloride occurred to produce 3-chloro-2-cyclohexenone cleanly.[17] In the second synthesis (Scheme III), diol **6** was cyclized to the dihydrobenzofuran **17** by treatment at 0 °C with $MsCl/NEt_3$ (91%). Acylation of **17** with 5-hexynoyl chloride under the conditions used to prepare **4** then afforded the desired bicyclic ketone **5** in 90% isolated yield.

In summary, an efficient method for the synthesis of *tert*-butyl hydroxylated di-*tert*-butylphenol compounds has been demonstrated. This new preparative sequence should provide ready access in the future to a host of important derivatives which possess this functionality.

Experimental Section

General Procedures. 5-Hexynoyl chloride was prepared from 5-hexyn-1-ol (Farchan Laboratories) as described in the literature.[18] 2-*tert*-Butylphenol was purchased from Aldrich Chemical Co. and 1,1-dichloro-2,2-difluoroethylene was obtained from SCM Specialty Chemicals (Gainesville, FL). Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl prior to use. All other materials were obtained from commercial sources and were used without further purification.

1-(2,2-Dichloro-1,1-difluoroethoxy)-2-(1,1-dimethylethyl)benzene (12). To a mixture of **7** (47.5 g, 316 mmol), 40% KOH (91 mL), and 40% Bu_4NOH (13 mL) was added at 0 °C a solution of 1,1-dichloro-2,2-difluoroethylene (100 mL) in CH_2Cl_2 (250 mL). The flask was tightly stoppered at 0 °C, and the mixture was warmed to room temperature and then stirred vigorously for 48 h. The reaction mixture was then poured into water and extracted with petroleum ether. The combined organic phase was washed with saturated NaCl and dried ($MgSO_4$). Concentration and short-path distillation gave 83.4 g (93%) of **12**: bp 95 °C (1 Torr); IR (film) 2970 (m), 1445 (m), 1310 (s), 1265 (s), 1235 (s), 1175 (s), 1165 (s), 835 (s), 755 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9 H), 5.95 (t, J = 7 Hz, 1 H), 7.0–7.5 (m, 4 H).

2-(1,1-Dimethylethyl)-6-[(methylthio)ethynyl]phenol (13). A solution of **12** (82.2 g, 291 mmol) in THF (875 mL) was treated at −78 °C with BuLi (2.74 M, 640 mL, 1.75 mol), keeping the temperature below −60 °C. The mixture was stirred at −78 °C for 6 h and was allowed to warm *very slowly* to room temperature; stirring was then continued overnight. The solution was cooled back to −78 °C, and to it was added methyl disulfide (41.1 g, 436 mmol). After warming to 25 °C, the mixture was stirred for 2 h and then poured into 0.1 N HCl. The aqueous portion was extracted with ether, and the combined organic extract was washed with saturated $NaHCO_3$ and saturated NaCl and then dried ($MgSO_4$). Examination of the reaction mixture by GC revealed a very clean product, showing very little else besides **13**. The volatile solvents were removed in the hood by distillation, with the pot temperature reaching ca. 110 °C. GC analysis at this point now showed an approximately 3:1 mixture of **13** and the corresponding thioester derived from hydration of the triple bond.[15] (It should be noted that this transformation was carried out several times on a smaller scale and uniformly provided pure **13** that was uncontaminated with thioester). Distillation using a Kugelrohr apparatus (110–140 °C, 0.5 Torr) afforded 43.5 g (ca. 68%) of an approximately 3:1 mixture of **13** and the derived thioester (spectra of pure **13**): IR (film) 3480 (m), 2960 (m), 1430 (s), 1225 (m), 745 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (s, 9 H), 2.50 (s, 3 H), 6.25 (s, 1 H), 6.80 (m, 1 H), 7.25 (m, 2 H).

7-(1,1-Dimethylethyl)-2(3*H*)-benzofuranone (14). A mixture of **13** (43.5 g, ca. 193 mmol; contained ca. 25% thioester), methanol (600 mL), and 3 N H_2SO_4 (600 mL) was heated under reflux overnight. The reaction solution was concentrated to about half of its original volume by distilling away the volatiles. It was then cooled to 25 °C and concentrated further by means of a water aspirator in the hood (this procedure removes all volatile sulfur-containing byproducts). The concentrated reaction mixture was poured into water and extracted with ether. The combined organic extract was washed with saturated $NaHCO_3$ and saturated NaCl and then dried ($MgSO_4$). The volatiles were removed under reduced pressure, and the crude lactone was recrystallized from hexane to afford 23.2 g of pure **14**. The mother liquor was flash chromatographed on silica gel (10% ethyl acetate/hexane) to afford an additional 2.01 g of **14**. The total yield of **14** was 25.2 g (69%): mp 99.5–100 °C; IR ($CHCl_3$) 2965 (s), 1795 (vs), 1430 (s), 1085 (s), 1070 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9 H), 3.65 (s, 2 H), 7.15 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 29.50, 32.56, 34.19, 122.15, 123.54, 123.90, 125.81, 134.16, 152.65, 174.03.

7-(1,1-Dimethylethyl)-3,3-dimethyl-2(3*H*)-benzofuranone (15). To a solution of **14** (3.80 g, 20.0 mmol) and methyl iodide (5.0 mL, 80 mmol) in THF (100 mL) was added potassium *tert*-butoxide (5.6 g, 50 mmol) portionwise at 0 °C. The mixture

(12) Zweifel, G.; Backlund, S. J. *J. Am. Chem. Soc.* **1977**, *99*, 3184.
(13) Boonstra, H. J.; Brandsma, L.; Wiegman, A. M.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1959**, *78*, 252. Abrams, S. R. *Can. J. Chem.* **1983**, *61*, 2423.
(14) Nooi, J. R.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1961**, *80*, 244. Brandsma, L.; Bos, H. J. T.; Arens, J. F. In *The Chemistry of Acetylenes*; Viehe, H. G., Ed.; Marcel Dekker Co.: New York, 1969; Chapter 11.
(15) Hydrolysis of **13** to the respective thioester proceeds readily under mild conditions. Hence, the crude reaction mixture must be completely dried prior to distillation to avoid occurrence of this side reaction.
(16) We acknowledge J. F. Ward, M. C. Coleman (The Procter & Gamble Co., Miami Valley Laboratories), and T. T. Hudec (Norwich Eaton Pharmaceuticals, Inc.; European Patent Application EP 321432, 1989) for their assistance with optimization of these Friedel–Crafts reaction conditions.
(17) Essentially the same results were obtained even when employing an excess (3 equiv) of $SnCl_4$ for the attempted Friedel–Crafts acylation of **6** using 5-hexynoyl chloride.
(18) Earl, R. A.; Vollhardt, K. P. C. *J. Org. Chem.* **1984**, *49*, 4786.

was stirred at 0 °C for 30 min and then was warmed to 25 °C and stirred for an additional 2 h. The reaction was poured into 0.1 N HCl, and the aqueous layer was extracted with ether. The combined organic extract was washed with saturated $NaHCO_3$ and saturated NaCl and then dried ($MgSO_4$). After removal of the solvents, the crude product was recrystallized from hexane to afford 2.21 g of pure **15**. The mother liquor was distilled using a Kugelrohr apparatus (160 °C, 0.5 Torr) to provide an additional 1.19 g of the title lactone. The total yield of **15** was 3.40 g (78%): mp 84–85 °C; IR ($CHCl_3$) 2970 (s), 1795 (vs), 1430 (s), 1280 (s), 1055 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ (off-resonance multiplicity) 25.38 (q), 29.58 (q), 34.21 (s), 42.09 (s), 120.32 (d), 124.14 (d), 125.59 (d), 134.13 (s, two carbons), 150.11 (s), 180.82 (s).

3-(1,1-Dimethylethyl)-2-hydroxy-β,β-dimethylbenzeneethanol (6). A solution of $LiAlH_4$ (1.14 g, 30.0 mmol) in ether (50 mL) was treated at 0 °C with **15** (5.45 g, 25.0 mmol). The reaction mixture was warmed to 25 °C and stirred for 1 h. The excess hydride was decomposed at 0 °C with 25 mL of ethyl acetate followed by 100 mL of a 1:1 mixture of saturated NH_4Cl and water. The resulting liquid was filtered through a thin pad of Celite, and the latter was washed well with ether. The organic phase was separated, washed with saturated NaCl, and then dried ($MgSO_4$). Concentration left 5.56 g of essentially pure **6**: mp 67–68 °C; IR (CCl_4) 3640 (m), 3290 (s, br), 2960 (s), 1425 (m), 1385 (m), 1245 (m), 1030 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 15 H), 1.85 (br s, alcoholic OH, 1 H), 3.65 (br s, 2 H), 6.6–7.3 (m, 3 H), 9.05 (s, phenolic OH, 1 H); ^{13}C NMR ($CDCl_3$) δ (off-resonance multiplicity) 25.45 (q), 29.99 (q), 34.97 (s), 39.75 (s), 74.13 (t), 118.96 (d), 125.25 (d), 125.58 (d), 133.33 (s), 138.25 (s), 155.28 (s).

TBDMS Ether of 6 (16). To a mixture of **6** (2.81 g, 12.7 mmol), *tert*-butyldimethylsilyl chloride (2.37 g, 15.8 mmol), and 4-(dimethylamino)pyridine (0.38 g, 3.2 mmol) in CH_2Cl_2 (60 mL) was added at room temperature triethylamine (5.23 mL, 38.0 mmol). The reaction mixture was stirred overnight at 25 °C and was then poured into water. The aqueous layer was extracted with ether, and the combined extract was washed with saturated NaCl and then dried ($MgSO_4$). The crude, concentrated solution was passed through a short column of silica gel, eluting with 2% ethyl acetate/hexane directly into a round-bottomed flask. Removal of the solvents then afforded 4.06 g (95%) of **16**: IR (film) 3225 (s, br), 2950 (s), 2930 (s), 1385 (s), 1250 (s), 1050 (s), 835 (s), 780 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (s, 6 H), 0.95 (s, 9 H), 1.45 (s, 15 H), 3.70 (s, 2 H), 6.6–7.3 (m, 3 H), 9.50 (s, 1 H).

1-[3-(1,1-Dimethylethyl)-4-hydroxy-5-(2-hydroxy-1,1-dimethylethyl)phenyl]-5-hexyn-1-one (4). A solution of **16** (4.38 g, 13.0 mmol) in CH_2Cl_2 was sequentially treated at −78 °C with 5-hexynoyl chloride (1.85 g, 14.3 mmol) and $SnCl_4$ (1.68 mL, 14.3 mmol). The mixture was stirred at −78 °C for 1 h and then was warmed to ca. −50 °C and stirred for 5 min. The reaction mixture was poured into 0.1 N HCl, and the layers were separated. The aqueous portion was extracted with ether, and the combined organic phases were washed with saturated $NaHCO_3$ and saturated NaCl and then dried ($MgSO_4$). TLC analysis (10% ethyl acetate/hexane) showed mainly the desired acylated silyl ether (R_f = 0.38), with only a trace of **16** remaining (R_f = 0.70). The crude, concentrated silyl ether was then diluted with THF (75 mL), and to it was added $Bu_4NF{\cdot}3H_2O$ (8.19 g, 26.0 mmol). After the mixture was stirred for 1 h at 25 °C it was poured into water, and the aqueous layer was extracted with ether. The combined extract was washed with saturated NaCl and then dried ($MgSO_4$). TLC analysis (20% ethyl acetate/hexane) showed predominantly **4** (R_f = 0.22) and a small amount of **5** (R_f = 0.56), with no silyl ether remaining. Flash chromatography through silica gel afforded 3.21 g (78%) of **4**: mp 91–93 °C; IR ($CHCl_3$) 3620 (m), 3310 (s), 3200 (m, br), 2970 (s), 2110 (w), 1655 (s), 1585 (s), 1270 (s), 635 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 15 H), 1.7–2.3 (m, 5 H), 3.05 (t, 2 H), 3.80 (d, 2 H), 5.40 (t, 1 H, alcoholic OH), 7.80 (s, 2 H), 10.95 (s, 1 H, phenolic OH); ^{13}C NMR ($CDCl_3$) δ (off-resonance multiplicity) 18.03 (t) 23.71 (t), 25.38 (q), 29.68 (q), 35.25 (s), 36.58 (t), 40.06 (s), 69.22 (d), 73.55 (t), 83.73 (s), 126.40 (d), 126.69 (d), 127.06 (s), 133.92 (s), 138.34 (s), 161.54 (s), 200.91 (s).

7-(1,1-Dimethylethyl)-2,3-dihydro-3,3-dimethylbenzofuran (17). To a solution of **6** (1.78 g, 8.00 mmol) in CH_2Cl_2 was added sequentially at 0 °C methanesulfonyl chloride (0.68 mL, 8.8 mmol) and triethylamine (2.80 mL, 20.0 mmol). The reaction was stirred for 1 h at 0 °C and then was poured into saturated NaCl. The aqueous layer was extracted with ether, and the combined organic phases were washed with saturated NaCl and dried ($MgSO_4$). Distillation using a Kugelrohr apparatus (110 °C, 0.5 Torr) provided 1.49 g (91%) of **17**: IR (film) 2960 (s), 2870 (m), 1425 (m), 995 (m), 745 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ (off-resonance multiplicity) 27.42 (q), 29.36 (q), 34.07 (s), 41.39 (s), 83.57 (t), 119.84 (d), 120.31 (d), 124.58 (d), 133.08 (s), 136.85 (s), 157.11 (s).

1-[7-(1,1-Dimethylethyl)-2,3-dihydro-3,3-dimethyl-5-benzofuranyl]-5-hexyn-1-one (5). A solution of **17** (1.65 g, 8.10 mmol) in CH_2Cl_2 (40 mL) was sequentially treated at −78 °C with 5-hexynoyl chloride (1.16 g, 8.90 mmol) and $SnCl_4$ (1.05 mL, 8.90 mmol). The mixture was stirred at −78 °C for 1 h and then was warmed to ca. −50 °C and stirred for 5 min. The reaction mixture was poured into 0.1 N HCl, and the layers were separated. The aqueous portion was extracted with ether, and the combined extract was washed with saturated $NaHCO_3$ and saturated NaCl and then dried ($MgSO_4$). Flash chromatography through silica gel (5% ethyl acetate/hexane, R_f = 0.23) provided 2.43 g (90%) of **5** as a colorless oil: IR (CCl_4) 3310 (m), 2960 (s), 2100 (w), 1665 (s), 1590 (m), 1405 (m), 1360 (m), 1185 (s), 1100 (m), 985 (m), 630 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 15 H), 1.9–2.5 (m, 5 H), 3.10 (t, 2 H), 4.30 (s, 2 H), 7.7–7.9 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ (off-resonance multiplicity) 17.99 (t), 23.32 (t), 27.57 (q), 29.16 (q), 34.18 (s), 36.61 (t), 41.07 (s), 69.02 (d), 83.92 (s), 84.71 (t), 120.67 (d), 126.45 (d), 130.39 (s), 132.92 (s), 137.63 (s), 161.62 (s), 198.28 (s).

Registry No. **3**, 112018-00-5; **4**, 124837-40-7; **5**, 124435-76-3; **6**, 124435-68-3; **7**, 88-18-6; **12**, 124837-34-9; **13**, 124454-63-3; **13** thioester, 139041-39-7; **14**, 124435-70-7; **15**, 124435-69-4; **16**, 124435-72-9; **17**, 124435-71-8; 5-hexynoyl chloride, 55183-45-4; 1,1-dichloro-2,2-difluoroethylene, 79-35-6.

Supplementary Material Available: ^{13}C and/or ^1H NMR spectra of all compounds described in the Experimental Section (15 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.