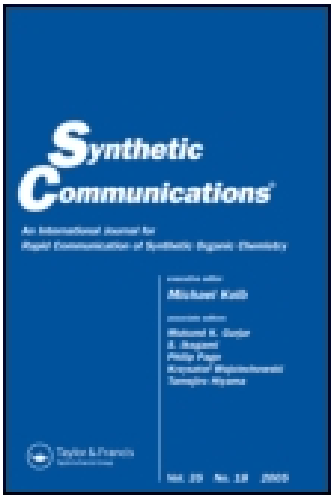


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

(±)-3,4,4a,5,6,7-Hexahydro-4a-Methyl-7,7-Diphenyl-1(2H)-Naphthtlenone

Richard A. Bunce [a] & R. Shawn Childress [a]
[a] Department of Chemistry , Oklahoma State University Stillwater , Oklahoma, 74078-3071
Published online: 23 Aug 2006.

To cite this article: Richard A. Bunce & R. Shawn Childress (1996) (±)-3,4,4a,5,6,7-Hexahydro-4a-Methyl-7,7-Diphenyl-1(2H)-Naphthtlenone, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 26:21, 4081-4089, DOI: 10.1080/00397919608003828

To link to this article: http://dx.doi.org/10.1080/00397919608003828

SYNTHETIC COMMUNICATIONS, 26(21), 4081–4089 (1996)

(±)-3,4,4a,5,6,7-HEXAHYDRO-4a-METHYL-7,7-DIPHENYL-1(2*H*)-NAPHTHALENONE

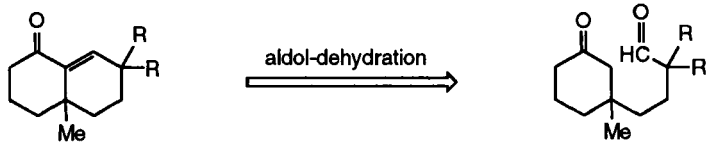
Richard A. Bunce* and R. Shawn Childress

Department of Chemistry, Oklahoma State University
Stillwater, Oklahoma 74078-3071

Abstract. The title compound was prepared in 48% overall yield using a seven-step sequence. The synthesis involves stepwise construction of a 3-formyl-3,3-diphenylpropyl side chain from the double bond of 3-ethenyl-3-methylcyclohexanone followed by aldol ring closure. The approach represents a general strategy for the synthesis of a number of (±)-7,7-diaryl-3,4,4a,5,6,7-hexahydro-1(2*H*)-naphthalenones.

Introduction. Our photochemical studies recently required access to (±)-3,4,4a,5,6,7-hexahydro-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (**1**). A review of the chemical literature indicated that **1** had not been previously reported. While the target structure did not appear to have any particular significance beyond our study,[1] it posed an interesting synthetic challenge and required the use of a novel strategy for its preparation. We describe here our synthesis of **1**.

Results and Discussion. Retrosynthetic analysis of **1** suggests that keto aldehyde **2** is the logical precursor.[2] Indeed, we recently reported a synthesis of (±)-3,4,4a,5,6,7-hexahydro-4a,7,7-trimethyl-1(2*H*)-naphthalenone (**3**) via inter-



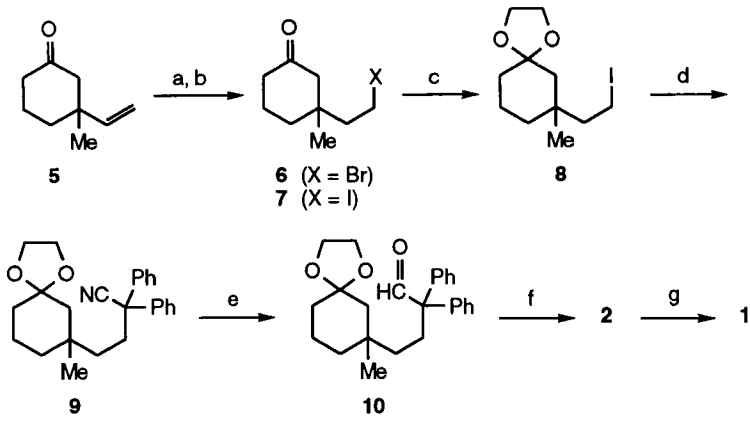
1 (R = Ph)
3 (R = Me)

2 (R = Ph)
4 (R = Me)

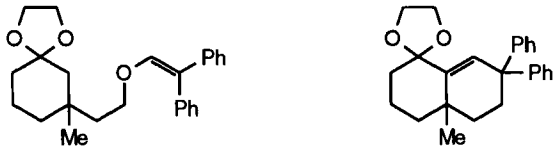
*Author to whom correspondence should be addressed.

mediate **4**.[3] This required (1) conjugate addition of 3,3-dimethyl-4-pentenylmagnesium bromide to 3-methyl-2-cyclohexen-1-one, (2) ozonolysis of the side chain double bond to give the aldehyde, and (3) acid-catalyzed aldol ring closure. In the 7,7-diphenyl-substituted case, the Grignard of 1-bromo-3,3-diphenyl-4-pentene[4] proved difficult to prepare[5] making an analogous approach unfeasible.

Our synthesis of **1** began from the known 3-ethenyl-3-methylcyclohexanone (**5**).[6] Anti-Markovnikov addition of HBr to the side chain double bond was carried out under photochemical conditions[7,8] to give 3-(2-bromoethyl)-3-methylcyclohex-



(a) HBr, hv, hexane, 83%; (b) NaI, acetone, 89%; (c) $(CH_2OH)_2$, *p*-TsOH, PhH, 98%; (d) Ph_2CHCN, KOH, MEK, 81%; (e) DIBAL-H, PhMe-hexane, 95%; (f) PPTS, 9:1 acetone-H_2O; (g) *p*-TsOH, PhMe, 86% from **10**.



anone (**6**) in 83% yield. Halide exchange followed by ketone protection with ethylene glycol then delivered the iodo ketal **8** in an 87% yield from **6**. Treatment of **8** with the anion of diphenylacetonitrile under phase-transfer conditions (KOH, MEK, reflux)[9] afforded the cyano ketal **9** in 81% yield; attempts to alkylate diphenylacetaldehyde directly using a related phase-transfer protocol (NaOH, *n*-Bu_4NI, PhMe-H_2O, reflux; then H_3O^+)[10] afforded predominantly the O-alkylation

product **11**. DIBAL-H reduction of nitrile **9** (-20→20 °C) provided ketal aldehyde **10** in 95% yield. Final conversion of **10** to **1** was best carried out by a two-step sequence involving (1) deprotection of the ketone using PPTS in 9:1 acetone-H_2O to give **2** and (2) aldol closure with *p*-TsOH in refluxing toluene. This procedure afforded **1** in an 86% yield from **10**. Direct reaction of **10** with *p*-TsOH in refluxing toluene containing added water proved less satisfactory, giving **1** (66%) along with its ethylene ketal **12** (18%). While ketal **12** was easily converted to the target naphthalenone (PPTS, acetone-H_2O, reflux), the overall yield by this route was slightly lower (81%).

Final purification by silica gel column chromatography afforded the title compound as a stable, light yellow solid. The seven step sequence requires a minimum of purification steps and gives the title compound in 48% overall yield. The current synthesis, thus, represents a clean and efficient route to **1** and should be adaptable to an entire family of related 7,7-diaryl-3,4,4a,5,6,7-hexahydro-1(2*H*)-naphthalenone derivatives.

Experimental Section

THF was distilled from $LiAlH_4$. Other reagents were used as received. All reactions were run under dry N_2 in oven-dried glassware. Reactions were monitored using one of the following methods: (1) TLC on hard-layer silica gel GF plates (Analtech) or (2) capillary GC with FI detection (SE-30 column, 6 m x 0.25 mm i.d., 0.25 μm film thickness) programmed between 50-300 °C. The NH_4Cl, 1 M HCl, $NaHCO_3$, 5% $Na_2S_2O_3$, and NaCl used in workup procedures refer to aqueous solutions. Preparative separations were performed using one of the following methods: (1) PTLC on 20- x 20-cm silica gel GF plates (Analtech) or (2) column chromatography on silica gel (Grace, grade 62, 60-200 mesh) containing UV-active phosphor (Sylvania no. 2282); band elution was monitored using a hand-held UV lamp. IR spectra are referenced to polystyrene. ^1H NMR and ^{13}C NMR were measured in $CDCl_3$ at 400 and 100 MHz, respectively, and are referenced to internal Me_4Si. High resolution mass spectra (HRMS, EI/DP) were obtained at 70 eV. Elemental analyses were ± 0.3%.

(±)-3-(2-Bromoethyl)-3-methylcyclohexanone (6). This compound was prepared using an adaptation of the procedure described by Molander and McKie.[7] A solution of 1.10 g (7.97 mmol) of 3-ethenyl-3-methylcyclohexanone[6] in 150 mL of spectrophotometric-grade hexane was placed in a 175-mL quartz tube

equipped with a magnetic stirrer. The reaction vessel was positioned adjacent to a Hanovia immersion well and the solution was purged with N_2 for 15 min prior to starting. The reaction was irradiated (450-W medium pressure mercury vapor lamp, Vycor filter) while dry HBr[8] gas was bubbled through the solution at a moderate rate. The reaction was monitored by GC until all of the starting material had been consumed. Excess HBr was removed by purging the reaction with N_2 for 15-30 min. The crude reaction mixture was washed with H_2O (2x), 5% $Na_2S_2O_3$ (1x), $NaHCO_3$ (1x), and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. The resulting dark brown oil was purified by silica gel column chromatography using 10% ether in hexanes. Band 2 afforded 1.44 g (6.61 mmol, 83%) of **6** as a pale yellow oil which crystallized on standing, mp. 24-26°C. IR (thin film) 1720, 1386 cm^{-1}; ^1H NMR δ 3.37 (m, 2 H), 2.30 (t, 2 H, J = 6.8 Hz), 2.23 (AB d, 1 H, J = 13.6 Hz), 2.14 (AB d, 1 H, J = 13.6 Hz), 1.90 (m, 4 H), 1,64 (m, 2 H), 0.97 (s, 3 H); ^{13}C NMR δ 210.9, 53.2, 45.2, 40.8, 39.7, 35.7, 27.6, 24.5, 21.9; HRMS *m/e* for $C_9H_{15}{}^{79}BrO$ calcd 218.0307, found 218.0307.

When the above procedure was scaled up to 7.90 g (57.2 mmol) of 3-ethenyl-3-methylcyclohexanone in 1 L of hexane using a Hanovia immersion apparatus, the yield of **2** was lowered to 58%.

(±)-3-(2-Iodoethyl)-3-methylcyclohexanone (7). A solution of 8.53 g (39.1 mmol) of **6** and 30 g (200 mmol) of NaI in 500 mL of acetone was heated at reflux for 24 h. The crude reaction mixture was cooled, concentrated under vacuum, diluted with H_2O, and ether extracted (3x). The combined ether extracts were washed with 5% $Na_2S_2O_3$ (1x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. This gave 9.24 g (34.7 mmol, 89%) of compound **7** as a dark yellow oil. This material was pure by NMR analysis and was used without further purification. IR (thin film) 1713, 1382, cm^{-1}; ^1H NMR δ 3.14 (m, 2 H), 2.29 (t, 2 H, J = 6.9 Hz), 2.21 (AB d, 1H, J = 13.6 Hz), 2.12 (AB d, 1 H, J = 13.6 Hz), 1.98 (m, 2 H), 1.89 (m, 2 H), 1.62 (m, 2 H), 0.95 (s, 3 H); ^{13}C NMR δ 210.9, 52.6, 46.9, 41.0, 40.8, 35.3, 24.1, 21.8, -1.3; HRMS *m/e* for $C_9H_{15}IO$ calcd 266.0169, found 266.0167.

(±)-7-(2-Iodoethyl)-7-methyl-1,4-dioxaspiro[4.5]decane (8). A mixture of 9.60 g (36.1 mmol) of **7** and 2.60 g (41.9 mmol) of ethylene glycol in 250 mL of benzene was treated with 50 mg of *p*-TsOH and heated under reflux for 12 h using a Dean-Stark apparatus to collect the H_2O produced. The cooled

reaction mixture was washed with $NaHCO_3$ (2x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. This gave 11.00 g (35.5 mmol, 98%) of ketal **8** as a light brown oil. This product was pure by NMR analysis and was used without further purification. IR (thin film) 1380 cm^{-1}; ^1H NMR δ 3.91 (s, 4 H), 3.16 (m, 2 H), 2.08 (dt, 1 H, J = 12.8, 5.1 Hz), 1.95 (dt, 1 H, J = 12.8, 5.1 Hz), 1.62 (m, 2 H), 1.57 (m, 2 H), 1.51 (AB d, 1 H, J = 13.7 Hz), 1.41 (AB d, 1 H, J = 13.7 Hz), 1.28 (m, 2 H), 0.97 (s, 3 H); ^{13}C NMR δ 108.9, 64.0 (2), 47.1, 44.1, 37.3, 36.7, 34.7, 25.4, 19.4, 1.0; HRMS *m/e* for $C_{11}H_{19}IO_2$ calcd 310.0431, found 310.0428.

(±)-7-(3-Cyano-3,3-diphenylpropyl)-7-methyl-1,4-dioxaspiro-[4.5]decane (9). The phase-transfer alkylation procedure of Adelstein and coworkers[9] was used. A mixture of 10.8 g (34.8 mmol) of **8**, 6.72 g (34.8 mmol) of diphenylacetonitrile, and 2.50 g (44.6 mmol) of pulverized KOH in MEK was heated under reflux with vigorous stirring. After 12 h, GC analysis indicated that a significant amount of starting material remained. An additional 1.0 g (17.9 mmol) of pulverized KOH was added and heating was continued for another 12 h. The mixture was cooled, the solution was filtered from the solid KOH using excess MEK, and the filtrate was concentrated under vacuum. The residue was taken up in ether and washed with 1 M HCl (1x), $NaHCO_3$ (1x), 5% $Na_2S_2O_3$ (1x), and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. The product was purified by chromatography on an 80 cm x 2.5 cm silica gel column eluted with 15-25% ether in hexanes. Band 3 yielded 10.5 g (28.1 mmol, 81%) of compound **9** as a pale yellow oil. IR (thin film) 3061, 3029, 2242, 1599, 1493, 1360, 753, 699 cm^{-1}; ^1H NMR δ 7.41-7.26 (complex, 10 H), 3.89 (m, 4 H), 2.34 (m, 2 H), 1.59-1.23 (complex, 10 H), 0.99 (s, 3 H); ^{13}C NMR δ 140.5, 140.2, 128.8, 128.7, 127.8, 126.9, 126.8, 122.4, 109.2, 64.1, 63.9, 51.8, 44.5, 38.1, 37.4, 34.8, 34.3, 34.1, 25.3, 19.5; HRMS *m/e* for $C_{25}H_{29}NO_2$ calcd 375.2200, found 375.2187.

Anal. Calcd for $C_{25}H_{29}NO_2$: C, 80.00; H, 7.73. Found: C, 79.91; H, 7.71.

Attempted Phase-Transfer Alkylation of Diphenylacetaldehyde with Iodo Ketal 7: (±)-7-(2-(2,2-Diphenylethenoxy)ethyl)-7-methyl-1,4-dioxaspiro[4.5]decane (11). The phase-transfer conditions of Buschmann and Zeeh[10] were used. A mixture of 170 mg (0.55 mmol) of **8**, 130 mg (0.66 mmol) of diphenylacetaldehyde, 66 mg (1.65 mmol) of finely ground NaOH, and 5 mg of tetrabutylammonium iodide was placed in a round-bottomed flask containing

0.25 mL of toluene and 0.25 mL of H_2O. This reaction mixture was stirred and heated at reflux for 4 h, then cooled to rt, and ether extracted (2x). The combined organic extracts were washed with 1 M HCl (1x), H_2O (1x), and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. The product was purified by PTLC eluted with 10% ether in hexanes. The slowest moving band yielded 80 mg (0.21 mmol, 38.5%) of compound **11** as a light yellow oil. IR (thin film) 3080, 3054, 3026, 1634, 1598, 1496, 1381, 766, 698 cm^{-1}; ^1H NMR δ 7.32 (d, 2 H, J = 8.4 Hz), 7.24-7.10 (complex, 8 H), 6.42 (s, 1 H), 3.91 (t, 2 H, J = 7.4 Hz), 3.81 (m, 4 H), 1.75 (dt, 1 H, J = 13.9, 7.2 Hz), 1.63 (dt, 1 H, J = 13.9, 7.2 Hz), 1.54 (m, 2 H), 1.48 (m, 2 H), 1.46 (AB d, 1 H, J = 13.6 Hz), 1.38 (AB d, 1 H, J = 13.6 Hz), 1.28-1.17 (complex, 2 H), 0.93 (s, 3 H); ^{13}C NMR δ 145.5 (2), 140.8, 137.8, 129.8, 128.3, 128.2, 127.8, 126.3, 126.2, 119.9, 109.1, 70.4, 64.0 (2), 45.0, 40.8, 37.6, 34.8, 34.7, 33.8, 26.3, 19.6; HRMS *m/e* for $C_{25}H_{30}O_3$ calcd 378.2196, found 378.2177.

Anal. Calcd for $C_{25}H_{30}O_3$: C, 79.36: H, 7.94. Found: C, 79.33; H, 7.93.

(±)-7-(3-Formyl-3,3-diphenylpropyl)-7-methyl-1,4-dioxaspiro-[4.5]decane (10). A solution of 2.48 g (6.61 mmol) of **9** in 100 mL of CH_2Cl_2 was cooled to -20 °C and treated with 9.92 mL (9.92 mmol) of a 1 M solution of DIBAL in hexane over 30 min. After addition was complete, stirring was continued for 2.5 h during which time the reaction warmed to 20 °C. The reaction was cooled to -20 °C and carefully quenched with 50 mL of 50% (w/w) aqueous citric acid. Stirring was continued until the two immiscible phases became clear. The organic layer was separated, washed with H_2O (2x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum to yield 2.37 g (6.27 mmol, 95%) of **10** as a viscous, colorless oil that was pure by GC and NMR. This product was used without further purification. IR (thin film) 3086, 3059, 3025, 2818, 2716, 1722, 1599, 1493, 756, 701 cm^{-1}; ^1H NMR δ 9.78 (s, 1 H), 7.36 (t, 4 H, J = 7.4 Hz), 7.30 (m, 2 H), 7.19 (m, 4 H), 3.89 (m, 2 H), 3.83 (m, 2 H), 2.26 (m, 2 H), 1.58-0.84 (complex, 10 H), 0.95 (s, 3 H); ^{13}C NMR δ 199.0 140.1, 140.0, 129.2, 128.7, 128.6, 127.2, 109.3, 64.1, 63.8, 63.6, 44.5, 37.3, 37.1, 34.9, 34.5, 27.9, 25.0, 19.6; HRMS *m/e* for $C_{25}H_{30}O_3$ calcd 378.2196, found 378.2199.

(±)-4-(1-Methyl-3-oxocyclohexyl)-2,2-diphenylbutanal (2). A solution of 2.35 g (6.22 mmol) of **10** and 1.04 g (4.14 mmol) of PPTS in 75 mL of 9:1 acetone-H_2O was heated at reflux for 36 h. The solution was cooled and concentrated under vacuum. The resulting oily residue was triturated with ether

(3x) and decanted away from the solid PPTS. The combined ether extracts were washed with H_2O (3x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum to yield 1.97 g of **2** containing *ca.* 10% of an impurity (by GC). A small amount was purified for analytical purposes using PTLC eluted with 5% ether in hexanes. The remainder of the material was used without further purification. IR (thin film) 3086, 3058, 3026, 2828, 2709, 1722, 1714, 756, 701 cm^{-1}; ^1H NMR δ 9.79 (s, 1 H), 7.37 (t, 4 H, J = 7.3 Hz), 7.31 (m, 2 H), 7.17 (t, 4 H, J = 7.8 Hz), 2.30-2.16 (complex, 4 H), 2.12 (AB d, 1 H, J = 13.4 Hz), 2.07 (AB d, 1 H, J = 13.4 Hz), 1.76 (m, 2 H), 1.60 (m, 1 H), 1.53 (m, 1 H), 1.01 (t, 2 H, J = 7.3 Hz), 0.90 (s, 3 H); ^{13}C NMR δ 211.9, 198.3, 139.9, 139.6, 128.9, 128.8, 127.4, 63.4, 53.7, 40.9, 38.5, 35.9, 35.5, 27.6, 24.5, 21.9; HRMS *m/e* for $C_{23}H_{26}O_2$ calcd 334.1934, found 334.1928.

Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.63; H, 7.78. Found: C, 82.41; H, 7.80.

(±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (1). Route A. A solution of 1.96 g of crude **2** and 50 mg of *p*-TsOH in 100 mL of toluene was heated under reflux in a 250 mL round-bottomed flask equipped with a Dean-Stark apparatus to collect the H_2O that was produced. After 12 h, the crude reaction mixture was cooled, washed with $NaHCO_3$ (2x), H_2O (1x), and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. The oil was eluted through a small plug of silica gel using 5% ether in hexanes to give 1.68 g (5.32 mmol, 86% from **10**) of **1** as a yellow oil which crystallized on standing. Slow recrystallization from ether gave an analytically pure sample, mp. 120-122 °C. UV (*t*-BuOH) 254 nm (ε 2429), 320 (120); IR (thin film) 3082, 3057, 3022, 1685, 1626, 1598, 1495, 1379, 762, 703 cm^{-1}; ^1H NMR δ 7.30-7.13 (complex, 10 H), 6.76 (s, 1 H), 2.64 (ddt, 1 H, J = 16.9, 5.1, 2.0 Hz), 2.37 (m, 3 H), 2.03 (qt, 1 H, J = 13.2, 4.4 Hz), 1.90 (m, 1 H), 1.69 (AB d, 1 H, J = 13.6 Hz), 1.60 (m, 3 H), 1.13 (s, 3 H); ^{13}C NMR δ 203.5, 249.0, 247.1, 144.6, 138.3, 127.8, 128.5, 128.3, 127.7, 126.5, 126.4, 49.4, 41.0, 38.9, 36.2, 35.4, 32.0, 25.3, 19.7; HRMS *m/e* for $C_{23}H_{24}O$ calcd 316.1828, found 316.1826.

Anal. Calcd for $C_{23}H_{24}O$: C, 87.34: H, 7.59. Found: C, 87.22; H, 7.61.

Route B. A mixture of 2.00 g (5.29 mmol) of **10**, 50 mg of *p*-TsOH, 150 mL of toluene, and 0.25 mL of H_2O was stirred and heated under reflux for 24 h using a Dean-Stark apparatus to collect H_2O from the reaction. The mixture was cooled to rt, washed with $NaHCO_3$ (2x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum. Purification on a 95 cm x 2.5 cm silica gel column

eluted with 5-10% ether in hexanes afforded 1.10 g (3.48 mmol, 66%) of **1** as a light yellow oil which crystallized on standing. The physical and spectral data matched those given above. Also isolated from this reaction was 0.35 g (0.97 mmol, 18%) of ethylene ketal **12**. IR (thin film) 3083, 3057, 3022, 1598, 1490, 756, 700 cm^{-1}; ^1H NMR δ 7.23 (m, 8 H), 7.16 (m, 2 H), 6.27 (s, 1 H), 3.94 (m, 1 H), 3.88 (t, 2 H, J = 6.1 Hz), 3.76 (m, 1 H), 2.36 (ddd, 1 H, J = 13.3, 10.1, 5.8 Hz), 2.23 (dm, 1 H, J = 12.5 Hz), 1.94 (m, 2 H), 1.72 (dd, 1 H, J = 13.3, 4.5 Hz), 1.64 (m, 1 H), 1.53 (dm, 1 H, J = 12.5 Hz), 1.41 (m, 2 H), 1.25 (s, 3 H), 1.24 (m, 1 H); ^{13}C NMR δ 149.9, 148.1, 140.7, 129.1, 128.3, 128.1, 127.9, 127.4, 125.7, 108.5, 64.9, 63.4, 49.2, 41.1, 37.9, 37.3, 35.9, 32.2, 24.8, 19.5; HRMS *m/e* for $C_{25}H_{28}O_2$ calcd 360.2090, found 360.2088.

Anal. Calcd for $C_{25}H_{28}O_2$: C, 83.33; H, 7.78. Found: C, 83.08; H, 7.81.

(±)-3,4,4a,5,6,7-Hexahydro-4a-methyl-7,7-diphenyl-1(2*H*)-naphthalenone (1) from Ethylene Ketal 12. A solution of 350 mg (0.97 mmol) of **12** and 100 mg (0.40 mmol) of PPTS in 10 mL of 9:1 acetone-H_2O was heated under reflux for 36 h. Reaction mixture was cooled and concentrated under vacuum. The resulting oily residue was triturated with ether (3x) and decanted away from the solid PPTS. The combined ether extracts were washed with H_2O (3x) and NaCl (1x), then dried ($MgSO_4$), and concentrated under vacuum to yield 260 mg (0.82 mmol, 84.5%) of **1** as pale yellow crystals which were pure by GC and NMR. When these crystals were combined with those from route B the yield of **1** was increased to 81%.

Acknowledgment: The authors wish to acknowledge the Oklahoma State University Center for Energy Research for support of this research. Partial Support by NSF (CHE-8718150) for our NMR facility and NSF (BSS-8704089) for our high resolution mass spectrometer is also appreciated.

References and Notes

1. The DE rings of several triterpenes incorporate the 3,4,4a,5,6,7-hexahydro-4a,7,7-trimethyl-1(2*H*)-naphthalenone ring skeleton, see ApSimon, J. W.; Fyfe, K. E.; Greaves, A. M. "The Total Synthesis of Natural Products," Wiley-Interscience: NY, **1984**, Vol. 6, pp. 85-139.

2. One other potential approach to the synthesis of fused rings bearing 7,7-disubstitution was deemed unsuitable because of steric hindrance to the initial Michael addition, see Meyer, W. L.; Brannon, M. J.; Burgos, C. G.; Goodwin, T. E.; Howard, R. W. *J. Org. Chem.* **1985**, *50*, 438-447.

3. Bunce, R. A.; Childress, R. S. *Org. Prep. Proc. Int.* **1995**, *26*, 709-713.

4. Bunce, R. A.; Childress, R. S. *Org. Prep. Proc. Int.* **1995**, *26*, 122-125.

5. The Grignard reagent of 1-bromo-3,3-diphenyl-4-pentene could not be produced under standard conditions (Mg, THF, reflux). Exposure of the bromide to Rieke magnesium at 0 °C for 30 min followed by quenching with aq. NH_4Cl resulted in recovery of 22% of the unreacted bromide, 37% of 3,3-diphenyl-1-pentene (quenched Grignard), 6% of 1,1-diphenylpropene (fragmented Grignard), and 20% of a mixture of dimers along with several unidentified minor compounds which could not be isolated in pure form.

6. Paquette, L. A.; Poupart, M.-A. *J. Org. Chem.* **1993**, *58*, 4245-4253.

7. Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *56*, 4112-4120.

8. The results for this reaction were best when commercial anhydrous HBr (Matheson) was used. The use of HBr generated by addition of Br_2 to tetralin (Duncan, D. R. *Inorganic Syntheses*; Booth, H. S., Ed.; McGraw-Hill, New York; **1939**, *1*, 151-152) gave yields in the 25-40% range.

9. Adelstein G. W.; Yen, C. H.; Dajani, E. Z.; Bianchi, R. G. *J. Med. Chem.* **1976**, *19*, 1221-1225.

10. Buschmann, E.; Zeeh, B. *Liebig's Ann. Chem.* **1979**, 1585-1590.