noflagellate of the genus *Amphidinium*.[4b] Amphidinolide B (3) possesses the tertiary methyl and tertiary hydroxyl groups at C-16, and the C-26 position is not oxygenated (methyl group), whereas amphidinolides G (1) and H (2) have the secondary methyl group at C-16 and the oxygenated methylene group on C-26.

Amphidinolide G (1) is a new cytotoxic 27-membered macrolide, while amphidinolide H (2) is a 26-membered macrolide bearing the similar molecular constitution and substitution pattern of 1.[14] These two compounds, especially 2, exhibited extremely strong cytotoxic activities against L1210 murine leukemia cells in vitro with the IC_{50} (50% inhibitory concentration) values of 0.0054 and 0.000 48 μg/mL[15] and KB human epidermoid carcinoma cells in vitro with IC_{50} values of 0.0059 and 0.000 52 μg/mL, respectively.[16]

Experimental Section

General Procedure. The 7.26 ppm resonance of residual $CHCl_3$ and 77.0 ppm resonance of $CDCl_3$ were used as internal references for ^1H and ^{13}C chemical shifts, respectively. FABMS were obtained using glycerol or diethanolamine as a matrix.

Isolation. The procedure for the algal cultivation has been previously described.[4c] The harvested cells (70 g, wet weight) from 160 L of culture were extracted with toluene–methanol (1:3, 200 mL × 3). After addition of 1 M NaCl (300 mL), the mixture was extracted with toluene (200 mL × 3). The toluene-soluble fraction was evaporated under reduced pressure to give a residue (1.0 g), which was subjected to silica gel column chromatography (Wako gel C-300, Wako Chemical, 2.2 × 37 cm) eluted with chloroform–methanol (95:5, 540 mL). The fraction (10 mg) eluting from 160 to 210 mL was further separated by SEP-PAK C_{18} cartridges (Waters, 10 × 12 mm) eluted with MeOH–H_2O (80:20, 20 mL). The eluate (6.9 mg) was then purified by HPLC (Develosil ODS-5, Nomura Chemical, 10 × 250 mm; flow rate 2.5 mL/min; UV detection at 254 nm; eluent MeOH–H_2O (88:12)) to afford compound 1 (1.4 mg, t_R 12.2 min) and compound 2 (1.2 mg, t_R 10.6 min).

Amphidinolide G (1): colorless amorphous powder; $[\alpha]^{22}_D$ −60.1° (*c* 0.15, $CHCl_3$); UV (MeOH) 222 nm (ϵ 11 000); IR (film) 3400, 1705, 1280, 1260, and 1120 cm^{-1}; ^1H and ^{13}C NMR (Table I); FABMS (positive ion, glycerol matrix) *m/z* 563 $(M + H)^+$, 545 $(M - H_2O + H)^+$, 527 $(M - 2H_2O + H)^+$, and 509 $(M - 3H_2O + H)^+$; FABMS (positive ion, diethanolamine (DEA) matrix) *m/z* 668 $(M + DEA + H)^+$ and 585 $(M + Na)^+$; HRFABMS *m/z* 668.4377 (M + DEA + H), calcd for $C_{36}H_{62}NO_{10}$ 668.4374.

Amphidinolide H (2): colorless amorphous powder; $[\alpha]^{18}_D$ −32.3° (*c* 0.2, $CHCl_3$); UV (MeOH) 222 nm (ϵ 10 000); IR (film) 3400, 1700, 1255, and 1130 cm^{-1}; ^1H and ^{13}C NMR (Table II); FABMS (positive ion, diethanolamine matrix) *m/z* 668 (M + DEA + H)$^+$, 650 $(M + DEA - H_2O + H)^+$; HRFABMS *m/z* 668.4407 (M + DEA + H), calcd for $C_{36}H_{62}NO_{10}$ 668.4374.

Acknowledgment. This study was supported in part by Grant-in-Aid (02151037) for Cancer Research from Ministry of Education, Science, and Culture, Japan.

Registry No. 1, 134781-23-0; 2, 134781-24-1.

Supplementary Material Available: ^1H–^1H COSY, ^{13}C NMR, NOESY, HMQC, HMBC, FABMS, HRFABMS, IR, and UV spectra of 1 and 2 (18 pages). Ordering information is given on any current masthead page.

(14) No interconversion between the two compounds (1 and 2) was observed.

(15) The cytotoxicity of amphidinolide H (2) is almost as potent as that of amphidinolide B (3, IC_{50} 0.000 14 μg/mL against L1210 cells).[4b]

(16) Before the cytotoxicity test, compounds 1 and 2 were further purified by HPLC (Develosil ODS-5, 10 × 250 mm) with MeOH–H_2O (88:12) to remove the impurities contained in the samples of the NMR experiments (see supplementary material).

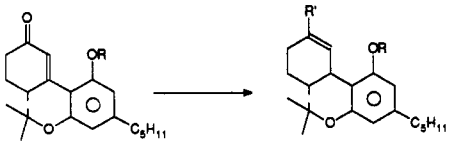
Regioselective Synthesis of 1-Formylcyclohexenes by One-Carbon Homologation

John W. Huffman,* Ming-Jung Wu, and H. Howard Joyner

Howard L. Hunter Chemistry Laboratory, Clemson University, Clemson, South Carolina 29634-1905

Received March 11, 1991

As one aspect of our general synthetic program directed toward the regio- and stereoselective synthesis of cannabinoids, we sought a method for the conversion of enone 1 to 11-oxocannabinoid 2.[1] Aldehyde 2 was to be a pre-



1 R = Me or MOM

2 R = Me or MOM, R' = CHO
3 R = Me or MOM, R' = CO_2H

cursor to 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol 3, a human metabolite of Δ^9-tetrahydrocannabinol, the major active component of marijuana. Although a number of procedures have been described for the preparation of unsaturated aldehydes by one-carbon homologation,[2] only two appeared attractive for the synthesis of 2. One of these, developed by Denmark,[2a] proceeds by conjugate reduction of an enone, trapping the derived enolate as the trimethylsilyl ether, and Rubottom oxidation to the TMS ether of an α-hydroxy ketone.[3] The TMS ether is cleaved, the hydroxyl group reprotected as the *tert*-butyldimethylsilyl ether; Horner–Emmons reaction,[4] followed by hydrolysis, provides the unsaturated aldehyde.[2a] The second procedure for regioselective synthesis of cyclohexenals entails palladium-catalyzed reaction of a vinyl triflate with carbon monoxide–tributytin hydride.[2b]

The attempted conversion of 1 to aldehyde 2 by both these procedures was unsuccessful, and in response to this problem, we developed a new synthetic procedure for the regioselective elaboration of cyclohexanones or cyclohexenones to 1-formylcyclohexenes. This procedure has been applied to the preparation of several unsaturated aldehydes in yields comparable to those reported by Denmark.[2a] In addition, the synthetic procedure is significantly shorter than Denmark's and does not require the isolation of sensitive silyl enol ethers.

This procedure, which is outlined in Scheme I, proceeds in three steps from an enone or saturated ketone, by formation of an α-phenylthio ketone, Wittig reaction with (methoxymethylene)triphenylphosphorane, or Warren's variation of the Horner–Emmons reaction.[4] Mercuric ion assisted acid hydrolysis provides directly the unsaturated aldehyde. This sequence has been applied to six substi-

(1) (a) Huffman, J. W.; Zhang, X.; Wu, M.-J.; Joyner, H. H. *J. Org. Chem.* **1989**, *54*, 5428. (b) Huffman, J. W.; Zhang, X.; Wu, M.-J.; Joyner, H. H.; Pennington, W. T. *J. Org. Chem.* **1991**, *56*, 1481. (c) Huffman, J. W.; Joyner, H. H.; Lee, M. D.; Jordan, R. D.; Pennington, W. T. *J. Org. Chem.* **1991**, *56*, 2081.

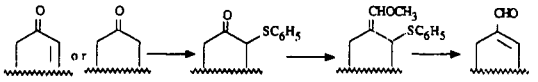
(2) (a) Jones, T. K.; Denmark, S. E. *J. Org. Chem.* **1985**, *50*, 4037. (b) Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 452. (c) Rousseau, G.; LePerchec, P.; Conia, J. M. *Synthesis* **1978**, 67. (d) Traas, P. C.; Boelens, H.; Takken, H. J. *Tetrahedron Lett.* **1976**, 2287. (e) Reutrakul, V.; Khanghae, W. *Tetrahedron Lett.* **1977**, 1377. (f) Taguchi, H.; Tanaka, S.; Yamamoto, H.; Nozaki, H. *Tetrahedron Lett.* **1973**, 2465 and other references cited in the above.

(3) Rubottom, G. M.; Gruber, J. M. *J. Org. Chem.* **1978**, *43*, 1599.

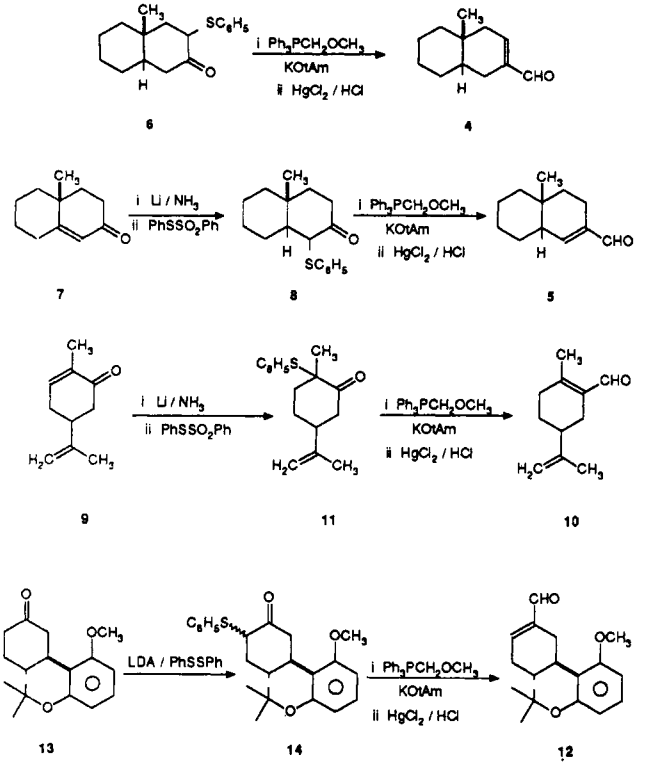
(4) (a) Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Chem. Commun.* **1977**, 314. (b) Earnshaw, C.; Wallis, C. J.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099.

0022-3263/91/1956-5224$02.50/0

Scheme I



Scheme II



tuted cyclohexanones or cyclohexenones and provides isolated, purified material in unoptimized overall yields of 29–53%.

Two monosubstituted cyclohexanones, 2-methylcyclohexanone and 4-*tert*-butylcyclohexanone, were converted to 2-(phenylthio)-6-methylcyclohexanone and 2-(phenylthio)-4-*tert*-butylcyclohexanone, respectively, as described by Trost.[5] Warren's variation of the Horner–Emmons reaction employing (methoxymethyl)diphenylphosphine oxide[4] provided the requisite phenylthio enol ethers. These enol ethers were neither purified nor extensively characterized (^{1}H NMR and IR only) but were subjected to acid hydrolysis in the presence of mercuric chloride to provide 1-formyl-6-methylcyclohexene and 1-formyl-4-*tert*-butylcyclohexene in 36 and 47% overall yields, respectively, from the starting cyclohexanone.

The two regioisomers of 2-formyl-10-methyl-*trans*-octalin (**4** and **5**) were also prepared to illustrate the regioselectivity of this procedure as shown in Scheme II. Aldehyde **4** was prepared from the known phenylthio ketone **6**[5] by McMorris's variation of the Wittig reaction,[6] followed by hydrolysis, in 58% yield. In this case, the Hormer–Emmons reaction failed, probably due to enolate formation by the strongly basic Warren reagent. Although reaction of the enolate obtained by Li/NH_3 reduction of **7** with phenyl disulfide provided significant quantities of **6** via enolate equilibration, phenyl benzenethiosulfonate[5] afforded α-phenylthio ketone **8** cleanly and in acceptable yield (54%). The phenylthio group was assigned equatorial stereochemistry based on the large coupling constant for the α-proton with the bridgehead proton (J = 18Hz). Wittig homologation followed by hydrolysis gave aldehyde **5** in an overall yield of 29% for three steps. As a second example in which the phenylthio ketone was prepared from an enolate generated by dissolving metal reduction, carvone (**9**) was converted to aldehyde **10** in 43% overall yield via phenylthio ketone **11**.

The aldehyde synthesis was also useful for the synthesis of a model 11-oxo-Δ^8-cannabinoid **12** (Scheme II). Ketone **13**[1c] was converted to phenylthio ketone **14** and thence to aldehyde **12** in an overall yield of 53%. Although **14** was obtained as a sharp-melting solid that was homogeneous to TLC, both ^{1}H and ^{13}C NMR indicated that it was a mixture (approximately 2:1) of two isomers. Comparison of the ^{1}H NMR spectrum with data obtained by Trost for the similar mixture of isomers of 2-(phenylthio)-4-*tert*-butylcyclohexanone indicates that the major isomer is that with an axial phenylthio group.[5] When this procedure was applied to the conversion of enone **1** to aldehyde **2** it was not possible to effect the synthesis of the intermediate phenylthio ketone. Trapping of the enolate derived from **1** on dissolving metal reduction, using either phenyl disulfide or phenyl benzenethiosulfonate, followed by aqueous workup, gave only the reduced, unsubstituted ketone. It is probable that steric hindrance arising from the aromatic methoxyl group prevents approach of the sulfur reagent. Although this approach was not successful for the synthesis of **2**, we were able to effect the conversion of **1** to acid **3** efficiently by an alternative route.[1a,b]

Experimental Section

General Methods. Melting points were determined using a Kofler hot stage and are uncorrected. All column chromatography was accomplished with 63–200-μm silica gel using hexane/ethyl acetate solutions as eluent unless otherwise noted. IR spectra were obtained as neat films between salt plates, as KBr pellets, or in solutions in $CHCl_3$. ^{1}H NMR spectra were recorded at 90, 200, or 300 MHz and ^{13}C spectra were recorded at 50.28 or 75.42 MHz using $CDCl_3$ as solvent. Mass spectral analyses were performed on a gas chromatograph/mass spectrometer at 70 eV. Ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone ketyl immediately before use. Toluene was distilled from sodium/benzophenone ketyl and then stored over freshly cut sodium wire for 24 h before use. Diisopropylamine and hexamethylphosphoric triamide (HMPA) were distilled from CaH_2, both under an atmosphere of N_2. Commercially available (Aldrich) solutions of *n*-butyllithium in hexanes were titrated with 1,3-diphenyl-2-propanone tosylhydrazone[7] as indicator prior to use. All reactions were carried out under an atmosphere of N_2 or Ar.

1-Methoxy-8-(phenylthio)-6,6a,7,8,10,10a-hexahydro-6,6-dimethyl-9*H*-dibenzo[*b*,*d*]pyran-9-one (14). To a stirred solution of 0.347 mmol of lithium diisopropylamide (LDA) containing a few crystals of dipyridyl at 0 °C was added 0.100 g (0.385 mmol) of **13**[1c] in 1 mL of dry THF. The solution was stirred at 0 °C for 1 h, and 0.168 g (0.77 mmol) of phenyl disulfide in 2 mL of dry THF was added. The mixture was warmed to ambient temperature, stirred for 16 h, quenched with 10% aqueous HCl, and extracted with ether. The organic layer was washed with 10% aqueous HCl and brine and dried ($MgSO_4$). Concentration afforded an oil that was chromatographed on silica gel to give 0.168 g (95%) of **14** (mixture of isomers at C-9) as a crystalline solid. Recrystallization from hexane and a few drops of ether gave **14** as white crystals, mp 130–132 °C: IR 1707 cm^{-1}; ^{1}H NMR δ 1.08, 1.46 (s, 3 H each), 3.63 (m, 0.67 H), 3.77 (s, 3 H), 3.79 (br s, 1 H) 3.85 (m, 0.33 H), 6.40 (dd, 2 H, J = 3 Hz), 7.06 (t, 1 H, J = 9 Hz), 7.12 (m, 5 H); ^{13}C NMR δ 16.5, 27.7, 33.2, 34.8, 35.5, 41.1, 42.9, 45.2, 47.3, 54.3, 55.1, 56.9, 76.3, 102.5, 110.6, 111.9, 127.5, 128.0, 129.0, 132.3, 158.6, 206.5; MS m/z (relative intensity) 369 (21),

(5) Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.
(6) Schow, S.; McMorris, T. *J. Org. Chem.* **1979**, *44*, 3760.
(7) Lipton, M. F.; Sorenson, C. M.; Sadler, A. C.; Shapiro, R. H. *J. Organomet. Chem.* **1980**, *186*, 155.

368 (90), 260 (17), 259 (68), 217 (47), 203 (11), 190 (19), 189 (100), 177 (60), 176 (15). Anal. Calcd for $C_{22}H_{24}O_3S$: C, 71.71; H, 6.56. Found C, 71.64; H, 6.58.

2-Methyl-2-(phenylthio)-5-(1-methylethenyl)cyclohexanone (11). To a stirred solution of 0.210 g (30 mg-atoms) of Li in 200 mL of liquid NH_3 at -78 °C was added dropwise a solution of 1.5 g (10.0 mmol) of (-)-carvone (**9**) in 10 mL of THF. After the solution was stirred at this temperature for 10 min, the excess Li was destroyed with isoprene and the NH_3 was evaporated, initially under a stream of N_2, and finally under vacuum at 40 °C for 15 min. The solid mass was blanketed with dry N_2 and dissolved in 40 mL of dry THF at -78 °C. This solution was transferred under N_2 pressure through a steel cannula to a solution of 5.0 g (20.0 mmol) of phenyl benzenethiosulfonate (Fluka) in 20 mL of THF at room temperature. After being stirred for 1 h, the reaction was quenched with 10% aqueous HCl, extracted with ether, washed with brine, and dried (Na_2SO_4). Evaporation and chromatography afforded 1.59 g (61%) of **11** as an yellow oil. IR 1702 cm^{-1}; ^1H NMR δ 1.23 (s, 3 H), 1.78 (s, 3 H), 3.37 (t, 1 H, J = 14 Hz), 4.89 (s, 2 H), 7.22-7.39 (m, 5 H); MS m/z (relative intensity) 262 (22), 261 (89), 260 (42), 243 (11), 218 (12). These properties agree with those reported for material prepared by a different route.[9]

1-(Phenylthio)-4a-methyl-*trans*-octahydro-2(1*H*)-naphthalenone (8). Reduction of 0.164 g (1.00 mmol) of 4a-methyl-*trans*-octahydro-2(1 *H*)-naphthalenone **7**[8] with Li in NH_3 and reaction with phenyl benzenethiosulfonate as described for the preparation of **11** gave 0.149 g (54%) of **8** as a pale yellow oil: IR 1715 cm^{-1}; ^1H NMR δ 1.04 (s, 3 H), 3.51 (d, 1 H, J = 18 Hz), 7.21-7.45 (m, 5 H); MS m/z (relative intensity) 275 (31), 274 (91), 219 (22), 218 (71), 217 (44), 185 (27), 109 (100). Anal. Calcd for $C_{17}H_{22}OS$: C, 74.41; H, 8.08. Found C, 74.27; H, 8.09.

4-*tert*-Butylcyclohexene-1-carboxaldehyde. A solution of 0.80 g (3.80 mmol) of (methoxymethylene)diphenylphosphine oxide in 5 mL of THF was added to a solution of 3.8 mmol of LDA in 5 mL of THF at -78 °C. The resulting solution was stirred at -78 °C for 30 min, and a solution of 0.500 g (1.90 mmol) of 2-(phenylthio)-4-*tert*-butylcyclohexanone[5] in 5 mL of THF was added dropwise over 15 min. The reaction mixture was stirred at -78 °C until TLC showed that consumption of the starting material was complete. The reaction was warmed to room temperature and stirred until TLC showed disappearance of the initial 1,2 adduct. The solution was diluted with water and extracted with ether, and the organic layer was washed with brine and dried (Na_2SO_4). Concentration afforded 0.299 g (54%) of crude enol ether, which was used without purification. A solution of 0.250 g (0.86 mmol) of the enol ether in 2 mL of acetonitrile and 0.934 g (3.5 mmol) of $HgCl_2$ in 3 mL of acetonitrile/water (4:1) was heated to 50 °C and stirred for 4 h. After being cooled, the reaction mixture was filtered through a Florisil column. The filtrate was diluted with water and extracted with ether, and the organic layer was washed with saturated aqueous NH_4Cl and brine and dried (Na_2SO_4). Concentration and chromatography on silica gel gave 0.135 g (94%) of aldehyde as an oil: ^1H NMR δ 0.91 (s, 9 H), 6.83 (m, 1 H), 9.43 (s, 1 H); MS m/z (relative intensity) 166 (6), 123 (19), 110 (47), 109 (30), 95 (39), 81 (31), 67 (22), 57 (100). This compound has been reported previously.[2d,10]

3-Methylcyclohexene-2-carboxaldehyde. From 0.264 g (1.20 mmol) of 2-(phenylthio)-6-methylcyclohexanone,[5] using the procedure described for the preparation of 4-*tert*-butylcyclohexene-1-carboxaldehyde, there was obtained 0.076 g (51%) of aldehyde, the spectral properties of which (IR, ^1H NMR) agree with those reproted.[11]

***trans*-4a-Methyl-1,1a,4,4a,5,6,7,8-octahydronaphthalene-2-carboxaldehyde (4).** To a solution of 1.85 g (5.32 mmol) of (methoxymethyl)triphenylphosphonium chloride in 2 mL of dry toluene at room temperature was added 1.5 mL of 3.55 M potassium *tert*-amylate in toluene (5.3 mmol). After the mixture was stirred for 10 min, a solution of 0.728 g (2.66 mmol) of phenylthio ketone **6**[5] in 2 mL of dry toluene was added in one portion. The solution was stirred for 1 h at room temperature, heated at reflux for 16 h, and cooled. The solution was diluted with water and extracted with ether, and the organic layer was washed with brine and dried (Na_2SO_4). Concentration afforded 0.394 g (65%) of crude enol ether, which was use in the next step without purification. A mixture of 0.260 g (0.86 mmol) of enol ether, 1.02 g (4.30 mmol) of $HgCl_2$ in 15 mL of THF/H_2O (4:1), and 1 drop of concentrated HCl was warmed at 50 °C for 4 h. After being cooled to ambient temperature, the reaction mixture was filtered through a Florisil column. The filtrate was diluted with water, extracted with ether, washed with saturated aqueous NH_4Cl and brine, and dried (Na_2SO_4). Removal of the solvent and distillation (bath temperature 65 °C (0.8 mm)) gave 0.136 g (89%) of aldehyde **4** as an air-sensitive oil: IR 1683 cm^{-1}; ^1H NMR δ 0.78 (s, 3 H), 6.72 (br s, 1 H) 9.41 (s, 1 H); MS m/z (relative intensity) 178 (78), 163 (20), 149 (26), 109 (38), 81 (100).

***trans*-4a-Methyl-1a,3,4,4a,5,6,7,8-octahydronaphthalene-2-carboxaldehyde (5).** Wittig reaction of 0.348 g (1.22 mol) of phenylthio ketone **8** followed by hydrolysis as described for the synthesis of **4** gave 0.120 g (53%) of **5** as white, air-sensitive crystals that melted below room temperature: IR 1689 cm^{-1}; ^1H NMR δ 0.76 (s, 3 H), 6.44 (br s, 1 H), 9.40 (s, 1 H); MS m/z (relative intensity) 178 (47), 163 (27), 160 (37), 149 (31), 147 (22), 109 (75), 67 (100).

2-Methyl-5-(1-methylethenyl)cyclohexene-1-carboxaldehyde (10). Wittig reaction of 0.278 g (1.07 mmol) of phenylthio ketone **11** followed by hydrolysis as described for the synthesis of **4** gave 0.125 g (71%) of **10** as an oil: IR 1672 cm^{-1}; ^1H NMR δ 1.75 (s, 3 H), 2.15 (s, 3 H), 4.71 (d, 2 H, J = 10 Hz), 10.15 (s, 1 H); MS m/z (relative intensity) 164 (32), 149 (26), 135 (24), 121 (36), 107 (41). This compound has been described previously.[12]

1-Methoxy-6a,7,10,10a-tetrahydro-6,6-dimethyl-6*H*-dibenzo[*b*,*d*]pyran-9-carboxaldehyde (12). Wittig reaction of 0.059 g (0.16 mmol) of phenylthio ketone **14** followed by hydrolysis as described for the preparation of **4** provided crude aldehyde **12**, which was purified by chromatography on silica gel to give 0.024 g (56%) of **12** as an air-sensitive oil: IR 1682 cm^{-1}; ^1H NMR δ 1.13, 1.43 (s, 3 H each), 3.77 (d, 1 H, J = 3.6 Hz), 3.82 (s, 3 H), 6.46 (t, 2 H, J = 8.1 Hz), 6.84 (br s, 1 H) 7.08 (t, 1 H, J = 8.1 Hz), 9.50 (s, 1 H); HRMS calcd for $C_{17}H_{20}O_2$ 272.1406, found 272.1386.

Acknowledgment. We thank the National Institute on Drug Abuse for support of this work under Grant DA-03590. We also thank Grace R. Zoorob for assistance in preparing starting materials and Dr. Qingmei Zha, Brown University, for the high-resolution mass spectral determination.

Supplementary Material Available: ^1H NMR spectra of **4**, **5**, and **12** (3 pages). Ordering information is given on any current masthead page.

(8) Heathcock, C. H.; Ellis, J. E.; McMurry, J. E.; Coppolino, A. *Tetrahedron Lett.* **1971**, 4995.
(9) Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 3554.
(10) Muzart, J.; Pale, P.; Pete, J. P. *J. Chem. Soc., Chem. Commun.* **1981**, 668.
(11) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147.
(12) deBotton, M. *Bull. Soc. Chim. Fr.* **1973**, 2472.

A Short Synthesis of Two Chiral Anthracycline AB Synthons

Herbert L. Holland* and Peter Viski

Department of Chemistry, Brock University, St. Catharines, Ontario L2S 3A1, Canada

Received February 19, 1991

The potent antitumor activity of the anthracyclines and their use in cancer chemotherapy has promoted a continued interest in the synthesis of this class of compounds. Anthracyclines with high antineoplastic activity, exemplified by daunomycin and its 4-demethoxy derivative,

0022-3263/91/1956-5226$02.50/0