on a 25 m × 0.25 mm Ni(HFB-1R-Cam)$_2$ column and also by the analysis of diastereomeric (2*R*,3*R*)-butanediol ketals on a 50 m × 0.25 mm methyl silicone column at 145 °C.

(*S*)-(+)-3,4,4-Trimethyl-2-pentanone: bp 85–86 °C (60 mm); IR ν_{max} (neat) 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 9 H, $C(CH_3)_3$), 1.1 (d, J = 7 Hz, 3 H, CH_3), 2.2 (s, 3 H, $COCH_3$), 2.46 (m, 1 H); $[\alpha]^{23}_D$ = +107.8° ± 0.02° (*c* 1, $CHCl_3$). The enantiomeric purity of this ketone was found to be 94% ee by capillary GC analysis of the diastereomeric (2*R*,3*R*)-butanediol ketals on a 30 m × 0.26 mm methyl silicone column.

Preparation of Achiral Ketones. Racemic 3-cyclohexyl-2-butanone and 4-phenyl-3-methyl-2-butanone were prepared[31] via alkylation of the sodio derivative of ethyl α-methylacetoacetate with cyclohexyl bromide and benzyl bromide, respectively, followed by base-catalyzed hydrolysis. Racemic 3,4,4-trimethyl-2-pentanone was prepared via the DCME reaction of racemic (1,2,2-trimethylpropyl)methoxymethylborane derived from 2-(1-*tert*-butylethyl)-1,3,2-dioxaborinane.

Determination of the Enantiomeric Purity of α-Chiral Ketones. The enantiomeric purity of these α-chiral ketones was determined by capillary GC analysis on a 25 m × 0.25 mm Ni-(HFB-1R Cam)$_2$ column or on a 50 m × 0.25 mm methyl silicone column. Further evidence for the minor enantiomer is provided by equilibration of these chiral ketones with 3 N NaOMe–MeOH and the capillary GC analysis of the equilibration product mixture.[13] Diastereomeric ketals derived from (2*R*,3*R*)-butanediol and α-chiral ketone were prepared by following the reported[13] literature procedure and analyzed on a 50 m × 0.25 mm methyl silicone column or a 30 m × 0.25 mm SPB-5 column.

Synthesis of Optically Active Amines from Borinate Esters 9a–c. The conversion of optically active borinate esters **9a–c** into the corresponding α-chiral amines has been achieved by following the reported procedure.[14] These chiral amines were further converted into the amine hydrochlorides by reaction with anhydrous HCl in EE. The spectral properties of these α-chiral amine hydrochlorides are as follows.

(*S*)-1-Cyclohexylethylamine: bp 72–74 °C (20 mm); ^{1}H NMR ($CDCl_3$) δ 1.1–1.9 (m, 14 H), 2.2 (br m, 2 H, NH_2), 3.43 (m, 1 H, $CHNH_2$); $[\alpha]^{23}_D$ = −11.68° (neat, *l* 0.5); converted to the corresponding amine HCl by reacting with anhydrous HCl in EE, mp >250 °C. The optical purity was found to be 96% ee by the capillary GC analysis of the MTPA amide[14] on a 50 m × 0.25 mm methyl silicone column at 200 °C.

(*S*)-(−)-1-Phenylethylamine hydrochloride: mp 148–150 °C; ^{1}H NMR (D_2O) δ 1.6 (d, J = 8 Hz, 3 H, CH_3) 4.52 [m, 1 H, $CHCH_3(NH_2)$], 4.70 (s, 3 H), 7.43 (m, 5 H, C_5H_5); $[\alpha]^{23}_D$ = −4.6° ± 0.02° (*c* 4, MeOH). The optical purity was found to be 99% ee by capillary GC analysis of the MTPA amide on a 50 m × 0.25 mm methyl silicone column at 200 °C. Presumably, 1-phenylethylamine might have upgraded from 88% ee to 99% ee during the preparation of the amine hydrochloride.

(*S*)-(+)-1-Methyl-2-phenylethylamine hydrochloride or (*S*)-amphetamine hydrochloride: mp 150–152 °C; ^{1}H NMR (D_2O) δ 1.30 (d, J = 8 Hz, 3 H, CH_3), 2.93 (m, 2 H, $PhCH_2$), 3.63 (m, 1 H), 4.70 (m, 3 H), 7.16–7.50 (m, 5 H, C_6H_5); $[\alpha]^{23}_D$ = +8.44° ± 0.02° (*c* 4, MeOH). The optical purity was found to be ≥99% ee by capillary GC analysis of the MTPA amide on a 50 m × 0.25 mm methyl silicone column at 210 °C.

(*S*)-(+)-3,3-Dimethyl-2-butylamine hydrochloride: mp >250 °C; ^{1}H NMR (D_2O) δ 1.0 (s, 9 H, CMe_3), 1.26 (d, J = 7 Hz, CH_3), 3.2 (m, 1 H, $CHNH_2$), 4.70 (s, 3 H); $[\alpha]^{23}_D$ = +2.80 ± 0.02° (*c* 4, MeOH). The optical purity was determined to be 96% ee by capillary GC analysis of the corresponding MTPA amide on a 50 m × 0.25 mm methyl silicone column at 180 °C.

Preparation of Racemic Primary Amines. The racemic primary amines required for the capillary GC analyses were prepared via $LiAlH_4$ reduction of the corresponding ketoximes.

Acknowledgment. We are grateful for the National Science Foundation (Grant CHE-8706102) and the National Institutes of Health (Grant GM 10937-23) for the financial support of this study.

Supplementary Material Available: ^{11}B NMR, ^{1}H NMR, ^{13}C NMR, and IR spectra for the compounds reported (55 pages). Ordering information is given on any current masthead page.

Angular Hydroxymethylation of Functionalized Decalin Systems

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Functionalized β-dicarbonyl bicyclic compounds **5** and **17** were hydroxymethylated at the angular position as the (benzyloxy)methoxy derivatives with diisopropylethylamine (DIPEA) and benzyl chloromethyl ether in the presence of paraformaldehyde. The stereochemistry of *cis*-8a-[[(benzyloxy)methoxy]methyl]-3-(phenylthio)-4a,5,6,8a-tetrahydronaphthalene-1,8(4*H*,7*H*)-dione (**12**) was confirmed by X-ray analysis of the ethylene ketal **16**.

Introduction

A number of natural products have a hydroxymethyl function at the angular position of a decalin system. Azadirachtin (**1**),[1] clerodin (**2**),[2] and sicannin (**3**)[3] are some of the examples in the terpenoid area. In steroids, it is known that biological hydroxylation of the angular methyl group to give the hydroxymethyl compound is the intermediate step in biological demethylation.

Because of our interest in the chemistry of insect antifeedants,[4] we became interested in the synthesis of analogues of azadirachtin (**1**) and clerodin (**2**). Both compounds are known to possess potent insect antifeeding activities. Furthermore, we have recently developed an annelation reaction based on tandem Michael–Claisen condensation of the siloxy diene **4** with α,β-unsaturated ketones.[5] The reaction has been used to construct the

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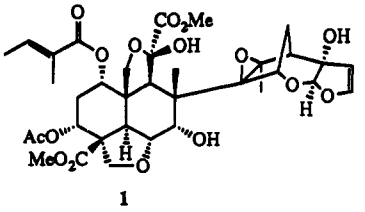

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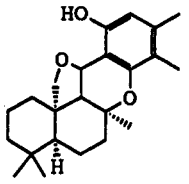

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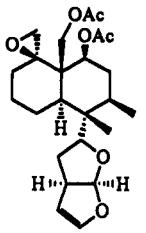

2

9-methyldecalin system and in the syntheses of some sesquiterpenes.[6] It seemed to us that hydroxymethylation of the functionalized decalin **5** may offer a facile entry into the azadirachtin (**1**) and clerodin (**2**) skeletons.

Results and Discussion

1. Hydroxymethylation with Benzyl Chloromethyl Ether. In a procedure similar to that described by Ley,[7] the Michael adduct **6** was treated with KO-*t*-Bu in THF to form the decalin **5** and the resulting anion **7** was quenched with formaldehyde in the hope of preparing **8** featuring the hydroxymethylene unit (Scheme I). However, even after repeated column chromatography, the product, if it were formed, could not be separated from the formaldehyde polymer. When the decalin **5** was treated with NaH in THF at 0 °C and the resulting anion **7** was reacted with benzyl chloromethyl ether, the O-alkylated products **9** and **10** were obtained in 35% and 43% yield, respectively (Scheme II). From the ^{1}H NMR spectra, it was quite clear that **9** and **10** were isomeric, and both were O-alkylated products. We tentatively assigned the structures of **9** and **10** as indicated in Scheme II. Replacing NaH with NaOEt again resulted in O-alkylation. The use of zinc triflate in CH_2Cl_2 or tetrabutylammonium hydroxide in benzene proved to be too mild, resulting only in recovery of unreacted decalin **5**.

When decalin **5** was treated with KO-*t*-Bu in THF or Cs_2CO_3 in acetonitrile and the resulting anion was quenched with benzyl chloromethyl ether, a C-alkylated compound was obtained in modest yields of 25–50%. Surprisingly, the product was not the expected **11** (Scheme III). Both NMR and mass spectral data indicated the presence of an extra "CH_2O" moiety. We were able to assign the structure of the product to be **12** on the basis of the following chemical transformation. Compound **12** was treated with Raney nickel in absolute ethanol at room temperature for 4 days, providing two products, **13** and **14** (Scheme IV). Compound **13**, the minor component, was the desulfurized product. Compound **14**, on the other hand, had two additional hydrogens. The spectral data were consistent with the structure assigned to **14**. Furthermore, the symmetry of the molecular structure, evident from the simplicity of the ^{1}H and ^{13}C NMR spectra, suggested that the incorporation of the $PhCH_2OCH_2OCH_2$ moiety must have taken place at the angular position. The yield of **12** from **5** could be improved somewhat by the use of diisopropylethylamine (DIPEA) in dichloroethane[8] and

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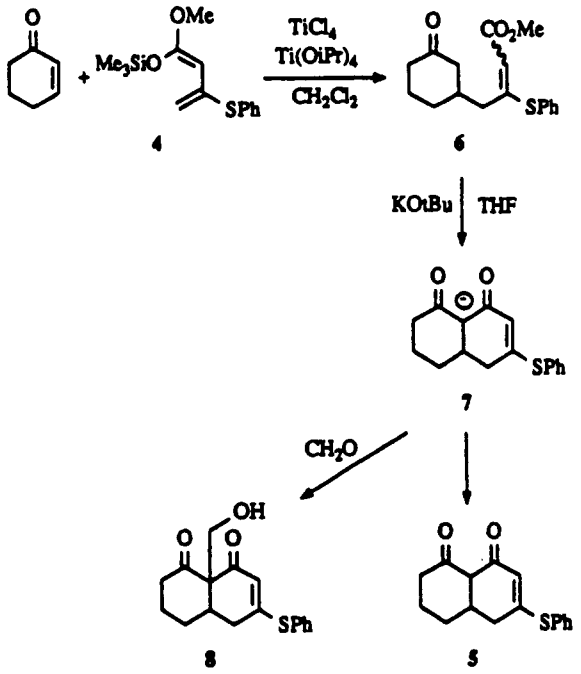
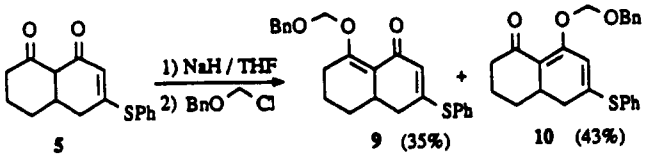
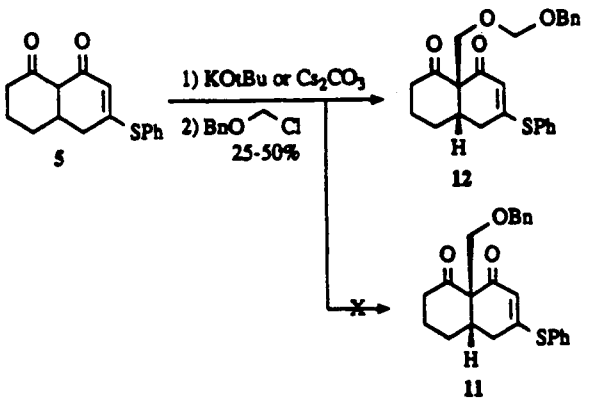
Scheme I



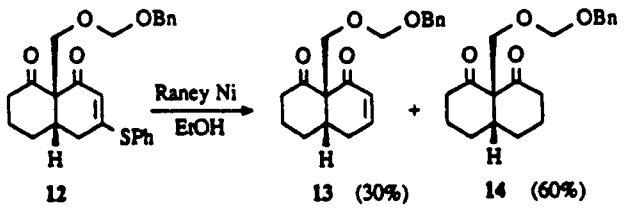
Scheme II



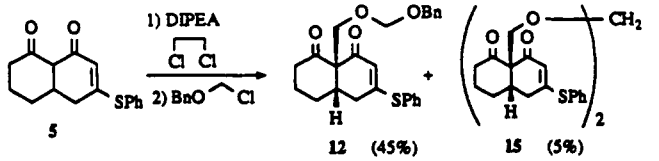
Scheme III



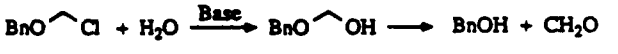
Scheme IV



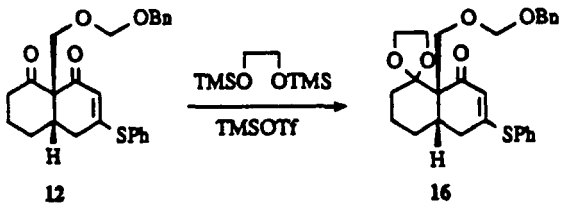
Scheme V



Scheme VI



Scheme VII



12 16

excess benzyl chloromethyl ether (5 equiv). Under such conditions, 12 could be obtained in 45% yield together with 5% of dimer 15 and 20% of recovered 5 (Scheme V).

The formation of product 12 and dimer 15 with the extra "CH_2O" can be rationalized if one accepts the presence of formaldehyde in the reaction mixture. The presence of formaldehyde could probably be due to the partial decomposition of the alkylating agent benzyl chloromethyl ether by a small quantity of water according to Scheme VI. When the alkylating agent was carefully distilled and then used in the reaction, the yield of product 12 decreased considerably. On the other hand, when paraformaldehyde (3 equiv) was added directly to the reaction mixture together with benzyl chloromethyl ether, the yield of 12 was improved substantially to 75%.

2. Stereochemistry. The angular hydroxymethylation described above was highly stereoselective in giving only one major isomer. The stereochemistry of 12 could not be assigned on the basis of spectroscopic information. Refluxing 12 with ethylene glycol in benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid on a Dean–Stark apparatus provided the ethylene ketal 16 in only 14% yield, together with 27% starting material and 20% decalin 5. Evidently, under the acidic conditions, 12 can undergo acid deacetalization followed by reverse aldol reaction. However, by using a variation of the Noyori conditions,[9] i.e., treatment of 12 with 1,2-bis(trimethylsiloxy)ethane in CH_2Cl_2 at −78 °C in the presence of trimethylsilyl triflate, followed by warming to −40 °C, ketal 16 (Scheme VII) could be obtained in 45% yield together with 35% starting material, but without formation of 5. Ketal 16 was crystalline, and X-ray structure determination confirmed the cis stereochemistry at the ring junction.

Previously, we had observed that methylation of 5 was stereoselective in giving mainly the trans isomer.[5] On the other hand, methylation of the corresponding *gem*-dimethyl-substituted decalin 17 or the hydrindan 18 gave preferentially the cis isomer.[10] The stereochemistry of angular alkylation is thus quite sensitive to structural variations. In the present hydroxymethylation, the cis aldol adduct 19 may well be kinetically favored over the corresponding trans adduct 20. Trapping of 19 by benzyl chloromethyl ether then gave 12 (Scheme VIII).

3. Other Hydroxymethylations. The trapping of the intermediate aldol 19 can also be accomplished with acetic anhydride. Thus treatment of 5 with DIPEA, paraformaldehyde, and acetic anhydride in dichloroethane gave the angular (acetoxymethoxy)methyl compound 21 in 60% yield, together with 33% of recovered 5 (Scheme IX). Interestingly in this case, 2 mol of "CH_2O" have been incorporated.

While the intermediacy of 19 was inferred from these products, 19 itself was too unstable to be isolated, presumably due to the ease of the reverse aldol reaction. We were able to demonstrate that, in the case of the keto ester 22, it was possible to isolate the intermediate aldol adduct 23. When 22 was treated under identical reaction conditions, 23 was isolated in 19% yield together with 73% of the [(benzyloxy)methoxy]methyl product 24 (Scheme X). It is remarkable that in none of these reactions was the (benzyloxy)methyl adduct ever observed.

Finally, reaction of the *gem*-dimethyl-substituted decalin 17 under similar reaction conditions gave the [(benzyloxy)methoxy]methyl compound 25 (Scheme XI). The reaction may therefore provide an entry into the azadirachtin skeleton as well. The stereochemistry of 25 was tentatively assigned to be cis on the basis of the similarity of its proton NMR spectrum with that of 12.

Conclusion

Reaction conditions have been found for angular hydroxymethylation of functionalized decalin systems. Compared to the existing methods of obtaining an angular hydroxymethyl function, such as remote functionalization of an angular methyl group,[11] or reduction of an angular ester functional group,[12] the present method may offer certain advantages. The cis stereoselectivity obtained is of some interest as well in that this gives easy access to the thermodynamically less stable isomer. Subsequent isomerization should then be able to provide entry into the more stable trans isomer.

Experimental Section

Melting points are uncorrected. The ^1H NMR spectral data are reported in parts per million relative to the $CHCl_3$ reference line. All mass spectra were recorded by using ammonia chemical ionization and are reported as *m/z* (relative intensity). Column chromatography was performed on Merck silica gel 60 (230–400 mesh). All glassware was predried in an oven at approximately 200 °C before being used.

Compound 5 was prepared according to a literature procedure.[5]

8-[(Benzyloxy)methoxy]-3-(phenylthio)-4a,5,6,7-tetrahydronaphthalen-1(4*H*)-one (9) and 1-[(Benzyloxy)methoxy]-3-(phenylthio)-4a,5,6,7-tetrahydronaphthalen-8(4*H*)-one (10). To a solution of the decalin 5 (0.093 g, 0.36 mmol) in 1 mL of THF at −5 °C under argon was added 97% sodium hydride (0.015 g, 0.36 mmol). The pale yellow mixture was stirred for 30 min, at which time benzyl chloromethyl ether (0.050 mL, 0.36 mmol) was added. After being stirred for 2 h at −5 °C, the mixture was diluted with ether and quenched with water. The aqueous layer was extracted with ether. The combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 EtOAc/hexanes) of the crude material provided 9 (0.050 g, 35%) as a lemon yellow oil and 10 (0.060 g, 43%) as a pale yellow oil.

9: ^1H NMR ($CDCl_3$) δ 7.23–7.54 (m, 10 H), 5.45 (d, *J* = 2 Hz, 1 H), 4.89 (s, 2 H), 4.65 (s, 2 H), 2.69–2.90 (m, 1 H), 2.20–2.50 (m, 4 H), 1.82–2.01 (m, 2 H), 1.49–1.75 (m, 1 H), 1.20–1.41 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 196.9, 159.1, 151.4, 137.2, 135.4, 134.6, 130.0, 129.8, 129.5, 128.4, 127.7, 119.1, 114.9, 93.5, 76.6, 70.3, 40.7, 36.6, 36.4, 30.5, 21.5; IR ($CHCl_3$) 2952, 1614, 1592, 1242 cm^{-1}; MS 393 (22, MH^+), 363 (14), 273 (100); exact mass calcd for $C_{24}H_{25}O_3S_1$ (MH^+) 393.1524, found 393.1524.

10: ^1H NMR ($CDCl_3$) δ 7.35–7.52 (m, 5 H), 7.31 (s, 5 H), 5.45 (d, *J* = 1.8 Hz, 1 H), 5.21 and 4.97 (AB, *J* = 6.9 Hz, 2 H), 4.67 (s, 2 H), 2.73–2.95 (m, 1 H), 2.25–2.51 (m, 4 H), 1.19–2.00 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 185.6, 161.8, 161.0, 137.3, 135.4, 129.9, 129.8, 128.3, 128.1, 127.7, 122.8, 116.4, 92.7, 70.4, 37.7, 36.3, 29.4, 28.1, 20.6; IR (neat) 2937, 1648, 1590, 1270, 748 cm^{-1}; MS 393 (31, MH^+), 363 (19), 273 (100); exact mass calcd for $C_{24}H_{25}O_3S_1$ (MH^+) 393.1524, found 393.1524.

***cis*-8a-[[(Benzyloxy)methoxy]methyl]-3-(phenylthio)-4a,5,6,8a-tetrahydronaphthalene-1,8(4*H*,7*H*)-dione (12).**

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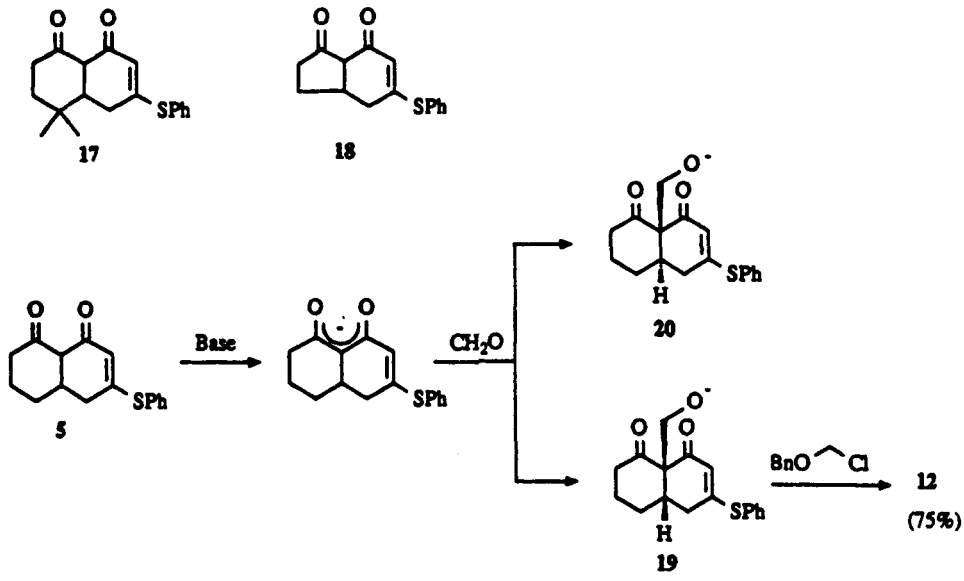
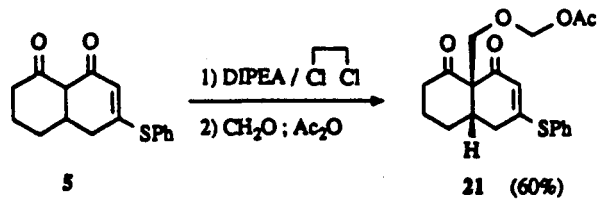
(11) Burke, S. D.; Silks, L. A., III; Strickland, S. M. S. *Tetrahedron Lett.* **1988**, *29*, 2761.
(12) Jackson, W. P.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1516.

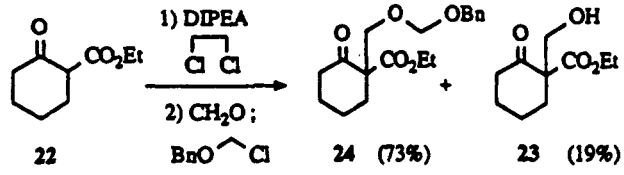
Scheme VIII



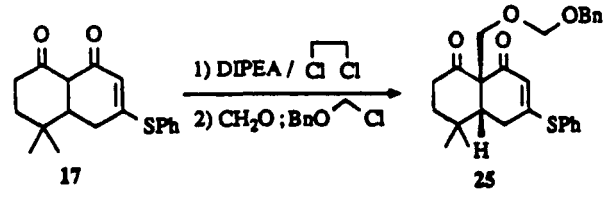
Scheme IX



Scheme X



Scheme XI



Cesium Carbonate Procedure. Cesium carbonate (0.338 g, 1.04 mmol) was weighed into a dried flask, which was then flame dried under argon. A solution of decalin **5** (0.166 g, 0.61 mmol) in 10 mL of CH_3CN was then added, followed 15 min later by benzyl chloromethyl ether (0.25 mL, 1.8 mmol). The pale yellow reaction mixture was stirred at 50 °C for 6 h. Then more benzyl chloromethyl ether (0.40 mL, 2.9 mmol) was added, and the mixture was stirred for another 20 h at 50 °C. The mixture was then diluted with ether and quenched with water. The aqueous layer was extracted with ether. The combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 EtOAc/hexanes) of the crude material provided **12** (0.122 g, 52%) as a yellow oil: ^1H NMR ($CDCl_3$) δ 7.25–7.52 (m, 10 H), 5.47 (d, J = 1.8 Hz, 1 H), 4.82 and 4.75 (AB, J = 8 Hz, 2 H), 4.67 and 4.57 (AB, J = 12 Hz, 2 H), 4.10 and 3.66 (AB, J = 10 Hz, 2 H), 2.75–3.05 (m, 2 H), 2.15–2.50 (m, 3 H), 1.57–2.09 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 205.6, 192.0, 165.5, 135.5, 130.4, 130.0, 128.4, 127.9, 127.7, 118.6, 95.4, 69.8, 66.0, 65.3, 40.1, 39.2, 33.3, 27.6, 24.6; IR (neat) 2936, 2860, 1717, 1646, 1576, 1442, 1331, 1208, 1106, 1045, 749 cm^{-1}; MS 423 (100, MH^+), 393 (74), 315 (36); exact mass calcd for $C_{25}H_{27}O_4S_1$ (MH^+) 423.1629, found 423.1630.

Alternative Procedure. To a solution of decalin **5** (0.690 g, 2.5 mmol) in 25 mL of 1,2-dichloroethane at 0 °C under argon was added diisopropylethylamine (0.45 mL, 2.5 mmol), followed 20 min later by benzyl chloromethyl ether (0.70 mL, 5.0 mmol). The reaction mixture was stirred at 75 °C for 16 h. At this time more benzyl chloromethyl ether (0.60 mL, 4.3 mmol) was added, and stirring was continued for an additional 3 h. The mixture was then diluted with ether and quenched with water. The aqueous phase was extracted with ether. The combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 EtOAc/hexanes) of the crude material provided **12** (0.425 g, 40%), in addition to the dimer **15** (0.075 g, 5%) and recovered starting material **5** (0.133 g, 20%). The spectral data for **12** are identical with those described above. The dimer **15** was a cream-colored solid with mp 194–195 °C: ^1H NMR ($CDCl_3$) δ 7.46–7.57 (m, 10 H), 5.50 (s, 2 H), 4.78 and 4.62 (AB, J = 6 Hz, 2 H), 4.05 and 3.65 (two superimposable AB, J = 10 Hz, 4 H), 3.10–3.26 (m, 2 H), 2.78–2.94 (m, 2 H), 2.13–2.50 (m, 6 H), 1.62–2.08 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 205.4, 192.1, 166.3, 135.6, 130.3, 129.9, 127.6, 118.5, 96.4, 66.1, 65.3, 40.2, 39.0, 33.4, 27.7, 24.5; IR ($CHCl_3$) 2944, 1717, 1641, 1577, 1333, 1220, 1038 cm^{-1}; MS 617 (3, MH^+), 316 (22), 315 (100), 285 (21), 273 (23); exact mass calcd for $C_{35}H_{37}O_6S_2$ (MH^+) 617.2032, found 617.2031.

Paraformaldehyde Procedure. To a solution of decalin **5** (0.785 g, 2.9 mmol) in 30 mL of 1,2-dichloroethane at 0 °C under argon was added diisopropylethylamine (0.63 mL, 3.6 mmol). After the solution was stirred for 20 min at 0 °C, the ice bath was removed and paraformaldehyde (0.783 g, 8.7 mmol) was added. After the mixture was stirred for 10 min at room temperature, benzyl chloromethyl ether (0.72 mL, 5.2 mmol) was added and the mixture was stirred at 70 °C for 14 h. The yellow mixture was then diluted with ether and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ether. The combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 EtOAc/hexanes) of the crude material afforded **12** (0.916 g, 75%). Th spectral data for the product were identical with those given above.

8a-[[(Benzyloxy)methoxy]methyl]-4a,5,6,8a-tetrahydronaphthalene-1,8(4*H*,7*H*)-dione (13) and 8a-[[(Benzyloxy)methoxy]methyl]-3,4,4a,5,6,8a-hexahydronaphthalene-1,8-(2*H*,7*H*)-dione (14). To a solution of **12** (0.380 g, 0.90 mmol) in 25 mL of absolute ethanol under argon was added a slurry of Raney nickel (2.204 g) in 5 mL of absolute ethanol. The reaction mixture was stirred at room temperature for 4 days. The Raney nickel catalyst was then filtered off through a Celite pad and washed with ethanol, and the solvent was removed. Column chromatography (1:4 EtOAc/hexanes) of the crude material provided **13** (0.085 g, 30%) and **14** (0.170 g, 60%).

13: ^1H NMR ($CDCl_3$) δ 7.25–7.40 (m, 5 H), 6.89–7.00 (m, 1 H), 6.06 (d, J = 12 Hz, 1 H), 4.80 and 4.75 (AB, J = 8 Hz, 2 H), 4.65 and 4.57 (AB, J = 12 Hz, 2 H), 4.09 and 3.73 (AB, J = 10 Hz, 2 H), 1.60–2.81 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 205.8, 196.2, 148.4, 137.9, 128.4, 128.0, 127.8, 127.6, 95.4, 69.7, 66.1, 65.9, 40.1, 39.0,

29.4, 27.8, 24.9; IR ($CHCl_3$) 2936, 1717, 1669, 1026 cm^{-1}; MS (CI, NH_3) 332 (80, M + NH_4^+), 285 (24), 256 (14), 255 (55), 208 (23), 207 (100); exact mass calcd for $C_{19}H_{23}O_4$ (MH^+) 315.1596, found 315.1596.

14: ^1H NMR ($CDCl_3$) δ 7.25–7.40 (m, 5 H), 4.78 (s, 2 H), 4.63 (s, 2 H), 4.03 (s, 2 H), 2.45 (t, J = 7 Hz, 4 H), 1.60–2.14 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 208.7, 137.9, 128.4, 127.9, 127.7, 95.3, 69.8, 68.9, 66.5, 42.4, 40.1, 26.9, 23.5; IR ($CHCl_3$) 2941, 1718, 1044 cm^{-1}; MS (CI, NH_3) 334 (100, M + NH_4^+), 258 (15), 257 (53), 210 (18), 209 (82), 192 (11); exact mass calcd for $C_{19}H_{25}O_4$ (MH^+) 317.1752, found 317.1753.

Ethylene Ketal of *cis*-8a-[[(Benzyloxy)methoxy]methyl]-3-(phenylthio)-4a,5,6,8a-tetrahydronaphthalene-1,8(4*H*,7*H*)-dione (16). To a solution of trimethylsilyl triflate (0.050 mL, 0.26 mmol) in 0.20 mL of CH_2Cl_2 at −78 °C under argon was added 1,2-bis(trimethylsiloxy)ethane (6.20 mL, 25 mmol) followed by **12** (0.119 g, 0.28 mmol) in 1.8 mL of CH_2Cl_2. Stirring was continued at −78 °C for 6 h. The solution was then warmed to −45 °C, stirred for 16 h, warmed to −20 °C, and stirred for an additional 2 h. The reaction was then quenched by addition of pyridine (0.030 mL, 0.37 mmol) at −78 °C and poured into saturated $NaHCO_3$. The mixture was extracted with ether. The combined organic extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 EtOAc/hexanes) of the crude material provided **16** (0.055 g, 38%) as a clear oil, in addition to recovered starting material **12** (0.043 g, 36%). Dissolving **16** in some ether resulted in the formation of colorless needles (mp 97–98 °C) whose structure was confirmed by X-ray analysis: ^1H NMR ($CDCl_3$) δ 7.26–7.51 (m, 10 H), 5.55, (d, J = 1.8 Hz, 1 H), 4.69 (s, 2 H), 4.54 (s, 2 H), 4.36 (AB, J = 10 Hz, 1 H), 3.69–3.88 (m, 5 H), 3.15–3.33 (m, 1 H), 2.81–2.97 (m, 1 H), 1.58–2.30 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 195.5, 165.9, 137.9, 135.4, 130.0, 129.7, 128.3, 127.8, 127.5, 121.9, 110.7, 95.1, 69.5, 67.1, 65.1, 64.6, 55.7, 34.0, 33.0, 32.8, 25.4, 18.6; IR ($CHCl_3$) 2946, 1649, 1638, 1593, 1292, 1212, 1104, 1079, 1039, 689 cm^{-1}; MS 467 (100, MH^+), 327 (76), 133 (38); exact mass calcd for $C_{27}H_{31}O_5S_1$ (MH^+) 467.1891, found 467.1892.

8a-[(Acetoxymethoxy)methyl]-3-(phenylthio)-4a,5,6,8a-tetrahydronaphthalene-1,8(4*H*,7*H*)-dione (21). To a solution of decalin **5** (0.093 g, 0.34 mmol) in 3.5 mL of 1,2-dichloroethane at 0 °C under argon was added diisoproylethylamine (0.070 mL, 0.40 mmol). After the solution was stirred at 0 °C for 20 min, the ice bath was removed and paraformaldehyde (0.095 g, 1.1 mmol) was added, followed 10 min later by acetic anhydride (0.080 mL, 0.84 mmol). The mixture was stirred at 70 °C for 4 h, at which time more paraformaldehyde (0.051 g, 0.56 mmol) was added. After being stirred overnight, the mixture was diluted with ether and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ether, and the combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 and then 1:2 EtOAc/hexanes) of the crude material afforded **21** (0.071 g, 60%) as a yellow oil, along with recovered decalin **5** (0.031 g, 33%): ^1H NMR ($CDCl_3$) δ 7.42–7.58 (m, 5 H), 5.45 (d, J = 2 Hz, 1 H), 5.30 and 5.22 (AB, J = 6 Hz, 2 H), 4.14 and 3.74 (AB, J = 10 Hz, 2 H), 2.10 (s, 3 H), 1.51–3.09 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 205.4, 191.6, 170.5, 166.0, 135.5, 130.5, 130.0, 127.3, 118.4, 89.4, 68.0, 65.2, 40.0, 38.9, 33.2, 27.6, 24.5, 21.0; IR ($CHCl_3$) 3013, 1741, 1717, 1646, 1577, 1230, 1013 cm^{-1}; MS 375 (9, MH^+), 345 (16), 315 (100), 176 (17); exact mass calcd for $C_{20}H_{23}O_5S_1$ (MH^+) 375.1267, found 375.1266.

Ethyl 1-(Hydroxymethyl)-2-oxocyclohexanecarboxylate (23) and Ethyl 1-[[(Benzyloxy)methoxy]methyl]-2-oxocyclohexanecarboxylate (24). To a solution of ethyl 2-oxocyclohexanecarboxylate (**22**) (0.68 mL, 4.3 mmol) in 40 mL of 1,2-dichloroethane at 0 °C under argon was added diisopropylethylamine (0.85 mL, 4.9 mmol). After the solution was stirred at 0 °C for 20 min, the ice bath was removed and paraformaldehyde (0.730 g, 8.1 mmol) was added, followed 10 min later by benzyl chloromethyl ether (1.18 mL, 8.5 mmol). The mixture was stirred at 70 °C for 6 h, diluted with ether, and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ether, and the combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:5 EtOAc/hexanes) of the crude material afforded **23** (0.238 g, 19%) and **24** (0.998 g, 73%), both as clear oils.

23: ^1H NMR ($CDCl_3$) δ 4.24 (q, J = 7.1 Hz, 2 H), 3.82 and 3.69 (AB, J = 11.4 Hz, 2 H), 2.23–2.93 (m, 4 H), 1.95–2.12 (m, 1 H), 1.40–1.84 (m, 4 H), 1.28 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 211.3, 171.5, 66.5, 62.5, 61.7, 40.9, 32.7, 26.8, 21.8, 14.0; IR (neat) 3553, 2986, 2938, 1739, 1694, 1458, 1311, 1199, 1064 cm^{-1}; MS 218 (100, M + NH_4^+), 201 (41, MH^+); exact mass calcd for $C_{10}H_{17}O_4$ (MH^+) 201.1128, found 201.1127.

24: ^1H NMR ($CDCl_3$) δ 7.29–7.37 (m, 5 H), 4.73 (s, 2 H), 4.57 (s, 2 H), 4.20 (dq, J = 7.2 and 2 Hz, 2 H), 3.96 and 3.75 (AB, J = 9.6 Hz, 2 H), 2.42–2.65 (m, 3 H), 1.96–2.12 (m, 1 H), 1.58–1.87 (m, 5 H), 1.25 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 205.9, 169.9, 137.5, 128.0, 127.5, 127.3, 94.5, 69.7, 68.9, 61.2, 61.1, 40.7, 33.3, 26.9, 21.7, 13.8; IR (neat) 2898, 1717, 1702, 1454, 1236, 1024 cm^{-1}; MS 338 (100, M + NH_4^+), 321 (8, MH^+), 308 (19), 213 (44); exact mass calcd for $C_{18}H_{25}O_5$ (MH^+) 321.1703, found 321.1702.

8a-[[(Benzyloxy)methoxy]methyl]-5,5-dimethyl-3-(phenylthio)-4a,5,6,8a-tetrahydronaphthalene-1,8(4*H*,7*H*)-dione (25). To a solution of decalin **17** (0.077 g, 0.26 mmol) in 2.7 mL of 1,2-dichloroethane at 0 °C under argon was added diisopropylethylamine (0.060 mL, 0.34 mmol). After the solution was stirred for 20 min at 0 °C, the ice bath was removed and paraformaldehyde (0.074 g, 0.82 mmol) was added, followed 10 min later by benzyl chloromethyl ether (0.060 mL, 0.43 mmol). The mixture was stirred at 70 °C for 3 h. At this time more paraformaldehyde (0.054 g, 0.61 mmol) was added, and stirring was continued overnight. The mixture was then diluted with ether and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with ether, and the combined ether extracts were dried ($MgSO_4$) and concentrated. Column chromatography (1:4 EtOAc/hexanes) of the crude material afforded **25** (0.033 g, 28%) as a yellow oil along with recovered decalin **17** (0.054 g, 70%): ^1H NMR ($CDCl_3$) δ 7.32–7.48 (m, 5 H), 5.44 (d, J = 2 Hz, 1 H), 4.82 and 4.76 (AB, J = 6.6 Hz, 2 H), 4.67 and 4.58 (AB, J = 10 Hz, 2 H), 4.12 and 3.54 (AB, J = 9.8 Hz, 2 H), 2.25–2.89 (m, 5 H), 1.60–1.71 (m, 2 H), 1.07 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 205.6, 192.5, 166.2, 137.8, 135.5, 130.5, 130.0, 128.0, 127.9, 119.5, 95.5, 69.9, 67.1, 63.7, 46.8, 40.1, 36.9, 34.3, 30.5, 28.6, 23.0; IR ($CHCl_3$) 2963, 1717, 1646, 1587, 1230, 1042 cm^{-1}; MS 451 (100, MH^+), 421 (65), 359 (24), 343 (96), 200 (47), 148 (37), 108 (52); exact mass calcd for $C_{27}H_{31}O_4S_1$ (MH^+) 451.1941, found 451.1943.

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra for compounds **9**, **10**, **12–16**, **21**, and **23–25** and tables of all atomic positional and thermal parameters and all atomic distances and angles for the crystallographic structure of ethylene ketal **16** (29 pages). Ordering information is given on any current masthead page.