Experimental Section

Radiochromatography scans were obtained using a Packard Model 7201 radiochromatogram scanner. Radioassays were obtained using a Packard Tri-Carb Model 574 liquid scintillation counter. Corrections for quenching were made by the channels ratio method. NaB^3H_4 and tritium gas were purchased from Amersham Corporation and Oak Ridge National Laboratories, respectively. NMR spectra were recorded on a Varian HA-100 spectrometer in $CDCl_3$ or Me_2SO-d_6 as noted and chemical shifts are reported in ppm (δ) from Me_4Si. Mass spectra were recorded on a Varian-MAT CH-4 spectrometer. NMR and mass spectra refer to nonradioactive reference standards.

6-Chloro-9α-bromo-11β,17α,21-trihydroxypregna-4,6-diene-3,20-dione BMD (BMD=bis(methylenedioxy) protecting group) (2). 2 was prepared in 97% yield from the corresponding $\Delta^{9(11)}$ compound by the method of Fried and Sabo.[1] Addition of water to the reaction mixture gave a white precipitate which was filtered and dried. This material was homogeneous by TLC (SiO_2; hexane–acetone, 2:1): NMR (Me_2SO) δ 1.10 (3 H, s, 18-CH_3), 1.60 (3 H, s, 19-CH_3), 4.37 (1 H, m, 11 α-H), 6.23 (1 H, d, J = 2 Hz, 7-H).

Tri-*n*-butyltin Tritide (6). Method a. Tritiated water (20 Ci; 30 Ci/matm; 0.3 mmol) was prepared on a vacuum line by the reaction of $^3H_2$ (20 Ci; 30 Ci/matm) with Pt_2O (100 mg). The ^3H_2O was distilled (on the vacuum line) from the reaction vessel into a 10-mL side-arm flask containing a rubber septum in the side arm. Freshly prepared Bu_3SnLi[8] (0.2 mmol) in THF was injected into the flask containing ^3H_2O. A precipitate of LiO^3H formed instantaneously, indicating that the reaction was complete.

Method b. A solution of *n*-Bu_3SnCl (85 mg; 0.26 mmol) in EtOH (1 mL) was added to NaB^3H_4 (9.8 mg; 0.26 mmol; 75.6 mCi; 293 mCi/mmol). The suspension was stirred at room temperature for 30 min until the NaB^3H_4 had completely reacted (disappearance of purple color) and a white precipitate (NaCl) had formed.

6-Chloro-11β,17α,21-trihydroxypregna-4,6-diene-3,20-dione BMD (4). To a solution of **2** (300 mg; 0.58 mmol) in THF (5 mL) was added *n*-Bu_3SnH (203 mg; 0.7 mmol). The reaction was stirred at room temperature for 18 h and then partitioned between brine and methyl ethyl ketone. The organic phase was dried over Na_2SO_4 and evaporated to dryness at reduced pressure. The residue was crystallized from methyl ethyl ketone to yield the product (160 mg, 63%) as off-white crystals. This material was chromatographically homogeneous (SiO_2; hexane–acetone, 4:1, run three times): NMR (Me_2SO-d_6) δ 1.08 (3 H, s, 18-CH_3), 1.30 (3 H, s, 19-CH_3), 4.15 (1 H, m, 11α-H), 6.43 (d, 1 H, J = 2 Hz, 7-H); mass spectrum *m/e* 420–422 (M^+).

6-Chloro-11β,17α,21-trihydroxy[9α-^{3}H]pregna-4,6-diene-3,20-dione BMD (4a). A solution of **2** (78 mg; 0.15 mmol) in THF (2 mL) was injected into a flask containing **6** [prepared by method a]. The reaction was stirred at room temperature for 18 h and labile tritiated materials were removed by distilling to dryness from EtOH two times on the vacuum line. The residue was partitioned between methyl ethyl ketone and water. The organic phase (1180 mCi) was dried over Na_2SO_4 and taken to dryness at reduced pressure. Chromatographic purification (2000 μm SiO_2 plates; hexane–acetone, 4:1, run three times) afforded pure **4a** (142 mCi). The radiochromatogram of this material was superimposable with standard **4**.

9α-Bromo-11β-fluoro-16α-methyl-17α,21-dihydroxypregn-4-ene-3,20-dione 21-Acetate (3). This substance was prepared from the corresponding $\Delta^{9(11)}$ compound by the method of Bowers[4] in 67% yield: mp 177 °C dec; NMR ($CDCl_3$) δ 0.9 (3 H, d, J = 2 Hz, 18-CH_3), 0.93 (3 H, d, J = 7 Hz, 16-CH_3), 1.6 (3 H, d, J = 4 Hz, 19-CH_3), 5.25 (d, J = 47 Hz, 11α-H); mass spectrum *m/e* 498–500 (M^+), 397–399, 317, 297.

11β-Fluoro-16α-methyl-17α,21-dihydroxypregn-4-ene-3,20-dione 21-Acetate (5). To a solution of **3** (600 mg; 1.05 mmol) in THF (25 mL) containing a trace of azobis(isobutyrylnitrile) was added *n*-Bu_3SnH (305 mg; 1.05 mmol). The reaction was heated at reflux for 30 min [TLC (toluene–EtOAc, 4:1) showed no starting material remaining] and partitioned between EtOAc and water. The organic phase was dried over Na_2SO_4 and evaporated to dryness at reduced pressure. Crystallization from CH_2Cl_2/CH_3OH afforded 325 mg (64%) of pure **5**: mp 279–279.5 °C; NMR ($CDCl_3$) δ 0.9 (3 H, d, J = 7 Hz, 16-CH_3), 0.95 (3 H, d, J = 2 Hz, 18-CH_3), 1.35 (3 H, d, J = 4 Hz, 19-CH_3), 3.07 (1 H, d, J = 47 Hz, 11α-H); mass spectrum *m/e* 420 (M^+), 319, 299.

9α-^{3}H-11β-Fluoro-16α-methyl-17α,21-dihydroxypregn-4-ene-3,20-dione 21-Acetate (5a). To **6** [prepared by method *b*] was added a solution of **3** (150 mg; 0.3 mmol) in EtOH (1 mL). The reaction was stirred at reflux for 30 min (radiochromatogram showed no further increase in size of product peak) and partitioned between EtOAc and water. The organic phase was taken to dryness at reduced pressure. Chromatographic purification (toluene–EtOAc, 4:1) of the residue afforded pure **5a** (11.3 mCi) in 60% yield: UV (MeOH) 242 nm (ϵ 16 700); specific activity 71.4 mCi/mmol (theory 73.3 mCi/mmol).

Registry No.—**1**, 688-73-3; **2**, 68238-03-9; **3**, 68225-92-3; **4**, 68213-12-7; **4a**, 68213-13-8; **5**, 68213-14-9; **5a**, 68213-15-0; **6**, 68213-16-1; **7**, 4226-01-1; **8**, 1461-22-9; 6-chloro-17α,21-dihydroxypregna-4,6,9(11)-triene-3,20-dione BMD, 68213-17-2; 16α-methyl-17α,21-dihydroxypregna-4,9(11)-diene-3,20-dione 21-acetate, 34542-56-0; NaB^3H_4, 35576-64-8.

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Reduction of Substituted Decalones. Stereochemical Reversal in the Lithium–Ammonia Reduction of Ketones

Paul A. Grieco,*[1a] Steven Burke,[1b] William Metz, and M. Nishizawa

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

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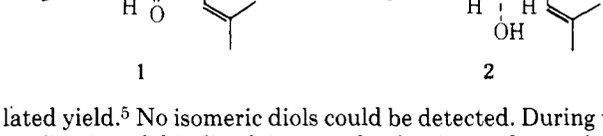
Several reports have appeared in the literature over the years describing "anomalous" dissolving metal (lithium–ammonia) reductions of cyclic ketones.[2] Past observations coupled with the recent report by Huffman and Copley describing the reduction (lithium–ammonia) of 24-nor-5β-cholan-12-one and 23,24-dinor-5β-cholan-12-one in the presence of a proton source (methanol)[3,4] prompt us to record our observations concerning the reduction of substituted decalones.

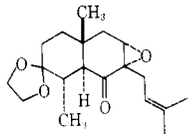
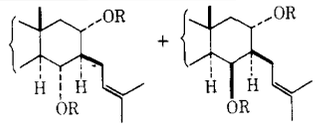
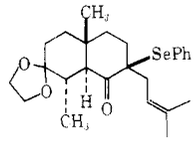
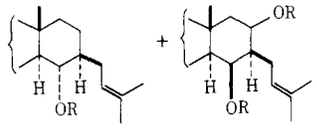
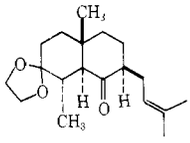
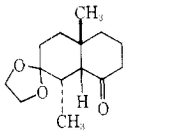
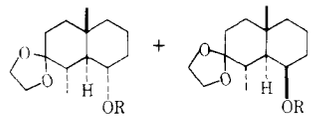
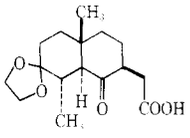
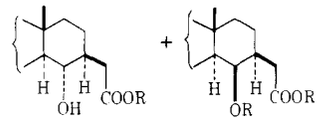
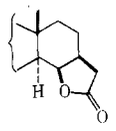
In conjunction with our efforts directed toward the total synthesis of cytotoxic sesquiterpene lactones, we had observed the smooth reduction (lithium–ammonium chloride–ammonia) of epoxy ketone **1** to the equatorial diol **2** in ca. 80% isolated yield.[5] No isomeric diols could be detected. During the application of this dissolving metal reduction to the synthesis of temisin,[6] we observed that reduction (lithium–ammonia) of epoxy ketone **3** under rigorously anhydrous conditions followed by quenching with solid ammonium chloride gave (78%) a mixture of the C-6 (steroid numbering) equatorial diol **4** and the C-6 axial diol **5** in a ratio of 1.8:1 (see Table I). Furthermore, if the strictly anhydrous conditions were not adhered to, the major product of the reaction was the C-6 axial diol **5**. For example, dissolving metal reduction of **3** in the presence of ammonium chloride gave as the major product



1 2

0022-3263/79/1944-0152$01.00/0

Table I. Reduction of Decalones[a,b]

ketone	products	method A % yield (ratio equatorial alcohol/axial alcohol)	method B % yield (ratio equatorial alcohol/axial alcohol)
 3	 4, R = H; 6, R = Ac — 5, R = H; 7, R = Ac	78 (1.8:1)	80 (1:25)
 8	 9, R = H; 11, R = Ac — 10, R = H; 12, R = Ac	97 (2.7:1)	97 (1:5.5)
 13	9 + 10	95 (8.5:1)	84 (0:84)
 14	 15, R = H; 17, R = Ac — 16, R = H; 18, R = Ac	99 (1.2:1)	99 (1:5.6)
 19	 20, R = H; 23, R = CH_3 — 21, R = H; 24, R = CH_3 —  22	81 (81:0)	69 (0:69)[c]

[a] Pinacol-type products which may arise from relatively long-lived radical anions were not observed. [b] Yields reported are based on isolated, chromatographically pure substances or crystalline material. [c] The ratio of axial alcohol **21** to the β-oriented γ-lactone **22** was 26:43.

(77% isolated) the "thermodynamically unstable" C-6 axial alcohol **5**, mp 144–145 °C, and ca. 3% of the "normal" product **4**, mp 97–98 °C. Rigorous confirmation of the structures assigned to diols **4** and **5** was obtained by examination of the 250 MHz NMR spectra of the corresponding diacetates **6** and **7**.

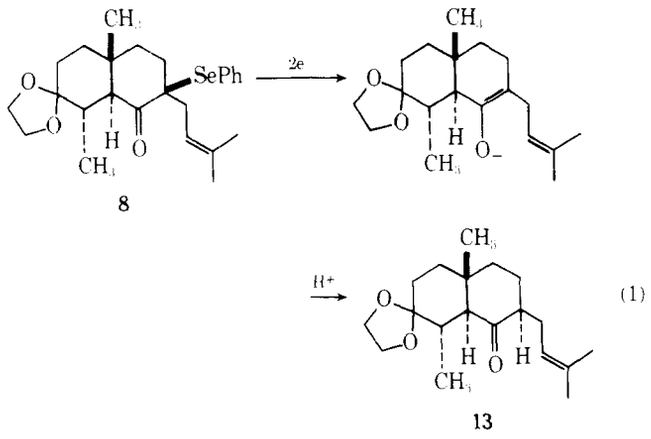
In view of the above results, we explored the reduction of a series of substituted 4-methyl-6-decalones (Table I) in order to ascertain the factors responsible for the stereochemical reversal observed during the reduction of **3** in the presence of ammonium chloride. The reductions were carried out as follows: addition of lithium to a solution of substrate in tetrahydrofuran–ammonia until the blue color persisted, followed by quenching with ammonium chloride (method A), and addition of lithium to a suspension of ammonium chloride in tetrahydrofuran–ammonia containing the dissolved substrate (method B).

In the case of keto acid **19**, reduction (method A) gave exclusively hydroxy (equatorial) acid **20** whereas application of method B revealed products derived exclusively from formation of an axial hydroxyl group. These results were similar to those obtained with the substituted decalone system **13**, in which reduction in the presence of ammonium chloride gave only formation of the axial alcohol. Reduction of **13** employing method A gave predominantly equatorial alcohol. Somewhat puzzling was the result obtained upon reduction (method A) of the simple decalone system **14**, in which the ratio of equatorial to axial alcohol was ca. 1:1.

As shown in Table I, reduction of β-keto selenide **8** with lithium in liquid ammonia (method A) provided, in near quantitative yield, a mixture of alcohols **9** and **10** in a ratio of 2.7:1. In contrast, reduction of **8** in the presence of a proton source (method B) gave **9** and **10** in a ratio of 1:5.5 in 97% yield. Reduction of **13** in the absence and in the presence of ammonium chloride gave more striking results (see Table I). For example, reduction of **13** with ammonium chloride present gave exclusively alcohol **10** in 84% yield, whereas use of strictly anhydrous conditions gave rise to a mixture of **9** and **10** in a ratio of 8.5:1. Qualitatively, the results obtained from the reduction of **8** and **13** utilizing methods A and B are the same.

It is somewhat surprising that the results from reduction of **8** and **13** are qualitatively the same since formation of ketone **13** in situ from **8** (eq 1) required initial reductive cleavage of the carbon–selenium bond and the presence of a proton source to protonate the regiospecifically generated enolate. In view of the necessity for a proton source (ammonium chloride), reduction of **13**,[9] generated from **8**, might be expected to give rise predominantly to the axial alcohol **10** employing either method A or B. This type of situation, where the enolate is protonated prior to reduction of the keto function, arises also during the reduction of epoxy ketone **3**.

The primary factor responsible for the observed stereochemical reversals in the reduction of ketones listed in the table appears to be steric in nature. We attribute this unusual behavior to the presence of the equatorial methyl group located at C-4 (steroid numbering); however, the exact nature



8 13 (1)

of this stereochemical interaction is not clear. In view of previously published work,[2,3] what appears to be an anomaly is the reduction of decalones **3** and **8**. For example, in the case of epoxy ketone **3**, one might have predicted, upon reduction employing either method A or B, the same ratio of equatorial to axial alcohol.

Experimental Section

Melting points were determined on a Fisher-Johns hot stage melting point apparatus. All melting points and boiling points are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 247 grating infrared spectrometer, and nuclear magnetic resonance (NMR) spectra were recorded at either 60 MHz (Varian A-60A or T-60 spectrometer) or 250 MHz as indicated. Chemical shifts are reported in parts per million (δ) relative to Me_4Si (δ_{Me_4Si} 0.0 ppm) as an internal standard. Low-resolution mass spectra were recorded on an LKB-9000 spectrometer. High-resolution spectra were recorded on a Varian MAT CH-5DF instrument. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

"Dry" solvents were dried immediately before use. Tetrahydrofuran was distilled from lithium aluminum hydride. Ammonia was distilled from sodium.

Reduction (Lithium–Ammonia) of *trans*-2,2-Ethylenedioxy-1α,10β-dimethyl-6α,7α-oxido-7β-(3-methyl-2-butenyl)-8-decalone (3). To a solution of 130 mg (0.406 mmol) of epoxy ketone **3**[6] in 8.6 mL of dry tetrahydrofuran and 13 mL of ammonia (distilled from sodium) at −33 °C was added 28.5 mg (4.06 mmol) of lithium wire, cut into small pieces. After the solution had been deep blue for 10 min, 246 mg (4.6 mmol) of ammonium chloride was added and the mixture was stirred at reflux for 20 min. The process was repeated, adding 28.5 mg of lithium followed by quenching with 246 mg of ammonium chloride after the blue color persisted for 10 min. The ammonia was allowed to evaporate, and the tetrahydrofuran was removed under reduced pressure. The residue was taken up in water and ethyl acetate. The aqueous layer was extracted repeatedly with ethyl acetate. The combined organic washes were dried over sodium sulfate and concentrated in vacuo, leaving 151 mg of crude product. Chromatography on silica gel (elution with ether–benzene, 1:2) gave 37 mg (28%) of the axial, equatorial diol **5**: mp 144–145 °C; R_f 0.48 (ether–benzene, 1:1); IR ($CHCl_3$) 3625, 3510, 3002, 2980, 2915, 2890, 2854, 1453, 1440, 1384, 1377, 1350, 1320, 1276, 1220, 1171, 1105, 1058, 1027, 1002, 950, 935, 922, 901 cm^{-1}. Anal. Calcd for $C_{19}H_{32}O_4$: C, 70.33; H, 9.94. Found: C, 70.08; H, 9.90.

For NMR analysis, diol **5** was converted to its corresponding diacetate **7** (see general procedure below): NMR (250 MHz) δ (CCl_4) 0.83 (d, 3 H, J = 7 Hz), 1.18 (s, 3 H), 1.53 (s, 3 H), 1.68 (s, 3 H), 1.95 (s, 3 H), 2.02 (s, 3 H), 3.86 (m, 4 H), 4.94 (td, 1 H, J = 12, 12, and 5 Hz), 5.12 (br t, 1 H), 5.35 (br s, 1 H).

Continued elution gave 65 mg (50%) of the diequatorial diol **4**: mp 97–98 °C; R_f 0.29 (ether–benzene, 1:1); IR ($CHCl_3$) 3615, 3520, 3015, 2935, 2895, 2860, 1485, 1459, 1448, 1392, 1382, 1358, 1282, 1230, 1188, 1110, 1060, 1009, 966, 958, 937, 910 cm^{-1}. Anal. Calcd for $C_{19}H_{32}O_4$: C, 70.33; H, 9.94. Found: C, 70.19; H, 9.89.

For NMR analysis, diol **4** was converted to the corresponding diacetate **6**: NMR (250 MHz) δ (CCl_4) 0.74 (d, 3 H, J = 7 Hz), 1.01 (s, 3 H), 1.48 (s, 3 H), 1.71 (s, 3 H), 1.94 (s, 6 H), 4.70 (td, 1 H, $J \approx$ 11, 11, and 4 Hz), 4.94 (t, 1 H, J = 11 and 11 Hz), 5.08 (br t, 1 H).

Reduction (Ammonium Chloride–Lithium–Ammonia) of 3. To a solution of 146 mg (0.455 mmol) of epoxy ketone **3**[6] in 10.5 mL of tetrahydrofuran and 14 mL of ammonia (distilled from sodium) at −33 °C containing 123 mg (2.30 mmol) of ammonium chloride was added 32 mg (4.55 mmol) of lithium wire, cut into small pieces. After the deep blue color persisted for 10 min, 147 mg (2.75 mmol) of ammonium chloride was added followed by an additional 32 mg (4.55 mmol) of lithium. The reaction was quenched by the addition of 147 mg (2.75 mmol) of ammonium chloride. The ammonia was allowed to evaporate, and the tetrahydrofuran was removed in vacuo. The residue was taken up in ethyl acetate and water, and the aqueous layer was extracted repeatedly with ethyl acetate. The combined ethyl acetate layers were dried over sodium sulfate and concentrated, leaving 143 mg of crude product. Chromatography on silica gel (elution with ether–benzene, 1:2) gave 112 mg (76%) of the axial, equatorial diol **5** (identical with that described above) and 4 mg (3%) of the equatorial, equatorial diol **4** (identical with that described above).

Reduction of *trans*-2,2-Ethylenedioxy-1α,10β-dimethyl-8-decalone (14). Method A (Lithium–Ammonia). In a typical reaction, lithium wire (59 mg, 8.4 mmol), cut in small pieces, was added to a solution (−33 °C) of 200 mg (0.84 mmol) of ketone **14**[7] in 19 mL of anhydrous tetrahydrofuran and 25 mL of dry ammonia. After refluxing for ca. 15 min, the reaction was quenched with 491 mg (9.19 mmol) of ammonium chloride and the ammonia was evaporated. The tetrahydrofuran was removed in vacuo, and the residue was taken up in water and extracted several times with ether. The combined ether extracts were dried over sodium sulfate and condensed. Chromatography of the crude product on silica gel (elution with ether–hexane, 1:3) gave in order of elution 89 mg (44%) of the axial alcohol **16** (R_f 0.44, 1:1 ether–hexane) which crystallized on standing [mp 99–100 °C; IR ($CHCl_3$) 3640, 3508, 3001, 2980, 2940, 2895, 2858, 1455, 1442, 1385, 1378, 1362, 1351, 1318, 1304, 1279, 1244, 1174, 1118, 1108, 1080, 1059, 1035, 1008, 995, 976, 953, 937, 909, 895 cm^{-1}; NMR δ ($CDCl_3$) 0.92 (d, 3 H, J = 7 Hz), 1.14 (s, 3 H), 3.9–4.2 (m, 5 H). Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.81; H, 9.97.] and 112 mg (55%) of the equatorial alcohol **15** as an oil (R_f 0.32, 1:1 ether–hexane) [IR ($CHCl_3$) 3680, 3620, 3490, 3005, 2985, 2955, 2944, 2890, 2853, 1464, 1380, 1362, 1358, 1342, 1310, 1281, 1242, 1218, 1185, 1149, 1138, 1107, 1097, 1075, 1058, 1011, 982, 975, 957, 940, 918, 901, 875, 862 cm^{-1}; NMR δ ($CDCl_3$) 0.93 (s, 3 H), 1.23 (d, 3 H, J = 7 Hz), 3.5–4.1 (m, 5 H)].

Axial alcohol **16** (89 mg, 0.37 mmol) was treated with 1 mL of acetic anhydride and 1 mL of triethylamine in the presence of 5 mg of 4-(dimethylamino)pyridine[8] at 25 °C for 2 h. The solution was concentrated, and the residue was taken up in ether and washed with water. The aqueous wash was extracted with ether, and the combined ether layers were dried over sodium sulfate and concentrated. Chromatography of the residue (elution with ether–hexane, 1:3) gave 84 mg (80%) of acetate **18**: R_f 0.68 (ether–hexane, 1:1); IR ($CHCl_3$) 2945, 2879, 2852, 1716, 1451, 1438, 1385, 1345, 1271, 1170, 1107, 1090, 1078, 1031, 969, 950, 924, 905, 892 cm^{-1}; NMR (250 MHz) δ ($CDCl_3$) 0.78 (d, 3 H, J = 8 Hz), 1.10 (s, 3 H), 2.03 (s, 3 H), 3.91 (m, 4 H), 5.09 (br s, 1 H). Anal. Calcd for $C_{16}H_{26}O_4$: M^+ (282.1831). Found: M^+ (282.1822).

Equatorial alcohol **15** (112 mg, 0.47 mmol) was treated with 1 mL of acetic anhydride in 1 mL of triethylamine at 25 °C for 2 h in the presence of 5 mg of 4-(dimethylamino)pyridine. Workup as above followed by chromatography of the residue (elution with ether–hexane, 1:3) gave 112 mg (85%) of equatorial acetate **17**: R_f 0.66 (ether–hexane, 1:1); IR ($CHCl_3$) 2990, 2954, 2892, 1722, 1464, 1455, 1381, 1366, 1354, 1322, 1303, 1276, 1258, 1210, 1187, 1160, 1145, 1122, 1098, 1072, 1056, 1027, 975, 955, 920, 904 cm^{-1}; NMR (250 MHz) δ ($CDCl_3$) 0.86 (d, 3 H, J = 8 Hz), 0.93 (s, 3 H), 1.98 (s, 3 H), 3.94 (m, 4 H), 4.82 (td, 1 H, J = 12, 12, and 5 Hz). Anal. Calcd For $C_{16}H_{26}O_4$: M^+ (282.1831). Found: M^+ (282.1814).

Reduction of *trans*-2,2-Ethylenedioxy-1α,10β-dimethyl-8-decalone (14). Method B (Ammonium Chloride–Ammonia–Lithium). To a solution of 200 mg (0.84 mmol) of decalone **14**[7] in 19 mL of dry tetrahydrofuran and 25 mL of anhydrous ammonia at −33 °C was added 224 mg (4.19 mmol) of ammonium chloride followed by 59 mg (8.4 mmol) of lithium wire, cut into small pieces. After the deep blue color persisted for 10 min, the reaction was quenched by the addition of 267 mg (5.00 mmol) of ammonium chloride. The ammonia was evaporated, and the tetrahydrofuran was removed in vacuo. The residue was taken up in water and the aqueous layer extracted repeatedly with ether. The combined ether layers were dried over sodium sulfate and condensed. Chromatography of the residue on silica gel (elution with ether–hexane, 1:3) gave 169 mg (84%) of the axial alcohol **16** (identical in all respects with that described above) and 31 mg (15%) of the equatorial alcohol **15** (identical in all respects with that described above).

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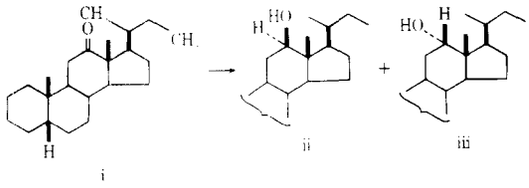
Registry No.—**3,** 68069-87-7; **4,** 68069-88-5; **5,** 68069-89-6; **6,** 68069-90-9; **7,** 68069-91-0; **8,** 68069-92-1; **9,** 68036-37-3; **10,** 68069-93-2; **11,** 68036-38-4; **12,** 68069-94-3; **13,** 68036-39-5; **14,** 61302-40-7; **15,** 68069-95-4; **16,** 68069-96-5; **17,** 68036-40-8; **18,** 68069-97-6; **19,** 68069-98-7; **20,** 68036-41-9; **21,** 68069-99-8; **22,** 68070-00-8; **23,** 68070-01-9; **24,** 68070-02-0.

Supplementary Material Available: Experimental details for the reduction of decalones **8, 13,** and **19** by method A and method B (3 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Fellow of the Alfred P. Sloan Foundation; (b) Andrew W. Mellon Predoctoral Fellow, 1975–1978.
(2) For a summary, see H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Menlo Park, Calif., 1972, pp 152–158; also see J. W. Huffman, D. M. Alabran, T. W. Bethea, and A. C. Ruggles, *J. Org. Chem.* **29,** 2963 (1964).
(3) J. W. Huffman and D. J. Copley, *J. Org. Chem.*, **42,** 3811 (1977), and references cited therein.
(4) When the reduction (lithium–ammonia) of 24-nor-5β-cholan-12-one (i) was carried out in the presence of methanol, there was produced (79% yield) a 29:71 ratio of the 12β-ol (ii) and the 12α-ol (iii), respectively.[3] However,



i

if methanol was added to quench the metal–ammonia reduction of i, the ratio of ii/iii changed to 81:19. Similarly, 23,24-dinor-5β-cholan-12-one (iv) upon reduction in the presence of methanol gave predominantly the C-12 axial alcohol.[3] The ratio of 12β-ol to 12α-ol was 27:73. The reduction of iv in the absence of methanol was not performed.
(5) P. A. Grieco, M. Nishizawa, T. Oguri, S. D. Burke, and N. Marinovic, *J. Am. Chem. Soc.*, **99,** 5773 (1977).
(6) For the structure and synthesis of temisin, see M. Nishizawa, P. A. Grieco, S. D. Burke, and W. Metz, *J. Chem. Soc., Chem. Commun.*, 76 (1978).
(7) P. A. Grieco and M. Nishizawa, *J. Chem. Soc., Chem. Commun.*, 582 (1976).
(8) W. Steglich and G. Höfle, *Angew. Chem., Int. Ed. Engl.*, **8,** 981 (1969).
(9) Decalone **13** was prepared by alkylation of the kinetic enolate [lithium diisoproplyamide, tetrahydrofuran, hexamethylphosphoramide, −78 °C] derived from decalone **14** with prenyl bromide and subsequent equilibration with sodium methoxide in methanol.

Regioselective Hydrosilylation–Desilylation: Convenient Preparation of a 2-(Trimethylsilyl)-1-alkene[1]

Paul F. Hudrlik,*[2a] Robert H. Schwartz,[2b] and John C. Hogan[2b]

Department of Chemistry, Howard University, Washington, D.C. 20059, and School of Chemistry, Rutgers University, New Brunswick, New Jersey 08903

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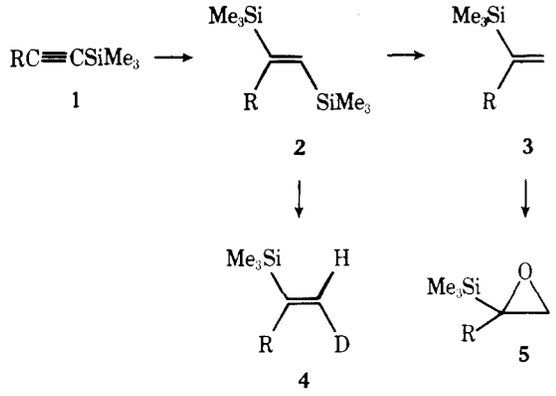
Vinylsilanes are compounds of increasing importance in organic synthesis,[3] in part because they undergo electrophilic substitution reactions with a variety of reagents and thus serve as vinyl anion equivalents[3,4] and in part because the derived α,β-epoxysilanes can serve as versatile vinyl cation equivalents.[5] A number of methods for the synthesis of vinylsilanes have been reported,[6,7] but few of these are suited for the preparation of 2-(trimethylsilyl)-1-alkenes.[7]

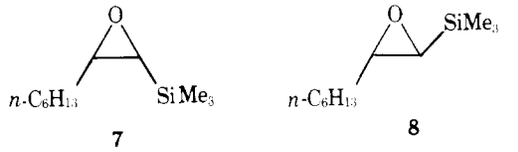
Scheme I



We wish to report a new method for the synthesis of vinylsilane **3** (R = n-C_6H_{13}), featuring a highly regioselective hydrosilylation and protiodesilylation sequence, shown in Scheme I, which should be applicable to the synthesis of other 2-(trimethylsilyl)-1-alkenes.[8] The protiodesilylation reaction has a precedent in the work of Dunogues et al., who reported that 1-phenyl-1,2-bis(trimethylsilyl)ethene (**2,** R = Ph) was converted to 1-phenyl-1-(trimethylsilyl)ethene (**3,** R = Ph) by prolonged treatment with refluxing acetic acid.[9]

We have found that chloroplatinic acid catalyzed hydrosilylation of 1-(trimethylsilyl)-1-octyne (**1,** R = n-C_6H_{13}) occurs in a highly regioselective manner to give (after treatment with MeMgBr) (*E*)-1,2-bis(trimethylsilyl)-1-octene (**2,** R = n-C_6H_{13}) in 96% yield. Only traces (not more than 4%) of what may be the alternate regioisomer (n-$C_6H_{13}CH{=}C(SiMe_3)_2$, **6**) could be detected by VPC but were not visible in the NMR. The stereochemistry of **2** was assigned by analogy to other chloroplatinic acid catalyzed hydrosilylations of alkynes which are known to occur exclusively in a syn manner.[10] The high regioselectivity observed here is noteworthy, since hydrosilylations of alkynes generally give mixtures of regioisomers, even with terminal alkynes.[11,12] It should also be noted that hydroborations[13] and hydroaluminations[14] of alkynylsilanes proceed with opposite regiochemistry to put the boron or aluminum on the carbon bonded to silicon.

Treatment of **2** with proton acids resulted in selective removal of the terminal trimethylsilyl group to give **3** (R = n-C_6H_{13}) in 96% yield. The optimum results were obtained using acetic acid containing about 5% water. The regiochemical purity of **3** was best determined by conversion to the epoxide **5.** Analysis by VPC showed that less than 0.1% of the cis or trans epoxides **7**[5b] or **8**[5b] were present, indicating the extremely high regioselectivity of the reaction.



A similar reaction using deuterated acetic acid gave the deuterated vinylsilane **4,** in which the deuterium was largely or completely cis to the alkyl group, consistent with retention of configuration in the desilylation step.[15,16]

Although the exact mechanism of the desilylation reaction is not known,[17] the regiochemistry can be rationalized by assuming addition of acetic acid to the double bond with Markownikoff orientation, followed by β-elimination of the resulting β-acetoxysilane. The fact that a simple alkyl group is sufficient to induce highly regioselective desilylation of a bis silylated alkene under conditions which maintain the stereoselectivity of the reaction suggests that the concept of regioselective desilylation of bis or higher silylated alkenes will

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