An Improved Synthesis of 18-Nor-17-ketosteroids and Application of the Method for the Preparation of (3β,5β,13α)- and (3β,5β,13β)-3-Hydroxygonan-17-one

Mingcheng Han and Douglas F. Covey*

Department of Molecular Biology & Pharmacology, Washington University School of Medicine, 660 South Euclid Avenue, St. Louis, Missouri 63110

Received June 17, 1996

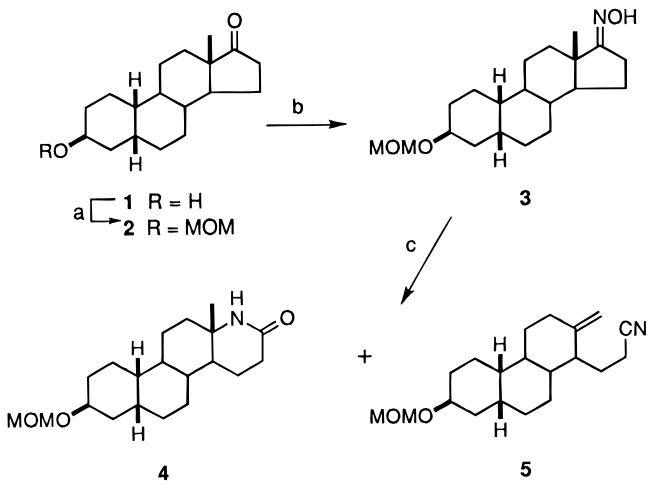
Introduction

Positive allosteric modulation of $GABA_A$ receptor function by neuroactive steroids is currently a topic of widespread physiological and pharmacological interest, and an enhanced knowledge of the structure−activity relationships of neuroactive steroids is expected to produce new drugs having a range of anesthetic, sedative/hypnotic, anticonvulsant, and anxiolytic activities.[1] Our ongoing investigations of neuroactive steroid analogues[2] required a general method that could be used to prepare different classes (gonanes and 18-norandrostanes) of 18-nor-17-ketosteroids. In this paper, we report modifications that improve the overall yield, convenience, and reliability of the "abnormal" Beckmann rearrangement route to 18-nor-17-ketosteroids. This route, which uses 17-ketosteroids as starting materials (for routes to 18-norsteroids proceeding through D-homosteroids or 20-ketosteroids see ref 3), was originally used by Chapman and Pinhey for the preparation of (3β,5α,13α)- and (3β,5α,13β)-3-(acetyloxy)-18-norandrostan-17-one.[4] Herein, the synthesis of the previously unreported (3β,5β,13α)- and (3β,5β,13β)-3-hydroxygonan-17-one (Scheme 2, **11a** and **11b**, respectively) is reported to demonstrate the improved synthetic route to 18-nor-17-ketosteroids. The major improvements involve the replacement of several steps required to recyclize the "abnormal" Beckmann rearrangement product into the 18-nor-17-ketosteroids.

Results and Discussion

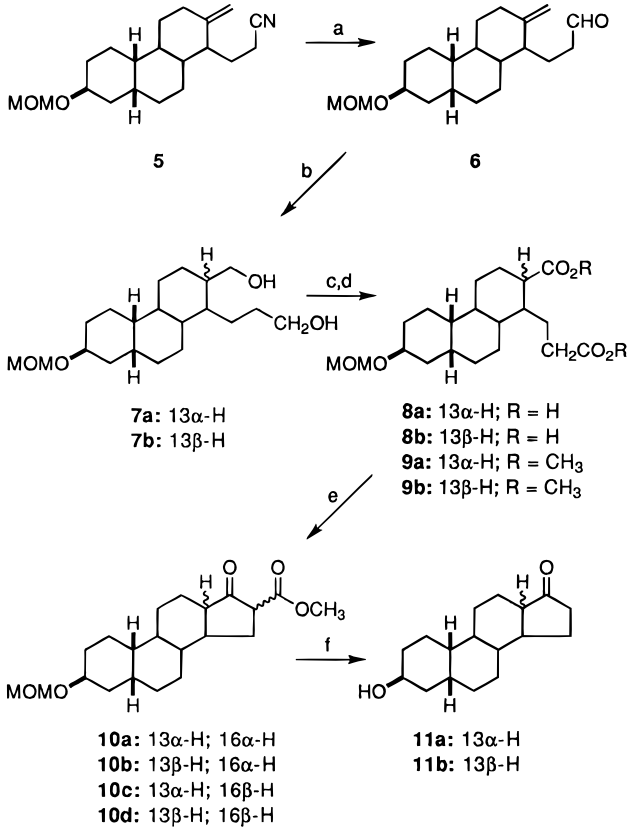
The starting material, (3β,5β)-3-hydroxyestran-17-one (**1**), was prepared in two steps (catalytic hydrogenation[5] followed by K-Selectride reduction at −78 °C) from commercially available 19-nortestosterone and the hydroxy group was reacted with chloromethyl methyl ether to give MOM derivative **2** in 99% yield (Scheme 1). The

Scheme 1[a]



[a] Reagents: (a) MOMCl, $(i\text{-}C_3H_7)_2$,NEt, CH_2Cl_2, 0 °C, 12 h; (b) $NH_2OH{\cdot}HCl$, $KHCO_3$, MeOH, reflux 2 h; (c) DCC, DMSO, TFA, benzene, room temperature, 1 h.

Scheme 2[a]



[a] Reagents: (a) DIBALH, CH_2Cl_2, −70 °C, 2 h; (b) $BH_3{\cdot}THF$ complex, THF, 0 °C, 4 h; (c) $KMnO_4$, 4 N NaOH, *t*-BuOH, room temperature, overnight; (d) CH_2N_2, EtOH, EtOEt, room temperature; (e) *t*-BuOK, benzene, reflux, overnight; (f) diethylene glycol, H_2O, 187−230 °C, 48 h.

MOM protecting group was chosen because although it is stable to the reagents and conditions used in steps a−e of Scheme 2, it is readily removed during the final decarboxylation step f. The reaction of compound **2** with $NH_2OH{\cdot}HCl$ and $KHCO_3$ (included to prevent loss of the MOM group by *in situ* formation of HCl) gave oxime **3** (89%). Reaction conditions (see Scheme 1) reported by Chapman and Pinhey[4] to be favorable to formation of

(1) (a) Gee, K. W.; McCauley, L. D.; Lan, N. C. *Crit. Rev. Neurobiol.* **1995**, *9*, 207. (b) Lambert, J. J.; Belelli, D.; Hill-Venning, C.; Peters, J. A. *Trends Pharmacol. Sci.* **1995**, *16*, 295. (c) McCarthy, M. M. *Hor. Behav.* **1995**, *29*, 131. (d) Olsen, R. V.; Sapp, D. W. *Adv. Biochem. Psychopharmacol.* **1995**, *48*, 57.

(2) (a) Covey, D. F.; Hu, Y.; Bouley, M. G.; Holland, K. D.; Rodgers-Neame, N. T.; Isenberg, K. E.; Zorumski, C. F. *J. Med. Chem.* **1993**, *36*, 627. (b) Hu, Y.; Zorumski, C. F.; Covey, D. F. *J. Med. Chem.* **1993**, *36*, 3956. (c) Hu, Y.; Zorumski, C. F.; Covey, D. F. *J. Org. Chem.* **1995**, *60*, 3619. (d) Han, M.; Hu, Y.; Zorumski, C. F.; Covey, D. F. *J. Med. Chem.* **1995**, *38*, 4548.

(3) (a) Johnson, W. S.; Bannister, B.; Pappo, R. *J. Am. Chem. Soc.* **1956**, *78*, 6331. (b) Johns, W. F. *J. Am. Chem. Soc.* **1958**, *80*, 6456. (c) Stork, G.; Khastgir, H. N.; Solo, A. J. *J. Am. Chem. Soc.* **1958**, *80*, 6457. (d) Yorka, K. V.; Truett, W. L.; Johnson, W. S. *J. Org. Chem.* **1962**, *27*, 4580. (e) Engel, Ch. R.; Lachance, P.; Capitaine, J.; Zee, J.; Mukherjee, D.; Merand, Y. *J. Org. Chem.* **1983**, *48*, 1954. (f) Davioud, E.; Schambel, P.; Viger, A.; Marquet, A. *Steroids* **1993**, *58*, 141.

(4) Chapman, J. C.; Pinhey, J. T. *Aust. J. Chem.* **1974**, *27*, 2421.

(5) Counsell, R. E. *Tetrahedron* **1961**, *15*, 202.

S0022-3263(96)01143-7 CCC: $12.00

"abnormal" Beckmann rearrangement products were utilized to convert oxime **3** into the easily separated lactam **4** (30%) and the "abnormal" product, carbonitrile **5** (53%). No attempt was made to enhance the formation of product **5** by varying the reaction conditions.

The Chapman and Pinhey sequence for the conversion of compounds similar to carbonitrile **5** into 18-nor-17-ketosteroids involves (1) epoxidation of the double bond with *m*-chloroperbenzoic acid; (2) rearrangement of the epoxide to a carboxaldehyde using BF_3·EtOEt; (3) Jones oxidation of the carboxaldehyde to the acid; (4) acid esterification using CH_2N_2; (5) cyclization to the diastereomeric (epimeric at C-13 and C-16) 17-oxo-16-carbonitriles using *t*-BuOK in benzene; and 7) HCl-catalyzed hydrolysis of the carbonitrile group followed by *in situ* decarboxylation to yield the 18-nor-17-ketosteroid. In this reaction sequence, we found that reactions 2 and 7 were particularly problematic. Highly variable, and sometimes major, amounts of a mixture of allylic alcohols were produced along with the carboxaldehyde in the BF_3·EtOEt rearrangement reaction; and in the final step, byproducts resulting from loss of the A-ring hydroxy group were also formed. These difficulties were avoided, and the yields of 18-nor-17-ketosteroid products were significantly enhanced by using the reaction sequence described below and outlined in Scheme 2.

The carbonitrile group of compound **5** was reduced by DIBALH to give aldehyde **6** (88%), and then a BH_3·THF complex was used for the simultaneous hydroboration of the double bond and reduction of the aldehyde group, thereby yielding the epimeric diols **7a** and **7b** (89%). Oxidation of the unseparated diols with $KMnO_4$ in 4 N NaOH/*t*-BuOH gave diacids **8a** and **8b** which were characterized as diesters **9a** and **9b** after esterification with CH_2N_2 (63% overall for both steps).[6] Cyclization and decarboxylation of the diesters were carried out using the methods reported by Johnson and colleagues in their total synthesis of racemic 18-norsteroids.[3d] Thus, treatment of the diesters with *t*-BuOK in benzene, followed by decarboxylation of the intermediate diastereomeric β-keto esters **10a**−**d** in aqueous diethylene glycol at 187−230 °C gave a crude product which was purified by chromatography to yield gonanes **11a** and **11b** (∼1:1, 80% for both steps).

The assignments of configuration at C-13 in steroids **11a** (13α) and **11b** (13β) were made by comparing ^{1}H NMR spectra of these compounds and authentic samples of (3β,5α,13α)-3-(acetyloxy)-18-norandrostan-17-one (mp 152−154 °C; lit.[4] mp 147−149 °C) and (3β,5α,13β)-3-(acetyloxy)-18-norandrostan-17-one (mp 106−108°C; lit.[4] mp 104−105 °C). The ^{1}H NMR spectra of steroid **11b** and the authentic (13β)-18-norsteroid contain a resonance for a single proton which appears as a non-first-order four-line multiplet centered at δ 2.28 and δ 2.37, respectively. This resonance, which is not observed in steroid **11a** and the authentic (13α)-18-norsteroid, is reasonably assigned as H-16β. A similar resonance which has been unambiguously assigned as H-16β is observed as a first order multiplet (J = 1.0 Hz, J = 8.5 Hz, J = 18.3 Hz) at δ 2.45 in the ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of 5α-androstan-17-one.[7]

(6) Other reaction conditions that gave less satisfactory results included $KMnO_4/H_2O$; $KMnO_4$/aqueous acetone; and $KMnO_4/H_2O$/benzene or CH_2Cl_2/18-crown-6.

(7) Schneider, H.-J.; Buchheit, U.; Becker, N.; Schmidt, G.; Siehl, U. *J. Am. Chem. Soc.* **1985**, *107*, 7027.

Experimental Section

General Methods. Melting points were determined on a Kofler micro hot stage and are uncorrected. NMR spectra were recorded in $CDCl_3$ at 300 MHz (^{1}H) or 75 MHz (^{13}C). IR spectra were recorded as films on a NaCl plate. Elemental analyses were carried out by M-H-W Laboratories, Phoenix, AZ. Solvents were used either as purchased or dried and purified by standard methodology. Solvents used for extractions were dried with Na_2SO_4, filtered, and removed on a rotary evaporator. Flash chromatography was performed using silica gel (32−63 μm) purchased from Scientific Adsorbents, Atlanta, GA. The Econosil HPLC column was purchased from Alltech Associates, Inc., Deerfield, IL.

(3β,5β)-3-(Methoxymethoxy)estran-17-one (2). Chloromethyl methyl ether (8.2 mL, 96 mmol) was added dropwise over 20 min to a stirred solution of (3β,5β)-3-hydroxyestran-17-one (**1**, mp 166−167 °C, lit.[5] mp 165−166.5 °C, 22 g, 80 mmol) and diisopropylethylamine (29 mL, 160 mmol) in dichloromethane (200 mL) at 0 °C. The reaction was allowed to warm to room temperature and continued for 12 h. The reaction solution was poured into brine (200 mL), and the separated water phase was extracted with dichloromethane (2 × 150 mL). The combined organic solvents were washed with 0.5 N HCl (2 × 150 mL), brine (2 × 150 mL), and water (2 × 150 mL). Solvent removal gave an oil which was purified by chromatography (silica gel, 15% EtOAc in hexanes) to yield product **2** (25.2 g, ca 99%) as colorless crystals: mp 56−57 °C (from EtOAc/hexanes); IR 1741 cm^{-1}; ^{1}H NMR δ 4.66 (s, 2H), 3.91 (m, 1H), 3.37 (s, 3H), 0.88 (s, 3H); ^{13}C NMR δ 221.39, 94.42, 71.94, 55.04, 50.49, 47.87, 41.06, 40.47, 38.06, 35.79, 31.55, 31.22, 30.97, 30.41, 25.14, 24.84, 24.29, 21.81, 21.58, 13.70. Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.81; H, 10.24.

(3β,5β)-3-(Methoxymethoxy)estran-17-one 17-Oxime (3). Compound **2** (14.5 g, 45 mmol) was added to a stirred mixture of $KHCO_3$ (16.0 g, 156 mmol) and NH_2OH·HCl (11 g, 156 mmol) in methanol (150 mL) and refluxed for 2 h. After cooling to room temperature, the reaction solution was poured into brine (200 mL) and extracted with EtOAc (2 × 150 mL). The combined organic solvents were washed with 0.5 N HCl (2 × 150 mL) and brine (2 × 200 mL). Solvent removal gave a solid which was purified by chromatography (silica gel, 40% EtOAc in hexanes) to yield oxime **3** (13.4 g, 89%) as colorless crystals: mp 125−126 °C (from EtOAc); IR 3283, 1679 cm^{-1}; ^{1}H NMR δ 4.66 (s, 2H), 3.91 (m, 1H), 3.37 (s, 3H), 0.91 (s, 3H); ^{13}C NMR δ 171.23, 94.50, 72.10, 55.14, 52.99, 44.24, 40.99, 40.58, 38.20, 34.12, 31.38, 31.06, 30.48, 25.57, 25.45, 25.04, 24.37, 22.99, 21.86, 17.15. Anal. Calcd for $C_{20}H_{33}NO_3$: C, 71.61; H, 9.91; N, 4.17. Found: C, 71.53; H, 9.84; N, 3.98.

(3β,5β)-3-(Methoxymethoxy)-17-aza-D-homoestran-17a-one (4) and [1*S*-(1α,4aβ,4bα,7α,8aα,10aα)]-7-(Methoxymethoxy)tetradecahydro-2-methylene-1-phenanthrenepropanenitrile (5). Trifluoroacetic acid (3.3 mL, 44.1 mmol) was added dropwise to a stirred solution of oxime **3** (21.0 g, 63 mmol) and DCC (39.0 g, 189 mmol) dissolved in DMSO (105 mL) and benzene (105 mL) under N_2 at room temperature. After 1 h, the reaction mixture was poured into brine (500 mL) and extracted with EtOEt (3 × 200 mL). The combined organic solvents were washed with saturated $NaHCO_3$ (200 mL), brine (2 × 200 mL), and water (200 mL). Solvent removal gave an oil which was purified by chromatography (silica gel, EtOAc:$CHCl_3$:hexanes; 5:35:60) to yield the less polar carbonitrile **5** (10.6 g, 53%) and the more polar lactam **4** (6.67 g, 30%).

Compound **4** was obtained as colorless crystals: mp 187−189 °C (from $CHCl_3$); IR 3172, 3066, 1681, 1610 cm^{-1}; ^{1}H NMR δ 5.94 (br s, 1H), 4.66 (s, 2H), 3.92 (m, 1H), 3.37 (s, 3H), 1.16 (s, 3H); ^{13}C NMR δ 171.76, 94.57, 71.98, 55.12, 54.49, 46.81, 41.91, 40.84, 39.96, 37.56, 31.40, 30.93, 30.67, 30.01, 25.91, 24.72, 24.43, 22.11, 21.49, 19.79. Anal. Calcd for $C_{20}H_{33}NO_3$: C, 71.61; H, 9.91; N, 4.17. Found: C, 71.59; H, 9.61; N, 4.03.

Compound **5** was obtained as an oil: IR 2245, 1692, 1645 cm^{-1}; ^{1}H NMR δ 4.80 (s, 1H), 4.66 (s, 2H), 4.48 (s, 1H), 3.92 (m, 1H), 3.37 (s, 3H); ^{13}C NMR δ 149.80, 120.01, 104.83, 94.37, 71.82, 54.96, 47.85, 46.70, 40.90, 36.65, 36.07, 32.00, 31.26, 30.70, 29.72, 25.56, 24.32, 23.64, 21.52, 14.63. Anal. Calcd for $C_{20}H_{31}NO_2$: C, 75.67; H, 9.77; N, 4.41. Found: C, 75.51; H, 9.80; N, 4.37.

[1*S*-(1α,4aβ,4bα,7α,8aα,10aα)]-7-(Methoxymethoxy)tetradecahydro-2-methylene-1-phenanthrenepropionalde-

hyde (6). DIBALH (6.3 mL, 6.3 mmol, 1.0 M in hexanes) was added to a solution of carbonitrile **5** (1.68 g, 5.2 mmol) in dichloromethane (30 mL) under N_2 at −70 °C. After 2 h, 1 N HCl (25 mL) was added and, after warming to room temperature, the reaction mixture was poured into water (150 mL) and extracted with EtOEt (3 × 150 mL). The combined organic solvents were washed with water (2 × 150 mL). Solvent removal gave an oil which was purified by chromatography (silica gel, 15% EtOAc in hexanes) to yield product **6** (1.49 g, 88%) as an oil: IR 2715, 1724, 1644 cm^{-1}; ^1H NMR δ 9.78 (t, J = 1.4 Hz, 1H), 4.75 (s, 1H), 4.66 (s, 2H), 4.49 (s, 1H), 3.92 (m, 1H), 3.37 (s, 3H); ^{13}C NMR δ 202.46, 150.58, 104.85, 94.36, 71.89, 54.95, 47.96, 46.75, 41.29, 40.96, 36.75, 36.31, 31.99, 31.40, 30.75, 29.82, 25.64, 24.37, 21.56, 19.44. Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.70; H, 9.83.

[1*S*-(1α,2α,4a*β*,4bα,7α,8aα,10aα)]-2-(Hydroxymethyl)-7-(methoxymethoxy)tetradecahydro-1-phenanthrenepropanol (7a) and [1*S*-(1α,2*β*,4a*β*,4bα,7α,8aα,10aα)]-2-(Hydroxymethyl)-7-(methoxymethoxy)tetradecahydro-1-phenanthrenepropanol (7b). BH_3·THF complex (11.2 mL, 11.2 mmol, 1.0 M in THF) was added dropwise to a stirred solution of compound **6** (1.8 g, 5.6 mmol) in THF (60 mL) at 0 °C. After 4 h, the reaction flask was cooled in ice, and 10% NaOH (30 mL) and 30% H_2O_2 (100 mL) were added. After 2 h and warming to room temperature, the reaction solution was poured into brine (100 mL), acidified to pH = 2, and extracted with EtOAc (3 × 100 mL). The combined organic solvents were washed with brine (3 × 100 mL). Solvent removal gave the mixture of epimeric products **7a** and **7b** (1.7 g, 89%) as a solid: IR 3328 cm^{-1}; ^1H NMR δ 4.66 (s, 2H), 3.91 (m, 1H), 3.65−3.59 (m, 4H), 3.37 (s, 3H); ^{13}C NMR δ 94.51, 72.17, 66.29, 63.33, 63.19, 59.96, 55.14, 45.12, 44.09, 43.14, 42.81, 41.93, 41.07, 41.00, 38.01, 37.49, 36.80, 31.69, 31.59, 30.95, 30.90, 30.55, 30.07, 29.89, 29.87, 27.49, 27.42, 25.83, 25.31, 24.57, 24.94, 24.57, 24.50, 24.38, 24.02, 21.59. Anal. Calcd for $C_{20}H_{36}O_4$: C, 70.55; H, 10.66. Found: C, 70.40; H, 10.55.

[1*S*-(1α,2α,4a*β*,4bα,7α,8aα,10aα)]-2-Carboxy-7-(methoxymethoxy)tetradecahydro-1-phenanthrenepropanoic Acid Dimethyl Ester (9a) and [1*S*-(1α,2*β*,4a*β*,4bα,7α,8aα,-10aα)]-2-Carboxy-7-(methoxymethoxy)tetradecahydro-1-phenanthrenepropanoic Acid Dimethyl Ester (9b). A mixture of epimeric diols **7a** and **7b** (1.6 g, 4.7 mmol), 4 N NaOH (75 mL), and $KMnO_4$ (8.3 g, 53 mmol) in *t*-BuOH (100 mL) was stirred overnight at room temperature. The reaction mixture then was poured into 5% Na_2SO_3 (100 mL), cooled in ice, and acidified with 3 N HCl until colorless. The solution was extracted with EtOAc (3 × 150 mL), and the combined organic solvents were washed with brine (3 × 100 mL). Solvent removal gave the epimeric diacids **8a** and **8b** which were dissolved in EtOH (20 mL) and EtOEt (20 mL) and esterified with an EtOEt solution of CH_2N_2. Solvent removal gave a crude product which was purified by chromatography (silica gel, 40% EtOAc in hexanes) to yield a mixture of epimeric diesters **9a** and **9b** (1.1 g, **9a**/**9b** = 1:1, 63%). This epimeric mixture was separated by HPLC (silica gel, 30% EtOAc in hexanes, 3 mL/min).

Compound **9a**[8] (first component) was obtained as colorless crystals: mp 50−52 °C (from EtOAc/hexanes); IR 1737 cm^{-1}; ^1H NMR δ 4.66 (s, 2H), 3.90 (m, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 3.37 (s, 3H), 2.79 (m, 1H); ^{13}C NMR δ 174.74, 174.17, 94.54, 72.16, 55.15, 51.50, 51.08, 43.48, 42.21, 41.91, 40.58, 37.17, 32.35, 31.39, 30.95, 30.03, 28.97, 25.87, 25.41, 25.16, 24.54, 21.56. Anal. Calcd for $C_{22}H_{36}O_6$: C, 66.64; H, 9.15. Found: C, 66.43; H, 8.90.

Compound **9b**[8] (second component) was obtained as colorless crystals: mp 79−80 °C (from EtOAc/hexanes); IR 1737 cm^{-1}; ^1H NMR δ 4.66 (s, 2H), 3.91 (m, 1H), 3.68 (s, 3H), 3.65 (s, 3H), 3.37 (s, 3H); ^{13}C NMR δ 175.89, 173.69, 94.22, 71.67, 54.75, 51.13, 51.07, 47.45, 43.85, 42.29, 40.55, 36.08, 31.13, 30.58, 29.67, 29.42, 28.91, 28.63, 24.81, 24.25, 24.18, 21.27. Anal. Calcd for $C_{22}H_{36}O_6$: C, 66.64; H, 9.15. Found: C, 66.68; H, 8.91.

(3*β*,5*β*,13α)-3-Hydroxygonan-17-one (11a) and (3*β*,5*β*,-13*β*)-3-Hydroxygonan-17-one (11b). A mixture of epimeric diesters **9a** and **9b** (400 mg, 1.01 mmol) and *t*-BuOK (1.0 g, 8.9 mmol) were dissolved in dry benzene (50 mL) and refluxed overnight under N_2. After cooling to room temperature, the reaction solution was added to a stirred mixture of 1 N HCl (200 mL) and ice (200 g). The products were extracted with EtOAc (3 × 150 mL), and the combined organic solvents were washed with brine (2 × 100 mL). After solvent removal, the crude solid product (**10a**−**d**, 313 mg) was added to diethylene glycol (50 mL) which contained H_2O (3 mL) and refluxed (ca. 187−230 °C) under N_2 for 48 h. After cooling to room temperature, the reaction solution was poured into brine (200 mL) and extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with water (2 × 100 mL). Solvent removal gave a solid which was purified by chromatography (silica gel, 30% EtOAc in hexanes) to yield a mixture of epimeric gonanes **11a** and **11b** (211 mg, 80%) which were separated by HPLC (silica gel, 30% EtOAc in hexanes, 3 mL/min).

Compound **11a** (first component) was obtained as colorless crystals: mp 154−155 °C (from EtOAc/hexanes); IR 3320, 1735 cm^{-1}; ^1H NMR δ 4.14 (m, 1H); ^{13}C NMR δ 220.09, 66.97, 50.27, 42.48, 42.31, 40.82, 35.14, 34.61, 33.15, 31.23, 29.57, 27.07, 26.24, 26.18, 23.18, 22.45, 20.86. Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.85; H, 9.80.

Compound **11b** (second component) was obtained as colorless crystals: mp 172−173 °C (EtOAc/hexanes); IR 3465, 1735 cm^{-1}; ^1H NMR δ 4.14 (m, 1H), 2.34 (m, 1H); ^{13}C NMR δ 218.68, 66.94, 55.37, 48.99, 48.10, 40.78, 37.57, 36.84, 33.23, 31.05, 29.83, 29.56, 26.93, 25.44, 24.99, 24.59, 21.40. Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.98; H, 9.81.

Acknowledgment. The work was supported by NIH grant GM 47969. Assistance was also provided by the Washington University High Resolution NMR Facility supported in part by NIH 1 S10 RR00204 and a gift from the Monsanto Co.

JO9611430

(8) The assignments of configuration at C-2 for compounds **9a** and **9b** are based on ^1H NMR data. A single line resonance with shoulders ($W_{1/2} \approx 12$ Hz), assigned as the equatorial H-2 resonance, is observed at δ 2.79 in compound **9a**. This resonance has a line shape very similar to the line shape of the equatorial H-3 proton in 5α-reduced 3α-hydroxysteroids. The axial H-2 resonance in compound **9b** occurs above δ 2.5 and is obscured by overlapping multiplets.