Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 77.24; H, 8.56; N, 6.65.

1-Benzoyl-2-methylpiperidine (6) was obtained as crystals from Skellysolve B: mp 46–49° (lit.[12] solid mp 44–45°). **1-Benzoyl-*cis*-2,6-dimethylpiperidine** (7) was obtained as crystals from benzoylation of commercially available (Eastman) 2,6-dimethylpiperidine and had mp 109–111° (lit.[13] mp 110°). **3-Benzoyl-3-azabicyclo[3.3.1]nonane** (8) was obtained as colorless crystals, mp 86–88°.

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.31; H, 8.47; N, 6.01.

(12) H. Bunzel, *Chem. Ber.*, **22**, 1053 (1889).

(13) R. K. Hill, T. H. Chan, and J. A. Joule, *Tetrahedron*, **21**, 147 (1965).

(+)-**1-Benzoyl-*trans*-decahydroquinoline** (9) has been described elsewhere.[14]

Registry No.—**1**, 17037-65-9; **2**, 17037-66-0; **3**, 17037-67-1; **4**, 17037-68-2; **5**, 17037-69-3; **6**, 17037-70-6; **7**, 17037-71-7; **8**, 17037-72-8; **9**, 17037-73-9.

Acknowledgment.—The author wishes to thank Dr. B. Vernon Cheney, Dr. Jackson B. Hester, Dr. Gunther S. Fonken, and Dr. George Slomp for many helpful comments and suggestions concerning this study.

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D-Homoannulation of 5α-Pregnane-3β,20β-diol 3-Acetate with Phosphorus Pentabromide

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3β-Acetoxy-17aα-bromo-17α-methyl-D-homo-5α-androstane (IIa) and its 17aβ-bromo epimer (IIIa) were obtained when 3β-acetoxy-5α-pregnan-20β-ol (I) was treated with phosphorus pentabromide. The 17α-methyl-D-homo structure was established by the synthesis of 17α-methyl-D-homo-5α-androstan-3β-ol (IVa). The assignment of the 17aα and 17aβ configurations for bromo compounds IIa and IIIa were based on spectral studies.

In the course of our studies on the synthesis of steroidal alkaloids, the need for the preparation of 3β-acetoxy-20α-bromo-5α-pregnane arose. This was sought by the treatment of 3β-acetoxy-5α-pregnan-20β-ol (I) with phosphorus pentabromide in chloroform in the presence of calcium carbonate. Two bromo compounds, IIa and IIIa, were obtained with yields of 32 and 6.8% respectively. Initially the two bromo compounds were assumed to be the epimeric 3β-acetoxy-20α- and -20β-bromo-5α-pregnanes with the major product IIa (acetate, mp 166–170°, $[\alpha]^{20}D$ −20.5°; alcohol, mp 170–175°, $[\alpha]^{20}D$ −15.3°) being assigned the α orientation and the minor product IIIa (acetate, mp 130–131°, $[\alpha]^{20}D$ +9.6°; alcohol, mp 184.5–186°, $[\alpha]^{20}D$ +10.9°) being assigned the opposite β orientation. This assignment is based on the fact that halogenation of alcohols by phosphorus pentahalides usually proceeds by a SN2 mechanism leading predominantly to inversion of configuration.[2,3]

An attempt to prepare the Grignard of IIa in an exploratory run using methyl iodide as an initiator[4a] resulted in a product which appeared to be derived from a coupling reaction.[5] To explore this route further as an approach to the synthesis of sterols (*e.g.*, cholestanol), IIa was treated with isohexylmagnesium bromide. The product to our mild surprise analyzed for the formulation $C_{21}H_{36}O$ (mol wt 304) and was subsequently ascribed the D-homo structure IVa. It was found also that the lithium aluminum hydride reduction of IIa led to IVa as well and that catalytic reduction over Raney nickel afforded the acetate IVb. See Scheme I.

The original assumption of IVa being perhaps 5α-pregnan-3β-ol resulting from the functional exchange[4b] of the 20α-bromo derivative with isohexylmagnesium bromide followed by hydrolytic cleavage was discarded in favor of the D-homo compound when the physical constants (melting point and rotation) of IVa and its derivatives (3-acetate, IVb, and 3-oxo, IVc) were not in agreement with those of authentic 5α-pregnan-3β-ol and its derivatives.[6,7] In addition the nmr data were more consonant with a D-homo product rather than a normal steroid. The proton resonance of an unperturbed C-18 methyl in 5α,14α steroids is observed at 0.692 ppm while that of the C-19 methyl is seen at 0.792 ppm.[8] Upon ring-D expansion, however, the former (C-18) has been observed to shift downfield to 0.792 ppm.[8,9] This is in harmony with compound IVa which displays a strong resonance peak (integrated for six protons) at 0.81 ppm for the C-18 and C-19 protons. Furthermore, it was considered mechanistically more probable for the D-homo rearrangement to occur earlier in the treatment with phosphorus pentabromide rather than during the reductive phase from IIa to IVa. It seems reasonable to assume that the rearrangement occurs through a C-20β ester–halide complex in a concerted process with the preferential migration of the C-16,17 bond to afford a product bearing a C-17α (equatorial) methyl function. This is comparable in manner with 5α-pregnane-3β,20β-diol 3-acetate 20-tosylate which un-

(1) Visiting Fellow, 1966–1968.

(2) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 392.

(3) G. Adam and K. Schreiber, *Tetrahedron*, **22**, 3581 (1966).

(4) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954: (a) p 38; (b) p 1060.

(5) A solution of CH_3I (0.34 g, 0.0024 mol) in 5 ml of ether was added to magnesium (0.41 g). As the reaction started, a mixture of compound IIa (1.0 g, 0.0024 mol) and CH_3I (1.36 g, 0.0096 mol) in 20 ml of ether was added dropwise and the mixture was refluxed for 3 hr. After hydrolysis with dilute H_2SO_4, the product isolated showed mol wt 318 in the mass spectrum.

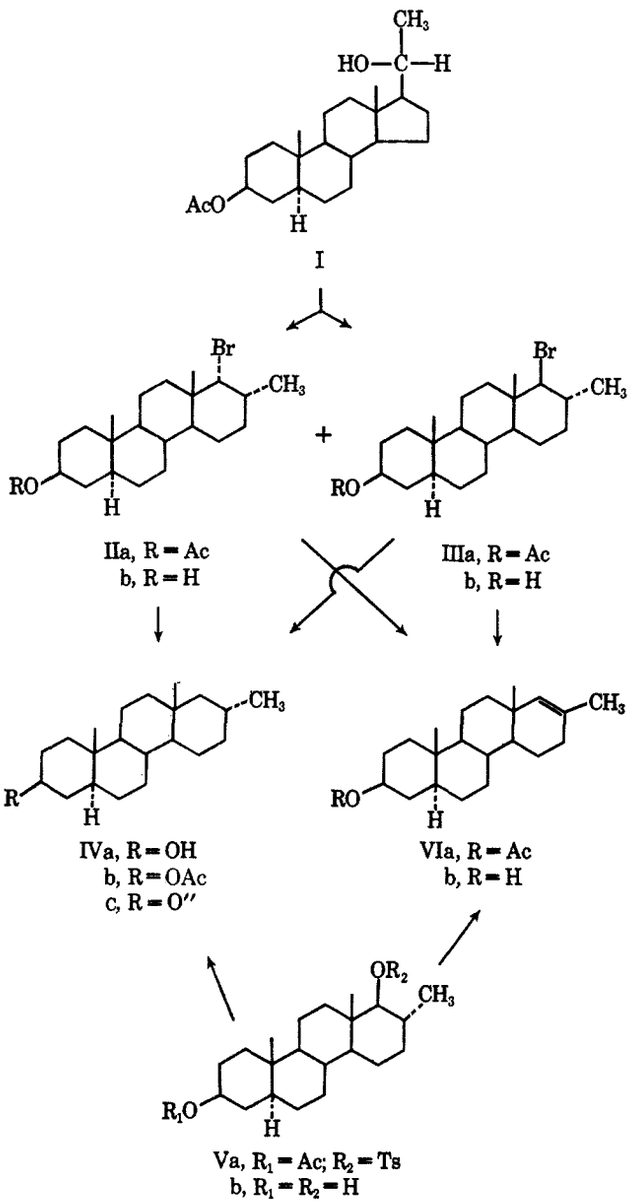
(6) L. Ruzicka, M. W. Goldberg, and E. Hardegger, *Helv. Chim. Acta*, **22**, 1294 (1939).

(7) L. Ruzicka, P. Meister, and V. Prelog, *ibid.*, **30**, 867 (1947).

(8) R. F. Zürcher, *ibid.*, **46**, 2054 (1963).

(9) N. R. Trenner, B. H. Arison, D. Taub, and N. L. Wendler, *Proc Chem. Soc.*, 214 (1961).

SCHEME I



dergoes solvolytic rearrangement to a 17α-methyl-D-homo compound.[10-13]

The proof of the ascribed structure for IVa was shown by its synthesis from uranediol 3-acetate 17a-tosylate (Va)[12] with lithium aluminum hydride. The product, 17α-methyl-D-homo-5α-androstan-3β-ol, proved to be identical (melting point, mixture melting point, ir spectra) with our compound IVa obtained from the reduction of the bromide IIa.[14] In the above metal hydride reduction, uranediol (Vb)[15] was also recovered as a by-product.[16,17]

That the bromo compounds IIa and IIIa differed only in orientation at C-17a was shown when the catalytic reduction of IIIa afforded the same 17α-methyl-D-homo product (IVb) as that obtained from the reduction of IIa. The assignment of the orientation of the bromine atoms in IIa and IIIa at C-17a was derived from spectral measurements. The nmr spectrum of IIa showed a doublet for a 17a proton centered at δ 4.08 ppm (J = 2 cps) whereas IIIa exhibited a doublet centered at 3.60 ppm with a coupling constant of 11 cps. The magnitude of the coupling constants indicated that the dihedral angles between C-17 and C-17a protons are approximately 60 and 180° for compounds IIa and IIIa, respectively.[18] Since it has been shown that the methyl function at C-17 has the equatorial orientation (C-17 proton, axial) in both compounds, the above studies would allow us the assignment of the 17aα orientation for the bromine atom in IIa and the 17aβ configuration for IIIa. The appearance of the chemical shift of the C-17a proton in IIIa at a higher field than that in IIa is also in line with our assignment, since it is known that axial ring protons absorb at higher fields than the equatorial protons in a six-membered system.[19-21]

The ir spectra of the compounds also support the assignment. Product IIa shows a C–Br stretching frequency at 683 cm^{-1}, whereas the corresponding frequency in IIIa appears at 694 cm^{-1}. An equatorial substituent in a cyclohexane ring usually appears at a higher frequency than its axial counterpart.[22,23]

It is of interest to note that in the Raney nickel reduction of IIa aside from the dehalogenated product IVb, a dehydrohalogenated compound (VIa), as judged from nmr spectrum (olefinic proton at 5.13 ppm), and the epimeric 17aβ-bromo compound IIIa were obtained. The origin of VIa is probably due to the alkalinity of the media, but the occurrence of IIIa is somewhat puzzling.[24] Studies along these lines are contemplated. Further reduction of IIIa with fresh catalyst affords IVb and the unsaturated product VIa in equal quantities. The structure of compound VIa was confirmed by its synthesis from uranediol 3-acetate 17a-tosylate (Va) with lithium chloride in dimethylformamide.[25]

Experimental Section[26]

3β-Acetoxy-5α-pregnan-20β-ol (I).—3β-Acetoxy-5α-pregnan-20-one (12.35 g, 0.0343 mol) was reduced in 240 ml of glacial

(10) W. Klyne, *Nature*, **166**, 559 (1950).

(11) H. Hirschmann and J. S. Williams, *J. Biol. Chem.*, **238**, 2305 (1963).

(12) H. Hirschmann, F. B. Hirschmann, and A. P. Zala, *J. Org. Chem.*, **31**, 375 (1966).

(13) H. Lee and M. Wolff, *ibid.*, **32**, 192 (1967).

(14) We are grateful to Dr. H. Hirschmann for sending us the ir spectrum of 17α-methyl-D-homo-5α-androstan-3β-ol which was obtained by reduction of 3β-acetoxy-17α-methyl-D-homo-5α-androstan-17a-one with amalgamated zinc in EtOH–HCl. The spectrum is identical with that of our compound IVa.

(15) The identity of this compound was established by comparison with a reference sample prepared from 5α-pregnane-3β,20β-diol 3-acetate 20-tosylate following the procedure of Hirschmann.[12]

(16) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

(17) A. S. Hussey, H. P. Liao, and R. H. Baker, *J. Amer. Chem. Soc.*, **75**, 4727 (1953).

(18) M. Karplus, *ibid.*, **85**, 2870 (1963).

(19) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p 47.

(20) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958).

(21) J. N. Shoolery and M. T. Rogers, *ibid.*, **80**, 5121 (1958).

(22) D. H. R. Barton, *Experientia, Suppl. II*, 121 (1955).

(23) D. H. R. Barton, J. E. Page, and C. W. Shoppee, *J. Chem. Soc.*, 331 (1956).

(24) One of the referees suggested that formation of IIIa in this reduction might possibly arise from bromide ion exchange.

(25) (a) R. P. Holysz, *J. Amer. Chem. Soc.*, **75**, 4432 (1953); (b) L. Ehmann, K. Heusler, Ch. Meystre, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **42**, 2548 (1959).

(26) Melting points were taken on a Kofler block and are uncorrected. Rotations were measured in chloroform solution with a Perkin-Elmer Model 141 polarimeter. Infrared spectra were recorded in carbon disulfide solution with a Perkin-Elmer Model 421 spectrophotometer. Nmr spectra were determined on the Model A-60 Varian Associates spectrometer using deuteriochloroform as the solvent with tetramethylsilane as the internal standard (TMS = 0.0 ppm). Microanalyses were performed by the Microanalytical Services Unit of this laboratory.

HAc with PtO_2 (4.94 g) for 4 hr according to the procedure of Klyne and Barton.[27] The crude product was chromatographed on silica gel and elution with benzene–ether (8:2) gave first the major product, 3β-acetoxy-5α-pregnan-20β-ol (I) (10.05 g, 81%): mp 170–172°; $[\alpha]^{20}D$ −10.4° (*c* 1.17) {lit. mp 168–169°; $[\alpha]^{20}D$ −6° ($CHCl_3$);[3] mp 171–173°, $[\alpha]^{20}D$ −7.8° ($CHCl_3$)[28]}.

Further elution with the same solvent system gave 3β-acetoxy-5α-pregnan-20α-ol (0.96 g, 8%): mp 135.5–136°; $[\alpha]^{22}D$ +0.4° (*c* 0.850) {lit.[28] mp 132–133°; $[\alpha]^{22}D$ +6° (EtOH)}.

3β-Acetoxy-17a-bromo-17α-methyl-D-homo-5α-androstanes (IIa and IIIa).—To 3β-acetoxy-5α-pregnan-20β-ol (I) (1 g, 0.0028 mol) in 80 ml of dried $CHCl_3$ was added $CaCO_3$ (1 g) and the mixture was cooled to 0° in an ice–water bath. Freshly prepared PBr_5 (4.8 g) was then added in small portions to the well-stirred mixture. The resulting mixture was stirred for 1 hr at 0° and an additional 2 hr at room temperature and then poured into a solution of $NaHCO_3$. The organic phase was separated and the aqueous phase was repeatedly extracted with $CHCl_3$. The combined extract was washed successively with water, dilute HCl, dilute $NaHCO_3$, and water and concentrated to dryness. The crude product upon recrystallization from acetone gave 3β-acetoxy-17aα-bromo-17α-methyl-D-homo-5α-androstane (IIa) (0.37 g, 32%) as needles: mp 166–170°; $[\alpha]^{20}D$ −20.5° (*c* 0.914); ir, 1736, 1245, 1026 (acetate), 683 and 644 cm^{-1} (C–Br); nmr, δ 0.80 (s, 3, 19-H), 0.97 (d, 3, *J* = 6 cps, 17α-CH_3), 1.02 (s, 3, 18-H), 2.0 (s, 3, OAc), and 4.08 (d, 1, *J* = 2 cps, 17aβ-H).

Anal. Calcd for $C_{23}H_{37}O_2Br$: C, 64.93; H, 8.77; Br, 18.78. Found: C, 65.09; H, 8.57; Br, 19.22.

The mother liquor, after repeated recrystallization from aqueous acetone, yielded the 17aβ-bromo epimer (IIIa) (0.089 g, 6.8%) as rods: mp 130–131°; $[\alpha]^{20}D$ +9.6° (*c* 0.963); ir, 1732, 1243, 1027 (acetate) and 694 cm^{-1} (C–Br); nmr, δ 0.80 (s, 3, 19-H), 0.96 (s, 3, 18-H), 1.07 (d, 3, *J* = 6 cps, 17α-CH_3), 2.02 (s, 3, OAc), and 3.60 (d, 1, *J* = 11 cps, 17aα-H).

Anal. Calcd for $C_{23}H_{37}O_2Br$: C, 64.93; H, 8.77; Br, 18.78. Found: C, 64.73; H, 8.55; Br, 18.90.

A mixture of IIa (0.1 g, 0.000261 mol) in 12 ml of 2% methanolic KOH was stirred at room temperature for 2 hr. The crude product, obtained after recrystallization from MeOH, afforded 17aα-bromo-17α-methyl-D-homo-5α-androstan-3β-ol (IIb) (0.074 g, 87%) as needles: mp 170–175°; $[\alpha]^{20}D$ −15.3° (*c* 1.05); ir, 3602, 1036 (OH), 682, and 647 cm^{-1} (C–Br).

Anal. Calcd for $C_{21}H_{35}OBr$: C, 65.78; H, 9.20; Br, 20.85. Found: C, 65.66; H, 9.14; Br, 20.83.

In a similar manner, compound IIIa (0.18 g, 0.000469 mol) was hydrolyzed with 20 ml of 2% methanolic KOH to give compound IIIb (0.14 g, 87%) as needles: mp 184.5–186°; $[\alpha]^{20}D$ +10.9° (*c* 0.695); ir, 3602, 1035 (OH), 693 and 648 cm^{-1} (C–Br).

Anal. Calcd for $C_{21}H_{35}OBr$: C, 65.78; H, 9.20; Br, 20.85. Found: C, 65.76; H, 9.05; Br, 20.89.

17α-Methyl-D-homo-5α-androstan-3β-ol (IVa). A.—A solution of compound IIa (1.2 g, 0.00288 mol) in 10 ml of *n*-propyl ether and 5 ml of THF was added dropwise to isohexylmagnesium bromide [prepared from magnesium (0.83 g) and isohexyl bromide (6.21 g)] in 15 ml of *n*-propyl ether. The mixture after refluxing overnight was poured into ice–water, hydrolyzed with dilute H_2SO_4, and extracted with ether. The dried ethereal solvent was evaporated and the crude residue was chromatographed on a silica gel column. Elution with benzene–ether (9:1) gave 17α-methyl-D-homo-5α-androstan-3β-ol (IVa) (0.67 g, 78%). Recrystallization from acetone–water yielded rods: mp 141–142°; $[\alpha]^{20}D$ +4.4° (*c* 1.0). The ir spectrum showed the following characteristic bands at 1380, 1088, 1072, 1050, 994, 957, 950, 932, 912, 898, and 838 cm^{-1}. The hydroxyl bands were at 3600 and 1034 cm^{-1}. Nmr signals were observed at δ 0.81 (s, 6, 18- and 19-H), 0.82 (d, 3, *J* = 6 cps, 17α-CH_3), 1.60 (s, 1, 3β-OH), and 3.54 (m, 1, 3α-H).

Anal. Calcd for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.98; H, 11.85.

B.—Compound IIa (0.425 g, 0.001 mol) in 10 ml of THF was added dropwise to the suspension of $LiAlH_4$ (0.456 g) in 15 ml of THF. The mixture was refluxed for 24 hr and poured into 50 ml of ether. Excess $LiAlH_4$ was decomposed by adding ice–water and the resulting mixture was extracted with ether. The ethereal solution was dried and evaporated leaving 0.27 g of a crude product which was chromatographed over a silica gel column. Elution with benzene–ether (8:2) gave compound IVa (0.23 g, 75%), mp 140–141°. The mixture melting point with a sample obtained from method A showed no depression. The ir spectra of the two samples were also in agreement.

C.—A solution of uranediol 3-acetate 17a-tosylate (Va)[12] (1.03 g, 0.002 mol) in 20 ml of THF was added dropwise to $LiAlH_4$ (0.912 g) in the same solvent and the mixture was refluxed for 24 hr. It was worked up as in method B. The crude product was chromatographed on silica gel and elution with benzene–ether (9:1) yielded compound IVa (0.37 g, 62%), mp 139–141°. A mixture melting point with a sample obtained from method A showed no depression. The ir spectrum was identical in all respects with a sample obtained from method A.

Further elution of the column with benzene–ether (7:3) gave uranediol (Vb) (0.168 g, 25%) which was recrystallized from methanol as needles: mp 213–214°; $[\alpha]^{20}D$ −0.2° (*c* 0.974) {lit. mp 216–219°, $[\alpha]^{20}D$ +3.7° ($CHCl_3$);[29] mp 215–216°, $[\alpha]^{23}D$ +5° (EtOH)[12]}. The mixture melting point with a sample prepared according to the procedure of Hirschmann[12] showed no depression. The ir spectra were also superposable.

Anal. Calcd for $C_{21}H_{36}O_2$: C, 78.69; H, 11.32. Found: C, 78.82; H, 11.02.

3β-Acetoxy-17α-methyl-D-homo-5α-androstane (IVb). A.—A solution of compound IVa (0.15 g, 0.000493 mol) in 2 ml of Ac_2O and 2 ml of pyridine was stirred at room temperature for an hour. Recrystallization of the crude product from aqueous acetone gave the 3-acetate (IVb) (0.153 g, 90%) as plates: mp 125–126°; $[\alpha]^{20}D$ −6.8° (*c* 0.990); ir, 1737, 1240, 1024 cm^{-1} (acetate); nmr, δ 0.80 (s, 6, 18- and 19-H), 0.81 (d, 3, *J* = 6 cps, 17α-CH_3), 2.01 (s, 3, OAc), and 4.70 (m, 1, 3α-H).

Anal. Calcd for $C_{23}H_{38}O_2$: C, 79.71; H, 11.05. Found: C, 79.45; H, 10.81.

B.—Compound IIa (0.5 g, 0.00118 mol) was reduced in 15 ml of EtOH with Raney nickel[30] (2 g) for 24 hr and the crude product was chromatographed on silica gel. Elution with benzene–hexane (4:6) gave, first, 3β-acetoxy-17α-methyl-D-homo-5α-androstane (IVb) (0.145 g, 36%) which had a melting point of 125–126°. It showed no depression of its melting point when mixed with a sample obtained by method A.

Further elution of the column with the same solvent yielded 3β-acetoxy-17-methyl-$\Delta^{17(17a)}$-D-homo-5α-androstene (VIa) (0.12 g, 30%). The later eluates afforded 3β-acetoxy-17aβ-bromo-17α-methyl-D-homo-5α-androstane (IIIa) (0.119 g, 24%) with mp 132–133°.

Compound VIa was recrystallized from acetone–water as rods: mp 119.5–120°; $[\alpha]^{20}D$ +21.3° (*c* 0.884); ir, 1732, 1237 and 1021 cm^{-1} (acetate); nmr, δ 0.83 (s, 6, 18- and 19-H), 1.62 (m, 3, 17-CH_3), 2.02 (s, 3, OAc), and 5.13 (m, 1, 17a-H).

Anal. Calcd for $C_{23}H_{36}O_2$: C, 80.18; H, 10.53. Found: C, 80.16; H, 10.64.

C.—Compound IIIa (0.14 g, 0.00033 mol) was hydrogenated in 15 ml of EtOH with Raney nickel[30] (1 g) for 24 hr. Chromatography of the crude product on silica gel using benzene–hexane (4:6) as an eluent afforded, first, 3β-acetoxy-17α-methyl-D-homo-5α-androstane (IVb) (0.052 g, 45%) of mp 125–126° followed by 3β-acetoxy-17-methyl-$\Delta^{17(17a)}$-D-homo-5α-androstene (VIa) (0.052 g, 45%) of mp 119–120°. The mixture melting point with a respective sample obtained by method B showed no depression.

17α-Methyl-D-homo-5α-androstan-3-one (IVc).—Compound IVa (0.058 g, 0.00019 mol) in 50 ml of acetone was oxidized with 1 ml of Kiliani chromic acid solution[31] at 20° for 10 min. The product after recrystallization from acetone gave the ketone IVc (0.055 g, 96%) as plates: mp 150–152°; $[\alpha]^{20}D$ +28.0° (*c* 0.940); ir, 1713 cm^{-1} (six-membered-ring ketone); nmr, δ 0.83 (s, 3, 18-H), 0.83 (d, 3, *J* = 6 cps, 17α-CH_3), and 0.99 (s, 3, 19-H).

Anal. Calcd for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.06; H, 11.35.

3β-Acetoxy-17-methyl-$\Delta^{17(17a)}$-D-homo-5α-androstene (VIa).—A mixture of uranediol 3-acetate 17a-tosylate (Va) (0.32 g,

(27) W. Klyne and D. H. R. Barton, *J. Amer. Chem. Soc.*, **71**, 1500 (1949).

(28) D. M. Glick and H. Hirschmann, *J. Org. Chem.*, **27**, 3212 (1962).

(29) R. V. Brooks, W. Klyne, E. Miller, and J. Y. F. Patterson, *Biochem. J.*, **51**, 694 (1952).

(30) Raney active nickel catalyst, Grade no. 28, W. R. Grace and Co., Chattanooga, Tenn.

(31) H. Kiliani, *Ber.*, **46**, 676 (1913).

0.0006 mol) and LiCl (0.05 g) in 20 ml of DMF was heated at 140° for 10 hr. The crude product was chromatographed on silica gel. Elution with benzene–hexane (4:6) gave 3β-acetoxy-17-methyl-$\Delta^{17(17a)}$-D-homo-5α-androstene (VIa) (0.18 g, 86%), mp 119–120.5°. It showed no depression of its melting point when mixed with the unsaturated product obtained by the reduction of the bromo compounds (IIa and IIIa) with Raney nickel. The ir spectra were also in agreement.

Hydrolysis of compound VIa with 2% methanolic KOH gave the free alcohol (VIb) which was recrystallized from aqueous acetone as plates: mp 128–129°; $[\alpha]^{20}D$ +50.8° (c 0.750). The infrared spectrum showed the hydroxyl bands at 3610 and 1035 cm^{-1}.

Anal. Calcd for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.36; H, 11.19.

Registry No.—I, 17182-23-9; IIa, 17182-24-0; IIb, 17182-25-1; IIIa, 17182-26-2; IIIb, 17182-27-3; IVa, 17182-28-4; IVb, 17182-29-5; IVc, 17182-67-1; VIa, 17182-68-2; VIb, 17182-69-3; phosphorus pentabromide, 7789-69-7.

Notes

D-Homoannulation of 3β-Acetoxy-5α-pregnan-20β-ol with Some Chlorinating Agents

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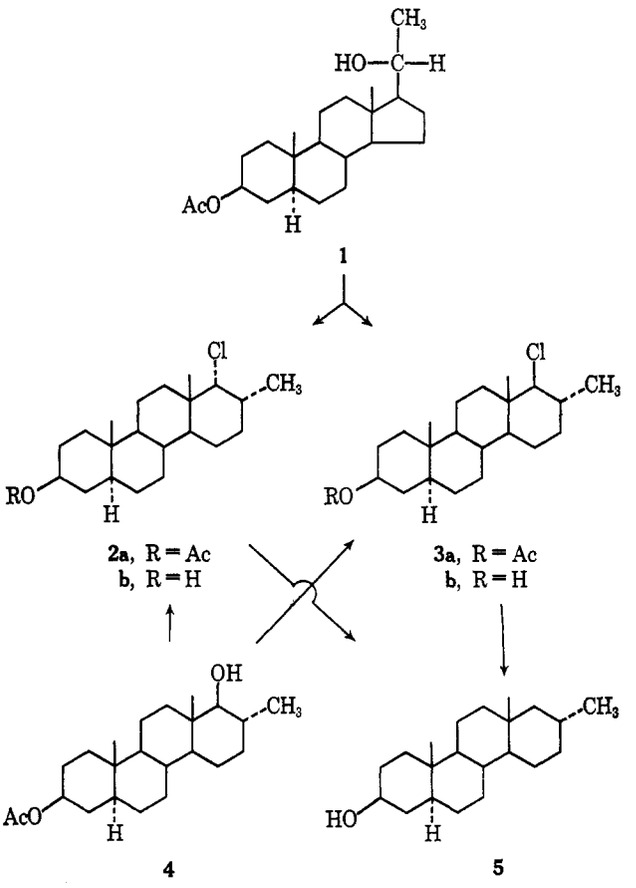
In continuance of our studies of the halogenation of 3β-acetoxy-5α-pregnan-20β-ol[2] (**1**), we wish now to report our observations on the treatment of **1** with several chlorinating agents. We find that chlorination of **1** with phosphorus pentachloride, sulfuryl chloride, or thionyl chloride, under the same conditions described by Adam and Schreiber,[3] leads to D-homoannulation, similar to our previous observation of **1** with phosphorus pentabromide,[2] to afford the two chloro derivatives, 3β-acetoxy-17aα- and -17aβ-chloro-17α-methyl-D-homo-5α-androstanes, **2a** and **3a**, and not 3β-acetoxy-20α- and -20β-chloro-5α-pregnanes[4] as reported.[3]

The halogenation of compound **1** with phosphorus pentachloride or sulfuryl chloride yields predominantly the chloro derivative **2a** (56% PCl_5 and 39% SO_2Cl_2) whereas thionyl chloride affords the chloro compound **3a** as the major product (63%).

The D-homo structure of **2a** and **3a** was established by their synthesis from the reaction of the known 3β-acetoxy-17α-methyl-D-homo-5α-androstan-17aβ-ol (**4**)[5a] with phosphorus pentachloride. The yields of **2a** and **3a** in the reaction were 56 and 18%, respectively. Lithium aluminum hydride reduction of both **2a** and **3a** to 17α-methyl-D-homo-5α-androstan-3β-ol (**5**)[2] further substantiated the D-homo assignment.



The possibility of D-homoannulation occurring on the silica gel column after the reaction, as in the manner reported for 3β-acetoxy-20-chlorobisnorallocholane,[6] is excluded since both **2a** and **3a** are obtained directly from the reaction mixture by crystallization without resort to chromatography.

The difference in the ratios of the rearrangement products obtained in the reaction of **1** with phosphorus pentachloride and thionyl chloride can be rationalized by assuming that, in the reaction with phosphorus

(1) Visiting Fellow, 1966–1968.

(2) R. T. Li and Y. Sato, *J. Org. Chem.*, **33**, 3632 (1968).

(3) G. Adam and K. Schreiber, *Tetrahedron Lett.*, 923 (1965); G. Adam and K. Schreiber, *Tetrahedron*, **22**, 3581 (1966).

(4) We wish to thank Professor K. Schreiber for sending us a sample of their 3β-acetoxy-20α-chloro-5α-pregnane for comparison purposes. The infrared spectrum of their sample is similar to our compound **2a**, but with a slight contamination by compound **3a**. This probably accounts for the discrepancies in melting point and optical rotation of their compounds with those of our samples.

(5) (a) H. Hirschmann, F. B. Hirschmann, and A. P. Zala, *J. Org. Chem.*, **31**, 375 (1966); (b) H. Hirschmann and J. S. Williams, *J. Biol. Chem.*, **238**, 2305 (1963).

(6) M. Uskokovic, M. Gut, and R. I. Dorfman, *J. Amer. Chem. Soc.*, **82**, 3668 (1960).