The analytical sample was prepared by crystallization from methanol–water: mp 144.5–147.5°; $\alpha^{27}D$ −65°; λ_{max} 315 mμ (ε 7700); 5.89, 5.95, 6.15, 6.40 μ.

Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.45; H, 9.08.

17α-Δ⁴-Pregnene-6,20-dione (24α).—To a 366-mg sample of 17α-pregnan-5α-ol-6,20-dione (**23α**) in 3.3 ml of pyridine at 0° was added 0.5 ml of thionyl chloride. After 20 min the reaction mixture was diluted and treated as described above for the preparation of **25α** to give 266 mg of a yellow solid: λ_{max} 241 mμ (ε 5400, 80% **24α**). Chromatography on silica gel with 4% ether gave 193 mg of material which was crystallized from isopropyl ether–hexane to give 134 mg (42%) of 17α-Δ⁴-pregnene-6,20-dione (**24α**), mp 134–136°.

Crystallization from methylene chloride–hexane furnished the analytical sample: mp 134.5–136°; $\alpha^{30}D$ −49°; λ_{max} 240 mμ (ε 6800); 5.87, 5.96, 6.18 μ.

Anal. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.10; H, 9.62.

17α-Δ⁴-Pregnen-3β-ol-6,20-dione Acetate (26α).—A 117-mg sample of 17α-pregnane-3β,5α-diol-6,20-dione 3-acetate (**20α**) in 0.5 ml of pyridine at 0° was treated with 0.02 ml of thionyl chloride as described above. Work-up gave 109 mg of a white solid: λ_{max} 234 mμ (ε 4200, 60% **26α**). Chromatography on neutral alumina with 10% ether in benzene followed by crystallization gave 48 mg (43%) of 17α-Δ⁴-pregnen-3β-ol-6,20-dione acetate (**26α**), mp 198–202°.

Crystallization from isopropyl ether afforded the analytical sample: mp 207–208°; λ_{max} 233 mμ (ε 7000); ($CHCl_3$) 5.76, 5.88, 6.10 μ.

Anal. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 74.34; H, 8.74.

Registry Nos.—**7α**, 16649-44-8; **8α**, 16649-22-2; **9α**, 16703-88-1; **9β**, 16649-23-3; **10α**, 16649-24-4; **10β**, 16703-89-2; **11α**, 16649-45-9; **12α**, 16649-25-5; **12β**, 2723-04-8; **13β**, 16649-46-0; **14α**, 16649-27-7; **14β**, 16649-28-8; **15α**, 16649-29-9; **15β**, 16649-30-2; **17β**, 16649-31-3; **18β**, 16649-32-4; **19α**, 16720-14-2; **21α**, 16649-33-5; **21β**, 16703-90-5; **22α**, 16649-47-1; **22β**, 16649-34-6; **23α**, 16649-35-7; **23β**, 16649-36-8; **24α**, 16649-37-9; **24β**, 16703-91-6; **25α**, 16649-38-0; **25β**, 16649-39-1; **26α**, 16649-40-4; **27α**, 16649-41-5; **28α**, 16649-42-6; **29α**, 16649-43-7.

Acknowledgment—Financial assistance from the National Institutes of Health (Grant A-3943) and the Squibb Institute of Medical Research is gratefully acknowledged. A. P. B. also wishes to acknowledge receipt of a NASA Predoctoral Fellowship. The ORD curves were obtained through the courtesy of M. Marsh of Eli Lilly and Co. A stimulating discussion with Dr. P. Diassi is also acknowledged.

C-18-Functional Steroids. V.[1a] Synthesis of Androstane Derivatives[1b]

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Received March 12, 1968

Methods for the preparation of C-18 functional androstane and androstene derivatives from pregnane compounds are described. C-20-hydroxy steroidal 18-nitriles are dehydrated to give the Δ^17,20^-olefins. Hydroxylation with osmic acid followed by periodate cleavage gives the corresponding 17β-alcohols. Less successful is the Beckmann rearrangement of 20-oximes derived from 18-nitriles which gives rise to 17β-amines. Degradation of these amines gives rise to mixtures of alcohols and olefins.

In continuing our study of C-18-substituted steroids, the preparation of C-18-substituted androstane derivatives was required. Some of these compounds have been obtained by total synthesis,[2,3] by microbiological conversions,[4] from conessine,[5–7] from iodine–lead tetraacetate treatment of C-20 carboxamides followed by removal of C-20,[8] and from C-18-functional pregn-20-ones *via* a Baeyer–Villiger degradation.[9] The present compounds were made by application of the Barton reaction to pregnane derivatives. A few of the substances obtained recently have been prepared from conessine.[10]

The synthetic problem involved was that a side chain is needed for the functionalization step[11] but its removal is necessary to obtain the final product. Since a method applicable to 3-keto-Δ⁴ analogs was sought, the use of ozonolysis, etc., for side-chain oxidation was contraindicated. A mild method, involving elimination, osmylation, and periodate cleavage was therefore employed. Although the 3-keto-Δ⁴ system is capable of reacting with OsO_4,[12] the side chain was attacked selectively under the conditions we employed.

Treatment of 20α-hydroxy-5α-pregnane with nitrosyl chloride in pyridine solution gave the corresponding nitrite ester which on photolysis furnished the 18-oxime **1**.[10a] Dehydration with acetic anhydride afforded the nitrile **2**[10a] (Scheme I). Saponification of the ester followed by treatment with *p*-toluenesulfonyl chloride produced the tosylate **4**. Elimination formed the *trans*-olefin **5**, the stereochemistry of which was assigned on the basis of the nmr spectrum as in our previous work.[1a] Hydroxylation with OsO_4 furnished one predominant diol, presumably the 20β-hydroxy compound

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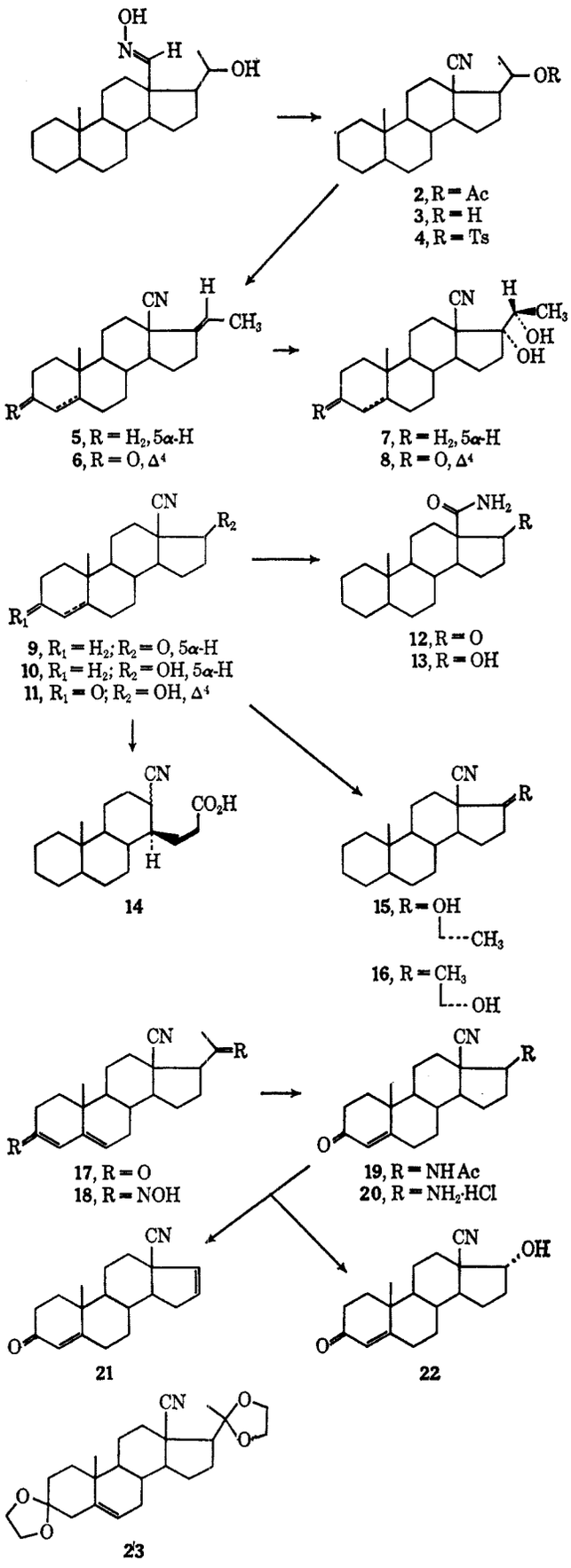
SCHEME I



7. Cleavage with periodic acid[13] gave the 17-ketone **9**, which on reduction with $LiAl(t\text{-}BuO)_3H$ afforded the 17β-ol **10**. The 17β configuration of the hydroxyl group was expected from the steric course of reduction and was further substantiated by the broad triplet[14] at 231 Hz due to the 17α proton in the nmr spectrum. The 17-methyl derivatives **15** and **16** were obtained by treatment of **9** with CH_3MgBr. The 17β-methyl configuration was assigned to **16**, in which deshielding of the methyl group by the nitrile function was evident in the nmr spectrum. Attempted hydrolysis of **9** with sodium hydroxide gave, *via* a reverse enolate condensation, a mixture of seco steroid C-13 epimers **14**, as shown by two angular methyl resonances and a D_2O exchangable proton resonance centered at 457 Hz in the nmr spectrum. A proton at 178 Hz, due to the 13-H which is geminal to the nitrile group, was also present. Successful hydrolysis of **9** to the 18-carboxamide **12** was achieved with sulfuric acid and reduction at C-17 gave **13**. The 3-keto-Δ^4 compounds **8** and **11** were obtained from **6**[1a] in analogous fashion.

A less fruitful removal of the side chain in the 3-keto-Δ^4 series involved the Beckmann rearrangement of C-20 oximes.[15]

Conversion of progesterone-18-nitrile[16] into the 3,20-bisethylenedioxy compound **23** was not a useful approach since the C-20 protecting group could not be hydrolyzed selectively. Enol ether formation at C-3 gave **17** which afforded the 20-oxime **18**. Beckmann rearrangement with $POCl_3$ gave in low yield the amide **19**, which on hydrolysis with concentrated HCl gave the amine **20**. Treatment of **20** with nitrous acid gave two products—one was the olefin **21** as shown by the nmr spectrum. The second compound, **22**, was shown to be a 17α-alcohol by nmr spectroscopy. The signal due to the 17β proton[14] was a broad doublet rather than a triplet as expected for a 17α proton. Moreover, the signal appeared 30 Hz downfield from the expected value for the 17β-hydroxy compound due to shielding by the nitrile group (*cf.* **11**). The course of the deamination differs in 18-nonfunctional steroids[17] but is similar in simple cyclopentylamines.[18]

Experimental Section[19]

18-Oximino-5α-pregnan-20α-ol (1).—Nitrosyl chloride was bubbled into a stirred, ice-cold solution of 8.5 g of 20α-hydroxy-5α-pregnane in pyridine, until a greenish brown color persisted. The resulting suspension was stirred for 5 min and poured into ice–water. The resulting precipitate was collected giving 9.0 g of 20α-hydroxy-5α-pregnane nitrite: ν_{max}^{KBr} 1645, 1605 cm^{-1}; nmr 44 (18-H_3), 48 (19-H_3), 84 (21-H_3, J = 6.5 Hz), 328 Hz (20-H, broad). The nitrite ester was air dried, dissolved in 200 ml of toluene, and subjected to photolysis for 6 hr with a 200-W

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(19) Melting points were determined with a Thomas–Hoover apparatus equipped with a corrected thermometer. Infrared spectra were obtained with a Beckman IR-8 or Perkin-Elmer 337 instrument. Microanalyses were performed by the Microanalytical Department, University of California at Berkeley. Optical rotations were obtained in a 0.5-dm tube with a Rudolph photoelectric polarimeter. Nmr spectra were obtained at a field strength of 60 MHz on samples in deuteriochloroform solution on a Varian A-60 or A-60A instrument, using tetramethylsilane as internal standard. When only small amounts of sample were available, a Varian C-1024 computer was used for time averaging.

medium-pressure mercury lamp equipped with a Pyrex filter. The solid which precipitated during the photolysis was separated to give 1 g of product. A second crop, mp 187–191°, obtained by concentration and washing with hexane, weighed 3 g. Recrystallization from benzene–hexane gave pure material: mp 198–200° (lit.[10a] mp 197–198° when prepared in another way); ν_{max}^{KBr} 3320, 3175, 3080 cm^{-1}; nmr 45.5 (19-H$_3$), 71 (21-H$_3$, J = 6.0 Hz), 238 (20-H, broad), 446 Hz (18-H).

20α-Hydroxy-5α-pregnane-18-nitrile Tosylate (4).—The product was obtained by treatment of 20α-hydroxy-5α-pregnane-18-nitrile[10] with p-toluenesulfonyl chloride in pyridine. Recrystallization from hexane–benzene gave the analytical sample: mp 133–136°; $[\alpha]^{20}D$ −67° (c 0.006, $CHCl_3$); nmr 48 (19-H$_3$), 83 (21-H$_3$) (J = 6.0 Hz), 287 (20-H, broad), 146 Hz (CH$_3$ of p-tosyl group).

Anal. Calcd for $C_{28}H_{39}NO_3S$: C, 71.60; H, 8.37; N, 2.98; S, 6.82. Found: C, 71.47; H, 8.11; N, 2.99; S, 6.74.

5α-Pregn-17-ene-18-nitrile (5).—A solution of 1.7 g of **4** in 50 ml of pyridine was heated under reflux for 3 days, poured into ice–water, and filtered. The precipitate (0.5 g) was purified by preparative tlc on silica gel to give 0.2 g of **5**, and 0.25 g of recovered **4**. The filtrate was evaporated to recover an additional 1.1 g of **4**. Compound **5** was recrystallized from methylene chloride to give the analytical sample: mp 90–91°; $[\alpha]^{20}D$ −38° (c 0.34, $CHCl_3$); nmr 50 (19-H$_3$), 96 Hz (21-H$_3$, J = 6.5 Hz).

Anal. Calcd for $C_{21}H_{31}NO$: C, 84.79; H, 10.50; N, 4.92. Found: C, 85.07; H, 10.42; N, 4.92.

17α,20β-Dihydroxy-5α-pregnane-18-nitrile (7).—A solution of 0.5 g of osmium tetroxide in 10 ml of anhydrous ether was added to a solution of 0.4 g of **5** in 40 ml of anhydrous ether. The solution turned black on mixing and was left for 48 hr at 27°. After evaporation of the solvent, the residue was dissolved in 50 ml of ethanol and mixed with a solution of 2.5 g of sodium sulfite in 120 ml of water. It was refluxed for 2 hr and filtered while hot. The residue was washed with a large quantity of hot ethanol and then with ether. The combined filtrate and washings were taken to dryness and the solid was treated with water and filtered. After washing with water, the solid was purified by preparative tlc to give 0.3 g of **7**: mp 172–173°; $[\alpha]^{20}D$ +41° (c 0.11, $CHCl_3$); nmr 49.5 (19-H$_3$), 73 (21-H$_3$, J = 6.0 Hz), 260 Hz (20-H, quartet, J = 6.0 Hz).

Anal. Calcd for $C_{21}H_{33}NO_2$: C, 76.09; H, 10.03; N, 4.23. Found: C, 76.24; H, 9.93; N, 4.31.

17α,20β-Dihydroxypregn-4-en-3-one-18-nitrile (8).—A solution of 0.5 g of 6[18] in 40 ml of anhydrous ether was hydroxylated with OSO_4 as described for **7**. Purification by preparative tlc gave 0.3 g of **8**: mp 241–242° after recrystallization from hexane–benzene–ethanol; $[\alpha]^{20}D$ +89° (c 0.32, $CHCl_3$); ν_{max}^{KBr} 3520, 3415, 2225, 1655, 1620 cm^{-1}; nmr 74 (19-H$_3$), 74 (21-H$_3$, doublet, J = 6.0 cps), 261 (20-H$_3$, quartet, J = 6.0 Hz), 345 Hz (4-H).

Anal. Calcd for $C_{21}H_{29}NO_3$: C, 73.44; H, 8.51; N, 4.08. Found: C, 73.26; H, 8.27; N, 4.13.

17-Oxo-5α-androstane-18-nitrile (9).—To a solution of 0.25 g of **7** in 50 ml of ethanol, there was added 10 ml of 10% aqueous $HIO_4 \cdot 2H_2O$. The solution was stirred with a magnetic stirrer for 12 hr and evaporated to dryness. The residue was washed with water and filtered giving 0.22 g of material showing one spot on tlc. Recrystallization from hexane gave the analytical sample: mp 139–141°; $[\alpha]^{20}D$ +42° (c 0.26, $CHCl_3$); ν_{max}^{KBr} 2230, 1770 cm^{-1}; nmr 51 Hz (19-H$_3$).

Anal. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.53; N, 4.91 Found: C, 79.85; H, 9.38; N, 5.06.

17β-Hydroxy-5α-androstane-18-nitrile (10).—A stirred solution of 0.18 g of **9** in anhydrous ether–tetrahydrofuran was cooled in ice and 0.8 g of LiAl(t-BuO)$_3$H was added. After 3 hr under ice cooling the excess reagent was decomposed with 5% acetic acid and the solution was extracted with ether. Evaporation of the solvent gave 0.15 g of solid which showed mainly one spot on tlc. Purification with preparative tlc and recrystallization from hexane gave the analytical sample: mp 180–183°; $[\alpha]^{20}D$ +13° (c 0.2, $CHCl_3$) (lit.[10b] mp 180°; $[\alpha]D$ +7° when prepared in another way); ν_{max}^{KBr} 3280 (broad), 2235 cm^{-1}; nmr 50 Hz (19-H$_3$).

Anal. Calcd for $C_{19}H_{29}NO$: C, 79.39; H, 10.17; N, 4.87. Found: C, 80.06; H, 9.49; N, 4.72.

17β-Hydroxyandrost-4-en-3-one-18-nitrile (11).—The product from periodate cleavage (*cf.* compound **9**) of **8** was purified by preparative tlc. A stirred ice-cold solution of 0.08 g of the cleavage product and 0.5 g of LiAl(t-BuO)$_3$H in 2 ml of tetrahydrofuran was stirred for 3 hr. The excess reagent was decomposed with 5% acetic acid and the solution was extracted with ether. The residue obtained on evaporation of ether showed mainly one tlc spot. It was dissolved in 20 ml of chloroform and stirred with 1 g of MnO_2 for 18 hr. The MnO_2 was filtered off and washed with chloroform several times. The combined chloroform solution was evaporated to dryness. The residue showed mainly one spot on tlc. Purification by preparative tlc gave 0.07 g of **11**: mp 193–194°; $[\alpha]^{20}D$ +149° (c 0.2, $CHCl_3$) (lit.[10b] mp 188°; $[\alpha]D$ +5° when prepared in another way).

Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 75.98; H, 8.23; N, 4.90.

17-Oxo-5α-androstan-18-carboxamide (12).—To 0.1 g of **9** there was added 1.5 ml of concentrated H_2SO_4 and 0.2 ml of water. This mixture, under nitrogen, was heated in an oil bath kept at 87° for 2.5 hr. It was cooled and poured into ice–water. The resulting precipitate was filtered and washed with water several times. Purification by preparative tlc gave 0.07 g of **12**: mp 167–168°; $[\alpha]^{20}D$ −38° (c 0.2, $CHCl_3$); ν_{max}^{KBr} 3500, 3460, 3400, 3300, 3180, 1740, 1690, 1630, 1600 cm^{-1}; nmr 47 Hz (19-H$_3$).

Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.38; H, 9.48; N, 4.83.

17β-Hydroxy-5α-androstane-18-carboxamide (13).—The product, obtained from LiAl(t-BuO$_3$)H reduction (*cf.* compound **11**) of 0.03 g of **12**, was purified by preparative tlc followed by recrystallization from hexane–benzene giving material of mp 211–213°; $[\alpha]^{20}D$ −11° (c 0.046, $CHCl_3$); ν_{max}^{KBr} 3450–3150 (broad), 1655, 1605 cm^{-1}; nmr 46 Hz (19-H$_3$).

Anal. Calcd for $C_{19}H_{31}NO_2$: N, 4.59. Found: N, 4.68.

13,17-Seco-5α,13ξ-androstan-17-oic Acid 18-Nitrile (14).—A solution of 0.1 g of **9** and 0.1 g of KOH in methanol was refluxed under nitrogen for 18 hr. On acidification with acetic acid, solid material precipitated which was purified by preparative tlc. Recrystallization from hexane–benzene gave the analytical sample: mp 166–168°; $[\alpha]^{20}D$ −48° (c 0.14, $CHCl_3$); nmr 43, 47.5 (both due to 19-H$_3$), 457 Hz (COOH, disappeared on addition of D_2O).

Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.09; H, 9.42; N, 4.67.

17β-Hydroxy-17α-methyl-5α-androstane-18-nitrile (15) and 17α-Hydroxy-17β-methyl-5α-androstane-18-nitrile (16).—To a solution of 0.1 g of **9** in 5 ml of anhydrous tetrahydrofuran and 5 ml of anhydrous ether, there was added slowly 3 ml of an ethereal 3 M methylmagnesium bromide solution. After refluxing for 10 hr, the reaction mixture was poured into ice–water and acidified with HCl to pH 1. It was extracted with ether and the combined extract was washed with water until the washings were neutral. Evaporation of the solvent gave a solid which showed (three) spots on tlc. Purification by preparative tlc gave, as the major product, 0.04 g of **15**: mp 169–170°; $[\alpha]^{20}D$ −13° (c 0.19, $CHCl_3$); ν_{max}^{KBr} 3455, 2240 cm^{-1}; nmr 50.5 (19-H$_3$); 75 Hz (17α-CH$_3$).

Anal. Calcd for $C_{20}H_{31}NO$: C, 79.68; H, 10.36; N, 4.65. Found: C, 79.73; H, 10.45; N, 4.75.

A second product, weighing 0.02 g, was identified as **16**: ν_{max}^{KBr} 3480, 2235 cm^{-1}; nmr 50 (19-H$_3$), 90.5 Hz (17β-CH$_3$).

Anal. Calcd for $C_{20}H_{31}NO$: C, 79.68; H, 10.36; N, 4.65. Found: C, 79.35; H, 10.13; N, 4.97.

A very small amount of **9** was recovered.

20-Oxopregna-3,5-diene-18-nitrile 3-Methyl Ether (17).—A solution of 2.0 g of 3,20-dioxopregn-4-ene-18-nitrile[16] and 0.10 g of p-toluenesulfonic acid in 20 ml of 2,2-dimethoxypropane and 20 ml of dimethylformamide was heated under reflux for 6 hr. After cooling, the solution was made alkaline with dilute NaOH solution and poured into ice–water. Recrystallization of the precipitated product from methylene chloride gave 1.8 g of sample: mp 202–207°; $[\alpha]^{20}D$ −51° (c 1, $CHCl_3$); nmr 60 (19-H$_3$), 132 (21-H$_3$), 214 Hz (3-CH$_3$O).

Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 76.97; H, 8.51; N, 4.26.

20-Oximinopregn-3,5-diene-18-nitrile 3-Methyl Ether (18).—A solution of 1.2 g of **17** and 1.2 g of hydroxylamine hydrochloride in pyridine was kept for 18 hr at 27° and poured into an ice–water mixture, and the resulting precipitate was collected. Recrystallization resulted in 0.90 g of analytical sample: mp 204–205°; $[\alpha]^{20}D$ −103° (c 1, $CHCl_3$); ν_{max}^{KBr} 3440, 3200, 2225, 1655, 1630 cm^{-1}; nmr 60.5 (19-H$_3$), 119 (21-H$_3$), 215 Hz (3-CH$_3$O).

Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.23; H, 8.36; N, 8.07.

3-Oxo-17β-acetamidoandrost-4-ene-18-nitrile (19.)—A solution of 0.5 g of **18** in 2.0 ml of pyridine was cooled in an ice bath and 1 ml of cold phosphorus oxychloride was added dropwise, while maintaining the temperature below 15°. After 3 hr, the mixture was poured into cold dilute HCl. This solution was extracted with methylene chloride and the combined extracts were washed with water and dried (Na_2SO_4). When the gummy residue from evaporation of the dried solvent was chromatographed on alumina, 0.20 g of 3,20-dioxopregn-4-ene-18-nitrile was recovered together with 0.06 g of **19**: mp 294–296°; $[\alpha]^{20}D$ +15° (*c* 1, $CHCl_3$); ν_{max}^{KBr} 3340, 2225, 1685, 1663, 1610, 1535 cm^{-1}; nmr 74 (19-H_3), 123 (CH_3CO–), 257 (17α-H, two broad peaks), 368 Hz (17β-NH, two broad peaks).

Anal. Calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 73.84; H, 8.09; N, 8.45.

17β-Aminoandrost-4-en-3-one-18-nitrile Hydrochloride (20).—To a solution of 0.27 g of **18** in 2 ml of ethanol and a small amount of tetrahydrofuran, there was added 2 ml of concentrated HCl. The solution was refluxed for 24 hr and poured into ice–water. The precipitate which formed (0.1 g) was filtered and shown to be starting material. The filtrate was evaporated to dryness under vacuum giving 0.15 g of almost pure **20**. Recrystallization from methylene chloride gave a hygroscopic sample: mp 240°; $[\alpha]^{20}D$ +90° (*c* 0.082, $CHCl_3$).

Anal. Calcd for $C_{19}H_{29}N_2OCl$: N, 8.37; Found: N, 8.60.

Androst-4,16-dien-3-one-18-nitrile (21) and 17α-Hydroxyandrost-4-en-3-one-18-nitrile (22).—To a stirred, ice-cold solution of 0.15 g of **20** in 2 ml of 50% acetic acid, there was added, dropwise, a solution of 0.5 g of $NaNO_2$ in 2 ml of 50% acetic acid. After 18 hr at 27° the solution was made alkaline and extracted with ether. The ethereal extract was mixed with 2 ml of 5% methanolic KOH solution and stirred for 0–5 hr. After addition of water and back extraction with ether, the combined ethereal extracts were evaporated to dryness giving solid material. Purification by preparative tlc resulted in two products. The major product (0.04 g) was shown to be **21**: mp 128–130° after recrystallization from hexane–benzene; $[\alpha]^{20}D$ +224° (*c* 0.19, $CHCl_3$).

Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.82; H, 8.16; N, 5.19.

The minor product (25 mg) was **22** as indicated by the doublet of the 17β proton. Recrystallization from hexane–benzene gave the analytical sample: mp 183–185°.

Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.33; H, 7.67; N, 5.89.

3,20-Bismethylenedioxypregn-5-ene-18-nitrile (23).—3,20-Dioxopregn-4-ene-18-nitrile[16] (0.80 g) was dissolved in 15 ml of hot ethylene glycol. The solution was acidified with 0.10 g of *p*-toluenesulfonic acid and very slowly distilled at 1.5 mm at 70° for 3 hr. The resulting suspension was made alkaline with a small amount of methanolic KOH and poured into an excess of ice-water. Recrystallization of the preciptated product from methylene chloride–hexane gave the analytical sample: mp 195–197°; $[\alpha]^{20}D$ −32° (*c* 1, $CHCl_3$); nmr 64 (19-H_3), 79 (21-H_3), 235 (20-ketal-H_4, slightly broad), 241 Hz (3-ketal-H_4).

Anal. Calcd for $C_{25}H_{35}NO_4$: C, 72.61; H, 8.53; N, 3.39. Found: C, 72.86; H, 8.26; N, 3.68.

Registry No.—**1**, 14418-17-8; 20α-hydroxy-5α-pregnane nitrite, 16797-50-5; **4**, 16778-28-2; **5**, 16778-29-3; **7**, 16778-30-6; **8**, 16778-31-7; **9**, 13583-64-7; **10**, 13583-63-6; **11**, 16778-34-0; **12**, 16797-45-8; **13**, 16797-46-9; **14**, 16797-49-2; **15**, 16777-99-4; **16**, 16778-00-0; **17**, 16778-01-1; **18**, 16778-02-2; **19**, 16778-03-3; **20**, 16778-04-4; **21**, 16797-47-0; **22**, 16778-05-5; **23**, 16778-06-6.

The Action of Bromine on a Chol-7-enic Acid Derivative

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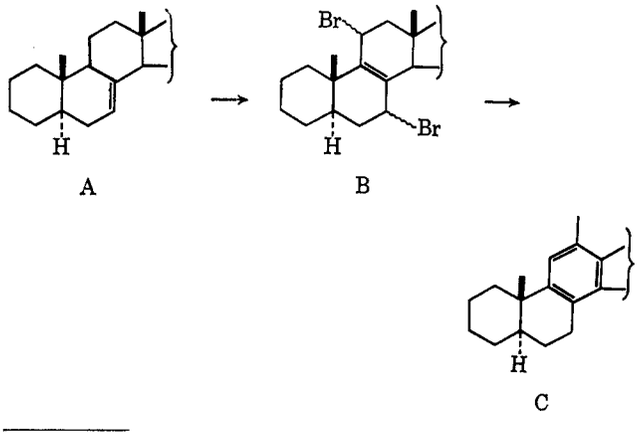
Received March 7, 1968

The behavior of a ring A/B *cis*-fused steroid unsaturated at C-7 toward bromine differs from that of the corresponding unsaturated ring A/B *trans*-fused steroids. On treatment with bromine, methyl 3α-ethoxycarbonyloxychol-7-enate yields methyl 14ξ-bromo-3α-ethoxycarbonyloxychol-7-enate. This allylic halide on dehydrobromination with silver acetate or alumina gives methyl 3α-ethoxycarbonyloxychola-7,14-dienate, and on debromination with zinc gives a mixture of methyl 3α-ethoxycarbonyloxychol-7-enate and methyl 3α-ethoxycarbonyloxychol-8-enate.

It has been shown[1] that bromine reacts with Δ^7-unsaturated steroids having rings A/B *trans*-fused (general part structure A) to yield, as major products, the 7,11-dibromo-Δ^8-unsaturated derivatives (part structure B) which are readily transformed into ring C benzenoid steroids (part structure C).[2,3] To ascertain if this route is feasible for the preparation of ring C benzenoid steroids in which rings A/B are *cis*-fused, we have examined the action of bromine on a Δ^7-unsaturated steroid derived from cholic acid.



A B C

Methyl cholate was selectively and quantitatively converted into the 3-ethoxycarbonyl derivative (**1**)[4] which was then dehydrated by the action of phosphorus oxychloride in pyridine to yield the known $\Delta^{7,11}$-diene (**2**)[5,6] (Scheme I). It has been reported[6] that the diene (**2**) undergoes selective hydrogenation of the Δ^{11}-ethylenic bond with platinum catalyst in acetic acid solution to yield the desired ester, methyl 3α-ethoxycarbonyloxychol-7-enate (**4**). In our hands, however, these condi-

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