Ethynylation of 17α-Hydroxypregnenolone 3-Acetate. Stereochemistry and Acid-Catalyzed Rearrangement of the Reaction Product[1]

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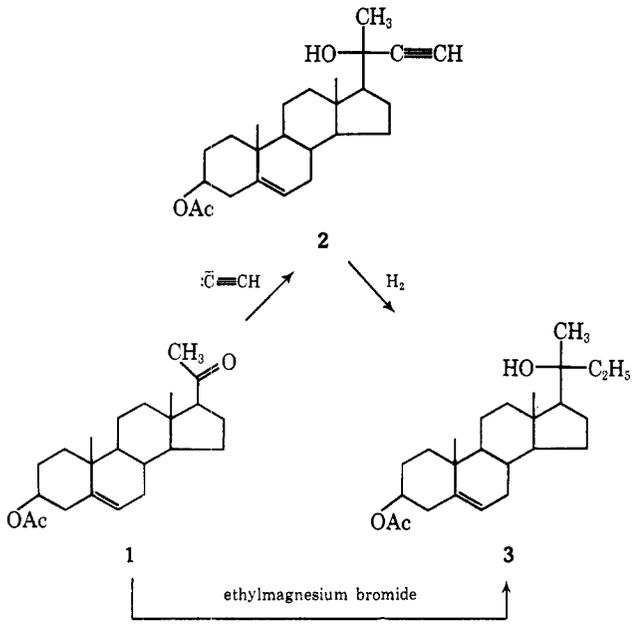
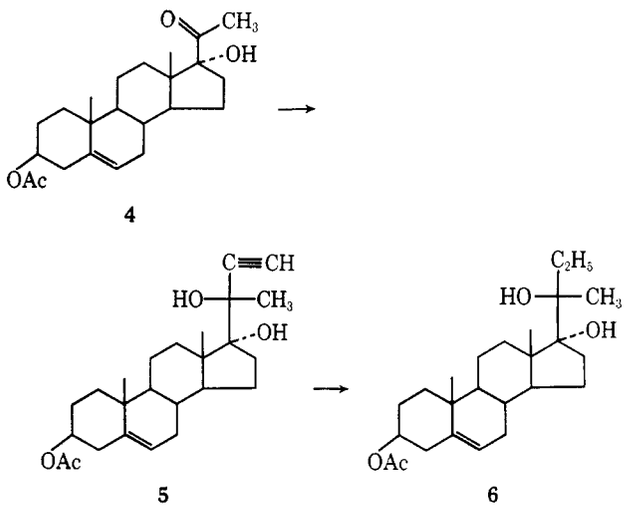
The ethynylation of 17α-hydroxypregnenolone 3-acetate (**4**) in the presence of lithium amide in liquid ammonia has been found to give only one product, **5**. The absolute configuration at C-20 of **5** has been determined by catalytic reduction to 20β-ethylpregn-5-ene-3β,17α,20α-triol (**6**), which has been independently synthesized by condensation of 17α-hydropregnenolone 3β-acetate with ethylmagnesium bromide. The synthesis of the 20-diastereoisomer of **6** by condensation of methylmagnesium bromide with the 21 homolog **7** of 17α-hydroxypregnenolone 3-acetate is also reported. The acetylenic glycol **5** underwent a Wagner–Meerwein rearrangement on treatment with formic acid or thionyl chloride. The structure and stereochemistry of the resulting D-homo ketone **17** has been determined. The reaction of **5** with thionyl chloride in the present of pyridine, however, gave a cyclic sulfite, **15**.

In 1959 Sondheimer, *et al.*,[2] showed that the ethynylation of 3β-acetoxypregn-5-en-20-one (**1**) with sodium acetylide in liquid ammonia was completely stereospecific, in contrast to the reduction of **1** with lithium aluminum hydride[3] which gives a 2:1 mixture of the two possible diastereoisomers. Subsequently we[4] repeated the above condensation and our results were in agreement with the observations of Sondheimer, *et al.*[2] Mijares, *et al.*,[5] have similarly observed that the reaction of **1** with isohexylmagnesium bromide is also stereospecific.



We have now carried out the ethynylation of **4**, which is the 17α-hydroxy derivative of **1**, and observed that only one (**5**) of the two possible diastereoisomers was formed. That **5** had the expected structure was deduced from the following observations. The infrared spectrum showed the presence of a –C≡CH group and periodate oxidation of **5** and its reduction product **6** gave androstenolone acetate showing, thereby, the presence of the intact steroid nucleus and a glycol group attached at the 17 position.



The reduction of a carbonyl group by metal hydride has much in common mechanistically with its alkylating reduction by the Grignard reagent or the acetylide ion. Therefore, Sondheimer, *et al.*,[2] assigned the 20α-ethynyl-20β-hydroxypregn-5-ene structure, **2**, to their product in analogy with the stereochemistry[3] of the major product (a 20β-hydroxypregnene derivative) formed by lithium aluminum hydride reduction of **1**. We have now confirmed their stereochemical assignment by identifying the catalytic reduction product of **2** as 3β-acetoxy-20α-ethylpregn-5-en-20β-ol (**3**) (20*S* configuration). An authentic sample of **3** was prepared by the condensation of ethylmagnesium bromide with **1**. A current report shows[6] that the tertiary alcohols formed by the stereospecific addition of Grignard reagents to pregn-5-en-20-one have the 20*S* configuration. The C-20 epimer (20*R*) of **3** (**3a**) was also synthesized by the condensation of methylmagnesium bromide with **10a**, obtained by catalytic reduction of the 16–17 double bond of **10** (described in a later section). It was

(1) Supported by the Atomic Energy Commission Contract AT(30-1)918 and Grant AM-03419 from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health.

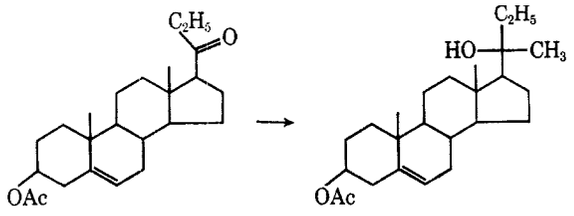
(2) F. Sondheimer, N. Danieli and Y. Mazur, *J. Org. Chem.*, **24**, 1278 (1959).

(3) W. Klyne and E. Miller, *J. Chem. Soc.*, 1972 (1950); J. K. Norymberski and G. F. Woods, *ibid.*, 3426 (1955).

(4) N. K. Chaudhuri and M. Gut, *J. Amer. Chem. Soc.*, **87**, 3737 (1965).

(5) A. Mijares, D. I. Cargill, J. A. Glassel, and S. Lieberman, *J. Org. Chem.*, **32**, 810 (1967).

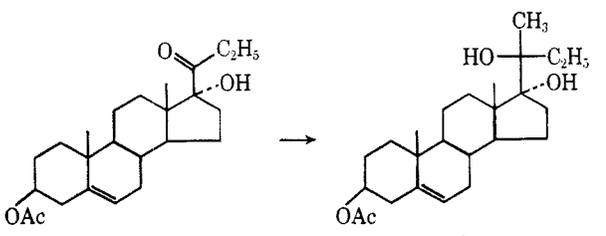
(6) N. K. Chaudhuri, J. G. Williams, R. Nickolson, and M. Gut, *ibid.*, **34**, 3759 (1969).



10a 3a

found to be different from the catalytic reduction product of **2**.

The absolute configuration of **5** at C-20 may be deduced by analogy with the stereochemistry of the addition of Grignard reagents to **4**. The conclusion will not, however, be unequivocal in view of the following considerations. The conformation of the side chain of **4** may be best described[7] as in A (Figure 1) to allow for the marked hydrogen bonding[8] between the 20-carbonyl and the 17α-hydroxyl groups. Rakhit and Engle[7] have shown that, during the course of the reduction with lithium aluminum hydride, a shift to the conformation B occurs by a rotation around the 17–20 bond to accommodate the metal atom between the two oxygen atoms and the result is the formation of a 17α,20α-dihydroxypregnene derivative. The stereochemistry (20*R*) of the tertiary alcohols formed by the addition of Grignard reagents to 17α-hydroxypregn-5-en-20-one may also be explained by a similar conformational change during the Grignard reaction, but, since the ethynylation reaction is carried out under a strongly basic condition, the dipolar interaction between the two oxygen atoms may drive the side chain into the conformation C which could lead to the formation of an alcohol having the opposite configuration. Hence we sought to provide an experimental proof for the absolute configuration of **5** at C-20. The ethynyl group of **5** was, therefore, catalytically reduced to an ethyl group and the two diastereoisomeric 20-ethyl-20-hydroxy compounds were synthesized for correlation studies. The 20*R* epimer **6** was prepared by the condensation of ethylmagnesium bromide with **4** and the 20*S* epimer **8** by the condensation of methylmagnesium bromide with **7**. The confirmation of the ring structures **6** and

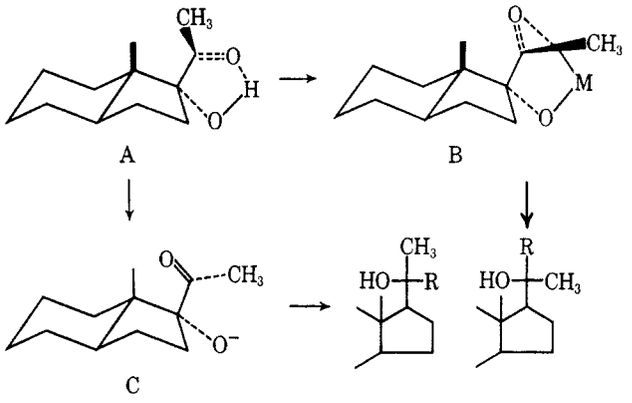


7 8

8 was obtained by periodate oxidation to androstenolone acetate. The most striking difference between these two 20 epimers, **6** and **8**, was in the position of the 21-methyl resonance peaks in their nmr spectra as noted previously by us[6] for similar epimeric pairs. The 21-methyl peak of **8** (20*S*) appeared 4 cps downfield relative to that of **6** (20*R*). The compound obtained by reduction of the ethynyl compound **5** was found to be identical with **6** and different from **8** showing thereby that the stereochemistry

(7) S. Rakhit and C. R. Engel, *Can. J. Chem.*, **40**, 2163 (1962).

(8) R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Amer. Chem. Soc.*, **74**, 2828 (1952).



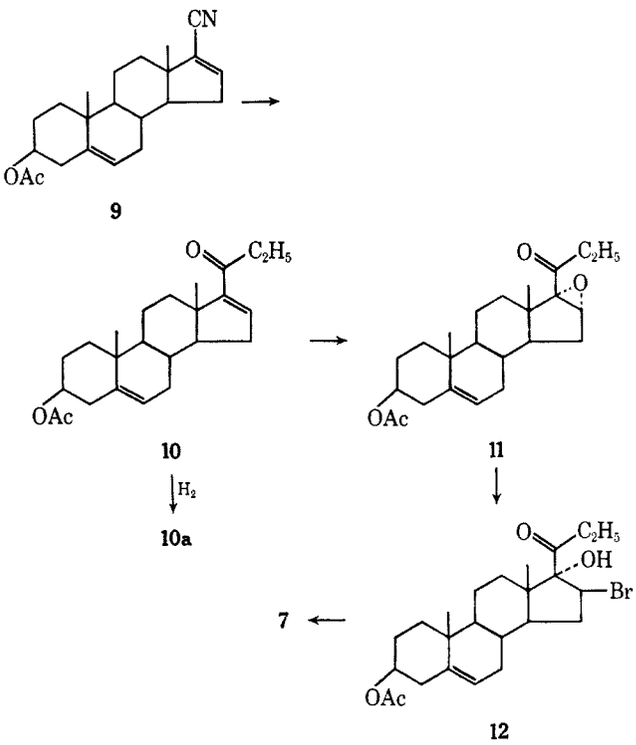
A B C

Figure 1.

of the ethynylation of **4** was indeed the same as that of the addition of Grignard reagents to **4**.

The 17α-hydroxy ketone **7** required for the above preparation was synthesized by the method of Julian, *et al.*,[9] from the unsaturated nitrile **9** as outlined in Scheme I. On reaction with ethylmagnesium bromide,

SCHEME I



9 10 11 10a 12 7

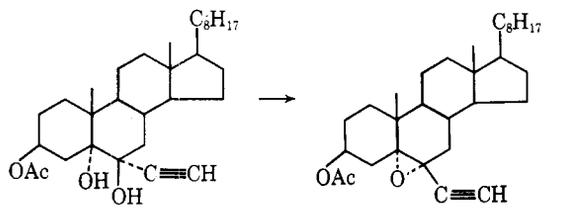
9 gave the α,β-unsaturated ketone **10** which was then epoxidized with alkaline hydrogen peroxide to give the 16,17-oxido ketone **11**. The oxido group of **11** was opened with hydrogen bromide to give the bromhydrin **12** which was then debrominated by catalytic hydrogenolysis in the presence of ammonium acetate[9] to give **7**.

In an attempt to invert the configuration at C-20 of the ethynyl glycol **5** *via* the formation and opening of a 17–20 oxide, **5** was treated with thionyl chloride both under SN2 (in the presence of pyridine) as well as SNi (absence of pyridine) conditions. However, in contrast to the reported[10] formation of the epoxide **14**

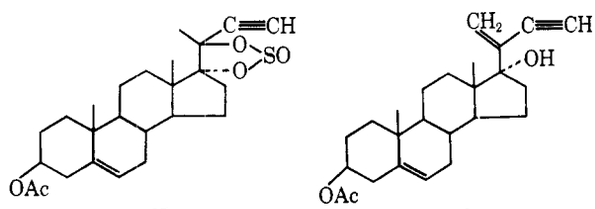
(9) P. J. Julian, E. W. Meyer, W. J. Karpel, and I. R. Waller, *ibid.*, **72**, 5145 (1950).

(10) B. Ellis, V. Petrow, and B. Waterhouse, *J. Chem. Soc.*, 2596 (1960).

from the acetylenic glycol **13** no epoxide was obtained under these conditions. Instead, in the presence of pyridine, the cyclic sulfite **15** was formed in almost quantitative yield. The structural assignment of **15** is



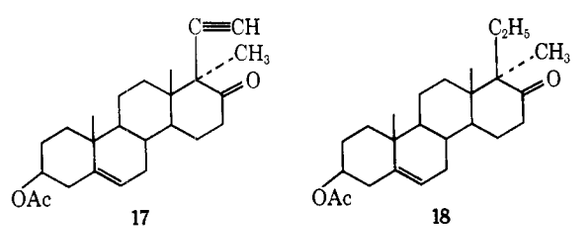
13 **14**



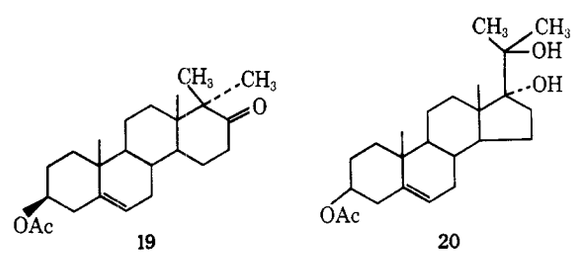
15 **16**

based on its infrared spectrum (presence of —C≡CH, absence of OH), elemental analysis (presence of sulfur) and mass spectrum which showed three very strong peaks at *m/e* 386 (M − HOAc), 322 (386 − SO_2) and 64 (SO_2). Chemical evidence in support of the structure **15** was obtained from the fact that the sulfite **15** was stable to acids but very readily hydrolyzed to the acetylenic glycol **5** under basic conditions (basic alumina).

The reaction with thionyl chloride in the absence of base was slow and did not go to completion even in 3 days. The minor product was easily identified by ir, uv, and nmr spectroscopy as the conjugated enyne **16** resulting from indirect dehydration of **5**. The major product was found, by infrared spectroscopy, to be a ketonic compound having an ethynyl group and no hydroxyl group. This ketone was readily formed in a much better yield when **5** was treated with formic acid. A D-homo-17-keto structure, **17**, resulting from a Wagner–



17 **18**



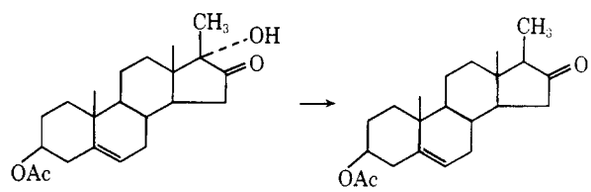
19 **20**

Meerwein rearrangement of **5** by the movement of the 13–17 bond seemed quite reasonable by analogy with the acid-catalyzed rearrangement[11] of the glycol **20** to the D-homo ketone **19**. The ketonic rearrangement product **17** and its reduction product **18** gave a positive Zimmerman test showing thereby the presence of a $-COCH_2-$ group and their infrared spectra showed a carbonyl band at 5.8 μ in agreement with their 17-keto structures and thus ruled out the alternative 17a-keto structures which usually have the carbonyl band shifted to 5.95–5.88 μ.[12] The 17-keto structures **17** and **18** were confirmed and their stereochemistry at the 17a position was established by studying the chemical shifts of the nmr signals of the various methyl groups of the three ketones **18**, **19**, and **22** (Table I). An au-

TABLE I

Compound	19-Me	18-Me	17a-Me (a)	17a-Me (e)
17	60	59	89	
18	59.5	44	68.5	
19	60	45.5	68.5	58
22	60	41		57

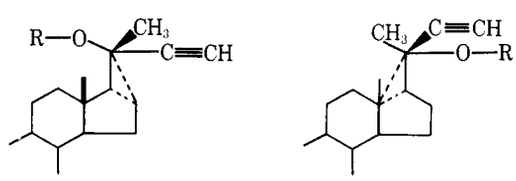
thentic sample of **22** was prepared by treating[13] **21** with phosphorus tribromide, followed by reduction of the bromo ketone with zinc and acetic acid to give **22**.



21 **22**

The 17a-methyl group of **22** must be equatorial since it was prepared under enolizable conditions. The nmr signal due to this equatorial secondary methyl group appeared at 57 cps (J = 6 cps) and therefore the 58-cps peak of **19** must be assigned to the 17a-equatorial methyl group and its 68.5-cps peak to the 17a-axial methyl group. Since the 17a-methyl peak of **18** appeared at 68.5 cps it must be axial. The 17a-ethyl group of **18** and hence the ethynyl group of **17** must, therefore be equatorial and β oriented.

Mechanistic consideration of the expansion of the D ring of **5** also leads to the same conclusion regarding the structure and stereochemistry of the rearrangement product **17**. In the transition state D (R = chlorosulfite or formate) required for the migration of the 16–17 bond, there is considerable steric interaction of



D E

the 1:3 diaxial type between the 21-methyl and 13-methyl group, but, owing to the linear nature of the ethynyl group, no such interaction exists in the transition state E (R = chlorosulfite or formate) required for the migration of the 13–17 bond. Steric factors are thus in favor of the migration of the 13–17 bond which is also favored by the electronic factors. The D-homo-annulation would, therefore, occur by the migration of

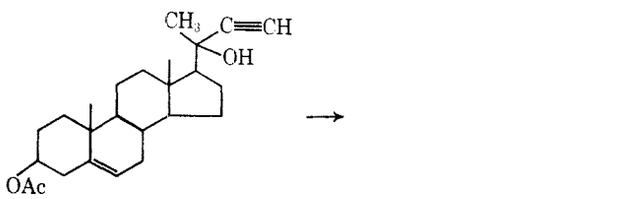
(11) M. Uskoković, M. Gut, and R. I. Dorfman, *J. Amer. Chem. Soc.*, **81**, 4561 (1959).

(12) D. K. Fukushima, S. Dobriner, M. S. Heffler, T. H. Kritchevsky, F. Herling, and G. Roberts, *ibid.*, **77**, 6585 (1955).

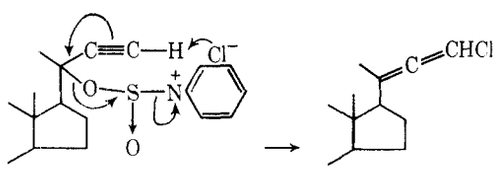
(13) L. Ruzicka and H. F. Meldahl, *Helv. Chim. Acta*, **22**, 421 (1939).

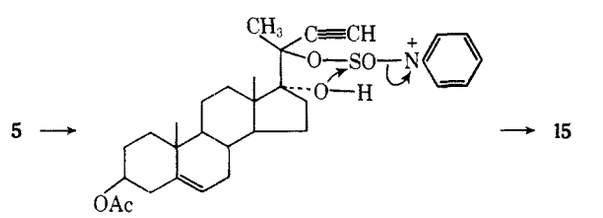
the 13–17 bond to give **17** in which the ethynyl group is β oriented.

It may be noted here that unlike the acetylenic carbinol[4] **23** and other tertiary acetylenic carbinols[14] the acetylenic glycol **5** did not give any chloroallene on reaction with thionyl chloride in the presence of pyridine. The formation of the chloroallene from a tertiary ethynylcarbinol takes place by the nucleophilic attack of a chloride ion on the ethynyl carbon and fission of the carbon–oxygen bond of the pyridinium sulfite. However, in the case of the acetylenic glycol **5**, the

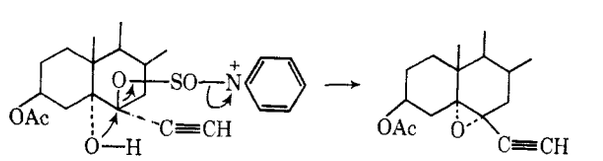


23





participation of the neighboring hydroxyl group readily leads to the formation of a five-membered cyclic sulfite **15** by a nucleophilic attack on the sulfur atom. In the case of the glycol **13** however, the 5α,6β-*trans*-diaxial stereochemistry is not favorable for the participation of the 5α-hydroxyl group to form a cyclic sulfite. Rather, the fission of the carbon–oxygen bond of the intermediate 6β-sulfite is preferred, by the nucleophilic attack of the 5α-hydroxyl on the 6 carbon atom to form a 5,6-oxide.



Experimental Section

Melting points are uncorrected. Nmr spectra were obtained in deuteriochloroform solution on a 60-Mc Varian Associates DA-60 spectrometer. Mass spectra were determined on a Varian Associates M-66 spectrometer. Ir spectra were determined as KBr pellets.

3β-Acetoxy-20α-ethylpregn-5-en-20β-ol (2).—This compound was prepared by the procedure of Sondheimer, *et al.*[2]

3β-Acetoxy-20α-ethylpregn-5-en-20β-ol (3). A. By Catalytic Reduction of 2.—To a solution of 250 mg of **2** in 20 ml of ethyl acetate was added 50 mg of 10% palladium-on-charcoal catalyst and the mixture was stirred in an atmosphere of hydrogen. The absorption of 2 mol of hydrogen was complete in 1 hr. After the usual work-up, **3** was crystallized from methanol: mp 179–182°; nmr data 52 (18-Me), 61.5 (19-Me), and 75.5 (21-Me) cps.

Anal. Calcd for $C_{25}H_{40}O_3$: C, 77.27; H, 10.38. Found: C, 77.40; H, 10.45.

B. From Pregnenolone Acetate by Grignard Reaction.—A benzene solution of 1 mmol of pregnenolone acetate was added to a cold ethereal solution of 5 mmol of ethylmagnesium bromide. The mixture was stirred for 2 hr at room temperature and then refluxed for 6 hr. After the usual work-up, the product was acetylated by treatment with acetic anhydride and pyridine. The acetate was crystallized from methanol, mp 178–181°; nmr was the same as that of **3**, obtained above, by catalytic hydrogenation.

3β-Acetoxy-20β-ethylpregn-5-en-20α-ol (3a).—This was prepared by condensing 1 mmol of the ketone **10** with 5 mmol of methylmagnesium bromide as described for the preparation of **3**. The reaction product was acetylated and the acetate was crystallized from acetone: mp 169–171°; nmr 52 (18-Me), 61.5 (19-Me), and 66.5 (21-Me) cps.

Anal. Calcd for $C_{25}H_{40}O_3$: C, 77.27; H, 10.38. Found: C, 77.47; H, 10.52.

3β-Acetoxy-20β-ethynylpregn-5-ene-17α,20α-diol (5).—A solution of lithium amide was prepared by dissolving 2 g of lithium in 250 ml of liquid ammonia. A stream of dry acetylene was passed through the solution at −33° for 2 hr. A solution of 10 g of 17α-hydroxypregnenolone acetate (**4**) in 100 ml of tetrahydrofuran was then added to the above solution (maintained at −78°) with stirring during 2 hr with a continuous flow of acetylene through the reaction mixture. The stirring was continued for an additional 3 hr at −33°. Solid ammonium chloride was added to the reaction mixture and the ammonia allowed to evaporate overnight. After the usual work-up, the residue was acetylated by treatment with acetic anhydride and pyridine at room temperature for 16 hr. The acetylated material was then chromatographed over a column of alumina and eluted with benzene, 5%, 10%, and 20% ethyl acetate in benzene. The eluates with 5 to 10% ethyl acetate in benzene gave small amounts of two hydroxy ketones[15] besides a small amount of the starting ketone. The eluate with 10–20% ethyl acetate in benzene gave 6 g of **5** which was crystallized from methanol: mp 175–177° (recrystallized from acetone–hexane gave mp 175–177°): ir bands at 2.7 and 2.9 (OH), 3.05 (≡CH), and 4.8 (C≡C) μ; nmr 59 (18-Me), 62 (19-Me), 94 (21-Me), and 154 (C≡CH) cps.

Anal. Calcd for $C_{25}H_{38}O_4$: C, 74.96; H, 9.06. Found: C, 75.21; H, 9.10.

3β-Acetoxy-20β-ethylpregn-5-ene-17α,20α-diol (6). A. By Catalytic Reduction of 5.—The procedure followed was the same as that described above for the preparation of **3**. The product was crystallized from methanol: mp 201–204°; nmr 54.5 (18-Me), 62 (19-Me), and 73 (21-Me) cps.

Anal. Calcd for $C_{25}H_{40}O_4$: C, 74.21; H, 9.97. Found: C, 74.43; H, 10.12.

B. From 17α-Hydroxypregnenolone Acetate by Grignard Reaction.—A solution of 6 equiv of ethylmagnesium bromide was treated with 17α-hydroxypregnenolone acetate. The procedure followed was the same as that used for other Grignard reactions described above. The product, after acetylation, was isolated by chromatography over alumina. It was crystallized from methanol, mp 200–205°.

3β-Acetoxy-20α-ethylpregn-5-ene-17α,20β-diol (8).—This was prepared by treatment of **7** with methylmagnesium bromide as described above for similar condensations. The product was crystallized from methanol: mp 191–194°; nmr 52.5 (18-Me), 62 (19-Me), and 77.5 (21-Me) cps.

Anal. Calcd for $C_{25}H_{40}O_4$: C, 74.21; H, 9.97. Found: C, 74.35; H, 9.85.

Periodate Oxidation of the Glycols 5, 6, and 8.—A methanol solution of the glycol was treated with an aqueous solution of sodium periodate and the pH was adjusted to 4. After the reaction was allowed to take place at room temperature for 48 hr, the product was isolated in the usual way.

3β-Acetoxy-21-methylpregn-5,16-dien-20-one (10).—A solution of ethylmagnesium bromide was prepared from 5 g of ethyl bromide and 1 g of magnesium turnings in 25 ml of dry ether. The solution was cooled in ice–water and to it was added with stirring a solution of 6 g of the unsaturated nitrile[6] **9** in 50 ml of dry benzene. The mixture was stirred at room temperature for

(14) Y. R. Bhatia, P. D. Landor, and S. R. Landor, *J. Chem. Soc.*, 24 (1959).

(15) The ir and nmr spectra of these ketones are consistent with D-homo structures.

1 hr and then refluxed for 4 hr. It was decomposed by pouring over ice and concentrated hydrochloric acid. The precipitated imine hydrochloride was filtered off and washed with cold ether. The hydrochloride was then dissolved in 20 ml of methanol and 2 ml of hydrochloric acid was added to the solution. The solution was diluted with water until turbid and then heated on steam bath for 15 min. After 30 min at room temperature, the solution was diluted and the precipitated solid removed by filtration. The solid (2.5 g) was acetylated by treatment with acetic anhydride and pyridine at room temperature. It was crystallized from methanol: mp 163–165°; λ_{max}^{MeOH} 240 mμ (ε 13,000); ir bands at 5.8 (acetate), 6.05 (conjd C=O), and 6.3 (conjd C=C) μ; nmr 55.5 (18-Me), 63.5 (19-Me), 320–325 (6 H), and 398–405 (16-H) cps; mass spectrum *m/e* 310 (base peak, M^+ − HOAc), 295 (310 − CH_3), 281 (310 − CH_3CH_2), etc.

Anal. Calcd for $C_{24}H_{34}O_3$: C, 77.80; H, 9.25. Found: C, 78.05; H, 9.36.

3β-Acetoxy-16α,17α-oxido-21-methylpregn-5-en-20-one (11).—A solution of 2 g of the unsaturated ketone **10** in 50 ml of methanol was cooled to 0° and treated successively with 4 ml of 4 *N* sodium hydroxide solution and 10 ml of 30% hydrogen peroxide solution. The solution was kept at 0° for 20 hr and then diluted with water. The precipitated solid was removed by filtration and washed with water. There was no uv absorption maximum, and the carbonyl band in the ir spectrum appeared at 5.85 μ.

This was converted into the 3-acetate (**11**) by treatment with acetic anhydride and pyridine. After crystallization from methanol it melted at 143–145°: nmr 62.5 (19-Me), 64 (18-Me), and mulitplet at 318–326 (6 H) cps.

Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.81. Found: C, 74.68; H, 8.93.

3β-Acetoxy-16β-bromo-17α-hydroxy-21-methylpregn-5-en-20-one (12).—A cold solution of 2 g of the above 16,17-oxido compound **11** in 10 ml of acetic acid was treated with a cold solution of 2 g of hydrobromic acid in 5 ml of acetic acid. After 10 min at 0° the solution was diluted with water and the precipitated solid was removed by filtration. It was washed with water to remove the acid and, after air drying, was used for the next step.

3β-Acetoxy-17α-hydroxy-21-methylpregn-5-en-20-one (1).—The above solid was dissolved in 100 ml of methanol. About 1 g of ammonium acetate and 500 mg of 5% palladium on charcoal was added to the above solution and stirred in an atmosphere of hydrogen for 2 hr. After the usual work-up, the product obtained showed three spots on thin layer chromatography. The major compound was isolated by crystallization from methanol: mp 203–207°; ir bands at 2.6 (OH), 5.8 (acetate), and 5.95 (20-keto) μ; nmr 42 (18-Me), 61.5 (19-Me), triplet centered at 63 (J = 7 cps, 22-Me), and multiplet at 320–325 (6 H) cps; mass spectrum *m/e* 388 (M^+, 20%), 328 (M^+ − HOAc, 98%), 310 (328 − H_2O, 8%), 271 (base peak) etc.

Anal. Calcd for $C_{24}H_{36}O_4$: C, 74.17; H, 9.31. Found: C, 74.35; H, 9.25.

3β-Acetoxy-21-methylpregn-5-en-20-one (10a).—To a solution of 1.1 g of the ketone **10** in 25 ml of ethyl acetate was added 200 mg of 5% palladium-on-charcoal and the mixture was stirred in an atmosphere of hydrogen. The absorption of 1 mol of hydrogen was complete in 90 min. After the usual work-up the product was crystallized from methanol: mp 165–173° (on recrystallization from acetone, the melting point was raised to 170–173°); ir bands at 5.8 (acetate) and 5.88 (20-keto) μ; nmr 38 (18-Me), 62 (19-Me), and multiplet at 320–325 (6 H) cps; mass spectrum *m/e* (M^+ − HOAc, base peak), 297 (312 − CH_3, 16%), 283 (312 − C_2H_5, 4%) etc.

The Reaction of 5 with Thionyl Chloride in the Presence of Pyridine. Formation of the Cyclic Sulfite 15.—A solution of 1 g of **5** in 25 ml of pyridine was cooled in an ice bath and 1 ml of thionyl chloride was added dropwise with stirring. After 5 min at 0°, the reaction mixture was poured over ice–water. The organic material was extracted with ethyl acetate and the extract was washed with cold 2 *N* hydrochloric acid and water. The residue obtained after removal of the solvent was crystallized from acetone–methanol: yield about 1 g; mp 187–192°; ir bands at 3.05 (C≡CH), 4.7 (C≡C, unusually intense compared to usual C≡C bands) μ; nmr 58 (18-Me), 61.5 (19-Me), 102 (21-Me), 172 (≡CH), and 318–326 (6 H) cps; mass spectrum *m/e* 386 (M^+ − HOAc, 75%), 322 (386 − SO_2, 65%), 307 (322 − CH_3, 15%), and among others 64 (SO_2, base peak).

Anal. Calcd for $C_{25}H_{34}O_5S$: C, 67.24; H, 7.68; S, 7.16. Found: C, 67.16; H, 7.74; S, 7.50.

The Reaction of 5 with Thionyl Chloride.—A solution of 1 g of **5** in 25 ml of dioxan was treated with 2 ml of thionyl chloride and left at room temperature for 72 hr. The solution was then poured over ice and the organic material was extracted with ethyl acetate. The extract was washed with water and dried; the solvent was removed. The oily residue showed three spots on thin layer chromatography. One of the spots was due to the unreacted material and the least polar spot absorbed in the ultraviolet. The three substances were separated by chromatography over a column of alumina. The least polar material (50 mg) had λ_{max}^{MeOH} 221 mμ. No further attempt was made to characterize it. The major product (0.5 g) obtained was further purified by crystallization from methanol: mp 222–227°; ir bands at 3.05 (≡CH), 4.7 (C≡C), and 5.8 μ; nmr 59 (18-Me), 61 (19-Me), 89 (17a-Me), and 143 (≡CH) cps; mass spectrum *m/e* 382 (M^+, 1%), 322 (M − HOAc, base peak), etc.

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.37; H, 8.68.

Catalytic Reduction of 17 to 18.—The reduction of 250 mg of **17** was carried out in the usual way with ethyl acetate as the solvent and 50 mg of 10% palladium on charcoal as the catalyst. The product was crystallized from acetone: mp 216–219°; nmr data, 44 (18-Me), 59.5 (19-Me), 68.5 (17a-Me), and 318–326 (6 H) cps.

Anal. Calcd for $C_{25}H_{38}O_3$: C, 77.67; H, 9.91. Found: C, 77.51; H, 10.10.

Treatment of 5 with Formic Acid. Formation of 17.—A solution of 500 mg of **5** in 0.5 ml of methylene chloride was treated with 5 ml of 97% formic acid and the solution was heated on the steam bath for 5 min. After the usual work-up, the product was purified by chromatography over alumina to give about 350 mg of **17**.

The Preparation of 19 and 20.—These were prepared according to the published procedure.[11] The melting point of **20** was however found to be 208–212° (lit.[11] 180–182°); nmr data of **20**, 53 (18-Me), 61.5 (19-Me), 78 and 81.5 (21- and 22-Me) cps.

Registry No.—**3**, 21902-59-0; **3a**, 21902-60-3; **5**, 21902-61-4; **6**, 21902-62-5; **7**, 21902-58-9; **8**, 21902-63-6; **10**, 21955-13-5; **10a**, 21927-82-2; **11**, 21902-64-7; **15**, 21927-83-3; **17**, 21927-84-4; **18**, 21927-85-5.

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