THE JOURNAL OF Organic Chemistry®

VOLUME 33, NUMBER 5

MAY 13, 1968

Synthesis of the Four Pairs of Side-Chain Epoxides Epimeric at Carbon 20 Derived from 5β-Pregnan-3α-ol[1]

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Received October 23, 1967

A study was made of the reduction of 21-bromo-3α,17-dihydroxy-5β-pregnan-20-one with sodium borohydride. Under the proper conditions 20β,21-oxido-5β-pregnane-3α,17-diol was the principal product. This compound, as well as the corresponding 20α,21-oxide, was also prepared by independent means *via* the 21-tosylates. Configurational assignment at C-20 for these epoxides is based on hydration to the 3α,17,20,21-tetrols and lithium aluminum hydride reduction to the 3α,17,20-triols. Reactions of the 17-hydroxy 20,21-oxides with periodic acid and hydrogen bromide are also described. Three other pairs of C-20-epimeric side-chain epoxides derived from 3α-hydroxy-5β-pregnane were prepared from the appropriate tosylate precursors. A comparison of the optical rotatory properties and infrared spectra of the eight epoxides and their derived acetates was also made, and the results are evaluated.

For some time we have been interested in the preparation of 5β-pregnan-20α-ols[2-5] which normally are minor products in the reduction of 20-ketopregnanes by complex metal hydrides. Sodium borohydride reduction of the bromodiolone 2[6] (Scheme I) was investigated with the expectation that a bulky substituent at C-21 might influence favorably the ratio of 20α- to 20β-ols formed in the reaction. It soon became evident that the type of solvent employed had a marked influence on the nature of the products which were generated. Reduction of 2 in dimethylformamide[7] afforded the 5β-pregnane-3α,17,20-triols in approximately 25% yield, indicating that both reductive elimination of bromine and reduction at C-20 had occurred. Since the 20β/20α ratio of 8:1 does not differ significantly from the epimeric mixture obtained by similar reduction of 17-hydroxy-20-ketopregnanes,[8] it is evident that no selective formation of the 20α epimer occurred.

Of greater interest, however, was the presence in the reaction mixture of a roughly equal amount of a chromatographically more mobile by-product. Subsequently it was found that this compound was the major product when the reduction was carried out in aqueous methanol and that the yield was proportional to the water content of the reaction solvent. Thus yields of 59 and 83% were realized in systems containing 15 and 44% (v/v) of water, respectively.

The mobile product was assigned the 20β,21-oxido-5β-pregnane-3α,17-diol (**3b**) structure on the basis of the following reactions: reduction with lithium aluminum hydride to 5β-pregnane-3α,17,20β-triol, hydration in aqueous, acidic tetrahydrofuran to 5β-pregnane-3α,-17,20β,21-tetrol, and oxidation with periodic acid to 3α-hydroxy-5β-androstan-17-one.

Formation of an epoxide must of necessity involve initial reduction of 2 to a 21-bromo-20-ol which rapidly undergoes cyclodehydrohalogenation in the alkaline medium. However, it was found that, if the reduction was carried out in absolute methanol for 5 min at 0°, the intermediate bromotriol **5b** could be recovered in high yield. Also isolated as a minor product in this reaction was a less mobile bromotriol which was shown to be the 20α epimer of **5b** (*vide infra*). As is evident from these results, one can control considerably the nature of the products formed by judicious selection of the reaction solvent system.

Steroidal epoxides have been prepared by a variety of methods,[9] but the author is aware of no systematic study centering on the synthesis of pairs of epoxides epimeric at C-20. This investigation therefore was extended to include the preparation not only of the 20α epimer of **3b**, but also the 21-hydroxy 17,20-oxides, the 17,20-oxides, and the 20,21-oxides derived from 5β-pregnan-3α-ol. None of these eight epoxides has been described previously. This paper is concerned chiefly with the synthesis of these latter com-

(1) This work was supported by a research grant (AM 01255) from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, U. S. Public Health Service.

(2) M. L. Lewbart and V. R. Mattox, *J. Org. Chem.*, **28**, 1773 (1963).

(3) M. L. Lewbart and V. R. Mattox, *ibid.*, **28**, 1779 (1963).

(4) M. L. Lewbart and J. J. Schneider, *ibid.*, **29**, 2559 (1964).

(5) M. L. Lewbart and J. J. Schneider, *J. Biol. Chem.*, **241**, 5325 (1966).

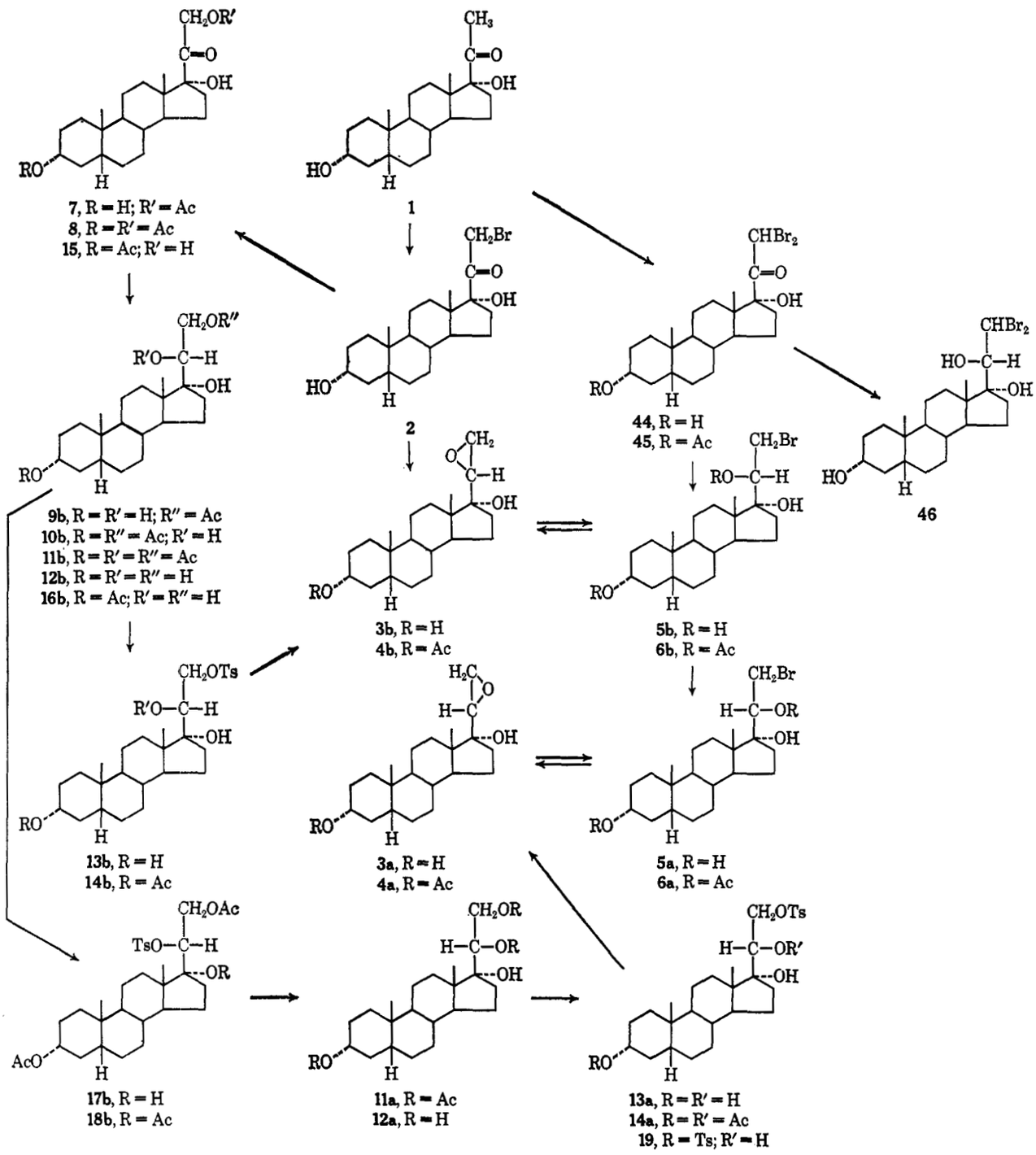
(6) B. A. Koechlin, T. H. Kritchevsky, and T. F. Gallagher, *J. Amer. Chem. Soc.*, **73**, 189 (1951).

(7) N. L. Wendler, R. P. Graber, and G. G. Hazen, *Tetrahedron*, **3**, 144 (1958).

(8) D. K. Fukushima and E. D. Meyer, *J. Org. Chem.*, **23**, 174 (1958).

(9) C. Djerassi, "Steroid Reactions," Holden-Day, Inc., San Francisco, Calif., 1963, pp 593–615.

SCHEME I



pounds. Only those reactions which are essential for proof of structure will be described. A second report dealing with further reactions will be submitted in the near future.

3α,17-Dihydroxy 20,21-Oxides (3a and 3b).—As a preliminary, it was judged essential to establish unequivocally the configuration at C-20 of the epoxide **3b** and its bromhydrin precursor **5b**. Conversion of **3b**, by reductive scission and by hydration, into 20β-ols argues for the same configuration in the epoxide, but the possibility of inversion at C-20, although unlikely, could not be ruled out. It was therefore decided to prepare both the epoxide and the bromohydrin by independent means, utilizing reactions which could not possibly result in inversion at C-20. Important intermediates in this projected scheme are the 21-tosyloxy-5β-pregnane-3α,17,20-triols which should be converted into the desired epoxides in the presence of alkali. The 20β epimer **13b** was prepared as follows. Reaction of the bromodiolone **2** with acetic acid in triethylamine[10] provided the 21-acetate **7**, which was reduced with sodium borohydride in dimethylformamide to the tetrol 21-acetate **9b**. Acetylation of **9b** gave the triacetate **11b**, resulting in an MD increment of +390 units, a value consistent with the 20β orientation of the hydroxyl group. Saponifi-

(10) W. T. Moreland, *J. Org. Chem.*, **21**, 820 (1956).

cation of **9b** afforded the free tetrol **12b** which, on treatment with an equivalent amount of tosyl chloride in pyridine, provided the 21-tosylate **13b**. Reaction of **13b** with alkali gave an epoxide identical with **3b**; treatment of **13b** with sodium bromide in diethylene glycol[11] afforded the bromotriol **5b**. These reactions unequivocally fix the 20β orientation in the oxide and bromohydrin since it is known that, in elimination reactions involving tosylates, inversion occurs only on the carbon atom which bears the leaving group.[12]

Preparation of 21-tosyloxy-5β-pregnane-3α,17,20α-triol (**13a**) was achieved by the following series of reactions. Acetylation of the α-ketol 21-acetate **7** gave the known 3,21-diacetate **8**.[6] This substance was characterized further by partial hydrolysis to the 3-monoacetate **15**. Reduction of **15** with sodium borohydride in dimethylformamide gave the amorphous tetrol 3-acetate **16b**; similar reduction of **8** afforded the tetrol diacetate **10b**. Reaction of **10b** with tosyl chloride in pyridine provided the 20β-tosylate diacetate **17b**. Strenuous acetylation of **17b**, under the conditions described by Fukushima, *et al.*,[13] gave the tosylate triacetate **18b** in only modest yield. However, reaction of **17b** in carbon tetrachloride with acetic anhydride and 60% perchloric acid for 1 min[14] supplied **18b** in a yield of nearly 90%. Reaction of **18b** with potassium acetate in acetic acid by the method of Fukushima, *et al.*,[13] which involves migration of the acetyl group from C-17 to C-20 with subsequent inversion at the latter position, provided the 20α-tetrol triacetate **11a**. Saponification of **11a** gave the free tetrol **12a** in an over-all yield from **8** of 47.6%. Reaction of **12a** with a limited amount of tosyl chloride in pyridine afforded the desired 21-monotosylate **13a** as well as a small amount of a crystalline 3,21-ditosylate (**19**). Treatment of **13a** with 1 equiv of alkali gave the 20α,21-epoxide **3a** in good yield. Utilizing reactions employed in characterizing its 20β epimer, **3a** was reduced with lithium aluminum hydride to 5β-pregnane-3α,17,20α-triol and, on oxidation with periodic acid, afforded 3α-hydroxy-5β-androstan-17-one in low yield. Treatment of **3a** under the same conditions of hydration which provided the 20β-tetrol **12b** in good yield from **3b** gave the 20α-tetrol **12a** as a minor product. The nature of the major product will be discussed in a forthcoming paper.

Both 20,21-oxido-5β-pregnane-3α,17-diols add hydrogen bromide normally; the sole products isolated were the 21-bromides in which the original configuration at C-20 was retained. The hydrogen bromide addition product **5a** of the 20α,21-epoxide was identical with the minor product isolated after sodium borohydride reduction of the bromodiolone **2**. In an analogous manner, cyclodehydrohalogenation of the 20α-bromotriol **5a** with alkali furnished its precursor, the 20α,21-oxide **3a**.

3α,21-Dihydroxy 17,20-Oxides (28a and 28b).—The key intermediates in the preparation of these compounds are the 20-tosyloxy-5β-pregnane-3α,17,21-triol 3,21-diacetates **17a** and **17b**. The 20β epimer **17b** was available from the previous reaction sequence. Synthesis of the 20α epimer **17a** (Scheme II) presented a much greater challenge, necessitating preparation of the tetrol 3,21-diacetate **10a** while leaving free the hydroxyl groups at C-17 and C-20. Initial attempts centered on the partial acetylation of 5β-pregnane-3α,17,20α,21-tetrol 3-monoacetate.[15] Under the proper conditions, the 3,21-diacetate was the major product as judged by paper chromatographic analysis. However, very little pure material was recovered after partition column chromatography, presumably because of partial isomerization to the 3,20-diacetate. As further evidence of its instability, it was noted that, when a pure sample of the 3,21-diacetate was subjected to thin layer chromatography on silica gel, two components corresponding to the two isomeric diacetates could be demonstrated. In contrast, the 20β epimer **10b** showed a single component when so chromatographed.[16] Because of these difficulties the following alternate series of reactions were carried out. The triolone **20** was prepared by hydrolysis of the 21-acetate **7** with a catalytic amount of alkali. Oxidation of **20** with methanolic cupric acetate,[17] followed by successive treatment of the amorphous glyoxal with sodium hydroxide and ethereal diazomethane,[3] gave the methyl 20α- and 20β-hydroxy-21-oates **21a** and **21b** which, after column chromatographic separation as the boric acid complexes,[18] were isolated in yields of 56 and 25%, respectively. Treatment of the more mobile ester **21b** in acetone solution with perchloric acid afforded in good yield a much more mobile, amorphous product (**23b**) which possessed no unacylable hydroxyl groups and which retained the carbomethoxyl function. That **23b** is the 17,20β-isopropylidene derivative was established by showing the identity of its lithium aluminum hydride reduction product (**26b**) with the saponification product of the acetonide obtained from the tetrol 21-monoacetate **9b**. In addition, the acetylation product (**25b**) of **26b** was identical with the acetonide prepared from the tetrol diacetate **10b**.

Conversion of the less mobile methyl ester **21a** into the 17,20α-acetonide **23a** also occurred in excellent yield. The amorphous product was reduced with lithium aluminum hydride to the dihydroxyacetonide **26a**. Acetylation of **26a** provided the diacetoxyacetonide **25a**, which was selectively hydrolyzed in aqueous acetic acid at 65° to the desired 3,21-diacetate **10a** in a yield of 70%. Acetylation of **10a** gave a triacetate identical with **11a** thus confirming the 20α configuration. Tosylation of **10a** provided the 20α-tosyloxy diacetate **17a**. Further evidence relating to the structure of **17a** was obtained by successive acetylation at C-17 and rearrangement of the amorphous tosylate triacetate **18a** with potassium acetate in acetic acid

(11) E. R. Buchan, D. H. Deutsch, and G. I. Fujimoto, *J. Amer. Chem. Soc.*, **75**, 6228 (1953).

(12) A. Rosowsky, "Heterocyclic Compounds with Three- and Four-Membered Rings," Part 1, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p. 147.

(13) D. K. Fukushima, N. S. Leeds, H. L. Bradlow, T. H. Kritchevsky, M. D. Stokem, and T. F. Gallagher, *J. Biol. Chem.*, **212**, 449 (1955).

(14) D. H. R. Barton, R. M. Evans, J. C. Hamlet, P. G. Jones, and T. Walker, *J. Chem. Soc.*, 747 (1954).

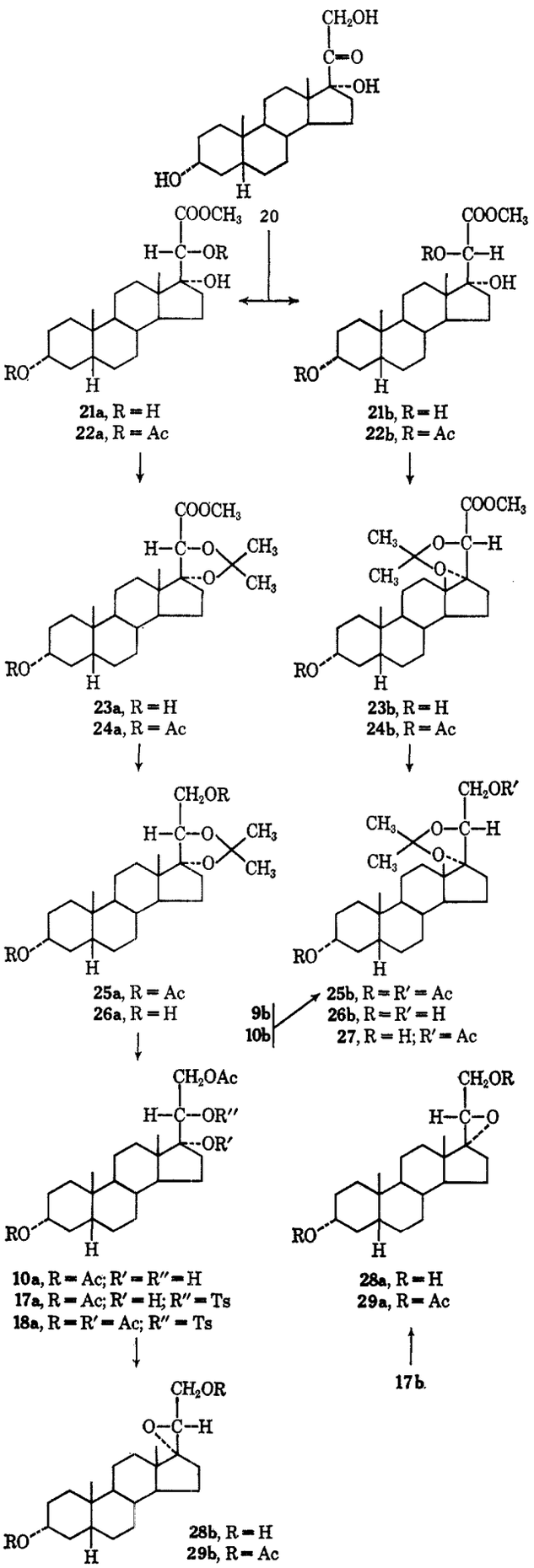
(15) The preparation of this compound by selective hydrolysis of the 20,21-acetonide will be detailed in a future communication.

(16) Since the ready isomerization of steroidal 20-acetoxy-17α,21-diols to 21-acetoxy-17α,20-diols has been reported [R. Gardi, R. Vitali, and A. Ercoli, *Gazz. Chim. Ital.*, **93**, 1642 (1963)], it is not unreasonable to assume that under the conditions of chromatography isomerization in the reverse direction also can occur. It is noteworthy that only the 20α epimer was unstable on silica gel.

(17) M. L. Lewbart and V. R. Mattox, *J. Org. Chem.*, **28**, 2001 (1963).

(18) J. J. Schneider and M. L. Lewbart, *Tetrahedron*, **20**, 943 (1964).

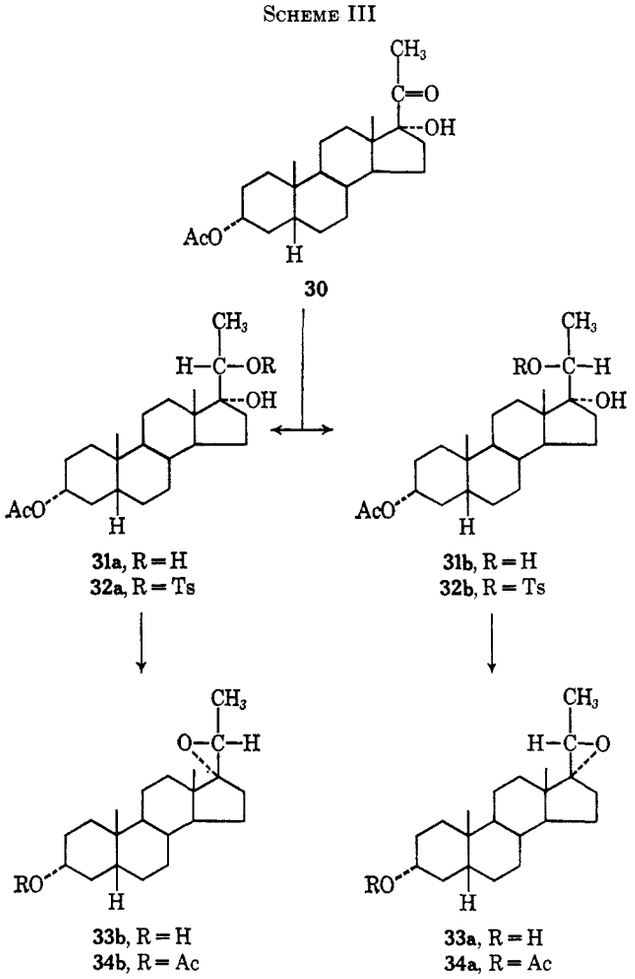
SCHEME II



to 5β-pregnane-3α,17,20β,21-tetrol 3,20,21-triacetate (**11b**). Inversion of the hydroxyl function at C-20 from α to β by the Fukushima method[13] has not been reported previously and, although of little practical value, represents a point of theoretical interest. The epimeric 20-tosyloxy diacetates **17a** and **17b** were converted smoothly in alkali into the 17,20β- and 17,20α-oxides (**28b** and **28a**), respectively. Both oxides were reduced by lithium aluminum hydride to the same product, namely, 5β-pregnane-3α,17,21-triol.[19]

3α-Hydroxy 17,20-Oxides (33a and 33b).—The necessary intermediates for the preparation of these oxides are the epimeric 20-tosylates **32a** and **32b** (Scheme III).

SCHEME III



Reduction of 17-hydroxypregnanolone acetate (**30**) with sodium borohydride in dimethylformamide followed by column chromatography in the presence of a borate buffer[18] provided the 20α- and 20β-pregnanetriol 3-acetates **31a** and **31b** in yields of 10 and 83%, respectively.

Unexpected difficulty was encountered in the tosylation of the 20β epimer **31b**. Reaction with excess tosyl chloride in pyridine at room temperature gave no product with the chromatographic mobility expected for the 20β-tosylate. In addition to some starting material, there were two very mobile products. One was obtained in crystalline form and, since its saponifi-

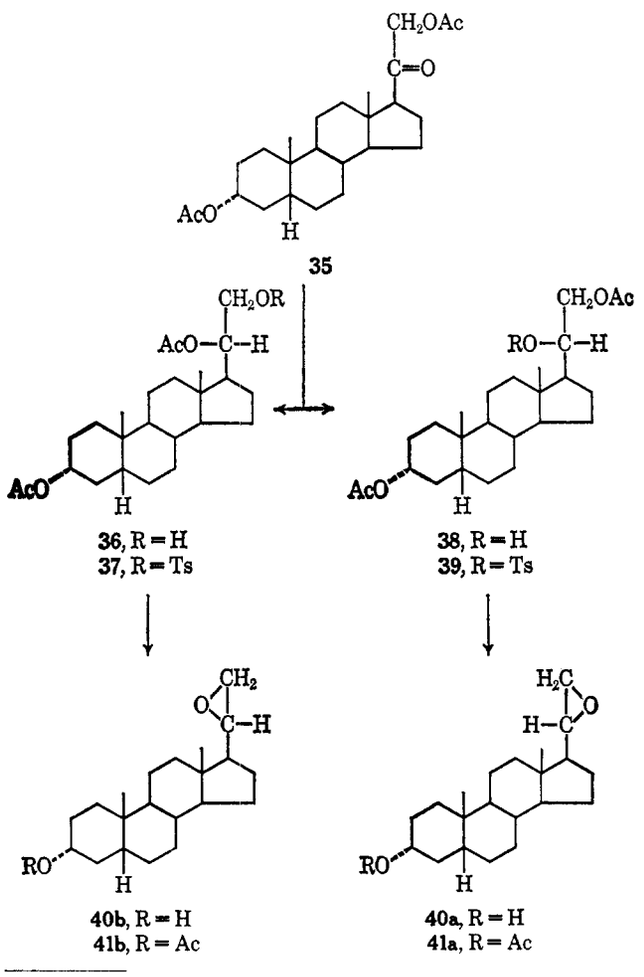
(19) The preparation of this compound as well as 5β-pregnane-3α,17-diol and 5β-pregnane-3α,21-diol will be presented in the following paper [M. L. Lewbart and J. J. Schneider, *J. Org. Chem.*, **33**, 1707 (1968)].

cation product possessed a carbonyl band in the infrared region, it was concluded that a D-homoannulation reaction, similar to that described by Williams, *et al.*,[20] had occurred. Tosylation of **31b** at −12° resulted chiefly in the formation of the desired tosylate. This product could not be crystallized directly from the reaction mixture and, when attempts were made to purify it by the relatively gentle techniques of partition column chromatography or countercurrent distribution, extensive formation of D-homoannulation products occurred. However, direct treatment with alkali of the reaction mixture obtained at −12° gave the 17,20α-oxide **33a** in surprisingly good yield.

Tosylation of the 20α-pregnanetriol 3-acetate **31a** at room temperature resulted in much less D-homoannulation than was encountered with its 20β epimer, but the qualitative pattern was similar. Reaction at 0° provided in high yield the crystalline 20α-tosylate **32a** which was converted with alkali into the 17,20β-oxide **33b**. Both oxides furnished 5β-pregnane-3α,-17-diol[19] on reductive scission with lithium aluminum hydride.

3α-Hydroxy 20,21-Oxides (40a and 40b).—Reduction of 3α,21-diacetoxy-5β-pregnan-20-one (**35**) with sodium borohydride in dimethylformamide[21] afforded a mixture of the 5β-pregnane-3α,20β,21-triol 3,20- and 3,21-diacetates (**36** and **38**, Scheme IV). The pure isomers

SCHEME IV



were isolated in only fair yield after column chromatography on silica gel since partial isomerization occurred under these conditions. However, one isomer, the 3,21-diacetate **38**, was prepared in excellent yield by reduction of **35** with sodium borohydride in absolute methanol at 0°.

The isomeric triol diacetates both provided crystalline tosylates.[22] The location of the tosyloxyl group on the side chain was determined by lithium aluminum hydride reduction of **37** to 5β-pregnane-3α,20β-diol and of **39** to 5β-pregnane-3α,21-diol.[19] Reaction of the 21-tosylate **37** with alkali resulted in elimination without inversion at C-20, affording the 20β,21-oxide **40b**; reaction of the 20-tosylate **39** with alkali resulted in elimination with inversion at C-20, providing the 20α,21-oxide **40a**. Lithium aluminum hydride reduction of **40a** gave 5β-pregnane-3α,20α-diol; similar reduction of **40b** gave 5β-pregnane-3α,20β-diol.

Molecular rotations taken at 365 and 589 mμ (D line of sodium) for the four pairs of epoxides and their acetates are recorded in Table I. When the values for epimeric pairs are compared, it is evident that there are no significant differences between the 17-hydroxy 20,21-oxides (pairs 3 and 4) and the 21-deoxy 17,20-oxides (pairs 5 and 6). For the 17-deoxy 20,21-oxides (pairs 1 and 2), the 20α epimers are more dextrorotatory than their 20β epimers as evidenced by positive Δ values. The opposite holds true for the 21-hydroxy 17,20-oxides (pairs 7 and 8) as reflected by negative Δ values. It would appear that, within the limits imposed by the few examples given here, configurational assignments for these last two types of epoxides could be made if new epimeric pairs are encountered. One additional point of interest arises when the molecular rotation values of the free and acetylated 3,21-dihydroxy 17,20-oxides (pairs 7 and 8) are compared. Acetylation increments of the 20α (+115 and +358 units) and 20β epimers (+156 and +489 units) are significantly larger than those calculated for the other three pairs of epoxides (+89 ± 9 and +262 ± 17 units) at the two wavelengths. Since acetylation of a 21-ol ordinarily causes no appreciable change in molecular rotation,[23] it must be concluded that the presence of an epoxide ring in an adjacent position promotes optical rotatory change after acetylation at C-21. A more subtle influence exerted by the stereochemical environment is suggested by the fact that the acetylation increment of the 20β epimer is roughly 1.5 times greater than that of the 20α epimer.

When the infrared spectra of the epoxides and their acetates were compared, there was noted typical but not invariable absorption in three regions. These consisted of weak bands at or near 3050 cm^{-1} (due to C–H stretch), weak to moderate bands in the vicinity of 1170 cm^{-1} (due to C–O–C stretch), and a strong band between 860 and 890 cm^{-1} (due to asymmetric stretching of the epoxide ring). In agreement with the results of Gunthard, *et al.*,[24] who studied steroidal ring epoxides, no characteristic band at 1250 cm^{-1}, which

(20) K. I. H. Williams, M. Smulowitz, and D. K. Fukushima, *J. Org. Chem.*, **30**, 1447 (1965).

(21) D. Taub, R. D. Hoffsommer, and N. L. Wendler, *J. Amer. Chem. Soc.*, **81**, 3291 (1959).

(22) The preparation of the 21-tosylate **37** has been reported recently [V. R. Mattox and W. Vrieze, *J. Org. Chem.*, **32**, 708 (1967)], but it was not obtained in crystalline form nor further characterized.

(23) L. H. Sarett, *J. Amer. Chem. Soc.*, **71**, 1175 (1949).

(24) H. H. Gunthard, H. Heusser, and A. Furt, *Helv. Chim. Acta*, **36**, 1900 (1953).

TABLE I

MOLECULAR ROTATIONS[a] AND INFRARED DATA OF STEROIDAL SIDE-CHAIN EPOXIDES AND THEIR ACETATES

					Molecular rotation data						Infrared data					
					Epimers						C—H stretch, ν_{max}		C—O—C stretch, ν_{max}		Asymmetric —C—C— \ / O stretch, ν_{max}	
					20α		20β									
Pair no.	C-3	C-17	C-20	C-21	M_{365}	M_D	M_{365}	M_D	$M_{365}^{20\alpha} - M_{365}^{20\beta}$	$M_D^{20\alpha} - M_D^{20\beta}$	20α	20β	20α	20β	20α	20β
1	α-OH	H		—O—	+248	+96	+106	+34	+142	+62	3042	3041	1161	1169	875	868
2	α-OAc	H		—O—	+512	+180	+375	+124	+137	+56	3050	3050	1171	1169	888	869
3	α-OH	OH		—O—	−127	−28	−75	−24	−52	−4	3060	3060	1165	Absent	877	878
4	α-OAc	OH		—O—	+144	+59	+204	+73	−60	−14	3050	3060	1165	1167	875	873
5	α-OH		—O—	H	+204	+79	+196	+78	+8	+1	3018[b]	Absent	1165	1167	886	882
6	α-OAc		—O—	H	+479	+165	+472	+167	+7	−2	3018[b]	Absent	1167	1168	885	886
7	α-OH		—O—	OH	+182	+64	+276	+109	−94	−45	Absent	Absent	1170	1170	888	Absent[c]
8	α-OAc		—O—	OAc	+540	+179	+765	+265	−225	−86	3020[b]	Absent	1171	1169	Absent	888

[a] Molecular rotations, M_{365} and M_D, are $[\alpha] \times$ mol wt/100. $M^{20\alpha} - M^{20\beta}$ differences will be referred to as Δ values in the text. [b] Shoulder. [c] There was a strong band at 937 cm^{-1} not present in the corresponding glycol which may be due to the oxide ring.

has been reported for most nonsteroidal epoxides,[25] was noted. It will be seen that, where the characteristic bands are present in both epimers, there is no significant difference in their frequency. Infrared analysis would therefore appear to be of limited utility in differentiating among the various classes of steroidal side-chain epoxides and in assigning configuration at C-20.

A comparison of the spectral properties of 17-hydroxypregnanolone (**1**), the bromodiolone **2**, and the dibromodiolone **44** is presented in Table II and further discussed.[26]

TABLE II

CARBONYL ABSORPTION IN THE ULTRAVIOLET AND INFRARED REGIONS OF 17-HYDROXYPREGNANOLONE (**1**) AND ITS 21-MONO- AND 21,21-DIBROMIDES (**2** AND **44**)

Compound	λ_{max}, mμ	ε	Δ, mμ	ν_{max}, cm^{-1}	Δ, cm^{-1}
1	295	61	...	1692	...
2	298	85	3	1719	27
44	318	58	23	1727	35

Experimental Section

Melting points were taken on a Fisher-Johns apparatus and are reported uncorrected. Optical rotations were determined at 365, 436, 546, and 589 mμ (D line of sodium) in a Zeiss 0.005° photoelectric polarimeter. Measurements were made in methanol solution in a 0.5-dm tube at a concentration of about 1% and at a temperature of 26 ± 1°. Infrared spectra were determined as KBr pellets with a Beckman IR-8 infrared spectrophotometer. A description of and references to the column, paper (pc), and thin layer (tlc) chromatographic techniques routinely employed in this laboratory appear in a previous paper.[4] Analyses were by E. Thommen, Basel, Switzerland, August Peisker-Ritter, Brugg, Switzerland, and Huffman Laboratories, Wheatridge, Colo.

Reactions mixtures from tosylations and large-scale (more than 50 mg) acetylations were processed by dilution with ice and water, extraction with methylene chloride, and successive washing of the organic phase with 1 *N* hydrochloric acid, 5% aqueous sodium bicarbonate solution, and water. The organic solvent was filtered through anhydrous sodium sulfate and concentrated to dryness *in vacuo*. Small-scale acetylations were processed by repeated additions of methanol and evaporation of the solvents with a stream of nitrogen. Ethyl acetate extracts were washed as required with acidic and/or alkaline brine and finally with neutral brine. The organic phase was dried by filtration through anhydrous sodium sulfate. Reaction mixtures from lithium aluminum hydride reductions were processed by inactivating excess reducing agent with additions of ethyl acetate, water, and 3 *N* sulfuric acid, dilution with an equal volume of ethyl acetate, washing the organic phase as required, and evaporating the solvent as above.

21-Bromo-3α,17-dihydroxy-5β-pregnan-20-one (2) and 21,21-Dibromo-3α,17-dihydroxy-5β-pregnan-20-one (44) from 1.—To a stirred solution of 3α,17-dihydroxy-5β-pregnan-20-one (5.84 g, 17.5 mmol) in chloroform (280 ml, Matheson ACS grade), bromine (3.25 g, 20.3 mmol) in chloroform (70 ml) was added dropwise over a 2-hr period. The clear, lemon-yellow solution was washed successively with cold, dilute sodium hydroxide solution and water, filtered through anhydrous sodium sufate, and concentrated to dryness. Repeated crystallization from ethyl acetate and acetone gave **2** as leaflets (5.33 g, mp 213–213.5° dec): $[\alpha]_{365}$ +533°, $[\alpha]_{436}$ +197°, $[\alpha]_{546}$ +93.1°, $[\alpha]_D$ +79.5°; reported[6] mp 206–209°, $[\alpha]^{30}D$ +79° (ethanol). When the residue from the combined mother liquors was examined by tlc, there was noted a more mobile contaminant which weakly absorbed 254-mμ irradiation. The mixture was chromatographed on a 41 × 790 mm silica gel column in benzene–ethyl acetate (2:1). Fractions (8 ml) were collected at 15-min intervals. Fractions 95–170 consisted of at least three components including **44**.

21,21-Dibromo-3α,17-dihydroxy-5β-pregnan-20-one (44).[26] Fractions 171–250.—Crystallization from ether gave prismatic needles (950 mg, mp 186.5° dec). The mother liquors were combined with fractions 95–170 (above) and yielded an additional 429 mg of **44**, containing only traces of impurities. The total yield of the dibromo product was 13.7%. For the analytical sample, recrystallized from ether and dried to constant weight at room temperature under a high vacuum over P_2O_5 had mp 188° (on stage at 183°); $[\alpha]_{365}$ +1010 $[\alpha]_{436}$ +263°, $[\alpha]_{546}$ +113°, $[\alpha]_D$ +94.7°; ν_{max} 3545 and 3350 cm^{-1} (free and associated hydroxyl).

Anal. Calcd for $C_{21}H_{32}Br_2O_3 \cdot (C_2H_5)_2O$: C, 53.01; H, 7.47; Br, 28.22. Found: C, 53.02; H, 7.44; Br, 30.88.

21,21-Dibromo-3α-acetoxy-17-hydroxy-5β-pregnan-20-one (45).

(25) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p 118.

(26) The presence of **44** (Scheme I) as a contaminant of **2** was suggested by Koechlin, *et al.*,[6] but it was not isolated as such by these workers. Assignment of the 21,21-dibromo structure followed from the bromine analysis and the presence of an unacetylable hydroxyl group in **45**, thus ruling out a 17,21-dibromide. Further evidence supporting the structure of **44** was obtained by its reduction with sodium borohydride to the dibromotriol **46** and to the bromotriol **5b** (*vide infra*).

When the spectral properties of the bromination products and the parent diolone **1** are compared, several points of interest emerge (Table II). Introduction of one bromine atom has only slight effect on λ_{max} of the low-intensity carbonyl absorption in the ultraviolet (Zeiss RPQ 20A recording spectrophotometer), but addition of a second bromine atom brings about a marked bathochromic shift of 23 mμ. Detection of the dibromide on thin layer chromatography plates with ultraviolet irradiation is apparently caused by a bathochromically displaced end absorption which is evidenced by a molecular extinction of 650 at 250 mμ. In contrast, the mono- and unsubstituted analogs possess extinctions of only 81 and 8 at the same wavelength. The infrared carbonyl frequency is displaced 27 cm^{-1} by substitution of one bromine atom at C-21. This shift is somewhat greater than the 20-cm^{-1} value reported by Jones, *et al.* [R. N. Jones, P. Humphries, F. Herling, and K. Dobriner, *J. Amer. Chem. Soc.*, **74**, 2830 (1952)], for the same compounds, but, since the earlier measurements were made in solution, the results are not strictly comparable. There is only slight additional displacement of the carbonyl band in the dibromide **44**. This observation is in agreement with that of G. P. Allen and M. J. Weiss [*ibid.*, **82**, 1709 (1960)] who reported a difference of 10 cm^{-1} between mono- and dibrominated derivatives of progesterone. Both the dibromodiolone **44** and its acetylation product **45** exhibit a weak band at 3050 cm^{-1}. Since this band is absent in the monobromide **2**, it is most likely attributable to C–H stretch at the trisubstituted 21-carbon atom.

—Reaction of 21,21-dibromo-3α,17-dihydroxy-5β-pregnan-20-one with pyridine and acetic anhydride and crystallization of the product from acetone gave rods: mp 212–212.5° dec (on stage at 200°) (recrystallization from methanol did not raise the melting point); $[\alpha]_{365}$ +1115°, $[\alpha]_{436}$ +310°, $[\alpha]_{546}$ +140°, $[\alpha]_D$ +119°; ν_{max} 3458 cm^{-1} (hydroxyl).

Anal. Calcd for $C_{23}H_{34}Br_2O_4 \cdot CH_3COCH_3$: C, 52.71; H, 6.81. Found: C, 52.53; H, 6.65.

From **fractions 275–430** there was obtained an additional 650 mg of **2**, mp 211.5° dec, raising the yield to 5.98 g (82.8%).

21-Bromo-5β-pregnane-3α,17,20β-triol (5b) and 21,21-Dibromo-5β-pregnane-3α,17,20β-triol (46) from 44.—To a solution of 21,21-dibromo-3α,17-dihydroxy-5β-pregnan-20-one (500 mg) in methanol (25 ml) at −10° was added sodium borohydride (375 mg). After 3 min at −10° excess acetic acid was added and, after evaporation of the solvent, the reaction mixture was diluted with water and extracted with ethyl acetate. Examination of the crude extract by tlc in ethyl acetate–benzene (2:1) showed that starting material (R_f 0.46) had beenc onverted entirely into two less mobile products. Both compounds (R_f 0.29 and 0.39) were Beilstein positive. The mixture was chromatographed in ethyl acetate–isooctane (3:2) on a 32 × 910 mm silica gel column. Fractions (7 ml) were collected every 15 min.

21,21-Dibromo-5β-pregnane-3α,17,20β-triol (46). Fractions 131–197.—Crystallization from ether gave 160 mg of prisms: mp 200–202°; $[\alpha]_{365}$ +56.3°, $[\alpha]_{436}$ +41.6°, $[\alpha]_{546}$ +27.6°, $[\alpha]_D$ +25.2°.

Anal. Calcd for $C_{21}H_{34}Br_2O_3$: C, 51.02; H, 6.93; Br, 32.33. Found: C, 51.12; H, 7.13; Br, 32.39.

21-Bromo-5β-pregnane-3α,17,20β-triol (5b). Fractions 205–305.—Crystallization from acetone gave prisms (180 mg, mp 163.5–164.5°; 39 mg, mp 148–150°). Recrystallization from acetone–ether gave the analytical sample: mp 165–166°; $[\alpha]_{365}$ +144°, $[\alpha]_{436}$ +94.5°, $[\alpha]_{546}$ +55.6°, $[\alpha]_D$ +48.1°.

Anal. Calcd for $C_{21}H_{35}BrO_3$: C, 60.71; H, 8.49; Br, 19.24. Found: C, 60.50; H, 8.64; Br, 19.17.

21-Bromo-5β-pregnane-3α,17,20β-triol 3,20-Diacetate (6b).—Acetylation of 21-bromo-5β-pregnane-3α,17,20β-triol and crystallization of the product from methanol gave needles: mp 198–199° dec; $[\alpha]_{365}$ +286°, $[\alpha]_{436}$ +182°, $[\alpha]_{546}$ +109°, $[\alpha]_D$ +95.5°.

Anal. Calcd for $C_{25}H_{39}BrO_5$: C, 60.11; H, 7.87. Found: C, 60.00; H, 7.89.

21-Bromo-5β-pregnane-3α,17,20α- (and 20β-) triols (5a and 5b) from 2.—To a solution of 21-bromo-3α,17-dihydroxy-5β-pregnan-20-one (2.5 g) in methanol (125 ml) at 0° was added sodium borohydride (1.5 g). After 5 min at 0° the product was recovered as in the preparation of **5b** and **46** from **44**. Crystallization from acetone afforded 1202 mg of **5b**, mp 164–165°. The remaining material was chromatographed on a 50 × 800 mm silica gel column in ethyl acetate–isooctane (3:1). Fractions (12 ml) were collected at 10-min intervals.

Crystallization from acetone of the residue from fractions 201–250 gave an additional 705 mg of **5b**, mp 164–165°. Since fractions 251–450 consisted of a mixture of **5a** and **5b**, the residues were rechromatographed on a 35 × 730 mm Celite column in toluene, 60; isooctane, 140; methanol, 150; 5% boric acid, 50 ml.[27] Fractions of 8 ml were collected at 15-min intervals.

The residue obtained by combining fractions 91–175 was partitioned between methylene chloride and very dilute sodium hydroxide solution. The organic layer was washed with water and concentrated to dryness. The residue was purified further by chromatography on a small silica gel column. Crystallization from acetone gave an additional 148 mg of **5b**, raising the yield of 21-bromo-5β-pregnane-3α,17-20β-triol to 2055 mg (81.8%).

21-Bromo-5β-pregnane-3α,17,20α-triol. Fractions 226–335.—The pooled material was recovered as above. Crystallization from acetone gave 74.8 mg (3% yield) of prisms: mp 172–172.5° (recrystallization from acetone gave the analytical sample); mp 174.5–175°; $[\alpha]_{365}$ +16.8°, $[\alpha]_{436}$ +12.6°, $[\alpha]_{546}$ +8.42°, $[\alpha]_D$ +7.15°.

Anal. Calcd for $C_{21}H_{35}O_3Br$: C, 60.71; H, 8.49; Br, 19.24. Found: C, 60.28; H, 8.39; Br, 18.93.

21-Bromo-5β-pregnane-3α,17,20α-triol 3,20-Diacetate (6a).—Acetylation of 21-bromo-5β-pregnane-3α,17,20α-triol in the usual manner and crystallization from *n*-hexane gave prisms in clusters: mp 174.5°; $[\alpha]_{365}$ −12.3°, $[\alpha]_{436}$ −6.18°, $[\alpha]_{546}$ −2.64°, $[\alpha]_D$ −1.76°.

Anal. Calcd for $C_{25}H_{39}O_5Br$: C, 60.11; H, 7.87. Found: C, 60.01; H, 7.91.

3α,17-Dihydroxy 20,21-Oxides. Reduction of 2 with Sodium Borohydride in Dimethylformamide.—To a solution of 21-bromo-3α,17-dihydroxy-5β-pregnan-20-one (500 mg) in dimethylformamide (11.25 ml) was added sodium borohydride (150 mg) in water (1.25 ml). After 1 hr at room temperature excess acetic acid was added and the solution was diluted with water and extracted with ethyl acetate. The crude product (350 mg) was chromatographed on a 32 × 690 mm Celite column in benzene, 300; *n*-hexane, 100; formamide, 12 ml. Fractions (7 ml) were collected at 15-min intervals.

20β,21-Oxido-5β-pregnane-3α,17-diol (3b). Fractions 51–101.—Crystallization from acetone gave plates (115 mg, mp 155–157°; 28 mg, mp 154–156°). The analytical sample had mp 156.5–158.5°; $[\alpha]_{365}$ −22.4°, $[\alpha]_{436}$ −13.4°, $[\alpha]_{546}$ −8.3°, $[\alpha]_D$ −7.03.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 74.98; H, 10.44.

20β,21-Oxido-5β-pregnane-3α,17-diol 3-Acetate (4b).—Acetylation of 20β,21-oxido-5β-pregnane-3α,17-diol (100 mg) with pyridine (0.2 ml) and acetic anhydride (0.2 ml) was carried out for 16 hr at room temperature. The crude product was chromatographed on a small silica gel column in isooctane–ethyl acetate (2:1). Crystallization of the purified product (50 mg) from *n*-hexane furnished prisms: mp 109–110°; $[\alpha]_{365}$ +54.2°, $[\alpha]_{436}$ +36.1°, $[\alpha]_{546}$ +21.8°, $[\alpha]_D$ +19.5°.

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64. Found: C, 73.75; H, 9.63.

5β-Pregnane-3α,17,20β-triol. Fractions 131–191.—Crystallization from acetone gave prisms (87 mg, mp 220–222°, 11.5 mg, mp 215.5–218°) which did not depress the melting point of an authentic sample of 5β-pregnane-3α,17,20β-triol.

5β-Pregnane-3α,17,20α-triol. Fractions 205–270.—Crystallization from acetone gave plates (13.5 mg, mp 254–255°) which possessed an infrared spectrum identical with that of 5β-pregnane-3α,17,20α-triol.

20β,21-Oxido-5β-pregnane-3α,17-diol (3b) from 2.—To a solution of 21-bromo-3α,17-dihydroxy-5β-pregnan-20-one (250 mg) in methanol (45 ml) was added sodium borohydride (150 mg) in water (25 ml). After 1.5 hr at room temperature excess acetic acid was added and most of the methanol was evaporated with a stream of nitrogen. The solution was diluted with water and extracted with ethyl acetate. The crude product was chromatographed on a 20 × 750 mm Celite column in benzene, 300; *n*-hexane, 100 ml, saturated with formamide. Fractions (6 ml) were collected every 15 min. Crystallization from acetone of the residues from fractions 28–58 gave plates (120 mg, mp 156–157°; 38 mg, mp 153–154°) in a yield of 82.7%. The infrared spectrum was identical with that of the mobile by-product obtained after reduction of **2** in dimethylformamide.

20β,21-Oxido-5β-pregnane-3α,17-diol (3b) from 5b.—21-Bromo-5β-pregnane-3α,17,20β-triol (25 mg) in methanol (10 ml) was treated with 0.1 *N* sodium hydroxide (2.5 ml) for 5 min at room temperature. After addition of an equivalent amount of 1 *N* hydrochloric acid, concentration to a small volume, and extraction with methylene chloride, the product crystallized from acetone as plates (9.5 mg, mp 156.5–158°; 5 mg, mp 154–155.5°). The infrared spectrum was identical with that of **3b** prepared by reduction of **2**.

21-Bromo-5β-pregnane-3α,17,20β-triol (5b) from 3b.—To a solution of 20β,21-oxido-5β-pregnane-3α,17-diol (50 mg) in chloroform (0.5 ml) was added 32% hydrogen bromide in acetic acid (0.05 ml). After 15 min at room temperature the solution was diluted with chloroform, washed, dried, and evaporated to dryness. The crude product was chromatographed on a 14 × 480 mm silica gel column in benzene–ethyl acetate (1:1). Fractions (2 ml) were collected every 10 min. Crystallization from ether of the contents of fractions 44–65 afforded a product (45 mg, mp 163.5–164°) which was indistinguishable from **5b** prepared by reduction of **2**.

Lithium Aluminum Hydride Reduction of 3b.—A solution of 20β,21-oxido-5β-pregnane-3α,17-diol (50 mg) and lithium aluminum hydride (50 mg) in ether (25 ml) was refluxed for 2 hr. Crystallization of the product from acetone provided needles (26 mg, mp 217.5–222°; 12.6 mg, mp 210–214°). A mixture melting point with a sample of 5β-pregnane-3α,17,20β-triol

(27) The improved separation of the bromotriols in the presence of boric acid can be exemplified by their paper chromatographic behavior. R_f values for **5a** and **5b** (in isooctane, 120; toluene, 80; methanol, 150; water, 50 ml) are 0.33 and 0.42, respectively. Substitution of 5% boric acid for water results in R_f values of 0.36 and 0.62.

was 217–219.5°. In addition, their paper chromatographic mobilities and infrared spectra were identical.

5β-Pregnane-3α,17,20β,21-tetrol (12b) from 3b.—To a solution of 100 mg of 20β,21-oxido-5β-pregnane-3α,17-diol in 12 ml of tetrahydrofuran (freshly distilled from lithium aluminum hydride) was added successively 4 ml of water and 4 ml of 1 *N* sulfuric acid. After 22.5 hr at room temperature, the solution was neutralized and concentrated *in vacuo* until turbidity developed. The product was recovered by extraction with ethyl acetate and further purified by chromatography on a 25 × 690 mm Celite column in toluene, 200; methanol, 70; water, 60 ml. Fractions (7.5 ml) were collected at a rate of four per hour. Fractions 115–195 gave, from acetone, hexagonal plates (68 mg, mp 221.5–223.5°; 6 mg, mp 217–219°). The analytical sample had mp 222.5–223.5°; $[\alpha]_{365}$ +43.1°, $[\alpha]_{436}$ +30.0°, $[\alpha]_{546}$ +18.7°, $[\alpha]_D$ +17.0°.

Anal. Calcd for $C_{21}H_{36}O_4$: C, 71.55; H, 10.30. Found: C, 71.51; H, 10.27.

5β-Pregnane-3α,17,20β,21-tetrol 3,20,21-Triacetate (11b).—Acetylation of **12b** in the usual manner afforded prismatic needles from ether: mp 159–160°; $[\alpha]_{365}$ +308°, $[\alpha]_{436}$ +197°, $[\alpha]_{546}$ +116°, $[\alpha]_D$ +102°.

Anal. Calcd for $C_{27}H_{42}O_7$: C, 67.75; H, 8.85; CH_3CO, 26.98. Found: C, 67.95; H, 8.82; CH_3CO, 27.75.

Periodic Acid Oxidation of 3b.—To 20 mg of 20β,21-oxido-5β-pregnane-3α,17-diol in 0.5 ml of ethanol was added 25 mg of H_5IO_6 in 0.5 ml of ethanol–water (8:2 v/v) 0.4 *N* in sulfuric acid. After 3 hr at room temperature the solution was diluted with ethyl acetate and washed several times with brine. Analysis of the extract by tlc in isooctane–ethyl acetate (1:1) showed a single product. After purification on a small silica gel column in the same system, the product crystallized as needles from aqueous methanol (12.4 mg, mp 150–152°; 1.5 mg, mp 148–150°). Recrystallization from a small volume of acetone provided a pure sample, mp 151.5–153.5° which did not depress the melting point of an authentic sample of 3α-hydroxy-5β-androstan-17-one. In addition, their infrared spectra were identical.

21-Acetoxy-3α,17-dihydroxy-5β-pregnan-20-one (7) from 2.—To a solution of 21-bromo-3α,17-dihydroxy-5β-pregnan-20-one (7 g) in acetone (150 ml) was added acetic acid (20 ml), then, slowly, triethylamine (33 ml).[10] The solution was refluxed for 1 hr, then concentrated in a stream of nitrogen. The product was recovered by dilution with water and extraction with ethyl acetate. Several crystallizations from ethyl acetate gave **7** as prisms (5.78 g, mp 225–227°) in a yield of 87.2%. The analytical sample had mp 226–228°; $[\alpha]_{365}$ +487°, $[\alpha]_{436}$ +200°, $[\alpha]_{546}$ +92.3°, $[\alpha]_D$ +78.5°.

Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.37; H, 9.24; CH_3CO, 10.96. Found: C, 70.11; H, 9.16; CH_3CO, 10.70.

3α,21-Diacetoxy-17-hydroxy-5β-pregnan-20-one (8).—Acetylation of 21-acetoxy-3α,17-dihydroxy-5β-pregnan-20-one (4 g) with pyridine (12 ml) and acetic anhydride (8 ml) was carried out for 4 hr at room temperature. A crystalline product separated after addition of ice and water. Recrystallization of the washed, dried product from acetone gave plates, mp 206–208°, in a total yield of 4.2 g (94.8%): $[\alpha]_{365}$ +496°, $[\alpha]_{436}$ +222°, $[\alpha]_{546}$ +108°, $[\alpha]_D$ +93.3°; reported[6] mp 205–206°, $[\alpha]_D$ +88° (EtOH).

3α,Acetoxy-17,21-dihydroxy-5β-pregnan-20-one (15) from 8.—To 434 mg (1 mmol) of 3α,21-diacetoxy-17-hydroxy-5β-pregnan-20-one in 40 ml of methanol was added 0.1 ml (0.1 mmol) of 1 *N* sodium hydroxide. After 2 hr at room temperature 3 drops of acetic acid was added, and the solution was concentrated to a small volume. Addition of water gave a crystalline precipitate which, on recrystallization from acetone, gave needles (254 mg, mp 186.5–189°; 57 mg, mp 184.5–186.5°) in a total yield of 83%. The analytical sample, recrystallized from acetone and dried to constant weight at 100° *in vacuo*, had mp 196–197.5°; $[\alpha]_{365}$ +448°, $[\alpha]_{436}$ +202°, $[\alpha]_{546}$ +101°, $[\alpha]_D$ +87.2°.

Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.37; H, 9.25. Found: C, 70.84; H, 9.29.

5β-Pregnane-3α,17,20β,21-tetrol 21-Acetate (9b) from 7.—To a solution of 21-acetoxy-3α,17-dihydroxy-5β-pregnan-20-one (500 mg) in dimethylformamide (12 ml) was added sodium borohydride (150 mg) in water (1.2 ml). After 1 hr at room temperature, the product was recovered in the usual fashion. Crystallization from acetone afforded needles (344 mg, mp 218–220°; 51 mg, mp 215–218°). Saponification of a sample provided the free tetrol **12b**, identical in all respects with the hydration product of **3b**. The analytical sample had mp 218–220°; $[\alpha]_{365}$ +67.2° $[\alpha]_{436}$ +45.8°, $[\alpha]_{546}$ +27.7°, $[\alpha]_D$ +25.0°.

Anal. Calcd for $C_{23}H_{38}O_5$: C, 70.01; H, 9.71; CH_3CO, 10.91. Found: C, 70.28; H, 9.91; CH_3CO, 10.78.

5β-Pregnane-3α,17,20β,21-tetrol 3-Acetate (16b) from 15.—To a solution of 3α-acetoxy-17,21-dihydroxy-5β-pregnan-20-one (250 mg) in dimethylformamide (6 ml) was added sodium borohydride (75 mg) in water (0.6 ml). After 1 hr at room temperature the product was recovered in the usual manner and chromatographed on a 25 × 660 mm silica gel column in ethyl acetate. Fractions (7.5 ml) were collected at 15-min intervals. The purified product was obtained from fractions 81–181 as a foam (206 mg) which, although homogeneous by tlc in ethyl acetate (R_f 0.25), could not be crystallized: $[\alpha]_{365}$ +98.5°, $[\alpha]_{436}$ +65.3°, $[\alpha]_{546}$ +39.4°, $[\alpha]_D$ +34.7°.

5β-Pregnane-3α,17,20β,21-tetrol 3,21-Diacetate (10b) from 8.—Reduction of 3α,21-diacetoxy-17-hydroxy-5β-pregnan-20-one (4 g) in dimethylformamide (100 ml) with sodium borohydride (1.2 g) in water (10 ml) was carried out for 1 hr at room temperature. After the addition of excess acetic acid and water (500 ml), the mixture was extracted with ethyl acetate. Successive crystallizations from aqueous acetone and acetone–*n*-hexane gave 2.9 g of **10b** as plates, mp 174.5–175°. The remaining material was chromatographed on a 38 × 740 mm silica gel column in benzene–ethyl acetate (3:2). Fractions (8 ml) were collected every 15 min. From fractions 151–265 was obtained an additional 493 mg of plates, mp 173–174°, raising the yield of **10b** to 3.39 g (84.1%). The analytical sample had mp 174.5–176°; $[\alpha]_{365}$ +137°, $[\alpha]_{436}$ +89.4°, $[\alpha]_{546}$ +53.5°, $[\alpha]_D$ +47.2°.

Anal. Calcd for $C_{25}H_{40}O_6$: C, 68.77; H, 9.24; CH_3CO, 19.72. Found: C, 68.84; H, 9.40; CH_3CO, 19.05.

20β-Tosyloxy-5β-pregnane-3α,17,21-triol 3,21-Diacetate (17b) from 10b.—A solution of 5β-pregnane-3α,17,20β,21-tetrol 3,21-diacetate (2 g) and tosyl chloride (2 g) in pyridine (10 ml) stood at room temperature for 90 hr. The product crystallized as leaflets from acetone–*n*-hexane: 2.49 g; mp 145° dec; $[\alpha]_{365}$ +214°, $[\alpha]_{436}$ +137°, $[\alpha]_{546}$ +81.7°, $[\alpha]_D$ +71.0°; ν_{max} 3550 (br) (hydroxyl), 1732 and 1240 (acetate), 1595, 1490, 1360, 1185, 1170, 1092, 808, 660 cm^{-1} (tosylate).[28]

Anal. Calcd for $C_{32}H_{46}O_8S$: C, 65.06; H, 7.85. Found: C, 65.30; H, 8.01.

20β-Tosyloxy-5β-pregnane-3α,17,21-triol Triacetate (18b) from 17b.—To a solution of 20β-tosyloxy-5β-pregnane-3α,17,21-triol 3,21-diacetate (1.2 g) in carbon tetrachloride (120 ml) was added a mixture of acetic anhydride (7.2 ml) and 60% perchloric acid (0.06 ml). After 1 min at room temperature methanol (5 ml) was added, and after dilution with an equal volume of carbon tetrachloride the solution was washed with cold, dilute sodium hydroxide solution and water. The product crystallized from methanol as needles (1147 mg, 89.2%), mp 120.5–121° dec. The compound darkens on standing. The analytical sample had mp 122.5° dec; $[\alpha]_{365}$ +138°, $[\alpha]_{436}$ +87.1°, $[\alpha]_{546}$ +73.0°, $[\alpha]_D$ +67.9°.

Anal. Calcd for $C_{34}H_{48}O_9S$: C, 64.54; H, 7.65. Found: C, 64.78; H, 7.71.

5β-Pregnane-3α,17,20α,21-tetrol 3,20,21-Triacetate (11a) from 18b.—A solution of 20β-tosyloxy-5β-pregnane-3α,17,21-triol triacetate (2.1 g) and potassium acetate (20 g) in a mixture of 96% acetic acid (200 ml) and acetic anhydride (10 ml) was refluxed for 3 hr. After standing for an additional 3 hr at room temperature, the solution was added to ice and water and extracted with methylene chloride. Crystallization of the product from acetone–ether and ether gave needles (1060 mg, mp 171–172°; 130 mg, mp 168–170°) in a yield of 74.8%.[29] Recrystallization from methanol gave the analytical sample as prismatic needles: mp 172–173°; $[\alpha]_{365}$ −52.5°, $[\alpha]_{436}$ −32.2°, $[\alpha]_{546}$ −18.8°, $[\alpha]_D$ −16.6°; ν_{max} 3475 (hydroxyl), 1735 and 1240 cm^{-1} (acetate).

Anal. Calcd for $C_{27}H_{42}O_7$: C, 67.76; H, 8.85. Found: C, 67.86; H, 8.83.

5β-Pregnane-3α,17,20α,21-tetrol (12a) from 11a.—Saponification of 5β-pregnane-3α,17,20α,21-tetrol 3,20,21-triacetate with methanolic sodium hydroxide and crystallization from methanol

(28) These are the principal bands in the infrared spectra of all tosylates described in this paper. For a more detailed listing of bands characteristic of steroidal tosylates, see Hirschmann, *et al.* [H. Hirschmann; F. B. Hirschmann, and A. P. Zala, *J. Org. Chem.*, **31**, 375 (1966)].

(29) Saponification of the material remaining in the mother liquors afforded 157 mg of 5β-pregnane-3α,17,20α,21-tetrol (**12a**), mp 263–264°.

gave prisms: mp 267–267.5°; $[\alpha]_{365}$ +14.4°, $[\alpha]_{436}$ +10.5°, $[\alpha]_{546}$ +6.70°, $[\alpha]_D$ +5.76°.

Anal. Calcd for $C_{21}H_{36}O_4$: C, 71.55; H, 10.30. Found: C, 71.31; H, 10.40.

21-Tosyloxy-5β-pregnane-3α,17,20β-triol (13b) from 12b.—A solution of 5β-pregnane-3α,17,20β,21-tetrol (500 mg) and tosyl chloride (355 mg) in pyridine (5 ml) stood for 24 hr at room temperature. The product crystallized from acetone as trapezoidal plates (352 mg, mp 185.5° dec). Silica gel chromatography of the mother liquor in benzene–ethyl acetate (1:1) afforded an additional 40 mg of **13b**, raising the yield to 55.7%. The analytical sample had mp 186° dec; $[\alpha]_{365}$ +69.0°, $[\alpha]_{436}$ +48.7°, $[\alpha]_{546}$ +30.1°, $[\alpha]_D$ +27.4°; ν_{max} 3540 and 3400 (free and associated hydroxyl), 1037 cm^{-1} (3α-hydroxyl).

Anal. Calcd for $C_{28}H_{42}O_6S$: C, 66.38; H, 8.36. Found: C, 66.59; H, 8.46.

21-Tosyloxy-5β-pregnane-3α,17,20β-triol 3,20-Diacetate (14b) from 13b.—Acetylation of 21-tosyloxy-5β-pregnane-3α,17,20β-triol in the usual manner and crystallization from ethanol gave plates: mp 133–134.5°; $[\alpha]_{365}$ +193°, $[\alpha]_{436}$ +124°, $[\alpha]_{546}$ +74.1°, $[\alpha]_D$ +64.8°.

Anal. Calcd for $C_{32}H_{46}O_8S$: C, 65.06; H, 7.85. Found: C, 65.43; H, 8.05.

20β,21-Oxido-5β-pregnane-3α,17-diol (3b) from 13b.—21-Tosyloxy-5β-pregnane-3α,17,20β-triol (25 mg) was treated with alkali as in the preparation of **3b** from **5b**. Crystallization from acetone gave 16 mg of needles, mp 157–158.5°, whose infrared spectrum was identical with that of **3b** prepared from **2**.

21-Bromo-5β-pregnane-3α,17,20β-triol (5b) from 13b.—A solution of 21-tosyloxy-5β-pregnane-3α,17,20β-triol (100 mg) and sodium bromide (1 g) in diethylene glycol (15 ml) was heated for 5 hr at 100°.[11] The cooled reaction mixture was diluted with water and extracted with ethyl acetate. The product was chromatographed on a 20 × 700 mm Celite column in isopropyl ether, 80; *n*-heptane, 120; methanol, 150; water, 50 ml. Fractions (7 ml) were collected at 15-min intervals. Since tlc analysis showed that fractions 52–67 contained both the bromtriol **5b** and a less mobile contaminant, the mixture was rechromatographed on a 16 × 670 mm silica gel column in benzene–ethyl acetate (1:1). Fractions (2 ml) were collected at 10-min intervals. Crystallization from ether of the residue from fractions 100–175 afforded plates (29 mg, mp 164.5–165.5°) which proved identical in all respects with **5b** prepared by sodium borohydride reduction of **2**.

21-Tosyloxy-5β-pregnane-3α,17,20α-triol (13a) and 3α,21-Ditosyloxy-5β-pregnane-17,20α-diol (19) from 12a.—A solution of 5β-pregnane-3α,17,20α,21-tetrol (500 mg) and tosyl chloride (355 mg) in pyridine (10 ml) stood for 12 hr at room temperature. The product was chromatographed on a 35 × 760 mm silica gel column in ethyl acetate–isooctane (2:1). Fractions (7 ml) were collected at 10-min intervals. Since fractions 45–85 (102 mg) contained several contaminants in addition to **19**, it was rechromatographed on a 20 × 770 mm silica gel column in isooctane–ethyl acetate (3:2). Fractions (3 ml) were collected at 12-min intervals.

3α,21-Ditosyloxy-5β-pregnane-17,20α-diol. Fractions 118–145.—Crystallization from acetone–*n*-hexane gave needles (30 mg, mp 135.5–136.5° dec; 9 mg, mp 133–133.5° dec). Recrystallization from methanol provided the analytical sample: mp 135° dec (on stage at 130°); $[\alpha]_{365}$ +14.3°, $[\alpha]_{436}$ +11.6°, $[\alpha]_{546}$ +7.17°, $[\alpha]_D$ +6.27°. The infrared spectrum showed intensification of the tosylate bands and absence of the band at 1035 cm^{-1}, characteristic of the 3α-hydroxyl group.

Anal. Calcd for $C_{35}H_{48}O_8S_2$: C, 63.62; H, 7.32. Found: C, 63.79; H, 7.43.

21-Tosyloxy-5β-pregnane-3α,17,20α-triol (13a). Fractions 235–400.—The amorphous tosylate (359 mg, 50%) was obtained as a filterable solid from methanol–water. The washed and dried product (332 mg) was homogeneous (R_f 0.21) by tlc in ethyl acetate–benzene (2:1): mp 93–95°; $[\alpha]_{365}$ −36.0°, $[\alpha]_{43}$ −23.4°, $[\alpha]_{546}$ −13.6°, $[\alpha]_D$ −11.4°.

Anal. Calcd for $C_{28}H_{42}O_6S$: C, 66.38; H, 8.36. Found: C, 66.13; H, 8.51.

21-Tosyloxy-5β-pregnane-3α,17,20α-triol 3,20-Diacetate (14a).—Acetylation of 21-tosyloxy-5β-pregnane-3α,17,20α-triol in the usual manner gave a product which could be obtained as a filterable solid from aqueous methanol: mp 78–81°; $[\alpha]_{365}$ −51.8°, $[\alpha]_{436}$ −32.0°, $[\alpha]_{546}$ −18.8°, $[\alpha]_D$ −16.7°.

Anal. Calcd for $C_{32}H_{46}O_8S$: C, 65.06; H, 7.85. Found: C, 64.79; H, 7.92.

20α,21-Oxido-5β-pregnane-3α,17-diol (3a) from 13a.—To a solution of 21-tosyloxy-5β-pregnane-3α,17,20α-triol (304 mg,0.6 mmol) in methanol (60 ml) was added 0.1 *N* sodium hydroxide (6.85 ml, 0.685 mmol). After 5 min at room temperature, the solution was diluted with water and extracted with ethyl acetate. The crude product (231 mg) was chromatographed on a 35 × 735 mm Celite column in isooctane, 150; toluene, 50; methanol, 160; water, 40 ml. Fractions (9 ml) were collected every 15 min. The pooled residues of fractions 236–325 afforded 165 mg of needles from acetone, mp 161.5–162°, in a yield of 82.5% (recrystallization from the same solvent did not raise the melting point): $[\alpha]_{365}$ −38.0°, $[\alpha]_{436}$ −19.7°, $[\alpha]_{546}$ −10.4°, $[\alpha]_D$ −8.39°.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.35; H, 10.33.

20α,21-Oxido-5β-pregnane-3α,17-diol 3-Acetate (4a).—Acetylation of 20α,21-oxido-5β-pregnane-3α,17-diol in the usual manner and purification of the product as in the preparation of **4b** gave needles from acetone–*n*-hexane: mp 155–156°; $[\alpha]_{365}$ +38.3°, $[\alpha]_{436}$ +27.6°, $[\alpha]_{546}$ +17.7°, $[\alpha]_D$ +15.6°.

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64. Found: C, 73.20; Y, 9.58.

Lithium Aluminum Hydride Reduction of 3a.—A solution of 20α,21-oxido-5β-pregnane-3α,17-diol (25 mg) and lithium aluminum hydride (50 mg) in ether (25 ml) was refluxed for 3 hr. A mixture melting point of the product with an authentic sample of 5β-pregnane-3α,17,20α-triol was 253.5–254°, and their infrared spectra were identical.

5β-Pregnane-3α,17,20α,21-tetrol (12a) from 3a.—To a solution of 20α,21-oxido-5β-pregnane-3α,17-diol (25 mg) in tetrahydrofuran (3 ml) was added successively water (1 ml) and 1 *N* sulfuric acid (1 ml). After 72 hr at room temperature the product was recovered as in the preparation of **12b** from **3b** and chromatographed on a 16 × 550 mm Celite column in toluene, 110; isooctane, 90; methanol, 150; water, 50 ml. Fractions (2 ml) were collected every 10 min. After the emergence of fraction 266, the mobile phase was changed to toluene, 140; isooctane, 60 ml. Crystallization of the pooled residues from fractions 155–180 gave needles (9.2 mg, mp 146–146.5°; 2.9 mg, mp 142–143.5°). The nature of this substance is under investigation.

5β-Pregnane-3α,17,20α,21-tetrol (12a).—The pooled residues from fractions 516–900 (7.9 mg) was crystallized from methanol to give 5 mg of needles, mp 266.5°, which were identical in all respects with the saponification product of **11a**.

Periodic Acid Oxidation of 3a.—20α,21-Oxido-5β-pregnane-3α,17-diol (20 mg) was treated with periodic acid as in the oxidation of **3b**. Analysis of the reaction mixture by tlc showed a ternary mixture which was chromatographed on a 10 × 280 mm silica gel column in isooctane–ethyl acetate (1:1). Fractions (0.5 ml) were collected at 5-min intervals. Fractions 32–48 contained an amorphous substance which was discarded.

Fractions 70–105.—The crude residue (3.3 mg) was crystallized from acetone to give 1.4 mg of needles which possessed an infrared spectrum identical with that of 3α-hydroxy-5β-androstan-17-one. Further elution afforded, from fractions 150–220, 6.6 mg of starting material **3a**.

21-Bromo-5β-pregnane-3α,17,20α-triol (5a) from 3a.—To a solution of 20α,21-oxido-5β-pregnane-3α,17-diol (75 mg) in chloroform (0.75 ml) was added 0.075 ml of 32% hydrogen bromide in acetic acid. After 15 min at room temperature the product was recovered as in the preparation of **5b** from **3b**. Crystallization from acetone and from acetone–*n*-hexane afforded prisms (72 mg, mp 171°; 6 mg, mp 168–169°) in a yield of 83.7%. The product was identical with the minor product obtained from **2** after reduction with sodium borohydride in methanol.

Reaction of the bromotriol **5a** with methanolic sodium hydroxide, as in the preparation of **3b** from **5b**, afforded the 20α,21-oxide **3a** as the sole product.

3α,21-Dihydroxy 17,20-Oxides. 3α,17,21-Trihydroxy-5β-pregnan-20-one (20) from 7.—To 2.78 g (7.1 mmol) of 21-acetoxy-3α,17-dihydroxy-5β-pregnan-20-one in 300 ml of methanol was added 0.71 ml of 1 *N* sodium hydroxide. After 2 hr at room temperature acetic acid was added. The solution was concentrated to a small volume, diluted with water, and extracted with methylene chloride. Several crystallizations from methanol gave 2.23 g (89.3%) of prisms: mp 202–204°; $[\alpha]_{365}$ +446°, $[\alpha]_{436}$ +181°, $[\alpha]_{546}$ +82.3°, $[\alpha]_D$ +68.5°; reported[30] mp 200–204° (214–216°), $[\alpha]^{27}D$ +60° (EtOH).

(30) F. Ungar and R. I. Dorfman, *J. Amer. Chem. Soc.*, **76**, 1197 (1954).

Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.62; H, 9.83.

Methyl 3α,17,20α- and 3α,17α,20β-Trihydroxy-5β-pregnan-21-oates (21a and 21b) from 20.—A solution of 3α,17,21-trihydroxy-5β-pregnan-20-one (1050 mg, 3 mmol) in methanol (150 ml) was oxidized with cupric acetate (300 mg, 1.5 mmol) for 1 hr in the manner described previously.[17] To a solution of the resulting amorphous glyoxal in 5 ml of methanol was added successively water (100 ml) and 1 *N* sodium hydroxide (10 ml). The initially turbid suspension became virtually clear in about 30 min. After 16.5 hr at room temperature the yellow solution was acidified and extracted with ethyl acetate. The mixture of C-20-epimeric glycolic acids was dissolved in methanol and esterified with diazomethane, affording 1170 mg of crude methyl esters. Two crystallizations from acetone gave 165 mg of **21b** as prisms, mp 202.5–204°. The remaining material was chromatographed on a 54 × 880 mm Celite column in toluene, 110; isooctane, 90; methanol, 140; 5% boric acid, 60 ml. Fractions (10 ml) were collected at intervals of 12 min.

Methyl 3α,17,20β-Trihydroxy-5β-pregnan-21-oate (21b). Fractions 285–385.—Partitioning between methylene chloride and water followed by crystallization from acetone gave an additional quantity of **21b** (99 mg, mp 203.5–205°; 26 mg, mp 201.5–203.5°) raising the yield to 290 mg (25.4%). The analytical sample had mp 205–206°; $[\alpha]_{365}$ +21.4°, $[\alpha]_{436}$ +12.4°, $[\alpha]_{546}$ +7.42°, $[\alpha]_D$ +5.77°; ν_{max} 3580, 3510, 3355 (free and associated hydroxyl), 1735 (sh), 1720 (sh), 1712 (carbomethoxyl), and 1037 cm^{-1} (3α-hydroxyl).

Anal. Calcd for $C_{22}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 69.02; H, 9.58.

Methyl 3α,20β-Diacetoxy-17-hydroxy-5β-pregnan-21-oate (22b).—Acetylation of methyl 3α,17,20β-trihydroxy-5β-pregnan-21-oate in the usual manner and crystallization from methanol gave prisms: mp 189–190°; $[\alpha]_{365}$ +114°, $[\alpha]_{436}$ +70.5° $[\alpha]_{546}$ +40.2°, $[\alpha]_D$ +35.0°.

Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.21; H, 8.68. Found: C, 67.14; H, 8.61.

Methyl 3α,17,20α-Trihydroxy-5β-pregnan-21-oate (21a). Fractions 480–680.—After partitioning between methylene chloride and dilute sodium hydroxide solution the ester crystallized from a small volume of benzene as hairy needles (639 mg, mp 94–97°) in a yield of 56% (it could not be crystallized from acetone–ether or acetone–*n*-hexane; recrystallization from benzene–*n*-hexane did not raise the melting point): $[\alpha]_{365}$ −13.1°, $[\alpha]_{436}$ −3.79°, $[\alpha]_{546}$ +0.69°, $[\alpha]_D$ +0.69°; ν_{max} 3450 (br) (associated hydroxyl), 1730 (carbomethoxyl), and 1038 cm^{-1} (3α-hydroxyl).

Anal. Calcd for $C_{22}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 69.87; H, 9.40.

Methyl 3α,20α-Diacetoxy-17-hydroxy-5β-pregnan-21-oate (22a).—Acetylation of methyl 3α,17,20α-trihydroxy-5β-pregnan-21-oate was carried out in the usual manner. The product could not be crystallized from anhydrous solvents. Addition of water to a methanol solution gave a filterable solid: mp 72.5–74°; $[\alpha]_{365}$ +114°, $[\alpha]_{436}$ +78.6°, $[\alpha]_{546}$ +48.3°, $[\alpha]_D$ +43.0°.

Anal. Calcd for $C_{26}H_{40}O_7$: C, 67.21; H, 8.68. Found: C, 67.10; H, 8.74.

Methyl 3α-Hydroxy-17,20β-isopropylidenedioxy-5β-pregnan-21-oate (23b) from 21b.—To a solution of methyl 3α,17,20β-trihydroxy-5β-pregnan-21-oate (100 mg) in acetone (100 ml) was added 70% perchloric acid (0.25 ml). The solution developed a yellow color slowly at room temperature. Analysis of an aliquot after 5 hr by tlc in ethyl acetate–isooctane (3:2) showed approximately 90% conversion of starting material (R_f 0.06) to a more mobile product (R_f 0.34). After a reaction time of 6.5 hr solid sodium bicarbonate (250 mg) was added, the solution was concentrated *in vacuo*, and the product was recovered by partitioning between methylene chloride and water. It was chromatographed on a 14 × 280 mm silica gel column in ethyl acetate–isooctane (3:2). Fractions (5 ml) were collected every 20 min. From fractions 6–9 a total of 91 mg of product was obtained which, although homogeneous by tlc, was not obtained in crystalline form: $[\alpha]_{365}$ +65.4°, $[\alpha]_{436}$ +41.9°, $[\alpha]_{546}$ +24.5°, $[\alpha]_D$ +21.3°; ν_{max} 1758, 1737 (sh) (carbomethoxyl), and 1038 cm^{-1} (3α-hydroxyl).

Acetylation in the usual manner gave the amorphous methyl 3α-acetoxy-17,20β-isopropylidenedioxy-5β-pregnan-21-oate (**24b**): $[\alpha]_{365}$ +109°, $[\alpha]_{436}$ +69.6°, $[\alpha]_{546}$ +40.1°, $[\alpha]_D$ +35.5°; ν_{max} 1758 (carbomethoxyl), 1733, 1240, and 1027 cm^{-1} (3α-acetoxyl); there was no absorption above 3000 cm^{-1}.

17,20β-Isopropylidenedioxy-5β-pregnane-3α,21-diol (26b) from 23b.—A solution of methyl 3α-hydroxy-17,20β-isopropylidenedioxy-5β-pregnan-21-oate (90 mg) and lithium aluminum hydride (150 mg) in ether (50 ml) was refluxed for 3 hr. The product was recovered without the use of mineral acid and crystallized from acetone–*n*-hexane as needles (49 mg, mp 177–177.5°; 20.5 mg, mp 176.5–177°). The analytical sample had mp 178–178.5°; $[\alpha]_{365}$ +30.2°, $[\alpha]_{436}$ +22.2°, $[\alpha]_{546}$ +14.2°, $[\alpha]_D$ +12.4°.

Anal. Calcd for $C_{24}H_{40}O_4$: C, 73.43; H, 10.27. Found: C, 73.46; H, 10.27.

17,20β-Isopropylidenedioxy-5β-pregnane-3α,21-diol Diacetate (25b) from 26b.—Acetylation of 17,20β-isopropylidenedioxy-5β-pregnane-3α,21-diol with pyridine and acetic anhydride gave a product which could not be crystallized from anhydrous solvents. Addition of water to a methanol solution gave a filterable solid, mp 69–71°, which was homogeneous (R_f 0.46) in the system isooctane–ethyl acetate (2:1): $[\alpha]_{365}$ +153°, $[\alpha]_{436}$ +101°, $[\alpha]_{546}$ +60.3°, $[\alpha]_D$ +53.2°.

Anal. Calcd for $C_{28}H_{44}O_6$: C, 70.55; H, 9.30; CH_3CO, 18.06. Found: C, 70.39; H, 9.20; CH_3CO, 15.36.

25b from 10b.—To a solution of 5β-pregnane-3α,17,20β,21-tetrol 3,21-diacetate (500 mg) in acetone (500 ml) was added 70% perchloric acid (1.25 ml). After 30 min at room temperature solid sodium bicarbonate (1.25 g) was added, and the product was recovered after removal of the acetone and partitioning between methylene chloride and water. Addition of water to a methanol solution gave a filterable solid (535 mg, mp 68–71°) whose infrared spectrum was indistinguishable from that of the acetylation product of **26b**.

17,20β-Isopropylidenedioxy-5β-pregnane-3α,21-diol 21-Acetate (27) from 9b.—To a solution of 5β-pregnane-3α,17,20β,21-tetrol 21-acetate (210 mg) in acetone (200 ml) was added 70% perchloric acid (0.5 ml). After 30 min at room temperature solid sodium bicarbonate (500 mg) was added, and the product was recovered as in the preparation of **25b** from **10b**. Crystallization from ether–*n*-hexane gave prisms (194 mg, mp 181–182.5°; 13 mg, mp 176–179°) in a yield of 89.7%. The compound was found to retain solvents tenaciously. A sample, recrystallized from ether–*n*-hexane and dried to constant weight *in vacuo* at 100°, had mp 184–184.5°; $[\alpha]_{365}$ +103°, $[\alpha]_{436}$ +69.3°, $[\alpha]_{546}$ +42.1°, $[\alpha]_D$ +37.8°.

Anal. Calcd for $C_{26}H_{42}O_5$: C, 71.85; H, 9.74. Calcd for $C_{26}H_{42}O_5 \cdot C_6H_{14}$: C, 73.80; H, 10.84; $CHCO_3$, 8.26. Found: C, 74.27; H, 10.29; CH_3CO, 10.53.

Another sample, recrystallized from ether and dried in the same manner, had mp 183.5–184°.

Anal. Calcd for $C_{26}H_{42}O_5 \cdot (C_2H_5)_2O$: C, 70.82; H, 10.30. Found: C, 71.10; H, 9.92.

26b from 27.—Saponification of a sample of 17,20β-isopropylidenedioxy-5β-pregnane-3α,21-diol 21-acetate and crystallization from acetone–*n*-hexane gave needles, mp 177–178°, which were identical in all respects with the lithium aluminum hydride reduction product of **23b**.

Methyl 3α-Hydroxy-17,20α-isopropylidenedioxy-5β-pregnan-21-oate (23a) from 21a.—To a solution of methyl 3α,17,20α-trihydroxy-5β-pregnan-21-oate (1 g) in acetone (1 l.) was added 70% perchloric acid (2.5 ml). After 8 hr at room temperature the product was recovered in the same fashion as was its 20β epimer (**23b**) and chromatographed on a 42 × 690 mm silica gel column in ethyl acetate–isooctane (3:2). Fractions (9 ml) were collected every 10 min. After the emergence of fraction 150 the system was changed to ethyl acetate. The pooled material from fractions 82–142 furnished 860 mg of **23a** which, although homogeneous by tlc, could not be crystallized: $[\alpha]_{365}$ −86.8°, $[\alpha]_{436}$ −51.7°, $[\alpha]_{546}$ −29.2°, $[\alpha]_D$ −25.4°; ν_{max} 1758, 1737 (carbomethoxyl), and 1040 cm^{-1} (3α-hydroxyl).

Fractions 176–281.—Crystallization from benzene–*n*-hexane gave 121 mg of starting material **21a**, mp 86–88°.

Methyl 3α-Acetoxy-17,20α-isopropylidenedioxy-5β-pregnan-21-oate (24a).—Acetylation of 3α-hydroxy-17,20α-isopropylidenedioxy-5β-pregnan-21-oate in the usual manner gave an amorphous product: $[\alpha]_{365}$ −20.0°, $[\alpha]_{436}$ −9.67°, $[\alpha]_{546}$ −4.52°, $[\alpha]_D$ −3.87°; ν_{max} 1758 (carbomethoxyl), 1732, 1240, and 1025 cm^{-1} (3α-acetoxyl); there was no absorption above 3000 cm^{-1}.

17,20α-Isopropylidenedioxy-5β-pregnane-3α,21-diol (26a) from 23a.—A solution of methyl 3α-hydroxy-17,20α-isopropylidenedioxy-5β-pregnan-21-oate (860 mg) and lithium aluminum hydride (1500 mg) in ether (250 ml) was refluxed for 4 hr. The product crystallized from acetone as multifaceted prisms (582 mg, mp 125–128°; 177 mg, mp 124–127°; 25 mg, mp 123–126°) in a

yield of 97.5%: $[\alpha]_{365}$ −89.2°, $[\alpha]_{436}$ −57.1°, $[\alpha]_{546}$ −33.9°, $[\alpha]_D$ −29.5°.

Anal. Calcd for $C_{24}H_{40}O_4$: C, 73.43; H, 10.27. Found: C, 73.32; H, 10.10.

17,20α-Isopropylidenedioxy-5β-pregnane 3α,21-Diacetate (25a).—Acetylation of 17,20α-isopropylidenedioxy-5β-pregnane-3α,21-diol (500 mg) with pyridine (2 ml) and acetic anhydride (2 ml) was carried out at room temperature for 17 hr. Crystallization from *n*-hexane gave cubes (458 mg, mp 128.5–129°; 104 mg, mp 127.5–128.5°) in a yield of 92.4%: $[\alpha]_{365}$ −22.2°, $[\alpha]_{436}$ −14.7°, $[\alpha]_{546}$ −8.15°, $[\alpha]_D$ −7.34°.

Anal. Calcd for $C_{28}H_{44}O_6$: C, 70.55; H, 9.30; CH_3CO, 18.06. Found: C, 70.57; H, 9.08; CH_3CO, 17.63.

5β-Pregnane-3α,17,20α,21-tetrol 3,21-Diacetate (10a) from 25a.—A solution of 17,20α-isopropylidenedioxy-5β-pregnane-3α,21-diol diacetate (562 mg) in 80% aqueous acetic acid (500 ml) was heated for 12 hr at 65 ± 2°. The cooled reaction mixture was diluted with 1 l. of water and extracted with methylene chloride. The combined organic phases were washed carefully with dilute sodium hydroxide until the aqueous layer was alkaline. After a final water wash the organic solvent was dried and evaporated. The residue (550 mg) was chromatographed on a 41 × 810 mm silica gel column in ethyl acetate–isooctane (1:1). Fractions (10 ml) were collected every 10 min. After the emergence of fraction 395 the system was changed to ethyl acetate. The residue from fractions 251–460 was charcoaled in and crystallized from acetone as feathery needles (276 mg, mp 191–192.5°; 47 mg, mp 190.5–191.5°; 39 mg, mp 188–189.5°) in a yield of 70.5%. The analytical sample had mp 191.5–192.5°; $[\alpha]_{365}$ +43.2°, $[\alpha]_{436}$ +28.5°, $[\alpha]_{546}$ +17.4°, $[\alpha]_D$ +15.6°.

Anal. Calcd for $C_{25}H_{40}O_6$: C, 68.77; H, 9.24. Found: C, 68.99; H, 9.29.

Material eluted from the column beyond this point was saponified to furnish 5β-pregnane-3α,17,20α,21-tetrol (**12a**), mp 264–266°, in a yield of 67 mg equivalent to 80.5 mg of **25a**. The total extent of hydrolysis of the acetonide group was therefore 86.2%.

20α-Tosyloxy-5β-pregnane-3α,17,21-triol 3,21-Diacetate (17a) from 25a.—A solution of 5β-pregnane-3α,17,20α,21-tetrol 3,21-diacetate (300 mg) and tosyl chloride (300 mg) in pyridine (1.5 ml) stood at room temperature for 71 hr. The product crystallized from acetone–*n*-hexane as trapezoidal plates (363 mg, mp 153–153.5° dec; 8 mg, mp 149.5–150° dec) in a yield of 91.3%. The analytical sample, crystallized from acetone–*n*-hexane, had mp 152.5° (on stage at 150°); $[\alpha]_{365}$ −89.2°, $[\alpha]_{436}$ −48.2°, $[\alpha]_{546}$ −27.7°, $[\alpha]_D$ −23.2°.

Anal. Calcd for $C_{32}H_{46}O_8S$: C, 65.06; H, 7.85. Found: C, 64.97; H, 7.80.

20α-Tosyloxy-5β-pregnane-3α,17,21-triol Triacetate (18a) from 17a.—To a solution of 20α-tosyloxy-5β-pregnane-3α,17,21-triol 3,21-diacetate (20 mg) in carbon tetrachloride (2 ml) was added a mixture of acetic anhydride (0.12 ml) and 70% perchloric acid (0.001 ml). After 1 min at room temperature the product was recovered as in the preparation of **18b** from **17b**. The product was obtained as a filterable solid from methanol–water (18 mg, mp 77–79°): there was no absorption in the hydroxyl region of the infrared spectrum; $[\alpha]_{365}$ −85.4°, $[\alpha]_{436}$ −54.9°, $[\alpha]_{546}$ −30.5°, $[\alpha]_D$ −24.4°.

5β-Pregnane-3α,17,20β,21-tetrol 3,20,21-Triacetate (11b) from 18a.—A solution of 20α-tosyloxy-5β-pregnane-3α,17,21-triol triacetate (16 mg) and potassium acetate (200 mg) in 96% acetic acid (2 ml) and acetic anhydride (0.1 ml) was refluxed for 3 hr. After standing 15 hr at room temperature, the reaction mixture was worked up as in the preparation of **11a** from **18b**. Crystallization from ether–*n*-hexane afforded rosettes (10.1 mg, mp 154–155°). Recrystallization from ether gave needles, mp 156.5–157.5°, which had an infrared spectrum identical with that of **11b**, the acetylation product of **9b**.

17,20β-Oxido-5β-pregnane-3α,21-diol (28b) from 17a.—To a solution of 20α-tosyloxy-5β-pregnane-3α,17,21-triol 3,21-diacetate (165 mg) in methanol (16.5 ml) was added 0.1 *N* sodium hydroxide (1.1 ml). After 18 hr at room temperature most of the solvent was removed with a stream of nitrogen. The concentrate was diluted with water and extracted with ethyl acetate. Crystallization from acetone gave trapezoidal prisms (82.5 mg, mp 195–198°; 9 mg, mp 193.5–196°) in a yield of 98%: $[\alpha]_{365}$ +82.5°, $[\alpha]_{436}$ +58.4°, $[\alpha]_{546}$ +36.6°, $[\alpha]_D$ +32.7°.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.63; H, 10.40.

17,20β-Oxido-5β-pregnane-3α,21-diol Diacetate (29b).—Acetylation of 17,20β-oxido-5β-pregnane-3α,21-diol in the usual manner and crystallization from methanol gave prisms: mp 145.5–146°; $[\alpha]_{365}$ +183°, $[\alpha]_{436}$ +121°, $[\alpha]_{546}$ +70.8°, $[\alpha]_D$ +63.3°.

Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.65; H, 9.13.

17,20α-Oxido-5β-pregnane-3α,21-diol (28a) from 17b.—A solution of 20β-tosyloxy-5β-pregnane-3α,17,21-triol 3,21-diacetate (500 mg) in 0.2 *N* methanolic potassium hydroxide (50 ml) stood for 1 hr at room temperature. Acetic acid (0.6 ml) was added, and the solution was concentrated nearly to dryness. The concentrate was diluted with water and extracted with methylene chloride. Crystallization from acetone gave needles (269 mg, mp 181–185°) in a yield of 95.2%. The analytical sample had mp 181–182°; $[\alpha]_{365}$ +54.5°, $[\alpha]_{436}$ +37.2°, $[\alpha]_{546}$ +21.5°, $[\alpha]_D$ +19.1°.

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.41; H, 10.35.

17,20α-Oxido-5β-pregnane-3α,21-diol Diacetate (29a).—Acetylation of 17,20α-oxido-5β-pregnane-3α,21-diol in the usual manner and crystallization from ethanol gave needles: mp 119.5–120°; $[\alpha]_{365}$ +129°, $[\alpha]_{436}$ +83.3°, $[\alpha]_{546}$ +49.6°, $[\alpha]_D$ +42.7°.

Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.52; H, 9.33.

3α-Hydroxy 17,20-Oxides. 5β-Pregnane-3α,17,20α-triol 3-Acetate (31a) and 5β-Pregnane-3α,17,20β-triol 3-Acetate (31b) from 30.—To a solution of 3α-acetoxy-17-hydroxy-5β-pregnan-20-one (1 g) in dimethylformamide (25 ml) was added sodium borohydride (300 mg) in water (2.5 ml). After 3 hr at room temperature dilute acetic acid was added, and a crystalline precipitate was filtered off, washed with water, and dried. Several recrystallizations from methanol gave **31b** as prisms (578 mg, mp 92.5–93.5°). The mother liquors and an ethyl acetate extract of the original aqueous filtrate were combined and chromatographed on a 46 × 920 mm Celite column in isooctane, 200; methanol, 170; pH 7.8 borate buffer, 30 ml.[18] Fractions (10 ml) were collected at a rate of four per hour.

5β-Pregnane-3α,17,20β-triol 3-Acetate. Fractions 101–175.—The residue was partitioned between methylene chloride and water. Crystallization from methanol gave an additional quantity of **31b** (200 mg, mp 91–93; 62 mg, mp 86–88°), raising the yield to 840 mg (83.5%). Saponification of a sample gave a product identical in all respects with 5β-pregnane-3α,17,20β-triol. The analytical sample had mp 143–144° with transient softening at 80–90°; $[\alpha]_{365}$ +75.8°, $[\alpha]_{436}$ +51.3°, $[\alpha]_{546}$ +32.4°, $[\alpha]_D$ +30.0°.

Anal. Calcd for $C_{23}H_{38}O_4 \cdot {}^1/_2H_2O$: C, 71.28; H, 10.14. Found: C, 71.58; H, 9.90.

5β-Pregnane-3α,17,20α-triol 3-Acetate. Fractions 268–338.—After a preliminary partitioning in the same fashion as the 20β-epimer, the product crystallized from acetone–*n*-hexane as needles (99 mg, mp 140.5–141°) in a yield of 9.85%: $[\alpha]_{365}$ +60.7°, $[\alpha]_{436}$ +38.3°, $[\alpha]_{546}$ +23.4°, $[\alpha]_D$ +19.6°. Saponification of **31a** gave a product identical in all respects with 5β-pregnane-3α,17,20α-triol.

Anal. Calcd for $C_{23}H_{38}O_4$: C, 72.97; H, 10.12. Found: C, 73.20; H, 10.32.

20α-Tosyloxy-5β-pregnane-3α,17-diol 3-Acetate (32a) from 31a.—A solution of 5β-pregnane-3α,17,20α-triol 3-acetate (500 mg) and tosyl chloride (500 mg) in pyridine (2.5 ml) stood for 20 hr at 0°. The product crystallized from acetone–*n*-hexane as rectangular prisms (528 mg, mp 122–122.5°; 141 mg, mp 118.5–119°) in a yield of 95%. The crystals tend to darken on standing at room temperature. The analytical sample had mp 122–122.5° (on stage at 120°); $[\alpha]_{365}$ −11.3°, $[\alpha]_{436}$ −4.95°, $[\alpha]_{546}$ −2.12°, $[\alpha]_D$ −1.41°.

Anal. Calcd for $C_{30}H_{44}O_6S$: C, 67.63; H, 8.32. Found: C, 67.58; H, 8.19.

17,20β-Oxido-5β-pregnan-3α-ol (33b) from 32a.—A solution of 20α-tosyloxy-5β-pregnane-3α,17-diol 3-acetate (200 mg) in 0.2 *N* methanolic potassium hydroxide (20 ml) stood for 2.5 hr at room temperature. The solution was added to 100 ml of methylene chloride and washed twice with water. Crystallization from ethyl acetate afforded rosettes (97 mg, mp 137–139°) in a yield of 81.2%: $[\alpha]_{365}$ +61.5°, $[\alpha]_{436}$ +43.4°, $[\alpha]_{546}$ +27.2°, $[\alpha]_D$ +24.9°.

Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.24; H, 10.84.

17,20β-Oxido-5β-pregnan-3α-ol 3-Acetate (34b).—Acetylation of 17,20β-oxido-5β-pregnan-3α-ol (25 mg) with pyridine (0.1 ml) and acetic anhydride (0.1 ml) for 18 hr at room temperature and crystallization from methanol gave needles (25 mg, mp 123–125°): $[\alpha]_{365}$ +131°, $[\alpha]_{436}$ +88.1°, $[\alpha]_{546}$ +52.5°, $[\alpha]_D$ +46.5°.

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.34; H, 9.73.

17,20α-Oxido-5β-pregnan-3α-ol (33a) from 31b.—A solution of 5β-pregnane-3α,17,20β-triol 3-acetate (200 mg) and tosyl chloride (200 mg) in pyridine (1 ml) stood for 68 hr at −12°. The amorphous tosylate, recovered in the usual manner, was dissolved in 20 ml of 0.2 *N* methanolic potassium hydroxide. After 2 hr at room temperature the solution was diluted with methylene chloride and washed several times with water. Crystallization from acetone provided needles (125 mg, mp 162–164°) in a yield of 79.3%. The analytical sample had mp 164–166°; $[\alpha]_{365}$ +64.0°, $[\alpha]_{436}$ +44.4°, $[\alpha]_{546}$ +27.5°, $[\alpha]_D$ +24.4°.

Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.59; H, 10.49.

17,20α-Oxido-5β-pregnan-3α-ol 3-Acetate (34a).—Acetylation of 17,20α-oxido-5β-pregnan-3α-ol (30 mg) in the usual manner and crystallization from methanol gave prisms (31 mg, mp 148.5–150°): $[\alpha]_{365}$ +133°, $[\alpha]_{436}$ +86.7°, $[\alpha]_{546}$ +51.7°, $[\alpha]_D$ +45.8°.

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.06; H, 9.80.

3α-Hydroxy 20,21-Oxides. 5β-Pregnane-3α,20β,21-triol 3,21-Diacetate (38) and 5β-Pregnane-3α,20β,21-triol 3,20-Diacetate (36) from 35.—To a solution of 3α,21-diacetoxy-5β-pregnan-20-one[17] (2 g) in dimethylformamide (25 ml) was added successively sodium bicarbonate (300 mg) and sodium borohydride (150 mg), each in 2.5 ml of water. After 4 hr at room temperature the solution was acidified, diluted with water, and extracted with ethyl acetate. The crude product was chromatographed on a 54 × 960 mm silica gel column in isooctane–ethyl acetate (4:3). Fractions (10 ml) were collected at intervals of 10 min.

5β-Pregnane-3α,20β,21-triol 3,21-Diacetate. Fractions 301–425.—Several crystallizations from ether gave prisms (719 mg, mp 133–134°) in a yield of 35.8%: $[\alpha]_{365}$ +147°, $[\alpha]_{436}$ +96.5°, $[\alpha]_{546}$ +58.0°, $[\alpha]_D$ +50.5°.

Anal. Calcd for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 71.30; H, 9.62.

5β-Pregnane-3α,20β,21-triol 3,20-Diacetate. Fractions 651–950.—Two crystallizations from ether gave needles (300 mg, mp 155–156°) in a yield of 14.9%: $[\alpha]_{365}$ +240°, $[\alpha]_{436}$ +154°, $[\alpha]_{546}$ +90.9°, $[\alpha]_D$ +80.2°.

Anal. Calcd for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 71.05; H, 9.58.

5β-Pregnane-3α,20β,21-triol 3,21-Diacetate (38) from 35.—To a stirred solution of 3α,21-diacetoxy-5β-pregnan-20-one (2.23 g) in methanol (200 ml) at 0° was added sodium borohydride (300 mg). After 20 min at 0° excess acetic acid was added, and the solution was concentrated to a small volume. The residue was partitioned between methylene chloride and water, and the product was crystallized from ether as prisms (1678 mg, mp 133.5–134°) in a yield of 75.4%. Its infrared spectrum was identical with that of the more mobile product obtained after reduction of **35** with sodium borohydride in dimethylformamide.

20β-Tosyloxy-5β-pregnane-3α,21-diol Diacetate (39) from 38.—A solution of 5β-pregnane-3α,20β,21-triol 3,21-diacetate (250 mg) and tosyl chloride (250 mg) in pyridine (1.25 ml) stood for 67 hr at room temperature. The product crystallized from methanol as prisms (272 mg, mp 106.5–107.5°; 25 mg, mp 103–104°) in a yield of 82%: $[\alpha]_{365}$ +184°, $[\alpha]_{436}$ +95.2°, $[\alpha]_{546}$ +56.0°, $[\alpha]_D$ +49.3°.

Anal. Calcd for $C_{32}H_{46}O_7S$: C, 66.87; H, 8.07. Found: C, 66.53; H, 8.18.

21-Tosyloxy-5β-pregnane-3α,20β-diol Diacetate (37) from 36.—A solution of 5β-pregnane-3α,20β,21-triol 3,20-diacetate (100 mg) and tosyl chloride (100 mg) in pyridine (0.5 ml) stood for 71 hr at room temperature. The product crystallized from methanol as prisms (111 mg, mp 133–134.5°) in a yield of 81.2%: $[\alpha]_{365}$ +133°, $[\alpha]_{436}$ +86.2°, $[\alpha]_{546}$ +51.1°, $[\alpha]_D$ +44.7°.

Anal. Calcd for $C_{32}H_{46}O_7S$: C, 66.87; H, 8.07. Found: C, 66.82; H, 7.89.

20α,21-Oxido-5β-pregnan-3α-ol (40a) from 39.—To a solution of 20β-tosyloxy-5β-pregnane-3α,21-diol diacetate (435 mg) in methanol (35 ml) was added 1 *N* sodium hydroxide (3 ml). After 3.5 hr at room temperature the solution was concentrated *in vacuo*, diluted with water, and extracted with ethyl acetate. The crude product was chromatographed on a 25 × 700 mm column of silica gel in isooctane–ethyl acetate (2:1). Fractions (7 ml) were collected at intervals of 15 min. Crystallization from acetone of the residues derived from fractions 111–152 gave prismatic needles (170 mg, mp 158.5–160°; 32 mg, mp 155–157°) in a yield of 88%: $[\alpha]_{365}$ +78.2°, $[\alpha]_{436}$ +55.4°, $[\alpha]_{546}$ +34.2°, $[\alpha]_D$ +30.2°.

Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.65; H, 10.44.

20α,21-Oxido-5β-pregnan-3α-ol Acetate (41a).—Acetylation of 20α,21-oxido-5β-pregnan-3α-ol, purification of the product on a small silica gel column and crystallization from methanol afforded leaflets: mp 125–127°; $[\alpha]_{365}$ +142°, $[\alpha]_{436}$ +95.2°, $[\alpha]_{546}$ +56.4°, $[\alpha]_D$ +50.2°.

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.76; H, 10.03.

20β,21-Oxido-5β-pregnan-3α-ol (40b) from 37.—A solution of 21-tosyloxy-5β-pregnane-3α,20β-diol diacetate (224 mg) in methanol (23 ml) was treated with 0.1 *N* sodium hydroxide (2 ml) for 3.5 hr at room temperature. The product, recovered as in the preparation of **40a**, was chromatographed on a 20 × 750 mm silica gel column in isooctane–ethyl acetate (2:1). Fractions (3 ml) were collected at 7.5-min intervals. From fractions 197–265 there was obtained, by crystallization from acetone–*n*-hexane, needles (90 mg, mp 153–155°; 4.5 mg, mp 152.5–153.5°) in a yield of 80%: $[\alpha]_{365}$ +33.3°, $[\alpha]_{436}$ +21.6°, $[\alpha]_{546}$ +12.6°, $[\alpha]_D$ +10.8°.

Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.10; H, 10.77.

20β,21-Oxido-5β-pregnan-3α-ol Acetate (41b).—Acetylation of 20β,21-oxido-5β-pregnan-3α-ol, purification of the product on a small silica gel column and crystallization from methanol gave plates: mp 133–134°; $[\alpha]_{365}$ +104°, $[\alpha]_{436}$ +67.1°, $[\alpha]_{546}$ +39.9°, $[\alpha]_D$ +34.5°.

Anal. Calcd for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.36; H, 10.02.

Lithium Aluminum Hydride Reduction of 40a.—A solution of 20α,21-oxido-5β-pregnan-3α-ol (10 mg) and lithium aluminum hydride (25 mg) in ether (20 ml) was refluxed for 4 hr. Crystallization of the product from methanol afforded needles, mp 233–233.5°, which had an infrared spectrum identical with that of 5β-pregnane-3α,20α-diol.

Lithium Aluminum Hydride Reduction of 37 and 40b.—20β,21-oxido-5β-pregnan-3α-ol (10 mg) and 21-tosyloxy-5β-pregnane-3α,20β-diol diacetate (10 mg) were treated separately with lithium aluminum hydride as in the reduction of **40a**. Crystallization of the product from each reaction gave prisms, mp 232.5–233°, which were identical in all respects with an authentic sample of 5β-pregnane-3α,20β-diol.

Registry No.—**3a,** 16064-95-2; **3b,** 16064-96-3; **4a,** 16064-97-4; **4b,** 16064-98-5; **5b,** 16064-99-6; **6a,** 16109-49-2; **6b,** 16065-00-2; **7,** 16065-01-3; **8,** 16065-02-4; **9b,** 16109-50-5; **10a,** 16109-51-6; **10b,** 16065-03-5; **11a,** 16065-04-6; **11b,** 16109-83-4; **12a,** 3615-89-2; **12b,** 977-24-2; **13a,** 16065-08-0; **13b,** 16065-09-1; **14a,** 16109-52-7; **14b,** 16065-10-4; **15,** 16109-53-8; **16b,** 16109-54-9; **17a,** 16065-11-5; **17b,** 16065-12-6; **18a,** 16065-13-7; **18b,** 16065-14-8; **20,** 68-60-0; **21a,** 16109-56-1; **21b,** 16109-57-2; **22a,** 16109-58-3; **22b,** 16109-59-4; **24a,** 16109-60-7; **24b,** 16109-61-8; **25a,** 16065-15-9; **25b,** 16065-16-0; **26a,** 16109-62-9; **26b,** 16109-63-0; **27,** 16065-17-1; **28a,** 16096-40-5; **28b,** 16065-18-2; **29a,** 16065-19-3; **29b,** 16096-41-6; **31a,** 16062-27-4; **31b,** 16062-26-3; **32a,** 16096-46-1; **33a,** 16096-42-7; **33b,** 16096-47-2; **34a,** 16065-20-6; **34b,** 16065-21-7; **37,** 16799-05-6; **39,** 16065-22-8; **40a,** 16062-30-9; 5β-pregnan-3α-ol, 4352-07-2; **40b,** 16096-43-8; **41a,** 16096-44-9; **41b,** 16062-21-8; **44,** 16062-22-9; **45,** 16062-23-0; **46,** 16062-24-1; 21-bromo-5β-pregnane-3α,17,20α-triol, 16096-45-0; 3α,21-ditosyloxy-5β-pregnane-17,20α-diol, 16062-25-2; 5β-pregnane-3α,20β,21-triol 3,21-diacetate, 16062-28-5; 5β-pregnane-3α,20β,21-triol 3,20-diacetate, 16062-29-6.