Rearrangements of the C-16,17 Ring-D Ketols of 14β-Steroids[1]

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The synthesis of the four isomeric C-16,17 ketol diacetates of 5α,14β-androstane-3β-ol are described. The stabilities of the four isomeric ketols were determined and compared with those of the corresponding compounds with the 14α structure. The rearrangements and sequential stability of the new ketols is discussed in terms of the altered steric environment of ring D with the 14β stereochemistry.

The stability of the four isomeric C-16,17 ketols of steroids with the more common 14α ring closure has been demonstrated to have the sequence 17β—OH, 16=O > 17α-OH, 16=O > 16α—OH, 17=O > 16β—OH, 17=O.[4,5] Since one of the explanations[5] for this order of rearrangement was based upon steric and conformational considerations it was of interest to extend these studies to the corresponding ketols with the 14β or *cis* ring fusion. It was anticipated that this change would materially alter both the steric and conformational environment at C-16 and C-17 with consequent modification of the stability of the ketols at these positions. This has been found to be true. The stability sequence in the 14β series is 17α—OH, 16=O > 17β—OH, 16=O > 16β—OH, 17=O > 16α—OH, 17=O.

The synthesis of the four isomeric C-16,17 ketols of the 14β series proceeded along the lines developed in the preparation of the analogous 14α compounds. The enol diacetate I[6] was the starting material and on treatment with perbenzoic acid gave the β-epoxy diacetate II which was not obtained crystalline. The oily compound II could be converted by contact with acid-washed alumina into the crystalline 16β-hydroxy-17-ketone 3-monoacetate (IIIa), m.p. 190–193°. Mild mineral acid treatment of II followed by reacetylation gave the ketol diacetate IIIb, identical with that obtained by acetylation of IIIa. Oxidation of the enol diacetate I with lead tetraacetate formed the epimeric 16α-acetoxy 17-ketone IV, m.p. 121–123°. The result of the lead tetraacetate oxidation is of interest in that it emphasizes the unique nature of the reaction. In both the 14α[4] and 14β series the reaction proceeds sterically opposite to the other reactions at that center. When the epoxy diacetate II was treated with dilute alcoholic alkali at room temperature and reacetylated a third isomeric ketol diacetate, 17α-acetoxy 16-ketone Vb, m.p. 194–197° was obtained. The preparation of the remaining possible ketol isomer required a somewhat more involved sequence. The 17α-acetoxy group in compound V could be cleanly removed with zinc in glacial acetic acid to give the acetate of the 16-keto compound VIb; hydrolysis afforded 3β-hydroxy-5α,14β-androstane-16-one (VIa), m.p. 146–147°. The enol diacetate of the ketone VIa could not be obtained crystalline but on the basis of the infrared spectrum and subsequent reactions it consisted mainly of the Δ^{16}-enol diacetate VII. Perbenzoic acid oxidation of VII led to the noncrystalline epoxide VIII which on rearrangement with acid and reacetylation gave the desired fourth isomeric ketol 16-oxo-5α,14β-androstane-3β,17β-diol diacetate IX, m.p. 144–145°.

The infrared spectra of the four compounds served to distinguish between the two pairs of epimeric ketols in that the 16-ketones V and IX exhibited methylene absorption alpha to a carbonyl at 1408 cm.$^{-1}$ (CCl_4), which was lacking in the two epimeric 17-ketones, III and IV. It was therefore necessary to establish the stereochemistry of the ring-D acetoxy groups in only one of each pair of epimers to arrive at the complete structure of all four isomers. This was accomplished for the 16β-acetoxy 17-ketone IIIb by an alternative synthesis from the known 16α,17α-epoxy-5α,14β-androstane-3β-ol (Xa).[6] The epoxy acetate Xb prepared from Xa was refluxed with glacial acetic acid. Acetolysis gave the 3β,16β,17α-triol 3,16-diacetate XI as the result of preferential attack at C-16. Oxidation of the free hydroxy group in XI gave the ketol diacetate IIIb identical in all respects with that obtained by the sequence leading from the enol acetate I. The epimer of IIIb is IV and it must therefore have the 16α-acetoxy 17-ketone structure.

The characterization of the other pair of epimers was achieved by degradative means. The 17α-acetoxy 16-ketone Vb was converted to the thioketal XIIb, m.p. 192–194°, by the boron trifluoride procedure of Fieser,[7] when milder methods failed. The thioketal of diacetate XIIb after removal of the acetate groups with base yielded

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(4) W. J. Johnson, B. Gastambide, and R. Pappo, *J. Am. Chem. Soc.*, **79**, 1991 (1957).

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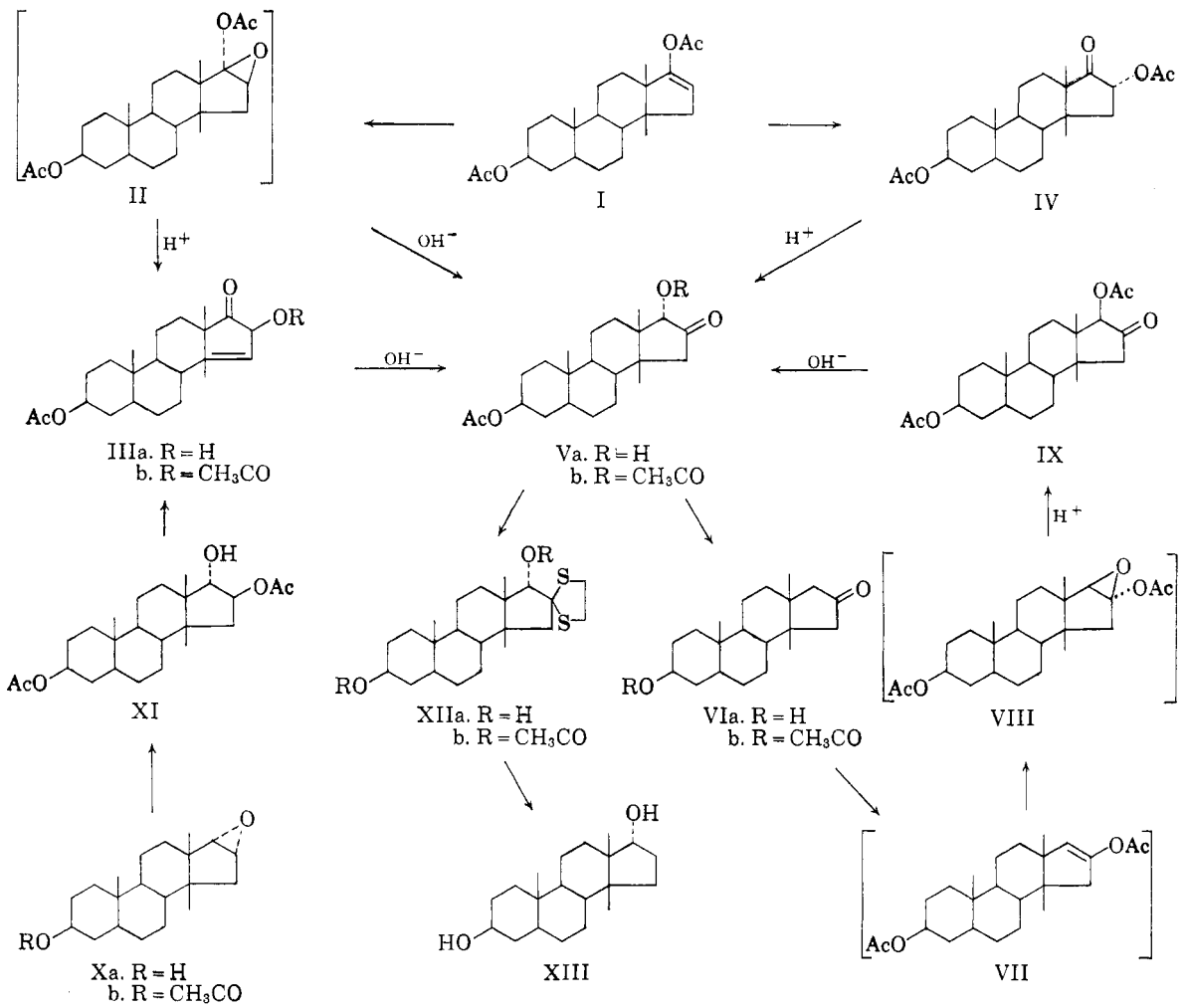

the thioketal diol XIIa, m.p. 236–239°, which was used at the next stage in order to minimize loss of the 17-oxygen during the desulfurization. Raney nickel desulfurization of XIIa proceeded without any evident hydrogenolysis at C-17 to give the 3β,17α-diol XIII, identical with that obtained by lithium aluminum hydride reduction of 3β-hydroxy-5α,14β-androstane-17-one.[8] The epimer of V is IX and hence its structure can be defined as 16-oxo-5α,14β-androstane-3β,17β-diol diacetate.

The rearrangement sequence of the four ketols in the 14α series has already been described.[5] In contrast, in the 14β series three of the isomeric ketols rearranged, under varying conditions, to the most stable ketol 17α-hydroxy-16-one V which was unchanged by both acid and base. In the 14β series the 16α-hydroxy 17-ketone IV was the least stable compound in that it rearranged on even mild acid treatment. The 16β-hydroxy 17-ketone III was stable to acid but isomerized completely on brief treatment with base at room temperature. Finally the 17β-hydroxy 16-ketone IX was unchanged by a similar two-hour exposure to alkali, but extending the time to twenty-four hours resulted in substantial epimerization to V.

It is evident that in the 14β series the relative stabilities of the 16-ketones (V and IX) and the 17-ketones (III and IV) are the same as in the 14α compounds, with the former being the more stable pair of epimers. The differences between the 14α and 14β series lie in the relative stabilities of the two epimers in each pair with the 14β compounds the reverse of those in the 14α series. Steric considerations can serve to explain this difference between the 14α and 14β ketols. While in the 14α series the dominant steric feature of the ring D is the axial C-18 β-methyl group, which makes the α face of ring D more available, in the 14β compounds the concave nature of the junction of rings C and D becomes more important. This steric arrangement results in substantial hindrance of the α side in contrast to the β, while the C-18 methyl group is now equatorially oriented with respect to ring D and does not appear to exert any important steric influence on that ring. The rate-determining step in enolization is abstraction of the proton alpha to the ketone. Accord-

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ingly, in the 16α-hydroxy 17-ketone IV the 16β-hydrogen is easily accessible and the compound enolizes and rearranges readily even in mild acid conditions. In the 16β-hydroxy 17-ketone, the 16α-hydrogen is hindered and hence requires the more vigorous alkaline conditions to effect enolization and rearrangement. In the case of 17 hydroxy epimers, the extent or rate of enolization need not be the determining factor, in that the nature of the product is very likely controlled by the stereochemistry of ketonization.[9] Thus the 17α-hydroxy 16-ketone may enolize readily but it will be a reversible reaction since the stereochemistry will favor protonation of the enol from the β side to regenerate the starting material. The 17β-hydroxy epimer on the other hand may enolize to a much smaller extent but would do so irreversibly since protonation of the enol will again be from the β side to give the 17α-hydroxy 16-keto epimer.

The 16-keto structure is preferred to the 17-ketone in both the 14α and 14β series. In the former case this preference was explained on the basis of conformational differences between ring D with a ketone at C-16 and one with a ketone at C-17.[5] These different conformations had adequate support from molecular models as well as from available experimental data.[10] In the 14β series, however, experimental data bearing on the conformation of ring D is incomplete. Furthermore, recent work from this laboratory[6] has shown that molecular models do not adequately represent the conformation of the 14β ring D. In view of this, any conformational explanation for the preference of the 16-ketones in the 14β ring D must await further knowledge of the spatial arrangement of the cis linked ring D. It is hoped that further work in progress in this laboratory will provide the data necessary for a definition of the 14β ring-D conformation.

Experimental[11]

17-Oxo-5α,14β-androstane-3β,16β-diol Diacetate (IIIb). A. By Acid Hydrolysis.—A solution of 65 mg. of 3β,17-diacetoxy-5α,14β-androst-16-ene (I) in 10 ml. of benzene containing 0.0002 *M* of perbenzoic acid was allowed to stand for 24 hr. at room temperature. The solution was diluted with ether and washed with aqueous sodium hydroxide containing ice and then with water. After drying the organic layer and evaporation of solvent, an oily residue was obtained. To the solution of the crude product in 5 ml. of methanol was added 1.25 ml. of 6 *N* aqueous sulfuric acid, and the mixture was allowed to stand at room temperature for 3 days. After dilution with ethyl acetate and washing with cold 1 *N* sodium hydroxide solution and water, the organic layer was dried and evaporated to give 51 mg. of crystalline material melting at 183–193°. Acetylation in the usual manner with acetic anhydride and pyridine and recrystallization from dilute methanol gave 51 mg. of IIIb, m.p. 142–145°, as white leaflets. The analytical sample melted at 144–146°; $[\alpha]^{28}D$ +24.9°.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.77. Found: C, 70.30; H, 8.61.

B. By Alumina.—Following the same procedure as above, 100 mg. of 3β,17-diacetoxy-5α,14β-androst-16-ene was treated with perbenzoic acid solution in benzene. The product was dissolved in petroleum ether, adsorbed on 5 g. of acid-washed alumina and allowed to stand overnight. Elution with 2:8 petroleum ether–benzene gave 33 mg. of crude 17-oxo-5α,14β-androstan-3β,16β-diol 3-acetate (IIIa). Recrystallization from dilute methanol gave white leaflets, m.p. 180–185°. The analytical sample melted at 190–193°; $[\alpha]^{28}D$ +31.2°.

Anal. Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.25. Found: C, 72.37; H, 9.53.

Elution with 5:5 benzene–ether and with pure ether gave, respectively, 11 mg. and 19 mg. of crystalline material, infrared spectra of which indicated it to be primarily IIIa. Acetylation in the usual manner and recrystallization from dilute methanol gave IIIb, m.p. 142–144°, white leaflets.

17-Oxo-5α,14β-androstan-3β,16α-diol Diacetate (IV).—To a solution of 50 mg. of 3α,17-diacetoxy-5α,14β-androst-16-ene(I) in 1 ml. of acetic acid containing 0.05 ml. of acetic anhydride was added 90 mg. of lead tetraacetate, and the reaction mixture was shaken occasionally until it was dissolved completely. After allowing to stand overnight, the solvent was removed under reduced pressure and the residue was diluted with ether, washed with water, and dried. Evaporation of solvent and recrystallization of the remaining semisolid material from dilute methanol gave 40 mg. of IV, m.p. 115–120°, white needles. The analytical sample melted at 121–123°; $[\alpha]^{23.5}D$ +54.8°.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.77. Found: C, 70.73; H, 8.60.

16-Oxo-5α,14β-androstane-3β,17α-diol (Va). A. By Base Hydrolysis.—Following the same procedure as above, 200 mg. of 3β,17-diacetoxy-5α,14β-androst-16-ene(I) was treated with perbenzoic acid solution in benzene. A solution of the crude product in 100 ml. of 0.04 *N* sodium hydroxide in 60% aqueous methanol was allowed to stand at room temperature for 3 hr. The solution was diluted with ethyl acetate, washed with water, and dried, and the solvent was evaporated to give 145 mg. of white crystalline material. Recrystallization from acetone–petroleum ether gave 80 mg. of Va, m.p. 165–170°. The analytical sample melted 168–171°.

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.23; H, 10.01.

Acetylation with acetic anhydride and pyridine in the usual manner and recrystallization from dilute methanol gave the diacetate Vb, m.p. 190–195°. The analytical sample melted at 194–197°; $[\alpha]^{28}D$ +74.3°.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.77. Found: C, 70.20; H, 8.93.

B. By Rearrangement from IV.—To the solution of 460 mg. of IV in 30 ml. of methanol was added 7.5 ml. of 6 *N* aqueous sulfuric acid, and the solution was allowed to stand at room temperature for 3 days. After dilution with ethyl acetate, washing with cold 5% sodium bicarbonate solution and water, and drying, the solvent was evaporated to give 360 mg. of crystalline material. Acetylation in the usual manner with acetic anhydride and pyridine and recrystallization from dilute methanol gave 261 mg. of Vb, m.p. 192–194°. Melting point of the mixture with the product obtained by procedure A showed no depression and the infrared spectra were identical in all respects.

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(10) C. W. Shoppee, R. H. Jenkins, and G. H. R. Summers, *J. Chem. Soc.*, 3048 (1958); F. V. Brutcher, T. Roberts, S. J. Barr, and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959); J. Fishman and C. Djerassi, *Experienta*, **16**, 138 (1960); J. Fajkos and J. Joska, *Chem. Ind.*, 872, 1162 (1960); J. Fajkos and J. Joska, *Collect. Chech. Chem. Commun.*, **25**, 2863 (1960); J. Fajkos and J. Joska, *ibid.*, **26**, 1118 (1961); J. Fishman, *J. Org. Chem.*, in press.

(11) Melting points were determined on a hot stage apparatus and are corrected. Rotations were determined in chloroform unless specified otherwise. The analyses were performed by Spang Microanalytical Laboratories.

C. By Rearrangement from IIIb.—A solution of 125 mg. of IIIb in 70 ml. of 0.04 *N* sodium hydroxide in 60% aqueous methanol was allowed to stand at room temperature for 4 hr. The solution was diluted with ethyl acetate, washed with water, and dried, and the solvent was evaporated to give semicrystalline material. The residue was taken up in benzene and chromatographed on 4 g. of acid-washed alumina. Elution with 8:2 ether–acetone gave 62 mg. of crystalline material, which was recrystallized from acetone and petroleum ether to give 16-oxo-5α,14β-androstane-3β,17α-diol (Va), white leaflets, m.p. 160–165°. Mixed melting point and infrared spectra were identical with those of an authentic sample. The diacetate (Vb) m.p. 191–192°, was obtained in the usual manner with acetic anhydride and pyridine, and was identical with the authentic sample by mixed melting point and infrared spectra comparison.

D. By Rearrangement from IX.—A solution of 10 mg. of IX in 7.5 ml. of 0.04 *N* sodium hydroxide in 60% aqueous methanol was allowed to stand at room temperature for 20 hr. The solution was diluted with ethyl acetate, washed with water, and dried, and the solvent was evaporated to give 10 mg. of oily product. This residue was taken up in benzene and chromatographed on 1 g. of acid-washed alumina. Elution with 8:2 ether–acetone and recrystallization from acetone and petroleum ether gave 4 mg. of white leaflets, m.p. 155–160°. This was identical with 16-oxo-5α,14β-androstane-3β,17α-diol (Va) by mixed melting point and infrared spectra. The diacetate, obtained in the usual manner was also identical with Vb by infrared spectra. The infrared spectrum of the acetylated mother liquor showed it to be impure Vb containing no discernible 3β,17β-diacetate IX.

E. By Base Hydrolysis of the Diacetate Vb.—A solution of 50 mg. of 16-oxo-5α,14β-androstane-3β,17α-diol diacetate (Vb) in 25 ml. of 0.04 *N* sodium hydroxide in 60% methanol was allowed to stand at room temperature for 20 hr. After the usual work-up 35 mg. of semicrystalline material was obtained, the infrared spectrum of which indicated it to be slightly impure Va. Recrystallization from petroleum ether–acetone gave leaflets, m.p. 165–170°, identical in all respects with Va. The infrared spectrum of the acetylated mother liquor did not show the presence of any 3β,17β-diacetate, IX.

5α,14β-Androstane-3β,16β,17α-triol 3,16-Diacetate (XI).—A solution of 120 mg. of the epoxy acetate Xb in 5 ml. of glacial acetic was boiled under reflux for 2 hr. The solvent was evaporated under reduced pressure, and the residue was extracted with chloroform. The organic extract was washed with cold 5% sodium bicarbonate solution, water, and dried. Upon evaporation of solvent the residue was taken up in 8:2 petroleum ether–benzene and chromatographed on 6 g. of acid-washed alumina. Elution with 5:5 petroleum ether–benzene gave 46 mg. of material, which crystallized from dilute methanol to give 28 mg. of XI, m.p. 147–151°, as white leaflets. On changing the solvent to pure benzene, there was obtained 23 mg. of crystalline material which was recrystallized from dilute methanol to give an additional 18 mg. of XI, m.p. 149–151°. The analytical sample of XI melted at 150–152°; $[\alpha]^{28}D$ +2.6°.

Anal. Calcd. for $C_{28}H_{36}O_5$: C, 70.37; H, 9.24. Found: C, 70.51; H, 9.29.

Oxidation of 5α,14β-Androstane-3β,16β,17α-triol 3,16-Diacetate.—A solution of 20 mg. of XI in 1 ml. of acetone was treated with 8 *N* chromic acid at room temperature for 30 min. Dilution with water and extraction with ether gave, after washing, drying and crystallization from dilute methanol, 12.5 mg. of 17-oxo-5α,14β-androstane-3β,16β-diol diacetate (IIIb), m.p. 144–146°, identical by infrared spectra comparison and mixed melting point with the authentic sample.

3β-Acetoxy-5α,14β-androstane-16-one (VIb).—To a stirred solution of 200 mg. of the diacetate Vb in 30 ml. of acetic acid containing 3 ml. of acetic anhydride was added 10 g. of zinc dust portionwise during 15 min. After boiling under reflux for 18 hr., the reaction mixture was filtered and the precipitate was washed with ethanol. The combined filtrates were concentrated and the residue was extracted with ether. The ether extract was washed with 5% sodium bicarbonate solution, water, and dried. After evaporation of solvent, the semisolid product (178 mg.) was chromatographed on 10 g. of alumina. Elution with increasing concentrations of benzene in petroleum ether yielded 145 mg. of crystalline material. Recrystallization from dilute methanol gave 136 mg. of VIb, m.p. 147–149°; $[\alpha]^{28}D$ +109.3°.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.92; H, 9.65.

3β-Hydroxy-5α,14β-androstane-16-one (VIa).—Hydrolysis of 25 mg. of the acetate VIb in 3 ml. of 5% methanolic potassium hydroxide gave, on recrystallization from chloroform–petroleum ether, 20 mg. of 3β-hydroxy-5α,14β-androstane-16-one (VIa), m.p. 146–147°, as white needles; $[\alpha]^{26}D$ +130.0°.

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.28; H, 10.21.

16,16-Ethylenedithio-5α,14β-androstane-3β,17α-diol (XIIa).—To a solution of 100 mg. of Vb in 3 ml. of glacial acetic acid was added 0.25 ml. of ethanedithiol and 0.25 ml. of boron trifluoride etherate, and the reaction mixture was allowed to stand at room temperature overnight. The solution was diluted with ether and washed with 5% sodium hydroxide solution, water, and dried. Upon evaporation of solvent, the remaining oily material was boiled in 5 ml. of 5% methanolic potassium hydroxide solution for 1 hr. After dilution with ethyl acetate, washing with water, and drying, the product obtained was chromatographed on 5 g. of alumina. Elution with 8:2 benzene–ether gave 48 mg. of crystalline material, which was recrystallized from acetone to give 38 mg. of XIIa, m.p. 235–238°, as white needles. The analytical sample melted at 236–238°; $[\alpha]^{26.5}D$ +28.9°.

Anal. Calcd. for $C_{21}H_{34}O_2S_2$: C, 65.91; H, 8.96. Found: C, 65.58; H, 8.85.

16,16-Ethylenedithio-5α,14β-androstane-3β,17α-diol Diacetate (XIIb).—A sample of XIIa (20 mg.) was acetylated in the usual manner with acetic anhydride and pyridine. On work-up, the product crystallized from methanol to give 16 mg. of XIIb, m.p. 189–191°. The analytical sample melted at 192–194°; $[\alpha]^{26.5}D$ +25.9°.

Anal. Calcd. for $C_{25}H_{38}O_4S_2$: C, 64.34; H, 8.21. Found: C, 64.28; H, 8.17.

Raney Nickel Desulfurization of XIIa.—To a solution of 20 mg. of XIIa in 5 ml. of ethanol was added 0.5 g. of Raney nickel, and the solution was boiled under reflux for 2.5 hr. After removing the nickel by filtration and evaporation of the solvent, 19 mg. of oily material was obtained. Recrystallization from dilute methanol gave 10 mg. of 5α,14β-androstane-3β,17α-diol (XIII), m.p. 180–183°, identical by infrared spectra comparison and mixed melting point with authentic sample.[8]

16-Oxo-5α,14β-androstane-3β,17β-diol Diacetate (IX).—To a solution of 140 mg. of the 16-ketone VIa in 10 ml. of isopropenyl acetate was added 12 drops of a catalyst solution (5 ml. of isopropenyl acetate and 0.1 ml. of concd. sulfuric acid). Approximately 5 ml. of the solvent was distilled over a period of 2 hr. An additional 5 ml. of the isopropenyl acetate containing 6 drops of catalyst solution was added, and the reaction mixture was concentrated to one-half of its volume by slow distillation over 2 hr. The solution was diluted with ether and washed with cold 5% sodium bicarbonate solution, water, and the solvent was evaporated. The residue was dissolved in petroleum ether and filtered through 1.5 g. of alumina. Upon concentration of filtrate there was obtained 145 mg. of an oily product which could not be crystallized. The oily material containing 5α,14β-androst-16-ene-3β,16-diol diacetate (VII) was dissolved in 20 ml. of benzene containing 0.0005 *M* of perbenzoic acid, and the reaction mixture was allowed to stand for 24 hr. at room temperature. The solution was diluted with ether and

washed with aqueous sodium hydroxide containing ice and then with water. After drying the organic layer and evaporation of solvent, an oily residue was obtained. Without purification the crude product was dissolved in 15 ml. of methanol and 3.75 ml. of 6 *N* aqueous sulfuric acid was added, and the mixture was allowed to stand at room temperature for 3 days. After dilution with ethyl acetate and washing with cold dilute sodium hydroxide solution and water, the organic layer was dried and evaporated to give 123 mg. of oily material. Acetylation in the usual manner with acetic anhydride and pyridine and recrystallization from methanol gave 80 mg. of IX, m.p. 187–193°, as white plates. The analytical sample melted at 194–195°; $[\alpha]^{27}D$ +15.2°.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.77. Found: C, 70.46; H, 8.92.

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Studies in the Sandalwood-Oil Series. I. The Structure, Synthesis, and Configuration of the Lactone of Tricycloekasantalic Acid[1]

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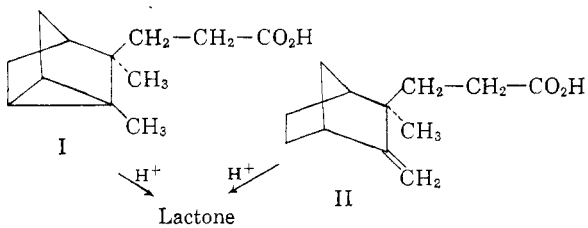
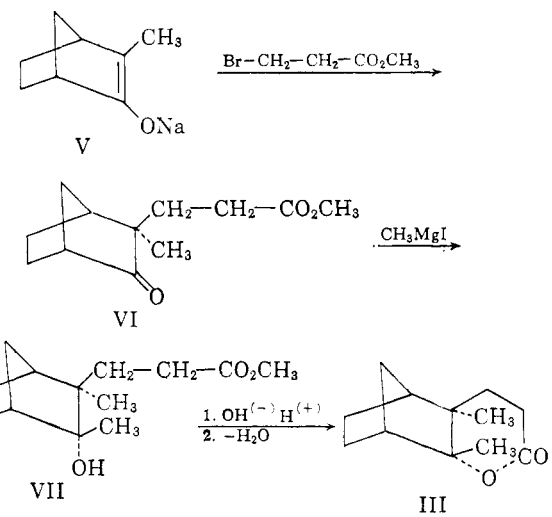
The structure, synthesis. and configuration of the lactone of tricycloekasantalic acid have been described. It has been shown that in the formation of this lactone (XII) from the acids (I) or (II) a rearrangement is involved.

In an attempt to convert tricycloekasantalic acid (I) (a degradation product of α-santalol, the chief constituent of the East Indian sandalwood-oil) into the isomeric acid (II) by boiling with dilute sulfuric acid, Semmler and Bode[3] obtained an isomeric lactone for which two structures (III) and (IV) have been proposed.[4,5] Structure III is based on a synthesis of the lactone by Bhattacharyya.[4] In this synthesis sodionormethylcamphor (V) was condensed with methyl β-bromopropionate, and the resultant keto ester (VI) was converted into the lactone either *via* the hydroxy ester (VII) or directly by treatment with two moles of methylmagnesium iodide.





Besides this synthesis, the structure (III) would appear to receive support from the fact that the same lactone is obtained by refluxing bicycloekasantalic acid (II) with formic acid.[6] Structure IV was suggested by Simonsen and Barton[5] by analogy with the lactone (VIII) prepared similarly[7] from teresantalic acid (IX). The formation of IV from bicycloekasantalic acid (II) was assumed by Simonsen and Barton to have involved a Wagner-Meerwein rearrangement.

The conflict between the structure (III), based on a straightforward synthesis, and that (IV) deduced from a reasonable analogy, prompted the present investigation.

The lactone gave, on hydrolysis with sodium hydroxide, the sodium salt of a hydroxy carboxylic acid which relactonized on acidification at 0°. If IV were correct then the hydroxy group of the acid, obtained on hydrolysis, ought to be second-

(1) The substance of this work was communicated to Professor P. de Mayo, and is briefly described by him in "The Mono- and Sesquiterpenoids," Interscience Publishers, Inc., New York, 1959, p. 128.

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