water (8:2:3:2). Concentration of the first part of the second hold-back volume gave 0.77 g. of IX, m.p. 220–221°. Concentration of the fourth hold-back volume gave 5 mg. of an unknown compound, m.p. 175–180° (not further purified); ν_{max}^{KBr} 1749, 1711, 1678 and 1618 cm^{-1}.

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Dehydration of a Steroidal β-Ketol with Chromatographic Adsorbents

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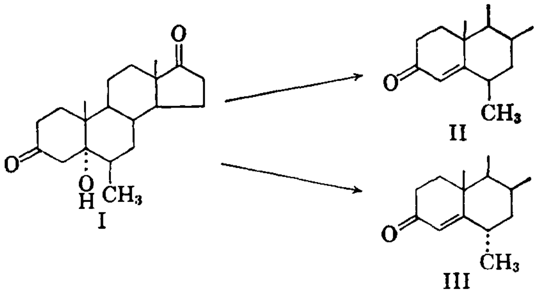
The preparation of steroidal 6-alkyl-Δ^4-3-ketones is usually accomplished by dehydration of the 6β-alkyl-5α-hydroxy-3-ketones which in turn arise from the action of an alkyl Grignard reagent on a 5α,6α-epoxide. A variety of basic and acidic conditions are available for the production of the 6α-alkyl derivatives[1] from this intermediate because of the great ease with which C_6 is epimerized subsequent to the dehydration step. For this same reason, however, the formation of the 6β-alkyl derivatives[2] has required careful attention to reaction conditions.

Quite by accident it was discovered that when the steroidal 5α-hydroxy-3-ketone system was chromatographed on Florisil[3] the eluates consisted of a mixture of dehydrated material along with the ketol. Further experiments in which the formation of the α,β-unsaturated ketone was followed by the appearance of its characteristic ultraviolet absorption demonstrated that the reaction was essentially complete after three hours at reflux in benzene in the presence of the Florisil. A good yield of 6β-methylandrost-4-ene-3,17-dione (II) was obtained from 6β-methyl-5α-hydroxyandrostan-3,17-dione (I)[1c] using these conditions.

This result led us then to attempt dehydration of I with the more strongly adsorbing aluminum oxide. In contrast to the previous case this reaction was quite fast and the only product isolated was 6α-methylandrost-4-en-3,17-dione (III).[4] Both procedures are characterized by the absence in the crude products of colored impurities thus allowing final crystallization with a minimum of loss.

Further examples of these methods will be described in forthcoming communications from this laboratory.



EXPERIMENTAL

6β-Methylandrost-4-ene-3,17-dione (II). A mixture of 5α-hydroxy-6β-methylandrostane-3,17-dione (I, 830 mg.),[1c] Florisil (8.3 g., 100–200 mesh), and benzene (166 ml.) was stirred at reflux temperature for 3 hr. The mixture was filtered and the solid was washed with ethyl acetate (500 ml.). Removal of the solvents from the combined filtrates followed by two recrystallizations of the resulting residue from aqueous methanol gave II; 570 mg.; m.p. 207–215°; $[\alpha]_D$ +135°; λ_{max} 241 mμ (ε 15,800). Reported[2a,5]: m.p. 207–212°; λ_{max} 242 mμ (ε 16,200); $[\alpha]_D$ +139°.

6α-Methylandrost-4-ene-3,17-dione (III). A. *By dehydration of ketol* I *with alumina*. Compound I (500 mg.) in benzene (100 ml.) was stirred at reflux temperature with basic aluminum oxide[6] (5.00 g., activity grade I) for 50 min. The mixture was filtered and the solid was washed with benzene (150 ml.). Removal of the solvent followed by one recrystallization of the resulting residue from aqueous methanol gave III; 250 mg.; m.p. 171–174°; $[\alpha]_D$ +181°. Reported[2a,5,7]: m.p. 164–167°; $[\alpha]_D$ +180°; λ_{max} 242 mμ (ε 15,650).

B. *By isomerization of the 6β-derivative* (II). A solution of Compound II (80 mg.) in ethanol (10 ml.) was refluxed with dilute sodium hydroxide (2 ml. of 0.1*N*) under nitrogen for 30 min. Dilution of the reaction mixture with water (200 ml.) containing dilute hydrochloric acid gave III; 46 mg.; m.p. 168.5–171.5°; λ_{max} 240 mμ (ε 14,520).

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(1) (a) H. J. Ringold, J. P. Ruelas, E. Batres, and C. Djerassi, *J. Am. Chem. Soc.*, **81**, 3712 (1959); (b) A. Bowers and H. J. Ringold, *J. Am. Chem. Soc.*, **80**, 3091 (1958); (c) M. Ackroyd, W. J. Adams, B. Ellis, V. Petrow, and I. A. Stuart-Webb, *J. Chem. Soc.*, 4099 (1957); (d) M. I. Ushakov and O. S. Madaeva, *J. Gen. Chem.* (*U.S.S.R.*), **9**, 436 (1939); *Chem. Abstr.*, **33**, 9309 (1939).

(2) (a) J. A. Campbell, J. C. Babcock, and J. A. Hogg, *J. Am. Chem. Soc.*, **80**, 4717 (1958); (b) R. B. Turner, *J. Am. Chem. Soc.*, **74**, 5362 (1952).

(3) A chromatographic magnesium silicate sold by the Floridin Co., Warren, Pa. Analysis: MgO, 15.5:; SiO_2, 84%; Na_2SO_4, 0.5%.

(4) An aqueous slurry of the Florisil was at least as basic as an aqueous slurry of the aluminum oxide thus demonstrating that this result was a consequence of the action of the adsorbent itself and not of the water soluble hydroxide.

(5) Compare also Ref. 1c; H. J. Ringold, E. Batres, and G. Rosenkranz, *J. Org. Chem.*, **22**, 99 (1957).

(6) A product of M. Woelm Eschwege supplied by Alupharm Chemicals.

(7) Compare also V. Grenville, D. K. Patel, V. Petrow, I. A. Stuart-Webb, and D. M. Williamson, *J. Chem. Soc.*, 4105 (1957); O. S. Madaeva, M. I. Ushakov, and N. F. Koscheleva, *J. Gen. Chem.* (*U.S.S.R.*), **10**, 213 (1940); *Chem. Abstr.*, **34**, 7292 (1940).