

spacing is remarkably short at 29 Å. and may signify a single-chain-length structure, but the fact that the intensities of various orders of long

spacing follow a sequence similar to those of the succinate suggests a double-chain-length structure. CINCINNATI 31, OHIO

COMMUNICATIONS TO THE EDITOR

THE STRUCTURE OF RUSCOGENIN¹

Sir:

Ruscogenin, isolated by Lapin and Sannié² in 1955 from *Ruscus aculeatus* L., was identified as 19-hydroxydiosgenin.³ However, we wish to report recent evidence which invalidates the structure proposed by the French workers. For purpose of clarity we shall assume that this new sapogenin is x-hydroxydiosgenin and later in this communication arrive at the most probable structure.

Recrystallized ruscogenin⁴ diacetate (m.p. 191–194°, $[\alpha]_{25}^{25D} -80.5^\circ$, 1.03% in CHCl_3 ; diol,⁵ m.p. 205–211°, $[\alpha]_{25}^{25D} -118^\circ$, 1% in CHCl_3) was degraded⁶ by methods well established in the sapogenin field⁷ to the oily diacetate of 5,16-pregnadiene-x,3-diol-20-one I in 70% yield. Beckmann rearrangement⁸ of the oxime (m.p. 188–197° dec.; C, 69.82; H, 8.02), followed by mild acid treatment yielded x-acetoxydehydroepiandrosterone acetate II (m.p. 97–99° and 147–149°; C, 71.44; H, 8.31), which on vigorous alkaline hydrolysis afforded x-hydroxydehydroepiandrosterone III (m.p. 195–197°; C, 74.71; H, 8.99). Diol III was stable to acid and reverted to II on acetylation. Controlled acid-catalyzed methanolysis of the diacetate II led, after chromatography, to x-acetoxydehydroepiandrosterone IV (m.p. 136.5–138°; C, 72.91; H, 8.97) in about 65% yield.

When the diol III was treated with aluminum isopropoxide and cyclohexanone in refluxing toluene, 1,4-androstadiene-3,17-dione⁹ (m.p. 139.5–140.5°; $\lambda_{\text{max}}^{\text{MeOH}}$ 243 m μ , ϵ 16,000) was obtained in approximately 30% yield, as shown by comparison (in-

fared and mixed m.p.), with an authentic sample prepared according to Djerassi and Scholz.^{9b} The monoacetate IV was carefully oxidized with chromic acid in acetone¹⁰ to an oily ketone V, which on treatment with potassium acetate in refluxing ethanol or aqueous potassium hydroxide in methanol at room temperature, again afforded 1,4-androstadiene-3,17-dione (m.p. 139–140.5°) in approximately 40% and 50% yield respectively. These results could best be rationalized by assuming the additional hydroxyl to be situated on carbon 1 of the steroid nucleus.

In order to obtain additional information as to the position and configuration of the functional groups, the diol III was reduced with sodium borohydride in methanol to 5-androstene-1,3 β ,17 β -diol VIa (m.p. 275–280° dec.; C, 74.24; H, 9.97; triacetate VIb, m.p. 145–147°; C, 69.24; H, 8.57), which on catalytic hydrogenation in presence of Adams catalyst in ethanol containing a trace of hydrochloric acid, afforded in 93% yield androstane-1,3 β ,17 β -triol VII (m.p. 217–219°; C, 74.01; H, 10.47). Triol VII was found to be different (infrared and mixed m.p.) from authentic androstane-1 α ,3 β ,17 β -triol (m.p. 236–238°; C, 73.71; H, 10.54), obtained from 1-androstene-3,17-dione by α -epoxidation with alkaline hydrogen peroxide, followed by stepwise reduction with sodium borohydride and lithium aluminum hydride.¹¹

Conclusive proof of structure was finally obtained when the triol VIa and its triacetate VIb were compared with authentic samples¹² of 5-androstene-1 β ,3 β ,17 β -triol, m.p. 270–278° dec. and its triacetate m.p. 147.5–148.5°. They were respectively found to be identical in all respects (infrared and mixed m.p.).

The positions of the two hydroxyl groups and of the double bond in ruscogenin are thus firmly established. In light of our results and the conversion of ruscogenin to diosgenin by Lapin and Sannié,² we conclude that this new sapogenin is very likely 1 β -hydroxydiosgenin.

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(1) After this work was completed a recent communication—D. Burn, B. Ellis and V. Petrow, *Proc. Chem. Soc.*, 119 (1957)—dealing with this subject, came to our attention.

(2) H. Lapin and C. Sannié, *Bull. Soc. Chim.*, 1552 (1955).

(3) C. Sannié and H. Lapin, *ibid.*, 1556 (1955).

(4) We wish to thank Mr. J. Monnet of Société des Usines Chimiques Rhône-Poulenc, for a generous supply of a mixture—as shown by paper chromatography and infrared analysis—of ruscogenin and its ring-F isomer.

(5) This sample of ruscogenin, derived from the diacetate, belonged to the "iso" series as shown by its infrared absorption spectrum.

(6) We are indebted to Dr. G. P. Mueller of this laboratory for his advice and help in this degradation.

(7) G. P. Mueller, R. E. Stobaugh and R. S. Winniford, *THIS JOURNAL*, **75**, 4888 (1953); M. E. Wall, H. E. Kenney and E. S. Rothman, *ibid.*, **77**, 5665 (1955); A. F. B. Cameron, R. M. Evans, J. C. Hamlet, J. S. Hunt, P. G. Jones and A. G. Long, *J. Chem. Soc.*, 2807 (1955).

(8) G. Rosenkranz, O. Mancera, F. Sondheimer and C. Djerassi, *J. Org. Chem.*, **21**, 520 (1956).

(9) (a) H. H. Inhoffen, G. Zühlsdorff and Huang-Minlon, *Ber.*, **73B**, 451 (1940); (b) C. Djerassi and C. R. Scholz, *J. Org. Chem.*, **13**, 697 (1948).

(10) C. Djerassi, R. R. Engle and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

(11) Cf. the extensive work of Tamm and co-workers—F. Salmann and C. Tamm, *Helv. Chim. Acta*, **39**, 1340 (1956), and earlier references on analogous systems, where it was shown that a similar sequence of reactions always led to the 1 α ,3 β -diol as the major product.

(12) R. M. Dodson, A. H. Goldkamp, R. D. Muir, *THIS JOURNAL*, **79**, 3920 (1957).