

COMMUNICATIONS TO THE EDITOR

THE STERIC STRUCTURE OF ESTRIOL AND RELATED STEROIDS

Sir:

Stodola, *et al.*,^{1,2} have shown that the zinc-acetic acid reduction of 16-oximino-17-ketosteroids followed by acetylation results in the formation of 16-keto-17-acetoxysteroids. The structure of the intermediate α -ketol was not determined.

We have found that 16-keto-17-acetoxysteroids made by the Stodola method possess the 17-group in the α -position, since Δ^5 -androstene-3(β),17-diol-16-one diacetate² so prepared readily forms a 16-diethyl thioacetal³ (m. p. 136.5–138°, uncor.) which, upon hydrogenolysis,³ yields the known Δ^5 -androstene-3(β),17(α)-diol diacetate^{4,5} identified by comparison with an authentic sample. Furthermore, we feel certain that no rearrangement occurs in the acetylation of α -ketols prepared by the Stodola method, and that these ketols are also 16-keto-17(α)-hydroxysteroids, because: (1) the acetylated α -ketol may be saponified to regenerate the original α -ketol from which it was prepared; (2) the same acetylated α -ketol results on esterification by long standing in pyridine-acetic anhydride or by almost instantaneous acetylation according to Ciusa and Sollazzo,⁶ the yields being virtually identical in both instances.

Hydrogenation of Δ^5 -androstene-3(β),17(α)-diol-16-one diacetate with Raney nickel in ethanol (Stodola, *et al.*)¹ or in ethyl acetate-ethanol (our confirmation) yields Butenandt's triol.⁷ Since this triol is known to be *cis*-oid at C₁₆-C₁₇,⁷ its structure must be Δ^5 -androstene-3(β),16(α),17(α)-triol. If Δ^5 -androstene-3(β),17(α)-diol-16-one (Stodola prepared, m. p. 200–202°, uncor.) is reduced with sodium amalgam in excess dilute ethanolic acetic acid (40°), both Butenandt's triol (*cis*-oid) and Hirschmann's triol⁸ (*trans*-oid) may be obtained. Hirschmann's triol (*trans*-oid at C₁₆-C₁₇)⁹ is therefore Δ^5 -androstene-3(β),16(β),17(α)-triol.

If, in the estrogen series, $\Delta^{1,3,5}$ -estratriene-3,17(α)-diol-16-one (Stodola prepared, m. p. 234–237°, uncor.) is reduced with sodium amalgam as

described, *cis*-oid isoestriol-A¹⁰ (acetone, m. p. 183.5–184.5°, uncor.) and *trans*-oid⁹ estriol are obtained. Isoestriol-A and estriol are therefore, respectively, $\Delta^{1,3,5}$ -estratriene-3,16(α),17(α)-triol and $\Delta^{1,3,5}$ -estratriene-3,16(β),17(α)-triol.

Ruzicka and co-workers^{11,12} have recently prepared in the estrogen and androstane series 16,17-glycols which they designated as $\Delta^{1,3,5}$ -estratriene-3,16(α),17(α)-triol¹¹ and androstane-3(β),16(α),17(α)-triol,¹² respectively. These two triols must be *cis*-oid at C₁₆-C₁₇, since they were formed through the osmium tetroxide addition to the proper Δ^{16} -steroid. However, as neither of the two triols is identical with isoestriol-A or with the saturated androstene-triol (m. p. 251–253°, uncor.) of Butenandt, we suggest that the two compounds are in reality $\Delta^{1,3,5}$ -estratriene-3,16(β),17(β)-triol and androstane-3(β),16(β),17(β)-triol.

(10) M. H. Huffman and H. H. Darby, *THIS JOURNAL*, **66**, 150 (1944).

(11) V. Prelog, L. Ruzicka and P. Wieland, *Helv. Chim. Acta*, **28**, 255 (1945).

(12) L. Ruzicka, V. Prelog and P. Wieland, *ibid.*, **28**, 1609 (1945).

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ON THE MAXIMUM IN THE EQUIVALENT CONDUCTIVITY OF TWO PARAFFIN-CHAIN SALTS IN WATER

Sir:

In a previous communication,¹ it was pointed out that the form of the $\Lambda-\sqrt{c}$ curve of *n*-octadecylpyridonium chloride in water is similar to that of the paraffin-chain electrolytes in general (*i. e.*, Λ decreases abruptly at the critical concentration), but that in water-methanol mixtures containing 10 to 35% of methanol (by wt.), Λ passes through a maximum at concentrations in the neighborhood of the critical concentration in water. Maxima in the $\Lambda-\sqrt{c}$ curves in suitable water-methanol mixtures, but not in water, have also been found for the following *n*-octadecyltrimethylammonium salts: chloride, bromate and formate. On the other hand, the corresponding nitrate, bromide and oxalate exhibit the usual "break point" phenomenon in mixtures containing 0 to 35% of methanol.

We now find that the existence of a maximum in Λ is not limited to water-methanol mixtures as is clearly shown in Fig. 1, where Λ has been plotted as a function of \sqrt{c} for *n*-hexadecylpyridonium iodate (curve 1) and *n*-octadecylpyridonium iodate (curve 2) in water at 25°. In the first mentioned case, the peak is approximately 1 Λ unit high, and in the second, approximately 10 Λ units.

(1) Evers, Grieger and Kraus, *THIS JOURNAL*, **68**, 1137 (1946).

(1) F. H. Stodola, E. C. Kendall and B. F. McKenzie, *J. Org. Chem.*, **6**, 841 (1941).

(2) F. H. Stodola and E. C. Kendall, *ibid.*, **7**, 336 (1942).

(3) S. Bernstein and L. Dorfman, *THIS JOURNAL*, **66**, 1152 (1946).

(4) L. Ruzicka and A. Wettstein, *Helv. Chim. Acta*, **18**, 1264 (1935).

(5) A. Butenandt and G. Hanisch, *Z. physiol. Chem.*, **237**, 89 (1935).

(6) R. Ciusa and G. Sollazzo, *Ann. chim. applicata*, **22**, 72 (1943).

(7) A. Butenandt, J. Schmidt-Thomé and T. Weiss, *Ber.*, **72**, 417 (1939).

(8) H. Hirschmann, *J. Biol. Chem.*, **160**, 363 (1943).

(9) M. N. Huffman and M. H. Lott, *ibid.*, **164**, 785 (1946).