COMMUNICATIONS TO THE EDITOR

THE STERIC STRUCTURE OF ESTRIOL AND RELATED STEROIDS

Sir:

Stodola, et al.,^{1,2} have shown that the zincacetic 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),17diol-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- $17(\alpha)$ -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- $3(\beta), 17(\alpha)$ 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- $3(\beta), 16(\alpha), 17$ -(α)-triol. If Δ^{5} -androstene- $3(\beta), 17(\alpha)$ -diol-16one (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-C₁₇⁹) is therefore Δ^{5} -androstene- $3(\beta)$, $16(\beta), 17(\alpha)$ -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

(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, 48, 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, 33, 72 (1943).

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

described, *cis*-oid isoestriol-A¹⁰ (acetonide, 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 16,17glycols which they designated as $\Delta^{1,3,5}$ -estratriene- $3,16(\alpha),17(\alpha)$ -triol¹¹ and androstane- $3(\beta),16(\alpha)$, $17(\alpha)$ -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- $3,16(\beta)$, $17(\beta)$ -triol and androstane- $3(\beta),16(\beta),17(\beta)$ -triol.

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

(11) V. Prelog, L. Ruzicka and P. Wielaud, Helv. Chim. Acta, 38, 255 (1945).

(12) L. Ruzicka, V. Prelog and P. Wieland, *ibid.*, **38**, 1609 (1945). DEPARTMENT OF BIOCHEMISTRY

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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) Bvers, Grieger and Kraus, THES JOURNAL, 65, 1187 (1946).

⁽⁸⁾ H. Hirschmann, J. Biol. Chem., 150, 363 (1943).

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