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-keto-steroids 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 diacetate[2] so prepared readily forms a 16-diethyl thioacetal[3] (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 C_{16}–C_{17},[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 triol[8] (*trans*-oid) may be obtained. Hirschmann's triol (*trans*-oid at C_{16}–C_{17}[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-A[10] (acetonide, m. p. 183.5–184.5°, uncor.) and *trans*-oid[9] 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)-triol[11] and androstane-3(β),16(α),17(α)-triol,[12] respectively. These two triols must be *cis*-oid at C_{16}–C_{17}, 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.

(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, **68**, 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).
(8) H. Hirschmann, *J. Biol. Chem.*, **156**, 363 (1943).
(9) M. N. Huffman and M. H. Lott, *ibid.*, **164**, 785 (1946).
(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).

DEPARTMENT OF BIOCHEMISTRY
SOUTHWESTERN MEDICAL COLLEGE MAX N. HUFFMAN
DALLAS, TEXAS MARY HARRIET LOTT

RECEIVED JUNE 11, 1947

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 Λ–$\sqrt{c}$ 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 Λ–$\sqrt{c}$ 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).

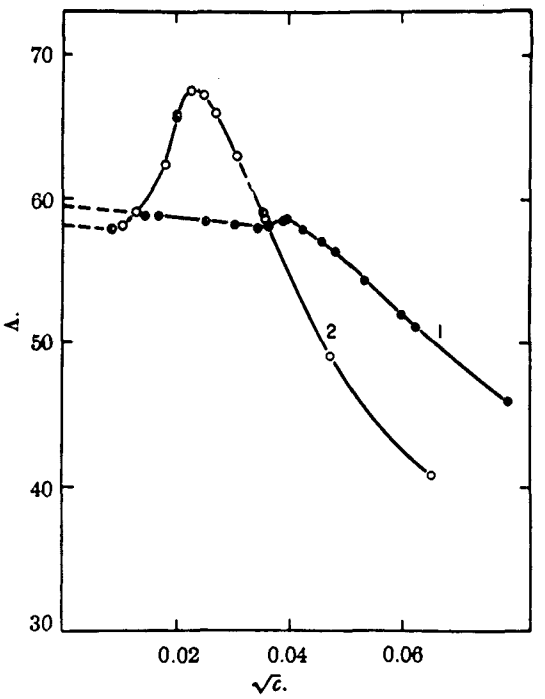

Fig. 1.—Conductance curves in water at 25°: (1) *n*-hexadecylpyridonium iodate; (2) *n*-octadecylpyridonium iodate.

While the addition of methanol in suitable amounts to water solutions of certain paraffin-chain salts gives rise to a maximum in Λ, the addition is not indispensable in some instances, nor is it sufficient to produce a maximum in others. It is evident that the phenomenon is closely related to the nature of the "gegenion."

Sufficient results have now been obtained to permit of formulating a fairly general description of the electrical conductance of solutions of paraffin-chain electrolytes in water–organic solvent mixtures; the details of this work will be presented in the near future.

GEORGE L. BROWN
DEPARTMENT OF CHEMISTRY PHILIP F. GRIEGER
BROWN UNIVERSITY E. CHARLES EVERS
PROVIDENCE, R. I. CHARLES A. KRAUS

RECEIVED JUNE 12, 1947

CUPRAMMONIUM-2,3-BUTANEDIOL COMPLEXES

Sir:

In connection with a study of the properties of cuprammonium-glucoside complexes the behavior of the optically active 2,3-butanediols in cuprammonium hydroxide solution has been observed.

In Table I are given the specific rotations for the D-(−)- and L-(+)-forms of the two butanediols in water (approx. 1% glycol concn.) and in cuprammonium (approx. 0.6%). The rotations were measured at 25°. The cuprammonium contained 15 g. of copper and 240 g. of ammonia per liter. The rotations on this solvent are calculated on the weight of glycol, not on the glycol-copper complex.

The magnitude of the optical rotations (1200°) in cuprammonium is striking. The sign and magnitude of the rotations indicate that the L-(+)-form may be oriented as are the 2- and 3-hydroxyl groups of substituted methyl glycoside and the D-(−)- form as are the 3- and 4-hydroxyl groups of substituted methyl glucoside. And such a condition is distinctly possible in view of the configurations which have been assigned to these two butanediols by Morell and Auernheimer.[1]

Specific rotations for the appropriately substituted methyl glucosides in cuprammonium have been reported.[2] They were +985° (436 mμ) for methyl 2-methyl-β-glucoside, and −1008° (436 mμ) for methyl 4-methyl-β-glucoside.

TABLE I

SPECIFIC ROTATION OF 2,3-BUTANEDIOL

Solvent and light source	L-(+)-form	D-(−)-form
Water, D-line	+ 11.8°	− 11.1°
Water, Hg blue line (436 mμ)	+ 20.6°	− 19.2°
Cuprammonium, Hg blue line	−1200°	+1200°

The samples of optically pure butanediols used in the investigation were supplied by Dr. Robert D. Coghill, formerly head of the fermentation division of the Northern Regional Research Laboratory.

(1) S. A. Morell and A. H. Auernheimer, THIS JOURNAL, **66**, 792–796 (1944).

(2) R. E. Reeves, *J. Biol. Chem.*, **154**, 49–55 (1944).

SOUTHERN REGIONAL RESEARCH LABORATORY
BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY
AGRICULTURAL RESEARCH ADMINISTRATION
U. S. DEPARTMENT OF AGRICULTURE
NEW ORLEANS 19, LA. RICHARD E. REEVES

RECEIVED APRIL 14, 1947

AN ALBUMIN FRACTION ISOLATED FROM HUMAN PLASMA AS A CRYSTALLINE MERCURIC SALT

Sir:

Following the addition of mercuric chloride to a solution of human serum albumin, a fraction of the albumin crystallized. The best yield was obtained when approximately one-third mole mercuric chloride per mole albumin was added to a 15% solution of Fraction V[1] or to human serum albumin crystallized with decanol,[2] in 15% ethanol at −5°, at *p*H 5.2, Γ/2 = 0.02. More than half the serum albumin separated after prolonged standing, or within a few days following seeding, in the form of rhombic or hexagonal plates. Sparingly soluble in water, the crystals dissolved readily in 0.02 *M* sodium chloride and could be recrystallized by the addition of ethanol.

(1) E. J. Cohn, L. E. Strong, W. L. Hughes, Jr., D. J. Mulford, J. N. Ashworth, M. Melin and H. L. Taylor, THIS JOURNAL, **68**, 459 (1946).

(2) These observations, which will presently be reported in full, followed upon, and are closely related to, the methods for the crystallization of serum albumins described elsewhere in this issue, Cohn, Hughes and Weare, *ibid.*, **69**, 1753 (1947).