# COMMUNICATIONS TO THE EDITOR

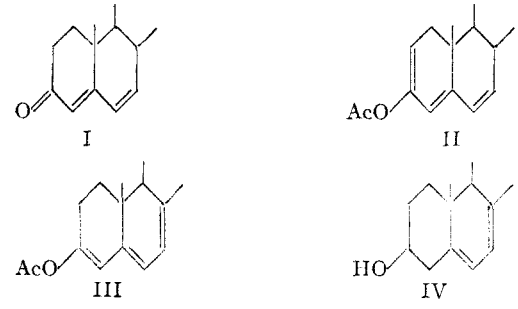
## A NEW METHOD FOR THE PREPARATION OF 7-DEHYDROCHOLESTEROL

*Sir:*

Recently there have been reported methods for introducing an oxygenated function into the 11-position of the steroid nucleus using 7-dehydro compounds as starting material.[1] We wish to report a new method for the introduction of a double bond into the 7-position. Previous methods for introducing such unsaturation have involved the preparation of 7-substituted steroids with subsequent elimination of the elements of water or acid from the 7,8-positions.[2] The new method involves the transposition of the more easily formed $\Delta^6$-double bond into the 7-position. As a model we have prepared 7-dehydrocholesterol, using as starting material $\Delta^{4,6}$-cholestadien-3-one (I). The latter compound can be prepared either from the $\Delta^5$-3-ol system by oxidation[3] or from the $\Delta^4$-3-one system by bromination and dehydrohalogenation.[4]

Depending upon conditions, acetylation of I yields one of the two possible enol acetates. Isopropenyl acetate and sulfuric acid, acetyl chloride and dimethylaniline or acetic anhydride and pyridine yield $\Delta^{2,4,6}$-3-acetoxycholestatriene (II); m. p. 89–91°; $[\alpha]^{25}D$ −21° ($CHCl_3$); $\lambda_{max.}^{EtOH}$ 302 mμ (log ε 4.1). Acetyl chloride and acetic anhydride (mixed) yields $\Delta^{3,5,7}$-3-acetoxycholestatriene (III); m.p. 91–93°; mixed with II m.p. 84–87°; $[\alpha]^{25}D$ −69° ($CHCl_3$); $\lambda_{max.}^{EtOH}$ 305, 316 (log ε 4.3), 330 mμ.[5] The assignment of structures II and III to the isomeric enol esters is made on the basis of the relative positions of the principal absorption maxima (302 and 316 mμ, respectively) and on the basis of the greater levorotary power of III. Confirmatory evidence for this assignment is the fact that III gives a positive Tortelli-Jaffé test[6] while II does not.

Reduction of III with sodium borohydride[7] in methanol-ether at room temperature proceeds rapidly and in high yield to a product which, on the basis of spectroscopic evidence, is essentially all in a $\Delta^{5,7}$-diene form; *i. e.*, the ultraviolet spectrum of the crude product is identical with that of 7-dehydrocholesterol. Presumably the reduction product is a mixture of the 3α- and 3β-hydroxy isomers. Over 70% of the crude material is precipitated by digitonin. Regeneration of the digitonide and crystallization of the product yields 7-dehydrocholesterol (IV); m.p. 142–143°; $[\alpha]^{25}D$ −115° ($CHCl_3$); $\lambda_{max.}^{EtOH}$ 271, 282 (log ε 4.1), and 293 mμ.

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(1) E. M. Chamberlin, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita and M. Tishler, THIS JOURNAL, **73**, 2396 (1951); L. F. Fieser, J. E. Herz and Wei-Yuan Huang, *ibid.*, **73**, 2397 (1951); G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3546 (1951).

(2) For leading references see v. J. Schmutz, H. Schaltegger and M. Sanz, *Helv. Chim. Acta*, **34**, 1111 (1951), and L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, pp. 179–182.

(3) C. Djerassi, "Organic Reactions," edited by R. Adams, Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, pp. 229–230.

(4) Ch. Meystre and A. Wettstein, *Experientia*, **2**, 408 (1946); H. H. Inhoffen, G. Stoeck and H. Martens, *Ann.*, **563**, 131 (1949).

(5) Compounds II and III have been further characterized by their carbon and hydrogen analyses, infrared spectra, and saponification equivalents.

(6) Tortelli-Jaffé, *Chem. Z.*, **39**, 14 (1915); U. Westphal, *Ber.*, **72**, 1243 (1939).

(7) E. Schwenk, M. Gut and J. Belisle, *Arch. Biochem.*, **31**, 456 (1951); T. F. Gallagher and B. Belleau, THIS JOURNAL, **73**, 4458 (1951); W. G. Dauben and J. F. Eastham, *ibid.*, **73**, 4463 (1951).

## STEROIDS. XXVIII.[1] INTRODUCTION OF THE 11-KETO AND 11α-HYDROXY GROUPS INTO RING C UNSUBSTITUTED STEROIDS (PART 2)

*Sir:*

Recently,[2] there was described the introduction of an oxygen function into position 11 of ring C unsubstituted steroids by performic acid oxidation of steroidal $\Delta^{7,9(11)}$-*allo*dien-3β-ols *via* 9α,11α-oxido-7-ones and thence $\Delta^{8(9)}$-11α-ol-7-ones (IV). We have now found that the by-products of the oxidation, which appear to be the isomeric $\Delta^{9(11)}$-7,8-oxides and/or $\Delta^{9(11)}$-7-ketone, are readily isomerized to $\Delta^{8(9)}$-7-ketones (I). A similar observation has already been recorded by Fieser and co-workers[3] in the bile acid series, where such derivatives represent the main products in the dichromate oxidation of steroidal $\Delta^{7,9(11)}$-dien-3-ols. The present communication deals with the facile conversion of such intermediates to 11-oxygenated steroids by a novel procedure, which promises to be of general applicability.

Performic acid oxidation of $\Delta^{7,9(11)}$-allopregnadien-3β-ol-20-one 3-acetate[4] proceeded exactly as described for the analogous 3β,20β-diol[2] yielding 9α,11α-oxidoallopregnane-7,20-dione-3β-ol acetate (m.p. 219–220°, $[\alpha]^{20}D$ −36° (all rotations in $CHCl_3$), $\lambda_{max.}^{CHCl_3}$ 1728 and 1700 cm.$^{-1}$, no free hydroxyl band, found: C, 71.06; H, 8.46), which was rearranged with alkali and acetylated to afford $\Delta^{8(9)}$-

(1) Paper XXVII, C. Djerassi, G. Rosenkranz, J. Pataki and St. Kaufmann, *J. Biol. Chem.*, in press.

(2) G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 3546 (1951).

(3) L. F. Fieser, J. E. Herz and W. Huang, *ibid.*, **73**, 2397 (1951); L. F. Fieser, *et al.*, *ibid.*, **73**, 4053 (1951).

(4) C. Djerassi, R. Romo and G. Rosenkranz, *J. Org. Chem.*, **16**, 754 (1951).