

slices could effect this conversion *in vitro*. Heard, *et al.*,<sup>3</sup> have added confirmatory *in vivo* evidence and West, *et al.*,<sup>4</sup> have shown that this conversion can occur in humans even in the absence of ovaries and adrenals. We now wish to report evidence for the formation of 17 $\alpha$ -hydroxyprogesterone and  $\Delta^4$ -androstene-3,17-dione from progesterone by ovarian tissue, thereby providing a link between progesterone and estradiol biogenesis. Recent publications by Slaunwhite and Samuels<sup>5</sup> and Lynn<sup>6</sup> have reported the conversion of progesterone to 17 $\alpha$ -hydroxyprogesterone and to androstenedione by testes homogenates.

Bovine ovarian tissue was homogenized according to the procedure of Hayano, *et al.*,<sup>7</sup> and incubated aerobically at 37° for four hours with 4.8 mg. of progesterone-4-C<sup>14</sup> ( $5.5 \times 10^6$  c.p.m.) and 10 mg. each of 17 $\alpha$ -hydroxyprogesterone and androstenedione. A neutral, ketonic extract was prepared<sup>7</sup> and chromatographed on alumina. The recovered 17 $\alpha$ -hydroxyprogesterone, eluted with ether-benzene (1:9), was mixed with unlabeled progesterone and submitted to two "washout" chromatograms on alumina to remove traces of progesterone-4-C<sup>14</sup>. The specific activity of the isolated 17 $\alpha$ -hydroxyprogesterone was 1190 c.p.m./mg. after the first recrystallization (m.p. 220–222° from acetone) and 1250 c.p.m./mg. after the second (m.p. 222–223°).<sup>8</sup> After dilution with 11 mg. of carrier, the 17 $\alpha$ -hydroxyprogesterone (4 mg.) was converted by hydrogenation over Pt catalyst in acetic acid and subsequent oxidation with periodic acid to 3 $\beta$ -hydroxyandrostane-17-one,<sup>8</sup> m.p. 177–177.5°, having a specific activity of 309 c.p.m./mg. (theoretical 369 c.p.m./mg.).

The androstenedione fraction, eluted from the alumina chromatogram by ligroin-benzene (2:8), was mixed with unlabeled progesterone and submitted to a "washout" 25 transfer countercurrent distribution using the system of Pearlman.<sup>9</sup> The fractions containing androstenedione were combined, diluted with carrier and purified by two additional countercurrent distributions followed by two chromatograms on paper using the propylene glycol-ligroin C system of Savard.<sup>10</sup> These procedures succeeded in eliminating two radioactive contaminants. The androstenedione eluted from the second paper chromatogram was purified through a column of alumina and recrystallized twice from ether-ligroin C. The specific activity after the first recrystallization (m.p. 170–172°) was 90 c.p.m./mg. and after the second<sup>8</sup> (m.p. 172–173°) 97 c.p.m./mg. The latter sample when repartitioned by a 50-transfer countercurrent procedure was distributed, as determined both by radioactivity and absorbance at 240 m $\mu$ ., in a manner

(3) R. D. H. Heard, P. H. Jellinek and V. J. O'Donnell, *Endocrinology*, **57**, 200 (1955).

(4) C. D. West, B. L. Damast, S. D. Sarro and O. H. Pearson, *J. Biol. Chem.*, **218**, 409 (1955).

(5) W. R. Slaunwhite, Jr., and L. T. Samuels, *ibid.*, **220**, 349 (1956).

(6) W. S. Lynn, *Fed. Proc.*, **15**, 305 (1956).

(7) M. Hayano, M. C. Lindberg, M. Wiener, H. Rosenkrantz and R. I. Dorfman, *Endocrinology*, **55**, 326 (1954).

(8) The identity was confirmed by infrared analysis and mixed melting point with an authentic sample.

(9) W. H. Pearlman, *Rec. Prog. Hor. Res.*, **9**, 27 (1954).

(10) K. Savard, *J. Biol. Chem.*, **202**, 457 (1953).

characteristic of pure androstenedione. The ultraviolet absorbing material from this distribution was recombined, purified over alumina and recrystallized from ether to yield androstenedione,<sup>8</sup> m.p. 171–173°, having 93 c.p.m./mg.

Thus the biogenesis of the two principal secretory products of the ovary, progesterone and estradiol, has been interrelated. In similar *in vitro* experiments with *corpora lutea* cholesterol has been shown<sup>11</sup> to be a precursor of progesterone and therefore a biosynthetic scheme in the ovary appears to be: cholesterol  $\rightarrow$  progesterone  $\rightarrow$  androstenedione (testosterone)  $\rightarrow$  estradiol. The intermediacy of androgens on the biogenetic pathways leading to the estrogens affords a new approach to the understanding of the origin and role of ovarian androgens. The occurrence of 17 $\alpha$ -hydroxylase in ovarian tissue makes it likely that 17 $\alpha$ -hydroxyprogesterone is an intermediate between progesterone and androstenedione in ovarian biosynthesis. Definitive proof of this is now being sought.

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(11) S. Solomon, R. Vande Wiele and S. Lieberman, unpublished results.

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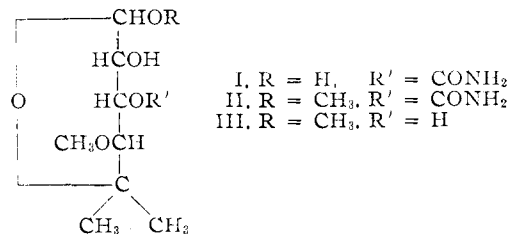
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## NOVOBIOCIN. V. THE CONFIGURATION OF THE ALDOSE MOIETY

Sir:

We have assigned the configuration of L-lyxose to 3-O-carbamyl-4-O-methylnovobiose (I).<sup>1,2</sup> This assignment is based in part on rules of optical rotation.

Hydrolysis of methyl 4-O-methylnovobiopyranoside (III)<sup>1,2</sup> with 0.1 *N* hydrochloric acid followed by reaction with *N*-benzyl-*p*-methoxyphenylhydrazine has yielded an *N*-benzyl-*p*-methoxyphenylhydrazone IV, m.p. 111–113°,  $[\alpha]_D^{25} -39^\circ$  (*c*, 1 in methanol). The negative optical rotation of IV allows assignment<sup>3</sup> of the C-2 hydroxyl group to the right in the Fisher projection formula.



(1) C. H. Shunk, C. H. Stammer, E. A. Kaczka, E. Walton, C. F. Spencer, A. N. Wilson, J. W. Richter, F. W. Holly and K. Folkers, *THIS JOURNAL*, **78**, 1770 (1956).

(2) H. Hneksema, E. L. Caron and J. W. Hinman, *ibid.*, **78**, 2019 (1956).

(3) It has been shown by B. Vataček, *Collection Czechoslov. Chem. Commun.*, **3**, 259 (1931), that *N*-benzylphenylhydrazones of aldoses having the C-2 hydroxyl located on the right have negative optical rotations.

The formation of a cyclic carbonate<sup>4</sup> of III from methyl 3-O-carbamyl-4-O-methylnovobiopyranoside (II) indicates that the C-2 and C-3 hydroxyl groups are *cis*. The preparation of a 2,3-isopropylidene derivative,  $[\alpha]^{25}_D -13^\circ$  (*c*, 1.36 in methanol), from III confirms<sup>5</sup> this conclusion.

(-)- $\alpha$ -Methoxy- $\beta$ -hydroxyisovaleric acid (V)<sup>1</sup> has been obtained by degradation of II. Its optical antipode, (+)- $\alpha$ -methoxy- $\beta$ -hydroxyisovaleric acid, was synthesized<sup>1</sup> from (-)- $\alpha,\beta$ -dihydroxyisovaleric acid (VI).<sup>6</sup> The rotation of VI in 1 *N*

(4) J. W. Hinman, H. Hoeksema, E. L. Caron and W. G. Jackson. *THIS JOURNAL*, **78**, 1072 (1956).

(5) J. A. Mills. *Advances in Carbohydrate Chem.*, **10**, 20 (1955).

(6) J. R. Sjolander, K. Folkers, E. A. Adelberg and E. L. Tatum. *THIS JOURNAL*, **76**, 1085 (1954).

hydrochloric acid is  $[\alpha]^{25}_D -14.7^\circ$  (*c*, 1.64); in 1 *N* sodium hydroxide,  $[\alpha]^{30}_D +4.8^\circ$  (*c*, 1.8). This shift in rotation indicates<sup>7</sup> that the C-2 hydroxyl in VI is on the right in the projection formula and, therefore, that the C-2 methoxyl in V is on the left. Since C-2 in V corresponds to C-4 in the aldose moiety, the methoxyl in compounds I-IV is on the left.

(7) M. Winitz, L. Bloch-Frankenthal, N. Izumiya, S. M. Birnbaum, C. G. Baker and J. P. Greenstein, *ibid.*, **78**, 2423 (1956).

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## BOOK REVIEWS

**Currents in Biochemical Research 1956.** Editor, DAVID E. GREEN, Institute for Enzyme Research, University of Wisconsin, Madison, Wisconsin. Interscience Publishers, Inc., 250 Fifth Avenue, New York 1, N. Y. 1956. xvi + 697 pp. 16.5 × 23.5 cm. Price, \$10.00.

In 1946, the first volume of "Currents in Biochemical Research" under the editorship of David E. Green made its appearance. Coming ten years later, the present volume under the same distinguished editor, has once more illuminated the progress of many areas of biochemistry. It is a pleasure to read the 27 lucid and stimulating essays which comprise the present volume. These cover many aspects, induced enzyme formation, photosynthesis, viruses, hormones, electron transfer reactions, protein and nucleic acid structure, enzyme kinetics, blood, muscle, and nerve physiology, and disease states, to mention only a few. As the editor points out "The past decade has witnessed a rate of progress vastly greater than any comparable period since the early beginnings of biochemistry as a science more than 100 years ago. There is little doubt that this phenomenal rate of development has been sparked by a revolution in methodology." There is good reason for the expression of pride in the accomplishments of a decade of distinguished achievement. There must also be some measure of perspective in what is well described as a revolution in methodology. Biochemists now possess tools and techniques, readily available, and applicable to the rapid solution of many problems, or at least to the quick and precise answering of the questions which the experimenter may ask himself. In this, the field of biochemistry is participating in and benefiting by the great engineering and technical progress of the current era. It is sometimes difficult, however, not to feel a twinge of reservation in what seems to be on occasion an equating of progress in ideas with progress in the development of machines. Some of the questions raised by Emil Fischer have been answered by recent chromatographic techniques, and the newly-hatched doctor of philosophy can turn out results faster and with higher precision than could Pasteur. Perhaps we should merely say that modern biochemistry is no better and no worse than in the days of Fischer and Pasteur, that its rate of production of penetrating concepts and ideas has not measurably changed, but that, thanks to modern tools, it may move a little faster.

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**Nuclear Magnetic Resonance.** BY ERNEST ROBERT ANDREW, Ph.D., F.R.S.E., Professor of Physics in the University of Wales (University College of North Wales, Bangor). University Press, Cambridge, 1955. xi + 265 pp., 14.5 × 22 cm. (Cambridge Monographs on Physics) Price \$6.50.

The utility of nuclear magnetic resonance studies in a wide variety of chemical problems is now well recognized. This is the first book on the subject, although a number of complete reviews have appeared. The excellent bibliography compiled by Andrew as part of this book lists these reviews as well as the pertinent references up to 1954.

The author has been one of the pioneers in the field, specializing in rotation and diffusion in organic crystals including polymers. This subject, which is of wide interest, is well treated in his book.

Outside of the Appendix, there are 220 pages which of course only allow a summary of this important and complicated subject. Nevertheless, the book is arranged so logically that the subject matter can be read almost like a novel with understanding and satisfaction. This reviewer was particularly pleased with the way in which nuclear magnetic resonance absorption was compared with the anomalous dispersion in the neighborhood of a spectroscopic absorption line and the correlation with the Lorentz theory clarified.

For a chemist who knows little of electrical engineering or electromagnetic theory, the chapter on experimental methods is too short to be thoroughly intelligible, but sufficient references are given to fill in the necessary detail.

The same may be said of the chapter on basic theory. Here, however, the order is so logical that a reader with very little background should grasp the general idea.

The choice of subject matter is well balanced up to the date of writing (1954). For example, there is a paragraph in Chapter 5 on water content in biological materials. The so-called chemical shift is only briefly discussed since at that time the subject was quite new. However, there is sufficient for the imaginative reader to see the application to problems of structural and analytical organic chemistry.

The chapter on metals will be of considerable interest to the chemist, as also will be the chapter on quadrupole effects. There are six appendices which deal with details of theory and give a useful list of substances investigated.

Needless to say, the reviewer recommends this book as a desirable part of the library of any physical chemist or physicist.

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