We have investigated electronic exchange between ferric and ferrous ions in 3 *M* perchloric acid using radioferric ion[3] as indicator. The concentration ratio of ferric to ferrous ions (R_0) was consistently close to 0.25 and the total iron concentration was 0.023 *M*. Exchange was allowed to proceed for periods up to nine days. No measurable oxidation of ferrous to ferric ion by air occurred in this time. Hydrolysis of ferric ion was slight.[4]

Measurement of exchange was dependent on partially separating ferric and ferrous ions by their diffusion from the exchange mixture across a sintered glass membrane[5] into 3 *M* perchloric acid.

Ferric and ferrous ion concentrations were determined colorimetrically at 480 mμ employing the thiocyanate method.

In thirty-minute diffusion periods at 25° ratios (R) of around 0.54 were obtained for ferric to ferrous ion concentrations in the diffusate. The average separation factor ($S = R_0/R$) of about 0.47 indicates ferric ion diffuses relatively more rapidly than ferrous ion.

If the half time for exchange is much greater than the time required for diffusion separation, it is possible to derive the relation

$$F = \left(\frac{A}{a_0 W} - 1\right)\frac{R_0 + 1}{S - 1}$$

where the fraction of equilibrium exchange (F) is related to the radioactivity of the diffusate (A, in counts min.$^{-1}$), the specific activity of ferric ion (a_0, in counts min.$^{-1}$ mmol.$^{-1}$), and the millimoles of ferric ion in the diffusate (W) through the separation terms previously defined.

Initial results, subject to deviations of ±5% by virtue of the separation technique used, are: for thirty minutes, 2.2 and 3.8% of equilibrium exchange and for one case of poor separation, 9.6%; for two days, 8.7%; for five days, 13.9%; for seven days, 26.2%; and for nine days, 30.7%. These figures give a half time for exchange[6] of 18.5 ± 2.5 days.

We gratefully acknowledge the interest shown by Professor T. de Vries. Experimental results for ferric–ferrous ion exchange under other conditions will be the subject of a later communication.

CHEMISTRY DEPARTMENT
PURDUE UNIVERSITY
LAFAYETTE, INDIANA
L. VAN ALTEN
C. N. RICE[7]

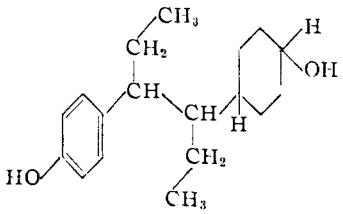
RECEIVED DECEMBER 13, 1947

(3) Supplied by U. S. Atomic Energy Commission.
(4) Rabinowitch and Stockmayer, THIS JOURNAL, **64**, 338 (1942).
(5) Northrop and Anson, *J. Gen. Physiol.*, **12**, 543 (1929).
(6) Mackay, *Nature*, **144**, 997 (1938).
(7) Present address: The Lilly Research Laboratories, Indianapolis 6, Indiana.,

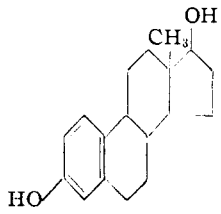
THE HEXAHYDRO DERIVATIVES OF *meso*-HEXESTROL

Sir:

After it was discovered that hexestrol is a highly potent estrogen, it became of considerable interest to prepare the hexahydro derivatives I since these bear a closer resemblance to the phenolic alcohol estradiol (II) than does the diphenol hexestrol itself. The activity of I would be of considerable significance in deciding whether the high physiological activities of hexestrol and diethylstilbestrol result from their superficial resemblance to the natural hormone II.



I



II

Our efforts to synthesize I (begun in 1940) have now proved successful, leading to the two stereoisomers corresponding in configuration at the bridge carbon atoms to *meso*-hexestrol. Recently Ungnade and Ludutsky [THIS JOURNAL, **69**, 2629 (1947)] reported the synthesis of the isomers of I related in configuration to the much less potent racemic hexestrol. In our synthesis hexestrol monomethyl ether was hydrogenated in the presence of copper chromium oxide catalyst at 240° and 425 atmospheres pressure, to obtain selective reduction of the phenolic ring. Demethylation of the mixture of methyl ethers by heating with methylmagnesium iodide at 170–190° gave a mixture of the phenolic alcohols I (soluble in Claisen alkali) in 40–50% yield. By recrystallization from dilute alcohol and benzene isomer A, m. p. 183–184° (cor.), was obtained. *Anal.* Calcd. for $C_{18}H_{28}O_2$: C, 78.2; H, 10.2. Found: C, 78.2; H, 9.9. The monobenzoate of A (Schotten–Baumann) melted at 68–69°. *Anal.* Calcd. for $C_{25}H_{32}O_3$: C, 78.9; H, 8.5. Found: C, 79.0; H, 8.6. Isomer B was obtained from the original filtrate and purified through the monobenzoate, m. p. 129.5–130° (cor.). *Anal.* Found: C, 79.0; H, 8.3. Saponification of the pure monobenzoate gave isomer B, which showed a variable melting point behavior. Recrystallization from benzene and from dilute methanol gave samples with the m. p. 133–134°; sublimation at 120° (0.01 mm.) resulted in material of m. p. 128–129.5°. When the 134° material was dried at 60° (0.1 mm.) the m. p. broadened to 134–141.5° (*Anal.* Found: C, 78.2; H, 10.0). Other samples melting as high as 143–145° were obtained. This behavior is indicative of polymorphism. Isomer B may be the same as the compound, m. p. 144–145°, obtained by Hoehn and Ungnade [THIS JOURNAL, **67**, 1617 (1945)] in low yield by hydrogenation of diethylstilbestrol.

Preliminary physiological assays carried out under the direction of Drs. R. K. Meyer and Elva Shipley Meyer of the Department of Zoology, indicate that both isomers are definitely weaker in

estrogenic activity in rats than diethylstilbestrol. Further tests are in progress.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN A. L. WILDS
MADISON 6, WISCONSIN WILLIAM B. MCCORMACK

RECEIVED JANUARY 19, 1948

STREPTOMYCIN, VII. DEGRADATION OF O-TETRAMETHYLSTREPTAMINE TO D,L-DIMETHOXYSUCCINIC ACID

Sir:

N,N′-Diacetylstreptamine (1,3-diacetamido-2,4,5,6-tetrahydroxycyclohexane)[1] was converted with dimethyl sulfate and sodium hydroxide to O-tetramethyl-N,N′-diacetylstreptamine (m. p. > 300°; *Anal.* Calcd. for $C_{14}H_{26}O_6N_2$: C, 52.81; H, 8.23; N, 8.81; CH_3O, 39.07. Found: C, 52.99; H, 8.28; N, 8.67; CH_3O, 40.1), which on hydrolysis with hydrochloric acid afforded O-tetramethylstreptamine dihydrochloride (m. p. > 300°; *Anal.* Calcd. for $C_{10}H_{22}O_4N_2 \cdot 2HCl$: C, 39.09; H, 7.87; N, 9.12; Cl, 23.08. Found: C, 38.76; H, 7.71; N, 8.98; Cl, 23.4). The free base (m. p. 83–84°; *Anal.* Calcd. for $C_{10}H_{22}O_4N_2$: C, 51.26; H, 9.46; N, 11.96. Found: C, 51.18; H, 9.38; N, 11.71) was oxidized with neutral potassium permanganate at room temperature. The methyl ester mixture formed from the oxidation products with methanolic hydrogen chloride yielded on distillation several fractions which were treated separately with methanolic ammonia or methylamine. From the lower-boiling fractions there were obtained D,L-dimethoxysuccinic acid diamide (m. p. 266–268° (dec.)[2]; *Anal.* Calcd. for $C_6H_{12}O_4N_2$: C, 40.90; H, 6.87; N, 15.90; CH_3O, 35.2. Found: C, 41.14; H, 6.76; N, 16.19; CH_3O, 35.0) and D,L-dimethoxysuccinic acid di-N-methylamide (m. p. 188–189°; *Anal.* Calcd. for $C_8H_{16}O_4N_2$: C, 47.04; H, 7.90; N, 13.72; CH_3O, 30.4. Found: C, 47.46; H, 8.05; N, 13.96; CH_3O, 30.5). Synthetic specimens of these hitherto undescribed amides, prepared from D,L-tartaric acid, showed the same melting points, undepressed by admixture of the degradation products. The diamide[3] and di-N-methylamide[4] of *meso*-dimethoxysuccinic acid melted at 255–257° (dec.) and 210–210.5°, respectively. The *meso*-diamide strongly depressed the melting point of the diamides derived from streptamine and from D,L-tartaric acid.

If, as appears highly probable, streptamine and streptidine are *meso* compounds, it follows from the above results that the 5-hydroxyl group is oriented *trans* with respect to the 4- and 6-hydroxyl groups (*xylo*-configuration), a spatial arrangement also encountered at the corresponding positions in *meso*inositol. This would limit the number of possible *meso* forms for streptamine to four.

Furthermore, there was isolated from high-boiling ester fractions prior to amidation a compound $C_{10}H_{17}O_6N$ (m. p. 109–110°; *Anal.* Calcd C, 48.57; H, 6.93; N, 5.67; $4CH_3O$, 50.1. Found: C, 48.74; H, 6.87; N, 5.65; CH_3O, 49.2) which should be either the 2,6-lactam of a 2-amino-3,4,5-trimethoxyadipic acid-1-methyl ester, or the 3,6-lactam of a 3-amino-2,4,5-trimethoxyadipic-1-methyl ester.

DIVISION OF ORGANIC CHEMISTRY O. WINTERSTEINER
SQUIBB INSTITUTE FOR MEDICAL RESEARCH
NEW BRUNSWICK, NEW JERSEY ANNA KLINGSBERG

RECEIVED JANUARY 19, 1948

(1) R. L. Peck, C. E. Hoffhine, E. W. Peel, R. P. Graber, F. W. Holly, R. Mozingo and K. Folkers, THIS JOURNAL, **68**, 776 (1946).

(2) All melting points reported are corrected.

(3) W. N. Haworth and E. L. Hirst, *J. Chem. Soc.*, 1858 (1926).

(4) W. N. Haworth and D. I. Jones, *ibid.*, 2349 (1927).

NEW BOOKS

SMALL WONDER—The Story of Colloids. By GESSNER G. HAWLEY. Alfred A. Knopf, New York, N. Y., 1947. 220 pp. Price $3.50.

The author certainly deserves full credit for his courage and, as many parts prove, skill in attempting to explain "to those who have the curiosity but lack the time to study more erudite treatises" what the term "colloid" implies. In his preface he also states, however, that "there is such a thing as having an embarrassment of subject matter" and "it is easy to become bewildered and get lost in it all." That has happened, and it is unfortunate because the reader who takes many of the written words at their face value will not get a more general, but often a wrong, understanding of colloids. This refers specifically to the author's definition of colloids, the history of this branch of science, to the explanation of their electrical properties, to the discussion of how natural rubber is obtained, or synthetic rubber produced.

The discussion of the electron microscope is by far too extensive for a book of this type, so much the more since its use in attempting to pry deeper into the structure of lyophilic colloids is becoming more and more questionable. It would have been far more appropriate to explain to the reader the tremendous developments of ultramicroscopic techniques and what has been achieved by their use.

The author has made a few serious mistakes which must be corrected. Plate XV is a cut-away view of a Sharples *super-* and not ultracentrifuge. The statement that the first periodical given over exclusively to colloid chemistry is the "Journal of Colloid Science," which appeared for the first time in January, 1946, is incorrect; the Germans have had the periodicals "Kolloid Zeitschrift" and "Kolloid-