In view of the unique character of the iron compound, and of the inherent difficulties in the precise formulation of the covalent complexes of the transition metals, particularly those with unsaturated hydrocarbons, detailed proposals with respect to the electronic structure of iron biscyclopentadienyl would be premature. However, it may be noted, that the number of electrons available (but not necessarily used) for iron to carbon binding, is eighteen (five π electrons for each cyclopentadienyl unit, plus the eight electrons of the iron atom). Thus the effective atomic number of the central iron atom is thirty-six (krypton structure) as in the ferrocyanide ion and in iron pentacarbonyl. Details of hybridization will determine the precise geometry of the molecule. For example, while the compound is formulated above as a pentagonal anti-prism, a prismatic structure (III) such as might result from split d^3p^2 plane pentagonal bonding, is not excluded.

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MICROBIOLOGICAL HYDROXYLATION OF PROGESTERONE

Sir:

The dehydrogenation of steroid alcohols by bacteria and the reduction of steroid ketones by yeasts has been studied in great detail by Mamoli, Vercellone, Butenandt and their collaborators.[1] Trufitt[2] has effected oxidative ring cleavage and removal of the steroidal side chain by the use of *Proactinomyces* species. We wish to report a novel type of microbiological oxidation, *viz.*, the introduction of one or more hydroxyl groups into the intact steroid nucleus by an unidentified actinomycete[3] in submerged culture.

In the example reported here progesterone (0.25 g./l.) was used as the substrate in a simple medium containing glycine, glutamate, soybean oil and inorganic salts. Media containing soybean meal, dried brewers' yeast or cornsteep liquor could be substituted for the above. After incubation for three days at 25° the culture was filtered and the oxidized steroids recovered from the filtrate by chloroform extraction followed by distribution between 80% methanol and hexane. The crystalline residue (8.7 g., from 17.5 g. of progesterone) from the alcoholic phase was chromatographed on magnesium silicate-celite and yielded three hitherto undescribed derivatives of progesterone. The major product eluted with chloroform-benzene 1:1 and also obtained directly by recrystallization of the above residue was 16α-hydroxyprogesterone (I), m.p. 225–226°; $[\alpha]^{23}D$ +158° (*c*, 0.65 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 239 mμ (ϵ = 17,000); $\lambda_{max.}^{Nujol}$ 3.04μ (OH); 5.90μ (20-keto); 6.02 and 6.20μ (3-keto, $\Delta^{4,5}$). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15. Found: C, 76.61; H, 9.36, Monoacetate, m.p. 134–135°; $[\alpha]^{22}D$ +107° (*c*, 0.33 in $CHCl_3$). *Anal.* Calcd. for acetyl: 11.6. Found: acetyl, 11.6. The position of the hydroxyl group in this substance followed from its conversion into the known Δ^{16}-dehydroprogesterone[4] (m.p. 190–191.5°[5]; $[\alpha]^{23}D$ +134.5° (*c*, 0.90 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 240 mμ (ϵ = 28,400) by means of aluminum butylate. The latter reaction has its analogy in the conversion of allopregnanetriol-3β,16α,20β (Marrian's triol) to Δ^{16}-allopregnenedione-3,20 by means of aluminum isopropylate.[6] The contributions to the molecular rotation made by the 16-hydroxyl group in the free ($[M]_D^{OH-H}$ = −82°) and in the acetylated form ($[M]_D^{OAc-H}$ = −205°) strongly suggest the α-orientation for that group.[7]

Preceding I in the chromatogram was pregnanol-16α-dione-3,20 (II) present in small amount only, m.p. 199–200°; $[\alpha]^{23}D$ +90.5° (*c*, 0.82 in $CHCl_3$)[8]; $\lambda_{max.}^{alc.}$ 284 mμ (ϵ = 65). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.85; H, 9.72. Found: C, 76.12; H, 9.73. The latter on treatment with aluminum *t*-butylate yielded Δ^{16}-pregnenedione-3,20, m.p. 196–198°; $[\alpha]_D$ +83°; $\lambda_{max.}^{alc.}$ 239 mμ (ϵ = 9100).[9]

A third substance present in small amount was eluted with chloroform–acetone 3:1, m.p. 215.5–16.5°; $[\alpha]^{24}D$ −39° (*c*, 0.76 in $CHCl_3$); $\lambda_{max.}^{alc.}$ 243 mμ (ϵ = 14,400). It had the composition of a dihydroxyprogesterone. *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 73.09; H, 8.68.

(1) For a review on this subject see the chapter by F. G. Fischer, "Biochemical Oxidations and Reductions" in Newer Methods of Preparative Organic Chemistry, Interscience Publishers, Inc., New York, N. Y., 1948.

(2) G. E. Turfitt, *Biochem. J.*, **42**, 376 (1948).

(3) The culture carries the designation MD-2428 in our own collection.

(4) A. Butenandt and J. Schmidt-Thomé, *Ber.*, **72**, 182 (1939); *cf.* also D. K. Fukushima and T. Gallagher, THIS JOURNAL, **73**, 196 (1951).

(5) A mixture melting point of this material with an authentic sample of Δ^{16}-dehydroprogesterone kindly supplied by Dr. Carl Djerassi (m.p. 188–190° after three recrystallizations) showed no depression.

(6) R. E. Marker and D. L. Turner, THIS JOURNAL, **62**, 2541 (1940).

(7) The average values for $[M]_D^{16\alpha-OH-H}$ and for $[M]_D^{16\alpha-OAc-H}$ are −64° and −284°, respectively, while those for 16β-substituted derivatives are +38° and +98°, respectively. *Cf.* H. Hirschmann and F. Hirschmann, *J. Biol. Chem.*, **184**, 259 (1950), and D. K. Fukushima and T. F. Gallagher, THIS JOURNAL, **73**, 196 (1951).

(8) The value for $[M]_D^{I-II}$ (+221°) is in good agreement with that for $[M]_D$ Δ^4-cholestenone-coprostanone (+203°).

(9) A. Butenandt, L. Mamoli and A. Heuser, *Ber.*, **72**, 1616 (1939).

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HYDRODEXTRAN

Sir:

A solution of degraded dextran has been shown to be an effective blood volume extender in clinical studies.[1] Occasional side reactions in man following dextran infusions have been observed.[2] At the present time, specifications for clinical dextran require a weight average molecular weight by light scattering of 75,000 ± 25,000 with the upper 5 to 10% having a weight average molecular weight not exceeding 200,000 and the lower 5 to 10% having a weight average molecular weight above 25,000.[3] In the usual preparation of clinical dextran, native

(1) B. Ingelman, *Upsala Läkarefören Förh.*, **54**, 107 (1949).

(2) Unpublished results reported to National Research Council, Subcommittee on Shock.

(3) U. S. Military Medical Purchase Description, 1-161-890, May 24 (1951).

dextran (a glucopyranose anhydride polymer obtained by fermentation of sucrose by *Leuconostoc mesenteroides* and possessing a weight average molecular weight of 5,000,000) is degraded by acid hydrolysis, and the hydrolyzate is fractionated by the addition of an organic solvent. Each dextran molecule formed by the rupture of the glycosidic bonds contains a terminal reducing group.[4] In this laboratory the reducing content per liter of a six per cent. solution of clinical dextran in isotonic saline solution was found to be equivalent to 200 mg. of glucose (Somogyi method).[5]

During the acid hydrolysis the 6-substituted terminal glucose unit may give rise to substituted 5-hydroxymethyl furfural derivatives which can rearrange to give products containing aldehydo, keto or carboxyl groups.[6] The molecular weight distribution of products containing these functional groups would not differ from that of fractionated and degraded dextran which can be expected to retain minute amounts of this material. Reduction of the terminal reducing group in clinical dextran as well as the reducing groups in rearranged products may lessen the possibility of reaction with carbohydrates, proteins or other materials in the blood that may give rise to clinical side reactions.

We have reduced all free reducing groups of clinical dextran by sodium borohydride, by sodium amalgam and by catalytic hydrogenation. Carboxyl-containing polymeric products were removed by treating a hydrodextran solution with alum and ammonia, filtering and passing the filtrate through exchange resins.

Hydrodextran (wt. average mol. wt. 66,000 by light scattering) was obtained as a fine white powder in quantitative yield from degraded dextran (wt. average mol. wt. 66,000) by reduction with sodium borohydride in aqueous solution. The specific rotation $[\alpha]^{21}D$ was $+196.6°$; the relative viscosity of a 6% solution (25°) was 3.42; the intrinsic viscosity (25°) was 0.21 dl./g.; boron content was 0.002% (spectrographic analysis). The product was non-reducing to Somogyi reagent.

It has been demonstrated that neutral, slightly acid or alkaline solutions of reducing sugars develop acidity and color during heating.[7] We have found that clinical dextran in similar solutions develops acidity and that clinical dextran in alkaline solutions develops color in addition. When a 6% solution of hydrodextran in isotonic saline solution was autoclaved for two hours at 121° at varying *p*H (6.4–10.4), less acidity and color developed than with dextran.

(4) I. Levi, W. L. Hawkins and H. Hibbert, THIS JOURNAL, **64**, 1959 (1942).

(5) M. Somogyi, *J. Biol. Chem.*, **70**, 599 (1926).

(6) W. A. van Ekenstein and J. J. Blanksma, *Ber.*, **43**, 2355 (1910).

(7) J. Dubourg and A. Lemaitre, *Chimie & Industrie*, **66**, No. 6, 815 (1951); A. Osol-G. E. Farrar, Dispensatory of U. S. of America, Lippincott Co., Philadelphia, 1950, p. 355.

J. T. BAKER CHEMICAL COMPANY MORRIS ZIEF
PHILLIPSBURG, NEW JERSEY JOSEPH R. STEVENS

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BOOK REVIEWS

Die Organischen Fluorverbindungen in Ihrer Bedeutung für die Technik. By GUNTHER SCHIEMANN, Direktor des Instituts fur Technische Chemie der Universität Istanbul, a. o. Professor an der Technischen Hochschule Hannover. Verlag von Dr. Dietrich Steinkopff, (16) Darmstadt, Holzhof-Allee 35, Germany. 1951. xi + 221 pp. 15.5 × 23 cm. Preis brosch. DM 24.-, geb. DM 26.-.

This book, which aims in general to cover the industrial applications of organic fluorine compounds, is divided into three main portions. They are (1) processes of technical interest (118 pp. in 39 short chapters) where the main emphasis has been placed; (2) purely scientific developments (37 pp. in 11 chapters) which have been treated more as a desirable supplement to the first part than as a complete review of existing material; and (3) a rather extensive patent review and bibliography (30 pp. in tabular form). The volume has been prepared by the author in the face of very unusual difficulties. The work was entirely completed and ready for printing in 1943 when the entire project had to be abandoned on account of the war; after which the treatise had to be reconstructed and brought fully up to date (1949) during the confused post-war aftermath. The resulting careful and methodical presentation which is fairly complete, with a minimum of irregularities, but which involved the incorporation of much new material, reflects the author's devotion to his task.

The compounds dealt with in the first part of the book have been classified as (1) aliphatic, (2) alkylaryl (mostly trifluoromethyl derivatives) and (3) aromatic; while under each of these headings the material has been further subdivided into (a) preparative methods, (b) physical properties, and (c) technical applications. The basic preparative methods of industrial or potentially industrial significance which are described include the replacement of chlorine by fluorine using anhydrous hydrogen fluoride with and without catalysts, similar exchanges using tri- and pentavalent antimony compounds, the addition of anhydrous hydrogen fluoride to unsaturates, as well as the use of this compound as a polymerization catalyst or reagent, and the replacement of the aromatic amino group by fluorine using either hydrogen fluoride or the author's well known fluoborate process. The preparation of a large number of more complex fluorine compounds from simpler intermediates by well known synthetic organic routes also has been described. Technical applications for organic fluorine compounds dealt with in this section, include their use as refrigerants such as the Freons (14 pp.), preservatives against decay and inflammability, solvents and selective solvents for separation and purification, dielectrics, unreactive oils and greases as well as plastics by polymerization (for the aliphatics); as dyestuffs carrying the trifluoromethyl group (9 pp.), insulating fluids, antiseptics, and intermediates (for the alkylaryls); and as dyestuffs carrying aromatic fluorine, pharmaceuticals, medicinals, insecticides and preservatives (for the aromatics).

The purpose of the second main division of the volume is to describe supplementary processes and materials of interest from the point of view of research and laboratory practice although not as yet of technical significance, but which on the whole would seem to foreshadow future industrial developments. This section does not purport to deal with