

Cl, 0.481 g., corresponding to the atomic ratio H:B:Cl = 1.98:2.00:4.03. A 0.0995-g. sample gave 0.0131 g. of boron and 0.0878 g. of chlorine, a total of 0.1009 g. The vapor density corresponds to a molecular weight of 163 (calcd., 163.5). The vapor tensions, measured between -63.5 and 22.5° , are satisfactorily reproduced by the equation: $\log P_{(\text{mm.})} = -1753/T + 8.057$.

Liquid tetrachlorodiborine at room temperature for seventy-two hours undergoes 21% decomposition, yielding boron trichloride, a very slightly volatile red substance and a white solid. The latter two must be hitherto unknown boron chlorides of as yet undetermined composition. At 0° the decomposition is much slower.

The following reactions of tetrachlorodiborine have been studied in preliminary fashion. (1) It yields the hitherto unknown *tetrabromodiborine* by treatment with boron tribromide, but does not react with boron trifluoride. (2) With dimethyl or diethyl ether it forms a liquid monoetherate and a solid dietherate. The latter has an appreciable dissociation pressure and is somewhat soluble in the ether. (3) It yields the corresponding tetramethoxy and tetraethoxy derivatives on treatment with the appropriate alcohols. (4) It reacts with lithium borohydride and aluminum borohydride to give boron hydrides among which diborane and dihydrotetraborane (B_4H_{10}) have been definitely identified; pentaboranes and decaboranes are probably present. It does not seem to react with lithium aluminum hydride at 0° . (5) It absorbs hydrogen at room temperature, by which reaction all of the chlorine is converted to boron trichloride, and the residue is a compound or mixture of the approximate composition $BH_{1.37}$ ($B_{10}H_{14}?$). (6) It reacts with ammonia in complex fashion. These and other reactions, as well as the preparative method, will receive further intensive study.

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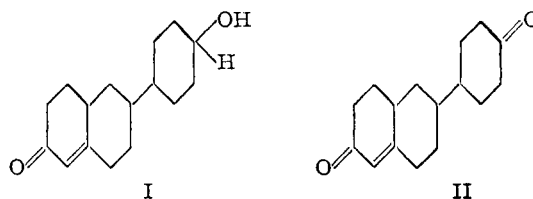
SYNTHESIS OF PHYSIOLOGICALLY ACTIVE ANALOGS OF TESTOSTERONE

Sir:

The discovery of several hundred compounds possessing the physiological activity of the estrogenic hormones has prompted a number of investigators to search for synthetic analogs having activity similar to the other steroid hormones. While some claims of activity for such analogs have been made, particularly in patents, so far as we are aware no such claim has yet been substantiated [*cf.*, for example, the reported androgenic activity for certain reduction products

related to diethylstilbestrol, apparently irrespective of configuration, Schoeller, Inhoffen, Steinruck and Höss, U. S. Patent 2,392,864 (Jan. 15, 1948)].

Since 1941 we have directed efforts toward the synthesis of analogs of the non-aromatic steroid hormones lacking ring C, and wish to report now the synthesis of two such analogs of the androgens: I, comparable to testosterone, and II, to androstenedione.



These α,β -unsaturated ketones were synthesized using the Robinson-Mannich base method [du Feu, McQuillin and Robinson, *J. Chem. Soc.*, 53 (1937)] with some modifications. Hydrogenation of 4,4'-dihydroxybiphenyl gave the three possible perhydro derivatives (m. p.'s $215-216^\circ$, $176.5-177^\circ$ and $194-195^\circ$, all m. p.'s cor.). Half-oxidation of the first two stereoisomers with chromium trioxide afforded the same 4-(4'-hydroxycyclohexyl)-cyclohexanone (III, probably *trans*), m. p. $129-130^\circ$. *Anal.* Calcd. for $C_{12}H_{20}O_2$: C, 73.4; H, 10.3. Found: C, 73.6; H, 10.1. When sufficient 195° diol becomes available, it will presumably lead to the other possible isomer. More complete oxidation gave 4-(4'-ketocyclohexyl)-cyclohexanone (IV), m. p. $115-116^\circ$. *Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.2; H, 9.3. Found: C, 74.3; H, 9.2.

Formylation of the keto alcohol (III) with ethyl formate and sodium methoxide, reaction of the derivative with the methiodide of 1-diethylaminobutanone-3 and cyclization with *ca.* 4% methanolic potassium hydroxide at room temperature gave 6-(4'-hydroxycyclohexyl)- Δ^{1-9} -octalene-2 (I), purified by chromatography on alumina and recrystallization from cyclohexane-ethyl acetate, m. p. $127-127.5^\circ$; max. $238.5 \text{ m}\mu$ ($E_{\text{molar}} = 16,870$). *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 77.4; H, 9.7. Found: C, 77.7; H, 9.8. The semicarbazone melted at $235-236^\circ$ (dec.). *Anal.* Calcd. for $C_{17}H_{27}N_3O_2$: C, 66.9; H, 8.9. Found: C, 67.0; H, 8.7.

Similarly, monoformylation of the diketone (IV), reaction with the Mannich base methiodide and cyclization gave 6-(4'-ketocyclohexyl)- Δ^{1-9} -octalene-2 (II), also obtained in small yield by oxidation of I (as the dibromide), m. p. $88.5-89.5^\circ$; max. $238 \text{ m}\mu$ ($E_{\text{molar}} = 16,400$). *Anal.* Calcd. for $C_{18}H_{22}O_2$: C, 78.0; H, 9.0. Found: C, 77.9; H, 8.7. The disemicarbazone decomposed at $256-257^\circ$. *Anal.* Calcd. for $C_{18}H_{23}N_6O_2$: C, 60.0; H, 7.8. Found: C, 59.9; H, 7.5.

Preliminary assays in day-old chicks, under the direction of Drs. R. K. Meyer and Elva G. Ship-

ley of the Department of Zoology, have indicated androgenic activity for the diketone II at a total dose of 2.5 mg. (26 to 83% increase in comb weight over the controls). A total dose of 0.012 mg. of testosterone propionate resulted in 40% increase. The keto alcohol I has given inconclusive results. Further investigation of physiological effects in other species awaits the preparation of additional material.

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SYNTHESIS OF VITAMIN A

Sir:

The appearance of an article by Schwarzkopf and collaborators¹ on the synthesis of vitamin A by the reduction of vitamin A esters with lithium aluminum hydride prompts us to record experimental work carried out in these laboratories.

Ethyl β -ionylidene acetate² was reduced with lithium aluminum hydride in 85% yield to β -ionylidene ethyl alcohol following the method of Milas and Harrington³ [b. p. 112–114° at 0.4 mm.; $\lambda_{\max}^{\text{isooctane}}$ 2840 Å., $E_1^{1\% \text{cm}}$ 1205]; *trityl ether* (m. p. 132–134°) *anal.* Found: C, 88.13; H, 8.47; $\lambda_{\max}^{\text{isooctane}}$ 2850 Å., $E_1^{1\% \text{cm}}$ 733.

Oxidation of β -ionylidene ethyl alcohol with manganese dioxide by the method used to convert vitamin A to the aldehyde⁴ produced a mixture of two stereoisomeric β -ionylideneacetaldehydes in 60% yield separable by chromatography into essentially equal amounts of *nor*- β -ionylideneacetaldehyde⁵ [b. p. 90–95° at 10⁻² mm.; n_D^{25}

1.5780; $\lambda_{\max}^{\text{isooctane}}$ 2650 Å., $E_1^{1\% \text{cm}}$ 567 and 3150 Å., $E_1^{1\%}$ 760, *anal.* Calcd. for C₁₅H₂₂O: C, 82.57; H 10.09. Found: C, 82.14; H, 10.36. *Semicarbazone*: m. p. 195–196°; $\lambda_{\max}^{\text{chloroform}}$ 3230 Å., $E_1^{1\% \text{cm}}$ 1330; *anal.* Found: C, 69.56; H, 8.82; N, 15.29]⁶ and *iso*- β -ionylidene acetaldehyde⁵ [b. p. 80–85° at 10⁻² mm.; n_D^{25} 1.5780; $\lambda_{\max}^{\text{isooctane}}$ 3180 Å., $E_1^{1\% \text{cm}}$ 904. *Anal.* Found: C, 82.14; H, 10.33. *Semicarbazone*: m. p. 175–176°, $\lambda_{\max}^{\text{chloroform}}$ 3175 Å., $E_1^{1\% \text{cm}}$ 1000. *Anal.* Found: C, 70.16; H, 9.07; N, 15.03]. *nor*- β -ionylideneacetaldehyde was condensed with acetone in the presence of aluminum *t*-butoxide whereby the previously described C₁₈-ketone was obtained⁷ in 80–85% yield; $\lambda_{\max}^{\text{isooctane}}$ 3360 Å.; *semicarbazone*: m. p. 186–188°; $\lambda_{\max}^{\text{chloroform}}$ 3490 Å., $E_1^{1\% \text{cm}}$ 1680. The C₁₈-ketone was converted by the Reformatsky reaction to the C₂₀-hydroxyester which was dehydrated by iodine to vitamin A ester and the latter saponified to vitamin A acid, m. p. 179–180°; $\lambda_{\max}^{\text{ethanol}}$ 3500 Å., $E_1^{1\% \text{cm}}$ 1415. From *iso*- β -ionylideneacetaldehyde there was obtained a more difficultly characterizable C₁₈-ketone exhibiting a broad band at 3340–3370 Å. indicating a mixture of the *nor* and *iso* forms. This ketone afforded vitamin A acid in the same yield as that obtained from the *nor* series (25%); m. p. 180.5–181.5°; $\lambda_{\max}^{\text{ethanol}}$ 3530 Å., $E_1^{1\% \text{cm}}$ 1510; mixed m. p. with acid from *nor* series, 180–181°. Both vitamin A acids on reduction with lithium aluminum hydride gave vitamin A exhibiting a single, well-defined maximum at 3260 Å., $E_1^{1\% \text{cm}}$ 1330 (80% yield) as measured in isooctane.

(6) The β -ionylidenealdehydes semicarbazones prepared by Kuhn and Morris, *Ber.*, **70**, 853 (1937), and by van Dorp and Arens, *Rec. trav. chim.*, **67**, 459 (1948), apparently have the *nor* configuration.

(7) Arens and van Dorp, *Rec. trav. chim.*, **65**, 338 (1946); Heilbron, Jones and O'Sullivan, *J. Chem. Soc.*, 866 (1946); Karrer, Jucker and Schick, *Helv. Chim. Acta*, **29**, 704 (1946).

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NEW BOOKS

Oxidation-Reduction Potentials in Bacteriology and Biochemistry. By L. F. HEWITT, Ph.D., B.Sc., F.R.I. C., Acting Director, Serum Research Institute, Carshalton, Surrey. Fifth Edition. Published by the London County Council, 1948, and may be purchased, either directly or through any Bookseller, from Staples, Ltd., 14, Great Smith Street, Victoria Street, Westminster, S.W.1. 130 pp. 17 × 25 cm. Price, 4s. 6d. By post, 4s. 10d.

The last previous edition of this small monograph was published in 1936. The present fifth edition follows the pattern of earlier ones. The first chapter contains a brief

outline of the theory of oxidation-reduction reactions and the mathematical expressions relating oxidation-reduction potentials to the components of the reactions. The second chapter describes the methods for measuring oxidation-reduction potentials and gives tables of oxidation-reduction indicators. The third chapter deals with oxidation-reduction systems of biological interest. In the fourth chapter, the bacteriological applications of oxidation-reduction studies are described. This fourth chapter is the most important in the monograph, since it constitutes the best review of the work in this particular field—a field to which the author himself has made many contributions. The monograph concludes with two short