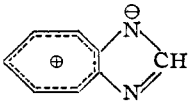
3.85), it seems not to be the bromine substitution product, but rather the bromine addition product.

These reactions indicate the large contribution of the structures of the type shown below for 1,3-diazazulene and the fact can also be explained by the large dipole moment.



We are deeply indebted to Dr. Riko Majima for his unfailing encouragement and to the Ministry of Education of Japan for financial support.

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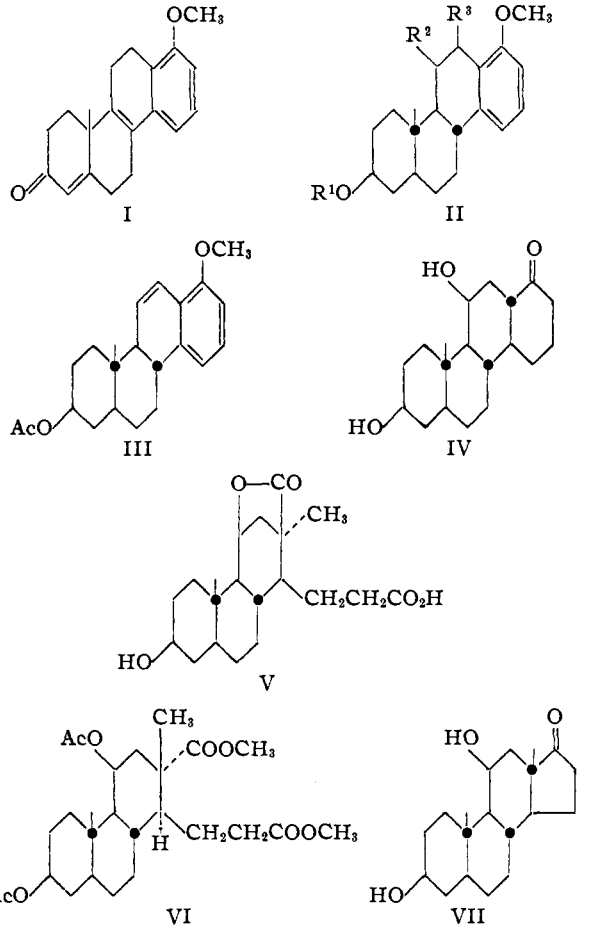
TOTAL SYNTHESIS OF AN 11-OXYGENATED STEROID

Sir:

We announce hereby the total synthesis of 3β,11β-dihydroxyandrostane-17-one (VII), a substance which has been isolated from beef adrenal glands[1] and has recently been found in human urine as a metabolite of compound "F."[2]

We have obtained *dl*-VII from the readily available tetracyclic ketone I, the conversion of which to *dl*-epiandrosterone has already been described.[3] Reduction of I with lithium[4] and alcohol (10%) in ammonia yielded the tetrahydro carbinol II (R^1 = R^2 = R^3 = H) isolated as the acetate II (R^1 = Ac, R^2 = R^3 = H), m.p. 151.3–152.3° (C, 76.8; H, 8.82), which upon treatment with lead tetraacetate in acetic acid was converted in good yield to the 12-acetoxy compound II (R^1 = Ac, R^2 = H, R^3 = OAc),[5] m.p. 206–212° (dec.) (C, 71.9; H, 8.04). On warming in acetic acid the 12-acetoxy group was readily eliminated[5] affording the 11,12-olefin III, m.p. 157.2–159° (C, 77.4; H, 8.36). Hydroxylation of the olefinic bond with peracid[6] (preferably performic acid) yielded a mixture of esters of stereoisomeric triols II (R^1 = H, R^2 = R^3 = OH) from which homogeneous components have been isolated, but which could be reduced directly by vigorous treatment with lithium and alcohol (40%) in ammonia[3] to simultaneously hydrogenolyze the substituent at C_{12}[7] and reduce the aromatic nucleus. After acid hydrolysis of the enol ether, a mixture of the 13,14- and 16,17-dehydroketones—IV(C=C at 13,14), m.p. 276–277°, λ_{max} 248 mμ (log ε 4.14) (C, 74.8; H, 9.52); and IV (C=C at 16,17), diacetate, m.p. 204–205°, λ_{max} 224.7 mμ (log ε 3.94) (C 71.1; H, 8.23)—crystallized readily in good yield. As in the 11-desoxy series[3] this mixture on hydrogenation over palladium in the presence of a trace of potassium hydroxide gave a single product, *dl*-3β,11β-dihydroxy-D-homo-18-nor-androstane-17a-one (IV), m.p. 256–257° (C, 74.3; H, 9.92).



The remaining steps were similar to those employed in the 11-desoxy series.[3] Conversion of IV to the fufurylidene derivative (diacetate, m.p. 246–248°, C, 71.6; H, 7.73) followed by methylation and acetylation gave *dl*-3β,11β-diacetoxy-17-furfurylidene-D-homoandrostane-17a-one, m.p. 256–258° (C, 72.5; H, 8.02) along with the 13-iso (preponderant) compound, m.p. 242–243° (C, 72.0; H, 7.68). These angularly methylated C_{13} epimers were ozonized, and the resulting dibasic acids esterified with diazomethane to give respectively *dl*-dimethyl 3β,11β-diacetoxyetioallohomobilianate (VI), m.p. 131.5–133° (C, 64.7; H, 8.12) and the 13-iso compound, m.p. 143.5–144.5° (C, 65.3; H, 8.56). The infrared spectrum of the former epimer was identical with that of authentic *d*-diester (oil, C, 65.3; H, 8.30), which was prepared by opening ring D[8] of *d*-VII produced from *allo*preg-

(1) T. Reichstein and J. Von Euw, *Helv. Chim. Acta*, **21**, 1197 (1938); **24**, 879 (1941).

(2) A. D. Kemp, A. Kappas, I. I. Salamon, F. Herling and T. F. Gallagher, *J. Biol. Chem.*, in press.

(3) W. S. Johnson, B. Bannister, B. M. Bloom, A. D. Kemp, R. Pappo, E. R. Rogier and J. Szmuszkovicz, THIS JOURNAL, **75**, 2275 (1953).

(4) *Cf.* A. L. Wilds and N. A. Nelson, *ibid.*, **75**, 5360 (1953).

(5) *Cf.* The acetoxylation and elimination reactions in a model series, W. S. Johnson, J. M. Anderson and W. E. Shelberg, THIS JOURNAL, **66**, 218 (1944).

(6) We are deeply indebted to Professor Gilbert Stork of Columbia University for encouraging us to exploit and helping us to properly apply this scheme for introducing the 11-oxygen via the 11,12-olefin. We wish to thank him particularly for giving us abundant unpublished information from his laboratory on methods of oxidizing the methoxydihydronaphthalene system.

(7) Under the milder (10% alcohol) conditions reduction stops at this stage affording after acetylation II (R^1 = Ac, R^2 = OAc, R^3 = H), m.p. 197.5–199° (C, 72.1; H, 8.14).

(8) By the method used in the estrone series, W. S. Johnson, D. K. Bannerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg and L. J. Chinn, THIS JOURNAL, **74**, 2832 (1952).

nan-3β,11β,17α,21-tetraol-20-one (Reichstein's substance V).[9]

Cyclization of the *dl*-diesters with potassium *t*-butoxide, followed by hydrolysis and decarboxylation, accomplished by heating with aqueous dioxane at 200–210°, gave after saponification *dl*-3β,11β-dihydroxyandrostane-17-one (VII), m.p. 249–251.5° (C, 74.4; H, 9.61), and the 13-iso compound, m.p. 216–217° (C, 74.3; H, 9.73). The diacetate of the former isomer melted at 217–217.5° (C, 70.7; H, 8.97) and had a characteristic infrared spectrum which was identical with that of authentic *d*-VII diacetate, m.p. 153.5–155°.[10,11]

It is noteworthy that when the acidic product from the ozonization in the 13-iso series was saponified to remove the acetate residues, and then isolated in the usual manner by acidification, the product was a lactonic acid, m.p. 264–266° (C, 68.4; H, 8.83; neut. equiv., 358), λ_{max}^{Nujol} 2.92 μ, 5.73 μ, 5.88 μ. The 5.73 μ band is indicative of a γ-lactone, and the compound is therefore represented by formula V. Since there is no doubt about the configuration at C_{13} in this compound, the formation of this lactone establishes unequivocally that the hydroxyl group at C_{11} is in the β-configuration. This observation coupled with the relationship of the C_{13} epimeric series to the natural steroids, thus constitutes conclusive confirmation of the C_{11} configuration of the natural 11-hydroxy steroids.

We are deeply grateful to the Research Committee of the Graduate School of the University of Wisconsin and to the Sterling-Winthrop Research Institute for generously supporting this program. We are also indebted to these agencies as well as to Merck and Co., Inc., for aiding the work in the 11-desoxy series.[3]

(9) We are indebted to Dr. G. Rosenkranz of Syntex, S. A., for supplying us with this substance and for providing us with unpublished details for its oxidation with sodium bismuthate.

(10) M. Steiger and T. Reichstein, *Helv. Chim. Acta*, **20**, 817 (1937).

(11) We wish to thank Dr. Max Tishler of Merck and Co., Inc., for supplying us with 17α-hydroxycorticosterone from which this product was prepared.

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1,2,3,4-TETRAPHENYLFULVALENE

Sir:

Recent theoretical calculations[1,2,3,4] predicting the properties of the hitherto non-existent fulvalene hydrocarbons has stimulated interest in their synthesis. It is the purpose of this Communication to report the synthesis of the first non-fused ring fulvalene, 1,2,3,4-tetraphenylfulvalene (I).

The addition of cyclopentadienylmagnesium bromide[5] to tetracyclone in a mixture of ethyl ether and benzene afforded 74% of the almost colorless 1-cyclopentadienyltetraphenylcyclopentadiene-1-ol (II), m.p. 197.6–198.6°. Calcd. for $C_{34}H_{26}O$: C, 90.63; H, 5.82. Found: C, 90.43; H, 6.00 (λ_{max} 242 mμ, log ϵ 4.45; λ_{max} 337 mμ, log ϵ 3.85 in methanol). The infrared showed a band at 2.83 microns, but none in the region 5.6–6.1 microns indicating the presence of an hydroxyl group, no carbonyl, and thus that 1,2-addition, and not 1,4-addition, had taken place.

In refluxing bromobenzene II gave a colorless maleic anhydride adduct (III), m.p. 251–252.5° (dec.). Calcd. for $C_{38}H_{28}O_4$: C, 83.2; H, 5.1. Found: C, 82.9; H, 5.4 (λ_{max} 223 mμ, log ϵ 4.43; λ_{max} 265 mμ, log ϵ 4.08). Strong bands at 5.42 and 5.65 microns are characteristic of the anhydride ring, band at 2.90 microns indicates the hydroxyl group.

Dehydration of II was effected with iodine in boiling benzene to give the brilliant orange-red I in 27% yield, m.p. 201–202°. Calcd. for $C_{34}H_{24}$: C, 94.41; H, 5.59. Found: C, 94.04; H, 5.51 (λ_{max} 278 mμ, log ϵ 4.34; $\lambda_{infl.}$ 320, log ϵ 3.07; λ_{max} 415 mμ, log ϵ 2.95). No hydroxyl band is present in the infrared.

When III was heated at 275° for 10 minutes 98% of the theoretical quantity of water is eliminated. The red product (IV), obtained in 20% yield, melts at 177–181°. Calcd. for $C_{38}H_{26}O_3$: C, 86.01, H, 4.94. Found: C, 85.93; H, 4.6 (λ_{max} 240 mμ, log ϵ 4.37; $\lambda_{infl.}$ 315 mμ, log ϵ 3.91; $\lambda_{infl.}$ 415 mμ, log ϵ 2.93). There was no band at 2.90 microns; the bands at 5.42 and 5.65 microns were still present. This anhydride did not depress the melting point of the maleic anhydride adduct from I in boiling toluene in 40% yield, m.p. 178–179° (m.m.p. 178–181°). The red color of the maleic anhydride adduct indicates that the phenylated fulvene system is intact in the molecule since non-phenylated fulvenes are yellow. Thus, maleic anhydride must add to the unsubstituted C-5 ring in both I and II.

The authors express their appreciation to Charles Pfizer Co., Inc., in whose laboratories this work was done, for their encouragement.

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RECEIVED MAY 13, 1954

THIOESTERASES FOR ACYL AND AMINOACYL MERCAPTANS[1]

Sir:

The recognition of the function of acyl mercaptans in biosynthetic processes[2] suggests a possible role of substituted or unsubstituted α-aminoacyl mercaptans as intermediates in peptide synthesis.[3,4,5] Such a concept would be supported by the occurrence of hydrolyzing and/or transferring thioesterases with a specificity directed toward the amino acid portion of the thioester. We wish to report on the presence in ox brain cortex and liver of a group of thioesterases able to catalyze the hydroly-

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(2) B. Pullman and G. Berthier, *Compt. rend.*, **229**, 717 (1949).

(3) G. Berthier, M. Mayot and B. Pullman, *J. phys. radium*, **12**, 717 (1951).

(4) A. Pullman and B. Pullman, *Disc. Faraday Soc.*, 46–52 (1950).

(5) E. D. Bergmann, G. Berthier, D. Ginsburg, Y. Hirshberg, D. Lavie, S. Pinchas, B. Pullman and A. Pullman (*Bull. soc. chim. France*, 661 (1951) have reported that cyclopentadienyllithium gives no well-defined product.

(1) This work was supported in part by grants from the National Institute of Neurological Disease and Blindness (Grant B-226) of the National Institutes of Health, Public Health Service, and by a contract between the Office of Naval Research and the Psychiatric Institute.

(2) F. Lynen, E. Reichert and L. Rueff, *Ann.*, **574**, 1 (1951).

(3) T. Wieland, W. Schafer and E. Bokelmann, *ibid.*, **573**, 99 (1951).

(4) H. Waelsch, *Adv. in Enzymol.*, **13**, 237 (1952).

(5) H. J. Strecker, "Glutathione Symposium," Academic Press, N. Y., 1954, in press.