converted to cholesterol by way of 2-carbon intermediates.

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THE STRUCTURE OF THE ANTIBIOTIC MYCOMYCIN

Sir:

We have deduced the structure of the highly unstable antibiotic mycomycin[1] as 3,5,7,8-tridecatetraene-10,12-diynoic acid (I).

$$HC{\equiv}C{-}C{\equiv}CH{=}C{=}CHCH{=}CH{-}CH{=}CHCH_2CO_2H$$

Mycomycin undergoes an unusual rearrangement in normal aqueous potassium hydroxide at 27° involving an allene to acetylene isomerization accompanied by migration of existing acetylenic bonds. The rearranged acid, isomycomycin, has been assigned the structure 3,5-tridecadiene-7,9,11-triynoic acid (II).

$$CH_3{-}C{\equiv}C{-}C{\equiv}C{-}C{\equiv}C{-}CH{=}CH{-}CH{=}CH{-}CH_2{-}CO_2H$$

I crystallizes in colorless needles from methylene chloride at −40°; m.p. 75° (dec. explosively) and $[\alpha]^{25}D$ −130° (*c*, 0.4, ethanol). (*Anal.* Calcd. for $C_{13}H_{10}O_2$: C, 78.76; H, 5.08; one C-methyl, 7.6; neut. equiv., 198; Found: C, 78.17; H, 5.36; C-methyl (Kuhn–Roth), 0.48; neut. equiv., 200). Ultraviolet absorption in diethyl ether: $\lambda^{m\mu}_{infl.}$ 256, ϵ 35,000; $\lambda^{m\mu}_{max.}$ 267, ϵ 61,000; $\lambda^{m\mu}_{max.}$ 281, ϵ 67,000.

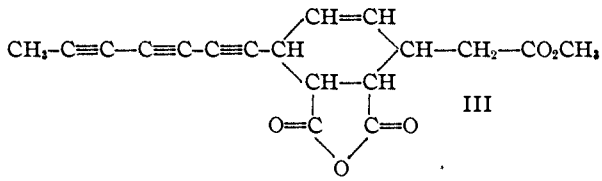
II crystallizes in colorless needles from ether–hexane, decomposes slowly above 140° and is optically inactive. (*Anal.* Found: C, 78.87; H, 5.43; C-methyl (Kuhn–Roth), 9.6; neut. equiv., 198). Ultraviolet absorption in diethyl ether: $\lambda^{m\mu}_{infl.}$ 246, ϵ 24,000; $\lambda^{m\mu}_{max.}$ 257.5, ϵ 58,000; $\lambda^{m\mu}_{max.}$ 267, ϵ 110,000; $\lambda^{m\mu}_{max.}$ 287.5, ϵ 14,000; $\lambda^{m\mu}_{max.}$ 305.5, ϵ 27,000; $\lambda^{m\mu}_{max.}$ 324, ϵ 41,000; $\lambda^{m\mu}_{max.}$ 347, ϵ 34,000.

Complete hydrogenation of I and II requires eight moles of hydrogen, quantitatively yielding *n*-tridecanoic acid, unequivocally identified by comparisons with an authentic sample.[2]

The infrared spectrum of I in dioxane has characteristic bands near 3180, 2200, 1930 and 1730 cm.$^{-1}$ attributed to ≡C—H, disubstituted —C≡C—, —CH=C=CH— and unconjugated —CO_2H[2a] functions, respectively. I reacts with acetylenic hydrogen reagents such as alcoholic silver nitrate. In view of the linear nature of the reduction product, the high order of optical activity of I can only be reconciled with its allenic function. The fine structure spacing ($\Delta\nu'$, 1900 cm.$^{-1}$) of the ultraviolet absorption maxima of I gives evidence that the two recognized acetylenic bonds are in conjugation.[3] The remaining two units of unsaturation are believed to be a conjugated diene, conjugated with the allenic group but not with the carboxyl group.

The location of the observed long wave length ultraviolet absorption maximum of I at 281 mμ limits the length of contributing conjugated multiple bonds to three units, part of which may be acetylenic.[4] The allene bond in the proposed 7,8-position of I performs a unique chromophoric role whereby the Δ^7 bond and the Δ^8 bond are conjugated with the 3,5-diene and 10,12-diyne, respectively, while the central carbon atom of the allene serves as an electronic insulator between the two resulting conjugated systems.[5] The two effectively isolated chromophores, each totaling three units of conjugation, explain the observed general light absorption zone of I.

The infrared spectrum of II in dioxane exhibits characteristic bands at 2200 cm.$^{-1}$ and 1730 cm.$^{-1}$ attributed to disubstituted —C≡C— and unconjugated —CO_2H,[2a] respectively. Monosubstituted acetylenic and allenic bands are absent. II analyzes for one C-methyl group, whereas I possesses none. II does not react with alcoholic silver nitrate, substantiating the absence of a ≡C—H function. The ultraviolet light absorption properties of II prove to be very similar to those recorded for compounds containing a conjugated dienetriyne grouping.[6,7] II reacts with ethereal diazomethane to form a methyl ester, crystallized from ether–hexane as colorless needles, m.p. 69–70°. A Diels–Alder reaction of the methyl ester of II with maleic anhydride gives a monoaddition product (III), crystallized from acetone–hexane as colorless plates, m.p. 177–178° (dec.). (*Anal.* Calcd. for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55; CH_3O, 10.00. Found: C, 69.59; H, 4.64; CH_3O, 10.89.) Ultraviolet light absorption in methanol: $\lambda^{m\mu}_{infl.}$ 215, ϵ 82,000; $\lambda^{m\mu}_{max.}$ 272.5, ϵ 450; $\lambda^{m\mu}_{max.}$ 289, ϵ 430; $\lambda^{m\mu}_{max.}$ 310, ϵ 170. These light absorption properties of III



III

bear striking resemblance to the unique light absorption behavior of the conjugated triacetylene grouping when it is the sole contributing chromo-

(1) E. A. Johnson and K. L. Burdon, *J. Bact.*, **54**, 281 (1947).

(2) Obtained through the courtesy of Dr. H. J. Harwood of Armour and Company.

(2a) In a comparison of infrared spectra determined in dioxane solution, the location of the C=O stretching frequency exhibited by I and II near 1730 cm.$^{-1}$ is the same as the corresponding band of their respective perhydro derivatives and authentic *n*-tridecanoic acid. If I and/or II contained a conjugated carboxyl group, this band would be expected to occur at a measurably lower frequency than the corresponding saturated derivative.

(3) T. Brunn, C. J. Haug and N. A. Sorensen, *Acta Chem. Scand.*, **4**, 850 (1950).

(4) I. M. Heilbron, E. R. H. Jones and R. A. Raphael, *J. Chem. Soc.*, 268 (1943); I. M. Heilbron, E. R. H. Jones and F. Sondheimer, *ibid.*, 1586 (1947).

(5) In a somewhat analogous situation, the ultraviolet light absorption of tetraphenylallene ($\lambda^{m\mu}_{max.}$ 267, ϵ 12,000) corresponds to that of 1,1-diphenylethylene ($\lambda^{m\mu}_{max.}$ 250, ϵ 11,000) and not to *trans,trans*-diphenyl-1,3-butadiene ($\lambda^{m\mu}_{max.}$ 328, ϵ 56,000).

(6) K. Stavholt and N. A. Sorensen, *Acta Chem. Scand.*, **4**, 1567 (1950).

(7) E. R. H. Jones, M. C. Whiting, J. B. Armitage, C. L. Cook and N. Entwistle, *Nature*, **168**, 900 (1951).

phore.[8,9] More detailed accounts of the above structural considerations will appear in subsequent publications.

(8) F. Bohlmann, *Chem. Ber.*, **84**, 785 (1951).
(9) E. R. H. Jones, personal communication.

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HYPOTENSIVE ALKALOIDS OF VERATRUM ESCHSCHOLTZII

Sirs:

In view of the present interest in the Veratrum Alkaloids as hypotensive agents, we wish to report the isolation from *Veratrum eschscholtzii Gray* of neogermitrine,[1] and a new alkaloid, for which we propose the name escholerine.

Preliminary fractionation of a crude chloroform extract which was based on the selective solubilities of the alkaloids and their salts, in conjunction with assays[2] for hypotensive activity in anesthetized dogs, yielded an amorphous fraction that accounted for the major part of the hypotensive activity in the crude extract. Further fractionation by two 8-plate Craig countercurrent distributions[3] yielded two fractions, A and B, each with a high hypotensive activity. Fraction A was resolved on a 24-plate distribution using 2 *M* acetate buffer at *p*H 5.5 and benzene as the solvent system. Neogermitrine was obtained from the material recovered from tubes 8 to 13 by crystallizing from acetone–water (m.p. 234–234.8 (cor.)); $[\alpha]^{25}D$ −79 ± 2°, (*c* 0.9 in pyridine); the sample was further identified by comparison of its infrared spectrum, and by a mixed melting point with an authentic sample of neogermitrine from *Veratrum viride Aiton* kindly provided by Dr. J. Fried.

Fraction B was distributed on a 24-plate Craig apparatus, using 0.5 *M* acetate buffer *p*H 5.0 and benzene–cyclohexane 25:75 as the immiscible phases. The material recovered from tubes 8 to 13, when crystallized from acetone–water, yielded escholerine (m.p. 235–235.3 with dec. (cor.); $[\alpha]^{25}D$ −30 ± 2° (*c* 1.0 in py.); +7 ± 2° (*c* 1.0 in $CHCl_3$)). The analytical data indicate the empirical formula $C_{41}H_{61}O_{13}N$; (calcd. C, 63.46; H, 7.92; N, 1.80; eq. wt., 775.9; found: C, 63.42, 63.59; H, 8.00, 7.97; N, 2.04; eq. wt., 782, 772; picrate, m.p. 259.5° (dec.), $(C_{41}H_{61}O_{13}N \cdot HOC_6H_2(NO_2)_3$: C, 56.17; H, 6.42; found: C, 56.41; H, 6.38); aurichloride, m.p. 191.4° (frothing), $(C_{41}H_{61}O_{13}N \cdot HAuCl_4$. C, 44.13; H, 5.60; Au, 17.67; found: C, 44.53; H, 5.61; Au, 17.21). Volatile acid determination, found: 3.7 equivalents of acid.

Hydrolysis of escholerine with 0.1 *N* methanolic potassium hydroxide afforded acetic acid, α-methylbutyric acid and a base that has so far resisted all attempts at crystallization. A mixture of the *p*-phenylphenacyl esters of the acids after chromatography on a silicic acid[4] column, yielded *p*-phenylphenacyl acetate, m.p. 110.8–111.2° (calcd. C, 75.58; H, 5.55; found, C, 75.38; H, 5.66) and *p*-phenylphenacyl α-methylbutyrate, m.p. 70–71° cor. (calcd. C, 77.01; H, 6.80; Found: C, 76.61; H, 6.80).

The hypotensive activity[5] of neogermitrine and escholerine in anesthetized dogs was found to be 0.13 μg. [0.12–0.15] and 0.30 μg. [0.26–0.36], respectively.

The isolation procedure has, in addition, yielded the alkaloids isorubijervine, jervine, rubijervine, pseudojervine and veratramine, already known as constituents of *Veratrum viride*, and small amounts of four apparently new crystalline alkamines and a new ester alkaloid which will be described more fully in a subsequent publication.

(1) J. Fried and P. Numerof, Abst. 119th meeting A.C.S., Cleveland, Ohio, April, 1951, 12L.
(2) Assays were run according to the method of G. L. Maison and J. W. Stutzman, *Arch. Int. Pharmacodyn.*, **85**, 357 (1951). Evaluations were made at Boston University School of Medicine, Boston, Mass.
(3) J. Fried, H. White and O. Wintersteiner, THIS JOURNAL, **72**, 4621–4630 (1950).
(4) J. G. Kurchner, Arthur H. Prater and A. J. Haagen-Smit, *Ind. Eng. Chem., Anal. Ed.*, **18**, 31 (1946).
(5) Expressed as micrograms per kilogram of dog per minute required for a ten minute intravenous infusion to lower the mean arterial blood pressure 30% when administered according to the method of G. L. Maison and J. W. Stutzman.[2] The bracketed numbers express the 95% confidence limits.

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MICROBIOLOGICAL OXYGENATION OF STEROIDS AT CARBON 11

Sir:

It is generally acknowledged that the most difficult series of steps in the partial synthesis of cortisone is that concerned with the introduction of oxygen at carbon 11 of the steroid nucleus.[1,2,3,4] We wish to report the oxygenation of steroids, *e.g.*, progesterone, at carbon 11 in a single step by means of common molds of the order *Mucorales* after a transformation period of 24–48 hours, in a lactalbumin digest–dextrose–cornsteep medium. Thus, from progesterone, a new 11-oxygenated steroid intermediate is made available for conversion to the cortical hormones. In these studies we have made use of the procedure of Zaffaroni, *et al.*,[5] for characterization of the transformation products.

The ability of several micro-organisms to oxidize a hydroxyl group or reduce a ketone group in a steroid is well recognized,[6] but heretofore the only microbiological oxygenation of a steroid carbon atom was reported by Krámli and Horváth[7] in the

(1) B. F. McKenzie, V. R. Mattox, L. L. Engel and E. C. Kendall, *J. Biol. Chem.*, **173**, 271 (1948).
(2) E. M. Chamberlain, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita and Max Tishler, THIS JOURNAL, **73**, 2396 (1951).
(3) L. F. Fieser, J. E. Herz and Wei-Yuan Huang, *ibid.*, **73**, 2397 (1951).
(4) G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3546 (1951).
(5) A. Zaffaroni, R. B. Burton and E. H. Keutmann, *Science*, **111**, 6 (1950).
(6) M. Welsch and C. Heusghem, *Compt. rend. soc. biol.*, **142**, 1074–1076 (1948).
(7) A. Krámli and J. Horváth, *Nature*, **160**, 639 (1947); **163**, 219 (1949).