to III and is assigned the structure IX. Copper-catalyzed decomposition of V in cyclohexene at 130° gave VII (43%); no evidence for the formation of a norcarane derivative could be obtained. Copper-catalyzed decomposition of I in either ethanol or cyclohexene gave II (91 and 94%, respectively).

We consider that these results are best interpreted in the following manner. In the decomposition of diazoisofenchone, a carbene (or carbene-copper complex[9]) is formed which in benzene or cyclohexene rearranges to VII by concerted migration of the *endo* C_5 methyl group and C_3-C_5 bond formation; in ethanol, reaction of the carbene with the solvent takes precedence over its rearrangement, giving IX. In the decomposition of diazocamphor, loss of nitrogen may be concerted with 1,3-hydrogen migration and C_3–C_5 bond formation, giving II directly.[10]

On this view, the migration of the methyl group in the formation of VII may be classed as intermediate between a 1,2 and 1,3 alkyl shift. The formation of VII from the carbene may equivalently be viewed as an insertion reaction of the carbene at the *endo* C_5–CH_3 bond. No simple insertion reactions of carbenes at carbon–carbon single bonds have been described,[11] although certain other rearrangement reactions of carbenes may be viewed as proceeding in this fashion.[12]

(9) P. Yates, *J. Am. Chem. Soc.*, **74**, 5376 (1952).

(10) W. Reusch, M. W. DiCarlo and L. Traynor, *J. Org. Chem.*, **26**, 1711 (1961), have shown that the related transformation of camphor hydrazone to tricyclene proceeds *via* intramolecular hydrogen transfer.

(11) *Cf.*, however, W. von E. Doering and M. Jones, unpublished work referred to by W. Kirmse, *Angew. Chem.*, **73**, 161 (1961).

(12) *Cf.* L. Friedman and H. Schechter, *J. Am. Chem. Soc.*, **83**, 3159 (1961); M. S. Newman and A. Arkell, *J. Org. Chem.*, **24**, 385 (1959).

(13) Department of Chemistry, University of Toronto, Toronto, Canada.

DEPARTMENT OF CHEMISTRY
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS

PETER YATES[13]
SAMUEL DANISHEFSKY

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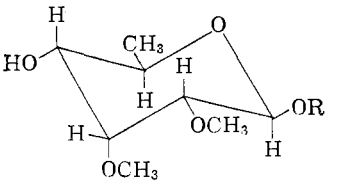
CHEMISTRY OF MYCINOSE: 6-DEOXY-2,3-DI-O-METHYL-D-ALLOSE

Sir:

Methanolysis of chalcomycin[1] yields methyl chalcoside[2] and methyl mycinoside I, m.p. 88–88.5°, $[\alpha]^{27}D$ −36° (*c* 1.6%, chloroform) [*Anal.* Calcd. for $C_9H_{18}O_5$: C, 52.41; H, 8.80; O, 38.79; OCH_3(3), 45.1; C-CH_3(1), 7.3. Found: C, 52.38; H, 8.80; O, 39.07; OCH_3, 45.2; C-CH_3, 8.13].

Aqueous hydrolysis of I gives crystalline mycinose II, m.p. 102–106° $[\alpha]^{25}D$ −46° → −42° (2 min.) → −36° (30 min.) → −29° (4 hr. and 24 hr.) (*c* 1.56%, water) [*Anal.* Calcd. for $C_8H_{16}O_5$: C, 49.99; H, 8.39; OCH_3(2), 32.29; C-CH_3(1), 7.82. Found: C, 49.94; H, 8.73; OCH_3, 31.98; C-CH_3, 7.42].

Mycinose is oxidized with bromine water to give a crystalline lactone, m.p. 134–135°, which



I, R = CH_3
II, R = H

exhibits no maximum in the ultraviolet and shows sharp bands at 2.90 and 5.68 μ in the infrared spectrum. [*Anal.* Calcd. for $C_8H_{14}O_5$: C, 50.52; H, 7.42; OCH_3(2), 32.63; C-CH_3(1), 7.90; mol. wt., 190.19. Found: C, 50.36; H, 7.69; OCH_3, 32.24; C-CH_3, 7.72; mol. wt. (by titration), 182.] Mycinose gives a positive iodoform test, reduces Fehling solution, and yields a pinkish-brown color with aniline hydrogen phthalate on papergrams; it does not reduce periodate, but the sodium borohydride reduction product takes up one mole to give acetaldehyde (0.75 mole as the 2,4-DNP) and a tetrose which was subsequently oxidized with nitric acid to give *meso*-dimethoxysuccinic acid, m.p. 162–163° [*Anal.* Calcd. for $C_6H_{10}O_6$: C, 40.45; H, 5.66; neut. equiv., 89.07. Found: C, 40.25; H, 5.83; neut. equiv., 91] which was identical with a synthetic sample (mixed m.p., R_f values, infrared spectrum). These data establish the structure of mycinose as a 6-deoxy-2,3-di-O-methylhexose.

Treatment of I with boron trichloride[3] for ten days at 4° and subsequent aqueous acid hydrolysis of the reaction product yields a crystalline sugar, m.p. 146–148°, $[\alpha]^{23}D$ −4.7° (7 min.) → 0° (40 min. and 3 hr.) (*c* 3%, water) [*Anal.* Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 44.18; H, 7.60], which was compared with a sample of 6-deoxy-β-D-allose prepared from digitoxin[4] and found to be identical (mixed m.p., paper chromatography and paper electrophoresis,[5] infrared spectrum, X-ray powder diagram). The phenylosazones[4] (m.p. 180–183°, $[\alpha]^{23}D$ −72° [*c* 0.6%, pyridine–ethanol 2:3]) of the above two sugar samples were also identical.

Exhaustive methylation of I with methyl iodide and silver oxide, then nitric acid oxidation, esterification with methanol in the presence of hydrogen chloride, and finally treatment with methylamine, gives *ribo*-2,3,4-trimethoxy-N,N′-dimethylglutaramide,[6] m.p. 147–147.5°, $[\alpha]^{25}D$ 0° (*c* 2%, chloroform) [*Anal.* Calcd. for $C_{10}H_{20}O_5N_2$: C, 48.37; H, 8.12; N, 11.28. Found: C, 48.47; H, 8.18; N, 11.50]. Thus, from the above, methyl mycinoside must be in the pyranose form as in I. Partial methylation of mycinose with methyl iodide and silver oxide gives I. Thus, mycinose probably exists in the pyranose form[7] as in II.

(1) Parke, Davis & Company, Belgian Patent 587,213, August 2, 1960.

(2) P. W. K. Woo, H. W. Dion and Q. R. Bartz, *J. Am. Chem. Soc.*, **83**, 3352 (1961).

(3) S. Allen, T. G. Bonner, E. J. Bourne and N. M. Saville, *Chem. & Ind.*, 630 (1958).

(4) F. Micheel, *Ber.*, **63**, 347 (1930).

(5) A. P. MacLennan and H. M. Randall, *Anal. Chem.*, **31**, 2020 (1959).

(6) P. A. Levene and J. Compton, *J. Biol. Chem.*, **116**, 183 (1936).

(7) N.m.r. spectroscopy shows that mycinose does not mutarotate in chloroform until acid is added. It is therefore reasonable to assume that, under the methylation conditions in methyl iodide, it also does not mutarotate.

The n.m.r spectra of I and II exhibit axial–axial splitting for H_1 and H_2 (I, $J_{1a,2a}$ = 7.6 cps.; II, $J_{1a,2a}$ = 8.6 cps.). The resulting absolute configuration at C-1, as indicated in II, agrees with that predicted, according to Hudson's rules, for a sugar in the D-series which mutarotates to a more positive value (*i.e.*, a β-D sugar).[8]

Thus, the second sugar obtained as a degradation product of chalcomycin has been isolated as 6-deoxy-2,3-di-O-methyl-β-D-allose.

(8) C. S. Hudson, "Advances in Carbohydrate Chem.," **3**, 15 (1948).

RESEARCH DIVISION
PARKE, DAVIS & COMPANY
DETROIT 32, MICHIGAN

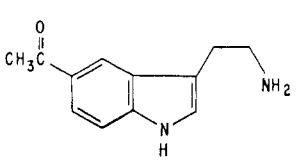
HENRY W. DION
PETER W. K. WOO
QUENTIN R. BARTZ

RECEIVED DECEMBER 22, 1961

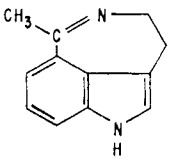
ACYLTRYPTAMINES. I. 5-ACETYLTRYPTAMINE AND RELATED COMPOUNDS

Sir:

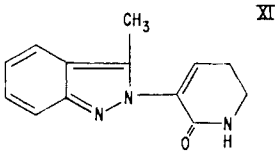
The interest in 5-hydroxytryptamine (serotonin) and the total synthesis of reserpine has resulted in the preparation of a multiplicity of tryptamines for use in biological and synthetic investigations. The results of our efforts in another field led to our preparation of a series of novel tryptamines having acyl groups in the benzene ring. The discovery of the unusual hypotensive[1] properties of 5-acetyltryptamine (I) and some interesting chemical transformations during this extensive synthetic program has prompted us to publish some of our findings at this time.



I



XI



XIII

The Japp-Klingemann reaction of *p*-acetylbenzenediazonium chloride with 2-oxopiperidine-3-carboxylic acid[2] gave the corresponding 3-(*p*-acetylphenyl)hydrazone of 2,3-piperidinedione (II, m.p. 229–231°, λ_{max}^{EtOH} 238 mμ, ε 10,800, 351 mμ, ε 42,000. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.66; H, 6.16; N, 17.13. Found: C, 63.40; H, 6.28; N, 16.93). Refluxing II with 88% formic acid for four hours gave 6-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]-indol-1-one (III; m.p. 370–372°, λ_{max}^{EtOH} 273 mμ, ε 42,250, 302 mμ, ε 8,800. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.27. Found: C, 68.35; H, 5.33; N, 12.08). Hydrolysis[3] of III in refluxing 2 *N* KOH in 60% aqueous ethanol gave 5-acetyl-2-carboxytryptamine (IV, m.p. 337–343°, λ_{max}^{EtOH} 266.5 mμ, ε 47,000, 303 mμ, ε 8,000. Calcd. for $C_{13}H_{14}N_2O_3 \cdot H_2O$: C, 59.08; H, 6.10; N, 10.60. Found: C, 59.04; H, 6.18; N, 10.77). Decarboxylation of IV in refluxing 20% hydrochloric acid containing 30% by volume glacial acetic acid gave 5-acetyltryptamine (I, m.p. 140–142°, λ_{max}^{EtOH} 254 mμ, ε 34,400, 299 mμ, ε 7,850. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 70.99; H, 6.93; N, 14.09).

Reaction of *m*-acetylbenzenediazonium chloride with 2-oxopiperidine-3-carboxylic acid gave the 3-(*m*-acetylphenyl)hydrazone of 2,3-piperidinedione (V, m.p. 204–206°, λ_{max}^{EtOH} 233 mμ, ε 19,500, 312.5 mμ, ε 21,200. Calcd. for $C_{13}H_{15}N_3O_2 \cdot 0.5H_2O$: C, 61.40; H, 6.34; N, 16.53. Found: C, 61.58; H, 6.59; N, 16.87). Refluxing V with 88% formic acid gave a mixture of 5-acetyl and 7-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-ones which were separated by fractional crystallization from absolute ethanol. The less soluble 7-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one (VI) had the m.p. 283–286°, λ_{max}^{EtOH} 248 mμ, ε 27,100, 315 mμ, ε 23,700. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.27. Found: C, 68.30; H, 5.38; N, 12.45. The more soluble 5-acetyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-1-one (VII) had the m.p. 241–243°, λ_{max}^{EtOH} 223 mμ, ε 24,500, 258 mμ, ε 11,800, 327 mμ, ε 10,090. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.40; H, 5.30; N, 12.27. Found: C, 68.62; H, 5.48; N, 12.06.

Hydrolysis of VI in refluxing 2 *N* KOH in 60% aqueous ethanol gave 6-acetyl-2-carboxytryptamine (VIII, m.p. 240–243°, λ_{max}^{EtOH} 249 mμ, ε 25,300, 309 mμ, ε 21,700. Calcd. for $C_{13}H_{14}N_2O_3 \cdot H_2O \cdot 0.5 \cdot C_2H_5OH$: C, 58.52; H, 6.66; N, 9.75. Found: C, 58.74; H, 6.40; N, 9.73). Decarboxylation of VIII in refluxing 20% hydrochloric acid gave 6-acetyltryptamine[4] (IX, m.p. 148–150°, λ_{max}^{EtOH} 233 mμ (shoulder), ε 15,500, 253 mμ, ε 21,400, 301 mμ, ε 12,900. Calcd. for $C_{12}H_{14}N_2O$: C, 71.26; H, 6.98; N, 13.85. Found: C, 71.38; H, 7.18; N, 14.08).

Hydrolysis of VII in refluxing 2 *N* KOH in 60% aqueous ethanol gave 4-acetyl-2-carboxytryptamine (X, m.p. 314–317°, λ_{max}^{EtOH} 216 mμ, ε 30,000, 245–52 mμ (shoulder), ε 13,900, 260 mμ, ε 15,000. Calcd. for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.59; H, 5.99; N, 11.46). Decarboxylation of X in refluxing 20% hydrochloric acid containing 30% by volume glacial acetic acid gave 3,4-dihydro-6-methyl-1H-azepino[5,4,3-cd]-indole[5] (XI, m.p. 272–277°, λ_{max}^{EtOH} 241 mμ, ε 18,250. Calcd. for $C_{12}N_{12}N_2$: C, 78.22; H, 6.57; N, 15.21. Found: C, 77.98; H, 6.59; N, 15.36).

Reaction of *o*-acetylphenyldiazonium chloride with 2-oxo-piperidine-3-carboxylic acid gave the 3-(*o*-acetylphenyl)hydrazone of 2,3-piperidinedione (XII, m.p. 231–234°, λ_{max}^{EtOH} 230 mμ, ε 17,300, 254 mμ, ε 11,700, 312.5 mμ, ε 14,700, 369 mμ, ε 13,200.

(1) We thank Dr. Max Ben of the Department of Pharmacology for the observation of this hypotensive activity in the dog.

(2) R. A. Abramovitch and D. Shapiro, *Chem. and Ind.*, 1255 (1955); *J. Chem. Soc.*, 4589 (1956).

(3) S. Keimatsu, S. Sugasawa and G. Kasuya, *J. Pharm. Soc.* (Japan), **48**, 762 (1928); *Chem. Abstr.*, **23**, 834 (1929).

(4) This compound showed pressor activity in the dog, according to Dr. M. Osborne of the Department of Pharmacology.

(5) This compound represents the first of a series of derivatives of the novel ring system 1H-azepino[5,4,3-cd]indole.