+17.2 p.p.m., and must be attributed to a hydrogen atom of an unusual character.

Biscyclopentadienylrhenium hydride is unaffected by water and reacts moderately quickly with air; it is readily soluble in, and may be crystallized from solvents such as petroleum ether, benzene and ether. It is only sparingly soluble in liquid ammonia and the solutions do not conduct electricity. It does not react with ferrous chloride in tetrahydrofuran solution to form ferrocene.

While a rhenium carbonyl hydride has been reported,[1] neither this compound nor the carbonyl hydrides of other second and third group transitional metals have been rigorously characterized and their properties studied. However, unlike the carbonyl hydrides of iron and cobalt, biscyclopentadienylrhenium hydride appears to have no basic properties and is unaffected by 6 *N* sodium hydroxide. On the contrary, it behaves as a proton acceptor (*cf.* NH_3) and will dissolve in dilute hydrochloric or sulfuric acids without evolution of hydrogen to form a unipositive cation $[(C_5H_5)_2ReH_2]^+$; on addition of sodium hydroxide to those solutions biscyclopentadienylrhenium hydride is liberated and can be recovered by solvent extraction. The ion gives precipitates with large anions such as silicotungstate, and a rose-pink reineckate has been characterized. That the hydridic hydrogen atoms are attached to the rhenium atom in the ion is indicated by a single proton resonance peak in the aqueous solution at a displacement of +18.9 p.p.m. relative to water.

The most reasonable structure for biscyclopentadienylrhenium hydride would seem to be one similar to that of ferrocene, with metal to ring bonds of the "sandwich bond" type. The nuclear magnetic resonance studies show that the hydridic hydrogen is unusually well diamagnetically shielded and the hydrogen atom is presumably buried in the electron density surrounding the metal atom in the exposed region between the cyclopentadienyl rings.

(1) W. Hieber and A. Fuchs, *Z. anorg. Chem.*, **248**, 256 (1941).

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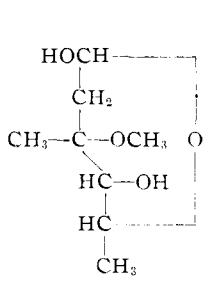
ERYTHROMYCIN. III. THE STRUCTURE OF CLADINOSE

Sir:

The isolation of cladinose from erythromycin was reported previously.[1,2] This is a $C_8H_{16}O_4$ compound containing two C–CH_3 groups, two hydroxyl groups and one methoxyl group. Evidence was presented for the presence of a hemiacetal grouping



and the moiety $CH_3\dot{C}HO$– with participation of this oxygen in the hemiacetal ring. These facts and further evidence given in this communication prove that cladinose has structure I.

Oxidation of cladinose with bromine formed a lactone (II). This compound lost the methoxyl group so readily that it was not possible to purify it, but it was characterized as its 3,5-dinitrobenzoate, m.p. 123–125° [Calcd. for $C_{15}H_{16}N_2O_9$: C, 48.91; H, 4.35; N, 7.62; CH_3O (1), 8.4. Found: C, 48.85; H, 4.33; N, 7.64; CH_3O, 8.7]. The infrared spectrum of the lactone was consistent with structure II, having absorption at 2.90 μ and 5.65 μ with a shoulder at 5.80 μ. The carbonyl absorption is indicative of a γ-lactone with a δ-lactone present as a minor component. Base treatment of II followed by neutralization resulted in the appearance of ultraviolet absorption at 211 mμ, ϵ 8400 which can be attributed to formation of a lactone having α,β unsaturation, probably III. Oxidation of base-treated II with periodate[3] formed two compounds. One of these was identified as acetaldehyde, 2,4-dinitrophenylhydrazone melting point and mixed melting point identical with an authentic sample. The other product, a liquid, formed a 2,4-dinitrophenylhydrazone, m.p. 250–251° dec. [Calcd. for $C_{11}H_{10}N_4O_6$: C, 44.90; H, 3.43; N, 19.03; mol. wt., 294. Found: C, 45.15; H, 3.68; N, 18.86; mol. wt., 289.6] and a semicarbazone, m.p. 214–215° [Calcd. for $C_6H_9N_3O_3$: C, 42.11; H, 5.26; N, 24.56. Found: C, 42.42; H, 5.36; N, 24.30]. An unambiguous synthesis proved that this compound is β-formylcrotonic acid (IV).

Ethyl β-hydroxymethylcrotonate[4] was oxidized to the aldehyde with manganese dioxide.[5] This was characterized by infrared and ultraviolet spectra and conversion to its 2,4-dinitrophenylhydrazone. The infrared spectrum showed aldehyde hydrogen absorption at 3.52 μ, ester carbonyl absorption at 5.85 μ, aldehyde carbonyl absorption at 5.90 μ and carbon–carbon double bond absorption at 6.08 μ. The ultraviolet absorption at 220 mμ, ϵ 10,170 (*cis*) and

(1) E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley and K. Gerzon, THIS JOURNAL, **76**, 3121 (1954).

(2) R. B. Hasbrouck and F. C. Garven, *Antibiotics and Chemotherapy*, **3**, 1040 (1953).

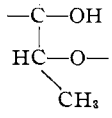
(3) It has been reported that cladinose does not react with periodate, but this is not absolute proof that there are not adjacent hydroxyl groups: see H. Klosterman and F. Smith, THIS JOURNAL, **74**, 5336 (1952).

(4) H. H. Sobotka and M. I. Rubin, U. S. Patent 2,390,335 (1945).

(5) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Herns, A. B. A. Jansen and F. Walker, *J. Chem. Soc.*, 1094 (1952).

230 mμ, ε 8,000 (*trans*) was consistent with the ethyl β-formylcrotonate structure.[6] The 2,4-dinitrophenylhydrazone melted at 199–200° [Calcd. for $C_{13}H_{14}N_4O_6$: C, 48.45; H, 4.38; N, 17.37; C_2H_5O (1), 13.9. Found: C, 48.38; H, 4.67; N, 17.03; C_2H_5O, 12.4]. Hydrolysis of this ester with 6 *N* hydrochloric acid gave β-formylcrotonic acid[7] (IV), 2,4-dinitrophenylhydrazone, m.p. 251° dec. [Calcd. for $C_{11}H_{10}N_4O_6$: C, 44.90; H, 3.43; N, 19.03. Found: C, 45.06; H, 3.55; N, 18.89]. This 2,4-dinitrophenylhydrazone did not depress the melting point of the same derivative obtained from the periodate oxidation product of base-treated II. The infrared spectra of the two 2,4-dinitrophenylhydrazones were identical.

The periodate oxidation of base-treated II with formation of acetaldehyde in conjunction with previous information indicated the presence of the grouping



The position of the other hydroxyl on C_1 has already been shown. The isolation of acetaldehyde and β-formylcrotonic acid by degradation of II is proof of a six carbon chain in cladinose. The appearance of α,β-unsaturation in II after base treatment indicates the β-position of the methoxyl group (C_3 in cladinose). The position of the second C–CH_3 group in II (C_3 in cladinose) is shown by formation of IV, and this fragment also indicates that base treatment of II eliminates the methoxyl group. These facts are consistent only with structure I for cladinose.

(6) T. Y. Shen and M. C. Whiting, *J. Chem. Soc.*, 1772 (1950).

(7) This compound has been reported from a natural product, but it was evidently not identical with the one isolated here: see I. J. Rinkes, *Rec. trav. chim.*, **48**, 1093 (1929).

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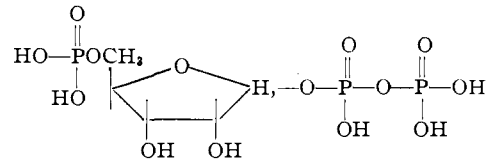
A SYNTHESIS OF β-D-RIBOFURANOSE-1-PHOSPHATE

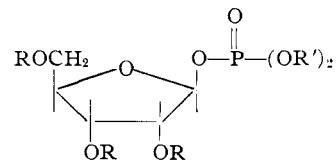
Sir:

Since the isolation by Kalckar[1] of ribose-1-phosphate as a product of the enzymatic "phosphorolysis" of certain nucleosides, two other related ribose derivatives have been discovered. Ribose-1,5-diphosphate[2] has been shown to be the coenzyme in the phosphoribomutase-catalyzed isomerization of ribose-1-phosphate to ribose-5-phosphate and 5-phosphoribose-1-pyrophosphate[3] (I) has been demonstrated to be a precursor in the enzymatic synthesis of nucleoside-5′-phosphates. Although the available evidence would appear to be conclusive as regards the location of the phosphate groups in these substances, the configurations at C_1 of the ribose moiety remain unknown. As part of our work aimed at the chemical synthesis of these compounds, we wish to report a synthesis of D-ribofuranose-1-phosphate. Also, evidence is presented which indicates that the configuration of the phosphate residue at C_1 in the synthetic sample is β, in contrast with the α configuration of a sample of ribose-1-phosphate prepared by the action of the fish muscle riboside phosphorylase[4] on guanosine.

2,3,5-tri-O-benzoyl D-ribofuranosyl-1-bromide, prepared according to Ness, *et al.*,[5] was treated in benzene solution at 5–8° with one equivalent of triethylammonium dibenzyl phosphate. Triethylamine hydrobromide which separated was removed by centrifugation and the sirup, presumably II, obtained after evaporation of benzene, was hydrogenated at 0° in anhydrous methyl alcohol, using freshly prepared 15% palladium–carbon catalyst. The methanolic solution of III was diluted with water and brought to and maintained at *p*H 10.5.



I



II, R = benzoyl, R′ = benzyl
III, R = benzoyl, R′ = H

Debenzoylation was complete after *ca.* 3 hours and ribose-1-phosphate was isolated as the barium salt and purified by the method of Kalckar[1]; yield on a 2-g. scale, 20%. *Anal.* Calcd. for $C_5H_9O_8PBa \cdot 1H_2O$: ribose, 39.1; P, 8.07. Found: ribose,[6] 38.8; P,[7] 7.9. The sample was non-reducing[8] and was free from inorganic phosphate.[9] Paper chromatography in several solvent systems showed the product to be homogeneous and identical with the enzymatically prepared sample of ribose-1-phosphate.[4] Furthermore, the two samples showed identical rates of hydrolysis in 0.1 *M* perchloric acid at room temperature. They were found to be much more labile than the following isomeric phosphates: D-ribopyranose-1-phosphate, synthesized as the crystalline barium salt from 2,3,4-tri-O-acetylribopyranosyl-1-bromide, ribose-2-phosphate,[10] ribose-3-phosphate[10] and ribose-5-phosphate. Enzymatic tests on the natural and the synthetic samples of ribose-1-phosphate were carried out as follows: Each sample (7.35 μM./cc.) was incubated at 37° with the fish muscle riboside phosphorylase in the presence of excess of hypoxanthine. After 3 hours, whereas *ca.* 90% of the natural sample had disappeared, with the concomitant liberation of an

(1) H. M. Kalckar, *J. Biol. Chem.*, **167**, 477 (1947).

(2) H. Klenow, *Arch. Biochem. Biophys.*, **46**, 186 (1953).

(3) A. Kornberg, I. Lieberman and E. S. Simms, THIS JOURNAL, **76**, 2027 (1954); I. Lieberman, A. Kornberg and E. S. Simms, *ibid.*, **76**, 2844 (1954).

(4) H. L. A. Tarr, *Fed. Proc.*, **14**, 291 (1955).

(5) R. K. Ness, D. W. Diehl and H. G. Fletcher, Jr., THIS JOURNAL, **76**, 763 (1954).

(6) A. H. Brown, *Arch. Biochem. Biophys.*, **11**, 269 (1946).

(7) R. A. Bonar and E. L. Duggan, *J. Biol. Chem.*, **212**, 697 (1955).

(8) M. Macleod and R. Robinson, *Biochem. J.*, **23**, 517 (1929).

(9) Determined by the method of O. H. Lowry and J. A. Lopez, *J. Biol. Chem.*, **162**, 421 (1946).

(10) We are grateful to Dr. Waldo E. Cohn of Oak Ridge National Laboratory for gifts of these substances.