

three weeks, at the end of which time there was a strong color test. The yield of biphenyl was 27%. In a check experiment the yield of biphenyl was 30%.

The trace of biphenyl reported earlier^{2c} indicates that the nickel cyanide used then was not completely anhydrous. This conclusion is reasonable when one recalls that in the former experiments a more vigorous reaction was reported.

Summary

In reactions of phenylmagnesium iodide with anhydrous halides of Group VIII metals, practically quantitative yields of biphenyl were ob-

tained with the halides of iron, cobalt, nickel, ruthenium, rhodium and palladium; and markedly reduced yields with the chlorides of osmium, iridium and platinum. The latter three halides also formed the corresponding organometallic compounds. The extent of the coupling reaction is suggested as a rough measure of the thermal instability of the intermediately formed organometallic compounds.

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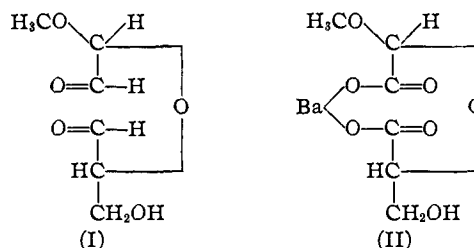
[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Periodic Acid Oxidation of Beta-Methyl-D-mannopyranoside¹

BY ERNEST L. JACKSON AND C. S. HUDSON

The oxidation of β -methyl-D-glucopyranoside by periodic acid and subsequent oxidation of the product, L'-methoxy-D-hydroxymethyl-diglycolic aldehyde (I), with bromine water kept neutral with barium carbonate has been shown by us² to produce the crystalline barium salt, barium L'-methoxy-D-hydroxymethyl-diglycolate (II). This crystalline barium salt has now been obtained by the application of these oxidation reactions to β -methyl-D-mannopyranoside and also to β -methyl-D-galactopyranoside, which previously has been oxidized by periodic acid to the dialdehyde² (I). The identity of the dialdehyde, the dibasic acid and the barium salt from the three β -methyl-D-aldohexosides is evident from the agreement of the rotations of corresponding compounds recorded in Table I. These methylglycosides, therefore, have the same configuration for carbon atom 1 and they possess the pyranoside ring

structure that is now generally accepted from the results of other methods of study,³ particularly methylation.



L'-Methoxy-D-hydroxymethyl-diglycolic aldehyde

Barium L'-methoxy-D-hydroxymethyl-diglycolate

TABLE I
ROTATIONS OF THE OXIDATION PRODUCTS OF THE β -METHYL-D-ALDOHEXOPYRANOSIDES

Substance	Methyl glyco-side [α] ^{20D}	Dialdehyde ^a [α] ^{20D}	Di-basic acid ^b [α] ^{20D}	Barium salt ^c [α] ^{20D}
β -Methyl-D-galactopyranoside	+ 1	-148.1 ^a	+45.0	+36.2
β -Methyl-D-glucopyranoside ²	-34	-150.6	+45.0	+35.9
β -Methyl-D-mannopyranoside	-69	-149.7	+45.4	+36.1

^a L'-Methoxy-D-hydroxymethyl-diglycolic aldehyde. Specific rotations calculated from the final [M]_D values of the oxidation solutions. ^b Determined by liberating the acid (*c*, 1.5) from its barium salt with an equivalent of hydrochloric acid. ^c *C*, 3.4.

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Jackson and Hudson, *THIS JOURNAL*, **59**, 994 (1937).

The data that have now been obtained for the alpha and beta methyl-pyranosides of glucose, galactose and mannose and the alpha methyl-pyranoside of gulose not only show the ring type of these substances and their alpha or beta classification, but also prove that these substances are homogeneous, no one of them being a molecular compound of an alpha and beta form, such as are known in the case of a certain xyloside⁴ (7 α -methyl-D-xylopyranoside:2 β -methyl-D-xylopyranoside) and a certain crystalline form of lactose⁴ (5 α -lactose:3 β -lactose). This conclusion follows from the fact that the solutions of the four α -methyl-hexopyranosides² show closely the same end rotation when they are oxidized by periodic acid to the dialdehyde, and likewise the three β -methyl-hexopyranosides when they are converted to their common dialdehyde. In il-

(3) Bott, Haworth and Hirst, *J. Chem. Soc.*, 2653 (1930); Pryde, *ibid.*, 1808 (1923); Haworth, Hirst and Jones, *ibid.*, 2428 (1927); Schlubach and Moog, *Ber.*, **56**, 1962 (1923); Müller, *ibid.*, **64**, 1820 (1931).

(4) Hockett and Hudson, *THIS JOURNAL*, **53**, 4454, 4455 (1931).

lustration of this proof, the compound xyloside, just mentioned, has been oxidized by periodic acid and the end molecular rotation has been found to be +9600 in contrast to the known² values of +16540 and -16,420 for the pure α - and β -methyl-D-xylopyranosides, respectively.

Experimental

Oxidation of β -Methyl-D-mannopyranoside with Periodic Acid.—Since β -methyl-D-mannopyranoside is known only as a sirup, an aqueous solution of the glycoside was prepared for oxidation from pure, crystalline β -tetraacetyl-methyl-D-mannopyranoside.⁵ A mixture of 9.1714 g. of the pure tetraacetate, 300 ml. of absolute methanol and 10 ml. of *N* barium methylate⁶ solution in methanol was kept at room temperature for three days and then diluted with water to exactly 500 ml. at 20°. For the determination of the rotation of the mannoside, 2 ml. of *N* hydrochloric acid was added to a 100-ml. aliquot of the deacetylation solution which then was concentrated cautiously *in vacuo* to dryness. A specific rotation⁷ of -68.9° in water for β -methyl-D-mannopyranoside was calculated from the rotation of the sirup (25 ml. of solution in water at 20°, 2-dm. tube; rotation, 5.42° to the left). Bott, Haworth and Hirst⁸ found about -68° in water. An aqueous solution of the mannoside was prepared for oxidation by the addition of 6 ml. of *N* sulfuric acid to 300 ml. of the deacetylation solution, removal of the barium sulfate by filtration and concentration of the solution *in vacuo* to a sirup which was made up to exactly 50 ml. in water at 20°. This solution contained 2.7898 g. of β -methyl-D-mannopyranoside calculated from the rotation (7.70° to the left; 2-dm. tube) and the specific rotation -69° of the mannoside. To 44.05 ml., containing 2.4577 g. of β -methyl-D-mannopyranoside, was added 50 ml. of 0.5331 *M* aqueous periodic acid solution at 20°. The solution, diluted with water to 100 ml. and kept in a 20° room, showed $[M]_D \times 10^{-2}$: -203.0 (3.9 min.); -209.9 (6.6 min.); -214.9 (10.0 min.); -221.6 (19.3 min.); -225.3 (27.7 min.); -229.7 (40.4 min.); -233.8 (65.1 min.); -237.6 (98 min.); -240.6 (149 min.); -242.7 (255 min.); -242.7 (24 hrs.). The specific rotation of *L'*-methoxy-D-hydroxymethyl-diglycolic aldehyde, calculated from the final rotation of the oxidation solution, is -149.7°. After twenty-four hours an analysis of 5 ml. of the solution showed 4% excess periodic acid, or the consumption of 2.02 molecular equivalents of the oxidant. *L'*-Methoxy-D-hydroxymethyl-diglycolic aldehyde was iso-

lated as a sirup, and from it was prepared barium *L'*-methoxy-D-hydroxymethyl-diglycolate in a yield of 73%, all as described for β -methyl-D-glucopyranoside.² The barium salt crystallized from water as characteristic fine needles of the dihydrate. After being dried at 100° *in vacuo* it showed a specific rotation of +36.1° in water (*c*, 3.4).

Anal. Calcd. for $C_8H_{13}O_7Ba$: Ba, 41.70. Found (dried at 100° *in vacuo*): Ba, 41.62.

Barium *L'*-Methoxy-D-hydroxymethyl-diglycolate from β -Methyl-D-galactopyranoside.—Crystalline barium *L'*-methoxy-D-hydroxymethyl-diglycolate was prepared in a yield of 70% from the dialdehyde obtained by the oxidation of β -methyl-D-galacto-pyranoside with periodic acid.² The pure, anhydrous barium salt showed the specific rotation +36.2° in water (*c*, 3.4).

Anal. Calcd. for $C_8H_{13}O_7Ba$: Ba, 41.70. Found (dried at 100° *in vacuo*): Ba, 41.62.

We are indebted to Dr. A. E. Knauf for the β -tetraacetyl-methyl-D-mannopyranoside and to Miss Edna M. Montgomery for the β -methyl-D-galactopyranoside.

Summary

The oxidation of β -methyl-D-mannopyranoside and also of β -methyl-D-galactopyranoside with periodic acid in aqueous solution and subsequent oxidation of the product with bromine water kept neutral with barium carbonate has yielded crystalline barium *L'*-methoxy-D-hydroxymethyl-diglycolate which had already been obtained by the application of these reactions to β -methyl-D-glucopyranoside. This proves that these three methyl-D-aldohexosides have the same configuration (beta) for carbon atom 1 and that they possess the pyranoside ring structure that is now generally accepted from methylation data.

The utility of the periodic acid oxidation reaction for testing the homogeneity of methyl-glycosides is illustrated by its application to a molecular compound (7 α -methyl-D-xylopyranoside: 2 β -methyl-D-xylopyranoside). Oxidation data now available prove the homogeneity of each of the alpha and beta methyl-pyranosides of D-glucose, D-galactose, and D-mannose and also of the alpha methyl-pyranoside of D-gulose.

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(5) Dale, *THIS JOURNAL*, **46**, 1046 (1924); Bott, Haworth, and Hirst, *ref.* 3.

(6) Weltzien and Singer, *Ann.*, **443**, 104 (1925); Isbell, *J. Research Natl. Bur. Standards*, **5**, 1185 (1930).

(7) Throughout the article the rotations are for sodium light and all specific rotations are at 20°.