The Direct Methyl Glycosidation of 2-Deoxy-D-*ribo*-hexose

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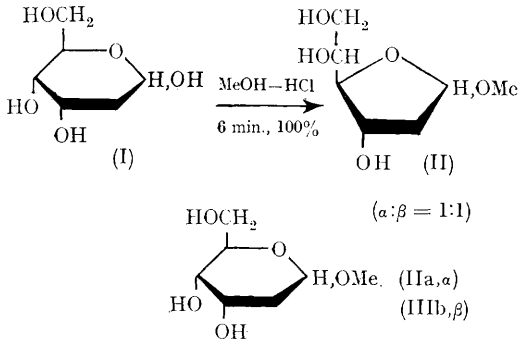
THE formation of furanoid derivatives of carbohydrates is an important problem and has recently received attention in attempts to synthesize potential anticancer nucleosides containing "false" sugar residues in their furanoid form. In general, the direct glycosidation of a monosaccharide is an unsatisfactory procedure for the preparation of furanoid derivatives, because it may lead either to pyranosides or to mixtures of glycosides, in which the proportion of furanoid isomers may be low. However, the methyl glycosidation of 2-deoxy-D-*erythro*-pentose gives a relatively high yield of a furanoside[1] that has been isolated only as a crystalline anomer mixture of methyl 2-deoxy-3,5-di-*O*-*p*-nitrobenzoyl-D-*erythro*-pentoside (75—85%),[2] or as a crystalline anomer mixture of methyl 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentoside (70%).[3] With 2-deoxy-D-*arabino*-hexose, we have recently shown that the direct methyl glycosidation of the hexose results in *ca.* 35% of methyl 2-deoxy-α-D-*arabino*-hexofuranoside, obtained in crystalline form after partition chromatography.[4]

We report the outcome of the direct methyl glycosidation of a monosaccharide which has no precedent. When 2·0 g. of 2-deoxy-D-*ribo*-hexose[5] (I) was added to 100 ml. of methanol containing 0·1% of hydrogen chloride at room temperature, all of the hexose (I) dissolved in 2 min. The reaction was continued for an additional 4 min. and then stopped by the addition of an excess of silver carbonate. The suspension was filtered, and the filtrate evaporated to a clear syrup that crystallized spontaneously. The product (II) gave values for carbon and hydrogen in excellent agreement with those calculated for a methyl glycoside, and had m.p. 93—95°, $[\alpha]_D$ + 39°, and n.m.r., septuplet δ 4·99 p.p.m. (anomeric protons). From the data, it was determined that the new glycoside was neither the α-pyranoside[6] (IIIa) [m.p. 97—99·5° $[\alpha]_D$ + 183°, and n.m.r., triplet δ 4·69 p.p.m. (anomeric proton)] nor the β-pyranoside[6] (IIIb) [m.p. 99—101°, $[\alpha]_D$ − 20°, and n.m.r., quadruplet δ 4·62 p.p.m. (anomeric proton)]. Recrystallization of (II) resulted in 85% recovery; this, coupled with the

n.m.r. data, suggested a 1 : 1 molecular compound of the anomers of methyl 2-deoxy-D-*ribo*-hexofuranoside. The components were, however, readily separable as their silylated derivatives on g.l.c.,† appearing as two, well-defined peaks of approximately equal area [retention times: 2·5 min. (α); 3·0 min. (β)]. Inspection of structures (II), (IIIa) and (IIIb) shows that only (II) will yield formaldehyde on treatment with periodate; estimation of formaldehyde produced in each case was made with chromotropic acid, giving zero values for (IIIa) and (IIIb), and 85%‡ for (II), the same as that for pure methyl 2-deoxy-α-D-*arabino*-hexofuranoside[4] used as a control.



It may be concluded, therefore, that the direct methyl glycosidation of 2-deoxy-D-*ribo*-hexose (I) results in 100% of crystalline furanoside in an anomer ratio of 1 : 1.

The authors thank Professor S. J. Angyal, University of New South Wales, for helpful discussions, Dr. Eleanor E. Storrs, Gulf South Research Institute, for the gas–liquid chromatography, and the National Cancer Institute for financial support.

(*Received, April 26th*, 1968, *Com.* 506.)

† Performed on a Micro-Tek model 220 instrument with a dual flame detector (column packing: 2% SE-52 on Chromosorb W).

‡ The failure to obtain values close to 100% is not due to the presence of pyranoid isomers, but may be ascribed to the low sensitivity of the Coleman Junior Model 6C spectrophotometer employed.

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[6] C. C. Bhat, K. V. Bhat, and W. W. Zorbach, to be published.