Carbohydrate Research
Elsevier Publishing Company, Amsterdam
Printed in Belgium

Note

Stereoselective hydroxylation of glycals

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(Received August 6th, 1969; in revised form, September 19th, 1969)

The mode of hydroxylation of glycals with perbenzoic acid, which probably involves an intermediate 1,2-epoxide, is dependent on the nature of the substituent at C-3. The hydroxyl group at C-2 is preferentially introduced *cis* to the substituent at C-3 when the latter is a hydroxyl group and *trans* if HO-3 is substituted. Numerous examples are known[1–3].

Treatment of glycals with hydrogen peroxide and osmium tetroxide in *tert*-butyl alcohol gave[4], predominantly, the aldose having *trans*-substituents at positions 2 and 3, regardless of substitution of HO-3.

Hydroxylation of glycals by perbenzoic acid has been used for the preparation of some relatively rare aldoses, for example, D-talose (32%) from D-galactal[2], and L-ribose (40%) from L-arabinal[3]. The disadvantage of this method is the instability of perbenzoic acid and the poor stereoselectivity of the reaction.

We have found that the hydroxylation of D-galactal by hydrogen peroxide in the presence of osmium tetroxide gives D-galactose and D-talose in the ratio 4:1. In the presence of selenium dioxide, vanadium pentoxide, or chromium trioxide, the ratio was *ca.* 2:1. However, the yield was relatively low, due to the formation of by-products. Whereas the hydroxylation of D-galactal in the presence of OsO_4, SeO_2, V_2O_5, or CrO_3 leads preferentially to products having *trans* 2,3-substituents, hydroxylation in the presence of molybdenum trioxide or tungsten trioxide affords almost exclusively *cis* 2,3-substituted products (Table I).

TABLE I

HYDROXYLATION OF D-GALACTAL BY HYDROGEN PEROXIDE IN THE PRESENCE OF VARIOUS OXIDES

Catalyst	*Yield* (%) D-*talose*+D-*galactose*	*Ratio* D-*talose*: D-*galactose*
MoO_3	90	9.5:0.5
WO_3	90	9:1
OsO_4	10	1:4
SeO_2	10	1:2
V_2O_5	5	1:2
CrO_3	5	1:2

The stereoselective, catalytic action of molybdenum trioxide was further demonstrated with D-glucal, D-arabinal, and D-xylal, by the formation of D-mannose, D-ribose, and D-lyxose, respectively (Table II). In addition to the main product, small proportions of the epimeric aldose and the corresponding 2-deoxyaldose are formed, the latter being the result of the addition of water due to the relatively acidic medium (pH 2.8). The stereoselectivity may be due, at least in part, to complex formation between HO-3 and peroxymolybdenic acid.

TABLE II

PRODUCTS ISOLATED FROM REACTION MIXTURES OBTAINED BY HYDROXYLATION OF GLYCALS (5 g) BY HYDROGEN PEROXIDE IN THE PRESENCE OF MOLYBDENUM TRIOXIDE

Glycal	*Reaction products* (*g*)		*Yield* (%)	*Ratio of aldoses*	R_F *values*
D-Glucal	D-Mannose	4.9	80.3	95.2	0.12
(*R_F* 0.49)	D-Glucose	0.3		4.8	0.09
	2-Deoxy-D-*arabino*-hexose	0.45			0.25
D-Galactal	D-Talose	4.8	78.7	95.0	0.15
(*R_F* 0.42)	D-Galactose	0.25		5.0	0.07
	2-Deoxy-D-*lyxo*-hexose	0.4			0.22
D-Arabinal	D-Ribose	5.75	89.1	97.5	0.19
(*R_F* 0.65)	D-Arabinose	0.15		2.5	0.12
	2-Deoxy-D-*erythro*-pentose	traces			0.34
D-Xylal	D-Lyxose	4.85	75.2	96.0	0.16
(*R_F* 0.65)	D-Xylose	0.2		4.0	0.14
	2-Deoxy-D-*threo*-pentose	0.3			0.37

EXPERIMENTAL

Melting points were determined on a Kofler microstage apparatus. Specific rotations were measured with a Bendix–Ericsson polarimeter, Type 143A. The fractionation of reaction mixtures was carried out by chromatography on columns (110 × 6 cm) of Whatman CF 12 cellulose with 5:1:4 butyl alcohol–ethanol–water. Sugars were identified by paper chromatography on Whatman No. 1 paper with detection by diphenylamine[5], and the amounts were determined by direct scanning of the detected chromatograms with an ERI-10 densitometer (Zeiss, Jena).

The starting glycals were synthesized by literature procedures: D-glucal[6], m.p. 57–60°, $[\alpha]_D^{24}$ $-8°$ (c 2, water); D-galactal[6], m.p. 98–100°, $[\alpha]_D^{24}$ $-6.6°$ (c 2, water); D-xylal, $[\alpha]_D^{24}$ $-245.4°$ (c 2, water); D-arabinal (prepared from 3,4-di-*O*-acetyl-D-arabinal[7] by Zemplén deacetylation), m.p. 80–82°, $[\alpha]_D^{24}$ $-197.4°$ (c 2, water).

Hydroxylation of D-*galactal in the presence of various oxides.* — D-Galactal (0.5 g) was dissolved in 5% aqueous hydrogen peroxide (5 ml), and one of the following oxides (10–15 mg) was added: MoO_3, WO_3, OsO_4, SeO_2, V_2O_5, and CrO_3. When OsO_4, SeO_2, V_2O_5, or CrO_3 was used, the reaction was complete within 4 h. In the presence of MoO_3 or WO_3, all of the D-galactal had reacted within 40 h. The reaction products were analysed by paper chromatography (Table I).

Hydroxylation of glycals in the presence of molybdenum trioxide. — To a solution of D-glycal (5 g) in 5% aqueous hydrogen peroxide (50 ml), molybdenum trioxide (40–50 mg) was added. After 48 h at room temperature, undissolved oxide was removed, and the excess of hydrogen peroxide was decomposed by treatment for 24 h at 22° with 5% palladised charcoal (0.1–0.2 g). The filtered mixture was then evaporated *in vacuo*. A solution of the residue in methanol (100 ml) was treated with charcoal and then chromatographed on cellulose. The results are summarized in Table II.

Preparation of D-*talose.* — A mixture of D-galactal (100 g) and molybdenum trioxide (1 g) in 5% aqueous hydrogen peroxide (1 litre) was kept for 48 h at room temperature. After filtration, 5% palladised charcoal (1–2 g) was added, and the mixture was stored for 48 h at 22°. The filtered mixture was evaporated *in vacuo*, and the syrupy residue was dried by two-fold evaporation with methanol. A solution of the residue in methanol (600 ml) was treated with charcoal and, after storage for 24 h at room temperature and thereafter for 24 h at 4°, gave D-talose (64 g), $[\alpha]_D^{24}$ +19.8° (*c* 1.6, water). Concentration of the mother liquor to half volume gave a further crop (21 g). The final mother liquor was subjected to cellulose chromatography to give D-talose (8.2 g), D-galactose (4.8 g), and 2-deoxy-D-*lyxo*hexose (7 g).

The crude, crystalline D-talose obtained above contained a small proportion of 2-deoxy-D-*lyxo*hexose. Recrystallization from methanol (8 ml per 1 g of crude D-talose) gave material having m.p. 130–133°, $[\alpha]_D^{24}$ +20.6° (*c* 1.5, water); lit.[2] m.p. 133–134°, $[\alpha]_D$ +21° (water).

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