Carbohydrate Research, 92 (1981) 154–156
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

Note

Preparation of carbohydrate isopropylidene derivatives with 2,2-dimethoxypropane in the presence of toluene-*p*-sulphonic acid

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(Received October 6th, 1980; accepted for publication, November 29th, 1980)

Carbohydrate derivatives can be converted into cyclic acetal-derivatives by treatment with the appropriate aldehyde or ketone in the presence of a suitable catalyst[1,2]. More recently, acetal exchange has been employed[3–6] and the most commonly used reagent is 2,2-dimethoxypropane in *N,N*-dimethylformamide or acetone in the presence of catalytic amounts of toluene-*p*-sulphonic acid. However, this process has the disadvantage of the removal of the last traces of *N,N*-dimethylformamide or of acetone-condensation products.

We now report a simple, rapid, and high-yielding method for the preparation of carbohydrate isopropylidene derivatives which is applicable to mono- and oligosaccharides. 2,2-Dimethoxypropane is used with toluene-*p*-sulphonic acid as catalyst at room temperature, but without any solvent. Similar reaction conditions were used for the preparation of isopropylidene derivatives of cyclitols from 2,2-diethoxypropane[7] and for isopropylidene derivative of lactose from 2,2-dimethoxypropane[8]. The time required for completion of the reaction depends on the solubility of the starting material in the reagent.

The following compounds were isopropylidenated: methyl α-L-, methyl β-L-, and benzyl α-L-rhamnopyranoside, methyl α-D- and methyl β-D-mannopyranoside, benzyl β-D-fucopyranoside, benzyl β-D-galactopyranoside, 1,2-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose, methyl 4-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranoside, and benzyl 2,3-*O*-isopropylidene-4-*O*-(4-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside.

The products, each of which was obtained in very good yield and easily isolated, were characterised by comparison with authentic samples and by ^{1}H-n.m.r. spectroscopy. The physical data were in good agreement with those reported in the literature, except for methyl 2,3:4,6-di-*O*-isopropylidene-α- and -β-D-mannopyranoside[9].

EXPERIMENTAL

General methods. — Melting points (uncorrected) were determined with a

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Kofler apparatus. T.l.c. was performed on Kieselgel G with detection by charring with sulphuric acid. Optical rotations were measured with a Perkin–Elmer 241 automatic polarimeter. ^{1}H-N.m.r. spectra (internal Me_4Si) were obtained by using a Jeol MH-100 (100 MHz) spectrometer.

Isopropylidenation reactions. — A mixture of methyl α-L-rhamnopyranoside[10] (5.34 g, 30 mmol), 2,2-dimethoxypropane (15.6 g, 150 mmol), and toluene-*p*-sulphonic acid (100 mg) was stirred for 10 min at room temperature. The mixture was then diluted with dichloromethane (50 ml), washed with 5% aqueous $NaHCO_3$ (20 ml) and water (3 × 20 ml), dried (Na_2SO_4), and concentrated, to give the syrupy 2,3-*O*-isopropylidene derivative (6.42 g, 98.1%), $[\alpha]_D$ −16° (*c* 1.1, acetone); lit.[11] $[\alpha]_D$ −15.9° (acetone). The 4-acetate had m.p. 66°; lit.[12] m.p. 61–63°.

Using essentially the foregoing procedure, but with the reaction times stated, the following conversions were effected.

Methyl β-L-rhamnopyranoside[13] (640 mg, 96 h) gave the syrupy 2,3-*O*-isopropylidene derivative (540 mg, 68.9%), $[\alpha]_D$ +80° (*c* 0.82, chloroform), R_F 0.66 (dichloromethane–acetone, 4:1). The 4-acetate was also a syrup, $[\alpha]_D$ +79° (*c* 2, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 3.61 (s, 3 H, OMe), 2.10 (s, 3 H, OAc), 1.61 and 1.38 (2 s, 6 H, CMe_2), and 1.25 (d, 3 H, $J_{5,6}$ 6.2 Hz, Me-5).

Benzyl α-L-rhamnopyranoside[14] (2.54 g, 15 min) gave the 2,3-*O*-isopropylidene derivative (2.67 g, 91.0%), m.p. 74–75° (from hexane), $[\alpha]_D$ −59° (*c* 0.7, chloroform); lit.[15,16] m.p. 73–75°, $[\alpha]_D$ −59.5°.

Methyl α-D-mannopyranoside[17] (1 g, 12 h) gave the 2,3:4,6-di-*O*-isopropylidene derivative (1.10 g; 78.2%), m.p. 76–77° (from ethanol), $[\alpha]_D$ +2° (*c* 0.5, methanol), $[\alpha]_D$ +2° (*c* 0.8, chloroform); lit.[18] m.p. 76–77°, $[\alpha]_D$ +3° (*c* 2.4, methanol).

Methyl β-D-mannopyranoside[13] (310 mg, 15 min) gave the 2,3:4,6-di-*O*-isopropylidene derivative (310 mg, 70.94%), m.p. 52–53° (from hexane), $[\alpha]_D$ −88° (*c* 1.27, chloroform), R_F 0.65 (dichloromethane–ethyl acetate, 9:1); lit.[9] gum, $[\alpha]_D$ −0.86° (*c* 1.98, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 4.72 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 3.56 (s, 3 H, OMe), 1.56, 1.50, 1.40, and 1.36 (4 s, 12 H, 2 CMe_2).

Benzyl β-D-fucopyranoside (1.27 g, 48 h) gave the 3,4-*O*-isopropylidene derivative as a syrup (0.9 g, 61.2%), $[\alpha]_D$ −8° (*c* 1.49, chloroform), R_F 0.43 (dichloromethane–ethyl acetate, 9:1); lit.[19] (for the L isomer) $[\alpha]_D$ +3° (*c* 2, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.40–7.15 (m, 5 H), 4.70 (q, 2 H, CH_2-Ph), 4.18 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 2.80 (b, 1 H, HO-2), 1.40 (d, 3 H, $J_{5,6}$ 6.3 Hz, Me-5), 1.48 and 1.30 (2 s, 6 H, CMe_2).

Benzyl β-D-galactopyranoside[20] (1 g, 24 h) gave the 3,4-*O*-isopropylidene derivative (1.12 g, 97%), m.p. 125° (from ethyl acetate–hexane), $[\alpha]_D$ −2° (*c* 1.26, chloroform); lit.[21] m.p. 123–124°, $[\alpha]_D$ −1.47° (*c* 1.12, chloroform).

1,2-*O*-Isopropylidene-6-*O*-toluene-*p*-sulphonyl-α-D-glucofuranose[23] (1.87 g, 3 h) gave the 1,2:3,5-di-*O*-isopropylidene derivative (1.67 g, 81%), m.p. 85–86°, $[\alpha]_D$ +25° (*c* 1.77, chloroform); lit.[22] m.p. 87°, $[\alpha]_D$ +27.1°.

Methyl 4-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranoside[24] (973 mg, 15 min) gave the syrupy 2,3:2′,3′-di-*O*-isopropylidene derivative as a syrup (1.17 g, 96.5%),

$[\alpha]_D$ −43° (*c* 0.86, chloroform), R_F 0.48 (dichloromethane–acetone, 9:1). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.52 (s, 1 H, H-1′), 4.81 (s, 1 H, H-1), 3.31 (s, 3 H, OMe), 2.84 (b, 1 H, HO-4′), and 1.60–1.18 (m, 18 H, 2 Me_2C, Me-5.5′).

Benzyl 2,3-*O*-isopropylidene-4-*O*-(4-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside[25] (293 mg, 30 min) gave the 2,3:2′,3′:2″,3″-tri-*O*-isopropylidene derivative (200 mg, 60%) as a syrup, $[\alpha]_D$ −71° (*c* 0.56, chloroform), R_F 0.48 (hexane–ethyl acetate, 3:1). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.30–7.20 (m, 5 H), 5.60 (s, 2 H, H-1′,1″), 5.09 (s, 1 H, H-1), 4.60 (q, 2 H, CH_2-Ph), 2.41 (b, 1 H, HO-4″), and 1.68–1.18 (m, 27 H, 3 Me_2C, Me-5,5′,5″).

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