Carbohydrate Research, 70 (1979) C13–C14

Preliminary communication

A facile synthesis of β-D-mannopyranosides

PER J. GAREGG and TOMMY IVERSEN

Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm (Sweden)

(Received January 9th, 1979; accepted for publication, January 15th, 1979)

Considerable success[1,2] has been achieved in the synthesis of 1,2-*cis*-glycosides having the *galacto* or *gluco* configuration, by using a non-participating group at C-2 and a suitable leaving-group at C-1. In disaccharide synthesis, however, few examples have been recorded of the use of this principle for preparing β-D-mannopyranosides[3,4].

We now report on a route to β-D-mannopyranosides, in four steps from D-mannose, including deprotection. D-Mannose was converted into the crystalline 2,3:4,6-di-*O*-cyclohexylidene-α-D-mannopyranose in 55% yield[5]; purification by chromatography was unnecessary. Treatment of the acetal with methanesulfonyl chloride in dichloromethane containing triethylamine afforded 2,3:4,6-di-*O*-cyclohexylidene-α-D-mannopyranosyl chloride that was sufficiently pure for direct use in the next reaction step; the mannosyl chloride may be crystallized. Treatment of the mannosyl chloride with the sodium alkoxide in a solution of the alcohol gave good yields of the methyl and isopropyl β-D-mannoside derivatives. Treatment of the mannosyl chloride in dichloromethane with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose in the presence of silver carbonate and molecular sieve (4 Å) afforded the β-linked disaccharide in 75% yield. Removal of cyclohexylidene[5] and isopropylidene groups with aqueous acetic acid at 100° afforded the known, crystalline 6-*O*-β-D-mannopyranosyl-D-galactose[6]. Preliminary experiments with carbohydrate aglycons containing secondary hydroxyl groups gave yields in the 30–60% range.

A solution of methanesulfonyl chloride (4.8 g) in dry dichloromethane (10 ml) was added dropwise to a stirred solution of 2,3:4,6-di-*O*-cyclohexylidene-α-D-mannopyranose[5] (3.4 g) in dry dichloromethane (100 ml) containing triethylamine[5,7] (10 ml). The solution was stirred at 40° for 2 h, cooled to room temperature, washed with water, dried over silica gel, filtered, and concentrated. The product was purified by filtration through a short column of silica gel [toluene–dichloromethane (1 : 1)]. 2,3:4,6-Di-*O*-cyclohexylidene-α-D-mannopyranosyl chloride (**1**; 3.0 g, 83%) was obtained as a chromatographically homogeneous (t.l.c.) syrup, $[\alpha]_D^{20}$ +47° (*c* 4.5, chloroform), which was used in the glycosylations described below. When crystallized from propan-2-ol, **1** had m.p. 87–88°, $[\alpha]_D^{20}$ +47° (*c* 3, chloroform).

A solution of **1** (1.0 g) in dry methanol (30 ml) containing sodium methoxide (0.25 g) was stirred at room temperature overnight, and then concentrated. The product was purified by passage through a column of silica gel (toluene—ethyl acetate, 4:1), to yield methyl 2,3:4,6-di-*O*-cyclohexylidene-β-D-mannopyranoside (0.9 g, 96%), m.p. 128—129° [from light petroleum (b.p. 40—60°)], $[\alpha]_D^{20}$ −82° (*c* 2, chloroform). A solution of the mannoside (1.6 g) in 80% aqueous acetic acid (15 ml) was heated at 100° for 1 h and then concentrated. The resulting syrup crystallized from propan-2-ol, to yield methyl β-D-mannopyranoside isopropylate[8,9] (0.8 g, 71%), m.p. 67—70°, $[\alpha]_D^{20}$ −57° (*c* 2, water).

The reaction of **1** with propan-2-ol (on the same scale and in the same manner as that described for methanol, except that a reaction temperature of 40° was used) gave syrupy isopropyl 2,3:4,6-di-*O*-cyclohexylidene-β-D-mannopyranoside (0.8 g, 75%), $[\alpha]_D^{20}$ −89° (*c* 3, chloroform).

Compound **1** (0.50 g) was added to a stirred mixture of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (0.26 g), silver carbonate (0.40 g), and molecular sieve (4 Å, 1.5 g) in dry dichloromethane (5 ml). The mixture was stirred in the dark at room temperature for 24 h, diluted with acetone, filtered, and concentrated. Purification on a column of silica gel (toluene—ethyl acetate, 3:1) yielded 6-*O*-(2,3:4,6-di-*O*-cyclohexylidene-β-D-mannopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**; 0.44 g, 75%), $[\alpha]_D^{20}$ −82° (*c* 1, chloroform).

A solution of **2** (0.3 g) in 60% aqueous acetic acid (15 ml) was heated at 100° for 3 h. The solution was concentrated to a syrup that crystallized from ethanol—water, to give 6-*O*-β-D-mannopyranosyl-D-galactose (0.11 g, 63%), m.p. 178—180°, $[\alpha]_{578}^{20}$ +22° (5 min) → 0° (24 h) (*c* 0.7, water), in agreement with literature values[6].

ACKNOWLEDGMENTS

We thank Professor Bengt Lindberg for his interest, the Swedish Natural Science Research Council for financial support, and Stiftelsen Bengt Lundqvists Minne for a maintenance grant (to T.I.).

REFERENCES

1 R. U. Lemieux, K. B. Hendricks, R. V. Stick, and K. James, *J. Am. Chem. Soc.*, 97 (1975) 4056—4062.
2 J.-R. Pougny, M. A. M. Nassr, N. Naulet, and P. Sinaÿ, *Nouv. J. Chim.*, 2 (1978) 389—395.
3 P. A. J. Gorin and A. S. Perlin, *Can. J. Chem.*, 39 (1961) 2474—2485.
4 H. Paulsen and O. Lockhoff, *Tetrahedron Lett.*, (1978) 4027—4030.
5 P. J. Garegg, T. Iversen, and T. Norberg, *Carbohydr. Res.*, in press.
6 G. Ekborg, B. Lindberg, and J. Lönngren, *Acta Chem. Scand.*, 26 (1972) 3287—3292.
7 P. J. Garegg, H. Hultberg, and T. Iversen, *Carbohydr. Res.*, 62 (1978) 173—174.
8 B. Helferich and G. Duve, *Chem. Ber.*, 91 (1958) 1790—1793.
9 H. S. Isbell and H. L. Frush, *J. Res. Natl. Bur. Stand.*, 24 (1940) 125—151.