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Note

A practical synthesis of *p*-nitrophenyl β-D-mannopyranoside

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p-Nitrophenyl glycosides are of interest in enzyme studies and in studies involving sugar residues linked to proteins by using *p*-aminophenyl glycosides obtainable by reduction of the nitro group. The synthesis of *p*-nitrophenyl β-D-mannopyranoside has so far posed a problem; two routes have been described. One involves the isolation of the β anomer, by chromatography, from the deacetylated mother liquors obtained in the synthesis of *p*-nitrophenyl α-D-mannopyranoside tetraacetate[1]; the other entails a multistep synthesis, also in rather low, overall yield[2].

We now report on a two-step procedure for the synthesis of *p*-nitrophenyl β-D-mannopyranoside from D-mannose in 32% overall yield, without resorting to chromatographic purification. D-Mannose is first converted[3] into crystalline 2,3:4,6-di-*O*-cyclohexylidene-α-D-mannopyranose. This, upon treatment with triphenylphosphine, *p*-nitrophenol, and diethyl azodicarboxylate[4,5] followed by mild hydrolysis with acid, affords crystalline *p*-nitrophenyl β-D-mannopyranoside.

EXPERIMENTAL

General methods. — Melting points are corrected. Concentrations were performed at reduced pressure and a bath temperature below 40°. Optical rotations were measured with a Perkin–Elmer 241 instrument. ^{1}H- and ^{13}C-n.m.r. spectra, recorded on a JEOL FX 100 spectrometer, were in agreement with the assigned structures.

2,3:4,6-*Di*-O-*cyclohexylidene*-α-D-*mannopyranose* (**1**). — 1-Ethoxycyclohexene[6] (50.5 g) was added dropwise, over a period of 1 h, to a stirred solution of D-mannose (18 g) and *p*-toluenesulphonic acid monohydrate (0.5 g) in dry *N*,*N*-dimethylformamide (250 ml) at 40°. The solution was kept at 13 mmHg, and the ethanol formed was continuously removed. The solution was stirred at this pressure and temperature for a further 1 h, diluted with diethyl ether, washed with saturated, aqueous sodium hydrogen carbonate, and water, and then concentrated at reduced pressure. The crystalline residue was recrystallised from light petroleum (40–60°)–dichloromethane, to yield **1** (18.9 g, 55%), m.p. 174–175°, $[\alpha]_D^{20}$ — 33° (*c* 1, chloroform).

Anal. Calc. for $C_{18}H_{28}O_6$: C, 63.5; H, 8.29. Found: C, 63.3; H, 8.24.

p-Nitrophenyl β-D-mannopyranoside (**2**). — A solution of diethyl azodicarboxylate (6.5 g) in toluene (50 ml) was added dropwise over a period of 15 min to a stirred solution of **1** (9 g), triphenylphosphine (10 g), and *p*-nitrophenol (5.2 g) in toluene (200 ml) at room temperature. The solution was stirred for a further 1 h at room temperature and then concentrated. A solution of the residue in acetic acid (100 ml) and water (25 ml) was heated at 100° for 2 h and then concentrated at reduced pressure. The residue was dissolved in water, and the solution was washed with chloroform. Concentration of the aqueous phase gave crystalline **2** (4.6 g, 58%). Recrystallisation from ethanol yielded the pure compound, m.p. 205–207°, $[\alpha]_D^{20}$ — 108° (*c* 1, water)[1,2,7].

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