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Note

Synthesis of *p*-nitrophenyl 1-thio-β-D-mannopyranoside*

KHUSHI L MATTA AND JOSEPH J BARLOW
Department of Gynecology, Roswell Park Memorial Institute, Buffalo, New York 14263 (U S A)
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Our continued interest in the synthesis of 1-thioaldopyranosides[2,3] in connection with work on the purification of glycosidases by affinity chromatography has led to a new synthesis of *p*-nitrophenyl 1-thio-β-D-mannopyranoside

The direct condensation of an aldose with a thiol in the presence of a strong acid as a catalyst has been known to produce a mixture of 1,2-*cis*- and 1,2-*trans*-1-thioaldosides with dithioacetates[4–6] Alternatively, the Helferich reaction, involving the reaction of a thiol with an *O*-acylated sugar derivative has also been found to give a mixture of 1,2-*cis*- and 1,2-*trans*-1-thioaldosides[7,8] Interestingly, the anomeric mixture of aryl 1-thioaldosides obtained by deacylation of the products from the Helferich reaction can be effectively separated on a column of cation-exchange resin using only water as the eluant[8] Lee *et al*[9] successfully employed this procedure for the preparation of some 1,2-*cis*-*p*-nitrophenyl 1-thio-D-aldopyranosides, including the title compound In recent investigations, we have shown that *O*-acylated 1,2-*trans*-*p*-nitrophenyl 1-thioglycopyranosides can conveniently be prepared by the reaction of an *O*-acylated glycosyl halide with sodium *p*-nitrobenzenethioxide (**2**) in dry *N*,*N*-dimethylformamide In the present study, this procedure has been extended to synthesis of the desired 1,2-*cis*-*p*-nitrophenyl 1-thio-D-mannopyranoside However, thin-layer chromatography (t l c) of the solid material obtained from the reaction of 4,6-di-*O*-acetyl-2,3-*O*-carbonyl-α-D-mannopyranosyl bromide[10,11] (**1**) with compound **2** under these conditions, followed by the usual processing, showed the presence of two distinct compounds, **4** and **5**, along with some unidentified, fast-moving impurities The desired compound **5** was isolated by chromatography of the crude material on a column of silica gel followed by fractional recrystallization The mother liquor of **5** was rechromatographed, to give pure **4** Treatment of derivatives **4** and **5**, respectively, with barium methoxide in anhydrous methanol produced *p*-nitrophenyl 1-thio-α-D-mannopyranoside (**8**) and its β anomer (**9**)

It may be mentioned that the anomeric configuration of the sugar derivative obtained from the reaction of bromide **1** with an aglycon derivative seems to be

*Carbohydrate Derivatives for Affinity Chromatography V For Part IV of the series, see ref 1
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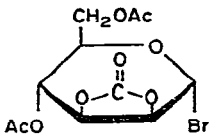
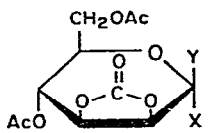
dependent on the solvent, the catalyst, and the nature of the aglycon[10 11]. In the present study, we have successfully separated both anomers from the mixture of *p*-nitrophenyl 1-thio-D-mannopyranosides In contrast, the reaction of this bromide (**1**) with sodium *p*-nitrophenoxide (**3**) produced mainly *p*-nitrophenyl 4,6-di-*O*-acetyl-2,3-*O*-carbonyl-*β*-D-mannopyranoside (**7**) As t l c of the solid material obtained under these conditions showed the presence of fast-moving material as a minor product (possibly, the *α* anomer **6**), no attempt was made to purify this minor product On treatment with barium methoxide under the usual conditions, pure compound **7** afforded the (known) *p*-nitrophenyl *β*-D-mannopyranoside (**10**)



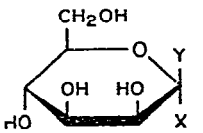
1

+ $NaZC_6H_4NO_2$-*p* ⟶

2 Z=S
3 Z=O



⟶



4 X = $SC_6H_4NO_2$-*p*, Y=H
5 X = H, Y = $SC_6H_4NO_2$-*p*
6 X = $OC_6H_4NO_2$-*p*, Y=H
7 X = H, Y = $OC_6H_4NO_2$-*p*

8 X = $SC_6H_4NO_2$-*p*, Y=H
9 X = H, Y = $SC_6H_4NO_2$-*p*
10 X = H, Y = $OC_6H_4NO_2$-*p*

1-Thioglycopyranosides are known to be competitive inhibitors for glycosidases[12] However, *p*-nitrophenyl 1-thio-*β*-D-mannopyranoside did not act as an inhibitor for the *β*-D-mannosidase present in an extract of *Aspergillus niger*[13]. Interestingly, the activity of this enzyme was also not inhibited by *N*-(6-aminocaproyl)-*β*-D-mannopyranosylamine prepared in our laboratory

EXPERIMENTAL

General — Melting points were determined with a Fisher–Johns apparatus and are uncorrected I r. spectra were recorded with a Perkin–Elmer Model 457 spectrophotometer. Optical rotations were measured with a Perkin–Elmer Model 141 Polarimeter The purity of the compounds was established by ascending, thin-layer chromatography conducted on plates coated with a 250-*μ*m layer of silica gel HF-254 (Merck, Darmstadt), and the spray reagent was potassium permanganate–sulfuric acid For column chromatography, the column packing was used without pretreat-

ment The elementary analyses were performed by Robertson Laboratory, Florham Park, New Jersey For the identification our synthetic derivative **10**, commercially available *p*-nitrophenyl *β*-D-mannopyranoside was purchased from Pierce Chemical Company, Rockford, Illinois

p-*Nitrophenyl 4,6-di*-O-*acetyl-2,3*-O-*carbonyl-1-thio*-D-*mannopyranosides* (**4**) *and* (**5**) — A mixture of 4,6-di-*O*-acetyl-2,3-*O*-carbonyl-α-D-mannopyranosyl bromide (**1**) (1 77 g, 5 mmoles, as a syrup) with freshly prepared sodium *p*-nitrobenzenethioxide (1 77 g, 10 mmoles) in anhydrous *N,N*-dimethylformamide (30 ml) was stirred for 18 h at room temperature, and then poured into water, the mixture was stirred for 1 h, kept cold for 6 h, and filtered The solid material was washed several times with cold water, air-dried, taken up in hot chloroform, and the suspension treated with carbon black and filtered through a Celite pad The brown-colored filtrate was cooled to room temperature, and passed through a column (2 2 × 80 cm) of silica gel which was washed with chloroform until most of the fast-moving impurities had been eluted Further elution was conducted with 19 1 chloroform–ethanol, but this did not separate the anomers **4** and **5** However, the fractions rich in these derivatives, along with the earlier fractions containing minor impurities, were combined, and evaporated to give 1 1 g of product, this was dissolved in hot, 1 1 chloroform–methanol (~100 ml), the solution concentrated to ~50 ml (in a hot-water bath), and then diluted with methanol (~50 ml), to give pure **5** as crystalline material which was recrystallized from chloroform–methanol, yield 0 45 g (21 1%), m p 195–197°, $[\alpha]_D^{23}$ −133 8° (*c* 1, chloroform), R_F 0 45 in solvent A (19 1 chloroform–ethanol), 0 38 in volvent B (19 1 benzene–methanol), ν_{max}^{KBr} 1800 (five-membered, cyclic carbonate), 1740 (OAc), 1600, 1590 (Ph), 1505, 1345 (NO_2), 745, and 687 cm^{-1} (Ph).

The mother liquor, rich in the α anomer, was evaporated to dryness, and a solution of the residue (0 6 g) in chloroform was passed through a column (2 2 × 50 cm) of silica gel Elution was conducted as already described Fractions thus obtained, containing almost pure **4**, were combined, evaporated, and the residue crystallized from methanol to give **4**, yield 0 35 g (16 4%), m p 115–116°, $[\alpha]_D^{23}$ +240° (*c* 1, chloroform), R_F 0 58 (solvent A) and 0 51 (solvent B), ν_{max}^{KBr} 1805 (five-membered cyclic carbonate), 1740 (OAc), 1600, 1580 (Ph), 1515, 1347 (NO_2), 747, and 690 cm^{-1} (Ph)

p-*Nitrophenyl 1-thio*-α-D-*mannopyranoside* (**8**) — Compound **4** (0 21 g) in methanol (30 ml) was treated with barium methoxide [1 ml, prepared by treating barium oxide (0 3 g) with methanol (10 ml), followed by centrifuging] The mixture was kept for 6 h at room temperature, made neutral with dil. acetic acid, and filtered The filtrate was stirred with Dowex 50 (H^+) cation-exchange resin for 15 min, and the suspension filtered. The resin was washed with methanol, and the filtrate and washings were combined, evaporated to dryness, and the residue crystallized from methanol–ether, to give pure **8**, yield 0 11 g (73 3%), m p 182–184°, $[\alpha]_D^{23}$ −320° (*c* 0 5, methanol). lit [9, 14] m p. 182–183°, $[\alpha]_D$ −285 0° (*c* 0 2, water)[9], m p. 186–188°, $[\alpha]_D$ −317 6° (*c* 0 89, methanol)[14]

p-*Nitrophenyl 1-thio-β-*D*-mannopyranoside* (**9**) — Treatment of compound **5** (0 2 g) in methanol (30 ml) with barium methoxide (1 ml), as described for the preparation of **8**, provided compound **9** as crystals in 80% yield, m p 208–211°, $[\alpha]_D^{23}$ −183° (*c* 0 5, methanol), lit [9] m p 172–174°, $[\alpha]_D$ −180° (*c* 0 2, water) The compound was examined by t l c in 3 2 benzene–methanol and 65 15 2 chloroform–methanol–water However, the mobility of compounds **8** and **9** in these solvent systems was almost the same

Anal Calc for $C_{12}H_{15}NO_7S$ C, 45 42, H, 4 76, N, 4 41, S, 10 08 Found C, 45 54, H, 4 78, N, 4 31, S, 10 32

p-*Nitrophenyl 4,6-di-*O*-acetyl-2,3-*O*-carbonyl-β-*D*-mannopyranoside* (**7**) — A solution of bromide **1** (0 88 g, 2 5 mmoles) and salt **3** (0 8 g, 5 mmoles) in anhydrous *N,N*-dimethylformamide (15 ml) was stirred for 18 h at room temperature The brown-colored solution thus obtained was poured into water (300 ml), and the mixture was stirred for 1 h, and kept cold for 6–8 h, the solid that separated was filtered off and air-dried (0 55 g, 50% yield) T l c of the solid showed a major spot having R_F 0.42 (solvent A) and a minor spot having R_F 0 72 (may be α anomer **6**) The air-dried material was taken up in hot ethanol (20 ml), and the suspension was treated with carbon black and filtered through a Celite pad When stored, the clear filtrate gave colorless crystals of **7**, yield 0 3 g (29 1%), m p 124–126°, $[\alpha]_D^{23}$ −140° (*c* 1, chloroform), ν_{max}^{KBr} 1810 (five-membered cyclic carbonate), 1745 (OAc), 1605, 1597 (Ph), 1520, 1345 (NO_2), 760, and 700 cm^{-1} (Ph) T l c of the mother liquor from **7** showed the presence of **7** along with a fast-moving, minor product No attempt was made to isolate this fast-moving material

Anal Calc for $C_{17}H_{17}NO_{11}$ C, 49 64, H, 4 17, N, 3 40 Found C, 49 49, H, 4 35, N, 3 38

p-*Nitrophenyl β-*D*-mannopyranoside* (**10**) — A solution of compound **7** (0 2 g) in anhydrous methanol (30 ml) was treated with barium methoxide (1 ml), and processed as described for the preparation of **7**, giving **10** in 70% yield, m p 204–207°, $[\alpha]_D^{23}$ −105° (*c* 0 5, water) Commercially available *p*-nitrophenyl β-D-mannopyranoside had m p 204–207°, $[\alpha]_D^{23}$ −103 6° (*c* 0 5, water)

ACKNOWLEDGMENTS

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