Tetrahedron Letters No. 47, pp 4307 - 4310, 1976. Pergamon Press. Printed in Great Britain.

STEREOSELECTIVE SYNTHESIS OF 1,2-cis-THIOGLYCOSIDES

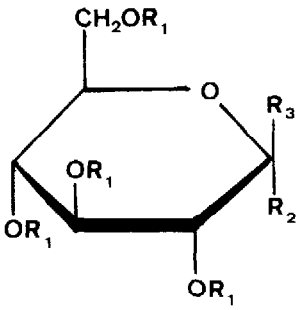
Michèle BLANC-MUESSER, Jacques DEFAYE and Hugues DRIGUEZ

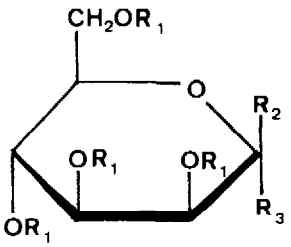
Centre de Recherches sur les Macromolécules Végétales, Centre National de la Recherche Scientifique, 53 X, 38041 GRENOBLE cédex, FRANCE.

(Received in UK 13 September 1976; accepted for publication 2 October 1976)

1,2-cis-p-Nitrophenyl 1-thioglycosides, potential ligands for the purification of glycosidases by affinity chromatography, are usually obtained in low yield together with the 1,2-trans isomers by the general reaction of an aldose with the thiol under strongly acidic conditions[1], or by Helferich reaction [2] involving, as for 1,2-cis-p-nitrophenyl analogues[3], fusion of the fully acetylated sugar with the thiol in the presence of a Lewis acid. p-Nitrophenyl 1-thio-α-D-glucopyranoside (1) and p-nitrophenyl 1-thio-β-D-mannopyranoside (2) were obtained in 3 and 8 % yield, respectively from the thioacetalation mixture by chromatography on a cation-exchange resin[1]. The very recent note of MATTA and BARLOW[4] prompts us to report at this time the results of our own investigations along similar lines.

In our hands, condensation under nitrogen of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl chloride[5] (3, 1 mmole) with p-nitrobenzenethiol (2 mmoles) in hexamethylphosphoramide (HMPA, 4-6 ml), for 1-2 h in the presence of aqueous satured potassium carbonate (2 mmoles) at room temperature, or sodium hydride (2 mmoles) at 70°[6] gave 24 and 60 % yields, respectively, of p-nitrophenyl 2,3,4,6-tetra-O-acetyl-1-thio-α-D-glycopyranoside[7] (4, m.p. 159-162° from dichloromethane-ether, $[\alpha]_D$ + 254°, c 0.82 chloroform)[8]. Similarly, p-nitrophenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-mannopyranoside (6) was prepared from 2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl bromide (5)[9], in 45 % yield by using either of the bases (m.p. 151-153° from dichloromethane-ether, $[\alpha]_D$ - 100°, c 1 chloroform). Zemplén catalytic deacetylation gave the expected α-D-glucoside m.p. 160-161°, $[\alpha]_D$ + 333°, c 0.24 water ; lit.[1] m.p. 149-150° $[\alpha]_D$ + 216.5°, c 0.2 water) and β-D-mannoside (2, m.p. 208-210° ; $[\alpha]_D$ - 170°, c 0.2 water) ; lit.[1]





1 $R_1 = R_3 = H$, $R_2 = SPhNO_2$

2 $R_1 = R_3 = H$, $R_2 = SPhNO_2$

3 $R_1 = Ac$, $R_2 = H$, $R_3 = Cl$

5 $R_1 = Ac$, $R_2 = H$, $R_3 = Br$

4 $R_1 = Ac$, $R_2 = SPhNO_2$, $R_3 = H$

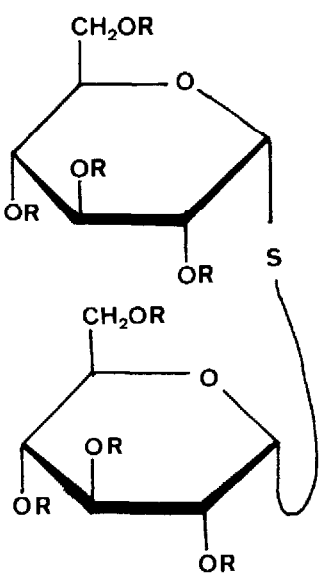
6 $R_1 = Ac$, $R_2 = SPhNO_2$, $R_3 = H$

7 $R_1 = Ac$, $R_2 = Br$, $R_3 = H$

9 $R_1 = Ac$, $R_2 = Cl$, $R_3 = H$

8 $R_1 = Ac$, $R_2 = H$, $R_3 = SPhNO_2$

10 $R_1 = Ac$, $R_2 = H$, $R_3 = SPhNO_2$



11 R = H

12 R = Ac

m.p. 172-174°, $[\alpha]_D$ - 180°, c 0.2 water).

An analogous reaction sequence was applied for the synthesis of α,α-thiotrehalose (11), a substrate of interest for studies on trehalases[10]. Reaction under nitrogen of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl chloride (3, 8 mmoles) with sodium sulfide (9 H_2O, 8 mmoles) in HMPA (8 ml) for 20 h at room temperature gave, after acetylation and purification by column chromatography (silica gel, 1:3 v/v diethyl ether-chloroform) the acetylated thiodisaccharide (12, 28 %, m.p. 191-193°, $[\alpha]_D$ + 200°, c 1.1 chloroform) from which α,α-thiotrehalose (11) was obtained as a foam after Zemplén deacetylation (m.p. 138-148° $[\alpha]_D$ + 358°, c 0.53 water).

The use of strong nucleophiles and a dipolar aprotic solvent suggest that these are SN_2 type reactions at the anomeric carbon atom[11]. In fact, this method has also been applied to the synthesis of 1,2-trans-p-nitrophenyl thioglycosides usually obtained in low yield from 1,2-cis-glycosyl-halides[12-14]. The foregoing conditions at room temperature provided the β-thioglucoside[12] (8) from the bromide(7) in 74 % yield by using aqueous potassium carbonate and, at 70°, the α-thiomannoside (10)[14] was obtained in 51 % yield from 2,3,4,6-tetra-O-acetyl-β-D-mannopyranosyl chloride[15,16,17] (9) with sodium hydride as a base.

This new type of displacement at the anomeric carbon atom is presently under investigation for access to mono- and oligoglycosides of biological interest.

REFERENCES AND FOOTNOTES

1 - J. SCHNEIDER, H.H. LIU and Y.C. LEE, Carbohydr. Res., 39 (1975), 156-159.

2 - B. HELFERICH and E. SCHMITZ-HILLEBRECHT, Ber. Dtsch. Chem. Ges., 66 (1933), 378-383.

3 - L. ROSENFELD and Y.C. LEE, Carbohydr. Res., 46 (1976), 155-158.

4 - K.L. MATTA and J.J. BARLOW, Carbohydr. Res., 48 (1976), 294-298.

5 - R.U. LEMIEUX, Methods Carbohydr. Chem., 2 (1963), 224-225.

6 - No reaction occurred at room temperature within 1 h. The reactions were monitored by t.l.c. on silica gel with ether-hexane (4:1 v/v) and stopped when the starting glycosyl halide was no longer detected.

7 - After purification on silica gel column with chloroform as solvent.

8 - All compounds described gave elemental microanalyses, ^{1}H (250 MHz) and mass-spectral data compatible with the proposed structures.

9 - W.A. BONNER, J. Am. Chem. Soc., 80 (1958), 3372-3329.

10 - E. BAR-GUILLOUX, J. DEFAYE, H. DRIGUEZ and D. ROBIC, Carbohydr. Res., 45 (1975), 217-236 and papers within quoted.

11 - C.J. CLAYTON, N.A. HUGUES and S.A. SAEED, J. Chem. Soc. (C), (1967), 444-448.

12 - G. WAGNER and C. LENK, Arch. Pharm., 295 (1962), 415-427.

13 - M.A. JERMYN, Aust. J. Chem., 10 (1957), 448-454.

14 - R.H. SHAH and O.P. BAHL, Carbohydr. Res., 32 (1974), 15-23.

15 - W. FORYTNYK and J.A. MILLS, J. Chem. Soc., (1959), 636-649.

16 - Kindly provided by Prof. B. Castro and Dr. J. Chapleur, University of Nancy.

17 - This compound was independently obtained from acetobromomannose by an adaptation of a method described[18] for syntheses of 1,2-trans-O-acetyl-glycosyl-halides from cis-isomers. To this glycosyl halide (5, 1 mmole), lithium chloride (3 mmoles) in HMPA (6 ml) is added and the mixture is shaken vigorously at room temperature for 1.5 h. Extraction as described gives the pure, crystalline β-chloride[15,16] (9) in 70 % yield.

18 - W.E. DICK and D. WEISLEDER, Carbohydr. Res., 46 (1976), 173-182.