Carbohydrate Research, 30 (1973) 414–417

Note

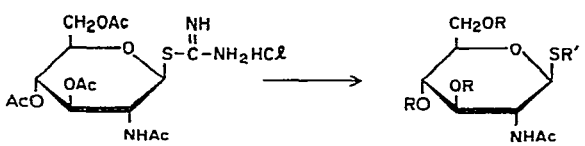
Synthesis of 2-acetamido-2-deoxy-1-thio-ß-D-glucopyranosides*

KHUSHI L. MATTA, EDWARD A. Z. JOHNSON, RAVINDAR N. GIROTRA, AND JOSEPH J. BARLOW
Department of Gynecology, Roswell Park Memorial Institute, Buffalo, New York 14203 (U. S. A.)
(Received, April 19th, 1973; accepted, in revised form, June 18th, 1973)

The affinity chromatography of some β-D-glycosidases has been accomplished by using insoluble affinity-supports obtained by coupling 1-thio-β-D-glycopyranosides to agarose[1,2]. For the isolation of 2-acetamido-2-deoxy-β-D-glucosidase, *p*-aminobenzyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside and related compounds have been prepared according to the methods in this report.

The starting material, 2-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-2-thiopseudourea hydrochloride (**1**), was obtained by reaction of 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranosyl chloride and powdered thiourea in acetone as described by Horton and Wolfrom[3]. The crystalline material **1**, without further purification, when submitted to reductive cleavage as described by Černý *et al.*[4] yielded 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranose (**2**) in 58% yield. Compound **2**, thus obtained, on reaction with benzyl bromide in the presence of potassium carbonate[2,4,5] produced benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-glucopyranoside (**3**) in 89% yield. Compound **3**, on exposure to a catalytic amount of sodium methoxide in methanol[6], furnished benzyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (**4**) in 80% yield.

The mercaptan **2**, on reaction with *p*-nitrobenzyl bromide under similar conditions, gave compound **5** which, on deacylation, yielded *p*-nitrobenzyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (**6**) in 66% yield. Hydrogenation of



1

2 R = Ac, R' = H
3 R = Ac, R' = CH_2Ph
4 R = H, R' = CH_2Ph
5 R = Ac, R' = $CH_2-C_6H_4-NO_2-(P)$
6 R = H, R' = $CH_2-C_6H_4-NO_2-(P)$
7 R = H, R' = $CH_2-C_6H_4-NH_2-(P)$

*This work was aided by Institutional Research Grant IN-54 of the American Cancer Society.

compound **6** with palladium–barium sulfate as catalyst produced *p*-aminobenzyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (**7**).

EXPERIMENTAL

General. — Melting points were taken on a Fisher–Johns apparatus and are uncorrected. N.m.r. spectra were obtained with a Varian A-60 instrument; chloroform-*d* was the solvent and tetramethylsilane the internal standard. I.r. spectra were recorded for potassium bromide discs with a Perkin–Elmer Model 457 spectrophotometer. Ascending t.l.c. was carried out on plates coated with a 0.25-mm layer of silica gel HF-254 (Merck, Darmstadt). The components were located with potassium permanganate and sulfuric acid. Optical rotations were measured with Perkin–Elmer polarimeter Model 141. Elementary analyses were performed by Robertson Laboratory, Florham Park, New Jersey.

*2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-*D*-glucopyranose* (**2**). — A solution of potassium pyrosulfite (5 g) in water (20 ml) was heated at 85° and chloroform (30 ml) was introduced followed by addition of compound[3] **1** (10 g). The reaction mixture was boiled for 15 min with constant stirring. After cooling, the organic layer was separated, washed with water, and dried (sodium sulfate). The solvent was evaporated under diminished pressure and the residue crystallized from ethyl acetate–petroleum ether to give compound **2** (4.8 g, 58%); m.p. 160–162°, $[\alpha]_D^{25}$ −16° (*c* 1, chloroform), lit.[7] m.p. 167–168°, $[\alpha]_D^{25}$ −14.5°.

*Benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-*D*-glucopyranoside* (**3**). — To a solution of compound **2** (1.8 g) in acetone (8 ml) was added benzyl bromide (0.9 g). A solution of potassium carbonate (0.63 g) in water (5 ml) was introduced, and the reaction mixture was agitated for 45 min at room temperature. The reaction mixture was diluted with an equal amount of water and extracted with chloroform. The extract was washed twice with water and then dried. After removal of sodium sulfate, the chloroform solution (40–50 ml) was diluted with anhydrous ether (15–20 ml) for crystallization of compound **3**; yield 2 g (89%), m.p. 199–202°, $[\alpha]_D^{27}$ −118° (*c* 1, chloroform); t.l.c. R_F 0.58 (9:1 benzene–methanol); ν_{max}^{KBr} 3340 (NH), 1745 (OAc), 1660, 1530 (–CONH), and 700 cm^{-1} (aromatic); n.m.r. data: τ 2.7 (5H, C_6H_5), 6.15 (2H, $SCH_2C_6H_5$), 7.86-7.96 (9H, OAc), 8.08 (3H, NAc), and 4.83 (doublet 1H, *J* 9 Hz, β-D-linkage).

Anal. Calc. for $C_{21}H_{27}NO_8S$: C, 55.61; H, 6.00; N, 3.08; S, 7.07. Found: C, 55.35; H, 6.23; N, 3.01; S, 7.20.

*Benzyl 2-acetamido-2-deoxy-1-thio-β-*D*-glucopyranoside* (**4**). — A solution of compound **3** (1 g) in abs. methanol (10 ml) was added to a solution of sodium methoxide (10 ml, prepared from 0.1 g of sodium). Fine crystals appeared in the reaction mixture, which was kept for 3 h at room temperature. A few drops of acetic acid were introduced for neutralization and the contents were cooled to 0° and filtered to give benzyl 2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (0.25 g). The mother liquor was evaporated and the residue obtained was crystallized from methanol to give

additional amounts of compound **4**; yield 0.58 g (80%); m.p. 225–227°, $[\alpha]_D^{27}$ −111° (*c* 1, water); t.l.c. R_F 0.71 (3:2 benzene–methanol); ν_{max}^{KBr} 3480–3200 (OH, NH), 1665, 1540 (–CONH), and 700 cm^{-1} (aromatic).

Anal. Calc. for $C_{15}H_{21}NO_5S$; C, 55.02; H, 6.47; N, 4.28; S, 9.79. Found: C, 54.80; H, 6.51; N, 4.05; S, 10.05.

p-*Nitrobenzyl 2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy-1-thio-β*-D-*glucopyranoside* (**5**). — A solution of compound **2** (2.2 g) in acetone (10 ml) and *p*-nitrobenzyl bromide (1.44 g) was treated with a solution of potassium carbonate (0.84 g) in water (12 ml). The product was isolated as described already for compound **3**. The compound was recrystallized from chloroform–ether; yield 2.8 g (93%); m.p. 217–219°, $[\alpha]_D^{27}$ −125° (*c* 1, chloroform); t.l.c. R_F 0.51 (9:1 benzene–methanol); ν_{max}^{KBr} 3300 (NH), 1745 (OAc), 1660, 1550 (CONH), 1520, 1375 (NO_2), and 1600, 725, 690 cm^{-1} (aromatic); n.m.r. data: τ 1.75, 2.5 (multiplet 4H, $C_6H_4NO_2$), 6.0 (2H, $SCH_2C_6H_4$), 7.85–7.92 (9H, OAc), 8.08 (3H, NAc), and 4.88 (doublet, *J* 9 Hz (1H, *β*-D-linkage).

Anal. Calc. for $C_{21}H_{26}N_2O_{10}S$; C, 50.93; H, 5.26; N, 5.62; S, 6.43. Found: C, 50.47; H, 5.47; N, 5.50; S, 6.63.

p-*Nitrobenzyl 2-acetamido-2-deoxy-1-thio-β*-D-*glucopyranoside* (**6**). — To compound **5** (2.4 g) in abs. methanol (25 ml) was added 10 ml of abs. methanol in which sodium (0.25 g) had been dissolved. The reaction mixture was kept for 3 h at room temperature and then neutralized with acetic acid and evaporated. The residue was twice crystallized from methanol to give compound **6**; yield 1.2 g (66%); m.p. 231–233°, $[\alpha]_D^{27}$ −116° (*c* 1, 50% methanol); t.l.c. R_F 0.73 (3:2 benzene–methanol); ν_{max}^{KBr} 3480–3200 (broad OH, NH), 1650, 1550 (CONH), 1570, 1340 (NO_2), 710, and 680 cm^{-1} (aromatic).

Anal. Calc. for $C_{15}H_{20}N_2O_7S$: C, 48.37; H, 5.41; N, 7.52; S, 8.61. Found: C, 48.10; H, 5.56; N, 7.40; S, 8.83.

p-*Aminobenzyl 2-acetamido-2-deoxy-1-thio-β*-D-*glucopyranoside* (**7**). — Compound **6** (0.5 g) was dissolved in abs. methanol (180 ml) and hydrogenated for 12 h at room temperature with a hydrogen pressure of 40 $lb.in^{-2}$ over palladium–barium sulfate (0.3 g). The catalyst was removed by passing the mixture through a Celite pad and the filtrate was evaporated under diminished pressure below 20°. The residue obtained was crystallized from abs. methanol to give compound **7** (0.33 g, 72%); m.p. 204–207°, $[\alpha]_D^{25}$ −120° (*c* 1, methanol); t.l.c. R_F 0.45 (3:2 benzene–methanol); ν_{max}^{KBr} 3400 (broad OH), 3310 (NH_2), 1645, 1545 (CONH), 745, and 680 cm^{-1} (aromatic).

Anal. Calc. for $C_{15}H_{22}N_2O_5S$: C, 52.61; H, 6.48; N, 8.18; S, 9.30. Found: C, 52.33; H, 6.30; N, 7.96; S, 9.65.

ACKNOWLEDGMENT

The authors are grateful to Dr. W. Korytnyk for providing infrared and optical rotation facilities.

REFERENCES

1 E. STEERS, JR., P. CUATRECASAS, AND H. B. POLLARD, *J. Biol. Chem.*, 246 (1971) 196.
2 M. CLAYSSENS, H. KERSTERS-HILDERSON, J. P. VAN WAUWE. AND C. K. DE BRUYNE, *FEBS Lett.*, 11 (1970) 336.
3 D. HORTON AND M. L. WOLFROM, *J. Org. Chem.*, 27 (1962) 1794.
4 M. ČERNÝ, J. VRKOČ, AND J. STANĚK, *Collect. Czech. Chem. Commun.*, 24 (1959) 64; M. ČERNÝ AND T. PACÁK, *ibid.*, 24 (1959) 2566.
5 M. CLAYSSENS AND C. K. DE BRUYNE, *Carbohyd. Res.*, 22 (1972) 460.
6 G. ZEMPLÉN AND E. PACSU, *Methods Carbohyd. Chem.*, 1 (1962) 215.
7 W. MEYER ZU RECKENDORF, AND W. A. BONNER, *J. Org. Chem.*, 26 (1961) 4596.