Carbohydrate Research, 232 (1992) 169–175
Elsevier Science Publishers B.V., Amsterdam

Note

Synthesis 1-thioglycosides from 1-sulfenates

Izabela Fokt and Wieslaw Szeja

Institute of Organic Chemistry and Technology, 44-100 Gliwice (Poland)

(Received April 12th, 1991; accepted December 30th, 1991)

Thioalkyl and thioaryl groups can be used to protect the anomeric position of sugars and can be activated to yield glycosyl donors [1,2]. Thioglycosides can be activated by mercury(II) sulfate [3], mercury(II) chloride [4,5], phenyl mercury trifluoromethanesulfonate [6], mercury(II) benzoate [7], mercury(II) nitrate [8], copper trifluoromethanesulfonate [9], and lead(II) perchlorate [10]. Generation of glycosyl donors involves the conversion of thioglycosides into glycosyl bromides [11–13] and glycosyl fluorides [14], and activation by use of methyl triflate [15–18], dimethyl(methyltio) sulfonium triflate [19], and nitrosyl tetrafluoroborate [20].

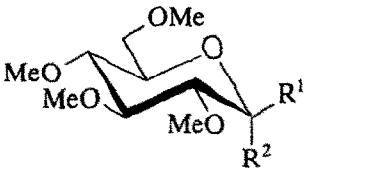
Numerous methods are available for the preparation of thioglycosides [21,22], of which the most general is the S_N2 reaction of alkali salts of thiophenols or alkanethiols with acetylglycosyl halides [24]. Acetylated alkyl 1-thio-D-glucopyranosides can be obtained by reaction of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose with alkyl bromides or iodides [25]. In order to prepare 1-thioglycosides with non-participating groups, these compounds were deacylated and subsequently alkylated, usually with benzyl halides. The trichloroacetimidate method has been used to synthesise thio sugars and thioglycosides from sugar derivatives with HO-1 unprotected [26]. A disadvantage of this procedure is the use of toxic and malodorous thiols and thiophenols.

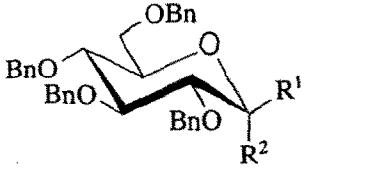
Carbohydrate sulfenates may be prepared [27] by the reaction of appropriate sugar derivatives with 2-nitrobenzenesulfenyl chloride or 2,4-dinitrobenzenesulfenyl chloride in the presence of triethylamine, and we now report a new synthesis of aryl 1-thioglycosides by deoxygenation of monosaccharide sulfenates with triethyl phosphite.

Thus, 2,3,4,6-tetra-*O*-methyl-1-*O*-(2-nitrophenylsulfenyl)-α-D-glucopyranose (**1a**), 2,3,4,6-tetra-*O*-benzyl-1-*O*-(2-nitrophenylsulfenyl)-α-D-glucopyranose (**2a**), 2,3,4,6-tetra-*O*-benzyl-1-*O*-(2-nitrophenylsulfenyl)-α,β-D-galactopyranose (**3a**,

Correspondence to: Dr. W. Szeja, Institute of Organic Chemistry and Technology, 44-100 Gliwice, Poland.

α,β-ratio 1 : 3), 2,3,4,6-tetra-*O*-benzyl-1-*O*-(2-nitrophenylsulfenyl)-α,β-D-mannopyranose (**4a**, α,β-ratio 4 : 1), 2,3 : 5,6-di-*O*-isopropylidene-1-*O*-(2-nitrophenylsulfenyl)-α-D-mannofuranose (**5a**), and 1-*O*-(2,4-dinitrophenylsulfenyl)-2,3 : 5,6-di-*O*-isopropylidene-α-D-mannofuranose (**5b**) were deoxygenated in benzene at room temperature or in chloroform at −50° to give **1b**–**4b**, **5c**, and **5d**, respectively. Each



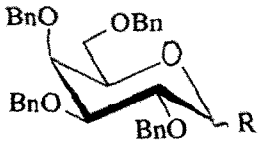


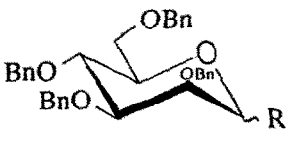
1a $R^1 = H$, $R^2 = -OS-C_6H_4-NO_2$

2a $R^1 = H$, $R^2 = -OS-C_6H_4-NO_2$

1b $R^1 = -S-C_6H_4-NO_2$, $R^2 = H$

2b $R^1 = -S-C_6H_4-NO_2$, $R^2 = H$



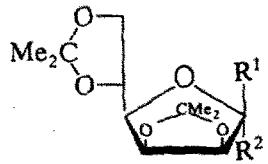


3a $R = -OS-C_6H_4-NO_2$

4a $R = -OS-C_6H_4-NO_2$

3b $R = -S-C_6H_4-NO_2$

4b $R = -S-C_6H_4-NO_2$



5a $R^1 = H$, $R^2 = -OS-C_6H_4-NO_2$

reaction proceeded with inversion of configuration at C-1 and similar results were obtained with trimethyl phosphite, triphenyl phosphite, and triethylphosphine.

5b $R^1 = H$, $R^2 = -OS-C_6H_3(NO_2)(O_2N)$

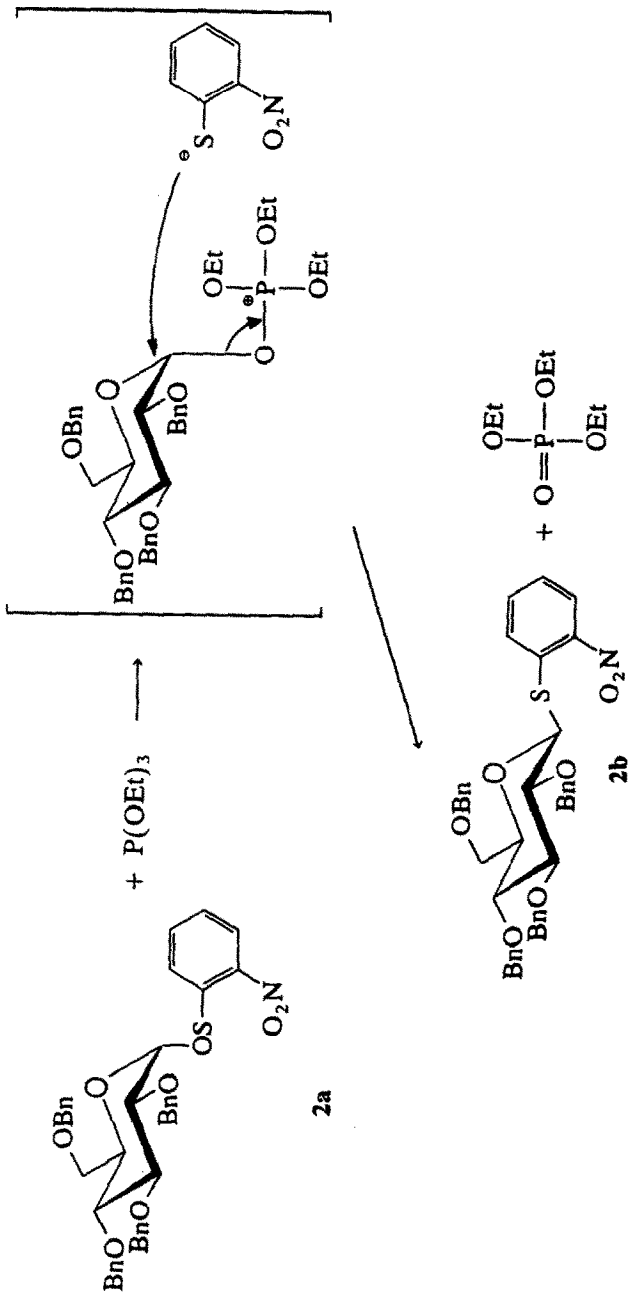
5c $R^1 = -S-C_6H_3(O_2N)$, $R^2 = H$

5d $R^1 = -S-C_6H_3(NO_2)(O_2N)$, $R^2 = H$

The reaction of 2,3,4,6-tetra-*O*-benzyl-1-*O*-(2-nitrophenylsulfenyl)-α-D-glucopyranose (**2a**) with triethyl phosphite was examined in more detail. The main products were 2-nitrophenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**2b**) and triethyl phosphate together with traces of 2,3,4,6-tetra-*O*-benzyl-D-glucose and ethyl 2-nitrophenyl sulphide. The reaction in $CDCl_3$ could be monitored by NMR spectroscopy. At temperatures down to −50°, only the ^{31}P resonances [28] of triethyl phosphite (δ 139.07) and triethyl phosphate (δ 0.5) could be observed; a signal for a phosphorylated intermediate formed from triethyl phosphite and **2a** could not be detected.

Phosphorus(III) compounds can be regarded as thiophilic reagents [29] and they can attack sulfenates [30] and sulfenamides [31] at the more electropositive sulfenyl sulfur atom. Phenyl sulfenamides treated with dialkyl or trialkyl phosphites form phosphorothioates [32]. The sulfur atom of 1,1-dimethanesulfenates is abstracted by trivalent phosphorus derivatives to afford the corresponding ethers [33]. Regioselective attack of trivalent phosphorus on sulfenates or sulfenamides has been observed. Thus, treatment of (2-benzothiazolyl)sulfenamides with dialkyl or trialkyl phosphites gave phosphoroamidates in excellent yields [32]. In a study of the abstraction from oxyphosphoranesulfenyl chlorides [$R^1R^2P(O)SCl$], Michalski et al. [34] found both deoxygenation and desulfuration. Barton et al. [35] found that benzyl methanesulfenate reacted with tributylphosphine in toluene at 20° to give the phosphine oxide and benzyl methyl sulfide, possibly by an abstraction process via a phosphorane intermediate and subsequent ionisation.

Our results are consistent with the following. Nucleophilic attack of triethyl phosphite at O-1 of **2a** to afford a phosphonium ion (Scheme 1). Attack of the liberated thiolate anion at C-1 then gives the thioglycoside **2b** and triethyl phosphate. Support for the above mechanism is the fact that, when the reaction was performed in the presence of a thiophilic reagent (silver trifluoroacetate) and a small amount of water, the main product was 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose.



Scheme 1.

EXPERIMENTAL

General.—Melting points were determined on a Kofler hot-stage and are uncorrected. Optical rotations were measured with a Zeiss Jena Polamat polarimeter. The ^{1}H- and ^{13}C-NMR spectra were recorded with Bruker (500 MHz), Varian (300 MHz), Gemini (200 MHz), and Tesla (80 MHz) instruments.

The progress of each reaction was monitored by TLC on Silica Gel 60 (0.2–0.063 mm, Merck).

Synthesis of thioglycosides.—To a solution of the sulfenate (1 mmol, prepared as described [27]) in dry benzene (30 mL) was added triethyl phosphite (0.50 g, 0.51 mL, 3 mmol). The mixture was stirred for 30 min at room temperature, then diluted with benzene (10 mL), washed with water, and dried ($MgSO_4$), and the solvent was evaporated. Column chromatography (benzene, 20:1 and 10:1 benzene–ether) of the residue gave the thioglycoside. The following compounds were prepared in this manner.

2-Nitrophenyl 2,3,4,6-tetra-*O*-methyl-1-thio-β-D-glucopyranoside (**1b**; 0.26 g, 69.5%), mp 117–118° (from benzene), $[\alpha]_{546}^{20}$ −128° (*c* 0.9, $CHCl_3$). ^{1}H-NMR data ($CDCl_3$): δ 3.40, 3.58, 3.63, 3.70 (4 s, each 3 H, 4 MeO), 2.95–3.83 (m, 6 H, H-2,3,4,5,6a,6b), 4.60 (d, 1 H, $J_{1,2}$ 8 Hz, H-1), 7.13–8.15 (m, 4 H, aromatic H).

Anal. Calcd for $C_{16}H_{23}NO_7S$: C, 51.45; H, 6.22; N, 3.75. Found: C, 51.12; H, 6.41; N, 3.32.

2-Nitrophenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-β-D-glucopyranoside (**2b**; 0.373 g, 55%), mp 116–118° (from benzene), $[\alpha]_{546}^{20}$ −104° (*c* 2.53, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H, δ 3.61–3.83 (m, 6 H, H-2,3,4,5,6a,6b), 4.53–4.99 (m, 9 H, H-1 and 4 PhCH_2), 7.2–7.33 (m, 22 H, aromatic H), 8.11 (dd, 1 H, aromatic H); ^{13}C, δ 69.22 (C-6), 73.49 (C-5), 79.30 (C-4), 80.89 (C-2), 85.69 (C-3), 86.82 (C-1), 125.51–138.47 (aromatic C).

Anal. Calcd for $C_{40}H_{39}NO_7S$: C, 70.87; H, 5.81; N, 2.07. Found: C, 70.59; H, 5.56; N, 2.20.

2-Nitrophenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α,β-D-galactopyranoside (**3b**; 0.383 g, 56.6%), α,β-ratio 3:1, syrup, $[\alpha]_{545}^{20}$ −21° (*c* 0.96, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H, δ 3.5–4.11 (m, 6 H, H-2,3,4,5,6a,6b), 4.34–5.01 (m, 9 H, H-1β and 4 PhCH_2), 5.8 (d, 1 H, $J_{1,2}$ 5.5 Hz, H-1α), 7.1–7.34 (m, 22 H, aromatic H), 7.78–8.07 (m, 2 H, aromatic H); ^{13}C, δ 84.71 (C-1α), 85.88 (C-1β).

Anal. Calcd for $C_{40}H_{39}NO_7S$: C, 70.87; H, 5.81; N, 2.07. Found: C, 70.89; H, 5.82; N, 2.28.

2-Nitrophenyl 2,3,4,6-tetra-*O*-benzyl-1-thio-α,β-D-mannopyranoside (**4b**; 0.434 g, 64%), α,β-ratio 1:4, syrup, $[\alpha]_{546}^{20}$ −2° (*c* 0.5, $CHCl_3$). NMR data ($CDCl_3$): ^{1}H, δ 3.54–4.03 (m, 6 H, H-1,2,3,4,5,6a,6b), 4.34–4.95 (m, 9 H, H-1β and 4 PhCH_2), 5.62 (d, 1 H, $J_{1,2}$ 2.4 Hz, H-1α), 7.11–7.25 (m, 22 H, aromatic H), 7.72–7.98 (m, 2 H, aromatic H); ^{13}C, δ 85.68 (C-1α), 86.16 (C-1β).

Anal. Calcd for $C_{40}H_{39}NO_7S$: C, 70.87; H, 5.81; N, 2.07. Found: C, 70.91; H, 5.65; N, 2.43.

2-Nitrophenyl 2,3:5,6-di-*O*-isopropylidene-1-thio-α-D-mannofuranoside (**5c**; 0.25 g, 56.6%), mp 138.5–139.5° (from benzene), $[\alpha]_{546}^{20}$ −239° (*c* 2.1, $CHCl_3$). ^{1}H-NMR data ($CDCl_3$): δ 1.43, 1.50, 1.63 (3 s, 12 H, 2 Me_2C), 3.73 (dd, 1 H, *J* 4, 6 Hz, H-4), 4.16 (m, 2 H, H-6a,6b), 4.38–4.65 (m, 1 H, H-5), 4.75–4.98 (m, 3 H, H-1,2,3), 7.18–8.17 (m, 4 H, aromatic H).

Anal. Calcd for $C_{18}H_{23}NO_7S$: C, 54.39; H, 5.48; N, 3.52. Found: C, 53.68; H, 5.93; N, 3.15.

2,4-Dinitrophenyl 2,3:5,6-di-*O*-isopropylidene-1-thio-α-D-mannofuranoside (**5d**; 0.135 g, 30%), mp 130° (dec) (from benzene), $[\alpha]_{546}^{20}$ −497° (*c* 3.25, $CHCl_3$). ^{1}H-NMR data ($CDCl_3$): δ 1.35, 1.4, 2.8 (3 s, 12 H, 2 Me_2C), 3.75 (dd, 1 H, *J* 3, 5.5 Hz, H-4), 4.13 (m, 2 H, H-6a,6b), 4.5 (m, 1 H, H-5), 4.73–4.98 (m, 3 H, H-1,2,3), 7.95 (d, 1 H, aromatic H), 8.3 (dd, 1 H, aromatic H), 8.89 (d, 1 H, aromatic H).

Anal. Calc. for $C_{18}H_{22}N_2O_9S$: C, 48.86; H, 5.02; N, 6.33; S, 7.25. Found: C, 48.54; H, 5.33; N, 6.35; S, 6.85.

Reaction of 2,3,4,6-tetra-O-benzyl-1-O-(2-nitrophenylsulfenyl)-α-D-glucopyranose (**2a**) *with triethyl phosphite in the presence of silver trifluoroacetate.*—To a solution of **2a** (1 mmol) in benzene (3 mL) was added triethyl phosphite (0.50 g, 0.51 mL, 3 mmol) and silver trifluoroacetate (0.22 g, 1 mmol). The mixture was stirred for 30 min at room temperature, then diluted with benzene (10 mL), washed with water, and dried ($MgSO_4$), and the solvent was evaporated. Column chromatography (benzene, 10:1 benzene–ether) of the residue gave 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose, mp 149–150° (from hexane); lit. [37] mp 151–152°.

ACKNOWLEDGMENT

The Polish Academy of Science is thanked for financial support (grant CPBP 01.13).

REFERENCES

1 P. Fügedi, P.J. Garegg, H. Lönn, and T. Norberg, *Glycoconjugate J.*, 4 (1987) 97–108.
2 R.R. Schmidt, *Angew. Chem. Int. Ed. Engl.*, 25 (1986) 212–235.
3 R.J. Ferrier, R.W. Hay, and N. Vethaviyasra, *Carbohydr. Res.*, 27 (1973) 55–61.
4 T.Y.R. Tsai, H. Jin, and K. Wiesner, *Can. J. Chem.*, 62 (1984) 1403–1405.
5 K. Wiesner, T.Y.R. Tsai, and H. Jin, *Helv. Chim. Acta*, 68 (1985) 300–314.
6 P.J. Garegg, C. Henrickson, and T. Norberg, *Carbohydr. Res.*, 116 (1983) 162–165.
7 J.W. van Cleve, *Carbohydr. Res.*, 70 (1979) 161–164.
8 S. Hanessian, C. Bacquet, and N. Lehong, *Carbohydr. Res.*, 80 (1980) c17–c22.
9 T. Mukaiyama, T. Nakatsuka, and S. Shoda, *Chem. Lett.*, (1979) 487–490.
10 P.G.M. Wuts and S.S. Bigelow, *J. Org. Chem.*, 48 (1983) 3489–3493.
11 M.L. Wolfrom and W. Groebke, *J. Org. Chem.*, 28 (1963) 2986–2988.
12 F. Weygand, H. Ziemann, and H.J. Bestmann, *Chem. Ber.*, 91 (1958) 2534–2536.
13 S. Koto, T. Uchida, and S. Zen, *Bull. Chem. Soc. Jpn.*, 46 (1973) 2520–2553.
14 K.C. Nicolaou, R.E. Dolle, D.P. Papahatjis, and J.L. Randall, *J. Am. Chem. Soc.*, 106 (1984) 4189–4192.
15 H. Lönn, *Carbohydr. Res.*, 139 (1985) 105–113.

16 H. Lönn, *Carbohydr. Res.*, 139 (1985) 115–121.
17 H. Lönn, *J. Carbohydr. Chem.*, 6 (1987) 310–316.
18 P. Fügedi and P.J. Garegg, *Carbohydr. Res.*, 149 (1986) c9–c12.
19 F. Dasgupta and P.J. Garegg, *Carbohydr. Res.*, 177 (1988) c13–c17.
20 V. Pozsgay and H.J. Jennings, *J. Org. Chem.*, 52 (1987) 4635–4637.
21 D. Horton and D.H. Hutson, *Adv. Carbohydr. Chem.*, 18 (1963) 123–200.
22 D. Horton, *Methods Carbohydr. Chem.*, 2 (1963) 368–373.
23 B. Capon, P.M. Collins, A.A. Levy, and W.G. Overend, *J. Chem. Soc.*, (1964) 3242–3254.
24 B. Helferich and P. Turk, *Chem. Ber.*, 89 (1956) 2215–2219, and references therein.
25 M. Černy and J. Pečak, *Chem. Listy*, 52 (1958) 2090–2093.
26 R.R. Schmidt and M. Stumpp, *Liebigs Ann. Chem.*, (1983) 1249–1256.
27 I. Fokt and W. Szeja, *Carbohydr. Res.*, 222 (1991) 271–276.
28 J. Emsley and D. Hall, *The Chemistry of Phosphorus*, Harper and Row, London, 1976.
29 J.I. Cadogan and R.K. Mackie, *Chem. Soc. Rev.*, 3 (1974) 87–137, and references therein.
30 E. Kühle, *The Chemistry of the Sulfenic Acids*, Thieme, Stuttgart, 1973.
31 L. Craine and M. Raban, *Chem. Rev.*, 89 (1989).
32 S. Torii, N. Sayo, and H. Tanaka, *Chem. Lett.*, (1980) 695–698.
33 D.H.R. Barton, G. Page, and D.A. Widdowson, *Chem. Commun.*, (1970) 1466.
34 B. Krawiecka, J. Michalski, J. Mikołajczyk, J. Omelańczuk, and A. Skowrońska, *J. Chem. Soc., Chem. Commun.*, (1974) 630–631.
35 D.H.R. Barton, D.A. Widdowson, and D.P. Manly, *J. Chem. Soc., Perkin Trans. 1*, (1975) 1568–1574.
36 L.L. Chang and D.B. Denney, *J. Chem. Soc., Chem. Commun.*, (1974) 84.
37 C.P.J. Glaudemans and H.G. Fletcher, Jr., *Methods Carbohydr. Chem.*, 6 (1972) 374–375.