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# Note

## Synthesis of sulfenates of sugar derivatives

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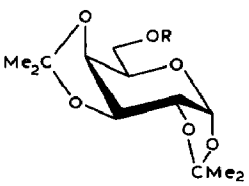
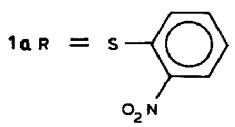
Sulfenates are widely used in organic synthesis[1] and they have been proposed as protecting groups in carbohydrate chemistry[2]. 2-Deoxyglycosides have been synthesised from glycals by Lewis-acid-mediated activation of benzenesulfenic esters[3]. The 6- and 4-phenylsulfenates of glucopyranosides have been prepared from suitably protected sugars and phenylsulfenyl chloride[4], but the products were not isolated and characterised.

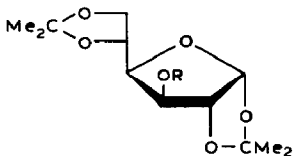
The most common method employed for the synthesis of sulfenates is the reaction of sulfenyl halides with alcohols or phenols in the presence of pyridine[1]. Sulfenamides can function as sulfenyl transfer reagents, *e.g.*, the thiophthalimides[5]. We now report on the synthesis of sulfenates of sugar derivatives.

The reactions of 2-nitrobenzenesulfenyl chloride with 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**1**) and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2**) were studied first. Treatment of **1** with sulfenyl chloride in the presence of tertiary amines gave the corresponding sulfenates in good yields. The presence of the nitro group in the benzene ring increases the stability of the sulfenates. Thus, the 2,4-dinitrobenzenesulfenates could be stored for several months at room temperature, whereas the benzenesulfenates required anhydrous conditions even in their preparation.

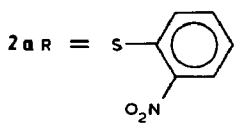



**1** R = H




**2** R = H

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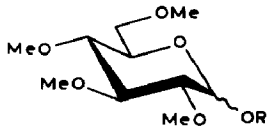
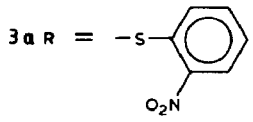
Phase-transfer catalysis[6] proved not to be useful for the synthesis of sugar sulfenates, and the application of thiophthalimides was also not successful.

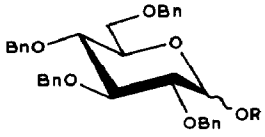
The synthesis of 1-sulfenates of sugar derivatives was studied next, using 2,3,4,6-tetra-*O*-methyl-D-glucopyranose (**3**). Reaction of **3** with the sulfenyl chloride in the presence of tertiary amines at room temperature rapidly gave an $\alpha,\beta$-mixture of the 1-sulfenates. The anomers were isolated and characterised on the basis of elemental analysis, n.m.r. data, and optical rotations (see Experimental section).

When pyridine or 2,4,6-trimethylpyridine was used as the base, similar $\alpha,\beta$-mixtures were obtained. Reactions at the anomeric centre can be improved by using metallated derivatives[7]. Treatment of **3** with sodium *tert*-pentylate followed by addition of the sulfenyl chloride gave an $\alpha,\beta$-mixture in which the $\beta$ anomer preponderated. Similar selectivity was observed when **3** reacted with 2-nitrophenylsulfenyl chloride under phase-transfer catalysis, but the yield was 20% lower. The higher content of $\beta$-sulfenate can be attributed to the higher nucleophilicity of the $\beta$-1-alkoxide due to the anomeric effect[8].

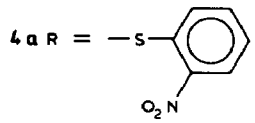


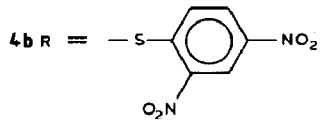

**3** R = H




**4** R = H

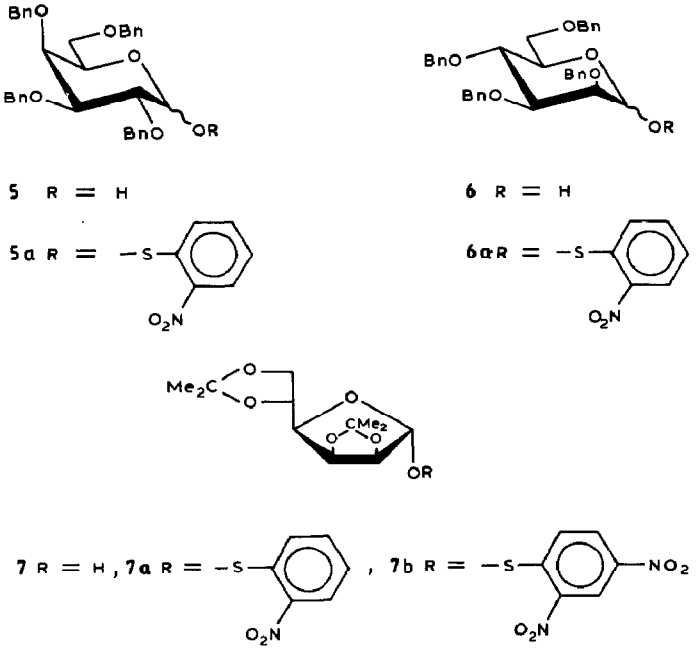



Reaction of 2,3,4,6-tetra-*O*-benzyl-D-gluco- (**4**), -D-galacto- (**5**), and -D-manno-pyranose (**6**) with 2-nitro- or 2,4-dinitro-benzenesulfenyl chloride in the presence of triethylamine gave $\alpha,\beta$-mixtures of 1-sulfenates with the $\alpha$ anomer preponderating. The poor stereoselectivity was not improved by the use of such tertiary amines as pyridine and 2,4,6-trimethylpyridine, and lowering of the temperature of reactions did not improve the stereoselectivity.

Excellent selectivites and yields of $\alpha$ isomer were obtained in the reaction of 2-nitro- and 2,4-dinitro-benzenesulfenyl chloride with 2,3:5,6-di-*O*-isopropylidene-$\alpha$-D-mannofuranose (**7**). The reaction of (**7**) with 2,4-dinitrobenzenesulfenyl chloride has been described[2], but the structure of the product was not determined, and the physical constants differ from those now reported. The 2-nitro- and 2,4-dinitro-benzenesulfenic esters could be stored without decomposition for prolonged periods with exclusion of

moisture, whereas the 1-benzenesulfenates decomposed during purification by column chromatography. The 1-sulfenates reacted with diethylamine to form sulfenamides and expose the anomeric hydroxyl group, and were hydrolysed in the presence of acid to give the parent sugar. They isomerised easily under anhydrous conditions in the presence of Lewis acids. Thus, treatment of the benzene solution of 2,3,4,6-tetra-*O*-methyl-1-*O*-(2-nitrophenylsulfenyl)-D-glucopyranose (**3a**, α,β-ratio 3:1) with titanium tetrachloride gave a 2:1 α,β-mixture.




## 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 $^{13}C$-n.m.r. spectra were recorded with Bruker (500 MHz), Gemini (200 MHz), Varian (300 MHz), and Tesla (80 MHz) instruments. The progress of all reactions was monitored by t.l.c. on Silica Gel 60 (Merck). Column chromatography was performed with Kieselgel 60 (0.2–0.063 mm, Merck). Phenylsulfenyl chloride[9], 2-nitrophenylsulfenyl chloride[10], and 2,4-dinitrophenylsulfenyl chloride[11] were prepared as described.

*Synthesis of sulfenates.* — To a solution of the sugar derivative (1 mmol) in dichloromethane (5 mL) was added the sulfenyl chloride (1 mmol). The mixture was cooled to 0° and a solution of triethylamine (0.30 g, 0.42 mL, 3 mmol) in dichloromethane (2 mL) was added. The mixture was stirred for 5 min, then washed with

aqueous 5% sulfuric acid (5 mL) and 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 sulfenate. The following compounds were prepared in this manner.

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2-nitrobenzenesulfenyl)-α-D-galactopyranose (**1a**; 0.31 g, 74.1%), syrup, $[\alpha]_{546}^{20}$ −92° (*c* 0.7, chloroform). $^1$H-N.m.r. data ($CDCl_3$): δ 1.35, 1.43, 1.55 (4 s, 12 H, 2 $Me_2C$), 3.33–4.66 (m, 6 H, H-2,3,4,5,6a,6b), 5.53 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 7.25 (dd, 1 H, aromatic H), 7.66 (td, 1 H, aromatic H), 7.85 (td, 1 H, aromatic H), 8.13 (dd, 1 H, aromatic H).

*Anal.* Calc. for $C_{18}H_{23}NO_8S$: C, 52.28; H, 5.61; N, 3.39; S, 7.79. Found: C, 52.45; H, 5.72; N, 3.41; S, 7.60.

1,2:5,6-Di-*O*-isopropylidene-3-*O*-(2-nitrobenzenesulfenyl)-α-D-glucofuranose (**2a**; 0.34 g, 81%), m.p. 87–90° (from benzene), $[\alpha]_{546}^{20}$ +53° (*c* 0.3, chloroform). $^1$H-N.m.r. data ($CDCl_3$): δ 1.35, 1.50 (2 s, 12 H, 2 $Me_2C$), 3.95–4.68 (m, 5 H, H-2,4,5,6a,6b), 4.90 (d, 1 H, $J_{1,2}$ 3 Hz, H-2), 5.99 (d, 1 H, H-1), 7.50–8.38 (m, 4 H, aromatic H).

*Anal.* Calc. for $C_{18}H_{23}NO_8S$: C, 52.28; H, 5.61; N, 3.39; S, 7.76. Found: C, 52.53; H, 5.69; N, 3.38; S, 7.79.

2,3,4,6-Tetra-*O*-methyl-1-*O*-(2-nitrobenzenesulfenyl)-α-D-glucopyranose (**3a**; 0.285 g, 73.5%), m.p. 102–103° (from benzene), $[\alpha]_{546}^{20}$ +244° (*c* 2.0, chloroform). $^1$H-N.m.r. data ($CDCl_3$): δ 3.1–3.9 (m, 18 H, H-2,3,4,5,6a,6b and 4 MeO), 5.01 (d, 1 H, $J_{1,2}$ 4 Hz, H-1), 7.23 (td, 1 H, aromatic H), 7.68 (td, 1 H, aromatic H), 8.2 (m, 2 H, aromatic H).

*Anal.* Calc. for $C_{16}H_{23}NO_8S$: C, 49.34; H, 5.96; N, 3.59; S, 8.23. Found: C, 49.27; H, 6.12; N, 3.06; S, 8.25.

2,3,4,6-Tetra-*O*-methyl-1-*O*-(2-nitrobenzenesulfenyl)-β-D-glucopyranose (**3a**; 0.095 g, 24.5%), m.p. 115–117° (from benzene), $[\alpha]_{546}^{20}$ −17° (*c* 0.8, chloroform). $^1$H-N.m.r. data ($CDCl_3$): δ 3.13–3.75 (m, 18 H, H-2,3,4,5,6a,6b and 4 MeO), 4.35 (d, 1 H, $J_{1,2}$ 7 Hz, H-1), 7.25 (td, 1 H, aromatic H), 7.52 (td, 1 H, aromatic H), 8.15 (m, 2 H, aromatic H).

*Anal.* Calc. for $C_{16}H_{23}NO_8S$: C, 49.34; H, 5.96; N, 3.59; S, 8.26. Found: C, 49.25; H, 6.01; N, 3.20; S, 8.26.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(2-nitrobenzenesulfenyl)-α-D-glucopyranose (**4a**; 0.46 g, 66%), m.p. 102–104° (from benzene), $[\alpha]_{546}^{20}$ +174° (*c* 1.0, chloroform). N.m.r. data ($CDCl_3$): $^1$H, δ 3.69–3.86 (m, 4 H, H-2,4,6a,6b), 4.01–4.20 (m, 2 H, H-3,5), 4.53, 4.66 (ABq, 2 H, 12 Hz, Ph$CH_2$), 4.5, 4.92 (ABq, 2 H, *J* 10.8 Hz, Ph$CH_2$), 4.71, 4.90 (ABq, 2 H, *J* 10.8 Hz, Ph$CH_2$), 5.08 (d, 1 H, $J_{1,2}$ 3.4 Hz H-1), 7.16–7.36 (m, 22 H, aromatic H), 8.02–8.26 (m, 2 H, aromatic H); $^{13}$C, δ 68.24 (C-6), 72.07 (C-5), 80.69 (C-2), 81.68 (C-3), 103.43 (C-1), 123.57–146.01 (aromatic C).

*Anal.* Calc. for $C_{40}H_{39}NO_8S$: C, 69.23; H, 5.68; N, 2.02; S, 4.62. Found: C, 68.83; H, 5.25; N, 2.16; S, 4.68.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(2,4-dinitrobenzenesulfenyl)-α-D-glucopyranose (**4b**; 0.53 g, 71%), m.p. 41–43° (from benzene), $[\alpha]_{546}^{20}$ +166° (*c* 1.3, chloroform). N.m.r. data ($CDCl_3$): $^1$H, δ 3.67–3.86 (m, 4 H, H-2,4,6a,6b), 4.48–5.44 (m, 8 H, 4 Ph$CH_2$), 6.41 (s, 1 H, H-1), 7.66 (dd, 1 H, aromatic H), 7.80 (dd, 1 H, aromatic H), 8.18 (d, 1 H, aromatic

H), 8.39 (d, 1 H, aromatic H), 9.01 (d, 1 H, aromatic H), 9.02 (d, 1 H, aromatic H); $^{13}C$, $\delta$ 67.98 (C-6), 72.41 (C-5), 80.53 (C-2), 81.59 (C-3), 104.59 (C-1), 120.54–153.20 (aromatic C).

*Anal.* Calc. for $C_{40}H_{38}N_2O_{10}S$: C, 65.02; H, 5.19; N, 3.79; S, 4.34. Found: C, 65.10; H, 5.04; N, 3.79; S, 4.28.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(2-nitrobenzenesulfenyl)-α-D-galactopyranose (**5a**; 0.157 g, 21.25%), syrup, $[\alpha]_{546}^{20}$ +23° (*c* 4.1, chloroform). N.m.r. data ($CDCl_3$): $^1H$, $\delta$ 3.56–4.30 (m, 6 H, H-2,3,4,5,6a,6b), 4.43–5.8 (m, 9 H, H-1 and 4 PhC$H_2$), 7.20–7.42 (m, 22 H, aromatic H), 8.05–8.25 (m, 2 H, aromatic H); $^{13}C$, $\delta$ 68.49 (C-6), 70.96 (C-5), 74.54 (C-4), 77.15 (C-2), 78.86 (C-3), 104.18 (C-1), 123.75–146.36 (aromatic C).

*Anal.* Calc. for $C_{40}H_{39}NO_8S$: C, 69.23; H, 5.68; N, 2.02. Found: C, 69.66; H, 5.48; N, 2.35.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(2-nitrobenzenesulfenyl)-β-D-galactopyranose (**5a**; 0.473 g, 63.75%), m.p. 103–105° (from benzene), $[\alpha]_{546}^{20}$ +78° (*c* 3.2, chloroform). N.m.r. data ($CDCl_3$): $^1H$, $\delta$ 3.36–4.30 (m, 6 H, H-2,3,4,5,6a,6b), 4.43–5.08 (m, 9 H, H-1 and 4 PhC$H_2$), 7.20–7.42 (m, 22 H, aromatic H), 8.05–8.25 (m, 2 H, aromatic H); $^{13}C$, $\delta$ 68.30 (C-6), 73.15 (C-5), 75.70 (C-4), 79.86 (C-2), 82.62 (C-3), 107.61 (C-1), 123.76–146.36 (aromatic C).

*Anal.* Calc. for $C_{40}H_{39}NO_8S$: C, 69.23; H, 5.68; N, 2.02. Found: C, 69.68; H, 5.50; N, 2.23.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(2-nitrobenzenesulfenyl)-D-mannopyranose (**6a**; 0.47 g, 64%), α,β-ratio 4:1, syrup, $[\alpha]_{546}^{20}$ +98° (*c* 2.4, chloroform). N.m.r. data ($CDCl_3$): $^1H$, $\delta$ 3.72–4.13 (m, 6 H, H-2,3,4,5,6a,6b), 4.53–4.86 (m, 9 H, H-1 and 4 PhC$H_2$), 4.96 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 7.27–7.39 (m, 22 H, aromatic H), 7.98–8.28 (m, 2 H, aromatic H); $^{13}C$, $\delta$ 69.07 (C-6α), 72.15 (C-6β), 79.03 (C-5α), 81.81 (C-5β), 103.80 (C-1α), 105.38 (C-1β), 122.54–145.73 (aromatic C).

*Anal.* Calc. for $C_{40}H_{39}NO_8S$: C, 69.23; H, 5.68; N, 2.02. Found: C, 69.59; H, 5.53; N, 2.32.

2,3:5,6-Di-*O*-isopropylidene-1-*O*-(2-nitrobenzenesulfenyl)-α-D-mannofuranose (**7a**; 0.34 g, 82%), syrup, $[\alpha]_{546}^{20}$ +215° (*c* 1.4, chloroform). $^1H$-N.m.r. data ($CDCl_3$): $\delta$ 1.37, 1.38, 1.44, 1.47 (4 s, 2 $Me_2C$), 3.33–4.50 (m, 5 H, H-3,4,5,6a,6b), 4.87 (d, 1 H, $J_{2,3}$ 1.4 Hz, H-2), 5.10 (s, 1 H, H-1), 7.18–7.38 (m, 1 H, aromatic H), 8.28–8.30 (m, 1 H, aromatic H).

*Anal.* Calc. for $C_{18}H_{23}NO_8S$: C, 52.28; H, 5.61; N, 3.39. Found: C, 51.91; H, 5.22; N, 3.07.

1-*O*-(2,4-Dinitrobenzenesulfenyl)-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**7b**; 0.42 g, 92%), m.p. 136° (from benzene), $[\alpha]_{546}^{20}$ +237° (*c* 1.9, chloroform). $^1H$-N.m.r. data ($CDCl_3$): $\delta$ 1.40, 1.48 (2 s, 12 H, 2 $Me_2C$), 4.03–4.53 (m, 5 H, H-3,4,5,6a,6b), 4.90 (d, $J_{2,3}$ 2 Hz, H-2), 5.18 (s, 1 H, H-1), 7.88 (d, 1 H, aromatic H), 8.46 (dd, 1 H, aromatic H), 8.89 (d, 1 H, aromatic H).

*Anal.* Calc. for $C_{18}H_{22}N_2O_{10}S$: C, 47.15; H, 4.85; N, 6.11; S, 6.99. Found: C, 47.45; H, 4.79; N, 5.67; S, 7.00.

*Synthesis of 2,3,4,6-Tetra-*O*-methyl-1-*O*-(2-nitrobenzenesulfenyl)-D-glucopyra-*

*nose* (**3a**). — To a solution of 2,3,4,6-tetra-*O*-methyl-D-glucopyranose (0.24 g, 1 mmol) in anhydrous benzene (3 mL) were added sodium hydride (50% dispersion in oil) (0.024 g, 1 mmol) and anhydrous *tert*-pentyl alcohol (0.088 g, 1 mmol), and the mixture was stirred for 15 min. A solution of 2-nitrobenzenesulfenyl chloride (0.19 g, 1 mmol) in benzene (2 mL) was then added dropwise during 20 min. Stirring was continued for 30 min, the mixture was washed with cold water until neutral and then dried ($MgSO_4$), and the solvent was evaporated in vacuum. Column chromatography (benzene, 20:1 and 10:1 benzene–ether) of the residue gave **3a** (0.25 g, 65%). $^1$H-N.m.r. data ($CDCl_3$): $\delta$ 4.43 (d, $J_{1,2}$ 7 Hz, H-1$\beta$), 5.01 (d, $J_{1,2}$ 3.3 Hz, H-1$\alpha$); $\alpha,\beta$-ratio 1:3.3.

*Isomerisation of* (**3a**). — To a solution of **3a** (1 mmol; $\alpha,\beta$-ratio, 3:1) in anhydrous carbon tetrachloride (5 mL) was added titanium tetrachloride (0.01 mmol). The mixture was kept at room temperature for 17 h, triethylamine (0.1 mol) was added, and the sulfenates were isolated (90%) by column chromatography. $^1$H-N.m.r. data ($CDCl_3$): $\delta$ 4.43 (H-1$\beta$), 5.01 (H-1$\alpha$); $\alpha,\beta$-ratio 2:1.

*Aminolysis of sulfenates*. — To a solution of the sulfenate (1 mmol) in benzene (5 mL) was added diethylamine (1.5 mmol), and the mixture was stirred at room temperature for 12 h. T.l.c. revealed only the parent sugar. The sulfenamide, isolated by column chromatography, was identical (i.r. spectrum) with the product prepared from the corresponding sulfenyl chloride and diethylamine[12].

ACKNOWLEDGMENT

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