Note

Blocking of hydroxyl groups in *O*-isopropylidenehexoses with the 2,4-dinitrobenzenesulfenyl group

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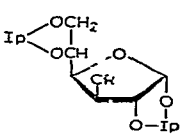
Recent publications[1–3] on utilization of the 2,4-dinitrobenzenesulfenyl group in nucleoside synthesis has prompted us to evaluate this group as a protecting group for hydroxyl functions in carbohydrates.

Hydroxyl groups in three kinds of *O*-isopropylidenehexoses (**1**, **6**, and **8**) were sulfenylated with a slight excess of 2,4-dinitrobenzenesulfenyl chloride in the presence of pyridine. The yields of the sulfenates, **2**, **7**, and **9** were 71, 70, and 83%, respectively. Although complete acid hydrolysis of the sulfenate **2** removed all of the protecting groups, giving D-glucose, acid hydrolysis under controlled conditions liberated only



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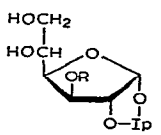

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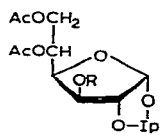

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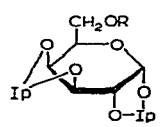

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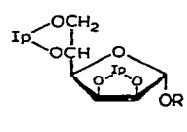

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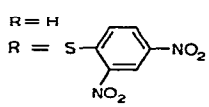

the 5,6-*O*-isopropylidene group (without hydrolysis of the sulfenyl group) giving **4**. The stability of the sulfenyl group and the remaining 1,2-*O*-isopropylidene group could not be differentiated. In mM methanolic sodium methoxide compound **5** gave a mixture of **3** and **4**, whereas under more vigorous conditions the former was the only product. Thus, the stability of the 2,4-dinitrobenzenesulfenyl group to acid is approximately equivalent to that of a 1,2-*O*-isopropylidenealdofuranose, and the susceptibility to alkali is of the same order as that of an acetyl group.

Removal of the sulfenyl group of **2** was easily achieved, either by reduction in methanolic solution with aluminium in the presence of mercuric acetate, or by hydrogenolysis with Raney nickel catalyst. The former provides an especially convenient method, since it permits deblocking in a neutral medium.

EXPERIMENTAL

General. — All evaporations were effected below 40° under diminished pressure. T.l.c. was performed on microscope slides coated with Wakogel B-5, and after development with benzene–ethyl acetate (1:1), the components were visualized by spraying with sulfuric acid and heating the plates in an oven. Melting points were determined on a hot stage with a Yanagimoto micro melting-point apparatus, and are uncorrected. Specific rotations were measured in a 1-dm tube. I.r. spectra were obtained with a Hitachi EPI G-2 i.r. spectrophotometer.

3-O-(2,4-Dinitrobenzenesulfenyl)-1,2;5,6-di-O-isopropylidene-α-D-glucofuranose (**2**). — 1,2:5,6-Di-*O*-isopropylidene-α-D-glucose (**1**, 1.56 g, 6.00 mmoles) and 2,4-dinitrobenzenesulfenyl chloride[4] (1.69 g, 7.20 mmoles) were dissolved in 1,2-dichloroethane (20 ml) by warming. The solution was cooled to room temperature and dry pyridine (1 ml) was added. After 1 h, the reaction mixture was filtered and crystalline impurities were washed with the solvent (5 ml). The combined filtrate and washings were extracted three times with water (20 ml), dried over calcium chloride, and evaporated to dryness. The residual syrup was crystallized from ethanol to give yellow needles (1.95 g, 71%) of the sulfenate **2**, m.p. 173–175°, $[\alpha]_D^{20}$ −90.1° (*c* 1.0, *p*-dioxane); ν_{max}^{KBr} 1600 (C=C of benzene ring), 1520 (NO_2), 1350 (NO_2), and 1000–1100 cm^{-1} (C–O–C).

Anal. Calc. for $C_{18}H_{22}N_2O_{10}S$: C, 47.16; H, 4.84; N, 6.11; S, 6.99. Found: C, 47.03; H, 4.77; N, 6.13; S, 6.92.

6-O-(2,4-Dinitrobenzenesulfenyl)-1,2;3,4-di-O-isopropylidene-α-D-galactopyranose (**7**). — From 1,2:3,4-di-*O*-isopropylidene-α-D-galactose (**6**, 2.60 g, 10.0 mmoles), 2,4-dinitrobenzenesulfenyl chloride (2.81 g, 12.0 mmoles), dry pyridine (0.5 ml), and 1,2-dichloroethane (50 ml), the sulfenate **7** (3.20 g, 70%) was obtained as yellow needles by a route similar to that used for the preparation of **2**; m.p. 136–137°, $[\alpha]_D^{20}$ −80.5° (*c* 1.0, *p*-dioxane); ν_{max}^{KBr} 1600 (C=C of benzene ring), 1520 (NO_2), 1350 (NO_2), and 1000–1100 cm^{-1} (C–O–C).

Anal. Calc. for $C_{18}H_{22}N_2O_{10}S$: C, 47.16; H, 4.84; N, 6.11; S, 6.99. Found: C, 47.31; H, 4.94; N, 6.10; S, 6.54.

1-O-(2,4-Dinitrobenzenesulfenyl)-2,3;5,6-di-O-isopropylidene-α-D-mannofuranose (**9**). — 2,3:5,6-Di-*O*-isopropylidene-α-D-mannose (**8**, 1.30 g, 5.00 mmoles) and 2,4-dinitrobenzenesulfenyl chloride (1.41 g, 6.00 mmoles) were dissolved in 1,2-dichloroethane (25 ml), and dry pyridine (0.5 ml) was added to this solution. After 1 h, the mixture was filtered and the filtrate evaporated to dryness. The residual syrup was dissolved in a small volume of benzene and applied to a column of Wakogel C-200 (60 g, 3 × 50 cm), which was eluted with benzene–ethyl acetate (1:1). Fractions containing the pure sulfenate **9** were combined and evaporated to dryness to give amorphous **9** (1.90 g, 83%). Crystallization from methanol afforded yellow needles; m.p. 147–148°, $[\alpha]_D^{20}$ −32.1° (*c* 1.0, *p*-dioxane); ν_{max}^{KBr} 1600 (C=C of benzene ring), 1520 (NO_2), 1350 (NO_2), and 1000–1100 cm^{-1} (C–O–C).

Anal. Calc. for $C_{18}H_{22}N_2O_{10}S$: C, 47.16; H, 4.84; N, 6.11; S, 6.99. Found: C, 47.29; H, 4.98; N, 6.19; S, 6.87.

3-O-(2,4-Dinitrobenzenesulfenyl)-1,2-O-isopropylidene-α-D-glucofuranose (**4**). — (*a*) The sulfenate **2** (1.50 g) was dissolved in ethyl acetate (65 ml) containing concentrated nitric acid (0.3 ml), and the solution was refluxed for 3 h. After cooling, the solution was neutralized with Dowex-1 (carbonate form), and evaporated to dryness. The residual syrup was crystallized from benzene to give the sulfenate **4** (980 mg, 71%) as yellow needles, m.p. 164–165°, $[\alpha]_D^{20}$ −112.7° (*c* 1.0, *p*-dioxane); ν_{max}^{KBr} 3540 (OH), 1600 (C=C of benzene ring), 1520 (NO_2), 1350 (NO_2), and 1000–1100 cm^{-1} (C–O–C).

Anal. Calc. for $C_{15}H_{18}N_2O_{10}S$: C, 43.06; H, 4.34; N, 6.70; S, 7.66. Found: C, 42.99; H, 4.27; N, 6.65; S, 7.20.

(*b*) The sulfenate **2** (415 mg) was dissolved in *p*-dioxane–water (5:2, 25 ml) and the solution was stirred with Amberlite IR-120 (H^+, 0.8 g) for 15 h under reflux. T.l.c. of the mixture gave three spots. The mixture was filtered and the filtrate evaporated to dryness. The residual syrup was dissolved in chloroform (10 ml) and extracted three times with water (15 ml). From the chloroform layer a yellow syrup (208 mg, 55%) of the sulfenate **4**, corresponding to the fastest-moving spot on t.l.c., was obtained, which was crystallized from benzene. The combined aqueous layers were extracted three times with ethyl acetate (15 ml), and the combined extracts were evaporated to dryness to give a yellow syrup (51 mg, 15%), corresponding to the middle spot. Attempted crystallization was unsuccessful, and further purification was not attempted. This product was presumed to be 3-*O*-(2,4-dinitrobenzenesulfenyl)-D-glucose, since it was positive to Fehling solution and gave a blue color in the sodium periodate–benzidine test. In the aqueous layer remaining from the ethyl acetate extraction, D-glucose was detected by paper chromatography.

5,6-Di-O-acetyl-3-O-(2,4-dinitrobenzenesulfenyl)-1,2-O-isopropylidene-α-D-glucofuranose (**5**). — The sulfenate **4** (245 mg) was dissolved in pyridine (2 ml) and acetic anhydride (0.56 ml) was added. The mixture was kept overnight and then poured into cold water (50 ml). The solid that separated was filtered off, washed with water, and dried *in vacuo*. Crystallization from ethanol afforded the acetate of **4** (194 mg, 66%), m.p. 139–140°, $[\alpha]_D^{20}$ +25.5° (*c* 1.0, *p*-dioxane); ν_{max}^{KBr} 1745 (C=O), 1600 (C=C of benzene ring), 1520 (NO_2), 1345 (NO_2), and 1000–1100 cm^{-1} (C–O–C).

Anal. Calc. for $C_{19}H_{22}N_2O_{12}S$: C, 45.42; H, 4.41; N, 5.58; S, 6.38. Found: C, 45.20; H, 4.44; N, 5.67; S, 6.54.

Susceptibility of **5** *to alkali.* — (*a*) Saponification of **5** in mM methanolic sodium methoxide for 72 h at 0° showed two spots by t.l.c., R_F 0.08 and 0.57. The R_F values of authentic **3** and **4** were 0.08 and 0.57, respectively. (*b*) Saponification of **5** in 20mM methanolic sodium methoxide for 30 min at 25°, and in saturated methanolic ammonia for 5 h at 0° gave a spot by t.l.c. having an R_F value (0.08) identical with that of **3**.

Desulfenylation of **2** *with aluminium.* — To a methanolic solution (20 ml) containing the sulfenate **2** (350 mg) and mercuric acetate (320 mg) was added finely divided aluminium foil (500 mg), and the mixture was kept for 5 h with occasional

shaking. The mixture was filtered and the filtrate evaporated to dryness. The residual syrup was dissolved in chloroform (30 ml) and extracted with water (100 ml). The chloroform layer was dried over calcium chloride and concentrated to low volume. Upon addition of petroleum ether 1,2-*O*-isopropylidene-α-D-glucose (**1**, 124 mg, 67%) separated as needles, m.p. and mixed m.p. 108–109° (lit.[5] 110–111°), $[\alpha]_D^{20}$ −15.2° (*c* 1.0, *p*-dioxane) (lit.[6] −19°, *c* 5, acetone). The i.r. spectrum agreed with the spectrum of authentic **1**, and the identity was also demonstrated by t.l.c.

Desulfenylation of **2** *by hydrogenolysis.* — The sulfenate **2** (960 mg) was dissolved in ethanol (150 ml) and hydrogenated at atmospheric pressure over Raney nickel W-2 (0.2 ml). The reaction mixture was decolorized with charcoal and filtered. The filtrate was evaporated to dryness to give a thick syrup, which was taken up in chloroform (10 ml), washed three times with water (10 ml), and dried over calcium chloride. The solvent was evaporated off and the residual syrup was crystallized from chloroform–petroleum ether to give the 1,2-*O*-isopropylidene-α-D-glucose (**1**, 240 mg, 54%) as needles, m.p. and mixed m.p. 109–112°, $[\alpha]_D^{20}$ −16.0° (*c* 1.0, *p*-dioxane). The i.r. spectrum was identical with that of authentic **1**, and the identity was also confirmed by t.l.c.

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