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Preliminary communication

The synthesis of sugar azidosulphates and azidodeoxy sugars from sugar chlorosulphates

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Carbohydrate chlorosulphates react with a variety of nucleophilic reagents[1]. Chloride causes C–O fission in sterically favoured chlorosulphonyloxy groups with the formation of chlorodeoxy sugars. Inversion of configuration results when reaction occurs at a chiral centre. By contrast, iodide causes S–O fission with the production of the parent hydroxy sugars with retention of configuration, while reaction with fluoride causes S–Cl fission with the formation of fluorosulphates. Khan[2] has questioned the bimolecular mechanism proposed for the chloride-displacement reaction, as chlorodeoxy derivatives and not azidodeoxy derivatives were obtained in the reaction of primary chlorosulphates with sodium azide. We report now on the synthesis of a number of carbohydrate azidosulphates and azidodeoxy sugars *via* the reaction of carbohydrate chlorosulphates with potassium azide in the presence of 18-crown-6-ether.

Treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-chlorosulphate[3] (1, 1 mol) with potassium azide (3 mol) and 18-crown-6-ether (0.03 mol) in acetone at room temperature for 24 h afforded, after column chromatography (silica gel), 2 (14%) and 3 (66%). Compound 3 was a syrup, $[\alpha]_D$ −151.1° (*c* 1.91, chloroform); $\nu_{max}^{CHCl_3}$ 2108 (N_3) and 1366 cm^{-1} (OSO_2N_3). The same products were obtained in the absence of crown ether, but the reaction time was approximately doubled.

5-Chloro-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranose 3-azidosulphate (5), m.p. 46–47°, $[\alpha]_D$ −153.2° (*c* 1.36, chloroform); $\nu_{max}^{CHCl_3}$ 2136 (N_3) and 1400 cm^{-1} (OSO_2N_3); was similarly synthesized from the chlorosulphate derivative 4 in 42% yield. Treatment of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose 6-chlorosulphate (6) with potassium azide (3 mol) and 18-crown-6-ether (0.01 mol) in acetone at room temperature for 48 h gave a mixture of 7 (73%), 8 (5.5%), and 9 (6.3%). Compound 7 had m.p. 72–73°, $[\alpha]_D$ −63.0° (*c* 1.09 chloroform); $\nu_{max}^{CHCl_3}$ 2136 (N_3) and 1376 cm^{-1}

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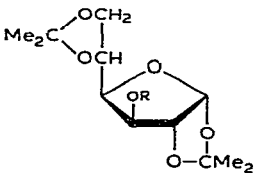
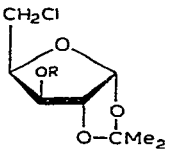
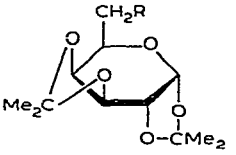


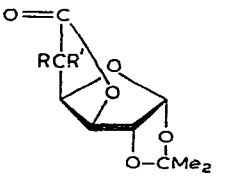
1 R = SO_2Cl
2 R = H
3 R = SO_2N_3



4 R = SO_2Cl
5 R = SO_2N_3



6 R = OSO_2Cl
7 R = OSO_2N_3
8 R = N_3
9 R = OH
10 R = Cl



11 R = OSO_2Cl, R′ =
12 R = H, R′ = N_3
13 R = N_3, R′ = H

(OSO_2N_3). Treatment of 7 with potassium azide (3 mol) and 18-crown-6-ether (1 mol) in acetone at room temperature gave 8. Compound 8 was also obtained directly from 6. The concentration of crown ether greatly influences the rate of reaction in the synthesis of 8 from both 6 and 7; thus, with 0.5 mol of crown ether, the reaction was incomplete after stirring at room temperature for 30 days, whereas the reaction was complete after 67 h in the presence of 1 mol of crown ether. The rate-limiting step in the production of 8 from 6 is the displacement of the azidosulphate group in the intermediate 7 by azide. That this process probably occurs by an S_N2 mechanism, rather than an intramolecular mechanism akin to an S_Ni, was demonstrated when the 6-chloro-6-deoxy derivative 10 was obtained by treatment of 7 with pyridinium chloride in acetone under reflux. At no stage during this reaction was an intermediate chlorosulphate detected, thus indicating direct replacement of the azidosulphate group by chloride.

Treatment of 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone 5-chlorosulphate (11) with potassium azide in the presence of 18-crown-6-ether gave, after 30 min, 12 (66%) and 13 (4%). Compound 12 had m.p. 111–113°, $[\alpha]_D$ +92.7° (*c* 1.41, chloroform); $\nu_{max}^{CHCl_3}$ 2102 (N_3) and 1786 cm^{-1} (lactone). Compound 13 was a syrup, $[\alpha]_D$ +40.2° (*c* 0.46, chloroform); $\nu_{max}^{CHCl_3}$ 2110 (N_3) and 1792 cm^{-1} (lactone).

All new compounds gave satisfactory elemental analyses and spectroscopic data.

ACKNOWLEDGMENTS

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2 R. Khan, *Carbohydr. Res.*, 25 (1972) 504–510.
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