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SULPHATES OF MONOSACCHARIDES AND DERIVATIVES

PART VIII[1]. INFRARED SPECTRA AND OPTICAL ROTATIONS OF SOME GLYCOSIDE SULPHATES

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ABSTRACT

The frequency of the infrared absorption peak due to the C-O-S group vibration near 850 cm^{-1} has been measured for a range of sugar and glycoside sulphates and their derivatives. The frequency is dependent upon the phase of the sample and the nature of substituents on the sugar, as well as on the position occupied by the sulphate group. The position of this peak cannot be used with certainty to predict the position of sulphate substitution. The molecular rotations of a number of D-glucoside and D-galactoside sulphates have been measured in aqueous solution and have been shown to differ very little from those of the parent glycosides, except in the case of glycoside 4,6-disulphates and 4,6-*O*-benzylideneglycoside sulphates. It is suggested that, except for 4,6-disulphates, the introduction of sulphate groups into a glycoside does not affect the optical rotation, and that these sulphates all have the expected *C1*(D) conformation in aqueous solution.

INTRODUCTION

In recent communications[2,3], we commented on the dangers inherent in using evidence, obtained from infrared spectra alone, in assigning positions to sulphuric ester groups on sugar rings. The assignments are based on the suggestion by Orr[4] that absorptions in the region 810–860 cm^{-1} and at *ca.* 1250 cm^{-1} are due to C-O-S and S=O group vibrations, respectively. An examination of a range of sugar and polysaccharide sulphates, in which the sulphate groups are at known positions on the hexopyranoside rings, had led to the proposal[5] that the absorptions in the 810–860 cm^{-1} band can be diagnostic for the position of the sulphate substituents. For a sulphate group on the equatorial C-6 of a hexopyranose in the *C1*(D) conformation, the absorption was at 810–820 cm^{-1}; sulphate at a secondary, equatorial position in the ring (*e.g.*, D-glucose 3-sulphate) gave an absorption at 830 cm^{-1}, and that at a secondary, axial position at *ca.* 850 cm^{-1} (*e.g.*, D-galactose 4-sulphate). Similar rules have been formulated for the analogous sulphonic esters of pyranose derivatives[6]. The recent synthesis of a range of sugar and glycoside sulphates has enabled a further systematic study to be made of the validity of these rules. In addition, the optical rotations of the glycoside sulphates have been used to examine any conformational changes consequent upon sulphation of the glycosides.

EXPERIMENTAL

The sugar and glycoside sulphates used in this study have been described in previous communications[1,3]. Optical rotations (sodium D-line) were measured at 20° in 1-dm tubes on a Perkin–Elmer 141 polarimeter, and concentrations were generally in the range 0.5–1.5 in water, unless otherwise stated (see Table II).

For the infrared spectra, three methods of preparing samples were tested: (*a*) the crystalline sulphate was ground with potassium bromide and pressed into a disc (KBr disc method); (*b*) the sulphate was ground in liquid paraffin (Nujol) and the mull layered between sodium chloride plates (Nujol mull method); and (*c*) an aqueous or aqueous alcoholic solution of the sulphate was evaporated to dryness on a silver chloride plate in a vacuum oven at 110° over phosphoric anhydride (evaporated film method). Spectra were recorded on either a Unicam SP200G spectrometer or, for greater definition, an a Perkin–Elmer Model 225 spectrometer.

RESULTS AND DISCUSSION

As a preliminary to the study of the infrared spectra of the sulphates, the effect of the method used in preparing the sample was investigated. The same sample of crystalline methyl α-D-glucopyranoside 2,3-di(barium sulphate) was used to prepare a KBr disc, a Nujol mull, and an evaporated film. Parts of the spectra recorded are depicted in Fig. 1. The evaporated film gave a spectrum with diffuse peaks in which little fine structure was apparent. The Nujol mull gave a spectrum showing sharp peaks with some fine detail, and the KBr disc gave a spectrum intermediate between the other two. It is obvious that the phase markedly influences the appearence of the

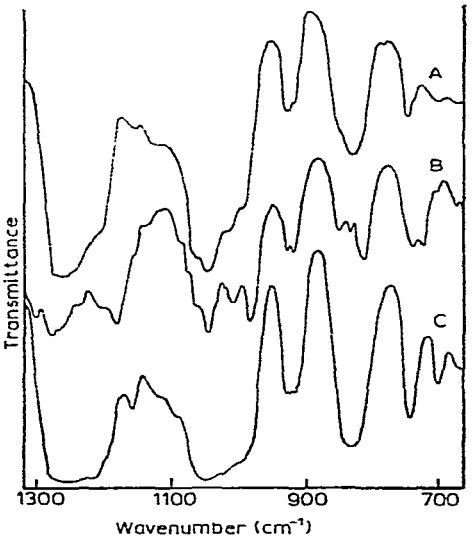

Fig. 1. Infrared spectra of methyl α-D-glucopyranoside 2,3-di(barium sulphate). A, KBr disc; B, Nujol mull; C, evaporated film.

spectrum, as has been pointed out by Spedding[7]. The greater spectral definition in the Nujol mull can be rationalised by considering the environment of the molecules in each medium. The specimen dispersed in Nujol still retains a microcrystalline structure in which the majority of the molecules are held rigidly in identical lattice environments, thus giving sharp absorption peaks. The solid solution in a KBr disc and the syrupy phase in an evaporated film allow more random environments for each molecule, and hence give rise to broader, more-diffuse absorptions[8]. The spectrum of a sugar sulphate in a Nujol mull will frequently show multiplicity, where the corresponding spectrum for a KBr disc shows a broad absorption in which the apparent peak occurs at the weighted mean of the individual absorptions.

The nature of the cation associated with the sugar sulphate anion appears to have little effect on the spectrum. Spectra of the barium, sodium, and potassium salts of the same sugar sulphate showed no apparent changes in absorption bands associated with the sulphate groups.

Table I records the principal absorption peaks in the regions 1200–1300 and 800–870 cm^{-1} for a range of sugar and glycoside sulphates, all measured as Nujol mulls on the barium salt. From Table I and previous results[3], it is apparent that the presence of different aglycone groups and substituents on a glycoside or sugar sulphate may profoundly alter the position of the absorption due to the C-O-S group vibration near 850 cm^{-1}. Extreme examples of this are methyl α-D-galactopyranoside 4-sulphate with a peak at 817 cm^{-1} compared with benzyl β-D-galactopyranoside 4-sulphate with the peak at 853 cm^{-1}, and methyl α-D-glucopyranoside 4,6-disulphate (828 cm^{-1}) compared with D-glucose 4,6-disulphate (855 cm^{-1}). The absorption band centred about 1250 cm^{-1}, due to the S=O group vibration, shows some variability, but is too broad to be of diagnostic importance.

We have previously shown that D-glucopyranose and D-galactopyranose derivatives which are sulphated at O-2 show anomalous infrared absorptions[3]. In confirmation of this, many, but not all, of the 2-sulphates listed in Table I display an absorption band near 850 cm^{-1}, whereas an equatorial sulphate would be expected to absorb at 830 cm^{-1}. That this is not always due to a change in ring conformation from *C1*(D) to *1C*(D) is apparent from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-disulphate and the corresponding galactose compound, both of which are locked in the *C1*(D) conformation by the benzylidene ring but still give bands near 850 cm^{-1}. It must, however, be emphasised that the majority of the spectra were obtained on crystalline samples and would, therefore, represent conformations and lattice effects peculiar to this phase. It is possible that, in the crystal lattice, some of the other sugar sulphates assume conformations other than the expected *C1*(D) form known to exist in solution for D-galactose and D-glucose. Only a crystallographic examination of these sulphates could finally settle this question, but it is possible to examine the conformations of the sugar sulphates in solution by simple methods.

Measurement of optical rotations and n.m.r. spectroscopy may both be used to study conformations in solution[9]. The former data will be reported in this paper, and the n.m.r. spectra will be given in the following paper. The optical rotations of free

TABLE I

INFRARED ABSORPTION PEAKS OF SUGAR SULPHATES

Sulphate	*S=O absorption*[a] (cm^{-1})	*C-O-S absorptions*[b] (cm^{-1})		
Methyl α-D-glucopyranoside 2,3-disulphate	1270	850(m)	830(m)	810(s)
α-D-Glucopyranose 2,3-disulphate	1255	860(s)	820(s)	
Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-disulphate	1265	850(s)	830(m)	
4,6-*O*-Benzylidene-D-glucose 2,3-disulphate	1275	835		
Methyl α-D-galactopyranoside 2,3-disulphate	1300	850(m)	825(s)	805(sh)
α-D-Galactopyranose 2,3-disulphate	1265	858(s)	830(s)	
Methyl β-D-galactopyranoside 2,3-disulphate	1305	832		
Methyl 4,6-*O*-benzylidene-α-D-galactopyranoside 2,3-disulphate	1250	856(m)	843(m)	829(s)
Methyl 4,6-*O*-benzylidene-β-D-galactopyranoside 2,3-disulphate	1285	870(m)	840(s)	805(m)
Methyl α-D-galactopyranoside 2,6-disulphate	1275	835(s)	810(sh)	
D-Galactose 2,6-disulphate	1255	840(s)	820(m)	
Benzyl β-D-galactopyranoside 2,6-disulphate	1240	863(s)	816(s)	
Methyl 3,4-*O*-isopropylidene-α-D-galactopyranoside 2,6-disulphate	1275	825		
Benzyl 3,4-*O*-isopropylidene-β-D-galactopyranoside 2,6-disulphate	1310	850		
Methyl α-D-glucopyranoside 4,6-disulphate	1235	828		
D-Glucose 4,6-disulphate	1250	855		
Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside 4,6-disulphate	1250	820(s)	810(s)	
2,3-Di-*O*-benzyl-D-glucose 4,6-disulphate	1255	830		
Methyl α-D-galactopyranoside 4-sulphate	1265	817		
β-D-Galactopyranose 4-sulphate	1280	845		
Benzyl β-D-galactopyranoside 4-sulphate	1255	853		
Methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside 4-sulphate	1290	852		
Benzyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside 4-sulphate	1280	848		

[a]Centre of broad absorption; [b]s = strong, m = medium, sh = shoulder.

TABLE II

MOLAR ROTATIONS OF GLYCOSIDES AND GLYCOSIDE SULPHATES[a]

Glycoside sulphate[b]	*Molecular rotation (degrees × 10^{-3})*	*Molecular rotation of parent glycoside (degrees × 10^{-3})*
Methyl α-D-glucopyranoside 2,3-disulphate	+30.1	+30.8
Methyl 4,6-*O*-benzylidene-α-D-glucopyranoside 2,3-disulphate	+14.7	+24.0
Methyl α-D-galactopyranoside 2,3-disulphate	+38.7	+38.4
Methyl β-D-galactopyranoside 2,3-disulphate	+1.2	0
Methyl 4,6-*O*-benzylidene-α-D-galactopyranoside 2,3-disulphate	+53.4	+45.7[c]
Methyl 4,6-*O*-benzylidene-β-D-galactopyranoside 2,3-disulphate	+16.8	−1.5
Methyl α-D-galactopyranoside 2,6-disulphate	+38.7	+38.4
Benzyl β-D-galactopyranoside 2,6-disulphate	−8.7	−8.0
Benzyl 3,4-*O*-isopropylidene-β-D-galactopyranoside 2,6-disulphate	−0.9	−0.5
Methyl α-D-galactopyranoside 4-sulphate	+37.3	+38.4
Benzyl β-D-galactopyranoside 4-sulphate	−8.6	−8.0
Methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside 4-sulphate	+60.8[c]	+62.0[c]
Benzyl 2,3,6-tri-*O*-benzoyl-β-D-galactopyranoside 4-sulphate	+14.2[d]	+13.1[c]
Methyl α-D-glucopyranoside 4,6-disulphate	+41.1	+30.8
Methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside 4,6-disulphate	+42.8	+7.0

[a]In water unless otherwise shown. [b]Barium salts. [c]In chloroform. [d]In pyridine.

sugar sulphates can be of little value in deciding the conformation, since slight variations in the mutarotational equilibrium will markedly affect the rotation; this discussion will therefore be confined to glycoside sulphates. Table II compares the molecular rotations of a range of glycoside sulphates with those of the parent glycosides (unsulphated). With a few exceptions, there is good agreement between the sulphated and parent compound. The agreement may be fortuitous in those cases where, for reasons of solubility, measurements were made in different solvents. Of particular interest, however, is the fact that large differences in molecular rotation between a glycoside and its sulphate occur only with 4,6-*O*-benzylidene derivatives, and with 4,6-disulphates. In those cases where the molecular rotation is not appreciably altered by sulphation, it implies that there can be no large change in molecular conformation consequent upon sulphation and that the sulphate group provides no additional contribution to the molecular rotation over that provided by a hydroxyl group. A further implication of this finding is that rotation about the C-O bond at the sulphated position allows the same population of the rotamer states as that in the parent hydroxyl compound—even where two sulphate groups are present on adjacent carbon atoms (*e.g.*, 2,3-disulphates).

The reason for the discrepancy in the case of 4,6-disulphates must imply some interaction between the sulphate groups in these two positions, since, as will be shown in a later paper, there is no conformational change in the ring to account for the difference[10]. It has been suggested that a large contribution to the magnitude of optical rotations in hexopyranose derivatives comes from groups on C-6 rotating about the exocyclic C-5–C-6 bond[11]. Charged sulphate groups on C-4 and C-6 may well modify the energetics of this rotation[12], and hence affect the molecular rotation. The reason for the discrepancy with 4.6-*O*-benzylidene derivatives is not readily explicable, especially in view of the fact that no conformational change is likely to have occurred. The general conclusion must remain that, in most cases, D-gluco- and D-galacto-pyranoside sulphates adopt the *CI*(D) conformation in aqueous solution.

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