Conformationally Dependent Oxygen Isotope Effects on the Infrared Spectra of 2,2-Dioxo-1,3,2-dioxathianes

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The isotope shift caused by ^{17}O or ^{18}O on the frequency of the symmetric and antisymmetric $>SO_2$ stretching modes of 2,2-dioxo-1,3,2-dioxathianes (six-membered cyclic sulphates) is strongly dependent on whether the heavy oxygen isotope is located in an axial or equatorial site.

A strategy has recently been developed for the synthesis of chiral [^{16}O,^{17}O,^{18}O]sulphate monoesters,[1] with a view to determining the stereochemical course of chemical and enzyme catalysed sulphuryl transfer reactions. N.m.r. spectroscopy, which has been successfully used for the analysis of chiral [^{16}O,^{17}O,^{18}O]phosphate monoesters,[2] does not commend itself for the analysis of chiral [^{16}O,^{17}O,^{18}O]sulphate monoesters since none of the isotopes of sulphur possesses a nuclear spin quantum number of $\frac{1}{2}$. Moreover the exocyclic oxygen atoms in a cyclic sulphate diester cannot be alkylated to render them chemically distinguishable as was possible with cyclic phosphate diesters.[3] The analysis of chiral [^{16}O,^{17}O,^{18}O]sulphate monoesters presents, therefore, a new conceptual problem.

The frequency of an i.r. vibrational mode is markedly affected if isotopic substitution occurs in the functional group responsible. However, the magnitude of the isotope shift is difficult to predict except in the simplest of molecules, but the shift caused by replacing ^{16}O with ^{18}O in a functional group could theoretically be up to 40 cm^{-1}.[4] We expected that the generalised anomeric effect[5] of the axial lone pairs of the ring oxygens on the axial exocyclic oxygen in 2,2-dioxo-1,3,2-dioxathianes, would ensure that the frequencies of the symmetric and antisymmetric $>SO_2$ vibrational modes were dependent on the location of the heavy oxygen isotope. If so, the isotope shift could form the basis of a method for the analysis of chiral [^{16}O,^{17}O,^{18}O]sulphate monoesters.

In order to explore the influence of oxygen isotopic substitution at the axial and equatorial sites of six-membered cyclic sulphate esters, 2,2-[^{18}O]dioxo-1,3,2-dioxathiane was prepared from 2-oxo-1,3,2-dioxathiane by oxidation with ruthenium [^{18}O]tetraoxide,[6] since this should exist as an equimolar mixture of chair conformations (neglecting the equilibrium isotope effect) with ^{18}O in the axial and equatorial sites, *viz.* equation (1).

The Fourier transform (F.t.) i.r. spectrum is shown in Figure 1(a) (the ^{18}O site is only about 60% enriched). It is evident from this spectrum that the ^{18}O shift in both the symmetric and antisymmetric stretching modes of the $>SO_2$ group is conformationally dependent. It is also apparent that the isotope shift is greater and the intrinsic line-width smaller in the symmetric stretching mode; consequently this vibrational mode should be the most useful for analytical purposes. Separate deconvolution of these two spectral regions gave the resolution enhanced spectrum shown in Figure 1(b).

In order to assign the conformations responsible for the two symmetric and two antisymmetric $>S[^{16}O,^{18}O]$ absorption bands in 2,2-[^{18}O]dioxo-1,3,2-dioxathiane, and to confirm this observation, the *cis*- and *trans*-cyclic sulphite esters obtained by treating (3*R*)-butane-1,3-diol with thionyl chloride were oxidised with ruthenium [^{18}O]tetraoxide to give the isotopomeric cyclic [^{18}O]sulphate esters. Since this oxidation is known to proceed with retention of configuration at sulphur,[6] the *cis*-sulphite must give the cyclic (R_s)-[^{18}O]sulphate (**1**) and the *trans*-sulphite must give the cyclic (S_s)-[^{18}O]sulphate (**2**). As expected, the (R_s)-isotopomer (**1**) possesses only one symmetric (1172 cm^{-1}) and one antisymmetric (1401 cm^{-1}) $>S[^{16}O,^{18}O]$ stretching vibration and likewise the (S_s)-isotopomer (**2**) possesses only one symmetric (1183 cm^{-1}) and one antisymmetric (1392 cm^{-1}) $>S[^{16}O,^{18}O]$ stretching vibra-

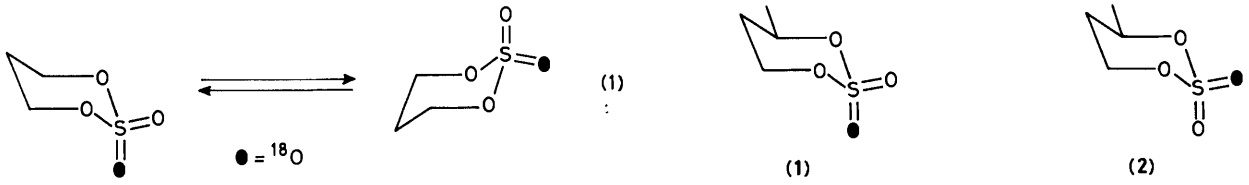


Table 1. The effect of oxygen isotopic substitution on the symmetric and antisymmetric $>SO_2$ stretching frequencies (cm^{-1}) of (4*R*)-4-methyl-2,2-dioxo-1,3,2-dioxathianes. Δ is the isotope shift from the $>SO_2$ frequency.

Isotope		Symmetric stretching frequency	Δ for symmetric stretching mode	Antisymmetric stretching frequency	Δ for antisymmetric stretching mode
Axial	Equatorial				
^{16}O	^{16}O	1201	—	1414	—
^{16}O	^{17}O	1192	9	1401	13
^{17}O	^{16}O	1186	15	1407	7
^{16}O	^{18}O	1183	18	1392	22
^{18}O	^{16}O	1172	29	1401	13
^{17}O	^{18}O	1170	31	1384	30
^{18}O	^{17}O	1163	38	1389	25
^{18}O	^{18}O	1157	44	1378	36

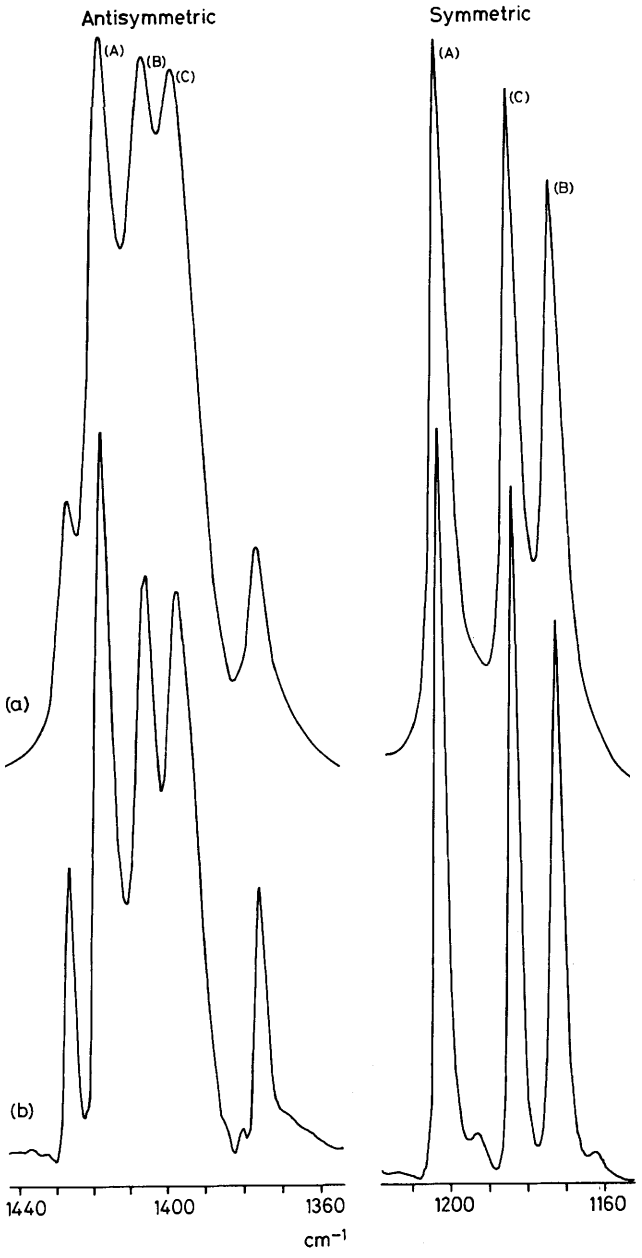
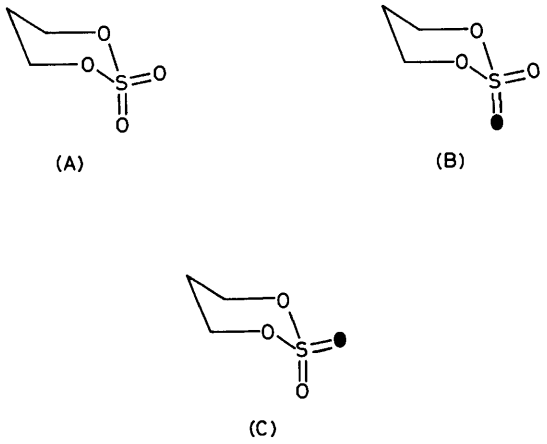


Figure 1. (a) The F.t. i.r. spectrum of the antisymmetric and symmetric $>SO_2$ stretching region of 2,2-[^{18}O]dioxo-1,3,2-dioxathiane and (b) the same spectrum after deconvolution with an enhancement factor of 1.68 and line-width at half height of 5 cm^{-1} for the antisymmetric $>SO_2$ stretching region and an enhancement factor of 1.50 and line-width at half height of 4 cm^{-1} for the symmetric $>SO_2$ stretching region. The spectra were measured on a Perkin-Elmer 1750 F.t. i.r. spectrometer at a resolution of 1 cm^{-1}.

tion, since the conformation with the methyl group equatorial should be preferred. Although these values differ slightly from those observed for 2,2-[^{18}O]dioxo-1,3,2-dioxathiane, the assignments shown in Figure 1 seem unambiguous.



The three stable oxygen isotopes, ^{16}O, ^{17}O, and ^{18}O can be arranged to give eight exocyclic isotopomers of (4*R*)-4-methyl-2,2-dioxo-1,3,2-dioxathiane. All eight isotopomers have been prepared and their F.t. i.r. spectra determined and resolution-enhanced by deconvolution. The frequencies of the symmetric and antisymmetric stretching modes for each isotopomer are shown in Table 1.

There are a number of features about these data worthy of comment. First, the overall isotope shift is greater for the symmetric stretching mode (*e.g.* $>SO_2 - >S^{18}O_2$, 44 cm^{-1}) than for the antisymmetric stretching mode ($>SO_2 - >S^{18}O_2$, 36 cm^{-1}). Secondly, the shift caused by a heavy oxygen isotope in an axial position is greater than in an equatorial position for the symmetric stretching mode, but the reverse is observed in the antisymmetric stretching mode. Thirdly, the shift caused by ^{18}O is about double that caused by ^{17}O in the same site in the symmetric stretching mode, but slightly less than double in the antisymmetric stretching mode. Fourthly, the isotope shifts are approximately additive. Finally, since each of the diastereo-isotopomeric pairs are distinguishable, especially in their symmetric stretching mode, i.r. spectroscopy should provide a means for analysing chiral [^{16}O,^{17}O,^{18}O]sulphate monoesters after stereospecific cyclisation to a chirally substituted six-membered cyclic sulphate.

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