Tetrahedron Letters No. 20, pp 1743 - 1746, 1977. Pergamon Press. Printed in Great Britain.

CONFORMATIONAL ANALYSIS OF SEVEN-MEMBERED RING SULFITE MOLECULES

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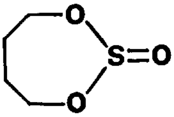
(Received in UK 28 February 1977; accepted for publication 4 April 1977)

In the last few years, considerable efforts have been directed toward elucidating the stereochemistry of five and six-membered ring sulfites. For ethylene sulfite in solution, n m r work based on a detailed analysis of vicinal coupling suggests the existence of twist-envelope forms which interconvert rapidely on the n m r time scale (1). For the six-membered ring, trimethylene sulfite both solid state (2) and solution studies (3) give evidence for a ring chair conformation with an axial S=O bond. The axial S=O bond is quoted to be 14.7 ± 4 kJ mol^{-1} more stable than the equatorial (4).

In line with our interest on the stereochemistry of seven membered-ring heterocyclic molecules (5)(6), we wish to report here preliminary results which give some insight on the stereochemistry of sulfites molecules 1, 2, 3 which, to our knowledge, have not been studied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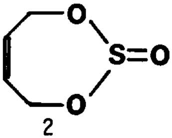
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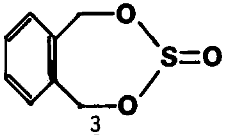
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up to date. Sulfites 1, 2 and 3 have been prepared according to standard procedures (7). An additional interest in choosing the three skeletons corresponding to molecules 1, 2 and 3, comes from conformational flexibility which have been reported on analogous 1,3-heterocyclic seven membered-rings (8)(9).

The ^{1}H and ^{13}C n m r spectra of the three sulfites 1, 2 and 3 have been recorded at room temperature. The spectral parameters which can be obtained are listed in Table 1.

For compound 1, the signal corresponding to protons attached to carbons 5 and 6 is highly degenerate and it has not been possible to obtain the $^{3}J(HH)$ ring proton couplings which would be of great help for conformational analysis. By homonuclear decoupling, the C_4C_7 protons system shows a simple AB spectrum ($^{2}J(HH)$ = -12.3 Hz). For compounds 2 and 3, the methylene protons show essentially an AB system with an additional triplet fine structure for sulfite 2 as due to the coupling with the ethylene protons.

The room temperature proton n m r spectra are compatible with a Cs symmetry chair or boat conformations (S=O bond axial or equatorial) or rapidly interconverting on the n m r time scale twist conformation.

In lowering the temperature down to -100°C, the ^{1}H n m r spectrum of sulfite 2 remains essentially unchanged albeit broadened at lower temperature by increasing viscosity. Conversely, the ^{1}H n m r spectrum of 3 shows significant changes on lowering the temperature. The lines of the AB system observed at room temperature broaden and eventually resolve in two AB systems (Figure) at -86°C. Such a modification of the n m r spectrum clearly indicates that, at room temperature, sulfite 3 exists as a mixture of at least two conformations.

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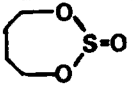
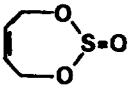
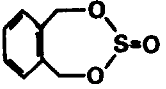
Table 1 : ^1H and ^{13}C parameters of sulfites 1, 2 and 3

Compounds	Chemical shifts * $H_{4,7}$	$H_{4',7'}$	$H_{5,6}$	$H_{5',6'}$	$C_{4,7}$	$C_{5,6}$	$^2J(H_{4,4'})$
 1	4.17	3.60	1.42	1.42	64.1	28.5	-12.3
 2	5.00	4.46	5.81	-	60.2	128.6	-14.0
 3	5.61	4.06	-	-	62.7	128.2	-14.0

* The proton n m r spectra were recorded in toluene, the chemical shifts are in ppm downfield from TMS. The ^{13}C n m r spectra were recorded in chloroform, the chemical shift are in ppm downfield from TMS.

A second piece of information from conformational analysis of sulfites 1, 2 and 3 can be obtained from infra-red study.

Two different ν(S=O) stretching frequencies at 1190 cm^{-1} and at 1230 cm^{-1} have been reported for the two diastereomers of 2-t-Butyl trimethylene sulfites (3a) and assigned to the axial (1190 cm^{-1}) and equatorial (1230 cm^{-1}) orientation of the S=O group. Since then a considerable body of work has been directed toward the stereochemical dependence of the ν(S=O) stretching frequency in six-membered ring sulfites (3d)(4)(10)(11). A rationale of the frequencies observed has been proposed as shown in Table 2 (12). We shall assume that only slight changes take place in ν(S=O) stretching frequency in going from a six to a seven-membered ring. Indeed, very small changes are observed in the ν(C=O) stretching frequency when the ring size increases in cyclic ketones (13).

Table 2 : ν(S=O) stretching frequency in six-membered ring sulfites,"a"refers to an axial orientation and "e" to an equatorial of the S=O group in a chair conformation of the ring. "i" refers to a twist conformation.

	CCl_4	CH_3CN	$\Delta\nu(CCl_4-CH_3CN)$
$\nu(SO_a)$ cm^{-1}	1193.5 ± 3.5	1186. ± 4.	7.5
$\nu(SO_i)$ cm^{-1}	1124. ± 2.	1211. ± 3.	13.
$\nu(SO_e)$ cm^{-1}	1245. ± 2.	1226. ± 2.5	19.

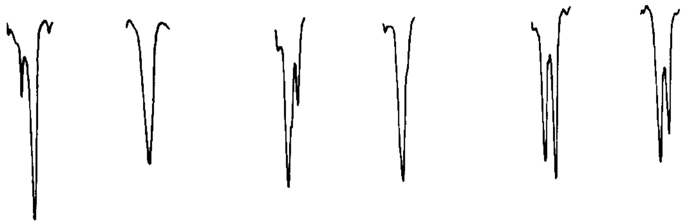
The infra-red spectra of sulfites 1, 2 and 3 were recorded in two different solvents (CCl_4 and CH_3CN). The absorption frequencies present in the 1000-1400 cm^{-1} region have been assigned to the S=O stretching frequency and are reported in table 3.

The ν(S=O) values shown in tables 2 and 3 and the differences observed by change of solvent are best interpreted in assigning the (1220-1214 cm^{-1}) frequency in CCl_4 to a twist conformation and the lower frequency (1184 cm^{-1}) to an axially oriented S=O group.

As a boat conformation with an axially oriented S=O bond seems to be very unlikely, sulfite 3 should exhibit a twist-chair equilibrium at room temperature, sulfite 2 will be in a predominantly twist conformation, and sulfite 1 in a chair conformation. The above conclusions are entirely consistent with the low temperature n m r observation performed on sulfites 2 and 3.

Table 3 : ν(S=O) stretching frequencies observed in sulfites 1; 2 and 3 in CCl_4 and CH_3CN.

	1		2		3	
	CCl_4	CH_3CN	CCl_4	CH_3CN	CCl_4	CH_3CN
ν(S=O) cm^{-1}	1214(S) 1184(W)	1197(S)	1219(S) 1184(W)	1204(S)	1220(S) 1184(W)	1210(S) 1179(S)



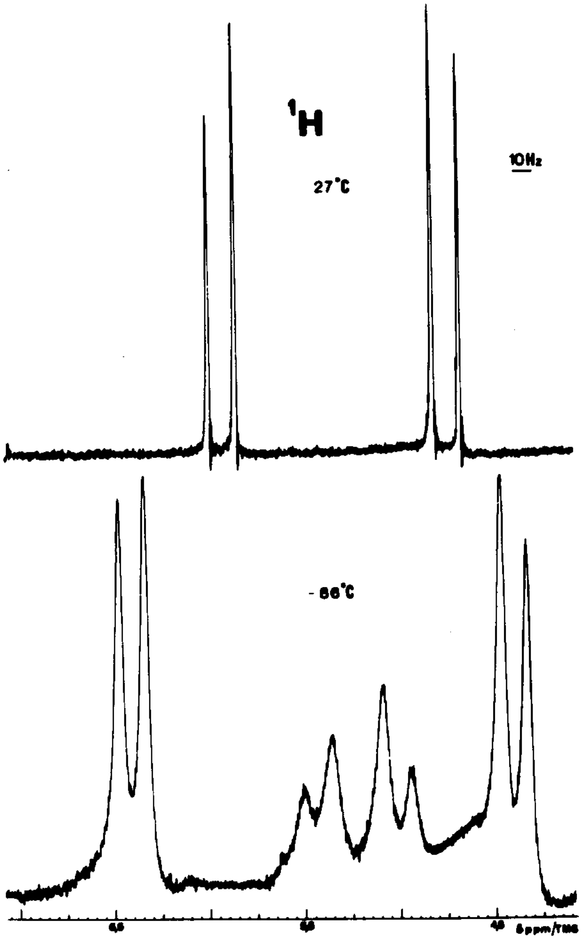


Figure : ^1H n m r spectrum of the methylene protons of sulfite 3, at room temperature (1 AB system), at low temperature (2 AB systems).

The peak areas corresponding to the low temperature spectra of the two AB systems observed in sulfite 3 correspond to a 5:2 ratio. The largest δ(AB) chemical shift difference observed in the predominant species strongly suggests that it corresponds to the chair conformation. Thus the ΔG difference between the chair and the twist conformation, taking into account the presence of two equivalent chair conformations is calculated to be 0.100 kJ mol^{-1}. A dnmr study of the variable temperature process observed in sulfite 3 gives a $\Delta G^{\neq}$ value of 2.42 kJ mol^{-1} at -74°C for the chair to twist equilibrium.

Further studies on the stereochemistry of substitued seven-membered ring sulfites are now in progress.

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