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Lanthanide Induced ^{17}O NMR Shifts of Diastereotopic Oxygen Atoms in 1-Thiadecalin 1,1-Dioxide and Related Compounds.

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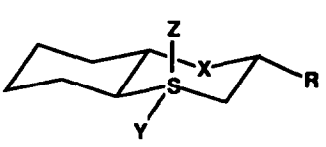
Abstract: Lanthanide-induced ^{17}O NMR shifts of diastereotopic sulfonyl oxygens provide a basis for determining equilibrium constants between diastereomeric Ln·sulfone complexes.

The importance of ^{17}O NMR spectroscopy in the structural analysis of organosulfur compounds containing the sulfonyl ($-SO_2-$) group has been well-documented.[1-3] These reports have focused on the relative ^{17}O NMR chemical shift differences caused by variations in the nature of substituents and differential steric effects arising from diastereomeric relationships.

The ^{17}O NMR diastereotopicities ($\Delta\delta_{SOaOb} = \delta_{SOa}-\delta_{SOb}$) of sulfonyl oxygens have been previously observed in both acyclic and cyclic sulfones.[2,3] Sulfonyl oxygens which are proximal (*i.e.*, α) to a stereogenic center may or may not exhibit individual resonances for each diastereotopic oxygen. For example, in 2-(phenylsulfonyl)butane the sulfonyl oxygens are isochronous, appearing at δ 141 ppm, whereas in 1,2-diphenyl-1-(phenylsulfonyl)ethane, two distinguishable resonances are observed at δ 140.3 and 145.4 ppm.[2] Sulfonyl oxygen diastereotopicity can also be enhanced by positioning the $-SO_2-$ group in a rigid heterocycle. Thus, *trans*-thiadecalin 1,1-dioxide (**1**), with axial and equatorial oxygens, exhibits ^{17}O NMR chemical shifts at δ 125.6 and 139.6 ppm. By analogy with the ^{17}O NMR shifts of the diastereomeric sulfoxides [*e.g.*, **2α** (δ 5.6 ppm); **2β** (δ -11.4 ppm)] where the high field resonance characterizes the axial S=O oxygen, the axial oxygen in **1** is assigned to δ 123.9 ppm.[3a] The results of several studies indicate that sulfonyl and sulfinyl oxygens occupying γ-gauche arrays with methylene or methyl groups experience considerable shielding compared to the γ-anti orientation.[3]



1) $X = CH_2$; $Y = Z = O$; $R = H$
2α) $X = CH_2$; $Y = O$; $Z = 2e^-$; $R = H$
2β) $X = CH_2$; $Z = O$; $Y = 2e^-$; $R = H$
3) $X = Y = Z = O$; $R = H$
4) $X = Y = Z = O$; $R = OEt$
5) $X = S$; $Y = Z = O$; $R = H$

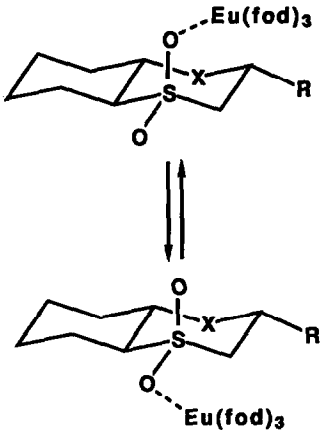
Table 1--Oxygen-17 LIS Studies on Thiadecalin Sulfones

Cmpd	Concen. (M)	Oxygen[a]	^{17}O Chemical Shift (δ, ppm)[b,c]	Linewidth (Hz)[c]	Induced Shift (ppm/M LSR)	K_{dias}
1	0.32	eq. S=O	139.6	146	1337	1.64
		ax. S=O	125.6	149	815	
3	0.29	eq. S=O	142.6	162	959	0.89
		ax. S=O	126.2	147	1073	
4	0.32	eq. S=O	145.9	251	538	0.68
		ax. S=O	133.3	255	792	
5	0.10	eq. S=O	141.1	205	1377	1.00
		ax. S=O	128.6	201	1371	

a) The ^{17}O NMR shifts of the ethereal oxygens are described in text. b) All oxygen-17 NMR spectra were recorded at 32°C for **1**, **3** and **4** and 23°C for **5** on a Varian XL-400 spectrometer operating at 54.2 MHz. c) In the absence of Eu(fod)$_3$.

Several recent reports suggest that ^{17}O NMR lanthanide-induced shifts (LIS) possess remarkable potential for understanding substrate-to-metal binding affinities of molecules containing monocoordinate oxygens.[4,5] These LIS's are largely a function of two variables: the non-bonded pseudocontact shift (Δ_{pc}) and the covalent contact shift (Δ_c). The latter term, Δ_c, is considered the dominant contributor and involves transfer of unshared electron density from the metal to oxygen. Thus, increases in the quantity of Eu(fod)$_3$ shift the equilibria toward the Eu^{+3}•substrate complex and result in progressive *upfield* ^{17}O NMR shifts of the coordinated oxygen nuclei. This effect should serve as a probe for assessing the steric inhibition to oxygen-metal binding. More importantly, nonequivalent oxygens should exhibit uniquely different binding aptitudes toward Eu(fod)$_3$. Their individual ^{17}O NMR shift responses should therefore be distinctive. To test this concept, the ^{17}O NMR spectra of thiadecalin 1,1-dioxide (**1**),[3] 1,4-oxathiadecalin 4,4-dioxides, **3** and **4**,[6a,6b] and 1,4-dithiadecalin 1,1-dioxide (**5**)[6a] were examined in the presence of Eu(fod)$_3$.

All four sulfones exhibited distinguishable sulfonyl oxygen resonances in the absence of Eu(fod)$_3$ (see Table 1). Oxathiadecalin 4,4-dioxide **3** exhibited SO_2 resonances at δ 142.6 and 126.2 ppm, as well as a resonance for an ethereal oxygen at δ 31.8 ppm. The sulfonyl resonances from oxathiadecalin **4** appeared at δ 145.9 and 133.3 ppm. Two resolvable, but very broad, resonances for the acetal oxygens were observed at δ 72.4 and 56.4 ppm. It is, however, not clear which of these signals arises from which oxygen. Finally, dithiadecalin sulfone



Scheme 1

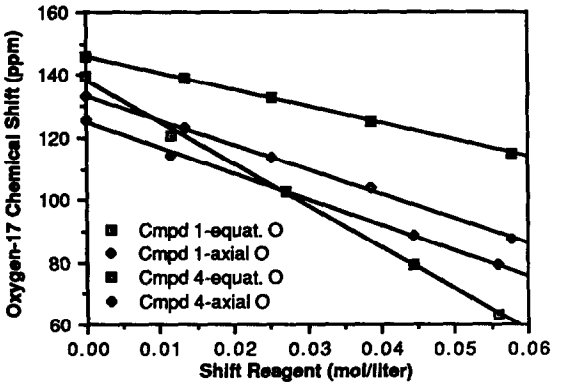


Figure 1--Lanthanide Induced Shifts for Sulfones 1 and 4.

5 displayed sulfonyl resonances at δ 141.1 and 128.6 ppm. For each of these compounds, it seems reasonable that the more shielded sulfonyl resonance belongs to the axial oxygen (*vide supra*).

After the initial spectra were recorded, several weighed increments of Eu(fod)$_3$ were added to the solutions of the sulfones and new spectra were recorded after each addition. In sulfone **1** (X=CH$_2$), the equatorial oxygen was more sensitive to Eu(fod)$_3$ than the axial oxygen, and consequently shifted upfield more rapidly. As a result, the two sulfonyl resonances became coincident, and then separated again (see Figure 1). In sulfones **3** and **4** (X=O), the axial oxygen showed the greater sensitivity to Eu(fod)$_3$. Finally, the results for sulfone **5** (X=S) appeared to fall between these two preferences, with the two sulfonyl resonances showing *identical* sensitivity to the presence of Eu(fod)$_3$. No LIS in the ethereal resonance of sulfone **3** was observed, suggesting that Eu^{3+} binds almost exclusively to the sulfonyl group. We were unable to follow the LIS of the acetal oxygens in **4**, due to the extreme line-broadening.

While the results indicate that one sulfonyl oxygen may ligate to Eu(fod)$_3$ more strongly than the other, our goal was to measure the binding affinities of the individual diastereotopic oxygens. To accomplish this, the ratio of the LIS's for the axial and equatorial oxygens were calculated for each sulfone. The LIS is equal to the fraction of substrate S which is bound to Eu^{+3} ($[Eu^{+3}\cdot S]/[S]$) times Δ_C for a hypothetical complex in which $[Eu^{+3}\cdot S]/[S]$ is unity:[7]

$$\delta_{ind} = \Delta_C[Eu^{+3}\cdot S]/[S] = \Delta_C K_b[Eu^{+3}]$$

where K_b is the binding constant between Eu^{+3} and one of the two diastereotopic oxygens. Thus, if we assume that the S=O oxygens have similar contact shifts, the ratio of the induced shifts should be the ratio of the axial and equatorial binding constants, or the equilibrium constant between the two diastereomeric complexes (see Scheme 1):

$$\delta_{ind,1}/\delta_{ind,2} \approx (K_{b,eq}/K_{b,ax}) = K_{dias}$$

K_{dias} for sulfone **1** is 1.64, favoring the equatorially-bound complex, while oxathiadecalin sulfones prefer binding through the axial oxygen (for **3**, K_{dias} = 0.89; for **4**, K_{dias} = 0.68). Unlike **1**, **3**, and **4**, dithiadecalin sulfone **5** shows no evidence of any binding preference (K_{dias} = 1.00). MM2 calculations[8] were performed on sulfones **1** and **3** to gain structural insight into the binding preferences. Sulfone **1** is slightly flattened about the sulfur atom (C_9-S-C_2-C_3, torsional angle τ = 56.3°), and Eu^{+3} binds to the more sterically accessible equatorial site. More importantly, puckering is observed at the C_4 position (C_{10}-C_4-C_3-C_2, τ = 62.4°). Replacement of C_4 with oxygen in sulfone **3** increases the puckering about C_9-O-C_2-C_3 (τ = 69.9°). This in turn appears to lead to further flattening about the sulfonyl sulfur (C_{10}-S-C_3-C_2, τ = 53.2°). We hypothesize that this decreases the steric inhibition by the 1,3 axial hydrogens to Eu^{+3} binding to the axial oxygen, leading to the observed reversal of binding preference in **3** and **4**.

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