

# Natural abundance $^{33}\text{S}$ NMR spectroscopy. The first spectra of several major compound types

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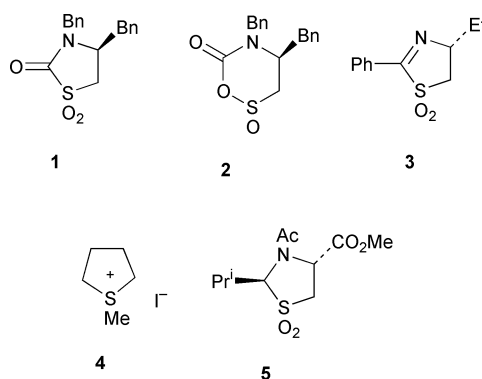
Using a high field, high power instrument,  $^{33}\text{S}$  NMR spectra have been obtained for several previously unobservable compound types including an aromatic isothiocyanate, a thiocyanate, a thiophenol, an alkyl aryl sulfide, a thiazole, a persulfate, a sulfinic acid and sulfinate salts, a sulfonylhydrazide and a sulfinyl halide. The range of data for sulfonyl fluorides and chlorides has also been extended considerably.

With a natural abundance of 0.76%, a nuclear spin of  $\frac{3}{2}$  and a substantial quadrupolar moment,  $^{33}\text{S}$  is far from ideal for NMR observation. Previous work has shown that the enormous diversity of chemical environments for sulfur is reflected in a chemical shift range of over 1000 ppm and line widths varying between 0.03 and >5000 Hz.<sup>1</sup> In  $^{33}\text{S}$  NMR the observed line width is dependent on the magnitude of the electric field gradient at the sulfur nucleus which in turn depends on the degree of symmetry around sulfur. Thus while narrow lines are observed for compounds with high molecular symmetry such as sodium sulfate ( $w_{1/2}$  6 Hz),  $\text{SF}_6$  ( $w_{1/2}$  <1 Hz) and sulfones and sulfonic acids ( $w_{1/2}$  10–300 Hz), compounds with lower molecular symmetry such as sulfoxides, sulfides and thiols ( $w_{1/2}$  2000–6500 Hz) give much broader lines making them close to the limit of observation with conventional instruments.  $^{33}\text{S}$  is best observed in solution by high power NMR techniques. High power enables short  $90^\circ$  pulse widths which in turn enables excitation of large spectral widths, ideal for broad lines. In addition chemical shift differences vary linearly with magnetic field strength but quadrupolar relaxation rates, and hence line widths, are independent of magnetic field. Thus a high power and high field NMR spectrometer is ideal for the study of  $^{33}\text{S}$  in solution.

Our attention was first drawn to this area in the course of previous studies in which a compound believed to be the 2-oxothiazolidine *S,S*-dioxide **1** was obtained.<sup>2</sup> Unexpectedly, this decomposed upon flash vacuum pyrolysis not only by loss of  $\text{SO}_2$  but also by loss of  $\text{CO}_2$  and this suggested that it might actually have the isomeric six-membered ring structure **2**. In order to differentiate between the two we followed the example of Trost and co-workers<sup>3</sup> who obtained the  $^{33}\text{S}$  NMR spectra of compounds thought to be either  $\text{RSO}_2\text{-CO}_2\text{Me}$  or  $\text{RS(O)-O-CO}_2\text{Me}$  and took the fact that a reasonably sharp signal was observed as proof of the first structure since the second would be expected to give a signal too broad to be observed. In our case, by analogy, a relatively sharp signal at  $\delta_{\text{S}} -6.5$  ( $w_{1/2}$  130 Hz) was taken as proof of structure **1** as opposed to **2**. We were also able to observe a signal at  $\delta_{\text{S}} +36.6$  ( $w_{1/2}$  200 Hz) for the novel 4,5-dihydrothiazole *S,S*-dioxide **3**.<sup>4</sup> We now report the observation of signals for the first time for a variety of compounds including several new compound types.

## Results and discussion

In the area of  $^{33}\text{S}$  NMR there has been some disagreement as to the most suitable reference with various authors favouring  $\text{CS}_2$ , sulfolane, aqueous  $\text{Cs}_2\text{SO}_4$  or aqueous  $\text{Na}_2\text{SO}_4$ . In this paper all



shifts are given relative to saturated aqueous  $\text{Na}_2\text{SO}_4$ . The known range of chemical shift for  $^{33}\text{S}$  NMR extends from  $\delta_{\text{S}} -594$  for  $\text{COS}^5$  to  $\delta_{\text{S}} +416$  for the sulfonium salt **4**.<sup>6</sup> The new results obtained here are summarised in order of increasing chemical shift in Table 1. It should be noted that for most of these examples the time required to obtain a spectrum was between 4 minutes and 2 hours. The signal for phenyl isothiocyanate is clearly at the limit of observability but the chemical shift agrees well with that for  $\text{COS}$  and is a good deal lower than the value of  $\delta_{\text{S}} -340$  ( $w_{1/2}$  4300 Hz) for ethyl isothiocyanate,<sup>7</sup> the only previous isothiocyanate to be observed. The signal observed for methyl thiocyanate is the first for any organic thiocyanate and the chemical shift is rather similar to that of  $\text{EtNCS}$  suggesting that the chemical shifts associated with  $\text{RNCS}$  and  $\text{RSCN}$  may be quite similar in general.

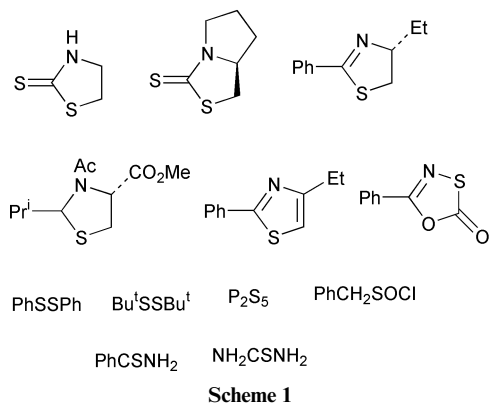
Because of the broad lines involved rather few thiols, sulfides and disulfides have been observed before. The only data previously reported for thiols are  $\delta_{\text{S}} -459$  for methanethiol<sup>5</sup> and  $\delta_{\text{S}} -415$  ( $w_{1/2}$  2100 Hz) for butane-1-thiol.<sup>7</sup> The signals observed here for phenylmethanethiol and thiophenol make it clear that introduction of an aryl group results in a significant increase in chemical shift. Apart from a series of saturated cyclic sulfides, the only previously reported value for a sulfide is  $\delta_{\text{S}} -428$  ( $w_{1/2}$  3300 Hz) for dimethyl sulfide.<sup>8</sup> Again it is clear that introduction of an aryl group results in a higher chemical shift for methyl phenyl sulfide, the first alkyl aryl sulfide to be observed. We were particularly interested to re-examine the case of diethyl disulfide since the reported value of  $\delta_{\text{S}} -501$  ( $w_{1/2}$  5120 Hz) was recorded in an early study<sup>9</sup> at only 4 MHz and the quality of the spectrum presented in that paper makes it doubtful whether any valid conclusion could be drawn. The chemical shift value for this, the only disulfide so far observed, also seems unexpectedly low compared to other thiols and sulfides. We were able to

**Table 1**  $^{33}\text{S}$  NMR data

Compound	Solvent	$\delta_{\text{S}}$	$w_{1/2}/\text{Hz}$
PhNCS	Neat	$-570 \pm 50$	23000
PhSMe	Neat	-390	19800
PhCH <sub>2</sub> SH	Neat	-379	6500
MeSCN	Neat	-369	4500
PhSH	Neat	-332	7000
EtSSEt	Neat	-297	10600
2-Methylthiazole	Neat	-72	4200
PhSO <sub>2</sub> NH <sub>2</sub>	Acetone	-25	980
K <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	H <sub>2</sub> O	-23	3000
PhSO <sub>2</sub> H	CHCl <sub>3</sub>	-20	610
4-MeC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> N(Me)NO	CHCl <sub>3</sub>	-18	5000
PhSO <sub>2</sub> <sup>-</sup> Na <sup>+</sup>	Aq. NaOH	-13	640
4-MeC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> <sup>-</sup> Na <sup>+</sup>	H <sub>2</sub> O	-11	>10000
PhSO <sub>2</sub> NHNH <sub>2</sub>	Acetone	-7	2300
HOCH <sub>2</sub> SO <sub>2</sub> <sup>-</sup> Na <sup>+</sup>	H <sub>2</sub> O	-5	500
PhSO <sub>2</sub> Cl	Neat	-0.1	6800
PhSO <sub>2</sub> F	Neat	+4	6400
EtSO <sub>2</sub> F	Neat	+17	2000
<b>5</b>	Acetone	+19	460
PhCH <sub>2</sub> SO <sub>2</sub> Cl	CHCl <sub>3</sub>	+23	5600
PhCH <sub>2</sub> SO <sub>2</sub> F	Neat	+25	5100
3-Methylisothiazole	Neat	+51	7700
EtSOCl	Neat	+218	6200

observe a strong although broad signal at  $\delta_{\text{S}} -297$ , a value which seems more in keeping with those for other aliphatic S<sup>II</sup> compounds.

Apart from a few saturated cyclic sulfides and sulfoxides and a good number of cyclic sulfones, only very few heterocyclic compounds have been observed before: thiophene<sup>7</sup> ( $\delta_{\text{S}} -119$ ), three substituted thiophenes and isothiazole<sup>5</sup> ( $\delta_{\text{S}} +53$ ), the only nitrogen containing heterocycle to be observed prior to our work. As well as compounds **1** and **3** mentioned in the introduction, a relatively sharp signal was also obtained for the thiazolidine *S,S*-dioxide **5**. The value obtained for 3-methylisothiazole is in excellent agreement with that for the unsubstituted compound while a considerable change in chemical shift is seen when we move to the isomeric 2-methylthiazole. It is worth mentioning at this stage that a considerable number of other compounds were also examined but had linewidths so large that the results cannot be considered reliable. These are shown in Scheme 1.



Only one sulfonyl fluoride, MeSO<sub>2</sub>F<sup>10</sup> ( $\delta_{\text{S}} +1$ ) and four sulfonyl chlorides, MeSO<sub>2</sub>Cl<sup>10</sup> ( $\delta_{\text{S}} +8$ ), EtSO<sub>2</sub>Cl<sup>10</sup> ( $\delta_{\text{S}} +19$ ), CF<sub>3</sub>SO<sub>2</sub>Cl<sup>11</sup> ( $\delta_{\text{S}} -21$ ) and TsCl<sup>11</sup> ( $\delta_{\text{S}} -16$ ) have been observed before. The three new fluorides and two chlorides shown in Table 1 fit well within the expected chemical shift range. The value obtained for ethanesulfonyl chloride, the first sulfonyl halide to be observed, is dramatically different but agrees with those for other compounds containing the SOCl unit such as thionyl chloride<sup>5</sup> ( $\delta_{\text{S}} +224$ ).

The values obtained for benzenesulfonamide are in good agreement with those for the previously observed sulfonamides, toluene-*p*-sulfonamide<sup>6</sup> [ $\delta_{\text{S}} -30$  ( $w_{1/2}$  1600 Hz)] and *N,N*-

dimethylmethanesulfonamide<sup>10</sup> [ $\delta_{\text{S}} -9$  ( $w_{1/2}$  300 Hz)]. We were successful in obtaining good signals for both *N*-methyl-*N*-nitrosotoluene-*p*-sulfonamide and benzenesulfonohydrazide which were noted by previous workers<sup>3</sup> as being unobservable.

Although a good number of sulfonic acids and sulfonates have been observed before, it appears that no derivative of a sulfinic acid has been observed. Both benzenesulfinic acid and its sodium salt gave reasonably sharp signals and sodium toluene-*p*-sulfinate was also observed in the same region although the signal in this case was much broader. The unusual sulfinate, sodium formaldehyde sulfoxylate, also gave a sharp signal in the same region. Although sodium sulfate is widely used as a reference, the only other oxy-anion of sulfur to have been observed before is sodium thiosulfate with  $\delta_{\text{S}} +33.5$  ( $w_{1/2}$  37 Hz) for the central sulfur atom. Potassium persulfate was found to give a rather broader signal at  $\delta_{\text{S}} -23$  with  $w_{1/2}$  3000 Hz.

In summary, we have been able to extend the range of compounds observable by  $^{33}\text{S}$  NMR considerably, but at the same time identify many types (Scheme 1) still outwith the capability of existing instrumentation. With an improvement in instrumentation particularly in the areas of high power and probe design we believe that natural abundance  $^{33}\text{S}$  NMR may be a useful method for solving a variety of structural problems in organosulfur chemistry.

## Experimental

Spectra were obtained on a Bruker MSL 500 instrument operating at 38.4 MHz. Liquid samples were run neat while solids were run as saturated solutions in the solvents shown in Table 1. RF power levels were adjusted so that 90° pulse widths between 10 and 20  $\mu\text{s}$  were obtained. Spectra were obtained using either a conventional quadrature or a quadrupole echo pulse sequence. Baseline artefacts were removed by subtracting data points from the FID as appropriate. All spectra were obtained on unspun samples in a solenoid probe. Chemical shifts are expressed in parts per million to high frequency of external aqueous sodium sulfate. Comparison with chemical shifts reported relative to CS<sub>2</sub> may be made using the equation  $\delta_{\text{S}}(\text{Na}_2\text{SO}_4) = \delta_{\text{S}}(\text{CS}_2) - 332$ .

Sulfur compounds were commercially available except for EtSO<sub>2</sub>F, PhSO<sub>2</sub>F and PhCH<sub>2</sub>SO<sub>2</sub>F,<sup>12</sup> EtSOCl,<sup>13</sup> and compound **5**<sup>14</sup> which were prepared by the literature methods.

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