Organic Magnetic Resonance, 1976, Vol. 8, pp. 108 to 114.

^{13}C NMR of Organosulphur Compounds

I—The Effects of Sulphur Substituents on the ^{13}C Chemical Shifts of Alkyl Chains and of S-Heterocycles

Giovanna Barbarella
DRF/Section Résonance Magnétique, C.E.A.-C.E.N.G., Grenoble, France

Pasquale Dembech and Anna Garbesi
Laboratorio C.N.R., Composti del Carbonio contenenti Eteroatomi, Ozzano Emilia (Bologna), Italy

Antonino Fava*
Istituto di Chimica Organica, Facoltà di Chimica Industriale, Università di Bologna, Italy

(Received 26 June 1975; accepted 18 August 1975)

Abstract—The ^{13}C NMR spectra have been determined of: (i) aliphatic compounds having at one end a functionalized sulphur atom (–SH, –S$^-$, –SMe, –S(O)Me, –SO$_2$Me and –S$^+$Me$_2$) and (ii) saturated sulphur heterocycles variously substituted at the S-atom (>S, >SO, >SO$_2$ and >S$^+$Me). The results are discussed in terms of the familiar deshielding effects for α- and β-carbons and shielding effects for γ-carbons, exerted by the sulphur atom itself and/or by the atoms or groups of which the sulphur function is made up. The γ-effect of the S-atom appears to be nearly independent of the nature of the S-function and of comparable magnitude to that of an aliphatic carbon (−2·5 ÷ −3·0 ppm). Surprisingly, however, a S—CH$_3$ group shields the carbon in γ position with respect to CH$_3$ by an amount (—5·4 ppm) which is more than twice that (−2·5 ppm) exerted by the aliphatic γ-carbon on the S-CH$_3$ carbon itself. As to the cyclic compounds, the shieldings of the α- and β-carbons can be rationalized in terms of the conformational orientation of the substituent at sulphur, and the equilibrium distribution of the conformers. The results confirm the great value of ^{13}C NMR for configurational and conformational assignment of S-heterocycles.

WITH the exception of a recent paper by Buchanan and collaborators, dealing with aryl methyl sulphides, sulphoxides and sulphones,[1] only scattered information is available in the literature on the ^{13}C chemical shifts of sulphur-containing organic compounds. The present report contributes some systematic observations on the effect of such sulphur functions as: thiol, –SH, the thiolate anion, –S$^-$, sulphide, –S–, sulphoxide, >S—O, sulphone, >SO$_2$ and the sulphonium cation, >S$^+$—R, on the ^{13}C chemical shifts of typical aliphatic and S-heterocyclic structures.

The main purpose of this work was to derive empirical criteria (additivity rules) to be used as groundwork for the conformational analysis of saturated sulphur heterocycles. The more numerous and systematic observations concern sulphoxides and sulphonium cations. We particularly concentrated on these functions since they are known to be pyramidal and configurationally stable. Therefore, when an integral part of a ring, they were expected to produce characteristic ^{13}C chemical shift effects that, while permitting facile configurational assignment, would also greatly aid the conformational assignment. Indeed, the few cyclic derivatives studied here fully confirm this expectation.†

Assignments are based on well established criteria, such as: (i) the signal multiplicity; (ii) the magnitude of the one-bond ^{13}C—H coupling, which is significantly larger for C-atoms bound to sulphur [$^1J(^{13}C—H) = 150$ to 140 Hz]; (iii) the additivity of deshielding effects produced by atoms at the α- or β-position, and shielding effects produced by atoms at the γ-position. In the same way as for other heteroatoms,[4] these substituent effects have also been found to act through the sulphur atom.

RESULTS

The results are collected in Tables 1, 3, 4 and 5. Table 1 reports the ^{13}C shieldings of aliphatic structures carrying at one end a sulphur atom which may be bound to other atoms or groups. In this Table the entire sulphur function is considered as a single unit and the shieldings are compared to those of the corresponding hydrocarbon. The results are summarised in Table 2 in the familiar form of α-, β-, γ- and δ-effects of the various sulphur functions. Table 3 reports the ^{13}C shieldings of aliphatic and cyclic sulphides as compared, in the form of α-, β- and γ-effects, to the corresponding aliphatic or alicyclic hydrocarbon where CH$_2$ replaces the heteroatom. Table 4 reports the ^{13}C shieldings of aliphatic and cyclic sulphoxides, sulphones and S-methyl sulphonium ions, in which the S-function is located at a non terminal position. The shieldings are compared to those of the corresponding sulphides, in the form of β-, γ- and δ-effects *by the substituents at the sulphur atom.*

Finally, Table 5 reports and compares the ^{13}C shifts of a conformationally anchored 6-membered sulphide, 4-isopropylthiane, and its isomeric *cis* and *trans* 1-oxides and 1-methylsulphonium cations.

† When this part of our work was completed, two communications appeared dealing with the ^{13}C NMR of isomeric, *cis* and *trans*, 6-membered sulphoxides[2] and S-methyl sulphonium cations[3] conformationally anchored by a 4-*t*-butyl group. These results[2,3] very closely match our own which have been obtained using the isopropyl as an anchoring group (see below).

* Author to whom correspondence should be addressed.

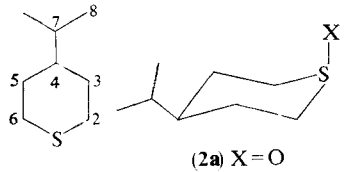
TABLE 1. ^{13}C CHEMICAL SHIFTS OF ORGANIC COMPOUNDS HAVING A SULPHUR-CONTAINING FUNCTION AT ONE END OF AN ALIPHATIC STRUCTURE

R	C-1 δ^{TMS}	C-1 α^a	C-2 δ^{TMS}	C-2 β^a	C-3 δ^{TMS}	C-3 γ^a	C-4 δ^{TMS}	C-4 δ^a	S—CH_3 δ^{TMS}
(a) Thiols, R—SH: CD_3OD solvent									
n-C_3H_7	26·4	+10·8	27·6	+11·5	12·6	−3·0			
n-C_4H_9	24·6	11·4	37·1	12·1	22·3	−2·7	13·9	+0·7	
(b) Thiolate anions, R—S^-: CD_3OD solvent									
n-C_3H_7	27·5	+11·9	30·2	+14·1	13·6	−2·0			
n-C_4H_9	24·7	+11·5	38·8	+13·8	22·5	−2·5	13·6	+0·4	
(c) Methyl sulphides, R—SMe: $CDCl_3$ solvent									
CH_3[b]	19·3	+21·6							
n-C_4H_9	34·1	20·9	31·4	+6·4	22·0	−3·0	13·7	+0·5	15·5
(d) Methyl sulphoxides, R—S(O)Me: $CDCl_3$ solvent									
$CH_3\delta$	40·1	+42·4							
n-C_3H_7	58·5	42·9	16·1	0·0	13·3	−2·3			38·6
n-C_4H_9	54·4	41·2	24·5	−0·5	22·0	−3·0	13·7		38·6
(e) Methyl sulphones, R—SO_2Me: $CDCl_3$ solvent									
$CH_3\delta$	42·6	+44·9							
n-C_3H_7	56·3	+40·7	16·3	+0·2	13·0	−2·6			40·3
n-C_4H_9	54·5	41·3	24·4	−0·6	21·7	−3·3	13·5	+0·3	40·4
(f) Dimethylsulphonium cations, R—SMe_2^+: D_2O solvent.[c]									
$CH_3\delta$	27·5	+29·8							
n-C_2H_5	38·2	+32·5	8·3	+2·6					24·3
n-C_3H_7	45·4	+29·5	17·7	+1·6	12·7	−2·7			24·8
n-C_4H_9	43·2	+30·2	25·7	+0·9	21·4	−3·4	13·7	+0·7	25·3
i-C_3H_7	47·5	+31·4	17·2	+1·6					22·2
i-C_4H_9	52·3	+28·0	25·2	0·0	21·5	−2·8			26·0
t-C_4H_9	54·8	+29·6	24·6	−0·3					20·6

[a] Chemical shift difference from the same carbon of the corresponding alkane.[5b] A positive sign indicates a downfield shift and *vice versa*.
[b] Neat. Ref. 44.
[c] The δ-values were converted to TMS as reference using the value $\delta^{TMS} = -1{\cdot}8$ ppm for the CH_3– resonance of $(CH_3)_3SiCD_2CD_2COONa$. The latter was used as internal standard in D_2O solvent.

TABLE 2. SHIELDING EFFECTS (PPM) OF SULPHUR FUNCTIONS IN 1-SUBSTITUTED ALKANES (R—X)

X	Carbon position α	β	γ	δ
$-S^-$	+11·7	+14·0	−2·3	+0·4
–SH	+11·1	+11·8	−2·9	+0·7
–SMe	+21·2	+6·4	−3·0	+0·5
$-S^+Me_2$	+30·1	+1·1	−3·0	+0·7
–SOMe	+41·8	−0·3	−2·7	+0·5
$-SO_2$Me	+41·0	−0·2	−2·9	+0·3



(1)

(2a) X=O
(2b) X=CH_3

(3a) X=O
(3b) X=CH_3

DISCUSSION

In analysing the shielding effects it is important to keep in mind that, when complex substituents are considered, the effect of the whole function is the combination of α-, β-, γ-, effects of the various atoms of which the substituent function is itself made up. Thus, for example, the effect of the –S(O)Me function at C-1 (α-effect) comprises, beside the α-effect of the S-atom, the β-effects at C-1 of both the oxygen atom and the methyl group. In turn the effect at C-2 (β-effect) comprises the γ-effect of these same atoms and groups, etc.† On this basis we will see that the various shielding effects may, on the whole, be satisfactorily understood.

Let us first consider the data concerning terminal sulphur functions (Table 1) as summarized for convenience of analysis in Table 2. The effects of a S-atom on the ^{13}C chemical shifts of an alkyl chain is best evinced by the shieldings of thiols and thiolate anions. The α-, β-, γ- and δ-effects appear to be very close to those of a carbon atom.[5b] The ionization of thiols to thiolates causes only minor deshielding effects, the larger effect being experienced by C-β, +2·2 ppm. These deshielding effects are difficult to rationalize also because of the dearth of systematic knowledge in the literature

† What in this context we call β-, γ-, · · · effects of oxygen are the shifts experienced by the β-, γ-, · · · carbon caused by replacement, at the sulphur atom, of a lone pair by a bonding pair to oxygen, which is not an exact definition for β-, γ-, · · · effects. These would be the shifts of the β-, γ-, · · · carbon caused by replacement of a bonding pair to hydrogen by a bonding pair to oxygen. The difference amounts to the β-, γ-, · · · effects of a lone pair with respect to a bonding pair to hydrogen. We will see below that the latter are quite small and can for a first approximation be neglected.

TABLE 3. ^{13}C CHEMICAL SHIFTS OF DIALKYL SULPHIDES, R—S—R, IN $CDCl_3$

	C-2[d]		C-3[d]		C-4[d]	
R	δ^{TMS}	α[a]	δ^{TMS}	β[a]	δ^{TMS}	γ[a]
C_2H_5	25·5	+2·9	14·8	+1·1		
n-C_3H_7	34·3	+1·9	23·2	+0·2	13·7	−0·2
$\widehat{S(CH_2)_4}$	(31·7)[b]	+5·2	(31·2)[b]	+4·7		
$\widehat{S(CH_2)_5}$	(29·1)[b]	+1·3	(27·8)[b]	0·0	26·6	−1·2
$\widehat{O(CH_2)_4}$[c]	68·6	+42·1	26·7	+0·2		
$\widehat{O(CH_2)_5}$[c]	69·7	+41·9	27·9	+0·1	25·1	−2·7

[a] Chemical shift difference from the same carbon in the alkane in which the heteroatom is replaced by $-CH_2-$. A + sign indicates a downfield shift and *vice versa*.
[b] Values in parentheses could be interchanged.
[c] Ref. 5b, p. 270.
[d] The numbering of carbon atoms is that normally used for heterocycles, i.e. number one is given to the heteroatom.

about the effect of putting a *localized* negative charge on a heteroatom.†

Functionalization of the S-atom causes an increase of the α-effect. Thus methylation, to give the methyl sulphide R—SMe, causes an increase of the α-effect by about 10 ppm. This effect can be viewed as a β-effect of the Me group being transmitted through the S-atom and having about the same magnitude as in alkanes (β-effect = +9·4 ppm).[5] It is interesting to observe that further methylation of the sulphide is accompanied by a further increase of the α-effect, again by 10 ppm, in agreement with the above interpretation and with the additivity rules.[5] A much larger α-effect is caused by oxidation of sulphide to sulphoxide (+20 ppm). If this has to be simply viewed as a β-effect of the oxygen atom, it appears to be unusually large (for instance the β-effect of OH is only about +10 ppm).[7] However, in this case, further substitution (oxidation) of the sulphur atom, sulphoxide → sulphone, surprisingly causes no further deshielding of C-1. Indeed, the α-effect of sulphone is just about the same as that of sulphoxide. This unexpected behaviour cannot be simply explained; it is, however, a dramatic demonstration of how very different are the properties of S—O bonds in sulphoxides and sulphones.†

† Although carboxylic acids are not strictly comparable, as the negative charge in the anion is delocalized, ionization also appears to have a deshielding effect, though of greater magnitude, on α-, β-, γ- and δ-carbons.[6]

† In contrast with this trend of ^{13}C shieldings, the α-proton shieldings vary in accordance with the effective electronegativity of the S-atom. For example, in the series Me_2S, Me_2SO, Me_2SO_2, Me_3S^+, the δ-values are 2·00, 2·49, 2·94, 2·94 ppm, respectively, and a similar sequence has been found by Allegra, Wilson and co-workers for the corresponding derivatives of tetrahydrothiophene.[8] The sequence also reflects the chemical behaviour (kinetic acidity) of the respective protons.[9]

TABLE 4. ^{13}C CHEMICAL SHIFTS OF DIALKYL SULPHOXIDES, SULPHONES AND S-METHYL SULPHONIUM CATIONS, R—X—R (X = SO, SO_2, S^+Me) IN $CDCl_3$

	C-2[c]						C-3[c]					
	–SO–		$-SO_2-$		S^+Me[a]		–SO–		$-SO_2-$		S^+Me[a]	
R	δ^{TMS}	β[b]	δ^{TMS}	β[b]	δ^{TMS}	β[b]	δ^{TMS}	γ[b]	δ^{TMS}	γ[b]	δ^{TMS}	γ[b]
C_2H_5	44·9	+19·4	46·2	+20·7	38·2	+12·7	6·8	−8·0	6·6	−8·2	8·3	−6·5
n-C_3H_7	54·4	+19·1	54·5	+20·3	43·5	+9·2	16·3	−6·9	15·5	−7·7	17·9	−5·3
$X(CH_2)_4$	54·3	+22·6	51·1	+20·4	46·5	+14·9	25·4	−5·8	22·7	−8·5	29·0	−2·2
$X(CH_2)_5$	48·2	+19·1	52·2	+23·1	37·5	+8·4	18·5	−9·3	24·3	−3·5	20·4	−7·4

	C-4[c]						S—CH_3[a]
	–SO–		$-SO_2-$		S^+Me[a]		S^+Me
R	δ^{TMS}	δ[b]	δ^{TMS}	δ[b]	δ^{TMS}	δ[b]	δ^{TMS}
C_2H_5							21·5
n-C_3H_7	13·4	−0·1	13·2	−0·3	12·9	−0·6	22·7
$\widehat{X(CH_2)_4}$							26·4
$\widehat{X(CH_2)_5}$	24·5	−2·1	23·9	−2·7	22·4	−4·2	22·2

[a] For the sulphonium cations the δ-values were converted to TMS as reference using the value $\delta^{TMS} = -1·8$ ppm for the CH_3 resonance of $(CH_3)_3SiCD_2CD_2COONa$. The latter was used as internal standard in D_2O solvent.
[b] Chemical shift difference from the same carbon of the corresponding sulphide (values in Table 3). A + sign indicates a downfield shift and *vice versa*. The Greek letters indicate the position of the C-atom with respect to the *substituent at the S-atom*.
[c] The numbering of carbon atoms is that normally used for heterocycles, i.e. number one is given to the heteroatom.

TABLE 5. ^{13}C CHEMICAL SHIFTS (δ^{TMS}) OF 4-ISOPROPYLTHIANE DERIVATIVES

	C-2, C-6		C-3, C-5		C-4		C-7	C-8	S^+-CH_3
Compound	δ^{TMS}	β[a]	δ^{TMS}	γ[a]	δ^{TMS}	δ[a]	δ^{TMS}	δ^{TMS}	δ^{TMS}
(1)	30·1		31·8		44·4		33·8	19·9	
(2a)[b]	46·7	+16·6	19·1	−12·7	43·0	−1·4	32·8	19·2	
(3a)[b]	52·3	+22·2	26·0	−5·8	42·8	−1·6	31·8	19·9	
(2b)[c]	35·6	+5·5	21·2	−10·6	40·5	−3·9	31·2	19·7	17·4
(3b)[c]	41·2	+11·1	26·9	−4·9	41·5	−2·9	32·6	19·4	25·7

[a] Chemical shift difference from the same carbon in 4-isopropylthiane. A + sign indicates a downfield shift and *vice versa*. The Greek letters indicate the position with respect to the *substituent at the S-atom*.
[b] $CDCl_3$ solvent.
[c] The δ-values were converted to TMS as reference using $\delta^{TMS} = -1·8$ for the CH_3 resonance of $(CH_3)_3SiCD_2CD_2COONa$. The latter was used as internal standard in D_2O.

As to the β-effects, they may be viewed mainly as γ-effects of the groups bound to the S-atom. In this interpretation one S—Me group appears to have a γ-effect of −5·4 ppm (RSH → RSMe) and two S—Me groups exactly twice as much, −10·7 ppm (RSH → RS^+Me_2). This γ-effect by a Me group bound to sulphur is large when compared to those observed in hydrocarbons (−2·5 ppm).[5] On the other hand, it is extremely interesting that the γ-effects produced *on the* $S—CH_3$ group by the γ-carbons of the aliphatic chain are instead quite normal, of the order of −2·5 to −3·0 ppm (Table 1, last columns, $R—S^+Me_2$ cations). This implies that the γ-effect is transmitted through the S-atom to the $S-CH_3$ group just as in a hydrocarbon chain, and the difference between the two types of γ-effects is related to the different nature of the C-atom exerting the γ-effect. This finding obviously rules out any interpretation of the γ-effect based wholly on steric grounds,[10] but is consistent with certain aspects of the γ-effect by electronegative atoms, which are becoming more and more documented in the recent literature.[11,12] This point will be more extensively discussed below in relation to 6-membered ring compounds.

The very small β-effect of the S(O)Me function (−0·3 ppm, compared to +6·4 of SMe) when viewed as a γ-effect of the S—O oxygen appears to be consistent with the generally greater γ-effect of electronegative heteroatoms with respect to carbon.[11,12] Thus, the γ-effect of sulphoxide oxygen amounts to −6·7 ppm. Surprisingly, however, further oxidation does not produce any further change of the γ-carbon shielding, and the two sulphone oxygens exert very nearly the same γ-effect as the single sulphoxide oxygen. This cannot be directly related to the different S—O bond length in sulphones and sulphoxides (1·44 against 1·51 Å)[13] because the shorter sulphone bond would actually decrease the C-γ—H · · · O distance, thus increasing the γ-effect.[11] Evidently the different γ-effect per oxygen atom must be related to the nature of the polar effect exerted through space by the two types of oxygen.

Examining now the shieldings of the C-atoms γ to the S-atom, the data of Table 2 show a surprising regularity: independently of the nature and the number of atoms bound to sulphur, the γ-effect of the S-atom remains remarkably constant at about −3 ppm. This is surprising in view of the observation, discussed above, that the γ-effect of a given atomic species depends on its chemical nature. However, we will see later that in thiane derivatives the γ-effect by sulphur appears to depend on its chemical combination (Table 4). Since in the 6-ring derivatives the γ-carbon can only be antiperiplanar to the S-atom, it is possible that the regularity observed in the acyclic compounds arises from the γ-effects of the various conformations averaging out accidentally to about the same value.

Before analysing the effects of the various sulphur functions at a non terminal position, it is useful to compare first the effects of substituting –S– for $–CH_2–$ in an alkane or cycloalkane. This comparison is shown in Table 3 which also includes some literature data on cyclic ethers. The α-, β- and γ-effects (S relative to CH_2) appear to be quite small in acyclic compounds and in the 6-membered sulphide, with only the exception of a significantly greater γ-effect in the latter (−1·2 against −0·2 ppm).† On the other hand, the 5-membered cyclic sulphide shows, with respect to thiane, relatively large deviations for both the α- and β-carbon, whose resonances appear to be shifted to significantly lower fields (~4 ppm). It is interesting to observe that, contrary to the cyclic sulphides, cyclic ethers (last two entries in Table 3) do not exhibit appreciable changes in α- and β-effects on changing ring size. This different behaviour might be related to the much greater degree of puckering allowed in thiolane with respect to oxolane or cyclopentane,[14] (due to the much longer C—S than C—O or C—C bond lengths and the smaller C—S—C bond angle)[8,15] and the correspondingly different hybridization of the thiolane carbons, which may reflect itself in the ^{13}C chemical shift.

We will now examine the effects of functionalizing the S-atom of an alkyl or cycloalkyl sulphide. These are shown in Table 4 which is divided into three parts reporting, respectively, the shieldings, δ^{TMS}, of C-1, C-2 and C-3, together with the differential shieldings with respect to the corresponding sulphides. The differential shieldings with respect to the corresponding hydrocarbon can be readily obtained by combining the data of Table 4 with those of Table 3. It is important to observe that the Greek letters in the column headings of Table 4 indicate the positions of the carbon atom from the *substituent* at sulphur.

An analysis of the data in Table 4 brings to light certain differences between acyclic and cyclic systems and, within the latter, between 5- and 6-membered rings. These differences are likely to reflect conformational factors insofar as, while the cyclic systems are conformationally more restricted, 5- and 6-membered rings may adopt quite different conformations. Thus, any analysis of the chemical shifts would require a detailed knowledge of the conformer population for both cyclic and acyclic compounds, which, except for the 6-rings, is largely unavailable at the present time.

The 6-membered cyclic derivatives can be examined in detail, however. The 6-ring sulphone, like the sulphide, is conformationally homogeneous insofar as the two chair conformations are equivalent; however, both sulphoxide and the S-methylsulphonium cation exist as mixtures of axial (a) and equatorial (e) conformers in rapid equilibrium. For thiane 1-oxide the axial conformer has been reported to be slightly favoured at equilibrium (62% at −90°)[16] while for the S-Me cation the equatorial conformer is slightly favoured (60% at 100°).[3] Thus, the shieldings observed are weighted averages of those pertaining to the individual conformers. The data of Table 5 illustrate the effects of the conformational orientation of the substituent (O or CH_3) at the S-atom on the ^{13}C shifts of the proximate carbons, and fully confirm the observations of Eliel and co-workers[3] and of Buchanan and Durst.[2] Thus, as observed for all 6-membered carbo- and heterocycles so far reported,[17] an axial substituent causes a smaller downfield shift

† Since in the 6-ring sulphide only chair conformations can be populated, in which the γ-carbon is antiperiplanar to the S-atom, this is likely to be a manifestation of the *anti* γ-effect by a heteroatom, as recently discussed by Eliel *et al.*[12] However, although these workers also reported an *anti* γ-effect of −1·2 ppm for thiane, their conclusion, based also on other data, was that sulphur does not cause an appreciable *anti* γ-shift.[12]

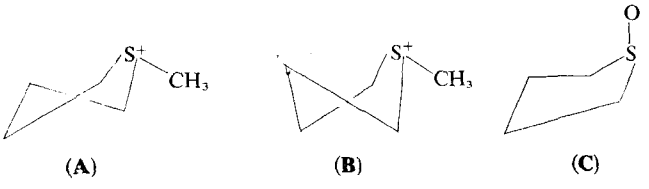
(β-effect) at C-2,C-6 and a greater upfield shift (γ-effect) at C-3,C-5 than the same substituent oriented equatorially.† The following differential shieldings in ppm, $\Delta\delta = \delta_a - \delta_e$, can be obtained from the data in Table 5 (the corresponding $\Delta\delta$ values for 4-*t*-butylthiane derivatives are given in parentheses). For sulphoxide: $\Delta\delta_{C2} = -5{\cdot}6$ ($-5{\cdot}5$),[2] $\Delta\delta_{C3} = -6{\cdot}9$ ($-7{\cdot}5$).[2] For the S-methylsulphonium ion: $\Delta\delta_{C2} = -5{\cdot}6$, $\Delta\delta_{C3} = -5{\cdot}7$ ($-6{\cdot}1$),[3] $\Delta\delta_{S\underline{C}H_3} = -8{\cdot}3$ ($-8{\cdot}9$).[3]

These differential shieldings are quite large and hence quite useful for structural assignment.§ Moreover, they can be applied to conformationally mobile systems to derive useful conformational information. For example, from the shifts of the conformationally fixed sulphide and sulphoxides (Table 5) and those of thiane and thiane 1-oxide (Table 4) the proportion of axial conformer in the latter can be estimated to be 62 or 51 % according to whether the shifts of C-2,C-6 or C-3,C-5 are considered. This is in good agreement with the known conformer distribution (~60 %).[16]

Beside their use for structural and conformational analysis, data such as those of Table 5 have other interesting features. One such feature is the large upfield shift of C-3,C-5 caused by functionalization of the S-atom. For axial isomers this is of course expected, in view of the γ *gauche* interaction between C-3,C-5 and the substituent itself. An upfield shift could also have been expected for an equatorial oxygen substituent (*anti* γ shift by an electronegative atom),[12] but it was quite unexpected that an equatorial CH_3 group should cause an upfield shift of $-4{\cdot}9$ ppm. Clearly the positive charge developed at the S-atom plays an important role, either acting inductively or through space. Another way of looking at it could be that, when bound to a positively charged centre, the methyl carbon behaves as if it were an electronegative heteroatom and exerts a sizeable *anti* γ shift. Independently of which view one chooses to describe this phenomenon, however, it gives rise to an interesting anomaly. That is, the incremental upfield shift of oxygen with respect to methyl on the *gauche* γ-carbon (axial isomers) is greater (by 1·2 ppm) than the incremental upfield shift of the *anti* γ-carbon (equatorial isomers), contrary to what is normally found.[12]

The data of Tables 4 and 5 bring to light another peculiarity. Functionalization of the S-atom is seen to cause little effect at C-4 (the carbon δ to the substituent at sulphur) in the acyclic derivatives, while producing sizeable upfield shifts in the 6-ring compounds. This behaviour is not without precedent. Thus, δ-effects are mildly deshielding in alkanes (+0·5 ppm), while in the cyclohexane series a shielding effect is observed with all substituents (up to -2 ppm).[19] Similarly, for organic phosphorous compounds, Quin and co-workers have observed a mildly deshielding δ-effect by substituents at the P-atom in acyclic structures,[4] but a shielding effect in phosphorinane derivatives.[17d] Analogous effects have also been reported in the piperidine series.[20] In the thiane series it appears to be the magnitude of the shielding which is unprecedented, reaching $-4{\cdot}2$ ppm in the thianium cation. In analysing the origin of these δ-effects, it should be observed that, because of the chair conformation prevalent in the 6-ring heterocyclics, the heteroatom can only be *anti* to the carbon. It may then be suggested that these apparent δ-effects should be viewed as changes of the *anti* γ-effect by the heteroatom attendant on functionalization of the latter. From this viewpoint it is remarkable that the effect increases along the series $>$S, $>$SO, $>SO_2$, $>S^+$—Me and parallels the effective electronegativity of (and positive charge on) the S-atom. This suggests the important factor in determining the *anti* γ-effect may not be the presence of lone pairs on the heteroatom (indeed the sulphone sulphur has no lone pair), as recently suggested.[12] An interpretation should perhaps be sought based on electrostatics, probably a field effect.[20,21]

For the 5-ring systems the available conformational information is scanty; henceforth the analysis of their ^{13}C NMR parameters is necessarily less detailed. However, the S-methylthiolanium cation, like thiolane itself,[13,22] appears to exist as a pair of rapidly equilibrating half-chair ring conformations (**A**, **B** below) in which the S^+—CH_3 group is quasi-equatorial.[23]



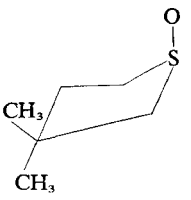
(A) **(B)** **(C)**

This conformational situation reflects itself in some remarkably consistent ^{13}C NMR effects: (i) the α-carbon resonates at an exceptionally low field, resulting in a very large β-effect by CH_3 bound to sulphur (+14·9 ppm); (ii) the β-carbon also resonates much further downfield than expected, resulting in a very small γ-effect by S^+—CH_3 [$-2{\cdot}2$ ppm, against $-7{\cdot}4$ in the conformationally mobile 6-ring sulphonium cation and against an average of $-5{\cdot}3$ ppm in acyclic sulphonium cations (Table 2)]; (iii) the S^+—$\underline{C}H_3$ resonance also appears at very low field (26·4 ppm) very near that observed for equatorial S^+—CH_3 in the 6-ring cation (25·7 ppm; Table 5). These observations are all consistent with the quasi-equatorial orientation of the S-methyl group and anticipate the great value of ^{13}C NMR in the conformational analysis of the thiolane ring.[24]

As to the 5-ring sulphoxide no definite conformational information is available. However, recent data from these laboratories have disclosed that 3,3-dimethylthiolane 1-oxide exists preferentially in an envelope conformation with the S-atom at the tip and the oxygen function quasi-axial.[25] Since the geminal methyls at C-3 are expected to favour, if anything, an increase of the torsional angle at C-3, C-4, one should conclude *a fortiori* that the parent ring sulphoxide also adopts the envelope conformation. If this analysis is correct,

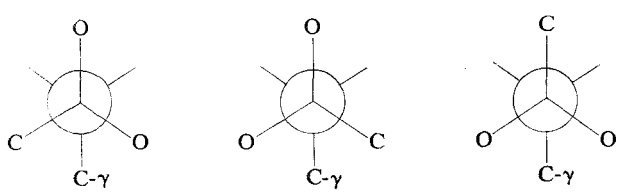
† In their paper,[2] Buchanan and Durst apply an electrostatic approach based on the S—O bond dipole, to afford an explanation of the differential shieldings of C-2,C-6 in the axial and equatorial isomeric sulphoxides. The purely electrostatic approach, however, fails to recognize the generality of the phenomenon, which is also applicable when no dipolar bonds are involved. For example, in methylcyclohexanes, C-2,C-6 is some 3·7 ppm upfield in the axial with respect to the equatorial isomer (conformer)[17a] and yet the bond dipoles must be negligible.

§ These differential shifts have proven to be an invaluable aid in the identification of stereoisomers of mono- and dimethyl substituted thiane 1-oxides and 1-methylthianium cations.[18]



and the conformation of thiolane 1-oxide is different from that of thiolane itself (half-chair)[14] the rationalization of the chemical shift differences of corresponding carbons in the two compounds becomes difficult if not impossible. Nevertheless, it is interesting to observe that in the sulphoxide, C-3, the carbon γ to oxygen, is 5·8 ppm upfield with respect to thiolane, a shift considerably smaller than that observed for the conformationally mobile 6-membered sulphoxide (−9·3 ppm). This difference is not unexpected and is accountable in terms of lesser puckering of thiolane with respect to thiane.†

A few concluding remarks on cyclic sulphones appear to be in order. No information being available about the conformation of the 5-ring sulphone, no sound comment can be made about its ^{13}C shieldings, which, however, compare closely to those of acyclic sulphones. On the other hand, the 6-ring sulphone appears to behave rather anomalously insofar as the C-3 and C-4 shieldings occur at an unexpectedly low field, giving rise to a larger than normal β-effect (+23·1 ppm) and a smaller than normal upfield γ-effect (−3·5 against about −8·0 ppm in acyclic sulphones). The latter is particularly striking and has no simple explanation. However, a conformational factor may, in part at least, be responsible for this anomaly: in either chair conformation of the 6-ring sulphone, one oxygen is *gauche* and the other is *anti* to C-γ (**C** and **D** below). Conformation **E**, where both oxygens are *gauche* to C-γ cannot be achieved in the cyclic compound, while



(C) **(D)** **(E)**

it is likely to be the more populated in the acyclic sulphones. Investigations on the temperature effect on the ^{13}C chemical shifts of suitable aliphatic sulphones appear to be desirable in this connection.

EXPERIMENTAL

Proton noise decoupled ^{13}C NMR spectra were recorded at 25·2 MHz on a Varian XL-100-15 spectrometer by the Fourier transform technique. The chemical shifts reported are within 0·2 ppm. Single frequency off-centre decoupled spectra were obtained by irradiating with a continuous wave frequency at about −4δ in the proton spectrum. The spectra were usually obtained from 1 to 2 M solutions; $CDCl_3$ solvent was used for sulphides, sulphoxides and sulphones; CD_3OD was used for thiols and thiolate anions. The latter were obtained by adding excess $CD_3O^-Na^+$ to the thiol solutions. In these solvents TMS was used as internal standard.

† This effect is particularly evident in the ^{13}C NMR of cyclopentanes with respect to cyclohexanes.[26]

The sulphonium cations were measured in D_2O using $(CH_3)_3SiCD_2CD_2COO^-Na^+$ as internal standard. The methyl resonance of the latter occurs at 1·8 ± 0·2 ppm upfield with respect to TMS. This value was obtained in various solvent mixtures of D_2O, acetone-d_6, DMSO-d_6 and dioxane.

Materials

The following were commercial samples (Fluka or Aldrich) purified by fractional distillation: n-C_3H_7SH, n-C_4H_9SH, dimethyl sulphide, dimethyl sulphoxide, dimethyl sulphone, thiolane, thiolane 1-oxide and thiolane 1,1-dioxide.

Most other products used in this work were known compounds and have been prepared by standard procedures: diethyl sulphide,[27] di-n-propyl sulphide,[27] n-butyl methyl sulphide,[28] thiane,[29] methyl n-propyl sulphoxide[30] n-butyl methyl sulphoxide,[31] diethyl sulphoxide,[27] di-n-propyl sulphoxide,[27] thiane 1-oxide,[15] diethyl sulphone,[27] di-n-propyl sulphone,[27] methyl n-propyl sulphone,[30] n-butyl methyl sulphone,[32] thiane 1,1-dioxide,[29] trimethylsulphonium iodide,[33] ethyldimethylsulphonium iodide,[34] dimethyl-n-propylsulphonium iodide,[34] n-butyldimethylsulphonium iodide,[34] dimethylisopropylsulphonium iodide,[34] dimethylisobutylsulphonium iodide,[34] diethylmethylsulphonium iodide,[35] methyldi-n-propylsulphonium iodide,[35] 1-methylthiolanium iodide,[29] 1-methylthianium iodide.[36]

tert-*Butyldimethylsulphonium fluoborate*, m.p. 196 to 197 °C, was prepared by methylation of t-butyl methyl sulphide with trimethyloxonium fluoborate in dichloromethane at 0 °C.

4-Isopropylthiane was prepared according to the reaction scheme reported in the literature for the preparation of 4-t-butylthiane:[37] (1) Reduction ($LiAlH_4$, Et_2O) of commercial diethyl 2-isopropylmalonate gave 2-isopropyl-1,3-propanediol (80%, b.p. 130 °C, 15 mm; Lit.[38] 133 °C, 18 mm). (2) Conversion ($MeSO_2Cl$, pyridine) of the diol to the dimesylate (95%, m.p. 84 to 85 °C); (3) Cyanidation (NaCN, 70% aq. EtOH, reflux, 50 h) of the dimesylate afforded 3-isopropylglutaronitrile (70%, b.p. 125 to 126 °C, 2 mm); (4) Saponification of the dinitrile (40% aq. sulphuric acid, reflux, 12 h) gave 3-isopropylglutaric acid (85%, m.p. 102 °C, Lit.[39] 101 to 102 °C); (5) Reduction ($LiAlH_4$, Et_2O) of the acid gave 3-isopropyl-1,5-pentanediol, (b.p. 146 °C, 15 mm; Lit.[40] 147 to 148 °C, 15 mm) which was converted to a low melting dimesylate (95%); (6) Cyclization of the dimesylate with Na_2S in EtOH according to standard procedure[29] afforded 4-isopropylthiane (60%, b.p. 210 °C, 760 mm, 84 to 85 °C, 15 mm). The overall yield of the entire sequence was about 20%.

cis- *and* trans-*4-Isopropylthiane 1-oxides* were obtained in a 30/70 mixture by oxidation of the sulphide with H_2O_2 in acetone,[41] b.p. 172 to 173 °C, 15 mm. The mixture was used as such to obtain the ^{13}C shifts. The assignment of the *trans* configuration to the major isomer was based (beside the ^{13}C NMR spectrum itself) on the 250 MHz proton NMR spectrum[24] and applying the well established criteria for assigning the configuration of sulphoxides (aromatic solvent shifts, lanthanide induced shifts, geminal coupling constants of α-methylene protons).[42]

cis- *and* trans-*4-Isopropyl-1-methylthianium fluoborates* were obtained as a 15/85 mixture by methylation of the sulphide with trimethyloxonium fluoborate in dichloromethane. The mixture was a low melting very hygroscopic semisolid and separation of the two isomers by fractional crystallisation was not achieved. Anal. Calc. for $C_9H_{19}SBF_4$: C, 43·92; H, 7·78; S, 13·03. Found: C, 44·05; H, 7·84; S, 12·95. The assignment of the *trans* configuration to the major isomer was based on the ^{13}C shifts themselves and was supported by a 250 MHz proton NMR study.[24] Heating the aqueous solution at 100 °C for 60 h led to equilibration of the isomers.[43] Careful integration (at 250 MHz) of the S$^+$—Me signals led to an equilibrium constant, *trans*/*cis* = 1·32 at 100 °C, in excellent agreement with that reported by Eliel and co-workers.[3]

Acknowledgement—The authors wish to thank Mr Robert Nardin for his skilful technical assistance. Financial support by C.N.R.-Rome is gratefully acknowledged by A. F.

REFERENCES

1. G. W. Buchanan, C. Reyes-Zamora and D. E. Clarke, *Can. J. Chem.* **52**, 3895 (1974).
2. G. W. Buchanan and T. Durst, *Tetrahedron Letters* 1683 (1975).

3. E. L. Eliel and R. L. Willer, *J. Amer. Chem. Soc.* **96,** 3021 (1974).
4. L. D. Quin, M. D. Gordon and S. O. Lee, *Org. Magn. Resonance* **6,** 503 (1974).
5. (a) D. M. Grant and E. G. Paul, *J. Amer. Chem. Soc.* **86,** 2984 (1964); (b) J. B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1974, Chapter 3.
6. R. Hagen and J. D. Roberts, *J. Amer. Chem. Soc.* **91,** 4504 (1969).
7. J. D. Roberts, F. J. Weigert, J. I. Kroschwitz and H. J. Reich, *J. Amer. Chem. Soc.* **92,** 1338 (1970).
8. G. Allegra, G. E. Wilson Jr, E. Benedetti, C. Pedone and R. Albert, *J. Amer. Chem. Soc.* **92,** 4002 (1970).
9. (a) J. Julien, H. Stahl-Lavriere and A. Trautmann, *Bull. Soc. Chim. France* 420 (1966); (b) J. Crosby and C. J. M. Stirling, *J. Amer. Chem. Soc.* **90,** 6869 (1968).
10. D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.* **89,** 5315 (1967); D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.* **88,** 4301 (1966); D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.* **94,** 5318 (1972).
11. D. D. Giannini, P. A. Kollman, N. S. Bhacca and M. E. Wolff, *J. Amer. Chem. Soc.* **96,** 5462 (1974).
12. E. L. Eliel, W. F. Bailey, L. D. Kopp, R. L. Willer, D. M. Grant, R. Bertrand, K. A. Christensen, D. K. Dalling, M. W. Duch, E. Wenkert, F. M. Schell and D. W. Cochran, *J. Amer. Chem. Soc.* **97,** 322 (1975)
13. U. De la Camp and H. Hope, *Acta Cryst.* **B26,** 846 (1970); H. L. Hammon, M. R. Smith and E. Kelso, *Acta Cryst.* **B28,** 246 (1972).
14. K. S. Pitzer and W. E. Donath, *J. Amer. Chem. Soc.* **81,** 3213 (1959).
15. R. Gerdil, *Helv. Chim. Acta* **57,** 489 (1974).
16. J. B. Lambert and R. G. Keske, *J. Org. Chem.* **31,** 3429 (1966).
17. For cyclohexanes, see: (a) D. K. Dalling and D. M. Grant, *J. Amer. Chem. Soc.* **89,** 6612 (1967) and **94,** 5318 (1972); (b) J. D. Roberts, F. J. Weigert, J. I. Kroschwitz and H. J. Reich, *J. Amer. Chem. Soc.* **92,** 1338 (1970). For phosphorinanes, see: (c) S. I. Featherman and L. D. Quin, *Tetrahedron Letters* 1955 (1973); (d) S. I. Featherman, S. O. Lee and L. D. Quin, *J. Org. Chem.* **39,** 2899 (1974); (e) L. D. Quin, A. T. McPhail, S. O. Lee and K. D. Onan, *Tetrahedron Letters*, 3476 (1974). For piperidines, see (f) M. W. Duch, PhD Thesis, University of Utah, 1970. Quoted in N. K. Wilson and J. B. Stothers, *Topics Stereochem.* **8,** 1 (1974).
18. G. Barbarella, P. Dembech, A. Garbesi and A. Fava, in preparation.
19. T. Pehk and E. Lippmaa, *Org. Magn. Resonance* **3,** 679 (1971).
20. M. W. Duch, PhD Thesis, University of Utah, 1970. Quoted by J. B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1974, p. 273.
21. J. G. Batchelor, J. H. Prestegard, R. J. Cushley and S. R. Lipsky, *J. Amer. Chem. Soc.* **95,** 6358 (1973).
22. Z. Nahlovska, B. Nalosky and H. M. Seip, *Acta Chem. Scand.* **23,** 3534 (1969).
23. A. Garbesi, G. Barbarella and A. Fava, *Chem. Commun.* 155 (1973); G. Barbarella, A. Garbesi, A. Boicelli and A. Fava, *J. Amer. Chem. Soc.* **95,** 8051 (1973).
24. G. Barbarella, to be published.
25. G. Barbarella, A. Garbesi and A. Fava, *J. Amer. Chem. Soc.* **97,** 5883 (1975).
26. M. Christl, H. J. Reich and J. D. Roberts, *J. Amer. Chem. Soc.* **93,** 3463 (1971).
27. W. Strecker and R. Spitaler, *Ber.* **59,** 1724 (1926).
28. A. I. Vogel and D. M. Cowan, *J. Chem. Soc.* 16 (1943).
29. E. V. Whitehead, R. A. Dean and F. A. Fidler, *J. Amer. Chem. Soc.* **73,** 3632 (1951).
30. C. C. Price and R. G. Gills, *J. Amer. Chem. Soc.* **75,** 4750 (1953).
31. P. Biscarini, G. Galloni and S. Ghersetti, *Boll. Sci. Fac. Chim. Ind. Bologna* **21,** 154 (1963).
32. F. Challenger, P. Taylor and B. Taylor, *J. Chem. Soc.* 48 (1942).
33. H. J. Emeleus and H. G. Heal, *J. Chem. Soc.* 1126 (1946).
34. C. K. Ingold, J. A. Jessop, K. I. Kuriyan and A. M. M. Mandour, *J. Chem. Soc.* 533 (1933).
35. D. Leaver and F. Challenger, *J. Chem. Soc.* 39 (1957).
36. G. Barbarella, A. Garbesi and A. Fava, *Helv. Chim. Acta* **54,** 2297 (1971).
37. J. Klein and H. Stoller, *J. Amer. Chem. Soc.* **95,** 7437 (1973).
38. M. Honjo, *Yaguku Zasshi* **77,** 589 (1957). *Chem. Abstr.* **51,** 16425^{f} (1957).
39. P. C. Guha and M. S. Muthanna, *Ber.* **71,** 2668 (1938).
40. M. Suchy and F. Sorm, *Chem. Listy Vedu Prum.* **52,** 1180 (1958). *Chem. Abstr.* **52,** 17317^{g} (1958).
41. A. Cerniani, G. Modena and P. E. Todesco, *Gazz. Chim. Ital.* **90,** 382 (1960).
42. R. Lett and A. Marquet, *Tetrahedron* **30,** 3365 (1974), give a comprehensive review of the ^{1}H NMR methods for establishing the configuration of cyclic sulphoxides.
43. N. Corsi, A. Garbesi and A. Fava, *Helv. Chim. Acta* **53,** 1499 (1970).
44. G. Miyajima and K. Nishimoto, *Org. Magn. Resonance*, **6,** 313 (1974).