STEREOCHEMISTRY OF ORGANIC SULPHUR COMPOUNDS. PART 14 .
SYNTHESIS AND CONFORMATION ANALYSIS OF 1-THIODERIVATIVES
OF 3,3-DIMETHYL-2-BUTANOL AND ITS ACETATES

E. Brunet[a], J.L. García-Ruano[a*], J.H. Rodríguez[a] and F. Alcudia[b]

[a]Departamento de Química Orgánica, Facultad de Ciencias
[b]Universidad Autónoma de Madrid, Canto Blanco, Madrid 28049
Departamento de Química Orgánica, Facultad de Farmacia,
Universidad de Sevilla
SPAIN

Abstract - The synthesis and conformational analysis of some
thioderivatives Bu^t-CHX-CH$_2$Y (X = OH and OAc; Y = SH, SMe,
SO$_2$Me and SMe$_2$) are reported. The conformational equilibra
have been established from ^{1}H-NMR data and high dilution ir stu-
dies. All the compounds exhibited almost monoconformational
behaviour around the C(1)-C(2) bond, due to strong steric fac-
tors. The observed vicinal coupling constants were used to
check the different parameterizations of Altona's equation for
our compounds with sulphur in distinct oxidation states. The
possible dihedral angle deformations were also evaluated.

INTRODUCTION

The study of several acyclic β-oxygenated thioderivatives[1] has shown that their
conformational equilibria are governed by a balance of steric and electrostatic
interactions and, when possible, by hydrogen bonding. In all instances, the eva-
luation of conformational populations (x_n) was carried out by means of equation |1|,
from the vicinal coupling constants ($J_{i,j}^{obs}$) and the corresponding theoretical ones
($J_{i,j}^n$) for each conformation. The latter were calculated by means of the Karplus
equation modified by Altona[2]. This modification seems to be one of the best
approaches as yet proposed in the literature for calculation of vicinal coupling
constants.

$$J_{i,j}^{obs} = \sum_n x_n J_{i,j}^n \qquad\qquad |1|$$

The use of calculated coupling constants was justified by the serious difficulties
encountered in obtaining rigid models with a similar geometry to that of each pos-
sible conformation of our systems. To this effect, we proposed to prepare acyclic
skeletons capable of exhibiting a monoconformational behaviour in order to check
the observed vicinal coupling with the calculated ones for the preferred rotamer.
This comparison would allow us to estimate the validity of this modified Karplus
type equation for our compounds containing sulphur in different oxidation states.
The interest of this evaluation would reside in the fact that these sulphur func-
tions are not commonly considered by authors in the parameterizations of these
equations.

Part 13. E. Brunet, J.L. García-Ruano, M.C. Martínez, J.H. Rodríguez and F. Alcu-
dia, Tetrahedron 40, 2023 (1984).

In this paper the synthesis and conformational analysis of 1-X-3,3-dimethyl-2-butanol (X = SH, SMe, SO_2Me and $^+SMe_2$) and their O-acetyl derivatives (see scheme 1) are reported.

We will also consider the existence of dihedral angle deformations[3]. The reliability of the predicted deformations by Altona's equation will give us a good indication of the applicability of the different parameterizations to our sulphur compounds.

RESULTS AND DISCUSSION

Compounds 1 to 7 were synthesized from 1-bromo-3,3-dimethyl-2-butanone following the reaction sequence shown in Scheme 1.
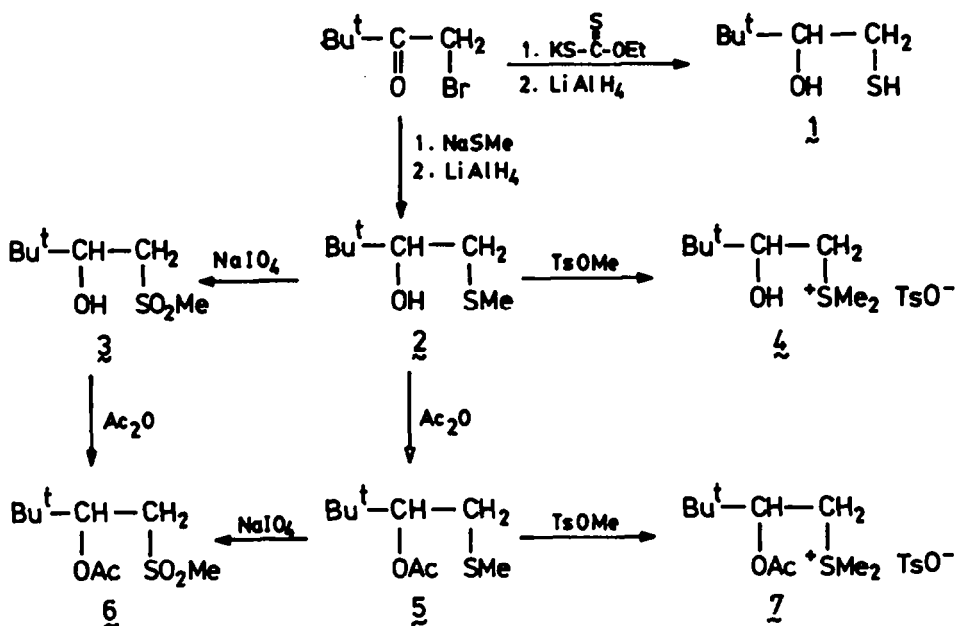
Scheme 1.

The reaction between 1-bromo-3,3-dimethyl-2-butanone and potassium ethyl xanthate or sodium methylthiolate, followed by lithium aluminium hydride reduction, yielded the thiol 1 and the thioether 2, respectively. The oxidation and methylation of the thioether gave the sulphone 3 and the sulphonium salt 4 (see experimental section). The acetyl derivatives were obtained from the corresponding hydroxycompounds by standard methods.

The [1]H-nmr parameters of compounds 1 to 7 are collected in Table 1. The hydroxy derivatives 1, 2 and 3, where intramolecular association through hydrogen bonding is possible, have been studied at different concentrations to evaluate the role played by this association in shifting the conformational equilibria. In addition, all the substrates have been observed in $CDCl_3$ and DMSO-d_6 in order to examine solvent effects.

Table 1. ^{1}H-NMR parameters of compounds 1-7 (R = H or $COCH_3$, R' = H or CH_3)

Compound	Solvent	Conc. (w/v)	δ (ppm) H(1)	H(2)	H(3)	SR	OR	t-Bu	$J_{1,2}$	$J_{1,3}$	$J_{2,3}$	$J_{1,OH}$	Others	x_A	x_B	x_C
1	a	10%	3.20	2.42	2.80	1.46	2.5^d	0.94	10.9	2.1	-13.4	-	$J_{2,SH}$=9.1; $J_{3,SH}$=8.0	94	-2	8
	a	1%	3.19	2.41	2.82	1.42	2.5^d	0.94	10.9	2.1	-13.4	-	" =9.3; " =7.7	94	-2	8
	a	0.1%	3.19	2.41	2.82	1.41	2.46	0.94	10.9	2.1	-13.5	3.2	" =9.3; " =7.7	94	-2	8
	a	0.01%	3.19	2.41	2.82	1.41	2.45	0.94	10.9	2.1	-13.5	3.2	" =9.4; " =7.6	94	-2	8
	b	5%	3.06	2.35	2.60	2.14	4.83	0.83	10.4	2.0	-13.1	6.1	" =5.2; " =10.2	89	-4	15
2	a	10%	3.31	2.40	2.75	2.10	2.85	0.94	11.1	2.0	-13.6	2.0		96	-3	7
	a	1%	3.30	2.39	2.75	2.10	2.72	0.94	11.1	2.1	-13.6	2.0		96	-2	6
	a	0.1%	3.30	2.39	2.75	2.10	2.79	0.94	11.1	2.1	-13.6	1.9		96	-2	6
	a	0.01%	3.30	2.39	2.75	2.10	2.79	0.94	11.2	2.2	-13.6	1.7		97	0	3
	b	5%	3.17	2.32	2.60	2.06	4.67	0.83	10.1	2.1	-13.2	6.0	$J_{3,OH}$=0.5	86	-4	18
3	a	2.5%	3.92	3.11	3.13	3.04	2.75	0.95	10.8	1.1	-14.7	3.7	$J_{3,OH}$=0.7	96	-15	19
	a	1%^{c}	3.93	3.11	3.13	-	-	-	10.3	1.5	-14.4	-	-	90	-11	21
	a	0.1%^{c}	3.93	3.10	3.13	-	2.72	-	10.3	1.6	-14.3	3.4	$J_{3,OH}$=0.7	90	-10	20
	a-b (4:1)		3.76	3.13	3.01	-	-	-	10.2	1.2	-14.3	-		90	-15	25
	(1:2)		3.70	3.13	2.98	-	-	-	10.3	1.3	-14.7	-		90	-13	23
	b	1%	3.59	3.14	3.01	3.00	5.27	0.84	10.2	1.3	-15.3	6.4	$J_{3,OH}$=0.8	89	-13	24
4	a	1%	3.73	3.55	3.43	3.11	-	0.88	11.4	3.0	-12.6	-		104	5	-9
	b	1%^{c}	3.55	3.40	3.43	2.85/2.89	-	0.88	11.5	3.2	-12.7	-		104	8	-12
5	a	2.5%	4.87	2.51	2.70	2.10	2.09	0.92	10.8	2.3	-14.1	-		93	0	7
	b	2.5%	4.76	2.48	2.78	2.06	2.04	0.89	10.9	2.4	-13.9	-		93	1	6
6	a	2.5%	4.33	3.16	3.21	2.95	2.12	0.95	10.4	1.6	-15.2	-		91	-10	19
	b	2.5%	5.16	3.33	3.48	2.98	2.02	0.88	10.2	1.5	-14.9	-		89	-11	22
7	a	0.1%	4.83	3.52	4.28	3.23/3.34	2.11	0.95	11.3	1.7	-13.5	-		108	-12	4
	b	0.1%	4.93	3.57	3.70	2.92/2.94	2.16	0.96	11.2	2.1	-13.4	-		105	-6	1

^{a} CDCl$_3$ ^{b} DMSO-d$_6$ ^{c} spectrum recorded at 360 MHz ^{d} broad signal ^{e} estimated from D' parametrization (see text)

The three staggered conformations that might be present in these compounds are depicted in Figure 1. The A rotamer with the t-butyl group flanked by two hydrogens must be greatly favoured on steric grounds. The other two conformers share a strong destabilizing $(Me/S)_{1,3-p}$ interaction (see Figure 2) capable by itself of largely restricting their participation in the equilibria. On the other hand, there must be serious limitations for the C-S bond to rotate freely in conformers B and C since position 1 (see Figure 2) should only be occupied by a lone electron pair, and a methyl group placed in position 2 would determine the appearance of a destabilizing $(Me/O)_{1,3-p}$ interaction. The first condition totally excludes the participation of B and C in the sulphones $\underset{\sim}{3}$ and $\underset{\sim}{6}$, and the second definitely precludes the participation of C. In addition, there are two $(Me/H)_{1,3-p}$ interactions in the B rotamers that would contribute to minimising their participation in conformational equilibria, although they are not very severe. This situation can be observed in sulphonium salts $\underset{\sim}{4}$ and $\underset{\sim}{7}$ in which position 1 is occupied by a lone electron pair, and a methyl group must hence be placed in position 2.

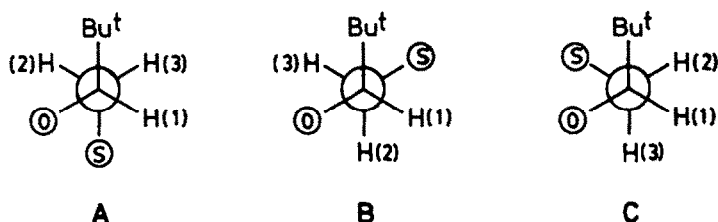Figure 1.   Staggered conformations of compounds $\underset{\sim}{1}$-$\underset{\sim}{7}$ around the C(1)-C(2) bond.
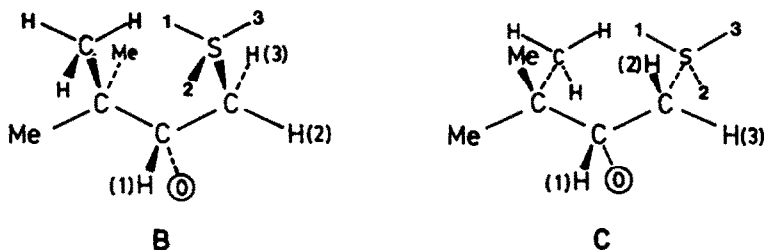

Figure 2.   Spatial arrangement of the substituents on sulphur in B and C rotamers.

This steric analysis suggests that a monoconformational behaviour may be expected for all the compounds, the rotamer A being the preferred one (only in thiol and thioethers could a slight participation of B and/or C be possible).

The disparity found in all compounds between the two vicinal couplings (see Table 1) evidenced a strong preference for A or B rotamers since in both conformations one methylenic proton has an anti arrangement and the other a gauche one with respect to H(1). We can state that A is the preferred conformation from the following: i) the steric factors argued above, ii) the predominance of A exhibited by other studied series with less severe steric restrictions (R=Me, Ph)[4,5,6], and iii) the long range coupling detected in $\underset{\sim}{2}$ and $\underset{\sim}{3}$ between the hydroxylic proton and only one methylenic proton (that which showed the lowest vicinal coupling with H(1)). This long range coupling is only possible when the protons involved are arranged in a "W"[7] (this arrangement is not feasible in B rotamer). The preference for A allows the assignment of H(2) and H(3) to spectrum signals as indicated in Table 1.

The conformation around the C-S bond could only be determined in a few cases. In the hydroxylated thiol $\underset{\sim}{1}$ and thioether $\underset{\sim}{2}$, the intramolecular hydrogen bonding

must contribute to the stabilization of the A rotamers. The most stable A conformers around the C-S bond are depicted in Figure 3.
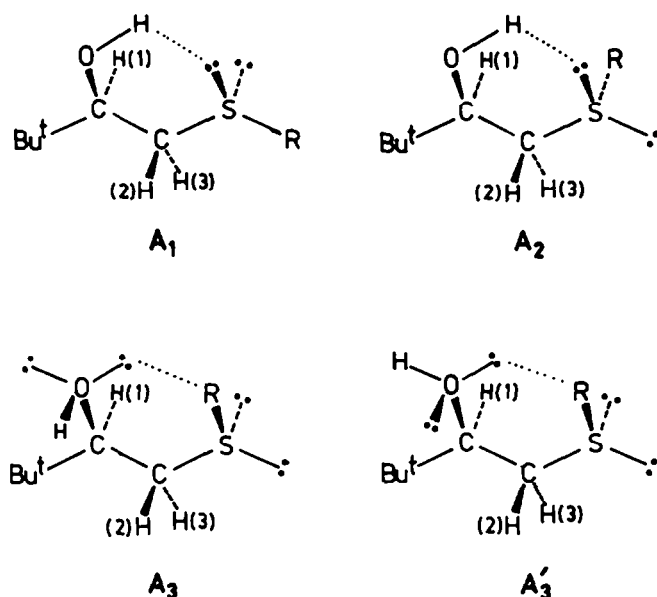

Figure 3. Favoured A rotamers for compounds $\underline{1}$ (R=H) and $\underline{2}$ (R=Me)

It must be noted that the consideration of rotamers similar to A_1 and A_2 is only reasonable while intramolecular association is possible. The rotamers A_3 and A'_3, that exhibit the S-H...O association, only have to be considered in the thiol $\underline{1}$ (R=H). The small value of $^3J_{1,OH}$=2 Hz found in the thioether 2, confirmed that its molecules must be intramolecularly hydrogen bonded because this low value is indicative of a dihedral angle close to 60º which is compatible with a stereochemis-try fixed by intramolecular association[8]. The $^3J_{1,OH}$ increased to 6 Hz in the presence of DMSO-d_6. This value has been suggested for systems bearing free rota-tion around the C-O bond[9] and may be in accordance with an extensive association with the solvent. At the same time, a constant $^4J_{3,OH}$ of c.a. 0.5 Hz was measured in DMSO-d_6. This coupling was not detectable in CDCl$_3$ because probably the pre-dominant rotamers A_1 and A_2 have not the suitable stereochemistry for a "W" arrange-ment of the protons. On the contrary, the free O-H rotation due to association with DMSO-d_6, provides for at least a fraction of the molecules to arrange their protons properly and exhibit the $^4J_{3,OH}$ coupling.

The situation is a little more complex for compound $\underline{1}$ because there are two possibilities of hydrogen bonding. Several authors have pointed out that the asso-ciation O-H...S is stronger than the O...H-S[10], so that the participation of A_1 and A_2 must be higher than those of A_3 and A'_3, although the latter should not be dis-regarded. This affirmation was based upon the observed $^3J_{1,OH}$ value for the thiol (3.2 Hz). This coupling still indicated a great number of molecules with the OH bonded group but it was slightly higher than that of the thioether, probably due to the participation of A_3 in which the involved protons are antiperiplanar. On the other hand, $^3J_{2,SH}$ in CDCl$_3$ was slightly higher than $^3J_{3,SH}$. Bearing in mind that the contribution of A_3 and A'_3 would favour the opposite situation and that in A_1 these vicinal couplings must be almost equal, this result pointed out the rela-tively large participation of A_2 (H(2) and $\underline{H}$-S in $\underline{anti}$-relationship) with respect to those of A_3 and A'_3. The observed variations when the solvent was changed were also significant. In DMSO-d_6, on the one hand $^3J_{1,OH}$ increased to 6.1 Hz and on the other, $^3J_{3,SH}$ doubled the value of $^3J_{2,SH}$. The first fact indicated free rotation

around the C-O bond (see above) and intramolecular O-H...S association was hence destroyed by DMSO-d$_6$. The second suggested that this solvent mainly associated with the OH group, reducing the participation of A$_1$ and A$_2$, but the S-H...O association seemed to be maintained (A$_3$ and A'$_3$ with the OH bonded to solvent must determine $^3J_{3,SH}$ to be higher than $^3J_{2,SH}$). Other evidence in support of intramolecular association can be found in the immutability of the chemical shift of the hydroxylic proton when compounds 1 and 2 were further diluted in CDCl$_3$. In both cases, this parameter increased its value in DMSO-d$_6$ in agreement with a strong association of OH with the solvent. Nevertheless, the most convincing proof of the important role played by intramolecular hydrogen bonding in these compounds was supplied by ir spectroscopy. The thiol 1 exhibited two bands, at 3650 and 3565 cm^{-1}, when diluted to 3.10^{-3}M in CCl$_4$ (the intermolecular interactions must be negligible at this concentration), corresponding to the free and bonded OH stretching absorptions respectively. The fraction of associated molecules could be established from the relative intensity of those bands[11] and represented 90%, in accordance with the qualitative deductions extracted from ^{1}H-nmr spectra. The thioether 2 showed a similar behaviour (absorptions at 3655 and 3520 cm^{-1}) and nearly all the molecules were associated (c.a. 95%). These data confirmed the suggested predominance of A$_1$ and A$_2$ in the conformational equilibria of the hydroxythiol and the hydroxythioether.

In the case of the sulphone 3, there is sufficient evidence to propose an almost statistical distribution of rotamer populations around the C-S bond. Before considering this problem, it must be noted that 3 is the only hydroxyderivative that showed a slight increase of H(2) shift value when CDCl$_3$ was changed for DMSO-d$_6$ (compare data at c=1% in both solvents). This fact involved a maintenance of the same conformational preference when the medium was varied and it had to be checked by recording the spectra at several CDCl$_3$:DMSO-d$_6$ mixtures (only two of them have been presented in Table 1) due to the small difference in chemical shift of the methylenic protons (the use of a 360 MHz spectrometer was also necessary). Returning to the problem of rotamer distribution around the C-S bond, the three possible conformations are depicted in Figure 4.
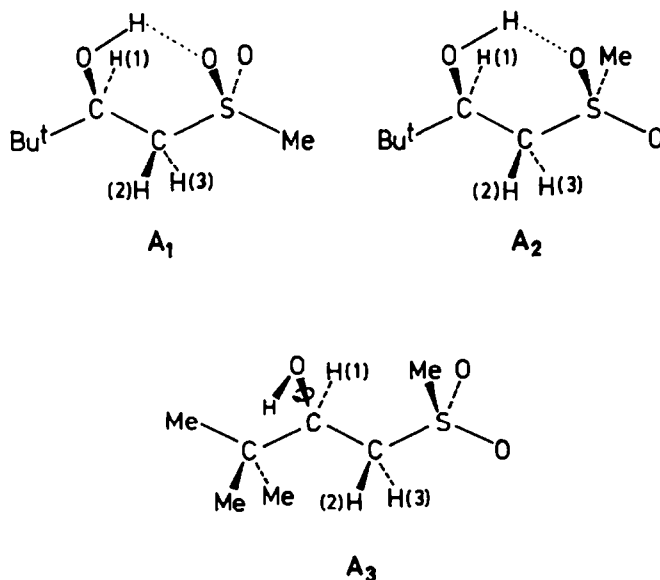

Figure 4.   Rotamers around the S-C(1) bond for the conformation A in sulphone 3 .

In principle, A$_1$ and A$_2$ would be favoured by intramolecular association with

respect to A_3 in which there is a $(Me/OH)_{1,3-p}$ destabilizing interaction on steric grounds. However, the ir spectrum of $\underline{3}$ in CCl_4 ($c=3.10^{-3}M$) showed two bands at 3645 and 3555 cm^{-1}, revealing a ratio of associated molecules of only 75% and hence, an important participation of non-hydrogen-bonded A_3 rotamer. On the other hand, the high magnitude of $^3J_{1,OH}$ (in comparison with that of the thioether $\underline{2}$) and the appearance of $^4J_{3,OH}$ (0.7 Hz) could only be explained by admitting a participation of A_3. At the same time, the methylsulphonyl signal exhibited an additional splitting due to a long range coupling with H(2) and H(3) ($^4J_{2,Me} = {}^4J_{3,Me} = 0.8$ Hz). The required arrangement for these couplings to be possible ("W" coplanar arrangement) suggested that the participation of A_2 (responsible for $^4J_{2,Me}$) and A_2 (responsible for $^4J_{3,Me}$) must be very similar. These results are not surprising according to the precedents observed in similar compounds. $^4J_{3,Me}$ was considerably higher than $^4J_{2,Me}$ in 2-methylsulphonyl-1-phenylethanol[4] and 3-methylsulphonyl-2-propanol[6], indicating that a rotamer similar to A_3 (with Ph or Me instead of Bu^t) predominated over A_2. This situation was attributed to the probable existence of an electrostatic attraction between the hydroxylic oxygen and the methyl group of the sulphone which shares the positive charge of sulphur by delocalization. Besides this, intramolecular hydrogen bonding was suggested to contribute very little to stabilising the A_1 and A_2 conformations. In the case of the sulphone $\underline{3}$, the arrangement of the hydroxylic proton, in contrast to the stereochemistry depicted in A_1 and A_2, introduces a $(Me/H)_{1,3-p}$ destabilizing interaction which would justify the lower participation of A_3 in $\underline{3}$ than in the preceding two series. The long range couplings $^4J_{2,Me}$ and $^4J_{3,Me}$ were also equal to 0.8 Hz in the acetoxysulphone $\underline{6}$, and therefore the contribution of intramolecular hydrogen bonding to the differential stabilization of rotamers around the C-S bond should be very small.

The lack of pertinent experimental data for sulphonium salts $\underline{4}$ and $\underline{7}$ and for acetoxythioether $\underline{5}$ did not permit the verification of the rotamer distribution around the C-S bond. It must be noted that the absence of additional splitting in methylenic signals, due to long range couplings, should not be considered as evidence for excluding the participation of the appropriately arranged rotamers. The electronic distribution at sulphur must be very different from the sulphone in these compounds and this factor may be responsible for these couplings not being transmitted.

THEORETICAL ANALYSIS OF CONFORMATION DEFORMATIONS

In previous papers[1,12] the conformational populations have been semiquantitatively calculated from the observed coupling constants by means of equation $|1|$. The diverse model $J^n_{i,j}$ values were obtained by Altona's equation[2], seemingly one of the best approaches as yet proposed in the literature. Among the different parameterizations indicated by Altona, three might be applicable to our compounds and they are identifiable in the original paper[2] by the letters Ⓐ, Ⓑ and Ⓓ. The first two equations were general and the latter was limited to substrates bearing the trisubstituted $CH-CH_2$ fragment. In the parameterizations Ⓐ and Ⓓ, the atom directly linked to the carbon chain is only considered for the substituent electronegativity effect. On the other hand, in Ⓑ the electronegativity value was modulated by the β-atoms. This parameterization was previously used by us because it allowed some differentiation among our sulphur functions (thiol, thioether, sulphoxide, sulphone and sulphonium salt). It was necessary to ascertain with some adequate model compounds which parameterization better filled our requirements. In the previously studied series, the existence of various rotamers in equilibrium complicated the attempts at checking the equation. On the contrary, the present series, with an almost certainly monoconformational behaviour, would allow making a theore-

tical analysis of experimental data.

As we have mentioned above, parameterization Ⓑ permitted some degree of differ-
entiation between sulphur functions but the resulting electronegativity range
(SH > SMe > $^+$SMe$_2$ > SOMe > SO$_2$Me) did not seem logical, probably because Altona did
not parameterize his equation with functionality in which the atom linked to the
carbon chain showed different oxidation states[14]. On the other hand, SMe, SO$_2$Me
and $^+$SMe$_2$ groups, although very different in electronic structure, must be con-
sidered identical as far as electronegativity is concerned in the Ⓐ and Ⓓ equations.
To avoid all these problems, we attempted to assert the validity of parameteriza-
tions Ⓐ and Ⓓ by introducing group, rather than atom, electronegativities. Hence-
forth we refer to these variants as Ⓐ̃ and Ⓓ̃ .

Thiols and thioethers share the same oxidation state and we used the Huggins
electronegativity value (2.5) for them. For the sulphonium salt, we increased that
value by 0.5 units, as this electronegativity increment is usually added when a
heteroatom passes from neutral to positively charged (for example, as a consequence
of protonation). To establish the values for the other two sulphur groups, we
used a similar procedure to that of Muller[15]. We measured the $\Delta\delta$ between α and β
protons of the C$_\beta$-C$_\alpha$-S fragment for each sulphur function under study in several
series of similar structure (2-thioderivatives of 1-phenylethanol[4], of _erythro_
and _threo_ 1,2-diphenylethanol[16,17], of 2-phenylethanol and 1-propanol[1], and 1-thio-
derivatives of 2-propanol[6]). Then the plot of the $\Delta\delta$ values of thioether and
sulphonium salt against their electronegativities (see above) obviously yielded a
straight line. The interpolation of sulphoxide and sulphone values rendered their
corresponding electronegativities (2.61 for SOMe and 2.83 for SO$_2$Me). Although this
scale must undoubtedly have certain limitations, it placed the sulphur functions in
the expected order (SMe < SOMe < SO$_2$Me < $^+$SMe$_2$).

The populations for the rotamers of Figure 1 (compounds 1 to 7), obtained by
means of both equation |1| and Ⓓ parameterization, are listed in Table 1. The other
parameterizations gave similar results. It can be seen from this table that some
populations showed a negative value and, in several cases, the participation of the
C rotamer was higher than expected from a steric point of view (see Figure 1). In
addition, the whole table is not consistent with a detailed analysis of the differ-
ent equilibria, taking into account the expected effects of solvent changes and the
interactions between heteroatomic functions. It must be noted that we considered
perfectly staggered rotamers for building Table 1 and it is well known that the
interactions among the groups may induce severe deformations in molecular geometry[3].
The larger the deviation from staggered, the higher the difference between actual
and calculated vicinal couplings and so the higher the errors in calculated popula-
tion values. We will use sulphones 3 and 6 to correlate the observed ^{3}J values with
a given geometry of the A rotamer because these compounds seemed to be the most mono-
conformational of the studied series. Especially considering that in B and C
rotamers, the distance between one methyl of the t-butyl group and the oxygen or
methyl group attached to the sulphur is shorter than the sum of Van der Waals radii.
This correlation will allow verification of the correctness of the aforementioned
parameterizations to our compounds.

The calculated dihedral α and β angles from the different parameterizations
Ⓐ to Ⓓ̃) and the $J_{1,3}$ and $J_{1,2}$ values of Table 1, are listed in Table 2. The
valence angle projection γ of methylenic protons is also indicated. The cosine type
relation between coupling constant and dihedral angle, determined the existence of
two values of α and two of β for each ^{3}J value of Table 1.

Table 2. Values of α, β and γ angles obtained from the different Altona parameterizations for sulphones 3 and 6

Parameterization	Solvent	Compound 3 (O = OH)			Compound 6 (O = OAc)		
		α	β	γ	α	β	γ
Ⓐ	CDCl$_3$	65	194	129	64	194	130
	DMSO-d$_6$	66	195	129	64	196	132
Ⓑ	CDCl$_3$	63	196	133	62	196	134
	DMSO-d$_6$	65	197	132	63	197	134
Ⓓ	CDCl$_3$	68	194	126	66	194	128
	DMSO-d$_6$	70	195	125	67	196	129
Ⓐ'	CDCl$_3$	62	194	132	61	193	132
	DMSO-d$_6$	64	195	131	61	196	135
Ⓓ'	CDCl$_3$	73	189	116	71	189	118
	DMSO-d$_6$	76	190	114	71	191	120
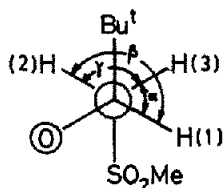
We have chosen the α value closer to 60º (the difference between the two α angles is always larger than 25º), and the β value that implies the γ value closer to 120º (the deformations of valence angles must be far less important[18]). On the other hand, we have only taken the values corresponding to c = 1% for the compounds registered at several concentrations in CDCl$_3$.

It can be seen from Table 2 that Ⓓ' was the only parameterization that gave reasonable γ values (close to 120º). Because, taking into account the nature of substituents at methylenic carbon, γ must never be higher than the value of an sp^3 angle (120º in Newman projection). This result is not surprising since Altona found the best agreement for trisubstituted ethyl groups with Ⓓ parameterization. The modification of electronegativity, made in the proper sense (see above), should tend to improve the results.

Once Ⓓ' appeared to be the more suitable parameterization, we tested the vicinal constants of compounds 1, 2 and 5, where a small participation of the other rotamers may perhaps be expected. The results obtained are collected in Table 3 (assuming a monoconformational behaviour).

Table 3. Values of α, β and γ angles obtained from compounds 1, 2 and 5 from Ⓓ' parameterization.

Compound	Solvent	α	β	γ
1	CDCl$_3$	60	189	129
	DMSO-d$_6$	61	194	133
2	CDCl$_3$	61	187	126
	DMSO-d$_6$	61	196	135
5	CDCl$_3$	58	190	132
	DMSO-d$_6$	58	189	131

The inconsistency of the obtained γ values (higher than 120º and particularly sudden changes when the solvent varied) may indicate the suggested participation of the other rotamers, which would be altered with solvent changes. To estimate the composition of these equilibria we admitted, in first approximation, that the only significant deformations would be those of the favoured rotamer (the contribution of the other rotamers is lower than 10%). Then, equation |1| was applied using the calculated parameters for various geometries of A rotamer (those of the B and C conformers correspond to staggered rotamers), and the resulting populations were analyzed separately. The results obtained for the thioether 2 in CDCl$_3$ are illustrative (see Table 4). When θ < 60º it can be seen that x_B was negative. The same

happened to x_C when $\theta > 65^\circ$. Therefore, reasonable populations could only be obtained when $60^\circ < \theta < 65^\circ$. Among these possible values of θ, the most reasonable would be that which minimized C participation (the most steric hindered rotamer), especially in compound $\underline{5}$ where intramolecular association is not possible or, in general, when the solvent is DMSO-d_6. Following this procedure, we have calculated the composition of equilibria for these three substrates in the two solvents. The results are summarized in Table 5, together with the θ value in A rotamer that yielded those populations.

Table 4. Rotamer populations calculated for several geometries of A in compound $\underline{2}$ from experimental data in CDCl$_3$.

	A parameters			Equilibria Compositions		
θ	$\beta(J_{1,2}^{calc.})$	$\alpha(J_{1,3}^{calc.})$		x_A	x_B	x_C
50	170(11.65)	50(3.44)		0.98	-0.18	0.20
55	175(11.66)	55(2.76)		0.96	-0.09	0.13
60	180(11.52)	60(2.17)		0.96	-0.02	0.06
61	181(11.47)	61(2.06)		0.96	0.00	0.04
64	184(11.29)	64(1.77)		0.97	0.03	0.00
65	185(11.22)	65(1.68)		0.97	0.05	-0.02
70	190(10.79)	70(1.30)		1.01	0.11	-0.11
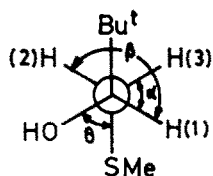
Table 5. Optimal geometry for A rotamer in compounds $\underline{1},\underline{2}$ and $\underline{5}$.

Compound	Solvent	θ	x_A	x_B	x_C
1	CDCl$_3$	65	0.95	0.04	0.01
	DMSO-d_6	70	0.93	0.07	0.00
2	CDCl$_3$	64	0.97	0.03	0.00
	DMSO-d_6	72	0.92	0.08	0.00
5	CDCl$_3$	65	0.93	0.07	0.00
	DMSO-d_6	64	0.95	0.05	0.00

The validity of the treatment is supported by the coherence of the obtained results. Both thiol $\underline{1}$ and thioether $\underline{2}$ exhibited a very high (although not exclusive) preference for A in CDCl$_3$ (see Table 5), being slightly diminished in DMSO-d_6. This diminution was followed by an increment of the angle subtended by the heteroatoms. This result is consistent with both the loss of association and the increase of effective volume of the heteroatomic functions as a consequence of solvation. On the other hand, the magnitude of the calculated variations was higher in the thioether $\underline{2}$ than in the thiol $\underline{1}$. This may be in agreement with the postulated survival of intramolecular S-H...O association in DMSO-d_6 by [1]H-nmr (see above), because the longer S-H bond must induce a higher θ angle between the heteroatoms. In thioether $\underline{5}$, the variations of angle and populations were not significant, as expected from the lack of interactions to be affected by medium polarity. Finally, it can also be observed that heteroatomic functions repel each other in the sulphone $\underline{3}$ but to a lesser extent than in compound $\underline{1}$. Additionally, no deformations were observed when this sulphone was dissolved in DMSO-d_6. These facts may reflect the small contribution of intramolecular hydrogen bonding in $\underline{3}$ (the association must be established through a six membered ring in which the OH...S distance is too long for effective hydrogen bonding).

In the case of sulphonium salts $\underline{4}$ and $\underline{7}$, the steric considerations made above, and the electrostatic attraction between the differently charged heteroatomic functions, strongly biased the conformational behaviour of these substrates. Unfortunately, it was not possible to study the deformations in the favoured rotamer for

when the $\textcircled{D}$ parameterization was applied to these compounds, the calculated $J_{1,2}$ value reached 11.3 Hz at a maximum corresponding to $\beta = 170^{\circ}$, but the higher observed value was 11.5 Hz. The explanation for this anomaly can most likely be found in the exceedingly high electronegativity value used for the sulphonium group. Although sulphur bears a positive charge, this can be delocalized over the methyl groups diminishing its actual electronegativity. This delocalization has been proposed for the $^+NMe_3$ group in acetylcholine[19].

Concluding this theoretical analysis, it can be stated that Altona's equation[2] can be applicable to thioderivatives with sulphur in different oxidation states. However, we think that the use of our electronegativity values, instead of those proposed by the author, improve the results. In spite of the inherent limitations of this equation[2], its application allows a very good semiquantitative approach to rotamer populations. Also the equation may result very valuable in developing molecular deformations, at least in homogeneous (monoconformational) systems. The validity of this study was supported in the present case by the reasonableness of the results obtained, although these should not be taken as quantitative as we have ignored some other geometrical aspects concerning vicinal coupling constants, i.e. valence angle deformations, whose magnitude is unknown in solution.

EXPERIMENTAL

Melting points were determined on a Buchi 594392 type S apparatus in open capillary tubes and are uncorrected. Elemental analyses were performed by the "Instituto de Química Orgánica (CSIC)" in Madrid with a Perkin Elmer model analyzer. Mass spectra were recorded in a Hitachi Perkin Elmer model RMU-6MG spectrometer at 70 eV. Mass data are reported in mass unit (m/e) and the values in brackets regard the relative intensity from the base peak (as 100%). IR spectra were obtained use a Pye Unicam SP-1100 spectrometer. Proton NMR spectra were recorded on a Bruker WM-200-SY (or WM-360) spectrometer in FT mode. Shifts are reported in ppm down field from internal TMS. In order to observe hydroxyl splitting, the deuterium chloroform was purified by distilling twice from phosphorous pentoxide and anhydrous potassium carbonate. The analyses of the spectra were carried out using a PANIC program on an ASPECT 2000 computer of the spectrometer. We estimate the reliability of all values to be 0.1 Hz and the root mean deviations for the calculated and the experimental lines were usually better than 0.05 Hz. The NMR parameters of compound 1-7 are listed in Table 1.

O-ethyl-S-(3,3-dimethyl-2-oxobutyl) thionodithiocarbonate
To a solution of 5 g (27.9 mmol) of 1-bromo-3,3-dimethyl-2-butanone in 30 ml of anhydrous acetone, 4.47 g (27.9 mmol) of potassium ethylxanthate in 100 ml of acetone were added and the mixture was stirred for 15 min at room temperature. The potassium bromide was filtered off and the solution evaporated. Distillation of the residue afforded 5.25 g (85%) of pure product, b.p. 88°/0.5 Torr. ν_{max} (film) 1715, 1225 and 1050 cm^{-1}. δ (CCl$_4$) 1.25 (9H, s, (CH$_3$)$_3$C), 1.45 (3H, t J=7.0 Hz, CH$_3$-CH$_2$), 4.22 (2H, s, CH$_2$S) and 4.37 (2H, q, J=7.0 Hz, CH$_2$-CH$_3$). Anal. calc. for C$_9$H$_{16}$O$_2$S: C 49.06, H 7.32, S 29.06; found: C 48.84, H 7.46, S 28.75.

3,3-dimethyl-1-mercapto-2-butanol 1
This was prepared following the procedure reported by Djerassi et al.[20] for similar compounds by reduction of the ethylxantate derivative with lithium aluminium hydride. Quantitative yield, b.p. 52°/30 Torr. ν_{max} (film) 3480 and 2560 cm^{-1}. M.S. 117(11), 115(16), 101(10), 87(27), 83(82), 69(20), 61(31), 57(100), 55(22), 47(13), 45(22), 43(47), 41(76) and 39(20).

3,3-dimethyl-1-methylthio-2-butanone
5.6 g (80 mmol) of sodium ethyl sulphide in 30 ml of anhydrous ethanol was slowly added to a solution of 12.6 g (70.4 mmol) of 1-bromo-3,3-dimethyl-2-butanone. The mixture was stirred at room temperature, diluted with 40 ml of water and extracted with chloroform. The organic extracts were dried and concentrated to yield 8 g (78%) of the ketosulphide, b.p. 69-70°/12 Torr. ν_{max} (film) 1700 cm^{-1}. δ (CCl$_4$) 1.18 (9H, s, (CH$_3$)$_3$C), 2.05 (3H, s, CH$_3$S) and 3.15 (2H, s, CH$_2$).

3,3-dimethyl-1-methylthio-2-butanol 2
A solution of 7.1 g (49 mmol) of 3,3-dimethyl-1-methylthio-2-butanone in 20 ml of anhydrous diethyl ether was added dropwise to 20 ml of ether containing 1.15 g (30 mmol) of lithium aluminium hydride. The suspension was refluxed for 4 h and the excess of hydride was destroyed by addition of 1.2 ml of water, 1.2 ml of 15% aqueous sodium hydroxide and 4 ml of water. The reaction mixture was diluted with 50 ml of chloroform and filtered. The filtrate was dried and evaporated. Distillation of the residue yielded 6.8 g (95%) of the sulphide 2, b.p. 79°/1.4 Torr.

ν_{max} (film) 3520 cm^{-1}. M.S. 148(25), 91(71), 87(32), 69(32), 62(100), 61(59), 57(46), 47(21), 43(27) and 41(57).

The acetyl derivative **5** was obtained by acetylation of **2** with acetic anydride and pyridine. Yield 88%, b.p. 100º/16 Torr. ν_{max} (film) 1745, 1240 and 1030 cm^{-1}. M.S. 130(39), 115(44), 91(9), 87(11), 83(16), 61(38), 57(19), 43(100) and 41(23), m* 101.7.

3,3-dimethyl-1-methylsulphonyl-2-butanol 3
A mixture of 0.5 g (3.4 mmol) of **2** in 10 ml of ethanol and 1.8 g (8.4 mmol) of sodium metaperiodate in 25 ml of water was refluxed for 14 h. 20 ml of water were added and the mixture was extracted with chloroform, the extract was dried and eva- porated yielding 0.45 g (74%) of **3**. This material was crystallized from benzene or carbon tetrachloride, m.p. 108-9º. ν_{max} (paraffinol) 3520, 1290 and 1135 cm^{-1}. M.S. 123(21), 85(10), 81(14), 79(9), 57(100), 43(9) and 41(26).

The acetyl derivative **6** was obtained from **3** by acetylation or from **5** by oxidation with sodium metaperiodate with similar yields (>90%). It was crystallized from benzene-light petroleum (1:1), m.p. 55-6º. ν_{max} (paraffinol) 1750, 1230, 1135 and 1030 cm^{-1}. Anal. calc. for $C_9H_{18}O_4S$: C 48.63, H 8.16, S 14.42, found C 48.43, H 8.38, S 14.56.

2-hydroxy-3,3-dimethylbuthyl dimethyl sulphonium p-toluenesulphonate 4
A mixture of 0.8 g (5.4 mmol) of **2** and 2 g (10.8 mmol) of methyl p-toluensulphonate was stirred at 30º for 100 h. The reaction mixture was washed with ether affording 1.2 g (66%) of **4**. Crystallized from chloroform, m.p. 148-9º. ν_{max} (paraffinol): 3300, 1225, 1130, 1035, 1015, 810 and 685 cm^{-1}. Anal calc. for $C_{15}H_{26}O_4S_2$: C 53.86, H 7.83, S 19.17; found C 54.25, H 8.12, S 19.32.

The acetyl derivative **7** was prepared from acetoxysulphide **5** following the procedure described in the synthesis of **4**. Reaction time 6 days. Yield 83%. It was crystal- lized from chloroform-diethyl ether (1:1), m-p. 122-5º. ν_{max} (paraffinol) 1730, 1250, 1210, 1130, 1035, 1015, 810 and 680 cm^{-1}. Anal. calc. for $C_{17}H_{28}O_5S$: C 54.23, H 7.50, S 17.03; found C 54.39, H 7.88, S 17.32.

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