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THE FIXING ROLE OF THE tert-BUTYL GROUP IN THE CONFORMATIONAL PROPERTIES OF ACYCLIC SULPHUR COMPOUNDS. SYNTHESIS AND CONFORMATIONAL ANALYSIS OF 2-tert-BUTYLTHIODERIVATIVES OF 1-PHENYLETHANOL AND THEIR O-METHYL ANALOGS

I.Fernandez, J.M.Llera, F.Zorrilla and F.Alcudia*

Dpto. de Quimica Organica y Farmaceutica. Facultad de Farmacia. Universidad de Sevilla. Prof. Garcia Gonzalez s/n. 41012 SEVILLA. SPAIN.

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Abstract: The synthesis and conformational analysis of the title compounds are reported. The conformational equilibria have been established from ^{1}H-NMR data and the role of hydrogen bonding in the hydroxylated compounds has been studied by high dilution IR spectroscopy. In all of these derivatives, the bulky But group blocks rotation around the **C-S** bond. The results for these compounds are compared with those reported for their analogous 2-methylthioderivatives. For sulphones and RR/SS sulphoxides, the possible dihedral angle deformations have also been evaluated.

Recently, we have reported the conformational properties of several series of cyclic[1] and acyclic derivatives[2] with the **X-C(1)-C(2)-Y** fragment in their structures (**X**: oxygen function, **Y**= SMe, SOMe, SO_2Me, $+SMe_2$). The study of the acyclic β-oxygenated thioderivatives showed that the position of the conformational equilibrium around **C(1)-C(2)** bond (Figure 1), determined by ^{1}H-NMR spectroscopy, was governed by a balance of steric, stereoelectronic and electrostatic interactions and, when possible, by hydrogen bonding. For these compounds, rotation around **C(2)-S** bond plays a crucial role because it affects all the possible *1,3-parallel* interactions between the substituents at **C(1)** and sulphur (see Figure 2). Nevertheless, the composition of the conformational equilibrium about this **C(2)-S** bond cannot be, in general, evaluated due to the lack of adequate spectroscopic parameters.

In the conformational analysis of cyclic systems, the bulky tert-butyl group has been widely used as an anchoring substituent[3], in order to simplify the conformational picture. From these

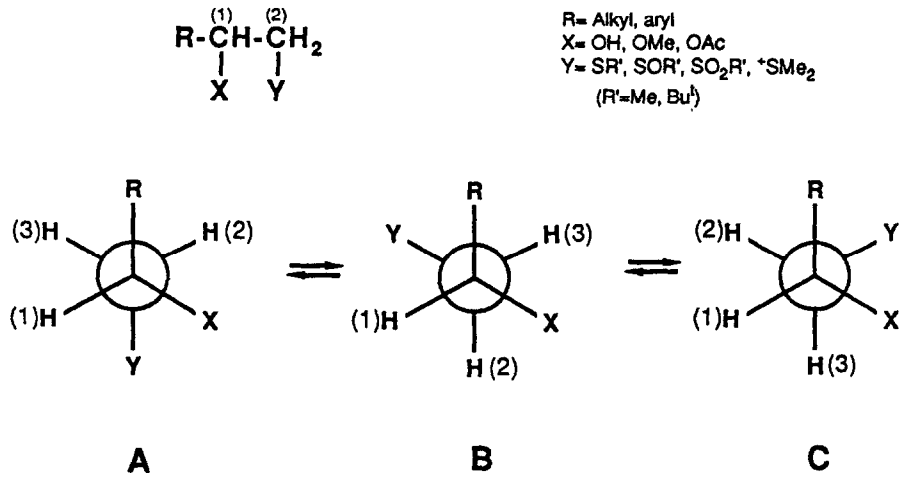
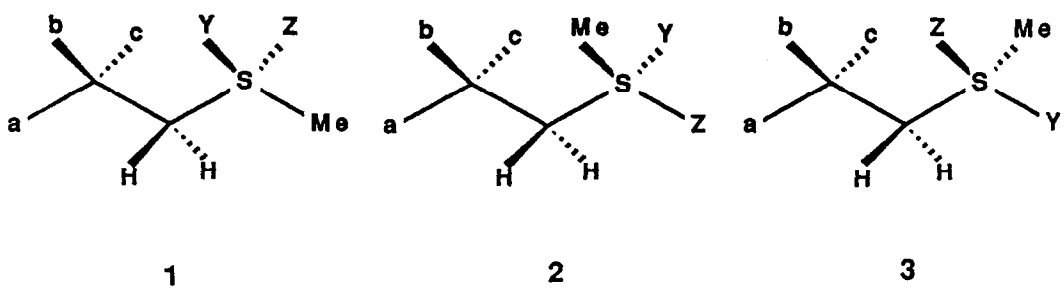


Figure 1: *Conformational equilibria around C(1)-C(2) bond of acyclic β-oxygenated sulphur derivativatives*



Rotamer **A**: a=R; b=OR'; c=H
Rotamer **B**: a=OR'; b=H; c=R
Rotamer **C**: a=H; b=R; c=OR'

Thioethers:Y=Z=:
α Sulphoxides:Y=:; Z=O
β Sulphoxides:Y=O; Z=:
Sulphones:Y=Z=O
Sulphonium salts:Y=Z=Me

Figure 2: *Rotamers 1,2 and 3 that arise from the rotation of the C(2)-S bond in each conformation of Figure 1*

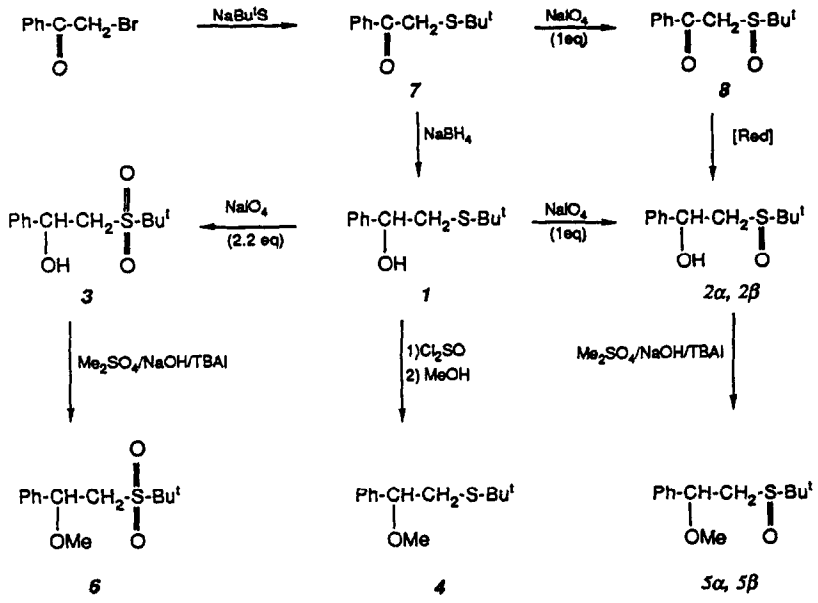
studies, assuming that no important geometric deformation exists for the derivatives under consideration[4], significant kinetic and spectroscopic data have been obtained[5]. On the contrary, since geometric deformations have often been invoked as inherent to fixing any conformation in acyclic derivatives, the Bu^t group, in spite of its interest, has hardly been used in the conformational study of these type of compounds[6]. Fortunately, it has recently been demonstrated that the Bu^t group can be efficiently used in order to block the rotation around a specific bond in acyclic substrates[2a,7]. With regard to geometrical deformations, they only seem to be meaningful when the steric factors are very severe[8].

With this in mind, the synthesis and conformational analysis of 2-tert-butylthioderivatives of 1-phenyl-ethanol and their O-methyl ethers have been carried out and the results are reported in this paper. The benefical Bu^t group, which hinders any rotation around the **C(2)-S** bond, facilitates the conformational analysis (for these compounds, only **1** type rotamers must be considered, see Figure 2). Thereby, the comparison between the obtained results for this series and those corresponding to the analogous methylthioderivatives[9,10], will show the relative stability of the different rotamers that result from the rotation around the **C(2)-S** bond for the methylthioderivatives. Thus, for methylsulphones and RS/SR methylsulphoxides (β isomers), an important contribution of the rotamers $\mathbf{A_2}$ and $\mathbf{A_3}$ (Figure 2), respectively, was proposed and theorethical calculations supported this hypothesis. On the contrary, for α sulphoxides (RR/SS configuration) and thioethers, the **1** type rotamers were considered as the only ones that participate in the conformational equilibria. According to that, the most important differences between methyl and tert-butyl-thioderivatives should be expected for sulphones and β sulphoxides. Additionally, the possible geometric deformations will be taken into account for these compounds, such as sulphones, in which severe $(\mathbf{RO/O\text{-}S})_{1,3\text{-parallel}}$ interactions are present.

RESULTS AND DISCUSSION

a) Synthesis

Compounds ***1-6*** were synthesized starting from bromoacetophenone following the reaction sequence shown in Scheme 1.



Scheme 1

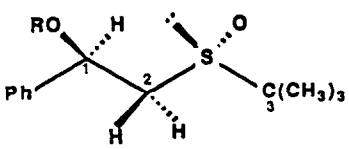
The reaction between bromoacetophenone and sodium tert-butylthiolate, followed by sodium borohydride reduction afforded the hydroxythioether ***1***.The oxidation of the sulphide with 1 eq. of $NaIO_4$ gave the hydroxysulphoxides ***2α*** and ***2β*** as a racemic mixture that was separated by column chromatography. The oxidation of ***1*** with an excess of sodium periodate produced sulphone ***3***. Methylation of ***2α***, ***2β*** and ***3*** using phase-transfer conditions yielded the corresponding β-methoxythioderivatives ***5α***, ***5β*** and ***6***. This method of methylation did not give satisfactory results for ***1***, and its O-methyl derivative ***4*** was obtained by treatment of the hydroxythioether with Cl_2SO, followed by methanolysis.

For diastereomeric β-oxygenated sulphoxides, the relative stereochemistry of both chiral centers was assigned by using three different methodologies:

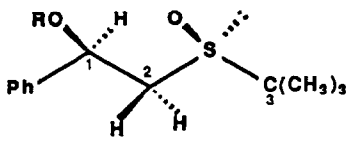
i) ^{13}C-NMR spectroscopy.- The diastereomer designed as ***2α*** presents **C(1)** and C(3) signals more shielded as compared with the ***2β*** isomer, while **C(2)** resonates at higher field in the latter diastereomer. The same spectroscopic differences are observed for the methoxysulphoxides

5α and *5β* (see Table 1). This behaviour, as has recently been proved by us[11,12], is in accordance with an RR/SS configuration for α isomers and an RS/SR one for β sulphoxides.

Table 1: *^{13}C Chemical shifts differences ($\delta_\alpha - \delta_\beta$) between diastereomeric sulphoxides 2 (α, β) and 5 (α, β) in $CDCl_3$ and DMSO-d_6*



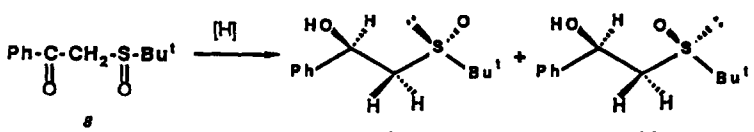
α



β

Comp.	R	Solvent	ΔC(1)	ΔC(2)	ΔC(3)	ΔC(C**Me**$_3$)	ΔC(O**Me**)
2	H	$CDCl_3$	+2.35	-2.38	+0.94	-0.31	-
		DMSO-d_6	+2.37	-0.62	+0.87	-0.14	-
5	Me	$CDCl_3$	+2.00	-0.64	+0.43	-0.33	-0.64
		DMSO-d_6	+1.99	-0.09	+0.63	-0.12	-0.30

ii) Stereoselective reduction of the β-ketosulphoxide *8* (obtained from β-ketothioether *7* by sodium metaperiodate oxidation, Scheme 1) with DIBAL and DIBAL/$ZnCl_2$ yielded the α and β isomer, respectively, in high diasteromeric excess[13] (Scheme 2). According to the literature data[2c,13,14], these results confirm the assignment made by the ^{13}C-NMR method.



[H]	2α	:	2β
DIBAL	88	:	12
DIBAL/Zn^{2+}	17	:	83

Scheme 2

iii) The very different conformational behaviour of α isomers, as compared with that of β ones, is closely related to the specific stereochemistry at both chiral centers, **C(1)** and sulphur[12]. As it will

be commented in the section on conformational analysis the results agree with the stereochemistry assigned by the two previous methods.

b) Conformational analysis

The ^{1}H-NMR parameters of compounds ***1-6***, significant in the following discussion, are collected in Table 2. In all instances, the spectra have been recorded in $CDCl_3$ at different concentrations and DMSO-d_6 in order to establish the role of the solvent nature on conformational equilibria.

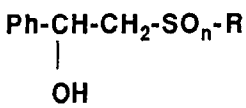
Table 2: *^{1}H-NMR parameters and conformational populations of 2-tertbutylthio derivatives of 1-phenylethanol, **1-3**, and their O-methylethers, **4-6**.*

			Chemical shifts (δ, ppm)					Coupling constants (Hz)					Conf.popul. (%)		
Comp	Solv[a]	Conc(w/v)	H(1)	H(2)	H(3)	Bu^t	OR	$J_{1,2}$	$J_{1,3}$	$-J_{2,3}$	$J_{1,OH}$	Others	X_A	X_B	X_C
1	A	6%	4.73	2.78	2.96	1.35	2.91	9.4	3.7	13.0	3.0	-	77	14	9
	A	3%	4.73	2.78	2.96	1.35	2.89	9.4	3.5	13.0	2.7	-	77	12	11
	A	0.5%	4.74	2.78	2.97	1.35	2.86	9.5	3.6	13.0	2.7	$J_{1,Ar}$=0.4	78	13	9
	B	4%	4.60	2.79	2.72	1.23	5.37	7.1	6.0	12.4	4.6	-	46	39	15
4	A	3%	4.26	2.95	2.73	1.30	3.24	8.3	5.0	12.4	-	-	61	30	9
	B	3%	4.23	2.86	2.70	1.21	3.11	7.4	5.7	12.7	-	-	50	37	13
2α	A	6%	5.33	2.78	2.77	1.22	5.16	10.2	2.5	12.5	4.8	-	92	0	8
	A	3%	5.33	2.79	2.76	1.23	4.80	10.3	2.3	12.6	4.8	-	93	-3	10
	B	3%	4.93	2.81	2.47	1.14	5.76	10.8	2.2	12.7	5.1	$J_{3,OH}$=0.9	100	-4	4
5α	A	3%	4.72	2.78	2.60	1.25	3.32	11.3	2.2	12.7	-	-	104	-1	-3
	B	3%	4.54	2.96	2.45	1.13	3.35	11.1	2.1	12.9	-	-	102	-3	1
2β	A	6%	5.36	2.90	2.63	1.25	4.86	9.8	2.5	12.7	1.4	$J_{3,OH}$=0.2	88	-2	14
	A	1%	5.39	2.90	2.62	1.27	4.81	10.0	2.2	12.6	1.2	$J_{3,OH}$=0.3	91	-6	14
	A	0.1%	5.39	2.90	2.62	1.26	4.81	10.1	2.3	12.7	1.2	$J_{3,OH}$<0.1	91	-4	13
	B	3%	4.94	2.75	2.95	1.10	5.63	6.0	7.9	12.7	4.0	$J_{1,Ar}$=0.5	29	63	8
5β	A	3%	4.62	3.05	2.78	1.88	3.26	5.1	9.5	12.3	-	-	13	82	4
	B	3%	4.49	2.82	3.03	1.09	3.35	5.4	9.0	12.8	-	-	18	77	5
3	A	6%	5.51	3.32	3.12	1.43	3.91	10.1	1.5	13.5	2.1	-	97	-16	18
	A	2%	5.52	3.32	3.12	1.44	3.89	10.2	1.5	13.4	2.0	$J_{1,Ar}$=0.5	98	-16	18
	A	0.5%	5.52	3.32	3.12	1.44	3.87	10.3	1.4	13.4	2.0	$J_{1,Ar}$=0.5	99	-17	17
	B	3%	5.14	3.43	3.25	1.30	5.66	8.3	3.3	14.0	5.0	$J_{3,OH}$=0.4	70	6	23
6	A	3%	4.87	3.48	3.08	1.42	3.30	9.0	2.8	14.0	-	-	80	1	19
	B	3%	4.69	3.56	3.27	1.30	3.36	8.8	3.2	14.2	-	-	77	61	18

a: A=$CDCl_3$, B=DMSO-d_6

The three possible staggered rotamers that result from rotation around **C(1)-C(2)** bond are depicted in Figure 1. The corresponding molar fraction deduced from coupling constants, by using the method reported in a previous paper[2e], are listed in Table 2. For hydroxylated derivatives ***1-3***, IR studies at high dilution have been carried out in order to establish the relative importance of intramolecular hydrogen bonding. The free and intramolecular associated **OH** stretching absorptions, as well as the ratio of associated molecules, are collected in Table 3. The corresponding values for the analogous methylthioderivatives are also indicated in this table for the purpose of comparison.

Table 3: *IR O-H stretching absorptions of 2-alkylthioderivatives of 1-phenylethanol 1-3, 9, 11 and 12*



Comp	n	R	Solv(Conc.Mol/l)	$\Delta\nu_{O-H}(cm^{-1})$ Free and (O-H--ring) associated	$\Delta\nu_{O-H}(cm^{-1})$ (O-H--O-S) intramolecular associated	$\Delta\nu(cm^{-1})$	% (O-H--O-S) associated molecules[a]
1	0	But	$CCl_4(5x10^{-4})$	3605	3510	95	75[b]
9	0	Me	$CCl_4(1x10^{-2})$	3635	3540	95	40[c]
2α	1	But	$CDCl_3(1x10^{-4})$	3590	-	-	0[b]
11α	1	Me	$CDCl_3(2x10^{-3})$	3600	3450[e]	150	50[d]
2β	1	But	$CDCl_3(7x10^{-4})$	3590	3370	220	70[b]
11β	1	Me	$CDCl_3(2x10^{-3})$	3602	3430	172	67[d]
3	2	But	$CDCl_3(7x10^{-4})$	3580	3514	66	90[b]
12	2	Me	$CDCl_3(1x10^{-3})$	3585	3515	70	25[b]

a:Estimated from the relative areas of both bands. b: This work. c:From ref 10a. d: From ref 10d. e:Intermolecular association has not been entirely destroyed and this band coresponds to dimers.

As can be seen in Table 2, the high participation of the rotamer **A** in $CDCl_3$ for the hydroxythioether ***1*** decreases in DMSO-d_6 or when the hydroxylic group is methylated (compound ***4***). This behaviour is, in general, similar to that of 1-phenyl-2-methylsulphenylethanol ***9*** and indicative of an important contribution of (**OH····S**) intramolecular association to the stabilization of

the rotamer **A1**. The $^3J(1,OH)$ values (2.7 Hz in $CDCl_3$ and 4.6 Hz in DMSO-d_6) support this hypothesis[15]. An important difference between ***1*** and its methyl analogue ***9*** can be found when their IR data are compared. As shown in Table 3, the hydroxythioether ***1*** has a much higher proportion of intramolecular associated molecules (75%) than ***9*** (40%). So, according to these IR data a higher proportion of rotamer **A**, intramolecularly associated, should be found for ***1***. Nevertheless, the ^{1}H-NMR parameters do not agree with the IR results indicating a similar value of X_A for both compounds (X_A=78% for ***1*** and X_A=74% for ***9***). Two reasons could be invoked to explain this behaviour:

i) The presence of the But group brings about a modification in the availability of the electron lone pairs at sulphur as a consequence of the opening of the **C-S-C** bond angle[6,16]. This could favour the intramolecular association in compound ***1*** by geometrical reasons.

ii) In order to avoid the (**S/O**) repulsive *gauche* effect[17], the contribution of a non-associated **A** type rotamer for the methylthioderivative ***9*** (A_2 in Figure 2) could be significant, justifying in this way the similar X_A values for ***1*** and ***9***, in spite of ***9*** having a lower proportion of hydrogen bonded molecules. If that was true, the participation of the rotamer A_2 should also be noticeable for those methylthioderivatives in which the hydrogen bonding is not feasible (***9*** in DMSO-d_6, as well as its O-methylderivative ***10*** in any solvent) and a higher X_A values should be observed for them as compared with their analogous tert-butyl derivatives, ***1*** and ***4***, respectively.

The comparison between the experimental results for the methylsulphenylderivatives (X_A=49% for ***9*** in DMSO-d_6; X_A=55% in $CDCl_3$ and 49% in DMSO-d_6 for ***10***) and the tert-butyl analogues (Table 2) does not support the second hypothesis. Therefore, the former explanation seems to be the only reasonable one.

The differences in the conformational properties between diastereomeric α and β sulphoxides, the comparison with several methyl analogues and ^{13}C-NMR data discussion have recently been reported by us[11,12]. The exclusive participation of the rotamer $^{\alpha}A_1$ (Figure 3) in sulphoxides ***2α*** and ***5α*** was justified by means of an $n \rightarrow \sigma^*_{S\text{-}C}$ stabilizing stereoelectronic interaction. For ***2β*** diastereomer, (**O-H····O-S**) intramolecular association and steric factors were invoked to explain the high participation of rotamer $^{\beta}A_1$ in $CDCl_3$, and the predominance of

conformer $^{\beta}\mathbf{B}_1$ when hydrogen bonding is not feasible (*2β* in DMSO-d_6 and *5β* in all solvents). These findings were in good agreement with the variation of J(1,OH) values[15] (see Table 2) and IR studies (Table 3).

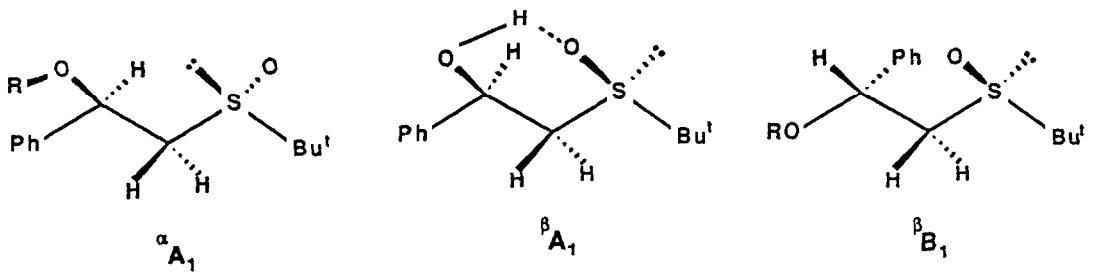


Figure 3: *Favoured conformations for α and β diastereomeric sulphoxides 2 and 5*

In the present paper, we will discuss some additional ^{1}H-NMR spectroscopic data that could reinforce the configurational assignment of the diastereomeric sulphoxides (see above). For *2α* and *2β* hydroxysulphoxides in $CDCl_3$, the different relative arrangement of substituents at both chiral centers in the predominant conformers, $^{\alpha}\mathbf{A}_1$ and $^{\beta}\mathbf{A}_1$ respectively, should cause significant differences between the chemical shifts of the protons of the ethane fragment. Taking into account the literature data, the $[\textbf{sulphinylic oxygen/H(1)}]_{1,3\text{- parallel}}$ disposition in the rotamer $^{\alpha}\mathbf{A}_1$ must deshield the **H(1)** proton[18], while the hydrogen bonding present in the conformer $^{\beta}\mathbf{A}_1$ induces a deshielding of the nearest protons[19], **H(1)** and **H(2)** (see Figure 3). The deshielding effects on **H(1)** in both diastereomers could justify the similar chemical shifts found for this proton. With regard to protons at α position to the sulphinylic function, **H(2)** and **H(3)**, according to Lett[20] no strict criterion can be given for our compounds. Nevertheless, one might reason that the similar relative environment of these protons when both isomers are compared should provide an almost identical absolute value for the differences between their chemical shifts, $|\delta H(2)-\delta H(3)|=\Delta$. The ^{1}H-NMR experimental data in Table 2, $\Delta_{2\alpha}$ =0.03 ppm and $\Delta_{2\beta}$ =0.28 ppm, can be explained by the previously commented deshielding effect of the hydrogen bonding on **H(2)** in the conformer $^{\beta}\mathbf{A}_1$.

In the case of the hydroxysulphone *3* in $CDCl_3$, an exclusive contribution of the rotamer **A** is observed. As in similar cases, a stabilizing electrostatic interaction between the hydroxylic oxygen

and the sulphonylic function ($O^{\delta-}/S^{\delta+}$) can be invoked in order to explain the high relative stability of this conformation[2,7,10]. In contrast with the methylsulphonyl derivatives[10], where there is sufficient evidence to propose an almost statistical distribution of rotamer population around the **C-S** bond, only the hydrogen bonded conformation $\mathbf{A_1}$, shown in Figure 4, is possible for the tert-butyl derivative ***3***. The IR studies of ***3*** and the 2-methylsulphonyl-1-phenylethanol ***12*** are in accord with this situation. Thus, a much higher proportion of (**O-H····O-S-O**) intramolecularly associated molecules for the former is observed (90% for ***3*** *vs.* 25% for ***12***, Table 3).

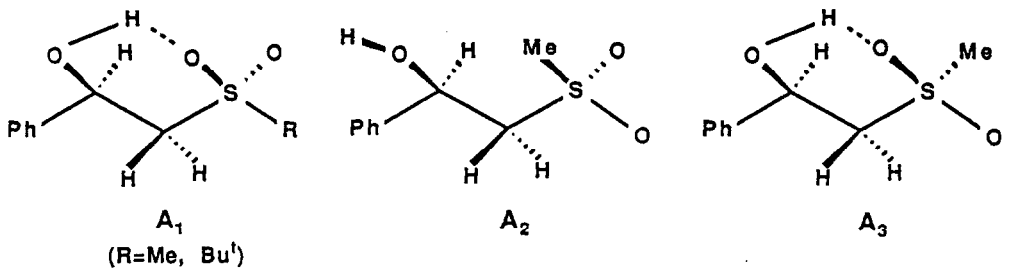


Figure 4: *Possible **A** type rotamers for 2-alkylsulphonyl derivatives of 1-phenylethanol **3** (R=Bu^t) and **12** (R=Me).*

The ^{1}H-NMR parameters for the hydroxylic protons are in agreement with IR data:

i) The difference between J(1,OH) values for ***12*** (3.0 Hz) and ***3*** (2.0 Hz) can be justified taking into account the participation of the non-intramolecularly-associated rotamer[15] for ***12*** ($\mathbf{A_2}$, Figure 4).

ii) For the methylsulphonyl derivative ***12***, a ^{4}J(3,OH) long range coupling constant is observed (1.0Hz), while the tert-butyl sulphone ***3*** does not exhibit this splitting. The required arrangement for this coupling constant to be possible ("W" coplanar disposition[21]) is again indicative of a non-participation of the rotamer$\mathbf{A_2}$ for ***3*** in contrast with an important contribution of this conformer for ***12***.

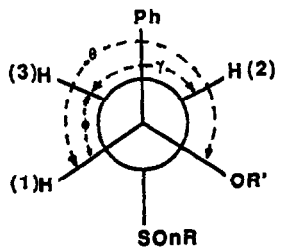
iii) As expected for a higher proportion of associated molecules in ***3***, the hydroxylic proton resonates at lower field in the tert-butyl derivative (3.89 ppm) than in its methyl analogue ***12*** (3.06 ppm).

As shown in Table 2, when hydrogen bonding is not possible (hydroxysulphone ***3*** in DMSO-d_6 and the O-methylderivative ***6*** in all solvents) the X_C value increases at the expense of X_A. Taking into account the different steric interactions present in these rotamers, $(Ph/O)_{1,3\text{-}p}$ in C_1 and $(O/H)_{1,3\text{-}p}$ in A_1, these results cannot be easily explained and must be attributed to deformations caused by the $(O/O)_{1,3\text{-}p}$ interaction present in the rotamer A_1. Additionally, for tertbutylsulphone ***3*** in DMSO-d_6 a $J_{3,OH}$=0.4 Hz was found (table 2) which indicates that a non associated A_1 type rotamer should be present and excludes the rotamer **B** from contributing to the conformational equilibrium. In the methylsulphonyl derivatives, hydroxylated and O-methylated, the $(O/O)_{1,3\text{-}p}$ destabilizing interaction can be substituted by a slightly stabilizing $(O/Me)_{1,3\text{-}p}$ one[22] (see conformation A_2 in Figure 4), the participation of the **A** type rotamer being almost independent of the possibility of intramolecular association.

The high negative values of X_B for ***3*** in $CDCl_3$ (Table 2), the more important contribution of rotamer **C** than expected from a steric point of view and the impossibility of justifying the afore mentioned conformational changes, required an analysis of the probable deformations in the tert-butylsulphones ***3*** and ***6***. It must be noted that we have considered perfectly staggered conformers for calculating rotamer population (Table 2) and it is well known that the interactions between the groups may induce severe deformations in molecular geometry[23]. Considering that, as in the methylsulphonyl analogues, only the **A** rotamer is populated, the dihedral ϕ and θ angles between the coupled protons [**H(1)**, **H(2)** and **H(3)**] can be evaluated from Altona equation[24]. The obtained values are gathered in Table 4, together with the valence angle projection γ of methylenic protons. The above mentioned monoconformational behaviour of methylsulphones ***12*** and ***13***, and sulphoxides ***2α*** and ***5β*** allowed us to apply the same methodology in order to check that, in these derivatives, there are no significant deformations, as expected. The cosine type relation between coupling constant and dihedral angle determines the existence of two ϕ angle values for each $J_{1,3}$ and two θ ones for each $J_{1,2}$. We have chosen the ϕ angles closer to 60° and the θ values that imply the γ angle closer to 120°. In all instances only deformations that avoid severe destabilizing interactions have been taken into account[2a].

As can be inferred from Table 4, the more important geometrical desviations are observed when an $(O/O)_{1,3\text{-}p}$ destabilizing interaction is present, that is, ***3*** in DMSO-d_6 and ***6*** in all cases.

Table 4: *Values of ϕ, θ and γ angles obtained from Altona equation for tert-butylsulphones 3 and 6, methylsulphones 12 and 13 and sulphoxides 2α and 5α.*



Comp.	R	R'	n	Solv	φ	θ	γ
3	Bu^t	H	2	$CDCl_3$	78	187	109
				DMSO-d_6	112	203	91
6	Bu^t	Me	2	$CDCl_3$	107	198	91
				DMSO-d_6	110	199	89
2α	Bu^t	H	1	DMSO-d_6	63	182	119
5α	Bu^t	Me	1	$CDCl_3$	62	172	110
				DMSO-d_6	62	176	114
12	Me	H	2	$CDCl_3$	68	187	119
				DMSO-d_6	58	189	131
13	Me	Me	2	$CDCl_3$	62	186	124
				DMSO-d_6	56	189	133

In Figure 5, a rotamer that shows the sense of θ and φ angle variation is depicted. The geometrical deformations bring about the rotation about the C(1)-C(2) bond in order to minimize the severe $(O/O)_{1,3\text{-}p}$ interaction, favouring at the same time, the stabilizing electrostatic attraction between the oxygen function (OH, OMe) and the positive end of the $S^{\delta+}\rightarrow O^{\delta-}$ dipole. The resulting conformer is almost an eclipsed one. In a similar way, Juaristi et al[25] have found that when the methyl group in the cis-5-methylsulphonyl-1,3-dioxane is substituted by a Bu^t one, the conformation changes from a perfectly staggered rotamer to an eclipsed one.

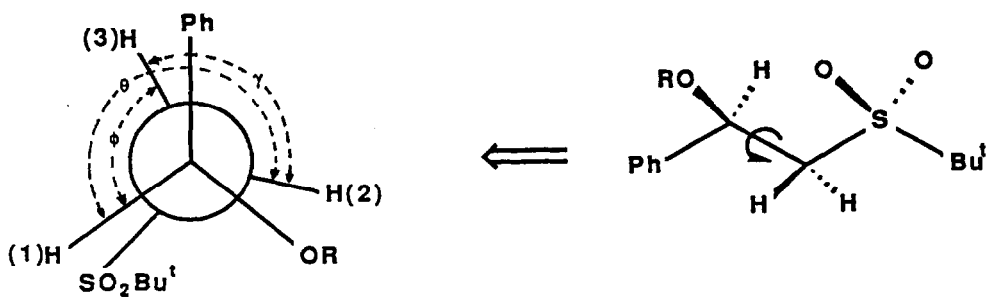


Figure 5: *Deformed A_1 type rotamer for sulphones 3 and 6 that result from rotation around C(1)-C(2) bond in order to avoid the $(RO/OS)_{1,3\text{-}p}$ destabilizing interaction.*

With regard to the lowering in the **H(2)-C-H(3)** angle (γ in Table 4), it could be a consequence of the Thorpe-Ingold effect[26]. The strong interactions between the sulphur and **C(1)** substituents must induce a higher **C(1)-C(2)-S** angle and, therefore, a decrease in the γ angle value.

On the other hand, the θ, ϕ and γ angles values for ***3*** in $CDCl_3$, the methylsulphones ***12*** and ***13***, and ***2α*** and ***5α*** sulphoxides, in all solvents, remain close to those for perfectly staggered conformations (60°, 180° and 120°, respectively).

EXPERIMENTAL SECTION.

The silica gel used in chromatography was Merck F-254 (TLC) or 60 (70-230 mesh) (column). Melting points were determined on a Buchi apparatus in open capillary tubes and are uncorrected. Elemental analyses were performed by the "Servicio de Analisis Elemental de los Servicios Tecnicos de la Universidad de Granada (STRUGA)". Mass spectra (MS) were recorded in an AEI MS-30 spectrometer at an ionizing voltage of 70 eV. Mass data are reported in mass unit (m/z) and the values in bracket regard the relative intensity from the base peak (as 100%). IR spectra were obtained on a Perkin-Elmer Model 1300 spectrometer. ^{1}H-NMR spectra were recorded on a Bruker WS-80-SY instrument. Chemical shifts are reported in parts per million downfield from internal Me_4Si. 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. Compound ***7*** was synthesized by the previously described method[13].

2-(tert-Butylsulphenyl)-1-phenylethanol (*1*).

Compund ***7*** (2.0 g, 9.6 mmol) was dissolved in 15 mL of methanol and treated with a solution of sodium borohydride (190 mg, 4.8 mmol) in methanol. After stirring for 10 minutes, the solution was concentrated. The residue was dissolved in 10 mL of water, stirred for one hour at room temperature and extracted with CH_2Cl_2 (6x40 mL). The extracts were dried and concentrated to yield 1.98 g (98%) of ***1***, b.p. 114-116°C/0.8 mmHg. IR(film) ν_{max}: 3420, 3080-3025, 2960-2860, 1480, 1455, 1365, 1165, 1060, 1030, 740 and 700 cm^{-1}. MS(EI): 210 M$^+$ (2), 193 (11), 106 (9), 104 (75) and 57 (100). ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.45-7.20 (m, 5H, C_6H_5), 4.73 (ddd, J=9.4, 3.5 and 2.7 Hz, 1H, CH), 2.96 (dd, J=3.5 and -13.0 Hz, 1H, CH_2), 2.78 (dd, J=9.4 and -13.0 Hz, 1H, CH_2), 2.89 (d, J=2.7 Hz, 1H,OH), 1.35 (s,9H, $C(CH_3)_3$).

2-(tert-Butylsulphinyl)-1-phenylethanol (*2α*) and (*2β*).

1 g (4.75 mmol) of ***1*** in 5 mL of ethanol was added to a solution of 1.02 g (4.75 mmol) of sodium metaperiodate in 10 mL of water at 0°C and the reaction mixture was stirred for 2h. The solvent was removed and the residue extracted with CH_2Cl_2 (5x30 mL). The extracts were dried and concentrated to give 0.99 g (93%) of the two diastereomeric sulphoxides as a colourless solid.

Separation of the isomers ***2α*** and ***2β*** was carried out by column chromatography (hexane:isopropanol, 30:1).

(RR/SS) Diastereomer, ***2α***: m.p. 113-114°C, crystallized from ethyl acetate. IR(KBr) ν_{max}: 3230, 3080-3020, 2980-2860, 1450, 1360, 1065, 1025, 990, 770, 710 and 700 cm^{-1}. ^{1}H-NMR($CDCl_3$), δ (ppm); 7.50-7.25 (m,5H,C_6H_5), 5.33 (ddd, J=10.3, 2.3 and 4.8 Hz, 1H, CH), 4.80 (d, J=4.8 Hz, 1H, OH). 2.79 (dd, J=10.3 and -12.6 Hz, 1H, CH_2), 2.76 (dd, J=2.3 and -12.6 Hz, 1H, CH_2), 1.23 (s, 9H, $C(CH_3)_3$). Anal. calc. for $C_{12}H_{18}SO_2$: C, 63.67, H, 8.02. Found: C, 63.81, H, 8.03.

(RS/SR) Diastereomer, ***2α***: m.p. 135-137°C, crystallized from ethyl acetate. IR(KBr) ν_{max}: 3280, 3080-3030, 2980-2880, 1475, 1460, 1440, 1370, 1045, 1030, 1020, 1010, 1000, 910, 780, 760 and 700 cm^{-1}. ^{1}H-NMR($CDCl_3$), δ (ppm): 7.50-7.25 (m, 5H, C_6H_5), 5.36 (ddd, J=9.8, 2.5 and 1.4 Hz, 1H, CH), 4.86 (d, J=1.4, 1H, OH), 2.90 (dd, J=9.8 and -12.7 Hz, 1H, CH_2), 2.63 (dd, J=2.5 and -12.7 Hz, 1H, CH_2), 1.25 (s, 9H, $C(CH_3)_3$). Anal. calc. for $C_{12}H_{18}SO_2$: C, 63.67, H, 8.02. Found: C, 63.64, H, 8.07.

2-(tert-Butylsulphonyl)-1-phenylethanol (*3*).

1 g (4.75 mmol) of ***1*** in 5 mL of ethanol was added to a solution of 2.36 g (11.0 mmol) of sodium metaperiodate in 10 mL of water and the reaction mixture was stirred for 4 hours at 50°C. The solvent was removed and the residue extracted with CH_2Cl_2 (5x50 mL). Usual work up of the extracts afforded 1.1 gr (96%) of 3, crystallized from ethyl acetate, m.p. 109-111°C. IR(KBr) ν_{max}:3455, 3050-3020, 2980-2890, 1275, 1110 and 710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.55-7.30 (m, 5H, C_6H_5), 5.52 (ddd, J=10.2, 1.5 and 2.0 Hz, 1H, CH), 3.89 (d, J=2.0 Hz, 1H, OH), 3.32 (dd, J=10.2 and -13.5 Hz, 1H, CH_2), 3.12 (dd, J=1.5 and -13.5 Hz, 1H, CH_2), 1.44 (s, 9H, $C(CH_3)_3$). Anal. calc. for $C_{12}H_{18}SO_3$: C, 59.47, H, 7.49. Found: C, 59.69, H, 7.55.

2-(tert-Butylsulphenyl)-1-methoxy-1-phenylethane (*4*).

0.15 mL (2.0 mmol) of Cl_2SO were added to a solution of 0.35 g (1.66 mmol) of ***1*** in 10 mL of CH_2Cl_2 and the reaction mixture was stirred for 2 h at room temperature. The removal of solvent gave 0.38 g (100%) of 2-(tert-butylsulphenyl)-1-chloro-1-phenylethanol, IR(film) ν_{max}: 3075-3020, 2950-2850, 1470, 1450, 1360, 1160 and 700 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ (ppm): 7.4 (m, 5H, C_6H_5), 4.96 (t, J=7.5 Hz, 1H, CH), 3.22 (d, J=7.5 Hz, 2H, CH_2), 1.30 (s, 9H, $C(CH_3)_3$). The chloroderivative was dissolved in absolute methanol and refluxed for 4 h. The solution was concentrated to yield 0.33 g (88.7%) of ***4*** as a colourless liquid that was purified by column chromatography (ether:hexane 1:1). IR(film) ν_{max}: 3080-3020, 2960-2860, 2820, 1450, 1360, 1110 and 700 cm^{-1}. MS(EI): 224 M^+ (2), 135 (9), 121 (100), 104 (16), 77 (10) and 57 (10). ^{1}H-NMR($CDCl_3$) δ (ppm): 7.34 (m, 5H, C_6H_5), 4.26 (dd, J=8.3 and 5.0 Hz, 1H, CH), 3.24 (s, 3H, OCH_3), 2.95 (dd, J=8.3 and -12.4 Hz, 1H, CH_2), 2.73 (dd, J=5.0 and -12.4 Hz, 1H, CH_2), 1.30 (s, 9H, $C(CH_3)_3$).

Methoxythioderivatives *5α*, *5β* and *6*: All of them were prepared by methylation of the corresponding hydroxy compounds, using the phase-transfer system Me_2SO_4/NaOH/TBAI, reported by Herz[27].

(RR/SS)-2-(tert-Butylsulphinyl)-1-methoxy-1-phenylethane, (*5α*).

Obtained from hydroxysulphoxide ***2α***, yield 99%. Crystallized from ether:hexane, m.p. 109-110°C. IR(KBr) ν_{max}; 3060-3020, 2980-2860, 2820, 1450, 1360, 1100, 1040, 770 and 715 cm^{-1}. ^{1}H-NMR($CDCl_3$), δ (ppm): 7.38 (m, 5H, C_6H_5), 4.72 (dd, J=11.3 and 2.2 Hz, 1H, CH), 3.32 (s, 3H, OCH_3), 2.78 (dd, J=11.3 and -12.7 Hz, 1H, CH_2), 2.60 (dd, J=2.2 and -12.7 Hz, 1H, CH_2), 1.25 (s, 9H, $C(CH_3)_3$). Anal. calc. for $C_{13}H_{20}SO_2$: C, 64.95, H,8.39. Found: C, 65.20, H, 8.47.

(RS/SR)-2-(tert-Butylsulphinyl)-1-methoxy-1-phenylethane, (*5β*).

Prepared from the corresponding hydroxysulphoxide ***2β*** as a colourless liquid, yield 82%. It was purified by colunm chromatography using ether as eluent. IR(film) ν_{max}: 3080-3030, 2970-2860, 2820, 1455, 1365, 1100, 1040, 760 and 705 cm^{-1}. MS(EI): 240 M^+ (1), 152 (65), 135 (20), 121 (100), 104 (70), 77 (16) and 57 (49). ^{1}H-NMR($CDCl_3$), δ (ppm): 7.40 (m,5H, C_6H_5), 4.62 (dd, J=5.1 and 9.5 Hz, 1H, CH), 3.26 (s, 3H, OCH_3), 3.05 (dd, J=5.1 and -12.3 Hz, 1H, CH_2), 2.78 (dd, J=9.5 and -12.3 Hz, 1H, CH_2), 1.88 (s, 9H, $C(CH_3)_3$).

2-(tert-Butylsulphonyl)-1-methoxy-1-phenylethane, (*6*).

Obtained from the hydroxysulphone ***3***, yield 97%. Crystallized from ether:hexane, m.p. 68-70°C. IR(KBr) ν_{max}: 3080-3040, 2980-2880, 2820, 1450, 1280, 1100, 980, 750 and 710 cm^{-1}. ^{1}H-NMR($CDCl_3$), δ (ppm): 7.39 (m,5H, C_6H_5), 4.87 (dd, J=9.0 and 2.8 Hz, 1H, CH), 3.48 (dd, J=9.0 and -14.0 Hz, 1H, CH_2), 3.08 (dd, J=2.8 and -14.0 Hz, 1H, CH_2), 3.30 (s, 3H, OCH_3), 1.42 (s, 9H, $C(CH_3)_3$). Anal. calc. for $C_{13}H_{20}SO_3$: C, 60.90, H, 7.86. Found: C, 61.09, H, 8.03.

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