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CONFIGURATIONAL ASSIGNMENT OF DIASTEREOISOMERS OF 2-METHYLSULPHINYL-1,2-DIPHENYLETHANOL AND OF THEIR O-METHYL AND O-ACETYL DERIVATIVES

E. Brunet, J.L. García Ruano*, M.C. Martínez, J.H. Rodríguez

Departamento de Química Orgánica. Facultad de Ciencias
Universidad Autónoma de Madrid. Cantoblanco. Madrid-34. Spain.

and

F. Alcudia

Departamento de Química Orgánica. Facultad de Farmacia
Universidad de Sevilla. Spain.

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Abstract.- The synthesis, isolation and conformational analysis of the diastereomeric 2-methylsulphinyl-1,2-diphenylethanol and of its O-methyl and O-acetyl derivatives are reported. Chemical correlations and the study of the influence of solvent polarity changes on the coupling constants have permitted the configurational assignment. Lanthanide shift reagents have been used also to this effect. The role of hydrogen bonding in the hydroxysulphoxides has been evaluated in diluted solutions by IR and NMR spectroscopy. A donor-acceptor interaction between oxygen and sulphur has been invoked to explain the differences in conformational behaviour between epimeric sulphoxides at sulphur atom.

INTRODUCTION

The conformational analysis of the two diastereoisomers of 2-methylsulphinyl-1-phenylethanol, and their O-methyl and O-acetyl derivatives[1], allowed us to assign their configurations, that were subsequently confirmed by X-ray diffraction studies[2]. The conformational criteria used in that paper seemed to be very valuable, firstly, to justify the dependence between configuration and conformational behaviour of every pair of diastereomeric beta-oxigenated sulphoxides and, secondly, to stablish the configuration itself.

In order to verify the validity of the method, we decided to carry out the isolation and the ^{1}H-NMR study of all the possible diastereoisomers of 2-methylsulphinyl-1,2-diphenylethanol, and their O-methyl and O-acetyl derivatives. The choice of these series was in part due to the fact that some of these compounds have been previously described by us[3,4], and in part because the configurational assignment of closely related compounds (erythro- isomers of 2-phenylsulphinyl-1,2-diphenylethanol), made by Kingsbury et al.[5], was the opposite to that deduced from our conformational criteria.

For Part 12, see reference 1.

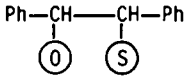
RESULTS AND DISCUSSION

The synthesis of the sulphoxides (7 to 12) was carried out by oxidation of the corresponding sulphides (1 to 6). The preparation of 1, 3, 4 and 6 have been described elsewhere[3,4]. The beta-methoxysulphide 2 was obtained by O-methylation of the corresponding beta-hydroxyderivative, that was unsuccesful in the case of compound 5. The synthesis of this sulphide was accomplished by reduction of the adequate sulphoxide as indicated in the experimental part. The oxidation of sulphides to sulphoxides yielded, in all cases, a pair of diastereoisomers that were only different in the relative configuration of the sulphur atom. Henceforth, we will refer to them as α or β.

Attempts to separate the isomers by fractional crystallization were only succesful in the hydroxysulphoxides, 7α + 7β, and 10α + 10β, naming α the isomer with higher melting point. To obtain the pure diastereoisomers of the methoxy and acetoxysulphoxides, it was neccesary to accomplish the independent O-methylation and acetylation of each diastereomeric hydroxysulphoxide. As long as the procedures used to perform these reactions did not affect the chirality of the substrates (see experimental part), we achieved also the chemical correlation of their configu-

Configuration	OH	SMe	oxdn. → SOMe (α)	+	SOMe (β)
erythro-	OH	1	7α (207-209°)[a]	+	7β (131-132°)
"	OMe	2	8α (119-120°)	+	8β (160-161°)
"	OAc	3	9α (141-143°)	+	9β (166-167°)
threo-	OH	4	10α (204-205°)	+	10β (94-95°)
"	OMe	5	11α (176-177°)	+	11β (189-190°)
"	OAc	6	12α (154-156°)	+	12β (98-99°)

a.- Melting point

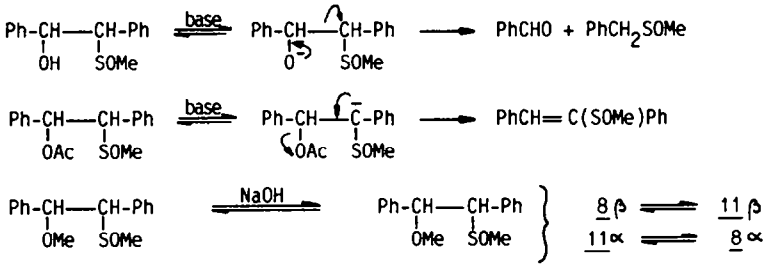


Scheme 1

rations. Thus, the diastereoisomers of the same denomination (α or β) within a series (erythro- or threo-), share the same relative configuration of their chiral centers. It must be noted that the α/β designation does not follow the melting point criterion in methoxy and acetoxy sulfoxides.

In order to correlate the configuration of both series of sulphoxides (erythro- and threo-) we tried the equilibration of the carbon chiral centers. The combination of Oppenauer oxidation and Meerwain-Poundorf-Verley reduction has been used to equilibrate secondary hydroxylic chiral carbons[6]. Unfortunately, the treatment of 7α, 7β, 10α and 10β with equimolecular amounts of aluminium isopropoxide in isopropanol, containing 2% of acetone, did not modify either of the substrates even after long periods (ca. 300 h) under reflux. The acidity of the benzylic proton near the methylsulphinyl group suggested the posibility of equilibrating C2 in basic media. The reactions carried out are given in the following scheme:

Attepmts to correlate beginning with hydroxysulphoxides were unfruitful. The reaction with NaH or metal hydroxides yielded mixtures where retrocondensation products were predominant. The situation was similar when the reactions were performed with the acetoxysulphoxides because a mixture of geometric isomers of methylsulphinylstilbene was isolated. Its formation from the corresponding carbanion is favourable because the OAc is a very good leaving group. When the methoxysulphoxydes were the starting materials (the OMe is a worse leaving group), olefins were also obtained but now, we were able to detect the resulting diastereoisomers from equilibration on C2. Definitively, in the reactions of erythro-8β and threo-11α with a 0.3% solution of NaOH in EtOH/H_2O (1:1), 11β and 8α could be detected respectively. These tests allowed us to affirm that the relative configuration of C1 was identical in the sulphoxides of the same denomination (α or β) in the erythro- and threo- series.



Scheme 2

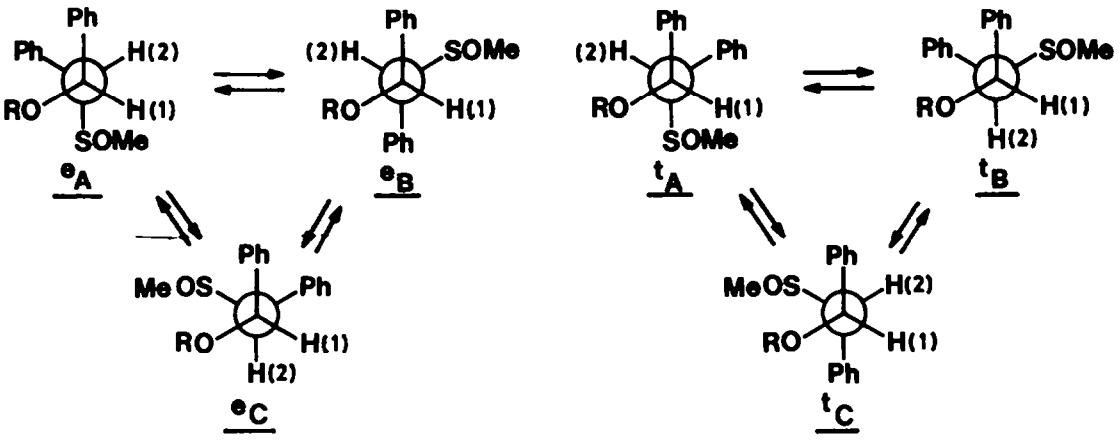


Figure 1.- Staggered conformations of the sulphoxides 7 to 12.

Table 1.- ^{1}H-RMN parameters of compounds 7 to 12.

Compd.	Solv.[a]	Chemical shifts (ppm) H(1)	H(2)	Me-S	Coupling consts. (Hz) $J_{1,2}$	$J_{1,2}$	Chemical shifts (ppm) Me-S	H(2)	H(1)	Solv.[a]	Compd.
7α[b]	A	5.74	3.83	2.37	2.7	7.3	2.09	3.53	5.61	A	7β
	B	5.47	4.03	2.21	3.0	8.6	2.12	3.92	5.19	B	
8α	A	5.17	3.64	2.30	3.0	9.3	2.06	3.58	4.92	A	8β
	B	5.03	4.10	2.25	3.3	9.8	2.00	4.05	4.82	B	
9α[b]	A	6.56	3.85	2.28	3.5	10.5	2.05	3.70	6.55	A	9β
	B	6.39	4.41	2.28	3.5	10.0	2.03	4.37	6.37	B	
10α[c]	A	5.50	3.73	2.14	10.0	9.5	2.51	3.92	5.55	A	10β
	B	5.11	3.98	1.99	10.8	8.3	2.40	4.33	5.42	B	
11α	A	4.86	3.62	2.06	10.6	5.7	2.39	4.14	5.04	A	11β
	B	4.79	4.18	2.50	11.0	8.6	2.42	4.51	5.01	B	
12α[c]	A	6.37	3.81	2.13	11.1	8.2	2.28	4.28	6.60	A	12β
	B	6.24	4.50	2.09	11.4	9.0	2.39	4.71	6.49	B	

a.- A = $CDCl_3$, B = DMSO-d_6. b.- Reference 3. c.- Reference 4.

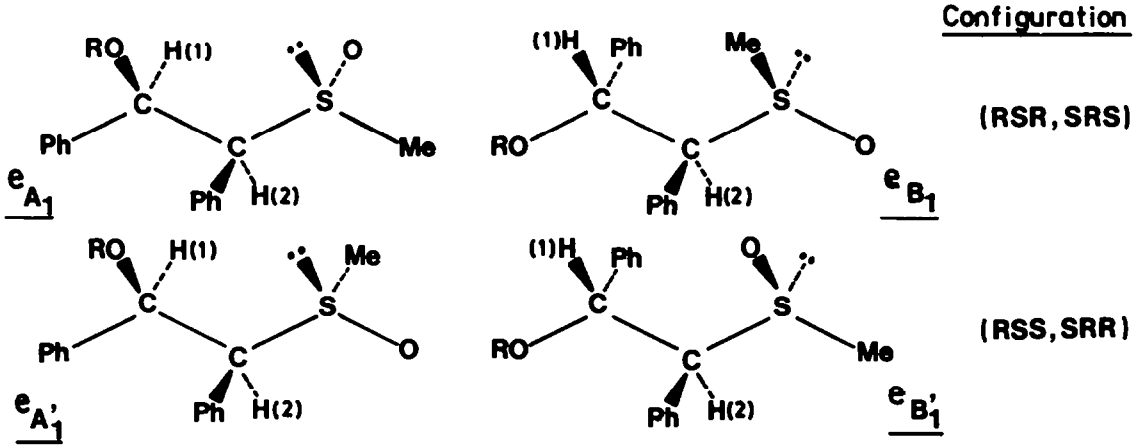


Figure 2.- More stable rotamers of erythro-sulphoxides 8 and 9, considering rotation around the C—S bond.

The staggered conformations of the sulphoxides (7 to 12) are depicted in fig. 1 and their ^{1}H-NMR parameters are listed in table 1. The remarkable differences of conformational behaviour of each pair of epimers at sulphur can be easily observed in this table by comparing their $J_{1,2}$ values. In the erythro- compounds, the α isomers exhibited a small value of $J_{1,2}$ reflecting a large predominance of ^eA and/or ^eC rotamers (see fig.1), whereas the β ones, where $J_{1,2}$ is higher, must share a great participation of ^eB rotamers with the protons in an anti relationship. In the threo- derivatives, the contribution to the equilibria of ^tA, with the protons in an anti arrangement, must be larger for α than for β isomers. In both series, the observed differences were lower in the hydroxysulphoxides than in their O-methyl and acetyl derivatives.

Three rotamers must be considered additionally for each conformation if one takes into account the rotation around the C—S bond. The more stable ones on steric grounds are drawn in fig. 2 for each diastereoisomer of erythro-sulphoxides 8 and 9, excluding those rotamers where an 1,3-parallel interaction is present between atoms of the second row (or the third) of the periodic table. Considering the conformations of fig. 2, it can be deduced that the (RSR,SRS) diastereoisomer should exhibit a large share of ^eA (lower $J_{1,2}$), whereas in the (RSS,SRR) one, the ^eB participation must be greater (higher $J_{1,2}$). This is the basis for the configurational assignment of our erythro-sulphoxides.

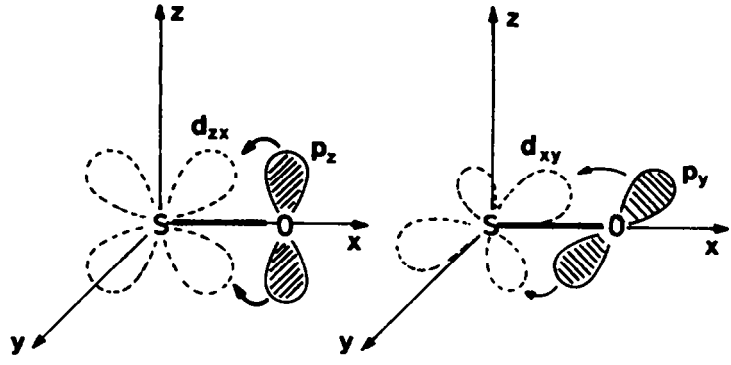
These conclusions can be easily drawn out from the following: i) the $(O/H)_{1,3-p}$ interaction in $^eA_1$ and $^eB_1'$ is slightly stabilizing[7], whereas the $(Me/H)_{1,3-p}$ in $^eB_1$ and $^eA_1'$ must be destabilizing[8]; ii) the anti arrangement of phenyl and methyl groups in benzylmethylsulphoxides is very destabilizing with respect to the gauche one[9]. Thus, $^eA_1$ and $^eB_1'$ would be more stable than $^eA_1'$ and $^eB_1$. These considerations allowed the assignment of the (RSS,SRR) configuration to the 8β and 9β isomers, that exhibited a higher value of $J_{1,2}$ (and hence, a larger participation of $^eB_1'$). Consequently, the (RSR,SRS) configuration could be assigned to the α isomers.

The predominance of $^eB'$ observed for β isomers suggested a steric control of equilibria because those rotamers have the minimum number of gauche interactions (see fig. 1). On the contrary, the conformational behaviour of α isomers, in which the predominance of ^eA was detected, required the existence of some sort of stabilizing interactions between the heteroatomic functions. The electrostatic attraction between the sulphur (electron defficient in sulphinyl group) and the oxygen of the OR group, proposed originally by Eliel in S-substitued 1,3-dioxanes[10], must contribute to the stabilization of A. Nevertheless, both the slight influence of solvent polarity in shifting conformational equilibria ($J_{1,2}$ was hardly affected from $CDCl_3$ to DMSO-d_6), and the significant differences between the diastereoisomers were not explained by this electrostatic interaction. On the other hand, the little magnitude of the $(O/H)_{1,3-p}$[7,11] and the $(Me/H)_{1,3-p}$[8] interactions does not seem enough to justify the almost exclusive participation of ^eA in α isomers, where up to three gauche interactions are present, among them the sterically very destabilizing $(Ph/Ph)_{1,2-g}$ interaction[12].

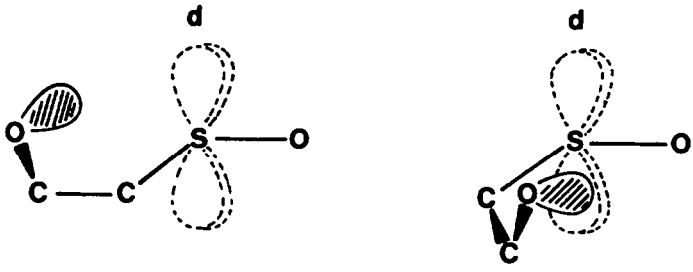
In principle, the distinct behaviour of diastereoisomers could be attributed to the tendency of alkyl groups, observed in benzylalkylsulphoxides, to adopt a gauche relationship with respect to the phenyl group[9], consequently minimizing the $^eA_1'$ participation in β isomers. Nevertheless, when one considers the results obtained for the diastereoisomers of 2-methylsulphinyl-1-phenyl-1-methoxy (and 1-acetoxy) ethane[1], where the preceding argument cannot be applied, one observes that the differences between these epimers were only slightly lower than those of the corresponding erythro- compounds. It may therefore be concluded that there must be other contributions to the stability of A in α isomers.

The electronic backdonation from p orbitals of oxygen to vacant d orbitals (adequately oriented) of sulphur is generally accepted for the S—O bond of the sulphinyl group. According to this and from an energetic viewpoint, any occupied orbital of a neighbouring oxygen could interact with a d orbital of a sulphinylic sulphur, even though both atoms were not directly bonded, provided there is an effective overlap between them. This kind of interaction, only possible when the oxygenated and the sulphur functions are gauche, could contribute to explaining the differences observed for both diastereoisomers, whenever it is feasible for this interaction to stabilize $^eA_1$ and, at the same time, to be inoperative in $^eA_1'$ (see fig. 2).

The two backdonation bonds that can be postulated for the S—O group are depicted in fig. 3a. The d orbital (d_{zy} in fig. 3) in the parallel



3a



3b 3c

Figure 3.- a) Backdonation from p (oxygen) to d (sulphur) orbitals for the sulphinyl group. b) Schematic conformation where the donor-aceptor-interaction is not possible (see text). c) Adequated arrangement for the donor-aceptor interaction (see text).

plane to that containing the filled p orbitals of oxygen, does not intervene in forming these bonds and is therefore the only available one that can interact in a similar way with the oxygen of the OR group in beta position. When the sulphinylic oxygen adopts an anti relationship with respect to the beta carbon (fig. 3b), the overlap between the occupied orbital of OR oxygen and the d_{zy} must be insignificant and resulting in the p—d interaction being inefficient. This geometry is attained in the $^{e}A_1$ rotamer (see fig. 2). On the contrary, if the sulphinylic oxygen and the beta carbon are gauche (see fig. 3c), the orbitals can overlap in a greater extent, due to their relative orientations, with the p—d interaction now being possible. This arrangement is only found in the $^{e}A_1$ rotamer.

Summing up, the existence of a weak interaction between oxygen p (or sp^3) and sulphur d orbitals, strongly dependent on the relative orientation of sulphinylic oxygen, can be rationally postulated as a factor that contributes to discriminate the conformational behaviour of the diastereoisomers.

A reconsideration of the results obtained in previously described series can bring new support to the preceding hipothesis. The behaviour of the isomers of 2-methylsulphinyl-1-phenylethanol[1] was completely compatible with that of the erythro- derivatives studied in this paper, and so it was possible for them to be explained in the same way. The observed differences between the epimers of 2-phenyl-2-methylsulphinylethanol and of 2-methylsulphinylpropan-1-ol[13] may also be justified in the light of this donor-acceptor interaction. The diastereoisomer of (RR,SS) configuration showed a clear predominance of the rotamer that bore the Ph and OR groups in anti arrangement (see fig. 4), whereas in the (RS,SR) epimer the participation of the rotamer with greater number of gauche interactions (and so, less favourable on steric grounds) was very important, and even the most populated in propane series. In fig. 4 it may be checked that these conformations can also gain stability by means of the aforementioned donor-aceptor interaction, because they share the same arrangement of heteroatoms to that depicted in fig. 3c.

Dealing with the threo-sulphoxides, 11 and 12, the configurational assignment may be accomplished from the data of table 1 and the simul-

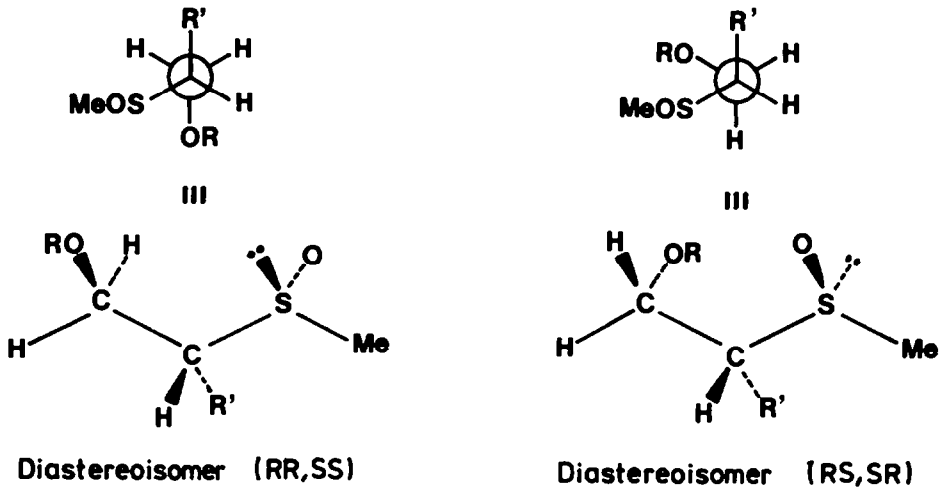


Figure 4.- Predominat rotamers observed for 2-phenyl-2-methylsulphinylethanol (R' = Ph) and 2-methylsulphinylpropan-1-ol (R' = Me).

taneous inspection of the rotamers collected in fig. 5, whose election has been discerned in the same manner as in erythro- compounds.

The fact that the observed differences between coupling constants of every couple of epimers at sulphur were smaller in the threo- than in the

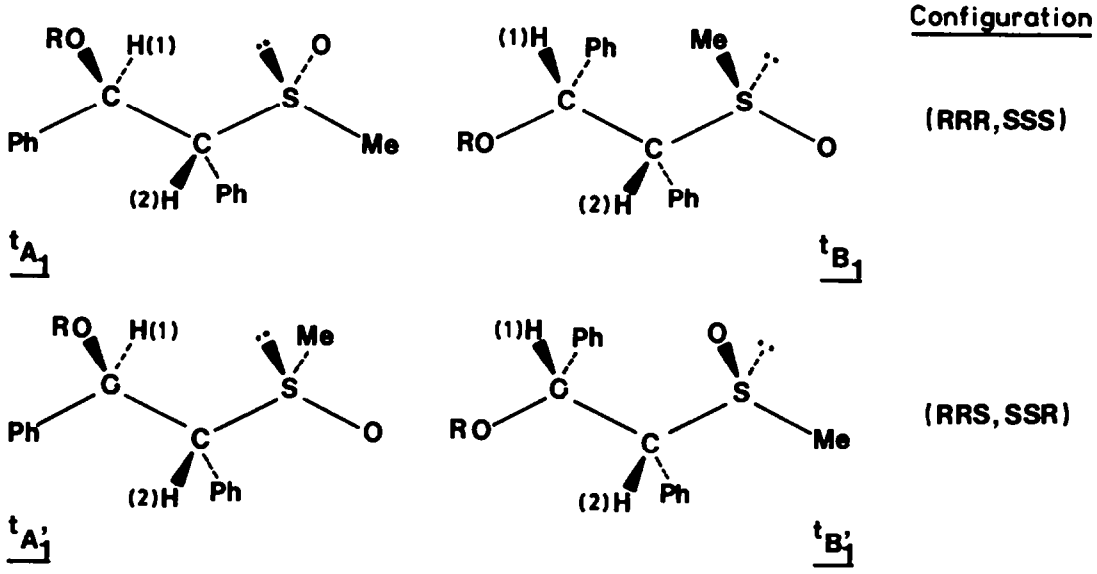


Figure 5.- More stable conformations of threo-sulphoxides 11 and 12, considering rotation around the C—S bond.

It can be easily deduced through identical criteria to that used in erythro- series, that $^{t}A_1$ participation in (RRR,SSSS) would be larger than that of $^{t}A'_1$ in (RRS,SSR). Thus, the (RRR,SSS) configuration must be assigned to α isomers, that exhibited a higher value of $J_{1,2}$ (see table 1), while the other configuration, (RRS,SSR), will correspond to β isomers, that showed a lower value of $J_{1,2}$ indicating a larger participation of ^{t}B rotamers.

erythro- compounds could be imputed to a balance of steric and electrostatic factors, the latter contributing to stabilize A rotamers in both sulphoxydes. In addition, the donor-acceptor interactions mentioned above remain operative only for α isomers because $^{t}A_1$ has a geometry similar to that of fig. 3c. Finally, there is some data in table 1 that hitherto we have not been able to explain satisfactorily: the remarkable difference in the $J_{1,2}$ value in $CDCl_3$ between 11β and 12β,

that disappeared in DMSO-d_6.

To understand the ^{1}H-NMR parameters of hydroxysulphoxides, one should consider intramolecular hydrogen bonding. The rotamers collected in fig. 6 can show this association without severe steric restrictions, and must be considered in the corresponding equilibria together with those conformations of figs. 2 and 5.

experimentally and it can also be noted that this increment disappeared in DMSO-d_6 (see table 1), where intramolecular associations are not feasible. Finally, there are two intramolecularly hydrogen bonded rotamers in 10α of which, $^tC_1$ must be more stable than $^tA_2$, the reason being that in the former the phenyl groups are in anti arrangement. The participation of $^tC_1$, which should decrease $J_{1,2}$, may be the explanation for

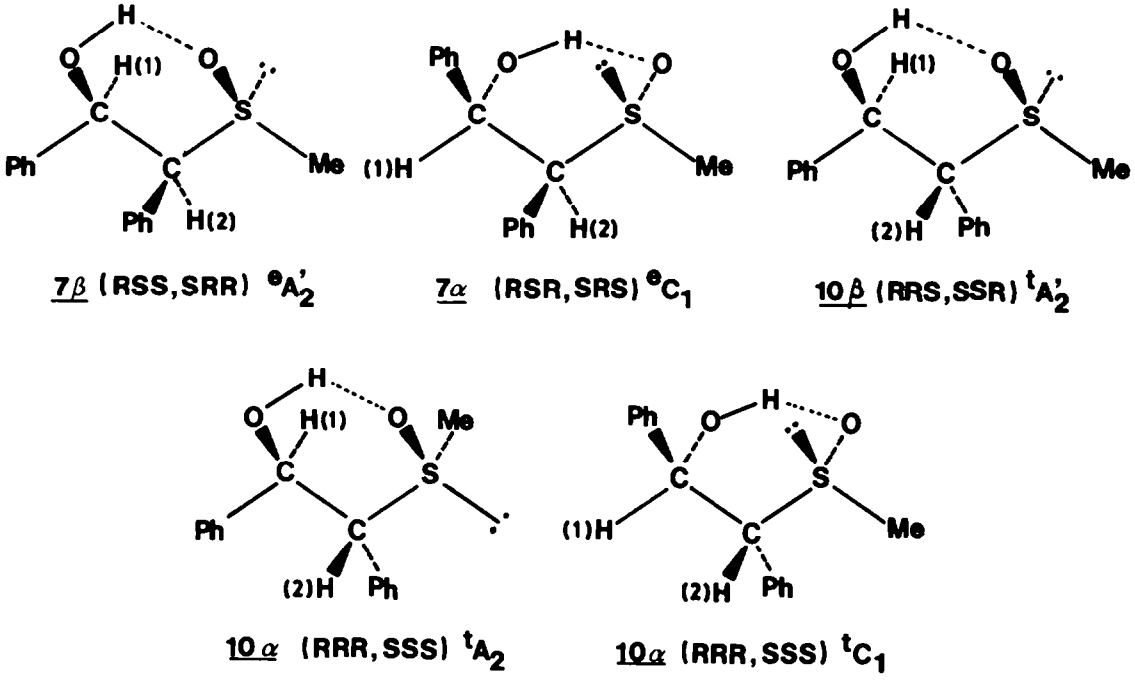


Figure 6.- Intramolecularly hydrogen bonded rotamers for erythro- and threo-hydroxysulphoxides 7 and 10.

The participation of $^eC_1$ in 7α would not substantially vary the observed $J_{1,2}$ value for 8α and 9α (ca. 3 Hz). In contrast, the stability of $^eA_2'$ (see fig. 6) for 7β must be higher than that of $^eA_1'$ (see fig. 2), because in the latter there was not any special interaction, such as donor-acceptor, to increase its stability and so, intramolecular hydrogen bonding must cause, whatever its magnitude may be, an increment in $^eA'$ population relative to that for 8β or 9β. Both predictions were confirmed experimentally. $J_{1,2}$ was similar for 7α, 8α and 9α, with a little influence of solvent polarity. On the contrary, $J_{1,2}$ for 7β was lower than the observed value for 8β and 9β, and was incremented when the solvent was changed to DMSO-d_6 (see table 1).

In the case of the threo-sulphoxides, the participation of $^tA_2'$ would be reflected by an increase of $J_{1,2}$ in 10β, relative to the observed values for 11β and 12β. This was observed the slightly lower value of that coupling in comparison with 11α and 12α. The decrease of $J_{1,2}$ for 10α when DMSO-d_6 was present supported this argument.

It can be seen that all available ^{1}H-NMR data were in agreement with the configurational assignment proposed by us. On the other hand, chemical correlations are also in accordance because 8β (assigned to the (RSS,SRR) configuration) has been related with 11β (assigned to the (RRS,SSR) one), by epimerizing the second chiral center. Likewise, 11α (RRR,SSS) was equilibrated with 8α (RSR,SRS).

With regard to erythro- and threo-1,2-diphenyl-2-phenylsulphinylethanols[5], Kingbury et al. isolated four diastereoisomers with very close characteristics to our hydroxysulphoxides. Their erythro- isomer with higher melting point showed a value of 2.9 Hz for $J_{1,2}$, and the threo- one,

a value of 10.2 Hz, both similar to those of 7α and 10α, respectively. The same occurred with the other isomers of lower melting point: $J_{1,2}$ was 8.2 Hz for erythro- and 9.5 Hz for threo- (compare these values with those in table 1 for 7β and 10β). These similitudes suggest that the configuration of comparable isomers must be identical. However, Kingsbury et al. assigned the opposite configuration for erythro- isomers to that proposed by us (in the threo- series the assignment coincided), being intramolecular hydrogen bonding considerations very important to stablish their conclusions. Their assignment was not also in accordance with the erythro-threo aforementioned correlation carried out chemically on our substrates.

In order to verify our assignment and the conformational criteria used to achieve it, we made a study with lanthanide shift reagents (LSR), and an evaluation of the intramolecular hydrogen bonding strength by ^{1}H-RMN an IR.

The use of LSR has allowed to resolve a great deal of configurational problems in cyclic substrates[14]. In the case of acyclic systems, the validity of the conclusions is usually limited by the coexistence of various rotamers in equilibrium, and the adition of LSR can cause changes in their relative populations. On the other hand, the results are sometimes ambiguous because they are compatible with distinct equilibrium compositions. In order to avoid these problems, we proceeded to study the methoxysulphoxides, that showed the most different conformational behaviour between the constituents of each diastereomeric pair, and displayed in some cases an almost total predominance of a single rotamer.

The isotropic shifts (relative to that observed for MeSO group) that H(1), H(2) and MeO suffered when $Eu(fod)_3$ was added to the corresponding product dissolved in $CDCl_3$, are listed in table 2. The $J_{1,2}$ values were constant for all compounds in every measurement and so, alterations of equilibrium compositions could be excluded, at least within the limits of the concentrations used. The first feature of table 2 is the small value of the slope for MeO protons. This fact clearly demonstrated that the coordination site was only the sulphinylic oxygen. The remaining data were totally consistent with the rotamer preference inferred above for each compound. Thus, the $^eB_1$ and $^tA_1$ rotamers were predominant for 8β and 11α respectively, where H(1) adopts an 1,3-parallel arrangement and H(2) is antiperiplanar, both with respect to the oxygen of the sulphinyl group. This could justify the very different slopes observed for H(1) and H(2) in these compounds, which was higher for the former because this proton is closer to the coordination site. In addition, as the conformational preference observed for 8β was slightly lower than that of 11α (smaler $J_{1,2}$ value), the fact that the H(1) and H(2) slopes of the former were closer each other than those of the latter resulted reasonable because the arrangement of protons in the less populated conformations ($^eA_1$ in 8β and $^tB_1$ in 11α) must tend to approximate their observed slopes.

Table 2.- LSR study of the beta-methoxy-sulphoxides 8 and 11. Relative slopes obtained from the representation of the isotropic shifts of the significative protons against that of the MeSO group.

Compound	H(1)	H(2)	MeSO	MeO
8α	1.34	1.19	1.00	0.24
8β	1.49	0.81	1.00	0.29
11α	1.62	0.76	1.00	0.26
11β	1.36	1.36	1.00	0.24

Finally, since intramolecular hydrogen bonding was used by Kingsbury[5] as an important factor for his assignment of configurations, we studied the changes of the additional splitting caused by the $J_{1,OH}$ vicinal constant in the ^{1}H-NMR spectra of hydroxysulphoxides (from $CDCl_3$ to DMSO-d_6), to evaluate the relative weight of inter-intramolecular associations. The results are summarized in table 3 and the following

Table 3.- Influence of solvent polarity changes on coupling constants of the hydroxy-sulphoxides 7 and 10.

Compd.	Solvent	Conc.	$J_{1,2}$	$J_{1,OH}$	$^4J_{2,OH}$
7α	$CDCl_3$	1[a]	2.8	5.0	0.8
	DMSO-d_6	1	3.0	4.4	1.2
7β	$CDCl_3$[b]	0.25	7.7	2.1	-
	"	5	7.4	-	-
	DMSO-d_6	5	8.6	-	-
10α	$CDCl_3$	1.8	10.2	4.0	-
	(8:1)[c]	1.8	10.5	4.4	-
10β	$CDCl_3$	10	9.2	0.9	-
	DMSO-d_6	10	8.4	3.8	-

a.- Weigt/vol. b.- Recorded at 400 MHz. c.- Mixture of solv.

features can be extracted: i) α isomers exhibited in $CDCl_3$ a $J_{1,OH}$ value higher than the isomers. This fact means that the molar fraction of intramolecularly hydrogen bonded species was more important for β than for α isomers (especially in 10β), because the intramolecular association disminishes the dihedral angle H—C—O-H, an so $J_{1,OH}$[15]; ii) The intramolecular association in $CDCl_3$ must be insignificant for 7α whereas it was not negligible for 10α. This can be inferred from the value of ca. 5 Hz for $J_{1,OH}$, accepted in the literature as characteristic of $^3J_{H,OH}$ when there is free rotation around the C—O bond[16]. Thus, the participation of $^eC_1$ (see fig. 6) in 7α should be negligible and this was also supported by the existence of a long range coupling (see $^4J_{2,OH}$ in table 2), that requires a "w" arrangement between the involved protons[17], only possible in $^eA_1$. On the other hand, the participation of $^tC_1$ must be of certain importance in 10α (see fig. 6); iii) In almost all the cases, the change to DMSO-d_6 provoked an increase of $J_{1,OH}$ couplings as a consequence of the obstructive effect of this solvent towards intramolecular association. In 7β it was not possible to measure this constant in DMSO-d_6 due to widening of signals. Even in $CDCl_3$, needed stronger magnetic fields (see footnote in table 3) and very dilute solutions to detect it.

The IR studies carried out in CS_2 diluted solutions were consistent with the conclusions outlined above (see table 4). As the frecuency changes between free and bonded OH absorptions is a measure of the hydrogen bonding strength, it can be concluded that intramolecular association was stronger in 10β ($\Delta\nu \simeq 226$ cm^{-1}) than in 7β ($\Delta\nu \simeq 184$ cm^{-1}). This fact can be explained according to the repulsion between the phenyl groups which must determine that their dihedral angle increases, resulting in a separation (in 7β) or an approximation (in 10β) of the heteroatomic functions. Therefore, in 7β the intramolecular association should be weaker than in 10β, in accordance with the experimental results.

Table 4.- Results obtained in the IR studies on carbon disulphide diluted solutions of the hydroxysulphoxides 7 and 10 (the relative areas of the bands are in parenthesis).

Compound	Concen.	ν_{OH} free	ν_{OH} associated
7α	neat		3200
	8.10^{-4}M	3600(1)	3180(23)
	1.10^{-4}M	3600(1)	3410-3140(6)
7β	neat		3185
	8.10^{-4}M	3586(1)	3400(3)
10α	neat		3180
	1.10^{-4}M	3597(1)	3410-3200(5)
10β	neat		3200
	8.10^{-4}M	3585(1)	3359(50)

From the existing relation between the number of associated molecules and the relative areas of the bonded and free OH absorptions[18] (see values in parentheses in table 4), it can be easily deduced that the number of associated molecules was higher for 10β (98%) than for 7β (70%). The conformational behaviour deduced from the ^{1}H-NMR spectra justified these facts. There, it was inferred that erythro-sulphoxide 7β had an important share of B rotamers (that exhibit an anti relationship between the heteroatoms), where intramolecular association is not possible.

The solubility of α isomers in CS_2 was sensibly lower than that of β ones. 7α compound exhibited a strong associated band centered at 3180 cm^{-1}, together with a stretching free OH absorption at 3600 cm^{-1}. The position of the associated band seemed too low to be typically intramolecular and therefore, we studied solutions even more diluted, observing that the relative intensity of both bands varied substantially (1:6) when $c \leq 10^{-4}$M. At the same time, the associated absorption widened and two maxima were observable at 3390 and 3200 cm^{-1}. These results showed clearly that the 3180 cm^{-1} absorption, observed at $c = 8.10^{-4}$M, corresponded to intermolecular associations, rather than intramolecular, which must be very strong to be detected even at so low concentrations.

Compound 10α at 10^{-4}M in CS_2 (higher concentrations were not reachable) exhibited a similar IR spectrum to that of 7α (see table 4).

The relative predominance of $^eA_1$ and $^tA_1$ with respect to the corresponding intramolecularly associated rotamers (deduced from the ^{1}H-NMR studies) was in accordance with the behaviour of α isomers in IR spectroscopy.

In conclusion, all these results contribute to confirm the conformational predictions previously established and also reinforce our configurational assignment.

Recently, Dr. García Blanco et al. have studied, following our instructions, 9α isomer by X-ray diffraction to get the definitive test. The results have confirmed the (RSR,SRS) configuration, and the preferred conformation in solid

state was very close to $^{e}A_1$[19], emphasizing the reliability of our conformational criteria for configurational assignment of beta-oxygenated sulphoxides. In addition, we can presume Kingsbury's assignment[5] to be incorrect.

Finally, it must be noted the higher melting point and the lower solubility of α isomers of these hydroxysulphoxides are compatible with a preference of $^{e}A_1$ and $^{t}A_1$, where strong intermolecular hydrogen bonding can take place, giving rise to dimers in a similar way to that of 2-methylsulphinyl-1-phenylethanol[1,2]. The β isomers, with a higher extent of intramolecular association, must share a lower melting point and a higher solubility. So, the quick criterion used in other hydroxysulphoxides for configurational assignment[1] can also be applied here since the α isomers (higher m. p.) have the same relative configuration at sulphur and beta-carbon. Efectively, 7α has the configuration ($\underline{C}^{R}C\underline{S},\underline{S}^{R}C\underline{S}^{R}C\underline{S}^{S}$) and 10$\alpha$ the ($\underline{C}^{R}C\underline{S}^{R}\underline{S},\underline{C}^{S}C\underline{S}^{S}\underline{S}^{S}$) one.

Actually, we are working in other sulphoxides with various substituents in beta-position, different from oxygenated, in order to obtain deffinitive information regarding the donor-aceptor interaction suggested in this paper.

EXPERIMENTAL

Melting points were determined on a Büchi 594392 type S apparatus in open capillary tubes and are uncorrected. Elemental microanalyses were performed by the "Instituto de Química Orgánica (CSIC)" in Madrid with a Perkin-Elmer model 240 analyzer. The silica-gel used in chromatography was Merck F-254 (TLC) or 60 (70 - 230 mesh)(column). Mass spectra were recorded in a Hitachi-Perkin-Elmer model RMU-6MG spectrometer at 70 eV. Mass data are reported in mass units (m/e) and the values in brackets regard the relative intensity from the base peak. IR spectra were taken as paraffinol dispersions (unless otherwise stated) on a Pye Unicam SP-1100 spectrometer. Proton NMR spectra were recorded on a Varian XL-100-15 spectrometer, coupled with a Varian 620/L computer of 16K, in the FT mode transforming 8K data points. Shifts are repoted in ppm downfield from internal TMS and are accurate within 0.1 Hz. In order to observe hydroxyl splitting, the deuterochloroform was purified by distilling twice from phosphorous pentoxide and anhidrous potassium carbonate. LSR study has been performed by adding known amounts of the reactive dissolved in deuterochloroform to a solution of the compound in the same solvent. Proton isotropic shifts have been represented against a reference proton (see text) and the relative slopes obtained by linear regression analysis.

erythro- and threo-2-methylthio-1,2-diphenylethanol (1 and 4) and their acetates (3 and 6).-

Their synthesis have been described elsewhere[3,4]. Alternativelly, compounds 1 and 4 were obtained directly from trans- and cis-stilbene oxides, respectivelly, as follows: 25.2 g (0.13 mol) of the appropiate stilbene oxide were dissolved in 50 ml of absolute methanol. Addition of 18.2 g (0.26 mol) of NaSMe (91 g of a 20% solution in methanol) was followed by refluxing (1 h) and standing at room temp. overnight. The excess of NaSMe was eliminated with 40 ml of water and the mixture worked up. Physical data of the obtained sulphides coincided with those of the previously described[3,4].

Erythro-1-methoxy-2-methylthio-1,2-diphenylethane (2).- The compound was obtained from 1 using the phase-transfer method for methylation reported by Herz[20], yielding 92%. The product was crystallized from ethanol, m.p. 90-92°. IR: ν_{max} 1605, 1100, 765, 740 and 700 cm^{-1}. ^{1}H-NMR: 1.72 (s, 3H, CH_3S), 3.14 (s, 3H, CH_3O), 3.93 (d, 1H, CHS), 4.48 (d, 1H, CHO) and 7.33 (m, 10H). Found: C, 74.3; H, 7.1; S, 12.2. Calcd. for $C_{16}H_{18}OS$: C, 74.4; H, 7.0; S, 12.4.

Threo-1-methoxy-2-methylthio-1,2-diphenylethane (5) Phase transfer methylation of compound 4 was unsuccesful. Its preparation was carried out from the sulphoxide 11 as follows: An equimolecular mixture of 11 (1.7 g, 6.2 mmol) and triphenylphosphine (1.6 g, 6.2 mmol) in CCl_4 (25 ml) was refluxed (1 h). The mixture concentrated to dryness and the residue redissolved in ethyl acetate. The triphenylphosphine oxide was separated by filtration through silica-gel and the evaporation of the filtrate afforded 1.4 g (87%). The material was crystallized from 50% aqueous ethanol, m.p. 66-67°. IR (KBr pellet) ν_{max}: 2850, 1600, 1100, 760, 730 and 700 cm^{-1}. ^{1}H-NMR: 1.85 (s, 3H, CH_3S), 3.25 (s, 3H, CH_3O), 4.00 (d, 1H, CHS), 4.40 (d, 1H, CHO) and 7.2 (m, 10H). Found: C, 74.8; H, 7.2; S, 12.7. Calcd. for $C_{16}H_{18}OS$: C, 74.4; H, 7.0; S, 12.4.

Erythro- and threo-2-methylsulphinyl-1,2-diphenylethanol (7 and 10).- They were obtained in good yields (85% or better) by oxidation with sodium metaperiodate or m-chloroperoxibenzoic acid, using general methods outlined in the literature[21]. In all cases a mixture of the two possible diastereisomers (7α + 7β; 10α + 10β) were obtained in variable compostion. The observed asimmetric induction will be described in a coming work. 7α and 7β were separated by treatment of the mixture with benzene at room temp. The insoluble diastereoisomer (m.p. 207-209°) labeled 7α has been previously described[3]. The soluble one, identified 7β, was crystallized from ethyl acetate, m.p. 131-132°. IR ν_{max}: 3450, 3190, 1060, 995

and 705 cm^{-1}. ^{1}H-NMR: 2.09 (s, 3H, CH_3S), 2.82 (d, 1H, OH), 3.53 (d, 1H, CHS), 5.61 (dd, 1H, CHO) 7.43 (m, 10H). Found: C, 69.0; H, 6.2; S, 12,5. Calcd. for $C_{15}H_{16}O_2S$: C, 69.2; H, 6.2; S, 12.3. The separation of 10α and 10β was accomplished by fractionated crystallization from benzene. The diastereoisomer of higher melting point (10α, 204-205°) crystallized first[4]. The other one 10β melted at 94-95°. IR (CCl_4) ν_{max}: 3200, 1090, 1060, 1010 and 695 cm^{-1}. ^{1}H-NMR: 2.51 (s, 3H, CH_3S), 3.92 (d, 1H, CHS), 5.55 (dd, 1H, CHO), 5.60 (d, 1H, OH) and 7.20 (m, 10H).

Erythro- and threo-1-methoxy-2-methylsulphinyl-1,2-diphenylethane (8 and 11).- The diastereoisomers α or β of 8 and 11 were prepared independently from the corresponding diastereomeric pure hydroxysulphoxides 7 and 10, repectively, as follows: To a solution of 10 mmol of a pure epimer of 7 or 10 in 20 ml of CH_2Cl_2, 21.1 mg of tetrabuthylammonium iodide and 2.1 ml of 50% aqueous sodium hydroxide were added. The mixture was vigorously stirred (15 min) and 3.8 g (30 mmol) of dimethyl sulphate were added at such a rate that the temp. was kept below 45°. After 12 h, the excess of sulphate was destroyed by addition of concentrated ammonium hydroxyde (6 ml). The mixture was poured into water (50 ml) and extracted several times with $CHCl_3$ The combined organic layers dried, the solvent distilled and the residue purified. Since the conditions used were mild and the reaction times short, the stereochemistry of the chiral centers should not be affected. Erythro-8β.- Benzaldehide and methylbenzylsulphoxide were detected as by-products. They were eliminated by washing with diethyl ether. Yield 73%. Cristallized from hexane, m.p. 160-161°. IR ν_{max}: 1600, 1095, 1050 and 700 cm^{-1}. ^{1}H-NMR: 2.06 (s, 3H, CH_3S), 3.14 (s, 3H, CH_3O), 3.58 (d, 1H, CHS), 4.92 (d, 1H, CHO) and 7.46 (m, 10H). Found: C, 69.7; H, 6.7; S, 11.8. Calcd. for $C_{16}H_{18}O_2S$: C, 70.0, H, 6.6; S, 11.7. Erythro-8α.- Cuantitative yield. Crystallized from diethyl ether, m.p. 119-120°. IR ν_{max}: 1600, 1585, 1100 and 1050 cm^{-1}. ^{1}H-NMR: 2.29 (s, 3H, CH_3S), 3.39 (s, 3H, CH_3O), 3.64 (d, 1H, CHS), 5.17 (d, 1H, CHO) and 7.25 (m, 10H). Found: C, 70.1; H, 6.9; S, 11.4. Calcd. for $C_{16}H_{18}O_2S$: C, 70.0; H, 6.6; S, 11.7. Threo-11α.- Yield 91%. Crystallized from CCl_4:hexane (3:1), m.p. 176-177°. IR ν_{max}: 1105, 1040, 760 and 705 cm^{-1}. ^{1}H-NMR: 2.06 (s, 3H, CH_3S), 3.36 (s, 3H, CH_3O), 3.62 (d, 1H, CHS), 4.86 (d, 1H, CHO), 7.33 (m, 10H). Found C, 69.8; H, 6.8; S, 11.9; Calcd. for $C_{16}H_{18}O_2S$ C, 70.0; H, 6.6; S, 11.7. Threo-11β.- Yield 78%. Purified by preparative TLC (ethyl acetate as eluent) and crystallized from hexane, m.p. 89—90°. IR ν_{max}: 1110, 1040, 760 and 705 cm^{-1}. ^{1}H-NMR: 2.39 (s, 3H, CH_3S), 3.32 (s, 3H, CH_3O), 4.14 (d, 1H, CHS), 5.04 (d, 1H, CHO), 7.25 (m, 10H). Found: C, 70.1; H, 6.8; S, 11.5. Calculated for $C_{16}H_{18}O_2S$: C, 70.0; H, 6.6; S, 11.7.

Erythro- and threo-2-methylsulphinyl-1,2-diphenylethyl acetate (9 and 12).- The diastereomeric acethoxysulphoxides were prepared independently from the corresponding hydroxysulphoxides 7α, 7β, 10α or 10β, by reaction with acetic anhidride and pyridine using standard procedures that should not alter the configuration of the chiral centers. The isomers 9α (m.p. 141-143°) and 12α (m.p. 154-156°) have been described elsewhere[3,4]. Erythro-9β.- Yield 96%. Crystallized from ethyl acetate, m.p. 166-167°. IR ν_{max}: 1735, 1235, 1220, 1040, 770, 750 and 700 cm^{-1}. ^{1}H-NMR: 1.79 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3S), 3.70 (d, 1H, CHS), 6.55 (d, 1H, CHO), 7.45 (m, 10H). Found: C, 67.4; H, 6.0; S, 10.9. Calcd. for $C_{17}H_{18}O_3S$: C, 67.5; H, 6.0; S, 10.6. Threo-12β.- Cuantitative yield. Crystallized from cyclohexane, m.p. 98-99°. IR ν_{max}: 1745, 1235, 1040, 770, 730 and 700 cm^{-1}. ^{1}H-NMR: 2.13 (s, 3H, CH_3CO), 2.28 (s, 3H, CH_3S), 4.28 (d, 1H, CHS), 6.60 (d, 1H, CHO), 7.23 (m, 10H). Found: C, 67.6; H, 6.1; S, 10.6. Calcd. for $C_{17}H_{18}O_3S$: C, 67.5; H, 6.0; S, 10.6.

Reaction of sulphoxides with base.- a) Sodium hydride.- An equimolecular amount of sodium hydride was added to 2 mmol of sulphoxide in 80 ml of anhidrous dioxane. The reaction mixture was stirred at room temp. until the starting sulphoxide was not detected. Then, hydrollized at 0° with water (25 ml), extracted with $CHCl_3$, dried and the solvent evaporated. Reaction of erythro-7α.- Time 70 h. Distillation of the crude yielded benzaldehide and benzylmethylsulphoxide. The residue was benzylmethylsulphone. Reaction of erythro—9α.- Time 21 h. The crude was purified by preparative TLC (ethyl acetate as eluent). The major product was further chromatographied (benzene: ethyl acetate 13:1) obtaining a mixture of Z- and E-1-methylsulphinyl-1,2-diphenylethylene. IR ν_{max}: 1600, 1575, 1495, 1450, 1065, 755 and 690 cm^{-1}. ^{1}H-NMR: 2.43 and 2.46 (s and s, 3H and 3H, CH_3S), 7.10-7.60 (m, 22H, CH and arom. protons). MS(m/e): 39(6), 51(13), 63(8), 76(7), 77 (12), 89(5), 137(7), 151(5), 176(8), 177(13), 178 (56), 179(100), 180(16), 242 (M^+, 2), 243 (M^++1, 20.3% rel. to M^+) and 244 (M^++ 2, 6.2% rel. to M^+). Reaction of erythro-8β.- Time 120 h. The

results were identical to those obtained for 9α. b) Sodium hydroxide.- The appropiate sulphoxide (65 mg, 0.25 mmol) was added to a solution of 40 mg (1 mmol) of sodium hydroxide in 15 ml of 50% aqueous ethanol. The mixture was stirred at room temp. and diluted with water. The clear solution was then extracted with CHC_3, the extracts dried and the solvent evaporated. Reaction of erythro-7α.- Time 96 h. The results coincided with those described above for the reaction with sodium hydride. Reaction of erythro-8β.- Time 288 h. The crude was analized by ^{1}H-NMR and identified as a mixture of starting material, threo-11β and 1-methylsulphinyl-1,2-diphenylethylene. Reaction of threo-11α.- Time 216 h at room temp. and 216 h at 50°. In both cases the crude was identified by ^{1}H-NMR as a mixture of starting material, erythro-8α and 1-methylsulphinyl-1,2-diphenylethylene.

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