Tetrahedron Vol. 49, No. 47, pp. 11009-11018, 1993
Printed in Great Britain

0040-4020/93 $6 00+.00

Stereoselective Reactions of $AlMe_3$ with Chiral Acyclic β-Ketosulfoxides.

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(*Received in UK* 6 *August* 1993; *accepted* 24 *September* 1993)

Abstract: The results obtained in the addition reactions of $AlMe_3$ to acyclic β-ketosulfoxides **1-5** are described. In the presence of ZnX_2 (X=Cl,Br) reactions proceed in high yield. The diastereoselectivities achieved, ranging from 70% to 90%, make these reactions useful for the asymmetric synthesis of tertiary methyl carbinols.

The stereoselective hydride reduction of β-ketosulfoxides has been the subject of extensive studies.[1] In the case of the reactions with DIBAL, the sulfinyl group is mainly responsible for the high diastereoselectivity observed in acyclic substrates.[2] The larger rigidity of the cyclic substrates determines a stereochemical evolution different from that observed for the acyclic ones, but the important role of the sulfinyl group in the control of the hydride approach to the carbonyl group is maintained in both cases.[3]

In contrast to these reactions, few studies concerning the stereoselective additions of other nucleophilic reagents to these chiral β-ketosulfoxides have been reported. Recently we described the highly diastereoselective addition of $AlEt_2CN$ to acyclic β-ketosulfoxides.[4] Although the steric course proposed for these hydrocyanations is different to that suggested in the case of DIBAL reductions (pentacoordinated *versus* tetracoordinated aluminium intermediates), the sulfinyl group is also the main responsible for the observed stereoselectivity. Once more, the stereochemical course of these reactions is depending on the cyclic or acyclic structure of the substrate.[5] To our knowledge, the only reported papers concerning the organometallic additions to chiral β-ketosulfoxides are related to Grignard[6], organotitanium[7] and organoaluminium[7,8] compounds. Concerning to the latter, important differences are observed in the reported results for the $AlMe_3$ reactions on cyclic (high yields and almost complete diastereoselectivity)[8] and acyclic (moderated yields and low diastereoselectivy)[7] substrates. As the experimental conditions used in both papers were different, it is necessary to study the reactions of the acyclic substrates using the conditions reported for the cyclic ones, in order to check if the different behaviour observed is due to the cyclic or acyclic character of the starting β-ketosulfoxides. The possibility of developing a new method to obtain tertiary carbinols with high optical purity, would confer an additional interest to this study.

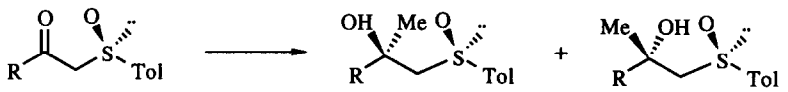
In the present paper we report the good yields and high diastereomeric excesses achieved in the reactions of $AlMe_3$ with acyclic β-ketosulfoxides in the presence of Lewis acids giving rise to acyclic tertiary methyl

carbinols. The stereochemical results obtained in these reactions are explained by assuming similar models to those proposed in DIBAL reductions.

RESULTS AND DISCUSSION

Enantiomerically pure acyclic β-ketosulfoxides R-CO-CH_2SOTol [R=Ph (**1**), 4-OMe-C_6H_4 (**2**), Et (**3**), *i*-Pr (**4**), *t*-Bu (**5**)] with the ***R*** configuration at sulfur, used as starting materials, were prepared as previously described[6,9] by reaction of the corresponding esters with (*R*)-methyl-*p*-tolyl sulfoxide in the presence of LDA.

Table 1. Results obtained in the reactions of $AlMe_3$ with β-ketosulfoxides **1-5**



1-5 **6A-10A** **6B-10B**

Entry	Start. Material	R	Lewis acid (1.6 eq)	Products (ratio)	Yield	a)
1	**1**	Ph	none	6A+6B (76:24)	40	30 (72)
2	**3**	Et	none	8A+8B (72:28)	15	72 (40)
3	**1**	Ph	$Mg(ClO_4)_2$	6A+6B (72:28)	38	30 (72)
4	**1**	Ph	$TiCl_4$	6A+6B (86:14)	60	b)
5	**1**	Ph	$ZnBr_2$	6A+6B (86:14)	90	
6	**1**	Ph	$ZnCl_2$[c)]	6A+6B (87:13)	90	
7	**1**	Ph	$ZnCl_2$ (0° C)	6A+6B (87:13)	90	
8	**1**	Ph	$ZnCl_2$ (-40° C)	6A+6B (79:21)	12	75 (4)
9	**1**	Ph	$ZnCl_2$ (-78° C)	6A+6B (45:55)		90 (4)
10	**1**	Ph	$ZnCl_2/AlMe_3$[d)]	6A+6B (85:15)	85	
11	**1**	Ph	$ZnCl_2$[e)]	6A+6B (90:10)	70	
12	**2**	MeO-C_6H_4	$ZnCl_2$	7A+7B (67:33)	90	
13	**3**	Et	$ZnCl_2$	8A+8B (87:13)	90	
14	**4**	*i*-Pr	$ZnCl_2$	9A+9B (87:13)	96	
15	**5**	*t*-Bu	$ZnCl_2$	10A+10B (95:5)	89	

[a] % of starting material recovered after the time (hours) indicated between brackets. [b] Thioether resulting in the reduction of **1** was also isolated in 15% yield. [c] Similar yields and diastereoisomeric excesses were obtained by increasing the $ZnCl_2$ 1 ratio (from 2 5 to 8 equiv of Lewis acid) [d] Substrate.$ZnCl_2$:$AlMe_3$ = 1:4:4 [e] Containing 1% of the Wilkinson catalyst

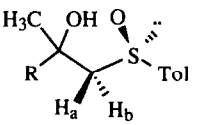
The reactions were carried out by slow addition of the β-ketosulfoxides **1-5** to a CH_2Cl_2 solution of $AlMe_3$. When Lewis acids were used, the sulfoxides were stirred with a suspension of the Lewis acid in CH_2Cl_2 (30 minutes to ensure complete association) and then added to a solution of $AlMe_3$ in the same solvent.

The order of reagent addition is critical to attain high conversions. The diastereomeric ratios of the carbinols were easily established from the ^{1}H-NMR spectra of the crude reaction mixtures. The results summarized in *Table 1* show that in most cases mixtures of epimeric carbinols **A** and **B** can be obtained in good yield.

In the absence of Lewis acids compounds **1** and **3** reacted with $AlMe_3$ (entries 1 and 2, *Table 1*) to give low yields of the β-hydroxysulfoxides (significant amount of the starting material was recovered unchanged, even using 4 equiv. of $AlMe_3$ and long reaction times) and the diastereoselectivity of the process was only moderate (de ≈ 50%). These results agree with those reported by Fujisawa[7] but contrast with those obtained by us in cyclic series[8], where reactions were instantaneous and highly diastereoselective. The conversion of the starting β-ketosulfoxide into an aluminium enolate[10] (unable to be attacked by the reagent) could explain the low conversion of the acyclic substrates even when an excess of the reagent was present.[11]

We chose compound **1** as model substrate to examine the effect of different Lewis acids and reaction conditions on the reactivity and diastereofacial selectivity of these reactions. The best results were obtained in the presence of $ZnCl_2$ (or $ZnBr_2$) at temperatures above 0° C, using a 1/2/1.6 molar ratio of substrate/$AlMe_3$/$ZnCl_2$. At lower temperatures the reactions were not completed and their stereoselectivities were lower (entries 8 and 9), probably as a consequence of an uncomplete chelation. $Mg(ClO_4)_2$ (entry 3) had no effect on the reaction, whereas the competitive reduction of the sulfoxide to the thioether took place in the presence of $TiCl_4$ (entry 4) decreasing the yield of hydroxy sulfoxide. The increase of the molar ratio $ZnCl_2$/$AlMe_3$ (entry 10) did not improve the results. However, the addition of a catalytic amount (5%) of tris-(triphenylphosphine) rhodium(I) chloride to the reaction medium[12] slightly increased the diastereoselectivity (entry 11), but the yield of the reaction was lower and the chromatographic purification of the products more difficult.

Table 2 Relevant NMR parameters for the configurational assignment of the epimeric sulfoxides **A** and **B**



	^{1}H-NMR								*^{13}C-NMR*	
	δ–CH_3		δ-$R^{a)}$		$^4J_{Me-a}$		δ-$CH_2^{b)}$		δ–CH_2	
Comp	A	B	A	B	A	B	A	B	A	B
6	2.00	1.60			0.6		0.18	0.14	73.67	67.99
7	1.98	1.58			0.4		0.19	0.14	73.65	68.32
8	1.58	1.31	1.61	1.89	0.4		0.33	0.22	72.65	67.09
9	1.57	1.20	1.79	2.32	0.8		0.30	0.10	74.08	66.50
10	1.63	1.18			1.0		0.38	0.11	76.17	

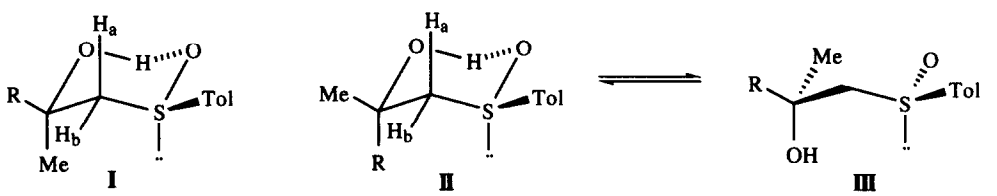
a) Protons at C-γ b) $\Delta\delta = \delta_a - \delta_b$

The above indicated optimal conditions were used on substrates **3-5** which gave mixtures of diastereomers, being epimer **A** the major ones in all cases, with *de* ranging from 74% to 90% (entries 13-15). The lower *de* obtained for compound **2** (24% *de*, entry 12) could be attributed to the presence of the *p*-methoxy group which is also able to associate with $ZnCl_2$ decreasing its effective concentration in the medium.[13]

The configurational assignment of the epimeric sulfoxides was initially based on their NMR parameters, being the most relevant collected in *Table 2*. The main systematic differences between both epimers, **A** and **B**, are the following: i) The δ values for the methyl group attached to the hydroxylic carbon are higher in epimers **A**, while those of the protons at C-γ on the aliphatic R groups[14] (compounds **8-10**) are lower in these epimers. ii) **A** epimers exhibit a long range coupling constant $^4J_{Me,a}$ which is absent in compounds **B**. iii) The chemical shifts differences between the protons of the CH_2 group next to the sulfinyl group ($[\delta_a-\delta_b]$ values) are larger in the **A** epimers (especially in compounds **8-10** when *R* is aliphatic). iv) The ^{13}C-δ values of the methylenic carbons are clearly higher in epimers **A**. All these facts support that the epimers **A**, obtained as the major components of the reactions of compounds **1-5** with $AlMe_3$, must be configurationally homogeneous exhibiting the same relative configuration.

In *Figure 1* the presumably most stable conformations for each of the possible epimers are depicted. The conformational equilibrium of the RR_S epimer must be strongly shifted towards rotamer **I**, which will be stabilized by steric effects (the most bulky R group in pseudoequatorial arrangement) and intramolecular hydrogen bonding. A significant contribution of two conformations **II** (intramolecularly associated) and **III** (with lower steric interactions) must be considered in the case of the SR_S epimers. Their relative population depends on the size of the R group. The fact that only epimers **A** exhibit a long range coupling constant $^4J_{Me,a}$ (*Table 2*) evidenced a W planar arrangement between the protons involved[15] only possible in rotamers **I**, and allowed us to assign the RR_S configuration to these major epimers.

Figure 1.- Favoured conformations for each epimeric hydroxy sulfoxides



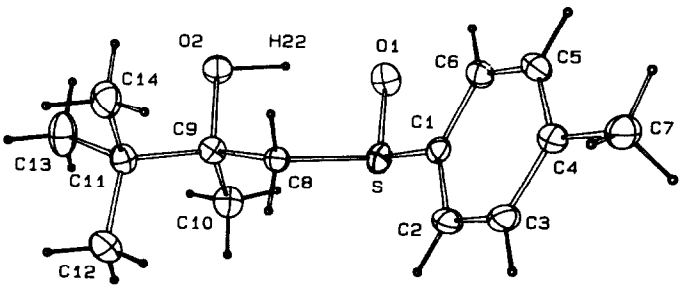
(R,R_S)-epimers (S,R_S)-epimers

In order to confirm this assumption we made a detailed study of the NMR behaviour of both epimers of compound **9** in dry $CDCl_3$. The chemical shift of the hydroxylic proton in compound **9A** is not affected by dilution (it remains constant at δ = 4.2 ppm when the concentration changes from 1 6 10^{-1} M to 1.6 10^{-3} M) indicating the existence of an intramolecular hydrogen bonding. On the other hand, the lower δ value observed for the OH proton in **9B** (3.6 ppm, also unchanged with dilution) and its small but significant long range coupling constant with the methyl group ($^4J_{Me,OH}$ = 0.4 Hz), undetectable in **9A**, are in accordance with the significant but not exclusive participation of the intramolecular hydrogen bonded rotamer **II** The fact that the

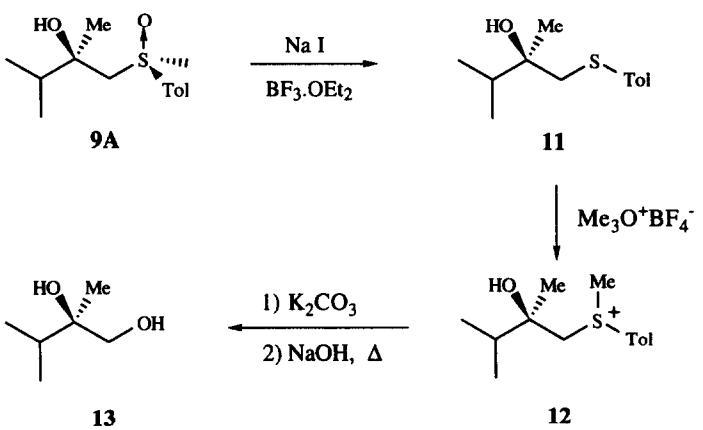
spatial arrangement of the CH_3 group in rotamer **I** (epimer **A**) was similar to that of the R group in rotamer **II** (epimer **B**) and vice versa (see *Figure 1*) explains the observed values of their chemicals shifts (*Table 2*).

Furthermore, the configuration of compound **10A** has been unequivocally determined as ***RR$_S$*** by X-Ray diffraction.[16] In the ORTEP diagram showed in *Figure 2* we can see that the favoured conformation in the solid state exhibit a spatial arrangement between the sulfinylic and hydroxylic oxygens which allows their intramolecular association through hydrogen bonding.

Figure 2 - ORTEP plot of [2R, (S)R]-2,3,3-trimethyl-1-(4'-methylpheyl)sulfinyl-2-butanol **10A**



The ***RR$_S$*** configuration assigned to compound **9A** from its NMR behaviour was also confirmed by chemical correlation with the known 2,3-dimethyl-1,2-butanediol **13**[17] (*Scheme 1*). The reduction of the hydroxysulfoxide **9A** with $BF_3{\cdot}OEt_2/NaI$[18] gave the thioether **11** whose alkylation with $Me_3O^+BF_4^-$ yielded the corresponding sulfonium salt **12**, which upon successive treatment with K_2CO_3[19] and NaOH[20] afforded the butanediol **13**, without isolation of the intermediate epoxide.

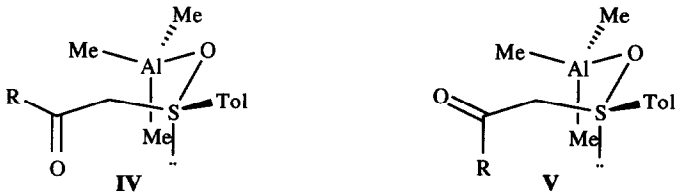


Scheme 1

As the sign of the specific rotation ($[\alpha]_D^{20} = 9.4°$, c = 0.17, $CHCl_3$) displayed by compound **13** was opposite to that described in the literature[17] for (*S*)-2,3-dimethyl-1,2-butanediol ($[\alpha]_D^{20} = -12°$, c = 1, $CHCl_3$)

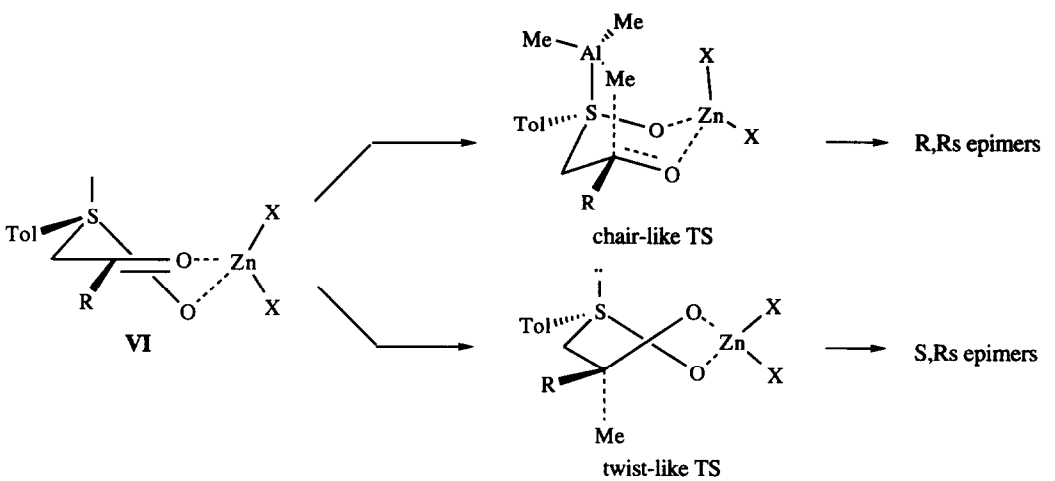
we assign the ***R*** configuration to the alcohol **13** obtained by us and subsequently the ***RR$_S$*** one to the starting hydroxysulfoxide **9A**.

These unequivocal assignments, in addition to the spectroscopic characteristic mentioned above, allowed us to assign the ***RR$_S$*** configuration to the major epimers **A** and the ***SR$_S$*** one to the minor epimers **B**.



Scheme 2

The stereochemical outcome of these reactions can be justified from models similar to those proposed in DIBAL reductions. In the absence of the Lewis acids, the intramolecular transfer of the methyl group from the associated species of the reagent on the sulfinyl oxygen (*Scheme 2*), must be hampered. The similar magnitude of the destabilizing interactions present in the two possible conformers **IV** *(R/Me)* and **V** *(R/Me)$_{1,3\text{-parallel}}$*, which become larger in the transition state, could account for the low stereoselectivity observed.



Scheme 3

In the presence of ZnX_2, the chelated species **VI** (*Scheme 3*) must be formed. The approach of the $AlMe_3$ from the top face must be favoured with respect to that from the bottom one, both from steric (*chair-like* TS more stable than *twist-like* TS) and stereoelectronic (association of the aluminium with the lone electron pair at sulfur) grounds. The fact that the stereoselectivity of the methylation was lower than that of the DIBAL

reduction[1] can also be explained from this model, taking into account that the $(Me/X)_{1,3\text{-}parallel}$ interaction developing in the favoured *chair-like* TS for methylation is more destabilizing than the $(H/X)_{1,3\text{-}parallel}$ interaction present in the corresponding TS for the reductions.

Acknowledgements. We thank the Dirección General de Investigación Científica y Técnica (DGICYT), for financial support (Grant PB92-0162) and Ministerio de Educación y Ciencia for completing a stay at University of East Anglia of one of us (M.C.C.).

EXPERIMENTAL

Melting points were determined on a Gallenkamp apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ with the Bruker WP-200-SY instrument. Chemicals shifts are given in parts per milion (δ), using tetramethylsilane as an internal standard. Opticals rotations were measured on a Perkin-Elmer 241 MC polarimeter. TLC analysis was performed on Merck (art. 554) silica gel plates and silica gel (230-400 mesh ASTM) from Merck was used for flash chromatography.

General Procedures for $AlMe_3$ Addition.

Method A: $AlMe_3$. To a 2 M solution of $AlMe_3$ (1.2 mmol) in hexane at room temperature a solution of β-ketosulfoxide (0.3 mmol) in 3 mL of CH_2Cl_2 was added dropwise. The reaction was monitored by TLC (eluent CH_2Cl_2/2-propanol 30:1). The mixture was decomposed with methanol at 0° C. The solvents were evaporated in vacuo, and the residue was diluted with a 5% aqueous sulfuric acid solution. The aqueous layer was extracted with CH_2Cl_2 and was dried with sodium sulfate.

Method B: $AlMe_3/ZnCl_2$. To a suspension of $ZnCl_2$ (12 mmol) in 10 mL of CH_2Cl_2 was added at room temperature a solution of β-ketosulfoxide (9.3 mmol) in 20 mL of CH_2Cl_2. The resulting mixture was stirred for 30 min and then added into a 2 M solution of $AlMe_3$ (18.6 mmol) in hexane at 0° C. The reaction was worked up as in method A.

***2-Phenyl-1-(4'-methylphenylsulfinyl)-2-propanol* 6.** Was prepared from (R)-1-phenyl-2-(4'-methylphenylsulfinyl)ethanone **1** following procedure B. Yield 90% as a 87:13 mixture of **6A** and **6B**. Both epimers can be obtained pure by flash chromatography (eluent diethyl ether/hexane 5:2). Major diastereomer **6A** [2R,(S)R]: $[\alpha]_D^{20}$= +150° (c= 2, $CHCl_3$); ^{1}H-NMR 7.60-7.10 (m, 9 H, Ar), 3.14 (dc part A of AB system, 1 H, J_{AB}= 13.3 Hz, $J_{A\text{-}Me}$= 0.6 Hz, CH_2SO), 2.96 (part B of AB system, 1 H, J_{AB} = 13.3 Hz, CH_2SO), 2.39 (s, 3 H, CH_3-Ar), 2.00 (d, 3 H, $J_{A\text{-}Me}$= 0.6 Hz, CH_3-C-OH).^{13}C-NMR: 146.2, 141.5 and 139.9 (3 C), 129.8, 128.0, 126.9, 124.4 and 123.7 (9 C), 73.7 (C-OH), 68.6 (CH_2), 28.4 (CH_3), 21.1 (CH_3-Ar); MS, 140 (100), 139 (39), 135 (74), 117 (27), 105 (23), 92 (88), 91 (66), 77 (44); Anal. calcd for $C_{16}H_{18}O_2S$: C, 70.04; H, 6.61. Found: C, 69.89; H, 6.74; IR, 3580, 3400, 1600, 1500, 1060, 1010, 818 cm^{-1}. Diastereomer **6B** [2S,(S)R]: $[\alpha]_D^{20}$= +158 ° (c= 1, $CHCl_3$); ^{1}H-NMR: 7.60-7.33 (m, 9 H, Ar), 3.29 y 3.15 (AB system, 2 H, J_{AB}= 13.2 Hz, CH_2SO), 2.41 (s, 3 H, CH_3-Ar), 1.60 (s, 3 H, CH_3).^{13}C-NMR: 145,5, 142.0 and 140.5 (3 C), 130.1, 128.6, 127.3, 125.1 and 124.0 (9 C), 75.0 (C-OH), 68.0 (CH_2), 32.0 (CH_3), 21.4 (CH_3-Ar).

***2-(4'-Methoxyphenyl)-1-(4'-methylphenylsulfinyl)-2-propanol* 7.** Was prepared from 2-(4'-methoxyphenyl)-1-(4'-methylphenylsulfinyl)ethanone **2** following procedure B as a 64:36 mixture of **7A** and **7B** which could not be separated (90 % yield). Major diastereomer **7A** [2R,(S)R]: ^{1}H-NMR 7.52-7.32 (AA'BB', 4 H, Ar), 7.39-6.85 (AA'BB', 4 H, Ar), 3.78 (s, 3 H, CH_3-O), 3.12 (part A of AB system, 1 H, J_{AB}= 13.4 Hz, CH_2SO), 2.93 (part B of AB system, 1 H, J_{AB} = 13.4 Hz, CH_2SO), 2.39 (s, 3 H, CH_3-Ar),

1.98 (s, 3 H, CH_3-C-OH). ^{13}C-NMR: 158.5, 141.7, 140.0 and 138.6 (4 C, Ar), 129.9, 125.7, 123.8 and 113.4 (8 C, Ar), 73.6 (C-OH), 68.5 (CH_2), 55.1 (CH_3O), 28.4 (CH_3), 21.2 (CH_3-Ar); Anal. calc for $C_{17}H_{20}O_3S$: C, 67.07; H,6.62. Found (from the mixture): C, 66.83; H, 6.79. Diastereomer **7B** [2S,(S)R]: ^{1}H-NMR 7.51-7.32 (AA'BB', 4 H, Ar), 7.30-6.95 (AA'BB', 4 H, Ar), 3.85 (s, 3 H, CH_3-O), 3.25 (part A of AB system, J_{AB} = 13.4 Hz, 1 H, CH_2SO), 3.11 (part B of AB system, 1 H, J_{AB} = 13.4 Hz, CH_2SO), 2.41 (s, 3 H, CH_3-Ar), 1.58 (s, 3 H, CH_3-C-OH). ^{13}C-NMR: 158.5, 141.7, 140.0 and 138.6 (4 C, Ar), 129.9, 126.1, 123.8 and 113.6 (8 C, Ar), 74.4 (C-OH), 68.3 (CH_2), 55.1 (CH_3O), 31.6 (CH_3), 21.2 (CH_3-Ar).

2-Methyl-1-(4'-methylphenylsulfinyl)-2-butanol ***8.*** Was prepared from (R)-1-(4'-methylphenylsulfinyl)-2-butanone **3** following procedure B. Yield 90% as a 87:13 mixture of **8A** and **8B**. Both epimers can be obtained pure by flash chromatography (eluent hexane/acetone 3:1). Diastereomer **8A** [2R,(S)R]: $[\alpha]_D^{20}$= +282° (c= 1.13, $CHCl_3$); ^{1}H-NMR 7.55 y 7.34 (AA'BB' system, 4 H, Tol), 2.99 y 2.66 (AB system, 2 H, J_{AB}= 13.3 Hz, CH_2SO), 2.42 (s, 3 H, CH_3-Ar), 1.61 (c, 2 H, J= 7.5 Hz, CH_2-CH_3), 1.58 (s, 3 H, CH_3-C-OH), 0.92 (t, 3 H, J= 7.4 Hz, CH_3-CH_2).^{13}C-NMR 141.7, 140.6 (2 C), 130.0 and 123.8 (4 C), 72.6 (C-OH), 66.6 (CH_2), 35.8 (CH_2-CH_3), 26.1 (CH_3-C-OH), 21.3 (CH_3-Ar), 7.8 (CH_3-CH_2); Anal. calc. for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02. Found: C, 63.47; H, 8.17; MS (NH_3): 227 (100) M^++1, 244 (67) M^++17. IR: 3600, 3410, 1600, 1490, 1380, 1365, 1025, 810 cm^{-1}. Diastereomer **8B** [2S,(S)R]: ^{1}H-NMR 7.54 y 7.33 (AA'BB' system, 4 H, Tol), 2.99 y 2.77 (AB , 2 H, J_{AB}= 13.5 Hz, CH_2SO), 2.42 (s, 3 H, CH_3-Ar), 1.89 (part AB of ABX_3 system, 2 H, $J_{AB\text{-}X}$= 7.4 Hz, CH_2-CH_3), 1.31 (s, 3 H, CH_3-C-OH), 1.02 (part X of ABX_3 system, 3 H, $J_{AB\text{-}X}$= 7.4 Hz, CH_3-CH_2); ^{13}C-NMR 141.6 and 140.7 (2 C), 129.9 and 123.8 (4 C), 72.8 (C-OH), 67.1 (CH_2), 34.3 (CH_2-CH_3), 26.7 (CH_3-C-OH), 21.2 (CH_3-Ar), 7.7 (CH_3-CH_2).

2,3-Dimethyl-1-(4'-methylphenyl)sulfinyl-2-butanol ***9.*** Was prepared from (R)-3-methyl-1-(4'-methylphenylsulfinyl)-2-butanone **4** following procedure B. Yield 86% as a 87:13 mixture of **9A** and **9B**. Both epimers can be obtained in a pure form by flash chromatography (eluent hexane/acetone 3:1). Diastereomer **9A** [2R,(S)R]: $[\alpha]_D^{20}$= +266° (c= 1, $CHCl_3$); ^{1}H-NMR 7.56 y 7.35 (AA'BB' system, 4 H, Tol), 2.95 (dc, part A of AB system, 1 H, J_{AB}= 13.2 Hz, $J_{A\text{-}Me}$= 0.8 Hz, CH_2SO), 2.65 (part B of AB system, 1 H, J_{AB} = 13.2 Hz, CH_2SO), 2.43 (s, 3 H, CH_3-Ar), 1.79 (sep, 1 H, J= 6.8 Hz, $CH(CH_3)_2$), 1.57 (d, 3 H, $J_{A\text{-}Me}$= 0.8 Hz, CH_3-C-OH), 0.93 (d, 3 H, J= 6.8 Hz, $(CH_3)_2CH$), 0.91 (d, 3 H, J= 6.8 Hz, $(CH_3)_2CH$); ^{13}C-NMR 141.1 and 140.4 (2 C), 129.5 and 123.4 (4 C), 74.1 (C-OH), 65.4 (CH_2), 37.9 ($CH(CH_3)_2$), 23.1 (CH_3), 20.8 (CH_3-Ar), 16.7 y 16.2 $(CH_3)_2CH$); IR: 3600, 3410, 1600, 1490, 1380, 1365, 1025, 810 cm^{-1}; Anal. calc. for $C_{13}H_{20}O_2S$: C,64.96; H, 8.39. Found: C, 64.56; H, 8.62. Diastereomer **9B** [2S,(S)R]: $[\alpha]_D^{20}$= +231° (c= 1, $CHCl_3$). ^{1}H-NMR: 7.55 y 7.34 (AA'BB' system, 4 H, Tol), 2.98 y 2.85 (AB system, 2 H, J_{AB}= 13.6 Hz, CH_2SO), 2.42 (s, 3 H, CH_3-Ar), 2.32 (sep, 1 H, J= 6.8 Hz, $CH(CH_3)_2$), 1.20 (s, 3 H, CH_3-C-OH), 1.07 (d, 3 H, J= 6.8 Hz, $(CH_3)_2CH$), 1.02 (d, 3 H, J= 6.8 Hz, $(CH_3)_2CH$).^{13}C-NMR: 141.6 and 140.9 (2 C), 130.0 and 123.8 (4 C), 75.0 (C-OH), 66.5 (CH_2SO), 37.1 ($CH(CH_3)_2$), 22.5 (CH_3), 21.3 (CH_3-Ar), 18.0 y 16.6 ($(CH_3)_2CH$).

2,3,3-Trimethyl-1-(4'-methylphenylsulfinyl)-2-butanol ***10.*** Was prepared from (R)-3,3-dimethyl-1-(4'-methylphenylsulfinyl)-2-butanone **5** following procedure B. Yield 89% as a 95:5 mixture of **10A** and **10B**. Major diastereomer **10A** [2R,(S)R] was obtained pure by crystallization in hexane, mp 105-106° C (hexane); $[\alpha]_D^{20}$= +278° (c= 2, $CHCl_3$). MS: 197 (80), 140 (61), 139 (100), 92 (37), 91 (24). ^{1}H-NMR: 7.56 y 7.36 (AA'BB' system, 4 H, Tol), 3.05 (dc part A of AB system, 1 H, J_{AB}= 13.3 Hz, $J_{A\text{-}Me}$= 1 Hz, CH_2SO), 2.67 (part B of AB system, 1 H, J_{AB}= 13.3 Hz, CH_2SO), 2.44 (s, 3 H, CH_3-Ar), 1.63 (d, 3 H,

J_{A-Me}= 1 Hz, CH_3-C-OH), 0.94 (s, 9 H, *terc*-Bu).^{13}C-NMR: 141.7 and 140.3 (2 C), 129.9 and 123.8 (4 C), 76.2 (C-OH), 63.7 (CH_2), 38.2 ($C(CH_3)_3$), 24.6 (3 C, *terc*-Bu), 22.0 (CH_3), 21.2 (CH_3-Ar). IR: (CH_2Cl_2): 3600, 3450, 2960, 1460, 1370, 1040 cm^{-1}. Anal. calc. for $C_{14}H_{22}O_2S$: C, 66.10; H, 8.72; S, 12.60. Found: C, 66.40; H, 8.61; S, 12.5. Compound **10B** [2S,(S)R] could not be obtained diastereomerically pure and was characterized in the mixture. ^{1}H-NMR 7.57 y 7.36 (AA'BB' system, 4H, Tol), 3.05 y 2.94 (AB system, 2H, J_{AB}= 13.4 Hz, CH_2SO), 2.43 (s, 3 H, CH_3-Ar), 1.18 (s, 3 H, CH_3-C-OH), 0.97 (s, 9 H, *terc*-Bu).

(R)-2,3-Dimethyl-1-(4'-methylphenylthio)-2-butanol 11. To a solution of 1.09 g (6.3 mmol, 3 eq) of NaI in 5 mL of CH_3CN was added a solution of 505 mg (2.1 mmol, 1 eq) of (R)-2,3-dimethyl-1-(4'-methylphenylsulfinyl)-2-butanol **9A** in 10 mL of CH_3CN. The mixture was coolded to 0° C prior to the dropwise adition of 0.8 mL of $BF_3.OEt_2$ in 5 mL of CH_3CN. After stirring during 40 min the mixture was poured into a separatory funnel with ice-water. The resulting solution was washed with a saturated aqueous $Na_2S_2O_3$ solution. The mixture was extracted with ether, dried over anhydrous sodium sulfate and concentrated in vacuo. Compound **11** was purified by flash chromatography (eluent ethyl acetate/hexane 1:10). Yield 77%. $[\alpha]_D^{20}$= +11.3° (c= 1.1, $CHCl_3$); ^{1}H-NMR: 7.32 and 7.08 (AA'BB' system, 4 H, Tol), 3.16 and 3.07 (AB system, 2 H, J_{AB} = 13.2 Hz, CH_2S), 2.31 (s, 3 H, CH_3-Ar), 1.86 (sep, 1 H, J= 7.0 Hz, $CH(CH_3)_2$), 1.14 (s, 3 H, CH_3-C-OH), 0.97 (d, 3 H, J= 6.9 Hz, $(CH_3)_2CH$), 0.89 (d, 3 H, J= 6.8 Hz, $(CH_3)_2CH$); ^{13}C-NMR: 136.4 and 133.3 (2 C), 130.3 and 129.7 (4 C), 74.5 (C-OH), 46.8 (CH_2S), 36.5 ($CH(CH_3)_2$), 22.3 (CH_3), 20.9 (CH_3-Ar), 17.7 (($CH_3)_2CH$), 17.0 (($CH_3)_2CH$); Anal. calc. for $C_{13}H_{20}OS$: C, 69.59; H, 8.99. Found: C, 69.48; 9.20; IR: 3520, 1600. 1490, 1390, 1375, 810 cm^{-1}.

(R)-2,3-Dimethyl-1,2-butanediol 13. To 170 mg (1.15 mmol, 1.6 eq) of trimethyloxonium tetrafluoroborate was added a solution of 161 mg of (R)-2,3-dimethyl-1-(4'-methylphenylthio)-2-butanol **11** in 4 mL of acetonitrile. The mixture was stirred for 20 min and then 2.2 mL of a 1 M aqueous potassium carbonate solution was added and the mixture was stirred overnight. Pure (R)-2,3-Dimethyl-1,2-epoxybutane could not be isolated due to its low boiling point. ^{1}H-NMR: 2.60 y 2.55 (AB system, 2 H, J_{AB}= 4.9 Hz, CH_2), 1.51 (sept, 1 H, J= 7.0 Hz, $CH(CH_3)_2$), 1.23 (s, 3 H, CH_3), 1.00 (d, 3 H, J= 6.8 Hz, $(CH_3)_2CH$), 0.94 (d, 3 H, J= 7.0 Hz, $(CH_3)_2CH$) (obtained directly from organic layer). 200 mg (4 mmol, 5.6 eq) of NaOH were then added to the reaction mixture and refluxed for 24 h. The crude was filtered and the solid and the aqueous layer were washed with ether. The organic layer was dried over magnesium sulfate and concentrated in vacuo. Yield 8%. $[\alpha]_D^{20}$= +9.4° (c= 0.17, $CHCl_3$); ^{1}H-NMR: 3.56 y 3.44 (AB system, 2H, J_{AB}= 11.1 Hz, CH_2), 1.83 (sept, 1H, J= 6.8 Hz, $CH(CH_3)_2$), 1.08 (s, 3H, CH_3), 0.96 (d, 3H, $(CH_3)_2CH$), 0.89 (d, 3H, $(CH_3)_2CH$)

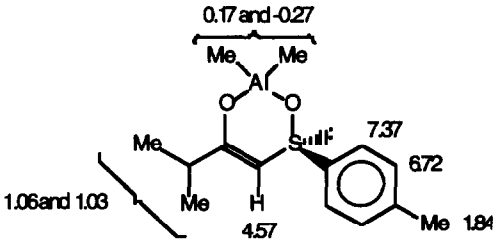
REFERENCES AND NOTES

1.-Carreño, M.C., García Ruano, J.L., Martin, A. M., Pedregal, C., Rodriguez, J.H., Rubio, A., Sanchez, J., Solladié, G. *J. Org. Chem.*, **1990**, *55*, 2120 and references cited therein.

2.-Barros, D., Carreno, M.C., Garcia Ruano, J. L., Maestro, M.C. *Tetrahedron Lett.*, **1992**, *33*, 2733.

3.-Preliminary results obtained from 2-*p*-tolylsulfinylcyclohexanone were previously reported (Carreño, M.C.; García Ruano, J.L.; Rubio, A. *Tetrahedron Lett.*, **1987**, *28*, 4861). A complete study of the reduction of cyclic substrates (5, 6 and 7 membered rings) has revealed significant differences between cyclic and acyclic substrates but, in both cases, the great importance of the sulfinyl group in the control of the stereoselectivity is mantained, (unpublished results). Similar differences have been found in the reduction of β-iminosulfoxides (see García Ruano, J.L., Lorente A., Rodríguez J.H., *Tetrahedron Lett.* **1992**, *33*, 5637 for acyclic substrates and Carreño, M.C., Domínguez, E., García Ruano, J.L , Rodríguez, J.H. *Tetrahedron*, **1991**, *47*, 10035 for imines derived from α-sulfinylcyclohexanone).

4.-García Ruano, J.L., Martín, A.M., Rodríguez, J.H. *J. Org. Chem.*, **1992**, *57*, 7235.
5.-Two different stereochemical pathways depending on the relative configuration of the starting ketosulfoxides (involving tetra or pentacoordinated intermediates), have been proposed to explain the results obtained in the highly stereoselective hydrocyanation of the α-sulfinylcycloalkanones (García Ruano, J.L., Martín, A.M., Rodríguez, J.H., unpublished results). Acyclic substrates evolved only through pentacoordinated intermediates (see *ref. 4*).
6.-Kunieda, N., Nokami, J., Kinoshita, M.*Chem. Lett.*, **1974**, 369.
7.-Fujisawa, T., Fujimura, A., Ukaji, Y. *Chem. Lett.* **1988**, 1541.
8.-Bueno, A.B., Carreño, M.C., Fischer, J., García Ruano, J.L., Peña, B, Peñas, L., Rubio, A. *Tetrahedron Lett.*, **1991**, *32*, 3191.
9.-García Ruano, J.L.; Martín, A.M.; Rodríguez, J.H. *An. Quim.*, **1990**, *86*, 71.
10.-The ^{1}H-nmr spectra of a C_6D_6 solution of compound **4** containing $AlMe_3$ (4 eq.) reveals the presence of the aluminium enolate. This compound is the major one in the crude mixture (> 70%) and exhibits the chemical shifts indicated below.



11.-The lower stability of the cyclic aluminumenolates would explain that their reactions became complete in the same conditions.
12.-Evans, D.A.; Hoveyda, A.H. *J. Org. Chem.*, **1990**, *55*, 5190.
13.-Addition of increasing amounts of catalyst to the reaction medium does not improve the results due to the low solubility of the $ZnCl_2$ in CH_2Cl_2. Although the reduction of β-ketosulfoxides with DIBAL/$ZnCl_2$ has been successfully conducted in THF, where the catalyst is soluble, reactions with $AlMe_3$ in this solvent were completely unfruitful.
14.-In *Table 2* only the protons at C-γ have been indicated. Nevertheless, the same effect is also observed for the CH_3-C-C(OH) protons in compounds **8** and **9** (in **10** the differences are too small), which are also slightly more deshielded in the **B** epimers (see experimental).
15.-Jochims, J.C.; Taigel, G.; Seeliger, A.; Lutz, P.; Driesen, H.E., *Tetrahedron Lett.*, **1977**, 4363.
16.-Crystals of **10A** belong to the orthorhombic space group $P2_12_12_1$, and accurate lattice constants of a = 19.020 (5), b = 10.269 (3), c = 7.580 (3) Å. All unique diffraction maxima [θ min/max (deg) = 3/55)] were colected using 2θ:θ scans and CuKα radiation ay -100° C. Of the 1121 reflections measured in this fashion, 1049 (94%) were judged observed [I>3σ(I)] and used in subsequent calculations. The structure, solved by the heavy atom method using Enraf-Nonius SDP/VAX package (B. A. Frenz, "The Enraf-Nonius CAD4-SDP" in *Computing in Crystallography*, Ed., H. Schenk, R. Olthof-Hazekamp, H, Van Koningveld, G. C. Bassi, pp. 64-71, Delft University Press, 1978), was refined to R = 0.038. The absolute structure was determined by comparing *xyz* and *-x-y-z* refinements. Tables of atomic coordinates, bond lengths and angles, and thermal parameters (supplementary material) are available on request from the Cambridge Crystallographic Data Centre.
17.- Mori, K.; Ebata, T.; Takechi, S. *Tetrahedron*, **1984**, *40*, 1761.
18.- Vankar, Y.D.; Trinadha Rao, C. *Tetrahedron Lett.*, **1985**, *26*, 2717.
19.- Solladié, G.; Demailly, G.; Greck, C. *Tetrahedron Lett.*, **1985**, *25*, 435.
20.- a) Chini, M.; Crotti, P.; Flippin, L.A.; Macchia, F. *J. Org. Chem.*, **1990**, *55*, 4265. b) Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.*, **1990**, *31*, 4664. c) Chini, M.; Crotti, P.; Macchia, F. *Tetrahedron Lett.*, **1990**, *31*, 5641 d) Chini, M.; Crotti, P.; Favero, L.; Macchia, F. *Tetrahedron Lett.*, **1991**, *32*, 4775.