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Enantioselective Oxidation of β-Hydroxythioethers[1]. Synthesis of Optically Active Alcohols and Epoxides

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Abstract: Optically pure β-hydroxysulfoxides may be obtained by direct oxidation of the parent thioethers with the modified Sharpless reagent developed in our laboratory. Necessary requisites for a successful asymmetric oxidation are both the protection of the OH function and the largest possible difference in size of the two groups linked to the thioether sulfur. This latter condition is fulfilled by using *S*-methyl derivatives. Examples referring to the oxidation of various *S*-methyl-β-hydroxythioethers, characterized by e.e. values up to 80%, which may be further increased (>98%) by crystallization, are presented. Results concerning the synthesis of optically active epoxides and alcohols starting from β-hydroxysulfoxides are also presented which, in some cases, allows the absolute configuration of the parent sulfoxide to be established.

A procedure of facile and general applicability for obtaining optically pure β-hydroxysulfoxides remains an important goal in organic synthesis in view of the applications, either as ligands or as building blocks, of such compounds in asymmetric reactions[2].

So far, optically active β-hydroxysulfoxides are obtained either *via* aldol-type reactions of α-sulfinyl anions with carbonyl compounds[3] or by reduction of β-ketosulfoxides with various hydride transfer agents[4]. The reagents containing the sulfinylic function are enantiomerically pure and their preparation is usually carried out *via* the Andersen[5] or related methods[6].

Aldol-type reactions afford the two diastereomeric β-hydroxysulfoxides in variable ratios, depending on the nature of the reagents[3]. Also the diastereoselection of the reduction of β-ketosulfoxides has been shown to depend on the hydride donors employed[4]. Thus, non-chelating hydride donors, such as di-*iso*-butylaluminium hydride, afford mainly one diastereomer, while chelating hydride donors, *e.g.* lithium aluminium hydride or DIBAL in the presence of zinc bivalent salts, provide the other diastereomeric β-hydroxysulfoxide. In both cases the level of diasteroselection is very high (d.r. up to 98%).

Other procedures involving the use optically pure β-hydroxythioethers, obtained by addition of thiolates to optically pure epoxides, have been reported[7]. The thioethers are oxidized to the corresponding *S*-oxides by conventional oxidizing agent, *e.g.* *m*-chloroperbenzoic acid. All the methods presented above need that an optically pure reagent, either a sulfoxide or an epoxide, is available.

A different and more direct approach is the asymmetric oxidation of racemic β-hydroxythioethers with a chiral, non racemic oxidizing agent.

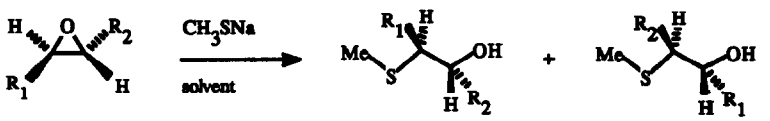
Recently we have developed a modification of the Sharpless reagent[8], effective in the enantioselective oxidation of thioethers[9]. Independently, another modification of the Sharpless reagent was developed by the Kagan's group[10]. Both systems (based on titanium (IV), diethyltartrate and an alkylhydroperoxide) have been found to enantioselectively oxidize the thioether sulfur in various classes of substrates[9,10,11].

Early studies on the application of our procedure to the oxidation of some β-hydroxythioethers provided rather disappointing results (e.e 20-47%)[12]. At any rate, such studies showed that enhanced enantioselectivities were achieved when the hydroxy function was protected either by forming a silyl ether or an acetate. A further improvement of the enantioselection was obtained by using protected *S*-methyl-β-hydroxythioethers[13]. Indeed, by maximizing the stereo and/or stereoelectronic differences between the two groups linked to the sulfur atom, an improvement of the enantioselection was obtained. Accordingly, e.e. values up to 80% were reached, *i.e.* values which may be considered of interest from a synthetic point of view. In this paper a full report of the results obtained by employing such an approach is presented. Also, data concerning the transformation of the optically enriched *S*-methyl-β-hydroxysulfoxides to chiral, non racemic epoxides and alcohols are discussed, that allow us to assign the absolute configuration of two of the *S*-methyl-β-hydroxysulfoxides synthesized. Some of this work has been subject of a preliminary communication[13].

Results

The series of *S*-methyl-β-hydroxythioethers employed in the present work have been synthesized *via* ring opening of suitable epoxides by sodium methanthiolate[14]. Such epoxides are shown in Scheme 1.

Scheme 1

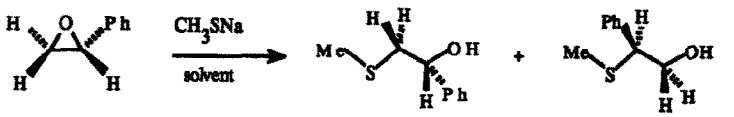


(±)-1 (±)-4 (±)-5
(±)-2 (±)-6 (±)-7
(±)-3 (±)-8

Substrate	R_1	R_2
(±)-styrene oxide (1)	H	Ph
(±)-*trans*-β-methylstyrene oxide (2)	Ph	CH_3
(±)-*trans*-3-hexene oxide (3)	CH_3CH_2	CH_3CH_2

The reaction of sodium methanthiolate with an epoxide is a stereospecific but not a regiospecific process[15]. As an example, when (±)-styrene oxide (1) is used and methanol is the solvent, equal amounts of the two regioisomers (±)-4 and (±)-5 are obtained. By assuming that the regioselectivity may be solvent dependent, we have tested various solvents in order to select the one which allows us to obtain predominantly one of the two isomeric alcohols (±)-4 or (±)-5. The pertinent results are collected in Table 1.

Table 1



(±)-1 (±)-4 (±)-5

Solvent	T°C	(±)-4:(±)-5	react.time(min)
DMSO	20	9:91	30
DMF	20	10:90	30
CH_3OH	40	50:50	30
CH_3CH_2OH	78	68:32	90
CF_3CH_2OH + CH_3COOH	20	70:30	60
CF_3CH_2OH	20	77:23	60
DMI[a]	20	93: 7	30

a. DMI=1,3-dimethyl-2-imidazolidinone

On the basis of the data of Table 1, (±)-4 has been prepared in trifluoroethanol. 1,3-Dimethyl-2-imidazolidinone was discounted because of its difficult removal. (±)-5 has been synthesized in *N,N*-dimethylformamide.

In the case of (±)-*trans*-β-methylstyrene oxide (2) we have found that the ring opening is highly regioselective when ethanol is used as solvent, thus providing the two isomers (±)-6 and (±)-7 in a 94:6 ratio. For this substrate only the isomer (±)-6 has been utilized in the asymmetric oxidation procedure.

In the case of (±)-*trans*-3-hexene oxide (3) there are no regiochemical problems and therefore the product (±)-8 was prepared by using ethanol as solvent.

As anticipated, we noticed that, at variance with the asymmetric epoxidation of allylic alcohols with the Sharpless reagent[7], the presence of a free hydroxy group in the substrate results in a lowering of optical yields in the β-hydroxythioethers oxidation[12,13]. Accordingly, the protection of the hydroxy functionality with suitable groups becames a necessary step of the procedure.

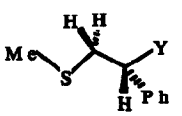
Therefore various protecting groups have been considered also with a view toward studying the effect of the nature and the bulkiness of the group on the stereochemistry. Thus, silylethers, acetyl derivatives and nitrobenzoates have been prepared. It is also important to mention that when the protected β-hydroxysulfoxides obtained are solid materials, an upgrading of the enantiomeric excess by crystallization could be predicted.

In the present study we used a substrate: Ti(IV): (+)-DET: hydroperoxide ratio of 4: 1: 4: 2 and the reactions were carried out in dichloroethane at -20°C.

It should be recalled that the substrates utilized are racemic compounds. Therefore the asymmetric oxidation of the sulfur atom also amounts to a kinetic resolution. Consequently a ratio 4 : 2 of the substrate and the hydroperoxide is required. Such an excess of the substrate turned out to be beneficial also as far as the chemical yields are concerned.

The results obtained in the asymmetric oxidation of (±)-4 where the alcoholic function is protected, are collected in Table 2. In the same Table data on the oxidation of the unprotected substrate are also reported for comparison purposes.

Table 2



sub. #	Y	ROOH	yield %	prod. #	diast. ratio a:b	e.e.a %	e.e.b %
(±)-4	OH	*t*-BuOOH	20	26	68:32	3	5
(±)-9	$OSiPh_3$	*t*-BuOOH	78	27	56:44	70	64
(±)-9	$OSiPh_3$	$PhCMe_2OOH$	85	27	50:50	80	75
(±)-10	OSi-*t*-$BuPh_2$	*t*-BuOOH	90	28	55:45	75	71
(±)-11	*o*-NO_2-benzoate	$PhCMe_2OOH$	71	29	53:47	54	50

Such results confirm the indications previously obtained[12] that the oxidation of β-hydroxythioethers, where the difference of the size of the two groups bound to sulfur is maximized and the hydroxy moiety is masked, may proceed with a high degree of enantioselectivity. In fact the e.e. values obtained for all the

derivatives reported in Table 2 range from fair to good while the e.e. observed for the unprotected *S*-methyl-β–hydroxythioether (±)-**4** is very low. Indeed such e.e. is even lower than those obtained for β-hydroxy thioethers substituted at the sulfur atom with alkyl groups other than methyl[12] (see Introduction). Moreover we have observed that the asymmetric oxidation of (±)-**4** provides also poor chemical yield.

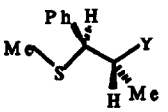
It may also be noticed that for all the derivatives reported in Table 2 there is almost no diastereoselection. Such a low level of recognition seems to be related to the absence in these substrates of a stereocenter directly connected to the sulfur atom. Such a hypothesis is also confirmed by the result obtained when compound (±)-**12**, derived from (±)-**5** protected as diphenyl-*tert*-butylsilylether, was subjected to the asymmetric oxidation. In this case, where an asymmetric carbon is present in α position to the sulfur, a d.r. = 87:13 and 74% and 66% e.e. for the two diastereomers **13a** and **13b** are obtained.

Another important observation is that the nature and the size of the protecting groups play only a marginal role as far as the enantioselectivity and the diastereoselectivity are concerned.

It is also worthy of mention that our data confirm previous observation[16] that, at least for this class of compounds, the use of cumyl hydroperoxide instead of *tert*-butylhydroperoxide improves the optical yield of the asymmetric oxidation.

Table 3 collects the data referring to the asymmetric oxidation of a series of (±)-**6** derivatives.

Table 3



sub. #	Y	ROOH	yield %	prod. #	diast.ratio a:b	e.e.$_a$ %	e.e.$_b$ %
(±)-**6**	OH	*t*-BuOOH	22	**24**	>99: 1	18	-
(±)-**14**	$OSiPh_3$	*t*-BuOOH	90	**17**	88:12	70	n.d.
(±)-**14**	$OSiPh_3$	$PhCMe_2OOH$	91	**17**	91: 9	78	70
(±)-**15**	$OSiMe_3$	$PhCMe_2OOH$	84	**30**	87:13	66	n.d.
(±)-**16**	acetate	$PhCMe_2OOH$	87	**31**	86:14	71	n.d.

It is evident from the e.e. and d.e. values reported above that the choice of the structure of β-hydroxythioether is crucial in determining the selectivity of the oxidizing system. In addition it may also be noticed that the presence of a stereocenter directly connected to the sulfur atom plays a relevant role in determining the diastereoselectivity which ranges from 86:14 up to 91:9. Moreover, the first entry of the Table 3 points again to a very negative effect exhibited by the free hydroxy group both on the optical and on the

chemical yields.

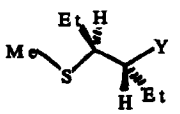
For derivatives of (±)-**4** where there is no stereocenter α- to the sulfur there is little d.e. observed (although e.e.>50%) and therefore little enantiomeric enrichment of the unreacted thioether is expected. However, for the derivatives of (±)-**5**, (±)-**6** and (±)-**8**, where there is a stereocenter α- to the sulfur, there is both a reasonable high d.e. and e.e., which implies that a significant enantiomeric enrichment of the unreacted thioether is to be expected: this was not investigated further.

In order to utilize the optically active sulfoxides obtained from (±)-**6** for synthetic purposes, the diastereomeric mixture (**17a** and **17b**) obtained by using the triphenylsilyl ether as protecting group was subjected to recrystallization and the major diastereomer (+)-**17a** was obtained with e.e.>98%.

The last class of *S*-methyl-β-hydroxythioethers protected at the hydroxy function examined, are the *trans*-3-hexene oxide (±)-**3** derivatives. Such alkyl derivatives were selected in order to test the relevance of the other group bound to the sulfur in determining the degree of enantioselectivity of the asymmetric oxidation, having established that the presence of the *S*-methyl moiety is a crucial feature.

Table 4 collects the results obtained with (±)-**8** (Y= OH) protected at the hydroxy functionality as silyl ether or as nitrobenzoates.

Table 4



sub. #	Y	ROOH	yield %	prod. #	diast.ratio a:b	e.e.$_a$ %	e.e.$_b$ %
(±)-**18**	$OSiPh_3$	$PhCMe_2OOH$	95	**32**	79:21	65	n.d.
(±)-**19**	*m,m*-dinitrobenzoate	$PhCMe_2OOH$	77	**22**	67:33	75	50
(±)-**20**	*o*-nitrobenzoate	$PhCMe_2OOH$	80	**23**	73:27	68	65
(±)-**21**	*p*-nitrobenzoate	$PhCMe_2OOH$	59	**33**	78:22	60	38

It can be seen that the substitution of an aryl group with an ethyl one does not change very much the degree of enantioselection (e.e. up to 75%). Moreover, also in this kind of substrates, where an α-stereocenter with respect to the sulfur is present, the d.e. values obtained may be considered satisfactory.

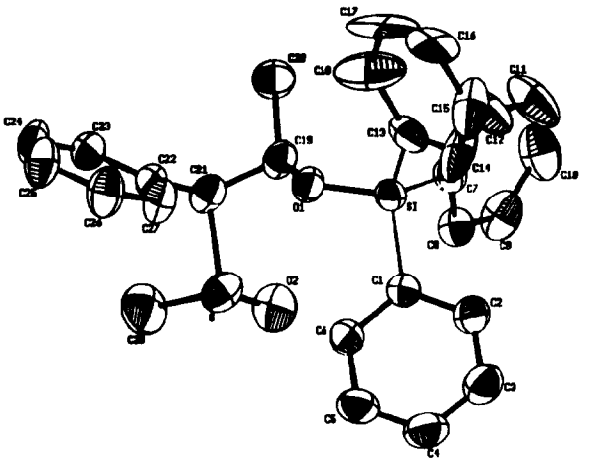
Unfortunately in this case the chromatographic separation of the diastereomeric mixture of the *m,m*-dinitrobenzoate derivatives (**22a** and **22b**), the one which gives the best results, was unsuccessful because of its low stability on silica-gel. In contrast, the two diastereomeric *o*-nitrobenzoatesulfoxides (**23a**) and (**23b**) could be separated by chromatography. Compound (-)-**23a**, obtained with an e.e.= 68%, was enantiomerically enriched up to e.e.> 98% by crystallization.

Applications.

Some of the optically active *S*-methyl-β-hydroxysulfoxides obtained with our methodology were converted to chiral, non racemic alcohols and epoxides by known procedures[17,18].

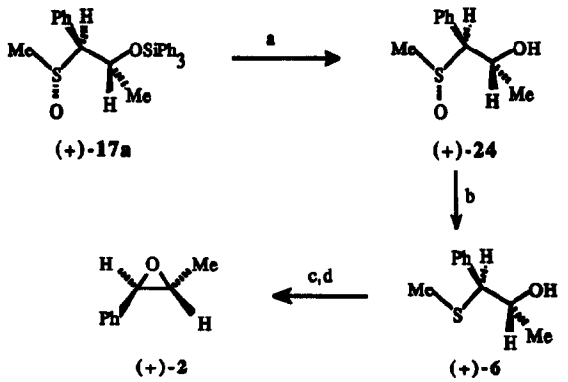
The major diastereomeric triphenylsilane (+)-**17a**, derived from (±)-β-methylstyrene oxide (**3**), was obtained in an optically pure form by simple crystallization (dichloromethane/pentane) $[\alpha]_D^{25}$= +19.6 (c=1.1, chloroform). Its relative stereochemistry was determined via diffrattometric analysis (Figure 1) to be 1-(R), 2-(S) and *S*-(R) if we assign the R configuration to the sulfinylic stereocenter, as it is likely in the light of the results reported below.

Figure 1.



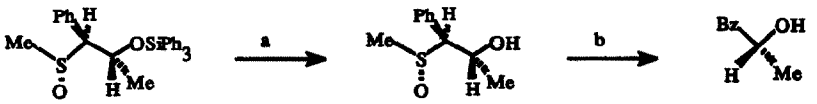
An optically pure sample of (+)-**17a** was transformed into (+)-(2R,3R)-β-methylstyrene oxide (**2**), $[\alpha]_D^{25}$= +49.2 (c=0.5, chloroform)[19a], (Scheme 2) and into (-)-(R)-1-methylphenethol (**25**) $[\alpha]_D^{25}$= -35.3 (c=3.0, chloroform)[20](Scheme 3) respectively.

Scheme 2.



a. n-Bu_4NF[21]; b. $NaI/I_2/Ph_3P$[22], c. Me_3OBF_4[17]; d. $NaOH/H_2O$[17].

Scheme 3.



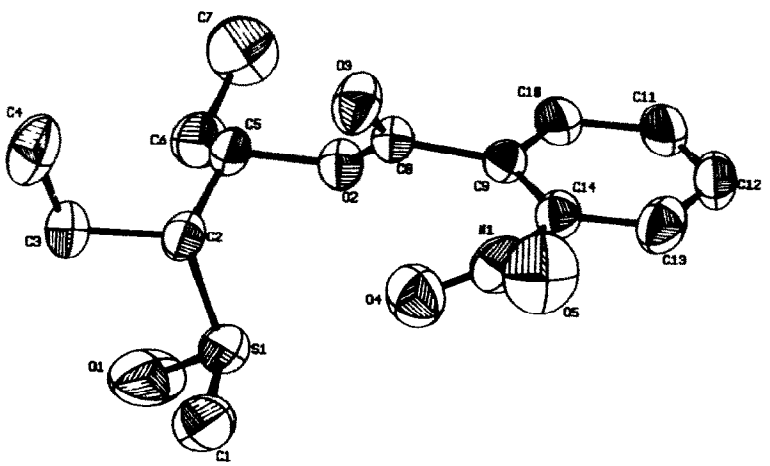
(+)-17a **(+)-24** **(-)-25**

a. *n*-Bu_4NF[21]; b. Raney/Nickel[23].

The absolute configurations of the epoxide (+)-2 and of the alcohol (-)-25 have been already determined by other authors[19,20], so that the correlation with the X-ray structure obtained for the triphenylsilane (+)-17a (figure 1), allows us to assign the R absolute configuration to the sulfinylic stereocenter. This absolute configuration is in agreement with previous results that showed the preference of our asymmetric oxidizing system[11] as well as that of Kagan[12] to afford R sulfoxides (at least for methyl aryl and methyl alkyl thioethers).

The major diastereomer (-)-23a, derived from (±)-*trans*-3-hexene oxide (3), obtained with a 68% e.e. $[\alpha]_D^{25}$=-69.6 (c=1.1, chloroform), was enantiomerically enriched by crystallization (dichloromethane/pentane), to give the optically pure sulfoxide, $[\alpha]_D^{25}$= -104.8 (c=1.1, chloroform). Also for compound (-)-23a the relative stereochemistry was determined *via* diffrattometric analysis (Figure 2) to be 1-(S), 2-(R) and *S*-(R) if we assign the R configuration to the sulfinyl stereocenter also in this case.

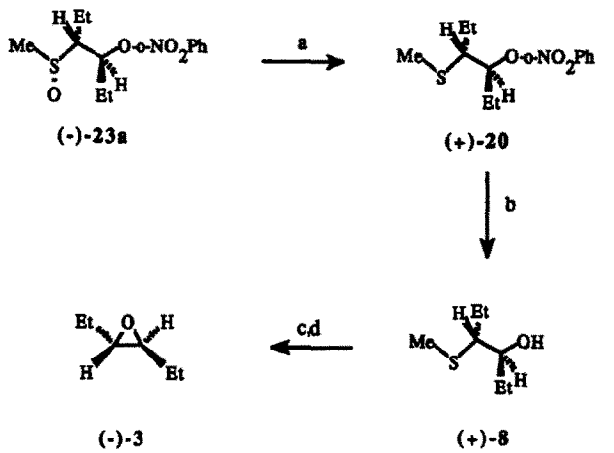
Figure 2.



The return to the resolved epoxide was carried out also with compound (-)-23a, by using a sample of a

50% enantiomeric purity. The same strategy previously used for the *S*-methyl-β-hydroxysulfoxide (+)-17a was essentially adopted (Scheme 4). On the basis of the hypothesis made above, the (2 S, 3 S)-epoxide should be obtained.

Scheme 4.



a. NaI/I_2/Ph_3P[22]; b. KOH/CH_3OH; c. Me_3OBF_4[17]; d. NaOH/H_2O[17]

The e.e. value of the epoxide (-)-3 was checked *via* g.c., using a capillary fused-silica column, coated with Ni(II)-bis-[1-S-(+)-3-heptafluorobutanoyl-10-ethylidencamphorate][24] and it was found to be 48.1 ± 1%. A support to the proposed absolute configuration of epoxide (-)-3 could be given by the elution order of the two enantiomers. In fact, normally when columns coated with Ni(II)-bis-[1-R-(+)-3-heptafluorobutanoylcamphorate] are used, the S and S,S enantiomers of aliphatic epoxides have a stronger interaction with the Ni(II) complex and therefore the R- and R,R-enantiomers are eluted first[24]. A similar behavior with the Ni(II)-bis-[1-S-(+)-3-heptafluorobutanoyl-10-ethylidencamphorate] coated columns may be expected, and in fact on our case the major enantiomer is the second in order of elution.

Another important point is that almost no loss of optical purity is experienced in the series of reactions shown in Scheme 2, 3, and 4.

In conclusion, we have presented here a novel methodology for obtaining chiral, non racemic *S*-methyl-β-hydroxysulfoxides with fairly good enantiomeric excesses (38-80%). In particular we have demonstrated the importance of protecting the hydroxy group in the β position for obtaining high enantioselections, showing at the same time that different protecting groups can be used.

Experimental.

^1H NMR spectra were determined on a Bruker WP200 (200 MHz) instrument; chemical shifts were

reported as δ units (ppm) downfield from tetramethylsilane. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), qui (quintet), m (multiplet). Coupling constant (J) are reported in Hz. Specific rotations were obtained with a Perkin-Elmer 241 polarimeter operating at λ=589 nm corresponding to the sodium D line. Mass spectra were determined on a GC Hewlett-Packard 5890/ Hewlett-Packard 5970 Mass selective detector. X-ray data were collected with a Phillips PW 1100 four-circle diffractometer. Crystal parameters and other diffractometric data are collected in Table 5. Boiling and melting points are uncorrected. Medium pressure chromatography was performed over silica gel (0.015-0.040 mm, Merck). Flash chromatography was performed over silica gel (0.040-0.063 mm, Merck). Radial chromatoghraphy was performed on a Chromatotron 7924 T (Harrison Research), over silica gel 60 (Merck, TLC PF 254). The enantiomeric excesses were determinated by ^{1}H NMR in the presence of (R)-(-) or (S)-(+)-2,2,2,-trifluoro-1-(9-anthryl)-ethanol (Aldrich), Pirkle CSA, (R)-(-)-*N*-(3,5-dinitrobenzoyl)-α-phenylethylamine, Kagan CSA[25] or tris-[3-(trifluoromethylhydroxymethylene)-(+)-camphorato]europium(III)derivative (Aldrich) Eu(hfc)$_3$. *tert*-Butyl-hydroperoxide (Fluka, 80%, 20% di-*tert*-butylperoxide) was purified by distillation under vacuum (b.p. 31°C/16 Torr) and stored at 4°C. Cumene hydroperoxide (80% in cumene) was stored on 4A molecular sieves at 4°C. (+)-Diethyl tartrate (Aldrich) was distilled under vacuum (b.p. 100-103°C/0.01Torr, $[\alpha]_D^{25}$=+8.5 (neat)), and stored under nitrogen. Titanium (IV)-tetra-*iso*-propoxide (Aldrich) was purified by distillation under vacuum (b.p. 58-60°C/0.1Torr). (±)-Styrene oxide (1) (Aldrich) was purified by distillation (b.p. 117°C/20 Torr). Dichloroethane, (Aldrich) was washed 3 times with 10% of concentrated H_2SO_4 and with H_2O several times until pH=7, dried overnight over $CaCl_2$, distilled over P_2O_5 and stored over molecular sieves. *N,N*-dimethylformamide was stirred overnight over calcium hydride and distilled under vacuum, 16 Torr. The other chemicals used were commercial products (Aldrich or Fluka) and were used without further purification.

Synthesis of (±)-trans-β-methylstyrene oxide (2) *and (±)-trans-3-hexene oxide* (3).

To a solution of 0.13 mol of alkene in 100 mL of dichloromethane at 0°C in the presence of potassium carbonate 0.14 mol of *m*-chloroperbenzoic acid dissolved in 300 mL of dichloromethane are slowly added under vigorous stirring. The reaction usually completes in 12 hrs. After removal by filtration of the *m*-chlorobenzoic acid formed, the organic layer is washed with a saturated solution of sodium metabisulfite, a saturated solution of sodium carbonate and brine. After drying over magnesium sulfate, product (±)-2 is obtained as colorless liquid by removing the solvent under vacuum, yield 88%, while product (±)-3, colorless liquid, is obtained after careful distillation of the solvent at atmospheric pressure, yield 85%.

(±)-*trans*-β-methylstyrene oxide (2): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.45 (3H, d, J=5.2); 3.04 (1H, dq, J=5.2, 2.1); 3.57 (1H, d, J=2.1); 7.20-7.40 (5H, m). MS (70 eV) m/z (%): 43(86); 50(21); 51(44); 63(34); 65(19); 77(38); 89(84); 90(100); 91(65); 92(18); 105(57); 133(34); 134(36, M^+).

(±)-*trans*-3-hexene oxide (3): ^{1}H-NMR-($CDCl_3$, TMS) δ (ppm): 0.99 (6H, t, J=6.0); 1.51-1.58 (4H, m); 2.66 (2H, t, J=6.0).

Synthesis of S-methyl-β-hydroxythioethers (±)-4, (±)-5, (±)-6, (±)-7, (±)-8

As a general procedure 0.14 mol of sodium methanthiolate is dissolved in 200 mL of the appropriate

solvent. To this solution, under stirring, 0.12 mol of the oxirane are slowly added. After the complete consuption of the epoxide the reaction mixture is quenched with 50 mL of a solution of 5% NaOH in water and extracted with dichloromethane. The organic phase is then washed with brine, dried over magnesium sulfate and the solvent removed under vacuum.

When (±)-styrene oxide (**1**) is the substrate and DMF is the solvent, products (±)-**4**:(±)-**5** are obtained in a ratio 10:90 with a chemical yield of 82%, when trifluoroethanol is used as solvent the ratio of the two isomers is 77:13, chemical yield 84%. The two products can be separated by medium pressure chromatography (ligth petroleum:ether 85:15) and were obtained as yellow oils.

(±)-2-(methylthio)-1-phenylethanol (**4**): ^{1}**H-NMR** ($CDCl_3$,TMS) δ (ppm) : 2.09 (3H, s); 2.70 (1H, dd, J=13.7, 8.8); 2.84 (1H, dd,J=13.7, 4.0); 4.74 (1H,dd, J=8.8, 4.0); 7.21-7.44 (5H, m), Elem. Anal., found, % (calcd for $C_9H_{12}OS$): C, 64.0 (64.2); H, 7.2 (7.2).

(±)-2-(methylthio)phenethyl alcohol (**5**) :^{1}**H-NMR** ($CDCl_3$,TMS) δ (ppm) 1.97 (3H, s); 3.87 (3H, s); 7.19-7.42 (5H, m); Elem. Anal., found, % (calcd for $C_9H_{12}OS$): C, 63.9 (64.2); H, 7.1 (7.2).

When (±)-*trans*-β-methylstyrene oxide is used, the solvent employed was refluxing ethanol, the reaction is completed in 60 min. Isomers (±)-**6** and (±)-**7**, are obtained in ratio 94:6, yield 79%, they can be separated by medium pressure chromatography (ligth petroleum:ether 80:20). They were obtained as yellow oils.

(1RS,2SR)-1-methyl-2-(methylthio)phenethyl alcohol (**6**) : ^{1}**H-NMR** ($CDCl_3$,TMS) δ (ppm): 1.25 (3H, d, J=6.1 Hz); 1.93 (3H,s); 2.10 (1H, -OH, d, J=4.6 Hz); 3.69 (1H, d, J=6.4 Hz); 4.09 (1H, ddq, J=4.6, 6.4, 6.1 Hz); 7.21-7.43 (5H, m).

(1RS,2SR)-1-phenyl-2-(methylthio)propanol (**7**): ^{1}**H-NMR** ($CDCl_3$,TMS) δ (ppm): 1.07 (3H, d, J=7.0); 2.14 (3H, s); 2.74 (1H, -OH, d, J=2,1); 3.01 (1H, dq, J=3.7, 7.0 Hz); 4.87 (1H, dd, J=3.7, 2.1); 7.24-7.42 (5H, m); Elem. Anal., found, % (calcd for $C_{10}H_{14}OS$): C, 65.8 (65.9); H, 7.7 (7.7).

Also in the case of (±)-*trans*-3-hexene oxide the solvent used was refluxing ethanol for 60 min. The product (±)-**8** has been purified by flash chromatography (ligth petroleum:ether 80:20) yield 70% and it was obtained as a yellow oil.

(3RS,4SR)-4-(methylthio)-3-hexanol (**8**): ^{1}**H-NMR** ($CDCl_3$,TMS) δ (ppm): 1.00 (3H, t, J=7.3), 1.05 (3H, t, J=7.3); 1.50 (3H, m); 1.70 (1H, m); 2.10 (3H, s); 2.15 (1H, s); 2.54 (1H, m); 3.63 (1H, m).

Synthesis of silyl derivatives. (±)-**9**, (±)-**10**, (±)-**14**, (±)-**15**, (±)-**18**.

To a solution of 32 mmol of silylchloride in anhydrous DMF under nitrogen at r.t. a solution of 36 mmol of triethylamine, 10 mmol of 4-*N*,*N*-dimethylaminopyridine and 30 mmol of β-hydroxythioether in DMF is slowly added. The reaction mixture is stirred at room temperature for 12 hrs, quenched with 50 mL of a saturated solution of ammonium chloride and extracted with dichloromethane. The organic layer is then washed with brine and dried over magnesium sulfate. The solvent is removed under vacuum. Products are purified by flash chromatography (light petroleum: dichloromethane 80:20).

(±)1-(methylthio)-2-phenyl-2-(triphenylsilyloxy)ethane (**9**) yield 84%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.72 (3H, s); 2.74 (1H, dd, J=13.4, 6.4); 2.89 (1H, dd, J=13.4, 6.4); 4.91 (1H, t, J=6.4); 7.19-7.45 (15H, m); 7.53-7.61 (5H, m); Elem. Anal., found, % (calcd for $C_{27}H_{26}OSSi$): C, 75.9 (76.0); H, 6.1 (6.1).

(±)-1-(*t*-butyldiphenylsilyloxy)-2-(methylthio)-1-phenylethane (**10**) yield 72%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.04 (9H, s); 1.63 (3H, s); 2.67 (1H, dd, J=13.7, 7.3); 2.80 (1H, dd, J=13.7, 5.5), 4.73 (1H, dd, J=7.3, 5.5); 7.18-7.78 (15H, m); Elem. Anal., found, % (calcd for $C_{25}H_{30}OSSi$): C, 73.6 (73.8); H, 7.5 (7.4).

(±)-1-(*t*-butyldiphenylsilyloxy)-2-(methylthio)-2-phenylethane (**12**) yield 73%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.98 (9H, s); 1.91 (3H, s); 3.93 (3H, m); 7.18-7.79 (15H, m); Elem. Anal., found, % (calcd for $C_{25}H_{30}OSSi$): C, 73.6 (73.8); H, 7.3 (7.4).

(1RS,2SR)-1-methyl-2-(methylthio)-2-phenyl-1-(triphenylsilyloxy)ethane (**14**) yield 81%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.26 (3H, d, J=6.1); 1.82 (3H,s); 3.70 (1H, d, J=6.1); 4.28 (1H, qui, J=6.1); 7.16-7.53 (20H, m); Elem. Anal., found, % (calcd for $C_{28}H_{28}OSSi$): C, 76,3 (76.3); H, 6.3 (6.4).

(1RS,2SR)-1-methyl-2-(methylthio)-2-phenyl-1-(trimethylsilyloxy)ethane (**15**) yield 71%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.02 (9H, s); 1.35 (3H, d, J= 6.4); 1.95 (3H, s); 3.7 (1H, d, J=6.4); 4.18 (1H, qui, J=6.4); 7.23-7.50 (5H, m); Elem. Anal., found, % (calcd for $C_{13}H_{22}OSSi$): C, 61.6 (61.3); H, 8.6 (8.7).

(3RS,4SR)-3-(methylthio)-4-(triphenylsilyloxy)hexane (**18**) yield 70%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.84 (3H, t, J=7.3); 0.91 (3H, t, J=7.3); 1.37 (4H, m); 1.84 (3H, s); 2.45 (1H, dt, J=5.2, 4.3); 3.85 (1H, dd, J=5.2, 0.9); 7.40 (10H, m); 7.67 (5H, m); Elem. Anal., found, % (calcd for $C_{25}H_{30}OSSi$): C, 73.5 (73.8); H, 7.5 (7.4).

Synthesis of (1RS,2SR)-1-methyl-2-(methylthio)phenethylacetate (**16**)

12.5 mmol of (±) **6** and 58 mmol of acetic anhydride are dissolved in 7 mL of pyridine. The stirred reaction mixture is left at r.t. for 12 hrs, then it is quenched with 10 mL of water and extracted with chloroform. The organic phase is washed with HCl 1M, with a 5% solution of sodium bicarbonate, dried over magnesium sulfate and the solvent is removed under vacuum. The product has been purified by flash chromatography (ligth petroleum:chloroform 1:1) yield 93%, and it was obtained as a colorless oil. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.31 (3H, d); 1.79 (6H, s); 3.58 (1H, d); 5.35 (1H, q); 7.22-7.40 (5H, m); Elem. Anal., found, % (calcd for $C_{12}H_{16}OS$): C, 65.2 (65.4); H, 7.3 (7.3).

Synthesis of nitrobenzoyl derivatives (±)-**11**, (±)-**19**, (±)-**20**, (±)-**21**.

To a solution of 3.2 mmol of the substrate, 6.4 mmol of pyridine and catalytic amount of dimethyldiaminopyridine in 5 mL of dichloromethane is added a solution of 6.4 mmol of the nitrobenzoyl chloride in 5 mL of dichloromethane. The reaction proceeds at r.t. in 1 hr, it is then quenched with 25 mL of water and extracted with dichloromethane. The organic phase is washed with HCl 1N, with a 5% solution of sodium bicarbonate, dried over magnesium sulfate and the solvent is removed under vacuum.

(±)-2-(methylthio)-1-phenylethyl-*o*-nitrobenzoate (**11**): the product is purified by flash chromatography (light

petroleum:ether 85:15) yield 81%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.05 (3H, s); 2.92 (1H, dd, J= 7.0, 13.7); 3.13 (1H, dd, J= 7.0, 13.7); 6.10 (1H, t, J=7.0); 7.32-7.45 (5H, m); 7.60-7.67 (2H, m); 7.75-7.81 (1H, m); 7.86-7.92 (1H, m); Elem. Anal., found, % (calcd for $C_{16}H_{15}NO_4S$): C, 60.7 (60.5); H, 4.6 (4.7); N, 4.3 (4.4).

(3RS,4SR)-3-(methylthio)-4-hexyl-*m,m*-dinitrobenzoate (**19**): the product has been purified by crystallization (methanol, activated coal), and it was obtained as a colorless solid, m.p. 103°-104°C, yield 65%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.99 (3H, t, J=7.7); 1.12 (3H, t, J=7.7); 1.52 (1H, m); 1.79-1.94 (3H, m); 2.12 (3H, s); 2.73 (1H, qui, J=4.6); 5.34 (1H, dt, J=4.6, 7.9); 9.17 (2H, d, J=2.1); 9.24 (1H, d, J=2.1); Elem. Anal., found, % (calcd for $C_{14}H_{18}N_2O_6S$): C, 48.8 (49.1); H, 5.4 (5.3); N, 8.1 (8.2).

(3RS,4SR)-3-(methylthio)-4-hexyl-*o*-nitrobenzoate (**20**): the product has been purified by flash chromatography (light petroleum:ethyl acetate 95:5) yield 78% and it was obtained as a colorless solid, m.p. 52°-53°C. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.02 (3H, t, J=7.3); 1.08 (3H, t, J=7.3); 1.40-1.55 (1H, m); 1.70-1.96 (3H,m); 2.11 (3H,s); 2.71 (1H, dt, J=4.5, 9.0); 5.26 (1H, dt, J=4.5, 8.1); 7.58-7.93 (4H, m); Elem. Anal., found, % (calcd for $C_{14}H_{19}NO_4S$): C, 56.8 (56.5); H, 6.5 (6.4); N, 4.7 (4.7).

(3RS,4SR)-3-(methylthio)-4-hexyl-*p*-nitrobenzoate (**21**): the product has been purified by flash chromatography (light petroleum:ethyl acetate 95:5) yield 76%. ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.98 (3H, t, J=7.0); 1.10 (3H, t, J=7.6); 1.35-1.64 (1H, m); 1.68-2.00 (3H, m); 2.11 (3H, s); 2.73 (1H, dt, J=5.2, 4.6); 5.27 (1H, dt, J=8.2, 4.6); 8.27 (4H, m); Elem. Anal., found, % (calcd for $C_{14}H_{19}NO_4S$): C, 56.7 (56.5); H, 6.5 (6.4); N, 4.6 (4.7).

Asymmetric oxidation of compounds (±)-**4**, (±)-**6**, (±)-**9**, (±)-**10**, (±)-**11**, (±)-**14**, (±)-**15**, (±)-**16**, (±)-**18**, (±)-**19**, (±)-**20**, (±)-**21**.

In a 100-ml round-bottom flask 2.84 mmol of titanium(IV)-tetraisopropoxide in 13 mL of dry dichloroethane and 11.34 mmol of (+)-diethyltartrate in 13 mL of dry dichloroethane were mixed under vigorous stirring at r.t.. The yellow, homogeneous solution was stirred at r.t. for 10 min, cooled to -20°C, and 5.67 mmol of the alkylhydroperoxide were added. The solution was stirred at -20°C for other 5 min, and a solution, 11.35 mmol in 20 ml of dry dichloroethane, of the β-hydroxythioether was added. The yellow solution was stirred at -20°C for 14-16 hrs, and, after disappearance of the oxidant, quenched with water and quickly warmed up to r.t. The mixture was stirred at r.t. for 1 h, filtered over Celite, and extracted with chloroform. The extracted was washed with 10% aqueous sodium metabisulfite, 5% aqueous sodium hydroxide, and brine, dried over magnesium sulfate, and concentrated under vacuum. The unreacted starting material was removed by flash chromatography (dichloromethane) and the oxidation products were recovered by eluting with methanol. The chemical yields are based on the equivalents of oxidant used and the diastereomeric ratio were determined by ^{1}H NMR on the mixture of the sulfoxides. The e.e. values were determined by ^{1}H NMR in the presence of chiral solvating agents.

2-(methylsulfinyl)-1-phenylethanol (**26a**) and (**26b**): the two diastereomers were obtained with a 20% chemical yield, r.d. 68:32. (**26a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.65 (3H, s); 2.94 (1H, dd, J=13.3, 2.7); 3.07 (1H, dd, J=13.3, 10.6); 5.35 (1H, dd, J=10.6, 2.7); 7.22-7.48 (5H, m). e.e.=3% determined in the

presence of (S)-(+)-Pirkle CSA, splitting signal at 2.65 ppm; (**26b**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.7 (3H, s); 2.95 (1H, dd, J=13.3, 3.3); 3.13 (1H, dd, J=13.3, 9.0); 5.38 (1H, dd, J=9.0, 3.3); 7.22-7.48 (5H, m). e.e.=5% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.70 ppm.

2-(methylsulfinyl)-1-phenyl-2-(triphenylsilyloxy)ethane (**27a**) and (**27b**): the diastereomers were obtained with a 78% chemical yield, d.r.=56:44 (with TBHP) or 85% chemical yield, d.r.=50:50(with CHP). (**27a**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.34 (2H, s); 2.99 (1H, dd, J=12.5, 7.0); 3.38 (1H, dd, J=12.5, 6.1); 5.22 (1H, dd, J=7.0, 6.1); 7.10-7.57 (20H, m). e.e.=70% (with TBHP) or 80% (with CHP) determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.34 ppm. (**27b**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.53 (3H, s); 2.93 (1H, dd, J=13.2, 2.8); 3.22 (1H, dd, J=13.1, 10.1); 5.35 (1H, dd, J=10.1, 2.8); 7.10-7.57 (20H, m). e.e.=64%. (with TBHP) or 75% (with CHP) determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.53 ppm.

1-(*t*-butyldiphenylsilyloxy)-2-(methylsulfinyl)-1-phenylethane (**28a**) and (**28b**) the two diastereomers were obtained with a 90% chemical yield, d.r.=55:45. (**28a**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.05 (9H, s); 2.29 (3H, s); 2.91 (1H, dd, J=12.5, 7.3); 3.28 (1H, dd, J=12.5, 5.8); 5.04 (1H, dd, J=7.3, 5.8); 7.04-7.75 (15H, m); e.e.=75% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.29. (**28b**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.07 (9H, s); 2.46 (1H, s); 2.91 (1H, dd, J=12.8, 3.4); 3.14 (1H, dd, J=12.8, 8.8); 5.18 (1H, dd, J=8.8, 3.4); 7.04-7.72 (15H, m); e.e.=71% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.46 ppm.

2-(methylsulfinyl)-1-phenylethyl-*o*-nitrobenzoate (**29a**) and (**29b**): the two diastereomers were obtained with a 71% chemical yield, d.r.=53:47. (**29a**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.66 (3H, s); 3.13 (1H, dd, J=8.6, 13.1); 3.56 (1H, dd, J=8.6, 13.1); 6.42 (1H, t, J=8.6); 7.26-7.95 (9H, m); e.e.=54% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.66 ppm.. (**29b**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 2.64 (3H, s); 3.12 (1H, dd, J=3.2, 13.4); 3.30 (1H, dd, J=10.0, 13.5); 6.44 (1H, dd, J=3.2, 10.0); 7.40-7.90 (9H, m); e.e.=50% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.64 ppm.

1-(*t*-butyldiphenylsilyloxy)-2-(methylsulfinyl)-2-phenylethane (**13a**) and (**13b**): the two diastereomers were obtained with a 89% chemical yield, d.r.=87:13. (**13a**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.98 (9H, s); 2.25 (3H, s); 3.70 (1H, dd, J=5.5, 3.7); 4.71 (1H, dd, J= 10.7, 3.7); 4.32 (1H, dd, J=10.7, 5.5); 7.15-7.38 (10H, m); 7.38-7.55 (5H, m); e.e.=74% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.25. (**13b**):^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.07 (9H, s); 2.18 (3H, s); 3.54 (1H, dd, J=9.6, 5.5); 4.05 (1H, dd, J=10.9, 5.5); 4.47 (1H, dd, J=10.9, 9.6); 7.11-7.24 (2H, m); 7.28-7.61 (10H, m); 7.47-7.74 (3H, m); e.e.=66% determined in the presence of (R)-(-)-Kagan's CSA, splitting signal at 2.18 ppm.

1-methyl-2-(methylsulfinyl)phenethyl alcohol (**24**) was obtained as a single diastereomer with a 22% chemical yield. (**24**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.19 (3H, d, J=6.5); 2.38 (3H, s); 3.4 (1H, broad); 3.64 (1H, d, J=2.7); 4.77 (1H, broad), 7.31-7.44 (5H, m); e.e.=18% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.38 ppm.

1-methyl-2-(methylsulfinyl)-2-phenyl-1-(triphenylsilyloxy)ethane (**17a**) and (**17b**) the two diastereomers were

obtained with a 90% chemical yield d.r.=88:12 (with TBHP), 91% chemical yield d.r=91:9 (with CHP). (**17a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.01 (3H, d, J=6.5); 2.28 (3H, s); 3.48 (1H, d, J=3.1); 4.9 (1H, dq, J=6.5 3.1); 7.28-7.49 (15H, m); 7.62-7.72 (5H, m); e.e.=70% (with TBHP), e.e.=78% (with CHP) determined in the presence of (S)-(+)-Pirkle CSA, splitting signals at 1.01 and 2.28 ppms. Compound **17a** was purified by crystallization (dichloromethane/pentane) and was obtained as a colorless solid, $[\alpha]_D^{25}$= +19.6 (c=1.1, $CHCl_3$), e.e.> 98%, determined in the presence of (S)-(+)-Pirkle CSA, no splitting of the signals at 1.01 and 2.28 ppms; Elem. Anal., found, % (calcd for $C_{28}H_{28}O_2SSi$): C, 73.4 (73.6); H, 6.1 (6.2). (X-ray data reported in Table 5).

Table 5. Crystallographic data for (1R, 2S, *S*R)-1-methyl-2-(methylsulfinyl)-2-phenyl-1-(triphenylsilyloxy) ethane (+)-**17a** and (3S, 4R, *S*R)-3-(methylsulfinyl)-4-hexyl-*o*-nitrobenzoate (-)-**23a**.

Compound		(+)-**17a**-$C_{28}H_{28}O_2SSi$	(-)-**23a**-$C_{14}H_{19}NO_5S$
Mol. wt.		456.664	313.368
Space group		$P2_1$	$P2_1$
Temp (°C)		21	21
Cell constants[26]:	a,Å	13.066 (2)	14.674 (2)
	b,Å	11.053 (2)	6.846 (1)
	c,Å	8.884 (2)	7.763 (1)
α, deg		90	90
β, deg		92.6 (2)	92.1 (2)
γ, deg		90	90
Cell vol. Å3		1281.7 (4)	779.3 (2)
Formula units/Unit cell		2	2
D_{calc}, g cm^{-1}		1.18	1.28
μ_{calc}, cm^{-1}		1.55	1.82
Diffractometer/Scan		ϑ-2ϑ	ϑ-2ϑ
Radiaton, graphite, monochromator		0.71070	0.71070
Max crystal dimensions, mm		0.3, 0.3, 0.5	0.5, 0.2, 0.5
Scan width, deg		1.2	1.2
Standard reflections		3	3
Decay of standards		10%	10%
Reflections measured		3407	2162
Reflections independent		3223	2033
2θ range, deg		50°	50°
Reflection observed		2711 $F \geq 7\sigma(F)$	1566 $F \geq 7\sigma(F)$
Structure solution		MULTAN 80	MULTAN 80
Computer programs		SHELX 76	SHELX 76
No. of parameters refined		289	265
Weights		$1/[\sigma^2(F)+0.003F^2]$	$1/[\sigma^2(F)+0.240F^2]$
R_{int}		0.031	0.008
R		0.044	0.057
R_w		0.051	0.060
Largest feature final diff. map		0.242	0.652

1-methyl-2-(methylsulfinyl)-2-phenyl-1-(trimethylsilyloxy)ethane (**30a**) and (**30b**) the two diastereomers were obtained with a 84% chemical yield d.r.=87:13. (**30a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.23 (9 H, s); 1.08 (3 H, d); 2.22 (3 H, s); 3.41 (1 H, d); 4.79 (1 H, dq); 7.18-7.55 (5 H, m); e.e=66% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.22 ppm. (**30b**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.23 (9 H, s); 1.28 (3 H, d); 1.93 (3 H, s); 3.49 (1 H, d); 4.13 (1 H, dq); 7.18-7.55 (5 H, m); e.e.% n.d.

1-methyl-2-(methylsulfinyl)-phenethylacetate (**31a**) and (**31b**) the two diastereomers were obtained with a 87% chemical yield d.r.=86:14. (**31a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.25 (3 H, d, J=6.4); 2.10 (3 H, s); 2.28 (3 H, s); 3.64 (1 H, d, J=3.7); 5.64- 5.79 (1 H, m); 7.18-7.55 (5 H, m); e.e.=71% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 3.64 ppm. (**31b**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.56 (3 H, d, J=6.1); 1.87 (3 H, s); 2.23 (3 H, s); 3.46 (1 H, d, J=8.2); 5.30-5.40 (1 H, m); 7.18- 7.55 (5 H, m); e.e.% n.d.

3-(methylsulfinyl)-4-(triphenylsilyloxy)hexane (**32a**) and (**32b**) the two diastereomers were obtained with a 95% chemical yield d.r.=79:21. (**32a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.87 (3 H, t, J= 7.3); 0.97 (3 H, t, J= 7.3); 1.56-1.85 (4 H, m); 1.85-2.08 (1 H, m); 2.29 (3 H, s); 4.06 (1 H, dt, J= 2.8, 5.8); 7.23-7.77 (15 H, m); e.e.=65% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.29 ppm. (**32b**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 0.70 (3 H, t, J= 7.6); 1.13 (3 H, t, J= 7.9); 1.56-1.85 (4 H, m); 2.41-2.51 (1 H, m); 2.54 (3H, s); 4.41 (1H, tm, J= 7.3); 7.23-7.77 (15 H, m); e.e.% n.d.

3-(methylsulfinyl)-4-hexyl-*m,m*-dinitrobenzoate (**22a**) and (**22b**) the two diastereomers were obtained with a 77% chemical yield d.r.=67:33. (**22a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.04 (3H, t, J= 7.3); 1.26 (3 H, t, J= 7.6); 1.83-2.17 (4 H, m); 2.61 (3 H, s); 2.72-2.83 (1 H, m); 5.55 (1H, m); 9.15 (2 H, d, J= 2.1); 9.28 (1H, t, 2.1); e.e.=75% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.61 ppm. (**22b**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.06 (3 H, t, J= 7.3); 1.23 (3 H, t, J= 7.3); 1.70-2.10 (4 H, m); 2.68 (3 H, s); 2.72-2.83 (1 H, m); 5.77 (1 H, m); 9.14 (2 H, d, J= 1.8); 9.25 (1 H, t, J= 1.8); e.e.=50% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.68 ppm.

3-(methylsulfinyl)-4-hexyl-*o*-nitrobenzoate (**23a**) and (**23b**). The two diastereomers were obtained with a 80% chemical yield, d.r.=73:27 and they were purified by medium pressure chromatography (ethyl acetate/light petroleum 80:20). Compound (-)-**23a** was obtained as a colorless solid, m.p.=69-70°C, $[\alpha]_D^{25}$= -69.6 (c=1.1, chloroform): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.02 (3H, t, J=7.4); 1.21 (3H, t, J=7.5); 1.61-2.10 (4H, m); 2.61 (3H, s); 2.76-2.84 (1H, m); 5.38-5.46 (1H, m); 7.61-7.73 (3H, m); 7.94-7.99 (1H, m); e.e.=68% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.61 ppm. Crystallization (dichloromethane/pentane), m.p.= 79.5 °C, $[\alpha]_D^{25}$=-104.8 (c=1.1, chloroform), e.e.> 98%, determined in the presence of (S)-(+)-Pirkle CSA, no splitting of the signal at 2.61 ppm; Elem. Anal., found, % (calcd for $C_{14}H_{19}NO_5S$): C, 53.5 (53.6); H, 6.1 (6.1); N, 4.3 (4.5). (X-ray data reported in Table 5). Compound (-)-**23b** was obtained as a pale yellow oil, $[\alpha]_D^{25}$= -39.9 (c=1.2, chloroform): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.05

(3H, t, J=7.4); 1.11 (3H, t, J=3.8); 1.41-1.85 (4H, m); 1.99-2.09 (1H, m); 2.63 (3H, s); 5.60 (1H, dt, J=2.56, 7.25); 7.59-7.70 (2 H, m); 7.80-7.91 (2 H, m); e.e.=65% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.63 ppm; Elem. Anal., found, % (calcd for $C_{14}H_{19}NO_5S$): C, 53.3 (53.6); H, 6.3 (6.1); N, 4.3 (4.5).

3-(methylsulfinyl)-4-hexyl-*p*-dinitrobenzoate (**33a**) and (**33b**) the two diastereomers were obtained with a 59% chemical yield d.r.=78:22. (**33a**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.02 (3H, t, J=7.3); 1.24 (3H, t, J=7.6); 1.78-2.16 (4H, m); 2.59 (3H, s); 2.78 (1H, ddd, J=0.6, 2.4, 3.0); 5.46 (1H, dd, J=0.6, 4.6); 8.21 (2H, d, J=8.0); 8.33 (2H, d, J=8.0); e.e.=60% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.59 ppm . (**33b**): ^{1}H-NMR ($CDCl_3$, TMS) δ (ppm): 1.04 (3H, t, J=7.3); 1.21 (3H, t, J=7.3); 1.69-2.17 (4H, m); 2.63 (3H, s); 2.70 (1H, m); 5.64 (1H, m); 8.25 (4H, m); e.e.=38% determined in the presence of (S)-(+)-Pirkle CSA, splitting signal at 2.63 ppm.

Deprotection of (1R,2S,*SR*)-*1-methyl-2-(methylsulfinyl)-2-phenyl-1-(triphenylsilyloxy)ethane*(+)-**17a**[21].
To a solution of 4.6 mmol of (+)-**17a** in 25 mL of dry THF were slowly added 4.6 mmol of tetra-*n*-butyl ammonium fluoride dissolved in 40 mL of THF. The mixture was then left, under stirring, at room temperature for 30 min. After consumption of the reagent the reaction was quenched with 35 mL of acidic water and extracted with ether. The organic phase was then washed with brine, dried over magnesium sulfate and the solvent was removed under vacuum. The product (+)-**24**, purified by radial chromatography (ethyl acetate:light petroleum 1:1), was obtained as a colorless solid, 56% yield, m.p. 188-189°C, $[\alpha]_D^{25}$=+162.8 (c=1.0, chloroform).

Deoxygenation of S-oxides (+)-(**24**) and (-)-(**23a**)[22].
A mixture of 0.76 mmol of triphenylphosphine and 0.76 mmol of iodine in 5 mL of acetonitrile was stirred at r.t. for 5 min. The brown mixture was then treated with the 0.69 mmol of the *S*-oxide and, after 2-3 min, with 0.83 mmol of sodium iodide. The mixture was refluxed for 1 h. After disappearance of starting material, the reaction was cooled to r.t. and quenched with 10% aqueous sodium metabisulfite. Extraction with dichloromethane, drying over sodium sulfate, removal of the solvent under vacuum, and flash chromatography (dichloromethane) afforded the corresponding thioether (85-95% yield). Compound (+)-**24** afforded (+)-**6**, $[\alpha]_D^{25}$= +185.6 (c=2.0, chloroform) and compound (-)-**23a** supplied the thioether (+)-**20**, m.p.= 51-52°C, $[\alpha]_D^{25}$=+21.2 (c=1.0, chloroform).

Deprotection of (+)-3-(methylthio)-4-hexyl-o-nitrobenzoate (+)-**20**
2.38 mmol of substrate and 2 mL of a solution of KOH (10%) in water were dissolved in 10 ml of methanol. The reaction proceeded at room temperature in 2 hrs. The reaction mixture was then acidified with HCl 1N. The *o*-nitrobenzoic acid formed was filtered off and the filtrate was extracted with dichloromethane. The organic phase was then washed with brine, dried over magnesium sulfate and the solvent was removed under vacuum. Purification by radial chromatography (light petroleum: ether 80:20) gave (+)-**8** as a

colorless oil, 89% yield, $[\alpha]_D^{25}$= +6.33 (c=1.3, chloroform).

Synthesis of optically active epoxides (+)-**2** *and* (-)-**3**[16].

0.25 mmol of *S*-methyl-β-hydroxythioether was dissolved in 5 mL of dichloromethane: nitromethane 1:1 under argon at 0°C. To the former solution was added 2.53 mmol of $(CH_3)_3O^+BF_4^-$. After the disappearance of the substrate (2 hrs) the solvent was removed under vacuum at 0°C. The crude was then dissolved in 5 mL of dichloromethane at 0°C and, under argon atmosphere, 20 mL of NaOH 0.5 N were added. The reaction then proceeds for 24 hrs and it was extracted with ether. The organic layer was washed with brine and dried over magnesium sulfate.

(+)-(1R,2R)-*trans*-β-methylstyrene oxide (**2**) was purified, after removal of the solvent under vacuum, by flash chromatography (light petroleum: dichloromethane 95:5), 60% yield, e.e > 98%, detected by ^{1}H NMR in $CDCl_3$, no splitting of any signal in the presence of Eu(hfc)$_3$[19b] $[\alpha]_D^{25}$=+49.2 (c=0.5, chloroform), $[\alpha]_{D\,lit.}^{25}$=+50 (c=1.17, chloroform)[19a].

(-)-*trans*-3-hexene oxide (**3**) was purified, after removal of the solvent at atmospheric pressure, lby ball to bal distillation; e.e. = 48.1%, determined *via* g.c., using a capillary fused-silica column, coated with Ni(II)-bis-[1-S-(+)-3-heptafluorobutanoyl-10-ethylidencamphorate][24], b.p. 107°C/760 Torr, $[\alpha]_D^{25}$= -8 (c=0.2, dichloromethane).

Reduction of (1R,2S,SR)-1-methyl-2-(methylsulfinyl)phenethyl alcohol (+)-**24**[23].

1.7 mmol of (+)-**24** and 1.70 g of Raney-Nickel are suspended in 15 mL of dry THF and the mixture is stirred at room temperature for 2 hrs. The suspension is then filtered over celite. The filtrate is extracted with ether and water, the organic phase is then washed with brine, dried over magnesium sulfate and the solvent is removed under vacuum. The product (-)-(R)-1-methylphenylethanol (**25**) was purified by distillation, b.p. 120°C, $[\alpha]_D^{25}$=-35.3 (c=3, chloroform), $[\alpha]_{D\,lit.}^{25}$=-33.7 (c=2, chloroform)[20]. **^{1}H-NMR** ($CDCl_3$, TMS) δ (ppm): 1.31 (3H, d, J=7.5); 2.64 (1H, d, J=6.4); 2.73 (1H, d, J=4.7); 3.96 (1H, m); 7.10-7.35 (5H, m).

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References and Notes

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1. Part 6. Part 5: Conte, V.; Di Furia, F.; Licini, G.; Modena, G. *Tetrahedron Lett.* **1989**, 30, 4859.
2. for some examples see Drabowicz, J.; Kielbasinski, P.; Mikolajczyk "Synthesis of Sulfoxides" Chapt. 8, pp. 233-378; Posner, G. "Asymmetric Synthesis Using α-Sulfinyl Carbanions and β-unsatured sulfoxides" Chapt.16, pp. 823-849, in "*The Chemistry of Sulphones and Sulphoxides*" Patai, S.; Rappoport, Z.; Stirling, C.J.M. Eds., J. Wiley & Sons Ltd., Colchester, Essex, UK (1988).
3. Durst, T.; Viau, R.; Van der Elzen *J. Chem. Soc., Chem. Commun.* **1971**, 1334; Kingsbury, C. H.; *J. Org. Chem.* **1972**, 37, 102; Farnum, D.G.; Veysoglu, T.; Carde, A. M.; Duhl-Emswiller, B.; Pancoast, T.A.; Reitz, T.J.; Carde, R.T. *Tetrahedron Lett.* **1977**, 4009; Demailly, G.; Greck, C.; Solladie', G. *Tetrahedron Lett.* **1984**, 25, 4113.
4. Annunziata, R.; Cinquini, M.; Cozzi, F. J. *Chem. Soc., Perkin Trans.* I **1979**, 1687; Solladie', G.; Damailly, G.; Grack, C. *J. Org. Chem.* **1985**, 50, 1552; Solladie', G.; Frachou, L.; Damailly, G.; Grack, C. *J. Org. Chem.* **1986**, 51, 1912.
5. Andersen, K.K. *J. Org. Chem.* **1964**, 29, 1953
6. for examples see: Mikolajczyk, M.; Drabowicz, J. "Chiral Organosulfur Reagents" in *Topics on Stereochemistry*, vol 13, pp 333-468, Allinger, N.L., Eliel, E.L.; Wilen, S.H. Eds., John Wiley & Sons Inc., New York, USA, (1982) and references cited in there.
7. De Lucchi, O.; Buso, M; Modena, G. *Tetrahedron Lett.* **1987**, 28, 107.
8. Sharpless, K.B.; Katsuki *J. Am. Chem. Soc.* **1980**, 102, 5974.
9. Di Furia, F.; Modena, G.; Seraglia, R. *Synthesis*, **1984**, 325.
10. Pitchen, P.; Kagan, H.B.*Tetrahedron Lett.* **1984**, 25, 1049; Pitchen, P.; Dunach, E.; Deshmukh, M.N.; and Kagan, H.B. *J. Am. Chem. Soc.* **1984**, 106, 8188; Dunach, E.; *Nouv. J. Chim.* **1985**, 9, 1; Nemecek, C.; Pitchen P.; Samuel, O.; Zhao, S. *Pure and Appl. Chem.* **1985**, 57, 1911; Nemecek, C.; Dunach, E.;Kagan, H.B.; *Nouv. J. Chim.* **1986**, 10, 761; Kagan H.B. *Phosphorous and Sulfur* **1986**, 27, 127.
11. Bortolini, O.; Di Furia, F.; Licini, G.; Modena, G.; Rossi, M. *Tetrahedron Lett.* **1986**, 27, 6257; Di Furia, F.; Licini, G.; Modena, De Lucchi, O. *Tetrahedron Lett.* **1989**, 30, 2575; Di Furia, F.; Licini, G.; Modena, G. *Gazz. Chim. It.* **1990**, 120, 165 ; Campestrini, S.; Conte, V., Di Furia, F.; Licini, G.; Modena, G. *Chim. Ind.* **1990**, 72, 408; Di Furia, F.; Licini, G.; Modena, G. *Bull. Soc. Chim. Fr.* **1990**, in press.
12. Bortolini, O.; Di Furia, F.; Licini, G.; Modena, G. *Phosphorous and Sulfur*, **1988**, 37, 171.
13. Conte, V.; Di Furia, F.; Licini, G.; Modena, G. *Tetrahedron Lett.* **1989**, 30, 4859.
14. Gozinski, J. *Synthesis*, **1984**, 629.
15. Iqbal, J.; Pandey, A.; Shukla, A.; Srivastava, R.R.; Tripathi, S. *Tetrahedron* **1990**, 46, 6423.
16. Zhao, S.; Samuel, O.; Kagan, H.B. *Tetrahedron* **1987**, 43, 5135.
17. Solladie', G.; Demailly, G.; Greck, C. *Tetrahedron Lett.* **1985**, 26, 435.
18. Solladie', G.; Greck, C.; Demailly, G.; Solladie'-Cavallo, *Tetrahedron Lett.* **1982**, 23, 5047.
19. a) Witkop, B.; Foltz, C.M. *J. Am. Chem. Soc.* **1957**, 79, 197; b) Castedo, L.; Castro, L. J.; Riguera, R.; *Tetrahedron Lett.* **1984**, 25, 1205..
20. Schmidt, M.; Amstutz, R.; Crass, G.; Seebach, D. *Chem. Ber.* **1980**, 113, 1691.
21. Corey, E.J.; Snider, B.B. *J. Am. Chem. Soc.* **1972**, 94, 2549.
22. Olah, G.A.; Gupta, B.G.B.; Narang, S.C. *Synthesis* **1978**, 137.
23. Kharasch, N.; Nudemburg, M. *J. Org. Chem.* **1951**, 16, 524.

24. Schurig, V.; Koppenhoefer, B.; Bürkle, W. *Angew. Chem. Int. Ed. Engl.* **1978**, 17, 937; Schurig, V.; Bürkle, W. *J. Am. Chem. Soc.* **1982**, 104, 7573; Schurig, V. *J. Chromatogr.* **1988**, 441, 135; Schurig, V.; Bürkle, W.; Hintzer, K.; Weber, R. *J. Chromatogr.* **1989**, 475, 23.
25. Deshmukh, M.; Dunach, E.; Juge, S.; Kagan, H.B. *Tetrahedron Lett.* **1984**, 25, 3467.
26. Last squares refinement of $(\sin\theta/\lambda)^2$ values for 25 reflections $7°<\theta<20°$.