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CHIRAL SULFUR-REAGENTS FOR THE PREPARATION OF OPTICALLY ACTIVE EPOXIDES

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Abstract: *Acyclic chiral sulfides which could be easily synthesized in both enantiomeric forms leading to poor yields and/or to racemic epoxides, Eliel's oxathiane reagent was used and proved to provide chiral trans diarylepoxides in high yield (70-80%) and enantiomeric purities up to 70-100%, with no rearrangment problems. It was also found that phase-transfer conditions were the easiest and the most efficient for these reactions.*

Résumé: *Nous avons montré que l'oxathiane d'Eliel est un bon réactif récupérable d'époxidation. Le benzylsulfonium correspondant conduit en effet à des trans diarylépoxydes dont la pureté optique peut atteindre 70 à 100% avec des rendements d'environ 80%. Les conditions de transfert de phase conduisent aux meilleurs résultats.*

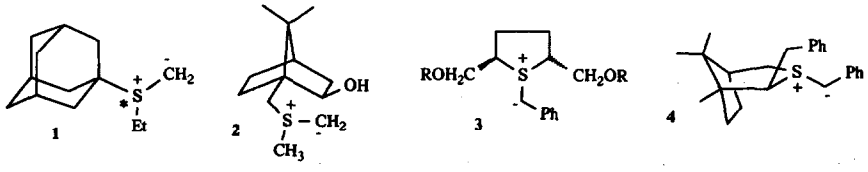
Introduction

During work on the asymmetric synthesis of adrenergic drugs[1-4] we have been confronted with the difficulty of obtaining optically pure epoxides and decided to investigate the use of chiral and optically pure sulfur-ylides to convert aldehydes into chiral epoxides.

Since the first report by Johnson and coll. in 1961[5] that sulfur-ylides could react with substituted benzaldehydes to give epoxides, the method has been extensively developed [6-9].

A number of reports[10-13] have also indicated that sulfonium-ylides were pyramidal at sulfur and were thus capable of exhibiting optical activity.

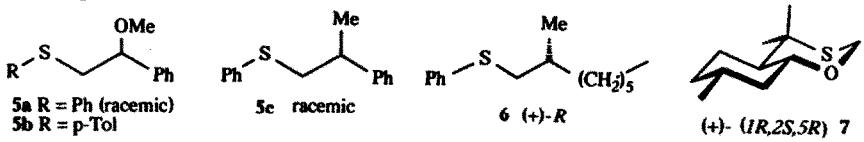
The first attempt to prepare optically active styrene oxide by this method has been performed by Trost and coll. in 1973[14], the reagent was the optically active adamantylethylsulfonium methylide **1** obtained from the corresponding resolved sulfonium, the chirality was at the sulfur-atom but the asymmetric induction happened to be nil.



Recently Furukawa and coll.[15] and then Durst and coll.[16,17] have reported the preparation of various trans-stilbene oxides in 43-47% e.e. (yield 20%)[15], 64-83% e.e. (yield= 27-41%)[16] and >96% e.e. (yield= 32-38%)[17] using respectively the optically pure ylides **2**, **3** and **4**, where the chirality was also situated at carbon-atoms.

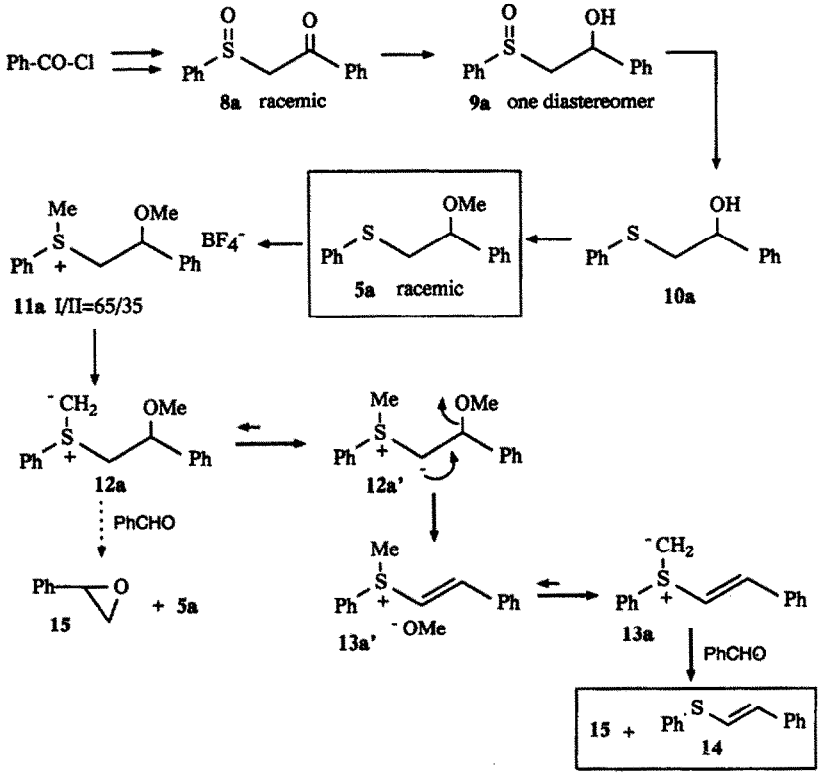
Results

We want to report here our results concerning the use of sulfides **5a**, **5c**, **6** and **7**.



Because sulfide **5b** is available in optically pure form (both *R* or *S*) from the method developed by Solladié and coll.[18] the less expensive racemic sulfide **5a** was investigated first to check if the desired epoxide was formed and if the sulfide could be recovered ; the two necessary conditions for the reaction to be synthetically useful.

Scheme 1

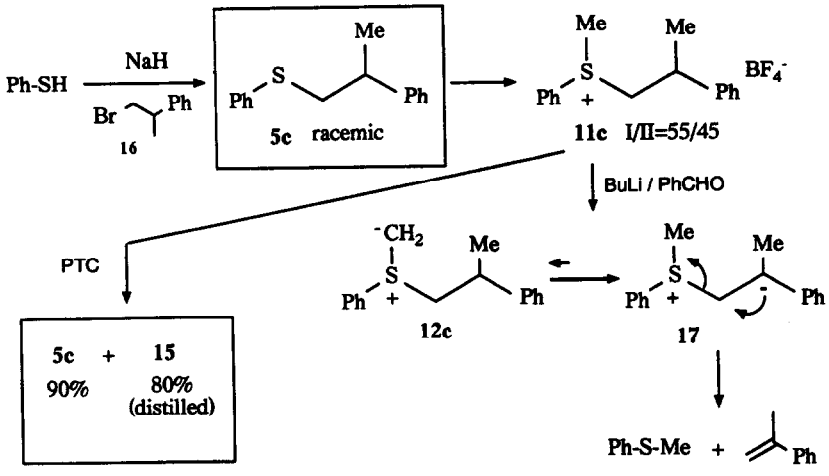


The racemic sulfide **5a** was synthesized in 5 steps and 46% total yield from benzoyl chloride as shown on scheme 1. The corresponding methylsulfonium salt **11a** was obtained in 90% yield as a 65/35 mixture of the two possible diastereomers and happened to provide in the Corey's conditions[19] the desired styrene oxide **15** but in low yield (20%).

Furthermore no starting sulfide **5a** could be recovered, only the vinyl sulfide **14** was obtained in about 20% yield. This suggested that the equilibrium between the two possible ylides **12a** and **12a'** was displaced toward **12a'** through decomposition into sulfonium **13a'** whose ylide **13a** then provided styrene oxide **15** and the vinyl sulfide **14**, scheme 1.

Sulfide **5c** with no methoxy-group was then synthesized in 87% yield from thiophenol, scheme 2, and the corresponding sulfonium salt **11c** was obtained as a 55/45 mixture of the two diastereomers. Under Corey's conditions[19] **11c** gave only α-methylstyrene and methylphenylsulfide suggesting that under these conditions the zwitterion **17** was formed as the main species, scheme 2. However under phase-transfer conditions the styrene oxide **15** was obtained in high yield, scheme 2.

Scheme 2

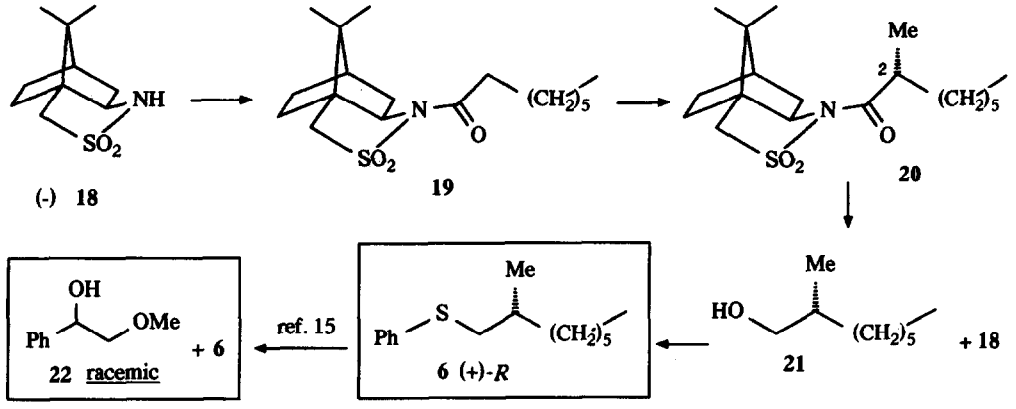


Optically pure sulfide **6**-(+)-*R* with no methoxy and/or phenyl-groups was synthesized using Oppolzer's chiral auxiliary[20], **18**.

Sultam A **18**, obtained in 50% total yield from (+)-*S*-camphorsulfonic acid[20,21], provided in 4 steps the (+)-*R*-sulfide **6**, scheme 3. It must be noticed that, with BuLi as a base, compound **20** was obtained as a single diastereomer in accord with literature results, the expected absolute configuration at C2 being *R*[22].

Under the liquid-solid two-phase Furukawa conditions[15] optically pure sulfide **6** provided, after chromatography, 50% of α-hydroxy-β-methoxyethylbenzene **22** but *racemic*; the starting sulfide **6** was recovered in 50% yield. This method was used in this case because it offered a way to save the expensive optically pure sulfide **6** which, in these conditions, worked as a mediator to transfer an alkyl group to the aldehyde and was used in non-stoichiometric ratio. However a clear limitation arised from the formation of MeOH (from the MeI used) and subsequent *in situ* opening of the epoxide formed[23].

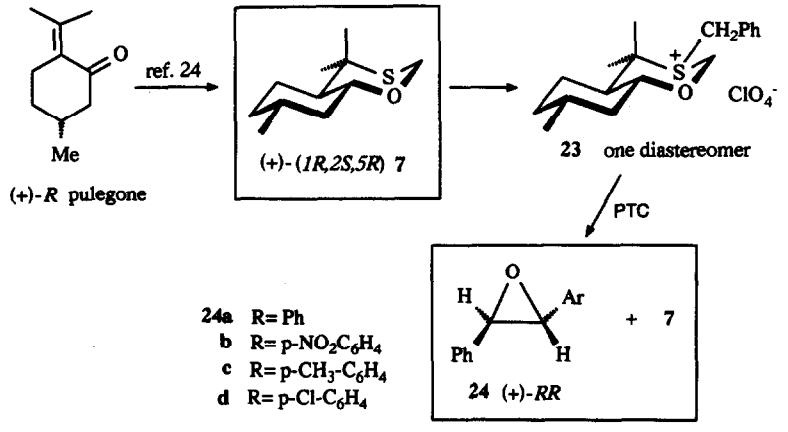
Scheme 3



However the α-hydroxy-ß-methoxy-ethylbenzene obtained being racemic, we turned to a cyclic and rigid sulfide.

Eliel's reagent, oxathiane 7, was obtained in the usual way[24], scheme 4.

Scheme 4



S-Alkylation of sulfide 7 with $PhCH_2Br$ in the presence of $AgClO_4$ afforded the sulfonium salt 23 in 70% yield. The ^1H NMR spectrum showed only one diastereomer (no splitting of any of the proton signals), it could thus be expected that, in basic medium, 23 will yield only one ylide .

Reaction of sulfonium salt 23 with benzaldehyde and substituted-benzaldehydes under phase-transfer conditions afforded only the trans-epoxides 24 in satisfying yield together with the starting sulfide 7. The results are given in the table.

Table : Preparation of arylphenylepoxides from 23 and under PTC

R-(CHO)	Trans Epoxide 24a-d yield	$[\alpha]_D$ (conc.)[a]	e.e.%	config.	recovered Sulfide 7 yield%
C_6H_5	80%	+169 (1.1)	72%[b]	*RR*	82%
p-NO_2-C_6H_4	60%	0[c] (1.15)	0%[b]		80%
p-CH_3-C_6H_4	75%	+92 (0.7)	26-32%[d]	*RR*	78%
p-Cl-C_6H_4	82%	+223 (1.35)	62-100%[e]	*RR*	80%

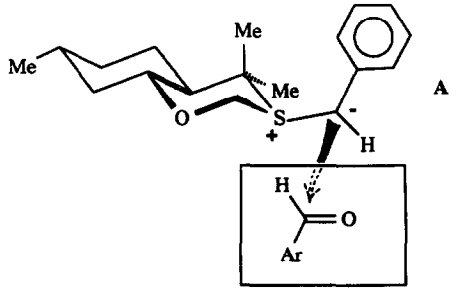
a) In EtOH. b) E.e.% determined by ^{1}H NMR using Eu(hfc)$_3$ as chiral reagent, by comparison with the racemic epoxide. c) In CH_2Cl_2. d) E.e.% determined from the different $[\alpha]_D$Max given in ref. 25: $[\alpha]_D$Max= +300 to +351, see also ref. 26. e) E.e.% determined from the different $[\alpha]_D$max given ref. 25: $[\alpha]_D$Max= +350 to +362 and ref. 15: $[\alpha]_D$Max= +214

No cis-epoxides were observed on the ^{1}H-NMR spectra (200 MHz) of the crude products[25]. After separation (flash chromatography) the e.e.'s of the epoxides were determined by ^{1}H NMR using Eu(hfc)$_3$ as chiral shift reagent and/or using the optical rotations when the $[\alpha]$Max were given in the literature[15,25,26].

It appeared that, in the four cases studied, the chemical yields are larger, 60-80%, than those generally obtained in the literature[15-17] (20-40%) and that the enantioselectivity was 72% for trans epoxide **24a** *and close to 100% for trans-epoxide* **24d**. *We do not yet have any clear understanding about the 0% e.e. obtained in the case of epoxide* **24b**.

The (+) rotations obtained clearly indicated that the configuration[17] of the major epoxides was *2R,3R*. As already invoked by Durst and coll.[17] this diastereoselectivity can be interpreted in terms of a preferred conformation A in the ylide[10-12] together with a sterically-directed approach of the aldehyde as shown on scheme 5.

Scheme 5



Conclusion

Eliel's oxathiane 7 appeared to be an efficient reagent for the preparation of trans diarylepoxides leading to high yields (about 80%) and to optical purities up to 72% and 100%. Furthermore, the starting oxathiane is recovered (no elimination possible) and can be used again.
It appeared also that the phase-transfer conditions, which allow to avoid undesirable side reactions was the most efficient method for the preparation of these aryl-epoxides.

Experimental part

Infra-Red spectra were recorded on a Perkin-Elmer 257 (ν in cm^{-1}). ^1H (200 MHz) and ^{13}C (50 MHz) NMR spectra were recorded on a Bruker AC-200 (δ in ppm refered to TMS, $\Delta\nu$ and J in Hz). Rotations were measured on a Perkin-Elmer 241 MC. M.p. were determined (uncorrected) on a Reichert Microscope. Flash-chromatography was performed using silicagel 70-230 Mesh purchased from Merck. Kieselgel 60 F_{254} (from Merck) were used for TLC. All the solvents were distilled before use: THF over Na/benzophenone, Et_2O over $LiAlH_4$, HMPT over calcium hydride, DMF and nitromethane over $CaSO_4$. All the reagents were reagent grade purchased from Aldrich and/or Janssen and used without further purification.

Synthesis of 1-methoxy-1-phenyl-2(phenylthio)ethane : **5a**

a) 1-phenyl-2-[(phenyl)sulfinyl]ethanone: **8a**

To a solution of LDA (42.8 mmol) in THF (60ml) at -30°C was added dropwise a solution of methyl phenyl sulfoxide (3g, 21.4 mmol) in THF (50 ml). The temperature was allowed to reach 0°C and the mixture stirred for 20 min. The temperature was then lowered to -78°C and a solution of benzoyl imidazolide [32 mmol; prepared from imidazole (4.36g, 64 mmol) and benzoyl chloride (37ml, 32 mmol)] in THF (40 ml)] was added slowly. After 2h at -78°C, the mixture was quenched with a saturated NH_4Cl solution (100ml). After extraction with ethyl acetate (3 x 100ml) the combined organic phases were washed successively with a 5% H_2SO_4 solution (10ml), a saturated NaCl solution (2 x 100ml) and dried over Na_2SO_4. After evaporation of the solvent under vacuum the residue was purified by chromatography (AcOEt/hex, 3/2): yield 70% .
Pale yellow solid, m.p. 60-65°C. R_f = 0.42 (AcOEt/hex.,3/2).
IR ($CHCl_3$) : ν_{CO}=1680.
^1H NMR ($CDCl_3$/TMS): 4.44 (2H, AB system, $\Delta\nu_{AB}$= 50, J_{AB}=14) ; 7.5 (6H, m, H arom) ; 7.7 (2H, m, H arom) ; 7.9 (2H, m, H arom).

b) 1-phenyl-2-[(phenyl)sulfinyl]ethanol: **9a**

To a solution of the above ß-keto-sulfoxide **8a** (0.5g, 2.05 mmol) in THF (5ml) was added $ZnCl_2$ (0,167g, 1.23 mmol), after 10min. stirring the temperature was lowered to -78°C and a 1M solution of Dibal in toluene (4.1 ml, 4.1 mmol) was added dropwise. After 1h stirring, methanol (10ml) and water (10ml) were added and the mixture was extracted with CH_2Cl_2 (2 x 20ml). The combined organic layers were washed with a 5% NaOH solution (2x10ml), dried over Na_2SO_4 and the solvent evaporated under vacuum. The residue was purified by chromatography (AcOEt/hex/CH_2Cl_2, 5/3/2): yield 84%, only one diastereomer observed[18].
White solid, m.p. 100-103°C. R_f= 0.3 (AcOEt/hex/CH_2Cl_2, 5/3/2).
IR ($CHCl_3$): ν_{OH} = 3400 (broad).

^{1}H NMR ($CDCl_3$/TMS): one diastereomer (cf.ref.18) ; 3.10 (2H, AB part of an ABX, $\Delta\nu_{AB}$=50, J_{AB}=13, J_{AX}~2.5, J_{BX}~9.5) ; 5.42 (1H, X part of the ABX, d.d, CH) ; 7.37 (5H, m, H arom) ; 7.52 (3H, m, H arom) ; 7.67 (2H, m, H arom).

c) 1-phenyl-2-phenylthioethanol: **10a**

To a suspension of $LiAlH_4$ (0.064g, 1.624 mmol) in Et_2O (10ml) was added a solution of the above hydroxysulfoxide **9a** (0.2g, 0.82mmol) in THF (10 ml). After stirring at room temperature for 1h were added successively a 5% NaOH solution (6ml) and water (0,13ml). The THF was evaporated and the acqueous layer extracted with ether (3 x 10ml). The organic layer was dried over Na_2SO_4, evaporated under vacuum and the residue purified by chromatography (AcOEt/hex, 3/2): yield 73%.
Pale yellow oil. R_f=0.58 (AcOEt/hex, 3/2).
IR (CCl_4): ν_{OH}= 3620, 3540 (broad).
^{1}H NMR ($CDCl_3$/TMS) : 2.85 (1H, d, J=2.5, OH) ; 3.22 (2H, AB part of an ABX, $\Delta\nu_{AB}$=48, J_{AB}=13.5, J_{AX}~9, J_{BX}~3.5, CH_2) ; 4.73 (1H, X part of the ABX, m, CH) ; 7.4 (10H, m, H arom.).

d) 1-methoxy-1-phenyl-2-phenylthioethane: **5a**

To a suspension of NaH (0.155g, 6.46 mmol) in THF (10ml) was added dropwise a solution of the above hydroxy-sulfide **10a** (0.62g, 2.7 mmol) in THF (10ml). After stirring for 0.5h at room temperature CH_3I (0.4 ml, 6.46 mmol) was added dropwise. The mixture was stirred overnight then water (1.5ml) was added slowly and the THF was evaporated under vacuum. The residue dissolved in Et_2O (10ml) was washed with water (2 x 10ml), dried over Na_2SO_4 and concentrated under vacuum. The residue is purified by chromatography (AcOEt/hex, 10/90) : yield ~ quantitative.
Colourless oil. R_f=0.43 (AcOEt/hex, 1/9).
IR (CCl_4): no ν_{OH}, ν_{OMe}= 2820.
^{1}H NMR ($CDCl_3$/TMS) : 3.15 (1H, A part of an ABX, J_{AB}=13 J_{AX}~4.5, CH_2); 3.25 (3H, s, OCH_3); 3.32 (1H, B part of the ABX, J_{AB}=13, J_{BX}~8, CH_2); 4.30 (1H, X part of the ABX, dd, CH); 7.4 (10H, m, H arom.).

Synthesis of 1-methyl-1-phenyl-2-phenylthioethane : **5c**

a) ß-Bromoisopropylbenzene.

Allyl bromide (87.5g, 0.72 mol) was added dropwise to a mixture of benzene (210 ml) and concentrated sulfuric acid (41 ml) at 40°C. Vigorous stirring and 40°C were maintained for 5h, then the reaction mixture was allowed to stand overnight. The benzene layer was separated, washed successively with concentrated sulfuric acid (30 ml), water (30 ml) and 5% acqueous NaOH (100 ml), and dried over Na_2SO_4. After concentration under vacuum the residue was distilled: b.p 103-105°/15mm Hg. Yield : 45%.
^{1}H NMR ($CDCl_3$/TMS): 1.45 (3H, d, J= 7, CH_3); 3.17 (1H, X part of an $ABXK_3$, sext., J= 7, 7.5 and 6.5, CH); 3.54 (2H, AB part of the $ABXK_3$, $\Delta\nu_{AB}$= 18, J_{AB}= 10, J_{AX} 7.5, J_{BX} 6.5, CH_2); 7.42 (5H, m, H arom.).

b) 1-methyl-1-phenyl-2-phenylthioethane : **5c**

To a suspension of NaH (0.27g, 11.16 mmoles) in DMF (10ml) was added slowly a solution of thiophenol (1.23ml ; 11.16 mmol) in DMF (5ml) and stirring maintained for 30 minutes. A solution of the above prepared bromide (2g, 10.15 mmol) in DMF (10ml) was then added dropwise and stirring maintained for 1h after the end of the addition . The mixture was then washed with H_2O (30ml) and extracted with AcOEt (3 x 10ml). The organic layer was washed with a 5% NaOH solution (10ml),

dried over Na_2SO_4 and evaporated, the residue was purified by chromatography to give the sulfide : yield 87%.
Colourless oil. R_f= 0.15 (hex).
^1H NMR ($CDCl_3$/TMS): 1.43 (3H, d, J= 6.5, CH_3); 3.10 (3H, m, CH_2-CH); 7.3 (10H, m, H arom.).
Anal. Calcd for $C_{15}H_{16}S$: C, 78.94; H, 7.01. Found: C, 79.20; H, 7.24.

Synthesis 1-phenylthio-2-methyloctane: **6**

a) N-octanoylbornane-10,2-sultam: **19**

A solution of sultam (-)-**18** (1.7g, 7.9 mmol) in toluene (30ml) was added dropwise at room temperature to a stirred suspension of NaH (0.52g, 11.84 mmol). After 2h stirring a solution of octanoyl chloride (32ml, 16.58 mmol) in toluene (30ml) was added slowly and the mixture stirred at room temperature for 2 more hours. After careful addition of water (20ml), the organic layer was separated, washed with a 15% NaOH solution (5ml), water (20ml) and dried over Na_2SO_4. The solvent was evaporated and the residue purified by chromatography to give **19**: yield 92%.
Pale yellow oil. R_f=0.25 (Et_2O/hex, 3/7).
$[\alpha]_D$= -88 (c, 1.4 ; $CHCl_3$). IR ($CHCl_3$) : ν_{CO}=1700.
^1H NMR $CDCl_3$/TMS) : 0.86 (3H, t, CH_3) ; 0.96 (3H, s, CH_3) ; 1.15 (3H, s, CH_3) ; 1.27 (12H, m, $6CH_2$) ; 1.66 (2H, m, CH_2) ; 1.88 (2H, m, CH_2) ; 2.08 (2H, m, CH_2) ; 2.70 (2H, AB part of an ABX_2, CH_2-CO); 3.45 (2H, AB system, $\Delta\nu_{AB}$=14, J_{AB}=13.5, CH_2-SO_2) ; 3.89 (1H, X part of an ABX, dd, CH-N).

b) (*2R*)-N-[(2-methyl)octanoyl]bornane-10,2-sultam: **20**

To a solution of octanoyl sultam **19** (2.5g, 7.32 mmol) in THF (40ml) was added slowly and at -78°C a 1M solution of n-BuLi in hexane (7.32ml, 7.32mmol). The mixture was stirred at -78°C for 1h, then CH_3I (1.37ml, 22mmol) in a mixture of THF (5ml) and HMPT (0,5ml) was added dropwise. After stirring at -78°C for 4h, a 0.1N solution of citric acid (10ml) and water (40ml) were added. The mixture was extracted with Et_2O (2 x 30 ml), the combined organic phases were dried over Na_2SO_4 and concentrated under vacuum, the residue was purified by chromatography (Et_2O/hex, 3/7): yield 80%.
White solid, m.p. 58-60°C. R_f=0.43 (Et_2O/hex, 3/7).
$[\alpha]_D$= -91 (c, 1.1; $CHCl_3$). IR ($CHCl_3$) : ν_{CO}=1700.
^1H NMR ($CDCl_3$(TMS) : 0.86 (3H, t, CH_3); 0.97 (3H, s, CH_3) ; 1.12 (3H, s, CH_3) ; 1.17 (3H, d, CH_3) ; 1.25 (12H, m, $6CH_2$) ; 1.70 (4H, m, $2CH_2$) ; 2.08 (2H, m, CH_2) ; 3.05 (1H, m.CH-CO) ; 3.47 (2H, AB system, $\Delta\nu_{AB}$=14, J_{AB}=13, CH_2-SO_2); 3.89 (1H, X part of an ABX, t, CH-N).

c) (*2R*)-1-hydroxy-2-methyloctane: **21**

A solution of **20** (2.6g, 7.3 mmol) in a 1/3 mixture of THF and Et_2O (40ml) was added dropwise to a stirred suspension of $LiAlH_4$ (18.2 mmol,0,69g) in Et_2O (30ml) at 0°C. After stirring at 0°C for 3h, a saturated NH_4Cl solution (40ml) was added then the mixture was extracted with Et_2O (5 x 20ml), the combined organic phases were dried over Na_2SO_4, the solvent evaporated under vacuum and the residue purified by chromatography (Et_2O/hex, 20/80) to give the starting sultam **18** (80%) and the desired alcohol **21**, yield: 75%.
Viscous oil. R_f=0.17 (Et_2O/hex., 2/8).
$[\alpha]_D$ = +38.2 (c, 0.24; EtOH). IR ($CHCl_3$) : ν_{OH}=3600, 3400.
^1H NMR ($CDCl_3$/TMS): 0.89 (3H, t, CH_3); 0.92 (3H, d, CH_3); 1.28 (11H, broad signal, $5CH_2$+OH): 1.6 (1H, m, CH) ; 3.47 (2H, AB part of an ABX, $\Delta\nu_{AB}$=17, J_{AB}=10, J_{AX}~6.5, J_{BX}~5.5 ; CH_2OH)

d) (+)(*2R*)-1-phenylthio-2 methyl octane: **6**

Sulfide **6** was synthesized in one step from alcohol **21** using Tanigawa's method[27].

To a suspension of NaH (0.09g, 3.65 mmol) in DMF (5ml) was added dropwise a solution of the alcohol **21** (0,5g, 3.5 mmol) in DMF (2mL), the mixture was stirred for 0.5h at room temperature then a solution of (N-methyl-N-phenylamino)triphenylphosphonium iodide (1.8g, 3.65 mmol) and thiophenol (0.37ml; 3.65 mmol) in DMF (10ml) was added. After stirring for 12h, water (30ml) was added, the mixture was then extracted with Et_2O (4 x 10ml). The combined organic layers were washed with HCl 0.1N (10ml), dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by chromatography (Et_2O/hex, 10/90) to give sulfide **6**, yield 85%.
Colourless oil. R_f=0.63 (Et_2O/hex, 1/9).
$[\alpha]_D$ = +26 (c, 3.8; $CHCl_3$).
^1H NMR ($CDCl_3$/TMS): 0.88 (3H, t, CH_3) ; 1.02 (3H, d, CH_3) ; 1.30 (10H, broad signal, $5CH_2$) ; 1.75 (1H, m, CH) ; 2.85 (2H, AB part of an ABX, $\Delta\nu_{AB}$=25, J_{AB}=12, J_{AX}~7, J_{BX}=6, CH_2-S) ; 7.3 (5H, m, H arom).

Preparation of oxathiane **7** *(Eliel's reagent)*
This reagent was prepared following the usual method [24].
R_f=0.65 (Et_2O/hex, 2/98). $[\alpha]_D$= +12 (c, 2.15; acetone).
^1H NMR ($CDCl_3$/TMS): 0.92 (3H, d, CH_3) ; 1.27 (3H, s, CH_3) ; 1.43 (3H, s, CH_3) ; 1.4-2 (8H, m, CH_2-CH) ; 3.35 (1H, td, J=10 and 4, CH-O) ; 4.70 (1H, A part of an AB, J_{AB}=11, S-CH_2-O) ; 5.03 (1H, B part of the AB, J_{AB}=11, S-CH_2-O).

Synthesis of sulfonium salts **11a and 11c.**
A solution of Me_3OBF_4 (1.8 ml, 0.64 mmol) in CH_3NO_2 (2ml) was added to a solution of the desired sulfide, **5a** or **5c** (0.49 mmol) in CH_3NO_2 (2ml). After stirring for 3h at room temperature CH_3NO_2 was evaporated.

-Methylphenyl [(α-methoxy)phenylethyl] sulfonium tetrafluoroborate: **11a.**

After evaporation of CH_3NO_2, the residue was dissolved in a minimum of MeOH and the salt precipitated by addition of Et_2O to give after filtration a white solid : yield 90%. m.p. 58-63°C (diastereomer mixture).
^1H NMR ($CDCl_3$/TMS) : two diastereomers in the ratio 65/35. **I***(major)* : 3.15 (3H, s, CH_3) ; 3.27 (3H, s, CH_3) ; 3.95 (1H, d.d, A part of an ABX, J_{AB}=13, J_{AX}~4, CH_2) ; 4.05 (1H, d.d, B part of the ABX, J_{BX}~10, CH_2) ; 4.45 (1H, d.d, X part of the ABX) ; 7.4 (5H, m, H arom) ; 7.7 (3H, m, H arom.) ; 8.0 (2H, m, H arom.). **II***(minor)* : 3.2 (3H, s, CH_3); 3.35 (3H, s, CH_3); 3.7 (1H, d.d, A part of an ABX, J_{AB}=13, J_{AX}~10 ; CH_2) ; 4.15 (1H, d.d, B part of the ABX, J_{BX}~3, CH_2) ; 4.95 (1H, d.d, X part of the ABX) ; 7.4 (5H, m, H arom.); 7.7 (3H, m, H arom) ; 7.95 (2H, m, H arom.).

-Methylphenyl [(α-methyl) phenylethyl]sulfonium tetrafluoroborate: **11c**
Oil. ^1H NMR (Acet.d6 /TMS) : Two diastereomers in the ratio 55/45. **I***(major)* : 1.40 (3H, d, CH_3) ; 3.04 (1H, m, CH) ; 3.34 (3H, s, CH_3) ; 4.2 (2H, m, overlapped with diast. II, CH_2) ; 7.3, 7.8 and 8 (10H, m, overlapped with diast.II, H arom). **II***(minor)* : 1.46 (3H, d, CH_3) ; 3.30 (1H, m overlapped with the CH_3 of diast.I, CH) ; 3.43 (3H, s, CH_3) ; 4.2 (2H, m, overlapped with diast.I, CH_2) ; 7.3, 7.8 and 8 (10H, m overlapped with diast.I, H arom.).

Synthesis of Sulfonium salt **23**

To a mixture of oxathiane **7** (618mg, 3.09 mmol) and $AgClO_4$ (770mg, 3.71 mmol) in anhydrous Et_2O (10ml) was added $PhCH_2Br$ (0.44ml, 3.71 mmol) at 0°C. After stirring at 0°C for 4h the solvent was evaporated and CH_2Cl_2 (10ml) was added, the AgBr precipitate was filtered out and the solution concentrated under vacuum. The solid was recrystallized in acetone/CH_2Cl_2, yield 75%.
White solid, m.p. 164°C.
$[\alpha]_D$ = -172 (c, 1.02; acetone).
^1H NMR (Acetone d6/DMSO d6, 10/1/TMS). One diastereomer : 0.96 (3H, d, CH_3) ; 1.78 (3H, s, CH_3) ; 1.84 (3H, s, CH_3) ; 1.1-2 (7H ring) ; 2.36 (1H, td, J=10 and 3, CH ring junction) ; 4.05 (1H, td, J=10 and 4, CH-O ring junction) ; 4.97 (2H, s, CH_2–Ph) ; 5.1 (1H, d, A part of an AB, J_{AB}=12, O-CH_2-S); 5.80 (1H, B part of the AB, O-CH_2-S) ; 7.5 and 7.62 (5H, m, H arom).
Anal. Calcd for $C_{18}H_{27}ClO_5S$: C, 55.36; H, 6.96. Found: C, 55.44; H, 6.70.

Preparation of Epoxides

a) Styrene oxide **15** from sulfides **5a** and **5c** using Corey's method[19]

A 1.42M solution of nBuLi in hexane (0.47 ml, 0.67 mmol) was added dropwise to sulfonium salt **5a** and/or **5c** (0.67 mmol) in THF (10ml) at 0°C. After 0.5h, a solution of benzaldehyde (0.068 ml ; 0.67 mmol) in THF (2 ml) was added. Stirring was maintained at 0°C for 1h and at r.t. for another 1h. After evaporation of THF under vacuum, water (20ml) was added and the new mixture extracted with ether (2 x 10ml). The combined organic phases were dried over Na_2SO_4 and the solvent evaporated under vacuum, the residue was analyzed by NMR before purification.

-Vinyl sulfide **14** from **5a**.
Yield 20%.
^1H NMR ($CDCl_3$/TMS): 6.75 (1H, d, A part of an AB, J_{AB} = 16, =CH); 6.92 (1H, d, B part of the AB, =CH); 7.5 (10H, m, H arom.).

-Styrene oxide **15** (racemic) from racemic **5c**.
Yield 80% distilled, Eb. 100° (25mm Hg).
^1H NMR ($CDCl_3$/TMS): 2.8 (1H, dd, A part of an ABX, ^2J = 5, $^3J_{trans}$ = 2.5, CH_2); 3.15 (1H, dd, B part of the ABX, ^2J = 5, $^3J_{cis}$ = 4, CH_2); 3.87 (1H, dd, X part of the ABX, CH); 7.4 (5H, m, H arom.).

b) α-Hydroxy-β-methoxyethylbenzene **22** from (+)-*R*-**6** using Furukawa's method[15]

To a solution of sulfide **6** (0.18g, 0.75 mmol) and KOH (0.14g, 2.47 mmol) in CH_3CN (5ml) was added a mixture of benzaldehyde (0.23ml, 2.27 mmol) and CH_3I (0.14ml, 2.27 mmol). After 18h, the mixture was filtred and evaporated. The residue was chromatographied (Et_2O/hex, 1/9) to give the starting sulfide **6** (89% recovered) and the opened styrene oxide, α-hydroxy-β-methoxyethylbenzene **22**, (yield 53%).

–α-Hydroxy-β-methoxyethylbenzene **22** racemic from (+)-*R*-**6**.
Yield 50% (refered to starting **6**). $[\alpha]_D$ = 0 (c, 1.12; $CHCl_3$).
^1H NMR ($CDCl_3$/TMS): 1.58 (1H, broad s, OH); 2.75 (2H, AB part of an ABX, $\Delta\nu_{AB}$ = 20, J_{AB} = 15, J_{AX} = 5, J_{BX} = 7, CH_2), 3.3 (3H, s, OCH_3); 4.45 (1H, X part of the ABX, CH); 7.35 (5H, m, H arom.).

c) (*R,R*)-1-aryl-2-phenyl oxirane **24a-d** from sulfonium **23** using phase-transfer conditions

To a mixture of sulfonium salt **23** (300mg, 0,75 mmol), the desired benzaldehyde (1.12 mmol) and $Et_3BuN^+Cl^-$ (catalytic amount) in CH_2Cl_2 (10ml) was added a 50% NaOH solution (3ml) at 0°C.

After stirring for 24h at 0°C, water (3ml) was added and the organic layer was separated and dried over Mg_2SO_4. The solvent was evaporated and the residue was purified by chromatography (Et_2O/hex, 2/98) to give the desired epoxide **24** and the starting sulfide **7**.

-(+)-24a from (+)-7.
Yield 80%. R_f = 0.24 (AcOEt/hex, 2/98). $[\alpha]_D$ cf text.
^1H NMR ($CDCl_3$/TMS): 3.9 (2H, s, CH); 7.39 (10H, broad s, H arom.). In the presence of Eu(hfc)$_3$ the 3.9 singlet split into two singlets in the ratio 87/13.

-Racemic 24b from (+)-7.
Yield 60%. R_f = 0.24 (AcOEt/hex, 2/98). $[\alpha]_D$ cf. Text.
^1H NMR ($CDCl_3$/TMS): 3.86 (1H, d, J = 1.7, CH); 3.98 (1H, d, J = 1.7, CH); 7.39 (5H, m, H arom.); 7;52 (2H, d, H arom.); 8.25 (2H, d, H arom.). In the presence of Eu(hfc)$_3$ the 3.86 and 3.98 doublets split into two doublets in the ratio 1/1 (non-equivalences: 0.05 and 0.15ppm respectively).

-(+)-24c from (+)-7.
Yield 75%. R_F = 0.21 (AcOEt/hex, 2/98). $[\alpha]_D$ cf. text.
^1H NMR ($CDCl_3$/TMS): 2.40 (3H, s, CH_3); 3.87 (2H, AB system, $\Delta\nu_{AB}$ = 4, J_{AB}trans = 1.5, 2CH); 7.22 (2H, d, H arom.); 7.34 (2H, d, H arom.); 7.38 (5H, m, H arom.). The AB system non-equivalence being too small, no clear splitting appeared with Eu(hfc)$_3$.
^{13}C NMR ($CDCl_3$/TMS): 21.3 (CH_3); 62.8 and 62.9 (CH); 125.5 (4 CH arom.); 128.3 (CH arom. para); 128.6 (2 CH arom.); 129.3 (2 CH arom.); 134.2 (C arom.); 137.3 (C arom.); 138.2 (C arom.).

(+)-24d from (+)-7.
Yield 82%. White crystal, mp 95°C (lit. 100°C). R_f = 0.24 (AcOEt/hex, 2/98). $[\alpha]_D$ cf. text.
^1H NMR ($CDCl_3$/TMS): 3.74 (2H, AB system, $\Delta\nu_{AB}$ = 5, J_{AB}trans = 1.5, 2 CH); 7.18 (2H, d, H arom.); 7.25 (7H, m, H arom.). The AB system non-equivalence being too small, no clear splitting appeared with Eu(hfc)$_3$.
^{13}C NMR ($CDCl_3$/TMS): 62.1 (CH); 62.8 (CH); 125.4 (2 CH arom.); 126.8 (2 CH arom.); 128.4 (1 CH arom.); 128.5 (2 CH arom.); 128.7 (2 CH arom.); 134.0 (C arom.); 135.6 (C arom.); 136.6 (C arom.).

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