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Asymmetric Epoxidation Using Chiral Sulfur Ylides

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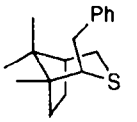
Abstract: Novel chiral sulfides, derived from pinene, have been prepared, converted to sulfonium salts and treated with base and aldehydes to generate non-racemic epoxides. Low to moderate enantioselectivities were obtained in the product epoxides and this possibly occurred as a result of using diastereomeric mixtures of sulfonium salts. Dibenzyl substituted sulfonium salts were also prepared to avoid formation of diastereomers but upon treatment with base and an aldehyde this gave the Stevens rearrangement product instead of epoxide.

Non-racemic epoxides can be prepared by the asymmetric oxidation of alkenes [1-9] or through the reaction of homochiral sulfur ylides with carbonyl compounds.[10-14] The latter strategy is potentially more general as the current asymmetric oxidation process only works well for a limited class of alkenes. There are now several examples of the reactions of chiral sulfur ylides with aldehydes and high enantioselectivities are beginning to emerge. Of the sulfides developed to date, Durst's sulfide **1**, gives the highest levels of enantioselectivity.[12] However, the synthesis of sulfide **1** requires a 6-steps in which some of the yields are quite low. To screen more rapidly a series of sulfides for their use in asymmetric epoxidation a shorter synthetic route is required.

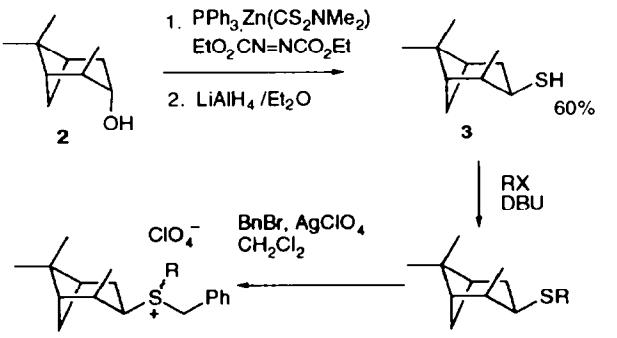


1

Due to the ready availability of homochiral alcohols we reasoned that chiral sulfides should be readily accessible by displacement of the hydroxyl group with a suitable thiol. In this paper we describe our success in achieving this objective and the results of the epoxidation process.

We chose (+)-isopinocampheol **2** as our homochiral alcohol [15] and attempted direct displacements of the alcohol with benzyl mercaptan and thiophenol under Mitsunobu conditions [16,17] and modifications thereof [18] but without success. Only starting material remained at the end of the reaction. However, we were successful at carrying out the required displacement using zinc N,N-dimethyl dithiocarbamate under modified Mitsunobu conditions. [19-21] Reduction of the dithiocarbamate with $LiAlH_4$ gave the known thiol **3**. [21] A range of sulfides **4a-c** and their corresponding sulfonium salts **5a-c** were prepared from this thiol by alkylation [22] as shown in scheme 1. Alkylation of **3** using *i*-PrI under conventional conditions was

extremely slow but when reactions were conducted in neat *i*-PrI good yields of the alkylated product **4b** were obtained.



2 **3**

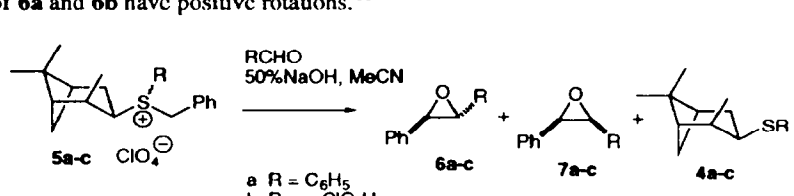
5a 82% (70:30)
5b 66% (55:45)
5c 40%

4a R = Me 72%
4b R = i-Pr 66%
4a R = Bn 63%

Scheme 1

Sulfonium salt formation using benzyl bromide proceeded in good yields but diastereomeric mixtures were obtained in the cases of **5a** and **5b**. As no new stereocentre is formed in alkylation of **4c** with benzyl bromide the sulfonium salt **5c** was obtained as a single diastereoisomer.

The sulfonium salts were treated with base and an aldehyde under two different conditions [either with a phase transfer catalyst (method A) or without (method B)] to give epoxides and the results are summarised in table 1. The epoxides were carefully separated by flash chromatography and their optical purity determined by chiral HPLC. It was not possible to determine the ee of **7b** by NMR or HPLC presumably because it is almost symmetrical and behaves as if it was a meso compound. The absolute stereochemistry of the products was determined by correlation with literature examples: the (R,R)-enantiomers of **6a** and **6b** have positive rotations.[10]



5a-c **6a-c** **7a-c** **4a-c**

a R = C_6H_5
b R = p-ClC_6H_4
c R = C_6H_{11}

Scheme 2

From our results, several points are worthy of note. It was found that the presence of phase transfer catalyst (PTC) had no substantial effect on the yields of the epoxides (entries 1 vs 2, 4 vs 5, 6 vs 7). This is somewhat surprising as literature examples often only describe reactions with PTC and we therefore expected reduced yields or reduced rates in the absence of PTC. The yields in reactions of the methyl substituted sulfonium salt (entries 1-5) are much higher than the isopropyl substituted sulfonium salt (entries 6-9) indicating that increased steric hindrance around the sulfur atom reduces yields. However, enantiomeric excesses are significantly lower with the smaller methyl substituted sulfonium salt compared to the isopropyl substituted sulfonium salt indicating that increased steric hindrance around the sulfur atom increases enantioselectivity.

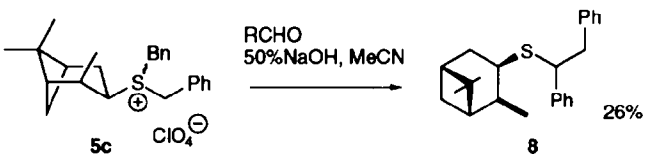
Table 1: Reactions of Sulfonium Salts with Aldehydes

entry	salt	aldehyde	reaction conditions[a]	trans epoxide **6**		cis epoxide **7**		recovered sulfide **4**
				yield	ee[b]	yield	ee[b]	
1	5a	PhCHO	A	66	0	6	meso	54
2	5a	PhCHO	B	67	13 (+)-(R,R)	20	meso	10
3	5a	p-ClC_6H_4CHO	B	62	12 (+)-(R,R)	8	c	22
4	5a	$C_6H_{11}CHO$	A	28	22[d]	6	28[d]	e
5	5a	$C_6H_{11}CHO$	B	27	14[d]	10	32[d]	e
6	5b	PhCHO	A	5	43 (+)-(R,R)	0	meso	e
7	5b	PhCHO	B	12	19 (+)-(R,R)	0	meso	e
8	5b	p-ClC_6H_4CHO	A	55	42 (+)-(R,R)	0	c	75
9	5b	$C_6H_{11}CHO$	A	f	-	f	-	e

a Reaction conditions as shown in scheme 2. Method A is in the presence of PTC and method B is without PTC. b. Enantiomeric excesses were determined by chiral HPLC using a chiralgel OD column. c Enantiomeric excess could not be determined by HPLC or NMR shift reagents. d The cis and trans isomers could not be separated and the yields indicated represent ratios of the two products with the sum being the total yield. The mixture had a negative rotation. e The starting sulfide could not be isolated in pure form. f No product was obtained in the reaction.

The enantiomeric excesses obtained are generally quite low and are significantly lower than the literature examples in which the starting sulfonium salts are single diastereoisomers. Our sulfonium salts, **5a** and **5b**, were a 30:70 and 45:55 mixture of diastereoisomers and this would presumably give rise to the same diastereomeric ratio of ylides. If epimerisation of the sulfur stereocentre in the ylide is slow then it is not unreasonable that ylides with opposite configuration at sulfur (the closest stereogenic centre to the approaching aldehyde) might give different, and possibly opposite, selectivities for the product epoxides. Indeed, Trost has demonstrated that sulphur ylides which possess chirality at sulfur are configurationally stable. [23] Therefore, this would suggest that during reactions of the diastereomeric mixture of ylides no epimerization at sulfur occurs and that the two diastereoisomers do not interconvert. They would therefore react independently, and probably give different and possibly opposite selectivities. This may account for the low enantioselectivities observed.

To avoid formation of diastereomeric salts, **5c** was prepared and treated with base in the presence of an aldehyde. However, no epoxide was obtained in this case. Instead, the major product isolated was **8** which presumably arose from a Stevens rearrangement.[24]



5c **8**

Conclusion

Our results show that homochiral sulfides can be readily prepared from homochiral alcohols. The ylides generated from such sulfides give low levels of enantioselectivities in epoxidation reactions and this probably results, in part, from the starting sulfonium salts being mixtures of diastereoisomers. Thus, for the preparation of epoxides with high enatioselectivity it appears to be essential that homochiral sulfides be designed such that high diastereoselectivity is obtained in sulfonium salt formation.

EXPERIMENTAL

Proton and carbon-13 magnetic reasonance spectra were recorded on a Bruker ACF-250 and on a Bruker WH-400 (400 MHz) spectrometer supported by an Aspect 2000 data system. Mass spectra were obtained on a Kratos MS 25 instrument operating in E.I., C.I. mode and on a Kratos MS 80 in +ve FAB mode. Melting points (m.p.) were determined on a Kofler Hot Stage Micro Melting Point Apparatus and stand uncorrected. Elemental micro analyses were carried out using a Perkin-Elmer 2400 Elemental Analyser CHN involving classical wet analysis for anions (Br, S, I, Cl). Infrared spectra were recorded in the range 4000-600cm^{-1} using a Perkin Elmer 157G Grating Infrared Spectrophotometer. Enantiomeric excesses (ee) were determined by chiral HPLC using a Chiralgel OD column and chiral GC using a Cylcodex-B column on a Perkin Elmer 8700 capillary GC machine. In the former case ratios of enantiomers were measured by UV monitoring at 212 nm. Solvents and reagents were dried and purified prior to use according to standard procedures. Petrol refers to petroleum ether boiling range 60-80°C. Ether was pre-dried over sodium wire and then refluxed over sodium benzophenone ketyl under a nitrogen atmosphere until anhydrous. Toluene was distilled over P_2O_5 and stored over 4Å molecular sieves under nitrogen. Hexane was distilled from calcium hydride and the fraction boiling at 69°C collected and stored over 4Å molecular sieves under nitrogen. Benzaldehyde and benzyl bromide were distilled prior to use. Thin layer chromatography (TLC) was used routinely to monitor the progress and purity of compounds. TLC was performed on Merck DC-alufolien Kieselgel 60 F_{254} sheets containing fluorescent indicator. TLC plates were visualised when possible by wavelength of 356nm ultraviolet light and by treatment with either a solution of phosphoromolybdic acid (5g in 100ml 95% absolute alcohol) or 0.5% (w/v) aqueous solution of potassium permanganate, followed by warming of the TLC plate. Purification of compounds was achieved by medium pressure chromatography using Kieselgel 60 F_{254} (layer thickness 0.2mm) and on C_{560}, 40-63 micron.

(1S, 2S, 3R)-N,N-Dimethyl Pinane-3-Dithiocarbamate: (+)-Isopinocampheol 2 (15.9g; 0.10mol) and dry triphenylphosphine (67.7g; 0.26mol) were dissolved in dry toluene (160ml) under nitrogen. Zinc N, N-dimethyl dithiocarbamate (31.5g; 0.1 mol) was added and the resulting suspension was protected from light and cooled to 0°C. Diethyl azodicarboxylate (43.79ml; 0.28mol) was **slowly** added and the reaction mixture was stirred at room temperature overnight. The reaction was complete according to TLC and was thus loaded onto a silica column and chromatographed eluting first with petroleum ether followed by Et_2O : petroleum ether 10/90 to give the crude product. The above product was rechromatographed for characterization to give the dithiocarbamate as beige crystals (17g; 66% yield); $[\alpha]_D$ +38.4 (c 1.06 in $CHCl_3$), lit.,[21] $[\alpha]_D$ +40.6 (c 5.7 in $CHCl_3$); ν_{max} /cm^{-1} (Nujol) 1140 (C=S); δ_H ($CDCl_3$) 4.7 (1H, ddd, *J* 10Hz, 10Hz, 9 Hz), 3.6 (3H, s), 3.4 (3H, s), 2.9 (1H, m), 2.5 (1H, m), 2.3 (1H, m), 1.95 (3H, m), 1.4 (1H, d, *J* 9 Hz), 1.2 (3H, s), 1.15 (3H, d, J 9Hz), 0.98 (3H, s).

(1S, 2S, 3R)-3-Pinanethiol 3: Lithium aluminium hydride (LAH) (3.85g; 0.1 moles) was **cautiously** added to a stirred solution of the above dithiocarbamate (10g; 0.04 moles) in dry ether (420ml) and the reaction mixture was refluxed overnight under nitrogen. Quenching of lithium aluminium hydride involved cooling of the reaction mixture to 0°C, **cautious** addition of ether and saturated sodium sulfate in water while stirring, until the evolution of gases ceased and the residues were white in colour. The reaction mixture was filtered and the filtrate dried over $MgSO_4$. Removal of the solvent *in vacuo* gave the crude product which was chromatographed eluting with petrol to give the thiol **3** as a pungent colourless liquid (6g; 90%), b.p.125-150°C/2mmHg, (lit.,[21] b.p.70-73°C/0.7mmHg); $[\alpha]_D$ -5.83 (c 1.32 in $CHCl_3$), (lit.,[21] $[\alpha]_D$ -8.6 (c 0.918 in $CHCl_3$)]; $\delta_H(CDCl_3)$ 3.75 (1H, dddd, *J* 10Hz, 10Hz, 9Hz, 7Hz, 3-H), 2.45 (2H, m), 2.2 (1H, m), 1.9 (3H, m), 1.42 (1H, d, *J* 7Hz, SH), 1.3 (1H, d, *J* 9Hz) 1.15 (3H, d, *J* 6Hz, 2-Me), 1.1 (3H, s, 8-Me or 9-Me), 1.0 (3H, s, 9-Me or 8-Me); m/z 170 (M^+).

(1S, 2S, 3R)-3-Pinanylmethyl Sulfide 4a: To a solution of 1,8-diazobicyclo(5.4.0.)undec-7-ene (DBU) (0.56ml; 3.8mmol) and thiol **3** (0.48ml; 3.8mmol) in dry toluene (12ml), iodomethane (0.24ml; 3.8mmol) was added and the resulting mixture was stirred at r.t. under nitrogen for 4h. The reaction mixture was washed with hydrochloric acid (HCl-2M) (7ml) and the organic layer was dried over $MgSO_4$. Toluene was evaporated *in vacuo* and the resulting crude product was purified by flash (column) chromatography with petrol to give the desired *sulfide* **4a** as a colourless oil (0.5g; 72%); b.p. 110°C/0.6mmHg; $[\alpha]_D$ -2.1 (c 1 in $CHCl_3$); $\delta_H(CDCl_3)$ 3.45 (1H, ddd, *J* 10Hz, 10Hz, 9Hz, 1-H), 2.55 (1H, m), 2.4 (1H, m), 2.2 (1H, m), 2.1 (3H, s, SCH_3), 1.9 (3H, m), 1.3 (1H, d, *J* 12Hz), 1.15 (3H, d, *J* 6Hz, 2-Me), 1.13 (3H, s, 9-Me or 8-Me), 1.0 (3H, s, 8-Me or 9-Me); (Found: M$^+$, 184.1274, $C_{11}H_{20}S$ requires M, 184.1286), m/z (E.I.) 184 (M^+, 100%).

(1S, 2S, 3R)-3-Pinanylisopropyl Sulfide 4b: To a stirred solution of 1,8-diazobicyclo(5.4.0.)-undec-7-en (DBU) (3.07ml; 0.02mol) and thiol **3** (2.61ml, 0.02mol) at 0°C, excess iodopropane (9ml; 0.1mol) was slowly added. The resulting "milky" solution was stirred at r.t. for about 7h (the reaction was complete according to TLC). The precipitated DBU-HBr salt was separated from the organic layer by addition of hydrochloric acid (HCl-2M) (20ml), water(10ml) and the aqueous layer was extracted with ether (2x20ml). The organic layers were combined and dried over $MgSO_4$. The ether was removed *in vacuo* to give the crude product which was chromatographed on silica eluting with petrol only to give the *sulfide* **4b** as a pale yellow oil (2.8g; 66%); $[\alpha]_D$ -2.66 (c 1.54 in $CHCl_3$); $\delta_H(CDCl_3)$ 3.6 (1H, ddd, *J* 10Hz, 10Hz, 9Hz, 3-H), 2.9 (1H, septet, *J* 6Hz), 2.55 (1H, m), 2.35 (1H, m), 2.2 (1H, m), 1.95 (3H, m), 1.4 (1H, m), 1.3 (3H, d, *J* 9Hz), 1.25 (3H, d, *J* 9Hz), 1.2 (3H, d, *J* 6H, 2-Me), 1.18 (3H, s), 0.98 (3H, s); δ_C 48.8 (C-1'), 41.3 (C-3), 39 (C-7), 38, 35.9, 35.7, 34, 27.9, 27.7, 23.6, 23.4, 23.2, 17.8 (CH_3) ; (Found: M$^+$, 212. 1610, $C_{13}H_{24}S$ requires M, 212.1599), m/z (E.I.) 212 (M^+, 100%).

(1S, 2S, 3R)-3-Pinanylbenzyl Sulfide 4c: Benzyl bromide ($PhCH_2Br$) (2.3ml; 18.7mmol) was added to a stirred mixture of DBU (2.63ml;17mmol) and thiol **3** (2.23ml; 17mmol) in dry toluene (10ml) at 0°C. The resulting reaction mixture was stirred at r.t. for 5h. The reaction was complete according to TLC and was washed with hydrochloric acid (HCl-2M) (8ml) and water (5ml). The organic layer was dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product. The excess of benzyl bromide was removed by evaporation at 125°C/1mmHg and the resulting mixture was chromatographed eluting with 1% di-isopropyl ether in petrol to give the desired *sulfide* **4c** (2.8g; 63%); $[\alpha]_D$ -2.25 (c:1.24 in $CHCl_3$);

δ_H($CDCl_3$) 7.25 (5H,m, Ph), 3.65 (2H, s, 11-H), 3.35 (1H, ddd, *J* 10Hz, 10Hz, 9Hz, 3-H), 2.40 (1H, m), 2.25 (1H, m), 1.85 (3H, m), 1.5 (1H, m), 1.15 (3H, d, *J* 6Hz, 2-Me), 1.1 (3H, s,), 0.95 (3H, s); δ_C 131.8, 128.8, 128.4, 126.8, 48.7 (C-3), 41.27, 37.6, 36.62, 35.9, 36.24, 35.39, 27.94, 27.7, 23.16, 17.5 (CH_3); (Found: M$^+$, 261.1668, $C_{17}H_{24}S$ requires M, 1261.1677), m/z (E.I.) 261(M+1).

Benzylmethyl [(1S, 2S, 3R)-3-pinanyl]sulfonium Perchlorate 5a: To a mixture of sulfide **4a** (0.39g; 2.12mmol) and silver perchlorate (0.52g; 2.53mmol) in dry ether (7ml) was added benzyl bromide (0.3ml; 2.53mmol) at 0°C. After stirring at 0°C for a day the solvent was evaporated and CH_2Cl_2 (8ml) was added. The AgBr precipitate was filtered off and the solution concentrated *in vacuo* to yield a brown oil. The resulting brown oil was triturated with *n*-pentane / EtOAc to give the title compound. The white solid was recrystallised from CH_2Cl_2 / Et_2O to give the *sulfonium salt* **5a** (0.63g; 82%) as a mixture of two diastereoisomers in the ratio 30:70; m.p. 96-100°C; (Found: C, 58.0; H, 7.53; Cl, 9.2; S, 8.76. $C_{18}H_{27}SClO_4$ requires C, 57.7; H, 7.25; Cl, 9.45; S, 8.55); $[\alpha]_D$ +0.67 (c 1.78 in Acetone); δ_H(DMSO): 7.5 (5H, m, Ph), 4.95^(1H, d, *J* 8Hz, 11-H_a or 11-H_b), 4.88*(1H, d, *J* 12Hz, 11-H_b or 11-H_a), 4.65*(1H, d, *J* 8Hz, 11-H_b or 11-H_a), 4.55^(1H, d, *J* 8Hz, 11-H_a or 11-H_b), 4.3 (1H, m, 3-H), 2.80 (3H, s, S-Me), 2.75 (1H, m), 2.25 (3H, m), 2.05 (2H, m), 1.4^(1H, d, *J* 8Hz), 1.35*(1H, d, *J* 8Hz), 1.3^(3H, s, 9-Me or 8-Me), 1.25*(3H, s, 9-Me or 8-Me), 1.15 (3H, d, *J* 8Hz, 2-Me), 1.05^(3H, s, 9-Me or 8-Me), 0.96*(3H, s, 9-Me or 8-Me); δ_C 131.2, 130.3, 129.9, 128.84, 49.5^(C-3), 48*(C-3), 46.9*(C-11), 43.5^(C-11), 39 (C-7), 34.9*(C-2), 33^(C-2), 27.6, 27.7, 27.16, 26.9, 23.5*, 23^, 20.3, 19.8, 17.03*, 16.6^; m/z (+ve FAB) 275 (M$^+$), 649 (2xM$^+$+ ClO_4). [*: major isomer, ^: minor isomer]

Benzylisopropyl[(1S, 2S, 3R)-3-pinanyl]sulfonium Perchlorate 5b: To a mixture of sulfide **4b** (2g; 9.43mmol) and silver perchlorate (3.9g; 18.8mmol) in dry ether (31ml) was added benzyl bromide (2.3ml; 18.8mmol) at 0°C. After stirring for 4 days, the solvent was evaporated and CH_2Cl_2 (35ml) was added, the AgBr precipitate was filtered and the solution concentrated *in vacuo* to yield a brown solid. The brown solid was triturated with *n*-pentane / EtOAc to give the *sulfonium salt* **5b** (2.5g; 66%) as a mixture of two diastereoisomers in the ratio 45:55; m.p.120°C; $[\alpha]_D$ -1.26 (c:2.03 in Acetone); δ_H(DMSO): 7.55 (5H, m, Ph), 4.81 (2H, m, 11-H_a or 11-H_b), 4.57 (1H, septet, *J* 6Hz, 12-H), 4.00*(1H, ddd, *J* 10Hz, 10Hz, 9Hz, 3-H), 3.82^(1H, ddd, *J* 10Hz, 10Hz, 9Hz, 3-H), 2.8*(1H, m, 2-H), 2.62^(1H, m, 3-H), 2.25 (2H, m), 2.05 (2H, m), 1.60 (4H, dd, *J* 12Hz, 9Hz), 1.4*and1.35^(3H, d, *J* 9Hz, 13-Me), 1.25^, 1.00*(3H, s, 9-Me), 1.2(3H, *J* 8Hz, 2-Me), 0.89*and 0.85^(3H, s, 8-Me); δ_C: 130.73, 130.5, 129.8, 129.7, 48.4*, 48.2^(C-3), 47.7, 46.1^, 45.8*, 43.5, 41.1, 37.6, 35.1^, 34.7*, 27.69*, 27.5^, 27.26, 23.6*, 23.4^, 19.3*, 19.1^(CH_3), 17, 16.6^, 16.0*(CH_3); m/z(E.I.) 303 (M$^+$), 705 (2xM$^+$+ ClO_4^-). [*:major isomer, ^: minor isomer]

Dibenzyl[(1S, 2S, 3R)-3-pinanyl]sulfonium Perchlorate 5c: To a mixture of sulfide **4c** (1g; 3.84mmol) and $AgClO_4$ (1.6g; 7.68mmol) in dry ether (15ml) was added benzyl bromide (0.9ml; 7.68mmol) at 0°C. After stirring for 4 days, the solvent was evaporated and CH_2Cl_2 (12ml) was added , the AgBr precipitate was filtered off. After evaporation of CH_2Cl_2, the residue was dissolved in a minimum amount of CH_2Cl_2 and the salt precipitated by addition of di-isopropyl ether to give, after filtration, the *sulfonium salt* **5c** as a beige solid (0.7g; 40%); m.p.123-125°C; $[\alpha]_D$ -4.92 (c:2.01 in Acetone); (Found: C, 63.74; H, 6.74; Cl, 8.05; S, 7.30 $C_{24}H_{31}SClO_4$ requires C, 63.9; H, 6.8; Cl, 7.86; S, 7.1); δ_H(DMSO) 7.35 (10H, m, 2xPh), 5.0 (1H, d, *J* 9Hz), 4.85 (1H, d, *J* 9Hz), 4.8 (1H, d, *J* 9Hz), 4.63 (1H, d, *J* 9Hz), 4.6 (1H, ddd, *J* 10Hz, 10Hz, 9Hz, 3-H), 2.7 (1H, m), 2.45 (1H, m), 2.25 (2H, m), 2.0 (2H,

m), 1.4 (1H, d, *J* 8Hz), 1.15 (3H, s, 9-H or 8-H), 1.05 (3H, d, *J* 8Hz, 2-Me), 0.9 (3H, s, 9-Me or 8-Me); m/z(+veFAB) 351 (M+), 801($2xM^+ + ClO_4^-$).

PREPARATION OF EPOXIDES

General Procedure A

To a mixture of sulfonium salt (1 mol. equivalent), aldehyde (1.5 mol. equivalent) and $CH_3N^+[(CH_2)_7CH_3]_3Cl^-$, (5-10 mol%) in CH_2Cl_2 (15ml per mmol of starting material) was added a 50% NaOH solution (50mmol per mmol of starting material) at 0°C. After stirring for about 24h at 0°C, water was added and the organic layer was separated and dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residue was purified by flash (column) chromatography.

General Procedure B

The same conditions as described in procedure A were employed without the presence of phase transfer catalyst $CH_3N^+[(CH_2)_7CH_3]_3Cl^-$.

(+)-(R, R)-1, 2-diphenyloxirane **6a** from **5a** [entry 1]: Following method A, using the sulfonium salt **5a** (0.1g; 0.26mmol) and benzaldehyde (0.04ml; 0.39mmol), **6a** (0.165mmol; 66%), **7a** (0.015mmol; 6%) were obtained, together with recovered sulfide **4a** (25mg; 54%) $[\alpha]_D$-2.19 (c:1 in $CHCl_3$); Trans isomer **6a**: m.p. 69°C [Lit [25] 69°C]; $\delta_H(CDCl_3)$ 7.4(10H, m, 2xPh), 3.9(2H, s, CH); 0% ee; Cis isomer **7a**: m.p.40°C, (lit.,[25]m.p. 39°C); $\delta_H(CDCl_3)$ 7.4(10H, m, 2xPh), 4.36(2H, s, CH), meso compound.

(+)-(R, R)-1, 2-diphenyloxirane **6a** from **5a** [entry 2]: Following method B, using the sulfonium salt **5a** (0.1g; 0.26mmol), and benzaldehyde (0.04ml; 0.39mmol), **6a** (0.174mmol; 67%), **7a** (0.078mmol; 20%) were obtained, together with recovered sulfide **4a** (5.2mg; 0.028mmol), $[\alpha]_D$-2.1 (c:1 in $CHCl_3$); Trans isomer, 13% ee.

(+)-(R, R)-1,2-diphenyloxirane **6a** from **5b** [entry 6]: Following method A, using the sulfonium salt **5b** (0.45g; 1.1mmol) and benzaldehyde (0.17ml; 1.67mmol) the title compound was obtained (0.06mmol; 5%); $[\alpha]_D$ +92 (c 1.31 in $CHCl_3$), 43% ee.

(+)-(R, R)-1,2-diphenyloxirane **6a** from **5b** [entry 7]: Following method B, using the sulfonium salt **5b** (0.05g; 0.125mmol) and benzaldehyde (0.02ml; 0.18mmol) the title compound was obtained (0.0142mmol; 12%), 19% ee.

(+)-(R, R)-1(p-chlorophenyl)-2-phenyloxirane **6b** from **5a** [entry 3]: Following method B, using the sulfonium salt **5a** (0.1g; 0.26mmol) and p-chlorobenzaldehyde (0.055g; 0.39mmol), **6b** (0.159mmol; 62%), **7b** (0.02mmol; 8%), were obtained; Trans isomer; m.p. 95°C, (lit.,[25] m.p. 99°C); $[\alpha]_D$+29.7 (c:1.21 in $CHCl_3$); $\delta_H(CDCl_3)$ 7.3 (9H, m, Ar), 3.78 (2H, AB system, J_{AB} 1.25Hz); 12% ee; Cis isomer; m.p.28°C, (lit.,[25] m.p. 30°C); $\delta_H(CDCl_3)$ 7.15(9H, m, Ar), 4.85(2H, AB system, J_{AB} 3.1Hz).

(+)-(R, R)-1(p-chlorophenyl)-2-phenyloxirane **6b** from **5b** [entry 8]: Following method A, using the sulfonium salt **5b** (0.45g; 1.1mmol) and p-chlorobenzaldehyde (0.23g; 1.65mmol), the title compound was

obtained (0.61mmol; 55%) together with the recovered sulfide **4b** (175mg; 0.83mmol, 75%) $[\alpha]_D$-2.69 (c:1.2 in $CHCl_3$); Trans isomer m.p.95°C; $[\alpha]_D$+40.4 (c:2.5 in CH_2Cl_2); 42% ee.

(-)-Cyclohexyl-3-phenyloxirane **6c** from **5a** [entry 4]: Following method A, using the sulfonium salt **5a** (0.1g; 0.26mmol) and cyclohexane carboxaldehyde (0.05ml; 0.39mmol), **6c**, **7c** (0.086mmol; 34%) were obtained as an 18:82 mixture of cis:trans isomers; $\delta_H(CDCl_3)$ 7.35 (5H, m, Ph), 4.10 (1H, d, *J* 10Hz), 3.70 (1H, d, *J* 5Hz), 2.9 (1H, dd, *J* 10, 10 Hz), 2.8 (1H, d, *J* 10, 5Hz), 2.0-0.90 (11H, m); trans isomer: 22% ee, cis isomer, 28% ee.

(-)-Cyclohexyl-3-phenyloxirane **6c** from **5a** [entry 5]: Following method B, using the sulfonium salt **5a** (0.1g; 0.26mmol) and cyclohexane carboxaldehyde (0.05ml; 0.39mmol), the epoxides **54c**, **55c** were obtained as a cis:trans mixture (27:73 ratio) (0.094mmol; 37%) and the ^1H nmr spectrum was identical to that described above; trans isomer :14% ee, cis isomer :32% ee; $[\alpha]_D$ -2.8 (c:1.11 in $CHCl_3$).

Attempted epoxide formation using sulfonium salt **5c**: Following method B, using the sulfonium salt **5c** (0.25g; 0.554mmol) and benzaldehyde (0.085ml; 0.831mmol), the sulfide **10** was isolated as an oil (0.05g; 26%); ν_{max} /cm^{-1} (Nujol) 3100-2900, 1600, 1580; $\delta_H(CDCl_3)$ 7.25 (10H, m, 2xPh), 4.0 (1H, m), 3.15 (3H, m), 2.45-1.65 (6H, m), 1.4-0.85 (10H, m).

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