Preparation of enantiomerically enriched bromohydrins from [*N*-(*p*-tolylsulfonyl)sulfoximino]oxiranes using *in situ* reduction of α-bromo aldehydes

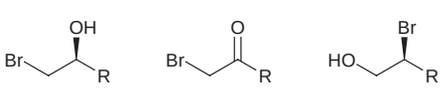
Peter L. Bailey,[a] Andrew D. Briggs,[a] Richard F. W. Jackson *[a] and Jörg Pietruszka [b]

[a] *Department of Chemistry, Bedson Building, The University of Newcastle, Newcastle upon Tyne, UK NE1 7RU*
[b] *Institut für Organische Chemie, Universität Hamburg, Martin-Luther-King Platz 6, D-20146 Hamburg 13, Germany*

Received (in Cambridge) 27th July 1998, Accepted 25th August 1998

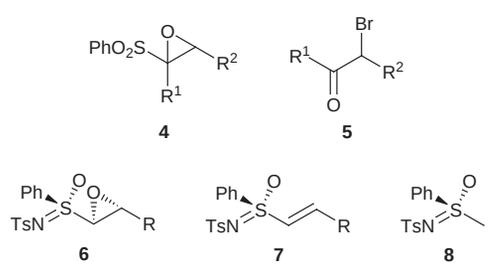
Treatment of enantiomerically pure [*N*-(*p*-tolylsulfonyl)sulfoximino]oxiranes **6** with $MgBr_2$ in the presence of tetrabutylammonium borohydride gives enantiomerically enriched bromohydrins **3**, together with small amounts of the primary alcohols **11**. The bromohydrins **3** are isolated in good yields with enantiomeric excesses in the range 70% to 91%. This process establishes that α-bromo aldehydes have sufficient configurational stability to be viable synthetic intermediates.

Optically active bromohydrins are useful synthetic intermediates, both in their own right and as precursors to optically active oxiranes. The preparation of secondary alcohols such as **1** by asymmetric reduction of the corresponding terminal bromo ketones **2** has been very well developed,[1–3] whilst methods for the preparation of the simple regioisomeric primary alcohols **3** are not so well developed.[4] A thorough investigation of the regioselectivity of ring-opening of terminal oxiranes with Lewis acidic metal halides has appeared,[5] and conditions which ensured selective halide attack at the secondary centre were reported. The stereochemical outcome of this process has not been established, so it is not yet clear whether this method will be effective for the preparation of optically active bromohydrins such as **3** (which is clearly dependant upon the rate of subsequent S_N2 attack by bromide ion). The reduction of enantiomerically pure α-bromo carboxylic acid derivatives has also been used. While α-bromo carboxylic acid can be prepared by the well-established diazotisation of α-amino acids in the presence of bromide ion, the lack of general methods for the preparation of these compounds has been rather limiting. However, an asymmetric synthesis of α-bromo carboxylic acids has been developed based on the bromination of enantiomerically pure esters derived from camphor-10-sulfonic acid.[6,7]



1 **2** **3**

It has been known for some time that treatment of sulfonyloxiranes **4** with $MgBr_2$ in diethyl ether (Et_2O) gives the corresponding α-bromo carbonyl compounds **5** in good yield.[8] We have therefore investigated the possibility that analogous enantiomerically pure [*N*-(*p*-tolylsulfonyl)sulfoximino]-oxiranes† **6**, for which we have developed an enantioselective synthesis based on the diastereoselective low-temperature epoxidation of *N*-(*p*-tolylsulfonyl)vinylsulfoximines **7** using lithium *tert*-butyl peroxide,[9,10] would be precursors to the corresponding enantiomerically enriched α-bromo aldehydes.‡ The necessary enantiomerically pure *N*-(*p*-tolylsulfonyl)vinylsulfoximines **7** were prepared using our previously described method starting from optically pure (*S*)-(+)-*S*-methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **8**.



4 **5** **6** **7** **8**

In a related study, Yamakawa has shown that treatment of enantiomerically pure sulfinyloxiranes with amine nucleophiles proceeds efficiently to give the corresponding α-amino carbonyl compounds with high enantiomeric excess.[12] However, in cases where the asymmetric carbon possesses an acidic proton, the products were obtained as racemates. It therefore appeared possible that enantiomerically pure α-bromo aldehydes **9**, which would be formed by initial bromide attack on [*N*-(*p*-tolylsulfonyl)sulfoximino]oxiranes **6**, would not be configurationally stable under the reaction conditions due to facile enolisation. The S_N2 reaction of enantiomerically pure α-bromo aldehydes with bromide ion was expected to provide an additional pathway for racemisation of the initially formed products.

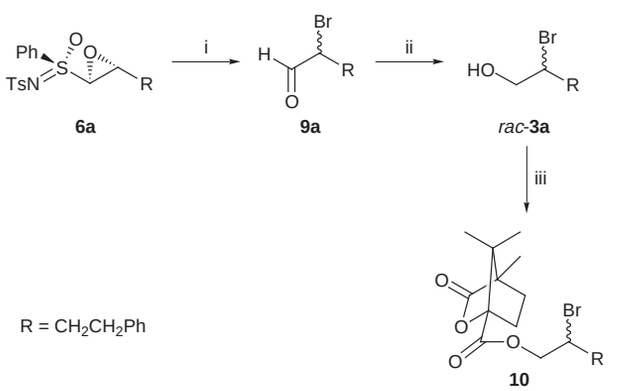
In a preliminary experiment we had established that the racemic *N*-(*p*-tolylsulfonyl)sulfoximino]oxirane **6** (R = ^{i}Pr) reacted with $MgBr_2$ in tetrahydrofuran (THF) at reflux to give 2-bromo-3-methylbutanal[13] in a low isolated yield (26%), due to the volatility of the product. Our attempts to perform the reaction in Et_2O, which is the solvent of choice for ring-opening reactions of sulfonyloxiranes,[8] were thwarted by the insolubility of the starting sulfoximinooxirane in Et_2O. However, it was established that ring-opening could be carried out at reflux using Et_2O–THF (4:1) as solvent. The evident reduction in reaction rate observed when using THF as solvent presumably reflects the enhanced coordinating ability of THF when compared to ether,[14,15] since coordination by magnesium to the oxirane oxygen is likely to be a necessary prelude to ring-opening by bromide.

† The IUPAC name for compounds of this type is sulfoximide, however for consistency with earlier work sulfoximine is used throughout this paper.
‡ This work has been the subject of a preliminary communication.[11]

Table 1 Preparation of vinylsulfoximines **7** and sulfoximinooxiranes **6**

R	Vinyl-sulfoximine	Yield (%)	Sulfoximino-oxirane	Yield (%)
CH_2CH_2Ph	**7a**	96	**6a**	98
$(CH_2)_6Me$	**7b**	92	**6b**	88
$(CH_2)_7Me$	**7c**	86	**6c**	85
^nBu	**7d**	76	**6d**	78
c-C_6H_{11}	**7e**	74	**6e**	84
$CH_2OTBDMS$	**7f**	58	**6f**	69

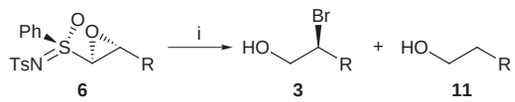
In order to investigate the stereochemical course of the ring-opening reaction, we have used the enantiomerically pure oxirane **6a** as a substrate. Diastereo- and enantiomerically pure oxirane **6a** was prepared by epoxidation of the corresponding *N*-(*p*-tolylsulfonyl)vinylsulfoximine **7a**,[9] derived from (*S*)-*S*-methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine.[16,17] A range of other sulfoximinooxiranes **6** were prepared in an analogous way, as reported in Table 1. The oxirane **6a** was treated with $MgBr_2$ [1.1 equiv., 4 h, Et_2O–THF (4:1), reflux] to give 2-bromo-4-phenylbutanal **9a** (60%), which was then reduced to 2-bromo-4-phenylbutan-1-ol **3a** ($NaBH_4$, EtOH) (89%) (Scheme 1). The alcohol was converted into the camphanate esters **10**, and ^1H NMR analysis showed that both diastereoisomeric esters had been formed as a 1:1 mixture, indicating that the original α-bromo aldehyde **9a** had been formed as a racemate.



Scheme 1 *Reagents and conditions*: i, $MgBr_2$, Et_2O–THF, reflux; ii, $NaBH_4$, EtOH; iii, (*S*)-camphanic chloride, DMAP, CH_2Cl_2.

We reasoned that the most effective method for prevention of the racemisation process was to include a hydride reducing agent together with $MgBr_2$ in the reaction mixture. By this means, the initially formed α-bromo aldehyde **9** should be reduced to the corresponding bromohydrin **3**, which would be much less susceptible towards nucleophilic attack by bromide ion, and hence the tendency towards racemisation would be reduced. In addition, racemisation *via* enol formation would be prevented. In the event, treatment of the oxirane **6a** with $MgBr_2$ (1.1 equiv.) and Bu_4NBH_4 (1.5 equiv.) in Et_2O–THF (4:1) at room temperature gave the required bromohydrin **3a** (49%), together with the primary alcohol **11a** (40%). The ee of the bromohydrin **3a** was established to be 80% (±10%) by analysis of the ^1H NMR spectrum of the camphanate ester **10a**. This result was deduced from integration of the methyl signals at δ 0.96 and 0.98, although the lack of baseline separation made a more precise determination difficult.

We eventually established that use of CH_2Cl_2 rather than THF as co-solvent gave superior yields of the desired bromohydrin **3a** at the expense of the alcohol **11a**. This result further illustrates the desirability of avoiding the use of THF as a solvent in reactions of $MgBr_2$ with sulfoximinooxiranes. The results from treatment of a range of enantiomerically pure [*N*-(*p*-tolylsulfonyl)sulfoximino]oxiranes **6** with $MgBr_2$ and Bu_4NBH_4 in Et_2O–CH_2Cl_2 (2:1) at room temperature are shown in Table 2. Good yields of the desired bromohydrins **3** are generally obtained, together with varying amounts of the corresponding primary alcohols **11** (Scheme 2). We presumed that



Scheme 2 *Reagents and conditions*: i, $MgBr_2$, Bu_4NBH_4, Et_2O–CH_2Cl_2, room temp., 2 h.

the ring-opening reaction would proceed with inversion of configuration (as indicated in Scheme 2) to give the bromohydrins of (*S*)-configuration. Circumstantial evidence in support of this presumption was provided by the negative optical rotation of the long chain bromohydrins **3a**–**c**, consistent with the negative optical rotation of (*S*)-2-bromohexadecan-1-ol, which had been prepared unambiguously from chiral pool precursors.[7] Since treatment of the [*N*-(*p*-tolylsulfonyl)sulfoximino]oxirane **6a** with Bu_4NBH_4 in Et_2O–CH_2Cl_2 (2:1) gave 4-phenylbutan-1-ol **11a** (90%), we concluded that by-products **11** are formed as a result of direct hydride attack on the [*N*-(*p*-tolylsulfonyl)-sulfoximino]oxiranes **6**, rather than by the (admittedly unlikely) subsequent reduction of the bromohydrins **3**. The clean formation of the bromohydrin **3e**, with none of the corresponding alcohol **11e**, must reflect the greater sensitivity to steric hindrance of the direct reduction process, compared with the ring-opening by bromide ion. The availability of the bromohydrins **3** provides a route to enantiomerically enriched terminal epoxides (by treatment with NaOMe).[6]

In view of the imprecision associated with the ee determination using NMR methods, a more direct and precise method was clearly required. We therefore investigated the use of GLC using modified cyclodextrins as stationary phases for this purpose.[18–20] By appropriate choice of stationary phase, the enantiomeric purity of each of the bromohydrins was established with a maximum error of ±0.5%. Our results are shown in Table 2. In some cases, it proved necessary to prepare the corresponding trifluoroacetate derivatives in order to permit good separation of the enantiomers. Our results demonstrate that simple α-bromo aldehydes **9**, whilst not completely configurationally stable under the reaction conditions, can be trapped effectively by reduction to the bromohydrins **3**, and that these bromohydrins possess a useful level of enantiomeric purity. A previous report has described the *in situ* preparation of enantiomerically pure α-bromo aldehydes at low temperature (most likely as the corresponding complex with magnesium cation), and their subsequent trapping with carbon nucleophiles.[21]

Experimental

General experimental procedures and instrumentation are as previously described.[22] *J* Values are given in Hz. $[a]_D$ Values are given in units of 10^{-1} deg cm^2 g^{-1}. Mass spectral peaks due to ^{79}Br only are recorded. Light petroleum refers to that fraction with boiling point range 40–60 °C. All organic extracts were dried over anhydrous $MgSO_4$, and solvent was removed using a rotary evaporator.

Preparation of vinylsulfoximines 7

The following vinylsulfoximines were prepared by the method described in our previous publications.[9,16]

(*S*)-(+)-(*E*)-*S*-Phenyl-*S*-(4-phenylbut-1-enyl)-*N*-(*p*-tolylsulfonyl)sulfoximine 7a. (*S*)-(+)-*S*-Methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **8** (3.09 g, 10 mmol) gave the pure vinylsulfoximine **7a** (4.08 g, 9.6 mmol, 96%), using hydrocinnamaldehyde as the aldehyde, as a colourless crystalline solid, mp

Table 2 Preparation of Bromohydrins **3**

Bromohydrin	Yield (%)	$[\alpha]_D$ of **3**[a]	Chiral phase[b]	Ee (%)	Yield of alcohol **11** (%)
3a	72	−71.6 (*c* 1.25, CH_2Cl_2)	A	87	22
3b[c]	71	−25.4 (*c* 2.5, CH_2Cl_2)	B	79	21
3c[c]	82	−22.7 (*c* 1.25, CH_2Cl_2)	B	76	15
3d	79	+18.8 (*c* 1.0, CH_2Cl_2)	C	70	16
3e	85	−22.9 (*c* 0.75, CH_2Cl_2)	A	71	0
3f[c]	67	+4.5 (*c* 1.0, CH_2Cl_2)	B	91	28

[a] In units of 10^{-1} deg cm^2 g^{-1}. [b] The stationary phases were as follows: A, octakis(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin;[20] B, octakis(2-*O*-methyl-3,6-di-*O*-pentyl)-γ-cyclodextrin;[20] C, octakis(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin.[19] [c] The bromohydrin was converted into the corresponding trifluoroacetate before GLC analysis.

89–90 °C; $[\alpha]_D^{20}$ +15.3 (*c* 1.1, CH_2Cl_2). Spectroscopic data were identical with those reported for the racemate.[9]

(*S*)-(+)-(*E*)-*S*-(Non-1-enyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine 7b. (*S*)-(+)-*S*-Methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine **8** (3.09 g, 10 mmol) gave the pure vinylsulfoximine **7b** (3.86 g, 9.2 mmol, 92%), using octanal as the aldehyde, as a colourless crystalline solid, mp 53–54 °C; $[\alpha]_D^{20}$ +22.0 (*c* 0.8, CH_2Cl_2). Spectroscopic data were identical with those reported for the racemate.[9]

(*S*)-(+)-(*E*)-*S*-(Dec-1-enyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine 7c. (*S*)-(+)-*S*-Methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine **8** (3.09 g, 10 mmol) gave the pure vinylsulfoximine **7c** (3.72 g, 8.6 mmol, 86%), using nonanal as the aldehyde, as a colourless crystalline solid, mp 55–56 °C; $[\alpha]_D^{20}$ +20.4 (*c* 1.0, CH_2Cl_2); ν_{max} (cm^{-1}, film) 1599, 1497, 1304, 1065, 814; δ_H (200 MHz, $CDCl_3$) 0.87 (3H, t, ^3J 6.5, CH_3CH_2), 1.24–1.45 (12H, m, 6 × CH_2), 2.20–2.28 (2H, m, CH_2CH=CH), 2.39 (3H, s, $CH_3C_6H_4SO_2$), 6.41 (1H, dt, ^3J 15.0 and 1.0, CH_2CH=C*H*), 7.00 (1H, dt, ^3J 15.0 and 7.0, CH_2CH=CH), 7.22–7.29 (2H, m, Ar), 7.49–7.67 (3H, m, Ar), 7.81–7.87 (2H, m, Ar), 7.91–7.97 (2H, m, Ar); *m*/*z* (EI) 434 (MH^+, 3.3), 433 (M^+, 1.6), 404 ($M^+ - CH_2Me$, 1), 296 (20), 278 (PhSNTs, 40%) (found: MH^+, 434.1817. $C_{23}H_{32}NO_3S_2$ requires 434.1823).

(*S*)-(+)-(*E*)-*S*-(Hex-1-enyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine 7d. (*S*)-(+)-*S*-Methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine **8** (3.09 g, 10 mmol) gave the pure vinylsulfoximine **7d** (2.86 g, 7.6 mmol, 76%), using pentanal as the aldehyde, as a colourless crystalline solid, mp 70–71 °C; $[\alpha]_D^{20}$ +17.6 (*c* 1.0, CH_2Cl_2)) (found: C, 60.3; H, 6.2; N, 3.6. $C_{19}H_{23}NO_3S_2$ requires C, 60.5; H, 6.1; N, 3.7%.); ν_{max} (cm^{-1}, film) 1599, 1499, 1308, 1059, 816; δ_H (200 MHz, $CDCl_3$) 0.88 (3H, t, ^3J 7.0, CH_3CH_2), 1.17–1.50 (4H, m, 2 × CH_2), 2.21–2.31 (2H, m, CH_2CH=CH), 2.40 (3H, s, $CH_3C_6H_4SO_2$), 6.41 (1H, dt, ^3J 15.0 and 1.5, CH_2CH=C*H*), 6.99 (1H, dt, ^3J 15.0 and 7.0, CH_2CH=CH), 7.22–7.25 (2H, m, Ar), 7.50–7.69 (3H, m, Ar), 7.82–7.86 (2H, m, Ar), 7.92–7.97 (2H, m, Ar); *m*/*z* (EI) 378 (MH^+, 31.5), 377 (M^+, 20.5), 348 ($M^+ - MeCH_2$, 40) 278 (PhSNTs, 80%) (found: MH^+, 378.1208. $C_{19}H_{24}NO_3S_2$ requires 378.1197).

(*S*)-(+)-(*E*)-*S*-(2-Cyclohexylethenyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine 7e. (*S*)-(+)-*S*-Methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **8** (3.09 g, 10 mmol) gave the pure vinylsulfoximine **7e** (2.98 g, 7.4 mmol, 74%). Physical and spectroscopic data were identical with those reported.[23,24]

(*S*)-(+)-(*E*)-*S*-[3-*tert*-(Butyldimethylsilyloxy)prop-1-enyl]-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine 7f. (*S*)-(+)-*S*-Methyl-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **8** (1.0 g, 3.23 mmol) gave the pure vinylsulfoximine **7f** (0.87 g, 1.88 mmol, 58%), using *tert*-butyldimethylsilyloxyacetaldehyde[25] as the aldehyde, as a colourless crystalline solid, mp 96–97 °C; $[\alpha]_D^{20}$ +27.2 (*c* 2.0, CH_2Cl_2); ν_{max} (cm^{-1}, KBr disc) 1599, 1495, 1298, 1063, 814; δ_H (200 MHz, $CDCl_3$) 0.00 (3H, s, $SiMe_AMe_BBu^t$), 0.02 (3H, s, $SiMe_AMe_BBu^t$), 0.86 (9H, s, $SiMe_AMe_BBu^t$), 2.38 (3H, s, $CH_3C_6H_4SO_2$), 4.38 (2H, m, CH_2O), 6.66 (1H, dt, ^3J 14.5 and 1.5, CH_2CH=C*H*), 7.07 (1H, dt, ^3J 14.5 and 3.0), 7.22–7.27 (2H, m), 7.51–7.70 (3H, m), 7.82–7.98 (4H, m); *m*/*z* (EI) 408 ($M^+ - Bu^t$, 58), 189 (30), 147 (100%) (found: $MH^+ - Bu^t$, 408.0735. $C_{18}H_{22}NO_4S_2Si$ requires 408.0759).

Preparation of sulfoximinooxiranes 6 §

The following sulfoximinooxiranes were prepared by the method described in our previous publication,[9] and in each case were diastereoisomerically pure as judged by ^1H NMR.

(*R*)-(−)-*S*-Phenyl-*S*-[*trans*-3-(2′-phenylethyl)oxiran-2-yl]-*N*-(*p*-tolylsulfonyl)sulfoximine 6a. (*S*)-(+)-(*E*)-*S*-Phenyl-*S*-(4-phenylbut-1-enyl)-*N*-(*p*-tolylsulfonyl)sulfoximine **7a** (0.85 g, 2 mmol) was converted into (*R*)-(−)-*S*-phenyl-*S*-[*trans*-3-(2′-phenylethyl)oxiran-2-yl]-*N*-(*p*-tolylsulfonyl)sulfoximine **6a** (0.86 g, 1.96 mmol, 98%) as a colourless crystalline solid, mp 96–97 °C; $[\alpha]_D^{20}$ +89.0 (*c* 1.2, CH_2Cl_2). Spectroscopic data were identical with those reported for the racemate.[9]

(*R*)-(−)-*S*-(*trans*-3-Heptyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine 6b. (*S*)-(+)-(*E*)-*S*-(Non-1-enyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **7b** (0.84 g, 2 mmol) was converted into (*R*)-(−)-*S*-(*trans*-3-heptyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6b** (0.77 g, 1.76 mmol, 88%) as a colourless crystalline solid, mp 55–56 °C; $[\alpha]_D^{20}$ +69.5 (*c* 1.1, CH_2Cl_2). Spectroscopic data were identical with those reported for the racemate.[9]

(*R*)-(−)-*S*-(*trans*-3-Octyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine 6c. (*S*)-(+)-(*E*)-*S*-(Dec-1-enyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **7c** (0.87 g, 2 mmol) was converted into (*R*)-(−)-*S*-(*trans*-3-octyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6c** (0.76 g, 1.70 mmol, 85%) as a colourless crystalline solid, mp 60–61 °C; $[\alpha]_D^{20}$ +118.8 (*c* 0.9, CH_2Cl_2); ν_{max} (cm^{-1}, film) 1599, 1497, 1323, 1069; δ_H (200 MHz, $CDCl_3$) 0.87 (3H, t, ^3J 6.5, CH_3CH_2), 1.22–1.75 (14H, m, 7 × CH_2), 2.40 (3H, s, $MeC_6H_4SO_2$), 3.37 (1H, dt, ^3J 1.5 and 5.0, CH_2CH[O]CH), 4.36 (1H, d, ^3J 1.5, CH_2CH[O]C*H*), 7.23–7.28 (2H, m, Ar), 7.56–7.78 (3H, m, Ar), 7.81–8.00 (4H, m, Ar); *m*/*z* (EI) 450 (MH^+, 0.5), 434 ($M^+ - Me$, 3%) (found: $M^+ - Me$, 434.1056. $C_{22}H_{28}NO_4S_2$ requires 434.1098).

(*R*)-(−)-*S*-(*trans*-3-Butyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine 6d. (*S*)-(+)-(*E*)-*S*-(Hex-1-enyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **7d** (0.76 g, 2 mmol) was converted into (*R*)-(−)-*S*-(*trans*-3-butyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6d** (0.62 g, 1.56 mmol, 78%) as a colourless crystalline solid, mp 85–87 °C; $[\alpha]_D^{20}$ −59.1 (*c* 0.9, CH_2Cl_2); ν_{max} (cm^{-1}, film) 1599, 1497, 1321, 1069; δ_H (200 MHz, $CDCl_3$) 0.85 (3H, t, ^3J 7.0, CH_3CH_2), 1.18–1.72 (6H, m,

§ In the names for compounds **6** *trans* describes the relative orientation between the R substituent and the sulfoximine group.

6 × CH_2), 2.40 (3H, s, *Me*C$_6$H$_4$SO$_2$), 3.37 (1H, dt, ^3J 1.5 and 5.0, CH$_2$C*H*[O]CH), 4.36 (1H, d, ^3J 1.5, CH$_2$CH[O]C*H*), 7.23–7.28 (2H, m, Ar), 7.56–7.78 (3H, m, Ar), 7.81–8.02 (4H, m, Ar); *m*/*z* (EI) 394 (MH$^+$, 0.6), 378 (M$^+$ − Me, 0.5), 278 (PhSNTs, 15%) (found: MH$^+$, 394.1161. $C_{19}H_{24}NO_4S_2$ requires 394.1147).

(*R*)-(−)-*S*-(*trans*-3-Cyclohexyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine 6e. (*S*)-(+)-(*E*)-*S*-(2-Cyclohexylethenyl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **7e** (0.79 g, 2 mmol) was converted into (*R*)-(−)-*S*-(*trans*-3-cyclohexyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6e** (0.69 g, 1.68 mmol, 84%) as a colourless crystalline solid, mp 93–94 °C; $[a]_D^{20}$ +83.2 (*c* 1.0, CH$_2$Cl$_2$); ν_{max} (cm^{-1}, film) 1599, 1497, 1327, 1067; δ_H (200 MHz, CDCl$_3$) 0.90–1.89 (11H, m, c-C$_6H_{11}$), 2.39 (3H, s, *Me*C$_6$H$_4$SO$_2$), 3.19 (1H, dd, ^3J 6.5 and 2.0, C*H*[O]CHS), 4.45 (1H, d, ^3J 2.0, CH[O]C*H*S), 7.19–7.28 (2H, m, Ar), 7.54–7.78 (3H, m, Ar), 7.81–7.99 (4H, m, Ar); *m*/*z* (EI) 404 (M$^+$ − Me, 3.4), 278 (PhSNTs, 40%) (found: M$^+$ − Me, 404.1062. $C_{20}H_{22}NO_4S_2$ requires 404.0990).

(*R*)-(−)-*S*-[*trans*-3-(*tert*-Butyldimethylsilyloxymethyl)oxiran-2-yl]-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine 6f. (*S*)-(+)-(*E*)-*S*-[3-(*tert*-Butyldimethylsilyloxy)prop-1-enyl]-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **7f** (0.90 g, 2 mmol) was converted into (*R*)-(−)-*S*-[*trans*-3-(*tert*-butyldimethylsilyloxymethyl)oxiran-2-yl]-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6f** (0.65 g, 1.48 mmol, 69%) as a colourless oil, $[a]_D^{20}$ +75.7 (*c* 0.65, CH$_2$Cl$_2$); ν_{max} (cm^{-1}, film) 1599, 1497, 1323, 1067; δ_H (200 MHz, CDCl$_3$) 0.00 (3H, s, Si*Me*$_A$Me$_B$Bu^t), 0.02 (3H, s, SiMe$_A$*Me*$_B$Bu^t), 0.82 (9H, s, SiMe$_A$-Me$_B$*Bu*^{t}), 2.39 (3H, s, *Me*C$_6$H$_4$SO$_2$), 3.53–3.57 (1H, m, CH$_A$-H$_B$C*H*[O]CH), 3.81 (1H, dd, ^3J 13.0 and 3.0, CH$_A$*H*$_B$CH-[O]CH), 3.93 (1H, dd, ^3J 13.0 and 3.0, C*H*$_A$H$_B$CH[O]CH), 4.55 [1H, d, ^3J 1.5, C*H*SO(NTs)Ph], 7.24–7.27 (2H, m, Ar), 7.56–7.78 (3H, m, Ar), 7.81–8.02 (4H, m, Ar); *m*/*z* (EI) 424 (M$^+$ − Bu^t, 3.1), 352 (M$^+$ − CH$_2$OSiMe$_2$Bu^t, 20), 278 (PhSNTs, 30%) (found: M$^+$ − Bu^t, 424.0761. $C_{18}H_{22}NO_5S_2Si$ requires 424.0710).

Direct preparation of 2-bromohydrins 3 *via in situ* reduction of 2-bromo aldehydes 9

General procedure. Magnesium bromide–diethyl ether (MgBr$_2$·Et$_2$O) (1.1 equiv.) and tetra-*n*-butylammonium borohydride (1.5 equiv.) were added to a solution of *S*-(*trans*-alkyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6** in dry diethyl ether (1 ml per 0.4 mmol) and dry dichloromethane (0.5 ml per 0.4 mmol) at room temp. The reaction mixture was stirred at room temp. and monitored by TLC until there was no longer any oxirane present (generally about 2 h). The reaction was quenched with phosphate buffer (pH 7; 1 ml per 0.3 mmol) and extracted with dichloromethane (3 × 1 ml per 0.3 mmol). The dichloromethane extracts were combined, dried (MgSO$_4$) and solvent removed under reduced pressure to give a yellow oil. The crude product was purified by flash column chromatography, using a 10% mixture of ethyl acetate in light petroleum as eluent, to give the pure bromohydrin **3**.

(*S*)-2-Bromo-4-phenylbutanol 3a. (*R*)-(−)-*S*-Phenyl-*S*-[*trans*-3-(2′-phenylethyl)oxiran-2-yl]-*N*-(*p*-tolylsulfonyl)sulfoximine **6a** (190 mg, 0.43 mmol) was treated with magnesium bromide–diethyl ether and tetra-*n*-butylammonium borohydride as described above at room temp. for 2 h. Normal work up and purification gave 2-bromo-4-phenylbutanol **3a** (70 mg, 0.31 mmol, 72%) as a colourless oil [86% ee as determined by GLC of **3a** using a 25 m fused silica capillary column, coated with a 1:1 mixture of octakis(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin and OV1701 at 190 °C, retention time (t_r) 56 min (major)/58 min (minor), carrier-gas H$_2$], $[a]_D^{20}$ −71.6 (*c* 1.25, CH$_2$Cl$_2$); ν_{max} (cm^{-1}, film) 3395, 1603, 1497, 750, 648; δ_H (200 MHz, CDCl$_3$) 2.04–2.20 (3H, m, CH_2Ph and O*H*), 2.66–2.99 (2H, m, CH_2CH$_2$Ph), 3.71–3.81 (2H, m, CH_2OH), 4.01–4.13 (1H, m, C*H*[Br]CH$_2$), 7.16–7.76 (5H, m, Ph); *m*/*z* (EI) 228 (M$^+$, 55), 131 (M$^+$ − Br, 98), 117 (M$^+$ − Br, CH$_2$OH, 62), 104 (M$^+$ − CH$_2$(OH)CHBr, 61), 91 (PhCH$_2$, 100%) (found: M$^+$, 228.0005. $C_{10}H_{13}OBr$ requires 228.0015) . 4-Phenylbutanol **11a** (14 mg, 0.09 mmol, 22%) was also isolated as a colourless oil, ν_{max} (cm^{-1}, film) 3343, 1603, 1496; δ_H (200 MHz, CDCl$_3$) 1.40–1.95 (5H, m, PhCH_2 and CH_2CH$_2$O*H*), 2.60–2.78 (2H, m, CH_2CH$_2$Ph), 3.60–3.68 (2H, m, CH_2OH), 7.13–7.96 (5H, m, Ph); *m*/*z* (EI) 150 (M$^+$, 85), 132 (M$^+$ − H$_2$O, 71), 117 (M$^+$ − Me, H$_2$O, 62), 104 (M$^+$ − CH$_2$CH$_2$, H$_2$O, 100), 91 (PhCH$_2$, 100%) (found: M$^+$, 150.1041. $C_{10}H_{14}O$ requires 150.1045).

(*S*)-2-Bromononanol 3b. (*R*)-(−)-*S*-(*trans*-3-Heptyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6b** (392 mg, 0.94 mmol) was treated with magnesium bromide–diethyl ether and tetra-*n*-butylammonium borohydride as described above at room temp. for 2 h. Normal work up and purification gave 2-bromononanol **3b** (148 mg, 0.67 mmol, 71%) as a colourless oil [79% ee as determined by GLC of the trifluoroacetyl derivative of **3b** using a 25 m fused silica capillary column, coated with a 1:1 mixture of octakis(2-*O*-methyl-3,6-di-*O*-pentyl)-γ-cyclodextrin and OV1701 at 86 °C, retention time 72 min (major)/74 min (minor), carrier-gas H$_2$], $[a]_D^{20}$ −25.4 (*c* 2.5, CH$_2$Cl$_2$); ν_{max} (cm^{-1}, film) 3380, 735, 684, 666; δ_H (200 MHz, CDCl$_3$) 0.89 (3H, t, *J* 6.5, *Me*CH$_2$), 1.28–1.72 (10H, m, 5 × CH$_2$), 1.79–1.90 (2H, m, CH_2CH[Br]), 2.11 (1H, br s, O*H*), 3.74–3.82 (2H, m, CH_2O), 4.09–4.21 (1H, m, C*H*Br); *m*/*z* (EI) 221 (M$^+$ − H, 6), 205 (M$^+$ − H$_2$O, 50), 143 (M$^+$ − Br, 60%) (found: M$^+$ − H, 221.0640. $C_9H_{18}OBr$ requires 221.0541). Nonanol **11b** was also isolated as a colourless oil (38 mg, 0.27 mmol, 28%).

(*S*)-2-Bromodecanol 3c. (*R*)-(−)-*S*-(*trans*-3-Octyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6c** (200 mg, 0.45 mmol) was treated with magnesium bromide–diethyl ether and tetra-*n*-butylammonium borohydride as described above at room temp. for 2 h. Normal work up and purification gave 2-bromodecanol **3c** (88 mg, 0.37 mmol, 82%) as a colourless oil [76% ee as determined by GLC of the trifluoroacetyl derivative of **3c** using a 25 m fused silica capillary column, coated with a 1:1 mixture of octakis(2-*O*-methyl-3,6-di-*O*-pentyl)-γ-cyclodextrin and OV1701 at 90 °C, retention time 116 min (major)/119 min (minor), carrier-gas H$_2$], $[a]_D^{20}$ −22.7 (*c* 1.25, CH$_2$Cl$_2$); ν_{max} (cm^{-1}, film) 3376, 723, 637; δ_H (200 MHz, CDCl$_3$) 0.88 (3H, t, *J* 6.5, *Me*CH$_2$), 1.28–1.61 (12H, m, 6 × CH_2), 1.79–1.90 (2H, q, *J* 7.5, CH_2CH[Br]), 2.05 (1H, t, *J* 6.5, O*H*), 3.61–3.89 (2H, m, CH_2O), 4.09–4.21 (1H, m, C*H*Br); *m*/*z* (EI) 238 (M$^+$, <1), 237 (M$^+$ − H, 1.2), 221 (M$^+$ − H$_2$O, 20), 177 (M$^+$ − (CH$_2$)$_2$-CH$_3$, H$_2$O, 10), 163 (M$^+$ − (CH$_2$)$_3$CH$_3$, H$_2$O, 15), 157 (M$^+$ − Br, 15) 139 (M$^+$ − Br, H$_2$O, 35%) (found: M$^+$, 238.0756. $C_{10}H_{21}OBr$ requires 238.0757). Decanol **11c** (11 mg, 0.07 mmol, 15%) was also isolated as a colourless oil.

(*S*)-2-Bromohexanol 3d. (*R*)-(−)-*S*-(*trans*-3-Butyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6d** (200 mg, 0.51 mmol) was treated with magnesium bromide–diethyl ether and tetra-*n*-butylammonium borohydride as described above at room temp. for 2 h. Normal work up and purification gave 2-bromohexanol **3d** (73 mg, 0.40 mmol, 79%) as a colourless oil [70% ee as determined by GLC of **3d** using a 25 m fused silica capillary column, coated with a 1:1 mixture of octakis(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin and OV1701 at 75 °C, retention time 28 min (minor)/33 min (major), carrier-gas H$_2$], $[a]_D^{20}$ +18.8 (*c* 1.0, CH$_2$Cl$_2$); ν_{max} (cm^{-1}, film) 3378, 733, 637; δ_H (200 MHz, CDCl$_3$) 0.92 (3H, d, *J* 7, *Me*CH$_2$), 1.23–1.64 (4H, m, MeCH_2CH_2), 1.80–1.91 (2H, m, CH_2CH[Br]CH$_2$), 2.06 (1H, br m, O*H*), 3.75–3.87 (2H, m, CH_2O), 4.09–4.21 (1H, m, C*H*Br); *m*/*z* (EI) 163 (M$^+$ − OH, 10), 83 (M$^+$ − OH, Br, 100%) (found: M$^+$ − OH, 163.0089. $C_6H_{12}Br$ requires 163.0123).

Hexanol **11c** (8 mg, 0.08 mmol, 16%) was also isolated as a colourless oil.

(*S*)-2-Bromo-2-cyclohexylethanol 3e. (*R*)-(−)-*S*-(*trans*-3-Cyclohexyloxiran-2-yl)-*S*-phenyl-*N*-(*p*-tolylsulfonyl)sulfoximine **6e** (200 mg, 0.48 mmol) was treated with magnesium bromide–diethyl ether and tetra-*n*-butylammonium borohydride as described above at room temp. for 2 h. Normal work up and purification gave 2-bromo-2-cyclohexylethanol **3e** (84 mg, 0.405 mmol, 85%) as a colourless oil [71% ee as determined by GLC of **3e** using a 25 m fused silica capillary column, coated with a 1:1 mixture of octakis(2,6-di-*O*-methyl-3-*O*-pentyl)-γ-cyclodextrin and OV1701 at 128 °C, retention time 21 min (minor)/25 min (major), carrier-gas H_2], $[\alpha]_D^{20}$ −22.9 (*c* 0.75, CH_2Cl_2); ν_{max} (cm^{-1}, film) 3370, 785, 660; δ_H (200 MHz, $CDCl_3$) 1.21–1.25 (6H, m, cyclohexyl), 1.75–2.10 (total 6H, m, cyclohexyl and O*H*), 3.80–3.95 (2H, t, *J* 6.0, CH_2O), 4.03–4.09 (1H, q, *J* 6.0, C*H*Br); *m*/*z* (EI) 207 (MH^+, 15), 189 ($MH^+ - H_2O$, 18), 83 (C_6H_{11}, 80%) (found: $MH^+ - H_2O$, 189.0290. $C_8H_{14}Br$ requires 189.0279).

(*S*)-2-Bromo-3-*tert*-butyldimethylsilyloxypropanol 3f. (*R*)-(−)-*S*-[*trans*-(3-*tert*-Butyldimethylsilyloxymethyl)oxiran-2-yl]-*S*-phenyl-*N*-(*p*-tolylsulfonyl)-sulfoximine **6f** (200 mg, 0.45 mmol) was treated with magnesium bromide–diethyl ether and tetra-*n*-butylammonium borohydride as described above at room temp. for 2 h. Normal work up and purification gave 2-bromo-3-*tert*-butyldimethylsilyloxypropanol **3f** (81 mg, 0.30 mmol, 67%) as a colourless oil [91% ee as determined by GLC of the trifluoroacetyl derivative of **3f** using a 25 m fused silica capillary column, coated with a 1:1 mixture of octakis(2-*O*-methyl-3,6-di-*O*-pentyl)-γ-cyclodextrin and OV1701 at 105 °C, retention time 13 min (minor)/14 min (major), carrier-gas H_2], $[\alpha]_D^{20}$ +4.5 (*c* 1.0, CH_2Cl_2); ν_{max} (cm^{-1}, film) 3395, 779, 671; δ_H (200 MHz, $CDCl_3$) 0.10 (6H, s, Si*Me*$_2$Bu^t), 0.90 (9H, s, SiMe$_2$*Bu*^{t}), 2.32 (1H, t, *J* 6.5, O*H*), 3.82–4.00 (4H, m, CH_2OSi and CH_2OH), 4.07–4.15 (1H, C*H*Br); *m*/*z* (EI) 211 ($M^+ - Bu^t$, 2), 131 ($M^+ - Bu^t$, Br, 60), 75 ($M^+ - Br$, SiBu^{t}Me$_2$, 100) (found: $M^+ - Bu^t$, 210.9793. $C_5H_{12}O_2BrSi$ requires 210.9790). 3-*tert*-Butyldimethylsilyloxypropanol **11f** (24 mg, 0.13 mmol, 28%) was also isolated as a colourless oil, which exhibited spectroscopic properties identical with those in the literature.[26]

Acknowledgements

We thank the EPSRC (SERC) for CASE studentships (P. L. B. and A. D. B.), the City of Hamburg for a scholarship (J. P.), the Ciba Fellowship Trust for an ACE award (R. F. W. J.), Professor W. A. König for providing access to GLC facilities, Professor O. Meth-Cohn (Sterling Organics) and Dr P. A. Brown (Roche Products) for helpful discussion, and Sterling Organics and Roche Products for support. We also thank Dr M. N. S. Hill, Mrs L. Cook, Mr D. Dunbar and Mr S. Addison for obtaining spectroscopic and other data, and Mr E. Hart for invaluable technical assistance.

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Paper 8/05839C