Diastereoselective conversion of sulfides into sulfoxides. 1,5- and 1,6-Asymmetric induction

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The diastereoselective oxidation of sulfides into sulfoxides has been achieved with enantiomerically pure dihydrooxazole auxiliaries. When an additional hydroxymethyl substituent is present, diastereocontrol is very high and 1,5-asymmetric induction has been achieved with up to 96:4 selectivity, and 1,6-asymmetric induction has been achieved with up to 97:3 selectivity in the absence of any additional chiral agents.

Introduction

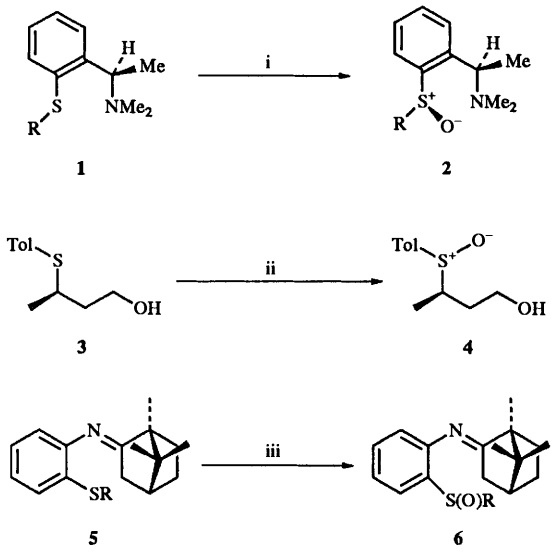
The utility of enantiomerically pure sulfoxides in asymmetric synthesis is an area of chemistry that has received increasing attention in recent years.[1] Sulfoxides have been used both as chiral auxiliaries[2] and as ligands in asymmetric catalysis.[3] It has been demonstrated that an enantiomerically pure sulfoxide may efficiently induce stereoselectivity in a variety of asymmetric reactions, including Diels–Alder reactions,[4] aldol reactions[5] and other carbon–carbon bond-forming processes.[6]

Several research groups have investigated the diastereoselective oxidation of chiral sulfides using achiral oxidants.[7] The proximity of a defined chirality centre has been exploited to relay stereochemistry to the newly formed sulfoxide. For example, Ohta and co-workers have reported the diastereoselective oxidation of aryl sulfides to aryl sulfoxides by means of the directing effects of *ortho*-substituents.[7a] By using sodium perborate as an oxidant, the sulfide **1** was oxidised to sulfoxide **2** in up to 78% diastereoisomeric excess (de) and with good chemical yield.

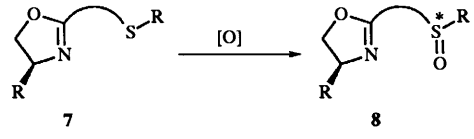
Seebach and Breitschuh utilised a hydroxy substituent to direct the diastereoselective oxidation of a series of sulfides **3** to sulfoxides **4** and De Lucchi and co-workers utilised (*R*)-camphor ketimines as chiral auxiliaries in their studies of chirality transfer in the conversion of sulfides **5** into sulfoxides **6**.[7b,7c] We were interested in the diastereoselective oxidation of sulfides tethered to a dihydrooxazole moiety. The 4,5-dihydrooxazole (oxazoline) unit has been widely used in asymmetric synthesis,[8] and it was envisaged that the approach of the oxidant to the sulfur atom could be influenced by the substituent at the 4-position on the 4,5-dihydrooxazole ring. We anticipated that the oxidation of sulfide **7** to sulfoxide **8** would generate simple bidentate ligands with a 4,5-dihydrooxazole moiety and a sulfoxide acting as the donor groups. Since these potential ligands possess two chirality centres, it would be possible to have matched and mismatched pairs between the 4*S* centre of the 4,5-dihydrooxazole ring and the S_S and R_S isomers of the sulfoxide.

Results and discussion

The sulfide substrates were prepared using conventional chemistry, in an analogous manner to ligand syntheses previously presented by this group.[9] 2-Fluorobenzonitrile **11** was treated with sodium toluene-*p*-thiolate to produce sulfide **12** in 75% yield.[10] The sulfide **12** was condensed with valinol,



Reagents and conditions: i, $NaBO_3 \cdot 4H_2O$, AcOH, room temp., 15 h, up to 78% de; ii, $VOacac_2$, Bu^{t}OOH, CH_2Cl_2, −20 °C, 6 h; iii, MCPBA

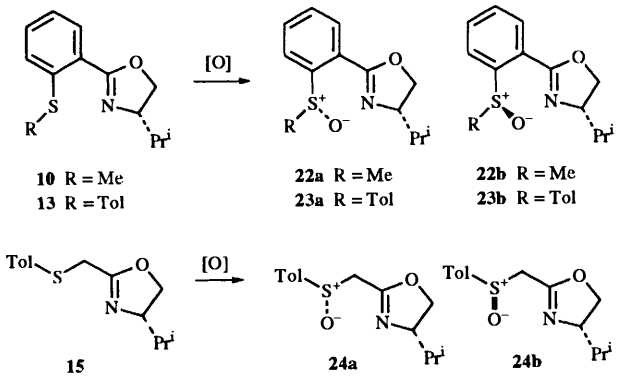


using zinc chloride as catalyst,[11] to form the sulfide **13** in 88% yield. Deprotonation of acetonitrile with lithium diisopropylamide (LDA) and quenching with di-*p*-tolyl disulfide at −78 °C in tetrahydrofuran (THF) afforded the sulfide **14**, which was converted into the dihydrooxazole **15** by condensation with valinol in the presence of zinc chloride as a catalyst. We also prepared a series of substrates that possessed a hydroxy group, since this functionality was expected to alter the interactions with the incoming oxidant. Similarly, the dihydrooxazole **16** was prepared in 91% yield by the zinc chloride-catalysed condensation of (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol and nitrile **14**. Furthermore, the dihydrooxazole **16** was converted into its triisopropylsilyl ether, **17** (Scheme 1). The formation of a dihydrooxazole from (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol and a suitable nitrile may also be carried out using potassium carbonate as a catalyst.[12] Thus,

2-(methylsulfanyl)benzonitrile **9** and benzonitrile **19** were converted into the corresponding dihydrooxazoles **18** and **20** respectively. Protection of the dihydrooxazole **20** as its *tert*-butyldimethylsilyl (TBDMS) derivative, followed by lithiation (directed by the dihydrooxazole moiety) and quenching of the lithiated species with di-*p*-tolyl disulfide introduced the *ortho*-substituent. Removal of the TBDMS group with tetrabutylammonium fluoride (TBAF) provided substrate **21** (Scheme 2), where the hydroxy group is potentially in a position to direct an oxidation of the sulfur atom.[13] With a series of sulfide substrates in hand the research turned to the investigation of directed oxidations.

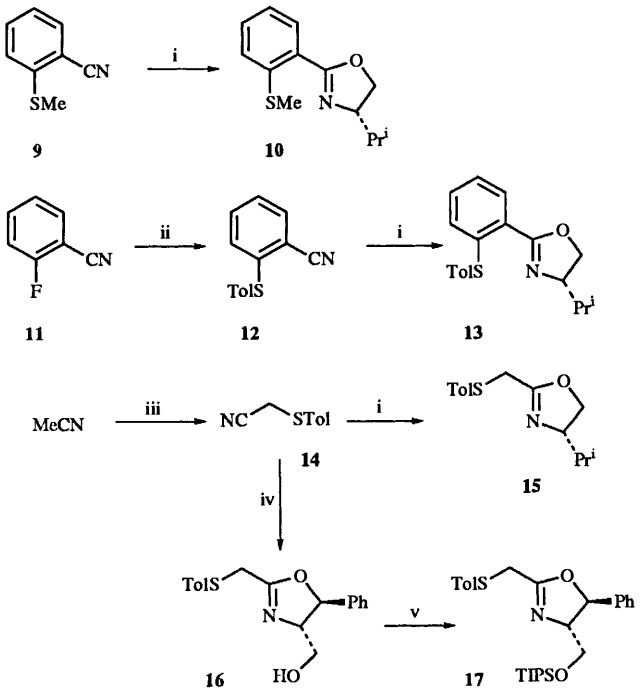
Sulfides **10**, **13** and **15** were oxidised under a variety of conditions to afford the sulfoxides **22a**:**22b**, **23a**:**23b** and **24a**:**24b** in variable isolated yield. The products were analysed further to determine any de and to identify the configuration of the major isomer (*vide infra*). The ratio of diastereoisomers was determined from either HPLC or NMR data. Oxidation of the diaryl sulfides is an example of 1,6-asymmetric induction, and oxidation of the alkyl aryl sulfides is an example of 1,5-asymmetric induction.

The sulfide **10** was oxidised in good yield but with low selectivity by *m*-chloroperbenzoic acid (MCPBA),[14] $NaIO_4$,[15] $NaBO_3$[16] and magnesium monoperoxyphthalate (MMPP).[17] Lower chemical yields were obtained using *tert*-butyl hydroperoxide with either titanium tetraisopropoxide or vanadyl acetylacetonate ($VOacac_2$) as the promoter, although in the latter case a reasonable diastereoselectivity was observed in the formation of sulfoxide **22a**. Results are given in Table 1. In the oxidation of this series of sulfoxides we assumed that the moderate degree of diastereoselectivity obtained is due to lack of organisation in the transition states. We therefore turned our attention to the use of a substituent capable of association with the incoming oxidising reagent.

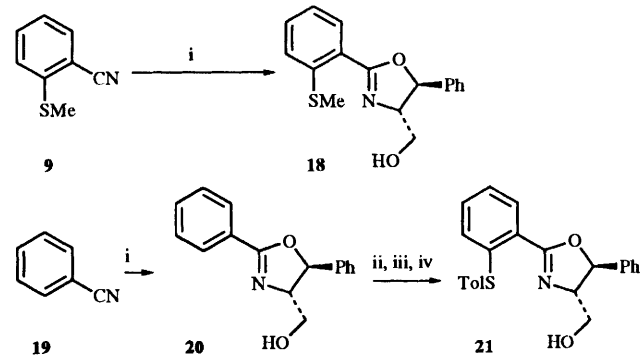


The series of sulfide substrates **16**–**18** and **21** derived from (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol were also oxidised under similar conditions to investigate the directing influence of the hydroxy group.[13] We were pleased to see that these substrates afforded much higher levels of diastereoselectivity in their oxidation reactions (see Table 2).

The diastereoselectivity of the MCPBA oxidation of the sulfides was seen to be influenced by the nature of the solvent. We believe that the presence of a protic solvent may disrupt hydrogen-bonding interactions between the substrate and the oxidising agent. The major diastereoisomer from the oxidation of sulfides **16**, **18** and **21** is seen to favour diastereoisomers **25a**, **27a** and **28a** respectively. The oxidation of silyl ether **17**, where the hydroxy group is masked, proceeds with only moderate selectivity to favour the diastereoisomer **26b**. The asymmetric induction is opposite to that observed for the substrate **16** which contains the free hydroxy group. The titanium tetraisopropoxide-promoted *tert*-butyl hydroperoxide oxidation of aryl sulfide **18** was highly diastereoselective and the selectivity could be enhanced still further by the use of an (*R*,*R*)-



Scheme 1 *Reagents and conditions:* i, (*S*)-(+)-valinol, cat. $ZnCl_2$, C_6H_5Cl, reflux; ii, TolSNa, THF, reflux; iii, LDA, THF, −78 °C; then TolS–STol; iv, (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol, cat. $ZnCl_2$, C_6H_5Cl, reflux; v, NEt_3, CH_2Cl_2; then TIPS triflate (Tol = *p*-tolyl)



Scheme 2 *Reagents and conditions:* i, (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol, glycerol, ethylene glycol, cat. K_2CO_3, 115 °C, 91%; ii, TBDMSCl, imidazole, DMF, 75%; iii, BuLi, TMEDA, Et_2O, TolS–STol, −65 °C, 13%; iv, TBAF, THF, 70%

(+)-DET-modified titanium reagent.[18] The oxidation of achiral aryl alkyl sulfides with the (*R*,*R*)-(+)-diethyltartrate-modified titanium reagent has been reported to afford the (*R*)-enantiomer of the sulfoxide selectively.[18]

We have independently prepared a series of diastereoisomerically pure sulfoxides. These compounds were prepared for two reasons. First, the further application of 4,5-dihydrooxazole sulfoxides as ligands would require compounds that were essentially diastereoisomerically pure and whose configuration at both chiral centres was known. Secondly, the ligands could be used as standards in the analysis of results from the oxidation chemistry.

The diastereoisomerically pure ligands were prepared by the application of technology first published by Andersen *et al.* in 1964.[19] Thus, the 4,5-dihydrooxazole **29** was *ortho*-lithiated with BuLi and quenched with the appropriate sulfinate ester to produce both compounds **23a** and **23b** in modest yield but as single diastereoisomers. The aryl sulfoxide **28b** was prepared in a similar manner to stereoisomers **23a** and **23b**. The dihydrooxazole **20** was protected as its TBDMS ether, *ortho*-lithiated, and the anion quenched with (−)-menthyl (*S*)-toluene-*p*-sulfinate; the protecting group was removed with

Table 1 Diastereoselective oxidations of sulfides **10**, **13** and **15**

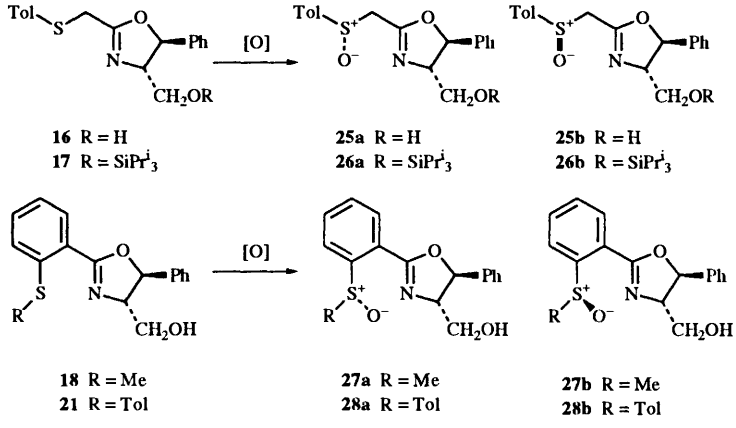
Sulfide	Conditions	Product	Ratio	Yield (%)
10	MCPBA, $CHCl_3$, −78 °C, 1.25 h	**22a**:**22b**	30:70[a]	94
10	$NaIO_4$, MeOH–water (1:1), 0 °C, 1 h	**22a**:**22b**	65:35	91
10	$NaBO_3 \cdot 4H_2O$, AcOH, 20 °C, 16 h	**22a**:**22b**	41:59	94
10	MMPP, EtOH–water (1:1), 50 °C, 1.5 h	**22a**:**22b**	38:62	90
10	Bu^{t}OOH, Ti(OPr^i)$_4$, CH_2Cl_2, −20 °C, 24 h	**22a**:**22b**	48:52	38
10	Bu^{t}OOH, Ti(OPr^i)$_4$, (+)-DET, CH_2Cl_2, −20 °C, 24 h	**22a**:**22b**	89:11	19
10	Bu^{t}OOH, Ti(OPr^i)$_4$, (−)-DET, CH_2Cl_2, −20 °C, 24 h	**22a**:**22b**	37:63	19
10	Bu^{t}OOH, VO(acac)$_2$, CH_2Cl_2, −20 °C, 24 h	**22a**:**22b**	85:15	77
13	MCPBA, $CHCl_3$, −78 °C, 1 h	**23a**:**23b**	28:72	57
15	MCPBA, $CHCl_3$, −78 °C, 1 h	**24a**:**24b**	37:63[b]	27
15	MCPBA, $CHCl_3$–MeOH (1:1), −78 °C, 1 h	**24a**:**24b**	37:63	26
15	MCPBA, $CHCl_3$–hexane (1:1), −78 °C, 1 h	**24a**:**24b**	26:74	48

[a] Ratio determined by capillary GLC using a BP1 column (SGE). [b] Ratio determined by inspection of the ^{1}H NMR spectrum.

Table 2 Diastereoselective oxidation of sulfides **16**–**18** and **21**

Sulfide	Conditions	Product	Ratio	Yield (%)
16	MCPBA, $CHCl_3$, −78 °C, 1 h	**25a**:**25b**	88:12[a]	11
16	MCPBA, $CHCl_3$–MeOH (1:1), −78 °C, 1 h	**25a**:**25b**	91:9	16
16	MCPBA, $CHCl_3$–hexane (1:1), −78 °C, 1 h	**25a**:**25b**	96:4	34
17	MCPBA, $CHCl_3$, −78 °C, 1 h	**26a**:**26b**	16:84	14
17	MCPBA, $CHCl_3$–MeOH (1:1), −78 °C, 1 h	**26a**:**26b**	42:58	15
17	MCPBA, $CHCl_3$–hexane (1:1), −78 °C, 1 h	**26a**:**26b**	31:69	24
18	MCPBA, MeOH, −70 °C, 1.25 h	**27a**:**27b**	57:43[b]	76
18	MCPBA, $CHCl_3$, −70 °C, 1 h	**27a**:**27b**	87:13	78
18	MCPBA, hexane–$CHCl_3$ (3:1), −70 °C, 1 h	**27a**:**27b**	96:4	76
18	Bu^{t}OOH, VO(acac)$_2$, CH_2Cl_2, −20 °C, 3 h	**27a**:**27b**	87:13	85
18	Bu^{t}OOH, Ti(OPr^i)$_4$, CH_2Cl_2, −20 °C, 24 h	**27a**:**27b**	97:3	41
18	Bu^{t}OOH, Ti(OPr^i)$_4$, L-DET, CH_2Cl_2, −20 °C, 24 h	**27a**:**27b**	99:1	32
21	MCPBA, $CHCl_3$, −20 °C, 1 h	**28a**:**28b**	80:20	90

[a] Ratio determined by inspection of the ^{1}H NMR spectrum. [b] Ratio determined by HPLC using a Bondapak C_{18} column (acetonitrile–water).



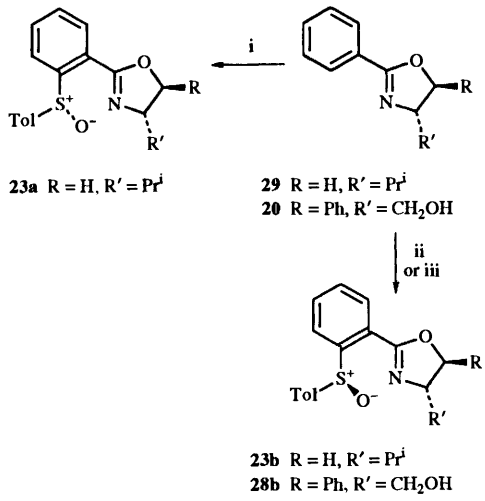
TBAF in THF to furnish compound **28b** in reasonable yield as a single diastereoisomer (Scheme 3). The crystal structures of compounds **23b** (Fig. 1) and **28b** (Fig. 2) clearly confirm the stereochemistry at the sulfur centres and are consistent with the fact that the reactions proceed with inversion at sulfur.

The sulfoxides **24a** and **24b** were also available in reasonable yield and as single diastereoisomers. Dihydrooxazole **30** was lithiated with LDA in THF and the anion was quenched with the appropriate sulfinate ester to afford sulfoxide **24a** or **24b**. In a similar manner, the diastereoisomers **26a** and **26b** were prepared from the dihydrooxazole **31**. The sulfoxides **26a** and **26b** were isolated as single diastereoisomers from the reaction mixture. The protecting group was removed from compounds **26a** and **26b** with TBAF in THF to liberate the free hydroxy group in the sulfoxides **25a** and **25b** (Scheme 4).

The diastereoisomerically pure sulfoxides allowed us to review our earlier oxidation chemistry and to determine the configuration of the major diastereoisomers of the products by analogy.

In the oxidations of compounds **10**, **13** and **15**, where the group at the 4-position of the 4,5-dihydrooxazole ring is an isopropyl group, only moderate levels of asymmetric induction were observed (up to 85:15), and the choice of reagent employed influenced the sense of asymmetric induction. We believe that there is too much flexibility in the transition states to provide highly asymmetric induction, and that rotation of the dihydrooxazole group leads to a poorly defined asymmetric environment (Fig. 3).

Much greater stereocontrol was observed in the oxidation of the hydroxymethyl series **16**–**18** and **21**. Thus, in the oxidation of the substrates **16**, **18** and **21** containing a free hydroxy group, there is a marked preference for the diastereoisomer where the approach of the oxidant is assisted by the presence of the hydroxy moiety. The importance of the hydroxy group in polar solvents appears to become less significant when MCPBA is used as the oxidant, presumably due to disruption of hydrogen bonding. Protection of the alcohol as its triisopropylsilyl (TIPS) ether leads to lower asymmetric induction (and in the opposite



23a R = H, R′ = Pr^i
29 R = H, R′ = Pr^i
20 R = Ph, R′ = CH_2OH
23b R = H, R′ = Pr^i
28b R = Ph, R′ = CH_2OH

Scheme 3 *Reagents and conditions:* i, BuLi, TMEDA, Et_2O, −65 °C; then (+)-menthyl (*R*)-toluene-*p*-sulfinate; ii, BuLi, TMEDA, −65 °C; then (−)-menthyl (*S*)-toluene-*p*-sulfinate; iii, TBDMSCl, imidazole, DMF; then BuLi, TMEDA, Et_2O, −65 °C; then (−)-menthyl (*S*)-toluene-*p*-sulfinate; then TBAF, THF

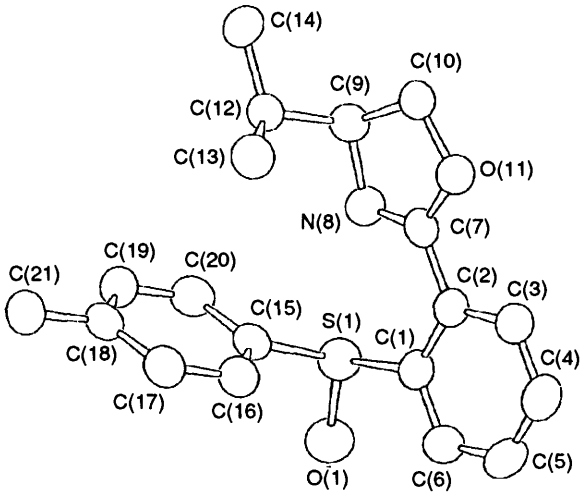


Fig. 1 X-Ray molecular structure of compound **23b**

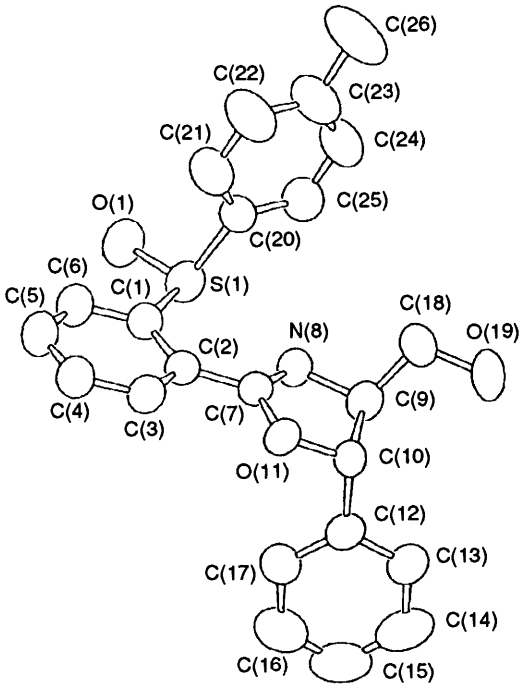
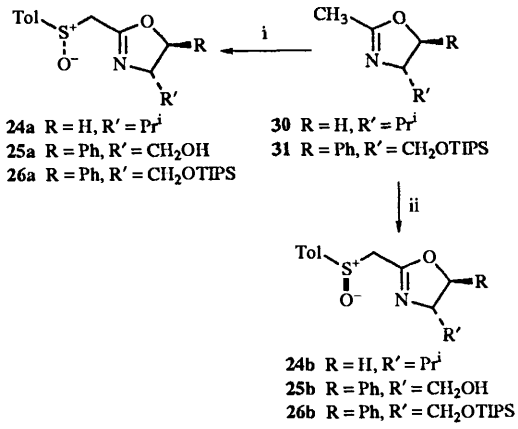


Fig. 2 X-Ray molecular structure of compound **28b**



24a R = H, R′ = Pr^i
25a R = Ph, R′ = CH_2OH
26a R = Ph, R′ = CH_2OTIPS
30 R = H, R′ = Pr^i
31 R = Ph, R′ = CH_2OTIPS
24b R = H, R′ = Pr^i
25b R = Ph, R′ = CH_2OH
26b R = Ph, R′ = CH_2OTIPS

Scheme 4 *Reagents and conditions:* i, LDA, THF, −78 °C; then (+)-menthyl (*R*)-toluene-*p*-sulfinate; ii, LDA, THF, −78 °C; then (−)-menthyl (*S*)-toluene-*p*-sulfinate (**26a**:**26b** to **25a**:**25b**); then TBAF, THF

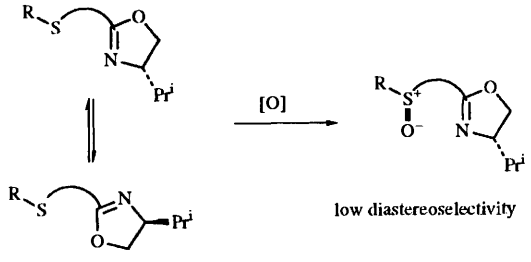


Fig. 3

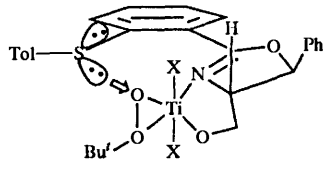


Fig. 4

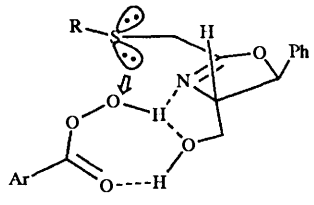


Fig. 5

sense), again indicating the importance of the free hydroxy group for good stereocontrol.

We speculate that co-ordination of the incoming reagent to both the hydroxy group and the dihydrooxazole nitrogen is required for good stereocontrol. A working model for the titanium-promoted oxidation of the dihydrooxazole **21** is indicated in Fig. 4. A working model for the MCPBA-promoted oxidation of the dihydrooxazole **16** is indicated in Fig. 5.

The involvement of the nitrogen atom is included to rationalise the high stereocontrol provided for both 1,5- and 1,6-asymmetric induction processes, which are notorious for providing only moderate diastereoselectivity.[20] The bidentate association to the incoming reagent provides a more tightly controlled environment in which asymmetric induction can occur efficiently. Research is in progress to try to confirm the proposed models for chirality transfer.

In conclusion, we have shown that enantiomerically pure 4,5-dihydrooxazoles are able to direct the oxidation of sulfides to

sulfoxides with reasonable levels of diastereocontrol. When the hydroxymethyl-substituted dihydrooxazole **18** was treated with *tert*-butyl hydroperoxide and titanium tetraisopropoxide the diastereocontrol was very high (97:3), and this diastereoselectivity could be enhanced still further by the co-operative effect of (*R*,*R*)-(+)-DET.

Substrates **15**–**17** provide examples of 1,5-asymmetric induction, and sulfides **10**, **13**, **18** and **21** provide examples of 1,6-asymmetric induction.

We have reported the use of 4,5-dihydrooxazole/sulfoxide systems as ligands for asymmetric catalysis elsewhere and are continuing to examine these ligands in a variety of reactions.[10]

Experimental

Commercially available solvents and reagents were used throughout without further purification, except for those detailed below or in previous publications.[9] ^{1}H and ^{13}C NMR spectra were recorded using a Bruker AC-250 instrument or a Bruker DPX-400 instrument. *J*-Values are in Hz. Capillary GLC was performed using a BP1 column (SGE). Analysis by HPLC was performed using a Bondapak C_{18} column, eluted with acetonitrile–water (1:3) at a flow rate of 1.2 cm^3 min^{-1} and with monitoring at a wavelength of 254 nm. IR spectra were recorded in the range 4000–600 cm^{-1} using a Nicolet FT-205 spectrometer, with internal calibration. High and low resolution mass spectra were recorded on a Kratos MS80 instrument. $[\alpha]_D$ values were measured using an Optical Activity AA100 polarimeter and are given in 10^{-1} deg cm^2 g^{-1}. Light petroleum refers to the fraction with distillation range 40–60 °C.

The preparation of compounds **10**,[9] **12**,[10] **13**[10] and **20**[21] has been detailed elsewhere.

[4-(Methylphenyl)sulfanyl]acetonitrile 14

A solution of acetonitrile (0.2 g, 4.87 mmol) in THF (2 cm^3) was cooled to −78 °C under nitrogen. LDA (9.7 cm^3, 14.6 mmol as a 1.5 mol dm^{-3} solution in THF) was added dropwise and the mixture was stirred for 1 h at −78 °C. To this mixture was added di-*p*-tolyl disulfide (2.4 g, 9.7 mmol) as a solution in THF (3 cm^3) over a period of 5 min. The solution was stirred at −78 °C for 2 h before being allowed to warm to ambient temperature. The reaction mixture was washed with saturated aq. ammonium chloride (20 cm^3) and the aqueous phase was washed with dichloromethane (5 × 30 cm^3). The combined organic phases were dried (Na_2SO_4), and concentrated under reduced pressure to leave an oily residue. This was purified by flash chromatography [light petroleum–diethyl ether (4:1)] to yield the *title compound* as an oil (583 mg, 73%) (Found: M$^+$, 163.0418. C_9H_9NS requires M, 163.0456); ν_{max}(neat)/cm^{-1} 2261 (CN); δ_H(250 MHz; $CDCl_3$) 7.49–7.18 (4 H, m, ArH), 3.51 (2 H, s, CH_2) and 2.36 (3 H, s, CH_3); δ_C(63 MHz; $CDCl_3$) 139.5, 133.1, 130.3 and 128.3 (arom C), 116.6 (CN), 22.0 (CH_2) and 21.1 (CH_3).

General procedure for the formation of 4,5-dihydrooxazoles using $ZnCl_2$ catalysis

In a 50 cm^3 Schlenk flask, zinc chloride (0.5 mmol) was melted under high vacuum and cooled under nitrogen to room temperature. Chlorobenzene (30 cm^3) was then added to the flask followed by the appropriate nitrile (10 mmol) and amino alcohol (15 mmol). The mixture was heated under reflux for 48 h, after which time the solvent was removed under reduced pressure to give an oily residue, which was dissolved in dichloromethane (30 cm^3). The solution was washed with water (3 × 20 cm^3) and the aqueous phase was back-extracted with dichloromethane (30 cm^3). The combined organic phases were dried (Na_2SO_4), and then concentrated under reduced pressure to give an oily residue, which was purified by flash chromatography to afford the product.

(4*S*)-4-Isopropyl-2-[(4-methylphenyl)sulfanylmethyl]-4,5-dihydro-1,3-oxazole 15

A *pale yellow oil* (80%) (Found: M$^+$, 249.1189. $C_{14}H_{19}NOS$ requires M, 249.1187); $[\alpha]_D^{20}$ −26.7 (*c* 0.374, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1665 (C=N); δ_H(250 MHz; $CDCl_3$) 7.36–7.08 (4 H, m, ArH), 4.25 (1 H, m, C*H*H′O), 4.00–3.72 (2 H, m, CH*H*′O and CHN), 3.60 (1 H, d, *J* 14.3, C*H*H′S), 3.53 (1 H, d, *J* 14.3, CH*H*′S), 2.31 (3 H, s, ArCH_3), 1.73–1.58 [1 H, m, C*H*(CH_3)$_2$], 0.88 (3 H, d, *J* 6.7, CHCH_3) and 0.81 (3 H, d, *J* 6.7, CHCH_3); δ_C(63 MHz; $CDCl_3$) 163.8 (C=N), 137.2, 130.8 and 129.6 (arom C), 72.3 (CHN), 70.6 (CH_2O), 32.4 (Ar*C*H$_3$), 31.6 (CH_2S), 20.9 [*C*H(CH_3)$_2$], 18.6 (CH*C*H$_3$) and 17.9 (CH*C*H$_3$).

(4*S*,5*S*)-4-Hydroxymethyl-2-[(4-methylphenyl)sulfanylmethyl]-5-phenyl-4,5-dihydro-1,3-oxazole 16

A *solid* (91%), mp 111–112 °C (Found: M$^+$, 313.1101. $C_{18}H_{19}NO_2S$ requires M, 313.1136); $[\alpha]_D^{20}$ +13.8 (*c* 0.362, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 3373 (OH) and 1651 (C=N); δ_H(250 MHz; $CDCl_3$) 7.41–7.12 (9 H, m, ArH), 5.35 (1 H, d, *J* 7.5, CHO), 4.07–4.01 (1 H, m, CHN), 3.89–3.78 (3 H, m, C*H*H′OH and CH_2S), 3.57 (1 H, dd, *J* 12.0 and 6.2, CH*H*′OH), 2.33 (3 H, s, ArCH_3) and 1.57 (1 H, br s, OH); δ_C(63 MHz; $CDCl_3$) 168.2 (C=N), 139.2, 137.8, 131.4, 130.4, 129.9, 129.8, 129.2, 128.8, 128.6, 128.3, 127.6 and 125.8 (arom C), 83.8 (CHO), 75.4 (CHN), 38.6 (CH_2OH), 31.6 (CH_2S) and 21.0 (Ar*C*H$_3$).

(4*S*,5*S*)-2-[(4-Methylphenyl)sulfanylmethyl]-5-phenyl-4-(triisopropylsiloxymethyl)-4,5-dihydro-1,3-oxazole 17

(4*S*,5*S*)-4-Hydroxymethyl-2-[(4-methylphenyl)sulfanylmethyl]-5-phenyl-4,5-dihydro-1,3-oxazole 16 (900 mg, 2.85 mmol) was dissolved in dichloromethane (30 cm^3). The solution was treated with triethylamine (348 mg, 3.44 mmol) and stirred for 5 min at ambient temperature. Triisopropylsilyl trifluoromethanesulfonate (1.05 g, 3.44 mmol) was added to the mixture in one portion and the solution was stirred for a further 15 min at room temperature. The mixture was washed with saturated aq. ammonium chloride (50 cm^3) and the aqueous phase was washed with dichloromethane (3 × 50 cm^3). The combined organic phases were dried (Na_2SO_4), and concentrated under reduced pressure to produce an oily residue. This was purified by flash chromatography [light petroleum–diethyl ether (2:1)] to yield the *title compound* as an oil (1.24 g, 93%) (Found: M$^+$, 469.2472. $C_{27}H_{39}NO_2SSi$ requires M, 469.2471); $[\alpha]_D^{20}$ −17.5 (*c* 0.286, $CHCl_3$), ν_{max}(neat)/cm^{-1} 1654 (C=N); δ_H(250 MHz; $CDCl_3$) 7.40–7.09 (9 H, m, ArH), 5.48 (1 H, d, *J* 5.9, CHO), 4.11 (1 H, m, CHN), 4.00 (1 H, dd, *J* 9.9 and 3.9, C*H*H′O), 3.84 (1 H, d, *J* 14.5, C*H*H′S), 3.77 (1 H, d, *J* 14.5, CH*H*′S), 3.64 (1 H, m, CH*H*′O), 2.32 (3 H, s, ArCH_3) and 1.13–0.99 (21 H, m, 3 × Pr^i); δ_C(63 MHz; $CDCl_3$) 164.6 (C=N), 141.1, 137.1, 136.1, 130.9, 128.6, 127.9, 127.3 and 125.4 (arom C), 84.2 (CHO), 76.6 (CHN), 65.3 (CH_2S), 31.8 (CH_2O), 21.1 (Ar*C*H$_3$), 17.7 [CH(*C*H$_3$)$_2$] and 11.9 (CH).

(4*S*,5*S*)-4-Hydroxymethyl-2-[2-(methylsulfanyl)phenyl]-5-phenyl-4,5-dihydro-1,3-oxazole 18

2-(Methylsulfanyl)benzonitrile **9** (1.49 g, 10 mmol) was added to a mixture of (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol (1.52 g, 9.1 mmol), potassium carbonate (0.25 g, 1.8 mmol), ethylene glycol (8 cm^3) and glycerol (4 cm^3) in one portion and the mixture was stirred at 115 °C for 18 h. The reaction mixture was cooled to ambient temperature before being diluted with distilled water (30 cm^3). The resulting white solution was extracted with dichloromethane (3 × 30 cm^3) and the combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography [diethyl ether–light petroleum (3:2)], to afford the *title compound* as colourless solid (1.28 g, 47%), mp 105–107 °C (Found: M$^+$, 299.0979; C, 67.7; H, 5.55; N, 4.7%. $C_{17}H_{17}NO_2S$

requires M, 299.0979; C, 68.10; H, 5.72; N, 4.68%); $[\alpha]_D^{25}$ 7.41 (*c* 4.7, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 3500 (OH) and 1644 (C=N); δ_H(250 MHz; $CDCl_3$) 7.87 (1 H, dd, *J* 1.5 and 7.7, ArH), 7.32 (7 H, m, ArH), 7.17 (1 H, m, ArH), 5.47 (1 H, d, *J* 7.3, CHO), 4.39 (1 H, m, CHN), 4.08 (1 H, m, C*H*H'OH), 3.76 (1 H, m, CH*H'*OH), 2.47 (3 H, s, CH_3S) and 2.38 (1 H, m, OH); δ_C(63 MHz; $CDCl_3$) 163.6 (C=N), 140.9, 140.7, 131.2, 130.2, 130.1, 128.8, 128.3, 125.7, 124.9, 124.6 and 123.8 (arom C), 82.2 (CHO), 77.3 (CHN), 63.9 (CH_2OH) and 15.9 (CH_3S); *m*/*z* (EI) 299 (23%), 284 (27), 268 (18), 166 (42), 151 (100) and 91 (80).

(4*S*,5*S*)-4-Hydroxymethyl-2-[2-(4-methylphenylsulfanyl)-phenyl]-5-phenyl-4,5-dihydro-1,3-oxazole 21

A mixture of (4*S*,5*S*)-4-hydroxymethyl-2,5-diphenyl-4,5-dihydro-1,3-oxazole **20** (1.5 g, 6 mmol), *tert*-butyl(chloro)-dimethylsilane (0.98 g, 6.5 mmol) and imidazole (0.89 g, 13 mmol) in dimethylformamide (DMF) (15 cm^3) was stirred under nitrogen for 16 h. After aqueous work-up, (4*S*,5*S*)-4-*tert*-butyldimethylsiloxymethyl-2,5-diphenyl-4,5-dihydro-1,3-oxazole was isolated as a yellow oil. Butyllithium (0.28 cm^3, 0.45 mmol) was added to a stirred solution of this silyl ether (150 mg, 0.4 mmol) and tetramethylethylenediamine (TMEDA) (142 mg, 1.2 mmol) in THF (4 cm^3) at −65 °C. The resulting brown solution was stirred at −65 °C for 15 min before the addition of a solution of di-*p*-tolyl disulfide (100 mg, 0.4 mmol) in THF (3 cm^3). Upon complete addition the reaction mixture was allowed to warm to ambient temperature and was stirred under nitrogen for 16 h. The reaction mixture was then diluted with diethyl ether (15 cm^3) and washed with distilled water (3 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure, to yield a pale yellow oil (26 mg, 13%). Removal of the *tert*-butyldimethylsilyl protecting group was effected by stirring with a solution of TBAF (0.014 cm^3, 0.05 mmol) in THF (3 cm^3) at room temperature. After aqueous work-up and purification by flash chromatography [ethyl acetate–light petroleum (7:3)] the *title compound* was isolated as a solid (12 mg, 63%), mp 112–114 °C (Found: M$^+$, 375.1293. $C_{23}H_{21}NO_2S$ requires M, 375.1293); $[\alpha]_D^{25}$ −17.64 (*c* 1.7, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 3530 (OH) and 1643 (C=N); δ_H(250 MHz; $CDCl_3$) 7.87 (1 H, dd, *J* 7.8 and 1.4, ArH), 7.39 (6 H, m, ArH), 7.23 (1 H, d, *J* 8.0, ArH), 7.22 (3 H, m, ArH), 7.13 (1 H, m, ArH), 6.85 (1 H, d, *J* 8.1, ArH), 5.53 (1 H, d, *J* 7.4, C*H*O), 4.44 (1 H, m, CHN), 4.12 (1 H, dd, *J* 11.6 and 3.4, C*H*H'OH), 3.79 (1 H, m, CH*H'*OH) and 2.40 (3 H, s, $ArCH_3$); δ_C(63 MHz; $CDCl_3$) 163.6 (C=N), 141.6, 140.6, 139.2, 135.3, 131.1, 130.5, 130.0, 129.1, 128.8, 128.3, 127.4, 125.8, 124.6 and 124.4 (arom C), 82.4 (CHO), 77.4 (CHN), 63.9 (CH_2OH) and 21.3 ($ArCH_3$); *m*/*z* (EI) 375 (50%), 344 (25), 238 (60) and 91 (100).

General procedures for the oxidation of (4*S*)-4-isopropyl-2-[2-(methylsulfanyl)phenyl]-4,5-dihydro-1,3-oxazole 10 and (4*S*)-4-isopropyl-2-[2-(4-methylphenylsulfanyl)phenyl]-4,5-dihydro-1,3-oxazole 13

Oxidant: **MCPBA**. A solution of MCPBA (0.43 mmol) in chloroform (3 cm^3) was added dropwise to a solution of a sulfide (0.43 mmol) in chloroform at −78 °C and the mixture was stirred until the reaction was deemed to have gone to completion by TLC. The reaction mixture was then diluted with dichloromethane (10 cm^3) and washed with saturated aq. sodium carbonate (2 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (8:2)] afforded the title compound. Diastereoisomeric ratios were determined by capillary GLC on a BP1 column (SGE).

(4S,R_S/S_S)-4-*Isopropyl*-2-[2-(*methylsulfinyl*)*phenyl*]-4,5-*dihydro*-1,3-*oxazole* **22a**:**22b**.—(94%) as a *pale yellow oil* (Found: M$^+$, 251.0 979. $C_{13}H_{17}NO_2S$ requires M, 251.0979) (**22a**:**22b** 89:11); $[\alpha]_D^{25}$ +180.3 (*c* 0.30, $CHCl_3$) (**22a**:**22b** 37:63); $[\alpha]_D^{25}$ +100.2 (*c*, 0.35, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1651 (C=N) and 1061 (S=O); δ_H(250 MHz; $CDCl_3$) 8.27 (1 H, dd, *J* 7.8 and 1.1, ArH), 7.87 (1 H, dd, *J* 7.7 and 1.1, ArH), 7.72 (1 H, dd, *J* 7.6 and 1.2, ArH), 7.53 (1 H, dd, *J* 7.6 and 1.2, ArH), 4.42 (1 H, m, CHN), 4.12 (2 H, m, CH_2O), 2.91 (3 H, s, CH_3S), 1.78 [1 H, m, C*H*(CH_3)$_2$], 1.03 (3 H, d, *J* 6.7, CHC*H*$_3$) and 0.98 (3 H, d, *J* 6.7, CHC*H*$_3$; δ_C(63 MHz; $CDCl_3$) 160.2 (C=N), 148.1, 131.8, 129.9, 129.1, 124.5 and 123.9 (arom C), 73.5 (CHN), 70.5 (CH_2O), 43.9 (CH_3S=O), 33.1 (*C*HCH$_3$), 19.0 (CH*C*H$_3$) and 18.8 (CH*C*H$_3$); *m*/*z* (EI) 251 (15%), 236 (100), 203 (50) and 136 (52).

(4S,R_S/S_S)-4-*Isopropyl*-2-[2-(4-*methylphenylsulfinyl*)*phenyl*]-4,5-*dihydro*-1,3-*oxazole* **23a**:**23b**.—(57%) as a *pale yellow oil* (Found: M$^+$, 327.12929. $C_{19}H_{21}NO_2S$ requires M, 327.1293); ν_{max}(neat)/cm^{-1} 1649 (C=N) and 1054 (S=O); δ_H(250 MHz; $CDCl_3$) 7.54–8.34 (4 H, m, ArH), 7.53 (2 H, d, *J* 7.9, ArH), 7.15 (2 H, d, *J* 7.9, ArH), 4.33 (1 H, m, CHN), 4.06 (2 H, m, CH_2O), 2.32 (3 H, s, ArC*H*$_3$), 1.76 [1 H, m, C*H*(CH_3)$_2$], 0.89 (3 H, d, *J* 6.7, CHC*H*$_3$) and 0.73 (3 H, d, *J* 6.7, CHC*H*$_3$); δ_C(63 MHz; $CDCl_3$) 160.6 (C=N), 146.9, 143.8, 140.8, 131.7, 130.1, 129.6, 129.4, 126.4, 125.5 and 125.2 (arom C), 73.2 (CHN), 69.8 (CH_2O), 32.4 (*C*HCH$_3$), 21.2 (Ar*C*H$_3$), 18.8 (CH*C*H$_3$) and 17.8 (CH*C*H$_3$); *m*/*z* (EI) 327 (100%) and 227 (40).

Oxidant: **sodium metaperiodate**. Sodium metaperiodate (49 mg, 0.23 mmol) was added to a solution of (4*S*)-4-isopropyl-2-[2-(methylsulfanyl)phenyl]-4,5-dihydro-1,3-oxazole **10** (53 mg, 0.23 mmol) in methanol–water, (1:1) at 0 °C. After 2 h the reaction mixture was diluted with dichloromethane (10 cm^3) and washed with distilled water (3 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (4:1)] yielded (4*S*,R_S/S_S)-4-isopropyl-2-[2-(methylsulfinyl)-phenyl]-4,5-dihydro-1,3-oxazole **22** as a pale yellow oil (51 mg, 91%). All data were consistent with those detailed above.

Oxidant: **magnesium monoperoxyphthalate**. A solution of MMPP (60 mg, 0.097 mmol) in distilled water (5 cm^3) was added to a stirred solution of (4*S*)-4-isopropyl-2-[2-(methylsulfanyl)phenyl]-4,5-dihydro-1,3-oxazole **10** (41 mg, 0.175 mmol) in ethanol (5 cm^3) and the resulting mixture was stirred for 1.5 h at 50 °C. The reaction mixture was then diluted with diethyl ether (20 cm^3) and washed with saturated aq. sodium carbonate (3 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (4:1)] yielded (4*S*,R_S/S_S)-4-isopropyl-2-[2-(methylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole **22** as a pale yellow oil (41 mg, 90%). All data were consistent with those detailed above.

Oxidant: **sodium perborate tetrahydrate**. Powdered sodium perborate tetrahydrate (20 mg, 0.13 mmol) was added to a solution of (4*S*)-4-isopropyl-2-[2-(methylsulfanyl)phenyl]-4,5-dihydro-1,3-oxazole **10** (30 mg, 0.13 mmol) in glacial acetic acid (2 cm^3). The reaction mixture was stirred at room temperature for 16 h before being poured onto 10% hydrochloric acid (10 cm^3). The aqueous solution was extracted with diethyl ether (3 × 15 cm^3) and the combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (4:1)] yielded (4*S*,R_S/S_S)-4-isopropyl-2-[2-(methylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole **22** as a pale yellow oil (30 mg, 94%). All data were consistent with those detailed above.

Oxidant: ***tert*-butyl hydroperoxide with vanadyl acetylacetonate**. *tert*-Butyl hydroperoxide (0.055 cm^3, 0.21 mmol) was added to a solution of (4*S*)-4,5-dihydro-4-isopropyl-2-[2-(methylsulfanyl)phenyl]-1,3-oxazole **10** (50 mg, 0.21 mmol) and

vanadyl acetylacetonate (5.9 mg, 0.021 mmol) in dichloromethane under nitrogen at −20 °C. The reaction mixture was stirred at −20 °C for 1 h before being kept in a freezer at −20 °C for 23 h. The reaction mixture was diluted with dichloromethane (15 cm^3) and washed with saturated aq. sodium carbonate (2 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (4:1)] yielded (4*S*,R_S/S_S)-4-isopropyl-2-[2-(methylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole **22** as a pale yellow oil (40 mg, 77%). All data were consistent with those detailed above.

Oxidant: *tert*-butyl hydroperoxide with titanium tetraisopropoxide. Titanium tetraisopropoxide (0.43 mmol) was added to a solution of diethyl tartrate (0.86 mmol) in dichloromethane (3 cm^3) at 20 °C under nitrogen. Distilled water (0.43 mmol) was added and the pale yellow solution was stirred until it became homogeneous. A solution of (4*S*)-4-isopropyl-2-[2-(methylsulfanyl)phenyl]-4,5-dihydro-1,3-oxazole **10** (0.43 mmol) in dichloromethane (3 cm^3) was added and the resultant mixture was cooled to −30 °C. *tert*-Butyl hydroperoxide was added in one portion and the reaction mixture was stirred for 1 h at −30 °C before being transferred to a freezer and kept at −20 °C for 23 h. Distilled water (10 mol equiv.) was added and the reaction mixture was stirred for 1 h at −20 °C, before being allowed to warm to ambient temperature.

The resulting gel was filtered through Celite and the filter was washed with dichloromethane (4 × 20 cm^3). The filtrate was vigorously stirred in a mixture of 2 mol dm^{-3} sodium hydroxide (40 cm^3) and saturated aq. sodium chloride (30 cm^3). The organic phase was separated, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (4:1)] yielded (4*S*,R_S/S_S)-4-isopropyl-2-[2-(methylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole **22** as a pale yellow oil (20 mg, 19%). The reaction was performed with both enantiomers of diethyl tartrate and also in the absence of a ligand (yield 77%). All data were consistent with those detailed above.

General procedure for the oxidation of (4*S*)-4-isopropyl-2-[(4-methylphenyl)methylsulfanyl]-4,5-dihydro-1,3-oxazole 15 by MCPBA

A mixture of (4*S*)-4-isopropyl-2-[(4-methylphenyl)sulfanylmethyl]-4,5-dihydro-1,3-oxazole **15** (100 mg, 0.4 mmol) and 50% MCPBA (138 mg, 0.8 mmol) was stirred for 1 h in the appropriate solvent at −78 °C. The reaction mixture was washed with conc. aq. sodium hydrogen carbonate (20 cm^3). The aqueous layer was washed with dichloromethane (20 cm^3) and the combined organics were dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue was purified by flash chromatography (ethyl acetate) to yield (4*S*,S_S/R_S)-4-isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole **24** as a pale yellow oil. Solvents: chloroform (yield 27%), chloroform–methanol (1:1) (yield 26%) and chloroform–hexane (1:1) (yield 48%). Diastereoisomeric ratios were determined by inspection of the ^1H NMR spectrum. All data were consistent with a mixture of (4*S*,S_S)-4-isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole **24a** and (4*S*,R_S)-4-isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole **24b** which is detailed below.

General procedure for the preparation of (4*S*,R_s)-4-isopropyl-2-[2-(4-methylphenylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole 23a and (4*S*,S_s)-4-isopropyl-2-[2-(4-methylphenylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole 23b

To a solution of (4*S*)-4-isopropyl-2-phenyl-4,5-dihydro-1,3-oxazole **29** (0.32 g, 1.7 mmol) and TMEDA (0.59 g, 5.1 mmol) in diethyl ether (4 cm^3) at −65 °C was added butyllithium (1.2 cm^3, 1.9 mmol) under an inert atmosphere. The resulting red solution was stirred at −65 °C for 2 h. A solution of menthyl toluene-*p*-sulfinate (0.5 g, 1.7 mmol) in diethyl ether (10 cm^3) was added slowly to the reaction mixture at −65 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 16 h under nitrogen. The reaction mixture was diluted with diethyl ether and washed successively with distilled water (2 × 15 cm^3) and brine (15 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford a yellow oil. Purification by flash chromatography [diethyl ether–light petroleum (7:3)] yielded the title compounds.

(4*S*,R_S)-4-Isopropyl-2-[2-(4-methylphenylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole 23a. A pale yellow oil (100 mg, 18%) (Found: M^+, 327.129 29. Calc. for $C_{19}H_{21}NO_2S$: M, 327.1293); $[\alpha]_D^{25}$ 156.5 (*c* 0.25, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1654 (C=N) and 1054 (S=O); δ_H(250 MHz; $CDCl_3$) 8.37 (1 H, dd, *J* 8.0 and 1.1, ArH), 7.85 (1 H, dd, *J* 7.7 and 1.2, ArH), 7.72 (1 H, dd, *J* 7.5 and 1.3, ArH), 7.62 (2 H, d, *J* 8.2, ArH), 7.51 (1 H, dd, *J* 7.5 and 1.3, ArH), 7.16 (2 H, d, *J* 8.3, ArH), 4.31 (1 H, m, CHN), 4.04 (2 H, m, CH_2O), 2.32 (3 H, s, ArCH_3), 1.78 [1 H, m, C*H*$(CH_3)_2$], 1.06 (3 H, d, *J* 6.7, CHCH_3) and 0.97 (3 H, d, *J* 6.7, CHCH_3); δ_C(63 MHz; $CDCl_3$) 160.2 (C=N), 146.9, 143.9, 140.9, 131.7, 130.1, 129.7, 129.5, 129.4, 126.6, 125.5, 125.3 and 124.9 (arom C), 73.3 (CHN), 70.5 (CH_2O), 33.1 (ArCH_3), 21.3 [*C*H$(CH_3)_2$], 18.8 (CHCH_3) and 18.7 (CHCH_3); *m*/*z* (EI) 327 (100%), 227 (27), 160 (40) and 132 (40).

(4*S*,S_S)-4-Isopropyl-2-[2-(4-methylphenylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole 23b. A solid (178 mg, 32%), mp 105–107 °C (Found: M^+, 327.12929. Calc. for $C_{19}H_{21}NO_2S$: M, 327.1293; C, 69.69; H, 6.25; N, 4.28%); $[\alpha]_D^{25}$ −251.2 (*c* 0.66, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 1649 (C=N) and 1054 (S=O); δ_H(250 MHz; $CDCl_3$) 8.33 (1 H, dd, *J* 8.0 and 1.1, ArH), 7.91 (1 H, dd, *J* 7.7 and 1.2, ArH), 7.62 (1 H, dd, *J* 7.5 and 1.3, ArH), 7.52 (2 H, d, *J* 8.2, ArH), 7.51 (1 H, dd, *J* 7.5 and 1.3, ArH), 7.16 (2 H, d, *J* 8.3, ArH), 4.34 (1 H, m, CHN), 4.08 (2 H, m, CH_2O), 2.32 (3 H, s, ArCH_3), 1.76 [1 H, m, C*H*$(CH_3)_2$], 0.89 (3 H, d, *J* 6.7, CHCH_3) and 0.73 (3 H, d, *J* 6.7, CHCH_3); δ_C(63 MHz; $CDCl_3$) 160.7 (C=N), 146.2, 143.6, 140.9, 131.8, 130.2, 130.2, 129.7, 129.4, 126.4, 125.6, 125.3 and 124.9 (arom C), 73.3 (CHN), 70.5 (CH_2O), 33.1 (ArCH_3), 21.3 [*C*H$(CH_3)_2$], 18.8 (CHCH_3) and 18.7 (CHCH_3); *m*/*z* (EI) 327 (100%) and 227 (40).

Crystal structure of (4*S*,S_S)-4-isopropyl-2-[2-(4-methylphenylsulfinyl)phenyl]-4,5-dihydro-1,3-oxazole 23b

Crystals suitable for X-ray analysis were prepared by recrystallisation of compound **23b** from warm hexane.

Crystal data.—$C_{19}H_{21}NO_2S$, M = 327.44. Orthorhombic, *a* = 13.929(1), *b* = 18.830(1), *c* = 6.440(2) Å, *V* = 1689.1(5) $Å^3$ (by least squares refinement on diffractometer angles for 20 automatically centred reflections, λ = 1.541 78 Å), space group $P2_12_12_1$ (#19), *Z* = 4, D_x = 1.288 g cm^{-3}. Clear, prism crystals. Crystal dimensions: 0.19 × 0.20 × 0.35 mm, μ(Cu-Kα) = 17.26 cm^{-1}.

Data collection and processing.[22]—Rigaku AFC7S diffractometer using ω scans. Graphite-monochromated Cu-Kα radiation; 1504 reflections measured ($0 < 2\theta < 120.1°$, $+h, k, l$), 1414 with $I > 3.00\sigma(I)$. An empirical absorption correction was applied (transmission factors: 0.9477–1.0000). The data were corrected for Lorentz and polarisation factors.

Structure analysis and refinement.—Direct methods. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The maximum peak in the final ΔF map was 0.20 e $Å^{-3}$. Final *R*- and R_w-values are 0.032 and 0.029. Programs and computers used and sources of scattering factor data are given in ref. 22. The X-ray molecular structure is presented in Fig. 1. Atomic coordinates, bond lengths, thermal parameters and angles have

been deposited at the Cambridge Crystallographic Data Centre.†

General procedure for the preparation of (4*S*,S_S)-4-isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole 24a and (4*S*,R_S)-4-isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole 24b

A 1.5 mol dm^{-3} solution of LDA (1.74 cm^3, 2.61 mmol) was added slowly to a solution of (4*S*)-4-isopropyl-2-methyl-4,5-dihydro-1,3-oxazole **31** in dry THF (5 cm^3) at −78 °C under an inert atmosphere. The resulting solution was stirred at −78 °C for 30 min before the slow addition of the appropriate menthyl toluene-*p*-sulfinate (384 mg, 1.3 mmol) in THF (5 cm^3). The mixture was stirred for 2 h before being allowed to warm to ambient temperature and quenched with saturated aq. ammonium chloride (20 cm^3). The mixture was diluted with diethyl ether (30 cm^3) and washed with saturated aq. ammonium chloride (20 cm^3). The aqueous phase was washed with diethyl ether (2 × 20 cm^3) and the combined organics were dried ($MgSO_4$), and concentrated under reduced pressure to yield a dark yellow oil. The crude product was purified by flash chromatography (ethyl acetate) to afford the *title compound*.

(4*S*,S_S)-4-Isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole 24a. A *pale yellow oil* (76%) (Found: M^+, 265.1140. $C_{14}H_{19}NO_2S$ requires M, 265.1136); $[\alpha]_D^{20}$ +100.0 (*c* 0.40, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1665 (C=N) and 1053 (S=O); δ_H(250 MHz, $CDCl_3$) 7.57 (2 H, d, *J* 8.2, ArH), 7.32 (2 H, d, *J* 8.0, ArH), 4.26 (1 H, m, CHN), 3.96–3.79 [3 H, m, CH_2O and C*H*H′S(O)], 3.64 [1 H, d, *J* 14.3, CH*H*′S(O)], 2.42 (3 H, s, ArCH_3), 1.65 [1 H, m, C*H*(CH_3)$_2$], 0.91 (3 H, d, *J* 6.7, CHCH_3) and 0.83 (3 H, d, *J* 6.7, CHCH_3); δ_C(63 MHz; $CDCl_3$) 158.6 (C=N), 143.1, 140.0, 129.8 and 124.2 (arom C), 72.5 (CHN), 70.8 (CH_2O), 55.8 [$CH_2S(O)$], 32.5 (ArCH_3), 21.3 [*C*H(CH_3)$_2$], 18.7 (CH*C*H_3) and 18.1 (CH*C*H_3).

(4*S*,R_S)-4-Isopropyl-2-[(4-methylphenyl)sulfinylmethyl]-4,5-dihydro-1,3-oxazole 24b. A *pale yellow oil* (47%) (Found: M^+, 265.1140); $[\alpha]_D^{20}$ −222.2 (*c* 0.27, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1632 (C=N) and 1034 (S=O); δ_H(250 MHz; $CDCl_3$) 7.58 (2 H, d, *J* 8.2, ArH), 7.33 (2 H, d, *J* 8.0, ArH), 4.22 (1 H, m, CHN), 3.96–3.83 [3 H, m, CH_2O and C*H*H′S(O)], 3.60 [1 H, d, *J* 14.3, CH*H*′S(O)], 2.42 (3 H, s, ArCH_3), 1.64 [1 H, m, C*H*(CH_3)$_2$], 0.89 (3 H, d, *J* 6.7, CHCH_3) and 0.84 (3 H, d, *J* 6.7, CHCH_3); δ_C(63 MHz; $CDCl_3$) 158.8 (C=N), 142.8, 140.2, 129.9 and 124.3 (arom C), 72.4 (CHN), 70.8 (CH_2O), 56.0 [$CH_2S(O)$], 32.4 (ArCH_3), 21.4 [*C*H(CH_3)$_2$], 18.6 (CH*C*H_3) and 18.1 (CH*C*H_3).

General procedure for the oxidation of (4*S*,5*S*)-4-hydroxymethyl-2-[(4-methylphenyl)sulfanylmethyl]-5-phenyl-4,5-dihydro-1,3-oxazole 16 and (4*S*,5*S*)-2-[(4-methylphenyl)sulfanylmethyl]-5-phenyl-4-triisopropylsiloxymethyl-4,5-dihydro-1,3-oxazole 17 with MCPBA

A mixture of sulfide **16** or **17** (0.4 mmol) and 50% MCPBA (138 mg, 0.8 mmol) was stirred for 1 h in the appropriate solvent at −78 °C. The reaction mixture was washed with conc. aq. sodium hydrogen carbonate (20 cm^3). The aqueous layer was washed with dichloromethane (20 cm^3) and the combined organics were dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was purified by flash chromatography (ethyl acetate) to yield the sulfoxide. Alcohols **25a**:**25b** solvents: chloroform (yield 11%), chloroform–methanol (1:1) (yield 16%) and chloroform–hexane (1:1) (yield 34%). Silyl ethers **26a**:**26b** solvents: chloroform (yield 14%), chloroform–methanol (1:1) (yield 15%) and chloroform–hexane (1:1) (yield 24%). Diastereoisomeric ratios were determined by inspection of the ^1H NMR spectrum. All data were consistent with those expected for a mixture of diastereoisomers of alcohols **25a**:**25b** or silyl ethers **26a**:**26b**. Data for the separate diastereoisomers are detailed below.

General procedure for the oxidation of (4*S*,5*S*)-4-hydroxymethyl-2-[2-(methylsulfanyl)phenyl]-5-phenyl-4,5-dihydro-1,3-oxazole 18 and (4*S*,5*S*)-4-hydroxymethyl-2-[2-(4-methylphenylsulfanyl)phenyl]-5-phenyl-4,5-dihydro-1,3-oxazole 21

Oxidant: MCPBA. A solution of MCPBA (0.43 mmol) in an appropriate solvent (3 cm^3) was added dropwise to a solution of a sulfide **18** or **21** (0.43 mmol) in the same solvent at −70 °C and the mixture was stirred until the reaction was deemed to have gone to completion by TLC chromatography. The reaction mixture was then diluted with dichloromethane (10 cm^3) and washed with saturated aq. sodium carbonate (2 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash chromatography [ethyl acetate–light petroleum (4:1)] afforded compounds **27a/b** and **28a/b**. Diastereoisomeric ratios were determined by HPLC analysis using a Bondapac C_{18} column (acetonitrile–water).

(4S,5S,R_S/S_S)-4-*Hydroxymethyl*-5-*phenyl*-2-[2-(*methylsulfinyl*)*phenyl*]-5-*phenyl*-4,5-*dihydro*-1,3-*oxazole* **27a**:**27b**.—(Found: M^+, 315.0929. $C_{17}H_{17}NO_3S$ requires M, 315.0929) (**27a**:**27b** 99:1), $[\alpha]_D^{25}$ +195.1 (*c* 0.50, $CHCl_3$) (**27a**:**27b** 73:27), $[\alpha]_D^{25}$ + 145.0 (*c* 0.40, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1649 (C=N) and 1062 (S=O); δ_H(250 MHz; $CDCl_3$) 8.27 (1 H, dd, *J* 7.8 and 0.9, ArH), 8.01 (1 H, dd, *J* 7.7 and 1.1, ArH), 7.73 (1 H, dd, *J* 7.5 and 1.2, ArH), 7.56 (1 H, dd, *J* 7.5 and 1.2, ArH), 7.37 (5 H, m, ArH), 5.55 (1 H, d, *J* 7.0, CHO), 4.34 (1 H, m, CHN), 4.01 (1 H, dd, *J* 11.5 and 3.9, C*H*H′OH), 3.79 (1 H, dd, *J* 11.5 and 3.9, CH*H*′OH), 2.91 (3 H, s, SCH_3) and 2.21 (1 H, br s, OH); δ_C(63 MHz; $CDCl_3$) 161.6 (C=N), 148.1, 140.2, 132.4, 130.2, 129.5, 128.7, 128.5, 125.4 and 124.1 (arom C), 82.7 (CHO), 77.2 (CHN), 63.8 (CH_2OH) and 43.9 (SCH_3); *m*/*z* (EI) 315 (5%), 270 (20) and 167 (100).

(4S,5S,R_S/S_S)-4-*Hydroxymethyl*-2-[2-(4-*methylphenylsulfinyl*)*phenyl*]-5-*phenyl*-4,5-*dihydro*-1,3-*oxazole* **28**.—All data were consistent with those detailed below.

All other oxidations, involving *tert*-butyl hydroperoxide with vanadyl acetoacetonate or titanium tetraisopropoxide, were performed in a likewise manner to those detailed above. All appropriate data were consistent with those detailed above.

(4*S*,5*S*,S_S)-4-Hydroxymethyl-5-phenyl-2-[(4-methylphenyl)sulfinylmethyl]-5-phenyl-4,5-dihydro-1,3-oxazole 25a

A solution of (4*S*,5*S*)-2-[(4-methylphenyl)sulfinylmethyl]-5-phenyl-4-(triisopropylsilyloxymethyl)-4,5-dihydro-1,3-oxazole **26a** (see below) (280 mg, 0.58 mmol) in THF (10 cm^3) was stirred with a 1 mol dm^{-3} solution of TBAF (0.7 cm^3, 0.7 mmol) for an hour at ambient temperature. The reaction mixture was diluted with diethyl ether (30 cm^3) and washed with saturated aq. ammonium chloride (30 cm^3). The organic phase was dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue was purified by flash chromatography (ethyl acetate) to yield the *title compound* as a solid (57 mg, 29%), mp 153–154 °C (Found: M^+, 329.0963. $C_{18}H_{19}NO_3S$ requires M, 329.1086); $[\alpha]_D^{20}$ −200.5 (*c* 0.374, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 3360 (OH), 1666 (C=N) and 1050 (S=O); δ_H(250 MHz; $CDCl_3$) 7.60–7.16 (9 H, m, ArH), 5.34 (1 H, d, *J* 7.0, CHO), 4.12 (1 H, m, CHN), 3.96 [2 H, m, CHH′O and C*H*H′S(O)], 3.80 [1 H, d, *J* 14.3, CH*H*′S(O)], 3.57 (1 H, m, CH*H*′O) and 2.42 (3 H, s, ArCH_3); δ_C(100.63 MHz; $CDCl_3$) 158.9 (C=N), 142.4, 141.0, 139.2, 138.6, 130.3, 130.1, 128.9, 128.6, 127.7 and 125.7 (arom C), 83.2 (CHO), 74.0 (CHN), 63.5 [$CH_2S(O)$], 54.8 (CH_2O) and 22.2 (ArCH_3).

(4*S*,5*S*,R_S)-4-Hydroxymethyl-5-phenyl-2-[(4-methylphenyl)-sulfinylmethyl]-5-phenyl-4,5-dihydro-1,3-oxazole 25b

The same procedure was used with **26b** as detailed above to give the *title compound* as a solid (29%), mp 156–157 °C (Found:

† See Instructions for Authors, in the January issue.

M^+, 329.0956); $[\alpha]_D^{20}$ 187.8 (*c* 0.426, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 3362 (OH), 1668 (C=N) and 1054 (S=O); δ_H(250 MHz; $CDCl_3$) 7.61–7.25 (9 H, m, ArH), 5.47 (1 H, d, *J* 7.3, CHO), 4.12 (1 H, m, CHN), 3.91 [2 H, m, C*H*H'O and C*H*H'S(O)], 3.76 [1 H, d, *J* 13.3, CH*H*'S(O)], 3.76 (1 H, m, CH*H*'O), 2.43 (3 H, s, ArCH_3) and 2.25 (1 H, br s, OH); δ_C(100.63 MHz; $CDCl_3$) 164.5 (C=N), 142.3, 141.2, 139.0, 138.7, 130.1, 129.8, 128.7, 128.6, 127.8 and 125.0 (arom C), 84.4 (CHO), 74.3 (CHN), 64.2 [$CH_2S(O)$], 56.7 (CH_2O) and 22.4 (ArCH_3).

(4*S*,5*S*,S_S)-2-[(4-Methylphenyl)sulfinylmethyl]-5-phenyl-4-(triisopropylsiloxymethyl)-4,5-dihydro-1,3-oxazole 26a

A solution of (4*S*,5*S*)-2-methyl-4-(triisopropylsilyloxymethyl)-5-phenyl-4,5-dihydro-1,3-oxazole **32** (see below) (500 mg, 1.44 mmol) in THF (5 cm^3) was cooled to −78 °C under nitrogen. LDA (2.88 cm^3, 4.32 mmol as a 1.5 mol dm^{-3} solution in THF) was added dropwise to the flask and the mixture was stirred for 1 h at −78 °C. To this mixture was added a solution of (+)-menthyl (*R*)-toluene-*p*-sulfinate (847 mg, 2.88 mmol) in THF (5 cm^3) over a period of 5 min. The solution was stirred at −78 °C for 2 h before being allowed to warm to ambient temperature. The reaction mixture was washed with saturated aq. ammonium chloride (20 cm^3) and the aqueous phase was washed with dichloromethane (5 × 30 cm^3). The combined organic phases were dried (Na_2SO_4), and concentrated under reduced pressure to leave an oily residue. This was purified by flash chromatography [light petroleum–diethyl ether (1:2)] to yield the *title compound* as a pale yellow oil (426 mg, 61%) (Found: M^+, 485.2406. $C_{27}H_{39}NO_3SSi$ requires M, 485.2420); $[\alpha]_D^{20}$ −145.3 (*c* 0.998, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1670 (C=N) and 1046 (S=O); δ_H(250 MHz; $CDCl_3$) 7.64–7.19 (9 H, m, ArH), 5.45 (1 H, d, *J* 6.4, CHO), 4.05 (1 H, m, CHN), 3.93 [2 H, m, C*H*H'O and C*H*H'S(O)], 3.68 [1 H, d, *J* 13.3, CH*H*'S(O)], 3.59 (1 H, dd, *J* 9.9, 7.2, CH*H*'O), 2.40 (3 H, s, ArCH_3) and 1.11–1.03 (21 H, m, 3 × Pr^i); δ_C(63 MHz; $CDCl_3$) 159.1 (C=N), 142.3, 140.3, 129.9, 128.5, 128.0, 125.4 and 124.5 (arom C), 84.4 (CHO), 76.6 (CHN), 65.1 [$CH_2S(O)$], 55.9 (CH_2O), 21.4 (ArCH_3), 17.7 [$CH(CH_3)_2$] and 11.8 [$CH(CH_3)_2$].

(4*S*,5*S*,R_S)-2-[(4-Methylphenyl)sulfinylmethyl]-5-phenyl-4-(triisopropylsiloxymethyl)-4,5-dihydro-1,3-oxazole 26b

The same procedure was used as detailed above, with the (−)-menthyl (*S*)-sulfinate, and gave the *title compound* as a pale yellow oil (64%) (Found: M^+, 485.2406); $[\alpha]_D^{20}$ +47.6 (*c* 0.21, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1671 (C=N) and 1047 (S=O); δ_H(250 MHz; $CDCl_3$) 7.60–7.27 (9 H, m, ArH), 5.45 (1 H, d, *J* 6.4, CHO), 4.03 (1 H, m, CHN), 3.94 [2 H, m, C*H*H'O and C*H*H'S(O)], 3.67 [1 H, d, *J* 13.3, CH*H*'S(O)], 3.59 (1 H, dd, *J* 9.9 and 7.2, CH*H*'O), 2.39 (3 H, s, ArCH_3) and 1.22–1.04 (21 H, m, 3 × Pr^i); δ_C(63 MHz; $CDCl_3$) 159.5 (C=N), 142.1, 140.2, 129.9, 128.5, 128.0, 125.5 and 124.3 (arom C), 84.5 (CHO), 76.4 (CHN), 65.1 [$CH_2S(O)$], 55.8 (CH_2O), 21.4 (ArCH_3), 17.9 [$CH(CH_3)_2$] and 11.8 [$CH(CH_3)_2$].

(4*S*,5*S*,S_S)-4-Hydroxymethyl-2-[2-(4-methylphenylsulfinyl)-phenyl]-5-phenyl-4,5-dihydro-1,3-oxazole 28b

A mixture of (4*S*,5*S*)-4-hydroxymethyl-2,5-diphenyl-4,5-dihydro-1,3-oxazole **20** (1.5 g, 6 mmol), *tert*-butyl(chloro)-dimethylsilane (0.98 g, 6.5 mmol) and imidazole (0.89 g, 13 mmol) in DMF (15 cm^3) was stirred for 16 h under an inert atmosphere. After aqueous work-up (4*S*,5*S*)-4-(*tert*-butyldimethylsiloxymethyl)-2,5-diphenyl-4,5-dihydro-1,3-oxazole was gained as an yellow oil. Butyllithium (0.75 cm^3, 1.2 mmol) was added to a solution of this compound (400 mg, 1.1 mmol) and TMEDA (380 mg, 3.3 mmol) in diethyl ether (10 cm^3 at −65 °C. The resulting brown solution was stirred at −65 °C for 15 min before the addition of a solution of (−)-menthyl (*S*)-toluene-*p*-sulfinate (320 mg, 1.1 mmol) in diethyl ether (5 cm^3). Upon complete addition the reaction mixture was allowed to warm to room temperature and was stirred for 16 h under nitrogen. The reaction mixture was then diluted with diethyl ether (15 cm^3) and washed with distilled water (3 × 10 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to yield a pale yellow oil. Purification by flash chromatography [diethyl ether–light petroleum (2:3)] gave (4*S*,5*S*,S_S)-4-(*tert*-butyldimethylsiloxymethyl)-2-[2-(4-methylphenylsulfinyl)phenyl]-5-phenyl-4,5-dihydro-1,3-oxazole (102 mg, 20%) as a yellow oil. Removal of the *tert*-butyldimethylsilyl group was effected by reaction with TBAF (0.16 cm^3, 0.16 mmol) in THF (7 cm^3) at ambient temperature. After aqueous work-up and purification by flash chromatography [ethyl acetate–light petroleum (4:1)] the *title compound* was achieved as a solid (53 mg, 84%), mp 137–139 °C (Found: M^+, 391.1242. $C_{23}H_{21}NO_3S$ requires M, 391.1242); $[\alpha]_D^{25}$ −134 (*c* 0.61, $CHCl_3$); ν_{max}/cm^{-1} 3380.9 (OH), 1650 (C=N) and 1068 (S=O); δ_H(250 MHz; $CDCl_3$) 8.47 (1 H, dd, *J* 8.0 and 1.1, ArH), 8.04 (1 H, dd, *J* 8.0 and 1.1, ArH), 7.81 (1 H, m, ArH), 7.58 (1 H, m, ArH), 7.47 (2 H, *J* 8.1, ArH), 7.30 (5 H, m, ArH), 7.16 (2 H, d, *J* 7.9, ArH), 5.37 (1 H, d, *J* 7.7, CHO), 4.20 (1 H, m, CHN), 3.77 (1 H, m, C*H*H'OH), 3.57 (1 H, m, CH*H*'OH) and 2.25 (3 H, s, ArCH_3); δ_C(63 MHz; $CDCl_3$) 161.5 (C=N), 145.6, 143.5, 141.4, 139.8, 132.1, 130.4, 130.1, 129.6, 128.8, 128.4, 126.9, 125.8, 125.7 and 124.6 (arom C), 82.6 (CHO), 77.1 (CHN), 63.3 (CH_2OH) and 21.2 (ArCH_3); *m*/*z* (EI) 391 (100%), 227 (61) and 104 (80).

Crystal structure of (4*S*,5*S*,S_S)-4-Hydroxymethyl-2-[2-(4-methylphenylsulfinyl)phenyl]-4,5-dihydro-5-phenyl-1,3-oxazole 28b

Crystals suitable for X-ray analysis were obtained by recrystallisation from Et_2O–$CHCl_3$ (3:1).

Crystal data.—$C_{23}H_{21}NO_3S$, M = 391.48. Monoclinic, *a* = 27.298(5), *b* = 7.998(2), *c* = 9.371(2) Å, *β* = 94.32(2)°, *V* = 2040.3(8) $Å^3$ (by least-squares refinement on diffractometer angles for 25 automatically centred reflections, *λ* = 1.541 78 Å), space group *C*2 (#5), *Z* = 4, D_x = 1.274 g cm^{-3}. Clear, block crystals. Crystal dimensions: 0.30 × 0.30 × 0.61 mm, *μ*(Cu-K*α*) = 17.26 cm^{-1}.

Data collection and processing.[22]—Rigaku AFC7S diffractometer using *ω* scans. Graphite-monochromated Cu-K*α* radiation; 1684 reflections, 1644 were unique, measured ($0 < 2\theta < 120.2°$, $+h$, $+k$, $\pm l$), 1610 with $I > 3.00\sigma(I)$. An empirical absorption correction was applied (transmission factors: 0.7903–1.0000). The data were corrected for Lorentz and polarisation factors.

Structure analysis and refinement.—Direct methods. Full-matrix least-squares refinement with all non-hydrogen atoms anisotropic and hydrogens in calculated positions. The maximum peak in the final ΔF map was 0.20 e $Å^{-3}$. Final *R*- and R_w-values are 0.037 and 0.041. The X-ray molecular structure is shown in Fig. 2. Programs and computers used and sources of scattering factor data are given in ref. 22. Atomic coordinates, bond lengths, thermal parameters and angles have been deposited at the Cambridge Crystallographic Data Centre.‡

(4*S*)-4-Isopropyl-2-phenyl-4,5-dihydro-1,3-oxazole 29

Zinc chloride (380 mg, 2 mmol) was melted under high vacuum and cooled under nitrogen. After cooling to room temperature the flask was charged with chlorobenzene (3 cm^3), benzonitrile (5 g, 48 mmol) and L-valinol (6.5 g, 63 mmol). The mixture was heated under reflux for 24 h. The reaction mixture was diluted with dichloromethane (50 cm^3) and washed with distilled water (3 × 30 cm^3). The combined organics were dried ($MgSO_4$), filtered, and concentrated under reduced pressure, to yield a brown oil. Purification by flash chromatography [light petroleum–diethyl ether (3:1)] afforded the *title compound* (6.9 g, 75%) as a pale yellow oil (Found: M^+, 189.1154. $C_{12}H_{15}NO$

‡ See Instructions for Authors, in the January issue.

requires M, 189.1154); $[\alpha]_D^{25}$ −72 (*c* 6.5, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1651 (C=N); δ_H(250 MHz; $CDCl_3$) 7.95 (2 H, m, ArH), 7.41 (3 H, m, ArH), 4.34 (1 H, m, CHN), 4.05 (2 H, m, CH_2O), 1.85 [1 H, m, C*H*$(CH_3)_2$], 1.04 (3 H, d, *J* 6.8, CHCH_3) and 0.91 (3 H, d, *J* 6.8, CHCH_3); δ_C(63 MHz; $CDCl_3$) 163.1 (C=N), 131.1, 128.1 and 128.0 (arom C), 72.5 (CHN), 69.9 (CH_2O), 32.7 [*C*H$(CH_3)_2$], 18.9 (CH*C*H_3) and 17.9 (CH*C*H_3); *m*/*z* (EI) 189 (77%) and 169 (100).

(4*S*)-4-Isopropyl-2-methyl-4,5-dihydro-1,3-oxazole 30

A solution of methyl acetimidate (1.27 g, 11.6 mmol) and valinol (1 g, 9.7 mmol) in dichloromethane (30 cm^3) was stirred for 16 h at ambient temperature. The reaction mixture was washed with saturated aq. sodium hydrogen carbonate. The organic phase was dried (Na_2SO_4), and concentrated under reduced pressure to afford the *title compound* as an oil (1.16 g, 94%) (Found: M^+, 127.1069. $C_7H_{13}NO$ requires M, 127.0997); $[\alpha]_D^{20}$ −86.21 (*c* 1.10, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1677 (C=N); δ_H(250 MHz; $CDCl_3$) 4.23 (1 H, m, CHN), 3.85 (2 H, m, CH_2O), 1.98 (3 H, s, CH_3), 1.70 [1 H, m, C*H*$(CH_3)_2$], 0.96 (3 H, d, *J* 6.8, CHCH_3) and 0.87 (3 H, d, *J* 6.8, CHCH_3); δ_C(63 MHz; $CDCl_3$) 164.0 (C=N), 72.1 (CHN), 69.9 (CH_2O), 32.4 [*C*H$(CH_3)_2$], 18.5 (CH*C*H_3), 17.9 (CH*C*H_3) and 13.5 (CH_3).

(4*S*,5*S*)-2-Methyl-5-phenyl-4-(triisopropylsiloxymethyl)-4,5-dihydro-1,3-oxazole 31

A solution of (1*S*,2*S*)-(+)-2-amino-1-phenylpropane-1,3-diol (1.14 g, 6.85 mmol) and methyl acetimidate (0.5 g, 4.56 mmol) in dichloromethane (30 cm^3) was stirred for 16 h at ambient temperature. The mixture was washed with water (50 cm^3) and the aqueous phase washed with dichloromethane (3 × 30 cm^3). The combined organic phases were dried (Na_2SO_4), and concentrated under reduced pressure to yield (4*S*,5*S*)-4-hydroxymethyl-2-methyl-5-phenyl-4,5-dihydro-1,3-oxazole as an oil (0.79 g, 91%). A solution of this compound (200 mg, 1 mmol) in dichloromethane (25 cm^3) was treated with triethylamine (127 mg, 1.26 mmol) and stirred for 5 min at room temperature. Triisopropylsilyl trifluoromethanesulfonate (385 mg, 1.26 mmol) was added to the mixture in one portion and the solution was stirred for a further 15 min at room temperature. The mixture was washed with saturated aq. ammonium chloride (50 cm^3) and the aqueous phase was washed with dichloromethane (3 × 50 cm^3). The combined organic phases were dried (Na_2SO_4), and concentrated under reduced pressure to produce an oily residue. This was purified by flash chromatography [light petroleum–diethyl ether (1 : 1)] to yield the *title compound* as an oil (322 mg, 93%) (Found: M^+, 347.2278. $C_{20}H_{33}NO_2Si$ requires M, 347.2280); $[\alpha]_D^{20}$ −52.6 (*c* 0.57, $CHCl_3$); ν_{max}(neat)/cm^{-1} 1675 (C=N); δ_H(250 MHz; $CDCl_3$) 7.33–7.29 (5 H, m, ArH), 5.43 (1 H, d, *J* 5.8, CHO), 4.05 (2 H, m, CHN and C*H*H′O), 3.74 (1 H, dd, *J* 9.8 and 6.9, CH*H*′O), 2.08 (3 H, s, CH_3) and 1.16–1.04 (21 H, m, 3 × Pr^i); δ_C(63 MHz; $CDCl_3$) 165.5 (C=N), 142.8, 128.5, 127.8 and 125.4 (arom C), 83.5 (CHN), 76.4 (CHO), 65.4 (CH_2), 17.7 [CH(*C*$H_3)_2$], 13.9 (CH_3) and 11.7 (*C*H).

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