Cycloaddition of Nitrile Oxides to Homochiral Vinyl Ethers

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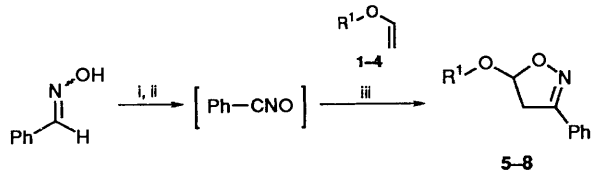
In the [3 + 2] cycloaddition of a range of nitrile oxides with homochiral vinyl ethers the diastereoselectivity observed is dependent on the chiral auxiliary used. A brief comparison is made with the diastereoselectivity of the corresponding [4 + 2] nitrosoalkene cycloaddition, and also to the nitrile oxide cycloaddition to chiral acrylic acid esters bearing the most successful auxiliaries from the vinyl ether study.

[3 + 2] Cycloaddition of nitrile oxides to double bonds[1] is an established synthetic protocol used to generate 4,5-dihydroisoxazoles. Additions to dipolarophiles such as acryloyl and crotyl derivatives[2] and allyl silanes[3] have been reported. The addition of nitrile oxides to homochiral allyl ethers has been extensively studied[4] and although addition to achiral vinyl ethers is known,[5] addition to chiral vinyl ethers to our knowledge has only been reported in one case.[6] As these products were of interest to us for a synthetic investigation underway in our laboratory[7] we undertook a more extensive study of nitrile oxide cycloaddition to homochiral vinyl ethers.[8]

Results and Discussion

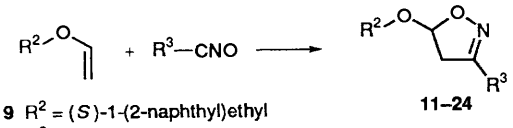
The vinyl ethers **1–4** were prepared by mercury(II) acetate catalysed exchange of the corresponding homochiral alcohols with butyl vinyl ether according to a literature procedure.[9] These were then reacted with benzonitrile oxide, which was generated from benzaldehyde oxime following the *N*-chlorosuccinimide–triethylamine protocol reported by Thomsen and Torssell (Scheme 1).[10] The 4,5-dihydroisoxazoles **5–8** were



Scheme 1 *Reagents and conditions:* i, *N*-chlorosuccinimide, $CHCl_3$, heat, 0.3 h; ii, Et_3N, $CHCl_3$, room temp.; iii, vinyl ether **1–4**, $CHCl_3$, room temp. then heat, 0.3 h

produced in 41–59% yield, but with disappointingly low diastereoselectivity (Table 1), the best diastereoisomer ratio being 1.9:1 [diastereoisomeric excess (d.e.) 31%] in the case of the 8-phenylmenthyl vinyl ether **2**.

Better results were obtained with the vinyl ethers **9** and **10** and the improved diastereoselection was also observed with a wider range of nitrile oxides, where diastereoisomeric excesses in the products **11** to **24** ranged from 33 to 60% (Scheme 2, Table 2).



9 R^2 = (*S*)-1-(2-naphthyl)ethyl
10 R^2 = (*S*)-1-phenylbutyl

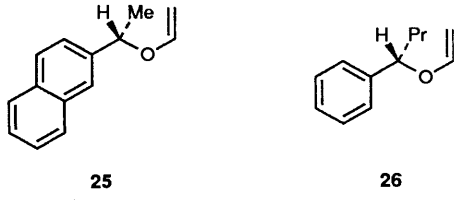
Scheme 2

Interestingly, similar trends in diastereoselection with auxiliary were observed by Posner and Wettlaufer[11] and Prapansiri and Thornton[12] who independently used related chiral vinyl ethers as dienophiles in inverse electron demand Diels–Alder reactions.

Table 1

	R^1	Yield (%)	Product	Diastereoisomer ratio[a] of isoxazoles **5–8**
1	(−)-Menthyl	41	**5**	1.4:1
2	8-Phenylmenthyl	51	**6**	1.9:1
3	(1*S*)-*endo*-Bornyl	45	**7**	1.3:1
4	(*R*)-PhCH(CO_2Me)	59	**8**	1.1:1

[a] The diastereoisomer ratio was measured from several peaks in the ^{13}C NMR spectrum of the crude product.



25 **26**

Fig. 1 The *syn*-staggered conformations of vinyl ethers **9** and **10**

Following the conclusions of extensive studies on the conformation of vinyl ethers[13] the most stable conformers of **9** and **10** are the *syn*-staggered forms **25** and **26** respectively (Fig. 1). Here the oxygen lone pairs are *anti* to the double bond leading to best overlap with the *anti*-bonding orbital of the alkene according to the bent bond theory.[14] The bulky naphthyl group (in **25**) or phenyl group (**26**) is situated in a co-planar, *anti* orientation with respect to the double bond. This leaves the alkyl and H groups attached to the chiral centre staggering the double bond so differentially shielding the two faces of the olefin. Evidence for the validity of the proposed conformation of the vinyl ethers has been revealed through the X-ray crystal structure determination of **11a**, the major diastereoisomer of isoxazole **11**.[8] In this isomer the newly created chiral centre at C-5 was shown to be *R* based on the known configuration of the auxiliary, *S*. The modest diastereoselection observed in this cycloaddition and the absolute configuration of the new chiral centre in the major isomer is consistent with attack of the dipole from the least hindered face.

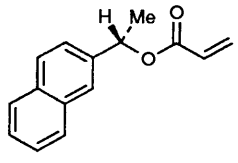
In explaining the poor diastereoselectivity observed with vinyl ethers **1–3** it can be seen that the chiral centre closest to the vinyl group is part of a carbocyclic ring and so the preferred conformation cannot be so clearly predicted as in the acyclic cases **9** and **10**. With the case of the methyl mandelate derived vinyl ether **4** there may well be electronic factors resulting from the ester function which changes the conformational preferences, so leading to poorer diastereoselection.

Table 2

Isoxazole	R^3	Vinyl ether	Crude[a] diastereoisomer ratio	Yield of isomer (%)
11	Ph	**9**	3:1	43
12	$Ph(CH_2)_2$	**9**	3:1	28
13	$4\text{-}NO_2C_6H_4$	**9**	4:1	26
14	Bu^t	**9**	3:1	53
15	Pr	**9**	4:1	37
16	Et	**9**	3:1	40
17	Me	**9**	3:1	37
18	Ph	**10**	2:1	33
19	$Ph(CH_2)_2$	**10**	4:1	44
20	$4\text{-}NO_2C_6H_4$	**10**	1:1	23
21	Bu^t	**10**	4:1	47
22	Pr	**10**	3:1	39
23	Et	**10**	4:1	35
24	Me	**10**	4:1	53

[a] The ratio of diastereoisomers of **11–24** was measured from several peaks in the ^{13}C NMR spectrum of the crude product. In the case of **11** the ratio was confirmed by ^1H NMR spectroscopy and by the isolation of both diastereoisomers. In products **12–24** the major product was isolated and fully characterised.

In a further study the two acrylate derivatives **27** and **28** were made, but [3 + 2] cycloaddition of benzonitrile oxide to these esters provided only 1 : 1 mixtures of diastereoisomers of **29** and **30** respectively. This result is not unexpected as not only is the



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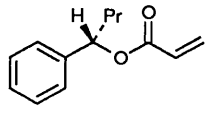

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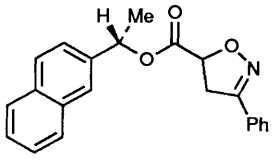

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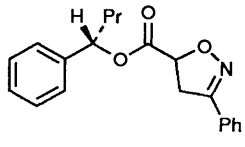

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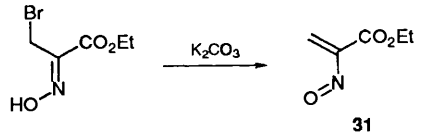
asymmetric induction now from a more remote centre (1,4-induction), but also more importantly there is the added factor of interconversion of the s-*cis* and s-*trans* acrylate conformers. Previous studies on nitrile oxide addition to acrylate[2a,b] and acrylamide[2c–f] derivatives have pinpointed control of this to be the most important factor in achieving good diastereoselection rather than simply the nature of the chiral auxiliary.

In order to synthesize six-membered homologues of the isoxazoles **11–24** the [4 + 2] cycloaddition of nitrosoalkenes to the vinyl ethers **9** and **10** was investigated. Nitrosoalkenes[15] have been shown to react with simple achiral vinyl ethers (in both inter-[16] and intra-molecular[17] senses) and in one example with a chiral glucose-derived vinyl ether.[18] Addition to silyl enol ethers[19] and lithium enolates[20] has also been reported. Gilchrist and Roberts have previously shown how the nitrosoalkene **31** can be generated *in situ*[21] for cycloadditions to achiral vinyl ethers (Scheme 3) and so this general reaction protocol was applied to the vinyl ethers **9** and **10**. Treatment of the oxime of ethyl bromopyruvate[21] with potassium carbonate generated the nitrosoalkene, which underwent cycloaddition to the vinyl ethers to yield the 6-alkoxy-5,6-dihydro-1,2-oxazines **32** and **33** in moderate yields (58 and 56% respectively). In this



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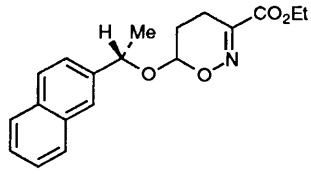
Scheme 3



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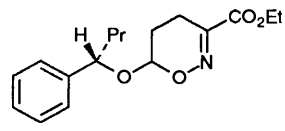

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case improved diastereoselectivity (5.8 : 1 and 6 : 1) was observed compared to the five-membered isoxazoles produced from the nitrile oxide cycloadditions. Assuming the same conformational preferences for the vinyl ethers it is likely that the improved diastereoselectivity results from steric interactions between the ethyl ester function on the heterodiene and the chiral auxiliary on the vinyl ether. This is more significant with the *endo* transition state which is to be expected based on previous reports[22] for other hetero-Diels–Alder reactions.

In conclusion we have reported that the homochiral vinyl ethers **9** and **10** undergo [3 + 2] cycloaddition with a range of nitrile oxides to produce 4,5-dihydro-1,2-isoxazoles **11–24** with moderate diastereoselection, and that also the six-membered 5,6-dihydro-1,2-oxazines **32** and **33** can be made *via* nitrosoalkene [4 + 2] heterocycloaddition to the same vinyl ethers.

Experimental

NMR spectra were recorded on a Bruker AM-300 spectrometer (^1H at 300 MHz and ^{13}C at 75 MHz). All coupling constants for AB systems have been corrected using the standard formula and DEPT experiments were used to assign the signals in the ^{13}C NMR spectra. Mass spectra and accurate mass measurements were made at the SERC Mass Spectrometry Centre, University College of Swansea and also at Leicester University. Elemental analyses were carried out by Butterworth Laboratories, Teddington, Middlesex. Infra-red spectra were recorded on a Perkin-Elmer 298 spectrometer and melting points were determined on a Kofler hot stage and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 141 polarimeter, with values of $[\alpha]_D$ given in units of 10^{-1} deg cm^2 g^{-1}. Flash chromatography was carried out according to the method of Still *et al.*,[23] using silica gel [Kiesel 60, 230–400 mesh (ASTM)] manufactured by Merck and Co. Ether refers to diethyl ether and light petroleum refers to the fraction boiling in the range 40–60 °C. Some of the oximes used as precursors to the nitrile oxides were commercially available, for example benzaldehyde oxime, *p*-nitrobenzaldehyde oxime and acetaldehyde oxime. The others were made by stirring the corresponding aldehyde and hydroxylamine hydrochloride overnight in pyridine. After removal of the solvent under reduced pressure the oximes were then purified using flash column chromatography. These oximes gave satisfactory ^1H NMR spectra.

(1R)-*Menthyl Vinyl Ether* **1**.[11a,12]—A solution of (1*R*)-menthol (5.0 g, 32.1 mmol) and a catalytic amount of mercury(II) acetate in butyl vinyl ether (50 cm^3) was heated under reflux for 6 h. Excess butyl vinyl ether was then removed under reduced pressure to give the *title compound* as a colourless liquid (2.88 g, 49%) after flash column chromatography [(10 : 1) light petroleum–ether], δ_H(300 MHz; $CDCl_3$) 0.77–1.70 (16 H, m), 2.03–2.15 (2 H, m), 3.52 (1 H, td, *J* 10.7 and 4.2, 1-H), 3.92 (1 H, dd, *J* 6.5 and 1.4, OCH=CH_{cis}), 4.26 (1 H, dd, *J* 14.1 and 1.4,

OCH=CH_{trans}) and 6.30 (1 H, dd, J_{trans} 14.1 and J_{cis} 6.5, OCH=CH_2); δ_C(300 MHz; $CDCl_3$) 16.4 (CH_3), 20.7 (CH_3), 22.1 (CH_3), 23.6 (CH_2), 25.9 (CH), 31.5 (CH), 34.5 (CH_2), 40.9 (CH_2), 47.9 (CH), 79.6 (CH), 87.4 (CH_2) and 151.1 (CH).

(1R)-8-*Phenylmenthyl Vinyl Ether* **2**.[11a,12]—In the same way as for compound **1** (1*R*)-8-phenylmenthol[24] (3.0 g, 12.9 mmol), butyl vinyl ether (40 cm^3) and a catalytic amount of mercury(II) acetate gave the *title compound* as a colourless liquid (770 mg, 23%) after flash column chromatography [(10:1) light petroleum–ether] δ_H(300 MHz; $CDCl_3$) 0.66–1.04 (6 H, m), 1.18–1.60 (9 H, m), 1.79 (1 H, ddd, J 11.7, 10.1 and 3.5), 2.00 (1 H, ddd, J 12.4, 5.9 and 3.8), 3.55 (1 H, td, J 9.9 and 4.2, 1-H), 3.93 (1 H, dd, J 6.6 and 1.3, OCH=CH_{cis}), 4.17 (1 H, dd, J 14.1 and 1.3, CH=CH_{trans}), 6.14 (1 H, dd, J_{trans} 14.1 and J_{cis} 6.6, OCH=CH_2), and 7.10–7.30 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 21.8 (CH_3), 24.9 (CH_3), 27.1 (CH_2), 29.2 (CH_3), 31.6 (CH), 34.6 (CH_2), 40.4 (C), 41.5 (CH_2), 51.5 (CH), 80.7 (CH), 87.7 (CH_2), 125.0 (CH), 125.8 (CH), 127.7 (CH), 150.1 (CH) and 150.5 (C).

(1S)-endo-*Bornyl Vinyl Ether* **3**.[11a,12]—In the same way as for compound **1** (1*S*)-*endo*-borneol (5.0 g, 32.5 mmol), butyl vinyl ether (50 cm^3) and a catalytic amount of mercury(II) acetate gave the *title compound* as a colourless liquid (3.99 g, 68%) after flash chromatography [(10:1) light petroleum–ether], δ_H(300 MHz; $CDCl_3$) 0.83–0.97 (9 H, m), 1.07 (1 H, dd, J 13.4 and 3.4), 1.18–1.32 (2 H, m), 1.65–1.76 (2 H, m), 1.96–2.06 (1 H, m), 2.16–2.26 (1 H, m), 3.92 (1 H, dd, J 6.7 and 1.6, OCH=CH_{cis}), 4.01 (1 H, ddd, J 9.5, 3.3 and 2.0, 1-H), 4.10 (1 H, dd, J 14.4 and 1.6, OCH=CH_{trans}) and 6.38 (1 H, dd, J_{trans} 14.4 and J_{cis} 6.7, OCH=OCH_2); δ_C(75 MHz; $CDCl_3$) 13.7 (CH_3), 18.9 (CH_3), 19.7 (CH_3), 26.7 (CH_2), 28.0 (CH_2), 36.4 (CH_2), 45.0 (CH), 47.7 (C), 49.2 (C), 83.8 (CH), 86.9 (CH_2) and 151.8 (CH).

Methyl (R)-2-*Phenyl*-2-*vinyloxyacetate* **4**.[12]—In the same way as for compound **1** (*R*)-methyl mandelate (4.5 g, 27.1 mmol), butyl vinyl ether (50 cm^3) and a catalytic amount of mercury(II) acetate gave methyl (*R*)-2-phenyl-2-vinyloxyacetate as a colourless liquid (703 mg, 14%) after flash column chromatography [(5:1) light petroleum–ether] and Kugelröhr distillation (160 °C/1 mmHg) δ_H(300 MHz; $CDCl_3$) 3.71 (3 H, s, CH_3), 4.15 (1 H, dd, J 6.8 and 2.7, OCH=CH_{cis}), 4.30 (1 H, dd, J 14.3 and 2.7, OCH=CH_{trans}), 5.31 (1 H, s, CH), 6.48 (1 H, dd, J_{trans} 14.3 and J_{cis} 6.8, OCH=OCH_2) and 7.28–7.51 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 52.5 (CH_3), 78.5 (CH), 89.6 (CH_2), 127.0 (CH), 128.7 (CH), 128.9 (CH), 134.9 (C), 149.7 (CH) and 170.0 (C).

(5RS)-5-[(1R)-*Menthyloxy*]-3-*phenyl*-4,5-*dihydroisoxazole* **5**.—A solution of benzaldehyde oxime (665 mg, 5.49 mmol), *N*-chlorosuccinimide (807 mg, 6.04 mmol) and pyridine (2 drops) in chloroform (30 cm^3) was heated under reflux for 20 min. The reaction mixture was then cooled to room temperature and solutions of (1*R*)-menthyl vinyl ether **1** (1.0 g, 5.49 mmol) and triethylamine (610 mg, 6.04 mmol) in chloroform (both 5 cm^3) were added consecutively in a dropwise fashion, after which the mixture was heated under reflux for 1 h. After removal of the solvent under reduced pressure, the product was purified by flash column chromatography (light petroleum) to give the *title compound* (677 mg, 41%) as an oily 1:1.38 mixture of diastereoisomers, R_f 0.37 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −52.5 (*c* 4, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1355s, 1085s, 930s, 830s and 755s; δ_H(300 MHz; $CDCl_3$) 0.63–1.68 (16 H, m), 2.03–2.16 (2 H, m) 3.11–3.49 (2.4 H, m, 4-H_2 and 0.4 1′-H), 3.62 (0.6 H, td, J 10.6 and 6.2, 1′-H), 5.73 (0.4 H, dd, J 6.7 and 1.8, 5-H), 5.81 (0.6 H, dd, J 6.5 and 1.6, 5-H), 7.34–7.45 (2 H, m, ArH and 7.59–7.69 (3 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 15.9 (CH_3), 16.3 (CH_3), 20.9 (CH_3), 21.0 (CH_3), 22.2 (CH_3), 22.3 (CH_3), 23.3 (CH_2), 23.4 (CH_2), 25.3 (CH), 25.7 (CH), 31.4 (CH), 31.6 (CH), 34.3 (CH_2), 34.4 (CH_2), 40.1 (CH_2), 41.6 (CH_2), 41.7 (CH_2), 43.1 (CH_2), 47.9 (CH), 48.3 (CH), 75.6 (CH), 80.7 (CH), 99.5 (CH), 104.8 (CH), 126.8 (CH), 128.6 (CH), 129.3 (C), 129.4 (C), 130.0 (CH), 156.7 (C) and 156.8 (C); m/z 302 [(M + H^+), 100%], 276 (13), 326 (26) and 148 (19) [Found: (M + H^+), 302.2120. $C_{19}H_{28}NO_2$ requires (M + H^+), 302.2120].

(5RS)-3-*Phenyl*-5-[(1R)-8-*phenylmenthyloxy*]-4,5-*dihydro-isoxazole* **6**.—In the same way as for compound **5**, benzaldehyde oxime (310 mg, 2.56 mmol), *N*-chlorosuccinimide (376 mg, 2.81 mmol), pyridine (2 drops), (1*R*)-8-phenylmenthyl vinyl ether **2** (660 mg, 2.56 mmol) and triethylamine (284 mg, 2.81 mmol) gave the *title compound* (495 mg, 51%) as a 1:1.94 mixture of diastereoisomers as a waxy white solid after flash column chromatography [(10:1) light petroleum–ether], R_f 0.21 [(6:1) light petroleum–ether]; $[\alpha]_D^{22}$ −44.4 (*c* 10, CH_2Cl_2); ν_{max}-(CH_2Cl_2)/cm^{-1} 1360s, 1190s, 1095s, 1080s, 840s and 680s; δ_H(300 MHz; $CDCl_3$) 0.76–1.54 (13 H, m), 1.56–1.74 (2 H, m), 1.81–1.94 (1 H, m), 2.15–2.38 (1.3 H, m), 2.43 and 3.10 (1.4 H, B and A of ABX system, J_{AB} 17.1, J_{AX} 6.8 and J_{BX} 1.7, 4-H), 2.93 (0.3 H, B of partially masked ABX system, J_{AB} 17.5 and J_{AX} 6.8, 4-H), 3.48 (0.3 H, td, J 10.3 and 4.3, 1′-H), 3.86 (0.7 H, td, J 10.6 and 3.6, 1′-H), 5.38 (0.3 H, X of partially masked ABX system, dd, J_{AX} 6.8 and J_{BX} 1.8, 5-H), 5.74 (0.7 H, X of ABX system, dd, J_{AX} 6.8 and J_{BX} 1.7, 5′-H), 6.89–6.93 (2 H, m, ArH) and 7.10–7.69 (8 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 22.0 (CH_3), 22.1 (CH_3), 24.5 (CH_3), 25.3 (CH_3), 26.7 (CH_2), 27.6 (CH_3), 29.2 (CH_3), 31.3 (CH), 31.5 (CH), 34.6 (CH_2), 34.9 (CH_2), 39.3 (CH_2), 39.7 (C), 39.8 (C), 41.4 (CH_2), 41.5 (CH_2), 43.9 (CH_2), 51.5 (CH), 75.4 (CH), 81.7 (CH), 97.6 (CH), 104.7 (CH), 124.0 (CH), 124.7 (CH), 125.3 (CH), 125.4 (CH), 126.7 (CH), 126.8 (CH), 126.84 (CH), 127.4 (CH), 127.7 (CH), 128.5 (CH), 128.57 (CH), 128.60 (CH), 129.3 (C), 129.5 (C), 130.0 (CH), 130.1 (CH), 152.1 (C), 153.1 (C), 156.8 (C) and 157.10 (C); m/z 378 [(M + H^+), 100%], 276 (73), 146 (34), 119 (29) [Found: (M + H^+), 378.2400. $C_{25}H_{32}NO_2$ requires (*M* + H^+), 378.2433].

(5RS)-5-[(1S)-endo-*Bornyloxy*]-3-*phenyl*-4,5-*dihydro-isoxazole* **7**.—In the same way as for compound **5**, benzaldehyde oxime (669 mg, 5.52 mmol), *N*-chlorosuccinimide (811 mg, 6.07 mmol), pyridine (2 drops), (1S)-*endo*-bornyl vinyl ether **3** (1.0 g, 5.52 mmol) and triethylamine (613 mg, 6.07 mmol) gave the *title compound* (741 mg, 45%) as an oily 1:1.31 mixture of diastereoisomers after flash column chromatography (light petroleum) R_f 0.61 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −21.9 (*c* 8, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1445s, 1385s, 1260s, 1110s, 1075s, 1035s, 960s, 850s, 745s and 685s; δ_H(300 MHz; $CDCl_3$) 0.79–1.29 (12 H, m), 1.46–1.76 (4 H, m), 1.97–1.26 (2 H, m), 3.91–4.01 (0.6 H, m, 1′-H), 4.08–4.16 (0.4 H, m, 1′-H), 5.42 (0.6 H, dd, J 10.8 and 5.4, 5-H), 5.43 (0.4 H, dd, J 10.7 and 5.4, 5-H), 7.33–7.42 (3 H, m, ArH) and 7.81–7.90 (2 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.3 (CH_3), 13.7 (CH_3), 18.81 (CH_3), 18.84 (CH_3), 19.7 (CH_3), 20.1 (CH_3), 20.5 (CH_3), 26.5 (CH_2), 26.7 (CH_2), 28.1 (CH_2), 28.3 (CH_2), 36.1 (CH_2), 37.5 (CH_2), 45.0 (CH), 47.2 (C), 47.5 (C), 48.9 (C), 49.4 (C), 81.5 (CH), 85.3 (CH), 103.1 (CH), 106.3 (CH), 127.0 (CH), 127.1 (CH), 128.30 (CH), 128.32 (CH), 132.8 (C), 132.9 (C) and 137.3 (C); m/z 300 [(M + H^+), 100%], 146 (83), 137 (87), 120 (71), 103 (29), 85 (52) and 83 (22) [Found: (M + H^+), 300.1964. $C_{19}H_{26}NO_2$ requires (*M* + H^+), 300.1964].

(5RS)-5-[(R)-α-(*Methoxycarbonyl*)*benzyloxy*]-3-*phenyl*-4,5-*dihydroisoxazole* **8**.—In the same way as for compound **5**, benzaldehyde oxime (252 mg, 2.08 mmol), *N*-chlorosuccinimide (306 mg, 2.29 mmol), pyridine (2 drops), methyl (*R*)-2-phenyl-2-vinyloxyacetate **4** (400 mg, 2.08 mmol) and triethylamine (231 mg, 2.29 mmol) gave the *title compound* (383 mg, 59%) as a 1:1.08 mixture of diastereoisomers as a white solid after flash

column chromatography [(2:1) light petroleum–ether]. The product was recrystallised from light petroleum, m.p. 117.5–119.5 °C; R_f 0.23 [(1:1) light petroleum–ether]; $[\alpha]_D^{22}$ −28.0 (*c* 10, CH_2Cl_2) (Found: C, 69.1; H, 5.5; N, 4.5. $C_{18}H_{17}NO_4$ requires C, 69.4; H, 5.5; N, 4.5%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1775s (C=O), 1370s, 1220s, 1185s, 1105s, 1080s, 940s and 860s; δ_H(300 MHz; $CDCl_3$) 3.30–3.47 (2 H, m, 4-H), 3.65 (1.5 H, s, OCH_3), 3.72 (1.5 H, s, OCH_3), 5.39 (0.5 H, s, OC*H*Ph), 5.49 (0.5 H, s, OC*H*Ph), 5.58 (0.5 H, dd, *J* 6.0 and 1.5, 5-H), 5.93 (0.5 H, dd, *J* 5.4 and 2.3, 5-H), 7.24–7.51 (8 H, m, ArH) and 7.62–7.69 (2 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 41.8 (CH_2), 42.2 (CH_2), 52.28 (CH_3), 52.34 (CH_3), 76.2 (CH), 77.0 (CH), 100.1 (CH), 101.1 (CH), 126.87 (CH), 126.92 (CH), 127.3 (CH), 127.8 (CH), 128.5 (CH), 128.66 (CH), 128.73 (CH), 128.8 (CH), 129.1 (CH), 130.4 (CH), 135.0 (C), 135.7 (C), 157.3 (C), 170.2 (C) and 171.0 (C); *m/z* 312 [(M + H^+), 2%], 149 (41), 147 (17), 146 (100), 121 (48), 107 (56), 105 (31), 103 (23), 91 (20), 79 (42) and 77 (89).

(S)-1-(2-*Naphthyl*)*ethyl Vinyl Ether* **9**.—Following the same procedure as for the preparation of compound **1**, (*S*)-1-(2-naphthyl)ethan-1-ol (5.0 g, 29.1 mmol), butyl vinyl ether (50 cm^3) and a catalytic amount of mercury(II) acetate gave the *title compound* as a colourless liquid (4.65 g, 81%) after flash column chromatography [(10:1) light petroleum–ether] R_f 0.71 [(10:1) light petroleum–ether]; ν_{max}(film)/cm^{-1} 1630m, 1190s, 1170s, 910s, 820s and 735s; δ_H(300 MHz; $CDCl_3$) 1.56 (3 H, d, *J* 6.5, CH_3), 3.94 (1 H, dd, *J* 6.7 and 1.7, OCH=CH_{cis}), 4.30 (1 H, dd, *J* 14.2 and 1.7, OCH=CH_{trans}), 4.99 (1 H, q, *J* 6.5, NaphC*H*O), 6.34 (1 H, dd, J_{trans} 14.2 and J_{cis} 6.7, OC*H*=CH_2), 7.37–7.45 (3 H, m, ArH) and 7.70–7.79 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 23.5 (CH_3), 77.4 (CH), 89.4 (CH_2), 123.7 (CH), 124.6 (CH), 125.8 (CH), 126.01 (CH), 127.6 (CH), 127.8 (CH), 128.4 (CH), 132.9 (C), 133.2 (C), 140.3 (CH) and 150.4 (CH); *m/z* 198 (M^+, 3%), 155 (100), 128 (13) (Found: M^+, 198.1045. $C_{14}H_{14}O$ requires M^+, 198.1045).

(S)-1-*Phenylbutyl Vinyl Ether* **10**.—Following the same procedure as for the preparation of compound **1**, (*S*)-1-phenylbutan-1-ol (5.5 g, 36.7 mmol), butyl vinyl ether (50 cm^3) and a catalytic amount of mercury(II) acetate gave the *title compound* as a colourless liquid (4.86 g, 75%) after flash column chromatography [(5:1) light petroleum–ether] R_f 0.60 [(10:1) light petroleum–ether]; ν_{max}(film)/cm^{-1} 1630s, 1185s, 1125m, 1045m and 700s; δ_H(300 MHz; $CDCl_3$) 0.91 (3 H, t, CH_3), 1.26–1.50 (2 H, m, CH_3CH_2), 1.62–1.74 (1 H, m, CH_3CH_2CH), 1.81–1.93 (1 H, m, CH_3CH_2CH), 3.93 (1 H, dd, *J* 6.6 and 1.6, OCH=CH_{cis}), 4.21 (1 H, dd, *J* 14.2 and 1.6, OCH=CH_{trans}), 4.69 (1 H, dd, *J* 7.5 and 5.7, PhC*H*O), 6.29 (1 H, dd, J_{trans} 14.2 and J_{cis} 6.6, OC*H*=CH_2) and 7.18–7.34 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.9 (CH_3), 18.8 (CH_2), 40.0 (CH_2), 81.3 (CH), 89.0 (CH_2), 126.2 (CH), 127.4 (CH), 128.3 (CH), 141.9 (C) and 150.8 (CH); *m/z* 176 (M^+, 2%), 133 (100) and 91 (100) (Found: M^+, 176.1201. $C_{12}H_{16}O$ requires M^+, 176.1201).

(5R)-5-[(S)-1-(2-*Naphthyl*)*ethoxy*]-3-*phenyl*-4,5-*dihydroisoxazole* **11**.—Following the same procedure as for the preparation of compound **5**, benzaldehyde oxime (1.22 g, 10.1 mmol), *N*-chlorosuccinimide (1.48 g, 11.1 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (2.0 g, 10.1 mmol) and triethylamine (1.12 g, 11.1 mmol) gave both diastereoisomers of the *title compound* as white solids after flash column chromatography [(10:1) light petroleum–ether]. The isomers were recrystallised from light petroleum. Major diastereoisomer, **11a** (1.39 g, 43%), m.p. 128–130 °C; R_f 0.15 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −67.9 (*c* 8, CH_2Cl_2) (Found: C, 79.5; H, 6.1; N, 4.4. $C_{21}H_{19}NO_2$ requires C, 79.5; H, 6.0; N, 4.4%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1075s, 935s, 925s, 845s and 820s; δ_H(300 MHz, $CDCl_3$) 1.52 (3 H, d, *J* 6.5, CH_3), 3.13–3.27 (2 H, m, 4-H), 5.14 (1 H, q, *J* 6.5, NaphC*H*O), 5.49 (1 H, dd, *J* 5.4 and 2.9, 5-H), 7.30–7.49 (6 H, m, ArH), 7.63–7.69 (2 H, m, ArH) and 7.78–7.85 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 23.9 (CH_3), 41.5 (CH_2), 74.9 (CH), 100.2 (CH), 124.2 (CH), 125.9 (CH), 126.0 (CH), 126.2 (CH), 126.8 (CH), 127.6 (CH), 127.8 (CH), 128.5 (CH), 128.6 (CH), 129.1 (CH), 130.2 (CH), 133.0 (C), 133.1 (C), 139.5 (C) and 156.9 (C); *m/z* 318 [(M + H^+), 17%] and 155 (100). Minor diastereoisomer, **11b** (0.463 g, 14%); m.p. 120–121 °C; R_f 0.10 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ +241.0 (*c* 2.73, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1360s, 1185s, 1080s and 845s; δ_H(300 MHz; $CDCl_3$) 1.58 (3 H, d, *J* 6.5, CH_3), 3.27 (1 H, A of ABX, *J* 17.4 and 1.8, 4-H), 3.39 (1 H, B of ABX, *J* 17.4 and 6.5, 4′-H), 5.10 (1 H, q, *J* 6.5, NaphC*H*O), 5.94 (1 H, dd, X of ABX, *J* 6.5 and 1.8, 5-H), 7.31–7.49 (6 H, m, ArH), 7.62–7.65 (2 H, m, ArH) and 7.74–7.80 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 21.7 (CH_3), 41.7 (CH_2), 74.9 (CH), 101.2 (CH), 124.56 (CH), 124.57 (CH), 125.6 (CH), 125.9 (CH), 126.8 (CH), 127.5 (CH), 127.9 (CH), 128.00 (CH), 128.6 (CH), 129.1 (C), 130.2 (CH), 132.8 (C), 133.1 (C), 140.5 (C) and 156.8 (C); *m/z* 317 (M^+, 11%), 155 (100), 129 (17) (Found M^+, 317.1415. $C_{21}H_{19}NO_2$ requires M^+ 317.1416).

(5R)-5-[(S)-1-(2-*Naphthyl*)*ethoxy*]-3-*phenethyl*-4,5-*dihydroisoxazole* **12**.—In the same way as for compound **5**, phenylpropionaldehyde oxime (377 mg, 2.53 mmol), *N*-chlorosuccinimide (371 mg, 2.78 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (500 mg, 2.53 mmol) and triethylamine (281 mg, 2.78 mmol) gave the major diastereoisomer of the *title compound* as a white solid (247 mg, 28%) after flash column chromatography [(10:1) light petroleum–ether]. The product was recrystallised from light petroleum, m.p. 123.5–125 °C; R_f 0.15 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −71.8 (*c* 10, CH_2Cl_2) (Found: C, 80.2; H, 6.7; N, 4.2. $C_{23}H_{23}NO_2$ requires C, 80.0; H, 6.7; N, 4.1%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1070s, 860s and 820s; δ_H(300 MHz; $CDCl_3$) 1.50 (3 H, d, *J* 6.5, CH_3), 2.51–2.69 (4 H, m, CH_2CH_2Ph), 2.83–2.88 (2 H, m, 4-H), 5.07 (1 H, q, *J* 6.5, NaphC*H*O), 5.27 (1 H, dd, *J* 5.0 and 3.2, 5-H), 7.09–7.26 (5 H, m, ArH), 7.36–7.45 (3 H, m, ArH) and 7.52–7.80 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 23.8 (CH_3), 29.3 (CH_2), 32.4 (CH_2), 43.8 (CH_2), 74.4 (CH), 99.2 (CH), 124.1 (CH), 125.8 (CH), 125.9 (CH), 126.1 (CH), 126.2 (CH), 127.6 (CH), 127.7 (CH), 128.2 (CH), 128.36 (CH), 128.41 (CH), 132.9 (C), 133.1 (C), 139.6 (C), 140.3 (C) and 158.5 (C); *m/z* 345 (M^+, 2%) and 155 (100).

(5R)-5-[(S)-1-(2-*Naphthyl*)*ethoxy*]-3-(4-*nitrophenyl*)-4,5-*dihydroisoxazole* **13**.—In the same way as for compound **5**, 4-nitrobenzaldehyde oxime (587 mg, 3.54 mmol), *N*-chlorosuccinimide (519 mg, 3.89 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (700 mg, 3.54 mmol) and triethylamine (393 mg, 3.89 mmol) gave the major diastereoisomer of the *title compound* as a white solid (333 mg, 26%) after flash column chromatography [(10:1) light petroleum–ether], m.p. 167.5–169.5 °C; R_f 0.17 [(4:1) light petroleum–ether]; $[\alpha]_D^{22}$ −9.0 (*c* 1, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1520s, 1340s and 850s; δ_H(300 MHz; $CDCl_3$) 1.55 (3 H, d, *J* 6.5, CH_3), 3.24–3.36 (2 H, m, 4-H), 5.16 (1 H, q, *J* 6.5, NaphC*H*O), 5.62 (1 H, dd, *J* 5.0 and 3.5, 5-H) and 7.40–8.37 (11 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 23.7 (CH_3), 40.9 (CH_2), 73.4 (CH), 101.1 (CH), 123.7 (CH), 123.8 (CH), 124.0 (CH), 124.1 (CH), 125.9 (CH), 126.0 (CH), 126.3 (CH), 127.4 (CH), 127.4 (CH), 127.6 (CH), 127.8 (CH), 128.6 (CH), 129.2 (CH), 130.3 (CH), 131.1 (CH), 133.0 (C), 135.1 (C), 139.1 (C), 148.3 (C), 155.4 (C) and 190.2 (C); *m/z* 362 (M^+, 1%), 155 (100) and 128 (11) (Found: M^+, 362.1270. $C_{21}H_{18}N_2O_4$ requires M^+, 362.1267).

(5R)-3-tert-*Butyl*-5-[(S)-1-(2-*naphthyl*)*ethoxy*]-4,5-*dihydroisoxazole* **14**.—In the same way as for compound **5**, pival-

aldehyde oxime (200 mg, 1.98 mmol), *N*-chlorosuccinimide (291 mg, 2.18 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (392 mg, 1.98 mmol) and triethylamine (220 mg, 2.18 mmol) gave the major diastereoisomer of the *title compound* as a white solid (311 mg, 53%) after flash column chromatography [(5:1) light petroleum–ether]. The product was recrystallised from light petroleum, m.p. 81–83 °C; R_f 0.10 [(5:1) light petroleum–ether]; $[\alpha]_D^{22}$ −81.3 (*c* 10, CH_2Cl_2) (Found: C, 76.4; H, 7.9; N, 4.7. $C_{19}H_{23}NO_2$ requires C, 76.7; H, 7.8; N, 4.7%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1075s, 935s and 850s; δ_H(300 MHz; $CDCl_3$) 1.20 [9 H, s, $C(CH_3)_3$], 1.49 (3 H, d, *J* 6.6, CH_3), 2.80 (2 H, d, *J* 4.0, 4-H), 5.07 (1 H, q, *J* 6.6, NaphC*H*O), 5.30 (1 H, t, *J* 4.0, 5-H), 7.38–7.47 (3 H, m, ArH) and 7.73–7.82 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 23.9 (CH_3), 27.4 (CH_3), 28.1 (CH_3), 29.3 (CH_3), 32.9 (C), 41.0 (CH_2), 74.3 (CH), 99.5 (CH), 124.2 (CH), 125.8 (CH), 125.9 (CH), 126.1 (CH), 127.6 (CH), 127.8 (CH), 128.4 (CH), 133.0 (C), 133.1 (C), 139.8 (C), 158.7 (CH) and 166.2 (C); *m*/*z* 298 [(M + H^+), 100%], 155 (43) and 144 (19).

(5R)-5-[(S)-1-(2-*Naphthyl*)*ethoxy*]-3-*propyl*-4,5-*dihydroisoxazole* **15**.—Following the same procedure as for the preparation of compound **5**, butyraldehyde oxime (220 mg, 2.53 mmol), *N*-chlorosuccinimide (371 mg, 2.78 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (500 mg, 2.53 mmol) and triethylamine (281 mg, 2.78 mmol) gave the major diastereoisomer of the *title compound* as a colourless oil (250 mg, 37%) after flash column chromatography [(3:1) light petroleum–ether], R_f 0.10 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ −173.6 (*c* 10, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1600m, 1510m, 1170s, 1080s, 940s, 865s and 750s; δ_H(300 MHz; $CDCl_3$)1.04 (3 H, t, *J* 7.3, $CH_2CH_2CH_3$), 1.58–1.75 (5 H, m, NaphCHCH_3 and $CH_3CH_2CH_2$), 2.44 (2 H, t, *J* 7.5, $CH_3CH_2CH_2$), 2.83 and 2.93 (2 H, B and A of ABX system, J_{AB} 17.5, J_{AX} 6.2 and J_{BX} 1.7, 4-H), 5.17 (1 H, q, *J* 6.5, NaphC*H*O), 5.40 (1 H, X of ABX system, dd, J_{AX} 6.2 and J_{BX} 1.7, 5-H), 7.49–7.58 (3 H, m, ArH) and 7.83–7.92 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.5 (CH_3), 19.6 (CH_2), 23.8 (CH_3), 29.3 (CH_2), 43.5 (CH_2), 74.3 (CH), 99.1 (CH), 124.1 (CH), 125.7 (CH), 125.8 (CH), 126.1 (CH), 127.5 (CH), 127.7 (CH), 128.3 (CH), 132.9 (C), 133.0 (C), 139.7 (C) and 159.2 (C); *m*/*z* 284 [(M + H^+), 100%], 155 (71) and 130 (24) [Found: (M + H^+), 284.1651. $C_{18}H_{22}NO_2$ requires (*M* + H^+), 284.1650].

(5R)-3-*Ethyl*-5-[(S)-1-(2-*naphthyl*)*ethoxy*]-4,5-*dihydroisoxazole* **16**.—In the same way as for compound **5**, propionaldehyde oxime (184 mg, 2.53 mmol), *N*-chlorosuccinimide (371 mg, 2.78 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (500 mg, 2.53 mmol) and triethylamine (281 mg, 2.78 mmol) gave the major diastereoisomer of the *title compound* as a white solid (248 mg, 40%) after flash column chromatography [(3:1) light petroleum–ether]. The product was recrystallised from light petroleum, m.p. 70.5–72 °C; R_f 0.11 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ −209.3 (*c* 10, CH_2Cl_2) (Found: C, 75.9; H, 7.2; N, 5.4. $C_{17}H_{19}NO_2$ requires C, 75.8; H, 7.1; N, 5.2%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1590m, 1100s, 955s, 870s, 860s and 840s; δ_H(300 MHz; $CDCl_3$) 1.16 (3 H, t, *J* 7.5, CH_2CH_3), 1.51 (3 H, d, *J* 6.5, NaphCH_3CHO), 2.34–2.48 (2 H, m, CH_2CH_3), 2.75 and 2.86 (2 H, B and A of ABX system, J_{AB} 17.5, J_{AX} 6.3 and J_{BX} 1.8, 4-H), 5.08 (1 H, q, *J* 6.5, NaphC*H*O), 5.32 (1 H, X of ABX system, dd, J_{AX} 6.3 and J_{BX} 1.8, 5-H), 7.30–7.58 (3 H, m, ArH) and 7.83–7.92 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 10.8 (CH_3), 21.2 (CH_2), 23.9 (CH_3), 43.6 (CH_2), 74.5 (CH), 99.3 (CH), 124.2 (CH), 125.8 (CH), 125.9 (CH), 126.2 (CH), 127.6 (CH), 127.8 (CH), 128.5 (CH), 133.0 (C), 133.1 (C), 139.8 (C) and 160.3 (C); *m*/*z* 269 (M^+, 4%), 156 (16), 155 (100), 154 (46), 153 (21), 129 (44), 128 (23) and 127 (26).

(5RS)-5-[(S)-1-(2-*Naphthyl*)*ethoxy*]-3-*methyl*-4,5-*dihydroisoxazole* **17**.—In the same way as for compound **5**, acetaldehyde oxime (145 mg, 2.53 mmol), *N*-chlorosuccinimide (371 mg, 2.78 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl vinyl ether **9** (500 mg, 2.53 mmol) and triethylamine (281 mg, 2.78 mmol) gave the *title compound* as a 2:1 mixture of diastereoisomers as a white solid (237 mg, 37%) after flash column chromatography [(2:1) light petroleum–ether]. The product was recrystallised from light petroleum, m.p. 92–95 °C; R_f 0.12 [(2:1) light petroleum–ether]; $[\alpha]_D^{22}$ −143.4 (*c* 8, CH_2Cl_2) (Found: C, 75.3; H, 6.8; N, 5.5. $C_{16}H_{17}NO_2$ requires C, 75.3; H, 6.7; N, 5.5%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1535s, 1415s, 1370s, 1070s, 925s, 835s and 750s; δ_H(300 MHz; $CDCl_3$) 1.49 (2 H, d, *J* 6.5, NaphCH_3CHO), 1.53 (1 H, d, *J* 6.5, NaphCH_3CHO), 1.97 (3 H, s, N=CCH_3), 2.71 (1 H, dd, *J* 17.6 and 1.1, 4-H), 2.82 (1 H, ddd, *J* 17.6, 6.2 and 1.1, 4-H), 5.00 (0.3 H, q, *J* 6.5, NaphC*H*O), 5.06 (0.7 H, q, *J* 6.5, NaphC*H*O), 5.29 (1 H, dd, *J* 6.2 and 1.8, 5-H), 7.37–7.48 (3 H, m, ArH) and 7.72–7.82 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 12.9 (CH_3), 13.9 (CH_3), 23.9 (CH_3), 25.2 (CH_3), 44.0 (CH_2), 45.1 (CH_2), 70.0 (CH), 74.6 (CH), 99.5 (CH), 100.7 (CH), 123.7 (CH), 123.9 (CH), 124.1 (CH), 124.2 (CH), 125.5 (CH), 125.8 (CH), 125.9 (CH), 126.2 (CH), 127.47 (CH), 127.54 (CH), 127.6 (CH), 127.8 (CH), 128.0 (CH), 128.5 (CH), 132.7 (C), 133.0 (C), 133.1 (C), 133.2 (C), 139.7 (C), 143.6 (C) and 155.8 (C); *m*/*z* 255 (M^+, 3%), 155 (100).

3-*Phenyl*-5-[(S)-1-*phenylbutoxy*]-4,5-*dihydroisoxazole* **18**.—Following the same procedure as for the preparation of compound **5**, benzaldehyde oxime (138 mg, 1.14 mmol), *N*-chlorosuccinimide (167 mg, 1.25 mmol), pyridine (2 drops), (*S*)-1-phenylbutyl vinyl ether **10** (200 mg, 1.14 mmol) and triethylamine (126 mg, 1.25 mmol) gave the major diastereoisomer of the *title compound* as a waxy white solid (111 mg, 33%) after flash column chromatography [(10:1) light petroleum–ether] R_f 0.43 [(3:1) light petroleum–ether; $[\alpha]_D^{22}$ −135.2 (*c* 5, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1490w, 1185m, 1080s, 930s and 845s; δ_H(300 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 7.3, CH_3), 1.21–1.43 (2 H, m, CH_3CH_2), 1.55–1.66 (1 H, m, CH_3CH_2CH), 1.74–1.86 (1 H, m, CH_3CH_2CH), 3.17–3.32 (2 H, m, 4-H), 4.81 (1 H, dd, *J* 7.5 and 6.2, PhC*H*O), 5.48 (1 H, dd, *J* 5.2 and 3.0, 5-H), 7.26–7.50 (2 H, m, ArH) and 7.61–7.71 (8 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.81 (CH_3), 18.82 (CH_2), 34.0 (CH_2), 41.5 (CH_2), 78.5 (CH), 100.0 (CH), 126.8 (CH), 127.1 (CH), 127.7 (CH), 128.4 (CH), 128.6 (CH), 129.2 (C), 130.2 (CH), 141.5 (C) and 156.9 (C); *m*/*z* 296 [(M + H^+), 46%], 164 (15), 146 (23), 133 (25), 83 (41) and 49 (100) [Found: (M + H^+), 296.1651. $C_{17}H_{22}NO_2$ requires (*M* + H^+), 296.1650].

5-[(S)-1-*Phenylbutoxy*]-3-*phenethyl*-4,5-*dihydroisoxazole* **19**.—In the same way as for compound **5**, 2-phenylpropionaldehyde oxime (677 mg, 4.55 mmol), *N*-chlorosuccinimide (668 mg, 5.0 mmol), pyridine (2 drops), (*S*)-1-phenylbutyl vinyl ether **10** (800 mg, 4.55 mmol) and triethylamine (505 mg, 5.0 mmol) gave the major diastereoisomer of the *title compound* as a colourless oil (645 mg, 44%) after flash column chromatography [(5:1) light petroleum–ether], R_f 0.20 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ −121.7 (*c* 10, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1445s, 1155s, 1060s, 970s, 865s and 750s; δ_H(300 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 7.3, $CH_3CH_2CH_2$), 1.17–1.42 (2 H, m, $CH_3CH_2CH_2$), 1.52–1.64 (1 H, m, CH_3CH_2CH), 1.72–1.84 (1 H, m, CH_3CH_2CH), 2.66–2.96 (6 H, m, CH_2CH_2Ph and 4-H), 4.74 (1 H, dd, *J* 7.5 and 6.1, PhC*H*O), 5.26 (1 H, dd, *J* 6.2 and 1.7, 5-H) and 7.02–7.34 (10 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.8 (CH_3), 18.8 (CH_2), 29.4 (CH_2), 32.6 (CH_2), 34.0 (CH_2), 43.8 (CH_2), 78.0 (CH), 99.1 (CH), 126.2 (CH), 127.0 (CH), 127.6 (CH), 128.19 (CH), 128.23 (CH), 128.35 (CH), 128.44 (CH), 140.4 (C), 141.6 (C) and 158.7 (C); *m*/*z* 323 (M^+, 6%), 133 (20), 132 (21), 131

(100), 107 (35) and 105 (34) (Found: M^+, 323.1885. $C_{21}H_{25}NO_2$ requires M^+, 323.1885).

3-(4-*Nitrophenyl*)-5-[(S)-1-*phenylbutoxy*]-4,5-*dihydro-isoxazole* **20**.—In the same way as for compound **5**, 4-nitrobenzaldehyde oxime (943 mg, 5.68 mmol), *N*-chloro succinimide (843 mg, 6.25 mmol), pyridine (2 drops), (*S*)-1-phenylbutyl vinyl ether **10** (1.0 g, 5.68 mmol) and triethylamine (631 mg, 6.25 mmol) gave the major diastereoisomer of the *title compound* as a white solid (433 mg, 23%) after flash column chromatography [(4:1) light petroleum–ether]. The product was recrystallised from methanol, m.p. 105–107 °C; R_f 0.10 [(4:1) light petroleum–ether]; $[\alpha]_D^{22}$ −63.1 (*c* 10, CH_2Cl_2) (Found: C, 67.2; H, 6.1; N, 8.2. $C_{19}H_{20}N_2O_4$ requires C, 67.0; H, 5.9; N, 8.2%) $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1535s, 1350s, 1085s, 860s and 840s; δ_H(300 MHz; $CDCl_3$) 0.89 (3 H, t, *J* 7.3, $CH_3CH_2CH_2$), 1.23–1.44 (2 H, m, $CH_3CH_2CH_2$), 1.58–1.70 (1 H, m, CH_3CH_2CH), 1.76–1.88 (1 H, m, CH_3CH_2CH), 3.29 and 3.37 (2 H, B and A of ABX system, J_{AB} 17.4, J_{AX} 6.1 and J_{BX} 2.3, 4-H), 4.84 (1 H, dd, *J* 10.3 and 6.4, PhCHO), 5.61 (1 H, X of ABX system, dd, J_{AX} 6.1 and J_{BX} 2.3, 5-H), 7.30–7.43 (4 H, m, ArH), 7.87–7.94 (3 H, m, ArH) and 8.23–8.46 (2 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.7 (CH_3), 18.7 (CH_2), 39.8 (CH_2), 40.8 (CH_2), 78.9 (CH), 100.9 (CH), 123.8 (CH), 124.1 (CH), 127.0 (CH), 127.4 (CH), 127.8 (CH), 128.4 (CH), 133.4 (CH), 135.2 (C), 141.0 (C), 148.3 (C) and 155.4 (C); *m/z* 192 [$(MH)^+$ − OCHPrPh, 81%], 164 (30), 149 (20), 135 (89), 134 (100), 133 (23), 118 (100), 108 (59) and 106 (66).

3-tert-*Butyl*-5-[(S)-1-*phenylbutoxy*]-4,5-*dihydroisoxazole* **21**.—In the same way as for compound **5**, pivalaldehyde oxime (459 mg, 4.55 mmol), *N*-chlorosuccinimide (668 mg, 5.0 mmol), pyridine (2 drops), (*S*)-1-phenylbutyl vinyl ether **10** (800 mg, 4.55 mmol) and triethylamine (505 mg, 5.0 mmol) gave the major diastereoisomer of the *title compound* as a colourless oil (590 mg, 47%) after flash column chromatography [(10:1) light petroleum–ether], R_f 0.10 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −197.4 (*c* 10, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1450s, 1360s 1175s, 1105s, 930s, 845s and 700s; δ_H(300 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 7.3, $CH_3CH_2CH_2$), 1.16–1.63 [12 H, m, $C(CH_3)_3$ and CH_3CH_2CH), 1.71–1.88 (1 H, m, CH_3CH_2CH), 2.80 and 2.89 (2 H, B and A of ABX system, J_{AB} 17.2, J_{AX} 5.8 and J_{BX} 2.0, 4-H), 4.75 (1 H, dd, *J* 7.8 and 6.0, PhCHO), 5.27 (1 H, X of ABX system, dd, J_{AX} 5.8 and J_{BX} 2.0, 5-H) and 7.21–7.36 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.8 (CH_3), 18.9 (CH_2), 28.1 (CH_3), 33.0 (C), 40.0 (CH_2), 41.0 (CH_2), 77.6 (CH), 99.1 (CH), 127.0 (CH), 127.6 (CH), 128.3 (CH), 141.8 (C) and 166.3 (C); *m/z* 275 (M^+, 3%), 232 (17), 150 (22), 133 (100), 126 (83), 117 (100) and 110 (56) (Found: M^+, 275.1885. $C_{17}H_{25}NO_2$ requires M^+, 275.1885).

5-[(S)-1-*Phenylbutoxy*]-3-*propyl*-4,5-*dihydroisoxazole* **22**.—In the same way, as for compounds **5** butyraldehyde oxime (247 mg, 2.84 mmol), *N*-chlorosuccinimide (417 mg, 3.13 mmol), pyridine (2 drops), (*S*)-1-phenybutyl vinyl ether **10** (500 mg, 2.84 mmol) and triethylamine (316 mg, 3.13 mmol) gave the major diastereoisomer of the *title compound* as a colourless oil (289 mg, 39%) after flash column chromatography [(5:1) light petroleum–ether] R_f 0.33 [(2:1) light petroleum–ether]; $[\alpha]_D^{22}$ −210.4 (*c* 5, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1600s, 1455s, 1175s, 870s and 765s; δ_H(300 MHz; $CDCl_3$) 0.85 (3 H, t, *J* 7.4, $CH_3CH_2CH_2CPh$), 0.94 (3 H, t, *J* 7.4, $N{=}CCH_2CH_2CH_3$), 1.17–1.38 (2 H, m, $CH_3CH_2CH_2CPh$), 1.49–1.65 (3 H, m, $NCCH_2CH_2CH_3$ and CH_3CH_2CHCPh), 1.69–1.80 (1 H, m, CH_3CH_2CHPh), 2.30–2.37 (2 H, m, $N{=}CCH_2CH_2CH_3$), 2.70 and 2.84 (2 H, B and A of ABX system, J_{AB} 17.4, J_{AX} 6.2 and J_{BX} 1.5, 4-H), 4.73 (1 H, dd, *J* 7.8 and 5.9, PhCHO), 5.24 (1 H, X of ABX system, dd, J_{AX} 6.2 and J_{BX} 1.5, 5-H) and 7.20–7.33 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.4 (CH_3), 13.7 (CH_3), 18.7 (CH_2), 19.7 (CH_2), 29.3 (CH_2), 39.9 (CH_2), 43.3 (CH_2), 77.7 (CH), 98.8 (CH), 126.9 (CH), 127.5 (CH), 128.2 (CH), 141.4 (C) and 159.1 (C); *m/z* 262 [$(MH)^+$, 100%], 242 (13), 150 (13), 130 (27), 112 (20) and 86 (25) [Found: $(M + H^+)$, 262.1810. $C_{16}H_{24}NO_2$ requires $(M + H^+)$, 262.1807].

3-*Ethyl*-5-[(S)-1-*Phenylbutoxy*]-4,5-*dihydroisoxazole* **23**.—In the same way as for compound **5**, propionaldehyde oxime (207 mg, 2.84 mmol), *N*-chlorosuccinimide (417 mg, 3.13 mmol), pyridine (2 drops), (S)-1-phenylbutyl vinyl ether **10** (500 mg, 2.84 mmol) and triethylamine (316 mg, 3.13 mmol) gave the major diastereoisomer of the *title compound* as a colourless oil (246 mg, 35%) after flash column chromatography [(5:1) light petroleum–ether], R_f 0.26 [(2:1) light petroleum–ether]; $[\alpha]_D^{22}$ −265.4 (*c* 10, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1605m, 1460s, 1175s, 1090s, 935s, 845s and 760s; δ_H(300 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 7.3, $CH_3CH_2CH_2$), 1.07–1.42 (5 H, m, $CH_3CH_2CH_2$ and CH_3CH_2CN), 1.53–1.64 (1 H, m, CH_3CH_2CH), 1.72–1.84 (1 H, m, CH_3CH_2CH), 2.35–2.46 (2 H, m, $NCCH_2CH_3$), 2.74 and 2.90 (2 H, B and A of ABX system, J_{AX} 17.4, J_{AB} 6.4 and J_{BX} 1.5, 4-H), 4.75 (1 H, dd, *J* 7.6 and 6.2, PhCHO), 5.28 (1 H, X of ABX system, dd, J_{AX} 6.4 and J_{BX} 1.5, 5-H), 7.23–7.26 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 10.9 (CH_3), 13.8 (CH_3), 18.9 (CH_2), 21.2 (CH_2), 40.0 (CH_2), 43.5 (CH_2), 78.4 (CH), 99.1 (CH), 127.0 (CH), 127.6 (CH), 128.4 (CH), 141.7 (C) and 160.4 (C); *m/z* 248 [$(M + H^+)$, 100%], 228 (10), 133 (10), 116 (17), 98 (14) and 91 (15) [Found: $(M + H^+)$, 248.1650. $C_{15}H_{22}NO_2$ requires $(M + H^+)$, 248.1651].

3-*Methyl*-5-[(S)-1-*Phenylbutoxy*]-4,5-*dihydroisoxazole* **24**.—In the same way as for compound **5**, acetaldehyde oxime (335 mg, 5.68 mmol), *N*-chlorosuccinimide (834 mg, 6.25 mmol), pyridine (2 drops), (*S*)-1-phenylbutyl vinyl ether **10** (1.0 g, 5.68 mmol) and triethylamine (631 mg, 6.25 mmol) gave the major diastereoisomer of the *title compound* as a colourless oil (696 mg, 53%) after flash column chromatography [(3:1) light petroleum–ether], R_f 0.12 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ −241.3 (*c* 10, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1415m, 1325s, 1170s, 1025s, 920s, 865s and 755s; δ_H(300 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 7.3, $CH_3CH_2CH_2$), 1.15–1.41 (2 H, m, $CH_3CH_2CH_2$), 1.52–1.64 (1 H, m, CH_3CH_2CH), 1.72–1.84 (1 H, m, CH_3CH_2CH), 2.02 (3 H, s, CH_3CN), 2.72 (1 H, d, *J* 17.6, 4-H), 2.89 (1 H, ddd, *J* 17.6, 6.4 and 1.1, 4-H), 4.75 (1 H, dd, *J* 7.5 and 6.2, PhCHO), 5.28 (1 H, dd, *J* 6.4 and 1.4, 5-H) and 7.23–7.36 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.0 (CH_3), 13.8 (CH_3), 18.8 (CH_2), 40.0 (CH_2), 45.1 (CH_2), 78.1 (CH), 99.3 (CH), 127.0 (CH), 127.6 (CH), 128.4 (CH), 141.6 (C) and 155.7 (C); *m/z* 234 (M^+, 4%), 190 (15), 150 (11), 133 (100), 117 (87) and 107 (69) (Found: M^+, 233.1420. $C_{14}H_{19}NO_2$ requires M^+, 233.1416).

(S)-1-(2-*Naphthyl*)*ethyl Prop*-2-*enoate* **27**.—A solution of (*S*)-1-(2-naphthyl)ethanol (1.0 g, 5.81 mmol) in THF (8 cm^3) was stirred under nitrogen at 0 °C, then butyllithium (3.82 cm^3, 6.10 mmol) was added dropwise. After 1 h acryloyl chloride (579 mg, 6.40 mmol) was added slowly and the reaction mixture stirred for 30 min. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate and then standard aqueous work-up yielded the *title compound* as a waxy white solid (1.23 g, 94%) after flash column chromatography [(10:1) light petroleum–ether], R_f 0.17 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −92.5 (*c* 20, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1715s (C=O), 1630m, 1400s, 1265s, 1125s, 1015s, 965s, 855s and 745s; δ_H(300 MHz; $CDCl_3$) 1.63 (3 H, d, *J* 6.6, CH_3), 5.75 (1 H, dd, *J* 10.3 and 1.5, $OCCH{=}CH_{cis}$), 6.12 (1 H, q, *J* 6.6, NaphCHO), 6.15 (1 H, dd, *J* 17.3 and 10.3, $OCCH{=}CH_{trans}$), 6.42 (1 H, dd, *J* 17.3 and 1.5, $OCCH{=}CH_2$), 7.37–7.47 (3 H, m, ArH) and 7.73–7.79 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 22.1 (CH_3), 72.5 (CH), 124.0

(CH), 124.9 (CH), 126.00 (CH), 126.03 (CH), 126.06 (CH), 126.1 (CH), 127.6 (CH), 127.9 (CH), 128.3 (CH), 128.6 (CH), 130.7 (CH_2), 132.9 (C), 133.1 (C), 138.8 (C) and 165.3 (C); *m/z* 226 (M^+, 100%), 172 (41), 155 (100), 127 (17) and 55 (42) (Found: M^+, 226.0994. $C_{15}H_{14}O_2$ requires M^+, 226.0994).

(S)-1-*Phenylbutyl Prop-2-enoate* **28**.—Following the same procedure as for the preparation of compound **27**, (*S*)-(−)-1-phenylbutan-1-ol (1.0 g, 6.67 mmol), butyllithium (4.16 cm^3, 7.0 mmol) and acryloyl chloride (664 mg, 7.33 mmol) gave the *title compound* as a colourless liquid (754 mg, 55%) after flash column chromatography [(10:1) light petroleum–ether] R_f 0.17 [(10:1) light petroleum–ether]; $[\alpha]_D^{22}$ −106.8 (*c* 5, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1725s (C=O), 1635m, 1405s, 1270s, 1190s, 1045s and 760s; δ_H(300 MHz; $CDCl_3$) 0.91 (3 H, t, *J* 7.3, CH_3), 1.23–1.42 (2 H, m, CH_3CH_2), 1.72–1.84 (1 H, m, CH_3CH_2CH), 1.88–1.99 (1 H, m, CH_3CH_2CH), 5.78 (1 H, dd, *J* 10.3 and 1.5, OCCH=CH_{cis}), 5.81 (1 H, dd, *J* 7.7 and 1.5, PhCHO), 6.13 (1 H, dd, J_{trans} 17.3 and J_{cis} 10.3, OCCH=CH_2), 6.40 (1 H, dd, *J* 17.3 and 1.5, OCCH=CH_{trans}) and 7.22–7.94 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.8 (CH_3), 18.8 (CH_2), 38.5 (CH_2), 76.0 (CH), 126.4 (CH), 127.8 (CH), 128.4 (CH), 128.7 (CH), 130.6 (CH_2), 140.7 (C) and 165.4 (C); *m/z* 204 (M^+, 7%), 161 (18), 133 (100), 117 (35), 91 (38), 71 (15) and 55 (65) (Found: M^+, 204.1150. $C_{13}H_{16}O_2$ requires M^+, 204.1150).

(5RS)-5-[(S)-1-(2-*Naphthyl*)*ethoxycarbonyl*]-3-*phenyl*-4,5-*dihydroisoxazole* **29**.—Following the same procedure as for the preparation of compound **5**, benzaldehyde oxime (268 mg, 2.21 mmol), *N*-chlorosuccinimide (325 mg, 2.43 mmol), pyridine (2 drops), (*S*)-1-(2-naphthyl)ethyl prop-2-enoate **27** (500 mg, 2.21 mmol) and triethylamine (245 mg, 2.43 mmol) gave the *title compound*, as a white solid, as an approximate 1:1 mixture of diastereoisomers (511 mg, 67%) after flash column chromatography [(10:1) light petroleum–ether]. The product was recrystallised from methanol, m.p. 112–114 °C; R_f 0.36 [(1:1) light petroleum–ether]; $[\alpha]_D^{22}$ +21.0 (*c* 1, CH_2Cl_2) (Found: C, 76.5; H, 5.7; N, 4.0. $C_{22}H_{19}NO_3$ requires C, 76.5; H, 5.5; N, 4.1%); ν_{max}(CH_2Cl_2)/cm^{-1} 1730s (C=O), 1600w, 1350s, 1200s, 1170s, 1060s, 880s and 855s; δ_H(300 MHz; $CDCl_3$) 1.61 (3 H, d, *J* 6.6, CH_3), 3.33–3.54 (2 H, m, 4-H), 5.05–5.15 (1 H, m, 5-H), 6.08 (1 H, q, *J* 6.6, NaphCHO) and 7.23–7.78 (12 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 21.9 (CH_3), 22.1 (CH_3), 38.5 (CH_2), 38.7 (CH_2), 73.9 (CH), 74.1 (CH), 78.1 (CH), 78.1 (CH), 123.7 (CH), 123.8 (CH), 124.8 (CH), 125.2 (CH), 126.0 (CH), 126.2 (CH), 126.24 (CH), 126.8 (CH), 127.5 (CH), 127.6 (CH), 127.9 (CH), 128.4 (CH), 127.43 (CH), 128.58 (CH), 128.61 (CH), 130.3 (CH) 132.9 (C), 138.0 (C), 138.1 (C), 155.9 (C), 169.2 (C) and 169.3 (C); *m/z* 345 (M^+, 8%) and 155 (100).

(5RS)-3-*Phenyl*-5-[(S)-1-*phenylbutoxycarbonyl*]-4,5-*dihydroisoxazole* **30**.—Following the same procedure as for the preparation of compound **5**, benzaldehyde oxime (297 mg, 2.45 mmol), *N*-chlorosuccinimide (360 mg, 2.70 mmol), pyridine (2 drops), (*S*)-1-phenylbutyl prop-2-enoate **28** (500 mg, 2.45 mmol) and triethylamine (273 mg, 2.70 mmol) gave the *title compound* (271 mg, 34%) as an oil, approximately 1:1 mixture of diastereoisomers after flash column chromatography [(3:1) light petroleum–ether], R_f 0.15 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ −33.9 (*c* 10, CH_2Cl_2); ν_{max}(film)/cm^{-1} 1735s (C=O), 1600w, 1355s, 1210s and 890s; δ_H(300 MHz; $CDCl_3$) 0.90 (1.5 H, t, *J* 7.3, CH_3), 0.92 (1.5 H, t, *J* 7.4, CH_3), 1.22–1.45 (2 H, m, CH_3CH_2), 1.72–2.02 (2 H, m, $CH_3CH_2CH_2$), 3.52–3.65 (2 H, m, 4-H), 5.11–5.19 (1 H, m, 5-H), 5.81 (1 H, dd, *J* 7.8 and 6.2, PhCHO), 7.14–7.43 (8 H, m, ArH) and 7.62–7.67 (2 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.7 (CH_3), 18.7 (CH_2), 38.2 (CH_2), 32.3 (CH_2), 38.6 (CH_2), 38.8 (CH_2), 77.5 (CH), 77.6 (CH), 78.16 (CH), 126.2 (CH), 126.5 (CH), 126.8 (CH), 127.9 (CH), 128.1 (CH), 128.4 (CH), 128.6 (CH), 139.9 (C), 155.8 (C), 169.3 (C); *m/z* 324 ([M + H^+], 100%), 192 (32), 146 (26), 133 (17), 108 (14) and 91 (26) [Found: (M + H^+), 324.1600. $C_{20}H_{22}NO_3$ requires (*M* + H^+), 324.1600].

3-*Ethoxycarbonyl*-6-[(S)-1-(2-*naphthyl*)*ethoxy*]-5,6-*dihydro*-4H-1,2-*oxazine* **32**.—Ethyl 3-bromo-2-hydroxyiminopropanoate[21] (0.40 g, 1.9 mmol) and (*S*)-1-(2-naphthyl)-ethyl vinyl ether **9** (0.68 g, 3.4 mmol) were dissolved in dichloromethane (10 cm^3), and to this mixture was added anhydrous K_2CO_3 (0.53 g, 3.83 mmol). After stirring overnight at room temperature the resulting orange solution was washed with water dried over $MgSO_4$ filtered then concentrated under reduced pressure to yield, after flash column chromatography [(6:1) light petroleum–ether], the two diasteroisomers of the *title compound*. Major diastereoisomer, **32a**, colourless crystals (from light petroleum) (0.287 g, 46%), m.p. 87–89 °C; R_f 0.40 [(1:1) light petroleum–ether]; $[\alpha]_D^{22}$ −114.5 (*c* 1.38, CH_2Cl_2); ν_{max}(CH_2Cl_2)/cm^{-1} 1720s (C=O), 1600w, 1290s, 1110s, 1095s, 1000s, 915s and 860s; δ_H(300 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.48 (3 H, d, *J* 6.6, ArCHCH_3), 1.62–1.73 (1 H, m), 1.89–1.98 (1 H, m), 2.41–2.61 (2 H, m), 4.25–4.40 (2 H, A and B of ABX$_3$, $CO_2CH_2CH_3$), 4.98 (1 H, t, *J* 2.6, 6-H), 5.11 (1 H, q, *J* 6.6, ArC*H*CH_3), 7.38–7.50 (3 H, m, ArH) and 7.68–7.83 (4 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 14.2 (CH_3), 15.6 (CH_2), 21.8 (CH_2), 23.6 (CH_3), 61.9 (CH_2), 74.6 (CH), 92.8 (CH), 124.0 (CH), 125.9 (CH), 126.0 (CH), 126.2 (CH), 127.6 (CH), 127.8 (CH), 128.5 (CH), 133.05 (C), 133.10 (C), 139.4 (C), 151.0 (C) and 163.3 (C); *m/z* 327 (M^+, 3%), 156 (14), 155 (100) (Found: M^+, 327.1473. $C_{19}H_{21}NO_4$ requires M^+, 327.1471). Minor diastereoisomer, **32b**, colourless oil (0.051 g, 8.0%), R_f 0.25 [(1:1) light petroleum–ether]; $[\alpha]_D^{22}$ +182.1 (*c* 1.38, CH_2Cl_2); ν_{max}(CH_2Cl_2)/cm^{-1} 1725s (C=O), 1605w, 1295s, 1255s, 1110s and 860s; δ_H(300 MHz; $CDCl_3$) 1.26 (3 H, t, *J* 7.2, $CO_2CH_2CH_3$), 1.58 (3 H, d, *J* 6.4, CHCH_3), 1.81–1.93 (1 H, m), 2.08–2.17 (1 H, m), 2.47–2.52 (2 H, m), 4.16–4.31 (2 H, A and B of ABX$_3$, $CO_2CH_2CH_3$), 5.13 (1 H, q, *J* 6.4, ArC*H*CH_3), 5.48 (1 H, t, *J* 2.6, 6-H) and 7.35–7.45 (3 H, m, ArH) and 7.70–7.85 (4 H, m, ArH); δ_C(75 MHz, $CDCl_3$) 14.0 (CH_3), 15.7 (CH_2), 21.5 (CH_3), 22.1 (CH_2), 61.8 (CH_2), 74.5 (CH), 93.5 (CH), 124.3 (CH), 124.4 (CH), 125.7 (CH), 125.9 (CH), 127.5 (CH), 127.91 (CH), 127.92 (CH), 132.8 (C), 133.1 (C), 140.5 (C), 150.8 (C) and 163.2 (CO); *m/z* (FAB) 328 [(M + H^+), 5%], 155 (100) [Found (EI): M^+, 327.1471. $C_{19}H_{21}NO_4$ requires M^+, 327.1471.

3-*Ethoxycarbonyl*-6-[(S)-1-*phenylbutoxy*]-5,6-*dihydro*-4H-1,2-*oxazine* **33**.—In the same way as for compound **32**, ethyl 3-bromo-2-hydroxyiminopropanoate[21] (0.67 g, 3.2 mmol), (*S*)-1-phenylbutyl vinyl ether **10** (0.67 g, 3.8 mmol) and anhydrous K_2CO_3 (0.53 g, 3.8 mmol) gave, after flash column chromatography [(6:1) light petroleum–ether], the two diasteroisomers of the *title compound*. Major diastereoisomer, **33a**, colourless oil (0.465 g, 48%), R_f 0.24 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ −148.2 (*c* 5, CH_2Cl_2); ν_{max}(CH_2Cl_2)/cm^{-1} 1720s (C=O), 1600w, 1290s and 1095s; δ_H(300 MHz; $CDCl_3$) 0.86 [3 H, t, *J* 7.4, $(CH_2)_2CH_3$], 1.15–1.43 (2 H, m), 1.36 (3 H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.51–1.62 (1 H, m), 1.67–1.84 (2 H, m), 1.92–2.00 (1 H, m), 2.47–2.54 (2 H, m), 4.33 (2 H, q, *J* 7.1, $CO_2CH_2CH_3$), 4.78 (1 H, dd, *J* 8.2 and 5.7, ArCHO), 4.98 (1 H, t, *J* 2.5, 6-H) and 7.24–7.37 (5 H, m, ArH); δ_C(75 MHz; $CDCl_3$) 13.6 (CH_3), 14.0 (CH_3), 15.6 (CH_2), 18.8 (CH_2), 21.8 (CH_2), 39.7 (CH_2), 61.7 (CH_2), 77.7 (CH), 92.2 (CH), 126.8 (CH), 127.6 (CH), 128.4 (CH), 141.2 (C), 151.0 (C) and 163.1 (CO); *m/z* (FAB) 306 [(M + H^+), 44%], 174 (100) and 133 (91) [Found: (EI) M^+, 305.1625. $C_{17}H_{23}NO_4$ requires M^+, 305.1627]. Minor diastereoisomer, **33b**, colourless oil (0.077 g, 8%), R_f 0.12 [(3:1) light petroleum–ether]; $[\alpha]_D^{22}$ +130.6 (*c* 5, CH_2Cl_2); ν_{max}(CH_2-

Cl_2)/cm^{-1} 1720s (C=O), 1605w, 1290s, 1110s, 1005s, 915s and 855s; δ_H(300 MHz; $CDCl_3$) 0.90 [3 H, t, *J* 7.3, $(CH_2)_2$ CH_3], 1.21–1.40 (3 H, m), 1.30 (3 H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.63–1.75 (1 H, m), 1.76–1.90 (1 H, m), 2.06–2.14 (1 H, m), 2.44–2.49 (2 H, m), 4.18–4.36 (2 H, A and B of ABX_3, $CO_2CH_2CH_3$), 4.73 (1 H, t, *J* 6.5, ArCHO), 5.36 (1 H, t, *J* 2.6, 6-H) and 7.17–7.34 (5 H, m, ArH); δ_C(75 MHz, $CDCl_3$) 13.9 (CH_3), 14.0 (CH_3), 15.7 (CH_2), 18.5 (CH_2), 21.9 (CH_2), 38.8 (CH_2), 61.6 (CH_2),79.8 (CH), 94.8 (CH), 126.1 (CH), 127.0 (CH), 127.9 (CH), 142.0 (C), 150.2 (C) and 163.2 (CO); *m/z* (FAB) 306 [(M + H^+), 56%], 174 (91), 154 (25) and 133 (100) [Found (EI): M^+, 305.1625. $C_{17}H_{23}NO_4$ requires M^+, 305.1627].

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