Chiral oxime ethers in asymmetric synthesis. Part 4.[1] Asymmetric synthesis of *N*-protected amines and β-amino acids by the addition of organometallic reagents to ROPHy/SOPHy-derived aldoximes

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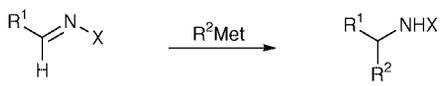
Addition of organolithium or Grignard reagents to (*R*)- or (*S*)-*O*-(1-phenylbutyl)aldehyde oximes **1** in the presence of boron trifluoride–diethyl ether results in the formation of hydroxylamines **2** in good to excellent diastereoselectivity. Subsequent cleavage of the N–O bond with zinc–acetic acid–ultrasound, and carbamate formation, gives *N*-protected amines **3** in good enantiomeric purity (77–100% ee). When allylmagnesium bromide was used as the organometallic reagent, the resulting hydroxylamines were converted into β-amino acid derivatives **4** and γ-amino alcohols **5**.

Introduction

Optically active nitrogen-containing compounds play a fundamental role in life processes. Even relatively simple chiral compounds such as amines, amino alcohols, and amino acids occupy vital roles such as hormones, neurotransmitters, building blocks, *etc.* In addition, amines and their substituted derivatives find increasing use as key intermediates in asymmetric synthesis as chiral ligands and chiral auxiliaries. Therefore the development of new methods for the diastereo- and enantioselective synthesis of amines has been a major objective for organic chemists.[2] Many of these methods are based on the nucleophilic addition of organometallic reagents to the C=N bond (Scheme 1), the stereochemistry of the addition being



Scheme 1 (X = alkyl, aryl, POR_2, SOR, SO_2R, NR_2, OR, SiR_3, *etc.*; Met = Li, Mg, Z, Ce, Sn, *etc.*).

controlled by the presence of a chiral auxiliary attached to the C or N atoms of the C=N bond, or by a chiral reagent–catalyst–ligand system.[3]

We have recently shown that the addition of organolithium or Grignard reagents to the C=N bond of oxime ethers derived from (***R***)- and (***S***)-***O***-(1-**p**henylbutyl)**hy**droxylamine (ROPHy/SOPHy) proceeds in a highly diastereoselective manner (Scheme 1, X = OCHPrPh).[4] The choice of the 1-phenylbutyl group as the chiral auxiliary on the oxime oxygen represents a significant improvement over the corresponding 1-phenethyl derivatives, and although the 2-methyl-1-phenylpropyl group gave better results,[4] the starting material for the preparation of the required hydroxylamine is not commercially available in both enantiomeric forms. Hence, although the use of oxime ethers derived from ROPHy/SOPHy represents something of a compromise, we have demonstrated the use of such auxiliaries in the asymmetric synthesis of the piperidine alkaloid (*R*)-(−)-coniine,[5] and α-amino acids.[1] We now describe the details of a new method for the asymmetric synthesis of *N*-protected amines, and, in the case of homoallylamines, their subsequent conversion into β-amino acid derivatives.[6]

Results and discussion

A range of aldoxime ethers **1** was readily prepared by reaction of the corresponding aldehyde with either ROPHy or SOPHy, prepared as previously described,[4] or more conveniently from the *N*-phthaloyl derivative of ROPHy or SOPHy by hydrazine hydrate-mediated deprotection followed by *in situ* reaction with the aldehyde. Alkyl, cycloalkyl, aromatic and heteroaromatic aldehydes all reacted satisfactorily. The (*E*)-oxime ethers **1** were separated from the (*Z*)-isomers, the amount of which varied from 0 to 33% according to the nature of the aldehyde substituent, by column chromatography and were isolated as colourless oils in moderate to excellent yield (Table 1). The naphthaldehyde-derived oxime **1j** and the thiazole derivative **1m** were solids, and on recrystallisation formed crystals suitable for X-ray analysis. In the case of the naphthaldehyde oxime **1j** the racemic derivative gave better crystals, and hence the analysis was carried out on the racemate. The X-ray crystal structures are shown in in Figs. 1 and 2,[7] and not only confirm the *E*-geometry about the C=N bond, but also the preferred *trans*-arrangement about the N–O bond. In both structures (and also in the ROPHy oxime of cinnamaldehyde[1]), the phenyl ring of the auxiliary adopts a conformation in which it is almost perpendicular to the planar CH=N–O oxime unit. Calculations at the semi-empirical level (Mopac Version 6.0, AM1 Hamiltonian[8]) support the fact that (in the gas phase) the *trans*-orientation about the N–O bond is the more stable, and that there is a high barrier to rotation about the N–O bond — ≈32 kJ mol^{-1} for the oxime ether $MeCH{=}NOCH_2Ph$. Interestingly, they also show that the conformation adopted by the phenyl ring (as shown in the X-ray crystal structures) is the minimum-energy conformation in the gas phase, and hence, in view of the low solvating power of toluene, probably also in solution.

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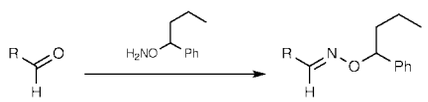
Table 1 Preparation of *O*-(1-phenylbutyl)aldehyde oximes **1**

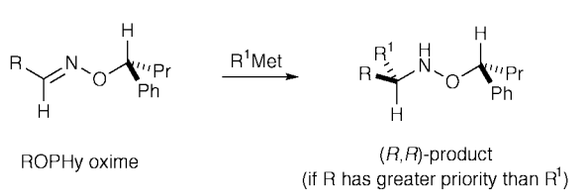


1

R	Oxime	Yield (%)
n-Pr	(*R*)-**1a**	58
Pr^i	(*R*)-**1b**	54
$CHEt_2$	(*R*)-**1c**	78
$H_2C{=}CHCH_2CH_2$	(*S*)-**1d**	62
$PhCH_2O(CH_2)_4$	(*R*)-**1e**	84
c-C_6H_{11}	(*R*)-**1f**	77
c-C_6H_{11}	(*S*)-**1f**	76
$PhCH_2$	(*R*)-**1g**	56
$PhCH_2$	(*S*)-**1g**	50
Ph	(*R*)-**1h**	98[a]
Ph	(*S*)-**1h**	88[a]
4-$MeOC_6H_4$	(*S*)-**1i**	75[b]
2-naphthyl	(*S*)-**1j**	78
2-pyridyl	(*S*)-**1k**	78
2-thienyl	(*S*)-**1l**	59
thiazol-2-yl	(*S*)-**1m**	47

[a] Racemate described in ref. 4. [b] Ref. 4.

The addition of organolithium and Grignard reagents to the oxime ethers **1** was carried out in toluene at −78 °C in the presence of boron trifluoride–diethyl ether and gave the corresponding hydroxylamines **2** in good yield (Table 2), although Grignard reagents appear to add efficiently to oximes of aliphatic aldehydes only. The use of toluene as solvent is essential for the success of the reaction, and although diethyl ether can be used as a co-solvent, for example when the Grignard reagent is supplied in diethyl ether, the use of THF is particularly deleterious both in terms of yield and stereoselectivity. We assume this is because it competes with the weakly Lewis basic oxime ether for the boron trifluoride (see below). The oxime ethers derived from heteroaromatic aldehydes gave poor results: no product was isolated from the addition of allylmagnesium bromide to the thiophene oxime **1l**, and the thiazole oxime **1m** gave only a poor yield of the hydroxylamine **2u**, and the diastereoisomeric excess (de) was only 20%. In the case of the phenylacetaldehyde oxime ethers **1g** the addition reactions were carried out at ≈−90 °C. In all except four cases (**2c**, **2g**, **2m** and **2u**), the diastereoselectivity of the addition was excellent (>90%); the de was determined from the ^{1}H NMR of the mixture, although in some cases it was impossible to obtain an accurate estimate of the de. These reactions are described as >90% de, *etc*., reflecting the limits of accuracy of NMR integration in certain cases. The stereochemistry of the new chiral centre was assigned on the basis of our previous work,[9] using the mnemonic that if the incoming group R^1 has a lower priority in the Sequence Rules than the existing group R, the new stereocentre has the same configuration as the auxiliary (Scheme 2), *i.e.* the nucleophile approaches from the side of



Scheme 2

the C=N bond opposite to the phenyl group of the auxiliary. However, this does not explain why the 1-phenylbutyl chiral auxiliary is more effective than the corresponding 1-phenethyl derivative. Unfortunately, the exact nature of the reacting

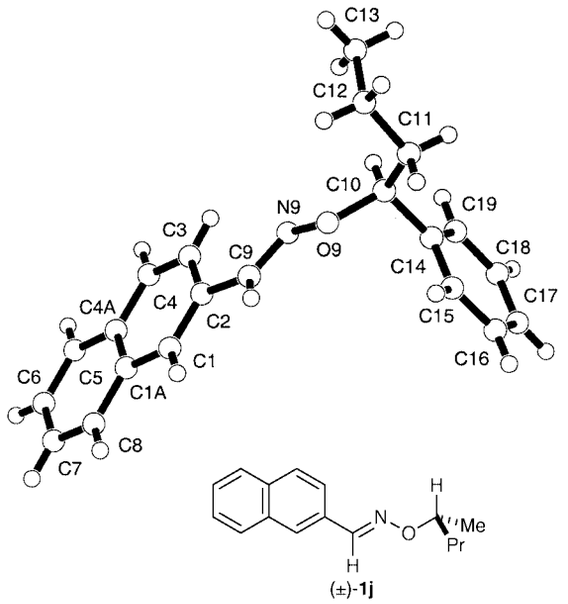


Fig. 1 X-Ray molecular structure of (±)-*O*-(1-phenylbutyl)-2-naphthaldehyde oxime (±)-**1j**, with crystallographic numbering scheme.

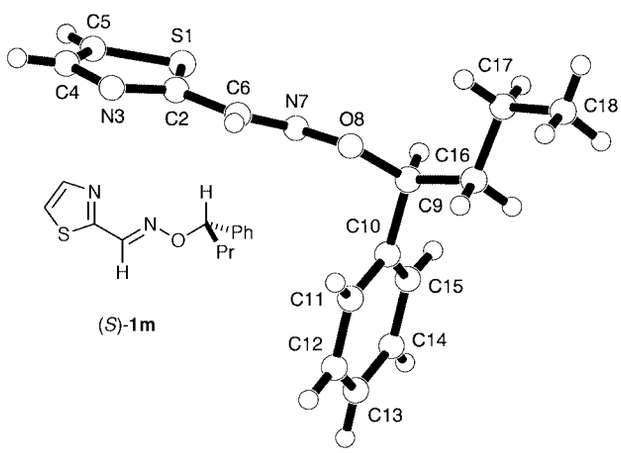
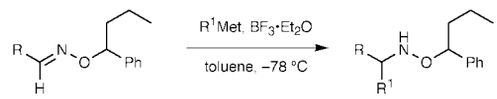


Fig. 2 X-Ray molecular structure of (*S*)-*O*-(1-phenylbutyl)thiazol-2-ylcarbaldehyde oxime (*S*)-**1m** with crystallographic numbering scheme.

oxime ether species in solution is not known; calculations (*vide supra*) suggest that there is a marginal preference for complexation of the boron trifluoride to oxygen rather than nitrogen, although the complex is much weaker than that formed between boron trifluoride and THF, which has a calculated equilibrium constant at least two orders of magnitude greater. The calculations also suggest that complexation significantly lowers the barrier to rotation about the N–O bond. Hence the involvement of non-planar non-*trans*-conformations of the oxime ether as the reacting species cannot be ruled out.

The N–O bond in hydroxylamines **2** was readily cleaved using the zinc–acetic acid–ultrasound protocol,[10] and the resulting amine was protected without purification as either its *tert*-butyl or benzyl carbamates **3**. The carbamates **3** were generally solids, and could be purified further by recrystallisation. The enantiomeric purity of the *N*-protected amines **3** was determined by HPLC analysis using a chiral stationary phase by comparison with the racemic product which was synthesised separately. As expected the observed enantiomeric excess (ee) of the carbamates **3** (Table 3) closely followed the de of the hydroxylamines **2**. In the case of the carbamates **3l** and **3m**, the protecting groups were removed by hydrogenolysis and acid treatment, respectively, to give the corresponding amines; comparison with literature data confirmed that the stereochemical assignments for **3l** and **3m** (Table 3) were correct.[11]

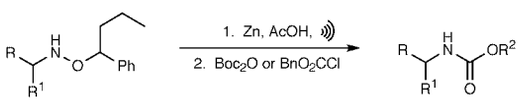
Table 2 Addition of organometallic reagents to *O*-(1-phenylbutyl)aldehyde oximes **1**



1 **2**

Oxime	R	R^1Met	Hydroxylamine	Yield (%)	de (%)
(*R*)-**1a**	*n*-Pr	Pr^iMgCl	**2a**	70	>90
(*R*)-**1a**	*n*-Pr	$PhCH_2MgCl$	**2b**	21	>90
(*R*)-**1b**	Pr^i	$H_2C{=}CHCH_2MgBr$	**2c**	78	86
(*R*)-**1c**	$CHEt_2$	$H_2C{=}CHCH_2MgBr$	**2d**	100	96
(*S*)-**1d**	$H_2C{=}CH(CH_2)_2$	PhLi	**2e**	91	>90
(*R*)-**1e**	$PhCH_2O(CH_2)_4$	*n*-PrMgCl	**2f**	98	>95
(*R*)-**1e**	$PhCH_2O(CH_2)_4$	PhLi	**2g**	61	83
(*R*)-**1f**	*c*-C_6H_{11}	*n*-BuLi	**2h**	95	>90
(*S*)-**1f**	*c*-C_6H_{11}	*t*-BuLi	**2i**	68	>90
(*R*)-**1f**	*c*-C_6H_{11}	PhLi	**2j**	77	>90
(*R*)-**1f**	*c*-C_6H_{11}	$H_2C{=}CHCH_2MgBr$	**2k**	80	96
(*S*)-**1f**	*c*-C_6H_{11}	$H_2C{=}CHCH_2MgBr$	**2l**	85	96
(*R*)-**1g**	$PhCH_2$	EtMgBr	**2m**	62	79
(*R*)-**1g**	$PhCH_2$	Pr^iMgCl	**2n**	92	91
(*S*)-**1g**	$PhCH_2$	*n*-BuLi	**2o**	72	>96
(*S*)-**1g**	$PhCH_2$	Bu^iLi	**2p**	67	>96
(*S*)-**1h**	Ph	*n*-BuLi	**2q**	72	>95
(*R*)-**1h**	Ph	$H_2C{=}CHCH_2MgBr$	**2r**	100	92
(*S*)-**1i**	4-$MeOC_6H_4$	$H_2C{=}CHCH_2MgBr$	**2s**	80	96
(*S*)-**1j**	2-naphthyl	*n*-BuLi	**2t**	50	>90
(*S*)-**1m**	thiazol-2-yl	$H_2C{=}CHCH_2MgBr$	**2u**	7	20

Table 3 Cleavage of hydroxylamines **2** and protection of resulting amines



2 **3**

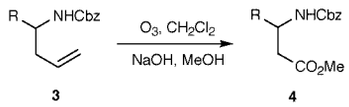
Hydroxylamine	R	R^1	Carbamate	R^2	Yield (%)	ee (%)[a]
2a	*n*-Pr	Pr^i	(*S*)-**3a**	Bn	58	91
2b	*n*-Pr	$PhCH_2$	(*S*)-**3b**	Bn	85	97[b]
2c	Pr^i	$H_2C{=}CHCH_2$	(*R*)-**3c**	Bn	47	78
2d	$CHEt_2$	$H_2C{=}CHCH_2$	(*R*)-**3d**	Bn	75	91
2e	$H_2C{=}CHCH_2CH_2$	Ph	(*R*)-**3e**	Bn	82	91[b]
2f	$PhCH_2O(CH_2)_4$	*n*-Pr	(*R*)-**3f**	*t*-Bu	85	88
2g	$PhCH_2O(CH_2)_4$	Ph	(*S*)-**3g**	*t*-Bu	31	77
2h	*c*-C_6H_{11}	*n*-Bu	(*R*)-**3h**	Bn	79	96[b]
2i	*c*-C_6H_{11}	*t*-Bu	(*R*)-**3i**	Bn	25	96
2j	*c*-C_6H_{11}	Ph	(*S*)-**3j**	Bn	62	100[b]
2k	*c*-C_6H_{11}	$H_2C{=}CHCH_2$	(*R*)-**3k**	Bn	67	92
2l	*c*-C_6H_{11}	$H_2C{=}CHCH_2$	(*S*)-**3k**	Bn	51	89
2n	$PhCH_2$	Pr^i	(*S*)-**3l**	Bn	37	98[b]
2o	$PhCH_2$	*n*-Bu	(*S*)-**3m**	*t*-Bu	78	>96[b]
2p	$PhCH_2$	Bu^i	(*S*)-**3n**	*t*-Bu	67	>96[b]
2q	Ph	*n*-Bu	(*S*)-**3o**	Bn	87	92[b]
2r	Ph	$H_2C{=}CHCH_2$	(*R*)-**3p**	Bn	66	95
2s	4-$MeOC_6H_4$	$H_2C{=}CHCH_2$	(*S*)-**3q**	Bn	62	98
2t	2-naphthyl	*n*-Bu	(*S*)-**3r**	Bn	83	91

[a] Enantiomeric excess (ee) obtained from HPLC analysis on a chiral stationary phase (Chiracel OD or ChiralPak AD) using hexane–propan-2-ol as eluent (from 99.5 : 0.5 to 92 : 8). [b] After recrystallisation.

With a range of homoallylamines in hand,[12] we next investigated their conversion into β-amino acid derivatives. The widespread occurrence of β-amino acids as constituents of a range of biologically active natural products, together with their role as precursors to β-lactams, and their incorporation into β-peptides with defined secondary structure,[13] has focused attention on these homologues of α-amino acids. The development of new methods for the asymmetric synthesis of β-amino acids is therefore of current interest, and several methods have been reported.[14] The most commonly used methods are summarised in Scheme 3: the homologation of α-amino acids using the Arndt–Eistert procedure,[15] the asymmetric conjugate addition of amines and amides to α,β-unsaturated carboxylic acid derivatives,[16] and the diastereoselective addition of ester enolate equivalents or allyl organometallic reagents to the C=N double bond of imines or hydrazones.[17] Other routes include the ring opening of aziridines,[18] biotransformations,[19] and a range of methods based on chiral auxiliaries, catalysts, and functional group interconversions.[20]

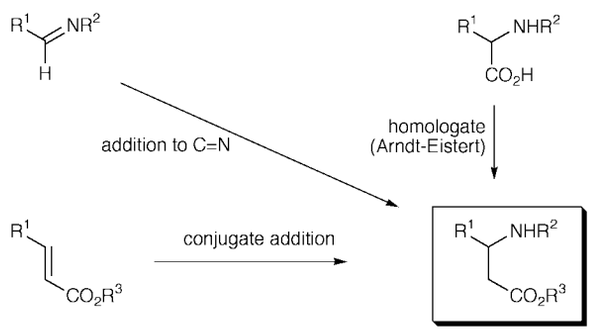
Initial attempts to cleave the alkene bond in the *N*-protected homoallylamines using ruthenium oxidants were unsatisfactory, but the double bond was readily cleaved by ozonolysis in methanolic sodium hydroxide[21] to give the *N*-Cbz amino esters **4** in moderate yield (Table 4). The configuration of the β-phenyl-β-alanine derivative **4d** was confirmed as (*R*) by comparison of its optical rotation with a literature value.[22]

Table 4 Oxidative cleavage of *N*-benzyloxycarbonyl homoallylamines



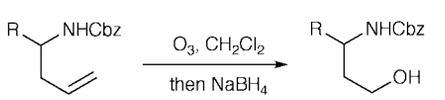
3 4

Homoallylamine	R	Carbamate	Yield (%)
3c	Pr^i	(*R*)-**4a**	36
3d	$CHEt_2$	(*R*)-**4b**	52
(*R*)-**3k**	*c*-C_6H_{11}	(*R*)-**4c**	39
3p	Ph	(*R*)-**4d**	41
3q	4-$MeOC_6H_4$	(*S*)-**4e**	33



Scheme 3

The method was also extended to the synthesis of γ-amino alcohols **5** by modification of the ozonolysis work-up conditions. Thus, the *N*-Cbz amines **3d** and **3k** were subjected to ozonolysis in dichloromethane, followed by reductive work-up to give the amino alcohols **5a** and **5b** in 56 and 50% yield, respectively (Scheme 4).

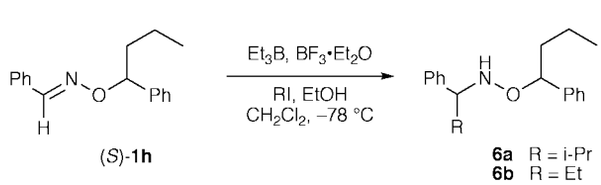


3d R = $CHEt_2$
(*S*)-**3k** R = *c*-C_6H_{11}

5a R = $CHEt_2$
5b R = *c*-C_6H_{11}

Scheme 4

Finally, since asymmetric induction in radical reactions is a topic of current interest, and oxime ethers are known to be good radical acceptors,[23] we briefly examined the addition of alkyl radicals to the SOPHy oxime of benzaldehyde, (*S*)-**1h** (Scheme 5). Using the conditions developed by Naito and co-



(*S*)-**1h**

6a R = i-Pr
6b R = Et

Scheme 5

workers,[23d] we found that the addition of isopropyl and ethyl radicals (from the corresponding iodoalkanes) to oxime ether **1h** did give the desired hydroxylamines **6**. However, in both cases the yield was poor, and the diastereoselectivity was worse (85% de for **6a**, 51% de for **6b**) than in the addition of organometallic reagents described above.

Hence we have established a new method for the asymmetric synthesis of *N*-protected amines including homoallylamines, *N*-protected β-amino esters and γ-amino alcohols based on the highly diastereoselective addition of organometallic reagents to oxime ethers. The routes are simple and versatile, tolerate a range of substituents, and further exemplify the synthetic utility of ROPHy/SOPHy-derived oximes.

Experimental

For general experimental details, see refs. 4 and 9. The hydroxylamines **2** were characterised as diastereoisomeric mixtures; the NMR data refer to the major diastereomer.

Preparation of oxime ethers: general method

A suspension of (*R*)- or (*S*)-*N*-(1-phenylbutoxy)phthalimide (6.00 mmol) in ethanol (20 mL) was heated until the phthalimide dissolved. Hydrazine hydrate (0.30 mL, 6.10 mmol) was added at this elevated temperature and a colourless precipitate was observed to form as the solution was slowly allowed to cool to room temperature. The aldehyde (7 mmol) was added at room temperature and the suspension was stirred until the reaction was adjudged complete by TLC (typically 2–16 h). The solvent was evaporated off, and tetrachloromethane (30 mL) and magnesium sulfate were added to the residue. The resulting suspension was filtered, the filtrate evaporated, and the residue purified by column chromatography (dichloromethane–light petroleum).

(*R*)-*O*-(1-Phenylbutyl)butyraldehyde oxime 1a. Obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with *n*-butyraldehyde, as an *oil* (58%), $[a]_D^{25}$ +7.7 (*c* 0.72, CH_2Cl_2); spectroscopic data identical to those previously reported for the (*S*)-isomer.[5]

(*R*)-*O*-(1-Phenylbutyl)isobutyraldehyde oxime 1b. Obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with isobutyraldehyde, as a *colourless oil* (54%) (Found: M^+, 219.1625. $C_{14}H_{21}NO$ requires *M*, 219.1623); $[a]_D^{22}$ +9.9 (*c* 0.95, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 2967, 1514, 1467, 1027, 923; δ_H (300 MHz; $CDCl_3$) 7.31 (6H, m, ArH, CHN), 5.02 (1H, t, *J* 7.2, OCH), 2.44 (1H, m, C*H*Me_2), 1.93 (1H, m, C*H*H), 1.71 (1H, m, CH*H*), 1.34 (2H, m, CH_2), 1.05 (3H, d, *J* 6.8, *Me*CMe), 1.03 (3H, d, *J* 6.8, MeC*Me*), 0.92 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 156.0, 142.6, 128.2, 127.2, 126.8, 84.5, 38.4, 29.3, 20.3, 20.2, 18.9, 14.1; *m*/*z* (EI) 219 (M^+, 1%), 133 (82), 117 (13), 107 (27), 91 (100), 77 (44), 51 (20).

(*R*)-2-Ethyl-*O*-(1-phenylbutyl)butyraldehyde oxime 1c. Obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with 2-ethylbutyraldehyde, as a *colourless oil* (78%) (Found: M^+, 247.1941. $C_{16}H_{25}NO$ requires *M*, 247.1936); $[a]_D^{20}$ +8.4 (*c* 1, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 2935, 1452, 1027, 924; δ_H (300 MHz; $CDCl_3$) 7.27 (6H, m, ArH, CHN), 5.06 (1H, t, *J* 6.8, OCH), 1.99 (1H, m, CH), 1.95 (1H, m, C*H*H), 1.75 (1H, m, CH*H*), 1.39 [6H, m, CH_2, $(MeCH_2)_2C$], 0.93 (3H, t, *J* 7.4, *Me*CH_2), 0.87 (3H, t, *J* 7.5, Me), 0.73 (3H, t, *J* 7.4, *Me*CH_2); δ_C (75 MHz; $CDCl_3$) 154.9, 142.6, 128.1, 127.1, 126.7, 84.3, 43.0, 38.3, 25.64, 25.58 18.8, 14.0, 11.5, 11.3; *m*/*z* (EI) 248 (MH^+, 1%), 204 (2), 176 (1), 150 (1), 133 (96), 117 (18), 105 (37), 91 (100), 84 (73), 77 (52), 71 (40), 65 (15), 51 (82).

(*S*)-*O*-(1-Phenylbutyl)pent-4-enaldehyde oxime 1d. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with pent-4-enal, as a *colourless oil* (62%); $[a]_D^{23}$ −13.9 (*c* 1.0, CH_2Cl_2) (Found: M^+, 231.1627. $C_{15}H_{21}NO$ requires *M*, 231.1623); ν_{max} (film)/cm^{-1} 3062, 3027, 2957, 2930, 2868, 1642, 1452; δ_H (300 MHz; $CDCl_3$) 7.45 (1H, t, *J* 5.8, CHN), 7.31 (5H, m, ArH), 5.76 (1H, m, H_2C=C*H*), 5.02 (3H, m, H_2C=CH, OCH), 2.22 (4H, m, 2 × CH_2), 1.90 (1H, m, C*H*H), 1.70 (1H, m, CH*H*), 1.37 (2H,

m, CH_2), 0.91 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 150.4, 142.6, 136.9, 128.2, 127.3, 126.7, 115.6, 84.6, 38.4, 30.8, 28.9, 18.9, 14.0; *m*/*z* (EI) 231 (M^+, 0.1%), 185 (2), 133 (61), 105 (13), 91 (100), 77 (18).

(*R*)-5-Benzyloxy-*O*-(1-phenylbutyl)pentaldehyde oxime 1e. The oxime was obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with 5-benzyloxypentanal,[24] as a *colourless oil* (84%); $[a]_D^{23}$ −132.2 (*c* 0.9, $CHCl_3$) (Found: M^+, 339.2196. $C_{22}H_{29}NO_2$ requires *M*, 339.2198); ν_{max} (neat)/cm^{-1} 3436, 2092, 1635, 1103; δ_H (300 MHz; $CDCl_3$) 7.44 (1H, t, *J* 6.2, CHN), 7.38–7.23 (10H, m, ArH), 5.03 (1H, t, *J* 6.8, OCH), 4.48 (2H, s, PhC*H*$_2$), 3.45 (2H, t, *J* 6.1, CH_2O), 2.17 (2H, q, *J* 6.8, CH_2), 1.92 (1H, m, C*H*H), 1.71–1.32 (7H, m, CH*H*, 3 × CH_2), 0.94 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 150.9, 142.7, 138.5, 128.4, 128.2, 127.6, 127.5, 127.2, 126.7, 84.9, 72.9, 69.8, 38.4, 29.3, 29.1, 13.5, 18.9, 14.1; *m*/*z* (EI) 339 (M^+, 0.2%), 248 (1), 207 (7), 149 (2), 133 (76), 105 (16), 91 (100), 77 (20).

(*R*)-*O*-(1-Phenylbutyl)cyclohexanecarbaldehyde oxime (*R*)-1f. Obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with cyclohexanecarbaldehyde, as a *colourless oil* (77%); $[a]_D^{22}$ +17.0 (*c* 0.98, CH_2Cl_2) (Found: M^+, 259.1936. $C_{17}H_{25}NO$ requires *M*, 259.1936); ν_{max} (CH_2Cl_2)/cm^{-1} 2935, 1449, 1027, 930, 686; δ_H (300 MHz; $CDCl_3$) 7.32 (6H, m, ArH, CHN), 5.04 (1H, t, *J* 6.3, OCH), 2.18 (1H, m, CH), 1.95 (1H, m, C*H*H), 1.74 (7H, m, CH*H*, 3 × CH_2), 1.29 (6H, m, 3 × CH_2), 0.92 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 155.0, 142.7, 128.1, 127.2, 126.8, 84.5, 38.5, 38.4, 30.5, 25.9, 25.4, 18.9, 14.1; *m*/*z* (EI) 259 (M^+, 1%), 149 (1), 133 (98), 127 (10), 117 (13), 107 (14), 91 (100), 83 (87), 77 (28).

(*S*)-*O*-(1-Phenylbutyl)cyclohexanecarbaldehyde oxime (*S*)-1f. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with cyclohexanecarbaldehyde, as a *colourless oil* (76%); $[a]_D^{22}$ −17.9 (*c* 1.1, CH_2Cl_2); spectroscopic data identical with those of the (*R*)-enantiomer.

(*R*)-*O*-(1-Phenylbutyl)phenylacetaldehyde oxime (*R*)-1g. Obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with phenylacetaldehyde, as a *colourless oil* (56%); $[a]_D^{20}$ −20.7 (*c* 1, CH_2Cl_2) (Found: M^+, 267.1635. $C_{18}H_{21}NO$ requires *M*, 267.1623); ν_{max} (film)/cm^{-1} 3437, 2958, 1652, 1635, 1496, 1454; δ_H (300 MHz; $CDCl_3$) 7.58 (1H, t, *J* 6.5, CHN), 7.33 (8H, m, ArH), 7.18 (2H, m, ArH), 5.16 (1H, t, *J* 7.0, OCH), 3.51 (2H, d, *J* 6.5, C*H*$_2$Ph), 1.99 (1H, m, C*H*H), 1.79 (1H, m, CH*H*), 1.51–1.38 (2H, m, CH_2), 0.99 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 149.5, 128.9, 128.7, 128.3, 127.4, 126.9, 126.8, 84.8, 38.5, 36.0, 19.0, 14.2; *m*/*z* (EI) 268 (MH^+, 4%), 267 (M^+, 1), 226 (8), 176 (3), 152 (1), 133 (75), 105 (24), 91 (100), 77 (26), 65 (26), 51 (14).

(*S*)-*O*-(1-Phenylbutyl)phenylacetaldehyde oxime (*S*)-1g. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with phenylacetaldehyde, as a *colourless oil* (50%); $[a]_D^{22}$ +22.5 (*c* 1, CH_2Cl_2); spectroscopic data identical with those of the (*R*)-enantiomer.

(*R*)-*O*-(1-Phenylbutyl)benzaldehyde oxime (*R*)-1h. Obtained from the cleavage of (*R*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with benzaldehyde, as a *colourless oil* (98%); $[a]_D^{20}$ +72.0 (*c* 0.85, CH_2Cl_2) (Found: M^+, 253.1470. $C_{17}H_{19}NO$ requires *M*, 253.1467); ν_{max} (film)/cm^{-1} 2959, 2933, 1493, 1448; δ_H (300 MHz; $CDCl_3$) 8.17 (1H, s, CHN), 7.56 (2H, m, ArH), 7.36 (8H, m, ArH), 5.23 (1H, t, *J* 6.8, OCH), 2.03 (1H, m, C*H*H), 1.82 (1H, m, CH*H*), 1.48 (2H, m, CH_2), 0.99 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 148.5, 142.5, 132.5, 129.6, 128.6, 128.3, 127.4, 127.0, 126.8, 85.5, 38.3, 18.9, 14.1; *m*/*z* (EI) 253 (M^+, 7%), 212 (5), 133 (92), 117 (7), 104 (22), 91 (100), 77 (35).

(*S*)-*O*-(1-Phenylbutyl)benzaldehyde oxime (*S*)-1h. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with benzaldehyde, as a *colourless oil* (88%); $[a]_D^{20}$ −68.0 (*c* 1.1, CH_2Cl_2); spectroscopic data identical with those of the (*R*)-enantiomer.

(*S*)-*O*-(1-Phenylbutyl)-*p*-anisaldehyde oxime 1i. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with *p*-anisaldehyde as previously described.[4]

(*S*)-*O*-(1-Phenylbutyl)-2-naphthaldehyde oxime 1j. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with 2-naphthaldehyde, as a *colourless solid* (78%); mp 78.5–81 °C (from light petroleum); $[a]_D^{20}$ −37.9 (*c* 5.6, CH_2Cl_2) (Found: C, 82.8; H, 6.9; N, 4.6. $C_{21}H_{21}NO$ requires C, 83.1; H, 7.0; N, 4.6%); ν_{max} (KBr)/cm^{-1} 3439, 3062, 3025, 2962, 2931, 2873, 1637, 1605, 1453; δ_H (300 MHz; $CDCl_3$) 8.34 (1H, s, CHN), 7.83 (5H, m, ArH), 7.44 (7H, m, ArH), 5.32 (1H, t, *J* 7.0, OCH), 2.12 (1H, m, C*H*H), 1.90 (1H, m, CH*H*), 1.50 (2H, m, CH_2), 1.04 (3H, t, *J* 7.4, Me); δ_C (75 MHz; $CDCl_3$) 148.8, 142.5, 134.1, 133.2, 130.3, 128.4, 128.3, 128.2, 127.9, 127.5, 126.9, 126.8, 126.5, 123.2, 85.7, 38.4, 19.0, 14.1; *m*/*z* (EI) 304 (MH^+, 11%), 303 (M^+, 0.1), 171 (5), 153 (16), 133 (68), 127 (31), 115 (14), 105 (14), 91 (100), 77 (23).

(*S*)-*O*-(1-Phenylbutyl)pyridine-2-carbaldehyde oxime 1k. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with pyridine-2-carbaldehyde, as a *colourless oil* (78%); $[a]_D^{22}$ +64.0 (*c* 1.1, $CHCl_3$) (Found: M^+, 254.1419. $C_{16}H_{18}N_2O$ requires *M*, 254.1419); δ_H (300 MHz; $CDCl_3$) 8.58 (1H, s, CHN), 8.23 (1H, s, ArH), 7.72 (1H, s, ArH), 7.62 (1H, s, ArH), 7.34 (6H, m, ArH), 5.24 (1H, t, *J* 7.2, OCH), 2.03 (1H, m, C*H*H), 1.84 (1H, m, CH*H*), 1.37 (2H, m, CH_2), 0.92 (3H, t, *J* 6.8, Me); δ_C (75 MHz; $CDCl_3$) 151.9, 149.5, 149.3, 142.2, 136.3, 128.3, 127.5, 126.8, 123.8, 120.9, 86.1, 38.3, 18.9, 14.0; *m*/*z* (EI) 254 (M^+, 0.7%), 133 (24), 122 (15), 91 (100), 78 (21), 77 (10), 66 (3), 65 (11), 55 (5), 53 (4), 52 (11), 51 (21), 50 (9).

(*S*)-*O*-(1-Phenylbutyl)thiophene-2-carbaldehyde oxime 1l. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with thiophene-2-carbaldehyde, as a *colourless oil* (59%); $[a]_D^{22}$ −116.5 (*c* 0.9 in CH_2Cl_2) (Found: M^+, 259.1031. $C_{15}H_{17}NOS$ requires *M*, 259.1047); ν_{max} (CH_2Cl_2)/cm^{-1} 2963, 1210, 1023, 951; δ_H (300 MHz; $CDCl_3$) 8.29 (1H, s, CHN), 7.34 (4H, m, ArH), 7.26 (2H, m, ArH), 7.15 (1H, m, ArH), 7.00 (1H, m, ArH), 5.17 (1H, t, *J* 6.7, OCH), 2.03 (1H, m, CH_2), 1.79 (1H, m, CH_2), 1.39 (2H, m, CH_2), 0.95 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 143.3, 142.2, 136.0, 129.0, 128.2, 127.4, 127.1, 127.1, 126.8, 85.6, 38.1, 18.9, 14.0; *m*/*z* (EI) 259 (M^+, 5%), 133 (70), 91 (100), 77 (18).

(*S*)-*O*-(1-Phenylbutyl)thiazol-2-ylcarbaldehyde oxime 1m. Obtained from the cleavage of (*S*)-*N*-(1-phenylbutoxy)phthalimide and subsequent condensation of the hydroxylamine with thiazole-2-carbaldehyde, as a *colourless solid* (47%); mp 73–74 °C (from aq. ethanol); $[a]_D^{22}$ −136.1 (*c* 1.0 in $CHCl_3$) (Found: C, 64.4; H, 6.2; N, 10.7. $C_{14}H_{16}N_2OS$ requires C, 64.6; H, 6.2; N, 10.8%); ν_{max} (KBr)/cm^{-1} 2958, 2932, 2872, 1485, 1454, 983; δ_H (300 MHz; $CDCl_3$) 8.36 (1H, d, *J* 0.9, CHN), 7.83 (1H, d, *J* 10.9, ArH), 7.39–7.26 (6H, m, ArH), 5.22 (1H, dd, *J* 6.7, 7.3 OCH), 2.02 (1H, m, C*H*H), 1.80 (1H, m, CH*H*), 1.48–1.34 (2H,

m, CH_2), 0.96 (3H, t, *J* 7.4, Me); δ_C (75 MHz; $CDCl_3$) 161.7 (C), 143.9 (CH), 143.5 (CH), 141.6 (CH), 128.3 (CH), 127.7 (CH), 126.8 (CH), 119.9 (CH), 86.6 (CH), 38.0 (CH_2), 18.9 (CH_2), 14.0 (CH_3); *m*/*z* (EI) 260 (M^+, 7%), 133 (52), 111 (4), 105 (8), 91 (100), 77 (7), 58 (3).

Organometallic addition reactions

General method. An oxime ether **1** (3.9 mmol) was dissolved in toluene (10 mL) and the solution was cooled to −78 °C. Boron trifluoride–diethyl ether (11.8 mmol) was added and the solution was stirred for 15 min. The organometallic reagent (11.8 mmol in its supplied solvent) was added dropwise over 15 min, and the mixture was stirred at −78 °C until all the starting material was consumed (typically 2–12 h). The reaction mixture was quenched at −78 °C with saturated aq. ammonium chloride, and allowed to warm up to room temperature. The solvent was removed under reduced pressure and the residue partitioned between dichloromethane (20 mL) and water (20 mL). The layers were separated and the aqueous layer was washed with further portions of dichloromethane (2 × 20 mL). The combined organic extracts were washed with brine and then dried ($MgSO_4$), filtered and evaporated. Column chromatography of the residue on silica gel (dichloromethane–light petroleum 1:2) gave the hydroxylamine **2**.

General method for allylmagnesium bromide addition to oxime ethers. An oxime ether **1** (3.9 mmol) was dissolved in toluene (10 mL) under nitrogen and cooled to −78 °C. Boron trifluoride–diethyl ether (11.8 mmol) was added, and the mixture stirred for 15 min. Allylmagnesium bromide (11.8 mmol) in diethyl ether was added dropwise over 15 min, and the mixture was stirred until all starting material was consumed (typically 2–12 h). The reaction mixture was quenched at −78 °C with water, allowed to warm to room temperature, and extracted with diethyl ether (3 × 15 mL). The combined extracts were dried (K_2CO_3), filtered and evaporated. The residue was purified by flash chromatography on silica gel using dichloromethane–light petroleum (1:2) as eluent to give the hydroxylamine **2**.

(S)-2-Methyl-N-[(R)-1-phenylbutoxy]hexan-3-ylamine ***2a***.—Obtained from the addition of isopropylmagnesium chloride to oxime ether (*R*)-**1a**, as a *colourless oil* (70%, >90% de) (Found: M^+, 263.2255. $C_{17}H_{29}NO$ requires *M*, 263.2249); ν_{max} (film)/cm^{-1} 2955, 2930, 2868, 1455, 1378; δ_H (300 MHz; $CDCl_3$) 7.30 (5H, m, ArH), 5.25 (1H, br s, NH), 4.55 (1H, dd, *J* 5.9, 7.9, OCH), 2.61 (1H, m, NCH), 2.00 (1H, m, C*H*H), 1.79 (1H, m, CH*H*), 1.33 (7H, m, CH, 3 × CH_2), 0.91 (12H, m, 4 × Me); δ_C (75 MHz; $CDCl_3$) 143.6, 128.3, 127.2, 126.6, 85.1, 65.6, 38.9, 29.8, 28.9, 20.2, 19.2, 19.0, 17.7, 14.3, 14.1; *m*/*z* (EI) 263 (M^+, 0.2%), 220 (0.3), 133 (38), 91 (100), 88 (33).

(S)-1-Phenyl-N-[(R)-1-phenylbutoxy]pentan-2-ylamine ***2b***.—Obtained from the addition of benzylmagnesium chloride to oxime ether (*R*)-**1a**, as a *colourless oil* (21%, >90% de) (Found: M^+, 311.2260. $C_{21}H_{29}NO$ requires *M*, 311.2249); ν_{max} (film)/cm^{-1} 3025, 2954, 2926, 2869, 1451; δ_H (300 MHz; $CDCl_3$) 7.30 (10H, m, ArH), 4.61 (1H, dd, *J* 5.5, 7.6, OCH), 2.99 (2H, m, PhCH_2), 2.72 (1H, m, NCH), 1.87 (1H, m, C*H*H), 1.45 (7H, m, CH*H*, 3 × CH_2), 0.99 (3H, t, *J* 7.1, Me), 0.90 (3H, t, *J* 6.7, Me); NH not observed; δ_C (75 MHz; $CDCl_3$) 143.4, 139.6, 129.6, 128.4, 128.3, 127.3, 126.6, 126.1, 85.4, 62.0, 38.9, 38.7, 33.9, 19.6, 19.3, 14.2, 14.2; *m*/*z* (EI) 311 (M^+, 0.2%), 220 (20), 179 (14), 149 (20), 133 (67), 105 (15), 91 (100), 77 (16).

(R)-2-Methyl-N-[(R)-1-phenylbutoxy]hex-5-en-3-ylamine ***2c***.—Obtained from the addition of allylmagnesium bromide to oxime ether (*R*)-**1b**, as a *colourless oil* (78%, 86% de) (Found: M^+, 261.2094. $C_{17}H_{27}NO$ requires *M*, 261.2093); ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2963, 2935, 2874, 1465, 916; δ_H (300 MHz; $CDCl_3$) 7.28 (5H, m, ArH), 5.74 (1H, m, CH=), 5.28 (1H, br s, NH), 5.03 (2H, m, =CH_2), 4.51 (1H, t, *J* 7.2, OCH), 2.56 (1H, m, NCH), 2.18 (2H, CH_2CH=), 1.78 (1H, m, C*H*H), 1.71 (1H, m, Me_2C*H*), 1.55 (2H, m, CH*H*), 1.36 (1H, m, CH_2), 0.92 (3H, t, *J* 7.3, Me), 0.89 (3H, d, *J* 6.8, *Me*$_2$C), 0.83 (3H, d, *J* 6.8, *Me*$_2$C); δ_C (75 MHz; $CDCl_3$) 143.1, 136.3, 128.2, 127.2, 126.8, 116.8, 84.9, 65.2, 38.5, 32.9, 28.6, 19.2, 19.1, 18.5, 14.1; *m*/*z* (EI) 261 (M^+, 6%), 239 (3), 220 (39), 218 (6), 184 (1), 178 (12), 162 (19), 141 (2), 133 (85), 117 (46), 112 (29), 104 (50), 100 (3), 91 (100), 77 (52).

(R)-5-Ethyl-N-[(R)-1-phenylbutoxy]hept-1-en-4-ylamine ***2d***.—Obtained from the addition of allylmagnesium bromide to oxime ether (*R*)-**1c**, as a *colourless oil* (100%, 96% de) (Found: M^+, 289.2403. $C_{19}H_{31}NO$ requires *M*, 289.2406); ν_{max} (CH_2Cl_2)/cm^{-1} 2962, 1638, 1453, 914, 686; δ_H (400 MHz; $CDCl_3$) 7.29 (5H, m, ArH), 5.79 (1H, m, CH=), 5.29 (1H, br s, NH), 5.07 (2H, m, CH_2=), 4.54 (1H, t, *J* 6.5, OCH), 2.89 (1H, m, NCH), 2.21 (2H, t, *J* 6.2, CH_2CH), 1.84 (1H, m, C*H*H), 1.59 (1H, m, CH*H*), 1.43 (1H, m, CH*H*Me), 1.38 (3H, m, C*H*Et$_2$, C*H*HMe, CH*H*Me), 1.27 (2H, m, CH*H*Me), 1.16 (1H, m, C*H*HMe), 0.93 (3H, t, *J* 7.3, Me), 0.86 (3H, t, *J* 7.3, *Me*CH_2), 0.81 (3H, t, *J* 7.3, *Me*CH_2); δ_C (75 MHz; $CDCl_3$) 143.2, 136.6, 128.2, 127.2, 126.8, 116.6, 84.9, 61.3, 41.8, 38.3, 32.2, 22.0, 21.8, 19.1, 14.1, 11.9, 11.6; *m*/*z* (EI) 289 (M^+, 0.1%), 248 (32), 218 (5), 203 (1), 166 (2), 157 (12), 133 (75), 116 (79), 105 (45), 91 (76), 86 (100), 77 (45), 70 (26), 55 (50), 51 (58).

(R)-1-Phenyl-N-[(S)-1-phenylbutoxy]pent-4-enylamine ***2e***.—Obtained from the addition of phenyllithium to oxime ether (*S*)-**1d**, as a *colourless oil* (91%, >90% de) (Found: M^+, 309.2188. $C_{21}H_{27}NO$ requires *M*, 309.2093); ν_{max} (film)/cm^{-1} 3058, 3026, 2955, 2930, 2869, 1641, 1495, 1456; δ_H (300 MHz; $CDCl_3$) 7.30 (10H, m, ArH), 5.71 (1H, m, H_2C=C*H*), 5.44 (1H, br s, NH), 4.95 (2H, m, *H*$_2$C=CH), 4.35 (1H, dd, *J* 5.5, 8.3, OCH), 4.00 (1H, dd, *J* 5.9, 8.2, NCH), 1.91 (2H, m, CH_2), 1.62 (2H, m, CH_2), 1.36 (1H, m, C*H*H), 1.15 (1H, m, CH*H*), 0.91 (2H, m, CH_2), 0.70 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 143.4, 142.5, 138.0, 128.3, 128.2, 127.9, 127.3, 127.2, 126.6, 114.9, 85.3, 65.2, 38.6, 32.9, 30.3, 18.9, 13.9; *m*/*z* (EI) 309 (M^+, 0.9%), 281 (1), 230 (7), 198 (6), 165 (13), 133 (26), 91 (100).

(R)-8-Benzyloxy-N-[(R)-1-phenylbutoxy]octan-4-ylamine ***2f***.—Obtained from the addition of *n*-propylmagnesium chloride to oxime ether (*R*)-**1e**, as a *colourless oil* (98%, >95% de) (Found: M^+, 383.2837. $C_{25}H_{37}NO_2$ requires *M*, 383.2824); ν_{max} (neat)/cm^{-1} 3430, 2954, 2924, 2865, 1146, 1103; δ_H (300 MHz; $CDCl_3$) 7.33 (10H, m, ArH), 5.00 (1H, br s, NH), 4.54 (1H, dd, *J* 7.6, 5.7, OCH), 4.51 (2H, s, PhCH_2), 3.46 (2H, t, *J* 6.5, CH_2O), 2.89 (1H, m, NCH), 1.81 (1H, m, C*H*H), 1.62–1.28 (13H, m, CH*H*, 6 × CH_2), 0.94 (3H, t, *J* 7.3, Me), 0.93 (3H, t, *J* 7.0, Me); δ_C (75 MHz; $CDCl_3$) 143.4, 138.7, 128.4, 128.3, 127.6, 127.5, 127.3, 126.6, 85.2, 72.9, 70.3, 60.2, 38.8, 34.4, 31.6, 30.0, 22.6, 19.3, 19.0, 14.4, 14.1; *m*/*z* (EI) 383 (M^+, 1%), 343 (3), 277 (6), 251 (48), 208 (48), 178 (57), 160 (24), 133 (74), 91 (100), 77 (49).

(S)-5-Benzyloxy-1-phenyl-N-[(R)-1-phenylbutoxy]pentylamine ***2g***.—Obtained from the addition of phenyllithium to oxime ether (*R*)-**1e**, as a *colourless oil* (61%, 83% de) (Found: M^+, 417.2674. $C_{28}H_{35}NO_2$ requires *M*, 417.2668); ν_{max} (neat)/cm^{-1} 3417, 2932, 2865, 1454, 1105; δ_H (300 MHz; $CDCl_3$) 7.83–7.26 (15H, m, ArH), 5.47 (1H, br s, NH), 4.47 (2H, s, PhCH_2), 4.39 (1H, dd, *J* 5.5, 9.8, OCH), 4.00 (1H, dd, *J* 6.0, 14.0, NCH), 3.40 (2H, t, *J* 6.5, CH_2O), 1.67–1.52 (5H, m, 2 × CH_2, C*H*H), 1.40–1.18 (3H, m, CH*H*, CH_2), 0.96 (2H, m, CH_2), 0.73 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 143.5, 142.7, 138.6, 134.8, 128.4, 128.34, 128.16, 127.92, 127.89, 127.7, 127.5, 127.4, 127.3, 127.2, 126.7, 126.6, 85.3, 72.9, 70.0, 65.9, 38.7, 33.7, 29.7, 22.8, 18.9, 13.9; *m*/*z* (EI) 417 (M^+, 0.5%), 312 (4), 285 (14), 212 (23), 133 (32), 106 (27), 91 (100), 77 (16).

(R)-1-Cyclohexyl-N-[(R)-1-phenylbutoxy]pentylamine ***2h***.—Obtained from the addition of *n*-butyllithium to oxime ether (*R*)-**1f**, as a *colourless oil* (95%, >90% de) (Found: M^+, 317.2729. $C_{21}H_{35}NO$ requires *M*, 317.2719); ν_{max} (film)/cm^{-1} 3030, 2957, 2923, 2850, 1490, 1452; δ_H (300 MHz; $CDCl_3$) 7.33

(5H, m, ArH), 5.29 (1H, br s, NH), 4.54 (1H, dd, *J* 6.1, 7.7, OCH), 2.58 (1H, dd, *J* 7.0, 5.3, NCH), 1.9–0.9 (27H, m, CH, 10 × CH_2, 2 × Me); δ_C (75 MHz; $CDCl_3$) 143.4, 128.3, 127.2, 126.7, 84.8, 65.1, 39.1, 38.7, 29.6, 28.9, 28.8, 28.4, 26.8, 26.7, 26.6, 23.0, 19.2, 14.2, 14.1; *m*/*z* (EI) 317 (M^+, 1%), 134 (24), 133 (85), 132 (27), 128 (45), 117 (29), 115 (10), 102 (100), 91 (100), 77 (29).

(R)-1-Cyclohexyl-2,2-dimethyl-N-[(S)-1-phenylbutoxy]-propylamine ***2i***.—Obtained from the addition of *tert*-butyllithium to oxime ether (*S*)-**1f**, as a *colourless oil* (68%, >90% de) (Found: MH^+, 318.2791. $C_{21}H_{36}NO$ requires *m*/*z*, 318.2797); ν_{max} (film)/cm^{-1} 3027, 2955, 2930, 2848, 1450, 1350; δ_H (300 MHz; $CDCl_3$) 7.31 (5H, m, ArH), 5.45 (1H, br s, NH), 4.55 (1H, dd, *J* 5.8, 7.5, OCH), 2.40 (1H, s, NCH), 1.80–1.10 (15H, m, CH, 7 × CH_2), 0.92 (3H, t, *J* 7.3, Me), 0.91 (9H, s, CMe_3); δ_C (75 MHz; $CDCl_3$) 143.9, 128.1, 127.0, 126.7, 83.9, 73.1, 38.8, 38.6, 35.5, 35.0, 28.5, 28.0, 27.5, 26.9, 26.5, 19.2, 14.1; *m*/*z* (EI) 318 (MH^+, 3%), 260 (100), 234 (3.0), 170 (1.7), 133 (19), 128 (69), 91 (30).

(S)-1-Cyclohexyl-N-[(R)-1-phenylbutoxy]benzylamine ***2j***.—Obtained from the addition of phenyllithium to oxime ether (*R*)-**1f**, as a *colourless oil* (77%, >90% de) (Found: M^+, 337.2407. $C_{23}H_{31}NO$ requires *M*, 337.2405); ν_{max} (film)/cm^{-1} 3257, 3027, 2925, 2848, 1486, 1445, 1353; δ_H (300 MHz; $CDCl_3$) 7.30 (10H, m, ArH), 5.61 (1H, br s, NH), 4.31 (1H, dd, *J* 5.3, 8.3, OCH), 3.75 (1H, d, *J* 7.7, NCH), 1.50 (7H, m, CH, 3 × CH_2), 1.35–0.70 (8H, m, 4 × CH_2), 0.65 (3H, t, *J* 7.2, Me); δ_C (75 MHz; $CDCl_3$) 138.6, 136.9, 123.4, 123.2, 122.6, 122.1, 121.7, 121.4, 80.0, 66.1, 35.6, 33.7, 25.4, 24.4, 21.2, 21.0, 13.1, 8.7; *m*/*z* (EI) 337 (M^+, 1%), 254 (35), 205 (68), 173 (38), 133 (79), 122 (94), 104 (26), 91 (100), 77 (27).

(R)-1-Cyclohexyl-N-[(R)-1-phenylbutoxy]but-3-enylamine ***2k***.—Obtained from the addition of allylmagnesium bromide to oxime ether (*R*)-**1f**, as a *colourless oil* (80%, 96% de) (Found: M^+, 301.2407. $C_{20}H_{31}NO$ requires *M*, 301.2406); ν_{max} (CH_2Cl_2)/cm^{-1} 2930, 1446, 1250, 916; δ_H (300 MHz; $CDCl_3$) 7.31 (5H, m, ArH), 5.80 (1H, m, CH=), 5.34 (1H, br s, NH), 5.06 (2H, m, $=CH_2$), 4.53 (1H, t, *J* 6.7, OCH), 2.60 (1H, m, NCH), 2.24 (2H, m, CH_2CH=), 1.79–1.07 (15H, m, cyclohexyl, CH_2CH_2), 0.92 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 143.3, 136.4, 128.2, 127.2, 126.7, 116.9, 84.9, 64.6, 38.7, 33.2, 29.7, 29.1, 26.6, 26.5, 19.2, 14.1; *m*/*z* (EI) 301 (M^+, 1%), 260 (46), 169 (26), 133 (78), 128 (86), 117 (52), 105 (54), 91 (100), 77 (65), 67 (59), 55 (76).

(S)-1-Cyclohexyl-N-[(S)-1-phenylbutoxy]but-3-enylamine ***2l***.—Obtained from the addition of allylmagnesium bromide to oxime ether (*S*)-**1f**, as a *colourless oil* (85%, 96% de), with identical spectroscopic properties to those of the enantiomer.

(R)-1-Phenyl-N-[(R)-1-phenylbutoxy)]butan-2-ylamine ***2m***.—Obtained from the addition of ethylmagnesium bromide to oxime ether (*R*)-**1g**, as a *colourless oil* (62%, 79% de) (Found: M^+, 297.2100. $C_{20}H_{27}NO$ requires *M*, 297.2093); ν_{max} (film)/cm^{-1} 3440, 3027, 2958, 2873, 1494, 1454, 1029; δ_H (300 MHz; $CDCl_3$) 7.36–7.16 (10H, m, ArH), 5.25 (1H, br s, NH), 4.58 (1H, dd, *J* 7.4, 6.1, OCH), 3.03 (1H, quintet, *J* 6.3, NCH), 2.74 (2H, d, *J* 6.6, $PhCH_2$), 1.84 (1H, m, C*H*H), 1.63–1.29 (5H, m, 2 × CH_2, CH*H*), 0.95 (3H, t, *J* 7.4, Me), 0.91 (3H, t, *J* 7.1, Me); δ_C (75 MHz; $CDCl_3$) 143.2, 139.1, 129.3, 128.34, 128.27, 127.2, 126.6, 126.1, 85.1, 63.1, 38.7, 37.7, 24.4, 19.3, 14.1, 10.3; *m*/*z* (EI) 297 (M^+, 1%), 268 (2), 239 (2), 218 (5), 194 (5), 165 (6), 133 (46), 91 (100).

(S)-3-Methyl-1-phenyl-N-[(R)-1-phenylbutoxy]butan-2-ylamine ***2n***.—Obtained from the addition of isopropylmagnesium chloride to oxime ether (*R*)-**1g**, as a *colourless oil* (92%, 91% de) (Found: M^+, 311.2242. $C_{21}H_{29}NO$ requires *M*, 311.2249); ν_{max} (film)/cm^{-1} 3440, 3027, 2958, 2871, 1494, 1463, 1029; δ_H (300 MHz; $CDCl_3$) 7.37–7.14 (10H, m, ArH), 5.24 (1H, br s, NH), 4.54 (1H, dd, *J* 7.3, 6.0, OCH), 2.92 (1H, m, NCH), 2.73 (1H, dd, *J* 4.1, 14.0, PhC*H*H), 2.46 (1H, dd, *J* 9.3, 14.0, PhCH*H*), 2.03 (1H, m, C*H*H), 1.76 (1H, m, CH*H*), 1.55–1.32 (3H, m, CH_2, CMe_2), 1.01 (3H, t, *J* 6.8, C*Me*Me), 0.98 (3H, t, *J* 6.8, CMe*Me*), (3H, t, *J* 7.1, Me); δ_C (75 MHz; $CDCl_3$) 143.2, 139.7, 129.1, 128.4, 128.2, 127.2, 126.5, 126.1, 85.0, 67.1, 38.7, 33.7, 19.2, 19.0, 18.0, 14.1; *m*/*z* (EI) 311 (M^+, 1%), 220 (10), 133 (20), 91 (100), 88 (36).

(S)-1-Phenyl-N-[(S)-1-phenylbutoxy]hexan-2-ylamine ***2o***.—Obtained from the addition of *n*-butyllithium to oxime ether (*S*)-**1g**, as a *colourless oil* (72%, >96% de) (Found: M^+, 325.2399. $C_{22}H_{31}NO$ requires *M*, 325.2405); ν_{max} (film)/cm^{-1} 3427, 2956, 2931, 1652, 1451; δ_H (300 MHz; $CDCl_3$) 7.25 (10H, m, ArH), 5.22 (1H, br s, NH), 4.56 (1H, dd, *J* 5.8, 9.8, OCH), 3.09 (1H, m, NCH), 2.73 (2H, dd, *J* 6.2, 3.2, CH_2Ph), 1.82 (1H, m, C*H*H), 1.60–1.29 (9H, m, 4 × CH_2, CH*H*), 0.95 (3H, t, *J* 7.3, Me), 0.89 (3H, t, *J* 7.1, Me); δ_C (75 MHz; $CDCl_3$) 143.3, 139.2, 129.4, 128.3, 128.3, 127.3, 126.7, 126.1, 85.1, 61.8, 38.7, 38.3, 31.5, 28.3, 22.9, 19.3, 14.2, 14.1; *m*/*z* (EI) 326 (MH^+, 11%), 268 (1), 234 (28), 210 (2), 193 (22), 176 (7), 163 (16), 149 (16), 133 (67), 117 (29), 91 (100), 77 (19), 65 (18).

(S)-4-Methyl-1-phenyl-N-[(S)-1-phenylbutoxy]pentan-2-ylamine ***2p***.—Obtained from the addition of isobutyllithium to oxime ether (*S*)-**1g**, as a *colourless oil* (67%, >96% de) (Found: M^+, 325.2405. $C_{22}H_{31}NO$ requires *M*, 325.2405); ν_{max} (film)/cm^{-1} 3425, 3029, 2956, 2871, 1635, 1496, 1454; δ_H (300 MHz; $CDCl_3$) 7.26 (10H, m, ArH), 5.17 (1H, br s, NH), 5.47 (1H, t, *J* 7.1, OCH), 3.16 (1H, q, *J* 6.5, NCH), 2.76 (2H, m, CH_2Ph), 1.71 (1H, m, C*H*H), 1.69–1.31 (5H, m, CH, 2 × CH_2), 1.18 (1H, m, C*H*Me_2), 0.95 (3H, t, *J* 7.3, Me), 0.87 (3H, t, *J* 6.5, C*Me*Me), 0.86 (3H, t, *J* 6.5, CMe*Me*); δ_C (75 MHz; $CDCl_3$) 143.3, 139.1, 129.4, 128.3, 128.2, 127.2, 126.6, 126.0, 85.6, 41.1, 28.6, 24.9, 23.0, 22.6, 19.2, 14.1; *m*/*z* (EI) 325 (M^+, 0.1%), 268 (1), 234 (21), 193 (6), 148 (2), 133 (53), 117 (26), 102 (63), 91 (100), 65 (14), 65 (14), 51 (78).

(S)-1-Phenyl-N-[(S)-1-phenylbutoxy]pentylamine ***2q***.—Obtained from the addition of *n*-butyllithium to oxime ether (*S*)-**1h**, as a *colourless oil* (72%, >95% de) (Found: M^+, 311.2258. $C_{21}H_{29}NO$ requires *M*, 311.2249); ν_{max} (film)/cm^{-1} 3252, 3032, 2955, 2930, 2873, 1449; δ_H (300 MHz; $CDCl_3$) 7.32 (10H, m, ArH), 5.39 (1H, br s, NH), 4.63 (1H, t, *J* 7.3, OCH), 4.00 (1H, dd, *J* 5.2, 8.8, NCH), 2.00 (1H, m, C*H*H), 1.87 (1H, m, CH*H*), 1.65 (2H, m, CH_2), 1.31 (6H, m, 3 × CH_2), 0.97 (3H, t, *J* 7.3, Me), 0.92 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 143.1, 141.7, 128.2, 128.1, 127.8, 127.31, 127.26, 126.8, 85.3, 65.8, 38.5, 33.5, 28.3, 22.8, 19.2, 14.1, 14.0; *m*/*z* (EI) 311 (M^+, 0.5%), 179 (67), 147 (56), 133 (77), 122 (75), 105 (21), 91 (100).

(R)-1-Phenyl-N-[(R)-1-phenylbutoxy]but-3-enylamine ***2r***.—Obtained from the addition of allylmagnesium bromide to oxime ether (*R*)-**1h**, as a *colourless oil* (100%, 92% de) (Found: M^+, 295.1938. $C_{20}H_{25}NO$ requires *M*, 295.1936); ν_{max} (CH_2Cl_2)/cm^{-1} 2962, 1640 1492, 1451, 1248, 918; δ_H (300 MHz; $CDCl_3$) 7.26 (10H, m, 2 × ArH), 5.72 (1H, m, =CH), 5.43 (1H, br s, NH), 5.03 (2H, m, $=CH_2$), 4.55 (1H, t, *J* 7.2, OCH), 4.07 (1H, dd, *J* 6.1, 7.6, NCH), 2.71 (1H, m, NCH), 2.42 (1H, m, CH_2CH=), 1.83 (1H, m, C*H*H), 1.60 (1H, m, CH*H*), 1.34 (2H, m, CH_2), 0.93 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 142.8, 140.9, 134.7, 128.3, 128.1, 127.8, 127.7, 127.4, 127.3, 126.7, 117.2, 85.2, 65.1, 38.3, 19.1, 14.1; *m*/*z* (EI) 295 (M^+, 0.2%), 164 (8), 163 (16), 146 (7), 134 (20), 132 (40), 91 (100), 77 (55).

(S)-1-(4-Methoxyphenyl)-N-[(S)-1-phenylbutoxy]but-3-enylamine ***2s***.—Obtained from the addition of allylmagnesium bromide to oxime ether (*S*)-**1i**, as a *colourless oil* (80%, >96% de) (Found: M^+, 325.2042. $C_{21}H_{27}NO_2$ requires *M*, 325.2042); ν_{max} (CH_2Cl_2)/cm^{-1} 2961, 1611, 1512, 1453, 1329, 1176, 1032, 916; δ_H (300 MHz; $CDCl_3$) 7.23 (5H, m, ArH), 7.15 (2H, d, ArH), 6.91 (2H, d, ArH), 5.65 (1H, m, CH=), 5.36 (1H, br s, NH), 5.02 (2H, m, CH_2=), 4.55 (1H, t, *J* 6.7, OCH), 3.79 (3H, s, OMe), 2.71 (1H, m, NCH), 2.45 (2H, m, CH_2CH=), 1.80 (1H, m, C*H*H), 1.56 (1H, m, CH*H*), 1.35 (2H, m, CH_2), 0.91 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 158.9, 142.9, 135.2, 132.8, 128.9, 128.2, 127.2, 126.7, 117.0, 113.6, 85.3, 64.5, 55.3, 38.4, 38.3, 19.2, 14.1; *m*/*z* (EI) 325 (M^+, 0.1%), 284 (35), 176 (13), 161

(57), 149 (3), 133 (69), 117 (24), 106 (8), 91 (100), 77 (53), 65 (28), 51 (29).

(S)-1-(2-Naphthyl)-N-[(S)-1-phenylbutoxy]pentylamine ***2t***.—Obtained from the addition of *n*-butyllithium to oxime ether (*S*)-**1j**, as a *colourless solid* (50%, >90% de); mp 76–77 °C (from ethanol) (Found: C, 83.1; H, 8.9; N, 3.8. $C_{25}H_{31}NO$ requires C, 83.1; H, 8.6; N, 3.9%); ν_{max} (KBr)/cm^{-1} 3437, 3058, 3027, 2954, 2929, 2867, 1638, 1455; δ_H (300 MHz; $CDCl_3$) 7.82 (3H, m, ArH), 7.66 (1H, s, ArH), 7.45 (2H, m, ArH), 7.37 (1H, dd, *J* 6.9, 8.5, ArH), 7.21 (5H, m, ArH), 5.47 (1H, br s, NH), 4.57 (1H, dd, *J* 6.2, 7.4, OCH), 4.11 (1H, dd, *J* 5.2, 9.0, NCH), 2.01 (1H, m, C*H*H), 1.76 (2H, m, CH_2), 1.57 (1H, m, CH*H*), 1.30 (6H, m, 3 × CH_2), 0.90 (3H, t, *J* 7.3, Me), 0.85 (3H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 142.9, 139.1, 133.3, 132.9, 128.2, 127.9, 127.8, 127.6, 127.2, 126.8, 126.7, 125.9, 125.8, 125.6, 85.2, 65.9, 38.5, 33.4, 31.8, 28.3, 22.8, 19.2, 14.1, 14.0; *m*/*z* (EI) 361 (M$^+$, 0.4%), 229 (12), 197 (31), 172 (19), 154 (10), 141 (43), 133 (31), 115 (5), 91 (100), 77 (6).

(S)-1-(Thiazol-2-yl)-N-[(S)-1-phenylbutoxy]but-3-enylamine ***2u***.—Obtained from the addition of allylmagnesium bromide to the oxime ether (*S*)-**1m**, as a yellow oil (7%, 20% de) (Found: MH$^+$, 303.1529. $C_{17}H_{23}N_2OS$ requires *m*/*z*, 303.1548); ν_{max} (film)/cm^{-1} 3079, 3029, 2958, 2931, 2871, 1494, 1454, 1027; δ_H (400 MHz; $CDCl_3$) 7.74 (1H, d, *J* 3.2, ArH), 7.35–7.24 (6H, m, ArH), 5.73 (1H, m, CH=), 5.65 (1H, br s, NH), 5.10 (2H, m, H_2C=), 4.63 (1H, t, *J* 6.1, OCH), 4.45 (1H, dd, *J* 6.1, 7.6, NCH), 2.57 (1H, m, C*H*HC=), 2.45 (1H, m, CH*H*C=), 1.68–1.21 (4H, 2 × CH_2), 0.80 (3H, t, *J* 7.4, Me); δ_C (100 MHz; $CDCl_3$) 173.2, 142.7, 142.1, 133.5, 128.4, 127.4, 126.5, 118.7, 118.5, 85.7, 62.6, 38.5, 37.8, 18.9, 13.9; *m*/*z* (EI) 303 (MH$^+$, 14%), 183 (5), 166 (100), 150 (100), 140 (40), 113 (19), 100 (26), 86 (55), 72 (20).

General method for the preparation of Boc-protected amines

Zinc dust (40 mmol) was added to a mixture of a hydroxylamine **2** (1 mmol) in acetic acid–water (6.5 mL; 1:1). The mixture was placed in a sonic bath at 40 °C and the reaction was followed by TLC until completion. The zinc was filtered off and washed with diethyl ether. The filtrate was basified with saturated aq. sodium bicarbonate solution and the aqueous layer exhaustively extracted with dichloromethane (8 × 15 mL). The extracts were combined, dried (Na_2SO_4), filtered and evaporated. The residue was dissolved in dichloromethane (7 mL), and di-*tert*-butyl dicarbonate (4 mmol) and DMAP (cat.) were added. The mixture was stirred at room temperature for 12 h. Saturated aq. sodium bicarbonate (10 mL) was added and the mixture stirred for 10 min before being extracted with dichloromethane (4 × 10 mL), and the organic extracts were combined, dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash chromatography on silica gel, eluting with dichloromethane–light petroleum (1:1).

General method for the preparation of Cbz-protected amines

Zinc powder (40 mmol) was added to a solution of the hydroxylamine **2** (1 mmol) in acetic acid (1 mL), water (1 mL) and THF (2 mL), and the mixture was place in a sonic bath at 50 °C until all the hydroxylamine had been consumed. The resulting mixture was filtered into a separating funnel, and the solid residue was washed successively with NaOH (2 M; 10 mL) and diethyl ether (10 mL). The washing was repeated once more and the ether layer was separated. The aqueous layer was washed with diethyl ether (2 × 20 mL). The combined washings were dried over (Na_2SO_4), filtered and the solvent removed under reduced pressure. The residue was dissolved in a mixture of THF (2 mL) and water (2 mL), potassium carbonate (1.1 mmol) was added and the mixture was stirred at room temperature. After 10 min, benzyl chloroformate (1.1 mL) was added carefully, and the heterogeneous solution was stirred vigourously for 1 h. Water (10 mL) and diethyl ether (10 mL) were added, the layers separated, and the aqueous layer was washed with two further portions of diethyl ether. The combined organic extracts were dried ($MgSO_4$), filtered and evaporated. Column chromatography of the residue on silica gel (dichloromethane–light petroleum gradient elution) gave the Cbz-protected amine.

(*S*)-(+)-*N*-Benzyloxycarbonyl-2-methylhexan-3-ylamine 3a. Obtained from the cleavage of hydroxylamine **2a** and protection, as a *colourless solid* (58%, 91% ee); mp 50–51 °C (from light petroleum); $[\alpha]_D^{25}$ +4.8 (*c* 1.0, CH_2Cl_2) (Found: C, 72.6; H, 8.9; N, 5.6. $C_{15}H_{23}NO_2$ requires C, 72.3; H, 9.3; N, 5.6%); ν_{max} (KBr)/cm^{-1} 3324, 2966, 2808, 1690, 1532, 1450, 1245; δ_H (300 MHz; $CDCl_3$) 7.33 (5H, m, ArH), 5.10 (2H, s, PhCH_2), 4.56 (1H, br d, *J* 9.0, NH), 3.53 (1H, m, NCH), 1.74 (1H, m, CH), 1.35 (4H, m, 2 × CH_2), 0.90 (9H, m, 3 × Me); δ_C (75 MHz; $CDCl_3$) 156.5, 136.8, 128.5, 128.0, 66.5, 56.1, 34.7, 32.1, 19.4, 19.2, 17.5, 14.1; *m*/*z* (EI) 249 (M$^+$, 1%), 206 (18), 162 (26), 107 (11), 91 (100).

(*S*)-(−)-*N*-Benzyloxycarbonyl-1-phenylpentan-2-ylamine 3b. Obtained from the cleavage of hydroxylamine **2b** and protection, as a *colourless solid* [85%, 92% ee, 97% ee (recrystallised)]; mp 81–83 °C (from light petroleum); $[\alpha]_D^{24}$ −6.6 (*c* 0.64, CH_2Cl_2) (Found: C, 76.8; H, 7.7; N, 4.7. $C_{19}H_{23}NO_2$ requires C, 76.7; H, 7.8; N, 4.7%); ν_{max} (KBr)/cm^{-1} 3426, 3329, 3027, 2955, 2925, 2868, 1701, 1537; δ_H (300 MHz; $CDCl_3$) 7.30 (10H, m, ArH), 5.12 (1H, d, *J* 12.3, PhC*H*HO), 5.07 (1H, d, *J* 12.6, PhCH*H*O), 4.63 (1H, br d, *J* 8.1, NH), 3.94 (1H, br m, NCH), 2.08 (2H, d, *J* 6.2, PhCH_2), 1.43 (4H, m, 2 × CH_2), 0.91 (3H, t, *J* 6.3, Me); δ_C (75 MHz; $CDCl_3$) 156.0, 138.1, 136.8, 129.5, 128.5, 128.4, 128.0 (2C), 126.4, 66.5, 52.0, 41.3, 30.4, 19.2, 13.0; *m*/*z* (EI) 297 (M$^+$, 0.9%), 206 (23), 189 (15), 162 (24), 108 (32), 98 (25), 91 (100), 77 (13).

(*R*)-(−)-*N*-Benzyloxycarbonyl-2-methylhex-5-en-3-ylamine 3c. Obtained from the cleavage of hydroxylamine **2c** and protection, as a *colourless oil* (47%, 78% ee) (Found: M$^+$, 247.1572. $C_{15}H_{21}NO_2$ requires *M*, 247.1572); $[\alpha]_D^{22}$ −30.0 (*c* 2.0, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 3055, 2989, 2306, 1721, 1421, 1269; δ_H (300 MHz; $CDCl_3$) 7.33 (5H, m, ArH), 5.79 (1H, m, CH=), 5.10 (2H, s, CH_2O), 5.04 (2H, m, CH_2=), 4.64 (1H, d, *J* 7.7, NH), 3.59 (1H, m, NCH), 2.24 (1H, m, C*H*HCH=), 2.16 (1H, m, CH*H*CH=), 1.75 (1H, m, C*H*Me$_2$), 0.93 (3H, d, *J* 7.6, Me), 0.90 (3H, d, *J* 7.6, Me); δ_C (75 MHz; $CDCl_3$) 156.4, 136.8, 134.8, 128.5, 128.4, 127.98, 127.97, 117.4, 66.5, 55.8, 36.9. 31.5, 19.2, 19.0, 17.7; *m*/*z* (EI) 247 (M$^+$, 1%), 234 (1), 190 (2), 162 (44), 149 (1), 118 (4), 107 (16), 91 (100), 83 (82), 77 (12), 65 (23), 51 (65).

(*R*)-(−)-*N*-Benzyloxycarbonyl-5-ethylhept-1-en-4-ylamine 3d. Obtained from the cleavage of hydroxylamine **2d** and protection, as a *colourless oil* (75%, 91% ee) (Found: M$^+$, 275.1885. $C_{17}H_{25}NO_2$ requires *M*, 275.1885); $[\alpha]_D^{22}$ −29.7 (*c* 0.97, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 3055, 2987, 2305, 1716, 1420, 1259; δ_H (300 MHz; $CDCl_3$) 7.33 (5H, m, ArH), 5.79 (1H, m, CH=), 5.09 (2H, s, CH_2O), 5.06 (2H, m, CH_2=), 4.63 (1H, d, *J* 8.5, NH), 3.83 (1H, m, NCH), 2.20 (2H, m, CH_2CH=), 1.43–1.16 [5H, m, (MeCH_2)$_2$C*H*], 0.92 [6H, t, *J* 7.0, (*Me*CH$_2$)$_2$C]; δ_C (75 MHz; $CDCl_3$) 156.2, 136.8, 135.0, 128.5, 128.00, 127.96, 117.3, 66.5, 52.2, 44.4, 37.0, 22.3, 21.7, 11.8, 11.5; *m*/*z* (EI) 275 (M$^+$, 0.2%), 234 (57), 204 (26), 190 (71), 160 (54), 146 (2), 118 (3), 107 (13), 91 (100), 83 (72), 65 (29), 51 (32).

(*R*)-(+)-*N*-Benzyloxycarbonyl-1-phenylpent-4-enylamine 3e. Obtained from the cleavage of hydroxylamine **2e** and protection, as a *colourless solid* [82%, 89% ee, 91% ee (recrystallised)]; mp 69–71 °C (from light petroleum); $[\alpha]_D^{24}$ +27.6 (*c* 1.0, CH_2Cl_2) (Found: C, 77.3; H, 7.1; N, 4.7. $C_{19}H_{21}NO_2$ requires C, 77.3; H, 7.2; N, 4.7%); ν_{max} (KBr)/cm^{-1} 3329, 3058, 3027, 2935, 2909, 2843, 1685, 1537, 1255; δ_H (300 MHz; $CDCl_3$) 7.25 (10H, m, ArH), 5.80 (1H, m, H_2C=C*H*), 5.06 (5H, m, PhCH_2, NH, H_2C=CH), 4.72 (1H, dd, *J* 7.8, 15.1, NCH), 2.06 (2H, m, CH_2),

1.88 (2H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 155.7, 142.3, 137.5, 136.4, 128.7, 128.5, 128.2, 127.4, 126.4, 115.4, 66.8, 55.0, 35.8, 30.4; *m*/*z* (EI) 296 (MH^+, 4%), 295 (M^+, 1), 240 (43), 196 (41), 160 (27), 145 (35), 132 (50), 117 (37), 104 (67), 91 (100), 77 (70).

(*R*)-(+)-8-Benzyloxy-*N*-(*tert*-butoxycarbonyl)octan-4-ylamine 3f. Obtained from the cleavage of **2f** and protection, as a *colourless oil* (85%, 88% ee); $[\alpha]_D^{24}$ +7.8 (*c* 0.54, $CHCl_3$) (Found: MH^+, 336.2549. $C_{20}H_{34}NO_3$ requires *m*/*z*, 336.2539); ν_{max} (neat)/cm^{-1} 3344, 2933, 2863, 1699, 1521, 1365; δ_H (300 MHz; $CDCl_3$) 7.34 (5H, m, ArH), 4.49 (2H, s, PhCH_2), 4.32 (1H, br d, *J* 6.2, NH), 3.55 (1H, br s, NCH), 3.46 (2H, t, *J* 6.4, CH_2O), 1.67–1.54 (2H, m, CH_2), 1.43 (9H, s, CMe_3), 1.43–1.28 (8H, m, 4 × CH_2), 0.90 (3H, m, Me); δ_C (75 MHz; $CDCl_3$) 155.7, 138.6, 128.3, 127.6, 127.5, 78.8, 72.9, 70.2, 50.4, 37.8, 35.4, 29.7, 28.4, 22.6, 19.1, 14.0; *m*/*z* (EI) 336 (MH^+, 3%), 292 (47), 278 (46), 262 (24), 234 (62), 212 (29), 206 (15), 192 (87), 172 (74), 130 (46), 116 (86), 107 (63), 91 (100), 77 (60).

(*S*)-(−)-5-Benzyloxy-*N*-(*tert*-butoxycarbonyl)-1-phenylpentylamine 3g. Obtained from the cleavage of **2g** and protection, as a *colourless oil* (31%, 77% ee); $[\alpha]_D^{22}$ −18.0 (*c* 2.0, $CHCl_3$) (Found: M^+, 369.2301. $C_{23}H_{31}NO_3$ requires *M*, 369.2304); ν_{max} (neat)/cm^{-1} 3338, 2975, 2935, 2861, 1699, 1496, 1170; δ_H (300 MHz; $CDCl_3$) 7.37–7.24 (10H, m, ArH), 4.83 (1H, br s, NH), 4.60 (1H, br s, NCH), 4.48 (2H, s, PhCH_2), 3.44 (2H, t, *J* 6.4, CH_2O), 1.76–1.59 (4H, m, 2 × CH_2), 1.51–1.27 (2H, m, CH_2), 1.42 (9H, br s, CMe_3); δ_C (75 MHz; $CDCl_3$) 144.1, 138.5, 128.5, 128.4, 127.7, 127.5, 127.1, 126.3, 72.9, 70.0, 54.1, 36.8, 29.4, 28.4, 23.0; *m*/*z* (EI) 369 (M^+, 1%), 268 (11), 206 (25), 161 (26), 150 (82), 106 (100), 91 (80).

(*R*)-(+)-*N*-Benzyloxycarbonyl-1-cyclohexylpentylamine 3h. Obtained from the cleavage of hydroxylamine **2h** and protection, as a *colourless solid* [79%, 96% ee (recrystallised)]; mp 98–99 °C (from light petroleum); $[\alpha]_D^{23}$ +13.0 (*c* 1.0, CH_2Cl_2) (Found: C, 75.2; H, 9.1; N, 4.5. $C_{19}H_{29}NO_2$ requires C, 75.2; H, 9.6; N, 4.6%); ν_{max} (KBr)/cm^{-1} 3437, 2925, 2850, 1690, 1639, 1537; δ_H (300 MHz; $CDCl_3$) 7.35 (5H, m, ArH), 5.12 (1H, d, *J* 12.1, PhC*H*H), 5.07 (1H, d, *J* 12.2, PhCH*H*), 4.54 (1H, br d, *J* 9.8, NH), 3.49 (1H, m, NCH), 1.8–0.9 (17H, m, CH, 8 × CH_2), 0.89 (3H, t, *J* 5.8, Me); δ_C (75 MHz; $CDCl_3$) 156.4, 136.8, 128.5, 128.1, 66.5, 55.8, 42.2, 32.1, 29.7, 28.3, 28.1, 26.5, 26.3, 26.3, 22.7, 14.1; *m*/*z* (CI) 304 (MH^+, 10%), 170 (100), 86 (60).

(*R*)-(−)-*N*-Benzyloxycarbonyl-1-cyclohexyl-2,2-dimethylpropylamine 3i. Obtained from the cleavage of hydroxylamine **2i** and protection, as a *colourless oil* (25%, 96% ee); $[\alpha]_D^{23}$ −1.0 (*c* 0.38, CH_2Cl_2) (Found: MH^+, 304.2282. $C_{19}H_{30}NO_2$ requires *m*/*z*, 304.2277); ν_{max} (KBr)/cm^{-1} 3577, 3345, 2925, 2848, 1696, 1532; δ_H (300 MHz; $CDCl_3$) 7.35 (5H, m, ArH), 5.15 (1H, d, *J* 12.2, PhC*H*H), 5.08 (1H, d, *J* 12.2, PhCH*H*), 4.75 (1H, br d, *J* 9.8, NH), 3.32 (1H, dd, *J* 11.0, 1.7, NCH), 1.69 (5H, m, CH, 2 × CH_2), 1.15 (6H, m, 3 × CH_2), 0.93 (9H, s, CMe_3); δ_C (75 MHz; $CDCl_3$) 156.9, 136.8, 128.5, 128.1, 66.7, 63.7, 38.5, 35.6, 33.9, 28.4, 27.3, 26.8, 26.4, 26.2; *m*/*z* (EI) 304 (MH^+, 2%), 246 (100), 220 (17), 176 (15), 91 (58).

(*S*)-(−)-*N*-Benzyloxycarbonyl-α-cyclohexylbenzylamine 3j. Obtained from the cleavage of hydroxylamine **2j** and protection, as a *colourless solid* [62%, 100% ee (recrystallised)]; mp 119–121 °C (from light petroleum–dichloromethane); $[\alpha]_D^{22}$ −23.4 (*c* 1.0, CH_2Cl_2) (Found: C, 78.0; H, 8.2; N, 4.2. $C_{21}H_{25}NO_2$ requires C, 78.0; H, 7.8; N, 4.3%); ν_{max} (KBr)/cm^{-1} 3437, 3360, 2919, 2853, 1690, 1521; δ_H (300 MHz; $CDCl_3$) 7.25 (10H, m, ArH), 5.25 (1H, br d, *J* 8.7, NH), 5.12 (1H, d, *J* 12.3, PhC*H*H), 5.04 (1H, d, *J* 12.3, PhCH*H*), 4.51 (1H, t, *J* 8.2, NCH), 1.90–0.90 (11H, m, CH, 5 × CH_2); δ_C (75 MHz; $CDCl_3$) 156.0, 141.7, 136.5, 128.5, 128.4, 128.20, 128.15, 127.1, 126.9, 66.8, 60.6, 43.4, 30.1, 29.3, 26.3; *m*/*z* (EI) 323 (M^+, 0.1%), 240 (77), 240 (65), 196 (62), 155 (5), 132 (26), 104 (25), 91 (100), 77 (31).

(*R*)-(−)-*N*-Benzyloxycarbonyl-1-cyclohexylbut-3-enylamine (*R*)-3k. Obtained from the cleavage of hydroxylamine **2k** and protection, as a *colourless solid* (67%, 92% ee); mp 69–71 °C (from light petroleum) (Found: C, 74.8; H, 8.7; N, 4.8. $C_{18}H_{25}NO_2 \cdot 0.1H_2O$ requires C, 74.7; H, 8.8; N, 4.8%) (Found: M^+, 287.1885. $C_{18}H_{25}NO_2$ requires *M*, 287.1885); $[\alpha]_D^{22}$ −16 (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 3435, 2931, 2854, 1721, 1507, 1448, 1340, 1213; δ_H (300 MHz; $CDCl_3$) 7.33 (5H, m, ArH), 5.75 (1H, m, CH=), 5.09 (2H, m, CH_2=), 5.02 (2H, s, CH_2O), 4.55 (1H, br d, *J* 9.0, NH), 3.58 (1H, m, NCH), 2.28 (1H, m, CH_2CH=), 2.14 (1H, m, CH_2CH=), 1.73 (5H, m, cyclohexyl), 1.09 (6H, m, cyclohexyl); δ_C (100 MHz; $CDCl_3$) 156.3, 136.7, 134.7, 128.5, 128.1, 117.5, 66.5, 55.2, 41.4, 39.7, 36.7, 28.3, 26.4, 26.2, 26.1; *m*/*z* (EI) 287 (M^+, 1%), 246 (51), 202 (61), 180 (3), 160 (44), 138 (10), 120 (3), 107 (34), 91 (100), 79 (39), 65 (51), 55 (50), 51 (31).

(*S*)-(+)-*N*-Benzyloxycarbonyl-1-cyclohexylbut-3-enylamine (*S*)-3k. Obtained from the cleavage of hydroxylamine **2l** and protection, as a *colourless solid* (51%, 89% ee); mp 67–68 °C (from light petroleum); $[\alpha]_D^{22}$ +19.2 (*c* 1.2, $CHCl_3$); identical spectroscopic properties with those of the enantiomer.

(*S*)-(−)-*N*-Benzyloxycarbonyl-3-methyl-1-phenylbutan-2-ylamine 3l. Obtained from the cleavage of **2n** and protection, as a *colourless solid* (37%, 98% ee); mp 103–104 °C (from light petroleum); $[\alpha]_D^{26}$ −2.0 (*c* 0.8, $CHCl_3$) (Found: C, 76.6; H, 8.1; N, 4.6. $C_{19}H_{23}NO_2$ requires C, 76.7; H, 7.8; N, 4.7%); ν_{max} (KBr)/cm^{-1} 3345, 2950, 2873, 1687, 1535, 1234, 1024; δ_H (300 MHz; $CDCl_3$) 7.35–7.17 (10H, m, ArH), 5.05 (1H, d, *J* 12.1, C*H*HO), 5.01 (1H, d, *J* 12.1, CH*H*O), 4.60 (1H, br d, *J* 9.5, NH), 3.83 (1H, m, NCH), 2.82 (1H, dd, *J* 6.0, 13.8, PhC*H*H), 2.69 (1H, dd, *J* 8.0, 13.8, PhCH*H*), 1.77 (1H, m, C*H*Me_2), 0.98 (3H, d, *J* 6.8, Me), 0.93 (3H, d, *J* 6.8, Me); δ_C (75 MHz; $CDCl_3$) 196.1, 156.6, 138.4, 136.7, 129.2, 128.5, 128.4, 127.9, 126.3, 66.5, 57.3, 38.6, 30.8, 19.6, 17.2; *m*/*z* (EI) 297 (M^+, 1%), 254 (100), 206 (79), 162 (81), 107 (13), 91 (100), 77 (14).

(*S*)-(−)-*N*-(*tert*-Butoxycarbonyl)-1-phenylhexan-2-ylamine 3m. Obtained from the cleavage of **2o** and protection, as a *colourless solid* (78%, >96% ee); mp 74–75 °C (from 50% aq. ethanol); $[\alpha]_D^{20}$ −9.5 (*c* 1.05, CH_2Cl_2) (Found: C, 73.9; H, 10.1; N, 4.9. $C_{17}H_{27}NO_2$ requires C, 73.6; H, 9.8; N, 5.0%); ν_{max} (KBr)/cm^{-1} 3367, 2977, 2921, 2857, 1683, 1527, 1365; δ_H (300 MHz; $CDCl_3$) 7.24 (5H, m, ArH), 4.28 (1H, br s, NH), 3.80 (1H, br s, NCH), 2.75 (2H, d, *J* 6.1, CH_2Ph), 1.41 (9H, s, CMe_3), 1.31 (6H, m, 3 × CH_2), 0.87 (3H, t, *J* 6.9, Me); δ_C (75 MHz; $CDCl_3$) 155.5, 138.4, 129.5, 128.2, 126.2, 33.9, 28.3, 28.15, 22.5, 14.0; *m*/*z* (CI) 278 (MH^+, 22%), 240 (2), 239 (14), 222 (4), 127 (5), 126 (15), 112 (11), 111 (36), 110 (13), 97 (16), 96 (22), 87 (11), 86 (68), 71 (19), 70 (100).

(*S*)-(−)-*N*-(*tert*-Butoxycarbonyl)-4-methyl-1-phenylpentan-2-ylamine 3n. Obtained from the cleavage of **2p** and protection, as a *colourless solid* (67%, >96% ee); mp 116–117 °C (from 50% aq. ethanol); $[\alpha]_D^{20}$ −23.6 (*c* 1.1, CH_2Cl_2) (Found: C, 74.0; H, 10.0; N, 5.0. $C_{17}H_{27}NO_2$ requires C, 73.6; H, 9.8; N, 5.0%); ν_{max} (KBr)/cm^{-1} 3407, 2098, 1683, 1652, 1365, 1172; δ_H (300 MHz; $CDCl_3$) 7.22 (5H, m, ArH), 4.27 (1H, br s, NH), 3.90 (1H, br s, NCH), 2.75 (2H, d, *J* 4.6, CH_2Ph), 1.75–1.61 (1H, m, C*H*Me_2), 1.40 (9H, s, CMe_3), 1.22 (2H, t, *J* 7.2, C$H_2$$CMe_2$), 0.88 (6H, t, *J* 6.4, CMe_2); δ_C (75 MHz; $CDCl_3$) 155.4, 138.3, 129.6, 128.2, 126.2, 78.9, 49.6, 43.6, 41.9, 28.4, 24.8, 23.2, 22.0; *m*/*z* (CI) 278 (MH^+, 87%), 239 (100), 222 (19), 186 (25), 179 (5), 178 (51), 159 (14), 134 (3), 133 (10), 117 (3), 116 (14), 112 (11), 88 (12), 87 (8), 86 (67).

(*S*)-(−)-*N*-Benzyloxycarbonyl-1-phenylpentylamine 3o. Obtained from the cleavage of hydroxylamine **2q** and protection, as a *colourless solid* [87%, 92% ee (recrystallised)]; mp 80–81 °C (from light petroleum); $[a]_D^{21}$ −24.0 (*c* 1.0, CH_2Cl_2) (Found: C, 76.8; H, 7.9; N, 4.7. $C_{19}H_{23}NO_2$ requires C, 76.7; H, 7.8; N, 4.7%); ν_{max} (KBr)/cm^{-1} 3419, 3334, 3031, 2950, 2930, 2855, 1680, 1534, 1257, 1045; δ_H (300 MHz; $CDCl_3$) 7.28 (10H, m, ArH), 5.12 (1H, d, *J* 12.2, PhC*H*H), 5.09 (1H, br s, NH), 5.04 (1H, d, *J* 12.2, PhCH*H*), 4.68 (1H, dd, *J* 7.3, 14.7, NCH), 1.76 (2H, m, CH_2), 1.27 (4H, m, 2 × CH_2), 0.88 (3H, t, *J* 6.9, Me); δ_C (75 MHz; $CDCl_3$) 155.7, 142.7, 136.5, 128.6, 128.5, 128.2, 127.3, 126.4, 66.8, 55.5, 36.5, 28.3, 22.5, 14.0; *m*/*z* (EI) 297 (M^+, 0.4%), 240 (77), 196 (70), 132 (20), 104 (27), 91 (100), 77 (21).

(*R*)-(+)-*N*-Benzyloxycarbonyl-1-phenylbut-3-enylamine 3p. Obtained from the cleavage of hydroxylamine **2r** and protection, as a *colourless solid* (66%, 95% ee); mp 68–69 °C (from light petroleum) (Found: C, 76.7; H, 6.6; N, 4.9. $C_{18}H_{19}NO_2$ requires C, 76.8; H, 6.8; N, 5.0%) (Found: M^+, 281.1416. $C_{18}H_{19}NO_2$ requires *M*, 281.1416); $[a]_D^{22}$ +43.6 (*c* 0.5, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 3437, 3061, 2929, 1721, 1503, 1419, 1251, 893; δ_H (300 MHz; $CDCl_3$) 7.28 (10H, m, ArH), 5.67 (1H, m, CH=), 5.13 (2H, m, =CH_2), 5.09 (2H, s, CH_2O), 5.08 (1H, br s, NH), 4.82 (1H, m, CHN), 2.54 (2H, m, CH_2CH=); δ_C (75 MHz; $CDCl_3$) 155.7, 142.0, 136.5, 133.8, 128.6, 128.5, 128.1, 127.3, 126.3, 126.2, 118.4, 66.8, 54.5, 41.0; *m*/*z* (EI) 281 (M^+, 0.1%), 240 (65), 196 (60), 132 (21), 107 (11), 91 (100), 77 (47), 65 (46).

(*S*)-(−)-*N*-Benzyloxycarbonyl-1-(4-methoxyphenyl)but-3-enylamine 3q. Obtained from the cleavage of hydroxylamine **2s** and protection, as a *colourless solid* (62%, 98% ee); mp 67–68 °C (from light petroleum) (Found: C, 73.3; H, 6.8; N, 4.5. $C_{19}H_{21}NO_3$ requires C, 73.0; H, 6.7; N, 4.4%) (Found: MH^+, 312.2249. $C_{19}H_{22}NO_3$ requires *m*/*z*, 312.1521); $[a]_D^{22}$ −36.6 (*c* 0.7, CH_2Cl_2); ν_{max} (CH_2Cl_2)/cm^{-1} 3433, 3054, 2986, 2305, 1718, 1511, 1260; δ_H (300 MHz; $CDCl_3$) 7.32 (5H, m, ArH), 7.21 (2H, d, *J* 8.5, ArH), 7.18 (2H, d, *J* 8.5, ArH), 5.66 (1H, m, CH=), 5.13 (2H, m, CH_2=), 5.09 (2H, s, CH_2O), 5.08 (1H, br s, NH), 4.76 (1H, d, *J* 6.1 NCH), 3.81 (3H, s, MeO), 2.43 (2H, m, CH_2CH=); δ_C (100 MHz; $CDCl_3$) 158.8, 155.6, 136.5, 134.1, 133.9, 128.5, 128.2, 127.5, 118.3, 114.0, 66.7, 55.3, 54.1, 41.0; one aromatic C not observed; *m*/*z* (EI) 312 (MH^+, 16%), 288 (1), 271 (70), 251 (45), 226 (58), 204 (29), 176 (19), 161 (100), 146 (8), 136 (67), 121 (42), 105 (12), 92 (39), 70 (36), 52 (3).

(*S*)-(−)-*N*-Benzyloxycarbonyl-1-(2-naphthyl)pentylamine 3r. Obtained from the cleavage of hydroxylamine **2t** and protection, as a *colourless oil* (83%, 91% ee); $[a]_D^{22}$ −22.2 (*c* 1.0, CH_2Cl_2) (Found: M^+, 347.1878. $C_{23}H_{25}NO_2$ requires *M*, 347.1885); ν_{max} (KBr)/cm^{-1} 3406, 3324, 3052, 2955, 2930, 2858, 1696, 1527, 1239; δ_H (300 MHz; $CDCl_3$) 7.80 (4H, m, ArH), 7.45 (8H, m, ArH), 5.27 (1H, d, *J* 8.4, NH), 5.15 (1H, d, *J* 12.2, PhC*H*H), 5.07 (1H, d, *J* 12.2, PhCH*H*), 4.88 (1H, dd, *J* 7.1, 13.8, NCH), 1.86 (2H, m, CH_2), 1.32 (4H, m, 2 × CH_2), 0.90 (3H, t, *J* 6.9, Me); δ_C (75 MHz; $CDCl_3$) 155.8, 140.2, 136.5, 133.4, 132.8, 128.6, 128.5, 128.22, 128.18, 128.0, 127.7, 126.2, 125.8, 125.2, 124.6, 66.8, 55.6, 36.4, 28.4, 22.5, 14.0; *m*/*z* (EI) 347 (M^+, 6%), 290 (28), 256 (38), 246 (47), 212 (13), 182 (14), 154 (17), 141 (10), 127 (15), 91 (100).

Deprotection reactions

(*S*)-(−)-3-Methyl-1-phenylbutan-2-ylamine. The *N*-Cbz-amine **3l** (64 mg, 0.21 mmol) was dissolved in methanol (5 mL) and Pd/C (5%; cat.) was added. The reaction mixture was stirred under a hydrogen atmosphere for 2.5 h. The catalyst was filtered off and washed with methanol. The methanol was evaporated and the residue was taken up in diethyl ether (5 mL). The mixture was acidified to pH 1 with hydrochloric acid (1 M) and extracted with diethyl ether (2 × 5 mL). The aqueous layer was basified to pH 14 with aq. sodium hydroxide (3 M) and extracted with dichloromethane (4 × 5 mL). The extracts were combined, dried (Na_2SO_4), filtered and evaporated to give the title compound as a *colourless oil* (41%); $[a]_D^{20}$ −38.7 (*c* 0.15, CH_2Cl_2) {lit.,[11a] $[a]_D$ −37.3 (*c* 0.12, CH_2Cl_2)}; δ_H (300 MHz; $CDCl_3$) 7.28–7.21 (5H, m, ArH), 2.90–2.80 (1H, m, PhC*H*H), 2.46–2.37 (1H, m, PhCH*H*), 1.75–1.64 (1H, m, C*H*Me_2), 1.19 (2H, br s, NH_2), 1.01 (3H, d, *J* 5.5, Me), 0.99 (3H, d, *J* 5.5, Me).

(*S*)-(+)-1-Phenylhexan-2-ylamine hydrochloride. The *N*-Boc-amine **3m** (140 mg, 0.5 mmol) was dissolved in 1,4-dioxane (4 mL). Conc. hydrochloric acid was added dropwise to the mixture until all of the amine was consumed (45 min). The 1,4-dioxane was removed *in vacuo* and the residue triturated with diethyl ether to give the title compound as a *colourless solid* (67%); mp 157–158 °C (lit.,[11b] 161–162 °C); $[a]_D^{20}$ +20.0 (*c* 0.2, H_2O) {lit.,[11b] $[a]_D^{20}$ +14.95 (H_2O)}; δ_H (400 MHz; $CDCl_3$) 8.46 (3H, br s, NH_3^+), 7.31–7.25 (5H, m, ArH), 3.47 (1H, br s, NCH), 3.24 (1H, PhC*H*H), 2.94 (1H, br s, PhCH*H*), 1.70–1.30 (6H, m, 3 × CH_2), 0.85 (3H, br s, Me).

General method for the preparation of Cbz-protected β-amino methyl esters

Ozone was passed through a solution of an *N*-Cbz-protected homoallylamine **3** (1.64 mmol) in CH_2Cl_2 (13 mL) and methanolic sodium hydroxide (3.3 mL; 2.5 M) at −78 °C. After 2 h (complete consumption of starting material) a yellow precipitate had formed. Diethyl ether (5 mL) and water (5 mL) were added and allowed to warm to room temperature. The mixture was exhaustively extracted with diethyl ether (5 × 5 mL). The extracts were combined, dried (Na_2SO_4), filtered and evaporated. Column chromatography on silica gel eluting with diethyl ether–light petroleum (1 : 1) gave the ester.

Methyl (*R*)-(−)-3-benzyloxycarbonylamino-4-methylpentanoate 4a. Obtained from the oxidative cleavage of the Cbz-protected homoallylamine **3c**, as a *colourless oil* (36%) (Found: M^+, 279.1471. $C_{15}H_{21}NO_4$ requires *M*, 279.1471); $[a]_D^{24}$ −24.6 (*c* 1.4, $CHCl_3$); ν_{max} (film)/cm^{-1} 3346, 2955, 1692, 1661, 1549, 1474, 1250; δ_H (300 MHz; $CDCl_3$) 7.35 (5H, m, ArH), 5.15 (1H, br s, NH), 5.10 (2H, s, CH_2O), 3.84 (1H, m, NCH), 3.65 (3H, s, OMe), 2.53 (2H, d, *J* 3.21, CH_2CO), 1.84 (1H, m, C*H*Me_2), 0.92 (6H, d, *J* 6.8, Me_2C); δ_C (100 MHz; $CDCl_3$) 172.1, 156.0, 136.6, 128.5, 128.0 (2 C), 66.6, 53.6, 51.7, 36.9, 31.7, 19.3, 18.5; *m*/*z* (EI) 279 (M^+, 2%), 236 (14), 206 (1), 192 (20), 162 (1), 144 (2), 128 (1), 108 (7), 91 (100), 79 (3), 65 (5), 55 (2).

Methyl (*R*)-(−)-3-benzyloxycarbonylamino-4-ethylhexanoate 4b. Obtained from the oxidative cleavage of the Cbz-protected homoallylamine **3d**, as a *colourless oil* (52%) (Found: M^+, 307.1783. $C_{17}H_{25}NO_4$ requires *M*, 307.1783); $[a]_D^{25}$ −18 (*c* 0.4, $CHCl_3$); ν_{max} (film)/cm^{-1} 3352, 2964, 2877, 1699, 1662, 1236; δ_H (300 MHz; $CDCl_3$) 7.34 (5H, m, ArH), 5.11 (1H, br s, NH), 5.09 (2H, s, CH_2O), 4.11 (1H, m, NCH), 3.63 (3H, s, OMe), 2.51 (2H, m, CH_2CO), 1.38–1.28 [5H, m, (CH_2Me)$_2$C, CH], 0.89 [6H, t, *J* 7.1, (*Me*CH_2)C]; δ_C (75 MHz; $CDCl_3$) 172.2, 156.0, 136.7, 128.4, 128.0 (2 C), 66.6, 51.6, 50.0, 44.2, 37.0, 22.0, 21.6, 11.4, 10.9; *m*/*z* (EI) 307 (M^+, 1%), 236 (22), 206 (4), 192 (34), 172 (1), 163 (6), 127 (2), 107 (6), 91 (100), 65 (11), 55 (7).

Methyl (*R*)-(−)-3-benzyloxycarbonylamino-3-cyclohexylpropanoate 4c. Obtained from the oxidative cleavage of the Cbz-protected homoallylamine (*R*)-**3k**, as a *colourless solid* (39%); mp 71–72 °C (Found: C 68.0; H, 8.0; N, 4.4%; M^+, 319.1783. $C_{18}H_{25}NO_4$ requires C, 67.7; H, 7.9; N, 4.4%) *M*, 319.1783); $[a]_D^{22}$ −14 (*c* 0.7, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3313, 2923, 2852, 2093, 1729, 1691, 1646, 1544; δ_H (300 MHz; $CDCl_3$) 7.35 (5H, m,

ArH), 5.10 (1H, br s, NH), 5.09 (2H, s, CH_2O), 3.80 (1H, m, NCH), 3.65 (3H, s, OMe), 2.54 (2H, d, *J* 5.3, CH_2CO), 1.66–1.80 (5H, m, cyclohexyl), 1.47 (1H, m, CH), 1.26–0.87 (5H, m, cyclohexyl); δ_C (75 MHz; $CDCl_3$) 172.3, 156.0, 136.7, 128.4, 128.0 (2 C), 66.6, 52.9, 51.6, 41.3, 36.6, 29.7, 29.0, 26.2, 16.0, 25.9; *m*/*z* (EI) 319 (M^+, 3%), 246 (1), 236 (17), 202 (2), 162 (2), 136 (1), 108 (11), 91 (100), 79 (6), 65 (7), 55 (12).

Methyl (*R*)-(+)-3-benzyloxycarbonylamino-3-phenylpropanoate 4d. Obtained from the oxidative cleavage of the Cbz-protected homoallylamine **3p**, as a *colourless solid* (41%); mp 65–66 °C (from *n*-hexane) (lit.,[22] 65 °C) (Found: C, 68.9; H, 6.2; N, 4.4%; M^+, 313.1314. Calc. for $C_{18}H_{19}NO_4$: C, 69.0; H, 6.1; N, 4.5%; *M*, 313.1314); $[\alpha]_D^{22}$ +17.1 (*c* 1, $CHCl_3$) {lit.,[22] for (*S*)-enantiomer $[\alpha]_D^{21}$ −15.8 (*c* 0.55, $CHCl_3$)}; ν_{max} (film)/cm^{-1} 3332, 3033, 2952, 1733, 1701, 1533, 1242; δ_H (300 MHz; $CDCl_3$) 7.30 (10H, m, ArH), 5.79 (1H, br s, NH), 5.18 (1H, m, NCH), 5.10 (2H, s, CH_2O), 3.60 (3H, s OMe), 2.86 (2H, m, CH_2CO); δ_C (75 MHz; $CDCl_3$) 171.2, 155.6, 140.8, 136.4, 128.7, 128.5, 128.1, 127.7, 126.2, 77.2, 66.9, 57.9, 40.5; *m*/*z* (EI) 313 (M^+, 2%), 240 (3), 222 (4), 196 (8), 178 (29), 164 (16), 146 (4), 121 (6), 107 (18), 104 (32), 91 (100), 77 (9), 65 (8), 51 (5).

Methyl (*S*)-(−)-3-benzyloxycarbonylamino-3-(4-methoxyphenyl)propanoate 4e. Obtained from the oxidative cleavage of the Cbz-protected homoallylamine **3q**, as a *colourless solid* (33%); mp 76–77 °C (from *n*-hexane) (Found: C, 66.5; H, 6.0; N, 4.1%; M^+, 343.1420. $C_{19}H_{21}NO_5$ requires C, 66.5; H, 6.2; N, 4.1%; *M*, 343.1420); $[\alpha]_D^{22}$ −26 (*c* 0.5, $CHCl_3$); ν_{max} (film)/cm^{-1} 3340, 1740, 1726, 1517, 1255; δ_H (300 MHz; $CDCl_3$) 7.33 (5H, m, ArH), 7.22 (2H, d, *J* 8.6, ArH), 6.85 (2H, d, *J* 8.6, ArH), 5.73 (1H, br s, NH), 5.10 (2H, s, CH_2O), 5.09 (1H, m, NCH), 3.78 (3H, s, OMe), 3.60 (3H, s, OMe), 2.83 (2H, m, CH_2CO); δ_C (100 MHz; $CDCl_3$) 171.3, 159.0, 155.5, 136.4, 132.9, 128.5, 128.1, 128.0, 127.6, 114.1, 66.8, 55.2, 51.8, 51.2, 40.6; *m*/*z* (EI) 343 (M^+, 11%), 298 (1), 283 (11), 252 (10), 226 (37), 208 (91), 193 (42), 176 (32), 162 (63), 151 (33), 134 (76), 119 (32), 107 (44), 91 (100), 77 (46), 65 (42), 51 (31).

General method for the preparation of Cbz-protected 1,3-amino alcohols

An *N*-Cbz-protected homoallylamine **3** (0.87 mmol) was dissolved in dichloromethane (5 mL) and cooled to −78 °C. Ozone was passed for 3 h and flushed with nitrogen. The reaction mixture was warmed to 0 °C and ethanol was added to homogenise the mixture. Sodium borohydride (1.91 mmol) in aq. ethanol (50%; 8 mL) was added dropwise to the reaction mixture, which was stirred for 12 h. The reaction mixture was poured into ice–water containing a few drops of HCl and extracted with diethyl ether (4 × 5 mL). The organic extracts were combined, dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash chromatography on silica gel, eluting with ethyl acetate–light petroleum (1 : 1).

(*R*)-(−)-3-Benzyloxycarbonylamino-4-ethylhexan-1-ol 5a. Obtained from the oxidative cleavage (with reductive work-up) of the protected homoallylamine **3d**, as a *colourless solid* (56%); mp 39–40 °C (Found: C, 68.8; H, 9.3; N, 4.9%; M^+, 279.1836. $C_{16}H_{25}NO_3$ requires C, 68.8; H, 9.0; N, 5.0%); *M*, 279.1834); $[\alpha]_D^{17}$ −10 (*c* 0.2, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3415, 3333, 2962, 2933, 2976, 1702, 1537, 1248, 1058; δ_H (300 MHz; $CDCl_3$) 7.34 (5H, m, ArH), 5.11 (1H, d, *J* 12.1, C*H*HO), 5.05 (1H, d, *J* 12.1, CH*H*O), 4.79 (1H, d, *J* 9.3, NH), 3.96 (1H, m, NCH), 3.65 (2H, m, C*H*$_2$OH), 3.10 (1H, br s, OH), 1.76 (1H, m, CH), 1.45–1.17 (6H, m, 3 × CH_2), 0.91 (6H, t, *J* 8.7, 2 × CH_3); δ_C (75 MHz; $CDCl_3$) 157.5, 136.4, 128.5, 128.2, 128.0, 66.9, 59.1, 49.1, 45.5, 35.6, 22.6, 22.1, 14.2, 11.9, 11.6; *m*/*z* (EI) 279 (0.3%), 262 (10), 236 (20), 222 (1), 208 (70), 190 (22), 164 (80), 146 (10), 108 (23), 91 (100), 77 (24), 65 (41), 55 (35).

(*S*)-(+)-3-Benzyloxycarbonylamino-3-cyclohexylpropan-1-ol 5b. Obtained from the oxidative cleavage (with reductive work-up) of the protected homoallylamine (*S*)-**3k**, as a *colourless solid* (50%); mp 90–91 °C (Found: C, 69.8; H, 8.63; N, 4.6. $C_{17}H_{25}NO_3$ requires C, 70.1; H, 8.6; N, 4.8%. Found: MH^+, 292.1915. $C_{17}H_{26}NO_3$ requires *m*/*z*, 292.1912); $[\alpha]_D^{17}$ +8 (*c* 0.5, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3382, 3326, 2909, 2852, 1687, 1664, 1535, 1621, 1049; δ_H (300 MHz; $CDCl_3$) 7.34 (5H, m, ArH), 5.13 (1H, d, *J* 12.1, CH*H*O), 5.06 (1H, d, *J* 12.1, CH*H*O), 4.66 (1H, br d, *J* 9, NH), 3.64 (3H, m, C*H*$_2$OH, NCH), 2.97 (1H, br s, OH), 1.87–1.66 (6H, m, 3 × CH_2), 1.40–0.94 (7H, m, 3 × CH_2, CH); δ_C (75 MHz; $CDCl_3$) 157.5, 136.4, 128.6, 128.2, 128.1, 67.0, 59.1, 52.4, 52.3, 35.5, 29.7, 28.7, 26.3, 26.2; *m*/*z* (CI) 292 (MH^+, 3%), 208 (1), 170 (8), 124 (10), 112 (28), 97 (67), 91 (13), 84 (34), 70 (100), 58 (7), 52 (81).

Radical additions

General method for the alkyl radical addition to the benzaldehyde oxime ethers. An oxime ether (0.50 g, 1.98 mmol), ethanol (0.29 mL, 4.94 mmol) and alkyl iodide (4.94 mmol) were dissolved in dichloromethane (5 mL). The mixture was cooled to −78 °C under nitrogen. Boron trifluoride–diethyl ether (1.25 mL, 9.88 mmol) was added and the mixture stirred for 15 min. Triethylborane (4.9 mL, 4.94 mmol) was added dropwise over a period of 30 min. The mixture was stirred at −78 °C for 5 h, and allowed to warm to room temperature overnight. Saturated aq. ammonium chloride (10 mL) was added, the layers separated and the aqueous layer extracted with diethyl ether (2 × 10 mL). The combined extracts were dried ($MgSO_4$), filtered and evaporated. The residue was purified by column chromatography on silica gel eluting with diethyl ether–light petroleum (1 : 20) to give the following compounds.

(S)-2-Methyl-1-phenyl-N-[(S)-1-phenylbutoxy]propylamine ***6a***.—Obtained from the addition of 2-iodopropane to the benzaldehyde oxime ether (*S*)-**1h**, as a *colourless oil* (11%, 85% de) (Found: MH^+, 298.2168. $C_{20}H_{28}NO$ requires *m*/*z*, 298.2171); ν_{max} (neat)/cm^{-1} 3430, 2958, 2933, 2851, 1454; δ_H (400 MHz; $CDCl_3$) 7.38–7.23 (10H, m, ArH), 5.51 (1H, br s, NH), 4.59 (1H, dd, *J* 6.9, 6.9, OCH), 3.79 (1H, d, *J* 6.8, NCH), 2.16 (1H, m, C*H*Me$_2$), 1.82 (1H, m, C*H*H), 1.57 (1H, m, CH*H*), 1.40–1.29 (2H, m, CH_2), 0.98 (3H, t, *J* 6.7, Me), 0.95 (3H, t, *J* 8.6, Me), 0.80 (3H, d, *J* 6.8, Me); δ_C (75 MHz; $CDCl_3$) 143.0, 140.5, 128.3, 128.1, 127.9, 127.3, 127.1, 126.8, 84.9, 71.1, 38.4, 30.5, 20.2, 19.2, 18.5, 14.1; *m*/*z* (CI) 298 (MH^+, 12%), 166 (10), 150 (100), 148 (29), 134 (11), 106 (30).

(S)-1-Phenyl-N-[(S)-1-phenylbutoxy]propylamine ***6b***.—Obtained from the addition of iodoethane to the benzaldehyde oxime ether (*S*)-**1h**, as a *colourless oil* (11%, de 51%) (Found: MH^+, 284.2019. $C_{19}H_{26}NO$ requires *m*/*z*, 284.2014); ν_{max} (neat)/cm^{-1} 3423, 2960, 2933, 2873, 1492, 1454; δ_H (400 MHz; $CDCl_3$) 7.9 (10H, m, ArH), 5.35 (1H, br s, NH), 4.65 (1H, dd, *J* 7.3, 7.3, OCH), 3.95 (1H, dd, *J* 5.0, 8.8, NCH), 2.05 (1H, m, C*H*H), 1.90 (1H, m, CH*H*), 1.76–1.00 (4H, m, 2 × CH_2), 0.98 (3H, t, *J* 7.3, Me), 0.88 (3H, t, *J* 7.4, Me); δ_C (75 MHz; $CDCl_3$) 143.1, 141.3, 128.30, 128.29, 127.9, 127.4, 127.3, 126.7, 85.4, 67.4, 38.6, 30.5, 26.7, 18.9, 14.2, 10.6; *m*/*z* (CI) 284 (MH^+, 32%), 166 (7), 150 (44), 136 (100), 134 (54), 106 (30), 91 (7).

Crystal data

Common to both determinations: Rigaku AFC7S diffractometer with Cu radiation. $T = 296$ K, all non-H atoms refined anisotropically. CCDC reference number 207/360. See http://www.rsc.org/suppdata/p1/1999/3443 for crystallographic files in .cif format.

(±)-*O*-(1-Phenylbutyl)-2-naphthaldehyde oxime (±)-1j. $C_{21}H_{21}NO$, $M = 303.4$, monoclinic, $P2_1/c$, $a = 18.514(3)$, $b = 7.606(2)$, $c = 12.166(1)$ Å, $\beta = 105.58(1)°$, $V = 1650$ Å^3, $\rho_{calc} = 1.22$ g cm^{-3}, $Z = 4$, μ(Cu-Kα) = 0.58 mm^{-1}; 2767 reflections

measured, 2676 independent (R_{int} 0.06), 1942 observed with $I > 2\sigma(I)$, to yield $R = 0.047$.

(*S*)-*O*-(1-Phenylbutyl)thiazol-2-ylcarbaldehyde oxime (*S*)-1m. $C_{14}H_{16}N_2OS$, $M = 260.4$, monoclinic, $P2_1$, $a = 9.087(3)$, $b = 7.841(4)$, $c = 10.648(3)$ Å, $\beta = 111.95(2)°$, $V = 704$ Å^3, $\rho_{calc} = 1.23$ g cm^{-3}, $Z = 2$, μ(Cu-Kα) = 1.96 mm^{-1}; 1226 reflections measured, 1148 independent (R_{int} 0.15), 839 observed with $I > 2\sigma(I)$, to yield $R = 0.039$; the Flack parameter, 0.05(7), did not allow an unambiguous determination of absolute stereochemistry to be made. The assignment of the (*S*)-configuration is based on the chemistry involved.

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