Chiral oxime ethers in asymmetric synthesis. Part 5.[1] Asymmetric synthesis of 2-substituted 5- to 8-membered nitrogen heterocycles by oxime addition–ring-closing metathesis

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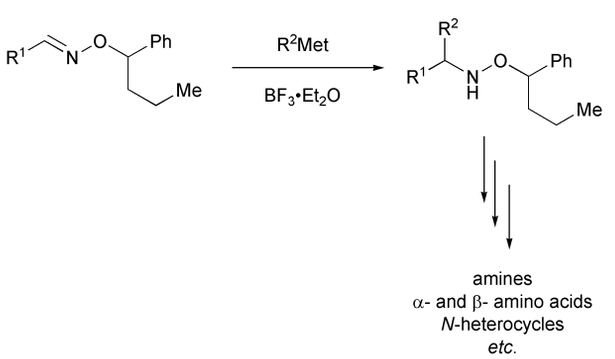
Addition of organometallic reagents to chiral oxime ethers **1** derived from an unsaturated aldehyde, or addition of an alkene containing organometallic to chiral aldoxime ethers **2** results in highly stereoselective formation of the hydroxylamines **6**. *N*-Allylation gives the dienes **7** which undergo ring-closing metathesis (RCM) reaction to give the 5-, 6-, and 7-membered nitrogen heterocycles **8**. Likewise, the benzyl carbamates **9**, also prepared by stereoselective addition to oxime ethers, were converted into dienes **10**, which underwent RCM to give the 5- to 8-membered azacycles **11**. The oxime addition–RCM protocol is thus a versatile method for the asymmetric synthesis of nitrogen heterocycles, further exemplified by the conversion of the unsaturated heterocycles into chiral piperidines, including the alkaloid (−)-coniine.

Introduction

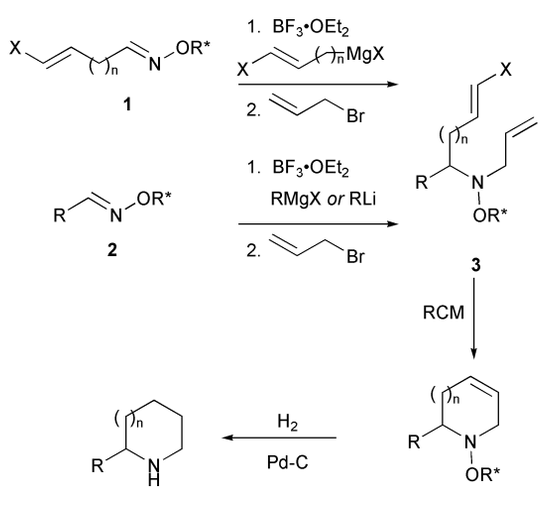
The development of methods for the asymmetric synthesis of pyrrolidines, piperidines and ring-fused derivatives such as indolizidines remains an area of current interest due to the presence of such saturated heterocyclic rings in a large range of biologically important compounds.[2–5] Almost invariably, these bioactive compounds, and in particular the naturally occurring derivatives, contain an asymmetric centre adjacent to the ring nitrogen atom. We have recently shown that such stereocentres α to nitrogen are readily established by the highly diastereoselective addition of organolithium or Grignard reagents to the C=N bond of chiral oxime ethers derived from (*R*)- and (*S*)-*O*-(1-phenylbutyl)hydroxylamine (ROPHy/SOPHy) (Scheme 1).



Scheme 1

The resulting hydroxylamines are versatile intermediates for the synthesis of chiral amines,[1] including 1-(2-thiazolyl)ethylamine components of thiazole-containing natural products,[6,7] α-amino acids,[8] β-amino acids,[1] and piperidine alkaloids.[9]

In continuation of our interest in the asymmetric synthesis of saturated nitrogen heterocycles,[9] we decided to investigate the combination of the highly diastereoselective addition reactions of ROPHy/SOPHy aldoximes with the ring-closing metathesis (RCM) reaction as a new route to this class of heterocycle. The RCM reaction is an extremely powerful synthetic method and, with the development of practical and reliable catalysts by Grubbs and others,[10,11] has been widely used in synthesis in the recent past.[12,13] The reaction tolerates a wide range of functional groups, and has been used for the synthesis of nitrogen heterocycles of varying ring size.[14–24] The proposed combination of oxime addition–RCM is shown in outline in Scheme 2, and we now describe the results of our work in this area in detail.[25]



Scheme 2

Results and discussion

As outlined in Scheme 2, the substrates for the RCM reaction are the chiral dienes **3**. These are accessible either by the addition of an organometallic reagent to an aldoxime ether **1** derived from an unsaturated aldehyde, or by addition of an alkene containing organometallic reagent to an alkyl or aryl aldoxime ether **2**, followed in both cases by *N*-allylation of the resulting hydroxylamine (Scheme 2). Both approaches were successful. Addition of organolithium reagents to the chiral oxime ethers **1a** and **1b** derived by reaction of cinnamaldehyde with ROPHy or SOPHy respectively,[8] and **1c** derived from 4-pentenal gave the corresponding hydroxylamines **6a**–**6e** in

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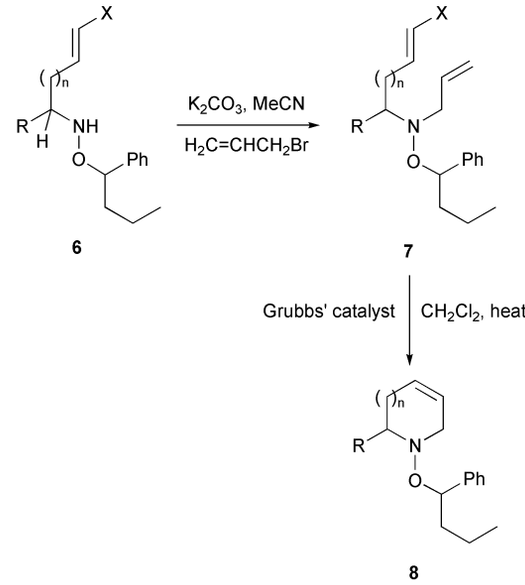
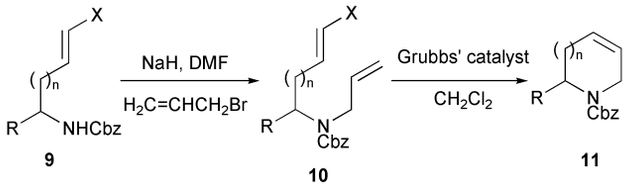
Table 1



	(*E*)-Oxime[a]	Organometallic addition	Hydroxylamine	Yield/% (de/%)[b]	R	X	*n*	Diene	Yield (%)	Heterocycle (configuration)	Yield (%)
1a	(*R*)-PhCH=CHCH=NOR*	MeLi[c]	**6a**	[d](>95)	Me	Ph	0	**7a**	72[d]	**8a** (*R*)	87
1a	(*R*)-PhCH=CHCH=NOR*	*n*-BuLi[c]	**6b**	[d](>95)	*n*-Bu	Ph	0	**7b**	66[d]	**8b** (*R*)	78
1b	(*S*)-PhCH=CHCH=NOR*	*i*-BuLi[e]	**6c**	95 (88)	*i*-Bu	Ph	0	**7c**	83	**8c** (*S*)	74
1a	(*R*)-PhCH=CHCH=NOR*	PhLi[c]	**6d**	62 (>95)	Ph	Ph	0	**7d**	52	**8d** (*S*)	51
1c	(*S*)-H_2C=$CHCH_2CH_2CH$=NOR*	PhLi	**6e**	[d](>95)	Ph	H	2	**7e**	74[d]	**8e** (*R*)	9
2a	(*S*)-$BnO(CH_2)_4CH$=NOR*	H_2C=$CHMgBr$	**6f**	[d](82)	$BnO(CH_2)_4$	H	0	**7f**	34[d]	**8f** (*R*)	35
2b	(*S*)-$(MeO)_2CH(CH_2)_3CH$=NOR*	H_2C=$CHMgBr$	**6g**	[d](79)	$(MeO)_2CH(CH_2)_3$	H	0	**7g**	28[d]	**8g** (*R*)	23
		H_2C=$CHLi$	**6g**	48 (>90)							
2c	(*S*)-*n*-PrCH=NOR*	H_2C=$CHCH_2MgBr$	**6h**	[d](87)	*n*-Pr	H	1	**7h**	39[d]	**8h** (*R*)	90
2e	(*R*)-PhCH=NOR*	H_2C=$CHCH_2MgBr$[f]	**6i**	[d](91)	Ph	H	1	**7i**	57[d]	**8i** (*R*)	53

[a] R* = 1-phenylbutyl; configuration as indicated [b] In general, the diastereomeric excess (de) of the organometallic addition is determined by integration of the 1H NMR signals of the C*H*N proton (indicated in **6**) for the two diastereomers. [c] This addition reaction is reported in ref. 8. [d] Yield over 2 steps. [e] The addition to the (*R*)-enantiomer of the oxime reported in ref. 8. [f] This addition reaction reported in ref. 1.

Table 2



Carbamate	Configuration (ee/%)[a]	R	X	*n*	*N*-allyl carbamate	Yield (%)	Heterocycle (configuration)	Yield (%)
9a[b]	*S* (89[c])	Me	Ph	0	**10a**	74	**11a** (*S*)	84
9b[d]	*R* (93[e])	*n*-Bu	Ph	0	**10b**	88	**11b** (*R*)	77
9c[b]	*R* (>95[e])	Ph	Ph	0	**10c**	63[f]	**11c** (*R*)	93
9d[g]	*R* (90)	*n*-Pr	H	1	**10d**	90	**11d** (*R*)	88
9e[h]	*S* (98)	4-MeO–C_6H_4	H	1	**10e**	97	**11e** (*S*)	91
9f[g]	*R* (82)	$BnO(CH_2)_3$	H	1	**10f**	83	**11f** (*R*)	98
9g[h]	*R* (90)	Ph	H	2	**10g**	89	**11g** (*R*)	65
9h[i]	*S* (92)	*n*-Pr	H	3	**10h**	81	**11h** (*S*)	19

[a] Enantiomeric excess (ee) was determined by HPLC on a chiral phase (ChiralCel OD using hexane–propan-2-ol (9:1) as eluant) by comparison with the racemate. [b] The preparation of the enantiomer is described in ref. 8. [c] Enantiomeric excess (ee) of the *N*-allyl derivative **10a** not **9a**. [d] Prepared as described in ref. 8. [e] Refers to the diastereomeric excess (de) of the immediate precursor to **9b**. [f] Allylation using allyl bromide–base caused double bond migration; prepared using allyl methyl carbonate–Pd(0); see text. [g] Prepared by addition of allylmagnesium bromide to the oxime ether, followed by cleavage of the N–O bond, and reaction with benzyl chloroformate; stereoselectivity refers to the de before cleavage of the N–O bond. [h] Prepared as described in ref. 1. [i] The preparation of the enantiomer is described in ref. 9.

excellent diastereomeric excess (de) (Table 1). Reaction with allyl bromide gave the dienes **7a**–**7e** in 32–74% yield over the two steps. In a similar manner, addition of vinyl or allyl organometallic reagents to oxime ethers **2a**–**2c**, **2d** and **2e** gave hydroxylamines **6f**–**6i** (79–91% de), allylation of which gave the dienes **7g**–**7i** (28–71% over two steps) (Table 1). The RCM reaction was carried out by heating the dienes **7** in dichloromethane in the presence of benzylidene bis(tricyclohexylphosphine)-dichlororuthenium (Grubbs' catalyst) and gave the expected heterocycles **8** in varying yield (Table 1). The 5-membered rings **8a**–**8d** were formed in good yield, although the dihydropyrroles **8f** and **8g** containing an oxygenated substituent were isolated in significantly poorer yield. The 6-membered rings **8h**, **8i** were also readily formed, but the yield of the 7-membered ring **8e** was extremely poor.

Although the above results indicate that the basic and nucleophilic hydroxylamine nitrogen atoms in **7** are tolerated in the RCM reaction, we also investigated a set of substrates **10** in which the nitrogen is rendered non-basic by protection as its benzyloxycarbonyl (Cbz) derivative. Thus a series of carbamates **9**, prepared as described previously[1,8] or as indicated in Table 2, was converted into the corresponding *N*-allyl derivatives **10** by reaction with allyl bromide in the presence of sodium hydride. In most cases this proved highly satisfactory and the dienes **10** were obtained in good yield (Table 2). In the case of **10c**, however, double bond migration occurred to give *N*-allyl-*N*-benzyloxycarbonyl-1,3-diphenyl-1-propenylamine in high yield, and therefore the allyl group was introduced using the palladium(0) catalysed reaction of allyl methyl carbonate.[26] The RCM reaction proceeded smoothly and gave dihydropyrrole **11a**–**11c** and tetrahydropyridines **11d**–**11f** in excellent yield (Table 2), although the dihydropyrrole **11a**–**11c** appeared somewhat unstable and could not be obtained analytically pure. The yield of the 7-membered ring **11g** was somewhat lower, whilst the 8-membered ring **11h** was formed in poor yield.

The versatility of the oxime addition–RCM sequence was further demonstrated by the subsequent reactions of the product heterocycles **8** and **11**. Thus hydrogenation of the dihydropyrrole **8c** and the tetrahydropyridine **8h** over palladium-on-charcoal in methanol resulted in simple alkene reduction to give the *N*-alkoxypyrrolidine **12** and -piperidine **13**. In principle, it should be possible to effect both the RCM reaction and the subsequent reduction of the double bond in the same reaction vessel using the same ruthenium catalyst as recently reported by Grubbs and co-workers,[27] although this possibility was not investigated. Hydrogenation of the tetrahydropyridine **8i** in methanol–acetic acid resulted in hydrogenation of the double bond and hydrogenolysis of the N–O bond to give (*R*)-2-phenylpiperidine isolated initially as its *N*-*tert*-butoxycarbonyl derivative **14**. Removal of the Boc-group gave the known (*R*)-heterocycle **15**[28] in good yield confirming the stereochemistry of the original addition reaction. In a similar manner, catalytic hydrogenation of the tetrahydropyridine **11d** resulted in double bond reduction and removal of the Cbz-group to give (*R*)-(−)-coniine isolated as its hydrochloride salt **16**.[29–31] Likewise the tetrahydropyridine **11e** and tetrahydroazepine **11g** were converted into the (*S*)-piperidine **17** and known (*R*)-2-phenylazepane **18**[28] respectively (Scheme 3).

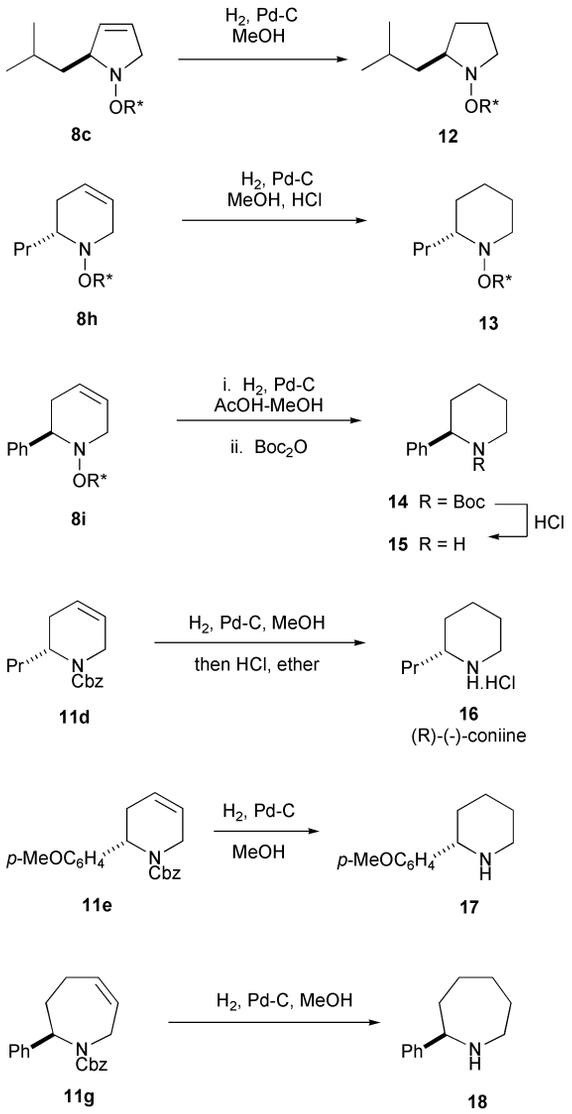
Experimental

General

Commercially available reagents and solvents were used throughout without further purification other than those detailed below. Light petroleum refers to the fraction that boils between 40 °C and 60 °C and was distilled from calcium chloride through a 36 cm Vigreux column before use. Diethyl ether (ether) and THF were distilled from sodium benzophenone ketyl under nitrogen prior to use. Dichloromethane was purified and dried by distillation from phosphorus pentoxide under nitrogen. Pyridine was distilled from calcium hydride whilst under nitrogen prior to use.

Analytical thin layer chromatography was carried out using aluminium or glass backed plates coated with Merck Kieselgel 60 GF_{254}. Developed plates were visualised under ultraviolet light (254 nm) and/or potassium permanganate or ninhydrin dip. Flash chromatography was carried out using Merck Kieselgel 60 H silica. Fully characterised compounds were chromatographically homogeneous.

IR spectra were recorded on a Nicolet Magna 550 spectrometer with internal calibration. Spectra were recorded as thin films on sodium chloride plates, in solution or potassium bromide discs. NMR spectra were recorded on Bruker AM 300, or Advance DRX 400 spectrometers at the frequencies stated. Chemical shifts are recorded in ppm and *J* values in Hz. Multiplets less than 0.2 ppm in width were recorded from the centre, those greater were reported as a range. Chemical shift



Scheme 3 (R* = 1-phenylbutyl)

values are referenced against chloroform at 7.27 ppm for $CDCl_3$, methanol at 3.35 ppm for CD_3OD, and DMSO at 2.50 ppm for d_6-DMSO, and are accurate to ±0.01 ppm (δ_H) and ±0.10 ppm (δ_C). High resolution mass spectra (CI and EI) were either obtained on a Kratos Profile HV3 spectrometer, on a Micromass GCT-TOF instrument, or at the EPSRC National Mass Spectrometry Service at the University of Wales, Swansea. Gas chromatography–mass spectrometry was carried out on a ThermoQuest Finnigan Trace 2000 series GCMS, with a 15 m Crossbond® 5% diphenyl–95% dimethylpolysiloxane column with a 0.25 mm internal diameter and CI/EI detection, which was used to obtain some of the low resolution spectra. Specific rotations were measured on an AA-1000 polarimeter.

General method for the preparation of *O*-(1-phenylbutyl) oximes 1 and 2

A suspension of *N*-(1-phenylbutoxy)phthalimide (3.0 g, 10.17 mmol) in ethanol (50 mL) was heated until the phthalimide dissolved. Hydrazine hydrate (0.6 mL, 12.4 mmol) was added at this elevated temperature and the reaction mixture was heated under reflux for a further 1 h. The solution was then allowed to cool to room temperature. The carbonyl compound (12 to 30 mmol) was added at room temperature and the reaction mixture stirred overnight. The solvent was evaporated under reduced pressure and the residue purified by column chromatography on silica gel eluting with ether:light petroleum (1:20).

(*E*)-(*R*)-*O*-(1-Phenylbutyl)cinnamaldehyde oxime 1a

Prepared as described previously.[8]

(*E*)-(*S*)-*O*-(1-Phenylbutyl)cinnamaldehyde oxime 1b

Prepared as described for the (*R*)-enantiomer;[8] mp 67 °C (lit.,[8] (*R*)-isomer mp 65–67 °C (light petroleum)); $[\alpha]_D^{25}$ −45.9 (*c* 1.12, CH_2Cl_2) (lit.,[8] (*R*)-isomer $[\alpha]_D^{20}$ +48.1 (*c* 1.0, CH_2Cl_2)).

(*S*)-*O*-(1-Phenylbutyl)pent-4-enaldehyde oxime 1c

Prepared as described previously.[1]

(*S*)-*O*-(1-Phenylbutyl)-5-benzyloxypentaldehyde oxime 2a

Prepared from 5-*O*-benzyloxypentanal[32] as a colourless oil (72%) exactly as described for the (*R*)-enantiomer;[1] $[\alpha]_D^{27}$ +6.2 (*c* 1.77, $CHCl_3$).

(*S*)-*O*-(1-Phenylbutyl)-5,5-dimethoxypentanaldehyde oxime 2b

Prepared from 5,5-dimethoxypentanal[33] as a colourless oil (*E* 51% + mixture *Z*/*E* 45%); (Found: MH^+, 294.2063. $C_{17}H_{27}NO_3$ + H requires 294.2069); $[\alpha]_D^{23}$ +12.1 (*c* 0.99, $CHCl_3$); ν_{max}(film)/cm^{-1} 3022, 2950, 2935, 2863, 2827, 1450, 1387, 1358, 1189, 1127, 1061, 922, 758, 697; δ_H (300 MHz; $CDCl_3$) 7.43 (1 H, t, *J* 6.2, N=CH), 7.29 (5 H, m, ArH), 5.02 (1 H, t, *J* 6.9, OCH), 4.33 (1 H, t, *J* 5.4, C*H*(OMe)$_2$), 3.29 (3 H, s, CH(O*Me*)(OMe)), 3.28 (3 H, s, CH(OMe)(O*Me*)), 2.17 (2 H, q, *J* 6.2, C*H*$_2$CH=N), 1.90 (1 H, m, OCHC*H*H), 1.76–1.24 (7 H, m, OCHCH*HCH*$_2$, C*H*$_2$C*H*$_2$), 0.93 (3 H, t, *J* 7.5, Me); δ_C (75 MHz; $CDCl_3$) 150.6 (N=CH), 142.7 (C), 128.2 (CH), 127.2 (CH), 126.7 (CH), 104.1 (CH), 84.5 (CH), 52.72 (OMe), 52.69 (OMe), 38.4 (CH_2), 31.7 (CH_2), 29.3 (CH_2), 21.8 (CH_2), 18.9 (CH_2), 14.0 (Me); *m*/*z* (CI) 294 (MH^+, 12%), 162 (76), 149 (32), 133 (82), 130 (100), 112 (59).

(*S*)-*O*-(1-Phenylbutyl)butyraldehyde oxime 2c

Prepared as described previously.[9]

(*R*)-*O*-(1-Phenylbutyl)butyraldehyde oxime 2d

Prepared as described previously.[1]

(*R*)-*O*-(1-Phenylbutyl)benzaldehyde oxime 2e

Prepared as described previously.[1]

(*S*)-*O*-(1-Phenylbutyl)-4-anisaldehyde oxime 2g

Prepared as described previously.[34]

(*E*)-(*S*)-*O*-(1-Phenylbutyl)-4-benzyloxybutanaldehyde oxime 2h

Prepared from 4-benzyloxybutanal as a colourless oil (76%); (Found: MH^+, 326.2117. $C_{21}H_{27}NO_2$ + H requires 326.2120); $[\alpha]_D^{26}$ +6.8 (*c* 1.46, $CHCl_3$); ν_{max}(film)/cm^{-1} 3083, 3058, 3027, 2955, 2930, 2868, 1455, 1358, 1204, 1107, 1030, 927, 733, 702; δ_H (300 MHz; $CDCl_3$) 7.46 (1 H, t, *J* 6.0, N=CH), 7.30 (10 H, m, ArH), 5.02 (1 H, t, *J* 6.8, OCH), 4.43 (2 H, s, C*H*$_2$Ph), 3.42 (2 H, t, *J* 6.4, OCH$_2$), 2.25 (2 H, m, CH$_2$), 1.91 (1 H, m, C*H*H), 1.73 (3 H, m, CH*H*, CH$_2$), 1.48–1.24 (2 H, m, CH$_2$), 0.92 (3 H, t, *J* 7.3, Me); on standing in $CDCl_3$, slow isomerisation to *Z*-isomer occurs; δ_C (100 MHz; $CDCl_3$) (mixture of *E* and *Z* diastereoisomers) 151.3 (N=CH), 150.5 (N=CH), 143.0 (C), 142.7 (C), 138.5 (C), 138.4 (C), 128.4 (CH), 128.3 (CH), 128.22 (CH), 128.16 (CH), 127.60 (CH), 127.57 (CH), 127.5 (CH), 127.3 (CH), 127.2 (CH), 126.7 (CH), 126.5 (CH), 84.9 (OCH), 84.5 (OCH), 73.0 (OCH$_2$), 72.9 (OCH$_2$), 69.7 (OCH$_2$), 69.3 (OCH$_2$), 38.5 (CH$_2$), 38.4 (CH$_2$), 26.9 (CH$_2$), 26.50 (CH$_2$), 26.46 (CH$_2$), 23.0 (CH$_2$), 18.90 (CH$_2$), 18.86 (CH$_2$), 14.03 (Me), 14.01 (Me); *m*/*z* (CI) 326 (MH^+, 8%), 193 (100), 166 (84), 150 (60), 106 (36), 70 (38).

General procedure for the addition of organometallic reagents to oxime ethers

The oxime ether (3.9 mmol) was dissolved in toluene (10 mL) under nitrogen and cooled to −78 °C. Boron trifluoride etherate (11.8 mmol) was added and the mixture stirred for 15 min. The organometallic reagent (11.8 mmol) was added dropwise over 15 min, and the mixture stirred until all starting material was consumed (typically 2–12 h). The reaction mixture was quenched at −78 °C with aqueous saturated ammonium chloride solution (10 mL), and allowed to warm to room temperature and was extracted with ether (3 × 15 mL), the extracts were combined, 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 **6**.

The organometallic addition to *O*-(1-phenylbutyl) oxime ethers and subsequent *N*-allylation to give dienes 7

The oxime ether (2.84 mmol) was dissolved in toluene (7.2 mL) under nitrogen and cooled to −78 °C. Boron trifluoride etherate (8.52 mmol) was added and stirred for 15 min. Organometallic reagent (8.52 mmol) 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 aqueous saturated ammonium chloride (10 mL), and allowed to warm to room temperature. The mixture was extracted with ether (3 × 15 mL), combined, dried (K_2CO_3), filtered and evaporated to give the hydroxylamine **6** used in the next step with no further purification.

The crude hydroxylamine **6** was dissolved in acetonitrile (14 mL) and potassium carbonate (0.785 g, 5.68 mmol) and allyl bromide (11.36 mmol) were added to the mixture. The reaction mixture was heated under reflux for 24 h. The mixture was cooled to room temperature and the solvent was removed *in vacuo*. Water (15 mL) and ether (15 mL) were added to the mixture and the layers separated. The aqueous layer was further extracted with ether (2 × 10 mL). The ethereal extracts were combined, dried (Na_2SO_4), and evaporated. The residue was purified by flash chromatography on silica gel using ether:light petroleum (1:40) as eluent giving the diene **7**.

(3*R*,1′*R*)-*N*-Allyl-*N*-(1-phenylbutoxy)-4-phenylbut-3-en-2-ylamine 7a

Obtained from the addition of methyllithium to the (*R*)-cinnamaldehyde oxime ether **1a** (>95% de) as described previously,[8] and subsequent *N*-allylation to give the title compound as a colourless oil (72% over 2 steps); (Found: MH^+, 336.2329. $C_{23}H_{29}NO$ + H requires 336.2327); $[\alpha]_D^{21}$ +61.8 (*c* 2.75, $CHCl_3$); ν_{max} (film)/cm^{-1} 3081, 3062, 3027, 2958, 2933, 2871, 1494, 1456, 1070, 970, 917, 748; δ_H (300 MHz; $CDCl_3$) 7.50–7.23 (10 H, m, ArH), 6.41 (1 H, d, *J* 16.0, PhCH=), 6.05 (1 H, dd, *J* 16.0, 7.5, C*H*=CHPh), 5.93 (1 H, m, C*H*=CH_2), 5.12 (2 H, m, =CH_2), 4.59 (1 H, t, *J* 6.6, OCH), 3.58 (1 H, m, NCH), 3.38 (2 H, m, CH_2CH=), 2.20–1.97 (1 H, m, C*H*H), 1.68 (1 H, m, CH*H*), 1.37–1.17 (2 H, m, CH_2), 1.24 (3 H, d, *J* 5.3, Me), 0.93 (3 H, t, *J* 7.2, Me); δ_C (100 MHz; $CDCl_3$) 142.7 (C), 137.3 (C), 134.7 (CH), 131.3 (CH), 130.8 (CH), 128.5 (CH), 128.0 (CH), 127.9 (CH), 127.4 (CH), 127.3 (CH), 126.4 (CH), 117.7 (CH_2), 85.4 (CH), 62.3 (CH), 57.8 (CH_2), 37.6 (CH_2), 19.2 (CH_2), 17.0 (Me), 14.2 (Me); *m*/*z* (FAB) 336 (MH^+, 13%), 203 (55), 186 (18), 131 (100).

(3*R*,1′*R*)-*N*-Allyl-*N*-(1-phenylbutoxy)-1-phenylhept-1-en-3-ylamine 7b

Obtained from the addition of *n*-butyllithium to the (*R*)-cinnamaldehyde oxime ether **1a** (>95% de) as described previously,[8] and subsequent *N*-allylation to give the title compound as a colourless oil (66% over 2 steps); (Found: M^+, 377.2711. $C_{26}H_{35}NO$ requires 377.2718); $[\alpha]_D^{22}$ +0.1 (*c* 1.3, $CHCl_3$); ν_{max} (film)/cm^{-1} 3029, 2956, 2927, 2861, 1500, 1456, 970; δ_H (300 MHz; $CDCl_3$) 7.31 (10 H, m, ArH), 6.36 (1 H, d, *J* 16.1, PhC*H*=), 6.13 (1 H, dd, *J* 16.1, 8.7, C*H*CN), 5.86 (1 H, m, C*H*=CH_2), 5.08 (2 H, m, =CH_2), 4.55 (1 H, dd, *J* 7.6, 6.5, OCH), 3.38 (3 H, m, NCH, NCH_2), 1.99 (1 H, m, C*H*H), 1.64 (1 H, m, CH*H*), 1.37–1.14 (8 H, m, 4 × CH_2), 0.92 (3 H, t, *J* 7.2, Me), 0.86 (3 H, t, *J* 6.7, Me); δ_C (100 MHz; $CDCl_3$) 142.8 (C), 137.3 (C), 134.9 (CH), 132.4 (CH), 129.5 (CH), 128.4 (CH), 127.9 (CH), 127.4 (CH), 127.2 (CH), 126.3 (CH), 117.4 (CH_2), 85.0 (CH), 67.6 (CH), 58.1 (CH_2), 37.6 (CH_2), 31.6 (CH_2), 28.7 (CH_2), 22.7 (CH_2), 19.2 (CH_2), 14.1 (Me), 14.0 (Me); one ArCH not observed; *m*/*z* (CI) 378 (MH^+, 1%), 245 (64), 188 (59), 173 (85), 133 (68), 105 (55), 90 (100), 77 (59).

(3*S*,1′*S*)-*N*-Allyl-*N*-(1-phenylbutoxy)-5-methyl-1-phenylhex-1-en-3-ylamine 7c

Obtained from the addition of isobutyllithium to the (*S*)-cinnamaldehyde oxime ether **1b** (95% yield, 88% de) as described previously for the (*R*)-enantiomer,[8] and subsequent *N*-allylation to give the title compound as a colourless oil (83%); (Found: MH^+, 378.2795. $C_{26}H_{35}NO$ + H requires 378.2797); $[\alpha]_D^{25}$ +11.1 (*c* 1.08, $CHCl_3$); ν_{max}(film)/cm^{-1} 3012, 2950, 2925, 2863, 1726, 1209, 927, 758, 666; δ_H (400 MHz; $CDCl_3$) 7.09 (10 H, m, ArH), 6.34 (1 H, d, *J* 16.0, PhC*H*=CH), 6.11 (1 H, dd, *J* 16.0, 8.6, PhCH=C*H*), 5.79 (1 H, m, C*H*=CH_2), 5.08 (2 H, m, =CH_2), 4.52 (1 H, t, *J* 6.1, OCH), 3.38 (3 H, m, NCH, NCH_2), 1.94 (1 H, m, NCHCH_2C*H*), 1.64–1.19 (6 H, m, NCHCH_2CH, OCHCH_2CH_2), 0.89 (3 H, t, *J* 7.3, Me), 0.84 (3 H, d, *J* 6.4, Me), 0.76 (3 H, d, *J* 6.4, Me); δ_C (100 MHz; $CDCl_3$) 142.7 (C), 137.3 (C), 135.0 (CH), 132.4 (CH), 129.4 (CH), 128.4 (CH), 128.1 (CH), 127.9 (CH), 127.3 (CH), 127.2 (CH), 126.3 (CH), 117.4 (=CH_2), 85.7 (CH), 85.1 (CH), 65.2 (CH), 58.0 (CH_2), 40.7 (CH_2), 37.6 (CH_2), 24.6 (CH), 23.4 (Me), 21.9 (Me), 19.1 (CH_2), 14.1 (Me); *m*/*z* (CI) 378 (MH^+, 70%), 230 (71), 173 (53), 166 (36), 150 (100).

(3*S*,1′*R*)-*N*-Allyl-*N*-(1-phenylbutoxy)-1,3-diphenylprop-1-en-3-ylamine 7d

Obtained from the addition of phenyllithium the (*R*)-cinnamaldehyde oxime ether **1a** (62% yield, >95% de) as described previously,[8] and subsequent *N*-allylation to give the title compound as a colourless oil (52%); $[\alpha]_D^{22}$ +28.6 (*c* 1.05, $CHCl_3$); ν_{max}(film)/cm^{-1} 3063, 3027, 2960, 2920, 2868, 1491, 1445, 963, 912, 733; δ_H (300 MHz; $CDCl_3$) 7.50–7.18 (15 H, m, ArH), 6.44 (1 H, d, *J* 15.7, PhC*H*=CH), 6.23–5.87 (2 H, m, C*H*=CH_2, C*H*=CHPh), 5.08 (2 H, m, =CH_2), 4.50 (1 H, dd, *J* 18.1, 5.5, NC*H*H), 4.35 (1 H, t, *J* 8.0, OCH), 3.42 (1 H, m, NCH), 3.20 (1 H, dd, *J* 14.5, 6.9, NCH*H*), 1.58 (1 H, s, OCHC*H*H), 1.43 (1 H, m, OCHCH*H*), 1.13–0.85 (2 H, m, CH_2), 0.74 (3 H, t, *J* 7.4, Me); δ_C (75 MHz; $CDCl_3$) 141.5 (C), 137.0 (C), 133.7 (C), 131.4 (CH), 128.8 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.9 (CH), 127.4 (CH), 127.3 (CH), 127.2 (CH), 126.5 (CH), 118.3 (=CH_2), 85.1 (OCH), 73.0 (NCH), 58.4 (NCH_2), 37.1 (CH_2), 18.9 (CH_2), 14.0 (Me).

(1*R*,1′*S*)-*N*-Allyl-*N*-(1-phenylbutoxy)-1-phenylpent-4-en-1-ylamine 7e

Obtained from the addition of phenyllithium to (*S*)-*O*-(1-phenylbutyl)pent-4-enaldehyde oxime **1c** (>95% de) as described above, and subsequent *N*-allylation to give the title compound as a colourless oil (74% over 2 steps); (Found: MH^+, 350.2484. $C_{24}H_{31}NO$ + H requires 350.2484); $[\alpha]_D^{25}$ −42.1 (*c* 1.07, $CHCl_3$); ν_{max}(film)/cm^{-1} 3079, 3060, 3027, 2956, 2922, 2865, 1635, 1488, 1450, 1103, 1061, 989, 904, 757, 695; δ_H (400 MHz; $CDCl_3$) 7.26 (10 H, m, ArH), 5.75 (2 H, m, 2 × =CH), 5.96 (4 H, m, 2 × =CH_2), 4.50 (1 H, t, *J* 6.5, OCH), 3.68 (1 H, dd, *J* 8.7, 5.6, NCH), 3.20 (1 H, m, NC*H*H), 2.97 (1 H, dd, *J* 14.1, 7.7, NCH*H*), 2.00–1.57 (6 H, m, OCHCH_2, NCHCH_2-

CH_2), 1.23 (1 H, m, C*H*HMe), 1.11 (1 H, m, CH*H*Me), 0.84 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 142.6 (C), 140.1 (C), 138.5 (CH), 134.5 (CH), 129.4 (CH), 128.1 (CH), 127.92 (CH), 127.86 (CH), 127.4 (CH), 127.1 (CH), 117.6 (=CH_2), 114.3 (=CH_2), 85.4 (CH), 68.5 (CH), 58.0 (CH_2), 37.1 (CH_2), 32.1 (CH_2), 30.7 (CH_2), 19.0 (CH_2), 14.1 (Me); *m*/*z* (CI) 350 (MH^+, 25%), 218 (34), 200 (79), 145 (42), 133 (100), 107 (26).

(3*R*,1′*S*)-*N*-Allyl-*N*-(1-phenylbutoxy)-7-benzyloxyhept-1-en-3-ylamine 7f

Obtained from the addition of vinylmagnesium bromide to (*S*)-[*O*-(1-phenylbutyl)]-5-benzyloxypentaldehyde oxime **2a** (82% de) and subsequent *N*-allylation to give the title compound as a colourless oil (34% over 2 steps); (Found: MH^+, 408.2910. $C_{27}H_{37}NO_2$ + H requires 408.2902); $[\alpha]_D^{28}$ −66.7 (*c* 1.26, $CHCl_3$); ν_{max}(film)/cm^{-1} 3068, 3027, 2950, 2930, 2858, 1716, 1649, 1450, 1414, 1358, 1102, 1030, 994, 912, 738, 692; δ_H (400 MHz; $CDCl_3$) 7.31 (10 H, m, ArH), 5.84 (1 H, m, =CH), 5.63 (1 H, br, =CH), 5.22 (1 H, dd, *J* 10.4, 1.9, =C*H*H), 5.02 (3 H, m, =CH*H*, =CH_2), 4.53 (3 H, m, CH_2Ph, OCH), 3.45 (2 H, t, *J* 6.5, OCH_2), 3.24 (1 H, dd, *J* 13.3, 7.8, NC*H*H), 3.15 (1 H, m, NCH*H*), 3.07 (1 H, m, NCH), 1.93 (1 H, m, OCHC*H*H), 1.75–1.16 (9 H, m, OCHCH*H*, 4 × CH_2), 0.90 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 142.8 (C), 138.7 (C), 136.6 (=CH), 134.8 (=CH), 128.3 (CH), 127.92 (CH), 127.88 (CH), 127.6 (CH), 127.5 (CH), 127.4 (CH), 118.0 (=CH_2), 117.3 (=CH_2), 85.7 (OCH), 72.8 (OCH_2), 70.4 (OCH_2), 67.6 (NCH), 57.9 (CH_2), 37.5 (CH_2), 32.0 (CH_2), 29.7 (CH_2), 23.0 (CH_2), 19.3 (CH_2), 14.1 (Me); *m*/*z* (CI) 408 (MH^+, 26%), 260 (35), 166 (82), 150 (100).

(3*R*,1′*S*)-*N*-Allyl-*N*-(1-phenylbutoxy)-7,7-dimethoxyhept-1-en-3-ylamine 7g

(a) Obtained from the addition of vinylmagnesium bromide to (*S*)-*O*-(1-phenylbutyl) 5,5-dimethoxypentanaldehyde oxime **2b** (79% de) and subsequent *N*-allylation to give the title compound as a colourless oil (28% of major diastereomer over 2 steps); (Found: MH^+, 362.2692. $C_{22}H_{35}NO_3$ + H requires 362.2695); $[\alpha]_D^{25}$ −71.2 (*c* 1.04, $CHCl_3$); ν_{max}(film)/cm^{-1} 3073, 3027, 2950, 2925, 2873, 2822, 1455, 1189, 1127, 1066, 1045, 999, 917, 758, 697, 666; δ_H (400 MHz; $CDCl_3$) 7.29 (5 H, m, ArH), 5.84 (1 H, m, NCH_2CH=CH_2), 5.60 (1 H, m, NCHC*H*=CH_2), 5.21 (1 H, dd, *J* 10.3, 1.9, NCH_2CH=C*H*H), 5.02 (3 H, m, NCH_2CH=CH*H*, NCHCH=CH_2), 4.51 (1 H, t, *J* 7.2, OCH), 4.33 (1 H, t, *J* 5.8, C*H*$(OMe)_2$), 3.31 (6 H, s, OMe), 3.22 (1 H, dd, *J* 13.3, 7.9, NCH), 3.08 (2 H, m, NCH_2), 1.91 (1 H, m, OCHC*H*H), 1.73–1.12 (9 H, m, OCHCH*HCH*$_2$, $CH_2CH_2CH_2$), 0.88 (3 H, t, *J* 7.4, Me); δ_C (100 MHz; $CDCl_3$) 142.7 (C), 136.5 (CH), 134.7 (CH), 127.92 (CH), 127.87 (CH), 127.4 (CH), 118.1 (=CH_2), 117.3 (=CH_2), 104.4 (CH), 85.6 (CH), 67.5 (CH), 57.8 (CH_2), 52.6 (OMe), 52.5 (OMe), 37.5 (CH_2), 32.4 (CH_2), 32.0 (CH_2), 21.5 (CH_2), 19.2 (CH_2), 14.1 (Me); *m*/*z* (CI) 362 (MH^+, 9%), 330 (39), 227 (14), 198 (39), 180 (56), 149 (26), 133 (100), 107 (34).

(b) Addition of vinyllithium to the above oxime ether proceded in *ca.* 90% de, and gave the addition product in 48% yield (the purified major diasteromer).

(1*R*,1′*R*)-*N*-Allyl-*N*-(1-phenylbutoxy)hept-1-en-4-ylamine 7h

Obtained from the addition of allylmagnesium bromide to (*S*)-*O*-(1-phenylbutyl)butyraldehyde oxime **2c**(87% de) and subsequent *N*-allylation to give the title compound as a colourless oil (39% over 2 steps); (Found: MH^+, 302.2478. $C_{20}H_{31}NO$ + H requires 302.2484); $[\alpha]_D^{22}$ −51.3 (*c* 1.19, $CHCl_3$); ν_{max}(film)/cm^{-1} 3078, 3027, 2955, 2935, 2868, 1639, 1450, 994, 912, 758, 702; δ_H (400 MHz; $CDCl_3$) 7.27 (5 H, m, ArH), 5.72 (2 H, m, 2 × =CH), 5.02 (4 H, m, 2 × =CH_2), 4.49 (1 H, t, *J* 7.1, OCH), 3.25 (1 H, dd, *J* 13.9, 7.2, NC*H*H), 3.18 (1 H, dd, *J* 13.9, 5.3, NCH*H*), 2.64 (1 H, m, NCH), 2.46 (1 H, m, NCHC*H*H), 1.98 (1 H, m, NCHCH*H*), 1.88 (1 H, m, OCHC*H*H), 1.56 (1 H, m, OCHCH*H*), 1.41–1.10 (6 H, m, CH_2CH_2Me, CH_2Me), 0.88 (3 H, t, *J* 7.3, Me), 0.78 (3 H, t, *J* 6.8, Me); δ_C (100 MHz; $CDCl_3$) 143.2 (C), 137.5 (=CH), 135.8 (=CH), 127.8 (CH), 127.7 (CH), 127.2 (CH), 116.6 (=CH_2), 115.5 (=CH_2), 85.1 (OCH), 63.4 (NCH), 59.9 (NCH_2), 37.8 (CH_2), 33.3 (CH_2), 33.0 (CH_2), 19.7 (CH_2), 19.1 (CH_2), 14.2 (Me), 14.1 (Me); *m*/*z* (ES) 302 (MH^+, 100%), 170 (75), 112 (75), 100 (50).

(1*R*,1′*R*)-*N*-Allyl-*N*-(1-phenybutoxy)-1-phenylbut-3-en-1-ylamine 7i

Obtained from the addition of allylmagnesium bromide to (*R*)-benzaldehyde oxime ether **2e** (91% de) as described previously,[1] and subsequent *N*-allylation to give the title compound as a colourless oil (57% over 2 steps); (Found: M^+, 335.2243. $C_{23}H_{29}NO$ requires 335.2249); $[\alpha]_D^{22}$ +8.48 (*c* 3.3, $CHCl_3$); ν_{max} (film)/cm^{-1} 3064, 3029, 2958, 2954, 2871, 1641, 1494, 1454, 995; δ_H(300 MHz; $CDCl_3$) 7.32 (10 H, m, ArH), 5.88 (1 H, m, NCH_2CH=), 5.56 (1 H, m, $NCHCH_2CH$=), 5.10–4.89 (4 H, m, 2 × =CH_2), 4.58 (1 H, dd, *J* 8.4, 6.0, OCH), 3.84 (1 H, dd, *J* 9.9, 4.6, NCH), 3.24 (1 H, m, NC*H*HC=), 3.02 (1 H, m, NCH*H*C=), 2.60 (1 H, m, NCC*H*HC=), 2.53 (1 H, m, NCCH*H*C=), 2.05 (1 H, m, C*H*H), 1.71 (1 H, m, CH*H*), 1.24 (2 H, m, CH_2), 0.93 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 142.6 (C), 140.0 (C), 136.0 (CH), 134.3 (CH), 129.3 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.5 (CH), 127.2 (CH), 117.8 (CH_2), 116.3 (CH_2), 85.5 (CH), 69.0 (CH), 57.4 (CH_2), 37.3 (CH_2), 36.3 (CH_2), 19.1 (CH_2), 14.2 (Me); *m*/*z* (CI) 335 (M^+, 0.4%), 294 (4), 220 (55), 205 (79), 186 (87), 162 (97), 146 (71), 133 (100), 104 (87), 92 (72), 77 (84).

General method for the preparation of Cbz-protected amines 9

Zinc dust (140.0 mmol) was added to a solution of hydroxylamine (3.5 mmol) in acetic acid:water (10 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 and washed with water. The filtrate was basified to pH 8 with aqueous potassium hydroxide solution (3 M). The solution was exhaustively extracted with dichloromethane (6 × 15 mL). The extracts were combined, dried (Na_2SO_4), filtered and evaporated. Sodium carbonate (7.0 mmol) was added to a solution of the residue dissolved in THF:water (50 mL, 1:1). The solution was cooled to 0 °C and benzyl chloroformate (3.5 mmol) was added dropwise. The mixture was allowed to warm to room temperature and was stirred for 12 h. The THF was evaporated under reduced pressure and extracted with ether (3 × 10 mL). The organic extracts were combined, dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash chromatography on silica gel.

(*S*)-*N*-Benzyloxycarbonyl-4-phenylbut-3-en-2-ylamine 9a

Prepared as described previously for the (*R*)-enantiomer in 26% yield, mp 90–91 °C (lit.,[8] for (*R*)-enantiomer mp 89–91 °C); $[\alpha]_D^{23}$ −55.4 (*c* 1.10, CH_2Cl_2) (lit.,[8] for (*R*)-enantiomer $[\alpha]_D^{20}$ +48.8 (*c* 1.0, CH_2Cl_2)).

(*R*)-*N*-Benzyloxycarbonyl-1-phenylhept-1-en-3-ylamine 9b

Prepared as described previously.[8]

(*R*)-*N*-Benzyloxycarbonyl-1,3-diphenylprop-2-en-1-ylamine 9c

Prepared as described previously for the (*S*)-enantiomer in 41% yield, mp 110–112 °C (lit.,[8] for (*S*)-enantiomer mp 110–111 °C); $[\alpha]_D^{21}$ +8.1 (*c* 1.10, CH_2Cl_2).

(*R*)-*N*-Benzyloxycarbonylhept-1-en-4-ylamine 9d

Addition of allylmagnesium bromide to oxime ether **2c** gave (4*R*,1′*S*)-*N*-(1-phenylbutoxy)hept-1-en-4-ylamine **6h** as a

colourless oil (51%, >95% de); (Found: MH^+, 262.2174. $C_{17}H_{27}NO$ + H requires 262.2171); $[a]_D^{18}$ −76.1 (*c* 0.9, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3421, 3075, 3029, 2958, 2933, 2874, 1639, 1454, 914; δ_H (300 MHz; $CDCl_3$) 7.31 (5 H, m, ArH), 5.81 (1 H, m, =CH), 5.29 (1 H, br s, NH), 5.09 (2 H, m, $=CH_2$), 4.56 (1 H, dd, *J* 7.7, 5.8, OCH), 2.85 (1 H, quintet, *J* 5.9, NCH), 2.34 (1 H, m, C*H*HCH=), 2.24 (1 H, m, CH*H*CH=), 1.80 (1 H, m, C*H*H), 1.57–1.26 (7 H, m, CH*H*, 3 × CH_2), 0.93 (3 H, t, *J* 7.3, Me), 0.86 (3 H, t, *J* 7.0, Me); δ_C(75 MHz; $CDCl_3$) 143.4 (C), 135.7 (CH), 128.3 (CH), 127.3 (CH), 126.6 (CH), 117.1 (CH_2), 85.3 (CH), 59.8 (CH), 38.9 (CH_2), 36.6 (CH_2), 33.5 (CH_2), 19.3 (CH_2), 19.2 (CH_2), 14.2 (Me), 14.1 (Me); *m*/*z* (CI) 262 (MH^+, 15%), 166 (10), 150 (21), 114 (100), 105 (6), 91 (4), 72 (52).

Cleavage of the above hydroxylamine and subsequent protection gave the title compound as a colourless solid (52%, 90% ee); mp 53–54 °C (from aq. ethanol); (Found: C, 73.0; H, 8.8; N, 5.6. $C_{15}H_{21}NO_2$ requires C, 72.8; H, 8.6; N, 5.7%); (Found: MH^+, 248.1649. $C_{15}H_{20}NO_2$ + H requires 248.1649); $[a]_D^{27}$ +20.7 (*c* 0.9, $CHCl_3$); ν_{max} (film)/cm^{-1} 3309, 3083, 3070, 2952, 1685, 1546, 1465, 1267, 1236; δ_H (300 MHz; $CDCl_3$) 7.33 (5 H, m, ArH), 5.77 (1 H, m, =CH), 5.12 (2 H, m, $=CH_2$), 5.09 (2 H, s, CH_2O), 4.57 (1 H, br d, *J* 8.4, NH), 3.72 (1 H, m, NCH), 2.23 (2 H, m, CH_2CH=), 1.42 (4 H, m, 2 × CH_2), 0.91 (3 H, t, *J* 6.4, Me); δ_C (75 MHz; $CDCl_3$) 155.7 (C), 142.3 (CH), 137.5 (C), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.4 (CH), 126.4 (CH), 115.4 (CH_2), 66.8 (CH_2), 55.0 (CH), 35.8 (CH_2), 30.3 (CH_2); *m*/*z* (CI) 248 (MH^+, 14%), 126 (12), 114 (100), 106 (25), 89 (11), 72 (56).

(*S*)-*N*-Benzyloxycarbonyl-1-(4-methoxyphenyl)but-3-en-1-ylamine 9e

Prepared as described previously.[1]

(*R*)-7-Benzyloxy-*N*-benzyloxycarbonylhept-1-en-4-ylamine 9f

Addition of allylmagnesium bromide to oxime **2h** gave (4*R*,1′*S*)-7-benzyloxy-*N*-(1-phenylbutoxy)hept-1-en-4-ylamine (88%, 82% de) as a colourless oil; (Found: MH^+, 368.2596. $C_{24}H_{33}NO_2$ + H requires 368.2589); $[a]_D^{24}$ −45.2 (*c* 1.15, $CHCl_3$); ν_{max}(film)/cm^{-1} 3068, 3027, 2955, 2930, 2863, 1460, 1358, 1096, 1025, 912, 738, 692; δ_H (400 MHz; $CDCl_3$) 7.30 (10 H, m, ArH), 5.78 (1 H, m, =CH), 5.31 (1 H, br s, NH), 5.09 (2 H, m, $=CH_2$), 4.53 (1 H, m, OCH), 4.47 (2 H, s, CH_2Ph), 3.41 (2 H, t, *J* 6.4, OCH_2), 2.84 (1 H, quintet, *J* 6.3, NCH), 2.35 (1 H, m, =CHC*H*H), 2.20 (1 H, m, =CHCH*H*), 1.86–1.19 (8 H, m, 4 × CH_2), 0.90 (3 H, t, *J* 7.2, Me); δ_C (100 MHz; $CDCl_3$) 143.3 (C), 138.6 (C), 135.5 (=CH), 128.34 (CH), 128.27 (CH), 127.6 (CH), 127.5 (CH), 127.3 (CH), 126.6 (CH), 117.3 ($=CH_2$), 85.3 (OCH), 72.8 (CH_2Ph), 70.4 (OCH_2), 59.8 (NCH), 38.8 (CH_2), 36.6 (CH_2), 28.0 (CH_2), 26.4 (CH_2), 19.2 (CH_2), 14.1 (Me); *m*/*z* (CI) 368 (MH^+, 24%), 166 (100), 150 (82), 110 (76), 58 (54).

Cleavage of the above hydroxylamine and subsequent protection gave the *title compound* (91%) as a colourless oil; (Found: MH^+, 354.2068. $C_{22}H_{27}NO_3$ + H requires 354.2069); $[a]_D^{25}$ +13.4 (*c* 1.42, $CHCl_3$); ν_{max}(film)/cm^{-1} 3324 (NH), 3063, 3032, 3001, 2945, 2848, 1701, 1532, 1450, 1360, 1250, 1069, 1020, 907, 738, 692; δ_H (400 MHz; $CDCl_3$) 7.34 (10 H, m, ArH), 5.78 (1 H, m, =CH), 5.09 (4 H, m, CH_2Ph, $=CH_2$), 4.68 (1 H, br d, *J* 8.1, NH), 4.50 (2 H, s, CH_2Ph), 3.74 (1 H, br, NCH), 3.49 (2 H, t, *J* 5.6, OCH_2CH_2), 2.25 (2 H, m, =CHCH_2), 1.67 (3 H, m, OCH_2CH_2, C*H*H), 1.47 (1 H, m, CH*H*); δ_C (100 MHz; $CDCl_3$) 156.1 (CO), 138.5 (C), 136.7 (C), 134.2 (=CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH),127.7 (CH), 127.6 (CH), 118.0 ($=CH_2$), 72.9 (CH_2), 70.0 (CH_2), 66.5 (CH_2), 50.5 (CH), 39.6 (CH_2), 31.3 (CH_2), 26.2 (CH_2); *m*/*z* (ES) 376 (M+Na, 100%), 371 (M+NH_4, 50), 354 (MH^+, 20), 193 (8), 97 (40), 65 (15).

(*R*)-*N*-Benzyloxycarbonyl-1-phenylpent-4-en-1-ylamine 9g

Prepared as described previously.[1]

(*S*)-*N*-Benzyloxycarbonylnon-8-en-4-ylamine 9h

Addition of pent-4-enylmagnesium bromide to the oxime ether **2d** gave (6*S*,1′*R*)-*N*-(1-phenylbutoxy)non-8-en-4-ylamine as a colourless oil (88%); $[a]_D^{25}$ +58.7 (*c* 0.8, CH_2Cl_2) (lit.,[9] for (*R*,*S*)-isomer $[a]_D^{25}$ −61.9 (*c* 0.62, CH_2Cl_2)); δ_H (300 MHz; $CDCl_3$) 7.33 (5 H, m,ArH), 5.84 (1 H, m, =CH), 5.21 (1 H, br s, NH), 5.03 (2 H, m, $=CH_2$), 4.58 (1 H, dd, *J* 7.9, 5.9, OCH), 2.84 (1 H, m, NCH), 2.10 (2 H, m, CH_2CH=), 1.59–1.31 (12 H, m, 6 × CH_2), 0.96 (3 H, t, *J* 7.3, Me), 0.91 (3 H, t, *J* 7.0 Me); δ_C (75 MHz; $CDCl_3$) 143.5 (CH), 138.9 (C), 128.3 (CH), 127.2 (CH), 126.6 (CH), 114.4 (CH_2), 85.2 (CH), 60.1 (CH), 38.9 (CH_2), 34.1 (CH_2), 31.7 (CH_2), 25.1 (CH_2), 19.3 (CH_2), 14.3 (Me), 14.1 (Me).

Cleavage of the above hydroxylamine and subsequent protection gave the title compound as a colourless oil (88%, 92% ee) mp 72–74 °C (from light petroleum) (lit.,[9] for (*R*)-enantiomer mp 71–73 °C); $[a]_D^{25}$ +2.3 (*c* 84, CH_2Cl_2) (lit.,[9] for (*R*)-enantiomer $[a]_D^{25}$ −1.5 (*c* 1.0, CH_2Cl_2); δ_H (300 MHz; $CDCl_3$) 7.33 (5 H, m, ArH), 5.78 (1 H, m, =CH), 5.13 (2 H, s, CH_2O), 5.00 (2 H, m, $=CH_2$), 4.48 (1 H, br d, *J* 9.2, NH), 3.65 (1 H, br s, NCH), 2.04 (2 H, m, CH_2) 1.51–1.19 (8 H, m, 4 × CH_2), 0.91 (3 H, t, *J* 6.5, Me); δ_C (75 MHz; $CDCl_3$) 156.1 (C), 138.6 (CH), 136.7 (C), 128.5 (CH), 128.1 (2 × CH), 114.7 (CH_2), 66.5 (CH_2), 51.0 (CH), 37.7 (CH_2), 34.9 (CH_2), 33.6 (CH_2), 25.1 (CH_2), 19.0 (CH_2), 14.0 (Me).

General method for the preparation of dienes 10 by allylation

Sodium hydride (2.040 mmol) was suspended in dry DMF (1 mL) and cooled to 0 °C under nitrogen. A solution of the Cbz-protected amine **9** (1.020 mmol) in dry DMF (1.5 mL) was added and the reaction mixture was allowed to warm to room temperature. After 30 min the reaction mixture was re-cooled to 0 °C. Allyl bromide (0.18 mL, 2.040 mmol) was added and the reaction mixture was allowed to warm to room temperature. After complete consumption of starting material (TLC) aqueous saturated ammonium chloride solution (2 mL) was added and the mixture was extracted with ether (3 × 10 mL). The combined organic extracts were washed with water (5 × 10 mL), dried (Na_2SO_4) and the mixture was filtered and evaporated. The residue was purified by column chromatography on silica gel eluting with light petroleum : ethyl acetate (10:1) to give the diene **10**.

(*S*)-*N*-Allyl-*N*-benzyloxycarbonyl-3-phenylbut-2-en-1-ylamine 10a

Obtained from the *N*-allylation of Cbz-amine **9a** as a colourless oil (74%, 89% ee); (Found: M + NH_4, 339.2062. $C_{21}H_{23}NO_2$+ NH_4 requires 339.2073); $[a]_D^{18}$ −62.1 (*c* 1.03, $CHCl_3$); ν_{max}(film)/cm^{-1} 3078, 3022, 2970, 2925, 1696 (C=O), 1450, 1403, 1250, 1143, 1020, 963, 912, 748, 687; δ_H (400 MHz; $CDCl_3$) 7.42–7.18 (10 H, m, ArH), 6.44 (1 H, d, *J* 15.8, PhC*H*=CH), 6.23 (1 H, dd, *J* 15.9, 5.5, PhCH=C*H*), 5.86 (1 H, m, C*H*=CH_2), 5.24–4.71 (5 H, m, $=CH_2$, CH_2Ph, NCH), 3.82 (2 H, m, NCH_2), 1.38 (3 H, d, *J* 6.9, Me); δ_C (100 MHz; $CDCl_3$) 156.0 (C=O), 136.8 (C), 136.7 (C), 135.6 (CH), 130.6 (CH), 130.2 (CH), 128.6 (CH), 128.4 (CH), 127.9 (CH), 127.8 (CH), 127.6 (CH), 126.4 (CH), 116.0 ($=CH_2$), 67.1 (CH_2), 53.2 (CH), 45.7 (CH_2), 18.0 (Me); *m*/*z* (CI) 339 (*M* + NH_4^+, 8%), 322 (MH^+, 16), 209 (12), 186 (10), 131 (100).

(*R*)-*N*-Allyl-*N*-benzyloxycarbonyl-1-phenylhept-1-en-3-ylamine 10b

Obtained from the *N*-allylation of Cbz-amine **9b** as a colourless oil (88%); (Found: MH^+, 364.2289. $C_{24}H_{29}NO_2$ + H requires 364.2276); $[a]_D^{23}$ +54.2 (*c* 0.83, $CHCl_3$); ν_{max} (film)/cm^{-1} 3081, 3062, 3029, 2956, 2931, 2871, 1697, 1456, 1407, 1241; δ_H (300 MHz; $CDCl_3$) 7.31 (10 H, m ArH), 6.49 (1 H, m, C*H*=CH), 6.22

(1 H, m, CH=C*H*), 5.24 (2 H, br s, CH_2O), 5.15 (2 H, m, $=CH_2$), 4.66 (1 H, m, NCH), 3.85 (2 H, br s, $CH_2CH=$), 1.62 (2 H, m, CH_2), 1.28 (4 H, m, 2 × CH_2), 0.91 (3 H, br t, *J* 7.0, Me); δ_C (75 MHz; $CDCl_3$) 156.2 (C), 136.8 (C), 135.6 (CH), 131.5 (CH), 129.2 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.6 (CH), 126.4 (CH), 116.4 (CH_2), 67.1 (CH_2), 58.5 (CH), 46.5 (CH_2), 32.1 (CH_2), 28.5 (CH_2), 22.5 (CH_2), 14.1 (Me); one ArC and one ArCH not observed; *m*/*z* (CI) 364 (MH^+, 11%), 230 (69), 192 (20), 173 (100), 108 (14), 91 (8).

(*R*)-*N*-Allyl-*N*-benzyloxycarbonyl-1,3-diphenylprop-2-en-1-ylamine 10c

To a solution of Cbz-amine **9c** (300 mg, 0.87 mmol) in anhydrous THF (2 mL), a solution of π-allylpalladium chloride dimer (3.2 mg, 0.0087 mmol, 1 mol %), triphenylphosphine (10 mg, 0.039 mmol, 4.5 mol %), and methyl allyl carbonate (0.21 mL, 1.75 mmol) were added at room temperature. The reaction mixture was heated under reflux overnight. The solvent was evaporated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with ethyl acetate:light petroleum (1:9) to give the title compound as a colourless oil (140 mg, 63%); (Found: M^+, 383.1884. $C_{26}H_{25}NO_2$ requires 383.1885); $[\alpha]_D^{25}$ +5.9 (*c* 2.20, $CHCl_3$); ν_{max}(film)/cm^{-1} 3058, 3027, 2929, 1696 (C=O), 1439, 1399, 1255, 1143, 968, 912; δ_H (400 MHz; $CDCl_3$) 7.32 (15 H, m, ArH), 6.53 (2 H, m, PhC*H*=C*H*), 5.97 (1 H, m, CH_2=C*H*), 5.73 (1 H, m, NC*H*Ph), 5.22 (2 H, AB, *J* 12.0, OCH_2), 5.03 (2 H, d, *J* 11.2, $=CH_2$), 4.01 (1 H, dd, *J* 15.9, 4.4, NC*H*H), 3.82 (1 H, dd, *J* 15.9, 5.8, NCH*H*); δ_C (100 MHz; $CDCl_3$) 156.2 (C=O), 139.8 (C), 136.7 (C), 136.6 (C), 135.1 (CH), 133.3 (CH), 128.6 (CH), 128.5 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.0 (CH), 126.6 (CH), 126.3 (CH), 116.5 ($=CH_2$), 67.3 (CH_2), 61.8 (CH); *m*/*z* (CI) 384 (MH^+, 10%), 248 (8), 209 (35), 193 (100).

(*R*)-*N*-Allyl-*N*-benzyloxycarbonylhept-1-en-4-ylamine 10d

Obtained from the *N*-allylation of Cbz-amine **9d** as a colourless oil (90%); (Found: MH^+, 288.1956. $C_{18}H_{25}NO_2$ + H requires 288.1963); $[\alpha]_D^{21}$ +15.6 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3075, 3033, 2958, 2931, 2871, 1699, 1456, 1409, 1240, 916; δ_H (300 MHz; $CDCl_3$; 60 °C) 7.31 (5 H, m, ArH), 5.87 (1 H, m, =CH), 5.73 (1 H, m, =CH), 5.15 (2 H, s, CH_2O), 5.05 (4 H, m, 2 × $=CH_2$), 4.08 (1 H, br s, NH), 3.77 (2 H, br s, $CH_2CH=$), 2.27 (2 H, m, $CH_2CH=$), 1.64–1.29 (4 H, m, 2 × CH_2), 0.89 (3 H, t, *J* 5.2, Me); δ_C (100 MHz; $CDCl_3$; 60 °C) 156.5 (C), 137.0 (C), 135.9 (CH), 135.5 (CH), 128.4 (CH), 127.9 (CH), 127.6 (CH), 116.9 (CH_2), 116.1 (CH_2), 66.8 (CH_2), 56.4 (CH), 45.8 (CH_2), 38.0 (CH_2), 34.8 (CH_2), 19.2 (CH_2), 13.9 (Me); *m*/*z* (CI) 288 (MH^+, 18%), 154 (100), 114 (38), 108 (33), 72 (27).

(*S*)-*N*-Allyl-*N*-benzyloxycarbonyl-1-(4-methoxyphenyl)but-3-en-1-ylamine 10e

Obtained from the *N*-allylation of Cbz-amine **9e** as a colourless oil (97%); (Found: MH^+, 352.1902. $C_{22}H_{25}NO_3$ + H requires 352.1912); $[\alpha]_D^{27}$ −91.1 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3075, 3033, 2954, 2935, 2836, 1695, 1513, 1456, 1405, 1249; δ_H (300 MHz; $CDCl_3$) 7.32 (7 H, m, ArH), 6.86 (2 H, AA′BB′, *J* 8.5 ArH), 5.79 (1 H, br s, =CH), 5.62 (1 H, br s, =CH), 5.38 (1 H, br s, NCH), 5.20 (2 H, s, CH_2O), 5.16–4.95 (4 H, m, 2 × $=CH_2$), 3.80 (3 H, s, OMe), 3.71 (1 H, m, C*H*H), 3.60 (1 H, dd, *J* 15.9, 6.5, CH*H*), 2.73 (2 H, t, *J* 7.2, $CH_2C=$); δ_C (100 MHz; $CDCl_3$) 159.0 (C), 156.4 (C), 136.9 (C), 135.3 (CH), 135.0 (CH), 131.7 (C), 129.3 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 117.4 (CH_2), 116.2 (CH_2), 113.7 (CH), 67.1 (CH_2), 58.1 (CH), 55.2 (OMe), 46.0 (CH_2), 35.7 (CH_2); *m*/*z* (CI) 352 (MH^+, 6%), 218 (32), 209 (12), 178 (9), 161 (100), 108 (8).

(*R*)-*N*-Allyl-7-benzyloxy-*N*-benzyloxycarbonylhept-1-en-4-ylamine 10f

Obtained from the *N*-allylation of Cbz-amine **9f** and purification by column chromatography on silica gel eluting with ether:light petroleum (1:2) as a colourless oil (83%); (Found: MH^+, 394.2379. $C_{25}H_{31}NO_3$ + H requires 394.2382); $[\alpha]_D^{22}$ +11.8 (*c* 1.02, $CHCl_3$); ν_{max}(film)/cm^{-1} 3068, 3027, 2940, 2853, 1690 (CO), 1455, 1409, 1358, 1327, 1230, 1148, 1102, 1030, 989, 912, 769, 738, 697; δ_H (400 MHz; DMSO, −10 °C) 7.29 (10 H, m, ArH), 5.80 (1 H, m, =CH), 5.68 (1 H, m, =CH), 5.16–4.95 (6 H, m, CH_2Ph, 2 × $=CH_2$), 4.42 (2 H, s, CH_2Ph), 3.96 (1 H, br, NCH), 3.74 (2 H, m, NCH_2), 3.40 (2 H, m, OCH_2), 2.26 (2 H, m, NCHCH_2), 1.53 (4 H, m, 2 × CH_2); δ_C (100 MHz; DMSO, −10 °C) 156.2 (CO), 139.3 (C), 137.6 (C), 136.2 (=CH), 136.1 (=CH), 128.7 (CH), 128.5 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 117.0 ($=CH_2$), 116.6 ($=CH_2$), 72.4 (CH_2), 69.9 (CH_2), 66.6 (CH_2), 57.0 (NCH), 46.4 (CH_2), 37.8 (CH_2), 29.5 (CH_2), 26.8 (CH_2); *m*/*z* (ES) 416 (*M* + Na, 100%), 411 (*M* + NH_4, 45), 394 (MH^+, 20), 97 (20).

(*R*)-*N*-Allyl-*N*-benzyloxycarbonyl-1-phenylpent-4-en-1-ylamine 10g

Obtained from the *N*-allylation of Cbz-amine **9g** as a colourless oil (89%); (Found: MH^+, 336.1952. $C_{22}H_{25}NO_2$ + H requires 336.1963); $[\alpha]_D^{25}$ +96.8 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3066, 3031, 2935, 1697, 1454, 1407, 1321, 1253, 1139, 916; δ_H (300 MHz; $CDCl_3$) 7.34 (10 H, m, ArH), 5.86 (1 H, br s, =CH), 5.67 (1 H, br s, =CH), 5.43 (1 H, br s, NCH), 5.24 (1 H, d, *J* 12.5, C*H*HO), 5.23 (1 H, d, *J* 12.5, CH*H*O), 5.02 (4 H, m, 2 × $=CH_2$), 3.75 (1 H, m, C*H*HCH=), 3.58 (1 H, dd, *J* 15.9, 6.7, CH*H*CH=), 2.14–1.98 (4 H, m, 2 × CH_2); δ_C (100 MHz; $CDCl_3$) 156.6 (C), 140.1 (C), 137.7 (CH), 136.8 (C), 135.2 (CH), 128.45 (CH), 128.38 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 116.3 (CH_2), 115.1 (CH_2), 67.2 (CH_2), 58.5 (CH), 46.0 (CH_2), 30.7 (CH_2), 30.3 (CH_2); *m*/*z* (CI) 336 (MH^+, 20%), 209 (34), 192 (11), 146 (11), 106 (20), 91 (6).

(*S*)-*N*-Allyl-*N*-benzyloxycarbonyl-1-propylhex-5-en-1-ylamine 10h

Obtained from the *N*-allylation of Cbz-amine **9h** as a colourless oil (81%); (Found: *M* + NH_4^+, 333.2543. $C_{20}H_{29}NO_2$ + NH_4 requires 333.2542); ν_{max} (film)/cm^{-1} 2958, 2931, 2863, 1697, 1456, 1409, 1328, 1238, 995, 912; δ_H (400 MHz; $CDCl_3$) *major rotamer* 7.31 (5 H, m, ArH), 5.95–5.66 (2 H, m, 2 × =CH), 5.29–4.91 (4 H, m, 2 × $=CH_2$), 5.15 (2 H, s, CH_2O), 4.12 (1 H, m, NCH), 3.73 (2 H, dd, *J* 4.4, 17.0, NCH_2), 2.03 (2 H, m, $CH_2CH=$), 1.51–1.26 (8 H, m, 4 × CH_2), 0.89 (3 H, t, *J* 5.4, Me); *minor rotamer* 3.96 (1 H, m, NCH), 0.87 (3 H, t, *J* 5.7, Me); δ_C (100 MHz; $CDCl_3$) *major rotamer* 156.7 (C), 138.6 (CH), 137.1 (C), 135.9 (CH), 128.4 (CH), 127.8 (CH),127.75 (CH), 116.1 (CH_2), 114.6 (CH_2), 66.9 (CH_2), 56.3 (CH), 45.2 (CH_2), 35.5 (CH_2), 33.5 (CH_2), 32.6 (CH_2), 25.7 (CH_2), 19.6 (CH_2), 13.9 (Me); *minor rotamer*138.5 (CH), 136.9 (C), 135.4 (CH), 128.2 (CH), 127.8 (CH), 127.68 (CH), 116.3 (CH_2), 67.0 (CH_2), 45.8 (CH_2), 35.8 (CH_2), 33.4 (CH_2), 32.9 (CH_2), 13.8 (Me); *m*/*z* (CI) 333 (*M* + NH_4^+, 64%), 316 (100), 300 (5), 272 (5), 182 (19), 125 (2).

General method for the preparation of nitrogen heterocycles 8 and 11 *via* ring-closing metathesis

The diene **7** or **10** (0.690 mmol) was dissolved in dry dichloromethane (4 mL) under nitrogen. To the solution was added benzylidene bis(tricyclohexylphosphine)dichlororuthenium (0.058 g, 0.0690 mmol, 10 mol%), and the mixture stirred (or heated under reflux) until complete consumption of starting material was observed (TLC, typically 2–4 h). The solvent was removed *in vacuo* and the residue purified by column chromatography on silica gel eluting with ethyl acetate:light petroleum (1:10) to give the azacycle **8** or **11**.

(2*R*,1′*R*)-2-Methyl-1-(1-phenylbutoxy)-2,5-dihydro-1*H*-pyrrole 8a

Obtained from the ring-closing metathesis of diene **7a** as a colourless oil (87%); (Found: M^+, 231.1629. $C_{15}H_{21}NO$ requires 231.1623); $[\alpha]_D^{22}$ +32.1 (*c* 1.65, $CHCl_3$); ν_{max} (film)/cm^{-1} 3064, 3031, 2960, 2929, 2871, 2825, 1454, 1369, 1355, 1027, 761; δ_H (300 MHz; $CDCl_3$) 7.31 (5 H, m, ArH), 5.60 (2 H, m, CH=CH), 4.65 (1 H, dd, *J* 7.8, 5.8, OCH), 4.01 (1 H, m, NCH), 3.52 (2 H, m, NCH_2), 1.86 (1 H, m, C*H*H), 1.62–1.28 (3 H, m, CH*H*, CH_2), 1.25 (3 H, d, *J* 6.7, Me), 0.95 (3 H, t, *J* 7.2, Me); δ_C (75 MHz; $CDCl_3$) 143.7 (C), 131.7 (CH), 128.1 (CH), 127.3 (CH), 127.2 (CH), 125.3 (CH), 86.1 (CH), 69.0 (CH), 62.6 (CH_2), 38.6 (CH_2), 19.4 (CH_2), 19.2 (Me), 14.1 (Me); *m*/*z* (EI) 231 (M^+, 1%) 150 (11), 133 (3), 117 (7), 107 (81), 99 (67), 91 (100), 79 (57), 68 (15).

(2*R*,1′*R*)-2-Butyl-1-(1-phenylbutoxy)-2,5-dihydro-1*H*-pyrrole 8b

Obtained from the ring-closing metathesis of diene **7b** as a colourless oil (78%); (Found: MH^+, 274.2176. $C_{18}H_{27}NO$ + H requires 274.2171); $[\alpha]_D^{22}$ +28.1 (*c* 2.35, CH_2Cl_2); ν_{max} (film)/cm^{-1} 2958, 2931, 2871, 1456, 1027, 761; δ_H (300 MHz; $CDCl_3$) 7.31 (5 H, m, ArH), 5.73 (1 H, m, =CH), 5.63 (1 H, m, =CH), 4.64 (1 H, dd, *J* 7.9, 5.7, OCH), 3.95 (1 H, m, NCH), 3.51 (2 H, qq, *J* 15.6, 2.0, NCH_2), 1.86 (1 H, m, C*H*H), 1.61–1.29 (9 H, m, CH*H*, 4 × CH_2), 0.97 (3 H, t, *J* 7.0, Me), 0.94 (3 H, t, *J* 7.3, Me); δ_C (75 MHz; $CDCl_3$) 143.8 (C), 130.3 (CH), 128.1 (CH), 127.2 (CH), 125.61 (CH), 125.60 (CH), 85.6 (CH), 74.7 (CH), 63.2 (CH_2), 38.5 (CH_2), 33.3 (CH_2), 28.8 (CH_2), 22.9 (CH_2), 19.4 (CH_2), 14.2 (Me), 14.1 (Me); *m*/*z* (CI) 274 (MH^+, 0.1%), 141 (9), 133 (9), 105 (18), 91 (100), 84 (49), (27).

(2*S*,1′*S*)-2-Isobutyl-1-(1-phenylbutoxy)-2,5-dihydro-1*H*-pyrrole 8c

Obtained from the ring-closing metathesis of diene **7c** after purification by column chromatography on silica gel eluting with ether:light petroleum (1:8) as a colourless oil (74%); (Found: MH^+, 274.2172. $C_{18}H_{27}NO$ + H requires 274.2171); $[\alpha]_D^{25}$ −28.1 (*c* 1.35, $CHCl_3$); ν_{max}(film)/cm^{-1} 3018, 2955, 1209, 758, 661; δ_H (400 MHz; $CDCl_3$) 7.28 (5 H, m, ArH), 5.71 (1 H, dq, *J* 6.3, 1.9, CH_2CH=C*H*), 5.61 (1 H, dq, *J* 6.3, 1.9, CH_2C*H*=CH), 4.66 (1 H, t, *J* 6.5, OCH), 4.02 (1 H, tt, *J* 7.2, 1.9, NCH), 3.49 (2 H, m, NCH_2), 1.82 (2 H, m, OCHCH_2), 1.55–1.25 (5 H, m, CH_2C*H*Me_2, CH_2Me), 0.99 (3 H, d, *J* 6.7, Me), 0.95 (3 H, d, *J* 6.6, Me), 0.91 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 143.8 (C), 130.6 (CH), 128.1 (CH), 127.3 (CH), 127.2 (CH), 125.4 (CH), 85.6 (CH), 73.3 (CH), 63.1 (CH_2), 43.0 (CH_2), 38.4 (CH_2), 25.7 (CH), 23.0 (Me), 22.9 (Me), 19.3 (CH_2), 14.0 (Me); *m*/*z* (EI) 274 (MH^+, 100%), 232 (18), 214 (55), 203 (65), 173 (71), 156 (51), 150 (88).

(2*S*,1′*S*)-2-Phenyl-1-(1-phenylbutoxy)-2,5-dihydro-1*H*-pyrrole 8d

Obtained from the ring-closing metathesis of diene **7d** after purification by column chromatography on silica gel eluting with ethyl acetate:light petroleum (1:50) as a colourless oil (51%); (Found: MH^+, 294.1860. $C_{20}H_{23}NO$ + H requires 294.1858); $[\alpha]_D^{22}$ −17.7 (*c* 1.13, $CHCl_3$); ν_{max}(film)/cm^{-1} 3053, 3027, 2950, 2925, 2863, 2822, 1450, 1025, 753; δ_H (400 MHz; $CDCl_3$) 7.31 (10 H, m, ArH), 5.71 (1 H, dq, *J* 6.3, 1.9, PhCHC*H*=CH), 5.64 (1 H, m, PhCHCH=C*H*), 4.97 (1 H, m, NCH), 4.33 (1 H, dd, *J* 7.7, 5.5, OCH), 3.60 (2 H, m, NCH_2), 1.68 (1 H, m, C*H*H), 1.45–1.02 (3 H, m, CH*H*, CH_2), 0.74 (3 H, t, *J* 7.1, Me); δ_C (100 MHz; $CDCl_3$) 143.8 (C), 142.1 (C), 130.3 (CH), 129.4 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 127.2 (CH), 127.1 (CH), 126.2 (CH), 85.4 (CH), 77.3 (CH), 62.6 (CH_2), 38.2 (CH_2), 19.1 (CH_2), 13.8 (Me); *m*/*z* (CI) 294 (MH^+, 86%), 200 (14), 162 (66), 144 (91), 133 (100).

(2*R*,1′*S*)-2-Phenyl-1-(1-phenylbutoxy)-2,3,4,7-tetrahydro-1*H*-azepine 8e

Obtained from the ring-closing metathesis of diene **7e** after purification by column chromatography on silica gel eluting with ether:light petroleum (3:80) as a colourless oil (9%); (Found: MH^+, 322.2171. $C_{22}H_{27}NO$ + H requires 322.2173); $[\alpha]_D^{25}$ −60.0 (*c* 0.3, $CHCl_3$); ν_{max}(film)/cm^{-1} 3063, 3027, 2960, 2925, 2868, 2812, 1731, 1685, 1486, 1450, 1214, 1030, 758, 697, 666; δ_H (400 MHz; $CDCl_3$) 7.48 (2 H, m, ArH), 7.30 (8 H, m, ArH), 5.83 (1 H, m, NCH_2CH=C*H*), 5.38 (1 H, m, NCH_2C*H*=CH), 4.22 (1 H, t, *J* 6.5, OCH), 4.00 (1 H, dd, *J* 7.2, 4.3, NCH), 3.38 (1 H, dd, *J* 14.5, 2.1, NC*H*H), 3.21 (1 H, dd, *J* 14.5, 7.6, NCH*H*), 2.29 (1 H, m, $NCHCH_2C$*H*H), 2.09 (1 H, m, $NCHCH_2CH$*H*), 1.93 (1 H, m, NCHC*H*H), 1.82 (1 H, m, NCHC*H*H), 1.35–1.12 (2 H, m, OCHCH_2), 0.83 (2 H, m, CH_2Me), 0.54 (3 H, t, *J* 6.7, Me); δ_C (100 MHz; $CDCl_3$) 144.8 (C), 142.9 (C), 134.2 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 127.3 (CH), 126.8 (CH), 125.8 (CH), 84.8 (CH), 75.1 (CH), 56.4 (CH_2), 37.0 (CH_2), 33.2 (CH_2), 25.5 (CH_2), 18.3 (CH_2), 13.8 (Me); *m*/*z* (ES) 322 (MH^+, 20%), 190 (6), 130 (100).

(2*R*,1′*S*)-2-(4-Benzyloxybutyl)-1-(1-phenylbutoxy)-2,5-dihydro-1*H*-pyrrole 8f

Obtained from the ring-closing metathesis of diene **7f** after purification by column chromatography on silica gel eluting with ether:light petroleum (1:20) as a colourless oil (35%); (Found: MH^+, 380.2587. $C_{25}H_{33}NO_2$ + H requires 380.2589); $[\alpha]_D^{28}$ −81.5 (*c* 0.54, $CHCl_3$); δ_H (400 MHz; $CDCl_3$) 7.28 (10 H, m, ArH), 5.72 (2 H, m, CH=CH), 4.58 (1 H, m, OCH), 4.46 (2 H, m, CH_2Ph), 3.95 (1 H, br, NC*H*H), 3.80 (2 H, m, NCH*H*, NCH), 3.29 (2 H, t, *J* 6.7, OCH_2), 1.82 (1 H, m, C*H*H), 1.55 (1 H, m, CH*H*), 1.43–0.98 (8 H, m, 4 × CH_2), 0.90 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 143.6 (C), 138.7 (C), 130.8 (CH), 128.3 (CH), 128.0 (CH), 127.6 (CH), 127.45 (CH), 127.37 (CH), 127.2 (CH), 125.2 (CH), 85.3 (OCH), 75.2 (NCH), 72.8 (CH_2Ph), 70.3 (OCH_2), 63.2 (NCH_2), 38.2 (CH_2), 32.7 (CH_2), 29.7 (CH_2), 22.6 (CH_2), 19.2 (CH_2), 14.0 (Me); *m*/*z* (CI) 380 (MH^+, 18%), 230 (100), 166 (60), 150 (88).

(2*R*,1′*S*)-2-(4,4-Dimethoxybutyl)-1-(1-phenylbutoxy)-2,5-dihydro-1*H*-pyrrole 8g

Obtained from the ring-closing metathesis of diene **7g** after purification by column chromatography on silica gel eluting with ether:light petroleum (1:17) as a colourless oil (23%); (Found: MH^+, 334.2394. $C_{20}H_{31}NO_3$ + H requires 334.2382); $[\alpha]_D^{25}$ −126.4 (*c* 1.25, $CHCl_3$); ν_{max}(film)/cm^{-1} 3063, 3022, 2955, 2930, 2868, 2822, 1450, 1383, 1363, 1194, 1127, 1071, 1050, 1020, 953, 907, 758, 697; δ_H (400 MHz; $CDCl_3$) *major diastereoisomer* 7.29 (5 H, m, ArH), 5.72 (2 H, m, CH=CH), 4.57 (1 H, t, *J* 7.5, C*H*$(OMe)_2$), 4.15 (1 H, t, *J* 5.8, OC*H*CH_2), 3.94 (1 H, dd, *J* 5.8, 1.1, NC*H*H), 3.78 (2 H, m, NCH*H*, NCH), 3.26 (3 H, s, CH(O*Me*)(O*Me*)), 3.25 (3 H, s, CH(OMe)(OMe)), 1.89–0.97 (10 H, m, OCHC$H_2C$$H_2$, $CH_2CH_2CH_2$), 0.90 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) *major diastereoisomer* 143.7 (C), 130.7 (CH), 128.0 (CH), 127.3 (CH), 127.2 (CH), 125.4 (CH), 104.4 (CH), 85.2 (CH), 75.1 (CH), 63.1 (CH_2), 52.6 (OMe), 52.5 (OMe), 32.7 (CH_2), 38.2 (CH_2), 32.5 (CH_2), 21.1 (CH_2), 19.3 (CH_2), 14.0 (Me); *m*/*z* (CI) 334 (MH^+, 8%), 302 (100), 170 (23), 152 (26), 133 (5), 120 (7).

(2*R*,1′*S*)-2-Propyl-1-(1-phenylbutoxy)-1,2,3,6-tetrahydropyridine 8h

Obtained from the ring-closing metathesis of diene **7h** after purification by column chromatography on silica gel eluting with ether:light petroleum (1:50) as a colourless oil (90%); (Found: MH^+, 274.2170. $C_{18}H_{27}NO$ + H requires 274.2171); $[\alpha]_D^{25}$ −100.8 (*c* 1.21, $CHCl_3$); ν_{max}(film)/cm^{-1} 3058, 3027, 2955, 2925, 2868, 2822, 1690, 1655, 1496, 1450, 1378, 1194, 1096,

1015, 907, 758, 696, 656; δ_H (400 MHz; $CDCl_3$) 7.30 (5 H, m, ArH), 5.72 (1 H, m, C*H*=CH), 5.50 (1 H, m, CH=C*H*), 4.55 (1 H, t, *J* 6.5, OCH), 3.24 (2 H, br s, NCH_2), 2.79 (1 H, m, NCH), 2.25–1.85 (3 H, m, CH_2, CH*H*), 1.78–1.50 (2 H, m, C*H*H, CH*H*), 1.44–1.13 (5 H, m, CH*H*, 2 × CH_2), 0.90 (6 H, t, *J* 7.3, 2 × Me); δ_C (100 MHz; $CDCl_3$) 143.5 (C), 128.0 (CH), 127.4 (CH), 127.2 (CH), 125.1 (=CH), 123.7 (=CH), 85.0 (OCH), 60.2 (NCH), 53.9 (NCH_2), 38.1 (CH_2), 34.0 (CH_2), 27.2 (CH_2), 19.5 (CH_2), 19.3 (CH_2), 14.2 (Me), 14.1 (Me); *m*/*z* (CI) 274 (MH^+, 90%), 166 (15), 150 (45), 126 (100).

(2*R*,1′*R*)-2-Phenyl-1-(1-phenylbutoxy)-1,2,3,6-tetrahydropyridine 8i

Obtained from the ring-closing metathesis of diene **7i** as a colourless oil (53%); (Found: M^+, 307.1934. $C_{21}H_{25}NO$ requires 307.1936); $[\alpha]_D^{25}$ +85.5 (*c* 2.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3062, 3031, 2958, 2951, 2871, 2815, 1494, 1454, 757; δ_H (400 MHz; $CDCl_3$) 7.55–6.90 (10 H, m, ArH), 5.86 (1 H, m, =CH), 5.68 (1 H, m, =CHCH_2N), 4.20 (1 H, dd, *J* 4.9, 9.8, OCH), 3.88 (1 H, br s, NCH), 3.65 (1 H, br s, NC*H*H), 2.68–2.37 (1 H, m, NCH*H*), 1.94 (1 H, br s, NCHC*H*H), 1.63 (1 H, m, NCHCH*H*), 1.31–0.85 (4 H, m, 2 × CH_2), 0.84 (3 H, t, *J* 5.1, Me); δ_C (100 MHz; $CDCl_3$) 141.7 (C), 128.7 (CH), 128.6 (CH), 128.5 (C), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 127.1 (CH), 124.3 (=CH), 124.0 (=CH), 84.5 (CH), 66.5 (CH), 55.8 (CH_2), 37.0 (CH_2), 34.0 (CH_2), 18.9 (CH_2), 14.1 (Me); *m*/*z* (EI) 307 (M^+, 1%), 175 (96), 133 (19), 121 (57), 105 (21), 91 (100), 77 (27).

(*S*)-1-Benzyloxycarbonyl-2-methyl-2,5-dihydro-1*H*-pyrrole 11a

Obtained from the ring-closing metathesis of diene **10a** after purification by column chromatography on silica gel eluting with ethyl acetate:light petroleum (1:10) as a colourless oil (84%); $[\alpha]_D^{16}$ +35.1 (*c* 0.57, $CHCl_3$); ν_{max}(film)/cm^{-1} 3015, 2960, 2890, 1702 (C=O), 1203, 760; δ_H (400 MHz; $CDCl_3$) *two rotamers* 7.35 (5 H, m, ArH), 5.72 (2 H, m, CH=CH), 5.17 (2 H, m, OCH_2Ph), 4.63 (1 H, m, NCH), 4.19 (2 H, m, NCH_2), 1.34 (first rotamer, 1.5 H, d, *J* 6.4, Me), 1.27 (second rotamer, 1.5 H, d, *J* 6.4, Me); δ_C (100 MHz; $CDCl_3$) *two rotamers* 154.8 (C=O), 154.4 (C=O), 137.0 (C), 136.9 (C), 132.0 (CH), 131.8 (CH), 128.5 (CH), 128.4 (CH),127.9 (CH), 127.8 (CH), 124.2 (CH), 123.9 (CH), 66.8 (OCH_2), 66.5 (OCH_2), 60.5 (CH), 59.8 (CH), 53.5 (NCH_2), 53.1 (NCH_2), 20.8 (Me), 19.8 (Me); a satisfactory mass spectrum could not be obtained.

(*R*)-1-Benzyloxycarbonyl-2-butyl-2,5-dihydro-1*H*-pyrrole 11b

Obtained from the ring-closing metathesis of diene **10b** as a colourless oil (77%); $[\alpha]_D^{20}$ −150.9 (*c* 0.53, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3057, 2934, 2902, 1685, 1463, 1255, 1084; δ_H (400 MHz; $CDCl_3$) *major rotamer* 7.33 (5 H, m, ArH), 5.75 (2 H, m, CH=CH), 5.21 (1 H, d, *J* 12.4, PhC*H*H), 5.17 (1 H, d, *J* 12.4, PhCH*H*), 4.60 (1 H, m, NCH), 4.27 (1 H, m, NC*H*H), 4.11 (1 H, dt, *J* 5.3, 2.0, NCH*H*), 1.84–1.44 (2 H, m, CH_2), 1.35–1.87 (4 H, m, 2 × CH_2), 0.89 (3 H, t, *J* 7.2, Me); *minor rotamer* 5.14 (1 H, d, *J* 12.4, PhC*H*H), 5.12 (1 H, d, *J* 12.4, PhCH*H*), 4.07 (1 H, dt, *J* 5.3, 2.0, NCH*H*), 0.84 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) *major rotamer* 154.4 (C), 137.1 (C), 130.2 (CH), 128.4 (CH), 128.2 (CH), 127.8 (CH), 124.7 (CH), 66.5 (CH_2), 64.8 (CH), 53.6 (CH_2), 32.9 (CH_2), 26.3 (CH_2), 22.8 (CH_2), 14.1 (Me); *minor rotamer* 154.8 (C), 136.9 (C), 130.1 (CH), 125.0 (CH), 66.8 (CH_2), 64.0 (CH), 54.1 (CH_2), 33.8 (CH_2), 26.6 (CH_2), 22.7 (CH_2), 14.0 (Me); a satisfactory mass spectrum could not be obtained.

(*R*)-1-Benzyloxycarbonyl-2-phenyl-2,5-dihydro-1*H*-pyrrole 11c

Obtained from the ring-closing metathesis of diene **10c** after purification by column chromatography on silica gel eluting with ether:light petroleum (1:10) as a colourless oil (93%); $[\alpha]_D^{25}$ +120.0 (*c* 0.75, $CHCl_3$); ν_{max}(film)/cm^{-1} 3020, 2981, 2921, 1715 (C=O), 1218, 740; δ_H (400 MHz; $CDCl_3$) *major rotamer* 7.36–6.92 (10 H, m, ArH), 5.91 (1 H, m, C*H*=CHCH_2), 5.75 (1 H, dq, *J* 6.3, 2.1, CH=C*H*CH_2), 5.51 (1 H, q, *J* 2.1, PhC*H*), 5.05 (1 H, d, *J* 12.6, OC*H*H), 4.97 (1 H, d, *J* 12.6, OCH*H*), 4.78–4.31 (2 H, m, NCH_2); *minor rotamer* 7.36–6.92 (10 H, m, ArH), 5.91 (1 H, m, C*H*=CHCH_2), 5.80 (1 H, dq, *J* 6.3, 2.1, CH=C*H*CH_2), 5.59 (1 H, q, *J* 2.1, PhC*H*), 5.19 (1 H, d, *J* 12.4, OC*H*H), 5.03 (1 H, d, *J* 12.4, OCH*H*), 4.78–4.31 (2 H, m, NCH_2); δ_C (100 MHz; $CDCl_3$) *major rotamer* 154.6 (C=O), 141.8 (C), 136.5 (C), 131.2 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 127.4 (CH), 126.9 (CH), 126.7 (CH), 124.7 (CH), 124.5 (CH), 68.0 (CH), 66.8 (CH_2), 54.3 (CH_2); *minor rotamer* 154.3 (C=O), 141.0 (C), 136.9 (C), 131.0 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 127.9 (CH), 127.6 (CH), 127.4 (CH), 126.9 (CH), 126.7 (CH), 124.7 (CH), 124.5 (CH), 68.4 (CH), 66.8 (CH_2), 53.7 (CH_2); a satisfactory mass spectrum could not be obtained.

(*R*)-1-Benzyloxycarbonyl-2-propyl-1,2,3,6-tetrahydropyridine 11d

Obtained from the ring-closing metathesis of diene **10d** as a colourless oil (88%); (Found: M^+, 259.1568. $C_{16}H_{21}NO_2$ requires 259.1572); $[\alpha]_D^{18}$ +24.5 (*c* 2.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3035, 2958, 2931, 2871, 1699, 1421, 1388, 1234, 1116, 1093; δ_H (400 MHz; $CDCl_3$) 7.34 (5 H, m, ArH), 5.70 (1 H, m, =CH), 5.62 (1 H, br s, =CH), 5.17 (1 H, d, *J* 12.5, C*H*HO), 5.14 (1 H, d, *J* 12.5, CH*H*O), 4.39 (2 H, m, NCH_2), 3.53 (1 H, br d, *J* 20, NCH), 2.41 (1 H, br d, *J* 17.2, C*H*HCH=), 1.89 (1 H, br d, *J* 17.2, CH*H*CH=), 1.44 (1 H, m, C*H*H), 1.24 (3 H, m, CH*H*, CH_2), 0.91 (3 H, br s, Me); δ_C (100 MHz; $CDCl_3$) 155.6 (C), 137.0 (C), 128.4 (CH), 127.9 (CH), 127.8 (CH), 123.3 (CH), 122.9 (CH), 66.9 (CH_2), 48.3 (CH), 39.9 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 19.5 (CH_2), 14.0 (Me); *m*/*z* (EI) 259 (M^+, 0.3%), 216 (14), 172 (19), 112 (7), 91 (100), 65 (11), 55 (18).

(*S*)-1-Benzyloxycarbonyl-2-(4-methoxyphenyl)-1,2,3,6-tetrahydropyridine 11e

Obtained from the ring-closing metathesis of diene **10e** as a colourless oil (91%); (Found: M^+, 323.1514. $C_{20}H_{21}NO_3$ requires 323.1521); $[\alpha]_D^{18}$ −95.4 (*c* 1.3, $CHCl_3$); ν_{max} (film)/cm^{-1} 3035, 2954, 2935, 2900, 2836, 1697, 1610, 1513, 1419, 1309, 1249, 1037; δ_H (300 MHz; $CDCl_3$) 7.33 (7 H, m, ArH), 6.83 (2 H, AA′BB′, *J* 8.3, ArH), 5.92 (1 H, br s, =CH), 5.67 (1 H, m, =CH), 5.64 (1 H, m, NCH), 5.24 (1 H, d, *J* 12.3, C*H*HO), 5.20 (1 H, d, *J* 12.3, CH*H*O), 4.32 (1 H, br d, *J* 18.1, NC*H*H), 3.79 (3 H, s, MeO), 3.40 (1 H, br d, *J* 18.1, NCH*H*), 2.72 (1 H, m, C*H*HC=), 2.54 (1 H, m, CH*H*C=); δ_C (75 MHz; $CDCl_3$) 158.6 (C), 155.6 (C), 136.8 (C), 132.6 (C), 128.5 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 124.2 (CH), 123.6 (CH), 113.7 (CH), 67.2 (CH_2), 55.2 (Me), 50.4 (CH), 40.3 (CH_2), 27.8 (CH_2); *m*/*z* (CI) 323 (M^+, 2%), 232 (31), 202 (14), 188 (33), 134 (17), 91 (100), 65 (9).

(*R*)-1-Benzyloxycarbonyl-2-(4-benzyloxypropyl)-1,2,3,6-tetrahydropyridine 11f

Obtained from the ring-closing metathesis of diene **10f** after purification by column chromatography on silica gel eluting with ether:light petroleum (1:2) as a colourless oil (98%, 87% ee); (Found: MH^+, 366.2067. $C_{23}H_{27}NO_3$ + H requires 366.2069); $[\alpha]_D^{24}$ +13.3 (*c* 1.05, $CHCl_3$); ν_{max}(film)/cm^{-1} 3032, 2930, 2853, 1701 (CO), 1419, 1337, 1224, 1112, 1025, 743, 692; δ_H (400 MHz; $CDCl_3$) 7.33 (10 H, m, ArH), 5.77–5.56 (2 H, m, CH=CH), 5.14 (2 H, AB, *J* 12.4, CH_2Ph), 4.54–4.23 (4 H, m, CH_2Ph, NCH, OC*H*H), 3.61–3.37 (3 H, m, NCH_2, OCH*H*), 2.44 (1 H, m, C*H*H), 1.93 (1 H, m, CH*H*), 1.75–1.44 (4 H, m, 2 × CH_2); δ_C (100 MHz; $CDCl_3$) 155.6 (CO), 138.6 (C), 136.9 (C), 128.5 (CH), 128.4 (CH), 128.0 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 123.3 (=CH), 122.8 (=CH), 72.9 (CH_2), 70.0

(NCH_2, first rotamer), 69.9 (NCH_2, second rotamer), 67.0 (CH_2), 48.5 (NCH, first rotamer), 48.0 (NCH, second rotamer), 39.8 (CH_2), 29.3 ($NCHCH_2$, first rotamer), 28.7 ($NCHCH_2$, second rotamer), 28.0 (CH_2), 26.6 (CH_2); *m/z* (ES) 753 (2*M* + Na, 50%), 748 (2*M* + NH_4, 20), 388 (*M* + Na, 100), 383 (40), 366 (MH^+, 25).

(*R*)-1-Benzyloxycarbonyl-2-phenyl-2,3,4,7-tetrahydro-1*H*-azepine 11g

Obtained from the ring-closing metathesis of diene **10g** as a colourless oil (65%); (Found: MH^+, 308.1655. $C_{20}H_{21}NO_2$ + H requires 308.1650); $[\alpha]_D^{22}$ +89.3 (*c* 1.2, $CHCl_3$); ν_{max} (film)/cm^{-1} 3062, 3027, 2933, 1699, 1456, 1448, 1415, 1236, 1205, 1116; δ_H (300 MHz; $CDCl_3$) 7.31 (10 H, m, ArH), 5.78 (1 H, m, =CH), 5.74 (1 H, m, =CH), 5.54 (1 H, dd, *J* 12.1, 5.2, NCH), 5.18 (2 H, s, CH_2O), 4.26 (1 H, dd, *J* 17.5, 5.8, NC*H*H), 3.70 (1 H, br d, *J* 17.5, NCH*H*), 2.39–2.18 (4 H, m, 2 × CH_2); δ_C (100 MHz; $CDCl_3$) 156.9 (C), 141.9 (C), 137.1 (C), 131.6 (CH), 128.5 (CH), 128.4 (CH), 127.9 (CH), 127.6 (CH), 127.5 (CH), 127.1 (CH), 126.2 (CH), 67.1 (CH_2), 59.2 (CH), 41.0 (CH_2), 31.8 (CH_2), 26.9 (CH_2); *m/z* (CI) 308 (MH^+, 34%), 174 (100), 106 (22), 91 (4).

(*S*)-1-Benzyloxycarbonyl-2-propyl-1,2,3,4,5,8-hexahydroazocine 11h

Obtained from the ring-closing metathesis of diene **10h** as a colourless oil (19%); (Found: M^+, 287.1886. $C_{18}H_{25}NO_2$ requires 287.1885); $[\alpha]_D^{20}$ +77.4 (*c* 1.24, $CHCl_3$); ν_{max} (film)/cm^{-1} 3012, 2956, 2931, 2873, 1697, 1454, 1415, 1236, 1213, 1099, 696; δ_H (400 MHz; $CDCl_3$) 7.32 (5 H, m, ArH), 5.56 (2 H, m, 2 × =CH), 5.19 (1 H, d, *J* 12.7, PhC*H*H), 5.14 (1 H, d, *J* 12.7, PhCH*H*), 4.44–4.17 (2 H, m, NCH_2), 3.53 (1 H, dd, *J* 4.5, 2.3, NCH), 2.33 (1 H, m, C*H*HCH=), 1.87 (1 H, m, CH*H*CH=), 1.53–1.21 (8 H, m, 4 × CH_2), 0.91 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 156 (C), 137.3 (C), 129.1 (CH), 128.3 (CH), 128.0 (CH), 127.4 (CH), 126.5 (CH), 126.1 (CH), 66.7 (CH_2), 56.1 (CH), 49.9 (CH_2), 36.4 (CH_2), 28.1 (CH_2), 22.9 (CH_2), 19.2 (CH_2), 14.1 (Me); *m/z* (EI) 287 (M^+, 2%), 244 (3), 200 (16), 152 (6), 116 (24), 91 (100).

Reactions of nitrogen heterocycles

(2*R*,1′*S*)-2-Isobutyl-1-(1-phenylbutoxy)pyrrolidine 12

Dihydropyrrole **8c** (45 mg, 0.22 mmol) was dissolved in methanol (7 mL) and hydrogenated over palladium on charcoal (6 mg, 10% w/w) for 3 h. The mixture was filtered through Celite and the solvent was removed in vacuo to give the title compound after purification by column chromatography on silica gel eluting with ether : light petroleum (1 : 30) as a colourless oil (33 mg, 74%); (Found: MH^+, 276.2326. $C_{18}H_{29}NO$ + H requires 276.2327); $[\alpha]_D^{25}$ −37.8 (*c* 0.90, $CHCl_3$); ν_{max}(film)/cm^{-1} 3063, 3027, 2945, 2930, 2863, 1465, 1450, 1363, 1102, 1055, 1025, 912, 753, 697; δ_H (400 MHz; $CDCl_3$) 7.28 (5 H, m, ArH), 4.58 (1 H, t, *J* 6.6, OCH), 2.92 (1 H, m, NCH), 2.76 (1 H, m, NC*H*H), 2.59 (1 H, m, NCH*H*), 1.86 (2 H, m, OCHC*H*H, NCHC*H*H), 1.71–1.37 (5 H, m, C*H*Me_2, OCHCH*H*, NCHCH*H*, NCH_2CH_2), 1.26 (4 H, m, $NCHCH_2$, CH_2Me), 0.95 (3 H, d, *J* 6.4, CH*Me*Me), 0.91 (6 H, m, CHMe*Me*, CH_2*Me*); δ_C (100 MHz; $CDCl_3$) 144.0 (C), 128.0 (CH), 127.15 (CH), 127.09 (CH), 85.1 (OCH), 66.5 (NCH), 56.0 (CH_2), 43.2 (CH_2), 38.8 (CH_2), 27.2 (CH_2), 26.0 (CH), 23.8 (Me), 22.4 (Me), 20.2 (CH_2), 19.3 (CH_2), 14.1 (Me); *m/z* (ES) 276 (MH^+, 100%), 144 (100).

(2*R*,1′*S*)-1-(1-Phenylbutoxy)-2-propylpiperidine 13

Tetrahydropyridine **8h** (33 mg, 0.12 mmol) was dissolved in methanol (7 mL) and hydrochloride acid (4 M in dioxane) (1 mL) and hydrogenated over palladium on charcoal (8 mg, 10% w/w) for 4 h. The catalyst was filtered through Celite and the solvent was removed *in vacuo* to give the title compound after purification by column chromatography on silica gel eluting with ether:light petroleum (1:30) as a colourless oil (30 mg, 91%); (Found: MH^+, 276.2328. $C_{18}H_{29}NO$ + H requires 276.2327); $[\alpha]_D^{28}$ −74.5 (*c* 1.06, $CHCl_3$); ν_{max}(film)/cm^{-1} 3032, 2955, 2925, 2863, 2822, 1450, 1368, 1091, 1030, 758, 697; δ_H (400 MHz; $CDCl_3$) *major diastereoisomer* 7.26 (5 H, m, ArH), 4.50 (1 H, t, *J* 7.0, OCH), 3.41 (1 H, br, NC*H*H), 2.49 (1 H, br, NCH*H*), 2.28 (1 H, br, NCH), 1.99 (2 H, m, C*H*H), 1.70–1.15 (13 H, m, CH*H*, 6 × CH_2), 0.90 (3 H, t, *J* 7.3, Me), 0.73 (3 H, br, Me); δ_C (100 MHz; $CDCl_3$) *major diastereoisomer*142.1 (C), 127.9 (CH), 127.6 (CH), 127.2 (CH), 84.5 (OCH), 66.7 (NCH), 57.6 (CH_2), 37.5 (CH_2), 35.1 (CH_2), 30.5 (CH_2), 25.8 (CH_2), 23.8 (CH_2), 19.1 (CH_2), 18.6 (CH_2), 14.3 (Me), 14.1 (Me); *m/z* (CI) 276 (MH^+, 56%), 166 (17), 150 (37), 128 (100).

(*R*)-1-(*tert*-Butoxycarbonyl)-2-phenylpiperidine 14

Dehydropiperidine **8i** (0.100 g, 0.326 mmol) was dissolved in a solution of methanol:acetic acid (1:1, 10 mL) and hydrogenated over palladium on charcoal (25% w/w) for 24 h. The catalyst was filtered and the solvent was removed *in vacuo*. The residue was basified with aqueous saturated sodium hydrogen carbonate solution and exhaustively extracted with dichloromethane (5 × 5 mL). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was dissolved in dichloromethane (5 mL) and di-*tert*-butyl dicarbonate (0.213 g, 0.978 mmol) and DMAP (cat.) were added and the reaction mixture stirred overnight. Aqueous saturated sodium bicarbonate solution was added and the mixture stirred for 10 min. The mixture was extracted with dichloromethane (3 × 5 mL) and the combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The residue was purified by column chromatography eluting with ether:light petroleum (1:10) to give the *title compound* as colourless solid (23%); mp 78–80 °C (from *n*-hexane); (Found: C, 73.1; H, 9.0; N, 5.0. $C_{16}H_{23}NO_2$ requires C, 73.5; H, 8.9; N, 5.4%); (Found: M^+, 261.1732. $C_{16}H_{23}NO_2$ requires 261.1729); $[\alpha]_D^{25}$ +83.7 (*c* 0.98, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 2964, 2937, 2859, 1681, 1415, 1159; δ_H (300 MHz; $CDCl_3$) 7.29 (5 H, m, ArH), 5.42 (1 H, br d, *J* 3.8, NCH), 4.05 (1 H, br d, *J* 13.4, NC*H*H), 2.77 (1 H, NCH_2CHH), 2.31 (1 H, m, NCH*H*), 1.88 (1 H, m, NCH_2CHH), 1.57 (4 H, m, 2 × CH_2), 1.47 (9 H, br s, CMe_3); δ_C (75 MHz; $CDCl_3$) 155.7 (C), 140.4 (C), 128.5 (CH), 126.5 (CH), 126.3 (CH), 79.5 (C), 53.2 (CH), 40.1 (CH_2), 28.5 (Me), 28.1 (CH_2), 25.5 (CH_2), 19.4 (CH_2); *m/z* (EI) 261 (M^+, 7%), 205 (61), 188 (16), 160 (50), 144 (11), 128 (29), 118 (19), 83 (100), 57 (62).

(*R*)-2-Phenylpiperidine 15

(*R*)-1-(*tert*-Butoxycarbonyl)-2-phenylpiperidine **14** (0.020 g, 0.077 mmol) was dissolved in dichloromethane (1 mL) and treated with HCl in ether (1 M, 0.76 mL, 0.766 mmol). After 30 min the reaction mixture was basified with aqueous sodium hydroxide solution (1 M) to pH 14 and extracted with dichloromethane (5 × 5 mL). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated to give the *title compound* as a colourless oil (82%); $[\alpha]_D^{21}$ +43.5 (*c* 0.23, CH_2Cl_2) (lit.,[28] $[\alpha]_D^{22}$ +49.5 (*c* 0.2, CH_2Cl_2); δ_H (400 MHz; $CDCl_3$) 7.30 (5 H, m, ArH), 3.61 (1 H, br d, *J* 8.9, NCH), 3.18 (1 H, br d, *J* 11.7, NC*H*H), 2.85 (1 H, m, NCH*H*), 1.90 (1 H, br d, *J* 10.0, C*H*H), 1.81 (1 H, br d, *J* 12.2, C*H*H), 1.68–1.26 (5 H, m, 2 × CH*H*, CH_2, NH); δ_C (100 MHz; $CDCl_3$) 144.0 (C), 128.4 (CH), 127.1 (CH), 126.7 (CH), 62.3 (CH), 47.7 (CH_2), 34.7 (CH_2), 25.7 (CH_2), 25.3 (CH_2).

(*R*)-2-Propylpiperidine hydrochloride [(−)-coniine hydrochloride] 16

Dehydropiperidine **11d** (0.023 g, 0.089 mmol) was dissolved in methanol (3 mL) and hydrogenated over palladium on charcoal

(10% w/w) for 1.5 h. The catalyst was filtered and the filtrate was treated with HCl in ether (1 M, 0.89 mL, 0.890 mmol) for 5 min. The solvent was removed *in vacuo* and the residue triturated with ether to give the *title compound* as a colourless solid (76%); mp 212–213 °C (from CH_2Cl_2–*n*-hexane) (lit.,[35] 217–218 °C); $[\alpha]_D^{22}$ −4.5 (*c* 0.66, EtOH) (lit.,[35] $[\alpha]_D^{24}$ −6.3 (*c* 0.62, EtOH); δ_H (400 MHz; $CDCl_3$) 9.44 (1 H, br s, NH), 9.18 (1 H, br s, NH), 3.46 (1 H, m, CHN), 2.93 (1 H, m, CHN), 2.81 (1 H, m, CHN), 2.16–1.41 (10 H, m, 5 × CH_2), 0.94 (3 H, t, *J* 7.3, Me); δ_C (100 MHz; $CDCl_3$) 57.2 (CH), 44.8 (CH_2), 35.4 (CH_2), 28.2 (CH_2), 22.4 (CH_2), 22.3 (CH_2), 18.6 (CH_2), 13.7 (Me).

(*S*)-2-(4-Methoxyphenyl)piperidine 17

Dehydropiperidine **11e** (0.042 g, 0.137 mmol) was dissolved in methanol (53 mL) and hydrogenated over palladium on charcoal (10% w/w) for 3 h. The catalyst was filtered and the solvent was removed *in vacuo* to give the *title compound* as a colourless oil (76%); (Found: MH^+, 192.1389. $C_{12}H_{17}NO$ + H requires 192.1388); $[\alpha]_D^{25}$ −73.1 (*c* 0.41, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3385, 2933, 2852, 1610, 1513, 1452, 1303, 1243, 1037; δ_H (300 MHz; $CDCl_3$) 7.27 (2 H, AA′BB′, *J* 8.3, ArH), 6.84 (2 H, AA′BB′, *J* 8.3, ArH), 3.78 (3 H, s, OMe), 3.53 (1 H, dd, *J* 2.4, 10.1, NCH), 3.17 (1 H, m, NC*H*H), 2.77 (1 H, dt, *J* 11.2, 2.8, NCH*H*), 2.10 (1 H, br s, NH), 1.77–1.47 (6 H, m, 3 × CH_2); δ_C (75 MHz; $CDCl_3$) 158.6 (C), 137.7 (C), 127.7 (CH), 113.7 (CH), 61.7 (CH), 55.2 (CH), 47.8 (CH_2), 34.9 (CH_2), 25.8 (CH_2), 25.4 (CH_2); *m*/*z* (CI) 192 (MH^+, 4%), 162 (43), 148 (27), 134 (100), 121 (29), 91 (48), 77 (38).

(*R*)-2-Phenylazepane 18

Dehydropiperidine **11g** (0.045 g, 0.147 mmol) was dissolved in methanol (5 mL) and hydrogenated over palladium on charcoal for 3 h. The catalyst was filtered and the was removed *in vacuo* to give the *title compound* as a colourless oil (85%); $[\alpha]_D^{25}$ +65.6 (*c* 0.64, CH_2Cl_2) (lit.,[28] $[\alpha]_D^{23}$ +62.0 (*c* 4.8, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3413, 3060, 2952, 2852, 1450, 1143; δ_H (300 MHz; $CDCl_3$) 7.29 (5 H, m, ArH), 3.75 (1 H, dd, *J* 9.6, 3.5, NCH), 3.14 (1 H, m, NC*H*H), 2.85 (1 H, m, NCH*H*), 1.98 (1 H, m, NH), 1.86–1.45 (8 H, m, 4 × CH_2); δ_C (75 MHz; $CDCl_3$) 147.1 (C), 128.4 (CH), 126.7 (CH), 126.4 (CH), 65.0 (CH), 48.3 (CH_2), 39.1 (CH_2), 30.9 (CH_2), 26.9 (CH_2), 26.2 (CH_2).

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