# Diastereoselective [2,3]-sigmatropic rearrangements of lithium *N*-benzyl-*O*-allylhydroxylamides bearing a stereogenic centre adjacent to the migration terminus

**Steven D. Bull, Stephen G. Davies,* Sara Hernández Domíngez, Simon Jones, Anne J. Price, Thomas G. R. Sellers and Andrew D. Smith**

*The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QY. E-mail: steve.davies@chemistry.ox.ac.uk*

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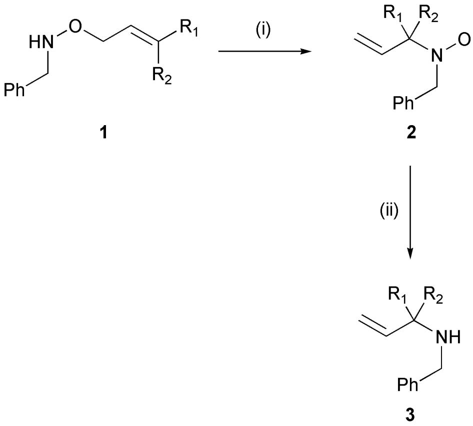
The diastereoselective [2,3]-sigmatropic rearrangements of lithium *N*-benzyl-*O*-allylhydroxylamides bearing a stereogenic centre adjacent to the migration terminus are examined. (*E*)-*N*-Benzyl-*O*-(4-phenylpent-2-enyl)-hydroxylamine rearranges in 30% de to afford *syn*-(3*RS*,4*RS*)-3-(*N*-benzyl-*N*-hydroxy)-4-phenylpent-1-ene as the major diastereoisomer, consistent with the rearrangement proceeding under moderate steric control. Rearrangements of both lithium (*E*)- and (*Z*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamides furnish *syn*-(1*RS*,2*RS*)-1-phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene in ≥90% and 88% de respectively, consistent with these rearrangements proceeding under chelation control.

## Introduction

Reactions that are capable of producing multiple functionalities both regio- and stereoselectively are essential for synthesis. Sigmatropic rearrangements,[1] in particular stereoselective [2,3]-sigmatropic shifts,[2] are one such class of transformations that have found extensive synthetic application.[3] Within this field, previous investigations from our laboratory have shown that, upon treatment with *n*-BuLi in THF, a range of *N*-benzyl-*O*-allylhydroxylamines **1** undergo an intramolecular [2,3]-sigmatropic rearrangement to afford *N*-benzyl-*N*-hydroxyallylamines **2**, which after subsequent reduction afford the corresponding *N*-benzyl-*N*-allylamines **3** in good yield.[4] The allylic amine functionality produced in this rearrangement protocol has been recognised both for its presence in molecules of biological interest,[5] and as a synthon for the introduction of a variety of other functional groups (Scheme 1).[6]



**Scheme 1** *Reagents and conditions:* (i) *n*-BuLi, THF, −78 °C to rt; (ii) Zn, $HCl_{(aq)}$, 80 °C.

Due to the expanding interest in the stereoselective synthesis of such compounds,[7] investigations concerning the rearrangement of chiral *N*-benzyl-*O*-allylhydroxylamines are described herein. It was envisaged that a stereogenic centre adjacent to the migration terminus could control the diastereoselectivity of the reaction, allowing the stereoselective synthesis of allylic amines (Fig. 1).

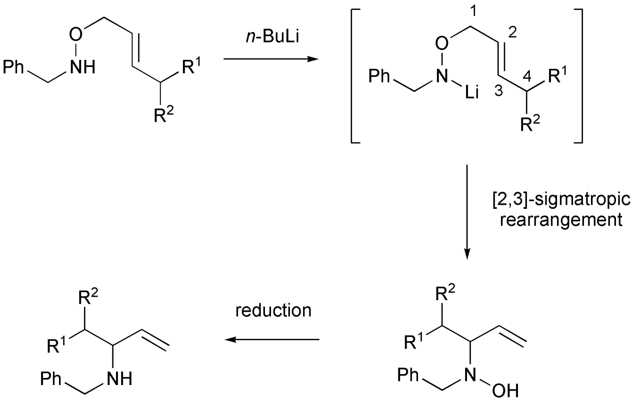


**Fig. 1**

We present herein our investigations concerning the effect of allylic C(4)-stereocentres bearing alkyl and alkoxy substituents on the diastereoselectivity of the N,O-rearrangement. Part of this work has been previously communicated.[8]

## Results

### Probing steric effects in the diastereoselective [2,3]-sigmatropic N,O-rearrangement

Initial attention was directed towards elucidating the level of diastereoselectivity imposed in the N,O-rearrangement on the basis of steric control through rearrangement of (*E*)-*N*-benzyl-*O*-(4-phenylpent-2-enyl)hydroxylamine **8**, which was prepared from racemic 2-phenylpropanal **4** in five steps. Wittig reaction of aldehyde **4** with ethyl (triphenylphosphoranylidene)acetate gave the (*E*)-α,β-unsaturated ester **5** in quantitative yield and in >95% de.[9] Subsequent DIBAL–H reduction gave the allylic alcohol **6** in 75% yield, followed by bromination with $PBr_3$ and bromide displacement with the potassium anion of benzaldehyde oxime to afford oxime **7** in 64% yield over two steps. Reduction of the C=N bond with pyridine–borane–HCl gave the desired substrate (*E*)-*N*-benzyl-*O*-(4-phenylpent-2-enyl)-hydroxylamine **8** in 78% yield (Scheme 2).

Deprotonation of (*E*)-*N*-benzyl-*O*-(4-phenylpent-2-enyl)-hydroxylamine **8** according to our established protocol[4] pro-

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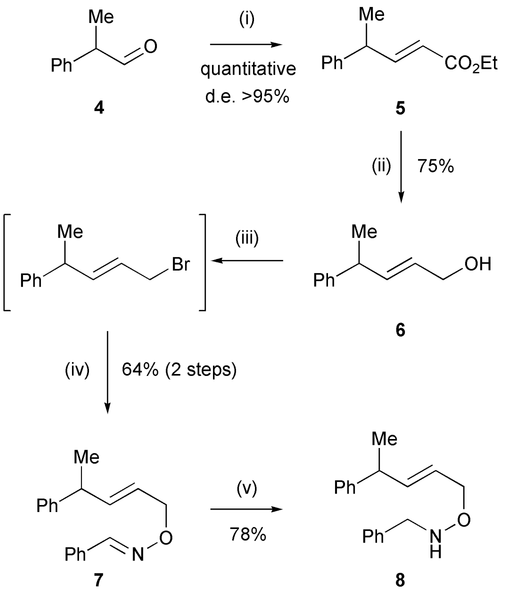
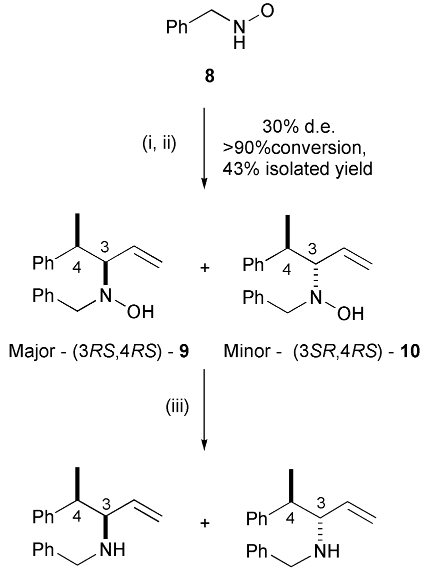


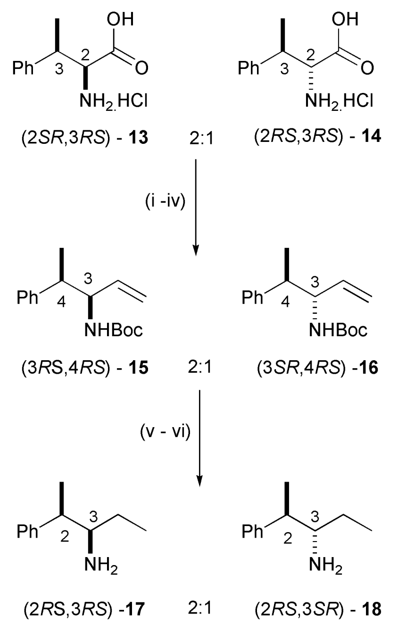
**Scheme 2** *Reagents and conditions:* (i) $Ph_3P{=}CHCO_2Et$ (1.0 eq.), THF; −78 °C to rt; (ii) DIBAL–H (2.5 eq.), $CH_2Cl_2$; −78 °C to rt; (iii) $PBr_3$, $Et_2O$, rt; (iv) PhCH=NOK, THF, rt; (v) $BH_3$–pyr, EtOH, HCl, rt.

moted the [2,3]-sigmatropic N,O-rearrangement, affording a mixture of allylic amines **9** and **10** in >90% conversion, but with only a moderate 30% diastereomeric excess.[9] In order to facilitate identification of the relative configuration within hydroxylamines **9** and **10**, separation by chromatography was attempted. However, **9** and **10** proved somewhat unstable to purification on silica, which furnished **9** and **10** as an inseparable mixture of diastereoisomers in 43% yield, much lower than that expected from the high levels of conversion apparent in the crude reaction mixture. Subsequent reduction of the mixture of hydroxylamines **9** and **10** (65 : 35, 30% de) to amines **11** and **12** was effected using Zn–HCl (aq), which also facilitated their separation by flash chromatography, affording the amines **11** and **12** in 53% (82% of theoretical) and 30% (86% of theoretical) yields respectively (Scheme 3).

The relative configurations within **11** and **12** were established *via* chemical correlation in which 2-amino-3-phenylbutanoic acid hydrochloride (commercially available[10] as a 2 : 1 mixture of (2*SR*,3*RS*)-**13** to (2*RS*,3*RS*)-**14** diastereoisomers)[11] was transformed into a mixture of the primary amines **17** and **18**. Thus, treatment of the mixture of **13** and **14** with thionyl chloride in methanol and subsequent *N*-Boc protection, followed by DIBAL–H reduction to the aldehyde and Wittig extension[12] gave a 2 : 1 ratio of *syn*-(3*RS*,4*RS*)-**15** to *anti*-(3*SR*,4*RS*)-**16** diastereoisomers of 3-(*N*-*tert*-butoxycarbonyl)-4-phenylpent-1-ene. Hydrogenation and *N*-Boc deprotection gave an authentic sample of a 2 : 1 mixture of *syn*-(2*RS*,3*RS*)- to *anti*-(2*RS*,3*SR*)-2-phenyl-3-aminopentane **17** and **18** respectively (Scheme 4).

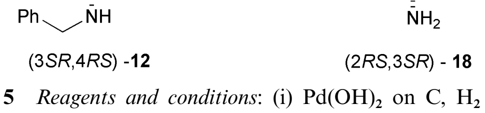


**Scheme 3** *Reagents and conditions:* (i) *n*-BuLi, THF, −78 °C then rt; (ii) $H_2O$; (iii) Zn, HCl (aq), 80 °C.



**Scheme 4** *Reagents and conditions*: (i) MeOH, $SOCl_2$, 0 °C to rt; (ii) $Boc_2O$, $NaHCO_3$, MeOH, 0 °C to rt; (iii) DIBAL–H (1.1 eq.), toluene −78 °C; (iv) $Ph_3PCH_3Br$ (1.05 eq.), *n*-BuLi, THF, −78 °C to rt; (v) $Pd(OH)_2$ on C, $H_2$ (1 atm), MeOH, rt; (vi) TFA, $CH_2Cl_2$, rt then $NaOH_{(aq)}$.

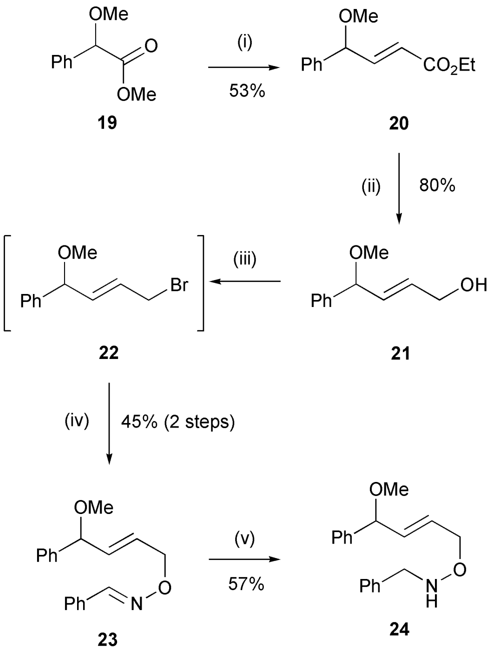
Concomitant hydrogenation and hydrogenolysis of the minor diastereoisomer (3*SR*,4*RS*)-**12** from the N,O-rearrangement of *O*-allylhydroxylamine **8** afforded *anti*-(2*RS*,3*SR*)-2-phenyl-3-aminopentane **18** (Scheme 5), which was shown by $^1H$ NMR spectroscopy to be identical to the minor component prepared from 2-amino-3-phenylbutanoic acid hydrochloride (Scheme 4). This protocol establishes unambiguously that the major diastereoisomer from the rearrangement of **8** is *syn*-(3*RS*,4*RS*)-3-(*N*-benzyl-*N*-hydroxy)-4-phenylpent-1-ene **9**, and that of the minor diastereoisomer is *anti*-(3*SR*,4*RS*)-3-(*N*-benzyl-*N*-hydroxy)-4-phenylpent-1-ene **10**.



**Scheme 5** *Reagents and conditions*: (i) $Pd(OH)_2$ on C, $H_2$ (1 atm), MeOH, rt.

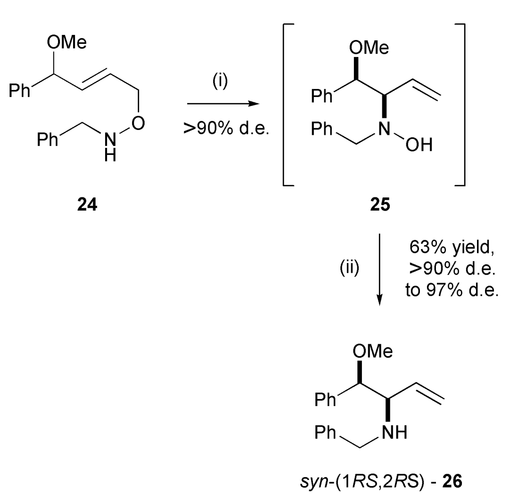
### Probing stereoelectronic and chelation effects in the diastereoselective [2,3]-sigmatropic N,O-rearrangement

In order to probe whether an alkoxy substituent would allow stereocontrol in the [2,3]-N,O-rearrangement, (*E*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamine **24** was prepared as a model substrate. Thus, methyl *O*-methylmandelate **19** was reduced with DIBAL–H in toluene at −78 °C and the resulting aldehyde treated *in situ* with ethyl (triphenylphosphoranylidene)acetate to afford the (*E*)-α,β-unsaturated ester **20** in an unoptimised 53% yield and >95% de. Reduction of ester **20** with DIBAL–H in toluene gave allylic alcohol **21** in 80% yield, which was subsequently treated with *N*-bromosuccinimide in the presence of triphenylphosphine to afford the unstable allylic bromide **22**. Treatment of the crude reaction product of the bromination reaction with the potassium anion derived from benzaldehyde oxime afforded oxime **23** in an overall 45% yield from allylic alcohol **21**. Reduction of oxime **23** with pyridine–borane–HCl gave the desired rearrangement substrate (*E*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamine **24** in 57% yield (Scheme 6).



**Scheme 6** *Reagents and conditions:* (i) DIBAL–H (1.1 eq.), toluene, −78 °C, then $Ph_3P{=}CHCO_2Et$ (1.1 eq.), −78 °C to rt; (ii) DIBAL–H (2.5 eq.), toluene, −78 °C; (iii) NBS (1.05 eq.), $Ph_3P$ (1.1 eq.), $CH_2Cl_2$, rt; (iv) PhCH=NOK, THF, rt; (v) $BH_3$–pyr, EtOH, HCl, 50 °C.

Treatment of hydroxylamine **24** with 1.1 equivalents of *n*-BuLi in THF at −78 °C, followed by warming to rt resulted in [2,3]-rearrangement, giving the required allyl amine **25** in >90% conversion and ≥90% de.[9] Zn–HCl reduction of the crude reaction mixture afforded *syn*-(1*RS*,2*RS*)-1-phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene **26** in 90% de, which was purified by chromatography furnishing *syn*-(1*RS*,2*RS*)-amine **26** in 63% yield and 97% de (Scheme 7).



**Scheme 7** *Reagents and conditions:* (i) *n*-BuLi, THF, −78 °C; (ii) Zn, HCl (aq), 80 °C.

The relative *syn*-(1*RS*,2*RS*) configuration within 1-phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene **26** was established by X-ray crystallographic analysis of its crystalline HCl salt, which unambiguously identified *syn*-(1*RS*,2*RS*)-**26** as the major diastereoisomer from the N,O-rearrangement of hydroxylamine **24** (Fig. 2).[8]

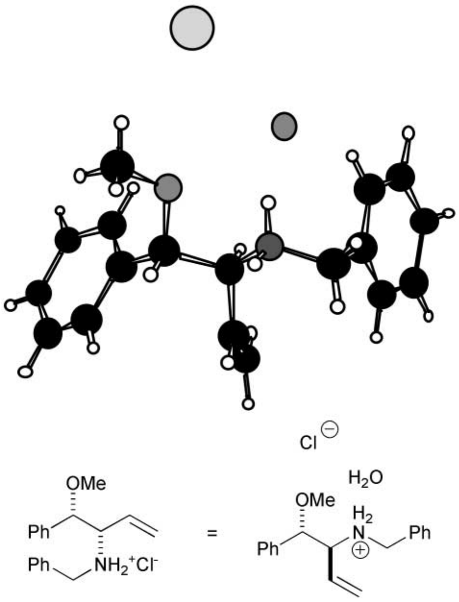
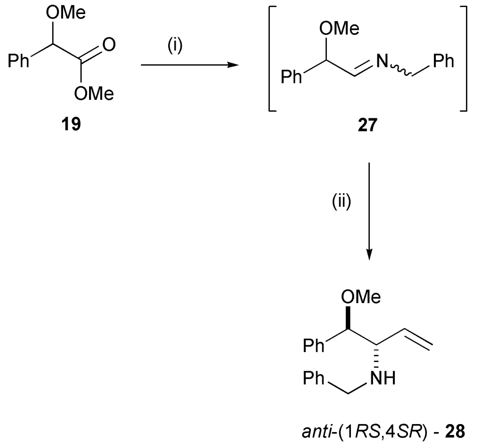


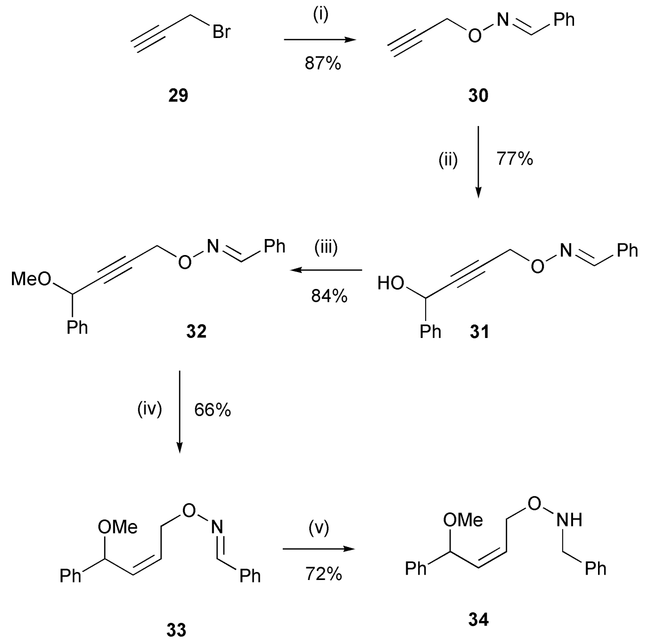
**Fig. 2** X-Ray crystal structure of hydrated *syn*-(1*RS*,2*RS*)-**26**·HCl.

The high diastereoselectivity (≥90%) observed upon rearrangement of (*E*)-hydroxylamine **24** was confirmed by the synthesis of an authentic sample of the minor *anti*-(1*RS*,2*SR*)-diastereoisomer **28** arising from the rearrangement and reduction protocol. Thus, methyl *O*-methylmandelate **19** was reduced to the corresponding aldehyde and, after *in situ* formation of the benzyl imine **27**, vinylmagnesium bromide addition afforded *anti*-(1*RS*,2*SR*)-1-phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene **28** in >95% de.[13] Comparison of the $^1$H NMR spectra from the crude reaction mixture of the Zn–HCl reduction of the crude rearrangement products allowed confirmation of the rearrangement diastereoselectivity as ≥90% de (Scheme 8).



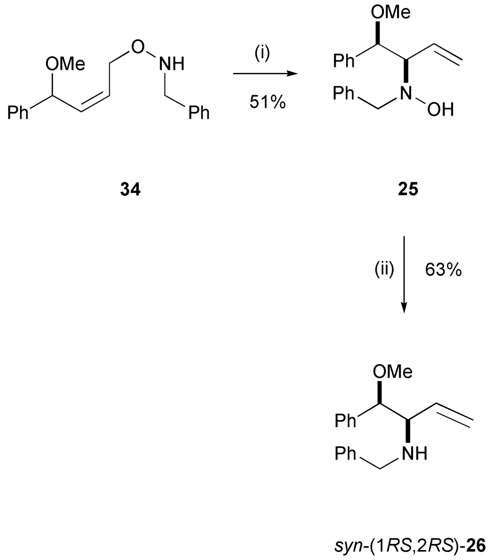
**Scheme 8** *Reagents and conditions:* (i) DIBAL–H (1.1 eq.), $CH_2Cl_2$, −78 °C then benzylamine (1.0 eq.), MeOH, −78 °C to rt; (ii) $BF_3{\cdot}Et_2O$ (3 eq.), $CH_2Cl_2$, −78 °C then vinylmagnesium bromide, −78 °C to rt.

To probe the influence of the double bond geometry in the N,O-rearrangement, the preparation and rearrangement of (*Z*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamine **34** was investigated. *O*-Alkylation of benzaldehyde oxime with propargyl bromide **29** gave the oxime **30** in 87% yield, with subsequent deprotonation and reaction with benzaldehyde affording the di-substituted alkyne **31** in 77% yield. *O*-Methylation afforded alkyne **32**, with hydrogenation with Lindlar's catalyst to the (*Z*)-alkene **33** and reduction of the imine with pyridine–borane–HCl furnishing the desired (*Z*)-amine **34** (Scheme 9).



**Scheme 9** *Reagents and conditions* (i) PhCH=NOK (1.1 eq.), THF, 0 °C to rt; (ii) LHMDS (1.1 eq.), THF, −78 °C, 30 min then PhCHO; (iii) NaH (1.1 eq.), THF, 0 °C then MeI (3 eq.), 0 °C to rt; (iv) Lindlar's catalyst, $H_2$ (4 atm), MeOH, rt; (v) $BH_3$–pyr, EtOH, 0 °C then EtOH–HCl, rt.

Treatment of (*Z*)-hydroxylamine **34** with *n*-BuLi under the standard rearrangement conditions gave a crude reaction mixture which indicated that the rearrangement had proceeded in >90% conversion and in 88% de to furnish *syn*-hydroxylamine **25**. Purification gave *syn*-**25** (identical to that formed from rearrangement of (*E*)-hydroxylamine **24**) in 98% de and in 51% yield. Further reduction of **25** with Zn–HCl furnished *syn*-(1*RS*,2*RS*)-1-phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene **26** in 98% de and 63% yield (Scheme 10).



**Scheme 10** *Reagents and conditions:* (i) *n*-BuLi, THF, −78 to rt; (ii) Zn, $HCl_{(aq)}$, 80 °C.

## Discussion

### Models for the diastereoselective N,O-rearrangement

The diastereoselectivity observed upon reaction of an acyclic C=C bond with an adjacent stereocentre have been widely investigated. Probably the most studied reaction in this field concerns 1,2-asymmetric induction for the conjugate addition of alkoxides,[14] amines,[15] carbon nucleophiles,[16] and metal amides[17] to α,β-unsaturated acceptors, with the levels of diastereoselectivity in these transformations generally being rationalised by a modified Felkin–Anh model as developed by Houk *et al.*[18] In the preferred transition state of such reactions, an allylic σ-bond is oriented antiperiplanar to the trajectory of the approaching reagent, with the conformational preference of the allylic stereocentre considered a combination of steric effects (approach *anti* to the largest allylic substituent) and stereoelectronic effects (approach *anti* to the best electron withdrawing group). Application of a modification of this model has been applied to [2,3]-sigmatropic Wittig rearrangements by Brückner,[19] and utilisation of this model for the rearrangement of (*E*)-*N*-benzyl-*O*-(4-phenylpent-2-enyl)hydroxylamine **8** predicts the predominant formation of *syn*-(3*RS*,4*RS*)-3-(*N*-benzyl-*N*-hydroxy)-4-phenylpent-1ene **11** (Fig. 3). To minimise steric interactions in the transition state, the allylic stereocentre will preferentially adopt a conformation whereby the nitrogen atom will attack *anti*- to the large C(4) phenyl substituent, with the C(4) hydrogen atom oriented onto the inside of the transition state model to minimise allylic strain. Rearrangement with the nitrogen *anti*-to the C(4) methyl group furnishes the minor *anti*-(3*SR*,4*RS*)-diastereoisomer **12**.

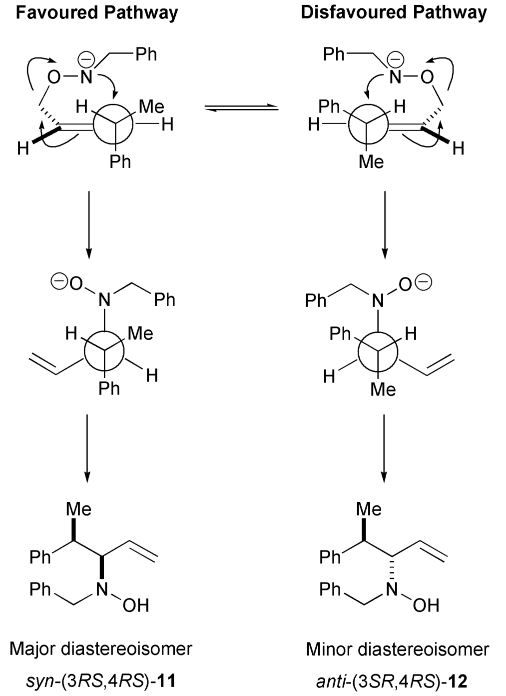


**Fig. 3** Steric control of diastereoselectivity.

Further application of this model to the rearrangements of (*E*)- and (*Z*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)-hydroxylamines **24** and **34** respectively predicts that these rearrangement processes would occur under stereoelectronic control. In this scenario, rearrangement of the lithium anion of (*E*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamine **24** would proceed *via* attack of the nitrogen atom *anti*- to the electron withdrawing methoxy substituent, giving rise to the *anti*-(1*SR*,2*RS*) diastereoisomer **28** (Fig. 4).

As the major diastereoisomer from rearrangement of **24** is actually the *syn*-(1*RS*,2*RS*) diastereoisomer **25**, it is clear that this form of stereoelectronic control is not the dominat factor in

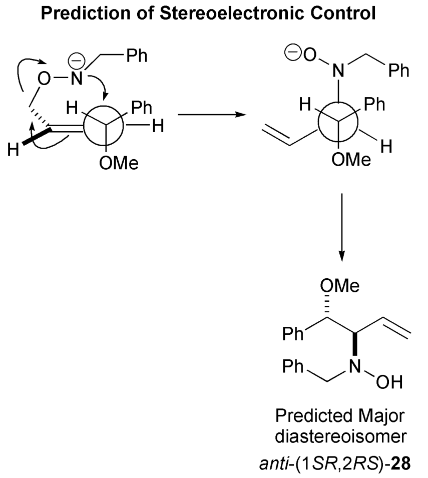


**Fig. 4** Stereoelectronic model predicts *anti*-(1*SR*,2*RS*)-**28** as the major diastereoisomer.

this rearrangement. As an alternative model, the possibility of the rearrangement pathway proceeding *via* a chelated transition state was evaluated.[20] Thus, allowing for lithium chelation between nitrogen and the C(4) oxygen substituent, a prediction for preferential attack onto the alkene functionality *syn* to the C(4)-OMe substituent, furnishing the observed *syn*-(1*RS*,2*RS*) diastereoisomer **25** can be made. Application of this model to the rearrangement of (*Z*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamine **34** also predicts the predominant formation of the *syn*-(1*RS*,2*RS*) diastereoisomer **25** (Fig. 5).[21]

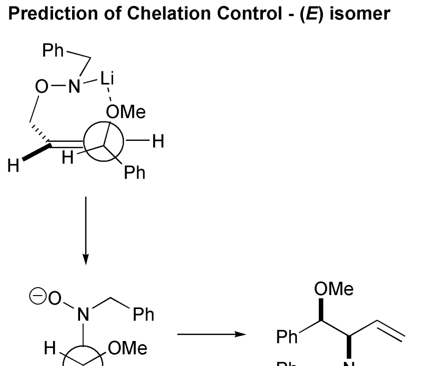


**Fig. 5** Chelation model predicts *syn*-(1*RS*,2*RS*)-**25** as the major diastereoisomer.

In conclusion, we have demonstrated that the diastereoselective [2,3]-sigmatropic rearrangements of lithium *N*-benzyl-*O*-allylhydroxylamides bearing a stereogenic centre adjacent to the migration terminus can proceed with high levels of diastereoselectivity. (*E*)-*N*-Benzyl-*O*-(4-phenylpent-2-enyl)hydroxylamine rearranges to afford *syn*-(3*RS*,4*RS*)-3-(*N*-benzyl-*N*-hydroxy)-4-phenylpent-1-ene as the major diastereoisomer in 30% de, consistent with the rearrangement proceeding under moderate steric control. Rearrangements of both (*E*)- and (*Z*)-*N*-benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamines furnish *syn*-(1*RS*,2*RS*)-1-phenyl-1-methoxy-3-*N*-benzylaminobut-3-ene with ≥90% and 88% de respectively, consistent with the rearrangement proceeding under chelation control. Current investigations within our laboratory are directed toward probing enantioselective [2,3]-sigmatropic N,O-rearrangements, and the application of this methodology to natural product synthesis.

## Experimental

### General experimental

Melting points were determined using a Gallenkamp hot stage apparatus, and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Paragon 1000 Fourier transform spectrometer. NMR spectra were recorded using Bruker DPX 400 ($^1$H 400 MHz, $^{13}$C 100 MHz), or Varian Gemini 200 ($^1$H 200 MHz, $^{13}$C 50 MHz) spectrometers. Chemical shifts ($\delta$) were recorded in ppm, coupling constants ($J$) were recorded in Hertz. Chemical shifts were referenced to residual protonated solvent. Spectra were recorded at rt unless otherwise stated. Assignment of carbon spectra was aided by DEPT editing. Low resolution mass spectra were recorded using a VG MASSLAB 20–250 spectrometer. High resolution mass spectra were obtained by Mr R. Procter using a VG Autospec spectrometer. Elemental analyses were obtained by Mrs Anne Douglas of the Inorganic Chemistry Laboratory, University of Oxford. Column chromatography was performed using silica (Merck, 70–320 mesh). TLC was performed on aluminium backed Kieselgel 60 F254 plates (Merck). Plates were developed using either a UV lamp (254 nm), 10% phosphomolybdic acid in ethanol, or $KMnO_4$ (1% solution in 2% aqueous acetic acid, containing 7% potassium carbonate). Benzaldehyde was distilled immediately prior to use from calcium hydride. THF was distilled from sodium benzophenone ketyl; $CH_2Cl_2$ was distilled from calcium hydride. All other solvents were used as supplied, without further purification. All yields quoted represent isolated yields. LHMDS was used as a commercially available 1.0 M solution in THF

**(*E*)-Ethyl 4-phenylpent-2-enoate 5.** 2-Phenylpropanal **4** (4.0 g, 3.96 mL, 29.9 mmol) was added dropwise to a stirred solution of $Ph_3P{=}CHCOOEt$ (10.4 g, 29.9 mmol) in THF (100 mL) at −78 °C and stirred for 1 h before warming to rt. After 72 h, aq sat $NH_4Cl$ (50 mL) was added, and the resultant solution extracted with EtOAc (3 × 50 mL), washed with sat brine (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. The resulting white solid was taken up in ice-cold petrol and filtered to remove $Ph_3PO$. Concentration *in vacuo* gave **5** {5.96 g, quantitative yield, >95% (*E*)} as a yellow oil which was utilised for further reactions without further purification although a small portion was purified for characterisation by column chromatography {10% EtOAc–petrol (40 : 60)} giving a pale yellow oil. $\nu_{max}$/cm$^{-1}$ (film) 2976 (m, C–H), 1718 (s, C=O), 1650 (m, C=C), 1452 (m, C=C aromatic); $\delta_H$ (400 MHz, $CDCl_3$) 1.28 (3H, t, $J$ 7.1, $CH_2CH_3$), 1.44 (3H, d, $J$ 7.1, $CHCH_3$), 3.63 (1H, m, $CHCH_3$), 4.19 (2H, q, $J$ 7.1, $OCH_2CH_3$), 5.81 (1H, d, $J$ 15.7, $CH{=}CHCOOEt$), 7.12 (1H, dd, $J$ 15.7, 6.7, $CH{=}CHCOOEt$), 7.19–7.35 (5H, m, aromatic $CH$); $\delta_C$ (50 MHz, $CDCl_3$) 14.1, 20.1 ($PhCHCH_3$ and $OCH_2CH_3$), 42.0 ($PhCH$), 60.3 ($OCH_2CH_3$), 120.2 ($CH{=}CHCOOEt$), 127.0, 127.6, 128.9 (aromatic $C$H), 143.6 (*ipso-C*), 152.9 ($CH_3CHCH{=}CH$), 167.0 ($COOEt$); *m*/*z* (APCI) 205 ($MH^+$, 100%), 177 (17%), 159 ($MH^+$ − EtOH, 45%), 131 (12%), 122 (15%), 105 (27%).

**(*E*)-4-Phenylpent-2-en-1-ol 6.** DIBAL–H (1.0 M solution in $CH_2Cl_2$, 36.8 mL, 36.8 mmol) was added dropwise to a stirred solution of **5** (3.0 g, 14.7 mmol) in $CH_2Cl_2$ (50 mL) at −78 °C and stirred for 1 h before being allowed to warm to rt overnight. $Na_2SO_4{\cdot}10H_2O$ (50 g) was added slowly and the resulting slurry stirred for a further hour and filtered through Celite®. The filtrate was diluted with further $CH_2Cl_2$ (50 mL) and washed with aq HCl (2 × 75 mL, 1 M), aq sat $NaHCO_3$ (2 × 75 mL) and sat brine (2 × 75 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {25% EtOAc–petrol (40 : 60)} gave **6** (1.78 g, 75%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 3340 (br, s, O–H), 2966 (m C–H), 1602 (w, C=C), 1452 (m, C=C aromatic): $\delta_H$ (400 MHz, $CDCl_3$) 1.40 (3H, d, *J* 7.0, C$\mathit{H}_3$), 1.58 (1H, br s, O*H*), 3.49 (1H, m, C*H*CH$_3$), 4.13 (2H, d, *J* 5.8, C$\mathit{H}_2$OH), 5.67 (1H, dt, *J* 15.4, 5.8, CH=C*H*CH$_2$), 5.89 (1H, dd, *J* 15.4, 6.7, CH=C*H*CH), 7.20–7.39 (5H, m, aromatic C*H*); $\delta_C$ (50 MHz, $CDCl_3$) 21.0 (*C*H$_3$), 41.9 (*C*HCH$_3$), 63.6 (*C*H$_2$OH), 126.4 (CH=*C*H), 127.4, 128.0, 128.7 (aromatic *C*H), 137.6 (*C*H=CH), 145.8 (*ipso-C*); *m*/*z* (APCI) 146 (10%), 145 (MH$^+$ − H$_2$O, 100%).

**Benzaldehyde (*E*)-*O*-(4-phenylpent-2-enyl)oxime 7.** $PBr_3$ (0.624 g, 0.22 mL, 2.80 mmol) was added dropwise to a stirred solution of **6** (1.0 g, 6.17 mmol) in $Et_2O$ (30 mL) at rt and was stirred for 18 h. Water (10 mL) was added slowly and the solution extracted into $Et_2O$ (3 × 30 mL), washed with aq sat $NaHCO_3$ (50 mL) and then sat brine (2 × 50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude bromide (1.23 g, 88%) as a yellow oil, which was used immediately in the next step. $\delta_H$ (200 MHz, $CDCl_3$) 1.39 (3H, d, C$\mathit{H}_3$), 3.52 (1H, m, C*H*CH$_3$), 3.98 (2H, d, C$\mathit{H}_2$Br), 5.65–6.02 (2H, m, C*H*=C*H*), 7.18–7.38 (5H, m, aromatic C*H*). KO$^t$Bu (1.22 g, 10.9 mmol) was added to a stirred solution of benzaldehyde oxime (1.32 g, 10.9 mmol) in THF (150 mL), and the mixture stirred for 30 min, after which time a solution of bromide (1.23 g, 5.45 mmol) in $Et_2O$ (10 mL) was added *via* cannula. The solution was stirred for 72 h at rt after which time aq phosphate pH 7 buffer (50 mL) was added and the resultant solution extracted into $Et_2O$ (3 × 50 mL), washed with sat brine (2 × 75 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give an orange oil. Purification by column chromatography {3% $Et_2O$–petrol (40 : 60)} afforded **7** (1.05 g, 73%) as a pale yellow oil. $\nu_{max}$/cm$^{-1}$ (film) 2966 (m, C–H), 1601 (w, C=C), 1492 (m, C=C aromatic); $\delta_H$ (400 MHz, $CDCl_3$) 1.40 (3H, d, *J* 7.0, C$\mathit{H}_3$), 3.53 (1H, m, C*H*CH$_3$), 4.68 (2H, d, *J* 6.3, C$\mathit{H}_2$O), 5.75 (1H, dt, *J* 15.5, 6.3, CH=C*H*CH$_2$O), 6.00 (1H, dd, *J* 15.5, 6.6, CH$_3$CHC*H*=CH), 7.19–7.61 (10H, m, aromatic C*H*), 8.11 (1H, s, C*H*=N); $\delta_C$ (50 MHz, $CDCl_3$) 21.0 (*C*H$_3$), 42.0 (Ph*C*HCH$_3$), 75.1 (*C*H$_2$O), 124.5 (*C*H=CH), 126.5, 127.3, 127.6, 128.7, 129.0, 130.0 (aromatic *C*H), 132.6 (*ipso-C*), 140.2 (*C*H=CH), 145.7 (*ipso-C*), 149.0 (*C*H=N); *m*/*z* (APCI) 266 (MH$^+$, 16%), 145 (100%), 123 (14%), 122 (62%), 106 (56%); HRMS calculated for $C_{18}H_{20}NO^+$: 266.1544. Found: 266.1544.

**(*E*)-*N*-Benzyl-*O*-(4-phenylpent-2-enyl)hydroxylamine 8.** Pyridine–borane complex (8 M in excess pyridine, 1.31 mL, 9.65 mmol) in EtOH (5 mL) was added to a stirred solution of **7** (1.05 g, 3.97 mmol) in EtOH (40 mL) at rt before cooling to 0 °C and the dropwise addition of 10% HCl in EtOH (15 mL) over 5 min. After stirring for a further 2 h the solution was neutralised with excess aq sat $NaHCO_3$, extracted into $CH_2Cl_2$ (3 × 50 mL), washed with aq $CuSO_4$ (2 × 50 mL, 1 M) and water (50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {20% $Et_2O$–petrol (40 : 60)} gave **8** (0.83 g, 78%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 3260 (br, N–H), 2965 (m, C–H), 1602 (w, C=C), 1494 (m, C=C aromatic), 1453 (m, C=C aromatic); $\delta_H$ (400 MHz, $CDCl_3$) 1.38 (3H, d, *J* 7.0, C$\mathit{H}_3$), 3.48 (1H, m, C*H*CH$_3$), 4.06 (2H, s, NHC$\mathit{H}_2$), 4.16 (2H, d, *J* 6.4, C$\mathit{H}_2$O), 5.58 (1H, dt, *J* 15.5, 6.4, CH=C*H*CH$_2$O), 5.68 (1H, br s, N*H*), 5.88 (1H, dd, *J* 15.5, 6.6, CH$_3$CHC*H*=CH), 7.19–7.36 (10H, m, aromatic C*H*); $\delta_C$ (50 MHz, $CDCl_3$) 21.0 (*C*H$_3$), 42.0 (Ph*C*HCH$_3$), 56.6 (Ph*C*H$_2$NH), 74.8 (*C*H$_2$O), 124.8 (*C*H=CH), 126.4, 127.5, 127.7, 128.7, 129.2 (aromatic *C*H), 137.7 (*ipso-C*), 139.8 (CH=*C*H), 145.8 (*ipso-C*); *m*/*z* (Probe CI (NH$_3$)) 269 (19%), 268 (MH$^+$, 100%), 145 (53), 106 (11), 91 (20); HRMS Calculated for $C_{19}H_{22}NO^+$: 268.1701. Found: 268.1696.

***syn*-(3*RS*,4*RS*)-3-(*N*-Benzyl-*N*-hydroxyamino)-4-phenylpent-1-ene 9 and *anti*-(3*SR*,4*RS*)-3-(*N*-benzyl-*N*-hydroxyamino)-4-phenylpent-1-ene 10.** *n*-BuLi (1.1 M, 1.5 mL, 1.65 mmol) was added to a stirred solution of **8** (400 mg, 1.50 mmol) in THF (28 mL) at −78 °C and stirred for 30 min before warming to rt over 1 h. Water (10 mL) was added slowly and the solution extracted into $Et_2O$ (3 × 30 mL), dried ($MgSO_4$), filtered and then concentrated *in vacuo*. Purification by column chromatography {10% $Et_2O$–petrol(40 : 60)–1% $Et_3N$} afforded an inseparable mixture of unstable diastereoisomers **9** and **10** (340 mg, 43%) as a colourless oil.

*syn*-(3*RS*,4*RS*)-**9**: $\delta_H$ (400 MHz, $CDCl_3$) 1.22 (3H, d, *J* 6.7, C$\mathit{H}_3$CH), 3.14–3.25 (2H, m, CH$_3$C*H* and NC*H*CH=CH$_2$), 3.68 (1H, d, *J* 13.4, NC*H*HPh), 3.93 (1H, d, *J* 13.4, NCH*H*Ph), 4.50 (1H, br s, O*H*), 5.12–5.19 (1H, m, CH=C*H*H), 5.44 (1H, d, *J* 10.3, CH=CH*H*), 6.01–6.08 (1H, m, C*H*=CH$_2$), 7.09–7.47 (10H, m, aromatic C*H*).

*anti*-(3*SR*,4*RS*)-**10**: $\delta_H$ (400 MHz, $CDCl_3$) 1.43 (3H, d, *J* 6.5, C$\mathit{H}_3$CH), 3.14–3.25 (2H, m, CH$_3$C*H* and NC*H*CH=CH$_2$), 3.74 (1H, d, *J* 13.5, NC*H*HPh), 3.99 (1H, d, *J* 13.5, NCH*H*Ph), 4.61 (1H, br s, O*H*), 4.90 (1H, d, *J* 17.4, CH=C*H*H), 5.12–5.19 (1H, m, CH=CH*H*), 5.72–5.98 (1H, m, C*H*=CH$_2$), 7.09–7.47 (10H, m, aromatic C*H*).

***syn*-(3*RS*,4*RS*)-3-(*N*-Benzylamino)-4-phenylpent-1-ene 11 and *anti*-(3*SR*,4*RS*)-3-(*N*-benzylamino)-4-phenylpent-1-ene 12.** Zinc powder (413 mg, 6.35 mmol) was added to a stirred solution of **9** and **10** (340 mg, 1.37 mmol) in aq HCl (30 mL, 1 M), and heated to 80 °C for 1 h. After cooling, the reaction mixture was made alkaline (pH 10) by the addition of aq NaOH (35 mL, 1 M) and extracted into $Et_2O$ (3 × 50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {20% $Et_2O$–petrol(40 : 60)} gave **12** (96 mg, 30%) and **11** (168 mg, 53%) as pale yellow oils.

*anti*-(3*SR*,4*RS*)-**12**: $\nu_{max}$/cm$^{-1}$ (film) 3328 (w, N–H), 3027 (m, C–H), 1603 (w, C=C), 1494 (m, C=C aromatic), 1453 (m, C=C aromatic); $\delta_H$ (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 7.1, C$\mathit{H}_3$), 2.94 (1H, m, CH$_3$C*H*), 3.14 (1H, dd, *J* 8.3, 5.8, CHC*H*NH), 3.60 (1H, d, *J* 13.6, NHC*H*HPh), 3.82 (1H, d, *J* 13.6, NHCH*H*Ph), 5.03 (1H, d, *J* 17.2, CH=C*H*H), 5.13 (1H, d, *J* 10.2, CH=CH*H*), 5.48–5.56 (1H, m, C*H*=CH$_2$), 7.19–7.31 (10H, m, aromatic C*H*); $\delta_C$ (50 MHz, $CDCl_3$) 17.0 (*C*H$_3$), 44.2 (CH$_3$*C*H), 51.0 (NH*C*H$_2$), 66.0 (NH*C*H), 117.1 (CH=*C*H$_2$), 126.5, 126.9, 128.2, 128.3, 128.5 (aromatic *C*H), 139.0 (*C*H=CH$_2$), 140.9 (*ipso-C*), 143.9 (*ipso-C*); *m*/*z* (APCI) 253 (15%), 252 (MH$^+$, 100%), 145 (96%). Calculated for $C_{18}H_{21}N$: C 86.0, H 8.4, N 5.6. Found C 85.95, H 8.4, N 5.35%.

*syn*-(3*RS*,4*RS*)-**11**: $\nu_{max}$/cm$^{-1}$ (film) 3326 (w, N–H), 3027 (m, C–H), 1603 (w, C=C), 1494 (m, C=C aromatic), 1453 (m, C=C aromatic); $\delta_H$ (400 MHz, $CDCl_3$) 1.18 (3H, d, *J* 7.0, C$\mathit{H}_3$), 2.71 (1H, m, CH$_3$C*H*), 3.03 (1H, app t, *J* 8.8, CHC*H*CH=CH$_2$), 3.52 (1H, d, *J* 13.8, NHC*H*H), 3.76 (1H, d, *J* 13.8, NHCH*H*), 5.18 (1H, d, *J* 17.1, CH=C*H*H), 5.28 (1H, d, *J* 10.1, CH=CH*H*), 5.62–5.71 (1H, m, C*H*=CH$_2$), 7.00–7.32 (10H, m, aromatic C*H*); $\delta_C$ (50 MHz, $CDCl_3$) 19.4 (*C*H$_3$), 44.3 (CH$_3$*C*H), 50.8 (NH*C*H$_2$Ph), 66.4 (NH*C*HCH=CH$_2$), 118.2 (CH=*C*H$_2$), 126.8, 128.0, 128.2, 128.4, 128.8 (aromatic *C*H), 140.0 (*C*H=CH$_2$), 140.6 (*ipso-C*), 144.5 (*ipso-C*); *m*/*z* (APCI) 253 (20%), 252 (MH$^+$, 100%), 145 (91%); HRMS Calculated for $C_{18}H_{22}N^+$: 252.1752. Found 252.1756.

***syn*-(3*RS*,4*RS*)-3-[*N*-(*tert*-Butoxycarbonyl)amino]-4-phenylpent-1-ene 15 and *anti*-(3*SR*,4*RS*)-3-*N*-(*tert*-butoxycarbonyl)-4-phenylpent-1-ene 16.** Thionyl chloride (2.41 g, 0.90 mL, 11.6 mmol) was added dropwise to a stirred solution of β-methylphenylalanine hydrochloride (1 g, 4.64 mmol, 2 : 1 *syn*-(2*SR*,3*RS*)-**13**: *anti*-(2*RS*,3*RS*)-**14**) in MeOH (20 mL) at 0 °C and allowed to warm to rt over 18 h. Concentration *in vacuo* afforded β-methylphenylalanine methyl ester hydrochloride as a white solid which was used without further purification. Di-*tert*-butyl dicarbonate (1.06 g, 4.88 mmol), followed by NaHCO$_3$ (1.49 g, 17.8 mmol) was added to a solution of the crude ester in MeOH (20 mL) cooled to 0 °C and allowed to warm to rt over 48 h. The reaction mixture was filtered through Celite® and the filtrate concentrated *in vacuo*. The resulting solid was redissolved in Et$_2$O, filtered and concentrated *in vacuo* to give the crude product as a white solid. Purification *via* column chromatography {25% Et$_2$O : petrol (40 : 60)} afforded a 2 : 1 *syn*-(2*SR*,3*RS*)- to *anti*-(2*RS*,3*RS*)-mixture of *N*-(*tert*-butoxycarbonyl)-3-methylphenylalanine methyl esters as a colourless viscous oil (0.411 g, 32% over 2 steps). $\nu_{max}$ (thin film)/cm$^{-1}$ 3365 (N–H, br), 2977 (C–H), 1714 (C=O, s br), 1454 (C=C aromatic, m); $\delta_H$ major diastereomer (400 MHz, CDCl$_3$) 1.37 (3H, m, CHC*H*$_3$), 1.41 (9H, s, C(C*H*$_3$)$_3$), 3.35 (1H, m, MeC*H*), 3.70 (3H, s, O*Me*), 4.47–4.54 (1H, m, C*H*NH), 4.80 (1H, br d, *J* 8.8, N*H*), 7.15–7.34 (5H, m, aromatic C*H*); $\delta_H$ minor diastereomer (400 MHz, CDCl$_3$) 1.37 (3H, m, CHC*H*$_3$), 1.41 (9, s, C(C*H*$_3$)$_3$), 3.19 (1H, m, MeC*H*), 3.57 (3H, s, OC*H*$_3$), 4.47–4.54 (1H, m, C*H*NH), 5.05 (1H, br, N*H*), 7.15–7.34 (5H, m, aromatic C*H*); $\delta_C$ major diastereomer (100 MHz, CDCl$_3$) 17.6 (CH*C*H$_3$), 28.2 (C*C*H$_3$), 42.1 (Me*C*H), 52.0 (*C*H$_3$O), 58.7 (NH*C*H), 79.9 (*C*Me$_3$), 127.2, 127.6, 128.5 (aromatic *C*H), 140.9 (*ipso-C*), 155.7 (*C*O$_2$Me), 172.3 (NH*C*OO$^t$Bu); $\delta_C$ minor diastereomer (100 MHz, CDCl$_3$) 16.5 (CH*C*H$_3$), 28.2 (C*C*H$_3$), 42.9 (Me*C*H), 51.9 (*C*H$_3$O), 59.0 (NH*C*H), 79.9 (*C*Me$_3$), 127.0, 127.6, 128.4 (aromatic *C*H), 141.3 (*ipso-C*), 155.1 (*C*O$_2$Me), 172.3 (NH*C*OO$^t$Bu); *m*/*z* (APCI$^+$) 249 (13%) 195 (13%), 194 (PhCH(Me)CH(NH$_4^+$)CO$_2$Me, 100%), 134 (94%), 121 (18%).

DIBAL–H (1.5 M in toluene, 1.05 mL, 1.57 mmol) was added dropwise to a stirred solution of 2 : 1 *syn*-(2*SR*,3*RS*)- to *anti*-(2*RS*,3*RS*)-*N*-(*tert*-butoxycarbonyl)-3-methylphenylalanine methyl esters (420 mg, 1.43 mmol) in toluene (20 mL) under Ar at −78 °C and stirred for 12 h at −78 °C before the dropwise addition of MeOH (5 mL). After warming to rt aq NaK[CH(OH)CO$_2$]$_2$ (20 mL, 1 M) was added and the solution was stirred for a further 1.5 h before being extracted into Et$_2$O (3 × 30 mL) and the combined organic extracts dried (MgSO$_4$), filtered and concentrated *in vacuo* to give crude aldehyde which was used without further purification. A stirred suspension of Ph$_3$PCH$_3$Br (1.07 g, 3.00 mmol) in THF (15mL) under N$_2$ was cooled to −78 °C and BuLi (1.69 M in hexanes, 1.69 mL, 2.86 mmol) was added dropwise. The solution was stirred at rt for 30 min, cooled to −78 °C and a solution of crude aldehyde in THF (10 mL) was added *via* cannula. The reaction mixture was warmed to rt and stirred for a further 4 h before the addition of water (20 mL). The organic material was extracted into Et$_2$O (3 × 30 mL), washed with sat brine (50 mL), dried (MgSO$_4$), filtered and then concentrated *in vacuo* to give the crude product as a yellow oil. Purification *via* column chromatography {15% Et$_2$O–petrol(40 : 60)} gave a 2 : 1 mixture of **15** and **16** as viscous, pale yellow oil (84 mg, 23%). $\nu_{max}$ (film)/cm$^{-1}$ 3349 (N–H, br), 2976 (C–H, m), 1703 (C=O, s), 1496 (C=C aromatic, m); $\delta_H$ major diastereomer **15** (400 MHz, CDCl$_3$) 1.29–1.33 (3H, m, C*H*$_3$CH), 1.40 (9H, s, C(C*H*$_3$)$_3$), 2.95 (1H, m, MeC*H*), 4.32–4.47 (2H, br m, N*H* and NHC*H*), 5.07–5.12 (2H, m, CH=C*H*$_2$), 5.70–5.79 (1H, m, C*H*=CH$_2$), 7.18–7.33 (5H, m, aromatic C*H*); $\delta_H$ minor diastereomer **16** (400 MHz, CDCl$_3$) 1.29–1.33 (3H, m, C*H*$_3$CH), 1.44 (9H, s, C(C*H*$_3$)$_3$), 2.95 (1H, m, MeC*H*), 4.32–4.47 (2H, br m, N*H* and NHC*H*), 5.07–5.12 (2H, m, CH=C*H*$_2$), 5.59–5.67 (1H, m, C*H*=CH$_2$), 7.18–7.33 (5H, m, aromatic C*H*); $\delta_C$ major diastereomer **15** (100 MHz, CDCl$_3$) 17.2 (*C*H$_3$CH), 28.3 ((*C*H$_3$)$_3$C), 43.8 (Me*C*H), 57.8 (*C*HN), 79.0 (*C*(CH$_3$)$_3$), 115.4 (CH=*C*H$_2$), 126.6, 128.0, 128.2 (5 × Ar*C*H), 137.1 (*C*H=CH$_2$), 142.4 (*ipso*-*C*H), 155.3 (NH*C*OO$^t$Bu); $\delta_C$ minor diastereomer **16** (100 MHz, CDCl$_3$) 17.2 (*C*H$_3$CH), 28.3 ((*C*H$_3$)$_3$C), 44.2 (Me*C*H), 57.9 (*C*HN), 79.0 (*C*(CH$_3$)$_3$), 115.5 (CH=*C*H$_2$), 126.6, 128.0, 128.3 (5 × Ar*C*H), 137.1 (*C*H=CH$_2$), 142.6 (*ipso*-*C*H), 155.3 (NH*C*OO$^t$Bu); *m*/*z* (APCI$^+$) 162 (44%, MH$_2^+$ − COO$^t$Bu), 146 (20), 145 (100, PhCH(Me)CHCH=CH$_2^+$); HRMS Calculated for C$_{16}$H$_{24}$NO$_2^+$: 262.1807. Found 262.1819.

***syn*-(2*RS*,3*RS*)-2-Phenyl-3-aminopentane 17 and *anti*-(2*RS*,3*SR*)-2-phenyl-3-aminopentane 18.** Pd(OH)$_2$ on carbon (20%, 10 mg, cat) was added to a stirred solution of **15** and **16** (62 mg, 0.238 mmol) in MeOH (5 mL) and stirred under H$_2$ (1 atm) for 18 h at rt. The crude reaction mixture was filtered through Celite® and concentrated *in vacuo*. Purification *via* column chromatography {15% Et$_2$O : petrol (40 : 60)} afforded a 2 : 1 mixture of *syn*-(2*RS*,3*RS*)-3-*N*-(*tert*-butoxycarbonyl)-1-ethyl-2-phenylpentane and *anti*-(2*RS*,3*SR*)-3-*N*-(*tert*-butoxycarbonyl)-1-ethyl-2-phenylpentane as a colourless oil (55 mg, 88%). $\nu_{max}$ (film)/cm$^{-1}$ 3351 (N–H, br), 2968 (C–H, s), 1703 (C=O, s), 1454 (C=C aromatic); $\delta_H$ major diastereomer (400 MHz, CDCl$_3$) 0.91 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 0.98–1.11 (1H, m, MeC*H*$_2$), 1.30–1.57 (13H, m, C*H*$_3$CHPh, C(C*H*$_3$)$_3$ and MeC*H*$_2$), 2.91–2.95 (1H, m, MeC*H*Ph), 3.63–3.72 (1H, m, C*H*NH), 4.16 (1H, br d, *J* 9.3, N*H*), 7.18–7.33 (5H, m, aromatic C*H*); $\delta_H$ minor diastereomer (400 MHz, CDCl$_3$) 0.85 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.30–1.57 (14H, m, C*H*$_3$CHPh, C(C*H*$_3$)$_3$ and MeC*H*$_2$), 2.91–2.95 (1H, m, MeC*H*Ph), 3.63–3.72 (1H, m, C*H*NH), 4.98 (1H, br d, *J* 9.7, N*H*), 7.18–7.33 (5H, m, aromatic C*H*); $\delta_C$ major diastereomer (100 MHz, CDCl$_3$) 10.6 (CH$_2$*C*H$_3$), 17.4 (*C*H$_3$CH$_2$), 26.0 (*C*H$_2$), 28.4 (C(*C*H$_3$)$_3$), 44.9 (Me*C*H), 56.7 (*C*HNH), 78.8 (*C*(CH$_3$)$_3$), 126.3, 128.2, 128.3 (aromatic *C*H), 142.9 (*ipso-C*), 156.0 (NH*C*=O); $\delta_C$ minor diastereomer (100 MHz, CDCl$_3$) 10.4 (CH$_2$*C*H$_3$), 19.1 (*C*H$_3$CH$_2$), 25.3 (*C*H$_2$), 28.4 (C(*C*H$_3$)$_3$), 43.3 (Me*C*H), 57.2 (*C*HNH), 78.9 (*C*(CH$_3$)$_3$), 126.4, 127.8, 128.2 (aromatic *C*H), 144.2 (*ipso-C*), 156.0 (NH*C*=O); *m*/*z* (APCI$^+$) 236 (18%), 208 (MH$_2^+$ − C(CH$_3$)$_3$, 32%), 164 (MH$_2^+$ − COO$^t$Bu, 60%), 147 (PhCH(Me)CH$^+$CH$_2$CH$_3$, 98%), 105 (100%); HRMS Calculated for C$_{16}$H$_{26}$NO$_2^+$: 264.1964. Found MH$^+$ 264.1969.

TFA (1 mL) was added to a stirred solution of a 2 : 1 mixture of *syn*-(2*RS*,3*RS*)-*N*-(*tert*-butoxycarbonyl)-1-ethyl-2-phenylpentane and *anti*-(2*RS*,3*SR*)-*N*-(*tert*-butoxycarbonyl)-1-ethyl-2-phenylpentane (37 mg, 0.14 mmol) in CH$_2$Cl$_2$ (2 mL) under Ar and the solution stirred for 1 h at rt before concentration *in vacuo*. The residue was dissolved in aq NaOH (10 mL, 1 M) and the organic material extracted into Et$_2$O (3 × 10 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo* to afford **17** and **18** as a pale yellow oil (20 mg, 85%). $\nu_{max}$ (thin film)/cm$^{-1}$ 3371 (N–H, br), 2961 (C–H, s), 1453 (C=C aromatic, m); $\delta_H$ major diastereomer (400 MHz, CDCl$_3$) 0.98 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.13–1.73 (7H, m, C*H*$_2$Me, N*H*$_2$ and C*H*$_3$CH$_2$), 2.60–2.68 (1H, m, MeC*H*), 2.72–2.81 (1H, m, C*H*NH$_2$), 7.19–7.34 (5H, m, aromatic C*H*); $\delta_H$ minor diastereomer (400 MHz, CDCl$_3$) 0.93 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.13–1.73 (7H, m, C*H*$_2$Me, N*H*$_2$ and C*H*$_3$CH$_2$), 2.72–2.81 (2H, m, C*H*NH$_2$ and MeC*H*), 7.19–7.34 (5H, m, aromatic C*H*); $\delta_C$ major diastereomer (100 MHz, CDCl$_3$) 10.4 (*C*H$_3$CH$_2$), 18.5 (*C*H$_3$CH), 27.4 (*C*H$_2$), 46.0 (Ph*C*HMe), 57.9 (*C*HNH$_2$), 127.1, 128.1, 128.4 (aromatic *C*H), 144.9 (*ipso-C*); $\delta_C$ minor diastereomer (100 MHz, CDCl$_3$) 10.9 (*C*H$_3$CH$_2$), 15.6 (*C*H$_3$CH), 27.9 (*C*H$_2$), 45.1 (Ph*C*HMe), 58.4 (*C*HNH$_2$), 126.3, 128.0, 128.3 (aromatic *C*H), 145.4 (*ipso-C*); *m*/*z* (APCI$^+$) 219 (14%), 164 (MH$^+$, 30%), 147 (M − NH$_2$, 55%), 105 (100%).

***anti*-(2*RS*,3*SR*)-2-Phenyl-3-aminopentane 18.** Pd(OH)$_2$ on carbon (20%, 10 mg, cat) was added to a solution of **12** (41 mg, 0.163 mmol) in MeOH (5 mL), and the solution stirred under H$_2$ (1 atm) for 18 h. The crude reaction mixture was filtered through Celite and concentrated *in vacuo* to give **18** (11 mg, 42%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 3340 (br, N–H), 2963 (s, C–H), 1455 (m, C=C aromatic); $\delta_H$ (400 MHz, CDCl$_3$) 0.93 (3H, t, *J* 7.4, CH$_2$C*H*$_3$), 1.15–1.29 (1H, m, C*H*$_2$CH$_3$), 1.30 (3H, d, *J* 6.9, C*H*$_3$CHPh), 1.41–1.52 (1H, m, C*H*$_2$CH$_3$), 1.98 (2H, br s, N*H*$_2$), 2.72–2.79 (1H, m, CH$_3$C*H*), 2.80–2.83 (1H, m, C*H*NH$_2$), 7.19–7.33 (5H, m, aromatic C*H*); $\delta_C$ (100 MHz, CDCl$_3$) 10.8 (CH$_2$CH$_3$), 15.9 (*C*H$_3$CHPh), 27.7 (*C*H$_2$CH$_3$), 45.0 (Ph*C*HCH$_3$), 58.4 (*C*HNH$_2$), 126.1, 127.9, 128.3 (aromatic *C*H), 145.2 (*ipso-C*); *m*/*z* (APCI) 219 (14%), 164 (MH$^+$, 21%), 147 (MH$^+$ − NH$_3$, 67%), 105 (100%); HRMS Calculated for $C_{11}H_{18}N^+$: 164.1439. Found 164.1437.

**(*E*)-Ethyl 4-phenyl-4-methoxybut-2-enoate 20.** DIBAL–H (1.5 M solution in toluene, 12.2 mL, 18.4 mmol) was added dropwise to a stirred solution of methyl *O*-methylmandelate **19** (3.0 g, 16.7 mmol) in toluene (80 mL) at −78 °C over 45 min whilst maintaining the temperature below −70 °C. After 2 hours, Ph$_3$P=CHCOOEt (6.39 g, 18.4 mmol) was added and the mixture warmed to rt over 18 h before the addition of Na$_2$SO$_4$·10H$_2$O (25 g) and the resulting slurry stirred for a further 1 h. The mixture was filtered through Celite®, diluted with toluene (100 mL) and washed successively with aq HCl (2 × 100 mL), aq sat NaHCO$_3$ (2 × 100 mL) and sat brine (2 × 100 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {10% Et$_2$O–petrol-(40 : 60)} gave **20** (1.96 g, 53%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 2983 (m, C–H), 1720 (s, C=O), 1658 (m, C=C aromatic); $\delta_H$ (400 MHz, CDCl$_3$) 1.28 (3H, t, *J* 7.1, CH$_2$C*H*$_3$), 3.34 (3H, s, OC*H*$_3$), 4.18 (2H, q, *J* 7.1, OC*H*$_2$CH$_3$), 4.78 (1H, d, *J* 5.5, CH$_3$OC*H*CH=CH), 6.08 (1H, d, *J* 15.7, CH=C*H*COOEt), 6.96 (1H, dd, *J* 15.7, 5.5, CHC*H*=CH), 7.30–7.40 (5H, m, aromatic C*H*); $\delta_C$ (50 MHz, CDCl$_3$) 14.1 (CH$_2$*C*H$_3$), 56.8 (O*C*H$_3$), 60.5 (O*C*H$_2$CH$_3$), 82.6 (Ph*C*HOCH$_3$), 121.1 (CH=*C*HCOOEt), 127.3, 128.5, 128.9 (aromatic *C*H), 139.1 (*ipso-C*), 147.5 (CH*C*H=CH), 166.6 (*C*OOEt); *m*/*z* (APCI) 189 (MH$^+$ − MeOH, 65%), 161 (94%), 133 (82%), 117 (28%), 115 (100%); Calculated for $C_{13}H_{16}O_3$: C 70.9, H 7.3. Found: C 70.9, H 7.5%.

**(*E*)-1-Phenyl-1-methoxybut-2-en-4-ol 21.** DIBAL–H (1.5 M in toluene, 15.2 mL, 22.7 mmol) was added dropwise to a stirred solution of **20** (2.0 g, 9.09 mmol) in toluene (50 mL) at −78 °C and stirred for 1 h followed by the dropwise addition of MeOH (10 mL). The solution was allowed to warm to rt and aq NaK[CH(OH)CO$_2$]$_2$ (75 mL, 1 M) was added. After 18 h, the organic material was extracted into toluene (3 × 50 mL), washed with sat brine (2 × 75 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {50% EtOAc–petrol (40 : 60)} gave **21** (1.30 g, 80%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 3380 (br s, O–H), 2933 (m, C–H), 1602 (w, C=C), 1453 (m, C=C aromatic); $\delta_H$ (400 MHz, CDCl$_3$) 1.38 (1H, t, *J* 6.1, O*H*), 3.33 (3H, s, OC*H*$_3$), 4.17 (2H, m, C*H*$_2$OH), 4.66 (1H, d, *J* 5.9, OC*H*CH=CH), 5.81–5.93 (2H, m, C*H*=C*H*), 7.27–7.39 (5H, m, aromatic C*H*); $\delta_C$ (50 MHz, CDCl$_3$) 56.3 (O*C*H$_3$), 56.6 (*C*H$_2$OH), 83.9 (CH$_3$O*C*H), 127.0, 128.0, 128.7 (aromatic *C*H), 131.8 (*C*H=*C*H), 141.0 (*ipso-C*); *m*/*z* (APCI) 161 (MH$^+$ − H$_2$O, 12%), 155 (17%), 147 (MH$^+$ − MeOH, 57%), 129 (100%), 122 (58%), 121 (29%).

**Benzaldehyde (*E*)-*O*-(4-phenyl-4-methoxybut-2-enyl)oxime 23.** PPh$_3$ (3.23 g, 11.7 mmol) was added to a stirred solution of **21** (1.9 g, 10.7 mmol) in CH$_2$Cl$_2$ (40 mL), followed by the addition of *N*-bromosuccinimide (2.09 g, 11.2 mmol) over 5 min and stirred at rt for 3 h before the addition of water (15 mL). The organic material was extracted into CH$_2$Cl$_2$ (3 × 30 mL), washed with brine (50 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo* to afford the crude bromide **22** as a pink solid, which was used immediately in the next step. KO$^t$Bu (2.18 g, 21.3 mmol) was added to a stirred solution of benzaldehyde oxime (2.39 g, 21.3 mmol) in THF (200 mL), and the mixture stirred for 30 min before the addition of a solution of bromide **22** (10.7 mmol) in THF (20 mL) *via* cannula. After 18 h, the reaction was quenched with aq phosphate pH 7 buffer (100 mL), extracted into Et$_2$O (3 × 100 mL), washed with sat brine (2 × 100 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {5% Et$_2$O–petrol (40 : 60)} gave **23** (1.36 g, 45% over two steps) as a yellow oil. $\nu_{max}$/cm$^{-1}$ (film) 2928 (m, C–H), 1602 (w, C=C), 1492 (m, C=C aromatic), 1448 (m, C=C aromatic); $\delta_H$ (400 MHz, CDCl$_3$) 3.36 (3H, s, OC*H*$_3$), 4.70–4.72 (3H, m, CH$_3$OC*H* and C*H*$_2$O), 5.89–6.03 (2H, m, C*H*=C*H*), 7.29–7.60 (10H, m, aromatic C*H*), 8.12 (1H, s, PhC*H*=N); $\delta_C$ (50 MHz, CDCl$_3$), 56.5 (*C*H$_3$O), 74.2 (*C*H$_2$O), 83.7 (CH$_3$O*C*H), 127.1, 127.3, 128.0, 128.2, 128.8, 128.9 (aromatic *C*H), 130.1 (*C*H=CH), 132.4 (*ipso-C*), 134.7 (CH=*C*H), 141.1 (*ipso-C*), 149.1 (*C*H=N); *m*/*z* (APCI) 250 (MH$^+$ − MeOH, 21%), 129 (22%), 122 (28%), 105 (17%), 104 (100%); Calculated for $C_{18}H_{19}NO_2$: C 76.8, H 6.8, N, 5.0. Found C 77.1, H 6.7, N 5.0%.

**(*E*)-*N*-Benzyl-*O*-(4-phenyl-4-methoxybut-2-enyl)hydroxylamine 24.** A solution of pyridine–borane complex (8 M in excess pyridine, 3.13 mL, 21.4 mmol) in EtOH (5 mL) was added to a stirred solution of **23** (0.80 g, 2.85 mmol) in EtOH (15 mL) at rt and the solution cooled to 0 °C before the addition of 10% HCl in EtOH (30 mL). The stirred reaction mixture was heated to 50 °C for 18 h, and cooled to rt before the solution was made alkaline to pH 10 by the addition of aq NaOH (50 mL, 1 M). The organic material was extracted into CH$_2$Cl$_2$ (3 × 60 mL) and the combined organic extracts washed with aq CuSO$_4$ (3 × 100 mL, 1 M) and water (100 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {8% Et$_2$O–petrol (40 : 60)} afforded **24** (0.462 g, 57%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 3250 (m, N–H), 2926 (m, C–H), 1602 (w, C=C), 1495 (m, C=C aromatic), 1453 (m, C=C aromatic); $\delta_H$ (400 MHz, CDCl$_3$) 3.32 (3H, s, OC*H*$_3$), 4.04 (2H, s, NHC*H*$_2$), 4.17 (2H, d, *J* 4.3, CH=CHC*H*$_2$), 4.63 (1H, d, *J* 4.4, CH$_3$OC*H*CH=CH), 5.68 (1H, br s, N*H*), 5.79–5.81 (2H, m, C*H*=C*H*), 7.28–7.38 (10H, m, aromatic C*H*); $\delta_C$ (50 MHz, CDCl$_3$) 56.4 (*C*H$_2$O), 56.6 (O*C*H$_3$), 74.1 (NH*C*H$_2$), 83.8 (CH$_3$O*C*H), 127.0, 127.7, 127.9, 128.6, 128.7 (aromatic *C*H), 129.2 (*C*H=CH), 134.3 (*C*H=CH), 137.7, 141.1 (*ipso-C*); *m*/*z* (Probe CI {NH$_3$}) 284 (MH$^+$, 19%), 253 (20%), 252 (MH$^+$ − MeOH, 100%); HRMS Calculated for $C_{18}H_{22}NO_2^+$: 284.1650. Found: 284.1655.

***syn*-(1*RS*,2*RS*)-1-Phenyl-1-methoxy-3-(*N*-benzyl-*N*-hydroxyamino)but-3-ene 25.** a. Preparation from rearrangement of (*E*)-**24**; *n*-BuLi (1.75 M solution in hexanes, 0.61 mL, 1.1 mmol) was added dropwise to a stirred solution of **24** (300 mg, 1.06 mmol) in THF (21 mL) at −78 °C and stirred for 1 h before warming to rt over 1 h. Water (10 mL) was added and the organic material was extracted into Et$_2$O (3 × 30 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo* to yield the crude product **25** (281 mg, 94%) as a colourless oil with identical spectroscopic properties to that prepared from rearrangement of (*Z*)-**34**.

b. Preparation from rearrangement of (*Z*)-**34**; *n*-BuLi (2.5 M solution in hexanes, 0.17 mL, 0.38 mmol) was added dropwise to a stirred solution of **34** (103 mg, 0.30 mmol) in THF (10 mL) at −78 °C and stirred for 1 h before warming to rt over 1 h. Water (25 mL) was added and the organic material was extracted into Et$_2$O (3 × 25 mL), dried (MgSO$_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {5% Et$_2$O–petrol (40 : 60)} gave **25** (53 mg, 51%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (KBr disc) 3338 (s, O–H), 2923 (m, C–H), 1494 (m), 1455 (s); $\delta_H$ (400 MHz, CDCl$_3$) 3.27 (3H, s, C*H*$_3$O), 3.50 (1H, m, CHC*H*NOH), 3.75 (1H, d, *J* 13.4, NC*H*HPh), 4.03 (1H, d, *J* 13.4, NCH*H*Ph), 4.51 (1H, d, *J* 7.2, CH$_3$OC*H*CH), 4.95 (1H, d, *J* 17.3, CH=C*H*H), 5.18 (1H, d, *J* 10.5, CH=CH*H*), 5.43 (1H, br s, O*H*), 5.77–5.88 (1H, m, C*H*=CH$_2$), 7.22–7.39 (10H, m, aromatic C*H*); $\delta_C$ (100 MHz, CDCl$_3$) 56.8 (O*C*H$_3$), 61.3 (Ph*C*H$_2$), 69.7, 84.8 (2 × *C*H), 120.7 (CH=*C*H$_2$), 127.1, 127.8, 127.9, 128.1, 128.2, 129.3 (aromatic *C*H), 132.1 (*C*H=CH$_2$), 137.8, 139.1 (*ipso-C*); *m*/*z* (APCI) 284 (MH$^+$, 40%), 252 (MH$^+$ − MeOH, 100%), 129 (60%), 106 (30%). Calculated for $C_{18}H_{19}NO_2$: C 76.3, H 7.5, N 4.9. Found: C 76.2, H 7.4, N 4.9%.

***syn*-(1*RS*,2*RS*)-1-Phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene 26.** Zinc powder (650 mg, 9.93 mmol) was added to a stirred solution of crude **25** (281 mg, 0.993 mmol) in aq HCl (1 M, 25 mL) and heated to 80 °C for 2 h. After cooling, aq NaOH (1 M, 30 mL) was added until pH 10, and the organic material extracted into $Et_2O$ (3 × 30 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by column chromatography {50% $Et_2O$–petrol (40 : 60)} gave **26** (168 mg, 63%) as a pale yellow oil which solidified on standing to a waxy cream solid. (Mp 41–43 °C); $\nu_{max}$/cm$^{-1}$ (film) 3330 (w, N–H), 2822 (m, C–H), 1603 (w, C=C), 1494 (m, C=C aromatic), 1453 (m, C=C aromatic); $\delta_H$ (400 MHz, $CDCl_3$) 3.21 (3H, s, $OCH_3$), 3.31 (1H, t, *J* 8.2, C*H*CH=CH$_2$), 3.62 (1H, d, *J* 13.2, NHC*H*H), 3.87 (1H, d, *J* 13.2, NHCH*H*), 4.07 (1H, d, *J* 8.2, CH$_3$OC*H*), 4.93 (1H, d, *J* 17.2, CH=C*H*H), 5.03 (1H, d, *J* 10.4, CH=CH*H*), 5.48–5.56 (1H, m, C*H*=CH$_2$), 7.23–7.35 (10H, m, aromatic C*H*); $\delta_C$ (100 MHz, $CDCl_3$) 51.2 (NH*C*H$_2$Ph), 56.8 (O*C*H$_3$), 66.9 (NH*C*HCH=CH$_2$), 86.6 (Ph*C*HOCH$_3$), 118.6 (*C*H=CH$_2$), 126.7, 127.8, 127.9, 128.0, 128.1, 128.3 (aromatic *C*H), 136.7 (*C*H=CH$_2$), 138.9 (*ipso-C*), 140.5 (*ipso-C*); *m*/*z* (APCI) 323 (13%), 269 (12%), 268 (MH$^+$, 100%), 237 (13%), 236 (MH$^+$ − MeOH, 82%); HRMS Calculated for $C_{18}H_{22}NO^+$: 268.1701. Found 268.1706.

***syn*-(1*RS*,2*RS*)-1-Phenyl-1-methoxy-3-(*N*-benzylamino)but-3-ene hydrochloride 26·HCl.** HCl (g) was bubbled through a solution of **26** (106 mg, 0.397 mmol) in $Et_2O$ (15 mL) for 2 min and the solvent removed *in vacuo* to afford the crude product **26**·HCl (108 mg, 85%) as a cream coloured solid. A small portion was purified for characterisation and X-ray crystallography by recrystallisation (1 : 3 petrol : $CH_2Cl_2$, white needles). Mp 167–169 °C; $\nu_{max}$/cm$^{-1}$ (KBr disc) 3361 (br, N–H), 2696 (br, C–H), 1602 (m, C=C), 1471 (C=C aromatic), 1454 (C=C aromatic); $\delta_H$ (400 MHz, $CD_3OD$) 3.28 (3H, s, C*H*$_3$O), 3.87 (1H, t, *J* 9.7, NH$_2$C*H*CH=CH$_2$), 4.20 (1H, d, *J* 13.3, NH$_2$C*H*HPh), 4.35 (1H, d, *J* 13.3, NH$_2$CH*H*Ph), 4.45 (1H, d, *J* 9.7, CH$_3$-OC*H*), 5.11 (1H, d, *J* 17.0, CH=C*H*H), 5.41 (1H, d, *J* 10.4, CH=CH*H*), 5.76–5.83 (1H, m, C*H*=CH$_2$), 7.31–7.55 (10H, m, aromatic C*H*); $\delta_C$ (100 MHz, $CD_3OD$) 48.5 (*C*H$_3$O), 56.9 (Ph*C*H$_2$NH$_2$), 67.1 (*C*HCH=CH$_2$), 83.5 (Ph*C*HOCH$_3$), 127.4 (CH=*C*H$_2$), 129.1 (*C*H=CH$_2$), 129.3, 129.8, 130.3, 130.6, 131.0 (aromatic *C*H), 132.4 (*ipso-C*), 137.4 (*ipso-C*); *m*/*z* (APCI) 323 (12%), 269 (15%), 268 (M$^+$, 100%), 237 (14%), 236 (83%).

***anti*-(3*RS*,4*SR*)-3-(*N*-Benzylamino)-1-phenyl-1-methoxybut-3-ene 28.** DIBAL–H (5.98 ml, 1.0 M in hexanes, 5.98 mmol) was added dropwise to a stirred solution of methyl *O*-methylmandelate (979 mg, 5.4 mmol) in $CH_2Cl_2$ (10 ml) at −78 °C. After two hours, benzylamine (0.59 ml, 5.44 mmol) was added, and the mixture allowed to reach rt over a period of 16 h. MeOH (5 ml) was then added, followed after 5 minutes by aqueous sodium potassium tartrate (20 ml, 1.0 M). After stirring for four hours, water (50 ml) was added and the resultant mixture extracted with $CH_2Cl_2$ (3 × 50 ml), dried ($MgSO_4$), and concentrated *in vacuo* to yield the crude imine **27** (1.0 g, 78% crude yield), which was used without purification in the next step. $\delta_H$ (200 MHz, $CDCl_3$) 3.41 (3H, s, OC*H*$_3$), 4.61 (2H, br s, C*H*$_2$Ph), 4.83 (1H, d, *J* 5.7, C*H*=N), 7.21–7.42 (10H, m, aromatic C*H*), 7.74 (1H, dt, *J* 5.7, 1.5).

$BF_3 \cdot Et_2O$ (0.57 mL, 4.66 mmol) was added to a stirred solution of the imine (371 mg, 1.55 mmol) in THF (10 ml) at −78 °C and stirried for 30 min before the addition of vinylmagnesium bromide (1.0 M in THF, 10 mL) over 5 minutes. After stirring at −78 °C for 30 min, the reaction mixture was allowed to warm to rt. After a further two hours, water (100 ml) was added, and the mixture extracted with $CH_2Cl_2$ (3 × 50 ml), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by column chromatography {20% $Et_2O$–petrol (40 : 60)} gave **28** (112 mg, 27%) as a pale yellow oil. $\nu_{max}$/cm$^{-1}$ (film) 3328 (w) (N–H), 2929 (m), 1495 (m), 1453 (s); $\delta_H$ (400 MHz, $CDCl_3$) 3.23 (1H, dd, *J* 8.4, 5.3, C*H*NH), 3.24 (3H, s, OC*H*$_3$), 3.59 (1H, d, *J* 13.6, PhC*H*H), 3.83 (1H, d, *J* 13.6, PhCH*H*), 4.26 (1H, d, *J* 5.3, C*H*OCH$_3$), 5.04 (1H, d, *J* 17.1, CH=C*H*H), 5.22 (1H, dd, *J* 10.2, 1.7, CH=CH*H*), 5.72 (1H, ddd, *J* 17.1, 10.2, 8.4, C*H*=CH$_2$), 7.19–7.37 (10H, m, aromatic C*H*); $\delta_C$ (50 MHz, $CDCl_3$) 50.7 (Ph*C*H$_2$), 57.2 (O*C*H$_3$), 65.7 (NH*C*H), 86.5 (*C*HOCH$_3$), 118.3 (CH=*C*H$_2$), 126.8, 127.7, 127.8, 128.1, 128.2, 128.3 (aromatic *C*H), 136.8 (*C*H=CH$_2$), 139.1, 140.4 (*ipso-C*); *m*/*z* (APCI) 268 (MH$^+$, 40%), 236 (MH$^+$ − MeOH, 70%), 161 (10%), 150 (15%), 129 (100%), 106 (15%); HRMS Calculated for $C_{18}H_{22}NO^+$: 268.1701. Found: 268.1699.

**Benzaldehyde *O*-prop-2-ynyloxime 30.** KO$^t$Bu (1.0 g, 9.1 mmol, 1.0 eq.) was added to a solution of benzaldehyde oxime (1.0 g, 8.25 mmol, 1.1 eq.) in THF (10 mL) at 0 °C. After 15 min propargyl bromide **29** (1.4 mL, 12.4 mmol) was added dropwise and stirred overnight before the addition of $NH_4Cl_{(aq)}$ (40 mL). The resultant mixture was extracted with $Et_2O$, dried, and concentrated *in vacuo*. Purification by column chromatography {20% $Et_2O$–petrol (40 : 60)} gave **30** (1.14 g, 87%) as a clear yellow oil. $\nu_{max}$/cm$^{-1}$ (film) 3293 (s, alkyne C–H), 2925 (m, C–H); $\delta_H$ (400 MHz, $CDCl_3$) 2.54 (1H, t, *J* 2.4, C≡C*H*), 4.80 (2H, d, *J* 2.4, C*H*$_2$C≡CH), 7.38–7.46 (3H, m, aromatic C*H*), 7.60–7.64 (2H, m, aromatic C*H*), 8.15 (1H, s, C*H*=N); $\delta_C$ (50 MHz, $CDCl_3$) 61.7 (*C*H$_2$), 74.8, 79.5 (2 × alkyne *C*), 127.3, 128.7, 130.2 (aromatic *C*H), 131.7 (*ipso-C*), 150.0 (*C*H=N); *m*/*z* (APCI) 160 (MH$^+$, 100%), 144 (25%), 129 (95%), 122 (30%), 106 (90%); HRMS Calculated for $C_{10}H_{10}NO^+$: 160.0762. Found: 160.0760.

**Benzaldehyde *O*-(4-hydroxy-4-phenylbut-2-ynyl)oxime 31.** LHMDS (1.0 M in THF, 6.29 mL, 6.29 mmol) was added to **30** (909 mg, 5.72 mmol) in THF (10 mL) at −78 °C. After 30 min, benzaldehyde (0.87 mL, 8.58 mmol) was added and the mixture stirred for a further hour at −78 °C and warmed to rt for 1 hour before the addition of $H_2O$ (30 mL) and the mixture extracted with EtOAc (3 × 30 mL), dried and concentrated *in vacuo*. Purification by column chromatography {30% $Et_2O$–petrol (40 : 60)} gave **31** (1.17 g, 77%) as a colourless oil. $\nu_{max}$/cm$^{-1}$ (film) 3400 (br, s, O–H), 3062 (m, C–H), 3029 (m, C–H), 2919 (m, C–H), 1957 (w), 1888 (w), 1811 (w); $\delta_H$ (400 MHz, $CDCl_3$) 2.99 (1H, br s, O*H*), 4.88 (2H, d, *J* 1.1, C*H*$_2$), 5.53 (1H, s PhC*H*OH), 7.31–7.42 (6H, m, aromatic C*H*), 7.57–7.64 (4H, m, aromatic C*H*), 8.13 (1H, s, C*H*=N); $\delta_C$ (100 MHz, $CDCl_3$) 62.1 (*C*H$_2$), 64.5 (*C*HOH), 82.5, 86.6 (*C*≡*C*), 126.8, 127.3, 128.4, 128.6, 128.8, 130.2 (aromatic *C*H), 131.7, 140.3 (*ipso-C*), 150.1 (*C*=N); *m*/*z* (APCI) 249 (MH$^+$ − $H_2O$, 10%), 117 (15%), 104 (100%). Calculated for $C_{17}H_{15}NO_2$: C 77.0, H 5.7, N 5.3. Found: C 76.9, H 5.7, N 5.3%.

**Benzaldehyde *O*-(4-methoxy-4-phenylbut-2-ynyl)oxime 32.** A solution of **31** (1.17 g, 4.40mmol) in THF (10 mL) was added by cannula to a stirred suspension of NaH (60% dispersion in mineral oil, 194 mg, 4.84 mmol, prewashed with pentane) in THF (10 mL) at 0 °C. After 30 min, methyl iodide (0.8 mL, 13.2 mmol) was added, and the mixture stirred for 18 h and allowed to reach rt. Methanol (10 mL), water (20 mL), and brine (10 mL) were then added, and the mixture extracted with EtOAc (3 × 30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification by column chromatography {50% $Et_2O$–petrol (40 : 60)} gave **32** (1.03 g, 84%) as a pale yellow oil. $\nu_{max}$/cm$^{-1}$ (film) 2929 (m, C–H), 1957 (w), 1895 (w), 1745 (m), 1668 (m), 1607 (m); $\delta_H$ (200 MHz, $CDCl_3$) 3.48 (3H, s, OC*H*$_3$), 4.92 (2H, d, *J* 1.7, C*H*$_2$), 5.20 (1H, t, *J* 1.7, PhC*H*OCH$_3$), 7.35–7.68 (10H, m, aromatic C*H*), 8.17 (1H, s, PhC*H*=N); $\delta_C$ (50 MHz, $CDCl_3$) 55.9 (O*C*H$_3$), 62.1 (O*C*H$_2$C≡C), 73.1 (*C*H(OCH$_3$)Ph), 83.8, 84.2 (*C*≡*C*), 127.5, 127.7, 128.7, 128.9, 130.3 (aromatic *C*H), 132.1, 138.4 (*ipso-C*), 150.1 (*C*H=N); *m*/*z* (APCI) 280 (MH$^+$, 20%), 117 (15%), 104 (100%); HRMS Calculated for $C_{17}H_{14}NO^+$ (MH$^+$ − MeOH): 248.1075. Found: 248.1082.

**(*Z*)-Benzaldehyde *O*-(4-methoxy-4-phenylbut-2-enyl)oxime 33.** Lindlar's catalyst (200 mg) was added to **32** (912 mg, mmol) in methanol (10 mL), and stirred under 4 atm $H_2$ for 4 days. The mixture was then filtered through Celite, and concentrated *in vacuo* before purification by column chromatography {10% $Et_2O$–petrol (40 : 60)} to give **33** (803 mg, 66%) as a colourless oil. $\nu_{max}/cm^{-1}$ (film) 2932 (s, C–H), 1955 (w), 1882 (w), 1812 (w), 1723 (m), 1602 (m); $\delta_H$ (400 MHz, $CDCl_3$) 3.38 (3H, s, $OCH_3$), 4.84 (1H, ddd, *J* 13.0, 6.1, 1.4, OC*H*H), 4.94 (1H, ddd, *J* 13.0, 6.8, 1.5, OCH*H*), 5.09 (1H, d, *J* 9.0, C*H*$OCH_3$), 5.78 (1H, app ddt, *J* 11.3, 9.0, 1.3, $CH_2$CH=C*H*), 5.87–5.93 (1H, m, $CH_2$-C*H*=CH), 7.28–7.41 (8H, m, aromatic C*H*), 7.56–7.60 (2H, m, aromatic C*H*), 8.11 (1H, s, C*H*=N); $\delta_C$ (50 MHz, $CDCl_3$) 56.8 ($OCH_3$), 70.4 ($CH_2$), 79.5 (Ph*C*H$OCH_3$), 127.1, 127.6, 128.2, 128.2, 129.0, 129.2, 130.4 (aromatic *C*H and *C*=C), 132.6 (*ipso-C*), 134.5 (C=*C*), 141.6 (*ipso-C*), 149.5 (Ph*C*=N); *m*/*z* (APCI) 250 ($MH^+$ − MeOH, 10%), 147 ($PhCHCH{=}CHCH_2OH^+$, 5%), 129 (15%), 122 ($PhCH{=}NHOH^+$, 15%), 104 (100%). Calculated for $C_{18}H_{19}NO_2$: C 76.8, H 6.8, N 5.0. Found: C 76.5, H 6.5, N 4.8%.

**(*Z*)-*N*-Benzyl-*O*-(4-methoxy-4-phenylbut-2-enyl)hydroxylamine 34.** Borane–pyridine complex (0.76 mL) was added to **33** (304 mg, 1.08 mmol) in EtOH (20 mL) at 0 °C, followed by the dropwise addition of 10% EtOH–HCl (30 mL) over 5 minutes before being allowed to warm to rt and stirred for a further 18 h. The reaction mixture was then basified with saturated aqueous $Na_2CO_3$, extracted with $CH_2Cl_2$ (3 × 40 mL), dried ($MgSO_4$), and concentrated *in vacuo* before purification by column chromatography {10% $Et_2O$–petrol (40 : 60)} to give **34** (221 mg, 72%) as pale yellow oil. $\nu_{max}/cm^{-1}$ (film) 3260 (m), 2928 (s), 1953 (w), 1861 (w), 1811 (w), 1602 (m); $\delta_H$ (400 MHz, $CDCl_3$) 3.29 (3H, s, $OCH_3$), 4.08 (2H, s, Ph$CH_2$), 4.29 (1H, dd, *J* 12.7, 4.6, OC*H*H), 4.39 (1H, dd, *J* 12.7, 6.0, OCH*H*), 4.93 (1H, d, *J* 7.8, C*H*$OCH_3$), 5.67–5.77 (2H, m, C*H*=C*H*), 7.25–7.38 (10H, m, aromatic C*H*); $\delta_C$ (50 MHz, $CDCl_3$) 56.2 ($OCH_3$), 56.6 (Ph$CH_2$), 69.8 ($OCH_2$), 78.9 (Ph*C*H), 126.6, 127.5, 127.6, 128.0, 128.5, 128.6, 129.0 (aromatic *C*H and *C*=C), 133.9 (C=*C*), 137.6, 141.3 (*ipso-C*); *m*/*z* (CI) 284 ($MH^+$, 15%), 252 ($MH^+$ − MeOH, 100%), 222 (10%), 161 (15%), 147 (25%), 130 (20%), 105 (25%), 92 (20%). Calculated for $C_{18}H_{21}NO_2$: C 76.3, H 7.5, N 4.9. Found: C 76.4, H 7.2, N 4.9%.

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19 (*a*) For other examples where the diastereoselectivity of the [2,3]-Wittig rearrangement has been rationalised in a similar manner see R. Brückner, *Chem. Ber.*, 1989, **122**, 193; (*b*) R. Brückner and H. Priepke, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 278; (*c*) E. Nakai and T. Nakai, *Tetrahedron Lett.*, 1988, **29**, 4587; (*d*) K. Mikami and T. Nakai, *Synthesis*, 1991, 594; (*e*) H. Priepke and R. Brückner, *Chem. Ber.*, 1990, **123**, 153.

20 (*a*) The need for a metal counter-ion in the [2,3]-Wittig rearrangement has been the cause of much debate. Theoretical calculations have shown that the preferred transition structure of the Wittig rearrangement required the lithium cation; see : Y.-D. Wu, K. N. Houk and J. A. Marshall, *J. Org. Chem.*, 1990, 1421; (*b*) However, in some cases *E*/*Z* and *anti*/*syn* ratios of products in the Wittig rearrangement have been shown to be independent of the metal counterion; see B. Kruse and R. Brückner, *Tetrahedron Lett.*, 1990, **31**, 4425.

21 For an example where the diastereoselectivity observed for a [2,3]-Wittig rearrangement has been rationalised *via* a chelated transition state see S. W. Scheuplein, A. Kusche, R. Brückner and K. Harms, *Chem. Ber.*, 1990, **123**, 917.