Diastereoselective acyclic aza-[2,3] Wittig sigmatropic rearrangements

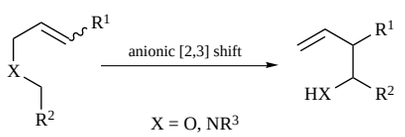
James C. Anderson,*,†,[a] Stephen C. Smith[b] and Martin E. Swarbrick[a]

[a] *Department of Chemistry, University of Sheffield, Sheffield, UK S3 7HF*
[b] *Zeneca Agrochemicals, Jealott's Hill Research Station, Bracknell, Berkshire, UK RG42 6EY*

The scope of anion-stabilising groups in promoting and controlling the diastereoselection of the aza-[2,3] Wittig sigmatropic rearrangement has been assessed by the syntheses of allylic amines 1c–g that have incorporated $SiPhMe_2$, Ph, SPh, SOPh and SO_2Ph respectively at the C-2 position. The subsequent anionic [2,3]-sigmatropic rearrangements are analysed with respect to the extent of diastereoselection of the product homoallylic amines 2 and 3. It appears that silicon not only is the most efficient at electronically facilitating this rearrangement, but its steric bulk controls the diastereoselectivity of the process exclusively. Phenyl and phenylthio substituents also have a similar, but decreased, effect on diastereoselection that mirrors their lower steric bulk in comparison to the silicon derivative. Sulfoxide and sulfone substituents are incompatible with the reaction conditions required for rearrangement.

Introduction

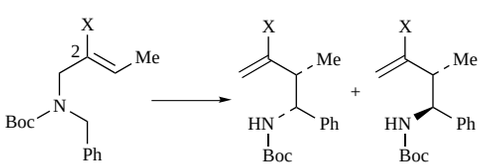
Despite the numerous synthetic applications of the [2,3] Wittig sigmatropic rearrangement of allylic ethers (Scheme 1, X = O),[1]



Scheme 1

the use of the aza congener (Scheme 1, X = N) has been limited by the reluctance of simple allyl amines to undergo this transformation.[2] The first unequivocal example of this rearrangement,[3] which is driven by relief of ring strain, has been extended by others to include vinyl aziridines.[4] The [2,3]-rearrangement of *N*-allyl nitrogen ylides has been shown to be potentially useful.[2e]

We have concentrated our efforts on the acyclic variant of this rearrangement and want to develop the aza-[2,3] Wittig sigmatropic process into a versatile method for the preparation of unnatural amino acids. To this end we have managed to markedly accelerate our preliminary reaction[5] and control the diastereoselectivity of the acyclic rearrangement by the incorporation of a trimethylsilyl group at the C-2 position of our substrate (Scheme 2).[6] We believe the silicon atom, due to



Scheme 2 *Reagents and conditions:* BuLi, Et_2O–HMPA (4:1); **a**, X = H, −78 to −40 °C, 14 h, 82%; **b**, X = $SiMe_3$, −78 °C, 10 min, 88%

its ability to stabilise adjacent negative charge,[7] is stabilising the transition state,[8] thus reducing the activation energy of the reaction. The inherent bulk of the silyl group is dictating the diastereoselection.[6] This strategy has allowed the acyclic aza-[2,3] Wittig rearrangement to become more applicable to a wider range of substrates.[9] We report here the first examples of other anion-stabilising groups successfully incorporated into rearrangement precursors **1**, that both facilitate and increase the synthetic scope of the aza-[2,3] Wittig rearrangement.

Our first concern was that we could not remove the trimethylsilyl group from **3**, presumably because the accepted mechanism would require the formation of an incipient primary carbocation.[10] Although there is a rich chemistry associated with vinyl silanes[10] that could be applied to compounds such as **3**, our methodology would be more versatile if the silyl group could also be removed at an early stage. An added incentive was that we could obtain unambiguous proof of diastereoselection from the desilylated product **3** (X = H).[5] Following an isolated report that the phenyldimethylsilyl group could be removed from the C-2 position of a vinyl silane with tetrabutyl ammonium fluoride (TBAF),[11] we sought to obtain **1c** (X = $SiPhMe_2$). We were also interested in the rearrangements of compounds analogous to **1**, where X = Ph, SPh, S(O)Ph and SO_2Ph (**1d–g** respectively); as all these groups are capable of stabilising an adjacent negative charge and could control diastereoselectivities in a manner similar to that found with $SiMe_3$ (*vide supra*).

Results and discussion

Allylic alcohols **4c–e** were prepared from the addition of the corresponding α-lithio-α-substituted vinyl precursors to acetaldehyde. In the case of the phenyldimethylsilane derivative **4c** we had to develop a reliable synthesis of (1-bromovinyl)-phenyldimethylsilane based upon a description in the literature of the triphenyl congener.[12] Addition of bromine to phenyldimethylvinylsilane and then elimination of hydrogen bromide with refluxing pyridine produced the desired halide in 62% yield. Allylic alcohols **4c–e** were then transformed into the desired rearrangement precursors **1c–e** *via* the established procedure for stereoselective conversion of secondary allylic alcohols to allyl amides **5c–e** (Scheme 3).[13] Compounds **1f** and **1g** were obtained from the controlled oxidation of **1e**.

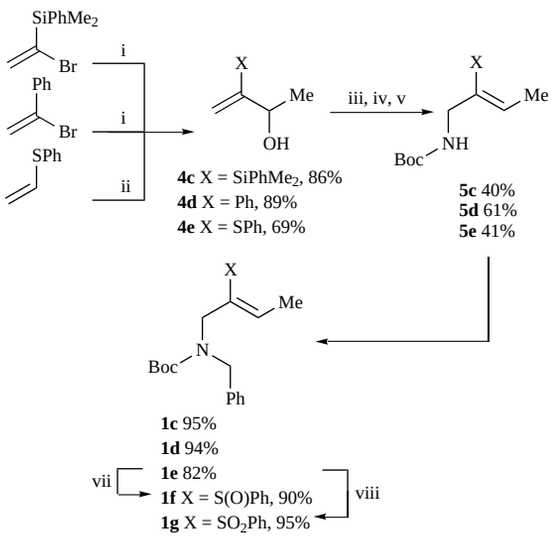
Rearrangement of **1c** was carried out by treatment with BuLi at −78 °C in tetrahydrofuran (THF) for 14 h to give the rearranged product **3c** in 81% yield with complete diastereoselectivity (Scheme 4). This diastereoisomer exhibited characteristic chemical shifts in its NMR spectrum that we had used to assign the trimethylsilyl analogue (Table 1).[6] Treatment with

†E-mail: j.anderson@sheffield.ac.uk

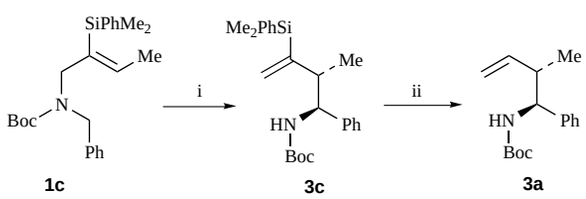
Table 1 Selected NMR data for **2** and **3**

	X	Diastereoselectivity[a] **2**:**3**	δ Me groups **2**; **3**[b]	*J* C-1H–C-2H **3**
1b	$SiMe_3$	<1:20	1.02; 0.66	10.4
1c	$SiPhMe_2$	**3** only	0.53	9.6
1d	Ph	1:7	0.80; 0.70	9.5
1e	SPh	1:4	1.13; 0.76	9.8

[a] Ratios of unpurified products determined by 250 MHz NMR. [b] [$^2H_6$]DMSO.



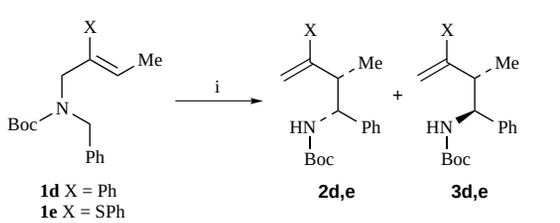
Scheme 3 *Reagents and conditions:* i, Bu^{t}Li, Et_2O, −78 °C, MeCHO; ii, BuLi, TMEDA, THF, −78 °C, MeCHO; iii, KH cat., Cl_3CCN; iv, xylenes, 140 °C; v, $(Boc)_2O$ then NaOH; vi, KH, BnBr; vii, *m*CPBA; viii, Oxone



Scheme 4 *Reagents and conditions:* i, BuLi, THF, −78 °C, 14 h; ii, TBAF, DMSO, 100 °C, 2 h

TBAF in DMSO under standard literature conditions[11] produced a single diastereoisomer of the desilylated product in 47% yield. This compound had an identical NMR spectrum to the minor diastereoisomer **3a** (Scheme 3), obtained from our first rearrangement, the structure of which had been proven by correlation to authentic isoleucine.[5]

Treatment of **1d** with BuLi in THF–HMPA (4:1) at −78 °C and then at −40 °C for 14 h led to a mixture of **2d** and **3d** in 71% yield with a diastereoisomeric ratio of 1:7 (Scheme 5).



Scheme 5 *Reagents and conditions:* i, BuLi, THF–HMPA (4:1), −78 °C, 1 h then −40 °C, 14 h

Similarly, treatment of **1e** under identical conditions led to an inseparable mixture by chromatography of **2e**, *N-tert*-butoxycarbonylbenzylamine and **3e** in 49% yield with a ratio of 1:2:4 (Scheme 5).

Samples of pure diastereoisomers **3d** and **3e** could be obtained by trituration of the chromatographed mixed products with cold light petroleum in 59 and 26% yield respectively. The diastereoselection could be ascertained from inspection of selected NMR characteristics (Table 1). As with the trimethylsilyl derivative, the large C-1H–C-2H coupling constant (Fig. 1) suggested conformations where the methyl substituents of the major diastereoisomer were shielded by the proximal phenyl ring.[6] This analysis was supported by the conversion of **3c** to **3a** (*vide supra*).

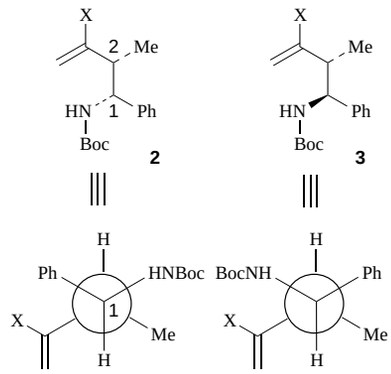
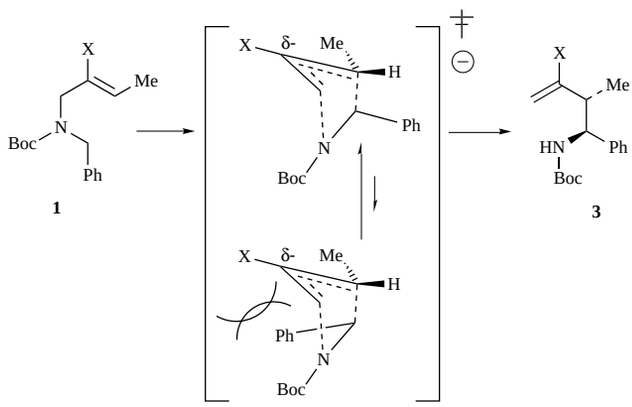


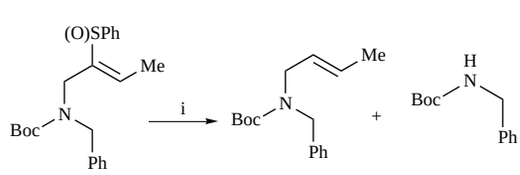
Fig. 1

These results support the proposed transition state model[6] (Scheme 6) for these rearrangements. The change in the extent of diastereoselection nicely mirrors the decrease in the steric bulk of the anion-stabilising vinyl substituents X, in the order $PhMe_2Si$ > Ph > SPh.



Scheme 6 Transition-state model for major diastereoisomer

We expected the sulfoxide **1f** and sulfone **1g** analogues to behave similarly; **1f** offering the potential of a chiral anion-stabilising vinyl substituent that could control the enantioselection of this particular variant of the process. Unfortunately, treatment of **1f** with BuLi under standard conditions led only to the desulfurised starting material **1a** (30%) and *N-tert*-butoxycarbonylbenzylamine (48%) (Scheme 7).



Scheme 7 *Reagents and conditions:* i, BuLi, THF–HMPA (4:1), −78 °C, 1 h then −40 °C, 14 h

Treatment of **1g** and **1f** under a range of similar conditions led to complex mixtures of products, none of which could be identified. We can only conclude that the sulfoxide and sulfone substituents render the system incompatible towards the strong base necessary to facilitate the anionic sigmatropic rearrangement.

The aza-[2,3] Wittig rearrangement has been shown to be accelerated by the incorporation of certain anion-stabilising vinyl substituents at the central vinyl carbon atom. The diastereoselection ranges from 4:1 to 20:1 depending on the steric bulk of the substituents X in allyl amines **1**, with silyl substituents emerging as the front runners. The phenyldimethylsilyl group, after its removal, has verified our structural assignments and increases the synthetic utility of the silicon-stabilised aza-[2,3] Wittig rearrangement. The phenyl and phenylthio substituents further expand the process. The use of the rearranged precursors as synthetic building blocks will be reported shortly and the investigation of other less obvious accelerating groups are underway.

Experimental

General details

Our general experimental details have been reported elsewhere.[6]

(1-Bromovinyl)phenyldimethylsilane

Bromine (1.84 ml, 0.036 mol, 1 equiv.) in carbon tetrachloride (20 ml + 2 × 5 ml wash) was added dropwise, *via* a cannula, to a stirred solution of phenyldimethylvinylsilane (5.78 g, 0.036 mol) in carbon tetrachloride (30 ml) at 0 °C. The solution was stirred for 10 min at 0 °C, washed sequentially with saturated aqueous sodium hydrogen carbonate containing some sodium hydrogen sulfite (3 × 50 ml) and brine (50 ml), dried over magnesium sulfate and concentrated *in vacuo* to give the crude dibromide (12.62 g) as a pale yellow oil. This crude product was dissolved in pyridine (50 ml) and refluxed for 14 h. After cooling to room temperature, the dark brown reaction mixture was diluted with diethyl ether (100 ml) and washed with water (70 ml). The aqueous layer was further extracted with diethyl ether (2 × 70 ml) and the combined organics washed repeatedly with a saturated copper sulfate solution until all of the pyridine had been removed, as indicated by the aqueous phase retaining a light blue colour. The organics were then washed with brine (70 ml), dried over magnesium sulfate and concentrated *in vacuo* to give a pale brown oil (5.63 g) which was purified by flash column chromatography (15 × 5 cm silica, light petroleum) to give the bromovinylsilane (5.32 g, 62%) as a colourless oil (Found: C, 50.2; H, 5.8; Br, 33.4. $C_{10}H_{13}BrSi$ requires C, 49.8; H, 5.4; Br, 33.1%); ν_{max}(thin film)/cm^{-1} 3071, 2962, 1592, 1429, 1397, 1250, 1114, 1070, 915; δ_H(250 MHz; $CDCl_3$) 0.49 [6H, s, $(CH_3)_2Si$], 6.17 (1H, d, *J* 1.7, C*H*H=), 6.35 (1H, d, *J* 1.7, CH*H*=), 7.30–7.70 (5H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) −3.4, 128.0, 129.8, 131.5, 134.1, 135.2, 136.7; *m/z* (EI$^+$) 241.9940 (31%, M$^+$. $C_{10}H_{13}{}^{81}BrSi$ requires *M*, 241.9949), 239.9962 (32, M$^+$. $C_{10}H_{13}{}^{79}BrSi$ requires *M*, 239.9970), 227 (51)/225 (50, M$^+$ − CH_3), 201 (100)/199 (100), 161 (23, M$^+$ − Br), 145 (37), 135 (97), 105 (46).

3-Phenyldimethylsilylbut-3-en-2-ol 4c

tert-Butyllithium (15.5 ml of a 1.7 M solution in pentane, 26.4 mmol, 2.1 equiv.) was added dropwise to a stirred solution of (1-bromovinyl)phenyldimethylsilane (3.03 g, 12.6 mmol) in diethyl ether (40 ml) at −78 °C. After complete addition, the reaction was stirred for 1 h at −78 °C. A solution of acetaldehyde (1.40 ml, 25.1 mmol, 2 equiv.) in diethyl ether (10 ml) was then added dropwise *via* a cannula. After stirring for a further hour at −78 °C, the reaction was allowed to warm to room temperature. Water (50 ml) was added, the mixture separated and the aqueous layer extracted with diethyl ether (3 × 30 ml). The combined organics were dried over magnesium sulfate and concentrated *in vacuo* to give a yellow oil (3.24 g) which was purified by flash column chromatography (15 × 5 cm silica, 15% ethyl acetate–light petroleum) to give **4c** (2.23 g, 86%) as a colourless oil (Found: C, 69.4; H, 8.8. $C_{12}H_{18}OSi$ requires C, 69.8; H, 8.8%); ν_{max}(thin film)/cm^{-1} 3358, 1428, 1250, 1111, 845; δ_H(250 MHz; $CDCl_3$) 0.42 (3H, s, CH_3Si), 0.44 (3H, s, CH_3Si), 1.20 (3H, d, *J* 6.4, CH_3CH), 1.39 (1H, d, *J* 4.3, O*H* by D_2O exchange), 4.44 (1H, qdt, *J* 6.4, 4.3, 1.2, CH_3CH), 5.45 (1H, dd, *J* 2.4, 1.2, C*H*H=), 5.91 (1H, dd, *J* 2.4, 1.2, CH*H*=), 7.30–7.65 (5H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) −2.3, −2.1, 24.1, 71.7, 124.7, 127.9, 129.1, 133.9, 138.4, 155.0; *m/z* (EI$^+$) 191.0893 (25%, M$^+$ − CH_3. $C_{11}H_{15}OSi$ requires *M* − CH_3, 191.0892), 137 (100), 135 (44), 105 (12), 75 (26).

3-Phenylbut-3-en-2-ol 4d

α-Bromostyrene (3 ml, 23.1 mmol) was converted to **4d** in an identical fashion to that for **4c** and was purified by flash column chromatography (15 × 5 cm silica, 15% ethyl acetate–light petroleum) to give a pale straw coloured oil (3.06 g, 89%);[14] δ_H(250 MHz; $CDCl_3$) 1.32 (3H, d, *J* 6.4, CH_3), 1.79 (1H, d, *J* 4.0, O*H* by D_2O exchange), 4.82 (1H, qd, *J* 6.4, 4.0, C*H*OH), 5.28 (1H, t, *J* 0.9, C*H*H=), 5.36 (1H, t, *J* 1.2, CH*H*=), 7.25–7.45 (5H, m, Ar*H*).

3-Phenylthiobut-3-en-2-ol 4e

Phenyl vinyl sulfide (5 ml, 0.038 mol) in tetrahydrofuran (40 ml + 2 × 10 ml wash) was added dropwise, *via* a cannula, to a stirred solution of butyllithium (16.1 ml of a 2.5 M solution in hexane, 0.040 mol, 1.05 equiv.) and TMEDA (6.1 ml, 0.040 mol, 1.05 equiv.) in tetrahydrofuran (120 ml) at −78 °C. After stirring at −78 °C for 2 h, a solution of acetaldehyde (4.2 ml, 0.077 mol, 2 equiv.) in tetrahydrofuran (10 ml + 2 × 2 ml wash) was added dropwise, *via* a cannula. Upon complete addition, the reaction was stirred for a further hour at −78 °C before being warmed to room temperature. Saturated aqueous ammonium chloride (100 ml) was added, the mixture separated and the aqueous layer further extracted with diethyl ether (3 × 70 ml). The combined organics were dried over magnesium sulfate and concentrated *in vacuo* to give a crude yellow oil (9.1 g) which was purified by flash column chromatography (15 × 7 cm silica, 20% ethyl acetate–light petroleum) to give the alcohol **4e** (4.75 g, 69%), as a yellow oil;[15] δ_H(250 MHz; $CDCl_3$) 1.43 (3H, d, *J* 6.4, CH_3), 1.93 (1H, br s, O*H* by D_2O exchange), 4.37 (1H, qt, *J* 6.4, 0.6, C*H*OH), 4.97 (1H, d, *J* 0.9, C*H*H=), 5.50 (1H, d, *J* 0.9, CH*H*=), 7.20–7.50 (5H, m, Ar*H*).

Preparation of compounds 1

We have previously reported general methods for the preparation of **1** from **4** *via* **5**.[6]

(*Z*)-*N*-*tert*-Butoxycarbonyl-2-(phenyldimethylsilyl)but-2-enylamine 5c. Compound **5c** was prepared in 40% yield from **4c** as a colourless oil; ν_{max}(thin film)/cm^{-1} 3356, 1703, 1505, 1366, 1249, 1171; δ_H(250 MHz; $CDCl_3$) 0.41 [6H, s, $(CH_3)_2Si$], 1.42 [9H, s, $(CH_3)_3C$], 1.64 (3H, dt, *J* 7.0, 1.2, CH_3CH=), 3.77 (2H, m, NCH_2CH=), 4.35 (1H, br s, N*H* by D_2O exchange), 6.31 (1H, qt, *J* 7.0, 1.2, CH_3CH=), 7.30–7.55 (5H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) −1.5, 17.8, 47.9, 79.1, 127.9, 128.9, 133.7, 134.8, 140.5, 155.4; *m/z* (CI$^+$) 306.1880 (13%, MH$^+$. $C_{17}H_{28}NO_2Si$ requires *M*H$^+$, 306.1889), 278 (17), 248 (13, M$^+$ − Bu^t), 234 (47), 172 (100), 135 (16), 57 (Bu^t).

(*E*)-*N*-*tert*-Butoxycarbonyl-2-phenylbut-2-enylamine 5d. Compound **5d** was prepared in 61% yield from **4d** as a colourless oil; ν_{max}(thin film)/cm^{-1} 3351, 1704, 1505, 1366, 1249, 1172, 702; δ_H(250 MHz; $CDCl_3$) 1.40 [9H, s, $(CH_3)_3C$], 1.59 (3H, dt, *J* 7.0, 1.2, CH_3), 3.97 (2H, m, NCH_2CH=), 4.55 (1H, br s, N*H* by D_2O exchange), 5.71 (1H, q, *J* 7.0, C*H*=), 7.15–7.40 (5H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) 14.5, 28.4, 47.4, 79.1, 123.0, 127.0, 128.2, 128.7, 138.3, 139.6, 155.8; *m/z* (EI$^+$) 247.1575 (3.8%, M$^+$. $C_{15}H_{21}NO_2$ requires *M*, 247.1572), 191 [100, MH$^+$ − $(CH_3)_3C$], 176 (9), 146 (6), 130 (37), 115 (8).

(*E*)-*N*-*tert*-Butoxycarbonyl-2-phenylthiobut-2-enylamine 5e. Compound **5e** was prepared in 41% yield from **4e** as a yellow solid, mp 52–54 °C (Found: C, 64.4; H, 7.5; N, 4.9; S, 11.6. $C_{15}H_{21}NO_2S$ requires C, 64.5; H, 7.6; N, 5.0; S, 11.5%); ν_{max}(thin film)/cm^{-1} 3348, 1702, 1584, 1507, 1478, 1366, 1249, 1170; δ_H(250 MHz; $CDCl_3$) 1.41 [9H, s, $(CH_3)_3C$], 1.90 (3H, dt, *J* 6.7,

1.2, CH_3), 3.77 (2H, d, *J* 5.5, NCH_2), 4.77 (1H, br s, N*H* by D_2O exchange), 6.25 (1H, q, *J* 6.7, CH_3C*H*=), 7.15–7.30 (5H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) 15.5, 28.4, 46.4, 79.3, 126.1, 128.9, 129.0, 130.8, 133.6, 134.6, 155.6; *m/z* (EI^+) 279.1291 (32%, M^+. $C_{15}H_{21}NO_2S$ requires *M*, 279.1293), 223 [$MH^+ - (CH_3)_3C$, 74], 162 (96), 149 (37), 129 (22), 114 (92), 57 (100).

(*Z*)-*N*-*tert*-Butoxycarbonyl-*N*-[2-(phenyldimethylsilyl)but-2-enyl]benzylamine 1c. Compound **1c** was prepared in 95% yield from **5c** as a colourless oil; ν_{max}(thin film)/cm^{-1} 1694, 1454, 1410, 1365, 1248, 1168, 1111; δ_H(250 MHz; $CDCl_3$) 0.38 [6H, s, (CH_3)$_2$Si], 1.45 [9H, s, (CH_3)$_3$C], 1.67 (3H, dt, *J* 7.0, 1.5, CH_3CH=), 3.93 (2H, br m, NCH_2), 4.31 (2H, br m, NCH_2), 6.12 (1H, q, *J* 7.0, CH_3C*H*=), 7.10–7.55 (10H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) −1.5, 17.7, 28.4, 48.7, 51.9, 79.6, 126.7, 127.1, 127.6, 127.8, 128.4, 128.8, 133.6, 138.4, 139.0, 155.9; *m/z* (EI^+) 395.2279 (9%, M^+. $C_{24}H_{33}NO_2Si$ requires *M*, 395.2281), 338 [17, $M^+ - (CH_3)_3C$], 324 (60), 262 (100), 135 (51), 91 (65).

(*E*)-*N*-*tert*-Butoxycarbonyl-*N*-(2-phenylbut-2-enyl)benzylamine 1d. Compound **1d** was prepared in 94% yield from **5d** as a pale yellow oil (Found: C, 78.1; H, 8.0; N, 3.95. $C_{22}H_{27}NO_2$ requires C, 78.3; H, 8.1; N, 4.15%); ν_{max}(thin film)/cm^{-1} 1694, 1454, 1416, 1365, 1243, 1167, 1124, 879, 700; δ_H(250 MHz; $CDCl_3$) 1.30 [9H, s, (CH_3)$_3$C], 1.55 (3H, m, CH_3), 3.87–4.40 (4H, m, CH_2NCH_2), 5.50 (1H, m, C*H*=), 7.00–7.30 (10H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) 14.4, 28.3, 48.3, 52.6, 79.5, 123.5, 124.0, 126.9, 127.1, 127.4, 128.1, 128.4, 128.8, 137.3, 138.3, 155.7; *m/z* (EI^+) 337.2037 (7%, M^+. $C_{22}H_{27}NO_2$ requires *M*, 337.2042), 281 [74, $MH^+ - (CH_3)_3C$], 132 (27), 91 (100), 57 (46).

(*E*)-*N*-*tert*-Butoxycarbonyl-*N*-(2-phenylthiobut-2-enyl)benzylamine 1e. Compound **1e** was prepared in 82% yield from **5e** as a yellow oil; ν_{max}(thin film)/cm^{-1} 1695, 1584, 1477, 1453, 1410, 1365, 1244, 1167, 1117, 878; δ_H(250 MHz; $CDCl_3$) 1.40 [9H, s, (CH_3)$_3$C], 1.94 (3H, dt, *J* 6.7, 1.5, CH_3), 3.87 (2H, m, NCH_2), 4.38 (2H, m, NCH_2), 6.03–6.17 (1H, m, CH_3C*H*=), 7.05–7.35 (10H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) 15.4, 28.3, 49.1, 51.1, 79.8, 125.8, 127.1, 127.3, 127.9, 128.3, 128.9, 133.4, 135.2, 138.0, 155.9; *m/z* (EI^+) 369.1770 (0.8%, M^+. $C_{22}H_{27}NO_2S$ requires *M*, 369.1763), 313 [1.2, $MH^+ - (CH_3)_3C$], 296 (4), 204 (100), 91 (58), 57 (25).

(*E*)-*N*-*tert*-Butoxycarbonyl-*N*-(2-phenylsulfinylbut-2-enyl)-benzylamine 1f

m-Chloroperbenzoic acid (0.56 g, 1 equiv.) was added portionwise to a stirred solution of (*E*)-*N*-*tert*-butoxycarbonyl-*N*-(2-phenylthiobut-2-enyl)benzylamine **1e** (1.20 g) in dichloromethane (30 ml) at room temperature. After 1 h, further dichloromethane (20 ml) was added, and the reaction mixture washed with saturated aqueous sodium hydrogen carbonate (3 × 50 ml), dried over magnesium sulfate and concentrated *in vacuo* to give a yellow oil (1.60 g). This was purified by flash column chromatography (15 × 3 cm silica, 30% ethyl acetate–light petroleum) to give the sulfoxide **1f** (1.13 g, 90%) as a viscous, pale yellow oil; ν_{max}(thin film)/cm^{-1} 1694, 1454, 1415, 1366, 1247, 1166, 1044, 749, 697; δ_H(250 MHz; $CDCl_3$) 1.37 [9H, m, (CH_3)$_3$C], 2.18 (3H, dt, *J* 7.3, 1.6, CH_3), 3.60–4.30 (4H, m, CH_2NCH_2), 5.90–6.30 (1H, m, CH_3C*H*=), 7.00–7.55 (10H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) 14.9, 28.3, 42.2, 50.1, 80.1, 123.9, 127.2, 127.7, 128.4, 129.1, 131.7, 134.6, 138.1, 140.6, 142.6, 155.8; *m/z* (EI^+) 385.1709 (19%, M^+. $C_{22}H_{27}NO_3S$ requires *M*, 385.1712), 329 [16, $MH^+ - (CH_3)_3C$], 312 [25, $M^+ - (CH_3)_3CO$], 284 [15, $M^+ - (CH_3)_3COCO$], 268 (47, $M^+ -$ PhSO), 204 (100), 158 (35), 144 (40).

(*E*)-*N*-*tert*-Butoxycarbonyl-*N*-(2-phenylsulfonylbut-2-enyl)-benzylamine 1g

A suspension of Oxone (5.79 g, 3 equiv.) and water (15 ml) was added portionwise to a stirred solution of **1e** (1.16 g) in methanol (25 ml) at 0 °C. Upon complete addition, the reaction was warmed to room temperature and stirred for 14 h. The methanol was removed *in vacuo*, the residue partitioned between water (15 ml) and dichloromethane (15 ml), the organic layer was separated and the aqueous layer further extracted with dichloromethane (3 × 15 ml). The combined organics were dried over magnesium sulfate and concentrated *in vacuo* to give a crude, yellow oil which was purified by flash column chromatography (15 × 3 cm silica, 20% ethyl acetate–light petroleum) to give the sulfoxide **1g** (1.20 g, 95%) as a viscous, pale yellow–green oil; ν_{max}(thin film)/cm^{-1} 1694, 1447, 1410, 1366, 1305, 1247, 1159, 1137, 1083, 729, 690; δ_H(250 MHz; $CDCl_3$) 1.40 [9H, m, (CH_3)$_3$C], 2.15 (3H, dt, *J* 7.6, 1.5, CH_3), 4.05 (2H, br m, NCH_2), 4.33 (2H, s, NCH_2), 6.00–6.35 (1H, br m, CH_3C*H*=), 7.05–7.90 (10H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) 14.7, 28.4, 48.2, 49.9, 80.6, 127.2, 127.6, 128.7, 129.4, 133.5, 136.8, 137.6, 138.1, 140.6, 141.5, 155.7; *m/z* (EI^+) 401.1658 (0.3%, M^+. $C_{22}H_{27}NO_4S$ requires *M*, 401.1661), 345 [10, $MH^+ - (CH_3)_3C$], 300 [37, $M^+ - (CH_3)_3COCO$], 204 (59), 150 (38), 144 (31), 106 (90), 91 (100), 77 (24), 57 (85).

(1*S,2*R**)-*N*-*tert*-Butoxycarbonyl-2-methyl-1-phenyl-3-(phenyldimethylsilyl)but-3-enylamine 3c**

Butyllithium (0.66 ml of a 2.5 M solution in hexane, 1.7 mmol, 1.2 equiv.) was added dropwise to a stirred soution of (*Z*)-*N*-*tert*-butoxycarbonyl-*N*-[2-(phenyldimethylsilyl)but-2-enyl]-benzylamine **1c** (0.55 g, 1.4 mmol) in tetrahydrofuran (11 ml) at −78 °C. After stirring for 14 h at −78 °C, the reaction was quenched by the addition of methanol (0.1 ml) and warmed to room temperature. The reaction mixture was then partitioned between saturated aqueous sodium hydrogen carbonate (20 ml) and diethyl ether (15 ml), the organic layer was separated and the aqueous layer further extracted with diethyl ether (3 × 15 ml). The combined organics were dried over magnesium sulfate and concentrated *in vacuo* to give a viscous pale yellow oil (0.63 g) which was purified by flash column chromatography (12 × 2.5 cm silica, 7% ethyl acetate–light petroleum) to give the title compound **3c** as a colourless oil (0.44 g, 81%) (Found: C, 72.4; H, 8.6; N, 3.8. $C_{24}H_{33}NO_2Si$ requires C, 72.9; H, 8.4; N, 3.5%); ν_{max}(thin film)/cm^{-1} 3425, 1702, 1496, 1366, 1250, 1171, 817, 734, 701; δ_H[250 MHz; (CD_3)$_2$SO] 0.42 [3H, s, (CH_3)Si], 0.47 [3H, s, (CH_3)Si], 0.53 (3H, d, *J* 7.0, =CCHCH_3), 1.15 [9H, s, (CH_3)$_3$C], 2.59 (1H, dq, *J* 9.6, 7.0, =CC*H*CH$_3$), 4.47 (1H, t, *J* 9.6, NC*H*Ph), 5.42 (1H, d, *J* 2.4, *H*HC=), 5.81 (1H, d, *J* 2.4, H*H*C=), 6.87 (1H, d, *J* 9.6, N*H* by D_2O exchange), 6.95–7.45 (10H, m, Ar*H*); δ_C(63 MHz; $CDCl_3$) −2.6, 19.7, 28.4, 42.2, 59.3, 79.0, 127.0, 127.1, 127.5, 128.0, 128.2, 129.3, 134.1, 137.9, 142.8, 152.9, 154.9; *m/z* (EI^+) 395.2274 (3.7%, M^+. $C_{24}H_{33}NO_2Si$ requires *M*, 395.2281), 382 (2), 262 (7), 206 (49), 172 (9), 150 (100), 135 (48), 106 (79), 91 (7), 57 (94).

(1*S,2*R**)-*N*-*tert*-Butoxycarbonyl-2-methyl-1,3-diphenylbut-3-enylamine 3d**

Butyllithium (1.64 ml of a 2.5 M solution in hexane, 4.1 mmol, 1.2 equiv.) was added dropwise to a stirred solution of (*E*)-*N*-*tert*-butoxycarbonyl-*N*-(2-phenylbut-2-enyl)benzylamine **1d** (1.15 g, 3.4 mmol) in tetrahydrofuran–HMPA (4:1, 23 ml) at −78 °C. After stirring for 1 h at −78 °C, the reaction was slowly warmed to −40 °C and stirred for 14 h before being quenched by the addition of methanol (0.2 ml). The reaction mixture was then partitioned between saturated aqueous sodium hydrogen carbonate (50 ml) and diethyl ether (30 ml), the organic layer was separated and the aqueous layer further extracted with diethyl ether (3 × 30 ml). The combined organics were dried over magnesium sulfate and concentrated *in vacuo* to give a viscous yellow gum (2.3 g) which was purified by flash column chromatography (12 × 4 cm silica, 10% ethyl acetate–light petroleum) to give a pale yellow solid (0.82 g, 71% of a 7:1 mixture of the title compound **3d** to the minor diastereoisomer **2d**). Trituration with ice-cold light petroleum furnished the major diastereoisomer only as a white powder (0.68 g, 59%), mp 123–124 °C (Found: C, 77.9; H, 7.7; N, 4.3. $C_{22}H_{27}NO_2$

requires C, 78.3; H, 8.1; N, 4.2%); ν_{max}(thin film)/cm^{-1} 3274, 1701, 1495, 1454, 1390, 1365, 1248, 1170, 701; δ_H[250 MHz; $(CD_3)_2SO$] 0.70 (3H, d, *J* 6.7, C*H*$_3$), 1.30 [9H, s, (C*H*$_3$)$_3$C], 3.02 (1H, dq, *J* 9.5, 6.7, CH$_3$C*H*C=), 4.53 (1H, t, *J* 9.5, NHC*H*Ph), 5.11 (1H, s, CH*H*=), 5.21 (1H, s, C*H*H=), 7.20–7.50 (11H, m, Ar*H* and N*H* by D_2O exchange); δ_C[63 MHz; $(CD_3)_2SO$] 18.7, 28.7, 43.8, 58.3, 78.0, 113.2, 127.2, 127.7, 127.9, 128.4, 128.7, 142.6, 142.9, 151.9, 155.2; *m/z* (EI$^+$) 337.2039 (0.4%, M$^+$. $C_{22}H_{27}NO_2$ requires *M*, 337.2042), 281 [3, MH$^+$ − $(CH_3)_3$C], 236 [10, M$^+$ − $(CH_3)_3$COCO], 206 (38), 196 (24), 150 (87), 106 (83), 91 (47), 57 (100).

(1*S**,2*R**)-*N*-*tert*-Butoxycarbonyl-2-methyl-1-phenyl-3-phenylthiobut-3-enylamine 3e

(*E*)-*N*-*tert*-Butoxycarbonyl-*N*-(2-phenylthiobut-2-enyl)benzylamine **1e** (0.72 g, 2.0 mmol) was treated with BuLi under exactly the same conditions and work up as for **3d** to give a viscous yellow oil (1.2 g) which was purified by flash column chromatography (15 × 3 cm silica, 10% ethyl acetate–light petroleum) to give a pale yellow solid (0.35 g, 49% of a 1:2:4 mixture of the minor diastereoisomer **2e**, *N*-*tert*-butoxycarbonylbenzylamine and the title compound **3e** respectively). Trituration with ice-cold light petroleum furnished the title compound only as a white powder (0.19 g, 26%), mp 121–122 °C; ν_{max}(thin film)/cm^{-1} 3375, 1679, 1512, 1368, 1292, 1250, 1171, 742, 704; δ_H[250 MHz; $(CD_3)_2SO$] 0.76 (3H, d, *J* 7.0, C*H*$_3$), 1.35 [9H, s, (C*H*$_3$)$_3$C], 2.76 (1H, dq, *J* 9.8, 7.0, CH$_3$C*H*C=), 4.60 (1H, s, CH*H*=), 4.70 (1H, t, *J* 9.5, NHC*H*Ph), 5.30 (1H, s, C*H*H=), 7.20–7.55 (11H, m, Ar*H* and N*H* by D_2O exchange); δ_C[63 MHz; $(CD_3)_2SO$] 17.7, 28.8, 46.9, 58.2, 78.1, 113.2, 127.4, 127.9, 128.6, 128.7, 129.9, 133.0, 134.1, 142.7, 149.4, 155.1; *m/z* (EI$^+$) 369.1767 (5%, M$^+$. $C_{22}H_{27}NO_2S$ requires *M*, 369.1762), 296 [5, M$^+$ − $(CH_3)_3$CO], 268 [3 M$^+$ − $(CH_3)_3$COCO], 260 (2, M$^+$ − Ph) 206 (63), 150 (100), 106 (87), 57 (96).

Attempted aza-[2,3] Wittig sigmatropic rearrangement of (*E*)-*N*-*tert*-butoxycarbonyl-*N*-(2-phenylsulfinylbut-2-enyl)benzylamine 1f

(*E*)-*N*-*tert*-Butoxycarbonyl-*N*-(2-phenylsulfinylbut-2-enyl)-benzylamine **1f** (63 mg, 0.16 mmol) was treated with butyllithium under exactly the same conditions and work up as for **3d** to give a viscous yellow oil (70 mg) which was purified by flash column chromatography (15 × 1 cm silica, 20% ethyl acetate–light petroleum) to furnish (*E*)-*N*-*tert*-butoxycarbonyl-*N*-but-2-enylbenzylamine **1a**[6] (13 mg, 30%) and *N*-*tert*-butoxycarbonylbenzylamine (16 mg, 48%).

(1*S**,2*R**)-*N*-*tert*-Butoxycarbonyl-2-methyl-1-phenylbut-3-enylamine 3a

Tetrabutylammonium fluoride (1.1 ml of a 1 M solution in tetrahydrofuran, 1.1 mmol, 5 equiv.) was added to a stirred solution of (1*S**,2*R**)-*N*-*tert*-butoxycarbonyl-2-methyl-1-phenyl-3-(phenyldimethylsilyl)but-3-enylamine **3c** (85 mg, 0.2 mmol) in dimethyl sulfoxide. After stirring for 2 h at 100 °C (oil bath temperature), the reaction mixture was cooled, diluted with ethyl acetate (10 ml), washed sequentially with water (4 × 10 ml) and brine (10 ml), dried thoroughly over magnesium sulfate and concentrated *in vacuo* to give an off-white solid (34 mg). Purification by flash column chromatography (15 × 1 cm silica, 10% ethyl acetate–light petroleum) furnished the title compound **3a** as a white solid (26 mg, 47%).[6]

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