The Silicon-Assisted Aza-[2,3]-Wittig Sigmatropic Rearrangement†

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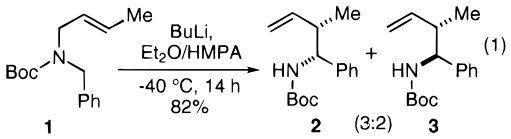
We have independently reported the first example of an acyclic aza-[2,3]-Wittig sigmatropic rearrangement (eq 1).[1] There are only two prior reports of true examples of this transformation, although they involved the use of cyclic precursors 1-benzyl-4-vinyl-2-azetidinone[2] and vinyl aziridines.[3] The ease with which these particular rearrangements occurred is undoubtedly due to relief of ring strain in the four- and three-membered ring substrates, respectively. There have been unsuccessful attempts to perform the acyclic variant which do not invoke this driving force.[4,5] Recently, Gawley has reported acyclic examples involving α-lithio pyrrolidines, but the desired products of the anionic rearrangements were contaminated with [1,2] products.[6] Higher yields and enantioselectivities were obtained *via* the corresponding ylide rearrangements.



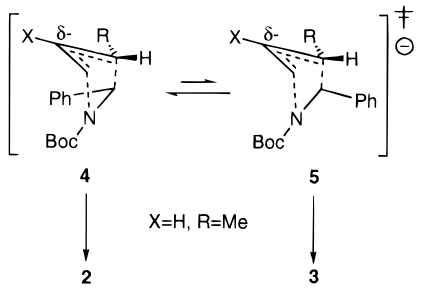
1 2 3

The rearrangement of Li-**1** occurred at −40 °C overnight and gave a 3:2 ratio of diastereoisomers. In accord with the calculated transition state structure of Houk[7] for the oxy-[2,3]-Wittig rearrangement[8] we attribute the poor diastereoselectivity in our rearrangement to the presumably small difference in transition state energies of **4** versus **5** (Scheme 1).

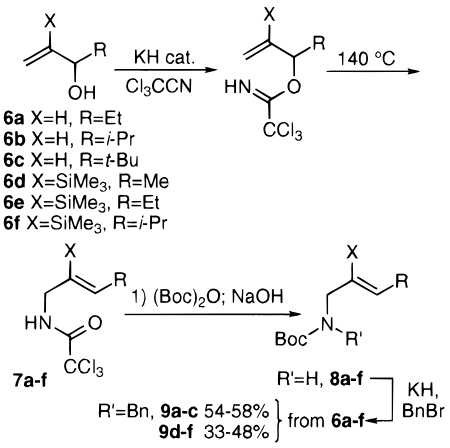
We now report details of how we have achieved reliably high yielding, diastereoselective rearrangements by judicious placement of a trimethylsilyl group in the precursor. This modification should now allow the aza-[2,3]-Wittig rearrangement wider scope in synthesis.

Our initial plans to enhance diastereoselection were to survey the effect of changing the bulk of R in **4** (Scheme

Scheme 1

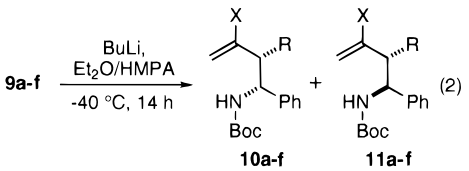


Scheme 2



1). We anticipated that increasing the steric bulk of R would favor **5** with respect to **4** so as to avoid a destabilizing 1,2 interaction. Preparation of the desired allylic amines **9a**−**c** was accomplished in four steps from the allylic alcohols **6a**−**c** *via* the established procedure for stereoselective conversion of secondary allylic alcohols to *E* allyl amides **7a**−**c** (Scheme 2).[9] Isolation of the free amine from the basic hydrolysis of the trichloroacetamides **7a**−**c** was low yielding, presumably due to the volatility of the amines involved. A more satisfactory procedure was to Boc protect the crude amide in situ and then remove the trichloroacetyl group by addition of 6 N NaOH with warming to 50 °C overnight. Standard *N*-benzylation of the purified Boc protected allylic amines **8a**−**c** gave the diastereomerically pure rearrangement precursors **9a**−**c** in 54−58% overall yield from **6a**−**c**.

Rearrangement under standard conditions[1] led to the Boc protected homoallylic amines **10** and **11** (eq 2, Table 1).



10a-f 11a-f

The sense of diastereoselection for the rearrangement of **9b** was assigned by comparison of its ^{1}H NMR spectra with that of the two diastereoisomers from eq 1. We noted that the Me group of major diastereoisomer **2** appeared at δ 0.96, upfield with respect to the Me group of minor diastereoisomer **3** δ 0.71. In both **2** and **3** the protons α to nitrogen appeared as doublets with the identical coupling constants (9.0 Hz). As the relative

† Dedicated to Clayton H. Heathcock on the occasion of his 60th birthday.

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§ Zeneca Agrochemicals.

(1) Anderson, J. C.; Siddons, D. C.; Smith, S. C.; Swarbrick, M. E. *J. Chem. Soc., Chem. Commun.* **1995**, 1835.

(2) Durst, T.; Elzen, R. V. D.; Le Belle, M. J. *J. Am. Chem. Soc.* **1972**, *94*, 9261.

(3) (a) Ahman, J.; Somfai, P. *J. Am. Chem. Soc.* **1994**, *116*, 9781. (b) Coldham, I.; Collis, A. J.; Mould, R. J.; Rathmell, R. E. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2739.

(4) (a) Broka, C. A.; Shen, T. *J. Am. Chem. Soc.* **1989**, *111*, 2981. (b) Murata, Y.; Nakai, T. *Chem. Lett.* **1990**, 2069. (c) Coldham, I. *J. Chem. Soc., Perkin Trans 1* **1993**, 1275.

(5) The rearrangement in ref 4a has been shown to proceed by a [1,2] mechanism.[4b]

(6) Gawley, R. E.; Zhang, Q.; Campagna, S. *J. Am. Chem. Soc.* **1995**, *117*, 11817.

(7) Wu, Y.-D.; Houk, K. N.; Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 1421. See also Mikami, K.; Uchida, T.; Hirano, T.; Wu, Y.-D.; Houk, K. N. *Tetrahedron* **1994** *50*, 5917.

(8) For a recent review see Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105.

(9) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901.

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Table 1. Aza-[2,3]-Wittig Rearrangements of 9a−c, X = H

	R	yield[a] (%)	diastereoselectivity[b] **10**:**11**
1	Me	82	3:2
9a	Et	69	1:1
9b	*i*-Pr	54	4:3
9c[c]	*t*-Bu	−	−

[a] Isolated yields of purified **10** and **11** together. [b] Ratios of unpurified products determined by 250-MHz NMR. [c] Low yield of impure material that could not be conclusively characterised.

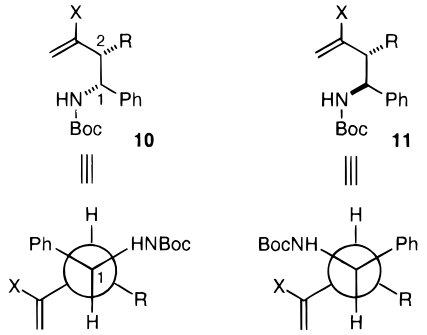

Figure 1.

Table 2. Selected NMR Data for 10 and 11

X	R	diastereoselectivity[a] **10**:**11**	*δ* R(Me groups) **10**:**11**[b]	*J* C_1H-C_2H
H	Me	3:2	0.96; 0.71	9.0 (**10** & **11**)
H	*i*-Pr	4:3	0.85, 0.81; 0.78, 0.75	10.1 (**10**); 9.3 (**11**)
$SiMe_3$	Me	<1:20	1.02; 0.66[c]	10.4 (**11**)[d]
$SiMe_3$	Et	1:18	0.73; 0.57[c]	10.2 (**11**)[d]
$SiMe_3$	*i*-Pr	1:11	0.84, 0.79; 0.71	9.8 (**11**)[d]

[a] Ratios of unpurified products determined by 250-MHz NMR. [b] DMSO-d_6. [c] Minor diastereoisomer visible from less selective reactions run at 0 °C. [d] *J* for **10** not visible.

stereochemistry of **2** and **3** have been proven by manipulation to known compounds,[1] these characteristics in the NMR spectrum of **2** and **3** can be rationalized by conformational analysis. By examining the Newmann projections of the energetically most favorable conformations of **2** and **3** (**10** and **11**, X = H, R = Me; Figure 1) it is only the *anti* diastereoisomer **11** in which the R group can feel the shielding effect of the proximal aromatic ring and thus account for the lower chemical shift of this substituent. The equivalence of the coupling constant between C_1H-C_2H (Figure 1) for both diastereoisomers and its magnitude indicates a *trans* diaxial arrangement[10] in each case and supports the conformations drawn. Products **10b** and **11b** have different chemical shifts for their isopropyl methyl groups. As the C_1H-C_2H coupling constant for this set of diastereoisomers is of the same magnitude as that for diastereoisomers **2** and **3** we assign the *syn* diastereoisomer **10b** to the major component that exhibits the lowest field signals for R (Figure 1 and Table 2).

Increasing the steric bulk of R (Me, Et, *i*-Pr) when X = H had little effect on the diastereoselection. Extremely bulky groups, such as *t*-Bu, are not compatible with this rearrangement. Increasing the steric bulk of R does not change the direction of diastereoselection as anticipated based upon the transition state model (Scheme 1).

Table 3. Aza-[2,3]-Wittig Rearrangements of 9d−f, X = $SiMe_3$

	R	yield[a] (%)	diastereoselectivity[b] **10**:**11**
9d	Me	88	<1:20
9e	Et	92	1:18
9f	*i*-Pr	94	1:11

[a] Isolated yields of purified **10** and **11** together. [b] Ratios of unpurified products determined by 250-MHz NMR.

In an attempt to circumvent these inherent problems to our system we expected that stabilizing the transition state in some way would allow milder reaction conditions and possibly enhanced diastereoselectivity. Taking note of the computed transition state structure for the oxy-[2,3]-Wittig rearrangement[7] (Scheme 1) there was predicted to be a small build up of negative charge at the central vinyl carbon during the rearrangement. Assuming a similar transition state structure for the aza variant, substitution at this carbon atom with an anion-stabilizing group should stabilize this transition state structure and promote the rearrangement. Additionally a bulky substituent at this position may increase diastereoselectivity by favoring structure **5** over **4** so as to avoid a destabilizing 1,3 interaction.

The trimethylsilylstabilizing group was selected due to the known propensity of silicon to stabilize an adjacent negative charge.[11,12] The steric bulk of the group should also maximize steric interactions.[13] Substrates **9d−f** were prepared (Scheme 2) in an analogous fashion to **9a−c** starting from the addition product of (1-lithiovinyl)-trimethylsilane with the requisite aldehyde[14] in comparable overall yields of 33−48%. The efficiency of preparing the *N*-(trichloroacetyl)-2-(trimethylsilyl)allylamines **7d−f** (60−78%) was compromised when exchange of protecting group on nitrogen was performed to give the *N*-Boc-2-(trimethylsilyl)allylamines. Unfortunately the precursor **9** where X = $SiMe_3$ and R = *t*-Bu could not be prepared by this route, failing at the formation of the trichloroacetimidate.

We were gratified to find that treatment of **9d** with *n*-BuLi at −78 °C in a mixture of Et_2O and HMPA consumed all starting material after 10 min. The product was formed as a major diastereoisomer (>15:1) in an isolated yield of 67%. We have subsequently found that by conducting the experiment in THF for 20 h there is no need for any HMPA, and that an 88% yield of rearranged material was obtained with a diastereoselectivity of >20:1 in favor of **11d**. Treatment of **9e**,**f** with *n*-BuLi led to mainly one rearranged product **11e**,**f** in high yields (Table 3). These rearrangements both proceeded at −78 °C, but the incorporation of HMPA as cosolvent was required to push the reaction to completion.

(10) These coupling constants may be slightly smaller than one would expect for a *trans* diaxial coupling, but it is known that electronegative substituents reduce coupling constants. Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon: New York, 1969, p 238 and references therein.

(11) Schleyer, P. v R.; Clark, T.; Kos, A. J.; Spitznagel, G. W.; Rohde, C.; Arad, D.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1984**, *106*, 6467.

(12) We have also investigated substitution by phenyl and thiophenyl, both of which promote the rearrangement, the results of which will be reported in due course.

(13) Trialkylsilyl groups have been used specifically to alter the stereochemical outcome of the resultant alkenes in oxy-[2,3]-Wittig rearrangements, but we have found no references to their use in control of diastereoselectivity in such rearrangements. Crawley, J. E.; Kaye, A. D.; Pattenden, G.; Roberts, S. M. *J. Chem. Soc., Perkin Trans 1* **1993**, 2001.

(14) Chan, T. H.; Mychajlowskij, W.; Ong, B. S.; Harpp, D. N. *J. Org. Chem.* **1978**, *43*, 1526.

The major diastereoisomer for these silicon-assisted rearrangements has been assigned as **11** on the basis of the difference in chemical shift of the R substituents Me groups for the two diastereoisomers as before (Figure 1, Table 2). Unambiguous proof of this assignment, by conversion of mixture **10**/**11d** to a mixture of **2**/**3**, was thwarted by the reluctance of the vinyl silane to undergo protodesilylation under reported conditions.[15]

It would seem that increasing the steric bulk of the R group in precursors **9d**−**f** (R = Me, Et or *i*-Pr) slightly erodes the diastereoselectivity of this process, but has no effect on the yield or the sense of diastereoselection. It is clear that in our systems the trialkylsilyl group is not only acting as a steric control element in a direction consistent with the transition state model (Scheme 1), but also increasing the rate of the reaction as planned. In view of the high diastereoselectivites observed we are confident that these rearrangements proceed by a concerted [2,3] sigmatropic mechanism.

We have shown that the aza-[2,3]-Wittig rearrangement is applicable to a variety of substrates containing a *trans* arrangement of alkyl groups on the alkene. The reaction can be accelerated by the judicious placement of an anion-stabilizing trimethylsilyl group, which greatly enhances the diastereoselectivity of these rearrangements. These results support the transition state model in Scheme 1 and indirectly, Houk's calculations on the transition state of related rearrangements.[7] We are currently extending this methodology to diastereo- and enantioselective variants and pursuing the synthesis of unnatural amino acids, which will all be reported in due course.

Experimental Section

General Methods. All nonaqueous reactions were performed under an oxygen-free atmosphere of nitrogen with rigorous exclusion of moisture from reagents and glassware. Thin layer chromatography was carried out using Merck 5554 60F silica gel coated aluminum plates and visualization was effected using ultraviolet light or by development using iodine, potassium iodoplatinate solution, potassium permanganate solution, or ceric ammonium molybdate solution. Flash chromatography[16] was performed using the indicated solvent system on BDH silica gel for flash chromatography (40−63 μm). ^{1}H and ^{13}C NMR spectra were recorded at 250 and 63 MHz, respectively, in $CDCl_3$ unless otherwise stated. Elemental analyses were obtained in the Department of Chemistry at the University of Sheffield.

Reagents and solvents were purified prior to use when necessary according to established procedures.[17] THF was distilled from K/benzophenone ketyl, Et_2O was distilled from Na/benzophenone ketyl, and CH_2Cl_2 and Et_3N were distilled from CaH. Allylic alcohols **6a**−**f** were obtained from the addition of either vinylmagnesium bromide or (1-lithiovinyl)trimethylsilane to the requisite aldehyde followed by distillation.

General Procedure for the Preparation of *N*-Boc-(*E*)-Allylic Amines 8. A solution of the crude *N*-trichloroacetyl-(*E*)-allylamine[18] **7** (1 equiv), $(Boc)_2O$ (1.5 equiv), and DMAP (0.1 equiv) in MeCN (4 mL/mmol) was stirred at 50 °C. After 1−4 h, NaOH (6 N, 12 equiv) was added and stirring continued for 14 h at 50 °C. The mixture was allowed to cool, the MeCN removed *in vacuo*, and the residue partitioned between H_2O and CH_2Cl_2. Upon separation the aqueous layer was further extracted with CH_2Cl_2, the combined organics were dried over $MgSO_4$ and filtered, and the solvent was removed *in vacuo*. Purification by flash-column chromatography eluting with EtOAc/light petroleum furnished the diastereomerically pure *N*-Boc-(*E*)-allylic amines **8** as mobile, colorless oils.

***N*-Boc-Pent-2(*E*)-enylamine (8a):** 71% from **6a**. IR (thin film) 3347, 1694, 1521 cm^{-1}; ^{1}H NMR δ 0.98 (3H, t, J = 7.6), 1.45 (9H, s), 2.03 (2H, quin q, J = 7.3, 1.2), 3.70 (2H, t, J = 5.5), 4.53 (1H, s, N*H*, by D_2O exchange), 5.41 (1H, dtt, J = 15.3, 6.1, 1.2), 5.63 (1H, dtt, J = 15.3, 6.1, 1.2); ^{13}C NMR δ 13.4, 25.2, 28.4, 42.5, 79.1, 125.3, 134.5, 155.7; MS (EI$^+$) m/z 185 (M$^+$). Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.82; H, 10.34; N, 7.56. Found: C, 64.69; H, 10.06; N, 7.67%.

***N*-Boc-4-Methylpent-2(*E*)-enylamine (8b):** 69% from **6b**. IR (thin film) 3347, 1699, 1522 cm^{-1}; ^{1}H NMR δ 0.96 (6H, d, J = 6.7), 1.45 (9H, s), 2.28 (1H, oct, J = 6.7), 3.66 (2H, t, J = 5.8), 4.50 (1H, s, N*H*, by D_2O exchange), 5.37 (1H, dtd, J = 15.3, 6.1, 0.9), 5.55 (1H, ddt, J = 15.3, 6.4, 1.2); ^{13}C NMR δ 22.2, 28.4, 30.7, 42.6, 79.2, 123.3, 140.0, 156.0; MS (EI$^+$) m/z 199 (M$^+$). Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.28; H, 10.63; N, 7.03. Found: C, 66.37; H, 10.59; N, 6.80%.

***N*-Boc-4,4-Dimethylpent-2(*E*)-enylamine (8c):** 68% from **6c**. IR (thin film) 3346, 1694, 1522 cm^{-1}; ^{1}H NMR δ 0.98 (9H, s), 1.43 (9H, s), 3.67 (2H, t, J = 5.5), 4.48 (1H, s, N*H*, by D_2O exchange), 5.32 (1H, dt, J = 15.6, 6.1), 5.58 (1H, dt, J = 15.6, 1.2); ^{13}C NMR δ 28.4, 29.5, 32.8, 42.8, 79.1, 121.1, 143.9, 155.7; MS (EI$^+$) m/z 213(M$^+$). Anal. Calcd for $C_{12}H_{23}NO_2$: C, 67.55; H, 10.87; N, 6.57. Found: C, 67.27; H, 10.77; N, 6.62%.

***N*-Boc-2-(Trimethylsilyl)but-2(*Z*)-enylamine (8d):** 52% from **6d**. IR (thin film) 3353, 1705 cm^{-1}; ^{1}H NMR δ 0.15 (9H, s), 1.40 (9H, s), 1.76 (3H, dt, J = 7.0, 1.2), 3.71 (2H, d, J = 4.6), 4.33 (1H, br s, N*H*, by D_2O exchange), 6.17 (1H, qt, J = 7.0, 1.3); ^{13}C NMR δ −0.2, 17.4, 28.4, 47.6, 79.0, 136.6, 138.7, 157.6; MS (EI$^+$) 243 (M$^+$). Anal. Calcd for $C_{12}H_{25}NO_2Si$: C, 59.21; H, 10.35; N, 5.75. Found: C, 59.16; H, 10.25; N, 5.60%.

***N*-Boc-2-(Trimethylsilyl)pent-2(*Z*)-enylamine (8e):** 34% from **6e**. IR (thin film) 3353, 1705 cm^{-1}; ^{1}H NMR δ 0.14 (9H, s), 0.96 (3H, t, J = 7.3), 1.43 (9H, s), 2.13 (2H, pen, J = 7.5), 3.71 (2H, d, J = 5.2), 4.32 (1H, br.s, N*H*, by D_2O exchange), 6.04 (1H, tt, J = 7.6, 1.2); ^{13}C NMR δ 0.01, 14.3, 25.0, 28.4, 47.6, 79.1, 135.0, 146.4, 154.5; MS (EI$^+$) 258 (M$^+$); HRMS $C_{13}H_{27}NO_2Si$ calcd 257.1811, found 257.1817.

***N*-Boc-2-(Trimethylsilyl)-4-methylpent-2(*Z*)-enylamine (8f):** 38% from **6f** as a white amorphous solid; mp 91−3 °C; IR (thin film) 3327,1683 cm^{-1}; ^{1}H NMR δ 0.13 (9H, s), 0.93 (6H, d, J = 6.7), 1.42 (9H, s), 2.53 (1H, d sept, J = 10.4, 6.4), 3.69 (2H, d, J =5.2), 4.29 (1H, br s, N*H*, by D_2O exchange), 5.82 (1H, dt, J = 9.2, 1.2); ^{13}C NMR δ 0.14, 22.9, 28.4, 30.8, 47.6, 79.0, 132.6, 152.1, 154.5; MS (EI$^+$) 271 (M$^+$). Anal. Calcd for $C_{14}H_{29}NO_2Si$: C, 61.94; H, 10.77; N, 5.16. Found: C, 61.87; H, 10.92; N, 5.14%.

General Procedure for Preparation of *N*-Boc-*N*-Benzyl Allylic Amines 9a−f. A solution of the *N*-Boc-allylic amine (1 equiv) in THF (2 mL/mmol) was added dropwise *via* cannula to a stirred suspension of KH (1.2 equiv of a 35% dispersion in mineral oil, washed twice with hexane) in an equal volume of THF at 0 °C. After stirring for 1 h at 0 °C, a solution of BnBr (1.2 equiv) in THF (total concentration 5 mL/mmol) was added and the reaction stirred for 1 h at 0 °C followed by 14 h at rt. Saturated aqueous $NaHCO_3$ was added, and the THF was removed *in vacuo*. The residue was partitioned between saturated aqueous $NaHCO_3$ and Et_2O and the aqueous further extracted with Et_2O. The combined organics were dried over $MgSO_4$ and filtered, and the solvent was removed *in vacuo* to give crude products which were purified by flash-column chromatography eluting with EtOAc/light petroleum to furnish the *N*-Boc-*N*-benzyl allylic amines **9a**−**f** as colorless oils.

***N*-Boc-*N*-[Pent-2(*E*)-enyl]benzylamine (9a):** 97%. IR (thin film) 1695 cm^{-1}; ^{1}H NMR δ 0.98 (3H, t, J = 7.6), 1.50 (9H, s), 2.06 (2H, quin q, J = 7.3, 1.2), 3.74 (2H, m), 4.40 (2H, s), 5.40 (1H, m), 5.53 (1H, m), 7.10−7.40 (5H, m); ^{13}C NMR δ 13.5, 25.2, 28.4, 47.9, 48.9, 79.5, 124.0, 126.9, 127.3, 128.3, 135.5; MS (EI$^+$) m/z 275 (M$^+$). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.95; H, 8.93; N, 5.14%.

***N*-Boc-*N*-(4-Methylpent-2(*E*)-enyl)benzylamine (9b):** 98% IR (thin film) 1695 cm^{-1}; ^{1}H NMR δ 0.96 (6H, d, J = 6.7), 1.48 (9H, s), 2.26 (1H, oct, J = 6.7), 3.75 (2H, m), 4.42 (2H, br s), 5.33 (1H, m), 5.47 (1H, m), 7.15−7.45 (5H, m); ^{13}C NMR δ 22.3,

(15) Fleming, I.; Dunoduès, J.; Smithers, R. *Org. React.* **1989**, *37*, 57. Protodesilylation of a terminal vinylsilane where the silyl group is on C2 is known to be difficult, presumably because the accepted mechanism would require the formation of an incipient primary carbocation.

(16) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(17) Perrin, D. D., Armarego, W. L. F., Eds. *Purification of Laboratory Chemicals*; Pergamon Press: New York.

(18) Prepared according to the procedure outlined in ref 9.

28.5 30.8, 48.0, 49.0, 79.6, 122.1, 127.0, 127.8, 128.4, 140.6; MS (EI^+) *m/z* 289 (M^+); HRMS $C_{18}H_{27}NO_2$ calcd 289.2042, found 289.2043.

***N*-Boc-*N*-(4,4-Dimethylpent-2(*E*)-enyl)benzylamine (9c):** 98%. IR (thin film) 1695 cm^{-1}; ^1H NMR δ 0.95 (9H, s), 1.48 (9H, s), 3.75 (2H, m), 4.39 (2H, s), 5.26 (1H, m), 5.49 (1H, m), 7.15−7.40 (5H, m); ^{13}C NMR δ 28.5, 29.5, 32.9, 48.2, 49.0, 79.6, 119.8, 127.0, 127.8, 128.3, 138.6, 144.4; MS (EI^+) *m/z* 303 (M^+). Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.05; H, 9.38; N, 4.65%.

***N*-Boc-*N*-[2-(Trimethylsilyl)but-2(*Z*)-enyl]benzylamine (9d):** 90%. IR (thin film) 1695 cm^{-1}; ^1H NMR δ 0.14 (9H, s), 1.46 (9H, s), 1.81 (3H, dt, J = 7, 1.5), 3.88 (2H, br s), 4.34 (2H, br s), 5.99 (1H, q, J = 7.0), 7.15−7.37 (5H, m); ^{13}C NMR δ -0.23, 17.3, 28.4, 48.3, 51.9, 79.6, 126.9, 127.5, 128.34, 138.5; MS (EI^+) 333 (M^+). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.26; H, 9.28; N, 4.08%.

***N*-Boc-*N*-[2-(Trimethylsilyl)pent-2(*E*)-enyl]benzylamine (9e):** 96%. IR (thin film) 1696 cm^{-1}; ^1H NMR δ 0.12 (9H, s), 0.98 (3H, t, J = 7.6), 1.45 (9H, s), 2.16 (2H, pent, J = 7.5), 3.85 (2H, br s), 4.36 (2H, br s), 5.83 (1H, t, J = 7.3), 7.13−7.38 (5H, m); ^{13}C NMR δ −0.01, 14.6, 25.0, 28.5, 48.3, 51.9, 79.6, 127.0, 127.6, 128.5, 138.5; MS (EI^+) 347 (M^+); HRMS $C_{20}H_{33}NO_2Si$ calcd 347.2281, found 347.2275.

***N*-Boc-*N*-[2-(Trimethylsilyl)-4-methylpent-2(*E*)-enyl]benzylamine (9f):** 100%. IR (thin film) 1696 cm^{-1}; ^1H NMR δ 0.11 (9H, s), 0.95 (6H, d, J = 6.4), 1.47 (9H, s), 2.60 (1H, d sept, J = 10.5, 6.5), 3.84 (2H, br s), 4.35 (2H, br s), 5.61 (1H, d, J = 10.4), 7.12−7.42 (5H, m); ^{13}C NMR δ 0.01, 23.0, 28.4, 30.7, 48.3, 51.7, 79.5, 126.9, 127.6, 128.3, 138.3; MS (EI^+) 361 (M^+); HRMS $C_{21}H_{35}NO_2Si$ calcd 361.2437, found 361.2444

General Experimental for the Aza-[2,3]-Wittig Sigmatropic Rearrangement of 1 and 9a−c. *n*-BuLi (2.5 M in hexanes, 1.2 equiv) was added slowly to a stirred solution of the *N*-Boc-*N*-allylbenzylamine **1** or **9a−c** (1 equiv) in Et_2O/HMPA (4:1, 5 mL/mmol) at −78 °C. After 1 h the reaction mixture was warmed to −40 °C and stirred for 14 h before being quenched by the addition of MeOH and partitioned between saturated aqueous $NaHCO_3$ and Et_2O. The aqueous was further extracted with Et_2O, and the combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting crude products were purified by flash-column chromatography (EtOAc/light petroleum or Et_2O/light petroleum) to furnish the rearranged products **2**, **3**, and **10a−c**, **11a−c**.

(1*R,2*S**)-*N*-Boc-2-Methyl-1-phenylbut-3-enylamine (2) and (1*S**,2*S**)-*N*-Boc-2-Methyl-1-phenylbut-3-enylamine (3):** 82% of **2**:**3**, in an inseparable ratio of 3:2, as a white amorphous solid; mp 95−7 °C; IR (thin film) 3374, 1681, 1527 cm^{-1}; ^1H NMR (DMSO-d_6) for **2** δ 0.96 (3H, d, J = 6.3), 1.34 (9H, s), 2.49−2.44 (2H, m), 4.35 (1H, t, J = 8.8), 4.79 (2H, d, J = 13.2), 5.57 (1H, dt, J = 17.1, 8.6), 7.17−7.28 (5H, m), 7.35 (2H, d, J = 9.1); ^1H NMR (DMSO-d_6) for **3** δ 0.71 (3H, d, J = 6.6), 1.33 (9H, s), 2.49−2.44 (2H, m), 4.29 (1H, t, J = 9.1), 4.95 (1H, d, J = 10.8), 5.00 (1H, d, J = 18.5), 5.77 (1H, dt, J = 17.8, 8.8), 7.17−7.28 (5H, m), 7.35 (2H, d, J = 9.1); ^{13}C NMR (100 MHz) for **2** δ 16.1, 28.3, 43.7, 58.5, 79.4, 115.8, 126.7, 127.2, 128.2, 139.6, 155.4; ^{13}C NMR (100 MHz) for **3** δ 17.0, 28.3, 43.1, 59.1, 79.4, 116.1, 126.9, 127.0, 127.2, 128.1, 139.8, 155.2; MS (CI, NH_3) 279 (MNH_4^+), 262 (MH^+). Anal. Calcd for $C_{16}H_{23}NO_2$: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.39; H, 9.07; N, 5.20%.

(1*R,2*S**)-*N*-Boc-2-Ethyl-1-phenylbut-3-enylamine (10a) and (1*S**,2*S**)-*N*-Boc-2-Ethyl-1-phenylbut-3-enylamine (11a):** 69% of **10a**:**11a**, in an inseparable ratio of 1:1, as a white amorphous solid; mp 132−43 °C; IR (thin film) 3386, 1683, 1520 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.68 (3H, t, J = 7.3), 0.77 (3H, t, J = 7.3), 1.03−1.20 (2H, m), 1.31 (9H, s), 1.53−1.57 (2H, m), 2.16−2.22 (1H, m), 4.35 (1H, t, J = 9.2), 4.37 (1H, t, J = 9.2), 4.70 (1H, dd, J = 16.8, 1.5), 4.80 (1H, dd, J = 10.4, 2.1), 4.97 (1H, d, J = 16.8), 5.02 (1H, d, J = 10.4), 5.35 (1H, dt, J = 17.1, 10.1), 5.54 (1H, dt, J = 16.8, 10.1), 7.15−7.29 (6H, m); ^{13}C NMR δ 11.6, 11.8, 23.8, 24.1, 28.3, 51.4, 51.8, 57.5, 79.3, 117.6, 117.9, 126.8, 126.9, 127.4, 127.9, 128.2, 138.0, 138.3, 142.3, 155.0, 155.3; MS (EI^+) 275 (M^+). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.96; H, 9.14; N, 4.99%.

(1*R,2*S**)-*N*-Boc-2-Isopropyl-1-phenylbut-3-enylamine (10b) and (1*S**,2*S**)-*N*-Boc-2-Isopropyl-1-phenylbut-3-enylamine (11b):** 54% of **10b**:**11b**, in an inseparable ratio of 4:3, as a white amorphous solid; mp 94−6 °C; IR (thin film) 3348, 1702, 1495 cm^{-1}; ^1H NMR (DMSO-d_6) for **10b** δ 0.81 (3H, d, J = 7.0), 0.85 (3H, d, J = 7.0), 1.31 (9H, s), 1.92−2.06 (1H, m), 2.22 (1H, br td, J = 11.5, 3.7), 4.48 (1H, t, J = 10.1), 4.55 (1H, dd, J = 17.1, 2.1), 4.77 (1H, dd, J = 10.4, 2.4), 5.38 (1H, dt, J = 17.1, 10.1), 7.09−7.31 (6H, m); ^1H NMR (DMSO-d_6) for **11b** δ 0.75 (3H, d, J = 7.0), 0.78 (3H, d, J = 6.7), 1.20−1.35 (10H, br s), 2.11−2.25 (1H, m), 4.58 (1H, t, J = 9.3), 4.92 (1H, dd, J = 16.8, 2.1), 5.07 (1H, dd, J = 10.1, 2.1), 5.67 (1H, dt, J = 16.8, 10.1), 7.09−7.31 (5H, m), 7.40 (1H, d, J = 9.3); ^{13}C NMR (100 MHz) for **10b** δ 17.2, 21.5, 21.7, 28.3, 54.7, 56.8, 79.2, 118.2, 126.8, 127.5, 128.0, 136.6, 140.7, 154.9; ^{13}C NMR (100 MHz) for **11b** δ 19.6, 27.3, 27.6, 28.3, 54.7, 56.6, 79.2, 118.9, 126.9, 127.5, 128.3, 135.6, 142.5, 155.2; MS (EI^+) 289 (M^+). Anal. Calcd for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.40; N, 4.84. Found: C, 74.55; H, 9.42; N, 4.66%.

(1*S,2*R**)-*N*-Boc-2-Methyl-1-phenyl-3-(trimethylsilyl)but-3-enylamine (11d).** *n*-BuLi (1.47 mL of 2.5M in hexanes, 3.67 mmol, 1.2 equiv) was added slowly to a stirred solution of **9d** (1.02 g, 3.06 mmol) in THF (20 mL) at −78 °C. After stirring for 20 h the reaction was quenched, worked up, and purified as for **10/11a−c** above to give **11d** (0.89 g, 88%) (ds 20:1), as a clear oil; IR (thin film) 3273, 1703, 1495, cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.17 (9H, s), 0.66 (3H, d, J = 7.0), 1.37 (9H, s), 2.60 (1H, dq, J = 10.4, 7.3), 4.46 (1H, t, J = 9.8), 5.43 (1H, d, J = 2.4), 5.73 (1H, d, J = 2.4), 7.08 (1H, d, J = 9.5), 7.20−7.40 (5H, m); ^{13}C NMR δ 0.4, 19.4, 28.7, 47.182, 58.8, 77.9, 126.6, 127.2, 127.9, 128.4, 143.3, 154.8, 155.1; MS (EI^+) 333 (M^+). Anal. Calcd for $C_{19}H_{31}NO_2Si$: C, 68.42; H, 9.37; N, 4.20. Found: C, 68.30; H, 9.36; N, 4.21%.

General Experimental for the Aza-[2,3]-Wittig Sigmatropic Rearrangement of 9e,f. *n*-BuLi (2.5 M in hexanes, 1.2 equiv) was added slowly to a stirred solution of the silyl-substituted *N*-Boc-*N*-allylbenzylamine **9e**,**f** (1 equiv) in THF/HMPA (4:1, 5 mL/mmol) at −78 °C. After stirring for 30 m the reaction was quenched, worked up, and purified as for **10/11a−c**.

(1*S,2*R**)-*N*-Boc-2-Ethyl-1-phenyl-3-(trimethylsilyl)but-3-enylamine (11e):** 92% (ds 18;1), as a clear oil; IR (thin film) 3352, 1702, 1496 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.15 (9H, s), 0.57 (3H, t, J = 7.3), 0.91−1.15 (2H, m), 1.31 (9H, s), 2.37 (1H, td, J = 10.4, 4.0), 4.42 (1H, t, J = 10.1), 5.54 (1H, d, J = 2.7), 5.70 (1H, d, J = 2.7), 7.02 (1H, d, J = 9.2), 7.18−7.32 (5H, m); ^{13}C NMR (100 MHz) δ −0.22, 12.2, 24.2, 28.3, 56.1, 58.3, 79.0, 126.9, 127.2, 128.1, 128.8, 143.0, 152.5, 154.8; MS (EI^+) 347 (M^+). Anal. Calcd for $C_{20}H_{33}NO_2Si$: C, 69.11; H, 9.57; N, 4.03. Found: C, 69.03; H, 9.66; N, 3.96%.

(1*S,2*R**)-*N*-Boc-2-Isopropyl-1-phenyl-3-(trimethylsilyl)but-3-enylamine (11f):** 94% (ds 11;1), as a clear oil; IR (thin film) 3445, 1722, 1701, 1494 cm^{-1}; ^1H NMR (DMSO-d_6) δ 0.03 (9H, s), 0.71 (6H, d, J = 6.7), 1.31 (9H, s), 1.21−1.41 (1H, m), 2.55 (1H, dd, J = 10.7, 5.5), 4.71 (1H, t, J = 9.8), 5.64 (1H, br d, J = 1.5), 5.79 (1H, d, J = 2.1), 6.81 (1H, d, J = 9.5), 7.18−7.39 (5H, m); ^{13}C NMR δ −1.0, 20.6, 21.8, 28.3, 29.3, 54.4, 56.3, 79.1, 126.76, 126.81, 128.1, 128.2, 143.3, 152.5, 155.0; MS (EI^+) 361 (M^+). Anal. Calcd for $C_{21}H_{35}NO_2Si$: C, 69.75; H, 9.76; N, 3.87. Found: C, 69.60; H, 9.66; N, 3.80%.

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Supporting Information Available: Copies of ^1H NMR spectra for compounds **8e**, **9b**,**e**, **f** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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