2-Ethynylaziridines as Chiral Carbon Nucleophiles: Stereoselective Synthesis of 1,3-Amino Alcohols with Three Stereocenters via Allenylindium Reagents Bearing a Protected Amino Group

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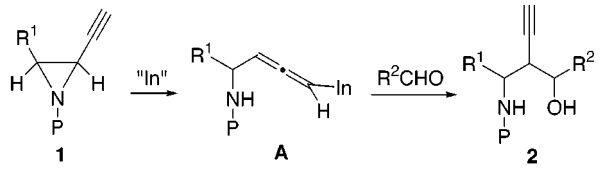
Allenylindium reagents bearing a protected amino group were effectively prepared from *N*-protected 3-alkyl-2-ethynylaziridines by treatment with InI in the presence of $Pd(PPh_3)_4$ and H_2O. Stereoselective addition of the allenylindium to aliphatic or aromatic aldehydes affords 1,3-amino alcohols bearing three contiguous chiral centers: while 2,3-*trans*-2-ethynylaziridines yield *syn*,*syn*-2-ethynyl-1,3-amino alcohols predominantly, 2,3-*cis*-aziridines give anti,syn isomers selectively. Synthesis of highly substituted ethynylazetidines is also described.

Introduction

Aziridines, three-membered azacycles, are widely used as carbon electrophiles since they easily undergo ring-opening reactions with a wide range of nucleophiles in a stereoselective manner.[1] Successful syntheses of chiral aziridines[2,3] in recent years make them more valuable intermediates for synthesis of various compounds bearing a nitrogen atom.[4,5] In contrast, the reactions of aziridines as carbon nucleophiles are scarcely known with the exception of a few examples: (1) aziridinyl anion reagents,[6] which are known as useful precursors of highly substituted aziridines, and (2) ring-opening reaction of aziridines with lithium naphthalenide.[7,8] The latter is an interesting reaction for reductive coupling of aziridines and electrophiles, in which stereochemistries of aziridines were not reflected in the products due to the configurational lability of the alkyllithium species.

Scheme 1



To demonstrate the utility of aziridines as chiral carbon nucleophiles, we planned to synthesize 2-ethynyl-1,3-amino alcohol **2** from ethynylaziridine **1** via allenylindium reagent **A** bearing an amino group (Scheme 1). Synthesis of the related amino alcohols bearing an ethynyl group was reported by Jacobi and co-workers, utilizing a combination of a modified Nicholas reaction and Curtius rearrangement.[9] However, our newly planned synthesis of **2** would have an advantage in ease of

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introduction of various alkyl or aryl group (R^2) by simply changing the aldehydes. While this study was in progress, the pioneering work on allenylindium reagents by Marshall and co-workers appeared.[10] Thus, treatment of propargylic mesylates with InI and aldehydes in the presence of catalytic palladium(0) affords ethynyl alcohols in good stereoselectivities via allenylindium reagents. However, it is a matter of interest to investigate the utility of ethynylaziridines as a precursor of an allenylindium reagent, the stability and reactivity of the allenylindium bearing an amino group, and regio- and stereoselectivity in both the reagent formation and addition to aldehydes. Herein we detail a highly stereoselective synthesis of the 2-ethynyl-1,3-amino alcohol **2** by umpolung of ethynylaziridines **1** with indium(I) and a catalytic amount of palladium(0).[11,12]

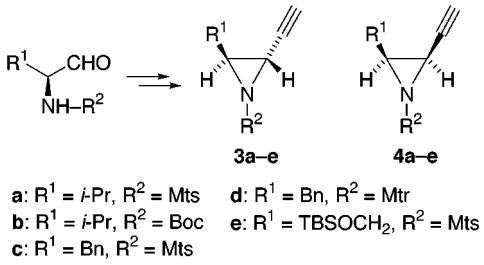
Results and Discussion

Synthesis of Ethynylaziridines from Natural Amino Acids. It is well documented that the reactivity of *N*-unsubstituted or *N*-alkylaziridines is relatively low; hence, activation by the introduction of an electron-withdrawing protecting group on the nitrogen atom of the aziridine is required. The choice of arylsulfonyl (Mts, Mtr, or Ts) or *tert*-butoxycarbonyl (Boc) as the activating group was based on the convenience of the introduction and deprotection of these groups.

According to our reported procedure,[13] we synthesized the 2-ethynylaziridines **3a**−**e** and **4a**−**e** via protected amino aldehydes derived from L-valine, L-phenylalanine, or L-serine (Scheme 2).[14]

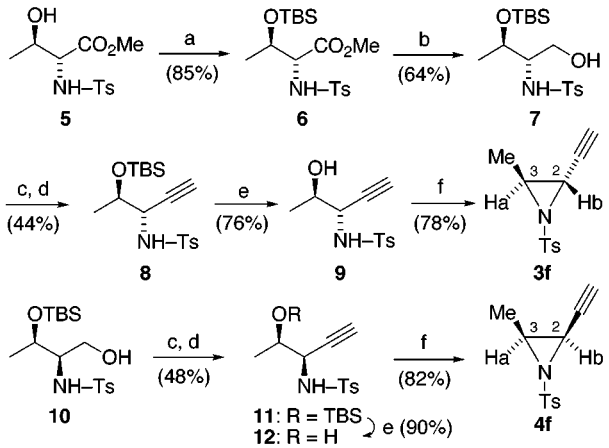
Ethynylaziridines **3f** and **4f** bearing a methyl substituent at C-3 were synthesized as shown in Scheme 3. The compound **5** was readily prepared from D-allothreonine following the literature.[15] Protection of **5** gave the silyl ether **6**, which was reduced by DIBAL-H to yield **7** in 64% yield. Successive treatment of the alcohol **7** with oxalyl chloride−DMSO−*N*,*N*-diisopropylethylamine, *t*-BuOK-dibromomethyltriphenylphosphonium bromide,[16] and *t*-BuOK gave the alkyne **8** in 44% overall yield. Deprotection of the TBS group of **8** by tetrabutylammonium fluoride gave **9**, which was readily converted into the desired 2,3-*trans*-2-ethynylaziridine **3f** by dehydration under Mitsunobu conditions.[13b,17] Similarly, the 2,3-*cis*-aziridine **4f** was synthesized from L-threonine starting from the known compound **10**[18] (see the Experimental Section).

Scheme 2[a]



[a] Abbreviations: Mts = 2,4,6-trimethylphenylsulfonyl; Mtr = 4-methoxy-2,3,6-trimethylphenylsulfonyl; TBS = *tert*-butyldimethylsilyl.

Scheme 3[a]



[a] Reagents and conditions: (a) TBSCl, imidazole, DMF; (b) DIBAL-H, toluene; (c) $(COCl)_2$, DMSO, CH_2Cl_2, then $(i\text{-Pr})_2NEt$; (d) $Ph_3P^+CHBr_2 \cdot Br^-$, *t*-BuOK, THF then *t*-BuOK; (e) TBAF, THF; (f) diethyl azodicarboxylate, PPh_3, THF.

Stereochemical assignments of the synthesized **3f** and **4f** were readily made by comparison of *J* values of the ring protons. The *trans*-ethynylaziridine **3f** shows smaller J_{Hab} values (J = 4.5 Hz) than that of cis isomer **4f** (J = 6.9 Hz).[13b]

Preparation of Allenylindium Reagents Bearing a Protected Amino Group. Having synthesized the requisite substrates, we initiated work on preparation of the allenylindium reagent from the ethynylaziridines **3a** (Scheme 4 and Table 1). The desired reagent could not be prepared using indium powder under various reaction conditions in the presence or absence of a palladium catalyst. Formation of allenylindium was observed using InI in DMF in the presence of $Pd(PPh_3)_4$, yielding an inseparable mixture of **13** and **14** after hydrolysis (54% yield; **13**:**14** = 84:16; Table 1, entry 1). Other solvents such as MeOH or THF were less effective (entries 2 and 3); however, we found that a promising result was obtained using THF−H_2O (1:1) as solvent (89% yield, **13**:**14** = 91:9; entry 4). Although one of

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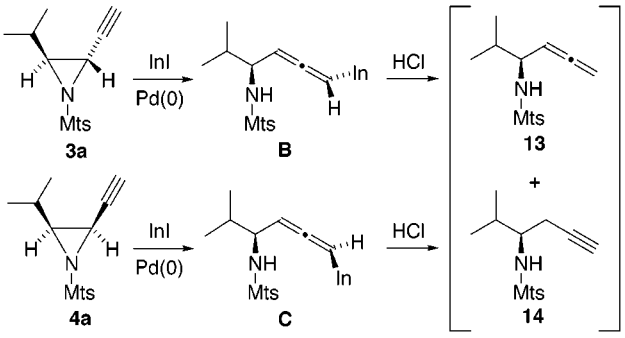
Table 1. Preparation of the Allenylindium Reagents from the Aziridines 3a and 4a[a]

entry	aziridine	catalyst	solvent	reaction time (min)	yield[b] (%)	ratio **13**:**14**[c]
1	**3a**	$Pd(PPh_3)_4$	DMF	20	54	84:16
2	**3a**	$Pd(PPh_3)_4$	MeOH	600	trace	ND
3	**3a**	$Pd(PPh_3)_4$	THF	90	34	86:14
4	**3a**	$Pd(PPh_3)_4$	THF−H_2O (1:1)	30	89	91:9
5	**3a**	$Pd(PPh_3)_4$	THF, H_2O (1 equiv)	90	41	85:15
6	**3a**	$Pd(PPh_3)_4$	THF−HMPA (4:1)	90	trace	ND
7	**3a**	$Pd(PPh_3)_4$	THF−HMPA (4:1), H_2O (1 equiv)	20	83	90:10
8	**3a**	none	THF−HMPA (4:1), H_2O (1 equiv)	90	6[d]	ND
9	**4a**	$Pd(PPh_3)_4$	THF−H_2O (1:1)	30	89	91:9
10	**4a**	$Pd(PPh_3)_4$	THF−HMPA (4:1), H_2O (1 equiv)	20	76	91:9

[a] All reactions were carried out at room temperature using palladium catalyst (5 mol %), InI (1.5 equiv). After being stirred at room temperature for the indicated time, the resulting allenylindium reagents were quenched with 1N HCl. [b] Combined isolated yields. [c] Ratios were determined by ^1H NMR (270 MHz). [d] A quite similar result was obtained using freshly opened equipment, which means that some allenylindium could be formed in the absence of palladium catalyst.[10]

Scheme 4

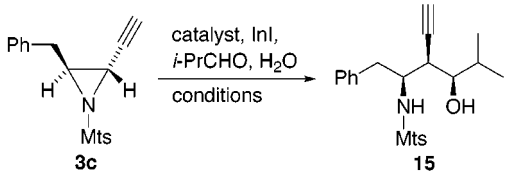


Marshall's conditions [InI, $Pd(PPh_3)_4$, THF−HMPA][10] was not effective for the reagent formation from the ethynylaziridine **3a** (entry 6), a similar result to THF−H_2O (entry 4) was obtained using THF−HMPA (4:1) in the presence of one equivalent of H_2O (entry 7). The corresponding 2,3-*cis*-aziridine **4a** also gave the allenylindium reagent by treatment with InI and $Pd(PPh_3)_4$ in THF−H_2O (entry 9) or THF−HMPA−H_2O (entry 10). Interestingly, it was found that the presence of H_2O is an important factor for the effective formation of the allenylindium bearing a protected amino group from 2-ethynylaziridines.

Reductive Coupling Reaction of 2-Ethynylaziridines with Aldehydes. To reveal the synthetic utility of allenylindium reagents bearing a protected amino group as chiral carbanions, we investigated their coupling reaction with aldehydes. A brief survey of the results with the aziridine **3c** and isobutyraldehyde is summarized in Table 2. The aziridine **3c** was treated with InI (1.3 equiv), isobutyraldehyde (1.5 equiv), and H_2O (1 equiv) in THF−HMPA (4:1) in the presence of $Pd(PPh_3)_4$ (5 mol %) or $Pd(dppf)Cl_2{\cdot}CHCl_3$ (5 mol %) to afford the desired amino alcohol **15** (62% and 61% yield, respectively). In both cases, the syn,syn adduct was the only isomer isolated (>97:3). To our dismay, THF or a mixed solvent of THF−H_2O was less effective for the addition reaction toward the aldehyde (entries 3−5).

Similarly, 2,3-*trans*-aziridines **3a**−**e** also gave syn,syn adducts **16**−**19** as the only isolable isomers. The results are summarized in Scheme 5. Substituents such as a benzyl (**3c** and **3d**) or silyloxy group (**3e**) caused no undesired side reaction. When 3-methyl-2-ethynylaziridine **3f** was employed, however, a small amount of

Table 2. Effects of Solvent and Catalyst in the Indium(I)-Mediated Reductive Coupling Reaction of the Ethynylaziridine 3c and Isobutyraldehyde[a]



entry	catalyst	solvent	yield[b] (%)
1	$Pd(PPh_3)_4$	THF−HMPA (4:1)	62
2	$Pd(dppf)Cl_2{\cdot}CH_2Cl_2$	THF−HMPA (4:1)	61
3	$Pd(PPh_3)_4$	THF	53
4	$Pd(PPh_3)_4$	THF−H_2O (10:1)	46
5	$Pd(PPh_3)_4$	THF−H_2O (1:1)	48

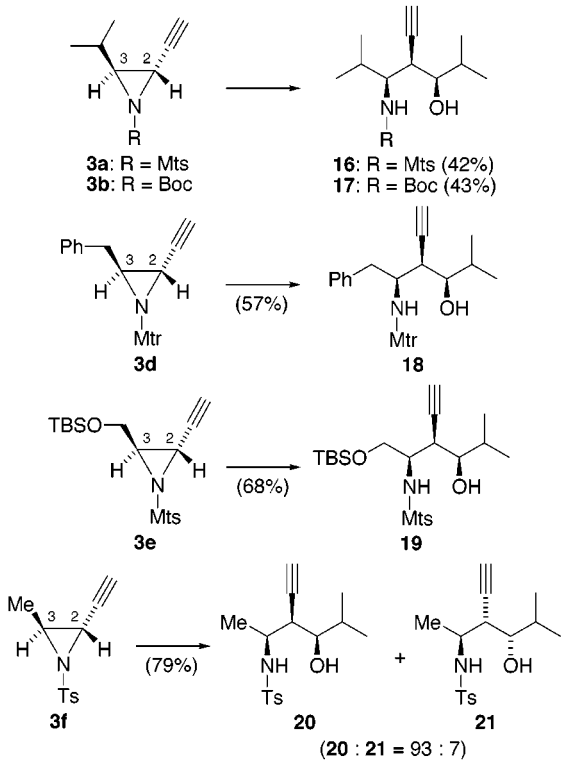
[a] All reactions were carried out at room temperature using palladium catalyst (5 mol %), InI (1.3 equiv), H_2O (1 equiv), and isobutyraldehyde (1.5 equiv). [b] Isolated yields.

anti,syn adduct **21** was isolated (**20**:**21** = 93:7). It turned out that the steric bulk of the substituent at C-3 of ethynylaziridines exerts a significant influence on the reactivity and selectivity of the allenylindium reagents: allenylindium from the 2-ethynylaziridines **3e** and **3f** bearing a relatively small substituent at C-3 was found to be more reactive toward the aldehydes yielding the corresponding amino alcohols **19** and (**20** and **21**) in higher yields, while the allenylindiums from 2,3-*trans*-2-ethynylaziridines **3a** and **3b** bearing a bulky isopropyl group showed lower reactivities, giving the corresponding amino alcohols **16** and **17** in lower yields (42% and 43%, respectively).

Next, the same reactions were conducted with the 2,3-*cis*-aziridines **4a**−**f** (Scheme 6). In sharp contrast to 2,3-*trans*-2-ethynylaziridines, it was found that 2,3-*cis*-aziridines **4a**−**f** gave anti,syn adducts **22**−**26** and **21** exclusively or predominantly under the identical reaction conditions. In the cases of **4a**−**e**, only the *anti,syn*-adducts were isolated. Not surprisingly, the *cis*-aziridine **4f** bearing a methyl substituent at C-3 afforded a separable mixture of **21** and **20** (**21**:**20** = 87:13) in high yield (79%), in line with the *trans*-aziridine **3f** (Scheme 5).

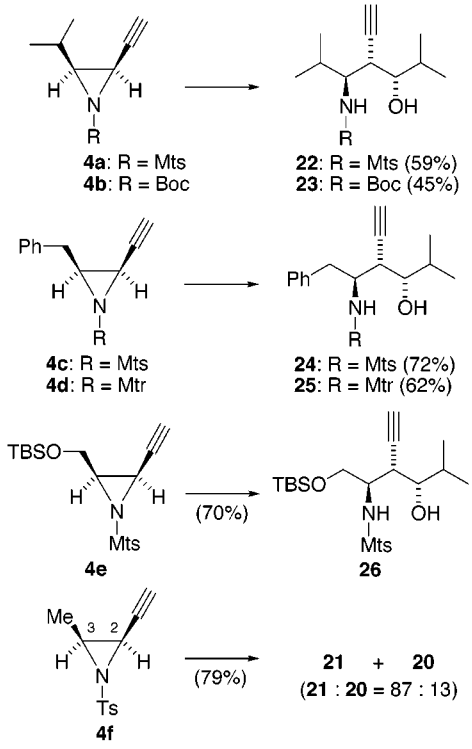
Other aromatic or aliphatic aldehydes could be analogously used for the present coupling reaction (Schemes 7 and 8). For example, the reaction of 2,3-*trans*-aziridine **3d** with benzaldehyde or acetaldehyde yielded **27** or **28**,

Scheme 5[a]



[a] Reaction conditions: $Pd(PPh_3)_4$ (5 mol %), InI (1.3 equiv), H_2O (1 equiv), isobutyraldehyde (1.5 equiv).

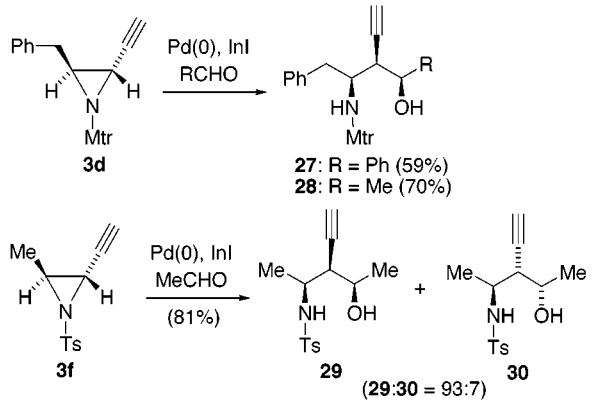
Scheme 6[a]



[a] Reaction conditions: $Pd(PPh_3)_4$ (5 mol %), InI (1.3 equiv), H_2O (1 equiv), isobutyraldehyde (1.5 equiv).

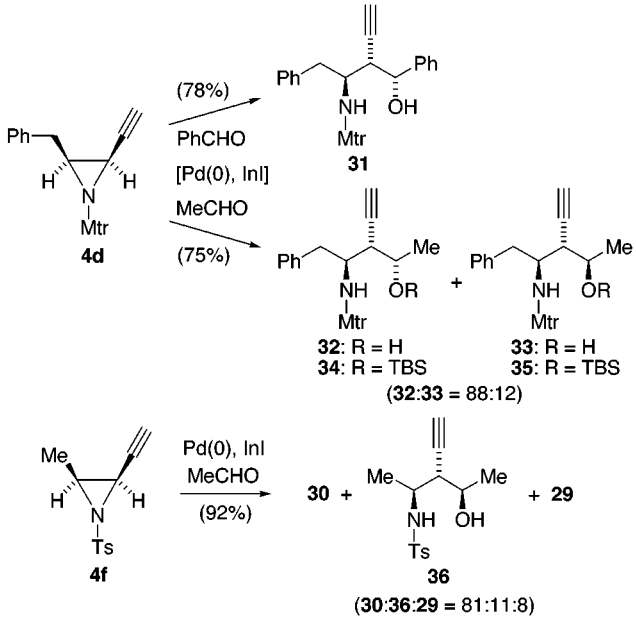
respectively, in good yields (Scheme 7). As expected, reaction of the 3-methyl-2-ethynylaziridine **3f** with acetaldehyde gave *syn*,*syn*-amino alcohol **29** predominantly along with a small amount of anti,syn isomer **30** (**29**:**30** = 93:7). It should be noted that, when employing acetaldehyde as an electrophile, although the 2,3-*trans*-aziridine **3d** yielded only *syn*,*syn*-**28**, the corresponding 2,3-*cis*-aziridine **4d** gave a mixture of the *anti*,*syn*-**32** and *anti*,*anti*-**33** (**32**:**33** = 88:12; Scheme 8). Similarly, the *cis*-aziridine **4f** yielded a small amount of anti,anti isomer **36** (Scheme 8; **30**:**36**:**29** = 81:11:8) which was not observed in the reaction mixture using *trans*-**3f** (Scheme 7).

Scheme 7[a]



[a] Conditions: $Pd(PPh_3)_4$ (5 mol %), InI (1.3 equiv), H_2O (1 equiv), aldehyde (1.5 equiv), THF/HMPA = 4:1, rt, 4 h.

Scheme 8[a]

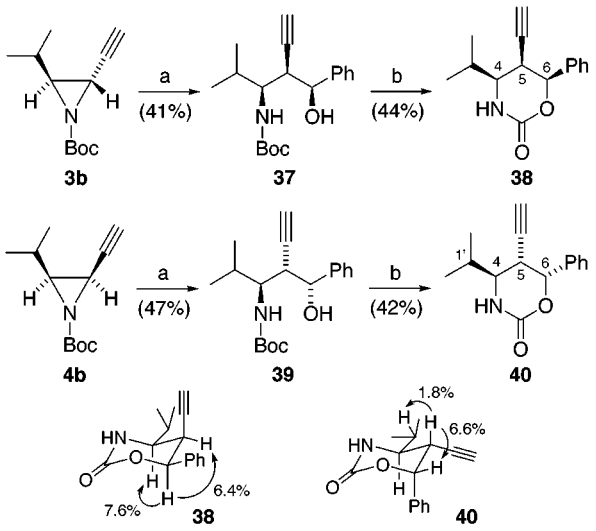


[a] Conditions: $Pd(PPh_3)_4$ (5 mol %), InI (1.3 equiv), H_2O (1 equiv), aldehyde (1.5 equiv), THF/HMPA = 4:1, rt, 4 h.

Thus, it was found that, whereas 2,3-*trans*-2-ethynylaziridines yield *syn*,*syn*-2-ethynyl-1,3-amino alcohols predominantly or exclusively by their treatment with InI, H_2O, and aldehydes in the presence of catalytic palladium(0), 2,3-*cis*-aziridines give anti,syn isomers selectively under the same reaction conditions.

All the isomeric mixtures in Schemes 5−8 except for (**32** and **33**) were easily separated by flash column chromatography and fully characterized by ^1H NMR, ^{13}C NMR, IR, and mass spectra or elemental analyses. Although the mixture of **32** and **33** was inseparable at

Scheme 9[a]



[a] Reaction conditions: (a) $Pd(dppf)Cl_2 \cdot CHCl_3$ (5 mol %), InI (1.3 equiv), H_2O (1 equiv), benzaldehyde (1.5 equiv); (b) NaH (1.5 equiv), THF/DMF (1:1), rt, 1.5 h.

this stage, these two isomers were isolated and characterized after derivatization into their silyl ethers **34** and **35** (see the Experimental Section).

Determination of Stereochemistries of 2-Ethynyl-1,3-amino Alcohols. Stereochemical assignments for the synthesized diastereomeric amino alcohols were readily made by their transformation into tetrahydro-1,3-oxazin-2-one derivatives as shown in Scheme 9. The amino alcohol **37**, prepared by the reaction of the 2,3-*trans*-2-ethynylaziridine **3b** with benzaldehyde, was treated with NaH to give the tetrahydro-1,3-oxazin-2-one **38**. Irradiation of the signal of 6-H led to NOE enhancement of the signals of 4-H and 5-H (7.6% for 4-H and 6.4% for 5-H). Similarly, in the case of **40** derived from 2,3-*cis*-aziridine **4b**, NOE was observed between [5-H and 6-H (6.6%)] and [5-H and 1′−H (1.8%)], as shown in structure **40** (Scheme 9).[19]

One plausible mechanism for the present reductive coupling reaction is shown in Figure 1. Attack of palladium(0) to ethynylaziridine from the opposite side of the C−N bond of the aziridine ring would produce the allenylpalladium(II) intermediate **42**, which would be converted into **43** by transmetalation with InI retaining the stereochemistry.[10] Coordination of the indium atom with carbonyl oxygen of aldehyde enables the approach of the aldehyde from the same side of the indium atom.[20] Since the unfavorable steric interaction between the substituents R and R^1 destabilizes **44**, the *syn*,*syn*-**45** will be obtained as a major isomer via **43**. Although the exact role of H_2O is unclear, protonation of the aza-anionic species **42** by H_2O is assumed to be an important factor for the effective formation of the allenylindium from 2-ethynylaziridines. For example, protonation of **42** might shift the equilibrium between **41** and **42** toward the latter. Similarly, the predominant formation of the *anti*,*syn*-amino alcohol **51** from the 2,3-*cis*-2-ethynylaziridine **47** can be rationalized by an analogous pathway as depicted in Figure 1.

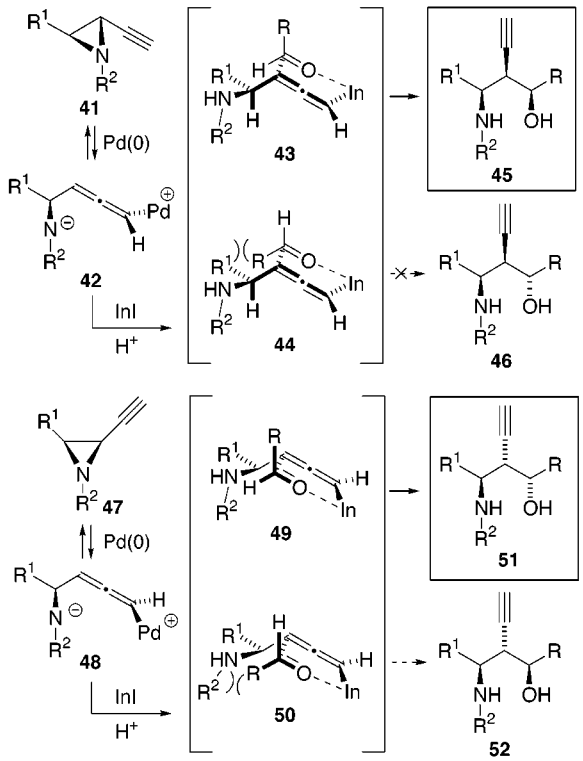


Figure 1. Plausible mechanistic pathway.

Synthesis of Highly-Substituted Azetidines under Mitsunobu Conditions. Chiral azetidines can be seen in several biologically active compounds,[21] and recently, they have attracted much attention due to their efficacy as chiral ligands for asymmetric syntheses.[22,23] To expand the synthetic utility of our novel reaction and to confirm the stereochemistries more strictly, we finally investigated the synthesis of highly substituted azetidines bearing three chiral centers under Mitsunobu conditions. Unfortunately, treatment of the *syn*,*syn*-amino alcohol **15** with diethyl azodicarboxylate and triphenylphosphine in THF afforded the desired azetidine **53** in poor yield (9%). The major product was the homoallylic amine **54** produced by *β*-elimination of the hydroxy group. However, the *syn*,*syn*-amino alcohols **27** and **29** yielded the desired ethynylazetidines **55** and **56**, respectively, in high yields. While the *anti*,*anti*-**36** gave

(19) Stereochemistries of **32** and **33** were determined by their transformation into a diastereomeric mixture of the corresponding azetidines and subsequent NOE experiment, in a similar way as shown in Scheme 10 (see the Supporting Information).

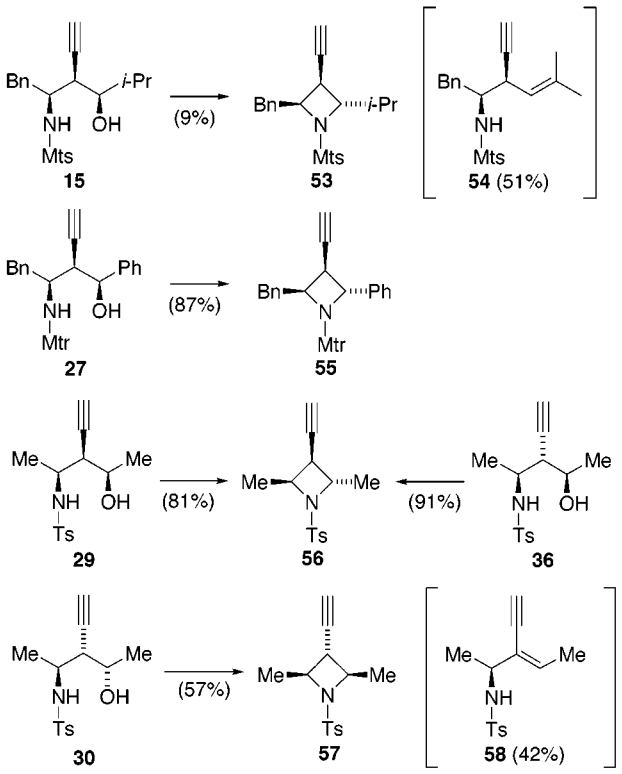
(20) Paquette, L. A.; Rothhaar, R. R. *J. Org. Chem*. **1999**, *64*, 217.

(21) (a) Dollé, F.; Dolci, L.; Valette, H.; Hinnen, F.; Vaufrey, F.; Guenther, I.; Fuseau, C.; Coulon, C.; Bottlaender, M.; Crouzel, C. *J. Med. Chem*. **1999**, *42*, 2251. (b) Holladay, M. W.; Wasicak, J. T.; Lin, N.-H.; He, Y.; Ryther, K. B.; Bannon, A. W.; Buckley, M. J.; Kim, D. J. B.; Decker, M. W.; Anderson, D. J.; Campbell, J. E.; Kuntzweiler, T. A.; Donnelly-Roberts, D. L.; Piattoni-Kaplan, M.; Briggs, C. A.; Williams, M.; Arneric, S. P. *J. Med. Chem*. **1998**, *41*, 407. (c) Knapp, S.; Dong, Y. *Tetrahedron Lett*. **1997**, *38*, 3813.

(22) (a) Doyle, M. P.; Davies, S. B.; Hu, W. *Chem. Commun*. **2000**, 867. (b) Shi, M.; Jiang, J.-K. *Tetrahedron*: *Asymmetry* **1999**, *10*, 1673. (c) Starmans, W. A. J.; Walgers, R. W. A.; Thijs, L.; de Gelder, R.; Smits, J. M. M.; Zwanenburg, B. *Tetrahedron* **1998**, *54*, 4991. (d) Starmans, W. A. J.; Thijs, L.; Zwanenburg, B. *Tetrahedron* **1998**, *54*, 629.

(23) For recent syntheses of azetidines, see: (a) Concellón, J. M.; Bernad, P. L.; Pérez-Andrés, J. A. *Tetrahedron Lett*. **2000**, *41*, 1231. (b) Anzai, M.; Toda, A.; Ohno, H.; Takemoto, Y.; Fujii, N.; Ibuka, T. *Tetrahedron Lett*. **1999**, *40*, 7393. (c) Rutjes, F. P. J. T.; Tjen, K. C. M. F.; Wolf, L. B.; Karstens, W. F. J.; Schoemaker, H. E.; Hiemstra, H. *Org. Lett*. **1999**, *1*, 717. (d) Starmans, W. A. J.; Doppen, R. G.; Thijs, L.; Zwanenburg, B. *Tetrahedron*: *Asymmetry* **1998**, *9*, 429. (e) Wessig, P.; Schwarz, J. *Helv. Chim. Acta* **1998**, *81*, 1803. (f) Alcaide, B.; Salgado, N. R.; Sierra, M. A. *Tetrahedron Lett*. **1998**, *39*, 467.

Scheme 10[a]



the azetidine **56** in good yield, the *anti*,*syn*-**30** yielded **57** in 57% yield and elimination product **58** in 42% yield (Scheme 10).

Stereochemistries of the azetidines **56** and **57** and (*E*)-geometry of the homoallylic amine **58** were confirmed by NOE analyses (see the Supporting Information).

As is revealed from these observations, highly substituted azetidines can be prepared from 2-ethynyl-1,3-amino alcohols derived from 2-ethynylaziridines, under the typical Mitsunobu conditions. However, yields of the azetidine synthesis have proven to be dependent on the structure of the starting amino alcohols.

Conclusion

In conclusion, we have demonstrated a novel utility of 2-ethynylaziridines as a precursor of chiral carbanions by umpolung with indium(I). Allenylindium reagents bearing a protected amino group were effectively formed by the treatment of 2-ethynylaziridines with InI, H_2O, and catalytic Pd(0). Reaction of the allenylindium, prepared from 2,3-*trans*-2-ethynylaziridines, with aldehydes afford *syn*,*syn*-2-ethynyl-1,3-amino alcohols selectively, while the reagents from 2,3-*cis*-aziridines give anti,syn isomers in high selectivities. This is the first example to demonstrate the utility of allenylindium reagents bearing an amino group as chiral carbanions. Highly substituted azetidines bearing three chiral centers are easily synthesized from the resulting amino alcohols under the typical Mitsunobu conditions.

Experimental Section

General Methods. Melting points are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported in parts per million downfield from internal Me_4Si (s = singlet, d = doublet, dd = double doublet, ddd = doublet of double doublet, t = triplet, q = quartet, m = multiplet). Optical rotations were measured in $CHCl_3$. For flash chromatography, silica gel 60 H (silica gel for thin-layer chromatography, Merck) or silica gel 60 (finer than 230 mesh, Merck) was employed. InI is available from the Aldrich and was crushed before use.

Known compounds **3a**−**e**,[13] **4a**−**e**,[13] **5**,[15] and **10**[18] were synthesized according to the literature.

Methyl (2*R*,3*R*)-3-*tert*-Butyldimethylsilyloxy-2-[*N*-(4-methylphenylsulfonyl)amino]butanoate (6). To a stirred mixture of **5** (5.60 g, 19.5 mmol) and imidazole (4.10 g, 60.1 mmol) in $CHCl_3$ (17 mL) and DMF (11 mL) at room temperature was added *tert*-butyldimethylsilyl chloride (5.31 g, 35.4 mmol) with stirring at 0 °C, and stirring was continued overnight. Water was added, and the whole was extracted with Et_2O. The extract was washed successively with 4% HCl, water, saturated $NaHCO_3$, and brine and then dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was purified by flash chromatography over silica gel with hexane−EtOAc (2:1) to give **6** (6.65 g, 85% yield) as colorless crystals: mp 72−74 °C (Et_2O−hexane); $[\alpha]^{26}_D$ −13.9 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3267 ($NHSO_2$), 1743 (C=O), 1348 ($NHSO_2$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.02 (s, 3H, SiMe), 0.03 (s, 3H, SiMe), 0.82 (s, 9H, CMe_3), 1.23 (d, J = 6.0 Hz, 3H, CMe), 2.42 (s, 3H, Ph-*Me*), 3.43 (s, 3H, OMe), 3.77 (dd, J = 9.6, 5.1 Hz, 1H, 2-H), 3.99 (qd, J = 6.0, 5.1 Hz, 1H, 3-H), 5.21 (d, J = 9.6 Hz, 1H, NH), 7.27−7.30 (m, 2H, Ph), 7.69−7.72 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.14, −4.50, 17.8, 20.7, 21.5, 25.5 (3C), 52.0, 61.8, 70.5, 127.3 (2C), 129.6 (2C), 136.6, 143.6, 170.2; MS (FAB) *m*/*z* 402 (MH^+, 100); HRMS (FAB) calcd $C_{18}H_{32}NO_5SSi$ (MH^+) 402.1771, found 402.1761. Anal. Calcd for $C_{18}H_{31}NO_5SSi$: C, 53.83; H, 7.78; N, 3.49. Found: C, 53.86; H, 7.68; N, 3.48.

(2*S*,3*R*)-3-*tert*-Butyldimethylsilyloxy-2-[*N*-(4-methylphenylsulfonyl)amino]butan-1-ol (7). Diisobutylaluminum hydride (1.0 M solution in toluene; 57 mL, 57 mmol) was added dropwise to a stirred solution of the ester **6** (6.54 g, 16.3 mmol) in a mixed solvent of toluene (27 mL) and $CHCl_3$ (11 mL) at −78 °C under nitrogen. Stirring was continued for 3 h at −50 °C, and saturated NH_4Cl was added dropwise with stirring. The mixture was made acidic with 4% HCl at 0 °C and extracted with a mixed solvent of Et_2O−EtOAc (1:1). The extract was washed with water and brine, and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was purified by chromatography over silica gel with hexane−EtOAc (3:1) to give **7** (3.90 g, 64% yield) as a colorless oil: $[\alpha]^{25}_D$ −24.1 (*c* 1.01, $CHCl_3$); IR (KBr) cm^{-1} 3520 (OH), 3282 ($NHSO_2$), 1327 ($NHSO_2$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 3H, SiMe), 0.08 (s, 3H, SiMe), 0.86 (s, 9H, CMe_3), 1.16 (d, J = 6.6 Hz, 3H, CMe), 2.43 (s, 3H, Ph-*Me*), 2.77 (dd, J = 9.9, 1.8 Hz, 1H, OH), 3.03 (qd, J = 6.6, 3.3 Hz, 1H, 3-H), 3.25 (ddd, J = 11.4, 9.9, 3.6 Hz, 1H, 1-C*H*H), 3.90 (ddd, J = 11.4, 2.7, 1.8 Hz, 1H, 1-CH*H*), 4.03−4.11 (m, 1H, 2-H), 5.30 (d, J = 8.1 Hz, 1H, NH), 7.29−7.32 (m, 2H, Ph), 7.44−7.77 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.0, −4.7, 17.8, 20.5, 21.5, 25.7 (3C), 58.4, 61.1, 72.2, 127.0 (2C), 129.8 (2C), 137.6, 143.5; MS (FAB) *m*/*z* 374 (MH^+, 100); HRMS (FAB) calcd $C_{17}H_{32}NO_4SSi$ (MH^+) 374.1821, found 374.1816.

(3*S*,4*R*)-4-*tert*-Butyldimethylsilyloxy-3-[*N*-(4-methylphenylsulfonyl)amino]-1-pentyne (8). To a stirred solution of oxalyl chloride (1.17 mL, 13.4 mmol) in CH_2Cl_2 (30 mL) at −78 °C under nitrogen was added dropwise a solution of DMSO (3.65 mL, 51.4 mmol) in CH_2Cl_2 (5 mL). After 30 min, a solution of the alcohol **7** (3.84 g, 10.3 mmol) in CH_2Cl_2 (10 mL) was added to the above reagent at −78 °C, and the mixture was stirred for 1 h. Diisopropylethylamine (12.2 mL, 72.0 mmol) was added to the above solution at −78 °C, and the mixture was stirred for 30 min with warming to 0 °C. The mixture was made acidic with 1 N HCl, and the whole was extracted with Et_2O. The extract was washed successively with water and brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give a crude aldehyde. A mixture of dibromomethyltriphenylphosphonium bromide (13.2 g, 25.7 mmol) and *t*-BuOK (2.77 g, 24.7 mmol) was dissolved in THF (100 mL) at room temperature under nitrogen. After the mixture was stirred for 5 min, a solution

of the above crude aldehyde in THF (10 mL) was added to this brown reagent at room temperature, and the mixture was stirred for 15 min. Additional *t*-BuOK (5.77 g, 51.4 mmol) was then added at room temperature, stirring was continued for 15 min, and brine was then added. The whole was extracted with Et_2O, and the extract was dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was flash chromatographed on a silica gel column with hexane−EtOAc (6:1) to give **8** (1.68 g, 44% yield) as a colorless oil: $[\alpha]^{25}_D$ +59.2 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3278 ($NHSO_2$), 2121 (C≡C), 1336 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 6H, $SiMe_2$), 0.87 (s, 9H, CMe_3), 1.21 (d, J = 6.0 Hz, 3H, CMe), 2.07 (d, J = 2.1 Hz. 1H, C≡CH), 2.43 (s, 3H, Ph-*Me*), 3.91−4.00 (m, 2H, 3-H and 4-H), 4.77 (d, J = 8.1 Hz, 1H, NH), 7.29−7.31 (m, 2H, Ph), 7.76−7.79 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.82, −4.43, 18.0, 19.9, 21.5, 25.7 (3C), 51.7, 70.4, 73.7, 79.0, 127.4 (2C), 129.5 (2C), 137.2, 143.5; MS (FAB) *m*/*z* 368 (MH^+, 100); HRMS (FAB) calcd $C_{18}H_{30}NO_3SSi$ (MH^+) 368.1716, found 368.1721.

(3*S*,4*R*)-4-Hydroxy-3-[*N*-(4-methylphenylsulfonyl)amino]-1-pentyne (9). To a solution of the alkyne **8** (1.66 g, 4.53 mmol) in THF (20 mL) was added tetrabutylammonium fluoride (1.0 M solution in THF; 5.44 mL, 5.44 mmol) at 0 °C with stirring, and the mixture was stirred for 1.5 h. The mixture was made acidic with 4% HCl, the whole was extracted with a mixed solvent of EtOAc−Et_2O (3:1), and the extract was washed with water, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. The filtrate was concentrated under reduced pressure to give an oily residue, which was purified by column chromatography over silica gel with hexane−EtOAc (1:1) to give **9** (872 mg, 76% yield) as colorless crystals: mp 141 °C (EtOAc−hexane); $[\alpha]^{26}_D$ +66.4 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3512 (OH), 3267 ($NHSO_2$), 2112 (C≡C), 1319 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (d, J = 6.3 Hz, 3H, CMe), 2.09 (d, J = 8.1 Hz, 1H, OH), 2.14 (d, J = 2.4 Hz, 1H, C≡CH), 2.43 (s, 3H, Ph-*Me*), 3.87−3.97 (m, 1H, 4-H), 4.05 (ddd, J = 9.3, 2.7, 2.4 Hz, 1H, 3-H), 5.24 (d, J = 9.3 Hz, 1H, NH), 7.30−7.32 (m, 2H, Ph), 7.77−7.80 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 21.6, 51.6, 69.8, 74.7, 78.2, 127.4 (2C), 129.6 (2C), 137.1, 143.7; MS (FAB) *m*/*z* 254 (MH^+, 21), 136 (100); HRMS (FAB) Calcd $C_{12}H_{16}NO_3S$ (MH^+) 254.0851, found 254.0849. Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 56.68; H, 5.93; N, 5.49.

(2*S*,3*S*)-2-Ethynyl-3-methyl-*N*-(4-methylphenylsulfonyl)aziridine (3f). To a mixture of the amino alcohol **9** (780 mg, 3.08 mmol) and PPh_3 (969 mg, 3.70 mmol) in THF (5 mL) was added dropwise diethyl azodicarboxylate (0.59 mL, 3.70 mmol) at 0 °C with stirring, and the mixture was stirred for 30 min. The mixture was concentrated under reduced pressure, and the residue was purified by column chromatography over silica gel with hexane−EtOAc (3:1) to give **3f** (565 mg, 78% yield) as colorless crystals; mp 91−92 °C (EtOAc−hexane); $[\alpha]^{26}_D$ +72.9 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3271 (NSO_2), 2127 (C≡C), 1331 (NSO_2); ^1H NMR (300 MHz, $CDCl_3$) δ 1.44 (d, J = 5.7 Hz, 3H, CMe), 2.38 (d, J = 1.8 Hz, 1H, C≡CH), 2.45 (s, 3H, Ph-*Me*), 3.03 (dd, J = 4.5, 1.8 Hz, 1H, 2-H), 3.13 (qd, J = 5.7, 4.5 Hz, 1H, 3-H), 7.33−7.36 (m, 2H, Ph), 7.86−7.88 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 21.6, 35.4, 44.7, 73.8, 77.1, 127.6 (2C), 129.6 (2C), 136.7, 144.4. MS (FAB) *m*/*z* 236 (MH^+, 100); HRMS (FAB) Calcd $C_{12}H_{14}NO_2S$ (MH^+) 236.0745, found 236.0727. Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.57; N, 5.95. Found: C, 61.10; H, 5.59; N, 5.87.

(3*R*,4*R*)-4-*tert*-Butyldimethylsilyloxy-3-[*N*-(4-methylphenylsulfonyl)amino]-1-pentyne (11). By a procedure identical with that described for the synthesis of **8** from **7**, **10** (7.00 g, 18.7 mmol) was converted into **11** (3.27 g, 48%) as colorless crystals: mp 73 °C (hexane); $[\alpha]^{26}_D$ −58.7 (*c* 1.03, $CHCl_3$); IR (KBr) cm^{-1} 3278 ($NHSO_2$), 2121 (C≡C), 1331 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 6H, $SiMe_2$), 0.89 (s, 9H, CMe_3), 1.21 (d, J = 6.3 Hz, 3H, CMe), 2.02 (d, J = 2.4 Hz. 1H, C≡CH), 2.43 (s, 3H, Ph-*Me*), 3.92 (ddd, J = 8.7, 2.7, 2.4 Hz, 1H, 3-H), 3.97 (qd, J = 6.3, 2.7 Hz, 1H, 4-H), 4.84 (d, J = 8.7 Hz, 1H, NH), 7.28−7.31 (m, 2H, Ph), 7.76−7.79 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.79, −4.55, 18.0, 20.2, 21.5, 25.8 (3C), 51.2, 70.6, 72.7, 81.0, 127.3 (2C), 129.4 (2C), 137.4, 143.4; MS (FAB) *m*/*z* 310 (100), 368 (MH^+, 97); HRMS (FAB) calcd $C_{18}H_{29}NO_3SSi$ (MH^+) 368.1716, found 368.1710. Anal. Calcd for $C_{18}H_{29}NO_3SSi$: C, 58.82; H, 7.95; N, 3.81. Found: C, 58.53; H, 7.80; N, 3.78.

(3*R*,4*R*)-4-Hydroxy-3-[*N*-(4-methylphenylsulfonyl)amino]-1-pentyne (12). By a procedure identical with that described for the synthesis of **9** from **8**, **11** (3.00 g, 8.16 mmol) was converted into **12** (1.85 g, 90% yield) as colorless crystals: mp 112 °C (EtOAc−hexane); $[\alpha]^{26}_D$ −82.2 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3521 (OH), 3269 ($NHSO_2$), 2119 (C≡C), 1327 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (d, J = 6.0 Hz, 3H, CMe), 2.12 (d, J = 1.8 Hz, 1H, C≡CH), 2.43 (s, 3H, Ph-*Me*), 2.44−2.50 (m, 1H, OH), 3.84−3.95 (m, 2H, 3-H and 4-H), 5.10 (d, J = 7.5 Hz, 1H, NH), 7.27−7.30 (m, 2H, Ph), 7.77−7.80 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 21.5, 51.7, 70.0, 73.9, 79.7, 127.4 (2C), 129.5 (2C), 136.8, 143.7; MS (EI) *m*/*z* 254 (MH^+, 0.3), 54 (100). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 56.80; H, 5.97; N, 5.48.

(2*R*,3*S*)-2-Ethynyl-3-methyl-*N*-(4-methylphenylsulfonyl)-aziridine (4f). By a procedure identical with that described for the synthesis of **3f** from **9**, **12** (2.00 g, 7.90 mmol) was converted into **4f** (1.53 g, 82% yield) as colorless crystals: mp 57 °C (EtOAc−hexane); $[\alpha]^{26}_D$ −91.9 (*c* 0.99, $CHCl_3$); IR (KBr) cm^{-1} 3288 ($NHSO_2$), 2129 (C≡C), 1327 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (d, J = 5.4 Hz, 3H, CMe), 2.20 (d, J = 1.8 Hz, 1H, C≡CH), 2.46 (s, 3H, Ph-*Me*), 3.01 (dq, J = 6.9, 5.4 Hz, 1H, 3-H), 3.31 (dd, J = 6.9, 1.8 Hz, 1H, 2-H), 7.34−7.37 (m, 2H, Ph), 7.82−7.85 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.3, 21.6, 33.6, 40.0, 72.7, 76.4, 127.8 (2C), 129.8 (2C), 134.7, 144.8; MS (EI) *m*/*z* 236 (MH^+, 0.14), 80 (100). Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 61.25; H, 5.57; N, 5.95. Found: C, 61.19; H, 5.62; N, 5.93.

General Procedure for Synthesis of 2-Ethynyl-1,3-amino Alcohols from 2-Ethynylaziridines. Synthesis of (3*R*,4*R*,5*S*)-4-Ethynyl-2-methyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]-6-phenylhexan-3-ol (15). To a solution of the aziridine **3c** (102 mg, 0.3 mmol) in a mixed solvent of THF (2.4 mL) and HMPA (0.6 mL) were added H_2O (5 μL, 0.3 mmol), isobutyraldehyde (41 μL, 0.45 mmol), InI (94.3 mg, 0.39 mmol) and $Pd(PPh_3)_4$ (17.3 mg, 5 mol %, 0.015 mmol) successively at room temperature. The mixture was stirred for 4 h at this temperature and quenched with 1 N HCl (1 mL). The whole was extracted with Et_2O, and the extract was washed with water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with hexane−EtOAc (5:2) gave **15** (76.3 mg, 62% yield): colorless needles; mp 123 °C (hexane−Et_2O); $[\alpha]^{23}_D$ +7.30 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3547 (OH), 3296 ($NHSO_2$), 2114 (C≡C), 1333 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.55 (d, J = 6.8 Hz, 3H, CMe), 0.64 (d, J = 6.8 Hz, 3H, CMe), 1.40−1.49 (m, 1H, 2-H), 2.10 (d, J = 5.4 Hz, 1H, OH), 2.29 (s, 3H, Ph-*Me*), 2.33 (d, J = 2.7 Hz, 1H, C≡CH), 2.62 (ddd, J = 5.9, 2.7, 2.4 Hz, 1H, 4-H), 2.66 (s, 6H, 2 × Ph-*Me*), 2.82 (dd, J = 13.5, 9.7 Hz, 1H, 6-C*H*H), 2.88 (dd, J = 13.5, 5.1 Hz, 1H, 6-CH*H*), 3.22 (ddd, J = 5.9, 5.4, 5.4 Hz, 1H, 3-H), 3.44−3.51 (m, 1H, 5-H), 5.21 (d, J = 8.1 Hz, 1H, NH), 6.95 (s, 2H, Ph), 7.03−7.06 (m, 2H, Ph), 7.17−7.26 (m, 3H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 15.5, 19.5, 21.0, 23.2 (2C), 30.9, 38.6, 40.5, 56.3, 74.8, 75.5, 80.2, 126.7, 128.6 (2C), 128.8 (2C), 132.0 (2C), 134.4, 137.0, 138.6 (2C), 142.2. MS (EI) *m*/*z* 415 (M + 2, 0.2), 250 (100). Anal. Calcd for $C_{24}H_{31}NO_3S$: C, 69.70; H, 7.56; N, 3.39. Found: C, 69.41; H, 7.40; N, 3.33.

(3*R*,4*R*,5*S*)-4-Ethynyl-2,6-dimethyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]heptan-3-ol (16). By a procedure identical with that described for the synthesis of **15** from **3c**, **3a** (58.3 mg, 0.2 mmol) was converted into **16** (30.7 mg, 42% yield): colorless oil; $[\alpha]^{23}_D$ −31.4 (*c* 1.13, $CHCl_3$); IR (KBr) cm^{-1} 3525 (OH), 3305 ($NHSO_2$), 2114 (C≡C), 1328 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.70 (d, J = 6.8 Hz, 3H, CMe), 0.85 (d, J = 6.8 Hz, 3H, CMe), 0.89 (d, J = 6.8 Hz, 6H, 2 × CMe), 1.59−1.71 (m, 1H, Me_2CH), 1.78−1.91 (m, 1H, Me_2CH), 2.20 (d, J = 4.3 Hz, 1H, OH), 2.25 (d, J = 1.6 Hz, 1H, C≡CH), 2.26 (s, 3H, Ph-*Me*), 2.62 (s, 6H, 2 × Ph-*Me*), 2.72−2.78 (m, 1H, 4-H), 3.01−3.07 (m, 1H, 3-H), 3.23 (ddd, J = 9.2, 6.8, 2.4 Hz, 1H, 5-H), 4.98 (d, J = 9.2 Hz, 1H, NH), 6.94 (s, 2H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 15.6, 19.2, 19.3, 19.6, 21.0, 23.1

(2C), 30.4, 33.3, 39.1, 59.1, 74.8, 76.0, 81.2, 131.8 (2C), 135.7, 138.0 (2C), 141.7; MS (FAB) *m/z* 366 (MH^+, 100); HRMS (FAB) calcd $C_{20}H_{32}NO_3S$ (MH^+) 366.2103, found 366.2113.

(3*R*,4*R*,5*R*)-6-*tert*-Butyldimethylsilyloxy-4-ethynyl-2-methyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]hexan-3-ol (19). By a procedure identical with that described for the synthesis of **15** from **3c**, **3e** (78.7 mg, 0.2 mmol) was converted into **19** (64.0 mg, 68% yield): colorless oil; $[\alpha]^{27}_D$ +15.6 (*c* 1.43, $CHCl_3$); IR (KBr) cm^{-1} 3552 (OH), 3311 ($NHSO_2$), 2116 (C≡C), 1335 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ −0.01 (s, 3H, SiMe), 0.00 (s, 3H, SiMe), 0.76 (d, *J* = 6.8 Hz, 3H, CMe), 0.84 (s, 9H, CMe_3), 0.90 (d, *J* = 6.8 Hz, 3H, CMe), 1.56−1.68 (m, 1H, 2-H), 2.14 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.28−2.30 (m, 1H, OH), 2.30 (s, 3H, Ph-*Me*), 2.65 (s, 6H, 2 × Ph-*Me*), 3.02−3.07 (m, 1H, 4-H), 3.12−3.18 (m, 1H, 3-H), 3.33−3.41 (m, 1H, 5-H), 3.51 (dd, *J* = 9.7, 7.3 Hz, 1H, 6-C*H*H), 3.66 (dd, *J* = 9.7, 3.8 Hz, 1H, 6-CH*H*), 5.11 (d, *J* = 8.4 Hz, 1H, NH), 6.96 (s, 2H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ −5.53, −5.48, 17.3, 18.2, 19.3, 21.0, 23.2 (2C), 25.8 (3C), 31.6, 37.6, 55.5, 62.8, 74.0, 75.4, 80.1, 131.9 (2C), 134.2, 138.8 (2C), 142.3; MS (FAB) *m/z* 468 (MH^+, 100), 119 (74); HRMS (FAB) calcd $C_{24}H_{42}NO_4SSi$ (MH^+) 468.2604, found 468.2605.

(3*R*,4*R*,5*S*)-4-Ethynyl-2-methyl-5-[*N*-(4-methylphenylsulfonyl)amino]hexan-3-ol (20) and Its (3*S*,4*S*,5*S*)-Isomer (21). By a procedure identical with that described for the synthesis of **15** from **3c**, **3f** (47.1 mg, 0.2 mmol) was converted into **20** (41.1 mg, 73% yield) and **21** (3.1 mg, 6% yield).

Compound **20**: colorless crystals; mp 114−115 °C (EtOAc−hexane); $[\alpha]^{26}_D$ −13.5 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3535 (OH), 3236 ($NHSO_2$), 2119 (C≡C), 1319 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.9 Hz, 3H, CMe), 0.91 (d, *J* = 6.6 Hz, 3H, CMe), 1.18 (d, *J* = 6.6 Hz, 3H, CMe), 1.67−1.78 (m, 1H, 2-H), 2.08 (d, *J* = 6.6 Hz, 1H, OH), 2.22 (d, *J* = 2.7 Hz, 1H, C≡CH), 2.43 (s, 3H, Ph-*Me*), 2.58 (ddd, *J* = 3.9, 3.9, 2.7 Hz, 1H, 4-H), 3.21 (ddd, *J* = 6.6, 6.6, 3.9 Hz, 1H, 3-H), 3.44−3.49 (m, 1H, 5-H), 5.08 (d, *J* = 7.2 Hz, 1H, NH), 7.30−7.33 (m, 2H, Ph), 7.76−7.79 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.2, 19.3, 20.7, 21.5, 31.8, 42.3, 51.3, 74.7, 76.2, 79.6, 127.2 (2C), 129.6 (2C), 137.5, 143.5. MS (FAB) *m/z* 310 (MH^+, 67), 69 (100); HRMS (FAB) calcd $C_{16}H_{24}NO_3S$ (MH^+) 310.1477, found 310.1479. Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53. Found: C, 61.86; H, 7.36; N, 4.50.

Compound **21**: colorless crystals; mp 173 °C (EtOAc−hexane); $[\alpha]^{26}_D$ −64.4 (*c* 0.99, $CHCl_3$); IR (KBr) cm^{-1} 3439 (OH), 3288 ($NHSO_2$), 2116 (C≡C), 1317 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.6 Hz, 3H, CMe), 1.02 (d, *J* = 6.6 Hz, 3H, CMe), 1.10 (d, *J* = 6.3 Hz, 6H, CMe), 1.81−1.93 (m, 1H, 2-H), 2.11 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.44 (s, 3H, Ph-*Me*), 2.48 (ddd, *J* = 7.4, 2.4, 2.4 Hz, 1H, 4-H), 2.63 (d, *J* = 6.6 Hz, 1H, OH), 3.46−3.59 (m, 2H, 3-H and 5-H), 4.59 (d, *J* = 9.3 Hz, 1H, NH), 7.31−7.34 (m, 2H, Ph), 7.56−7.78 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0 (2C), 19.7, 21.5, 31.9, 43.1, 50.5, 73.5, 74.3, 80.6, 127.1 (2C), 129.8 (2C), 137.4, 143.7; MS (FAB) *m/z* 310 (MH^+, 100); HRMS (FAB) calcd $C_{16}H_{24}NO_3S$ (MH^+) 310.1477, found 310.1500.

(3*S*,4*S*,5*S*)-4-Ethynyl-2,6-dimethyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]heptan-3-ol (22). By a procedure identical with that described for the synthesis of **15** from **3c**, **4a** (87.4 mg, 0.3 mmol) was converted into **22** (64.7 mg, 59% yield): colorless crystals; mp 66 °C (hexane−Et_2O); $[\alpha]^{27}_D$ −35.1 (*c* 1.45, $CHCl_3$); IR (KBr) cm^{-1} 3537 (OH), 3302 ($NHSO_2$), 2116 (C≡C), 1313 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.46 (d, *J* = 6.8 Hz, 3H, CMe), 0.82 (d, *J* = 6.8 Hz, 3H, CMe), 0.86 (d, *J* = 6.8 Hz, 3H, CMe), 1.02 (d, *J* = 6.5 Hz, 3H, CMe), 1.87−2.01 (m, 1H, Me_2CH), 2.09 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.28−2.35 (m, 1H, Me_2CH), 2.29 (s, 3H, Ph-*Me*), 2.55 (d, *J* = 9.5 Hz, 1H, OH), 2.64 (s, 6H, 2 × Ph-*Me*), 3.04−3.07 (m, 1H, 4-H), 3.34−3.40 (m, 1H, 3-H), 3.48 (ddd, *J* = 10.3, 10.0, 3.0 Hz, 1H, 5-H), 4.73 (dd, *J* = 10.3, 4.1 Hz, 1H, NH), 6.94 (s, 2H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 15.8, 19.1, 19.8, 20.3, 21.0, 23.3 (2C), 29.7, 32.0, 40.5, 59.2, 73.1, 74.0, 80.8, 131.8 (2C), 135.3, 138.1 (2C), 142.0; MS (EI) *m/z* 367 (M + 2, 0.2), 254 (100). Anal. Calcd for $C_{20}H_{31}NO_3S$: C, 65.72; H, 8.55; N, 3.83. Found: C, 65.44; H, 8.70; N, 3.61.

(3*S*,4*S*,5*S*)-4-Ethynyl-2-methyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]-6-phenylhexan-3-ol (24). By a procedure identical with that described for the synthesis of **15** from **3c**, **4c** (67.9 mg, 0.26 mmol) was converted into **24** (60.0 mg, 72% yield): colorless oil; $[\alpha]^{24}_D$ −10.5 (*c* 1.00, $CHCl_3$); IR (KBr) cm^{-1} 3516 (OH), 3296 ($NHSO_2$), 2116 (C≡C), 1319 ($NHSO_2$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.78 (d, *J* = 6.9 Hz, 3H, CMe), 1.00 (d, *J* = 6.6 Hz, 3H, CMe), 1.79−1.93 (m, 1H, 2-H), 2.17 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.28 (s, 3H, Ph-*Me*), 2.53−2.56 (m, 1H, OH), 2.56 (s, 6H, 2 × Ph-*Me*), 2.61 (ddd, *J* = 7.5, 2.4, 2.4 Hz, 1H, 4-H), 2.86 (dd, *J* = 14.1, 5.7 Hz, 1H, PhC*H*H), 3.04 (dd, *J* = 14.1, 6.0 Hz, 1H, PhCH*H*), 3.36−3.42 (m, 1H, 3-H), 3.74−3.84 (m, 1H, 5-H), 5.05 (d, *J* = 9.3 Hz, 1H, NH), 6.87 (s, 2H, Ph), 7.02−7.20 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.9, 19.1, 20.8, 23.3 (2C), 32.3, 38.7, 39.9, 55.6, 74.1, 74.5, 80.8, 126.7, 128.5 (2C), 129.3 (2C), 132.0 (2C), 134.5, 136.2, 138.5 (2C), 142.0; MS (FAB) *m/z* 414 (MH^+, 100); HRMS (FAB) calcd $C_{24}H_{32}NO_3S$ (MH^+) 414.2103, found 414.2101.

(3*S*,4*S*,5*R*)-6-*tert*-Butyldimethylsilyloxy-4-ethynyl-2-methyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]hexan-3-ol (26). By a procedure identical with that described for the synthesis of **15** from **3c**, **4e** (78.7 mg, 0.2 mmol) was converted into **26** (65.8 mg, 70% yield): colorless oil; $[\alpha]^{28}_D$ −5.91 (*c* 0.930, $CHCl_3$); IR (KBr) cm^{-1} 3541 (OH), 3311 ($NHSO_2$), 2118 (C≡C), 1326 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.02 (s, 3H, SiMe), 0.03 (s, 3H, SiMe), 0.86 (d, *J* = 5.9 Hz, 3H, CMe), 0.87 (s, 9H, CMe_3), 1.08 (d, *J* = 6.5 Hz, 3H, CMe), 1.91−2.03 (m, 1H, 2-H), 2.08 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.31 (s, 3H, Ph-*Me*), 2.64 (s, 6H, 2 × Ph-*Me*), 2.74 (ddd, *J* = 10.3, 2.4, 2.4 Hz, 1H, 4-H), 2.98 (dd, *J* = 10.3, 3.2 Hz, 1H, 6-C*H*H), 3.22 (d, *J* = 5.9 Hz, 1H, OH), 3.24−3.36 (m, 1H, 5-H), 3.60 (ddd, *J* = 9.5, 5.9, 2.4 Hz, 1H, 3-H), 3.89 (dd, *J* = 10.3, 0.8 Hz, 1H, 6-CH*H*), 5.43 (d, *J* = 9.7 Hz, 1H, NH), 6.97 (s, 2H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ −5.56, −5.45, 18.3, 18.9, 20.1, 21.0, 23.0 (2C), 25.8 (3C), 31.9, 37.9, 54.5, 61.7, 73.0, 73.8, 80.7, 132.0 (2C), 133.9, 138.6 (2C), 142.5; MS (FAB) *m/z* 468 (MH^+, 100), 119 (78); HRMS (FAB) calcd $C_{24}H_{42}NO_4SSi$ (MH^+) 468.2604, found 468.2585.

(2*S*,3*S*,4*S*)-2-*tert*-Butyldimethysilyloxy-3-ethynyl-4-[*N*-(4-methoxy-2,3,6-trimethylphenylsulfonyl)amino]-5-phenylpentane (34) and Its (2*R*,3*S*,4*S*)-Isomer (35). By a procedure identical with that described for the preparation of **15** from **3c**, the aziridine **4d** (73.9 mg, 0.2 mmol) was converted into an inseparable mixture of **32** and **33** (73.9 mg, 75%; **32**:**33** = 88:12, ^1H NMR) by treatment with $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol), InI (62.8 mg, 0.26 mmol), MeCHO (17 μL, 0.3 mmol) and H_2O (4 μL, 0.2 mmol) in a mixed solvent of THF (0.8 mL) and HMPA (0.2 mL). To a stirred solution of the above diastereomixture (38 mg, 0.0914 mmol) in DMF (1 mL) were added imidazole (15.6 mg, 0.229 mmol) and *tert*-butyldimethylsilyl chloride (13.4 mg, 0.11 mmol) at room temperature. The mixture was stirred at room temperature for 48 h and was made acidic with 0.5 N HCl. The whole was extracted with Et_2O and the extract was washed with water and dried ($MgSO_4$). Usual workup followed by flash chromatography over silica gel with hexane−$CHCl_3$−EtOAc (15:6:1) gave, in order of elution, **34** (42.1 mg, 87% yield) and **35** (4.6 mg, 10% yield).

Compound **34**: colorless needles; mp 138 °C (hexane−Et_2O); $[\alpha]^{18}_D$ −20.6 (*c* 0.96, $CHCl_3$); IR (KBr) cm^{-1} 3307 ($NHSO_2$), 2114 (C≡C), 1308 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ −0.01 (s, 3H, SiMe), 0.00 (s, 3H, SiMe), 0.79 (s, 9H, CMe_3), 1.15 (d, *J* = 6.2 Hz, 3H, 1-Me), 2.00 (s, 3H, Ph-*Me*), 2.05 (d, *J* = 2.4 Hz, 1H, C≡CH), 2.30 (s, 3H, Ph-*Me*), 2.59 (s, 3H, Ph-*Me*), 2.61−2.64 (m, 1H, 3-H), 2.83 (dd, *J* = 14.3, 7.0 Hz, 1H, 5-C*H*H), 2.89 (dd, *J* = 14.3, 5.4 Hz, 1H, 5-CH*H*), 3.61−3.70 (m, 1H, 4-H), 3.78 (s, 3H, OMe), 3.92−4.00 (m, 1H, 2-H), 5.49 (d, *J* = 6.8 Hz, 1H, NH), 6.45 (s, 1H, Ph), 6.89−6.93 (m, 2H, Ph), 7.03−7.05 (m, 3H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ −4.53, −4.22, 12.1, 18.1, 18.2, 20.9, 24.8, 25.8 (3C), 37.9, 43.5, 55.0, 55.5, 69.2, 73.1, 81.8, 111.8, 124.9, 126.2, 127.9 (2C), 129.2 (2C), 129.5, 136.8, 138.1, 139.1, 158.9. Anal. Calcd for $C_{29}H_{43}NO_4SSi$: C, 65.74; H, 8.18; N, 2.64. Found: C, 65.82; H, 8.17; N, 2.67.

Compound **35**: colorless oil; $[\alpha]^{21}_D$ −50.2 (*c* 0.235, $CHCl_3$); IR (KBr) cm^{-1} 3307 ($NHSO_2$), 2114 (C≡C), 1308 ($NHSO_2$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.03 (s, 3H, SiMe), 0.08 (s, 3H,

SiMe), 0.89 (s, 9H, CMe_3), 1.33 (d, J = 5.9 Hz, 3H, 1-Me), 1.98 (s, 3H, Ph-*Me*), 2.02 (s, 3H, Ph-*Me*), 2.23 (d, J = 2.7 Hz, 1H, C≡CH), 2.57 (s, 3H, Ph-*Me*), 2.66 (dd, J = 14.3, 11.3 Hz, 1H, 5-CHH), 2.95 (dd, J = 14.3, 3.5 Hz, 1H, 5-CHH), 3.14 (ddd, J = 9.2, 4.1, 2.7 Hz, 1H, 3-H), 3.81−3.93 (m, 2H, 2-H and 4-H), 3.85 (s, 3H, OMe), 4.57 (d, J = 9.7 Hz, 1H, NH), 6.46 (s, 1H, Ph), 6.85−6.87 (m, 2H, Ph), 6.98−7.12 (m, 3H, Ph); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ −4.35, −3.60, 12.0, 17.6, 18.1, 23.2, 24.9, 26.0 (3C), 35.5, 47.0, 52.4, 55.5, 68.8, 73.6, 82.0, 111.6, 124.8, 126.1, 128.0 (2C), 128.2, 128.7 (2C), 137.0, 138.6, 139.4, 159.0; MS (FAB) *m*/*z* 530 (MH^+, 100), 472 (93); HRMS (FAB) calcd $C_{29}H_{44}NO_4SSi$ (MH^+) 530.2761, found 530.2772.

(4*S*,5*R*,6*S*)-5-Ethynyl-4-isopropyl-6-phenyl-tetrahydro-1,3-oxazin-2-one (38). To a stirred suspension of NaH (5.6 mg, 0.14 mmol) in DMF (0.5 mL) under argon was added **37** (37 mg, 0.117 mmol) in dry THF (0.5 mL) at room temperature, and the mixture was stirred for 1 h. The mixture was poured into ice water (3 mL) saturated with NH_4Cl, and the whole was extracted with Et_2O. The extract was washed with water, and dried ($MgSO_4$). Usual workup gave a crystalline mass, which was recrystallized from hexane−CH_2Cl_2 to give **38** (12.5 mg, 44% yield): colorless crystals; mp 233 °C; $[\alpha]^{27}_D$ −113 (*c* 0.550, $CHCl_3$); IR (KBr) cm^{-1} 3290 (NHCO), 2117 (C≡C), 1704 (NHCO), 1394 (NHCO); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.01 (d, J = 6.0 Hz, 3H, CMe), 1.10 (d, J = 6.0 Hz, 3H, CMe), 1.95−2.03 (m, 1H, Me_2CH), 2.07 (d, J = 2.5 Hz, 1H, C≡CH), 3.10−3.11 (m, 1H, 5-H), 3.27 (dd, J = 9.8, 3.7 Hz, 1H, 4-H), 5.35 (d, J = 1.8 Hz, 1H, 6-H), 5.69 (br s, 1H, NH), 7.34−7.41 (m, 3H, Ph), 7.47−7.49 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.6, 19.1, 30.8, 35.7, 60.8, 75.0, 75.4, 79.2, 126.1 (2C), 128.2 (2C), 128.5, 136.5, 153.3; MS (FAB) *m*/*z* 244 (MH^+, 74), 116 (100); HRMS (FAB) calcd $C_{15}H_{18}NO_2$ (MH^+) 244.1337, found 244.1325.

(4*S*,5*S*,6*R*)-5-Ethynyl-4-isopropyl-6-phenyltetrahydro-1,3-oxazin-2-one (40). By a procedure identical with that described for the synthesis of **38** from **37**, **39** (40.0 mg, 0.126 mmol) was converted into **40** (13.0 mg, 42% yield) as colorless crystals: mp 195 °C (hexane−$CHCl_3$); $[\alpha]^{25}_D$ +19.3 (*c* 0.500, $CHCl_3$); IR (KBr) cm^{-1} 3234 (NHCO), 2123 (C≡C), 1713 (NHCO), 1413 (NHCO); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.03 (d, J = 7.0 Hz, 3H, CMe), 1.06 (d, J = 6.5 Hz, 3H, CMe), 1.94−2.01 (m, 1H, Me_2CH), 2.15 (d, J = 2.5 Hz, 1H, C≡CH), 3.12−3.14 (m, 1H, 5H), 3.23 (ddd, J = 5.5, 5.5, 2.5 Hz, 1H, 4-H), 5.42 (d, J = 3.0 Hz, 1H, 6-H), 6.45 (br s, 1H, NH), 7.34−7.45 (m, 5H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.4, 19.1, 31.5, 33.6, 59.1, 74.2, 76.3, 78.9, 126.4 (2C), 128.2 (2C), 128.5, 136.2, 154.0; MS (FAB) *m*/*z* 244 (MH^+, 86), 116 (100); HRMS (FAB) calcd $C_{15}H_{18}NO_2$ (MH^+) 244.1337, found 244.1348.

(2*R*,3*R*,4*S*)-4-Benzyl-3-ethynyl-*N*-(4-methoxy-2,3,6-trimethylphenylsulfonyl)-2-phenylazetidine (55). By a procedure similar to that described for the synthesis of **3f** from **9**, **27** (15.5 mg, 0.032 mmol) was converted into **55** (13 mg, 87% yield) by treatment with PPh_3 (34 mg, 0.13 mmol) and diethyl azodicarboxylate (71 μL, 0.13 mmol) in THF at 0 °C for 15 min: colorless oil; $[\alpha]^{27}_D$ +6.71 (*c* 0.65, $CHCl_3$); IR (KBr) cm^{-1} 3292 (NSO_2), 2119 (C≡C), 1311 (NSO_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.02 (s, 3H, Ph-*Me*), 2.37 (d, J = 2.4 Hz, 1H, C≡CH), 2.49 (s, 3H, Ph-*Me*), 2.54 (s, 3H, Ph-*Me*), 3.35 (ddd, J = 7.8, 6.9, 2.4 Hz, 1H, 3-H), 3.62 (dd, J = 14.7, 10.8 Hz, 1H, PhC*H*H), 3.70−3.76 (m, 1H, PhCH*H*), 3.74 (s, 3H, OMe), 4.88 (ddd, J = 10.8, 7.8, 3.0 Hz, 1H, 4-H), 5.15 (d, J = 6.9 Hz, 1H, 2-H), 6.26 (s, 1H, Ph), 7.04−7.39 (m, 10H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.8, 18.0, 24.1, 35.26, 35.31, 55.4, 66.1, 71.0, 75.8, 80.2, 111.6, 124.8, 126.3, 126.7 (2C), 128.0 (2C), 128.2 (2C), 128.3, 129.1, 129.7 (2C), 137.3, 137.6, 139.2, 140.0, 159.4; MS (FAB) *m*/*z* 460 (MH^+, 5.1), 185 (100); HRMS (FAB) calcd $C_{28}H_{30}NO_3S$ (MH^+) 460.1946, found 460.1945.

(2*S*,4*S*)-3-Ethynyl-2,4-dimethyl-*N*-(4-methylphenylsulfonyl)azetidine (56). By a procedure similar to that described for the synthesis of **3f** from **9**, **29** (13.3 mg, 0.047 mmol) was converted into **56** (10 mg, 81% yield) by treatment with PPh_3 (55.4 mg, 0.21 mmol) and diethyl azodicarboxylate (33 μL, 0.21 mmol) in THF at 0 °C for 10 min: colorless crystals; mp 72 °C (EtOAc−hexane); $[\alpha]^{24}_D$ +14.2 (*c* 0.34, $CHCl_3$); IR (KBr) cm^{-1} 3271 (NSO_2), 2118 (C≡C), 1336 (NSO_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (d, J = 6.0 Hz, 3H, CMe), 1.41 (d, J = 6.0 Hz, 3H, CMe), 2.25 (d, J = 2.5 Hz, 1H, C≡CH), 2.44 (s, 3H, Ph-*Me*), 3.00 (ddd, J = 9.0, 6.5, 2.5 Hz, 1H, 3-H), 4.22 (dq, J = 6.5, 6.0 Hz, 1H, 2-H), 4.44 (dq, J = 9.0, 6.0 Hz, 1H, 4-H), 7.30−7.32 (m, 2H, Ph), 7.71−7.73 (m, 2H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 20.2, 21.5, 33.3, 60.4, 64.9, 74.0, 79.7, 127.5 (2C), 129.6 (2C), 137.3, 144.1. MS (FAB) *m*/*z* 264 (MH^+, 82), 136 (100); HRMS (FAB) calcd $C_{14}H_{18}NO_2S$ (MH^+) 264.1058, found 264.1063.

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Supporting Information Available: Experimental procedures for **17**, **18**, **23**, **25**, **27**−**31**, **36**, **37**, **39**, **53**, **54**, **57**, and **58**; NOE experiment of **56**−**58**; ^{1}H NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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