Stereoselective Synthesis of 2-Alkenylaziridines and 2-Alkenylazetidines by Palladium-Catalyzed Intramolecular Amination of α- and β-Amino Allenes

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Whereas palladium-catalyzed reaction of *N*-arylsulfonyl-α-amino allenes with an aryl iodide (4 equiv) in the presence of potassium carbonate (4 equiv) in DMF at around 70 °C affords the corresponding 3-pyrroline derivatives, the reaction in refluxing 1,4-dioxane under otherwise identical conditions yields exclusively or most predominantly the corresponding 2-alkenylaziridines bearing an aryl group on the double bond. Similarly, *N*-arylsulfonyl-*β*-amino allenes can be also cyclized into the corresponding alkenylazetidines bearing a 2,4-*cis*-configuration under palladium-catalyzed cyclization conditions in DMF.

Introduction

Transition metal-catalyzed cyclization of allenes[1] bearing a (pro-) nucleophilic functionality such as oxygen,[2−4] nitrogen,[5−10] and carbon[11,12] has attracted much attention in recent years, and many stereoselective processes have been developed. Particularly, cyclization of amino allenes using such metals as Pd(0 or II),[5−7] Ag(I),[8] and organolanthanides[9] has become quite useful methodology for the synthesis of five- or six-membered azacycles, and several groups have applied such cyclization to the total synthesis of natural products.[5c,8b,8g] It is well documented that cyclization of amino allene **1** with a one- or two-carbon tether between the allene and the nitrogen atom ($n = 1$ or 2) yields five- or six-membered azacycles selectively by path A (Scheme 1), while an amino allene bearing a longer carbon tether ($n = 3$ or 4) also affords five- or six-membered rings via path B. In contrast, ring-closure of amino allenes bearing a shorter carbon chain ($n = 1$ or 2) yielding three- or four-membered azacycles (path B) had been unprecedented until quite recently.[6,7]

Currently, chiral aziridines bearing an alkenyl group on one of the aziridine-ring carbons are widely used as building blocks for the stereoselective synthesis of biologically and synthetically important compounds.[13,14] Chiral azetidines also constitute an important class of compounds since they can be seen in several biologically active compounds[15] and used as efficient chiral ligands for asymmetric syntheses.[16] Recent development of aziri-

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(1) For recent reviews, see: (a) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (b) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199. (c) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (d) Hashmi, A. S. K. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3590.

(2) (a) Walkup, R. D.; Park, G. *Tetrahedron Lett.* **1987**, *28*, 1023. (b) Walkup, R. D.; Guan, L. G.; Mosher, M. D.; Kim, S. W.; Kim, Y. S. *Synlett* **1993**, 88. (c) Ma, S.; Shi, Z. *J. Org. Chem.* **1998**, *63*, 6387. (d) Kang, S.-K.; Yamaguchi, T.; Pyun, S.-J.; Lee, Y.-T.; Baik, T.-G. *Tetrahedron Lett.* **1998**, *39*, 2127. (e) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **1999**, *121*, 7943. (f) Ma, S.; Li, L. *Org. Lett.* **2000**, *2*, 941. (g) Labrosse, J.-R.; Lhoste, P.; Sinou, D. *Org. Lett.* **2000**, *2*, 527.

(3) (a) Olsson, L.-I.; Claesson, A. *Synthesis* **1979**, 743. (b) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1991**, *56*, 4913. (c) Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 7180. (d) Marshall, J. A.; Bartley, G. S. *J. Org. Chem.* **1994**, *59*, 7169. (e) VanBrunt, M. P.; Standaert, R. F. *Org. Lett.* **2000**, *2*, 705.

(4) (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2285. (b) Yoneda, E.; Kaneko, T.; Zhang, S.-W.; Onitsuka, K.; Takahashi, S. *Org. Lett.* **2000**, *2*, 441.

(5) (a) Lathbury, D.; Vernon, P.; Gallagher, T. *Tetrahedron Lett.* **1986**, *27*, 6009. (b) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4257. (c) Fox, D. N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *J. Am. Chem. Soc.* **1991**, *113*, 2652. (d) Kimura, M.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1992**, *57*, 6377. (e) Davies, I. W.; Scopes, D. I. C.; Gallagher, T. *Synlett* **1993**, 85. (f) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, *60*, 482. (g) Desarbre, E.; Mérour, J.-Y. *Tetrahedron Lett.* **1996**, *37*, 43. (h) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 5421. (i) Karstens, W. F. J.; Stol, M.; Rutjes, F. P. J. T.; Hiemstra, H. *Synlett* **1998**, 1126. (j) Kang, S.-K.; Baik, T.-G.; Hur, Y. *Tetrahedron* **1999**, *55*, 6863. (k) Grigg, R.; MacLachlan, W. S.; MacPherson, D. T.; Sridharan, V.; Suganthan, S.; Thornton-Pett, M.; Zhang, J. *Tetrahedron* **2000**, *56*, 6585. (l) Kang, S.-K.; Kim, K.-J. *Org. Lett.* **2001**, *3*, 511.

(6) A portion of this study was reported in preliminary communications: (a) Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1999**, *64*, 2992. (b) Anzai, M.; Toda, A.; Ohno, H.; Takemoto, Y.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 7393.

(7) (a) Kang, S.-K.; Baik, T.-G.; Kulak, A. N. *Synlett* **1999**, 324. (b) 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.

(8) (a) Claesson, A.; Sahlberg, C.; Luthman, K. *Acta Chem. Scand.* **1979**, B*33*, 309. (b) Arseniyadis, S.; Sartoretti, J. *Tetrahedron Lett.* **1985**, *26*, 729. (c) Lathbury, D.; Gallagher, T. *J. Chem. Soc. Chem. Commun.* **1986**, 114. (d) Grimaldi, J.; Cormons, A. *Tetrahedron Lett.* **1986**, *27*, 5089. (e) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4253. (f) Fox, D. N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *J. Chem. Soc., Chem. Commun.* **1989**, 1073. (g) Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 10012.

(9) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633.

(10) For palladium-catalyzed intermolecular amination of allenes, see: (a) Shimizu, I.; Tsuji, J. *Chem. Lett.* **1984**, 233. (b) Besson, L.; Goré, J.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 3857. (c) Al-Masum, M.; Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1997**, *38*, 6071.

(11) (a) Trost, B. M.; Gerusz, V. J. *J. Am. Chem. Soc.* **1995**, *117*, 5156. (b) Meguro, M.; Kamijo, S.; Yamamoto, Y. *Tetrahedron Lett.* **1996**, *37*, 7453. (c) Trost, B. M.; Michellys, P.-Y.; Gerusz, V. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1750. (d) Kamijo, S.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 1747. (e) Meguro, M.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 694. (f) Ma, S.; Zhao, S. *Org. Lett.* **2000**, *2*, 2495.

(12) Walkup, R. D.; Park, G. *J. Am. Chem. Soc.* **1990**, *112*, 1597.

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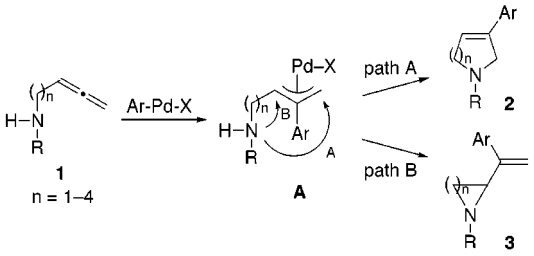
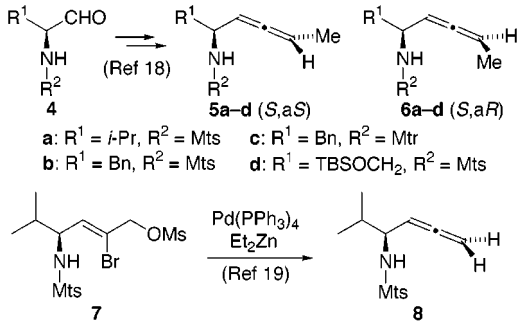
Scheme 1. Cyclization of Amino Allenes



dine and azetidine chemistry prompts us to synthesize these compounds bearing a wide variety of alkenyl groups via cyclization of amino allenes. It was of considerable interest to determine whether amino allenes can be cyclized into strained aziridines and azetidines using a transition-metal-based catalytic system and whether the axial chirality of the amino allenes influences the chemo- and stereoselectivity of the cyclization process.

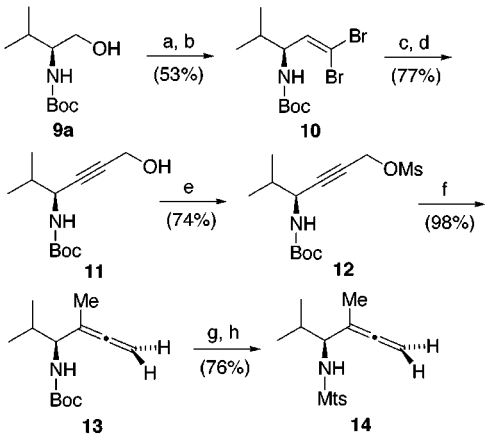
At almost the same time that we communicated our palladium-catalyzed cyclization of amino allenes into aziridines[6a] and azetidines,[6b] two independent communications describing a similar cyclization of β-amino allenes **1** ($n = 2$, Scheme 1) into azetidines **3** ($n = 2$) appeared.[7] Thus, Kang and co-workers reported the palladium-catalyzed cyclization of an *N*-protected amino allene with hypervalent iodonium salts to afford a mixture of four- and six-membered azacycles, albeit only in a single example.[7a] Rutjes, Hiemstra, and their co-workers also communicated that predominant formation of alkenylazetidines over a six-membered ring can be accomplished by exposure of some β-amino allenes to $Pd(PPh_3)_4$, K_2CO_3, and aryl- or alkenyl halides (or triflates) in DMF only when the reaction was stopped right after the consumption of the starting material.[7b] They also described that prolonged reaction time causes isomerization of alkenylazetidines into the corresponding six-membered rings. In this paper, we present a full account of our investigation into a highly stereoselective synthesis of *N*-protected-3-alkyl-2-alkenylaziridines and azetidines from amino allenes. This is a first example of metal-catalyzed aziridination of amino allenes.[17]

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: (a) $(COCl)_2$, DMSO, CH_2Cl_2, then $(i\text{-Pr})_2NEt$; (b) CBr_4, PPh_3, Et_3N; (c) *n*-BuLi (3 equiv), then DMF; (d) $NaBH_4$; (e) MsCl, Et_3N; (f) MeCu(CN)Li·2LiCl; (g) TFA; (h) MtsCl, Et_3N.

Results and Discussions

Synthesis of Amino Allenes from α-Amino Acids. The requisite nonracemic *N*-sulfonylated amino allenes **5** and **6** bearing a methyl group at the terminal sp^2-carbon atom were prepared in high yields starting from natural α-amino acids following the published procedure (Scheme 2).[18] The terminal allene **8** was also prepared by palladium(0)-catalyzed reduction of allylic bromomesylate **7** as we described recently.[19]

The amino allene **14** bearing a methyl substituent on the allenic carbon neighboring the amino group was synthesized from (*S*)-valinol as shown in Scheme 3. Thus, *N*-protected amino alcohol **9a** was treated successively with oxalyl chloride−DMSO−*N*,*N*-diisopropylethylamine and $CBr_4-PPh_3-Et_3N$ affording the dibromide **10** in 53%

(13) (a) Hudlicky, T.; Luna, H.; Price, J. D.; Rulin, F. *J. Org. Chem.* **1990**, *55*, 4683. (b) Pearson, W. H.; Bergmeier, S. C.; Degan, S.; Lin, K.-C.; Poon, Y.-F.; Schkeryantz, J. M.; Williams, J. P. *J. Org. Chem.* **1990**, *55*, 5719. (c) Spears, G. W.; Nakanishi, K.; Ohfune, Y. *Synlett* **1991**, 91. (d) Wipf, P.; Fritch, P. C. *J. Org. Chem.* **1994**, *59*, 4875. (e) Davis, F. A.; Reddy, V. *Tetrahedron Lett.* **1996**, *37*, 4349. (f) Jeong, J. U.; Tao, B.; Sagasser, I.; Henniges, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1998**, *120*, 6844. (g) Cossy, J.; Blanchard, N.; Meyer, C. *Tetrahedron Lett.* **1999**, *40*, 8361. (h) Chuang, T.-H.; Sharpless, K. B. *Org. Lett.* **1999**, *1*, 1435. (i) Deng, W.-P.; Li, A.-H.; Dai, L.-X.; Hou, X.-L. *Tetrahedron* **2000**, *56*, 2967.

(14) (a) Ibuka, T.; Nakai, K.; Habashita, H.; Hotta, Y.; Fujii, N.; Mimura, N.; Miwa, Y.; Taga, T.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 652. (b) Ibuka, T.; Mimura, N.; Aoyama, H.; Akaji, M.; Ohno, H.; Miwa, Y.; Taga, T.; Nakai, K.; Tamamura, H.; Fujii, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 999. (c) Ibuka, T.; Mimura, N.; Ohno, H.; Nakai, K.; Akaji, M.; Habashita, H.; Tamamura, H.; Miwa, Y.; Taga, T.; Fujii, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2982. (d) Toda, A.; Aoyama, H.; Mimura, N.; Ohno, H.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1998**, *63*, 7053. (e) Ohno, H.; Ishii, K.; Honda, A.; Tamamura, H.; Fujii, N.; Takemoto, Y.; Ibuka, T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3703. (f) Ishii, K.; Ohno, H.; Takemoto, Y.; Osawa, E.; Yamaoka, Y.; Fujii, N.; Ibuka, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2155. (g) Ohno, H.; Hamaguchi, H.; Tanaka, T. *Org. Lett.* **2000**, *2*, 2161.

(15) (a) Knapp, S.; Dong, Y. *Tetrahedron Lett.* **1997**, *38*, 3813. (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) 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.

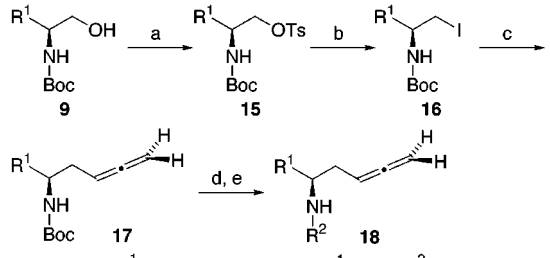
(16) (a) Starmans, W. A. J.; Thijs, L.; Zwanenburg, B. *Tetrahedron* **1998**, *54*, 629. (b) Starmans, W. A. J.; Walgers, R. W. A.; Thijs, L.; de Gelder, R.; Smits, J. M. M.; Zwanenburg, B. *Tetrahedron* **1998**, *54*, 4991. (c) Shi, M.; Jiang, J.-K. *Tetrahedron: Asymmetry* **1999**, *10*, 1673. (d)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

(17) For related cyclizations of allenes into three-membered rings, see refs 2d, 2e, and 11f.

(18) Ohno, H.; Toda, A.; Fujii, N.; Takemoto Y.; Tanaka, T.; Ibuka, T. *Tetrahedron* **2000**, *56*, 2811. See also: Ohno, H.; Toda, A.; Takemoto, Y.; Fujii, N.; Ibuka, T. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2949.

(19) Ohno, H.; Toda, A.; Oishi, S.; Tanaka, T.; Takemoto, Y.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **2000**, *41*, 5131.

Scheme 4[a]



9a, 15a–17a: R^1 = *i*-Pr
9b, 15b–17b: R^1 = *i*-Bu
9c, 15c–17c: R^1 = Bn
9d, 15d–17d: R^1 = $TBSOCH_2$
9e, 15e–17e: R^1 = $MeO_2C(CH_2)_2$

18a: R^1 = *i*-Pr, R^2 = Mts
18b: R^1 = *i*-Bu, R^2 = Mts
18c: R^1 = *i*-Bu, R^2 = Ts
18d: R^1 = *i*-Bu, R^2 = *o*-Ns
18e: R^1 = Bn, R^2 = Mts
18f: R^1 = Bn, R^2 = Ts
18g: R^1 = $TBSOCH_2$, R^2 = Mts
18h: R^1 = $MeO_2C(CH_2)_2$, R^2 = Mts
18i: R^1 = $MeO_2C(CH_2)_2$, R^2 = Mtr

[a] Reagents: (a) TsCl, Et_3N, DMAP; (b) NaI; (c) Zn, $BrCH_2CH_2Br$, TMSCl, then CuCN, LiCl, then propargyl tosylate; (d) TFA; (e) $ArSO_2Cl$, Et_3N.

Table 1. Synthesis of β-Amino Allenes 18

SM	yield of **15**	yield of **16**	yield of **17**	yield of **18**
9a	**15a**: 81%	**16a**: 42%	**17a**: 67%	**18a**: 21%
9b	**15b**: 70%	**16b**: 57%	**17b**: 62%	**18b**: 74%
				18c: 85%
				18d: 66%
9c	**15c**: 73%	**16c**: 19%	**17c**: 14%	**18e**: 94%
				18f: 80%
9d	**15d**: 70%	**16d**: 27%	**17d**: 49%	**18g**: 15%
9e	**15e**[a]	**16e**[a]	**17e**: 65%	**18h**: 45%
				18i: 54%

[a] For the synthesis of **15e** and **16e**, see ref 20a.

yield (two steps). After treatment of **10** with *n*-BuLi and DMF, the resulting aldehyde was reduced to the propargyl alcohol **11** with $NaBH_4$ without purification. After mesylation of **11**, organocopper-mediated reaction of the mesylate **12** gave **13**, which was then converted into the sulfonamide derivative **14**.

Next, β-amino allenes **18** were synthesized by the reaction of amino acid-derived zinc/copper reagents with propargyl tosylate (Scheme 4).[20] Tosylation of the amino alcohols **9** followed by iodination with NaI provided **16** in variable yields (Table 1). The zinc/copper reagents of the type RCu(CN)ZnI were prepared by treatment of **16** with zinc and CuCN·2LiCl, which were then allowed to react with propargyl tosylate to yield the *N*-Boc-amino allenes **17**. The *N*-sulfonylated amino allenes **18** were then synthesized by deprotection of **17** with TFA, followed by sulfonylation with an Mts, Ts, or Mtr group. The yields are summarized in Table 1.

Cyclization of α-Amino Allenes into Alkenylaziridines. With the synthesized amino allenes in hand, we next investigated the cyclization of α-amino allenes under various reaction conditions. We first applied the known cyclization condition of amino allenes according to the literature.[5e] To our initial dismay, exposure of **5a** and **6a** to $Pd(PPh_3)_4$, K_2CO_3, and iodobenzene in DMF afforded undesired five-membered rings **19a** and **20a**, although in a stereoselective manner (Scheme 5). Other known

Scheme 5

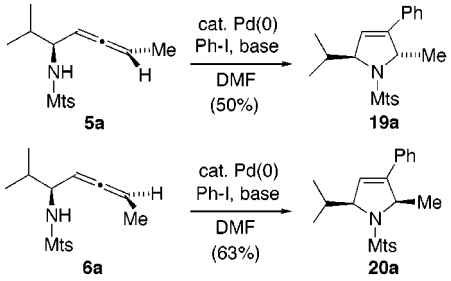
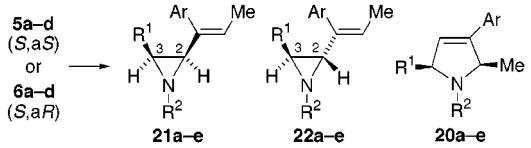


Table 2. Palladium(0)-catalyzed Aziridination of the α-Amino Allenes 5 and 6[a]



20a–22a: R^1 = *i*-Pr, R^2 = Mts, Ar = Ph
20b–22b: R^1 = *i*-Pr, R^2 = Mts, Ar = 4-MePh
20c–22c: R^1 = Bn, R^2 = Mts
20d–22d: R^1 = Bn, R^2 = Mtr
20e–22e: R^1 = $TBSOCH_2$, R^2 = Mts

entry	allene	reaction time (h)	ArI	product ratio[b]	yield[c] (%)
1	**5a**	6	PhI	**21a**/**22a** = 82:18	80
2[d]	**5a**	2	PhI	**21a**/**22a** = 84:16	83
3	**5a**	6	4-MePhI	**21b**/**22b** = 91:9	64
4	**5b**	4.5	PhI	**21c**/**22c** = 85:15	79
5	**5c**	4	PhI	**21d**/**22d** = 80:20	79
6	**5d**	1.2	PhI	**21e**/**22e** = 72:28	74
7	**6a**	2.5	PhI	**21a**/**22a**/**20a** = 2:90:8	79
8	**6a**	3.5	4-MePhI	**21b**/**22b**/**20b** = 12:85:3	44
9	**6b**	4	PhI	**21c**/**22c**/**20c** = 17:67:16	73
10	**6c**	4	PhI	**21d**/**22d**/**20d** = 17:78:5	77
11	**6d**	1.2	PhI	**21e**/**22e**/**20e** = 23:64:13	71

[a] All reactions were carried out in 1,4-dioxane under reflux using $Pd(PPh_3)_4$ (4−20 mol %), K_2CO_3 (4 equiv) and ArI (4 equiv) unless otherwise stated. [b] Ratios were determined by ^1H NMR (270 MHz) or isolation. [c] Combined isolated yields. [d] $Pd(OAc)_2/4PPh_3$ (10 mol %) was used.

cyclization using Ag(I) again resulted in the formation of a five-membered ring as the sole isolable product.

After considerable unsuccessful experimentation, the expected aziridine formation could be realized when the palladium(0)-catalyzed cyclizations were conducted in 1,4-dioxane. The results are summarized in Table 2. Typically, a dioxane solution of the amino allene **5a**, iodobenzene (4 equiv), potassium carbonate (4 equiv), and a catalytic amount of $Pd(PPh_3)_4$ (4 mol %) was refluxed under argon yielding 2,3-*cis*- and 2,3-*trans*-2-alkenylaziridines **21a** and **22a** in an 82:18 ratio in a good combined yield (Table 2, entry 1). Arylation takes place on the central carbon of the allenic moiety, in the same manner as is described in the previous cyclization of amino allenes.[5,21] The most dominant factor in determining the site of intramolecular amination was found to be the solvent employed. Although its exact role was unclear, dioxane was the solvent of choice for the aziridination of amino allenes. THF can also be used; however, prolonged reaction time is necessary to achieve high

(20) (a) Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Turner, D. *J. Org. Chem.* **1995**, *60*, 2210. (b) Duddu, J.; Eckhardt, M.; Furlong, H.; Knoess, H. P.; Berger, S.; Knochel, P. *Tetrahedron* **1994**, *50*, 2415. (c) Karstens, W. F. J.; Stol, M.; Rutjes, F. P. J. T.; Hiemstra, H. *Synlett*, **1998**, 1126.

(21) In quite limited cases, arylation on the terminal carbon of the allenic moiety, leading to the amination onto the central carbon, was also reported by Hiemstra: Karstens, W. F. J.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett.* **1997**, *38*, 6275. See also, ref 5i.

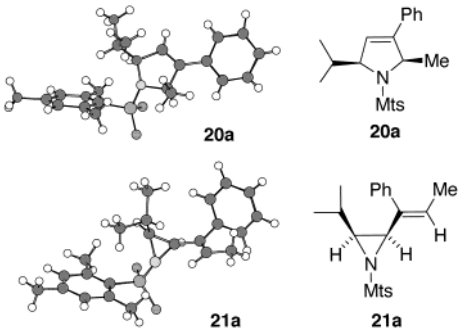
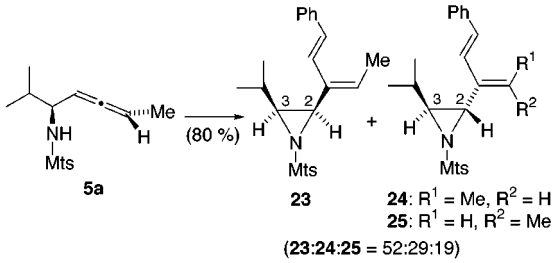


Figure 1. Crystal structures of **20a** and **21a**.

Scheme 6[a]



[a] Reaction conditions: *β*-bromostyrene (4 equiv), $Pd(PPh_3)_4$ (4 mol %), K_2CO_3 (4 equiv), dioxane, reflux, 1 h.

conversion. Although $Pd(PPh_3)_4$ proved to be the most convenient catalyst, $Pd(OAc)_2$/4PPh_3 was equally efficacious (entry 2, Table 2). Similarly, by using *p*-iodotoluene instead of iodobenzene, the expected aziridines **21b** and **22b** were obtained in good yield (entry 3).

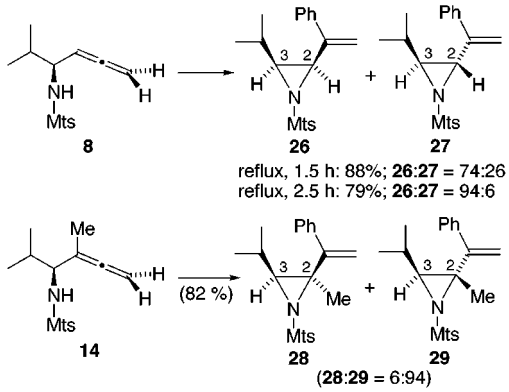
As is revealed from Table 2, while all the (*S*,a*S*)-amino allenes **5** yield the corresponding aziridines (**21** and **22**) exclusively (entries 1−6), allenes **6** with (*S*,a*R*)-configuration afford the desired aziridines (**21** and **22**) along with a small amount of the corresponding pyrroline **20** (entries 7−11). Furthermore, although amino allenes **5** with (*S*,a*S*)-configuration yield the 2,3-*cis*-aziridines **21** predominantly (entries 1−6), the isomeric amino allenes **6** afford 2,3-*trans*-aziridines **22** as major products (entries 7−11). In all cases examined, the relative configuration between the aryl and the methyl group on the double bond in the aziridines is *cis*.

Confirmation of the structure and stereochemistry of the pyrroline **20a** and the alkenylaziridine **21a** was based on single-crystal X-ray data (Figure 1). The constitution of the other aziridines was deduced from ^{1}H NMR spectral data (see the Supporting Information).

Alkenyl halides can be used instead of aryl halides in the present aziridination of amino allenes (Scheme 6). For example, when the (*S*,a*S*)-amino allene **5a** was subjected to palladium-catalyzed cyclization reaction in dioxane in the presence of *β*-bromostyrene, 1,3-dienylaziridines **23**−**25** were obtained as a chromatographically separable mixture in 80% combined yield. However, it should be noted that a small amount of 2,3-*trans*-*Z*-alkenylaziridine **25** was isolated, although such isomers could not be detected in the reaction mixture using aryl halide (Table 2).

Next, cyclization of the terminal allenes **8** and **14** bearing no axial chirality was investigated (Scheme 7). A mixture of the amino allene **8**, $Pd(PPh_3)_4$ (10 mol %), iodobenzene, and K_2CO_3 was heated in dioxane under reflux for 1.5 h affording a separable mixture of 2,3-*cis*-

Scheme 7[a]



[a] Reaction conditions: Ph-I (4 equiv), $Pd(PPh_3)_4$ (10 mol %), K_2CO_3 (4 equiv), dioxane, reflux.

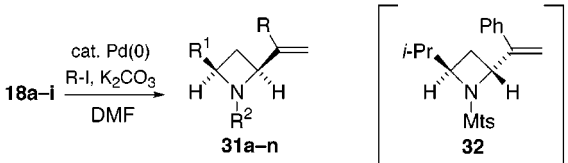
aziridine **26** and 2,3-*trans*-**27** (74:26). Interestingly, prolonged reaction time (2.5 h) raised the stereoselectivity to 94:6, although such effect was hardly observed using internal allenes **5** or **6** (Table 2). These results suggested that the less stable 2,3-*trans*-2-alkenylaziridine **27** was isomerized into the relatively more stable *cis*-isomer **26** under the cyclization conditions (vide infra). This 2,3-*cis*-selectivity is in striking contrast to the formation of related epoxides,[2d,e] in which the *trans*-alkenylepoxides are preferably formed. Interestingly, the terminal amino allene **14** bearing a methyl substituent gave an isomeric mixture of **28** and **29** in which the *trans*-isomer **29** predominated (**28**:**29** = 4:96), presumably due to the thermodynamic control.

Cyclization of *β*-Amino Allenes into Alkenylazetidines. Having established the novel synthetic method of various alkenylaziridines from α-amino allenes, we next proceeded to cyclization of *β*-amino allenes for the synthesis of alkenylazetidines. Considering the results of the palladium-catalyzed cyclization of α-amino allenes, we anticipated that the choice of 1,4-dioxane would also be suitable for the cyclization of *β*-amino allenes. Treatment of the *β*-amino allene **18a** and iodobenzene, K_2CO_3, and catalytic $Pd(PPh_3)_4$ in dioxane yielded an isomeric mixture of 2,4-*cis*- and 2,4-*trans*-3-alkyl-2-alkenylazetidines **31a** and **32** (82:18; Table 3, entry 1), while in DMF, unexpectedly, 2,4-*cis*-isomer **31a** was afforded exclusively (entry 2).

Similar results were obtained using other *β*-amino allenes **18b**, **18c**, **18e**−**i** bearing a variety of alkyl (isobutyl, benzyl, siloxymethyl, or methoxycarbonylethyl group) and *N*-protecting groups (Mts, Ts, Mtr), affording the 2,4-*cis*-4-alkyl-2-alkenylazetidines **31b**, **31c**, **31e**−**i** in good to excellent yields (entries 3, 4 and 6−10). However, the amino allene **18d** bearing a *o*-nitrophenylsulfonyl (*o*-Ns) group yielded a considerable amount of the six-membered ring **33** along with the desired azetidine **31d** (**31d**/**33** = 62:38; entry 5), in analogy with the results reported by Hiemstra: an amino allene bearing a strong electron-withdrawing *p*-nitrophenylsulfonyl (*p*-Ns) group on the nitrogen atom yields a six-membered ring exclusively under similar reaction conditions, while *N*-toluenesulfonylated amino allene gives a four-membered ring predominantly.[7b]

Other aryl- or alkenyl groups such as a 3-nitrophenyl, (*E*)-styryl, or 4-methylphenyl group can also be introduced on the double bond of the alkenylazetidines (entries 11−16).

Table 3. Palladium(0)-Catalyzed Azetidine Synthesis from the β-Amino Allenes[a]

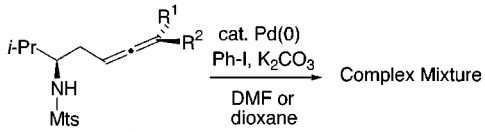


31a: R^1 = *i*-Pr, R^2 = Mts, R = Ph
31b: R^1 = *i*-Bu, R^2 = Mts, R = Ph
31c: R^1 = *i*-Bu, R^2 = Ts, R = Ph
31d: R^1 = *i*-Bu, R^2 = *o*-Ns, R = Ph
31e: R^1 = Bn, R^2 = Mts, R = Ph
31f: R^1 = Bn, R^2 = Ts, R = Ph
31g: R^1 = $TBSOCH_2$, R^2 = Mts, R = Ph
31h: R^1 = $MeO_2C(CH_2)_2$, R^2 = Mts, R = Ph
31i: R^1 = $MeO_2C(CH_2)_2$, R^2 = Mtr, R = Ph
31j: R^1 = *i*-Bu, R^2 = Mts, R = 3-NO_2Ph
31k: R^1 = *i*-Bu, R^2 = Mts, R = (*E*)-CH=CHPh
31l: R^1 = *i*-Bu, R^2 = Ts, R = (*E*)-CH=CHPh
31m: R^1 = $MeO_2C(CH_2)_2$, R^2 = Mts, R = (*E*)-CH=CHPh
31n: R^1 = Bn, R^2 = Mts, R = 4-MePh
31o R^1 = Bn, R^2 = Ts, R = 4-MePh

entry	allene	RI	reaction time (h)	product ratio[b]	yield[c] (%)
1[d]	**18a**	PhI	4	**31a**/**32** = 82:18	91
2	**18a**	PhI	2	**31a** = 100	98
3	**18b**	PhI	3.5	**31b** = 100	84
4	**18c**	PhI	3	**31c** = 100	89
5	**18d**	PhI	0.75	**31d**/**33** = 62:38	87
6	**18e**	PhI	1	**31e** = 100	84
7	**18f**	PhI	1	**31f** = 100	89
8	**18g**	PhI	1.5	**31g** = 100	53
9	**18h**	PhI	1	**31h** = 100	67
10	**18i**	PhI	1.5	**31i** = 100	73
11	**18b**	3-NO_2PhI	1	**31j** = 100	22
12	**18b**	PhCH=CHBr	0.75	**31k** = 100	68
13	**18c**	PhCH=CHBr	0.75	**31l** = 100	81
14	**18h**	PhCH=CHBr	0.5	**31m** = 100	75
15	**18e**	4-MePhI	0.5	**31n** = 100	66
16	**18f**	4-MePhI	1.5	**31o** = 100	81

[a] All reactions were carried out in DMF at 70 °C using $Pd(PPh_3)_4$ (10 mol %), K_2CO_3 (4 equiv) and RI (4 equiv) without otherwise stated. [b] Ratios were determined by ^1H NMR (270 MHz) or isolation. [c] Combined isolated yields. [d] Reaction was conducted in 1,4-dioxane under reflux.

Scheme 8

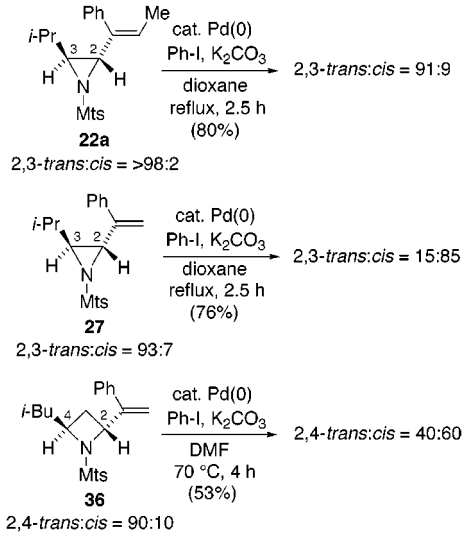


34: R^1 = H, R^2 = Me
35: R^1 = Me, R^2 = H

Stereochemical assignments for the synthesized alkenylazetidines were readily made by NOE experiments (see the Supporting Information).

Unfortunately, as shown in Scheme 8, both isomers of internal β-amino allenes **34** and **35**, prepared from (*S*)-valine (see the Supporting Information), afforded complex mixtures of unidentified products under the palladium-catalyzed cyclization conditions in DMF or dioxane. From the above results, it is found that the cyclization of terminal allenes bearing a protected amino group on the β-position yields alkenylazetidines exclusively by proper choice of the solvent and *N*-protecting group, although internal β-amino allenes are not suitable for palladium-catalyzed cyclization.

Scheme 9



Consideration of the Origin of the Stereoselectivities of the Palladium-Catalyzed Cyclization of Amino Allenes. Finally, we investigated the isomerization reaction of alkenylaziridines and azetidines under palladium-catalyzed cyclization conditions, to obtain some information on the origin of the stereoselectivity of the cyclization of the amino allenes. First, upon exposure of the 2,3-*trans*-2-alkenylaziridine **22a** having a methyl substituent on the double bond to the cyclization conditions, isomerization was observed only to a small extent (Scheme 9). In contrast, the *trans*-aziridine **27** lacking a methyl substituent was easily isomerized into the corresponding 2,3-*cis*-isomer under the identical reaction conditions (*cis*/*trans* = 85:15).

Our previous studies on the alkenylaziridines revealed that 2,3-*cis*-2-alkenylaziridines are relatively more stable than their 2,3-*trans*-isomers, and that 2,3-*trans*-isomers can be easily isomerized into their *cis*-isomers upon treatment with palladium(0), via η^3-allylpalladium(II) intermediates.[14b,14c,22] Considering the results shown in Scheme 9, the aziridine **27** is assumed to be reactive enough toward palladium(0) to undergo equilibration even in the presence of iodobenzene. However, since the reactivity of **22a** would be significantly low, presumably due to steric hindrance, palladium(0) reacts with iodobenzene preferably than with **22a**, to form phenylpalladium(II) iodide. Accordingly, the stereoselective formation of alkenylaziridines **22** and **23** bearing a methyl substituent (Table 2) would be controlled kinetically (vide infra), while the 2,3-*cis*-selective formation of **26** (Scheme 7) would be thermodynamically controlled.

A plausible rationale for the stereoselectivities of the aziridination reaction of internal amino allenes is depicted in Figure 2.[23] The phenylpalladium(II) iodide (**37**), formed in situ from iodobenzene and Pd(0), would generate η^3-allylpalladium complexes by the reaction with (*S*,a*S*)-**5** approaching from the less hindered face. Predominant formation of the complex **A** (path A) over **B** (path B) can be expected due to the relatively small steric repulsion of **37** with a methyl group than with an aminomethyl group (R_L). The *cis*-*E*-alkenylaziridine **21**

(22) Ohno, H.; Toda, A.; Fujii, N.; Miwa, Y.; Taga, T.; Yamaoka, Y.; Osawa, E.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 1331.
(23) For another possible mechanism for palladium-catalyzed intramolecular amination, see refs 5d, 5e, and 21.

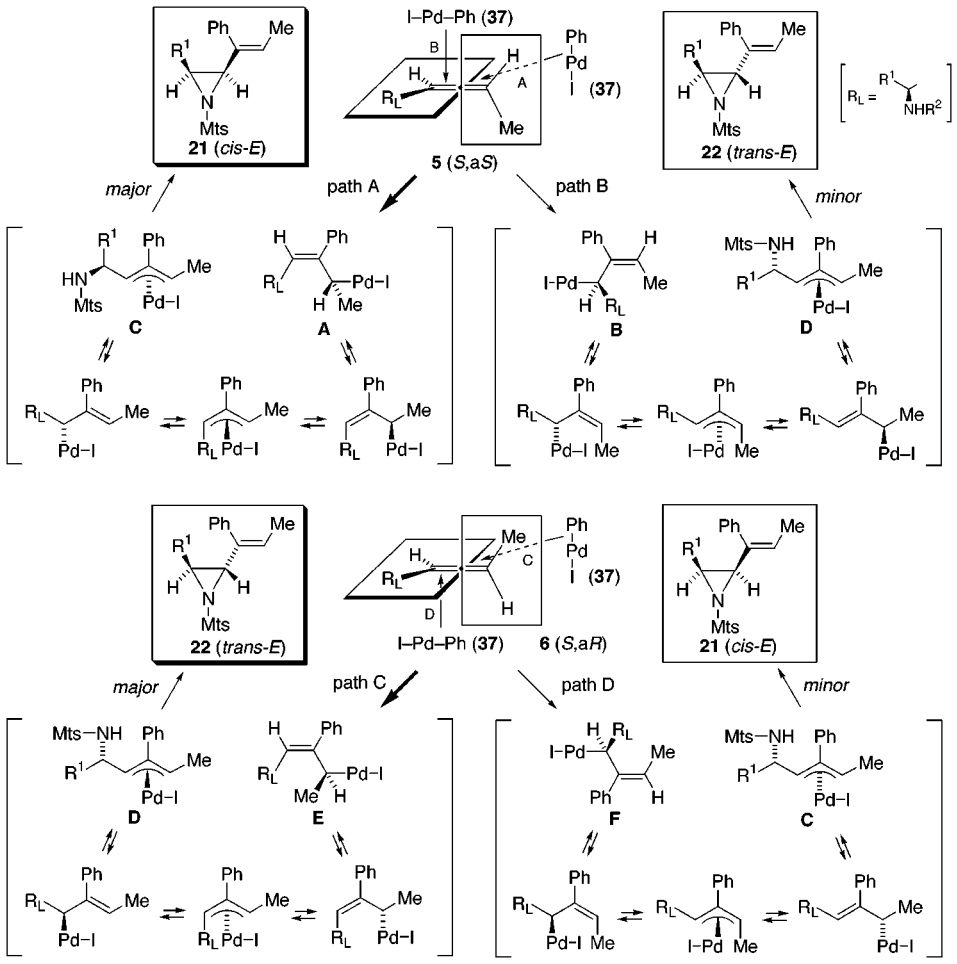


Figure 2. One plausible rationale for the stereoselective aziridination of (*S*,a*S*)-**5** and (*S*,a*R*)-**6**.

would be formed as a main product by the intramolecular nucleophilic attack of the nitrogen onto the stable *syn*-η^3-allylpalladium complex **C** derived from **A**[24] via $\sigma-\pi-\sigma$ mechanism, reproducing palladium(0). Formation of the minor *cis*-*E*-alkenylaziridine **22** can be rationalized by path B, in that the allylpalladium complex **B** is isomerized into the stable **D**, followed by cyclization (path B). Similarly, the predominant formation of the *trans*-*E*-alkenylaziridine **22** from (*S*,a*R*)-**6** can be explained by preferable complexation of **37** from the less hindered side of **6**, isomerization of the allylpalladium intermediate **E** into **D**, and aziridination (path C). As described above, the significant effect of the solvent on the regioselectivity of the reaction was not rationalized at the present stage of our understandings.

Figure 3 shows a plausible pathway for the preferable formation of 2,4-*cis*-2-alkenylazetidine **31** over its 2,4-*trans* isomer **32** (Table 3). The two π-allylpalladium complexes **G** and **I**, which would be generated by the reaction of β-amino allene **18** and phenylpalladium(II) iodide, are expected to be interconvertible via a $\pi-\sigma-\pi$-mechanism. Since unfavorable steric interaction between the arylsulfonyl and allyl groups (in **K**) or arylsulfonyl and R^1 groups (in **L**) would destabilize these conformers, predominant formation of 2,4-*cis*-azetidine **31** via the

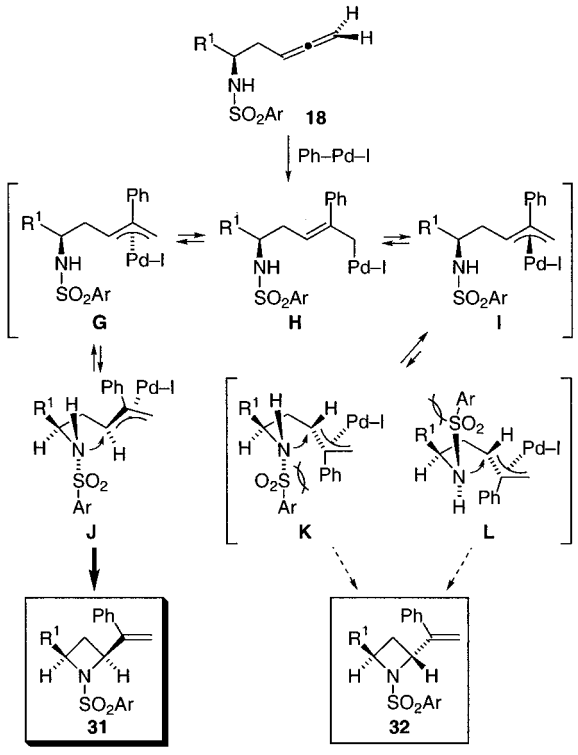


Figure 3. Palladium-catalyzed stereoselective formation of 2,4-*cis*-azetidine **31** from β-amino allene **18**.

(24) It is known that *syn*-η^3-allylpalladium complexes are relatively more stable than other isomers, even if the central carbon of the allyl group is substituted by an aryl group. For example, see ref 1c.

conformer **J** is readily understood.[25] In addition, the predominant formation of 2,4-*cis*-azetidines would also be influenced by palladium(0)-catalyzed equilibration, as can be seen in the isomerization reaction of **36** (Scheme 9).

Conclusion

The described procedures provide reliable methodology for the intramolecular amination of *N*-protected amino allenes to the corresponding alkenylaziridines and alkenylazetidines bearing an aryl or alkenyl group on the double bond. Whereas palladium-catalyzed reaction of (*S*,a*S*)-*N*-arylsulfonyl-2,3-dienylamines (α-amino allenes) with an aryl iodine in the presence of potassium carbonate in refluxing 1,4-dioxane yields 2,3-*cis*-*E*-2-alkenylaziridines bearing an aryl group on the double bond predominantly, reaction of (*S*,a*R*)-2,3-dienylamines affords 2,3-*trans*-*E*-isomers preferably. In contrast, palladium-catalyzed cyclization of *N*-arylsulfonyl-3,4-dienylamines (*β*-amino allenes) in DMF gives 2,4-*cis*-2-alkenylazetidines exclusively, although a small amount of 2,4-*trans*-isomers is formed when 1,4-dioxane is used as the solvent. As far as we are aware, this is the first report detailing the palladium-catalyzed cyclization of amino allenes into three-membered azacycles.

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.

(3*S*)-1,1-Dibromo-3-[*N*-(*tert*-butoxycarbonyl)amino]-4-methylpent-1-ene (10). To a stirred solution of oxalyl chloride (3.49 mL, 36.4 mmol) in CH_2Cl_2 (60 mL) at −78 °C under argon was added dropwise a solution of DMSO (9.93 mL, 140 mmol) in CH_2Cl_2 (10 mL). After 30 min, a solution of the alcohol **9a** (5.69 g, 28 mmol) in CH_2Cl_2 (15 mL) was added to the above reagent at −78 °C, and the mixture was stirred for 1 h. Diisopropylethylamine (34.3 mL, 196 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 saturated citric acid and the whole was extracted with Et_2O. The extract was washed successively with water, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Concentration under reduced pressure gave a crude aldehyde. To a stirred solution of CBr_4 (18.6 g, 56 mmol) in CH_2Cl_2 (100 mL) was added PPh_3 (29.4 g, 112 mmol) at 0 °C, and the mixture was stirred at this temperature for 20 min. To the stirred mixture was added Et_3N (4.26 mL, 30.8 mmol) at 0 °C and the stirring was continued for 10 min. The crude aldehyde in CH_2Cl_2 was added dropwise to the above reagent at −78 °C with stirring, and the mixture was stirred for 2 h with warming to 0 °C. *n*-Hexane (300 mL) was added to the mixture, and insoluble materials were removed by filtration. Concentration under reduced pressure gave an oily residue, which was purified by flash chromatography over silica gel with *n*-hexane−EtOAc (10:1) to give **10** (5.26 g, 53% yield) as colorless needles from *n*-hexane: mp 81 °C; $[\alpha]^{27}_D$ +29.6 (*c* 1.63, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) *δ* 0.95 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 1.45 (s, 9H), 1.77−1.90 (m, 1H), 4.12 (br s, 1H), 4.55 (br s, 1H), 6.30 (d, *J* = 9.2 Hz, 1H). Anal. Calcd for $C_{11}H_{19}Br_2NO_2$: C, 37.00; H, 5.36; N, 3.92. Found: C, 37.08; H, 5.31; N, 3.62.

(4*S*)-4-[*N*-(*tert*-Butoxycarbonyl)amino]-5-methylhex-2-yn-1-ol (11). To a stirred solution of the dibromoalkene **10** (3.07 g, 8.6 mmol) in THF (17 mL) under argon was added dropwise *n*-BuLi (1.53 M in *n*-hexane; 16.9 mL, 25.8 mmol) at −78 °C. After 20 min, DMF (1.32 mL, 17.2 mmol) in THF (3 mL) was added dropwise at −78 °C and the mixture was stirred for 1 h with warming to 0 °C. Saturated citric acid (5 mL) was added to the mixture at 0 °C and stirring was continued for 10 min with warming to room temperature. Concentration under reduced pressure gave an oily residue, which was extracted with Et_2O. The extract was washed with water, and dried over $MgSO_4$. Usual workup gave a crude aldehyde. To a stirred solution of the crude aldehyde in EtOH (10 mL) was added $NaBH_4$ (325 mg, 8.6 mmol) at 0 °C and the mixture was stirred for 10 min at this temperature. The mixture was made acidic with citric acid, concentrated, and extracted with a mixed solvent of Et_2O−EtOAc (3:1). The extract was washed with water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (3:1) gave **11** (1.50 g, 77% yield) as a colorless oil: $[\alpha]^{21}_D$ −70.7 (*c* 1.08, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) *δ* 0.98 (d, *J* = 6.8 Hz, 6H), 1.45 (s, 9H), 1.82−1.95 (m, 2H), 4.27−4.38 (m, 3H), 4.70−4.78 (m, 1H); MS (FAB) *m*/*z* 228 (MH^+), 172 (base peak), 154, 128, 57; HRMS (FAB) calcd for $C_{12}H_{22}NO_3$ (MH^+) 228.1600, found 228.1596.

(4*S*)-4-[*N*-(*tert*-Butoxycarbonyl)amino]-5-methyl-*O*-methanesulfonylhex-2-yn-1-ol (12). To a stirred mixture of the alcohol **11** (750 mg, 3.3 mmol) and Et_3N (2.28 mL, 16.5 mmol) in THF (7 mL) was added dropwise methanesulfonyl chloride (0.767 mL, 9.9 mmol) at −78 °C. The mixture was stirred for 30 min with warming to 0 °C. Saturated $NaHCO_3$ (2 mL) was added at −78 °C, and stirring was continued vigorously for 30 min at room temperature. The whole was extracted with Et_2O, and the extract was washed successively with saturated citric acid, water, saturated $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (3:1) gave **12** (744 mg, 74% yield) as a colorless oil: $[\alpha]^{27}_D$ −61.5 (*c* 0.81, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) *δ* 0.99 (d, *J* = 7.0 Hz, 6H), 1.45 (s, 9H), 1.85−1.97 (m, 1H), 3.12 (s, 3H), 4.32−4.41 (m, 1H), 4.70−4.77 (m, 1H), 4.87−4.88 (m, 2H); MS (FAB) *m*/*z* 306 (MH^+), 250 (base peak), 206, 154, 110, 93, 57; HRMS (FAB) calcd $C_{13}H_{24}NO_5S$ (MH^+) 306.1375, found 306.1387.

(4*S*)-4-[*N*-(*tert*-Butoxycarbonyl)amino]-3,5-dimethylhexa-1,2-diene (13). To a stirred solution of CuCN (823 mg, 9.2 mmol) and LiCl (778 mg, 18.4 mmol) in dry THF (10 mL) under argon was added by syringe MeLi (1.14 M in Et_2O; 8.07 mL, 9.2 mmol) at −78 °C, and the mixture was stirred for 10 min with warming to 0 °C. The mesylate **12** (702 mg, 2.3 mmol) in dry THF (4 mL) was added to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with a solution of 1:1 saturated NH_4Cl−28% NH_4OH (10 mL). The mixture 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 *n*-hexane−EtOAc (15:1) gave **13** (509 mg, 98% yield) as colorless crystals from cold *n*-hexane: mp 31 °C; $[\alpha]^{26}_D$ −67.9 (*c* 0.95, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) *δ* 0.86 (d, *J* = 7.0 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 1.45 (s, 9H), 1.69 (t, *J* = 3.0 Hz, 3H), 1.82−1.93 (m, 1H), 3.84 (br s, 1H), 4.48−4.57 (m, 1H), 4.68−4.78 (m, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$) *δ* 16.9, 17.1, 22.2, 28.6, 30.5, 57.7, 76.6, 79.3, 100.3, 156.1, 205.9; MS (FAB) *m*/*z* 226 (MH^+), 170 (base peak), 169, 126, 116, 109, 57; HRMS (FAB) calcd $C_{13}H_{24}NO_2$ (MH^+) 226.1807, found 226.1809.

(4*S*)-3,5-Dimethyl-4-[*N*-(2,4,6-trimethylphenylsulfonyl)-amino]hexa-1,2-diene (14). Trifluoroacetic acid (1 mL) was added to **13** (253 mg, 1.12 mmol) at room temperature with stirring, and the mixture was stirred for 30 min at this

(25) Formation of aza-anionic planar intermediates cannot be ruled out. However, these planar intermediates would not explain the observed 2,4-*cis*-selective azetidine formation since there would be no unfavorable steric interaction in such intermediates leading to the 2,4-*trans*-azetidines. As shown in Figure 1 (X-ray), a nitrogen of the sulfonamide group has a tetrahedral geometry. Accordingly, if the anionic intermediate is formed, it will be cyclized into the azetidine via a nonplanar transition state similar to **J**, **K**, and **L**.

temperature. Concentration under reduced pressure gave a residual oil, which was dissolved in $CHCl_3$ (1 mL). To the above solution, Et_3N (1 mL) and 2,4,6-trimethylphenylsulfonyl chloride (295 mg, 1.35 mmol) were added at 0 °C, and the mixture was stirred for 1.5 h at room temperature. Saturated $NaHCO_3$ (0.5 mL) was added to the mixture with vigorous stirring, and stirring was continued for 30 min at room temperature. The whole was extracted with Et_2O, and the extract was washed successively with saturated citric acid, water, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (10:1) gave **14** (261 mg, 76% yield) as colorless needles from *n*-hexane: mp 128 °C; $[\alpha]^{30}_D$ −14.6 (*c* 0.99, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.83 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 6.5 Hz, 3H), 1.47 (t, J = 3.2 Hz, 3H), 1.71−1.83 (m, 1H), 2.29 (s, 3H), 2.63 (s, 6H), 3.36−3.42 (m, 1H), 4.53−4.57 (m, 2H), 4.66 (d, J = 9.2 Hz, 1H), 6.93 (s, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 16.0, 17.8, 19.8, 21.1, 23.4, 31.3, 61.7, 77.1, 99.1, 132.0, 135.0, 139.0, 142.0, 205.9. Anal. Calcd for $C_{17}H_{25}NO_2S$: C, 66.41; H, 8.20; N, 4.56. Found: C, 66.34; H, 7.97; N, 4.34.

General Procedure for Synthesis of the Tosylates (15) from (9). Synthesis of (2*S*)-2-[*N*-(*tert*-Butoxycarbonyl)-amino]-3-methyl-*O*-(4-methylphenylsulfonyl)butan-1-ol (15a). To a stirred solution of the alcohol **9a** (2.03 g, 10 mmol) and Et_3N (5.0 mL, 36 mmol) in THF (15 mL) were added *p*-toluenesulfonyl chloride (2.28 g, 12 mmol) at room temperature, and the mixture was stirred for 48 h at this temperature. Saturated $NaHCO_3$ was added to the mixture, and the whole was extracted with Et_2O. The extract was washed successively with saturated citric acid, water, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup gave a crystalline mass, which was recrystallized from *n*-hexane−Et_2O (2:1) to give **15a** (2.9 g, 81% yield) as colorless crystals: mp 74 °C; $[\alpha]^{10}_D$ −26.7 (*c* 1.25, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H), 1.41 (s, 9H), 1.73−1.88 (m, 1H), 2.45 (s, 3H), 3.45−3.55 (m, 1H), 4.01 (dd, J = 10.0, 3.5 Hz, 1H), 4.08 (dd, J = 10.0, 3.5 Hz, 1H), 4.60 (d, J = 8.9 Hz, 1H), 7.34−7.37 (m, 2H), 7.77−7.80 (m, 2H). Anal. Calcd for $C_{17}H_{27}NO_5S$: C, 57.12; H, 7.61; N, 3.92. Found: C, 56.96; H, 7.57; N, 3.67.

General Procedure for Synthesis of the Iodides (16) from (15). Synthesis of (2*S*)-2-[*N*-(*tert*-Butoxycarbonyl)-amino]-1-iodo-3-methylbutane (16a). To a stirred solution of the tosylate **15a** (14.5 g, 40.6 mmol) in Me_2CO (100 mL) was added NaI (12.2 g, 81.2 mmol) at room temperature, and the mixture was stirred in the dark at this temperature for 24 h. Concentration under reduced pressure gave a crystalline residue. Water was added and the whole was extracted with Et_2O. The extract was washed with water and dried over $MgSO_4$. Usual workup gave a crystalline mass, which was recrystallized from cold *n*-hexane to give **16a** (6.28 g, 42% yield) as colorless crystals: mp 68 °C; $[\alpha]^{28}_D$ −24.1 (*c* 1.12, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H), 1.45 (s, 9H), 1.70−1.84 (m, 1H), 3.06−3.16 (m, 1H), 3.33 (dd, J = 10.3, 4.3 Hz, 1H), 3.41 (dd, J = 10.3, 4.3 Hz, 1H), 3.57 (d, J = 8.9 Hz, 1H). Anal. Calcd for $C_{10}H_{20}INO_2$: C, 38.35; H, 6.44; N, 4.47. Found: C, 38.42; H, 6.22; N, 4.53.

General Procedure for Synthesis of β-Amino Allenes (17) from (16). Synthesis of (5*R*)-5-[*N*-(*tert*-Butoxycarbonyl)amino]-6-methylhepta-1,2-diene (17a). Zinc powder (5.23 g, 80 mmol) was washed successively with 0.1 N HCl (3 × 4 mL), EtOH (3 × 4 mL), and Et_2O (3 × 4 mL), and was dried by heating under reduced pressure at 120 °C for 2 h. Dry DMF (4 mL) and 1,2-dibromoethane (0.2 mL, 1.6 mmol) was added at room temperature. After exothermic reaction was completed, the mixture was stirred for 5 min at 60 °C. After cooling, TMSCl (0.2 mL, 1.6 mmol) was added to the mixture at room temperature, and the mixture was sonicated at this temperature for 30 min. The zinc was allowed to settle and the supernatant was removed by syringe. Dry DMF (5 mL) was added and the iodide **16a** (3.13 g, 10 mmol) in dry DMF (8 mL) was added at 0 °C with stirring, and the mixture was stirred for 30 min at this temperature. A solution of CuCN (200 mg, 2.2 mmol) and LiCl (190 mg, 4.4 mmol) in dry THF (5 mL) was added to the mixture at −78 °C, and stirring was continued for 10 min. Propargyl tosylate (2.91 g, 15 mmol) in dry THF (3 mL) was added to the above stirring reagent at −78 °C, and the mixture was stirred for 30 min with warming to 0 °C and an additional 30 min at 0 °C. The mixture was quenched with NH_4Cl and the whole was extracted with Et_2O. The extract was washed successively with saturated citric acid, water, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) gave **17a** (1.5 g, 67% yield) as a colorless oil: $[\alpha]^{15}_D$ −55.4 (*c* 1.03, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.89 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H), 1.44 (s, 9H), 1.75−1.80 (m, 1H), 2.04−2.10 (m, 1H), 2.19−2.25 (m, 1H), 3.47−3.53 (m, 1H), 4.35−4.40 (m, 1H), 4.67 (ddd, J = 7.0, 2.7, 2.7 Hz, 2H), 5.05 (tdd, J = 7.0, 7.0, 7.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 17.7, 19.3, 28.4, 31.4, 31.9, 55.5, 74.5, 86.4, 155.8, 209.5. MS (FAB) *m*/*z* 226 (MH^+), 170 (base peak), 130, 116; HRMS (FAB) calcd $C_{13}H_{24}NO_2$ (MH^+) 226.1807, found 226.1797.

General Procedure for Synthesis of (18) from (17). (5*R*)-6-Methyl-5-[*N*-(2,4,6-trimethylphenylsulfonyl)amino]-hepta-1,2-diene (18a). Trifluoroacetic acid (3 mL) was added to **17a** (1.4 g, 6.22 mmol) at room temperature with stirring, and the mixture was stirred for 4 h at this temperature. Concentration under reduced pressure gave a residual oil, which was dissolved in $CHCl_3$ (2 mL). To the above solution, Et_3N (4 mL) and 2,4,6-trimethylphenylsulfonyl chloride (1.5 g, 6.84 mmol) were added at 0 °C, and the mixture was stirred for 3 h at room temperature. Saturated $NaHCO_3$ was added to the mixture with vigorous stirring, and stirring was continued for 10 min at room temperature. The whole was extracted with Et_2O, and the extract was washed successively with saturated citric acid, water, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (4:1) gave **18a** as a crystalline mass, which was recrystallized from *n*-hexane to give pure **18a** (400 mg, 21% yield) as colorless crystals: mp 99 °C; $[\alpha]^{23}_D$ −68.0 (*c* 0.63, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.78 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 6.8 Hz, 3H), 1.79−1.90 (m, 1H), 2.04−2.11 (m, 2H), 2.30 (s, 3H), 2.64 (s, 6H), 3.07 (dddd, J = 8.4, 5.9, 5.9, 5.9 Hz, 1H), 4.47 (d, J = 8.4 Hz, 1H), 4.63 (ddd, J = 6.8, 2.8, 2.8 Hz, 2H), 4.80 (tdd, J = 6.8, 6.8, 6.8 Hz, 1H), 6.94 (s, 2H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 18.1, 18.8, 21.1, 23.4, 30.9, 31.4, 59.0, 73.5, 85.5, 132.1, 135.0, 138.9, 142.1, 209.7. Anal. Calcd for $C_{17}H_{25}NO_2S$: C, 66.41; H, 8.20; N, 4.56. Found: C, 66.25; H, 8.47; N, 4.56.

(2*S*,5*S*)-5-Isopropyl-2-methyl-*N*-(2,4,6-trimethylphenylsulfonyl)-3-phenyl-3-pyrroline (19a). To a stirred mixture of the amino allene **5a** (46.1 mg, 0.15 mmol), $Pd(PPh_3)_4$ (6.9 mg, 0.006 mmol; 4 mol %), and K_2CO_3 (82.8 mg, 0.6 mmol) in DMF (1 mL) under argon was added PhI (0.0673 mL, 0.6 mmol), and the mixture was heated at 70 °C for 4 h. Water (2 mL) was added to the mixture, and the whole was extracted with Et_2O. The extract was washed with water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (9:1) gave **19a** (23 mg, 40% yield). Colorless oil: $[\alpha]^{27}_D$ +226 (*c* 0.92, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.51 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 7.0 Hz, 3H), 1.34 (d, J = 6.2 Hz, 3H), 1.99−2.10 (m, 1H), 2.29 (s, 3H), 2.69 (s, 6H), 4.74 (ddd, J = 5.0, 3.4, 2.0 Hz, 1H), 5.13−5.21 (m, 1H), 5.88 (dd, J = 2.0, 1.4 Hz, 1H), 6.93 (m, 2H), 7.27−7.37 (m, 5H); MS (FAB) *m*/*z* 384 (MH^+), 382, 341, 340 (base peak), 200, 158, 119; HRMS (FAB) calcd $C_{23}H_{30}NO_2S$ (MH^+) 384.1997, found 384.1991.

General Procedure for Palladium(0)-Catalyzed Cyclization of Amino Allenes in 1,4-Dioxane. Synthesis of (4*R*,5*S*,2*E*)-4,5-Epimino-6-methyl-*N*-(2,4,6-trimethylphenylsulfonyl)-3-phenylhept-2-ene (21a) and Its (4*S*,5*S*,2*E*)-Isomer (22a) from the Amino Allene (5a) (Entry 1 in Table 2). To a stirred mixture of the amino allene **5a** (23.1 mg, 0.075 mmol), $Pd(PPh_3)_4$ (8.7 mg, 0.0075 mmol; 10 mol %), and K_2CO_3 (41.4 mg, 0.3 mmol) in 1,4-dioxane (1 mL) under argon was added PhI (0.0336 mL, 0.3 mmol), and the mixture was heated under reflux for 6 h. Water (1 mL) was

added to the mixture, and the whole was extracted with Et_2O. The extract was washed with water and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (15:1) gave, in order of elution, 2,3-*trans*-aziridine **22a** (4.1 mg, 14% yield) and 2,3-*cis*-aziridine **21a** (18.9 mg, 65% yield). Compound **21a**: colorless crystals from *n*-hexane; mp 82 °C; $[\alpha]^{28}_D$ −39.2 (*c* 0.40, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.67 (d, J = 6.3 Hz, 3H), 0.70 (d, J = 6.4 Hz, 3H), 1.35−1.47 (m, 1H), 1.64 (dd, J = 7.1, 1.3 Hz, 3H), 2.31 (s, 3H), 2.50 (dd, J = 9.8, 7.1 Hz, 1H), 2.74 (s, 6H), 3.71 (ddq, J = 7.1, 1.3, 1.3 Hz, 1H), 5.82 (qd, J = 7.1, 1.3 Hz, 1H), 6.95−6.96 (m, 2H), 7.13−7.17 (m, 2H), 7.22−7.35 (m, 3H). Anal. Calcd for $C_{23}H_{29}NO_2S$: C, 72.03; H, 7.62; N, 3.65. Found: C, 72.11; H, 7.82; N, 3.46. Compound **22a**: colorless oil; $[\alpha]^{29}_D$ +25.8 (*c* 1.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (d, J = 6.7 Hz, 3H), 1.14 (d, J = 6.4 Hz, 3H), 1.43 (dd, J = 7.0, 0.9 Hz, 3H), 2.20−2.29 (m, 1H), 2.30 (s, 3H), 2.34 (dd, J = 9.8, 4.3 Hz, 1H), 2.64 (s, 6H), 3.44 (ddd, J = 4.3, 0.9, 0.6 Hz, 1H), 5.70 (qd, J = 7.0, 0.6 Hz, 1H), 6.80−6.84 (m, 2H), 6.91 (s, 2H), 7.18−7.21 (m, 3H); MS (FAB) *m*/*z* 384 (MH^+), 201, 200 (base peak), 185, 158, 119, 91, 73; HRMS (FAB) calcd $C_{23}H_{30}NO_2S$ (MH^+) 384.1997, found 384.1991.

(4*R*,5*S*,2*E*)-4,5-Epimino-6-methyl-3-(4-methylphenyl)-*N*-(2,4,6-trimethylphenylsulfonyl)hept-2-ene (21b) and Its (4*S*,5*S*,2*E*)-Isomer (22b) (Entry 3 in Table 2). By a procedure identical with that described for the aziridination of **5a** with PhI, the amino allene **5a** (500 mg, 1.63 mmol) was converted into **21b** (376 mg, 58% yield) and **22b** (35 mg, 6% yield) by treatment with $Pd(PPh_3)_4$ (188 mg, 0.163 mmol; 10 mol %), K_2CO_3 (900 mg, 6.52 mmol), and 4-iodotoluene (1.42 g, 6.52 mmol) in 1,4-dioxane under reflux for 6 h. Compound **21b**: colorless crystals from *n*-hexane; mp 85−87 °C; $[\alpha]^{27}_D$ −36.8 (*c* 0.95, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.67 (d, J = 6.5 Hz, 3H), 0.70 (d, J = 6.2 Hz, 3H), 1.34−1.48 (m, 1H), 1.63 (dd, J = 7.3, 1.1 Hz, 3H), 2.31 (s, 3H), 2.35 (s, 3H), 2.50 (dd, J = 9.7, 7.3 Hz, 1H), 2.74 (s, 6H), 3.68−3.71 (m, 1H), 5.79 (qd, J = 7.3, 1.1 Hz, 1H), 6.96 (s, 2H), 7.04−7.15 (m, 4H). Anal. Calcd for $C_{24}H_{31}NO_2S$: C, 72.51; H, 7.86; N, 3.52. Found: C, 72.22; H, 7.99; N, 3.42. Compound **22b**: colorless oil; $[\alpha]^{27}_D$ +37.1 (*c* 0.65, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.00 (d, J = 6.8 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H), 1.43 (d, J = 7.0 Hz, 3H), 2.18−2.29 (m, 1H), 2.30 (s, 6H), 2.35 (dd, J = 9.5, 4.3 Hz, 1H), 2.64 (s, 6H), 3.43 (d, J = 4.3 Hz, 1H), 5.68 (q, J = 7.0 Hz, 1H), 6.70−6.73 (m, 2H), 6.91 (s, 2H), 6.99−7.02 (m, 2H); MS (FAB) *m*/*z* 398 (MH^+), 215, 214 (base peak), 200, 199, 172, 157, 119; HRMS (FAB) calcd $C_{24}H_{32}NO_2S$ (MH^+) 398.2154, found 398.2154.

(4*R*,5*S*,2*E*)-4,5-Epimino-*N*-(2,4,6-trimethylphenylsulfonyl)-3,6-diphenylhex-2-ene (21c) and Its (4*S*,5*S*,2*E*)-Isomer (22c) (Entry 4 in Table 2). By a procedure identical with that described for the aziridination of **5a**, the amino allene **5b** (107 mg, 0.3 mmol) was converted into **21c** (87 mg, 67% yield) and **22c** (15 mg, 12% yield) by treatment with $Pd(PPh_3)_4$ (13.9 mg, 0.012 mmol; 4 mol %), K_2CO_3 (166 mg, 1.2 mmol), and PhI (0.135 mL, 1.2 mmol) in 1,4-dioxane under reflux for 4.5 h. Compound **21c**: colorless oil; $[\alpha]^{31}_D$ −98.6 (*c* 0.69, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.73 (dd, J = 7.3, 1.4 Hz, 3H), 2.29 (s, 3H), 2.53 (dd, J = 14.3, 8.9 Hz, 1H), 2.57 (s, 6H), 2.70 (dd, J = 14.3, 4.9 Hz, 1H), 3.06 (ddd, J = 8.9, 6.8, 4.9 Hz, 1H), 3.74 (ddd, J = 6.8, 1.4, 1.1 Hz, 1H), 6.05 (qd, J = 7.3, 1.1 Hz, 1H), 6.81−7.36 (m, 12H); MS (FAB) *m*/*z* 432 (MH^+), 249, 248 (base peak), 233, 158, 156, 119, 91; HRMS (FAB) calcd $C_{27}H_{30}NO_2S$ (MH^+) 432.1997, found 432.1989. Compound **22c**: colorless oil; $[\alpha]^{28}_D$ +61.2 (*c* 1.15, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.42 (d, J = 6.8 Hz, 3H), 2.32 (s, 3H), 2.66 (s, 6H), 2.75 (ddd, J = 10.3, 3.8, 3.8 Hz, 1H), 3.26 (dd, J = 14.3, 10.3 Hz, 1H), 3.50 (dd, J = 14.3, 3.8 Hz, 1H), 3.66 (d, J = 3.8 Hz, 1H), 5.66 (q, J = 6.8 Hz, 1H), 6.69−6.72 (m, 2H), 6.94 (s, 2H), 7.08−7.29 (m, 8H); MS (FAB) *m*/*z* 432 (MH^+), 249, 248, 233, 221, 207, 158, 147, 119, 91, 73 (base peak), 55; HRMS (FAB) calcd $C_{27}H_{30}NO_2S$ (MH^+) 432.1997, found 432.2004.

(4*R*,5*S*,2*E*)-4,5-Epimino-*N*-(4-methoxy-2,3,6-trimethylphenylsulfonyl)-3,6-diphenylhex-2-ene (21d) and Its (4*S*,5*S*,2*E*)-Isomer (22d) (Entry 5 in Table 2). By a procedure identical with that described for the aziridination of **5a**, the amino allene **5c** (116 mg, 0.3 mmol) was converted into **21d** (88 mg, 63% yield) and **22d** (22 mg, 16% yield) by treatment with $Pd(PPh_3)_4$ (13.9 mg, 0.012 mmol; 4 mol %), K_2CO_3 (166 mg, 1.2 mmol), and PhI (0.135 mL, 1.2 mmol) in 1,4-dioxane under reflux for 4 h. Compound **21d**: colorless needles from *n*-hexane−Et_2O (3:1); mp 94 °C; $[\alpha]^{30}_D$ −120 (*c* 0.66, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.74 (dd, J = 7.3, 1.4 Hz, 3H), 2.09 (s, 3H), 2.51 (dd, J = 14.3, 9.2 Hz, 1H), 2.52 (s, 3H), 2.57 (s, 3H), 2.72 (dd, J = 14.3, 4.3 Hz, 1H), 3.04 (ddd, J = 9.2, 7.0, 4.3 Hz, 1H), 3.75 (ddd, J = 7.0, 1.4, 1.4 Hz, 1H), 3.86 (s, 3H), 6.08 (qd, J = 7.3, 1.4 Hz, 1H), 6.41 (s, 1H), 6.83−7.02 (m, 5H), 7.17−7.39 (m, 5H). Anal. Calcd for $C_{28}H_{31}NO_3S$: C, 72.85; H, 6.77; N, 3.03. Found: C, 72.69; H, 6.76; N, 2.97. Compound **22d**: colorless oil; $[\alpha]^{29}_D$ +56.0 (*c* 0.68, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.43 (d, J = 7.0 Hz, 3H), 2.16 (s, 3H), 2.62 (s, 3H), 2.66 (s, 3H), 2.75 (ddd, J = 10.0, 4.3, 4.1 Hz, 1H), 3.27 (dd, J = 14.3, 10.0 Hz, 1H), 3.48 (dd, J = 14.3, 4.1 Hz, 1H), 3.67 (d, J = 4.3 Hz, 1H), 3.88 (s, 3H), 5.69 (q, J = 7.0 Hz, 1H), 6.55 (s, 1H), 6.71−6.76 (m, 2H), 7.08−7.32 (m, 8 H); MS (FAB) *m*/*z* 462 (MH^+), 247, 246 (base peak), 213, 158, 149, 119, 91; HRMS (FAB) calcd $C_{28}H_{32}NO_3S$ (MH^+) 462.2103, found 462.2110.

(4*R*,5*R*,2*E*)-6-(*tert*-Butyldimethylsiloxy)-4,5-epimino-*N*-(2,4,6-trimethylphenylsulfonyl)-3-phenylhept-2-ene (21e) and Its (4*S*,5*R*,2*E*)-Isomer (22e) (Entry 6 in Table 2). By a procedure identical with that described for the aziridination of **5a**, the amino allene **5d** (41 mg, 0.1 mmol) was converted into **21e** (26 mg, 54% yield) and **22e** (10 mg, 21% yield) by treatment with $Pd(PPh_3)_4$ (23.1 mg, 0.02 mmol; 20 mol %), K_2CO_3 (55.2 mg, 0.4 mmol), and PhI (0.0443 mL, 0.4 mmol) in 1,4-dioxane under reflux for 1.2 h. Compound **21e**: colorless oil; $[\alpha]^{27}_D$ −62.4 (*c* 0.67, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.10 (s, 6H), 0.79 (s, 9H), 1.65 (dd, J = 7.3, 1.4 Hz, 3H), 2.31 (s, 3H), 2.70 (s, 6H), 3.08 (ddd, J = 7.3, 6.2, 6.2 Hz, 1H), 3.53−3.56 (m, 2H), 3.62 (ddq, J = 7.3, 1.4, 1.4 Hz, 1H), 5.85 (qd, J = 7.3, 1.4 Hz, 1H), 6.95 (s, 2H), 7.17−7.34 (m, 5H); MS (FAB) *m*/*z* 486 (MH^+), 428, 303, 302, 170, 158, 119, 89, 75, 73 (base peak); HRMS (FAB) calcd $C_{27}H_{40}NO_3SSi$ (MH^+) 486.2498, found 486.2490. Compound **22e**: colorless oil; $[\alpha]^{27}_D$ +50.0 (*c* 0.66, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.89 (s, 9H), 1.50 (d, J = 7.0 Hz, 3H), 2.31 (s, 3H), 2.63 (s, 6H), 2.74 (ddd, J = 8.4, 4.1, 3.8 Hz, 1H), 3.54 (d, J = 3.8 Hz, 1H), 4.02 (dd, J = 10.8, 8.4 Hz, 1H), 4.29 (dd, J = 10.8, 4.1 Hz, 1H), 5.71 (q, J = 7.0 Hz, 1H), 6.93 (s, 2H), 6.96−7.00 (m, 2H), 7.19−7.23 (m, 3H); MS (FAB) *m*/*z* 486 (MH^+), 428, 303, 302, 170, 147, 119, 89, 75, 73 (base peak); HRMS (FAB) calcd $C_{27}H_{40}NO_3SSi$ (MH^+) 486.2498, found 486.2504.

(3*R*,4*S*)-3,4-Epimino-5-methyl-*N*-(2,4,6-trimethylphenylsulfonyl)-2-phenylhex-1-ene (26) and Its (3*S*,4*S*)-Isomer (27). By a procedure identical with that described for the aziridination of **5a**, the amino allene **8** (50 mg, 0.17 mmol) was converted into **26** (48 mg, 76% yield) and **27** (2 mg, 3% yield) by treatment with $Pd(PPh_3)_4$ (19.6 mg, 0.017 mmol; 10 mol %), K_2CO_3 (94 mg, 0.68 mmol), and PhI (0.076 mL, 0.68 mmol) in 1,4-dioxane (0.5 mL) under reflux for 2.5 h. Compound **26**: colorless crystals from *n*-hexane; mp 83 °C; $[\alpha]^{23}_D$ −95.5 (*c* 0.33, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.72 (d, J = 6.8 Hz, 3H), 0.77 (d, J = 6.8 Hz, 3H), 1.34−1.48 (m, 1H), 2.31 (s, 3H), 2.68−2.79 (m, 1H), 2.76 (s, 6H), 3.83 (d, J = 7.3 Hz, 1H), 5.26 (s, 1H), 5.57 (s, 1H), 6.97 (s, 2H), 7.29−7.37 (m, 3H), 7.45−7.48 (m, 2H); MS (FAB) *m*/*z* 370 (MH^+), 187, 186 (base peak), 171, 144, 119, 117, 116, 91; HRMS (FAB) calcd $C_{22}H_{28}NO_2S$ (MH^+) 370.1841, found 370.1847. Compound **27**: colorless oil; $[\alpha]^{23}_D$ −2.94 (*c* 0.34, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.08 (d, J = 6.8 Hz, 3H), 1.20 (d, J = 6.5 Hz, 3H), 2.20−2.34 (m, 1H), 2.29 (s, 3H), 2.60 (dd, J = 9.5, 4.6 Hz, 1H), 2.68 (s, 6H), 3.58 (d, J = 4.3 Hz, 1H), 5.08 (s, 1H), 5.30 (s, 1H), 6.91 (s, 2H), 7.23−7.29 (m, 5H); MS (FAB) *m*/*z* 370 (MH^+), 187 (base peak), 186, 144, 119, 117, 55; HRMS (FAB) calcd $C_{22}H_{28}NO_2S$ (MH^+) 370.1841, found 370.1831.

(3*R*,4*S*)-3,4-Epimino-3,5-dimethyl-*N*-(2,4,6-trimethylphenylsulfonyl)-2-phenylhex-1-ene (28) and Its (3*S*,4*S*)-Isomer (29). By a procedure identical with that described for the aziridination of **5a**, the amino allene **14** (61.5 mg, 0.20 mmol) was converted into **28** (4 mg, 5% yield) and **29** (59 mg,

77% yield) by treatment with $Pd(PPh_3)_4$ (23.1 mg, 0.02 mmol; 10 mol %), K_2CO_3 (110 mg, 0.80 mmol), and PhI (0.090 mL, 0.80 mmol) in 1,4-dioxane (1.5 mL) under reflux for 1 h. Compound **28**: colorless oil; $[\alpha]^{35}_D$ −72.9 (*c* 0.78, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.40 (d, J = 6.7 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H), 1.27−1.32 (m, 1H), 2.00 (s, 3H), 2.28 (s, 3H), 2.67 (s, 6H), 2.80 (d, J = 8.9 Hz, 1H), 5.51−5.53 (m, 2H), 6.92 (s, 2H), 7.28−7.35 (m, 3H), 7.42−7.44 (m, 2H); MS (FAB) *m*/*z* 384 (MH^+), 200 (base peak), 119; HRMS (FAB) calcd $C_{23}H_{30}NO_2S$ (MH^+) 384.1997, found 384.2001. Compound **29**: colorless oil; $[\alpha]^{35}_D$ −165 (*c* 0.45, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.51 (d, J = 6.7 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H), 1.51−1.54 (m, 1H), 1.65 (s, 3H), 2.28 (s, 3H), 2.63 (d, J = 9.8 Hz, 1H), 2.66 (s, 6H), 5.68 (s, 1H), 5.69 (s, 1H), 6.90 (s, 2H), 7.26−7.34 (m, 3H), 7.41−7.44 (m, 2H); MS (FAB) *m*/*z* 384 (MH^+), 201, 200 (base peak); HRMS (FAB) calcd $C_{23}H_{30}NO_2S$ (MH^+) 384.1997, found 384.1983.

(2*S*,4*R*)-4-Isopropyl-*N*-(2,4,6-trimethylphenylsulfonyl)-2-(1-phenylvinyl)azetidine (31a) and Its (2*R*,4*R*)-Isomer (32) (Entry 1 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18a** (50 mg, 0.16 mmol) was converted into **31a** (47 mg, 75% yield) and **32** (10 mg, 16% yield) by treatment with $Pd(PPh_3)_4$ (18.5 mg, 0.016 mmol; 10 mol %), K_2CO_3 (88 mg, 0.64 mmol), and PhI (0.072 mL, 0.64 mmol) in 1,4-dioxane under reflux for 4 h. Compound **31a**: colorless crystals from *n*-hexane; mp 75 °C; $[\alpha]^{25}_D$ −14.0 (*c* 0.29, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 1.80 (ddd, J = 10.7, 8.1, 8.1 Hz, 1H), 2.00−2.11 (m, 1H), 2.28 (s, 3H), 2.42 (ddd, J = 10.7, 8.9, 8.9 Hz, 1H), 2.64 (s, 6H), 4.31 (ddd, J = 8.9, 8.1, 5.0 Hz, 1H), 4.98 (dd, J = 8.9, 8.1 Hz, 1H), 5.12 (m, 1H), 5.14 (m, 1H), 6.90 (m, 2H), 7.15−7.20 (m, 2H), 7.24−7.30 (m, 3H). Anal. Calcd for $C_{23}H_{29}NO_2S$: C, 72.03; H, 7.62; N, 3.65. Found: C, 71.83; H, 7.70; N, 3.70. Compound **32**: colorless oil; $[\alpha]^{25}_D$ +75.9 (*c* 0.49, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80 (d, J = 6.7 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H), 2.05 (ddd, J = 11.0, 8.6, 6.7 Hz, 1H), 2.27 (s, 3H), 2.37 (ddd, J = 11.0, 8.9, 4.8 Hz, 1H), 2.56 (s, 6H), 2.67−2.77 (m, 1H), 4.53 (ddd, J = 8.6, 4.8, 3.8 Hz, 1H), 5.01 (m, 1H), 5.05 (d, J = 0.8 Hz, 1H), 5.21 (ddd, J = 8.9, 6.7, 0.8 Hz, 1H), 6.86 (m, 2H), 7.13−7.18 (m, 2H), 7.23−7.27 (m, 3H); MS (FAB) *m*/*z* 384 (MH^+), 254, 183, 120, 119 (base peak), 91; HRMS (FAB) calcd $C_{23}H_{30}NO_2S$ (MH^+) 384.1998, found 384.2003.

(2*S*,4*S*)-4-Isobutyl-*N*-(2,4,6-trimethylphenylsulfonyl)-2-(1-phenylvinyl)azetidine (31b) (Entry 3 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18b** (48 mg, 0.15 mmol) was converted into **31b** (50 mg, 84% yield) by treatment with $Pd(PPh_3)_4$ (17 mg, 0.015 mmol; 10 mol %), K_2CO_3 (83 mg, 0.60 mmol), and PhI (0.067 mL, 0.60 mmol) in DMF at 70 °C for 3.5 h. Colorless crystals from *n*-hexane: mp 85 °C; $[\alpha]^{25}_D$ −19.5 (*c* 0.92, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (d, J = 6.2 Hz, 6H), 1.50−1.63 (m, 2H), 1.72 (ddd, J = 10.8, 8.1, 8.1 Hz, 1H), 1.79−1.90 (m, 1H), 2.29 (s, 3H), 2.60−2.70 (m, 1H), 2.63 (s, 6H), 4.34−4.45 (m, 1H), 5.01 (dd, J = 8.6, 8.1 Hz, 1H), 5.10 (s, 2H), 6.90 (s, 2H), 7.16−7.32 (m, 5H). Anal. Calcd for $C_{24}H_{31}NO_2S$: C, 72.51; H, 7.86; N, 3.52. Found: C, 72.67; H, 7.94; N, 3.37.

(2*S*,4*S*)-4-Isobutyl-*N*-(4-methylphenylsulfonyl)-2-(1-phenylvinyl)azetidine (31c) (Entry 4 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18c** (50 mg, 0.17 mmol) was converted into **31c** (55 mg, 88% yield) by treatment with $Pd(PPh_3)_4$ (20 mg, 0.017 mmol; 10 mol %), K_2CO_3 (94 mg, 0.68 mmol), and PhI (0.076 mL, 0.68 mmol) in DMF at 70 °C for 3 h. Colorless oil: $[\alpha]^{28}_D$ −79.4 (c 1.04, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (d, J = 6.2 Hz, 6H), 1.50−1.67 (m, 3H), 1.85−1.96 (m, 1H), 2.40 (ddd, J = 10.5, 8.6, 8.6 Hz, 1H), 2.46 (s, 3H), 3.87−3.99 (m, 1H), 4.61 (dd, J = 8.6, 7.8 Hz, 1H), 5.46 (s, 1H), 5.66 (s, 1H), 7.25−7.37 (m, 7H), 7.25−7.76 (m, 2H); MS (FAB) *m*/*z* 370 (MH^+), 368, 240 (base peak), 214, 155, 91, 69, 55, 43; HRMS (FAB) calcd $C_{22}H_{28}NO_2S$ (MH^+) 370.1841, found 370.1833.

(2*S*,4*S*)-4-Isobutyl-*N*-(2-nitrophenylsulfonyl)-2-(1-phenylvinyl)azetidine (31d) and 2-Isobutyl-*N*-(2-nitrophenylsulfonyl)-5-phenyl-2*H*,3*H*,6*H*-azine (33) (Entry 5 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18d** (40 mg, 0.12 mmol) was converted into **31d** (26 mg, 54% yield) and **33** (16 mg, 33% yield) by treatment with $Pd(PPh_3)_4$ (19 mg, 0.012 mmol; 10 mol %), K_2CO_3 (66 mg, 0.48 mmol), and PhI (0.054 mL, 0.48 mmol) in DMF at 70 °C for 0.75 h. Compound **31d**: colorless oil; $[\alpha]^{18}_D$ −65.9 (*c* 0.18, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H), 1.53−1.69 (m, 2H), 1.76 (ddd, J = 11.1, 7.6, 7.6 Hz, 1H), 1.96−2.04 (m, 1H), 2.58 (ddd, J = 11.1, 8.4, 8.4 Hz, 1H), 4.32−4.44 (m, 1H), 5.04 (dd, J = 8.4, 7.6 Hz, 1H), 5.39 (s, 1H), 5.58 (s, 1H), 7.30 (m, 5H), 7,60−7.75 (m, 3H), 7.95−7.99 (m, 1H); MS (FAB) *m*/*z* 401 (MH^+), 271 (base peak), 214, 186, 156, 130, 105, 61, 59, 41; HRMS (FAB) calcd $C_{21}H_{25}N_2O_4S$ (MH^+) 401.1535, found 401.1527. Compound **33**: colorless oil; $[\alpha]^{28}_D$ −54.2 (*c* 0.16, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87 (d, J = 6.3 Hz, 3H), 0.91 (d, J = 6.3 Hz, 3H), 1.26−1.39 (m, 1H), 1.50−1.68 (m, 2H), 2.05−2.11 (m, 1H), 2.52−2.60 (m, 1H), 4.00−4.07 (m, 1H), 4.19−4.27 (m, 1H), 4.57 (d, J = 17.8 Hz, 1H), 6.03−6.07 (m, 1H), 7.28−7.40 (m, 5H), 7.63 (m, 3H), 8.05 (m, 1H); MS (FAB) *m*/*z* 401 (MH^+, base peak), 343, 271, 214, 186, 154, 136, 130, 91, 77, 55, 41; HRMS (FAB) calcd $C_{21}H_{25}N_2O_4S$ (MH^+) 401.1535, found 401.1545.

(2*S*,4*S*)-4-Benzyl-*N*-(2,4,6-trimethylphenylsulfonyl)-2-(1-phenylvinyl)azetidine (31e) (Entry 6 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18e** (48 mg, 0.14 mmol) was converted into **31e** (49 mg, 84% yield) by treatment with $Pd(PPh_3)_4$ (16.2 mg, 0.014 mmol; 10 mol %), K_2CO_3 (77.3 mg, 0.56 mmol), and PhI (62.8 μL, 0.56 mmol) in DMF at 70 °C for 1 h. Colorless oil: $[\alpha]^{28}_D$ +12.4 (*c* 1.27, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81 (ddd, J = 10.7, 8.1, 8.1 Hz, 1H), 2.30 (s, 3H), 2.45 (ddd, J = 10.6, 8.5, 8.5 Hz, 1H), 2.68 (s, 6H), 2.82 (dd, J = 13.2, 10.4 Hz, 1H), 3.29 (dd, J = 13.2, 4.0 Hz, 1H), 4.51 (dddd, J = 10.4, 8.5, 8.1, 4.0 Hz, 1H), 4.98 (dd, J = 8.5, 8.1 Hz, 1H), 5.13−5.15 (m, 2H), 6.92−6.93 (m, 2H), 7.09−7.28 (m, 10H); MS (FAB) *m*/*z* 432 (MH^+), 340, 302, 248, 183, 119 (base peak), 91; HRMS (FAB) calcd $C_{27}H_{30}NO_2S$ (MH^+) 432.1997, found 432.1983.

(2*S*,4*S*)-4-Benzyl-*N*-(4-methylphenylsulfonyl)-2-(1-phenylvinyl)azetidine (31f) (Entry 7 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18f** (42 mg, 0.128 mmol) was converted into **31f** (46 mg, 89% yield) by treatment with $Pd(PPh_3)_4$ (14.8 mg, 0.0128 mmol; 10 mol %), K_2CO_3 (70.7 mg, 0.512 mmol), and PhI (57.3 μL, 0.512 mmol) in DMF at 70 °C for 1 h. Colorless oil: $[\alpha]^{30}_D$ −39.5 (*c* 0.98, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.74 (ddd, J = 11.1, 7.6, 7.6 Hz, 1H), 2.24 (ddd, J = 11.1, 8.6, 8.6 Hz, 1H), 2.45 (s, 3H), 2.96 (dd, J = 13.5, 9.2 Hz, 1H), 3.21 (dd, J = 13.5, 3.5 Hz, 1H), 4.03−4.14 (m, 1H), 4.55 (dd, J = 8.6, 7.6 Hz, 1H), 5.41 (s, 1H), 5.57 (s, 1H), 7.12−7.33 (m, 10H), 7.34−7.38 (m, 2H), 7.75−7.78 (m, 2H); MS (FAB) *m*/*z* 404 (MH^+), 312, 274, 248, 155, 91 (base peak); HRMS (FAB) calcd $C_{25}H_{26}NO_2S$ (MH^+) 404.1684, found 404.1682.

(2*S*,4*R*)-4-(*tert*-Butyldimethylsiloxy)-*N*-(2,4,6-trimethylphenylsulfonyl)-2-(1-phenylvinyl)azetidine (31g) (Entry 8 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18g** (30 mg, 0.073 mmol) was converted into **31g** (18 mg, 53% yield) by treatment with $Pd(PPh_3)_4$ (8.5 mg, 0.0073 mmol; 10 mol %), K_2CO_3 (40 mg, 0.29 mmol), and PhI (0.031 mL, 0.29 mmol) in DMF at 70 °C for 1.5 h. Colorless oil: $[\alpha]^{28}_D$ +14.9 (*c* 0.25, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 2.13 (ddd, J = 10.5, 7.8, 7.8 Hz, 1H), 2.28 (s, 3H), 2.48 (ddd, J = 10.5, 8.9, 8.9 Hz, 1H), 2.63 (s, 6H), 3.63 (dd, J = 8.1, 2.7 Hz, 1H), 3.84 (dd, J = 10.5, 4.6 Hz, 1H), 4.42−4.51 (m, 1H), 5.03 (dd, J = 8.9, 7.8 Hz, 1H), 5.09 (s, 1H), 5.13 (s, 1H), 6.88 (s, 2H), 7.16−7.28 (m, 5H); MS (FAB) *m*/*z* 486 (MH^+), 428, 356, 298, 173, 119 (base peak), 73; HRMS (FAB) calcd $C_{27}H_{40}NO_3SSi$ (MH^+) 486.2498, found 486.2506.

Methyl (2′*S*,4′*R*)-3-[*N*-(2,4,6-Trimethylphenylsulfonyl)-4-(1-phenylvinyl)azetidin-2-yl]propanoate (31h) (Entry 9 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18h** (28 mg, 0.080 mmol) was converted into **31h** (23 mg, 67% yield) by treatment with $Pd(PPh_3)_4$ (9.2 mg, 0.0080 mmol; 10 mol %), K_2CO_3 (44 mg, 0.32 mmol), and PhI (0.036 mL, 0.32 mmol) in DMF at 70

°C for 1 h. Colorless oil: $[\alpha]^{25}_D$ −24.1 (*c* 0.34, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.72 (ddd, J = 10.5, 8.2, 8.2 Hz, 1H), 1.93−2.06 (m, 1H), 2.14−2.25 (m, 1H), 2.29 (s, 3H), 2.31−2.39 (m, 2H), 2.56−2.67 (m, 1H), 2.63 (s, 6H), 3.67 (s, 3H), 4.36−4.46 (m, 1H), 5.00 (dd, J = 8.6, 8.1 Hz, 1H), 5.07 (s, 1H), 5.09 (s, 1H), 6.90 (s, 2H), 7.13−7.29 (m, 5H); MS (FAB) *m*/*z* 428 (MH^+), 298, 244, 229, 183, 154, 119 (base peak), 98, 91, 77; HRMS (FAB) calcd $C_{24}H_{30}NO_4S$ (MH^+) 428.1896, found 428.1900.

Methyl (2′*S*,4′*R*)-3-[*N*-(4-Methoxy-2,3,6-trimethylphenylsulfonyl)-4-(1-phenylvinyl)azetidin-2-yl]propanoate (31i) (Entry 10 in Table 3). By a procedure similar to that described for the aziridination of **5a**, the amino allene **18i** (35 mg, 0.092 mmol) was converted into **31i** (30 mg, 73% yield) by treatment with $Pd(PPh_3)_4$ (10.6 mg, 0.0092 mmol; 10 mol %), K_2CO_3 (50 mg, 0.36 mmol), and PhI (0.040 mL, 0.36 mmol) in DMF at 70 °C for 1.5 h. Colorless oil: $[\alpha]^{22}_D$ −15.8 (*c* 0.22, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.73 (ddd, J = 11.1, 7.8, 7.8 Hz, 1H), 1.94−2.06 (m, 1H), 2.12 (s, 3H), 2.15−2.24 (m, 1H), 2.33−2.39 (m, 2H), 2.58−2.67 (m, 1H), 2.61 (s, 3H), 2.63 (s, 3H), 3.66 (s, 3H), 3.84 (s, 3H), 4.36−4.46 (m, 1H), 5.01 (dd, J = 8.4, 7.8 Hz, 1H), 5.11 (s, 1H), 5.13 (s, 1H), 6.50 (s, 1H), 7.12−7.27 (m, 5H); MS (FAB) *m*/*z* 458 (MH^+), 328, 244, 213, 197, 149 (base peak), 134, 119, 91; HRMS (FAB) calcd $C_{25}H_{32}NO_5S$ (MH^+) 458.2002, found 458.2010.

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Supporting Information Available: Experimental procedures for **15b**−**d**, **16b**−**d**, **17b**−**e**, **18b**−**i**, **20a**−**e**, **23**−**25**, **31j**−**o**, **34**, and **35**; NOE experiment of the synthesized aziridines and azetidines; ^1H NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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