Reactions of *N*-Arylsulfonyl-2,3-*cis*- and *N*-Arylsulfonyl-2,3-*trans*-3-alkyl-2-vinylaziridines with Organocopper Reagents: Importance of 2,3-*cis*-Stereochemistry in Controlling Regio- and Stereoselectivity

Ayako Toda, Hiroshi Aoyama, Norio Mimura, Hiroaki Ohno, Nobutaka Fujii, and Toshiro Ibuka*

Graduate School of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan

Received May 28, 1998

Although reactions of 2,3-*trans*-*N*-arylsulfonyl-3-alkyl-2-alkenylaziridines with organocopper reagents give a mixture of two or three products, the corresponding 2,3-*cis*-isomers provide a highly efficient route to synthetically important nonracemic (*E*)-allylamines. It is also found that the reaction proceeds via the well-known anti-S_N2' pathway.

Development of synthetic methods that provide ready access to nonracemic allylamines from alkenylaziridines with a high level of regio- and (*E*)-stereoselectivity as well as high chemical yields represents a challenge to synthetic organic chemists. Recently, great advances have been reported in the ring opening of activated and unactivated aziridines[1] by both carbon (e.g., enolates,[2] enediolates,[3] malonates and related reagents,[4] organolithiums,[5] Grignard reagents,[6] organocopper reagents,[7] and Wittig reagents[8]) and heteroatom nucleophiles (e.g., amines,[9] thiols or thiophenolates,[10] and alcohols[11]). Although extensive stereochemical and mechanistic studies by Marshall[12] and Marino[13] on the ring-opening reaction of vinyloxiranes and related compounds with organocopper reagents have shown that an anti-S_N2' pathway is highly favored for substitution, until recently S_N2' ring-opening reactions of vinylaziridines[14,15] and their derivatives[16] with organocopper reagents for the synthesis of various synthetically useful allylamines had been rare.

We now detail a regio- and (*E*)-stereoselective S_N2' ring-opening strategy involving organocopper reagents for converting nonracemic *N*-protected 2,3-*cis*- and 2,3-*trans*-3-alkyl-2-alkenylaziridines to the synthetically important *N*-protected allylamines in high yields. Synthesis of a nonracemic vinylglycine derivative is also presented.

* Phone: 81-75-753-4528. Fax: 81-75-753-4570. E-mail: tibuka@pharmsun.pharm.kyoto-u.ac.jp.

(1) For reviews of syntheses and reactions of activated and unactivated aziridines, see: Pawda, A.; Woolhouse, A. D. In *Comprehensive Heterocyclic Chemistry*; Lwowski, W., Ed.; Pergamon: Oxford, 1984; Vol. 7, pp 47−93. Kasai, M.; Kono, M. *Synlett* **1992**, 778. Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. Osborn, H. M. I.; Sweeney, J. *Tetrahedon: Asymmetry* **1997**, *8*, 1693. Rayner, C. M. *Synlett* **1997**, 11. Ibuka, T. *Chem. Soc. Rev.* **1998**, *27*, 145.

(2) Stamm, H.; Weiss, R. *Synthesis* **1986**, 392.

(3) (a) Stamm, H.; Weiss, R. *Synthesis* **1986**, 395. (b) Brigaud, T.; Laurent, E.; Tardivel, R.; Cebulska, Z.; Bartnik, R. *J. Chem. Res., Synop.* **1994**, 330. (c) Matsumoto, K.; Iida, H.; Uchida, T.; Yabe, Y.; Kakehi, A. *Chem. Express* **1993**, *8*, 609.

(4) Stamm, H.; Assithianakis, P.; Buchholz, B.; Weiss, R. *Tetrahedron Lett.* **1982**, *23*, 5021.

(5) Howson, W.; Osborn, H. M. I.; Sweeney, J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2439.

(6) Oppolzer, W.; Flaskamp, E. *Helv. Chim. Acta* **1977**, *60*, 204.

(7) (a) Eis, M. J.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 1153. (b) Duréault, A.; Greck, C.; Depezay, J. C. *Tetrahedron Lett.* **1986**, *27*, 4157. (c) Duréault, A.; Tranchepain, I.; Depezay, J.-C. *J. Org. Chem.* **1989**, *54*, 5324. (d) Kozikowski, A. P.; Ishida, H.; Isobe, K. *J. Org. Chem.* **1979**, *44*, 2788. (e) Church, N. J.; Young, D. W. *Tetrahedron Lett.* **1995**, *36*, 151. (f) Tanner, D.; Groth, T. *Tetrahedron* **1997**, *53*, 16139. (g) Tanner, D.; Birgersson, C.; Dhaliwal, H. K. *Tetrahedron Lett.* **1990**, *31*, 1903. (h) Tanner, D.; Somfai, P. *Tetrahedron* **1988**, *44*, 619.

(8) Baldwin, J. E.; Adlington, R. M.; Robinson, N. G. *J. Chem. Soc., Chem. Commun.* **1987**, 153.

(9) (a) Shigematsu, N.; Setoi, H.; Uchida, I.; Shibata, T.; Terano, H.; Hashimoto, M. *Tetrahedron Lett.* **1988**, *29*, 5147. (b) Nakajima, K.; Tanaka, T.; Morita, K.; Okawa, K. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 283. (c) Cernerud, M.; Adolfsson, H.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 2655. (d) Maligres, P. E.; See, M. M.; Askin, D.; Reider, P. J. *Tetrahedron Lett.* **1997**, *38*, 5253.

(10) (a) Tomalia, D. A.; Sheetz, D. P.; Ham, G. E. *J. Org. Chem.* **1970**, *35*, 47. (b) Nakajima, K.; Oda, H.; Okawa, K. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 520. (c) Lin, P.-Y.; Bellos, K.; Stamm, H.; Onistschenko, A. *Tetrahedron* **1992**, *48*, 2359. (d) Legters, J.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1989**, *30*, 4881.

(11) (a) Nakajima, K.; Neya, M.; Yamada, S.; Okawa, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3049. (b) Bodenan, J.; Chanet-Ray, J.; Vessiere, R. *Synthesis* **1992**, 288. (c) For an aziridine ring-opening reaction with acetic acid, see: Atkinson, R. S.; Ayscough, A. P.; Rattrell, W. T.; Raynham, T. M. *Tetrahedron Lett.* **1998**, *39*, 4377.

(12) (a) Marshall, J. A.; Audia, V. H.; Jenson, T. M.; Guida, W. C. *Tetrahedron* **1986**, *42*, 1703. (b) Marshall, J. A.; Audia, V. H. *J. Org. Chem.* **1987**, *52*, 1106. (c) Marshall, J. A.; Trometer, J. D. *Tetrahedron Lett.* **1987**, *28*, 4985. (d) Marshall, J. A.; Trometer, J. D.; Clearly, D. G. *Tetrahedron* **1989**, *45*, 391. (e) Marshall, J. A. *Chem. Rev.* **1989**, *89*, 1503. (f) Marshall, J. A.; Blough, B. E. *J. Org. Chem.* **1990**, *55*, 1540. (g) Marshall, J. A.; Blough, B. E. *J. Org. Chem.* **1991**, *56*, 2225. (h) Marshall, J. A.; Crute, T. D., III.; Hsi, J. D. *J. Org. Chem.* **1992**, *57*, 115.

(13) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675. Marino, J. P.; Hatanaka, N. *J. Org. Chem.* **1979**, *44*, 4467. Marino, J. P.; Abe, H. *Synthesis* **1980**, 872. Marino, J. P.; Abe, H. *J. Org. Chem.* **1981**, *46*, 5379. Marino, J. P.; Abe, H. *J. Am. Chem. Soc.* **1981**, *103*, 2907. Marino, J. P.; Jaén, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165. Marino, J. P.; Fernández de la Pradilla, R.; Laborde, E. *J. Org. Chem.* **1984**, *49*, 5279. Marino, J. P.; Fernández de la Pradilla, R.; Laborde, E. *J. Org. Chem.* **1987**, *52*, 4898. Fernàndez de la Pradilla, R.; Rubio, M. B.; Marino, J. P. Viso, A. *Tetrahedron Lett.* **1992**, *33*, 4985. Marino, J. P.; Viso, A.; Fernández de la Pradilla, R.; Fernàndez, P. *J. Org. Chem.* **1991**, *56*, 1349. Marino, J. P.; Anna, L. J.; Fernández de la Pradilla, R.; Martínez, M. V.; Montero, C.; Viso, A. *Tetrahedron Lett.* **1996**, *37*, 8031.

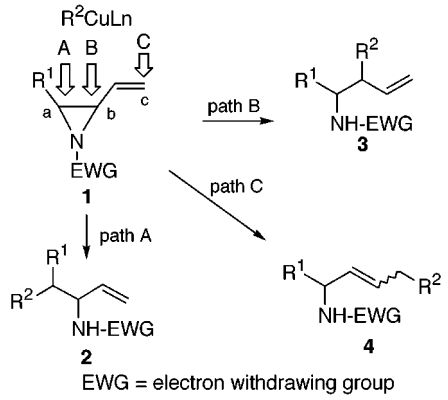
(14) Cantrill, A. A.; Jarvis, A. N.; Osborn, H. M. I.; Ouadi, A.; Sweeney, J. B. *Synlett* **1996**, 847.

(15) A preliminary communication of this work has appeared: Aoyama, H.; Mimura, N.; Ohno, H.; Ishii, K.; Toda, A.; Tamamura, H.; Otaka, A.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1997**, *38*, 7383.

(16) (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) Wipf, P.; Fritch, P. C. *J. Org. Chem.* **1994**, *59*, 4875. (c) Fujii, N.; Nakai, K.; Tamamura, H.; Otaka, A.; Mimura, N.; Miwa, Y.; Taga, T.; Yamamoto, Y.; Ibuka, T. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1359. (d) Ibuka, T.; Akaji, M.; Mimura, N.; Habashita, H.; Nakai, K.; Tamamura, H.; Fujii, N.; Yamamoto, Y. *Tetrahedron Lett.* **1996**, *37*, 2849. (e) 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. (f) Wipf, P.; Henninger, T. C. *J. Org. Chem.* **1997**, *62*, 1486.

S0022-3263(98)01015-9 CCC: $15.00
Published on Web 09/15/1998

Scheme 1



EWG = electron withdrawing group

Results and Discussion

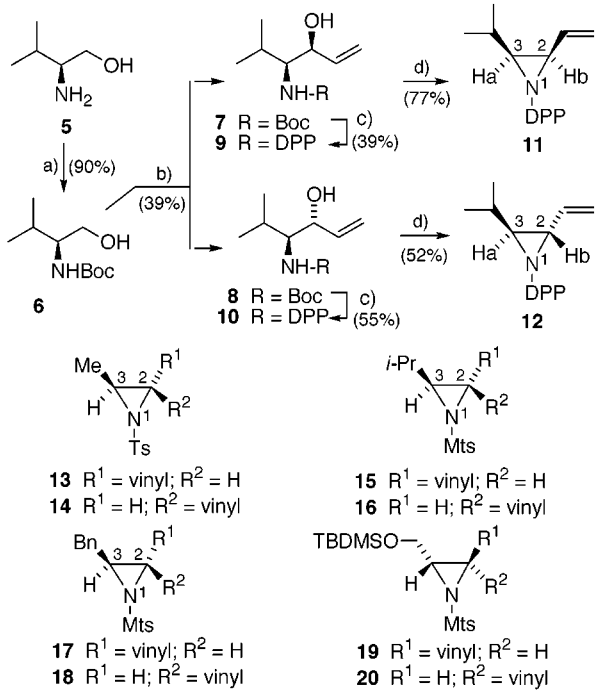
As shown in Scheme 1, three different products from the reaction of 2-vinylaziridine **1** with an organocopper reagent could be envisioned. If an organocopper reagent reacts with vinylaziridine **1** by an S_N2 mechanism, it will produce either **2** or **3**. If the reagent attacks by an S_N2' mechanism, it will generate either (*E*)- or (*Z*)-allylamine **4** or a mixture of (*E*)- and (*Z*)-configurational isomers.

The regio- and stereoselectivity of the ring-opening reaction is expected to be controlled by a delicate balance of steric and electronic factors. Thus, it is not an easy matter to predict whether path A, B, or C is the major reaction pathway in the reaction of 2-alkenylaziridines with organocopper reagents.

Synthesis of Nonracemic 2,3-*cis*- and 2,3-*trans*-3-Alkyl-2-vinylaziridines. It is well documented that the reactivity of *N*-unsubstituted- or *N*-alkylaziridines toward nucleophiles is relatively low; hence, activation by the introduction of an electron-withdrawing protecting group on the nitrogen atom of the aziridine is required. The term "activated aziridines" has been introduced by Ham for aziridines that easily undergo nucleophilic S_N2-type ring opening.[17] The *N*,*N*-diphenylphosphinoyl group serves as a good activating group.[18] Alternatively, arylsulfonyl groups work as most effective activating groups.[19] The *N*-arylsulfonyl groups can withstand a wide range of chemical manipulations and yet be removed by the use of HBr−AcOH,[7e,20] SmI_2,[21] TFA−thioanisole,[22] Na−Hg,[23] or Na−liquid NH_3.[24]

The requisite 2,3-*cis*/*trans* pair of *N*,*N*-diphenylphosphinoyl-3-alkyl-2-vinylaziridines **11** and **12** were prepared from the known (*S*)-valinol **5**[25] by a sequence of reactions as shown in Scheme 2 (for details, see Experimental Section). The 2,3-*cis* or -*trans* stereochemistry of the aziridines **11** and **12** was inferred from ^{1}H NMR spectral analyses. The 2,3-*cis*-aziridine **11** shows a *J*(Hab) value (J = 6.5 Hz) larger than that of the 2,3-*trans*-isomer **12** (J = 3.2 Hz). The data are in good agreement with ^{1}H NMR data for related compounds.[22,26] The 2,3-*cis*/*trans* pair of *N*-tosylaziridines **13** and **14** was readily synthesized by our published method[22] from (*S*)-threonine and (*D*)-allo-threonine, respectively. Other 2,3-*cis*/*trans* pairs of *N*-2,4,6-trimethylbenzenesulfonylaziridines (**15** and **16**), (**17** and **18**), and (**19** and **20**) were prepared from (*S*)-valinol, (*S*)-phenylalanine, and (*R*)-serine, respectively, following literature procedure.[22]

Scheme 2



Abbreviations: DPP = diphenylphosphinoyl; Boc = *tert*-butoxycarbonyl; Ts = *p*-toluenesulfonyl; Mts = 2,4,6-trimethylbenzenesulfonyl; Bn = benzyl; TBDMSO = *tert*-butyldimethylsilyl; *Reagents*: a) Boc_2O -Et_3N; b) i. Swern oxidation in *n*-hexane-$CHCl_3$ (3:2); ii . vinyl-MgCl-$ZnCl_2$ in THF; c) i. TFA; ii. DPPCl - Et_3N in DMF; d) PPh_3 - diethyl azodicarboxylate.

Ring-Opening Reactions of Activated 2-Alkenyl-3-alkylaziridines with Organocopper Reagents. Synthesis of Nonracemic Allylamines. The ring-opening reaction of activated 2,3-*trans*-2-vinylaziridine with some nucleophiles has been examined independently by Sweeney and co-workers[14] and our group.[15] However, the synthetic utility of this transformation remains unexplored. At first, we briefly studied the scope of the methylcopper-mediated reaction by using the two stereoisomeric substrates **11** and **12** (Scheme 3 and Table 1).

To our initial dismay, reaction of the 2,3-*cis*-vinylaziridine **11** with 4 molar equiv of methylcopper (MeCu·LiI·LiBr) or lower-order cyanocuprate [MeCu(CN)Li·LiBr] recovered the starting material unchanged (Table 1, entries 1 and 2). Similar results were obtained by reaction of 2,3-*trans*-isomer **12** with MeCu·LiI or MeCu(CN)Li (Table 1, entries 5 and 6). Although the *N*,*N*-diphenylphosphinoyl (DPP) group is a potentially useful

(17) Ham, G. E. *J. Org. Chem.* **1964**, *29*, 3052.
(18) (a) Osborn, H. M. I.; Sweeney, J. B. *Synlett* **1994**, 145. (b) Berry, M. B.; Craig, D.; Jones, P. S.; Rowlands, G. J. *Chem. Commun.* **1997**, 2141. (c) Cantrill, A. A.; Osborn, H. M. I.; Sweeney, J. *Tetrahedron* **1998**, *54*, 2181. (d) Hou, X.-L.; Yang, X.-F.; Dai, L.-X.; Chen, X.-F. *Chem. Commun.* **1998**, 747.
(19) Greene, T. W.; Wuts, P. G. M. In *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1991.
(20) Baldwin, J. E.; Spivey, A. C.; Schofield, C. J.; Sweeney, J. B. *Tetrahedron* **1993**, *49*, 6309.
(21) Vedejs, E.; Lin, S. *J. Org. Chem.* **1994**, *59*, 1602.
(22) 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.
(23) Craig, D.; McCague, R.; Potter, G. A.; Williams, M. R. V. *Synlett* **1998**, 55 and 58.
(24) Ibuka, T.; Nakai, K.; Akaji, M.; Tamamura, H.; Fujii, N.; Yamamoto, Y. *Tetrahedron* **1996**, *52*, 11739.
(25) McKennon, M. J.; Meyers, A. I.; Drauz, K.; Schwarm, M. *J. Org. Chem.* **1993**, *58*, 3568.
(26) (a) Coutrot, P.; Elgadi, A.; Grison, C. *Heterocycles* **1989**, *28*, 1179. (b) Davis, F. A.; Zhou, P. *Tetrahedron Lett.* **1994**, *35*, 7525. (c) Davis, F. A.; Zhou, P.; Reddy, G. V. *J. Org. Chem.* **1994**, *59*, 3243. (d) Ziegler, F. E.; Belema, M. *J. Org. Chem.* **1994**, *59*, 7962.

Scheme 3

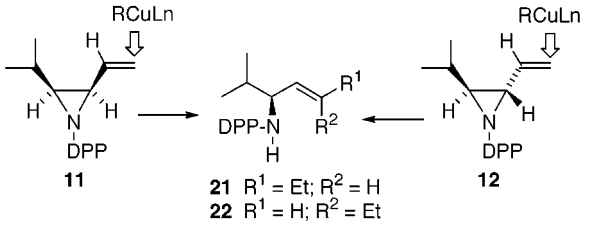
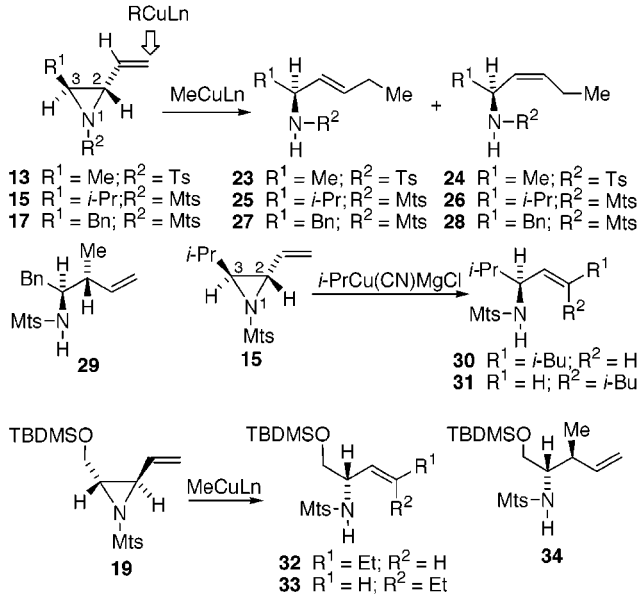


Table 1. Methylcopper-Mediated Reactions of Vinylaziridines 11 and 12[a]

entry	substr	reagent	product ratio **21**:**22**	combd isoltd yld (%)
1	**11**	MeCu·LiI·LiBr (4 equiv)		recovered
2	**11**	MeCu(CN)Li·LiBr (4 equiv)		recovered
3	**11**	Me_2CuLi·LiI·2LiBr (4 equiv)	89:11	93
4	**11**	$Me_2Cu(CN)Li_2$·2LiBr (4 equiv)	99:1	99
5	**12**	MeCu·LiI·LiBr (4 equiv)		recovered
6	**12**	MeCu(CN)Li·LiBr (4 equiv)		recovered
7	**12**	$Me_2Cu(CN)Li_2$·2LiBr (4 equiv)	99:1	93

[a] All reactions were carried out in THF under a positive pressure of argon at −78 °C for 30 min. All methylcopper reagents have been prepared by treatment of CuI or CuCN with ethereal MeLi as the LiBr complex. All product ratios were determined by HPLC.

Scheme 4



Abbreviations: Bn = benzyl; Ts = *p*-toluenesulfonyl; Mts = 2,4,6-trimethylbenzenesulfonyl; TBDMS = *tert*-butyldimethylsilyl

protecting and activating group, it is clear that activation by the DPP group is considerably lower than that by arylsulfonyl groups. However, the ring-opening reaction was accomplished by using a Gilman-type reagent, Me_2CuLi·LiI·LiBr, to yield an 89:11 mixture of (*E*)- and (*Z*)-allylamines **21** and **22** in favor of the (*E*)-isomer **21** (Table 1, entry 3). The (*E*)-allylamine **21** could be isolated readily after flash chromatography. Thus, of the three possible regioisomeric products, ring-opening products via path C (Scheme 1) were formed exclusively. It should be clearly noted that while there is ^{1}H NMR spectroscopic evidence to support the presence of the (*Z*)-allylamine **22**, the (*Z*)-isomer **22** could not be isolated in a pure state by various silica gel columns.

The most regio- and (*E*)-selective S_N2' type ring-opening reaction was realized by the reaction of **11** or **12** with a higher order cuprate, $Me_2Cu(CN)Li_2$·2LiBr[27] (Me_2CuLi·LiCN·2LiBr[28]), to yield almost exclusively allylamine **21** (Table 1, entries 4 and 7). Thus, the stereoselectivity markedly changes by use of the higher-order cuprate, $Me_2Cu(CN)Li_2$·2LiBr instead of the Gilman-type reagent, Me_2CuLi·LiI·2LiBr[29] (compare entry 3 with 4, Table 1). Thus, the higher-order cyanocuprate, $Me_2Cu(CN)Li_2$·2LiBr, prepared from 2 equiv of methyllithium as the LiBr complex and an equivalent of CuCN, is the reagent of choice because with it the most (*E*)-selective anti-S_N2' substitution reaction to the *N*-DPP-2-vinylaziridine substrate occurs.

Next, the scope of the organocopper-mediated reaction was determined by using the four 2,3-*trans* substrates **13**, **15**, **17**, and **19** bearing an *N*-arylsulfonyl group.

As can be seen from Scheme 4 and Table 2 (entries 1−10), regardless of the type of organocopper reagent, mixtures of two or three products were obtained from all reactions of 2,3-*trans*-2-vinylaziridines. It is of interest, however, that all of these ring-opening reactions exhibit high levels of regioselectivity and (*E*)-stereoselectivity (>85%). In all cases studied in the 2,3-*trans* series of substrates, 3−15% yields of (*Z*)-allylamines **24**, **26**, **28**, **31**, and **33** were obtained after flash chromatography. Although both (*E*)- and (*Z*)-products, e.g., (**23** and **24**) and (**25** and **26**), are the result of an S_N2' reaction, the loss of stereocontrol, though slight, is undesirable in synthesis. In addition, minor products (**29** and **34**, 2−3% yield) that would have originated via the S_N2 pathway were also isolated from the reactions of vinylaziridines **17** and **19**.

In contrast, upon the exposure of 2,3-*cis*-3-alkyl-2-vinylaziridines **14**, **16**, **18**, and **20** to organocopper reagents, the corresponding (*E*)-allylamines were exclusively produced in very high yields (Scheme 5 and Table 2, entries 11−19). In all cases examined in the 2,3-*cis* series of substrates, reaction products were shown to be a single (*E*)-allylamine by ^{1}H NMR and HPLC analyses (compare entries 1−10 with entries 11−19).

Thus, it is found that whereas *N*-arylsulfonyl-2,3-*trans*-3-alkyl-2-vinylaziridines gave mixtures of two or three products, 2,3-*cis*-isomers gave exclusively the corresponding (*E*)-allylamines in high yields. Since 2,3-*trans*-3-alkyl-2-vinylaziridines could be transformed into the corresponding 2,3-*cis*-isomers by the Pd(0)-catalyzed isomerization reactions,[22] we believe that the present organocopper chemistry could be used for the selective synthesis of (*E*)-allylamines.

(27) Lipshutz, B. H.; Wilhelm, R. S.; Kozlowski, J. A. *Tetrahedron* **1984**, *40*, 5005. Lipshutz, B. H.; Sharma, S.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 4032. Although the organocopper reagent prepared from CuCN and 2 equiv of MeLi·LiBr may be represented as Me_2CuLi·LiCN·2LiBr by analogy to Gilman reagent, Me_2CuLi·LiI·2LiBr, for the cuprate prepared from CuI and 2 equiv of MeLi·LiBr as suggested by Dr. Bertz,[28a−c] the formula $Me_2Cu(CN)Li_2$·2LiBr has been used throughout this paper as a matter of convenience. We are not concerned about the exact constitution, but watch the reactive species as a reagent system. See also: Lipshutz, B. H. *Synthesis* **1987**, 325. Lipshutz, B. H. In *Organometallic in Synthesis*; Schlosser, M., Ed.; Wiley: New York, 1994; p 283.

(28) (a) Bertz, S. H. *J. Am. Chem. Soc.* **1990**, *112*, 4031. (b) Bertz, S. H.; Miao, G.; Eliksson, M. *J. Chem. Soc., Chem. Commun.* **1996**, 815. (c) Bertz, S. H.; Dabbagh, G.; He, X.; Power, P. P. *J. Am. Chem. Soc.* **1993**, *115*, 11640. See also: Stemmler, T.; Penner-Hahn, J. E.; Knochel, P. *J. Am. Chem. Soc.* **1993**, *115*, 348. Synder, J. P.; Spangler, D. P.; Behling, J. R.; Rossiter, B. E. *J. Org. Chem.* **1994**, *59*, 2665.

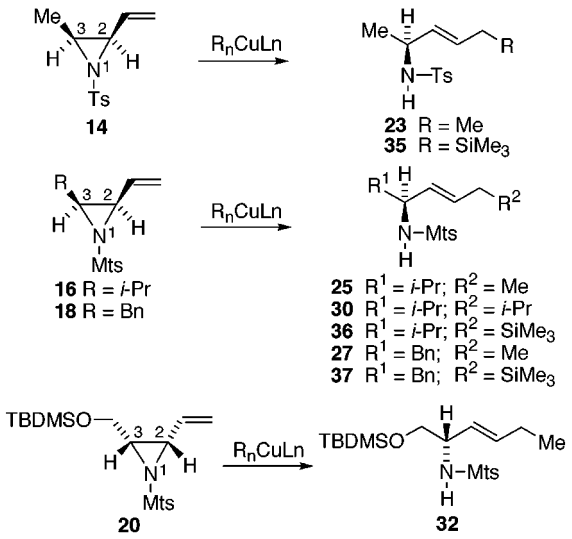
(29) Similar results were obtained by treatment of (2*R*,3*S*)-2,3-*cis*-*N*,*N*-diphenylphosphinoyl-3-(1-methylpropyl)-2-vinylaziridine, prepared from (*S*)-isoleucine, with methylcopper reagents.

Table 2. Organocopper-Mediated Reactions of 2,3-*trans*- and 2,3-*cis*-3-Alkyl-2-vinylaziridines[a]

entry	reactant	reagent	mol equiv	product(s)	combd yld (%)	ratio[b]
1	**13**	MeCu·LiI·LiBr	5	**23** + **24**	99	96:4
2	**13**	MeCu(CN)Li·LiI	4	**23** + **24**	99	89:11
3	**15**	MeCu·2LiI	5	**25** + **26**	98	92:8
4	**15**	MeCu(CN)Li·LiI	5	**25** + **26**	95	85:15
5	**15**	Me_2CuLi·LiI·LiBr	5	**25** + **26**	99	93:7
6	**15**	*i*-PrCu(CN)MgCl	5	**30** + **31**	99	85:15
7	**17**	MeCu·LiI·LiBr	5	**27** + **28** + **29**	99	93:4:3
8	**17**	MeCu(CN)Li·LiI	5	**27** + **28** + **29**	95	95:3:2
9	**19**	MeCu·2LiI	5	**32** + **33** + **34**	93	93:4:3
10	**19**	MeCu(CN)Li·LiI	5	**32** + **33** + **34**	89	94:4:2
11	**14**	MeCu·LiI·LiBr	5	**23**	91	100
12	**14**	$Me_3SiCu(CN)Li$	5	**35**	98	100
13	**16**	MeCu(CN)Li·LiI	5	**25**	99	100
14	**16**	*i*-PrCu(CN)MgCl	5	**30**	99	100
15	**16**	$Me_3SiCu(CN)Li$	5	**36**	99	100
16	**18**	MeCu(CN)Li·LiI	5	**27**	99	100
17	**18**	$Me_3SiCu(CN)Li$	5	**37**	87	100
18	**20**	MeCu(CN)Li·LiI	5	**32**	98	100
19	**20**	MeCu·2LiI	5	**32**	87	100

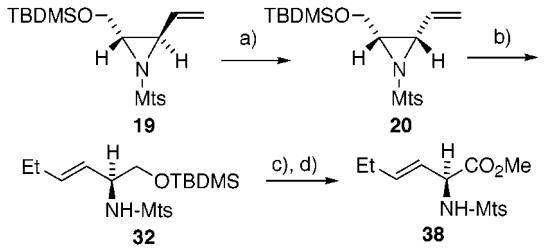
[a] All reactions were carried out in dry THF under slight positive argon pressure. Product ratios were determined by reverse-phase HPLC. All compounds were isolated by flash chromatography and fully characterized. [b] Values correspond to the products in the same order as given in column 5.

Scheme 5



Abbreviations: Ts = *p*-toluenesulfonyl; Mts = 2,4,6-trimethylbenzenesulfonyl; Bn = benzyl; TBDMS = *tert*-butyldimethylsilyl;

Scheme 6



Abbreviations: Mts = 2,4,6-trimethylbenzenesulfonyl;TBDMS = *tert*-butyldimethylsilyl. *Reagents:* a) $Pd(PPh_3)_4$, 4 mol%, 80%; b) MeCu(CN)Li·LiI, 98%; c) 47% HF in MeCN, 96%; d) i. Swern oxid., ii. Jones oxid., iii. diazomethane, 20%

Unsaturated amino acids such as vinylglycines[30] are of particular biological interest as receptor antagonists[31] and enzyme inhibitors.[32] Vinylglycinol[33] and butadienylglycine[34] have also attracted much interest in recent years. Vinylglycine analogue **38** was synthesized from 2,3-*trans*-ziridine **19** in the following manner. Exposure of **19** to 4 mol % of $Pd(PPh_3)_4$ in THF followed by flash chromatography over silica gel gave 2,3-*cis*-isomer **20** in 80% yield, which was then treated with MeCu(CN)Li·LiI to yield exclusively the desired (*E*)-allylamine **32**. The (*E*)-allylamine **32** was transformed into the vinylglycine analogue **38** following a well-established sequence of reactions.

As can be seen from Table 2, there remains the question of why only the 2,3-*cis*-aziridines were exclusively transformed into the corresponding (*E*)-allylamines.[35] To facilitate *ab initio* calculations, the most simple system, *N*-mesyl-2,3-*cis*-3-methyl-2-vinylaziridine **39** and its 2,3-*trans*-isomer **40**, was chosen for investigation of the theoretical aspects.[22] *Ab initio* calculations suggest that the energy difference between the conformers **39-A** and **39-B** of **39** is ca. 10.2 kcal mol^{-1} at the RHF/6-31G** level (Scheme 7). In addition, consideration of the nonbonded interactions in the conformers **39-A** and **39-B** reveals that in conformer **39-B**, which could lead to (*Z*)-allylamine **42**, a substantial nonbonded interaction exists to destabilize **39-B** in comparison with **39-A**. As a result, the reaction of 2,3-*cis*-3-alkyl-2-vinylaziridine **39** with organocopper reagents would be expected to afford exclusively the corresponding (*E*)-allylamine **41**. Thus, the exclusive formation of (*E*)-allylamines from 2,3-*cis*-aziridines (Scheme 5 and Table 2, entries 10−19) may be rationalized by assuming a similar preferred conformation of type **39-A** (Scheme 7).

(30) Dardenne, G.; Casimir, J.; Marlier, M.; Larsen, P. O. *Phytochemistry* **1974**, *13*, 1897. Havlícek, L.; Hanus, J. *Collect. Czech. Chem. Commun.* **1991**, *56*, 1365.

(31) Fagg, G. E.; Olpe, H. R.; Pozza, M. F.; Baud, J.; Steinmann, M.; Schmutz, M.; Portet, C.; Baumann, P.; Thedinga, K.; Bittiger, H.; Allgeier, H.; Heckendorn, R.; Angst, C.; Brundish, D.; Dingwall, J. G. *Br. J. Pharmacol.* **1990**, *99*, 791. Ibuka, T.; Suzuki, K.; Habashita, H.; Otaka, A.; Tamamura, H.; Mimura, N.; Miwa, Y.; Taga, T.; Fujii, N. *J. Chem. Soc., Chem. Commun.* **1994**, 2151.

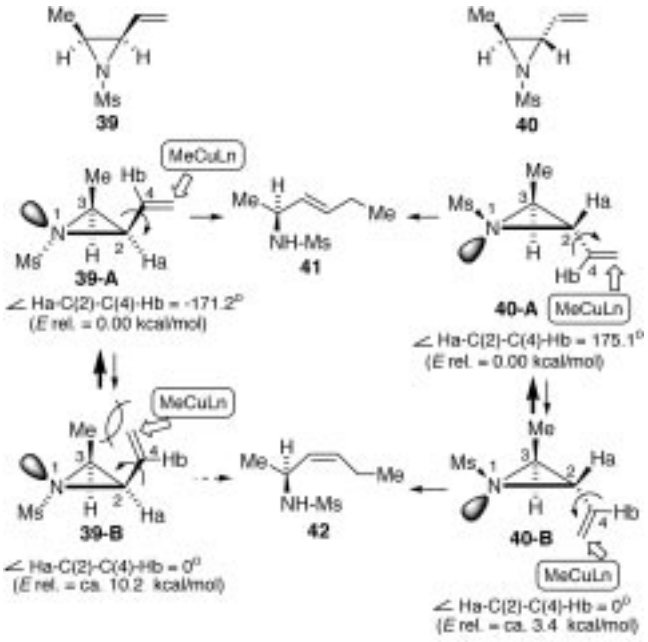
(32) Sufrin, J. R.; Lombardini, J. B.; Keith, D. D. *Biochem. Biophys. Res. Commun.* **1982**, *106*, 251.

(33) Trost, B. M.; Bunt, R. C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 99.

(34) Cameron, S.; Khambay, B. P. S. *Tetrahedron Lett.* **1998**, *39*, 1987.

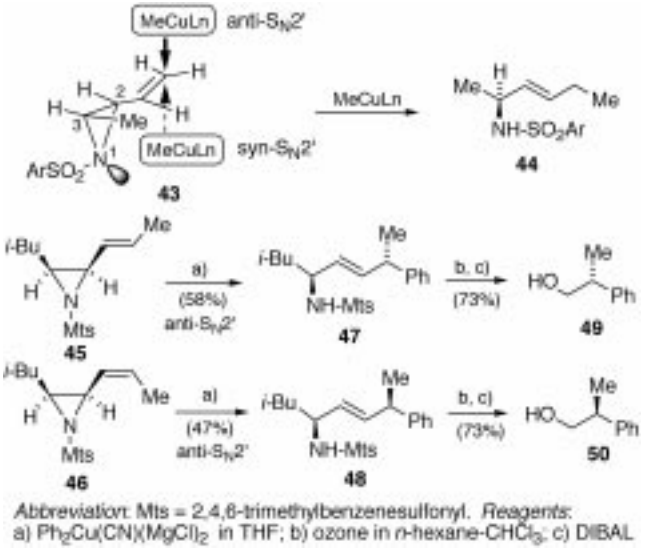
(35) For (*E*)-selective S_N2' reactions, see: Trost, B. M.; Klun, T. P. *J. Org. Chem.* **1980**, *45*, 4256−4257.

Scheme 7



Abbreviation: Ms = methanesulfonyl. Energies are relative to the lowest energy at the HF/6-31G** level.

Scheme 8



Abbreviation: Mts = 2,4,6-trimethylbenzenesulfonyl. *Reagents:* a) $Ph_2Cu(CN)(MgCl)_2$ in THF; b) ozone in *n*-hexane-$CHCl_3$; c) DIBAL

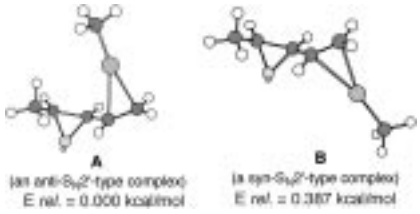
On the other hand, the energy difference between possible conformers **40-A** and **40-B** of 2,3-*trans*-aziridine **40** is predicted to be somewhat smaller (ca. 3.4 kcal/mol). Consequently, formation of a mixture of (*E*)- and (*Z*)-allylamines **41** and **42** would be expected. In actuality, the treatment of *N*-arylsulfonyl-2,3-*trans*-3-alkyl-2-vinylaziridines with organocopper reagents gave the corresponding mixtures of (*E*)- and (*Z*)-allylamines (Table 2, entries 1−10).

Needless to say, the ground state and the reactive conformer are not necessarily the same. In addition, the precise dihedral angle of the reactive conformer would not be near 180° (e.g., **39-A** and **40-A**) or 0° (e.g., **39-B** and **40-B**). Although it is difficult to explain the differences in regioselection (S_N2 versus S_N2'), the picture used in Scheme 7 is representative of our current level of understanding of the stereoselective organocopper-mediated S_N2' ring-opening reactions of *N*-arylsulfonyl-3-alkyl-2-vinylaziridines.

Next, we investigated the S_N2' substitution to determine if the reaction proceeds via an anti- or syn-S_N2' pathway (Scheme 8).[36] Both anti- and syn-S_N2' reactions of a vinylaziridine like **43** (Scheme 8) with organocopper reagents should lead to a single product **44**. If the usual preference for an anti-S_N2' pathway is assumed,[37] an organocopper reagent would be expected to approach 2,3-*cis*-vinylaziridines such as **43** from the side anti to the N(1)−C(2) bond (Scheme 8). However, the mechanism of the S_N2' reaction has been a matter of some controversy since its discovery.[38] The intermolecular S_N2' reactions of allylic carbamates,[39] ammonium salts,[40] some oxiranes,[41] (allyloxy)benzothiazoles,[42] and some γ-mesyloxy-α,β-enoates[43] with organocopper reagents take place by via the syn-S_N2' pathway.

The following experiment shows how the above problem has been clarified. Thus, the reaction of (*E*)-aziridine **45** with a higher order diphenylcyanocuprate, $Ph_2Cu(CN)(MgCl)_2$, provided anti-S_N2'-substitution product **47** as a single product. The absolute configuration at the

(36) Although the detailed mechanism of organocopper S_N2' substitution is still a question, evidence shows the reversible formation of a cuprate−substrate (d−π*) complex in the initial step (Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1981**, *46*, 2144. Goering, H. L.; Seitz, E. P., Jr.; Tseng, C. C. *J. Org. Chem.* **1981**, *46*, 5304. Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3063.). To gain an understanding of the relative stabilities of two methylcopper−substrate (d−π*) complexes, we undertook ab initio calculations at the RHF/LANL1DZ level of theory. Effective core potential (ECP) for Cu and double-ζ were used for other elements. To reduce the size, two model systems **A** and **B** of methylcopper−substrate (d−π*) complexes were chosen. However, it was found that the energy difference between geometries **A** and **B** was predicted to be only 0.387 kcal/mol.



(37) (a) Lipshutz, B. H.; Sengupta, S. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons: New York, 1992; p 135. (b) Lipshutz, B. H. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: London, 1995; Vol. 12, pp 59−130. (c) Ibuka, T.; Yamamoto, Y. In *Organocopper Reagents*; Taylor, R. J. K., Ed.; Oxford Unversity Press: Oxford, 1994; pp 154−157. (d) Ibuka, T.; Nakao, T.; Nishii, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1986**, *108*, 7420. (e) Ibuka, T.; Tanaka, M.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 967. (f) Ibuka, T.; Akimoto, N.; Tanaka, M.; Nishii, S.; Yamamoto, Y. *J. Org. Chem.* **1989**, *54*, 4055. (g) Ibuka, T.; Tanaka, M.; Nishii, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4864. (h) Ibuka, T.; Habashita, H.; Funakoshi, S.; Fujii, N.; Oguchi, Y.; Uyehara, T.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 801. (i) Ibuka, T.; Habashita, H.; Otaka, A.; Fujii, N.; Oguchi, Y.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1991**, *56*, 4371.

(38) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901.

(39) (a) Gallina, C.; Ciattini, P. G. *J. Am. Chem. Soc.* **1979**, *101*, 1035. (b) Ganilla, C. *Tetrahedron Lett.* **1982**, *23*, 3093. (c) Goering, H. L.; Kantner, S. S.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 715. (d) Fleming, I.; Thomas, A. P. *J. Chem. Soc., Chem. Commun.* **1986**, 1456. (e) RajanBabu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 7128. (f) Greene, A. E.; Coelho, F.; Depres, J.-P.; Brocksom, T. J. *Tetrahedron Lett.* **1988**, *29*, 5661. (g) Underiner, T. L.; Goering, H. L. *J. Org. Chem.* **1989**, *54*, 3239.

(40) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1985**, *107*, 6137. Hutchinson, D. K.; Hardinger, S. A.; Fuchs, P. L. *Tetrahedron Lett.* **1986**, *27*, 1425. Hutchinson, D. K.; Fuchs, P. L. *Tetrahedron Lett.* **1986**, *27*, 1429. Pan, V.; Hutchinson, D. K.; Nantz, M. H.; Fuchs, P. L. *Tetrahedron* **1989**, *45*, 467. Berglund, R. A.; Braish, T. F.; Jakubowski, J. A. Fuchs, P. L. *Bioorg. Med. Chem.* **1991**, *1*, 649.

(41) Ziegler, F. E.; Cady, M. A. *J. Org. Chem.* **1981**, *46*, 122.

(42) Valverde, S.; Bernabé, M.; Garcia-Ochoa, S.; Gómez, A. M. *J. Org. Chem.* **1990**, *55*, 2294.

(43) Ibuka, T.; Taga, T.; Habashita, H.; Nakai, K.; Tamamura, H.; Fujii, N.; Chounan, Y.; Nemoto, H.; Yamamoto, Y. *J. Org. Chem.* **1993**, *58*, 1207.

phenylated carbon center was established by conversion of **47** into the known (*R*)-2-phenylpropan-1-ol **49**[44] through a two-step sequence of reactions illustrated in Scheme 8. In a similar manner, the isomeric (*Z*)-propenylaziridine **46** was converted into the known (*S*)-2-phenylpropan-1-ol **50**[45] via the anti-S_N2' intermediate **48**. We have shown unequivocally that organocopper reagents attack alkenylaziridines to give overall anti-S_N2' products.

In summary, we have demonstrated that although reactions of 2,3-*trans*-*N*-arylsulfonyl-3-alkyl-2-alkenylaziridines with organocopper reagents give a mixture of two or three products, the corresponding 2,3-*cis*-isomers provide a highly efficient route to synthetically important nonracemic (*E*)-allylamines. It is also found that the reaction proceeds via a net anti-S_N2' pathway.

Experimental Section

General Methods. All reactions were carried out under a positive pressure of argon. All glassware and syringes were dried in an electric oven at 100 °C prior to use. All melting points are uncorrected. For flash chromatographies, silica gel 60 H (silica gel for thin-layer chromatography, Merck) or silica gel 60 (finer than 230 mesh, Merck) was employed.

(3*S*,4*S*)-4-(*N*-*tert*-Butoxycarbonyl)amino-5-methylhex-1-en-3-ol (7) and (3*R*,4*S*)-4-(*N*-*tert*-Butoxycarbonyl)amino-5-methylhex-1-en-3-ol (8). To a stirred solution of oxalyl chloride (12.5 mL, 0.13 mol) in 80 mL of *n*-hexane−$CHCl_3$ (3:2) at −78 °C under argon was added dropwise a solution of DMSO (28.4 mL, 0.40 mol) in 50 mL of *n*-hexane−$CHCl_3$ (3:2). After 30 min, a solution of the alcohol **6** (20.3 g, 0.1 mol) in 50 mL of *n*-hexane−$CHCl_3$ (3:2) was added to the above reagent at −78 °C, and the mixture was stirred for 30 min. *N*,*N*-Diisopropylethylamine (86.9 mL, 0.50 mol) was added dropwise to the above solution at −78 °C, and the mixture was stirred for 30 min with warming to 0 °C. The mixture was extracted with Et_2O and the extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration under reduced pressure gave a crude aldehyde. To a stirred solution of $ZnCl_2$ (13.6 g, 0.10 mol) in 100 mL of dry THF at −78 °C was added vinylmagnesium chloride (187.5 mL, 1.6 M solution in THF, 0.30 mol). After the mixture was stirred at this temperature for 10 min, a solution of the above crude aldehyde in 50 mL of dry THF was added dropwise to the organometallic reagent and the mixture was stirred at this temperature for 2 h. The mixture was quenched with 10 mL of saturated NH_4Cl. The mixture was extracted with Et_2O−EtOAc (1:1), and the extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$, and brine and dried over $MgSO_4$. The usual workup led to a mixture of products as a colorless oil, which was separated by flash chromatography over silica gel eluting with *n*-hexane−EtOAc 5:1, yielding, in order of elution, **7** (6.63 g, 29% yield) and **8** (2.20 g, 10% yield). **7**: colorless needles from *n*-hexane; mp 41 °C; $[\alpha]^{23}_D$ −61.14 (*c* 0.99, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (d, J = 6.8 Hz, 3 H), 0.99 (d, J = 6.7 Hz, 3 H), 1.43 (s, 9 H), 1.91 (m, 1 H), 2.22 (d, J = 4.1 Hz, 1 H), 3.27 (m, 1 H), 4.26 (m, 1 H), 4.75 (d, J = 8.1 Hz, 1 H), 5.18 (ddd, J = 10.5, 0.6, 0.6 Hz, 1 H), 5.29 (ddd, J = 17.1, 1.4, 1.4 Hz, 1 H), 5.91 (ddd, J = 17.1, 10.5, 5.8 Hz, 1 H). Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11. Found: C, 62.81; H, 10.10; N, 6.06. **8**: colorless needles from *n*-hexane−Et_2O (4:1); mp 69 °C; $[\alpha]^{24}_D$ −31.78 (*c* 1.076, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.94 (d, J = 6.8 Hz, 3 H), 0.99 (d, J = 6.8 Hz, 3 H), 1.45 (s, 9 H), 1.69−1.82 (m, 1 H), 2.71 (d, J = 5.4 Hz, 1 H), 3.50 (m, 1 H), 4.27 (m, 1 H), 4.44 (d, J = 7.8 Hz, 1 H), 5.25 (d, J = 10.8 Hz, 1 H), 5.36 (d, J = 17.3 Hz, 1 H), 5.87 (ddd, J = 17.3, 10.8, 5.9 Hz, 1 H). Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11. Found: C, 62.55; H, 10.15; N, 6.03.

(3*S*,4*S*)-4-(*N*-Diphenylphosphinoyl)amino-5-methylhex-1-en-3-ol (9). Trifluoroacetic acid (2 mL) was added to 229 mg (1.0 mmol) of the alcohol **7** at 0 °C, and the mixture was stirred for 1 h with warming to room temperature. The mixture was concentrated under reduced pressure to an oily residue, which was made alkaline with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with brine and concentrated under reduced pressure to leave a colorless oil. To the oil in 2 mL of DMF were added successively 0.166 mL (1.2 mmol) of Et_3N and 260 mg (1.1 mmol) of diphenylphosphinoyl chloride in 5 mL of DMF. After the mixture was stirred for 14 h at 0 °C, 3 mL of saturated $NaHCO_3$ was added with stirring. The mixture was made acidic with saturated citric acid and extracted with EtOAc. The extract was washed with water, 5% $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration followed by flash chromatography over silica gel with *n*-hexane−EtOAc (1:2) gave 129 mg (39% yield) of the title compound **9**: colorless needles from Et_2O; mp 159−160 °C; $[\alpha]^{22}_D$ −73.67 (*c* 1.20, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (d, J = 6.8 Hz, 3 H), 0.91 (d, J = 6.5 Hz, 3 H), 1.84−1.99 (m, 1 H), 2.68−2.79 (m, 1 H), 2.94 (dd, J = 11.1, 4.2 Hz, 1 H), 3.97 (ddd, J = 7.0, 7.0, 1.5 Hz, 1 H), 5.16 (dd, J = 10.4, 1.0 Hz, 1 H), 5.30 (dd, J = 13.0, 1.0 Hz, 1 H), 5.33 (s, 1 H), 5.77 (ddd, J = 17.6, 10.4, 7.6 Hz, 1 H), 7.41−7.58 (m, 6 H), 7.88−8.01 (m, 4 H); LRMS (FAB), *m*/*z* 330 (MH^+, base peak). HRMS (FAB), *m*/*z* calcd for $C_{19}H_{25}NO_2P$ (MH^+) 330.1623, found 330.1620.

(3*R*,4*S*)-4-(*N*-Diphenylphosphinoyl)amino-5-methylhex-1-en-3-ol (10). By use of a procedure identical with that described for the preparation of **9** from **7**, the alcohol **8** (1.374 g, 6.0 mmol) was converted into 1.081 g (55% yield) of the title compound **10**: colorless needles from Et_2O; mp 113 °C; $[\alpha]^{21}_D$ −102 (*c* 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.95 (d, J = 6.8 Hz, 3 H), 1.05 (d, J = 6.8 Hz, 3 H), 1.53−1.67 (m, 1 H), 2.70 (dd, J = 11.9, 3.2 Hz, 1 H), 2.78−2.89 (m, 1 H), 4.32−4.37 (m, 1 H), 5.32 (ddd, J = 10.5, 1.6, 1.6 Hz, 1 H), 5.51 (ddd, J = 17.0, 1.6, 1.6 Hz, 1 H), 5.76 (d, J = 11.1 Hz, 1 H), 5.90 (ddd, J = 17.0, 10.5, 4.9 Hz, 1 H), 7.42−7.57 (m, 6 H), 7.89−7.98 (m, 4 H). Anal. Calcd for $C_{19}H_{24}NO_2P$: C, 69.28; H, 7.43; N, 4.25. Found: C, 69.14; H, 7.47; N, 4.13.

(2*R*,3*S*)-*N*-Diphenylphosphinoyl-3-isopropyl-2-vinylaziridine (11). Triphenylphosphine (2.46 g, 9.4 mmol) and diethyl azodicarboxylate (1.60 mL, 10.1 mmol) were added to a stirred solution of the alcohol **9** (1.28 g, 3.9 mmol) in 20 mL of dry THF at 0 °C, and the mixture was stirred at this temperature for 30 min. The mixture was concentrated under reduced pressure to an oil, which was flash chromatographed over silica gel with *n*-hexane−EtOAc (1:1) to give 938 mg (77% yield) of the title compound **11**: colorless crystals from *n*-hexane−Et_2O (5:1); mp 67−68 °C; $[\alpha]^{25}_D$ −11.0 (*c* 1.036, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.57 (d, J = 6.8 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H), 1.43−1.58 (m, 1 H), 2.58 (ddd, J = 16.2, 9.5, 6.5 Hz, 1 H), 3.29 (ddd, J = 14.0, 7.3, 6.5 Hz, 1 H), 5.27 (dd, J = 10.2, 1.4 Hz, 1 H), 5.39 (dd, J = 17.0, 1.4 Hz, 1 H), 5.77 (ddd, J = 17.0, 10.2, 7.3 Hz, 1 H), 7.39−7.52 (m, 6 H), 7.86−7.94 (m, 4 H). Anal. Calcd for $C_{19}H_{22}NOP$: C, 73.29; H, 7.12; N, 4.50. Found: C, 73.21; H, 7.12; N, 4.45.

(2*S*,3*S*)-*N*-Diphenylphosphinoyl-3-isopropyl-2-vinylaziridine (12). By use of a procedure identical with that described for the preparation of **11** from **9**, the alcohol **10** (987 mg, 3.0 mmol) was converted into 481 mg (52% yield) of the title compound **12** by treatment with PPh_3 (4.56 g, 14.7 mmol) and diethyl azodicarboxylate (3.88 mL, 24.6 mmol) in THF (10 mL) at 0 °C for 14 h followed by the usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (3:1). **12:** colorless needles from *n*-hexane−Et_2O (3:1); mp 68 °C; $[\alpha]^{21}_D$ −95.38 (*c* 1.04, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.67 (d, J = 6.7 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 1.55−1.73 (m, 1 H), 2.68 (ddd, J = 15.7, 7.3, 3.2 Hz, 1 H), 3.01 (ddd, J = 12.3, 9.5, 3.2 Hz, 1 H), 5.03 (dd, J = 10.0, 1.3 Hz, 1 H), 5.21 (dd, J = 17.0, 1.3 Hz, 1 H), 6.04 (ddd, J = 17.0, 10.0, 10.0 Hz, 1 H), 7.30−7.52 (m, 6 H), 7.80−7.99 (m, 4 H). Anal. Calcd

(44) Roger, R.; Neilson, D. J. *J. Chem. Soc.* **1960**, 627. Johnson, R. A.; Hall, C. M.; Krueger, W. C.; Murray, H. C. *Bioorg. Chem.* **1973**, *2*, 99.

(45) Watson, M. B.; Youngson, G. W. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1597.

for $C_{19}H_{22}NOP$: C, 73.29; H, 7.12; N, 4.50. Found: C, 73.34; H, 7.18; N, 4.56.

(*E*,3*S*)-3-(*N*-Diphenylphosphinoyl)amino-2-methylhept-4-ene (21). To a stirred suspension of CuCN (50 mg, 0.64 mmol) in 2 mL of dry THF under argon was added by a syringe MeLi·LiBr (0.86 mL, 1.1 M solution in THF) at −78 °C, and the mixture was stirred at this temperature for 10 min. The aziridine **11** (50 mg, 0.16 mmol) in 1 mL of dry THF was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 2 mL of a 1:1 saturated NH_4Cl−28% NH_4OH solution. The mixture was extracted with EtOAc, and the extract was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was flash chromatographed over silica gel with EtOAc to give 52 mg (99% yield) of a 99:1 mixture of **21** and **22** as a crystalline mass. Recrystallization from *n*-hexane−EtOAc (5:1) gave pure **21** as colorless needles: mp 150−151 °C; $[\alpha]^{22}_D$ +12.14 (*c* 1.008, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (d, J = 7.0 Hz, 6 H), 0.93 (t, J = 7.8 Hz, 3 H), 1.78−1.92 (m, 1 H), 1.93−2.03 (m, 2 H), 2.89 (dd, J = 9.2, 6.8 Hz, 1 H), 3.44 (m, 1 H), 5.31 (dd, J = 15.4, 7.0 Hz, 1 H), 5.46 (dt, J = 15.4, 5.9 Hz, 1 H), 7.38−7.50 (m, 6 H), 7.83−7.96 (m, 4 H); LRMS (FAB), *m*/*z* 328 (MH^+, base peak); HRMS (FAB), *m*/*z* calcd for $C_{20}H_{27}NOP$ (MH^+) 328.1830, found 328.1835. The (*Z*)-isomer **22** could not be isolated. In a similar manner, the 2,3-*trans*-aziridine **12** was converted into a 99:1 mixture of **21** and **22** in 93% combined yield (Table 1, entry 7).

(*E*,2*S*)-2-[*N*-(4-Methylbenzene)sulfonyl]amino-3-hexene (23) and Its (*Z*,2*S*)-Isomer (24). (Table 2, entry 1). To a stirred suspension of CuI (328 mg, 1.73 mmol) in THF (2 mL) at −78 °C was added dropwise a solution of MeLi·LiBr (1.16 mL, 1.73 mmol, 1.5M in Et_2O), and the mixture was allowed to warm to 0 °C. The mixture was cooled to −78 °C, and a solution of the aziridine **13** (82 mg, 0.344 mmol) in THF (2 mL) was added dropwise under stirring. After 30 min, 2 mL of a 1:1 solution of 28% NH_4OH and saturated NH_4Cl was added to the mixture. The whole was extracted with Et_2O, and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave a 96:4 mixture of **23** and **24** in 99% combined yield as a colorless oil. The mixture was chromatographed over silica gel with *n*-hexane−$CHCl_3$−EtOAc (80:120:1) to yield, in order of elution, 83.5 mg of **23** and 3.5 mg of **24**. **23**: $[\alpha]^{25}_D$ −25 (*c* 0.55, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, J = 7.4 Hz, 3 H), 1.16 (d, J = 6.7 Hz, 3 H), 1.86 (m, 2 H), 2.41 (s, 3 H), 3.86 (m, 1 H), 4.55 (d, J = 7.4 Hz, 1 H), 5.15 (dddd, J = 15.4, 6.5, 1.6, 1.6 Hz, 1 H), 5.44 (dddd, J = 15.4, 6.3, 6.3, 1.2 Hz, 1 H), 7.25−7.30 (m, 2 H), 7.72−7.76 (m, 2 H); LRMS (FAB), *m*/*z* 254 (MH^+, base peak); HRMS (FAB), *m*/*z* calcd for $C_{13}H_{20}NO_2S$ (MH^+) 254.1215, found 254.1212. **24**: colorless oil; $[\alpha]^{19}_D$ +68.2 (*c* 0.355, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, J = 7.5 Hz, 3H), 1.17 (d, J = 6.8 Hz, 3 H), 1.82 (dddd, J = 11.8, 7.5, 7.5, 1.6 Hz, 1 H), 1.89 (dddd, J = 11.8, 7.5, 7.5, 1.6 Hz, 1 H), 2.42 (s, 3 H), 4.17 (dddd, J = 9.0, 6.4, 6.4, 0.9 Hz, 1 H), 4.31 (d, J = 6.4 Hz, 1 H), 5.06 (dddd, J = 10.7, 9.0, 1.6, 1.6 Hz, 1 H), 5.26 (dtd, J = 10.7, 7.5, 0.9 Hz, 1 H), 7.28 (d, J = 8.4 Hz, 2 H), 7.73 (dt, J = 8.4, 2.0 Hz, 2 H). LRMS (FAB), *m*/*z* 254 (MH^+); HRMS (FAB), *m*/*z* calcd for $C_{13}H_{20}NO_2S$ (MH^+) 254.1215; found 254.1219.

(*E*,2*S*)-2-[*N*-(4-Methylbenzene)sulfonyl]amino-3-hexene (23) (Table 2, entry 11). By use of a procedure similar to that described for the preparation of **23** and **24** from **13**, 47.4 mg (0.2 mmol) of the 2,3-*trans*-vinylaziridine **14** was converted into 46 mg (91% yield) of the title compound **23** as a colorless oil: $[\alpha]^{25}_D$ −26 (*c* 0.407, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, J = 7.4 Hz, 3 H), 1.16 (d, J = 6.7 Hz, 3 H), 1.86 (m, 2 H), 2.41 (s, 3 H), 3.86 (m, 1 H), 4.55 (d, J = 7.4 Hz, 1 H), 5.15 (dddd, J = 15.4, 6.5, 1.6, 1.6 Hz, 1 H), 5.44 (dddd, J = 15.4, 6.3, 6.3, 1.2 Hz, 1 H), 7.25−7.30 (m, 2 H), 7.72−7.76 (m, 2 H). LRMS (FAB), *m*/*z* 254 (MH^+, base peak). HRMS (FAB), *m*/*z* calcd for $C_{13}H_{20}NO_2S$ (MH^+) 254.1215, found 254.1218.

(*E*,3*S*)-2-Methyl-3-[*N*-(2,4,6-trimethylbenzene)sulfonyl]amino-4-heptene (25) (Table 2, entry 13). To a stirred slurry of CuCN (61 mg, 0.68 mmol) in 1 mL of dry THF under argon was added by a syringe 0.17 mL (0.68 mmol) of a 1.0 M solution of MeLi·LiI in Et_2O at −78 °C, and the mixture was allowed to warm to room temperature and stirred at this temperature for 15 min. A solution of the 2,3-*cis*-vinylaziridine **16** (50 mg, 0.17 mmol) in dry THF (1 mL) was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 4 mL of a 1:1 saturated NH_4Cl−28% NH_4OH solution. The mixture was extracted with Et_2O−EtOAc (1:1), and the extract was washed with a saturated NaCl solution and dried over $MgSO_4$. Concentration under reduced pressure gave a colorless oil, which was purified by flash chromatography over silica gel eluting with *n*-hexanes−EtOAc (4:1) to give 52 mg of the title compound **25** in 99% yield: colorless crystals from *n*-hexane−Et_2O (3:1); mp 87−88 °C; $[\alpha]^{20}_D$ +31.9 (*c* 0.97, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.74 (t, J = 7.3 Hz, 3 H), 0.81 (d, J = 6.5 Hz, 3 H), 0.87 (d, J = 6.5 Hz, 3 H), 1.64−1.81 (m, 3 H), 2.28 (s, 3 H), 2.61 (s, 6 H), 3.46 (td, J = 7.6, 5.7 Hz, 1 H), 4.40 (d, J = 7.6 Hz, 1 H), 4.97 (dddd, J = 15.3, 8.4, 1.4, 1.4 Hz, 1 H), 5.23 (dddd, J = 15.3, 6.2, 6.2, 0.5 Hz, 1 H), 6.91 (s, 2 H). Anal. Calcd for $C_{17}H_{27}NO_2S$: C, 65.98; H, 8.79; N, 4.53. Found: C, 65.71; H, 8.75; N, 4.40.

(*E*,2*S*)-1-Phenyl-2-[*N*-(2,4,6-trimethylbenzene)sulfonyl]-amino-3-hexene (27) (Table 2, entry 16). By use of a procedure similar to that described for the preparation of **25** from **16**, 50 mg (0.15 mmol) of the 2,3-*cis*-vinylaziridine **18** was converted into 52 mg (99% yield) of the title compound **27** as colorless needles from *n*-hexane−Et_2O (3:1): mp 50−51 °C; $[\alpha]^{19}_D$ −13.0 (*c* 1.04, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.77 (t, J = 7.4 Hz, 3 H), 1.76−1.86 (m, 2 H), 2.27 (s, 3 H), 2.50 (s, 6 H), 2.77 (m, 2 H), 3.89 (m, 1 H), 4.42 (d, J = 6.2 Hz, 1 H), 5.10 (dddd, J = 15.3, 7.6, 1.5, 1.5 Hz, 1 H), 5.36 (dddd, J = 15.3, 5.1, 5.1, 0.5 Hz, 1 H), 6.87 (s, 2 H), 7.02−7.08 (m, 2 H), 7.17−7.27 (m, 3 H). Anal. Calcd for $C_{20}H_{27}NO_2S$: C, 70.55; H, 7.61; N, 3.90. Found: C, 70.52; H, 7.68; N, 3.90.

(*E*,3*S*)-2,7-Dimethyl-3-[*N*-(2,4,6-trimethylbenzene)sulfonyl]amino-4-octene (30) (Table 2, entry 14). To a stirred slurry of CuCN (35 mg, 0.40 mmol) in 1 mL of dry THF under argon was added by a syringe 0.28 mL (0.40 mmol) of a solution of 1.4 M-PrMgCl in Et_2O at −78 °C, and the mixture was allowed to warm to 0 °C and stirred at this temperature for 15 min. A solution of the 2,3-*cis*-vinylaziridine **16** (29 mg, 0.10 mmol) in dry THF (1 mL) was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 6 mL of a 1:1 saturated NH_4Cl−28% NH_4OH solution. The mixture was extracted with Et_2O−EtOAc (1:5), and the extract was washed with a saturated NaCl solution and dried over $MgSO_4$. Concentration under reduced pressure gave a colorless oily residue, which was purified by flash chromatography over silica gel eluting with *n*-hexane−EtOAc (4:1) to give the *trans*-alkene **30** (33 mg, 99% yield) as a colorless oil: $[\alpha]^{21}_D$ −0.85 (*c* 3.79, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.74 (d, J = 6.5 Hz, 3 H), 0.76 (d, J = 6.5 Hz, 3 H), 0.82 (d, J = 7.0 Hz, 3 H), 0.86 (d, J = 7.0 Hz, 3 H), 1.39 (m, 1 H), 1.55−1.78 (m, 3 H), 2.28 (s, 3 H), 2.62 (s, 6 H), 3.46 (dd, J = 8.1, 5.1 Hz, 1 H), 4.43 (d, J = 7.8 Hz, 1 H), 5.01 (dddd, J = 15.2, 7.8, 1.1, 1.1 Hz, 1 H), 5.18 (dt, J = 15.2, 6.8 Hz, 1 H), 6.91 (s, 2 H); LRMS (FAB), *m*/*z* 338 (MH^+); HRMS (FAB), *m*/*z* calcd for $C_{19}H_{32}NO_2S$ (MH^+) 338.2154, found 338.2144.

(*E*,2*S*)-1-(*tert*-Butyldimethylsiloxy)-2-[*N*-(2,4,6-trimethylbenzene)sulfonyl]amino-3-hexene (32) (Table 2, entry 18). By use of a procedure similar to that described for the preparation of **25** from **16**, 515 mg (1.3 mmol) of the 2,3-*cis*-vinylaziridine **20** was converted into 526 mg (98% yield) of the title compound **32** by treatment with MeCu(CN)Li·LiI followed by flash chromatography over silica gel eluting with *n*-hexanes−EtOAc (8:1): colorless needles from *n*-hexane−Et_2O (2:1); mp 67−68 °C; $[\alpha]^{21}_D$ +19.7 (*c* 1.03, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.03 (s, 6 H), 0.79 (t, J = 7.3 Hz, 3 H), 0.87 (s, 9 H), 1.77−1.87 (m, 2 H), 2.29 (s, 3 H), 2.61 (s, 6 H), 3.44 (dd, J = 9.9, 5.9 Hz, 1 H), 3.53 (dd, J = 9.9, 4.3 Hz, 1 H), 3.62−3.71 (m, 1 H), 5.03−5.13 (m, 2 H), 5.49 (dddd, J = 15.4, 5.9, 5.9, 0.6 Hz, 1 H), 6.92 (s, 2 H). Anal. Calcd for $C_{21}H_{37}NO_3SSi$: C, 61.27; H, 9.06; N, 3.40. Found: C, 61.36; H, 9.06; N, 3.43.

(*E*,4*S*)-1-Trimethylsilyl-4-[*N*-(4-methylbenzene)sulfonyl]-amino-2-pentene (35) (Table 2, entry 12). To a stirred solution of THF−HMPA (3:1; 4 mL) under argon were added by syringe 0.20 mL (1.00 mmol) of $Me_3SiSiMe_3$ and 0.62 mL (1.00 mmol) of 1.6 M *n*-BuLi in *n*-hexane at −78 °C, and the mixture was stirred for 1 h. To a slurry of CuCN (89 mg, 1.00 mmol) in 1 mL of dry THF was added a solution of the above reagent, and the mixture was allowed to warm to −30 °C and stirred at −78 °C for 5 min. A solution of the 2,3-*cis*-vinylaziridine **14** (24 mg, 0.10 mmol) in dry THF (1 mL) was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 4 mL of a 1:3 saturated NH_4Cl−28% NH_4OH solution. The mixture was extracted with EtOAc, and the extract was washed with saturated brine and dried over $MgSO_4$. Concentration under reduced pressure gave a colorless oil, which was purified by flash chromatography over silica gel eluting with *n*-hexane−EtOAc (8:1) to give the title compound **35** (31 mg, 98% yield) as a colorless oil: $[\alpha]^{17}_D$ −48.5 (*c* 0.231, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.07 (s, 9 H), 1.16 (d, J = 6.6 Hz, 3 H), 1.32 (m, 2 H), 2.42 (s, 3 H), 3.83 (m, 1 H), 4.33 (d, J = 7.3 Hz, 1 H), 5.05 (dddd, J = 15.7, 8.1, 0.8, 0.8 Hz, 1 H), 5.42 (dddd, J = 15.7, 8.4, 8.4, 1.0 Hz, 1 H), 7.26−7.30 (m, 2 H), 7.72−7.76 (m, 2 H). LRMS (FAB), *m*/*z* 312 (MH^+); HRMS (FAB), *m*/*z* calcd for $C_{15}H_{26}NO_2SSi$ (MH^+) 312.1453, found 312.1442.

(*E*,4*S*)-5-Methyl-1-trimethylsilyl-4-[*N*-(2,4,6-trimethylbenzene)sulfonyl]amino-2-hexene (36) (Table 2, entry 15). By use of a procedure similar to that described for the preparation of **35** from **14**, 29 mg (0.10 mmol) of the 2,3-*trans*-vinylaziridine **16** was converted into 36 mg (99% yield) of the title compound **36** as a colorless oil: $[\alpha]^{17}_D$ −46.3 (*c* 0.468, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.09 (s, 9 H), 0.80 (d, J = 6.8 Hz, 3 H), 0.86 (d, J = 6.8 Hz, 3 H), 1.20 (m, 2 H), 1.66−1.78 (m, 1 H), 2.28 (s, 3 H), 2.62 (s, 6 H), 3.44 (m, 1 H), 4.39 (d, J = 7.4 Hz, 1 H), 4.88 (ddd, J = 15.1, 8.1, 1.4 Hz, 1 H), 5.21 (ddd, J = 15.1, 7.5, 7.5 Hz, 1 H), 6.91 (s, 2 H). LRMS (FAB), *m*/*z* 368 (MH^+). HRMS (FAB), *m*/*z* calcd for $C_{19}H_{34}NO_2SSi$ (MH^+) 368.2079; found 368.2087.

(*E*,4*S*)-5-Phenyl-1-trimethylsilyl-4-[*N*-(2,4,6-trimethylbenzene)sulfonyl]amino-2-pentene (37) (Table 2, entry 17). By use of a procedure similar to that described for the preparation of **35** from **14**, 34 mg (0.10 mmol) of the 2,3-*cis*-vinylaziridine **18** was converted into 36 mg (87% yield) of the title compound **37** as colorless needles: mp 69−70 °C; $[\alpha]^{20}_D$ −39.4 (*c* 0.966, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.13 (s, 9 H), 1.24 (m, 2 H), 2.28 (s, 3 H), 2.52 (s, 6 H), 2.74 (dd, J = 13.5, 7.3 Hz, 1 H), 2.81 (dd, J = 13.5, 6.2 Hz, 1 H), 3.87 (m, 1 H), 4.39 (d, J = 6.2 Hz, 1 H), 4.99 (dddd, J = 15.1, 7.6, 1.4, 1.4 Hz, 1 H), 5.31 (dddd, J = 15.1, 8.6, 1.0, 1.0 Hz, 1 H), 6.88 (s, 2 H), 7.03−7.07 (m, 2 H), 7.14−7.26 (m, 3 H); LRMS (FAB), *m*/*z* 416 (MH^+). HRMS (FAB), *m*/*z* calcd for $C_{23}H_{34}NO_2SSi$ (MH^+) 416.2079, found 416.2075.

Methyl (*E*,2*S*)-2-[*N*-(2,4,6-Trimethylbenzene)sulfonyl]-amino-3-hexen-1-enoate (38). To a stirred solution of the alkene **32** (502 mg, 1.22 mmol) in 4 mL of MeCN were added 3 mL of 46% HF and 2 mL of H_2O at 0 °C, and the mixture was stirred for 16 h at room temperature and for 4 h at 50 °C. The mixture was made basic with 3 mL of 28% NH_4OH and extracted with EtOAc. The extract was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was purified by flash chromatography over silica gel with *n*-hexane−EtOAc (3:1) to give (*E*,2*S*)-2-*N*-[(2,4,6-trimethylbenzene)sulfonyl]amino-3-hexen-1-ol as a colorless oil (347 mg, 96% yield): $[\alpha]^{23}_D$ +14.1 (*c* 1.01, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.80 (t, J = 7.6 Hz, 3 H), 1.84 (m, 1 H), 2.17 (t, J = 5.4 Hz, 3 H), 2.29 (s, 3 H), 2.63 (s, 6 H), 3.45−3.62 (m, 2 H), 3.67−3.79 (m, 1 H), 5.07 (d, J = 7.3 Hz, 1 H), 5.10 (dd, J = 15.4, 7.3 Hz, 1 H), 5.45 (ddd, J = 15.4, 6.2, 6.2 Hz, 1 H), 6.94 (s, 2 H); LRMS (FAB), *m*/*z* 298 (MH^+); HRMS (FAB), *m*/*z* calcd for $C_{15}H_{24}NO_3S$ (MH^+) 298.1477, found 298.1472. To a stirred solution of oxalyl chloride (0.12 mL, 3.6 mmol) in 70 mL of CH_2Cl_2 was added dropwise DMSO (0.77 mL, 10.8 mmol) in 2 mL of *n*-hexane−$CHCl_3$ (1:1) at −78 °C under argon, and the mixture was stirred at this temperature for 30 min. To the above mixture was added 357 mg of (*E*,2*S*,)-2-*N*-[(2,4,6-trimethylbenzene)sulfonyl]amino-3-hexen-1-ol in 2 mL of $CHCl_3$ at −78 °C. After 30 min, *N*,*N*-diisopropylethylamine (86.9 mL, 0.50 mol) was added at −78 °C under stirring, and the mixture was stirred at this temperature for 30 min. The mixture was made acidic with saturated citric acid and the whole was extracted with Et_2O. The extract was washed with water and 5% $NaHCO_3$ and dried over $MgSO_4$. Concentration under reduced pressure gave a crude aldehyde as a colorless oil. The oily crude aldehyde in acetone (3 mL) was oxidized with Jones' reagent. Methylation with diazomethane followed by the usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) gave 78 mg (20% yield) the title compound **38** as a colorless oil: $[\alpha]^{27}_D$ +42.1 (*c* 0.737, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, J = 7.4 Hz, 3 H), 1.92 (m, 1 H), 2.29 (s, 3 H), 2.63 (s, 6 H), 3.58 (s, 3 H), 4.44 (dddd, J = 8.1, 8.1, 1.5, 1.5 Hz, 1 H), 5.21 (dddd, J = 15.1, 8.1, 1.5, 1.5 Hz, 1 H), 5.33 (d, J = 8.1 Hz, 1 H), 5.73 (ddd, J = 15.1, 6.5, 1.5 Hz, 1 H), 6.94 (s, 2 H); LRMS (FAB), *m*/*z* 326 (MH^+); HRMS (FAB), *m*/*z* calcd for $C_{16}H_{24}NO_4S$ (MH^+) 326.1426, found 326.1432.

(*E*,2*S*,5*S*)-7-Methyl-2-phenyl-5-*N*-[(2,4,6-trimethylbenzene)sulfonyl]aminooct-3-ene (47). To a stirred solution of CuCN (172 mg, 1.92 mmol) and LiCl (189 mg, 3.84 mmol) in 3 mL of dry THF under argon was added by a syringe 3 mL (3.84 mmol) of PhMgBr (1.3 M solution in THF) at − 78 °C, and the mixture was stirred at this temperature for 30 min. The aziridine **45** (154 mg, 0.48 mmol) in 4 mL of dry THF was added dropwise to the above reagent at −78 °C with stirring, and the stirring was continued for 30 min followed by quenching with 4 mL of a 3:5 mixture of saturated NH_4Cl−28% NH_4OH. The mixture was extracted with Et_2O, and the extract was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was flash chromatographed over silica gel with *n*-hexane−EtOAc (9:1) to give 90 mg (47% yield) of the title compound **47**: colorless needles from *n*-hexane; mp 82−83 °C; $[\alpha]^{19}_D$ −18.15 (*c* 0.981, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (d, J = 6.5 Hz, 3 H), 0.85 (d, J = 6.8 Hz, 3 H), 1.07 (d, J = 6.8 Hz, 3 H), 1.21−1.45 (m, 2 H), 1.62 (m, 1 H), 2.27 (s, 3 H), 2.57 (s, 6 H), 3.11 (m, 1 H), 3.75 (m, 1 H), 4.52 (d, J = 7.3 Hz, 1 H), 4.95 (ddd, J = 15.2, 7.8, 1.4 Hz, 1 H), 5.44 (ddd, J = 15.2, 5.9, 0.5 Hz, 1 H), 6.86 (s, 2 H), 6.94−6.97 (m, 2 H), 7.15−7.28 (m, 3 H). Anal. Calcd for $C_{24}H_{33}NO_2S$: C, 72.14; H, 8.32; N, 3.51. Found: C, 71.86; H, 8.37; N, 3.36.

(*E*,2*R*,5*S*)-7-Methyl-5-(2,4,6-trimethylbenzenesulfonyl))amino-2-phenyloct-3-ene (48). By use of a procedure identical with that described for the preparation of **47** from **45**, the aziridine **46** (321 mg, 1.0 mmol) was converted into 233 mg (58% yield) of the title compound **48** as a colorless oil: $[\alpha]^{23}_D$ − 27.5 (*c* = 0.898, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.81 (d, J = 6.8 Hz, 6 H), 1.12 (d, J = 7.0 Hz, 3 H), 1.19−1.42 (m, 2 H), 1.58 (m, 1 H), 2.29 (s, 3 H), 2.61 (s, 6 H), 3.18 (m, 1 H), 3.74 (m, 1 H), 4.39 (d, J = 7.8 Hz, 1 H), 5.02 (ddd, J = 15.4, 8.1, 1.4 Hz, 1 H), 5.43 (ddd, J = 15.4, 10.0, 7.0 Hz, 1 H), 6.92 (s, 2 H), 6.90−7.02 (m, 2 H), 7.14−7.29 (m, 3 H); LRMS (FAB), *m*/*z* 400 (MH^+); HRMS (FAB), *m*/*z* calcd for $C_{24}H_{34}NO_2S$ (MH^+) 400.2310, found 400.2314.

(*R*)-2-Phenylpropan-1-ol (49) and (*S*)-*N*-[(2,4,6-Trimethylbenzene)sulfonyl]leucinol. Ozone was bubbled through a solution of the alkene **47** (80 mg, 0.20 mmol) in 6 mL of *n*-hexane−$CHCl_3$ (1:1) at − 78 °C until a blue color persisted. Zinc powder (5 g) was added to the mixture, and the mixture was stirred for 10 min, during which time it was allowed to warm to 0 °C. To the above mixture at −78 °C was added dropwise 10.0 mL (10.0 mmol) of a 1.0 M toluene solution of DIBAL, and the mixture was allowed to warm to room temperature. Saturated NH_4Cl (3 mL) was added with vigorous stirring at −78 °C. The mixture was extracted with Et_2O−EtOAc (1:1), and the extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$, and brine and dried over $MgSO_4$. The usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) gave, in order of elution, (2*R*)-2-phenylpropan-1-ol **49** (20 mg, 73% yield) and (*S*)-*N*-[(2,4,6-trimethylbenzene)sulfonyl]leucinol (44 mg, 73% yield).

49: a colorless oil; $[\alpha]^{23}_D$ +16.53 (*c* 1.471, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.27 (d, J = 6.9 Hz, 3 H), 1.45 (broad s, 1 H), 2.94 (qd, J = 6.9, 6.9 Hz, 1 H), 3.68 (m, 2 H), 7.20−7.25 (m, 3 H), 7.30−7.36 (m, 2 H); LRMS (EI), *m*/*z* 136 (M^+), 106, 105 (base peak), 91, 79, 77. HRMS (EI), *m*/*z* calcd for $C_9H_{12}O$ (M^+) 136.0888, found 136.0893. (*S*)-*N*-[(2,4,6-Trimethylbenzene)sulfonyl]leucinol: colorless needles from *n*-hexanes−Et_2O (2:1); mp 112−113 °C; $[\alpha]^{20}_D$ −21.93 (*c* 0.963, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.65 (d, J = 6.8 Hz, 3 H), 0.77 (d, J = 6.8 Hz, 3 H), 1.22−1.34 (m, 1 H), 1.42−1.50 (m, 1 H), 2.07 (broad s, 1 H), 2.30 (s, 3 H), 2.66 (s, 6 H), 3.23−3.29 (m, 1 H), 3.40−3.48 (m, 1 H), 3.53−3.59 (m, 1 H), 4.78 (broad s, 1 H), 6.94 (s, 2 H). Anal. Calcd for $C_{15}H_{25}NO_3S$: C, 60.17; H, 8.42; N, 4.68. Found: C, 59.97; H, 8.46; N, 4.59.

(*S*)-2-Phenylpropan-1-ol (50) and (*S*)-*N*-[(2,4,6-Trimethylbenzene)sulfonyl]leucinol. By use of a procedure identical with that described for the preparation of **49** and (*S*)-*N*-[(2,4,6-trimethylbenzene)sulfonyl]leucinol from **47**, the alkene **48** (80 mg, 0.20 mmol) was converted into 20 mg (73% yield) of (2*S*)-2-phenylpropan-1-ol **50** and 44 mg (73% yield) of (*S*)-*N*-[(2,4,6-trimethylbenzene)sulfonyl]leucinol. **50**: a colorless oil; $[\alpha]^{21}_D$ −16.09 (*c* 0.513, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 1.27 (d, J = 6.9 Hz, 3 H), 1.34 (broad s, 1 H), 2.94 (qd, J = 6.9, 6.9 Hz, 1 H), 3.68 (m, 2 H), 7.20−7.25 (m, 3 H), 7.30−7.36 (m, 2 H). LRMS (CI), *m*/*z* 137 (MH^+, base peak); HRMS (CI), *m*/*z* calcd for $C_9H_{13}O$ (MH^+) 137.0966, found 137.0967. (*S*)-*N*-[(2,4,6-Trimethylbenzene)sulfonyl]leucinol: colorless crystals from *n*-hexane−$CHCl_3$ (2:1); $[\alpha]^{21}_D$ −22.5 (*c* 0.845, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.65 (d, J = 6.8 Hz, 3 H), 0.77 (d, J = 6.8 Hz, 3 H), 1.22−1.34 (m, 1 H), 1.42 (m, 2 H), 1.42−1.55 (m, 1 H), 2.07 (broad s, 1 H), 2.30 (s, 3 H), 2.66 (s, 6 H), 3.25 (m, 1 H), 3.44 (m, 1 H), 3.53−3.59 (m, 1 H), 4.78 (broad s, 1 H), 6.96 (s, 2 H); LRMS (FAB), *m*/*z* 300 (MH^+, base peak). HRMS (FAB), *m*/*z* calcd for $C_{15}H_{26}NO_3S$ (MH^+) 300.1633, found 300.1636.

Acknowledgment. Financial support from a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture, Japan, is gratefully acknowledged. We are grateful to Professor T. Taga and Dr. Y. Miwa, Kyoto University, for helpful discussions.

Supporting Information Available: Experimental details of reactions of **15**, **17**, and **19** with organocopper reagents; synthetic methods of compounds **26**, **45**, **46**, and an authentic sample of **50**; and copies of ^1H NMR spectra for compounds **9**, **21**, **23**, **24**, **26**, **28**−**31**, **33**−**38**, **45**, **46**, and **48**−**50** that have no combustion analysis (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9810157