A Thermodynamic Preference of Chiral *N*-Methanesulfonyl and *N*-Arenesulfonyl 2,3-*cis*-3-Alkyl-2-Vinylaziridines over Their 2,3-*Trans*-Isomers: Useful Palladium(0)-Catalyzed Equilibration Reactions for the Synthesis of (*E*)-Alkene Dipeptide Isosteres

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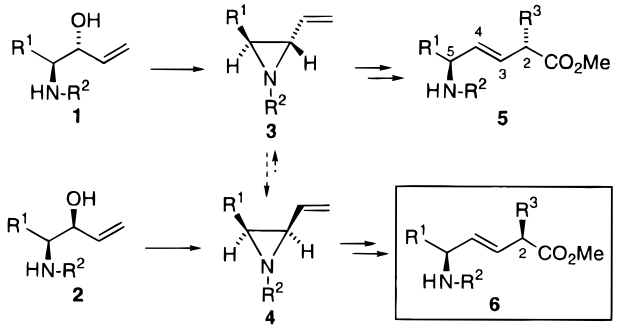
Received September 13, 1996[⊗]

Palladium(0)-catalyzed reactions of *N*-methanesulfonyl- or *N*-(arenesulfonyl)-3-alkyl-2-vinylaziridines reveal that 2,3-*cis*-isomers are more stable than the corresponding 2,3-*trans*-isomers in accord with *ab initio* calculations. A highly stereoselective synthetic route to (*E*)-alkene dipeptide isosteres having desired stereochemistries from 2,3-*cis*-3-isobutyl-2-vinylaziridine by the use of organocopper chemistry is also presented.

The aziridine ring framework can be found in many synthetic and natural compounds of biological importance.[1] Currently, there is significant interest in the synthesis and reaction of aziridines and their *N*-activated analogues.[2] Due to their very high reactivity and ability to function as carbon electrophiles, activated aziridines,[3] notably 2-vinylaziridines[4] and their derivatives,[5] are versatile synthetic intermediates for the synthesis of biologically important compounds.

Recently, we proposed that peptides involving (*E*)-alkene dipeptide isosteres of type **6** may represent a novel class of potent bombesin receptor antagonists (Scheme 1).[6] Merck[7] and Dupont Merck[8] groups, Panek,[9] and Bartlett[10] have also reported that peptides containing (*E*)-alkene dipeptide isosteres show potent biological activity. One of the simplest methods for the synthesis of alkene isosteres such as **5** and **6** via aziridine derivatives of type **3** and **4** involves the use of chiral *anti*- and *syn*-amino alcohols **1** and **2**, which in turn could be synthesized from various chiral amino aldehydes.[11,12] However, when a

Scheme 1



R^1 = alkyl; R^2 = Boc, Ts, etc.; R^3 = alkyl

[⊗] Abstract published in *Advance ACS Abstracts,* February 1, 1997.

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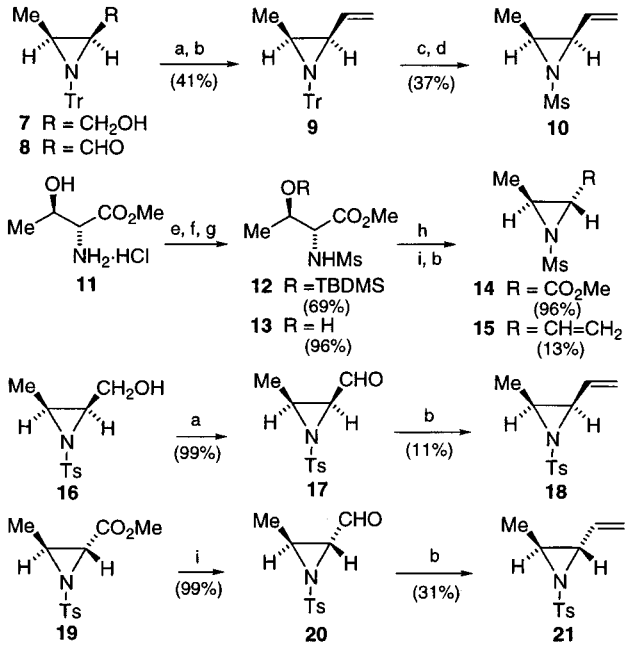
S0022-3263(96)01760-4 CCC: $14.00

chiral *N*-protected amino aldehyde derived from a natural α-amino acid is reacted with organometallic reagents such as vinylmagnesium bromide, a mixture of *anti*- and *syn*-amino alcohols **1** and **2** is always obtained.[12] Usually, *N*-monoprotected amino aldehydes exhibit low facial diastereoselectivity.[13] While less stereoselective, the synthetic procedure involving reactions of *N*-protected amino aldehydes with vinylmagnesium halides still remains the only practical route to amino alcohols **1** and **2**.[12,14,15] The ratio of isomers is highly dependent on the structure of the starting material, the reagent, the solvent, and the temperature of the reaction. Thus, the highly stereoselective synthesis of either *anti*- or *syn*-amino alcohols **1** or **2** and hence 2,3-*trans*- or 2,3-*cis*-3-alkyl-2-vinylaziridines **3** or **4** from readily available amino aldehydes has hitherto been difficult. This rather low stereoselectivity in the reaction of amino aldehydes with organometallic reagents such as vinylmagnesium halides frequently hinders their use in many synthetic applications.[7,12,16]

As part of an ongoing program aimed at the synthesis of biologically active peptides containing (*E*)-alkene isosteres,[17] we needed a reliable procedure for the synthesis of activated *cis*-3-alkyl-2-vinylaziridines **4** as key synthetic intermediates. In this context, we looked for a convenient method for the transformation of undesired 2,3-*trans*-3-alkyl-2-vinylaziridines of general formula **3** into desired 2,3-*cis*-isomers of type **4**. Recently, palladium(0)-catalyzed carbonylations of vinylaziridines to β-lactams have been achieved successfully by Ohfune[4c] and Tanner.[4d] It was expected that palladium(0)-catalyzed isomerization of 2,3-*trans*-3-alkyl-2-vinylaziridines **3** into the corresponding desired *cis*-isomers **4** could occur *via* π-allyl palladium complexes. Here we detail a study involving the palladium(0)-catalyzed equilibrated reaction of chiral *N*-(methanesulfonyl)- and *N*-(arenesulfonyl)-3-alkyl-2-vinylaziridines and *N*-(arenesulfonyl)-4-alkyl-5-vinyloxazolidin-2-ones.[18]

Scheme 2



Reagents: a) $(COCl)_2$-DMSO, *i*-Pr_2NEt; b) $Ph_3P{=}CH_2$ in THF; c) TFA in $CHCl_3$; d) MsCl - Et_3N; e) *i*-Pr_2NEt - MsCl in $CHCl_3$ - DMF; f) imidazole - TBDMSCl; g) aq. HF in MeCN - MeOH; h) PPh_3 - diethyl azodicarboxylate; i) DIBAL in toluene

Results and Discussion

Synthesis of 2,3-*Cis*/*Trans*-Pairs of Chiral *N*-(Methanesulfonyl)- or *N*-(Arenesulfonyl)-3-alkyl-2-vinylaziridines and 4,5-*Cis*/*Trans*-Pairs of Chiral *N*-(Arenesulfonyl)-4-alkyl-5-vinyloxazolidin-2-ones. The requisite homochiral 2,3-*cis*/*trans*-pairs of *N*-(methanesulfonyl)- and *N*-tosyl-3-methyl-2-vinylaziridines (**10** and **15**, and **18** and **21**) were prepared in acceptable yields from the known (2*S*,3*S*)-*N*-trityl-3-methyl-2-aziridinemethanol (**7**),[11,17t] D-*allo*-threonine methyl ester hydrochloride (**11**),[11] (2*S*,3*S*)-*N*-tosyl-3-methyl-2-aziridinemethanol (**16**),[11] and methyl (2*R*,3*S*)-3-methyl-*N*-tosylaziridine-2-carboxylate (**19**),[11] respectively, according to the usual method as shown in Scheme 2 (for details, see Experimental Section).

The chiral 2,3-*cis*/*trans*-pairs of aziridines (**24** and **25**, and **28** and**29**) were synthesized from the known allyl alcohols **22** and **23**[12,14] by a sequence of reactions as shown in Scheme 3 (for details, see Experimental Section). It should be clearly noted that although *N*-(*tert*-butoxycarbonyl)aziridines **24** and **25** are rather labile oily compounds, the *N*-(mesitylenesulfonyl)aziridines **28** and **29** are stable crystalline substances.

In a similar manner, the chiral 2,3-*cis*/*trans*-pair of *N*-(mesitylenesulfonyl)aziridines **38** and **39** bearing a *tert*-

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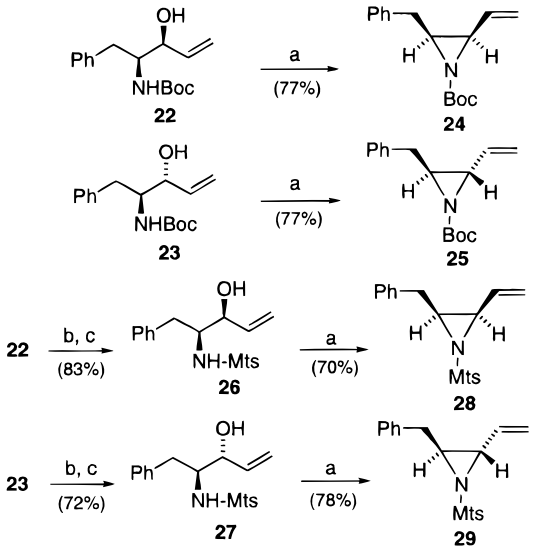
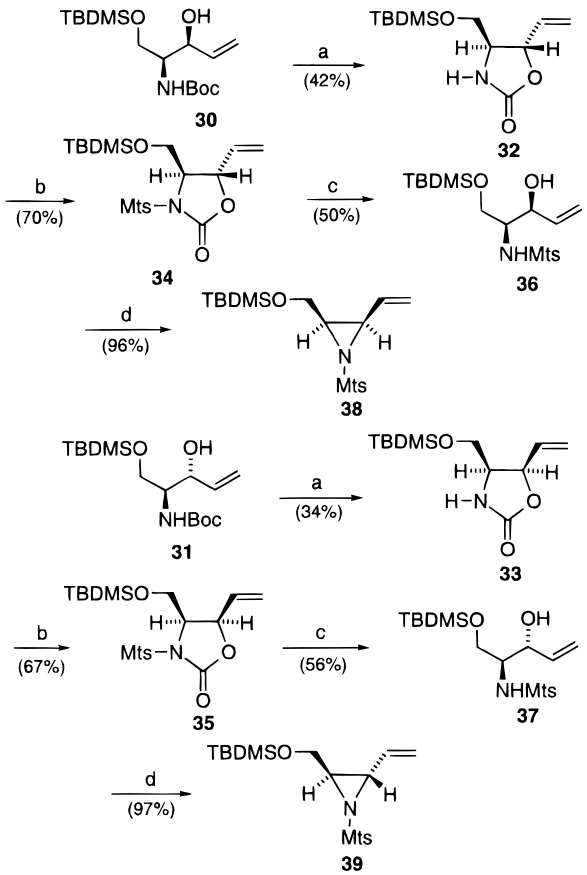
Scheme 3



Abbreviations: Mts = 2,4,6-trimethylbenzenesulfonyl.
Reagents: a) PPh_3 - diethyl azodicarboxylate; b) TFA; c) Et_3N - MtsCl

Scheme 4

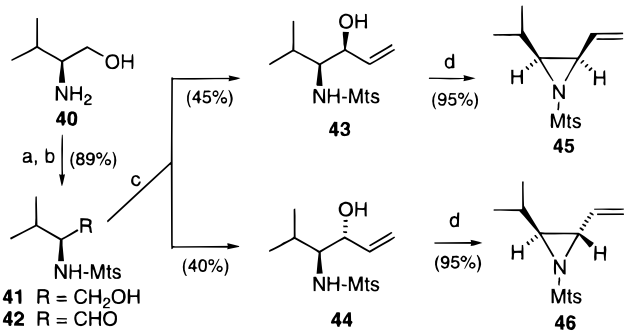


Abbreviations: Mts = 2,4,6-trimethylbenzenesulfonyl
Reagents: a) NaH in THF; b) NaH-MtsCl; c) KOH-MeOH; d) PPh_3 - diethyl azodicarboxylate

butyldimethylsilyl group was prepared from the known allyl alcohols **30** and **31**[12] by a sequence of reactions as shown in Scheme 4 (for details, see Experimental Section).

The 2,3-*cis*/*trans*-pair of chiral aziridines **45** and **46** bearing an isopropyl group was synthesized from (*S*)-valinol **40**[19] as shown in Scheme 5. (*S*)-Valinol was treated successively with 2-mesitylenesulfonyl chloride

Scheme 5



Abbreviations: Mts = 2,4,6-trimethylbenzenesulfonyl
Reagents: a) MtsCl-Et_3N; b) $(COCl)_2$-DMSO, *i*-Pr_2NEt; c) vinyl-MgBr; d) PPh_3-diethyl azodicarboxylate

in the presence of triethylamine, oxalyl chloride−dimethyl sulfoxide−*N*,*N*-diisopropylethylamine, and vinyl magnesium bromide to give a separable 53:47 mixture of allyl alcohols **43** and **44** in 85% combined yield. Exposure of **43** and **44** to triphenylphosphine−diethyl azodicarboxylate in THF gave the aziridines **45** and **46**, respectively, in high isolated yields (for details, see Experimental Section).

Finally, as shown in Scheme 6, the 2,3-*cis*/*trans*-pairs of chiral aziridines (**62** and **63**, **64** and **65**, and **68** and **69**) and the 4,5-*cis*/*trans*-pairs of *N*-arenesulfonyl 4,5-disubstituted-oxazolidin-2-ones (**54** and **55**, and **56** and **57**) were prepared from (*S*)-leucinol **47**[19] by a sequence of reactions similar to that described for the synthesis of the vinylaziridines **45** and **46** (for details, see Experimental Section). The choice of 2,2,5,7,8-pentamethylchroman-6-sulfonyl (Pmc)[20] and *p*-nitrobenzenesulfonyl (PNBS)[21] as both protective and activating groups was based primarily on their ease of deprotection (for details, see Experimental Section).

As can be seen from Table 1, the 2,3-*cis*-aziridines (Table 1, entries 1−8) show JH_{ab} values (J = 6.8−7.3 Hz) larger than the JH_{ab} values (J = 4.1−4.5 Hz) of the 2,3-*trans*-isomers (Table 1, entries 9−16). In addition, the H_a protons in the 2,3-*trans*-3-alkyl-2-vinylaziridines always resonate at higher field (δ 3.07−3.23) than those of the 2,3-*cis*-isomers (δ 3.28−3.45), respectively. The data are in agreement with ^{1}H NMR data for related compounds.[22] It should be clearly noted that the 2,3-*cis*-aziridines (Table 1, entries 1−8) show JH_{ac} values (J = 6.8−7.1 Hz) smaller than the JH_{ac} values (J = 8.7−9.5 Hz) of the 2,3-*trans*-isomers (Table 1, entries 9−16).

Although the 2,3-*cis*- or 2,3-*trans* stereochemistry of *cis*/*trans* pairs of the aziridines listed in Table 1 was inferred from ^{1}H NMR spectral analyses, the structures of 2,3-*cis*- and 2,3-*trans*-*N*-tosyl-3-methyl-2-vinylaziridines **18** and **21** were unequivocally ascertained by single crystal X-ray analyses (Figure 1).[23] In their solid states both compounds **18** and **21** are characterized by a well-

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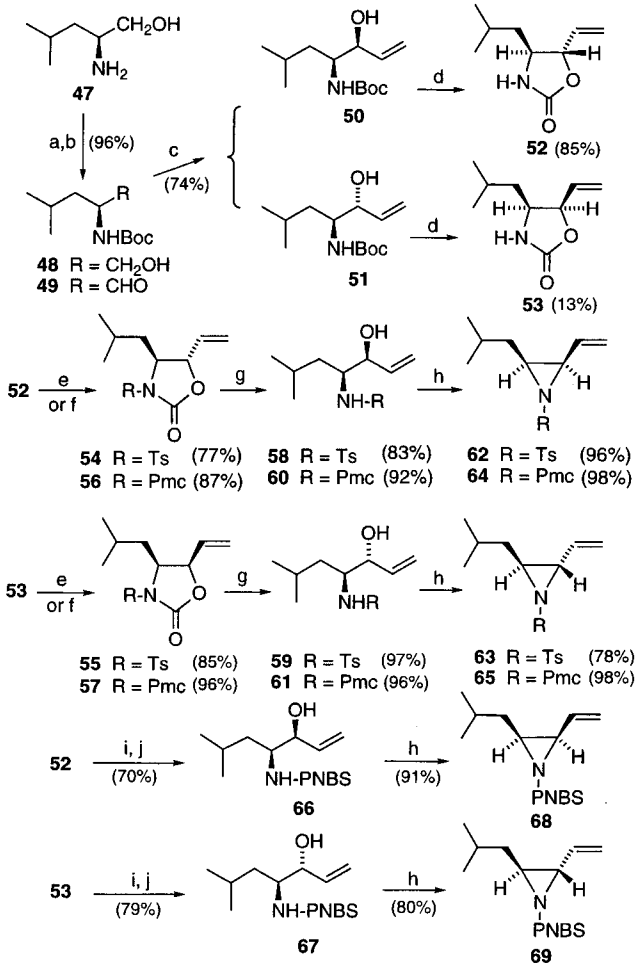
Scheme 6



Abbreviations: Pmc = 2,2,5,7,8-pentamethyl-6-chromansulfonyl; PNBS = *p*-nitrobenzenesulfonyl

Reagents: a) Boc_2O - Et_3N; b) $(COCl)_2$ - DMSO - $(i\text{-}Pr)_2NEt$; c) vinyl-MgCl in THF; d) NaH - THF - DMF; e) NaH - TsCl; f) NaH - PmcCl; g) aq. KOH in MeOH; h) PPh_3 - diethyl azodicarboxylate; i) KOH-MeOH-H_2O; j) PNBSCl - Et_3N

known pyramidal configuration of the ring nitrogen atom.[24] X-ray analysis of 2,3-*trans*-3-methyl-2-vinylaziridine (**21**) indicates that the *p*-tosyl group is pointed away from the vinyl group at the C-2 position (**21-A**, Figure 1). The origin of this conformation could come from the repulsion between the vinyl group and the *p*-tosyl group in **21**. On the other hand, the asymmetric unit of 2,3-*cis*-3-methyl-2-vinylaziridine (**18**) contains two crystallographically independent molecules **18-A** and **18-B**. The *p*-tosyl group in the conformer **18-A** is pointed toward the vinyl group, while it is pointed away from the vinyl group in the isomeric conformer **18-B**. As can be seen from Figure 1, the *p*-tosyl groups on the aziridine nitrogen in the solid state conformations **18-A**, **18-B**, and **21-A** are *trans* with respect to the methyl group at the C(3)-position.

Finally, stereochemical assignments for 4,5-*trans*/*cis*-pairs of 4-alkyl-5-vinyloxazilidin-2-ones (**54** and **55**, and **56** and **57**), which are required for the Pd(0)-catalyzed decarboxylative equilibrated reactions, are based on ^1H NMR spectral analyses (for structures **54**−**57**, see Scheme 6). The 4,5-*cis*-oxazolidin-2-ones **55** and **57** show $JH_{4,5}$ values (J = 6.9 Hz) larger than the $JH_{4,5}$ values (J = 2.3−2.5 Hz) of the corresponding 4,5-*trans*-isomers **54** and **56**. In addition, the proton at the C-5 position in the 4,5-*trans*-compounds resonates at higher field (δ 4.60−4.70) than those of the 4,5-*cis*-isomers (δ 4.97−4.98). The data are in agreement with ^1H NMR data for related compounds.[12,25,26]

Calculations of Relative Stabilities of 2,3-*Cis*-Disubstituted Aziridines and Their 2,3-*Trans*-Isomers. Recently, Lewis acid-catalyzed isomerizations of stereochemistry at the C-2 or C-3 position of aziridines have been observed for some 2,3-disubstituted aziridines.[27] Although, the relative thermodynamic stabilities of 2,3-*cis*-disubstituted aziridines and their 2,3-*trans*-isomers are dependent on the nature of the substituents at the C-2 and C-3 positions, as well as the *N*-protecting or activating group, Huisgen *et al*. reported experimental studies on the relative stability of 1,2,3-trisubstituted aziridines and discovered that 2,3-*trans*-aziridines are more stable.[28] Jørgensen *et al*. also recently reported that an *N*-protected 2,3-*cis*-aziridine could be transformed into an *N*-deprotected 2,3-*trans*-aziridine.[29] Accordingly, at first sight, the isomerization of *N*-activated 2,3-*trans*-3-alkyl-2-vinylaziridines into their 2,3-*cis*-isomers did not look promising. In spite of their synthetic utility, the relative themodynamic stabilities of both unactivated and activated 2,3-*cis*- and 2,3-*trans*-3-alkyl-2-vinylaziridines are poorly understood.[30]

In order to gain an understanding of the relative stabilities of 2,3-*cis*- and 2,3-*trans*-disubstituted aziridines, we undertook *ab initio* molecular orbital calculations involving full optimizations using the GAUSSIAN 92 quantum mechanical package (revision C).[31,32] In order to reduce the size of the system such that *ab initio* calculations could be employed, two model systems of 2,3-

(23) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre. 12 Union Road, CB2 1EZ, UK.

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(28) (a) Huisgen, R.; Scheer, W.; Huber, H. *J. Am. Chem. Soc.* **1967**, *89*, 1753. (b) Huisgen, R.; Scheer, W.; Mäder, H. *Angew. Chem.* **1969**, *81*, 619.

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(31) All *ab initio* calculations were performed using the program GAUSSIAN 92 on a CRAY Y-MP2E/264 at the Supercomputer Laboratory, Institute for Chemical Research, Kyoto University. GAUSSIAN 92, Revision C: Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Forseman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. Gaussian Inc., Pittsburgh, PA, 1992.

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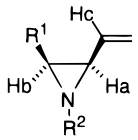
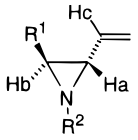
Table 1. ^{1}H NMR Chemical Shifts for H_a and H_b and Spin−Spin Coupling Constants for JH_{ab} and JH_{ac} of the Selected 2,3-*cis*- and 2,3-*trans*-Vinylaziridines in $CDCl_3$[a]



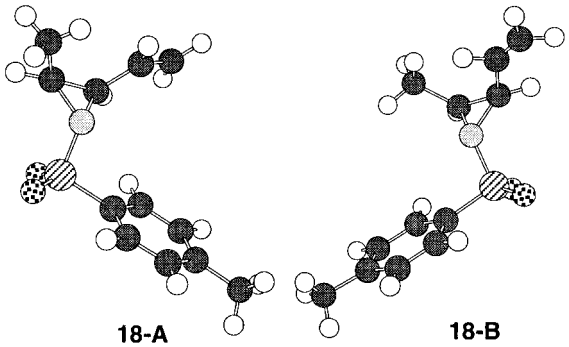
A (2,3-*cis*)



B (2,3-*trans*)

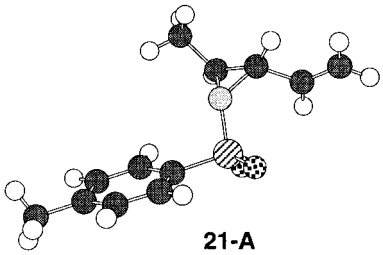
entry	compound	2,3-*cis*/*trans*	R^1	R^2	H_a (δ)	H_b (δ)	JH_{ab} (Hz)	JH_{ac} (Hz)
1	**10**	*cis*	Me	Ms	3.28	3.01	6.8	6.8
2	**18**	*cis*	Me	Ts	3.32	3.03	7.3	6.9
3	**28**	*cis*	$PhCH_2$	Mts	3.48	3.10	7.3	6.8
4	**38**	*cis*	$TBDMSOCH_2$	Mts	3.44	3.07	6.9	6.9
5	**45**	*cis*	*i*-Pr	Mts	3.41	2.56	7.0	7.0
6	**62**	*cis*	*i*-Bu	Ts	3.31	2.96	7.1	7.1
7	**64**	*cis*	*i*-Bu	Pmc	3.38	2.96	6.9	6.9
8	**68**	*cis*	*i*-Bu	PNBS	3.45	3.13	7.2	7.0
9	**15**	*trans*	Me	Ms	3.09	2.93	4.4	8.8
10	**21**	*trans*	Me	Ts	3.13	2.97	4.4	8.7
11	**29**	*trans*	$PhCH_2$	Mts	3.20	3.14	4.2	9.1
12	**39**	*trans*	$TBDMSOCH_2$	Mts	3.23	3.17	4.1	8.9
13	**46**	*trans*	*i*-Pr	Mts	3.11	2.80	4.2	9.5
14	**63**	*trans*	*i*-Bu	Ts	3.07	2.94	4.4	9.1
15	**65**	*trans*	*i*-Bu	Pmc	3.08	2.92	4.2	9.1
16	**69**	*trans*	*i*-Bu	PNBS	3.18	3.03	4.5	9.0

[a] All ^{1}H NMR spectra were recorded in $CDCl_3$ at 300 K, and chemical shifts are reported in parts per million downfield from internal TMS. For designations H_a, H_b, and H_c, see structures **A** and **B**. Abbreviations: Mts = mesitylenesulfonyl; Pmc = 2,2,5,7,8-pentamethylchroman-6-sulfonyl; PNBS = *p*-nitrobenzenesulfonyl.



18-A
(1*R*,2*R*,3*S*)-2,3-*cis*

18-B
(1*R*,2*R*,3*S*)-2,3-*cis*

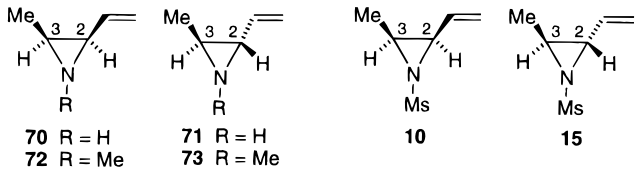


21-A
(1*R*,2*S*,3*S*)-2,3-*trans*

Figure 1. Crystal structures and solid state conformations of **18** and **21**: **18-A** and **18-B**, 2,3-*cis*-*N*-tosyl-3-methyl-2-vinylaziridine. **21-A**, 2,3-*trans*-*N*-tosyl-3-methyl-2-vinylaziridine.

cis−*trans* pairs (**70** and **71**, and **72** and **73**) were chosen (Scheme 7). Both theoretical and experimental aspects were carried out with 2,3-*cis*- and 2,3-*trans*-*N*-(methanesulfonyl)-3-methyl-2-vinylaziridines **10** and **15** (Scheme 7).[33] All conformational minima were fully optimized up to the extended 6-31G** basis set. Harmonic frequencies were calculated for each conformer using the 6-31G** basis set. The minimum conformations all have positive frequencies, which is an indication of a true minimum on the potential surface. Energy calculations for the aziridines were performed with the second order Møller−Plesset electron correlation (MP2) on the RHF/6-31** optimized geometries.[34]

Scheme 7



70 R = H
72 R = Me

71 R = H
73 R = Me

10

15

We initiated our study to determine the relative stabilities of a 2,3-*cis*−*trans* pair of 3-methyl-2-vinylaziridines **70** and **71** (Figure 2). The geometries of 2,3-*cis*-3-methyl-2-vinylaziridine **70-A** and its nitrogen invertomer **70-B** as well as 2,3-*trans*-3-methyl-2-vinylaziridine **71-A** and its nitrogen invertomer **71-B** were located with *ab initio* calculations involving full optimizations at the RHF/6-31G** level. It was found that the energy minimum **71-A** of the 2,3-*trans*-aziridine **71** was predicted to be 0.25 kcal/mol lower than the energy minimum **70-A** of the 2,3-*cis*-aziridine **70** at the MP2/6-31G** level.

The dihedral angle between the C(2)−H(2) bond and the C(4)−H(4) bond for the most stable conformation **71-A** of 2,3-*trans*-3-methyl-2-vinylaziridine (**71**) was predicted to be −177.9°, a spatial arrangement known as antiperiplanar. In normal allylic compounds, this conformation is favored.[35−37] On the other hand, the angle

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(34) For references dealing with the 6-31G** basis set and Møller−Plesset perturbation theory, see: Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. In *Ab Initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986.

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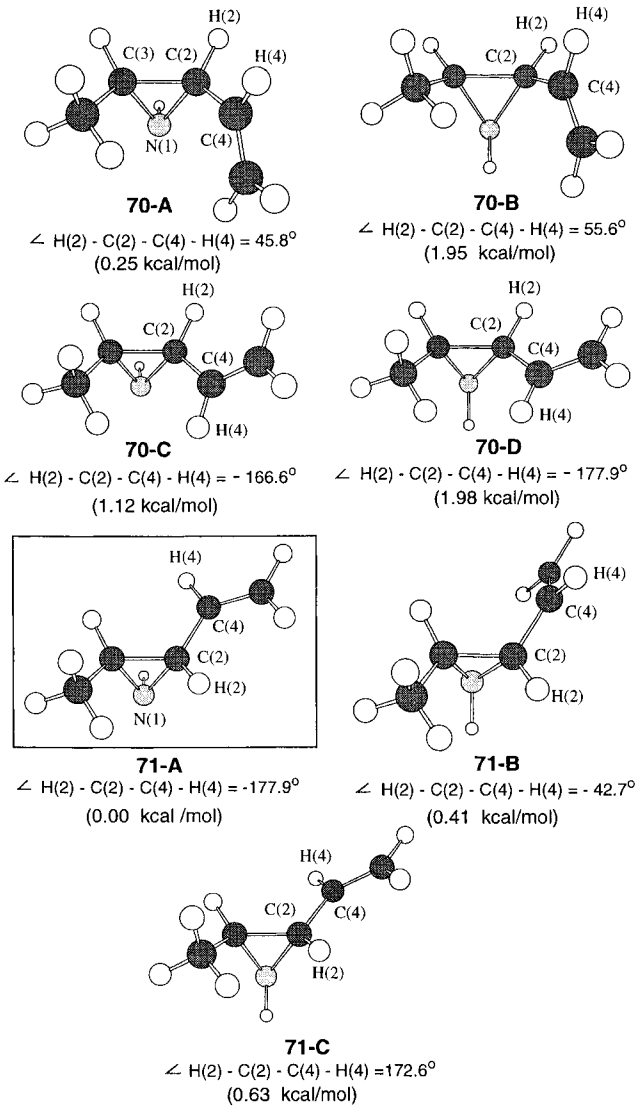


Figure 2. RHF/6-31G** optimized geometries of model compounds **70** and **71**. Energies are relative to the lowest energy at the MP2/6-31G** level. **70-A**: (1*R*,2*R*,3*S*)-2,3-*cis*-3-methyl-2-vinylaziridine. **70-B**, **70-C**, and **70-D**: geometries of the local energy minima of 2,3-*cis*-3-methyl-2-vinylaziridines **70**. **71-A**: the lowest energy geometry of (1*R*,2*S*,3*S*)-2,3-*trans*-3-methyl-2-vinylaziridine. **71-B**: the lowest energy minimum of the nitrogen invertomer **71-A**. **71-C**: geometry of one of the local energy minima of (1*S*,2*S*,3*S*)-2,3-*trans*-3-methyl-2-vinylaziridine **71**.

between the C−H bonds on adjacent carbon atoms C(2) and C(4) for the energy minimum **70-A** of 2,3-*cis*-3-methyl-2-vinylaziridine (**70**) was estimated to be only 45.8°. Likewise, the dihedral angles between the C(2)−H(2) bond and the C(4)−H(4) bond in the local minima **70-B** and **71-B** (the nitrogen invertomers of **70-A** and **71-A**) were predicted to be only 55.6° and −42.7°, respectively, as shown in Figure 2. It should be clearly noted that the geometries **70-C**, **70-D**, as well as **71-C** with the larger dihedral angles (almost antiperiplanar arrangements) were predicated to be less stable.

Thus, as can be seen from Figure 2, 2,3-*trans*-disubstituted aziridine **71** is predicted to be more stable than its 2,3-*cis*-disubstituted isomer **70** in agreement with the literature data.[28,29]

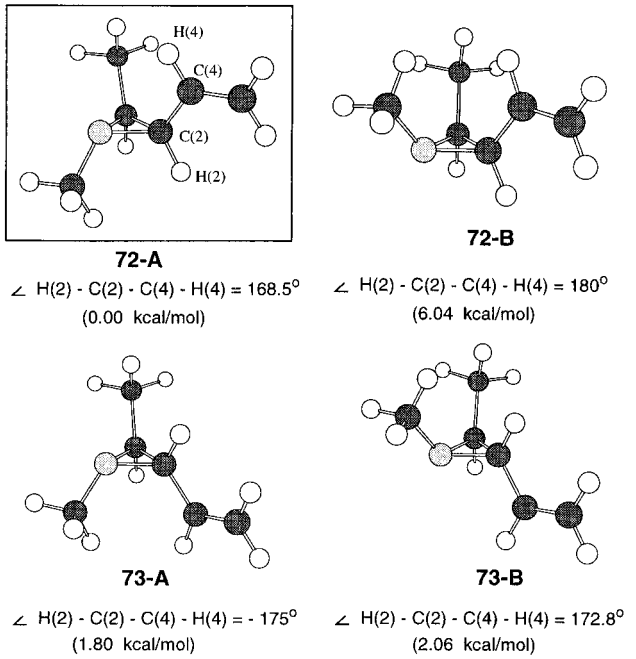


Figure 3. RHF/6-31G** optimized geometries of model compounds **72** and **73**. Energies are relative to the lowest energy at the MP2/6-31G** level. **72-A** and **72-B**: 2,3-*cis*-1,3-dimethyl-2-vinylaziridine and its nitrogen invertomer, respectively. **73-A** and **73-B**: 2,3-*trans*-1,3-dimethyl-2-vinylaziridine and its nitrogen invertomer.

In *N*-substituted aziridines, the interactions between the *N*-substituent and the substituents at the C(2) and/or C(3)-positions may have marked conformational consequences. In this context, relative energies of a *cis*/*trans*-pair of *N*-methyl-2,3-disubstituted aziridines (**72** and **73**) were investigated (Figure 3). The energy minimum **72-A** of 2,3-*cis*-*N*-methyl-3-methyl-2-vinylaziridine (**72**) was predicted to be ca. 1.80 kcal/mol lower than the energy minimum **73-A** of 2,3-*trans*-isomer **73**, as can be seen from Figure 3. Interestingly, unlike 2,3-*cis*- and 2,3-*trans*-3-methyl-2-vinylaziridines shown in Figure 2, the dihedral angle between the C(2)−H(2) bond and the C(4)−H(4) bond for the optimized geometries **72-A**, **72-B**, **73-A**, and **73-B** were estimated to be 168.5−180°. Thus, calculations suggest that 2,3-*cis*-*N*-methyl-3-methyl-2-vinylaziridine (**72**) would be more stable than its 2,3-*trans*-isomer **73**.

Finally, in 2,3-*cis*/*trans* pairs, would 2,3-*cis*-*N*-mesyl-2,3-substituted aziridines or their 2,3-*trans*-isomers be expected to be the more stable isomers? The relative stabilities of a 2,3-*cis*−*trans* pair of *N*-mesyl-3-methyl-2-vinylaziridines **10** and **15** were investigated (Figure 4). The energy minimum **10-A** of 2,3-*cis*-*N*-mesyl-3-methyl-2-vinylaziridine (**10**) was predicted to be approximately 1.43 kcal/mol lower than the energy minimum **15-A** of 2,3-*trans*-isomer **15** at the MP2/6-31G** level. Assuming $\Delta S° = 0$, this energy difference is calculated to give the equilibrated product ratio of 94:6 (2,3-*cis*-**10**:2,3-*trans*-**15**) at 0 °C in the gas phase. As will be described later, this prediction proved to be quite close to the experimental results in solution. Optimized geometry **10-B** is the model for estimating the repulsion between the *N*-mesyl group and the substituents at the C-2 and C-3 positions. When compared to conformer **10-A**, this amounts ~6.5 kcal/mol in energy difference.

(37) (a) Khan, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 650. (b) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841. (c) Broeker, J. L.; Hoffmann, R. W.; Houk, K. N. *J. Am. Chem. Soc.* **1991**, *113*, 5006. (d) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1124.

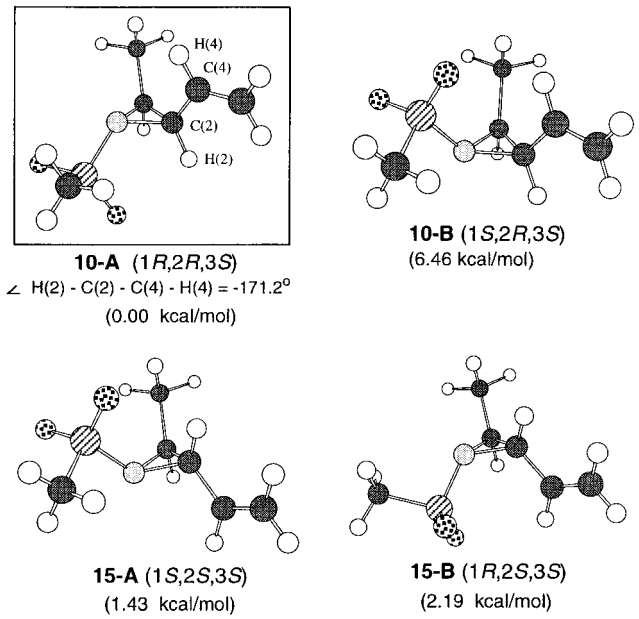


Figure 4. RHF/6-31G** optimized geometries of 2,3-*cis*-*N*-mesyl-3-methyl-2-vinylaziridine (**10**) and its 2,3-*trans*-isomer (**15**). Energies are relative to the lowest energy at the MP2/6-31G** level. **10-A**: the lowest energy geometry of **10**. **10-B**: the optimized geometry of the nitrogen invertomer of **10-A**. **15-A**: the lowest energy geometry of **15**. **15-B**: the optimized geometry of the nitrogen invertomer of **15-A**.

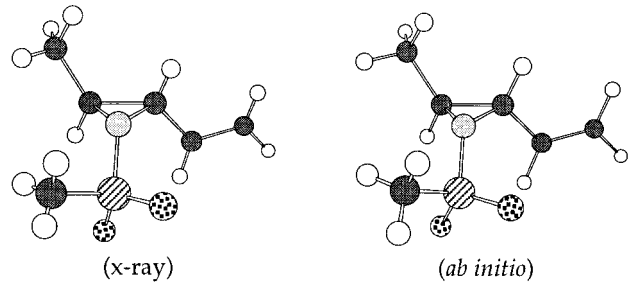


Figure 5. Solid-state conformation of 2,3-*trans*-*N*-mesyl-3-methyl-2-vinylaziridine (**15**) (left). One of the local minima of (1*R*,2*S*,3*S*)-*N*-mesyl-3-methyl-2-vinylaziridine (**15**) at the RHF/6-31G** level (right).

It is found that one of the local energy minima, **15-B**, shown in Figure 4, is quite similar to the solid-state conformation[23] of 2,3-*trans*-*N*-mesyl-3-methyl-2-vinylaziridine (**15**) [compare the solid-state conformation (left) with the geometry (right) obtained by computations in Figure 5]. The methyl group in the methanesulfonyl group is pointed away from the vinyl group presumably for steric reasons. Although the crystal structure conformation and the gas phase geometry need not to be the same, in the solid state, the methanesulfonyl or arenesulfonyl group on the aziridine nitrogen of 3-alkyl-2-vinylaziridines and their derivatives[17j,t] is usually *trans* with respect to the alkyl group at the C-3 position (see also Figure 1).

Table 2 summarizes the above results obtained by calculations. Entry 1 shows that 2,3-*trans*-3-methyl-2-vinylaziridine (**71**) is predicted to be more stable than its 2,3-*cis*-isomer **70** in accord with precedents.[28] On the other hand, entries 2 and 3 show that 2,3-*cis*-3-methyl-2-vinylaziridines, bearing a methyl or mesyl group on the nitrogen atom, are calculated to be more stable. The lone electron pairs on the nitrogen atom of the stable nitrogen invertomers of 2,3-*cis* compounds **72** and **10** are predicted to be on the same side of the aziridine-ring plane as the C(2)- and C(3)-substituents, presumably for mere steric reasons. On the contrary, in the stable conformation **15-A** (Figure 4) of 2,3-*trans*-3-methyl-2-vinylaziridine (**15**), the *N*-methanesulfonyl group is predicted to be on the same side of the plane of the aziridine-ring as the C(3)-methyl group. Thus, the nitrogen configuration depends on a subtle balance of stereoelectronic factors.[38] Table 3 summarizes total and relative energies of the critical points.

Table 2. Predicted Relative Stabilities of 2,3-*Cis*/*Trans*-Pairs of Compounds 70 and 71, 72 and 73, and 10 and 15

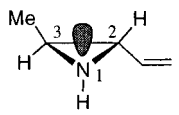
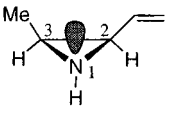
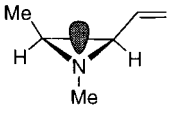
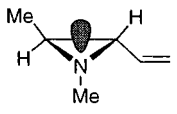
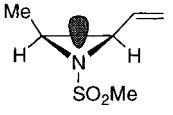
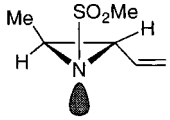
Entry	Predicted to be more stable compounds	Predicted to be less stable compounds
1	 **71**	 **70**
2	 **72**	 **73**
3	 **10**	 **15**

Table 3. Total and Relative Energies of the Critical Points[a]

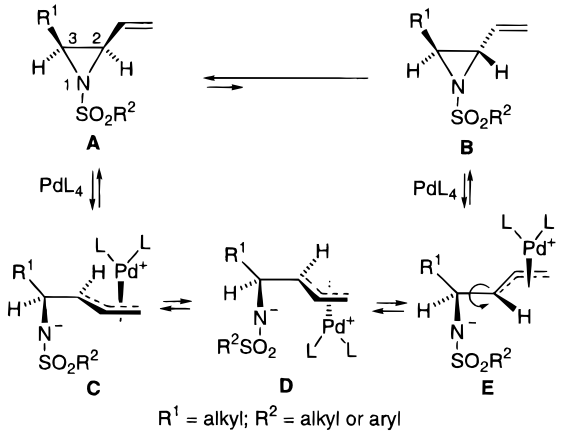
RHF/6-31G** geometry	MP2/6-31G**//RHF/6-31G**	
	E^b	ΔE^c
2,3-*cis*- and 2,3-*trans*-3-Methyl-2-vinylaziridines **70** and **71**		
70-A (2,3-*cis*)	−249.84097	0.25
70-B (2,3-*cis*)	−249.83826	1.95
70-C (2,3-*cis*)	−249.83975	1.12
70-D (2,3-*cis*)	−249.83820	1.98
71-A (2,3-*trans*)	−249.84136	0.00
71-B (2,3-*trans*)	−249.84071	0.41
71-C (2,3-*trans*)	−249.84035	0.63
2,3-*cis*- and 2,3-*trans*-*N*-Methyl-3-methyl-2-vinylaziridines **72** and **73**		
72-A (2,3-*cis*)	−288.00965	0.00
72-B (2,3-*cis*)	−288.00002	6.04
73-A (2,3-*trans*)	−288.00678	1.80
73-B (2,3-*trans*)	−288.00637	2.06
2,3-*cis*- and 2,3-*trans*-*N*-Mesyl-3-methyl-2-vinylaziridines **10** and **15**		
10-A (2,3-*cis*)	−835.18669	0.00
10-B (2,3-*cis*)	−835.17640	6.46
15-A (2,3-*trans*)	−835.18441	1.43
15-B (2,3-*trans*)	−835.18300	2.19

[a] The character of all energy minima and transition states was confirmed with calculation of force constant analyses at the Hartree−Fock level. Energy calculations at the MP2 level were performed on the RHF/6-31G** optimized geometries (single point calculations). [b] Total energies in atomic units (Hartree). [c] kcal/mol. Energies are relative to the lowest energy.

Palladium(0)-Catalyzed Equilibrated Reactions of 2,3-*cis*- and 2,3-*trans*-3-Alkyl-2-vinylaziridines. Since the energy difference in the gas phase is calculated

(38) For nitrogen configuration of some aziridine derivatives, see: Häner, R.; Olano, B.; Seebach, R. *Helv. Chim. Acta* **1987**, *70*, 1676.

Scheme 8

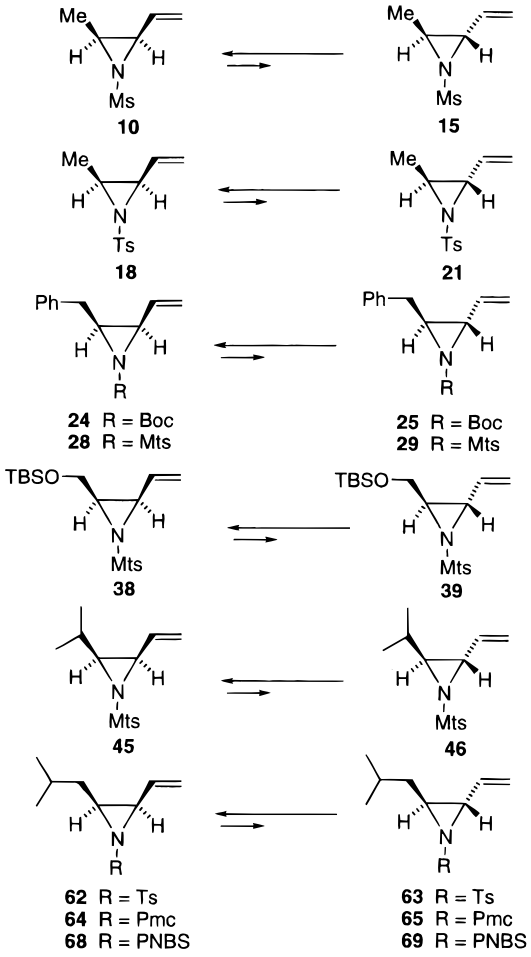


to give the equilibrated product ratio of 94:6 (2,3-*cis*-**10**:2,3-*trans*-**15**) at 0 °C, it was our expectation that the palladium(0)-catalyzed equilibrated reaction of *N*-activated 2,3-*trans*-3-alkyl-2-vinylaziridines **B** would aid in producing the desired 2,3-*cis*-isomers **A** preferentially *via* π-allyl palladium complexes **E**, **D**, and **C** as shown in Scheme 8. However, we were still apprehensive as to the possible success of palladium(0)-catalyzed isomerizations, because of a recent report disclosing that the exposure of an *N*-activated 2-vinylaziridine to palladium(0)-catalyst led to the isolation of an aziridine-ring-opened product.[39]

To our delight, upon treatment with 5 mol % of Pd(PPh_3)$_4$ in THF at 0 °C, 2,3-*trans*-*N*-mesyl-3-methyl-2-vinylaziridine (**15**) gave a 98:2 mixture of 2,3-*cis*-*N*-mesyl-3-methyl-2-vinylaziridine (**10**) and its 2,3-*trans*-isomer (**15**) in 90% isolated yield in good agreement with the computational prediction. So far THF appears to be the solvent of choice for this equilibrated reaction. An essentially identical result was obtained following treatment of 2,3-*cis*-*N*-mesyl-3-methyl-2-vinylaziridine (**10**) under the same reaction conditions (Scheme 9 and entries 1 and 2, Table 4). Thus, a good agreement was observed between predicted and experimental results, thereby providing feedback information about the reliability of the calculation procedure used here.

As stated in the calculation section, in order to facilitate *ab initio* calculations, the most simple systems **10** and **15** bearing an *N*-mesyl group were chosen for theoretical aspects. We anticipated that the relative energies of the *N*-arenesulfonyl 2,3-*cis*/*trans* 3-alkyl-2-vinylaziridines would not be significantly influenced by the change of the *N*-activating group.[40] In this context, in order to establish the observed equilibria in *N*-mesylaziridines **10** and **15** as general trends, the same chemical analyses were carried out for various 2,3-*cis*/*trans* pairs of *N*-Boc- and *N*-(arenesulfonyl)-3-alkyl-2-vinylaziridines (Scheme 9). Results obtained by exposure to the palladium(0) catalyst(s) for the 2,3-*cis*/*trans*-pairs of activated aziridines are summarized in Table 4. Except for the *N*-Boc-aziridines **24** and **25** (entries 8 and 9, Table 4), it is readily apparent from Table 4 that the equilibrated reactions give satisfactory results. The low combined isolated yields in entries 8 and 9 could be attributed to the low stability of the **24** and **25** toward

Scheme 9. Pd(0)-Catalyzed Equilibrated Reactions



Abbreviations: Mts = 2-mesitylenesulfonyl ; Pmc = 2,2,5,7,8-pentamethyl-6-chromansulfonyl; PNBS = *p*-nitrobenzenesulfony

silica gel flash chromatography. In the presence of PPh_3, tris(dibenzylideneacetone)dipalladium [$Pd_2(dba)_3$] could be used equally well (entries 3, 5, and 7, Table 4). However, dibenzylideneacetone was found to hinder product purification by silica gel flash chromatography.

At the outset, changing the steric bulk of the *N*-activating group and the alkyl group at the C-3 position was considered to change the 2,3 *cis*−*trans* ratio of the equilibrated products. Interestingly, as can be seen from Table 4, neither the bulk of the *N*-activating group (Ms, Ts, Mts, Pmc, PNBS) nor the 3-alkyl group (Me, isopropyl, isobutyl, *tert*-butyldimethylsiloxymethyl, or benzyl) exerts significant influence on the *cis*−*trans* ratios of the reactions at equilibrium. It should be clearly noted that although we usually stir reaction mixtures for 5−20 h, reactions described above generally attained equilibrium at 0 °C in THF within 60 min as can be seen from Figure 6.

Having established conditions for the equilibrated reactions of *cis*- and *trans*-3-alkyl-2-vinylaziridines, the reaction of five-membered heterocycles **54**−**57** with Pd(PPh_3)$_4$ was briefly investigated (Scheme 10). As expected, when either the 4,5-*trans*-oxazolidin-2-one **54** or the 4,5-*cis*-isomer **55** was treated with 5 mol % of Pd(PPh_3)$_4$, a 97:3 mixture of the *cis*-3-isobutyl-2-vinylaziridine **62** and its *trans*-isomer **63** were formed in good yield *via* a decarboxylative ring closure. A similar trend was

(39) Matano, Y.; Yoshimune, M.; Suzuki, H. *J. Org. Chem.* **1995**, *60*, 4663.

(40) Reduction of the size of systems for computations. Gung, B. W.; Fouch, R. A.; Zou, D. *J. Org. Chem.* **1996**, *61*, 4200.

Table 4. Palladium(0)-Catalyzed Equilibrated Reactions of *N*-Activated 3-Alkyl-2-vinylaziridines[a]

entry	reactant	catalyst[b] (mol %)	conditions	product ratio[c] 2,3-*cis*:2,3-*trans*	combined isolated yield %
1	**10**	A (5)	0 °C, 18 h	**10**:**15** = 98:2	97
2	**15**	A (5)	0 °C, 15 h	**10**:**15** = 98:2	90
3	**15**	B (4)	0 °C, 18 h	**10**:**15** = 98:2	75
4	**18**	A (2)	0 °C, 18 h	**18**:**21** = 96:4	97
5	**18**	B (4)	0 °C, 18 h	**18**:**21** = 95:5	80
6	**21**	A (2)	0 °C, 18 h	**18**:**21** = 96:4	95
7	**21**	B (4)	0 °C, 18 h	**18**:**21** = 95:5	74
8	**24**	A (4)	0 °C, 10 h	**24**:**25** = 91:9	46
9	**25**	A (4)	0 °C, 20 h	**24**:**25** = 90:10	48
10	**28**	A (4)	0 °C, 3 h	**28**:**29** = 94.6:5.4	82
11	**29**	A (4)	0 °C, 1 h	**28**:**29** = 93.8:6.2	94
12	**38**	A (4)	0 °C, 1 h	**38**:**39** = 91.6:8.4	90
13	**39**	A (4)	0 °C, 15 h	**38**:**39** = 92.5:7.5	66
14	**45**	A (4)	0 °C, 24 h	**45**:**46** = 95.5:4.5	99
15	**46**	A (4)	0 °C, 24 h	**45**:**46** = 95.3:4.7	97
16	**62**	A (5)	0 °C, 18 h	**62**:**63** = 97:3	96
17	**63**	A (5)	0 °C, 18 h	**62**:**63** = 96:4	97
18	**64**	A (4)	0 °C, 18 h	**64**:**65** = 96:4	99
19	**65**	A (4)	0 °C, 18 h	**64**:**65** = 97:3	99
20	**68**	A (4)	0 °C, 5 h	**68**:**69** = 93:7	87
21	**69**	A (4)	0 °C, 5 h	**68**:**69** = 93:7	88

[a] All reactions were carried out in THF (ca. 0.05 molar solution) under a positive pressure of argon. [b] A = $Pd(PPh_3)_4$; B = $Pd_2(dba)_3$·$CHCl_3$:PPh_3 = 1:8. [c] Product ratios for entries 1−3 and 4−21 were determined by capillary gas chromatography (0.2 mm × 50 m) and reverse phase HPLC, respectively.

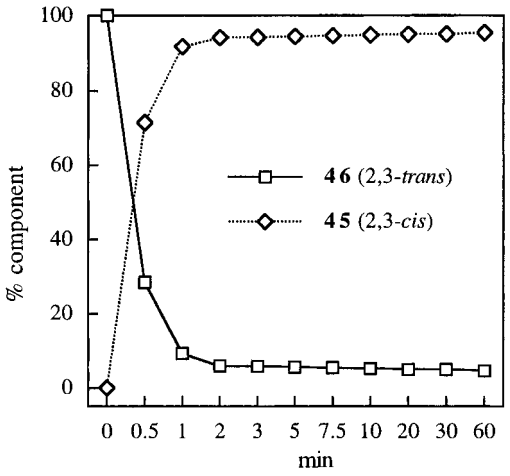
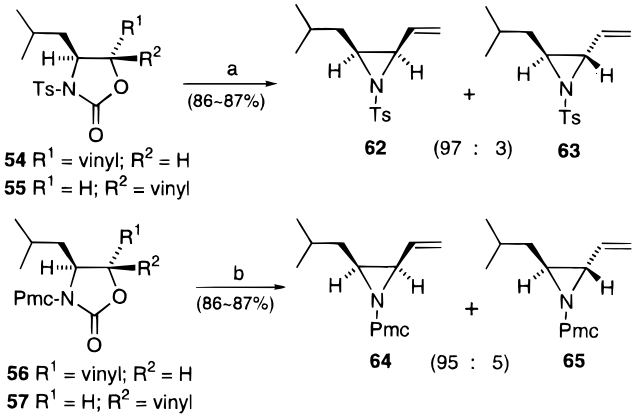


Figure 6. Plot showing the variation in the percentage composition of a mixture of 2,3-*cis*-*N*-Mts-3-isopropyl-2-vinylaziridine (**45**) and its 2,3-*trans*-isomer (**46**) formed by treatment of **46** with 5 mol % of $Pd(PPh_3)_4$ in THF at 0 °C.

noted for the reaction of oxazolidin-2-ones **56** and **57** (Scheme 10).

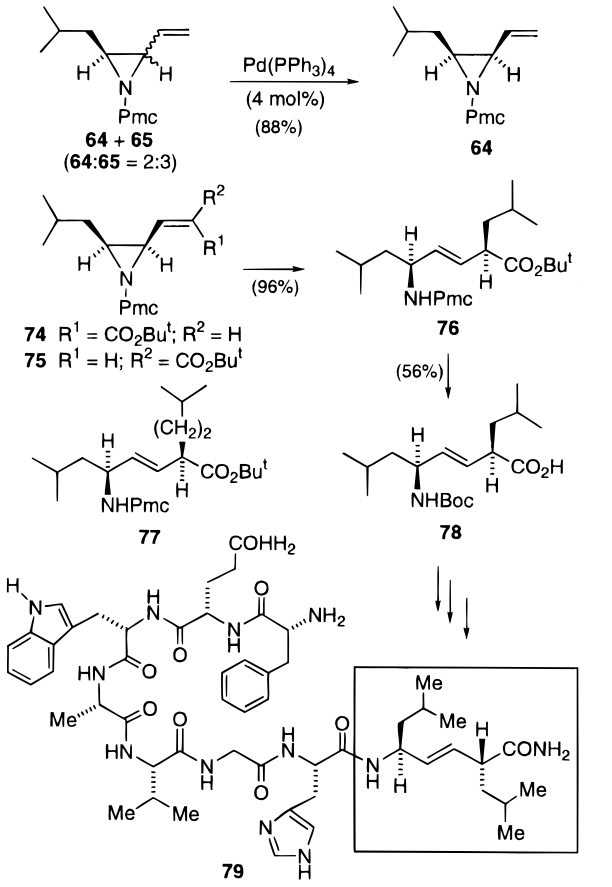
Synthetic Application to the Synthesis of (*E*)-Alkene Dipeptide Isosteres. To demonstrate the utility of these equilibrated reactions, we have used this chemistry for the synthesis of (*E*)-alkene dipeptide isosteres such as **77** and **78** (Scheme 11). The importance of optically active (*E*)-alkene isosteres as key intermediates for the synthesis of various types of polypeptides has been demonstrated by many groups.[6−10,12,41] It has also been disclosed that the stereochemistry at the α-carbon center in (*E*)-alkene dipeptide isosteres is one of the essential factors for enzyme inhibition.[42] We have also recently reported that the synthetic isosteric peptide **79**, containing a dipeptide isostere **78**, is a potent bombesin receptor antagonist with no agonist activity.[6] As stated before, the efficient synthesis of chiral 2,3-*cis*-3-alkyl-2-vinylaziridines is one of the keys to stereocontrol over the new chiral centers of the (*E*)-alkene isosteres.

Scheme 10



Reagents and Conditions: a) $(PPh_3)_4Pd$ (5 mol %) in THF; 0 °C, 18 h; b) $(PPh_3)_4Pd$ (4 mol %) in THF; 0 °C, 15 h or rt, 7 h

Scheme 11



(41) (a) Shue, Y.-K.; Tufano, M. D.; Nadzan, A. M. *Tetrahedron Lett.* **1988**, *29*, 4041. (b) Kaltenbronn, J. S.; Hudspeth, J. P.; Lunney, E. A.; Michniewicz, B. M.; Nicolaides, E. D.; Repine, J. T.; Roark, W. H.; Steir, M. A.; Tinney, F. J.; P. K. W. Woo, P. K. W.; Essenburg, A. D. *J. Med. Chem.* **1990**, *33*, 838. (c) Scarso, A.; Degelaen, J.; Viville, R.; De Cock, E.; van Marsenille, M.; van der Auwera, L.; Tourwe, D.; van Binst, G. *Bull. Soc. Chim. Belg.* **1991**, *100*, 381. (d) Touwe, D.; De Cock, E.; van Marsenille, M.; van der Auwera, L.; van Binst, G.; Viville, R.; Degelaen, J.; Scarso, A. *Peptides 1988*; Jung, G., Bayer, E., Eds.; Walter de Gruyter: Berlin and New York, 1989; p 562. (e) Tourwe, D.; Couder, J.; Ceusters, M.; Meert, D.; Burks, T. F.; Kramer, T. H.; Davis, P.; Knapp, R.; Yamamura, H. I.; Leysen, J. E.; van Binst, G. *Int. J. Pept. Protein Res.* **1992**, *39*, 131.

(42) Cox, M. T.; Gormley, C. F.; Hayward, C. F.; Petter, N. N. *J. Chem. Soc., Chem. Commun.* **1980**, 800. Fujimoto, K.; Doi, R.; Hosotani, R.; Wada, M.; Lee, J.-U.; Koshiba, T.; Ibuka, T.; Habashita, H.; Nakai, K.; Fujii, N.; Imamura, M. *Life Sci.*, **1997**, *60*, 29.

The Pd(0)-catalyzed equilibrated reaction has been successfully applied to the synthesis of (*E*)-alkene dipeptide isosteres. Typically, when a 2:3 mixture of the 2,3-*cis*- and 2,3-*trans*-aziridines **64** and **65** (4.5 g) was allowed to stand at 0 °C in THF in the presence of 4 mol % of $Pd(PPh_3)_4$ for 18 h, subsequent flash chromatographic separation of a 96:4 *cis*/*trans* mixture of **64** and **65** led to the isolation of the desired 2,3-*cis*-aziridine **64** in an 88% yield (see Experimental Section). Exposure of **64** to ozone followed by *tert*-butyl (triphenylphosphoranylidene)-acetate yielded a separable 1:12.6 mixture of (*Z*)- and (*E*)-α,β-unsaturated esters **74** and **75** in 83% combined yield. When *tert*-butyl (triphenylphosphoranylidene)acetate was substituted for the anion of *tert*-butyl diethylphosphonoacetate,[43] only the desired (*E*)-unsaturated ester **75** was obtained in a comparable isolated yield. Reaction of **75** with isobutyl-Cu(CN)MgCl or isopentyl-Cu(CN)-MgCl in THF at −78 °C for 30 min yielded stereospecifically the required (*E*)-alkene dipeptide isostere **76** or **77** in high isolated yields.[17j,t] The absolute configuration at the alkylated carbon center in (*E*)-alkene isosteres can be determined by a circular dichroism measurement. We have previously reported that given the sign of the n → π* Cotton effect, the absolute configuration at the α-position in the (*E*)-alkene isosteres can be determined.[44] The isostere **76** shows a negative n → π* Cotton effect (Δε: −8.78, 222 nm, in isooctane). Similarly, **77** exhibits a negative Cotton effect (Δε: −7.82, 222 nm, in isooctane). Consequently, the absolute configuration at the alkylated carbon center in the isosteres **76** and **77** was assigned as *R*. Deprotection of both the *N*- and carboxy protecting groups in **76** followed by *tert*-butoxycarbonylation yielded the NH-Boc-isostere **78**, which can be used for the synthesis of the potent bombesin antagonist **79**.[6]

In summary, we have developed a reliable procedure for the isomerization of the undesired 2,3-*trans*-3-alkyl-2-vinylaziridines into the desired 2,3-*cis*-isomers by means of palladium(0)-catalyzed equilibrated reactions. 2,3-*trans*-2,3-Disubstituted NH aziridine **71** shown in Figure 2 is predicted to be more stable than the corresponding *cis*-isomer **70**. On the contrary, as shown in Figures 3 and 4 and Table 2 (entries 2 and 3), 2,3-*cis*-disubstituted aziridines with an *N*-methyl or mesyl group are predicted to be more stable than their 2,3-*trans*-isomers. Use of $Pd(PPh_3)_4$ has thus overcome the problematic stereoselectivity in the synthesis of allylic alcohols from protected chiral amino aldehydes and has put the method on a sound synthetic footing.

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. All NMR spectra were recorded in $CDCl_3$ unless otherwise specified. 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. For HPLC, Cosmosil-5SL (10 × 200 mm, Nacalai Tesque) was employed. The enantiomeric excess (ee) was determined using chiral HPLC columns (Chiralcel OD or Chiralcel OB, Daicel, or ChiraSpher, Merck).

(2*R*,3*S*)-3-Methyl-*N*-trityl-2-vinylaziridine (9). To a stirred solution of oxalyl chloride (2.5 mL, 26 mmol, 1.5 equiv) in dry CH_2Cl_2 (200 mL) at −78 °C under argon was added dropwise a solution of DMSO (7.36 mL, 103.8 mmol, 6 equiv) in CH_2Cl_2 (20 mL). After 20 min, a solution of the trityl alcohol **7**[11] (5.7 g, 17.3 mmol) in CH_2Cl_2 (20 mL) was added to the above reagent at −78 °C, and the mixture was stirred for 1 h. Diisopropylethylamine (21 mL, 0.12 M) was added dropwise to the above solution at −78 °C, and the mixture was stirred for 2 h with warming to 0 °C. The reaction was quenched with 40 mL of a saturated aqueous NH_4Cl solution at −78 °C with vigorous stirring. The mixture was extracted with Et_2O, and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave a crude aldehyde as a colorless oil. To a stirred solution of the above oily aldehyde in THF (50 mL) at 0 °C was added a THF solution (200 mL) of methylenetriphenylphosphorane, preprared from methyltriphenylphosphonium bromide (24.7 g, 69.2 mmol) and *n*-BuLi (43.2 mL, 69.2 mmol, 1.6 M in *n*-hexane), and the mixture was stirred for 30 min at 0 °C. The reaction was quenched with 20 mL of a 5% NH_4Cl solution at −78 °C with vigorous stirring. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) gave 2.3 g (41% yield) of the title compound **9** as a colorless oil. $[\alpha]^{26}_D$ −70 (*c* 0.99, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, *J* = 5.6 Hz, 3 H), 1.44 (m, 1 H), 1.67 (m, 1 H), 5.18−5.25 (m, 2 H), 5.88 (m, 1 H), 7.17−7.28 (m, 9 H), 7.45−7.49 (m, 6 H). LRMS (CI, reagent gas: methane) *m*/*z*, 326 (MH^+), 271, 248, 240 (base peak). HRMS (CI, reagent gas: methane) *m*/*z*, calcd for $C_{24}H_{24}N$ (MH^+) 326.1909; found: 326.1915.

(2*R*,3*S*)-*N*-(Methanesulfonyl)-3-methyl-2-vinylaziridine (10). To a solution of the *N*-tritylaziridine **9** (550 mg, 1.7 mmol) in 3 mL of $CHCl_3$ at 0 °C was added 2 mL of TFA, and the mixture was stirred for 2 h. Concentration under reduced pressure gave an oily residue, which was used without purification for the next step. To a stirred solution of the above oily residue in 5 mL of $CHCl_3$ at −60 °C were added successively 2 mL of Et_3N and 0.5 mL of methanesulfonyl chloride with vigorous stirring, and the whole was stirred for 3 h at 0 °C. It was then cooled to 0 °C, and a saturated $NaHCO_3$ solution (10 mL) was added with vigorous stirring. The mixture was extracted with EtOAc, and the extract was washed successively with 5% 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 (3:1) gave 100 mg (37% yield) of the title compound **10** as a colorless oil. $[\alpha]^{25}_D$ −94.8 (*c* 0.736, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (d, *J* = 5.8 Hz, 3 H), 3.01 (m, 1 H), 3.03 (s, 3 H), 3.28 (m, 1 H), 5.38−5.55 (m, 2 H), 5.68 (ddd, *J* = 14.1, 10.2, 6.8 Hz, 1 H). LRMS (FAB) *m*/*z*, 162 (MH^+, base peak), 149, 113, 82, 57. HRMS (FAB) *m*/*z*, calcd for $C_6H_{12}NO_2S$ (MH^+) 162.0589; found: 162.0580.

Methyl *O*-(*tert*-Butyldimethylsilyl)-*N*-(methanesulfonyl)-D-*allo*-threoninate (12). To a stirred solution of D-*allo*-threonine methyl ester hydrochloride (**11**) (5.7 g, 33.6 mmol) in a mixture of 20 mL of $CHCl_3$ and 20 mL of DMF at −78 °C were added successively *N*,*N*-diisopropylethylamine (14.6 mL, 0.168 M) and methanesulfonyl chloride (3.12 mL, 40.3 mmol), and then the mixture was allowed to warm to 0 °C. After 2 h, imidazole (9.13 g, 134 mmol) and *tert*-butyldimethylsilyl chloride (6.088 g, 40.3 mmol) were added to the mixture with stirring at 0 °C, and stirring was continued for 48 h, followed by quenching with aqueous 5% $NaHCO_3$ (20 mL). The mixture was extracted with Et_2O, and the extract was washed successively 5% citric acid, water, 5% $NaHCO_3$, and water and then 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 7.5 g (69% yield) of the title compound **12** as a colorless oil. $[\alpha]^{25}_D$ −8.3 (*c* 1.77, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.092 (s, 3 H), 0.10 (s, 3 H), 0.89 (s, 9 H), 1.20 (d, *J* = 6.3 Hz, 3 H), 3.01 (s, 3 H), 3.79 (s, 3 H), 4.12−4.21 (m, 2 H), 5.09 (d, *J* = 7.7 Hz, 1 H). LRMS (FAB) *m*/*z*, 326 (MH^+), 310, 268 (base peak), 266, 208, 194, 159. HRMS (FAB) *m*/*z*, calcd for $C_{12}H_{28}NO_5SSi$ (MH^+) 326.1457; found: 326.1444.

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Methyl *N*-(Methanesulfonyl)-D-*allo*-threoninate (13). To a stirred solution of the silyl ether **12** (2.5 g, 7.67 mmol) in a mixture of MeCN (18 mL), MeOH (3 mL), and water (0.6 mL) was added 1.5 mL of 46% aqueous HF, and the mixture was stirred at 50 °C for 1 h. The mixture was made basic with 28% NH_4OH at 0 °C and concentrated under reduced pressure to leave a colorless semisolid, which was purified by flash chromatography over silica gel eluting with *n*-hexane−EtOAc (1:2) to give 1.55 g (96% yield) of the title compound **13** as a colorless syrup. $[\alpha]^{25}_D$ −0.86 (*c* 1.72, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.21 (d, J = 6.3 Hz, 3 H), 2.74 (d, J = 7.0 Hz, 1 H), 3.04 (s, 3 H), 3.82 (s, 3 H), 4.16−4.26 (m, 2 H), 5.63 (d, J = 8.3 Hz, 1 H). LRMS (FAB) *m*/*z*, 212 (MH^+, base peak), 194, 152, 134. HRMS (FAB) *m*/*z*, calcd for $C_6H_{14}NO_5S$ (MH^+) 212.0593; found: 212.0596.

Methyl (2*R*,3*S*)-*N*-(Methanesulfonyl)-3-methylaziridine-2-carboxylate (14). Triphenylphosphine (2.34 g, 8.93 mmol) and diethyl azodicarboxylate (1.2 mL, 7.56 mmol) were added to a stirred solution of the alcohol **13** (1.45 g, 6.87 mmol) in 20 mL of THF at 0 °C, and the mixture was allowed to warm to room temperature and stirred at this temperature for 1 h. The mixture was concentrated under reduced pressure to an oil, which was flash chromatographed on a silica gel column. Elution with *n*-hexane−EtOAc (3:2) gave 1.28 g (96% yield) of the title compound **14** as a colorless oil. Kugelrohr distillation, 115 °C (1 Torr); $[\alpha]^{25}_D$ +102.6 (*c* 1.16, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.67 (d, J = 6.0 Hz, 3 H), 3.08−3.16 (m, 1 H), 3.14 (s, 3 H), 3.29 (d, J = 4.0 Hz, 1 H), 3.79 (s, 3 H). Anal. Calcd for $C_6H_{11}NO_4S$: C, 37.3; H, 5.74; N, 7.25. Found: C, 37.21; H, 5.80; N, 7.24.

(2*S*,3*S*)-*N*-(Methanesulfonyl)-3-methyl-2-vinylaziridine (15). Diisobutylaluminum hydride in toluene (4.8 mL, 4.8 mmol; 1.0 M solution) was added dropwise to a stirred solution of the ester **14** (744 mg, 4 mmol) in 13 mL of toluene at −78 °C under argon. After 1 h, a saturated NH_4Cl solution (2 mL) was added dropwise with vigorous stirring. The mixture was made acidic with 15% citric acid at 0 °C and extracted with $CHCl_3$. The extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave a crude aldehyde as a colorless oil. To a stirred solution of the above oily aldehyde in THF (10 mL) at 0 °C was added a THF solution (30 mL) of methylenetriphenylphosphorane, preprared from methyltriphenylphosphonium bromide (4.11 g, 11.5 mmol) and *n*-BuLi (7.19 mL, 11.5 mmol, 1.6 M in *n*-hexane), and the mixture was stirred for 30 min at 0 °C. The reaction was quenched with 2 mL of a 5% NH_4Cl solution at 0 °C with vigorous stirring. The mixture was concentrated under reduced pressure to a semisolid, which was flash chromatographed on a silica gel column. Elution with *n*-hexane−EtOAc (2:1) gave 100 mg of a colorless solid, which was recrystallized from cold *n*-hexane−Et_2O (4:1) to give the title compound **15** (80 mg, 12.4% yield) as colorless crystals: mp 48 °C; $[\alpha]^{25}_D$ −40.5 (*c* 0.682, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (d, J = 5.8 Hz, 3 H), 2.93 (ddd, J = 11.6, 5.8, 4.4 Hz, 1 H), 3.05 (s, 3 H), 3.09 (dd, J = 8.8, 4.4 Hz, 1 H), 5.34−5.38 (m, 1 H), 5.50−5.56 (m, 1 H), 5.86 (ddd, J = 17.1, 10.2, 8.8 Hz, 1 H). LRMS (CI: reagent gas, methane) *m*/*z*, 162 (MH^+, base peak), 146, 120, 106, 84, 83, 82. HRMS (CI: reagent gas, methane) *m*/*z*, calcd for $C_6H_{12}NO_2S$ (MH^+) 162.0589; found: 162.0589.

(2*R*,3*S*)-3-Methyl-*N*-(4-methylbenzenesulfonyl)-2-vinylaziridine (18). By use of a procedure similar to that described for the preparation of **9** from **7**, the known 2-aziridinemethanol **16**[11] (2.892 g, 12 mmol) was converted into the title compound **18** (300 mg, 11% yield): colorless crystals from *n*-hexane−Et_2O (4:1); mp 84 °C; $[\alpha]^{26}_D$ −1.0 (*c* 1.05, $CHCl_3$); ee > 99% (Chiralcel OB, 2-PrOH: *n*-hexane = 85:15); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (d, J = 5.8 Hz, 3 H), 2.44 (s, 3 H), 3.03 (ddd, J = 11.7, 7.3, 5.8 Hz, 1 H), 3.32 (m, 1 H), 5.27−5.31 (m, 1 H), 5.60 (ddd, J = 17.2, 10.3, 6.9 Hz, 1 H), 7.31−7.34 (m, 2 H), 7.80−7.84 (m, 2 H). Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.45; H, 6.47; N, 5.82.

(2*S*,3*S*)-3-Methyl-*N*-(4-methylbenzenesulfonyl)-2-vinylaziridine (21). By use of a procedure similar to that described for the preparation of **15** from **14**, the known ester **19**[11] (1.8 g, 6.69 mmol) was converted into the title compound **21** (500 mg, 31% yield): colorless crystals from *n*-hexane−Et_2O (5:1); mp 83 °C; $[\alpha]^{26}_D$ −87.4 (*c* 0.633, $CHCl_3$); ee > 98% (Chiralcel OB, 2-PrOH: *n*-hexane = 85:15); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (d, J =5.8 Hz, 3 H), 2.44 (s, 3 H), 2.97 (m, 1 H), 3.13 (dd, J = 8.7, 4.4 Hz, 1 H), 5.29−5.32 (m, 1 H), 5.41−5.48 (m, 1 H), 5.91 (ddd, J = 17.1, 10.2, 8.7 Hz, 1 H), 7.27−7.33 (m, 2 H), 7.80−7.84 (m, 2 H). Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90. Found: C, 60.78; H, 6.40; N, 5.86.

(2*R*,3*S*)-3-Benzyl-*N*-(*tert*-butoxycarbonyl)-2-vinylaziridine (24). Triphenylphosphine (262 mg, 1 mmol, 2 equiv) and diethyl azodicarboxylate (0.326 mL of a 40% solution in toluene, 0.75 mmol, 1.5 equiv) were added to a stirred solution of the alcohol **22** (139 mg, 0.5 mmol) in 4 mL of THF at 0 °C, and the mixture was stirred at this temperature for 5 h. The mixture was concentrated under reduced pressure to an oil, which was flash chromatographed on a silica gel column. Elution with *n*-hexane−EtOAc (5:1) gave 100 mg (77% yield) of the title compound **24** as a colorless oil. $[\alpha]^{25}_D$ −42.9 (*c* 0.81, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9 H), 2.67−2.79 (m, 2 H), 2.84−2.96 (m, 1 H), 3.05 (dddd, J = 6.4, 6.4, 0.8, 0.8 Hz, 1 H), 5.36 (ddd, J = 10.4, 1.7, 0.8 Hz, 1 H), 5.41 (ddd, J = 17.1, 1.7, 0.8 Hz, 1 H), 5.79 (ddd, J = 17.1, 10.4, 6.4 Hz, 1 H), 7.18−7.31 (m, 5 H). LRMS (FAB) *m*/*z*, 260 (MH^+), 259, 204 (base peak), 160, 143, 91, 57. HRMS (FAB), *m*/*z*, calcd for $C_{16}H_{22}NO_2$ (MH^+) 260.1650; found: 260.1643.

(2*S*,3*S*)-3-Benzyl-*N*-(*tert*-butoxycarbonyl)-2-vinylaziridine (25). By use of a procedure similar to that described for the synthesis of the vinylaziridine **24** from **22**, 277 mg (1 mmol) of **23** was converted into 200 mg (77% yield) of the title compound **25** as a colorless oil by treatment with PPh_3 (262 mg) and diethyl azodicarboxylate (0.434 mL of a 40% solution in toluene) in THF (5 mL) at 0 °C for 5 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1). $[\alpha]^{25}_D$ −16 (*c* 0.84, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 2.61−2.71 (m, 2 H), 2.88 (dd, J = 7.3, 3.0 Hz, 1 H), 3.05 (m, 1 H), 5.23−5.50 (m, 3 H), 7.19−7.36 (m, 5 H). LRMS (FAB) *m*/*z*, 260 (MH^+), 259, 204 (base peak), 158, 143, 91, 57. HRMS (FAB), *m*/*z*, calcd for $C_{16}H_{22}NO_2$ (MH^+) 260.1650; found: 260.1652.

(3*S*,4*S*)-5-Phenyl-4-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-penten-3-ol (26). Trifluoroacetic acid (15 mL) was added to 1.385 g (5 mmol) of the alcohol **22**[12,14] at 0 °C, and the mixture was stirred for 1 h. The solution 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 50 mL of $CHCl_3$ were added successively 15 mL of Et_3N and 1.31 g (6 mmol) of mesitylenesulfonyl chloride. After being stirred for 1 h at 0 °C, 10 mL of 10% $NaHCO_3$ was added to it, and the mixture was stirred for 30 min. The mixture was made acidic with 20% citric acid and extracted with EtOAc and the extract was washed with water and dried over $MgSO_4$. Concentration followed by flash chromatography over silica gel with *n*-hexane−EtOAc (2:1) gave 1.493 g (83% yield) of the title compound **26**. Colorless crystals from *n*-hexane−Et_2O (2:1); mp 92−93 °C; $[\alpha]^{27}_D$ −42.0 (*c* 1.02, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.99 (d, J = 3.8 Hz, 1 H), 2.28 (s, 3 H), 2.56 (s, 6 H), 2.65 (dd, J = 13.8, 6.5 Hz, 1 H), 2.93 (dd, J = 13.8, 8.6 Hz, 1 H), 3.43 (m, 1 H), 4.10 (m, 1 H), 4.96 (d, J = 8.6 Hz, 1 H), 5.05−5.25 (m, 2 H), 5.69 (ddd, J = 17.3, 10.5, 5.7 Hz, 1 H), 7.00−7.21 (m, 5 H); LRMS (FAB) *m*/*z*, 360 (MH^+), 302, 183, 119 (base peak), 91. HRMS (FAB), *m*/*z*, calcd for $C_{20}H_{26}NO_3S$ (MH^+) 360.1633; found: 360.1631.

(3*R*,4*S*)-5-Phenyl-4-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-penten-3-ol (27). By use of a procedure identical with that described for the preparation of **26** from **22**, the known alcohol **23**[12,14] (730 mg, 2.635 mmol) was converted into 677 mg (72% yield) of the title compound **27**. Colorless crystals from *n*-hexane−Et_2O (2:1); mp 72−73 °C; $[\alpha]^{27}_D$ −43.9 (*c* 1.00, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.72 (d, J = 6.8 Hz, 1 H), 2.27 (s, 3 H), 2.43 (s, 6 H), 2.61 (dd, J = 14.5, 8.9 Hz, 1 H), 2.68 (m, 1 H), 2.77 (dd, J = 14.5, 5.7 Hz, 1 H), 3.48 (m, 1 H), 4.38 (m, 1 H), 4.86 (m, 1 H), 5.30 (ddd, J = 10.5, 1.5, 1.5 Hz, 1 H), 5.39 (ddd, J = 17.5, 1.5, 1.5 Hz, 1 H), 5.89 (ddd, J = 17.5, 10.5, 5.7 Hz, 1 H), 6.70−7.26 (m, 5 H). Anal. Calcd for

$C_{20}H_{25}NO_3S$: C, 66.82; H, 7.01; N, 3.90. Found: C, 66.56; H, 7.04; N, 3.87.

(2*R*,3*S*)-3-Benzyl-*N*-(2,4,6-trimethylbenzenesulfonyl)-2-vinylaziridine (28). By use of a procedure similar to that described for the synthesis of **24** from **22**, 213 mg (0.593 mmol) of the allyl alcohol **26** was converted into 141 mg (70% yield) of the title compound **28** by treatment with PPh_3 (187 mg, 1.1 mmol) and 0.098 mL (0.622 mmol) of diethyl azodicarboxylate in THF (2 mL) at 0 °C for 5 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (9:1). Colorless crystals from *n*-hexane−Et_2O (2:1); mp 73−74 °C; $[\alpha]^{26}_D$ −25.7 (*c* 1.01, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.29 (s, 3 H), 2.58 (s, 6 H), 2.65 (dd, J = 14.6, 7.8 Hz, 1 H), 2.75 (dd, J = 14.6, 5.7 Hz, 1 H), 3.10 (m, 1 H), 3.48 (dd, J = 7.3, 6.8 Hz, 1 H), 5.37 (m, 1 H), 5.50 (m, 1 H), 5.79 (ddd, J = 17.0, 10.5, 6.8 Hz, 1 H), 6.80−7.20 (m, 5 H). Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10. Found: C, 70.19; H, 6.78; N, 3.98.

(2*S*,3*S*)-3-Benzyl-*N*-(2,4,6-trimethylbenzenesulfonyl)-2-vinylaziridine (29). By use of a procedure identical with that described for the synthesis of **28** from **26**, 655 mg (1.825 mmol) of the allyl alcohol **27** was converted into 488 mg (78% yield) of the title compound **29**. Colorless crystals from *n*-hexane−Et_2O (2:1); mp 109−110 °C; $[\alpha]^{31}_D$ −32.8 (*c* 0.993, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3 H), 2.54 (s, 6 H), 2.67 (dd, J = 14.3, 7.0 Hz, 1 H), 2.99 (dd, J = 14.3, 5.1 Hz, 1 H), 3.14 (m, 1 H), 3.20 (dd, J = 9.1, 4.2 Hz, 1 H), 5.35 (m, 1 H), 5.50 (m, 1 H), 6.07 (ddd, J = 17.0, 10.2, 9.1 Hz, 1 H), 6.80−7.14 (m, 5 H). Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10. Found: C, 70.51; H, 6.90; N, 4.10.

(4*S*,5*S*)-4-[(*tert*-Butyldimethylsiloxy)methyl]-5-vinyloxazolidin-2-one (32). To a stirred suspension of sodium hydride (435 mg, 9 mmol) in a mixture of THF (25 mL) and DMF (15 mL) at 0 °C was added 3 g (9 mmol) of the alcohol **30**[12] in 10 mL of THF. The stirring was continued for 18 h at rt followed by quenching with 15 mL of 20% citric acid at −78 °C with vigorous stirring. The mixture was extracted with Et_2O and the extract was washed successively with brine, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (3:1) gave 960 mg (42% yield) of the title compound **32** as a colorless oil. $[\alpha]^{30}_D$ −42.0 (*c* 0.948, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.89 (s, 9 H), 3.60−3.67 (m, 3 H), 4.74 (m, 1 H), 5.30 (ddd, J = 10.5, 1.0, 1.0 Hz, 1 H), 5.41 (ddd, J = 17.0, 1.0, 1.0 Hz, 1 H), 6.02 (broad s, 1 H), 5.92 (ddd, J = 17.0, 10.5, 6.5 Hz, 1 H); LRMS (FAB) *m*/*z*, 258 (MH^+, base peak), 200, 156, 115, 73. HRMS (FAB) *m*/*z*, calcd for $C_{12}H_{24}NO_3Si$ (MH^+) 258.1525; found: 258.1530.

(4*S*,5*R*)-4-[(*tert*-Butyldimethylsiloxy)methyl]-5-vinyloxazolidin-2-one (33). By use of a procedure identical with that described for the synthesis of the oxazolidin-2-one **32** from **30**, 1.0 g (3.02 mmol) of the alcohol **31**[12] was converted into 265 mg (34.1% yield) of the title compound **33**. Colorless crystals from *n*-hexane; mp 78 °C; $[\alpha]^{29}_D$ −53.8 (*c* 1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.059 (s, 3 H), 0.062 (s, 3 H), 0.89 (s, 9 H), 3.53 (dd, J = 10.5, 7.3 Hz, 1 H), 3.59 (dd, J = 10.5, 4.9 HZ, 1 H), 3.89 (ddd, J = 12.1, 7.6, 4.6 Hz, 1 H), 5.09 (dddd, J = 8.1, 6.8, 1.1, 1.1 Hz, 1 H), 5.34 (broad s, 1 H), 5.37 (ddd, J = 10.5, 1.0., 1.0 Hz, 1 H), 5.49 (ddd, J = 17.2, 1.0, 1.0 Hz, 1 H), 5.90 (ddd, J = 17.2, 10.5, 6.8 Hz, 1 H). Anal. Calcd for $C_{12}H_{23}NO_3Si$: C, 55.99; H, 9.01; N, 5.44. Found: C, 56.12; H, 9.25; N, 5.39.

(4*S*,5*S*)-4-[(*tert*-Butyldimethylsiloxy)methyl]-*N*-(2,4,6-trimethylbenzenesulfonyl)-5-vinyloxazolidin-2-one (34). Mesitylenesulfonyl chloride (3.4 g, 15.6 mmol) in 10 mL of THF and **32** (2.0 g, 7.8 mmol) in 15 mL of THF were successively added to a stirred suspension of sodium hydride (0.588 g, 23.4 mmol) in THF (2 mL) at 0 °C. The stirring was continued for 1 h followed by quenching with 10 mL of 20% citric acid at −78 °C with vigorous stirring. The mixture was made alkaline with 5% $NaHCO_3$ and extracted with EtOAc. The extract was successively washed with brine and water and dried over $MgSO_4$. Usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (9:1) gave 2.73 g (70% yield) of the title compound **34** as a crystalline mass. Recrystallization from *n*-hexane gave **34** as colorless crystals; mp 99 °C; $[\alpha]^{30}_D$ +72.3 (*c* 1.15, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3 H), 0.14 (s, 3 H), 0.87 (s, 9 H), 2.30 (s, 3 H), 2.64 (s, 6 H), 4.00 (s, 1 H), 4.02 (s, 1 H), 4.21 (m, 1 H), 4.96 (m, 1 H), 5.32 (d, J = 10.5 Hz, 1 H), 5.39 (d, J = 17.3 Hz, 1 H), 5.88 (ddd, J = 17.3, 10.5, 5.1 Hz, 1 H), 6.97 (s, 2 H). Anal. Calcd for $C_{21}H_{33}NO_5SSi$: C, 57.38; H, 7.57; N, 3.19. Found: C, 57.10; H, 7.56; N, 3.12.

(4*S*,5*R*)-4-[(*tert*-Butyldimethylsiloxy)methyl]-*N*-(2,4,6-trimethylbenzenesulfonyl)-5-vinyloxazolidin-2-one (35). By use of a procedure identical with that described for the synthesis of the oxazolidin-2-one **34** from **32**, 500 mg (1.945 mmol) of the oxazolidin-2-one **33** was converted into 573 mg (67% yield) of the title compound **35**. Colorless crystals from *n*-hexane−EtOAc (3:1); mp 133 °C; $[\alpha]^{27}_D$ +129 (*c* 0.952, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.12 (s, 3 H), 0.15 (s, 3 H), 0.92 (s, 9 H), 2.30 (s, 3 H), 2.68 (s, 6 H), 3.86 (d, J = 11.5 Hz, 1 H), 4.13 (dd, J = 11.5, 3.2 Hz, 1 H), 4.40 (dd, J = 7.6, 2.7 Hz, 1 H), 4.98 (t, J = 7.6 Hz, 1 H), 4.46 (d, J = 10.3 Hz, 1 H), 5.50 (d, J = 17.5 Hz, 1 H), 6.13 (ddd, J = 17.6, 10.3, 7.6 Hz, 1 H), 6.98 (s, 2 H). Anal. Calcd for $C_{21}H_{33}NO_5SSi$: C, 57.38; H, 7.57; N, 3.19. Found: C, 57.53; H, 7.65; N, 3.12.

(3*S*,4*S*)-5-(*tert*-Butyldimethylsiloxy)-4-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-penten-3-ol (36). To a stirred solution of the oxazolidin-2-one **34** (2 g, 4.56 mmol) in 15.3 mL of MeOH−H_2O (2:1) at 0 °C was added 2.3 g of KOH, and the mixture was stirred for 15 h at room temperature. The solution was concentrated under reduced pressure and extracted with Et_2O. The extract was washed with brine and dried over $MgSO_4$. Usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (7:3) gave 947 mg (50% yield) the title compound **36** as a crystalline mass. Recrystallization from *n*-hexane−Et_2O (2:1) gave colorless crystals; mp 104 °C; $[\alpha]^{31}_D$ −21 (*c* 0.944, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.018 (s, 3 H), 0.021 (s, 3 H), 0.87 (s, 9 H), 2.30 (s, 3 H), 2.63 (s, 6 H), 2.99 (d, J = 2.2 Hz, 1 H), 3.17 (m, 1 H), 3.59 (dd, J = 10.3, 4.6 Hz, 1 H), 3.70 (dd, J = 10.3, 2.4 Hz, 1 H), 4.32 (m, 1 H), 5.05 (ddd, J = 10.5, 1.5, 1.5 Hz, 1 H), 5.20 (d, J = 8.6 Hz, 1 H), 5.25 (ddd, J = 17.2, 1.5, 1.5 Hz, 1 H), 5.54 (ddd, J = 17.2, 10.5, 5.7 HZ, 1 H), 6.94 (s, 2 H). Anal. Calcd for $C_{20}H_{35}NO_4SSi$: C, 58.07; H, 8.53; N, 3.39. Found: C, 57.96; H, 8.45; N, 3.37.

(3*R*,4*S*)-5-(*tert*-Butyldimethylsiloxy)-4-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-penten-3-ol (37). By use of a procedure similar to that described for the synthesis of the amino alcohol **36** from **34**, 395 mg (0.9 mmol) of the oxazolidin-2-one **35** was converted into 207 mg (56% yield) of the title compound **37** as a colorless oil. $[\alpha]^{28}_D$ +23.0 (*c* 1.087, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.01 (s, 6 H), 0.86 (s, 9 H), 2.30 (s, 3 H), 2.66 (s, 6 H), 2.97 (d, J = 8.6 Hz, 1 H), 3.21 (m, 1 H), 3.53 (dd, J = 10.3, 3.8 Hz, 1 H), 3.82 (dd, J = 10.3, 3.0 Hz, 1 H), 4.11 (m, 1 H), 5.21 (ddd, J = 10.5, 1.5, 1.5 Hz, 1 H), 5.30 (ddd, J = 17.2, 1.5, 1.5 Hz, 1 H), 5.37 (d, J = 8.6 Hz, 1 H), 5.80 (ddd, J = 17.2, 10.5, 5.1 Hz, 1 H), 6.96 (s, 2 H). LRMS (FAB) *m*/*z*, 414 (MH^+), 396, 356, 213, 173, 167, 119, 89, 73 (base peak). HRMS (FAB) *m*/*z*, calcd for $C_{20}H_{36}NO_4SSi$ (MH^+) 414.2134; found: 414.2144.

(2*R*,3*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-*N*-(2,4,6-trimethylbenzenesulfonyl)-3-vinylaziridine (38). By use of a procedure similar to that described for the synthesis of the vinylaziridine **24** from **22**, 413 mg (1 mmol) of the allyl alcohol **36** was converted into 379 mg (96% yield) of the title compound **38** as a colorless oil. $[\alpha]^{28}_D$ +0.12 (*c* 1.04, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.09 (s, 3 H), −0.06 (s, 3 H), 0.79 (s, 9 H), 2.30 (s, 3 H), 2.69 (s, 6 H), 3.07 (m, 1 H), 3.44 (dddd, J = 6.9, 6.9, 1.0, 1.0 Hz, 1 H), 3.58 (dd, J = 17.0, 1.5 Hz, 1 H), 3.61 (dd, J = 17.0, 1.5 Hz, 1 H), 5.28 (m, 1 H), 5.41 (m, 1 H), 5.66 (ddd, J = 17.0, 10.0, 6.5 Hz, 1 H), 6.940 (s, 1 H), 6.942 (s, 1 H). LRMS (FAB) *m*/*z*, 396 (MH^+), 338, 308, 241, 212, 177, 154, 119, 89, 73 (base peak), 59. HRMS (FAB) *m*/*z*, calcd for $C_{20}H_{34}NO_3SSi$ (MH^+) 396.2028; found: 396.2026.

(2*R*,3*S*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-*N*-(2,4,6-trimethylbenzenesulfonyl)-3-vinylaziridine (39). By use of a procedure similar to that described for the preparation of **24** from **22**, 187 mg (0.453 mmol) of the allyl alcohol **37** was converted into 174 mg (97% yield) of the title compound **39** as a colorless oil. $[\alpha]^{28}_D$ +0.12 (*c* 1.04, $CHCl_3$); ^{1}H NMR (270 MHz,

$CDCl_3$) δ −0.13 (s, 3 H), −0.10 (s, 3 H), 0.78 (s, 9 H), 2.84 (s, 3 H), 2.69 (s, 6 H), 3.17 (m, 1 H), 3.22 (dd, J = 8.9, 4.1 Hz, 1 H), 3.60 (dd, J = 11.5, 5.4 Hz, 1 H), 3.75 (dd, J = 11.5, 3.8 Hz, 1 H), 5.36 (dd, J = 10.2, 1.0 Hz, 1 H), 5.56 (dd, J = 17.0, 1.0 Hz, 1 H), 6.12 (ddd, J = 17.0, 10.2, 9.6 Hz, 1 H), 6.919 (s, 1 H), 6.922 (s, 1 H). LRMS (FAB) *m/z*, 396 (MH^+), 338, 308, 241, 212, 177, 154, 119, 89, 73 (base peak), 59. HRMS (FAB) *m/z*, calcd for $C_{20}H_{34}NO_3SSi$ (MH^+) 396.2028; found: 396.2034.

(*S*)-*N*-(2,4,6-Trimethylbenzenesulfonyl)valinol (41). To a stirred solution of (*S*)-valinol **40** (11.74 g, 0.114 M) and Et_3N (63 mL, 0.456 M) in THF (30 mL) at 0 °C was added 2,4,6-trimethylbenzenesulfonyl chloride (25 g, 0.114 M), and the mixture was stirred for 1 h. The reaction was quenched with 20 mL of 5% $NaHCO_3$ at 0 °C with stirring. The mixture was extracted with EtOAc, and the extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$, and brine and dried over $MgSO_4$. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (4:1) gave 29 g (89% yield) of the title compound **41** as a colorless crystalline mass. Recrystallization from *n*-hexane−Et_2O (2:1) gave colorless crystals: mp 71 °C; $[\alpha]^{20}_D$ −37.8 (*c* 1.13, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.75 (d, J = 6.6 Hz, 3 H), 0.80 (d, J = 6.9 Hz, 3 H), 1.76 (m, 1 H), 2.30 (s, 3 H), 2.35 (m, 1 H), 2.66 (s, 6 H), 2.98 (m, 1 H), 3.60 (m, 2 H), 5.14 (m, 1 H), 6.95 (s, 2 H). Anal. Calcd for $C_{14}H_{23}NO_3S$: C, 58.92; H, 8.12; N, 4.91. Found: C, 58.84; H, 8.42; N, 4.90.

(3*S*,4*S*)-5-Methyl-4-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-hexen-3-ol (43) and (3*R*,4*S*)-5-Methyl-4-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-hexen-3-ol (44). To a stirred solution of oxalyl chloride (5.68 mL, 59.3 mmol, 1.3 equiv) in dry CH_2Cl_2 (70 mL) at −78 °C under argon was added dropwise a solution of DMSO (9.7 mL, 137 mmol, 3 equiv) in CH_2Cl_2 (20 mL). After 20 min, a solution of the alcohol **41** (13 g, 45.6 mmol) in CH_2Cl_2 (20 mL) was added to the above reagent at −78 °C, and the mixture was stirred for 1 h. Diisopropylethylamine (39.6 mL, 228 mmol, 5 equiv) was added dropwise to the above solution at −78 °C, and the mixture was stirred for 2 h with warming to 0 °C. The reaction was quenched with 20 mL of a saturated aqueous NH_4Cl solution at −78 °C with vigorous stirring. 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 as a colorless oil. To a stirred solution of CuCN (410 mg, 4.56 mmol) and LiCl (386 mg, 9.12 mmol) in 40 mL of THF at −78 °C was added *via* syringe vinylmagnesium bromide (96 mL; 1 M solution in THF; 96 mmol, 2.1 equiv). After being stirred at this temperature for 10 min, a solution of the above crude aldehyde in THF (50 mL) was added dropwise to it, and the mixture was allowed to warm to −40 °C and stirred at this temperature for 30 min, followed by quenching with 30 mL of a mixture of 5% NH_4Cl−28% NH_4OH (1:1). The mixture was concentrated under reduced pressure and extracted with Et_2O. 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 4:1, yielding, in order of elution, **44** (5.673 g, 40% yield) and **43** (6.38 g, 45% yield). **43**: Colorless needles from *n*-hexane−Et_2O (2:1); mp 119 °C; $[\alpha]^{20}_D$ −36.2 (*c* 0.918, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.75 (d, J = 6.9 Hz, 3 H), 0.83 (d, J = 6.5 Hz, 3 H), 1.85 (m, 1 H), 2.14 (d, J = 4.0 Hz, 1 H), 2.29 (s, 3 H), 2.64 (s, 6 H), 3.06 (m, 1 H), 4.15 (m, 1 H), 4.94 (m, 1 H), 4.95−5.02 (m, 1 H), 5.16−5.22 (m, 1 H), 5.63 (ddd, J = 16.8, 10.2, 6.3 Hz, 1 H), 6.93 (s, 2 H). Anal. Calcd for $C_{16}H_{25}NO_3S$: C, 61.71; H, 8.09; N, 4.50. Found: C, 61.54; H, 8.14; N, 4.44. **44**: Colorless prisms from *n*-hexane−Et_2O (1:1); mp 103 °C; $[\alpha]^{20}_D$ −24.9 (*c* 2.56, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.77 (d, J = 6.6 Hz, 3 H), 0.78 (d, J = 6.6 Hz, 3 H), 3.12 (m, 1 H), 2.30 (s, 3 H), 2.52 (d, J = 6.6 Hz, 1 H), 2.65 (s, 6 H), 3.12 (ddd, J = 9.9, 6.3, 3.6 Hz, 1 H), 4.25 (m, 1 H), 4.78 (d, J = 9.5 Hz, 1 H), 5.23−5.37 (m, 2 H), 5.82 (ddd, J = 17.2, 10.6, 5.3 Hz, 1 H), 6.95 (s, 2 H). Anal. Calcd for $C_{16}H_{25}NO_3S$: C, 61.71; H, 8.09; N, 4.50. Found: C, 61.52; H, 8.34; N, 4.47.

(2*R*,3*S*)-3-Isopropyl-*N*-(2,4,6-trimethylbenzenesulfonyl)-2-vinylaziridine (45). Triphenylphosphine (4.8 g, 18.5 mmol, 1.2 equiv) and diethyl azodicarboxylate (2.9 mL, 18.5 mmol, 1.2 equiv) were added to a stirred solution of the alcohol **43** (4.79 g, 15.4 mmol) in 40 mL of THF at 0 °C, and the mixture was allowed to warm to room temperature and stirred at this temperature for 1 h. The mixture was concentrated under reduced pressure to an oil, which was flash chromatographed on a silica gel column. Elution with *n*-hexane−EtOAc (5:1) gave 4.3 g (95% yield) of the title compound **45** as a crystalline mass. Recrystallization from cold *n*-hexane gave **45** as colorless prisms; mp 46 °C; $[\alpha]^{20}_D$ −11.1 (*c* 1.37, $CHCl_3$); ee > 99% (Chiralcel OB, *n*-hexane−*i*-PrOH = 98:2); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.78 (d, J = 6.9 Hz, 3 H), 0.88 (d, J = 6.6 Hz, 3 H), 1.43 (m, 1 H), 2.30 (s, 3 H), 2.56 (dd, J = 9.9, 7.0 Hz, 1 H), 2.70 (s, 6 H), 3.41 (t, J = 7.0 Hz, 1 H), 5.25−5.44 (m, 2 H), 5.65 (ddd, J = 17.2, 10.2, 7.0 Hz, 1 H), 6.95 (s, 2 H). Anal. Calcd for $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.25; H, 8.13; N, 4.73.

(2*S*,3*S*)-3-Isopropyl-*N*-(2,4,6-trimethylbenzenesulfonyl)-2-vinylaziridine (46). By use of a procedure identical with that described for the preparation of **45** from **43**, the alcohol **44** (4.26 g, 13.7 mmol) was converted into the title compound **46** (3.81 g, 95% yield). **46**: colorless prisms from *n*-hexane−Et_2O (2:1); mp 67 °C; $[\alpha]^{20}_D$ −89.1 (*c* 2.10, $CHCl_3$); ee > 99% (Chiralcel OB, *n*-hexane−*i*-PrOH = 98:2); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.70 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H), 1.51 (m, 1 H), 2.29 (s, 3 H), 2.70 (s, 6 H), 2.80 (dd, J = 7.6, 4.2 Hz, 1 H), 3.11 (dd, J = 9.5, 4.2 Hz, 1 H), 5.34 (d, J = 9.5 Hz, 1 H), 5.50 (d, J = 17.0 Hz, 1 H), 6.17 (triplets of d, J = 17.0, 9.5 Hz, 1 H), 6.93 (s, 2 H). Anal. Calcd for $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.35; H, 8.01; N, 4.52.

(*S*)-*N*-(*tert*-Butoxycarbonyl)leucinol (48). To a stirred solution of (*S*)-leucinol **47** (23.4 g, 0.2 M) in dry DMF (250 mL) and Et_3N (55.8 mL, 0.4 M) under argon was added Boc_2O (43.6 g, 0.2 M) with stirring at 0 °C. After 18 h, water (60 mL) was added, and the mixture was stirred for 1 h. 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 46 g (96% yield) of the title compound **48** as a colorless oil. Kugelrohr distillation, 141 °C (5 Torr); $[\alpha]^{20}_D$ −28.36 (*c* 0.952, $CHCl_3$); IR ($CHCl_3$) cm^{-1}: 3500 (NH and OH), 1709, 1690 (CO); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.930 (d, J = 6.3 Hz, 3 H), 0.933 (d, J = 6.8 Hz, 3 H), 1.25−1.35 (m, 2 H), 1.45 (s, 9 H), 1.55−1.80 (m, 1 H), 2.30 (broad s, 1 H), 3.40−3.75 (m, 3 H), 4.55 (broad s, 1 H). Anal. Calcd for $C_{11}H_{23}NO_3$: C, 60.80; H, 10.67; N, 6.45. Found: C, 60.85; H, 10.83; N, 6.39.

(4*S*,5*S*)-4-(2-Methylpropyl)-5-vinyloxazolidin-2-one (52) and Its (4*S*,5*R*)-Isomer (53). To a stirred solution of oxalyl chloride (25 mL, 0.26 M, 1.3 equiv) in dry CH_2Cl_2 (300 mL) at −78 °C under argon was added dropwise a solution of DMSO (56.7 mL, 0.8 M) in CH_2Cl_2 (100 mL). After 20 min, a solution of the alcohol **48** (46 g, 0.2 M) in CH_2Cl_2 (100 mL) was added to the above reagent at −78 °C, and the mixture was stirred for 1 h. Diisopropylethylamine (139 mL, 0.8 M) was added dropwise to the above solution at −78 °C, and the mixture was stirred for 2 h with warming to 0 °C. The reaction was quenched with 200 mL of a saturated aqueous NH_4Cl solution at −78 °C with vigorous stirring. The mixture was extracted with Et_2O, and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave a crude aldehyde as a colorless oil. To a stirred mixture of vinylmagnesium chloride (300 mL, 2 M solution in THF; 0.6 M) and zinc chloride (54.4 g, 0.4 mol) in THF (350 mL) at −78 °C was added a solution of the above crude aldehyde in 200 mL of THF, and the mixture was stirred for 1 h with warming to 0 °C. The reaction was quenched with 100 mL of 5% citric acid at −78 °C with vigorous stirring. The mixture was concentrated under reduced pressure and extracted with Et_2O. The extract was washed successively with 5% citric acid, water, 5% $NaHCO_3$, and water and then dried over $MgSO_4$. The usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (4:1) gave 35.5 g (74% yield) of an inseparable mixture of the alcohols **50** and **51** as a colorless oil. To a stirred suspension of sodium hydride (4.3 g, 180 mmol) in a mixture of THF (300 mL) and DMF (100 mL) at 0 °C was added 23.2 g (95.5 mmol) of a mixture of alcohols (**50** and **51**) in 50 mL of THF. The stirring was continued for 18 h at rt

followed by quenching with 100 mL of 5% citric acid at −78 °C with vigorous stirring. The mixture was extracted with Et_2O, and the extract was washed successively with 5% HCl, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (2:1) gave 13.7 g (85% yield) of **52**, and further elution gave 2.1 g (13% yield) of **53**. **52**: a colorless oil; Kugelrohr distillation, 185 °C (1 mmHg); $[\alpha]^{20}_D$ −54 (*c* 1.12, $CHCl_3$); IR ($CHCl_3$) cm^{-1}: 3500−3250 (NH and OH), 1743 (CO); ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (d, J = 6.4 Hz, 3 H), 0.94 (d, J = 6.6 Hz, 3 H), 1.30−1.80 (m, 3 H), 3.61 (m, 1 H), 4.53 (m, 1 H), 5.32 (dt, J = 10.3, 1.0 Hz, 1 H), 5.42 (dt, J = 17.1, 1.0 Hz, 1 H), 5.91 (ddd, J = 17.1, 10.3, 6.8 Hz, 1 H). Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.26. Found: C, 64.08; H, 8.97; N, 8.12. **53**: a colorless oil; Kugelrohr distillation, 180 °C (1 mmHg); $[\alpha]^{20}_D$ −24 (*c* 0.846, $CHCl_3$); IR ($CHCl_3$) cm^{-1}: 3500−3250 (NH and OH), 1740 (CO); ^1H NMR (200 MHz, $CDCl_3$) δ 0.90 (d, J = 6.6 Hz, 3 H), 0.95 (d, J = 6.6 Hz, 3 H), 1.21 (ddd, J = 13.4, 9.3, 3.4 Hz, 1 H), 1.43 (ddd, J = 13.4, 10.3, 4.9 Hz, 1 H), 1.45−1.70 (m, 1 H), 3.97 (ddd, J = 10.3, 8.1, 4.2 Hz, 1 H), 5.04 (m, 1 H), 5.34−5.49 (m, 2 H), 5.89 (ddd, J = 17.0, 10.3, 6.8 Hz, 1 H), 6.24 (broad s, 1 H). Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.26. Found: C, 63.80; H, 8.97; N, 8.26.

(4*S*,5*S*)-*N*-(4-Methylbenzenesulfonyl)-4-(2-methylpropyl)-5-vinyloxazolidin-2-one (54). To a stirred suspension of sodium hydride (0.48 g, 20 mmol) in a mixture of THF (10 mL) and DMF (25 mL) at 0 °C were added successively 1.69 g (10 mmol) of **52** in 5 mL of THF and 2.48 g (13 mmol) of *p*-toluenesulfonyl chloride. The stirring was continued for 18 h at room temperature followed by quenching with 10 mL of 10% NH_4Cl at −78 °C with vigorous stirring. The mixture was extracted with Et_2O, and the extract was washed successively with 5% HCl, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) gave 2.49 g (77% yield) of the title compound **54** as a crystalline mass. Recrystallization from *n*-hexane−Et_2O (2:1) gave **54** as colorless crystals; mp 109 °C; $[\alpha]^{20}_D$ −30.36 (*c* 1.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, J = 6.5 Hz, 3 H), 0.99 (d, J = 6.4 Hz, 3 H), 1.62−1.77 (m, 2 H), 1.88−1.99 (m, 1 H), 2.45 (s, 3 H), 4.15 (ddd, J = 10.3, 3.5, 2.5 Hz, 1 H), 4.60 (dddd, J = 6.1, 2.5, 1.2, 1.2 Hz, 1 H), 5.23−5.33 (m, 3 H), 5.75 (ddd, J = 17.0, 10.5, 6.1 Hz, 1 H), 7.32−7.36 (m, 2 H), 7.89−7.92 (m, 2 H). Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42; H, 6.55; N, 4.33. Found: C, 59.24; H, 6.64; N, 4.04.

(4*S*,5*R*)-*N*-(4-Methylbenzenesulfonyl)-4-(2-methylpropyl)-5-vinyloxazolidin-2-one (55). By use of a procedure similar to that described for the preparation of the tosylate **54** from **52**, the oxazolidin-2-one **53** (0.66 g, 4 mmol) was converted into the title compound **55** (1.2 g, 85% yield). Colorless crystals from $CHCl_3$−Et_2O (1:1); mp 156 °C; $[\alpha]^{25}_D$ +39.7 (*c* 1.21, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (d, J = 6.3 Hz, 3 H), 0.99 (d, J = 6.7 Hz, 3 H), 1.56−1.72 (m, 3 H), 2.45 (s, 3 H), 4.48 (m, 1 H), 4.98 (dddd, J = 6.9, 6.9, 1.0, 1.0 Hz, 1 H), 5.44 (ddd, J = 10.5, 1.0, 1.0 Hz, 1 H), 5.50 (ddd, J = 17.1, 1.0, 1.0 Hz, 1 H), 5.82 (ddd, J = 17.1, 10.5, 6.9 Hz, 1 H), 7.33−7.37 (m, 2 H), 7.93−7.98 (m, 2 H). Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42; H, 6.55; N, 4.33. Found: C, 59.15; H, 6.60; N, 4.32.

(4*S*,5*S*)-4-(2-Methylpropyl)-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-5-vinyloxazolidin-2-one (56). To a stirred suspension of sodium hydride (0.72 g, 30 mmol) in a mixture of THF (50 mL) and DMF (80 mL) at 0 °C were added successively 3.38 g (20 mmol) of **52** in 10 mL of THF and 6.66 g (22 mmol) of 2,2,5,7,8-pentamethyl-6-chromansulfonyl chloride. The stirring was continued for 18 h at room temperature followed by quenching with 100 mL of 10% citric acid at −78 °C with vigorous stirring. The mixture was concentrated under reduced pressure followed by extracted with Et_2O. The extract was washed successively with 5% HCl, 5% $NaHCO_3$, and water and dried over $MgSO_4$. Usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (9:1) gave 7.58 g (87% yield) of the title compound **56** as a crystalline mass. Recrystallization from *n*-hexane−Et_2O (10:1) gave pure **56** as colorless crystals, mp 134 °C; $[\alpha]^{25}_D$ +124 (*c* 1.54, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (d, J = 6.5 Hz, 3 H), 1.02 (d, J = 6.5 Hz, 3 H), 1.32 (s, 3 H), 1.33 (s, 3 H), 1.69−1.89 (m, 4 H), 2.08−2.17 (m, 1 H), 2.11 (s, 3 H), 2.52 (s, 3 H), 2.54 (s, 3 H), 2.64 (m, 2 H), 4.22 (ddd, J = 7.2, 3.1, 2.3 Hz, 1 H), 4.69 (dddd, J = 5.8, 2.3, 1.3, 1.3 Hz, 1 H), 5.31−5.43 (m, 2 H), 5.87 (ddd, J = 17.1, 10.5, 5.8 Hz). Anal. Calcd for $C_{23}H_{33}NO_5S$: C, 63.42; H, 7.64; N, 3.22. Found: C, 63.43; H, 7.74; N, 2.93.

(4*S*,5*R*)-4-(2-Methylpropyl)-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-5-vinyloxazolidin-2-one (57). By use of a procedure similar to that described for the synthesis of **56** from **52**, 950 mg (5.6 mmol) of the oxazolidin-2-one **53** was converted into 2.34 g (96% yield) of the title compound **57** by treatment with 2,2,5,7,8-pentamethyl-6-chromansulfonyl chloride (2.04 g, 6.72 mmol) and NaH (0.202 g, 8.4 mmol) in a mixture of THF (15 mL) and DMF (60 mL) at room temperature for 18 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (9:1). Recrystallization from *n*-hexane−Et_2O (10:1) gave **57** as colorless crystals, mp 131 °C; $[\alpha]^{30}_D$ +123.2 (*c* 1.45, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (d, J = 6.3 Hz, 3 H), 1.01 (d, J = 6.3 Hz, 3 H), 1.32 (s, 3 H), 1.33 (s, 3 H), 1.75−1.86 (m, 5 H), 2.13 (s, 3 H), 2.56 (s, 3 H), 2.58 (s, 3 H), 2.67 (m, 2 H), 4.49 (m, 1 H), 4.97 (dddd, J = 6.9, 6.9, 1.0, 1.0 Hz, 1 H), 5.47 (ddd, J = 10.5, 1.0, 1.0 Hz, 1 H), 5.54 (ddd, J = 17.1, 1.0, 1.0 Hz, 1 H), 5.88 (ddd, J = 17.1, 10.5, 6.9 Hz, 1 H). Anal. Calcd for $C_{23}H_{33}NO_5S$: C, 63.42; H, 7.64; N, 3.22. Found: C, 63.56; H, 7.79; N, 3.11.

(3*S*,4*S*)-6-Methyl-4-[(4-methylbenzenesulfonyl)amino]-1-hepten-3-ol (58). To a stirred solution of the oxazolidin-2-one **54** (1.371 g, 4.24 mmol) in 25 mL of MeOH−H_2O (4:1) was added 1.90 g (34 mmol, 8 equiv) of KOH at 0 °C, and the mixture was stirred under reflux for 4 h. The mixture was made acidic with 5% citric acid and concentrated under reduced pressure to leave an oily residue. This oily residue was extracted with $CHCl_3$, and the extract was washed with water and dried over $MgSO_4$. The usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (3:1) gave 1.05 g (83% yield) of the title compound **58**. Colorless crystals from *n*-hexane−Et_2O (1:1); mp 89 °C; $[\alpha]^{20}_D$ −37.9 (*c* 0.71, $CHCl_3$); ^1H NMR (270 MHz, $CDCl_3$) δ 0.68 (d, J = 6.3 Hz, 3 H), 0.79 (d, J = 6.6 Hz, 3 H), 1.19 (m, 1 H), 1.34−1.52 (m, 2 H), 2.11 (d, J = 4.3 Hz, 1 H), 2.23 (s, 3 H), 3.32 (ddd, J = 12.9, 5.3, 4.0 Hz, 1 H), 4.06 (m, 1 H), 4.73 (d, J = 8.6 Hz, 1 H), 5.09−5.25 (m 2 H), 5.73 (ddd, J = 17.2, 10.6, 6.6 Hz, 1 H), 7.27−7.31 (m, 2 H), 7.74−7.77 (m, 2 H). Anal. Calcd for $C_{15}H_{23}NO_3S$: C, 60.58; H, 7.79; N, 4.71. Found: C, 60.42; H, 7.98; N, 4.55.

(3*R*,4*S*)-6-Methyl-4-[(4-methylphenylsulfonyl)amino]-1-hepten-3-ol (59). By use of a procedure similar to that described for the preparation of the allyl alcohol **58** from **54**, the oxazolidin-2-one **55** (0.72 g, 2.23 mmol) was converted into the title compound **59** (0.64 g, 97% yield) by treatment with 1.93 g of KOH in 30 mL of MeOH−H_2O (2:1) under reflux for 2 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (3:1). Colorless needles from *n*-hexane−Et_2O (3:1); mp 60 °C; $[\alpha]^{25}_D$ −21.9 (*c* 0.858, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.58 (d, J = 6.6 Hz, 3 H), 0.78 (d, J = 6.6 Hz, 3 H), 1.17 (m, 2 H), 1.43 (m, 1 H), 2.43 (s, 3 H), 2.50 (d, J = 6.6 Hz, 1 H), 3.76 (m, 1 H), 4.11 (m, 1 H), 4.74 (d, J = 9.6 Hz, 1 H), 5.21−5.32 (m, 2 H), 5.78 (ddd, J = 17.2, 10.6, 5.3 Hz, 1 H), 7.27−7.33 (m, 2 H), 7.78−7.81 (m, 2 H). Anal. Calcd for $C_{15}H_{23}NO_3S$: C, 60.58; H, 7.79; N, 4.71. Found: C, 60.55; H, 7.77; N, 4.60.

(3*S*,4*S*)-6-Methyl-4-[(2,2,5,7,8-pentamethyl-6-chromansulfonyl)amino]-1-hepten-3-ol (60). By use of a procedure identical with that described for the preparation of the allyl alcohol **58** from **54**, the oxazolidin-2-one **56** (5.65 g, 13 mmol) was converted into the title compound **60** (4.9 g, 92% yield) as a colorless oil by treatment with 5.82 g of KOH in 70 mL of MeOH−H_2O (5:2) followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (3:1). $[\alpha]^{30}_D$ −24.1 (*c* 0.755, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.66 (d, J = 6.2 Hz, 3 H), 0.75 (d, J = 6.4 Hz, 3 H), 1.10−1.52 (m, 5 H), 1.31 (s, 6 H), 1.83 (t, J = 6.8 Hz, 2 H), 2.13 (s, 3 H), 2.28 (d, J = 4.2 Hz, 1 H), 2.54 (s, 3 H), 2.56 (s, 3 H), 2.64 (t, J = 6.9 Hz, 2 H), 3.32 (m, 1 H), 4.06 (m, 1 H), 4.70 (d, J = 8.9 Hz, 1

H), 5.10 (ddd, J = 11.7, 1.3, 1.3 Hz, 1 H), 5.22 (ddd, J = 17.0, 1.3, 1.3 Hz, 1 H), 5.43 (ddd, J = 17.0, 10.4, 6.4 Hz, 1 H). LRMS (FAB) *m*/*z*, 410 (MH^+), 352, 267, 251, 219, 203 (base peak), 147, 126. HRMS (FAB) *m*/*z*, calcd for $C_{22}H_{36}NO_4S$ (MH^+) 410.2365; found: 410.2368.

(3*R*,4*S*)-6-Methyl-4-[(2,2,5,7,8-pentamethyl-6-chromansulfonyl)amino]-1-hepten-3-ol (61). By use of a procedure similar to that described for the preparation of the allyl alcohol **58** from **54**, the oxazolidin-2-one **57** (1.5 g, 3.44 mmol) was converted into the title compound **61** (1.35 g, 96% yield). Colorless needles from *n*-hexane; mp 105 °C; $[\alpha]^{25}_D$ −14.9 (*c* 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.61 (d, J = 6.5 Hz, 3 H), 0.77 (d, J = 6.7 Hz, 3 H), 1.09−1.26 (m, 2 H), 1.32 (s, 6 H), 1.36−1.53 (m, 1 H), 1.83 (t, J = 6.8 Hz, 2 H), 2.13 (s, 3 H), 2.55 (m, 1 H), 2.57 (s, 3 H), 2.58 (s, 3 H), 2.65 (t, J = 6.8 Hz, 2 H), 3.39 (m, 1 H), 4.18 (m, 1 H), 4.58 (d, J = 9.2 Hz, 1 H), 5.24 (ddd, J = 10.6, 1.6, 1.6 Hz, 1 H), 5.31 (ddd, J = 17.2, 1.6, 1.6 Hz, 1 H), 5.78 (ddd, J = 17.2, 10.5, 5.1 Hz, 1 H). Anal. Calcd for $C_{22}H_{35}NO_4S$: C, 64.51; H, 8.61; N, 3.42. Found: C, 64.24; H, 8.57; N, 3.33.

(2*R*,3*S*)-*N*-(4-Methylbenzenesulfonyl)-3-(2-methylpropyl)-2-vinylaziridine (62). By use of a procedure similar to that described for the synthesis of the vinylaziridine **45** from the *N*-protected amino alcohol **43**, 0.75 g (2.52 mmol) of **58** was converted into 675 mg (96% yield) of the title compound **62** by treatment with PPh_3 (858 mg, 3.28 mmol) and diethyl azodicarboxylate (0.52 mL, 3.28 mmol) in THF (15 mL) at room temperature for 1 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1). **62**: a colorless oil; $[\alpha]^{25}_D$ −7.1 (*c* 0.70, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (d, J = 6.7 Hz, 3 H), 0.88 (d, J = 6.7 Hz, 3 H), 1.34 (m, 2 H), 1.59 (m, 1 H), 2.43 (s, 3 H), 2.96 (ddd, J = 7.1, 6.2, 6.2 Hz, 1 H), 3.31 (tt, J = 7.1, 0.7 Hz, 1 H), 5.26 (ddd, J = 10.2, 0.7, 0.7 Hz, 1 H), 5.39 (ddd, J = 17.1, 0.7, 0.7 Hz, 1 H), 5.59 (ddd, J = 17.1, 10.2, 7.1 Hz, 1 H), 7.28−7.32 (m, 2 H), 7.78−7.84 (m, 2 H). LRMS (FAB) *m*/*z*, 280 (MH^+, base peak), 155, 139, 124 (base peak), 91. HRMS (FAB) *m*/*z*, calcd for $C_{15}H_{22}NO_2S$ (MH^+) 280.1371; found: 280.1377.

(2*S*,3*S*)-*N*-(4-Methylbenzenesulfonyl)-3-(2-methylpropyl)-2-vinylaziridine (63). By use of a procedure similar to that described for the synthesis of the vinylaziridine **62** from **58**, 560 mg (1.88 mmol) of the allyl alcohol **59** was converted into 411 mg (78% yield) of the title compound **63** by treatment with PPh_3 (640 mg, 2.44 mmol) and diethyl azodicarboxylate (0.387 mL, 2.44 mmol) in THF (10 mL) at rt for 1 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1). Colorless crystals from *n*-hexane, mp 61 °C; $[\alpha]^{25}_D$ −71 (*c* 0.60, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (d, J = 6.7 Hz, 6 H), 1.39 (m, 1 H), 1.60 (m, 2 H), 2.43 (s, 3 H), 2.94 (ddd, J = 8.7, 5.6, 4.4 Hz, 1 H), 3.07 (dd, J = 9.1, 4.4 Hz, 1 H), 5.32 (dd, J = 10.2, 1.0 Hz, 1 H), 5.45 (dd, J = 17.0, 1.0 Hz, 1 H), 6.01 (ddd, J = 17.0, 10.2, 9.1 Hz, 1 H), 7.28−7.32 (m, 2 H), 7.80−7.84 (m, 2 H). Anal. Calcd for $C_{15}H_{21}NO_2S$: C, 64.49; H, 7.58; N, 5.02. Found: C, 64.54; H, 7.72; N, 4.90.

(2*R*,3*S*)-3-(2-Methylpropyl)-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-2-vinylaziridine (64). By use of a procedure similar to that described for the synthesis of the vinylaziridine **62** from **58**, 230 mg (0.562 mmol) of the allyl alcohol **60** was converted into 216 mg (98% yield) of the title compound **64** as a colorless oil by treatment with PPh_3 (191 mg, 0.73 mmol) and diethyl azodicarboxylate (0.115 mL, 0.73 mmol) in THF (10 mL) at room temperature for 30 h followed by flash chromatography over silica gel with *n*-hexane−EtOAc (5:1). $[\alpha]^{30}_D$ +5.3 (*c* 0.68, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H), 1.24−1.44 (m, 5 H), 1.31 (s, 3 H), 1.57 (m, 1 H), 1.82 (t, J = 6.8 Hz, 2 H), 2.12 (s, 3 H), 2.59 (s, 3 H), 2.61 (s, 3 H), 2.65 (t, J = 6.8 Hz, 1 H), 2.96 (m, 1 H), 3.38 (tt, J = 6.9, 0.7 Hz, 1 H), 5.26 (ddd, J = 10.3, 0.7, 0.7 Hz, 1 H), 5.37 (ddd, J = 17.1, 0.7, 0.7 Hz, 1 H), 5.63 (ddd, J = 17.1, 10.3, 6.9 Hz, 1 H). LRMS (FAB) *m*/*z*, 392 (MH^+), 390, 267, 251, 219, 203, 147, 124 (base peak). HRMS (FAB) *m*/*z*, calcd for $C_{22}H_{34}NO_3S$ (MH^+) 392.2259; found: 392.2248.

(2*S*,3*S*)-3-(2-Methylpropyl)-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-2-vinylaziridine (65). By a procedure similar to that described for the synthesis of the vinylaziridine **62** from **58**, 1.28 g (3.12 mmol) of the allyl alcohol **61** was converted into 1.20 g (98% yield) of the title compound **65** as a colorless oil by treatment with PPh_3 (1.06 g, 4.06 mmol) and diethyl azodicarboxylate (0.64 mL, 4.06 mmol) in THF (10 mL) at room temperature for 30 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1). $[\alpha]^{30}_D$ −57.1 (*c* 0.963, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (d, J = 6.5 Hz, 3 H), 0.88 (d, J = 6.6 Hz, 3 H), 1.311 (s, 3 H), 1.316 (s, 3 H), 1.39 (dt, J = 13.1, 7.7 Hz, 1 H), 1.52−1.74 (m, 2 H), 1.82 (t, J = 6.8 Hz, 2 H), 2.12 (s, 3 H), 2.58 (s, 3 H), 2.60 (s, 3 H), 2.64 (t, J = 6.8 Hz, 1 H), 2.92 (ddd, J = 7.5, 5.3, 4.7 Hz, 1 H), 3.08 (dd, J = 9.1, 4.2 Hz, 1 H), 5.25−5.29 (m, 1 H), 5.40−5.46 (m, 1 H), 6.01 (ddd, J = 17.0, 10.2, 9.1 Hz, 1 H). LRMS (FAB) *m*/*z*, 392 (MH^+), 390, 267, 251, 219, 203, 147, 124 (base peak). HRMS (FAB) *m*/*z*, calcd for $C_{22}H_{34}NO_3S$ (MH^+) 392.2259; found: 392.2250.

(3*S*,4*S*)-4-[*N*-(4-Nitrobenzenesulfonyl)amino]-6-methyl-1-hepten-3-ol (66). To a stirred solution of the oxazolidin-2-one **52** (1.69 g, 10 mmol) in 30 mL of MeOH−H_2O (1:1) at 0 °C was added KOH (1.68 g, 30 mmol), and the mixture was refluxed for 5 h. The mixture was concentrated under reduced pressure followed by extraction with $CHCl_3$ (30 mL). The extract was washed with brine and dried over $MgSO_4$. To a stirred dried chloroform extract were added successively Et_3N (3 mL) and *p*-nitrobenzenesulfonyl chloride (2.43 g, 11 mmol) at 0 °C, and the stirring was continued for 30 min at room temperature. It was then cooled to 0 °C, and a saturated $NaHCO_3$ solution (10 mL) was added with vigorous stirring. The mixture was extracted with EtOAc, and the extract was washed successively with 5% 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 (3:1) gave 2.3 g (70% yield) of the title compound **66**. Colorless crystals from Et_2O, mp 82 °C; $[\alpha]^{10}_D$ −25.2 (*c* 2.02, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (d, J = 6.2 Hz, 3 H), 0.84 (d, J = 6.4 Hz, 3 H), 1.26−1.37 (m, 1 H), 1.41−1.58 (m, 2 H), 1.84 (d, J = 3.7 Hz, 1 H), 3.44 (dddd, J = 14.5, 9.0, 5.7, 3.4 Hz, 1 H), 4.10 (m, 1 H), 4.92 (d, J = 9.1 Hz, 1 H), 5.07 (ddd, J = 10.4, 1.2, 1.2 Hz, 1 H), 5.21 (ddd, J = 17.2, 1.2, 1.2 Hz, 1 H), 5.67 (ddd, J = 17.2, 10.4, 6.1 Hz, 1 H), 8.02−8.07 (m, 2 H), 8.32−8.36 (m, 2 H). Anal. Calcd for $C_{14}H_{20}N_2O_5S$: C, 51.21; H, 6.14; N, 8.53. Found: C, 51.10; H, 6.10; N, 8.52.

(3*R*,4*S*)-4-[*N*-(4-Nitrobenzenesulfonyl)amino]-6-methyl-1-hepten-3-ol (67). By use of a procedure similar to that described for the preparation of **66** from **52**, the oxazolidin-2-one **53** (1.69 g, 10 mmol) was converted into the title compound **67** (2.595 g, 79% yield) as a colorless semisolid. $[\alpha]^{10}_D$ −20.6 (*c* 1.03, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.69 (d, J = 6.5 Hz, 3 H), 0.83 (d, J = 6.6 Hz, 3 H), 1.14−1.34 (m, 2 H), 1.38−1.54 (m, 1 H), 2.11 (d, J = 5.3 Hz, 1 H), 3.50 (m, 1 H), 4.17 (m, 1 H), 5.00 (d, J = 9.1 Hz, 1 H), 5.77 (ddd, J = 17.2, 10.6, 5.2 Hz, 1 H), 5.26 (ddd, J = 10.5, 1.5, 1.5 Hz, 1 H), 5.27 (ddd, J = 17.2, 1.5, 1.5 Hz, 1 H), 8.08−8.12 (m, 2 H), 8.33−8.38 (m, 2 H). LRMS (FAB) *m*/*z*, 329 (MH^+), 311 (base peak), 295, 271, 255, 215, 186. HRMS (FAB) *m*/*z*, calcd for $C_{15}H_{21}N_2O_5S$: (MH^+) 329.1171; found: 329.1162.

(2*R*,3*S*)-3-(2-Methylpropyl)-*N*-(4-nitrobenzenesulfonyl)-2-vinylaziridine (68). By use of a procedure similar to that described for the synthesis of the vinylaziridine **45** from **43**, 2.20 g (6.7 mmol) of the allyl alcohol **66** was converted into 1.9 g (91% yield) of the title compound **68** as a colorless oil by treatment with PPh_3 (2.11 g, 8.04 mmol) and diethyl azodicarboxylate (1.27 mL, 8.04 mmol) in THF (10 mL) at 0 °C for 18 h followed by flash chromatography over silica gel with *n*-hexane−EtOAc (4:1). $[\alpha]^{10}_D$ +9.4 (*c* 1.64, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (d, J = 6.6 Hz, 3 H), 0.92 (d, J = 6.7 Hz, 3 H), 1.30−1.49 (m, 2 H), 1.57−1.71 (m, 1 H), 3.12 (m 1 H), 3.45 (m, 1 H), 5.30 (ddd, J = 10.2, 0.7, 0.7 Hz, 1 H), 5.39 (ddd, J = 17.1, 0.7, 0.7 Hz, 1 H), 5.59 (ddd, J = 17.1, 10.2, 7.0 Hz, 1 H), 8.12−8.16 (m, 2 H), 8.35−8.40 (m, 2 H). LRMS (FAB) *m*/*z*, 311 (MH^+), 295, 186, 124 (base peak). HRMS (FAB) *m*/*z*, calcd for $C_{14}H_{19}N_2O_4S$ (MH^+) 311.1065; found: 311.1064.

(2*S*,3*S*)-3-(2-Methylpropyl)-*N*-(4-nitrobenzenesulfonyl)-2-vinylaziridine (69). By a procedure similar to that described for the synthesis of the vinylaziridine **45** from **43**, 2.5

g (8.06 mmol) of **67** was converted into 1.9 g (80% yield) of the title compound **69** as a colorless oil by treatment with PPh_3 (2.1 g, 8.06 mmol) and diethyl azodicarboxylate (1.27 mL, 8.06 mmol) in THF (10 mL) at 0 °C for 30 min followed by flash chromatography over silica gel with *n*-hexane−EtOAc (4:1). $[\alpha]^{10}_D$ −68.9 (*c* 1.21, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, J = 6.4 Hz, 3 H), 0.92 (d, J = 5.9 Hz, 3 H), 1.37−1.48 (m, 1 H), 1.56−1.73 (m, 2 H), 3.03 (m, 1 H), 3.18 (dd, J = 9.0, 4.5 Hz, 1 H), 5.38 (m, 1 H), 5.50 (m, 1 H), 5.95 (ddd, J = 19.2, 10.2, 9.0 Hz, 1 H), 8.11−8.15 (m, 2 H), 8.34−8.39 (m, 2 H). LRMS (FAB) *m*/*z*, 311 (MH^+), 303, 186, 124 (base peak). HRMS (FAB) *m*/*z*, calcd for $C_{14}H_{19}N_2O_4S$ (MH^+) 311.1065; found: 311.1069.

General Procedure for Equilibrated Reaction of *N*-(Arenesulfonyl)-3-alkyl-2-vinylaziridines with Tetrakis(triphenylphosphine)palladium(0). Equilibrated Reaction of (2*S*,3*S*)-3-Methyl-*N*-(4-methylbenzenesulfonyl)-2-vinylaziridine (21). To a stirred solution of the 2,3-*trans*-vinylaziridine **21** (237 mg, 1 mmol) in 5 mL of dry THF at 0 °C under argon was added by syringe a solution of $Pd(PPh_3)_4$ (23 mg, 0.02 mmol, 2 mol %) in 3 mL of dry THF, and the mixture was stirred at 0 °C for 18 h. Concentration under reduced pressure at 0 °C followed by flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) gave 225 mg (95% yield) of a mixture of **18** and **21** (**18**:**21** = 96:4) as a crystalline mass. Recrystallization from *n*-hexane−Et_2O (4:1) gave 191 mg (80.6% yield) of 2,3-*cis*-vinylaziridine **18** as colorless crystals. The mother liquor was concentrated under reduced pressure to leave 32.3 mg of a colorless semisolid. The residual semisolid was treated with 3 mg of $Pd(PPh_3)_4$ in 4 mL of dry THF for 16 h at 0 °C. Usual work up followed by flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) and recrystallization from *n*-hexane−Et_2O (4:1) gave 24 mg (10.1% yield) of pure **18**. The product **18** thus obtained amounts to 215 mg (90.7% yield).

Palladium(0)-Catalyzed Equilibrated Reaction of (2*S*,3*S*)-3-Isopropyl-*N*-(2,4,6-trimethylbenzenesulfonyl)-2-vinylaziridine (46). By use of a procedure similar to that described for the preparation of **18** from **21**, the 2,3-*trans*-aziridine **46** (293 mg, 1 mmol) was converted into the 2,3-*cis*-aziridine **45** by treatment with $Pd(PPh_3)_4$ (46.2 mg, 0.04 mmol, 4 mol %) in 15 mL of dry THF at 0 °C for 24 h followed by usual workup and flash chromatography over silica gel with *n*-hexane−EtOAc (5:1). Recrystallization from cold *n*-hexane gave **45** (219 mg, 75% yield) as colorless crystals. The mother liquor was concentrated under reduced pressure to leave 60 mg of a colorless semisolid. This residual semisolid was treated with 9.5 mg of $Pd(PPh_3)_4$ in 5 mL of dry THF for 16 h at 0 °C. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc (5:1) and recrystallization from cold *n*-hexane gave 45 mg (15.3% yield) of pure **45**. The product **45** thus obtained amounts to 264 mg (90% yield). Mp 46 °C; $[\alpha]^{20}_D$ −11.6 (*c* 1.09, $CHCl_3$); ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.78 (d, J = 6.9 Hz, 3 H), 0.88 (d, J = 6.6 Hz, 3 H), 1.43 (m, 1 H), 2.30 (s, 3 H), 2.56 (dd, J = 9.9, 7.0 Hz, 1 H), 2.70 (s, 6 H), 3.41 (t, J = 7.0 Hz, 1 H), 5.25−5.44 (m, 2 H), 5.65 (ddd, J = 17.2, 10.2, 7.0 Hz, 1 H), 6.95 (s, 2 H). Anal. Calcd for $C_{16}H_{23}NO_2S$: C, 65.49; H, 7.90; N, 4.77. Found: C, 65.32; H, 7.83; N, 4.65.

Palladium(0)-Catalyzed Equilibrated Reaction of a 2:3 Mixture of (2*R*,3*S*)-3-(2-Methylpropyl)-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-2-vinylaziridine (64) and Its (2*S*,3*S*)-Isomer (65). To a stirred solution of a 2:3 mixture of the 2,3-*cis*- and 2,3-*trans*-aziridines **64** and **65** (4.5 g, 11.45 mmol) in 15 mL of dry THF at 0 °C was added by syringe a solution of $Pd(PPh_3)_4$ (529 mg, 0.458 mmol, 4 mol %) in 5 mL of dry THF, and the mixture was stirred at 0 °C for 18 h. Concentration under reduced pressure at 0 °C followed by flash chromatography on a short silica gel column with *n*-hexane−EtOAc (5:1) gave 4.46 g (99% yield) of a mixture of **64** and **65** (**64**:**65** = 96:4, HPLC) as a colorless oil, which was flash chromatographed on silica gel eluting with *n*-hexane−EtOAc to give the desired compound **64** (3.96 g, 88% yield) as a colorless oil.

Equilibrated Reaction of (2*S*,3*S*)-3-(2-Methylpropyl)-*N*-(4-nitrobenzenesulfonyl)-2-vinylaziridine (69) with Pd(PPh$_3$)$_4$. To a stirred solution of the 2,3-*trans*-aziridine **69** (236 mg, 0.761 mmol) in 3 mL of dry THF under a positive pressure of argon at 0 °C was added by syringe a solution of $Pd(PPh_3)_4$ (35.1 mg, 4 mol %) in 2 mL of dry THF, and the mixture was stirred at 0 °C for 5 h. Concentration under reduced pressure at 0 °C followed by flash chromatography on a short silica gel column with *n*-hexane−EtOAc (3:1) gave a mixture of **68** and **69** (**68**:**69** = 93:7) as a colorless oil. The mixture was flash chromatographed on a silica gel column. Elution with *n*-hexane−EtOAc (6:1) gave 195 mg (82% yield) of the 2,3-*cis*-aziridine **68** as a colorless oil, and further elution gave 14 mg (6% yield) of the 2,3-*trans*-aziridine **69** as a colorless oil.

***tert*-Butyl (4*R*,5*S*,2*Z*)-4,5-Epimino-7-methyl-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-2-octenoate (74) and *tert*-Butyl (4*R*,5*S*,2*E*)-4,5-Epimino-7-methyl-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-2-octenoate (75).** Ozone was bubbled through a solution of the vinylaziridine **64** (2.7 g, 6.92 mmol) in EtOAc (30 mL) at −78 °C until a faint blue color persisted. To the mixture at −78 °C were added 2 g of triphenylphosphine and *tert*-butyl (triphenylphosphoranilidene)acetate (5.20 g, 13.84 mmol), and the mixture was stirred for 3 h with warming up to 0 °C. The mixture was concentrated under reduced pressure to leave a semisolid, which was purified by flash chromatography over silica gel eluting with *n*-hexane−EtOAc (5:1) to give the (*Z*)-enoate **74** (782 mg, 23% yield). Continued elution gave the (*E*)-enoate **75** (1.35 g, 40% yield). Compound **74**, colorless crystals from Et_2O, mp 113 °C; $[\alpha]^{30}_D$ −1.4 (*c* 0.997, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, J = 6.6 Hz, 3 H), 0.87 (d, J = 6.6 Hz, 3 H), 1.32 (s, 6 H), 1.34−1.64 (m, 3 H), 1.82 (t, J = 6.8 Hz, 2 H), 2.12 (s, 3 H), 2.58 (s, 3 H), 2.60 (s, 3 H), 2.64 (t, J = 6.8 Hz, 2 H), 3.10 (dd, J = 7.4, 6.7 Hz, 1 H), 4.40 (dd, J = 7.6, 6.7 Hz, 1 H), 5.80 (dd, J = 11.6, 6.7 Hz, 1 H), 5.87 (d, J = 11.6 Hz, 1 H). LRMS (FAB) *m*/*z*, 492 (MH^+), 436, 352, 267, 251, 203, 168 (base peak), 147. HRMS (FAB) *m*/*z*, calcd for $C_{27}H_{42}NO_5S$ (MH^+) 492.2783; found: 492.2791. Compound **75**, a colorless oil; $[\alpha]^{30}_D$ −38.3 (*c* 0.737, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 1.20−1.60 (m, 3 H), 1.32 (s, 6 H), 1.47 (s, 9 H), 1.83 (t, J = 6.8 Hz, 2 H), 2.13 (s, 3 H), 2.59 (s, 3 H), 2.60 (s, 3 H), 2.65 (t, J = 6.8 Hz, 2 H), 3.02 (dd, J = 7.3, 5.9 Hz, 1 H), 3.42 (td, J = 7.3, 1.0 Hz, 1 H), 5.97 (dd, J = 15.6, 1.0 Hz, 1 H), 6.57 (dd, J = 15.6, 7.1 Hz, 1 H). LRMS (FAB) *m*/*z*, 492 (MH^+), 490, 434, 267, 251, 224 (base peak), 203, 168, 147. HRMS (FAB) *m*/*z*, calcd for $C_{27}H_{42}NO_5S$ (MH^+) 492.2783; found: 492.2782.

***tert*-Butyl (4*R*,5*S*,2*E*)-4,5-Epimino-7-methyl-*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)-2-octenoate (75).** Ozone was bubbled through a solution of the vinylaziridine **64** (0.80 g, 2.046 mmol) in CH_2Cl_2 (15 mL) at −78 °C until a faint blue color persisted. To the mixture at −78 °C was added 0.5 g of zinc powder, and the mixture was stirred for 1 h with warming up to 0 °C. The inorganic precipitates were removed by filtration through a short column of silica gel. The filtrate was concentrated under reduced pressure to leave a crude aldehyde as a colorless oil. To a stirred suspension of LiCl (173 mg, 4.092 mmol) in MeCN (10 mL) under argon at room temperature were added *tert*-butyl diethylphosphonoacetate (0.96 mL, 4.092 mmol), diisopropylethylamine (0.71 mL, 4.092 mmol), and finally the above oily aldehyde in 5 mL of MeCN. The mixture was stirred for 1 h at room temperature. Usual workup followed by flash chromatography over silica gel eluting with *n*-hexane−EtOAc (3:1) afforded the (*E*)-enoate **75** (860 mg, 85.6% yield) as a colorless oil. $[\alpha]^{30}_D$ −38.5 (*c* 1.64, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 1.20−1.60 (m, 3 H), 1.32 (s, 6 H), 1.47 (s, 9 H), 1.83 (t, J = 6.8 Hz, 2 H), 2.13 (s, 3 H), 2.59 (s, 3 H), 2.60 (s, 3 H), 2.65 (t, J = 6.8 Hz, 2 H), 3.02 (dd, J = 7.3, 5.9 Hz, 1 H), 3.42 (td, J = 7.3, 1.0 Hz, 1 H), 5.97 (dd, J = 15.6, 1.0 Hz, 1 H), 6.57 (dd, J = 15.6, 7.1 Hz, 1 H). Anal. Calcd for $C_{27}H_{41}NO_5S$: C, 65.96; H, 8.41; N, 2.85. Found: C, 65.93; H, 8.48; N, 2.85.

***tert*-Butyl (2*R*,5*S*,3*E*)-7-Methyl-2-(2-methylpropyl)-5-[*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)amino]-3-octenoate (76).** To a stirred solution of CuCN (954 mg, 10.6 mmol) and LiCl (896 mg, 21.2 mmol) in 20 mL of dry THF

under argon was added by syringe isobutylmagnesium chloride (1.1 M solution in THF; 9.64 mL, 10.6 mmol) at −78 °C, and the mixture was allowed to warm to 0 °C and stirred at this temperature for 10 min. The enoate **75** (1.3 g, 2.65 mmol) in 5 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 20 mL of a 1:1 saturated NH_4Cl−28% NH_4OH solution. The mixture was extracted with Et_2O, and the extract was washed with water and dried over $MgSO_4$. Concentration under reduced pressure gave an oily residue, which was flash chromatographed on silica gel, eluting with *n*-hexane−EtOAc (4:1) to give the title compound **76** (1.40 g, 96% yield) as a colorless oil. $[\alpha]^{20}_D$ −39.8 (*c* 1.22, $CHCl_3$); $\Delta\epsilon$ −8.72 (222 nm in isooctane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (d, J = 6.6 Hz, 3 H), 0.80 (d, J = 6.6 H, 3 H), 0.81 (d, J = 6.5 Hz, 3 H), 0.83 (d, J = 6.7 Hz, 3 H), 1.00 (m, 1 H), 1.17−1.60 (m, 6 H), 1.31 (s, 6 H), 1.39 (s, 9 H), 1.83 (t, J = 6.8 Hz, 2 H), 2.12 (s, 3 H), 2.535 (s, 3 H), 2.538 (s, 3 H), 2.65 (t, J = 6.8 Hz, 2 H), 2.74 (m, 1 H), 3.71 (m, 1 H), 4.33 (d, J = 7.4 Hz, 1 H), 5.25 (m, 2 H). LRMS (FAB) *m*/*z*, 549 (M^+), 492, 448, 284, 267 (base peak), 203, 147. HRMS (FAB) *m*/*z*, calcd for $C_{31}H_{51}NO_5S$ (M^+) 549.3488; found: 549.3495.

***tert*-Butyl (2*R*,5*S*,3*E*)-7-Methyl-2-(3-methylbutyl)-5-[*N*-(2,2,5,7,8-pentamethyl-6-chromansulfonyl)amino]-3-octenoate (77).** By use of a procedure similar to that described for the reaction of **75** with *i*-BuCu(CN)MgCl, the α,*β*-enoate **75** (391 mg, 0.8 mmol) was converted into the *β*,*γ*-enoate **77** (430 mg, 96%) as a colorless oil by treatment with isopentyl-Cu(CN)MgCl (3.2 mmol, 4 equiv) in 7.5 mL of THF at −78 °C for 30 min. $[\alpha]^{20}_D$ −42.6 (*c* 1.13, $CHCl_3$); $\Delta\epsilon$ −7.82 (222 nm in isooctane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.79 (d, J = 6.5 Hz, 6 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.97−1.61 (m, 8 H), 1.32 (s, 6 H), 1.40 (s, 9 H), 1.83 (t, J = 6.8 Hz, 2 H), 2.12 (s, 3 H), 2.53 (s, 3 H), 2.55 (s, 3 H), 2.60 (dd, J = 8.1, 6.3 Hz, 1 H), 2.65 (t, J = 6.8 Hz, 2 H), 3.71 (m, 1 H), 4.31 (d, J = 7.3 Hz, 1 H), 5.22 (dd, J = 15.5, 7.2 Hz, 1 H), 5.33 (dd, J = 15.5, 8.0 Hz, 1 H). LRMS (FAB) *m*/*z*, 563 (M^+), 506, 462, 267 (base peak), 203, 147, 57.

(2*R*,5*S*,3*E*)-5-[*N*-(*tert*-Butyloxycarbonyl)amino]-7-methyl-2-(2-methylpropyl)-3-octenoic Acid (78). To a stirred solution of the *N*-Pmc derivative **76** (840 mg, 1.53 mmol) in 10 mL of TFA under argon was added by syringe 0.5 mL of thioanisole at room temperature, and the mixture was stirred at this temperature for 24 h. The mixture was concentrated under reduced pressure to leave an oily residue. To a solution of the oily residue in 15 mL of $CHCl_3$ were added diisopropylethylamine (4 mL) and Boc_2O (1.0 g) under stirring at 0 °C, and the mixture was stirred for 3 h. The mixture was made acidic with 20% citric acid and extracted with EtOAc. Usual workup followed by flash chromatography over silica gel with *n*-hexane−EtOAc gave the title compound **78** (280 mg, 56% yield) as a crystalline mass. Colorless crystals from cold *n*-hexane; mp 97 °C; $[\alpha]^{20}_D$ −61.0 (*c* 0.95, $CHCl_3$); $\Delta\epsilon$ −4.19 (219 nm in isooctane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (d, J = 6.2 Hz, 3 H), 0.90 (d, J = 6.6 Hz, 3 H), 0.91 (d, J = 6.4 Hz, 6 H), 1.22−1.42 (m, 2 H), 1.44 (s, 9 H), 1.48−1.69 (m, 3 H), 3.07 (m, 1 H), 4.11 (m, 1 H), 4.39 (broad s, 1 H), 5.45 (dd, J = 15.5, 6.0 Hz, 1 H), 5.56 (dd, J = 15.5, 8.3 Hz, 1 H). Anal. Calcd for $C_{18}H_{33}NO_4$: C, 66.02; H, 10.16; N, 4.28. Found: C, 65.85; H, 9.97; N, 4.21.

Acknowledgment. We thank Dr. T. R. Burke, Jr., NCI, NIH, Bethesda, MD, for reading the manuscript and providing useful comments. This work was supported in part by Grant-in-Aid for Scientific Researches (B and C) from the Ministry of Education, Science and Culture of Japan, to which the authors' thanks are due.

Supporting Information Available: Copies of ^{1}H NMR spectra of compounds **9**, **10**, **12**, **13**, **15**, **24**−**26**, **32**, **37**−**39**, **60**, **62**, **64**, **65**, **67**−**69**, **74**−**77** are available (23 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS; see any current masthead page for ordering information.

JO961760O