Formation of Scalemic Aziridines via the Nucleophilic Opening of Aziridines

Stephen C. Bergmeier* and Punit P. Seth
Division of Medicinal Chemistry, College of Pharmacy, The Ohio State University, Columbus, Ohio 43210

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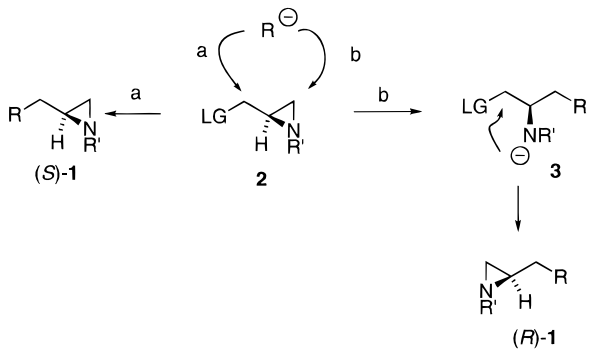
Introduction

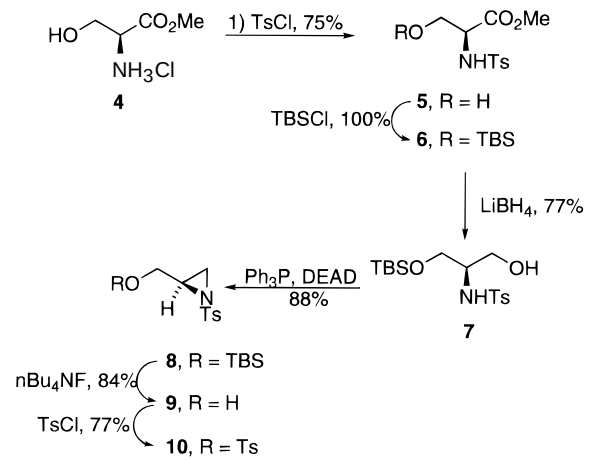
As part of our work in the preparation of aziridine−allylsilanes[1] we had need of a method for the preparation of simple monosubstituted, scalemic aziridines such as **1**. The preparation of scalemic aziridines has been well covered in a number of reviews.[2] Two methods seemed particularly well suited for the preparation of the types of aziridines needed for our work. First, an amino acid can be converted into a substituted aziridine.[3] The use of amino acids, however, is quite limiting as to the identity of R. Second, the aziridination of an olefin with PhI=NTs and a copper catalyst has been shown to be useful in some cases.[4] While this method can be extremely useful, again the choice of R can be limited. For example, other olefins in the molecule can be a problem, and optimal yields are only obtained with cyclic or strained olefins.

Our plan (Scheme 1) was to prepare the aziridine **2** and to examine the reactivity of this molecule with a variety of organometallic reagents. The reaction of the aziridine ring with cuprates, organolithium reagents, and Grignard reagents is well known.[5] We were not certain where nucleophilic attack would take place with an aziridine such as **2**, and a variety of products are possible. If nucleophilic attack takes place at the tosyl ester, (*S*)-**1** would be the result. We had hoped that attack would take place on the aziridine ring and lead to intermediate **3**, which would then recyclize to form aziridine (*R*)-**1**. A similar strategy has been used in reactions of glycidyl tosylate.[6] In that case, when glycidyl tosylate was reacted with heteroatom nucleophiles, displacement of the tosylate was observed to be the major reaction pathway. Reaction of glycidal tosylate with organometallic reagents, however, gave products resulting from exclusive epoxide ring opening. In our case, such a strategy would allow the preparation of a number of monosubstituted aziridines from a single aziridine precursor. The preparation of the precursor aziridine **10**, in optically pure form from (*R*)-serine is well known.[7]

Scheme 1



Scheme 2



Results and Discussion

The preparation of aziridine **10** was carried out as shown in Scheme 2. The readily available (*S*)-serine was esterified and tosylated, and the free hydroxyl was protected as a *tert*-butyldimethylsilyl ether. Reduction of the methyl ester was most efficiently carried out with lithium borohydride to produce **7**.[8] The aziridine ring was then formed via a Mitsunobu reaction.[9] Desilylation of **8** yields aziridine **9** in 44% overall yield from (*S*)-serine. Tosylation produces the desired *N*-tosyl,*O*-tosylaziridine **10**.

* To whom correspondence should be addressed. Telephone: 614-292-5499. E-mail: bergmeier.1@osu.edu.

(1) Bergmeier, S. C.; Seth, P. P. *Tetrahedron Lett.* **1995**, *36*, 3793.

(2) For exhaustive discussions of the synthesis and reactions of aziridines see: (a) Aziridines, Azirines and Fused-ring Derivatives. Padwa, A.; Woolhouse, A. D. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 7; Lwowski, W., Ed., pp 80−93. (b) Aziridines. Deyrup, J. A. In *The Chemistry of Heterocyclic Compounds*; Weissberger, A., Taylor, E. C., Eds.; Wiley: New York, 1983; Vol. 42; Hassner, A., Ed., pp 11−83. (c) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. (d) Kametani, T.; Honda, T. *Adv. Heterocycl. Chem.* **1986**, *39*, 181.

(3) For some examples of the synthesis of chiral nonracemic aziridines from amino acids see: (a) Bergmeier, S. C.; Lee, W. K.; Rapoport, H. *J. Org. Chem.* **1993**, *58*, 5019 and references therein. (b) Baldwin, J. E.; Farthing, C. N.; Russell, A. T.; Schofield, C.; Spivey, A. C. *Tetrahedron Lett.* **1996**, *37*, 3761. (c) Osborn, H. M. I.; Cantril, A. A.; Sweeney, J. B. *Tetrahedron Lett.* **1994**, *35*, 3159. (d) Ho, M.; Chung, J. K. K.; Tang, N. *Tetrahedron Lett.* **1993**, *34*, 6513. (e) Berry, M. B.; Craig, D. *Synlett*, **1992**, 41. Also see ref 7 and references cited therein.

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(7) Fujii, N.; Nakai. K.; Habashita H.; Hotta, H.; Tamamura, T.; Otaka. A.; Ibuka, T. *Chem. Pharm. Bull.* **1994**, *42*, 2241.

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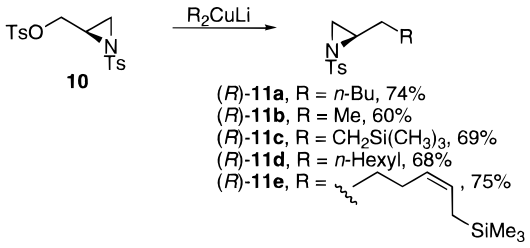
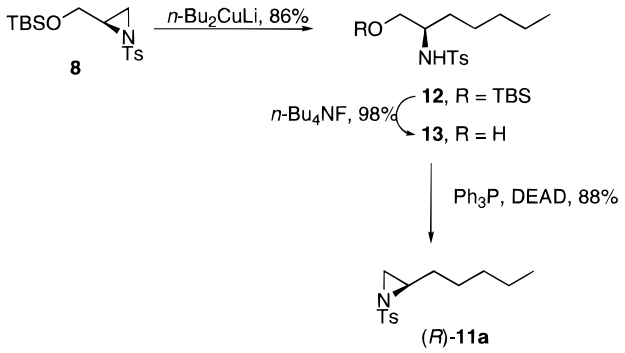
Scheme 3



Scheme 4

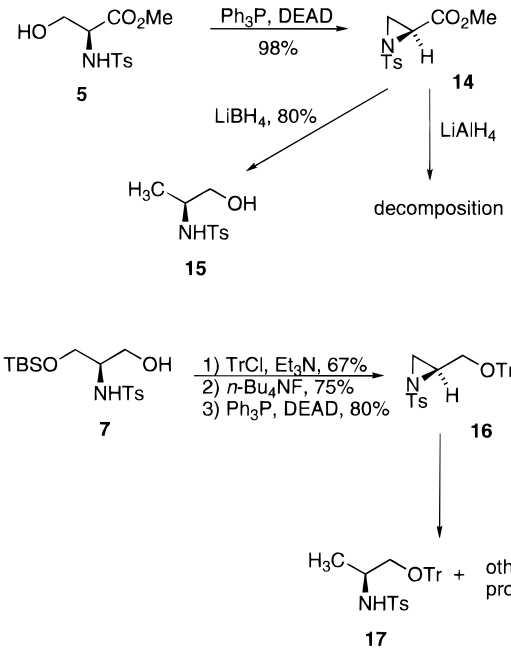


We were pleased to find that the reaction of **10** with *n*-Bu_2CuLi gave only a single product (**11a**) in good yield (Scheme 3). As **11a** could have either the *S* or *R* configuration, or a mixture of the two, the absolute stereochemistry needed to be determined. In order to unambiguously assign the absolute stereochemistry, the aziridine **11a** with the *R* configuration was prepared by an alternate route (Scheme 4). Starting from aziridine **8**, reaction with *n*-Bu_2CuLi gave a single ring-opened product **12**. Desilylation and aziridine formation via a Mitsunobu reaction gave **11a** with the *R* configuration. This compound was identical with respect to optical rotation with **11a** prepared via the single-step aziridine opening/aziridine reformation reaction.

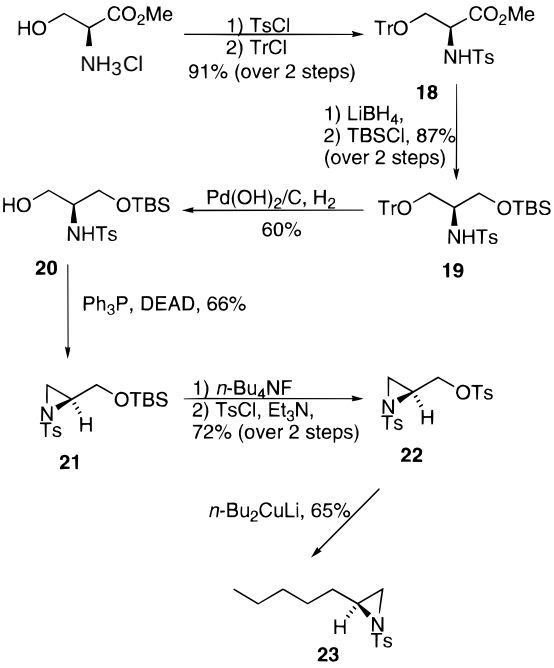
Further proof of the stereochemical integrity of **11a** was desired. For this purpose, the enantiomer of **11a**, aziridine **23**, was prepared from the aziridine tosylate **22**. A number of routes which could lead us to **22** from (*S*)-serine were examined (Scheme 5). The aziridine ester **14** was prepared from **5** via a Mitsunobu reaction. Reduction of the ester using $LiAlH_4$ resulted in decomposition products. Reduction using $LiBH_4$ gave only the completely reduced product **15**. Another route which was attempted involved protection of the free hydroxyl of **7** with a trityl group. Desilyation followed by a Mitsunobu reaction gave the trityl-protected aziridine **16**. Hydrogenation of **16** using Pd on charcoal gave a mixture of products. The major product **17** was found to be the one arising from hydrogenolysis of the aziridine ring.[10]

The method which ultimately worked is depicted in Scheme 6. The methyl ester of (*S*)-serine was *N*-tosylated, followed by tritylation of the free hydroxyl group to provide **18**. Reduction of the methyl ester and protection of the resulting alcohol with *tert*-butyldimethylsilyl chloride gave **19**. Removal of the trityl group proved to

Scheme 5



Scheme 6



be difficult. Use of palladium on activated charcoal resulted in long reaction times and low yields of **20**. Hydrogenation using 100 wt % of Pearlman's catalyst provided **20** in a 33% yield (60% considering recovered starting material). Use of more vigorous conditions resulted in complete removal of the trityl as well as the silyl protecting group. Detritylation using formic acid in ether provided the desired product in only 39% yield.[11] As before, the aziridine **21** was formed via a Mitsunobu reaction of the vicinal amido alcohol. Deprotection of the silyl group, followed by tosylation of the alcohol, produced **22**. Aziridine **22** was then treated with *n*-Bu_2CuLi to provide **23**.

The comparison of **11a** and it's enantiomer, **23**, showed clear differentiation in the ^1H NMR when combined with the chiral solvating reagent (*S*)- or (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol. The identification of the peaks arising from the (*S*) enantiomer **23** allowed us to assign

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(11) Bessodes, M.; Komiotis, D.; Antonakis, K. *Tetrahedron Lett.* **1986,** *27*, 579.

(12) In a typical experiment, 3−5 mg of the aziridine and 20−30 mg of the solvating agent were dissolved in benzene-d_6 (0.5−0.6 mL). In the case of **11a** and **23**, the doublet at 1.05 ppm, corresponding to one of the methylene protons on the aziridine ring, was shifted to 1.46 ppm for **23** (*S* enantiomer) and 1.44 ppm for **11a** (*R* enantiomer).

an optical purity of >97% to the (*R*)-aziridine, **11a**.[12] Chiral shift agent (+)-Eu(hfc)$_3$ was not as effective as the chiral solvating reagent in resolving the two enantiomers.

Satisfied that the reaction of **10** with a cuprate would provide **11** via a ring-opening−ring-closing sequence, we turned our attention to the use of other organometallic reagents. Neither *n*-BuLi nor *n*-BuMgBr provided any of the desired product; only decomposition of **10** was seen.

We next wished to examine the use of other organocuprate reagents. The cuprates derived from commercially available methyllithium, hexyllithium, and [(trimethylsilyl)methyl]lithium gave acceptable yields of the corresponding aziridines **11**−**11d** (Scheme 3). When methyl lithium was used, an additional product that we have identified as *N*-tosyl-3-pentanamine was formed. We believe that this product arises from the reaction of Me_2CuLi with the product **11b**.[13] Through the use of the chiral solvating agent, the enantiomeric purity of aziridines **11**−**11d** was determined to be >97%.

We now turned our attention to the use of noncommercially available organolithium reagents in this reaction. To this end the known alkyl iodide 6-iodo-1-(trimethylsilyl)-2-hexene[14] was prepared starting from 3,4-dihydro-2*H*-pyran.[15] The iodide was cleanly converted to the corresponding organolithium reagent by treating it with *t*-BuLi at −78 °C in Et_2O.[16] Treatment of the intermediate organolithium with CuI resulted in the formation of an insoluble cuprate which did not provide very good yields of **11e** (30−34%). This problem was overcome by the addition of *n*-Bu_3P[17] to the reaction, producing **11e** in 75% yield.

We also attempted to prepare and use a cuprate prepared from *s*-BuLi. Although this reagent did provide us with some of the desired aziridine, this reaction was not as clean as the reactions using the cuprates derived from primary organolithiums. Similarly cuprates derived from phenyllithium, vinyllithium, and vinylmagnesium bromide only resulted in the decomposition of **10**.

In conclusion, we have developed a novel method for the preparation of enantiomerically pure monosubstituted aziridines via the reaction of an aziridine tosylate with a primary organocuprate reagent. The attack of the cuprate takes place at the least-substituted carbon of the aziridine ring, resulting in the formation of ring-opened intermediates. These intermediates can then undergo a ring closure by displacement of the tosyl ester. With the help of chiral solvating reagents, the optical purity of the aziridines thus formed was judged to be >97%.

Experimental Section[18]

(2*R*)-2-[[[(4-Methylphenyl)sulfonyl]oxy]methyl]-1-[(4-methylphenyl)sulfonyl]aziridine (10). Et_3N (2.9 g, 29.2 mmol) was added to a solution of **9**[19] (13.6 g, 14.6 mmol) and DMAP (180 mg, 1.5 mmol) in CH_2Cl_2 (15 mL) at 0 °C. *p*-Toluenesulfonyl chloride (2.9 g, 15.3 mmol) was added to the reaction over a period of 5 min. After the addition was complete, the solution was warmed to rt and allowed to stir for another 90 min. The reaction was diluted with CH_2Cl_2 (20 mL) and quenched by the addition of 1 M HCl (15 mL). The two layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic layers were combined, washed with saturated $NaHCO_3$ solution (15 mL) and brine, dried ($MgSO_4$), and concentrated. Chromatography (35% EtOAc in hexanes) gave 4.28 g (75%) of **10** as a white solid. $[\alpha]_D$ +18.7° (*c* 8.4, EtOAc), ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.71 (d, 2H, J = 8.35), 7.61 (d, 2H, J = 8.37), 7.30 (m, 4H), 4.01 (dd, 1H, J = 4.79, 11.24), 3.84 (dd, 1H, J = 6.32, 11.18), 2.98−2.90 (m, 1H), 2.61 (d, 1H, J = 7.07), 2.39 (s, 6H), 2.13 (d, 1H, J = 4.28). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 145.0, 144.8, 134.4, 132.6, 129.8, 129.6, 127.9, 127.7, 68.4, 36.6, 30.8, 21.4. Anal. Calcd for $C_{17}H_{19}NO_5S_2$: C, 53.52; H, 5.02; N, 3.67. Found: C, 53.20; H, 4.76; N, 3.69.

General Procedure for the Preparation of Aziridines 11a−d. A solution of the desired organolithium (1−1.35 mmol) was added to a cold (−78 °C) suspension of CuI (95 mg, 0.5 mmol) in THF (1.5 mL). The resulting solution was warmed to −40 °C and allowed to stir for 10 min after which it was cooled to −78 °C. A solution of **10** (195 mg, 0.5 mmol), dissolved in THF (1 mL) was added to the reaction via cannula under a positive pressure of nitrogen. The reaction was allowed to stir at −78 °C for 60 min after which it was quenched by the addition of saturated NH_4Cl solution at −78 °C, and the aqueous solution was extracted with EtOAc (2 × 5 mL), dried ($MgSO_4$), and concentrated. Chromatography gave the aziridines **11a**−**d**.

(*R*)-2-Pentyl-*N*-[(4-methylphenyl)sulfonyl]aziridine (11a). Prepared by the general procedure using *n*-BuLi (1 mmol, 0.43 mL of a 2.3 M solution in hexanes) to give 99 mg (74%) of **11a** as a colorless oil. R_f 0.23 (6% EtOAc in hexanes), $[\alpha]_{365}$ +18.5° (*c* 3.0, EtOAc), ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.79 (d, 2H, J = 8.21), 7.29 (d, 2H, J = 8.31), 2.63 (m, 1H), 2.59 (d, 1H, J = 6.95), 2.40 (s, 3H), 2.02 (d, 1H, J = 4.33), 1.6−1.1 (m, 8H), 0.78 (m, 3H). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 144.3, 135.5, 129.5, 128.0, 40.4, 33.6, 31.2, 31.1, 26.3, 22.3, 21.5, 13.7. Anal. Calcd for $C_{14}H_{21}NO_2S$: C, 62.88; H, 7.91; N, 5.20. Found: C, 62.86; H, 7.81; N, 5.20.

(*R*)-2-Ethyl-*N*-[(4-methylphenyl)sulfonyl]aziridine (11b). Prepared by the general procedure using MeLi (1.2 mmol, 1.05 mL of a 1.14 M solution in Et_2O) to give 67 mg (60%) of **11b** as a colorless oil. R_f 0.21 (6% EtOAc in hexanes), $[\alpha]_{365}$ −7.9° (*c* 3.2, EtOAc), ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.82 (d, 2H, J = 8.35), 7.33 (d, 2H, J = 7.96), 2.69 (m, 1H), 2.61 (d, 1H, J = 6.97), 2.44 (s, 3H), 2.07 (d, 1H, J = 4.48), 1.6 (m, 1H), 1.35 (m, 1H), 0.83 (t, 3H, J = 7.42). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 144.3, 135.4, 129.5, 127.9, 41.6, 33.4, 24.4, 21.5, 10.6. Anal. Calcd for $C_{11}H_{15}NO_2S$: C, 58.63; H, 6.71; N, 6.21. Found: C, 58.56; H, 6.52; N, 6.21.

(*R*)-2-[2-(Trimethylsilyl)ethyl]-*N*-[(4-methylphenyl)sulfonyl]aziridine (11c). Prepared by the general procedure using [(trimethylsilyl)methyl]lithium (1.2 mmol, 1.53 mL of a

(13) This di-opening product is seen to a small extent with all of the organocuprate reagents (5−10%), but due to the small size of the methylcuprate, increased amounts are seen (up to 25−30%). The amount of di-opening product formed was reduced when the reaction was not allowed to warm to rt and quenched at −78 °C. Warming the reaction to rt also resulted in some loss of optical purity of the products. The aziridines formed in this manner had ee in the range of 92−95%.

(14) Padwa, A.; Zhang, Z. J. *Heterocycles* **1994**, 441. These workers prepared 6-iodo-1-(trimethylsilyl)-2-hexene in six steps from butanediol. We prepared the iodide from the corresponding alcohol in 80% yield by tosylation and displacement by iodide. The alcohol was prepared by the method of Wenkert[15] in 36% yield from dihydropyran in a single step. The olefins formed by this coupling reaction predominantly have the *Z* configuration.

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(16) (a) Bailey, W. F.; Punzalan, E. R. *J. Org. Chem*. **1990**, *55*, 5404. (b) Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem*. **1990**, *55*, 5406.

(17) O'Reilly, J. M.; Lin, J. M.; Duax, W. L.; Brueggemeier. R. W. *J. Med. Chem*. **1995**, *38*, 2842.

(18) General methods: Thin layer chromatography (TLC) was performed on Whatman precoated silica gel F_{254} aluminum foils. Visualization was accomplished with UV light and/or phosphomolybdic acid solution followed by heating. Purification of the reaction products was carried out by flash column chromatography using glass column dry packed with silica gel (230−400 mesh ASTM) according to the method of Still.[20] ^{1}H NMR spectra referenced to TMS were recorded using a Bruker AF 250 or Bruker AF 270 model spectrometer. Data are reported as follows: chemical shift in ppm from internal standard tetramethylsilane on the δ scale, multiplicity (b = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), integration, coupling constant (Hz). All reactions were carried out under an atmosphere of nitrogen unless specified otherwise. Glassware was flame dried under a flow of nitrogen. Tetrahydrofuran and diethyl ether was distilled over sodium/benzophenone ketyl immediately prior to use. Dichloromethane was distilled over CaH_2 prior to use. Organolithium reagents used for the reactions were purchased from Aldrich Chemical Co. or prepared via the method of Negishi.[16] (*S*)- and (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol was purchased from Aldrich Chemical Co.

(19) Compound **9** was prepared by the method of Fujii et al.[7] These workers prepared the *S* enantiomer of **9** starting from (*R*)-serine. We started from natural (*S*)-serine to prepare compound **9** which was identical in all respects to the enantiomer reported in ref 7 except for the optical rotation $[\alpha]_D$ +29.9° (*c* 9.9, EtOAc), which was the opposite.

(20) Still, C. W.; Kahn, M.; Mitra, A. *J. Org. Chem*. **1978**, *50*, 2923.

0.78 M solution in pentane) to give 102 mg (69%) of **11c** as a colorless oil. R_f 0.27 (6% EtOAc in hexanes), $[\alpha]_{365}$ −32.7° (*c* 3.0, EtOAc), ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.78 (d, 2H, J = 8.29), 7.28 (d, 2H, J = 8.58), 2.69 (m, 1H), 2.55 (d, 1H, J = 6.91), 2.39 (s, 3H), 2.01 (d, 1H, J = 4.58), 1.39 (m, 2H), 0.36 (t, 2H, J = 8.67), −0.11 (s, 9H). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 144.1, 135.3, 129.4, 127.9, 42.6, 33.7, 25.8, 21.4, 13.1, −2.1. Anal. Calcd for $C_{14}H_{23}NO_2SiS$: C, 56.52; H, 7.79; N, 4.71. Found: C, 56.34; H, 7.98; N, 4.68.

(*R*)-2-Heptyl-*N*-[(4-methylphenyl)sulfonyl]aziridine (11d). Prepared by the general procedure using *n*-hexyllithium (1.35 mmol, 0.75 mL of a 1.8 M solution in hexanes) to give 100 mg (68%) of **11d** as a colorless oil. $[\alpha]_{365}$ +23.8° (*c* 3.9, EtOAc), ^{1}H NMR ($CDCl_3$, 270 MHz), δ 7.79 (d, 2H, J = 8.29), 7.29 (d, 2H, J = 8.07), 2.55 (m, 1H), 2.59 (d, 1H, J = 6.97), 2.40 (s, 3H), 2.02 (d, 1H, J = 4.48), 1.6−1.1 (m, 12H), 0.83 (t, 3H, J = 6.68). ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 144.3, 135.3, 129.5, 128.0, 40.4, 33.7, 31.6, 31.3, 29.0, 28.9, 26.7, 22.5, 21.5, 14.0. Anal. Calcd for $C_{16}H_{25}NO_2S$: C, 65.04; H, 8.52; N, 4.74. Found: C, 64.87; H, 8.24; N, 4.74.

(*R*)-2-[7-(Trimethylsilyl)hept-5-enyl]-*N*-[(4-methylphenyl)-sulfonyl]aziridine (11e). *t*-BuLi (3.7 mmol, 4.16 mL of a 0.89 M solution in pentane) was added to a solution of 6-iodo-1-(trimethylsilyl)-2-hexene[14] (500 mg, 1.8 mmol) in Et_2O (5 mL) at −78 °C. The reaction was stirred at −78 °C for 10 min after which it was warmed to rt and allowed to stir for 1 h. The reaction was recooled to −78 °C, and a solution of CuI (119 mg, 0.63 mmol) and nBu$_3$P (0.75 mL, 3.0 mmol) in Et_2O (5 mL) was added to the reaction via cannula. The reaction was warmed to −40 °C for 10 min after which it was cooled to −78 °C and allowed to stir for another 40 min. A solution of **10** (240 mg, 0.63 mmol) in THF:Et_2O (1:1, 2 mL) was added to the cuprate solution, and the reaction was stirred for another 60 min after which it was quenched by the addition of saturated NH_4Cl solution at −78 °C. The aqueous solution was extracted with EtOAc (2 × 5 mL), dried ($MgSO_4$), and concentrated. Chromatography (7% EtOAc in hexanes) gave 173 mg (75%) of **11e** as a colorless oil. R_f 0.26 (6% EtOAc in hexanes). $[\alpha]_{365}$ +34.0° (*c* 3.0, EtOAc). ^{1}H NMR ($CDCl_3$, 270 MHz), δ 7.79 (d, 2H, J = 8.28), 7.30 (d, 2H, J = 8.51), 5.35 (m, 1H), 5.15 (m, 1H), 2.69 (m, 1H), 2.59 (d, 1H, J = 6.98), 2.41 (s, 3H), 2.02 (d, 1H, J = 4.49), 1.85 (m, 2H), 1.39 (d, 2H, J = 8.18), 1.6−1.1 (m, 6H), −0.03 (s, 9H). ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 144.3, 135.4, 129.5, 127.9, 127.0, 125.6, 40.3, 33.6, 31.2, 29.1, 26.7, 26.4, 21.5, 18.4, −1.8. Anal. Calcd for $C_{19}H_{31}NO_2SiS$: C, 62.42; H, 8.55; N, 3.83. Found: C, 62.45; H, 8.51; N, 3.84.

Alternate Preparation of (*R*)-2-Pentyl-*N*-[(4-methylphenyl)sulfonyl]aziridine (11a). *n*-BuLi (1.21 mL of a 2.3 M solution in hexanes, 2.8 mmol) was added to a suspension of CuI (270 mg, 1.4 mmol) in THF (2.8 mL) at −40 °C. The bluish black solution that was formed was allowed to stir at −40 °C for 40 min. A solution of **8**[7] in THF (1 mL) was added to the cuprate solution, and the reaction was allowed to stir at −78 °C for 60 min after which it was warmed to rt and stirred for another 60 min. The reaction was quenched by the addition of saturated NH_4Cl solution (10 mL), and the aqueous layer was extracted with EtOAc (2 × 10 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated. Chromatography (8% EtOAc in hexanes) gave 249 mg (86%) of **12** as a colorless oil. ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.72 (d, 2H, J = 8.31), 7.25 (d, 2H, J = 8.15), 4.73 (d, 1H, J = 8.29), 3.40 (dd, 1H, J = 3.27, 9.96), 3.30 (dd, 1H, J = 4.28, 9.95), 3.15 (m, 1 H) 1.63−1.08 (m, 8 H), 0.81 (s, 12H), −0.06 (s, 3H), -0.08 (s, 3H). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 143.1, 138.6, 129.5, 127.1, 64.3, 55.1, 32.1, 31.5, 25.8, 25.2, 22.4, 21.4, 18.2, 13.8, −5.6. nBu$_4$NF (0.8 mL of 1 M solution in THF, 0.8 mmol) was added dropwise to an ice cold solution of **12** (240 mg, 0.63 mmol) in THF (1.5 mL). The solution was stirred for 1 h after which it was diluted with water and extracted with EtOAc (2 × 5 mL). The layers were separated, and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography (3% MeOH in $CHCl_3$) gave 180 mg (98%) of **13** as a colorless oil. ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.75 (d, 2H, J = 8.18), 7.25 (d, 2H, J = 8.36), 5.36 (m, 1H), 3.5 (m, 2H), 3.28 (m, 2H), 2.76 (m, 1 H), 2.37 (s, 3H), 1.36−1.00 (m, 8 H), 0.73 (t, 3H, J = 6.47). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 143.3, 137.9, 129.6, 127.1, 64.8, 55.7, 31.6, 31.3, 25.1 22.3, 21.3, 13.7. Diethyl azodicarboxylate (120 mg, 0.70 mmol) was slowly added to a stirred solution of **13** (180 mg, 0.63 mmol) and triphenylphosphine (180 mg, 0.70 mmol) in THF (3.5 mL) at 0 °C. The reaction was allowed to stir for 4 h after which all the solvent was removed by concentration under reduced pressure to give a thick brown oil. Chromatography (10% EtOAc in hexanes) gave 143 mg (88%) of **11a** as a colorless oil. Analytical data was identical to that reported for **11a** prepared by reaction of n-Bu$_2$CuLi with **10**.

Methyl *O*-(Triphenylmethyl)-*N*-[(4-methylphenyl)sulfonyl]-(*S*)-serinate (18). Et_3N (6.2 mL, 45.0 mmol) was added dropwise to a cold stirring suspension of methyl (*S*)-serinate hydrochloride (3.1 g, 20.0 mmol) in CH_2Cl_2 (20 mL). The suspension was stirred for 30 min at 0 °C. *p*-Toluensulfonyl chloride (3.8 g, 20.0 mmol) was added to the reaction in small portions over 10 min. After the addition was completed, the reaction was warmed to rt and allowed to stir for 8 h. The reaction was then cooled to 0 °C followed by a further addition of triethylamine (4 mL, 28.0 mmol). Trityl chloride (11.1 g, 40.0 mmol) was then added to the reaction in small portions over 10 min, and the whole was stirred at rt for 10 h. The reaction was then diluted with CH_2Cl_2 (40 mL) and washed successively with 1 M HCl, saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated. Chromatography (8% EtOAc in hexanes) provided 9.41 g (91%) of **18** as a white solid. $[\alpha]_D$ +5.8° (*c* 7.9, EtOAc), ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.67 (d, 2H, J = 8.30), 7.35 (m, 17H), 5.51 (d, 1H, J = 9.18), 4.05 (m, 1H), 3.54 (s, 3H), 3.43 (dd, 1H, J = 3.4 Hz, 9.06), 3.34 (dd, 1H, J = 3.58, 9.07), 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 170.2, 143.4, 143.2, 137.2, 129.6, 128.5, 127.8, 127.2, 127.1, 86.8, 77.5, 77.0, 76.5, 64.6, 56.1, 52.4, 21.4. HRMS Calcd for $C_{30}H_{29}NO_5S$ 515.1767, found 515.1757.

***O*-(Triphenylmethyl)-*O*-(*tert*-Butyldimethylsilyl)-*N*-[(4-methylphenyl)sulfonyl]-(*S*)-serinol (19).** A solution of **18** (1.4 g, 2.7 mmol) in THF:EtOH (1:2, 12 mL) was treated with anhydrous LiCl (340 mg, 8.1 mmol) followed by $NaBH_4$ (300 mg, 8.1 mmol) at 0 °C. After the addition of all the $NaBH_4$, the reaction was warmed to rt and stirred for 6 h. The reaction was quenched by addition of acetone (2 mL) followed by addition of 5% HCl until the reaction became clear. The solution was extracted with Et_2O (2 × 10 mL), dried ($MgSO_4$), and concentrated. The crude oil was dissolved in CH_2Cl_2 (3 mL). DMAP (30 mg, 0.27 mmol) and Et_3N (0.64 mL, 4.6 mmol) were added to the above solution, and the whole was cooled in an ice bath. *tert*-Butyldimethylsilyl chloride (810 mg, 5.4 mmol) was added to the cold solution, and the reaction was allowed to stir overnight at rt. The mixture was then diluted with CH_2Cl_2 (5 mL), washed successively with 1 M HCl, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated. Chromatography (10% EtOAc in hexanes) provided 1.42 g (87%) of **19** as a white solid. $[\alpha]_D$ +6.2° (*c* 3.4, EtOAc), ^{1}H NMR ($CDCl_3$, 250 MHz), δ 7.65 (d, 2H, J = 8.27), 7.35 (m, 17H), 4.90 (d, 1H, J = 7.61), 3.81 (dd, 1H, J = 3.60, 9.88), 3.63 (dd, 1H, J = 6.07, 9.86), 3.37 (m, 1H), 3.28 (dd, 1H, J = 4.52, 8.95), 3.0 (dd, 1H, J = 6.18, 8.97), 2.41 (s, 3H), 0.83 (s, 9H), 0.0 (d, 6H). ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 143.6, 143.0, 138.0, 129.5, 128.5, 127.7, 127.0, 126.9, 86.8, 62.1, 61.9, 54.6, 25.8, 21.4, 18.1, −5.6.

***O*-(*tert*-Butyldimethylsilyl)-*N*-[(4-methylphenyl)sulfonyl]-(*S*)-serinol (20).** A mixture of the protected diol **19** (250 mg, 0.41 mmol) and 250 mg of 20% $Pd(OH)_2$/C in EtOAc (2 mL) was hydrogenated at atmospheric pressure for 24 h. The reaction mixture was then filtered through a bed of Celite and evaporated. Chromatography (20% EtOAc in hexanes) gave 50 mg (34%) of the detritylated product **20** as well as 106 mg of the starting material **19** (43%). Analytical data was identical to that reported in literature.[7]

(2*S*)-2-[[[(4-Methylphenyl)sulfonyl]oxy]methyl]-1-[(4-methylphenyl)sulfonyl]aziridine (22). Prepared on a 1.1 mmol scale using the same procedure for the conversion of **8** to **10**. Analytical data was identical to that reported for **10** except for $[\alpha]_D$ −20.4° (*c* 3.0, EtOAc).

(*S*)-2-Pentyl-*N*-[(4-methylphenyl)sulfonyl]aziridine (23). Prepared using the same procedure for the conversion of **10** to **11a**. Analytical data was identical to that reported for **11a** except for $[\alpha]_{365}$ −16.6° (*c* 1.5, EtOAc).

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of **18** and **19** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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