Palladium-Catalyzed Rearrangement of Allylic Sulfoximines: Application to the Asymmetric Synthesis of Chiral Allylic Amines

Stephen G. Pyne* and Zemin Dong

Department of Chemistry, University of Wollongong, Wollongong, New South Wales, 2522, Australia

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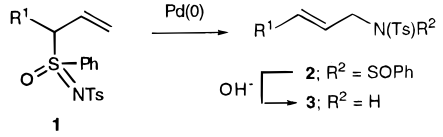
The palladium(0)-catalyzed reactions of the primary and secondary allylic sulfoximines **7**, **9**, **11**, **13, 15**, **17**, and **19** gives allylic sulfinamides without 1,3-allylic rearrangement. These compounds were not isolated but were converted to their corresponding *N*-tosyl allylic amines, primary and secondary **8**, **10**, **12**, **14**, **16**, **18**, and **20**, respectively. In the case of the optically active secondary allylic sulfoximines **17** and **19,** chiral *N*-tosyl allylic secondary amines were formed in high enantiomeric purities.

Introduction

Chiral amines are important compounds in organic synthesis. They have been employed as chiral bases,[1a] nucleophiles,[1b] auxiliaries,[1c] and ligands[1d] for asymmetric synthesis. In particular, allylic amines are useful compounds for organic synthesis[2] and have been featured as the key structural components of peptide isosteres.[3] We recently reported a novel method for the synthesis of primary *N*-tosyl allylic amines **3** via the palladium(0)-catalyzed rearrangement of α-substituted allylic sulfoximines **1** to allylic sulfinamides **2**[4,5] (eq 1).

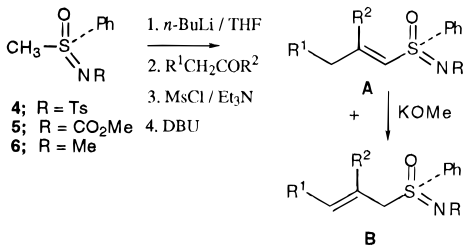


1 (1)

This type of rearrangement reaction has been reported to occur under thermal induction but only in the case of γ-phenyl allylic sulfoximines.[6] In these compounds the phenyl substituent may facilitate the rearrangement process by providing stabilization of an ion pair or other intermediate. These thermally induced rearrangements, however, proceed with poor regioselectivity and poor yields of conversion.[6] Interestingly, semiempirical[7] and *ab initio*[8] calculations indicate that allylic sulfinamides are thermodynamically much more stable than their isomeric allylic sulfoximines and that the free energy barrier, for conversion of allylic sulfoximines to their corresponding allylic sulfinamides, must be relatively large.

Results and Discussion

The primary allylic sulfoximines **7**, **9**, **11**, **13**, and **15** (Table 1) were prepared from racemic or (*S*)-*N*-tosyl-,[9] *N*-methoxycarbonyl-,[10] or *N*-methyl-[11] *S*-methyl-*S*-phenylsulfoximines **4, 5**, **and 6** respectively, according to the general literature procedures[12] (eq 2). In general, a



(2)

mixture of the vinyl sulfoximine **A** and the allylic sulfoximine **B** was obtained. Treatment of this mixture with KOMe/THF gave exclusively the desired allylic sulfoximine **B**.[13]

Treatment of a THF solution of the acyclic allylic sulfoximines **7** or **9** (*E*:*Z* = 58:42) with 5 mol % of tetrakis(triphenylphosphine)palladium(0) ($Pd(PPh_3)_4$) at room temperature for 10 min resulted in a bright red solution. Evaporation of the THF *in vacuo* and exposure of the crude reaction mixture to 10% aqueous sodium hydroxide and MeOH (1:10) at room temperature for 2 h gave the primary *N*-tosyl allylic amines **8** and **10**, respectively, in good yields (Table 1, entries 1 and 2). In both cases the rearrangement reactions were completely regioselective and resulted in products without 1,3-allylic rearrangement. In the case of **9** a 90:10 mixture of the (*E*) and (*Z*) geometric isomers of **10** was obtained. The regiochemistry of these reactions can be understood in terms of the formation of the Pd−allylic cation complex **C** followed by

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(1) For some recent examples, see: (a) Nishibayashi, Y.; Arikawa, Y.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1996**, *61*, 1172. (b) Davies, S. G.; McCarthy, T. D. *Synlett* **1995**, 700. (c) Matulenko, M. A.; Meyers, A. I. *J. Org. Chem.* **1996**, *61*, 573. (d) Miao, G.; Rossiter, B. E. *J. Org. Chem.* **1995**, *60*, 8424.

(2) Wei, Z.-Y.; Knaus, E. E. *Synthesis* **1994**, 1463 and references cited therein.

(3) Spaltenstein, A.; Carpino, P. A.; Miyake, F.; Hopkins, P. B. *J. Org. Chem.* **1987**, *52*, 3759.

(4) Pyne, S. G.; Dong, Z.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1995**, 445.

(5) Pyne, S. G.; Dong, Z. *Tetrahedron Lett.* **1995**, *36*, 3029.

(6) Gais, H.-J.; Scommoda, M.; Lenz, D. *Tetrahedron Lett.* **1994**, *35*, 7361.

(7) Harmata, M.; Claassen, R. J., II. *Tetrahedron Lett.* **1991**, *32*, 6497. Pyne, S. G.; Boche, G. *Tetrahedron* **1993**, *49*, 8449.

(8) Harmata, M.; Glaser, R.; Chen, G. S. *Tetrahedron Lett.* **1995**, *36*, 9145.

(9) Johnson, C. R.; Kirchhoff, R. A.; Reischer, R. J.; Katekar, G. F. *J. Am. Chem. Soc.* **1973**, *95*, 4287.

(10) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424.

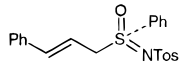
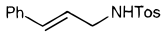
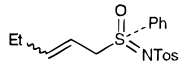
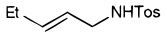
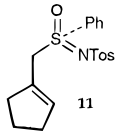
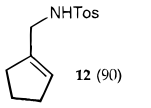
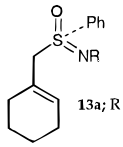
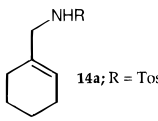
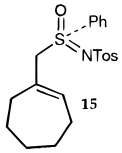
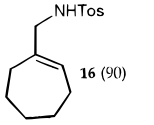
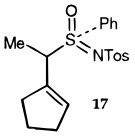
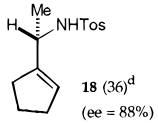
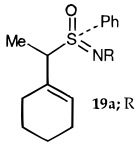
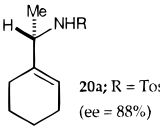
(11) Schaffner-Sabba, K.; Tomaselli, H.; Henrici, B.; Renfroe, H. B. *J. Org. Chem.* **1977**, *42*, 952.

(12) Pyne, S. G. *J. Org. Chem.* **1986**, *51*, 81.

(13) Gais, H.-J.; Muller, H.; Bund, J.; Scommoda, M., Brandt, J.; Raabe, G. *J. Am. Chem. Soc.* **1995**, *117*, 2453.

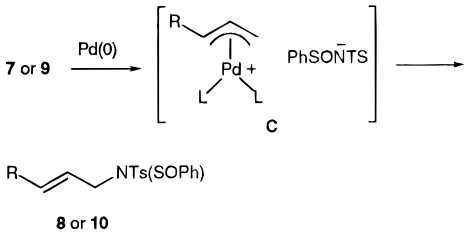
S0022-3263(96)00510-5 CCC: $12.00

Table 1. Synthesis of N-Protected Allylic Amines via Treatment of Allylic Sulfoximines with Palladium(0) and Then with Base

entry	substrate	time[a] (min)	product (yield[b] (%))
1	 **7**	10	 **8** (87)
2	 **9** (*E* : Z = 58 : 42)	10	 **10** (95; *E* : *Z* = 90 : 10)
3	 **11**	10	 **12** (90)
4	 **13a;** R = Tos	10	 **14a;** R = Tos (89)
5	**13b;** R = CO_2Me	30	**14b;** R = CO_2Me (66)
6	**13c;** R = Me	60	**14c;** R = Me (21)[c] + PhSONHMe (68)
7	 **15**	10	 **16** (90)
8	 **17**	10	 **18** (36)[d] (ee = 88%)
9	 **19a;** R = Tos	10	 **20a;** R = Tos (59)[d] (ee = 88%)
10	**19b;** R = CO_2Me	30	**20b;** R = CO_2Me (40)[d] (ee = 34%)

[a] Time for the palladium catalyzed reaction. [b] After base treatment with aqueous sodium hydroxide and then purification by column chromatography on silica gel. [c] Yield of the corresponding *N*-tosyl derivative that was formed by treating the crude reaction mixture with tosyl chloride/pyridine. [d] Overall yield from their respective sulfoximines **11**, **13a**, and **13b**.

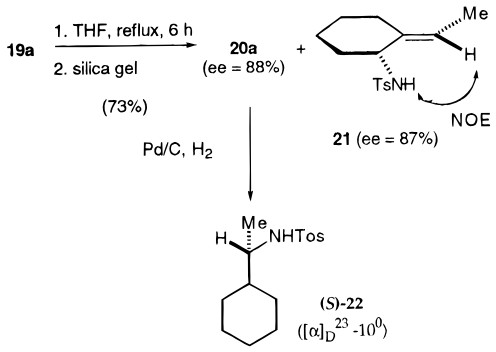
addition of the sulfinamide anion to the least substituted terminus of the allylic cation moiety of **C** (eq 3).



8 or **10** (3)

Formation of the more stable *syn* complex **C** (R = Et) would be expected from the initial mixture of *syn* and *anti* Pd−allylic cation complexes that could arise from the reaction of (*Z*)- and (*E*)-**9** with $Pd(PPh_3)_4$, respectively.[14] The palladium-catalyzed reactions of the cyclic *N*-tosyl allylic sulfoximines **11**, **13a**, and **15** were also completely regioselective and gave, after base hydrolysis, the *N*-tosyl primary allylic amines **12**, **14a**, and **16**, respectively, without 1,3-allylic transposition and in good overall yields (Table 1, entries 3, 4, and 7). The *N*-methoxycarbonyl and *N*-methyl allylic sulfoximines, **13b** and **13c**, also underwent rearrangement to their corresponding allylic sulfinamides with $Pd(PPh_3)_4$; however, those reactions were much slower than that of the related *N*-tosyl analogue **13a**. Qualitatively, the relative rates of the reactions of **13a**, **13b**, and **13c** correlated closely with the electron-withdrawing ability of the *N*-substituent of the sulfoximine. Thus while **13a** reacted in 10 min, **13b** required a reaction time of 30 min while the reaction of *N*-methyl compound **13c** was complete only after 1 h. In the later reaction the yield of the *N*-methyl allylic amine **14c** was low (21%, isolated as its less volatile *N*-tosyl derivative) and the major product isolated was *N*-methyl phenyl sulfinamide (68%). This major product is thought to arise via deprotonation of the intermediate Pd−allylic cation complex by the relatively basic *N*-methyl phenyl sulfinamide counteranion. This would also eventually give 3-methylenecyclohexene that was not isolated due to its volatility.

Scheme 1



Chiral α-Substituted Allylic Sulfoximines

In principle the palladium(0)-catalyzed rearrangement reaction of optically active α,γ-disubstituted allylic sulfoximines can give rise to optically active allylic amines. The success of this reaction depends upon the regioselectivity and diastereoselectivity of the rearrangement reaction. Methylation of the (*S*)-allylic sulfoximines **11**, **13a**, and **13b** (ee = 96%) by first deprotonation with LDA at −78 °C and then methylation with MeI gave the corresponding methylated allylic sulfoximines **17**, **19a**, and **19b**, respectively in 96−98% de. Sulfoximines **17** and **19a** were unstable and their attempted purification by chromatography on silica gel gave complex mixtures that included rearranged allylic sulfinamides. Heating a THF solution of **19a** at reflux for 6 h, followed by purification on silica gel, gave an inseparable 45:55 mixture of the rearranged *N*-tosyl allylic amines **20a** and **21**, respectively, in a combined yield of 73%. These compounds could be separated by preparative HPLC. The

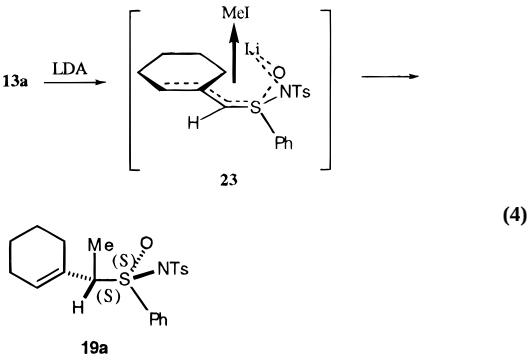
(14) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedon: Asymmetry* **1992**, *3*, 1089.

absolute (*S*) stereochemistry of **20a** was determined by a comparison of the specific rotation of its *N*-tosyl(1-cyclohexylethyl)amine derivative **22** ($[\alpha]^{23}_D$ −10° (*c* 0.4, $CHCl_3$) with that prepared from tosylation of commercially available (*R*)-(1-cyclohexylethyl)amine according to Scheme 1. (*R*)-*N*-tosyl(1-cyclohexylethyl)amine had a specific rotation of $[\alpha]^{23}_D$ +24.0° (*c* 0.5, $CHCl_3$).

The absolute stereochemistry assigned to **21** is more tenuous and is based on mechanistic considerations (Scheme 2). The (*E*) stereochemistry of **21** was established by a NOESY experiment that showed a cross peak between the alkene proton and the NH group. The enantiomeric purities of **20a** and **21** were determined to be 88% and 87%, respectively (92% and 91% ee corrected for the ee of **4**), by ^{1}H NMR studies using the chiral shift agent europium tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorate]. These studies resulted in well-resolved separate signals for the α-methyl group of **20a** and the vinyl methyl group of **21** for the two enantiomers of these compounds respectively, in both racemic and optically active preparations of these compounds.

Treatment of the crude methylation products **17**, **19a**, or **19b** with 5 % mol $Pd(PPh_3)_4$ in THF, followed by base hydrolysis, gave the related *N*-protected allylic amines **18**, **20a**, or **20b**, respectively (Table 1). These reactions were completely regioselective and gave none of the 1,3-allylic rearrangement products (e.g. **21**). The stereochemical sense of all these reactions were identical and like **20a**, which was obtained from the thermal rearrangement of **19a**, these compounds had the (*S*) absolute stereochemistry. While the enantiomeric purities of **18** and **20a** were high [both had an ee of 88% (92% corrected)] that of **20b** was only moderate (ee 34% from analysis by chiral HPLC).

The α-methylated allylic sulfoximines **17**, **19a**, and **19b** were too unstable to prepare crystals for X-ray crystallographic analysis. However, on the basis of our previous work,[15] we would predict that these compounds had the (*S*) stereochemistry at the α-carbon (eq 4). Our suggested

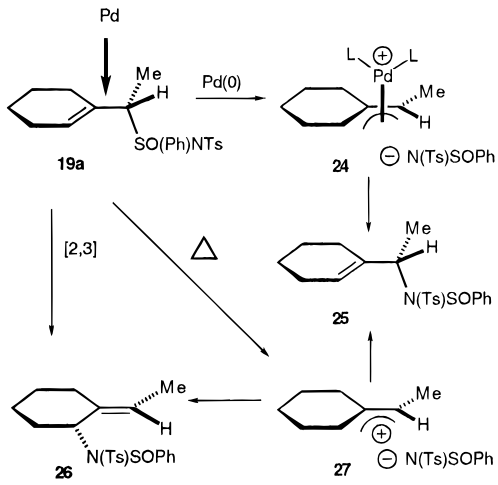


(4)

structure (**23**) for lithiated **13a** is shown in eq 4. This type of structure is also supported by single-crystal X-ray structural studies by Gais on related lithiated allylic sulfoximines.[16] Methylation of **23** would be expected to occur *syn* to lithium and *anti* to the S−Ph group (eq 4).

If this stereochemical assignment is correct then the thermal and palladium(0)-induced rearrangement reactions on **19a** can be rationalized as depicted in Scheme 2.

Scheme 2



The reactive conformation of **19a** would be expected to be that shown in Scheme 2 from stereoelectronic considerations[14,17] and in order to minimize allylic $A^{1,3}$ strain.[17] Attack of palladium(0) on the conformation **19a** would be expected to occur *anti* to the sulfoximine leaving group for stereoelectronic reasons to give the Pd−allylic cation complex **24** with the planar chirality shown. Addition of the sulfinamide anion to the allylic cation moiety would be expected to occur *anti* to palladium[14] to give sulfinamide **25** with the (*S*)-stereochemistry at the carbon of the newly created C−N bond. The thermal rearrangement of **19a** may proceed via the intimate ion pair **27**, followed by collapse of this intermediate to give **25** or **26**. Alternatively, some or all of **26** may arise from a [2,3]-sigmatropic rearrangement.[18] In the later scenario, collapse of the ion pair intermediate **27** would necessarily be regioselective and give only **25**.

From this study, however, it is not possible to distinguish between the different possible reaction pathways.

In conclusion, the palladium(0)-catalyzed rearrangement of certain primary and secondary allylic sulfoximines to give *N*-protected allylic amines has been shown to be highly regioselective and in the case of the later compounds highly enantioselective. Further extensions and applications of this methodology for asymmetric synthesis are under active investigation.

Experimental Section

General procedures were as described previously.[19] All NMR spectra were recorded in $CDCl_3$ solution at 400 MHz (^{1}H NMR) or 100 MHz (^{13}C NMR) unless otherwise noted. Chiral HPLC analysis was carried out using a Waters pump model 510 and a Regis D-naphthylalanine (Pirkle) 4.6 × 250 mm column at a flow rate of 0.6 mL/min using isopropyl alcohol/hexane (0.5:99.5) as eluent. The UV detector was a Waters series 450 variable wavelength detector operating at 254 nm.

(15) Pyne, S. G.; Dong, Z.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1994**, 751.

(16) Gais, H.-J.; Lenz, D.; Raabe, G. *Tetrahedron Lett.* **1995**, *36*, 7437.

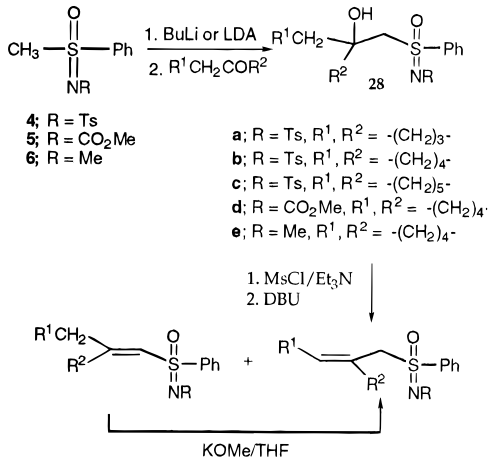
(17) Hoffman, *R. W. Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 563.

(18) For the [2,3]-sigmatropic rearrangements of allylic selenilimines, sulfilimines, and tellurimides, see refs a, b, and c, respectively: (a) Frankhauser, J. E.; Peevey, R. M.; Hopkins, P. B. *Tetrahedron Lett.* **1984**, *25*, 15. (b) Tamura, Y.; Sumoto, K.; Minamikawa, J.; Ikeda, M. *Tetrahedron Lett.* **1972**, 4137. (c) Nishibayashi, Y.; Srivastava, S. K.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **1995**, *36*, 6725. (d) For more recent references, see: Dolle, R. E.; Li, C.-S.; Novelli, R.; Kruse, L. I.; Eggleston, D. *J. Org. Chem*, **1992**, *57*, 128. Nishibayashi, Y.; Chiba, T.; Ohe, K.; Uemura, S. *J. Chem. Soc. Chem. Commun.* **1995**, 1243 and references cited therein.

(19) Pyne, S. G.; Dong, Z.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2607.

Racemic samples were always run to ensure separation of both enantiomers.

Preparation of Allylic Sulfoximines, A General Procedure:



To a solution of the sulfoximine (**5**, **6**, or **7**) (1 mmol) in dry THF (3 mL) at −78 °C was added *n*-BuLi or LDA (1.3 equiv) and the solution was stirred at −78 °C under N_2 for 40 min. The carbonyl compound (1.2 equiv) was added, and the reaction mixture was stirred for a further 1 h and then quenched by the addition of a saturated solution of aqueous NH_4Cl (0.2 mL) at −78 °C. Water (15 mL) was added, and the mixture was extracted with CH_2Cl_2 (2 × 20 mL). The combined extracts were dried ($MgSO_4$) and evaporated and the crude products were purified by column chromatography on silica gel. Elution with ethyl acetate/hexane gave the corresponding alcohol. In the case of alcohols **28** (R^1 = Ph, R^2 = H, R^3 = Ts) and **28** (R^1 = Et, R^2 = H, R^3 = Ts) the crude products were used in the next reaction directly. The purified or crude alcohol (1 mmol) was dissolved in dry CH_2Cl_2 (6 mL) and the solution was cooled to 0 °C. Triethylamine (5 equiv) was added then methanesulfonyl chloride (MsCl) (3 equiv) was added dropwise over 10 min. After 2 h of stirring at 0 °C, DBU (6 equiv) was added and after 10 min the reaction mixture was warmed to rt and then stirred for overnight. The reaction was diluted with ether (40 mL), and the mixture was washed with water (25 mL), a saturated aqueous solution of NH_4Cl (25 mL) and a 10% aqueous solution of Na_2CO_3 (25 mL). The ether layer was dried ($MgSO_4$) and evaporated. The crude reaction mixture was treated with potassium methoxide in dry MeOH for 72 h according to the method of Gais.[13] The crude reaction mixtures were purified by column chromatography on silica gel. Elution with ethyl acetate/hexane gave allylic sulfoximines **7**, **9, 11, 13a, 13b, 13c,** and **15**.

Alcohols 28: 1-[*N*-Tosyl-*S*-phenylsulfonimidoyl]methylcyclopentanol (28a). Yield 95%. ^{1}H NMR (300 MHz): δ 7.95−7.93 (2H, m), 7.77−7.73 (2H, m), 7.66−7.62 (1H, m), 7.56−7.51 (2H, m), 7.21 (2H, d, J = 7.5 Hz), 3.96 (1H, d, J = 14.4 Hz), 3.53 (1H, d, J = 14.4 Hz), 3.64-3.30 (1H, br), 2.37 (3H, s), 2.18−1.57 (8H, br). ^{13}C NMR (75 MHz): δ 142.6, 140.4, 138.6, 134.0, 129.3, 129.0, 127.8, 126.3, 79.5, 66.7, 39.9, 39.3, 23.0, 22.7, 21.2.

1-[*N*-Tosyl-*S*-phenylsulfonimidoyl]methylcyclohexanol (28b). Yield 81%. ^{1}H NMR: δ 8.00−7.97 (2H, m), 7.78 (2H, d, J = 8.4 Hz), 7.71−7.67 (1H, m), 7.62−7.58 (2H, m), 7.24 (2H, d, J = 8.4 Hz), 3.73 (1H, d, J = 14.4 Hz), 3.59 (1H, s), 3.31 (1H, d, J = 14.4 Hz), 2.40 (3H, s), 1.74−1.31 (8H, m). ^{13}C NMR (75 MHz): δ 142.8, 140.6, 139.4, 134.2, 129.5, 129.2, 127.8, 126.5, 72.0, 66.9, 37.7, 37.1, 25.0, 21.54, 21.50, 21.4.

1-[*N*-Tosyl-*S*-phenylsulfonimidoyl]methylcycloheptanol (28c). Yield 96%. ^{1}H NMR: δ 8.01−7.97 (2H, m), 7.79−7.77 (2H, m), 7.70−7.67 (1H, m), 7.62−7.57 (2H, m), 7.24 (2H, d, J = 8 Hz), 3.70 (1H, d, J = 14.4 Hz), 3.69 (1H, s), 3.30 (1H, d, J = 14.4 Hz), 2.40 (3H, s), 1.91−1.69 (4H, m), 1.63−1.48 (4H, m), 1.44−1.25 (4H, m). ^{13}C NMR: δ 142.9, 140.4, 139.4, 134.2, 129.6, 129.2, 127.8, 126.6, 76.2, 67.8, 41.2, 40.5, 29.5, 29.4, 21.7, 21.6, 21.5.

1-[*N*-(Methoxycarbonyl)-*S*-phenylsulfonimidoyl]methylcyclohexanol (28d). Yield 22%. ^{1}H NMR: δ 7.96−7.94 (2H, m), 7.70−7.66 (1H, m), 7.63−7.59 (2H, m), 4.69 (1H, s), 3.61 (3H, s), 3.53 (1H, d, J = 14 Hz), 3.26 (1H, d, J = 14 Hz), 2.06−2.02 (1H, m), 1.79-1.68 (4H, m), 1.55−1.42 (4H, m), 1.32−1.25 (1H, m). ^{13}C NMR (75 MHz): δ 158.6, 139.2, 133.9, 129.7, 127.5, 71.9, 65.6, 53.1, 38.6, 36.9, 25.2, 21.7, 21.6.

1-[*N*-Methyl-*S*-phenylsulfonimidoyl]methylcyclohexanol (28e). Yield 78%. ^{1}H NMR (300 MHz): δ 7.90−7.86 (2H, m), 7.63−7.54 (3H, m), 6.44 (1H, br), 3.27 (1H, d, J = 13.5 Hz), 3.12 (1H, d, J = 13.5 Hz), 2.62 (3H, s), 2.20−2.10 (1H, br), 1.97−1.86 (1H, m), 1.82−1.50 (5H, m), 1.41−1.24 (3H, m). ^{13}C NMR: δ 139.1, 133.0, 129.5, 128.9, 71.7, 64.4, 39.2, 36.7, 28.9, 25.4, 22.0, 21.7.

Allylic sulfoximines: (*E*)-*N*-Tosyl-*S*-phenyl-*S*-(3-phenyl-2-propenyl)sulfoximine (7). Yield 29% overall from **4**. ^{1}H NMR (300 MHz): δ 7.92−7.88 (4H, m), 7.71−7.64 (1H, m), 7.58−7.50 (2H, m), 7.35−7.17 (7H, m), 6.31 (1H, d, J = 15.9 Hz), 6.01 (1H, dt, J = 15.9, 7.5 Hz), 4.42 (2H, dddd, J = 0.9, 7.5, 0.9, 7.5 Hz), 2.38 (3H, s). ^{13}C NMR (75 MHz) δ 142.8, 141.1, 140.8, 135.3, 135.2, 134.3, 129.24, 129.21, 128.8, 128.7, 128.6, 126.7, 126.6, 113.0, 62.3, 21.5. MS (ES + ve): m/z 412 (M + H$^+$, 15), 296 (20), 251 (30), 183 (35), 117 (100).

(*E*)- and (*Z*)-*N*-Tosyl-*S*-phenyl-*S*-(2-pentenyl)sulfoximine (9). Yield 49% overall from **4**. ^{1}H NMR (300 MHz): (major, (*E*)-isomer) δ 7.92−7.85 (4H, m), 7.67 (1H, tt, J = 7.5, 1.5 Hz), 7.58−7.53 (2H, m), 7.24 (2H, d, J = 8.1 Hz), 5.51 (1H, dt, J = 15.6, 6.3 Hz), 5.38−5.27 (1H, m), 4.27−4.12 (2H, m), 2.38 (3H, s), 1.97 (2H, pent, J = 7.5 Hz), 0.84 (3H, t, J = 7.5 Hz); (minor, (*Z*)-isomer) δ 5.78−5.69 (1H, m), 4.42−4.25 (2H, m), 1.63 (2H, dpent, J = 7.5, 1.5 Hz), 0.67 (3H, t, J = 7.5 Hz). ^{13}C NMR (75 MHz) (on mixture): δ 145.5, 143.0, 142.6, 141.0, 135.4, 134.2, 134.1, 129.13, 129.06, 128.5, 126.6, 113.8 (*E*), 113.4 (*Z*), 62.0 (*E*), 57.0 (*Z*), 29.6 (*Z*), 25.6 (*E*), 21.4 (*E*), 20.6 (*Z*), 13.1 (*Z*), 12.7 (*E*); MS (ES + ve): m/z 364 (M + H$^+$, 22), 296 (100), 125 (20). HRMS calcd for $C_{18}H_{21}NO_3S_2$ = 363.09626; found 363.09684.

***N*-Tosyl-*S*-phenyl-*S*-(1-cyclopent-1-enylmethyl)sulfoximine (11).** Yield 97% from **28a**. ^{1}H NMR (300 MHz): δ 7.91−7.85 (4H, m), 7.69−7.64 (1H, m), 7.57−7.52 (2H, m), 7.24 (2H, d, J = 8.1 Hz), 5.49 (1H, br), 4.41 (1H, d, J = 13.8 Hz), 4.35 (1H, d, J = 13.8 Hz), 2.38 (3H, s), 2.27−2.15 (4H, m), 1.76 (2H, p, J = 7.5 Hz). ^{13}C NMR (75 MHz) δ 142.6, 141.0, 138.1, 135.9, 134.1, 129.8, 129.1, 129.0, 128.5, 126.6, 60.6, 34.8, 32.8, 23.5, 21.4. MS (ES + ve): m/z 376 (M + H$^+$, 30), 296 (100), 106 (50), 104 (100). HRMS calcd for $C_{19}H_{21}NO_3S_2$ = 375.09626; found 363.09535.

***N*-Tosyl-*S*-phenyl-*S*-(1-cyclohex-1-enylmethyl)sulfoximine (13a).** Yield 82% from **28b**. ^{1}H NMR: δ 7.91−7.85 (4H, m), 7.69−7.65 (1H, m), 7.58−7.54 (2H, m), 7.24 (2H, d, J = 8.8 Hz), 5.38 (1H, br), 4.21 (1H, d, J = 14 Hz), 4.06 (1H, d, J = 14 Hz), 2.39 (3H, s), 2.05−1.78 (4H, m), 1.51−1.41 (4H, m). ^{13}C NMR: δ 142.6, 141.0, 135.6, 134.1, 129.2, 129.1, 128.8, 126.6, 124.9, 66.7, 28.7, 25.7, 22.4, 21.5, 21.2. MS (ES + ve): m/z 390 (M + H$^+$, 25), 296 (100), 125 (25).

***N*-(Methoxycarbonyl)-*S*-phenyl-*S*-(1-cyclohex-1-enylmethyl)sulfoximine (13b).** Yield 68% from **28d**. ^{1}H NMR (300 MHz) δ 7.91−7.88 (2H, m), 7.70−7.64 (1H, m), 7.60−7.55 (2H, m), 5.36 (1H, broad), 4.13 (1H, d, J = 13.5 Hz), 4.03 (1H, d, J = 13.5 Hz), 3.68 (3H, s), 2.10−1.80 (4H, m), 1.54−1.43 (4H, m). ^{13}C NMR (75 MHz): δ 159.5, 135.7, 134.8, 133.7, 129.0, 128.5, 125.1, 64.3, 53.0, 28.6, 25.6, 22.4, 21.2. MS (ES + ve): m/z 294 (M + H$^+$, 100), 200 (20), 104 (15). HRMS calcd for $C_{15}H_{19}NO_3S$ = 293.10854; found 293.109809.

***N*-Methyl-*S*-phenyl-*S*-(1-cyclohexenylmethyl)sulfoximine (13c).** Yield 81% from **28e.** ^{1}H NMR (300 MHz): δ 7.83−7.78 (2H, m), 7.61−7.48 (3H, m), 5.32 (1H, broad), 3.76 (2H, s), 2.71 (3H, s), 2.20−2.05 (1H, m), 1.94−1.80 (3H, m), 1.58−1.40 (4H, m). ^{13}C NMR (75 MHz): δ 137.1, 132.9, 132.6, 129.8, 128.9, 126.6, 65.0, 29.8, 28.8, 25.6, 22.6, 21.5. MS (ES + ve): m/z 250 (M + H$^+$, 40), 156 (100), 124 (15).

***N*-Tosyl-*S*-phenyl-*S*-(1-cycloheptylmethyl)sulfoximine (15).** Yield 96% from **28c**. ^{1}H NMR: δ 7.92−7.90 (2H, m), 7.87−7.85 (2H, m), 7.66−7.65 (1H, m), 7.58−7.54 (2H, m),

7.24 (2H, d, J = 8 Hz), 5.45 (1H, t, J = 6 Hz), 4.32 (1H, d, J = 13.6 Hz), 4.03 (1H, d, J = 13.6 Hz), 2.38 (3H, s), 2.21−2.08 (2H, m), 1.93 (2H, broad), 1.70−1.56 (2H, m), 1.42−1.26 (4H, m). ^{13}C NMR: δ 142.6, 141.0, 140.9, 135.7, 134.1, 130.7, 129.1, 129.0, 128.8, 126.6, 68.9, 33.4, 31.7, 28.8, 26.04, 26.02, 21.5. MS (ES + ve): m/z 404 (M + H$^+$, 15), 296 (100), 233 (50).

General Method of Methylation of Allylic Sulfoximines 11, 13a, and 13b. To a solution of the allylic sulfoximine (**11**, **13a**, or **13b**) (1 mmol) in dry THF (3 mL) was added LDA (1.3 equiv) at −78 °C, and the reaction mixture was stirred for 40 min. The orange red solution was treated with CH_3I (2 equiv) at −78 °C, and the reaction was stirred for a further 1 h at −78 °C and was quenched by the addition of a saturation aqueous solution of NH_4Cl (0.5 mL) at −78 °C. The reaction was warmed to rt, poured into water (10 mL), and extracted with CH_2Cl_2 (2 × 20 mL). The extracts were concentrated and dried under vacuum to leave a light yellow oil that decomposed upon attempted purification by column chromatography on silica gel.

***N*-Tosyl-*S*-phenyl-*S*-(1-cyclopent-1-enylethyl)sulfoximine (17).** ^{1}H NMR (in part): δ 7.84−7.19 (9H, m), 5.46 (1H, br), 4.31 (1H, q, J = 7.2 Hz), 2.36 (3H, s), 1.53 (3H, d, J = 7.2 Hz).

***N*-Tosyl-*S*-phenyl-*S*-(1-cyclohex-1-enylethyl)sulfoximine (19a).** ^{1}H NMR: δ 7.89−7.86 (2H, m), 7.83−7.81 (2H, m), 7.67−7.63 (1H, m), 7.57−7.53 (2H, m), 7.23−7.21 (2H, m), 5.40 (1H, br), 3.88 (1H, q, J = 7.4 Hz), 2.38 (3H, s), 1.98−1.83 (2H, m), 1.74−1.69 (2H, m), 1.55 (3H, d, J = 7.4 Hz), 1.46−1.32 (4H, m). ^{13}C NMR δ 142.4, 141.2, 135.7, 134.2, 133.9, 129.4, 129.1, 129.0, 128.9, 126.6, 70.2, 26.3, 25.6, 22.4, 21.5, 21.4, 11.8.

***N*-(Methoxycarbonyl)-*S*-phenyl-*S*-(1-cyclohex-1-enylethyl)sulfoximine (19b).** ^{1}H NMR (300 MHz): δ 7.84−7.81 (2H, m), 7.64−7.61 (1H, m), 7.57−7.55 (2H, m), 5.39 (1H, br), 3.92 (1H, q, J = 7.2 Hz), 2.62 (3H, s), 2.25−1.32 (8H, m), 1.66 (3H, d, J = 7.2 Hz). ^{13}C NMR (75 MHz): δ 159.5, 133.5, 132.2, 129.9, 129.0, 128.9, 124.7, 65.8, 53.0, 26.4, 25.5, 22.4, 21.5, 12.1. HRMS calcd for $C_{16}H_{21}NO_3S$ = 307.12419; found 307.126527.

General Method of Palladium(0)-Catalyzed Allylic Sulfoximine to Allylic Sulfonamide Rearrangement. To a stirred solution of the pure allylic sulfoximine (**7, 9, 11, 13a, 13b, 13c, or 15**) or the crude allylic sulfoximine (**17, 19a, or 19b**) (1 mmol) in dry THF (20 mL) was added freshly prepared tetrakis(triphenylphosphine)palladium(0) (58 mg, 5 mol %) under N_2 at rt. After TLC analysis indicated complete consumption of the starting allylic sulfoximine, the reaction was diluted with ether (20 mL) and then washed with water (20 mL). The orange solution was concentrated to leave a thick dark red oil. The oil was dissolved in a 1:10 mixture of 10% aqueous NaOH (2 mL) and MeOH (20 mL) at room temperature, and the reaction mixture was stirred for 2 h. The MeOH was then removed. Water (10 mL) was added, and the mixture was neutralized by the addition of a 5% aqueous solution of HCl to pH 7. The mixture was extracted with CH_2Cl_2 (2 × 20 mL), and the combined extracts were dried ($MgSO_4$) and concentrated to leave a dark red oil which was purified with column chromatography. Elution with ethyl acetate/hexane gave the allylic sulfonamide.

***(E)*-*N*-Tosyl-*N*-[1-(3-phenyl-2-propenyl)]amine (8).** ^{1}H NMR: δ 7.78 (2H, d, J = 8 Hz), 7.33−7.24 (7H, m), 6.45 (1H, d, J = 16 Hz), 6.02 (1H, dt, J = 16, 6.4 Hz), 4.46 (1H, br), 3.76 (2H, dt, J = 6.4, 1.2 Hz), 2.43 (3H, s). ^{13}C NMR: δ 143.6, 137.0, 136.0, 133.2, 129.8, 128.6, 128.0, 127.2, 126.4, 124.0, 45.5, 21.5. MS (ES + ve): m/z 288 (M + H$^+$, 25), 149 (30), 117 (100), 115 (85), 91 (40). HRMS calcd for $C_{16}H_{17}NO_2S$ = 287.09798; found 287.09776.

***(E)*- and *(Z)*-*N*-Tosyl-*N*-(1-pent-3-enyl)amine (10).** ^{1}H NMR (300 MHz): δ 7.75 (2H, d, J = 8.1 Hz), 7.31 (2H, dd, J = 8.1, 0.9 Hz), 5.60 (1H, dtt, J = 15.3, 6.3, 1.2 Hz), 5.30 (1H, dtt, J = 15.3, 6.3, 1.5 Hz), 4.34 (1H, br), 3.53 (2H, tq, J = 6.3, 1.2 Hz), 2.43 (3H, s), 1.95 (2H, pentq, J = 7.5, 1.2 Hz), 0.91 (3H, t, J = 7.5 Hz). ^{13}C NMR (75 MHz): δ 143.3, 137.2, 136.5, 129.6, 127.2, 123.5, 45.3, 25.1, 21.4, 13.1. MS (ES + ve): m/z 240 (M + H$^+$, 55), 206 (100), 172 (85), 104 (50), 69 (95). HRMS calcd for $C_{12}H_{17}NO_2S$ = 239.09798; found 239.097496.

***N*-Tosyl-*N*-(1-cyclopent-1-enyl)methylamine (12).** ^{1}H NMR (300 MHz): δ 7.75 (2H, dt, J = 8.4, 1.8 Hz), 7.30 (2H, dd, J = 8.4, 0.9 Hz), 5.49 (1H, s), 4.84 (1H, br), 3.60 (2H, d, J = 4.8 Hz), 2.43 (3H, s), 2.25−2.12 (4H, m), 1.84−1.74 (2H, m). ^{13}C NMR (75 MHz): δ 143.2, 139.3, 137.1, 129.5, 127.5, 127.1, 43.7, 33.1, 32.2, 23.2, 21.4. MS (ES + ve): m/z 252 (M + H$^+$, 25), 106 (50), 104 (100), 81 (95). HRMS calcd for $C_{13}H_{17}NO_2S$ = 251.09798; found 251.097812.

***N*-Tosyl-*N*-(1-cyclohex-1-enyl)methylamine (14a).** ^{1}H NMR: δ 7.43 (2H, d, J = 8 Hz), 7.30 (2H, d, J = 8 Hz), 5.34 (1H, s), 4.59 (1H, broad), 3.43 (2H, d, J = 6.4 Hz), 2.43 (3H, s), 1.91 (2H, br), 1.85 (2H, br), 1.54−1.45 (4H, m). ^{13}C NMR (75 MHz): δ 143.2, 137.3, 132.9, 129.5, 127.1, 125.3, 49.6, 26.2, 24.9, 22.3, 22.0, 21.4. MS (ES + ve): m/z 266 (M + H$^+$, 10), 110 (100). HRMS calcd for $C_{14}H_{19}NO_2S$ = 265.11362; found 265.11318.

***N*-(Methoxycarbonyl)-*N*-(1-cyclohex-1-enyl)methylamine (14b).** ^{1}H NMR: δ 5.57 (1H, s), 4.67 (1H, broad), 3.68 (5H, broad, CH_2 and CH_3), 2.03−1.97 (2H, br), 1.96−1.90 (2H, br), 1.68−1.52 (4H, m). ^{13}C NMR: δ 157.1, 134.6, 122.8, 52.1, 47.1, 26.3, 24.9, 22.5, 22.3. MS (ES + ve): m/z 170 (M + H$^+$, 100), 106 (50), 104 (100), 88 (95). HRMS calcd for $C_9H_{15}NO_2$ = 169.11026; found 169.110059.

***N*-Methyl-*N*-(1-cyclohex-1-enyl)methylamine (14c).** The title compound was prepared from **13c** (200 mg, 0.8 mmol) according to the general method described above except that the crude rearrangement products were dissolved in MeOH (4 mL) and treated with trifluoroacetic acid (0.12 mL, 1.6 mmol) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C, and the solvent was then removed *in vacuo* at 35 °C. The residue was dissolved in ether (10 mL) and extracted with a 15% aqueous solution of HCl (2 × 5 mL). The aqueous layers were combined and cooled to 5 °C. CH_2Cl_2 (10 mL) was added, and the resulting biphasic mixture was carefully neutralized to pH 9 with solid $NaHCO_3$. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic extracts were washed with water (20 mL) and brine (20 mL) then dried ($MgSO_4$) and concentrated to give a colorless oil. The title compound was then converted to its less volatile *N*-tosyl derivative for characterization using the following procedure. The oil was dissolved in pyridine (2 mL) and tosyl chloride (152 mg, 0.8 mmol) was added in one portion at 0 °C. After 10 min, the reaction was warmed to rt and was then stirred overnight. Water (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (2 × 10 mL). The combined extracts were washed with a 10% aqueous solution of HCl (10 mL) and then water (20 mL). The extract was dried ($MgSO_4$) and concentrated to give the crude product which was purified by column chromatography. Elution with 10% ethyl acetate/hexane gave 47 mg (21% overall yield) of *N*-methyl-*N*-tosyl-*N*-(1-cyclohex-1-enyl)methylamine and *N*-methylphenylsulfinamide (68%) (^{1}H NMR (300 MHz) δ 7.72−7.69 (2H, m), 7.52−7.50 (3H, m), 4.18 (1H, br), 2.55 (3H, d, J = 3.9 Hz); MS (EI + ve) m/z 156 (M + H$^+$, 30), 64 (100)).

***N*-Methyl-*N*-tosyl-*N*-(1-cyclohex-1-enyl)methylamine Derivative of 14c.** ^{1}H NMR (300 MHz): δ 7.66 (2H, d, J = 8.4 Hz), 7.32 (2H, d, J = 8.4 Hz), 5.55 (1H, s), 3.42 (2H, s), 2.57 (3H, s), 2.43 (3H, s), 2.03−1.95 (4H, br), 1.68−1.52 (4H, br). ^{13}C NMR (75 MHz): δ 143.1, 132.7, 129.6, 127.6, 127.5, 126.6, 56.9, 33.7, 26.0, 25.2, 22.5, 22.3, 21.5. MS (ES + ve): m/z 280 (M + H$^+$, 60), 186 (10), 102 (25), 95 (100).

***N*-Tosyl-*N*-(1-cyclohept-1-enyl)methylamine (16).** ^{1}H NMR: δ 7.74 (2H, dt, J = 8.2 Hz), 7.30 (2H, dd, J = 8, 0.4 Hz), 5.65 (1H, t, J = 6 Hz), 4.48 (1H, t, J = 6 Hz), 3.42 (2H, d, J = 5.6 Hz), 2.43 (3H, s), 2.06−2.00 (4H, m), 1.71−1.65 (2H, m), 1.44−1.37 (4H, m). ^{13}C NMR: δ 143.3, 139.1, 137.0, 130.3, 129.6, 127.1, 51.4, 32.1, 30.6, 28.1, 26.7, 26.6, 21.5. MS (EI + ve): m/z 280 (M + H$^+$, 10), 124 (100). HRMS calcd for $C_{15}H_{21}NO_2S$ = 279.12927; found 279.12959.

***N*-Tosyl-*N*-1-(1-cyclopent-1-enyl)ethylamine (18).** ^{1}H NMR: δ 7.73 (2H, d, J = 8 Hz), 7.28 (2H, d, J = 8 Hz), 5.41 (1H, s), 4.45 (1H, d, J = 8 Hz), 4.03 (1H, pent, J = 7.2 Hz), 2.42 (3H, s), 2.19−2.10 (3H, m), 2.00−1.90 (1H, m), 1.80−1.70 (1H, m), 1.69−1.58 (1H, m), 1.2 (3H, d, J = 7.2 Hz). ^{13}C NMR (100 MHz): δ 144.1, 143.0, 138.0, 129.4, 127.2, 126.3, 50.1,

32.0, 31.3, 29.7, 23.0, 21.5, 20.9. MS (ES + ve): *m*/*z* 266 (M + H^+, 20), 109 (20), 95 (100). ee = 88%. $[\alpha]^{24}_D$ −29.2° (*c* 0.12, $CHCl_3$).

***N*-Tosyl-*N*-(1-cyclohex-1-enylethyl)amine (20a).** ^{1}H NMR: δ 7.71 (2H, d, *J* = 8 Hz), 7.27 (2H, d, *J* = 8 Hz), 5.44 (1H, s), 4.61 (1H, broad), 3.83 (1H, p, *J* = 6.8 Hz), 2.42 (3H, s), 1.84−1.75 (3H, m), 1.65−1.60 (1H, m), 1.49−1.44 (1H, m), 1.39−1.31 (2H, m), 1.24−1.19 (1H, m), 1.15 (3H, d, *J* = 6.8 Hz). ^{13}C NMR: δ 142.9, 138.1, 136.8, 129.3, 127.3, 123.9, 55.5, 24.8, 23.5, 22.1, 22.0, 21.5, 20.4. MS (ES + ve): *m*/*z* 280 (M + H^+, 37), 264 (12), 198 (10), 172 (8), 155 (15), 124 (14), 109 (100). HRMS calcd for $C_{15}H_{21}NO_2S$ = 279.12927; found 279.12896. ee = 88%. $[\alpha]^{22}_D$ −8.0° (*c* 0.2, $CHCl_3$).

***N*-(Methoxycarbonyl)-*N*-(1-cyclohex-1-enylethyl)-amine (20b).** ^{1}H NMR: δ 5.60 (1H, br), 4.61 (1H, br), 4.11 (1H, br), 3.66 (3H, s), 2.03−1.86 (4H, m), 1.65−1.53 (4H, m), 1.22 (3H, d, *J* = 7.2 Hz). ^{13}C NMR: δ 156.2, 138.5, 121.2, 51.7, 26.7, 25.2, 24.8, 22.6, 22.3, 19.7. MS (ES + ve): *m*/*z* 184 (M + H^+, 60), 109 (50), 104 (100). HRMS calcd for $C_{10}H_{17}NO_2$ = 183.12591; found 183.126251. ee = 34%. $[\alpha]^{25}_D$ −26.7° (*c* 0.6, $CHCl_3$).

Thermal Rearrangement of 19a. A solution of **19a** (440 mg, 1.1 mmol) in dry THF (10 mL) under N_2 was heated to reflux for 6 h, and the solvent was removed. The crude products were purified by column chromatography on silica gel. Elution with 10% ethyl acetate/hexane gave a mixture (225 mg, 73%, 45:55) of **20a** and **21**. Compounds **20a** and **21** could be separated by preparative HPLC.

***(E)*-*N*-Tosyl-*N*-(2-ethylidenecyclohexyl)amine (21).** ^{1}H NMR: δ 7.72 (2H, d, *J* = 8 Hz), 7.27 (2H, d, *J* = 8 Hz), 5.23 (1H, q, *J* = 6.4 Hz), 4.57 (1H, s), 3.74 (1H, s), 2.42 (3H, s), 2.11−2.05 (1H, m), 1.97−1.91 (1H, m), 1.66-1.58 (2H, m), 1.45 (3H, d, *J* = 6.4 Hz), 1.54−1.36 (5H, m). ^{13}C NMR: δ 143.0, 138.1, 137.1, 129.3, 127.1, 117.9, 57.5, 34.8, 26.5, 25.5, 23.1, 21.5, 12.4. MS (ES + ve): *m*/*z* 280 (M + H^+, 35), 172 (10), 155 (13), 124 (18), 109(100). HRMS calcd for $C_{15}H_{21}NO_2S$ = 279.12927; found 279.12937. $[\alpha]^{27}_D$ −25.9° (*c* 0.6, $CHCl_3$).

***(R)*-*N*-Tosyl-*N*-(1-cyclohexylethyl)amine (22).** (*R*)-(−)-(1-Cyclohexylethyl)amine (100 mg, 0.8 mmol) was dissolved in pyridine (2 mL), and tosyl chloride (150 mg, 0.8 mmol) was added in portions at 0 °C. The reaction mixture was allowed to warm to rt and was stirred overnight. Water was added, and the mixture was extracted with CH_2Cl_2 (2 × 15 mL). The combined extracts were washed with a 10% aqueous solution of HCl (10 mL) and water (2 × 10 mL), then dried ($MgSO_4$), and concentrated to give the crude product that was purified with column chromatography. Elution with 25% ethyl acetate/hexane gave **(+)-22** (185 mg, 84%). ^{1}H NMR (300 MHz): δ 7.75 (2H, d, *J* = 8.4 Hz), 7.29 (2H, d, *J* = 8.4 Hz), 4.35 (1H, d, *J* = 8.7 Hz), 3.15 (1H, m), 2.43 (3H, s), 1.74−1.50 (5H, m), 1.30−0.80 (5H, m), 0.93 (3H, d, *J* = 6.9 Hz). ^{13}C NMR (100 MHz): δ 142.9, 138.3, 129.4, 126.9, 54.3, 43.4, 28.6, 28.4, 26.2, 26.1, 21.4, 18.1. $[\alpha]^{22}_D$ +24.0° (*c* 0.5, $CHCl_3$).

***(S)*-*N*-Tosyl-*N*-(1-cyclohexylethyl)amine (22).** A solution of **20a** (100 mg, 0.36 mmol) in ethyl acetate (3 mL) and $CHCl_3$ (0.2 mL) at rt was stirred overnight in the presence of 10% palladium on carbon (10 mg) under an atmosphere of H_2. The mixture was filtered through a bed of celite 521, and the celite was washed with ethyl acetate (200 mL). The washings were concentrated and the crude product was purified by PTLC to give of **(−)-22** (4 mg, 4%). The ^{1}H NMR of this compound was identical to **(*R*)-22** above: $[\alpha]^{23}_D$ −10.0° (*c* 0.4, $CHCl_3$).

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Supporting Information Available: Copies of the ^{1}H NMR spectra for all compounds (except **17**) reported in the Experimental Section (27 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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