Asymmetric Copper-Catalyzed [2,3]-Sigmatropic Rearrangements of Alkyl- and Aryl-Substituted Allyl Sulfides

Douglas W. McMillen,* Norbert Varga, Beth Ann Reed, and Claudia King

Department of Chemistry, Indiana University, South Bend, Indiana 46634-7111

Received November 30, 1999

The asymmetric copper-catalyzed generation and subsequent [2,3]-sigmatropic rearrangement of sulfur ylides is strongly dependent on the structure of the starting allyl sulfide. A series of alkyl and aryl substituted allyl sulfides (**2a**−**i**) were reacted with ethyl diazoacetate in the presence of copper triflate (CuOTf) and a C_2-symmetric bis-oxazoline ligand (**5a**−**c**). The degree of asymmetric induction ranged from 2.8% for allyl methyl sulfide (**2a**) to 60% for (1*S*,2*S*,5*R*)-(+)-allyl menthyl sulfide (**2d**). The enantioselectivity of the reactions was also dependent on the electronic nature of the sulfide; allyl phenyl sulfide (**2e**) gave a 14% ee, whereas allyl *p*-methoxyphenyl sulfide (**2i**) produced only an 8% ee. The stereochemistry of **2d** and (1*R*,2*S*,5*R*)-(+)-allyl menthyl sulfide (**7**) was assigned on the basis of NMR spectroscopic experiments.

Introduction

Sulfur ylides have recently been investigated as intermediates in enantioselective syntheses.[1] To prevent pyramidal inversion of sulfur ylides (E_{act} < 25 kcal/mol), many approaches force the configuration at the sulfur by including it in a rigid ring system.[1a] However, this is not always necessary, particularly for intramolecular reactions. Trost and Hammen, for example, demonstrated that the base-catalyzed [2,3]-sigmatropic rearrangement of 1-adamantylallylethylsulfonium flouroborate to the chiral sulfide proceeded with >94% ee.[2] This stereoselectivity is due to the ease of the [2,3]-sigmatropic rearrangement and the strict conformational requirements of the five-member transition state.

The asymmetric metal-catalyzed [2,3]-sigmatropic rearrangement of chiral sulfur ylides has also been recently investigated. Uemura and co-workers were the first to report the use of this methodology in the Cu(I)/bis-oxazoline-catalyzed reaction of *trans*-cinnamyl phenyl sulfide with ethyl diazoacetate.[3] Product selectivities up to 20% ee were observed. Higher enantioselectivities (up to 64%) have been achieved with *trans*-cinnamyl phenyl sulfide using a chiral cobalt(III)−salen catalyst and the sterically larger *tert*-butyl diazoacetate.[4] The presence of a discrete sulfur ylide has been proposed for this latter catalytic system since the diastereoselectivities of the [2,3]-sigmatropic reactions were independent of the catalysts. This proposal is consistent with previous observations for the metal-catalyzed reactions of sulfides and diazo compounds.[5] Thus, formation of an optically active sulfide (**4**) from a chiral metal carbenoid (**1**) likely involves two asymmetric steps (Scheme 1). In the first step, the chiral metal carbenoid (**1**) must distinguish between the heterotopic lone pairs of **2** to form an optically active sulfur ylide (**3**). The second step is the [2,3]-sigmatropic rearrangement of sulfur ylide **3**, with transfer of chirality to the configurationally stable sulfide **4**. Since the [2,3]-sigmatropic rearrangement of **3** likely proceeds with high enantioselectivity,[2] the observed low enantiomeric excesses of the metal-catalyzed reactions[3,4] are attributed to low asymmetric induction upon forming the sulfur ylide (**3**).

Despite the low enantiomeric excesses observed for the [2,3]-sigmatropic rearrangements employing a Cu(I)/bis-oxazoline catalyst,[3] we decided to use this system in our studies due to the commercial availability of a significant number of C_2-bisimine ligands allowing the catalytic system to be readily modified in a systematic manner. Also, in the cyclopropanation reactions of olefins with diazo compounds,[1b,6] which are mechanistically similar to sulfur ylide generation,[7] copper(I) salts coordinated to C_2-bisimine ligands have generated high enantioselectivities.

Results and Discussion

Catalytic Reactions. Considering the high enantiomeric selectivity achieved in the cyclopropanation of styrene with copper triflate and bis-oxazoline ligand **5a**,[8] this catalyst was initially used to study the [2,3]-sigmatropic rearrangements of several alkyl- and aryl-substituted allyl sulfides (**2**) with ethyl diazoacetate (**6**) (Scheme 2). Although the product yields were largely invariant to the substituents, significant differences in the enantioselectivities were observed (Table 1). The reaction of allyl methyl sulfide (**2a**) gave the lowest enantioselectivity (2.8%) (entry 1). A significant increase in selectivity was obtained by using the bulkier adamantyl allyl sulfide (**2b**) and allyl trityl sulfide (**2c**), respec-

(1) Reviews: (a) Li, A.-H.; Dai, L.-X.; Aggarwal, V. K. *Chem. Rev.* **1997**, *97*, 2341. (b) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron*: *Asymmetry* **1998**, *9*, 1. (c) Doyle, M. P. *Pure Appl. Chem.* **1998**, *70*, 1123.

(2) Trost, B. M.; Hammen, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 962.

(3) Nishibayashi, Y.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1245.

(4) (a) Fukuda, T.; Katsuki, T. *Tetrahedron Lett.* **1997**, *38*, 3435. (b) Fukuda, T.; Irie, R.; Katsuki, T. *Tetrahedron* **1999**, *55*, 649.

(5) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094.

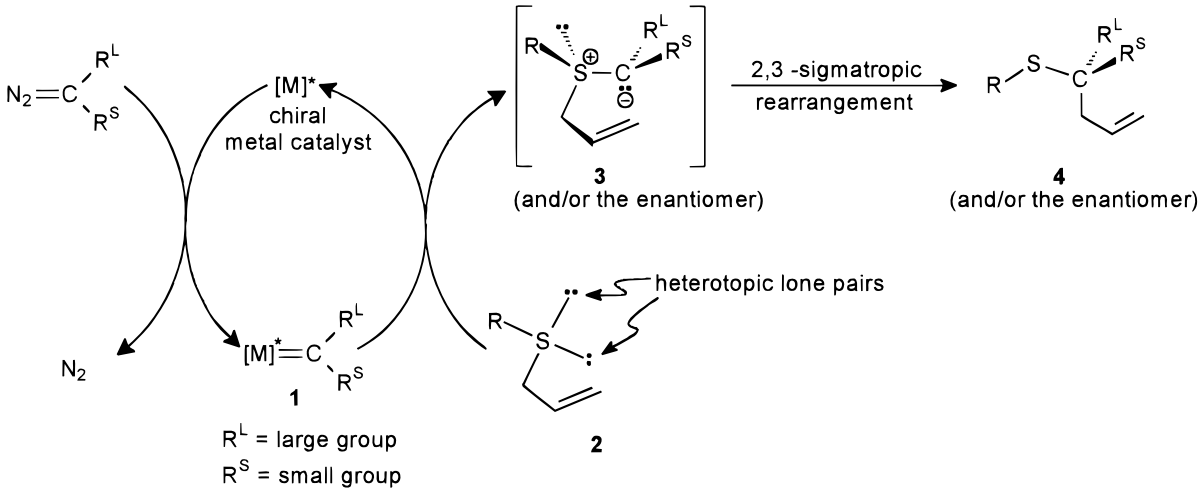
(6) Reviews: (a) Doyle, M. P.; Protopopova, M. N. *Tetrahedron* **1998**, *54*, 7919. (b) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. (c) Singh, V. K.; DattaGupta, A.; Sekar, G. *Synthesis* **1997**, 137. (d) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497.

(7) Tamblyn, W. H.; Hoffman, S. R.; Doyle, M. P. *J. Organomet. Chem* **1981**, *216*, c64.

(8) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726.

10.1021/jo991842n CCC: $19.00
Published on Web 03/18/2000

Scheme 1. Proposed Pathway for the Asymmetric Metal-Catalyzed Generation of a Chiral Sulfide



Scheme 2. Asymmetric Copper-Catalyzed Reaction of Aryl- and Alkyl-Substituted Allyl Sulfides (2) with Ethyl Diazoacetate (6)

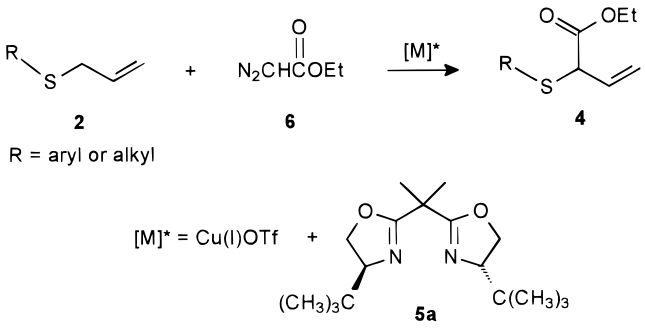


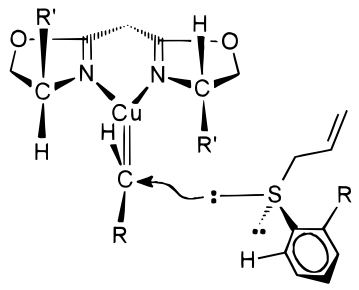
Table 1. Dependence of the Percent Enantiomeric Excess and Yield on the Structure of the Allyl Sulfide

entry[a]	compd **2** or **4**	substituent (R=)	ligand	ee (%)	yield (%)
1	**a**	methyl	**5a**	2.8	58
2	**b**	adamantyl	**5a**	26	62
3	**c**	trityl	**5a**	27	66
4	**d**	(+)-menthyl	**5a**	60	72
5	**d**	(+)-menthyl		21	40
6	**e**	phenyl	**5a**	14	59
7	**f**	2-methylphenyl	**5a**	14	58
8	**g**	2-isopropylphenyl	**5a**	12	65
9	**h**	2,6-dimethylphenyl	**5a**	52	62
10	**i**	4-methoxyphenyl	**5a**	8.0	63
11	**b**	adamantyl	**5b**	12	60
12	**b**	adamantyl	**5c**	20	72
13	**h**	2,6-dimethylphenyl	**5b**	11	64
14	**h**	2,6-dimethylphenyl	**5c**	39	62
15	**b**	adamantyl	**5a**	21	37
16	**e**	phenyl	**5a**	7.1	62
17	**i**	4-methoxyphenyl	**5a**	3.0	63

[a] Entries 1−14 were performed in $CHCl_3$ while entries 15−17 were performed in CH_2Cl_2.

tively (entries 2 and 3). Since the adamantyl group had been effectively employed by Trost and Hammen for the enantioselective base-catalyzed [2,3]-sigmatropic rearrangement,[2] the lower selectivities observed for the metal-catalyzed reactions likely occur during the generation of the sulfur ylides and not from the [2,3]-sigmatropic rearrangements. To increase the selectivity, (1*S*,2*S*,5*R*)-(+)-allyl menthyl sulfide (**2d**) was synthesized and used to generate the sulfur ylide. The resulting enantioselectivity of 60% (entry 4) is the largest value reported to date for an asymmetric copper-catalyzed reaction. The presence of ligand **5a** is clearly important since the diastereoselectivity was 3-fold greater (entry 4) than without the ligand (entry 5).

To further determine the importance of sterics on selectivity, a number of allyl aryl sulfides were synthesized and systematically investigated (entries 6−10). Allyl phenyl sulfide (**2e**) was used as the standard for comparison, and the observed 14% ee was similar to that reported for the [2,3]-sigmatropic rearrangement of *trans*-cinnamyl phenyl sulfide using the same catalyst.[3] The selectivity was unaffected by monosubstitution in the ortho-position of the phenyl ring; allyl *o*-methylphenyl sulfide (**2f**) and allyl *o*-isopropylphenyl sulfide (**2g**) gave 14 and 12% ee, respectively (entries 7 and 8). The experimentally similar enantiomeric excesses of **2e**−**g** and the modest increases in selectivities obtained with **2b** and **2c** versus **2a** suggest that the aryl and alkyl groups are directed away from the steric bulk of the catalyst (eq 1). This steric restriction does not lead to high

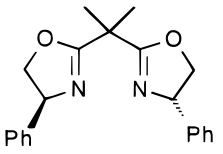


(1)

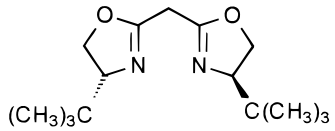
enantioselectivities due to rotation around the sulfur−carbon bond, which permits nucleophilic attack by either heterotopic lone pair on the metal carbenoid without a significant change in the orientation of the alkyl or aryl groups. Although the ortho-substituents of **2f** and **2g** can be directed away from either lone pair, an ortho,ortho-disubstituted aryl group would have one of the ortho-substituents directed at the reactive site. In accordance with this expectation, the [2,3]-sigmatropic reaction of allyl 2,6-dimethylphenyl sulfide (**2h**) proceeded with a significant increase in enantioselectivity (entry 9); the 52% ee is the largest selectivity reported for the reaction of an achiral sulfide with ethyl diazoacetate.

To determine the dependence of enantioselectivity on the structure of the bis-oxazoline ligand, ligands **5b** and

5c were compared to **5a** in the [2,3]-sigmatropic rearrangement of adamantyl allyl sulfide (**2b**) and allyl 2,6-dimethylphenyl sulfide (**2h**), respectively (entries 11−14).



5b

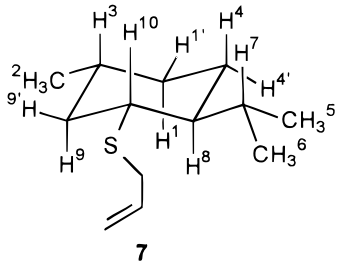


5c

The importance of the *tert*-butyl group was demonstrated by the higher selectivities achieved with ligand **5a** versus **5b**; the enantiomeric excess was doubled for **2b** (entries 2 and 11) and increased by more than a factor of 4 for **2h** (entries 9 and 13). However, ligand **5a** also gave higher enantioselectivities than **5c** for the reactions of **2b** (entries 2 and 12) and **2h** (entries 9 and 14). These differences in selectivity were unexpected since **5a** differs from **5c** at a position remote to the reactive site (the two oxazoline rings of **5a** are bridged by an isopropyl group instead of a methylene group). Although it is possible that the increase in selectivity is due to the additional steric requirements of the remote methyl groups, the inductive donation of electron density by the methyl groups to the electron-deficient copper may also play a role. This latter interpretation is consistent with the observation that allyl *p*-methoxyphenyl sulfide (**2i**) gave an 8% ee (entry 10) versus the 14% ee observed for **2e** (entry 6). A variety of para-substituted derivatives of **2h** are currently being synthesized to further investigate the nature of this influence on enantioselectivity.

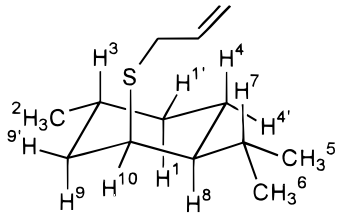
Stereochemistry of the Allyl Menthyl Sulfides. In the preparation of allyl menthyl sulfide by the reaction of menthyl mercaptan with allyl bromide,[9] two compounds were isolated in yields of 22 and 13%, respectively.[10] The molecular formula of $C_{13}H_{24}S$ for both compounds is consistent with the data from the mass spectra and elemental analyses (see the Experimental Section).

The structure of the minor isomer (1*R*,2*S*,5*R*)-(−)-allyl menthyl sulfide (**7**) was established by COSY and proton-decoupling experiments. The axial orientations of H3, H8, H9, and H10 were based on the magnitude of the shared coupling constants (12 Hz). This requires the methyl, allylthio, and isopropyl groups to be equatorial. Since the starting material for the reaction was initially (2*S*,5*R*)-menthone, this establishes the configuration of the carbon bonded to the allyl thio group as *R*.



7

The major isomer has been isolated previously and identified as allyl menthyl sulfide.[9] This connectivity is consistent with our data. However, to our knowledge, the stereochemical arrangement of the groups around the cyclohexane ring has not been established. On the basis of the reaction conditions, the major isomer must differ from the minor isomer at the carbon bearing the allylthio functionality. This assumption implies that the major isomer is (1*S*,2*S*,5*R*)-allyl menthyl sulfide (**2d**). This assignment is supported by the ^{1}H NMR spectrum (300 MHz). Proton H10 of **2d** is shifted 0.68 ppm downfield (to 3.12 ppm) relative to that observed for **7**. This downfield shift suggests that H10 is equatorial. Although the coupling constants to H10 could not be determined because the signal was a broad singlet, the measured baseline width of 10.6 Hz is in agreement with the expected 3.0 Hz couplings of equatorial H10 to three protons. The broadness of H10 is likely due to the conformational rotations of the nearby allylthio and isopropyl groups. On the basis of the chemical shift similarity of the isopropyl methyl groups ($\Delta\delta$ = 6.6 Hz) of **2d**, the conformational freedom of the isopropyl group may be less restricted than observed for **7** ($\Delta\delta$ = 75 Hz). The broadness of H10 cannot be due to a conformational equilibrium between **2d** and its chair conformer as this would place both the isopropyl and methyl groups axial. On the basis of the above analysis, the major isomer is (1*S*,2*S*,5*R*)-(+)-allyl menthyl sulfide ($[\alpha]^2_D$ = 76.8 in $CHCl_3$).



2d

Conclusion

The low enantioselectivities observed for the copper-catalyzed generation of sulfur ylides is due to a lack of discrimination of the heterotopic lone pairs of sulfur by the catalysts. When the sterically demanding allyl 2,6-dimethylphenyl sulfide (**2h**) was used, a significant increase in asymmetric induction was observed. Thus, copper(I)/bisimine catalysts are suitable for the asymmetric generation of sulfur ylides and their in situ [2,3]-sigmatropic rearrangement to stable sulfides. However, the steric requirements for high enantioselectivities are much greater than typically observed for the asymmetric copper-catalyzed cyclopropanation reactions. Since the increases in the enantioselectivities of the sulfur ylide reactions were not deleterious to the product yields, sterically larger ligands than **5a**−**c** may be used. In addition, as demonstrated by the difference in asymmetric induction of **2d** and **2i**, electronic factors may also be important.

Experimental Procedures

General Methods. All catalytic reactions were conducted under an atmosphere of dry, deoxygenated nitrogen in glassware that had been flame-dried and cooled under a dynamic

(9) Wilson, S. R.; Caldera, P.; Jester, M. A. *J. Org. Chem.* **1982**, *47*, 3319.

(10) The synthesis of allyl menthyl sulfide from menthyl mercaptan instead of directly from the thioketal of (−)-menthone (ref 9) was due to the ease of purification. The mixture of **2d** and **7** was more easily separated from unreacted thiol than from unreacted thiolketal.

vacuum and then back-filled with nitrogen. Chloroform was washed three times with water, dried over potassium carbonate, distilled from P_2O_5 under nitrogen, and stored over 4 Å molecular sieves in the dark. Portions were then distilled from P_2O_5 under nitrogen immediately prior to use. Dichloromethane was distilled from calcium hydride under a nitrogen atmosphere. Ethyl ether was distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Pentane and hexanes were fractionally distilled before use. Hexamethylphosphoramide (Aldrich) and ethanol, denatured with methanol and 2-propanol (Fisher), were used as purchased. Copper(I) trifluoromethanesulfonate benzene complex and the chiral ligands, 2,2′-isopropylidenebis[(4S)-4-*tert*-butyl-2-oxazoline] (**5a**), 2,2′-isopropylidenebis[(4S)-4-phenyl-2-oxazoline] (**5b**), and 2,2′-methylenebis[(4S)-4-*tert*-butyl-2-oxazoline] (**5c**) were purchased (Aldrich), stored in a MBraun LabMaster100 inert-atmosphere box, and used as received. Ethyl diazoacetate was also purchased (Aldrich), refrigerated, and used without further purification. 1-Adamantylthiol[11] and allyl phenyl sulfide (**2e**)[12] were prepared according to reported procedures. Allyl methyl sulfide (**2a**), 2-methylbenzenethiol, 4-methoxybenzenethiol, 2-isopropylbenzenethiol (90%), 2,6-dimethylbenzenethiol, 1,2-ethanedithiol (tech), (−)-menthone (90%), and 2.5 M butyllithium were used as received (Aldrich) as were triphenylmercaptan (Fisher) and thiophenol (Fisher).

The catalytic reactions were maintained at a constant temperature using a Neslab Exatrol heater. A model 365 ATI Orion pump was used for the injection of ethyl diazoacetate. All reactions were monitored by TLC carried out on UV-active 250-μm Whatman silica gel plates using a 15:1 hexanes/ethyl ether mobile phase. Liquid chromatography was done using a Selecto Scientific silica gel column (63−200 μm). Routine ^{1}H and ^{13}C NMR spectra were obtained on Anasazi Aii FT-NMR (60 MHz) and General Electric GN 300 spectrometers. The COSY and proton-decoupling experiments were done on a Varian VXN 500 spectrometer. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; m, multiple; b, broad. Infrared spectroscopy was done using a Nicolet Avatar 360 FT-IR. GC/MS data were obtained on a Perkin-Elmer Autosystem XL/Turbomass instrument using a PE-5MS fused silica capillary column (20 m × 0.180 mm) with helium as the carrier (1.0 mL/min, split ratio = 50:1). As referenced in the detailed data section for each of the sulfides, the GC temperature program was as follows: method 1, 50 °C (5 min), 2.5 °C/min ramp, 110 °C (31 min); method 2, 50 °C (10 min), 5.0 °C/min ramp, 75 °C (20 min); method 3, 100 °C (5 min), 4.0 °C/min ramp, 200 °C (20 min); or method 4, 100 °C (180 min), 2.0 °C/min ramp, 150 °C. The data were reported as relative intensity versus *m*/*z*. Enantiomeric excess determination was done on a Beckman System Gold HPLC instrument with the 166 UV detector. Baseline separation of the enantiomers was achieved with a Chiracel OD column (250 × 4.6 mm) using a 0.15% 2-propanol/hexane mobile phase at a flow rate of 1.0 mL/min.

Adamantyl Allyl Sulfide (2b). Adamantanethiol[11] (5.0 g, 0.030 mol) was added to a solution of sodium ethoxide in ethanol (prepared by adding sodium (12 g, 0.052 mol) to 600 mL of ethanol). Allyl bromide (3.9 mL, 0.045 mol) was then added by an addition funnel over a 5 min period and the reaction mixture stirred at reflux under a nitrogen atmosphere for 1 h. A white solid gradually formed leaving a clear yellow solution. The mixture was gravity filtered and the filtrate combined with 1/3 amount of ethyl ether as well as 1/3 amount of saturated NaCl. The opaque yellow organic layer was separated and dried with anhydrous Na_2CO_3 and then Na_2SO_4. Rotary evaporation (20 mmHg, 30 °C) of the solvent gave a clear yellow oil that was further purified by distillation (bp 89.6−92.5 °C$^{1.0\ mmHg}$) to give a clear and colorless oil (4.0 g, 64%): IR (neat) 3079 (w), 1636 (w), 987 (m), 912 (m); ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.5−2.3 (m, 15H), 3.0−3.3 (m, 2H), 4.8−5.3 (m, 2H), 5.5−6.2 (m, 1H); ^{13}C NMR (15 MHz, $CDCl_3$) 29.16, 29.50, 36.08, 43.24, 44.18, 115.07, 134.61; GS/MS (method 1, t_R = 54.8 min) 210 (1), 209 (2), 208 (11), 135 (100). Anal. Calcd for $C_{13}H_{20}S$: C, 74.94; H, 9.67. Found: C, 74.56; H, 9.83.

Allyl 2-Methylphenyl Sulfide (2f). This compound was synthesized on the basis of the published procedure for allyl phenyl sulfide.[12] A mixture of 2-methylbenzenethiol (5.0 g, 0.040 mol) and 15% aqueous NaOH (12 mL, 0.045 mol) was heated to 50 °C. To the rapidly stirring mixture was added allyl bromide (3.8 mL, 0.044 mol) dropwise over a 5 min period. The cloudy mixture was heated an additional 40 min and then allowed to cool. The two-phase mixture was separated and the upper organic layer dried with anhydrous $CaCl_2$ until it was clear, and then distilled (bp 50.2−52.2 °C$^{1.0\ mmHg}$ (lit.[13] 42 °C$^{1.0\ mmHg}$)) to give a clear and colorless oil (3.8 g, 58%): IR (neat) 3082 (w), 3060 (w), 1636 (w), 1589 (m), 1469 (s), 987 (m), 919 (m) 743 (s); ^{1}H NMR (60 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.3−3.6 (m, 2H), 4.8−5.3 (m, 2H), 5.5−6.3 (m, 1H), 6.9−7.4 (m, 4H).

Allyl 4-Methoxyphenyl Sulfide (2i). This compound was synthesized in the same manner as **2f**. A clear and colorless oil (3.2 g, 54%) was isolated after vacuum distillation (bp 66.0−67.8 °C$^{1.0\ mmHg}$). ^{1}H NMR and IR spectroscopic analyses were consistent with the literature.[14]

Allyl Menthyl Sulfides (2d and 7). This compound was synthesized from menthyl mercaptan[9] on the basis of a published procedure.[9] Under a nitrogen atmosphere, 2.5 M *n*-butyllithium (16 mL, 0.040 mol) was added dropwise over a 10 min period to an ice-cooled solution of menthyl mercaptan (4.0 g, 23.2 mmol) in 50 mL of ethyl ether. The ice bath was removed and the yellow solution allowed to warm. After 30 min, the solution was again cooled in an ice bath. Allyl bromide (2.2 mL, 25.4 mmol) and then HMPA (3.0 mL) were added to the flask resulting in a dark colored mixture. After being warmed to room temperature, the reaction mixture was quenched with 100 mL of water, the layers were separated, and the aqueous layer was extracted twice with 20 mL portions of pentane. The combined organic layers were dried with anhydrous Na_2SO_4 to give a clear and colorless solution. Rotary evaporation (20 mmHg, 30 °C) of the solvent gave a clear and colorless oil (4.8 g) that was further purified by vacuum distillation (bp 52.9−58.0 °C$^{1.0\ mmHg}$) to give a diastereomeric mixture of **2d** and **7**. The diastereomers were separated by column chromatography (4 × 45 cm silica; hexanes eluant): major isomer (1.09 g, 22%), minor isomer (0.614 g, 13%).

Major isomer (**2d**): $[\alpha]^2_D$ = 76.8 (*c* = 10.00, $CHCl_3$); IR (neat) 3080 (w), 1634 (w), 989 (m), 913 (m); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (d, 3H, *J* = 6.6 Hz), 0.86 (d, 3H, *J* = 6.9 Hz), 0.89 (d, 3H, *J* = 6.6 Hz), 0.97−1.21 (m, 4H), 1.52−1.76 (m, 3H), 1.81−2.00 (m, 2H), 3.06 (b, 1H), 3.09 (bd, 2H, *J* = 7.1 Hz), 5.00−5.13 (m, 2H), 5.71−5.86 (m, 1H); ^{13}C NMR (15 MHz, $CDCl_3$) 20.59, 20.91, 22.08, 26.12, 26.21, 29.61, 33.95, 35.21, 40.14, 44.49, 48.55, 115.13, 134.85; GS/MS (method 1, t_R = 34.4 min) 214 (1), 213 (3), 212 (20), 95 (100). Anal. Calcd for $C_{13}H_{24}S$: C, 73.52; H, 11.39. Found: C, 73.23; H, 11.64.

Minor isomer (**7**): $[\alpha]^2_D$ = −77.1 (*c* = 7.38, $CHCl_3$); IR (neat) 3080 (w), 1634 (w), 989 (m), 913 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.74 (d, 3H, *J* = 7.0 Hz), 0.83−0.94 (m, 1H), 0.87 (d, 3H, *J* = 7.0 Hz), 0.89 (d, 3H, *J* = 7.0 Hz), 0.95−1.05 (m, 1H), 1.09 (q, 1H, *J* = 12.4 Hz), 1.18 (tt, 1H, *J* = 12.2 Hz, 2.8 Hz), 1.29−1.40 (m, 1H), 1.67−1.74 (m, 2H), 2.05−2.12 (m, 1H), 2.38 (dh, 1H, *J* = 2.8 Hz, 7.0 Hz), 2.44 (dt, 1H, *J* = 2.8 Hz, 12.2 Hz), 3.12 (ab, 1H, *J* = 13.9 Hz, 6.7 Hz), 3.18 (ab, 1H, *J* = 13.9 Hz, 7.9 Hz), 5.03−5.13 (m, 2H), 5.76−5.88 (m, 1H,); ^{13}C NMR (15 MHz, $CDCl_3$) 15.10, 22.14, 22.16, 24.56, 26.94, 32.63, 33.00, 34.54, 43.49, 45.40, 46.52, 115.05, 133.96; GS/MS (method 1, t_R = 34.5 min) 214 (1), 213 (4), 212 (25), 95 (99), 41 (100). Anal. Calcd for $C_{13}H_{24}S$: C, 73.52; H, 11.39. Found: C, 73.31; H, 11.62.

Allyl 2-Isopropylbenzene Sulfide (2g). Under a nitrogen atmosphere, 2.5 M *n*-butyllithium (21 mL, 0.053 mol) was added dropwise to an ice-cooled solution of 2-isopropylbenzenethiol (7.2 g, 0.047 mol) in 100 mL of ethyl ether. The ice bath was removed and the yellow solution allowed to warm.

(11) Khullar, K. K.; Bauer, L. *J. Org. Chem.* **1971**, *36*, 3038.
(12) Onishi, A.; Fujiyama, H.; Oda, R. JP Patent 54040527, 1979.
(13) Vizgert, R. V.; Sendega, R. V. *Zh. Org. Khim.* **1969**, *5*, 488.
(14) Crudden, C. M.; Alper, H. *J. Org. Chem.* **1995**, *60*, 5579.

After 30 min, the solution was again cooled in an ice bath. Dropwise addition of allyl bromide (4.5 mL, 0.052 mol) gave a colorless solution that became dark brown upon addition of HMPA (8 mL). After warming to room temperature, the reaction mixture was quenched with 100 mL of water, the layers were separated, and the aqueous layer was extracted twice with 30-mL portions of pentane. The combined organic layers were dried with anhydrous Na_2SO_4 to give a clear and colorless solution. Rotary evaporation (20 mmHg, 30 °C) of the solvent gave a clear and colorless oil (9.5 g) that was further purified by distillation (bp 71.7−75.2 °C$^{1.0\ mmHg}$ (lit.[15] 90−100 °C$^{2.0\ mmHg}$)) to give a clear and colorless oil (5.2 g, 57%). The ^{1}H NMR analysis was consistent with the literature.[15]

Allyl 2,6-Dimethylbenzene Sulfide (2h).[16] Under a nitrogen atmosphere, 2.5 M *n*-butyllithium (16 mL, 0.040 mol) was added dropwise to an ice-cooled solution of 2,6-dimethylbenzenethiol (5.0 g, 0.036 mol) in 60 mL of ethyl ether. The ice bath was removed and the cloudy and colorless solution allowed to warm. After 30 min, the solution was again cooled in an ice bath. Dropwise addition of allyl bromide (4.5 mL, 0.052 mol) followed by HMPA (6 mL) gave a dark brown mixture. After being warmed to room temperature, the reaction mixture was quenched with 100 mL of water, the layers were separated, and the aqueous layer was extracted twice with 30 mL portions of pentane. The combined organic layers were dried with anhydrous Na_2SO_4 to give a clear and colorless solution. Rotary evaporation (20 mmHg, 30 °C) of the solvent gave a clear and light yellow oil (6.0 g) that was further purified by distillation (bp 45.3−49.3 °C$^{1.0\ mmHg}$) to give a clear and colorless oil (4.4 g, 69%): IR (neat) 3081 (w), 3055 (w), 1634 (w), 1581 (w), 1460 (s), 771 (s); ^{1}H NMR (60 MHz, $CDCl_3$) δ 2.50 (s, 6H), 3.1−3.4 (m, 2H), 4.8−5.1 (m, 2H), 5.4−6.2 (m, 1H), 7.04 (s, 3H); ^{13}C NMR (15 MHz, $CDCl_3$) 21.90, 38.03, 115.47, 126.47, 126.97, 132.76, 141.85.

Allyl Trityl Sulfide (2e). Under a nitrogen atmosphere, a solution of triphenylmethylthiol (5.0 g, 0.018 mol) in 50 mL of ethyl ether was cooled in an ice bath to give a cloudy mixture. The dropwise addition of 2.5 M *n*-butyllithium (8.0 mL, 0.020 mol) gradually gave a cloudy orange solution. The ice bath was removed and the solution allowed to warm. After 30 min, the solution was again cooled in an ice bath. Dropwise addition of allyl bromide (1.8 mL, 0.020 mol) and then HMPA (3 mL) gave a yellow-green solution. After being warmed to room temperature, the reaction mixture was quenched with 100 mL of water, the layers were separated, and the aqueous layer was extracted twice with 20 mL portions of pentane. The combined organic layers were dried with anhydrous Na_2SO_4 to give a clear-yellow solution. Rotary evaporation (20 mmHg, 30 °C) of the solvent gave a powdery yellow solid (6.0 g). Recrystallization from 95% ethanol gave off-white needles (4.3 g, 74%): IR (neat) 3083 (w), 3055 (w), 1637 (m), 1593 (m), 911 (s), 744 (s), 700.86 (s); ^{1}H NMR (60 MHz, $CDCl_3$) δ 2.7−3.0 (m, 2H), 4.8−5.3 (m, 2H), 5.3−6.1 (m, 1H), 7.0−7.7 (m, 15H); ^{13}C NMR (15 MHz, $CDCl_3$) 35.61, 117.50, 126.64, 127.89, 129.69, 133.14, 144.92; mp 100.9−102.3 °C.

Representative Procedure: Asymmetric [2,3]-Sigmatropic Rearrangement of Adamantyl Allyl Sulfide. In an inert-atmosphere box, copper triflate benzene complex (0.0110 g, 0.0393 mmol of copper) and ligand **5a** (0.0118 g, 0.0401 mmol) were added to a 10 mL Shlenck tube. After the addition of 3.0 mL of chloroform, the solution was stirred for 1 h. The blue-green solution was then transferred by filter canula into a 10 mL Shlenck tube containing the allyl sulfide (2.10 mmol) in chloroform (2.0 mL). The flask was then placed in a bath maintained at 20 ± 1 °C and ethyl diazoacetate (0.20 mL, 1.90 mmol) in chloroform (4.0 mL) injected over a 1 h period. After being stirred for an additional 12 h, the yellow solution was transferred to a round-bottom flask and the volume of the solution reduced on a rotary evaporator (20 mmHg, 30 °C) for 20 min. The resulting green oil was then placed under a high vacuum (0.5 mmHg) for 2 h. The crude oil (0.612 g) was purified by column chromatography (1 × 30 cm silica; 30 mL of 40:1 hexanes/ether followed by 200 mL of 15:1 hexanes/ether). After removal of the solvent by rotary evaporation, a clear and colorless oil was obtained (0.375 g, 67%). The oil was identified as ethyl 2-(adamantylthio)-4-pentenoate (**4b**): TLC R_f = 0.32; IR (neat) 3078 (w), 1733 (s), 1641 (w), 995 (m); ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.26 (t, 3H, J = 7.1 Hz), 1.5−2.3 (m, 15H), 2.3−2.7 (brm, 2H), 3.2−3.5 (m, 1H), 4.16 (q, 2H, J = 7.1 Hz), 4.8−5.3 (m, 2H), 5.4−6.1 (m, 1H); ^{13}C NMR (15 MHz, $CDCl_3$) 14.73, 30.25, 36.621, 38.44, 42.06, 43.85, 46.51, 60.94, 116.99, 133.91, 172.58; GS/MS (method 3, t_R = 28.8 min) 294 (2), 135 (100); HPLC (214 nm) t_R = 14.5 min (major), 17.0 (minor). Anal. Calcd for $C_{17}H_{26}O_2S$: C, 69.34; H, 8.90. Found: C, 69.40; H, 8.98.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society through Grant No. 32440-GB1, for their financial support. D.W.M. also thanks Indiana University−South Bend for financial support through a Summer Faculty Fellowship and a Grant-in-Aid Award. N.V. received financial support for one summer through the Student Mentor Academic Research Team (SMART) award. We also thank the University of Notre Dame for use of their high-field FT-NMR spectrometers and, in particular, Don Schifferl for obtaining the COSY and proton-decoupled spectra.

Supporting Information Available: The characterization of **4a**,**c**−**i**, the structural assignment and the ^{1}H NMR, COSY, and homonuclear decoupled spectra for **7**, and the ^{1}H NMR spectrum for **2d**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO991842N

(15) Atkinson, R. S.; Judkins, B. D.; Patwardhan, B. *J. Chem. Soc., Perkin Trans. 2* **1979**, *11*, 1490.

(16) For a different synthetic procedure, see: Cere, V.; Massaccesi, F.; Pollicino, S.; Ricci, A. *Synth. Commun.* **1996**, *26*, 899.