Notes

Asymmetric Cyclopropanation of Allylic Alcohols Employing Sulfonamide/Schiff Base Ligands

Jaume Balsells and Patrick J. Walsh*

P. Roy and Diane T. Vagelos Laboratories, University of Pennsylvania, Department of Chemistry, 231 South 34th Street, Philadelphia, Pennsylvania 19104-6323

pwalsh@sas.upenn.edu

Received November 1, 1999

Many biologically active natural products contain chiral cyclopropanes. Interest in the synthesis of these and other products with cyclopropane subunits has fueled the effort to develop improved methodology for the enantioselective cyclopropanation of olefins. Much of this work has employed diazo compounds to generate metal carbenes that can add to olefins to provide cyclopropanes.[1] However, this methodology has not found wide application to asymmetric transfer of methylene units (CH_2).[2]

Efforts to develop methylene group transfer reagents for cyclopropanation reactions have focused on the use of diiodomethane. The stoichiometric transfer of a methylene unit to allylic alcohols has been reported to give high enantioselectivities.[3−7] Successful catalytic asymmetric cyclopropanation of allylic alcohols have been achieved with TADDOL[8] and bis(sulfonamide) ligands.[9−12] The bis(sulfonamide) system was developed by Kobayashi[9−12] and improved by Denmark.[13] The active reagent in this cyclopropanation reaction is believed to be I−Zn−CH_2−I.[14−16]

We have been interested in the synthesis of sulfonamide-based ligands[17−19] and their application to asymmetric catalysis.[20−23] Here we describe the catalytic asymmetric cyclopropanation of allylic alcohols using sulfonamide/Schiff base ligands. Enantioselectivities as high as 88% have been achieved at high catalyst loadings

Results and Discussion

Methods to monoderivatize *trans*-1,2-diaminocyclohexane have generally resulted in formation of substantial amounts of mono and bis(derivatized) products.[24−27]

We have found that formation of the aminosulfonamides (**1**−**6**) can be cleanly accomplished employing a slight excess of the diamine (1.5 equiv) relative to the sulfonyl chloride (Scheme 1).[18] The reaction was performed in the presence of triethylamine or diisopropylethylamine. Reaction of the aminosulfonamides with salicylaldehyde derivatives cleanly afforded the sulfonamide/Schiff base ligands.

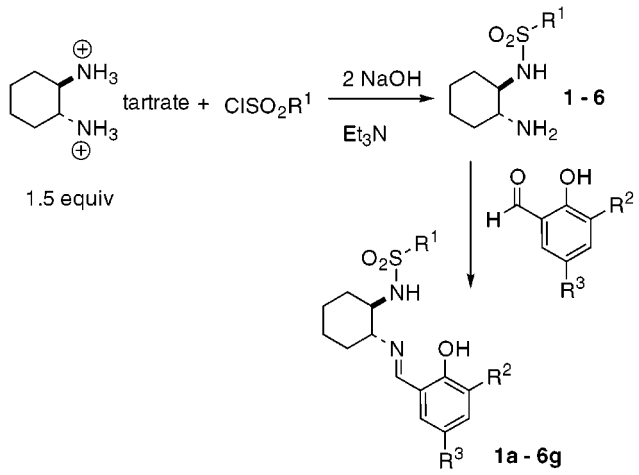
The conditions used for the asymmetric cyclopropanation reactions were based on the two-flask method of Denmark (Scheme 2).[14] In a Schlenk flask under a nitrogen atmosphere, *trans*-cinnamyl alcohol, the ligand, dichloromethane, and diethylzinc were combined (solution A). In a second Schlenk flask iodine, dichloromethane and diethylzinc were mixed, followed by CH_2I_2 (solution B). Solution A was then combined with solution B. The reactions were complete after 1 h at room temperature. After workup, the reaction mixture was distilled. The reactions were very clean, with isolated yields consistently >90%. Using this procedure, the ligand was not recovered. However, when the reaction mixture was chromatographed after workup, the ligand was isolated in 80−99% yield.

The modular nature of sulfonamide/Schiff base ligands permitted assembly of a wide range of ligand architectures. The first generation was designed to determine how R^2 and R^3 affected the enantioselectivity of the catalyst. Ligands containing two sulfonamides (R^1) and three salicylaldehyde derivatives (R^2 and R^3) were examined in the asymmetric cyclopropanation reaction using 10 mol % ligand (Scheme 2). The results (Table 1)

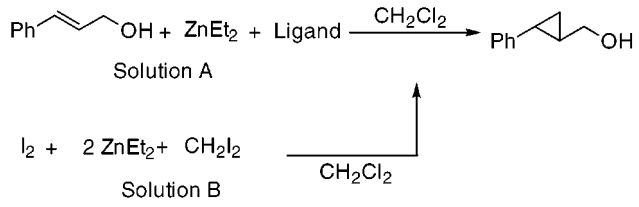
(1) Doyle, M. P.; McKervey, A. M.; T, Y. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley and Sons: New York, 1998.
(2) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339−345.
(3) Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651−2652.
(4) Charette, A. B.; Juteau, H.; Lebel, H.; Molinaro, C. *J. Am. Chem. Soc.* **1998**, *120*, 11943−11952.
(5) Kitajima, H.; Ito, K.; Aoki, Y.; Katsuki, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 207−217.
(6) Ukaji, Y.; Nishimura, M.; Fujisawa, T. *Chem. Lett.* **1992**, 61−64.
(7) Ukaji, Y.; Sada, K.; Inomata, K. *Chem. Lett.* **1993**, 1227−1230.
(8) Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367−11368.
(9) Imai, N.; Sakamoto, K.; Takahashi, H.; Kobayashi, S. *Tetrahedron Lett.* **1994**, *35*, 7045−7048.
(10) Imai, N.; Takahashi, H.; Kobayashi, S. *Chem. Lett.* **1994**, 177−180.
(11) Takahashi, H.; Yoshioka, M.; Ohno, M.; Kobayashi, S. *Tetrahedron Lett.* **1992**, *33*, 2575−2578.
(12) Takahashi, H.; Yoshioka, M.; Shibasaki, M.; Ohno, M.; Imai, N.; Kobayashi, S. *Tetrahedron* **1995**, *51*, 12013−12026.
(13) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 584−594.
(14) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 3390−3401.
(15) Denmark, S. E.; Edwards, J. P.; Wilson, S. R. *J. Am. Chem. Soc.* **1992**, *114*, 2592−2602.
(16) Charette, A. B.; Marcoux, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 4539−4549.
(17) Diltz, S. I.; Aguirre, G.; Ortega, F.; Walsh, P. J. *Tetrahedron: Asymmetry* **1997**, *8*, 3559−3562.
(18) Balsells, J.; Mejorado, L.; Phillips, M.; Ortega, F.; Aguirre, G.; Somanathan, R.; Walsh, P. J. *Tetrahedron: Asymmetry* **1998**, *9*, 4135−4142.
(19) Ho, D. E.; Betancort, J. M.; Woodmansee, D. H.; Larter, M. L.; Walsh, P. J. *Tetrahedron Lett.* **1997**, *38*, 3867−3870.
(20) Pritchett, S.; Woodmansee, D. H.; Davis, T. J.; Walsh, P. J. *Tetrahedron Lett.* **1998**, *39*, 5941−5944.
(21) Pritchett, S.; Woodmansee, D. H.; Gantzel, P.; Walsh, P. J. *J. Am. Chem. Soc.* **1998**, *120*, 6423−6424.
(22) Balsells, J.; Walsh, P. J. *J. Am. Chem. Soc.* **2000**, *122*, 1802−1803.
(23) Balsells, J.; Walsh, P. J. *J. Am. Chem. Soc.* **2000**, *122*, 3250−3251.
(24) Xu, D.; Prasad, K.; Repic, O.; Blacklock, T. J. *Tetrahedron Lett.* **1995**, *36*, 7357−7360.
(25) Neumann, W. L.; Franklin, G. W.; Sample, K. R.; Aston, K. W.; Weiss, R. H.; Riley, D. P.; Rath, N. *Tetrahedron Lett.* **1997**, *38*, 3143−3146.
(26) Wennemers, H.; Yoon, S. S.; Still, W. C. *J. Org. Chem.* **1995**, *60*, 1108−1109.
(27) Jentgens, C.; Bienz, S.; Hesse, M. *Helv. Chim. Acta* **1997**, *80*, 1133−1143.

10.1021/jo991704y CCC: $19.00
Published on Web 07/20/2000

Scheme 1



Scheme 2



indicated the importance of the 3-methoxy group in **1a** and **2a**. It is also clear from Table 1 that large substituents on the Schiff base resulted in low enantioselectivities (**1c** and **2c**).

The second generation of ligands maintained the vanillin imine and optimized R^1. As illustrated in Table 2, large sulfonamide groups such as R^1 = 2,4,6-trimethylbenzene (**3a**) or R^1 = 2,4,6-triisopropylbenzene (**4a**) led to significant drops in the enantioselectivities. Smaller groups such as Me (**5a**) and ^{n}Bu (**6a**) give the highest enantioselectivities, even surpassing the 1-naphthyl derivative **2a** in Table 1.

The methyl derivative **5a** gave the highest enantioselectivity of all the ligands at 10 mol % but the precursor **5** was difficult to isolate due to its water solubility. Because the *n*-butyl derivative **6a** gave comparable enantioselectivity to **5a** (20 mol %) and was easily prepared on large scale, it was used for the remainder of the study.

Using 10, 20, 40, and 50 mol % ligand (Table 2), the product ee values increased with increasing catalyst loading. This indicates that the background reaction, the reaction that occurs without the participation of the chiral ligand and generates racemic product, was competitive with the ligand accelerated process.[28]

The third generation ligands explored the use of different substituents at R^2 (OMe vs H, Cl, Br, and NO_2) and the effect of electron-withdrawing substituents at R^3 (H vs Br and NO_2) on the turnover frequency and the enantioselectivity (Table 3).

In these experiments, the sulfonamide R^1 group was held constant (^{n}Bu). Ligands with R^2 = H (**6b**), Cl (**6d**), Br (**6e**), and NO_2 (**6f**) showed steep decreases in the ee

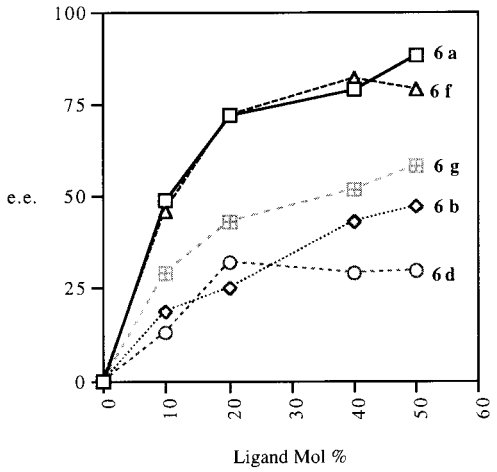
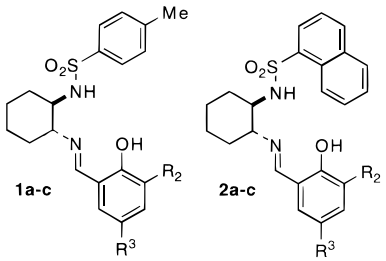


Figure 1. Plots of the enantioselectivities of ligands **6a**, **6b**, **6d**, **6f**, and **6g** as a function of catalyst loading.

Table 1. Initial Examination of the Effect of R^2 and R^3 on the Enantioselectivities Using *trans*-Cinnamyl Alcohol (Scheme 2)



ligand	R^1	R^2	R^3	ee
1a	4-C_6H_4−Me	OMe	H	44
1b	4-C_6H_4−Me	H	H	22
1c	4-C_6H_4−Me	^{t}Bu	^{t}Bu	2
2a	1-naphthyl	OMe	H	56
2b	1-naphthyl	H	H	37
2c	1-naphthyl	^{t}Bu	^{t}Bu	0

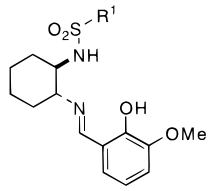
of the product, affirming the importance of R^2 = OMe. At this point it is not known if the role of the methoxy group is solely to define part of the chiral environment of the catalyst or if the zinc is interacting with the lone pair electrons on the oxygen.

It was thought that an electron-withdrawing substituent at R^3 might increase the Lewis acidity and turnover frequency of the catalyst. Changing from R^3 = H (**6a**) to R^3 = Br (**6h**) had little effect on the enantioselectivity at 10−40 mol %. At 50 mol %, the enantioselectivity showed a slight decrease with R^3 = Br while **6a** climbed another 11% in enantioselectivity. Introduction of a nitro group at R^3 (**6g**) resulted in a marked decrease in enantioselectivities at all ligand mole percents tested. A plot of the catalyst loading vs product ee values is illustrated in Figure 1. Unfortunately, little sign of a leveling off of the enantioselectivities was observed with increasing catalyst loadings indicating that the background reaction is competitive with the ligand accelerated pathway.[28]

Ligand **6a**, which performed the best with *trans*-cinnamyl alcohol, was then examined with a range of allylic alcohols at 20 and 50 mol % ligand (Table 4). Inspection of the results in Table 4 indicates that the yields are high and the ee values are moderate except for the trisubstituted allylic alcohol (Table 4, entry 3). The bis(sulfonamide) system also exhibited low enantioselectivity with this substrate (5% ee).[29] The enantioselectivities of trans allylic alcohols are superior to their

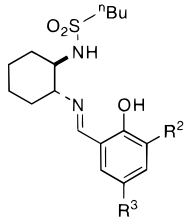
(28) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059−1070.
(29) Denmark, S. E.; Christenson, B. L.; O'Connor, S. P.; Noriaki, M. *Pure Appl. Chem.* **1996**, *68*, 23−27.
(30) Pritchett, S.; Gantzel, P.; Walsh, P. J. *Organometallics* **1999**, *18*, 823−831.

Table 2. Second Generation Ligands. Optimization of the Sulfonamide Group R^1 with R^2 = OMe and R^3 = H in the Asymmetric Cyclopropanation of *trans*-Cinnamyl Alcohol



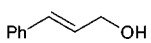
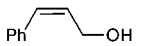
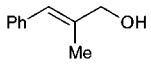
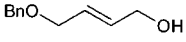
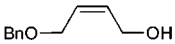
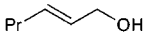
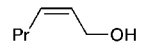
catalyst mol %	**3a**, R^1 = 2,4,6-C_6H_2-Me_3	**4a**, R^1 = 2,4,6-C_6H_2-$^iPr_3$	**1a**, R^1 = 4-C_6H_4-Me	**5a**, R^1 = Me	**6a**, R^1 = ^{n}Bu
10	5	8	44	68	49
20	6	9	54	74	72
40					79
50			81		88

Table 3. Third Generation Ligands. Reoptimization of the Schiff Base Group (R^2 and R^3) and Examination of the Effect of Electron-Withdrawing Substituents on the Enantioselectivity with Sulfonamide R^1 = ^{n}Bu



catalyst mol %	**6a**, R^2 = OMe, R^3 = H	**6b**, R^2 = H, R^3 = H	**6d**, R^2 = Cl, R^3 = Cl	**6e**, R^2 = Br, R^3 = Br	**6f**, R^2 = NO_2 R^3 = NO_2	**6g**, R^2 = OMe, R^3 = Br	**6h**, R^2 = OMe, R^3 = NO_2
10	49	19	14	13	2	46	29
20	72	25	24	32	5	72	43
40	79	43		29		82	52
50	88	47		30		79	58

Table 4. Asymmetric Cyclopropanations with Ligand 6a

Entry	Substrate	20 Mol% **6a** ee (yield)	50 Mol% **6a** ee (yield)	Config. (major enant.)
1		72 (98)	88 (98)	1R,2R
2		40 (96)	66 (96)	1S,2R
3		0 (90)	0 (96)	--
4		78 (96)	89 (98)	1R,2R
5		47 (95)	72 (92)	1S,2R
6		57 (92)	66 (91)	1R,2R
7		49 (90)	62 (93)	1S,2R

[a] See Supporting Information for details of ee determinations.

cis analogues. Interestingly, the sense of enantioselectivity of (*R*,*R*)-**6a** and (*R*,*R*)-bis(sulfonamide)-based catalysts for trans allylic alcohols was the same. However, the facial selectivity of these catalysts was opposite in the cyclopropanation of the *cis* allylic alcohols.[13]

Conclusions

The results of this investigation into the catalytic asymmetric cyclopropanation of allylic alcohols represent the first application of our sulfonamide/Schiff base ligands to asymmetric catalysis. These ligands permit the cyclopropanation of trans allylic alcohols with good to high enantioselectivities in most cases and excellent yields. The modular nature of the ligands and their ease of assembly allow rapid tailoring of the chiral environment. The observation that increasing the Lewis acidity of the catalyst (**6g** and **6h** vs **6a**) does not lead to an increase in turnover frequency is consistent with the idea that the chiral assembly of the ligand and metal serve as a scaffolding to bring the reacting partners together.[13] This is in contrast to the more common role of Lewis acid catalysts, which is to electronically activate the substrate through coordination.

Experimental Section

General. Details concerning handling of air-sensitive compounds and purification of solvents have been previously reported.[30] Carbon multiplicities were assigned by DEPT experiments at either 50 or 125 MHz. Elemental analyses were performed at the University of Pennsylvania. Unless otherwise specified, all reagents were purchased from Aldrich Chemical Company and used without further purification. Diethylzinc solutions (2 M) were prepared with hexanes in the drybox and stored in glass vessels sealed with Teflon stoppers.

Enantiomeric excesses were determined using HPLC (25-cm CHIRALCEL OD-H or 25 cm CHIRALCEL OB-H) or GC (30-m Supelco β-DEX) methods.

Synthesis and Characterization of the Aminosulfonamides 1−6. The procedure for the preparation of compounds **1**−**4** has been described.[18] An optimized procedure is described for the synthesis of **5** and **6** that can be used to synthesize **1**−**4**.

To a stirred solution of (*R*,*R*)-1,2-diaminocyclohexane tartrate salt (5.28 g, 20.0 mmol) in 26 mL of a 2 N NaOH solution were added 200 mL of dichloromethane and triethylamine (1.61 g, 15.96 mmol). The mixture was cooled to 0 °C, and a solution of *n*-butyl sulfonyl chloride (2.09 g, 13.3 mmol) in 133 mL of dichloromethane was added dropwise over 90 min. After the addition was complete, the mixture was allowed to warm to room temperature and stirred overnight. The resulting solution was washed with water (3 × 150 mL), and the organic phase was dried. Finally, the solvent was removed at reduced pressure. In this manner **6** was isolated as an oil in 61% yield (1.90 g, 8.12 mmol). Data for **6**: $[\alpha]_D$ = −35.5 (*c* 0.62, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.95 (t, J = 7.5 Hz, 3H), 1.1−1.2 (m, 4H), 1.2−1.3 (m, 3H), 1.46 (q, J = 7.5 Hz, 2H), 1.68−1.76 (m, 2H), 1.78−1.86 (m, 2H), 1.96 (dd, J_1 = 2.0 Hz, J_2 = 13.0 Hz, 1H), 2.10−2.17 (m, 1H), 2.39 (t, J = 10.5 Hz, 1H), 2.87 (td, J_1 = 4.5

Hz, J_2 = 11.0 Hz, 1H), 3.0−3.1 (m, 2H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 125 MHz) δ 13.5 (CH_3), 21.5 (CH_2), 24.8 (CH_2), 25.0 (CH_2), 25.7 (CH_2), 33.6 (CH_2), 35.7 (CH_2), 53.6 (CH_2), 55.0 (CH), 60.4 (CH) ppm; IR (film) 3436, 1639 cm^{-1}; ME (ES^+) *m*/*z* 235.2 (M + H, 100%).

Data for **5**: the product was prepared as **6** above and obtained as an oil in 25% yield (100 mg, 0.52 mmol); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.1−1.4 (m, 4H), 1.6−1.8 (m, 2H), 1.9−2.0 (m, 1H), 2.0−2.2 (m, 1H), 2.3−2.5 (m, 1H), 2.6−3.0 (m, 3H), 3.02 (s, 3H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 24.6 (CH_2), 24.9 (CH_2), 33.3 (CH_2), 35.3 (CH_2), 41.5 (CH_3), 54.7 (CH), 60.5 (CH) ppm.

Synthesis and Characterization of 1−6(a−g). The procedure for the preparation of compounds **1−6(a−g)** has been described in a previous paper. [18] Data for the new compounds **5a** and **6a−g** is described herein.

Data for **5a**: the oily product was obtained as a 4:1 mixture of diastereomers in 99% yield (171 mg, 0.52 mmol); $[\alpha]_D$ = −158.0 (*c* 0.1.12, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.2−1.6 (m, 3H), 1.6−2.0 (m, 4H), 2.2−2.3 (m, 1H), 2.70 (s, 3H), 2.9−3.1 (m, 2H), 3.3−3.4 (m, 2H), 3.82 (s, 3H, minor), 3.85 (s, 3H, major), 6.7−7.0 (m, 3H), 8.24 (s, 1H, minor), 8.36, (s, 1H, major) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) major diastereomer δ 23.5 (CH_2), 24.4 (CH_2), 33.5 (CH_2), 33.8 (CH_2), 40.9 (CH_3), 55.8 (CH), 57.6 (CH), 71.6 (CH_3), 114.3 (C), 118.0 (CH), 118.1 (CH), 123.1 (CH), 148.3 (C), 151.6 (C), 165.7 (CH) ppm; minor diastereomer δ 23.7 (CH_2), 24.4 (CH_2), 32.7 (CH_2), 33.8 (CH_2), 40.9 (CH_3), 55.8 (CH), 57.6 (CH), 71.9 (CH_3), 113.9 (C), 117.6 (CH), 118.2 (CH), 123.1 (CH), 148.1 (C), 151.7 (C), 164.7 (CH) ppm; IR (film) 3454, 1631 cm^{-1}; ME (ES^+) *m*/*z* 327.4 (M + H, 100%), 349.3 (M + Na, 85%), 675.8 (2M + Na, 25%).

Data for **6a**: 99% yield (735 mg, 1.99 mmol); mp 185−186 °C; $[\alpha]_D$ = −2.6 (*c* 0.51, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.50 (t, J = 7.5 Hz, 3H), 0.8−2.0 (m, 11H), 2.2−2.4 (m, 1H), 2.6−2.9 (m, 2H), 2.9−3.1 (m, 1H), 3.2−3.4 (m, 1H), 3.84 (s, 3H), 5.23 (d, J = 8.0 Hz, 1H), 6.7−7.0 (m, 3H), 8.37 (s, 1H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 12.9 (CH_3), 20.8 (CH_2), 23.4 (CH_2), 24.4 (CH_2), 25.2 (CH_2), 33.6 (CH_2), 34.3 (CH_2), 52.9 (CH_2), 55.7 (CH_3), 57.5 (CH), 71.7 (CH), 114.2 (C), 117.9 (CH), 118.1 (CH), 122.9 (CH), 148.3 (C), 151.6 (C), 165.5 (CH) ppm; IR (film) 3047, 1642 cm^{-1}; ME (ES^+) *m*/*z* 339.4 (M + H, 100%), 361.4 (M + Na, 10%). Anal. Calcd for $C_{18}H_{28}N_2O_4S$: C, 58.67; H, 7.66; N, 7.60. Found: C, 58.40; H, 7.94; N, 7.31.

Data for **6b**: 100% yield (603 mg, 1.78 mmol); mp 112−114 °C; $[\alpha]_D$ = −132.3 (*c* 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.57 (t, J = 7.4 Hz, 3H), 0.8−1.9 (m, 11H), 2.2−2.4 (m, 1H), 2.6−3.1 (m, 3H), 3.2−3.5 (m, 1H), 4.62 (d, J = 8.2 Hz, 1H), 6.8−7.0 (m, 2H), 7.2−7.4 (m, 2H), 8.36 (s, 1H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 13.2 (CH_3), 21.1 (CH_2), 23.8 (CH_2), 24.8 (CH_2), 25.4 (CH_2), 34.0 (CH_2), 34.6 (CH_2), 53.4 (CH_2), 57.9 (CH), 72.9 (CH), 117.1 (CH), 118.5 (C), 118.9 (CH), 131.5 (CH), 132.6 (CH), 161.0 (C), 165.4 (CH) ppm; IR (film) 3279, 1631 cm^{-1}; ME (ES^+) *m*/*z* 369.4 (M + H, 100%), 391.4 (M + Na, 10%). Anal. Calcd for $C_{17}H_{26}N_2O_3S$: C, 60.33%; H, 7.74; N, 8.28. Found: C, 60.70; H, 8.01; N, 8.27.

Data for **6c**: 99% yield (1.22 g, 2.99 mmol); mp 111−114 °C; $[\alpha]_D$ = −113.7 (*c* 0.51, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.64 (t, J = 7.2 Hz, 3H), 1.0−2.0 (m, 11H), 2.2−2.4 (m, 1H), 2.6−2.9 (m, 2H), 3.1 (td, J_1 = 3.0 Hz, J_2 = 10.0 Hz, 1H), 3.2−3.5 (m, 1H), 5.23 (b, 1H), 7.16 (d, J = 2.6 Hz, 2H), 7.40 (d, J = 2.6 Hz, 2H), 8.30 (s, 1H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 13.2 (CH_3), 21.1 (CH_2), 23.6 (CH_2), 24.6 (CH_2), 25.5 (CH_2), 33.5 (CH_2), 34.3 (CH_2), 53.3 (CH_2), 57.7 (CH), 71.6 (CH), 119.1 (CH), 122.6 (CH), 123.2 (C), 129.2 (C), 132.5 (C), 157.0 (C), 164.1 (CH) ppm; IR (film) 2934, 1631 cm^{-1}; ME (ES^+) *m*/*z* 407.3, 409.3 (M + H, 100%), 429.4, 431.3 (M + Na, 90%). Anal. Calcd for $C_{17}H_{24}Cl_2N_2O_3S$: C, 50.13; H, 5.94; N, 6.88. Found: C, 50.48; H, 6.24; N, 6.50%.

Data for **6d**: 99% yield (1.48 g, 2.98 mmol); mp 117−120 °C; $[\alpha]_D$ = −103.7 (*c* 0.51, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.65 (t, J = 7.4 Hz, 3H), 1.0−2.0 (m, 11H), 2.2−2.4 (m, 1H), 2.6−2.9 (m, 2H), 3.1 (td, J_1 = 3.2 Hz, J_2 = 10.0 Hz, 1H), 3.2−3.5 (m, 1H), 5.11 (b, 1H), 7.33 (d, J = 2.2 Hz, 2H), 7.69 (d, J = 2.2 Hz, 2H), 8.28 (s, 1H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 13.2 (CH_3), 21.1 (CH_2), 23.6 (CH_2), 24.6 (CH_2), 25.5 (CH_2), 33.6 (CH_2), 34.3 (CH_2), 53.3 (CH_2), 57.7 (CH), 71.4 (CH), 109.4 (CH), 112.7 (C), 119.5 (CH), 132.9 (C), 138.0 (C), 158.4 (C), 164.0 (CH) ppm; IR (film) 3454, 1640 cm^{-1}; ME (ES^+) *m*/*z* 495.3, 497.4, 499.3 (M + H, 50%, 100%, 50%), 517.3, 519.3, 521.4 (M + Na, 30%, 60%, 30%). Anal. Calcd for $C_{17}H_{24}Br_2N_2O_3S$: C, 41.15; H, 4.87; N, 5.64. Found: C, 41.11; H, 4.89; N, 5.30.

Data for **6e**: 99% yield (1.28 g, 2.98 mmol); mp 99−101 °C; $[\alpha]_D$ = −69.3 (*c* 0.51, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.81 (t, J = 7.2 Hz, 3H), 1.2−2.0 (m, 11H), 2.1−2.3 (m, 1H), 2.9−3.1 (m, 2H), 3.4−3.6 (m, 1H), 3.6−3.9 (m, 1H), 6.27 (b, 1H), 8.52 (d, J = 3.0 Hz, 2H),, 8.66 (s, 1H), 8.89 (d, J = 3.0 Hz, 2H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 13.3 (CH_3), 21.3 (CH_2), 23.7 (CH_2), 24.6 (CH_2), 25.5 (CH_2), 31.2 (CH_2), 33.2 (CH_2), 54.3 (CH_2), 56.7 (CH), 66.1 (CH), 117.6 (C), 128.5 (CH), 131.5 (CH), 137.0 (C), 140.2 (C), 166.7 (C), 170.7 (CH) ppm; IR (film) 3436, 1650 cm^{-1}; ME (ES^-) *m*/*z* 427.4 (M + H, 100%).

Data for **6f**: the product was recrystallized from $CHCl_3$; 92% yield (1.15 g, 2.57 mmol); mp 193−194 °C; $[\alpha]_D$ = −94.4 (*c* 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.60 (t, J = 7.4 Hz, 3H), 0.9−2.0 (m, 11H), 2.2−2.4 (m, 1H), 2.6−3.1 (m, 3H), 3.2−3.4 (m, 1H), 3.87 (s, 3H), 4.7−4.9 (m, 1H), 6.99 (s, 2H), 8.28 (s, 1H), 13.66 (s, 1H) ppm; ^{13}C {^{1}H} NMR ($CDCl_3$, 50 MHz) δ 13.2 (CH_3), 21.1 (CH_2), 23.6 (CH_2), 24.6 (CH_2), 25.5 (CH_2), 33.6 (CH_2), 34.4 (CH_2), 53.3 (CH_2), 56.2 (CH_3), 57.7 (CH), 72.2 (CH), 109.5 (C), 117.3 (CH), 119.0 (CH), 124.9 (C), 149.6 (C), 151.2 (C), 164.5 (CH) ppm; IR (film) 3280, 1631 cm^{-1}; ME (ES^+) *m*/*z* 447.4, 449.5 (M + H, 100%). Anal. Calcd for $C_{17}H_{27}BrN_2O_4S$: C, 48.32; H, 6.08; N, 6.26. Found: C, 48.12; H, 6.05; N, 6.07.

Data for **6g**: the product precipitated from the reaction mixture as a yellow powder, and after overnight stirring, the solid was vacuum filtered and dried; 92% yield (1.18 g, 2.85 mmol); mp 267−269 °C; $[\alpha]_D$ = −153.0 (*c* 0.10, $CHCl_3$); ^{1}H NMR (DMSO, 500 MHz) δ 0.29 (t, J = 7.0 Hz, 3H), 0.6−1.2 (m, 6H), 1.3−1.5 (m, 3H), 1.6−1.8 (m, 2H), 2.4−2.6 (m, 2H), 2.9−3.1 (m, 3H), 3.45 (s, 3H), 6.95 (d, J = 8.5 Hz, 1H), 7.07 (d, J = 2.0 Hz, 1H), 7.80 (d, J = 2.0 Hz, 1H), 8.30 (d, J = 6.5 Hz, 1H), 13.5 (b, 1H) ppm; ^{13}C {^{1}H} NMR (DMSO, 125 MHz) δ 13.6 (CH_3), 21.1 (CH_2), 24.1 (CH_2), 24.5 (CH_2), 25.8 (CH_2), 31.8 (CH_2), 34.4 (CH_2), 52.8 (CH_2), 56.0 (CH_3), 56.1 (CH), 65.1 (CH), 106.2 (C), 112.0 (CH), 125.6 (C), 133.4 (CH), 152.3 (C), 166.7 (C), 172.0 (CH) ppm; IR (film) 3453, 1642 cm^{-1}; ME (ES^+) *m*/*z* 414.5 (M + H, 100%). Anal. Calcd for $C_{17}H_{27}N_3O_6S$: C, 52.29; H, 6.58; N, 10.16. Found: C, 51.74; H, 6.57; N, 9.98.

(1*R*,2*R*)-2-Phenylcyclopropylmethanol. General Procedure Using Different Promoters. In a dry 25-mL round-bottom flask (flask A) were combined *trans*-cinnamyl alcohol (123 mg, 0.91 mmol) and ligand (**6b**, 165 mg, 0.45 mmol). Vacuum (0.5 Torr) was applied for 1 min, and then the flask was put under atmosphere of nitrogen. This was repeated twice followed by the addition of 10 mL of CH_2Cl_2. To this solution was slowly added diethylzinc (143 μL, 1.4 mmol, 1.1 equiv) to give a colorless solution, which was maintained at room temperature for another 30 min. To a 25-mL Schlenk flask similarly equipped (flask B) were added iodine (456 mg, 1.80 mmol, 1.0 equiv) and CH_2Cl_2 (20 mL). When the iodine was completely dissolved, diethylzinc (186 μL, 1.80 mmol, 2.0 equiv) was slowly added to give a white slurry. After 5 min, diiodomethane (145 mL, 1.80 mmol, 1.0 equiv) was added, and the contents of the flask were stirred at room temperature for an additional 5 min. After this time, the contents of flask A were transferred via cannula to flask B. The reaction was quenched after 1 h by addition of 13 mL of a 2 N NaOH solution. The organic phase was separated, and the aqueous solution was extracted twice with 30 mL of CH_2Cl_2. The combined organic extracts were dried with sodium sulfate, and the solvent was removed in vacuo. Distillation of the residue at reduced pressure (bp 109 °C, 0.6 Torr) yielded 134 mg of (1*R*,2*R*)-2-phenylcyclopropylmethanol (98%, 88.3% ee) as a colorless oil.

This procedure was used for the cyclopropanation of all other allylic alcohols. Spectroscopic data for all cyclopropanes matched those reported in the literature.[4,13]

Acknowledgment. This work was supported by a CAREER award to P.J.W. from the National Science Foundation (CHE-9733274).

Supporting Information Available: Details of the ee determinations. This material is available free of charge via the Internet at http://pubs.acs.org.

JO991704Y