Enantioselective Hydrosilylation of Ketones with a Chiral Titanocene Catalyst

Mary Beth Carter, Birgit Schiøtt, Alberto Gutiérrez, and Stephen L. Buchwald*

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received June 1, 1994[⊗]

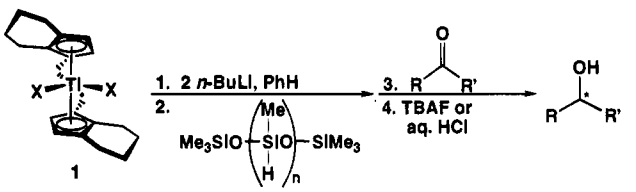
Abstract: The first efficient asymmetric hydrosilylation of aromatic ketones with an early transition metal chiral catalyst affords alcohols with excellent enantioselectivity. The reaction is general for aromatic ketones and exhibits a moderate degree of functional group compatibility.

The asymmetric reduction of prochiral ketones has been explored extensively. A variety of different catalytic systems for both asymmetric hydrogenation and hydrosilylation have been reported.[1-3] Previously we noted the ease with which the hydrosilylation of esters to yield primary alcohols could be effected using titanocene dichloride as a precatalyst.[4a,c] This, combined with our success with a catalyst derived from complex **1**[5] for the asymmetric hydrogenation of imines[6] and olefins,[7] led us to investigate the use of a similar system for the hydrosilylation of ketones.[8]

Sequential treatment of **1** (4.5 mol %) in benzene with 2 equiv of *n*-butyllithium (relative to **1**) and 5 equiv of polymethylhydrosiloxane[9] (relative to ketone) provides the active catalyst (Scheme 1). The hydrosilylation reactions proceed, in general, at room temperature under an argon atmosphere for 0.8–4.5 days. After optimizing our conditions using acetophenone, we explored the scope of this methodology (Tables 1–3). Our results indicate that aromatic ketones (Table 1, entries 1 and 5) are reduced with the highest enantioselectivity. Although the hydrosilylation of 1-acetyl-1-cyclohexene (Table 1, entry 3) also proceeds with good enantioselectivity, a small amount (4–10%) of reduction of the olefin moiety occurs. Ketones without α unsaturation are reduced with poor enantioselectivity (Table 1, entries 2 and 4). All the unsaturated ketones tested were reduced to the (*S*)-enantiomer of the corresponding alcohols with the (*R*,*R*,*R*)-enantiomer of precatalyst **1**. The two saturated ketones examined (Table 1, entries 2 and 4) were reduced to the (*R*)-enantiomer of the corresponding alcohols with the (*R*,*R*,*R*)-enantiomer of precatalyst **1**. This stereoselectivity provides insight into a possible mechanism for this process (vide infra).

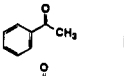
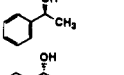
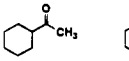
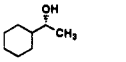
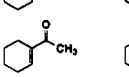
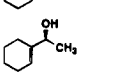
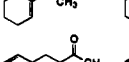
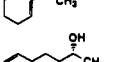
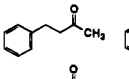
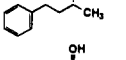
Ortho- and *para*-substituted aromatic ketones were reduced to alcohols with high enantioselectivity in most cases (Table 2). While chloro- and fluoro-substituted acetophenones were effectively reduced, *p*-(trifluoromethyl)acetophenone (Table 2,

Scheme 1



X_2 = 1,1'-binaphth-2,2'-diolate

Table 1

Entry	Ketone	Alcohol[a]	Time (d)	%ee	yield (%)
1			0.9	97[b]	73
2			4	24[c]	67
3			3 1	85[d] 90[e]	70 72
4			0.8	12[f]	88
5			3	95[g]	84

[a] Reactions were run using 4.5 mol % **1** as the (*R*,*R*,*R*)-diastereomer. The absolute configuration was determined by comparison of the optical rotation with literature references. [b] Percent ee determined by GC analysis using a cyclodex-B column. [c] Percent ee determined by HPLC analysis using a Chiralcel OD HPLC column of the naphthoyl ester. [d] Percent ee and absolute configuration determined by ^1H and ^{19}F NMR of the Mosher ester; contains 4% 1-cyclohexylmethanol. [e] Reaction run using 9 mol % **1** and 10 equiv of silane; percent ee and absolute configuration determined by ^1H and ^{19}F NMR of the Mosher ester; contains 10% 1-cyclohexylmethanol. [f] Percent ee determined by HPLC analysis using a Chiralcel OB HPLC column of the benzoyl ester. [g] Percent ee determined by HPLC analysis using a Chircel OB HPLC column.

[⊗] Abstract published in *Advance ACS Abstracts*, October 15, 1994.

(1) Hydrosilylation: (a) Brunner, H.; Nishiyama, H.; Itoh, K. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 6. (b) Nishiyama, H.; Yamaguchi, S.; Park, S.-B.; Itoh, K. *Tetrahedron: Asymmetry* **1993**, *4*, 143 and references therein.

(2) Hydrogenation: (a) Takaya, H.; Ohta, T.; Noyori, R. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 1. (b) Noyori, R. *Asymmetric Catalysis In Organic Synthesis*; John Wiley & Sons, Inc.: New York, 1994; Chapter 2. (c) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062.

(3) Reduction: (a) Singh, V. K. *Synthesis* **1992**, 605. (b) Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1993**, *34*, 5227.

(4) (a) Berk, S. C.; Kreutzer, K. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 5093. (b) Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 3751. (c) Barr, K. J.; Berk, S. C.; Buchwald, S. L. *J. Org. Chem.* **1994**, *59*, 4323.

(5) (a) Wild, F. R. W. P.; Zsolnai, L.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1982**, *232*, 233. (b) Collins, S.; Kuntz, B. A.; Hong, Y. *J. Org. Chem.* **1989**, *54*, 4154. (c) Collins, S.; Kuntz, B. A.; Taylor, N. J.; Ward, D. G. *J. Organomet. Chem.* **1988**, *342*, 21.

(6) (a) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1992**, *114*, 7562. (b) Willoughby, C. A.; Buchwald, S. L. *J. Org. Chem.* **1993**, *58*, 7627.

(7) Broene, R. D.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 12569.

(8) After the completion of our work, Halterman and co-workers reported a similar asymmetric hydrosilylation of alkyl aryl ketones using chiral titanium catalysts. However, the enantioselectivity realized was low. Halterman, R. L.; Ramsey, T. M.; Chen, Z. *J. Org. Chem.* **1994**, *59*, 2642. Preliminary results were described in the following: Halterman, R. *Chem. Rev.* **1992**, *92*, 965.

(9) Our original work employed triethoxysilane as the hydride source, which produces equivalent results, and, although this reaction is faster, because of the potential hazards[4c] of this reagent we strongly discourage its use. Polymethylhydrosiloxane is also attractive from an economic point of view as it is only $0.08/g from Aldrich.

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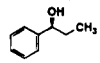
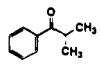
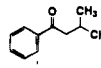
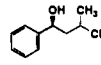
Table 2

Entry	Ketone	Alcohol[a]	Time (d)	%ee	yield (%)
1			0.9	97[b]	73
2			0.8	91[c]	77
3			8	94[c,d]	51
4			2	90[b]	78
5			1	95[c]	88
6			0.9	96[c]	84
7			2	94[c]	85
8			0.8	87[c]	62
9			1	96[c]	75
10			1	97[c]	89
11			8	65[d,e]	66

[a] Reactions were run using 4.5 mol % **1** as the (*R,R,R*)-diastereomer. The absolute configuration was determined by comparison of the optical rotation with literature sources. [b] Percent ee determined by GC analysis using a cyclodex-B column. [c] Percent ee determined by HPLC analysis using a Chiralcel OB HPLC column. [d] Did not go to completion. [e] Percent ee determined by ^{19}F NMR of the Mosher ester.

Table 3

Entry	Ketone	Alcohol[a]	Time (d)	%ee	yield (%)
1			1	95[b]	96
2			4.5	92[b,c]	79
3			2.5	94[b]	78
4			2.5	82[b,d]	88
5			1	82[b,d]	88
6			1.6	92[b]	68
7			3.5	91[b]	92

[a] Reactions were run using 4.5 mol % **1** as the (*R,R,R*)-diastereomer. The absolute configuration was determined by comparison of the optical rotation with literature sources. [b] Percent ee determined by HPLC analysis using a Chiralcel OB HPLC column. [c] Reaction run with 10 mol % **1** and 10 equiv of silane. [d] 1.5 equiv of $PhSiH_3$ as silane.

entry 11) was reduced to the corresponding alcohol with only a moderate level of enantioselectivity. Addition of 9,10-dihydroanthracene[10] increased the enantioselectivity of the reaction to 81−91%, but did not increase the reaction rate. This provides evidence that the catalyst, in this case, is being converted, by a radical process, into a species which also hydrosilylates ketones but with little or no enantioselectivity. This hydrosilylation procedure tolerates aromatic bromides,

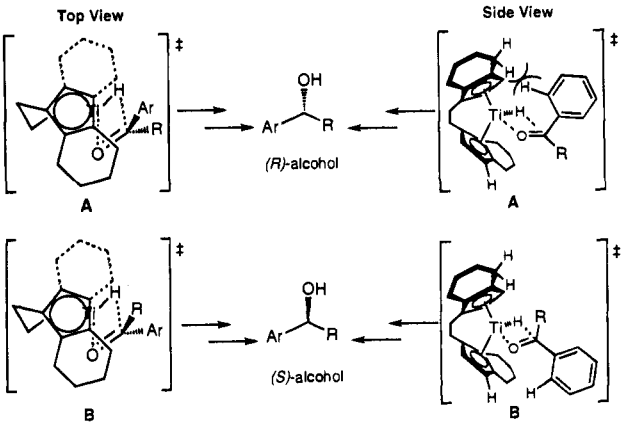


Figure 1.

unlike the related hydrogenation of imines.[11] Both *o*- and *p*-bromoacetophenone (Table 2, entries 3 and 9) are reduced to the corresponding alcohols with high levels of enantioselectivity. However, the reduction of *o*-bromoacetophenone does not proceed to completion. Initially we presumed that catalyst deactivation was due to a side reaction operating via a radical mechanism, but the addition of 9,10-dihydroanthracene[10] had no effect on the rate, enantioselectivity, or degree of conversion of the reaction. While earlier reports suggested that a titanium(III) hydride species would reductively cleave an aromatic bromide,[12] neither acetophenone nor 1-phenylethanol was detected by GC analysis of the crude reaction mixtures. Possible explanations for these conflicting observations are (1) that there are different titanium species involved in each reaction or (2) that different hydrogen sources affect the reactivity of the titanium catalyst.

We have also examined how the size of the alkyl group of the alkyl aryl ketone affects the hydrosilylation reaction. A variety of ketones with branched aliphatic groups were hydrosilylated (Table 3). All ketones were reduced to the (*S*)-enantiomers of the corresponding alcohols with moderate to good levels of enantioselectivity. Bulkier substrates required the use of additional catalyst and/or longer reaction times. Aryl cyclobutyl and aryl cyclohexyl ketones (Table 3, entries 4 and 5) were transformed with better enantioselectivity when phenylsilane was used in place of polymethylhydrosiloxane.

It has been postulated,[4,6,7,13] that the active species in these reductions is a titanium(III) hydride. To account for the stereoselectivity of this reaction, we propose the transition state model[14] shown in Figure 1. Analysis of the metallocene orbitals as determined by Lauher and Hoffmann[16] indicates that the ketone should approach the titanium complex from the side. If one assumes that the aromatic (or olefinic) group and the carbonyl group remain in conjugation throughout the reaction,[17]

(10) Narayanan, B. A.; Amatore, C.; Casey, C. P.; Kochi, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6351.

(11) Willoughby, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8952.

(12) Colomer, E.; Corriu, R. *J. Organomet. Chem.* **1974**, *82*, 367.

(13) (a) Sato, F.; Jinbo, T.; Sato, M. *Tetrahedron Lett.* **1980**, *21*, 2171. (b) Nakano, T.; Nagai, Y. *Chem. Lett.* **1988**, 481.

(14) We have been unable to identify the exact nature of the catalytic species in this reaction. It is possible that a variety of titanium species are present in the solution including titanium(III) hydrides, silyl titanium(IV) hydrides, bimetallic silyl titanium hydrides, and bimetallic titanium hydrides. All of these have been previously reported in the literature[15] and may be capable of reducing ketones. However, our basic model does not change whether the catalyst is a titanium(III) hydride or a titanium(IV) hydrido silyl species.

(15) (a) Harrod, J. F.; Mu, Y.; Samuel, E. *Can. J. Chem.* **1992**, 2980. (b) Harrod, J. F.; Ziegler, T.; Tschinke, V. *Organomet.* **1990**, *9*, 897. (c) Samuel, E.; Mu, Y.; Harrod, J. F.; Dromzee, Y.; Jeannin, Y. *J. Am. Chem. Soc.* **1990**, *112*, 3435. (d) Aitken, C. T.; Harrod, J. F.; Samuel, E. *J. Am. Chem. Soc.* **1986**, *108*, 4059.

(16) Laugher, J. W.; Hoffmann, R. *J. Am. Chem. Soc.* **1976**, *98*, 1729.

the aromatic group should not rotate to minimize interactions with the catalyst. The ketone thus prefers to approach the complex as shown in transition state B to minimize steric interactions between the cyclohexyl portion of the tetrahydroindenyl ligand and the aromatic ring of the ketone. Reaction through transition state B results in the (*S*)-alcohol as observed. In transition state **A**, the aromatic group of the ketone would be forced into close contact with the cyclohexyl portion of the tetrahydroindenyl ligand, thus destabilizing **A** relative to **B**. The observed configuration of products is consistent with this model. For unconjugated ketones (e.g., Table 1, entry 2) rotation of the side chain can occur upon approach to the catalyst to minimize steric interactions. In these cases the sizes of the groups on the ketone are similar and poor enantioselectivity is observed.

In summary, we have presented the first method to hydrosilylate aromatic ketones with high enantioselectivity using an early transition metal catalyst. Further efforts to design asymmetric catalysts for the reduction of prochiral substrates are underway.

Experimental Section

General Techniques. Reactions were generally run under an atmosphere of argon in sealed Schlenk flasks that were base washed and dried in an oven at 150 °C overnight. Benzene was distilled under nitrogen from sodium benzophenone ketyl. The ketones and the silanes were passed through a plug of neutral alumina prior to use. Melting points were obtained using a Haake Buchler melting point apparatus in an open capillary tube and are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker AC-250 (250 MHz) or a Varian XL-300 (300 MHz) instrument. Chemical shifts are reported in δ units, parts per millio (ppm) downfield from tetramethylsilane (TMS). Coupling constants are reported in hertz (Hz). Infrared spectra (IR) were obtained on a Perkin-Elmer 1600 Series FTIR and are recorded in cm^{-1}. Optical rotations were recorded on a Perkin-Elmer polarimeter 241. Enantiomeric excesses were determined by GC analysis using a cyclodex-B column, HPLC analysis using a Chiralcel OB or OD column, or ^{19}F NMR (Varian VXR-500, 470.268 MHz) of the Mosher ester.[18]

General Procedure for the Hydrosilylation of Ketones. A solution of *n*-butyllithium in hexanes (0.090 mmol) was added to the center of a solution of **1**[5,19] (0.045 mmol) in anhydrous benzene (1.0 mL) under an atmosphere of argon in a Schlenk tube. After 5 min, polymethylhydrosiloxane (5.0 mmol) was added and formation of a precipitate was observed. After an additional 5 min, ketone (1.0 mmol) was added, the precipitate disappeared, and bubbling occurred. The reaction was monitored by TLC or GC analysis until complete. The reaction mixture was diluted with THF (5 mL) and quenched with a solution of 1.0 M TBAF in THF (6.0 mL). **CAUTION**: vigorous bubbling! After 2 h the reaction was concentrated *in vacuo*, diluted with ether (25 mL), washed with 0.5 M aqueous HCl (25 mL), 0.5 M aqueous NaOH (25 mL), and saturated aqueous NaCl (12 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give an oil. The product was purified by flash column chromatography[20] (ether–pentane) and characterized by ^{1}H NMR and optical rotation. The results reported in this paper are the average of at least two runs.

Alternative Workup. The reaction mixture was diluted with acetone (5 mL) and quenched with 10% aqueous HCl (1 mL). After 2 h the reaction mixture was concentrated *in vacuo*, diluted with ether (25 mL), washed with water (10 mL), 0.5 M aqueous NaOH (10 mL), and saturated aqueous NaCl (10 mL), dried ($MgSO_4$), and concentrated *in vacuo* to give an oil. The product was purified by flash column chromatography[20] (ether–pentane) and Kugelrohr distillation and characterized by ^{1}H NMR and optical rotation.

(*S*)-**1-Phenylethanol**: 0.9 day; 97% ee; 73% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.48 (d, J = 6.47 Hz, 3 H), 2.04 (br s, 1 H), 4.87 (q, J = 6.34 Hz, 1 H), 7.23–7.36 (m, 5 H); IR (neat) 606, 699, 761, 899, 997, 1011, 1029, 1078, 1099, 1204, 1303, 1369, 1451, 1493, 2875, 2927, 2973, 3028, 3062, 3085, 3356 cm^{-1}; $[\alpha]_D$ −49.5° (*c* 0.0489, CH_2Cl_2) (lit.[21] $[\alpha]_D$ 48.6° (*c* 1.0, CH_2Cl_2), 96.2% ee (*R*)).

(*R*)-**1-Cyclohexylethanol**: 4 days; 24% ee; 67% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.02–1.34 (m, 6H), 1.16 (d, J = 6.34 Hz, 3 H), 1.38 (br s, 1 H), 1.65–1.88 (m, 5 H), 3.50–3.57 (m, 1 H); IR (neat) 892, 938, 1043, 1062, 1098, 1128, 1269, 1373, 1449, 2852, 2924, 2969, 3356 cm^{-1}; $[\alpha]_D$ −1.6° (*c* 0.0368, $CHCl_3$) (lit.[22] $[\alpha]_D$ −3.4° (*c* 1.1, $CHCl_3$), 94% ee (*R*)).

(*S*)-**1-(1-Cyclohexenyl)ethanol**:[23] 1 day; 9 mol % **1**, 10 equiv of silane; 90% ee; 72% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 1.26 (d, J = 6.42 Hz, 3 H), 1.39 (br s, 1 H), 1.54–1.67 (m, 4 H), 1.89–2.05 (m, 4 H), 4.16 (q, J = 6.38 Hz, 1 H), 5.67 (br s, 1 H).

(*R*)-**4-Phenyl-2-butanol**: 0.8 day; 12% ee; 88% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.23 (d, J = 6.34 Hz, 3 H), 1.43 (br s, 1 H), 1.67–1.87 (m, 2 H), 2.61–2.82 (m, 2 H), 3.75–3.90 (br m, 1 H), 7.15–7.37 (m, 5 H); IR (neat) 699, 746, 954, 1031, 1055, 1082, 1128, 1373, 1454, 1485, 1603, 2860, 2927, 2965, 3026, 3062, 3084, 3355 cm^{-1}; $[\alpha]_D$ −2.1° (*c* 0.0621, $CHCl_3$) (lit.[24] $[\alpha]_D$ 17.45° (*c* 2.04, $CHCl_3$), >95% ee (*S*)).

(*S*)-**1-(2-Naphthyl)ethanol**: 3 days; 95% ee; 84% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 1.23 (d, J = 6.34 Hz, 3 H), 1.43 (br s, 1 H), 1.67–1.87 (m, 2 H), 2.61–2.82 (m, 2 H), 3.75–3.90 (br m, 1 H), 7.15–7.37 (m, 5 H); $[\alpha]_D$ −52.3° (*c* 0.0520, $CHCl_3$) (lit.[1b] $[\alpha]_D$ 49.6° (*c* 1.1, $CHCl_3$), 89% ee (*R*)); mp 69.7–70.5 °C (lit.[25] mp 71–72 °C).

(*S*)-**1-(2′-Methoxyphenyl)ethanol**: 0.8 day; 91% ee; 77% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.51 (d, J = 6.55 Hz, 3 H), 2.62 (d, J = 5.30 Hz, 1 H), 3.89 (s, 3 H), 5.09 (qd, J = 6.21, 6.21 Hz, 1 H), 6,88 (d, J = 8.19 Hz, 1 H), 6.96 (t, J = 7.49 Hz, 1 H), 7.22–7.35 (m, 2 H); IR (neat) 582, 612, 754, 802, 898, 1030, 1050, 1078, 1125, 1161, 1175, 1194, 1236, 1284, 1365, 1403, 1483, 1492, 1587, 1601, 2836, 2929, 2969, 3033, 3060, 3384 cm^{-1}; $[\alpha]_D$ −57.6° (*c* 0.0363, toluene) (lit.[21] $[\alpha]_D$ 48.9° (*c* 1.1, toluene), 81.5% ee (*R*)).

(*S*)-**1-(2′-Bromophenyl)ethanol**:[26] 9 days; alternative workup; 94% ee; 59% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 1.49 (d, J = 6.36 Hz, 3 H), 1.99 (d, J = 3.36 Hz, 1 H), 5.25 (qd, J = 6.38, 3.63 Hz, 1 H), 7.13 (dt, J = 7.65, 1.65 Hz, 1 H), 7.35 (dt, J = 7.43, 1.03 Hz, 1 H), 7.52 (dd, J = 7.92, 1.20 Hz, 1 H), 7.60 (dd, J = 7.76, 1.61 Hz, 1 H); IR (neat) 608, 668, 723, 754, 900, 1008, 1024, 1045, 1071, 1091, 1128, 1200, 1268, 1346, 1368, 1440, 1469, 1568, 2927, 2973, 3064, 3345 cm^{-1}; $[\alpha]_D$ −50.5° (*c* 0.0305, $CHCl_3$); mp 51.0–52.4 °C.

(*S*)-**1-(2′-Chlorophenyl)ethanol**: 2 days; 90% ee; 78% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.49 (d, J = 6.42 Hz, 3 H), 2.01 (br s, 1 H), 5.29 (qd, J = 6.29, 2.46 Hz, 1 H), 7.17–7.35 (m, 3 H), 7.60 (dd, J = 7.73, 1.81 Hz, 1 H); IR (neat) 609, 692, 729, 754, 900, 1009, 1036, 1048, 1073, 1094, 1133, 1202, 1266, 1348, 1369, 1437, 1474, 1574, 1595, 2929, 2975, 3088, 3354 cm^{-1}; $[\alpha]_D$ −56.5° (*c* 0.0463, $CHCl_3$) (lit.[27] $[\alpha]_D$ 18.5° (neat), 70% ee (*R*)).

(*S*)-**1-(2′-Methylphenyl)ethanol**: 1 day; 95% ee; 88% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.47 (d, J = 6.41 Hz, 3 H), 1.74 (d, J = 2.66 Hz, 1 H), 2.35 (s, 3 H), 5.14 (qd, J = 6.32, 3.07 Hz, 1 H), 7.12–7.28 (m, 3 H), 7.52 (d, J = 7.31 Hz, 1 H); IR (neat) 727, 759, 896, 1006, 1050, 1077, 1128, 1271, 1368, 1460, 1488, 2927, 2971, 3345 cm^{-1}; $[\alpha]_D$ −58.6° (*c* 0.0665, ethanol) (lit.[28] $[\alpha]_D$ −14° (*c* 0.4, ethanol), 25% ee (*S*)).

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(*S*)-**1-(4′-Methylphenyl)ethanol**: 0.9 day; 96% ee; 84% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.48 (d, J = 6.48 Hz, 3 H), 1.78 (br s, 1 H), 2.35 (s, 3 H), 4.87 (qd, J = 6.43, 2.33 Hz, 1 H), 7.22 (AB, J = 7.89 Hz, $\Delta\nu$ = 25.92 Hz, 4 H); IR (neat) 819, 899, 1010, 1089, 1117, 1202, 1368, 1415, 1451, 1514, 2868, 2924, 2972, 3021, 3356 cm^{-1}; $[\alpha]_D$ −54.1° (*c* 0.0532, $CHCl_3$) (lit.[21] $[\alpha]_D$ 51.6° (*c* 1.0, $CHCl_3$), 93.8% ee (*R*)).

(*S*)-**1-(4′-Chlorophenyl)ethanol**: 2 days; 94% ee; 85% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 1.43 (d, J = 6.93 Hz, 3 H), 1.78 (br s, 1 H), 4.84 (br q, 1 H), 7.27 (s, 4 H); IR (neat) 778, 829, 898, 1013, 1089, 1112, 1201, 1272, 1295, 1338, 1371, 1408, 1453, 1493, 2886, 2928, 2973, 3346 cm^{-1}; $[\alpha]_D$ −48.9° (*c* 0.0613, ether) (lit.[29] $[\alpha]_D$ 45.61° (*c* 1.5, ether), 90% ee (*R*)).

(*S*)-**1-(4′-Methoxyphenyl)ethanol**: 0.8 day; 87% ee; 62% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.48 (d, J = 6.44 Hz, 3 H), 1.79 (br s, 1 H), 3.81 (s, 3 H), 4.86 (q, J = 6.40 Hz, 1 H), 7.10 (AB, J = 8.63 Hz, $\Delta\nu$ = 105 Hz, 4 H); IR (neat) 808, 832, 898, 1006, 1035, 1088, 1116, 1176, 1204, 1245, 1302, 1369, 1455, 1513, 1586, 1612, 2836, 2931, 2969, 3382 cm^{-1}; $[\alpha]_D$ −46.2° (*c* 0.0273, $CHCl_3$) (lit.[22] $[\alpha]_D$ 52.1° (*c* 1.0, $CHCl_3$), 87% ee (*R*)).

(*S*)-**1-(4′-Bromophenyl)ethanol**: 1 day; 96% ee; 75% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.47 (d, J = 6.52 Hz, 3 H), 1.88 (br s, 1 H), 4.87 (q, J = 6.32 Hz, 1 H), 7.36 (AB, J = 8.43 Hz, $\Delta\nu$ = 54.8 Hz, 4 H); IR (neat) 772, 824, 899, 1009, 1086, 1112, 1201, 1271, 1295, 1370, 1403, 1448, 1489, 2877, 2926, 2973, 3346 cm^{-1}; $[\alpha]_D$ −37.5° (*c* 0.0666, $CHCl_3$) (lit.[30] $[\alpha]_D$ 37.71° (*c* 5.4, $CHCl_3$), 90% ee (*R*)).

(*S*)-**1-(4′-Fluorophenyl)ethanol**: 1 day; 97% ee; 89% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 1.44 (d, J = 6.32 Hz, 3 H), 1.74 (d, J = 3.25 Hz, 1 H), 4.85 (qd, J = 6.43, 3.25 Hz, 1 H), 6.96−7.03 (m, 2 H), 7.27−7.33 (m, 2 H); IR (neat) 570, 836, 899, 1013, 1084, 1157, 1223, 1371, 1509, 1604, 2974, 3346 cm^{-1}; $[\alpha]_D$ −47.4° (*c* 0.0576, $CHCl_3$) (lit.[30] $[\alpha]_D$ −41.0° (*c* 1.30, $CHCl_3$), >97% ee (*S*)).

(*S*)-**1-[4′-(Trifluoromethyl)phenyl]ethanol**: 6 days; alternative workup; 61% ee; 67% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.51 (d, J = 6.45 Hz, 3 H), 1.87 (br d, J = 3.26 Hz, 1 H), 4.96 (qd, J = 6.36, 3.51 Hz, 1 H), 7.55 (AB, J = 8.20 Hz, $\Delta\nu$ = 28.48 Hz, 4 H); IR (neat) 605, 630, 738, 842, 900, 1016, 1068, 1124, 1206, 1327, 1372, 1416, 1451, 1621, 2881, 2932, 2978, 3346 cm^{-1}; $[\alpha]_D$ −10.8° (*c* 0.0578, MeOH) (lit.[31] $[\alpha]_D$ −24.7° (*c* 1.9, MeOH), 84% ee (*S*)).

(*S*)-**1-Phenylpropanol**: 1 day; 95% ee; 96% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 0.92 (t, J = 7.39 Hz, 3 H), 1.69−1.83 (m, 2 H), 1.87 (d, J = 2.94 Hz, 1 H), 4.59 (td, J = 6.59, 3.07 Hz, 1 H), 7.39−7.23 (m, 5 H); IR (neat) 700, 766, 974, 1013, 1045, 1097, 1201, 1270, 1331, 1378, 1453, 1493, 2876, 2932, 3964, 3029, 3062, 3362 cm^{-1}; $[\alpha]_D$ −46.7° (*c* 0.0409, $CHCl_3$) (lit.[22] $[\alpha]_D$ 49.0° (*c* 1, $CHCl_3$), 96% ee (*R*)).

(*S*)-**2-Methyl-1-phenylpropanol**: 4.5 days; 10 mol % **1**; 10 equiv of silane; 92% ee; 79% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 0.76 (d, J = 7.09 Hz, 3 H), 0.96 (d, J = 6.72 Hz, 3 H), 1.78 (br d, J = 3.30 Hz, 1 H), 1.92 (dsept, J = 6.73, 6.73 Hz, 1 H), 4.32 (dd, J = 6.84, 3.19 Hz, 1 H), 7.20−7.33 (m, 5 H); IR (neat) 701, 760, 1022, 1124, 1366, 1383, 1453, 1468, 2872, 2930, 2959, 3029, 3386 cm^{-1}; $[\alpha]_D$ −45.7° (*c* 0.0623, ether) (lit.[32] $[\alpha]_D$ 34.8° (*c* 4.90, ether), 73% ee (*R*)).

(*S*)-**3-Methyl-1-phenylbutanol**: 2.5 days; 94% ee; 78% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 0.91 (d, J = 6.49 Hz, 3 H), 0.91 (d, J = 6.56 Hz, 3 H), 1.45−1.53 (m, 1 H), 1.62−1.75 (m, 2 H), 1.73 (d, J = 3.14 Hz, 1 H), 4.68−4.74 (m, 1 H), 7.20−7.33 (m, 5 H); IR ($CDCl_3$) 1047, 1368, 1385, 1454, 1467, 1493, 2870, 2928, 2959, 3605 cm^{-1}; $[\alpha]_D$ −39.9° (*c* 0.0504, *n*-heptane) (lit.[33] $[\alpha]_D$ −28.7° (*c* 16.6, *n*-heptane), 95% ee (*S*)); mp 49.6−50.6 °C (lit.[35] 50.0−50.5 °C).

(*S*)-**1-Cyclohexyl-1-phenylmethanol**: 2.5 days; 1.5 equiv of $PhSiH_3$; 82% ee; 88% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 0.82−1.29 (m, 7 H), 1.30−1.49 (br d, 1 H), 1.51−1.75 (m, 3 H), 1.75 (d, J = 3.45 Hz, 1 H), 4.33 (dd, J = 7.30, 3.34 Hz, 1 H), 7.19−7.32 (m, 5 H); $[\alpha]_D$ −20.9° (*c* 0.0507, PhH) (lit.[35] $[\alpha]_D$ −28.27° (*c* 3.29, PhH) (*S*)); mp 63.1−69.1 °C.

(*S*)-**1-Cyclobutyl-1-phenylmethanol**:[36] 1 day; 1.5 equiv of $PhSiH_3$; 82% ee; 88% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.79−2.14 (m, 7 H), 2.55−2.68 (m, 1 H), 4.58 (dd, J = 7.93, 3.17 Hz, 1 H), 7.24−7.39 (m, 5 H); IR (neat) 699, 754, 1008, 1028, 1049, 1133, 1194, 1282, 1430, 1452, 1492, 3028, 3061, 3374 cm^{-1}; $[\alpha]_D$ −29.7° (*c* 0.0519, $CHCl_3$).

(*S*)-**1-Indanol**: 1.6 days; 92% ee; 68% yield; ^{1}H NMR ($CDCl_3$, 250 MHz) 1.76 (d, J = 6.67 Hz, 1 H), 1.88−2.01 (m, 1 H), 2.42−2.56 (m, 1 H), 2.76−2.88 (m, 1 H), 3.00−3.12 (m, 1 H), 5.24 (td, J = 6.33, 5.85 Hz, 1 H), 7.22−7.42 (m, 4 H); $[\alpha]_D$ 28.7° (*c* 0.0230, $CHCl_3$) (lit.[1b] $[\alpha]_D$ −29.8° (*c* 1.1, $CHCl_3$) (*S*)); mp 71.6−72.6 °C (lit.[25] mp 72 °C).

(*S*)-**1-Tetralol**: 3.5 days; 91% ee; 92% yield; ^{1}H NMR ($CDCl_3$, 300 MHz) 1.58−1.99 (m, 5 H), 2.63−2.84 (m, 2 H), 4.74 (br s, 1 H), 7.05−7.09 (m, 1 H), 7.13−7.21 (m, 2 H), 7.37−7.42 (m, 1 H); $[\alpha]_D$ 29.0° (*c* 0.0462, $CHCl_3$) (lit.[37] $[\alpha]_D$ 25.8° (*c* 3.1, $CHCl_3$) (*S*)); mp 32.9−34.9 °C (lit.[38] mp 33 °C).

Acknowledgment. We thank the National Institutes of Health (GM46059) for support of this research. S.L.B. acknowledges the Camille & Henry Dreyfus Foundation for a Teacher-Scholar Award. M.B.C. acknowledges the National Institutes of Health for a postdoctoral fellowship (CA09298-02). We are grateful to C. A. Willoughby for helpful discussions and P. A. Petillo for his help with calculations.

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