Titanocene-Catalyzed Asymmetric Ketone Hydrosilylation: The Effect of Catalyst Activation Protocol and Additives on the Reaction Rate and Enantioselectivity

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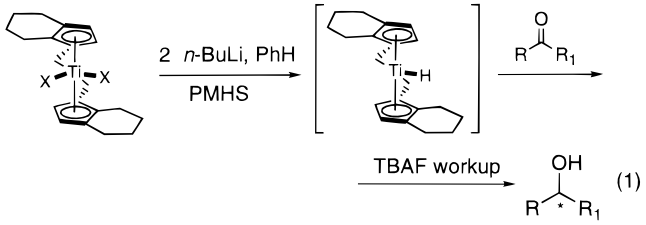
Abstract: The efficient asymmetric hydrosilylation of ketones with a chiral titanocene catalyst has been realized. In this procedure, (*R*,*R*)-ethylenebis(tetrahydroindenyl) titanium difluoride (**1**) was used as the precatalyst, and alcohol additives were employed. Aromatic and α,β-unsaturated ketones were reduced to the corresponding alcohols with a high level of enantioselectivity.

Introduction

The asymmetric hydrosilylation of ketones provides an effective route to optically active secondary alcohols. While the asymmetric hydrosilylation of prochiral ketones using late transition-metal catalysts has been extensively explored,[1] we reported only recently the first hydrosilylation of ketones with a chiral titanocene catalyst which afforded the corresponding alcohols in high enantiomeric purity (eq 1).[2] Since our report,

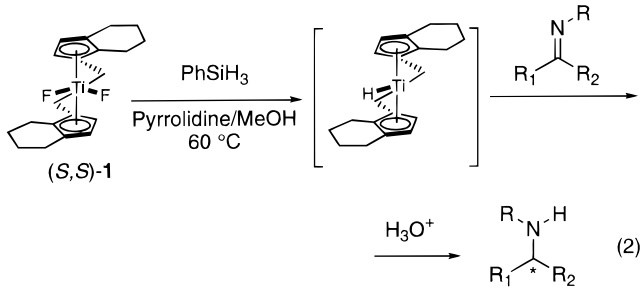


X_2 = 1,1'-binaphth-2,2'-diolate

PMHS = polymethylhydrosiloxane = $Me_3SiO(SiMeHO)_nSiMe_3$

other asymmetric hydrosilylation reactions of ketones using chiral titanium catalysts have been reported.[3−6] However, the enantioselectivity realized in these studies was very low even with aromatic ketones,[3−5] which were the optimal substrates for our catalytic system.

Recently, we have shown that the precatalyst (*S*,*S*)-(EBTHI)−TiF_2 (EBTHI = ethylenebis(tetrahydroindenyl)) **1** can be activated with phenylsilane and that the resulting titanocene hydride is highly effective in the asymmetric hydrosilylation of prochiral imines (eq 2).[7,8] We also found that the substrate



scope in this process could be significantly increased if certain primary amines were slowly added to the reaction mixture. We therefore chose to reinvestigate the ketone hydrosilylation reaction using (*R*,*R*)-**1** with and without the inclusion of additives. Herein, we report the results of those studies.

Results

In our previous study, (EBTHI)Ti-catalyzed hydrosilylation of aromatic ketones afforded the product alcohols with a high enantiomeric excess, but it was necessary to use high catalyst loadings (4.5−10 mol %) to obtain complete conversion of substrate to product in a reasonable reaction time (1−4.5 days). Since the (EBTHI)Ti-catalyzed imine hydrosilylation was facilitated by added primary amines,[8] we surmised that the analogous ketone hydrosilylation reaction might also be promoted by additives. In preliminary studies on the hydrosilylation of 4-methylacetophenone and isobutyrophenone,[9] we screened a number of possibilities and found that primary alcohols are more effective as additives than either secondary alcohols or primary amines (Table 1). Among the primary alcohols we examined, MeOH was eventually chosen because its low boiling

(1) (a) Brunner, H.; Nishiyama, H.; Itoh, K. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 6. (b) Lee, S.; Lim, C. W.; Song, C. E.; Kim, I. O. *Tetrahedron: Asymmetry* **1997**, *8*, 4027. (c) Hayashi, T.; Hayashi, C.; Uozumi, Y. *Tetrahedron: Asymmetry* **1995**, *6*, 2503. (d) Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500.

(2) Carter, M. B.; Schiøtt, B.; Gutiérrez, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 11667.

(3) Halterman, R. L.; Ramsey, T. M.; Chen, Z. *J. Org. Chem.* **1994**, *59*, 2642.

(4) Xin, S.; Harrod, J. F. *Can. J. Chem.* **1995**, *73*, 999.

(5) Imma, H.; Mori, M.; Nakai, T. *Synlett* **1996**, 1229.

(6) Rahimian, K.; Harrod, J. F. *Inorg. Chim. Acta* **1998**, *270*, 330.

(7) Verdaguer, X.; Lange, U. E. W.; Reding, M. T.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 6784.

(8) Verdaguer, X.; Lange, U. E. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1998**, *37*, 1103.

(9) In our previous report, isobutyrophenone was reduced to the alcohol product (92% ee, 79% isolated yield) with 10 mol % catalyst and 10 equiv PMHS in 4.5 days.[2]

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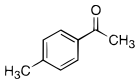
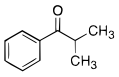
Table 1. Effect of Different Additives on the Assymetric Hydrosilylation of Ketones

(*R,R*)-**1** (2 mol %) → 1) Activation, 2) PMHS, Ketone → slow addition of additive, r.t. → Secondary alcohol product

Ketone	Additive (equiv)	Time of addition (h)	Conversion[a] (%)	ee (%)
	MeOH (4)	3	97	97
	i-BuNH$_2$ (4)	4	50	–
	None[b]	39[c]	17	90
	MeOH (5)	5	94	99
	EtOH[d] (5)	6	96	99
	i-PrOH (5.5)	5.5	65	–
	n-BuOH[e] (3.8)	14	92	
	(7.0)	32	95	99

[a] Determined by GC after aqueous work-up upon completion of addition of indicated amounts of additives. [b] Reaction was carried out at 60 °C. [c] Time of reaction with no additive. [d] 10 equiv PMHS was used instead of 6 equiv. [e] 1 mol % of **1** was used.

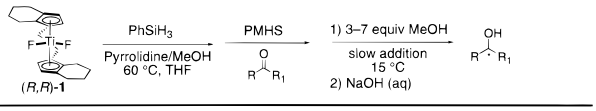
point facilitates product isolation. It is important to note that the use of different alcohol additives did not affect the enantioselectivity of the process. This is in contrast to imine hydrosilylation for which different amine additives produced secondary amine product with varying levels of enantiomeric excess.[8]

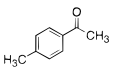
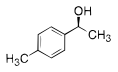
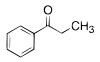
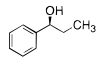
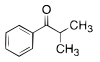
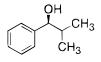
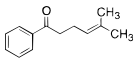
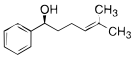
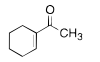
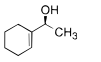
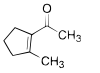
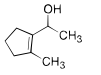
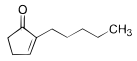
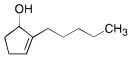
Slow addition of MeOH, using a syringe pump, to the homogeneous reaction mixture over 4−13 h resulted in a great enhancement of the reaction rate, compared to that previously reported, allowing the reduction of the catalyst greatly to 0.5−2 mol % (Table 2).[10] In addition, the alcohol products were found to have a higher ee than those in our previous study. Bulky aromatic ketones such as isobutyrophenone (entry 3) and cyclohexylphenyl ketone (entry 4) were reduced with excellent levels of enantioselectivities within 12 h and α,β-unsaturated ketones (entries 6−8) were reduced in 1,2-fashion to afford the corresponding allylic alcohols of high ee.

Most of the reactions in this work were conducted in THF; in our previous study the use of THF as solvent afforded products with variable levels of ee. In the present study, the ee of the product was the same for reactions conducted in either THF or toluene (entry 2). Additionally, the current procedure does not require that the activating agent (in the previous instance, *n*-BuLi) be added to the center of the reaction mixture.[2]

The hydrosilylation reactions of dialkyl ketones were also briefly investigated. The product secondary alcohols, however, were formed with only low to moderate levels of enantiomeric excess (Table 3). Cyclohexylmethyl ketone was reduced to the corresponding alcohol of the same ee (23% ee) as in our previous study.[2] As expected, as the steric bulk of the alkyl side chain increased, the rate of reaction was found to decrease. With *tert*-butylmethyl ketone, the reaction rate becomes so slow that the addition of methanol had no beneficial effect.

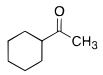
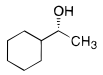
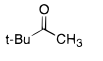
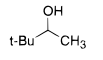
Table 2. Enantioselective Hydrosilylation of Ketones[a]



Entry	Ketone	Alcohol	Mol % catalyst	Time (h)[b]	ee (%)[c]	Yield (%)[d]
1			1	5	98	87
2			1	12[e]	98	86
			0.5	13	98	86
3			1	8	99	86
4			1	10	>98	80
5			2	6	97[f]	84
6			2	5	96	87[g]
7			2	4.5	97	90
8			2	4	84	90

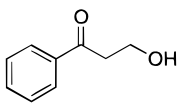
[a] Reactions were run using (*R,R*)-(EBTHI)TiF$_2$. All data represent the average of at least two runs except entry 2. [b] MeOH (3−7 equiv) was added during the course of the reaction time. [c] Percent ee was determined by chiral GC analysis (Chiraldex GTA or BPH column). [d] >95% pure by ^{1}H NMR and GC. [e] Toluene was used instead of THF. [f] Percent ee was determined by HPLC analysis using a Chiralcel OJ column. [g] Contaminated with 5% 1-cyclohexylethanol.

Table 3. Hydrosilylation of Dialkyl Ketones[a]

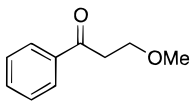
Entry	Ketone	Alcohol	Time (h)	ee (%)	Conversion (%)
1			6	23	>98
2			11	50	92
3[b]			17	53	30

[a] 1 mol% (*R,R*)-**1**, 5 equiv PMHS, slow addition of MeOH. [b] MeOH was added until the catalyst was deactivated.

Substrates possessing proximal heteroatoms are poorer substrates for the hydrosilylation reaction. The presence of a potential coordinating heteroatom close to the ketone carbonyl significantly slows the reaction, leading to low levels of conversion to product.[11] However, the enantioselectivity of the reaction was still high. Ketones **2** and **3** having β-hydroxy and



2



3

β-methoxy groups, respectively, were reduced to the corre-

(10) For analysis by GC, an aliquot was removed from the reaction mixture and subjected to aqueous workup. It was found that, even under more forcing reaction conditions (prolonged reaction time, higher catalyst loadings, high temperatures), the ketone (<3%) was observable after aqueous workup except in the case of isobutyrophenone where ~5% of the starting ketone was observed. This starting ketone may arise from the corresponding silyl enol ether, a side product invoked in several ketone hydrosilylation reports.[1b−1d] To investigate this further, an experiment using infrared spectroscopy was carried out. The progress of the hydrosilylation reaction of 4-methylacetophenone with (*R,R*)-**1** (5 mol %) was monitored over 6 h with an ASI 1000React IR probe, following the C=O stretching band of the ketone (1686 cm^{-1}). The absorbance of the C=O stretching decreased to baseline in 4 h, and the reaction was continued for another 2 h. There was no change in the intensity during the next 2 h. However, ketone was still detected by GC after hydrolysis of the reaction mixture, and the ratio of alcohol product and ketone was 98:2.

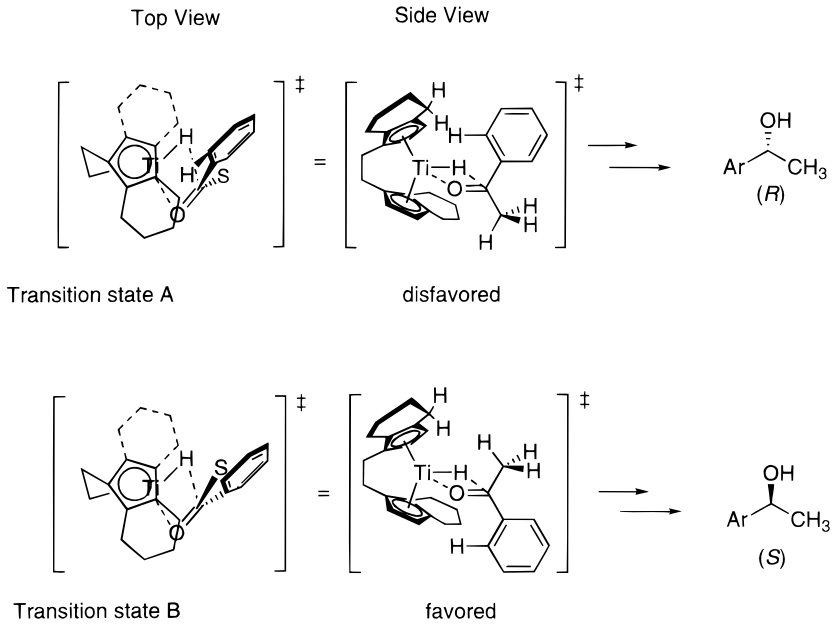


Figure 1.

sponding alcohols under the standard reaction conditions using PMHS (~50% conversion) with the same level of enantioselectivity (96% and 98% ee, respectively) as for ketones with similar steric demands in Table 2.

Discussion

As in the previous study, we observed that conjugation of the carbonyl group is necessary to achieve high levels of enantioselectivity. To explain this phenomenon, we proposed a transition-state model for the reaction in which the ketone approaches the titanium complex from the side(Figure 1).[2] For substrates in which the carbonyl is conjugated to an aromatic ring or a double bond (e.g., aromatic ketones and α,β-unsaturated ketones), the enone moiety is in a coplanar arrangement. As a result, transition state A is disfavored because of unfavorable steric interactions between the aromatic ring and the tetrahydroindenyl ring (Figure 1). In contrast, no such interaction exists for transition state B, and thus it is preferred. In saturated ketones such a conjugation does not exist, allowing the alkyl side chain to rotate to minimize steric interactions. This resulted in a very small energy difference between the two transition states.

Harrod and Rahimian recently reported that the enantioselectivity for the (EBTHI)Ti-catalyzed hydrosilylation of acetophenone was consistently much higher (~99% ee) when they generated active catalyst by adding *n*-BuLi rather than MeLi (7−53% ee) to the precatalyst (EBTHI)−Ti(binaphtholate).[6] They attributed the difference in ee to the formation of different catalytic species when the different modes of activation were employed. In their study, benzene was used for the hydrosilylation reaction utilizing *n*-BuLi, while THF was used for the hydrosilylation reaction using MeLi. We previously observed that variable levels of enantioselectivity were seen for reactions run in different solvents in the *n*-BuLi based activation protocol.[12] We therefore felt that the difference in ee might be explained in an alternative manner. Pentavalent silicon species formed by the reaction of hydrosilanes with a nucleophile such as F^- or an alkali metal alkoxide are capable of hydrosilylating ketones[13] and this nonselective hydrosilylation reaction is known to be dependent on both the solvent and silane employed.[13d] Such a reduction pathway catalyzed by pentavalent hydrosilicate species formed from lithium binaphtholate in the reaction mixture may be a major factor in the reaction which utilized MeLi in THF. This would explain the lower ee's in THF solution observed by Harrod and Rahimian, as well as the lower ee's that we had observed in solvents other than benzene utilizing our previous activation protocol (*n*-BuLi, (EBTHI)−Ti(binaphtholate)).

Harrod and Rahimian also proposed that the active silane species in our previously reported catalytic system is actually $MeSiH_3$, not PMHS. We have confirmed their observation that PMHS undergoes a partial redistribution reaction to $MeSiH_3$ and new polymeric materials in the presence of a titanocene catalyst. (**Caution**: $MeSiH_3$ is generated in these procedures. Due precaution should be taken including a consideration of the possible buildup of pressure.)[14] However, we are unsure whether methylsilane is the active silane species in the hydrosilylation reaction. When the hydrosilylation of **2** was carried out with different silanes, we found that the ee of the product depended on whether $PhSiH_3$ (~0% ee) or PMHS (96% ee) was used, indicating that a nonselective pathway was taking place in the protocol involving $PhSiH_3$. We reason that, in the

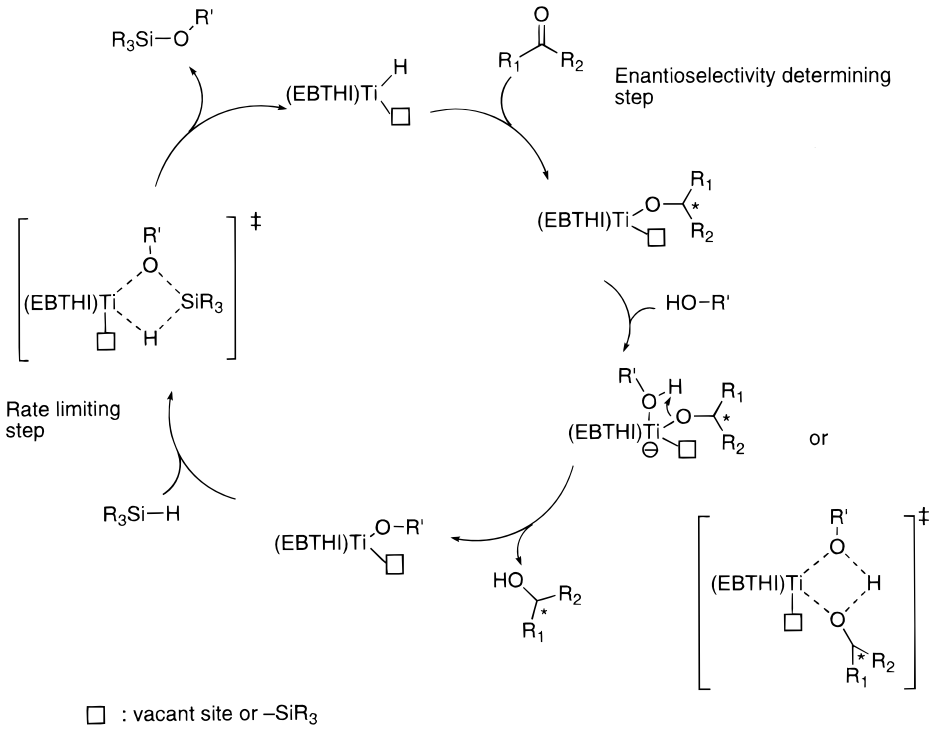
(11) With 2 mol % **1** and 5 equiv PMHS, we observed ~50% conversion for both ketones **2** and **3** before catalyst deactivation. When a solution of ketone **2** in THF was added slowly via syringe pump, we obtained ~90% conversion with no change in the ee of the product.

(12) With PMHS as the silane, the alcohol product which was isolated had a 2−30% ee when the reaction was carried out in THF and 14% ee when diethyl ether was used as solvent: Carter, M. B., unpublished results.

(13) (a) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371. (b) Furin, G. G.; Vyazankina, O. A.; Gostevsky, B. A.; Vyazankin, N. S. *Tetrahedron* **1988**, *44*, 2675. (c) Schiffers, R.; Kagan, H. B. *Synlett* **1997**, 1175. (d) The reactivity of silanes has been shown to decrease in the order: $(EtO)_3SiH > (EtO)_2Si(Me)H > PMHS$[13a] or $(EtO)_3SiH > (EtO)_2Si(Me)H > Ph_2SiH_2$.[13b] The reactivity of silanes increases as the coordinating ability of the solvent increases: HMPA > DMF > THF ≫ CH_2Cl_2.[13a] It has been reported that ketones could be reduced asymmetrically by a catalytic amount of the monolithio salt of (*R*)-binol in the presence of $(MeO)_3SiH$ or $(EtO)_3SiH$. When THF was used as solvent, the reduction of acetophenone proceeded faster but with a lower enantioselectivity (0% ee, 88% yield) than when diethyl ether was used (31% ee, 33% yield). Other solvents were not effective in this reaction catalyzed by hypervalent trialkoxysilanes.[13c]

(14) (a) Urben, P. G. *Bretherick's Handbook of Reactive Chemical Hazards*, 5th ed.; Butterworth-Heinemann: Boston, 1995; Vol. I, p 205. (b) Lewis, R. J., Sr. *Sax's Dangerous Properties of Industrial Materials*, 8th ed.; Van Nostrand Reinhold: New York, 1994; Vol. III, p 2397.

Scheme 1



presence of $PhSiH_3$, the primary hydroxyl group of **2** initially reacts with the silane producing the silyl ether.[15] Reduction of the carbonyl group to the corresponding diol product via intramolecular hydrogen transfer[16] from the silane subsequently occurs with no selectivity. It is possible that this intramolecular reduction takes place faster than the asymmetric reduction pathway catalyzed by the titanocene catalyst. To the extent that methylsilane and phenylsilane should behave similarly, if methylsilane were the active silane species in our reactions with PMHS, we would expect that the ee of the product alcohol would be closer to that seen when $PhSiH_3$ is employed. This finding, of course, does not shed light on what the actual silane group participating in the σ-bond metathesis is, but is suggestive of what it is not.

In analogy to what we have proposed for the imine hydrosilylation carried out with slow addition of primary amine, a possible catalytic cycle for the modified ketone hydrosilylation process is shown in Scheme 1.[17] In this mechanism, the enantioselectivity-determining step and the rate-determining step are different, as they are in the titanocene-catalyzed hydrogenation of imines.[19] That $-OR'$ is smaller than $-O(CH(R_1)(R_2))$ increases the rate of σ-bond metathesis in the rate-determining step; the rate of the process is enhanced. The additive is not involved in the enantioselectivity-determining step; thus, it does not change the inherent selectivity of the process. We believe that the uniformly consistent ee's arise because use of the additive greatly enhances the rate of the catalytic asymmetric hydrosilylation reaction, whereas nonselective reduction pathways are minimized when the new activation protocol is employed.

In summary, by applying a protocol which involves the slow addition of a primary alcohol to the titanocene-catalyzed asymmetric hydrosilylation reaction of ketones, improved turnover numbers and high enantioselectivities were realized. The use of the new activation protocol obviates the need to use alkyllithium reagents for catalyst activation and broadens the choice of solvent by minimizing other deleterious nonselective pathways for ketone reduction.

Experimental Section

General Methods. Toluene and THF were distilled under argon or nitrogen from sodium benzophenone ketyl. Polymethylhydrosiloxane (PMHS) was used after filtration through a plug of alumina under argon. Alcohols (MeOH, EtOH, *i*-PrOH, *n*-BuOH) were purchased from Aldrich in sure-seal bottles, transferred via cannula into a Schlenk tube and degassed using three freeze−pump−thaw cycles. Substrate ketones were commercially available with the following exceptions: 5-methyl-1-phenylhex-4-en-1-one (Table 2, entry 5) was prepared by the literature procedure.[20] Ketone **2** was obtained from ethyl benzoyl acetate by protection of the ketone carbonyl (ethylene glycol, *p*-TsOH), reduction of the ester moiety ($LiAlH_4$) to afford a hydroxy ketal, followed by deketalization (PPTS, aqueous acetone). Ketone **3** was obtained in a similar fashion as for **2** by methylation of the hydroxy ketal (NaH, MeI) followed by cleavage of the ketal. These ketones were purified by column chromatography and/or Kugelrohr distillation. Commercial ketones were passed through a plug of alumina and stored over 3 Å molecular sieves prior to use. Phenylsilane and pyrrolidine were stored under argon in a Schlenk tube and were manipulated under an argon atmosphere. Flash chromatography was performed on ICN SiliTech 32−63D, 60A. All ^1H NMR spectra are reported in δ units, parts per million (ppm) downfield from tetramethylsilane. ^{13}C NMR spectra are reported in ppm referenced to the center peak of deuteriochloroform (77 ppm). Infrared spectra (IR) were obtained on ASI ReactIR 1000 and are recorded in cm^{-1}. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter.

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(17) We have been unable to identify the exact nature of the catalytic species. It is possible that several titanium species are present in the solution including titanium(III) hydrides, silyl titanium(IV) hydrides, and bimetallic titanium hydrides which have been reported in the literature.[18].
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General Procedure for the Asymmetric Hydrosilylation of Ketones. To a solution of (*R*,*R*)-**1** (7.0 mg, 0.02 mmol) in anhydrous THF (1 mL) were added phenylsilane (12 μL, 0.1 mmol), pyrrolidine (8 μL, 0.1 mmol), and MeOH (4 μL, 0.1 mmol) sequentially under an atmosphere of argon in a resealable Schlenk tube. The reaction mixture was then heated at 60 °C until the color of the solution turned from yellow to green. The Schlenk tube was removed from the oil bath and cooled to room temperature. PMHS (5 equiv relative to ketone) and ketone (1 or 2 mmol) were added successively. The Schlenk tube was resealed and transferred to a glovebox. A gastight syringe was charged with methanol (>7 equiv) and slow addition of the methanol into the Schlenk tube was initiated by means of a syringe pump. During the course of the addition, the progress of the reaction was monitored by GC and/or TLC. The addition of methanol was allowed to continue until the ratio of product to staring material did not change, and at this point the reaction was stopped. Typically this occurred before 5 equiv of MeOH had been added. (**CAUTION**: The evolution of gas was observed in this reaction. Therefore, it is advised that the addition be carried out in a system open to an inert atmosphere to avoid the buildup of pressure). Workup: The reaction mixture was diluted with THF (10 mL), and the resulting solution was added to an aqueous solution of NaOH (10 mL, 2 M) with vigorous stirring. The biphasic mixture was stirred until the organic layer became clear (several hours). The aqueous layer was extracted with ether (3 × 20 mL), and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The product was purified by column chromatography, and its ^{1}H spectrum was compared against either the literature data or that of authentic material (derived from sodium borohydride or Luche[21] reduction of the corresponding ketone). The reported isolated yields are the average of at least two runs, and the products were of >95% purity by GC and ^{1}H NMR. The absolute configuration of the alcohol was determined by optical rotation in the cases where it had previously been determined. The ee was determined by GC analysis of the alcohol itself or the corresponding acetate derivative using a Chiraldex BPH or GTA column or by HPLC analysis using a Chiralcel OB or OJ column as indicated below.

(*S*)-1-(4-Methylphenyl)ethanol:[2] 87% yield; 98% ee was measured by GC on a GTA column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.27 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 7.8 Hz, 2H), 4.87 (q, J = 6.5 Hz, 1H), 2.34 (s, 3H), 1.80 (br s, 1H), 1.48 (d, J = 6.5 Hz, 3H); $[\alpha]_D$ −63.0° (*c* 1.0, $CHCl_3$) (lit.[22] $[\alpha]_D$ 51.6° (*c* 1.0, $CHCl_3$), 93.8% ee (*R*)).

(*S*)-1-phenylpropanol:[2] 86% yield; 98% ee was measured by GC on a BPH column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.25−7.35 (m, 5H), 4.59 (t, J = 6.6 Hz, 1 H), 1.72−1.85 (m, 3H), 0.92 (t, J = 7.4 Hz, 3H); $[\alpha]_D$ −49.2° (*c* 1.18, $CHCl_3$) (lit.[23] $[\alpha]_D$ 49.0° (*c* 1.0, $CHCl_3$), 96% ee (*R*)).

(*S*)-2-Methyl-1-phenylpropanol:[2] 86% yield; 99% ee was measured by GC on a GTA column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.24−7.37 (m, 5H), 4.36 (d, J = 6.9 Hz, 1H), 1.94 (d sept, J = 6.9 Hz, 1H), 1.82 (s, 1H), 1.00 (d, J = 7.2 Hz, 3H), 0.80 (d, J = 6.9 Hz, 3H); $[\alpha]_D$ −50.9° (*c* 0.65, diethyl ether) (lit.[24] $[\alpha]_D$ 34.8° (*c* 4.90, diethyl ether), 73% ee (*R*)).

(*S*)-1-Cyclohexyl-1-phenylmethanol:[2] 80% yield; >98% ee was measured by GC on a BPH column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.25−7.38 (m, 5H), 4.38 (d, J = 7.2 Hz, 1H), 1.98−2.02 (br d, 1H), 1.58−1.81 (m, 5H), 1.36−1.40 (br d, 1H), 0.91−1.27 (m, 5H); $[\alpha]_D$ −29.2° (*c* 0.22, benzene) (lit.[25] $[\alpha]_D$ −28.27° (*c* 3.29, benzene), (*S*)).

(*S*)-1-Phenyl-5-methylhex-4-en-1-ol:[26] 84% yield; 97% ee was measured by HPLC on a OJ column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.26−7.36 (m, 5H), 5.15 (br t, J = 7.2 Hz, 1H), 4.68 (dd, J = 5.5 Hz, 7.7 Hz, 1H), 1.95−2.06 (m, 2H), 1.73−1.87 (m, 3H), 1.70 (s, 3H), 1.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 144.95, 132.52, 128.61, 127.66, 126.10, 123.98, 74.45, 39.21, 25.96, 24.68, 17.94; IR (neat) 3354, 2968, 2926, 2860, 1494, 1451, 1378, 1061, 1015, 833 cm$^{-1;}$ $[\alpha]_D$ −13.9° (*c* 1.73, $CHCl_3$) (lit.[26] $[\alpha]_D$ −10.7° (*c* 1.60, $CHCl_3$), 96% ee (*S*)).

(*S*)-1-(1-Cyclohexenyl)ethanol:[2] 87% yield; 96% ee was measured by GC on a GTA column; ^{1}H NMR ($CDCl_3$, 300 MHz) 5.67 (br s, 1H), 4.17 (q, J = 6.4 Hz, 1H), 2.02 (m, 4H), 1.50−1.70 (m, 4H), 1.39 (br s, 1H), 1.26 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 141.41, 121.67, 72.32, 25.07, 23.82, 22.83, 22.78, 21.67; $[\alpha]_D$ −11.2° (c 0.36, $CHCl_3$) (lit.[27] $[\alpha]_D$ 7.60° (*c* 1.54, $CHCl_3$), 61% ee (*R*)).

1-(2-Methyl-cyclopent-1-enyl)ethanol:[28] 90% yield; 97% ee was measured by GC on a GTA column; ^{1}H NMR ($CDCl_3$, 300 MHz) 4.71 (q, J = 6.5 Hz, 1H), 2.35−2.44 (m, 2H), 2.30 (t, J = 7.5 Hz, 2H), 1.73−1.84 (m, 2H), 1.68 (s, 3H), 1.36 (br s, 1H), 1.26 (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 137.86, 134.28, 64.60, 39.03, 30.51, 21.82, 21.75, 13.90; IR (neat) 3335, 2972, 2953, 2926, 2895, 2841, 1675, 1444, 1405, 1382, 1336, 1289, 1185, 1069, 1015, 984, 880 cm^{-1}; $[\alpha]_D$ −27.6° (*c* 1.01, $CHCl_3$).

2-Pentyl-cyclopent-2-enol: 90% yield; 84% ee was measured by GC on a BPH column; ^{1}H NMR ($CDCl_3$, 300 MHz) 5.53 (s, 1H), 4.65 (br s, 1H), 2.08−2.46 (m, 5H), 1.65−1.74 (m, 1H), 1.42−1.56 (m, 2H), 1.26−1.39 (m, 5H), 0.90 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 146.71, 127.09, 79.10, 34.22, 32.03, 29.81, 28.19, 27.60, 22.76, 14.28; IR (neat) 3312, 2957, 2926, 2856, 1459, 1316, 1046, 926, 826 cm$^{-1;}$ $[\alpha]_D$ −30.3° (*c* 1.26, $CHCl_3$).

(*S*)-1-Phenyl-propane-1,3-diol:[29] 96% ee was measured by HPLC on a OB column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.24−7.36 (m, 5H), 4.94 (dd, J = 3.8 Hz, 8.5 Hz, 1H), 3.83 (t, J = 5.5 Hz, 2H), 2.91 (br s, 2H), 1.86−2.06 (m, 2H); $[\alpha]_D$ −65.7° (*c* 1.67, $CHCl_3$) (lit.[29] $[\alpha]_D$ −70.5° (*c* 1.015, $CHCl_3$), >98% ee (*S*)).

(*S*)-3-Methoxy-1-phenyl-1-propanol:[30] 98% ee was measured by GC on a GTA column; ^{1}H NMR ($CDCl_3$, 300 MHz) 7.24−7.38 (m, 5H), 4.91 (ddd, J = 3.2 Hz, 3.9 Hz, 8.0 Hz, 1H), 3.53−3.62 (m, 2H), 3.37 (s, 3H), 3.32 (d, J = 3.2 Hz, 1H), 1.90−2.05 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) 144.59, 128.56, 127.50, 125.88, 73.80, 71.43, 59.16, 38.75; $[\alpha]_D$ −39.0° (*c* 1.77, cyclopentane) (lit.[31] $[\alpha]_D$ 30.1° (*c* 0.74, cyclopentane), 80% ee (*R*)).

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