Chiral Metallocenes. 3.[1] The Enantioselective Reduction of C=X Bonds (X = O or CH_2) by the Chiral *ansa*-Metallocenes (*R*)- or (*S*)-[$TiCl_2(\eta^5:\eta^5$-$C_5Me_4SiMe_2C_5H_3R^*)$] (R* = Menthyl or Neomenthyl)

Paul Beagley, Philip J. Davies, A. John Blacker,[2] and Colin White*

Department of Chemistry, University of Sheffield, Sheffield S3 7HF, England

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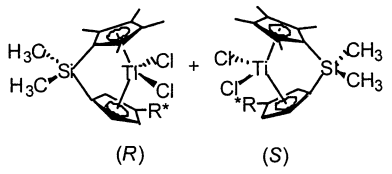
After activating with *n*-BuLi, the two diastereoisomers of [$TiCl_2(\eta^5:\eta^5$-$C_5Me_4SiMe_2C_5H_3R^*)$] (**1a**, R* = menthyl), which have different faces of the asymmetric cyclopentadienyl ring coordinated to the titanium, catalyze the hydrosilylation of ketones, with the $\mathbf{(1a)}_R$ diastereomer being more enantioselective than the $\mathbf{(1a)}_S$ isomer. For example, with the $\mathbf{(1a)}_R$ catalyst, hydrosilylation of acetophenone gives, after hydrolysis, *S*-PhCH(OH)Me in 82% ee, whereas only 16% ee of *R*-PhCH(OH)Me is obtained with the corresponding $\mathbf{(1a)}_S$ catalyst. Inspection of the crystal structures of both $\mathbf{(1a)}_R$ and $\mathbf{(1a)}_S$ allows this difference in stereoselectivity to be rationalized. Highest ee's and rates of hydrosilylation were observed with aryl ketones containing electron-donating groups in the ring. The diastereoisomer $\mathbf{(1a)}_R$ catalyzes the hydrogenation of alkenes; thus, 2-phenyl-1-butene, PhC(Et)=CH_2, is hydrogenated in 53% ee (*S*). The same reduction carried out with a 1.4:1 mixture of *R* and *S* diastereoisomers of the corresponding $TiCl_2(\eta^5:\eta^5$-$C_5Me_4SiMe_2C_5H_3R^*)$ (**1b**, R* = neomenthyl) gives 36% ee of *R*-PhCH(Me)Et.

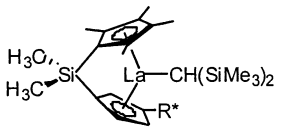
Introduction

As part of a program to develop chiral cyclopentadienyl catalysts we recently reported the synthesis of the chiral titanocenes [$TiCl_2(\eta^5:\eta^5$-$C_5Me_4SiMe_2C_5H_3R^*)$] (**1a**, R* = menthyl or **1b**, neomenthyl).[3] In addition to the



1a R* = menthyl. **1b** R* = neomenthyl

chiral substituent, these 1,3-substituted metallocenes exhibit planar chirality, and in the case of the menthyl compound we were able to separate the two diastereoisomers $\mathbf{(1a)}_R$ and $\mathbf{(1a)}_S$ and to determine their absolute configurations by X-ray crystallography. The corresponding neomenthyl derivatives were isolated as a 1.4:1 mixture of the *R* and *S* diastereoisomers, which defied further attempts to separate them. Marks and co-workers have reported that complexes of the type **2**, which are the Lanthanide analogues of **1a** and **1b**,



2 (R* = menthyl or neomenthyl)

catalyzed the hydrogenation of nonfunctionalized alkenes in = 96% ee.[4] This is a remarkable result; for example, rhodium(I)/chiral bis(phosphine) catalysts, which are so successful in the catalytic hydrogenation of functionalized alkenes, typically hydrogenate nonfunctionalized alkenes with 20% ee.[5] Only recently have catalysts been reported that rival those of Marks, and these are the iridium/phosphine-oxazoline catalysts developed by Pfaltz[6] and the cationic zirconocene catalysts reported by Buchwald and co-workers.[7] Organo-

* Corresponding author. Tel: 0114-222 9310. Fax: 0114 2738673. E-mail: Colin.white@sheffield.ac.uk.

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lanthanide complexes are, however, notoriously moisture-sensitive, and synthesising and handling them requires special techniques. We therefore wondered if our less moisture-sensitive titanium complexes could give as impressive results in enantioselective synthesis as those obtained by Marks and co-workers, and we report here the catalytic properties of these complexes, in particular their ability to catalyze the hydrosilylation of ketones and the hydrogenation of alkenes.[8] These studies also contribute to the considerable interest over the past decade in chiral metallocenes[9] which has been fueled by their spectacular successes in catalyzing stereoselectively a wide range of organic transformations[10] including the stereospecific polymerization of 1-alkenes.[11]

Results and Discussion

Hydrosilylation Studies. Although catalytic asymmetric hydrosilylation of ketones was first reported over thirty years ago[12] and has been studied extensively ever since,[13] there is, as far as we are aware, no industrial process using this reaction nor any general protocol for this procedure to be used by organic chemists as standard methodology to produce chiral alcohols. Further, although various chiral titanocenes have been used to catalyze this reaction, the literature is full of conflicting results; for example, the bis-tetrahydroindenyl complex $[TiCl_2\{(\eta^5{:}\eta^5\text{-}C_9H_{10})_2CH_2CH_2\}]$ is reported to hydrosilylate acetophenone in 12% ee[14] and 97% ee.[15] Equally puzzling is the range of protocols used to activate titanocenes for hydrosilylation. Thus, not only are different alkylating agents added to activate titanocenes but the literature is full of advice on how to add these activating agents; for example, "*n*-BuLi must be added to the centre of the solution and not allowed to run down the side of the glassware to achieve reproducible results".[15] Clearly, as others have pointed out,[16] the activation procedure has a profound effect upon both the rate and the enantioselectivity of the hydrosilylation reaction, and therefore we started our studies by trying to develop an activation protocol that would give us consistent results using *n*-BuLi as the activator and acetophenone as the substrate. We were also aware that a major restriction in the commercialization of the hydrosilylation reaction is the relatively high cost of the silanes normally used, and therefore our initial studies were conducted with the cheap and readily available poly(methylhydrosiloxane), PMHS, $Me_3SiO(SiMeH)_nOSiMe_3$.[17] Our initial studies were also conducted with a 1% catalyst loading of **(1a)$_R$**, i.e., PhCOMe:[Ti]:BuLi = 100:1:2.

Table 1. Effect of Catalyst Loading on the Enantioselective Hydrosilylation of Acetophenone by $PhSiH_3$ in Toluene at 25 °C Using (1a)$_R$ -2*n*-BuLi

mol % catalyst	time (h)	% conversion	% ee of S alcohol
5	1	42	76
	3	81	84
	24	100	82
4	1	39	66
	3	60	68
	24	92	68
3	1	30	63
	3	63	64
	24	100	60
2	1	35	68
	3	70	68
	24	98	64
1	1	32	67
	3	53	67
	24	97	60
0.5	1	12	
	3	21	60
	24	33	47
	48	36	46

Using such conditions, hydrosilylation readily proceeded, but the rate, and more importantly the enantioselectivity, of the reaction was very variable. Thinking that adventitious traces of water might be responsible for the inconsistencies, we carried out experiments in which various amounts of water were added. We found that water did have a detrimental effect on the activity of the catalyst, but to our surprise, limited amounts of water actually improved the enantioselectivity. The optimum enantioselectivity (ca. 70% ee) appeared to be achieved with 1−1.25 equiv of water to titanium catalyst. Another trend that we consistently observed is that the enantioselectivity of the catalyst decreased as the reaction proceeded. After many frustrating inconsistent experiments we found that consistent results and the highest entantioselectivities could be guaranteed only if the reaction proceeded quickly. Thus, high ee's were achieved by replacing PMHS with a more reactive silane, $PhSiH_3$, and using a higher catalyst loading as illustrated in Table 1.

The main features illustrated in Table 1 are as follows:

(i) The ee's are generally higher (and more consistent) with higher catalyst loading.

(ii) The $PhSiH_3$ is more reactive than PMHS. This is illustrated using a 1% catalyst loading when virtually

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complete reduction (97%) of acetophenone is achieved using $PhSiH_3$ after 24 h at room temperature, whereas with PMHS, under the same conditions, only 55% reduction occurs over 3 days.

(iii) The initial ee's at lower catalyst weightings are high but drop before the reaction reaches completion; for example, at a 0.5 mol % catalyst loading the ee is initially in the 60+ region but falls to 46% ee.

We interpret these changes in the enantioselectivity of the reaction as indicating that as the reaction proceeds, a secondary catalytic species forms during the reaction which produces either lower ee, the racemic product, or the opposite enantiomer. Thus, by using a higher catalyst loading or a more reactive silane most of the hydrosilylation reaction is complete before this secondary species is generated in sufficient quantities to influence the enantioselectivity. This would also explain the effect of water on the reaction when PMHS is used; that is, adding small amounts of water destroys the catalyst, and so the conversion goes down but the enantioselectivity improves because any catalysis that occurs is by the primary catalytic species and the secondary species does not have time to be generated. At this stage we can only speculate on the nature of this secondary catalytic species, but we favor it being a monocyclopentadienyl species formed by hydrogen transfer to one of the cyclopentadienyl ligands, probably the one bearing the menthyl group. Such hydrogen transfers are known,[18] and the η^4-cyclopentadiene thus formed would be readily displaced. Monocyclopentadienyl catalysts are known to give lower enantioselectivities than metallocenes,[9c] and this would explain the drop in enantioselectivity as the reaction proceeded. Alternatively, if the hydrogen transfer process was reversible, this would provide a mechanism for epimerizing the catalyst.

Having developed a protocol of using a relatively high catalyst loading and a reactive silane, a reexamination of the literature revealed that for dichlorotitanocene catalysts highest enantioselectivities were reported using just such conditions,[15] whereas deviating from these conditions led to lower enantioselectivities,[14,19] thus explaining some of the anomalous results in the literature.

We next examined the effect of solvent. It is clear from Table 2 that THF accelerates the reaction and (vide ante) that might have been expected to lead to high enantioselectivity, whereas in fact the converse is true. It appears therefore that the coordinating nature of THF has a detrimental effect on the hydrosilylation reaction using **(1a)$_R$**. In contrast, other workers have successfully used THF for titanocene-catalyzed hydrosilylation reactions.[14,19] One difficulty in interpreting solvent effects is that, in addition to the hydrosilylation reaction itself, the solvent may have a significant effect upon the activation stage since the nature of the activating agent (*n*-BuLi) in solvents such as hexane is very different from that in coordinating solvents such as THF. Indisputable is that toluene is the best solvent to use to obtain high enantioselectivity with the titanocene catalyst **(1a)$_R$**; therefore toluene was adopted as the solvent of choice for such reactions.

Table 2. Effect of Solvent on the Enantioselective Hydrosilylation of Acetophenone by $PhSiH_3$ in Toluene at 25 °C Using 5 Mol % (1a)$_R$ -2*n*-BuLi

solvent	time (h)	% conversion	ee of *S* alcohol
THF	1	87	6
	3	100	0
toluene	1	44	59
	3	100	63
benzene	1	78	36
	3	98	42
hexane	1	67	17
	3	96	21
no solvent	1	51	14
	3	60	11
	24	79	7

Table 3. Enantioselective Hydrosilylation of Acetophenone Derivatives, p-$RC_6H_4C(O)Me$ by $PhSiH_3$ in Toluene at 65 °C Using 5 Mol % (1a)-2*n*-BuLi

			(*R*)-catalyst		(*S*)-catalyst	
R	σ_p	time (h)	% conversion	% ee (*S*)	% conversion	% ee (*R*)
MeO	−0.27	1	100	63	100	23
Me	−0.17	1	100	53	100	6
H	0	1	100	59		
H[a]		24[a]	100[a]	82[a]	100[a]	16[a]
F	0.06	1	100	66	38	12
Cl	0.23	1	33	48	18	13
		3	87	46	39	0
		24	100	44		
Br	0.23	1	57	28		
		3	79	22		
		20	81	20		
CF_3	0.54	1	86	14		
		3	99	14		
NO_2	0.78	1	4	1	9	2 (S)
		3	13	1		
Cl[b]		1	96	48	8	8
		3			14	13

[a] At 25 °C. [b] Ortho derivative.

Using our new experimental protocol we hydrosilylated a range of ketones, and the results are presented in Tables 3 and 4. From these tables it is evident that the **(1a)$_R$** diastereomer consistently shows greater enantioselectivity than the corresponding **(1a)$_S$** diastereomer. Also, although both contain a menthyl substituent, the two diastereoisomers give rise to opposite enantiomers of the product, indicating that the planar chirality is the major factor controlling the stereochemistry of the product. We have previously reported the crystal structures of both **(1a)$_R$** and **(1a)$_S$**, and these are illustrated in Figure 1. The major difference between the structures is that the catalyst face of **(1a)$_R$** is more hindered than **(1a)$_S$** because the ^{i}Pr of the menthyl substituent group points across the face of the catalyst toward where one would expect a substrate to be coordinated. The *S*-catalyst diastereoisomer has the same menthyl group attached but in a different orientation; this means the carbon with the ^{i}Pr group is pointing toward the back of the catalyst away from the side where it is proposed that coordination of the ketone takes place. Thus, the area at the catalyst face that is occupied by an ^{i}Pr group in the *R*-diastereoisomer is occupied by a proton in the case of the *S*-diastereoiso-

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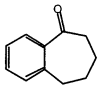
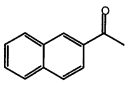
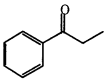
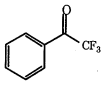
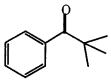
Table 4. Enantioselective Hydrosilylation of a Range of Ketones by $PhSiH_3$ in Toluene for 1 h at 65 °C Using 5 Mol % (1a)-2*n*-BuLi

Substrate	$(1a)_R$		$(1a)_S$	
	% conversion	% e.e. (*S*)	% conversion	% e.e. (*R*)
	No reaction			
	96	43	94	10
	100	0	100	0
	99	36		
	94[a]	28[a]		
	100	62	100	25
	9	6	15	2
	10	5	9	5
	58[b]	2		

[a] Reaction time = 3 h. [b] In hexane.

mer. If these structural differences are maintained in solution, this would rationalize the observed relative efficiencies of $(1a)_R$ and $(1a)_S$ in asymmetric synthesis. Inspection of the crystal structures of $(1a)_R$ and $(1a)_S$ also allows the correct configuration of the products to be rationalized. Thus, as depicted in Figure 2, in each diastereomer the titanium atom may be considered to be sitting in an open four-sided box with the bridging $SiMe_2$ group making up the back of box, the large C_5Me_4 group making up the top of the box, and the smaller cyclopentadienyl ligand at the bottom. The bulky menthyl group then makes up either a right or a left side in $(1a)_R$ and $(1a)_S$, respectively. Thus, the ketone can approach only from the open side or the front (Figure 2). Buchwald,[15] by adapting Lauher and Hoffmann's theoretical analysis of metallocene orbitals,[20] has argued that for maximization of the metal hydride HOMO/ketone LUMO overlap, the ketone should approach from the side rather than the front (Figure 2). This would correctly account for the stereochemistry of the alcohols formed by $(1a)_R$ and $(1a)_S$. As a note of caution, however, one must bear in mind that this presupposes that the enantioselectivity is determined by the kinetics of complexation of the ketone and that subsequent hydrogen transfer is fast.

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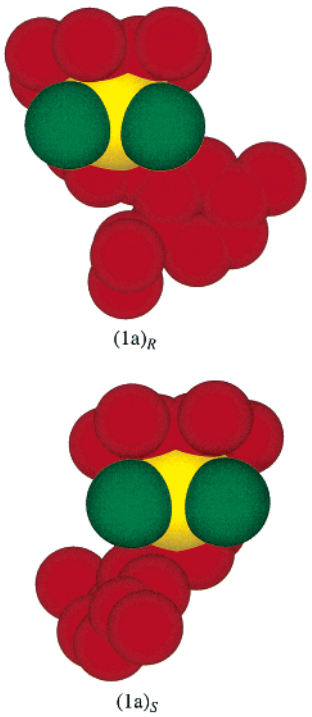


Figure 1. Crystal structures of $(1a)_R$ and $(1a)_S$[3].

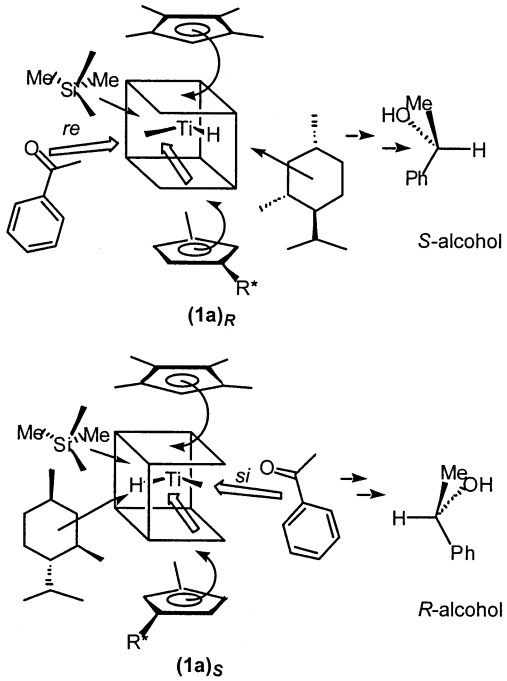


Figure 2. Proposed origin of enantioselection in the hydrosilylation reactions.

Another major trend apparent from Table 4 is that the presence of electron-donating groups in the aryl ring has a beneficial effect both on the rate of reaction and on the enantioselectivity observed. There is a broad correlation between both the rate and enantioselectivity with the inverse of the Hammet parameter σ_p[21], and it is curious that Halterman,[19] using a related binaphthyl-derived titanocene, observed the opposite trend, whereas Buchwald,[15] using an ethylenebis(tetrahydroindenyl)-titanium system, noted that an aromatic substituent was essential for high stereoselectivity but found no correlation between the electron density in the aromatic

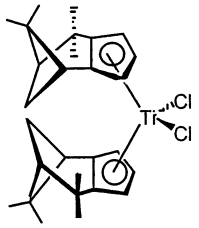
Table 5. Hydrogenation of Alkenes at 1 atm over 48 h

catalyst	substrate	solvent	temp (°C)	% conversion	ee (%)
(*R*)/(*S*)-1b 1.4:1 mixture	2-phenyl-1-butene	hexane/THF (10:1)	20	57	36 (*R*)
(*R*)/(*S*)-1b 1.4:1 mixture	2-phenyl-1-butene	hexane/THF (10:1)	−20	23	35 (*R*)
(1a)$_R$	2-phenyl-1-butene	hexane/THF (10:1)	20	100	48 (*S*)
(1a)$_R$	2-phenyl-1-butene	hexane/THF (10:1)	−30	26	53 (*S*)
(1a)$_R$	2-phenyl-1-butene	THF	20	66	31 (*S*)
(1a)$_R$	2-phenyl-1-pyrroline	THF	60	100	60 (*S*)

ring. Our observation that electron donors in the aromatic ring promote higher enantioselectivity suggests that in the key intermediate there is a secondary interaction between the highly electropositive titanium center and the electron-rich aromatic ring which leads to a more rigid transition state and hence the higher ee's. This would also rationalize why THF, although promoting the hydrosilylation reaction, has a detrimental effect upon the stereoselectivity since any weak interaction between the catalyst and the aromatic ring would not be able to compete with a coordinating solvent like THF, which is in excess. Further support for an interaction between the titanium and the aromatic ring comes from X-ray studies[22] and other spectroscopic methods,[23] which show that titanocenes of the type $[TiCp_2X_2]$ can form adducts with suitable Lewis bases. There is also indirect evidence in the literature to support the proposal that aromatic rings can interact with catalysts of this type. For example, during the $[TiCl_2\{(\eta^5{:}\eta^5\text{-}C_9H_{10})_2CH_2CH_2\}]$-catalyzed reduction of 2-phenyl-1-pyrroline by deuterium, half the deuterium is incorporated at the chiral center, but the remainder is mainly incorporated in the aromatic ring at the ortho position;[24] this strongly suggests an interaction between the titanium and the aromatic ring at some stage in the reaction.

Table 4 shows that the seven-membered ring benzosuberone was not reduced under these conditions; in contrast, the less bulky six- and five-membered ring derivatives tetralone and indanone reacted readily, but tetralone gave lower ee's than acetophenone and the five-membered ring derivative indanone gave a racemic product. Similarly, the 2-acyl naphthalene is more reactive than the corresponding 1-acyl naphthalene; this again is probably a steric effect, but it is not at all apparent why these naphthyl derivatives should give lower ee's than acetophenone. Replacing the methyl group of acetophenone by ethyl has a modest beneficial effect upon the enantioselectivity, but substituting the methyl group with a bulky ^{t}Bu or an electron-withdrawing CF_3 group has a distinct detrimental effect upon both the rate and the enantioselectivity. The alkyl ketone pinacolone was readily reduced but with low enantioselectivity.

Hydrogenation Studies. To compare our results with other catalysts, our studies were carried out predominantly with 2-phenyl-1-butene, which has in effect become the standard test substrate for the enantioselective reduction of unfunctionalized alkenes. We also used the recommended activating procedure using 6 equiv of *n*-BuLi per Ti.[25] Despite this, we observed a variable induction period before hydrogenation proceeded. The results obtained are presented in Table 5. The 53% ee obtained with **(1a)$_R$** is greater than that obtained for all titanocenes except for **3**, which gives comparable enantioselectivity,[26,27] and **4**, which gives 77% ee at −75 °C.[26,28] However, **(1a)$_R$** is considerably



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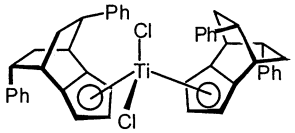

4

easier to synthesize than either **3** or **4** and hence easier to modify in a systematic way in order to enhance the enantioselectivity. It is frustrating that we were unable to separate the diastereoisomers of the corresponding neomenthyl complex **1b** because this is clearly a more stereoselective catalyst since a 1.4:1 enriched mixture of the two diastereomers gives (*R*)-2-phenylbutane in 30% ee at room temperature. This illustrates that the chiral substituent on the asymmetric cyclopentadienyl ligand plays a significant role in the enantioselectivity of these catalysts.

To test if these catalysts would tolerate the presence of a functional group, we briefly examined the hydrogenation of 2-phenyl-1-pyrroline. Although we had to increase the temperature to 60 °C to obtain reasonable rates, this enamine was readily reduced with 60% ee.

It is interesting to compare the enantioselectivity obtained with that reported by Marks for the same chiral ligand complexed to various lanthanides. Whereas **(1a)$_R$** gives (*S*)-2-phenylbutane, the corresponding (*R*)-$[Sm\{CH(SiMe_3)_2\}\{(\eta^5{:}\eta^5\text{-}C_5Me_4SiMe_2C_5H_3(menthyl)\}]$, i.e., (*R*)-Sm menthyl diastereoisomer, gives (*R*)-2-phenylbutane in only 16% ee at room temperature; in contrast, the (*S*)-Sm menthyl, which was not separated completely from the (*R*)-epimer, is much more stereoselec-

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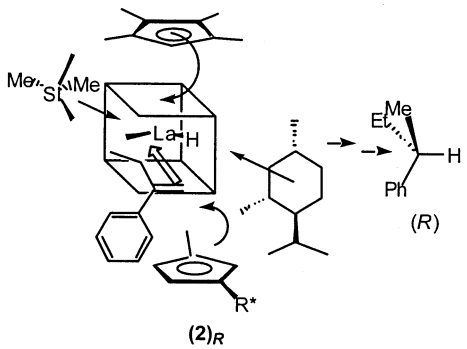

Figure 3. Frontal approach of the alkene to the corresponding lanthanide-hydride intermediate **(2)$_R$**.

tive, giving >80% ee (*S*)-2-phenylbutane. We address first the question as to why the same chiral directing group attached to Ti and Sm should give opposite products. This can be rationalized by proposing that in the case of the titanium catalyst the hydrogen is delivered as the alkene approaches laterally, i.e., the same direction of approach as a ketone (Figure 2). In contrast, Marks proposes that in the samarium case the alkene approaches along a frontal trajectory (Figure 3). For both catalysts the phenyl substituent on the substrate is orientated to avoid the bulky menthyl substituent.

We were surprised to find that the titanium catalyst was less stereoselective than the samarium catalyst since in both cases the enantioselection is assumed to take place in a [MH(η^5:η^5-$C_5Me_4SiMe_2C_5H_3$R*)(alkene)] (R* = menthyl) intermediate. We had presumed that the smaller titanium atom would involve a more crowded intermediate, leading to higher stereoselectivity. It is, however, pertinent that Marks and co-workers noted, but did not explain, that the ee obtained in the reduction of 2-phenyl-1-butene decreased markedly with decreasing radius of the lanthanide catalyst used.

Conclusions

The catalyst **(1a)$_R$**, which is relatively straightforward to synthesize and crystallize out optically pure, gives enantioselectivities in both the hydrosilylation and the hydrogenation reactions which compare well with many similar titanocene catalysts. Both the planar chirality of the asymmetric cyclopentadienyl ligand and the chiral substituent play a significant role in determining the enantioselectivity. Realistically, however, these catalysts are not likely to find wide general use. In the case of the hydrosilylation reactions the activation procedure is too capricious, and this seems to be a general feature of titanocene catalysts activated by lithium alkyls. In contrast, the titanocene difluoride catalysts developed by Buchwald and co-workers which are activated by slow continuous addition of methanol seem to be greatly superior.[16a] Similarly, as hydrogenation catalysts, these do not have the activity to make them practical catalysts. Again this seems to be a general feature of titanocenes in that under conditions that give high enantioselective hydrogenation the most stereoselective catalysts have turnover rates of 4 cycles h^{-1}.[25,27] Presumably, the steric crowding that is responsible for their high enantioselectivity is also responsible for their low activity. Such turnover rates compare very badly with the iridium/phosphine-oxazoline catalysts developed by Pfalt and also Marks lanthanide metallocene catalysts; not only are these catalysts more enantioselective for the reduction of nonfunctionalized alkenes but their turnover rates are several orders of magnitude greater than any reported chiral titanocene.

Experimental Section

General Methods. All reactions of moisture-sensitive reagents were performed under nitrogen. THF was heated under reflux over sodium benzophenone ketyl and distilled under nitrogen, hexane was dried by distillation from $LiAlH_4$ under nitrogen, whereas toluene and diethyl ether were heated under reflux over sodium and freshly distilled under nitrogen prior to use. (*R*)- and (*S*)-dichloro{1-(η^5-3′-menthylcyclopentadienyl)-1′-(η^5-2,3,4,5-tetramethylcyclopentadienyl)dimethylsilane}titanium, **(1a)$_R$** and **(1a)$_S$**,[3] (*RS*)-dichloro{1-(η^5-3′-neomenthylcyclopentadienyl)-1′-(η^5-2,3,4,5-tetramethylcyclopentadienyl)dimethylsilane}titanium, **(1b)$_{RS}$**,[3] and 2-phenyl-1-pyrroline[29] were prepared by the reported literature procedures. 2-Phenyl-1-butene was prepared from phenylpropanone (propiophenone) via Wittig reaction with methylenetriphenylphosphine[30] and stored over sodium metal, under nitrogen.

Procedure for Hydrosilylation of Ketones Using PMHS. All solvents, ketones, and the silane were thoroughly degassed with argon prior to use, and the hydrosilylation reactions were carried out under argon in reaction flasks shielded from the light by aluminum foil.

Activation. *n*-BuLi (2 equiv) was added at room temperature to the center of a solution of **(1a)$_R$** (20 mg, 0.04 mmol) in toluene (1 cm^3) and then the mixture stirred for 5 min.

Hydrosilylations. PMHS (1.5 equiv, relative to the ketone) was added to the activated catalyst and the mixture stirred for a further 5 min before adding the ketone. Stirring was continued throughout the reaction. If higher temperatures were required, the mixture was placed in an oil bath immediately after the addition of ketone. In cases where water was added this was added as a 0.14 M toluene solution via a syringe.

Workup Procedure. Samples of the alcohols were prepared in vials by the addition of acetone and 0.1 M HCl (similar results were obtained if the silyl ether was cleaved with TBAF or MeOH). After bubbling had ceased, the HCl was neutralized with a saturated solution of $NaHCO_3$. The product was then extracted with diethyl ether and run through a plug of $MgSO_4$.

Product Analysis. Conversions and ee's were determined using either a Perkin-Elmer 8420 or an 8600 gas chromatograph fitted with a flame ionization detector and a 30 m α- or β-Chiradex column. Hydrogen was used as the carrier gas, and the conditions that allowed the alcohol product enantiomers to be separated are given in the Supporting Information. The identity of the major enantiomer was confirmed by measuring the sign of the optical rotation of the reaction mixture and comparing it with the literature.[15,31]

Procedure for Hydrosilylation of Ketones Using $PhSiH_3$. Activation. A stock solution of *n*-BuLi in toluene was prepared (0.08 M, i.e., 0.08 mmol/cm^3).[32] The stock solution of *n*-BuLi (1 cm^3) was added at room temperature to the titanium

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(32) Many ketones were added as solutions in toluene (0.5 cm^3); in these cases a more concentrated solution of *n*-BuLi (0.16 mmol/cm^3) was prepared and the catalyst activated using 0.5 cm^3 of this solution.

catalyst (20 mg, 0.04 mmol) in toluene (0.2 cm^3), and the mixture was shaken and then stirred rapidly for 5 min.

Hydrosilylations. Phenylsilane (108 μL, 0.88 mmol) was added to the above catalytic solution; the reaction was stirred for a further 5 min before adding the ketone (0.8 mmol). The reaction vessel was then placed in an oil bath at 65 °C. The work up was performed in the same way as described above.

Procedure for Catalytic Hydrogenations. At room temperature these were carried out in a 20 cm^3 Schlenk tube attached to a 1 bar hydrogenation apparatus using a ratio of catalyst:cocatalyst:substrate of 1:6:100. 2-Phenyl-1-butene was freshly distilled under argon, and all solutions were degassed by bubbling hydrogen through them for 15 min. In a typical experiment, the oven-dried Schlenk tube was attached to the hydrogenation apparatus and allowed to cool under a stream of hydrogen gas. A 12 mm PTFE magnetic flea was added to the reaction vessel, the apparatus was then evacuated (=0.1 mmHg), and the atmosphere was replaced with hydrogen. This was carried out three times to remove trace amounts of oxygen. Degassed hexane (5 cm^3) and 2-phenyl-1-butene (0.5 cm^3, 4.27 mmol) were added via syringe. The required amount of cocatalyst was added via syringe and the solution stirred rapidly via a 1 cm magnetic flea for 5 min. The catalyst (20 mg, 0.04 mmol) was added into a separate Schlenk tube and then evacuated and placed under nitrogen. The catalyst was dissolved in THF (0.5 cm^3), and the solution degassed and transferred via a 1 cm^3 syringe to the rapidly stirred reaction solution. The red catalyst solution turned yellow, and the reaction was stirred for 48 h in the dark, after which time the catalyst was removed by passing the reaction solution through a short (3 cm × 5 cm) column of alumina eluting with hexane. The relative amounts of 2-phenylbutane and 2-phenyl-1-butene were determined via GC (DB 1 or DB 5 capillary column, 100 °C isothermal). The product was purified by Kugelrohr distillation (75 °C, 30 mmHg). NMR spectroscopic data were in agreement with the literature.[33] The specific rotation of the sample was measured via polarimetry and the enantiomeric excess calculated on the basis of a quoted value for the specific rotation of an optically pure sample of (*S*)-2-phenylbutane ($[\alpha]^{20}$ +28.4, EtOH).[4]

Low-temperature catalytic hydrogenation experiments were carried out using a similar procedure, but the reaction solution was not lowered into the cold bath until uptake of dihydrogen was observed (via the level of oil in the gas buret); that is, formation of the active catalyst took place at room temperature.

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Supporting Information Available: Table of GC conditions for chiral alcohol analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

OM020618C

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