Asymmetric Hydrosilylation of Prochiral Ketones Catalyzed by Rh(I) Complexes and (-)-Sparteine

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Summary: (-)-Sparteine has been used as an added chiral ligand for the enantioselective hydrosilylation of prochiral ketones catalyzed by neutral, cationic and zwitterionic rhodium(I) complexes.

INTRODUCTION

The enantioselective catalytic synthesis of chiral alcohols, useful intermediates in organic chemistry, has attracted a great deal of attention among chemists in recent years.[1] Enantioselective hydrosilylation of prochiral carbonyl compounds in the presence of chiral catalysts has been extensively studied over the last decade as a convenient asymmetric reaction model and as a route to optically active alcohols.[2] A large number of catalysts, mostly rhodium complexes with chiral ligands, have been used in such reactions. These catalysts have been previously synthesized or prepared *in situ* by introducing the chiral ligand into the reaction mixture containing an achiral transition metal complex. In the hydrosilylation of ketones using *in situ* catalysts, consisting of a rhodium complex and optically active phosphines, low to average asymmetric inductions have been achieved[2], while some nitrogen-containing ligands (in particular, pyridinethiazolidines[3], C_2-symmetrical bis(oxazolinylpyrdines)[4a] and bioxa(thia)zolins[4b,5] were shown to be highly efficient in terms of both chemical and optical yield.

In the present work, the rhodium(I) catalyzed hydrosilylation of alkyl aryl and heteroaryl ketones was examined using (-)-sparteine (**1**) as an added chiral ligand. To our knowledge, this ligand has not been used for hydrosilylations, although there are several examples of
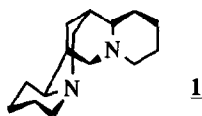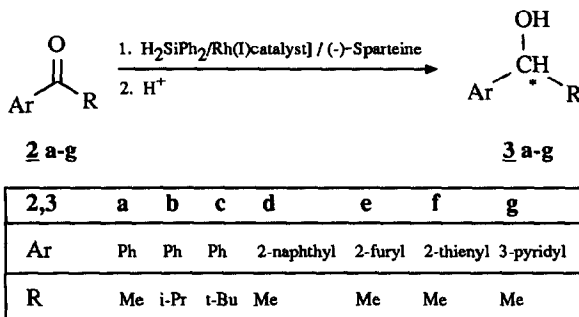
asymmetric reactions carried out in the presence of **1**, such as palladium catalyzed allylic alkylations,[6] Reformatsky reactions,[7] as well as Grignard-induced anionic polymerizations[8] and some other reactions involving sparteine modified organometallic reagents.[9]

RESULTS AND DISCUSSION

The hydrosilylation of aromatic and heteroaromatic ketones was carried out using neutral ([Rh(cod)Cl]$_2$,cod=cis,cis-1,5-cyclooctadiene), cationic ([Rh(dppb)(cod)]$^+$BF$_4^-$. dppb = 1,4-bis(diphenylphosphino)butane) and zwitterionic ([Rh$^+$(cod)BPh$_4^-$) rhodium(I) complexes. The reactions were carried out at 0 - 25°C either neat or in tetrahydrofuran (THF). In most cases, diphenylsilane was used as a hydrosilylation agent, and the latter was generally employed in 10-25% molar excess. The concentration of the metal catalyst in all cases was 0.1 mol. % based on the ketone. The amount of chiral ligand **1** was varied from 1 to 20 molar equivalents with respect to rhodium. The reactions were monitored by GC and GC/MS and the silyl ethers formed were quantitatively converted into the corresponding secondary alcohols by treatment with aqueous HCl in acetone, according to the procedure of Brunner and Riepl[10], or by using the strongly acidic cation-exchange resin, Amberlyst 15 (A15)[11]. The latter method is substantially simpler and comprises addition of a stoichiometric amount of A15 to the reaction mixture, followed by 2-3 hours stirring at room temperature. It should be noted that, in the case of acid-sensitive furan derivatives, the use of A15 was the only possible method for desilylation.

The catalytic system [Rh(cod)Cl]$_2$/**1** was at first studied in detail in the hydrosilylation of acetophenone (**2a**) with diphenylsilane. When the mixture of **2a**, H$_2$SiPh$_2$ (1.1 mol-equiv.), [Rh(cod)Cl]$_2$ (0.1 mol %) and chiral ligand **1** (0.1 mol %) was stirred at room temperature, the

$$\text{Ar} \overset{O}{\underset{}{\parallel}} \text{R} \quad \xrightarrow[\text{2. H}^+]{\text{1. H}_2\text{SiPh}_2/\text{Rh(I)catalyst] / (-)-Sparteine}} \quad \text{Ar} \overset{OH}{\underset{*}{\underset{}{\overset{|}{CH}}}} \text{R}$$

2 a-g   **3** a-g

2,3	a	b	c	d	e	f	g
Ar	Ph	Ph	Ph	2-naphthyl	2-furyl	2-thienyl	3-pyridyl
R	Me	i-Pr	t-Bu	Me	Me	Me	Me

hydrosilylation occurred slowly (4 days) to give the diphenylsilyl ether of 1-phenylethanol in high yield. Desilylation of the latter afforded the corresponding carbinol (**3a**) isolated by vacuum distillation in 86% yield. The product was optically active; however, its optical purity was only 6%. Decreasing the reaction temperature to 0°C drastically decreases the rate of hydrosilylation and both the chemical and optical yield of alcohol **3a** remained almost the same. An increase in excess chiral ligand also does not influence the reaction (Table 1).

TABLE 1.   Hydrosilylation of acetophenone (**2a**) with H_2SiPh_2 catalyzed by [Rh(cod)Cl]$_2$ in the presence of (-)-Sparteine (the molar ratio **2a** : H_2SiPh_2 : Rh catalyst = 1:1.1:0.001)

Temperature, °C	**1**:[Rh] (mol)	Reaction time, days	Yield of (S)-PhCH(OH)CH$_3$,%	ee, %[a]
25	1 : 1	4	86	6
0	1 : 1	14	82	8
25	2 : 1	4	82	6
0	2 : 1	14	78	6
25	4 : 1	4	84	6
0	4 : 1	14	78	5
25	10 : 1	4	83	6
0	10 : 1	14	80	6

[a] Based on optical rotation measurements, see footnote b in Table 2.

The hydrosilylations of some other aromatic and heteroaromatic ketones were also carried out in the presence of [Rh(cod)Cl]$_2$/**1** (Table 2). As anticipated, isobutyrophenone (**2b**) and 2,2-dimethylpropiophenone (**2c**), which are more sterically hindered than **2a**, react with H_2SiPh_2 more slowly, whereas the reactivities of 2-acetonaphthone (**2d**), 2-acetylfuran (**2e**), 2-acetylthiophene (**2f**) and 3-acetylpyridine (**2g**) are similar to that of **2a**. In all cases, the corresponding secondary alcohols (**3b-g**) were isolated in fair chemical yields in optically active form (after desilylation of silyl ethers). Their optical purities (16 - 34%) are substantially higher than that of carbinol **3a**. The maximum asymmetric induction (34%) is observed in the case of pyridine derivatives. However, this value is lower than that achieved when using [Rh(cod)Cl]$_2$/pyridinethiazolidine[3b] and also N-benzyl-N-methylephedrinium tetrahalozinkate.[13] Furyl (**3e**) and thienyl carbinols (**3f**) are formed with optical purities similar to those achieved using the [Rh(cod)Cl]$_2$/pyridinethiazolidine catalytic system.[3b] In general, (-)-sparteine in conjunction with [Rh(cod)Cl]$_2$ is a considerably less effective chiral ligand than previously reported nitrogen-containing chiral ligands.[2-5] For this reason, we have examined the possibility of using **1** as an added chiral ligand for hydrosilylations catalyzed by cationic and betaine-like rhodium(I) complexes.

In order to estimate the catalytic activity of the cationic complex [Rh(cod)(dppb)]$^+$BF$_4^-$, it was first tested in the reaction of acetophenone with different hydrosilanes in the absence of any added ligand. The experimental findings revealed that the catalyst is only quite active in the

TABLE 2. Hydrosilylation of ketones **2** with H_2SiPh_2 catalyzed by [Rh(cod)Cl]$_2$ in the presence of (-)-sparteine (the molar ratio **2** : H_2SiPh_2 : Rh catalyst : **1** = 1 : 1.1 : 0.001 : 0.004; 25°C)

Ketone	Reaction time, days	Product (S)	Yield, %[a]	ee, %[b]
2a	4	**3a**	84	6
2b	6	**3b**	80	16
2c	6	**3c**	78	22
2d	4	**3d**	65	11
2e	4	**3e**	73	19
2f	4	**3f**	77	15
2g	4	**3g**	65	34 (42)[c]

[a] Isolated yield.   [b] Based on maximum reported $[\alpha]_D$ r .t. values: -45.5 (c=3.0, MeOH) for (S)-**3a**,[12] + 47.7 (c=7,Et$_2$O) for (R)-**3b**,[13] -32.2 (c=1.0,MeOH) for (S) - **3c**,[14] + 55.8 (c=4.8,CHCl$_3$) for (R)-**3d**,[15] 17.0 (c=6,EtOH) for (S)-**3e**,[16] -23.3 (c=1.5,CHCl$_3$) for (S)-**3f**,[17], +40.2 (c=0.87,MeOH) for (R)-**3g**.[18]   [c] Based on NMR analysis using chiral shift reagent Pr(tfc)$_3$.

case of diphenylsilane (Table 3). When HSiEt$_3$ or HSiMe$_2$Ph is used, 100% conversion of the starting material cannot be achieved. Therefore, these silanes are unsuitable for the preparative synthesis of secondary alcohols via hydrosilylation.

TABLE 3. Hydrosilylation of acetophenone (**2a**) catalyzed by [Rh(cod)(dppb)]$^+$BF$_4^-$ (the molar ratio **2a** : H_2SiPh_2 : Rh catalyst = 1 : 1.1 : 0.001; 25°C)

Silane	Reaction time, h	Conversion of **2a**, %[a]
HSiEt$_3$	24	10(15)[b]
HSiMe$_2$Ph	24	24
H_2SiPh_2	0.5	100
H_2SiPh_2[c]	4.5	100

[a] GC data;   [b] after 48 h reaction;   [c] reaction mixture diluted with THF (50 vol. %).

The dilution of the reaction mixture with THF decreases the reaction rate but it still remains quite high and all subsequent experiments were carried out using THF as the solvent. The hydrosilylation of ketone **2a** with H_2SiPh_2 in THF catalyzed by the cationic Rh(I) complex occurs more slowly in the presence of ligand **1** than without the latter. Moreover, this effect becomes more pronounced with an increasing amount of **1** in the reaction mixture until the

ligand : Rh ratio reaches 10 : 1 (Table 4). Therefore, the addition of **1** results in the formation of sparteine-containing catalytic species which are less reactive than [Rh(cod)(dppb)]$^+$BF$_4^-$ itself. The extent of asymmetric induction also increases with the rise of the chiral ligand

TABLE 4. Hydrosilylation of acetophenone (**2a**) with H$_2$SiPh$_2$ catalyzed by [Rh(cod)(dppb)]$^+$BF$_4^-$ in the presence of (-)-sparteine (**2a** : H$_2$SiPh$_2$: Rh catalyst = 1 : 1.1 : 0.001; solvent: THF)

[Rh] : **1**	Reaction time, h	Isolated yield of (S) - **3a**, %	ee, %[a]	Number of runs
1:1	9	70	4	1
1:2	16	65±2	4	2
1:4	28	70±4	9±2	3
1:10	48	77±3	21±2 (23[b],22[c])	3
1:12	48	68	20	1
1:20	48	79	22 (24[b])	1

[a] Based on optical rotation measurements (see footnote (b) in Table 2);
[b] Based on NMR analysis of (+)-MTPA esters; [c] Based on NMR analysis using Pr(tfc)$_3$ as shift-reagent.

concentration (to a 10-fold excess). Under optimum conditions, the optical purity of alcohol **3a** is higher than in the case of the neutral Rh(I) complex, although it does not exceed ca. 20% (Table 4).

More sterically hindered alkyl aryl ketones (**2b**, **2c** and **2d**) as well as heteroaryl ketones (**2e** and **2f**) can also be hydrosilylated using the [Rh(cod)(dppb)]$^+$BF$_4^-$/**1** system. Desilylation affords the corresponding chiral alcohols in fair chemical yields. Their optical purities are somewhat higher than that of **3a**. The maximum value (30%) is obtained in the case of the most hindered ketone **2c** (Table 5).

TABLE 5. Hydrosilylation of ketones **2** with H$_2$SiPh$_2$ catalyzed by [Rh(cod)(dppb)]$^+$BF$_4^-$ in the presence of sparteine (the molar ratio **2** : H$_2$SiPh$_2$: Rh catalyst: **1** = 1 : 1.1 : 0.001 : 0.01 25°C; solvent : THF)

Ketone	Reaction time, h	Product (S)	Isolated yield, %	ee, %[a]	Number of runs
2a	48	**3a**	77±3	22±2 (23[b],22,[c])	3
2b	120	**3b**	72±3	27±1	2
2c	144	**3c**	82±4	30±3	3
2d	48	**3d**	75	14±1	2
2e	48	**3e**	63±2	23	2
2f	48	**3f**	83±2	19±0.5	2

[a],[b],[c] See footnotes to Table 4.

The hydrosilylation of **2** was also carried out in the presence of the zwitterionic rhodium(I) catalyst, $Rh^+(cod)BPh_4^-$.[20] In the absence of solvent, this complex smoothly catalyses the reaction of **2a** with H_2SiPh_2, although its activity is somewhat less than that of the cationic Rh(I) complex. Under similar conditions, 100% conversion of **2a** is achieved in 72 h. at room temperature (cf. Table 3). The dilution of the reaction mixture with THF does not influence the activity of the catalyst. To our knowledge, this is the first example of zwitterionic-complex-catalyzed hydrosilylation.[21]

As in the case of the cationic Rh(I) complex, the introduction of chiral ligand **1** decreases

TABLE 6.   Hydrosilylation of ketones **2** with H_2SiPh_2 catalyzed by $Rh^+(cod)BPh_4^-$ in the presence of sparteine (the molar ratio **2** : H_2SiPh_2 : Rh catalyst: **1** = 1 : 1.25 : 0.001 : 0.01; 25°C; solvent : THF)

Ketone	Reaction time, days	Product (S)	Isolated yield, %	ee, %[a]	Number of runs
2a	7	**3a**	75±5	37±3 (41[b],28[c])	3
2b	9	**3b**	68±5	34±2	3
2c	9	**3c**	64±2	30±1	3
2d	6	**3d**	83±3	21±1	2

[a,b,c] See footnotes to Table 4.

the catalytic activity of the zwitterionic complex. In the case of acetophenone, the hydrosilylation results in 37% optical yield of carbinol **3a**. Surprisingly, the optical purities of secondary alcohols obtained from the more sterically hindered ketones **2b** and **2c** are somewhat less (31 - 35%). Similar values of optical yield were also obtained in hydrosilylations of acetonaphthone (Table 6).

In conclusion, the hydrosilylation of prochiral alkyl aryl and alkyl heteroaryl ketones with diphenylsilane in the presence of neutral, cationic and zwitterionic rhodium(I) complexes as the metal catalyst and (-)-sparteine as an added chiral ligand affords the corresponding secondary alcohols (after desilylation of the silyl ethers) in good chemical yield and low to moderate optical purity. The maximum asymmetric induction is observed when $Rh^+(cod)BPh_4^-$ is used as the metal catalyst.

EXPERIMENTAL

All ketones, silanes and $[Rh(cod)(dppb)^+BF]_4^-$ were Aldrich products. $[Rh(cod)Cl]_2$[22] and $Rh^+(cod)BPh_4^-$[20] were prepared as described in the literature. Amberlyst 15 (4.6 mg equiv. H^+/g was purchased from Fluka. (-)-Sparteine sulfate (Fluka) was transformed to the free base and distilled in vacuo before use. THF was distilled from sodium/benzophenone. GC analysis

was carried out on a Varian Vista 6000 gas chromatograph equipped with a column packed with 1.5% OV-17 + 1.95% OV-210 on Chromosorb W-HP (100-200 mesh). ^{1}H NMR spectra were obtained on a Gemini 200 MHz spectrometer using $CDCl_3$ as the solvent and Me_4Si as the internal standard. A VG 7070E spectrometer was used for mass spectral determinations. Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

Representative Procedure: To a solution of acetophenone (2a, 1.2 g, 1.17 ml, 10 mmol) in THF (3 ml) was added the rhodium(I) catalyst, $Rh^+(cod)BPh_4^-$ (5.3 mg, 0.01 mmol) and the mixture was stirred under N_2 at room temperature for 30 min. Diphenylsilane (2.3 g, 2.32 ml, 12.5 mmol) was added by syringe and stirring was continued at room temperature until the reaction was complete (7 days). After completion of the reaction, Amberlyst 15 (2.72 g, 12.5 mmol H^+) was added and the reaction mixture was stirred for 3 h at room temperature. Amberlyst 15[11] was filtered off, the filtrate was evaporated and the residue was distilled in vacuo affording 0.91 g (75%) of (S)-1-phenylethanol (3a), $[\alpha]_D^{20}$ - 16.8 (c = 3.0, MeOH), ee 37% (see Table 6).

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