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Rh(I)-Catalyzed Asymmetric Hydrosilylation and Hydroboration/Oxidation Reactions Using Berens Ligand

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Abstract: The Berens ligand **2** was used in a number of Rh(I)-catalyzed asymmetric hydrosilylations of acetophenones under standard conditions, affording the corresponding 1-arylalcohols in ees up to 65%. Some novel Rh catalysts were generated in situ from the neutral precatalyst $[Rh(\mu\text{-}Cl)(COD)]_2$ and screened in the catalytic asymmetric hydroboration/oxidation of styrenes, gave enantioselectivities of up to 62%.

Keywords: Catalytic asymmetric synthesis, chiral diphosphine, hydroboration, hydrosilylation

INTRODUCTION

The synthesis of enantiomerically pure or enriched 1-aryl alcohols is an important endeavor because they are widely used as chiral building blocks in organic synthesis. Over the past two to three decades, both Rh(I)-catalyzed asymmetric hydrosilylation of arylketones[1] and hydroboration/oxidation of styrenes[2] have been shown to be alternative routes to these compounds. In the case of the hydrosilylation reaction, exceedingly mild conditions are used as compared to the corresponding

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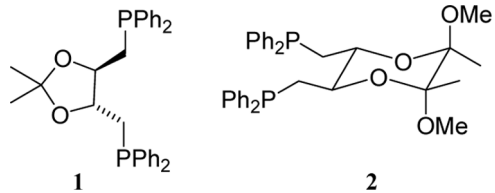
hydrogenation, thus making this an attractive alternative method to access enantiomerically enriched 1-aryl alcohols. In the late 1980s, Nishiyama and Itoh made a significant breakthrough with the introduction of the PyBox ligand system.[3]

The asymmetric hydroboration/oxidation of olefins pioneered by Burgess in the late 1980s using chiral Rh(I) catalysts is another alternative, simple, yet efficient approach to enantiomerically enriched 1-arylalcohols.[4] Burgess used both 4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane (DIOP) **1** (Fig. 1) and 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) as chiral diphosphines in these studies, but observed in the case of styrene substrates that the ees were modest with a maximum ee of 27% using α-methylstyrene. By using an analogous Rh(I) catalyst with BINAP, Hayashi and Ito improved the ees for styrene and derivatives.[5] ChiraPhos,[6] Josiphos,[7] 1-(2-diphenylphosphino-1-naphthyl)-isoquinoline (QUINAP),[8] and 2-(2′-diphenylphosphino-4′,6′-di-tert-butyl-1′-phenyl)-3-methylpyridine (PYPHOS)[9] have also afforded good results.

Unfortunately, in most cases these ligands are difficult to prepare and/or expensive, necessitating the discovery of less expensive alternatives or the reemployment of cheaper ones with a good track record in other asymmetric processes.

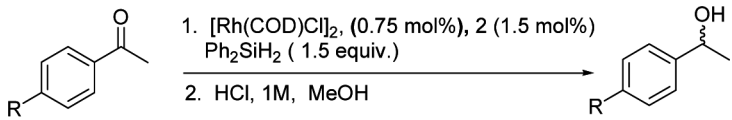
With a view to re-employing "reliable" known chiral ligands in catalytic asymmetric synthesis, we have recently successfully employed Berens DIOP analog **2**[10] (Fig. 1)—which has enjoyed considerable success for catalytic asymmetric hydrogenations[11]—in a series of catalytic asymmetric alkylations.[12] These encouraging results led us to investigate the potential of **2** in Rh(I)-catalyzed arylketone hydrosilylations and the hydroboration/oxidation of styrenes leading to 1-arylethanol products. In this article, we report our results on the application of in situ prepared Rh(I) catalysts derived from **2** for these asymmetric catalytic applications.



1 **2**

Figure 1. Tartaric acid–derived C_2-symmetric diphosphines.

Table 1. Rh-catalyzed asymmetric hydrosilylations of acetophenones **3** and **4** with ligand **2**



3 R = H
4 R = OMe

5
6

Entry	Substrate	Solvent	Temp (°C)	Time (h)	Conv.[a] (%)	Ee[b] (%)
1	**3**	Toluene	0	40	44	6 (*S*)
2	**3**	THF	0	45	43	19 (*S*)
3	**3**	CH_2Cl_2	25	42	50	29 (*S*)
4	**3**	Et_2O	25	21	60	21 (*S*)
5	**3**	Benzene	25	21	76	28 (*S*)
6	**3**	DCE	25	17	64	49 (*S*)
7	**3**	MeCN	25	22	9	38 (*S*)
8	**3**	DME	25	21	65	41 (*S*)
9	**3**	DCE	85	15	74	41 (*S*)
10	**3**	DCE	50	15	81	41 (*S*)
11	**3**	DCE	0	21	14	36 (*S*)
12	**3**	DCE	−30	6	11	30 (*S*)
13	**4**	THF	25	25	58	54 (*S*)
14	**4**	DME	25	25	33	50 (*S*)
15	**4**	Toluene	25	15	20	65 (*S*)

[a]Determined by GC.
[b]Determined by GC using a Cyclodex B capillary column.

RESULTS AND DISCUSSION

Rh(I)-Catalyzed Asymmetric Hydrosilylations

A number of Rh(I)-catalyzed hydrosilylations were carried out with acetophenone **3** and 4-methoxyacetophenone **4** under standard conditions[13] (Table 1). A number of satisfactory ees were obtained (38–65%). It was the more bulkier 4-methoxyacetophenone **4** that gave the best ees (Table 1, entries 13–15, 50–65%). (*S*)-1-Phenylethanol **5** and (*S*)-1-(4-methoxyphenyl)ethanol **6** were the major enantiomers. No solvent effects on ee were discernable, as both coordinating and non-coordinating solvents gave similar results. On lowering the reaction temperature, instead of an increase in ee (as anticipated), there was a slight decrease (Table 1, entries 10–12). We next focused our attention on Rh(I)-catalyzed asymmetric hydroboration/oxidation reactions.

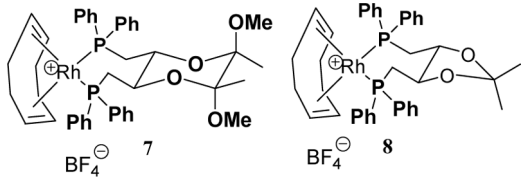


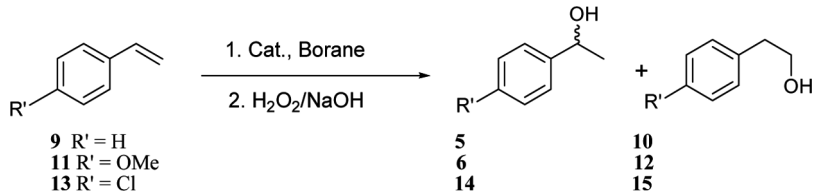
Figure 2. Cationic Rh(I) diphosphine complexes screened in the hydroboration of vinylarenes.

Rh(I)-Catalyzed Asymmetric Hydroboration/Oxidation of Styrenes

Our initial studies started with the hydroboration of styrene and derivatives using the pre-prepared cationic rhodium catalysts **7** and **8** (Fig. 2, Scheme 1), which were obtained by reacting $Rh(COD)_2BF_4$ with Berens' diphosphine **2** and DIOP **1** in 85% and 52% yields, respectively.[14] Various conditions were tested but only a maximum ee of 16% was obtained despite excellent regioselectivities and conversions.

We also reacted ligands **1** and **2** with $[Rh(\mu\text{-Cl})(COD)]_2$ to form the active catalyst in situ. The cheapness of $[Rh(\mu\text{-Cl})(COD)]_2$ relative to the corresponding $Rh(COD)_2BF_4$ catalyst was the main impetus behind this study. In this series of experiments, catecholborane (CatBH) (Table 2) and pinacolborane (PinBH) (same quantities as indicated in Table 2) were used.

In this study, enantioselectivities superior to those obtained with preformed complexes **7** and **8** were obtained for styrene (ees of 30–62%, Table 2, entries 3 to 6). This was also observed by Fernandes's group in their studies, but no explanation was given.[15] It was the reaction using ligand **2** that gave the higher ees as expected. Substrates **11** and **13** gave very low enantioselectivities. With styrene **9** at rt, (*S*)-**5** was slightly preferred (Table 2, entries 1 and 2), but interestingly, when the temperature was lowered to 0 °C or to −78 °C, the major enantiomer became (*R*)-**5** for ligand **2** (Table 2, entries 5 and 6). The precise explanation for this is not known at this juncture, but perhaps the active chiral catalyst lifetime is



Scheme 1. Catalytic asymmetric hydroboration/oxidation of some styrene substrates.

Table 2. Hydroborations of styrenes **9**, **11**, and **13** using in situ generated neutral catalysts derived from **1** and **2**[a]

Entry	Olefin (mol%)	Ligand	Borane	Temp.	Conv. (%)[b]	Branched–linear[b] (% major)	Ee (%)[c,d]
1	9	2	CatBH	rt	26	1:1.6 (62%)	3 (*S*)
2	9	1	CatBH	rt	38	1:3.4 (77%)	2 (*S*)
3	9	1	CatBH	0 °C	58	1.4:1 (58%)	30 (*S*)
4	9	1	CatBH	−78 °C	72	2.6:1 (72%)	32 (*S*)
5	9	2	CatBH	0 °C	72	2.6:1 (72%)	52 (*R*)
6	9	2	CatBH	−78 °C	75	3.1:1 (76%)	62 (*R*)
7	11	2	CatBH	rt	66	1.2:1 (55%)	18 (*S*)
8	13	2	CatBH	rt	21	1:3.7 (79%)	<2 (*S*)
9	13	1	CatBH	rt	22	1:3.5 (77%)	<2 (*S*)

[a]Standard conditions: vinyl arene/CatBH/ligand/pre-catalyst 1/1.1/0.027/0.013 in THF, rt, ca. 15 h.

[b]Determined by GC analysis.

[c]The percentage ee of the branched alcohol was determined by chiral GC analysis (on a cyclosil-B capillary column).

[d]The major isomer is indicated in parentheses.

enhanced at these temperatures or a more constrained metal complex is present.[15] With 4-methoxystyrene **11**, this switch did not occur.

The regioselectivities were generally inferior to those obtained using catalysts **7** and **8**[14] (a maximum of 90% was achieved using PinBH with **9** (not shown in Table 2), and although at rt 2-phenylethanol **10** was preferred, on lowering the temperature to 0 °C and to −78 °C, it was (*S*)-**5** that was preferred. In the case of 4-methoxystyrene **11**, the opposite effect was observed. With 4-chlorostyrene **13**, the linear regioisomer **15** was preferred at rt with both **1** and **2** (Table 2, entries 8 and 9).

The substrate conversions were not as high as those achieved with the preformed catalysts **7** and **8**[14]: a maximum conversion of 66% was achieved. 4-Chlorostyrene **13** gave modest conversions (21 and 22%, for ligands **2** and **1**, respectively) at rt.

On comparing the effectiveness of CatBH with PinBH at rt with 4-methoxystrene **11**, one can see that the branched regiosomer **6** was preferred with the former, while the linear regioisomer **12** was preferred with the latter hydroborating reagent. Attempts at obtaining and characterizing the active neutral complex formed between **2** and $[Rh(\mu\text{-}Cl)(COD)]_2$ were unsuccessful.

In the case of the hydrosilylation reaction of simple aromatic ketones, Berens ligand **2** has potential as the corresponding 1-arylethanols

were obtained with reasonable ees. With regards to the vinylarene hydroborations leading to 1- and 2-arylethanols, we obtained some promising ees (a maximum of 62% was obtained). We are currently exploring these complexes and derivatives in other asymmetric catalytic transformations.

EXPERIMENTAL

General Methods

All reagents were obtained from Aldrich, Fluka, Alfa Aesar, or Acros. Solvents were dried using common laboratory methods.

Gas chromatographic (GC) analyses of the products were performed on a Hewlett Packard (HP) 6890 series instrument equipped with a cyclodex-B and cyclosil-B capillary column (30 m, 250 μm, 0.25 μm) (Agilent 112–2532). In all cases, the conversions were determined by determining the ratio of the peak areas for the ketone or olefin substrates and of the 1-arylethanol and 2-arylethanol product in the hydroboration reactions. The configurational assignments for the chiral alcohol products were made on comparison with literature values.[16,17]

The ^{1}H NMR spectra were recorded on a Bruker AMX300, a Varian 300, a Bruker Avance 400, and a Mercury 400 instrument using $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were recorded on a VG Autospec M (Waters-Micromass) spectrometer using the FAB technique. Infrared (IR) spectra were measured with a Perkin-Elmer Paragon 1000 model. Microanalysis was performed on a Carlo-Erba EA 1108 instrument.

The catalytic asymmetric hydrosilylation reactions were conducted using standard conditions.[13]

Catalytic Hydroboration/Oxidation Reactions

The ligand (0.045 mmol) was added to $[Rh(\mu\text{-}Cl)(COD)]_2$ (11.1 mg, 0.022 mmol) in THF (2 ml). After stirring for 10 min, the vinylarene substrate was added (0.2 ml, 1.5 mmol) along with the borane (1.1 equiv., 1.65 mmol), and the mixture was stirred for 4 h. Afterward EtOH (2 ml), aqueous NaOH (2 M, 2 ml), and aqueous H_2O_2 (30%, 2 ml) were added, and the reaction mixture was left stirring overnight.

The reaction mixture was extracted with Et_2O (3×20 ml), and the organic phase washed with a 2 M aqueous NaOH solution (20 ml), water (20 ml), and brine (20 ml). The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product, which was analyzed by gas chromatography (GC).

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