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Ruthenium-Catalysed Hydrogenation of Aromatic Ketones using Monodentate Phosphoramidite Ligands

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Abstract: A ruthenium pre-catalyst containing two equivalents of the bulky monodentate phosphoramidite 3,3'-dimethyl-PipPhos and one equivalent of a chiral diamine such as 1,2-diphenylethylenediamine or 1,2-diaminocyclohexane was used for the asymmetric hydrogenation of aromatic ketones. A range of substituted and unsubstituted aryl alkyl ketones was hydrogenated using only 0.1 mol% of this catalyst with full conversions and enantioselectivities up to 97%. The phosphoramidite and diamine ligands

matched when both had the same configuration, i.e., *S*-phosphoramidite with *S,S*-diamine. In that case the product was obtained with high enantioselectivity and the *R*-configuration. The mismatched case produced the product in lower *ee*. The product configuration was determined by the configuration of the diamine ligand. A mechanistic proposal was made.

Keywords: asymmetric hydrogenation; homogeneous catalysis; ketones; phosphoramidites; ruthenium

Introduction

Asymmetric hydrogenation has blossomed into a mature technology, both on the laboratory scale as well as in production.^[1] For the reduction of aromatic ketones, the [Ru(PP)(NN)Cl₂] catalyst (PP = chiral bis-phosphine such as BINAP, NN = chiral diamine such as 1,2-cyclohexanediamine) developed by Noyori and co-workers remains the golden standard.^[2] It is a highly enantioselective catalyst, which in addition is very fast, allowing its economic use in production. After Noyori's seminal publications a range of similar catalysts were developed in which BINAP was replaced by other bisphosphines.^[3,4] The asymmetric hydrogenation of aliphatic ketones has remained more problematic, with most ketones being reduced with low to medium enantioselectivities.^[5] The use of alcohol dehydrogenases (ADH) for the enantioselective reduction of ketones has made remarkable progress in the last decade, and now can be considered the method of choice for the enantioselective reduction of aliphatic ketones.^[5]

Until the year 2000 the use of bidentate ligands was considered a *conditio sine qua non* in asymmetric hy-

drogenation reactions. In that year three groups separately introduced the first examples of the use of chiral monodentate phosphorus ligands in rhodium-catalysed asymmetric hydrogenation. Pringle and co-workers developed the use of monodentate phosphonites,^[6] Reetz and co-workers developed the use of monodentate phosphites^[7] and we have developed the use of monodentate phosphoramidites.^[8] These ligands were all used in the hydrogenation of C=C double bonds, obtaining very good results (fast reactions and *ees* > 99%). By now these ligands are well accepted and have proven their usefulness on a range of different substrates.^[9] In our patent on the use of rhodium and ruthenium phosphoramidite complexes for asymmetric hydrogenation we have shown the first examples of the use of a ruthenium(bis-MonoPhos)(diamine) dichloride complex as a ketone hydrogenation catalyst with moderate *ees*.^[10] Better results were obtained by Wills and co-workers who tested a range of BINOL-based monodentate ligands in ruthenium-catalysed aromatic ketone hydrogenation.^[11] Full conversion and excellent *ees* (up to 99%) were reached in the hydrogenation of acetophenones, using the monodentate phosphonite ligand BrXuPhos

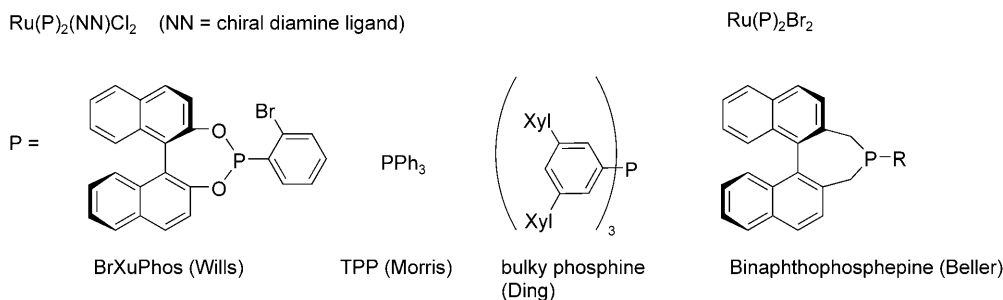


Figure 1. Ruthenium catalysts based on monodentate ligands for asymmetric ketone hydrogenation.

(Figure 1) in combination with 1,2-diphenylethylene-1,2-diamine (DPEN) (denoted as NN in Figure 1).

Morris replaced the BINAP in Noyori's Ru-complex by two monodentate triphenylphosphine ligands. With this catalyst he obtained 60% *ee* in the asymmetric hydrogenation of acetophenone.^[12] Ding substantially improved this catalyst by using very bulky triarylphosphines.^[13] Using tris(3,5-dixylylphenyl)phosphine in combination with the chiral diamine DPEN they reached up to 95% *ee* in the Ru-catalysed hydrogenation of acetophenone. Beller tested a range of monodentate phosphorus ligands in the Ru-catalysed asymmetric hydrogenation of β -keto esters. Best results were obtained with the bis-naphthyl-based phosphepine ligands they had developed earlier.^[14]

Here we report on the use of monodentate phosphoramidites in the Ru-catalysed asymmetric hydrogenation of acetophenones. A clear advantage of the use of phosphoramidite ligands is their easy accessibility. They can be made from the BINOLs in a very simple two-step procedure and virtually any amine or aniline can be used to make a ligand.^[15] In contrast, ligands like BINAP or the monodentate ligands described by the groups of Ding and Beller all require a difficult multi-step synthesis. The ease of synthesis of the phosphoramidites has allowed the development of a protocol for their parallel synthesis in the robot. This enabled the synthesis of 96 ligands in a single day followed by their testing in hydrogenation the next day.^[16] Finally, because of their monodentate nature, it is possible to synthesise catalysts that contain two different ligands. This tremendously increases the available diversity.^[17,18] A mixed phosphoramidite/phosphine rhodium catalyst is used by DSM in a ton-scale process.^[19]

Results

For the preparation of the phosphoramidite-based catalysts we followed the procedure of Noyori.^[2] Thus, the pre-catalyst was made by heating $[\text{RuCl}_2(\text{cymene})]_2$ with four equivalents of MonoPhos (**1a**) for 3 h in DMF at 90 °C. This resulted in the forma-

tion of a complex, which displayed a single peak in the ³¹P NMR at 148.8 ppm which we tentatively assign the structure $[\text{Ru}(\mathbf{1})_2(\text{DMF})_n\text{Cl}_2]$. After three hours, a chiral 1,2-diamine or another auxiliary ligand was added and this mixture was left stirring at room temperature overnight. The structure of the resulting complex will be discussed later. After removal of the solvent the complex was used directly without further purification in the hydrogenation reactions. In initial experiments, we screened a limited number of ligands **1a–d** and **2** (Figure 2), a limited number of auxiliary ligands (Figure 3), bases and solvents.

These experiments were carried out on a 1-mmol scale in well-stirred vials in an autoclave at 50 bar H₂. Some experiments were performed on 10-mmol scale directly in the autoclave. The first experiments used

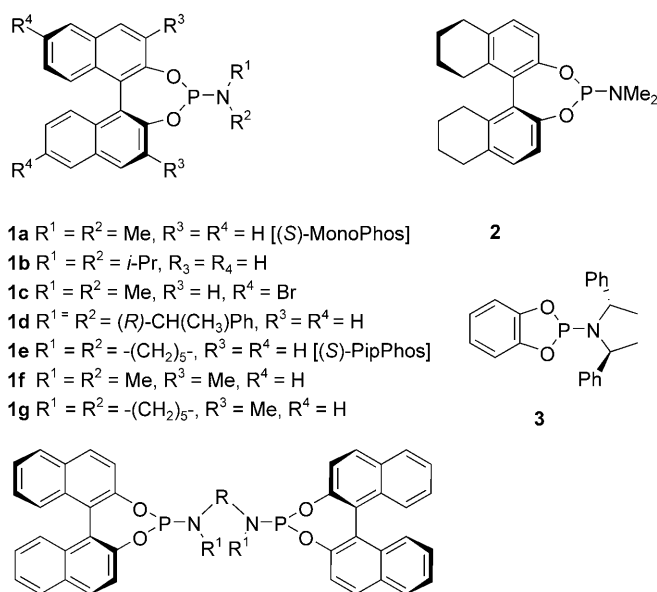


Figure 2. Monodentate and bidentate phosphoramidite ligands.

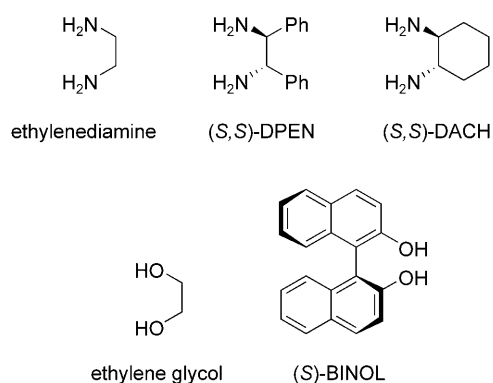


Figure 3. Diamines and other auxiliary ligands.

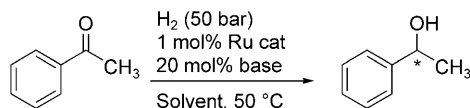
the catalyst based on MonoPhos **1a** and were performed in MeOH as solvent using K_2CO_3 as base.

Use of ethylenediamine as auxiliary ligand gave near complete conversion in 4 h but the product 1-phenylethanol was obtained in disappointingly low *ee* (Table 1, entry 1). Better results were obtained using (S,S)-1,2-diphenylethylenediamine. Not only is the reaction much faster, but the *ee* also increased to 58%. Using the diamine with the reversed configuration leads to a similar *ee*, however, the configuration of the product has also reversed. These 3 experiments suggest that the diamine plays a dominant role in the determination of the enantioselectivity and that the chirality of the phosphoramidite is only of minor im-

portance. The catalyst was not very soluble in non-polar solvents such as dichloromethane and EtOAc leading to negligible conversions (entries 4, 5).

To rule out the possibility that the solubility of the base also plays a role, we also tested Cs_2CO_3 as base; this did not improve matters (entry 5). Surprisingly, use of NMP also led to poor conversions; in this case the coordinative nature of the solvent may be the culprit. Thus, protic solvents such as methanol and 2-propanol (entries 7, 8) turn out to be the best for these hydrogenations. Potassium bases seem best; rate and *ee* were lower when Cs_2CO_3 was used (entry 7). $KO-t-Bu$ also is an excellent base for this reaction (entry 8). Although only two equivalents of base are needed to convert the dichloride into the dihydride, Noyori and co-workers have shown that an excess may lead to increased rate; hence the 5- to 20-fold excess in most experiments.^[20] Gratifyingly, the bis-(isopropyl)amine-based phosphoramidite **1b** in combination with (S,S)-DPEN led to an improved *ee* of 67% (entry 9). Here we see a clear match/mismatch effect with respect to the *ee* (entries 9, 10). Again, the configuration of the product changed with the configuration of the diamine used. Use of ligand **1c** containing 6,6'-dibromo substituents on the BINOL gave similar results as with ligand **1a** (entries 11, 12). Use of the octahydro-BINOL-based ligand **2** led to 60% *ee* in the case of the matched ligands; the mismatched combination led to only 39% *ee* (entries 13, 14). Use of ethylene glycol or BINOL as auxiliary ligand in

Table 1. Initial screening of ligands and conditions in the Ru-phosphoramidite-catalysed hydrogenation of acetophenone.^[a]

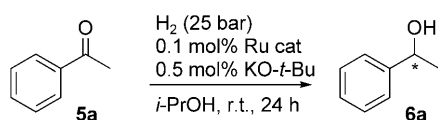


Entry	Ligand	Auxiliary Ligand	Base	Solvent	<i>t</i> (h)	Conv. [%]	<i>ee</i> [%]
1	1a	ethylenediamine	K_2CO_3	MeOH	4	95	9 (<i>S</i>)
2	1a	<i>S,S</i> -DPEN	K_2CO_3	MeOH	0.75	93	58 (<i>R</i>)
3	1a	<i>R,R</i> -DPEN	K_2CO_3	MeOH	2.5	95	56 (<i>R</i>)
4	1a	<i>S,S</i> -DPEN	K_2CO_3	CH_2Cl_2	2.5	0	–
5	1a	<i>S,S</i> -DPEN	Cs_2CO_3	EtOAc	22	2	–
6	1a	<i>S,S</i> -DPEN	K_2CO_3	NMP	16	3	–
7	1a	<i>S,S</i> -DPEN	Cs_2CO_3	<i>i</i> -PrOH	22	18	47 (<i>R</i>)
8	1a	<i>S,S</i> -DPEN	$KO-t-Bu$	<i>i</i> -PrOH	16	100	52 (<i>R</i>)
9	1b	<i>S,S</i> -DPEN	K_2CO_3	MeOH	2.5	98	67 (<i>R</i>)
10	1b	<i>R,R</i> -DPEN	K_2CO_3	MeOH	0.5	53	52 (<i>S</i>)
11	1c	<i>S,S</i> -DPEN	K_2CO_3	MeOH	1	49	57 (<i>R</i>)
12	1c	<i>R,R</i> -DPEN	K_2CO_3	MeOH	1	50	55 (<i>S</i>)
13	2	<i>S,S</i> -DPEN	K_2CO_3	MeOH	3.8	94	60 (<i>R</i>)
14	2	<i>R,R</i> -DPEN	K_2CO_3	MeOH	0.5	39	39 (<i>S</i>)
15	1a	ethylene glycol	K_2CO_3	MeOH	16	59	1
16	1a	<i>S</i> -BINOL	K_2CO_3	MeOH	2.5	16	15

^[a] *Conditions*: reaction on 1-mmol scale in 5 mL of solvent, S/C=100.

^[b] All ligands were made from BINOLs with the *S*-configuration.

^[c] 10 mol% of $KO-t-Bu$, S/C=1000 was used.

Table 2. Ligand screening in the asymmetric hydrogenation of acetophenone.^[a]

Entry	Ligand	Diamine	Conv. ^[c] [%]	ee ^[c] [%]
1	3	DPEN	40	rac
2	4a	DPEN	20	10
3	4b	DPEN	50	12
4	4c	DPEN	13	41
5	1d ^[c]	DPEN	100	41
6	1e	DPEN	100	52
7	1e	DACH	100	55
8	1e	ethylenediamine	100	34
9	1f	DPEN	100	90
10	1g	DPEN	100	97
11	1g	DACH	100	97
12 ^[d]	1g	DACH	0	–
13	BINAP	DPEN	100	87

^[a] Experiments were performed in the Endeavor apparatus on 2-mmol scale in 4 mL solvent.

^[b] All experiments were performed with (*R*)-BINOL-based ligands and (*R,R*)-diamine, unless noted otherwise. This combination leads to the product with the *S*-configuration.

^[c] (*S,RR*)-**1d** was used in combination with (*S,S*)-DPEN.

^[d] Transfer hydrogenation experiment.

^[e] Conversion and *ee* were determined by chiral GC.

combination with MonoPhos **1a** resulted in low enantioselectivities (entries 15, 16).

Having thus established that protic solvents, potassium bases and diamine auxiliary ligands are the best we continued screening more monodentate and bidentate phosphoramidite ligands and this time also included enantiopure 1,2-cyclohexanediamine as auxiliary ligand. (Table 2). These screening experiments were all performed at ambient temperature with a substrate/catalyst ratio (*S/C*) of 1000 in *i*-PrOH using KO-*t*-Bu as base.

Use of ligand **3**, in which the chirality stems solely from the amine part and in which the BINOL has been replaced by catechol, in combination with (*R,R*)-DPEN led to a relatively slow reaction; the product alcohol was obtained in racemic form (entry 1).^[21] Next, we tested three bidentate phosphoramidite ligands (entries 2–4). Again, slow reactions ensued and the enantioselectivities ranged from low to moderate. This is comparable to the results in the rhodium-catalysed asymmetric hydrogenation of *N*-acylated dehydroamino acids, where use of these ligands also led to slow rates and very low enantioselectivities.^[8a]

As the improvement obtained going from ligand **1a** to ligand **1b** suggested that bulk on the amino sub-

stituent could be beneficial we tested ligand **1d** containing the bulky bis-1-phenylethylamino group. Gratifyingly, full conversion was obtained, although the enantioselectivity was a disappointing 41% (entry 5). PipPhos (**1e**) has been an extraordinary successful ligand in the Rh-catalysed hydrogenation of enamides.^[22] In the hydrogenation of acetophenone using DPEN or DACH as auxiliary ligand full conversion was achieved with a product *ee* of 51% (entries 6, 7). Use of ethylenediamine instead of DPEN did not improve matters, and the product was obtained with 34% *ee* (entry 8). Next, we examined ligands in which the cone angle has been substantially increased by the presence of methyl substituents in the 3 and 3' positions. Use of 3,3'-dimethyl-MonoPhos **1f** in combination with DPEN led to full conversion and we obtained the product in 90% *ee* (entry 9). Although this is already very good, by using 3,3'-dimethyl-PipPhos **1g** we could further improve upon this result. This ligand has been used with great success in the asymmetric hydrogenation of α -alkylated cinnamic acids culminating in its application in a ton-scale production process of an intermediate for the blood pressure-lowering agent AliskirenTM.^[19] In the present study this ligand also turned out to be the key to success as the product, 2-phenylethanol, could be obtained in 97% *ee* with both DPEN or DACH as auxiliary ligands (entries 10, 11). Considering that the use of 2-propanol could lead to product formation *via* transfer hydrogenation we performed a control experiment without hydrogen to verify this (entry 12). No conversion ensued after overnight reaction at room temperature, establishing that this is a true hydrogenation reaction. These results compare well with the experiment in which BINAP was used as a ligand and in which only 87% *ee* was obtained (entry 13). It should be noted of course that using other BINAP analogues or other bidentate bisphosphines can also lead to very high enantioselectivities.^[3]

Having thus established the good performance of the ruthenium catalyst based on **1g** with DACH or DPEN as auxiliary ligands we established the scope of its application by screening a range of substituted and unsubstituted aromatic ketones (Table 3). We found that especially the *para*- and *ortho*-substituted acetophenones are hydrogenated very well using this system (entries 2, 4). No conversion was obtained with *o*-hydroxyacetophenone (entry 3). The acidic functionality presumably protonates the amido ligand of the active catalyst. Both electron-withdrawing as well as electron-donating substituents were well tolerated at the *para*-position and *p*-chloro- and *p*-methoxy-substituted 1-phenylethanol were obtained with excellent *ees* (entries 5, 6).

meta-Substituted acetophenones were hydrogenated in good yield, although the enantioselectivity of the product alcohols was somewhat lower (en-

Table 3. Results of hydrogenation reactions using different substrates.^[a]

Entry	R ¹	R ²	Alcohol	Conv. ^[b] [%]	ee ^[c] [%]
1	H	Me	6a	100	97
2	2-Me	Me	6b	100	97
3	2-OH	Me	6c	0	–
4	2-OMe	Me	6d	100	96
5	4-OMe	Me	6e	100	97
6	4-Cl	Me	6f	100	95
7	3-Br	Me	6g	100	65
8	3-Cl	Me	6h	100	83
9	3-OMe	Me	6i	< 10	–
10	3,5-CF ₃	Me	6k	100	95
11	1-acetonaphthone		8a	100	93
12	2-acetonaphthone		8b	100	94
13	H	C ₂ H ₅	6l	100	91
14	H	<i>n</i> -Pr	6m	100	93
15	H	<i>i</i> -Pr	6n	< 10	–
16	H	CH ₂ Cl	6o	< 10	–
17	H	CF ₃	6p	< 10	–

^[a] For conditions see Table 2. All hydrogenations were performed using (*R*)-**1g** in combination with (*R,R*)-DACH leading to the *S*-products.

^[b] Conversions were determined *via* ¹H NMR.

^[c] The *ees* were determined *via* chiral GC.

tries 7,8). Surprisingly, *m*-methoxyacetophenone was a poor substrate and only 10% conversion was obtained after overnight reaction (entry 9). Gratifyingly, the hydrogenation of 3,5-bis(trifluoromethyl)acetophenone yielded the alcohol in 100% conversion and 95% *ee*. This alcohol is an intermediate for the antiemetic AprepitantTM (entry 10).^[23] Both 1- and 2-acetonaphthones were hydrogenated with excellent *ee* (entries 11, 12). Although propiophenone (entry 13) and butyrophenone (entry 14) were hydrogenated with very high enantioselectivity, surprisingly, 2-methylpropiophenone was a sluggish substrate (entry 15). Also electron-withdrawing substituents on the 2 position of acetophenone led to poor conversions (entries 16, 17).

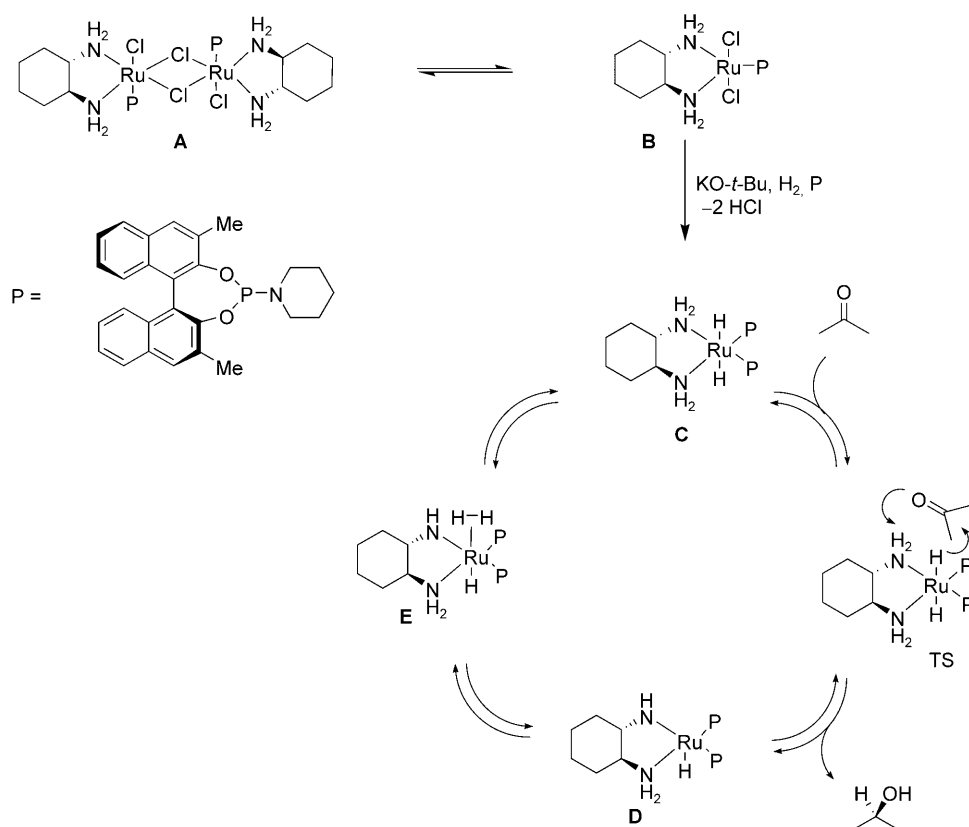
Mechanistic Aspects

Reaction of [RuCl₂(*cymene*)₂] with four equivalents of MonoPhos (**1a**) for 3 h in DMF at 90 °C results in the formation of a complex which displayed a single peak in the ³¹P NMR at 148.8 ppm which we tentatively assign the structure [Ru(**1**)₂(DMF)_{*n*}Cl₂]. The ¹H NMR shows broad absorptions and no X-ray struc-

ture could be obtained. After three hours, a chiral 1,2-diamine or another auxiliary ligand was added and this mixture was left stirring at room temperature overnight. The resulting product shows two signals in the ³¹P NMR at 147.7 (free **1a**) and at 172.2. This latter peak presumably belongs to the ruthenium complex. Similar results were obtained when using 3,3'-dimethyl-PipPhos (**1g**). We observe a single peak for [Ru(**1g**)₂(DMF)_{*n*}Cl₂] at 149 ppm and two peaks after reaction with DACH, one of which is from **1g** at 147.2 ppm and the other at 173.4 ppm, which we ascribe to the ruthenium complex. As the presence of a rather large residual ligand peak suggests that the complex contains only a single phosphoramidite ligand per ruthenium, we repeated the entire procedure with only 1 equivalent of **1g** per ruthenium and indeed, in this case a product was obtained which showed mostly the peak in the ³¹P NMR at 173.4 ppm with only small amounts of **1g** showing up. Unfortunately, extensive attempts to establish the exact structure of this complex failed on account of its instability upon attempted isolation. In several crystallisation attempts, products were obtained that, surprisingly, had lost large amounts of the phosphoramidite. Several attempts to obtain electrospray mass spectra also failed to give meaningful results, although several peaks were observed that clearly belong to a dimeric ruthenium species. From the stoichiometry of the experiments only a limited number of structures would seem to be possible. These could be either dimeric or monomeric [Ru(P)(NN)Cl₂] (structures **A** and **B** in Scheme 1). Previously, we have shown that reaction of bulky 3,3'-disubstituted phosphoramidites with dimeric [Ir(COD)Cl]₂ leads to formation of [Ir(COD)(P)Cl], irrespective of the amount of phosphoramidite ligand.^[24] This iridium catalyst was highly active and enantioselective for the asymmetric hydrogenation of *N*-acylated dehydroamino esters.

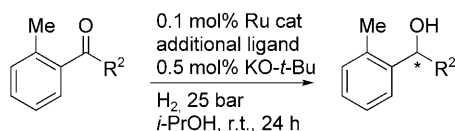
To gain more information about the true nature of the catalytically active species, we performed a range of experiments (Table 4). First, hydrogenation of *o*-methylacetophenone using the precatalyst with Ru/**1g**=1 led to formation of the alcohol in 75% *ee* (entry 1). Addition of an additional 0.5 equivalents of **1g** to the 1: 1 complex gave the product in 90% *ee* and finally addition of 1.0 equivalent of **1g** led to full restoration of the *ee* to 97% as in the original procedure (entries 2, 3). Addition of more than one equivalent of **1g** led to a reduction of *ee* again (entry 4).

It is also possible to add a different ligand, which we illustrated by the addition of 0.5 and 1.0 equivalent of PPh₃ (entries 5,6). Surprisingly, this led to lower rates and enantioselectivities, which is in stark contrast to our results with rhodium where the rate increased in all cases.^[18b] These experiments suggest that although in the precatalyst the ruthenium complex contains only a single phosphoramidite ligand, in



Scheme 1. Proposed mechanism for the asymmetric hydrogenation of ketones

Table 4. Hydrogenation results using the putative $[\text{RuCl}_2(\mathbf{1g})(\text{DACH})]_n$ as catalyst precursor.



Entry	Extra equiv. of ligand	Conv. [%]	ee [%]
1	0	100 (18 h)	75
2	0.5 of 1g	100 (17 h)	90
3	1.0 of 1g	100 (16 h)	97
4	1.5 of 1g	100 (14 h)	89
5	0.5 of PPh_3	50 (24 h)	31
6	1.0 of PPh_3	50 (24 h)	38

the active and enantioselective catalyst 2 equivalents of **1g** are bound to ruthenium. We propose a mechanism, similar to the mechanism described by Morris and co-workers for asymmetric hydrogenations with $[\text{Ru}(\text{PPh}_3)_2(\text{DPEN})\text{Cl}_2]$, in which the ultimate catalyst that reacts with the ketone is a ruthenium dihydride (structure **C** in Scheme 1).^[25]

It is conceivable that although the dichloride (**A** or **B**) is too sterically encumbered to accommodate two bulky phosphoramidites this is less problematic for

the dihydride **C**. Thus, once the precatalyst has been converted into the dihydride by the action of $\text{KO-}t\text{-Bu}$ and H_2 , the second phosphoramidite can bind to the ruthenium. The resulting dihydride **C** reacts with the ketone in a six-membered transition state (**TS**), similar to the Morris mechanism. The resulting 16 electron complex **D** reacts with hydrogen to form the dihydrogen complex **E** which reconverts to the dihydride **C**.

A preliminary examination of the reaction kinetics seems to confirm the reaction is zero order in substrate as in the Morris mechanism (Figure 4). In this experiment a turnover frequency of 50 h^{-1} was reached. Higher rates can probably be obtained at 50°C .

Conclusions

In conclusion, we have developed a catalyst that is able to hydrogenate a wide range of aryl alkyl ketones with high enantioselectivities using only 0.1 mol% in methanol or 2-propanol. The precatalyst is in essence a ruthenium dichloride complex containing one 3,3'-dimethyl-PipPhos ligand and one chiral diamine or possibly a dimer thereof. It is proposed that during treatment with $\text{KO-}t\text{-Bu}$, an extra equivalent

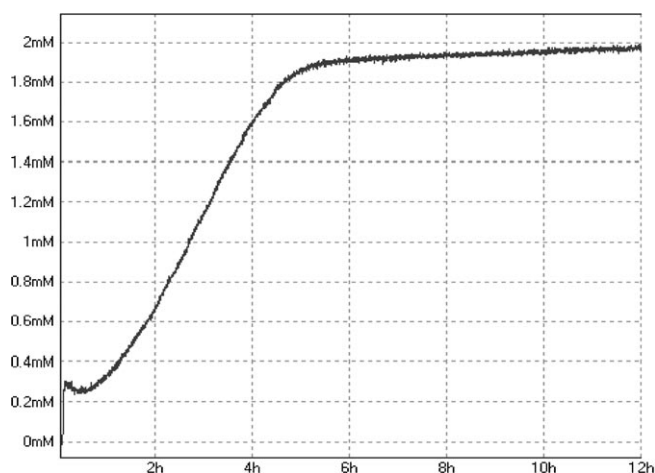


Figure 4. Hydrogen uptake curve of the hydrogenation of acetophenone with $[\text{Ru}(\mathbf{1g})_2(\text{DPEN})\text{Cl}_2]_n$ plus 1 equivalent of $\mathbf{1g}$ (S/C=218, room temperature, 25 bar H_2).

of $\mathbf{1g}$ and hydrogen this precatalyst is transformed into a ruthenium complex that contains two phosphoramidite ligands and one chiral diamine; presumably this is a dihydride.

Experimental Section

Ligands $\mathbf{1a}$,^[26] $\mathbf{1b}$,^[27] $\mathbf{1c}$,^[28] $\mathbf{1d-f}$,^[27] $\mathbf{1g}$,^[29] $\mathbf{2}$,^[28] $\mathbf{3}$,^[30] $\mathbf{4a}$ ^[27] and $\mathbf{4b}$ ^[31] were synthesised according to previously reported procedures from the literature.

Synthesis of the Pre-Catalyst Comprising Ru, (R)-3,3'-Dimethyl-PipPhos and (R,R)-DACH

A Schlenk flask was flame-dried and 62 mg $[\text{RuCl}_2(\text{cymene})_2]$ (0.1 mmol) and 160 mg of (R)-3,3'-dimethyl-PipPhos (0.4 mmol) were added. The Schlenk tube was degassed by three cycles of vacuum/ N_2 and then kept under N_2 and the solids were dissolved in 5 mL of dry DMF. This mixture was heated for 3 h at 90 °C. After three hours the mixture was allowed to cool down to room temperature. Subsequently, 23 mg (R,R)-DACH (0.2 mmol) was added. After overnight stirring, DMF was evaporated under reduced pressure. The resulting solid was subjected to azeotropic distillation with toluene (2 × 5 mL) and washed twice with 5 mL hexane. The obtained solid was used in hydrogenation reactions without further purification. ^{31}P NMR (162 MHz, CDCl_3): $\delta = 173.4$; ^1H NMR (400 MHz, CDCl_3): $\delta = 8.05$ (d, 1H, $J = 36$ Hz), 7.90–7.70 (m, 6H), 7.39–7.11 (m, 13H), 5.87 (dd, 2H, $J = 22$ Hz, $J = 120$ Hz), 5.85 (d, 2H, $J = 22$ Hz), 2.95–2.51 (m, 15H), 2.37–2.36 (m, 6H) 1.99–0.79 (m, 50H).

Hydrogenation Procedure

Most experiments were performed in small autoclaves in an Endeavor apparatus that can be pressurised to 25 bar. To a glass liner for an autoclave 2 mmol of substrate was added. To the substrate was added 0.1 mol% of preformed catalyst of example $\mathbf{3}$ and 10 μL of a 1 M solution of KO-*t*-Bu in *i*-

PrOH. To this 3.7 mL *i*-PrOH were added. The liner was put into one of the parallel autoclaves and subjected to three vacuum/nitrogen cycles. Then, while stirring, 25 bars of hydrogen pressure were applied. After 24 h the autoclave was carefully vented and the glass liner taken out. From the reaction mixture a sample was taken and filtered over a silica plug to prepare a GC sample. The sample containing the product alcohol was analysed by chiral GC.

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