More than 100,000 Turnovers with Immobilized Ir-Diphosphine Catalysts in an Enantioselective Imine Hydrogenation

Benoit Pugin,* Heidi Landert, Felix Spindler, Hans-Ulrich Blaser

Solvias AG, R 1055.6, P.O. Box, 4002 Basel, Switzerland
Fax: (+41)-61-6866311, e-mail: benoit.pugin@solvias.com

Received: May 15, 2002; Accepted: July 18, 2002

Dedicated to Roger Sheldon, a chemist with an amazing E(nthusiasm) factor, on the occasion of his 60th birthday.

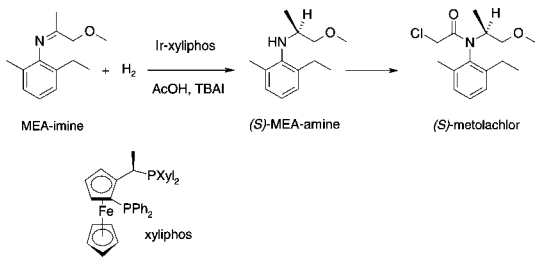
Abstract: A modular concept to prepare immobilized enantioselective catalysts is described, consisting of a functionalized xyliphos ligand covalently attached to a support *via* a linker. Immobilized xyliphos bound to silica and to polystyrene as well as soluble dimeric xyliphos and an extractable analogue were prepared and tested in the Ir-catalyzed hydrogenation of a hindered *N*-arylimine used for the production of (*S*)-metolachlor. The best heterogeneous catalyst **9b** exhibited TON's >100,000 and TOF's up to 20,000 h^{-1}, the best values so far for immobilized catalysts. The immobilized catalysts gave similar enantioselectivities but lower activities and higher deactivation rates than the homogeneous analogues. These negative effects were tentatively explained by the higher local catalyst concentration on the support surface leading to an increased tendency to deactivation by irreversible dimer formation. Separation of these catalysts by filtration and extraction is easy and efficient.

Keywords: enantioselective imine hydrogenation; extractable Ir-xyliphos; immobilized Ir-xyliphos; modular immobilization concept; silica-bound xyliphos

Introduction

One obvious drawback of homogeneous catalysts is the problem of their separation from the reaction mixture. Attachment of the active metal complexes to insoluble or water soluble carriers is an attractive strategy allowing separation by filtration or extraction.[1] However, immobilization usually affects the catalytic performance of the catalyst. Sometimes this effect is positive, e.g., when catalyst deactivation *via* dimerization is prevented by site isolation.[2a] Unfortunately, practical experience has shown that more often catalytic activity and/or selectivity decrease with immobilization. For technical applications, several requirements should be met in order to make immobilized enantioselective catalysts practically useful: Besides sufficient selectivity, easy preparation or commercial availability, relatively high activities (turnover frequency, TOF) and productivities (turnover number, TON) are required because immobilization raises catalyst costs by a factor of 2–5. The development of extremely efficient immobilized catalysts is therefore of very high importance.

Different immobilization approaches are possible and all have their advantages and disadvantages. We have chosen the covalent attachment of the metal complex at the chiral ligand *via* a suitable bifunctional linker and have found this to be a very versatile strategy to obtain catalysts bound to both organic moieties and inorganic solids.[2] Here we report on the immobilization of the Ir-xyliphos complex, a very active catalyst for the enantioselective hydrogenation of the sterically hindered MEA-imine (see Scheme 1). MEA-amine is an intermediate for *(S)*-metolachlor, the most important herbicide of Syngenta, which is presently produced on a >10,000 tons/year scale with the homogeneous complex.[3] The investigations were carried out parallel to the development of the homogeneous process in order to have a further option for catalyst separation.



Scheme 1. Structure of starting imine, products and xyliphos ligand.

  1615-4150/02/34409-974–979 $ 17.50-.50/0

Results

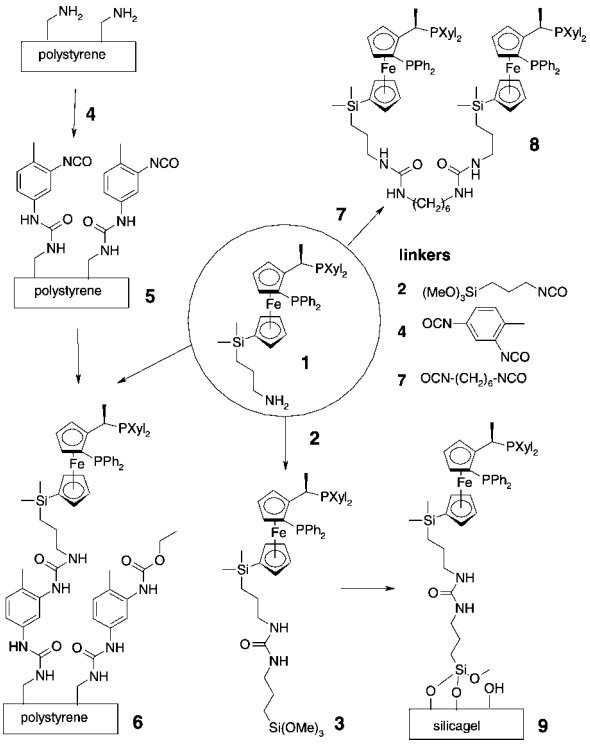
Preparation of the Functionalized and Immobilized Ligands

Over the last few years we have developed a modular system combining functionalized ligands with different supports and isocyanate linkers in order to have a systematic and quick access to a variety of immobilized chiral catalysts.[2] We have applied this modular system to immobilize xyliphos on silica gel and various organic moieties as depicted in Scheme 2.

For the preparation of the ligand immobilized on silica, we started with the functionalized xyliphos **1** carrying an amino function[4] which was reacted first with 3-isocyanato-propyltrimethoxysilane **2** to give **3** and then with silica to give **9** as described before.[2b] As support we used silica Grace 332 that gave the best results for Rh-catalyzed hydrogenations.[2b] Grace 332 has a relatively homogeneous pore size (average 19 nm), a pore volume of 1.55 mL/g and a high specific surface of 320 m^2/g. Three immobilized xyliphos ligands **9a – c** with loadings of 0.10, 0.042 and 0.013 mmol ligand/g support, respectively, were synthesized.

To prepare the polymer-bound ligand, we used commercial aminomethylated polystyrene cross-linked with 1% divinylbenzene. This support has to be swollen with an appropriate solvent (e.g., toluene) to allow adequate mass transport. Earlier work with Rh complexes immobilized on this support gave similar ee's but only about 1/10 of the activity of their homogeneous analogues.[2c] To immobilize **1** on polystyrene, the amino groups of the aminomethylated polystyrene were first reacted with an excess of 2,4-diisocyanato-toluene **4** to give the reactive polymer **5**, then the functionalized xyliphos **1** was added. The remaining isocyanate groups were reacted with an excess of ethanol to give the immobilized ligand **6** with a loading of 0.116 mmol/g.

The di-xyliphos compound **8** was prepared by reaction of **1** with 1,6-diisocyanatohexane **7** in order to simulate a high local catalyst concentration.[2a] A water extractable xyliphos **12** was made by reacting xyliphos ligand **10** carrying a chloroalkyl chain with diethyl malonate followed by hydrolysis (see Scheme 3). Under basic conditions, the functionalized ligand **12** can be extracted into the water phase.



Scheme 2. Functionalized xyliphos, linkers and immobilized ligands.

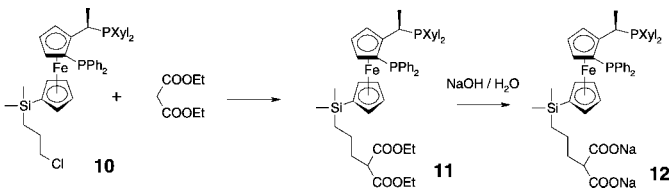
Hydrogenations

A standard protocol originally developed for the homogeneous Ir-xyliphos was used where the hydrogenation reaction is carried out in presence of acetic acid and iodide[5] (see experimental section). Table 1 summarizes a number of control experiments with the homogeneous Ir-xyliphos systems (xyliphos, functionalized xyliphos **3**, dimeric xyliphos **8**, water extractable xyliphos **12**). Table 2 shows the results with the silica and polystyrene bound Ir catalysts with xyliphos-SiO_2 **9a – c** and xyliphos-PS **6**, respectively. In all cases, the TOF values are calculated for the whole reaction time.

Discussion

The main objective of this work was to determine the limits of the performance of separable catalysts and to assess their potential in comparison with the homogeneous Ir-xyliphos system which is actually used in the production of (*S*)-metolachlor. All catalysts were tested with various substrate/catalyst ratios (s/c) between 20,000 and 120,000. In addition, some experiments were carried out to identify factors that may influence the catalytic performance.

Under our test conditions the homogeneous catalysts can be used at s/c ratios up to 120,000 with TOF's



Scheme 3. Water-soluble xyliphos ligand.

Table 1. Control experiments with the homogeneous Ir-xyliphos systems.

Entry	Ligand	s/c[a]	TOF [h^{-1}][b]	ee [%]	Comment
1.1	xyliphos	50,000	60,000	79	re-use[c]: +25,000 TON in 6.5 h
1.2	xyliphos	50,000	42,857	78	100 mg SiO_2 added (Grace 332)
1.3	xyliphos	120,000	55,385	80	
1.4	funct. xyliphos **3**	50,000	28,571	80	
1.5	extract. xyliphos **12**	120,000	36,000	79	
1.6	dimeric xyliphos **8**	50,000	4,167	n.d.	re-use[c]: +3000 TON in 3.5 h

Reaction conditions: 19.5 g MEA-imine, 2 mL acetic acid, 10 mg tetrabutylammonium iodide (TBAI), 80 bar, 25 – 30 °C, 100% conversion.
[a] Mol substrate/mol Ir.
[b] Overall TOF.
[c] Another portion of substrate was added to the hydrogenation mixture without separation of the catalyst.

Table 2. Hydrogenation with immobilized Ir-xyliphos systems.

Entry	Ligand	s/c[a]	TOF [h^{-1}][b]	ee [%]	Comment
2.1	xyliphos-SiO_2 **9b**	20,000	10,000	77	
2.2	xyliphos-SiO_2 **9b**	20,000	20,000	76	ligand/Ir = 2
2.3	xyliphos-SiO_2 **9b**	120,000	12,000	78	ligand/Ir = 2
2.4	xyliphos-SiO_2 **9b**	250,000	9,750	75	ligand/Ir = 2, 50 °C, 78% conv.
2.5	xyliphos-SiO_2 **9a**	50,000	2,146	77	93% conversion
2.6	xyliphos-SiO_2 **9b**	50,000	6,000	78	re-use[c]: no reaction in 2 h
2.7	xyliphos-SiO_2 **9c**	50,000	1,732	77	97% conversion
2.8	xyliphos-PS **6**	50,000	1,140	73	95% conversion
2.9	xyliphos-PS **6**	50,000	1,500	70	50 °C

Reaction conditions: 19.5 g MEA-imine, 2 mL acetic acid (5 mL toluene for xyliphos-PS), 10 mg TBAI, 80 bar, 25 – 30 °C, 100% conversion unless otherwise noted.
[a,b,c] See Table 1.

between 29,000 and 60,000 h^{-1} and ee's between 78 and 80%. While the TON and TOF values were significantly lower than those of the actual production process,[5] these results serve well as standards for comparison. Some comments: The Ir-xyliphos catalyst was re-used but with a significant loss in activity, furthermore the addition of silica barely affected the catalyst activity (entries 1.1 and 1.2). While in the catalytic reactions the two substituted xyliphos **3** and **12** gave similar activity as the parent ligand (entries 1.4 and 1.5), this was no longer the case for the dimeric analogue **8** (entry 1.6) which was much less active both on first and on second use.

The most important result of Table 2 is the unprecedented activity (TOF up to 20,000 h^{-1}) and productivity (TON up to 195,000) of the silica-bound catalysts (entries 2.1 – 2.4). The highest TON's/TOF's reported in the literature for covalently attached diphosphine catalysts are in the range of 10,000/2000 h^{-1} for Rh [1,6] and of 33,000/400 h^{-1} for Ru.[7] Nevertheless, compared to the very active soluble catalysts, the TOF's for the heterogenized analogs are lower by a factor of 2 – 5 while the enantioselectivities are only slightly affected. The influence of immobilization on activity and productivity becomes more pronounced with increasing s/c ratio as illustrated by entries 2.1 and 2.6. As already observed for other catalytic systems, the polystyrene-bound complexes (entries 2.8, 2.9) are much less active, maybe because mass transport is slower in the polymer matrix than in the large pores of the silica gel. In contrast to the homogeneous reactions several hydrogenations with the immobilized systems practically stopped before complete conversion and re-use seems not to be possible (compare entries 1.1 and 2.6). These results indicated that the immobilized catalysts were more susceptible to deactivation than free Ir-xyliphos catalyst and that they have a certain lifetime and gradually deactivate.

As already mentioned, we designed a number of experiments in order to find possible reasons for the lower activity (TOF's < 20,000 compared to 60,000 h^{-1} for xyliphos) as well as the faster deactivation of the immobilized catalysts. The following changes go along with the covalent binding of a homogeneous catalyst on a support:

i) Functionalization of the ligand. The additional functional groups which are in close proximity to the catalytic center may interact in a detrimental way. A comparison of the performance of xyliphos and the functionalized ligand **3** indicates that if such interactions are present they are not significant enough to account

for the lower performance of the immobilized catalysts (compare entries 1.1 and 1.4).

ii) New chemical environment. Binding a metal complex to a support can lead to interactions with surface functional groups (e.g., free OH). The fact that addition of silica gel to the homogeneous catalyst does not significantly change its performance (entry 1.2) shows that silica gel is not a strong catalyst poison. However, this result does not exclude the possibility that the close proximity of metal center and surface groups could enhance such interactions.

iii) High local catalyst concentration. The phenomenon of catalyst deactivation by irreversible formation of inactive dimers (or oligomers) is well known for Ir-diphosphine catalysts.[8–10] In a previous study with Ir-ppm and Ir-diop catalysts albeit under different reaction conditions (lower s/c, lower MEA-imine concentration, no acid, in presence of solvent), we have observed significantly higher productivities of the immobilized catalysts. This result was attributed to site isolation of the surface bound catalytic species because among other effects, the activity and productivity increased with lower catalyst loading[2a, 9]. Even though the Ir-xyliphos are known to have little tendency for deactivation, we wanted to test this hypothesis as well. For this purpose, we prepared the dimeric ligand **8** and immobilized ligands **9a – c** with varying metal loadings of 0.10, 0.042 and 0.0013 mmol/g in order to investigate the influence of the local catalyst concentration for the present system (entries 2.5 – 2.7). Even though the results are not quite conclusive because the system with 0.042 mmol/g exhibited the highest activity, there is little doubt that the local concentration does have a strong effect on catalyst activity. This was confirmed with the dimeric xyliphos ligand **8** that simulates a metal loading similar to the one of the silica bound catalysts (assuming regular distribution). Ligand **8** has a maximum length of approx. 3.6 nm. Assuming two catalyst molecules in a spherical ball with a diameter of 3.6 nm, the local catalyst concentration is about 0.15 molar. The concentration of the free Ir-xyliphos catalyst varied between $2.5.10^{-4}$ molar for s/c 20,000 and 5.10^{-5} molar for s/c 100,000. Thus, with ligand **8** a catalyst concentration is simulated that is more than 500 times higher than the free Ir-xyliphos catalyst and probably comparable to the situation on the surface of the silica. Indeed, the hydrogenation results show that catalysts with the dimeric xyliphos **8** have TON's and TOF's in the same range as xyliphos immobilized on the silica (compare entries 1.6 and 2.5 – 2.7). The fact that lowering the catalyst loading by increasing the L/M ratio from 1.2 to 2 (compare entries 2.1 and 2.2), gives significantly more active catalysts is another indication that catalyst deactivation is indeed enhanced by the proximity of the Ir complexes.

iv) Limited mass transport in pores. A rough estimation shows that the catalyst immobilized on Grace 332 with a loading of 0.1 mmol/g would have to exchange the complete pore volume in about 2 – 3 seconds. As basis we assumed a TOF of 120,000 h^{-1} as observed in the initial reaction phase for the homogeneous Ir-xyliphos, a pore volume of 1.55 mL/g and an imine concentration of 4.3 mmol/L. With a loading of 0.042 mmol/g the exchange time would be about 6 s. If this exchange rate cannot be attained, this would mean that part of the immobilized catalysts in the pores is not working. While this can explain the lower activity of the immobilized catalyst, it does not account for the observed enhanced deactivation.

At this time we favor the explanation that catalyst deactivation is enhanced by the proximity of the Ir complexes but it has to be stressed that deactivation is much less pronounced than for Ir catalysts with other diphosphines.[9] We stopped our investigations at this stage because it became clear that due to the much higher activity and productivity, the catalyst of choice for the production process would be the unfunctionalized xyliphos and that catalyst separation would be accomplished by distillation of (*S*)-metolachlor.[5]

Separation of Immobilized Catalysts

The silica gel- as well as the polystyrene-bound catalysts can be separated by simple filtration. Analysis of the Ir content revealed that in all cases > 95% of the catalyst was removed. The Ir catalyst with the water-soluble ligand **12** could be separated with > 90% efficiency by extraction into 1 N NaOH and we are confident that this can be improved if the number of carboxylic acid functions in the side chain is increased.

Conclusions

The modular concept allows us to prepare a large variety of immobilized and extractable enantioselective catalysts. The preferred support is wide pore silica whereas polystyrene is not a suitable carrier. The silica-bound and the extractable catalysts are feasible for industrial applications (TON > 100,000, TOF up to 20,000 h^{-1}). The lower activity of the immobilized catalysts is tentatively explained by the higher local catalyst concentration on the support surface leading to an increased tendency to deactivation by irreversible dimer formation. Separation of these catalysts by filtration and extraction is easy and efficient. Although these immobilized catalysts exhibit unprecedented catalyst activity and productivity, the results demonstrate that heterogenization leads to highly complex systems that are difficult to control.

Experimental Section

General

All experiments were carried out under argon. The functionalized ligands **1** and **10** were prepared as previously described.[4] Silica Grace 332 with a particle size of 35–70 μm was obtained from Grace. Aminomethylated polystyrene cross-linked with 1% divinylbenzene with 0.56 mmol amine groups/g was purchased from Novabiochem.

$(EtO)_3Si$-Xyliphos (3)

0.7 mL (2.6 mmol) of 1-triethoxysilyl-3-isocyanatopropane were slowly added to a solution of 1.5 g (1.99 mmol) of aminated xyliphos **1** in 10 mL of dichloromethane. After stirring overnight the solvent was removed under reduced pressure. Chromatography (silica gel Merck 60, hexane/ethyl acetate, 3/2) gave the pure product in 74% yield. ^{1}H NMR ($CDCl_3$, characteristic signals): δ = 0.03 (s, 3H, Si-CH_3), 0.11 (s, 3H, Si-CH_3), 0.48 (m, 2H, CH_2-Si-cp), 0.61 [m, 2H, CH_2-Si$(OEt)_3$], 1.2–1.8 (m, 4H, C$H_2$$CH_2$NHCONHC$H_2CH_2$), 1.22 (t, J = 7 Hz, 9H, O-CH_2-CH_3), 1.47 (m, 3H, CH-CH_3), 2.20 and 2.28 [two s, 6H, Ph(CH_3)$_2$], 2.95–3.25 (m, 4H, CH_2-NHCONH-CH_2), 3.83 (q, J = 7 Hz, 6H, O-CH_2), 6.7–7.8 [m, 16H, P$(C_6H_5)_2$, P$C_6H_3(Me)_2$]; ^{31}P NMR ($CDCl_3$): δ = – 25.2 (d, PPh_2), 6.7 (d, $PXyl_2$), J_{PP} = 21 Hz.

Preparation of the Polystyrene-Bound Ligand 6

600 mg of aminomethylated polystyrene were dried at 50 °C in a high vacuum for 2 hours. After addition of 6 mL of THF, the mixture was slowly stirred, resulting in polymer swelling, and was subsequently treated with 1,3 mmol of tolylene-2,4-diisocyanate **4.** After 2 hours, the excess of **4** was removed by washing 5 times with 10 mL THF. The polymer was reslurried in 6 mL of THF, treated with an orange solution of 60 mg (0.096 mmol) **1** in 2 mL THF and stirred for 2 hours at 40 °C, with the polymer becoming yellow and the solution being decolorized. Subsequently, 5 mL of ethanol and a spatula tip of 1,4-diazabicyclo[2.2.2]octane were added and the mixture gently stirred overnight at room temperature. The solution was then filtered, the yellow polymer washed four times with THF and twice with diethyl ether and subsequently dried at 40 °C in a high vacuum. Microanalysis: 0.72% P. This corresponds to a loading of 0.116 mmol ligand/g.

Bis-Xyliphos (8)

22 microliters (0.134 mmol) of hexamethylene-diisocyanate were added to a solution of 200 mg (0.27 mmol) aminated Xyliphos **1** in 5 mL dichloromethane. After stirring overnight the dichloromethane was removed under reduced pressure and the raw material was purified by chromatography (silica gel Merck 60, ethyl acetate). Product **8** was obtained as an orange solid in 65% yield. ^{1}H NMR ($CDCl_3$, characteristic signals): δ = 0.1 [s, 12H (Si$(CH_3)_2$], 0.5 (m, 4H, Si-CH_2), 2.2 (s, 12H, Ph-CH_3), 2.35 [s, 12H, Ph$(CH_3)_2$], 2.9–3.2 (m, 8H, CH_2-N), 3.2–4.8 (m, cyclopentadiene-H and CH-CH_3), 6.7–7.7 (m, 32H, Ph-H); ^{31}P NMR ($CDCl_3$): δ = – 25.2 (d, PPh_2), 6.7 (d, $PXyl_2$), J_{PP} 21 Hz.

General Procedure for the Preparation of the Silica Gel-Bound Ligands 9a–c

A solution of ligand **3** in toluene (4.5 mL/g silica gel) was added to silica gel Grace 332 that was previously dried under vacuum at 130 °C for three hours and then set under argon. This mixture was then heated to 90 °C and gently stirred for 20 h. After cooling to room temperature and sedimentation of the silica gel, the supernatant solution was removed with a syringe. The silica gel was washed several times with methanol and finally dried under reduced pressure at 40–50 °C.

9a: 3.3 g silica gel, 400 mg (0.4 mmol) ligand **3**; microanalysis, P 0.62%. This corresponds to a ligand loading of 0.1 mmol/g.

9b: 6.3 g silica gel, 300 mg (0.3 mmol) ligand **3**; Microanalysis, P 0.26%. This corresponds to a ligand loading of 0.042 mmol/g.

9c: 7.5 g silica gel, 120 mg (0.12 mmol) ligand **3**; Microanalysis, P 0.08%. This corresponds to a ligand loading of approx. 0.013 mmol/g.

Preparation of the Extractable Xyliphos Ligand 12

1 g (1.3 mmol) **10** were added to a freshly prepared solution of 38 mmol sodium ethoxide and 11.6 mL (76 mmol) diethyl malonate in 23 mL ethanol and stirred for 20 hours at 80–90 °C in presence of 100 mg potassium iodide. After evaporation of the solvent the mixture was treated with 10 mL 2 N HCl and extracted in water/ethyl acetate. The organic phase was then dried with sodium sulfate. Chromatography (silica gel Merck 60, hexane/ethyl ester, 10/1) gave pure **11** in 92% yield. ^{1}H NMR ($CDCl_3$): δ = 0.0 (s, 3H, Si-CH_3), 0.08 (s, 3H, Si-CH_3), 0.5 (m, 2H, CH_2-Si), 1.2 (t, 6H, O$CH_2$$CH_3$) 1.48 (t, 3H, CH-C$H_3$), 1.82 [m, 2H, C$H_2$-CH(COOEt)$_2$], 2.15 and 2.25 (two s, 12H, Ph-CH_3), 3.2–4.4 [m, 9H, $C_5H_3FeC_5H_4$, CH-CH_3, CH(COOEt)$_2$], 4.15 (q, 4H, OC$H_2$$CH_3$), 6.7–7.7 [m, 16H, P$(C_6H_5)_2$ and P$(C_6H_3Me_2)$]; ^{31}P NMR ($CDCl_3$): δ = – 25.2 (d, PPh_2), 6.8 (d, $PXyl_2$), J_{PP} = 21 Hz.

12: A mixture of 700 mg (0.78 mmol) **11** in 25 mL ethanol and 1 g KOH in 1.5 mL water was stirred at room temperature for 1 hour. After evaporation of the ethanol, the slurry was extracted in toluene/diethyl ether/water. The water phase with the product was washed with ethyl acetate, then toluene was added. The pH was set to 2–3 whereby the product went into the toluene phase, which was dried with sodium sulfate and then evaporated. Product **12** was obtained in 90% yield. ^{1}H NMR ($CDCl_3$): δ = 0.0 (s, 3H, Si-CH_3), 0.08 (s, 3H, Si-CH_3), 0.57 (m, 2H, CH_2-Si), 1.55 (m, 3H, C-CH_3), 1.95 [m, 2H, CH_2-CH(COOH)$_2$], 2.15 and 2.3 (two s, 12H, Ph-CH_3), 3.2–4.4 [m, 9H, $C_5H_3FeC_5H_4$, CH-CH_3, CH(COOH)$_2$], 6.7–7.7 [m, 16H, P$(C_6H_5)_2$ and P$(C_6H_3Me_2)$]; ^{31}P NMR ($CDCl_3$): δ = – 25.9 (d, PPh_2), 8.4 (d, $PXyl_2$).

Typical Hydrogenation Procedure

The catalyst precursors were prepared by mixing the ligand and $[Ir(cod)Cl]_2$ (unless otherwise noted in a ratio of 1.2 ligand/1

Ir) in small amounts of THF and evaporating the solvent. For the hydrogenation experiments, MEA-imine, acetic acid (AcOH) and tetrabutylammonium iodide (TBAI) were then added to these preformed Ir complexes. The resulting mixture was then pressed with argon through a capillary into a 50-mL steel autoclave that was flushed with argon. The autoclave was then sealed, flushed three times with hydrogen pressurizing typically to 20 bars, finally charged with hydrogen to the specified pressure and the reaction started by switching on the stirrer. The course of the reaction could be followed by the hydrogen uptake. After the hydrogenation, the solvent was evaporated and the conversion determined by gas chromatography [column: DB17/30W, 15 m (JWC Scientific Inc.), temperature program: 60 °C/1min. to 220 °C, ΔT: 10 °C/min]. The enantiomeric excess of the MEA-amine was determined by HPLC (column: Daicel Chiracel-OD; solvent: hexane/2-isopropanol, 99.7:0.3).

References

[1] *Chiral Catalyst Immobilization and Recycling*, (Eds.: D. E. De Vos, I. F. J. Vankelecom, P. A. Jacobs), Wiley-VCH, Weinheim, **2000**.

[2] a) B. Pugin, *J. Mol. Catal.* **1996**, *107*, 273; b) B. Pugin, M. Müller, *Stud. Surf. Sci. Catal.* **1993**, *78*, 107; c) B. Pugin (Ciba-Geigy AG), *EP Patent* 728768 A2, **1996**; *Chem. Abstr.* **1996**, *125*, 248834.

[3] G. M. Ramos Tombo, H. U. Blaser, in *Pesticide Chemistry and Bioscience*, (Eds.: G. T. Brooks, T. R. Roberts), Royal Society of Chemistry, Cambridge, **1999**, p. 33.

[4] C. Köllner, B. Pugin, A. Togni, *J. Am. Chem. Soc*. **1998**, *120*, 10274.

[5] H. U Blaser, H. P. Buser, K. Coers, R. Hanreich, H. P. Jalett, E. Jelsch, B. Pugin, H. D. Schneider, F. Spindler, A. Wegmann, *Chimia* **1999**, *53*, 275.

[6] U. Nagel, E. Kinzel, *J. Chem. Soc. Chem. Commun*. **1986**, 1098.

[7] T. Ohkuma, H. Takeno, Y. Honda, R. Noyori, *Adv. Synth. Catal.* **2001**, *4*, 343.

[8] R. Crabtree, *Acc. Chem. Res.* **1979**, *12*, 331; D. Chadosh, R. Crabtree, H. Felkin, S. Morehouse, G. Morris, *Inorg. Chem*. **1982**, *21*, 1307; H. H. Wang, L. H. Pignolet, *Inorg. Chem*. **1980**, *19*, 1470.

[9] H. U. Blaser, B. Pugin, F. Spindler, A. Togni, *C. R. Chimie* **2002**, *5*, in press.

[10] H. U. Blaser, F. Spindler, in *Comprehensive Asymmetric Catalysis*, Vol. I, (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto),Springer, Berlin, **1999**, p. 247.