# A Heterogenization of Homochiral Ferrocenylphosphine Ligand for Rh(I)-Catalyzed Enantioselective Hydrosilylation of Acetophenone

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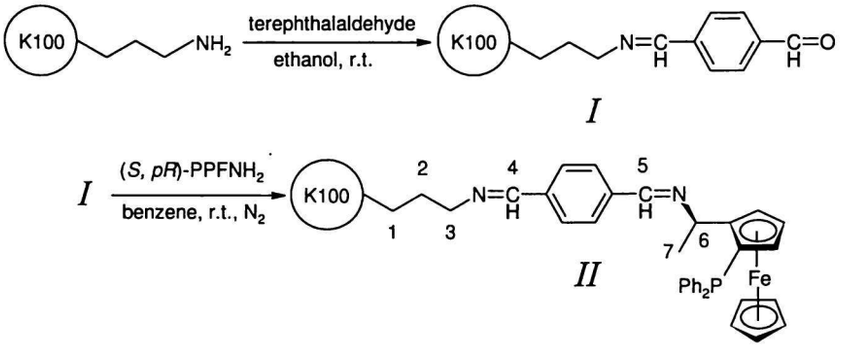
A homochiral ferrocenylphosphine ligand (*S*, *pR*)-PPFNH$_2$ has been immobilized to aminopropylated Kieselgel 100 (AMP-K-100) modified with terephthalaldehyde. The heterogeneous catalytic system Rh(I)/imino-phosphine ligand was examined at an enantioselective hydrosilylation of acetophenone and achieved results were compared to its homogeneous analogue.

Transition-metal complexes of homochiral ferrocenylphosphine ligands are known as effective homogeneous catalysts used in enantioselective syntheses [1, 2]. Nevertheless the application of homogeneous catalytic systems in industry is limited due to complications with the catalyst recovery [3]. The heterogenization of catalytic systems such as immobilization of homochiral ferrocene ligands to solid supports (insoluble polymers [4, 5], silica gel [6—9], mesoporous silica gel (MCM-41) [10, 11] or dendrimers [12—15]) opens the possibility for efficient recovery of the catalytic system.

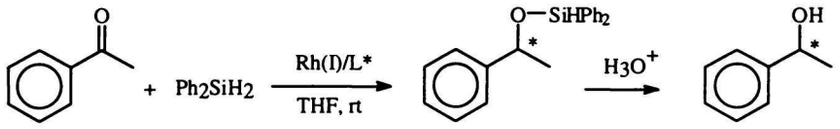
*Hayashi* and coworkers [16] described hydrosilylation of prochiral ketones with diphenylsilane catalyzed by the Rh(I)/(*R*, *S*)-*N*,*N*-dimethyl-1-[2-dimethylphosphinoferrocenyl]ethylamine complex with modest enantioselectivity (49 % ee for acetophenone). Recently, *Hayashi*'s group [17] prepared the iminophosphine ligands, which were found to be very effective for the Rh(I)-catalyzed enantioselective hydrosilylation of prochiral ketones to give alcohols with high enantioselectivity (up to 90 % ee). The importance of imino group for enantioselectivity was demonstrated by the hydrosilylation of acetophenone with (*S*, *pR*)-PPFA or (*S*, *pR*)-PPFNH$_2$ ligand giving the product with opposite configuration and different ee (16 % ee or 39 % ee, respectively).

The main goal of our work was to immobilize a homochiral ferrocenylphosphine ligand *via* imino bond to surface of silica K-100. The prepared immobilized ligand was examined as a component of heterogeneous catalytic system for enantioselective hydrosilylation of acetophenone.

The (*S*, *pR*)-PPFNH$_2$ ligand for immobilization was prepared according to the procedure described by *Hayashi* and coworkers [18]. Immobilization of (*S*, *pR*)-PPFNH$_2$ was performed analogously as described [19]. Aminopropylated K-100 (loading 1 mmol g$^{-1}$) was suspended in ethanol, terephthalaldehyde was added and resulting suspension was stirred at room temperature (Scheme 1). The functionalized inorganic support was suspended in dry benzene, solution of the




*Scheme 1*




*Scheme 2*

**Table 1.** Results of the Rh(I)-Catalyzed Enantioselective Hydrosilylation of Acetophenone

| Ligand | $t$/h | Conversion of ketone to alcohol/% | ee/% |
|---|---|---|---|
| (*S*, *R*)-*N*-Benzylidene-1-[2-diphenylphosphinoferrocenyl]ethylamine | 1 | 98 | 80 (*S*) |
| K-100—(*S*, *R*)-PPFA (*II*) | 1 | 23 | 28 (*S*) |
| K-100—(*S*, *R*)-PPFA (*II*) | 5 | 56 | 12 (*S*) |
| K-100—(*S*, *R*)-PPFA (*II*) reused | 5 | 15 | 6 (*S*) |
| K-100—(*S*, *R*)-PPFA (*II*) reloaded with Rh(I) | 5 | 37 | 6 (*S*) |

ferrocene ligand (*S*, *pR*)-PPFNH$_2$ was added. Resulting yellow solid (*I*) was filtered off, washed with benzene, ethanol, and diethyl ether, dried at 50 °C under high vacuum. Functionalization was determined by AAS (Fe) and found to be 0.25 mmol g$^{-1}$.

To test the prepared immobilized ligand, we decided to explore the Rh(I)-catalyzed enantioselective hydrosilylation of acetophenone with diphenylsilane (Scheme 2).

The reaction was carried out according to *Hayashi*'s procedure [17]: acetophenone (2 mmol) in THF (2 cm$^3$) reacted with diphenylsilane (2.5 mmol) in the presence of 1 mole % Rh(I)/L* (in the mole ratio 1:1.5) at room temperature under nitrogen. A ratio $n$(ketone):$n$(alcohol) was determined by $^1$H NMR spectrum of the products after hydrolysis, enantioselectivity was determined by GC analysis (30 % permethylated $\beta$-cyclodextrin in OV-1 as the active phase). The first reaction was carried out with a homogeneous catalytic system generated from homochiral ferrocene ligand (*S*, *R*)-*N*-benzylidene-1-[2-diphenylphosphinoferrocenyl]ethylamine [17] and [RhCl(hexa-1,5-diene)]$_2$. *Hayashi* and coworkers described enantioselectivity 87 % ee (*S*) ($n$(ketone):$n$(alcohol) = 2:98) and we achieved the same results (Table 1). The reaction catalyzed by the heterogeneous system Rh(I)/immobilized ligand *II* was incomplete (23 % conversion) giving the product of the same configuration (*S*) with low enantioselectivity (28 % ee). To increase the yield, the reaction time was prolonged to 5 h. The product was obtained in higher yield (56 %), but enantioselectivity dropped (12 % ee (*S*)). Our next experiment was to test catalytic activity of the regenerated catalyst. The catalyst was filtered off, washed with THF, and dried in vacuum. Under the same reaction conditions, activity of the reused catalyst was low. Only 15 % conversion and 6 % ee (*S*) were detected. The possible explanation of the decrease of catalytic activity could be leaching of transition-metal during the regeneration process. The regenerated heterogeneous catalyst was therefore reloaded with Rh(I) spieces in the subsequent experiment. The increase of conversion was observed (37 %), but enantioselectivity was low again (6 % ee (*S*)) (Table 1).

The results show that catalytic centres are partly destroyed during the reaction to diminish both the activity and enantioselectivity of the recycled catalyst. This is confirmed by comparing the results obtained after 1 h (28 % ee) and 5 h (12 % ee). This is probably caused by the hydrolysis of imino bonds on both sides of the terephthalaldehyde linker. This is supported by the presence of aldehydic carbon $C_5$ at $^{13}$C CP MAS NMR ($\delta$ = 162) in case of hydrolysis of imino bond closer to cyclopentadienyl ring or carbon $C_3$ ($\delta$ = 41) which can be ascribed to 3-aminopropylated silica gel in the reused catalyst.

The attempts to immobilize the ligand to the aminopropylated HMS (Hexagonal Mesoporous Silica gel) using terephthalaldehyde were not successful even when the period of the modification of the HMS with terephthalaldehyde was prolonged to 25 h. This failure may be attributed to a small pore size of the solid support, lower reactivity of the amino groups or interactions between the surface of silica gel and the linker.

## EXPERIMENTAL

Acetophenone, terephthalaldehyde, diphenylsilane, and rhodium catalyst [RhCl(hexa-1,5-diene)]$_2$ were purchased from Aldrich and used without further purification. Silica gels K-100 and HMS were obtained from the University of York in UK. The (*S*, *pR*)-PPFNH$_2$ ligand was prepared according to the procedure described by *Hayashi* and coworkers [18]. Standard procedures have been used for purification and drying of the solvents. $^1$H NMR ($\delta$) spectra of samples were obtained from $CDCl_3$ solutions on a Varian Gemini 2000 spectrometer operating at 300 MHz frequency with tetramethylsilane as internal standard. $^{13}$C CP

MAS ($\delta$) spectrum of modified silica gel was obtained on a Bruker 300MSL spectrometer at 75 MHz operating frequency. $^{31}$P CP MAS ($\delta$) spectrum of modified silica was obtained on a Bruker at 162 MHz operating frequency with reference to $NH_4H_2PO_4$. Diffuse reflectance FTIR (DRIFTS) spectrum of modified silica gel was measured as a mass mixture of 5 % sample and 95 % KBr in an environmental chamber at 150 °C under vacuum on a Bruker Equinox FTIR.

### Modification of AMP-K100 with Terephthalaldehyde

2 g of aminopropylated silica K-100 (loading 1 mmol $g^{-1}$) were suspended in ethanol (40 $cm^3$), terephthalaldehyde (268 mg; 2 mmol) was added and the resulting suspension was stirred at room temperature for 2 h. Solid was filtered off, washed with ethanol and dried at 50 °C under high vacuum. Colourless powder (1.95 g) was obtained.

### Immobilization of Ferrocene Ligand to Inorganic Support

To a functionalized AMP-K100 (1 g) suspended in dry benzene (10 $cm^3$), a solution of the ferrocene ligand (*S, pR*)-PPFNH$_2$ (423 mg; 1 mmol) in dry benzene (10 $cm^3$) was added and the reaction mixture was stirred under argon at room temperature for 24 h. Resulting yellow solid (*II*) was filtered off, washed with benzene, ethanol, and diethyl ether, dried at 50 °C under high vacuum. Product was obtained as a yellow powder (0.966 g). Functionalization was determined by AAS (Fe) and found to be 0.25 mmol $g^{-1}$. $^{13}$C CP MAS NMR spectrum ($\delta$): 9 ($C_1$), 23 ($C_2$ + $C_7$), 63 ($C_6$), 70—90 (ferrocene + $C_3$), 115—140 ($PPh_2$), 179 ($C_4$), 190 ($C_5$). $^{31}$P CP MAS spectrum ($\delta$ ): −21 ($PPh_2$cp). DRIFTS spectrum ($\tilde{\nu}/cm^{-1}$): 1100 (SiOR), 1569, 1605 (aromatics), 1642 (—CH=N—), 2834, 2938 (—$CH_{aliph}$), 3051 (—$CH_{arom}$), 3648 (SiOH).

### Rh(I)-Catalyzed Enantioselective Hydrosilylation of Acetophenone

Mixture of [RhCl(hexa-1,5-diene)]$_2$ (2.2 mg, 0.005 mmol, 1 mole %) and ligand (7.7 mg, 0.015 mmol, 1.15 eqv. of homogeneous one or 66 mg, 0.015 mmol, 1.15 eqv. of immobilized one) in dry THF (1 $cm^3$) was stirred at room temperature for 1 h. Then acetophenone (0.12 $cm^3$, 1 mmol) and diphenylsilane (0.23 $cm^3$, 1.25 mmol, 1.25 eqv.) were added. Reaction was observed on the TLC ($SiO_2$, $\varphi$(iHx—EtOAc) = 4:1). Catalytic system was then filtered off and the mixture was hydrolyzed by dropwise addition of 1 $cm^3$ of methanolic solution of hydrochloric acid ($c$ = 1 mol $dm^{-3}$, $\varphi$(HCl—MeOH) = 1:1) during 10 min and additional stirring for 20 min. Mixture was then extracted with 2 × 10 $cm^3$ of $Et_2O$. Organic phase was dried over $Na_2SO_4$ and evaporated. Crude product was purified by distillation. Conversion of ketone to alcohol was determined by $^1$H NMR spectrum of the mixture of the products after hydrolysis, enantiomeric excess was determined by GC analysis (30 % permethylated $\beta$-cyclodextrin in OV-1 as the active phase).

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## REFERENCES

1. Hayashi, T., in *Ferrocenes. Homogeneous Catalysis. Organic Synthesis. Materials Science* (Togni, A. and Hayashi, T., Editors.) Pp. 105, 173. VCH, Weinheim, 1995.
2. Richards, J. and Locke, A. J., *Tetrahedron: Asymmetry 1998*, 2377.
3. Blaser, H. U. and Pugin, B., *Chiral Reactions in Heterogeneous Catalysis.* (Jannes, G. and Dubois, V., Editors.) P. 33. Plenum Press, New York, 1993.
4. Švec, F., *Pokroky chemie: Polymerní katalyzátory.* (Progress in Chemistry: Polymer Catalysts.) Academia, Prague, 1987.
5. Stille, J. K., *React. Polym. 10*, 165 (1989).
6. Pugin, B., *Eur. Pat. Appl. EP 729, 969; Chem. Abstr. 125*, 276188z (1996).
7. Pugin, B., *PCT Int. Appl. WO 9632, 400; Chem. Abstr. 126*, 8302r (1997).
8. Pugin, B., *PCT Int. Appl. WO 9702, 232; Chem. Abstr. 126*, 185879e (1997).
9. Price, P. M., Clark, J. H., and Macquarrie, D. J., *J. Chem. Soc., Dalton Trans. 2000*, 101.
10. Johnson, B. F. G., Raynor, S. A., Shephard, D. S., Mashmeyer, T., Thomas, J. M., Sankar, G., Bromley, S., Oldroyd, R., Gladden, L., and Mantle, M. D., *Chem. Commun. 1999*, 1167.
11. Raynor, S. A., Thomas, J. M., Raja, R., Johnson, B. F. G., Bell, R. G., and Mantle, M. D., *Chem. Commun. 2000*, 1925.
12. Eggeling, E. B., Hovestad, N. J., Jastrzebski, J. T. B. H., Vogt, D., and van Koten, G., *J. Org. Chem. 65*, 8857 (2000).
13. Schneider, R., Kolner, C., Weber, I., and Togni, A., *Chem. Commun. 1999*, 2415.
14. Kolner, C., Pugin, B., and Togni, A., *J. Am. Chem. Soc. 120*, 10274 (1998).
15. Oosterom, G. E., van Haacen, R. J., Reck, J. N. H., Kramer, P. C. J., and van Leeuwen, P. W. N. M., *Chem. Commun. 1999*, 1119.
16. Hayashi, T., Yamamoto, K., and Kumada, M., *Tetrahedron Lett. 49—50*, 4405 (1974).
17. Hayashi, T., Hayashi, C., and Uozumi, Y., *Tetrahedron: Asymmetry 6*, 2503 (1995).
18. Hayashi, T., Mise, T., Fukushima, M., Katogani, M., Nagashima, M., Hamada, Y., Matsumoto, A., Kawakami, S., Kanishi, M., Yamamoto, K., and Kumada, M., *Bull. Chem. Soc. Jpn.* 53, 1138 (1980).
19. Chisem, I. C., Chisem, J., and Clark, J. H., *New J. Chem. 1998*, 81.