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The economic use of precious chiral diphosphine ligands—DuPHOS and its rhodium(I) COD and NBD complexes

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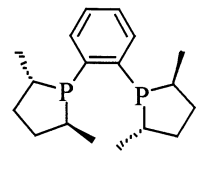
Abstract—The use of cationic Rh(DuPHOS) precatalysts for asymmetric hydrogenation bearing NBD (norbornadiene) as counter ligand has significant advantages over the application of the related COD (cyclooctadiene) complexes. Liberation of the active catalysts by hydrogenation of COD requires much more time than complete asymmetric hydrogenation of a prochiral substrate proceeding in parallel. Due to this feature expensive DuPHOS ligands are wasted by more than 50%.

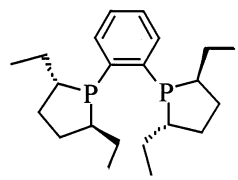
Chiral diphosphines play a pivotal role as ligands in rhodium(I) catalyzed asymmetric hydrogenation.[1] In particular C_2-symmetric 1,2-bisphospholanes like DuPHOS and BPE,[2] PennPHOS,[3] RoPHOS,[4] BASPHOS[5] or bisphosphetanes such as CnrPHOS[6] form highly enantioselective catalysts for the hydrogenation of a range of different prochiral olefins. Due to their excellent and versatile catalytic performance, utilization for industrial applications may be envisaged. Unfortunately, the synthesis of these ligands consists of several steps and requires expensive reagents. Due to this fact, only a few of them are commercially available and the price is extremely high. In order to benefit from the whole amount of chiral ligands synthesized or purchased, economic application is therefore highly desired. In the overwhelming cases, as precatalysts rhodium(I) complexes bearing COD (cyclooctadiene) as counter ligand to the chiral diphosphine are used. In particular, cationic [Rh(COD)(chiral ligand)]$^+$ complexes have seen broad application. In a related frequently utilized methodology the precatalyst is prepared in situ for example by mixing the chiral ligand with [Rh(COD)$_2$]$^+$.[7] In both methods the catalytically active species, e.g. solvent complexes, are generated by hydrogenation of the stabilizing diolefin.

Recently, we reported that prehydrogenation of Rh(I)(COD) complexes bearing chiral 1,4-diphosphines as ligands (seven-membered chelates) takes considerably longer than generally assumed.[8] Moreover, our investigations revealed that the asymmetric hydrogenation of prochiral olefins like dehydroamino acid derivatives takes place parallel to that of the diolefin.[9]

Herein we report that this feature is even much more expressed for corresponding five-membered chelates based on 1,2-bisphospholanes.[10] As a typic example we have chosen the hydrogenation of methyl (*Z*)-*N*-acylaminocinnamates using a catalyst containing as chiral ligands (*S*,*S*)-Me-DuPHOS [1,2-bis(2,5-dimethyl-phospholanyl)benzene] and (*S*,*S*)-Et-DuPHOS [1,2-bis(2,5-diethyl-phospholanyl)benzene], respectively.[2]



(*S*,*S*)-Me-DuPHOS



(*S*,*S*)-Et-DuPHOS

Hydrogenation experiments have been carried out under normal pressure and isobaric conditions with an automatically registrating gas measuring device (1.0 atm overall pressure over the solution). The experiments were performed with 0.01 mmol precatalyst and 1.0 mmol of prochiral olefin in 15.0 ml of MeOH at 25°C. In our first approach methyl (*Z*)-*N*-benzoylaminocinnamate was hydrogenated. In one run the catalyst was prepared in situ by the reaction of

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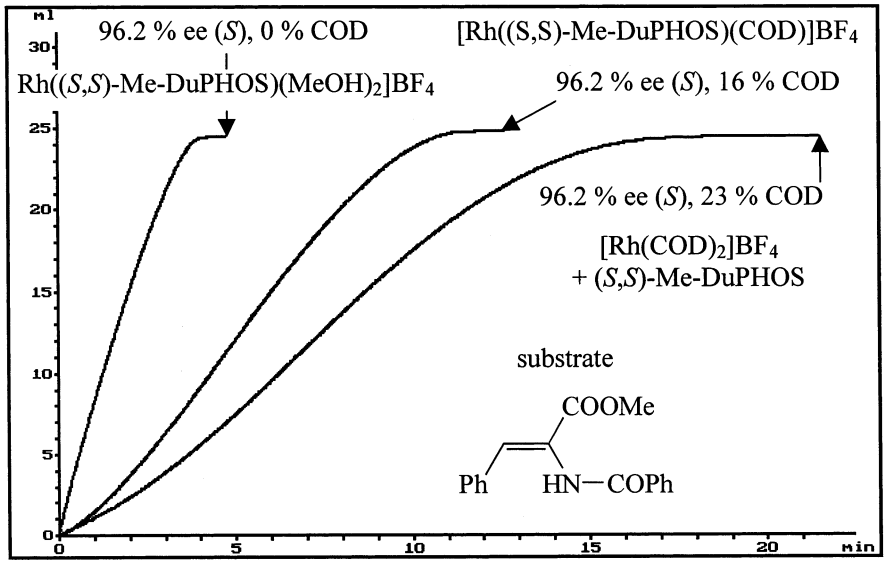

Figure 1. Different methods to apply the catalyst for the asymmetric hydrogenation of methyl (*Z*)-*N*-benzoylaminocinnamate with a rhodium(I) catalyst containing ((*S*,*S*)-Me-DuPHOS.

$[Rh(COD)_2]BF_4$ with one equivalent of (*S*,*S*)-Me-DuPHOS. In another run the precatalyst was used directly as $[Rh((S,S)\text{-Me-DuPHOS})(COD)]BF_4$. In the final run the solvent complex $[Rh((S,S)\text{-Me-DuPHOS})(MeOH)_2]BF_4$ was applied, which has been generated by prior hydrogenation of the precatalyst taking ca. 90 min (^{31}P NMR control). The hydrogen uptake for all three trials is depicted in Fig. 1. The results from the first two experiments indicate that there was still COD[11] present after the completion of the asymmetric hydrogenation.[12] It is noteworthy that the enantioselectivity remained constant.

As can be clearly seen, there is more COD left after the completion of asymmetric hydrogenation than when the catalyst was prepared in situ. In other words for the asymmetric hydrogenation under the usual reaction conditions only a part of the expensive catalyst is consumed. It should be stressed that the amounts of COD given in the figure concern the amount which is left after the whole hydrogenation process. That means during the asymmetric hydrogenation the concentration of the COD complex is—time dependent—much higher, and therefore the concentration of the active catalyst is still lower as at the end.

We next compared the COD precatalyst with the corresponding NBD complex. Precatalysts of the latter type can be easily prepared following the procedure of Schrock and Osborn by the reaction of Rh(NBD)acac with the chiral ligand and subsequent addition of HBF_4.[13] Another quite general methodology developed

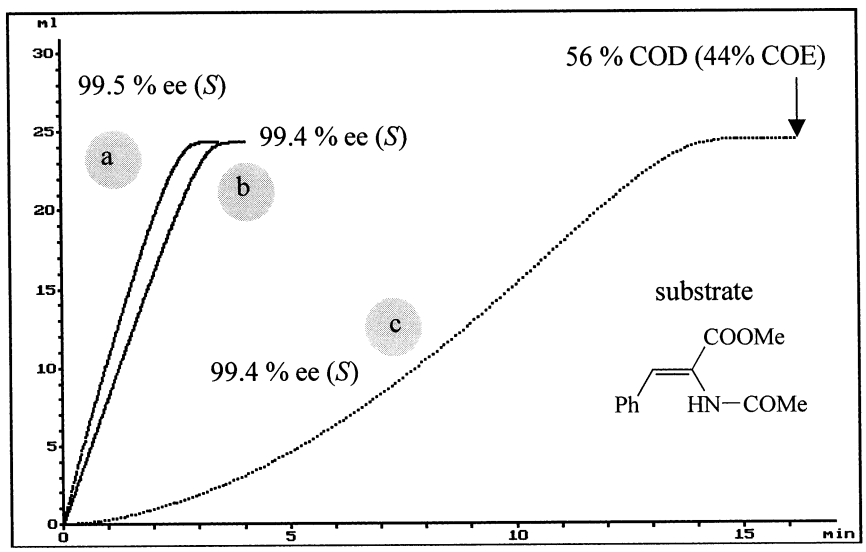

Figure 2. Asymmetric hydrogenations of methyl (*Z*)-*N*-acetylaminocinnamate with catalysts bearing (*S*,*S*) Et-DuPHOS. a: $[Rh((S,S)\text{-Et-DuPHOS})(MeOH)_2]BF_4$, b: $[Rh((S,S)\text{-Et-DuPHOS})(NBD)]BF_4$, c: $[Rh((S,S)\text{-Et-DuPHOS})(COD)]BF_4$.

in our laboratory consists in the treatment of the relevant COD complexes with an excess of NBD.[14]

$$[Rh(COD)(P–P^*)]BF_4 \underset{}{\overset{NBD}{\rightleftharpoons}} [Rh(NBD)(P–P^*)]BF_4$$

As a model reaction we have chosen the hydrogenation of methyl (*Z*)-*N*-acetylaminocinnamate with the (*S*,*S*)-Et-DuPHOS catalyst. The diphosphine was again used either as COD or NBD precatalyst or as its solvent complex. Results are depicted in Fig. 2. As expected, by application of the COD complex there is still unchanged COD at the end of the asymmetric hydrogenation (56%). Surprisingly, NBD and solvent complex exhibited almost similar activities. Obviously, the hydrogenation of NBD is much faster than that of the COD. It should be noted that the time required for conversion of half of the substrate with the COD complex is six times as long as with the NDB complex.

Our preliminary results clearly demonstrate that the use of NBD precatalyst in the asymmetric hydrogenation has significant advantages over the application of the usually sold and applied COD complexes. By utilization of NBD precatalysts costs of ligands and catalysts can be significantly reduced. Work is in progress to rationalize the different behaviour of these both types of related Rh(diolefin) precatalysts.

Acknowledgements

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References

1. For some recent reviews see: Brown, J. M. In *Comprehensive Asymmetric Catalysis;* Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999, 121–182. Nagel, U.; Albrecht, J. In *Topics in Catalysis* 1998, *5*, 3–23. Burk, M. J.; Bienewald, F. In *Transition Metals for Organic Synthesis*; Beller, M.; Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998, Vol II, 13–25.
2. See e.g. Burk, M. J.; Gross, M. F.; Harper, T. G. P.; Kalberg, C. S.; Lee, J. R.; Martinez, J. P. *Pure & Applied Chem*. **1996**, *68*, 37–44. Burk, M. J.; Allen, J. G.; Kiesmann, W. F. *J. Am. Chem. Soc*. **1998**, *120*, 657–663. Albrecht, J.; Nagel, U. *Angew. Chem*. **1996**, *108*, 444–446. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 407–409. Burk, M. J.; Kalberg, C. S.; Pizzano, A. *J. Am. Chem. Soc*. **1998**, *120*, 4345–4353. Burk, M. J.; Johnson, N. B.; Lee, J. R. *Tetrahedron Lett*. **1999**, *40*, 6685–6688; Burk, M. J.; Pizzano, A.; Martin, J. A. *Organometallics* **2000**, *19*, 250–260.
3. Jiang, Q.; Jiang, Y.; Xiao, D.; Cao, P.; Zhang, X. *Angew. Chem*. **1998**, *110*, 1203–1207; *Angew. Chem., Int. Ed. Engl*. **1998**, *37*, 1100–1103.
4. Holz, J.; Quirmbach, M.; Schmidt, U.; Heller, D.; Stürmer, R.; Börner, A. *J. Org. Chem*. **1998**, *63*, 8031–8034. Li, W.; Zhang, Z.; Xiao, D.; Zhang, X. *Tetrahedron Lett*. **1999**, *40*, 6701–6704. Yan, Y.-Y.; RajanBabu, T. V. *J. Org. Chem*. **2000**, *65*, 900–906. Li, W.; Zhang, Z.; Xiao, D.; Zhang, X. *J. Org. Chem*. **2000**, *65*, 3489–3496. Yan, Y.-Y.; RajanBabu, T. V. *Org. Lett*. **2000**, *2*, 199–202.
5. Holz, J.; Heller, D.; Stürmer, R.; Börner, A. *Tetrahedron Lett*. **1999**, *40*, 7059–7062.
6. Marinetti, A.; Genêt, J. P.; Jus, S.; Blanc, D.; Ratovelomanana-Vidal, V. *Chem. Eur. J*. **1999**, *5*, 1160–1165. Marinetti, A.; Labrue, F.; Genêt, J. P. *Synlett* **1999**, *12*, 1975–1977. Marinetti, A.; Jus, S.; Genêt, J. P. *Tetrahedron Lett*. **1999**, *40*, 8365–8368. Marinetti, A.; Jus, S.; Genêt, J. P.; Ricard, L. *Tetrahedron* **2000**, *56*, 95–100.
7. Brunner, H. In *Applied Homogeneous Catalysis with Organometallic Compounds;* Cornils, B.; Herrmann, W. A., Eds.; VCH, Weinheim, **1996**, 201–219. Sometimes $[Rh(COD)Cl]_2$, which is also a common and commercial available precursor, is used.
8. Heller, D.; Kortus, K.; Selke, R. *Liebigs Ann*. **1995**, 575–581. Heller, D.; Holz, J.; Borns, S.; Spannenberg, A.; Kempe, R.; Schmidt, U.; Börner, A. T*etrahedron: Asymmetry* **1997**, *8*, 213–222.
9. Baumann, W.; Mansel, S.; Heller, D.; Borns, S. *Mag. Reson. Chem*. **1997**, *35*, 701–706.
10. For a detailed and more exhaustive study on the behaviour of COD and NBD complexes of chiral 1,2-diphosphines, see Drexler, H.-J.; Baumann, W.; Spannenberg, A.; Fischer, C.; Heller, D. *J. Organometal. Chem*. in press.
11. The COD was determined by GC. NMR investigations revealed that the precatalyst remained unchanged in the solution. For more detailed information, compare Ref. 10.
12. This feature is not unique for the special catalytic system considered here in detail. Thus, in the hydrogenation of (*Z*)-*N*-acetylaminocinnamic acid with $[Rh((S,S)\text{-Et-DuPHOS})(COD)]BF_4$ as precatalyst under the same conditions in MeOH 41% COD was left. In *i*-PrOH as solvent 36% COD remained after complete conversion of methyl (*Z*)-*N*-acetylcinnamate as substrate.
13. Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc*. **1971**, *93*, 2397–2407.
14. Heller, D.; Borns, S.; Baumann, W.; Selke, R. *Chem. Ber*. **1996**, *129*, 85–89.