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Counter-ligand and solvent dependent oxygen–metal interactions of hemilabile coordinating hydroxy groups in chiral diphosphine rhodium(I) hydrogenation catalysts †

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Abstract

In cationic Rh[(*R*,*R*)-1,4-bis(diphenylphosphino)butane-2,3-diol] complexes the interaction of the hemilabile coordinating hydroxy groups with the metal is strongly dependent upon the nature of the counter-ligand and the solvent. As a result of the 'arm-off, arm-on' mechanism the conformation of the chirality inducing backbone is changed. Spectroscopic and catalytic investigations demonstrate that the η^3-coordination mode of the tetradentate ligand is responsible for the deceleration of the asymmetric hydrogenation. By the assistance of the second HO-group the Rh–O interaction can be suspended.

1. Introduction

The understanding of the chirality transfer in metal catalyzed enantioselective synthesis is the key for a rational design of highly efficient catalysts. In particular chiral bis-diarylphosphine metal complexes have been widely investigated in order to discover relationships between distinguished conformations of the chirality inducing backbone and the product configuration or the degree of enantioselection.[1] Unfortunately, most rules presented in the literature have been deduced from structural data collected with easily accessible precatalysts[2] or with analogous complexes of other metals.[3] This approach does not reflect the change of steric and electronic circumstances in the course of the catalytic cycle. However, it is obvious that the interaction of the substrate or/and the reagent with the metal center also has an influence on the conformation of the chirality inducing unit.[4]

Of particular interest is the behavior of ether groups which have been incorporated into the diphosphine ligand as hemilabile ligands[5] in order to support the stereodiscriminating ability of the catalyst. Examples

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† Dedicated to Prof. Dr. Y. Belokon on the occasion of his 60th birthday.

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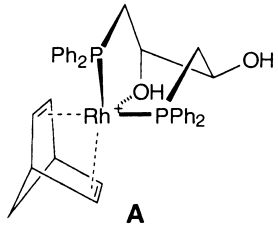
are Rh(I) hydrogenation catalysts based on DIPAMP[1,2-bis(*o*-anisylphenylphosphino)ethane)][6] and its DIOP-hybrids,[7,8] Dioxop,[9]CDP[10] or RoPHOS.[11] In crystal structures of a pertinent methoxy substituted five-membered diphosphine Pd-chelate[12] and a DIPAMP–Rh–substrate adduct,[13] respectively, a close proximity of the ether group and the metal was found. Brown et al. detected in solution alkyl rhodium-hydride complexes, where coordination of the methoxy group on the metal *trans* to the hydride was assumed.[14] However, due to the conformationally rigid structure of five-membered Rh-chelates investigated, serious steric compressions are operative and a clear cut distinction between sterically driven effects and hemilabile coordination is not possible. Therefore, it is not surprising that Imamoto et al. achieved similarly good results in the asymmetric hydrogenation when in DIPAMP the polar methoxy groups were replaced by ethyl groups.[15] Based on these findings they concluded the dominance of steric effects.

We recently investigated the asymmetric hydrogenation of functionalized olefins with Rh(I)-complexes based on ligands with a 1,4-bis(diphenylphosphino)butane skeleton. To elucidate the effects caused by polar groups one[16] or two *threo* arranged hydroxy or methoxy groups[17] were incorporated into the carbon chain. These studies showed that in methanol the catalytic effect on the enantioselectivity (increase) and reactivity (decrease) was much more pronounced with the hydroxy than with the methoxy group bearing catalysts.

The X-ray structural analysis of the precatalyst [Rh(**1**)(norbornadiene)]BF_4 [with **1**=(*R*,*R*)-1,4-bis(diphenylphosphino)butane-2,3-diol] revealed that one of the hydroxy groups interacts strongly with the metal.[17] The distance between the oxygen and the rhodium center is 2.4 Å. In the structure which was maintained also in methanol the seven-membered diphosphine-Rh chelate adopts the boat conformation **A**.



A

Prompted by these results we anticipated that the strongly polar and small hydroxy group in the conformationally flexible seven-membered chelate could also serve as indicator for electronic changes at the metal center during a catalytic reaction. As model complexes we have investigated two important intermediates involved in the asymmetric hydrogenation of methyl (*Z*)-*N*-acetylaminocinnamate (AMe) in methanol. Starting from the catalyst precursor [Rh(**1**)(nbd)]BF_4, the catalytically active species [Rh(**1**)$(MeOH)_2$]BF_4 was generated by hydrogenation of the diolefin. Then methyl (*Z*)-*N*-acetylaminocinnamate was added to displace the solvent by coordination of the bidentate electronically non-symmetrical substrate.

2. Results and discussion

In Fig. 1a the $^{31}P\{^1H\}$ NMR spectrum of [Rh(**1**)(nbd)]BF_4 in CD_3OD is shown. The spectrum at ambient temperature is characterized by a broad doublet at δ 18.1. After a coalescence temperature at 243 K the initial resonance had disappeared. At 189 K two sets of double doublets at δ 44.0 (J_{Rh-P}=141.5 Hz, J_{P-P}=41.4 Hz) and δ −2.7 (J_{Rh-P}=129.1 Hz) can be observed. This pattern is uniquely consistent with one oxygen atom bound to the metal and the formation of the boat conformation **A** (Scheme 1).

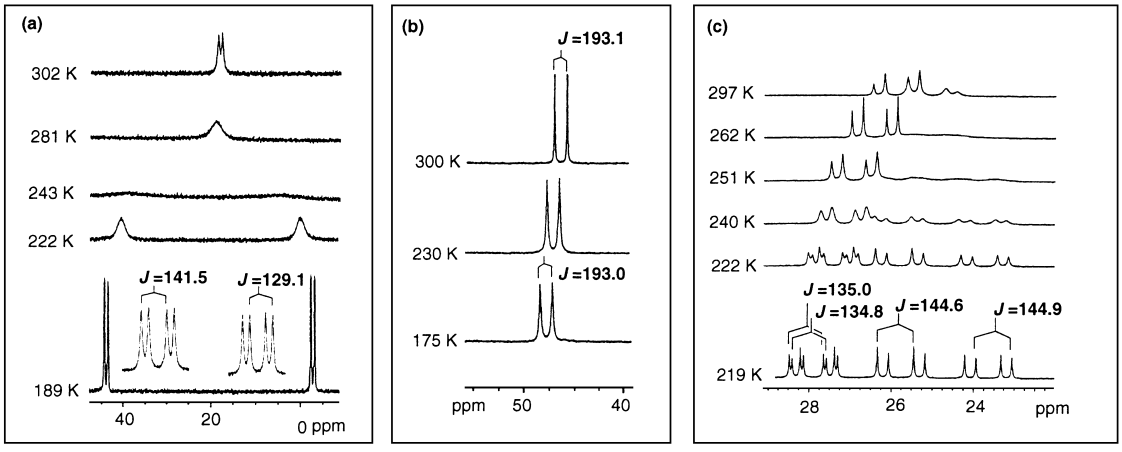


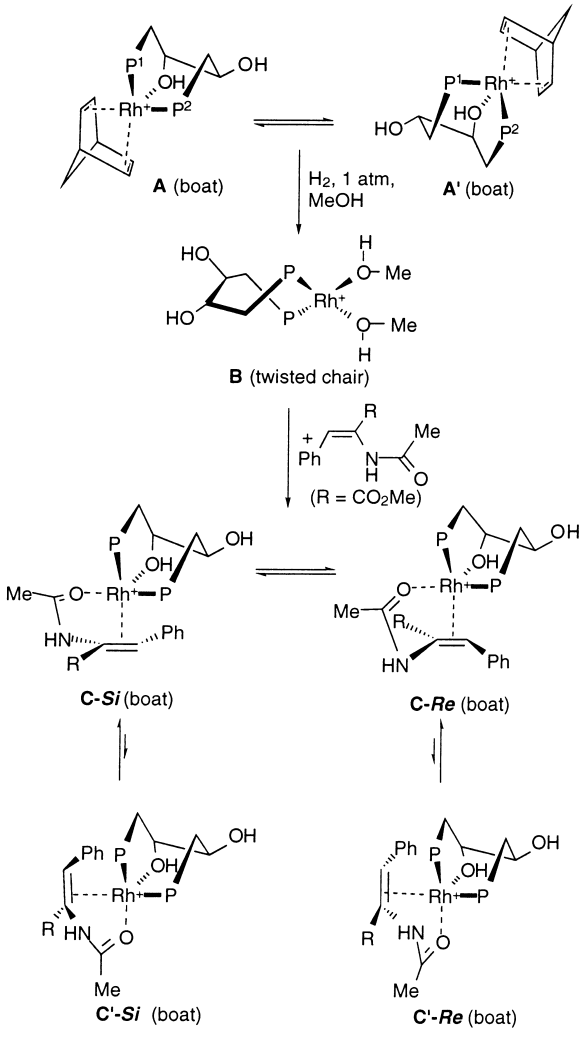
Figure 1. $^{31}P\{^1H\}$ NMR spectra in CD_3OD at different temperatures: (a) [Rh(**1**)(nbd)]BF_4; (b) [Rh(**1**)$(MeOH)_2$]BF_4; (c) [Rh(**1**)(AMe)]BF_4; coupling constants $J_{P–Rh}$ are indicated in hertz

The resonance at δ 44.0 characterizes a phosphorus (P^1) which is involved in a O–P five-membered chelate.[18] The phosphorus (P^2) in the fused O–P six-membered ring is characterized by the signal at high-field and a remarkably small $^{103}Rh–^{31}P$ coupling of 129.1 Hz.[18b] The typical change of the band shapes with decreasing temperature shows that the single doublet observed at 302 K characterizes a rapid exchange of these two phosphine signals. This interchange of high-field with low-field and low-field with high-field phosphorus resonances caused by the alternate coordination of the two hydroxy groups is not distinguishable on the NMR time scale at ambient temperatures. Due to the C_2-symmetry of the ligand boat structures **A** and **A′** are identical.

The precatalyst was exposed for 30 min to 1 atm hydrogen in order to remove norbornadiene by hydrogenation and to generate the catalytically active species. The ^{31}P NMR spectrum of the bis-methanol complex at room temperature shows a doublet at δ 47.5 (Fig. 1b). In comparison to the nbd-complex of **1** the shift to lower field is caused by the strong σ-donor but weak π-acceptor properties of the *O*-coordinated solvent.[19] Cooling of the mixture leads to a small shift of the doublet to lower field and a broadening of the signal caused by the viscosity of methanol. No dynamic phenomenon is observed at all accessible temperatures.

This is a clear indication that, in contrast to the precatalyst, in the catalytically active species the interaction of the hydroxy groups with the metal is inoperative. The complex exists exclusively in the C_2-symmetric twisted chair conformation[20] **B** (Scheme 1). This behavior can be rationalized by the decrease of the Lewis-acidity of rhodium(I) caused by the coordination of methanol, hence the interaction of the metal with the HO-group (Lewis-base) is disfavored. Our results illustrate clearly that not only steric interaction forces the hydroxy group to approach the metal,[21] but also attractive interactions play a decisive role.

By addition of a fivefold molar excess of methyl (*Z*)-*N*-acetylaminocinnamate (AMe) catalyst–substrate complexes were formed. It is noteworthy, that in contrast to corresponding complexes of related 1,4-diphosphines like (*R*,*R*)-DIOP under the same conditions the solvent-complex cannot be detected in the NMR spectrum.[22] This result agrees well with the small Michaelis constant measured in the hydrogenation of AMe with [Rh(**1**)$(MeOH)_2$]BF_4. The $^{31}P\{^1H\}$ NMR spectrum of the catalyst–substrate complex at 297 K shows an ABX pattern with different line widths for the A and B part (Fig. 1c). The upfield signals broaden as the temperature is lowered further. Finally, two well-separated ABX patterns become visible characterizing four phosphorus nuclei of two diastereomeric substrate



Scheme 1. The counter-ligand dependent O–Rh-interaction in different stages of the asymmetric hydrogenation of AMe (*P*–Ph groups are omitted)

complexes in a ratio of 1:0.76.[23] The most striking features are the close chemical shift of all resonances and two small ^{103}Rh–^{31}P coupling constants of 134.8 Hz and 135.0 Hz [J_{P-P} 44.6 Hz and 43.2 Hz]. This pattern is entirely different to those described by Brown for AMe–catalyst complexes of (*R*,*R*)-DIOP and DPPB [1,4-bis(diphenylphosphino)butane], respectively, where large differences between the chemical shifts were reported (e.g. for the AMe–Rh–DIOP complex: $\Delta\delta$=25 ppm). In these spectra the signal at low-field characterizes the phosphorus situated *trans* to the electron donating carbonyl group. The phosphine bound *trans* to the π-accepting olefin moiety has a resonance at high-field. In all instances ^{103}Rh–^{31}P couplings larger than 150 Hz have been observed. These reports combined with the conclusions derived from the NMR spectra of the di-olefin (norbornadiene) and the bis-methanol complex of **1** provide the key to the particular structures of the catalyst–substrate complexes presented herein. Thus, the unique pattern of the spectrum can be rationalized by the assumption of tripodal coordination of the hydroxyphosphine ligand. In principle, due to the stereofacial coordination of prochiral AMe on rhodium the alternate coordination of both hemilabile HO-ligands should produce

a spectrum characterizing four diastereomeric substrate complexes (**C**–*Si*, **C**–*Re*, **C**′–*Si*, **C**′–*Re*). Only two of them were observed. We suggest that the phosphine *trans* to the carbonyl oxygen is involved in the six-membered O–P–Rh chelate (**C**–*Si*, **C**–*Re*). As discussed above, the formation of a six-membered ring is indicated by the shift of the signal to higher field. Obviously, in the AMe–catalyst complex this tendency is counterbalanced by the *trans* coordination of the weakly π-accepting C=O-group, which caused a shift to lower field. The observation of the characteristically small ^{103}Rh–^{31}P coupling constants (vide supra) supports this conclusion. On the other hand, the signal of the phosphorus *trans* to the olefin, in 7-membered chelates normally observed at high-field, is displaced to lower field due to the formation of the additional 5-membered ring (vide supra). Based on this analysis the occurrance of all resonances in the narrow range between δ 23–29 becomes clear. In addition, the spectra were simulated and iteratively fitted[24] to the experimental spectra in order to verify the phosphorus interchange.[25] The line-shape analysis indicates that high-field signals exchange with high-field and the low-field with low-field signals, respectively. These results give evidence for the proposed **C**–*Si*/**C**–*Re*-interconversion. A simple HO-recoordination/coordination (**C**–*Si*/**C**′–*Si* or **C**–*Re*/**C**′–*Re*) would give an exchange of the high-field resonance with low-field, as observed with the nbd-complex (**A**).

The preceeding discussion shows that electronically different counter-ligands can significantly influence the ‘arm-off, arm-on’ mechanism between a hemilabile ligand and a metal and consequently the conformation of the chiral catalyst. Furthermore, our results provide evidence that the coordination of the HO-group takes place stereoselectively in catalyst–substrate complexes with electronically non-symmetrical substrates.

It is important to note that the tripodal coordination mode of the ligand and the bidentate coordination of the prochiral dehydroamino acid produces 18-electron Rh(I)-complexes. For the subsequent addition of hydrogen, decomplexation of the hemilabile ligand is necessary. We suggest that this feature is responsible for the lowering of the hydrogenation rate observed in the presence of hemilabile HO- and MeO-ligands.[16,17] In other words, the concentration of the inactive catalyst–substrate complexes and the rate of decomplexation, respectively, determine the rate of the hydrogenation.

Evidence for this hypothesis came from the hydrogenation of AMe in a non-polar solvent. In contrast to the reaction in methanol, in CH_2Cl_2 the hydrogenation proceeded six times faster. Interestingly, the dramatic increase in the reaction rate was not accompanied by a significant change in the enantioselectivity. In methanol methyl (*R*)-*N*-acetylphenylalaninate was obtained with 35.6% ee, whereas in methylenchloride the (*R*)-product was produced with 37.1% ee. The temperature dependent ^{31}P{^{1}H} NMR spectra of [Rh(**1**)(nbd)]BF_4 in CD_2Cl_2/$CHCl_2F$ (Fig. 2) differ strikingly from those observed in CD_3OD. At 322 K a doublet at δ 19.1 is observed with a ^{103}Rh–^{31}P coupling of 141.7 Hz. After cooling the signal broadens and at ca. 184 K two additional broad signals become visible. However, in contrast to the spectra in CD_3OD at low temperature a doublet at δ 20.9 with a ^{103}Rh–^{31}P coupling of 143.7 Hz dominates the spectrum. That means at low temperature preferentially a C_2-symmetric complex featuring no Rh–O-interactions is present. The corresponding complex with tripodal coordination of the chiral ligand can be observed only in a small quantity. The stepwise change in the dominance of η^3- versus η^2-species could be illustrated by addition of CD_2Cl_2 to the complex in CD_3OD. These results are best explained with the formation of an intramolecular hydrogen bond between the HO-groups in the non-polar solvent (**B**, Scheme 2). In the IR spectrum in CH_2Cl_2 a strong band at 3499 cm^{-1} gives evidence for this species. The minor O–Rh coordinated complex is characterized by two weak bands at 3400 cm^{-1} and 3589 cm^{-1}. Obviously, the strong intramolecular hydrogen bond is more favored than the (weak) interaction of one of the hydroxy groups with rhodium. When the Rh–O-interaction is removed the hydrogenation can operate unhindered. In contrast, in an excess of methanol the intramolecular hydrogen bond is cleaved and the Rh–O-interaction dominates. The complex is converted into an inactive

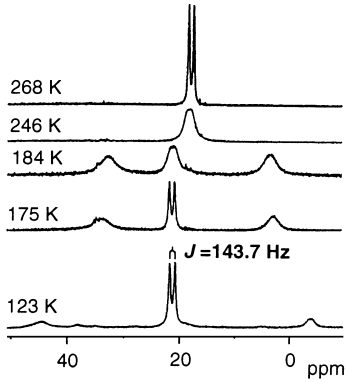
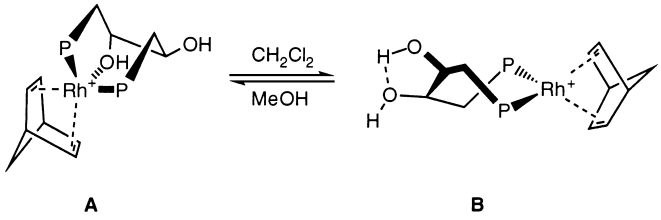


Figure 2. $^{31}P\{^{1}H\}$ NMR spectra of [Rh(**1**)(nbd)]BF_4 in CD_2Cl_2:$CHCl_2F$ (1:10) at different temperatures

state. Macroscopically, the diminution of the concentration of the active catalyst–substrate complex is expressed in the deceleration of the hydrogenation.



Scheme 2. Equilibrium between η^3- and η^2-coordination mode of the ligand in dependence of the solvent

Our results provide arguments to explain the well-known decelerating effect of hemilabile alkoxy and hydroxy ligands on the asymmetric hydrogenation.[17,26] However, up to now, the rationalization of their beneficial effect on the enantioselectivity remains speculative. Probably, pre-equilibria of diastereomeric non-active substrate–catalyst complexes, as shown above, selectively influence the concentrations of diastereomeric catalytically active catalyst–substrate complexes. Work is in progress to verify this hypothesis.

3. Summary

In chiral Rh-complexes with (*R*,*R*)-1,4-bis(diphenylphosphino)butane-2,3-diol as chiral ligand the interaction of the hemilabile coordinating HO-groups with the metal center is strongly dependent upon the nature of the counter-ligand and solvent employed. Due to their strong π-accepting properties, olefins strengthen the attractive interaction between the HO-group and the metal. Counter-ligands with reduced π-accepting properties such as methanol disfavor these interactions. As a result of this fluxional behavior the conformation of the chirality inducing backbone is altered. The coordination of electronically non-symmetric chelating substrates like methyl (*Z*)-*N*-acetylaminocinnamate can induce stereoselective interactions between diastereotopic HO-groups of the chiral hydroxyphosphine ligand and the metal center. Complexes considered herein with η^3-coordinated ligands are not active in the hydrogenation. Only by decomplexation of the hemilabile ligand can the addition of the hydrogen molecule to rhodium(I) proceed. The decomplexation may be advantageously assisted by a second HO-group able to compete with the metal for the metal bound HO-group in non-polar solvents like methylenechloride.

Acknowledgements

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