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Trinuclear Rhodium Complexes and Their Relevance for Asymmetric Hydrogenation

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Abstract: Various trinuclear rhodium complexes of the type $[Rh_3(PP)_3(\mu_3\text{-}OH)_x(\mu_3\text{-}OMe)_{2-x}]BF_4$ (where PP = Me-DuPhos, dipamp, dppp, dppe; different ligands and μ-bridging anions) are presented, which are formed upon addition of bases such as NEt_3 to solvate complexes $[Rh(PP)(solvent)_2]BF_4$. They were extensively characterized by X-ray diffraction and NMR spectroscopy (^{103}Rh, ^{31}P, ^{13}C, ^{1}H). Their in situ formation resulting from basic additives (NEt_3) or basic prochiral olefins (without addition of another base) can cause deactivation of the asymmetric hydrogenation. This effect can be reversed by means of acidic additives.

Keywords: asymmetric catalysis · hydrogenation · rhodium · kinetics · phosphine ligands

Introduction

Investigations on the asymmetric hydrogenation, especially of dehydroamino acid derivatives, with cationic rhodium complexes have for decades been of academic and industrial interest. In the established mechanistic concepts[1] the so-called solvate complexes play a fundamental role. Since they are very sensitive and difficult to handle owing to their high reactivity usually diolefin complexes of the type [Rh(PP*)-(diolefin)]anion (PP* = chelating chiral bisphosphine) are applied as precatalysts or are generated by conversion of a respective bis-diolefin complex $[Rh(diolefin)_2]$anion with one equivalent of the chiral ligand. By hydrogenating the diolefin, mostly (*Z*)-1,5-cyclooctadiene (cod) or 2,5-norbornadiene (nbd), the actual catalyst, that is, the solvate complex, is formed.[2]

Already in 1977 Halpern et al. described polynuclear rhodium complexes. Besides the possibility of the formation of an arene-bridged dimer $[Rh(dppe)(BF_4)]_2$ (dppe = 1,2-bis-(diphenylphosphino)ethane)[3] a trinuclear complex of the type $[Rh_3(dppe)_3(\mu_3\text{-}OMe)_2]^+$ was characterized.[4] The latter one forms by addition of NEt_3 and other bases such as KOMe to the solvate complex $[Rh(dppe)(MeOH)_2]BF_4$. As a structural principle it was found that three rhodium centers form a regular triangle whereas each bidentate dppe ligand is coordinated to a rhodium cation. The P-Rh-P plane is perpendicular to the Rh_3 plane, and μ_3-bridging methoxy anions are located above and below the Rh_3 plane. An analogous structure of $[Rh_3(binap)_3(\mu_3\text{-}OH)_2]ClO_4$ (binap = (2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl)) has been reported by Saito et al.[5]

In the first publications on asymmetric hydrogenation with monodentate phosphines and chelating bis-phosphines, respectively, the influence of NEt_3 additives on the enantioselectivity was investigated.[6] Such basic additives are still common practice.[7] Thus, it is rather surprising that trinuclear complexes which can result from such additives are practically not discussed as part of catalytic systems with very few exceptions.[8] The objective of this work therefore was to investigate the influence of trinuclear complexes on the activity of asymmetric hydrogenations.

Results and Discussion

By following the method of adding base (NEt_3) to a respective solvate complex described by Halpern et al. we succeed-

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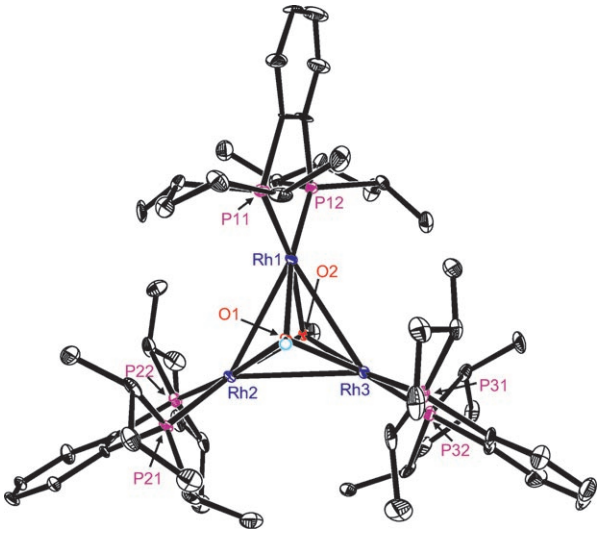

Figure 1. X-ray structure of the cation in $[Rh_3((S,S)\text{-Me-DuPhos})_3(\mu_3\text{-OH})(\mu_3\text{-OMe})]BF_4$ (ORTEP, 30% probability ellipsoids). The hydrogen atoms (except H of the OH bridge) are omitted for clarity.

ed in synthesizing several new trinuclear complexes in yields of isolated product of up to 90%. In Figure 1 a selected X-ray structure is presented.[9] As shown in the example different anions above and below the Rh_3 plane are possible[10] as are different ring sizes in the phosphine ligands (see the Supporting Information).

The bonds between the rhodium atoms of about 3 Å are longer than Rh–Rh bonds previously described in the literature.[11,12] The X-ray structures prove that ideal symmetry does not exist in the crystal owing to irregular Rh–Rh distances. However, those differences apparently compensate on the NMR time scale since the ^{31}P NMR spectra of the complexes with similar bridging anions exhibit only a doublet. In the case of dissimilar anions eight peaks are observed (ddd).

The chemical shifts in the ^{31}P NMR spectrum of the trinuclear complexes lie in the range of several species which could be present in the catalytic system.[13] Here, ^{103}Rh NMR spectroscopy renders an adequate method to unequivocally distinguish between species. The respective spectrum with the Me-DuPhos ligand (Figure 2) proves that also species with dissimilar μ_3-bridging anions can be discriminated in this way. The trinuclear complexes exhibit a high formation tendency and stability. They are stable in solution over a long period of time[15] and as solids are relatively stable in air.[16]

To resolve the question of whether trinuclear complexes are suitable diolefin-free precatalysts for asymmetric hydrogenation the test substrate methyl (*Z*)-α-acetamido cinnamate (MAC) was hydrogenated with $[Rh_3(dipamp)_3(\mu_3\text{-}OH)_2]BF_4$ under standard conditions (0.01 mmol Rh; 1.0 mmol prochiral olefin; 15.0 mL methanol; 25.0 °C; 101.3 kPa; Figure 3).[17] For reasons of comparison the same figure additionally shows the hydrogenation of MAC with the solvate complex $[Rh(dipamp)(MeOH)_2]BF_4$ and with

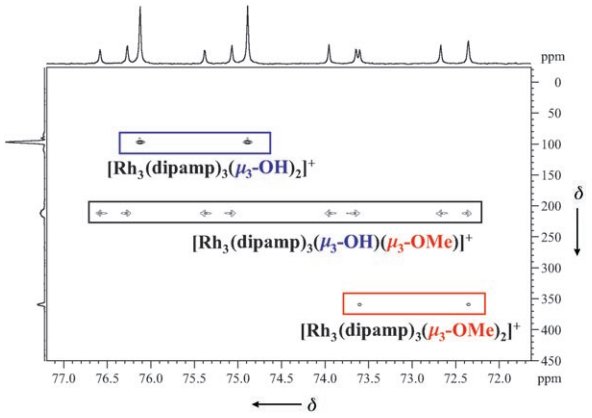

Figure 2. ^{31}P-^{103}Rh HMQC spectrum of trinuclear Me-DuPhos complexes with different μ_3-bridging anions in CD_2Cl_2.[14]

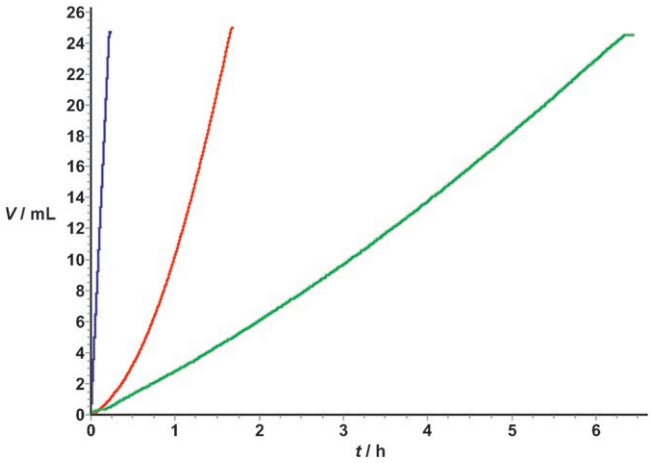

Figure 3. Comparison of hydrogen consumption curves of the hydrogenation of methyl (*Z*)-α-acetamido cinnamate (MAC) with different dipamp complexes: $[Rh(dipamp)(MeOH)_2]BF_4$ (blue), $[Rh(dipamp)(cod)]BF_4$ (red), $[Rh_3(dipamp)_3(\mu_3\text{-}OH)_2]BF_4$ (green); each 0.01 mmol Rh; 1.0 mmol MAC; 15.0 mL methanol; 25.0 °C; 101.3 kPa.[18]

the cod complex $[Rh(dipamp)(cod)]BF_4$. The hydrogen consumption curve proves that hydrogenations can be performed using the trinuclear complexes in principle. However, considerable induction periods occur that are even more pronounced than with the analogous cod complex.

The trinuclear complex itself is not active in the hydrogenation owing to a lack of coordination sites. However, the equilibrium between the trinuclear complex and the solvate complex, which is apparently strongly shifted to the side of the trinuclear complex[15] is—in the presence of prochiral olefin in excess—disturbed by the formation of diastereomeric catalyst–substrate complexes which then further react with hydrogen. This leads to a continuous decrease of the trimer concentration. Macroscopically, the induction period, that is, the period of increasing hydrogenation activity, is observed.

As already mentioned, enantioselective catalyses have been described in the presence of basic additives such as NEt_3.[7,8] Since the hydrogenation of MAC with the solvate

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complex $[Rh(dipamp)(MeOH)_2]BF_4$ proceeds as a pseudo-zero-order reaction (saturation range of the underlying *Michaelis–Menten* kinetics[1a]), it is easily quantified and thus suitable to determine the influence of NEt_3 additives on activity.

Figure 4 shows the hydrogen consumption for the system MAC/$[Rh(dipamp)(MeOH)_2]BF_4$. In comparison, analogous hydrogenations were performed in which different amounts of NEt_3 were added (NEt_3/Rh = 1 to 35) to the reaction solution after each ca. 20% conversion of the prochiral olefin. The addition of base results in an instant color change of the reaction solutions from red/orange to red/brown and an activity loss that is the more significant the higher the NEt_3/Rh ratio. After a very short transition period an approximately constant activity is reached again. The ^{31}P NMR spectrum after completion of the hydrogenation reveals only the typical signals of the trinuclear complex.[19]

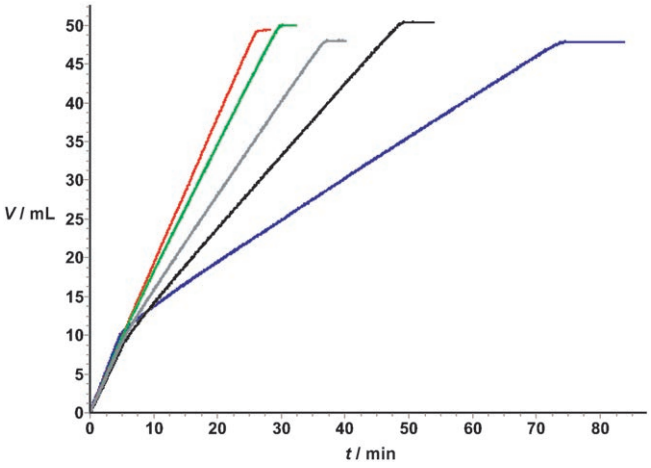

Figure 4. Hydrogen consumption curves of the hydrogenation of MAC with $[Rh(dipamp)(MeOH)_2]BF_4$ (red). Addition of NEt_3 to analogous hydrogenations after ca. 20% conversion: green = 0.01 mmol, gray = 0.05 mmol, black = 0.1 mmol, blue = 0.35 mmol (each 0.01 mmol Rh; 2.0 mmol MAC; 15.0 mL methanol; 25.0 °C; 101.3 kPa).

Thus, it could be quantified for the first time that basic additives such as NEt_3 can negatively influence the catalytic activity owing to the fast formation of practically non-hydrogenation-active trinuclear complexes. In principle it is possible—and exploratory analyses prove it (see the Supporting Information)—that some prochiral olefins can be basic enough to initiate the formation of inactive trinuclear complexes, without other basic additives!

The formation of trinuclear complexes in the presence of base suggests that by subsequent addition of acid the reverse reaction to the solvate complexes can be accomplished.[20] Hydrogenations with trinuclear complexes as precatalysts indeed show that upon addition of HBF_4, with BF_4^- already present in the system as an anion, the hydrogenation activity increases considerably (Figure 5). Within the range of reproducibility the same activity (and selectivity) as with the solvate complex is observed at an acid/Rh ratio of 100. Apparently, in the presence of an appropriate excess of acid the inactive trinuclear complexes are—at least in the example shown here—completely transformed into the active solvate complex $[Rh(dipamp)(MeOH)_2]BF_4$.

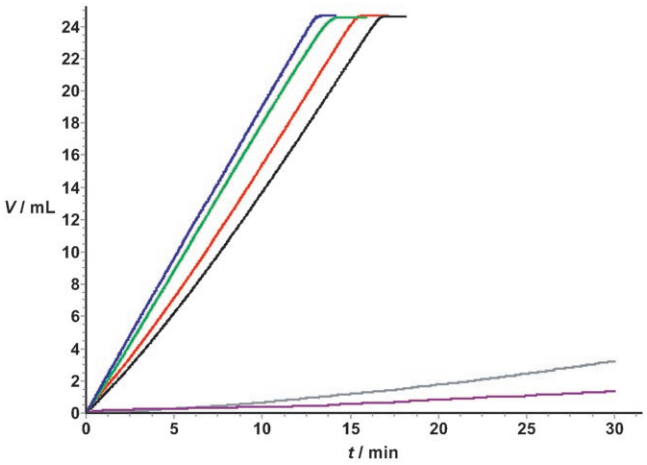

Figure 5. Hydrogenation of MAC with dipamp complexes: blue = $[Rh(dipamp)(MeOH)_2]BF_4$ as reference; trinuclear complex $[Rh_3(dipamp)_3(\mu_3\text{-}OH)_2]BF_4$ with acid as additive: green: HBF_4/Rh = 100, red: HBF_4/Rh = 30, black: HBF_4/Rh = 10; gray = $[Rh(dipamp)(cod)]BF_4$; violet = $[Rh_3(dipamp)_3(\mu_3\text{-}OH)_2]BF_4$ (each 0.01 mmol Rh; 1.0 mmol MAC; 15.0 mL methanol; 25.0 °C; 101.3 kPa.).

The relevance of the results becomes evident considering that the addition of acid in asymmetric hydrogenations is described even for industrial processes.[21] The actual reasons for that, however, remain partly unclear. The degradation of catalytically inactive trinuclear species described here is *a possible explanation* for the known effect of activity increase after addition of acid to a hydrogenation system.[22]

Conclusions

In summary, the application of newly described, stable trinuclear rhodium complexes as diolefin-free precatalysts for asymmetric hydrogenation is in principle possible; however, those hydrogenations are macroscopically characterized by a comparatively low activity. It could be proven that basic additives such as NEt_3 commonly used to manipulate enantioselectivities can lead to a deactivation by formation of the respective trinuclear complexes. Exploratory analyses furthermore showed that appropriate prochiral olefins can be basic enough to initiate the formation of trinuclear complexes *without* other basic additives. By means of acidic additives, however, the formation of trinuclear complexes can be thwarted or the decomposition of trinuclear complexes can be accelerated.

Experimental Section

All reactions and manipulations were performed in a dry argon atmosphere using standard Schlenk-type techniques. Hydrogenation experiments were performed as described in reference [2b]. All ^1H and ^{31}P NMR spectra were taken on a Bruker 300MHz spectrometer. All ^{13}C

and ^{103}Rh NMR experiments were carried out on a Bruker 400MHz spectrometer. Diffraction data were collected on a STOE-IPDS II diffractometer [$\lambda(Mo_{K\alpha}) = 0.71073$ Å]. The structures were solved by direct methods (SHELXS-97 (Sheldrick, 1997)) and refined by full-matrix least-square techniques against F^2 (SHELXL-97). XP (Siemens Analytical X-ray Instruments, Inc.) was used for structure representations. As observation criterion, $I > 2\sigma(I)$ was used. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed into theoretical positions and were refined by using the riding model.

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[3] Regarding the possible influence of arene complexes on the *activity* of asymmetric hydrogenations, see: D. Heller, H.-J. Drexler, A. Spannenberg, B. Heller, J. You, W. Baumann, *Angew. Chem.* **2002**, *114*, 814–817; *Angew. Chem. Int. Ed.* **2002**, *41*, 777–780.

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[8] W. Leitner, J. M. Brown, H. Brunner, *J. Am. Chem. Soc.* **1993**, *115*, 152–159.

[9] Further examples as well as a tabular summary of important bond lengths and angles can be found in the Supporting Information. CCDC 680135–680141 contain the supplementary crystallographic data to this publication. These data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ; Fax:(+44) 1223-336-033; E-mail: deposit@ccdc.cam.ac.uk.

[10] In principle there are two ways of gaining trinuclear complexes with dissimilar μ_3-bridging anions: firstly by direct formation from a respective solvate complex and, for example, a NEt_3/H_2O mixture; or by subsequent exchange of one anion (see the Supporting Information).

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[12] In metal atom clusters direct metal–metal bonds exist, whereas in "Werner complexes" nuclei are bridged by μ-bridging ligands.

[13] The Supporting Information provides all NMR data of the synthesized trinuclear complexes as well as NMR data of several dipamp complexes.

[14] An analogous spectrum for the dipamp ligand can be found in the Supporting Information.

[15] After addition of NEt_3 to the solvate complex [Rh(dipamp)-$(MeOH)_2$]BF_4, the ^{31}P NMR spectrum exhibits signals of the trinuclear complex only. The solvate complex which is expected from the equilibrium is not observed in a period of weeks.

[16] The ^{31}P NMR spectrum of [Rh_3((*S,S*)-dipamp)$_3$(μ_3-OMe)$_2$]BF_4 that had been exposed to air for 10 days shows only two species: the doublet of the trinuclear complex and a singlet (most likely of an oxide) at $\delta = 31$ ppm (ratio of integrals trinuclear complex/oxide = 70:30).

[17] The general procedure for hydrogenations is described in: "Kinetics in Homogeneous Hydrogenation: Interpretation and Measurement": H.-J. Drexler, A. Preetz, T. Schmidt, D. Heller in *Handbook of Homogeneous Hydrogenation* (Eds.: H. G. deVries, C. Elsevier), Wiley-VCH, Weinheim, **2007**, chap. 10, pp. 257–293.

[18] While the hydrogenations with the solvate complex and with the cod complex result in an *ee* value of 96%, the hydrogenation with the trinuclear complex gives reproducibly 89% *ee*. The reasons remain unclear.

[19] In addition, an arene complex with the hydrogenation product is observed, as unequivocally proven by ^{103}Rh NMR spectroscopy; $J_{P-Rh} = 206$ Hz, ^{31}P-^{103}Rh HMQC: $\delta_{Rh} = -967.2$ ppm.

[20] Halpern et al. explicitly exclude this in reference [4]: "When base (OMe^- or a sterically hindered amine such as triethylamine) was added to a methanolic solution of [Rh(diphos)]$^+$ an irreversible (i.e., not reversed by addition of acid) yellow to red-brown color change was observed, to yield a new species, [Rh_3(diphos)$_3$($OMe)_2$]$^+$".

[21] H. U. Blaser, F. Spindler, M. Studer, *Appl. Catal. A* **2001**, *221*, 119–143 (Table 5).

[22] It should also be kept in mind that the addition of acid to a basic substrate can as well lead to a protonation of the latter. Thus, it could not act as a base anymore to initiate the formation of trinuclear complexes. In this context the importance of the order in which components are added to the reaction solution to be hydrogenated becomes clear.

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