Enantioselectivity Control with Metal Colloids as Catalysts

Helmut Bönnemann* and Gerhard A. Braun

Abstract: Metal colloids protected with chiral molecules can lead to a new type of enantioselective catalyst combining good selectivity control with an extraordinarily high activity in hydrogenation reactions. This concept has been applied for the first time in the form of platinum sols stabilized by the alkaloid dihydrocinchonidine.

Keywords
asymmetric synthesis · catalysis · colloids · hydrogenations · platinum

Mono- and multimetal colloids of 1–10 nanometer size have been shown to be efficient catalysts for various chemical reactions such as hydrogenation,[1] oxidation,[2] hydrosilylation,[3] and C–C bond formation.[4] In addition, colloidal metal precursors have been used for the formation of high-performance fuel-cell catalysts.[5] In colloids the metal particles are protected sterically or eletrostatically to prevent agglomeration. The protecting shell present at the surface of the nanoparticle has been demonstrated to have a decisive influence on the regioselectivity[6] and stereoselectivity[7] in the hydrogenation of olefins and substituted aromatics. We have recently reported for the first time that metal colloids protected by a chiral stabilizer can induce enantioselectivity in catalytic hydrogenation.[8] The concept leading to this new type of catalyst is an extension to colloidal metals of the well-known heterogeneous enantioselective catalyst.

Supported platinum particles modified by cinchona alkaloids are known to catalyze the hydrogenation of 2-oxoesters[9a–c] and -acids[9d] to the corresponding 2-hydroxy compounds in optical yields of up to 95% *ee*.[9e] This reaction has been investigated systematically with respect to the catalyst preparation,[10] reaction conditions,[11] kinetics,[12] and mass transfer phenomena.[13] Further, the structural elements of the modifier required to induce enantioselectivity have been studied in detail by Pfaltz et. al.[14] The interaction between the modifier and the substrate on the surface can be rationalized with the help of computer modeling,[15] and the reaction rate and enantioselectivity have both been monitored as a function of conversion.[16]

Platinum sols stabilized by dihydrocinchonidine (**1**, Figure 1) can be synthesized in different particle sizes by the reduction of platinum tetrachloride with formic acid in the presence of different amounts of alkaloid. The resulting nanoparticles induce enantioselectivity in the hydrogenation of ethyl 2-oxopropionate (ethyl pyruvate) with optical yields of 75–80% *ee* (Scheme 1).[8] Turnover frequencies (ca. 1 s^{-1}) and enantiomeric excess were both found to be independent of the particle size.

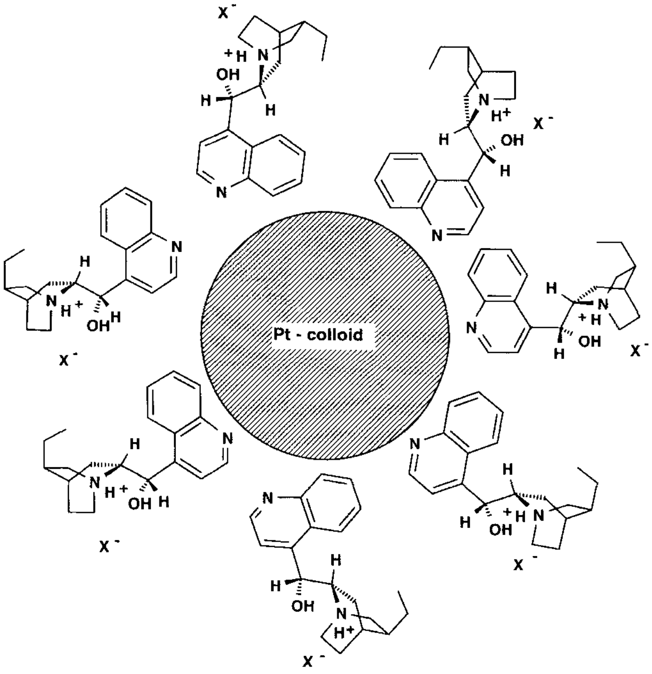
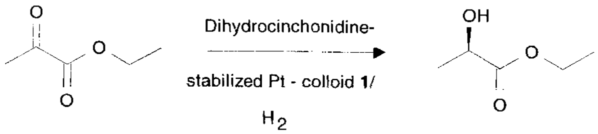


Figure 1. Schematic representation of the cinchona-stabilized platinum colloid (**1**, X = AcO, Cl).

In order to evaluate the catalytic characteristics of colloidal platinum, we compared the efficiency in the reaction shown in Scheme 1 of Pt nanoparticles in "quasi-homogeneous" phase with that of supported colloids of the same charge and of a



Scheme 1. Enantioselective hydrogenation of ethyl pyruvate.

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conventional heterogeneous platinum catalyst. The result is shown in Table 1. The conventional catalyst E4759 from Engelhardt Inc. gives the highest optical yields (91.4% *ee*). The difference between the enantioselectivity of the colloidal system (81.3% *ee*) and that of the conventional catalyst is not insignificant, since the higher the enantioselectivity, the more difficult it becomes to improve any further. The difference may derive from the fact that the convential catalyst was pretreated with hydrogen at 400 °C, a procedure that was shown to improve catalytic performance.[9a, b] This was not possible in the case of the colloidal system. However, the turnover frequency of the "quasi-homogeneous" colloidal platinum exceeds the heterogeneous systems by a factor of 3. We initially assumed this effect to be the result of mass transport limitations in the case of the supported catalysts and investigated this possibility using the Koros–Nowak criterion,[17] which relates the activity of a heterogeneous catalyst to the number of active centers in the absence of mass or heat-transfer limitations. Heterogeneous catalysts prepared, for example, by supporting colloidal metal particles of defined size are well-suited to fulfill this criterion, since the metal loading and consequently the number of active centers can be varied over a broad range without altering the basic preparation mode or the particle size of the metal component.[18] Figure 2 demonstrates that the size of the preformed metal particles remains unaffected by the adsorption on the support surface.

Table 1. Reaction rate, turnover frequency, and optical yield achieved with different platinum catalysts in the enantioselective hydrogenation of ethyl 2-oxopropionate.

Catalyst	*R* [a] [mol s^{-1} m^{-3}]	TOF [b] [s^{-1}]	*ee* [%]
Pt colloid ("quasi-homogeneous")	5.47	35.8	81.3
supported Pt colloid	1.77	10.2	75.4
E4759 [c]	1.14	13.2	91.4

[a] *R* is the molar rate per unit volume of the reaction phase. The reactions were performed in a reaction volume of 15 mL with a 3 M concentration of ethyl 2-oxopropionate. The amount of platinum metal was 1 mg in all cases. H_2 pressure was 9 MPa, reaction temperature 292 K, 5 mg dihydrocinchonidine was added to the reaction mixture in all cases. [b] The colloids had a dispersion of $D = 0.52$, estimated as described in ref. [8]; TOF is given by (mol substrate)(mol surface platinum atom)$^{-1}$(second)$^{-1}$. [c] E4759 is a heterogeneous catalyst consisting of platinum on aluminum oxide from Engelhardt Inc.; dispersion specified, $D = 0.24$.

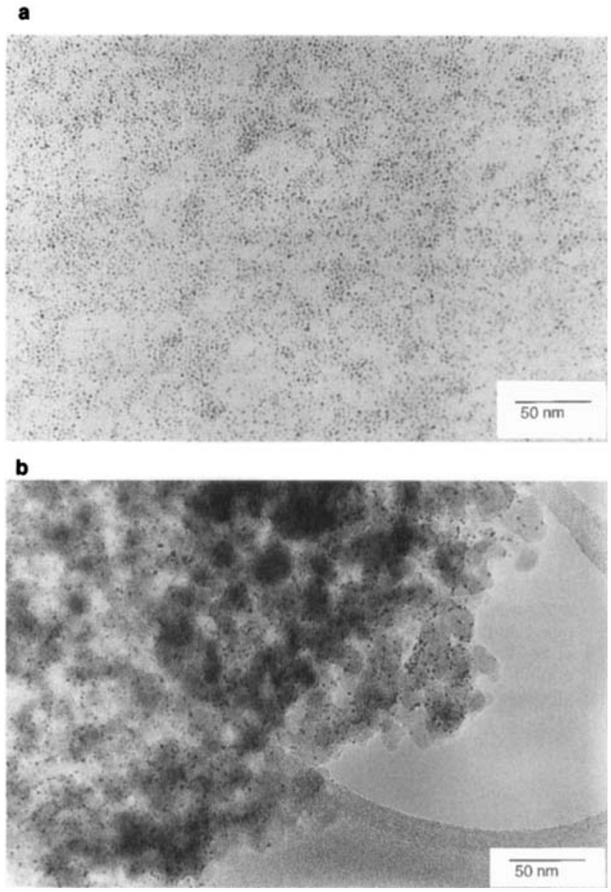

Figure 2. Transmission electron micrographs of platinum colloids from dihydrocinchonidine-stabilized sols: a) as synthesized and b) after being supported on silica.

Table 2. Activity and selectivity as a function of catalyst amount and metal loading.

Catalyst [mg]	Metal loading [% (g/g)]	Pt [mg]	*R* [mol s^{-1} m^{-3}]	TOF [s^{-1}]	*ee* [%]
120	1	1.2	1.9	9.0	74.4
20	5	1	1.6	8.9	75.4
70	1	0.7	1.2	9.6	73.6
10	5	0.5	0.8	9.6	74

An inspection of Table 2 reveals that the turnover frequency is constant in all cases, suggesting that only the metal loading (i.e. the number of active centers) governs the reaction rate. This provides evidence for the absence of mass and heat transport phenomena. Up to now, we have no conclusive explanation for the considerable enhancement in the catalytic activity observed with our colloidal metal catalyst in "quasi-homogeneous" phase. Further, the enhanced activity does not correlate with enantioselectivity, as might be expected from a kinetic model.[19]

The enhancement in the catalytic activity along with good selectivity control is the most promising incentive for the development of colloidal metal catalysts having properties between those of classical homogeneous complex catalysts and the established heterogeneous systems.

Future developments in the field of enantioselectivity control using colloidal metal as catalysts may center on specific variation of the metal core, for example, by the use of metal alloys, or a more controlled construction of the metal particle surface by hydrothermal treatment. A second line of innovation may come from new types of chiral stabilizers. In this respect, the use of polymers containing cinchona building blocks or chiral dendrimers could lead to an alternative type of colloidal metal catalyst showing activity at higher reaction temperatures.

Abstract in German: Mit *chiralen Molekülen geschützte Metallkolloide liefern eine neue Art enantioselektiver Katalysatoren, die zu guten Selektivitäten und außerordentlichen Aktivitäten bei Hydrierungen führen. Platinsole, die durch das Alkaloid Dihydrocinchonidin stabilisiert werden, sind das erste Beispiel für Verbindungen, die nach diesem Konzept arbeiten.*

A new type of metal colloid protected with chiral stabilizer may derive from another well-known heterogeneous enantioselective catalyst, the nickel/tartrate system,[20] which is certainly a good candidate for the colloidal approach to catalytic enantioselectivity control.

The ultimate research goal in this field, however, is to develop highly active nanostructured metal colloids protected by a new generation of chiral stabilizers providing efficient enantioselectivity control in the transformation of specific prochiral substrates into valuable fine chemicals.

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Corrigendum: In the paper "Control of the Helical Chirality in Octahedral Complexes by a Chiral Macrobicyclic Cavity Possessing Six Convergent Hydroxyl Groups" by P. Baret, V. Beaujolais, D. Gaude, C. Coulombeau and J.-L. Pierre (*Chem. Eur. J.* **1997**, *3*, 969–973; June issue) the legend to Figure 4 should read as follows:

Stereoviews of Λ-(a*S*,a*S*,a*S*) (top) and Δ-(a*S*,a*S*,a*S*) (bottom) $[LFe]^{3-}$ complexes (generated by molecular modelling).