Role of ligands in homogeneous catalysis based on transition metals*

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The role of ligands in homogeneous catalysis by transition metals and the promising lines of research related to simulation of biocatalytic processes are considered.

Key words: homogeneous catalysis, transition metal complexes, biocatalysis, ligands.

Homogeneous transition metal based catalysis has seen a rapid growth in recent years, mainly due to selectivity advantages. Selectivity (chemo, regio, stereo) is needed for new processes and products or for replacement of old processes and products. Environmental demands for pure products and for processes producing no by-products (green chemistry) provide additional, enticing opportunities.

An essential part of practising homogeneous catalysis is selecting ligands or tailoring ligands. The major share of homogeneous catalysts applied by industry is based on monodentate phosphorous ligands as is evident from hydroformylation applying $XRh(CO)(R_3P)_2$ complexes. Only lately, ligands such as cyclopentadienyl (as metallocenes) or ligands containing bidentate nitrogen groups have found practical application. However, if one looks at systems based on biological ligands, quite a different picture is observed. Besides the cooperation between the ligand and the metal strong steering impacts stem from the mutual influence of different reaction centers (bi- and multi-functional catalysis); involvement of several metal atoms and ionic complexes; preferred participation of oxygen-, nitrogen- and sulfur-containing ligands rather than phosphorus ones; interactions at hydrophobic/hydrophilic interfaces; and self-organization of a catalyst system. One can conclude that homogeneous catalysis is still in its infancy and that emulating the nature may be a good approach to advance homogeneous catalysis.

For considerations of applicability, a comparison of homogeneous, heterogeneous, and bio-catalysis is of interest (Table 1).

For industry, the operation conditions are of great significance. Industry prefers processes at low pressure and temperature. The catalysts of choice must be selective and must possess good activity and stability. It is obvious from Table 1 that homogeneous and biocatalysts offer many advantages over heterogeneous catalysts, especially regarding selectivity. Looking only at enantioselectivity, which is so important for the manufacture of optically pure compounds needed in "life science chemistry", biocatalysts even surpass homogeneous systems. Learning from nature or a bio-inspired approach could certainly assist the advancement of homogeneous catalysis.

The search for bio-inspired impacts on homogeneous catalysis can be focused on the following points: ligands and bio-inspiration, use of metals and bio-inspiration, and the role of bio-inspired reaction conditions. The last two topics will not be elucidated within the framework of this paper. The considerations will be based almost exclusively on ligands.

Ligands and biocatalysis

The majority of ligands used in biological systems (Fig. 1) are based on oxygen, nitrogen, and sulfur coordinating groups. Phosphorous, the working horse in homogeneous catalysis, is missing here. The ligands can be coordinated in monodentate or polydentate fashions, as is well known from metalloenzymes or complexes in proteins. Polymetallic and ionic systems are also very common.

Historically, homogeneous catalysis has developed around monodentate R_3P ligands. It is Wilke´s great contribution to have recognized for the first time the method to control the distribution of the cyclic butadiene oligomers, *viz.*, cyclooctadiene, cyclododecatriene and vinylcyclohexene, by variation of the R_3P or $(RO)_3P$ ligands.[1]

* Dedicated to O. M. Nefedov on the occasion of his 70th birthday.

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Table 1. Comparison of homogeneous (I), heterogeneous (II), and biological (III) types of catalysis

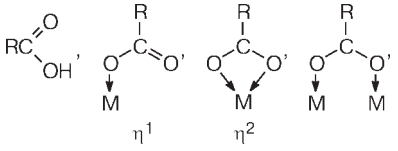
Parameter	I	II	III
Catalyst	Metal (bulk or supported)	Metal/ligand	Complex systems, often with specific ligands
Pressure/bar	1—300	1—300	~1
T/°C	~20—400	<200	15—50
pH	From acidic to alkaline	From acidic to alkaline	5—10
Medium	Mainly gas phase	Liquid phase	Hydrophobic/hydrophilic interface
Selectivity	Variable, often poor	High	Very high (regio-, enantio-)
Activity/stability	Variable	Variable	Variable
Diffusion	Difficult	Easy	Easy, toward the complex

The so-called "ligand tailoring" emerged and is practised effectively, for instance, in Shell´s hydroformylation process for converting olefins into linear alcohols or DuPont´s hydrocyanation of butadiene to give adiponitrile. Both processes embracing million tons of products are based on high regioselectivity.

Ligands

Monodentate ROH, RSH, R_nNH_m, N-heterocyclic

Bidentate



amino acids

sulfur-containing

Tridentate Mainly, nitrogen-, sulfur, and oxygen-containing

Tetradentate Porphyrin, corrin

Complexes

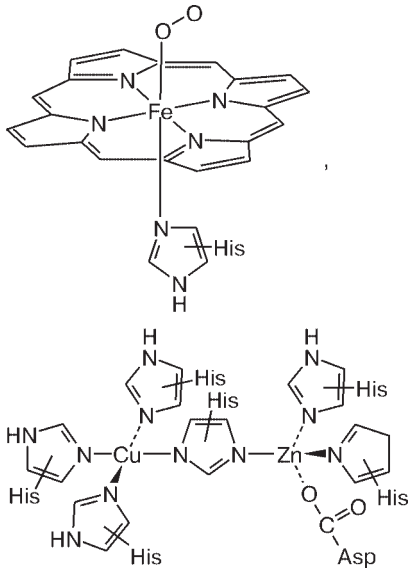
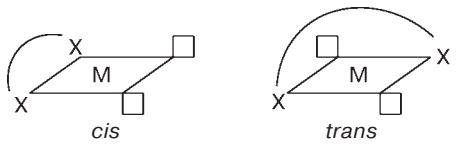


Fig. 1. Ligands and complexes in biological systems.

Bidentate ligands in homogeneous catalysis. Many research groups have used bidentate ligands in homogeneous catalytic reactions. Here reference should only be given to the numerous papers dealing with asymmetric syntheses. The high enantiomeric excess (*ee*) values reached by chelating ligands may be considered as a bridge to biocatalysis in which bidentate ligands are frequently used (see Fig. 1). The steric control of reactions is crucial for nature, which achieves this in various ways.

A bidentate ligand can consist of electronically identical or nonidentical heteroatoms. This gives rise to various pathways of catalytic reactions, which are well established in organometallic coordination chemistry.

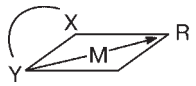
cis- or trans-Position of electronically identical X∩X chelating ligands. In square planar complexes, electronically identical X∩X chelating ligands can favor either *cis*- or *trans*-position.



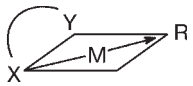
It is well known that alkyl complexes with *cis*-arranged X∩X groups are very unstable and easily undergo β-elimination (Eq. 1), whereas *trans*-complexes are quite stable.

$$L_nM—CH_2—CH_2—R \longrightarrow L_nMH + CH_2=CH—R \qquad (1)$$

cis- or trans-Position of electronically different X∩Y chelating ligands. In square planar complexes with electronically different X∩Y chelating ligands, one can differentiate whether a group R is in *cis*- or *trans*-position with respect to X or Y.



R is in the *trans*-position relative to Y

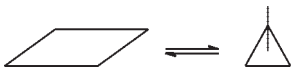


R is in the *trans*-position relative to X

Apical or equatorial position. In bipyramidal complexes, the X∩X and X∩Y chelating ligands can be coordinated

in apical and equatorial positions giving rise to equatorial-equatorial or apical-equatorial modes of coordination.[2]

Structural changes. Square planar complexes can be converted to tetrahedral structures (Eq. (2)).

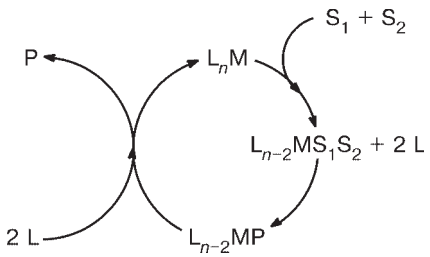


(2)

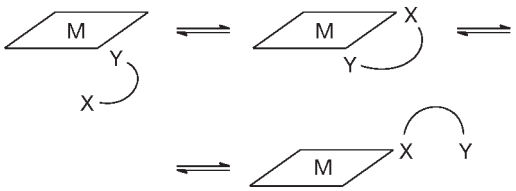
Square planar complexes are unsaturated and easily coordinate other ligands, which can be important for substrate coordination.

Hemilabile structures. Ligands in organometallic complexes can dissociate (Scheme 1), thus creating free coordination sites (reaction centers), which can be used by incoming substrate molecules (for example, $S_1 + S_2$) to yield product P in a catalytic cycle.

Scheme 1



In the case of X⌒Y chelating ligands, either X or Y atom can split off (Eq. (3)).



(3)

This so-called hemilabile ligand behavior[3] can be used (i) to create a free coordination site, (ii) to preserve a free coordination site for concomitant ligand displacement, and (iii) to create a vacant site in the *cis*- or *trans*-position relative to a third group (for example, a metal—carbon bond).

The author has long been interested in bidentate ligands of the P⌒O type; these are used successfully in the SHOP (Shell higher olefin process), which is one of the largest-scale applications of homogeneous catalysis by a transition metal.[1]

For understanding of the methods of ligand design (ligand tailoring), easy synthesis routes and built-in chemical properties should be given.

The P⌒O ligands offer great potential regarding the ligand tailoring and the variation of chemical properties

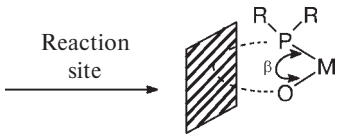
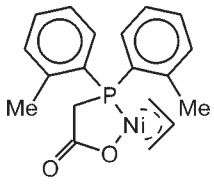


Fig. 2. Model representation of the catalytic site of a biological system with a P⌒O bidentate ligand; β is the opening angle.

of complexes as functions of the donor capacity, the chelating effect, labile equilibrium between the mono- and bidentate ligand coordination, the Tolman cone angle, the opening angle (β), and the symmetry and rigidity of the reaction site (Fig. 2).

In order to elucidate the mechanism of C—C bond formation in olefin conversions, we synthesized the square planar crystalline complex **1**, which (when dissolved in toluene) catalyzes the oligomerization of ethylene yielding oligomers that are 99% linear and contain up to 98% α-olefins.



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The oligomers obtained follow a Schulz—Flory type molecular-mass distribution. Obviously the rate of chain propagation *vs.* the rate of β-elimination (see Eq. (1)) is responsible for the molecular-mass selectivity in the oligomer distribution, and the selectivity can be finely tuned by various methods.

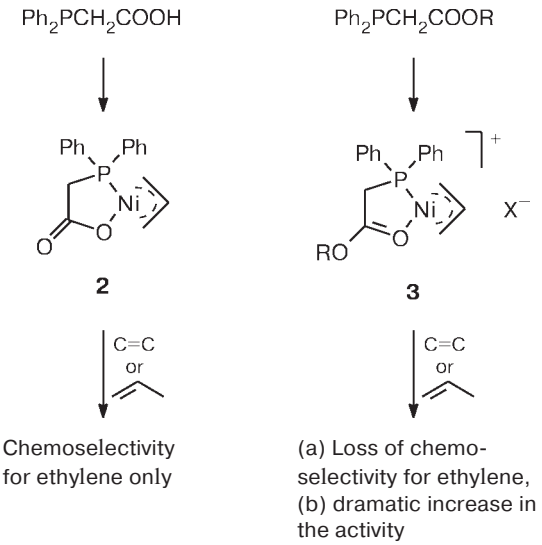
1. *Substituents at the P atom.* Alkyl or bulky groups at phosphorus result in higher molecular masses.[3] Substituents at the *ortho*-position of the benzene rings of complex **1** also favor high-molecular-mass oligomers up to polyethylene[4] (*ortho*-effect).

2. *Ring size in the Ni—K²—P⌒O chelate.* An increase in the Ni—K²—P⌒O chelate ring size from five- to six- or seven-membered ring significantly diminishes the catalytic activity.[5] The complexes become paramagnetic, which is indicative of a tetrahedral geometry (see Eq. (2)).

3. *Ionic or neutral complexes.* To investigate the impact of ionic complexes, we have synthesized complexes **2** and **3** (Scheme 2).[5] Both catalyze ethylene oligomerization. Whereas neutral complex **2** is chemoselective for ethylene only, ionic complex **3** has lost chemoselectivity and reacts with other α-olefins giving branched oligomers. In addition, a dramatic activity increase is observed with ionic complexes.[6] Again, parallels to ionic biological systems may be drawn. It may be suggested for academic research that the impact of cationic or anionic complexes upon chemical reactions should be investi-

gated in greater detail using organometallic model reactions.

Scheme 2



The success with P⌒O chelating ligands in ethylene oligomerization has prompted us to use P⌒O type ligands in various other type of reaction.

Reaction of ethylene with carbon monoxide. Cationic palladium complexes with P⌒O ligands allow the catalytic conversion of ethylene and CO into strongly alternating polyketones.[7]

Reaction of ethylene with sulfur dioxide. In the presence of cationic P⌒O—Pd complexes, ethylene and SO_2 can be converted into strongly alternating polysulfones.[8]

Reaction of ethylene with acrylates. Ethylene and acrylate can condense[9] to give CH_2=CH—CH_2—COOR due to the action of cationic P⌒O—Pd complexes.

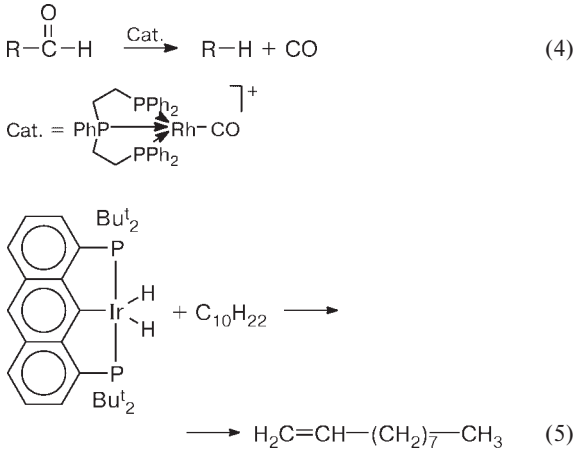
Hydroformylation of epoxides. In the presence of hemilabile P⌒O chelating ligands, epoxides can be selectively hydroformylated to give β-hydroxyaldehydes in high yields.[10]

Hydrovinylation of styrene. The hydrovinylation of styrene with ethylene offers a special challenge regarding chemo-, regio-, and enantioselectivity. In the presence of [η^3-C_4H_7Pd(Ph_2PC*H)(Me)COOEt]SbF_6, this reaction gives[11] 3-phenylbut-1-ene with 86% conversion and with an optical purity of 33%.

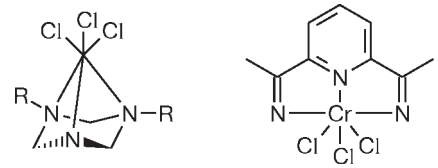
It is very surprising that chelates formed by P⌒O ligands catalyze six absolutely different reactions described above. We speculate and postulate that the enforcing square planarity *via* the P⌒O chelate is the real driving force of this unique behavior of the ligand. If this is correct, great importance in homogeneous catalysis rests on the geometrical structure. The possibility of obtaining a desired geometrical structure would be enhanced by the use of polydentate ligands. Indeed, also nature uses polydentate ligands to enforce geometrical structures, as is exemplified in porphyrins frequently encountered in metalloenzymes.

If one searches through the literature for polydentate ligands (with a denticity of >2) applied in homogeneous catalysis, the results are disappointing. Whereas such a vast amount of data is available on monodentate ligands, reports on polydentate ligands are sparse. However, some interesting examples exist.

Tridentate ligands in homogeneous catalysis. An interesting decarbonylation reaction using a tridentate ligand (Eq. (4))[12] and a unique dehydrogenation reaction yielding α-olefins (Eq. (5))[13] have been reported.



In a study[14] that we carried out in close collaboration with R. D. Köhn´s research group (University of Bath), we have found that complex **4** allows the conversion of ethylene and other α-olefins to trimers. Surprisingly, another chromium complex with a tridentate ligand (**5**) reacts with ethylene to give α-olefins conforming to the Schulz—Flory molecular-mass distribution.[14]



4 **5**

This difference might be due to different modes of coordination of the tridentate ligands. We postulate that in complex **4**, three coordination sites in facial coordination are occupied giving rise to trimers only, whereas in complex **5**, the ligand coordination is meridional, leading to α-olefins with a Schulz—Flory type distribution.

The use of tridentate ligands sheds light once again on the modes of coordination possible for chelating ligands, which makes them quite unique.

Tetradentate ligands in homogeneous catalysis. Numerous papers dealing with the use of tetradentate ligands, such as porphyrins, in homogeneous catalytic oxidation reactions can be found in the literature. Many researchers have attempted to mimic natural enzymes.[15] Chiral (salen) metal complexes are known[16] to catalyze an array asymmetric nucleophilic and electrophilic reactions. However, only a few systematic studies have been carried out with tetradentate A—B—C—D ligands with various heteroatom combinations.

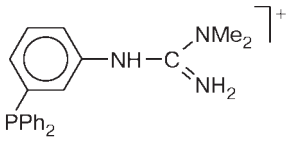
Prospects for the search for new ligands

A number of promising lines for future research can be foreseen:

Ligands. More emphasis on the role of polydentate ligands in homogeneous catalysis should be given. Previously, the success with phosphorus-containing ligands has diverted researchers´ attention from ligands containing the N, O, and S heteroatoms, used almost exclusively by the nature. For instance, amino acids may provide very useful ligands.

Cooperation between ligand fragments and the catalyst center is frequently observed in biological systems. This is also known in some cases in organometallic chemistry. More research is needed to untangle this delicate interplay.

Ligands or ligand fragments provided by nature should be included in catalytic investigations. Recently,[17] we have successfully used guanidinium based ligands (**6** and **7**) in hydroformylation using ionic liquids.



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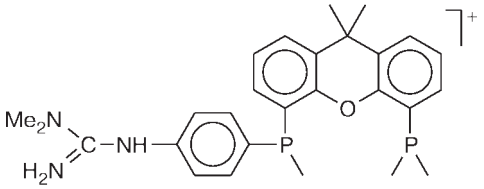

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The ligands active in redox processes shows great promise for electrochemical control.[18]

In coordination chemistry, which forms the backbone of homogeneous catalysis, stoichiometric and catalytic model reactions involving ionic complexes are seldom encountered. When one considers the importance of ionic complexes in biosystems, one can foresee here a great potential for future research.

Metals. The research in homogeneous catalysis is based to a large extent on a monometallic approach. Conversely, biocatalysts often contain more than one metal. The interaction between two or more different metals seems to be important. Very often, we are far from understanding how nature utilizes polymetallic systems. Here we definitely need a better understanding *via* research.

We should not be disillusioned by the former failures in cluster chemistry. These may have been due to selection of wrong reactions for testing the catalytic behavior. For instance, in the presence of synthesis gas, many clusters tend to decompose.

Nature is using a limited number of metals. The metals not used by nature, *e.g.* noble metals, can be introduced into biological ligand systems *via* metal exchange. In nature, two or more enzymes are often involved in a coupled system of reactions. The use of multifunctional organometallic complexes can give rise to cascades of reactions. For instance, dehydrogenation induced by one catalyst may be coupled with hydroformylation on the active sites of a second catalyst (tandem reactions).

Reaction conditions. The biocatalytic processes in nature are extremely complex. For instance, iron porphyrin complexes can stoichiometrically transport oxygen but at the same time maintain a multiplicity of catalytic functions such as participation in redox processes with electron transport and in consecutive reactions with intermediate formation of O_2^{2-}, NO_2^-, SO_3^{2-}, *etc*. Enzymes can be activated by the addition of inorganic ions, probably, *via* stabilization of certain conformations.

The pH, temperature, and heat- and mass-transfer have a crucial impact on enzymatic systems. The nature accomplishes all these phenomena in very sophisticated ways. What can we learn here?

Medium effects are essential in either deactivating or assisting adsorption and desorption. A very delicate interplay exists between hydrophobic and hydrophilic phase interactions.

An important field in enzyme chemistry is the influence of co-factors and co-enzymes. Do parallels exist to homogeneous catalysis by transition metal complexes?

Within the framework of this paper, only a very limited number of thoughts could be raised. The author, however, hopes to stimulate a discussion on bio-inspired ligands in homogeneous catalysis.

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