Inorganica Chimica Acta, 50 (1981) 11–19

Mechanistic Aspects of Homogeneous Catalytic Hydrogenation and Related Processes

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The roles of transition metal complexes in catalysis are discussed in the light of recent studies on the kinetics and mechanisms of homogeneous catalytic hydrogenation reactions.

Introduction

Among the most significant developments in inorganic and organometallic chemistry during the past several decades are those associated with the roles of coordination compounds, especially of transition metals, in the homogeneous catalysis of reactions involving the formation or dissociation of H–H, C–H and C–C bonds [1–5]. Illustrative of the catalytic processes encompassed by these developments are the examples listed in Table I. Contributing to the intensive interest and research that this field has attracted are the novel chemistry connected with such catalytic processes, their relevance as possible models for related heterogeneous and enzymic catalyst systems, as well as important technological applications such as the hydroformylation of olefins, the oxidation of ethylene to acetaldehyde and the carbonylation of methanol to acetic acid (examples I, II and III, respectively, of Table I).

The field encompassed by such catalytic systems is still relatively young, having developed for the most part within the past twenty-five years. The mechanistic aspects of reactions such as those cited in Table I are far from completely appreciated and are still being clarified. Nevertheless, the past few years have witnessed some impressive advances in our detailed understanding of such mechanisms and in the development of approaches to their elucidation. The present article discusses some of these developments, as illustrated particularly by our recent studies on two homogeneous catalytic hydrogenation reactions, namely hydrogenation of olefins catalyzed by 'Rh(PPh_3)$_3$Cl' (Wilkinson's catalyst) and the asymmetric hydrogenation of prochiral olefins to yield optically active products, catalyzed by chiral cationic rhodium phosphine complexes (eqns. 1 and 2, respectively). The latter sys-

TABLE I. Selected Homogeneous Catalytic Processes.

I. Hydroformylation of Olefins (Oxo Process)

$$RCH{=}CH_2 + CO + H_2 \xrightarrow{Co^I \text{ or } Rh^I} RCH_2CH_2\overset{O}{\overset{\|}{C}}H$$

II. Oxidation of Olefins (Wacker Process)

$$CH_2{=}CH_2 + O_2 \xrightarrow{Pd^{II}\ (Cu^{II})} CH_3\overset{O}{\overset{\|}{C}}H$$

III. Carbonylation of Methanol to Acetic Acid

$$CH_3OH + CO \xrightarrow{Rh^I\ (HI)} CH_3\overset{O}{\overset{\|}{C}}OH$$

IV. Hydrocyanation of Butadiene to Adiponitrile

$$CH_2{=}CHCH{=}CH_2 + 2HCN \xrightarrow{Ni^0} NC{-}CH_2CH_2CH_2CH_2{-}CN$$

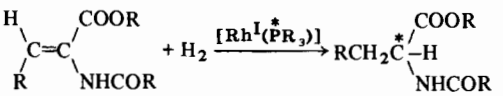
V. Synthesis of 1,4-Hexadiene

$$CH_2{=}CHCH{=}CH_2 + CH_2{=}CH_2 \xrightarrow{Rh^I} CH_2{=}CHCH_2CH{=}CHCH_3$$

VI. Olefin Dismutation

$$2CH_2{=}CHCH_3 \xrightarrow{W \text{ or } Mo\ (?)} CH_2{=}CH_2 + CH_3CH{=}CHCH_3$$

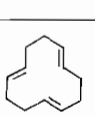
VII. Asymmetric Catalytic Hydrogenation of Prochiral Olefins



>90% L (or D)

VIII. Cyclotrimerization of Butadiene

$$3CH_2{=}CHCH{=}CH_2 \xrightarrow{Ni^0}$$



IX. Rearrangements of Strained Hydrocarbons

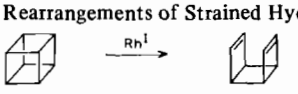


TABLE II. Elementary Processes in Homogeneous Catalysis.

I.	Ligand Dissociation	
	(1) *Heterolytic:* $M-L \rightleftharpoons M + :L$	[L = CO, PR_3 *etc.*]
	(2) *Homolytic:* $M\text{-}R \rightleftharpoons M^{\bullet} + R^{\bullet}$	
II.	Dissociation of Saturated Molecules (H_2 *etc.*)	
	(1) *Electrophilic:* $M^{+} + H_2 \rightleftharpoons MH + H^{+}$	[$M^{+} = Ag^{+}$ *etc.*]
	(2) *Oxidative Addition:* $M + H_2 \rightleftharpoons M\begin{smallmatrix}H\\H\end{smallmatrix}$	[$M = Rh^{I}, Ir^{I}$ *etc.*]
	(3) *Homolytic:* $2M + H_2 \rightleftharpoons 2M-H$	[$M = Co^{II}$ *etc.*]
III.	'Insertion' Reactions	
	(1) $M-R + CO \rightleftharpoons \left[M\begin{smallmatrix}C^{O}\\R\end{smallmatrix}\right] \rightleftharpoons M-\overset{O}{\overset{\|}{C}}-R$	
	(2) $M-H + \diagdown C{=}C\diagup \rightleftharpoons \left[\diagdown C{=}C\diagup \;\; M-H\right] \downarrow M-C-C-H$	

tem also serves to illustrate the remarkable selectivities that can be achieved with certain homogeneous catalysts.

$$RCH{=}CH_2 + H_2 \xrightarrow{\text{'Rh(PPh}_3\text{)}_3\text{Cl'}} RCH_2CH_3 \qquad (1)$$

$$\begin{matrix}H\\ \diagdown\\ C{=}C\\ \diagup\\ R_1\end{matrix}\begin{matrix}COOR_2\\ \diagup\\ \\ \diagdown\\ NHCOR_3\end{matrix} + H_2 \xrightarrow{[\text{'Rh}(\overset{*}{P}_2)\text{'}]^{+}} \begin{matrix}COOR_2\\ \diagup\\ R_1CH_2\overset{*}{C}-H\\ \diagdown\\ NHCOR_3\end{matrix} \qquad (2)$$

General Mechanistic Considerations

Mechanisms of reactions such as those exemplified by Table I are typically multi-step processes, involving discrete hydrido- and organo-metallic intermediates, as exemplified by the schematic representation of eqn. 3 (where L = ligand) which encompasses a sequence of oxidative addition [6], migratory insertion [7] and reductive elimination steps that is common to the mechanisms of many homogeneous catalytic hydrogenation reactions [7]. These reactions, and others listed in Table II, constitute the 'elementary steps' which contribute to the stepwise pathways of many other homogeneous catalytic processes such as those listed in Table I. The mechanisms that have been proposed for several of these reactions and that serve to illustrate this theme are depicted in Table III.

$$\left[L_nRh^{I}\right] \xrightarrow{H_2} \left[L_nRh\begin{smallmatrix}H\\H\end{smallmatrix}\right] \xrightarrow{C=C} \left[L_nRh\begin{smallmatrix}\diagdown C{=}C\diagup\\H\\H\end{smallmatrix}\right] \rightarrow \left[L_nRh\begin{smallmatrix}C-C-H\\ \diagdown\;\diagup\\H\end{smallmatrix}\right] \xrightarrow{-H-C-C-H} \left[L_nRh\right] \qquad (3)$$

Alternative suggestions involving 'concerted' mechanisms have been advanced from time to time, for example in connection with the olefin metathesis reaction and with the rearrangements of strained carbocyclic compounds (examples VI and IX, respectively, of Table I). However, in virtually every case where such suggestions have been tested they have been shown to be incorrect and alternative stepwise mechanisms have been demonstrated. Thus, the Rh(I)-catalyzed rearrangement of cubane (example IX of Table I) proceeds through the mechanistic pathway of eqn. 4b rather than that of eqn. 4a. This theme has been reviewed elsewhere and

TABLE III. Proposed Mechanisms of Some Homogeneous Catalytic Processes.

$Rh(PPh_3)_3Cl$-Catalyzed Hydrogenation of Olefins (P = PPh_3)

$$[Rh^{I}P_3Cl] \xrightarrow{H_2} [Rh^{III}P_3H_2Cl] \underset{P}{\overset{C=C}{\rightleftharpoons}} [Rh^{III}P_2(C=C)H_2Cl] \xrightarrow{P} [Rh^{III}P_3(-C-C-H)HCl] \rightarrow H-C-C-H$$

Hydroformylation of Olefins (Oxo Process)

$$[H-Co^{I}(CO)_4] \underset{CO}{\overset{C=C}{\rightleftharpoons}} [H-Co^{I}(CO)_3(C=C)] \rightarrow [R-Co^{I}(CO)_3] \xrightarrow{CO} [RC(=O)-Co^{I}(CO)_3] \xrightarrow{[H]} RCH=O$$

CO, H_2

Carbonylation of Methanol to Acetic Acid

$$CH_3OH \underset{H_2O}{\overset{HI}{\rightleftharpoons}} CH_3I$$

$$[Rh^{I}I_2CO)_2]^- \rightarrow [Rh^{III}I_3(CO)_2(CH_3)]^- \rightarrow [Rh^{III}I_3(CO)(CCH_3)]^- \rightarrow CH_3C(=O)I$$

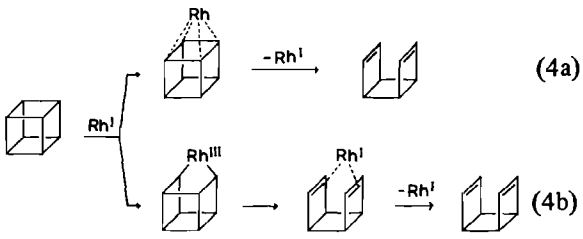
$$CH_3C(=O)I \xrightarrow[HI]{H_2O} CH_3C(=O)OH$$

Palladium Chloride-Catalyzed Oxidation of Olefins (Wacker Process)

$$[Pd^{II}Cl_4]^{2-} \underset{Cl^-}{\overset{C_2H_4}{\rightleftharpoons}} [Pd^{II}Cl_3(CH_2=CH_2)]^- \underset{H^+}{\overset{H_2O}{\rightleftharpoons}} [Pd^{II}Cl_3(CH_2CH_2OH)]^{2-} \rightarrow [Pd^0] + CH_3CHO$$

O_2, HCl

further comment at this stage is considered unnecessary [9].

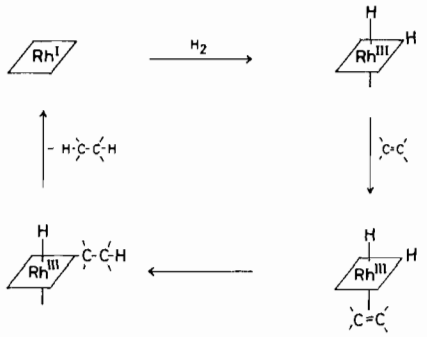


Although susceptibility to detailed mechanistic elucidation frequently is cited as an advantageous feature of homogeneous catalytic processes, compared with heterogeneous ones, only rarely until recently has such elucidation been achieved for processes of the type depicted in Table I. Mechanisms such as those proposed in Table III often are based on considerations of plausibility, or on analogies with known chemistry of related 'model' systems, rather than on firm evidence. Thus, even at this stage there is no direct evidence for key intermediates such as $[RCo(CO)_n]$ and $[PdCl_3(CH_2CH_2OH)]^{2-}$ in the widely accepted mechanisms of two of the oldest and most extensively investigated (as well as industrially important) homogeneous catalytic processes, namely the hydroformylation of olefins (Oxo process) [10] and the palladium chloride-catalyzed oxidation of ethylene (Wacker process) [11], respectively (see Tables I and III).

'$Rh(PPh_3)_3Cl$'-Catalyzed Hydrogenation of Olefins

Even when the nature of the stepwise sequence that constitutes the pathway of a catalytic process is recognized, as in the examples of Table III, the mechanism frequently is understood only in schematic terms which do not encompass a detailed description of the compositions and configurations of all the intermediate species and of the kinetics of the component elementary steps. The problems connected with the achievement of such a detailed description are illustrated by reference to the catalysis of the hydrogenation of olefins by '$Rh(PPh_3)_3Cl$' which has been extensively studied by many workers since its initial discovery in 1965 [12–21]. The widely accepted mechanism for this reaction, based on the chemistry expected for rhodium complexes, on the actual observations of species related to the proposed intermediates and, to some degree,

on kinetic evidence, is depicted schematically by eqn. 5.



(5)

The problems of elucidating the details of such a mechanistic scheme are compounded not only by its multistep character but also by the fact that each of the 'intermediates' in the proposed catalytic sequence may actually coexist in several forms related through labile ligand dissociation and/or substitutional processes. Thus, at the present stage of characterization of this system the initial 'catalyst' of the mechanistic sequence of eqn. 5, *i.e.*, $[Rh^I]$, has been shown to encompass at least four different species, *i.e.*, $[Rh(PPh_3)_3Cl]$, $[Rh(PPh_3)_2Cl]$, $[Rh(PPh_3)_2(\rangle C{=}C\langle)Cl]$ and $[Rh_2(PPh_3)_4Cl_2]$ [16, 17]. Each of the three other 'intermediates' of the sequence also corresponds to several species (at least 3, 2 and 2, respectively). At the same time, each of the 'elementary' steps comprising the successive stages of the catalytic sequence may actually encompass several parallel reactions. Thus, what appears at the schematic level to be a fairly simple mechanistic scheme actually corresponds to a reaction system of great complexity involving a large number of participating species and a correspondingly large number of simultaneous and consecutive reaction steps [15–18, 21].

The situation just described reflects the characteristic labilities of the species corresponding to the various stages of the catalytic cycle. Such lability is widespread in homogeneous catalytic systems and, indeed, can frequently be recognized as an essential feature of catalytic activity, a requirement of which is the facile incorporation of reactants (*e.g.*, olefins or CO) into the coordination sphere of the catalyst, and facile elimination of products from the coordination sphere, through substitution or dissociative processes. The widely recognized importance of 'coordinatively unsaturated' species in catalysis is linked to this theme.

In view of the complexity of such systems, attempts to deduce 'mechanisms' from kinetic studies on the overall catalytic reactions (although frequently attempted) generally lead to results that are incomplete and of questionable reliability. This is illustrated by the history of attempts to deduce the mechanism of the '$Rh(PPh_3)_3Cl$'-catalyzed hydrogenation of olefins. Such attempts over the years have yielded a variety of different (in some cases incompatible) 'rate-laws' [12–14, 19, 20]. Each of these rate-laws can be (and has been) fitted to a variant of the general mechanistic scheme represented by eqn. 5, with component rate and equilibrium constants derived by fitting the rate-law to rate measurements

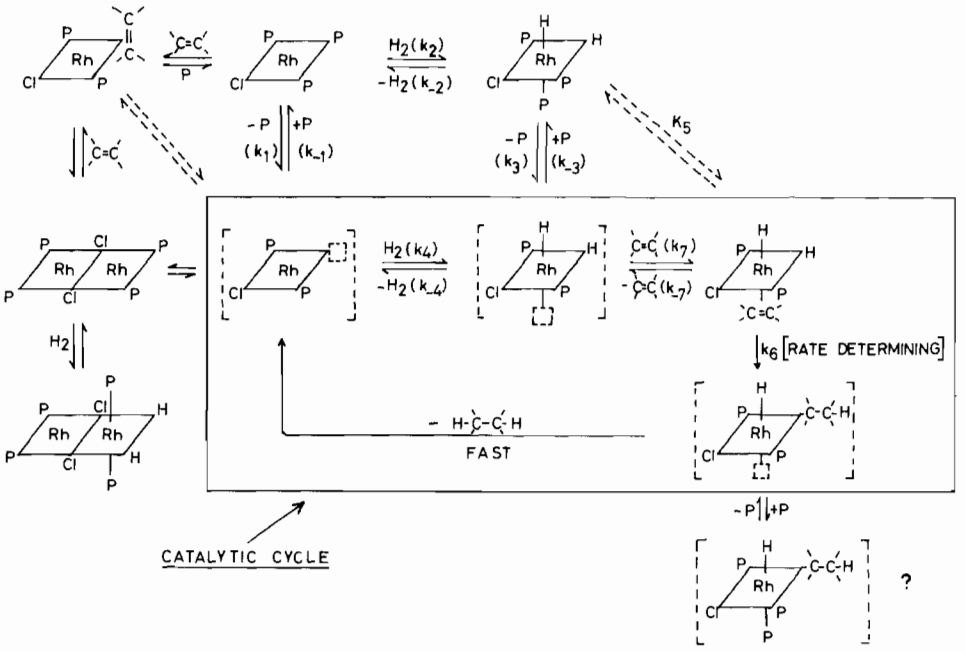


Fig. 1. Mechanism of the '$Rh(PPh_3)_3Cl$'-catalyzed hydrogenation of cyclohexene.

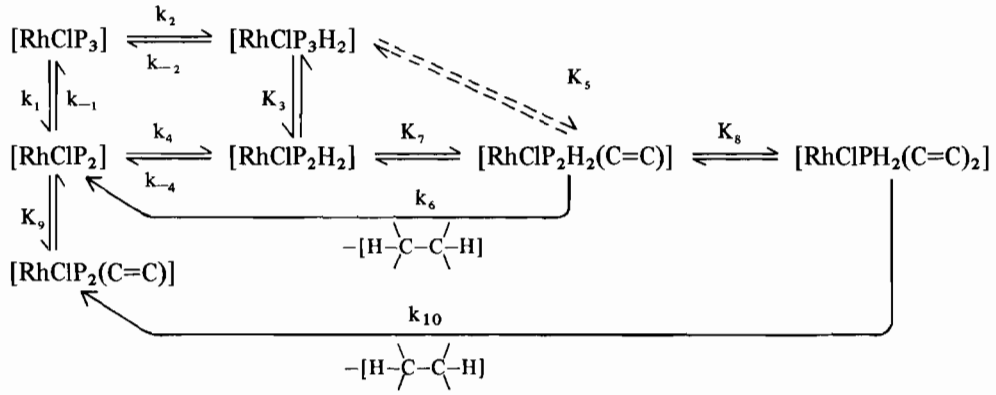


Fig. 2. Mechanism of the 'Rh(PPh$_3$)$_3$Cl'-catalyzed hydrogenation of styrene.

of the overall catalytic reaction. The number of mutually compensating parameters (up to seven!) in each case is sufficiently large to accommodate the *imposed* fit within the experimental error. Such a procedure provides neither a rigorous test of the proposed mechansim nor a meaningful evaluation of the desired parameters.

Elucidation of the mechanistic features of a system of this complexity usually can be achieved only by examining the individual stages (*i.e.*, the various intermediate species and component elementary steps) separately and directly. We have recently accomplished this in the case of the 'Rh(PPh$_3$)$_3$Cl'-catalyzed hydrogenation of olefins in studies which have depended critically upon the use of ^{31}P NMR spectroscopy, since this technique provides information not only about the compositions but, at least in favorable cases, also about the configurations and labilities of species actually present in solution [15–18, 21]. These studies have resulted in elucidation of the mechanistic scheme depicted in Fig. 1. The following features are noteworthy.

1. The rate-law derived for this mechanism is given by eqn. 6 (where P = PPh$_3$). In contrast to earlier derivations, all the rate- and equilibrium-constants in eqn. 6 have been evaluated with a high degree of reliability from *direct* measurements on the individual (stoichiometric) stages of the reaction sequence, rather than from kinetic measurements on the overall reaction. The values obtained in this way (for the hydrogenation of cyclohexene in benzene at 25 °C) are $k_1 = 0.68$ sec^{-1}, $k_2 = 4.8\ M^{-1}$ sec^{-1}, $k_{-2} = 2.8 \times 10^{-4}$ sec^{-1}, $K_5 = 3.0 \times 10^{-4}$, $k_{-1}/k_4 = 1.0$, $K_1K_9 = 3.5 \times 10^{-4}$, $k_6 = 0.22$ sec^{-1}. Thus, the excellent agreement between the rates calculated from eqn. 6, using these values, and the measured catalytic rates, over a wide range of concentration conditions, is not a forced one and provides a reliable test of the mechanism at the given level of detail.

$$[k_{CAT}]^{-1} = \frac{[Rh]_{TOT}}{RATE} = \frac{1}{k_6} + \frac{[P]}{K_5k_6[\rangle C{=}C\langle]} + \frac{[P]}{K_1k_4[H_2]} \qquad (6)$$

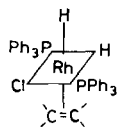
2. At least five rhodium-containing species have been directly observed in this reaction system and characterized either in solution (by ^{31}P NMR) or as isolated solids. These include: [Rh(PPh$_3$)$_3$Cl], [Rh(PPh$_3$)$_2$(C=C)Cl], [Rh$_2$(PPh$_3$)$_4$Cl$_2$], [Rh(PPh$_3$)$_3$H$_2$Cl] and [Rh$_2$(PPh$_3$)$_4$H$_2$Cl$_2$] [17]. *None* of these actually lies within the catalytic cycle depicted by Fig. 1 and, to the extent that these species accumulate in the system, they contribute to reduction of the catalytic rate. This emphasizes the unreliable, and often misleading, mechanistic conclusions that may be derived by simply identifying the predominant species under catalytic conditions (or isolated from such solutions), unless such studies are coupled with kinetic measurements which serve to define the roles of such species (as well as the 'undetected' species derived from them) in the reaction mechanism.

3. For the hydrogenation of styrene (which coordinates more strongly than cyclohexene; $K_5 = 1.7 \times 10^{-3}$), corresponding studies reveal an expanded mechanism, depicted schematically in Fig. 2 and related to the mechanism of Fig. 1 through the superposition of a parallel path involving a monophosphine bis-olefin complex, [Rh(PPh$_3$)(C=C)$_2$H$_2$Cl] [21]. The latter, previously unsuspected, path accounts for most of the rate of catalytic hydrogenation of styrene under the conditions commonly employed for this catalyst. The rate-law derived for this mechanism is given by eqn. 7, where the independently determined additional constants for styrene (in benzene at 25 °C) are: $K_5 = 1.7 \times 10^{-3}$; $k_6 = 0.11$ sec^{-1}; $K_9/k_4 = 5 \times 10^{-4}$ sec and $k_{10}K_8 = 1.0 \times 10^{-4}$ sec^{-1}.

$$[k_{CAT}]^{-1} = \frac{[Rh]_{TOT}}{RATE} =$$

$$= \frac{([C{=}C] + K_5^{-1}[P])[P]}{(k_{10}K_6[C{=}C] + k_6[P])[C{=}C]} + \frac{K_1K_9[C{=}C] + [P]}{K_1k_4[H_2]} \quad (7)$$

Examination of the kinetic and mechanistic features of this catalytic system and of the structure of the key intermediate, **1**, emphasizes the importance of a number of themes, notably: (a) The requirement of several coordination sites (in this case three coordination sites, two for the coordination of H atoms and one for the coordination of the olefinic substrate). (b) Substitution lability, for example in accommodating the rapid interconversion of $[Rh(PPh_3)_3H_2Cl]$ and $[Rh(PPh_3)_2(C{=}C)H_2Cl]$. (C) Accessibility of different coordination numbers for a given oxidation state to accommodate several of the component reactions, notably, $[Rh(PPh_3)_3Cl] \rightarrow [Rh(PPh_3)_2Cl] + PPh_3$; $[Rh(PPh_3)_3H_2Cl] \rightarrow [Rh(PPh_3)_2H_2Cl] + PPh_3$; and $[Rh(PPh_3)_2(C{=}C)H_2Cl] \rightarrow [Rh(PPh_3)_2(\text{-}C\text{-}C\text{-})HCl]$. (d) Accessibility of different oxidation states, in this case to accommodate oxidative addition of H_2 to $[Rh^I(PPh_3)_3Cl]$ (or $[Rh^I(PPh_3)_2Cl]$) and the reductive elimination of the alkane product from $[Rh^{III}(PPh_3)_2(\text{-}C\text{-}C\text{-})HCl]$. (e) The potentially important role of the 'spectator' ligands (*i.e.*, PPh_3 and Cl) in regulating catalytic activity (for example the enhancement of the rate of hydrogenation of styrene when a PPh_3 ligand is replaced by a second styrene ligand) and, where relevant (as in the asymmetric catalytic hydrogenation reactions discussed below), in regulating catalytic selectivity.



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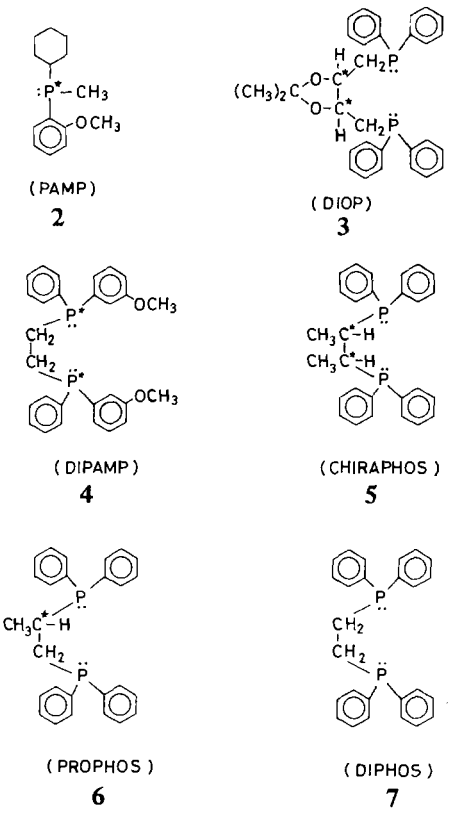
Asymmetric Catalytic Hydrogenation

The use of chiral catalysts to effect the asymmetric hydrogenation of prochiral olefinic substrates with high optical yields represents one of the most impressive achievements to data in catalytic selectivity, matched only by the comparable stereoselectivity of enzymic catalysts [22–24]. Notably high optical yields, approaching 100% enantiomeric excess, have been achieved in the hydrogenation of prochiral enamides to the corresponding amides, using homogeneous cationic rhodium complexes containing chiral phosphine (especially chelating di-(tertiary phosphine)) ligands as catalysts (eqn. 2) [22–27]. The commercial synthesis of L–DOPA by such a route constitutes an important practical application of this extraordinarily stereoselective catalyis.

Examples of some of the chiral ligands that have been found to be effective in such asymmetric catalytic hydrogenation reactions are depicted by **2** to **6**. Ligands **4**, **5** and **6** are simple derivatives of the familiar chelating ligand, 1,2-bis(diphenylphosphino) ethane (DIPHOS, **7**). Equally satisfactory results have been obtained, whether the site of chirality is the coordinating phosphorus atom (**4**) or a substituent or backbone carbon atom (**3**, **5** or **6**) [25–27].



Various studies have demonstrated the empirical dependence of the rates and stereoselectivities of such reactions on the electronic and structural features of the catalysts and substrates [22–27]. However, a fundamental understanding of these themes, and a rational approach to the design and modification of such catalysts, must rest ultimately upon a detailed understanding of the catalytic mechanism. Furthermore, to accommodate the stereochemical features of the reaction such a mechanistic description must encompass the actual interception and structural characterization of the stereoregulating intermediate(s), as well as the kinetic information necessary to define the reaction pathway and to establish whether or not a given species that may be identified in the reaction system is actually an intermediate in the catalytic cycle.

We have recently accomplished such a mechanistic elucidation of the hydrogenation of prochiral enamides (eqn. 2) catalyzed by cationic rhodium complexes containing DIPHOS and certain chiral derivatives thereof [28–31].

The catalyst precursors in such hydrogenation reactions are typically diene adducts such as [Rh(DIPHOS)NOR)]$^+$ (8, NOR = norbornadiene). H_2 reacts rapidly with such complexes in methanol and related solvents according to eqn. 8 and forms the solvated complex [Rh(DIPHOS)S'_2]$^+$ (9, S' = methanol). The latter is the starting point for the catalytic hydrogenation cycle which is depicted in Fig. 3 for the substrate methyl-(Z)-α-acetamidocinnamate (MAC) [28, 30].

The formation of the adduct **10** is rapid and essentially complete (K_{eq} = [**10**]/[**9**][MAC] = 5.3 × 10^3 M^{-1} at 25 °C) even at moderate (≳0.1 *M*) MAC concentrations. The structure of the [Rh(DIPHOS)(MAC)]$^+$ adduct (**10**) was established by NMR (^{31}P, ^{13}C and ^{1}H) spectroscopy and by single crystal X-ray analysis of the BF_4-salt, revealing chelation of the MAC substrate to the Rh atom through the carbonyl oxygen of the amide group as well as through normal symmetrical (η^2) coordination of the C=C bond.

At room temperature the second step of the catalytic cycle, *i.e.*, the oxidative addition of H_2 to **10**, corresponding to the rate-law, $-d[\mathbf{10}]/dt = k_{10}[\mathbf{10}][H_2]$ (where k_{10} = 1.0 × 10^2 M^{-1} sec^{-1}, $\Delta H^{\ddagger}_{10}$ = 6.3 Kcal $mole^{-1}$, $\Delta S^{\ddagger}_{10}$ = −28 cal $mole^{-1}$ deg^{-1})

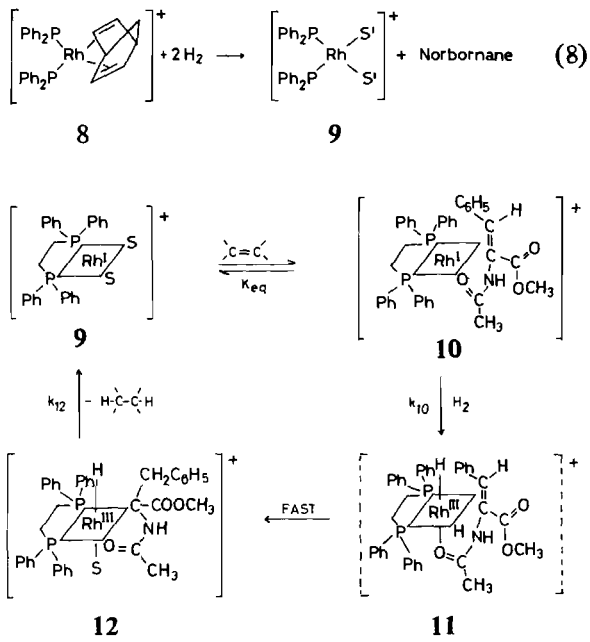


Fig. 3. Mechanism of the [Rh(DIPHOS)(MeOH)$_2$]$^+$-catalyzed hydrogenation of MAC. (S = MeOH)

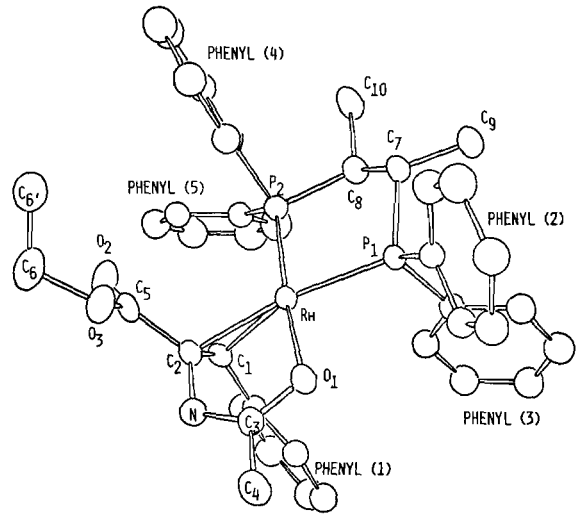
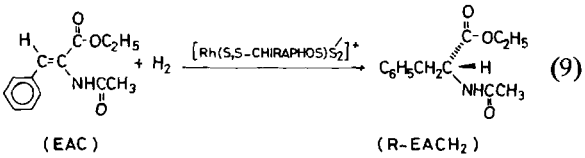


Fig. 4. Structure of [Rh(S,S-CHIRAPHOS)(EAC)]$^+$.

was found to be rate-determining for the overall catalytic hydrogenation reaction. However, the final product-forming reductive elimination step, corresponding to the rate-law, $-d[\mathbf{12}]/dt = k_{12}[\mathbf{12}]$ (where k_{12} = 44 sec^{-1} at 25 °C, $\Delta H^{\ddagger}_{12}$ = 17.0 kcal $mole^{-1}$ and $\Delta S^{\ddagger}_{12}$ = 6 cal $mole^{-1}$ deg^{-1}) exhibited a sufficiently higher activation energy compared with k_{10} that this step became rate-determining below −40 °C, permitting the intermediate **12** to be intercepted and characterized. The structure of **12**, as deduced from ^{1}H, ^{13}C and ^{31}P NMR spectral measurements, is depicted in Fig. 3 [30]. *Although such hydridoalkyl complexes have frequently been postulated as intermediates in homogeneous catalytic hydrogenation reactions this represents the first instance in which such an intermediate has actually been intercepted and characterized.*

Catalytic systems involving chiral derivatives of DIPHOS, notably DIPAMP (**4**) and CHIRAPHOS (**5**), were found to exhibit essentially similar behavior, as reflected in the formation of catalyst–substrate adducts analogous to **10** (with similar formation constants, K_{eq}, and similar electronic and NMR spectral characteristics) and apparently similar reaction mechanisms. Especially significant results were obtained for the system involving the hydrogenation of ethyl-(Z)-α-acetamidocinnamate (EAC) catalyzed by [Rh(S,S-CHIRAPHOS)S'_2]$^+$ which yields N-acetyl-(R)-phenylalanine ethyl ester (R-EACH$_2$) in high optical yield (>95% enantiomeric excess in methanol at 25 °C) according to eqn. 9.



Only a single diastereomer of the [Rh(S,S-CHIRAPHOS)(EAC)]$^+$ adduct, *i.e.*, of the analog of **10**, could be detected in solution by NMR, indicating that the second diastereomer (with which it is in rapid equilibrium) must be present to the extent of less than 5%. The absolute configuration of the dominant diastereomer was established by single crystal X-ray analysis which revealed the structure depicted in Fig. 4 [31].

According to the generally accepted interpretation of the mechanistic scheme of Fig. 3, the addition of H_2 should occur to the Rh-coordinated face of the olefin in the Rh–olefin adduct. The isolated diastereomer of [Rh(S,S-CHIRAPHOS)(EAC)]$^+$ (Fig. 4) corresponds to coordination of the (C_α-re) face of EAC to the rhodium atom. Addition of H_2 to this face would yield *N-acetyl-(S)-phenylalanine ethyl ester* whereas the predominant product of reaction (9) is the R isomer. Thus, it is concluded that most of the reaction product arises not from the dominant [Rh(S,S-CHIRAPHOS)(EAC)]$^+$ adduct which was identified and isolated, but rather from the minor diastereomer in which the opposite (*i.e.*, C_α-si) face of EAC is coordinated to the Rh atom. The latter, while present in concentrations too small to be detected, apparently is sufficiently more reactive toward H_2 than the major diastereomer (*i.e.*, in the step corresponding to **10** → **11** in Fig. 3) that it dominates the stereoselectivity of the reaction. This conclusion is supported by comparison of the rates of the [Rh(DIPHOS)S_2']$^+$- and [Rh(S,S-CHIRAPHOS)S_2']$^+$-catalyzed hydrogenation of EAC. The apparent value of k_{10} for the latter reaction was found to be *ca.* 60 times smaller than for the former, a result consistent with the conclusion that only a minor diastereomer of [Rh(S,S-CHIRAPHOS)-(EAC)]$^+$ contributes to the overall reaction of the latter with H_2.

Thus, these studies lead to the important conclusion that, contrary to most earlier suggestions [27, 32–36], *it is not the preferred mode of the initial binding of the prochiral olefinic substrate to the chiral catalyst but rather differences in the rates of the subsequent reactions of the diastereomeric catalyst-substrate adducts that determine the enantioselectivity in the asymmetric catalytic hydrogenation of prochiral olefinic substrates.*

It is noteworthy that, according to this interpretation, the reversibility of the initial catalyst-olefin adduct formation (**9** ⇄ **10**) should be reduced by increasing the rate of the subsequent H_2 oxidative addition step (**10** → **11**). Thus, at sufficiently high H_2 concentrations, the rate of the catalytic reaction should become determined by the initial binding of the prochiral olefinic substrate to the catalyst, rather than by the subsequent reaction of the resulting adduct with H_2. *This predicts that the enantioselectivity should decrease, with the possibility of eventual reversal of the absolute stereochemistry, with increasing H_2 pressure.* This would appear to explain the inverse dependence of optical yield on the H_2 partial pressure which has been observed for virtually every asymmetric hydrogenatin [22, 25, 37] catalyst system thus far examined, and for which a satisfactory explanation had not previously been advanced. The widespread observation of such an inverse dependence of optical yield on the H_2 partial pressure suggests that our conclusion concerning the origin of enantioselectivity in such catalyst systems may be quite general.

Concluding Remarks

The current phase of research in homogeneous catalysis has been marked by impressive advances, which are still continuing, in our understanding of the detailed mechanisms of homogeneous catalytic processes and of the component elementary steps and intermediates. These advances have resulted in considerable measure from (a) improved methods for the detection and characterization of species in solution, notably by NMR spectroscopy, and (b) the utilization of low temperature studies to intercept and characterize species that are too labile to be detected under ambient conditions.

Mechanistic studies, such as those described in this article, have repeatedly emphasized the essential need for *kinetic* measurements to define reaction pathways and to establish whether any particular species which may be present in the reaction system under catalytic conditions is an intermediate in the catalytic cycle. *That such kinetic measurements are essential for the elucidation of catalytic mechanisms is hardly surprising in view of the fact that catalysis is, by definition, purely a kinetic phenomenon.* Nevertheless, this point warrants repeated emphasis in view of the many studies directed at the elucidation of catalytic phenomena that are restricted to the characterization of catalytic systems by structural and spectroscopic techniques without relating the results to the catalytic reaction through essential kinetic measurements. This is a widespread limitation of much past and current research, not only on homogeneous catalytic systems, but also on heterogeneous and enzymic catalysis.

A striking feature of the two catalytic systems that have been discussed in some detail in this article is that the 'stable' species that accumulate in sufficiently high concentrations to be detected under the conditions of catalytic reactions, generally are not themselves intermediates in the catalytic cycles but, rather, labile 'reservoirs' for the actual catalytic intermediates which usually do not accumulate in sufficient concentrations to be detected. In this connection it is not altogether surprising that species

that are sufficiently stable to accumulate in appreciable concentrations and whose lifetimes are sufficiently long to permit detection, especially by NMR, should be insufficiently reactive to be intermediates in catalytic cycles with high turnover frequencies. At the same time such 'reservoir' species play an important role in stabilizing the catalytic system since the catalytic intermediates themselves are likely to be too unstable to sustain the catalyst in solution and prevent its deactivation through decomposition processes such as deposition of metal or formation of inert clusters. This feature of catalytic systems has important consequences for the elucidation of catalytic mechanisms that extend not only to homogeneous, but also to heterogeneous and enzymic catalysts.

Acknowledgement

Support of our research on the themes discussed in this article through grants from the National Science Foundation is gratefully acknowledged.

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