

Opportunities in homogeneous catalysis

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Abstract - An account is given of part of our exploratory journey through homogeneous catalysis, aimed at finding potential applications of homogeneous catalysis in the synthesis of (large-scale) industrial chemicals. The intimate interplay between the neutral ligands and associated anions in electrophilic, cationic transition metal complex catalysts, determining the catalyst activity and selectivity in a variety of reactions, has been chosen as the theme of this presentation. To illustrate this theme, we report a variety of findings, made in our study of reactions such as the carbonylation of olefins, hydroformylation of formaldehyde and olefins, reductive carbonylation of nitro-aromatic compounds and olefin dimerization.

INTRODUCTION

The "Golden Age" of innovation in the large-scale industrial application of homogeneous catalysis lasted about a quarter of a century and ended in the second half of the 1970s. Despite the relatively low level of innovation in the past decade, we believe that the prospects for industrial application of homogeneous catalysis in the future are excellent. This optimistic view is based on the observation of several factors which present major challenges to the chemical industry:

* environmental considerations not only require the development of new, ecologically sound products, but also the development of new, less environmentally demanding processes for a variety of existing products;

* changes to new feedstocks necessitated by future limitations in the availability of cheap petroleum-based resources; although still abundantly available now, it is predicted that the cost of these resources will again escalate by the end of the century. Processes starting from synthesis gas (CO/H_2) will have a considerable advantage because this feedstock can be produced from coal or organic refuse;

* considerable growth in demand for specialty, "effect" chemicals, i.e. chemicals or polymers with special optical, electronic or other properties, and fine chemicals such as pharmaceuticals and agrochemicals.

These factors will certainly require new technologies to be developed, and in view of the long lead time involved in developing a new process and/or a new product, it is now the time to uncover and explore these new technologies, for the production of both new and existing chemicals. We expect that organometallic chemistry and homogeneous catalysis will be at the heart of many of the new developments to come.

In this paper we give an account of part of our exploratory journey through homogeneous catalysis, undertaken with the aim and hope to uncover potential applications in the synthesis of (large-scale) industrial chemicals. In the course of these studies we became fascinated by the potentials of electrophilic, cationic transition-metal complex catalysts. In particular, the intimate interplay between ligands and accompanying anions observed in determining their (re)activity towards a variety of substrates and the selectivity of a variety of reactions they catalyse, has intrigued us. We have chosen this aspect as the theme of this paper.

EXPERIMENTAL

The experiments were carried out in 250-ml Hastelloy C, magnetically stirred autoclaves using standard techniques. Products were analysed by conventional GLC and/or NMR techniques.

Averaged reaction rates were calculated on the basis of amounts of product and reaction time (0.30–5 h). Molar selectivities are based on the amounts of product formed and starting material converted. Catalyst precursors (e.g. Pd(OAc)₂, ligands etc.), reactants, solvents and other chemicals were all used as commercially available and were generally of p.a. quality.

HYDROFORMYLATION OF FORMALDEHYDE

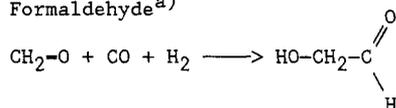
An extensive study of the direct synthesis of ethylene glycol from syngas has been carried out by several research groups (ref.1). This synthesis is characterized by severe reaction conditions, a relatively low selectivity to ethylene glycol and very high catalyst costs.

As an alternative approach we have considered the Rh-catalysed hydroformylation of formaldehyde as part of a three-step, indirect process to ethylene glycol:



For the present purpose we will only discuss the catalysis of reaction (2). The reaction is catalysed by Rh-based homogeneous catalysts under mild conditions. Using Rh(acac)(CO)₂ as catalyst precursor in the presence of phosphines, we found that hydroformylation is co-catalysed by protonic acids, i.e. both rate and selectivity strongly depend on the type of ligand and acid used. Some typical examples are shown in Table 1.

TABLE 1. Hydroformylation of Formaldehyde^{a)}



Ligand (mmol)	Acid promoter (mmol)	Temperature (°C)	Formaldehyde ^{e)} conversion rate (mol/(mol Rh.h))	Selectivity to glycol aldehyde ^{f)} (%)
1 PPh ₃ ^{b)} (2)	-	85	60	36
2 ditto	p-toluenesulphonic acid (4)	85	150	98
3 ditto	CH ₃ COOH (45)	85	300	70
4 PBu ₃ ^{c)} (2)	ditto	80	400	20
5 P(PhpCl) ₃ ^{d)} 2.5	-	80	< 30	< 60
6 ditto	CH ₃ COOH (90)	80	270	94
7 ditto	CH ₃ O-CH ₂ COOH (20)	80	300	98

a) Catalyst precursor: 0.5 mmol Rh(acac)(CO)₂; 50 ml dimethylacetamide as solvent, 7.5 g formaldehyde as paraformaldehyde intake, CO/H₂ = 1, 60 bar (constant pressure).

b) PPh₃ = triphenylphosphine

c) PBu₃ = tributylphosphine

d) P(Ph pCl)₃ = tris(p-chlorophenyl)phosphine

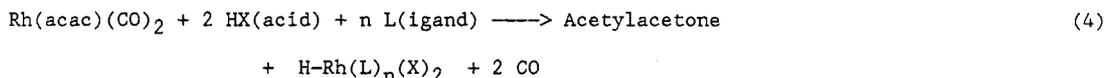
e) rate averaged over first hour

mol glycol aldehyde

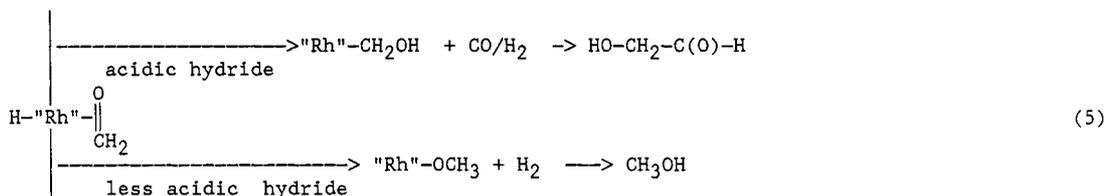
f) selectivity = $\frac{\text{mol glycol aldehyde}}{\text{mol CH}_3\text{OH} + \text{mol glycol aldehyde}} \times 100 \%$

First of all, experiments 1 and 5 show the low activity and selectivity observed for reaction (2) when only phosphines and no acids are used. A strong acid (e.g. *p*-toluene-sulphonic acid) raises the selectivity to almost 100 %, while at the same time the reaction rate increases considerably. A weak acid, such as a carboxylic acid, further increases the reaction rate, but at the cost of selectivity (cf. experiments 2 and 3). Replacing triphenylphosphine by the more basic tributylphosphine further reduces the selectivity, i.e. the main reaction appears to be hydrogenation of formaldehyde (experiment 4). By contrast, when phosphines less basic than triphenylphosphine, such as tris(*p*-chlorophenyl)phosphine, are combined with weakly acidic anion donors, both a high activity and a high selectivity are observed (experiments 6 and 7).

To explain these observations we hypothesize that cationic hydrido-Rh complexes are the actual catalyst species, generated via:



The crucial factor governing the selectivity in formaldehyde hydroformylation, we believe to be the acidity of the rhodium hydride:



The acidity of the hydride, in turn, is determined by the ligand/anion combination in the catalytic complex. We can now make it plausible that relatively basic phosphines - because they generate a larger electron density on Rh - will lead to less acidic Rh-hydride species and a low selectivity for hydroformylation. By combination with anions (X) of high electron affinity (such as non-coordinating tosylate anions) the electron density on Rh can be reduced, thus leading to a more acidic rhodium hydride and to a higher selectivity for formaldehyde hydroformylation.

When using more strongly electron-donating, coordinating anions, such as methoxyacetate and acetate, the required acidity of rhodium hydride can only be obtained by combination with strongly electron-accepting phosphines, such as tris(*p*-chlorophenyl)phosphine. It thus appears that fine tuning of the electrophilic properties of the cationic Rh centre in the catalyst species, brought about by a proper choice of their ligand and anion constituents, allows one to carefully control catalyst activity and selectivity.

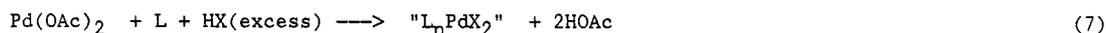
In the next sections we will demonstrate the key role of electrophilicity of cationic Pd^{2+} in bringing forth a highly specific activation of a variety of substrates such as olefins, carbon monoxide and nitro compounds and thus in allowing them to react under very mild reaction conditions.

CARBONYLATION OF OLEFINS

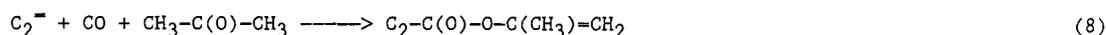
Catalysts for the carbonylation of olefins:



in which $\text{R}' = \text{H}$, alkyl, aryl or acetyl, can be generated by combining a cationic Pd^{2+} source, e.g. as a carboxylate, with a relatively large molar excess of monodentate phosphines (L) and a strong protonic acid (HX). It is believed that catalysts of the type " L_nPdX_2 " are generated via:



As an interesting application of reaction (6) we discuss the synthesis of vinyl esters, which can occur when HOR' is replaced by an enolizable ketone, e.g. acetone, as hydroxy reactant:



This reaction proceeds rapidly to its thermodynamic equilibrium (~ 30 % conversion of acetone) with a selectivity > 95 % (at 110 °C, $P_{CO}=P_{C_2} = 20$ bar), when catalysed by a $Pd(OAc)_2$ / triphenylphosphine/ p-toluenesulphonic acid (e.g. 1/30/20) catalyst. It demonstrates that the very low stationary enol concentration is sufficient and also that keto \rightleftharpoons enol interconversion is fast enough for the reaction to proceed effectively. Replacing the acid component by one containing more coordinating anions, e.g. phenylphosphonic acid, results in relatively slow reaction rates yielding, instead of the product of reaction (8), mainly vinyl ethyl ketone via:



The very nature of this product implies catalysis of reaction (9) by "XPd-H" species (cycle A in Figure 1), in contrast to catalysis by "XPd-carbo-alkoxy" species (cycle B in Figure 1), which we consider the most probable catalytic pathway for reaction (8).

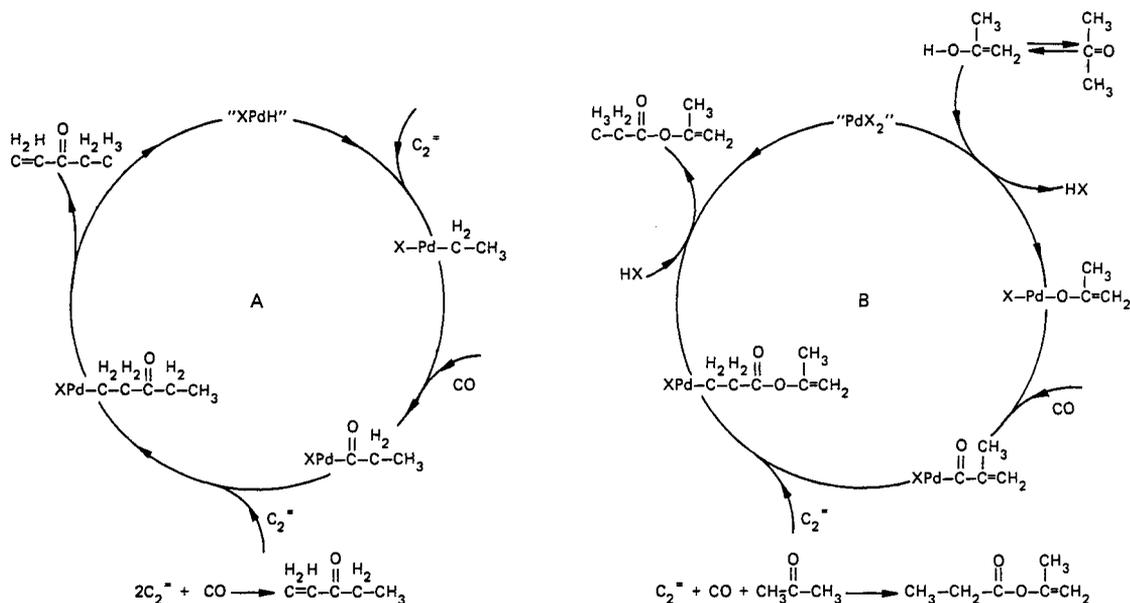
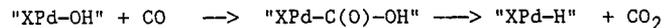


FIG. 1: CATALYTIC OLEFIN-CARBONYLATION CYCLES

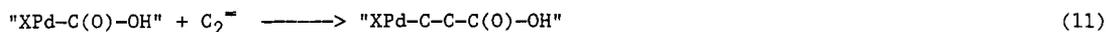
A: "Pd-H" CYCLE

B: "Pd-CARBO-ALKOXY" CYCLE

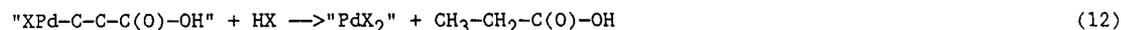
The generation of the initial "XPd-H" species most probably proceeds in situ by a partial water gas shift reaction:



Apparently, generation of cationic "XPd-H" species is favoured when X is a more strongly coordinating anion. When X is a weakly coordinating anion, the intermediate "XPd-C(O)-OH" is sufficiently electrophilic to activate ethene and to force it rapidly to react:



followed by:



Thus any trace of water is rapidly and catalytically converted to propionic acid, of which indeed traces are observed under these conditions.

HYDROFORMULATION OF OLEFINS

Having shown that cationic "XPd-H" species can play a role in the catalysis of reaction (10) we will now discuss our attempts to find catalysts of this type which are active in the

hydroformylation of olefins. We hypothesize that in this case "XPd-H" species could be generated by reaction with H₂ via:

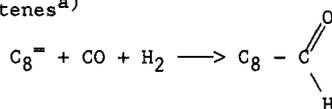


and which, supposedly, can then take part in a hydroformylation catalytic cycle (ref. 2).

However, no active catalysts can be generated using a monophosphine in combination with a variety of anions ranging from coordinating to non-coordinating types. More satisfying results are obtained when the monophosphine is replaced by chelating 2-4-carbon-atom-bridged diphosphines. For one particular example, bis(diphenylphosphino)propane, we demonstrate in Table 2 the peculiar effects brought about by the anion choice. Apparently, intermediately strong coordinating anions are required; in particular with trifluoroacetic acid as the anion source good results are obtained. Experiments 5 and 6 show that with these catalysts it is also possible to convert octenes containing internal olefinic bonds to linear aldehydes with a selectivity of ~ 67 %. It can thus be concluded that olefin isomerization takes place concurrently with hydroformylation and that hydroformylation of terminal olefinic bonds takes place at a rate that is 4 to 5 times faster than that of olefinic bonds located at internal positions.

To our knowledge these catalyst systems present the first examples of good activity Pd-based olefin hydroformylation catalysts.

TABLE 2. Hydroformylation of Octenes^{a)}



Exp. No.	Ligand (mmol)	Anion source (mmol)	Temperature (°C)	Octene (ml)	Conversion rate ^{c)} (mol olefin / (mol Pd.h))	Sel. to aldehyde ^{d)} (%)	Linearity ^{e)} of product (%)
1	(Ph) ₂ P-(CH ₂) ₃ P(Ph) ₂ ^{b)} 0.3	p-toluene-sulphonic acid (2)	125	octene-1 (20)	< 10	-	-
2	ditto	phenylphosphonic acid (1)	125	ditto	40	97	62.4
3	ditto	CF ₃ COOH (2)	125	ditto	120	97	74.6
4	ditto	ditto	140	ditto	300	92	66.7
5	ditto	ditto	125	internal octenes (20)	30 ^{f)}	97	66.5
6	ditto	ditto	145	ditto	100	85 ^{g)}	65.9

a) Catalyst precursor: 0.1 mmol Pd(OAc)₂, 50 ml diglyme as reaction solvent; CO/H₂ = 1; P = 60 bar

b) Ph = phenyl

c) conversion rate averaged over 5 h reaction time

d) selectivity to aldehydes = $\frac{\text{mol aldehydes}}{\text{mol aldehydes} + \text{mol alcohol} + \text{mol alkane}} \times 100 \%$

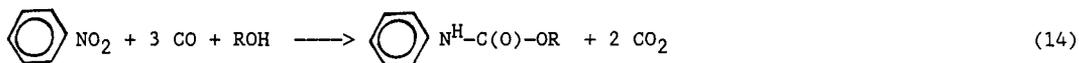
e) linearity of product = $\frac{\text{mol n-aldehydes}}{\text{mol n-aldehydes} + \text{mol branched aldehydes}} \times 100 \%$

f) diphenyl ether as reaction solvent

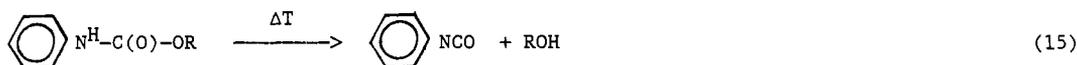
g) methyl benzoate as reaction solvent; 12 % alcohol, 3 % alkane selectivity

REDUCTIVE CARBONYLATION OF NITROAROMATIC COMPOUNDS

A potentially attractive route to isocyanates proceeds via the synthesis of carbamates:



followed by pyrolysis of the carbamate:



We will discuss some of our results obtained in the catalysis of reaction (14) by homogeneous cationic Pd catalysts, with $\text{ROH}=\text{CH}_3\text{OH}$.

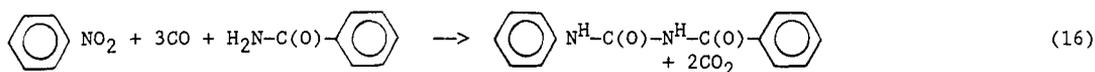
Irrespective of the anion type used a low activity and selectivity are obtained, under the desired mild reaction conditions, when monodentate ligands such as phosphines and pyridines are used in the catalyst complex. However, the results summarized in Table 3 show that very active and selective catalysts can be generated when chelating bidentate ligands are employed.

The intimate interplay between the ligand and anion of the catalyst is again quite remarkable. For optimal results it is required that biphosphines are combined with a weak acid anion source, i.e. those containing coordinating anions; by far the best results are obtained by combining bipyridyl-type ligands with strong acid anion sources i.e. those containing weakly or non-coordinating anions. The anions can also be provided in the form of their salts, e.g. as copper tosylate (experiment 7). In separate experiments we have also demonstrated that pre-synthesized complexes e.g.

$\text{Pd}(1,10\text{-phenanthroline})_2(\text{tosylate})_2$ as catalyst precursor, and in the presence of some excess of ligand, are as effective as the three-component catalyst systems shown in Table 3. The delicately balanced electrophilicity of the catalyst complex, required to effectively catalyze reaction (14), can apparently be achieved in two ways: on the one hand, by applying "hard"-base electron-donating ligands, such as phenanthroline, combined with anions having relatively strong electron affinity, i.e. non-coordinating or weakly coordinating anions. On the other hand, similar electrophilic properties can result by applying "soft"-base ligands, having the relatively strong ability to accept d-electron density from Pd^{2+} , such as diphosphines, in combination with anions having the possibility of covalent coordination (e.g. carboxylate anions) to Pd^{2+} as a means to adjust its electrophilicity. Of course, these considerations can remain only qualitative as long as many details about the mechanism are unknown.

The electrophilicity of intermediate complexes will be determined not only by ligand and anion but also by the reactants which take part in intermediate complexes of the catalytic cycle. In searching for these effects we found an interesting application when methanol in reaction (14) was replaced by an aromatic amide:

A $\text{Pd}(\text{OAc})_2/2,2'\text{-bipyridyl}/\text{Cu}(\text{tosylate})_2$ catalyst allows the very efficient synthesis of acylureas, e.g.:



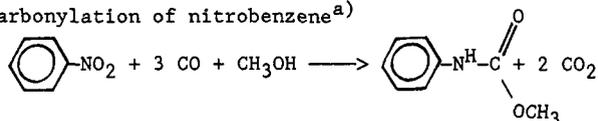
Acylurea yields of 90 % (both on nitro compound and on amide) can be obtained under mild reaction conditions similar to those applied for reaction (14).

In the chemistry discussed so far, carbon monoxide is essential as reactant (and is therefore also present as catalyst ligand); in what follows, we will show an example of the use of cationic metal catalysts in olefin activation in the absence of carbon monoxide.

DIMERIZATION OF OLEFINS

Some of the active carbonylation catalysts of the type discussed above appear to turn into active olefin dimerization catalysts when applied to olefin substrates in the absence of carbon monoxide.

Some typical experimental results are summarized in Table 4. Examples 1 and 2 show the use of monodentate phosphine-based, three-component ($\text{L}+\text{Pd}(\text{OAc})_2+\text{HX}$) catalysts; the effect of the anion, weakly coordinating tosylate vs strongly coordinating chloride, on the dimerization rate is noteworthy. A much higher ethene dimerization activity is displayed by catalysts containing chelating diphosphines, i.e. both by those generated in situ from the three

TABLE 3. Reductive carbonylation of nitrobenzene^{a)}

Exp. No.	Ligand (mmol)	Anion source ^{b)} (mmol)	Reaction rate ^{c)} (mol nitrobenzene / (mol Pd.h))	Selectivity ^{d)} (%)
1	(Ph) ₂ P-(CH ₂) ₃ P(Ph) ₂ 1.5	TBA (16)	500	95
2	ditto	p-toluene-sulphonic acid (1)	100	60
3	ditto	HCl (1)	150	80
4	1,10-phenanthroline (1.5)	TBA (16)	700	90
5	ditto	p-toluene-sulphonic acid (1)	> 1600 ^{e)}	96
6	ditto	phenylphosphonic acid (1)	1000	95
7	ditto	Cu(tosylate) ₂ (0.5)	> 1600 ^{e)}	98

a) Catalyst precursor: 0.033 mmol Pd(OAc)₂; 7.5 ml nitrobenzene in 50 ml methanol; T = 135 °C, P = .60 bar

b) TBA = 2,4,6 trimethylbenzoic acid

c) Reaction rate averaged over 1-5 reaction period

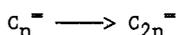
d) Selectivity based on nitrobenzene; main by-products: azo- and azoxybenzene

e) conversion of nitrobenzene = 100 %

components, Pd(OAc)₂, diphosphine and acid, and by pre-synthesized neutral complexes (experiments 3 and 4). The latter observation is in strong contrast to results obtained with neutral complexes based on monophosphines, e.g. (P(Ph)₃)₂Pd(tosylate)₂, which, in the presence of olefins and alcohols or water, decompose via a Wacker-type reduction to Pd metal and do not display any significant dimerization activity in protic solvents. In aprotic solvents, however, only a mediocre activity is observed, similar to that of analogous complexes reported by Sen et al. (ref. 3).

Protic solvents, such as alcohols or even water, are essential to efficient dimerization catalysis by cationic Pd complexes. We take this as an indication that anion-cation separation in the catalyst complex is a prerequisite for the underlying catalysis and thus underlines the importance of non-coordinating or weakly coordinating anions.

Although the diphosphine-based catalysts display a high activity for ethene dimerization they are hardly capable of catalysing propene dimerization (experiment 5). A solution to this problem is to choose bipyridyl-type ligands: experiments 6-8 show, for example, that 1,10-phenanthroline-based catalysts - the ones that proved so effective in the reductive carbonylation of nitro compounds (Table 3) - whether those generated in situ or the pre-

TABLE 4. Dimerisation of olefins^{a)}

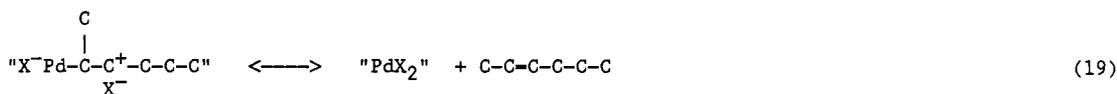
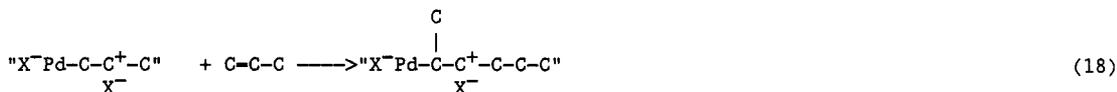
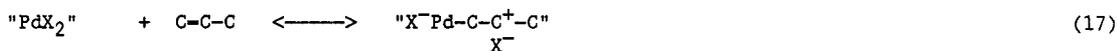
Exp. No.	Ligand (mmol)	Anion source (mmol)	Olefin	Temperature (°C)	Conv. rate (mol/mol Pd.h)	Selectivity to dimer (%)
1	P(Ph) ₃ (3)	p-toluenesulphonic acid (2)	C ₂ ⁻ (40 bar)	95	200	98 (C ₄ ⁻)
2	ditto	Hydrochloric acid (2)	ditto	95	30	98 (C ₄ ⁻)
3	Ph ₂ P-(CH ₂) ₃ P(Ph) ₂ (0.15)	p-toluenesulphonic acid (2)	ditto	95	6000	98 (C ₄ ⁻)
4	0.1 Pd(Ph ₂ P-(CH ₂) ₃ PPh ₂)(tosylate) ₂ ^{b)}		ditto	95	6000	98 (C ₄ ⁻)
5	ditto		C ₃ ⁻ (40 ml)	95	< 30	-
6	1,10-phenanthroline (0.2)	ditto (1)	C ₂ ⁻ (40 bar)	90	7500	93 (C ₄ ⁻) 7 (C ₆ ⁻)
7	0.5 Pd(1,10-phenanthroline) ₂ (tosylate) ₂ ^{b)}		C ₂ ⁻ (40 bar)	70	7000	90 (C ₄ ⁻) 6 (C ₆ ⁻) 3 (C ₈ ⁻)
8	ditto		C ₃ ⁻ (50 ml)	75	1250	94 (C ₆ ⁻) (linearity 60%!) 6 (C ₉ ⁻)

a) Catalyst precursor: 0.1 mmol Pd(OAc)₂, reaction solvent 50 ml methanol

b) Complexes synthesized by adding phosphine ligand in 1:1 ratio, or, 1,10-phenanthroline ligand in 2:1 ratio to Pd(tosylate)₂ in methanol as solvent at room temperature; complexes isolated by cold filtration.

synthesized neutral complexes, have a high activity not only for ethene but also for propene dimerization (oligomerization). Of the propene dimers and trimers, 60 and 25 %, respectively, are linear.

The following catalytic cycle for olefin dimerization by cationic "PdX₂" complexes can be envisaged:



Such a proposed mechanism does not invoke the intermediacy of Pd-hydrido species (in a conventional Ziegler-type catalytic cycle), but emphasizes the electrophilic properties of the catalyst complex.

Whatever the mechanism, the results once again demonstrate the versatility of cationic L_nPdX_2 complexes in catalysing a variety of reactions between a variety of substrates, with their key property, electrophilicity, being governed and tunable by the choice of ligand and anion constituents.

CONCLUDING REMARKS

We have given an impression of our exploratory journey through part of homogeneous catalysis. The emphasis has been placed on the phenomenology of the discovery of catalyst systems for a variety of reactions, rather than on mechanistic considerations and explanations. The experimental results lead to the construction of working hypotheses which are then used as direction indicators for the next experiments. The results of these experiments lead to elimination or reconstruction of hypotheses from which new experiments follow, etc. Of course, hypotheses do not necessarily represent the physical truth nor does their validity require a full proof in advance; we simply use them as long as the results fit with expectations based upon them. It is our experience that those hypotheses which in hindsight proved to be false have been extremely valuable in directing the research to areas of originally unforeseen opportunities; having a wrong hypothesis is by far better than having no hypothesis at all!

The leading hypothesis which has directed the underlying research concerns the tuning of the electrophilicity of cationic transition metal complexes used as homogeneous catalysts for a variety of reactions. It has been amply demonstrated that the choice of both the ligand and anion constituents in these catalysts is crucial to their (re)activity and the selectivity of reactions they catalyse.

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