70. Cationic Palladium(II), Platinum(II), and Rhodium(I) Complexes as Acetalisation Catalysts

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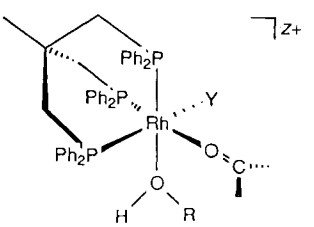
(1.III.90)

The use of $[Pd(H_2O)_2(Ph_2PCH_2CH_2PPh_2)](CF_3SO_3)_2$ as a catalyst for the acetalisation of a variety of aldehydes and ketones and for *trans*-acetalisation is described. It is also shown that $[Pt(H_2O)_2(PH_2PCH_2CH_2PPh_2)](CF_3SO_3)_2$ is at least as effective as the corresponding Pd compound, while much lower reaction rates are observed with $[Rh(MeOH)_2(Ph_2PCH_2CH_2PPh_2)][BF_4]$.

Introduction. – The protection of the C=O groups of aldehydes and ketones is generally carried out by transforming them into acetals. The reaction is acid-catalysed and protonic, as well as *Lewis* acids are commonly used [1]. There are, however, many synthetically important acetals which cannot be prepared by established methods, as they fail to give the desired product. Thus, the search for new catalysts is still actively pursued. Furthermore, acetals are increasingly used either as active substances or as intermediates for the preparation of enantiomerically pure compounds [2]. As a consequence, the preparation of chiral acetals from prochiral substrates remains a desirable goal.

In recent years, an increasing number of reports have described the use of transition-metal complexes as catalysts for this reaction [3]. The latest of them [4] describes the use of a family of Rh(III) complexes $[RhCl_x(MeCN)_{3-x}(triphos)](CF_3SO_3)_{3-x}$ (**1**; $x = 1$–3, triphos = $CH_3C(CH_2PPh_2)_3$).

The mechanistic pathway postulated for this reaction centers on the formation of an intermediate of type **1a**. Thus, catalyst activity can be attributed to the *Lewis* acidity of the complex cation and to its ability to act as a template for the simultaneous activation of the carbonyl compound and of the alcohol.



1a

$z = 3$ for Y = uncharged ligand; $z = 2$ for Y = anionic ligand.

If this is the case, it can be expected that any cationic complex *a*) in which two 'active sites' in mutually *cis*-positions can be easily generated, *e.g.* by the presence of weakly coordinated ligands, and *b*) where the bonds between the metal center and the O donors

are labile, should be able to act as an acetalisation catalyst. To test this idea, we have prepared complexes of Pd(II), Pt(II), and Rh(I) with a chelating diphosphine and tested their activity as acetalisation catalysts.

Results. – The most extensively tested catalyst was $[Pd(H_2O)_2(Ph_2PCH_2CH_2PPh_2)](CF_3SO_3)_2$ (**2**) [5]. The successful acetalisation reactions are listed in the *Table*. A standard catalyst/substrate ratio of 1:2000 was used. A variety of reagents and/or methods to remove H_2O produced during the reaction were employed.

Although, with one exception, the yields were determined by gas chromatography, previous experience with the Rh(III)-catalysed reaction [4] leads one to expect that also in the case of the Pd(II)-catalysed reaction, no difficulty should be encountered in carrying out preparations on a laboratory scale (see also *Experimental*).

The major difference observed between the Pd(II) and Rh(III) complexes is that, if benzene solutions of the former are used and H_2O produced is removed by azeotropic distillation, decomposition of the catalyst occurs. However, this problem can be avoided by using CH_2Cl_2 as solvent, although the lower reaction temperature causes a decrease in reactivity. As a consequence, a number of acetalisation reactions, which can be carried out in refluxing benzene using the Rh(III) catalyst, either do not take place or occur at very slow rates, when the Pd compound, in refluxing CH_2Cl_2, is used. Some of these examples are summarized in the *Experimental*.

The Pt(II) catalyst $[Pt(H_2O)_2(Ph_2PCH_2CH_2PPh_2)](CF_3SO_3)_2$ (**3**) was tested only on a limited number of substrates. The systems actually tested correspond to *Entries 1*, *3*, *4*, and *5* in the *Table*. The reaction conditions used were identical with those described for the Pd(II)-catalysed reactions, and the reaction times, selectivities, and yields were comparable. However, it was found that with this compound acetalisation reactions could be carried out in refluxing benzene, without catalyst decomposition. As no other advantages of the Pt(II) catalyst came to light during these screening tests, more extended studies were not carried out.

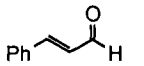
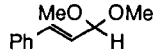
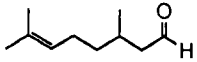
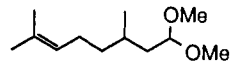
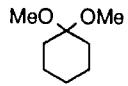
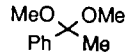
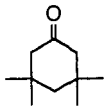
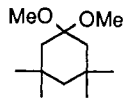
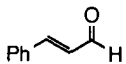
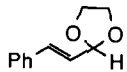
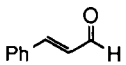
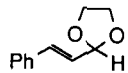
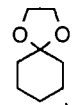
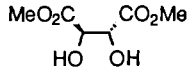
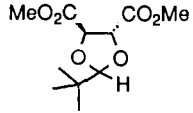
The activity of the Rh complex $[Rh(MeOH)_2(Ph_2PCH_2CH_2PPh_2)][BF_4]$ (**4**) [6] was tested on a very limited number of substrates. Using the reagents and conditions described for the Pd(II)-catalysed reaction under *Entries 3* and *4*, it was found that these reactions occurred much more slowly. Thus, for the Rh(I)-catalysed reaction using the substrate and conditions listed in *Entry 3*, only 8% conversion had occurred within 10 min and a 90% yield of product required 8 h. Therefore, this catalyst system was not investigated further.

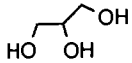
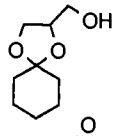
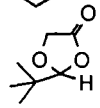
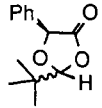
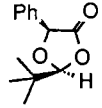
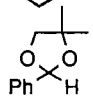
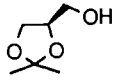
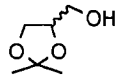
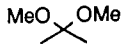
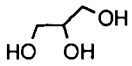
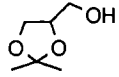
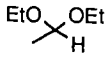
Finally, it was found that the Pd(II) and Pt(II) catalysts, **2** and **3**, respectively, showed reaction rates which were comparable with those of the Rh(III) catalysts **1** for the reaction of cyclohexanone and MeOH, using the conditions described in [4]. This is not the case for reactions which occur more slowly, *e.g.* for the substrates and reaction conditions of *Entry 5* in the *Table*. Here, it was found that the reaction with the Pt(II) catalyst was slightly faster than that with the Pd compound as, within 10 min, a 95% conversion had occurred with Pt, while only a 73% conversion had occurred with Pd.

Discussion. – The data mentioned above clearly show that the Pt-metal complexes, **2**, **3**, and **4** are, to differing degrees, catalysts for the acetalisation reaction.

The major factor influencing reactivity appears to be the ionic charge of the complex, +2 being the lowest charge giving acceptable reaction rates under mild conditions. The

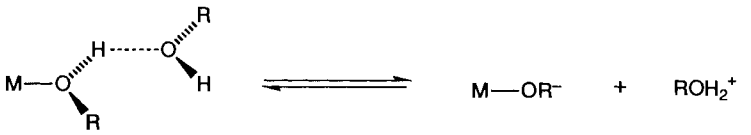
Table. *Some Acetalisation Reactions Catalysed by* $[Pd(H_2O)_2(dppe)](CF_3SO_3)_2$ (dppe = $Ph_2PCH_2CH_2PPh_2$; catalyst/substrate ratio 1: 2000)

Entry	Substrates I	II	Ratio [I]/[II]	Solvent	Drying process	Temp./ time [h]	Product	Yield [a] [%]
1		MeOH	1:4	–	[b]	r.t./24		90
2		MeOH	1:2	–	[b]	r.t./3		98
3		MeOH	1:2	–	[b]	r.t./02		98
4		MeOH	1:4	–	[b]	r.t./24		98
5		MeOH	1:5	–	[b]	r.t./3		90
6		HO OH	1:1.5	C_6H_6 [c]	[d]	r.t./8		90
7		HO OH	1:1	CH_2Cl_2 [e]	[f]	[g]/12		95
8			1:1.5	C_6H_6 [c]	[d]	r.t./8		98
9			1:1	CH_2Cl_2 [e]	[f]	[g]/8		95
10			1:0.8	CH_2Cl_2 [e]	[f]	[g]/8		95
11			1:1	CH_2Cl_2 [e]	[f]	[g]/8		92

12			1:1.2	CH_2Cl_2[e])	[f])	[g])/12		99
13			1:1	CH_2Cl_2[e])	[f])	[g])/12		99
14			1:1	CH_2Cl_2[e])	[f])	[g])/4		99[h])
15			1:1	CH_2Cl_2[e])	[d])	r.t./60		85[j])[i])
16			3:1	CH_2Cl_2[e])	–	r.t./8		95
17			1:1	CH_2Cl_2[e])	–	r.t./8		95
18			1:20	CH_2Cl_2[e])	–	r.t./4		99[k])
19			1:1	CH_2Cl_2[e])	–	r.t./12		92
20			1:3	CH_2Cl_2[e])	–	r.t./8		90

[a]) Unless otherwise stated, these were determined by GC.
[b]) Trimethyl orthoformate (2 equiv.) was added to the reaction mixture.
[c]) 2 Equiv. of solvent were used.
[d]) Tri(isopropyl) orthoformate (2 equiv.) was added to the reaction mixture.
[e]) 40–50 Equiv. of solvent were used.
[f]) Azeotropic distillation with solvent recycling over molecular sieves.
[g]) Temp. of refluxing CH_2Cl_2, *ca.* 40°.
[h]) *cis*/*trans* ratio: 5:1.
[i]) Isolated yield.
[j]) Diastereoselectivity > 99% by GC.
[k]) Racemic product.

Scheme 1



effect of the charge is two-fold: *1*) to form the M–O bonds, which are expected to be largely electrostatic, and *2*) to favour the deprotonation of the coordinated alcohol with formation of the alkoxide which, directly or indirectly, is involved in the nucleophilic attack at the coordinated C=O group (*Scheme 1*). Another important feature for efficient catalysis is the lability of the M–O bond, as this must be cleaved after H_2O and product formation (*Scheme 2*). Clearly, if the rate of this substitution reaction is slow, the catalyst will not be efficient. As a consequence, the presence of a ligand exerting a high *trans*-effect [7] in *trans*-position to the M–O bond will be essential, particularly with a kinetically inert metal center of the 2nd and 3rd transition series. This effect will be most pronounced in a low-spin d^6-metal center such as Rh(III) [8], but it is likely to be significant also in the Pt(II) compound [8].

Scheme 2

Tertiary phosphine ligands are well-suited for this purpose because of their high *trans*-effect [9]. Furthermore, the presence of this donor in the auxiliary ligand will impart particular stability to the catalyst *a*) because of the great strength of the Pt–P bond and *b*) because of the presence of a chelating system.

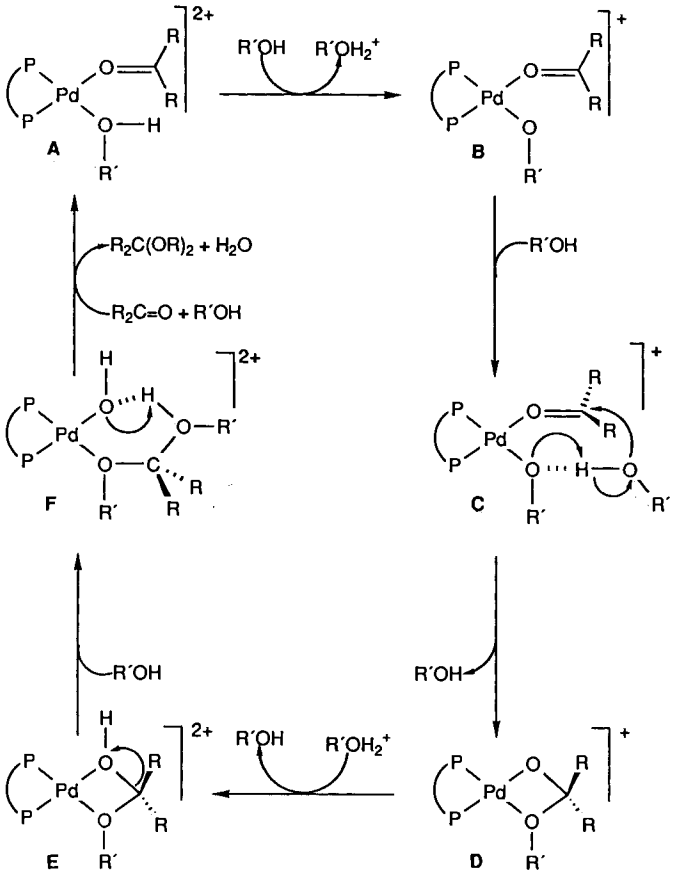
The influence on the reaction rate of the *trans*-effect of the donor atom of the auxiliary ligand was mentioned in [4] where it was shown that the Rh(III) complexes with tertiary arsine donors gave slower reaction rates than those with the corresponding phosphine donors.

The mechanistic pathway that can be postulated for the acetalisation reaction using the square-planar complexes **2**, **3**, and **4** is similar to that put forward for the Rh(III)-catalysed reaction [4], and is summarized in *Scheme 3*. There, the transformation of intermediate **B** into **D** has been postulated as occurring by way of a cyclic six-membered species **C**, as structures of this type appear to be favoured in organic reactions. Furthermore, the formation of strong H-bonds between an alcohol and an alkoxide coordinated to Pd has been recently described [11]. However, the coordination chemistry of Pt complexes with bidentate O-donor ligands, forming four-membered rings, *e.g.* CO_3^{2-}, RCO_2^-, is well established [12], and thus, it cannot be excluded that intermediate **B** gives **D** by a direct intermolecular reaction.

Finally, a comment is required on the point, whether the metal center is directly involved in the catalytic cycle as proposed in *Scheme 3*, or whether it merely serves to favour the deprotonation of the coordinated alcohol, and it is the proton, thus liberated, which brings about a classical acid catalysis.

As was the case for the Rh(III)-catalysed reaction, the evidence for direct metal participation in the catalytic cycle is unambiguous, albeit indirect. The case rests on the

Scheme 3. *A Possible Mechanistic Pathway for the Pd(II)-Catalysed Acetalisation Reaction*



following evidence: *a*) the Pt-metal catalysts mentioned above successfully acetalise acid-sensitive substrates and *b*) promote reaction in cases where protons do not. Furthermore, when suitable substrates are used, protons and transition metals produce different selectivities. Finally, the above catalysts are active in *trans*-acetalisation reactions under conditions where protons cannot be involved.

One must then assume that the protons liberated during the transformation **A**→**B** in *Scheme 3* are less active for the acetalisation reaction than the metal centers, probably because the latter activate both C=O compounds and alcohol and places them in mutually *cis*-positions.

While the thermal instability of the Pd catalyst reduces the range of its applications, the price of the Pd(II) salts relative to those of Rh(III) and Pt(II) as well as the commercial availability of the diphosphine ligand makes complex **2** the catalyst of choice when the reaction does not require higher temperatures.

The extension of the use of this type of catalyst to complexes with chiral diphosphines is obvious and is currently being tested.

The authors gratefully acknowledge the financial support of the *Forschungskommission* of the ETH-Zürich, and Messrs. *U. E. Bucher* and *T. R. Ward* for valuable assistance with the manuscript preparation.

Experimental. – All operations involving free phosphines were performed in deoxygenated solvents under Ar. The reagents and solvent (*purum* or *puriss.* quality) used for the acetalisation reactions were employed as received from *Fluka AG*. The ^{31}P-NMR spectra were recorded on a *Bruker AM-200* spectrometer operating at 81.01 MHz. A positive sign of the chemical shift denotes a resonance to low field of the external H_3PO_4 reference. The same instrument was used for ^{1}H-NMR spectra. A soln. of $[Rh(MeOH)_2(Ph_2PCH_2CH_2PPh_2)][BF_4]$ was prepared as described in [6] and used directly. The other catalysts were prepared as described below.

$[Pd(H_2O)_2(Ph_2PCH_2CH_2PPh_2)](CF_3SO_3)_2$ (**2**). Silver trifluoromethanesulfonate (178.5 mg, 0.694 mmol) was added to a suspension of $[PdCl_2(Ph_2PCH_2CH_2PPh_2)]$ [5] in 20 ml of acetone to which one drop of H_2O had been added. The mixture was stirred for 1 h at r.t., filtered over *Celite*, and the soln. evaporated to a 5-ml volume under reduced pressure. The white precipitate formed by addition of 50 ml of Et_2O was filtered off and washed with hexane and dried under high vacuum. Yield 80%. ^{1}H-NMR (CD_2Cl_2): 7.8–7.6 (*m*, Ph); 5.45 (br. *s*, H_2O); 2.64 (*m*, CH_2). $^{31}P\{^1H\}$-NMR (CD_2Cl_2): 74.5. The corresponding perchlorate salt has been described in [5], but no NMR data have been reported.

$[Pt(H_2O)_2(Ph_2PCH_2CH_2PPh_2)](CF_3SO_3)_3$ (**3**) was prepared as described for **2**. ^{1}H-NMR (CD_2Cl_2): 7.8–7.5 (*m*, Ph); 5.42 (br. *s*, H_2O); 2.52 (*m*, CH_2). $^{31}P\{^1H\}$-NMR (CD_2Cl_2): 36.76 (*s*, $^1J(Pt,P) = 3975$).

Method 1: Acetalisation Reaction Using Trimethyl Orthoformate as Dehydrating Agent. The catalyst (5 µmol) was added to a soln. of the aldehyde or ketone (10 mmol) in MeOH (1–5 equiv.) to which the ortho ester (2 equiv.) had been added. The reaction was monitored by GC.

Method 2: Acetalisation Reaction Using Tri(isopropyl) Orthoformate. This reaction was carried out as described above using the aldehyde or ketone (10 mmol), the diol (1–1.5 equiv.), the ortho ester (2 equiv.), and the catalyst (5 µmol) in CH_2Cl_2 (2 equiv.). The soln. was stirred at r.t. and product formation monitored by GC. At the end of the reaction, the product could be worked up either by bulb-to-bulb distillation or crystallization of the residue, after the solvent had been evaporated under reduced pressure.

Method 3: Acetalisation Using a Molecular Sieve as a Drying Agent. The aldehyde or ketone (20 mmol), the alcohol (1–2 equiv.), the catalyst (0.01 mmol), and CH_2Cl_2 (50 ml) were placed in a pear-shaped flask. The molecular sieve (4 Å, 1 g per mmol C=O compound) was placed in a cotton bag suspended above the liquid. The stirred soln. was refluxed under Ar for the time specified in the *Table*. The catalyst was removed by evaporating the soln. on a rotary evaporator, the residue was taken up in Et_2O, and the soln. filtered off over an aluminia column.

No product was obtained, when the following reagents were reacted with the Pd(II) catalyst using *Method 3*: 1. 2,2-dimethyl-1,3-dioxolane and 4-(*tert*-butyl)pyrochatechol; 2. benzalacetone and ethylene glycol; 3. cinnamaldehyde and (+)-L-mandelic acid; 4. isophorone and glycolic acid.

Furthermore, the reaction of bromomethyl 2,4-dichlorophenyl ketone using *Method 1* gave a 10% yield of product after a 24 h, while the reaction of the same ketone with pentane-1,2-diol resulted in the formation of the corresponding product in 5% yield after 8 h.

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