DALTON

Nitrile hydration catalysed by palladium(II) complexes

Natalia V. Kaminskaia and Nenad M. Kostić *

Department of Chemistry, Iowa State University, Ames, IA 50011, USA

The palladium(II) complexes $[Pd(H_2O)_4]^{2+}$, *cis*-$[Pd(en)(H_2O)_2]^{2+}$, *cis*-$[Pd(Met\text{-}OMe)(H_2O)_2]^{2+}$, *cis*-$[Pd(dtcol)(H_2O)_2]^{2+}$ and $[Pd(dien)(H_2O)]^{2+}$, which contain aqua, ethane-1,2-diamine (en), methionine methyl ester (Met-OMe), 1,5-dithiacyclooctan-3-ol (dtcol), and diethylenetriamine (dien) ligands, catalysed selective hydration of various nitriles, yielding the corresponding carboxamides. Further hydrolysis to carboxylic acids was not detected. The catalysed reactions are enhanced as much as 10^6-fold over the uncatalysed ones. Equilibrium constants for co-ordination of nitriles to palladium(II) complexes were determined or estimated. Since carboxamides do not detectably co-ordinate to palladium(II) in solutions containing water, the product of hydration does not inhibit the reaction. Carboxamidate anion, however, co-ordinates to palladium(II) in acetone solution. Kinetic effects of the following factors were examined: catalyst concentration, substrate concentration, pD value, water concentration, electrophilicity of the nitrile group in the substrate, and electron donation and *trans* effect of the ancillary ligands in the catalyst. In the reaction catalysed by the four chelate complexes no intermediates were detected. In the hydration of $CHCl_2CN$ catalysed by $[Pd(H_2O)_4]^{2+}$ palladium(II)–iminol complexes were observed as intermediates. In aqueous solutions only bidentate iminol co-ordination was detected. In acetone solutions the more labile unidentate iminol co-ordination was observed as well. The substrate (nitrile), the product (carboxamide), and an iminol intermediate were monitored in the cycle catalysed by $[Pd(H_2O)_4]^{2+}$. This reaction was analysed in terms of the Michaelis–Menten model of enzyme kinetics, and microscopic rate constants were determined for the pathways involving and not involving the iminol intermediate. Internal attack on the nitrile ligand by the aqua (not hydroxide) ligand and external attack on the nitrile ligand by solvent water occur at similar rates. A general scheme of catalysis is devised on the basis of the kinetic experiments.

Hydration of nitriles and the formation of corresponding carboxamides [equation (1)] is an important reaction both in

$$R\text{–}C{\equiv}N + H_2O \longrightarrow R\text{–}C(=O)NH_2 \qquad (1)$$

the laboratory and in industry. This reaction is catalysed by various acids and bases, but many of these classical methods require harsh conditions and give low yields.[1–3] The undesirable further hydrolysis of carboxamides into carboxylic acids cannot be avoided, because this reaction is faster than hydration, especially under basic conditions. Extreme acidity and basicity can, however, be avoided if transition-metal complexes are used. Such studies have been done with several transition metals, often under forcing conditions.[4–18] Labile complexes served as catalysts. Inert complexes allowed reactive intermediates to be trapped and gave kinetic and stereochemical information about the mechanisms of hydration. The main advantage of transition-metal complexes over acids and bases is their selectivity. In the presence of these complexes, carboxamides are not converted into carboxylic acids.

Palladium(II) complexes were used for nitrile hydration in a few studies.[19–21] These studies dealt with a reaction of considerable practical importance, conversion of acrylonitrile into acrylamide, but they did not really contribute to understanding of the hydration mechanisms.

Palladium(II) complexes proved remarkably useful in our laboratory as promoters and catalysts for selective hydrolytic cleavage of peptides[22–26] and proteins.[27] In the course of this research, working with solutions in acetonitrile, we observed hydration of this solvent. Since this unexpected reaction was 'clean' and fast we studied it. We report here on hydration of several nitriles catalysed by several palladium(II) aqua complexes. We examine the effects of the aqua ligands, ancillary ligands, solvent, and the pH value on the rate of hydration and present a general mechanism for this reaction. Since nitrile hydratases, which catalyse reaction (1) *in vivo*, are metalloenzymes,[28–31] investigation of catalysis by transition-metal complexes may contribute to an understanding of these important but little-studied enzymes.

Experimental

Reagents

The deuterium-containing compounds D_2O, $DClO_4$ and NaOD, and the salts $K_2[PdCl_4]$ and $NaClO_4$, were obtained from Sigma Chemical Co and Aldrich Chemical Co. Acetaldoxime, dimethyl ketoxime and 1,5-dithiacyclooctan-3-ol (dtcol) were obtained from Sigma Chemical Co. and Aldrich Chemical Co. Anhydrous $AgClO_4$ (explosive substance!) was obtained from G. Frederich Smith Chemical Co. These and all other chemicals were of reagent grade.

Palladium(II) complexes

Since almost all the reaction mixtures contained D_2O (so that ^1H NMR spectroscopy can be used) the formulas H_2O, H^+ and OH^- in this article almost always mean D_2O, D^+ and OD^-. The following complexes were prepared by published procedures: *cis*-$[Pd(en)Cl_2]$[32] (en = ethane-1,2-diamine), $[Pd(dien)I]I$[33] (dien = diethylenetriamine), *cis*-$[Pd(Met\text{-}OMe)Cl_2]$ (Met-OMe = methionine methyl ester),[34] $[Pd(H_2O)_4][ClO_4]_2$[25] and *cis*-$[Pd(dtcol)Cl_2]$.[35] The halide ligands were aquated by stirring a solution of the halogeno complex and an equivalent amount of anhydrous $AgClO_4$ for 4 h at 35 °C, in the dark. The solid AgCl or AgI was filtered off in the dark, and a fresh solution of the aqua complex was used in further experiments. The complexes *cis*-$[Pd(en)(H_2O)_2]^{2+}$, $[Pd(dien)(H_2O)]^{2+}$, *cis*-$[Pd(Met\text{-}OMe)(H_2O)_2]^{2+}$ and [Pd-

$(H_2O)_4]^{2+}$, all with ClO_4^- as the counter anion, had the respective absorption maxima at 340–345, 365, 360 and 380–382 nm. Published values for the first and the last complex[32,36–38] agree with our values. The complexes $[Pd(en)(H_2O)_2]^{2+}$ and $[Pd(H_2O)_4]^{2+}$ were also prepared in acetone solution by the aforementioned procedures.

Nitriles and carboxamides

These chemicals are the starting materials and products in reaction (1). Acetonitrile, chloroacetonitrile, dichloroacetonitrile, chloroacetamide, dichloroacetamide and 4-nitrobenzamide were obtained from Aldrich Chemical Co, benzonitrile, 4-nitrobenzonitrile and acetamide from Sigma Chemical Co, 4-methoxybenzonitrile from Eastman Organic Chemicals and $CH_3C^{15}N$ containing 99% nitrogen-15 from Cambridge Isotope Laboratories, Inc. Solutions of chloronitriles and of aromatic nitriles were kept in the dark and handled carefully because they decompose in the light, albeit very slowly.

Measurements

Proton, ^{13}C and ^{15}N NMR spectra at 300 and 400 MHz of solutions in D_2O and in mixtures of D_2O and $(CD_3)_2CO$ with acetone, $SiMe_4$ or [^{15}N]aspartate as an internal reference, were measured with Varian VXR 300, Nicolet NT 300 and Bruker DRX 400 spectrometers. Water-suppression experiments were done with a Varian Unity 500 spectrometer at 500 MHz. The 1–1 echo sequence, consisting of an excitation pulse $90°_x$–τ_1–$90°_{-x}$ and a refocusing pulse $90°_\varphi$–τ_2–$90°_{-\varphi}$, does not introduce any phase errors.[39a] For good suppression we recorded 32–320 scans. The solvent in the water-suppression experiments was water–D_2O (9:1), and the temperature was 21 °C. The sample temperature in all NMR experiments was kept within ±0.1 °C. The UV/VIS spectra were recorded with an IBM 9430 spectrophotometer. The pH values were measured with a Fisher 925 instrument and a Phoenix Ag–AgCl reference electrode. The corrected values in deuteriated solvents[39b] are designated pD.

Stability of nitriles

In control experiments concerning 'background' hydration of nitriles in the absence of palladium(II) complexes the nitrile concentration was 0.50 mol dm^{-3}, pD values were in the range 0.50–3.0, the solvent was D_2O–$(CD_3)_2CO$ (1:1), and the temperature was 40 °C. These solutions were occasionally checked by ^1H NMR spectroscopy for the presence of carboxamides.

Co-ordination of substrates to the catalysts

Ultraviolet-visible spectra of 10 mmol dm^{-3} palladium(II) aqua complexes were recorded in the absence of nitriles and in the presence of different concentrations of them; the solvent was water (in the case of acetonitrile) or acetone–water (5:1) (in the case of chloronitriles). A D_2O solution that was 0.50 mol dm^{-3} in *cis*-$[Pd(en)(H_2O)_2]^{2+}$ and 2.50 mol dm^{-3} in acetonitrile was incubated for 2 h at 20 °C, the conditions at which hydration does not occur to an extent detectable by NMR spectroscopy. The solution was then examined by ^{13}C NMR spectroscopy at 20 and 60 °C. Two solutions in D_2O were prepared for ^{15}N NMR experiments. One was 0.20 mol dm^{-3} in *cis*-$[Pd(en)(H_2O)_2]^{2+}$ and 1.0 mol dm^{-3} in $CH_3C^{15}N$ at pD 2.5. The other was 0.5 mol dm^{-3} in *cis*-$[Pd(en)(H_2O)_2]^{2+}$ and 0.50 mol dm^{-3} in $CH_3C^{15}N$ at pD 2.5. Equilibrium constants for binding of nitriles were obtained from ^1H NMR spectra at 20 °C. The concentration of *cis*-$[Pd(en)(H_2O)_2]^{2+}$ and of $[Pd(dien)(H_2O)]^{2+}$ was 0.050 mol dm^{-3}, the nitrile concentration was 0.050 mol dm^{-3}, and the solvent was D_2O–$(CD_3)_2CO$ (1:1) at pD 2.7. In the study of the kinetic effects of pH the ionic strength was kept constant at 0.40 mol dm^{-3} by addition of $NaClO_4$.

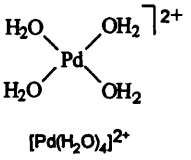
Kinetics of hydration

Reaction (1) was followed by ^1H NMR spectroscopy. Various nitriles and various freshly prepared palladium(II) aqua complexes, were mixed in different mole ratios and at different concentrations. Since the nitriles and the complexes differ widely in solubility, acetone and water had to be mixed in different proportions in the solvents used for different experiments. In a typical experiment, the palladium(II) aqua complex in D_2O was diluted to 20 mmol dm^{-3} with $(CD_3)_2CO$, pD was adjusted with $DClO_4$ or NaOD, and the required amount of nitrile was added as a solution in $(CD_3)_2CO$ having the correct pD value. The final solvent for the reaction was D_2O–$(CD_3)_2CO$ (1:5), unless stated otherwise. When hydration was slow the pD of the final mixture was adjusted again. The final concentration of the palladium(II) complex, which is the catalyst, was 17 mmol dm^{-3}, unless stated otherwise. Acquisition of the spectra began as soon as possible, and the temperature was kept at 40 ± 0.1 °C. The initial pD value is reported. As will be explained below, pD changes of 0.5 or less at pD < 3.5 do not affect the rate of the reaction and could be neglected. The ^1H resonances of the nitrile (substrate), of the carboxamide (product), and of an intermediate (when it was observed) were integrated with estimated errors of ±5%. The concentrations of these three substances were determined on the basis of these integrals and the initial concentration of the nitrile. The dependence of the hydration rate on water concentration was studied with *cis*-$[Pd(en)(H_2O)]^{2+}$ as a catalyst, in mixtures of D_2O and $(CD_3)_2CO$ as solvents, at pD 2.9. The dependence of the hydration rate on pD was studied with the same catalyst, in D_2O–$(CD_3)_2CO$ (1:1) as solvent.

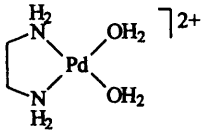
In Michaelis–Menten experiments the $[Pd(H_2O)_4]^{2+}$ concentration was 0.029 mol dm^{-3}, the $CHCl_2CN$ concentration was varied from 0.086 to 1.00 mol dm^{-3}, and the solvent was D_2O–$(CD_3)_2CO$ (1:1) at pD 0.95. Variation of concentrations with time was simulated with the program KINSIM.[39c] Agreement between the simulated and experimental profiles was taken as confirmation of the correctness of the kinetic model.

Detection of reactants and products

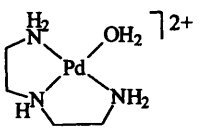
Nitriles and carboxamides were detected, and carboxylic acids sought, by ^1H NMR spectroscopy. In many experiments reaction mixtures were spiked with the pure chemical of interest. In ^1H NMR experiments concerning nitrile co-ordination to palladium(II) sharp resonances of free nitrile and broad resonances of co-ordinated nitrile ligands were integrated. The corresponding chemical shifts are δ 2.07 and 2.50 for CH_3CN and δ 4.50 and 4.80 for CH_2ClCN. In the experiments concerning nitrile hydration the following singlet resonances were monitored: CH_3CN at δ 2.07, $CH_3C(O)NH_2$ at δ 1.78, CH_2ClCN at δ 4.50, $CH_2ClC(O)NH_2$ at δ 4.03, $CHCl_2CN$ at δ 7.08 and $CHCl_2C(O)NH_2$ at δ 6.26. The following multiplet resonances were monitored: C_6H_5CN at δ 7.45 and 7.65, $C_6H_5C(O)NH_2$ at δ 7.50 and 7.90, 4-O_2N-C_6H_4CN at δ 7.95 and 8.40, 4-$O_2NC_6H_4C(O)NH_2$ at δ 8.15 and 8.25, 4-$CH_3OC_6H_4CN$ at δ 7.00 and 7.61, and 4-$CH_3OC_6H_4C(O)NH_2$ at δ 6.91 and 7.91. All of these reactions were studied in D_2O–$(CD_3)_2CO$ (1:1). In pure $(CD_3)_2CO$ the following resonances were observed: $CHCl_2CN$ at δ 7.03, free $CHCl_2C(O)NH_2$ at δ 6.32, and $CHCl_2C(O)NH_2$ N-co-ordinated to palladium(II) at δ 6.20. These chemical shifts could deviate from the stated values by up to 0.10 ppm, depending on the composition of the reaction mixture and other conditions.



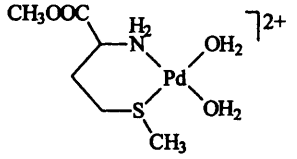
$[Pd(H_2O)_4]^{2+}$



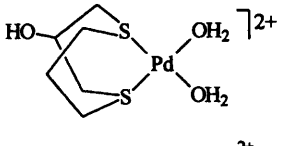
cis-$[Pd(en)(H_2O)_2]^{2+}$



$[Pd(dien)(H_2O)]^{2+}$



cis-$[Pd(Met\text{-}OMe)(H_2O)_2]^{2+}$



cis-$[Pd(dtcol)(H_2O)_2]^{2+}$

Results and Discussion

The catalysts

The palladium(II) complexes used in this study are as shown above. Their protonation states and net charges are consistent with the reaction conditions (2.0 < pD < 3.0) and the pK_a values of the aqua ligands.[32,36–38,40] Ultraviolet-visible spectra of the aqua complexes were unchanged in acetone solutions, evidence that acetone does not detectably co-ordinate to palladium(II). In order to avoid formation of bridged oligomers, these catalysts were always prepared fresh before the hydration experiments.

Detection of nitrile co-ordination to palladium(II)

The observed blue shift of the d–d absorption bands of palladium(II) complexes upon nitrile co-ordination is consistent with the relative strengths of the ligand fields of the nitrile and aqua ligands.[4] Similar shifts were observed upon nitrile co-ordination to cobalt(III).[15,16a] The nitrile must be present in a large molar excess over the palladium(II) complex in order to compete with the solvent water.

Carbon-13 NMR spectra in Fig. 1 confirm the co-ordination and show that nitrile is a labile ligand to palladium(II). At 20 °C both the methyl resonances (at δ 1.02 and 2.46) and the nitrile resonance (at δ 120–125) are broad; the latter possibly consists of two overlapping signals. At 60 °C both kinds of carbon atoms give rise to sharp resonances, at 1.63 and 122.5. The chemical shifts at 60 °C are averages of the corresponding values at 20 °C. Evidently, the rate of nitrile co-ordination at room temperature is relatively high, comparable to the intrinsic rate of the ^{13}C NMR experiment. These qualitative experiments are corroborated by quantitative ^1H NMR experiments below. The exchange between the free and the bound nitrile, or between the nitrile and water in the co-ordination sphere, is accelerated as the temperature rises. Since the chosen palladium(II) complex is a relatively poor catalyst for hydration, and because the chosen nitrile is a relatively poor substrate for this reaction, no carboxamide was observed in these ^{13}C NMR experiments. Therefore, co-ordination of the substrate to the catalyst could be studied without complications.

Nitrogen-15 NMR spectra in Fig. 2 give some qualitative information about the nitrile co-ordination because these spectra arise from the atom that becomes directly bonded to the palladium(II). When the nitrile (free at δ 246.4) is present

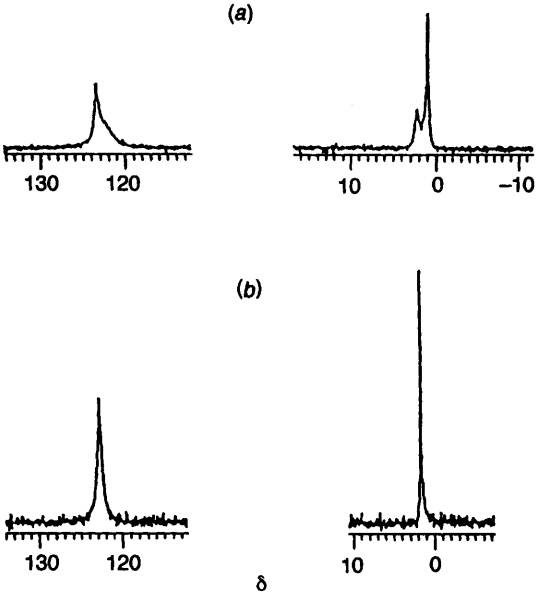


Fig. 1 Carbon-13 NMR resonances of CH_3CN in an aqueous solution at pD 2.5 that was initially 2.50 mol dm^{-3} in CH_3CN and 0.50 mol dm^{-3} in *cis*-$[Pd(en)(H_2O)_2]^{2+}$ at (*a*) 20 °C and (*b*) 60 °C

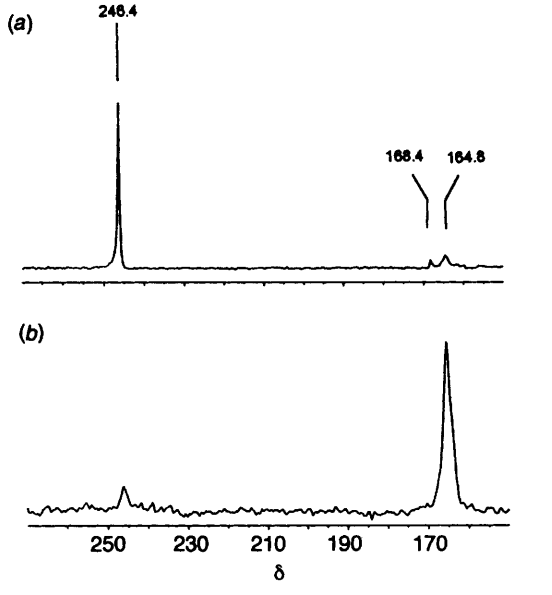
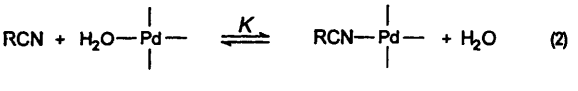


Fig. 2 Nitrogen-15 NMR resonances of 99%-enriched $CH_3C^{15}N$ in aqueous solutions at 20 °C and pD 2.5 having the following initial concentrations of $CH_3C^{15}N$ and *cis*-$[Pd(en)(H_2O)_2]^{2+}$: (*a*) 1.00 and 0.20; and (*b*) 0.50 and 0.50 mol dm^{-3}

in a five-fold excess over the complex [Fig. 2(*a*)] the complexes *cis*-$[Pd(en)(CH_3C^{15}N)(H_2O)]^{2+}$ (at δ 164.8) and *cis*-$[Pd(en)(CH_3C^{15}N)_2]^{2+}$ (at δ 168.4) are formed. When the nitrile and the complex are equimolar [Fig. 2(*b*)] the bis(nitrile) complex does not form to a detectable extent. Concentrations cannot be deduced from the ^{15}N NMR spectra because the relaxation time depends on whether the nitrile is free or co-ordinated.

Equilibrum constants for nitrile co-ordination to palladium(II)

The equilibrium (2) was quantitatively studied by ^1H NMR



spectroscopy because of the sensitivity of this method. The results for various nitriles and palladium(II) complexes are given

Table 1 Experimentally determined and estimated equilibrium constants for displacement of an aqua ligand by a nitrile ligand [equation (2)] at 20 °C

Entering ligand	Complex	K/dm^3 mol^{-1} Determined	Estimated
CH_3CN	*cis*-$[Pd(en)(H_2O)_2]^{2+}$	22 ± 2	
	$[Pd(dien)(H_2O)]^{2+}$	0.37 ± 0.04	
	$[Pd(H_2O)_4]^{2+}$	5.4*	
CH_2ClCN	*cis*-$[Pd(en)(H_2O)_2]^{2+}$	2.7 ± 0.3	
	$[Pd(dien)(H_2O)]^{2+}$		0.04
$CHCl_2CN$	*cis*-$[Pd(en)(H_2O)_2]^{2+}$		0.3
	$[Pd(dien)(H_2O)]^{2+}$		0.004
	$[Pd(H_2O)_4]^{2+}$		0.05

* Ref. 38(*b*).

in Table 1. The reactants are mixed in equimolar concentrations, so that only the mononitrile complexes are formed, as shown in equation (2). The K values of 22 and 0.37 dm^3 mol^{-1} remain unchanged at pD values 1.45, 1.70, 1.90, 2.27, 3.20, 3.65 and 4.10. This independence is understandable because the pK_a value of *cis*-$[Pd(en)(H_2O)_2]^{2+}$ is 5.6,[32] well outside of the range in which we studied nitrile co-ordination and subsequent hydration.

Since hydration of CH_3CN is undetectably slow, co-ordination of this nitrile was studied easily. Hydration of CH_2ClCN at 20 °C was slow enough not to interfere with the study of co-ordination. The corresponding three values of the equilibrium constant in Table 1 are accurate. Considering the differences among the complexes, our values generally agree with the literature value of 5.4 dm^3 mol^{-1}.[38b]

Proton NMR spectra did not give evidence of binding of CH_2ClCN to $[Pd(dien)(H_2O)]^{2+}$, and $CHCl_2CN$ underwent hydration too rapidly for the co-ordination to be studied. For these reasons, the last four values in Table 1 are estimates. The first four numbers show that a chloro substituent in the nitrile lowers the binding constant approximately ten-fold (from 22 to 2.7 dm^3 mol^{-1}) and that replacement of ethane-1,2-diamine by diethylenetriamine in the palladium(II) complex lowers it approximately 60-fold (from 22 to 0.37 dm^3 mol^{-1}). Both of these effects are easily understood. Electronegative substituents lessen the Lewis basicity and donor ability of nitriles. The tridentate complex has only one aqua ligand and is bulkier than the bidentate complex. Extrapolations from the first four numbers give the last four. For example, $0.1 \times 2.7 \approx 0.3$ and $(0.1)^2 \times 0.37 \approx 0.04$.

The main conclusion from Table 1 is that binding of $CHCl_2CN$ to palladium(II) catalysts is undetectable. This lability of complexes is favourable for turnover, as will be discussed below.

Uncatalysed hydration of nitriles

The stability of nitriles was tested in control experiments at 40 °C without the palladium(II) complexes. The conditions were made especially favourable for hydration, more so than in the catalysed reactions. The concentration was higher, the pD was lower, and the solvent contained more D_2O. Even dichloroacetonitrile, which undergoes hydration more easily than any other nitrile used in this study, did not show any conversion into dichloroacetamide after 13 months. Given the sensitivity of ^1H NMR spectroscopic detection in a 500 mmol dm^{-3} solution of the nitrile, we conservatively estimate the half-life of the uncatalysed reaction to be longer than 75 y. Deuteriation of $CHCl_2CN$, *i.e.* exchange with the solvent D_2O, was not detected.

Dependence of hydration rate on catalyst concentration

The experiments summarized in Fig. 3 were done with a

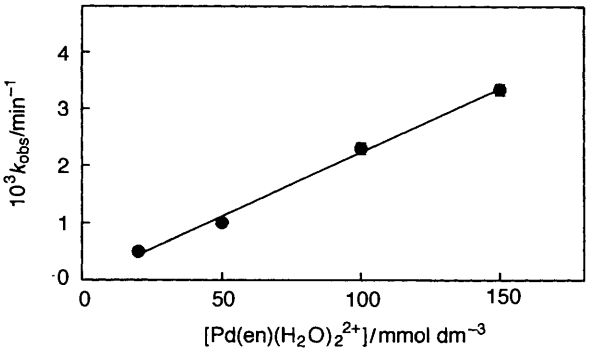


Fig. 3 Hydration of $CHCl_2CN$ and formation of $CHCl_2C(O)NH_2$ at 40 °C in solutions that were initially 0.2 mol dm^{-3} in $CHCl_2CN$ and in which the concentration of the catalyst, *cis*-$[Pd(en)(H_2O)_2]^{2+}$, was 0.020, 0.050, 0.100 and 0.150 mol dm^{-3}. The solvent was D_2O–$(CD_3)_2CO$ (1:1)

palladium(II) catalyst that is relatively inefficient, so that the hydration reaction (1) would be relatively slow and easy to monitor. Evidently, the reaction is of first order with respect to the catalyst concentration. With the substrate-to-catalyst mole ratio of 10:1 the reaction was completed in several hours, and no carboxylic acid was detected.

Dependence of hydration rate on substrate concentration

The initial rates method was used in kinetic studies.[39d] Initial rates, v_i, of $CHCl_2CN$ hydration were obtained in a series of experiments run in the first 11 min of the reaction, during which time the nitrile concentration changed little from the initial value, $[CHCl_2CN]_0$. The linear plot in Fig. 4 obeys equation (3),

$$v_i = -d[CHCl_2CN]/dt = k_{obs}[CHCl_2CN]_0 \quad (3)$$

and its slope [equation (4)] gave directly $k_{obs} = 0.28$ h^{-1}. This

$$k_{obs} = v_i/[CHCl_2CN]_0 \quad (4)$$

rate constant was obtained with the catalyst *cis*-$[Pd(Met\text{-}OMe)(H_2O)_2]^{2+}$ and with an equimolar concentration and small molar excesses of the nitrile over this catalyst. The results show that there is no saturation of the catalyst complex by the substrate under these conditions. Indeed, the equilbrium constant for nitrile co-ordination is low (see above).

Dependence of hydration rate on pH

Hydration of $CHCl_2CN$ catalysed by the tridentate complex $[Pd(dien)(H_2O)]^{2+}$ was independent of pD in the range $1.4 \leqslant pD \leqslant 5.6$. The complex $[Pd(dien)(CHCl_2CN)]^{2+}$ lacks aqua ligands; the water for hydration must come from the solvent. We assume that hydration involving the complex *cis*-$[Pd(en)(CHCl_2CN)_2]^{2+}$, which also lacks aqua ligands, will likewise be independent of pH.

The dependence of the hydration rate on pD, shown in Fig. 5, therefore comes from an acid–base process involving an aqua ligand. Since the catalyst is $[Pd(en)(H_2O)_2]^{2+}$, the complex responsible for the pD dependence is *cis*-$[Pd(en)(CHCl_2\text{-}CN)(H_2O)]^{2+}$; its acid-dissociation constant is K_a. The experimental data in Fig. 6 were fitted by equation (5),

$$k_{obs} = \frac{k_{H_2O}[H^+] + K_a k_{OH}}{K_a + [H^+]} \quad (5)$$

derived from Scheme 1. The fitted parameters are as follows: $k_{H_2O} = (7.2 \pm 0.1) \times 10^{-4}$ min^{-1}, $k_{OH} = (24 \pm 2) \times 10^{-4}$ min^{-1} and $K_a = (8.0 \pm 0.1) \times 10^{-6}$ mol dm^{-3}. The last value corresponds to p$K_a = 5.1 \pm 0.1$ in D_2O as a solvent.

The fitted value of k_{OH} is only *ca.* three times greater than

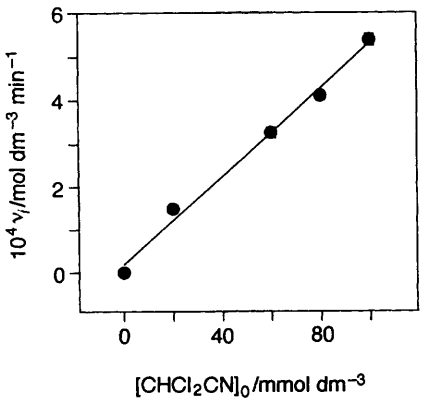


Fig. 4 Initial rate at 40 °C for hydration of $CHCl_2CN$ and formation of $CHCl_2C(O)NH_2$ depending on the nitrile concentration. The solutions were 0.20 mol dm^{-3} in the catalyst, *cis*-$[Pd(Met\text{-}OMe)(H_2O)_2]^{2+}$, and contained different initial concentrations of $CHCl_2CN$. The solvent was D_2O–$(CD_3)_2CO$ (1 : 4)

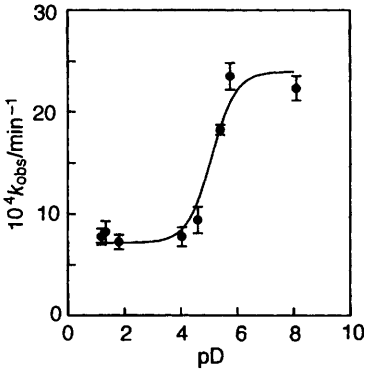


Fig. 5 Initial rate at 40 °C for hydration of $CHCl_2CN$ and formation of $CHCl_2C(O)NH_2$ depending on the initial pD value in solution. The solutions were initially 0.017 mol dm^{-3} in the catalyst, *cis*-$[Pd(en)(H_2O)_2]^{2+}$, and 0.170 mol dm^{-3} in the nitrile. The solvent was D_2O–$(CD_3)_2CO$ (1 : 5). The solid line is a fitting by equation (5)

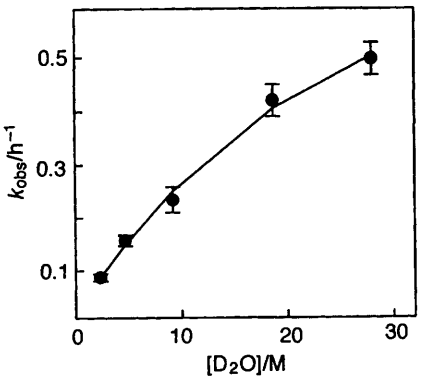
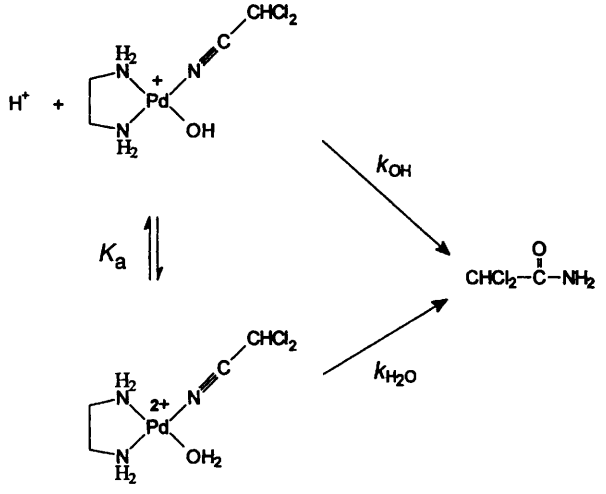


Fig. 6 Rate constant at 40 °C and pD 2.9 for hydration of $CHCl_2CN$ and formation of $CHCl_2C(O)NH_2$ depending on the ratio of D_2O and $(CD_3)_2CO$ in the solvent. The solutions were initially 0.017 mol dm^{-3} in the catalyst, *cis*-$[Pd(en)(H_2O)_2]^{2+}$, and 0.170 mol dm^{-3} in the nitrile. The solid line is only a guide to the eye



Scheme 1

k_{H_2O}. In other words, the 'jump' in Fig. 5 is smaller than is expected on the basis of the fact that the hydroxide ligand is much more nucleophilic than the aqua ligand. These observations are caused by the well known tendency of palladium(II) aqua complexes to form polynuclear μ-hydroxo complexes at pH values similar to and greater than the pK_a value of the aqua ligand. Since these polynuclear complexes are inactive as catalysts, the rate enhancement with increasing pH value beyond the pK_a is relatively small. The increased reactivity of the mononuclear hydroxo complex is partially offset by its decreasing concentration. Fortunately, formation of these polynuclear complexes is only slight at pH < pK_a, so that the early part of the plot in Fig. 6 and the pK_a value are acceptable.

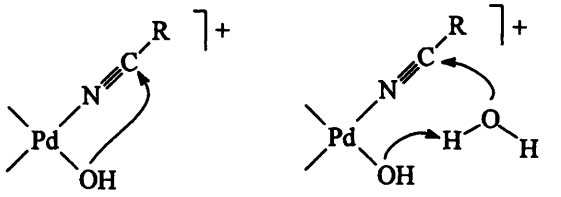
This pK_a value can be compared with those published for the following palladium(II) aqua complexes: *ca.* 3 for $[Pd(H_2O)_4]^{2+}$;[38a,d] 5.6 for *cis*-$[Pd(en)(H_2O)_2]^{2+}$;[32] 7.3 for *cis*-$[Pd(en)(H_2O)Cl]^+$;[32] and 7.5, 8.1 and 8.2 for a series of complexes $[Pd\{R_2N(CH_2)_2NH(CH_2)_2NR_2\}(H_2O)]^{2+}$ in which R = H, Me or Et, respectively.[40] These pK_a values follow the order of increasing electron-donating ability of the three ligands other than the aqua ligand under consideration: $(H_2O)_3$ < en, H_2O < en, Cl^- < dien < $Me_2N(CH_2)_2NH(CH_2)_2NMe_2$ < $Et_2N(CH_2)_2NH(CH_2)_2NEt_2$. Our experiments show that $CHCl_2CN$, with its two electron-withdrawing substituents, is a much weaker donor than CH_3CN and probably weaker than the aqua ligand. The π-accepting ability of nitriles,[4] strengthened by the chloro substituents in $CHCl_2CN$, enhances the acidity of the aqua ligand. On the basis of this analysis the series of ligand triplets can be interpolated with the triplet relevant to the process in equation (4): $(H_2O)_3$ < en, $CHCl_2CN$ < en, H_2O. This ordering is consistent with the pK_a value obtained from Fig. 5.

The hydroxo complexes may be somewhat better catalysts than their aqua precursors for two reasons, illustrated in Scheme 2. The hydroxo ligand is both a stronger nucleophile and a stronger general base than the aqua ligand. Kinetic experiments, however, cannot distinguish between those two mechanisms, *i.e.* between the internal and external nucleophilic attacks on the co-ordinated nitrile. Labelling experiments were conclusive in similar studies of cobalt(III) complexes, which are inert,[41] but these experiments are inapplicable to these palladium(II) complexes, which are labile.

The small increase in the rate of hydration in neutral and weakly basic solutions is not advantageous in practical catalysis, because increasing pD increases the rate of the undesirable hydrolysis of carboxamide into carboxylate. For this reason, we continued studying the catalysis of hydration in acidic solutions. All the reactions except those concerning the kinetic effects of pD were done in the interval 2.0 < pD < 3.0. Fig. 5 shows that in this range the rate of hydration is independent of pD, and therefore small changes in the pD during the reaction are inconsequential.

Dependence of hydration rate on water concentration

The dependence shown in Fig. 6 is approximately linear when the concentration of D_2O in the reaction mixture is relatively low. At higher concentrations of D_2O the rate constant begins to level off. A true plateau was unattainable because of the



Scheme 2

insolubility of $CHCl_2CN$ in solvents that contain mostly water. The observed rate constant in pure water can be estimated at 0.6 h^{-1}. The somewhat different value of 0.28 h^{-1} (see above) was obtained at different concentrations of reagents and in a different mixture of D_2O and $(CD_3)_2CO$ as a solvent.

Dependence of hydration rate on substrate electrophilicity

Table 2 shows a marked increase in the rate of hydration as the electron-withdrawing ability of the substituents increases in a series of similar nitriles. Table 1 shows a parallel decrease in the binding affinity of the nitrile for palladium(II). Evidently, reactivity is enhanced more by the electrophilicity of the nitrile carbon atom than by the substrate binding to the catalyst. Since electron-withdrawing substituents make the nitrile group more electrophilic and the carboxamide group a weaker ligand, the trend in Table 2 is consistent with either nucleophilic attack on the co-ordinated nitrile or the release of the carboxamide from palladium(II) as the rate-limiting step in the catalytic cycle for hydration. Electronic effects of the substituents by themselves do not reveal the rate-limiting step in the reaction.

Dependence of hydration rate on ancillary ligands bound to palladium(II)

Table 3 shows a considerable kinetic effect of the ligands that remain bound to palladium(II) during the catalytic reaction. The following two factors (and possibly others) may enhance the reactivity. If the reaction involves internal attack, the nucleophilicity and lability of the attacking aqua ligand are beneficial. Whether the reaction involves internal attack, by an aqua ligand, or external attack, by a solvent molecule, the lability of the carboxamide ligand, which is the reaction product, may facilitate its release. The actual importance of these factors depends on the rate-limiting step in the reaction mechanism. Catalysis by the hydroxide ligand as a general base, which was a realistic possibility in neutral and weakly basic solutions and was discussed in the subsection on pH effects above, is not a possibility here. At $2.0 < pD < 3.0$, the interval in which our reactions were carried out, the aqua ligands are not deprotonated to any significant extent. Good electron donors, such as the nitrogen and sulfur atoms, are expected to weaken the palladium(II)–ligand σ bonding and lessen the nucleophilicity of the aqua ligand. Conversely, weak donors such as aqua ligands are expected to strengthen this σ bonding and to enhance the nucleophilicity of the other aqua ligand.

Since it contains the most nucleophilic aqua ligand, even though it has the least affinity for binding of the nitrile (Table 1), the complex $[Pd(H_2O)_4]^{2+}$ is more effective than the other complexes. For the aforementioned electronic reason, the bidentate ligands methionine ester (an S,N-donor), ethylenediamine (an N,N-donor), and a substituted 1,5-dithiacyclooctane (an S,S-donor) lessen the catalytic effectiveness of the palladium(II). The three bidentate complexes in Table 3 can be compared in terms of the electron-donating and *trans*-labilizing effects of the thioether and amine ligands. For a conclusive analysis, however, the rate-limiting step has to be known.

That the diethylenetriamine (dien) complex is only about 20 times less reactive than the ethane-1,2-diamine (en) complex can be explained with reference to Scheme 3. The reaction was studied at pD 2.5, below the pK_a values for both complexes, which are 7.5 and 5.6 respectively. Under these conditions the nucleophilic hydroxide ligand in the ethylenediamine complex is virtually absent. Although a free water molecule attacking the diethylenetriamine complex is more nucleophilic than the aqua ligand in the ethylenediamine complex, the aqua ligand is proximate to the substrate because both are co-ordinated to the same palladium(II). The similarity of the observed rate constants indicates that the two factors are nearly balanced. Comparison of microscopic rate constants (see below) further supports this conclusion.

The complex $[Pd(H_2O)_4]^{2+}$ differs from the other four catalysts in Table 3. In its presence the rate constants for disappearance of the nitrile and appearance of the carboxamide are unequal. This interesting finding, reproduced multiple times, will be explained in the subsection following the next one.

Table 2 Effect of substituents on the rate constant for hydration of nitriles and formation of corresponding carboxamides catalysed by 17 mmol dm^{-3} $[Pd(H_2O)_4]^{2+}$

mole ratio catalyst : substrate	Substrate	k_{obs}/h^{-1} at 40 °C
1:10	CH_3CN	0.0016 ± 0.0001
	CH_2ClCN	0.042 ± 0.003
	$CHCl_2CN$*	5.22 ± 0.16
1:1	$4\text{-}CH_3OC_6H_4CN$	0.010 ± 0.001
	C_6H_5CN	0.023 ± 0.001
	$4\text{-}O_2NC_6H_4CN$	0.35 ± 0.04

* For disappearance of the nitrile. The rate constant for the appearance of the carboxamide is different. See the main text.

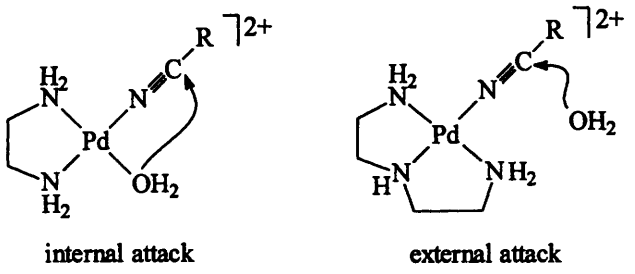
Table 3 Rate constant for disappearance of $CHCl_2CN$ and appearance of $CHCl_2C(O)NH_2$ in solutions that were initially 170 mmol dm^{-3} in the nitrile and 17 mmol dm^{-3} in the palladium(II) aqua complex

Catalyst	k_{obs}/h^{-1} at 40 °C
$[Pd(H_2O)_4]^{2+}$	5.22 ± 0.16*
cis-$[Pd(Met\text{-}OMe)(H_2O)_2]^{2+}$	1.05 ± 0.01
cis-$[Pd(en)(H_2O)_2]^{2+}$	0.39 ± 0.02
cis-$[Pd(dtcol)(H_2O)_2]^{2+}$	0.05 ± 0.01
$[Pd(dien)(H_2O)]^{2+}$	0.020 ± 0.002

* For disappearance of the nitrile. The rate constant for the appearance of the carboxamide is different. See the main text.

Lack of affinity between carboxamides and palladium(II)

Carboxamides can co-ordinate to transition metals *via* the oxygen or the nitrogen atom.[42–45] In platinum(II) complexes, in which both co-ordination modes of acetamide have been observed, the former is kinetically favoured, and the latter is thermodynamically favoured.[43] Various experiments showed that acetamide and dichloroacetamide do not detectably bind to $[Pd(H_2O)_4]^{2+}$ under the conditions used for the hydration reactions. Routine ^1H NMR spectra showed only one resonance of the proton bound to the carbon atom, that of the free carboxamide, even when the amide was present in a 10- or 50-fold molar excess over the complex. Since this proton is distant from the possible donor atoms in the amide group, these routine experiments were augmented with those obtained with suppression of the solvent water, so that exchangeable amide protons could be observed directly. Again, identical spectra were obtained with and without the $[Pd(H_2O)_4]^{2+}$ complex. Evidently, neither $CH_3C(O)NH_2$ nor $CHCl_2C(O)NH_2$ displaces the aqua ligand in palladium(II) complexes. The same conclusion was reached in the study of co-ordination, discussed



Scheme 3

above. This finding, that the carboxamides are labile ligands to palladium(II), rules out inhibition of nitrile hydration by co-ordination of the product, carboxamide, to the catalyst. Without the inhibition, the catalysts are more efficient.

Treatment of *cis*-$[Pd(en)(H_2O)_2]^{2+}$ with $CHCl_2C(O)NH_2$ in neat $(CD_3)_2CO$, a solvent not used for the hydration reactions, yielded a mixture of free (δ 6.32) and N-co-ordinated (δ 6.20) carboxamide. These ^1H NMR chemical shifts agree with the reported values, which show that the carboxamide resonance moves upfield upon N-co-ordination and downfield upon O-co-ordination.[43] In the absence of water, there is a partial co-ordination of $CHCl_2C(O)NH_2$ to the palladium(II) catalyst.

Observed intermediate in the reaction catalysed by $[Pd(H_2O)_4]^{2+}$

Now we turn to the catalyst $[Pd(H_2O)_4]^{2+}$. It differs from the other four catalysts in Table 3, as mentioned in subsection before the previous one. Hydration of $CHCl_2CN$ is conveniently followed by ^1H NMR spectroscopy because the only protons in the reaction mixture (other than those in water) belong to the species in the catalytic cycle. Since experiments with the catalyst and the substrate in the mole ratios 1:1, 1:5, 1:10, 1:50 and 1:100 yielded similar results, only one set of spectra is shown in Fig. 7. The declining resonance at δ 7.08 is due to the free substrate, $CHCl_2CN$, and the growing resonance at δ 6.26 is due to the free product of hydration, $CHCl_2C(O)NH_2$. This assignment was easily confirmed by spiking the reaction mixture with these compounds; the existing resonances were enhanced, and no new ones appeared.

The resonance that grows over time at δ 6.68, 0.40 ppm upfield from that of $CHCl_2CN$ and 0.42 ppm downfield from that of $CHCl_2C(O)NH_2$, cannot be due to either co-ordinated nitrile or N-co-ordinated carboxamide. First, the binding constant for this nitrile and this catalyst (Table 1) is too low for the complex to be detected in these reaction mixtures. Co-ordination of other nitriles to other catalysts, which was observed, occurs rapidly (during the mixing of the solutions) and causes downfield movement by 0.30 ppm or more. Secondly, N-co-ordination of this carboxamide to another catalyst, which was observed under different conditions, causes an upfield movement by 0.12 ppm. These studies of co-ordination were discussed above. Although O-co-ordination is expected to cause a downfield shift comparable to the one we observe,[43] we rule out this possibility because the evidence in the preceding subsection rules out co-ordination of $CHCl_2C(O)NH_2$ to palladium(II) under the conditions used for the hydration. Clearly, the resonance at δ 6.68 appears too slowly and at a 'wrong' position to be due simply to the complex of the catalyst with the substrate or with the product of hydration.

Several facts show that the resonance at δ 6.68, observed without exception in repeated kinetic experiments, is due to an intermediate in the conversion of the nitrile into the carboxamide. It does not arise when nitrile alone is left in solution. When $[Pd(H_2O)_4]^{2+}$ is absent so is the resonance. As the concentration of the catalysts is raised the intensity of the resonance increases. Clearly, the compound giving rise to the resonance at δ 6.68 is not simply in equilibrium with the free

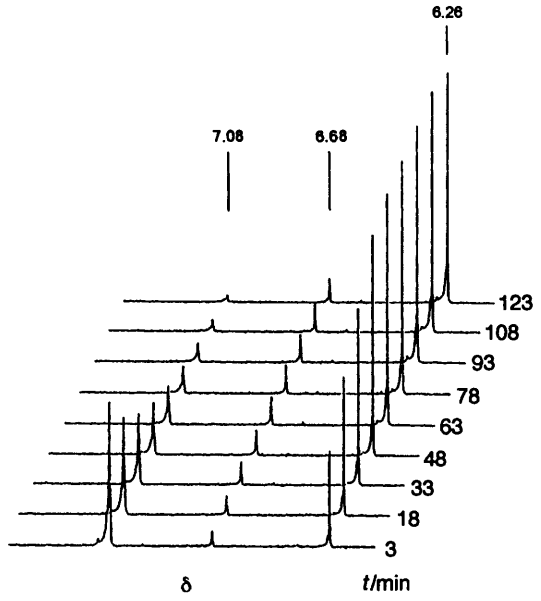
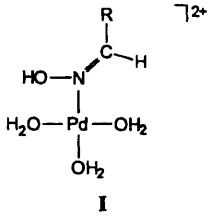


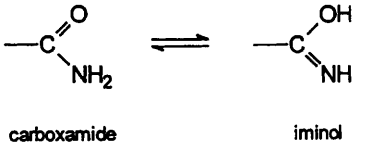
Fig. 7 Progress in time for hydration of $CHCl_2CN$ catalysed by $[Pd(H_2O)_4]^{2+}$. Their respective initial concentrations were 0.085 and 0.017 mol dm^{-3}. The solvent was D_2O–$(CD_3)_2CO$ (1:2). The ^1H NMR spectra shown are a subset of a larger set recorded at shorter intervals. The mixing time is taken as zero



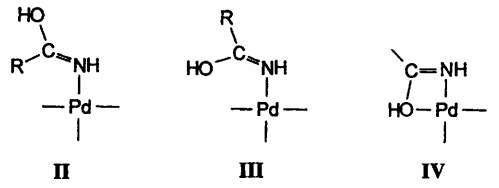
I

nitrile. Near the end of the reaction, when the nitrile is no longer evident in the ^1H NMR spectrum, the resonance in question is still evident, see Fig. 7. Concomitant decrease of it and increase of the resonance of the carboxamide show that the intermediate is converted into the product. Since oximes can give amides under certain conditions[46] and because oximes can co-ordinate to palladium(II),[47] we considered the possibility that the intermediate may be a complex of the type **I**. The first evidence against it came from ^1H NMR chemical shifts. The value for acetaldoxime (δ 1.65) is not intermediate between the values for acetonitrile (δ 2.07) and acetamide (δ 1.78). Co-ordination to palladium(II) raises the shift beyond δ 2.07 and worsens the discrepancy. In control experiments, acetaldoxime and dimethyl ketoxime in the presence of $[Pd(H_2O)_4]^{2+}$ at pD 3.0 gave only acetaldehyde and acetone, respectively. The respective yields were 10 and 100%. Since ^1H NMR spectra showed neither carboxamides nor nitriles, we rejected the oxime hypothesis without attempting similar experiments with dichloroacetaldoxime.

The near equidistance of the middle resonance from the resonances of $CHCl_2CN$ (δ 0.40) and of $CHCl_2C(O)NH_2$ (δ 0.42) suggests that it is due to an intermediate in the conversion of the nitrile into the carboxamide, a species with partial characteristics of both. An iminol, the minor tautomer of carboxamide [equation (6)], satisfies this requirement. It



(6)



resembles both the nitrile and a carboxamide in having both a multiple carbon–nitrogen bond and a carbon–oxygen bond. (This resemblance may be the reason for occasional misnaming in the literature of iminol ligands as amide ligands.) Iminols can be stabilized by transition metals, and both uni- and bi-dentate modes of co-ordination have been examined crystallographically.[16a,45,46] Therefore there are good precedents for possible iminol intermediates in the hydration reaction, which are shown below. The two unidentate ligands are geometrical *syn* and *anti* isomers; the intermediate **IV**, containing bidentate iminol, cannot show geometrical isomerism. Corresponding iminolates are unlikely, because deprotonation is suppressed in the acidic solutions used in our study.

Kinetic mechanism involving the intermediate

The following symbols will be used in this subsection: Pd for $[Pd(H_2O)_4]^{2+}$, the catalyst; N for $CHCl_2CN$, the substrate; C for the catalyst–substrate complex; I for the intermediate, which has the ^1H chemical shift of δ 6.68; and A for $CHCl_2C(O)NH_2$, the product of hydration. The simple scheme in equation (7) is inconsistent with Fig. 8. At a time around

$$N \longrightarrow I \longrightarrow A \qquad (7)$$

20–30 min the concentration of the intermediate still increases while the rate of formation of carboxamide is already decreasing.

Scheme 4 shows the formation of the carboxamide by two paths, only one of which involves the intermediate. The concentrations of N, I and A are known at all times, but the exact value of the equilibrium constant, K, cannot be determined because the complex C is undetectable by NMR spectroscopy (see above). Therefore, a complete kinetic expression for Scheme 4 cannot be derived. We did, however, determine the rate constants for the most important part of the mechanism, the triangle in Scheme 4. We analysed it in terms of the familiar Michaelis–Menten model of enzymatic catalysis, treating the complex C (not the intermediate, I) as the Michaelis complex; see equation (8) in which the subscript T stands for total concentration.

$$[C] = \frac{[Pd]_T[N]}{K_m + [N]} \qquad (8)$$

The UV/VIS spectroscopic experiments showed that the equilibrium in Scheme 4 is established in less than 2 s upon mixing of $[Pd(H_2O)_4]^{2+}$ and $CHCl_2CN$. More quantitatively,[38b] the equilibrium between this complex and CH_3CN at concentrations used in this study is established within *ca.* 0.2 s. Since the estimated equilibrium constant K is *ca.* 0.05 dm^3 mol^{-1} (see Table 1), the complex C does not accumulate to a detectable concentration. Although the true initial concentration $[C]_0$ is zero, the complex C reaches its maximum concentration very rapidly, practically at the beginning of the hydration reaction. After that it disappears, relatively slowly, with the same rate constants as for the substrate, N. Equation (8) can be simplified in two limiting cases. First, if $K_m \ll [N]$ then $[C] \approx [Pd]_T = 0.029$ mol dm^{-3}. This case clearly does not apply, for the concentration of the complex is undetectably low. Secondly, if $K_m \gg [N]$ then equation (8) reduces to (9), which shows that the Michaelis constant, K_m, can be considered as the

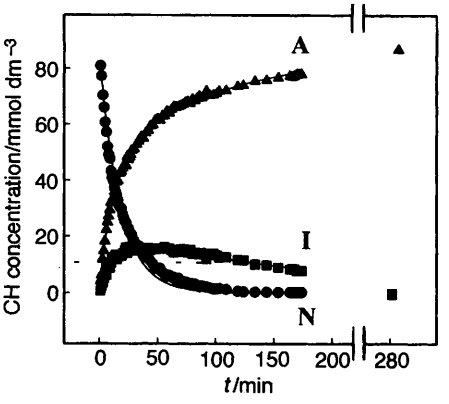
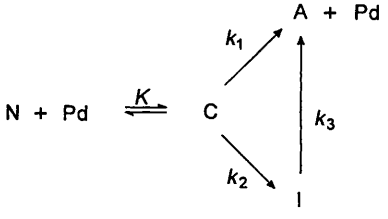


Fig. 8 Concentrations, determined by ^1H NMR spectroscopy, of $CHCl_2CN$ (●), $CHCl_2C(O)NH_2$ (▲), and the iminol intermediate (■) during hydration of the nitrile and formation of the carboxamide catalysed by $[Pd(H_2O)_4]^{2+}$. The initial concentrations of the nitrile and the catalyst were 0.086 and 0.029 mol dm^{-3}, respectively. The solvent was D_2O–$(CD_3)_2CO$ (1 : 1) at pD 0.95. Note the break in the time axis and final concentrations of the three species after the hydration reaction was completed. Since the final concentrations of the nitrile and of the intermediate are both nil, the corresponding points overlap and only one is shown



Scheme 4

$$[C] = \frac{[Pd]_T}{K_m}[N] \qquad (9)$$

dissociation constant of the complex C. Since the formation constant in Table 1 is low, the dissociation constant is indeed relatively large. Our determination of $K_m = 5$ mol dm^{-3} qualitatively agrees with the estimate of 1/0.05 = 20 mmol dm^{-3} from Table 1. Since the highest concentration of $CHCl_2CN$ in this series of experiments was 0.086 mol dm^{-3}, the assumption in this limiting case is justified. Also, because the quotient $[Pd]_T/K_m$ in equation (9) is constant, the unobservable [C] is proportional to the observable [N]. This is the main result of this analysis.

Fitting of the kinetic data [equations (10)–(12)] yielded

$$[N]_T = [N]_0 e^{-(k_1+k_2)t} \qquad (10)$$

$$[I]_T = \frac{k_2[C]_0}{k_3 - (k_1 + k_2)}[e^{-(k_1+k_2)t} - e^{-k_3 t}] \qquad (11)$$

$$[A]_T = [C]_0\left\{1 - \left[1 + \frac{k_2[C]_0}{k_3 - (k_1 + k_2)}\right]e^{-(k_1+k_2)t} + \frac{k_2[C]_0}{k_3 - (k_1 - k_2)}e^{-k_3 t}\right\} \qquad (12)$$

consistent values of the microscopic rate constants: $k_1 + k_2 = 0.056 \pm 0.008$, 0.074 ± 0.010 and 0.08 ± 0.01 min^{-1} from equations (10), (11) and (12) respectively; and $k_3 = 0.005 \pm 0.001$ and $0.010 + 0.001$ min^{-1} from equations (11) and (12), respectively. The average values are $(k_1 + k_2)_{av} = 0.071 \pm 0.018$ min^{-1} and $k_{3av} = 0.0072 \pm 0.0025$ min^{-1}. Simulations with the program KINSIM matched the

experimental data for the following parameters: $k_1 = 0.04$, $k_2 = 0.016$ and $k_3 = 0.0072$ min^{-1}. The relative magnitudes of these rate constants show that the pathway *via* the iminol complex is a minor one. Indeed, an aqua ligand is less nucleophilic than a free water molecule.

Chemical mechanism and the iminol intermediate

Although either a uni- or bi-dentate iminol intermediate (see formulas above) can result from either mechanism of hydration, unidentate iminol may be more likely in the external attack (k_1), whereas bidentate iminol may be more likely in the internal attack (k_2). These rate constants differ little (see the preceding subsection) because the reaction is studied at pD 0.95, below the pK_a value for palladium(II) aqua complexes, which is 3.[38a,d] Co-ordination of the aqua ligand and the nitrile to the same palladium(II) raises the probability of internal attack, but the free water involved in the external attack is more nucleophilic than the aqua ligand. On balance, the two mechanisms in Scheme 4 are approximately equally effective.

All three resonances in Fig. 7 were followed until completion of the reaction, and the results are shown in Fig. 8. There is complete conversion of the nitrile into the carboxamide. The chemical shifts give a clue about the mode of iminol co-ordination. When the hydration is studied in aqueous (D_2O) solution the intermediate gives only the resonance at δ 6.68. This fact argues for the bidentate iminol complex, which cannot exist as geometric isomers.

The reaction in reagent grade $(CD_3)_2CO$, which contains *ca.* 0.5% water (as judged from its ^{1}H NMR spectrum), is completed in *ca.* 10 min, faster than the reaction in D_2O–$(CD_3)_2CO$ (1 : 1). Since acetone is a weaker ligand than water it does not compete with $CHCl_2CN$ for binding to palladium(II), and the concentration of complex C in Scheme 4 is increased. The resonances at δ 6.79, 6.81 and 6.82, which occur during the reaction, can be assigned to the bidentate iminol and the isomers of the unidentate iminol (designated **II** and **III** above). At the end of the reaction these resonances are gone, and those at δ 6.32, 6.24 and 6.20 remain. The first is due to free $CHCl_2C(O)NH_2$ in $(CD_3)_2CO$ solution. The last two probably are due to the *syn* and *anti* isomers of the amidate ligand shown in **V** and **VI**. Their chemical shifts agree with published values for similar complexes.[43,48]

Unidentate iminol complexes may form by two pathways: directly in the external attack and by opening of the bidentate iminol complex, in the internal attack (Scheme 5). Owing to their lability, these complexes are evident in acetone solution, but not in aqueous solution. Water displaces unidentate iminol ligands easier than bidentate ones.

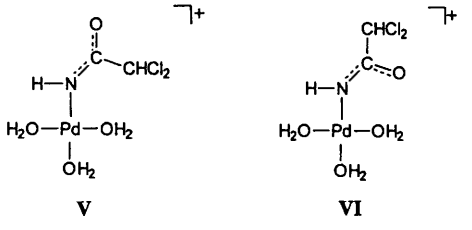
Overall mechanism and turnover in hydration

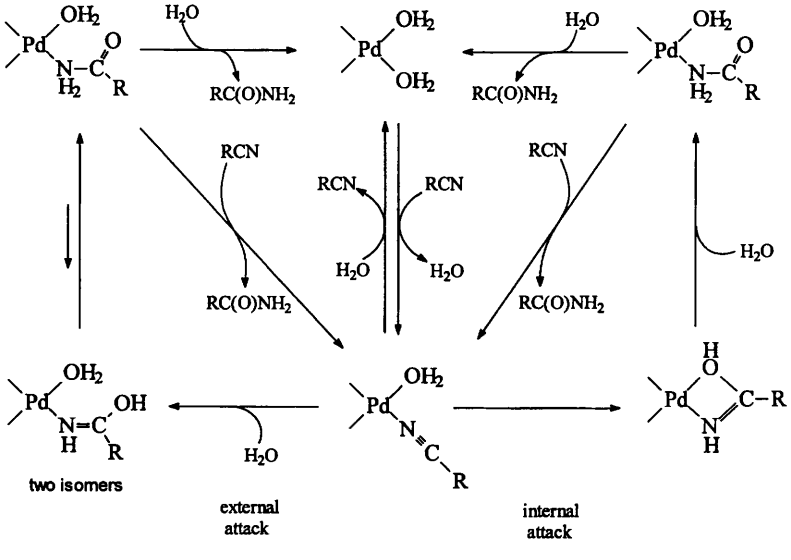
The experimental facts discussed above are integrated in the mechanism in Scheme 5. It is best followed beginning with the catalytic aqua complex, shown in the upper centre. The mechanism consists of two connected cycles, each of them made up of the following four steps: co-ordination of the nitrile to the catalyst (the central vertical); attack of water and formation of a co-ordinated iminol (the lower horizontal); tautomeric rearrangement of the iminol into amide, which is more stable (the side vertical); and release of the carboxamide. This last step can occur in two ways. If the nitrile concentration is relatively low, the carboxamide is displaced by water, and the catalytic aqua complex is restored (the upper horizontal). If the nitrile concentration is relatively high, the carboxamide is displaced by this substrate, and the substrate–catalyst complex is formed (the diagonals). Since co-ordination of nitrile is a fast process, this 'diagonal' step may be important. The species in the two upper corners of the rectangular Scheme 5 may be identical, but this could not be shown in the layout.

The two connected cycles differ only in the origin of the nucleophile, it can be an aqua ligand attacking internally or a solvent water attacking externally. The resulting intermediates, the complexes containing the bidentate and the unidentate iminol, may be in equilibrium with each other.

Conclusion

The uncatalysed hydration of nitriles has a half-life longer than *ca.* 1 × 10^6 h. Palladium(II) aqua complexes accelerate these reactions approximately 10^6-fold under the same conditions. Since the vinyl group resembles the CH_2Cl and $CHCl_2$ groups in its electron-withdrawing ability, the results of this study may be relevant to hydration of acrylonitrile. Acrylamide, the product of this last reaction, is an important industrial chemical.[49]





Scheme 5

Acknowledgements

This work was supported by National Science Foundation Grant CHE-9404971. N. M. K. also thanks the A. P. Sloan Foundation for a Research Fellowship.

References

1 B. C. Challis and J. A. Challis, in *The Chemistry of Amides*, ed. A. Zabicky, Wiley, New York, 1970.
2 P. L. Compagnon and M. Miocque, *Ann. Chim. (Paris)*, 1970, **5**, 11.
3 L. S. Hegedus and L. G. Nade, *Compendium of Organic Synthetic Methods*, Wiley, New York, 1977.
4 B. N. Storhoff and C. L. Huntley, jun., *Coord. Chem. Rev.*, 1977, **23**, 1.
5 R. W. Hay, in *Comprehensive Coordination Chemistry*, ed. G. W. Wilkinson, Pergamon, Oxford, 1987, sect. 61.4.5.
6 N. E. Dixon and A. M. Sargeson, in *Zinc Enzymes*, ed. T. G. Spiro, Wiley, New York, 1983, ch. 7.
7 P. F. B. Barnard, *J. Chem. Soc. A*, 1969, 2140.
8 S. Komiya, S. Suzuki and K. Watanabe, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 1440.
9 D. Pinnell, G. B. Wright and R. B. Jordan, *J. Am. Chem. Soc.*, 1972, **94**, 6104.
10 D. A. Buckingham, A. M. Sargeson and A. Zanella, *J. Am. Chem. Soc.*, 1972, **94**, 8246.
11 M. A. Bennett and T. Yoshida, *J. Am. Chem. Soc.*, 1973, **95**, 3030.
12 S. E. Diamond, B. Grant, G. M. Tom and H. Taube, *Tetrahedron Lett.*, 1974, **46**, 4025.
13 R. L. De La Vega, W. R. Ellis, jun. and W. L. Purcell, *Inorg. Chim. Acta*, 1983, **68**, 97.
14 C. M. Jensen and W. C. Trogler, *J. Am. Chem. Soc.*, 1986, **108**, 723.
15 S. S. Massoud and A. M. Ismail, *Polyhedron*, 1992, **11**, 1269.
16 (*a*) J. H. Kim, J. Britten and J. Chin, *J. Am. Chem. Soc.*, 1993, **115**, 3618; (*b*) N. M. Kostić, *Chemtracts-Inorg. Chem.*, 1993, **5**, 238.
17 R. Cini, F. P. Fanizzi, F. P. Intini, L. Maresca and G. Natile, *J. Am. Chem. Soc.*, 1993, **115**, 5123.
18 R. Breslow, R. Fairweather and J. Keana, *J. Am. Chem. Soc.*, 1967, **89**, 2135.
19 G. Villain, P. Kalck and A. Gaset, *Tetrahedron Lett.*, 1980, **21**, 2901.
20 G. Villain, G. Constant and A. Gaset, *J. Mol. Catal.*, 1980, **7**, 355.
21 G. Villain and A. Gaset, *J. Mol. Catal.*, 1981, **12**, 103.
22 N. M. Kostić, *Comments Inorg. Chem.*, 1988, **8**, 137.
23 I. E. Burgeson and N. M. Kostić, *Inorg. Chem.*, 1991, **30**, 4299.
24 L. Zhu and N. M. Kostić, *J. Am. Chem. Soc.*, 1993, **115**, 4566.
25 L. Zhu and N. M. Kostić, *Inorg. Chim. Acta*, 1994, **217**, 21.
26 E. N. Korneeva, M. V. Ovchinnikov and N. M. Kostić, *Inorg. Chim. Acta*, 1996, **243**, 9; T. N. Parac and N. M. Kostić, *J. Am. Chem. Soc.*, 1996, **118**, 51; 5946.
27 L. Zhu, L. Qin, T. N. Parac and N. M. Kostić, *J. Am. Chem. Soc.*, 1994, **116**, 5218.
28 T. Nagasawa and H. Yamada, *Trends Biotechnol.*, 1989, **7**, 153.
29 M. J. Nelson, H. Jin, I. M. Turner, jun., G. Grove, R. C. Scarrow, B. A. Brennan and L. Que, jun., *J. Am. Chem. Soc.*, 1991, **113**, 7072.
30 H. Jin, I. M. Turner, jun., M. J. Nelson, R. J. Gurbiel, P. E. Doan and B. M. Hoffman, *J. Am. Chem. Soc.*, 1993, **115**, 5290.
31 J. Honda, H. Kandori, T. Okada, T. Nagamune, Y. Shichida, H. Sasabe and I. Endo, *Biochemistry*, 1994, **33**, 3577.
32 H. Hohmann and R. Van Eldik, *Inorg. Chim. Acta*, 1990, **174**, 87.
33 G. W. Watt and W. A. Cude, *Inorg. Chem.*, 1968, **7**, 335.
34 L. M. Volshtein and M. F. Mogilevkina, *J. Chem. Soc. A*, 1967, 642.
35 C. Drexler, H. Paulus and H. Elias, *Inorg. Chem.*, 1991, **30**, 1297.
36 L. Rasmussen and C. K. Jorgensen, *Acta Chem. Scand.*, 1968, **22**, 2313.
37 L. I. Elding, *Inorg. Chim. Acta*, 1972, **6**, 647.
38 (*a*) L. I. Elding, *Inorg. Chim. Acta*, 1976, **20**, 65; (*b*) L. Helm, L. I. Elding and A. E. Merbach, *Helv. Chim. Acta*, 1984, **67**, 1453; (*c*) T. Shi, personal communication; (*d*) A. F. M. Siebert, Ph.D. Thesis, University of Bochum, 1995.
39 (*a*) V. Sklenár and A. Bax, *J. Magn. Reson.*, 1987, **74**, 469; (*b*) A. K. Covington, M. Paabo, R. A. Robinson and R. G. Bates, *Anal. Chem.*, 1968, **40**, 700; (*c*) B. A. Barshop, S. F. Wrenn and C. Frieden., *Anal. Biochem.*, 1983, **130**, 134; (*d*) J. H. Espenson, *Chemical Kinetics and Reaction Mechanisms*, McGraw-Hill, New York, 1981.
40 G. Mahal and R. Van Eldik, *Inorg. Chem.*, 1985, **24**, 4165.
41 P. A. Sutton and D. A. Buckingham, *Acc. Chem. Res.*, 1987, **20**, 357.
42 H. Sigel and R. B. Martin, *Chem. Rev.*, 1982, **82**, 385.
43 T. C. Woon and D. P. Fairlie, *Inorg. Chem.*, 1992, **31**, 4069.
44 T. C. Woon, W. A. Wickramasinghe and D. P. Fairlie, *Inorg. Chem.*, 1993, **32**, 2190.
45 D. P. Fairlie, T. C. Woon, W. A. Wickramasinghe and A. C. Willis, *Inorg. Chem.*, 1994, **33**, 6425.
46 B. G. Challis and J. A. Challis, in *Comprehensive Organic Chemistry*, ed. A. Zabicky, Pergamon, Oxford, 1979, vol. 2, p. 957.
47 R. C. Mehrotra, in *Comprehensive Coordination Chemistry*, ed. G. W. Wilkinson, Pergamon, Oxford, 1987, vol. 2, p. 269.
48 R. Cini, P. A. Caputo, F. P. Intini and G. Natile, *Inorg. Chem.*, 1995, **34**, 1130.
49 F. Matsuda, *Chemtech*, 1977, **7**, 306.

Received 30*th April* 1996; *Paper* 6/03024F