Reactions of Coordinated Nitriles. Nucleophilic Attack by Amines on *cis*-Dichlorobisbenzonitrileplatinum(II)

CHRISTOPHER A. AMODIO

Department of Chemistry, St. Mary's College, Strawberry Hill, Twickenham TW1 4SX, U.K.

and KEVIN B. NOLAN*

Department of Chemistry, University of Surrey, Guildford GU2 5XH, U.K.

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Abstract

The reactions of *cis*-$PtCl_2(C_6H_5CN)_2$ with primary amines, RNH_2, in chloroform at 30 °C have been investigated spectrophotometrically. With n-$C_3H_7NH_2$ and n-$C_4H_9NH_2$ as attacking nucleophiles two distinct reaction steps were observed and the products of these were isolated in the case of the former amine. The product of the first reaction is the amidine complex *trans*-$[PtCl(n\text{-}C_3H_7NH_2)\{C_6H_5C(NHC_3H_7)=NH\}_2]^+$ which, in the second reaction undergoes replacement of coordinated Cl^- by amine. The kinetics of these reactions were studied with n-butylamine as reacting nucleophile. For the first reaction the observed rate law is of the form, rate = k_3 [complex] $[RNH_2]^2$, while the second reaction follows the expected second order kinetic behaviour. With diethylamine as attacking nucleophile only the first of these reactions was observed.

Introduction

The activation of nitriles with respect to attack by nucleophiles in the coordination sphere of metal ions has recently attracted considerable interest. An example of such nitrile activation occurs in the complex $[Co(NH_3)_5CH_3CN]^{3+}$ which undergoes base catalysed hydrolysis some 2×10^6 times faster than the hydrolysis of the free ligand [1]. The complex *cis*-$[Co(en)_2(NH_2CH_2CN)Cl]^{2+}$ (en = 1,2-diaminoethane), despite not having the nitrile ligand directly coordinated to the metal, is also highly susceptible to attack by nucleophiles [2]. This high reactivity arises from the juxtapositioning of the nitrile group and coordinated nucleophilies such as OH^- or RNH^-, which are generated under certain conditions. In weakly basic solution, for example, attack by an amido conjugate base, derived from an en ligand, on the nitrile group leads to formation of an amidine, while in acid solution containing Hg^{2+} a chelated glycinamide complex is obtained by a mechanism involving attack by coordinated OH^- (the conjugate base of the initial aquation product) on the nitrile.

One of the earliest reported reactions of a coordinated nitrile was that of the complex *cis*-$PtCl_2(CH_3CN)_2$ which on treatment with Ag^+ and H_2O changed colour from pale yellow to blue [3]. The product of this reaction was shown to contain acetamidine ligands [4]. A number of other 'platinum blues' have since been prepared by the reaction of aqueous solutions of platinum(II) and amides [5, 6]. The structures of these materials have been the subject of much speculation because of their unusual colours. Interest in this area has been further aroused by the realisation that platinum blues are also obtained when the aquation product of the antitumour drug *cis*-$PtCl_2(NH_3)_2$ reacts with uracil, thymine and related pyrimidine bases [5]. It has also been recently discovered that pyrimidine platinum blues possess antitumour activity of their own [6, 7]. On the basis of structural studies it appears that the platinum blues are oligomeric, mixed valence, paramagnetic species containing platinum chains which are responsible for the colour [8]. The reaction of *cis*-$PtCl_2(CH_3CN)_2$ with ammonia has also been investigated. The product, although initially thought to be the six-coordinate platinum(II) complex $[Pt(NH_3)_4(CH_3CN)_2]Cl_2$ [9], was later shown by X-ray crystallography to be the acetamidine complex *trans*-$[Pt(NH_3)_2\{CH_3C(NH_2)=NH\}_2]^{2+}$ [10]. Similar products have been obtained by the reaction of other platinum(II) complexes, *cis*-$PtX_2(RCN)_2$ (X = Cl, Br; R = alkyl or aryl) and primary amines [11]. In this paper we report results of our studies on the reactions between *cis*-$PtCl_2(C_6H_5CN)_2$ and amines in chloroform solution.

*Author to whom correspondence should be addressed.

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Experimental

The complex *cis*-$PtCl_2(C_6H_5CN)_2$ was obtained as a yellow precipitate after cooling a solution of $PtCl_2$ in benzonitrile, which had been stirred at 100 °C for one day [12]. *Anal.* Calc. for $C_{14}H_{10}N_2Cl_2Pt$: C, 35.6; H, 2.12; N, 5.93. Found: C, 36.0; H, 2.18; N, 6.05%.

The reaction between n-propylamine and *cis*-$PtCl_2(C_6H_5CN)_2$ in $CHCl_3$ occurs in two steps. The products of these reactions were isolated as follows.

Product of Reaction 1

A solution of *cis*-$PtCl_2(C_6H_5CN)_2$ (0.3 g) in n-propylamine/$CHCl_3$ (5×10^{-3} mol dm^{-3}, 100 cm^3) was allowed to stand at room temperature for 1 h. A more concentrated solution of n-propylamine in $CHCl_3$ (0.1 mol dm^{-3}, 15 cm^3) was added to this and the reaction mixture then quickly cooled to 0 °C. The solution was evaported to dryness under reduced pressure leaving a yellow oily residue which was extracted into diethyl ether. The filtrate obtained after filtration of this solution was treated with petroleum ether (40–60) whereupon a yellow complex was precipitated. An IR spectrum of this material showed an intense ν(C=N) band at 1650 cm^{-1} and also a weak ν(C≡N) band at 2250 cm^{-1}, indicative of the presence of unreacted starting complex. The above procedure was repeated until the ν(C≡N) band completely disappeared from the spectrum of the isolated material. *Anal.* Calc. for $C_{23}H_{37}Cl_2N_5Pt$: C, 42.5; H, 5.70; N, 10.79. Found: C, 42.1; H, 5.68; N, 10.23%.

Product of Reaction 2

cis-$PtCl_2(C_6H_5CN)_2$ (0.3 g) in n-propylamine/$CHCl_3$ (0.1 mol dm^{-3}, 100 cm^3) was stirred for 1 h at room temperature, during which time its original yellow colour gradually disappeared. After the addition of a little neat n-propylamine (*ca.* 1 cm^3) to the colourless solution it was evaporated under reduced pressure and the resulting oily residue was triturated with diethylether. Recrystallisation from a cyclohexane/chloroform solvent mixture gave a product with satisfactory C, H, N, elemental analysis. *Anal.* Calc. for $C_{26}H_{46}Cl_2N_6Pt$: C, 44.0; N, 11.86; H, 6.57. Found: C, 44.07; H, 6.71; N, 11.54%.

Instrumentation

UV spectra were recorded on Pye-Unicam SP 800 and SP 1800 spectrophotometers and IR spectra on a Perkin-Elmer 577 spectrophotometer.

Results and Discussion

Heating a solution of $PtCl_2$ in benzonitrile gives the complex $PtCl_2(C_6H_5CN)_2$ which can be precipitated in high yield simply by cooling the solution. A number of such nitrile complexes $PtX_2(RCN)_2$ (R = CH_3 [11, 13], C_2H_5 [13], i-C_3H_7 [13], n-C_4H_9 [13], C_6H_5 [11, 13]; X = Cl, Br) have been prepared, usually by the addition of the appropriate nitrile to an aqueous solution of K_2PtX_4. On the basis of infrared spectroscopy these complexes have been assigned *cis* configurations in contrast to the analogous palladium complexes which are *trans* [11]. The main evidence for these assignments is provided by the ν(M–X) regions in the far infrared spectra. On symmetry grounds *cis* complexes should have two ν(M–X) absorption bands (symmetry A_1 and B_2) whereas *trans* complexes should only have one (symmetry B_{2u}) [11]. The ν(M–X) regions in the spectra of the platinum(II) complexes conform to the former pattern and of the palladium(II) complexes to the latter [11].

Addition of NH_3 to *cis*-$PtCl_2(CH_3CN)_2$ results in the replacement of Cl^- ligands by NH_3, addition of NH_3 to the nitrile and isomerisation, giving the bis acetamidine complex *trans*-$[Pt(NH_3)_2\{CH_3C(NH_2)=NH\}_2]^{2+}$ as final product. We wished to establish the sequence of these events but in this system either insolubility of reacting complex or precipitation during the course of the reaction interfered with spectrophotometric studies in many of the common solvents. The reaction between *cis*-$PtCl_2(C_6H_5CN)_2$ and n-butylamine in chloroform however provided us with a system uncomplicated by precipitation or solvation throughout the course of the reaction. At 30 °C two distinct reaction steps were observed spectrophotometrically, the first at lower concentrations (Fig. 1) and the second at higher concentrations (Fig. 2) of amine. Because of the lower volatility of n-butylamine relative to chloroform however, we

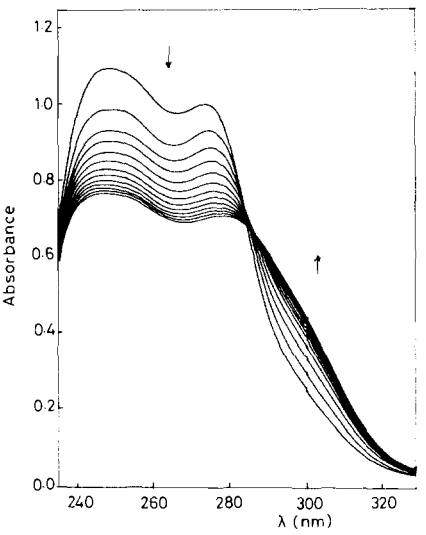


Fig. 1. UV spectra of *cis*-$PtCl_2(C_6H_5CN)_2$ in a solution of n-$C_4H_9NH_2$ in $CHCl_3$ (0.005 mol dm^{-3}) at 30.0 ±0.1 °C as a function of time (reaction 1). The time interval between spectral scans is 122 s.

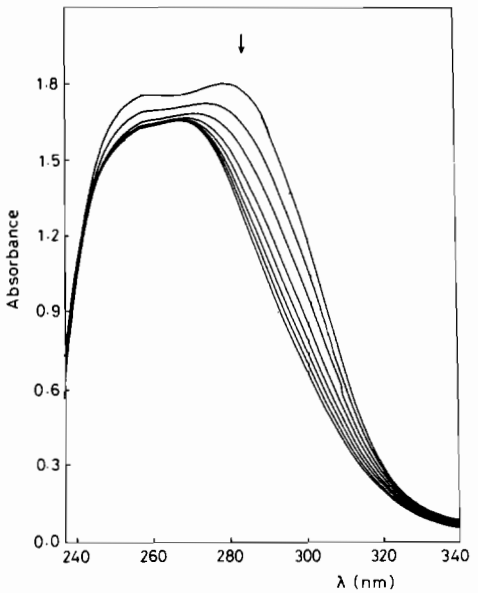


Fig. 2. UV spectra of *cis*-$PtCl_2(C_6H_5CN)_2$ in a solution of $n\text{-}C_4H_9NH_2$ in $CHCl_3$ (0.1 mol dm^{-3}) at 30.0 ±0.1 °C (reaction 2). Time interval between scans is 122 s.

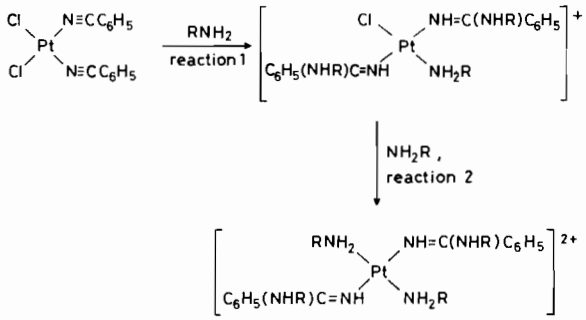
were unable to isolate and characterise the product of the first reaction in this system, because of interference from the second reaction as the solution was evaporated to dryness (and the amine concentration increased) even at low temperatures. The above two reactions were also observed with n-propylamine and because of the greater volatility of this amine relative to the solvent we were easily able to isolate the product of the first reaction without contamination from the final product. The isolation procedure for the products of the reactions between *cis*-$PtCl_2(C_6H_5CN)_2$ and n-propylamine is described in the experimental section.

On the basis of C,H,N, microanalytical data and infrared spectroscopy (no ν(C≡N) absorption but ν(C=N) at 1660 cm^{-1}) the product of reaction 2 is clearly the amidine complex $[Pt(n\text{-}C_3H_7NH_2)_2\{C_6H_5\text{-}C(NHC_3H_7)=NH\}_2]Cl_2$. On the basis of the established configuration of the product of the reaction between NH_3 and *cis*-$PtCl_2(CH_3CN)_2$, we assign a *trans* configuration to this product. According to C,H,N, microanalysis the product of reaction 1 contains one less n-propylamine ligand than the product of reaction 2. Its infrared spectrum is very similar to that of the final product and contains no ν(C≡N) absorption but instead a ν(C=N) band at 1650 cm^{-1}. It therefore appears that reaction 2 involves the replacement of a Cl^- ligand by amine and the overall reaction sequence may be represented by Scheme 1.

We have studied the kinetics of these reactions (R = n-C_4H_9) in chloroform at 30 °C. Both reactions were followed spectrophotometrically under pseudo

TABLE I. Kinetic Data for the Reactions between *cis*-$PtCl_2(C_6H_5CN)_2$ and n-butylamine in Chloroform at 30 °C

$[n\text{-}BuNH_2]$ (mol dm^{-3})	k_{obs} (s^{-1})	$k_{obs}/[n\text{-}BuNH_2]^2$ (dm^6 mol^{-2} s^{-1})
(a) Reaction 1		
0.0025	4.58×10^{-4}	73.3
0.005	1.83×10^{-3}	73.2
0.0075	4.00×10^{-3}	71.1
0.01	7.00×10^{-3}	70.0
$[n\text{-}BuNH_2]$ (mol dm^{-3})	k_{obs} (s^{-1})	$k_{obs}/[n\text{-}BuNH_2]$ (dm^3 mol^{-1} s^{-1})
(b) Reaction 2		
0.1	1.11×10^{-3}	1.11×10^{-2}
0.3	3.18×10^{-3}	1.06×10^{-2}
0.5	5.27×10^{-3}	1.05×10^{-2}

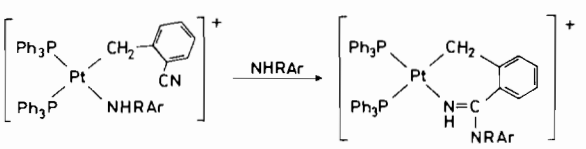


Scheme 1.

first order conditions, the first by monitoring the absorbance decrease at 275 nm and the second from the absorbance decrease at 315 nm. Results of these investigations are presented in Table I. Reaction 2 follows second order kinetics with a calculated rate constant of $(1.07 \pm 0.04) \times 10^{-2}$ dm^3 mol^{-1} s^{-1}. Reaction 1 on the other hand obeys the rate expression (eqn. 1) with $k_3 = 71.9 \pm 1.9$ dm^6 mol^{-2} s^{-1}. On examining the literature to find a precedent

$$\text{rate} = k_3[\text{complex}][RNH_2]^2 \quad (1)$$

for this type of behaviour we came across some relevant examples, including the only previous kinetic study on the addition of amines to coordinated nitriles [14, 15]. Complex **1** obtained by reaction of the dimer $[(Ph_3P)_2Pt(\mu\text{-}CH_2C_6H_4CN)]_2$ with secondary anilines was found to undergo further reaction in dichloromethane to give the amidine product **2** [14].



1 **2**

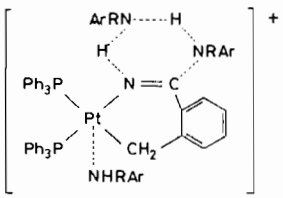
The rate expression for this reaction is of the form:

$$\text{rate} = k_2[\text{complex}][\text{NHRAr}] + k_3[\text{complex}][\text{NHRAr}]^2 \quad (2)$$

While the first order amine term in this rate expression has been attributed to nucleophilic attack by external amine on the nitrile group an alternative mechanism involving rapid pre-equilibrium formation of an amido conjugate base, eqn. 3, followed by intramolecular nucleophilic attack on the nitrile carbon is also a very likely possibility

$$Pt^{II}\text{–NHRAr} + \text{NHRAr} \rightleftharpoons Pt^{II}\text{–}N^{-}\text{RAr} + NH_2RAr^{+} \quad (3)$$

The second order term in amine has been explained on the basis of rapid pre-equilibrium formation of an aniline dimer which adds to the nitrile via the six-membered cyclic activated complex **3**. Amine dimers as attacking nucleophiles have also been implicated in the aminolysis of metal carbene complexes [16] in the aminolysis of esters in aprotic solvents [17] and in other reactions.



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To account for the second-order dependence on amine concentration in reaction 1 of the present work, we propose a similar rate determining step which involves attack by amine dimer on the carbon of one of the nitrile ligands. Subsequent rapid steps involving addition of amine to the second nitrile, replacement of Cl^- (*trans* to the amidine ligand) by amine and isomerization lead to the product of reaction 1. The order of these events cannot be predicted on the basis of the available information.

We have also investigated the reaction between *cis*-$PtCl_2(C_6H_5CN)_2$ and diethylamine in chloroform at 30 °C. In this case only one reaction was observed and this was characterised by a UV spectral change similar to those observed for reaction 1 between primary amines and the nitrile complex. The kinetics of this reaction were investigated under pseudo first order conditions ($[NHEt_2] \gg [\text{complex}]$) by following the absorbance increase at 310 nm. The results of these investigations (Table II) are consistent with the rate expression in eqn. 4. It therefore seems that in this reaction parallel pathways involving attack by

$$\text{rate} = [\text{complex}]\{k_2[NHEt_2] + k_3[NHEt_2]^2\} \quad (4)$$

TABLE II. Kinetic Data for the Reaction between *cis*-$PtCl_2(C_6H_5CN)_2$ and Diethylamine in Chloroform at 30 °C

$[NHEt_2]$ (mol dm^{-3})	k_{obs} (s^{-1})	$k_{obs}/[NHEt_2]$ (dm^3 mol^{-1} s^{-1})
0.02	6.00×10^{-4}	3.00×10^{-2}
0.05	1.95×10^{-3}	3.90×10^{-2}
0.10	5.19×10^{-3}	5.19×10^{-2}
0.20	1.56×10^{-2}	7.80×10^{-2}

amine and amine dimer on the nitrile group are observed. From the linear plot of $k_{obs}/[NHEt_2]$ *vs.* $[NHEt_2]$, k_3 was found to equal 0.26 ± 0.01 dm^6 mol^{-2} s^{-1} and k_2 to equal $(2.52 \pm 0.05) \times 10^{-2}$ dm^{-3} mol^{-1} s^{-1}. Attack by diethylamine dimer on the nitrile group is therefore some 270 times slower than attack by n-butylamine dimer, an observation which may be attributed to steric effects in the reaction involving the secondary amine.

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