A ^{1}H Nuclear Magnetic Resonance Study of the Mechanism of the Reaction between *cis*-Dichlorobis(dimethyl sulfoxide)-platinum(II) and Nitrogen Donors

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The product of the reaction between equimolar amounts of *cis*-[Pt(dmso)$_2$Cl$_2$] (dmso = dimethyl sulfoxide) and heterocyclic nitrogen bases (L) in nitromethane depends upon the steric requirements of the base. Strongly hindered ligands such as 2-methylquinoline and 2,6-dimethylpyridine give *cis*-[Pt(dmso)(L)Cl$_2$], while the less bulky 2-chloropyridine, 2,4-dimethylpyridine and pyridine give the corresponding *trans* isomer which later isomerises very slowly to the *cis* form. The analogous cationic bis(dimethyl sulfoxide) complexes have been prepared as their tetrafluoroborate salts, *cis*-[Pt(dmso)$_2$(L)Cl][BF$_4$] and their reactions with chloride in nitromethane solution have been studied by ^{1}H NMR spectroscopy. It is concluded that these ionic cations are intermediates in the replacement of dimethyl sulfoxide by L and that all of the stages take place with complete retention of configuration. The reaction products are accounted for in terms of an interplay between the normal *trans* effect advantage of chloride over the nitrogen donors and the steric repulsion arising from a 2,6-disubstituted pyridine in the axial site of the trigonal-bipyramidal intermediate and/or transition states.

The reactions between *cis*-[Pt(dmso)$_2$Cl$_2$] (dmso = dimethyl sulfoxide) and nitrogen-donor ligands have been investigated by a number of different groups using a variety of techniques. Rochon and co-workers[1] reported that the reaction of this complex with the stoichiometrically required amount of heterocyclic nitrogen bases (L) such as substituted pyridines or nucleosides in dimethyl sulfoxide solution led to the formation of *trans*-[Pt(dmso)(L)Cl$_2$] which then underwent a slow isomerisation to the *cis* form. It was concluded that the initial reaction was the displacement of dimethyl sulfoxide, which, if correct, makes this one of the few examples of substitution at a planar four-co-ordinate d^8 metal substrate that takes place with stereochemical change [equation (1)].

$$cis\text{-}[Pt(dmso)_2Cl_2] + L \longrightarrow trans\text{-}[Pt(dmso)(L)Cl_2] + dmso \quad (1)$$

Marzilli and co-workers[2] examined this reaction with a wider range of nucleosides in dimethyl sulfoxide solution and found that *trans* species were formed as in (1) except in the case of the reaction of cytidine (Cyd) with a two-fold excess of the complex. They found direct evidence for the formation of the ionic intermediate, *cis*-[Pt(dmso)$_2$(Cyd)Cl]$^+$, and concluded that the first stage in this reaction was the displacement of the chloride by the nitrogen donor. In a later paper[3] the authors extended this conclusion to the reaction with the substituted pyridines.

Some years ago, we examined the kinetics of the displacement of dimethyl sulfoxide from *cis*-[Pt(dmso)$_2$Cl$_2$] by a variety of substituted pyridines R-py in 1,2-dimethoxyethane solution and showed that the reaction product was *cis*-[Pt(dmso)(R-py)Cl$_2$].[4]

The use of dimethyl sulfoxide as a solvent for the study of these reactions seemed inappropriate to us since the solvent could also function as a nucleophile (n^0_{Pt} = 2.56[5]) and, in any case, would obscure important information about species containing dmso. For this reason we have used ^{1}H NMR spectroscopy to make an extensive examination of the reactions indicated in (1), carried out in CD_3NO_2 solution, and have also isolated and characterised a number of cationic complexes of the type *cis*-[Pt(dmso)$_2$(L)Cl][BF$_4$] and studied their reactivity. The results are reported in this paper.

Experimental

Preparations.—Dipotassium tetrachloroplatinate(II) was obtained from Johnson Matthey, dimethyl sulfoxide, the inorganic salts, and solvents were reagent grade products. Commercial heterocyclic bases were purified by distillation over KOH.

The compounds *cis*-[Pt(dmso)$_2$Cl$_2$],[6] K[Pt(dmso)Cl$_3$][7] and [Pt$_2$(dmso)$_2$(μ-Cl)$_2$Cl$_2$][8] were prepared by known methods while [AsPh$_4$][Pt(dmso)Cl$_3$] was precipitated from an aqueous solution of the sodium salt by adding the stoichiometric amount of [AsPh$_4$]Cl and was recrystallised from chloroform–pentane.

The complexes *trans*-[Pt(dmso)(L)Cl$_2$] [L = 2,4-dimethylpyridine (2,4Me$_2$-py), 2-chloropyridine (2Cl-py), 2-methylquinoline (2Me-quin) and pyridine (py)] were prepared by the method of Kong *et al.*[9] by adding the appropriate base to an aqueous solution of K[Pt(dmso)Cl$_3$]. The product which is precipitated from solution was recrystallised from chloroform–diethyl ether and obtained in yields in excess of 90%. The complex *cis*-[Pt(dmso)(py)Cl$_2$] was prepared by the method of Rochon and co-workers.[1]

trans-[Pt(dmso)(2,6Me$_2$-py)Cl$_2$]. A solution of 2,6Me$_2$-py (0.048 g, 0.44 mmol) in chloroform (1 cm^3) was added with stirring to a solution of [Pt$_2$(dmso)$_2$(μ-Cl)$_2$Cl$_2$] (0.15 g, 0.22 mmol) in the same solvent (10 cm^3) and the reaction mixture was allowed to stand at room temperature overnight. Diethyl ether (20 cm^3) was then added to precipitate the crude product as a pale yellow solid which was recrystallized from chloroform–pentane. Yield 86% (Found: C, 23.9; H, 3.30; Cl, 15.9; N, 3.10. $C_9H_{15}Cl_2NOPtS$ requires C, 23.95; H, 3.35; Cl, 15.7; N, 3.10%).

cis-[Pt(dmso)(2Cl-py)Cl$_2$]. Sodium chloride (0.014 g, 0.24 mmol) was added to a suspension of *trans*-[Pt(dmso)(2Cl-py)Cl$_2$] (0.1 g, 0.24 mmol) in water (5 cm^3) and the mixture was stirred for 2 d at 70 °C. The white solid which formed was

filtered off, washed twice with water and air-dried. The yield was almost quantitative (Found: C, 18.4; H, 2.15; Cl, 23.5; N, 3.10. $C_7H_{10}Cl_3NOPtS$ requires C, 18.4; H, 2.20; Cl, 23.2; N, 3.05%).

cis-[Pt(dmso)(2,6Me_2-py)Cl_2]. A solution of 2,6Me_2-py (0.026 g, 0.24 mmol) in nitromethane (0.5 cm^3) was added, with stirring, to a solution of *cis*-[Pt(dmso)$_2Cl_2$] (0.1 g, 0.24 mmol) in the same solvent (5 cm^3) and the reaction mixture set aside. After some days the reaction product began to precipitate as large, yellowish, crystals. The reaction mixture was allowed to stand at room temperature for two weeks and then the precipitate was filtered off, washed once with a small quantity of nitromethane, then twice with diethyl ether and air-dried. Yield 80% (Found: C, 23.7; H, 3.35; Cl, 15.8; N, 3.10. $C_9H_{15}Cl_2NOPtS$ requires C, 23.95; H, 3.35; Cl, 15.7; N, 3.10%).

cis-[Pt(dmso)(2Me-quin)Cl_2] was prepared in a similar way. The compound is much more soluble in nitromethane and did not precipitate from the solution; after one week the volume of the solvent was reduced and diethyl ether was added dropwise to give white crystals which were filtered off and washed with ether, then air dried. Yield 85% (Found: C, 29.6; H, 3.15; Cl, 14.5; N, 2.8. $C_{12}H_{15}Cl_2NOPtS$ requires C, 29.6; H, 3.10; Cl, 14.55; N, 2.9%).

The cationic complexes *cis*-[Pt(dmso)$_2$(L)Cl][BF_4] (L = 2,6Me_2-py, 2Me-quin, 2,4Me_2-py, 2Cl-py or py) were prepared by the following procedure: to a solution of *cis*-[Pt(dmso)$_2Cl_2$] (0.3 g, 0.71 mmol) in nitromethane (15 cm^3) a solution of the stoichiometric amount of Ag[BF_4] in the same solvent (5 cm^3) was added with stirring and a white precipitate of AgCl immediately started to form. A solution of the stoichiometric amount of the appropriate heterocyclic nitrogen base in nitromethane (1 cm^3) was then added, with stirring, and the mixture was stored in the dark. After a period of time ranging from 2 d (for L = 2,6Me_2-py or 2Me-quin) to 30 min (in the other cases), the AgCl was filtered off and the solution concentrated to 5 cm^3 on a rotary evaporator. The crude product was then precipitated by adding diethyl ether (10 cm^3) and was recrystallized from a filtered nitromethane solution by careful addition of diethyl ether, washed twice with diethyl ether and dried *in vacuo* over P_2O_5. In all cases the yields were practically quantitative (Found: L = 2,6Me_2-py: C, 22.6; H, 3.80; Cl, 6.15; N, 2.40. $C_{11}H_{21}BClF_4NO_2PtS_2$ requires C, 22.75; H, 3.65; Cl, 6.10; N, 2.40. L = 2,4Me_2-py: C, 23.0; H, 3.60; Cl, 6.05; N, 2.45. $C_{11}H_{21}BClF_4NO_2PtS_2$ requires C, 22.75; H, 3.65; Cl, 6.10; N, 2.40. L = 2Me-quin: C, 27.3; H, 3.40; Cl, 5.70; N, 2.30. $C_{14}H_{21}BClF_4NO_2PtS_2$ requires C, 27.3; H, 3.45; Cl, 5.75; N, 2.25. L = 2Cl-py: C, 18.5; H, 2.75; Cl, 12.0; N, 2.35. $C_9H_{16}BClF_4NO_2PtS_2$ requires C, 18.4; H, 2.75; Cl, 12.1; N, 2.40. L = py: C, 19.5; H, 3.10; Cl, 6.40; N, 2.55. $C_9H_{17}BClF_4NO_2PtS_2$ requires C, 19.6; H, 3.10; Cl, 6.40; N, 2.55%).

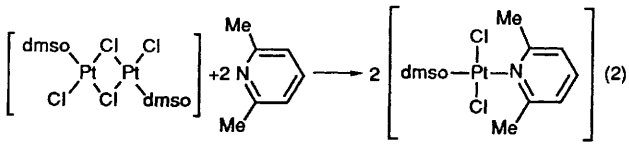
The reaction of trans-[Pt(dmso)(2Cl-py)Cl_2] *with dmso*. To a solution of *trans*-[Pt(dmso)(2Cl-py)Cl_2] (0.1 g, 0.22 mmol) in acetone (10 cm^3), a solution of the stoichiometric amount of dmso in the same solvent (0.5 cm^3) was slowly added with stirring; after a few minutes a pale-yellow precipitate started to form. The mixture was cooled in an ice-bath and stirred for a further 30 min. The resulting precipitate was collected by filtration, washed with cold acetone, diethyl ether and air-dried. The compound was identified as *trans*-[Pt(dmso)$_2Cl_2$] by IR spectroscopy and the yield was practically quantitative.

Apparatus.—Infrared spectra of Nujol mulls between NaCl or polyethylene (below 600 cm^{-1}) plates were recorded with a Perkin Elmer 683 spectrophotometer. Proton NMR spectra of CD_3NO_2 solutions, using $SiMe_4$ as internal standard, were recorded with a Varian EM390 spectrometer. Conductance measurements were carried out with a CDM 83 Radiometer Copenhagen conductivity meter and CDC 334 immersion electrode. Electronic spectra were obtained with a Cary 219 spectrophotometer.

Results

(*i*) *The Preparation of the Complexes*.—Although the details of the preparations are given in the previous section it is useful to make some general comments.

(*a*) *Uncharged complexes*. Addition of 2,4Me_2-py, 2Cl-py, 2Me-quin or py to an aqueous solution of K[Pt(dmso)Cl_3] led to the formation of pure *trans*-[Pt(dmso)(L)Cl_2] but NMR spectrometry indicated that the reaction with 2,6Me_2-py gave a mixture of the *cis* and *trans* isomers. The product was also shown to be contaminated with some platinum metal. Pure *trans*-[Pt(dmso)(2,6Me_2-py)Cl_2] was prepared by the bridge-splitting reaction [equation (2)]. The IR spectrum of the



(2)

compound showed only one band assigned to ν_{Pt-Cl} (347 cm^{-1}) in accordance with the *trans* configuration.

Only one of the complexes of the type *cis*-[Pt(dmso)(L)Cl_2], namely that with L = pyridine, could be obtained conveniently by isomerising the *trans* isomer in dmso solution. This process is too slow to be practicable with the most sterically hindered species, 2,6Me_2-py and 2Me-quin; the *cis* complexes of these ligands were best prepared by treating *cis*-[Pt(dmso)$_2Cl_2$] with an equimolar amount of the base in nitromethane solution (the reason for the success of this method will be made clear later). IR spectra showed two bands assigned to ν_{Pt-Cl} (320, 350, and 328, 348 cm^{-1} for L = 2,6Me_2-py and 2Me-quin respectively). In the case of the reaction with the least basic ligand, 2Cl-py, elemental analysis indicated that a mixture of compounds had been obtained after the *trans* isomer was allowed to stand for several days in dmso solution. The changing NMR spectrum of a mixture of the *trans* compound and a two-fold excess of dmso in CD_3NO_2 solution showed a slow conversion to a mixture of *cis*-[Pt(dmso)$_2Cl_2$] and *cis*-[Pt(dmso)(2Cl-py)Cl_2]; a trace of *trans*-[Pt(dmso)$_2Cl_2$] was also present in the early stages of the reaction. Owing to the very low basicity of 2-chloropyridine, it is likely that equilibrium (3) was set up in

trans-[Pt(dmso)(2Cl-py)Cl_2] + dmso $\rightleftharpoons$ *trans*-[Pt(dmso)$_2Cl_2$] + 2Cl-py (3)

solution followed by the dmso-catalysed isomerisation of the *trans*-[Pt(dmso)$_2Cl_2$] complex to the *cis* species. When the reaction represented by (3) was carried out in acetone, in which *trans*-[Pt(dmso)$_2Cl_2$] is completely insoluble, the latter was precipitated almost quantitatively. This offers an alternative route, with better yield, for the synthesis of this species and avoids the time consuming synthesis of the dimer, [Pt_2(dmso)$_2$(μ-Cl)$_2Cl_2$].[8]

The compound *cis*-[Pt(dmso)(2Cl-py)Cl_2] was obtained as a sole product of the chloride-catalysed isomerisation of the *trans* isomer in aqueous solution (IR: ν_{Pt-Cl} 325 and 345 cm^{-1}). In the ^1H NMR spectrum of the compound (CD_3NO_2 solution) two methyl resonances of co-ordinated dmso are observed, each with ^{195}Pt satellites; the same pattern is found for the corresponding complex of 2Me-quin (see Table 1). This is consistent with the plane of ligand L being out of the co-ordination plane of the metal. (In the solid state, the 2Me-py ligand in *cis*-[Pt(dmso)(2Me-py)Cl_2] is perpendicular to the co-ordination plane of the metal.[10]) The ligand is thus prochiral and the appearance of two methyl peaks indicates that the two enantiomers do not interconvert rapidly at 35 °C by a process which requires the bulk of the ligand L to move from one side of the co-ordination plane to the other.

Table 1 Proton NMR data[a]

Complex	dmso Resonances	Upfield Resonances 2-Me	4-Me
$[AsPh_4][Pt(dmso)Cl_3]$	3.28 (21.9)		
cis-$[Pt(dmso)_2Cl_2]$	3.52 (23.3)		
trans-$[Pt(dmso)(py)Cl_2]$	3.41 (20.6)		
cis-$[Pt(dmso)(py)Cl_2]$	3.46 (24.0)		
trans-$[Pt(dmso)(2,4Me_2\text{-py})Cl_2]$	3.40 (20.6)	3.02 (9.6)	2.45
trans-$[Pt(dmso)(2,6Me_2\text{-py})Cl_2]$	3.40 (20.7)	3.18 (11.7)	
cis-$[Pt(dmso)(2,6Me_2\text{-py})Cl_2]$	3.45 (23.4)	3.24 (13.8)	
trans-$[Pt(dmso)(2Cl\text{-py})Cl_2]$	3.44 (22.5)		
cis-$[Pt(dmso)(2Cl\text{-py})Cl_2]$	3.43 (24.6)		
	3.50 (24.6)		
trans-$[Pt(dmso)(2Me\text{-quin})Cl_2]$	3.50 (21.3)	3.44[b]	
cis-$[Pt(dmso)(2Me\text{-quin})Cl_2]$	3.40 (25.0)	3.46 (13.2)	
	3.46 (25.2)		
cis-$[Pt(dmso)_2(py)Cl][BF_4]$	3.64 (26.7)		
	3.70 (22.4)		
cis-$[Pt(dmso)_2(2,4Me_2\text{-py})Cl][BF_4]$	3.59 (26.2)	3.02 (9.17)	2.49
	3.64 (26.5)		
	3.70 (22.4)		
cis-$[Pt(dmso)_2(2,6Me_2\text{-py})Cl][BF_4]$	3.66 (26.9)	3.21 (11.1)	
	3.75 (23.4)		
cis-$[Pt(dmso)_2(2Me\text{-quin})Cl][BF_4]$	3.55 (26.4)	3.43 (11.3)	
	3.65 (27.2)		
	3.81 (23.4)		
	3.85 (23.9)		
cis-$[Pt(dmso)_2(2Cl\text{-py})Cl][BF_4]$	3.65 (26.7),		
	3.69 (26.6)		
	3.76 (24.8)		

[a] Spectra were recorded on CD_3NO_2 solutions, chemical shifts are in ppm downfield from $SiMe_4$ and coupling constants (J_{Pt-H} in parentheses) are given in Hz. [b] Not determined because of superimposition of the ^{195}Pt satellites with dmso resonances.

(*b*) *Cationic complexes.* The ^1H NMR spectra of the cationic complexes show that, in every case, the two dmso ligands are sulfur-bonded and *cis* to each other; usually two methyl resonances belonging to non-equivalent dmso molecules, each with ^{195}Pt satellites, are observed. The one with the larger coupling constant is assigned to the dmso *cis* to L on the basis that (*i*) in the neutral mixed complexes, the coupling constant is always larger in the *cis*- than in the corresponding *trans*-isomer, and (*ii*) when L is unsymmetrically substituted at the 2 and 6 positions the resonance with the larger coupling constant appears as a doublet for the reasons discussed above.

(*ii*) *The Reactions of cis-*$[Pt(dmso)_2Cl_2]$ *with Pyridines in Equimolar Concentrations.*—The progress of the reaction between *cis*-$[Pt(dmso)_2Cl_2]$ and L, in CD_3NO_2 solution, was monitored by NMR spectrometry. Three types of behaviour could be observed depending upon the nature of L.

(*a*) The reactions with $2,4Me_2$-py or py were complete within the time required for mixing the reagents (*ca.* 2 min) under the experimental conditions employed ([complex] = [L] = 0.060 mol dm^{-3}, T = 35 °C); only the signals for the products, *trans*-[Pt(dmso)(L)Cl] and dmso, were observed in the first recorded spectrum. The *trans* compound then slowly changed to the *cis* isomer; in the case of L = pyridine, about 10% was converted after 15 h.

(*b*) The reactions with 2Cl-py were slow enough to be followed by ^1H NMR spectroscopy. The spectra, taken at times over a period of several days, showed the progressive formation of *trans*-$[Pt(dmso)(2Cl\text{-py})Cl_2]$ and free dimethyl sulfoxide in equimolar amounts. The subsequent *trans* to *cis* isomerisation was much slower. After 4 d, only 10% had been converted to the *cis* isomer whereas the starting dichlorobis(dimethyl sulfoxide)platinum(II) complex and the *trans* product were present in roughly equimolar amounts. By analysing the spectra

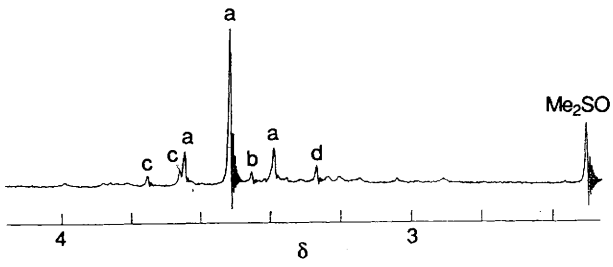


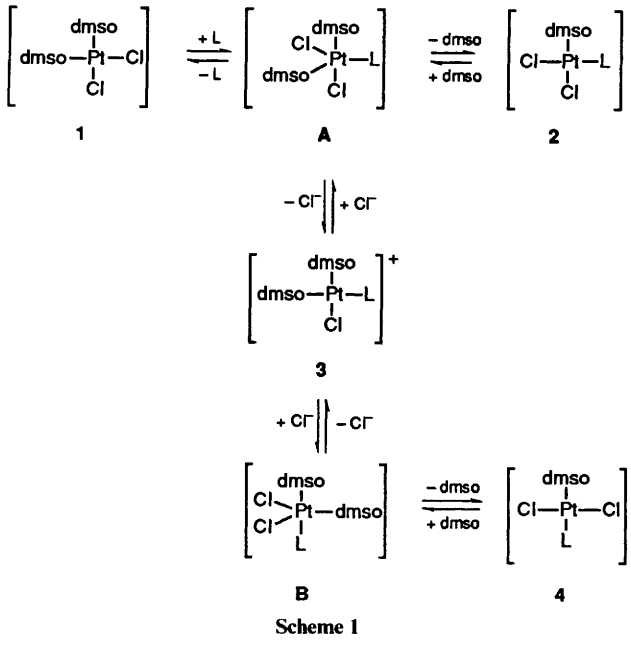
Fig. 1 Proton NMR spectrum (90 MHz; standard $SiMe_4$), in the region of the methyl proton resonances of dmso, for the reaction between *cis*-$[Pt(dmso)_2Cl_2]$ and 2,6-dimethylpyridine in equimolar ratio in CD_3NO_2, taken 110 min after mixing. The proton resonances are identified as: *cis*-$[Pt(dmso)_2Cl_2]$ (a), *cis*-$[Pt(dmso)(2,6Me_2\text{-py})Cl_2]$ (b), *cis*-$[Pt(dmso)_2(2,6Me_2\text{-py})Cl]^+$ (c) and $[Pt(dmso)Cl_3]^-$ (d)

recorded in the early stage of the reaction (6 h), where the isomerisation process does not interfere, the rate constant for the formation of the *trans* product was determined. The data obey equation (4) for a second-order reaction with equal

$$\frac{2A_F/A_T}{1 - 2(A_F/A_T)} = c_0 k_{obs} t \qquad (4)$$

concentrations of reactants; A_F and A_T are the measured areas under the peaks of free dmso and of all the dmso-containing species respectively at time t, and c_0 is the initial concentration of reactants. A plot of the left-hand term in the equation against time was linear with negligible intercept, the slope giving the second-order rate constant k_{obs} = (1.4 ± 0.1) × 10^{-3} dm^3 mol^{-1} s^{-1}.

(*c*) The reactions with the sterically-hindered bases $2,6Me_2$-py and 2Me-quin could also be followed by NMR. In the early stages of the reaction with $2,6Me_2$-py four resonances assigned to species containing co-ordinated dmso other than *cis*-$[Pt(dmso)_2Cl_2]$ were observed in the NMR spectrum (Fig. 1), together with the signal for free dmso. The two peaks at δ 3.75 and 3.66 were assigned to *cis*-$[Pt(dmso)_2(2,6Me_2\text{-py})Cl]^+$ and the one at δ 3.45 was assigned to *cis*-$[Pt(dmso)(2,6Me_2\text{-py})Cl_2]$ (see Table 1). The remaining resonance at δ 3.29 corresponded to none of the known compounds; however, on addition of $[AsPh_4][BF_4]$ it shifted to a δ value identical to that of the salt $[AsPh_4][Pt(dmso)Cl_3]$, whereas the other resonances remained unchanged. With time, *cis*-$[Pt(dmso)(2,6Me_2\text{-py})Cl_2]$ became the predominant complex, and eventually precipitated from solution. The concentrations of the two ionic complexes remained equal throughout the reaction and reached a maximum of *ca.* 10% of the total platinum species present (as judged from peak heights). Thereafter, the signals for these species started to decrease and new signals appeared that were assigned to *trans*-$[Pt(dmso)(2,6Me_2\text{-py})Cl_2]$. The signal heights indicated that the ionic species were replaced by an equivalent amount of the latter compound. Conductance measurements confirmed the formation and subsequent consumption of ionic intermediates and a maximum conductivity of 4.2 × 10^{-4} ohm^{-1} cm^{-1} was reached approximately 2 h after the reagents were mixed. In order to calculate the concentrations of the intermediate *cis*-$[Pt(dmso)_2(2,6Me_2\text{-py})Cl][Pt(dmso)Cl_3]$, we determined the equivalent conductances of *cis*-$[Pt(dmso)_2(2,6Me_2\text{-py})Cl][BF_4]$, $[AsPh_4][BF_4]$ and $[AsPh_4][Pt(dmso)Cl_3]$ in the concentration range 10^{-2}–10^{-4} mol dm^{-3}. The Onsager plots were all linear and those for the first two electrolytes coincided within experimental error, indicating that the equivalent conductances of *cis*-$[Pt(dmso)_2(2,6Me_2\text{-py})Cl]^+$ and $[AsPh_4]^+$ were similar. It was therefore concluded that the conductance of $[AsPh_4][Pt(dmso)Cl_3]$ was equal to that of the intermediate whose maximum concentration (reached in the 1:1 reaction) could thus be calculated to be 7 × 10^{-3} mol dm^{-3} which is *ca.* 11% of the initial concentration of reactants. This is in good agreement with the NMR analysis.



Scheme 1

The reaction with 2Me-quin was faster and gave *cis*-[Pt(dmso)(2Me-quin)Cl_2]; the transient species, *cis*-[Pt(dmso)$_2$(2Me-quin)Cl][Pt(dmso)Cl_3] also appeared in the initial stages of the reaction but the maximum amount (*ca.* 1%) was very much less.

(*iii*) *Reactions of the Cationic Complexes with Chloride.*—The reactions of the cationic complexes *cis*-[Pt(dmso)$_2$(L)Cl][BF_4] with an equimolar amount of [$AsPh_4$]Cl (added as a solid) were also followed by NMR spectroscopy; the experimental conditions (solvent, temperature and concentration) were the same as those in the experiments previously described.

The compound [Pt(dmso)$_2$(2Cl-py)Cl][BF_4] reacted quantitatively in the time required for mixing the reagents giving *cis*-[Pt(dmso)$_2$$Cl_2$] and free amine which then reacted in the way described above.

When L was py or 2,4Me_2-py, the first recorded spectrum was that of an equimolar mixture of *trans*-[Pt(dmso)(L)Cl_2] and free dmso. However, when chloride was added to an acidified (0.5 mol dm^{-3} CF_3CO_2H) solution of the cationic complex, the predominant reaction product in the first recorded spectrum was *cis*-[Pt(dmso)$_2$$Cl_2$]. The amount of *trans*-[Pt(dmso)(L)Cl_2] which was formed at the same time, was *ca.* 30 and 20% of the initial concentration of reactants for L = py and 2,4Me_2-py respectively.

The cationic complexes with L = 2,6Me_2-py and 2Me-quin also reacted rapidly with Cl^-, but gave *cis*-[Pt(dmso)(L)Cl_2] + dmso whether or not trifluoroacetic acid was added.

Discussion

The experimental results presented in this paper can be accounted for by the reaction pathways shown in Scheme 1 each of which passes through the indicated five-co-ordinate intermediate (A mechanism) or single transition-state (I_a mechanism) and occurs with retention of configuration.

The isomer formed in the reaction of **1** with equimolar amounts of L depends on the amount of steric hindrance at the positions *ortho* to the nitrogen donor. For example, when L = highly hindered 2,6Me_2-py or 2Me-quin, the *cis* isomer, **2**, is formed. In all other cases the product is the *trans* isomer, **4**. In all but one of the cases examined, reaction **1** ⟶ **4** is complete soon after mixing the reagents under the experimental conditions employed. The reaction with the least basic nucleophile 2Cl-py takes place more slowly and only in this case could the kinetics of dmso displacement be examined. These followed a simple second-order rate law and there was no evidence for the build-up of measurable concentrations of intermediates such as **3**. We must therefore consider the problem as to whether or not **4** is formed by the two consecutive displacement reactions in the above scheme.

In those cases where the *cis* complex is apparently formed directly, *i.e.*, **1** ⟶ **2**, there is direct experimental evidence for the presence of *cis*-[Pt(dmso)$_2$(L)Cl]$^+$ as a transient species in solution. However, this does not necessarily imply that the reaction proceeds through **3**. Indeed, the presence of [Pt(dmso)Cl_3]$^-$ as the counter ion, strongly suggests that build up of **3** is the result of a reaction that is parallel to and competitive with the formation of **2** and is a consequence of chloride abstraction by equilibrium (5).

$$cis\text{-}[Pt(dmso)_2Cl_2] + Cl^- \rightleftharpoons [Pt(dmso)Cl_3]^- + dmso \quad (5)$$

The observation that it is a transient species that gives rise to an equal amount of the *trans*-[Pt(dmso)(L)Cl_2] complex (see Results section) can be accounted for by the well known reaction [equation (6)].[11]

$$[Pt(dmso)Cl_3]^- + L \longrightarrow trans\text{-}[Pt(dmso)(L)Cl_2] + Cl^- \quad (6)$$

This behaviour is similar in many respects to that reported by Marzilli and co-workers[2] for the reaction of **1** with cytidine in dmso solution when only with the least reactive nucleoside and in the presence of an excess of the substrate did they have direct evidence for the formation of *cis*-[Pt(dmso)$_2$(Cyd)Cl]$^+$ as a transient species in solution. It is significant that, in spite of the fact that the product of the concentrations of the reagents in the cytidine reaction ($0.01 \times 0.02 = 2 \times 10^{-4}$ mol^2 dm^{-6}) was half that used in the corresponding reaction with the more reactive 7-methylinosine ($0.01 \times 0.02 = 4 \times 10^{-4}$ mol^2 dm^{-6}), the rate of build-up of the mixed complexes was nearly the same in both cases (see Figs. 1 and 3 of ref. 2).

For *cis*-[Pt(dmso)$_2$$Cl_2$] to compete with *cis*-[Pt(dmso)$_2$(L)Cl]$^+$ in reacting with Cl^-, both reactions must, obviously, have similar rates. Although the latter reaction was too fast to measure from changes in the NMR spectra, it was possible to follow the kinetics of the reaction **3** ⟶ **2** at lower reagent concentrations using spectrophotometry. For L = 2,6Me_2-py and 2Me-quin, studied under pseudo-first-order conditions ([complex] = 10^{-4} mol dm^{-3}, [LiCl] = 10^{-2} mol dm^{-3}) in methanol–water (95:5% v/v) at 25 °C, the change in absorbance is, indeed, first order, and the second-order rate constants, $k_{obs}/[Cl^-]$, could be estimated as $(6.22 \pm 0.01) \times 10^{-2}$ and (0.129 ± 0.002) dm^3 mol^{-1} s^{-1} respectively.

The isolation of the cationic species **3** as their tetrafluoroborate salts, allowed us to study their reactions with equimolar amounts of chloride ion. When L = 2,6Me_2-py or 2Me-quin, dmso is displaced and the product is **2**. When L = 2,4Me_2-py or py a mixture of **4** and **1** is obtained and, when L is 2Cl-py only L is displaced and **1** is formed. These observations can be accounted for by considering the effect of steric and electronic effects.

There are three possible leaving groups. The ligand L can only be displaced through intermediate **A** to give **1**. The most basic heterocyclic ligands are likely to be most strongly bound and in the appropriate complexes the displacement of dimethyl sulfoxide can be observed. Which of the two will be displaced ought to depend upon the relative *trans* effects of Cl and L. Since Cl usually exerts a greater *trans* effect than these nitrogen donors one might expect that the *trans*-dichloro species, **4**, will be preferred kinetically. However when there is steric hindrance from *ortho* substituents on the pyridine (as far as steric hindrance is concerned, quinoline can be looked upon as an *ortho*-substituted pyridine) the effect on the stability of the five-

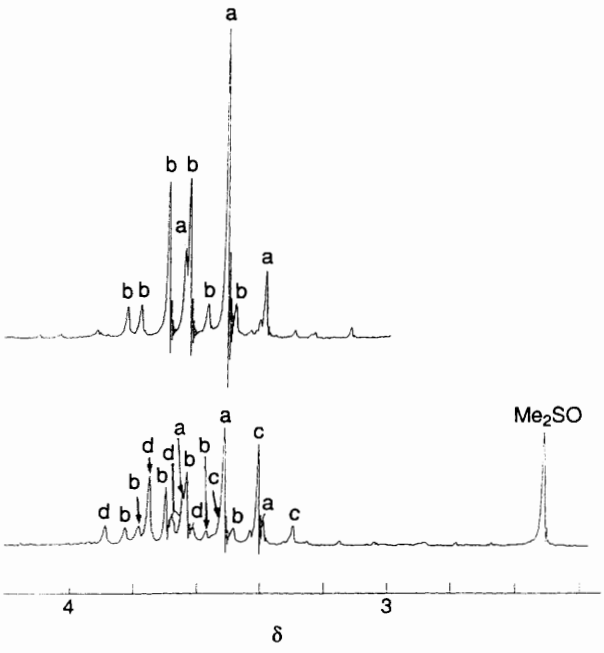


Fig. 2 Proton NMR spectrum (90 MHz; standard $SiMe_4$), in the region of the methyl proton resonances of dmso, of an equimolar mixture of *cis*-$[Pt(dmso)_2Cl_2]$ and *cis*-$[Pt(dmso)_2(py)Cl][BF_4]$ dissolved in CD_3NO_2, (*a*), before and (*b*), 20 min after the addition of 2-chloropyridine. Proton resonances are identified as: *cis*-$[Pt(dmso)_2Cl_2]$ (a), *cis*-$[Pt(dmso)_2(py)Cl]^+$ (b), *trans*-$[Pt(dmso)(py)Cl_2]$ (c) and *cis*-$[Pt(dmso)_2(2Cl\text{-}py)Cl]^+$ (d)

co-ordinate intermediates (transition states) represented by **A** and **B** in Scheme 1 becomes important. When L takes an axial position in the trigonal bipyramid, as in **B**, this steric hindrance is much greater and the destabilisation much more than when it lies in the trigonal plane, as in **A**. Consequently, with the bulky and strongly basic 2,6Me_2-py and 2Me-quin, the product predicted by applying the classical *trans* effect would require passage through the destabilised intermediate **B**, and so the pathway through **A** is preferred and **2** is formed instead. When the steric hindrance is too small to interfere, the displacement of dmso leads to the formation of the predicted isomer. The basicity of 2Cl-py is low enough for its displacement to dominate the reaction of the cationic complex with chloride.

The same reasoning can account for the observation of Rochon *et al.*[12] that the product of the solvolytic displacement of Cl^- from $[Pt(2,6Me_2\text{-}py)Cl_3]^-$ in dimethylformamide (dmf), reaction (7), has a *trans* configuration in spite of the fact that

$$[Pt(2,6Me_2\text{-}py)Cl_3]^- + Ag^+ + dmf \longrightarrow trans\text{-}[Pt(2,6Me_2\text{-}py)(dmf)Cl_2] + AgCl \quad (7)$$

chloride should have a larger *trans* effect than 2,6-dimethylpyridine.

It is clear that **4** is generated by the displacement of dmso from the cationic species **3**, even though the concentration ratio of the products, [**1**]/[**4**] indicates that the relative rate of displacement of L from **3** is always greater than that for the displacement of dmso ([**1**]/[**4**] = 70/30 for L = py, 80/20 for L = 2,4Me_2-py and even larger in the case of L = 2Cl-py).

In the cases where the *trans*-$[Pt(dmso)(L)Cl_2]$ isomer is the main product of reaction of **1** with L, the reversibility of the formation of the cationic species does not invalidate the assumption that the latter is an intermediate of the reaction under steady-state conditions. On the contrary, the unfavourable position of the equilibrium, **1** $\rightleftharpoons$ **3**, for the weakly basic 2Cl-py accounts for the fact that the reaction with 2-chloropyridine is much slower than that with 2,4-dimethylpyridine even though the steric hindrance of the two nucleophiles is similar and the dependence of nucleophilicity upon basicity is usually small in substitution reactions of Pt^{II}.

Although none of these facts are inconsistent with the proposal that the cationic complex, **3**, is an intermediate in the formation of the *trans* complex, **4**, there was no direct evidence that it is actually present in the reaction mixture generated by the addition of L to *cis*-$[Pt(dmso)_2Cl_2]$. In order to clarify this point we examined the consequence of adding the stoichiometric amount of 2-chloropyridine to a solution containing equimolar amounts of **1** and *cis*-$[Pt(dmso)_2(py)Cl][BF_4]$ and followed the subsequent changes by ^1H NMR spectroscopy (Fig. 2). In the early stages of the reaction, the spectra clearly show the build up of the concentrations of *cis*-$[Pt(dmso)_2(2Cl\text{-}py)Cl]^+$ and *trans*-$[Pt(dmso)(py)Cl_2]$. Since it has been shown that the direct exchange reaction (8), which could also account for the above

$$cis\text{-}[Pt(dmso)_2(py)Cl]^+ + 2Cl\text{-}py \longrightarrow cis\text{-}[Pt(dmso)_2(2Cl\text{-}py)Cl]^+ + py \quad (8)$$

observation, occurs much more slowly than the reaction forming *cis*-$[Pt(dmso)_2(2Cl\text{-}py)Cl]^+$ in the competition experiment, it is concluded that the exchange of ligand in the cationic species must involve the displacement of chloride from *cis*-$[Pt(dmso)_2Cl_2]$ [equation (9)], together with the consumption of the released chloride in reaction (10).

$$cis\text{-}[Pt(dmso)_2Cl_2] + 2Cl\text{-}py \longrightarrow cis\text{-}[Pt(dmso)_2(2Cl\text{-}py)Cl]^+ + Cl^- \quad (9)$$

$$cis\text{-}[Pt(dmso)_2(py)Cl]^+ + Cl^- \longrightarrow trans\text{-}[Pt(dmso)(py)Cl_2] + dmso \quad (10)$$

It should be noted that the exchange of labelled dmso between **1** and **2** is fast when L = py [equation (11)], but this cannot interfere with the process discussed above.

$$cis\text{-}[Pt(*dmso)_2Cl_2] + cis\text{-}[Pt(dmso)_2(py)Cl]^+ \longrightarrow cis\text{-}[Pt(dmso)_2Cl_2] + cis\text{-}[Pt(*dmso)_2(py)Cl]^+ \quad (11)$$

Since the consumption of chloride by reaction (10) is fast it has been assumed that reaction (9) is the rate-determining step and that, since the chloride ion released has been scavenged, it is irreversible. Owing to the number of resonances within a relatively narrow range of frequencies, it was only possible to estimate that the second-order rate constant for reaction (9) was approximately 0.02 $dm^3\ mol^{-1}\ s^{-1}$. If this rate constant is designated as $k_{1,3}$ then combining it with the value of k_{obs} determined for the formation of *trans*-$[Pt(dmso)(2Cl\text{-}py)Cl_2]$ (see Results section) using the expression, $k_{obs} = k_{1,3}/(1 + k_{3,1}/k_{3,4})$, which assumes steady-state conditions for intermediate **3**, we can estimate $k_{3,1}/k_{3,4} = 13$. This accounts for the absence of **4** when Cl^- is added to **3**.

Finally, we have shown that **3**, on reacting with Cl^- can either give **2** but not **1** (when L = 2,6Me_2-py or 2Me-quin) or **1** but not **2** (when L = 2Cl-py, py or 2,4Me_2-py). This cannot be accounted for in terms of basicity (the least basic ligands being lost in preference to dmso) since the basicities of 2,4Me_2-py and 2,6Me_2-py are similar. Once again the steric requirements of the ligand L seem to play a major role in determining the course of reaction, in this case controlling which ligand will leave the five-co-ordinate intermediate **A**. It is possible that it does so by changing hybridization in the trigonal plane; for example when L is a 2,6-substituted pyridine, angles will be very close to 120°. It is significant that most stable five-co-ordinate platinum(II) complexes isolated until now have a very bulky ligand in the trigonal plane.[13] It may also be that the position of the amine plane relative to the trigonal one is important in altering, for example, the relative amount of π-back bonding of ligands L and dmso.

Acknowledgements

We thank the Italian Ministry of University and Research and the Italian Research Council (CNR-Rome) for financial support.

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Received 18*th May* 1992; *Paper* 2/02557D