in **2**. However we must emphasize that there is no evidence even at 140 °C that any axial–equatoral exchange occurs in **2**. Moreover since couplings of the methyl isocyanide protons to two different platinum atoms are observed in **2** even at 140 °C, exchange of isocyanide ligands between the two metals is also ruled out in this complex. In most cases where barriers to rearrangement processes at a metal center have been measured it has been noted that the barrier for a third-row transition metal is larger than for a second-row metal.[19] However in the present case where **1** and **2** are compared, the difference in barrier height between these two is more striking than usual.

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Registry No. $[Pd_2(CN\text{-}t\text{-}C_4H_9)_6](PF_6)_2$, 59561-00-1; $[Pd_2(CN\text{-}C_6H_5)_6](PF_6)_2$, 60039-64-7; $[Pd_2(CNCH_3)_5\{P(C_6H_5)_2\}](PF_6)_2$, 60039-66-9; $[Pd_2(CNCH_3)_4\{P(C_6H_5)_3\}_2](PF_6)_2$, 60125-83-9; $[Pd(CNCH_3)_2\{P(C_6H_5)_3\}_2](PF_6)_2$, 61258-88-6; $[PdPt(CNCH_3)_5\{P(C_6H_5)_3\}](PF_6)_2$, 61288-82-2; $[PdPt(CNCH_3)_4\{P(C_6H_5)_3\}_2](PF_6)_2$, 60125-87-3; $[Pt_2(CNCH_3)_5\{P(C_6H_5)_3\}](BF_4)_2$, 60039-68-1; $Pd_2(CNCH_3)_4I_2$, 61258-82-0; $Pd_2(CNC_6H_5)_4I_2$, 61258-85-3; $Pd_2(CNCH_3)_4(SCN)_2$, 61258-83-1; $Pd_2(CNCH_3)_4Cl_2$, 61258-81-9; $Pd_2(CN\text{-}t\text{-}C_4H_9)_4I_2$, 61258-84-2; $[Pd_2(CNCH_3)_6](PF_6)_2$, 56116-48-4; $[PdPt(CNCH_3)_6](PF_6)_2$, 60767-38-6; $[Pt_2(CNCH_3)_6](BF_4)_2$, 60767-37-5; $[Pd(CNCH_3)_4](PF_6)_2$, 38317-62-3; $Pd(CNC_6H_5)_2$, 41021-81-2; $Pd(CNCH_5)_2I_2$, 61302-31-6.

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Kinetics of the Chelate Effect. Ring Closing and Ring Opening in *cis*-Dichloro(dimethyl sulfoxido)(2-aminoethylammonium)platinum(II) Chloride

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The kinetics of the reaction *cis*-$[Pt(dmso)(enH)Cl_2]^+ \rightleftarrows [Pt(dmso)(en)Cl]^+ + H^+ + Cl^-$ (dmso = S-bonded dimethyl sulfoxide, enH = monodentate 2-aminoethylammonium, and en = 1,2-diaminoethane) have been studied in both directions in aqueous solution at 30.0 °C, μ = 2.0 ($LiClO_4$). The specific rate constant for the approach to equilibrium, k_{obsd}, is given by the expression $k_{obsd} = (k^f_{Cl}K_a'[Cl^-] + k^f_{H_2O}K_a''K_{Cl})[H^+]^{-1}([Cl^-] + K_{Cl})^{-1} + k^r_{Cl}[Cl^-]$. This is interpreted in terms of a rapid equilibrium between the chloro and aquo open-chain species (chloride trans to dmso), equilibrium constant $K_{Cl} = 6.2 \times 10^{-4}$ M, and rapid acid–base equilibria between these complexes and their reactive bases (equilibrium constants K_a' and K_a'', respectively) which undergo first-order ring closure with rate constants k^f_{Cl} and $k^f_{H_2O}$, respectively; $k^f_{Cl}K_a' = 1.50 \times 10^{-4}$ M^{-1} s^{-1} and $k^f_{H_2O}K_a'' = 5.91 \times 10^{-3}$ M^{-1} s^{-1}. The second-order rate constant for ring opening, $k^r_{Cl} = 1.0 \times 10^{-4}$ M^{-1} s^{-1}. This behavior is compared to that of an analogous system involving two monodentate cyclohexylamine ligands and the consequences of chelation are examined.

Introduction

The study of the chelate effect has a long history in the field of complex formation equilibrium constants[1] and from time to time attempts have been made to investigate the chelate effect from a kinetic point of view by measuring the rates of ring opening and ring closing. Much of the published work relates to octahedral complexes where the substitution is generally dissociatively activated and an examination of the chelate effect would have to include an analysis of the rate of ring closure in terms of effective aggregate formation constants in an I_d mechanism or competition for five-coordinate intermediates in a D mechanism.[2-4] For associatively activated systems the kinetics of ring closing and ring opening can, in principle, be analyzed much more easily in terms of rate constants and the active participation of the solvent in either solvolytic or anation processes can be bypassed. Many studies have now been made of the kinetics of ring closing in square-planar systems, some superficial and some in con-

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siderable depth. The classic study of Carter and Beattie[5] described the kinetics of ring closure of *trans*-$[Pt(enH)_2Cl_2]^{2+}$ and compared it with parallel reactions involving monodentate amines but they were unable to measure the reverse (ring opening) reaction because of the high stability of the complex. The displacement of chelated amines from palladium has been analyzed in terms of ring opening and ring closing[6-8] but many of the reversible steps are too fast to follow and can only be treated as equilibria.

In our studies of the substitution reactions of platinum(II)–dimethyl sulfoxide complexes we were able to use the strong trans-labilizing effect of S-bonded dimethyl sulfoxide to examine the forward and reverse processes in two series of reactions

$$cis\text{-}[Pt(dmso)(am)Cl_2] + am' \rightleftarrows cis\text{-}[Pt(dmso)(am)(am')Cl]^+ + Cl^-\ ^9 \quad (1)$$

$$[Pt(dmso)Cl_3]^- + am \rightleftarrows trans\text{-}[Pt(dmso)(am)Cl_2] + Cl^-\ ^{10} \quad (2)$$

In both cases it was possible to evaluate the equilibrium quotient in terms of the ratio of the appropriate rate constants for the forward and the reverse processes. The first of these reactions presents an ideal opportunity to compare the behavior of a pair of cis monodentate amines with that of a chelated diamine. To this end we have initiated a study of the kinetics of ring opening and closing in order to investigate such aspects as the effect of ring size and flexibility upon the parameters of the chelation phenomenon. This paper reports the reaction where the chelating diamine is 1,2-diaminoethane and compares it with that involving monodentate cyclohexylamine analogues.

Experimental Section

Preparations. Chloro(dimethyl sulfoxido)(1,2-diaminoethane)platinum(II) was prepared by the method of Romeo et al.[11] in which *cis*-$[Pt(dmso)_2Cl_2]$ was reacted with ethylenediamine in methanol.

Anal. Calcd for $C_4H_{14}N_2OCl_2PtS$: C, 11.9; H, 3.46; N, 6.93; Cl, 17.5; S, 7.9. Found: C, 11.9; H, 3.31; N, 7.17; Cl, 17.3; S, 7.7.

***cis*-Dichloro(dimethyl sulfoxido)(2-aminoethylammonium)platinum(II) Chloride.** [Pt(dmso)(en)Cl]Cl (0.16 g) was dissolved in methanol (8 cm^3) and a fivefold excess of concentrated hydrochloric acid (0.15 cm^3) was added to the solution which was kept at room temperature. After a while, white crystals separated and were filtered off, washed with a solution of methanolic hydrochloric acid and then ether, and air-dried.

Anal. Calcd for $C_4H_{15}N_2OCl_3PtS$: C, 10.9; H, 3.41; N, 6.37; Cl, 24.0. Found: C, 10.9; H, 3.23; N, 6.46, Cl, 24.2.

The infrared spectrum is characterized by a very strong absorption at 1195 cm^{-1} assigned to ν(S–O) and characteristic of S-bonded dimethyl sulfoxide.[12] A strong peak at 444 cm^{-1} is assigned to ν(Pt–S) and a pair of strong peaks at 327 and 343 cm^{-1} is assigned to ν(Pt–Cl), the splitting being characteristic of a pair of cis chlorines. The chelated (monochloro) complex has only one peak (344 cm^{-1}) in this region.[11]

Kinetics. The reactions were started by adding a weighed amount of the complex to 10.0 cm^3 of a solution of all the other reagents that had been brought to the reaction temperature in the spectrophotometer cell. Slower reactions were followed with an Optica CF4R double-beam recording spectrophotometer and the spectra were scanned repeatedly over the range 220–420 nm. Many of the slower and all of the faster reactions were followed with a Beckman DU single-beam monochromator equipped with a Saitron 301 thermostated cell compartment, a Saitron 301 photometer with scale expansion facilities, and a Servoscribe RE511.20 potentiometric recorder which plotted the absorbance at a convenient wavelength as a function of time. The fastest reactions were followed with a standard Durrum–Gibson stopped-flow spectrophotometer.

The first-order rate constants were obtained from the slope of the plot of ln $(A_t - A_\infty)$ against time, where A_t and A_∞ are the absorbances of the reaction mixture at time t and after 8–10 half-lives, respectively. At the lowest chloride ion concentrations there was a significant increase in $[Cl^-]$ as the ring-closing reaction proceeded (20% in the worse case) and the rate constant was determined from the initial slope of the curved semilogarithmic plot. In all other cases the reaction was followed under pseudo-first-order conditions.

Table I. Slopes and Intercepts of the Linear Plots of k_{obsd} vs. $[H^+]^{-1}$ as a Function of $[Cl^-]$ for the Reaction *cis*-$[Pt(dmso)(enH)Cl_2]^+ \rightarrow [Pt(dmso)(en)Cl]^+ + H^+ + Cl^-$ [a-c]

$10^2[Cl^-]$ /M[d]	Range of $[H^+]$ variation/M^{-1}	$10^3 \times$ slope/s^{-1} M^{-1}	$10^3 \times$ intercept/s^{-1}
0.125	0.066-1.0	2.09 ± 0.04	0.02 ± 0.24
0.175	0.066-0.80	1.66 ± 0.01	0.14 ± 0.11
0.275	0.066-0.80	1.21 ± 0.02	−0.16 ± 0.12
0.425	0.066-0.50	0.87 ± 0.05	−0.17 ± 0.38
0.625	0.066-0.80	0.669 ± 0.005	0.05 ± 0.02
0.825	0.066-0.80	0.547 ± 0.003	−0.02 ± 0.02
1.03	0.066-0.80	0.469 ± 0.009	−0.01 ± 0.08
1.53	0.066-0.80	0.371 ± 0.005	0.00 ± 0.04
2.03	0.080-0.80	0.334 ± 0.006	0.00 ± 0.04
10.0	0.050-0.80	0.158 ± 0.002	0.07 ± 0.02
30.0	0.040-0.80	0.129 ± 0.003[e]	0.07 ± 0.02
50.0	0.052-0.52	0.158 ± 0.006	0.13 ± 0.06
100.0	0.040-0.80	0.173 ± 0.001	0.06 ± 0.02

[a] At 30.0 °C. [b] μ = 2.0 ($LiClO_4$) except where otherwise stated. [c] [Complex] = 2.5 × 10^{-4} M. [d] Chloride concentration at the start of the reaction. [e] μ = 2.3.

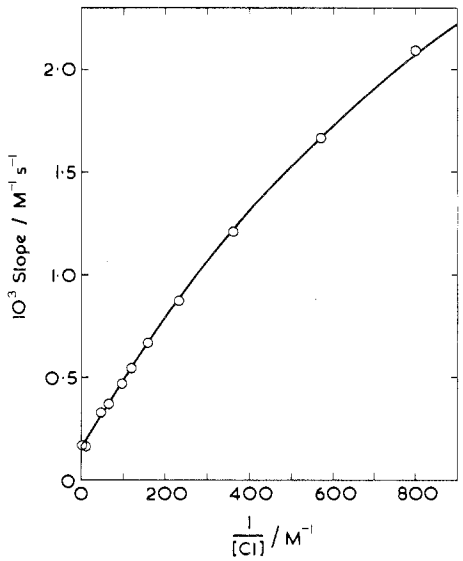


Figure 1. Slope of the plot of k_{obsd} vs. $[H^+]^{-1}$, S, for the ring-closing reaction of $[Pt(dmso)(enH)Cl_2]^+$ in water at 30.0 °C, μ = 2.0, plotted as a function of $[Cl^-]^{-1}$. The curve is calculated from the derived constants.

Results

(a) Kinetics of Ring Closing. The spectrum of an aqueous solution of trans-$[Pt(dmso)(enH)Cl_2]Cl$ changes, at a rate that is sensitive to the concentrations of the chloride and acid present, into one that is identical with that of an authentic sample of the chelated $[Pt(dmso)(en)Cl]^+$ cation. Although there are no isosbestic points in the region 420–220 nm, there is no evidence for the appearance of any significant quantity of any light-absorbing intermediate. Reactions were carried out at 30.0 °C and at constant ionic strength ($LiClO_4$, μ = 2.0), and the effects of the variation of $[H^+]$, added as aqueous $HClO_4$, and $[Cl^-]$, added as LiCl, were studied. Plots of k_{obsd} against $[H^+]^{-1}$ give very good straight lines whose intercepts are zero within experimental error, except at the very highest chloride concentrations where there is a finite positive intercept. The values of the slopes and intercepts obtained from a linear least-squares analysis of the data are collected in Table I. The slopes decrease as the chloride ion concentration is increased, reaching a limiting value when $[Cl^-] > 0.10$ M, but a plot of slope vs. $[Cl^-]^{-1}$ is not linear (Figure 1). The intercept, when $[Cl^-]^{-1} = 0$, corresponds to the limiting slope at the highest chloride concentration, $S_\infty = 1.50 \times 10^{-4}$ M^{-1} s^{-1}, and a plot of $(S - S_\infty)^{-1}$ against $[Cl^-]$ gives a very good straight line

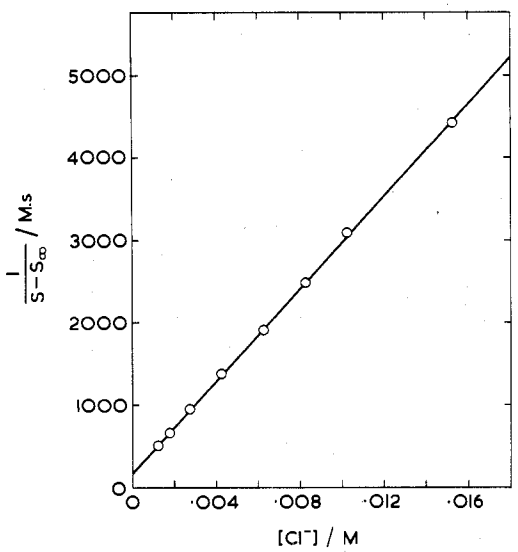


Figure 2. Plot of $(S - S_\infty)^{-1}$ as a function of $[Cl^-]$.

(Figure 2) with a slope of (2.80 ± 0.02) × 10^5 s and an intercept of 174 ± 13 M s.

(b) Kinetics of Ring Opening. Unless the reaction is studied in the presence of high concentrations of acid and chloride, only the chelate can be detected at equilibrium. Indeed, the back-reaction does not make any contribution to the approach to equilibrium starting from the open-chain complex until the chloride concentration is greater than 0.1 M. Even then, the contribution to the overall process is small and the experimental error is proportionally large. The kinetics of the reactions in which [Pt(dmso)(en)Cl]Cl is the starting material were analyzed in one of two ways. (i) By using values of A_∞ calculated on the assumption that all of the material would be converted to the ring-opened species, ln $(A_\infty^{calcd} - A_t)$ was plotted against t and the initial slope of the curve taken to be k^r, the pseudo-first-order rate constant for ring opening. (ii) At higher acid concentrations, where the extent of ring opening at equilibrium was quite significant, the data were analyzed in terms of a first-order approach to equilibrium, using the experimental value for A_∞. The rate constant thus obtained, $k_{obsd} = k^f + k^r$, and the value of k^f calculated from the established rate law for ring closing at the appropriate chloride and acid concentrations was subtracted leaving k^r. The rate constants are collected in Table II where it will be seen that k^r is essentially independent of $[H^+]$ but directly proportional to $[Cl^-]$.

(c) The Kinetics of the Reaction *cis*-[Pt(dmso)(chx)Cl_2] + chx ⇄ *cis*-[Pt(dmso)(chx)$_2$Cl]$^+$ + Cl^- (chx = Cyclohexylamine). The reaction was studied in much the same way as the analogous process in methanol.[9] The entry of the amine was studied in water containing 5% methanol in order to ensure complete solution of the amine. The pH was not determined and the solution was unbuffered and no extra electrolyte was added to increase the ionic strength. The reactions were too fast for the normal mixing and scanning techniques and had to be followed by stopped-flow spectrophotometry. The reverse reaction was studied in the presence of sufficient acid (1.0 × 10^{-3} M) to ensure that it went to completion. The rate constants are collected in Table III. The entry of amine follows the usual two-term rate law for substitution in Pt(II) complexes, $k_{obsd} = k^f_1 + k^f_{Cl}[am]$, where $k^f_1 = 0.15 \pm 0.01$ s^{-1} and $k^f_{Cl} = 3.79 \pm 0.04$ M^{-1} s^{-1} at 30.0 °C. The reverse reaction could not be studied under conditions of constant ionic strength because the perchlorate of the complex cation precipitated from solutions containing sufficient $LiClO_4$ to maintain an ionic strength of 2.0. The ionic strength therefore varies with the concentration of lithium chloride. This reaction between two ions of opposite charge has a negative primary salt effect on the k^r_{Cl} contribution to the rate of reaction and the slope of the plot of k_{obsd} vs. $[Cl^-]$ decreases as the concentration of chloride increases. Assuming that the two-term rate law would apply under conditions of constant ionic strength, k^r_{Cl} is estimated to be 1.5 × 10^{-4} M^{-1} s^{-1} at 30.0 °C (μ = 0.7) and k^r_1 is probably less than 1.3 × 10^{-5} s^{-1} under the same conditions. The contribution made to the reaction by the solvolytic pathway is negligible at the higher chloride concentrations.

Table II. Rate Constants for the Opening of the Chelate Ring in [Pt(dmso)(en)Cl]$^+$ in Aqueous Solution[a-c]

$[H^+]$/M	$[Cl^-]$/M	$10^4 k_{obsd}$/ s^{-1} [d]	$10^4 k^f$/ s^{-1} [e]	$10^4 k^r$/ s^{-1}	$10^4 k^r$/ $[Cl^-]^{-1}$/ M s^{-1}
0.050	1.6			1.64[f]	1.0
0.065	1.2			1.15[f]	1.0
0.10	1.2			1.32[f]	1.1
0.10	1.4			1.53[f]	1.1
0.14	1.8			1.85[f]	1.0
0.20	0.8			0.85[f]	1.1
0.20	1.0			0.94[f]	0.9
0.20	1.3			1.16[f]	0.9
0.20	1.8			1.94[f]	1.1
0.80	1.5			1.65[f]	1.1
1.70	0.30	1.23	0.95	0.28	0.9
1.80	0.20	1.08	0.93	0.15	0.8
2.00	0.50[g]	1.33	0.78	0.55	1.1

[a] Temperature 30.0 °C. [b] μ = 2.0 ($LiClO_4$) except where stated. [c] [Complex] = 1.0 × 10^{-3} M. [d] Specific rate constant for approach to equilibrium. [e] $k^f = (k^f_{Cl}K_a'[Cl^-] + k^f_{H_2O}K_a''K_{Cl})[H^+]^{-1}(K_{Cl} + [Cl^-])^{-1}$. [f] Initial slopes of curved semilogarithmic plot. [g] μ = 2.5.

Table III. Rate Constants for the Reaction

cis-[Pt(chx)(dmso)Cl_2] + chx $\underset{k^r}{\overset{k^f}{\rightleftarrows}}$ *cis*-[Pt(chx)$_2$(dmso)Cl]$^+$ + Cl^- [a-c]

$[Cl^-]$/mM	[chx]/mM	k^f/s^{-1} [d]	$10^4 k^r$/s^{-1} [e]
	5.0	0.160	
	9.4	0.183	
	18.7	0.212	
	37.5	0.276	
	75	0.47	
	150	0.70	
	200	0.94	
	400	1.68	
	600	2.41	
90			0.25
540			1.01
720			1.18

[a] chx = cyclohexylamine. [b] Temperature 30.0 °C. [c] [Complex] = 5.0 × 10^{-4} M. [d] In 5% methanol–95% water. [e] In 1.0 × 10^{-3} M aqueous perchloric acid.

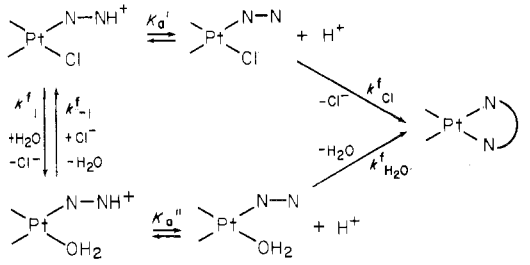
Discussion

The chelate ring-closing reaction, which could be studied conveniently and precisely, obeys a rate law that contains a well-defined inverse first-order dependence on $[H^+]$ over the wide range of concentration studied and a more complex dependence on $[Cl^-]$. The $[H^+]^{-1}$ dependence is similar to that observed by Carter and Beattie[5] in the ring-closing reactions of *trans*-[Pt(enH)$_2$Cl$_2$]$^{2+}$ in the range of pH where the concentration of the reactive unprotonated species is very small when compared to the total amount of complex present. They observed no intercept in the plot of k_{obsd} vs. $[H^+]^{-1}$ for the closure of the first ring but a significant intercept and a smaller slope for a similar plot of the data associated with the closure of the second ring suggest that the lack of intercept simply means that the solvolytic rate constant is too small to be

observed in the first stage. They did not observe retardation by added chloride. It is not possible to account for chloride retardation by any simple process that interferes with the direct displacement of coordinated chloride by amine and we do not feel that ion association between the $-NH_3^+$ and free chloride would be relevant, especially in aqueous solution. Chloride retardation can be very important if there is a significant solvolytic pathway for reaction where chloride and amine can compete for the solvento intermediate or where the solvento complex can offer a more favorable pathway for ring closure. The absence of an intercept in the plot of k_{obsd} vs. concentration of nucleophile would be another consequence of this type of interference.

The two mechanisms are already well established in reactions involving the entry of monodentate ligands into four-coordinate planar complexes and can be represented as follows in the context of ring closure. Mechanism I is es-

Mechanism I



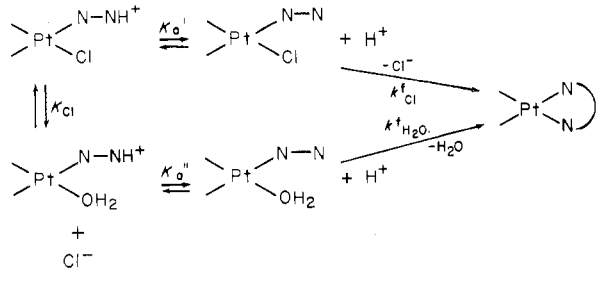
sentially a mass law retardation of substitution in the solvento complex by the leaving group chloride, and its monodentate equivalent is well-known in the substitution reactions of the sterically hindered $[Pt(PEt_3)_2(R)X]$ complexes.[13] It is found when the nucleophile is relatively weak or is buffered at low concentrations so that the product of the rate constant for chloride anation of the solvento complex and the concentration of chloride is comparable in magnitude to the analogous product for the entering nucleophile. Assuming that the reverse (ring opening) reaction can be neglected this mechanism leads to the rate law

$$k_{obsd} = k^f_1 k^f_{H_2O} K_a''(k^f_{-1}[H^+][Cl^-] + k^f_{H_2O}K_a'')^{-1} + k^f_{Cl}K_a'(K_a' + [H^+])^{-1}$$

The second term is identical with that found by Beattie[5] and simplifies to $k_2K_a'[H^+]^{-1}$ when $[H^+] >> K_a'$. The first term, which simplifies to the usual k^f_1 when $k^f_{H_2O}K_a'' >> k^f_{-1}\cdot[H^+][Cl^-]$, will only produce the observed inverse hydrogen ion concentration dependence if $k^f_{-1}[H^+][Cl^-] >> k^f_{H_2O}K_a''$. Under these circumstances the overall rate law will simplify to $k_{obsd} = [H^+]^{-1}(k^f_1 k^f_{H_2O}K_a''(k^f_{-1})^{-1}[Cl^-]^{-1} + k^f_2K_a')$ so that the relationship between the slopes of the plots of k_{obsd} vs $[H^+]^{-1}$ at constant $[Cl^-]$ and the concentration of chloride should be of the form slope $= a[Cl^-]^{-1} + b$. However, it can be seen quite clearly in Figure 1 that a plot of slope vs. $[Cl^-]^{-1}$ is strongly curved and so this mechanism can be eliminated.

Mechanism II has been found in reactions where solvolysis

Mechanism II



is fast and reversible, and subsequent substitution, which takes place in both the chloro and the solvento complex, is relatively slow.[14,15] This differs from Mechanism I in that the substrate is partitioned between the chloro and the much more reactive aquo species and, at low enough $[Cl^-]$, the latter species can be present in large amounts. Under favorable conditions this should be observable as a dependence of the initial spectrum on the concentration of chloride. Such a dependence has been observed in a parallel study of this reaction in methanol where the rates are slower and the spectral scans can be carried out at the low chloride ion concentrations required.[16] This mechanism leads to the rate law

$$k_{obsd} = ([Cl^-] + K_{Cl})^{-1}\{k^f_{Cl}K_a'[Cl^-](K_a' + [H^+])^{-1} + k^f_{H_2O}K_a''K_{Cl}(K_a'' + [H^+])^{-1}\}$$

which, if K_a' and K_a'' are much smaller than $[H^+]$, reduces to

$$k_{obsd} = (k^f_{Cl}K_a'[Cl^-] + k^f_{H_2O}K_a''K_{Cl})([Cl^-] + K_{Cl})^{-1}[H^+]^{-1}$$

This predicts an exact inverse first-order dependence on the hydrogen ion concentration over the whole range of conditions where the mechanism holds and a dependence of the slope of the plot of k_{obsd} vs. $[H^+]^{-1} \equiv S$, at constant $[Cl^-]$, on chloride concentration that should take the form $S = (a[Cl^-] + b)([Cl^-] + c)^{-1}$. This is, indeed, the observed form of the relationship. The data were analyzed as follows. The intercept in Figure 1 is the value of S when $[Cl^-]^{-1} = 0$ is taken as S_∞, the limiting value of the slope as $[Cl^-]$ becomes very large, and it is easy to see that $S_\infty = a$. Therefore $S - S_\infty = (a[Cl^-] + b)([Cl^-] + c)^{-1} - a = (b - ac)([Cl^-] + c)^{-1}$, so that a plot of $(S - S_\infty)^{-1}$ against $[Cl^-]$ should be a straight line with slope $(b - ac)^{-1}$ and intercept $c(b - ac)^{-1}$. This is indeed so (Figure 2) when S_∞ is taken as 1.50×10^{-4} M^{-1} s^{-1}, the slope is $(2.80 \pm 0.02) \times 10^5$ s, and the intercept is 174 ± 13 M s. Therefore, $c \equiv K_{Cl}$ = intercept/slope $= 6.2 \times 10^{-4}$ M, $a \equiv k^f_{Cl}K_a' = 1.50 \times 10^{-4}$ M^{-1} s^{-1}, and $b \equiv k^f_sK_a'' = 5.91 \times 10^{-3}$ M^{-1} s^{-1}. These numbers were further checked by reinserting them in the original expression and calculating values for the pseudo-first-order rate constant at the appropriate acid and chloride concentrations, k_{calcd}. Agreement was generally very good. The experimental observations are therefore in full agreement with Mechanism II and it remains to check whether the actual first-order rate constant for the solvolysis of $[Pt(dmso)(enH)Cl_2]^+$ is indeed large enough for the solvolysis to behave as a rapidly attained equilibrium. While the reaction cannot be examined directly, it is not unreasonable to assume that k^f_1 for this reaction will be no smaller than the value found for the analogous reaction involving the monodentate amine cyclohexylamine (chx)

$$cis\text{-}[Pt(dmso)(chx)Cl_2] + chx \rightarrow cis\text{-}[Pt(dmso)(chx)_2Cl]^+ + Cl^-$$

Since the basicity of monoprotonated ethylenediamine is less than that of cyclohexylamine, it would be expected to exert a stronger cis-labilizing effect,[9,10] and the lability of the complex might be further enhanced by an ion-pair interaction between the free $-NH_3^+$ end of the ligand and the departing Cl^-.[17] Thus, the observed value of $k^f_1 = 0.15$ s^{-1} for the cyclohexylamine system is probably significantly smaller than the value for the ethylenediamine system and one can be certain therefore that solvolytic equilibrium is rapidly established.

Unlike Carter and Beattie,[5] we were unable to separate the rate constants from the equilibrium constants in $k^f_{Cl}K_a'$ and $k^f_{H_2O}K_a''$ because the reaction was far too fast to follow in the pH region where $[H^+] << K_a'$ and K_a''. In basic solution, ring closure is complete within the 2-ms mixing time of the stopped-flow spectrophotometer. We have therefore assumed

that their values for K_{a1} (1.2×10^{-8} M) and K_{a2} (1.1×10^{-8} M), evaluated directly from the kinetics of ring closure of *trans*-$[Pt(enH)_2Cl_2]^{2+}$ and *trans*-$[Pt(en)(enH)Cl]^{2+}$, are not likely to differ much from K_a' and K_a''. It is unlikely that the difference in the natures of the ligands attached to the platinum will have any effect on the inductive forces transmitted through the ethylenediamine but the change in the overall charge may have some influence. However, Hay and Nolan[18] in a study of the reactions of *cis*-$[Co(en)_2(enH)X]^{3+}$ (X = Cl, Br) at 25 °C, μ = 0.1, have shown that the acidity of coordinated enH^+ is not much less than that of free enH_2^{2+}. Using the approximation that $K_a' = K_a'' = 10^{-8}$ M (the gross nature of this approximation is such that the difference in ionic strength and temperature can be ignored) we estimate $k^f_{Cl} = 1.5 \times 10^4$ s^{-1} and $k^f_{H_2O} = 5.9 \times 10^5$ s^{-1}. The 40-fold greater substitutional lability of the aquo complex over the chloro complex compares well with the 28-fold difference found in an analogous way for $[Pt(C_2H_4)Cl_3]^-$ and *trans*-$[Pt(C_2H_4)(H_2O)Cl_2]$.[15]

It is of interest to compare the rate constant for ring closing with the value estimated for the entry of an independent monodentate amine under otherwise identical conditions. Elsewhere[9] we have shown that the second-order rate constant for the reaction

cis-$[Pt(dmso)(am)Cl_2]$ + am′ → *cis*-$[Pt(dmso)(am)(am')Cl]^+ + Cl^-$

is insensitive to the basicity of the entering amine, am′, but varies with the pK_a of the protonated amine cis to the leaving chloride according to $\log k_2 = -0.4pK_a(amH^+) + c$. This work was done in methanol and it was our original intention to study the ring closing and opening reactions in the same solvent. However, the rates of ring closing are extremely sensitive to the quantity of water present in nearly dry methanol[16] (a phenomenon not observed in the similar reactions with monodentate amines). This is probably due to the great sensitivity of K_a' and K_a'' to the composition of the solvent mixture in this region. It is known that the pK_a of acetic acid changes from 7.68 in 95% methanol–water to 9.63 in dry methanol.[19] We have reexamined the above reaction in water with am = am′ = cyclohexylamine. The pK_a of cyclohexylamineH^+ (10.66)[20] is very close to that of enH^+ (10.71)[20] and so this amine serves as a good model to estimate the cis effect of ethylenediamine. The change of solvent from methanol to water does not appear to have a dramatic effect upon the value of k^f_{Cl} which increases from 1.73 M^{-1} s^{-1} in methanol (30.0 °C) to 3.79 M^{-1} s^{-1} in water (30.0 °C). On the other hand, k^f_1 undergoes a dramatic 50-fold increase from 3.0×10^{-3} to 0.15 s^{-1}. We therefore estimate that the rate constant for the entry of a second ethylenediamine into *trans*-$[Pt(dmso)(en)Cl_2]$ should also be 3.8 M^{-1} s^{-1}. In order to achieve the observed first-order rate constant of 1.5×10^4 s^{-1} it would be necessary for the uncoordinated end of the ethylenediamine to exert an effective molarity of 4×10^3 M, which is even higher than the 8×10^2 M estimated in a similar way for the ring-closure reactions of *trans*-$[Pt(enH)_2Cl_2]^{2+}$. Statistical analysis of the distribution of the free end of a chelate would suggest that the effective molarity of the free end of the ethylenediamine is of the order of 30 M. This phenomenon is well-known from ring-closing reactions of organic substrates and has been reviewed recently.[21] Effective molarities many orders of magnitude greater than this are common and it has been suggested that the "close-packing" analysis gives a gross underestimation and that more formal arguments based on changes of degrees of freedom could predict entropic rate accelerations equivalent to effective molarities of up to 10^8 M in solution.[22] In the absence of accurate temperature-dependence data no purpose will be served in discussing the relative importance of entropic rate acceleration and potential energy differences. A more simple-minded and pictorial view would be that, in the average conformation of $[Pt(dmso)(en)Cl_2]$ in its ground state, the arrangement of the, as yet, uncoordinated amine with respect to the rest of the complex and the overall solvation of the species resembles the reacting $[Pt(dmso)(am)Cl_2]$ + am system at a point well along the first (bond making) part of the reaction coordinate.

Because of the greater stability of the chelated complex, the extent of the ring-opening reaction can never be large under the experimental conditions that we have used and so the rate constants are imprecise. Nevertheless, it is clear that the rate constant for ring opening is independent of $[H^+]$ and linearly proportional to $[Cl^-]$. The second-order rate constant $k^r_{Cl} = 1.0 \times 10^{-4}$ M^{-1} s^{-1} at 30.0 °C can be compared with the estimated value for the rate constant for the displacement of a monodentate (but still coordinated) ethylenediamine by chloride under the cis effect of a similar ethylenediamine species. We have already shown that the rate constant for the displacement of the amine trans to dmso by chloride obeys the relationship $\log k^r_{Cl} = -0.91pK_a(amH) + c'$ in methanol at 30.0 °C[9] and, assuming that the change in solvent does not change the magnitude of the exponent, we can use the rate constant for the reaction of the bis(cyclohexylamine) complex, 1.5×10^{-4} M^{-1} s^{-1}, the pK_a of $chxH^+$ (10.66), and the pK_a of monocoordinated enH^+ (7.9),[5] which is not much different from the pK_a of enH_2^{2+} itself (7.56),[20] to calculate that k^r_{Cl} (no ring) = $10^{[\log 1.5\times10^{-4}-0.91(7.9-10.66)]} = 4.9 \times 10^{-2}$ M^{-1} s^{-1} which is about 500 times greater than the observed value. It has been estimated that the steric restrictions associated with the opening of a tight chelate ring might account for a 40-fold decrease in the rate of a dissociatively activated reaction[23] and these rough calculations indicate that the bond-breaking part of this associatively activated process is even more affected.

The equilibrium constant for the cyclohexylamine system is $k^f_{Cl}/k^r_{Cl} = 3.79/1.5 \times 10^{-4} = 2.5 \times 10^4$. This is some 17 times greater than that observed in methanol (1.49×10^3) probably reflecting the greater ability of water to solvate the ionic species on the right-hand side of the equation. The equilibrium constant for the ring closure of ethylenediamine, 1.5×10^4 $s^{-1}/1.0 \times 10^{-4}$ M^{-1} $s^{-1} = 1.5 \times 10^8$ M, is very much larger than that estimated for a comparable chloro(amine) complex changing to a bis(amine) complex but the comparison must be made with care because the numbers are dimensionally different. It is clear, nevertheless, that the very large increase in stability, which is the chelate effect, arises from a much larger than expected rate constant for ring closing and a smaller than expected rate constant for ring opening.

Registry No. *cis*-$[Pt(dmso)(enH)Cl_2]Cl$, 61587-65-3; $[Pt(dmso)(en)Cl]^+$, 24598-61-6; *cis*-$[Pt(chx)(dmso)Cl_2]$, 50830-89-2; chx, 108-91-8.

Supplementary Material Available: Table of observed pseudo-first-order rate constants for the reaction $[Pt(dmso)(enH)Cl_2]^+ \rightarrow [Pt(dmso)(en)Cl]^+ + H^+ + Cl^-$ (4 pages). Ordering information is given on any current masthead page.

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Ternary Complexes in Solution. 25.[1] Influence of Alkyl Side Chains with Hydroxy or Thioether Groups on the Stability of Binary and Ternary Copper(II)–Dipeptide Complexes

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Equilibrium constants have been measured potentiometrically for protonation and Cu^{2+} coordination of glycyl-L-serine, glycyl-L-threonine, glycyl-*S*-methylcysteine, or glycyl-L-methionine [=glycyl(α-alkyl-*S*/*O*)glycines] and L-serylglycine, L-threonylglycine, *S*-methyl-L-cysteinylglycine, or L-methionylglycine [=(α-alkyl-*S*/*O*-glycyl)glycines]. For two of these dipeptides, glycyl-*S*-methyl-L-cysteine and *S*-methyl-L-cysteinylglycine, synthetic routes have been developed. Besides the binary complexes CuL^+ and Cu(L–H), the mixed-ligand complexes with 2,2′-bipyridyl, viz., Cu(bpy)L^+ and Cu(bpy)(L–H), were also studied. The results were evaluated by comparison with data obtained earlier for glycyl(*N*- or α-alkyl)glycinates and (*N*- or α-alkylglycyl)glycinates. For the glycyl(α-alkyl-*S*/*O*)glycinates, the stability of CuL^+ depends only on the basicity of the amino group, while for the complexes with (α-alkyl-*S*/*O*-glycyl)glycinates, there is a considerable increase in stability attributable to an interaction of the hydroxy or thioether groups with an apical coordination position of Cu^{2+}. With the (α-alkyl-*S*/*O*-glycyl)glycinates, the ionization of the amide proton is also somewhat facilitated; i.e., Cu(L–H) is somewhat more stable for these dipeptides than it is with glycylglycinate, whereas those of the glycyl(α-alkyl-*S*/*O*)glycinates are of the same stability. However, from detailed considerations it is concluded that the donor atom of the side chain in both types of dipeptides coordinates in Cu(L–H). The results obtained for the ternary systems resemble those of the binary ones; the main difference is that deprotonation of the amide group in the complexes is shifted toward higher pH values. The possible structures of these binary and ternary complexes are discussed.

The deprotonated peptide nitrogen is considered important in protein–copper binding,[4,5] and thus the coordination of peptides has received considerable attention.[6–12] Complex formation between Cu^{2+} and peptides in aqueous solution starts with the terminal amino group and not from the carboxylate end, forming chelates involving the terminal amino moiety and the oxygen of the neighboring amide group. These complexes are usually deprotonated at the amide group in the pH range 4–7, and chelates are formed by the coordination of Cu^{2+} to the deprotonated nitrogen of the amide group. This holds usually not only for binary but also for ternary, i.e., mixed-ligand, complexes.[13–15]

In order to learn how coordination may be altered by the kind of amino acids in the two terminal residues of such peptides or proteins, we have studied the simplest models—dipeptides; they contain all of the binding sites of interest. The first aim was to evaluate the influence of bulky alkyl groups on the stability and acidity of complexes formed in binary copper(II)–dipeptide and ternary 2,2′-bipyridyl–copper(II)–dipeptide systems.[15] Depending on the position of the alkyl group in the dipeptide, either the stability or the acidity of the complexes is altered: for the glycyl(*N*- or α-alkyl)glycinates, the stability of CuL^+ depends only on the basicity of the amino group, while for the complexes with (*N*- or α-alkylglycyl)glycinates, a considerable decrease in stability is observed. In contrast, with (*N*- or α-alkylglycyl)glycinates ionization of the amide proton is facilitated; i.e., Cu(L–H) is more stable for these dipeptides than with glycylglycinate, whereas the corresponding complexes of the glycyl-α-alkylglycinates are less stable.

In the present work, binary copper(II)–dipeptide and ternary 2,2′-bipyridyl–copper(II)–dipeptide systems with dipeptides containing alkyl side chains with hydroxy or thioether groups have been studied; the influence of these potentially weakly coordinating groups[16–18] on the stability of complexes was evaluated. The hydroxy- or thioether-substituted dipeptides studied, together with three dipeptides used for comparisons, are indicated in Figure 1.

Experimental Section

A. Synthesis. Materials. Ionac A-310 was a gift from the Ionac Chemical Co., Birmingham, N.J. Carbobenzoxy chloride, carbobenzoxyglycine, glycine ethyl ester hydrochloride, and *N*,*N*′-dicyclohexylcarbodiimide were purchased from Sigma Chemical Co., St. Louis, Mo. Ethyl chloroformate, triethylamine, and trifluoroacetic acid were from Eastman Organic Chemicals, Rochester, N.Y. *S*-Methyl-L-cysteine, *N*-methylmorpholine, acetonitrile, and iodomethane were obtained from Aldrich Chemical Co., Milwaukee, Wis. Pyridine was from Allied Chemical Corp., Morristown, N.J., and Dowex 1-X2 and Dowex 50W-X8 were from Bio-Rad Laboratories, Richmond, Calif.

Thin-layer chromatography was performed on silica gel plates (N-HR) from Brinkman Instrument Co., Los Angeles, Calif. The following solvent systems were used: butanol–acetic acid–water (=BAW, 4:1:1 v/v/v), chloroform–methanol (=CM, 19:1 v/v), and chloroform–methanol–acetic acid (=CMA, 18:1:1 v/v/v). Paper chromatography was performed on Whatman No. 1 paper using ascending butanol–acetic acid–water (=BAW, 2:1:1 v/v/v).