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Kinetics and Mechanism of the Fundamental Substitution Processes during Complex Formation of the (Diethylenetriamine)palladium(II) Center with Nucleic Bases, Nucleosides, and 5′-Nucleotides in Aqueous Solution

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The complexation of Pd(dien)Cl^+ and Pd(dien)OH_2^{2+} (dien ≡ diethylenetriamine) with nucleic free bases, nucleosides, and 5′-nucleotides was studied kinetically as a function of the nucleobase and added chloride ion concentration at neutral pH, a fixed ionic strength, and 25 °C to contribute to the understanding of the substitution behavior of related antitumor complexes. The kinetics of the reactions with the free bases and the nucleosides markedly deviate from normal square-planar substitution kinetics in that the usually fast anation step following the rate-determining solvolysis reaction is slowed down to such an extent by these nucleic acid entities that it becomes rate-determining under all conditions. The kinetic data enable a clear distinction among three different mechanisms to be made according to which the free bases and the nucleosides enter the coordination sphere depending on the complexation capability and the concentration of the entity concerned. The results for the 5′-nucleotides indicate that neither spontaneous solvolysis nor subsequent anation is the rate-determining step but that a secondary substitution process best accounts for the observations. The investigation includes a temperature- and pressure-dependence study of some of the measured rate constants. The results are compared and discussed in reference to appropriate activation parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, and $\Delta V^{\ddagger}$) reported in the literature.

Introduction

Some excellent reviews have appeared recently in which the complexation of platinum(II) and palladium(II) complex ions with different nucleic acid moieties is described in relation to the antitumor activity of *cis*-[$Pt(NH_3)_2Cl_2$] and its derivatives.[1-3] The chemical aspects mainly focused on include the location of the binding sites[4a-c] of the various nucleobases and the structure[4d,e] and stability order/constants[4f,g] of the resulting complex species. The ascertainment of these aspects by using the square-planar $Pd(dien)^{2+}$ (dien ≡ diethylenetriamine) center as a more reactive representative of platinum(II) complexes of which many are antitumor agents, has been proven successful.[4f,g,5,6] Despite the evidence that the binding reactions are kinetically rather than thermodynamically controlled,[5,7] detailed kinetic studies of the fundamental substitution processes occurring when platinum(II) and palladium(II) centers react with nucleobases remain very limited.[8]

Recent studies[9-13] in this laboratory of the substitution kinetics of sterically hindered dien complexes of palladium(II) with various ligands in aqueous solution demonstrated a remarkable difference in reactivity between chloro, aqua, and hydroxo complexes, a result that has important consequences for the antitumor activity of related species. Building on this experience, we now investigated kinetically the reaction between the $Pd(dien)^{2+}$ center and the various nucleic bases, nucleosides, and 5′-nucleotides presented in Figure 1 to reveal the nature of the rate-determining step(s) in each case. The advantage of the selected system is that only one coordination site is available to interact with the nucleobase and that this is a rather labile site compared to that of related platinum(II) complexes. It is thus hoped that this study should throw more light on the intimate mechanism of the antitumor activity of the latter complexes.

Experimental Section

The complexes [Pd(dien)Cl]ClO_4 and [Pd(dien)Cl]Cl were prepared according to standard procedures, the isolation of the latter complex being simplified by using ethanol instead of a precipitating salt for reasons outlined previously.[14] The chemical analyses and UV/visible spectral data were in good agreement with those obtained for previous preparations. The in situ conversion of these two complexes into the aqua species Pd(dien)OH_2^{2+} was done in the usual way be precipitating chloride with 1 or 2 equiv of $AgClO_4$, respectively. The ligand solutions were prepared by using the free bases and the nucleosides as pure compounds and the 5′-nucleotides as disodium salts, the only exceptions being adenine and A (hemisulfate salts) and AMP (sodium salt). The concentration of each of the complex solutions was held constant at 1×10^{-3} mol dm^{-3}, and the concentrations of the ligand solutions were varied between 5×10^{-3} and 4×10^{-2} mol dm^{-3} when equal volumes of complex and ligand solutions were mixed, in fulfilment of pseudo-first-order requirements. The pH of solutions of the free bases and the nucleosides, measured with a Metrohm E520 pH-meter, was left unadjusted in the range $5 < pH < 7$, the only exceptions being the solutions of adenine and A having pH <3 in the concentration range concerned. The solutions of these two ligands were used at their natural pH value of 2.8 and a pH value of 5.0 obtained by the addition of an appropriate amount of a standard NaOH solution. The nucleotide solutions all had, with the exception of AMP (sodium salt), pH >8 and were adjusted to pH ~6

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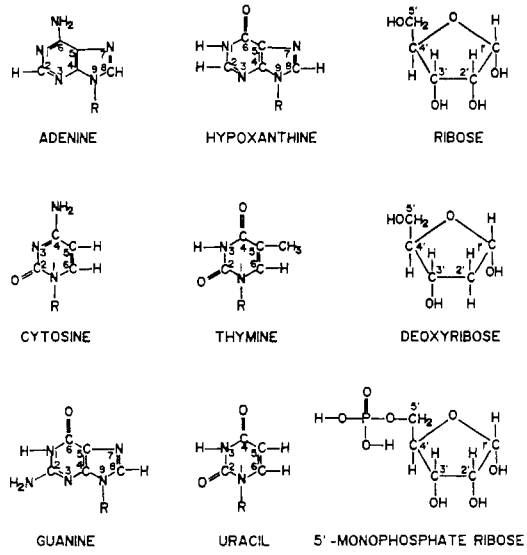


Figure 1. Nucleic free bases (R = H), nucleosides (R = ribose or deoxyribose), and nucleotides (R = 5′-monophosphate ribose). The abbreviations A, C, G, I, T, and U in the text represent the nucleosides adenosine, cytidine, guanosine, inosine, thymidine, and uridine respectively, whereas MP (for 5′-monophosphate) added to these symbols indicates the corresponding nucleotides. The nucleobases bind to the sugars by displacement of OH^- at $C_{1'}$.

with an appropriate amount of a standard $HClO_4$ solution to protonate the 5′-phosphate residue ($pK_a \sim 6.3$)[5] that could otherwise serve as an alternative coordination site. The chloro and aqua complex solutions exhibit pH values of 5.5 and 4.5 respectively, so that when complex solutions were mixed with equal volumes of ligand solution, almost neutral pH conditions existed for all the reactions under consideration. In this way the deprotonation of the aqua complex species ($pK_a = 7.4$)[10] and protonation of the nucleobase coordination sites ($pK_a(N7) = -1.6$, 1.2, and 2.2 for purine nucleosides A, I, and G respectively; $pK_a(N3) = 4.3$, 9.6, and 9.3 for pyrimidine nucleosides C, T, and U respectively)[5] could be prevented (except for thymine and uracil and their derivatives). Our earlier work[11] showed that there are no suitable buffers that do not coordinate to these very labile $Pd(dien)Cl^+$ and $Pd(dien)OH_2^{2+}$ species. The total ionic strength of the final reaction mixture was adjusted to 0.1 mol dm^{-3} by adding to the ligand solutions prior to mixing the necessary amounts of a standard $NaClO_4$ solution. The $[Cl^-]$ dependence of the various reactions was studied by using solutions of the two different chloro complexes mentioned above, the one having a total chloride content twice as large as the other ($[Cl]_T = 1 \times 10^{-3}$ and 2×10^{-3} mol dm^{-3} on mixing), and a third solution having a higher total chloride content ($[Cl]_T = 5 \times 10^{-3}$ mol dm^{-3}) through the addition of an appropriate amount of solid NaCl to a solution of either of the two complexes.

The spectral changes resulting from mixing of complex and ligand solutions were recorded with a Perkin-Elmer Lambda 5 spectrophotometer over the range $250 < \lambda < 400$ nm to establish a suitable wavelength at which kinetic measurements could be performed. These measurements were executed on a Durrum D110 stopped-flow spectrophotometer connected to a Tektronix 5111A oscilloscope for a visual display of the reaction course and an Apple II microcomputer for the evaluation of the corresponding pseudo-first-order rate constant by using an advanced data acquisition and analysis program.[15] The temperature dependence of the rate constants for the nucleosides was determined by performing measurements at three different temperatures in the range $18 < T < 32$ °C as controlled from an ancillary Haake NK22 cryostat. The pressure dependence of the rate constants for the nucleosides resulted from measurements at five different pressures in the range $5 < p < 100$ MPa on a locally developed high-pressure stopped-flow system.[16] The temperature for these measurements was fixed at 12 °C to allow the rate constants to fall within the measuring limits of the equipment.

Results and Discussion

Figure 2 shows the UV/visible spectra of aqueous solutions of the complexes $Pd(dien)Cl^+$ (one chloride ion per complex molecule

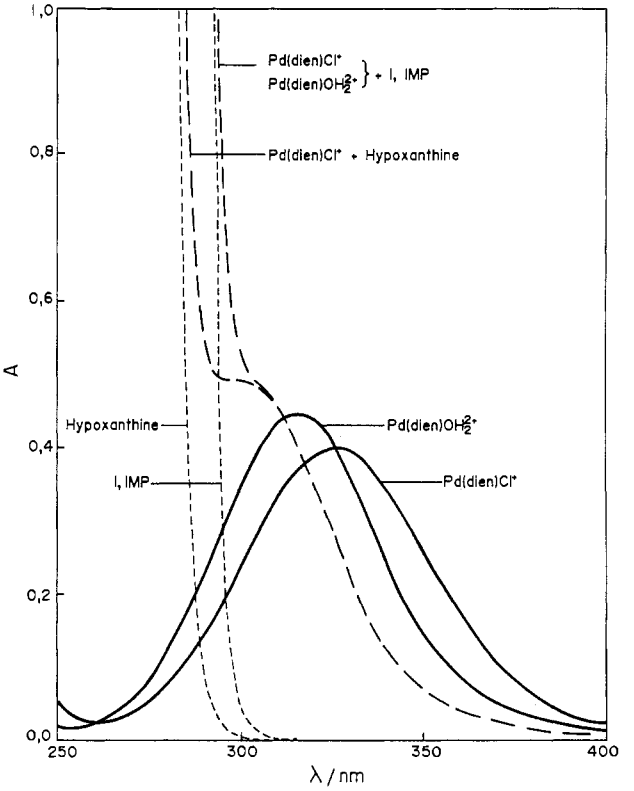
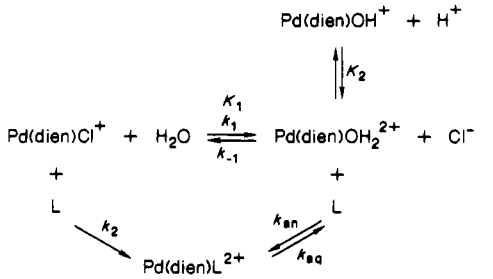


Figure 2. Spectral changes during reaction of the $Pd(dien)^{2+}$ center with L = hypoxanthine, I, and IMP. Conditions: [complex] = 1×10^{-3} mol dm^{-3}; [L] = 1×10^{-2} mol dm^{-3}; ionic strength = 0.1 mol dm^{-3}.

Scheme I



free in solution) and $Pd(dien)OH_2^{2+}$, of the ligands hypoxanthine, I, and IMP (10-fold concentration excess over complex solutions except for hypoxanthine with 5-fold excess due to relative insolubility), and of the products resulting from mixing equal volumes of the complex and the ligand solutions. These spectra are representative of those recorded for all the other mutually related free bases, nucleosides, and 5′-nucleotides, a striking feature being the perfect overlap of the three product spectra at wavelengths, e.g. $\lambda = 340$ nm, suitable for kinetic measurements. This suggests that principally the same product is formed in all three cases; it is also immaterial whether the reaction is performed with a chloro or an aqua complex.

The observed rate constants for the nucleic free bases and the nucleosides as incoming ligands are presented in Table I. The pH values are those of the ligand solution prior to mixing. The reaction pH is assumed to be equal to the ligand solution pH for the reactions with the chloro complex ($1 \times 10^{-3} < [Cl]_T < 5 \times 10^{-3}$ mol dm^{-3}) and equal to the average pH for the reactions with the aqua complex ($[Cl]_T = 0$). The reason for this is that the chloro complex solutions have a pH of 5.5 so that the reaction pH will mainly be determined by the pH of the ligand solution, whereas the aqua complex solution has a pH of 4.5 and thus contributes to the reaction pH (except for adenine and A at pH 2.8).

The substitution reactions at the square-planar $Pd(dien)Cl^+$ and $Pd(dien)OH_2^{2+}$ centers in aqueous solution generally proceed

(15) The program is an improved version of the MCS-1 Hi-Tech Stopped-Flow Data Aquisition and Analysis Program, Mark III, 1982. Further information can be obtained from the authors.
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Table I. Rate Data for Reaction of Pd(dien)OH$_2^{2+}$ ([Cl]$_T$ = 0) and Pd(dien)Cl$^+$ ($1 \times 10^{-3} < [Cl]_T < 5 \times 10^{-3}$ mol dm^{-3}) with Free Bases and Nucleosides[a]

nucleobase L	[L]/ mol dm^{-3}	pH[c]	k_{obsd}/s^{-1} [Cl]$_T$ = 0	[Cl]$_T$ = 1×10^{-3}	[Cl]$_T$ = 2×10^{-3}	[Cl]$_T$ = 5×10^{-3}	k_{an}/dm^3 mol^{-1} s^{-1}
adenine, A	5×10^{-3}	2.8 for adenine,	11.7 ± 0.6	6.4 ± 0.2	4.4 ± 0.1		1840 ± 101
	1×10^{-2}	5.0 for A	21.6 ± 2.1	12.5 ± 0.2	7.8 ± 0.1	4.3 ± 0.2	
	2×10^{-2}		36.0 ± 2.2	21.9 ± 0.8	14.5 ± 0.3	7.7 ± 0.1	
adenine	5×10^{-3}	5.0	40.4 ± 0.8	18.7 ± 0.2	14.8 ± 0.2	7.2 ± 0.2	7835 ± 98
	1×10^{-2}	5.0	78.1 ± 1.8	26.9 ± 0.4	21.5 ± 0.2	14.5 ± 0.3	
cytosine, C	5×10^{-3}	6.7	16.5 ± 1.6	8.7 ± 0.1	6.6 ± 0.2	3.7 ± 0.1	3230 ± 13
	1×10^{-2}	6.8	32.7 ± 0.6	17.2 ± 0.5	12.7 ± 0.9	6.8 ± 0.5	
	2×10^{-2}	7.2	64.5 ± 0.8	26.5 ± 1.2	19.8 ± 0.5	12.5 ± 0.7	
G[b]	5×10^{-3}	5.8	165 ± 28[d]				32636 ± 146
	1×10^{-2}	5.8	326 ± 29[d]				
hypoxanthine, I	5×10^{-3}	5.8	130 ± 4	31.7 ± 1.5	25.4 ± 0.8	18.3 ± 0.1	26091 ± 36
	1×10^{-2}	5.4	261 ± 10	37.3 ± 0.6	34.0 ± 0.4	27.5 ± 0.9	
	2×10^{-2}			43.6 ± 1.2	41.3 ± 1.2	37.0 ± 0.2	
thymine, T	5×10^{-3}	6.2	0.30 ± 0.01	0.21 ± 0.01	0.16 ± 0.00	0.12 ± 0.00	18.8 ± 0.4
	1×10^{-2}	5.9	0.42 ± 0.01	0.30 ± 0.01	0.24 ± 0.00	0.17 ± 0.00	
	2×10^{-2}	5.9	0.63 ± 0.01	0.46 ± 0.00	0.36 ± 0.00	0.25 ± 0.01	
	4×10^{-2}	6.0	0.98 ± 0.03		0.55 ± 0.01	0.36 ± 0.00	
uracil, U	5×10^{-3}	5.7	0.41 ± 0.01	0.32 ± 0.00	0.25 ± 0.00	0.18 ± 0.00	31.1 ± 0.4
	1×10^{-2}	5.8	0.58 ± 0.01	0.43 ± 0.01	0.34 ± 0.01	0.23 ± 0.00	
	2×10^{-2}	5.7	0.87 ± 0.01	0.63 ± 0.01	0.52 ± 0.01	0.33 ± 0.00	
	4×10^{-2}	5.6	1.53 ± 0.03		0.74 ± 0.01	0.49 ± 0.02	

[a] Conditions: [complex] = 1×10^{-3} mol dm^{-3}; ionic strength = 0.1 mol dm^{-3}; temperature = 25 °C; wavelength = 340 nm. [b] Guanine omitted due to insufficient solubility for workable concentration level. [c] Natural pH except for preadjusted pH 5.0 in the case of adenine and A (cf. Experimental Section). [d] k_{obsd} obtained by extrapolation of data measured at reduced [compelx] and [L] (cf. Results and Discussion).

according to the mechanism shown in Scheme I to which the well-known two-term rate law $k_{obsd} = k_1 + k_2[L]$ applies and for which anation, i.e. $k_{an}[L]$, is usually a fast, non-rate-determining step. The solvolysis rate constant k_1, which is independent of [L], can be determined from the intercept of k_{obsd} vs. [L] for the reaction of L with the *chloro* complex. The values $k_1 = 37.8 \pm 0.4$ s^{-1} and $k_1 = 43.8 \pm 0.5$ s^{-1} previously[9] determined this way by reacting the chloro complex with L = OH$^-$ and L = I$^-$, respectively, were complemented in this study by the value $k_1 = 35.0 \pm 3.5$ s^{-1} obtained by using L = I$^-$ over an extended range of concentrations. The anation rate constant k_{an} can be determined from the slope of k_{obsd} vs. [L] for the reaction of L with the *aqua* complex. The values so obtained vary according to the nucleophilicity or complexation capability of various L, k_{obsd} in most cases being immeasurably large due to the lability of the aqua complex. A value of $k_{obsd} > 10^3$ s^{-1}, for example, is extrapolated for the anation of Pd(dien)OH$_2^{2+}$ with Cl$^-$ at a ligand to complex concentration ratio of 10:1 by using published anation[10,16] and ligand substitution[9,12] rate data for more sterically hindered dien complexes.

The rate constants k_{obsd} for the nucleic bases and the nucleosides reacting with the *chloro* complex ([Cl]$_T$ = 1×10^{-3} column) are in view of the foregoing not solvolysis rate constants k_1 since the intercepts of k_{obsd} vs. [L] are in all cases smaller than the expected value of $35 < k_1 < 45$ s^{-1}. The corresponding rate constants k_{obsd} for the reaction of the *aqua* complex ([Cl]$_T$ = 0 column) show a linear dependence on [L], except those for thymine and T and uracil and U, allowing anation rate constants k_{an} to be calculated from the slope of k_{obsd} vs. [L]. These rate constants are presented in the last column of Table I. The slope of k_{obsd} vs. [L] for the reactions with thymine and T and with uracil and U could despite the occurrence of an intercept be considered as the anation rate constant k_{an} since the intercept in these two cases had been proven to be the aquation rate constant k_{aq}. This was done experimentally by reacting the product species obtained on mixing the aqua complex and the nucleic entity in a 1:1 ratio with various concentrations of excess HClO$_4$ (10-fold minimum as required for pseudo-first-order conditions) to effect the reverse aquation reaction and checking whether the same intercept is obtained as when the forward anation reaction is performed. The positive outcome of this experiment is demonstrated in Figure 3 for uracil and U as a representative example by plotting k_{obsd} as a function

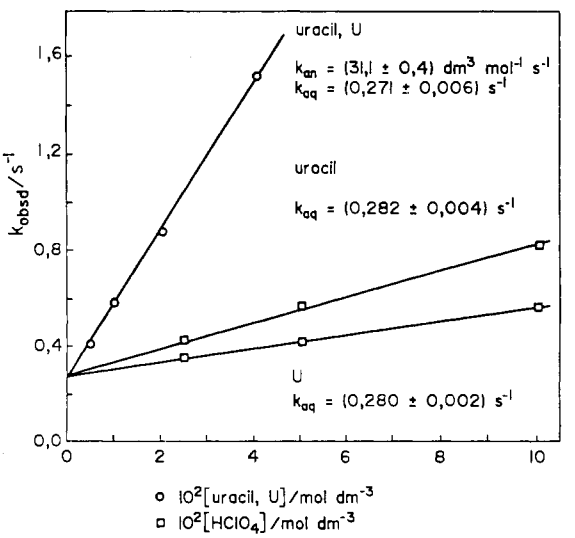

Figure 3. Determination of k_{an} (slope) and k_{aq} (intercept) for L = uracil and U by performing forward anation (Pd(dien)OH$_2^{2+}$ + L) and reverse aquation (Pd(dien)L^{2+} + HClO$_4$) reactions. Conditions: [complex] = 1×10^{-3} mol dm^{-3}; ionic strength = 0.1 mol dm^{-3}; temperature = 25 °C.

of [uracil] and [U] for the forward anation reaction and k_{obsd} as a function of [HClO$_4$] for the reverse aquation reaction. The common intercepts support the rate law

$$k_{obsd} = k_{aq} + k_{an}[L] \quad (1)$$

for the overall substitution process with $k_{aq} = 0.239 \pm 0.015$ s^{-1} and $k_{aq} = 0.278 \pm 0.025$ s^{-1} for thymine and T and for uracil and U, respectively. The reverse aquation comes into operation with the protonation of the nucleobase on acidification (cf. quoted pK values) such that the forward anation cannot occur anymore, and k_{aq} becomes the rate-determining step. The [H$^+$] dependence of k_{obsd} is ascribed to an acid-catalyzed aquation process, during which the product species Pd(dien)L^{2+} is protonated to produce a more reactive species.

The question arises as to which reaction path is measured when the chloro complex is reacted with the various ligands in Table I. The decrease in k_{obsd} with an increase in [Cl$^-$] (from [Cl]$_T$ =

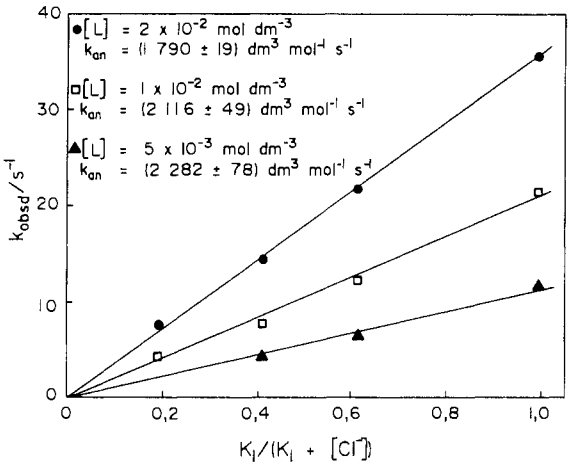

Figure 4. Graphical presentation of the rate law (eq 3) for the reaction of the $Pd(dien)^{2+}$ center with L = adenine (pH 2.8) and A (pH 5.0) representing the *first* mechanistic model. Data were taken from Table I.

0 column to $[Cl]_T = 5 \times 10^{-3}$ column) strongly suggests that the anation reaction path is measured under *all* the experimental conditions, the increasing $[Cl^-]$ leading to smaller fractions of the aqua species

$$f_{Pd(dien)OH_2^{2+}} = K_1[H^+]/\{[H^+][Cl^-] + K_1[H^+] + K_1K_2\} \approx K_1/(K_1 + [Cl^-]) \quad (2)$$

due to a shift of the chloro $\rightleftarrows$ aqua equilibrium toward the chloro species according to Scheme I, for which $K_1 = 10^{-3.00}$ [13] and $K_2 = 10^{-7.38}$,[10] $[H^+]$ is given by either the pH of the ligand solution or the average pH of the ligand and aqua solution as explained above and $K_1K_2 \ll K_1[H^+]$. This implies that, since

$$k_{obsd} = k_{an}f_{Pd(dien)OH_2^{2+}}[L] = k_{an}K_1[L]/(K_1 + [Cl^-]) \quad (3)$$

for the anation path (cases where $k_{aq} = 0$ only), it should be possible to fit *all* the data for a given ligand on one line by plotting k_{obsd} vs. $K_1/(K_1 + [Cl^-])$. $[Cl^-]$ was obtained from the sum of $[Pd(dien)OH_2^{2+}] = \{K_1[H^+]/([H^+][Cl^-] + K_1[H^+] + K_1K_2)\}[Pd]_T$ and $[Pd(dien)OH^+] = \{K_1K_2/([H^+][Cl^-] + K_1[H^+] + K_1K_2\}[Pd]_T$ through inserting the added chloride ion concentration in these expressions and correcting it for the chloride ion released by the chloro complex by repeating the calculation in such a way that each newly calculated value of $[Cl^-]$ was introduced for the next calculation until constant values were obtained.

A plot of k_{obsd} vs. $K_1/(K_1 + [Cl^-])$ for adenine (pH 2.8) and A (pH 5.0) as a representative example is shown in Figure 4, the average of the resulting values of k_{an}, viz. $k_{an} = (2062 \pm 250)$ dm^3 mol^{-1} s^{-1}, being in good agreement with the experimental value of k_{an} in Table I. The validity of eq 3 also holds for cytosine and C, for which an average value $k_{an} = (3265 \pm 43)$ dm^3 mol^{-1} s^{-1} was obtained from a similar plot. The presentation of the kinetic data this way shows that, whereas in normal square-planar substitution the solvolysis path is rate-determining and the subsequent anation path is very fast, the nucleic entities under consideration slow down the anation path to such an extent that it becomes rate-determining. This retardation of the anation path should be related to the relatively poor complexation capabilities of the nucleic entities. Since $k_{an}[L] < k_1, k_{-1}[Cl^-]$ ($k_{-1} = k_1/K_1 = 3.5 \times 10^4$ dm^3 mol^{-1} s^{-1} from the values quoted above), the solvolysis process preceding the anation step can be regarded as a fast preequilibration comprising the opposing reaction steps k_1 and k_{-1}. This preequilibration is, however, not observed as a separate fast step as in the cases where Tris[17] and HCO_3^- [18] react with palladium(II)–dien complexes. The reason is that, unlike the two cases mentioned, no pH jump occurs on mixing the complex species with the nucleobases so that all of the aqua species in solution remains in that form and can rapidly react with free chloride to produce the chloro species. A further reason for not observing the preequilibration is that the reverse step is so fast (cf. quoted value for k_{-1}) that it can not be captured within the stopped-flow time scale.

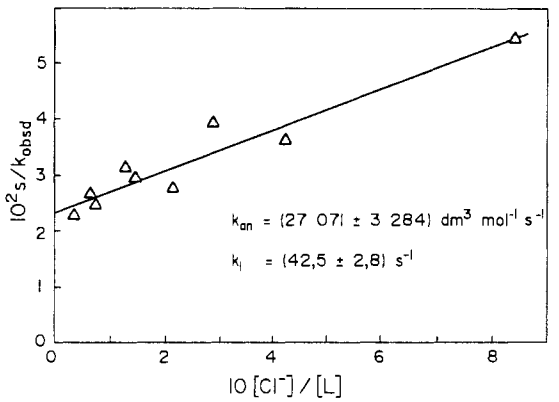

Figure 5. Graphical presentation of the rate law (eq 5) for the reaction of $Pd(dien)Cl^+$ with L = hypoxanthine and I representing the *second* mechanistic model. Data were taken from Table I.

The data for hypoxanthine and I and for adenine at neutral pH (pH ~5) cannot be presented in the same way as in Figure 4 since the values of k_{obsd} for $1 \times 10^{-3} < [Cl]_T < 5 \times 10^{-3}$ mol dm^{-3} in Table I are too small to be associated with the values of $K_1/(K_1 + [Cl^-])$ calculated for the presentation in Figure 4. Since it follows from Table I that in these cases $k_{an}[L] \sim k_1, k_{-1}[Cl^-]$, the solvolysis process preceding the anation step can no longer be regarded as a fast preequilibration. The situation is rather one where the aqua species reacts with the incoming nucleic ligand at a rate comparable with that at which it is formed in solution by solvolysis, implying that the stationary state approximation should be applied to determine the correct expression for the aqua complex concentration in the equation $d[product]/dt = k_{an}[Pd(dien)OH_2^{2+}][L]$. The rate law

$$k_{obsd} = k_{an}k_1[L]/(k_{-1}[Cl^-] + k_{an}[L]) \quad (4)$$

derived in this way, offers in its inversed form

$$1/k_{obsd} = k_{-1}[Cl^-]/k_{an}k_1[L] + 1/k_1 = [Cl^-]/K_1k_{an}[L] + 1/k_1 \quad (5)$$

the possibility to fit the data by plotting $1/k_{obsd}$ vs. $[Cl^-]/[L]$. The values of k_{an} and k_1 obtainable from the slope and the intercept can then be compared with the known values of these rate constants to check the validity of the applied model. This is done in Figure 5 for hypoxanthine and I as a representative example, the value $k_{an} = (27071 \pm 3284)$ dm^3 mol^{-1} s^{-1} being in good agreement with the corresponding value of k_{an} from Table I and the value $k_1 = 42.5 \pm 2.8$ s^{-1} being in reasonable agreement with the value $35 < k_1 < 45$ s^{-1} mentioned earlier. The validity of the model is also supported by the realistic values $k_{an} = (8084 \pm 827)$ dm^3 mol^{-1} s^{-1} and $k_1 = 33.1 \pm 5.6$ s^{-1} obtained from a similar plot for adenine at neutral pH. The two ligands under consideration thus represent cases where the anation reaction path is slowed down to such an extent that it becomes rate-determining, but unlike the former case where it becomes so slow that the preceding solvolysis process could be regarded as a fast preequilibration, it now remains fast enough to compete with the preceding solvolysis process and thereby restrict the presence of the aqua species to a constant, infinitely small concentration.

The values of k_{obsd} for the reaction of G with $Pd(dien)Cl^+$ are omitted from Table I, because they were measured at a 10-fold lower complex and ligand concentration due to poor ligand solubility and could not be extrapolated directly (by multiplication with 10) as in the case of the reaction with $Pd(dien)OH_2^{2+}$ since the fraction of aqua complex available in solution at a given $[Cl]_T$

(17) Breet, E. L. J.; van Eldik, R., submitted for publication in *Inorg. Chem.*
(18) Breet, E. L. J.; van Eldik, R., prepared for publication.

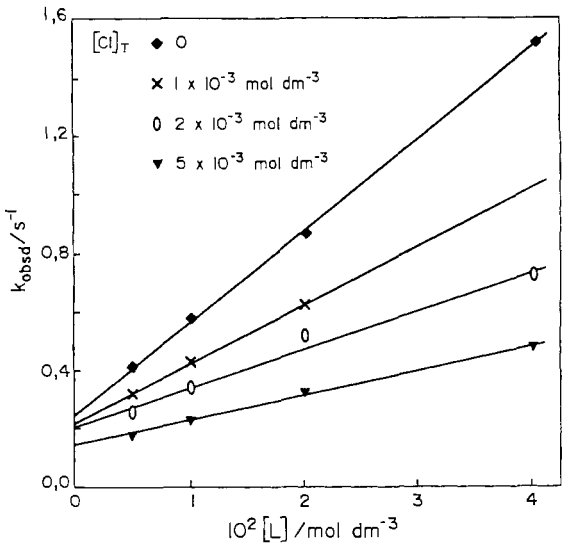

Figure 6. Graphical presentation of rate-law (equation (6)) for reaction of Pd(dien)$^{2+}$ centre with L = uracil, U representing *third* mechanistic model. Data taken from Table I.

is quite different at the two complex concentration levels. The measured data could, however, be fitted with eq 3 at low [L] and with eq 4 at high [L], indicating that k_{an}[L] for G lies on the border of a preequilibrium and steady-state treatment under the prevailing conditions and that a sufficient change in [L] causes a changeover between the two. The importance of the relative magnitudes of k_{an}[L], k_1, and k_{-1}[Cl$^-$] for distinguishing between the two introduced mechanistic models is thereby emphasized. The term k_{an}[L] is determined by the complexation capabilities of the various nucleic entities and so governs the preequilibrium or steady-state condition.

A third mechanistic case is presented by the ligands thymine and T and uracil and U. The k_{obsd} vs. [L] plots for uracil and U, given in Figure 6 as a representative example, can be described by the equation $k_{obsd} = k' + k''$[L], where both the intercept k' and the slope k'' show a [Cl$^-$] dependence such that $1/k' = k_a + k_b$[Cl$^-$] and $1/k'' = k_c + k_d$[Cl$^-$]. The experimental rate law is thus

$$k_{obsd} = 1/(k_a + k_b[Cl^-]) + \{1/(k_c + k_d[Cl^-])\}[L] = k_A/(k_B + [Cl^-]) + \{k_C/(k_D + [Cl^-])\}[L] \quad (6)$$

with $k_A = 1/k_b$, $k_B = k_a/k_b$, $k_C = 1/k_d$, and $k_D = k_c/k_d$, such that $k_A = (8.3 \pm 2.2) \times 10^{-4}$ mol dm^{-3} s^{-1}, $k_B = (4.5 \pm 1.2) \times 10^{-3}$ mol dm^{-3}, $k_C = (4.4 \pm 0.2) \times 10^{-2}$ s^{-1}, and $k_D = (2.5 \pm 0.1) \times 10^{-3}$ mol dm^{-3} for thymine and T and $k_A = (1.4 \pm 0.1) \times 10^{-3}$ mol dm^{-3} s^{-1}, $k_B = (5.6 \pm 0.2) \times 10^{-3}$ mol dm^{-3}, $k_C = (5.3 \pm 0.6) \times 10^{-2}$ s^{-1}, and $k_D = (2.0 \pm 0.3) \times 10^{-3}$ mol dm^{-3} for uracil and U. It was already shown (eq 1) that the *slope* of the k_{obsd} vs. [L] plot for [Cl]$_T$ = 0 (Figure 3) equals the anation rate constant k_{an}. If it is assumed that anation is also rate-determining for $1 \times 10^{-3} < [Cl]_T < 5 \times 10^{-3}$ mol dm^{-3} as in the two preceding mechanistic cases, the preequilibrium treatment is probably most applicable on account of the lower reactivity observed for these ligands, and the corresponding rate constant is given by eq 3. This equation equals the second right-hand side term of eq 6 for $k_{an}K_1 = k_C$ and $K_1 = k_D$, from which a value $k_{an} = 18.0 \pm 1.0$ dm^3 mol^{-1} s^{-1} for thymine and T and a value $k_{an} = (27.1 \pm 3.8)$ dm^3 mol^{-1} s^{-1} for uracil and U, in good agreement with the corresponding values of k_{an} in Table I, can be derived. In addition, the value $K_1 \sim 2 \times 10^{-3}$ mol dm^{-3} is quite acceptable when the error limit of the literature value $K_1 = (1.0 \pm 0.5) \times 10^{-3}$ mol dm^{-3} [13] is taken into account.

The *intercept* of the k_{obsd} vs. [L] plot for [Cl]$_T$ = 0 (Figure 3) was shown (eq 1) to equal the aquation rate constant k_{aq}. The fact that the intercept decreases with increasing [Cl$^-$] for $1 \times 10^{-3} < [Cl]_T < 5 \times 10^{-3}$ mol dm^{-3} strongly suggests that, in the same way as an increasing [Cl$^-$] decreases the fraction of aqua complex

Scheme II

$$Pd(dien)L^{2+} + Cl^- \overset{Q}{\rightleftharpoons} (Pd(dien)L^{2+} \cdot Cl^-)$$

in solution to undergo the forward anation reaction, the fraction of the product species available in solution to undergo the reverse aquation reaction is decreased by an increasing [Cl$^-$]. The rate constant for the reverse aquation reaction would then be given by

$$k_{obsd} = k_{aq} f_{Pd(dien)L^{2+}} \quad (7)$$

It could indeed be shown experimentally, by repeating the measurements with which k_{aq} (Figure 3) had been determined but using various [NaCl] instead of various [HClO$_4$] to effect the reverse reaction, that a totally different reaction with rate constants about 10 times smaller than those for the reverse aquation reaction occurs. The exact nature of this competitive reaction reducing the fraction of product species available for aquation has not been established, but a reasonable possibility might be the formation of an encounter complex, viz. an ion pair, according to Scheme II. The fraction of reacting species in solution is then given by

$$f_{Pd(dien)L^{2+}} = 1/(1 + Q)[Cl^-] \quad (8)$$

which, on substitution in eq 7, yields

$$k_{obsd} = (k_{aq}/Q)/\{(1/Q) + [Cl^-]\} \quad (9)$$

This expression equals the first right-hand side term of eq 6 for $k_{aq}/Q = k_A$ and $1/Q = k_B$, from which the values $Q = 224 \pm 58$ dm^3 mol^{-1} and $k_{aq} = 0.18 \pm 0.05$ s^{-1} for thymine and T and the values $Q = 179 \pm 8$ dm^3 mol^{-1} and $k_{aq} = 0.25 \pm 0.01$ s^{-1} for uracil and U can be derived. The values of k_{aq} are in good agreement with the experimental values obtained in the acidification experiments (Figure 3). The values of Q are rather high for pure ion-pair formation constants, indicating that there must be some specific interaction between the nucleobase ligand and chloride ion. Recent studies on complexation reactions of similar 2+-charged palladium(II) complexes with HSO_3^- resulted in equally large encounter complex formation constants,[19] hydrogen bonding being thought responsible for the observed effect. Whatever the nature of this interaction, the suggested formation of an unreactive encounter complex does present a realistic fit of the observed data.

The nucleic ligands thymine and T and uracil and U thus react with the Pd(dien)$^{2+}$ center according to a mechanism having, as in the two previous cases, the anation path following the initial solvolysis process as its rate-determining step. In this case, however, the reactivity of the incoming ligands is so poor that k_{an}[L] $\sim k_{aq}$, i.e. the reverse aquation reaction becomes significant and contributes to the overall observed rate constant. The reverse aquation reaction is, however, strongly affected by the presence of chloride ion due to a competitive reaction that probably involves ion pairing.

The temperature and pressure dependencies of the rate constants k_{obsd} for the reactions of the aqua complex ([Cl]$_T$ = 0) with the nucleosides are presented in Tables II and III, respectively. The data are analyzed according to eq 3 (with $f_{Pd(dien)OH_2^{2+}} = 1$) or, where applicable, according to eq 1 to report activation parameters for both the forward anation and the reverse aquation steps. Table II shows that there is only a small variation in the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ among the various nucleosides.

The activation enthalpy order $\Delta H^{\ddagger}$(G) $\sim \Delta H^{\ddagger}$(I) $< \Delta H^{\ddagger}$(C) $< \Delta H^{\ddagger}$(A) $< \Delta H^{\ddagger}$(U) $< \Delta H^{\ddagger}$(T) neatly corresponds with the anation rate constant order k_{an}(G) $> k_{an}$(I) $> k_{an}$(C) $> k_{an}$(A) $> k_{an}$(U) $> k_{an}$(T) in Table I and, with the exception of U and T relative to the other nucleosides, with the stability constant order G7 > I7 > U3 > T3 > C3 > A7 in the literature.[4f] The difference between the anation rate and stability orders with respect to U and T probably lies in the degree of deprotonation of the coordination site (pK_a(N3) > 9 in both cases) at neutral pH and emphasizes that the complexation reactions studied are rather

(19) Mahal, G.; van Eldik, R. *Inorg. Chem.*, in press.

Table II. Temperature Dependence of Reaction of $Pd(dien)OH_2^{2+}$ with Nucleosides[a]

nucleoside L	T/°C	[L]/ mol dm^{-3}	k_{obsd}/s^{-1}	k_{an}/ dm^3 mol^{-1} s^{-1}	$\Delta H^{\ddagger}_{an}$/ kJ mol^{-1}	$\Delta S^{\ddagger}_{an}$/ J K^{-1} mol^{-1}	k_{aq}/s^{-1}	$\Delta H^{\ddagger}_{aq}$/ kJ mol^{-1}	$\Delta S^{\ddagger}_{aq}$/ J K^{-1} mol^{-1}
A	18	1×10^{-2}	14.8 ± 0.5	1435 ± 18	26.0 ± 2.4	−95.3 ± 8.1			
		2×10^{-2}	28.6 ± 1.1						
	25	1×10^{-2}	19.9 ± 0.4	1817 ± 69					
		2×10^{-2}	36.0 ± 2.2						
	32	1×10^{-2}	25.7 ± 0.9	2461 ± 44					
		2×10^{-2}	49.0 ± 1.5						
C	18	1×10^{-2}	25.3 ± 1.2	2530 ± 0	25.3 ± 1.6	−92.9 ± 5.4			
		2×10^{-2}	50.6 ± 2.0						
	25	1×10^{-2}	32.6 ± 0.7	3224 ± 15					
		2×10^{-2}	64.4 ± 1.0						
	32	1×10^{-2}	42.9 ± 1.4	4281 ± 4					
		2×10^{-2}	85.6 ± 0.7						
G	18	5×10^{-3}	128 ± 21	25055 ± 218	21.8 ± 1.8	−85.6 ± 6.0			
		1×10^{-2}	250 ± 14						
	25	5×10^{-3}	165 ± 28	32636 ± 146					
		1×10^{-2}	326 ± 29						
	32	5×10^{-3}	202 ± 25	39673 ± 291					
		1×10^{-2}	396 ± 46						
I	18	5×10^{-3}	107 ± 3	21491 ± 36	18.4 ± 0.0	−98.7 ± 0.1			
		1×10^{-2}	215 ± 7						
	25	5×10^{-3}	132 ± 2	26309 ± 36					
		1×10^{-2}	263 ± 10						
	32	5×10^{-3}	165 ± 8	31909 ± 436					
		1×10^{-2}	318 ± 8						
T	18	1×10^{-2}	0.27 ± 0.01	12.2 ± 0.2	39.5 ± 1.6	−88.3 ± 5.3	0.14 ± 0.00	45.3 ± 2.7	−105 ± 9
		2×10^{-2}	0.39 ± 0.01						
		4×10^{-2}	0.63 ± 0.01						
	25	1×10^{-2}	0.42 ± 0.01	18.8 ± 0.4			0.24 ± 0.02		
		2×10^{-2}	0.63 ± 0.01						
		4×10^{-2}	0.98 ± 0.03						
	32	1×10^{-2}	0.62 ± 0.02	27.0 ± 0.3			0.36 ± 0.01		
		2×10^{-2}	0.89 ± 0.02						
		4×10^{-2}	1.44 ± 0.05						
U	18	1×10^{-2}	0.36 ± 0.00	22.2 ± 0.4	35.9 ± 2.2	−95.6 ± 7.2	0.15 ± 0.01	55.6 ± 4.2	−69.6 ± 14.0
		2×10^{-2}	0.59 ± 0.01						
		4×10^{-2}	1.04 ± 0.05						
	25	1×10^{-2}	0.58 ± 0.01	31.1 ± 0.4			0.28 ± 0.03		
		2×10^{-2}	0.87 ± 0.01						
		4×10^{-2}	1.53 ± 0.03						
	32	1×10^{-2}	0.90 ± 0.03	46.0 ± 0.5			0.44 ± 0.01		
		2×10^{-2}	1.38 ± 0.02						
		4×10^{-2}	2.28 ± 0.05						

[a] Conditions: [complex] = 1×10^{-3} mol dm^{-3}; ionic strength = 0.1 mol dm^{-3}; wavelength = 340 nm.

kinetically than thermodynamically controlled. The rate constants in Table III exhibit within experimental error practically no pressure dependence. It is also reflected in the corresponding values of $\Delta V^{\ddagger}$, so that with major solvational changes not expected to contribute toward $\Delta V^{\ddagger}$, the intrinsic component is assumed to be almost zero. This means that during the associative bond formation suggested by the negative values of $\Delta S^{\ddagger}$ in Table II, the overlap of the van der Waals radii hardly occurs, possibly as a result of steric hindrance due to the size of the entering anating molecule. The solvolysis reactions of related sterically hindered complexes exhibit for associative substitution significantly negative values of $\Delta V^{\ddagger} = -12 \pm 2$ cm^3 mol^{-1} for charged leaving groups (Cl^-, I^-, etc.)[12] but more positive values $-4 < \Delta V^{\ddagger} < -3$ cm^3 mol^{-1} for neutral leaving groups (pyridine, NH_3, etc.).[20] The small negative values of $\Delta V^{\ddagger}$ reported in Table III for the reverse aquation step fit this trend. The steric hindrance on the entering ligand thus presumably accounts for the almost zero value of $\Delta V^{\ddagger}$ for the forward anation step, while the neutral nature of the ligand depicts the value of $\Delta V^{\ddagger}$ for the reverse aquation step.

The rate constants k_{obsd} for the nucleotides as incoming ligands are presented in Table IV. There are a few reasons why they are considered to be the rate constants for a *secondary* reaction and not for the rate-determining anation reaction as in the case of the free bases and the nucleosides.

First, it is known that the nucleotides react faster than the nucleosides, the enhancing effect being AMP/A ~ 3 and GMP/G ~ 15 in the case of *cis*-$[Pt(NH_3)_2(OH_2)_2]^{2+}$.[8c] This should lead, even when the enhancing effect is not more pronounced with the labile $Pd(dien)^{2+}$ center, to immeasurably large rate constants for the majority of the nucleotides. The measured rate constants are, however, much smaller than those for the free bases and the nucleosides, possibly indicating that a secondary reaction is observed. The primary reaction probably involves very rapid coordination by the phosphate group. The extrapolation of the tabulated data to zero [L] leads to intercepts that can not be correlated with the value of the solvolysis rate constant k_1, again suggesting that the observed reaction is a secondary substitution process.

Second, the rate constants k_{obsd} for the nucleotides, unlike those for the free bases and the nucleosides, show no $[Cl^-]$ dependence, except for TMP and UMP. This $[Cl^-]$ independence also supports the idea of a secondary reaction since the primary anation reaction depends on $[Cl^-]$. The exception to the $[Cl^-]$ independence in the case of TMP and UMP probably stems from the $[Cl^-]$ dependence of the reverse reaction involving the product species and chloride ion as described earlier in this paper (cf. further discussion).

Third, plots of k_{obsd} vs. [L] for the ligands TMP and UMP show that only the intercepts depend on $[Cl^-]$, the slopes of the various straight lines, unlike those in Figure 6 for uracil and U, being

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Table III. Pressure Dependence of Reaction of $Pd(dien)OH_2^{2+}$ with Nucleosides[a]

nucleoside L	p/bar	10^2[L]/ mol dm^{-3}	k_{obsd}/s^{-1}	k_{an}/ dm^3 mol^{-1} s^{-1}	$\Delta V^{\ddagger}_{an}$/ cm^3 mol^{-1}	k_{aq}/s^{-1}	$\Delta V^{\ddagger}_{aq}$/ cm^3 mol^{-1}
A	50	1	9.9 ± 0.6	987 ± 60	−2.0 ± 0.4		
	250	1	9.8 ± 0.5	979 ± 50			
	500	1	10.1 ± 0.5	1011 ± 50			
	750	1	10.5 ± 0.9	1049 ± 90			
	1000	1	10.6 ± 0.8	1057 ± 80			
C	50	1	15.5 ± 1.2	1548 + 120	1.5 ± 0.7		
	250	1	15.5 ± 0.6	1546 ± 60			
	500	1	14.6 ± 1.5	1456 ± 150			
	750	1	14.6 ± 0.3	1459 ± 30			
	1000	1	14.7 ± 0.3	1473 ± 30			
T	50	1	0.43 ± 0.03	16.4 ± 1.2	−0.6 ± 2.2	0.28 ± 0.03	−0.8 ± 1.1
		2	0.63 ± 0.03				
		4	0.93 ± 0.03				
	250	1	0.43 ± 0.02	16.7 ± 3.2		0.30 ± 0.09	
		2	0.69 ± 0.07				
		4	0.95 ± 0.03				
	500	1	0.43 ± 0.03	17.0 ± 1.7		0.28 ± 0.05	
		2	0.65 ± 0.02				
		4	0.95 ± 0.01				
	750	1	0.43 ± 0.02	16.6 ± 1.9		0.29 ± 0.05	
		2	0.65 ± 0.02				
		4	0.94 ± 0.02				
	1000	1	0.45 ± 0.02	17.0 ± 1.7		0.30 ± 0.05	
		2	0.67 ± 0.01				
		4	0.97 ± 0.02				
U	50	1	0.52 ± 0.03	29.1 ± 0.7	−0.8 ± 2.2	0.22 ± 0.02	−6.3 ± 4.6
		2	0.79 ± 0.02				
		4	1.39 ± 0.05				
	250	1	0.53 ± 0.01	27.8 ± 0.6		0.25 ± 0.02	
		2	0.79 ± 0.02				
		4	1.36 ± 0.03				
	500	1	0.57 ± 0.01	26.1 ± 1.4		0.33 ± 0.04	
		2	0.87 ± 0.03				
		4	1.36 ± 0.06				
	750	1	0.58 ± 0.01	26.9 ± 0.4		0.32 ± 0.01	
		2	0.86 ± 0.02				
		4	1.39 ± 0.04				
	1000	1	0.58 ± 0.01	30.7 ± 0.2		0.27 ± 0.01	
		2	0.88 ± 0.02				
		4	1.50 ± 0.02				

[a] Conditions: [complex] = 1×10^{-3} mol dm^{-3}; ionic strength = 0.1 mol dm^{-3}; temperature = 12 °C; wavelength = 340 nm.

Table IV. Rate Data for Reaction of $Pd(dien)OH_2^{2+}$ ($[Cl]_T = 0$) and $Pd(dien)Cl^+$ ($1 \times 10^{-3} < [Cl]_T < 2 \times 10^{-3}$ mol dm^{-3}) with 5′-Nucleotides[a]

			k_{obsd}/s^{-1}		
nucleotide L	10^2[L]/mol dm^{-3}	pH[b]	$[Cl]_T = 0$	$[Cl]_T = 1 \times 10^{-3}$	$[Cl]_T = 2 \times 10^{-3}$
AMP	1	5.4	20.4 ± 0.6	19.7 ± 0.3	20.4 ± 1.7
	2		25.3 ± 1.0	26.3 ± 0.4	25.0 ± 0.7
CMP	1	6.0	8.5 ± 0.2	8.3 ± 0.1	7.9 ± 0.4
	2		10.3 ± 0.5	10.1 ± 0.1	10.0 ± 0.2
	4		13.7 ± 0.5		
GMP	1	6.0	40.2 ± 3.2	40.4 ± 0.7	40.5 ± 0.7
	2		45.7 ± 5.6	46.8 ± 1.2	47.3 ± 0.2
IMP	1	6.0	36.3 ± 3.2	39.4 ± 0.7	39.5 ± 0.9
	2		41.3 ± 3.0	43.8 ± 0.4	43.9 ± 0.3
TMP	1	6.0	0.36 ± 0.00	0.31 ± 0.00	0.28 ± 0.01
	2		0.41 ± 0.00	0.36 ± 0.00	
UMP	1	6.0	0.70 ± 0.01	0.60 ± 0.00	0.37 ± 0.01
	2		0.83 ± 0.01	0.76 ± 0.00	0.52 ± 0.00

[a] Conditions: [complex] = 1×10^{-3} mol dm^{-3}; ionic strength = 0.1 mol dm^{-3}; temperature = 25 °C; wavelength = 340 nm. [b] Preadjusted except for natural pH 5.4 in the case of AMP (cf. Experimental Section).

independent of $[Cl^-]$. Since the slope of such lines can be related to the anation reaction path, which is quite dependable on $[Cl^-]$, the constancy of the slopes is pointing toward a reaction other than the anation reaction observed with the free bases and the nucleosides. The $[Cl^-]$ dependence of the intercept, which can be related to the reverse aquation path, can be interpreted in the same way as for the corresponding free bases and nucleosides.

The exact nature of the secondary reaction observed with the nucleotides as incoming ligand is still to be established. A realistic possibility is that the phosphate-bonded nucleotide complex produced in the primary (not observed) process undergoes ring closure or a reaction with a second nucleotide molecule (see work performed by Reily and Marzilli in ref 8f). This requires ring opening of the dien ligand, a feature that has only been observed

for similar complexes in which S-bonded ligands are present.[19] The [L] dependence of the data suggests the secondary reaction to be a substitution process, the intercept being due to either the reverse solvolysis step or a parallel dissociative ring-opening reaction of the dien ligand followed by a non-rate-determining substitution step.

To summarize, the principal feature of the reactions involving the nucleic free bases and the nucleosides is that, contrary to normal square-planar substitution, the solvolysis of $Pd(dien)Cl^+$ is not the rate-determining step but the subsequent anation of $Pd(dien)OH_2^{2+}$ is instead. The spontaneous solvolysis preceding the rate-determining anation can, depending on the relative magnitudes of k_1, $k_{-1}[Cl^-]$, and $k_{an}[L]$ (cf. Scheme I), either be treated as a preequilibration (k_1, $k_{-1}[Cl^-] > k_{an}[L]$, eq 3, Figure 4) or a steady-state controlling step (k_1, $k_{-1}[Cl^-] \sim k_{an}[L]$, eq 4, Figure 5), a change-over between the two for a given nucleic moiety being effected by a sufficient change in its concentration. The reverse aquation following the rate-determining anation becomes sufficiently significant in a few cases (Figures 3 and 6) to contribute to the observed rate constant (eq 1 and 6) and competes in the presence of chloride ion with a reaction that probably involves ion pairing (cf. Scheme II). The rate-determining step of the reactions involving the 5′-nucleotides is neither spontaneous solvolysis nor subsequent anation but a secondary substitution that is still to be identified. The mentioned anation, reverse aquation, and other subsequent reactions are expected to play an important role in the intimate mechanism of the interaction of related antitumor complexes with nucleic acid moieties. The approach of various authors, for instance, to slow down the reactions of *cis*-$[Pt(NH_3)_2Cl_2]$ with AMP and GMP by studying them in a large excess of chloride[4e,8c] had been based on the supposition that hydrolysis of *cis*-$[Pt(NH_3)_2Cl_2]$ is the rate-determining step[21] and that this hydrolysis is hampered by high chloride ion concentrations,[2,8a] but we arrived at a different explanation for the retardation in view of our results. Similarly, some other aspects that may contribute to the fundamental understanding of the substitution behavior of related antitumor complexes are being investigated in more detail in our laboratories.

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Registry No. A, 73-24-5; C, 71-30-7; G, 73-40-5; I, 68-94-0; T, 65-71-4; U, 66-22-8; AMP, 61-19-8; CMP, 63-37-6; GMP, 85-32-5; IMP, 131-99-7; TMP, 365-07-1; UMP, 58-97-9; $Pd(dien)OH_2^{2+}$, 53773-87-8; $Pd(dien)Cl^+$, 17549-31-4.

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Two-Electron Transfer Accompanied by Metal–Metal Bond Formation. Synthesis and Electrochemistry of Dinuclear Molybdenum and Tungsten Carbonyl Thiolates

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The binuclear, thiolate-bridged complexes $[Et_4N]_2[M_2(CO)_8(SR)_2]$ (M = Mo, W; R = Ph, *t*-Bu, Bz) (**1**), are prepared by refluxing $M(CO)_6$ with $[Et_4N]SR$ in acetonitrile. On the basis of analytical, spectroscopic, and conductometric data, they are characterized as 2:1 electrolytes with the dinuclear dianions consisting of two metal(0)–$(CO)_4$ fragments bridged by two μ-SR moieties. The complexes are converted to the corresponding M^I_2 dimers, $M_2(CO)_8(SR)_2$ (**2**), by two-electron electrochemical oxidation (in a single step) (eq i) or treatment with a mild chemical oxidant, to the solvolyzed M^I_2 dimers, $M_2(CO)_6(MeCN)_2(SR)_2$ (**3**), by

$$[M_2(CO)_8(SR)_2]^{2-} \rightleftharpoons [M_2(CO)_8(SR)_2] + 2e^- \quad \text{(i)}$$

oxidation in acetonitrile, and to the monomeric M^0 species, $[M(CO)_5(SR)]^-$ (**4**) (for M = Mo, R = Ph, *t*-Bu), by treatment with excess CO. Interconversion of **1**–**4** by means of redox, solvolysis, and carbonylation reactions and the influence of the solvolysis and carbonylation reactions on electrode reactions (eq i) are described. Oxidation of the M^0_2 to the M^I_2 dimers is accompanied by formation of a single metal–metal bond and significant rearrangement within the $M_2(SR)_2$ core. These changes apparently supply the driving force that enables two-electron transfer to occur in a single step. Comparisons with structurally analogous compounds indicate that contractions of ~1.0 Å in the M–M bond distance and of ~25° in the M–S–M bridge angle accompany $M^0_2 \rightarrow M^I_2$ oxidation. Despite these large displacements in nuclear coordinates, electrode reaction i exhibits Nernstian two-electron behavior by cyclic voltammetry at 0.1 V s^{-1}. This kinetically facile behavior suggests that the nuclear rearrangement involved in conversion of $[M_2(CO)_8(SR)_2]^{2-}$ to $M_2(CO)_8(SR)_2$ is concerted in such a way that a low activation energy barrier is presented to electron transfer.

Introduction

The reactions of thiols and thiolates with metal complexes have received increasing attention in the recent literature. In particular, the chemistry of molybdenum with these reagents has come increasingly under study, with virtually all oxidation states (0–VI) of this metal represented. Mo–SR bonding usually is accompanied in the higher oxidation states by coordination of strong π-donor oxo ligands to the metal and in the lower oxidation states by the presence of π-acceptor ligands such as CO. These coligands provide favorable conditions for Mo–SR binding by moderating the effective nuclear charge of the metal. Compounds with an exclusively Mo–SR coordination shell are known but occur in a smaller number of cases. Examples[1–6] of various oxidation levels

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