Monatshefte für Chemie 138, 1–11 (2007)
DOI 10.1007/s00706-006-0568-z
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Thermodynamic and Kinetic Studies on Reactions of Pt(II) Complexes with Pyrazole, Pyridazine, and 1,2,4-Triazole

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Received April 6, 2006; accepted (revised) June 19, 2006
Published online December 14, 2006 © Springer-Verlag 2006

Summary. Substitution reactions of the complexes $[Pt(\mathit{dien})H_2O]^{2+}$ and $[PtCl(\mathit{dien})]^+$, where *dien* = diethylentriamine or 1,5-diamino-3-azapentane, with some nitrogen-donor ligands such as 1,2,4-triazole, pyrazole, and pyridazine, were studied in an aqueous 0.10 *M* $NaClO_4$ at *pH* = 2.5 using variable-temperature spectrophotometry and ^1H NMR spectroscopy. The second-order rate constants indicate that the aqua complex, $[Pt(\mathit{dien})H_2O]^{2+}$, is more reactive than the corresponding chloro complex, $[PtCl(\mathit{dien})]^+$. The reactivity of the used ligands follows the order: 1,2,4-triazole > pyridazine > pyrazole. Activation parameters were determined for all reactions and the negative entropies of activation ($\Delta S^{\neq}$) support an associative ligand substitution mechanism.

Keywords. Platinum(II); Kinetics; Mechanism; Azoles; Diazines.

Introduction

In the last a few years our work has been concentrated on the study of reactions of different Pd(II) and Pt(II) complexes with sulphur- and nitrogen-bonding nucleophiles including some biomolecules [1–6]. These interactions could be very important not only from the fundamental point of view. Since some Pt(II) complexes have been used as anticancer drugs [7], these interactions are also very important in biology and medicine. Coordination compounds of Pd(II) and Pt(II) with tridentate ligands such as diethylentriamine (*dien*), bis(2-pyridylmethyl)amine (*bpma*) or 2,2′:6′,2″-terpyridine (*terpy*) provide very useful substrates for studies on ligand substitution reactions of square-planar complexes. However, these tridentate ligands form very stable mononuclear complexes with Pd(II) and Pt(II) even in very acidic *pH* [8, 9].

The five-membered ring containing two or three nitrogen atoms (azoles) were found to be of great interest from a bioinorganic chemistry point of view, since the

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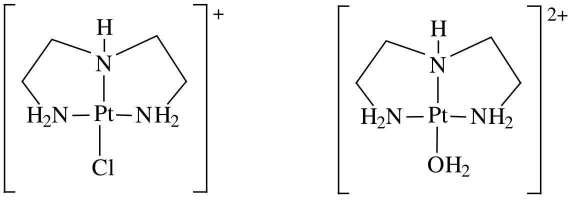
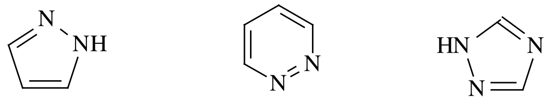


$[PtCl(dien)]^+$ **$[Pt(dien)(H_2O)]^{2+}$**



pyrazole **pyridazine** **1,2,4-triazole**

Formulae 1

imidazole group of histidine acts as a ligand in most of the known haemoproteins [10]. Moreover, azoles were found to inhibit the binding of CO to the sodium dithionite-reduced ferrous cytochrome and the activity of reconstituted P-450 by binding to cytochrome in a one-to-one stoichiometry. Imidazole derivatives and 1,2,4-triazole [11] are considered to be of potential interest to coordination chemists because they can be used to link studies on the metal binding properties of nitrogenous bases with information on the proton affinities in the gas phase [12, 13], in aqueous solutions and aprotic solvents [14], and on their H-bonding capacities [15].

Recently we published the results of complex-formations between Pd(II) complexes with azoles and diazines [16]. As an extension of that work we studied and report here the kinetics of the complex-formation between monofunctional $[Pt(dien)H_2O]^{2+}$ and $[PtCl(dien)]^+$ complexes with nitrogen-donor ligands, such as 1,2,4-triazole, pyrazole, and pyridazine, in an aqueous $0.10\,M$ $NaClO_4$. All reactions were studied as a function of nucleophile concentration and temperature. The reactions on $[Pt(dien)H_2O]^{2+}$ were studied at $pH = 2.5$, while the substitution on the chloro complex was studied in the presence of $5\,mM$ NaCl. The studied reactions can be presented by Eqs. (1) and (2).

$$[Pt(dien)H_2O]^{2+} + L \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} [Pt(dien)L]^{2+} + H_2O \qquad (1)$$

$$[PtCl(dien)]^{+} + L \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} [Pt(dien)L]^{2+} + Cl^- \qquad (2)$$

The structures of the complexes and ligands are shown as Formulae 1.

Results and Discussion

The observed pseudo-first-order rate constants, k_{obsd}, as a function of the total concentration of nucleophile are described by Eq. (3) for reaction (1).

$$k_{obsd} = k_{-1} + k_1[\text{nucleophile}] \qquad (3)$$

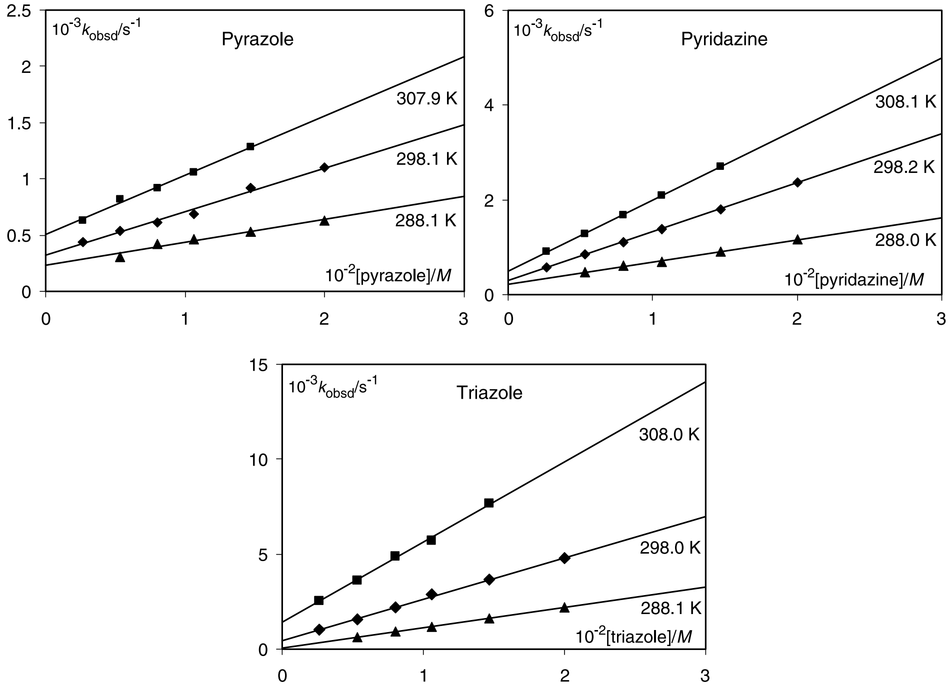


Fig. 1. Observed *pseudo*-first order rate constants, k_{obsd}, as a function of ligand concentration and temperature for the substitution reactions on $[Pt(dien)(H_2O)]^{2+}$ complex in $0.10\,M$ $NaClO_4$ at $pH = 2.5$

A least-squares fit of the data according to Eq. (3), resulted in values for the forward anation rate constants (k_1) and the reverse aquation rate constant (k_{-1}) according to reaction (1). The second-order rate constants (k_1) were obtained directly from the slope from plot of k_{obsd} *vs.* entering nucleophile concentration [17]. The experimental results are summarized in Fig. 1, and rate constants and activation parameters for reaction (1) are given in Table 1.

In the case of the chloro complex $[PtCl(dien)]^+$, reaction (2) proceeds according to two parallel associative reaction paths [17]. One involves the rate-determining formation of a solvento-complex (k_3-path in Scheme 1) followed by rapid substitution of the coordinated solvent molecule (S). The other reaction involves direct nucleophilic attack by the entering ligand (k_2-path in Scheme 1).

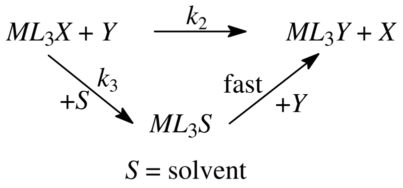
The observed pseudo-first order rate constant (k_{obsd}) as a function of the total concentration of entering nucleophile is given by Eq. (4).

$$k_{obsd} = k_3 + k_2[\text{nucleophile}] \qquad (4)$$

The solvolysis rate constant (k_3) independent of the concentration of L, is usually small and contributes little to the observed rate. It can be determined from the intercept of the graph of k_{obsd} *vs.* $[L]$. The second-order rate constants (k_2) characterizing the formation of the product complex, can be evaluated from the slope of a plot k_{obsd} *vs.* $[L]$. All reactions of the chloro complex were studied in the presence of a slight excess of chloride ions (5 mM) to suppress spontaneous solvolysis reactions. The experimental results for the displacement of chloride from

Table 1. Rate constants and activation parameters for the substitution reactions of monofunctional Pt(II) complexes in 0.10 *M* NaClO4

	λ / nm	T / K	10^2k_2 / $M^{-1}\,s^{-1}$	10^4k_3 / s^{-1}	$\Delta H^{\neq}$ / kJ mol^{-1}	$\Delta S^{\neq}$ / JK^{-1}mol^{-1}
			$[PtCl(dien)]^+$			
Pyrazole	290	288.0	0.45 ± 0.05	1.61 ± 0.06	22 ± 2	-215 ± 6
		298.0	0.67 ± 0.04	2.15 ± 0.05		
		308.0	0.88 ± 0.08	2.91 ± 0.08		
Pyridazine	440	288.0	0.73 ± 0.06	1.38 ± 0.07	28 ± 6	-190 ± 20
		298.2	1.29 ± 0.07	2.31 ± 0.08		
		308.1	1.71 ± 0.07	3.27 ± 0.07		
1,2,4-Triazole	330	288.0	4.15 ± 0.04	4.14 ± 0.05	30 ± 4	-165 ± 11
		298.1	7.12 ± 0.03	5.39 ± 0.04		
		308.0	10.10 ± 0.20	7.07 ± 0.03		
			$[Pt(dien)(H_2O)]^{2+}$			
	λ / nm	T / K	10^2k_1 / $M^{-1}\,s^{-1}$	10^4k_{-1} / s^{-1}	$\Delta H^{\neq}$ / kJ mol^{-1}	$\Delta S^{\neq}$ / JK^{-1}mol^{-1}
Pyrazole	280	288.1	2.04 ± 0.02	2.31 ± 0.03	33 ± 7	-163 ± 22
		298.1	3.88 ± 0.02	3.20 ± 0.03		
		307.9	5.25 ± 0.03	5.09 ± 0.03		
Pyridazine	285	288.0	4.68 ± 0.02	2.22 ± 0.02	41 ± 8	-129 ± 26
		298.2	10.30 ± 0.11	2.87 ± 0.01		
		308.1	15.01 ± 0.20	4.90 ± 0.02		
1,2,4-Triazole	260	288.1	10.6 ± 0.1	0.68 ± 0.02	49 ± 1	-94 ± 3
		298.0	21.8 ± 0.5	4.56 ± 0.06		
		308.0	42.2 ± 0.2	14.1 ± 0.1		



Scheme 1

$[PtCl(dien)]^+$ are also summarized in Table 1, and presented in Fig. 2. As can be seen, in all cases k_{obsd} depends linearly on the entering ligand concentration.

The coordinated water molecule on Pd(II) and Pt(II) centres has been shown to be very labile and can easily be substituted by stronger nucleophiles [18]. Indeed, the aqua complex, $[Pt(dien)H_2O]^{2+}$, is much more reactive than the corresponding chloro complex, $[PtCl(dien)]^+$ (see Table 1).

The kinetic data clearly show that these nitrogen-containing nucleophiles are very good entering ligands for Pt(II) complexes. From a comparison of the reactivity (Table 1) it can be concluded that 1,2,4-triazole (five-membered ring) is the most

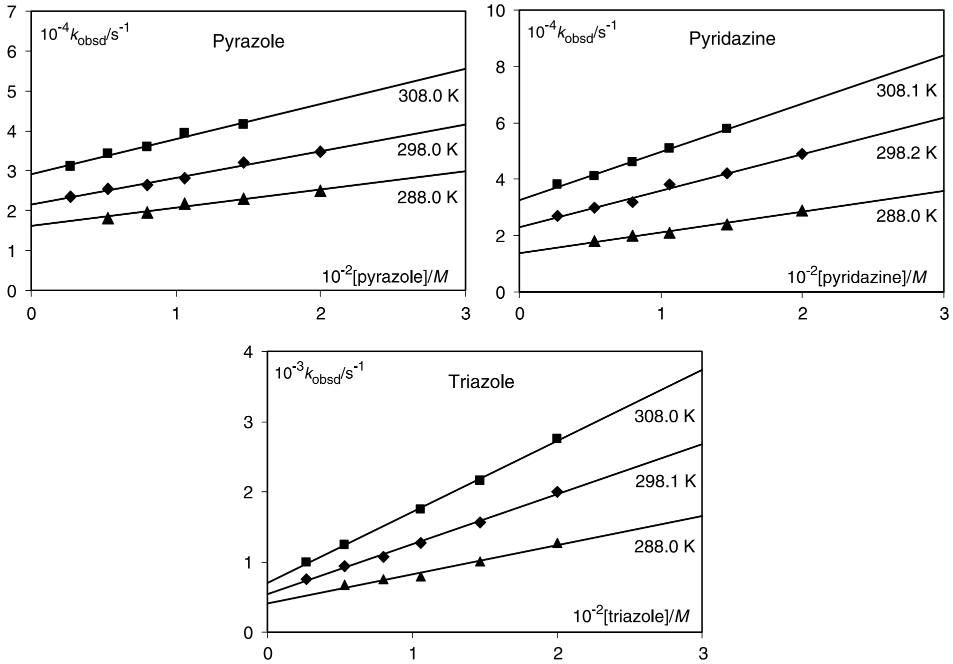


Fig. 2. Observed *pseudo*-first order rate constants, k_{obsd}, as a function of ligand concentration and temperature for the substitution reactions on $[PtCl(\textit{dien})]^+$ complex in 0.10 M $NaClO_4$, $[Cl^-] = 5$ mM

reactive ligand. Pyridazine (six-membered ring) is more reactive than pyrazole. This order of reactivity is in relation with their acidity. The pK_a values for the used ligands are: 2.30 for 1,2,4-triazole, 2.33 for pyridazine, and 2.52 for pyrazole [19].

These results are in agreement with the already published results with Pd(II) complexes [16]. Of course, Pd(II) complexes are much more reactive than Pt(II) complexes. The difference in the reactivity of the nucleophiles used can be explained in terms of electronic effects. However, the sensitivity of the reaction rate on the entering ligands is in line with that expected for an associative mode of activation.

The second order rate constants were studied as a function of temperature. The obtained activation parameters, $\Delta H^{\neq}$ and $\Delta S^{\neq}$, are summarized in Table 1. All available activation parameters support the operation of an associative mechanism [17]. The significantly negative activation entropies for the forward reactions (1) and (2) suggest that the activation process in the studied systems seems to be strongly dominated by formation [17]. The results are in an excellent agreement with similar data reported for related systems [16].

NMR Results

The substitution reaction of the $[PtCl(\textit{dien})]^+$ complex with 1,2,4-triazole was also studied by ^{1}H NMR spectroscopy as *pseudo*-first order reaction with large excess of the nucleophile. The chemical shifts from the *dien*-system of unreacted $[PtCl(\textit{dien})]^+$ complex are between 2.9–3.2 ppm. On the other hand, the chemical shifts of the *dien*-system from the substituted product are between 3.2–3.4 ppm. The downfield moving of these signals is the result of changed chemical environ-

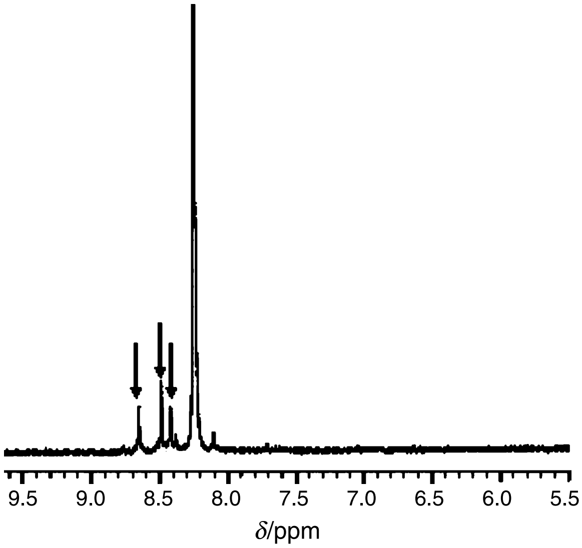


Fig. 3. ^{1}H NMR spectra of the reaction of $[PtCl(\textit{dien})]^+$ and 1,2,4-triazole

ment of the tridentate ligands caused by substitution of the chloro ligand. The ^{1}H NMR spectra of the substitution reaction of the $[PtCl(\textit{dien})]^+$ with studied nucleophile is presented in the Fig. 3.

The NMR spectra of five-membered 1,2,4-triazole consists of one singlet at 8.37 ppm, what is evidence of the presence of two CH-groups shaped with nitrogen atoms. In the process of substitution of the $[PtCl(\textit{dien})]^+$ complex with 1,2,4-triazole theoretically two types of products can be obtained. One when the platinum is coordinated through the N(1) or N(2) atoms, and the other with the coordination *via* N(4). First product of coordination will give two different signals in ^{1}H NMR spectra because the influence of metal ion is not equal for both protons. The other way of reaction will give only one signal. The obtained signals of products are at 8.55, 8.61, and 8.80 ppm. Taking into account the chemical shifts, and the intensity of these signals it can be concluded that the signal at 8.61 ppm corresponded to product where the platinum is coordinated to N(4). Other two equal-intensity singlets, at 8.55 and 8.80 ppm, present the chemical shifts of protons when the platinum is coordinated *via* N(1) or N(2) atoms.

Materials and Methods

Chemicals and Solutions

The complex $[PtCl(\textit{dien})]Cl$ was prepared as described in the literature [20]. The chemical analysis, UV-VIS spectra, and ^{1}H NMR spectral data were in good agreement with those obtained in earlier preparations [1–3]. The chloro complex was converted into the aqua analogues in solution by addition of an equivalent of $AgClO_4$, heating to 40°C for 1 h, and removing the AgCl precipitate by filtration through a 0.1 μm pore membrane filter. Great care was taken to ensure that the resulting solution was free of Ag^+ ions. Since perchlorate ions do not coordinate to

Pt(II) [21], the kinetics of the complex formation reactions were studied in perchlorate medium. The ionic strength of the solutions was adjusted to $0.10\,M$ with $NaClO_4$ (Merck, pa). The complex, $[Pt(dien)H_2O]^{2+}$ was stable under selected experimental conditions ($pH = 2.5$), and the hydrolysis of the complex was negligible [22]. The reactions of the chloro complex were also studied at $pH = 2.5$, adjusted in a similar way as for the aqua complex, only to the solutions of the chloro complex 5 m*M* NaCl was added to prevent solvolysis. Ligand stock solutions were prepared without further purification shortly before use by dissolving the chemicals: 1,2,4-triazole (Fluka), pyrazole and pyridazine (Acros). Highly purified, deionised water was used in the preparation of all solutions.

Kinetic Measurements

Spectral changes resulting from mixing Pt(II) complex and ligand solutions were recorded over the wavelength range 220–550 nm to establish a suitable wavelength at which kinetic measurements could be performed. The kinetics of the substitution of coordinated water or chloro were followed spectrophotometrically by monitoring the change in absorbance at suitable wavelengths. Reactions were initiated by adding $0.5\,cm^3$ of Pt(II) complex solution to $2.5\,cm^3$ of thermostated ligand solution in the UV-VIS spectrophotometric cell, and they were followed for at least 8 half-lives. Complex formation was monitored as an increase in absorbance for pyrazole at 290 nm, for pyridazine at 285 nm, and as a decrease in absorbance at 260 nm for 1,2,4-triazole. The reactions were studied under *pseudo*-first order conditions with ligand at least in a 10-fold excess. The ionic strength of the reaction mixtures was kept constant at $0.10\,M$ with $NaClO_4$ and *pH* was 2.5. The temperature was controlled throughout all kinetic experiments to $\pm 0.1^\circ C$.

The observed *pseudo*-first order rate constants, k_{obsd}, were calculated as the average value from two to three independent kinetic runs. Observed experimental data are reported in Tables A1–A6 (Appendix) and are summarized in Figs. 1 and 2.

NMR Measurements

NMR measurements were performed by a Varian Gemini 200 MHz spectrometer. Reactions were carried out in a NMR tube. D_2O (Aldrich Chemical Company, Inc) was used as a solvent. The chemical shifts were reported in ppm relative to *TSP* (sodium trimethylsilylpropane-3-sulphonate, $\delta = 0$). The reactions were studied at 298 K.

pD measurements were also performed at 298 K. The *pH* meter was calibrated with Fischer-certified buffer solutions of $pH = 4.00$, 7.00, and 11.00. Meter readings were corrected for the deuterium isotope effect by adding 0.4 units to the display readout. The *pD* was adjusted with $0.01–0.05\,M$ solutions of NaOD and DCl.

Acknowledgements

The authors gratefully acknowledge financial support from the Ministry of Science of Republic of Serbia (Project No: 142008Б). Also, the authors sincerely thank Mrs. *B. Mojsilović* for the NMR experiments.

Appendix

Table A1. Observed *pseudo*-first order rate constants as a function of ligand concentration and temperature for the reaction between $[Pt(dien)](H_2O)]^{2+}$ complex and pyridazine in 0.1 M $NaClO_4$, $pH = 2.5$

T/K	$10^{-2}\, c_{pyrazole}/M$	$10^{-3}\, k_{obsd}/s^{-1}$
288.1	0.53	0.31(6)
	0.80	0.42(6)
	1.06	0.46(6)
	1.47	0.53(5)
	2.00	0.63(6)
298.1	0.27	0.44(6)
	0.53	0.54(6)
	0.80	0.61(5)
	1.06	0.69(5)
	1.47	0.92(6)
	2.00	1.10(5)
307.9	0.27	0.63(6)
	0.53	0.82(5)
	0.80	0.92(5)
	1.06	1.06(6)
	1.47	1.28(5)

Table A2. Observed *pseudo*-first order rate constants as a function of ligand concentration and temperature for the reaction between $[Pt(dien)(H_2O)]^{2+}$ complex and pyridazine in 0.1 M $NaClO_4$, $pH = 2.5$

T/K	$10^{-2}\, c_{pyridazine}/M$	$10^{-3}\, k_{obsd}/s^{-1}$
288.0	0.53	0.48(6)
	0.80	0.61(5)
	1.06	0.69(5)
	1.47	0.90(5)
	2.00	1.17(4)
298.2	0.27	0.57(6)
	0.53	0.84(5)
	0.80	1.11(5)
	1.06	1.38(4)
	1.47	1.79(5)
	2.00	2.37(4)
308.1	0.27	0.91(5)
	0.53	1.28(4)
	0.80	1.67(5)
	1.06	2.09(4)
	1.47	2.71(4)

Table A3. Observed *pseudo*-first order rate constants as a function of ligand concentration and temperature for the reaction between $[Pt(dien)(H_2O)]^{2+}$ complex and 1,2,4-triazole in 0.1 M $NaClO_4$, $pH = 2.5$

T/K	$10^{-2}\, c_{\text{triazole}}/M$	$10^{-3}\, k_{\text{obsd}}/s^{-1}$
288.1	0.53	0.65(5)
	0.80	0.91(5)
	1.06	1.18(6)
	1.47	1.62(5)
	2.00	2.20(6)
298.0	0.27	1.03(6)
	0.53	1.56(5)
	0.80	2.19(5)
	1.06	2.87(4)
	1.47	3.67(5)
	2.00	4.77(5)
308.0	0.27	2.53(6)
	0.53	3.63(5)
	0.80	4.90(4)
	1.06	5.74(4)
	1.47	7.66(5)

Table A4. Observed *pseudo*-first order rate constants as a function of ligand concentration and temperature for the reaction between $[PtCl(dien)]^{+}$ complex and pyrazole in 0.1 M $NaClO_4$ $[Cl^-] = 5\,mM$

T/K	$10^{-2}\, c_{\text{pyrazole}}/M$	$10^{-4}\, k_{\text{obsd}}/s^{-1}$
288.0	0.53	1.82(6)
	0.80	1.97(6)
	1.06	2.17(5)
	1.47	2.31(6)
	2.00	2.50(5)
298.0	0.27	2.34(6)
	0.53	2.54(5)
	0.80	2.65(5)
	1.06	2.81(5)
	1.47	3.21(6)
	2.00	3.47(4)
308.0	0.27	3.10(5)
	0.53	3.42(5)
	0.80	3.61(6)
	1.06	3.94(5)
	1.47	4.15(4)

Table A5. Observed *pseudo*-first order rate constants as a function of ligand concentration and temperature for the reaction between $[\mathrm{PtCl}(dien)]^+$ complex and pyridazine in 0.1 M $\mathrm{NaClO_4}$, $[\mathrm{Cl^-}] = 5\,\mathrm{m}M$

T/K	$10^{-2}\,c_{\mathrm{pyridazine}}/M$	$10^{-4}\,k_{\mathrm{obsd}}/\mathrm{s}^{-1}$
288.0	0.53	1.8(6)
	0.80	2.0(6)
	1.06	2.1(5)
	1.47	2.4(5)
	2.00	2.9(6)
298.2	0.27	2.7(6)
	0.53	3.0(5)
	0.80	3.2(5)
	1.06	3.8(6)
	1.47	4.2(5)
	2.00	4.9(5)
308.1	0.27	3.8(6)
	0.53	4.1(6)
	0.80	4.6(5)
	1.06	5.1(5)
	1.47	5.8(4)

Table A6. Observed *pseudo*-first order rate constants as a function of ligand concentration and temperature for the reaction between $[\mathrm{PtCl}(dien)]^+$ complex and 1,2,4-triazole in 0.1 M $\mathrm{NaClO_4}$, $[\mathrm{Cl^-}] = 5\,\mathrm{m}M$

T/K	$10^{-2}\,c_{\mathrm{triazole}}/M$	$10^{-3}\,k_{\mathrm{obsd}}/\mathrm{s}^{-1}$
288.0	0.53	0.67(6)
	0.80	0.75(6)
	1.06	0.80(6)
	1.47	1.01(5)
	2.00	1.27(5)
298.1	0.27	0.76(6)
	0.53	0.94(5)
	0.80	1.07(5)
	1.06	1.27(6)
	1.47	1.56(5)
	2.00	2.00(4)
308.0	0.27	1.00(5)
	0.53	1.25(5)
	1.06	1.75(4)
	1.47	2.16(5)
	2.00	2.76(4)

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