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Influence of Solvent on Ligand-Substitution Reactions of Pt^{II} Complexes as Function of the π-Acceptor Properties of the Spectator Chelate

Christian F. Weber[a] and Rudi van Eldik*[a]

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A detailed kinetic study of the substitution reactions of $[Pt^{II}(L^3)Cl]^+$ complexes, where L^3 represents a tridentate N-donor chelate which contains different numbers of π-acceptor pyridine units, with thiourea as a function of nucleophile concentration, temperature and pressure was undertaken in a series of solvents of different polarity, viz. 1-pentanol, 1-propanol, ethanol, methanol and water. The substitution behaviour of $[Pt(diethylenetriamine)Cl]^+$ (**aaa**), $[Pt\{2,6\text{-bis(aminomethyl)pyridine}\}Cl]^+$ (**apa**), $[Pt\{bis(2\text{-pyridylmethyl)amine}\}Cl]^+$ (**pap**) and $[Pt(terpy)Cl]^+$ (**ppp**) was studied in the selected solvents. In the case of alcoholic solutions, an increase in the substitution rate with increasing length of the carbon chain was observed, which is ascribed to the possible role of van der Waals forces in stabilizing the transition state. In the case of methanol and water as solvent, the second-order rate constants correlate with the polarity of the solvent. The activation parameters for the substitution of the **aaa**, **apa**, **pap**, and **ppp** complexes in methanol and water were determined, from which evidence for an associative mechanism was obtained. The introduction of π-acceptor ligands leads to a higher electrophilicity of the platinum(II) centre and consequently a higher lability of the complex. The reactivity of the complexes is controlled by a combination of solvent and π-acceptor effects.

Introduction

We are interested in the effect of solvent on ligand-substitution reactions of Pt^{II} complexes because of the high activity of some Pt complexes against certain tumour cells.[1] For this reason ligand-substitution reactions of square-planar (low-spin d^8) Pt^{II} complexes are among the best investigated dynamic processes in chemistry.[2] Up to now the kinetic and thermodynamic data show that in nearly all cases the substitution mechanism has an associative character,[2,3] according to which the entering ligand forms a bond with the metal centre prior to bond cleavage with the leaving group, which involves an increase in the coordination number of the Pt centre from four (square-planar) to five (trigonal-bipyramidal) in the transition state. In some rare cases ligand-substitution reactions on Pt^{II} complexes follow a dissociative reaction mechanism.[4–6]

The rate constants for such ligand-substitution reactions vary considerably and depend on the nature of the solvent, entering nucleophile, spectator ligand, leaving group, charge on the complex and pH. For a series of (aqua)Pt^{II} complexes with a varying number of π-acceptor ligands (viz. pyridine ligands), it was shown that the π-acceptor effect controls the substitution rate since it causes a decrease in the electron density and an increase in electrophilicity of the Pt^{II} centre.[7] Kotowski et al. determined rate and activation parameters for the reaction of *trans*-$[Pt(py)_2(NO_2)Cl]$ with pyridine in nitromethane, methanol, ethanol and dichloromethane.[8,9] The solvent dependence of the activation volume, $\Delta V^{\neq}$, could be used to separate intrinsic and solvational volume contributions which result from changes in bond lengths and angles, and changes in polarity, dipole interactions and electrostriction during formation of the transition state of the reaction, respectively. Such information is crucial for a full understanding of the intimate nature of the substitution mechanism.[8,9]

In this paper we report the effect of solvent on ligand-substitution reactions of Pt^{II} complexes as a function of the π-acceptor properties of the spectator chelate. The investigated reaction is given in Equation (1).

$$[Pt(L^3)Cl]^+ + TU \xrightarrow{k_2} [Pt(L^3)TU]^{2+} + Cl^- \qquad (1)$$

Thiourea (TU) was used as a neutral entering ligand such that the overall reaction is accompanied by charge creation on which basis a characteristic solvent dependence is to be expected. In addition, formation of the five-coordinate transition state may involve changes in dipole moment which will affect the activation parameters, especially the entropy and volume of activation. The selected Pt^{II} complexes are $[Pt(diethylenetriamine)Cl]^+$ (**aaa**), $[Pt\{2,6\text{-bis(aminomethyl)pyridine}\}Cl]^+$ (**apa**), $[Pt\{bis(2\text{-pyridylmethyl)amine}\}Cl]^+$ (**pap**) and $[Pt(2,2'{:}6',2''\text{-terpyridine})Cl]^+$ (**ppp**), where **a** and **p** represent amine and pyridine, respectively. The structures of the complexes[7] and adopted abbrevi-

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[a] Institute for Inorganic Chemistry, University of Erlangen-Nürnberg,
Egerlandstr. 1, 91058 Erlangen, Germany

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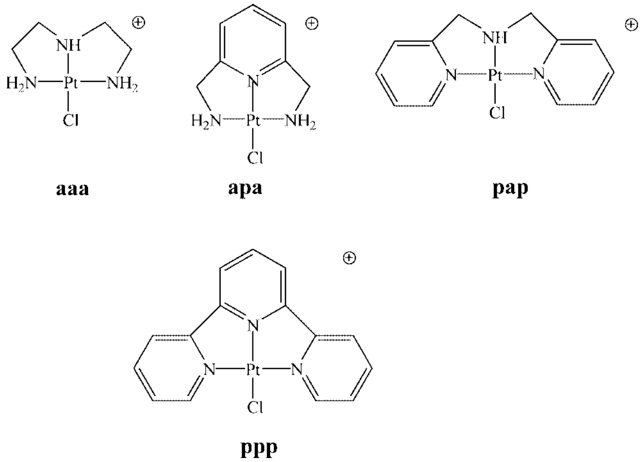
Table 1. The employed solvents and the corresponding dielectric constant ε (25 °C) and boiling points (101.3 kPa).

Solvent	1-Pentanol	1-Propanol	Ethanol	Methanol	Water	Formamide
Dielectric constant	13.9	20.45	24.55	32.66	78.36	109.5
Boiling point [°C]	138	97	78.3	64.5	100	210

ations are summarized in Scheme 1. A series of solvents of different polarity were selected and are summarized in Table 1.[10] We report the effect of the solvent on the π-acceptor properties, activation parameters and polar nature of the transition state for the studied reaction.



Scheme 1.

Results and Discussion

In order to investigate the solvent dependence of ligand-substitution reactions on Pt^{II} complexes as a function of the π-acceptor property of the spectator chelate, a total of four (chloro)Pt^{II} complexes were synthesized and characterized. More information on the crystal structure of the complexes is available from the literature.[7] Solutions of the complexes were prepared by dissolving known amounts of the chloro complexes in the selected solvents in the presence of 0.002 M LiCl in order to prevent spontaneous solvolysis reactions. The solubility of the complexes differed significantly and UV/Vis spectra were recorded to monitor the solvolysis reactions.

The ligand-substitution reactions were studied as a function of the thiourea (TU) concentration, temperature and pressure for the series of solvents. An example of the UV/Vis spectral changes and a representative kinetic trace are shown in Figures 1 and 2, respectively. The wavelengths used to monitor the reactions are listed in Table 2. All kinetic traces showed excellent fits to a single exponential function. We studied the effect of the concentration of trifluoromethanesulfonic acid on the observed rate constants for the substitution reactions of the **apa** complex in water and methanol. In water as solvent, following $k_{\text{obsd.}}$ values were obtained at 25 °C (concentration of trifluoromethanesulfonic acid is given in parentheses): 0.0497 s^{-1} (0.001 M), 0.0439 s^{-1} (0.01 M), and 0.0466 s^{-1} (0.02 M) for [TU] = 0.0274 M. From these results it is clear that no significant protonation of thiourea occurs in water in the acidity range employed in this study. For the same reaction in methanol the following values were found: 0.0151 s^{-1} (0.001 M), 0.0141 s^{-1} (0.01 M), and 0.0125 s^{-1} (0.02 M) for [TU] = 0.0367 M. The observed trend is ascribed to partial protonation of thiourea at higher acid concentrations. Apparently, there is quite some confusion in the literature concerning the protonation constant of thiourea. We have therefore performed a reinvestigation (experimental and theoretical) of the protonation constant of thiourea in different solvents and will report the results separately.[11] Furthermore, the influence of low concentrations of water on the rate constants for the reactions in methanol and propanol was also studied. In methanol as solvent the following $k_{\text{obsd.}}$ values were obtained at 25 °C (vol.% of water is given in parentheses): 0.0141 s^{-1} (as received), 0.01503 s^{-1} (1 vol.%), 0.01514 s^{-1} (2 vol.%), 0.01403 s^{-1} (3 vol.%), 0.01438 s^{-1} (4 vol.%) and 0.01460 s^{-1} (5 vol.%) for [TU] = 0.0367 M. In propanol as solvent the following values were obtained: 0.0212 s^{-1} (as received), 0.0215 s^{-1} (1 vol.%), 0.0205 s^{-1} (2 vol.%), 0.0199 s^{-1} (3 vol.%), 0.0197 s^{-1} (4 vol.%) and 0.0194 s^{-1} (5 vol.%) for [TU] = 0.0265 M. It follows that low concentrations of water have no significant effect on the observed rate constant.

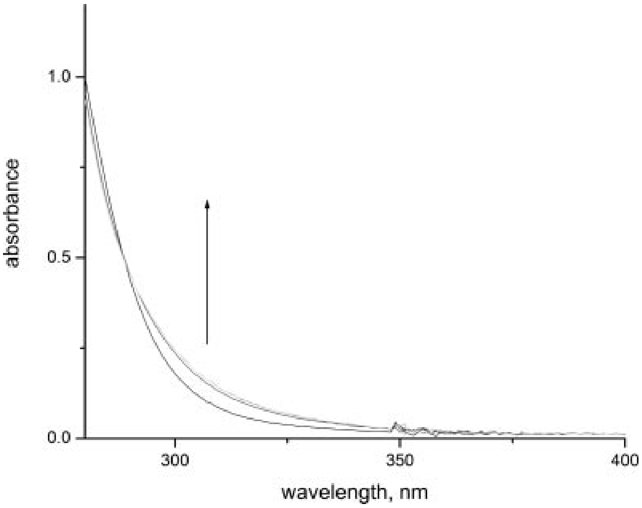


Figure 1. UV/Vis spectral changes recorded for the reaction between the **apa** complex and thiourea in water at 25 °C. The concentrations of **apa** and thiourea are 1.9 × 10^{-4} M and 0.0106 M, respectively.

The observed pseudo-first-order rate constants, $k_{\text{obsd.}}$, were plotted against the thiourea concentration, and for all studied reactions a linear dependence with a negligible in-

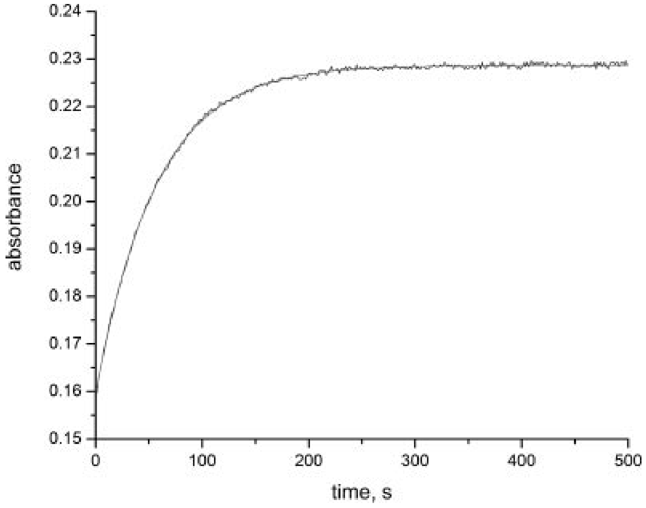


Figure 2. Typical kinetic trace for the reaction between the **apa** complex and thiourea in water at 25 °C. Experimental conditions: [**apa**] = 0.95×10^{-4} M, [TU] = 0.0106 M, 0.002 M LiCl, pH = 2 (0.01 M trifluoromethanesulfonic acid).

Table 2. Summary of the wavelengths [nm] used in the kinetic experiments.

Solvent	Complex			
	aaa	apa	pap	ppp
1-Pentanol	–	300	–	336
1–Propanol	–	300	300	336
Ethanol	–	300	300	333
Methanol	–	300	300	333
Water	300	305	285	336

tercept was observed. Two typical plots are shown in Figures 3 and 4, respectively, from which it follows that $k_{\text{obsd.}}$ can be expressed by Equation (2), where k_2 is the second-order rate constant for the overall reaction in Equation (1). The corresponding plots for all other studied reactions are reported as Supporting Information (see also the footnote on the first page of this article).

$$k_{\text{obsd.}} = k_2\,[\text{TU}] \qquad (2)$$

The values of k_2 for the substitution of chloride by thiourea on complexes of the type $[\text{Pt}^{II}(\text{L}^3)\text{Cl}]^+$ are summarized in Table 3 for the selected solvents. Formamide (FMA) was in general unsuitable as solvent due to the rapid displacement of chloride by the solvent and formation of $[\text{Pt}(\text{L}^3)\text{-FMA}]^{2+}$. Also the substitution reactions of **aaa** in methanol and **pap** in 1-pentanol could not be studied due to the formation of insoluble products. The higher charge on the product led to a decrease in solubility in relative nonpolar solvents. The k_2 values show that the substitution reactions in water and methanol depend on polarity, viz. the k_2 values decrease with decreasing polarity. Changing the solvent from water to methanol causes a fourfold deceleration in the case of **apa**, a sixfold deceleration in the case of **pap** and a twofold deceleration in the case of **ppp**. This can be related to the creation of charge during the overall displacement of the chloride anion by neutral thiourea, viz. leading to a partial increase in polarity in the transition state of the process. According to the Hughes–Ingold rules a decrease in solvent polarity results in a decrease in the rates of those reactions in which the charge density is larger in the activated complex than in the initial reactants. The change to a less polar solvent will decrease the reaction rate when the activated complex is more polar than the initial reactants.[12] In the case of water as solvent the polar transition state is even more stabilized.

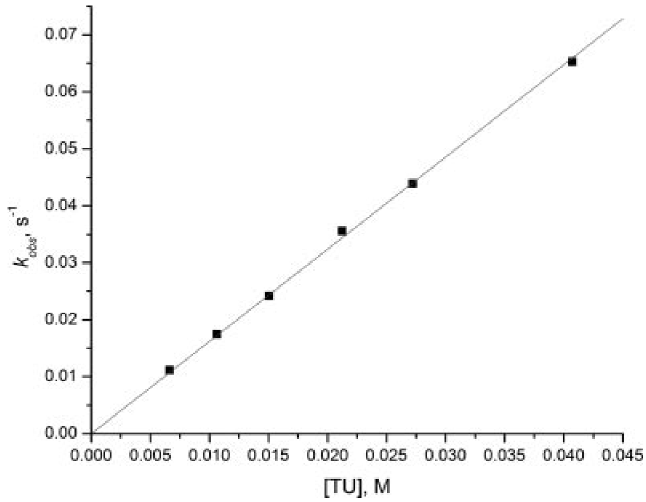


Figure 3. Plot of $k_{\text{obsd.}}$ vs. thiourea concentration for the **apa** complex in water. Experimental conditions: [**apa**] = 1.9×10^{-4} M. 25 °C, 0.002 M LiCl, pH = 2 (0.01 M trifluoromethanesulfonic acid).

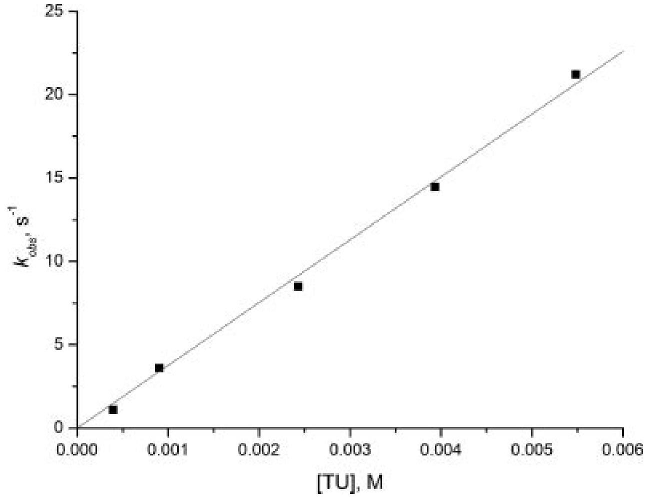


Figure 4. Plot of $k_{\text{obsd.}}$ vs. thiourea concentration for the **ppp** complex in 1-propanol. Experimental conditions: [**ppp**] = 1.16×10^{-4} M. 25 °C, 0.002 M LiCl, 0.01 M trifluoromethanesulfonic acid.

On changing the solvent to methanol, ethanol, 1-propanol and 1-pentanol, an acceleration of all substitution reactions for the complexes **apa**, **pap** and **ppp** was observed. This tendency was also observed by Kotowski et al.[9] for substitution reactions on related Pt^{II} complexes. Various attempts were undertaken to correlate the reported second-order rate constants with physical parameters that describe

Table 3. Summary of the second-order rate constants for the displacement of chloride by thiourea in complexes of the type $[Pt^{II}(L^3)Cl]^+$ in a range of solvents. Experimental conditions: 25 °C, 0.002 M LiCl, pH = 2 (0.01 M trifluoromethanesulfonic acid).

Solvent	k_2 [M^{-1} s^{-1}]			
	aaa	**apa**	**pap**	**ppp**
1-Pentanol	–	0.90 ± 0.03	–[a]	2570 ± 58 2640 ± 80
1-Propanol	–	0.793 ± 0.006	0.878 ± 0.012	3768 ± 71
Ethanol	–	0.410 ± 0.003	0.784 ± 0.010	3323 ± 63
Methanol	–[a]	0.385 ± 0.002	0.588 ± 0.003	1344 ± 21
Water	0.538 ± 0.007	1.62 ± 0.01	3.67 ± 0.02	2797 ± 42

[a] Formation of colloid particles.

the solvent properties. No direct correlation could be found for solvent polarity or the possible influence of hydrogen bonding. Furthermore, no correlation was found between the second-order rate constant and the Kamlet and Taft solvatochromic parameters that measure the solvent hydrogen-bond donor acidity (α), solvent hydrogen-bond acceptor basicity (β) and solvent dipolarity/polarizability (π^*).[13] The only apparently meaningful correlation that could be found is based on the observation that an increase in the van der Waals forces with increasing carbon-chain length of the alcohols seemed to play an important role. With increasing carbon-chain length the van der Waals forces, as indicated by the boiling points of the solvents, increase to the point that they become stronger than the hydrogen bonding network.[14] The boiling points of the employed alcohols are listed in Table 1. A similar trend is observed in the second-order rate constants. A comparison of both trends is shown in Figure 5, from which it is concluded that van der Waals forces apparently contribute significantly to the stabilization of the transition state. A referee suggested that the longer-chain alcohols could behave as nano-micelles with the alcohol portions directed toward the evolving charge centre. In this way the reaction in the higher alcohols could occur inside a polar sphere, not in contact with the non-polar alcohol tails.

It is well known that the rate of associative substitution reactions strongly depend on the nucleophilicity of the entering nucleophile, viz. the stronger the nucleophile, the faster the rate of the substitution reaction. The four complexes **aaa**, **apa**, **pap** and **ppp** show different k_2 values in the same solvent. In water as solvent we obtained a second-order rate constant of 0.54 M^{-1} s^{-1} for the reaction between **aaa** and TU at 25 °C, 1.62 M^{-1} s^{-1} for **apa**, 3.67 M^{-1} s^{-1} for **pap** and 2797 M^{-1} s^{-1} for **ppp** as reactant. In methanol as solvent we found 0.39 M^{-1} s^{-1} for **apa**, 0.59 M^{-1} s^{-1} for **pap** and 1344 M^{-1} s^{-1} for **ppp** as reactant. This shows that the second-order rate constants increase with increasing number of π-acceptor ligands on the spectator chelate. π-Acceptor ligands have the ability to withdraw electron density from the Pt^{II} centre, thus making it more electrophilic for a nucleophilic attack and enabling stabilization of the electron-rich, five-coordinate transition state. This results in a reduction of the activation barrier and an acceleration of the reaction. The π-acceptor effect is also used to account for the unusually high lability of the **ppp** complex. This effect was investigated in more detail for Pt^{II} complexes in which the number of pyridine ligands was varied systematically.[7] The **ppp** complex shows the highest reactivity relative to the corresponding **aaa** complex due to π-back-bonding from the Pt^{II} centre to the empty π*-orbitals of the pyridine moieties of the terpy ligand.

The activation parameters ($\Delta H^{\neq}$, $\Delta S^{\neq}$ and $\Delta V^{\neq}$) were determined for the substitution reaction of the **aaa** complex in water and of the **apa**, **pap** and **ppp** complexes in methanol and water, respectively, and are listed in Table 4. Two representative plots showing typical temperature and pressure

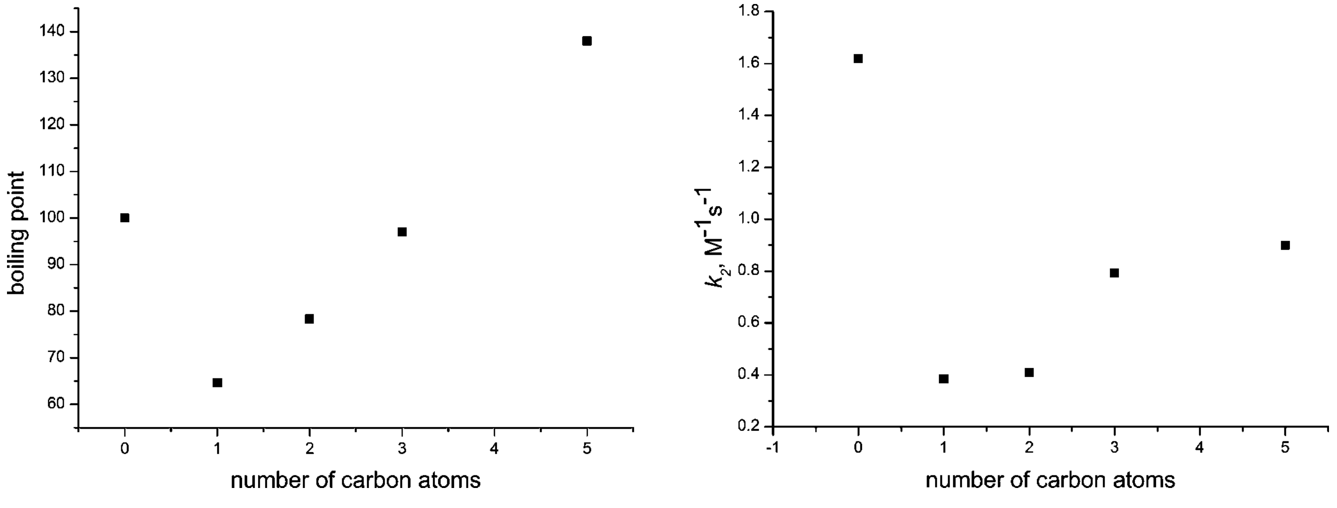


Figure 5. Plots of k_2 and boiling point vs. number of carbon atoms of the employed solvents.

Table 4. Rate and activation parameters for the reaction of the **aaa**, **apa**, **pap**, and **ppp** complexes with thiourea (TU) in water and methanol as solvent at 25 °C.

Complex	Solvent	k_2 [M^{-1} s^{-1}]	$\Delta H^{\neq}$ [kJ mol^{-1}]	$\Delta S^{\neq}$ [J K^{-1} mol^{-1}]	$\Delta V^{\neq}$ [cm^3 mol^{-1}]
aaa	water	0.538 ± 0.007	40 ± 1	-116 ± 4	-5.9 ± 0.2
apa	methanol	0.385 ± 0.002	63 ± 1	-42 ± 4	-6.65 ± 0.06
apa	water	1.62 ± 0.01	49 ± 1	-77 ± 4	-10.4 ± 0.5
pap	methanol	0.588 ± 0.003	55 ± 1	-65 ± 3	–[a]
pap	water	3.67 ± 0.02	46 ± 1	-81 ± 2	-7.0 ± 0.3
ppp	methanol	1344 ± 21	35 ± 1	-67 ± 3	-2.6 ± 0.1
ppp	water	2797 ± 42	29 ± 1	-82 ± 2	–[b]

[a] Not possible to measure. [b] Not possible due to low solubility of **ppp** in water.

dependences are reported in Figures 6 and 7, respectively. The corresponding plots for all other studied reactions are reported as Supporting Information. The acceleration of the substitution reactions by pressure is indicative of an associative substitution mechanism, which is supported by the negative $\Delta S^{\neq}$ values. The decrease in entropy is associated with a highly structured transition state which is accompanied by a decrease in volume due to the compact nature of the transition state as a result of bond formation and an increase in solvation due to an increase in polarity of the transition state.[15]

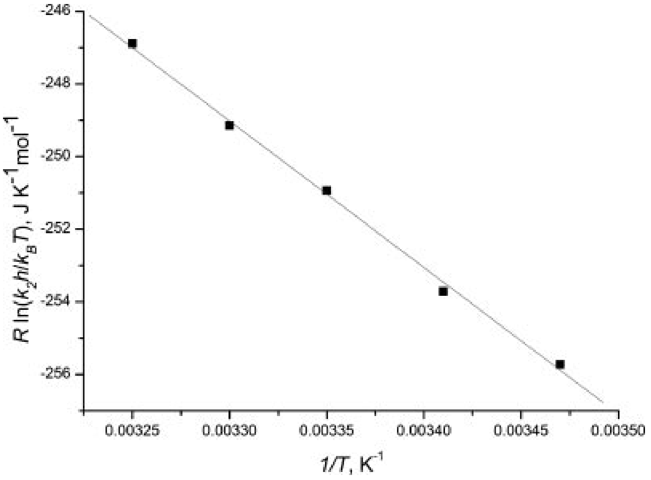


Figure 6. Temperature dependence of the reaction of the **aaa** complex with thiourea in water. Experimental conditions: [**aaa**] = 3.36×10^{-4} M, [TU] = 0.271 M, 0.002 M LiCl, pH = 2 (0.01 M trifluoromethanesulfonic acid).

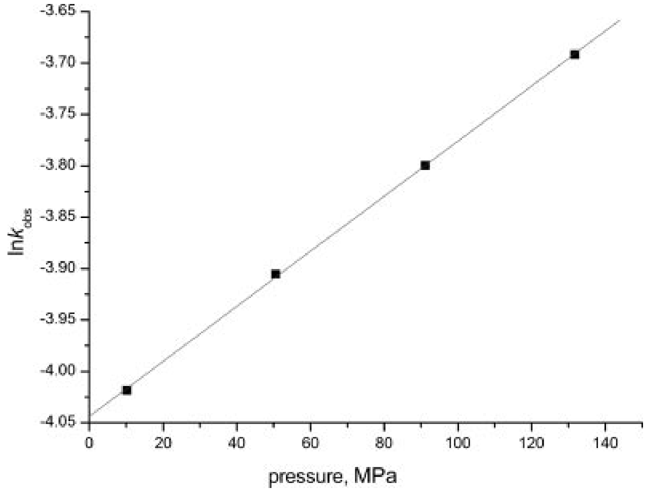


Figure 7. Pressure dependence of the reaction of the **apa** complex with thiourea in methanol. Experimental conditions: [**apa**] = 4.75×10^{-4} M, [TU] = 0.059 M, 25 °C, 0.002 M LiCl, 0.01 M trifluoromethanesulfonic acid.

For all investigated reactions, changing the solvent from methanol to water leads to more negative entropies of activation and in the case of **apa** the volume of activation changes from –6.6 to –10.4 cm^3 mol^{-1}, which corresponds to the tendency shown by the entropies of activation. $\Delta S^{\neq}$ decreases from –42 to –77 J K^{-1} mol^{-1} in the case of **apa**, from –65 to –81 J K^{-1} mol^{-1} for **pap** and from –67 to –82 J K^{-1} mol^{-1} **ppp** on changing the solvent from methanol to water. This can be ascribed to a larger number of highly structured water molecules as compared to the number of structured methanol molecules in the second coordination sphere of the transition state, in which hydrogen bonding plays a major role. Activation volumes were found to be –5.9 cm^3 mol^{-1} for the reaction of **aaa** with TU in water, –7.0 cm^3 mol^{-1} for **pap** in water and –2.6 cm^3 mol^{-1} for **ppp** in methanol. These values parallel the trends in the activation entropies and can be interpreted in a similar way.

As mentioned above, changing the solvent from methanol to water causes an acceleration of all studied reactions. Thus, in general an increase in solvent polarity leads to higher rate constants and lower $\Delta H^{\neq}$ values. We observed a change in $\Delta H^{\neq}$ from 63 to 49 kJ mol^{-1} for the reaction of **apa** with thiourea, from 55 to 46 kJ mol^{-1} for **pap** and from 35 to 29 kJ mol^{-1} for **ppp** on changing the solvent from methanol to water. In the case of **apa**, the decrease in $\Delta H^{\neq}$ is more significant than for **pap** and **ppp** for the two solvents. This must be related to the increase in the number of pyridine ligands which causes an increase in the electrophilicity of the Pt^{II} centre and apparently makes $\Delta H^{\neq}$ less sensitive to the polarity of the solvent.

Conclusions

The effect of solvent on ligand-substitution reactions of Pt^{II} complexes as a function of the π-acceptor property of the spectator chelate was studied systematically. Four mono(chloro)Pt^{II} complexes were synthesized and characterized. A series of solvents were selected as a function of polarity, viz. 1-pentanol, 1-propanol, ethanol, methanol, water, and formamide. The ligand-substitution reactions were studied as a function of the nucleophile (thiourea) concentration, temperature and pressure. Formamide as solvent was ruled out due to the formation of solvento complexes.

In the case of alcohols as solvent, we observed a systematic increase in the second-order rate constant with increasing length of the carbon chain of the alcohol and ascribed it to a possible role of van der Waals forces in stabilizing the transition state of the substitution process. An increase in rate constant was observed in going from methanol to water, which is in line with the expected trend in terms of the polarity of the solvent, viz. a more polar solvent will stabilize the polar transition state formed through the associative attack of the neutral nucleophile. The negative $\Delta S^{\neq}$ and $\Delta V^{\neq}$ values are indicative of an associative substitution mechanism. The magnitude of $\Delta V^{\neq}$ favours the operation of an associative interchange (I_a) mechanism and can be interpreted in terms of an intrinsic volume collapse due to bond formation with the entering nucleophile, accompanied by solvational changes resulting from changes in the polarity of the five-coordinate transition state. In all investigated reactions, a change in polarity from a relative nonpolar to a polar solvent resulted in more negative entropies and volumes of activation. Furthermore, the results suggest that in the case of water as solvent a larger number of structured water molecules are present in the second coordination sphere of the transition state, as compared to the number of structured methanol molecules in the case of methanol as solvent.

The four complexes **aaa**, **apa**, **pap**, and **ppp** showed in the same solvent a steady increase in rate constant with increasing electrophilicity of the platinum centre. The π-acceptor pyridine ligands have the ability to withdraw electron density from the Pt^{II} centre to make it more electrophilic which is accompanied by an increase in rate constant for nucleophilic attack. In the case of the **ppp** complex the rate constant is much less solvent dependent than in the case of the **apa** and **pap** complexes, indicating that a highly electrophilic metal centre will lead to a less polar transition state making the substitution reaction less solvent dependent.

Experimental Section

General: All chemicals used were of analytical reagent grade and of the highest purity commercially available. The ligands diethylenetriamine, bis(2-pyridylmethyl)amine and 2,2′:6′,2′′-terpyridine were purchased from Aldrich. K_2PtCl_4 was obtained from Strem. K_2PtCl_4 was separated from metallic Pt and K_2PtCl_6 by dissolution in water and filtering.[16] All chemicals were used without further purification. Ultra pure water was used for the spectroscopic as well as kinetic measurements. The organic solvents used were of analytical reagent grade (see Results and Discussion).

Synthesis of Complexes

[Pt(diethylenetriamine·HCl)Cl$_2$]: The complex was prepared in a similar way as described by Mahal and van Eldik.[17] K_2PtCl_4 (0.5 g, 1.2 mmol) was dissolved in water (8 mL), filtered and diethylenetriamine (0.240 mL, 0.23 g, 2.27 mmol) was added. The pH of the solution was adjusted to ca. 3 by the addition of HCl, followed by heating to reflux for 3 d. The yellow solution was filtered, concentrated to ca. 2.5 mL and cooled with ice. A yellow product precipitated, which was recrystallized from 1 M HCl (0.315 g, 65%). $C_4H_{14}Cl_3N_3Pt$ (405.6): calcd. C 11.9, H 3.5, N 10.4; found C 11.64, H 3.51, N 10.15.

[Pt(diethylenetriamine)Cl]Cl:[17] The above prepared compound was dissolved in water and the pH adjusted to 10 with LiOH. After that, the solution was heated at 80 °C for 30 min during which the pH was kept at 10 with LiOH. The colourless solution was cooled, the pH adjusted to 4 with HCl, concentrated and cooled. White crystals precipitated, which were washed with ethanol and ether (0.182 g, 63%). $C_4H_{13}Cl_2N_3Pt$ (369.2): calcd. C 13.0, H 3.5, N 11.4; found C 12.72, H 3.53, N 11.14.

[Pt(diethylenetriamine)Cl]CF$_3$SO$_3$ (aaa):[18] Concentrated solutions of [Pt(diethylenetriamine)Cl]Cl (0.161 g, 0.4 mmol) and Ag(CF_3SO_3) (0.112 g, 0.4 mmol) were prepared in warm water. The Ag(CF_3SO_3) solution was added dropwise and AgCl precipitated immediately. After repeated filtration, the solvent was removed and the product was dried (0.149 g, 77%). $C_5H_{13}ClF_3N_3O_3PtS$ (482.8): calcd. C 12.44, H 2.71, N 8.70, S 6.64; found C 12.62, H 2.66, N 8.46, S 6.52.

[Pt{2,6-bis(aminomethyl)pyridine}Cl]Cl·H$_2$O (apa): The ligand 2,6-bis(aminomethyl)pyridine was prepared according to a method used to synthesize 6-(aminomethyl)-2,2′-bipyridine[19] by using 2,6-bis(bromomethyl)pyridine[20] as starting material.[7] The corresponding platinum complex was prepared as described in the literature[7] and was obtained in the same quality (0.260 g, 38%). $C_7H_{13}Cl_2N_3OPt$ (421.2): calcd. C 19.95, H 3.09, N 9.98 ;found C 19.76, H 3.19, N 9.76. ^1H NMR (300 MHz, D_2O): δ = 7.7 (t, 1 H, 1 CH, *para*), 7.25 (d, 2 H, 2 CH, *meta*), 4.25 (s, 4 H, 2 CH_2) ppm.

[Pt{bis(2-pyridylmethyl)amine}Cl]CF$_3$SO$_3$ (pap): K_2PtCl_4 (0.2 g, 0.48 mmol) was dissolved in 0.005 M HCl (200 mL) and then 97% bis(2-pyridylmethyl)amine (0.1 mL) was added. The solution was stirred under reflux for 3 d and then cooled to room temperature. The colourless solution was filtered and concentrated to about 10 mL. Addition of saturated CF_3SO_3Na solution (2–3 mL) produced the precipitate of the desired complex. This was collected by filtration, washed with small amounts of water, ethanol and ether, and dried under vacuum. $C_{13}H_{13}ClF_3N_3O_3PtS$ (578.9): calcd. C 26.97, H 2.26, N 7.26, S 5.54; found C 26.49, H 2.16, N 7.05, S 5.57. ^1H NMR (400 MHz, D_2O): δ = 8.70 (d, 2 H, 2 CH, *ortho*), 8.05 (td, 2 H, 2 CH, *para*), 7.52 (d, 2 H, 2 CH, *meta*), 7.41 (dd, 2 H, 2 CH, *meta*) ppm.

[Pt(2,2′:6′,2′′-terpyridine)Cl]CF$_3$SO$_3$ (ppp): A mixture of K_2PtCl_4 (0.5 g, 1.2 mmol) and 2,2′:6′,2′′-terpyridine (terpy) (0.33 g, 1.4 mmol) in water (25 mL) was stirred under reflux until a clear red solution had formed, which took about 75 h. The solution was filtered and concentrated to about 3 mL. The red trihydrate salt of [Pt(2,2′:6′,2′′-terpyridine)Cl]Cl precipitated upon cooling. This was collected by vacuum filtration, washed with dilute 0.1 M HCl and acetone, and the product [Pt(2,2′:6′,2′′-terpyridine)Cl]Cl·3H_2O was dried under vacuum (0.181 g, 28%).[21] Concentrated solutions of [Pt(2,2′:6′,2′′-terpyridine)Cl]Cl·3H_2O (0.161 g, 0.3 mmol) and Ag(CF_3SO_3) (0.075 g, 0.3 mmol) were prepared in warm water. The Ag(CF_3SO_3) solution was added dropwise and AgCl precipitated immediately. An additional red precipitate was observed. The solution was stirred at room temperature for 1 h, diluted to 250 mL and stirred at 60 °C overnight. After repeated filtration, the solvent was removed and the product was dried (0.108 g, 61%). $C_{16}H_{11}ClF_3N_3O_3PtS$ (612.9): calcd. C 31.36, H 1.81, N 6.86, S 5.23; found C 30.81, H 1.83, N 6.65, S 5.18.

Instrumentation and Measurements: A Carlo Erba Elemental Analyser 1106 and 1108, and NMR spectroscopy (Bruker Avance DPX 300 and DRX 400) were used for chemical analysis and compound characterization. UV/Vis spectra for the study of slow reactions were recorded with a Varian Cary 1G spectrophotometer, equipped with a thermostatted cell holder. The chloro complexes all show absorbance maxima between 280 and 340 nm. Addition of an excess of thiourea causes a large increase in absorbance below 350 nm. Appropriate wavelengths (see Table 2) were selected to monitor the substitution of chloride by thiourea. Kinetic measurements for fast reactions were studied with an Applied Photophysics SX 18MV stopped-flow instrument. For experiments at elevated pressure (1–130 MPa), a laboratory-made high-pressure stopped-flow instrument was used.[22] The temperature of the instruments was controlled with an accuracy of ±0.1 °C. Thiourea (TU) was selected as entering ligand since its high nucleophilicity prevents the back reaction. LiCl solutions (0.002 M) were used to avoid spontaneous solvolysis of the chloro complexes. In the case of alcohol as solvent, trifluoromethanesulfonic acid (0.01 M) was used to avoid formation of alcoholate species that can compete as nucleophiles (see Results and Discussion). The ligand-substitution reactions were studied under pseudo-first-order conditions by using at least a ten-fold excess of TU. All listed rate constants represent an average value of at least five kinetic runs under each experimental condition.

Supporting Information (see also footnote on the first page of this article): Plots showing the concentration, temperature, and pressure dependence of the reactions between the Pt^{II} complexes and thiourea.

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[1] B. Lippert, *Cisplatin. Chemistry and Biochemistry of a Leading Anticancer Drug*, Wiley-VCH, Weinheim, **1999**.
[2] R. G. Wilkins, *Kinetics and Mechanisms of Reactions of Transition Metal Complexes*, VCH, Weinheim, **1991**.
[3] M. L. Tobe, J. Burgess, *Inorganic Reaction Mechanisms*, 1st ed., Addison Wesley Longman Limited, Essex, UK, **1999**.
[4] G. Alibrandi, D. Minniti, L. Monsù Scolaro, R. Romeo, *Inorg. Chem.* **1989**, *28*, 1939.
[5] R. Romeo, A. Grassi, L. Monsù Scolaro, *Inorg. Chem.* **1992**, *31*, 4383.
[6] M. R. Plutino, L. Monsù Scolaro, R. Romeo, A. Grassi, *Inorg. Chem.* **2000**, *39*, 2712.
[7] A. Hofmann, D. Jaganyi, O. Q. Munro, G. Liehr, R. van Eldik, *Inorg. Chem.* **2003**, *42*, 1688.
[8] M. Kotowski, R. van Eldik, in: *Inorganic High Pressure Chemistry, Kinetics and Mechanisms* (Ed.: R. van Eldik), Elsevier, Amsterdam, **1986**, chapter 4.
[9] M. Kotowski, D. A. Palmer, H. Kelm, *Inorg. Chem.* **1979**, *18*, 2555.
[10] C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, Wiley-VCH, Weinheim, Germany, **2003**, p. 472.
[11] W. C. Schiessl, N. K. Summa, C. F. Weber, S. Gubo, C. Dücker-Benfer, R. Puchta, N. J. R. van Eikema Hommes, R. van Eldik, *Z. Anorg. Allg. Chem.*, in press.
[12] Ref.[10], p. 163ff.
[13] Ref.[10], p. 431ff.
[14] H. R. Christen, F. Vögtle, Organische Chemie, *Von den Grundlagen zur Forschung*, Otto Salle Verlag, Frankfurt am Main, **1988**, vol. 1, p. 191.
[15] M. L. Tobe, J. Burgess, *Inorganic Reaction Mechanisms*, Addison Wesley Longman Limited, Essex, UK, **1999**, p. 10.
[16] G. Arena, G. Calogero, S. Campagna, L. M. Scolaro, V. Ricevuto, R. Romeo, *Inorg. Chem.* **1998**, *37*, 2763.
[17] G. Mahal, R. van Eldik, *Inorg. Chim. Acta* **1987**, *127*, 203.
[18] Triflate as anion increases the solubility of the complex.
[19] R. Ziessel, J.-M. Lehn, *Helv. Chim. Acta* **1990**, *73*, 1149.
[20] W. Baker, K. M. Buggle, J. F. W. McOmie, D. A. M. Watkins, *J. Chem. Soc.* **1958**, 3594.
[21] M. Howe-Grant, S. J. Lippard, *Inorg. Synth.* **1980**, *20*, 101.
[22] R. van Eldik, W. Gaede, S. Wieland, J. Kraft, M. Spitzer, D. A. Palmer, *Rev. Sci. Instrum.* **1993**, *64*, 1355.

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