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Synthesis and Reactivity of [PdCl(*terpy*)]Cl

Radovan Karkalić and **Živadin D. Bugarčić***

University of Kragujevac, Faculty of Science, Department of Chemistry,
YU-34000 Kragujevac, Yugoslavia

Summary. [PdCl(*terpy*)]Cl · $3H_2O$ has been synthesized both by interaction of $[PdCl_4]^{2-}$ and *cis*-[Pd(*DMSO*)$_2$Cl$_2$] with *terpy* (2,2′:6′,2″-terpyridine). Complex formation of $[PdCl(terpy)]^+$ with *L*-cysteine, *S*-methyl-*L*-cysteine, and *L*-methionine was studied as a function of temperature (298–308 K) using of stopped-flow spectrophotometry in methanol-water (95:5 (v/v)). The ionic strength and acidity of the solutions were adjusted to $0.10\,mol \cdot dm^{-3}$ with CH_3SO_3H. The second-order rate constant for the reaction of $[PdCl\ (terpy)]^+$ with *L*-cysteine amounts to $9.60 \pm 0.5\,M^{-1}s^{-1}$. *L*-Methionine and *S*-methyl-*L*-cysteine are unreactive under the same experimental conditions. The entropy of activation is strongly negative, which is compatible with an associative mechanism.

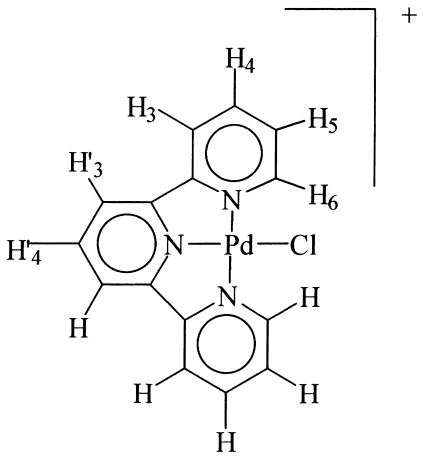
Keywords. Palladium; Complex; *terpy*; Thiol; Reactivity.

Introduction

Although substitution reactions of square-planar complexes in general and of Pt(II) and Pd(II) in particular have received much attention over the last two decades, the interest in this field continues uninterruptedly as demonstrated by the high number of reports appearing annually. This interest mainly forcuses on the effect of steric hindrance, helation of ligands, antitumor activity, and substituents of biological importance. The chemistry of Pt(II) and Pd(II) complexes is very similar, but Pd(II) analogues exhibit *ca.* 10^4–10^5-fold higher reactivity [1, 2]. In a recent study [3–5], we have investigated the substitution reactions of $[PtCl(terpy)]^+$ with different thiols including biologically important molecules.

Platinum and palladium terpyridine complexes have first been synthesized by *Morgen* and *Burstall* [6] and later by several workers [7–9]. With the present investigation of the substitution behaviour and associated kinetics of Pd(II) we extend our previous work on $[PdCl(terpy)]^+$. The complex chloro-(2,2′:6′,2″-terpyridine)-palladium(II), $[PdCl(terpy)^+$(see below), contains a tridentate aromatic nitrogen donor; only the chloride ion is displaced under ordinary conditions. This contribution describes new routes for the synthesis of $[PdCl(terpy)]^+$ as well as its substitution reactions with thiols and thioethers.

* Corresponding author



Results and Discussion

Figure 1 shows the UV/Vis spectra of the product resulting from mixing equal volumes of complex and ligand solutions; $\lambda = 258\,\text{nm}$ is suitable for kinetic measurements. The observed *pseudo*-first-order rate constant k_{obsd} were obtained from a least-squares fit of at least three half-lives of the reactions; the values given in Table 1 represent the average of two to five experiments. The second-order rate constants were obtained by fitting the dependence of the observed rate constants on the concentration of excess ligand to straight lines using a least-squares algorithm as above (Fig. 2).

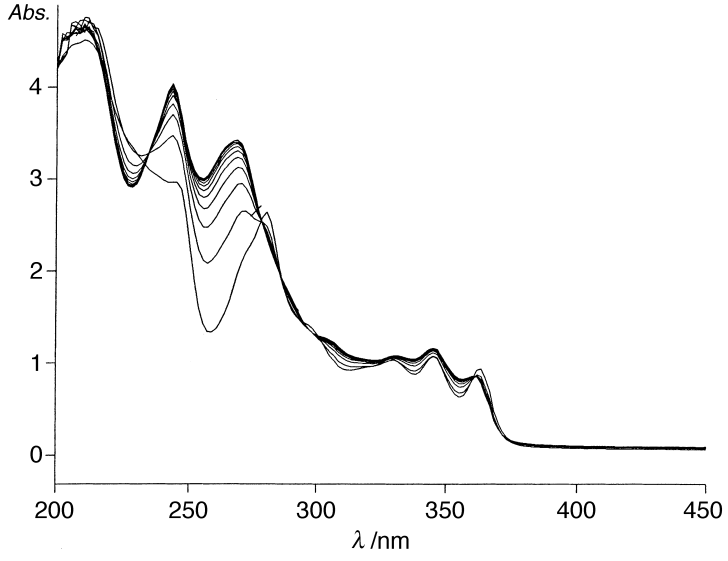


Fig. 1. UV/Vis spectroscopic changes during the reaction of the $[PdCl(terpy)]^+$ with *L*-cysteine; conditions: $[\text{complex}] = 2\times10^{-4}\,\text{mol}\cdot\text{dm}^{-3}$; $[L\text{-cyst.}] = 8\times10^{-3}\,\text{mol}\cdot\text{dm}^{-3}$; MeOH/$H_2O$ solutions (95:5 (v/v)); $I = 0.10\,\text{mol}\cdot\text{dm}^{-3}$ (CH_3SO_3H), 25°C, $\Delta t = 30\,\text{s}$

Table 1. *Pseudo*-first-order rate constants for the displacement of chloride from $[PdCl(terpy)]^+$ by *L*-cysteine in MeOH/H_2O (95:5 (v/v)); $I = 0.10\,mol \cdot dm^{-3}$ (CH_3SO_3H) 25.0°C; complex concentration: $1 \times 10^{-4}\,mol \cdot dm^{-3}$; numbers of runs in parentheses

t/°C	$10^3 \times$[*L*-cysteine]/mol · dm^{-3}	$10^2 \times k_{obsd}$/s^{-1}
25.0	1.22	158 ± 0.08 (3)
	2.54	2.96 ± 0.04 (5)
	4.06	4.42 ± 0.05 (2)
	6.10	5.86 ± 0.07 (4)
	7.11	7.20 ± 0.10 (3)
	10.16	9.98 ± 0.11 (4)
29.9	1.22	2.35 ± 0.06 (3)
	2.54	4.26 ± 0.08 (5)
	4.06	5.89 ± 0.11 (4)
	7.11	10.88 ± 0.06 (2)
	10.16	13.54 ± 0.04 (3)
35.1	1.22	3.12 ± 0.05 (4)
	2.54	5.49 ± 0.02 (3)
	4.06	7.85 ± 0.12 (5)
	7.11	13.09 ± 0.08 (2)
	10.16	18.98 ± 0.10 (3)

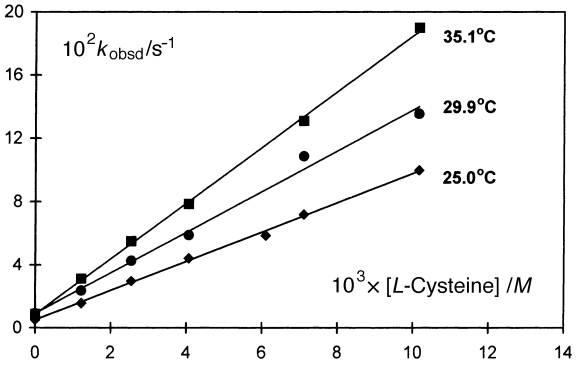


Fig. 2. Observed *pseudo*-first-order rate constants as a function of excess of *L*-cysteine

Substitution reactions at the square-planar $[PdCl(terpy)]^+$ moiety proceed according to the well-known two-term rate law $k_{obsd} = k_1 + k_2 \cdot [L]$. The solvolysis rate constant k_1, which is independent of $[L]$, can be determined from the intercept of the graph of k_{obsd} *vs.* $[L]$, is small and contributes little to the observed rates. The second-order rate constants k_2 characterizing the formation of the new complex can be determined from the slope of a plot of k_{obsd} *vs.* $[L]$. Second-order rate constants for the formation of the complexes between $[PdCl(terpy)]^+$ and $[PtCl(terpy)]^+$ with *L*-cysteine are given in Table 2. From the data of this table it appears that the Pd(II) complex is *ca.* 10^3 times more reactive than its Pt(II) analogue.

Table 2. Second-order rate constants and activation parameters for the reactions of $[PdCl(terpy)]^+$ and $[PtCl(terpy)]^+$ with *L*-cysteine in MeOH/H_2O (95:5 (v/v)); $I = 0.10\,mol \cdot dm^{-3}$ (CH_3SO_3H)

$[PdCl(terpy)]^+$					
L	$k_2/M^{-1}s^{-1}$	k_1/s^{-1}	$\Delta H_2^{\neq}$/kJ · mol^{-1}	$\Delta S_2^{\neq}$/J · K^{-1} · mol^{-1}	Ref.
L-Cysteine, 25.0°C	9.60 ± 0.5	0.005	42 ± 3	-112 ± 8	this work
L-Cysteine, 29.9°C	12.86 ± 0.4	0.009			this work
L-Cysteine, 35.0°C	17.59 ± 0.7	0.009			this work
S-Methyl-*L*-cysteine	unreactive				this work
L-methionine	unreactive				this work
$[PtCl(terpy)]^+$					
L-Cysteine, 25°	1.06×10^{-2}	0.0002	47 ± 5	-114 ± 5	[3]
S-Methyl-*L*-cysteine	unreactive				[3]
L-methionine	unreactive				[3]

The rate constants obtained at three different temperatures allow the calculation of the corresponding activation parameters *via* a fit to the *Eyring* equation [10]. The activation entropy is strongly negative which is compatible with an associative mode of activation (I_a or *A* mechanism). The results support a strong contribution from bond formation in the activation process and indicate that the leaving group is still tightly bound to the metal center in the transition state.

S-Methyl-*L*-cysteine and *L*-methionine seem to be unreactive under the same experimental conditions, and the spectrum of the $[PdCl(terpy)]^+$ remains unchanged within several hours even in the presence of a large excess of ligands. Their unreactivity was suprising in view of the expected affinity of the soft nucleophilic thioether moiety toward the soft electrophilic Pt(II) or Pd(II) atoms [11], especially since the *terpy* ligand accelerates the displacement of the fourth ligand. For example, $[PtCl(terpy)]^+$ and $[PdCl(terpy)]^+$ are approximately 10^3–10^4 times more reactive than their aliphatic homologs, $[PtCl(dien)]^+$ and $[PdCl(dien)]^+$ toward various small nucleophiles [12, 13].

The difference can be explained to a certain extend by steric effects of $[PdCl(terpy)]^+$ and the thioethers, but this cannot be the main reason. The same behaviour has been observed with $[PtCl(terpy)]^+$ and other thioethers [4, 5]. Since the thiol used in the experiments prevails in its undissociated state (protolysis constants for cysteine: $pK_{a1} = 1.9$, $pK_{a2} = 8.10$, $pK_{a3} = 10.1$ [14]), this means that the substitution is immediately followed by deprotonation of the product $[Pd(terpy)(RSH)]^{2+}$ and the reaction leads to the formation of the thiolate complex $[Pd(terpy)(SR)]^+$ observed for reactions between Pt(II) complexes and thiols [4, 5, 15]. It seems, therefore, that thioethers do not react because the resulting *bis*-cationic products cannot be stabilized by deprotonation [4, 5]. Therefore, even if there is not significant difference in the nucleophilicity of thiols and thioethers, a difference is clearly evident in the relative stability of the reaction product.

Experimental

Chloro-(2,2′:6′,2″-terpyridine)-palladium(II) chloride trihydrate ([PdCl(terpy)]Cl · 3H$_2$O)

1) From [PdCl$_4$]$^{2-}$ and terpy

0.0901 g $PdCl_2$ were dissolved under reflux in a mixture of 10 cm^3 H_2O and 3 cm^3 concentrated HCl. The clear solution was filtered, and a solution of *terpy* (0.1198 g in 10 cm^3 methanol) was added dropwise to the warm solution of [PdCl$_4$]$^{2-}$. The *pH* of the solution was carefully adjusted to 4.5–5.0 by addition of NaOH. The clear bright yellow solution was filtered and allowed to stand at room temperature until crystals precipitated. The bright yellow complex was filtered off, washed with water and diethyl ether, dried an air, and recrystallized from a minimum amount of 0.1 *N* HCl at 40–50°C. The bright yellow needles were collected by filtration, washed with water and diethyl ether, and dried an air.

Yield: 0.2172 g (92%); found: C 43.47, N 9.87, H 2.92; calcd.: C 43.90, N 10.24, H 2.68.

2) From cis-[PdCl$_2$(DMSO)$_2$ and terpy

cis-[$PdCl_2$(*DMSO*)$_2$] was prepared according to the method described by *Wayland* and co-workers [16, 17]. To a stirred suspension of 0.07247 g *cis*-[$PdCl_2$(*DMSO*)$_2$] in 20 cm^3 methanol a solution of 0.05905 g *terpy* in 10 cm^3 of methanol was added, and the resulting mixture was refluxed. After a few minutes the solution became bright yellow. Refluxing was continued for an additional hour to ensure completion of the reaction. The yellow precipitate was filtered off, washed with water and diethyl ether, and dried on air.

Yield: 0.091 g (90%); found: C 44.11, N 10.58, H 2.86; calcd.: C 43.90, N 10.24, H 2.68; ^{1}H NMR (200 MH, CD_3OD, δ, ppm): H_6 7.97, H_5 7.48, $H_{4,4'}$ 8.18, $H_{3,3'}$ 8.09.

Kinetic Measurements

[PdCl(*terpy*)]$^+$, *L*-cysteine (Fluka, 99.5%), *L*-methionine (Fluka, 99%), and *S*-methyl-*L*-cysteine (Fluka, 99%) were dissolved in aqueous methanol (MeOH: H_2O = 95:5 (v/v)). The ionic strength and acidity of the solutions were adjusted to 0.10 mol · dm^{-3} with CH_3SO_3H (Aldrich, 90%).

The UV/V is spectroscopic changes resulting from mixing of complex and ligand solutions were recorded with a Perkin-Elmer Lambda 16 spectrophotometer from 200 to 450 nm to establish a suitable wavelength at which kinetic measurements could be performed. These measurements were executed using a Hi-Tech stopped-flow spectrophotometer. The reaction between [PdCl(*terpy*)]$^+$ and *L*-cysteine was initiated by mixing equal volumes of complex and ligand solutions directly in the stopped-flow instrument and followed by observing the increase in absorbance at 258 nm. The complex formation reactions were followed under *pseudo*-first-order conditions with the concentration of ligand in at least 10-fold excess over that of the complex. Measurements at different temperatures were performed between 298 and 308 K. All kinetic runs were best described by a single exponential. Kinetic date were collected and analyzed using the OLIS computer program [18].

Acknowledgements

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