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Interaction of 2-aminopyrimidine with dichloro-[1-alkyl-2-(naphthylazo) imidazole]palladium(II) complexes : Kinetic and mechanistic studies

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Abstract

Background: The anticancer properties of *cis*platin and palladium(II) complexes stem from the ability of the *cis*-MCl_2 fragment to bind to DNA bases. However, *cis*platin also interacts with non-cancer cells, mainly through bonding molecules containing -SH groups, resulting in nephrotoxicity. This has aroused interest in the design of palladium(II) complexes of improved activity and lower toxicity. The reaction of DNA bases with palladium(II) complexes with chelating N,N/donors of the *cis*-MCl_2 configuration constitutes a model system that may help explore the mechanism of *cis*platin's anticancer activity. Heterocyclic compounds are found widely in nature and are essential to many biochemical processes. Amongst these naturally occurring compounds, the most thoroughly studied is that of pyrimidine. This was one of the factors that encouraged this study into the kinetics and mechanism of the interaction of 2-aminopyrimidine (2-NH_2-Pym) with dichloro-{1-alkyl-2-(α-naphthylazo)imidazole}palladium(II) [Pd(α-NaiR)Cl_2, **1]** and dichloro-{1-alkyl-2-(β-naphthylazo)imidazole}palladium(II) [Pd(β-NaiR)Cl_2, **2]** complexes where the alkyl R = Me (**a**), Et (**b**), or Bz (**c**).

Results: 2-NH_2-Pym reacts with **1a**, **1b**, and **1c** to yield [{1-alkyl-2-(α-naphthylazo)imidazole}bis(2-aminopyrimidine)]palladium(II) (**3a, 3b, 3c**) dichloride and with **2a, 2b,** and **2c** to yield [{1-alkyl-2-(β-naphthylazo)imidazole}bis(2-aminopyrimidine)]palladium(II) (**4a, 4b, 4c**) dichloride in an acetonitrile (MeCN) medium. The products were characterized using spectroscopic techniques (FT-IR, UV-Vis, NMR). The ligand substitution reactions follow second order kinetics – first order dependence on the concentration of the Pd(II) complex and 2-NH_2-Pym. Addition of LiCl to the reaction does not influence its rate. The thermodynamic parameters (standard enthalpy of activation, $\Delta^{\ddagger}H^{\circ}$ and standard entropy of activation, $\Delta^{\ddagger}S^{\circ}$) were determined from variable temperature kinetic studies. The magnitude of the second order rate constant, k_2, at 298 K, was shown to increase thus: **b <a <c** as well as **1 <2**.

Conclusion: The kinetics of the reaction between Pd(II) complexes (**1** and **2**) and 2-NH_2-Pym were examined spectrophotometrically at 530 nm in MeCN under pseudo-first-order conditions. The reaction rate is largely influenced by the π-acidity of the chelating ligand, with substitution in the naphthyl azoimidazole backbone influencing the rate of the substitution process. The activation parameters, $\Delta^{\ddagger}H^{\circ}$ and $\Delta^{\ddagger}S^{\circ}$, were determined and support the kinetic rate data.

Background

The anticancer properties of *cis*-$Pt(NH_3)_2Cl_2$ or *cis*platin [1-9] have given impetus to research in the field of platinum chemistry. This anticancer activity stems from the binding of the *cis*-$PtCl_2$ fragment with DNA bases. However, *cis*platin also interacts with non-cancer cells, through bond formation with -SH groups, resulting in nephrotoxicity. The anticancer properties of biologically important palladium(II) complexes [10-14] have aroused interest in the design of platinum(II) and palladium(II) [4] and ruthenium(II/III) [8,9] complexes of better activity and lower toxicity.

Mono-dentate ligands can bind in both *cis*- and *trans*-arrangements around a metal center, with the stability of the isomers dependent upon several factors. Bidentate ligands, however, are more reliable for the preparation of *cis*-complexes, in particular those of palladium(II) and platinum(II) [15-22]. The reaction of DNA bases with Pt(II) complexes with chelating N,N/donors of the *cis*-MCl_2 configuration constitutes a model system that may permit the exploration of the mechanism of *cis*platin's anticancer activity. The kinetics and mechanism of reactions involving Pd(II) complexes [23-27] prompted us to study palladium(II) *cis*platin analogues. The kinetics and mechanism of the substitution reactions involving Pd(II) complexes of 1-alkyl-2-(arylazo)imidazoles (**i**) (Figure 1) with adenine [28], cytosine [29], 2-mercapto-pyridine [30], 2-amino-pyrimidine [31], picolinic acid [32,33], and 8-hydroxy quinoline [34,35] have been reported.

In order to introduce greater steric crowding around the target metal center, we aim to use different ligands containing the azoimine chelating mode (-N=N-C=N-). This will allow the mechanism of nucleophilic interaction with the metal centre under different local environments to be elucidated. Naphthyl azoimidazoles ((**ii**) in Figure 1) are chemical analogues to phenyl azoimidazoles ((**i**) in Figure 1) but with a greater degree of steric crowding and electron donating ability.

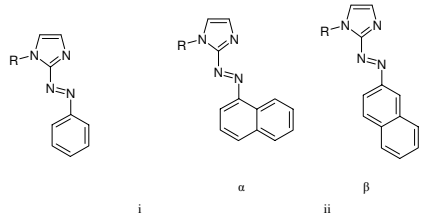
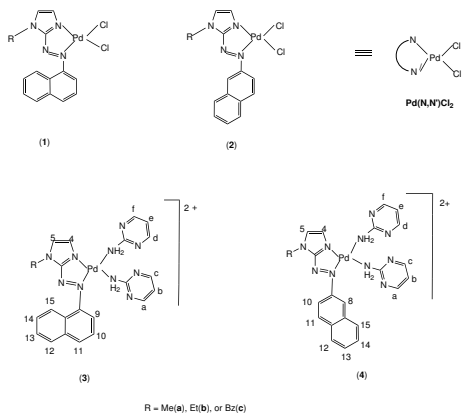


Figure 1
Phenylazoimidazole (**i**) and Naphthylazoimidazole (**ii**).

Heterocyclic compounds are found widely in nature, being essential to many biochemical processes, with the most thoroughly studied that of pyrimidine. Such ring systems form the building units of many valuable chemotherapeutic agents (Bleomycine), vitamins (Vitamin B_1), drugs (hyprotic, antibacterial, antimalarial), nucleic acids (cytosine and uracil). This fact has encouraged us to study the reactions of pyrimidine derivatives with different metal complexes [36,37]. In this study we present the kinetic and mechanistic studies of the reaction of 2-NH_2-Pym with **1** and **2**.

Results and Discussion

The two classes of naphthyl azoimidazole palladium (II) complexes,**1** and **2**, have been used in this work, that is, Pd(α-NaiR)Cl_2 (**1**) and Pd(β-NaiR)Cl_2 (**2**) [where α-NaiR = 1-alkyl-2-(α-naphthylazo)imidazole, β-NaiR = 1-alkyl-2-(β-naphthylazo)imidazole, and R = Me (**a**), Et (**b**) or Bz (**c**)]. The ligands belong to the asymmetric bidentate N,N/donors type and form dichloropalladium(II) complexes. Hereafter we shall use the abbreviation, Pd(N,N/)Cl_2 (see Scheme 1), when referring to the complex.



Scheme 1

The reaction kinetics between Pd(N,N/)Cl_2 and 2-NH_2-Pym were examined spectrophotometrically. The reaction is first order with respect to the Pd(II) complex because k_{obs}-values are almost steady when all variants are constant, other than that of the complex concentration. The k_{obs}-values (Table 1) and the linear plots for the k_{obs} *versus* initial molar concentration of 2-NH_2-Pym, $[2\text{-}NH_2\text{-Pym}]_0$ (Figures 2 and 3) indicate the reaction is first order with respect to 2-NH_2-Pym. The slope of the plot gives the second order rate constant (k_2). The small intercept (k_0) value indicates the minor existence of a solvent assisted pathway to the overall reaction products, because MeCN is a coordinating solvent.

The reaction rate increases with temperature as expected from the Eyring equation. Activation parameters, standard enthalpy of activation (Δ‡H°) and standard entropy of

activation (Δ‡S°) was calculated using Eyring plots (Figures 4 and 5), which are recorded in Table 2. The activation parameter values support the experimental k2-values. The order for the Δ‡H° and Δ‡S° values is : b > a > c and 1 > 2. The iso-kinetic plot (Figure 6) suggests an identical mechanism as that for the reaction of Pd(N,N/)Cl2 with 2-NH2-Pym. Kinetic studies in the presence of externally added Cl- ions (LiCl) reveal that the rate as well as kobs almost remain unchanged with variation of [Cl-]0 when all other variants are constant, thus supporting the mechanism outline (see Scheme 2). The dissociation of the first Pd-Cl bond is the rate-determining step, and is therefore not affected by externally Cl- ion as LiCl. The reaction product was isolated and characterized as [Pd(N,N/)(2-NH2-Pym)2](ClO4)2.

The overall nucleophilic substitution process involves direct displacement of 2 Cl- ions by 2-NH2-Pym (see Scheme 3), with the observed rate expressed as :

$$\text{Rate} = \{k_0 + k_2\,[2\text{-NH}_2\text{-Pym}]_0\,[\text{Pd(N,N/)Cl}_2] = k_{obs}\,[\text{Pd(N,N/)Cl}_2],$$
$$\text{with, } k_{obs} = k_0 + k_2\,[2\text{-NH}_2\text{-Pym}]_0 \text{ and } k_2 = \text{k/K}.$$

where k_0 and k_2 are the intercept and the slope of the plot of k_{obs}*versus* $[2\text{-NH}_2\text{-Pym}]_0$ respectively. The values of k_0 and k_2 are constant when the temperature is constant. The nucleophile is an N donor ligand. It is probable that the basic N coordinates quickly with the positively charged metal centre. The first step of the reaction is the formation of a five-coordinated square pyramidal species (**X**) from

Table 1:

$Pd(NN/)Cl_2$	10^3 [2-NH_2- Pym]$_0$ (mol dm^{-3})	$10^3 k_{obs}$ (s^{-1})	k_2 ($dm^3\ mol^{-1}\ s^{-1}$)	k_0 (s^{-1})
1a	1.00	3.28	2.53	0.67
	3.00	8.12		
	5.00	13.45		
	7.00	18.17		
	10.00	26.03		
1b	1.00	3.06	2.24	0.69
	3.00	7.32		
	5.00	11.70		
	7.00	16.43		
	10.00	23.11		
1c	1.00	3.35	2.68	0.61
	3.00	8.95		
	5.00	14.25		
	7.00	20.05		
	10.00	28.15		
	1.00	4.20		
2a	3.00	11.95	3.85	0.33
	5.00	19.33		
	7.00	27.35		
	10.00	38.80		
	1.00	3.76		
2b	3.00	10.52	3.65	0.11
	5.00	18.46		
	7.00	26.79		
	10.00	35.97		
2c	1.00	4.47	4.13	0.19
	3.00	13.06		
	5.00	19.65		
	7.00	29.52		
	10.00	41.63		

Observed pseudo-first-order rate constants (k_{obs}) for the reactions of 2-aminopyrimidine with dichloro-{1-alkyl-2-(α-naphthylazo)imidazole}palladium(II) (**1**) and dichloro-{1-alkyl-2-(β-naphthylazo)imidazole}palladium(II) (**2**)complexes where the alkyl R = Me(**a**), Et(**b**), or Bz(**c**) in MeCN : $[Pd(NN/)Cl_2]_0 = 1.0 \times 10^{-4}$ mol dm^{-3}, Temperature = 298 K.

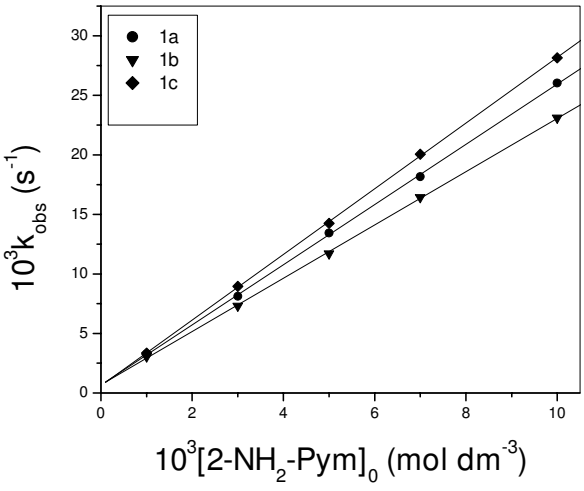


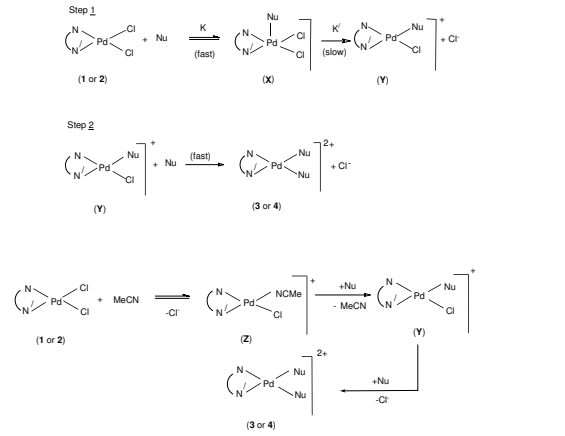
Figure 2
Plots of *kobs versus* [2-NH2-Pym]0 for the reactions: Pd(α-NaiR)Cl2 + 2-NH2-Pym in MeCN; where [Pd(α-NaiR)Cl2]0 = 1.00 × 10-4 mol dm-3 and temperature = 298 K.

the complex (**1** or **2**) with 2-NH_2-Pym. This species quickly converts into a more stable four coordinated square planar species (**Y**) by dissociation of first Pd-Cl bond. The second nucleophile coordinates rapidly with the mono positive species (**Y**), forming the final product (**3** or **4**) by simultaneous dissociation of second Pd-Cl bond. Because the first Pd-Cl bond cleavage is possibly slow, the step is therefore rate determining. This is supported by there being no effect on reaction rate from externally added Cl^- as LiCl. A plausible mechanism, outlined in Scheme 2, initially involves two competing steps : the first, a solvation step where coordinating solvent, MeCN, forms a solvated species Pd(N,N/)Cl_2(MeCN) (**Z**); and the second, a nucleophilic attack by 2-NH_2-Pym (Scheme 2). Though the steric crowding of the α-/β-naphthyl group in N,N/chelating ligand is significant its strong electron withdrawing ability resulting from conjugation, stabilizes the chelated Pd(N,N/) species, rather than resulting in dechelation.

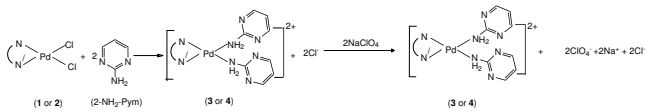
The kinetic data in Table 1 reveal that the magnitude of k_2 increases thus : **b <a <c**. This is because of the electron withdrawing tendency of Bz group is greater than that of Me whilst that of the Me group it is slightly greater than for Et.

Conclusion

The kinetics of the interaction between Pd(N,N/)Cl_2 and 2-NH_2-Pym were examined spectrophotometrically at 530 nm in MeCN under pseudo-first-order reaction conditions. The reactions are first order with respect to the Pd(II) complex and 2-NH_2-Pym. The rate of reaction is largely influenced by the π-acidity of the chelating ligand; substitution in the naphthyl azoimidazole backbone influences greatly the rate of the substitution. The reaction activation parameters, $\Delta^{\ddagger}H^{\circ}$ and $\Delta^{\ddagger}S^{\circ}$, were calculated and correlate well with the kinetic rate data. The products isolated from the reaction between Pd(N,N/)$Cl_2$and 2-NH_2-Pym in MeCN were characterized by spectroscopically, and the composition being confirmed as [Pd(N,N/)(2-NH_2-Pym)$_2$](ClO_4)$_2$.



Scheme 2



Scheme 3

Experimental

The Pd(II) complexes were prepared according to a reported procedure [38,18]. 2-aminopyrimidine was obtained from Sigma-Aldrich. Acetonitrile (MeCN) was purified using a known procedure [39,40]. All kinetic and spectroscopic measurements were recorded on an Agilent 8453E UV-visible Spectroscopy System. Quartz cells (1.0 cm path length) from Hellma were used. IR spectra (KBr pellet) were recorded on a FT-IR Spectrophotometer Spectrum RX1, Perkin-Elmer. H^1 NMR spectra were carried out on a 300 MHz Bruker NMR instrument in CD_3CN using TMS as the internal standard. Microanalyses were carried out on a Perkin-Elmer 2400 CHN elemental analyzer. The specific conductance was measured on a JENCONS 4010 Conductivity Meter. Rate constants and standard deviations were calculated by linear regression using a PC-based programme, Microcal-origin version Origin-6.1.

For the kinetic measurements, stock solutions of the Pd(II) complexes (*ca.* 10^{-3} mol dm^{-3}) and of 2-amino-pyrimidine (2-NH_2-Pym) (*ca.* 10^{-2} mol dm^{-3}) were prepared in dry MeCN. Solutions of different concentrations were

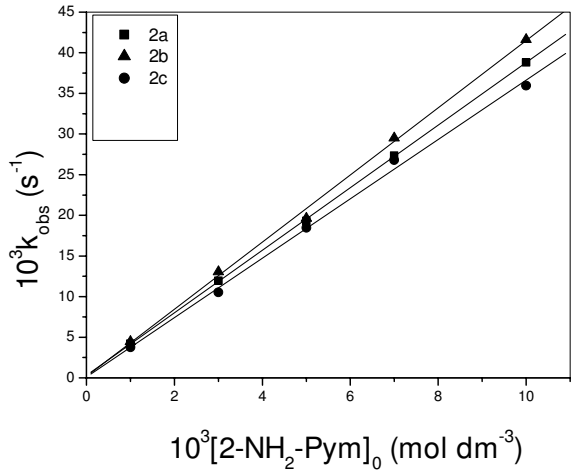


Figure 3
Plots of *kobs versus* [2-NH2-Pym]0 for the reactions: Pd(β-NaiR)Cl2 + 2-NH2-Pym in MeCN, where [Pd(β-NaiR)Cl2]0 = 1.00 × 10-4 mol dm-3 and temperature = 298 K.

prepared by quantitatively diluting stock solutions using dry MeCN. All experiments were performed at 298 K (unless otherwise stated) by mixing the required volumes of the thermostated reactants, before being transferred into the absorption cells (1.0 cm length). On addition of 2-amino-pyrimidine (2-NH_2-Pym) to the solution of Pd(N,N/)Cl_2 (**1** or **2**) in MeCN the orange solution changes to yellow-orange. The influence of the addition of 2-amino-pyrimidine (2-NH_2-Pym) on the spectra of Pd(α-NaiEt)Cl_2 (**1b**) is shown in the Figure 7. The change proceeds through a single isosbestic point at *ca*. 412 nm. The decrease in absorbance of the reaction mixture was recorded automatically at *ca*. 530 nm as a function of time. A_∞ was measured after ~24 h of mixing, when the absorbance became constant. In all experiments, the initial molar concentration of 2-NH_2-Pym, [2-NH_2-Pym]$_0$ was kept at least ten times higher than Pd(II) complex concentration so as to maintain pseudo-first-order kinetic conditions. Pseudo-first-order rate constants, k_{obs}, were obtained from the slopes of the plots of (A_t-A_∞) *versus* time (Figure 8) where A_t = absorbance of the reaction mixture at time, t(s) after mixing of 2-NH_2-Pym solution, and A_∞ = absorbance of same after completion of the reaction.

Synthesis of [Pd(α-NaiEt)(2-NH_2 – Pym)$_2$](ClO$_4$)$_2$ (3b-diperchlorate)

To the MeCN solution of the complex Pd(α-NaiEt)Cl_2 (25 mg, 5.85 × 10^{-2} mmol), 2-NH_2-Pym (5.6 mg, 5.89 × 10^{-2} mmol) was added and the resulting orange-colored solution stirred for about 24 h. Next, the solution was filtered and allowed to evaporate to dryness at room temperature. The resulting mass was then dissolved in methanol, before the addition of an aqueous solution of 1 g of $NaClO_4$. The resulting brown precipitate was filtered and washed with water. The dried product was then chromatographed over silica gel, with MeCN eluting an orange band. A yield of 29 mg (65.91%) was obtained.

All other complexes were prepared using the same procedure with yields varying from 58–70%.

Microanalytical data of the products are as follows: For [Pd(α-NaiMe)(2-NH_2-Pym)$_2$](ClO$_4$)$_2$ (**3a**- diperchlorate): *Anal*. Found: C, 36.02; H, 3.04; N, 19.59%. Calc. for $C_{22}H_{22}O_8N_{10}PdCl_2$: C, 36.10; H, 3.01; N, 19.14%. For [Pd(α-NaiEt)(2-NH_2-Pym)$_2$](ClO$_4$)$_2$ (**3b**-diperchlorate) *Anal*. Found: C, 37.10; H, 3.30; N, 18.69%. Calc. for $C_{23}H_{24}O_8N_{10}PdCl_2$: C, 37.03; H, 3.22; N, 18.78%. For [Pd(α-NaiBz)(2-NH_2-Pym)$_2$](ClO$_4$)$_2$(**3c**-diperchlorate) *Anal*. Found: C, 41.72; H, 3.21; N, 17.11%. Calc. for $C_{28}H_{26}O_8N_{10}PdCl_2$: C, 41.62; H, 3.22; N, 17.34%. For [Pd(β-NaiMe)(2-NH_2-Pym)$_2$](ClO$_4$)$_2$ (**4a**-diperchlorate) : *Anal*. Found: C, 36.18; H, 3.02; N, 19.36%. Calc. for $C_{22}H_{22}O_8N_{10}PdCl_2$: C, 36.10 ;H, 3.01; N,19.14%. For [Pd(β-NaiEt)(2-NH_2-Pym)$_2$](ClO$_4$)$_2$ (**4b**-diperchlorate) *Anal*. Found: C, 37.08; H, 3.25; N, 18.75%. Calc. for $C_{23}H_{24}O_8N_{10}PdCl_2$: C, 37.03; H, 3.22; N, 18.78%. For [Pd(β-NaiBz)(2-NH_2-Pym)$_2$](ClO$_4$)$_2$ (**4c**- diperchlorate) *Anal*. Found: C, 41.60; H, 3.23; N, 17.30%. Calc. for $C_{28}H_{26}O_8N_{10}PdCl_2$: C, 41.62; H, 3.22; N, 17.34%.

Product characterization

To the MeCN solution of the complex, Pd(N,N/)Cl_2, 2-NH_2-Pym was added and the orange-colored solution was stirred for about 24 h. Next the solution was filtered and allowed to evaporate to dryness at near to room temperature. The resulting solid was dissolved in methanol, before the addition of aqueous $NaClO_4$. The brown precipitate was filtered, washed with water and cold MeCN. The dried product was chromatographed over silica gel with MeCN eluting an orange-red band. Finally the micro-analytical data in addition to U.V.-Vis, IR, NMR (Table 3) spectral data were obtained for the dried product. The molar conductivity data for the compound in a MeCN solution (Λ_M = 120–155 S cm^2 mol^{-1}) showed the 1:2 electrolytic nature of the complexes. The IR spectra of the complexes display stretch at 1350–1370 cm^{-1} which corresponds to ν(N=N), thus showing a red shift of 10–15 cm^{-1} with respect to Pd(N,N/)Cl_2 [25]. This may be attributed to the charge delocalization from the coordinated 2-NH_2-Pym to the chelated N,N/ligand. The binding mode was indirectly established by the disappearance of two ν(Pd-Cl) bands corresponding to the *cis*-$PdCl_2$ configuration [21,38,41]. All the complexes exhibit a structure-less band at 1090 – 1100 cm^{-1} corresponding to ν(ClO_4), suggesting lack of a significant interaction in the solid state [42]. The coordi-

nated 2-NH_2-Pym shows ν(NH_2) as a doublet at *ca*. 3135 and 3200 cm^{-1}.

The electronic spectra of the complexes were recorded in the range of 900 – 200 nm in MeCN. The absorptions below 400 nm are due to intramolecular charge transfer and therefore do not need to be considered further. The absorption band in the range 500 – 530 nm for all the complexes is absent in free ligands, and may represent charge transfer transitions localized on the metallated fragment [43].

The H NMR spectra of the complexes were recorded in CD_3CN (Table 3). The proton-numbering is outlined in Scheme 1. The data reveal that the signals in the complexes are shifted downfield relative to the free ligand values [34] supporting the coordination of ligand to Pd(II). An important feature of the spectra is the general shifting observed for the imidazole protons 4-H and 5-H to lower δ-values relative to naphthyl protons (6-H – 13-H); the imidazole protons are shifted by 0.1–0.2 ppm compared to the free ligand position.

This supports the strong preference of the binding of imidazole-N to Pd(II). The Naphthyl protons appear as multiplets except for the broad singlet for 6-H and doublet for 8-H (in [Pd(α-/β-NaiR)(2-NH_2-Pym)$_2$](ClO_4)$_2$) and a doublet for 15-H in the case of all the complexes. The 1-alkyl group appears as a singlet to -N(1)-CH_3 of Me group in [Pd(α-/β-NaiMe)(2-NH_2-Pym)$_2$](ClO_4)$_2$; quartet to -N(1)-CH_2-, triplet to -CH_3 of Et group in [Pd(α-/β-NaiEt)(2-NH_2-Pym)$_2$](ClO_4)$_2$ and also singlet to – N(1)-

Table 2:

$Pd(N,N')Cl_2$	Temperature (K)	k_2 ($dm^3\ mol^{-1}\ s^{-1}$)	$\Delta^{\ddagger}H°$ (kJ mol^{-1})	$\Delta^{\ddagger}S°$ (J $K^{-1}mol^{-1}$)
1a	293	2.03	29.12	-139.51
	298	2.53		
	303	3.12		
	308	3.82		
	313	4.66		
1b	293	1.80	33.84	-124.46
	298	2.24		
	303	2.93		
	308	3.69		
	313	4.62		
1c	293	2.31	23.30	-158.38
	298	2.68		
	303	3.26		
	308	3.84		
	313	4.50		
2a	293	3.38	14.44	-185.32
	298	3.85		
	303	4.26		
	308	4.76		
	313	5.30		
2b	293	3.18	21.16	-162.87
	298	3.85		
	303	4.41		
	308	5.14		
	313	5.98		
2c	293	3.82	9.52	-201.16
	298	4.13		
	303	4.49		
	308	4.85		
	313	5.23		

Second order rate constants (k_2) at different temperatures and activation parameters for the reactions of 2-aminopyrimidine with dichloro-{1-alkyl-2-(α-naphthylazo) imidazole}palladium(II) (**1**) and dichloro-{1-alkyl-2-(β-naphthylazo)imidazole} palladium(II) (**2**)complexes where the alkyl R = Me(**a**), Et(**b**), or Bz(**c**) in MeCN : $[Pd(N,N')Cl_2]_0 = 1.0 \times 10^{-4}$ mol dm^{-3}, $[2\text{-}NH_2\text{- Pym}]_0 = 1.0 \times 10^{-3}$ mol dm^{-3}.

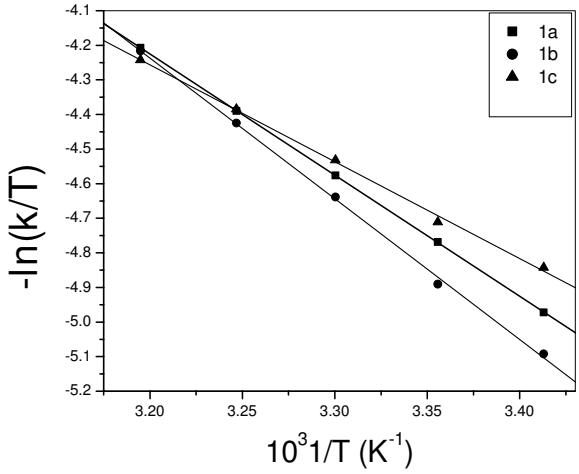


Figure 4
Plots of ln (*k*/T) *versus* (1/T) for the reactions: Pd(α-NaiR)Cl2 + 2-NH2-Pym in MeCN.

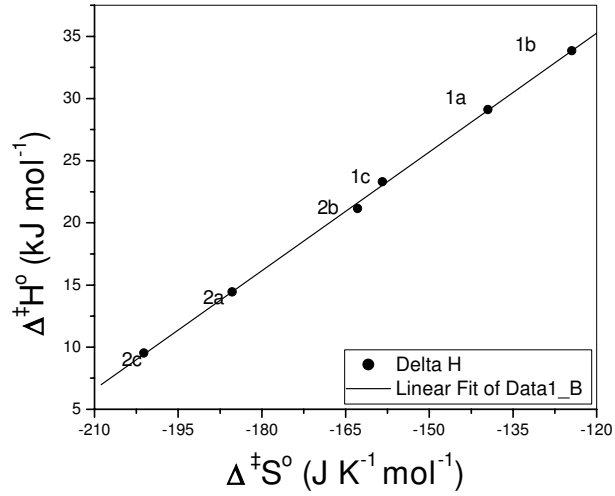


Figure 6
Plot of Δ‡H0 *versus* Δ‡S0, i.e., iso-kinetic plot for the reactions: Pd(R/aiR)Cl2 + 2-NH2-Pym in MeCN.

CH_2- of Bz group in [Pd(α-/β-NaiBz)(2-NH_2-Pym)$_2$](ClO_4)$_2$ complexes. The δ(NH_2) appears as a broad band at *ca*. 4.30 ppm which is shifted to higher chemical shift with respect to δ(NH_2) when the -NH_2 group is non coordinated. This also supports coordination of -NH_2 to Pd(II). Pyrimidine protons (a-H to c-H,) appear between 8.5 to 9.0 ppm, which confirms the coordination of 2-NH_2-Pym compared with the free amine [44].

Authors' contributions

This work was prepared by AM's research group: PKG helped design and carry out the experiments in addition to drafting the manuscript. SS carried out the IR and ^{1}H NMR spectra analysis and product characterization and participated in the discussion of the manuscript. This

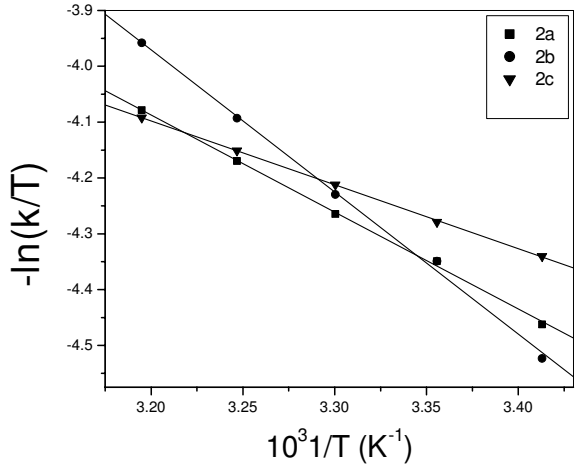


Figure 5
Plots of ln(*k*/T) *versus* (1/T) for the reactions: Pd(β-NaiR)Cl2 + 2-NH2-Pym in MeCN.

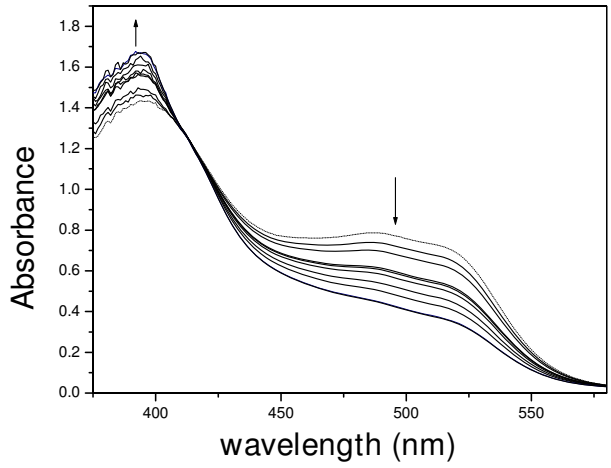


Figure 7
Spectra of Pd(α-NaiEt)Cl2 in MeCN and the reaction mixture of Pd(α-NaiEt)Cl2 and 2-NH2-Pym in MeCN solution at 298 K. The arrows indicate decrease and increase of band intensities over the course of the reaction.

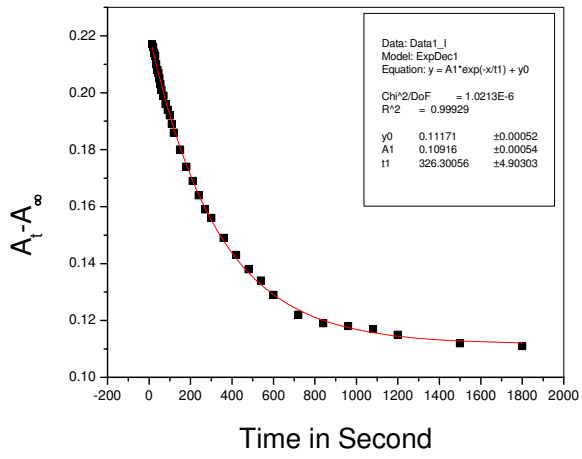


Figure 8
Plot of (At-A∞) *versus* time(s) for reaction, where, [Pd(α-NaiEt)Cl2]0 = 1.0 × 10-4 mol dm-3, [2-NH2-Pym]0 = 1.0 × 10-3 mol dm-3, and temperature = 298 K.

project was based on the ideas of AM and carried out with his guidance and consultation.

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Table 3: H NMR spectral data of 3a-, 3b-, 3c-, 4a-, 4b-, and 4c-perchlorates in CD_3CN

Compound[h]	δ, ppm (J, Hz)										
	4-H[a]	5-H[a]	8-H[b]	9-H	10-H	11–15-H[c]	N(1)-CH_3	N(1)-CH_2	N(1)-CH_2-CH_3	a,c-H[d]	b,-H[e]
3a-diperchlorate	7.01	6.83		7.88 (7.0)[d]	7.59[c]	7.60	4.12			9.03 (7.0)	8.54 (7.0)
3b-diperchlorate	7.03	6.86		7.90 (7.0)[d]	7.62[c]	7.62		4.30 (9.0)[g]	1.65 (7.0)[e]	9.05 (7.0)	8.55 (7.0)
3c-diperchlorate	7.05	6.90		7.92 (7.0)[d]	7.72[c]	7.63		5.71[b, f]		9.08 (7.0)	8.57 (7.0)
4a-diperchlorate	7.02	6.81	8.01		7.81 (7.0)[d]	7.81	4.15			9.05 (7.0)	8.58 (7.0)
4b-diperchlorate	7.03	6.87	8.05		7.83 (7.0)[d]	7.83		4.32 (9.0)[g]	1.61 (7.0)[e]	9.08 (7.0)	8.59 (7.0)
4c-diperchlorate	7.07	6.92	8.10		7.88 (7.0)[d]	7.88		5.75[b, f]		9.10 (7.0)	8.61 (7.0)

[a] Broad singlet; [b] Singlet; [c] Multiplet, [d] Doublet, [e] Triplet, [f] Ph-H : 7.45 – 7.55 ppm, [g] Quartet; [h] δ(NH_2): 4.26–4.32 (broad) ppm

References

1. Lippard S J, Bertini I, Gray HB, Lippard SJ, Valentine JS, Eds: **Bioinorganic Chemistry.** *University Science Books: Mill Valley, CA* 1994:505.
2. Beer PD: **Transition-metal receptor systems for the selective recognition and sensing of anionic guest species.** *Acc Chem Res* 1998, **31:**71-80.
3. Yoo J, Sohn YS, Do YK: **Synthesis, structures and antitumor activity of the first crown ester-linked bipyridyl platinum complexes.** *J Inorg Biochem* 1999, **73:**187-193.
4. Li J, Zheng ML, King I, Doyle TW, Chan SH: **Biological Properties of Citrus Flavonoids Pertaining.** *Curr Med Chem* 2001, **8:**121-133.
5. Banerjee P: **Interaction of nitrogen bases with some platinum(II) and palladium(II) complexes – usual and unusual features.** *Coord Chem Rev* 1999, **190–192:**19-28.
6. Lippert B: **Impact of Cisplatin on the recent development of Pt coordination chemistry: a case study.** *Coord Chem Rev* 1999, **182:**263-295.
7. Kato M, Takahashi J, Sugimoto Y, Kosuge C, Kishi S, Yano S: **Selective formation of integrated stacks of (α-diimine)(ethylenediamine)platinum(II) and neutral π systems of the phenanthrene type.** *J Chem Soc Dalton Trans* 2001:747-752.
8. Chen H, Parkinson JA, Pearsons S, Coxall RA, Gould RO, Sadler PJ: **Organometallic Ruthenium(II) Diamine Anticancer Complexes: Arene-Nucleobase Stacking and Stereospecific Hydrogen-Bonding in Guanine Adducts.** *J Am Chem Soc* 2002, **124:**3064-3082.
9. Velders AH, Kooijman H, Spek AL, Hassnoot JG, de Vos D, Reedijk J: **Strong Differences in the in Vitro Cytotoxicity of Three Isomeric Dichlorobis(2-phenylazopyridine)ruthenium(II) Complexes.** *Inorg Chem* 2000, **39:**2966-2967.
10. Kovala-Demertzi D, Boccarelli A, Demertzis MA, Coluccia M: **In vitroAntitumor Activity of 2-Acetyl Pyridine 4N-Ethyl Thiosemicarbazone and Its Platinum(II) and Palladium(II) Complexes.** *Chemotherapy* 2007, **53:**148-152.
11. Divsalar A, Saboury AA, Mansoori-Torshizi H, Hemmatinejad B: **Comparative and Structural Analysis of the Interaction between β-Lactoglobulin type A and B with a New Anticancer component (2,2/-Bipyridin n-Hexyl DithiocarbamatoPd (II) nitrate).** *Bulletin of the Korean Chem Soc* 2006, **27:**1801-1808.
12. Butour JL, Wimmer S, Wimmer F, Castan P: **Palladium(II) compounds with potential antitumour properties and their platinum analogues: a comparative study of the reaction of some orotic acid derivatives with DNA in vitro.** *Chemico-Biological Interactions* 1997, **104:**165-178.
13. Umreiko DS, Kachurina DN, Chernikova IE, Novitskii GG, Sinitsyn NM, Buslaeva TM, Efanov VI: **Structure and anti-tumor activity of Palladium complexes with hexamethylenetetramine.** *Zdravookhranenie Belorussii* 1986, **12:**22-24.
14. Fiallo MML, Garnier-Suillerot A: **Metal Anthracycline Complexes as a New Class of Anthracycline Derivatives. Pd(II)-Adriamycin and Pd(II)-Daunorubicin Complexes: Physicochemical Characteristics and Antitumor Activity.** *Biochemistry* 1986, **25:**924-930.
15. Misra TK, Das D, Sinha C, Ghosh PK, Pal CK: **Chemistry of Azoimidazoles: Synthesis, Spectral Characterization, Electrochemical Studies, and X-ray Crystal Structures of Isomeric Dichloro Bis [1-alkyl-2-(arylazo)imidazole] Complexes of Ruthenium(II).** *Inorg Chem* 1998, **37:**1672-1678.
16. Byabartta P, Santra PK, Misra TK, Sinha C, Kennard CHL: **Synthesis, spectral characterisation, redox studies of isomeric dichloro-bis-[1-alkyl-2-(naphthyl-(α/β)-azo)imidazole]ruthenium(II). Single crystal X-ray structure of blue-green dichloro-bis-[1-ethyl-2-(naphthyl-α-azo)imidazole]ruthenium(II).** *Polyhedron* 2001, **20:**905-913.
17. Santra PK, Misra TK, Das D, Sinha C, Slawin AMZ, Woollins JD: **Chemistry of azopyrimidines. Part II. Synthesis, spectra, electrochemistry and X-ray crystal structures of isomeric dichloro bis[2-(arylazo)pyrimidine] complexes of ruthenium(II).** *Polyhedron* 1999, **18:**2869-2878.
18. Pal S, Das D, Chattopadhyay P, Sinha C, Panneerselvam K, Lu T-H: **Synthesis, spectral and electrochemical properties of 1-alkyl-2-(naphthyl-β-azo)imidazole complexes of platinum(II) and the reaction with pyridine bases. Single-crystal X-ray structure of dichloro-[1-ethyl-2-(naphthyl-β-azo)imidazole]platinum(II).** *Polyhedron* 2000, **19:**1263-1270.
19. Rauth GK, Pal S, Das D, Sinha C, Slawin AMZ, Woollins JD: **Synthesis, spectral characterization and electrochemical studies of mixed-ligand complexes of platinum(II) with 2-(arylazo)pyridines and catechols. Single-crystal X-ray structure of dichloro{2-(phenylazo) pyridine}platinum(II).** *Polyhedron* 2001, **20:**363-372.
20. Roy R, Chattopadhyay P, Sinha C, Chattopadhyay S: **Synthesis, spectral and electrochemical studies of arylazopyridine complexes of palladium(II) with dioxolenes.** *Polyhedron* 1996, **15:**3361-3369.
21. Das D, Nayak MK, Sinha C: **Chemistry of azoimidazoles. Synthesis, spectral characterization and redox studies of N(1)-benzyl-2-(arylazo) imidazolepalladium(II) chloride.** *Transition Met Chem* 1997, **22:**172-175.
22. Das D, Sinha C: **Synthesis, spectral and electrochemical characterization of (dithiocarbamato) (arylazoimidazole)Palladium(II) perchlorates.** *Transition Met Chem* 1998, **23:**309-311.
23. Bugarčić ŽD, Nandibewoor ST, Hamza MSA, Heinemann F, van Eldik R: **Kinetics and mechanism of the reactions of Pd(II) complexes with azoles and diazines. Crystal structure of $[Pd(bpma)(H_2O)](ClO_4)_2 \cdot 2H_2O$.** *Dalton Trans* 2006:2984-2990.
24. Breet E, van Eldik R: **Hydrogen carbonate inhibited and induced substitution reactions of labile square-planar diethylenetriaminepalladium (II) complexes.** *Berichte der Bunsen-Gesellschaft* 1998, **102:**1418-1427.
25. Shoukry A, Rau T, Shoukry M, van Eldik R: **Kinetics and mechanisms of the ligand substitution reactions of bis(amine)(cyclobutane-1,1-dicarboxylato)palladium(II).** *J Chem Soc, Dalton Trans* 1998:3105-3112.
26. Hohmann H, Suvachittanont S, van Eldik R: **A kinetic study of the substitution behaviour of aqua and chloro complexes of ethylenediaminepalladium(II) in aqueous solution.** *Inorg Chim Acta* 1990, **177:**51-58.
27. Berger J, Kotowski M, van Eldik R, Frey U, Helm L, Merbach AE: **Kinetics and Mechanism of Solvent-Exchange and Anation Reactions of Sterical Hindered Diethylenetriamine Complexes of Palladium (11) in Aqueous Solution.** *Inorg Chem* 1989, **28:**3759-3765.
28. Saha S, Ghosh PK, Mahapatra A: **Interaction Between Pd(RaaiR')Cl_2 and Adenine: Reaction Dynamics and Mechanism [RaaiR' = 1-alkyl-2-(arylazo)imidazole].** *Transition Met Chem* 2005, **30:**706-711.
29. Saha S, Majumdar T, Mahapatra A: **Mechanism of Interaction of DNA Bases with Pd(II)-azoimidazoles: The Cytosine Case.** *Inorg Reac Mech* 2006, **6:**19-29.
30. Saha S, Majumdar T, Mahapatra A: **Kinetic and mechanistic studies of the interaction of 2-mercapto pyridine with dichloro[1-alkyl-2-(arylazo)imidazole] palladium(II) complexes.** *Transition Met Chem* 2006, **31:**1017-1023.
31. Saha S, Majumdar T, Mahapatra A: **Kinetic and mechanistic studies on the interaction of 2-aminopyrimidine with dichloro[1-alkyl-2-(arylazo)imidazole]palladium (II) complexes.** *Indian J Chem* 2006, **45A:**877-881.
32. Saha S, Sarkar PK, Mahapatra A: **Kinetics and Mechanism of the Reactions of Picolinic Acid with Dichloro-{1-alkyl-2-(arylazo)imidazole}palladium(II) Complexes.** *Transition Met Chem* 2006, **31:**389-395.
33. Ghosh PK, Saha S, Mahapatra A: **Pd-Cl cleavage of dichloro-[1-alkyl-2-(naphthylazo) imidazole] palladium(II) complexes by picolinic acid : Kinetic and mechanistic studies.** *Polyhedron* 2007 in press.
34. Saha S, Mahapatra A: **Interaction Between Pd(RaaiR/)Cl_2 and HQ: Reaction Dynamics and Mechanism (RaaiR/= 1-alkyl-2-(arylazo)imidazole; HQ = 8-Quinolinol).** *Inorg React Mech* 2006, **6:**71-80.
35. Ghosh PK, Saha S, Mahapatra A: **Mechanistic studies on the Pd-Cl cleavage of dichloro-[1-alkyl-2-(naphthylazo)imidazole]palladium(II) complexes by 8-quinolinol.** *Polyhedron* 2007, **26:**2655-2662.
36. Zamora F, Kunsman M, Sabat M, Lippert B: **Metal-Stabilized Rare Tautomers of Nucleobases. Imino Tautomer of Adenine in a Mixed-Nucleobase Complex of Mercury(II).** *Inorg Chem* 1997, **36:**1583-1587.
37. Jolibois F, Cadet J, Grand A, Subra R, Rega N, Barone V: **Structures and Spectroscopic Characteristics of 5,6-Dihydro-6-thymyl and 5,6-Dihydro-5-thymyl Radicals by an Integrated Quan-**

tum Mechanical Approach Including Electronic, Vibrational, and Solvent Effects. *J Am Chem Soc* 1998, **120:**1864-1871.
38. Dinda J, Das D, Santra PK, Sinha C, Falvello LR: **Cyclopalladation versus hydroxylation. A case of pH dependence.** *J Organomet Chem* 2001, **629:**28-38.
39. Roy R, Das D, Banerjee M, Sinha C, Mahapatra A: **Nucleophilic ligand displacement in dichloro[2-(arylazo)heterocycle]palladium(II) complexes by benzimidazole – a kinetic and mechanistic study.** *Trans Met Chem* 2001, **26:**205-211.
40. Roy R, Misra TK, Sinha C, Mahapatra A, Sanyal A: **Kinetics and mechanism of nucleophilic substitution of dichloroarylazopyridinepalladium(II) by pyridine bases.** *Transition Met Chem* 1997, **22:**453-458.
41. Pal CK, Chattopadhyay S, Sinha C, Bandyopadhyay D, Chakravorty A: **Facile regiospecific aromatic hydroxylation in palladium azopyridines and structural characterization of phenolato product.** *Polyhedron* 1994, **13:**999-1003.
42. Goswami S, Kharmawphlang W, Deb AK, Peng SM: **Monovalent copper complexes of N-aryl-pyridine-2-aldimine. Synthesis, characterization and structure.** *Polyhedron* 1996, **15:**3635-3641.
43. Wakatsuki Y, Yamazaki M, Grutasch PA, Santhanam M, Ku AC: **Study of intramolecular sensitization and other excited-state pathways in orthometalated azobenzene complexes of palladium (II).** *J Am Chem Soc* 1985, **107:**8153-8159.
44. Baikalova LV, Zyryanov IA, Afonin AV, Trofimov BA: **Features of 2-, 3-Aminopyridines and 2-Aminopyrimidine Condensation with 2-Formylimidazoles.** *Russian Journal of Organic Chemistry* 2002, **38:**1674-1680.