Tanzania Journal of Science 44(2): 45-63, 2018 ISSN 0856-1761, e-ISSN 2507-7961

A TRANS INFLUENCE AND π-CONJUGATION EFFECTS ON LIGAND SUBSTITUTION REACTIONS OF Pt(II) COMPLEXES WITH TRIDENTATE PENDANT N/S-DONOR LIGANDS

Grace A Kinunda
Chemistry Department, University of Dar es Salaam,
P. O. Box 35061, Dar es Salaam, Tanzania
E-mail:kinundag2010@gmail.com/kinundag@udsm.ac.tz

ABSTRACT

*The rate of displacement of the chloride ligands by three neutral nucleophiles (Nu) of different steric demands, namely thiourea (TU), N,N'-dimethylthiourea (DMTU) and N,N,N,'N-tetramethylthiourea (TMTU) in the complexes viz; [Pt(II)(bis(2-pyridylmethyl)amine)Cl]ClO_4, (**Pt1**), [Pt(II){N-(2-pyridinylmethyl)-8-quinolinamine}Cl]Cl, (**Pt2**), [Pt(II)(bis(2-pyridylmethyl)sulfide)Cl]Cl, (**Pt3**) and [Pt(II){8-((2-pyridylmethyl)thiol)quinoline}Cl]Cl, (**Pt4**) was studied under pseudo first-order conditions as a function of concentration and temperature using a stopped-flow technique and UV-Visible spectrophotometry. The observed pseudo first-order rate constants for substitution reactions obeyed the simple rate law* $k_{obs} = k_2[\mathrm{Nu}]$. *The results have shown that the chloro ligand in **Pt(N^S^N)** complexes is more labile by two orders of magnitude than **Pt(N^N^N)** complexes due to the high trans labilizing effect brought by the S-donor atom. The quinoline based Pt(II) complexes (**Pt2** and **Pt4**) have been found to be slow than their pyridine counterparts **Pt1** and **Pt3** due to poor π-acceptor ability of quinoline. Second-order kinetics and large negative activation entropies support an associative mode of activation.*

Key words: Substitution, nucleophiles, *pseudo* first-order, associative, entropy

INTRODUCTION

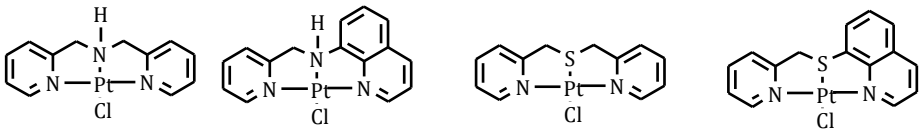
The substitution kinetics of different platinum(II) complexes towards biomolecules with sulfur donor atoms is very important from a biological and bioinorganic point of view (Banerjee 2000). Over the last few decades, there has been a great interest in studying the substitution reactions of monofunctional Pt(II) complexes, especially those with tridentate ligands, such as diethylenetriamine (dien), bis(2-pyridylmethyl)amine (bpma) or 2,2':6',2-terpyridine (terpy) as non-leaving groups (Hofmann et al. 2003, Soldatović and Bugarčić 2005, Summa et al. 2006, It has been shown that small structural modifications in the non-labile chelate ligand can produce significant changes in the substitutional reactivity of the Pt(II) complexes. Most importantly, the reactivity of these Pt(II) complexes is significantly increased when π-back donation of electron density from the metal centre into the non-leaving ligand is involved. For example, chloride substitution in $[Pt(terpy)Cl]^+$ in methanol is 10^2 to 10^4 times faster than for the cationic $[Pt(dien)Cl]^+$ (Pitteri et al. 1995, Romeo et al. 2000). This difference has been attributed to the stabilization of the five-coordinate transition state relative to the ground state brought about by the delocalization of the π-electron density, which is back-donated from platinum *d*π-orbitals into the π*-molecular orbitals of the terpy ligand (Mambanda and Jaganyi 2017).

Addition of electron-donating groups on the ancillary positions of the terpy ligand has been shown to weaken this stabilization resulting in retarded rates of substitution of the chloride (Reddy and Jaganyi 2008). The opposite is true for electron-withdrawing groups (Jaganyi et al. 2008). On the other hand, increasing the number and varying the position (*cis*/*trans*) of π-acceptor groups such as pyridine affects the electronic communication in the system hence affecting the reactivity of the Pt(II) centre (Jaganyi et al. 2001). Studies by Hofmann et al. (2003) and Papo and Jaganyi (2015) showed that *cis* π-back donation of electron density is stronger than the *trans* π-back donation. It has also been shown that while the *cis* σ-donor effect slows down the reactivity of the Pt(II) complex, the *trans* σ-donor accelerates the rate of substitution reaction (Mambanda and Jaganyi 2011, 2017). Pitteri et al. (1994, 1995, 2005) studied substitution reactions of Pt(II) complexes containing neutral tridentate chelating ligands with sulfur and nitrogen donors of the type N^S^N and N^N^N (where N^S^N = bis(2-pyridylmethyl)sulphide and N^N^N = bis(2-pyridylmethyl)amine) using ionic, neutral and pyridine nucleophiles. The reactivity data of the Pt(II) complexes indicated that apart from the π-interaction of the pyridine rings, the lability of the leaving group also depended on the nature or number of the donor atoms *trans* and/or *cis* to the replaceable chloride ligand. For example, Pt(N^S^N) complexes were found to be more reactive than their Pt(N^N^N) counterparts. The high reactivity of Pt(N^S^N) complexes was attributed to the strong *trans*-labilization effect of the coordinated sulfur which results into elongation of the Pt–Cl bond at the ground state (Pitteri et al. 1994, 1995, 2005). Such labilization has also been illustrated by earlier studies by Hofmann et al. (2003) and Papo and Jaganyi (2015) when *trans* donor atoms of the tridentate chelate were varied from N to C. The reactivity of Pt(N^C^N) complexes was found to be higher compared with the Pt(N^N^N) complexes owing to the strong *trans*-labilizing effect of Pt–C that induces high intrinsic reactivity (Hofmann et al. 2003, Papo and Jaganyi 2015). This is due to the ability of the Pt–C bond to labilize the leaving group in square-planar metal complexes through the kinetic *trans*-effect.

Recent studies have shown that introduction of isoquinoline and quinoline ligand in the non-labile chelated framework can decrease the substitution rate of the Pt(II) complex in the range of 3-5 orders of magnitude due to the fact that isoquinoline and quinoline are net σ-donors (Ongoma and Jaganyi 2012, Kinunda and Jaganyi 2014, Wekesa and Jaganyi 2014).

A search in the literature domain shows limited information on the factors which influence the reactivity of Pt(II) complexes bearing ligands with extended π-conjugation and different *trans* donor atoms. It is from this background that the current study was occasioned to investigate the competing roles of π-backbonding through the extended chelate and the strong σ-donor *trans* effect of sulfur atom on the reactivity of Pt(II) metal complex within the chelate framework. To achieve this, the *cis* positioned pyridyl group was systematically replaced with a quinoline group, and in *trans* position with N and S donor atoms. Therefore, chloride substitution of platinum(II) complexes with the general formulae [Pt(N^N^N)Cl] and [Pt(N^S^N)Cl namely: [Pt(II)(bis(2-pyridylmethyl)amine)Cl]ClO_4, (**Pt1**), [Pt(II){N-(2-pyridinylmethyl)-8-quinolinamine}Cl]Cl, (**Pt2**), [Pt(II)(bis(2-pyridylmethyl)sulfide)Cl]Cl, (**Pt3**) and [Pt(II){8-((2-pyridylmethyl)thiol)quinoline}Cl]Cl, (**Pt4**) (Scheme 1) were studied using thiourea

nucleophiles of different steric demand; thiourea (TU), 1,3-dimethyl-2-thiourea (DMTU) and 1,1,3,3,-tetramethyl-2-thiourea (TMTU). The thiourea nucleophiles were chosen because of their good solubility, neutral character, different nucleophilicity, steric hindrance, binding properties and biological relevance (Ashby 1990, Murray and Hartley 1981, Reedijk 1999). In addition, thiourea is a very useful nucleophile since it combines the ligand of thiolates (σ-donor) and thioethers (σ-donor and π-acceptor) and is used as a protecting agent to minimize nephrotoxicity following cisplatin treatment (Reedijk 1999). DFT calculations were performed in an effort to account for the observed reactivity of the complexes.



Pt1 **Pt2** **Pt3** **Pt4**

Scheme 1: Structures of the complexes investigated.

MATERIALS AND METHOD

Thiosemicarbazide (99.0%), 8-bromoquinoline (98%), 8-aminoquinoline (98%), 2-picolyl chloride hydrochloride (98%), 8-mercaptoquinoline hydrochloride (98%), NaO^tBu (97%), pyridine-2-carboxaldehyde (99%), lithium perchlorate (98%) and sodium borohydride (98%) were obtained from Aldrich. Potassium tetrachloroplatinate (K_2PtCl_4, 99.99%) was procured from Strem. All other chemicals were of the highest purity commercially available and were used without further purification. Solvents were dried by standard methods (Carlsen et al. 1979) and distilled prior to use. Synthetic work was performed under nitrogen atmosphere using standard Schlenk techniques and vacuum-line systems.

Synthesis of the ligands

Ligands di-(2-picolyl)sulfide (**dps**) 8-((2-pyridylmethyl)thiol)quinoline (**NSNQ**) and N-(2-pyridinylmethyl)-8-quinolinamine (**NNNQ**) were synthesized following literature methods by Sung et al. (2005), Canovese et al. (2006) and Kinunda and Jaganyi (2014), respectively. Character identification data of the ligands were in agreement with the proposed structures.

dps: Yield: brown oil, 712.8 mg, 66%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ/ppm = 8.52 (br-d, 2H), 7.61 (td, 2H), 7.35 (d, 2H), 7.13 (ddd, 2H), 3.81 (s, 4H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ/ppm = 158.5, 149.5, 136.6, 123.3, 121.9 and 37.6. *Anal. calcd*. for $C_{12}H_{12}N_2S$: C 66.67, H 5.55, N 12.96. *Found*: C 66.16, H 5.36, N 13.01. TOF MS ES$^+$: *m*/*z*, $[M+Na]^+$ = 239.06.

NSNQ: Yield yellow powder, 572.3 mg, 90%. ^{1}H NMR ($CDCl_3$, 400 MHz,): δ/ppm = 8.94(br-d, 1H), 8.54 (d, 1H), 8.11(dd, 1H), 7.63-7.52 (m, 4H), 7.45-7.35 (m, 2H), 7.14 (t, 1H), 4.47 (s, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ/ppm = 157.7, 149.3, 149.0, 145.6, 137.7, 136.9, 136.4, 128.3, 126.7, 125.3, 124.4, 123.0, 122.1, 121.7, 37.7. *Anal. Calcd*. for $C_{15}H_{12}N_2S$: C 71.43, H 4.76, N 11.11, S 12.70. *Found* C 71.41, H 4.70, N 11.19, S 12.72. TOF MS ES$^+$: *m*/*z*, $[M+Na]^+$ = 275.06.

NNNQ: Yield yellow oil, 686.7 mg, 63%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ/ppm = 8.76(td, 1H), 8.62 (d, 1H), 8.05(ddd, 1H), 7.60 (td, 1H), 7.42-7.29 (m, 3H), 7.14 (dd, 1H), 7.09(dd, 1H), 6.92(dd, 1H), 6.63(d, 1H), 4.71 (s, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz): δ/ppm = 159.3, 149.3, 147.6, 136.7, 136.3, 127.7, 127.4, 122.0, 121.4, 121.3, 116.3, 114.5, 110.2, 105.6, 49.3. TOF MS ES$^+$: *m*/*z*, $[M + 23]^+$ = 258.10.

Synthesis of Pt(II) Complexes

Complexes **Pt1**, **Pt2**, **Pt3** and **Pt4** were synthesized according to the published procedures (Annibale et al. 2005, Weber and van Eldik 2005, Kinunda and Jaganyi 2014). Platinum precursor *cis*/*trans*-$PtCl_2(SMe_2)_2$ was synthesized as described in literature (Darensbourg et al. 2007). The purity of all the Pt(II) complexes were confirmed by NMR, elemental analysis and LC-MS.

Pt1: Yield: 242.3 mg, yellow powder (95%). ^{1}H NMR (DMSO-d_6, 400 MHz,): δ/ppm = 8.82(dd, 2H), 8.60 (br s, 1H), 8.23(ddd, 2H), 7.76 (d, 2H), 7.63 (t, 2H), 4.92(m, 2H), 4.51 (dd, 2H). ^{13}C NMR (DMSO, 400 MHz): δ/ppm = 167.4, 149.4, 141.4, 125.7, 123.4, 59.4. ^{195}Pt NMR (DMSO-d_6, 400 MHz): δ/ppm = 2344.8. *Anal. Calcd.* for $C_{12}H_{13}N_3PtCl_2O_4$: C 27.22, H 2.46, N 7.94. *Found* C 26.72, H 2.45, N 7.62. TOF MS ES$^+$: *m*/*z*, $[M + H]^+$ = 430.05.

Pt2: Yield: 15.1 mg, (57%). ^{1}H NMR (DMSO-d_6, 400 MHz,): δ/ppm =8.91 (d, 1H), 8.78(dd, 1H), 8.64 (dd, 1H), 8.54 (dd, 1H), 8.40 (td, 1H), 8.29 (ddd, 1H), 8.17-8.09 (m, 1H), 7.93 (m, 1H), 7.76 (m, 2H), 7.64 (m, 1H), 7.57 (s, 2H). ^{13}C NMR (DMSO, 400 MHz,): δ/ppm = 159.8, 148.7, 147.6, 135.7, 135.3, 128.7, 128.4, 125.0, 122.4, 121.7, 115.3, 113.5, 109.2, 106.6, 51.1. ^{195}Pt NMR (DMSO-d_6, 400 MHz): δ/ppm = 2314.8. *Anal. Calcd*. for $C_{15}H_{13}N_3PtCl_2$: C 35.93, H 2.59, N 8.38. *Found* C 35.44, H 2.39, N 7.91. TOF MS ES$^+$: *m*/*z*, $[M+H]^+$ = 466.04.

Pt3: Yield yellowish brown powder, 56.3 mg, 63%. ^{1}H NMR (DMSO-d_6, 400 MHz): δ/ppm = 8.98 (dd, 2H), 8.27 (td, 2H), 7.90 (d, 2H), 7.67 (t, 2H), 4.85 (m, 4H). ^{13}C NMR (DMSO-d_6, 400 MHz): δ/ppm = 166.6, 156.6, 150.1, 142.0, 137.5 and 17.7. ^{195}Pt NMR (DMSO-d_6, 400 MHz): δ/ppm = 2960.7. *Anal. calcd*. for $C_{12}H_{12}N_2SPtCl_2$: C 29.87, H 2.49, N 5.81, S 6.64. *Found*: C 29.35, H 2.29, N 5.90, S 6.48. TOF MS ES$^+$: *m*/*z*, $[M+H]^+$ = 447.01.

Pt4: Yield orange powder, 138.3 mg, 61%. ^{1}H NMR (DMSO-d_6, 400 MHz,): δ/ppm = 9.44(dd, 1H), 8.93 (dd, 1H), 8.65(dd, 1H), 8.46-7.89 (m, 4H), 7.31-7.14 (m, 2H), 6.63 (d, 1H), 4.86 (d, 2H). ^{13}C NMR (DMSO, 400 MHz,): δ/ppm = 157.7, 149.3, 149.0, 145.6, 137.7, 136.9, 136.4, 128.3, 126.7, 125.3, 124.4, 123.0, 122.1, 121.7, 37.7. ^{195}Pt NMR (DMSO-d_6, 400 MHz): δ/ppm = 2149.3. *Anal. Calcd*. for $C_{15}H_{12}N_2SPtCl_2$: C 34.75, H 2.32, N 5.40, S 6.18. *Found* C 34.21, H 2.06, N 4.96, S 6.32. TOF MS ES$^+$: *m*/*z*, $[M+ H]^+$ = 483.01.

Preparation of Complex and Nucleophile Solutions for Kinetic Analysis

Stock solutions of the complexes were prepared by dissolving the known amounts in 2% DMF to improve the solubility and topped up with 98% of methanolic solution of constant ionic strength of 0.1 M. The ionic strength of the solution was maintained using sodium perchlorate ($NaClO_4$, 0.09 M) and lithium chloride (LiCl, 0.01 M) because perchlorate anion is non-coordinating (Appleton et al. 1984). 10 mM LiCl was added to the solvent system to prevent any possibility of solvolysis of the chloro ligand. The resulting complex concentrations were approximately 0.2 mM for **Pt1**, **Pt3** and **Pt4** and 0.26 mM for **Pt2** before mixing with nucleophile solutions. A total of three

neutral nucleophiles, *viz.* TU, DMTU and TMTU with different steric hindrance were used as entering nucleophiles. Solutions of these nucleophiles were prepared fresh before use by dissolving in a 0.1 M $NaClO_4$/LiCl methanolic solution. Nucleophiles concentrations of approximately 40, 30, 20 and 10-fold in excess over that of the metal complex were prepared by diluting the stock solution which was 50-fold in excess over that of Pt complex. These concentrations were chosen to maintain the *pseudo* first-order conditions and to push the reaction to completion.

Physical Measurements and Instrumentation

^{1}H, ^{13}C and ^{195}Pt NMR spectra were recorded on a Bruker Avance III 500 or Bruker Avance III 400 at frequencies of 500 MHz or 400 MHz and 125 MHz/100 MHz using either a 5 mm BBOZ probe or a 5 mm TBIZ probe. All chemical shifts are quoted relative to the relevant solvent signal at 30 ˚C unless stated otherwise. Elemental (CHN) analysis of the ligands and complexes were performed on Carlo Erba Elemental Analyzer 1106. Low resolution electron-spray ionization (ESI^+) mass spectra of the samples were recorded on a Waters Micromass LCT Premier spectrometer operated in positive ion mode. UV-Visible spectra and kinetic measurements of slow reactions were recorded on a Cary 100 Bio UV-Visible spectrophotometer with a cell compartment thermostated by a Varian Peltier temperature controller having an accuracy of ± 0.05 ˚C. Kinetic measurements of fast reactions were monitored using an Applied Photophysics SX 20 stopped-flow reaction analyser coupled to an online data acquisition system. The temperature of the instrument was controlled to within ± 0.1 ˚C.

Computational Calculations

Density Functional Theoretical (DFT) calculations were performed using a well-established approach for the third row transition metal complexes, to identify the energy-minimized structures based on B3LYP/LANL2DZ (Los Alamos National Laboratory 2 double ζ) level theory, with inner core electrons of Pt replaced by relativistic effective core potential (ECP) (Beck 1993, Lee et al. 1988, Hay and Wadt 1985). The singlet states were used due to low electronic spin of Pt(II) complexes. The frontier molecular orbitals of these complexes were generated in Gauss view 5.0 using the same level of theory. The influence of the methanol solvent was evaluated *via* single-point computations using the CPCM (Barone and Cossi 1998, Cossi et al. 2003) formalism. Gaussian09 suite of programs was used for all DFT computations (Frisch et al. 2009).

Kinetic Measurements

The working wavelengths (Table SI 1) were determined by recording spectra of the reaction mixture over the wavelength range of 200 to 650 nm using Cary 100 Bio UV-Visible spectrophotometer. All kinetic experiments were performed under *pseudo* first-order conditions for which the concentration of the nucleophile was always at least a 10-fold excess. Kinetic data were graphically analysed using the software package, Origin 7.5® (Origin7.5 2003). The activation parameters, $\Delta H^{\#}$ and $\Delta S^{\#}$, were obtained by studying temperature dependence of the rate constant in the range of 15–35 ˚C at an interval of 5 ˚C with the nucleophile concentration held constant at 30 times the concentration of the metal complex.

RESULTS

Computational Analysis

In order to understand the role of the structural and electronic differences that

exist in the complexes on the observed kinetic results, computational studies were carried out at the DFT level of theory. Geometry-optimized structures as well as the key data are presented in Tables 1 and 2. For all investigated complexes, the HOMO is located on the dz^2 orbital of the metal and the LUMO is populated on the aromatic region of the ligand. Complexes **Pt1**, **Pt3** and **Pt4** show maximum overlap of the *d*π-orbitals of the metal with the π*-orbitals of the ligand. This is expected to enhance the π-back bonding character which will result into increase in reactivity of the metal centre. Generally, the electrophilicity indices show that quinoline based complexes (ω = 6.067 for **Pt2** and ω = 6.155 for **Pt4**) are less electrophilic compared to pyridine based complexes (ω = 7.518 for **Pt1** and ω = 7.608 for **Pt3**) with **Pt(N^S^N)** being superior in electrophilicity. **Pt2** and **Pt4** are characterized by the rise in LUMO energy level making them inaccessible for π-back donation. The HOMO-LUMO energy gap decreases with increasing π-conjugation in the order of 3.65 ≳ 3.57 < 3.51 < 3.41 for **Pt3**, **Pt1**, **Pt2** and **Pt4** respectively. The NBO charges are more positive by 0.17 units for **Pt(N^N^N)** complexes than **Pt(N^S^N)** indicating that the reactivity of the complexes towards substitution cannot sorely be explained by NBO charges but rather how electrons have been distributed within the complexes.

Table 1: Geometry optimized structures and DFT-calculated (B3LYP/LanL2DZ) HOMOs and LUMOs of the investigated complexes

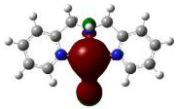
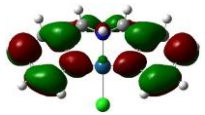
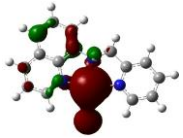
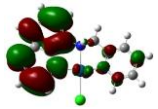
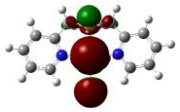
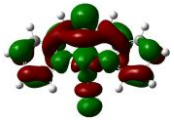
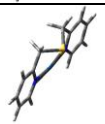
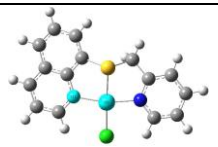
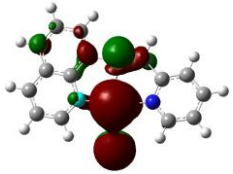
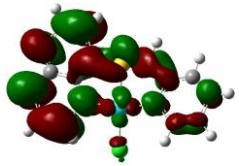
Complex Structure	HOMO	LUMO	Planarity
 **Pt1**			
 **Pt2**			
 **Pt3**			
 **Pt4**			

Table 2: Summary of DFT calculated parameters of the complexes studied

Property	**Pt1**	**Pt2**	**Pt3**	**Pt4**
HOMO-LUMO energy				
LUMO /eV	-3.396	-2.860	-3.445	-2.974
HOMO/eV	-6.967	-6.371	-7.097	-6.388
ΔE /eV	3.571	3.511	3.652	3.414
NBO charges				
Pt	0.540	0.550	0.365	0.380
$N_{q/py}$	-0.510	-0.495	-0.507	-0.499
N_{py}	-0.510	-0.509	-0.507	-0.506
Dipole moment (Debye)	14.005	12.071	11.125	10.738
Electrophilicity index (ω)	7.518	6.067	7.608	6.418
Bond Length (Å)				
Pt–N/S_{trans}	2.051	2.062	2.392	2.396
Pt–Cl	2.440	2.437	2.444	2.442
Bond Angles (˚)				
N/s_{trans}–Pt–Cl	179.43	178.35	175.15	176.25
$N_{q/py}$–Pt–N_{py}	165.94.	165.12	168.56	166.19

q and py are quinoline and pyridine respectively

Kinetic Measurements

The kinetics of the substitution of coordinated chloride by thiourea nucleophiles was investigated under *pseudo* first-order conditions in order to drive the reactions to completion. Conventional UV-Visible spectrophotometry and Stopped-Flow technique were used for kinetic measurements by following the change in absorbance at suitable wavelengths as a function of time. The selected wavelengths are recorded in Table SI 3 **(ESI)**. The kinetic traces obtained at suitable wavelengths gave excellent fits to first-order exponential decay to generate the observed *pseudo* first-order rate constants, k_{obs} at the specific concentration of the nucleophile and temperature. A typical Stopped-Flow kinetic trace at 375 nm recorded by mixing methanol solutions of **Pt3** (0.2 mM) and 6 mM of TU at ionic strength of 0.1 M ($NaClO_4$) is shown in Fig. 1.

An example of the UV-Visible spectra obtained from the reaction between **Pt2** and TU is shown in Fig. 2. Inset to figure 2 is the corresponding kinetic trace recorded at 375 nm.

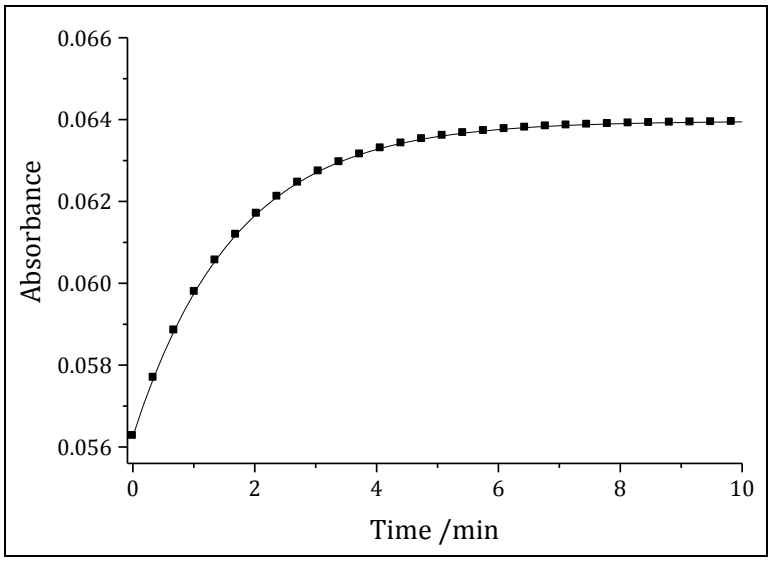


Figure 1: Stopped-Flow kinetic trace of **Pt3** (0.2 mM) with 6 mM thiourea at 298 K in methanol, I = 0.1 M ($NaClO_4$/LiCl)

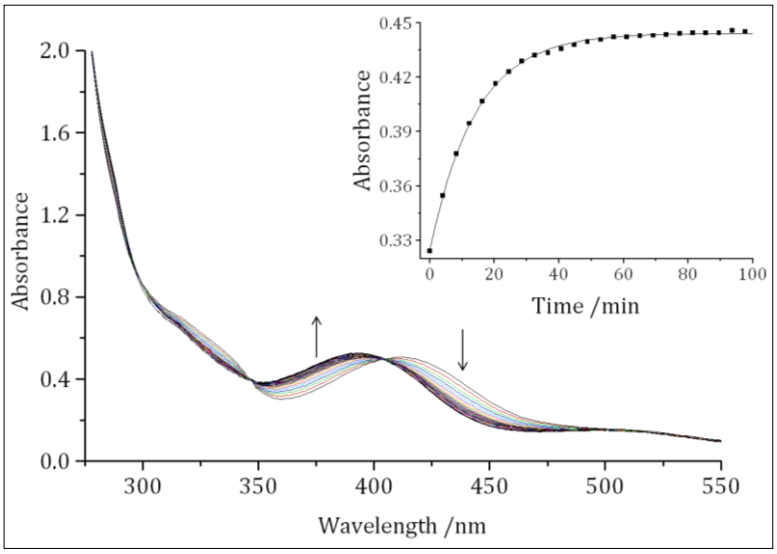


Figure 2: UV-Vis spectra recorded as a function of time for the reaction between **Pt2** and 6 mM of thiourea at 25 ˚C in methanol, I = 0.1 M ($NaClO_4$/LiCl). Inset is the kinetic trace obtained at 375 nm.

When the obtained k_{obs} values were plotted against the concentration of the entering nucleophile, a linear dependence on the nucleophile concentration with zero intercepts was observed for all complexes. The absence of a noticeable intercept is ascribed to the stronger binding of the soft thiourea nucleophiles to the metal centre (Schmülling et al. 1992, Hofmann et al. 2003). Representative plots are shown in Fig. 3 (also figures SI 5 and 7) and the observed rate constants obeys the rate law $k_{obs} = k_2[\mathrm{Nu}]$, typical of nucleophilic substitution at planar tetra-coordinate d^8 metal complexes in which k_2 is the second-order rate constant for the direct attack of the nucleophile (Nu) at the metal centre.

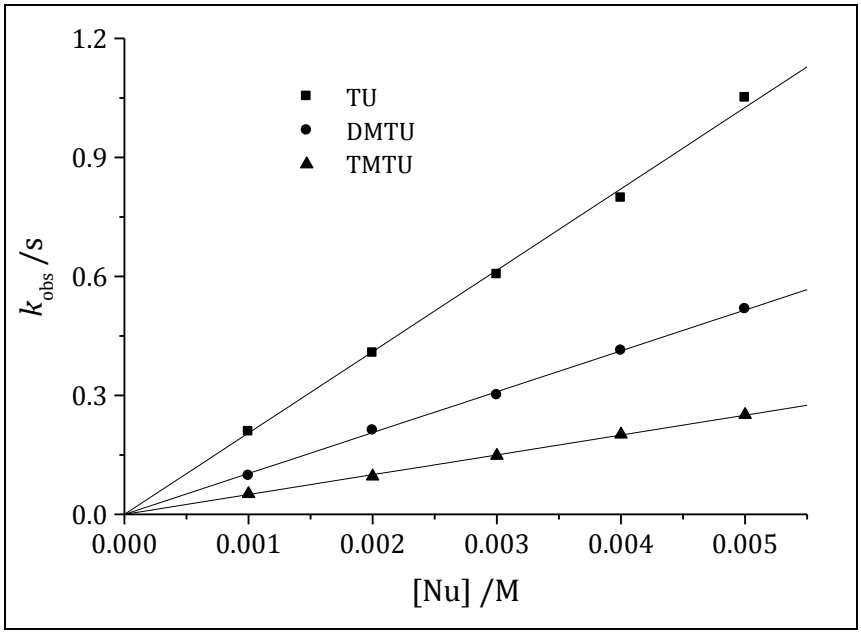


Figure 3: Dependence of k_{obs} on the concentration of entering nucleophile for the chloride substitution of **Pt3** (0.2 mM) in methanol, *I* = 0.1 M ($NaClO_4$/LiCl), T= 25 ˚C.

The values of the second-order rate constants, k_2, were obtained from the slope of individual plot at 25 ˚C and are summarised in Table 3. The temperature dependence of the second-order rate constants was investigated over a temperature range of 15-35 ˚C. Typical Eyring plots are shown in Fig. 4 (also figures SI 6 and 8).

The enthalpy of activation, ($\Delta H^{\#}$) and entropy of activation, ($\Delta S^{\#}$) were determined using the Eyring equation (Eyring 1935). These activation parameters are summarized in Table 3.

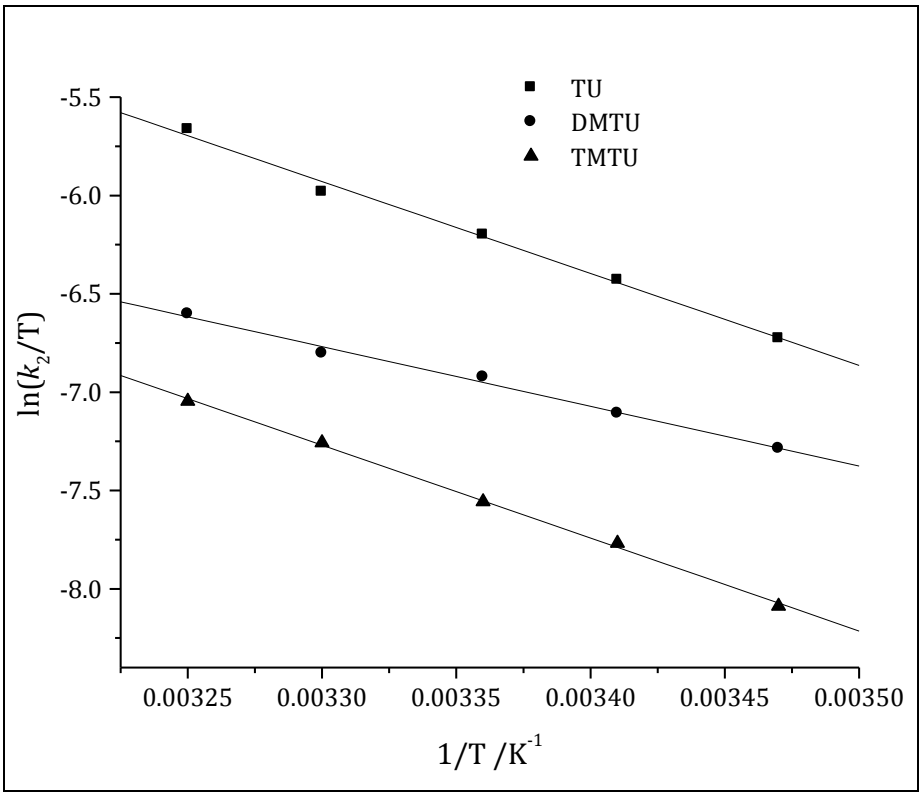
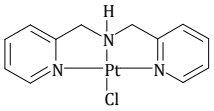
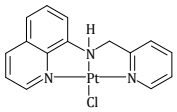
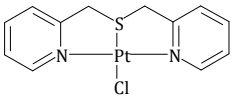
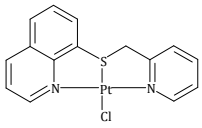


Figure 4: Eyring plots for the reaction of **Pt3** with a series of neutral nucleophiles at various temperatures in the temperature range 15-35 ˚C.

Table 3: Summary of k_2 values and activation parameters

Complex	Nu	k_2 / M^{-1} s^{-1}	$\Delta H^{\#}$ /kJ mol^{-1}	$\Delta S^{\#}$ /J K^{-1} mol^{-1}
 **Pt1**	TU			
	DM	0.50 ± 0.01	50 ± 2	-130 ± 6
	TU	0.16 ± 0.004	75 ± 3	-58 ± 10
	TM	0.03 ± 0.001	77 ± 1	-109 ± 4
	TU			
 **Pt2**	TU			
	DM	0.29 ± 0.003	59 ± 3	-104 ± 10
	TU	0.13 ± 0.001	51 ± 1	-138 ± 3
	TM	0.05 ± 0.001	59 ± 2	-150 ± 5
	TU			
 **Pt3**	TU			
	DM	205.19 ± 2.40	25 ± 2	-132 ± 5
	TU	103.07 ± 0.79	28 ± 1	-173 ± 3
	TM	49.99 ± 0.35	38 ± 1	-122 ± 4
	TU			
 **Pt4**	TU			
	DM	21.03 ± 0.49	35 ± 1	-170 ± 3
	TU	11.07 ± 0.19	38 ± 1	-158 ± 3
	TM	2.07 ± 0.03	48 ± 5	-125 ± 16
	TU			

DISCUSSION

In this paper, the substitution behaviour of mono-functional Pt(II) complexes with thiourea-based nucleophiles is described. Thiourea nucleophiles have been chosen due to their good solubility, neutral character and high nucleophilicity. In general, thiourea coordinates through sulfur to typical electrophilic reaction partners such as Pt(II), Pd(II) and Co(III) metals. This is because sulfur-donor atoms have a high affinity for Pt(II) complexes (Lippert 1999, Guo and Sadler 2000, Bugarčić 2007). The reactivity of the complexes towards substitution of chloride by all the nucleophiles investigated follows the trend **Pt3** > **Pt4** > **Pt1** > **Pt2**. This can be explained by the *trans*-labilizing effect and π-interactions between the filled *d*π-orbitals of the metal with the empty π*-orbitals of the ligand. Looking at the structures of the investigated Pt(II) complexes, the donor atom *trans* to leaving group is either N or S, and the *cis*-coplanar ligands in **Pt2** and **Pt4** is quinoline and pyridine moieties whereas in **Pt1** and **Pt3** the *cis* ligands comprise of two pyridine rings.

The high reactivity of **Pt3** and **Pt4** complexes which is two orders of magnitude higher than **Pt1** and **Pt2** complexes is attributed to the sulfur atom which is known to be a σ-donor atom and is positioned *trans* to the leaving group. It is known that a group with strong σ-donor properties will weaken the bond *trans* to it in the ground state (σ-

trans effect and *trans* influence). This is because the bonding character shares a greater amount of metal *p*-orbitals in the transition state than in the ground state (transitional state σ-effect) (Chval et al. 2008, Langford and Gray 1965). On the other hand, strong π-acceptor groups accelerate the substitution reaction by accommodating the excess electron charge induced on the metal through a bimolecular attack of the entering group resulting into stabilization of the penta-coordinate transition state (Orgel 1956).

Comparing the σ-donicity of the *trans* atoms, N and S in these two sets of complexes investigated, sulfur is superior owing to the fact that it is less electronegative compared to nitrogen (Wang et al. 2015). The *trans* effect of sulfur causes electrostatic destabilization of the ligand in the *trans* position and this is observed in Pt–Cl bond length elongation (Table 2). Thus, the higher reactivity of **Pt3** and **Pt4** complexes compared to **Pt1** and **Pt2** complexes is mainly due to the stronger *trans*-labilizing effect of the Pt–S bond which induces a high intrinsic reactivity. Also, by being bigger in size, the greater polarizability of the sulfur allows some charge transfer to move away from the metal through the σ-framework as the incoming group becomes bound (Pitteri et al. 2005, Nkabinde et al. 2017). Such labilization and polarizability has clearly been demonstrated in a number of studies (Bugarčić 2004, Bogojeski 2010, Hochreuther 2012). In addition, the HOMO-LUMO maps show that there is a metal to ligand π-interactions through the sulfur bridge in **Pt3** and **Pt4**, whose strength helps to stabilize the five coordinate transition state by making the complexes more reactive towards substitution reaction. This is facilitated by the lone pair of electrons in the *p*-orbitals of S which forms π-bonds with platinum *d*π-orbitals to such an extent that the metal centre achieves an 18-electron configuration.

Complexes **Pt1** and **Pt3** react faster than **Pt2** and **Pt4**. The difference in reactivity between these two sets of complexes can be explained by the degree of π-backbonding character of pyridine compared to quinoline ligand. The two pyridine rings in the chelate framework of **Pt1** and **Pt3** increase the lability of the leaving group due to their electron-withdrawing effect from the metal centre through π-back bonding. The π-back bonding increases the total positive charge of the Pt(II) atom by a decrease of electron density in the *xz* plane hence facilitates a nucleophilic attack and stabilizes corresponding penta-coordinated transition state. The decrease in reactivity of **Pt2** and **Pt4** is due to the poor π-acceptor property of the quinoline ligand (Ongoma and Jaganyi 2012, Kinunda and Jaganyi 2014, Wekesa and Jaganyi 2014). This adds electron density into the Pt(II) metal centre resulting in the retardation of the incoming nucleophiles through repulsion. Results on the dampening of the rate of substitution reactions of Pt(II) complexes as an outcome of *cis* σ-effect with carbon donor atom has been reported (Hofmann et al. 2003, Reddy and Jaganyi 2008). The high reactivity of **Pt1** and **Pt3** when compared to **Pt2** and **Pt4** is supported by high value of dipole moment due to its π-withdrawing character of two pyridine rings compared to the quinoline moiety.

Having a close look on DFT data, the NBO charges show that **Pt1** and **Pt2** complexes are more positive than **Pt3** and **Pt4**. The low NBO charges observed for **Pt3** and **Pt4** is attributed to the strong σ-donor effect of the *trans* sulfur atom. This reduces the total (positive) NBO charge of the Pt(II) atom by an increase of electron density in the *xy* plane leaving the metal centre less positive.

For **Pt1** and **Pt2** complexes, the electronegativity of *trans* nitrogen helps to quench the electron density on the metal centre rendering high NBO charges. Therefore, if the NBO charge distribution in the complexes controls the reactivity towards the approach of the nucleophile, then the chloride leaving group in **Pt1** and **Pt2** complexes could have been more labile than in **Pt3** and **Pt4** complexes. This was not the case with the reactivity data observed.

Previous studies have used NBO charges as an indicator for the electron density around the Pt(II) centre (Mambanda and Jaganyi 2011, Ongoma and Jaganyi 2012). Nevertheless, the challenge of NBO charge has always been the small magnitude of difference and sometimes inconsistence with reactivity (Ongoma and Jaganyi 2012, Ongoma and Jaganyi 2013). Inspired by the success of global electrophilicity index in predicting the chemical reactivity and addressing NBO charge inadequacies, electrophilicity index were incorporated in the study to unknot the intrinsic electronic properties of Pt(II) complexes. Electrophilicity index possesses adequate information regarding structure, stability, reactivity, toxicity, bonding, interactions and dynamics (Chattaraj et al. 2006 and 2011, Parthasarathi et al. 2003 and 2004, Mebi 2011, Domingo et al. 2003, Cedillo and Contreras 2012). The quantification of the electrophilicity concept is based on the maximum energetic stabilization of a species that arises from accepting charge. The electrophilicity indices in Table 2 show that generally, quinoline based complexes, **Pt2** and **Pt4** are less electrophilic therefore should be less reactive than their **Pt1** and **Pt3** counterparts with two pyridine rings. Also **Pt(N^S^N)** complexes have high values of electrophilicity indices which is in harmony with the observed rate constants

In addition, the low reactivity of **Pt2** compared to **Pt1** and that of **Pt4** compared to **Pt3** despite their high positive NBO charges observed can be explained by the *trans* labilizing effect through σ-donation of electrons by carbon atom through t*rans* N/S-donor atom. **Pt1** and **Pt3** have one extra sp^3 carbon which can further donate electron density into the N/S leading to a high *trans* labilizing effect than **Pt2** and **Pt4**. This is evidenced by the increase in NBO charges of the Pt complexes upon substitution of the sp^3 carbon in **Pt1**(0.540) and **Pt3**(0.365) with an sp^2 carbon as for **Pt2**(0.550) and **Pt4**(0.380). The σ-donation effect strengthens the Pt–N/S_{trans} bond at the expense of Pt–Cl (Table 2) bond resulting in the ground state destabilization and an increase in the reaction rate of substitution of the leaving chloride group. The reactivity trend is well supported by the calculated electrophilicity indices.

The substitution of coordinated chloride by the most sterically hindered nucleophiles TMTU shows a clear dependence on the steric bulk of the nucleophile. The values of the rate constants for the substitution reaction of **Pt3** decrease in the order TU (205 M^{-1} s^{-1}) > DMTU (103 M^{-1} s^{-1}) > TMTU (50 M^{-1} s^{-1}). It was observed that the most sterically hindered nucleophile TMTU shows by far the lowest reactivity.

The trend in the reactivity of the investigated complexes for the different nucleophiles can also be seen in the activation enthalpies for the investigated reactions. Generally, as the reaction becomes slower, the process is less favoured resulting in high activation enthalpy due to destabilization of the transition state. Accordingly, the activation entropy becomes more negative with acceleration of the reaction due to low disorder in the transition state. This general comment is valid in our results with some exceptions in few cases.

CONCLUSION

The general reactivity trend for the complexes is **Pt3 > Pt4 > Pt1 > Pt2**. The difference in the rate of substitution of all the complexes is purely electronic in origin. The rate constants for the substitution of chloro ligand in **Pt3** (k_2 = 205.19 M^{-1} s^{-1}) and **Pt4** (k_2 = 21.03 M^{-1} s^{-1}) complexes decrease to k_2 = 0.50 M^{-1} s^{-1} for **Pt1** and k_2 = 0.29 M^{-1} s^{-1} for **Pt2** complexes due to the high *trans* labilizing effect brought by the S-donor atom. Moreover, complexes with two pyridine rings (**Pt1** and **Pt3**) are superior in reactivity by two orders of magnitude than those with quinoline moiety in a ligand framework (**Pt2 and Pt4**). The dominance in reactivity is explained by a better ability of the pyridine ring to delocalize negative charge away from the reaction centre which eventually leads to an increase in the electrophilicity of the metal centre. The net σ-donor effect of quinoline moiety in **Pt4** is overwhelmed by the *trans* effect of sulfur atom leading to high substitution reactions relative to **Pt2**. The substitution of chloride in **Pt1**, **Pt2**, **Pt3** and **Pt4** complexes by thiourea nucleophiles has been characterized by sensitivity to the steric of the incoming ligand. The large negative entropies and small activation enthalpies suggest that formation of the transition is accompanied by a net increase in bonding.

ACKNOWLEDGEMENTS

The author is gratefully indebted to the University of Dar es Salaam through World Bank Project for financial support and Prof. D. Jaganyi, University of KwaZulu-Natal (South Africa) for his guidance.

ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

The available ESI includes a number of NMR and mass spectra, wavelengths for kinetic measurements, concentration dependence and Eyring plots for determination of second order rate constant and activation parameters and HOMO-LUMO energy diagram of the investigated complexes.

REFERENCES

Annibale G, Bortoluzzi M, Marangoni G and Pitteri B 2005 An improved method for the preparation of tetra-coordinate platinum(II) chloro-complexes containing bidentate or terdentate ligands starting from *cis*/*trans*-[$PtCl_2(SMe_2)_2$]. *Transit. Met. Chem.* **30**(6), 748–750.

Appleton TG, Hall JR, Ralph SF and Thomson CSM 1984 Reactions of platinum(II) aqua complexes. 2. ^{195}Pt NMR study of reactions between the tetraaquaplatinum(II) cation and chloride, hydroxide, perchlorate, nitrate, sulfate, phosphate and acetate. *Inorg. Chem*. **23**: 3521–3525.

Ashby MT 1990 Concerning the spatial nature of metal-thiolate π bonding. *Comments Inorg. Chem.* **10**: 297–313.

Banerjee P 1999 Interaction of nitrogen bases with some platinum(II) and palladium(II) complexes-usual and unusual features. *Coordinat. Chem. Rev.* **190–192**: 19–28.

Barone V and Cossi M 1998 Quantum calculation of molecular energies and energy gradients in solution by a conductor solvent model. *J. Phys. Chem. A.* **102**: 1995–2001.

Becke AD 1993 Density-functional thermochemistry. III. The role of exact exchange. *Chem. Phys*. **98**: 5648.

Bogojeski J, Bugarčić, ŽD, Puchta R, van Eldik R 2010 Kinetic studies on the reactions of different bifunctional platinum(II) complexes with selected nucleophiles. *Eur. J. Inorg. Chem.* 5439–5445.

Bugarčić ŽD, Soldatović T, Jelić R, Alguero B, Grandas A 2004 Equilibrium, kinetic

and HPLC study of the reactions between platinum(II) complexes and DNA constituents in the presence and absence of glutathione. *Dalton Trans.* **22**: 3869–3877.

Bugarčić ŽD, Rosić J, Petrović B, Summa N, Puchta R, van Eldik R 2007 Kinetics and mechanism of the substitution reactions of [PtCl(bpma)](+), [PtCl(glymet-S,N,N)] and their aqua analogues with L:-methionine, glutathione and 5'-GMP. *J. Biol. Inorg. Chem*. **12**: 1141−1150.

Canovese L, Visentin F, Chessa G, Uguagliati P, Levi C, Dolmella A, Bandoli G 2006 Role of the ligand and of the size and flexibility of the palladium−ancillary ligand cycle on the reactivity of substituted alkynes toward palladium(0) complexes bearing potentially terdentate nitrogen−sulfur−nitrogen or nitrogen−nitrogen−nitrogen ligands: Kinetic and structural study. *Organometallics* **25**: 5355–5365.

Carlsen L, Egsgaard H, Anderson JR 1979 Purification of acetonitrile. *Anal Chem*. **51**: 1593–1595.

Chattaraj PK, Sarkar U and Roy DR 2006 Electrophilicity Index. *Chem. Rev*. **106**(6): 2065–2091.

Chattaraj PK, Giri S and Duley S 2011 Update 2 of: Electrophilicity Index. *Chem. Rev*. **111**(2): 43–75.

Cedillo A, Contreras R 2012 A Local Extension of the Electrophilicity Index Concept. *J. Mex. Chem. Soc.* **56**(3): 257–260.

Chval Z, Sip M, Burda JV 2008 The *trans* effect in square-planar platinum(II) complexes-a density functional study. *J. Comput. Chem*. **29**: 2370–2380.

Cossi M, Scalmani G, Rega N, Barone V 2003 Energies, structures and electronic properties of molecules in solution with the C-PCM solvation model. *Comput. Chem.* **24**: 669–681.

Darensbourg MY, Hill GS, Irwin MJ, Levy CJ, Rendina LM, Puddephatt RJ, Andersen RA and Mclean L 2007 Platinum(II) complexes of dimethyl sulfide. *Inorg. Synth.* **32**: 149−153.

Domingo LR, Perez, P, Contreras R 2003 Electronic contributions to the sigma(σ) parameter of the Hammett equation. *J. Org. Chem*. **68**: 6060–6062.

Eyring H 1935 The activated complex in chemical reactions. *J. Chem. Phys*. **3**:107.

Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Vreven T, Montgomery JA, Peralta JE, Ogliaro F, Bearpark M, Heyd JJ, Brothers E, Kudin KN, Staroverov VN, Kobayashi R, Normand J, Raghavachari K, Rendell A, Burant JC, Iyengar SS, Tomasi J, Cossi M, Rega N, Millam JM, Klene M, Knox JE, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Martin RL, Morokuma K, Zakrzewski VG, Voth GA, Salvador P, Dannenberg JJ, Dapprich S, Daniels AD, Farkas O, Foresman JB, Ortiz JV, Cioslowski J and Fox DJ, Gaussian 09, Revision *A.1*, Wallingford CT, **2009**.

Guo ZJ and Sadler PJ 2000 Medicinal inorganic chemistry. *Adv. Inorg. Chem.* **49**: 183–306.

Hay PJ and Wadt, WR 1985 Ab initio effective core potentials for molecular calculations. Potentials for the transition metal atoms Sc to Hg. *Chem. Phys*. **82**: 270–283.

Hochreuther S, Nandibewoor ST, Puchta R and van Eldik R 2012 Thermodynamic and kinetic behaviour of [Pt(2-

methylthiomethylpyridine)$(OH_2)_2]^{2+}$. *Dalton Trans.* **41**: 512–522.

Hofmann A, Jaganyi D, Munro OQ, Liehr G, van Eldik, R 2003 Electronic tuning of the lability of Pt(II) complexes through pi-acceptor effects. Correlations between thermodynamic, kinetic, and theoretical parameters. *Inorg. Chem*. **42**: 1688–1700.

Hofmann A and van Eldik R 2003 Thermodynamic and kinetic study of the interaction between the Pt(II) centres in $[Pt_2$(*N*,*N*,*N*′,*N*′-tetrakis(2-pyridylmethyl)diamine)$(H_2O)_2]^{4+}$. Influence of the bridging ligand. *Dalton Trans*. 2979–2985.

Hofmann A, Dahlenburg L and van Eldik R 2003 Cyclometalated analogues of platinum terpyridine complexes: kinetic study of the strong σ-donor *cis* and *trans* effects of carbon in the presence of a π-acceptor ligand backbone. *Inorg. Chem.* **42**(20): 6528–6538.

Jaganyi D, Hofmann A and van Eldik R 2001 Controlling the lability of square-planar Pt(II) complexes through electronic communication between pi-acceptor ligands. *Angew. Chem. Int., Ed*. **40**: 1680–1683.

Jaganyi D and Tiba F 2003 Substitution of $[Pt(terpy)H_2O]^{2+}$ and $[Pt(bpma)H_2O]^{2+}$ with thiols in acidic aqueous solution. terpy = 2,2′:6′2″-terpyridine; bpma = bis(2-pyridylmethyl)amine. *Transit. Met. Chem.* **28**: 803–807.

Jaganyi D, Tiba F, Munro OQ, Petrovi´c B and Bugarčić ZD 2006 Kinetic and mechanistic study on the reactions of $[Pt(bpma)(H_2O)]^{2+}$ and $[Pd(bpma)(H_2O)]^{2+}$ with some nucleophiles. Crystal structure of $[Pd(bpma)(py)](ClO_4)_2$. *J. Chem. Soc., Dalton Trans.* 2943–2949.

Jaganyi D, Tiba F, Munro OQ, Petrovi´c B and Bugarčić ZD 2006 Kinetic and mechanistic study on the reactions of $[Pt(bpma)(H_2O)]^{2+}$ and $[Pd(bpma)(H_2O)]^{2+}$ with some nucleophiles. Crystal structure of $[Pd(bpma)(py)](ClO_4)_2$. *J. Chem. Soc., Dalton Trans.* 2943–2949.

Jaganyi D, de Boer K, Gertenbach J and Perils J 2008 Kinetic and mechanistic investigation into the influence of chelate substituents on the substitution reactions of platinum(II) terpyridine complexes. *Int. J. Chem. Kinet.* **40**: 808–818.

Kinunda G and Jaganyi D 2014 Understanding the electronic and π-conjugation roles of quinoline on ligand substitution reactions of platinum (II) complexes. *Transit. Met. Chem*. **39**(4): 451–459.

Langford CH and Gray HB 1965 Ligand Substitution Processes, Benjamin, New York

Lee CT, Yang WT and Parr RG 1988 Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. *Phys. Rev. B*. **37**: 785–789.

Lippert B (Ed.) 1999 Cisplatin: Chemistry and biochemistry of a leading anticancer drug. Zürich: Verlag Helvetica Chimica. Acta.

Mambanda A and Jaganyi D 2011 Understanding the role of the flexible bridging linker through kinetics and mechanistic study of Pt(II) amphiphiles derived from a bis(2-pyridylmethyl)amine chelate head group. *Dalton Trans*. **40**: 79–91.

Mambanda A and Jaganyi D 2017 Chapter six-Controlling the lability of square-planar Pt(II) complexes through electronic and π-conjugation: Correlation between kinetics and theoretical parameters. *Adv. Inorg. Chem.* **70**: 243–276.

Mebi CA 2011 DFT study on structure, electronic properties and reactivity of

cis-isomers of $[(NC_5H_4\text{-}S)_2Fe(CO)_2]$. *J. Chem. Sci.* **123**(5): 727–731.

Murray SG and Hartley FR 1981 Coordination chemistry of thioethers, selenoethers, and telluroethers in transition-metal complexes. *Chem. Rev.* **81**: 365–414.

Nkabinde SV, Kinunda G and Jaganyi D 2017 Mechanistic study of the substitution reactions of [Pt(II)(bis(2-pyridylmethyl)amine) $H_2O](ClO_4)_2$ and [Pt(II)(bis(2-pyridylmethyl) sulfide)$H_2O](ClO_4)_2$ with azole nucleophiles. Crystal structure of [Pt(II)(bis(2-pyridylmethyl) sulfide)Cl]ClO_4. *Inorg. Chim. Acta* **466**: 298–307.

Ongoma PO and Jaganyi D 2012. The π-acceptor effect in the substitution reactions of tridentate N-donor ligand complexes of platinum(II): A detailed kinetic and mechanistic study. *Dalton Trans*. **41**: 10724–10730

Ongoma PO and Jaganyi D 2013 Mechanistic elucidation of linker and ancillary ligand substitution reactions in Pt(II) dinuclear complexes *Dalton Trans*. **42**: 2724–2734.

Orgel LE 1956 An electronic interpretation of the *trans* effect in platinous complexes. *J. Inorg. Nucl. Chem*. **2**: 137–140.

Origin7.5^{TM} SRO, v7.5714 (B5714), 2003 Origin Lab Corporation, Northampton, One, Northampton, M. A, 01060, USA.

Parthasarathi R, Padmanabhan J, Subramanian V, Maiti B, Chattaraj PK 2003 Chemical Reactivity Profiles of Two Selected Polychlorinated Biphenyls. *J. Phys. Chem. A*. **107**: 10346–10352.

Parthasarathi R, Subramanian V, Roy DR and Chattaraj PK 2004 Electrophilicity index as a possible descriptor of biological activity. *Bioorg. Med. Chem*. **12**: 5533–5543.

Pitteri B, Marangoni G and Cattalini L 1994 Reactivity of neutral nitrogen donors in planar d^8 metal complexes. Part 2. The system [2,6-bis(methylsulfanyl-methyl)pyridine]chloroplatinum(II) with pyridines and amines in methanol. Effect of basicity, π-acceptor capacity and steric hindrance. *J. Chem. Soc. Dalton Trans*. 3539–3543.

Pitteri B, Marangoni G, Cattalini L and Bobbo T 1995 Nucleophilic displacement of halides from monocationic platinum(II) complexes containing neutral tridentate chelating ligands with sulfur and nitrogen donors: kinetics and equilibria. *J. Chem. Soc. Dalton Trans*. 3853–3859

Pitteri B, Marangoni G and Cattalini L 1995 The reactivity of cationic platinum(II) complexes containing the tridentate ligand bis(2-pyridylmethyl)sulphide. *Polyhedron* **14**: 2331–2338.

Pitteri B, Annibale G, Marangoni G, Cattalini L, Visentin F, Bertilasi V and Gilli P 2001 The role of the non-participating groups in substitution reactions at cationic Pt(II) complexes containing tridentate chelating nitrogen donors. Crystal structure of {Pt[bis(2-pyridylmethyl)amine](py)}$(CF_3SO_3)_2$. *Polyhedron* **20**: 869–880.

Pitteri B, Bortoluzzi M and Marangoni G 2005 Nucleophilic substitution reactions at planar tetra-coordinate bis-cationic-platinum(II) complexes. kinetics of displacement of pyridine from {Pt[2,6-bis(methylthiomethyl)pyridine](py)}$^{2+}$, {Pt[bis(2-pyridylmethyl)amine] (py)}$^{2+}$ and {Pt[bis(2-(pyridylmethyl)sulphide](py)}$^{2+}$ cations. *Transit. Met. Chem.* **30**: 1008–1013.

Reedijk J 1999 Why does Cisplatin reach Guanine-N7 with competing S-donor ligands available in the cell? *Chem. Rev.* **99**: 2499–2510.

Reddy D and Jaganyi D 2008 Controlling the extent of pi-backbonding in platinum(II) terpyridyl systems: A detailed kinetic, mechanistic and

computational approach. *Dalton Trans*. 6724–6731.

Romeo R, Plutino MR Scolaro LM, Stoccoro S and Minghetti G 2000 Role of cyclometalation in controlling the rates of ligand substitution at platinum(II) complexes. I*norg. Chem*. **39**: 4749–4755.

Schiessl WC, Summa NK, Weber CF, Gubo S, Dücker-Benfer C, Puchta R, van Eikema Hommes NJR and van Eldik R 2005 Experimental and theoretical approaches to the protonation of thiourea: a convenient nucleophile in coordination chemistry revisited. *Z. Anorg. Allg. Chem*., **631**: 2812–2819.

Schmülling M, Ryabov AD and van Eldik R 1992 Steric and electronic tuning of the lability of square planar d^8 metal complexes: platinum(II)≡palladium(II). *J. Chem. Soc. Chem. Commun*. 1609–1611.

Soldatović T and Bugarčić ŽD 2005 Study of the reactions between platinum(II) complexes and L-methionine in the presence and absence of 5'-GMP. *J. Inorg. Biochem*. **99**: 1472–1479.

Summa N, Schiessl W, Puchta R, van Eikema Hommes, N and van Eldik R 2006 Thermodynamic and kinetic studies on reactions of Pt(II) complexes with biologically relevant nucleophiles. *Inorg. Chem*. **45**: 2948–2958.

Sung ND, Choi KY, Lee HH, Lee KC, Kim MJ 2005 Synthesis and characterization of mononuclear copper(II) and dinuclear cadmium(II) complexes with di-(2-picolyl)sulfide. *Transit. Met. Chem.* **30**: 273–277.

Papo TR and Jaganyi D 2015, Tuning the π-backbonding and σ-*trans* effect of N^C^N coordinated Pt(II) complexes. Kinetic and computational study. *J. Coord. Chem.* **68**(5): 794–807.

Wang J, Ma R, Zhou Z, Liu G, and Liu Q 2015 Magnesiothermic synthesis of sulfur-doped graphene as an efficient metal-free electrocatalyst for oxygen reduction. *Sci Rep.* **5**: 930–9312.

Weber CF and van Eldik R 2005 Influence of solvent on ligand-substitution reactions of pt^{ii} complexes as function of the-acceptor properties of the spectator chelate. *Eur. J. Inorg. Chem*. 4755–4761.

Wekesa IM and Jaganyi D 2014 Kinetic and mechanistic studies of 1,3-bis(2-pyridylimino)isoindolate Pt(II) derivatives. Experimental and new computational approach. *Dalton Trans.* **43**: 2549–2558.