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Published in:
Inorganica Chimica Acta

DOI:
10.1016/j.ica.2018.03.039

Publication date:
2018

Document Version
Peer reviewed version

Citation for published version (APA):
Josephsen, J. (2018). Diaminehalogenoplatinum(II) complex reactions with DMSO. *Inorganica Chimica Acta*, *478*, 54-58. https://doi.org/10.1016/j.ica.2018.03.039

Research paper

Diaminehalogenoplatinum(II) complex reactions with DMSO

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Abstract

The platinum(II) complexes [Pt(N-N)X_2] (X = Cl, Br, and I; (N-N) = 1,2-ethanediamine (en) and 1,3-propanediamine (tn)) have been synthesised; their reactions with DMSO in DMSO to substitute halogenide were followed using changing integrals of NMR-spectroscopic signals. The rate constant for [PtenCl_2] was found to be $1.0*10^{-4}$ s^{-1} at 300 K and from kinetic runs at different temperatures the energy of activation was estimated as 82 kJ*mol^{-1} in this case.

The rate constant depends on the size of halogenide and was found to be forty times larger for [PtenI_2] than for its dichloro-analogue. In the tn-series reactions were a little faster than in the en-series.

For all six [Pt(N-N)X_2] complexes the solvolysis stopped at the coordination of one DMSO and the six new [Pt(N-N)DMSOX]X were isolated and characterised. Further the [PtenDMSOCl]$^+$ was isolated as its nitrate and perchlorate. DMSO exchange reactions (in DMSO) of [PtenDMSOX]$^+$ were found to be slightly slower than the solvolysis reactions, iodide again giving rise to the most labile system.

Ion pair formation in DMSO was found to be modest to almost negligible with a formation constant of 30 M^{-1} in the case of [PtenDMSOCl]Cl as the largest.

Keywords: Platinum(II) diamine complexes; Substitution reaction rates; DMSO

1 Introduction

DMSO (dimethylsulphoxide) as a solvent has been used in studies of biological effects of several *cis*-bis(amine)dihalogenoplatinum(II) complexes [1] in cases where the solubility in water was too low. DMSO is a good solvent for many of these complexes and is also known to act as a ligand and to form well defined coordination compounds with metal ions including platinum(II) [2].

The solvolysis in DMSO of *cis*-diammindichloroplatinum(II) (*cis*-DDP) has been shown to be extensive [3]. Such reactions complicate the interpretation of kinetic data in biological assays when DMSO is used as a solvent. The same is true for aqueous solutions in which a *cis-trans* equilibration also takes place. Indeed, it has been shown that the cytotoxicity is inhibited of currently used platinum drugs dissolved in DMSO [4,5].

In our earlier kinetic studies of biological effects of platinum(II) complexes we have used the diaqua-derivatives of dichloro-1,2-ethanediaminplatinum(II) (PtenCl_2), thus avoiding problems with low solubility and complex kinetics due to *cis-trans* equili-bration and the simultaneous hydrolysis in aqueous solution of these complexes [4].

A kinetic study of solvolysis in DMSO of PtenCl_2 (and a number of N- and C-substituted analogues) [6] has shown that only one chloride is substituted by DMSO in the coordination sphere. Qualitative studies of the fate of halogenides in some *cis*-diaminedihalogenoplatinum(II) analogues in DMSO [3,7] demonstrated that iodide behaved as a faster leaving group than bromide and chloride. This is the opposite order of that found in classical kinetic studies [8] of the reaction of bis-(2-aminoethyl)aminehalogenoplatinum(II) (PtdienX^+) with pyridine in aqueous solution. Further studies with other entering groups showed that there is little or no difference between the three halogenides as leaving groups in DMSO [9]. In order to shed light upon the apparent kinetic difference from aqueous solution a quantitative study of DMSO reaction rates was undertaken in some (diamine)dihalogenoplatinum(II) systems varying only the halogenides as the leaving group.

2 Experimental

2.1 Materials

K_2PtCl_4 was purchased from Johnson Matthey Ltd. and 1,2-ethanediamine (en) and 1,3-propanediamine (tn) for synthesis were obtained from Fluka; standard solvents and dimethylsulphoxide were of analytical grade, and ^{15}N-1,2-ethanediamine dihydrochloride (<96% ^{15}N) was from Prochem (BOC) Ltd.

2.2 Syntheses

2.2.1 Dichloro-1,2-ethanediamineplatinum(II). [PtenCl$_2$]

2 ml of an aqueous solution of 1.75 mmol en, 3.5 mmol of sodium chloride (in the case of the ^{15}N-enriched compound 1.75 mmol of the dihydrochloride and 3.50 mmol of sodium hydroxide) and 1.75 mmol of potassium tetrachloroplatinate(II) was stirred in the dark at room temperature overnight and then cooled at 4 °C. The yellow precipitate was filtered from an almost colourless solution and washed with ice-cold 0.1 M HCl and ethanol and dried in the air. The product was recrystallised by dissolving it on the glass filter in almost boiling 10^{-3} M HCl giving 0.35 g (60%) yellow needles after cooling, filtration, and washing as before. With larger quantities, a 0.5 M aqueous solution of en was simply added slowly to an equivalent amount of a stirred 0.25 M solution of K_2PtCl_4 at room temperature in the dark. (*Anal.* Calc. for $PtC_2H_8N_2Cl_2$: Pt, 59.82; C, 7.37; H, 2.47; N; 8.59; Cl, 21.74. Found: Pt, 59.90; C, 7.22; H, 2.40; N; 8.50; Cl, 21.7%.)

2.2.2 Dichloro-1,3-propanediamineplatinum(II). [PttnCl$_2$]

This compound was prepared in the same way as the en analogue on a 2 mmol scale. Yield 65%. (*Anal.* Calc for $PtC_3H_{10}N_2Cl_2$: Pt, 57.36; C, 10.59; H, 2.96; N; 8.24; Cl, 20.85. Found: Pt, 57.35; C, 10.50; H, 2.86; N; 8.15; Cl, 20.9%.)

2.2.3 Dibromo-1,2-ethanediamineplatinum(II). [PtenBr$_2$]

K_2PtCl_4 (1.0 g, 2.4 mmol) and KBr (2.85 g, 24 mmol) in 20 ml of water was heated at 60 °C for an hour to give a dark red solution. After cooling to 40 °C, 2.4 ml of 1.0 M aqueous solution of en was added in the dark and the stirring was continued for an hour. The yellow precipitate was separated from a yellowish solution and washed with water and ethanol. Yield 0.86 g (85%). (*Anal.* Calc for $PtC_2H_8N_2Br_2$: Pt, 47.01; C, 5.79; H, 1.94; N; 6.75. Found: Pt, 47.28; C, 5.93; H, 1.74; N; 6.82%.)

*2.2.4 *Dibromo-1,3-propanediamineplatinum(II). [PttnBr$_2$]*

This compound was prepared in the same way as the en analogue. Yield 85%. (*Anal.* Calc for $PtC_3H_{10}N_2Br_2$: Pt, 45.47; C, 8.40; H, 2.35; N; 6.53. Found Pt, 45.39; C, 8.48; H, 2.24; N; 6.52%.)

2.2.5 Diiodo-1,2-ethanediamineplatinum(II). [PtenI$_2$]

K_2PtCl_4 (1.0 g, 2.4 mmol) and KI (4.0 g, 24 mmol) in 20 ml of water was stirred at room temperature for 10 min to give a dark greenish brown solution. 2.4 ml of 1.0 M aqueous solution of en was added in the dark and the stirring was continued for an hour. The yellow precipitate was separated from an almost colourless solution and washed with water and ethanol, Yield 1.1 g (90%) after recrystallization from water. (*Anal.* Calc for $PtC_2H_8N_2I_2$: Pt, 38.33; C, 4.72; H, 1.58; N; 5.50; I, 49.87. Found Pt, 38.40; C, 4.63; H, 1.56; N; 5.50; I, 49.9%.)

2.2.6 Diiodo-1,3-propanediamineplatinum(II). [PttnI$_2$]

This compound was prepared in the same way as the en analogue. Yield 90%. (*Anal.* Calc for $PtC_3H_{10}N_2I_2$: Pt, 37.30; C, 6.89; H, 1.93; N; 5.36; I, 48.53. Found Pt, 37.36; C, 6.86; H, 1.86; N; 5.30; I, 48.3%.)

2.2.7 Chloro(dimethylsulphoxide)-1,2-ethanediamineplatinum(II) chloride [PtClen(DMSO)]Cl

$PtenCl_2$ (0.5 g, 1.5 mmol) was dissolved in 2 ml of DMSO and left for 24 h in the dark, after which 20 ml of acetone was added under stirring. The resulting white precipitate (0.5 g, 80%) was washed with acetone. (*Anal.* Calc for $PtC_4H_{14}N_2SOCl_2$: Pt, 48.26; C, 11.89; H, 3.49; N, 6.93. Found: Pt, 47.9; C, 12.06; H, 3.47; N; 6.87%.)

2.2.8 Chloro(dimethylsulphoxide)-1,3-propanediamineplatinum(II) chloride [PtCltn(DMSO)]Cl

This compound was prepared in the same way as its en-analogue with the same yield, (0.5 g, 80%) and washed with acetone. (*Anal.* Calc for $PtC_5H_{16}N_2SOCl_2$: C, 14.4; H, 3.86; N, 6.70. Found: C, 14.7; H, 3.85; N, 6.69%.)

*2.2.9 *Bromo(dimethylsulphoxide)-1,2-ethanediamineplatinum(II) bromide [PtBren(DMSO)Br*

$PtenBr_2$ (0.5 g, 1.5 mmol) was dissolved in 2 ml of DMSO and left for 24 h in the dark, after which 20 ml of acetone was added under stirring. The resulting white precipitate (0.5 g, 80%) was washed with acetone. (*Anal.* Calc for $PtC_4H_{14}N_2SOBr_2$: C, 9.74; H, 2.86; N, 5.68. Found: C, 10.0; H, 2.91; N; 5.8%.)

*2.2.10 *Bromo(dimethylsulphoxide)-1,3-propanediamineplatinum(II) bromide [PtBrtn(DMSO)]Br*

This compound was prepared in the same way as its en-analogue with the same yield, (0.5 g, 80%) and was washed with acetone. (*Anal.* Calc for $PtC_5H_{16}N_2SOBr_2$: Pt, 38.47; C, 11.84; H, 3.18; N, 5.52. Found: Pt, 38.36; C, 11.88; H, 3.12; N; 5.45%.)

*2.2.11 *Iodo(dimethylsulphoxide)-1,2-ethanediamineplatinum(II) iodide [PtIen(DMSO)]I*

PtenI$_2$ (0.5 g, 1 mmol) was dissolved in 2 ml of DMSO and left for 4 h in the dark, after which 8 ml of ethanol was added. The drop wise addition under stirring of 30 ml of toluene resulted in a yellow precipitate (0.5 g, 80%), which was washed with toluene and ethanol. (*Anal.* Calc for $PtC_4H_{14}N_2SOI_2$: Pt, 33.23; C, 8.18; H, 2.40; N, 4.77. Found: Pt, 33.47; C, 8.21; H, 2.39; N; 4.80%.)

2.2.12 *Iodo(dimethylsulphoxide)-1,3-propanediamineplatinum(II) iodide [PtItn(DMSO)]I

This compound was prepared in the same way as its en-analogue with the same yield. (*Anal.* Calc for $PtC_5H_{16}N_2SOI_2$: Pt, 32.45; C, 9.99; H, 2.68; N, 4.66. Found: Pt, 32.50; C, 10.10; H, 2.67; N; 4.65%.)

2.2.13 *Chloro(dimethylsulphoxide)-1,2-ethanediamineplatinum(II) nitrate [PtClen(DMSO)]NO$_3$

[PtClen(DMSO)]Cl (548 mg, 1.36 mmol) and $AgNO_3$ (228 mg, 1.34 mmol) was stirred in 50 ml of methanol in the dark after which the suspension was filtered through a glass fibre filter on a Büchner funnel to leave a colourless solution. 50 ml of ether was added under stirring and the resulting white precipitate (0.5 g, 90%) was washed with ether. %. (*Anal.* Calc for $PtC_4H_{14}N_3SO_4Cl$: Pt, 45.29; C, 11.15; H, 3.28; N, 9.76. Found: Pt, 45.2; C, 11.28; H, 3.15; N, 9.63%.)

2.2.14 *Chloro(dimethylsulphoxide)-1,2-ethanediamineplatinum(II) perchlorate [PtClen(DMSO)]ClO$_4$

[PtClen(DMSO)]Cl (206 mg, 0.51 mmol) and $AgClO_4$ (108 mg, 0.51 mmol) was stirred in 20 ml of methanol in the dark after which the suspension was filtered through a glass fibre filter on a Büchner funnel to leave a colourless solution. 40 ml of ether was added under stirring and the resulting white precipitate (0.5 g, 90%) was washed with ether. (*Anal.* Calc for $PtC_4H_{14}N_2SO_5Cl_2$: C, 10.26; H, 3.01; N, 5.98%. Found: C, 10.10; H, 3.01; N, 5.93%.)

2.3 Instrumentation and ^{1}H NMR data

^{1}H NMR-spectra (DMSO-d_6) were recorded at 27 °C using an AC250 MHz or an Avance III HD (400 MHz) both from Bruker. ^{195}Pt NMR-spectra (DMSO-d_6) were recorded using a Varian Inova (600 MHz) at different temperatures. ^{1}H NMR data are given in Table 1.

~~2.4 ^{1}H NMR data~~

~~See Table 1~~ (As indicated in my respose to Q3 Table 1 lay out could be improved: Shading of row 10 plus a special marking of some of the data obtained at 250 MHz. **Either** the numbers should be in italics while the word "shaded" in brackets is replaced by "in italics" **or** by ¤ followed by appropriate marking of the relevant data as entered. The last option has been introduced as corrections.)

Table 1 Data obtained at 400 MHz or 250 MHz¤ ~~(shaded)~~ both at 300 K. *exact chemical shifts are dependent on concentration; c: coordinated DMSO; l liberated, non-deuterated DMSO; #these signals happen to coincide with that of the sharp non-deuterated DMSO-signal. The combined signal in these cases is significantly broader at the base than pure DMSO in DMSO-d_6 but not separated as for [PtenIDMSO]I. §Coinciding with the DMSO-d_5 signal from the solvent.

Numbers in ppm	CH_2	DMSO l	DMSO c	NH_2
[PtenCl$_2$]	2.24			5.31
*[PtenClDMSO]Cl	2.54#	2.54	3.41	6.11; 6.48
*[PtenClDMSO]NO$_3$	2.54#	2.54	3.40	6.04; 6.17
[PtenClDMSO]ClO$_4$	2.54#	2.54	3.39	6.02; 6.09
[PtenBr$_2$]	2.21¤			5.33¤
*[PtenBrDMSO]Br	2.54#¤			6.06; 6.30¤
[PtenI$_2$]	2.20			5.28
*[PtenIDMSO]I	2.58(m); 2.46(m)	2.54	3.60	5.94; 6.20
Numbers in ppm	1-CH_2	2-CH_2	DMSO c	NH_2
[PttnCl$_2$]	2.41¤	1.54¤		4.87¤
*[PttnClDMSO]Cl	2.70¤	1.77¤	3.41¤	5.53; 5.64¤

[PttnBr$_2$]	2.48¤	1.64¤		4.92¤
*[PttnBrDMSO]Br	2.56; 2.77¤	1.79¤		5.47; 5.60¤
[PttnI$_2$]	2.50§	1.68		4.81
*[PttnIDMSO]I	2.82	1.78	3.62	5.40; 5.53

3 Results

The syntheses of [Pt(N-N)X$_2$] were performed around room temperature with an excess of halide present, and were found to work well without by-products, since their solubility in aqueous media is low. Each of the six [Pt(N-N)X$_2$] complexes readily dissolve in DMSO at room temperature and reacts at different speeds to form [Pt(N-N)X(DMSO)]$^+$ + X$^-$. No further reaction was observed on the time scale studied (typically 4–24 h) in agreement with previous results [6].

The products [Pt(N-N)X(DMSO)]X were isolated from DMSO by adding a less polar solvent. The chloro(dimethylsulphoxide)-1,2-ethanediamineplatinum(II) was also isolated as nitrate and perchlorate salts. Several of the 14 complexes described are new: In the experimental section the complexes without a CAS number has been marked by an asterisk.

3.1 Kinetics of solvolysis

Kinetics of the reactions in DMSO of all the compounds were studied by recording the intensities of the ^{1}H NMR signals of the amine-protons, considered proportional to the concentrations. The initial spectrum showed in each case one not too broad signal around 5 ppm. In the subsequent spectra (cf. Fig. 1), this signal gradually vanished, while two different signals gradually appeared (approximately at 0.8 ppm downfield). The kinetics was clearly pseudo first-order, and the rate constants given in Table 2 indicate that the lability of X$^-$ in the tn-series is a little higher than in the analogous [PtenX$_2$] complexes. In both series the rate constants were found to increase in the order X = Cl < I.

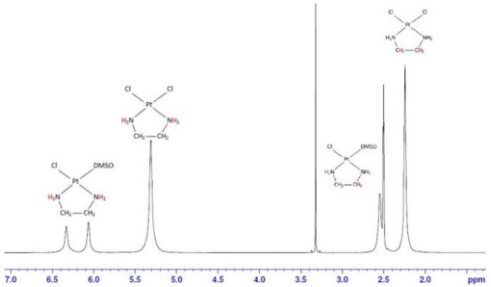

Fig. 1 400 MHz ^{1}H NMR spectrum at 300 K showing appearing and disappearing signals (in red) recorded 47 min after dissolution of solid PtenCl$_2$ in d$_6$-DMSO (0.15 M). (Water at 3.33 ppm and DMSO at 2.50 ppm.) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2 Pseudo first-order rate constants k$_1$ for [Pt(N-N)X$_2$]+DMSO → Pt(N-N)X(DMSO)]$^+$+X$^-$.

k$_1$ (s^{-1})	N-N = en	N-N = tn
Cl	1.03 ± 0.02·10^{-4}	1.48 ± 0.02·10^{-4}
Br	1.09 ± 0.02·10^{-3}	2.59 ± 0.03·10^{-3}
I	4.37 ± 0.06·10^{-3}	*1.3 ± 0.1·10^{-2}

* Data obtained at 295 K.

Inspection of the gradually appearing non-equivalent amine proton signals (cf. Fig. 1) reveals that the chemical shifts move a little further downfield as the concentration of [Pt(N-N)X(DMSO)]$^+$ increases. The largest change was 0.25 ppm observed for one signal of [PtenCl$_2$] and when positions of the changing signals were extrapolated back to t = 0 they coincided with those of the corresponding signals δ$_{ion}$ of [PtenCl(DMSO)]$^+$ as its perchlorate. This is

illustrated in Fig. 2, where the amine proton signals have been recorded in a kinetic run.

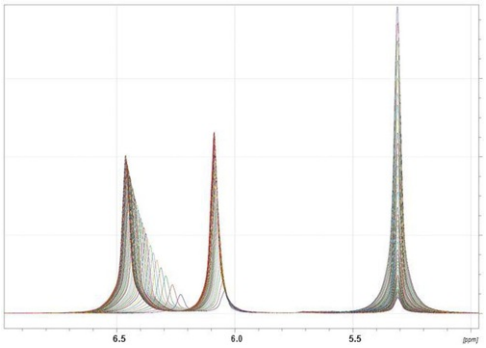

Fig. 2 Amine-proton signals in ^{1}H NMR spectra (400 MHz at 300 K) ($\Delta t = 10$ min.) during solvolysis of $PtenCl_2$ in d_6-DMSO ($C_{Pt} = 0.15$ M). Disappearing signals to the right (5.31 ppm); appearing signals to the left (moving towards 6.11 ppm and 6.48 ppm, respectively). The positions of the last two signals can be extrapolated back to 6.0 and 6.1 ppm, respectively at $t = 0$. The extrapolations back to $t = 0$ are not very accurate since the initial changes are large; still the values estimated are essentially the same as 6.02 and 6.09 ppm obtained from the spectrum of $[PtenCl(DMSO)]ClO_4$ in d_6-DMSO.

3.2 Ion pair formation

The observed small changes in chemical shifts, δ_{obs}, for the amine protons as the solvolysis proceeds, cf. Fig. 2, has been taken as evidence of the ion pair $[Pt(N\text{-}N)X(DMSO)]^+$, X^- being in fast equilibrium with its solvated ions in DMSO, assuming δ_{pair} to be different from δ_{ion}. δ_{obs} is thus interpreted as $\delta_{pair}\ \alpha_{pair} + \delta_{ion}\ \alpha_{ion}$, and since $\alpha_{ion} = 1\text{-}\alpha_{pair}$, each of the two α's can be expressed in terms of δ_{obs}, δ_{pair} and δ_{ion}. Among these δ_{obs} is an observable in the single experiment, δ_{pair} is unknown, but a constant parameter, and δ_{ion} is known from the spectrum of a salt of $[Pt(N\text{-}N)X(DMSO)]^+$ with negligible ion pair formation.

Substituting α's with the combination of the three chemical shifts in the equilibrium expression, $K_{pair} = \frac{\alpha_{pair}}{\alpha_{ion}^2 \cdot C_{Pt}}$, gives $K_{pair} = \frac{(\delta_{obs} - \delta_{ion}) \cdot (\delta_{pair} - \delta_{ion})}{(\delta_{obs} - \delta_{pair})^2 \cdot C_{Pt}}$ with the two unknown constants K_{pair} and δ_{pair}. From two experiments with two different stoichiometric concentrations, C_{Pt}, of $[Pt(N\text{-}N)X_2]$ both of these constants can be estimated.

$[PtenCl_2]$ exhibited the largest changes in signal positions of all cases studied, which made an extrapolation back to reaction start less accurate. To get a reliable δ_{ion} the product was isolated as its nitrate and as its perchlorate anticipating that ion pair formation in DMSO would be insignificant in both solutions. The low field signal of the nitrate and the perchlorate were, however observed at 6.20 and 6.09 ppm resp. (65 mM, 27 °C in both cases) and decreased 0.03 ppm for the nitrate but remained unchanged for the perchlorate when the concentration was reduced by a factor of 3 in both cases. In one experiment the two different concentrations were $C_{Pt} = 43$ mM and 201 mM and the corresponding δ_{obs} were found at 6.35 ppm and 6.50 ppm, resp. With $\delta_{ion} = 6.09$ ppm (from the spectrum of $[PtenCl(DMSO)]ClO_4$), δ_{pair} was found to be 6.70 ppm leading to the value $K_{pair} = 29.2 \pm 1.1\ M^{-1}$ at 300 K, which is sufficient to cause a displacement of the appearing chemical shifts further as observed. Small changes in chemical shifts of other signals were also observed, but K_{pair}'s derived in the same way as outlined above were less accurate. Also, for the other 5 $[Pt(N\text{-}N)X_2]$ complexes, chemical shifts of appearing signals only changed little or very little during a kinetic run. These small changes in chemical shifts either did not allow an estimate or gave less accurate estimates of K_{pair} being smaller than $3 \cdot 10^1\ M^{-1}$ in all cases.

The ion pair formation interpretation was further consistent with the following small experiment: To a solution of $[PtenClDMSO]ClO_4$ (23 mM) was added solid LiCl to give 40 mM of non-coordinated chloride; the low field signal changed to lower fields at a position which agreed within 0.02 ppm with that calculated using $K_{pair} = 30\ M^{-1}$ at 300 K.

3.3 Temperature variation

The rate of solvolysis of $[PtenCl_2]$ was also studied using ^{195}Pt NMR at different temperatures. ^{15}N-labelling (I = ½) was used because ^{14}N (I = 1) often gives rise to line broadening due to quadrupole relaxation. In this case it turned out not to give any problems in the analysis of data. The appearing signal (at −3296 ppm relative to Na_2PtCl_6) and the disappearing signal (at −2334 ppm) were followed at 20 °C (for $[Pt^{15}N\text{-}enCl_2]$ and $[Pt^{14}N\text{-}enCl_2]$), and at 27, 34 and 41 °C (for $[Pt^{14}N\text{-}enCl_2]$ only). The consistent rate constants of solvolysis in DMSO are given in Table 3. An Arrhenius plot gave an activation energy $82 \pm 3\ kJ\ mol^{-1}$. From an Eyring plot activation parameters ΔH^* and ΔS^* were found to be $79 \pm 2\ kJ\ mol^{-1}$ and $-56 \pm 3\ J\ mol^{-1}\ K^{-1}$, respectively. The negative entropy of activation found confirms that the substitution mechanism is associative.

Table 3 Pseudo first-order rate constants k_{Cl} for $[PtenCl_2] + DMSO \rightarrow [Pt(en)Cl(DMSO)]^+ + Cl^-$ at different temperatures, measured using ^{195}Pt NMR data.

t °C	20	27	34	41
k 10^4 s	0.52 ± 0.01	1.12 ± 0.01	2.73 ± 0.03	4.8 ± 0.1

Small changes of chemical shifts were also observed during these experiment and rough estimates of K_{pair} obtained from the ^{195}Pt NMR data at different temperatures were of the same order of magnitude ($10^1\,M^{-1}$) but less accurate.

3.4 DMSO exchange rates

While the solvolysis reactions studied apparently stopped at $[Pt(N\text{-}N)X(DMSO)]^+$, DMSO was found to be labile:

[PtenCl(DMSO)]NO_3 and [PtenI(DMSO)]I were dissolved in DMSO-d_6 and the exchange rate of DMSO was measured by following the disappearing signal (at $3.6 > \delta > 3.4$ ppm) of the coordinated DMSO and the increasing uncoordinated DMSO signal in ^{1}H NMR.

The rate constants ($4.8 \pm 0.02 \cdot 10^{-5}\,s^{-1}$ for $[PtenCl(DMSO)]^+$ and $4.1 \pm 0.02 \cdot 10^{-3}\,s^{-1}$ for $[PtenI(DMSO)]^+$ at 300 K) revealed that DMSO exchange was comparable in rate with substitution of the first halogenide by DMSO, cf. Table 2, and confirmed that iodide had a greater *cis*-labilising effect than chloride

4 Discussion

In agreement with qualitative observations [3,6] the rate of solvolysis in DMSO of di(amine)dihalogenoplatinum(II) (1,2-ethanediamine and 1,3-propanediamine) was found to decrease in the order of decreasing size of halogenide. The rates were invariably larger in the tn-systems than the analogous en-systems, most so with iodide as the leaving group.

Our findings in Tables 2 and 3 agree with literature data. Thus, the rate constant for $[PtenCl_2]$ + DMSO at 30 °C was found to be $1.53 \cdot 10^{-4}\,s^{-1}$ [6]. In addition, this substitution in dichloro-8-aminoquinoline-platinum(II) measured in dimethylformamide solution at 40 °C was found to proceed with the rate constant $3.8 \cdot 10^{-4}\,M^{-1}\,s^{-1}$ [10]; extrapolation to pure DMSO gives $5.4 \cdot 10^{-4}\,s^{-1}$, which agrees well with data of Table 3. Agreement was also found with corresponding data for *cis*-$[Pt(NH_3)_2Cl_2]$ + DMSO ($\sim 1.5 \cdot 10^{-4}\,s^{-1}$ at 30 °C calculated from data in [3]) and ($0.933 \cdot 10^{-4}$ at 30 °C and $1.35 \cdot 10^{-4}\,s^{-1}$ at 33 °C) [11]. From the latter study, the activation energy was found to be $82 \pm 2\,kJ\,mol^{-1}$, which compares well with our findings in the $[PtenCl_2]$ system.

In their early studies of $[PtdienX]^+ + py \rightarrow [Ptdienpy]^+ + X$ in aqueous solution, Basolo, Gray and Pearson [8] demonstrated a large variation in reaction rates for different leaving groups X. Variations were relatively small for X being a halogenide (only a factor of 3.5, X being Cl and I); still a decrease in the order $X = Cl > Br > I$ was observed. This trend in reaction rates was rationalised in terms of an associative bimolecular reaction mechanism with the bond rupture being the determining factor and being in accord with the observation, that the order of lability was opposite to the order of stability in the larger series of leaving groups including as different ligands X as nitrate and cyanide in $[PtdienX]^+$.

We found the opposite order of reaction rates of DMSO with $[PtenX_2]$ through the halogenides, (the reaction rate being 40 times faster when X = I than when X = Cl). The exchange of DMSO in $[PtenI(DMSO)]^+$ was also found to be significantly faster than in its chloride-analogue (ratio of exchange rate constants ~ 80). Numbers are comparable with DMSO exchange in $[PtenCH_3(DMSO)]^+$ [12] for which a first-order rate constant $1.2 \times 10^{-4}\,s^{-1}$ at 25 °C can be estimated by extrapolating the concentration of DMSO to that in pure DMSO.

The opposite order of rates is not due to different solvation in DMSO and in water of the leaving halogenide, since chloride has the largest solvation energy in both media [13]. Also, reaction rates for the hydrolysis of $[Pt(H_2O)_3X]^+$ were found to increase through the series $X = Cl < Br < I$ [14] in aqueous solution. In this case, the rate was at least two orders of magnitude higher with iodide than with chloride. Likewise, the reaction in aqueous ethanol of $[PtdienX]^+$ [15] with dimethyl sulphide followed the same rate pattern (ratio ~4) as reactions with DMSO in DMSO [16], so other unspecified solvent effects are not dominating either.

Iodide was also a faster leaving group than chloride when azide and other stronger nucleophiles as thiourea was used instead of pyridine in the reactions with $[PtdienX]^+$ (30 °C, aqueous solution, [9]). The differences were, however, small (a factor of ~2 between the rates with iodide and chloride as the leaving group). It was suggested that among a larger series of leaving ligands, the three halogenides behave almost at equal rates [17], embracing the earlier findings with only small differences in rates; this should indicate, that bond breaking is not rate determining.

4 Conclusion

Our findings clearly support the view that iodide is generally the fastest leaving group of the three halogenides in most square planar platinum(II) systems mentioned here.

However, variations due to entering nucleophile and/or solvent may in the case of the three halogenides as leaving groups cause a reduction of or even efface [17] the difference in reaction rates in the few cases reported [8].

Acknowledgments

We thank Jens Abildgaard and Morten Kall for their early assistance in this project, Pauli Kofod for recording the ^{195}NMR spectra, and Katrine Bøg for performing the C, H, N, X and Pt analyses.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ica.2018.03.039.

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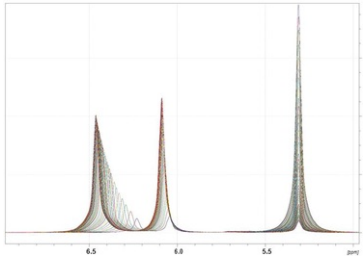
Appendix A. Supplementary data

Multimedia Component 1

Supplementary data 1

Graphical abstract

Kinetics of solvolysis of [PtenCl$_2$] followed by ^{1}H NMR. Signals of amine protons signals in [PtenCl$_2$] (right-staying at 5.31 ppm) and [PtenDMSOCl]$^+$ (left changing due to ion pair formation).



Highlights

- Kinetics of substitution in [PtdiamineX$_2$] in DMSO by ^{1}H and ^{195}Pt NMR.
- Ion pair formation in DMSO of [PtdiamineDMSOX]$^{+}$, X^{-}.
- 7 new [PtdiamineDMSOX]$^{+}$ salts isolated and characterised.

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