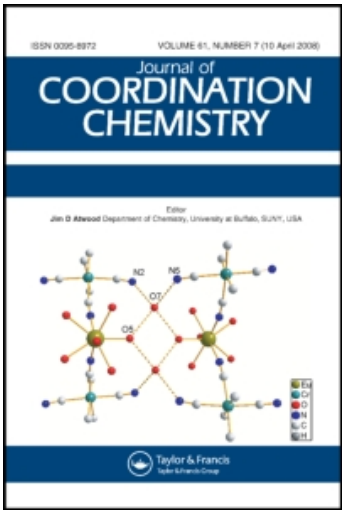

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Synthesis, spectroscopic and thermal studies on platinum(II) complexes of 5-nitrosouracil derivatives

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Synthesis, spectroscopic and thermal studies on platinum(II) complexes of 5-nitrosouracil derivatives

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Three complexes were obtained during reactions of 6-amino-1-methyl-5-nitrosouracil, 6-methylamino-1-methyl-5-nitrosouracil and 6-methylamino-1-benzyl-5-nitrosouracil with K_2PtCl_4. The complexes were isolated in good yields as powdery precipitates and characterized through elemental analysis, infrared and ^1H NMR spectroscopies, and thermal analysis. The pyrimidine bases easily substitute chloro ligands as a neutral monodentate ligand form. The exocyclic oxygen atoms are the probable binding sites rather than ring or exocyclic nitrogen atoms. *trans* Square planar structures were proposed in all cases.

Keywords: Platinum(II); Pyrimidine derivatives; IR; ^1H NMR; TG

1. Introduction

The discovery of the anti-tumor of *cis*-platin by Rosenberg and his co-workers [1], used for patient treatment in 1975 has led to large interest in all aspects of Pt coordination compounds with nucleic acids. A great number of Pt(II) complexes with monodentate nucleobases forming square-planar coordination units have been investigated [2]. The structurally characterized complexes contain one or two nucleobases, with the other coordination sites about platinum occupied by Cl, and/or ligands containing N donors. A structural characterization of a complex containing three cytosines [3] and a preliminary report on a tetrakis(9-methylguanine)platinum(II) complex [4] have been reported.

Pyrimidine bases have a large number of positions to bind a metal ion including their heterocyclic and amidic nitrogen atoms. The exocyclic nitrogen and/or oxygen atoms of some pyrimidine derivatives bind with metal ions [5]. Bidentate coordination involving N(1) and O(2) has been observed for a Ag^+-uracil complex, and through O(4) and N of NO group for some uracil derivatives [6, 7]. For the unsubstituted uracil anion, the binding site is preferentially N1 [8]. However, the N3 linkage isomer of a Pt(II) complex containing UH- has also been crystallized recently [9]. Most of the observed solid-state structures involve unidentate pyrimidine coordination. However, N(3) is the most probable coordination site when that atom is available [10–14].

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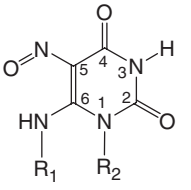
Determination of binding site(s) of pyrimidine bases to platinum ions is a step towards understanding the bioinorganic chemistry of these complexes [15], however, there is a limited number of metal complexes with 5-nitrosouracil derivatives [6, 7, 16]. The present investigation deals with preparation and characterization of Pt(II) complexes with three derivatives of 5-nitrosouracil (**I**).



AMNU: $R_1 = H; R_2 = CH_3$
MAMeNU: $R_1 = CH_3; R_2 = CH_3$
MABNU: $R_1 = CH_3; R_2 = CH_2Ph$

(**I**)

2. Experimental

All of the chemical used throughout this investigation were of analytical reagent grade and used without further purification.

^{1}H NMR spectra of uracil ligands and their Pt(II) complexes were recorded on a Varian Gemini 200 spectrometer, operating at 200 MHz for ^{1}H using dimethylsulfoxide-d_6 as solvent. Solvent signal (^{1}H) was used as an internal reference. Infrared spectra of the reactants and the obtained complexes were recorded from KBr pellets (4000–400) using a Buck scientific 500-IR spectrophotometer. Microanalyses were performed using CHNS-932 (LECO) and Vario-EL (elmentar Analysensysteme) elemental analyzers. Chlorine was determined by burning the substance in oxygen with platinum contact and subsequent titration with mercuric nitrate towards diphenylcarbazide. Thermal analyses, TG were carried out using a Shimadzu TGA-50 H computerized thermal analysis system. The system includes data processing with the ChromotPac C-R3A. The rate of heating of the samples was $10^\circ C\,min^{-1}$. Sample masses varied between 2.0 and 5.0 mg were analyzed under N_2 flow of $30\,mL\,min^{-1}$.

2.1. *Synthesis of complexes*

2.1.1. $[PtCl_2(AMNU)_2]$ (1). To a solution of K_2PtCl_4 (124.5 mg, 0.30 mmol) in water-acetone (1 : 1, 10 mL), a solution of 6-amino-1-methyl-5-nitrosouracil (AMNU) (102.1 mg, 0.60 mmol) in acetone (50 mL) was added. The reaction mixture was left overnight with stirring. The formed dark green powder of complex **1** was filtered off, washed several times with a few drops of acetone and dried *in vacuo*. Yield: 152.0 mg (83.6%).

Anal. found: C, 19.94; H, 2.17; Cl, 11.44; N, 18.59. Anal. Calcd for $C_{10}H_{12}Cl_2N_8O_6Pt$ (606.25): C, 19.81; H, 2.00; Cl, 11.70; N, 18.48.

2.1.2. [$PtCl_2$(MAMNU)$_2$] (2). To a solution of K_2PtCl_4 (83.0 mg, 0.20 mmol) in water–ethanol (1 : 1, 10 mL), a solution of 6-methylamino-1-methyl-5-nitrosouracil (MAMNU) (73.7 mg, 0.40 mmol) in ethanol (60 mL) was added. The reaction mixture was left overnight with stirring. The dark reddish-brown powder of complex **2** was filtered off, washed several times with a few drops of acetone and dried *in vacuo*. Yield: 96.0 mg (75.7%).

Anal. found: C, 22.98; H, 2.96; Cl, 11.00; N, 17.85. Anal. Calcd for $C_{12}H_{16}Cl_2N_8O_6Pt$ (634.31): C, 22.72; H, 2.54; Cl, 11.18; N, 17.67.

2.1.3. [$PtCl_2$(MABNU)$_2$] (3). To a solution of K_2PtCl_4 (124.5 mg, 0.30 mmol) in water–methanol (1 : 1, 10 mL), a solution of 6-methylamino-1-benzyl-5-nitrosouracil (MABNU) (156.2 mg, 0.60 mmol) in methanol (60 mL) was added. The reaction mixture was left overnight with stirring. The dark brown precipitate of complex **3** was filtered off, washed several times with a few drops of acetone and dried *in vacuo*. Yield: 160.0 mg (67.8%).

Anal. found: C, 35.70; H, 4.40; Cl, 9.24; N, 14.89. Anal. Calcd for $C_{24}H_{24}Cl_2N_8O_6Pt$ (786.48): C, 36.65; H, 3.08; Cl, 9.02; N, 14.25.

3. Results and discussion

[$PtCl_2$(AMNU)$_2$] (**1**), [$PtCl_2$(MAMNU)$_2$] (**2**) and [$PtCl_2$(MABNU)$_2$] (**3**) complexes were obtained during the reaction at room temperature of the respective ligand with potassium tetrachloroplatinate(II) in a molar ratio of 2 : I. The same complexes are obtained on carrying out the reactions using a molar ratio of Pt(II): pyrimidine of either 1 : 1 or 1 : 2. Chemical analysis together with the data obtained from ^{1}H NMR and IR indicate that, the pyrimidine bases interact with $PtCl_4^{2-}$ via ligand substitution reactions as a neutral ligand and the suggested coordination site is the exocyclic oxygen, O(4). The three pyrimidine–Pt(II) complexes are readily soluble only in dimethyl sulfoxide (dmso) and slightly soluble in water, methanol, ethanol or acetone. All compounds were characterized by microanalyses, IR and ^{1}H NMR spectroscopies. Identity of complex **3** was also confirmed by thermal analysis.

3.1. *^{1}H NMR spectra*

The proton NMR spectra of 6-amino-1-methyl-5-nitrosouracil, 6-methyl-amino-1-methyl-5-nitrosouracil, 6-methylamino-1-benzyl-5-nitrosouracil and their isolated platinum(II) complexes (**1**, **2**, **3**) in dmso-d_6 were obtained and the spectra assigned consistent with related pyrimidine bases [17–19] (table 1).

All the signals observed in the spectra of the free ligands are also reflected in their corresponding complexes indicating that these pyrimidine bases interact with Pt(II) as

Table 1. ^{1}H NMR chemical shifts (δ in ppm) of 5-nitrosouracil derivatives and their complexes in dmso d_6.

Compound	R_2			6-N*H*CH$_3$	6-NHC*H*$_3$	N(3)–*H*
	–C*H*$_3$	C*H*$_2$*P*h				
AMNU	3.33	–		7.31	–	11.70
[PtCl$_2$(AMNU)$_2$] (**1**)	3.29	–		7.24	–	11.95
MAMNU	3.20	–		10.60	3.10	14.20
[PtCl$_2$(MAMNU)$_2$] (**2**)	3.24	–		10.80	3.10	13.85
MABNU	–	5.00	7.25–7.34	13.90	3.10	11.35
[PtCl$_2$(MABNU)$_2$] (**3**)	–	5.10	7.29–7.38	12.03	3.30	11.15

neutral ligands. Furthermore, almost all the signals observed in the spectra of the complexes are downfield from the free ligands because decrease in the electron density on the pyrimidine results from coordination with Pt(II). For comparison, in a previous investigation [6] on the interaction of 1-methyl-5-nitrosouracil and its 6-methyl derivative with Co(II) and Cu(II), we found that pyrimidine bases interact with Co(II) as a bidentate ligand in the anionic form through the exocyclic oxygen and nitrogen atoms. This interaction was associated with dissociation of the iminic or N(3) proton depending on the nature of substituents on the pyrimidine. Both ligands interact with Cu(II) monodentate in the neutral form. These results are inconsistent with the crystallographic data [10–14] obtained for metal pyrimidine complexes precluding sweeping generalities about the nature of interaction of metal ions with pyrimidines.

3.2. *IR Analysis*

Assignments of the well-characterized bands in the infrared spectra of the pyrimidine ligands and the obtained complexes are given in table 2. The formation of Pt(II)–pyrimidine complexes is strongly supported by observing the main infrared bands of the ligands in the product spectra. However, the bands of the ligands in the spectra of complexes reveal small shifts in intensities compared with those of the free ligands. This should be attributed to the expected symmetry and electronic structure changes upon complex formation.

Two bands are observed in the spectrum of AMNU at 3278 and 3202 cm^{-1} characteristic [17, 18] for the antisymmetric and symmetric stretching vibration of the NH_2 group. Similar bands are observed in the corresponding Pt(II) complex **1** spectrum at 3300 and 3193 cm^{-1}. The N–H bond (exocyclic nitrogen) of the ligands MAMNU and MABNU and their complexes **2** and **3** shows its stretching vibration mode at 3208, 3198, 3221 and 3206 cm^{-1}, respectively. The N(3)–H bond stretch associated with the three ligands and their complexes is observed in its expected region [6] around 3100 cm^{-1}. The presence of amino protons in the free ligand spectra as well as in spectra of their complexes was also supported by bands in the region 1680–1632 cm^{-1}, characteristic to bending, $\delta(NH_2)$ or δ(CNH) [20, 21], see table 2. The assignments of various N–H bond stretches are consistent with the data obtained from ^{1}H NMR spectra and support the suggestion that pyrimidine interact with Pt(II) in the neutral form.

Table 2. Characteristic infrared frequencies* (cm^{-1}) and tentative assignments for 5-nitrosouracil derivatives and their complexes.

AMNU	MAMNU	MABNU	1	2	3	Assignments**
3278 m			3300 br			ν_{as}(N–H); NH_2
	3208 m	3193 m		3221 m	3206 m	ν_s(N–H); exocyclic
3202 m			3193 m			ν_s(N–H); NH_2
3104 m	3092 m	3102 w	3072 m	3064 m	3098 w	ν(N(3)–H)
		3058 s			3064 m	ν(C–H); phenyl
2930 m	2930 m	2950 w	2945 w	2921 m	2923 w	ν_{as}(C–H); CH_3
2875 m	2875 m	2855 m	2850 w	2851 m	2851 w	ν_s(C–H); CH_3
1745 vs	1750 vs	1740 s	1703 vs	1705 vs	1704 vs	ν(C=O)
1670 s	1650 s	1680 vs	1651 sh	1632 s	1650 sh	$\delta(NH_2)$, δ(CNH)
1618 s	1620 s	1624 s	1583 vs	1558 vs	1585 vs	ν(C=C)
1510 s	1508 s	1503 s	1515 w	1502 ms	1501 ms	ν(N=O)
–	–	–	1268 m	1295 m	1293 w	ν(C–O)
450 m	460 m	451 m	442 m	457 m	455 w	δ(CNO)
–	–	–	425 w	425 w	422 w	ν(Pt–O)

*s, strong; m, medium; v, very; w, weak; br, broad. **ν, stretching; δ, deformation.

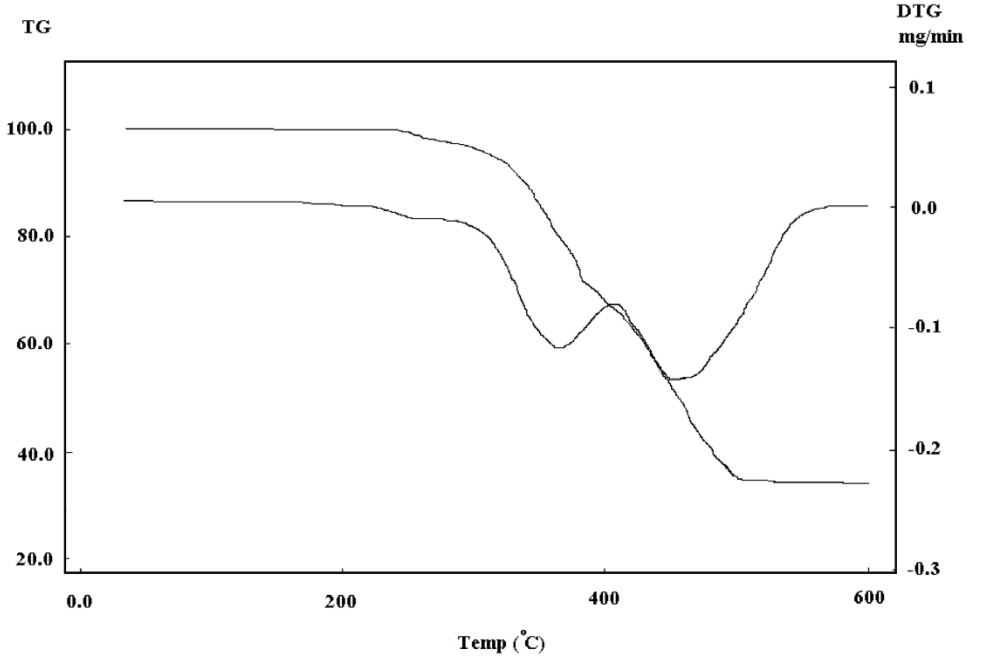


Figure 1. Thermogravimeteric (TG) and derivative (DTG) analysis of $[PtCl_2(MABNU)_2]$.

In the three complexes, the stretching vibration corresponding to ν(C=O) was observed around 1704 cm^{-1}, lower by nearly 45 cm^{-1} in comparison with the free ligands. The ν(N=O) was observed around 1508 cm^{-1} for free ligands and their complexes [7, 21, 22]. The shift to lower wavenumber for ν(C=O) is attributed to coordination. This mode of coordination agrees quite well with the interaction of the ligands in a neutral form and could be supported by observing two new bands in the

spectra of complexes not present in the spectra of the free ligands. The first band is observed around 1295 cm^{-1}, attributed to ν(C–O) associated with the coordinated C=O group [6, 20, 21, 23]. The second band is observed at 425 cm^{-1} due to the stretching of Pt(II)–O.

Three different derivatives of 5-nitrosouracil are capable of substituting two chloro ligands and coordinating to Pt(II) via oxygen of the carbonyl group in a neutral form. The most probable structure with these complexes is a square planar with two pyrimidine ligands in *trans* positions, as chloro ligand exerts a weaker trans effect than pyrimidine.

3.3. *Thermal analysis*

Thermogravimetric (TG) and differential thermal analysis (DTG) were carried out for complex **3** under N_2 flow (figure 1). The data obtained support the proposed structure; decomposition of the complex occurs in the temperature range of 361–500°C, where two maxima at 361 and 455°C are observed. The total weight loss of 64.00% agrees quite well with the calculated value of 62.61% due to the loss of the two ligand molecules leaving Pt(II)Cl_2 as the final product.

References

[1] (a) B. Rosenberg, L. VanCamp, J.E. Trosko, V.H. Mansour. *Nature*, **222**, 385 (1969); (b) B. Rosenberg. *Interdiscip. Sci. Rev.*, **32**, 134 (1978).
[2] E. Zangrando, F. Pichierri, L. Randaccio, B. Lippert. *Coord. Chem. Revs*, **156**, 275 (1996).
[3] R. Fagiani, C.J.L. Lock, B. Lippert. *Inorg. Chem. Acta*, **106**, 75 (1985).
[4] H.-J. Korte, R. Bau. *Inorg. Chem. Acta*, **79**, 251 (1983).
[5] B. Lippert. *Coord. Chem. Rev.*, **200–202**, 487 (2000).
[6] S M. Teleb. *Spectrochim. Acta*, **A**(60), 3093 (2004).
[7] J.M. Salas-Pergrin, M.N. Moreno-Carretero, E. Colacio-Rodriguez. *Can. J. Chem.*, **63**, 3573 (1985).
[8] R. Fagiani, B. Lippert, C.J.L. Lock. *Inorg. Chem.*, **19**, 295 (1980).
[9] H. Rauter, E.C. Hillgeris, A. Erxleben, B. Lippert. *J. Am. Chem. Soc.*, **116**, 616 (1994).
[10] T.J. Kistenmacher, T. Sorrell, L.G. Marzilli. *Inorg. Chem.*, **14**, 2479 (1975).
[11] T.J. Kistenmacher, D.J. Szalda, L.G. Marzilli. *Acta Crystallogr.*, **B31**, 2416 (1975).
[12] L.D. Kosturko, C. Folzer, R.F. Stewart. *Biochem.*, **13**, 3949 (1974).
[13] K. Saito, R. Terashima, T. Sakaki, K. Tomita. *Biochem. Biophys. Res. Commun.*, **61**, 83 (1974).
[14] D.J. Szalda, L.G. Marzilli, T.J. Kistenmacher. *Inorg. Chem.*, **14**, 2076 (1975).
[15] (a) L.G. Goodman, A. Gilman. *The Pharmacological basis of Therapeutics* (Joel G. Hardman, 10 ed, New York, NY [u. a.]: McGraw-Hill Med. Publ., 2001); (b) J.A.R. Navarro, J.M. Salas, M.A. Romero, R. Vilaplana, F. Gonzalez, R. Faure. *J. Med. Chem.*, **41**(3), 332 (1998); (c) P.J.S. Miguel, P. Lax, M. Willermann, B. Lippert. *Inorg. Chim. Acta*, **357**, 4552 (2004).
[16] F. Belanger-Gariepy, R. Faure, F. Hueso, M.N. Moreno, J.A.R. Navarro, J.M. Salas. *Polyhedron*, **17**, 1747 (1998).
[17] J.M. Salas-Pergrin, M.N. Moreno-Carretero, M.A. Romero-Molina, E. Colacio-Rodriguez. *Rev. Chim. Miner.*, **21**, 233 (1984).
[18] J.M. Salas-Pergrin, M.N. Moreno-Carretero, J.D. Lopez-Gonzalez, A. Garcia-Rodriguez. *An. Quim.*, **80B**, 437 (1984).
[19] G.C. Stocco, A. Tamburello, M.A. Girasolo. *Inorg. Chim. Acta*, **78**, 57 (1983).
[20] H. Günzler, H. Gremlich. *IR Spectroscopy An Introduction*, Wiley-VCH Verlag GmbH 69469, Weinheim (F.R.G.) (2002).
[21] K. Nakamoto. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 4th Edn, Wiley, New York (1986).
[22] M.N. Moreno-Carretero, J.M. Salas-Peregrin, A. Sanches-Rodrigo, I. Nogueras-Montiel. *An. Quim.*, **79B**, 547 (1983).
[23] J.S. Garcia-Mino, J.D. Lopez-Gonzalez, M.N. Moreno-Carretero, J.M. Salas-Pergrin. *An. Quim.*, **77b**, 335 (1981).