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# A Dinuclear Platinum(II) N4Py Complex: An Unexpected Coordination Mode For N4Py

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Supporting Information

**ABSTRACT:** The polypyridyl compound *N*,*N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine (N4Py) acts as a bridging ligand and coordinates to two Pt(II) ions giving an unexpected diplatinum(II) complex, whose photophysical and anticancer properties were investigated.

The polypyridyl compound *N*,*N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine (N4Py) has been extensively used as a pentadentate ligand to bind to octahedral metal ions such as iron,[1] manganese,[2] ruthenium,[3] copper,[4] zinc,[4a] cobalt,[5] and nickel[6] forming mononuclear complexes. Owing to the ability of the N4Py scaffold to stabilize metal complexes at different oxidation states, N4Py complexes have been developed as catalysts for various reactions including oxidation of a variety of biological[1e,f] and nonbiological[1c,g−i,2b,c,3a,b] substrates, oxygen evolution,[2a] and hydrogen production.[5,6] Our interest in the reactivity of five-coordinate Pt(II) complexes[7] and the coordination chemistry of N4Py[4a] led us to examine the use of N4Py for the synthesis of a five-coordinate platinum complex. Herein, we report the synthesis and crystal structure of an unexpected diplatinum(II) N4Py complex. Additionally, the photophysical and anticancer properties of this complex were examined.

The N4Py ligand was prepared according to our previously reported method.[4a] Heating an equimolar mixture of N4Py and *cis*-$[Pt(DMSO)_2Cl_2]$ (DMSO = dimethyl sulfoxide) in nitromethane ($CH_3NO_2$) at reflux for 3 h resulted in a color change from yellow to green. The $^1$H NMR spectrum of the green reaction mixture in $d_7$-*N*,*N*-dimethylformamide ($d_7$-DMF) was complicated and suggested that a range of platinum-containing species were generated in the reaction (Supporting Information). Consistently, peaks corresponding to N4Py complexes containing one and two Pt(II) ions were observed in the high resolution electrospray ionization (HRESI) mass spectrum (Supporting Information). While it proved impossible to separate the mono- and diplatinum complexes from the reaction mixture, the results suggested that N4Py could potentially be acting as a bridging ligand and forming diplatinum N4Py species. As such, we then investigated the reaction of N4Py with two equivalents of *cis*-$[Pt(DMSO)_2Cl_2]$ in $CH_3NO_2$. Refluxing the mixture for 70 min resulted in a color change from yellow to greenish yellow, which was accompanied by precipitation of a yellow solid (Figure 1).

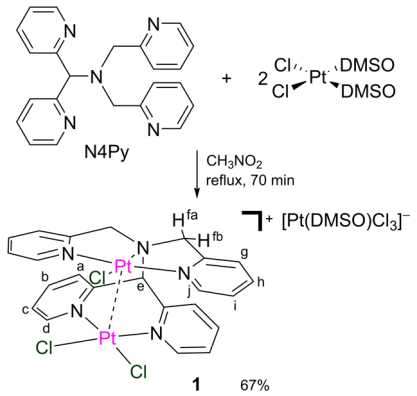


**Figure 1.** Synthesis of the diplatinum(II) N4Py complex $[Cl_2Pt(N4Py)PtCl][Pt(DMSO)Cl_3]$ (**1**).

In contrast to the spectrum obtained for the 1:1 reaction, the $^1$H NMR spectrum of the yellow product in $d_7$-DMF shows only one set of downfield shifted N4Py proton signals, indicating coordination of N4Py to Pt(II) ion(s) and formation of only one Pt N4Py complex (Supporting Information). Two singlet signals were observed in the methyl region of the spectrum; the signal at 4.54 ppm is due to free $CH_3NO_2$, whereas the signal at 3.36 ppm, flanked by $^{195}$Pt satellites ($^3J_{H-Pt}$ = 20.6 Hz), is presumably due to methyl groups of a DMSO ligand coordinated to Pt. This methyl signal is shifted upfield compared with the singlet signal (3.67 ppm, $^3J_{H-Pt}$ = 21.5 Hz) observed for the methyl protons of *cis*-$[Pt(DMSO)_2Cl_2]$. The HRESI mass spectrum of the yellow product shows prominent peaks corresponding to the diplatinum N4Py species $[Cl_2Pt(N4Py)PtCl]^+$ at $m/z$ = 862.0165 and fragments of this species in the positive mode (Supporting Information) and $[Pt(DMSO)Cl_3]^-$ at $m/z$ = 377.8864 in the negative mode. This suggests that the yellow product is $[Cl_2Pt(N4Py)PtCl][Pt(DMSO)Cl_3]$. Integration of the $^1$H NMR signals due to $[Cl_2Pt(N4Py)PtCl]^+$, $[Pt(DMSO)Cl_3]^-$ (at 3.36 ppm), and $CH_3NO_2$ reveals that the ratio of

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these components in the product is 1:1:0.5. The formulation of the product $[Cl_2Pt(N4Py)PtCl][Pt(DMSO)Cl_3]\cdot 0.5CH_3NO_2$ ($\mathbf{1}\cdot 0.5CH_3NO_2$) was confirmed by elemental analysis.

The solid state structure of **1** was determined by X-ray crystallography. Yellow crystals of $\mathbf{1}\cdot DMF\cdot 0.5CH_3NO_2$ were obtained by vapor diffusion of diethyl ether into a DMF solution of the complex. The crystal structure of **1** unequivocally shows that N4Py acts as a bridging ligand and coordinates to two Pt(II) centers in the $[Cl_2Pt(N4Py)PtCl]^+$ cation (Figure 2). The aliphatic amine (N5) and two picolyl

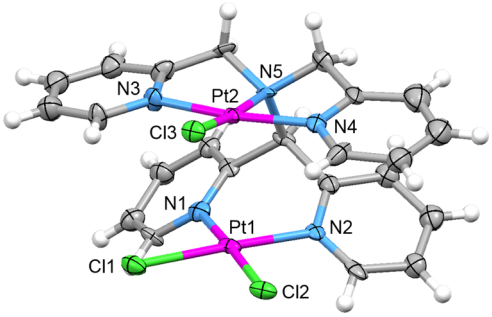


**Figure 2.** Crystal structure of the $[Cl_2Pt(N4Py)PtCl]^+$ cation shown as a thermal ellipsoid plot (50% probability level). Selected distances (Å) and angles (deg): Pt1···Pt2 3.1268(8), Pt1−N1 2.04(2), Pt1−N2 2.03(1), Pt1−Cl1 2.305(3), Pt1−Cl2 2.303(4), Pt2−N3 1.97(1), Pt2−N4 2.00(1), Pt2−N5 2.04(1), Pt2−Cl3 2.304(4); N1−Pt1−Cl2 176.9(4), N2−Pt1−Cl1 178.1(4), N1−Pt1−N2 90.4(5), N3−Pt2−N4 168.3(5), N5−Pt2−Cl3 174.0(4).

amine (N3 and N4) nitrogen donors of N4Py coordinate to Pt2 in a tridentate fashion, whereas the remaining two nitrogen donors (N1 and N2) of N4Py coordinate to Pt1 in a bidentate fashion. The remaining sites on the square coordination plane of both Pt(II) centers are occupied by chlorido ligands. The $[Cl_2Pt(N4Py)PtCl]^+$ cation adopts an X-wing like conformation; presumably the folded structure is stabilized by both Pt···Pt (3.1268(8) Å) and $\pi-\pi$ stacking interactions between pyridyl rings (centroid−centroid distances are 3.622 and 3.704 Å and angles between the ring normal of the pyridine plane and the centroid vector ranging from 10° to 28°). Both Pt(II) centers are four-coordinate and display square planar geometries; $\tau_4$ values[8] for Pt1 and Pt2 are 0.04 and 0.13, respectively.

It was of interest to examine whether the folded structure of $[Cl_2Pt(N4Py)PtCl]^+$ observed in the solid state exists in the solution state. The $^1H$ and $^{13}C$ NMR spectra of **1** in $d_7$-DMF suggest that it possesses a mirror plane (Figure 3a and Supporting Information). This is consistent with both folded and unfolded conformations, where there is no Pt···Pt interaction, and the N−C bond that covalently linked the two halves in $[Cl_2Pt(N4Py)PtCl]^+$ is rotated by 180° (Supporting Information). However, all pyridyl proton signals of **1**, except $H_a$, $H_d$, and $H_j$, are shifted upfield when compared with the corresponding proton signals in complexes **2b** and **3** (Figure 3), which can be considered as mononuclear analogs of the top and bottom halves, respectively, of the $[Cl_2Pt(N4Py)PtCl]^+$ cation. The upfield shifts are consistent with $\pi-\pi$ stacking of pyridyl rings from the top and bottom halves of $[Cl_2Pt(N4Py)PtCl]^+$. Interestingly, the pyridyl proton signals of $H_d$ and $H_j$ are slightly downfield shifted (0.10 ppm). This is presumably due to the close proximity of these protons to the electronegative chlorido ligand(s) on the top/bottom half of

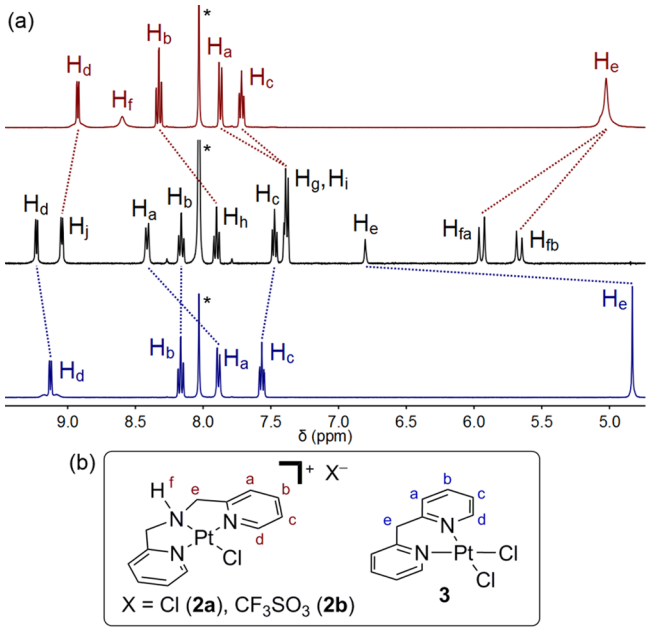


**Figure 3.** (a) Stacked partial $^1H$ NMR spectra (400 MHz, $d_7$-DMF, 298 K) of **2b** (top), **1** (middle), and **3** (bottom). The asterisk (*) denotes the residue solvent peak. (b) Structures of complexes **2a**, **2b**, and **3**.

$[Cl_2Pt(N4Py)PtCl]^+$ supporting the postulate that the cation exists in the folded conformation in solution.

More importantly, through-space interactions between $H_a$ and $H_{fb}$, $H_a$ and $H_g$, and $H_e$ and $H_{fb}$ were observed in the two-dimensional $^1H-^1H$ ROESY NMR spectrum (Supporting Information). On the basis of density functional theory (DFT) calculations, the distances between these three pairs of protons are expected to be much shorter in the folded conformer compared with the unfolded conformer (Supporting Information), suggesting that the folded structure of $[Cl_2Pt(N4Py)PtCl]^+$ exists in solution. Furthermore, DFT calculations (with a DMF solvation field) show that the folded structure is more energetically favorable than the unfolded conformer by 12.2 kJ $mol^{-1}$ (at 298 K).

The photophysical properties of diplatinum complex **1** were examined and compared with those of the corresponding monoplatinum complexes **2** and **3**. The electronic absorption spectrum of **1** shows a distinct band at 420 nm that is not observed for either monoplatinum complex (Supporting Information). Time-dependent DFT calculations suggest that this is an MLCT transition involving an antibonding orbital composed of the platinum $d_{z^2}$ orbitals (HOMO) and a delocalized $\pi^*$ orbital located on the ligand (LUMO). A Pt−Pt bonding orbital derived from the $d_{z^2}$ orbitals makes up the HOMO−10 orbital.

While compound **3** is not emissive, as expected for Pt(II) dichloride complexes,[9] compounds **1** and **2a** were found to be very weakly emissive in DMF solution (Supporting Information). Complex **2a** exhibits a broad emission band at 629 nm while **1** shows vibronic peaks at 621 and 577 nm reminiscent of the emission spectra of Pt(II) terpyridine complexes in low-temperature glasses.[10] The presence of vibronic structure is consistent with the structural rigidity of **1** in both the ground and excited states.

It is well established that platinum(II) compounds can display anticancer properties.[11] Analogs of the two mono-


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platinum complexes **2a** and **3** have been tested as potential anticancer agents,[12] and there has been considerable interest in the antiproliferative properties of multiplatinum species including di- and triplatinum complexes[13] containing the di(2-picolyl)amine (dpa) binding motif present in **2a**. Mindful of the possibility of **1** acting as a cytotoxic agent through a DNA binding mechanism, testing was carried out against two cancer cell lines: A549 (lung cancer) and MDA MB 231 (breast cancer). The complex displayed moderate cytotoxicity against A549 cells ($IC_{50} \approx 40$ $\mu$M, compared with an $IC_{50}$ of $9.4 \pm 0.3$ $\mu$M for cisplatin, Supporting Information). The complex displayed lower cytotoxicity against MDA MB 231 cells ($IC_{50}$ >40 $\mu$M, Supporting Information), again lower than cisplatin ($IC_{50}$ $41.2 \pm 3.9$ $\mu$M)[14] despite this cell line being cisplatin-resistant.[15] Disappointingly, it therefore appears that **1** has limited potential as an anticancer agent.

In conclusion, the reaction of N4Py with two equivalents of Pt(II) ions gave the unexpected diplatinum complex **1**. X-ray crystallography, NMR spectroscopy, and DFT calculations suggest that **1** exists in the folded conformer in both solid and solution states. Both electronic absorption and emission spectra of **1** show distinct features that were not observed in monoplatinum complexes **2** and **3**. The antiproliferative properties of **1** against two cancer cell lines A549 (lung cancer) and MDA MB231 (breast cancer) were moderate to low, suggesting that the structure of **1** would require modification before it could act as a potent anticancer agent.

Herein, we have reported the first observation of the ubiquitous N4Py ligand acting as a bridging ligand and forming a unexpected diplatinum(II) complex. The ability of N4Py to bridge two square planar metal centers should be general. This property could be utilized in the preparation of both homo and mixed dimetallic N4Py complexes. Such systems may display interesting catalytic and photophysical properties, and studies toward these types of systems are currently underway.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental procedures, selected NMR and mass spectra, crystal structures, DFT calculations, electronic absorption and emission spectra, FT-IR and FT-Raman spectra, details for cytotoxicity studies, .xyz files, and CIFs giving crystallographic data for **1**, **2b**, and **3** (CCDC reference numbers 1055682−1055684). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.5b01032.

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### Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

### Notes

The authors declare no competing financial interest.

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