

Synthesis and Characterization of Platinum(II) and Palladium(II) Complexes with 2,5-Dimethyl-4-Hydroxyprimidine

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Summary: The binding of Pt(II) and Pd(II) ions to 4-amino-2,5-dimethyl-1-pyrimidine (ADMPY) has been compared with the binding of the same metal ions to 2,5-dimethyl-4-hydroxy pyrimidine (HDMPY), analogue of ADMPY in which the amino group has been replaced by a hydroxyl group. A brief comparison is made with the corresponding Pt(II) and Pd(II) complexes of thiamine and oxythiamine. In this paper we report the synthesis, elemental analyses, infrared spectra data, proton and carbon-13 nuclear magnetic resonance studies of these new complexes.

A complete assignment of ^1H and ^{13}C NMR spectra resonances is presented for both the ligand and the complexes. The results show that the metallation site is N-1' position of the ligand in agreement with earlier works [1-3], however, the chemical shifts observed for this ligand upon complexation are larger than the corresponding chemical shifts observed for the 4-amino-2,5-dimethyl-pyrimidine analogue contrary to the thiamine/oxythiamine system.

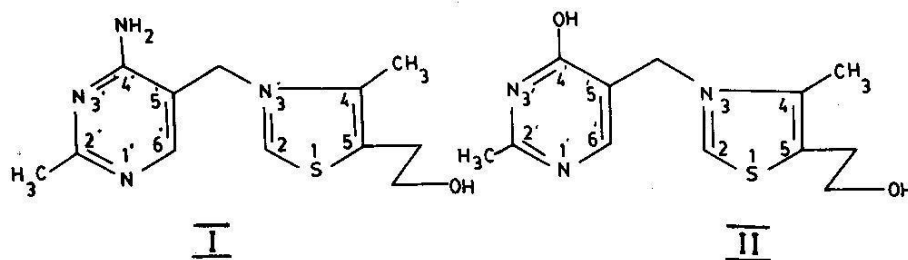
Introduction

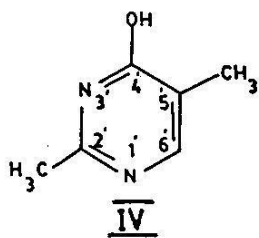
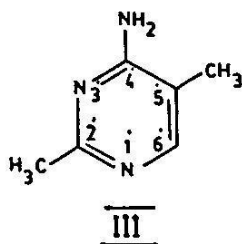
Recently we reported the synthesis and characterization of Pd(II) complexes of 4-amino-2,5-dimethyl pyrimidine [1] where we claimed N-1' position of the ligand as the coordination site in agreement with the previous reports [2,3]. In another paper from our laboratory [4], we reported correlation between ligand basicity and chemical shifts upon metal coordination to thiamine and oxythiamine (structures I and II). Since then we have been curious as to whether this ligand basicity/chemical

shift correlation is unique to thiamine /oxythiamine system or it could be extended to some similar systems. A very good example of such a system could be 4-amino-2,5-dimethyl pyrimidine and 2,5-dimethyl-4-hydroxypyrimidine-(structure (III) and (IV)).

Experimental

Potassium tetrachloroplatinate(II), potassium tetrachloropalladate(II) and deuterated dimethyl sulfoxide were purchased from Aldrich Chemical





company and were used without further purification.

Preparation of 2,5-dimethyl-4-hydroxypyrimidine:

Five grams (40.60 mmol) of 4-amino-2,5-dimethyl pyrimidine were dissolved in 150 ml of 6N HCl and refluxed for ten hours. Having been evaporated to dryness, the residue was dissolved in 80 ml of water. The pH of the resulting solution was then adjusted to 5 and evaporated to dryness. The residue was extracted with chloroform, evaporation of which yielded 92% of 2,5-dimethyl-4-hydroxypyrimidine. The melting point was determined to be $175 \pm 0.5^\circ\text{C}$ [5].

Preparation of Pt(II) and Pd(II) Complexes:

The platinum(II) and palladium (II) complexes were prepared as described earlier [1]. Anal. Calcd. for $\text{Pt}(\text{HDMPY})_2\text{Cl}_2 \cdot \text{H}_2\text{O}$, $\text{C}_{12}\text{H}_{18}\text{N}_4\text{O}_3$ PtCl_2 (Mw = 532) : C, 27.07; H, 3.38; N, 10.53%. Found: C, 26.78; H, 3.06; N, 10.47%.

Anal. Calcd. for $\text{Pd}(\text{HDMPY})_2\text{Cl}_2 \cdot \text{H}_2\text{O}$, $\text{C}_{12}\text{H}_{18}\text{N}_4\text{O}_3\text{PdCl}_2$ (Mw = 443.3)
C, 32.51; H, 4.06; N, 12.63%.
Found: C, 32.62; H, 3.78; N, 12.61%.

Proton and carbon-13 NMR spectra were run on Varian FT-80A 20 MHz, using DMSO-d_6 as solvent TMS as internal reference standard. The infrared spectra were recorded on Perkin-Elmer IR NO 297 Spectrophotometer, employing KBr pellets with polystyrene as reference. The melting points were determined in capillaries and were uncorrected.

Results and Discussion

^1H NMR Spectra:

The proton NMR chemical shifts are given in Table 1. The assignments of the resonances are based on previous studies including off-resonance techniques [1,2,6]. Three resonances are observed for the free ligand and they were assigned as follows: a singlet at δ 1.85 ppm is due to 5'- CH_3 while the singlet at δ 2.20 ppm is ascribed to 2'- CH_3 signal. The most downfield resonance is unequivocally assigned to C6'-H proton.

In $\text{Pt}(\text{HDMPY})_2\text{Cl}_2$ complex, 5'- CH_3 signal hardly shifted (δ 0.02

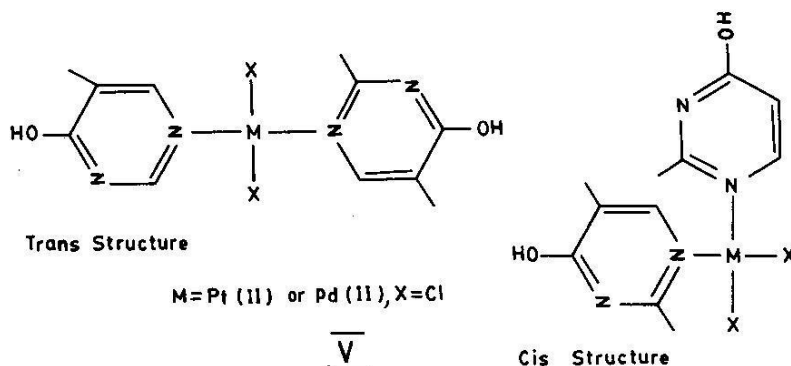


Table-1: $^1\text{H-NMR}$ Chemical Shifts of the Ligand and Its Pt(II) and Pd(II) Complexes

PROTON	HDMPY	Pt(HDMPY) $_2$ Cl $_2$ ·H $_2$ O	Pd(HDMPY) $_2$ Cl $_2$ ·H $_2$ O
5'-CH $_3$	1.85	1.87	1.89
2'-CH $_3$	2.20	2.94	3.01
C6'-H	7.63	8.00	8.00

ppm). While 2'-CH $_3$ and C6'-H shifted downfield by δ 0.74 and δ 0.37 ppm, respectively. In Pd(HDMPY) $_2$ Cl $_2$ complex, 5'-CH $_3$, 2'-CH $_3$ and C6'-H protons shifted downfield by δ 0.04, 0.81 and δ 0.37 ppm, respectively. These downfield chemical shifts in Pt(II) and Pd(II) complexes compared to the free ligand are strong indication for N-1'-metal covalent bond. These chemical shifts are comparable to those observed in Pt(II)-nucleoside complexes reported by Kong and Theophanides [7,8]. These findings are also consistent with the work of Adeyemo et al.[3,9], Adeyemo and Raval [1], Theophanides et al.[2] and some other authors [6,10]. In order to provide a sound argument for our claim that N-1' position of the ligand is the coordination site, we have considered other alternative binding sites (N-3' and/or C4'-OH). If binding were through the phenolic group, one would expect 5'-CH $_3$ protons to be shifted downfield by about twice as much as 2'-CH $_3$ protons since 5'-CH $_3$ and 2'-CH $_3$ protons are ortho and meta, respectively to the phenolic group. It has been suggested in a paper on Pt(II)-pyridine complexes that the downfield shifts of the meta and para protons are roughly only half of that of the ortho protons [11]. Since our observation is contrary to

this hypothesis, we concluded that the phenolic group is not likely to be the coordination site. Another potential donor atom is N-3' position of HDMPY. Again, considering N-3' as the coordination site, one would expect 2'-CH $_3$ and C4'-OH protons which are ortho to this assumed coordination site to be shifted downfield by about twice as much as 5'-CH $_3$ and C6'-H protons which are meta and para, respectively to N-1' position. It is interesting to observe that a downfield shift of 0.37 ppm of C6'-H proton is roughly half the downfield shift of δ 0.81 ppm of 2'-CH $_3$ protons. Along the same line of reasoning, one would expect C4'-OH signal to shift downfield by about twice as much as 5'-CH $_3$ and C6'-H protons. Unfortunately, we could not observe C4'-OH signal. Although, 5'-CH $_3$ protons were observed (δ 0.02 or 0.04 ppm downfield shift), this was not a strong evidence in favour of N-3' as a possible coordination site.

^{13}C NMR Spectra:

The ^{13}C NMR chemical shifts are given in Table 2. The assignments for the free ligand and its Pt(II) complexes are reported for the first time. The spectra were recorded for the ligand and its complexes in the same solvent (DMSO- d_6) for effective comparison.

Table-2: ^{13}C -NMR Chemical Shifts of the Ligan and Its Pt(II) and Pd(II) Complexes.

CARBON	HDMPY	Pt(HDMPY) $_2$ Cl $_2$.H $_2$ O	Pd(HDMPY) $_2$ Cl $_2$.H $_2$ O
C4'	162.85	160.98	160.60
C2'	157.07	160.48	160.45
C6'	150.48	151.46	-
C5'	121.03	123.08	122.04
2'-CH $_3$	20.82	23.08	23.04
5'-CH $_3$	12.58	12.26	12.20

The free ligand shows six resonances as expected. The resonance at δ 162.50 ppm is assigned to C4' carbon while the signals at δ 157.07 and δ 150.48 ppm are attributed to C2' and C6' carbons, respectively. Other signals, C5', 2'-CH $_3$ and 5'-CH $_3$ are assigned to δ 121.03, δ 20.82 and δ 12.58 ppm, respectively. Complexation causes downfield shift of carbons adjacent to the coordination site [12].

In Pt(HDMPY) $_2$ Cl $_2$ complex, C4' shifted upfield to δ 160.98 ppm, representing a shift of δ 1.87 ppm. Another upfield shifted resonance is 5'-CH $_3$ (δ 0.32 ppm). All other signals experienced downfield shift. The C2', C6', C5' and 2'-CH $_3$ carbons shifted by δ 3.41, δ 0.98, δ 2.05 and δ 2.26 ppm, respectively. The chemical shifts in Pd(HDMPY) $_2$ Cl $_2$ complex are similar to those of Pt(HDMPY) $_2$ Cl $_2$ except that C6' signal could not be observed. This finding is consistent with our experience in Pd(ADMPY) $_2$ Cl $_2$ complex reported [1] earlier. Thus ^{13}C NMR results provided additional support for the assumption that Pt(II) and Pd(II) are coordinated through N-1' position of the ligand.

Infrared Spectra:

The IR tentative assignments are given in Table 3. Although the free ligand (HDMPY) and its Pt(II) and Pd(II) complexes show many bands between 1700 and 600 cm^{-1} , we shall concentrate on those bands which are relevant to our interpretation.

The appearance of a broad band around 3500 cm^{-1} supports the presence of water in Pt(II) and Pd(II) complexes. The non-involvement in bonding of the phenolic oxygen with metals is indicated by the non-removal of the $\nu(\text{C-OH})$ band of the ligand in the complexes [2,13,14]. This band appears at 1045, 1030 and 1020 cm^{-1} in the ligand and at 1065, 1040 and 1025 cm^{-1} in Pt(HDMPY) $_2$ Cl $_2$ and at 1062, 1040 and 1025 cm^{-1} in Pd(HDMPY) $_2$ Cl $_2$ complexes.

Strong evidence for the involvement of the ring nitrogen in the complexes can be appreciated by considering the bands around 1600 cm^{-1} . The free ligand and its complexes show two bands in this region. At 1665 and 1610 cm^{-1} for the ligand, at 1675 and 1625 cm^{-1} for the Pt(II) complex and

Table-3: Infrared Spectra Data (cm^{-1}) of the Compounds.

HDMPY	Pt(HDMPY) ₂ Cl ₂ ·H ₂ O	Pd(HDMPY) ₂ Cl ₂ ·H ₂ O	Assignments
3400-3200 br	3600-3400 br	3600-3400 br	$\nu(\text{HOH}) + \nu(\text{OH})$
-	3200-2850 br	3200-2850 br	$+\nu(\text{CH})$
1665s	1685s	1675s	ring stretching
-	1675s	1670s	coupling
1610s	1625sh	1625sh	
-	1575m	1583m	Skeletal C = C,
-	-	1558m	C = N stretching
-	-	1520m	
1490m	1490m	-	
1450m	-	-	
1435w	1430m	1430m	
1380s	1380m	1375m	
1318m	1340-1310 br		
1285sh	1270w	1255w	
	1265w		
1200w	-	-	
1185s	-	1185w	
1170s	1165m	1164m	
-	-	1130sh	
1045sh	1065m	1062w	
1030m	1040m	1040w	$\nu(\text{C-OH})$ stretching
1020s	1025m	1025w	
950s	-	-	
935s	920w	930w	
775s	775m	980m	
764s	770m	770w	
743m	740w	700w	
594m	620m	630m	

Abbreviations: s = strong; m = medium; w = weak; sh = shoulder

at 1673 and 1625 cm^{-1} for the Pd(II) complex. This observation is in very good agreement with Pt(II) and Pd(II) complexes of thiamine reported earlier [2] and also consistent with the Pt(II) and Pd(II) complexes of pyridine previously reported [15]. It is interesting to observe that the corresponding bands in pyridine and its Pt(II) and Pd(II) complexes occur at lower frequencies than in the pyrimidine moiety in very good agreement with other independent studies [16,17].

In summary, the absence of complex ^1H and ^{13}C NMR spectra eliminates the possibility of having polymeric units [18]. Three proton resonances were observed for the free ligand as well as for the Pt(II) and Pd(II) complexes. Six carbon-13 resonances were observed for the free ligand as well as in the Pt(II) complex while five resonances were observed for the Pd(II) complex. These facts coupled with the elemental analyses strongly suggest that our complexes are simple and symmetric 2:1 (ligand : metal) complexes. The fact that 2'- CH_3 and C6'-H protons which are adjacent to the assumed coordination site (N-1') shifted downfield by about $\delta 0.80$ and $\delta 0.37$ ppm, respectively confirmed coordination through N-1' position of the ligand. The most downfield shifted carbon resonances are C2' ($\delta 3.41$ ppm), 2'- CH_3 (2.26 ppm) and C6' ($\delta 0.98$ ppm) carbons which are adjacent to the assumed coordination site also lends support to our assumption that Pt(II) and Pd(II) are coordinated through N-1' position of the ligand. Finally, the IR spectra indicate the involvement of the ring nitrogen and more specifically N-1' position through a shift to higher frequencies of the bands around 1600 cm^{-1} as HDMPY

goes to Pt(II) and Pd(II) complexes. All these findings are in good agreement with earlier reports [1-18]. The Kurnakov [19] test was performed on these new complexes and this was found to be positive, establishing the fact that cis isomers are preferred to trans isomers. This finding is in very good agreement with earlier report [18].

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