Studies Involving Labile Vitamin B_1 Metal Complexes.
Part 2. Infrared, Nuclear Magnetic Resonance Studies, Structure and Binding Site Determination

ADEGBOYE ADEYEMO*, ABDULLAH SHAMIM, ANNE TURNER and KOLA AKINADE

Department of Chemistry, Howard University, Washington, D.C. 20059, U.S.A.

Received September 20, 1982

Potassium tetrachloroplatinate(II) reacts with labile Vitamin B_1, $Hg(Th)Cl_4 \cdot H_2O$ (1:1 mol ratio) in warm aqueous medium to form the very stable trinuclear complex, $HgPt_2(Th)Cl_6$. Two structures are proposed – one in which mercury is presumably two-coordinated and platinum is penta-coordinated, and another in which mercury is tetracoordinated and platinum is penta-coordinated through chlorine bridges. On the contrary, the same metal salt reacts with $Zn(Th)Cl_4 \cdot H_2O$ and $Cd(Th)Cl_3 \cdot H_2O$ to form dinuclear complexes, $ZnPt(Th)Cl_3$ and $CdPt(Th)Cl_3$ in which zinc or cadmium is two-coordinated and platinum is tetracoordinated. These novel tri- and dinuclear complexes were characterized by ^1H, ^{13}C NMR, IR and elemental analysis.

Introduction

Recently, we reported [1] the preparation and nuclear magnetic resonance studies of the new heterodinuclear complex, $HgPd(Th)Cl_3$, in which we observed an unusual oxidation state of metal/metals which it was hoped would provide a mechanism whereby mercury poisoning could be prevented in biological systems. Such a mechanism may be workable if the oxidation of thiamine by metal ions proceeds by inner-sphere mechanism [6, 7]. In view of the clear-cut evidence for metal–thiamine bonding in recent papers [1, 8, 9], we should, at least in the very near future, be able to propose some mechanisms whereby mercury [1], cadmium [2, 3] or manganese [4, 5] poisoning can be prevented in biological systems.

Experimental

Thiamine chloride hydrochloride, potassium tetrachloroplatinate(II) and deuterated dimethyl sulfoxide were obtained from Aldrich Chemical Company and were used without further purification.

Infrared spectra were recorded on a Beckman 621 Infrared Grating Spectrophotometer in KBR pellets. The proton and carbon-13 NMR spectra were recorded on a Nicolet 200 MHz High Resolution Spectrophotometer. All chemical shifts were measured and expressed in parts per million relative to DMSO-d_6.

The tri- and dinuclear complexes were prepared as described earlier [1] with slight modification. The trinuclear complex, $HgPt_2(Th)Cl_6$, was prepared by adding a warmed and filtered solution of 2.0 g of K_2PtCl_4 in 60 ml of distilled water to a warmed and filtered solution of 3.0 g of $Hg(Th)Cl_4 \cdot H_2O$ in 60 ml of water. The resulting mixture turned yellow immediately and precipitation followed at once. The precipitate was allowed to remain under the mother liquor for 1 hour before being filtered, washed with water, acetone and diethyl ether. The orange colored solid complex isolated was air-dried for 24 hours and finally oven-dried at 120 °C for 12 hours. The yield was 1.0 g. The dinuclear complexes, $CdPt(Th)Cl_3$ and $ZnPt(Th)Cl_3$ were similarly prepared with yields of 0.72 and 0.62 g, respectively. Elemental analyses were performed by Galbraith Laboratories Inc. of Knoxville, Tennessee and Atlantic Microlab. of Atlanta, Georgia. *Anal.* Calcd. for $HgPt_2(Th)Cl_6$ (Mw = 1369): C, 21.59; H, 2.55; Cl, 15.94%. Found: C, 21.61; H, 2.66; Cl, 16.23%. Calcd. for $CdPt(Th)Cl_3 \cdot H_2O$ (Mw = 679.85): C, 21.18; H, 2.94; N, 8.24%. Found: C, 21.79; H, 3.00; N, 8.46%. Calcd. for $ZnPt(Th)Cl_3 \cdot 2H_2O$ (Mw = 667.84): C, 21.56; H, 3.14; N, 8.37%.

---

*Author to whom correspondence should be addressed.

0020-1693/83/0000-0000/$03.00

TABLE I. ^{13}C NMR Chemical Shifts of Free Ligand and Its Platinum Complexes in Parts per Million (ppm).

Compound	4-CH_3	$2'\text{-CH}_3$	$5\text{-}\alpha\text{-CH}_2$	Bridged CH_2	$5\text{-}\beta\text{-CH}_2$	C-5′	C-5	C-4	C-6′	C-2	C-4′	C-2′
Thiamine•HCl	11.63	21.13	29.33	49.88	59.65	105.28	135.31	142.13	146.65	155.23	161.23	163.00
$HgPt_2(Th)_2Cl_6$	11.50	27.17	29.31	50.08	59.59	106.56	135.97	142.03	154.55	157.85	160.67	167.32
$CdPt(Th)Cl_3$	11.55	27.17	29.36	50.08	59.64	106.56	135.88	142.03	154.97	158.07	160.81	167.27
$ZnPt(Th)Cl_3$	11.68	27.17	29.36	50.08	59.59	106.56	135.97	142.13	155.96	158.05	160.79	167.07

TABLE II. ^{1}H NMR Chemical Shifts of Free Ligand and Its Platinum Complexes in Parts per Million (ppm).

Proton	Vitamin B_1	$HgPt_2(Th)Cl_6$	$CdPt(Th)Cl_3$	$ZnPt(Th)Cl_3$
4-CH_3	2.600	2.407	2.415	2.413
$2'\text{-CH}_3$	2.570	2.888	2.884	2.888
5-CH_2	3.100	3.023	3.019	3.023
CH_2OH	3.670	3.631	3.625	3.629
$5'\text{-CH}_2$	5.700	5.432–5.475	5.465–5.512	5.451–5.496
C-6′-H	8.470	8.459–8.531	8.547	8.478–8.545
C-2-H	10.00	9.613–9.782	9.846	9.625–9.820

TABLE III. Selected IR Data of the New Complexes, $ZnPt(Th)Cl_3$, $CdPt(Th)Cl_3$ and $HgPt_2(Th)Cl_6$ in cm^{-1}.[a]

$ZnPt(Th)Cl_3$:	290m, 300m, 570s, 608s, 745sh, 766s, 990sh, 1045s, 1158sh, 1220m, 1350m, 1450s, 1540m, 1605s, 1640sh, 3000m, 3200–3000m
$CdPt(Th)Cl_3$:	295m, 320m, 575s, 610s, 768s, 867m, 930m, 994sh, 1040s, 1160sh, 1224s, 1294m, 1350m, 1430–1458br, 1537s, 1585–1610br, 3000m, 3140–3200m
$HgPt_2(Th)Cl_6$:	300br, 525sh, 570s, 608s, 766s, 866w, 927sh, 990sh, 1047br, 1160sh, 1222s, 1346m, 1450m, 1535m, 1600s, 1640sh, 1640sh, 3000m, 3150–3300m

[a] Abbreviations: m = medium, sh = shoulder, s = strong, w = weak, br = broad.

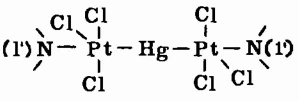
Results and Discussion

Table I shows the ^{13}C NMR chemical shifts of the ligand and its complexes. In agreement with the previous works [1, 8], the most downfield shifted carbons are those adjacent to N-1′ position of the pyrimidine moiety of the ligand. As shown in Table I, C-2′, $2'\text{-CH}_3$ and C-6′ carbons shifted by 4.6 and 9.0 ppm, respectively. The fact that all other carbons remain essentially unaffected indicates that Pt(II) is directly bound to the ligand via the N-1′ position. It is very interesting to observe a remarkable difference between the chemical shifts enjoyed by C-6′ in the platinum and palladium complexes. While C-6′ shifted downfield by about 12 ppm in the palladium complex [1], the same carbon shifted downfield by about 9.0 ppm in the platinum complex. This result indicates a much stronger interaction between Pd(II) and ligand.

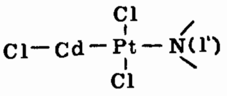
Proton NMR data provides additional support for metal–nitrogen interaction in these complexes. Table II lists the chemical shifts for the ligand and the complexes. The most downfield shifted resonances are 2′-CH_3 and C-6′-H with about 0.3 and 0.1 ppm, respectively. All other resonances either remain unaffected or are slightly shifted upfield. Thus the proton nuclear magnetic resonance also confirms that Pt(II) is preferentially bound to the ligand via the N-1′ position.

Table III shows selected IR data of the new complexes. Thiamine chloride hydrochloride shows strong bands at 3450, 3435, 3270 and 3075 cm^{-1} [8] due to OH, NH_2 and CH aromatic and aliphatic stretching motions. In the complexes, $ZnPt(Th)Cl_3$, $CdPt(Th)Cl_3$ and $HgPt_2(Th)Cl_6$, the strong bands between 3200 and 3300 cm^{-1} are ascribed to OH stretchings while bands between 3000 and 3150 cm^{-1} are ascribed to NH_2 stretchings. The band at about 1640 cm^{-1} is attributed to the metalated pyrimidine ring stretching motion of thiamine. Evidence for M–Cl stretchings is confirmed by the medium band between 290 and 320 cm^{-1} [8, 11] in these complexes. The strong band at 575–525 cm^{-1} is ascribed to a metal–nitrogen bond [10].

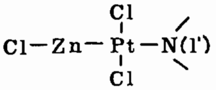
Thus the infrared spectroscopic data are supportive of the structures (I–IV) proposed for these new complexes. We hope that X-ray crystal studies or X-ray powdered diffraction will shed more light on the proposed structures.



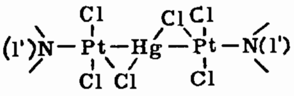
Structure I



Structure II



Structure III



Structure IV

Acknowledgements

The authors wish to express their gratitude to Dr. J. B. Morris for his moral and financial support. We would also like to thank Mr. Parker for his support and Mrs. Flowers for typing this manuscript.

References

1 A. Adeyemo, *Inorg. Chim. Acta, 66,* L3 (1982).
2 M. Yasuda, T. Fugita and S. Morimoto, *Yakugku Zasshi, 94,* 153 (1974).
3 T. Abe, Y. Itokawa and K. Inoue, *Nippon Eiseigaku Zasshi, 26,* 498 (1972).
4 V. A. Mikhailov, *Vopr. Gig. Fiziol. Tr. Profpatol. Prom. Toksikol. Sverdl. Nauchn.-Issled. Inst. Gig. Tr. Profpatol, Sb., 6,* 268 (1962).
5 A. P. Dorinovskaya, *Klin., Patog. Profil Profzabol. Khim. Etop.; Predpr. Tsvetn. Chern. Metall., 2,* 57 (1969).
6 K. Kobayashi, *Vitamins, 45,* 239 (1972).
7 J. Holzbecher and D. E. Ryan, *Anal. Chim. Acta, 64,* 333 (1973).
8 N. Hadjiliadis, J. Markopoulos, G. Pneumatikakis, D. Katakis and N. Theophanides, *Inorg. Chim. Acta, 25,* 21 (1977).
9 R. E. Cramer, R. B. Maynard and J. A. Ibers, *J. Am. Chem. Soc., 103,* 76 (1981).
10 K. P. Beaumont, C. A. McAuliffe and M. E. Friedman, *Inorg. Chim. Acta, 25,* 241 (1977).
11 R. G.Goel, W. O. Ogini and R. C. Strivastava, *Inorg. Chem., 20,* 3612 (1981).