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Synthesis and Characterization of Novel Vitamin B_1 Metal Complexes

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The reactions of thiamine hydrochloride with some transition metal salts have been studied. While the nitrates or chlorides of group 2B metals conveniently afford 1:1 (metal:ligand) complexes with this organic ligand, nitrates or chlorides of other metals form different type of complexes under the same experimental conditions. The formulation of the products isolated is $M(Th)X_4$ where M = Zn(II), Cd(II), Hg(II) and X = Cl. These complexes have been characterized by elemental analysis, infrared, proton and carbon-13 NMR techniques.

Introduction

The chemistry of interactions of thiamine hydrochloride and its derivatives with metal ions is very interesting since thiamine hydrochloride has a wide variety of coordination sites [1].

White and Drago [2] studied the interaction in solution between thiamine pyrophosphate and Ni(II)/Co(II) employing ^1H nmr and ^{31}P nmr techniques and then concluded that N-1′ position of the pyrimidine ring was indirectly bound to the metal *i.e.* through a water molecule. Marzotto *et al.* [3] stated that Cu(II) binds to pyrimidine moiety of thiamine in solution. Recently, Theophanides *et al.* [4] in their paper 'Interaction of Thiamine and its Phosphate Esters with Pt(II) and Pd(II),' claimed metal-to-nitrogen bond, the first of its kind. Earlier [5], we proposed the possibility of Zn(II), Cd(II) and Hg(II) binding at N-3′ and/or NH_2 position of the pyrimidine ring.

This work was motivated in order to synthesize these complexes and compare the results obtained by dissolving the solid crystals in DMSO-d_6 with the results obtained by mixing the ligand and metal ion in the solvent [5] since Zn(II), Cd(II) and Hg(II) are labile metal ions.

Experimental

Thiamine hydrochloride and dimethyl sulfoxide were purchased from Aldrich Chemical Company. Cadmium chloride and nitrate salts of zinc, cadmium and mercury were obtained from Fisher Scientific Company, while mercuric chloride and zinc chloride were products of Baker Chemical Company.

Preparations of the Complexes

These complexes were prepared by mixing aqueous solutions of thiamine hydrochloride and metal nitrate salts (2:1 mole ratio). The resulting solution was allowed to evaporate at room temperature to about a quarter of its original volume. The crystals obtained were thoroughly rinsed with ice cold distilled water, dried at room temperature and finally oven dried at 100 °C for about 60 minutes.
Anal. Calcd. for $C_{12}H_{18}N_4OSCl_4Zn$: C, 30.48; H, 3.81; N, 11.85; S, 6.79; Cl, 30.01; Zn, 13.84%. Found: C, 30.11; H, 4.11; N, 11.74; S, 6.62; Cl, 29.72; Zn, 13.77%.
Anal. Calcd. for $C_{12}H_{18}N_4OSCl_4Cd$: C, 27.72; H, 3.47; N, 10.78; S, 6.17; Cl, 27.30; Cd, 21.64. Found: C, 26.82; H, 3.91; N, 10.47; S, 6.05; Cl, 26.40; Cd, 20.86%.
Anal. Calcd. for $C_{12}H_{18}N_4OSCl_4Hg$: C, 23.70; H, 2.96; N, 9.22; S, 5.28; Cl, 23.24; Hg, 33.01. Found: C, 23.49; H, 2.96; N, 8.89; S, 5.11; Cl, 22.66; Hg, 33.07%.
Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

^1H NMR spectra were recorded, using EM-360 MHz Spectrometer. Tetramethylsilane (TMS) was used as an internal reference standard with DMSO-d_6 as solvent. Ir spectra were recorded on Beckman 700 model Spectrometer. ^{13}C NMR spectra were recorded on carbon-13 Fourier Transform-Twenty MHz NMR Spectrometer (CFT-20MH$_z$ NMR Spectrometer) fully computerized and equipped with the optional alpha numeric printer.

Results and Discussion

Although both the nitrate and the chloride salts of group 2B metals form 1:1 (ligand:metal) complexes with thiamine hydrochloride, crystallization process seems much easier with the nitrate than the

TABLE I. ^{1}H NMR Chemical Shifts of Thiamine•HCl and its Zn(II), Cd(II), and Hg(II) Complexes in ppm (δ).

Compound	C-2-H	C-4'-NH$_2$	C-6'-H	C-5'-CH$_2$	OCH$_2$	C-5-CH$_2$	C-4-CH$_3$	C-2'-CH$_3$
Thiamine•HCl	10.05	9.30	8.42	5.67	3.67	3.10	2.60	2.57
Zn(Th)Cl$_4$	8.90	9.03	8.42	5.67	3.68	3.08	2.59	2.58
Cd(Th)Cl$_4$	9.88	9.05	8.42	5.55	3.72	3.12	2.60	2.59
Hg(Th)Cl$_4$	9.91	9.05	8.46	5.57	3.73	3.13	2.62	2.60

TABLE II. ^{13}C^a NMR Chemical Shifts of Thiamine•HCl and its Zn(II), Cd(II), and Hg(II) Complexes in ppm (δ).

Compound	4-CH$_3$	2'-CH$_2$	5- -CH$_2$	Bridged CH$_2$	OCH$_2$
Thiamine•HCl	11.63	21.12	29.33	49.88	59.56
Hg(Th)Cl$_4$	11.73	21.42	29.41	49.85	59.59
Cd(Th)Cl$_4$	11.68	21.39	29.38	49.85	59.56
Zn(Th)Cl$_4$	11.66	21.42	29.31	49.84	59.54

	C-5'	C-5	C-4	C-6'	C-2	C-4'	C-2'
Thiamine•HCl	105.28	135.31	142.13	146.65	155.23	161.83	163.13
Hg(Th)Cl$_4$	105.14	135.46	142.12	146.67	155.11	161.99	163.18
Cd(Th)Cl$_4$	105.11	135.49	142.12	146.73	155.16	162.01	163.23
Zn(Th)Cl$_4$	104.92	135.32	141.98	146.59	155.01	162.01	163.19

$^{a\,13}$C NMR data were obtained from two different instruments.

chloride salts of these metals. This result may be ascribed to the lability of nitrate ion. The results obtained by mixing the ligand and metal salts in the solvent [5] were identical to the results obtained by the preparation of solid complexes. These results are expected since Zn(II), Cd(II) and Hg(II) are labile metal ions. Other solid complexes isolated include, Fe(II)-thiamine (%Fe = 0.046), Fe(III)-thiamine (%Fe = 0.019), Ni(II)-thiamine (%Ni = 1.0), Cr(II)-thiamine (%Cr = 0.18) complexes. These results may imply that these metal ions are not complexing with thiamine, in which case the very low percentage of these metal ions may be regarded as contamination. Detailed studies will be reported in the near future.

Infrared spectrum of the metal free ligand is identical to those of its Zn(II), Cd(II) and Hg(II) complexes. This result is consistent with earlier work [5]. ^{1}H NMR and ^{13}C NMR chemical shifts are listed in Tables I and II, respectively. The spectra are not presented since they are identical to the previous ones [5]. The chemical shifts observed in both the proton and carbon-13 NMR are much smaller than those obtained by Theophanides *et al.* [4]. This observation may be due to weak interaction, which may argue for outer sphere complexes.

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