Interaction of Pt(II) and Pd(II) with Oxythiamine: Correlation between Ligand Basicity and Chemical Shifts

ADEGBOYE ADEYEMO*, ABDULLAH SHAMIM and ANNE TURNER

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

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Introduction

Although the binding of Ni(II) and Mn(II) to thiamine phosphate and thiamine pyrophosphate has been compared with the binding of the same metal ions to oxythiamine phosphate and oxythiamine pyrophosphate, analogues of thiamine in which the C-4′ amino group has been replaced by an -OH group, the studies were purely solution studies which may be somewhat complex. We are of the opinion that by isolating the solid complexes first and then carrying out the studies we may have a better understanding of these systems. Gallo and Sable [1, 2] have concluded that the strength of the metal ion–pyrimidine interaction depends strongly both on the coordination affinity of the metal ion and on the ligand basicity. We wish to obtain ^{13}C NMR data on metal–oxythiamine complexes, compare this set of data with those obtained on metal–thiamine complexes [3] and hence draw a correlation between chemical shifts and ligand basicity.

It should be borne in mind that in thiamine the N-1′ position of pyrimidine ring is more basic (pK = 5.0) than in oxythiamine (pK = 2.3). In principle this difference in ligand basicity should be reflected in the chemical shifts. While efforts are well under way to obtain crystals of metal–thiamine phosphate/pyrophosphate and metal–oxythiamine phosphate/pyrophosphate complexes for X-ray studies, we report for the first time ^{13}C NMR studies on solid platinum–oxythiamine complexes.

Experimental

Oxythiamine, potassium tetrachloroplatinate(II), potassium tetrachloropalladate(II), tetramethylsilane and deuterated dimethyl sulfoxide were used as obtained from Aldrich Chemical Company. The platinum and palladium oxythiamine complexes were prepared by mixing aqueous solutions of metal and ligand in 1:2 and 2:1 mol ratio. The pH of oxythiamine solutions were adjusted to 2.2, 5.2 and 8.7, respectively. The solid complexes isolated were found to be 1:1 stoichiometric complexes.

Carbon-13 NMR spectra were recorded on a Nicolet 200 MHz High Resolution Spectrometer, employing deuterated imethyl sulfoxide as solvent. The

*Author to whom correspondence should be addressed.

TABLE I. Carbon-13 NMR Chemical Shifts of Oxythiamine and Its Platinum(II) Complexes.

Carbon	Oxythiamine	Pt–Oxythiamine (pH = 2.2)	Pt–Oxythiamine (pH = 5.2)	Pt–Oxythiamine (pH = 8.7)
C-4′	161.49	160.58	160.96	160.47
C-2′	159.75	160.38	160.32	160.30
C-2	157.08	156.50	156.54	156.69
C-6′	146.98	153.60	153.58	153.61
C-4	140.82	140.77	140.72	140.82
C-5	133.98	134.03	134.03	134.12
C-5′	116.27	115.20	115.15	115.49
O-CH_2	58.62	58.67	58.62	58.76
5′-CH_2	48.53	49.21	49.16	49.25
5-CH_2	28.48	28.46	28.44	28.53
2′-CH_3	18.39	20.33	20.28	20.43
4-CH_3	10.58	10.63	10.58	10.68

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^{13}C chemical shifts were expressed in parts per million (ppm) downfield from TMS.

Results and Discussion

Table I shows the ^{13}C NMR chemical shifts of oxythiamine and its platinum(II) complexes. The signal C-6′ of oxythiamine occurs at 146.98 ppm whereas in the platinum–oxythiamine complexes it occurs at 153.60 ppm, a downfield shift of about 6.6 ppm. This chemical shift is about half that reported for C-6′ signal in platinum–thiamine complexes [3]. The C-2′ resonance occurs at 159.75 ppm in oxythiamine whereas it occurs on average at 160.12 ppm in the platinum–oxythiamine complexes, a modest downfield shift of about 0.87 ppm. Another conspicuously downfield shifted resonance is 2′-CH_3, which on the average shifted by about 1.96 ppm. While it is clear that the coordination site is N-1′ position of the pyrimidine ring, the observed chemical shifts are smaller than in the corresponding shifts in thiamine analogues. It should be borne in mind that N-1′ position of the pyrimidine moiety of thiamine is about 500 times more basic than N-1′ position of oxythiamine. The smaller chemical shifts observed for C-6′ C-2′ and 2′-CH_3 resonances in platinum–oxythiamine complexes compared to the same resonances in platinum–thiamine complexes [3] may be establishing a correlation between chemical shifts and ligand basicity. The 5′-CH_2 resonance also shifted downfield by about 0.68 ppm. Other resonances either shifted upfield slightly or remained essentially constant.

In order to create a competition between N-1′ position and the phenolic group of this ligand for metal ion, some complexes were isolated at pH 8.7 which is about the pK of the phenolic group [4]. In all the different metal:ligand ratios tried only 1:1 stoichiometric complexes were isolated and the preferential binding site was N-1′ position of the ligand.

Another remarkable observation in this study is that platinum–oxythiamine complexes were easily isolated in the pH range studied whereas palladium–oxythiamine complexes were isolated only with sodium iodide solution. Although palladium–oxythiamine complexes may exist in solution in chloride form, large ions are required to obtain these complexes in solid form, which is not the case with platinum–oxythiamine complexes.

It is hoped that the X-ray crystal studies will show some differences in the platinum/palladium–oxythiamine complexes and platinum/palladium–thiamine complexes in terms of nitrogen–metal bond length and the like. Meanwhile work is in progress to obtain crystals of various complexes especially the metal–thiamine phosphate/pyrophosphate and oxythiamine analogues so as to establish whether N-1′, the terminal phosphate group or both are simultaneously used in binding divalent metal ions.

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