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Complexes of Tetrahydrothiamine with Pt(II)

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Recently, we reported the reactions of Pt(II) and Pd(II) with thiamine and its phosphate esters [1, 2]. These were the first examples of thiamine metal complexes presenting direct metal–ligand bonds. In continuation of our studies on interactions of these metals with thiamine derivatives, we now present a preliminary account of the interactions of Pt(II) with tetrahydrothiamine (THTH). THTH possesses one pyrimidine and one thiazolidine molecule. Since in the case of thiamine the metal prefers to coordinate to the pyrimidine moiety (N_1' of pyrimidine) rather than to thiazole, it was interesting to compare the donor properties of thiazolidine, in the case of the reduced form of thiamine, to those of pyrimidine towards Pt(II).

THTH is prepared by the action of $NaBH_4$ [3, 4] on thiamine. This ligand reacts with K_2PtX_4 (X = Cl, Br) at pH ~ 5.5 producing yellow precipitates as follows:

$$K_2PtX_4 + 2THTH \xrightarrow{pH \sim 5.5} Pt(THTH)_2X_2 + 2KX \qquad (1)$$

When the reaction is carried out at pH ~1 (0.1 N HX) two HX molecules could be retained by the complex.

$$K_2PtX_4 + 2THTH \xrightarrow[0.1\ N\ HX]{pH \sim 1} Pt(THTH)_2X_2 \cdot 2HX + 2KX \qquad (2)$$

The same complex could also be obtained when the $Pt(THTH)_2X_2$ was treated with HX, reversibly:

$$Pt(THTH)_2X_2 + 2HX \underset{H_2O}{\overset{0.1\ N\ HX}{\rightleftharpoons}} Pt(THTH)_2X_2 \cdot 2HX \qquad (3)$$

The ligand could also retain one HX molecule in acidic solutions reversibly:

$$THTH \underset{H_2O}{\overset{0.1\ N\ HX}{\rightleftharpoons}} (THTH) \cdot HX$$

The analytical results agree with the assigned formulae. Some physical measurements of the ligands and the complexes are given in the Table.

THTH has two pK values, as is found by pH metric titrations, $pK_1 \sim 3.1$ and $pK_2 \sim 7.1$, in the acidic and neutral region.

In the complex $Pt(THTH)_2Cl_2$ the first value is almost constant, while the second is decreased to about ~5.6 (see Table I).

The first is assigned to the protonation of the N_1' of the pyrimidine moiety. In thiamine the N_1' has a pK of about 5 [1]. The second is most probably due to ionization of a ring proton of thiazolidine or to

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TABLE I. Physical Data of the Complexes.

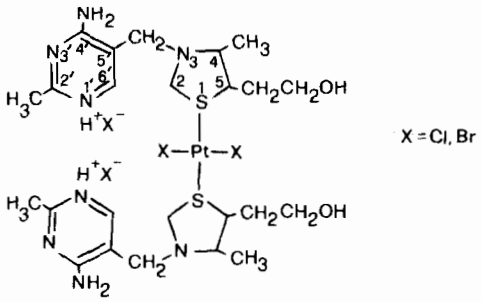
Compounds	^1H nmr(ppm) C_6'-H Solvent	pK	Molar Conductance		IR bands				
			Value	Solvent	νOH νOD	νNH_2 νND_2	δNH_2 δND_2	ring stretch	νPt–Cl
THTH[a]	7.78 DMSO-d_6	3.1	–	–	3400	3150	1645	1618	
THTH[a]	8.25 DMSO + 2dCF_3COOH	7.1	–	–	2545	2310	1225	1554	
THTH·HCl	8.40 DMSO-d_6		54.8	DMF	3400	3400	1650	1603	
THTH·HCl	8.55 DMSO + 2dCF_3COOH		149.4	H_2O	2500	2500	1260	1540	
THTH·HCl	8.43 DMSO + 2dD_2O				2250	2250		1650	
THTH·HCl	8.40 0.1 NDCl				3400	3400	1648	1603	
$Pt(THTH)_2Cl_2$	7.88 DMSOd_6		6.5	DMF	2540	2340	1218	1545	335
$Pt(THTH)_2Cl_22HCl$	8.41 0.1 NDCl	3.0	78	DMF	3400	3400	1655	1605	330
$Pt(THTH)_2Cl_22HCl$	8.50 DMSO-d_6	5.6	194.2	H_2O				1578	
$Pt(THTH)_2Cl_22HCl$	8.53 DMSO + 2dCF_3COOH								

[a]THTH = Tetrahydrothiamine.

the side No. 5 primary alcoholic group. It seems therefore that the N'_1 position is the protonation site, since it can retain reversibly one HX molecule in the ligand or the complexes, depending on pH.

This is further confirmed by the chemical shift of the proton at C'_6 which is shown at 7.78 ppm in DMSO-d_6 solutions in the free ligand, THTH. It was shifted to 8.25 when two drops of CF_3COOH were added to the solution [5]. In the protonated THTH·HCl it is found at 8.40 ppm in DMSO-d_6 or 0.1 N DCl solutions. The addition of two drops of CF_3COOH causes a further shift to 8.55 ppm possibly due to the protonation of N'_3 also in solution. The same behavior is also shown by the complexes $Pt(THTH)_2Cl_2$ and $Pt(THTH)_2Cl_2 \cdot 2HCl$. In the first, the C'_6-H is almost unshifted in DMSO-d_6 solutions as compared to the free ligand (7.88 ppm), while in the second it is shown at ~8.50 ppm (see Table). The molar conductances in DMF or H_2O solutions also agree with the retention of HX molecules by the ligand and the complexes. THTH·HCl is a 1:1 electrolyte while $Pt(THTH)_2Cl_2 \cdot 2HCl$ is 1:2. Certain ir bands, given also in the Table, indicate that the NH_2 and OH groups are free in the complexes. The single νPt–Cl bands shown at ~330 cm^{-1} in the complexes, absent from the spectra of the bromo analogs, indicate a *trans* configuration.

Therefore, the metallation site in the case of THTH seems to be the sulfur atom of the thiazolidine molecule, while the N'_1 site is the protonation site, in a *trans* configuration as follows:



The sulfur atom of d(+)-biotin has also been found to interact with Pt(II) and Pd(II) in their complexes [6]. The complexes are unstable in alkaline solutions. Sulfur involvement in bonding with Pt(II) lowers the second pK value of the ligand by ~1.5 units, thus causing decomposition at high pH values. These reactions are under study and will be forthcoming.

References

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