JOURNAL OF ENGINEERING annals OF FACULTY OF ENGINEERING HUNEDOARA

POSSIBLE USE OF METAL COMPLEXES OF POLYAMINOPOLYPHOSPHONIC ACIDS

Imre LABADI[1], Károly MOGYORÓSI[1], Ecaterina PRINCZ[2]

[1] University of Szeged, Department of Inorganic & Analytical Chemistry, Szeged, HUNGARY
[2] Institute for Chemistry of Timisoara of Romanian Academy, Timisoara, ROMANIA

Abstract

The development of nuclear resonance (NMR) imaging techniques as a clinical diagnostic modality has prompted the need of compounds, which enhance the image contrast between normal and diseased tissue and/or indicate the status of organ or blood flow. Complexes of paramagnetic transition metal and lanthanide ions with polyamino-polycarboxylic acids have been studied earlier in this respect in detail.

Owning to the structural similarities between the polyamino-polycarboxylic acids and polyamino-polyphosphonic acids, the lanthanide and transition metal complexes of the later ones were prepared and studied. The ethylenediamino-tetramethylene-phosphonic acid (EDTMP) and 1,3-propanediamine-tetramethylene-phosphonic acid(PDTMP) were chosen as ligand, and lanthanide ions (Eu(III), La(III), Gd(III), Sm(III)) or transition metal ions (Fe(III), Zn(II), Cu(II), Ni(II), Mn(II), VO(II)) used for preparation of metal complexes. The preparation of complexes were performed at different pH (pH= 1, 3 and 5). The composition of the complexes was determined by metal ion analysis and the complexes were studied by thermal analysis and IR spectroscopy.

The thermal behaviour of the transition metal complexes of EDTMP and PDTMP permit a suggestion for their use as a precursor compound to prepare different phosphate compounds, having interesting magnetic properties.

Keywords:

polyamino-polyphosphonates, lanthanide complexes, transition metal complexes, MRI agents, precursors for metal phosphates

1. INTRODUCTION

Throughout history, metals and metal compounds have been used in medicine to treat a variety of ailments. An even more recent development is the use of paramagnetic metal complexes for enhancing contrast of magnetic resonance imaging (MRI) in the non-invasive diagnostics of diseases and tumours. Paramagnetic metal ions function as contrast agents by increasing the relaxation rates of the observed water protons near the ion, through interactions between the electron spins of the paramagnetic centre and the nuclei of the water hydrogens [1–2].

Numerous complexes with polyaminopolycarboxylic acids have been studied as potential contrast agents [3–10]. The structural similarities between the polyamino-polycarboxilic and polyaminopolyphosphonic acids determined the study of these ligands as chelating agents. Replacement of the carboxylic groups by organophosphonic acid groups determines the specific nature of the polyamino-polyphosphonic acids due to the presence of tetrahedral phosphonic group as compared to planar carboxylic group and greater polarisability of the PO bond [11, 12].

Our studies had been focused to the synthesis and characterization of some lanthanide and transition metal complexes with two of the polyamino-polyphosphonic acids (EDTMP, PDTMP), because exchange reactions between the lanthanide complexes used as contrast agents in MRI and end transmetalation by transition metalions may place in the human body. By this way a dangerous free lanthanide ions could be appeared [13-14] and owning to this phenomenon the use of lanthanide complexes of the EDTMP and PDTMP, as an MRI agents reagents, will forms a new problem.

An another practical importance of the polyamino-polyphosphonic acids and their metal complexes is the use of them as a precursor of different metalpolyphosphates. For instance in the last 10-20 years an increased interest could be observed against the new iron phosphates, pyrophosphates, alkali-iron phosphates- pyrophosphates as compounds having special magnetic properties. The metal complexes of polyamino-polyphosphonic acids were proofed as a candidate as precursors for preparation of the above mentioned metal phosphates, pyrophosphates[15].

In the present work the complexes of different lanthanide-, transition metal complexes of EDTMP and PDTMP were isolated from solution having different pH and their IR spectra and thermal stabilities were studied in order to determine their compositions, their stability and the binding mode of the water molecules in the complexes.

2. EXPERIMENTAL

Preparation of the ligands

The investigated polyamino-polyphosphonic acids (EDTMP and PDTMP) were synthesized by us via a Mannich reaction of 1,2-ethylenediamine or 1,3-propanediamine with phosphorous acid and formaldehyde, as described earlier [16, 17].

pK values of the ligands(EDTMP, PDTMP)

The protonation constants and the complex stability constants were determined by potentiometric titration [20]. The pK values of the ligands determine the possible composition of the metal complexes prepared at different pH and different ligand metal ratio. At low pH (1-3), 2-5 proton could be replaced by sodium and other metal-ion. At higher pH all proton could be replaced by sodium ion and different metal-ion.

Table 1. pK values of the EDTMP and PDTMP (H_8L) determined by us. The pK values of the EDTMP[] and PDTMP [18]

Ligand	pK_1	pK_2	pK_3	pK_4	pK_5	pK_6	pK_7	pK_8
EDTMP	<1	1.5	3.02	5.2	6.4	7.85	10.00	11.00
PDTMP	<2	<2	4.05	5.10	5.89	6.85	10.00	11.40

Preparation of the metal complexes

The preparation of the complexes was performed as followings:

The ligands (EDTMP and PDTMP) was mixed with the appropriate metal nitrate or acetate in ratio 1:1, 1:2 and the pH of the solution was adjusted by adding sodium hydroxide solution. The formed precipitate was filtered, washed, dried and stored in exsiccatore. The metal-ion and sodium contents of the complexes were determined.

Table 2. The general composition of the investigated metal complexes of EDTMP and PDTMP[18,19]

Ligand (L)	Composition	Metal ions (M)
EDTMP	$M_4(H_4L)_3\ xH_2O$	La(III), Sm(III)
EDTMP	$MH_5L\ xH_2O$	La(III), Sm(III)
EDTMP	$MNa_5L\ xH_2O$	La(III), Sm(III)
PDTMP	$MNa_5L\ xH_2O$	Eu(III), La(III), Gd(III), Sm(III)
EDTMP PDTMP	MH5L xH2O, $MNa_2H_3L\ xH_2O$ $MNa_5L\ xH_2O$	Fe(III)
EDTMP, PDTMP	$MH_6L\ xH_2O$ $M_2H_4L\ xH_2O$	Co(II), Ni(II), Zn(II), Cu(II), VO(II)

The composition of the complexes

The composition of the investigated complexes is shown in Table 2. Comparing the pK values of the ligands and the pH values of the preparation of the complexes, the gained composition of the complexes could be interpret easily.

The IR spectra of the ligands and of the metal complexes

The characteristic bands of the ligands are presented in Table 3-4.

Table 3. Characteristic bands of EDTMP and their assignation [18]

Band maximum(cm^{-1})	Assignation
3402s, 3246s	ν(OH, water)
3026s,3014s	$\nu(\equiv NH^+)$
2954s, 2924vs, 2854s	ν_{as} and ν_{sym} of CH_2
2767m, 2611m, 2308m	ν (OH, POH)
1653m, broad	δHOH
1461m, 1438m, 1413w, 1379, 1321w	δCH_2 or/and ν(C–N)
1261s,1207s, 1121vs,1008vs, 953vs	ν (P=O, P–O(H))
838w, 792w, 776w,748w	ν(C–P)
573m, 532m, 487m	ν (OH, POH)

Table 4. Characteristic bands of PDTMP and their assignation [19]

Band maximum(cm^{-1})	Assignation
3372s	ν(OH, water)
3024s,3005s	$\nu(\equiv NH^+)$
2950s, 2921vs, 2849s	ν_{as} and ν_{sym} of CH_2
2773m, 2612m, 2288m	ν (OH, POH)
1657m, broad	δHOH
1485m, 1437m, 1411w, 1344	δCH_2 or/and ν(C–N)
1248s,1167s, 1050s, 980s, 944s	ν (P=O, P–O(H))
838w, 792w, 776w,748w	ν(C–P)
602m, 585m, 548m, 512m, 482m	ν (OH, POH)

The IR spectra, characteristic bands of metal complexes changed, related to the IR spectra of the ligands, showing the formation of complex between the metal ion and ligands [18, 19].

3. THE THERMAL BEHAVIOUR OF THE EDTMP, PDTMP AND THEIR METAL COMPLEXES

Both the EDTMP and PDTMP ligands have 2 water molecules, as a crystal water, which release the solid material on heating in two steps (below 150 °C and between 150 and 200 °C, 1.5 and 0.5 mole water, respectively)[16,17].

The thermoanalytical studies of the metal complexes of EDTMP, PDTMP show that the complexes of EDTMP, PDTMP contain two types of water molecules. This fact is very important from point of view of possible medicinal use of these complexes.

From the thermal decomposition of the metal complexes of EDTMP, PDTMP several conclusions could be drawn:

1. One of the final decomposition products is the metal-pyrophosphate, sodium-pyrophosphate.
2. The free OH groups of the EDTMP, PDTMP losses water molecules on heating, so they form polyphosphates with different composition and probably with different structure.

REFERENCES

[1] D. E. Reichert, J. S. Lewis and C. J. Anderson, Coord. Chem. Rev., 184 (1999) 3
[2] L. Thunus, and R. Lejeune, Coord. Chem Rev. 184 (1999) 125
[3] R.B. Lauffer : Chem. Rev., 87 (1987) 901.
[4] L.Thunus, R.Lejeune: Coord.Chem.Rev., 184(1999) 125.
[5] S. Aime, M. Botta, M. Fasano, E. Terreno, Chem. Soc. Rev., 27 (1998) 19.
[6] R. Ruloff, R. N. Muller, D. Pubanz, A. E. Merbach, Inorg. Chim. Acta, 275-276 (1998) 15.
[7] S. Jurisson, D. Berning, Wei Jia and Dangshe Ma: Chem. Rev., 93 (1993) 1137.
[8] A. N. Pudovik: Chemistry of Organophosphorus Compounds, MIR Publishers, Moscow, 1983, 150
[9] K. Sawada, T. Miyagawa, T. Sahaguchi, K. Doi, J. Chem. Soc. Dalton Trans., 1993, 3777.
[10] L. V. Ruzajkina, B. A. Rjabuhin, A. N. Jermakov, I. N. Marov, L. S. Davidova, E. B. Krutko, Zh. Neorg. Khim **25** (1980) 3254
[11] I.V. Tananaiev, E.N. Bereznev, G. S. Terjosin, O. B. Kuznecova, L.V.Goeva, Zh. Neorg.Khim.,26(1981) 278-280
[12] T.S. Terjosin, L.K Gharitonova, N. N. Novikova, M. V. Rudomino, Zh. Neorg. Khim 22(1977) 2115
[13] M. I. Kabachnik, N. M. Djatlova, T, Ya. Medvegy, Yu. F. Belugin, V. V. Sidoren-ko, Dokl. AN **175** (1967) 351
[14] B. V. Zhadanov and N. M. Djatlova, Zh. Fiz. Khim 48 (1969) 744
[15] Z. Rzacynska and A. Bartyzel, J. Therm. Anal. Cal. 68 (2002) 937
[16] N. Palta, B. V. Rao, S. N. Dubey and D. M. Puri; Polyhedron 3 (1984) 527.
[17] E.N. Rizkalla, Rev. Inorg. Chem. 5 1983(223l
[18] E. Princz, I. Szilágyi, K. Mogyorosi and I Lbadi, J. Therm. Anal. and Calorimetry 69(2002), 427-439
[19] E. Printz, K. Mogyorosi and I. Labadi, J. Thermal Anal. and Calorimetry 77 (2004) 767-776
[20] I. Labadi to be published