

Synthesis, Characterization and Thermodynamic Study of a Novel N-Functionalized Macrocycle and Its Metal Complexes

JIAN-HONG BI*†, LI-QIN CHEN‡, ZHI-QIANG XU‡, FU-XIN XIE

XIANG-DA ZHAO, SHI-SHENG NI, JI-DE XU**

Department of Chemistry, Anhui University, Hefei-230 039, PR China

A new N-carboxymethyl derivative of the tetraazamacrocyclic ligand LH₄ (5,7,12,14-tetramethyl-1,4,8,11-tetraazamacrocyclotetradecane-N,N',N''N'''-tetraacetic acid) and its complexes with Cu²⁺, Co²⁺, Ni²⁺, UO²⁺ and Th⁴⁺ have been synthesized and characterized by elemental analyses, UV, IR, ¹H NMR spectra and X-ray powder diffraction. The stability constants of mononuclear complexes of LH₄ with the ions above were determined at 35 ± 0.1, 45 ± 0.1 and 55 ± 0.1°C in 0.5 mol L⁻¹ KNO₃ solution by means of potentiometric and computer fitting. The ΔH and ΔS of the coordination reactions in the solution were given.

Key Words: N-Functionalized macrocycle, Metal complexes.

INTRODUCTION

Synthetic aza-macrocyclic compounds and their metal complexes have been one of the most studied groups of compounds in recent years¹⁻³. There are several reasons for this interest in macrocyclic complexes, *e.g.*, the synthetic challenge, the exceptional kinetic and thermodynamic properties that enable practical applications of these compounds, and the possibility of using them as models for systems of biological interest⁴⁻⁶.

In this paper, we describe the synthesis of a novel N-carboxymethyl pendant arms macrocyclic ligand: 5,7,12,14-tetramethyl-1,4,8,11-tetraazamacrocyclotetradecane-N,N',N''N'''-tetraacetic acid (LH₄, Fig. 1) as well as the preparation of its metal complexes with Cu²⁺, Co²⁺, Ni²⁺, UO²⁺ and Th⁴⁺. We have successfully developed a potentiometric technique and use it to determine the stability constants of the complexes in aqueous. The ΔH and ΔS of LH₄ complexation with ions have been calculated by a linear computer fitting program these metal.

†Present address: Department of Chemistry, Anhui Institute of Education, Hefei-230061, PR China.

‡Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland A1B 3X7, Canada.

**Department of Chemistry, University of California, Berkeley, 94720-1460, USA.

EXPERIMENTAL

All chemicals used were of analytical grade. The solvents were purified by conventional methods. The parent macrocycle *c*-meso-meso-Me₄[14]aneN₄ was prepared by the methods of Hay⁷ and characterized by elementary analysis and infrared spectroscopy.

Infrared spectra and UV-Vis spectra were obtained with a Nicolet 170 SX and a Shimadzu UV-240 spectrometer, respectively. ¹H NMR spectra were recorded on a JEOL FX-90Q spectrometer. X-ray powder diffraction measurement was made with a XD-3A X-ray diffractometer. Microanalyses were determined by the Centre of Structure and Elemental Analysis, China University of Science and Technology.

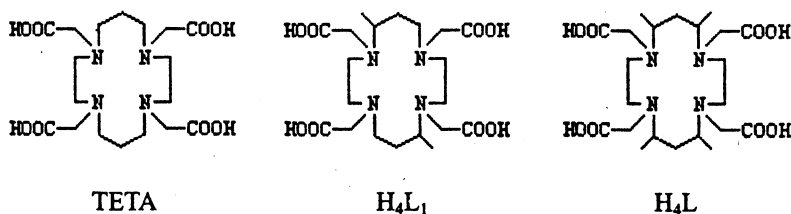


Fig. 1 Structural formulae of TETA, H₄L₁ and H₄L

Syntheses of macrocyclic ligand H₄L

H₄L·5H₂O (A): To 8.4 g (0.06 mol) of bromoacetic acid in 30 mL dry methanol, 0.06 mol of KOH in 60 mL dry methanol was added. Then 3.8 g (0.01 mol) of *c*-meso-meso-Me₄[14]ane-N₄ in 40 mL dry methanol and 9 g (0.065 mol) of powdered anhydrous potassium carbonate were added. The mixture was refluxed with stirring for 20 h, cooled and the white precipitate of KHCO₃ was filtered off. After nearly complete evaporation of the solvent, the residue dissolved in 30 mL of water and the solution was acidified to pH 2 with concentrated hydrochloric acid. The product H₄L·5H₂O (A) sedimented as white or light cream needles upon standing at 0°C overnight. The crystals (4.1 g) were recrystallized from water.

H₄L·4HCl·4H₂O (B): After 3.5 g (6 mmol) of compound A dissolved in 7 mL diluted KOH solution, 4 mL concentrated hydrochloric acid was added. While the solution cooled slowly, the macrocyclic ligand was precipitated as powder, then the colourless crystals (3.1 g) were obtained by recrystallization with water. ¹H NMR(D₂O): δ 0.9–1.2 (12H, CH₃); 1.8–2.2 (4H, —CH₂—); 3.35br (12H, N—CH₂—, N—CH—); 3.98br (8H, N—CH₂COOH). X-ray powder diffraction: 2θ° 9.30, 10.86, 15.76, 21.26, 25.42, 27.72, 31.60; d, Å 9.50, 8.14, 5.62, 4.18, 3.50, 3.22, 2.83; I/I₀ 22.1, 45.4, 31.2, 53.5, 22.2, 100.0, 61.3. The product was titrated by KOH and AgNO₃.

Syntheses of the complexes

Complexes of transition metals: 0.25–1.2 mmol of the required transition metal salt, dissolved in 10–15 mL water, was added to a solution of compound B (0.3–0.5 mmol in 10–20 mL water). The pH was adjusted to 4 with KOH, then the mixture was stirred and refluxed for 2 h. The corresponding metal complex crystals were obtained upon standing. These were collected and air dried.

Uranyl and thorium complexes: By a similar procedure to that described above, 1.2 mmol of the appropriate metal salt was dissolved in 15 mL dry methanol; 0.5 mmol of compound B in 15 mL dry methanol was added.

Potentiometric Equilibrium Measurements and Computational

Measurements: The experimental set-up used was described before⁸. Typical concentrations of experimental solutions were $5 \times 10^{-3} - 5 \times 10^{-4} \text{ mol L}^{-1}$ of ligand with equal molar concentrations of metal ions and then titrated with 0.4 mol L^{-1} KOH solution at $35 \pm 0.1^\circ\text{C}$, $45 \pm 0.1^\circ\text{C}$ and $55 \pm 0.1^\circ\text{C}$ in 0.5 mol L^{-1} KNO_3 solution. All solutions were prepared using double-distilled deionized water.

Calculation of equilibrium constants: Computations of equilibrium constants were made using a program based on the improved TITFIT techniques^{8,9}.

RESULTS AND DISCUSSION

Elemental analysis and UV spectra

Composition of the ligand and the complexes: Elementary analysis results and UV spectra data of mononuclear transition metal complexes are given in Table-1 and 2. The synthesis of the new complexone-like macrocycle H_4L by alkylation of the cyclic tetramine with bromoacetic acid is straight forward. The complexes of H_4L , which has eight potential coordinating atoms, were studied in part in solution but mainly by preparing several crystalline compounds. According to the elemental analysis, H_4L forms 1 : 1 complexes with Cu^{2+} and Ni^{2+} , 2 : 1 complexes with UO_2^{2+} and Th^{4+} , 1 : 1 or 2 : 1 complexes with Cu^{2+} ion.

TABLE-1
YIELD, COLOURS AND ELEMENTAL ANALYSIS

Complex (Colour)	% Analysis found (calcd.)				
	C	H	N	M	Yield (%)
$\text{H}_4\text{L} \cdot 5\text{H}_2\text{O}$ (white)	45.78 (45.66)	8.91 (9.05)	9.62 (9.68)	—	70
$\text{H}_4\text{L} \cdot 4\text{HCl} \cdot 4\text{H}_2\text{O}$ (colourless)	36.37 (36.47)	7.53 (7.51)	7.94 (7.73)	—	73
$\text{CuLH}_2 \cdot 3\text{H}_2\text{O}$ (light blue)	10.38 (10.52)	43.46 (43.73)	7.08 (7.34)	9.12 (9.27)	67
$\text{Cu}_2\text{L} \cdot 4\text{H}_2\text{O}$ (dark blue)	18.51 (18.60)	38.58 (38.65)	6.24 (6.49)	8.19 (8.20)	60
$\text{Ba}[\text{CuL} \cdot 2\text{H}_2\text{O}]$ (green)	28.13 (27.84)	36.35 (36.62)	5.26 (5.59)	7.59 (7.77)	60
$\text{CoLH}_2 \cdot 2\text{H}_2\text{O}$ (orange)	10.04 (10.13)	45.19 (45.42)	7.08 (7.28)	8.87 (9.62)	64
$\text{NiLH}_2 \cdot 2\text{H}_2\text{O}$ (violet)	10.00 (10.10)	45.41 (45.45)	7.02 (7.28)	10.01 (9.63)	56
$(\text{UO}_2)_2\text{L} \cdot 4.5\text{H}_2\text{O}$ (light yellow)	42.95 (43.37)	23.88 (24.07)	4.37 (4.13)	5.17 (5.10)	65
$\text{Th}_2\text{L} \cdot 4\text{NO}_3 \cdot 8\text{H}_2\text{O}$ (white)	35.02 (34.60)	19.36 (19.70)	3.51 (3.90)	8.26 (8.35)	60

TABLE-2
UV SPECTRA OF THE Cu²⁺, Co²⁺, Ni²⁺ COMPLEXES IN H₂O (pH = 11)

Compound	CuH ₂ L	CoH ₂ L	NiH ₂ L		^a CuH ₂ L ₁	^a CoH ₂ L ₁	^a NiH ₂ L ₁
λ _{max} (nm)	665	500	350	577	653	504	342,554
ε(m ⁻¹ cm ⁻¹)	38	16.5	29	13.8	40	4.5	96.2
Assignment	² E _g → ² T _{2g}	⁴ T _{1g} (F)→ ⁴ T _{1g} (P)	A(F)→T(P)	A(F)→T(F)			

^aMe₂[14]aneN₄-4ac¹⁰.

Deprotonated 1 : 1 complexes can be obtained by addition of NaOH to the complexes MLH₂. This allows us to study their absorption spectra in aqueous solution (Table-2). MLH₂ have absorption properties very similar to those of ML₁H₂, which exhibit octahedral geometry with a MN₂O₂(H₂O)₂ chromophore. We suggest that in the 1 : 1 complexes of the type MLH₂ the metal ion is not incorporated into the macrocyclic ring, but is coordinated by two amino-nitrogen atoms and two carboxylate groups.

IR spectrum

The IR spectral data of ligand and its complexes and their assignments are given in Table-3. The detailed study of the IR spectra of amino carboxylic acid complexes¹¹ has shown that the absorption of the carboxylic group (COOH) appears at 1750–1700 cm⁻¹, that of the coordinated carboxylate (COO⁻... M²⁺) at 1650–1590 cm⁻¹, and that of the free carboxylate (COO⁻) at 1630–1575 cm⁻¹. The IR results of Table-3 indicate that at least one amino group of the ring must

TABLE-3
KEY IR SPECTRAL BANDS (cm⁻¹) FOR LIGANDS AND THEIR METAL COMPLEXES

Complex	v(OH)	v(NH ⁺)	v(COOH)	v(COO ⁻)	v(C—N)	(Coord.) NO ₃	UO ₂ ²⁺ (ν ₁)
H ₄ L·5H ₂ O	3450	2600	1704	1663, 1599	1330, 1307		
H ₄ L·4HCl·4H ₂ O	3420	2600	1740	—	1355, 1320		
CuH ₂ L·3H ₂ O	3410	2500	1750	1620	1310, 1280		
Cu ₂ L·4H ₂ O	3415	—	—	1620	1305, 1275		
Ba[CuL·2H ₂ O]	3400	—	—	1625	1300, 1270		
CoH ₂ L·2H ₂ O	3400	2500	1751	1595	1310, 1285		
NiH ₂ L·2H ₂ O	3410	2500	1751	1590	1310, 1280		
(UO ₂) ₂ L·4.5H ₂ O	3405	—	—	1630	1300, 1276		930
Th ₂ L·4NO ₃ ·8H ₂ O	3420	—	—	1625	1300, 1270	742, 813, 1033	

be protonated and that the carboxylic functions are in the COOH as well as in the COO⁻ or COO⁻...M²⁺ form. Because protonation of one amino group excludes coordination of the metal ion by the complete tetraazacycloalkane unit, we must consider as donor both nitrogen and oxygen atoms. This agrees with the results of UV spectra.

Thermodynamic properties

Stability constants: Only mononuclear species ML was formed (the error square sum $QS \leq 3.0 \times 10^{-3}$). We have checked the possibility of formation of other species, but they are not formed under our experimental conditions. These mononuclear complexes show a marked tendency to protonate and their stability constants are listed in Table-4. Because of the space obstruction of macrocyclic pendant arms, the stability of M-LH₄ is less than those of M-TETA. For the transition metal ions, the Irving-Williams order of stability is observed.

Enthalpies of the coordination reaction: The temperature-dependent data of equilibrium constant in Table-4 can be used to calculate ΔH and ΔS for reactions *via* a Van't Hoff analysis by a linear computer fitting program and the calculated results are given in Table-5. The data of Table-5 show that all values of ΔH are negative, *i.e.*, the stability constants decrease when the temperature is increased.

TABLE-4
STABILITY CONSTANTS OF THE COMPLEXES (I = 0.5 MOL/L KNO₃)

Ion	H ₄ L (35°C)			H ₄ L (45°C)			H ₄ L (55°C)			^a TETA (20°C)		
	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	ML, MLH, MLH ₂	
Cu ²⁺	18.73, 11.97, 4.68	16.65, 11.26, 4.14	15.24, 10.81, 3.75	21.60, 14.60, 7.36								
Co ²⁺	14.36, 9.84, 3.61	13.22, 9.35, 3.88	12.47, 8.84, 2.43	16.56, 9.95, 2.63								
Ni ²⁺	16.90, 10.66, 4.28	14.55, 9.69, 3.88	13.41, 9.01, 3.60	19.91, 13.35, 6.52								
UO ₂ ²⁺	10.47, 5.29	8.91, 3.84	6.82	— — —								
Th ⁴⁺	13.35, 6.60	12.04, 5.10	10.54, 4.00	— — —								

TABLE-5
CALCULATED ΔH AND ΔS FOR IONIC COMPLEXATION WITH LH₄

Equilibrium	A1	A2	A3	B1	B2	B3	C1	C2	C3	D1	D2	E2
R	0.996	0.994	0.997	0.999	1.000	0.995	0.984	0.996	0.996	0.995	0.998	0.997
$-\Delta H$ (kJ/mol)	338.1	112.4	90.1	113.7	96.7	113.9	338.6	159.8	65.9	352.3	271.5	251.8
$-\Delta S$ (J/K mol)	740.8	136.5	203.2	287.7	125.3	300.1	779.2	315.5	132.2	941.8	625.0	692.0

(A1: CuL = Cu²⁺ + L, A2: CuL = Cu²⁺ + LH, A3: CuLH₂ = Cu²⁺ + LH₂; B1: CoL = Co²⁺ + L, B2: CoLH = Co²⁺ + LH, B3: CoLH₂ = Co²⁺ + LH₂; C1: NiL = Ni²⁺ + L, C2: NiLH = Ni²⁺ + LH, C3: NiLH₂ = Ni²⁺ + LH₂; D1: UO₂L = UO₂²⁺ + L, D2: UO₂LH = UO₂²⁺ + LH; E1: ThL = Th⁴⁺ + L)

^a[14]aneN₄-4ac (I = 0.1 mol/L KCl)¹²

ACKNOWLEDGEMENTS

This project was supported from the National Natural Science Foundation of China, the Nature Science Foundation of Anhui Universities, Anhui Institute of Education and the National Key Laboratory of the Coordination Chemistry, Nanjing University, China.

REFERENCES

1. J.H. Bi, F.X. Xie, L.Q. Chen and S.S. Ni, *China Chem. Lett.*, **7**, 862 (1996)
2. S. Aime, M. Botta, M. Fasano and E. Terreno, *Chem. Soc. Rev.*, **27**, 19 (1998).
3. P. Caravan, T.J. Ellison, T.J. Mc Murry and R.B. Laufer, *Chem. Res.*, **99**, 2293 (1999).
4. J.D. Xu, S.S. Ni and Y.J. Lin, *Inorg. Chem.*, **27**, 4651 (1988).
5. K.P. Wainwright, *Coord. Chem. Rev.*, **166**, 35 (1997).
6. M. Botta, *J. Eur. Inorg. Chem.*, 399 (2000).
7. R.W. Hay, M.P. Pujar and F. McLaren, *Chem. Soc. Dalton. Trans.*, **8**, 1531 (1982).
8. J.H. Bi, *Master Thesis*, Anhui University, Hefei, China (1988).
9. A.D. Zuberbuhler and T.A. Kaden, *Talanta*, **19**, 201 (1982).
10. H. Hafliker and T.A. Kaden, *Helv. Chim. Acta*, **62**, 683 (1979).
11. K. Nakamoto, "Infrared Spectra of Inorganic and Coordination Compounds, 3rd Edn., J. Wiley & Sons, New York (1978).
12. R. Delgado and R.F. Silva, *Talanta*, **29**, 815 (1982).

(Received: 14 March 2002; Accepted: 27 May 2002)

AJC-2737