Notes

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Decreased Overall Basicity of a Series of New N,N'-Bis(carboxymethyl) Macrocyclic Ether–Bis(lactone) Ligands Derived from EDTA and the Ring Size Effect on the Stability Constants of Their Lanthanide Complexes

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The idea of combining the characteristics of both open-chain and macrocyclic ligands for the preparation of novel metal ion selective reagents is of current interest. Previously, we have reported the unusual thermodynamic and kinetic properties of lanthanide complexes of 1,7-diaza-4,10,13-trioxacyclopentadecane-N,N'-diacetic acid (K21DA) and 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane-N,N'-diacetic acid (K22DA) for which the lighter lanthanides, e.g., Eu(III) ion, form stronger complexes than the heavier ones.[1-5] The two ligands, K21DA and K22DA with the respective 15- and 18-membered rings and two ionizable pendant acetic acid moieties, allow the formation of stable lanthanide complexes; therefore, the discernment of size selectivity toward lanthanides in aqueous solution is possible.

In order to examine the effects of the position of the nitrogen donor atoms and the relative coordination sites of the two carboxylate groups on lanthanide complexation, we have prepared a series of N,N'-bis(carboxymethyl) macrocyclic ether–bis(lactone) ligands (Figure 1, 1–4) derived from EDTA. The ligand protonation constants and their lanthanide complex formation constants have been determined for these four ligands and two noncyclic structural analogues (Figure 1, 5 and 6). The results are reported in this paper.

Experimental Section

Synthesis of Ligands. The dianhydride of EDTA was prepared by the method of Lennon.[6] The yield was 97.1%, mp 191–192 °C (lit. mp 195 °C). The preparation of the final ligands (1–4) involved the reactions between the EDTA dianhydride and poly(ethylene glycol) [HOCH$_2$CH$_2$(OCH$_2$CH$_2$)$_n$OH, n = 0, 1, 2, 3] to give the title compounds according to published procedures.[7] A typical synthetic procedure is described as below: 12.2 mmol (2.83 g) of EDTA dianhydride was dissolved in 200 mL of dioxane with continuous stirring for 0.5 h. Poly(ethylene glycol) (12.2 mmol) in 30 mL of dioxane was then added to this solution in a dropwise fashion at 90–95 °C over the next 0.5 h. The solution was then refluxed for 40 h, cooled, and evaporated under reduced pressure. The solid obtained was recrystallized from acetone. The white crystalline products obtained were characterized by IR and NMR spectroscopy, molecular weight determination (mass spectrometry, Finnigan MRT 4510), and elemental analysis. Analytical data for ligands 1–4 are given in Table I.

Materials and Standard Solutions. A 1 × 10^{-2} M ligand stock solution was prepared and standardized by standard tetramethylammonium hydroxide solution. Carbonate-free tetramethylammonium hydroxide solution (0.05 M) was prepared by diluting a 20% (CH$_3$)$_4$NOH–methanol solution from Aldrich Chemical Co. The aqueous (CH$_3$)$_4$NOH solution was standardized by using potassium hydrogen phthalate. The standard metal salt solutions having concentrations of about 0.01 M were prepared from reagent grade nitrates (Ce, Pr, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu), chlorides (La, Nd), or sulfate (Sm). The metal solutions were standardized by EDTA complexometric titrations using Xylenol Orange
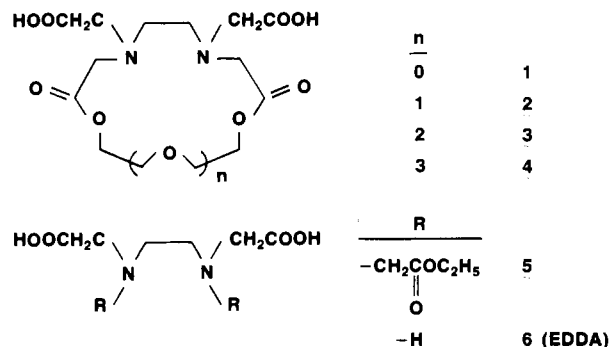

Figure 1. Formulas of macrocyclic and noncyclic ligands related to EDTA.
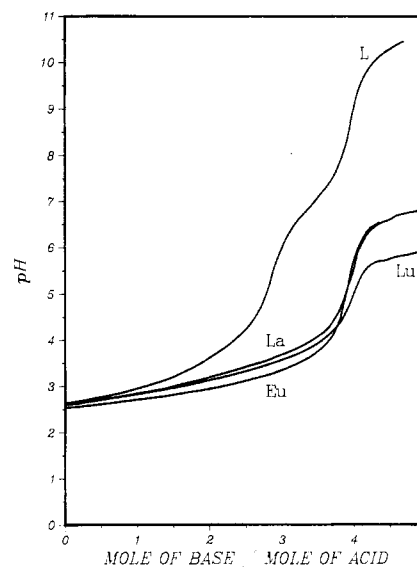

Figure 2. Potentiometric equilibrium curves of ligand 2 and 1:1 ratios of ligand 2 with several lanthanide ions. [Ln] = [2] = 1.0 × 10^{-3} M; 25 ± 0.1 °C; μ = 0.10, (CH$_3$)$_4$NCl.

(all lanthanide ions) as indicator. A 1 M solution of (CH$_3$)$_4$NCl was prepared and determined by passing aliquots of the solution into a cation-exchange (Dowex 50W-X8 resin) column in the H$^+$ form and by titrating the displaced H$^+$ ions with standard KOH solution.

Potentiometric Titration. All titrations were carried out at a constant ionic strength of 0.10 M (CH$_3$)$_4$NCl. Boiled deionized water was used for all experiments. A Model 750 Fisher Acument selective analyzer in conjunction with a Fisher combination electrode was employed to monitor the pH (±0.001 pH unit). The sample solution was prepared by pipeting exact amounts of each stock solution into a titration vessel so that the final mixture is 1 × 10^{-3} M in both the ligand and the metal salt. An additional amount of standardized HCl solution was also added into the titration mixture so that the final ligand would be in the form H$_2$L·2HCl. The water-jacketed titration vessel with a 50-mL capacity was purchased from Brinkmann together with a five-hole cover. Electrode, buret, and temperature probe were fitted into these holes. The vessel was always maintained at 25.0 ± 0.1 °C by using a constant-temperature circulating bath from Van Waters and Rogers. Prior to each titration, the pH meter was standardized at pH 4.00 and 7.00 ± 0.02 with Fisher buffer solu-

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Table I. Analytical Data for Ligands 1–4

compd (yield, %)	anal. found (calcd)			mp, °C	M_r: exptl, m/z (calcd)	IR, cm^{-1}	^{1}H NMR, δ
	% C	% H	% N				
1 (14.0)	45.25 (45.28)	5.66 (5.66)	8.81 (8.54)	181–182	318 (318)	1740, 1700, 1200	3.10 (4 H, s, NCH$_2$CH$_2$N), 3.60 (4 H, s, COCH$_2$N), 3.74 (4 H, s, NCH$_2$COOH), 4.50 (4 H, s, COOCH$_2$)
2 (20.3)	46.23 (46.40)	6.05 (6.09)	7.86 (7.73)	161–162.5	362 (362)	1730, 1700, 1220	3.26 (4 H, s, NCH$_2$CH$_2$N), 3.69–3.81 (8 H, m, COCH$_2$N, COOCH$_2$CH$_2$O), 3.98 (4 H, s, NCH$_2$COOH), 4.39 (4 H, s, COOCH$_2$)
3 (21.6)	47.12 (47.29)	6.49 (6.40)	6.52 (6.90)	155–156	406 (406)	1735, 1720, 1220	3.26 (4 H, s, NCH$_2$CH$_2$N), 3.62 (4 H, s, OCH$_2$CH$_2$O), 3.68–3.81 (8 H, m, COCH$_2$N, COOCH$_2$CH$_2$O), 4.00 (4 H, s, NCH$_2$COOH), 4.38 (4 H, t, COOCH$_2$)
4 (25.3)	47.85 (48.00)	6.55 (6.66)	6.04 (6.22)	137–138	405 (M$^+$ – CO$_2$H) (450)	1735, 1715, 1200	3.26 (4 H, s, NCH$_2$CH$_2$N), 3.63 (8 H, s, OCH$_2$CH$_2$O), 3.68–3.82 (8 H, m, COOCH$_2$CH$_2$O, COCH$_2$N), 3.98 (4 H, s, NCH$_2$COOH), 4.34 (4 H, t, COOCH$_2$)

Table II. Logarithmic Protonation Constants and Stability Constants of Ligands and Metal Complexes of Interest[a]

	1	2	3	4	5	6
H$^+$	6.44	6.82	6.97	7.20	7.33	9.59
	3.49	3.84	3.75	3.91	3.66	6.53
La^{3+}	5.48	7.23	8.46	8.35	10.25	7.04
Ce^{3+}	5.55	7.40	8.44	8.57	9.95	7.48
Pr^{3+}	5.92	7.74	8.67	8.85	10.14	7.84
Nd^{3+}	5.93	8.08	9.18	9.04	10.35	8.06
Sm^{3+}	6.13	8.58	9.37	9.71	10.36	8.28
Eu^{3+}	6.06	8.80	10.03	9.89	10.36	8.38
Gd^{3+}	5.63	8.61	9.59	10.04	10.23	8.13
Td^{3+}	6.12	8.54	9.56	9.54	10.42	8.18
Dy^{3+}	6.40	8.73	9.31	9.49	10.39	8.31
Ho^{3+}	6.30	8.48	9.44	9.13	10.49	8.42
Er^{3+}	6.36	8.08	8.78	9.08	10.21	8.59
Tm^{3+}	6.53	7.98	8.56	8.94	10.44	8.75
Yb^{3+}	6.64	7.92	8.52	9.01	10.66	8.93
Lu^{3+}	6.80	7.71	8.57	8.93	10.39	9.09

[a] K^M_{ML} = [ML]/[M][L]; ionic strength = 0.10; 25.0 ± 0.1 °C. Standard deviations are all within ±0.10 log K unit.

tions. The (CH$_3$)$_4$NOH solution was delivered from a 5-mL buret with a reading accuracy of ±0.01 mL. All titrations were performed two to three times, and reproducible results were obtained. Oxygen-free nitrogen gas was bubbled through the titrate solution on several occasions, and no significant difference was found if the step is neglected. All equilibrium calculations were performed with use of computer programs described elsewhere.[1,4] Data points in the metal buffer region of 20–80% metal complexation were employed for the calculation of stability constants. The averaged values are presented together with the standard deviations calculated from those valid data points.

Results and Discussion

Ligand Protonation Constants. A typical potentiometric titration equilibrium curve for ligand 2 is shown in Figure 2. The calculated values of the protonation constants of the two basic nitrogen sites for all ligands (1–6) are listed in Table II. When a non acid carbonyl group is attached to the nitrogen donor through a methylene spacer for 1–5, the log K values decrease by 2 to 3 units as compared to EDDA (6). This is presumably due to the strong electron-withdrawing ability of the carbonyl group, which decreases the basicity of the amine nitrogen. Similar observations happen to a large number of dipeptides for which the primary amine (–NH$_2$) nitrogens one methylene group away from the peptide bond show decreased basicity.[8] The same is seen for hydroxyethyl group substitution at the amine nitrogen for a hydrogen atom.

For the purpose of calculating the stability constants of complexes, the third and fourth protonation constants of ligands 1–5 are estimated to be 2.37 and 1.66, which are the same as those of EDDA, respectively.

Stability of Lanthanide Complexes. Some representative lanthanide complex formation equilibrium curves are also shown in Figure 2. The logarithmic stability constants of the lanthanide complexes of ligands 1–5 are listed in Table II together with those of Ln–EDDA complexes.

By examining the values of these constants, the following conclusions can be made:

(1) The trend observed for ligand 1 with respect to different lanthanide metal ions is the same as that of EDDA; i.e., the heavier lanthanide ions have greater formation stability. This indicates that complex formation stability of ligand 1 is governed mainly by charge density. This is presumably because the 12-membered ring of ligand 1 is too small for lanthanide ions to show any size selectivity. Because of the noninvolvement of the ring, the stability constants are all smaller than the corresponding complexes of other ligands with some size selectivity, i.e., 2–4.

(2) For ligands 2–4, the value of the stability constant of the lanthanide complex first increases as the atomic number of the metal increases. A maximum value is observed for a middle lanthanide ion, and the stability decreases for the heavy lanthanide ions. The middle lanthanide ion showing the greatest complex formation stability is in general either Eu(III) or its nearby neighbors in the periodic table. This kind of small selectivity for each macrocyclic ligand toward a middle or the lighter lanthanides is also seen for other neutral crown ethers and the like,[10,11] indicating the involvement of the size selectivity of the macrocycle. The 18- and 21-membered ring compounds (3 and 4) form relatively stronger complexes than the 15-membered one (2), indicating the larger macrocycles are normally more flexible for a suitable match of ring size of the ligand with the ionic radius of the metal.

(3) The lanthanide complex formation constants of ligands 2–4 are all smaller than those of K21DA[4] and K22DA,[1] where K21DA is 1,7-diaza-4,10,13-trioxacyclopentadecane-N,N'-diacetic acid and K22DA is 1,10-diaza-4,7,13,16-tetraoxacyclooctadecane-N,N'-diacetic acid. This is mainly due to the decrease in nitrogen donor basicity. If the protonation constants of K21DA are used for ligand 2 to evaluate the lanthanide complex formation constants of ligand 2, little difference is observed between the new Ln–ligand 2 complexes and Ln–K21DA complexes. Similar results are seen for the 18-membered ring analogues. This indicates that, at least for 15- and 18-membered ring macrocycles, the positions of the nitrogen donor atoms and the corresponding carboxylic acid pendent arms are probably not very significant in determining the lanthanide complex formation stabilities as long as five-membered chelate rings are formed. The statement may not work if six-membered ring(s) are involved because substantial conformational changes may occur for the ligand upon complexation. This is illustrated by the lanthanide complex formation stabilities of DOTA (12-membered ring) and TETA (14-membered ring), i.e., tetraacetic acid derivatives of 12- and 14-membered ring tetraaza macrocycles.[12] The DOTA complexes exhibit stability constants 10 orders of magnitude greater than those of TETA, apparently due to conformational differences in the free and complexed forms of the ligands.[13,14]

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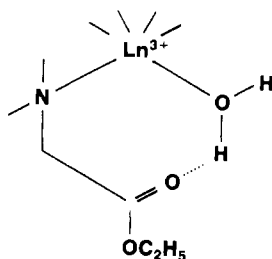
Figure 3. Pseudochelate ring formation between the acetate ester carbonyl group and the coordinated water molecule.

(4) The lanthanide complex formation constants of ligands **2–4** are sometimes greater for the lighter and middle lanthanide ions as compared to those of EDDA (**6**), even though the protonation constants are smaller for ligands **2–4**. This further substantiates the size selectivity of the macrocycles toward the lighter and middle lanthanide ions. On the other hand, the lanthanide complex formation constants of ligand **5** are always greater than the corresponding ones of EDDA (**6**), despite the facts that the protonation constants of ligand **5** are 2–3 orders of magnitude smaller and both ligands do not possess macrocyclic rings.

This probably can be explained by the possibility of pseudochelate ring formation pictured in Figure 3 between the acetate ester carbonyl groups and coordinated water molecules for Ln–ligand **5** complexes. This kind of pseudochelate ring formation may add additional thermodynamic stability to the complex formation.

In summary, the crown ether-like behavior for lanthanide complexes, i.e., selectivity toward the lighter or middle lanthanide ion, is also seen for macrocyclic ligands with ionizable functional pendant arms in aqueous solution. This seems to be true regardless of where the ionizable functional groups are located in the macrocycle ring. However, with the addition of electron-withdrawing or electron-donating groups, the complexation ability of the macrocyclic ligands can be further modified.

Acknowledgment. This material was prepared with the support of U.S. Department of Energy Grant No. DE-FG05-84ER13292; however, any opinions, findings, conclusions, or recommendations expressed herein are those of the authors and do not necessarily reflect the views of DOE.

Registry No. **1,** 93031-52-8; **2,** 93031-53-9; **3,** 93031-54-0; **4,** 93049-99-1; **5,** 17619-53-3; **6,** 5657-17-0.

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Convenient Synthesis of and Additional Characterization Data for Vanadyl Hydrogen Phosphate Tetrahydrate

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In 1985, Leonowicz et al.[1] reported the single-crystal structure of a polymeric oxovanadium(IV) orthophosphate hydrate with empirical formula $VOHPO_4 \cdot 4H_2O$. They observed its transformation to $(VO)_2P_2O_7$[2] at 773 K and suggested that $VOHPO_4 \cdot$

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$0.5H_2O$[3] might be formed by elimination of water from the tetrahydrate. In the same month, Garbassi et al.[4] reported a microcrystalline compound (phase P2) with composition and properties similar to $VOHPO_4 \cdot 4H_2O$, which they assumed to be $(VO)_2P_2O_7 \cdot 9H_2O$. Earlier, Poloiko and Teterevkov[5] reported limited characterization data for a compound with the same empirical formula. In addition, an identical composition was disclosed in a 1984 U.S. Patent,[6] which described a process for the manufacture of maleic anhydride by *n*-butane selective oxidation on VPO catalysts.[7]

As part of a study of vanadium phosphates, various $VOHPO_4$ hydrates were prepared as precursors to $(VO)_2P_2O_7$. In this note, I report a high-yield synthesis of single-phase $VOHPO_4 \cdot 4H_2O$ and present vibrational spectral, bulk magnetic susceptibility, and thermal data for this compound. A method for the quantitative conversion of this hydrate to $VOHPO_4 \cdot 0.5H_2O$ is described.

Experimental Section

Materials. Johnson Matthey Puratronic grade V_2O_5, obtained from Alfa, was used as received. D_3PO_4 (85% in D_2O), DI (53% in D_2O), and D_2O (99.8 atom % D) were obtained from Sigma. All other chemicals were ACS reagent grade from Fisher.

Instrumentation. Magnetic susceptibility data were collected from 4 to 300 K by using a George Associates force magnetometer system. The magnetic field gradient was measured by using a National Bureau of Standards cylindrical Pt susceptibility standard. Field intensity was measured with a calibrated Hall probe. GaAs thermometry was used to measure sample temperature, which was controlled to better than ±0.08 K from 4.2 to 50 K. Replicate susceptibility measurements of HgCo(NCS)$_4$ from 4.2 to 300 K were fit to the Curie–Weiss law with $C = 2.358 \pm 0.003$ and $\theta = -1.92 \pm 0.04$ K, in essential agreement with accepted values[8] of 2.351 ± 0.001 and -1.86 ± 0.01 K, respectively. The magnetic susceptibility of $[(CH_3)_2NHCH_2CH_2NH(CH_3)_2]CuCl_4$ was also measured from 4.2 to 50 K to give $C = 0.439$ and $\theta = -0.15$ K, in close agreement with published values[8] of 0.433 and –0.07 K, respectively ($N\alpha = -217 \times 10^{-6}$ cgsu and $\chi_{dia} = 60 \times 10^{-6}$ cgsu). Susceptibility data were fit to appropriate theoretical expressions by using a local computer program that incorporated the Simplex minimization algorithm.[9] Vacuum desiccation of $VOHPO_4 \cdot 4H_2O$ during susceptibility measurements was minimized by sealing samples in poly(tetrafluoroethylene) cylinders with threaded closures.

Powder X-ray diffraction patterns were obtained by using a Sintag/Seifert automated powder diffractometer with an EG&G Ortec germanium crystal energy dispersive detector. Cu $K\alpha_1$ radiation (154.051 pm) was used to index the patterns. Laser Raman spectra were recorded on a Ramanor U-1000 spectrophotometer at Washington University, St. Louis, MO. The laser (514.532 nm) was operated at 100-mW power. Thermal analysis curves were obtained by using a Mettler TA-1 thermal analyzer.

Syntheses. $VOHPO_4 \cdot 4H_2O$. *Caution!* This synthesis liberates iodine vapor. All operations should be conducted in a hood.

A mixture of 85% H_3PO_4 (28 g) and V_2O_5 (20 g) in distilled water (70 mL) was stirred at 80 °C for 30 min to give the hydrate of $VOPO_4$. This mixture was heated to 90 °C and treated dropwise with 57% aqueous HI (50 g). After this addition, the mixture was stirred at 90 °C for 1 h. Water was added to maintain a volume of 150 mL. The product mixture was suction filtered to remove I_2. The dark green filtrate was boiled with a subsurface N_2 purge until I_2 evolution ceased. The dark blue solution was diluted to 150 mL, filtered, and stirred at room temperature for 20 h to precipitate a blue solid. The solid was collected,

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