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Synthesis of Bis[(4,10-diaza-4,10-ditosyl-benzo-12-Crown-4) 4′-yl] Diaminoglyoxime and Its Complexes

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Abstract. A new macrocyclic ligand (HL) has been synthesised by reaction of 4′-amino-4,10-diaza-4,10-ditosyl-benzo-12-crown-4 with 1,2-dichloroethanedial-dioxime. Protonation constants of the ligand and overall formation constants have been calculated from potentiometric data using the program TITFIT. Both amino and hydroxyimino groups provide donor atoms together with hydroxyl ions at higher pH values.The order of formation constants of the mononuclear complexes are $U(VI)O_2$>Cu(II)>Ni(II)=Co(II)>Cd(II).

Key words: Crown ethers, preparation, protonation constants, formation constants.

1. Introduction

The stable complexes of the macrocyclic polyethers with alkali and transition metal salts are important subjects of intensive investigations since the studies of Pedersen in 1967 [2–6]. The development of syntheses for new macrocyclic systems of potential interest for discrimination studies has been a major thrust of research programs [7–9]. In particular emphasis has been given to the preparation of new oxygen-nitrogen donor macrocycles [10–12]. These ligands, which incorporate various combinations and numbers of donor atoms, are intermediate in structure between the crown polyethers and the category of macrocycles which incorporate mainly nitrogen donors [13, 14].

Small-ring, mixed oxygen and nitrogen donor macrocycles interact strongly with a variety of heavy metal cations [15]. Changes in the ring donors e.g. replacing nitrogen by oxygen or sulphur atoms, may also affect the kinetics but the corresponding ligands have received less attention. Regardless of whether the met-

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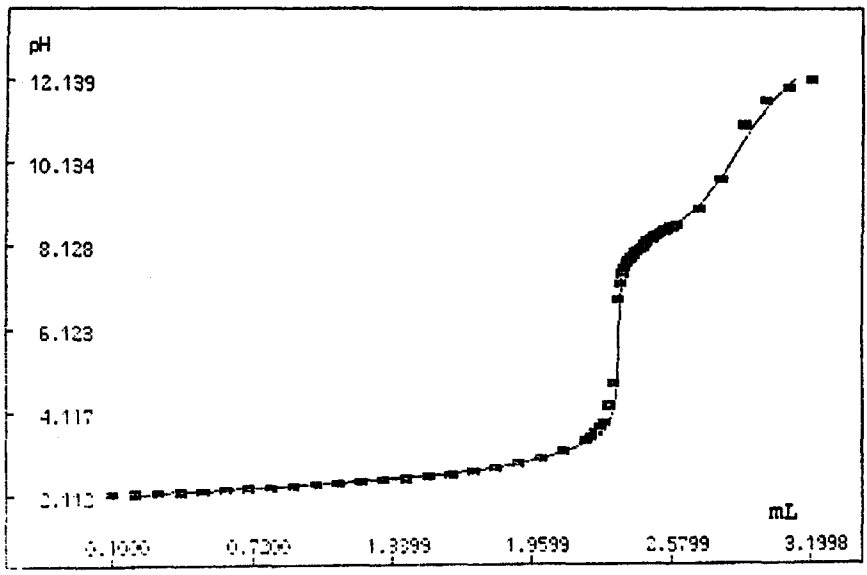


Figure 1. Titration curve of HL.

al complexes of this type of macrocycles are usually less stable than those of the full nitrogen derivatives, they have faster formation reactions [16–19], which may be important in many analytical, medical or other applications.

Addition of macrocyclic groups on to the transition metal complexes of soft donors also enhance their solubility in various organic solvents and their reactivities in solution chemistry is unambiguous. Although it is generally possible to isolate a single complex by changing the reaction conditions, there is usually more than one species in equilibrium in solution. With the aid of computer programs, it has become possible to obtain reliable results for the stability of each species [20–22].

We are confident that potentiometric titration alone can be effectively used to estimate the complex species in different pH ranges by carefully applying different mathematical procedures related to least squares regression. The computer programs enable one to calculate overall protonation or formation constants which minimise the sum-of-squares residual between observed and calculated potential values.

The aim of this study is to synthesise a new vic-dioxime ligand with macrocyclic side groups containing N and O donors, namely bis [(4,10-diaza-4,10-ditosyl-benzo-12-crown-4)4′-yl]diaminoglyoxime and to investigate its protonation and complexation in the presence of the Co(II), Cu(II), Ni(II), Cd(II) or $U(VI)O_2$ ions in solution.

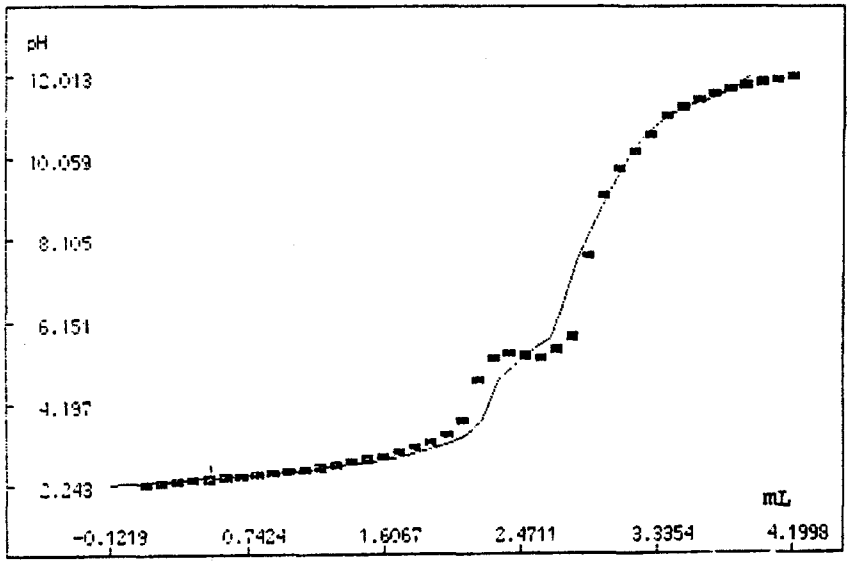


Figure 2. Titration of HL in the presence of Cu^{++}.

2. Experimental

2.1. Reagents

Doubly distilled and deionized water was used throughout the potentiometric experiments which were carried out under an atmosphere of purified nitrogen. Concentrations of stock solutions of metal ions were standardised by atomic absorption spectroscopy. All other chemicals employed were of the highest grade available. Unless specified otherwise, reagent-grade reactants and solvents were used as received from chemical suppliers. DMF was dried overnight over K_2CO_3, filtered and distilled from CaH_2 under reduced pressure. High purity sodium nitrate (Merck) was used as supporting electrolyte and the ionic medium was 1.0 M $NaNO_3$ at the beginning of each potentiometric titration. The starting solutions for each potentiometric experiment were obtained by adding successively to the titration vessel a known volume of ligand solution, and an exact volume of metal chloride, then the required quantities of sodium nitrate (Merck), used as supporting electrolyte in order to minimise variations of the activity coefficients in spite of wide changes in the concentrations of the reagents, and a sufficient amount of doubly distilled water was added to make up the total volume V_0, which was 25.0 ± 0.1 mL. Carbonate-free sodium hydroxide solution was prepared and standardised by potentiometric titration. 1,2-Dichloroethanedial-dioxime was prepared according to the reported procedure [23, 24].

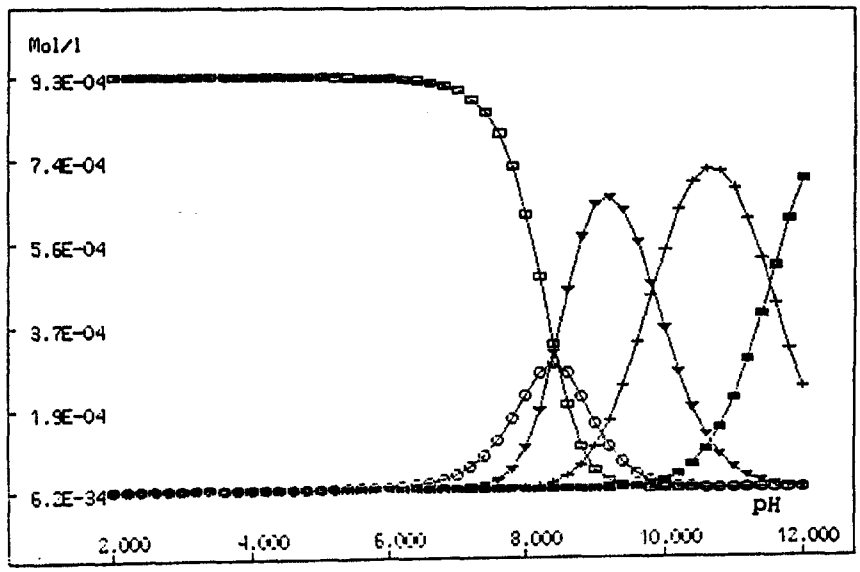


Figure 3. Typical distribution diagrams for HL. (■■■ L^-, ++++ LH, ▼▼▼ LH_2^+, ○○○ LH_3^{++}, □□□ LH_4^{+++}).

2.2. SYNTHESIS

2.2.1. *4′-Nitro-4,10-diaza-4,10-ditosyl-benzo-12-crown-4* (**1**)

4′-Nitro-4,10-diaza-4,10-ditosyl-benzo-12-crown-4 (**1**) was synthesised according to the reported procedure [12, 22].

2.2.2. *4′-Amino-4,10-diaza-4,10-ditosyl-benzo-12-crown-4* (**2**)

4′-Nitro-4,10-diaza-4,10-ditosyl-benzo-12-crown-4 (1.5 g, 2.6 mmol) was dissolved in isopropyl alcohol (100 mL). 0.5 g Pd/C (10%) catalyst and hydrazine hydrate (10 mL 100%) were added. After refluxing the mixture for 1 hour under nitrogen, it was filtered and the solvent was evaporated. The residue was dissolved in chloroform and then washed with water. The organic layer was separated, dried (Na_2SO_4) and the solvent was evaporated. The resulting oily product (1.0 g, 70%) was used in the following reaction without any further purification. IR (KBr): ν = 3320(NH_2), 1343, 1162(SO_2) cm^{-1}.

Anal. calcd. for $C_{26}H_{31}O_6S_2$ (545): C, 57.25; H, 5.69; N, 7.70. *Found*: C, 57.08; H, 5.58; N, 7.78.

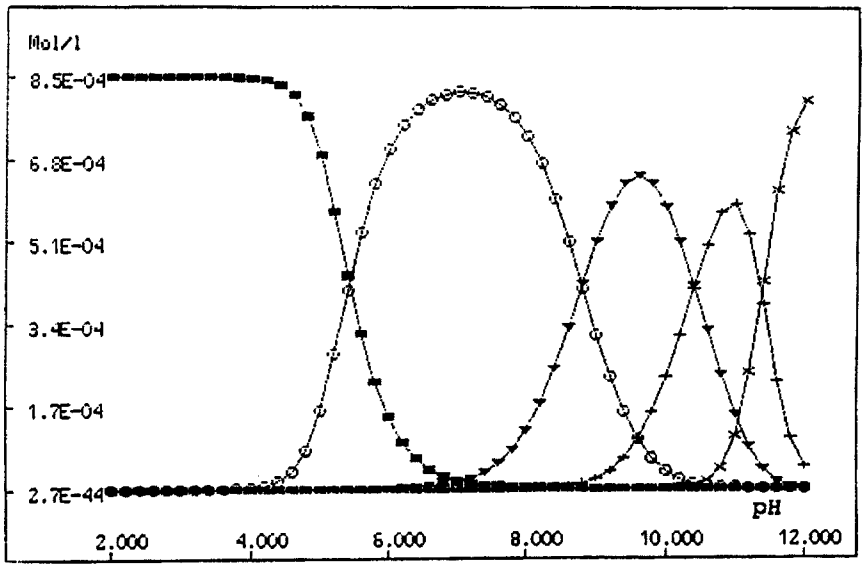


Figure 4. Typical distribution diagrams for the Cu^{2+}—HL system. (■■■ Cu^{2+} ++++ CuL, ▼▼▼ CuLH, ○○○ $CuLH_2$, □□□ CuL(OH)).

2.2.3. *Bis[(4,10-Diaza-4,10-ditosyl-benzo-12-crown-4)4′-yl] diaminoglyoxime* (**HL**)

1,2-Dichloroethanedial-dioxime (0.70 g, 4.44 mmol) dissolved in absolute ethanol (28 mL) was added dropwise into a solution of 4′-amino-4,10-diaza-4,10-ditosyl-benzo-12-crown-4 (4.85 g, 8.90 mmol) containing solid $NaHCO_3$ in excess (2.8 g). The mixture was stirred for 1.5 hours at 60–65 °C on the water bath. A brown precipitate obtained when the solution was cooled to room temperature and it was filtered off, washed with absolute ethanol and then this solution was cooled to 0 °C. Dried diethyl ether was then added and stirred, precipitation of a light-yellow solid occurred. It was filtered, washed with dried diethyl ether to obtain 1.0 g (30%) of (**HL**). mp 88–90 °C; IR(KBr): ν = 3420(OH), 1343, 1162(SO_2) cm^{-1}; ^1H NMR($CDCl_3$) δ = 8.36–6.69 (m, 22H, Ar-H), 5.58 (s, 2H, NH), 4.02 (t, 12H, OCH_2), 3.36 (q, 12H, NCH_2), 2.42 (s, 12H, —CH_3). (—OH protons were not observed in $CDCl_3$, but the spectrum in DMSO-d_6 indicated the D_2O exchangeable —OH protons at 9.77 ppm).

Anal. calcd. for $C_{54}H_{62}N_8O_{14}S_4$ (1174): C, 55.20; H, 5.28; N, 9.54. *Found*: C, 55.4; H, 5.22; N, 9.62.

2.2.4. *$(HL)_2Ni$ Complex*

In order to prepare the $(HL)_2Ni$ complex HL (0.1 mmol, 0.1174g) was dissolved in 5 mL of absolute ethanol and 0.05 mmol of $NiCl_2 \cdot 6H_2O$ (0.0119 g) was added

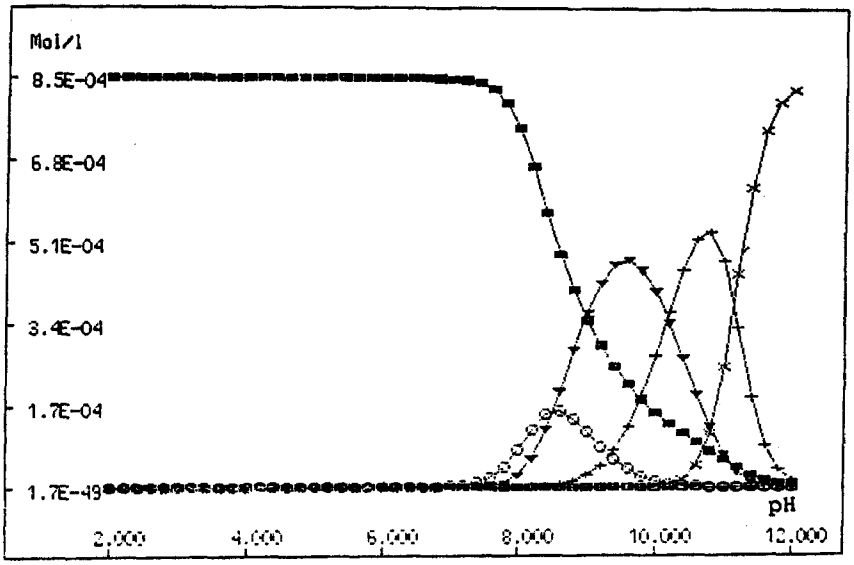


Figure 5. Typical distribution diagrams for the Ni^{2+}—HL system. (■■■ Ni^{2+}, ++++ NiL, ▼▼▼ NiLH, ○○○ $NiLH_2$, ×× NiL(OH)).

to this solution. This mixture was heated at 60 °C. An orange-red precipitate was obtained when the solution was cooled to room temperature. It was filtered, washed with absolute ethanol and dried diethyl ether and dried. The product was slightly soluble in DMSO. Yield 0.085 g (70%). m.p. 179–181 °C; IR(KBr): ν = 3420(OH), 1343, 1160 and 1120 (C—O—C) cm^{-1}; ^1H NMR(DMSO) δ = 9.77 (s, 2H, O—H···O) (it appeared with D_2O), 7.95 (d, 4H, Ar-H), 7.91 (s, 4H, N-H) (it appeared with D_2O), 8.15 (s, 4H, Ar-H), 7.69 (d, 8H, Ar-H), 7.52 (d, 8H, Ar-H), 7.30 (d, 8H, Ar-H), 7.12 (d, 8H, Ar-H), 6.88 (d, 8H, Ar-H), 3.75 (s, 24H, CH_2O), 3.02 (s, 24H, CH_2-N), 2.31 (s, 12H, Ts-CH_3), 2.27 (s, 12H, Ts-CH_3).

Anal. calcd. for $C_{108}H_{122}N_{16}O_{28}S_8Ni$: C, 53.89; H, 5.073; N, 9.315; Ni, 2.44. *Found:* C, 54.2; H, 5.0; N, 9.1; Ni, 2.50.

2.3. Potentiometric Titrations

Potentiometric titrations were carried out using a Metrohm E-415 dosimeter and a Metrohm E-510 pH meter. A Metrohm 6.0204.000 combined glass electrode was used for pH and e.m.f. measurements. The ionic strength was kept constant at 1.0 M $NaNO_3$. All titration solutions were prepared as a total volume of 25.0 mL and thermostatted at 25.0±0.1 °C. The solution in the titration vessel was stirred by means of a magnetic stirrer. A stream of nitrogen was blown over the surface of the solution. All the alkalimetric titrations were carried out at 25.0±0.1 °C and I = 1.0 mol/L $NaNO_3$ for solutions of binary systems containing copper(II), nickel(II),

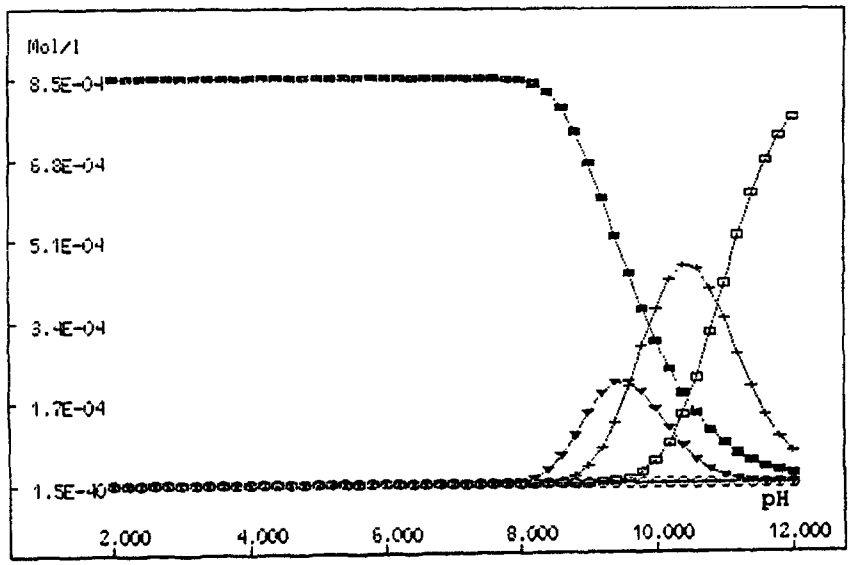


Figure 6. Typical distribution diagrams for the Co^{2+}—HL system. (■■■ Co^{2+}, ++++ CoL, ▼▼▼ CoLH, □□□ CoL(OH)).

cobalt(II), cadmium(II), uranyl(VI) and ligand at different molar ratios. Acetone was added to obtain homogeneous solutions.

The following solutions were prepared to obtain the pH-titration curves:

Solution A: $HClO_4$ (2.5 mL,0.1 M), $NaNO_3$ (5 mL, 1.0 M), acetone (17.5 mL),

Solution B: $HClO_4$ (2.5 mL, 0.1 M), $NaNO_3$ (5 mL, 1.0 M), solution of HL in acetone (2.5 mL, 0.01 M), acetone (15 mL)

Solution C–F: $HClO_4$ (2.5 mL, 0.1 M), $NaNO_3$ (5 mL, 1.0 M), solution of HL in acetone (2.5 mL, 0.01 M), aqueous solution of metal salt (i.e. $CuCl_2.2H_2O$, $CdCl_2.2H_2O$, $NiCl_2.6H_2O$, $CoCl_2.6H_2O$, $UO_2(AcO)_2.4H_2O$) (2.5 mL, 0.01 M), acetone (15 mL).

These solutions were titrated with progressive addition of 0.1 M NaOH titrant in increments of 0.1 mL. The corresponding change in the pH of the solution was measured. The values of proton activity and pK_w for these solutions have been calculated from solution A as 1.39 and 15.60 respectively.

3. Results and Discussion

3.1. Synthesis

The new macrocyclic ligand (HL) has been synthesised by reaction of 1,2-dichloroethanedial-dioxime with [4′-amino-4,10-diaza-4,10-ditosyl-benzo-12-crown-4], which was prepared by catalytic reduction of the 4′-nitro derivative (**1**) in isopropanol with hydrazine hydrate (Scheme). Under these reduction conditions, the

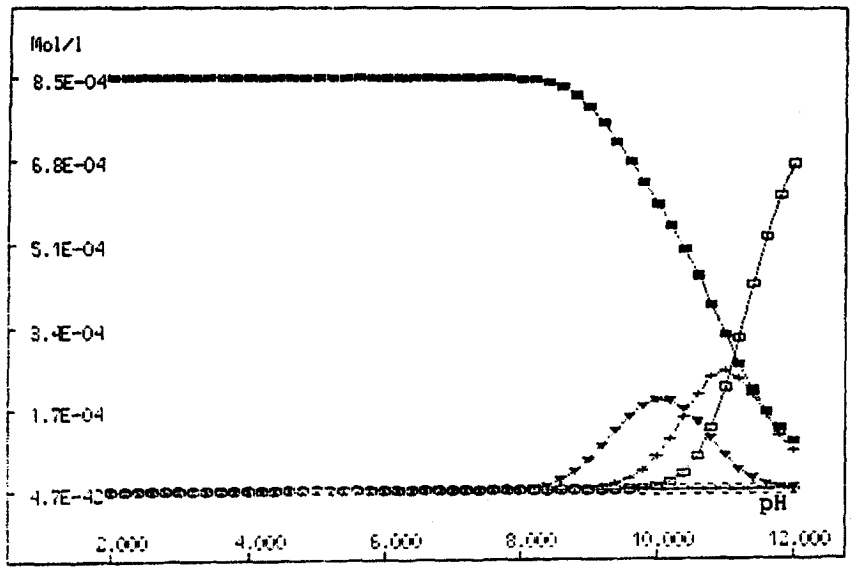


Figure 7. Typical distribution diagrams for the Cd^{2+}—HL system. (■■■ Cd^{2+}, ++++ CdL, ▼▼▼ CdLH, □□□ CdL(OH)).

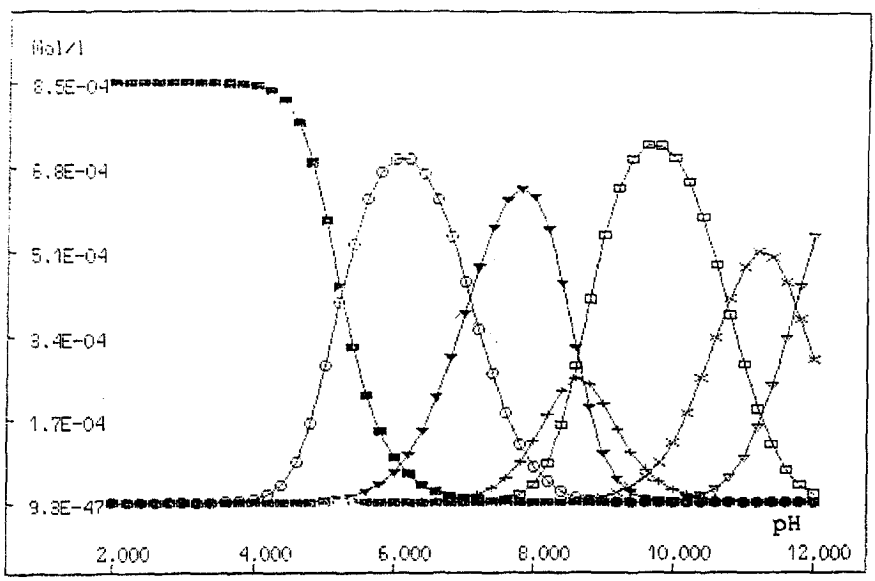
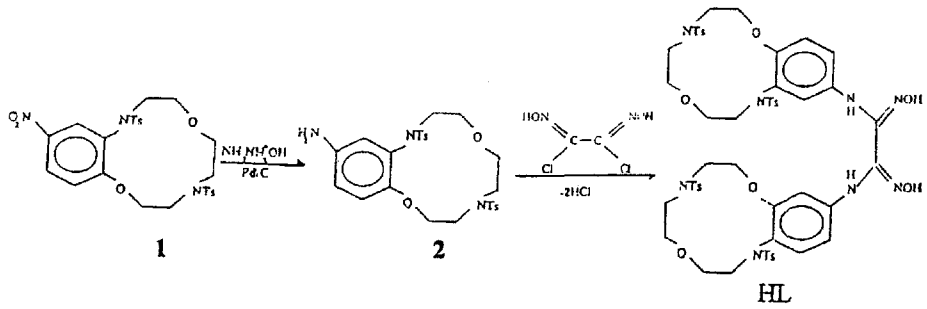


Figure 8. Typical distribution diagrams for the UO_2^{2+}—HL system. (■■■ UO_2^{2+}, ++++ UO_2L, ▼▼▼ UO_2LH, ○○○ UO_2LH, □□□ $UO_2L(OH)$, ××× $UO_2L(OH)_2$, ▽▽▽ $UO_2L(OH)_3$).

tosylated macrocyclic group remains intact. The new compounds were characterised by elemental analysis together with IR and ^1H NMR spectra. As a consequence of the hydrogen bridge between the (OH) group of (HL) and the azomethine

group (O—H· · ·N), the chemical shift for this proton comes at a lower field (13.02 ppm). Although the ^{1}H NMR spectrum of HL in $CDCl_3$ gave well resolved peaks for aliphatic and aromatic CH protons, OH protons could be observed only in DMSO-d_6 solutions at 9.77 ppm and they were characterised by D_2O exchange.



Although the new ligand (HL) carries a 12-membered N_2O_2-macrocyclic group as an additional donor site, the complexation through these donors has been hindered to a large extent due to the presence of the electron withdrawing bulky tosyl groups on the aza-functions. Therefore the interaction of transition metal ions with (HL) is mainly through the oxime moiety and the macrocyclic group functions as a bulky substituent.

3.2. PROTONATION EQUILIBRIUM

Initially the cumulative protonation constants of the ligand were calculated by the TITFIT program. The calculated protonation and formation constants ($\log \beta_{xyz}$) of the ligand are given in Table I. In the normal aqueous titration range, the ligand can liberate four protons; one from the protonated amino group (N-H) and one from the (OH) group of the hydroxylamine.

The values for the macroscopic protonation constants for the ligand are $\log K_1 = 11.52$, $\log K_2 = 9.82$, $\log K_3 = 8.37$, $\log K_4 = 8.46$ and they correspond to the following equations:

$$L^- + H^+ \rightleftharpoons HL$$

$$HL + H^+ \rightleftharpoons H_2L^+$$

$$H_2L + H^+ \rightleftharpoons H_3L^{2+}$$

$$H_3L^{2+} + H^+ \rightleftharpoons H_4L^{3+}$$

Titration data obtained for HL in the presence of Cu(II), Ni(II), Co(II), Cd(II) and U(VI)O_2 ions were processed by the program TITFIT to observe the protonated, neutral as well as the hydroxyl complexes [25]. Cumulative formation constants of the species encountered in the case of five metal ions are summarised in Table I.

Table I. Protonation and metal ion complex stability constants of HL at 25 °C and I = 1.0 M $NaNO_3$.

Metal ion	Species	log β^a
H^+	HL	11.52 (1)
	H_2L^+	21.34 (1)
	H_3L^{2+}	29.71 (1)
	H_4L^{3+}	38.17 (1)
Cu^{2+}	ML	11.50 (1)
	MLH	21.91 (1)
	MLH_2	30.70 (1)
	ML(OH)	−6.32 (1)
Co^{2+}	ML	5.40 (1)
	MLH	15.02 (1)
	ML(OH)	−5.52 (1)
Ni^{2+}	ML	5.82 (1)
	MLH	16.00 (1)
	MLH_2	24.50 (1)
	ML(OH)	−9.25 (1)
Cd^{2+}	ML	4.05 (1)
	MLH	14.50 (1)
	ML(OH)	−7.01
UO_2^{2+}	ML	15.34 (1)
	MLH	24.04 (1)
	MLH_2	31.10 (1)
	ML(OH)	6.78 (1)
	$ML(OH)_2$	−3.98 (1)
	$ML(OH)_3$	−15.71 (1)

[a] Mean value and standard deviation between two batches.

The titration curves for the ligand (HL) and HL/Cu mixtures are shown in Figures 1, 2. The relative importance of various species in each pH range is also shown by distribution diagrams in Figures 3–8.

Some general observations about the behaviour of the various systems are as follows: In the case of the Cu—HL system, complexation begins at pH ≈ 4.0 with the formation of $[CuLH_2]^{3+}$ and then $[CuLH]^{2+}$ appears at pH values above pH = 7.0 (Figure 4).While almost 50% of the $[CuHL]^{2+}$ has been converted into the $[CuL]^+$ complex at pH ≈ 9.0, the concentration of completely deprotonated $[CuL]^+$ product only reaches up to 52% of the metal ion around pH = 6.2. The CuL(OH) complex appears at pH ≈ 10.5

The diagram given in Figure 5 shows that complexes are formed in the solution containing Ni(II) and HL. Complexation begins at pH ≈ 8.0 with the formation of $[NiLH_2]^{3+}$. Then the monoprotonated $[NiLH]^{2+}$ and deprotonated $[NiL]^+$ complexes show maximum concentration at pH 8.5 and 10.5, respectively. The conver-

sion ratios are about 59% $[NiLH]^{2+}$ and 61% $[NiL]^{+}$. The monohydroxo complex [NiL(OH)] appears at pH = 10.0. The complexation behaviour of Co(II) with HL begins at pH=8.0 with the formation of $[CoLH]^{2+}$ and then $[CoL]^{+}$ appears at pH values above pH = 9.0 and shows maximum concentration at pH = 10.0 (41%) (Figure 6). The monohydroxo complex [CoL(OH)] begins at pH=10.0.

A close look at the diagram given in Figure 7 shows that similar complexes are formed in the solution containing Cd(II) and HL as in the case of Co(II). The $U(VI)O_2$-HL system gives a completely different range of complex ions (Figure 8). The high coordination number of this *f*-block element enables the coordination of one or two of the tetradentate ligands together with one or two hydroxo ions. The distribution diagram in Figure 8 shows that the complexation behaviour of $U(VI)O_2$ with HL begins at pH $\approx$ 4.0 with the formation of $[UO_2L(OH)]$ and then $[UO_2LH]$ appears at pH $\approx$ 6.0 and shows maximum concentration at pH=8.0. The monohydroxo complex and dihydroxo complex begin at pH 4.0 and 8.0. The trihydroxo complex appeared at pH $\approx$ 9.0 and showed maximum concentration at pH$\approx$12.

Acknowledgement

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