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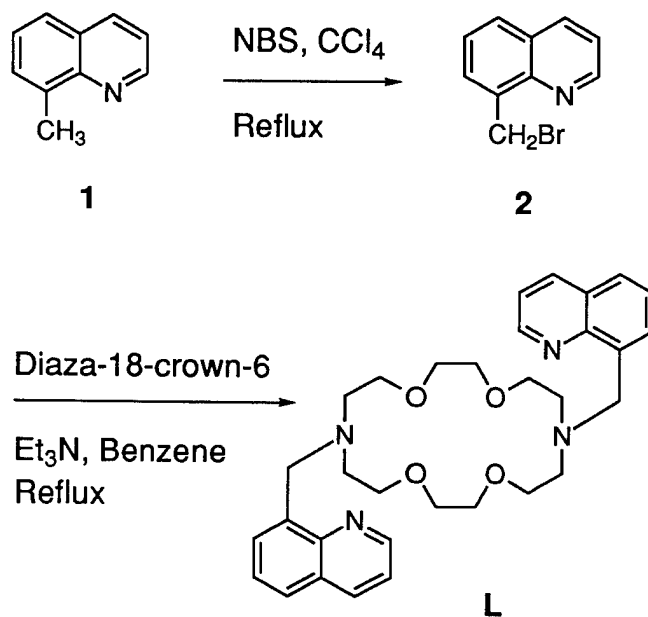
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Results and Discussion

Synthesis. The synthetic route to ligand 7,16-bis(quinolin-8-ylmethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane **L** is depicted in Scheme 1. Intermediate 8-bromomethylquinoline (**2**) was easily isolated as crystals from EtOH in an 88% yield after the reaction of 8-methylquinoline (**1**) with NBS in the presence of benzoyl peroxide in refluxing CCl_4 . The reaction of diaza-18-crown-6 with 8-bromomethylquinoline (**2**) in the presence of Et_3N as base in anhydrous benzene gave **L** in an 87% yield after purification by column chromatograph on silica gel and recrystallization from $\text{CH}_2\text{Cl}_2/\text{EtOH}$.

Complexation Thermodynamics. Interactions of **L** with Na^+ , K^+ , Mg^{2+} , Ba^{2+} , Co^{2+} , Cu^{2+} , Ni^{2+} , and Zn^{2+} were evaluated by calorimetric and UV-visible spectrophotometric titrations¹⁻³ in absolute MeOH solution. The values of equilibrium constants ($\log K$) and enthalpy (ΔH) and entropy changes ($T\Delta S$) for these interactions are listed in Table 1. With the exception of Ni^{2+} , ligand **L** forms stable complexes with the metal ions studied ($\log K > 3$). We first intended to determine the stability constant for the interaction of Ni^{2+} with **L** by the calorimetric method. The very small reaction heat suggested a weak complexation for which the $\log K$ value cannot be accurately calculated due to insufficient heat. Therefore, we used a spectroscopic method³⁸ to evaluate the interaction and obtained a $\log K < 1.5$ which is consistent



Scheme 1. Syntheses of Bis(quinolin-8-ylmethyl)-substituted ligand **L**

with the calorimetry study. The ligand shows a good selectivity for Cu^{2+} over Ni^{2+} by about three orders of magnitude. Among the metal ions studied, Ba^{2+} forms the most stable complex with the ligand. Selectivity factors for Ba^{2+} over the other cations are more than two orders of magnitude.

The calorimetric titration indicated that ligand **L** forms a binuclear complex with Cu^{2+} . Both 1:1 and 2:1 ($\text{Cu}^{2+}:\text{L}$) complexes are observed while all other cations studied form only 1:1 complexes. The data in Table 1 indicate that differences in thermodynamic quantities between 1:1 and 2:1 $\text{Cu}^{2+}\text{-L}$ complexation are small. The binuclear Cu^{2+} complex with a tetraazacrown ether containing two 8-hydroxyquinoline arms has been previously observed in our laboratory.⁴ Most of the binuclear Cu(II) complexes reported were formed with all-nitrogen-containing macrocyclic ligands.⁵⁻⁹ To the best of our knowledge, the Cu(II) complex described in this paper is the first binuclear Cu(II) complex formed with a diaza-18-crown-6 ligand.

It can be seen in Table 1 that entropy effects play a major role in the complexation of Mg^{2+} , Ba^{2+} , and Co^{2+} . The high stability constant of $\text{Ba}^{2+}\text{-L}$ results from both enthalpy and entropy effects. On the other hand, the formation of Mg^{2+} and Co^{2+} complexes is essentially entropy driven.

Experimental Section

Preparation of 8-Bromomethylquinoline (2) (Scheme 1). 8-Bromomethylquinoline was prepared by a similar manner as that described by Kimura et.al.¹⁰ A solution of 8-methylquinoline (**1**) (12.6 g, 88 mmol) in 400 mL of CCl_4 was refluxed with NBS (16.0 g, 90 mmol) in the presence of benzoyl peroxide (0.7 g) for 12 h. The hot solution was filtered and the

Table 1. Thermodynamic Quantities for the Interactions of Macrocyclic Ligand **L** with Metal Ions in Methanol Solution^a

cation	log <i>K</i>	ΔH	$T\Delta S$
Na ⁺	3.73 ± 0.02	-22.5 ± 0.3	-1.2
K ⁺	4.58 ± 0.03	-39.1 ± 0.3	-13.0
Mg ²⁺	4.02 ± 0.07	9.9 ± 0.6	32.8
Ba ²⁺	6.73 ± 0.08 ^c	-19.4 ± 0.4 ^c	19.0
Co ²⁺	3.21 ± 0.06	14.4 ± 0.8	32.7
Cu ²⁺ (1) ^b	4.43 ± 0.04	-35.7 ± 0.5	-10.4
Cu ²⁺ (2) ^b	4.15 ± 0.04	-32.8 ± 0.6	-9.11
Ni ²⁺	< 1.5		
Zn ²⁺	3.66 ± 0.08		

^a Both ΔH and $T\Delta S$ values are in kJ/mol. Except Cu²⁺, all thermodynamic parameters are for 1:1 interactions. The log *K* values for Ni²⁺ and Zn²⁺ interactions were evaluated at 23 °C by UV-visible spectrophotometric titrations and other log *K* values were determined at 25 °C by calorimetric titrations.

^b Thermodynamic parameters for Cu²⁺(1) and Cu²⁺(2) refer to the formation of 1:1 complex Cu²⁺L and 2:1 complex (Cu²⁺)₂L (from Cu²⁺ and Cu²⁺L), respectively.

^c Determined by a competitive calorimetric titration.

brown filtrate was evaporated under reduced pressure. The residue was dissolved in 50 mL of CHCl_3 , and the solution was washed twice with saturated aqueous Na_2CO_3 and once with water. The organic phase was dried (Na_2SO_4) and evaporated. The residue was recrystallized from EtOH to give 17.2 g (88%) of **2** as white crystals. The mp and NMR spectral data were identical to those reported.¹⁰

7,16-Bis(quinolin-8-ylmethyl)-1,4,10,13-tetroxa-7,16-diazacyclooctadecane monohydrobromide (L) (Scheme 1). A solution of **2** (2.0 g, 9.0 mmol) in 50 mL of benzene was added dropwise to a solution of diaza-18-crown-6 (1.0 g, 3.8 mmol) and Et_3N (1.6 g, 15.8 mmol) in 50 mL of benzene under N_2 . The mixture was stirred at room temperature for 20 h and then refluxed for 2 h. The solvent was evaporated under reduced pressure. The residue was treated with a mixture of water and CHCl_3 (1:2). The organic layer was separated, washed with water, and dried (Na_2SO_4). After evaporation, the residue was purified by column chromatography on silica gel with acetone as eluent. The product was recrystallized from $\text{CH}_2\text{Cl}_2/\text{EtOH}$ to give 1.81 g (87%) of **L**·HBr as yellow crystals, mp 95-96 °C; ^1H NMR: δ 2.93 (t, 8H), 3.66 (m, 16H), 4.43 (s, 4H), 7.36 (dd, 2H), 7.52 (d, 2H), 7.65 (dd, 2H), 8.02 (d, 2H), 8.11 (dd, 2H), 8.90 (dd, 2H); ^{13}C NMR (CDCl_3): δ 54.78, 54.86, 70.33, 71.00, 120.95, 126.53, 126.74, 128.36, 129.20, 136.54, 138.23, 147.02, 149.42; HRMS: m/z calcd. for $\text{C}_{32}\text{H}_{41}\text{O}_4\text{N}_4$ ($\text{M}+\text{H}$)⁺: 545.3130, found: 545.3132. Anal. Calcd for $\text{C}_{32}\text{H}_{40}\text{N}_4\text{O}_4\cdot\text{CH}_2\text{Cl}_2\cdot\text{H}_2\text{O}$: C, 61.20; H, 6.85. Found: C, 61.24; H, 6.62.

Calorimetric Measurements. Values of $\log K$, ΔH , and $T\Delta S$ for the interactions of metal ions (except Ni^{2+} and Zn^{2+}) with **L** were determined as described earlier¹ in absolute MeOH

solutions at 2.50 ± 0.1 °C by titration calorimetry using a Tronac Model 450 calorimeter equipped with a 20-mL reaction vessel. The metal ion solutions were titrated into the macrocyclic ligand solutions and the titrations were carried out to a 2-fold excess of metal ions. In general, concentrations of the ligands were $(2.2 - 3.2) \times 10^{-3}$ M and those of the metal ions 7.5×10^{-2} M (K^+) - 0.1 M. In the case of Cu^{2+} , concentration of the ligand was 1.5×10^{-3} M and that of Cu^{2+} , 5.1×10^{-2} M. After a 2:1 (Cu^{2+} :L) complex was observed, the Cu^{2+} concentration was increased to 0.11 M. The method used to process the calorimetric data and to calculate the $\log K$ and ΔH values has been described.² Calorimetric titrations showed no detectable heat for the Ni^{2+} -L interaction and a white precipitate was observed when the ligand ($(1.5 - 2.1) \times 10^{-3}$ M) was titrated with Zn^{2+} . Therefore, $\log K$ values for Ni^{2+} and Zn^{2+} interactions were evaluated by a UV-visible spectrophotometric method.

UV-Visible Spectral Measurements. UV-visible spectra were recorded at 23 ± 1 °C in a 1-cm quartz cell by using a Hewlett-Packard 8453 spectrophotometer. Absolute MeOH was used as the solvent. For the determination of stability constants, a 5.0×10^{-5} M L solution (2.50 mL) was titrated by Ni^{2+} or Zn^{2+} solution and the UV-visible spectra were recorded after each titration. The method described by Bourson and Valeur³ was employed to calculate $\log K$ values. Absorbance data at 280 and 284 nm were used to make the calculations for L- Zn^{2+} and L- Ni^{2+} interactions respectively. Since nickel nitrate showed a weak absorption at 284 nm in MeOH solution ($\epsilon = 10.9 \text{ M}^{-1}\text{cm}^{-1}$), the values of ligand absorbance were corrected by subtracting the Ni^{2+} absorption.

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