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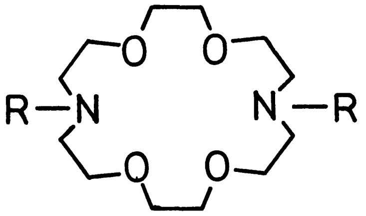
CROWN COMPLEXANE. 1,10-DIAZA-4,7,13,16-TETRAOXACYCLOOCTADECANE-N,N'-DIPROPIONIC ACID [1)]

Makoto TAKAGI, Masato TAZAKI, and Keihei UENO
Department of Organic Synthesis, Faculty of Engineering,
Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812

The title compound (**1**, H_2L), a new type of complexane chelating agent, was synthesized and the complexation properties were examined by potentiometric method. The successive acid dissociation constants (in pKa unit) were 2.61 (H_4L^{2+}), 3.63 (H_3L^+), 8.20 (H_2L) and 8.92 (HL^-) at 25.0 °C and μ = 0.10M (KNO_3). The conditional stability constants (in log K_{ML} unit) for $M^{II}L$ were <2 (Mg^{2+}), 4.0 (Ca^{2+}), 4.4 (Sr^{2+}) and 3.8 (Ba^{2+}). Interaction with Co^{2+}, Ni^{2+} and Zn^{2+} was comparable to the alkaline earth metals. Cu^{2+} interacted strongly but in a complicated manner.

Macrocyclic polyethers, commonly known as crown ethers, have such remarkable property to complex selectively with alkali and alkaline earth metal ions that intensive efforts have been made in its application to various fields of chemistry.[2)] Coordination behavior of crown ethers with metal ions is generally governed by relative size of the cavity of the ether and the ionic radius of the metal ion to be complexed. On the other hand, complexanes, a class of polyamino-polycarboxylic acids such as ethylenediaminetetraacetic acid (EDTA), have been known to be versatile complexing agents for a wide variety of metal ions. As an extension of our program[1b)] on the development of a new complexane-type chelating agent we speculated that a crown ether which has amino-acid moiety in itself will not only exhibit the specificity in complexing behavior toward alkali and alkaline earth metal ions according to its crown ring size but also the increased stability of the resulting complex as compared with the corresponding parent crown ether. To realize this concept we have started with the molecular design and synthesis of a new complexane **1** (H_2L) and investigated its complexing behavior toward alkaline earth and the first row transition metals.



1; R = CH_2CH_2COOH

2; R = CH_2CH_2CN

Preparation of **1**: A solution of 2.5 g (9.5 mmol) of commercial Kryptofix-22 (E. Merck Laboratories) in 15 ml (230 mmol) of acrylonitrile was refluxed for 8 h and then concentrated under reduced pressure. The residual oil (**2**) was converted into the picrate and washed thoroughly with methanol (yield, quantitative). The picrate was converted into the hydrochloride, and the latter was hydrolyzed with refluxing methanolic potassium hydroxide (20 - 30 h). The hydrolysis mixture was neutralized with concentrated hydrochloric acid, the solid potassium chloride removed by filtration from methanolic solution, and finally, **1** was isolated by means of Amberlite IR-120B cation exchange resin. Reprecipitation from methanol-acetone gave 2.5 g of **1**, colorless crystalline powder, mp 128.5 - 130 °C; yield, 65 %. IR (nujol or hexachlorobutadiene mull) 2200 - 1900 (weak, broad, $\geq\overset{+}{N}H$), 1620 (strong, COO^-), 1120 cm^{-1} (strong, C-O-C). NMR (D_2O; δ, ppm from DSS) 2.62 (t, J = 7.5 Hz, 4H), 3.3 - 3.6 (m, 12H), 3.75 (s, 8H), 3.8 - 4.0 (m, 8H). Found: C, 52.86; H, 8.49; N, 6.86 %. Calcd for $C_{18}H_{34}N_2O_8$: C, 53.19; H, 8.43; N, 6.89 %. Interestingly, the IR spectrum of **1** taken in KBr disk gave rise to a free COOH band of medium strength at 1710 cm^{-1} in addition to the strong COO^- band at 1600 cm^{-1}, suggesting that the complexation of the macrocycle with K^+ ion in KBr matrix occurred during the sample preparation. Diperchlorate salt of **1** ($H_4L^{2+}\cdot 2ClO_4^-$) was prepared by reacting **1** with excess concentrated perchloric acid in ethanol. White crystals. IR (nujol mull) 3500 - 2400 (strong, COOH, $\geq\overset{+}{N}H$), 1745 cm^{-1} (strong, COOH). Found: C, 35.55; H, 6.03; N, 4.48 %. Calcd for $C_{18}H_{36}Cl_2N_2O_{16}$: C, 35.59; H, 5.97; N, 4.61 %. The monoperchlorate ($H_3L^+\cdot ClO_4^-$) was obtained by reprecipitating the diperchlorate salt from methanol-ether. White crystals. IR (nujol mull) 3200 - 2200 (strong, COOH, $\geq\overset{+}{N}H$), 1730 (strong, COOH), 1585 cm^{-1} (strong, COO^-). Found: C, 42.60; H, 6.96; N, 5.50 %. Calcd for $C_{18}H_{35}ClN_2O_{12}$: C, 42.65, H, 6.96, N, 5.53 %.

Potentiometric measurement: The acid dissociation constants were determined by titrating **1** with 0.1 N KOH at 25.0 °C and μ = 0.10 M (KNO_3) using the same apparatus previously described.[3)] The acid dissociation equilibria are defined in eq 1 - 4.

$$H_4L^{2+} \rightleftharpoons H_3L^+ + H^+ \qquad Ka_1 = \frac{[H_3L^+]\,[H^+]}{[H_4L^{2+}]} \tag{1}$$

$$H_3L^+ \rightleftharpoons H_2L + H^+ \qquad Ka_2 = \frac{[H_2L]\,[H^+]}{[H_3L^+]} \tag{2}$$

$$H_2L \rightleftharpoons HL^- + H^+ \qquad Ka_3 = \frac{[HL^-]\,[H^+]}{[H_2L]} \tag{3}$$

$$HL^- \rightleftharpoons L^{2-} + H^+ \qquad Ka_4 = \frac{[L^{2-}]\,[H^+]}{[HL^-]} \tag{4}$$

$$M^{2+} + L^{2-} \rightleftharpoons ML \qquad K_{ML} = \frac{[ML]}{[M^{2+}]\,[L^{2-}]} \tag{5}$$

pKa values obtained by titrating the diperchlorate salt of **1** were 2.61 (pKa_1), 3.63 (pKa_2), 8.20 (pKa_3) and 8.92 (pKa_4). Both pKa_3 and pKa_4 values are much smaller than those expected for β-aminopropionic acid.[4] The increased acidity of the two ammonium protons may be attributed to the complex formation between **1** (HL^- and L^{2-}) and K^+ ion in the medium.

One to one molar mixture of H_2L and $M^{II}(NO_3)_2$ (M^{II} = Mg^{2+}, Ca^{2+}, Sr^{2+}, Ba^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}) was titrated under the same conditions as described above. The titration curves illustrated in Fig. 1 show that alkaline earth metals are complexed according to eq. 5. The conditional stability constants K_{ML}'s were evaluated using Bjerrum's equations as described earlier.[5] The results are summerized in Table 1. In the case of Co^{2+}, Ni^{2+} and Zn^{2+}, the pH became unstable at a>1, and the precipitates, most probably the metal hydroxides, were finally formed (Fig. 2). The pH depression (as compared with the titration in the absence

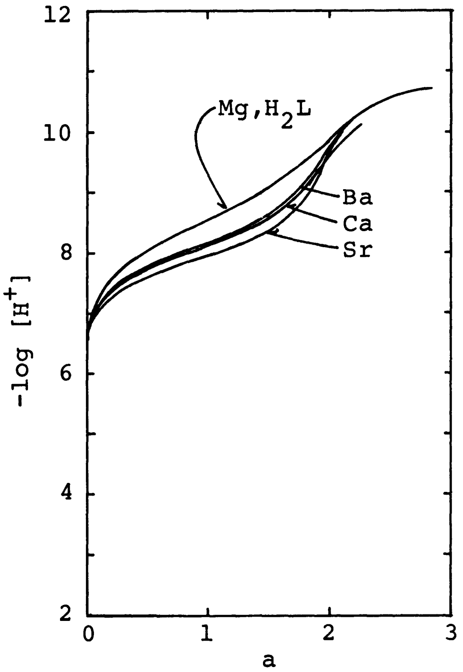


Fig. 1. Titration curves for alkaline earth metal - **1**. $[M^{2+}]_0$ = $[\mathbf{1}]_0$ = 0.001 M, μ = 0.10 M(KNO_3), 25.0°C. a; mol KOH added per mol H_2L.

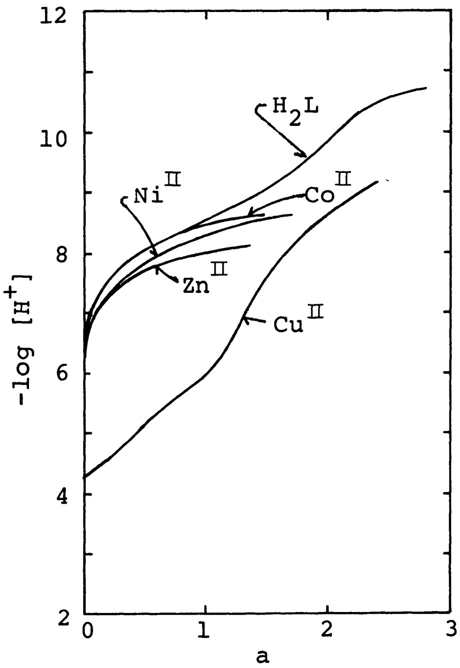


Fig. 2. Titration curves for transition metal - **1**. $[M^{2+}]_0$ = $[\mathbf{1}]_0$ = 0.001 M, μ = 0.10 M(KNO_3), 25.0°C. a; mol KOH added per mol H_2L.

Table 1 Conditional stability constants. 25.0 °C, μ = 0.10 M (KNO_3)

M^{2+}	Mg	Ca	Sr	Ba
$\log K_{ML}$	<2	4.0	4.4	3.8

of metals) at the first halves of the titration curves suggests that the extent of interaction of these transition metals is comparable to that of alkaline earth metals, but the limited data excluded the explicit mathematical treatment. Cu^{2+} interacted strongly with **1** but in a complicated manner.

The stability sequence of alkaline earth metal ions, Mg << Sr > Ca > Ba (>> Mg), is substantially different from that observed in the ordinary complexanes6), suggesting that the interaction of M^{2+} with 1 involves the coordination of the eighteen-membered macrocycle. The poor interaction of Mg^{2+} under the present experimental conditions should be ascribed to the competitive complexation of **1** with 100 times excess of K^+ ion. More drastic differences in the stability may be expected, if ionic strengh of the medium is adjusted with Bu_4N^+ salt which has little interaction with the ligand macrocycle. The analytical applications of this interesting new ligand are now under progress.

References and Notes

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