

LIPOPHILIC (HYDROPHOBIC) CYCLAMS
WITH LONG ALKYL SIDE-CHAINS

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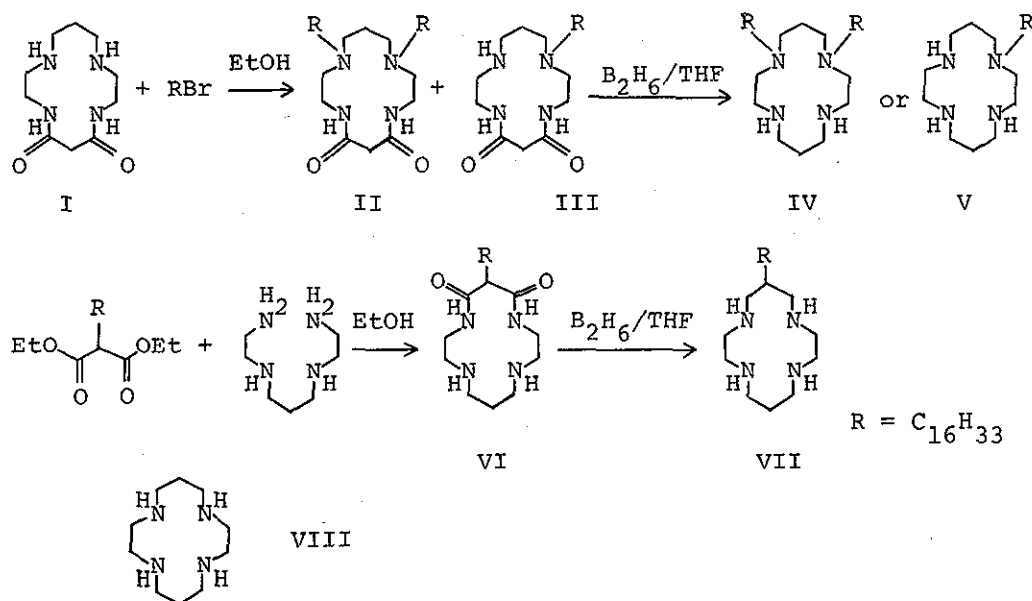
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One or two long alkyl chains were introduced either on carbon or nitrogen atom of cyclam (1,4,8,11-tetraazacyclotetradecane) via the direct alkylation or the condensation of the alkylmalonate with the tetramine followed by the borane reduction. Long alkyl substituted cyclams thus obtained are sparingly soluble in water and can extract heavy metal ions from aqueous solution to an organic phase.

Macrocyclic polyamines form very stable complexes with various heavy metal ions in water.¹⁾ For the successful application of such unique ligands to extract heavy metals from (dilute) aqueous solution, it is necessary for polyamines to be fixed on the (water insoluble) polymer²⁾ or to be converted to the oil not miscible with water. We have already reported the synthesis of cyclams substituted on the ring carbon.³⁾ Now we wish to report the synthesis of lipophilic cyclams with long alkyl side chains on C or N which are practically insoluble in

water. Also their binding characteristics toward heavy metal ions are described.

Scheme 1



Diamide II was obtained by refluxing 10.0 g (43.9 mmol) of diamide of cyclam³⁾ I and 26.7 g (87.8 mmol) of cetyl bromide in ca.100 ml EtOH overnight followed by the silica gel column chromatography (eluent: CHCl_3) and the recrystallization from EtOH (7.20 g, 23.3 % yield). After treatment of 6.9 g (10.23 mmol) of II with a THF solution of B_2H_6 ⁴⁾ was obtained 4.5 g of IV (70 % yield). IV: Mp (as a 4 HCl salt) 180–181°C; ir (KBr), 3300, 2925, 2850, 2800, 1460, 1380, 1140, 1110, 1070, and 720 cm^{-1} ; nmr (CDCl_3), δ 0.92 (methyl protons, 6H), 1.33 (methylene protons of cyclam, 22H). Analysis (as a 4 HCl Salt), Found: C, 77.52; H, 13.71; N, 8.77. Calcd: C, 77.71; H, 13.66; N, 8.63.

Similarly was obtained III by refluxing 7.99 g (35.0 mmol) of the diamide I and equivalent amount (10.7 g) of cetyl bromide in 100 ml EtOH overnight followed by the silica gel column chromatography (eluent, CHCl_3 : EtOH = 10 : 1) and the recrystallization from EtOH- H_2O (2.71 g, 17.0 % yield). On treatment of III with B_2H_6 /THF was obtained V in 60 % yield. V: Mp (as a 4 HCl salt) 197—198°C; ir (KBr), 3300, 2925, 2850, 2800, 1460, 1360, 1280, 1140, 1120, 1070, and 720 cm^{-1} ; nmr (as a 4 HCl salt, in D_2O), δ 0.95 (methyl protons, 3H), 1.37 (methylene protons of cetyl group, 32H), 3.62 (methylene protons of cyclam, 18H). Analysis (as a 4 HCl salt), Found: C, 52.39; H, 9.87; N, 9.08. Calcd: C, 52.25; H, 10.30; N, 9.38.

A solution of 24.2 g of diethyl cetylmalonate (63 mmol) and 10.0 g of N,N-bis(2-aminoethyl)-1,3-propanediamine (63.0 mmol) in EtOH was refluxed for 4 days to give VI in 28.3 %, then treatment of IV with B_2H_6 /THF gave a white amorphous solid VII in 35.3 % yield. VII: Mp 132—133°C; ir (KBr), 3260, 3180, 2920, 2850, 2800, 1460, 1330, 1200, 1120, 1060, 965, 820, and 720 cm^{-1} ; nmr (CDCl_3), δ 0.8 (methyl protons, 3H), 1.25 (methylene protons of cetyl group, 31H), 1.73 (amine protons, 4H), 2.63 (methylene protons of cyclam). Analysis, Found: C, 73.48; H, 13.76; N, 12.79. Calcd: C, 73.52; H, 13.29; N, 13.19.

N-substituted cyclam IV, V are easily soluble in nonpolar solvents such as CH_2Cl_2 , CHCl_3 , petroleum ether or benzene but solubility is rather poor in ethyl ether, THF or EtOH. While C-substituted cyclam VII is easily soluble in benzene, CHCl_3 , CH_2Cl_2 , THF or EtOH. These lyophilic macrocyclic amines IV, V, VII are

all insoluble or sparingly soluble in water. Extraction of Cu^{++} from aqueous to CHCl_3 solution was attempted by shaking 5 ml of an aqueous solution of Cu^{++} ($1.0 \times 10^{-2} \text{M}$) with 5 ml of CHCl_3 solution of IV, V, or VII ($1.5 \times 10^{-2} \text{M}$) for 30 sec. Under the present condition more than 99.5 % of Cu^{++} was extracted by every cyclic polyamine used as shown in Table. To be noteworthy is that the

Table. Concentration of residual metal ions in aqueous layer (ppm)

		Cu^{++} (635) ^{a)}	Ni^{++} (587) ^{a)}	Co^{++} (589) ^{a)}
IV	pH 6	1.4	106	198
	pH 13	2.2	—	—
V	pH 6	1.7	66	93
	pH 13	3.3	—	—
VII	pH 6	*	*	*
	pH 13	0.8	2.0	586

a) Initial concentration of each metal ion in aqueous layer (ppm). * M-L complex.

extraction of Cu^{++} by the polyamine oil is remarkably fast and within 2 sec more than half of Cu^{++} in aqueous solution was transferred to the organic layer.⁵⁾ And very interestingly, the extraction rate was very sensitive to the nature of metal ion to be extracted. According to our preliminary experiments, a possibility exists that between two of more metal ions of very similar stability constants toward cyclic polyamines, one can be extracted much faster than others, leading to the successfully discriminating extraction.

References and Note

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5. This extraction rate is ca. 5,000 times faster than that using the cyclam chemically bound on polystyrene.⁶⁾
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