

Macrocyclic-metal cation interactions involving polyaza macrocycles bonded to silica gel via a nitrogen donor atom

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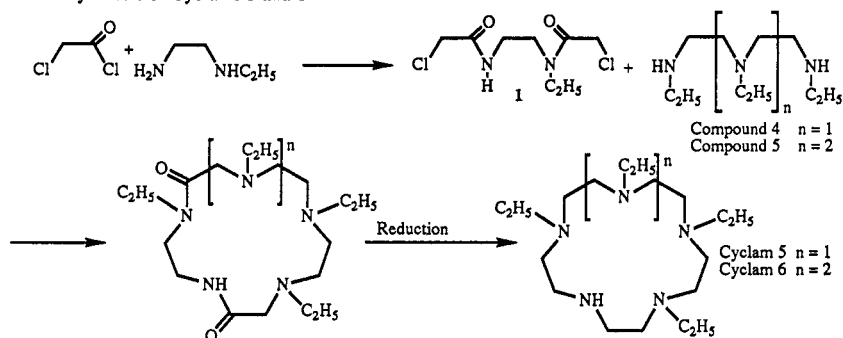
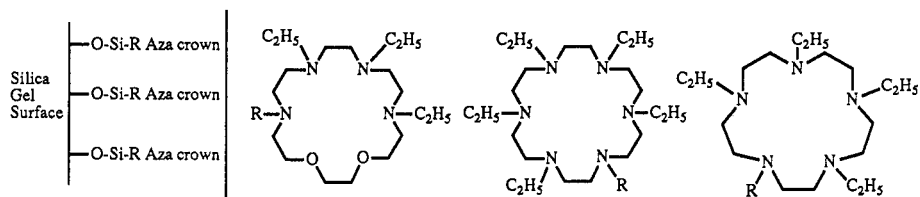
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Abstract - Macrocycles are noted for the remarkable selectivities which certain of them show toward metal ions. This selectivity has been studied extensively for free macrocycles in single solvent systems. However, there is a need for new systems that are more economical and with engineering feasibility which incorporate macrocycles to perform actual separations. Stable silica gel-bound macrocycles maintain the macrocycle for reuse in performing actual separations. The polyaza macrocycles 1,4,7,10-tetraaza-18-crown-6, pentaaza-15-crown-5, and hexaaza-18-crown-6 have been synthesized with the macrocycle covalently bonded to silica gel via one of the nitrogen donor atoms. These bound macrocycles have selective and strong interactions with the soft heavy metal cations as well as proton chemistry which have now been quantified by the measurement of equilibrium constants. These interactions are similar to those of the analogous unbound macrocycles. Separations of ppb levels of heavy metal cations from concentrated matrices of other cations such as the alkali and alkaline earth cations have also been made. The bound macrocycles apparently show a greater tendency towards cavity size-based selectivity than the analogous unbound ligands. This is presumably due to increased ligand rigidity caused by the donor atom attachment to the solid support.

INTRODUCTION

The strong and selective interactions of macrocycles with specific metal ions make these ligands ideal candidates for use as reagents in performing difficult metal ion separations (ref. 1,2). In particular, the use of macrocycles to separate very dilute metal ions in the presence of other more concentrated metal ions is of interest. Much of the previous work using macrocyclic ligands to perform separations has involved the solvent extraction of metal ions from aqueous solutions into organic phases or the membrane transport of metal ions from an aqueous source phase through an organic membrane phase containing the ligand into an aqueous receiving phase. Selective extraction and/or transport of many cations using macrocyclic ligands has been reported (ref. 3-7).

Major problems in using macrocyclic ligands in solvent extraction and liquid membrane systems are (a) maintaining the very expensive ligands in the organic phase (even a very slow loss of these materials from the organic layer of a liquid membrane or solvent extraction system often cannot be tolerated); (b) loss of extraction effectiveness when low concentrations of metal ions are involved; and (c) the relatively slow kinetics of extraction. One way to overcome these problems is the covalent attachment of the macrocyclic ligands to a solid support. Early efforts to accomplish such chemical bonding involved the use of benzo-crown ethers and hydrophobic solid supports or amide bonding groups of relatively low stability (ref. 8). Electron withdrawing benzo substituent groups on macrocycles reduce cation-macrocycle interaction (ref. 1) and hydrophobic supports greatly reduce these interactions relative to those of the analogous unbound macrocycle due to the lack of wetting of the solid. We have described the use of ether and alkyl chains to connect the carbon framework of ether and diaza macrocycles to the siloxy component of silica gel (ref. 9-15). The resulting bond is permanent and the system can be used almost indefinitely to perform separations, recoveries, and determinations without measurable loss of the crown. Furthermore, the bound macrocycles studied thus far have been found to have approximately the same affinity as the corresponding unbound macrocycles for metal ions in aqueous solution (ref. 9,10). The silica gel bound macrocycles studied previously include 15-crown-5, 18-crown-6, 21-crown-7, pyridino-18-crown-6, and 1,10-diaza-18-crown-6. The bonding to silica gel of 1,4,7,10-tetraaza-18-crown-6 via one of the nitrogen donor atoms and the synthesis of triaza crowns and some cyclam macrocycles with additional functionalities which can be attached to silica gel have recently been reported (ref. 15-21). We herein report the binding to silica gel of pentaaza-15-crown-5 and hexaaza-18-

Scheme 1 Synthesis of Cyclams 5 and 6**Scheme 2** Silica Gel Bound Polyaza Macrocycles

crown-6 via nitrogen donor atoms along with an analysis of the interesting metal ion binding properties of these polyaza macrocycles. The polyaza macrocycles are of interest because of their strong and selective interactions with toxic and/or valuable heavy metal cations.

SYNTHESIS OF SILICA GEL-BOUND CYCLAM 5

The pentaaza-15-crown-5 (cyclam 5) and hexaaza-18-crown-6 (cyclam 6) macrocycles were synthesized as shown in Scheme 1 (ref. 19). First, compound 1 of Scheme 1 was mixed with either *N,N',N''*-triethyldiethylenetriamine (for cyclam 5) or *N,N',N'',N'''*-tetraethyl-triethylenetetraamine (for cyclam 6) in an equimolar ratio in acetonitrile with sodium carbonate added to make the solution basic. High dilution techniques are not necessary. After 48-72 hours, the reaction mixture was filtered and evaporated. Chloroform was then added and the resulting material was filtered and evaporated. The resulting product was subjected to column chromatography using methanol as the mobile phase. The diamide was reduced to the amine by adding diborane in tetrahydrofuran (Aldrich 1 M, 70 ml) to 2 g of the diamide in THF. This mixture was then refluxed overnight. The final cyclam products were purified by chromatography on alumina using toluene/ethanol:10/1 as the mobile phase. Each of the cyclams was then attached to silica gel by first reacting the dry silica gel with the appropriate silane in toluene at reflux and then adding the macrocycle. This mixture was allowed to react for 24 hours and then filtered and dried. The polyaza macrocycles attached to silica gel are shown in Scheme 2.

COMPLEXATION AND SEPARATION RESULTS**Metal ion complexation**

Log K values for the interaction of the silica gel-bound polyaza macrocycles with metal ions have been determined as done previously with other silica gel-bound macrocycles (ref. 9,10). Small amounts of the silica gel material were equilibrated with known concentrations of the cations in well defined matrices. After equilibrium was reached, the amount of bound cation was measured by stripping the gel with an acidic solution. The metal concentration in the eluate was then determined by atomic absorption spectrophotometry. Binding of the cations of interest to the silica gel sites was made negligible by including an excess of a cation (e.g. Mg^{2+}) which does not complex with the macrocycle but competes effectively with the cations of interest for plain silica gel as measured in plain silica gel experiments. The equilibrium expression for 1:1 cation-macrocycle interaction is equation (1), where f is the fraction of ligand sites containing bound cations, K_1 through K_6 are stepwise protonation

$$K = \frac{f(1 + K_1[H^+] + K_1K_2[H^+]^2 + K_1K_2K_3[H^+]^3 + K_1K_2K_3K_4[H^+]^4 + K_1K_2K_3K_4K_5[H^+]^5 + K_1K_2K_3K_4K_5K_6[H^+]^6)}{(1 - f)[M^{n+}]} \quad (1)$$

constants for the cyclam, and $[M^{n+}]$ and $[H^+]$ are the equilibrium molar free cation and proton concentrations, respectively. Interactive competition for the cation of interest was included in the free molar concentration term using the equilibrium constant compilations of

TABLE 1. Log K values^a at 25°C for the interaction of the silica gel-bound polyaza macrocyclic ligands (L) 1,4,7,10-tetraaza-18-crown-6 (A₄18C6), pentaaza-15-crown-5 (A₅15C5), and hexaaza-18-crown-6 (A₆18C6) and the analogous free ligands (in parentheses) with metal cations (M) and protons (H).

Cation	Interaction	A ₄ 18C6 ^b	A ₅ 15C5	A ₆ 18C6
Ag ⁺	ML/M·L	9.3(≈8) ^c	9.3(≈8) ^c	9.3(≈8) ^c
Ag ⁺	HML/ML·H	6.9	7.2	8.4
Ag ⁺	H ₂ ML/HML·H	----	4.8	5.7
Hg ²⁺	ML/M·L	23.7	25.0(28.5)	28.8(29.1)
Pb ²⁺	ML/M·L	11.6	12.0(17.3)	14.0(14.1)
Cd ²⁺	ML/M·L	9.8	10.1(19.2)	11.2(17.9)
Cd ²⁺	HML/ML·H	----	7.7	7.2
Cu ²⁺	ML/M·L	12.9(15.5)	13.9(28.3)	16.3
Cu ²⁺	HML/ML·H	----	7.2	----
Zn ²⁺	ML/M·L	8.4(10.9)	9.3(19.1)	10.0(17.8)
Ni ²⁺	ML/M·L	8.3(12.49)	9.0	9.8(19.6)
K ⁺ , Ca ²⁺	ML/M·L ^d	<2.0	<2.0	<2.0(0.8, 2.5)
Sr ²⁺	ML/M·L ^d	<2.0	<2.0	<2.0(3.2)
Na ⁺ , Mg ²⁺	ML/M·L ^d	<2.0	<2.0	<2.0
Ba ²⁺ , Fe ³⁺	ML/M·L ^d	<2.0	<2.0	<2.0
H ⁺	HL/H·L	10.0(9.67)	10.0(10.73)	11.4(10.07)
H ⁺	H ₂ L/H·HL	8.6(8.85)	8.9(9.53)	8.3(9.11)
H ⁺	H ₃ L/H·H ₂ L	2.9	3.8(5.88)	5.6(8.61)
H ⁺	H ₄ L/H·H ₃ L	2.0	2.8(1.6)	3.2(3.97)
H ⁺	H ₅ L/H·H ₄ L	----	2.3(1.0)	1.5(≈2)
H ⁺	H ₆ L/H·H ₅ L	----	----	1.3(≈1)

^aThe bound ligand log K values have deviations between ± 0.1 and ± 0.3 . Data for unbound ligands taken from (ref. 1,22). ^bUnbound ligand data for 1,4,10,13-tetraaza-18-crown-6. ^cUnbound macrocycle log K values are for 1,10-diaza-18-crown-6. Minimal change is observed in the log K value for Ag⁺ with increasing nitrogen substitution beyond two nitrogen donor atoms (ref. 1,22). ^dInteractions below detection.

Martell and Smith (ref. 22). The total number of moles of ligand sites was determined by quantitatively loading every macrocycle site with a strongly binding cation under appropriate matrix and concentration conditions. The protonation constants were determined by repeating the experiments at several pH values for at least one cation and curve-fitting the results according to equation (1).

The results of the log K measurements are given in Table 1. Unlike the crown ethers, the database of unbound polyaza macrocycle-cation interaction is somewhat meager as seen in Table 1 and the values have not been confirmed by others. In fact, the increase in the protonation and metal cation log K with the unbound cyclam 5 appears to be a result of using the less accurate polarographic rather than potentiometric mode of measurement (ref. 1). However, the expected increase in log K values for soft metal cation-macrocycle interaction with increasing nitrogen donor atom substitution is evident with both the bound and unbound macrocycles. The proton chemistry of the polyaza macrocycles is also very similar to that of the unbound aza macrocycles (ref. 1). The first two consecutive protonation constants are rather large but then a substantial drop in strength of interaction occurs for the remaining protons. This drop in interaction strength differs from the behavior of noncyclic polyethylene amines (ref. 22) due to the closer proximity of the nitrogen atoms in the cyclic structures. Although some similarities between the bound and unbound macrocycles were observed, there are significant differences. In particular, size based selectivity appears to be enhanced by the attachment to the solid support via a donor atom. The soft metal cations with ionic radii similar to the macrocycle cavity radii (Ag⁺, Hg²⁺, and Pb²⁺) (ref. 1) have interaction constants with the bound macrocycles quite similar to those of the analogous unbound macrocycles. However, the macrocycle interactions of the intermediate sized Cd²⁺ and the small sized Cu²⁺, Zn²⁺, and Ni²⁺ ions, which are much smaller than a rigid macrocycle cavity radius with these macrocycles, are significantly reduced in going from the unbound to bound macrocycles. Macrocycle attachment to the solid support through a nitrogen donor atom appears to have introduced a degree of rigidity to the normally quite flexible polyaza macrocycles (ref.1).

Parts per billion cation separation, removal and concentration

An aqueous solution which mimics potable water (4 mM Na⁺, 0.4 mM Mg²⁺, 0.1 mM Ca²⁺, 0.1 mM K⁺, 0.1 mM NO₃⁻, 4 mM Cl⁻, 0.4 mM SO₄²⁻, and 1.8 mM HCO₃⁻) was spiked with 100 ppb Pb²⁺, 100

ppb Ag⁺, 4 ppb Hg²⁺, and 20 ppb Cd²⁺. Fifteen liters of this solution was passed through separate 2.0 g columns containing one of the three bound polyaza macrocycles at a flowrate of ~100 ml/min with effluent samples taken every 5 liters. The level of Hg²⁺ coming through the columns was always undetectable (< 1 ppb), the Pb²⁺ and Ag⁺ levels increased from ~10 to ~20 to ~30 ppb, while Cd²⁺ came out of the columns at a virtually constant 10 ppb level. These data indicate that with all of these cations except the strongly binding Hg²⁺ there is some kinetic control involved with the interactions and these kinetics are similar for all three materials. Thermodynamically, the materials are capable of quantitative removal of all four cations at the ppb level for many liters under the experimental conditions even assuming just one theoretical plate for the column (see Table 1). The kinetic removal rates are still excellent considering the 100 ml/min flow rate and the small amount of material (2g) and material height (3.25 cm) used. The relatively rapid kinetics are particularly impressive in comparison to chelating ion exchange resins which are typically attached to polystyrene and other hydrophobic organic polymers (ref. 23,24). The columns were then eluted with 3 M HNO₃ and the removed heavy metals were quantitatively recovered in concentrated form (600-fold) using 25 ml of eluent. In conclusion, the silica gel bound polyaza macrocycles appear to be useful in making viable soft metal cation separation, removal, recovery, and concentration operations. However, the binding of macrocycles to silica through donor atoms rather than carbon atoms does change the properties of unbound macrocycles. In some cases, these changes may be used to obtain desired selectivities.

Acknowledgements

The authors are grateful for funding by the Utah State Centers of Excellence Program, IBC Advanced Technologies, Orem, Utah, and by Serpentix Conveyor Corporation, Westminster, Colorado. We also appreciate the work of Wade Walke, David Cash, Trent Rasmussen, and Rob Terry in performing the bound macrocycle log K and separation experiments and analyses.

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