

Krzysztof E. Krakowiak [a], Garren E. Maas [a], Jerald S. Bradshaw [b]\*,  
Jon K. Hathaway [b], and Reed M. Izatt [b]

[a] IBC Advanced Technologies, Inc., P.O. Box 656, Provo, UT 84603

[b] Department of Chemistry, Brigham Young University, Provo, UT 84602

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4,10-Diaza-15-crown-5, 4,10-diaza-18-crown-6, 4,13-diaza-21-crown-7, and 4,16-diaza-24-crown-8 were prepared by an improved method from the appropriate oligoethylene glycol diiodides and diamines. The thermodynamic values of  $\log K$ ,  $\Delta H$  and  $\Delta S$  for the interaction of 4,10-diaza-18-crown-6 with  $\text{Pb}^{2+}$  and  $\text{Ag}^+$  were determined by a calorimetric titration method and compared with thermodynamic values for interactions of 4,13-diaza-18-crown-6 with the same cations. The thermodynamic values were found to be different for the two diaza-crown ligands. 4,10-Diaza-18-crown-6 and its 4,13-diaza-crown analog formed precipitates when treated with  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Ni}^{2+}$  so that no thermodynamic data are reported for these interactions.

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### Introduction.

There is a continuing interest in the synthesis and metal ion complexing properties of diaza-crown ethers [1]. The diaza-crowns have complexation properties that are intermediate between those of the all-oxygen crowns, which strongly complex alkali and alkaline earth metal ions, and those of the all-nitrogen cyclams, which strongly complex heavy-metal cations [2]. These mixed complexation properties make the diaza-crowns interesting to researchers in many areas. For example, the diaza-crowns have important uses as molecular receptors [3], as well as being valuable intermediates for the synthesis of cryptands [1,4], lariat ethers [5] and macrotricyclic ligands [2,4c,6]. Diaza-crowns have been incorporated into polymers [1b,7], attached to synthetic polymers as the diaza-crown or in the form of a cryptand [8] or attached to silica gel [9].

From the many methods reported for the preparation of diaza-crown ethers [1], the high-dilution process of reacting a diamine with a diacid dichloride [4a,10], the templated ring closure procedure using a diamine and a dihalogen compound or a ditosylate [11], cyclization of  $\alpha,\omega$ -diesters with  $\alpha,\omega$ -diamines [12] and the Richman-Atkins [13] method using a ditosylamide and a ditosylate are the most useful. Among these methods, the high-dilution technique is most commonly used. However, this process is inconvenient because the cyclization step requires a simultaneous addition of the diamine and diacid dichloride to a large volume of a dry solvent over an extended period of time. The Richman-Atkins method, the second most used procedure, has many steps and it is inconvenient to remove the protecting *N*-tosyl groups in the last step. The most convenient (and inexpensive) method to prepare the diaza-crowns

in the laboratory is the one-step template procedure. Up to now, only two diaza-crowns have been prepared by the template procedure. Kulstad and Malmsten [11] reported that diaza-crown ethers could be prepared by reacting a diaminoether with a diiodoether using sodium or potassium carbonate as the base. Their yield was only 17% for 4,10-diaza-15-crown-5 (**1**) but 44% for 4,13-diaza-18-crown-6 (**3**). The metal ion binding properties of **3** have been reported with over 30 different references and over 250  $\log K$  values measured under various conditions [2]. Surprisingly, only one study of the thermodynamic properties of 4,10-diaza-18-crown-6 (**2**) has been reported. This latter investigation reported the  $\log K$  values for the interaction of **2** with four metal ions [14].

We report here the preparation of other diaza-crown ethers using this convenient one-step template procedure from available and inexpensive starting materials. 4,13-Diaza-21-crown-7 (**4**) and 4,10-diaza-18-crown-6 (**2**) (Figure 1) were prepared in good yields (41% and 43%, respectively). 4,16-Diaza-24-crown-8 (**5**) was prepared in only a 14% yield, but this method is still useful in the laboratory when small amounts of this large diaza-crown are needed in a short time. Diaza-crowns **1**, **3** and **4** are available commercially. Also reported here are the thermodynamic values of  $\log K$ ,  $\Delta H$ , and  $\Delta S$  for the interaction of **2** with  $\text{Ag}^+$  and  $\text{Pb}^{2+}$ . The interactions of **2** and **3** with  $\text{Co}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Ni}^{2+}$  gave precipitates.

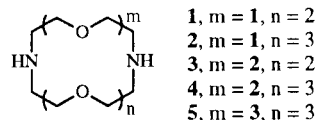
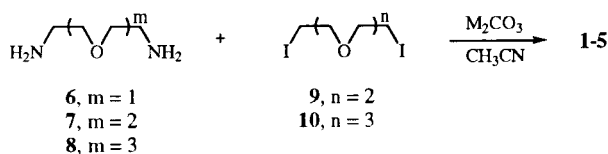


Figure 1. Diaza-crown Ethers

## Results and Discussion.

$\alpha,\omega$ -Diaminoethers 1,5-diamino-3-oxapentane (**6**), 1,8-diamino-3,6-dioxaoctane (**7**) or 1,11-diamino-3,6,9-trioxaundecane (**8**) were treated with  $\alpha,\omega$ -diiodoethers 1,8-diiodo-3,6-dioxaoctane (**9**) or 1,11-diiodo-3,6,9-trioxaundecane (**10**) in acetonitrile in the presence of sodium or potassium carbonate to form the diaza-crowns (see Scheme 1). Macrocycle **1** was prepared previously [11], but we obtained a yield of 28% instead of the reported 17%. A yield of 43% was obtained for diaza-crown **2** which was purified in the same manner as **1** using silica gel column chromatography. Diaza-crown **4** was prepared using both potassium and cesium carbonates as the base giving similar yields. The product was separated by distillation under vacuum. Using this procedure, 4,13-diaza-21-crown-7 (**4**), would cost less than \$5/gram to prepare. This is much cheaper than the commercial cost of over \$730/gram. 4,16-Diaza-24-crown-8 (**5**) was the most difficult to obtain. In this case, diamine **8** was treated with diiodide analog **10** to give **5** in only a 14% yield. Ligand **5** was also obtained using the ditosylate derivative of tetraethylene glycol instead of diiodo **10** in about the same yield. 4,13-Diaza-18-crown-6 (**3**) was prepared from **7** and **9** as reported [11]. After purification, diaza-crown **3** exhibited a higher mp than that reported and only one tlc spot was observed (silica gel, methanol/ammonium hydroxide:10/1). Commercial diaza-crown **3** exhibited two spots on tlc and had a lower mp. This procedure would also be useful for the preparation of diaza-crown ethers containing alkyl substituents.

Scheme 1  
Preparation of Diaza-crowns 1-5



The starting materials were commercially available except for diiodide **10** which was prepared from 1,11-dichloro-3,6,9-trioxaundecane using sodium iodide in acetone. The physical properties of diaza-crowns **1-5** were the same as those reported for **1-5** prepared by other methods [4a,13c].

The thermodynamic values of  $\log K$ ,  $\Delta H$ , and  $\Delta S$  for the interaction  $\text{Ag}^+$  and  $\text{Pb}^{2+}$  with **2**, as determined by a titration calorimetric technique, are shown in Table 1. Table 2 shows the ionic radii of these metal ions and the  $\log K$  values for the interaction of the metal ions with diaza-crown **3** under the same conditions.

The interaction  $\text{Co}^{2+}$  with **2** and **3** resulted in precipi-

Table 1  
Thermodynamic Values of  $\log K$ ,  $\Delta H$ , and  $\Delta S$  for the Interaction of 4,10-Diaza-18-Crown-6 (**2**) with  $\text{Pb}^{2+}$  and  $\text{Ag}^+$  in Water at 25°

Cation	$\log K$	$\Delta H$ (kJ/mole)	$\Delta S$ (J/K mole)	Anion
$\text{Pb}^{2+}$	$4.50 \pm 0.08$	$-25.8 \pm 1.5$	-0.37	$\text{NO}_3^-$
$\text{Ag}^+$	$5.26 \pm 0.06$	$-18.7 \pm 0.5$	38.0	$\text{NO}_3^-$

Table 2  
Ionic Radii [a] Thermodynamic Values of  $\log K$  [b] for the Interaction of 4,13-Diaza-18-crown-6 (**3**) with  $\text{Pb}^{2+}$  and  $\text{Ag}^+$  in Water at 25°

Cation	$\log K$	Ionic Radii
$\text{Pb}^{2+}$	6.9	1.19 Å
$\text{Ag}^+$	7.8	1.15 Å

[a] Ref 15. [b] Ref 1.

tates. The solution also changed from a rose-pink color to blue. This suggests that the nitrogen donor atoms are involved in the complexation since the final pH of the solution was slightly acidic. The interaction of  $\text{Cd}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Ni}^{2+}$  with **2** and **3** also gave precipitates. However,  $\text{Cd}^{2+}$ ,  $\text{Cu}^{2+}$ , and  $\text{Ni}^{2+}$  complexes with **2** and **3** do not undergo color changes so visual inspections gave no structural information. Due to the formation of the precipitates, no thermodynamic values are reported.

The highest  $\log K$  value measured was for the interaction of  $\text{Ag}^+$  with **2**. However, this value is over 2  $\log K$  units lower than the value for the interaction of  $\text{Ag}^+$  with **3**. Although  $\text{Ag}^+$  forms strong complexes with nitrogen donor atoms, it also strongly prefers linear coordination. Certainly, **2** is less able than **3** to meet this requirement.

The interaction of  $\text{Pb}^{2+}$  with **2** is also more than 2  $\log K$  units less than the value for the interaction of  $\text{Pb}^{2+}$  with **3**.  $\text{Pb}^{2+}$  usually forms octahedral complexes [16] and has approximately the same radius as that of the ligand cavity. The difference must arise from the inability of **3** to satisfy the geometric preference of  $\text{Pb}^{2+}$ .

Thus, it is evident that the interactions of **2** with some transition metal ions do not mimic the interactions of **3** with those same metal ions as the previous study may have suggested [14]. Especially affected are metal ions which prefer nitrogen donor atoms over oxygen donor atoms and have rigid complex geometry requirements.

## EXPERIMENTAL

Compounds **6-8** were obtained from the Texaco Chemical Company. Compounds **6** and **7** are also available from Aldrich and Fluka Chemical Companies. Compound **9** and 1,11-dichloro-3,6,9-trioxaundecane were purchased from Aldrich and Parish Chemical Companies. The purity of **2** for the calorimetric titrations was determined to be greater than 98% by titration

with a standard salt solution. Cadmium nitrate (Allied Chemical, AR), cobaltous nitrate (Spectrum, A.C.S.), cupric nitrate (Fisher A.C.S.), lead nitrate (Allied Chemical, AR), and silver nitrate (EM Science, GR) were used as purchased.

Preparation of Diaza-crowns **1**, **2**, **4** and **5** (Scheme 1).

Diiodo compounds **9** and **10** (0.01 mole) and 0.01 mole of diamine **6**, **7** or **8** were added to 200 ml of acetonitrile containing 0.1 mole of the appropriate metal carbonate (see Table 3). The mixture was stirred and refluxed for 48 hours or, for the preparation of **5**, 7 days. The solvent was evaporated and the residue was mixed with 100 ml of a mixture of water and methylene chloride or chloroform. The aqueous layer was extracted four times with 50 ml portions of methylene chloride or chloroform. The combined organic layers were dried over anhydrous magnesium sulfate and filtered. The solvent was evaporated and **1**, **2**, and **5** were purified by column chromatography on silica gel using methanol/ammonium hydroxide as the eluent with a gradient mixture from 40/1 to 5/1. The solvents were evaporated and a small amount of toluene or methylene chloride was added to the residue. The solution was filtered through a glass filter (to remove silica compounds). In the case of **1** and **2**, white solids were obtained when the solvent was removed; mp for **1**, 87-90° (lit mp 88-91° [4a]) and for **2**, 95-98° (lit mp 96-98° [13c]). Diaza-crown **4** was obtained by distillation, bp 162-164°/0.07 mm Hg. Diaza-crown **5** was an oil which could be distilled using a vacuum greater than 0.02 mm Hg. These macrocycles had the same spectral and physical properties as reported [4a,13c]. The yields are given in Table 3.

Table 3  
Reactants, Base, and Yields for the Preparation of  
Some Diaza-crown Ethers

Reactants	Product	Base	Yield (%)	Name of Product
6 + 9	1	Na <sub>2</sub> CO <sub>3</sub>	28	4,10-diaza-15-crown-5
6 + 10	2	Na <sub>2</sub> CO <sub>3</sub>	43	4,10-diaza-18-crown-6
7 + 10	4	K <sub>2</sub> CO <sub>3</sub>	45	4,13-diaza-21-crown-7
7 + 10	4	Cs <sub>2</sub> CO <sub>3</sub>	40	4,13-diaza-21-crown-7
8 + 9	4	K <sub>2</sub> CO <sub>3</sub>	41	4,13-diaza-21-crown-7
8 + 10	5	K <sub>2</sub> CO <sub>3</sub>	14	4,16-diaza-24-crown-8

Thermodynamic Properties for the Interaction of **2** with Ag<sup>+</sup> and Pb<sup>+</sup>.

Thermodynamic measurements were done using a Tronac model 450 isoperibol calorimeter. The measurements were made in distilled, deionized water. The heats of dilution were averaged and subtracted. The volume of the titrate was 20 ml. The volume of the titrant was 1.76 ml. The final molar ratio of metal ion to ligand was approximately 2:1. For each titration, 20 lead points, 100 titration points and 20 trail points were taken. For each system, a minimum of 3 titrations were done with each metal ion. The calculation of log *K*, Δ*H*, and Δ*S* values was done on a VAX 11/780 computer using programs developed earlier [17]. The accuracy of the instrument was tested by determining the thermodynamic quantities in methanol for the interaction of sodium nitrate with 18-crown-6. The values of log *K* (4.31 ± 0.02) and Δ*H* (-33.1 ± 0.1 kJ/mole) for the latter interaction are in excel-

lent agreement with literature values [1a].

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