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Ten new diazadithiacrown ethers containing two 8-hydroxyquinoline (HQ) sidearms attached through the HQ 7-positions and four new diazadithiacrown ethers containing two HQ sidearms attached through the HQ 2-positions have been prepared. Some of these new ligands also contain a hydroxymethyl substituent. The starting macrocyclic diazadithiacrown ethers were obtained by treatment of a bis(_-chloroamide) with the appropriate dimercaptan using K_2CO_3 as the base followed by reduction of the resulting macrocyclic dithiadiamide by BH_3-THF or by $NaBH_4$ in the presence of BF_3-ether as a catalyst. HQ-containing ligands **23-32** were synthesized by a Mannich reaction of the secondary macrocyclic diamines with the substituted-8-hydroxyquinoline. HQ-containing ligands **33-36** were prepared by reductive amination of the secondary macrocyclic diamines with 8-hydroxyquinoline-2-carbaldehyde.

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Syntheses of Diazadithiacrown Ethers Containing Two 8-Hydroxyquinoline Side Arms

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Introduction

In general, the complexing ability and selectivity of lariat ethers for metal ions can be varied by changing certain parameters such as the acidity of the phenolic OH group; the size of the crown ether ring; type, number, and position of the complexing crown ether heteroatoms; the stereochemistry imposed by the arms which connect the phenolic group to the macroring; and the pH of media. For example, diaza-18-crown-6 containing two 5-chloro-8-hydroxyquinoline (CHQ) groups attached through the CHQ 7-position (**1**, Figure 1) exhibits a stronger affinity for Mg^{2+} than for Ba^{2+} (log *K* value in MeOH for Mg^{2+} is 6.82, for Ba^{2+} 3.60) and its isomer, diaza-18-crown-6 bearing two CHQ groups attached through the CHQ 2-position (**4**), has a stronger affinity for Ba^{2+} than for Mg^{2+} (log *K* value in MeOH for Ba^{2+} is 12.2).[1] Ligands **3** and **5**, the HQ analogs of **1** and **4**, respectively (**1** and **4** with the chlorine atoms removed), do not exhibit the same complexing properties as do **1** and **4**.[2] Increasing the number of macroring nitrogen atoms and changing the size of macroring could change the affinity of the ligand toward the heavy metal ions. For example, for ligand **5**, the log *K* value in MeOH for Cu^{2+} is 4.39 while its tetraaza-15-crown-5 analog (**6**) has a log *K* value for Cu^{2+} of 15.5.[3] Ligand **2**, which has a 5-nitro substituent on each 8-hydroxyquinoline, has a high affinity and selectivity for Hg^{2+} and has proven to be a chemosensor for Hg^{2+}.[4] Diaza-18-crown-6 with two 4-methyl(or nitro)-6-aminophenol groups attached through the phenol 2-positions (**7** and **8**) form dinuclear complexes with one Cu^{2+} complexed to the two 6-aminophenols and one Na^+ in the macroring cavity.[5]

Diazadithia(or trithia)crown ethers **9** containing two HQ side arms have also been synthesized.[6,7] These new azathia ligands have poor solubilities in MeOH and, therefore, their complexing properties with metal ions cannot be conveniently studied. A few of ligands **9** have a hydroxymethyl substituent attached to the macroring and are thereby more soluble in methanol. Herein, we report the synthesis of a series of new diazadithiacrown ethers bearing two 5-substituent(or 2-methyl)-HQ side-arms. Some of these new ligands contain a hydroxymethyl group on the macroring. A report on the affinities of some of these new ligands for metal ions and their possible use as sensors for metal ions will be reported in due course.

Results and Discussion

The CHQ and HQ side arms are best attached to the diazadithiacrown ethers through macroring NH groups. Macrocyclic ligands containing two secondary amine functions have conveniently been prepared by the crab-like synthesis using bis(α-chloroamide)s.[3,6,8-10] The NH functions of the secondary bis(α -chloroamide)s are unreactive toward alkylating agents including thiols.[6,11] In the present case, bis(α -chloroamide)s **10-12** were treated with the appropriate dimercaptans using K_2CO_3 as the base to form macrocyclic diamides **13-15** in yields of 46%-61% as shown in Scheme 1. The macrocyclic diamides were in turn reduced to the desired diazadithiacrown ethers **16**, **17**, and **22** by either B_2H_6-THF or the $NaBH_4$-BF_3-THF complex (Scheme 1). Ligands **18-21** shown in Scheme 1 were prepared as reported.[6] Satisfactory elemental analyses were obtained for the new macrocyclic diamides or for new HQ and CHQ armed ligands **23-36** prepared from them.

The Mannich aminomethylation reaction has been used to attach HQ and CHQ groups to the azacrown ethers through HQ and CHQ 7-positions.[2,6,12-14] In the present case, the appropriate diazadithiacrown ether (**16-22**) and the appropriate HQ derivative were treated with paraformaldehyde in refluxing benzene in the one-step aminomethylation reaction[2,6,15,16] to give the bis(2- or 5-substituted-8-quinolin-7-ylmethyl)-substituted ligands **23-32** (Scheme 2).

The products of the Mannich reaction of the diazadithiacrown ethers with HQ (**23** and **27**) and 8-hydroxyquinaldine (**26**) were mixtures. Each of these two starting materials has no substituent on the quinoline 5-position. Thus, both the 5 and 7 positions could be aminomethylated under these reaction conditions. Although we did not look for the side products in these reactions, we recently showed by a careful ^{1}H NMR analysis that when diazatrithiacrown ether **18** was treated with 8-hydroxyquinaldine, the product mixture proved to be about 90% of the desired product where both quinoline substituents were attached through the 8-hydroxyquinaldine 7-position, about 9% of the product with one 8-hydroxyquinaldine attached through its 7-position and the other through its 5-position and the remaining product had both 8-hydroxyquinaldine groups attached through their 5-positions. Thus, we suspect that products **23**, **26** and **27** are mixtures where the HQ groups are attached through their 7-and 5-positions.

HQ has been attached to diaza-18-crown-6[2] and a series of tetraaza-15(and 16)-crown-5 ligands[3] through the HQ 2-position by a reductive amination process using $NaBH(OAc)_3$.[17] In the present case, 8-hydroxyquinoline-2-carbaldehyde and the appropriate ligand (**16-18** or **20**) were treated with $NaBH(OAc)_3$ to form the bis(8-hydroxyquinolin-2-ylmethyl)-substituted ligands **33-36** in yields of 46% - 66% (Scheme 3). It is important to note that the hydroxy group of HQ did not have to be protected for this reaction as previously reported.[3]

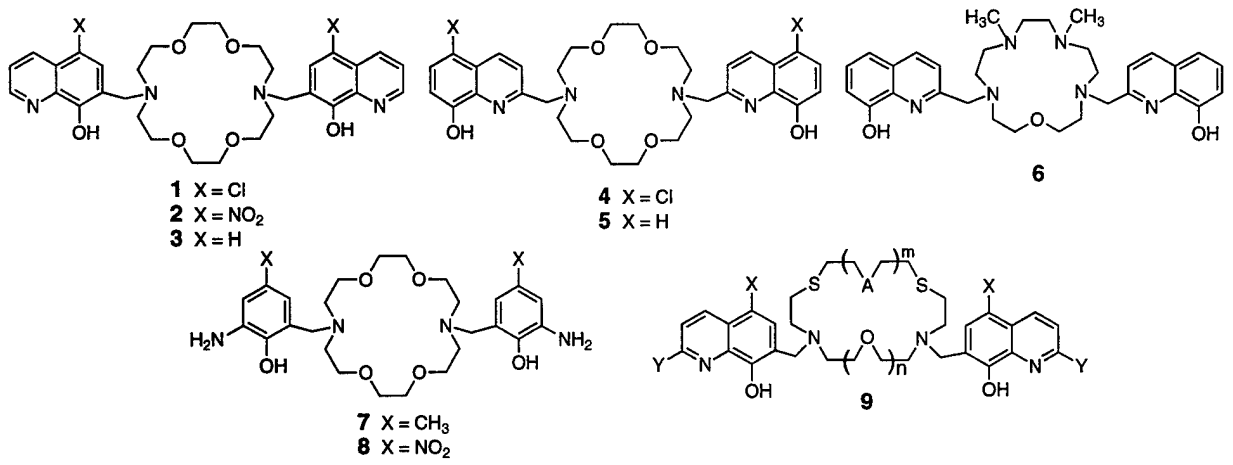
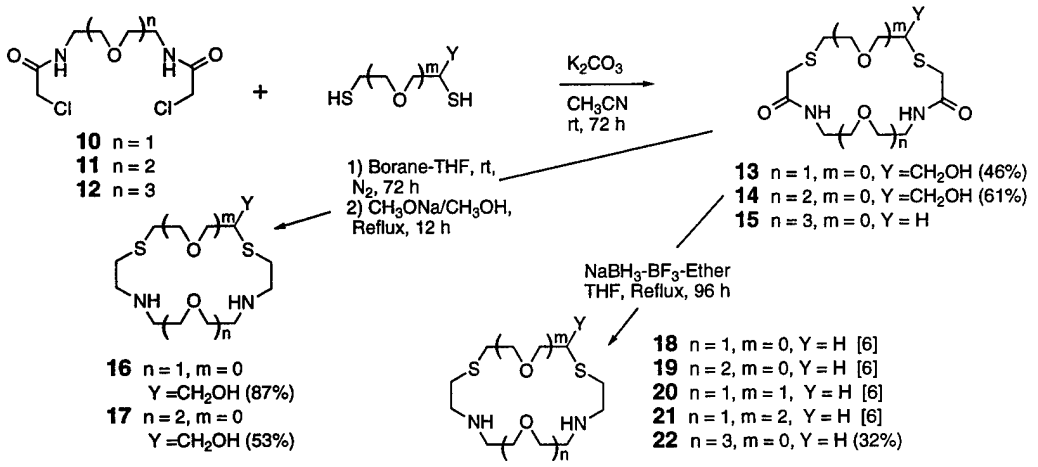
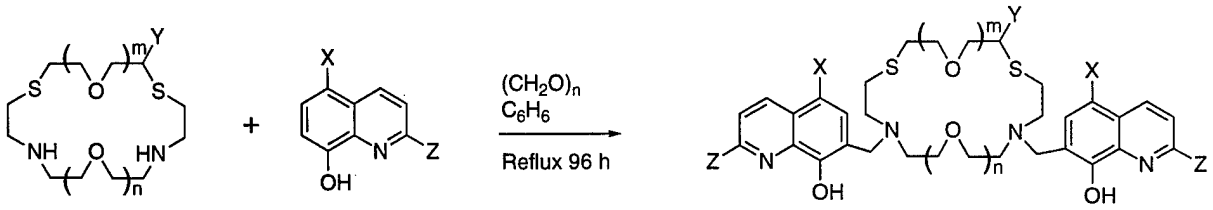


Figure 1. Compounds Mentioned in the Introduction.



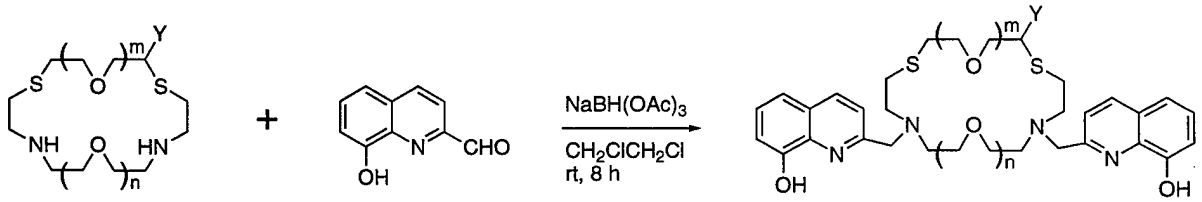
Scheme 1. Preparation of Diazadithiacrown Ethers **16**, **17** and **22**.



16-22

23 n = 1, m = 0, Y = CH_2OH, X, Z = H (64%)
24 n = 1, m = 0, Y = CH_2OH, X = CH_3, Z = H (34%)
25 n = 1, m = 0, Y = CH_2OH, X = Cl, Z = H (57%)
26 n = 1, m = 0, Y = CH_2OH, X = H, Z = CH_3 (64%)
27 n = 2, m = 0, Y = CH_2OH, X, Z = H (64%)
28 n = 2, m = 0, Y = CH_2OH, X = CH_3, Z = H (34%)
29 n = 2, m = 0, Y = CH_2OH, X = Cl, Z = H (57%)
30 n = 1, m = 2, Y = H, X = CH_3, Z = H (56%)
31 n = 1, m = 2, Y = H, X = Cl, Z = H (60%)
32 n = 3, m = 0, Y = H, X = Cl, Z = H (57%)

Scheme 2. Preparation of 8-Hydroxyquinoline-substituted Diazadithiacrown Ethers **23-32** by the Mannich Reaction.



33 n = 1, m = 0, Y = CH_3OH (66%)
34 n = 1, m = 0, Y = H (53%)
35 n = 2, m = 0, Y = CH_3OH (64%)
36 n = 1, m = 1, Y = H (46%)

Scheme 3. Preparation of 8-Hydroxyquinoline-substituted Diazadithiacrown Ethers **33-36** by Reductive Amination.

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