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Form Approved
OMB No. 0704-0188

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1. AGENCY USE ONLY (Leave blank)		2. REPORT DATE April 17, 2001	3. REPORT TYPE AND DATES COVERED Technical Report	
4. TITLE AND SUBTITLE Synthesis of Bis-8-Hydroxyquinoline-Armed Diazatrithia-15-Crown-5 and Diazatrithia-16-Crown-5 Ligands			5. FUNDING NUMBERS N00014-98-1-0485 98PR05020-00	
6. AUTHOR(S) R. Todd Bronson, Jerald S. Bradshaw, Paul B. Savage, Krzysztof E. Krakowiak, and Reed M. Izatt			8. PERFORMING ORGANIZATION REPORT NUMBER Technical Report No 25	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Department of Chemistry and Biochemistry Brigham Young University Provo, UT 84602				
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Dr. Stephen W. McElvany (Program Officer) Office of Naval Research 800 No Quincy Street Arlington, VA 22217-5660			10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
1. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release; distribution unlimited			12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 words) <p>The synthesis of a series of diazatrithia-15-crown-5 and diazatrithia-16-crown-5 ligands containing two 8-hydroxyquinoline side arms are reported. The ligands were prepared by a two-step process. First, diazatrithiacrown ethers 11 and 12 were prepared by treating bis(α-chloroamide) 5 with various dimercaptans followed by reduction using a boron-THF complex. Hydroxymethyl-substituted macrocycle 12 was rearranged to hydroxy-substituted diazatrithia-16-crown-5 in refluxing aqueous HCl. Macrocyclic diamines 11-13 were converted to either 5-chloro-8-hydroxyquinolin-7-ylmethyl-substituted diazatrithiacrown ethers 14-16 by a Mannich aminomethylation reaction or to 8-hydroxyquinolin-2-ylmethyl-substituted diazatrithiacrown ethers 17-19 by reductive amination using 8-hydroxyquinoline-2-carboxaldehyde.</p>				
14. SUBJECT TERMS			15. NUMBER OF PAGES	
20010501 092			16. PRICE CODE NA	
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT Unlimited	

OFFICE OF NAVAL RESEARCH

Grant N00014-98-1-0485

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**Synthesis of Bis-8-Hydroxyquinoline-Armed Diazatrithia-
15-Crown-5 and Diazatrithia-16-Crown-5 Ligands**

by

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Synthesis of Bis-8-Hydroxyquinoline-Armed Diazatrithia-15-Crown-5 and Diazatrithia-16-Crown-5 Ligands

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Results and Discussion

Synthesis of Diazatrithia Crown Ethers. Secondary ring nitrogen atoms in crown ethers offer a convenient site for attachment of alkyl substituents. The crab-like synthesis of diazacrown ethers using the bis(α -chloroacetamide)s provides a relatively high yield method to form macrocycles containing two secondary amine functions.^{1b,2} In this regard, bis(α -chloroamide) **5** was treated with various dimercaptans in MeCN using a carbonate base to form macrocyclic diazatrithiadiamides **6-8** in good yields (Scheme 1). As expected, the larger 2:2 cycloaddition products, macrocyclic tetraamides **9** and **10**, were also isolated in two cases in small yields. The NMR spectra of **9** and **10** were similar to those of **6** and **8**, respectively. High dilution techniques helped minimize the production of these undesired by-products. Macrocyclic diazatrithia ligands **11** and **12** were prepared by reducing macrocyclic diamides **6** and **8**, respectively, using a borane-THF complex. Initially, work up of the borane reduction products was done in refluxing 6 M HCl, but this process caused the formation of unexpected rearrangement and ring opened products as discussed below. Exposure to 6 M HCl at room temperature for a period of 10 minutes, along with extraction, was adequate for freeing the desired product from boron giving diazatrithia-18-crown-6 (**11**) and hydroxymethyl-substituted diazatrithia-15-crown-5 (**12**) in good yields.

The rearrangement product of **12** proved to be a new hydroxy-substituted diazatrithia-16-crown-5 (**13**) (Scheme 2). Ligand **13** is also of value in our research program. In an acid environment with heating, the protonated primary hydroxyl group from **12** becomes a leaving group when attacked by the neighboring ring sulfur atom. This leads to a charged epithio intermediate that is in turn attacked by water at the carbon atom most able to support a positive charge, forming **13**. A minor product from this reaction resulted from the intramolecular attack by a neighboring ring nitrogen atom forming **13a** in a very low-yield. A trace amount of another compound which has very similar properties to those of **13a** was also observed. This material could be a result of the attack of the other ring nitrogen atom on the epithio intermediate.

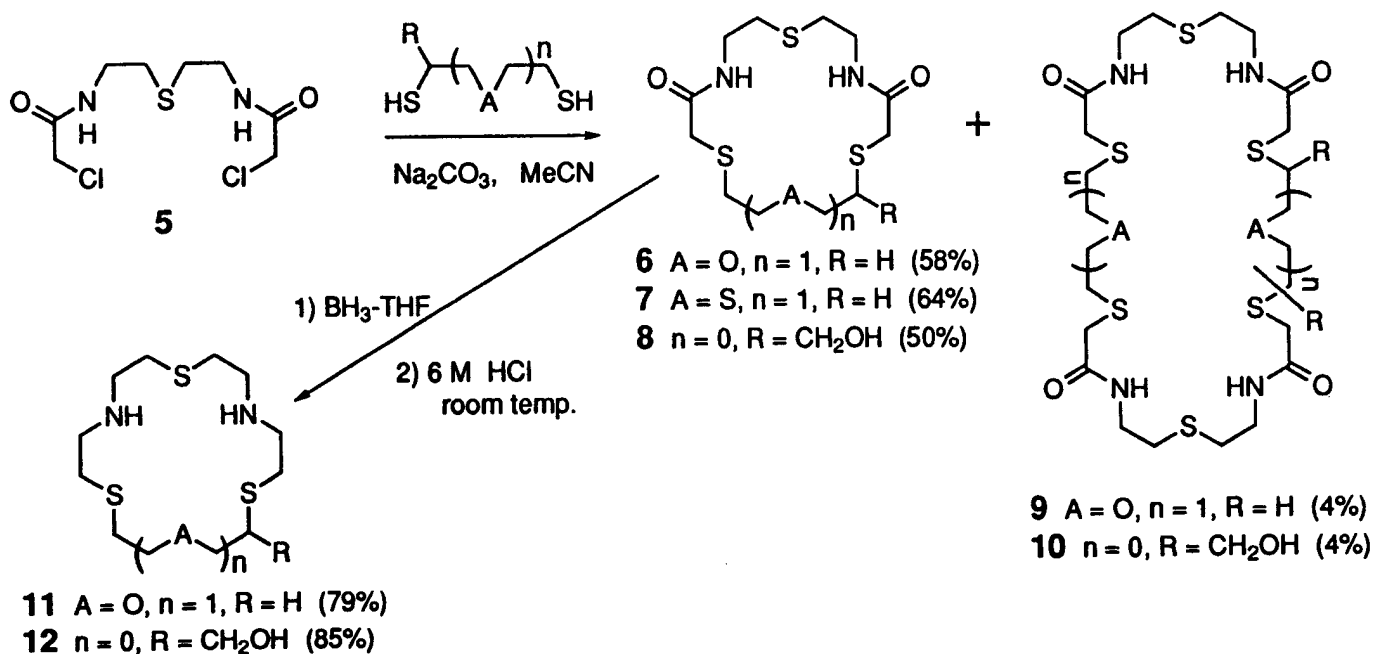
Synthesis of 8-Hydroxyquinoline-substituted Ligands. Ligands **14-16** with the CHQ units attached at the CHQ 7-position were formed using Mannich reaction conditions as shown in Scheme 3.^{1d,3} The best results were achieved by first forming the *N,N'*-bis(methoxymethyl)diazacrown ethers by stirring the diaza crowns in methanol and a slight excess of paraformaldehyde.³ After removal of methanol and addition of benzene to the mixtures, CHQ was added and the mixtures were refluxed. Benzene

proved to be a good reaction solvent since there were few side products. Products **14-16** were purified using radial chromatography.

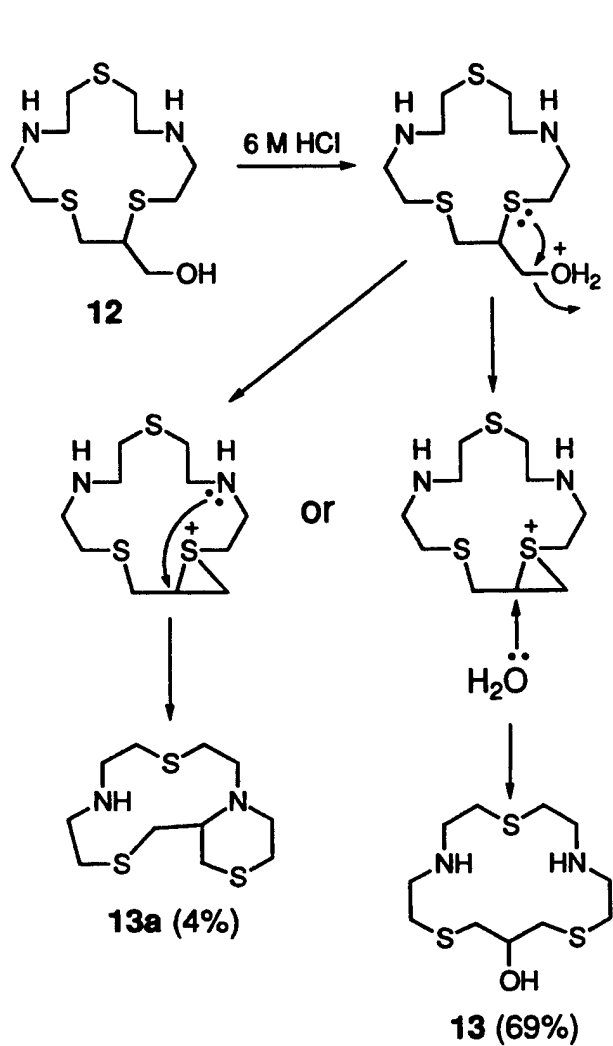
Compounds **17-19** (Scheme 4) were obtained in good yields using a reductive amination procedure.^{1a,1b} Ligands **17-19** with the 8-hydroxyquinoline side arms attached at their 2-positions were more readily isolated than compounds **14-16** with CHQ units attached at their 7-positions.

References

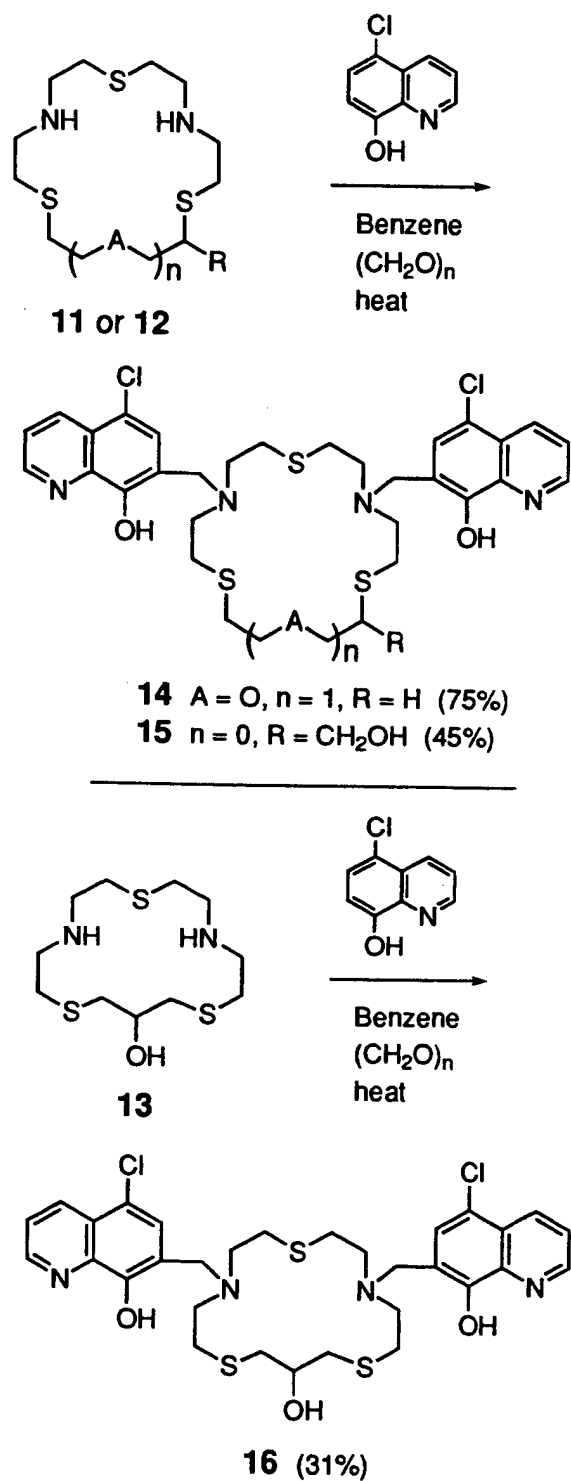
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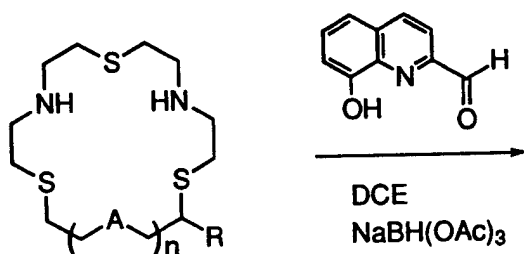
Scheme 1. Syntheses of diazatrithiacrown ethers **11** and **12** containing two unsubstituted nitrogen atoms



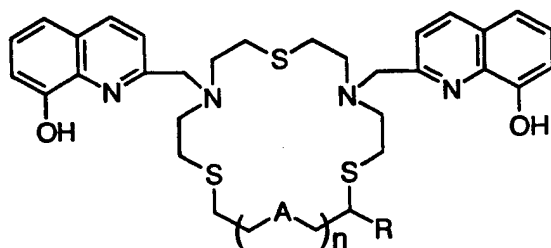
Scheme 2. Rearranged crown ethers **13** and **13a**



Scheme 3. Syntheses of 5-chloro-8-hydroxyquinolin-7-ylmethyl-substituted crown ethers via the Mannich reaction

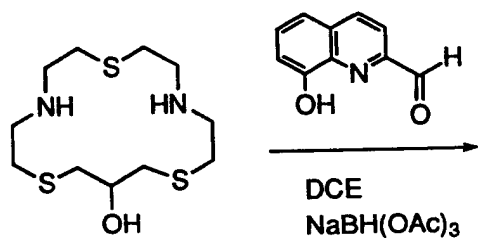


11 or 12

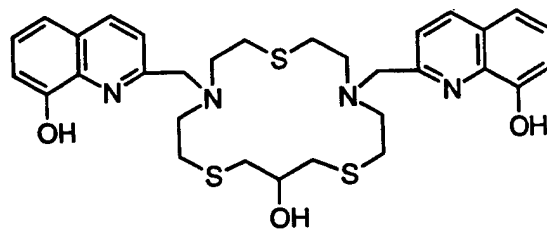


17 A = O, n = 1, R = H (75%)

18 n = 0, R = CH₂OH (69%)



13



19 (64%)

Scheme 4. Syntheses of 8-hydroxy-quinolin-2-ylmethyl-substituted crown ethers via reductive amination