

## The Discovery of Crown Ethers\*

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I regret that I have nothing new to add to this field in which so many able investigators have obtained interesting results extending the scope of my discovery. So I must resort to old material, perhaps so old that some have forgotten, and some of the younger of you never knew of it. Briefly, I will recount how I discovered the crown ethers and the fun I had doing so [1, 2].

In 1961, at Dr. H. E. Schroeder's suggestion, I began research on vanadium compounds. We hoped that an understanding of the effect of various ligands on the catalytic behavior of vanadium might lead to the development of superior catalysts for the polymerization of olefins. We also hoped to find means for suppressing the pro-oxidant catalytic action of residual vanadium in the resulting polymers. There was then little understanding of the effects of structure on contemporary vanadium catalysts. Most were discovered empirically by reactions of inorganic vanadium compounds, such as vanadium tetrachloride or vanadyl chloride ( $\text{VOCl}_2$ ), with various aluminum alkyls.

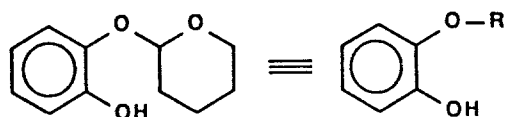
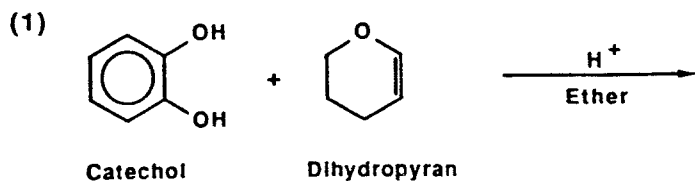
I decided to study the effects of uni- and multidentate phenolic ligands on the catalytic properties of VO. To this end, I had synthesized the desired ligands up to and including the quadridentate. Now I was preparing the quinquedentate, bis[2-(*o*-hydroxyphenoxy)ethyl] ether **3** by reacting a catechol derivative with a protected hydroxy group **1** with bis(2-chlorethyl) ether in the presence of sodium hydroxide (Figure 1). The sample of the partly protected catechol **2** was known to be contaminated with about 10% unreacted catechol, but it was used without further purification.

A brownish goo was the product of the reaction, and in my initial attempt to recover the desired quinquedentate ligand, I obtained a colorless crystalline by-product in 0.4% yield. This fibrous substance had an intriguing combination of properties: (1) elementary analysis fitted benzo-9-crown-3, a possible product of the reaction of the contaminant catechol with bis(2-chlorethyl) ether; (2) it was little soluble in methanol but solubilized by sodium hydroxide; (3) its UV spectrum was that of a phenolic compound but without a hydroxyl group which would have explained the solubilization by sodium hydroxide; and (4) its UV spectrum was altered by the base in a way we had never seen before (Figure 2).

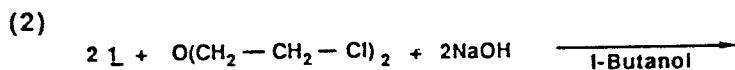
There was no known cause for the solubilization in methanol by sodium hydroxide without an appropriate functional group. To complete the picture, the product was submitted for molecular weight determination.

In the meantime, I was greatly excited to discover that the unknown was solubilized in methanol by any methanol-soluble salt of the alkali metals. Therefore,

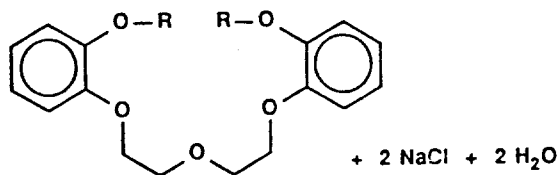
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1.

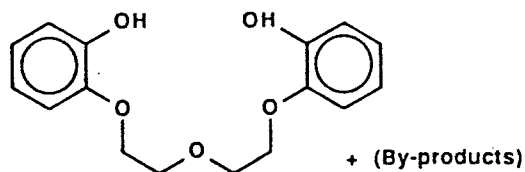
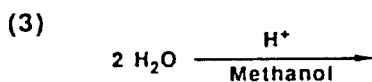


Bis(2-chloroethyl) ether



Protected Intermediate

2.



Bis-[2-(o-hydroxyphenoxy)ethyl] ether

3.

Fig. 1. Synthesis of bis-[2-*o*-hydroxyphenoxy]ethyl ether.

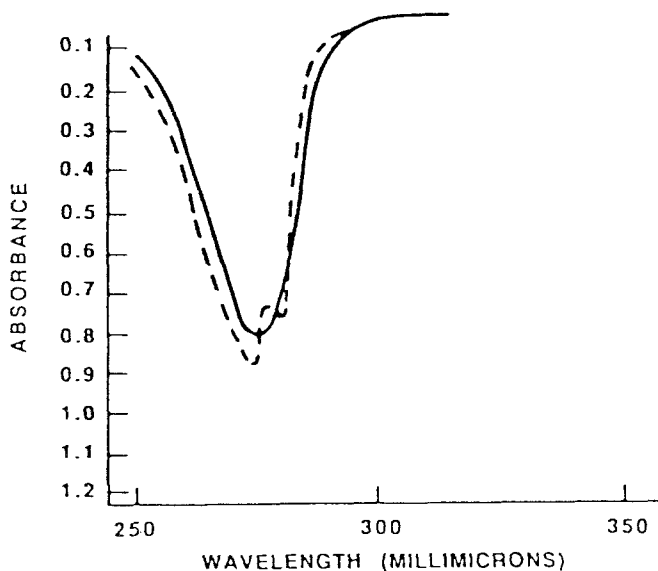
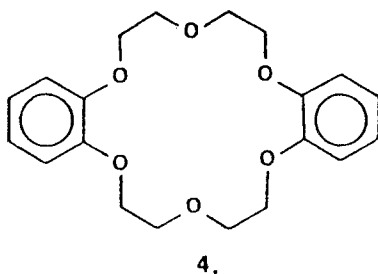


Fig. 2. Effect of NaOH on the ultraviolet spectrum of dibenzo-18-crown-6, **4**. (---, after addition of NaOH). Soluble sodium salts have the same effect.

solubilization by sodium hydroxide was due to the sodium cation and not to the base! Its molecular weight was found to be double that of benzo-9-crown-3, namely corresponding to dibenzo-18-crown-6, **4** in Figure 2. The mystery was solved; in my synthesis of the quinquedentate ligand, nature had lent a hand to produce a hexadentate ligand by reacting two molecules of the contaminant catechol with two molecules of bis(2-chlorethyl) ether and thus closing the ring.

Thus did I discover dibenzo-18-crown-6, the first crown ether and the first synthetic compound capable of complexing the alkali metal cations. So now, with the realization that I had something very unusual and with the utmost curiosity and anticipation, I devoted all my energies to the study of this fascinating class of ligands by synthesizing a great variety of macrocyclic polyethers and determining their interaction with inorganic cations. I was specially interested in the stability of the 'complexes' and the reason for their behavior. For example, I found that for maximum stability of its salt complex, each cation has an optimum size of the ring

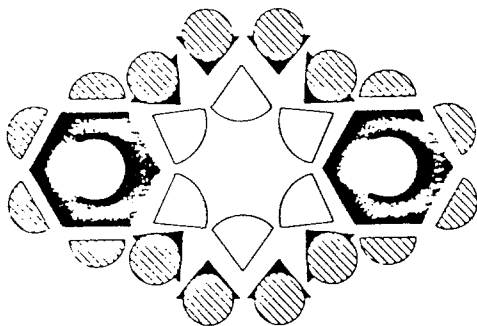


Fig. 3. Courtauld model of dibenzo-18-crown-6, 4.

of the polyether. A complex can form even if the fit is not the best by forming a sandwich complex consisting of two molecules of polyether per cation. The thermal stability of some salt complexes, e.g., KCNS is attested to by their having melting points higher than those of the components.

When their unique properties were realized, an exhilarating period of research was inaugurated. Every successful experiment produced a significantly novel result and led to new thoughts on what to synthesize and also as to the many potential uses of these extraordinary substances. I also derived great esthetic pleasure from the structure of the crown ethers as shown by the Courtauld model (Figure 3); so simple, elegant, and effective a means for the trapping of hitherto recalcitrant alkali cations. The crown nomenclature was created because the official names of crown ethers were so complex and hard for me to remember.

It might appear that the work on the crown ethers was mine alone save for the help of an able laboratory technician. True, the concepts and decisions were mine, but there was a host of indispensable collaborators who made all this possible. I would be more than remiss were I not to make the following acknowledgement; to the management of the Elastomer Chemicals Department of the du Pont Company for support in every way for almost a decade; to the Analytical Groups of the Company who made all their resources available; for consultations with the technical staff of the company, and the versatile skill of my laboratory technician.

And now, I place myself again in the kindly hands of my friend and mentor, Herman Schroeder, I cannot adequately express my gratitude to him for all of his actions on my behalf.

## References

1. C. J. Pedersen: *J. Am. Chem. Soc.* **89**, 7017 (1967).
2. C. J. Pedersen: in *Synthetic Multidentate Macrocyclic Compounds*, R. M. Izatt and J. J. Christensen (eds.), Academic Press, New York, Ch 1, 1978.