

# THE DISCOVERY OF CROWN ETHERS

Nobel lecture, December 8, 1987

by

CHARLES J. PEDERSEN

E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

Ladies and Gentlemen, Dear Colleagues,

This is a wonderful day in my life, and I am looking forward to sharing my thoughts with you.

Before I begin, I would like to convey the warm greetings of the people of Salem County, New Jersey - where I have lived for many years - to the people of Sweden. Salem County is where a very early Swedish settlement was established in 1643. Next year we will join with the people of our neighboring state of Delaware to celebrate the 350th anniversary of the first landing of Swedes in the New World at The Rocks in Wilmington, Delaware. We look forward to the visit of His Majesty King Carl XVI Gustaf and Her Majesty Queen Silvia and others from Sweden to our celebration next April.

Now I would like to discuss the discovery of the crown ethers. I will divide my lecture into three parts.

First, because every discovery takes place in more than a scientific context, I would like to touch on my life and background. In the weeks since it was announced that I would share this year's prize in chemistry, people have expressed as much interest in my early life as they have in my later work. So I think it appropriate to express myself on the matter. It may also be that details of my past have more than casual bearing on my work.

Second, I would like to describe for you my research program and some of the specific events that led to the discovery of the first crown ether. Since I am the only one who knows at firsthand the excitement and pleasure of the discovery, I will devote a portion of my time to sharing this experience with you.

And third, I would like to discuss the properties and preparation of crown ethers. In doing so, I hope I will convey to you that I was always a "hands-on" chemist; I took satisfaction from what I did in the laboratory. Also, I was very much an industrial chemist and was always interested in the potential application of my work. In fact, when I submitted my first major paper on the discovery of the crown ethers, the editor of the *Journal of the American Chemical Society*, Marshall Gates, remarked that my descriptions were replete with industrial jargon. Fortunately he published the paper anyway.

*Personal background*

Let me start then with how I began life and went on to discover the crown ethers.

My father, Brede Pedersen, was born in Norway in 1865 and trained as a marine engineer. Due to sibling disharmony, he left home for good as a young man and shipped out as an engineer on a steam freighter to the Far East. He eventually arrived in Korea and joined the fleet of the Korean customs, which was administered by the British. He rose in rank and later joined one of the largest Japanese steamship lines and became a chief engineer. Then a tragedy occurred that changed the course of his life. A childhood disease took the life of my elder brother while my father was away from home on a long journey. He abandoned the sea and became a mechanical engineer at the Unsan Mines in what is now the northwestern section of present-day North Korea.

My mother, Takino Yasui, was born in 1874 in Japan. She had accompanied her family to Korea when they decided to enter a large-scale trade in soybeans and silkworms. They established headquarters not far from the Unsan Mines, where she met my father.

The Unsan Mines were an American gold and lumber concession, 500 square miles in area. It had been granted by the Emperor of Korea to an American merchant named James R. Morse prior to 1870. I was conceived there in mid-winter just before the start of the Russo-Japanese war. Frequent incursions by Cossacks across the Yalu River into the region of the mines were considered to endanger my mother, so she and several American ladies were sent south by carriage to the railhead for safety. I was thus born on October 3, 1904, in the southern Port of Fusan, the largest in Korea. My arrival was doubly welcomed because mother was still grieving the loss of her firstborn. She devoted the next 10 years to overseeing my education and that of my sister, Astrid, five years my senior, in foreign language schools.

I spent my first and last winter at the mines when I was 4 years old. The region was known for severe weather due to the confluence of the Siberian steppes, Mongolian Gobi Desert and the mountains of Korea. Large Siberian tigers still roamed the countryside and were frightened away with bells on the pony harnesses. Wolves killed children during the cold winter nights, and foxes slept on roofs against the chimneys to keep warm.

Because the Unsan Mines were an American enclave - the top management being all Americans - great emphasis was placed on making life as American as possible. The country club was the center of social activities and life was considerably more gentle than at the typical gold mine of the legendary American West. So my contacts with Americans began early, and I spoke English which was the common language at the mines.

I do not know if such an environment had a lifelong influence on me, but I can speculate that perhaps it did. Freedom of the Americans to administer their affairs in taking care of themselves in the wilds where things could not be ordered for overnight delivery no doubt taught a certain independent approach to problem solving. As for chemistry, I recall that the gold was recovered by the cyanide process, and the monthly cleanup day was marked by the pervasive

odor of the process. The pouring of the molten gold was always a beautiful sight, and that might have started my interest in chemistry. Also, my sister claimed that I loved to play with a collection of colorful Siberian minerals.

Foreign language schools did not exist in Korea then, and so at the age of 8, I was sent to a convent school in Nagasaki. When I was 10 years old, my mother took me to Yokohama where she remained with me for a year as I began my studies at St. Joseph College. St. Joseph was a preparatory school run by a Roman Catholic religious order of priests and brothers called the Society of Mary. There I received a general secondary education and took my first course in chemistry.

When it came time for me to start my higher education, there was no question of where it would be obtained. I had lived among Americans and had determined, with my father's encouragement, to study in America. I selected the University of Dayton in Ohio for two reasons: First, we had family friends in Ohio, and secondly, the same organization, the Society of Mary, ran both St. Joseph College and the University of Dayton.

My four years in Dayton and a year in graduate school at Massachusetts Institute of Technology were pleasant and taken up with activities that made me into an American. This perhaps also molded my scientific character and represented something of a personal metamorphosis. The sequence - Dayton first and then MIT - was also good, making a false start by a young man much less likely. The University of Dayton was a college of 400 men, most of them living in dormitories under strict monastic regimen. Training of the spirit was considered as important as training of the body and soul. I enjoyed all phases of the training. I became vice president of my graduating class, won letters in tennis and track and a gold medal for excellence that reflected my four years of performance there. Excellence in general was encouraged; I was even awarded a gold medal for conduct.

MIT was another matter. Boston, where I lived, is an old city of great charm and a center of the arts. I did not apply myself to my courses as I should, but my extracurricular activities contributed to the formation of my ultimate character. It was while studying at MIT that I first felt the exhilaration of utter freedom. MIT was considered deficient in the humanities, but with a little effort that deficiency could be remedied delightfully by visiting second-hand book stores. Why second-hand books appealed to me more than library books still remains a mystery - though it possibly was the prospect of finding unexpected treasures. I celebrated my graduation from MIT as a chemist by taking a walking tour of the Presidential Range in New Hampshire.

In spite of the urging of James F. Norris - a very prominent professor and my research advisor - I did not remain at MIT to take a Ph.D. My bills were still being paid by my father, and I was anxious to begin supporting myself. In 1927, I obtained employment at Du Pont through the good offices of Professor Norris, and I was fortunate enough to be directed to research at Jackson Laboratory by William S. Calcott. My career of 42 years had begun.

The research environment at Du Pont during those years was not altogether typical of industrial laboratories of the time. The company had formed the

nucleus of a basic research department that in a few years' time would have scientists such as Wallace Carothers and the young Paul Flory working on the polymer studies that led to nylon and other breakthroughs. And in general, Du Pont was a productive center of research where many interesting and important problems were being solved. For example, one day while visiting Julian Hill at the Du Pont Experimental Station in Wilmington, Delaware, I observed him pull the first oriented fiber of a polyester. On another occasion, at Jackson Laboratory, across the Delaware River in New Jersey where I worked, I noticed commotion in the laboratory of Roy Plunkett, which was across the hall from my own. I investigated and witnessed the sawing open of a cylinder from which was obtained the first sample of Teflon<sup>®</sup> fluoropolymer. At Jackson Laboratory, during that time, other important advances were taking place in tetraethyl lead and new petroleum chemicals, new elastomers, and a new series of fluorocarbons for refrigeration and aerosols. The atmosphere was vibrant and exciting, and success was expected. It was in this atmosphere I began my career.

As a new scientist I was initially set to work on a series of typical problems, the successful solution of which buoyed my research career (Ref. 1-5). After a while, I began to search for oil-soluble precipitants for copper, and I found the first good metal deactivator for petroleum products (Ref. 6-8). As a result of this work, I developed a great interest in the effects of various ligands on the catalytic properties of copper and the transition elements generally, and I worked in that field for several years. I noticed a very unusual synergistic affect wherein a metal deactivator greatly increased the efficacy of antioxidants (Ref. 9-10).

So more and more, I became interested in the oxidative degradation of the substrates themselves, particularly petroleum products and rubber. As my interests moved in that direction, I left off working on metal deactivators and coordination chemistry. By the mid-1940s, I was in full career, having established myself in the field of oxidative degradation and stabilization (Ref. 11-13). I was independent in terms of the problems I might choose and had achieved the highest non-management title then available to a scientist at Du Pont. During the 1940s and 1950s, my interests became more varied. For example, I became interested in the photochemistry of new phthalocyanine adducts and of quinoneimine dioxides. I found some polymerization initiators, discovered that ferrocene was a good antiknock agent for gasoline, and made some novel polymers (Ref. 14-23).

#### *Discovery of the crown ethers*

But then there arose a challenging opportunity that led me back to ligand chemistry. In response to my desire to contribute to the elastomer field, my colleague Herman Schroeder suggested that there was an interesting problem in the coordination chemistry of vanadium. This sparked my curiosity, and I began work with the initial goal of understanding factors which govern catalytic activity of vanadium in oxidation and polymerization. This was a relatively unexplored area, and previous work had been empirical. It was my work in this

## Copper Complex of N,N'-(1,2-Propylenebis)(Salicylideneimine)

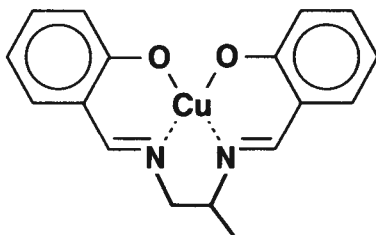


Fig. 1

area that led to the discovery of crown ethers, which I will now describe.

As I have related, I studied for many years the autoxidation of petroleum products and rubber and its retardation by antioxidants. Autoxidation is greatly catalyzed by trace metals, such as copper and vanadium. Hence, I had developed the compounds referred to earlier, namely the "metal deactivators" which suppress the catalytic activity of the metal salts by converting them into inactive multidentate complexes. The first of these was N,N'-(1,2-propylenebis)(salicylideneimine) shown in Figure 1 - an excellent deactivator for copper which has been used industrially for many years.

In 1960 when I returned to investigations in coordination chemistry, I decided to study the effects of bi- and multidentate phenolic ligands on the

## Synthesis of Bis[2-(o-Hydroxyphenoxy)Ethyl]Ether

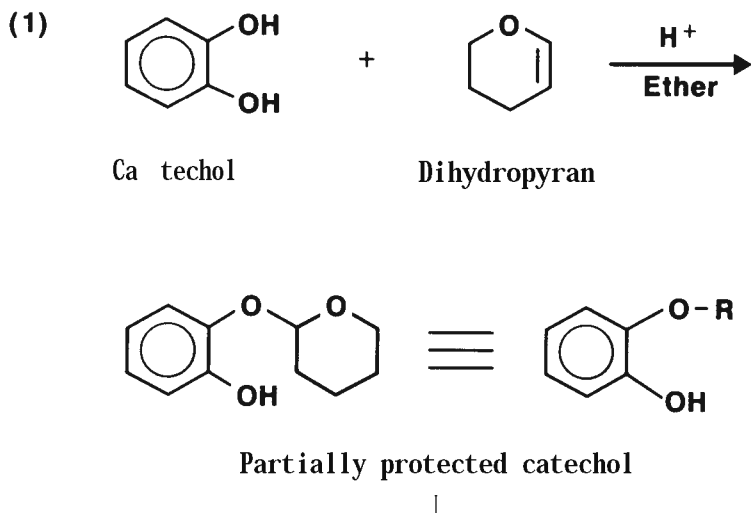


Fig. 2.

catalytic properties of the vanadyl group, VO (Ref. 24). The multidendate ligand I selected is the bis[2-(*o*-hydroxyphenoxy)ethyl] ether whose synthesis is depicted in Figure 2. As I proceeded, I knew that the partially protected catechol was contaminated with about 10 percent unreacted catechol. But I decided to use this mixture for the second step anyway since purification would be required at the end. The reactions were carried out as outlined and gave a product mixture in the form of an unattractive goo. Initial attempts at purification gave a small quantity (about 0.4 percent yield) of white crystals which drew attention by their silky, fibrous structure and apparent insolubility in hydroxylic solvents.

The appearance of the small quantity of the unknown should have put me in a quandary. I probably was not the target compound because that would be obtained in a higher yield. My objective was to prepare and test a particular compound for a particular purpose. Had I followed this line, I would have doomed the crown ethers to oblivion until such a time as another investigator would retrace my steps and make the better choice at the critical moment. Crown ethers, however, were in no danger, because of my natural curiosity. Without hesitation, I began study of the unknown

It was fortunate that I used an ultraviolet spectrophotometer to follow the reactions of the phenols. These compounds and their ethers in neutral methanol solutions absorb in the region of 275 millimicrons. On treatment with alkali, the absorption curve is not significantly altered if all the hydroxyl groups are covered, but it is shifted to longer wavelengths and higher absorption if one or more hydroxyl groups are still free, as shown by the dashed curve in Figure 3.

### Synthesis of Bis[2-(*o*-Hydroxyphenoxy)Ethyl] Ether

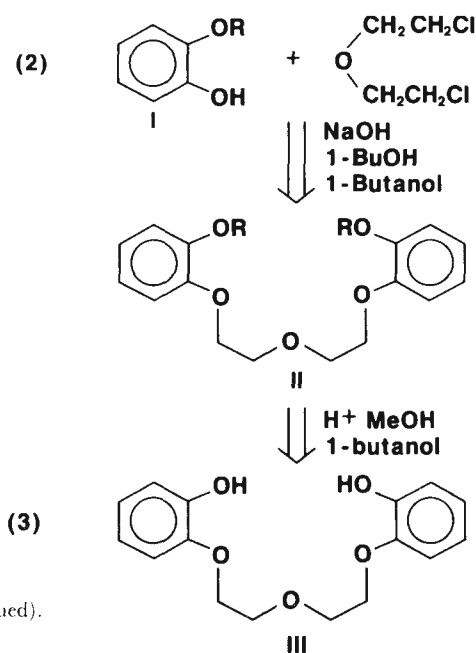


Fig. 2 (continued).

## Effect of NaOH on Ultraviolet Spectrum

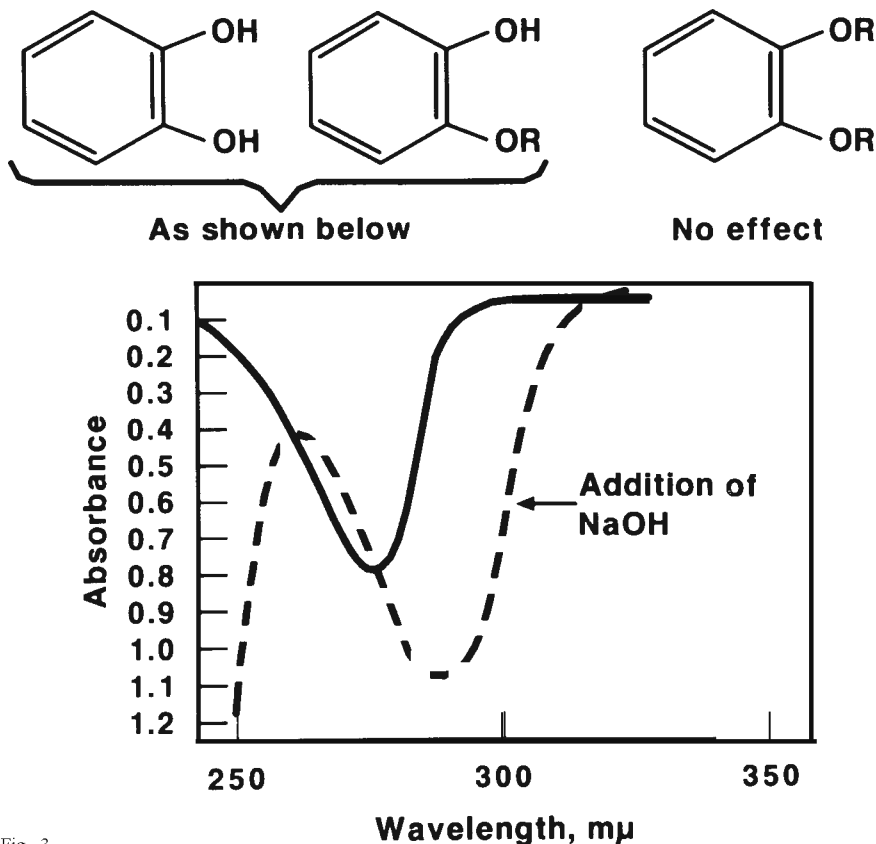


Fig. 3.

The unknown product was very little soluble in methanol, and the neutral solution gave an absorption curve characteristic for a phenolic compound. The solution was made alkaline with sodium hydroxide with the expectations that the curve would either be unaffected or shifted to longer wavelengths. The resulting spectrum, however, showed neither effect, but rather the one shown in Figure 4. At the same time, I noticed that the fibrous crystals were freely soluble in methanol in the presence of sodium hydroxide. This seemed strange since the compound did not contain a free phenolic group, a fact confirmed by its infrared and NMR spectra. I then found that the compound was soluble in methanol containing any soluble sodium salt. Thus, the increased solubility was due not to alkalinity but to sodium ions. But there was no obvious explanation for the behavior of the compound because its elementary analysis corresponded with that for a 2,3-benzo-1,4,7-trioxacyclononane, (Figure 5) a plausible product from the reaction of catechol and bis(2-chloroethyl)ether in the presence of sodium hydroxide. However, the moment of revelation came when I learned that its molecular weight was exactly twice that of the above compound. The true structure was that of an 18-membered ring, dibenzo-18-

## Effect of Sodium Hydroxide on the Ultraviolet Spectrum of Dibenzo-18-Crown-6 in Methanol

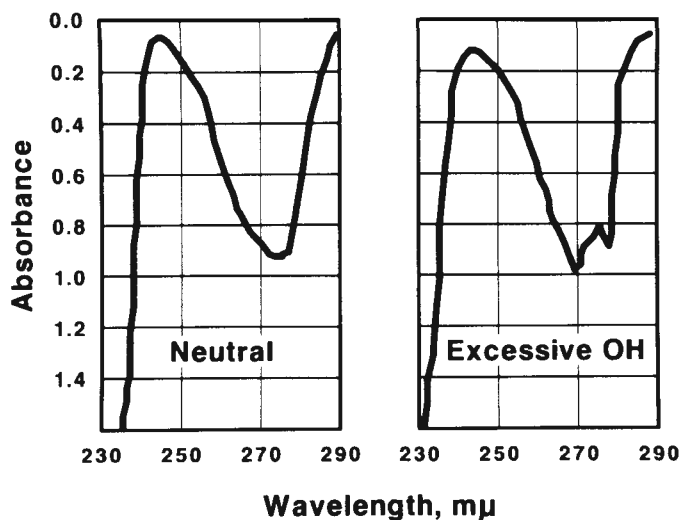


Fig. 4.

crown-6, the first and most versatile of the aromatic crown compounds, depicted in Figure 6. The shape is that of a torus or a doughnut.

It seemed clear to me now that the sodium ion had fallen into the hole in the center of the molecule and was held there by the electrostatic attraction between its positive charge and the negative dipolar charge on the six oxygen atoms symmetrically arranged around it in the polyether ring. Tests showed that other alkali metal ions and ammonium ion behaved like the sodium ion so that, at long last, a neutral compound had been synthesized which formed stable complexes with alkali metal ions. Up to that point, no one had ever found a synthetic compound that formed stable complexes with sodium and potassium.

## 2,3-Benzo-1,4,7-Trioxacyclononane

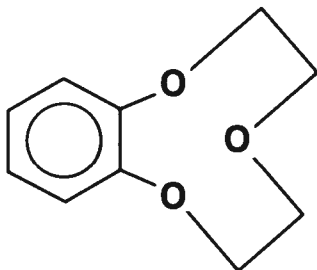
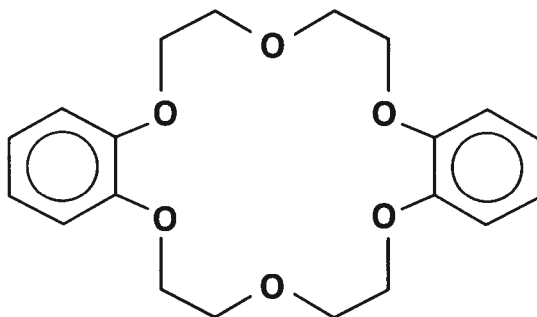


Fig. 5.



## Dibenzo-18-Crown-6



### 2,3,11,12-Dibenzo-1,4,7,10,13,16-Hexaoxacyclo-octadeca-2,11-Diene

Fig. 6.

My excitement, which had been rising during this investigation, now reached its peak and ideas swarmed in my brain. One of my first actions was motivated by esthetics more than science. I derived great esthetic pleasure from the three-dimensional structure as portrayed in the computer-simulated model in Figure 7. What a simple, elegant and effective means for the trapping of hitherto recalcitrant alkali cations! I applied the epithet "crown" to the first member of this class of macrocyclic polyethers because its molecular model looked like one and, with it, cations could be crowned and uncrowned without physical damage to either as shown for the potassium complex in Figure 8. As my studies progressed, I created the system of crown nomenclature chiefly because the official names of the crown ethers were so complex and hard for me to remember. It is a source of special satisfaction to me that this system of abbreviated names, devised solely for the ready identification of the macrocyclic polyethers, has been retained by the scientific establishment. In Figure 9 I have illustrated how the nomenclature system is made up of the side-ring substituents, the total number of oxygen atoms in the main ring and the size of the ring.

Another aspect of this discovery filled me with wonder. In ordinary organic reactions only rings of 5, 6, or 7 members form easily. Here a ring of 18 atoms had been formed in a single operation by the reaction of two molecules of catechol, which was present as a minor impurity, with two molecules of bis(2-chloroethyl)ether. Further experiments revealed that dibenzo-18-crown-6 can be synthesized from these intermediates in a 45 percent yield without resorting to high dilution techniques. This was most unexpected and some good reason must exist for such an unusual result. I concluded that the ring-closing step, either by a second molecule of catechol or a second molecule of bis(2-chloroethyl)ether, was facilitated by the sodium ion which, by ion-dipole interaction, "wrapped" the molecular pieces around itself to form a three-quarter circle and

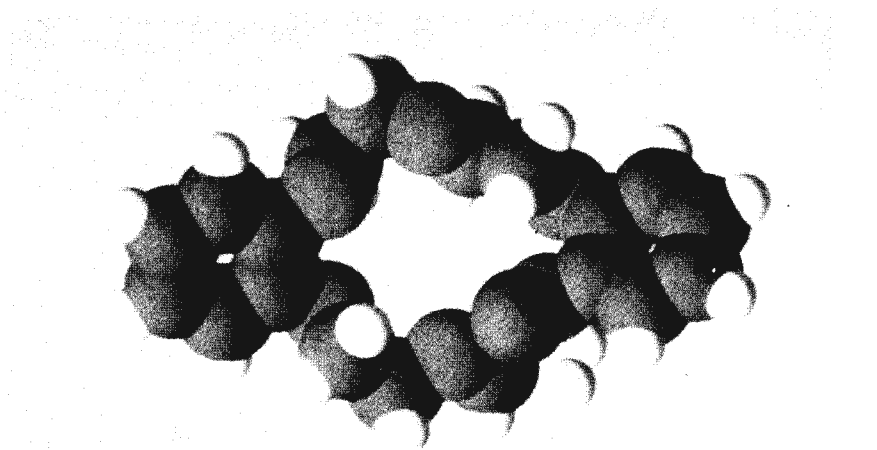


Fig. 7

disposed them for the final ring closure in much the same fashion as is involved in the synthesis of the porphyrins and phthalocyanines. Later experiments appear to support this hypothesis. The yields of dibenzo-18-crown-6 are higher when it is prepared with sodium or potassium hydroxide than when lithium or tetramethylammonium hydroxide is used. Lithium and the quaternary ammonium ions are not strongly complexed by the polyether. The best complexing agents are rings of 15 to 24 atoms including 5 to 8 oxygen atoms. They are formed in higher yields than smaller or larger rings, or rings of equal sizes with only four oxygen atoms. Finally, even open-chain polyethers such as 3,4,12,13-dibenzo-2,5,8,11,14-pentaoxapentadeca-3,12-dienc (Figure 10) were found to form complexes with sodium and potassium ions.

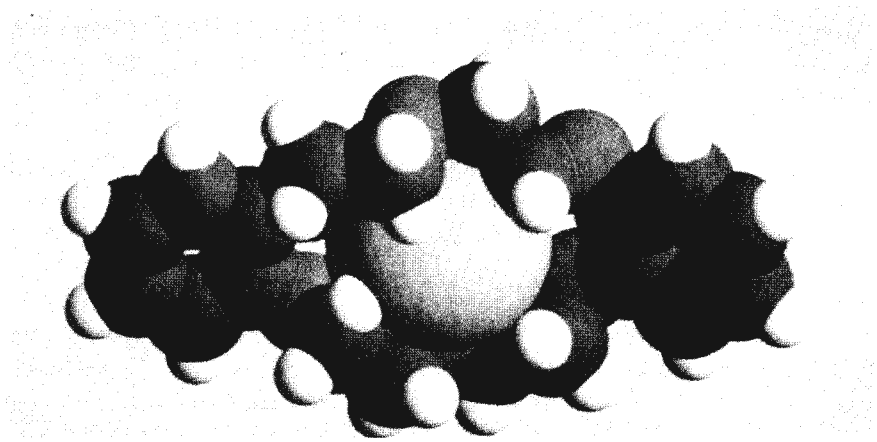
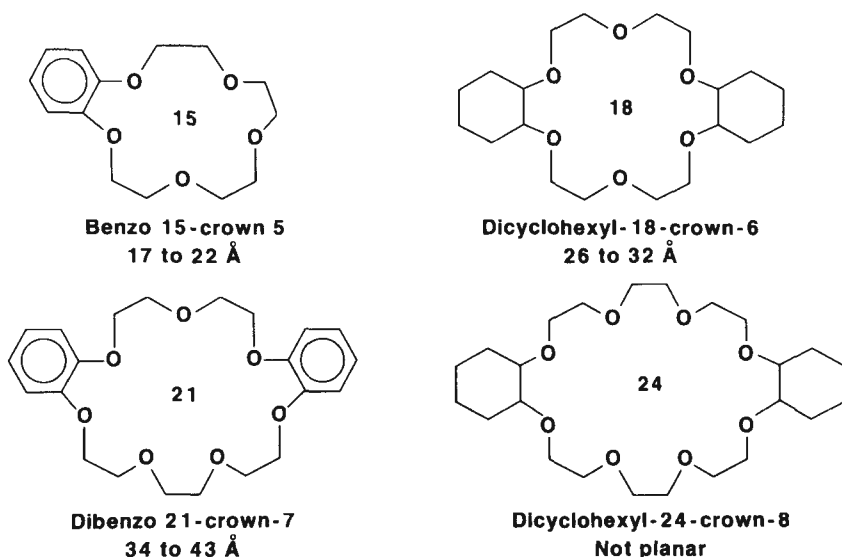


Fig. 8

### Some Macrocyclic Polyethers



**The numbers within the diagrams are the numbers of atoms in the polyether rings. The numbers under the names are the estimated diameters of the holes in Å.**

Fig. 9

Thus did I discover dibenzo-18-crown-6, the first crown ether and the first neutral synthetic compound capable of complexing the alkali metal cations (Ref. 25-26, 36).

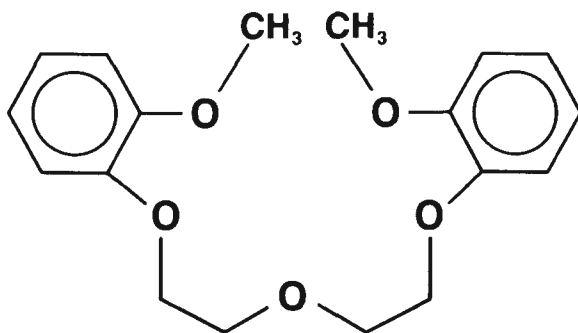
With the realization that I had something very unusual and with the utmost curiosity and anticipation, I devoted all my energies over the next several years to the study of this fascinating class of ligands and their interaction with inorganic cations. Every successful experiment produced a significantly novel result and led to new thoughts on what to synthesize and also as to the many potential uses of these extraordinary substances.

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

#### *Preparation and properties of macrocyclic polyethers*

Spurred by curiosity regarding the factors involved in the stability of the salt complexes (such as the relative sizes of the hole and the cation, and the number and symmetrical arrangement of the oxygen atoms in the polyether ring), I initiated an extensive program of syntheses. Ultimately, about 60 macrocyclic polyethers were prepared containing 12 to 60 atoms to a polyether ring including 4 to 10 oxygen atoms and some with nitrogen and sulfur atoms. Many of these compounds were found to be useless as complexing agents, but they

## Dibenzo - 18 - Crown - 6



## 3,4,12,13-Dibenzo - 2,5,8,11,14-Pentaoxa-pentadeca - 3,12-Diene

Fig. 10.

served to define the effective ones which are compounds containing 5 to 10 oxygen atoms in the ring, each separated from the next by 2 carbon atoms. I also noted that even whole molecules such as the thioureas formed complexes with some crown compounds. I accomplished all this working alone with the help of my able technician, Ted Malinowski.

Some of the general properties of the aromatic macrocyclic polyethers are as follows: They are neutral, colorless compounds with sharp melting points, and are little soluble in water and alcohols, fairly soluble in aromatic solvents, and very soluble in methylene chloride and chloroform. They undergo substitution reactions characteristic for aromatic ethers (halogenation, nitration, etc.), and form formaldehyde resins when treated with paraformaldehyde under acid conditions. They are decomposed by reactions which cause the scission of ethers.

The saturated macrocyclic polyethers are obtained most simply by catalytically hydrogenating the aromatic compounds using ruthenium catalyst. Bridge-bond isomers are obtained from compounds containing two or more aromatic side-ring substituents. For example, dibenzo-18-crown-6 gives a mixture of stereoisomers of dicyclohexyl-18-crown-6. The saturated polyethers are colorless, viscous oils or solids of low melting points. They are thermally stable but, like the aromatic compounds, must be protected from oxygen at high temperatures. They are, as a group, very much more soluble than the aromatic compounds in all solvents, and most of them are even soluble in petroleum ether.

The unique property of the macrocyclic polyethers as complexing agents is their preference for alkali metal ions, which do not form complexes with the numerous ligands used for the transition metal ions. The crown compounds form stable crystalline complexes and solutions of the complexes with some or

# Diameters of Holes in Ångström Units

<u>Macrocyclic Polyethers</u>	<u>Diameters</u>
<b>All 14-crown-4</b>	<b>1.2-1.5</b>
<b>All 15-crown-5</b>	<b>1.7-2.2</b>
<b>All 18-crown-6</b>	<b>2.6-3.2</b>
<b>All 21-crown-7</b>	<b>3.4-4.3</b>

Table I.

all of the cations of alkali and alkaline earth metals plus ammonium ions and others. Some of them, for example, dicyclohexyl-18-crown-6, also form complexes with Co(II), and some other transition metal ions. The saturated compounds are better complexing agents than the corresponding aromatic compounds.

Three criteria have been used for the formation of complexes between macrocyclic polyethers and salts: (a) isolation of the complexes as crystals; (b) characteristic changes in the ultraviolet spectra of the aromatic compounds; and (c) changes in the solubilities of the polyethers and salts in different solvents.

As is evident from Table 1, these compounds have holes of different diameters in the center of the polyether rings. The uncomplexed cations also differ in size, given in Table 2 in Ångstroms units: sodium 1.94, potassium 2.66, ammonium 2.86, rubidium 2.94, and cesium 3.34. Depending, therefore, on the relative sizes of the hole and the cation, crystalline complexes with polyether/cation ratios of 1:1, 3:2, and 2:1 have been prepared as illustrated in Table 3. The aromatic macrocyclic polyethers tend to give high melting complexes which are not readily soluble in aprotic solvents, while the saturated compounds give lower melting complexes which are more soluble. Most of the pure complexes are decomposed by water, the rate and extent of decomposition depending on the proportion of water and the temperature.

It was postulated from the beginning that complexes of macrocyclic polyethers containing less than seven oxygen atoms consisted of a cation surrounded by the oxygen atoms arranged symmetrically in a single plane. The essential correctness of this view of the structure has been confirmed by Professor M. R. Truter and her collaborators who have been the first to determine the structures of a number of crystalline salt complexes of crown compounds by X-ray diffraction methods (Ref. 27).

All macrocyclic polyethers containing one or more benzo groups have a characteristic absorption maximum at 275 millimicrons in methanol, and the shapes of the curves are altered by the addition of complexable salts as was shown in *Figure 4*. The spectral evidence is nearly always confirmed by the other two criteria.

## Complexable Cations and Their Diameters in Ångström Units

<u>Group I</u>		<u>Group II</u>		<u>Group III</u>		<u>Group IV</u>	
<b>Li</b>	<b>1.36</b>						
<b>Na</b>	<b>1.94</b>						
<b>K</b>	<b>2.66</b>	<b>Ca</b>	<b>1.98</b>				
<b>Cu(I)</b>	<b>1.92</b>	<b>Zn</b>	<b>1.48</b>				
<b>Rb</b>	<b>2.94</b>	<b>Sr</b>	<b>2.26</b>				
<b>Ag</b>	<b>2.52</b>	<b>Cd</b>	<b>1.94</b>				
<b>Cs</b>	<b>3.34</b>	<b>Ba</b>	<b>2.68</b>	<b>La</b>	<b>2.30</b>		
<b>Au(I)</b>	<b>2.88</b>	<b>Hg(II)</b>	<b>2.20</b>	<b>Tl(I)</b>	<b>2.80</b>	<b>Pb(II)</b>	<b>2.40</b>
<b>Fr</b>	<b>3.52</b>	<b>Ra</b>	<b>2.80</b>				
<b>NH<sub>4</sub></b>	<b>2.86</b>						

Table 2.

Macrocyclic polyethers and complexable salts mutually increase their solubilities in solvents wherein the complexes are soluble. Sometimes these effects are spectacular, for instance, the solubility of the potassium thiocyanate complex is about a tenth of a mole per liter, a 100-fold increase. Some of the saturated polyethers, such as dicyclohexyl-18-crown-6, have the useful property of solubilizing alkali metal salts, particularly those of potassium, in aprotic solvents. Crystals of potassium permanganate, potassium tertiary-butoxide, and potassium palladous tetrachloride ( $\text{PdCl}_2 + 2\text{KCl}$ ) can be made to dissolve in liquid aromatic hydrocarbons merely by adding dicyclohexyl-18-crown-6. This is dramatic for the crown complex of potassium permanganate which colors toluene purple. Benzylpotassium is rendered soluble in n-heptane by the polyether, but the polyether ring is gradually decomposed by this organometallic compound. The solubilizing power of the saturated macrocyclic polyethers permits ionic reactions to occur in aprotic media. It is expected that this property will find practical use in catalysis, enhancement of chemical reactivity, separation and recovery of salts, electrochemistry, and in analytical chemistry.

The complexing efficiencies of saturated macrocyclic ethers can be ranked numerically by measuring the relative distribution of a colored alkali metal salt (such as picrate) between an immiscible organic solvent and water in the presence of the crown ether as depicted. If the polyether is ineffective, the organic phase will be colorless; if the polyether is very powerful, most of the color will be in the organic phase. The efficiencies of the polyether will lie between these two limits as shown in Table 4 (Ref. 28-35).

Dr. H. K. Frensdorff has determined the stability constants for 1:1 complexes of many macrocyclic polyethers with alkali metal ions by potentiometry with

## Crystalline Complexes of Polyethers

<u>Crystalline Complex</u>	<u>Mole Ratio<sup>a</sup></u>
<b>Benzo-15-crown-5</b>	
NaI	1:1
KCNS	2:1
<b>Dibenzo-15-crown-5</b>	
KCNS	2:1
<b>Dibenzo-18-crown-6</b>	
KCNS	1:1
NH <sub>4</sub> CNS	1:1
RbCNS	1:1
RbCNS	2:1
CsCNS	2:1
CsCNS	3:2
<b>Dicyclohexyl-18-crown-6</b>	
KI <sub>3</sub>	1:1
CsI <sub>3</sub>	3:2
<b>Dibenzo-24-crown-8</b>	
KCNS	1:1
KCNS	1:2
<b>Dibenzo-30-crown-10</b>	
KCNS	1:1
NaCNS	1:2
<sup>a</sup> (Polyether):(salt).	

Table 3.

cation-selective electrodes. Selectivity toward the different cations varies with polyether ring size, the optimum ring size being such that the cation just fits into the hole, that is 15-18 for sodium ion, 18 for potassium ion, and 18-21 for cesium ion (Ref. 33).

That concludes my remarks on the discovery, properties and preparation of the crown ethers. It remains only for me to mention certain individuals who contributed to the success of my research and to add a few words concerning my interest and hope for the future of research in this area.

First, I want to remember on this occasion my wife Susan who died in 1983. It would have been wonderful to share with her all that has happened to me of late as we shared everything else during our marriage of 36 years.

Next, I would like to thank the Du Pont Company. They encouraged me to pursue my research on crown ethers, even when it was evident that, at least initially, my work might not have a significant practical impact. At another company, I might not have met with such encouragement and latitude.

Within the company I received support from certain individuals. I appreciate the advice and counsel of my close friend, Dr. Herman Schroeder, who was

## Extraction Results''

<u>Polyether</u>	<u>Picrate Extracted (%)</u>			
	<u>Li<sup>+</sup></u>	<u>Na<sup>+</sup></u>	<u>K<sup>+</sup></u>	<u>Cs<sup>+</sup></u>
<b>Dicyclohexyl- 14-crown-4</b>	<b>1.1</b>	<b>0</b>	<b>0</b>	<b>0</b>
<b>Cyclohexyl- 15-crown-5</b>	<b>1.6</b>	<b>19.7</b>	<b>8.7</b>	<b>4.0</b>
<b>Dibenzo- 18-crown-6</b>	<b>0</b>	<b>1.6</b>	<b>25.2</b>	<b>5.8</b>
<b>Dicyclohexyl- 18-crown-6</b>	<b>3.3</b>	<b>25.6</b>	<b>77.8</b>	<b>44.2</b>
<b>Dicyclohexyl- 21-crown-7</b>	<b>3.1</b>	<b>22.6</b>	<b>51.3</b>	<b>49.7</b>
<b>Dicyclohexyl- 24-crown-8</b>	<b>2.9</b>	<b>8.9</b>	<b>20.1</b>	<b>18.1</b>

### <sup>a</sup>Two-phase liquid extraction: methylene chloride and water.

Table 4.

always interested in my research and whose companionship has meant so much to me during the many years we have known each other. I also thank my friend Dr. Rudolph Pariser, who has been tireless in his efforts to assure recognition for my accomplishments.

Finally, I want to thank the analytical groups of the company for making all their resources available to me; my technical colleagues for their scientific consultation; and our academic friends for their interest.

Of course, I must mention my respect and admiration for the two scientists with whom I share this year's prize. If I may use an analogy reflecting my youth at the Unsan gold mines, I see the discovery of the crown ethers as comparable to the finding of a new field with a lot of action in it. Professor Cram and Professor Lehn staked claims to particular veins of rich ore and went on to discover gold mines of their own.

I know that the crown ethers continue to create great interest among biologists for studying the mechanism of transport of ions across cell membranes (Ref. 36). But whether it be in biology or some other field, it is my fervent wish that before too long it matters not by whom the crown ethers were discovered but rather that something of great benefit to mankind will be developed about which it will be said that were it not for the crown compounds it could not be.



## REFERENCES

1. F. B. Downing, A. E. Parmalee and C. J. Pedersen, U.S.P. 2,004,160 (6/11/35) to Du Pont.
2. F. B. Downing and C. J. Pedersen U.S.P. 2,008,753 (7/23/35) to Du Pont; also 2,087,103 (7/11/37).
3. R. G. Clarkson and C. J. Pedersen, U.S.P. 2,054,282 (7/15/36) to Du Pont.
4. L. Spiegler and C. J. Pedersen, U.S.P. 2,087,098 (7/13/37) to Du Pont.
5. F. B. Downing and C. J. Pedersen, U.S.P. 2,121,397 (6/21/38) to Du Pont.
6. F. B. Downing and C. J. Pedersen, U.S.P. 2,181,121 (11/28/39) to Du Pont.
7. C. J. Pedersen, *Oil & Gas Journal*, p. 97, July 27, (1939).
8. C. J. Pedersen, *Ind. & Eng. Chem.*, 41, 824, (1949).
9. C. J. Pedersen, *Delaware Symposium*, Dec. 1, (1948). Prooxidant Catalytic Activity of Metal Chelates.
10. C. J. Pedersen, *Symposium on Chelate Chemistry*. Centenary Celebration of Brooklyn Polytechnic Institute, New York, N.Y. Published in *Advances in Chelate Chemistry*, p. 113 (1954).
11. C. J. Pedersen, *Delaware Chemical Symposium*, Jan. 21, (1950). Mechanism of Decomposition of Perbenzoic Acid Compared with Benzoyl Peroxide.
12. C. J. Pedersen, Antioxidants, *Encyclopedia Britannica*, (1953).
13. C. J. Pedersen, *J. Org. Chem.*, 22, 127 (1957); U.S.P. 2,662,895-7 (12/15/53); U.S.P. 2,681,347 (6/15/54); U.S.P. 2,741,531 (5/12/56); U.S.P. 2,831,805 (4/22/58) all to Du Pont.
14. C. J. Pedersen, *Ind. & Eng. Chem.*, 48, 1881 (1956).
15. C. J. Pedersen, *J. Am. Chem. Soc.*, 79, 2295 (1957).
16. C. J. Pedersen, *J. Am. Chem. Soc.*, 79, 5014 (1957); U.S.P. 2,681,918 (6/22/54); U.S.P. 2,741,625 (4/10/56); U.S.P. 2,831,805 (4/22/58) all to Du Pont.
17. C. J. Pedersen, U.S.P. 2,867,516 (1/6/59) to Du Pont.
18. C. J. Pedersen, U.S.P. 3,341,311 (9/12/67) to Du Pont.
19. C. J. Pedersen, U.S.P. 3,038,299-300 (6/12/62) to Du Pont.
20. C. J. Pedersen, *J. Org. Chem.*, 23, 252 & 255 (1958).
21. J. Diekmann and C. J. Pedersen, *J. Org. Chem.*, 28, 2879 (1963). See also *Chem. Rev.*, 67, 611 (1967, p. 617).
22. C. J. Pedersen, U.S.P. 3,232,914 (2/1/66) to Du Pont.
23. C. J. Pedersen, U.S.P. 3,320,214 (5/16/67) to Du Pont.
24. C. J. Pedersen, U.S.P. 3,361,778 (1/2/68) to Du Pont.
25. C. J. Pedersen, *J. Am. Chem. Soc.*, 89, 2495, 7017 (1967).
26. C. J. Pedersen, *Aldrichimica Acta*, (4) 1, 1 (1971).
27. M. R. Truter and C. J. Pedersen, *Endeavor*, XXX (111), 142 (1971).
28. C. J. Pedersen, *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, 27, 1305 (1968).
29. C. J. Pedersen, *J. Am. Chem. Soc.*, 92, 386 (1970).
30. C. J. Pedersen, *J. Am. Chem. Soc.*, 92, 391 (1970).
31. C. J. Pedersen, *J. Org. Chem.*, 36, 254 (1971).
32. C. J. Pedersen, *J. Org. Chem.*, 36, 1690 (1971).
33. C. J. Pedersen and H. K. Frensdorff, *Angew. Chem.*, 84, 16 (1972); *ibid.* (int. Ed.), 11, 16 (1972).
34. C. J. Pedersen, *Org. Syn.*, 52, 66 (1972).
35. C. J. Pedersen, U.S.P. 3,562,295, (2/9/71); U.S.P. 3,622,577 (11/23/71); U.S.P. 3,686,225 (8/12/72); U.S.P. 3,687,978 (8/12/72); with M. Bromeis U.S.P. 3,847,949 (1/12/74); U.S.P. 3,856,813 (12/24/74); U.S.P. 3,873,569 (3/25/75); U.S.P. 3,987,061 (10/19/76); U.S.P. 3,998,838 (12/21/76); with M. Bromeis U.S.P. 4,031,111 (6/21/77); all to Du Pont.
36. C. J. Pedersen in *Current Topics in Macrocyclic Chemistry in Japan*, Ed. E. Kimura, Hiroshima Univ. School of Medicine (1987), p. 1. H. E. Schroeder 5.