SYNTHESIS AND COMPLEXING PROPERTIES

OF QUATERENES

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By

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ABSTRACT

Several macrocyclic ethers (quaterenes) with limited cavity sizes were synthesized and characterized by infrared, ultraviolet and mass spectroscopy. Their complexing ability with selected metal ions was investigated to examine the analytical potential of the ligands. Unfortunately, no appreciable reaction could be detected by ultraviolet and proton NMR spectroscopy and by picrate extraction. It was concluded that the quaterenes are of not much interest as analytical ligands.

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I. INTRODUCTION

GENERAL

Since Werner proposed his coordination theory in 1893 (1) and especially in the last three decades, appreciable progress has been made in the understanding and development of organic chelating agents in coordination chemistry.

Research on multidentate chelating agents has been stimulated by a number of factors such as their interesting and often unique stereochemical properties, their widespread appearance in biological systems, and the many analytical applications found for sequestering agents. This interest has led to the synthesis and study of a wide variety of new chelating agents. The design, synthesis and application of such ligands provide an ideal field for collaboration between organic and analytical chemists.

Most chelating agents are unselective in their reactions with metal ions but their selectivity can be increased often by appropriate control of pH and by the use of suitable complexing agents to mask interfering ions. For example, 8-hydroxyquinoline forms water-insoluble precipitates with more than 30 metal ions (2,3) but the judicious choice of pH and complexing agents can enhance the selectivity appreciably. There is, however, a limit to which selectivity can be increased by these factors. During the last 30 years, a considerable amount of research has been done to determine the factors that affect the stability of metal chelates and thus govern their selectivity (4-7). The following factors are considered to be important in determining both the stability of metal chelates and the gross selectivity of the chelating agents (4,5): the size and number of chelate rings formed, the basicity of the donor atoms, the polarizability of the donor atoms; steric effects from suitably placed substituents in the ligand, and metal-ion properties such as ionization potential, charge-to-radius ratio and polarizability.

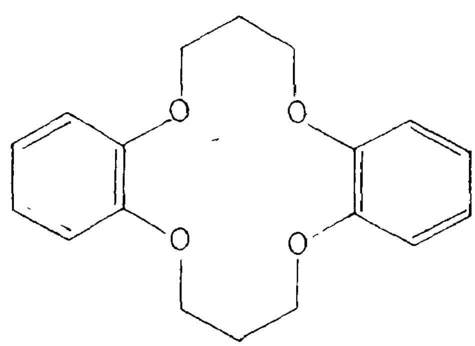
More recently, attention has been devoted to the study of metal chelates of macrocyclic ligands (8) and, in particular, to those of macrocyclic ligands of biological significance (e.g., ligands with a porphyrin nucleus, valinomycin and nonactin (9-11)). Studies of the antibiotics valinomycin and nonactin in turn stimulated the discovery of the "crown" macrocyclic polyethers by Pedersen (8). This thesis is concerned with macrocyclic ethers based on the tetrafuran, reduced tetrafuran, and mixed furan/pyrrole macrocyclic systems. These compounds are termed quaterenes and mixed quaterenes.

A historical introduction of the macrocyclic polyethers and of the quaterenes follows.

Historical

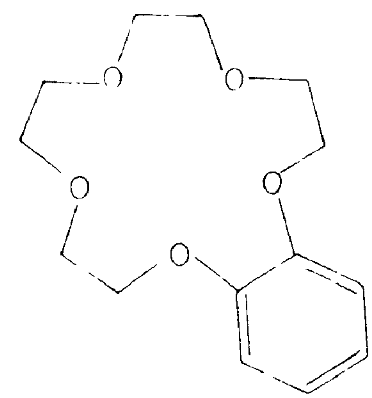
In the search for new and selective ligands, Pedersen synthesized over 60 cyclic polyethers containing from 9 to 30 atoms and 3 to 9 oxygen atoms, respectively (8,12). Pedersen noted that many of these cyclic polyethers formed stable complexes with alkali metal salts. This uncommon phenomenon was reminiscent of the behaviour which had been observed previously for certain biological materials and antibiotics (9,11). Since Pedersen's initial observation, several cyclic polyethers, such as cyclohexyl-18-crown-6 (13) and the structurally related antibiotics nonactin and valinomycin (14), have been shown to exhibit varying degrees of biological activity related to the process of active ion-transport (15). For example, Eisenman et al. (13) found the stability sequence for alkali metal ion complexes of cyclohexyl-18-crown-6 to be: $K^+ > Rb^+ > Cs^+ > Na^+ > Li^+$, which is identical to the permeability sequence for these metal ions across the mitochondrial membrane.

The most effective complexing agents are found among those cyclic polyethers which contain 5 to 10 oxygen atoms and in which the binding sites are separated by two carbon atoms. The structure and trivial names of three cyclic polyethers are given below:

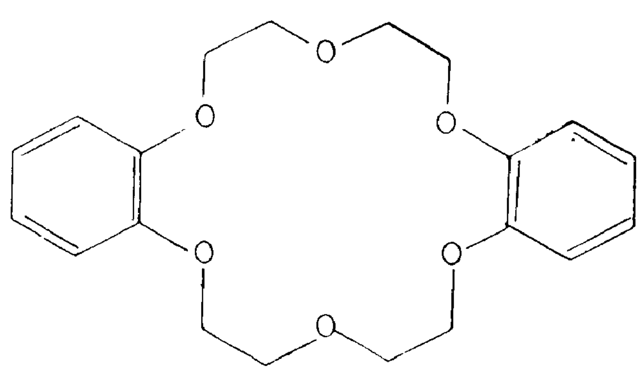


(I) Perhydrodibenzo-[14]-crown-4

The stoichiometry of the complexes formed by these ligands is one to one. The cation is encircled by the oxygen atoms of the polyether rings and held there by dipole-charge interactions. Certain crystalline complexes show stoichiometric ratios (ligand to cation) of two to one and three to one (16). Cyclic polyethers have been reported to form complexes with several cations such as, Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, RNH_3^+, Ag^+, Au^+,



(II) Perhydrobenzo-[15]-crown-5

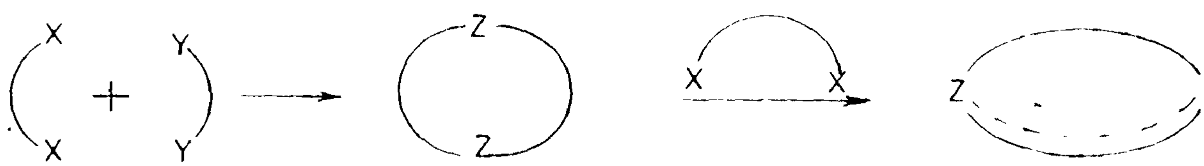


(III) Dibenzo-[18]-crown-6

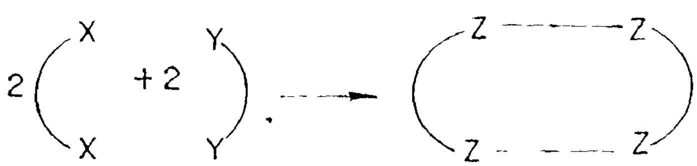
Ca^{2+}, Sr^{2+}, Ba^{+2}, Ra^{+2}, Zn^{+2}, Cd^{+2}, Hg^{+}, Hg^{+2}, La^{+3}, Tl^{+}, Ce^{+3}, and Pb^{+2} (8). A large number of parameters determine the stability of these complexes. These parameters include: cation size, type and charge; ligand cavity size, donor-atom number and type; and ring conformation (8,12).

IUPAC names of many of the polyethers are too complicated for repeated use (17). Therefore, a system of trivial names has been devised and is based on the following: (1) the number and kind of hydrocarbon rings; (2) the total number of atoms in the polyether ring; (3) the class name "crown" and (4) the number of oxygen atoms in the polyether ring. Thus, 2,3,11,12-dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene is called dibenzo-18-crown-6 (III).

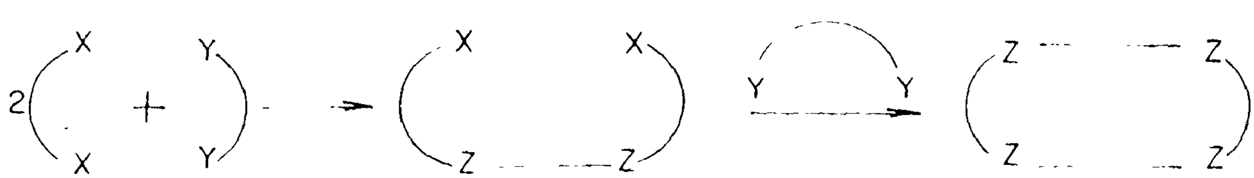
Corey and Petersen (18) introduced systematic procedures for varying the number of donor atoms by insertion of edges, vertices, and rings containing two or more edges. Macrocyclic systems can be obtained by elimination of one or more edges simultaneously as shown in the schematic reaction below.



(1)



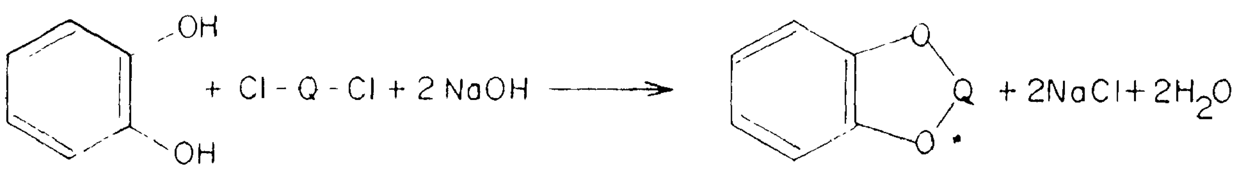
(2)



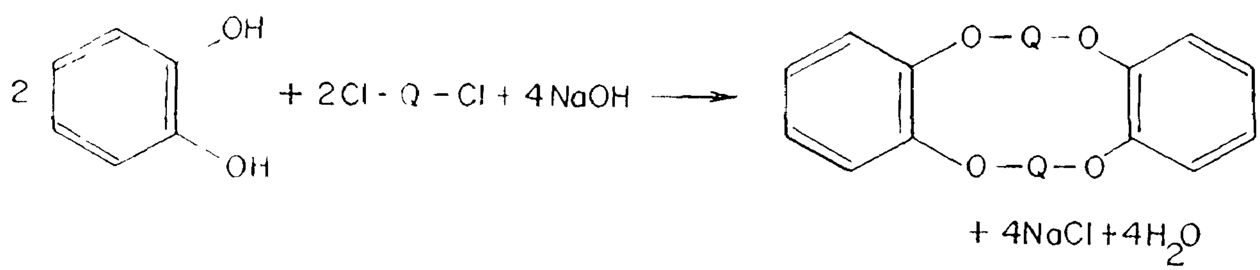
(3)

Here, -X is -OH or -SH (these groups are converted into O^- or S^- by base prior to reaction) and -Y is a leaving group, in general a halogen or tosylate.

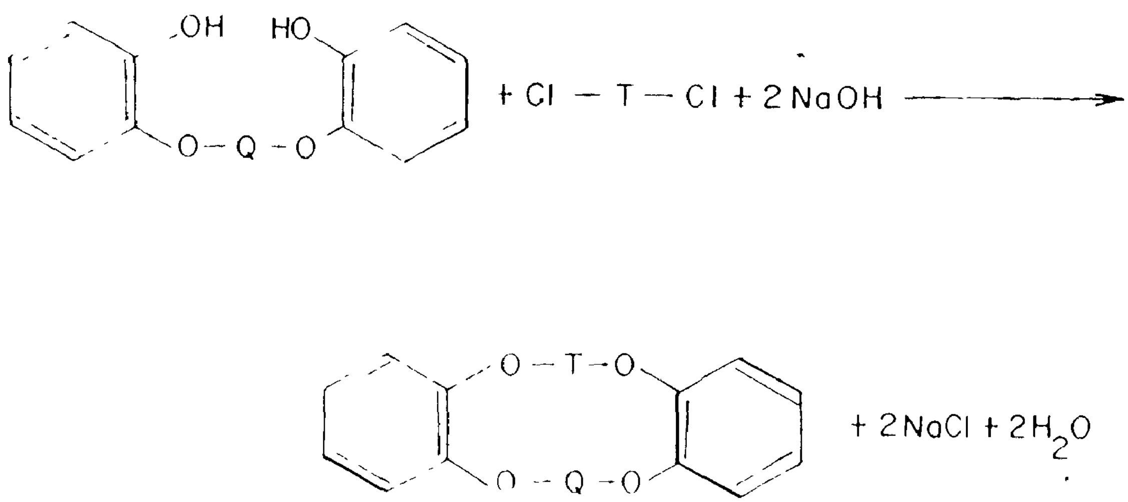
The preparation of the cyclic polyethers is shown in the following equations. The method involves a straightforward condensation in which Q and T represent organic groups which may or may not be identical, and which are generally of the type $-(CH_2CH_2O)_nCH_2CH_2-$ (8,12). Polymerization can be minimized by high dilution techniques or by template synthesis (19).



(4)



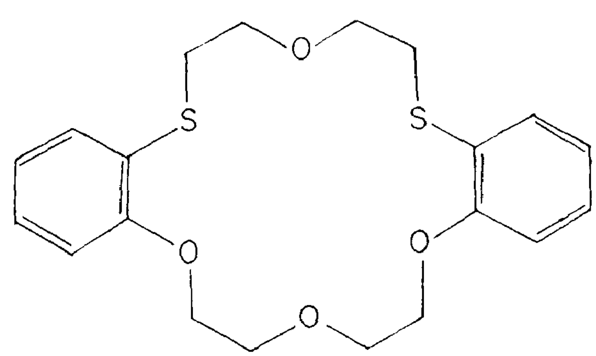
(5)



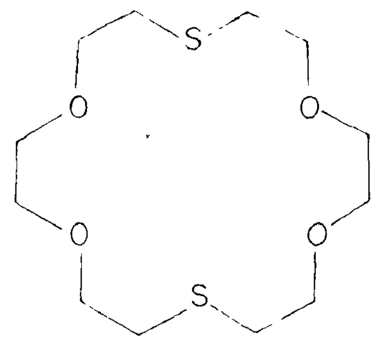
(6)

The condensation is usually done in 1-butanol under reflux for 12 to 24 hours. The first method is used for the preparation of monobenzo crown compounds while the second is used for the dibenzo crown compounds. The third method may require protection of one of the hydroxyl groups by a benzyl or tetrahydropyranyl group (followed by removal of the protective group before the cyclization step (17)). This method is most convenient for synthesis of uneven numbered polyether rings such as perhydrobenzo-15-crown-5 (II).

Macrocyclic rings containing donor atoms other than oxygen have been reported, e.g., one or more sulphur atoms have been substituted (19,20). They are prepared by similar condensation methods in which the hydroxyl groups are replaced by thiol groups. Examples are shown in structures (IV) and (V).

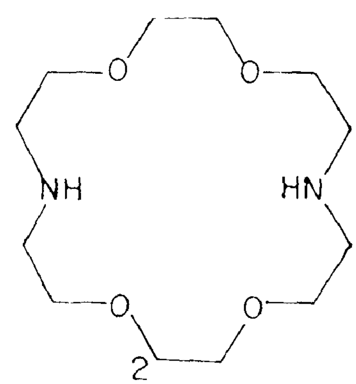


(IV) 2,3,11,12-dibenzo-1,7,13,16-tetroxa-4,10-dithiocyclo-octadeca-2,11-diene.

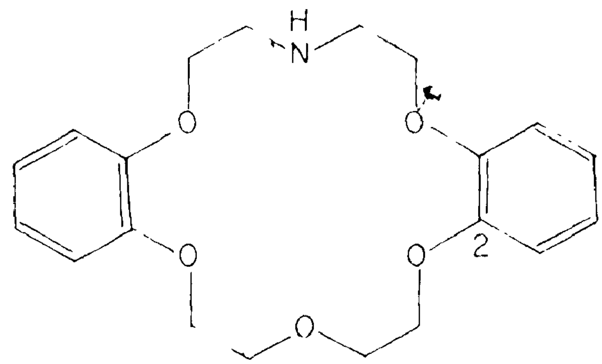


(V) 1,4,10,13-tetroxa-7,16-dithiocyclo-octadeca ether

Other macrocyclic compounds having one or two NH or NR groups replacing oxygen (21,22) have also been prepared. Synthesis of these compounds involves the condensation of a linear diamine (e.g., $(CH_2OCH_2CH_2NH_2)_2$) with a diacid chloride (e.g., $(CH_2OCH_2COCl)_2$) in high dilution, followed by reduction with $LiAlH_4$ or B_2H_6 (23,24). Examples are shown in structures (VI) and (VII).



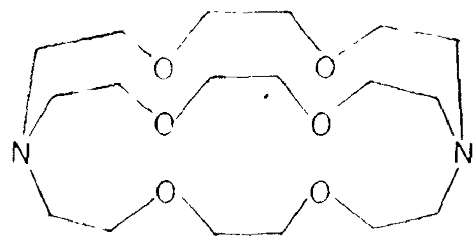
(VI) 1,4,10,13-tetroxa-7,16-diaminocyclo-octadeca ether



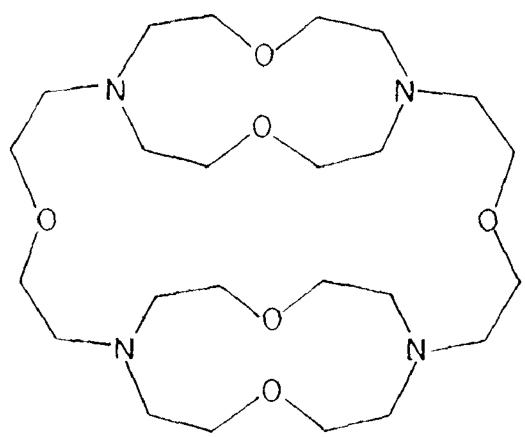
(VII) 2,3,11,12-dibenzo-1,4,10,13,16-quintoxa-7-aminocyclo-octadeca-2,11-diene

All benzo compounds can be catalytically hydrogenated to the corresponding 1,2-cyclohexyl polyether. Hydrogenation can be accomplished in 2-butanol at 100°C and 7-10 atmospheres over a ruthenium catalyst (8). The product is best purified by column chromatography on alumina. The benzo-substituted macrocyclic polyethers are colourless crystalline compounds. Melting points increase with the number of benzo groups while the solubility in water, alcohol and other common solvents is found to decrease. The polyethers are readily soluble in methylene chloride and chloroform (8). The saturated polyethers are colourless viscous liquids or solids of low melting points. They are considerably more soluble than the benzo compounds in all solvents.

With nitrogen as the bridging atom, the synthesis of macrobicyclic ligands has been made possible (22-25). The preparation is an extension of method (1) used for the synthesis of monocyclic diamine polyethers. These are commonly called "cryptates". Examples of some cryptates are shown below (structures (VIII) and (IX)).



(VIII) [2.2.2] macrobicyclic diamine



(IX) [2.2.2] macrotricyclic tetramine

Both the cyclic polyethers and cryptates have been characterized by elemental analysis, melting points, NMR, infrared, and UV-visible spectroscopy, and molecular weight determination (8,12,17,26).

Nature of the Metal Complexes of Macrocyclic Polyethers

The following general discussion relates to the metal complexes of macrocyclic polyethers. The principles mentioned here however, should apply equally well to the metal-ligand interactions in the quaterenes and are thus discussed in some detail.

The most important property of macrocyclic polyethers is their ability to form complexes with alkali, alkaline-earth and some transition-metal salts. The following factors influence the stability of the metal complexes (8): (1) the relative size of the ion and the cavity in the polyether ring; (2) the number of donor atoms in the polyether ring; (3) the coplanarity of the oxygen atoms; (4) the symmetrical placement of the donor atoms; (5) the basic strength of the donor atoms; (6) steric effects in the polyether ring; (7) the tendency of the metal ion to associate with the solvent; and (8) the metal-ion charge to radius ratio. The number of oxygen atoms in the ring is correlated with the preference of the ligand for a particular metal ion, as judged by measurements of stability constants of 1:1 complexes (17), isolation of crystalline complexes (16), and extraction into organic solvents (27). These results have led to the postulate that the ion is held in the center of the ring (formed by the coplanar oxygen atoms) by electrostatic attractive forces between the cation and the negatively charged oxygen dipole. Cation-ligand interaction is opposed by the interaction (28,29) of the cation with the medium (i.e., solvation). The ligand should be able to replace, as completely as possible, the solvation shell of the cation. Optimum results are obtained when the cation is in contact with the oxygen atoms. If the cavity is too large, ligand deformations are introduced which cause destabilization of the complex. If the cation is too large to lie in the plane of the ring, a stable complex is not formed. The greater the number of oxygen atoms, the more stable is the complex formed, provided that the oxygen atoms are coplanar and symmetrically placed in the ring. Optimally, the number of binding sites should be equal to or higher than the solvation number of the cation (30,31). However, when seven or more oxygen atoms are present in the polyether ring, they cannot arrange themselves in a coplanar configuration, but they can arrange themselves around the surface of a right circular cylinder with the vertices of the C-O-C angles pointed toward the center of the cylinder. This configuration, termed "cylindrical symmetry" by Pedersen (8), allows the formation of stable metal complexes. For alkali-metal and alkaline-earth complexes, the stability is expected to decrease on replacement of oxygen by nitrogen or sulphur atoms in the sequence O > N > S. This is explained on the basis of electrostatic interactions (8). Substitution of groups in the chelating molecule may alter its basic strength, thereby increasing or reducing its complexing power (32). Substitution may introduce steric effects which, in extreme cases, may prevent chelation altogether (24).

The solvent plays an important role in the formation of complexes. Complexation processes between ligand (L) and cation (M^{n+}) in solvent (S) is represented by the following general equation:

$$(L)S_x + (M^{n+})S_y \rightleftharpoons (ML^{n+})S_z + (x+y-z)S$$

The stability (and selectivity) of complexation is influenced by the interaction of the cation and ligand with the solvent, as well as with each other. The solvation energy of the metal ion is more important than that of the ligand and is usually an inverse function of the ionic radius for a series of ions of like charge (33). The stability of the metal complexes increases as solvent polarity decreases. The above factors are shown by comparison of

TABLE I. Stability Constants of Polyether-Cation Complexes in Water at 25°C, in l/mol (21).

Polyether*	Li^+	Na^+	K^+	Pb^+	Cs^+	NH_4^+	Ag^+	Sr^{+2}	Ba^{+2}
perhydrobenzo-15-crown-5 (1.7 - 2.2)	< 1.0	< 0.3	0.6	-	-	-	-	-	-
perhydrobenzo-18-crown-6 (2.6 - 3.2)	< 0.7	0.8	1.9	-	0.8	1.1	1.8	-	-
perhydrodibenzo-18-crown-6									
isomer A(2.6 - 3.2)	0.6	1.7	2.2	1.5	1.2	1.4	2.3	3.2	2.6
isomer B(2.6 - 3.2)	-	1.4	1.8	0.9	0.9	0.8	1.8	2.6	3.3
perhydrodibenzo-21-crown-7 (3.4 - 4.3)	-	-	-	-	1.9	-	-	-	-

* The number in brackets is the estimated cavity diameters in A°. The ionic radii (in A°) of the ions are: Li^+, 0.60; Na^+, 0.95; K^+, 1.33; Rb^+, 1.48, Cs^+, 1.67; NH_4^+, 1.43; Ag^+, 1.26, Sr^{+2}, 1.13. Ba^{+2}, 1.35.

data in Tables I and II, obtained in water and in methanol respectively. The stability constants are greater by a factor of 10^3-10^4 in methanol.

As an example of the trends apparent in Table I, examination of the data for perhydrodibenzo-18-crown-6 is instructive. For like-charged ions, the smaller ions form complexes of lower stability primarily because of extensive hydration. The larger ions such as Rb^+ and Cs^+ are less extensively hydrated but are too large to fit into the cavity of the ligand in such a way as to attain the position of maximum charge density in the plane of the ether oxygen atoms. Ag^+ is a weakly hydrated cation of suitable size and thus forms a more stable complex than the other unipositive ions. The divalent ions such as Sr^{+2} and Ba^{+2} form the more stable complexes because of their high charge density (providing stronger ion-dipole interaction) and also because of their suitable size.

Table II. Stability Constants of Polyether-Cation Complexes in Methanol at 25 C (21).

Polyether	Log K Na^+	K^+	Cs^+
tetramethyl-12-crown-4	1.4	-	-
perhydrodibenzo-14-crown-4	2.2	1.3	-
perhydrobenzo-15-crown-5	3.7	3.6	2.8
18-crown-6	4.3	6.1	4.6
perhydrodibenzo-18-crown-6			
(isomer A)	4.1	6.0	4.6
(isomer B)	3.7	5.4	3.5
dibenzo-18-crown-6	4.4	5.0	3.6
dibenzo-21-crown-7	2.4	4.3	4.2
dibenzo-24-crown-8	-	3.5	3.8
dibenzo-30-crown-10	2.0	4.6	-
pentaglyme $CH_3(OCH_2CH_2)_5OCH_3$	1.5	2.2	-

With regard to relative size of the ring and the ion, the optimum ring size is one which provides the closest fit between the cation and the hole (Figure 1).

As expected, ion-pair formation between the cationic polyether complex and the anion is more extensive in solvents of low polarity. In water or other highly solvating media, both species are separately solvated and no anion effect on complex stability is expected (35). The effect of anions on solubility is extremely important in solvents of low polarity. While complexation of the cation is an obvious prerequisite for solubilization, the anion also plays an important role, as illustrated by the data in Table III below.

Table III. Solubilization of Alkali-metal Halides in Organic Solvents by Addition of 50 mmol/ℓ of Perhydro-dibenzo-18-crown-6 (17).

Solvent	Methanol (mmol/ℓ)	Solubility (mmol/ℓ)*				
		NaCl	NaBr	KCl	KBr	KI
C_6H_6	0	0.01	1.8	0.03	2.3	9.2
	250	0.48	24	8.7	30	46
CCl_4	0	0.03	2.7	0.6	4.1	0.8
	250	1.1	28	8.8	34	15
$CHCl_3$	0	1.8	37	21	41	43
	250	5.7	41	34	44	44
CH_2Cl_2	0	1.8	35	17	41	43
	250	5.8	42	33	42	44
THF	0	0.02	1.2	0.1	3.6	45
	250	0.04	5	0.4	13	50

* Salt concentrations after agitation of the polyether solution with enough salt to give 50 mmol/ℓ solution.

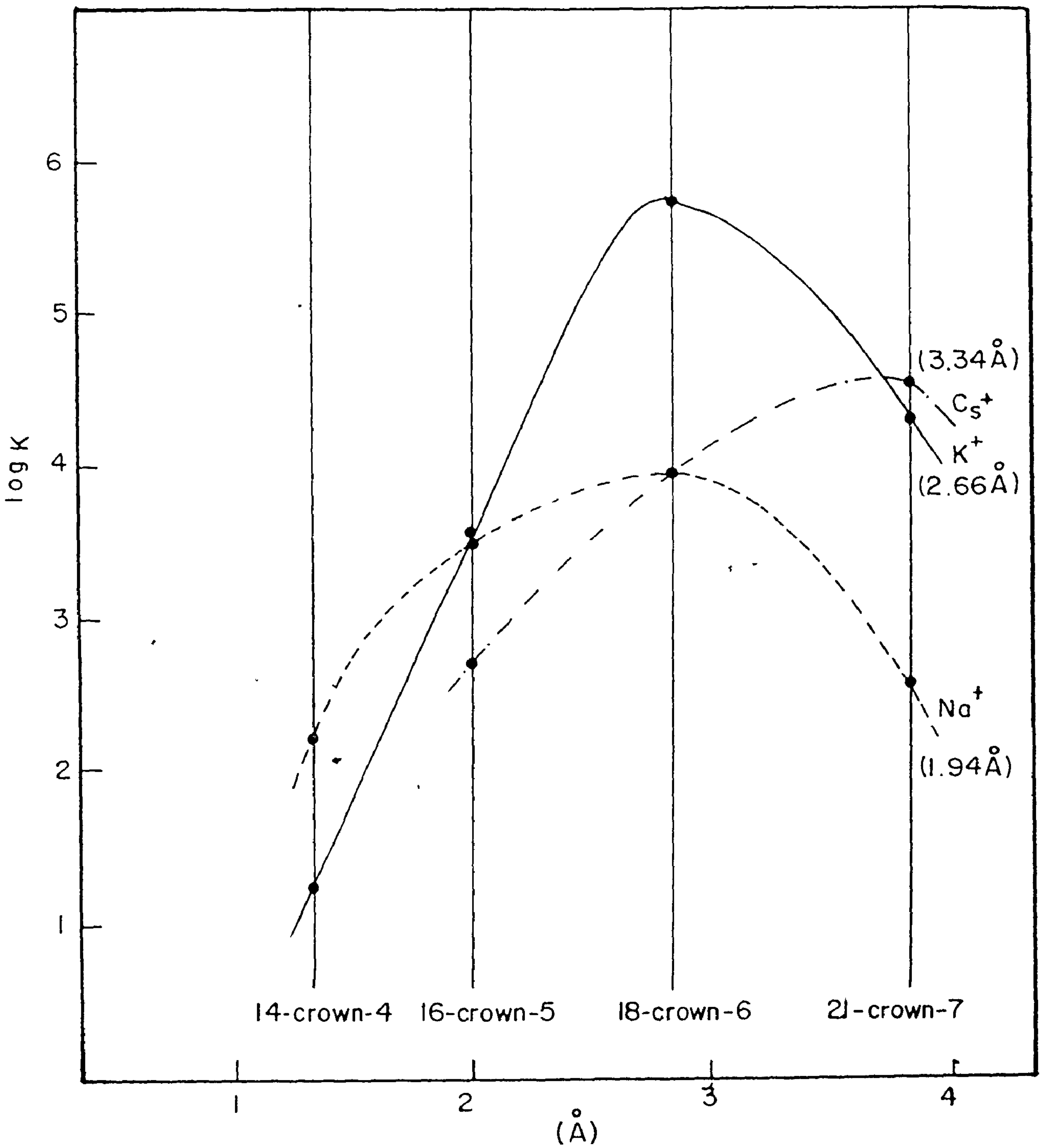


Figure 1. Dependence of log K on Cation Diameter/Ring Size Ratio.

Detection of Complex Formation

The solution stability of the 1:1 metal complexes is measured by the equilibrium constant* for the reaction:

$$M^{n+} + L \overset{K}{\rightleftharpoons} ML^{n+}$$

where

$$K = \frac{[ML^{n+}]}{[M^{n+}][L]}$$

A variety of methods have been used for the determination of values of K, e.g., potentiometric methods involving the use of cation-selective electrodes (21), conductimetry (36) and spectroscopic methods (37).

The detection of polyether/metal-ion complexes in the first instance can be achieved in a number of ways: by alteration of salt solubility; by changes in ultraviolet spectra; by solvent extraction of the complex as an ion-pair; by isolation of the complexes as solids; by changes in NMR spectra; by potentiometry; and by conductimetry (17). Some of these methods are briefly discussed below.

One of the simplest ways in which polyether complex formation manifests itself is the solubilization of ionic compounds in organic solvents. For instance, Table IV shows the increase in solubility of some salts in methanol in the presence of dibenzo-18-crown-6. The greatest percentage increase tends to occur with salts that are least soluble in methanol in the absence of the polyether. The solubilization of ionic compounds in aprotic solvents (including aromatic hydrocarbons) is of practical significance (17,38-43), as will be discussed in the next section.

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* It is customary to measure the concentration equilibrium constant rather than the activity constant.

TABLE IV. Effect of Dibenzo-18-crown-6* on Solubilities of Salts in Methanol at 30°C (8).

Salt	Solubility (M) Salt	Complex	Ratio (complex)/(salt)
sodium oxalate	0.00036	0.0011	3.1
sodium carbonate	0.028	0.14	5.0
sodium bicarbonate	0.046	0.24	5.2
sodium chloride	0.21	0.52	2.5
sodium nitrite	0.51	1.09	2.1
potassium iodate	0.00004	0.0015	38
sodium bromate	0.0017	0.018	11
sodium nitrate	0.031	0.28	9.0
sodium chloride	0.057	0.23	4.0

* present in excess.

The most widely used means for demonstration of complexation are characteristic changes in the ultraviolet spectra of aromatic polyethers, provided that the salts themselves do not absorb in the ultraviolet region. The benzo and dibenzo polyethers have a characteristic absorption maximum at 275 nm in methanol. In general, complexation causes the appearance of a second peak about 6 nm to the long wavelength side of the major peak (8,44). In some instances, the spectral changes are barely noticeable and complexation requires confirmation by other methods.

A particularly simple method for the detection of complex formation consists of extraction of the complex formed, usually as its picrate ion-pair. An organic solution of the polyether is shaken with an aqueous solution of the metal picrate in the presence of excess hydroxide. If complexation occurs, the charged complex will be transferred as the picrate ion-pair to the organic phase (12,27,44). The partition coefficient can be determined and related to the stability of the complex. Extraction is efficient only if the anion is large and polarizable, such as is the picrate anion. The picrate anion has an absorption maximum near 360 nm which is useful for easy analysis. In the absence of complexation, picrate remains in the aqueous phase (yellow) and the organic phase is colourless. This method is more useful than the ultraviolet absorption method because complexing efficiencies of the various polyethers can be ranked numerically (12,38,44). Polyethers that do not absorb in the region of 270 nm (i.e., non-benzopolyethers) can also be thus evaluated. Table V shows some typical results obtained for various polyethers. The extraction efficiencies

TABLE V. Extraction* of Picrates into Methylene Chloride Containing Polyethers (44).

Polyether	Picrate extracted (%)			
	Li^+	Na^+	K^+	Cs^+
di(tert-butylperhydrobenzeno)-14-crown-4	1.1	0	0	0
tert-butylperhydrobenzo-15-crown-5	1.6	19.7	8.7	4.0
dibenzo-18-crown-6	0	1.6	25.2	5.8
perhydrodibenzo-18-crown-6	33	25.6	77.8	44.2
perhydrodibenzo-21-crown-7	3.1	22.6	51.3	49.7
perhydrodibenzo-24-crown-8	2.9	8.9	20.1	18.1

*For equal volumes of water and CH_2Cl_2. Initial concentrations: alkali hydroxide 0.1M; alkali picrate 7×10^{-5}M; polyether 7×10^{-5}M.

are in accordance with stability constants measured by other means for these systems. Eisenman et al. (13,45), have used the picrate extraction technique in an extensive investigation of the complexing of the alkali cations by macrocyclic antibiotics (13). The data showed that factors other than the stability of the complex affect extraction efficiencies. These are the solubility of the polyether, metal salt and its complex in the solvent involved and the nature of the anion directly involved in complex formation. Also, extraction efficiencies are lowered in solvents of very low dielectric constants, although better selectivity is obtained in such solvents.

Changes in the NMR spectra are easy to observe and the technique has become increasingly popular in the study of polyether and cryptate complexes. On complexation, changes occur in the chemical shifts of the CH_2 protons. Such changes in the chemical shifts were used to demonstrate the formation of a complex between the [2.2.2] bicyclic cryptate (VIII) and KF (26).

Complexation was also demonstrated for sodium, potassium, rubidium, calcium, strontium, and barium salts in both D_2O and $CDCl_3$ (28-31). The NMR spectra are temperature dependent and can be used to determine the rate of exchange in metal complexes (26). Further, use of low polarity solvents such as $CDCl_3$ and C_6D_6, provides opportunity to observe the formation of complexes that would normally be unstable in water.

The most positive test for the formation of a complex is the isolation of the complex. It was originally reported (8) that the stoichiometry of these complexes is always 1:1 regardless of the metal-ion valence. Later studies showed, however, that this is not always the case. Complexes with stoichiometric ratios of 2:1 and 3:2 (ligand: metal-ion) have been reported (16,46). These ratios were found for isolated solid complexes (47-49).

Considerable interest has been shown in the properties of the polyether compounds because of their similarities to naturally-occurring antibiotics. For this reason, some of the larger polyethers such as dibenzo-30-crown-10, which forms a 1:1 complex with potassium ion, have received special attention (50). The structure is similar to the wrap-around structure of the potassium complex of the antibiotic nonactin. Several cyclic polyethers have been synthesized in which one or more sulphur or nitrogen atoms have been substituted for oxygen (19). As expected, complexation of alkali and alkaline-earth cations is decreased but complexation with Ag(I) is enhanced (21). With nitrogens as donor atoms, complexation in solutions is pH sensitive since protonation of the ligand competes with complex formation.

Applications of Crown Ethers

The crown ethers have achieved importance in synthetic organic chemistry. Their synthetic utility is derived from their ability to solvate cations in a non-polar environment. In most cases, the transfer of salts into the non-polar solvent is a direct solid/liquid phase transfer, although in a few instances, it is a liquid/liquid transfer. Application of crown ethers to organic synthesis is already extensive. Gokel and Durst (51) have recently reviewed this subject and mention is made below of only a few outstanding examples.

Pedersen showed that potassium hydroxide could be solubilized in toluene by dicyclohexyl-18-crown-6 to produce a powerful base for the high-yield hydrolysis of esters (8,52). Sam and Simmons found that direct solid/liquid phase transfer of potassium permanganate into benzene by dicyclohexyl-18-crown-6 (purple benzene) is a mild yet effective oxidant, e.g., α-pinene can be oxidized to pinonic acid, stilbene to benzoic acid and diphenylmethane to benzophenone (43). Solubilization of potassium periodate and potassium iodate by 18-crown-6 transforms catechols to o-quinones in high yield (53). Potassium superoxide can be solubized by dicyclohexyl-18-crown-6 or 18-crown-6 in both DMSO and benzene to give a very nucleophilic oxygen anion which reacts with alkyl halides and tosylates to produce alcohols or dialkyl peroxides, depending on the solvent (54,55). The ability of the macrocyclic polyethers to draw salts into non-polar solvents has been utilized in reactions involving fluoride. Thus, 18-crown-6 assists the solubilization of KF in either acetonitrile or benzene and the poorly solvated fluoride anion ("bare fluoride") exhibits potent nucleophilic properties (56). Although the carboxylate anion is not a good nucleophile in polar solvents, in non-polar media it is quite nucleophilic ("bare acetate"). In this regard, potassium acetate brought into acetonitrile by 18-crown-6 reacts gradually with n-heptyl bromide to yield n-heptyl acetate (57). Other reactions involving "bare acetate" have been reviewed by Gokel and Durst (51). Other uses to which cyclic polyethers have been put include: (i) the dissolution of potassium and cesium metal in tetrahydrofuran and diethylether by perhydrodibenzo-18-crown-6, which promises to extend greatly the range of solvents in which solvated electrons and related species can be obtained (58); (ii) their study as models for macrocyclic antibiotics in ionic transport phenomena across biological and artificial membranes (59,60); and (iii) analytical applications which are dependent on ion discrimination. These are dealt with separately below.

Potential analytical applications of cyclic polyethers are based on the cation-discriminating properties of these ligands. For example, selectivity toward cations varies with polyether ring size, the optimum ring size being one for which the cation just fits into the hole. Thus, separations of alkali-metal and/or alkaline-earth cations by solvent extraction procedures should be possible. Pedersen has separated KSCN from CoSCN on this basis (12), and Jepson and Dewitt have even separated the isotopes ^{40}Ca and ^{44}Ca using dicyclohexyl-18-crown-6 (61). The separation of erbium from praseodymium by use of dibenzo-18-crown-6 has also been reported (62). The development of ion-selective electrodes based on the use of discriminating polyethers should also be possible. Indeed, Rechnitz and Eyal (63) have examined several cyclic polyethers in relation to their use as neutral ion carriers in liquid-membrane electrodes. There is no fundamental limitation to the type of cation that can be measured potentiometrically by ion-selective electrodes if suitable carrier molecules can be found and in this connection the design and synthesis of certain cyclic polyethers may prove useful.

Finally, in a somewhat different analytical application of crown ethers, Cram and co-workers (64,65) have designed optically active crown ethers, such as dibinaphthyl-22-crown-6, which extract alkyl ammonium salts from water into chloroform. The optically pure S,S crown ether prefers the R-enantiomer of phenethylamine hexafluorophosphate over the S-enantiomer by a ratio of about two to one. This recognition allows partial resolution of amines on a preparative scale by simple extraction methods. The same approach has been extended by Stoddart and co-workers (66) who accomplished selective extraction of certain enantiomeric amines as their salts.

Synthesis and Complexing Properties of Quaterenes: Statement of the Problem

The usefulness of chelating agents in analytical chemistry increases as their selectivity increases. The selectivity of the cyclic polyethers is determined primarily by the cavity size and cation diameter. Examination of tables of stability constants (17) reveals that for Na^+, maximum stability occurs between perhydrodibenzo-15-crown-5 and 18-crown-6; for K^+, at 18-crown-6; and for Cs^+ between 18-crown-6 and 21-crown-7. The optimum ring sizes are exactly those which provide the closest fit between cation and hole, as seen in Table VI.

TABLE VI. Polyether Ring Size and Metal-Ion Diameters

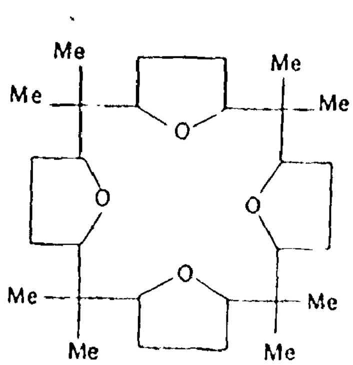
Polyether*	Hole Diameter meter (A°)**	Favoured Ion	Ionic Diameter (Crystal) A°
14-crown-4	1.2 - 1.5	Li^+	1.20
15-crown-5	1.7 - 2.2	Na^+	1.90
18-crown-6	2.6 - 3.2	K^+	2.66
21-crown-7	3.4 - 4.3	Cs^+	3.34

* Polyethers are perhydrodibenzo types.

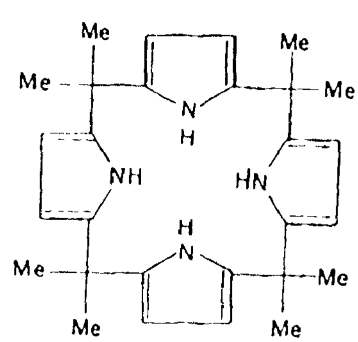
** Hole diameters, as estimated by Pedersen, based on Corey-Pauling-Koltun models for lower limit and Fisher-Hirschfelder-Taylor models for upper limit.

Potentially, the most selective polyethers should be the ones with the smallest cavities since only the smallest cations would be capable of effective complexation while the larger ions would be excluded from the cavity. In Table VI, the smallest cavity is associated with perhydrodibenzo-14-crown-4 (1.2 - 1.5 Å). The compounds tetramethyl-12-crown-4, and dibenzo-12-crown-4 have been synthesized (8,67) and would obviously possess even smaller cavities. Their dimensions have not yet been reported. In general, there appears to be little data on the stability of complexes formed by the polyethers containing smaller sized cavities. These ligands are likely poor complexing agents because of the smaller number of donor atoms available for complexation to the smaller cations, ions which would be strongly solvated.

Nevertheless, Chastrette and Chastrette (16) reported that the reduced form (X) of 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetroxaquaterene forms a complex with Li^+ in both ethanol and chloroform and that Li^+ acts as a template by coordination to the furan oxygen during the synthesis of unreduced X . In view of this report, it was decided to further examine the complexing properties of X and its unreduced form in the present work. In addition, a study of the complexing properties of mixed quaterenes was undertaken. These quaterenes are compounds in which one to four furan rings are systematically replaced by pyrrole rings, complete substitution yielding 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetrazaquaterene (XI).



(X)



(XI)

The cavity diameters of the quaterenes, obtained by comparison of their Courtauld models with the Courtauld models of various polyethers, were estimated to be in the range 1.5 - 1.6 A° (approximately the same size as the 14-crown-4 polyether). It was thought that successive substitution of furan by pyrrole would lead to an interesting shift in complexing ability from, for example, the alkali-metal ions to ions like Ag^{+}, Cd^{+2}, Ni^{+2} and Cu^{+2} reflecting the increased covalent character of the metal-donor bond. Frensdorff (21) had found that substitution of two ether oxygens by two NH groups in 18-crown-6 dramatically increases the stabilities of the Ag^{+} complex (21).

The syntheses of X in its unsaturated form has been reported previously by Ackman, Brown and Wright (68). The synthesis of the mixed quaterenes was first reported by Brown and French (69). The general procedure described in each paper was followed in the present study. Certain modifications, specified later, led to improved yields of intermediates and of the final compounds.

II. EXPERIMENTAL SECTION

A. Apparatus

Proton magnetic resonance spectra were recorded on either a Varian T-60 or HA-100 instrument.

Mass spectra were obtained on a Hitachi Perkin-Elmer RMU-6A mass spectrometer.

Infrared spectra were recorded on either a Beckmann IR-5 or a Perkin-Elmer Model 337 grating spectrophotometer. The bands at 2851.5, 1944.5 and 1028.3 cm^{-1} of a polystyrene film were used to calibrate each spectrum. Compounds soluble in $CHCl_3$ or CCl_4 were prepared in sealed liquid cells with sodium chloride windows. The spectra of insoluble compounds were taken in potassium bromide pellets.

Spectra in the ultraviolet-visible region were recorded on a Bausch and Lomb Spectronic 600 instrument. The spectrophotometer was equipped with a Sargent Recorder Model SRL. Fused silica cells (1.00 cm pathlength) were used.

Elemental analysis reported in this thesis were performed by A.B. Gygli, Microanalysis Laboratories Limited, Toronto, Ontario, or by Alfred Bernhardt, Mikroanalytisches, Laboratrium, Elbach über Englelskirchen, West Germany.

All melting points were taken on a Mel-Temp capillary melting point apparatus. The thermometer was calibrated at several temperatures, up to 263°C.

The catalytic reduction of the quaterene compounds was carried out in a Parr shaker-type hydrogenation apparatus, Specification Number 3911. High-pressure hydrogenations were carried out in a Parr rocker autoclave type apparatus (Specification Number 400), fitted with a high-pressure hydraulic pump.

The pH meter was a Corning Model-7 type, equipped with a single combination-type electrode (Sargent Model S-30072-15).

B. Material

1. Reagents

Boron trifluoride etherate (Fisher Scientific Company) was purified by distillation over calcium hydroxide. As recommended by Zweifel and Brown (70), a small amount of diethyl ether was added to ensure its excess. The fraction boiling over the range 125-126°C (atmospheric pressure), was collected for use.

Pyrrole (Fisher Scientific Company), which had darkened owing to air oxidation, was distilled to a clear, colourless liquid (boiling range 128-130°C).

Analytical grade 1,4-dioxane (British Drug House) was purified by refluxing over sodium for at least 36 hours, followed by fractional distillation through a one-meter column packed with glass helices. The fraction boiling in the range 100.5 - 101.0°C was collected and used within 24 hours.

All other reactants and solvents, such as $CHCl_3$, CCl_4, acetone, ethanol, and all inorganic reagents were sufficiently pure for the purpose intended.

2. Synthesis

The mixed quaterenes and their intermediates were prepared by the method described by Brown et al. (69) while the tetroxaquaterene was prepared as described by Ackman et al. (68). The original procedures were modified to some extent and are described in detail below. The reaction sequences for the syntheses are given in Figures 2 and 3 which follow. The ligands were characterized by elemental analysis and by infrared, proton magnetic resonance and mass spectroscopy. The data are presented under Results and Discussion.

(a) 2-Acetylfuran. This compound was prepared by the reaction of furan and acetic anhydride in the presence of borontrifluoride etherate as described by Heid and Levine (71). On distillation (2 mm pressure), a colourless oil was obtained (42-44°C) which solidified in the receiver. The yield on several preparations varied from 70 to 80 percent.

(b) 2-Dimethylfurylcarbinol. This compound was prepared by the method of Reichstein et al. (72), with some modifications. An ether solution of methylmagnesium iodide (0.193 moles), prepared as described by Feisér and Feiser (73), was placed in a 500-ml 3-necked flask fitted with a mercury-seal stirrer, reflex condenser, a nitrogen inlet, and a dropping funnel. The solution of the Grignard reagent was cooled in an ice-bath and with vigorous stirring, a dilute solution of acetylfuran (0.182 moles) in ether (100 ml) was added dropwise. A gentle stream of nitrogen was passed through the reaction vessel at all times. The ice-bath was removed and stirring was continued for two hours at room temperature; then 100 g of chipped ice was added slowly to decompose the yellow complex and the solution was next saturated with K_2CO_3. After removal of the ether phase, the system was extracted several times with ether and the

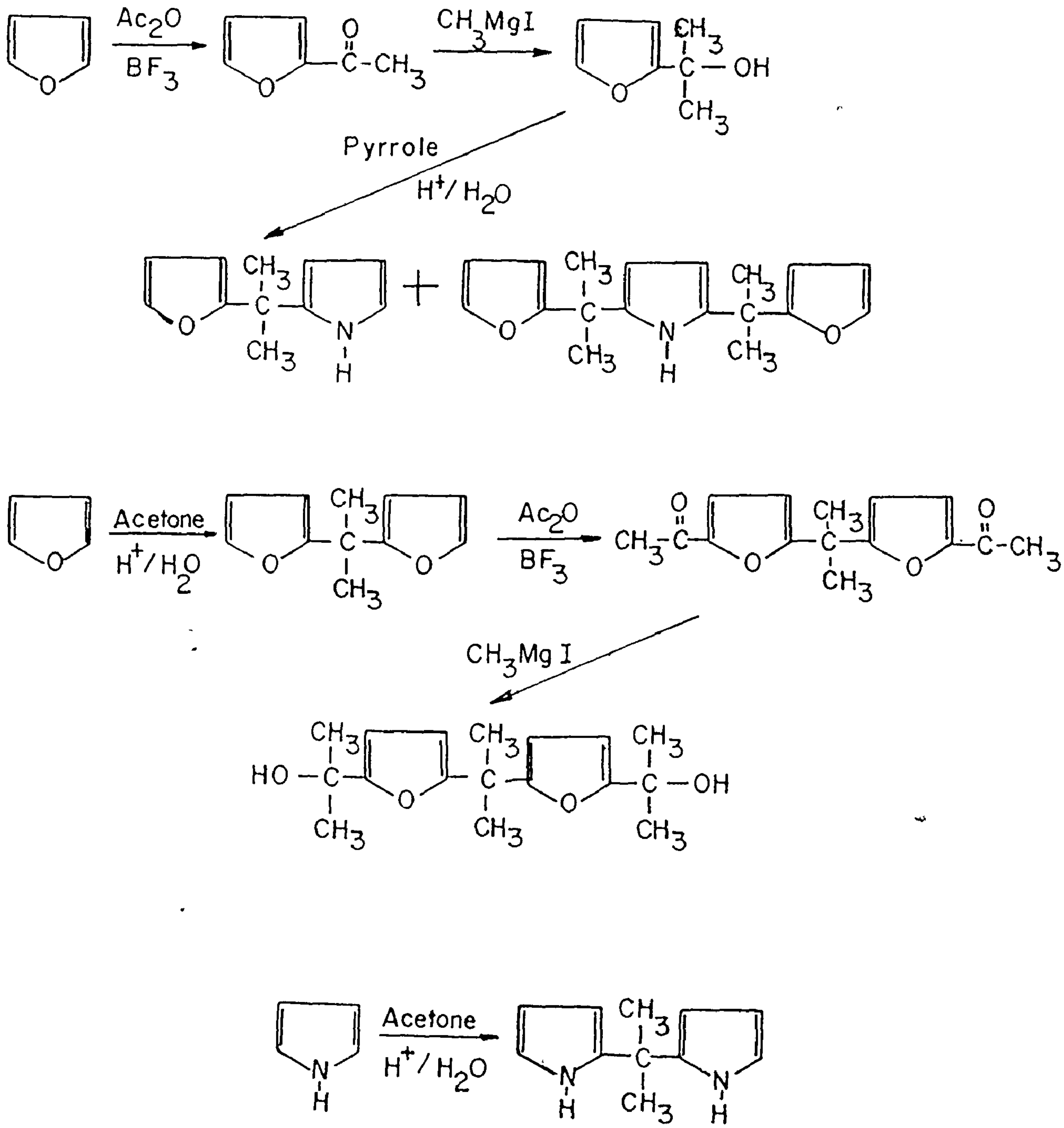
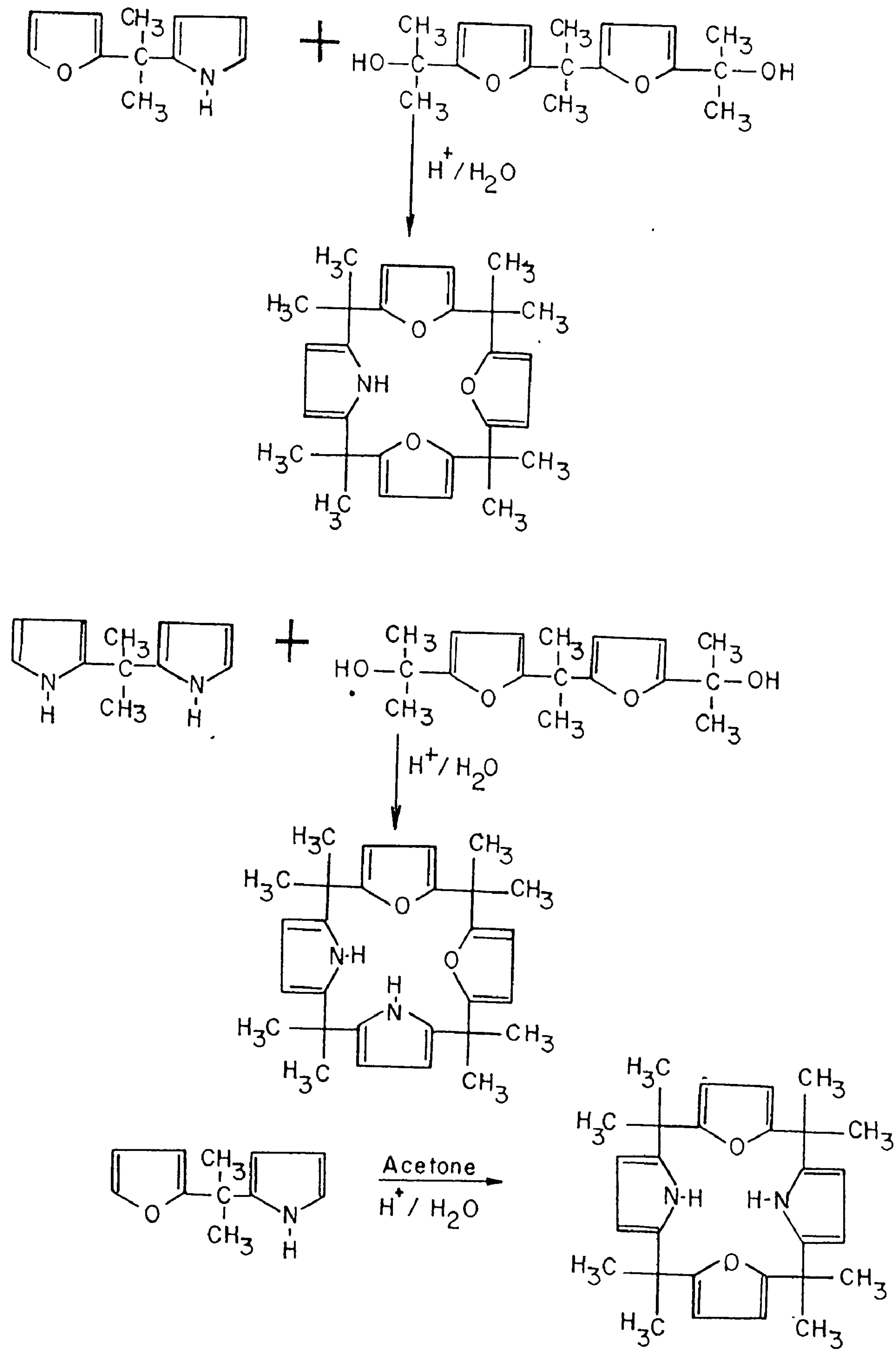


Figure 2. The Synthesis of Mixed Quaterenes

Figure 2. (continued)



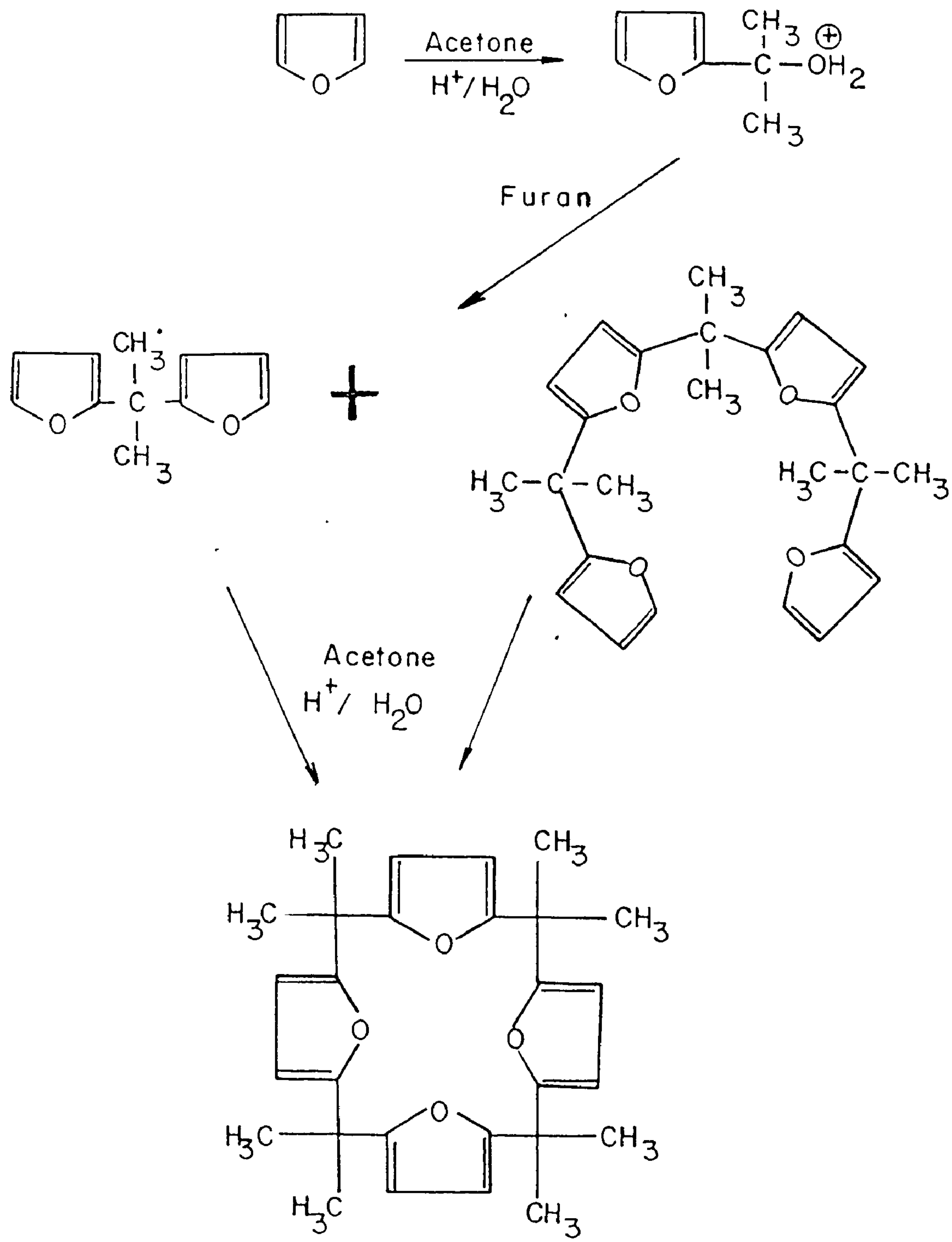


Figure 3. The Synthesis of Tetrafuran-16-Crown-4.

combined ether solutions were washed with a 10% K_2CO_3 solution and then dried over anhydrous K_2CO_3. The ether was removed by distillation and then the residue was fractionated under reduced pressure (2-3 mm). A colourless liquid was collected over the range 50-55°C. The yield varied on several preparations from 70 to 80 percent.

(c) 2-Furyl-2-pyrrylpropane. The following procedure is a modification of that used by Brown and French (69). A solution of purified pyrrole (0.45 moles), 60 ml of absolute ethanol, and 0.39 moles of 2-dimethylfurylcarbinol was placed in a 500-ml flask equipped as described above. The solution was cooled to 0°C and then 10 ml of concentrated hydrochloric acid was added dropwise with stirring over a period of 20 minutes. The reaction mixture turned yellow initially, and then dark green. The ice-bath was removed and stirring was continued for two hours at room temperature. Addition of 100 ml of water resulted in the formation of two phases. A 10% sodium carbonate solution was added and the organic layer was extracted several times with chloroform and then dried over anhydrous sodium sulphate. After the removal of the chloroform by rotary evaporation, and of the excess pyrrole by distillation under reduced pressure, the residual oil was fractionally distilled under vacuum (2-3 mm). The product, a colourless oil, distilled as the first fraction (90-95°C). The yield varied from 30 to 40 percent.

(d) 2,5-Bis (dimethylfurfuryl) pyrrole. The second fraction, from the above distillation, a yellowish oil, distilled at 150-170°C (2 mm). The yield was about 15 percent.

(e) 2,2-Difurylpropane. The following procedure is similar to that described by Ackman, Brown and Wright (68), with slight modifications. Furan (5.0 moles), absolute ethanol (150 ml) and acetone (2.5 moles) were placed in a 3-necked flask and cooled to 0°C. Concentrated hydrochloric acid (100 ml) was added dropwise with stirring over a period of 45 minutes. After separation and washing with 5% Na_2CO_3 solution, the organic layer was extracted several times with chloroform. The chloroform was removed by distillation and the residue was fractionated in vacuo (1 mm). The product was a colourless oil, collected over the range 42-45°C. The yield was 40% (literature, 20.5% (68)).

(f) 2,2-Bis-(5-acetylfuryl)propane. The method of synthesis for this compound was essentially similar to that reported by Brown and French (69). The product was collected at 180-185°C (4 mm); yield, approximately 50 percent. The disemicarbazone derivative melted at 230°C (literature 235°C (69)).

(g) 2,2-Bis-(5-isopropylolfuryl)propane. The following procedure is similar to that for the preparation of 2-dimethylfurylcarbinol. The methylmagnesium iodide (0.123 moles) was present in slight excess of 2,2-bis (5-acetylfuryl) propane (0.0537 moles). The latter compound was dissolved in 100 ml of ether and added dropwise with stirring. The ether phase was separated and the system extracted with ether. The combined ether phases were quickly chilled in an acetone-dry ice mixture and the ether decanted. This procedure was repeated several times; leaving a slightly sticky yellow solid. It was not possible to obtain the white crystals reported by Brown and French (69) without loss of most of the product. Melting point 90-93°C (literature, 91-92°C (69)); yield, 40-50%.

(h) 2,2-Dipyrrylpropane. The procedure below is a modification of that reported by Brown and French (69). A solution of pyrrole (one mole), 70 ml of absolute ethanol, and 18.4 ml of acetone was placed in a 500-ml flask equipped as described in section (b). The mixture was cooled to 10°C and 3 ml of concentrated hydrochloric acid were added dropwise with stirring over a period of 15 minutes. Stirring was continued for one hour at 0°C, and then two hours at room temperature, during which time the solution turned yellowish-green. Water (100 ml) was added and the resulting mixture was neutralized with sodium carbonate. The organic layer was extracted several times with chloroform and dried over sodium sulphate. The chloroform was distilled at atmospheric pressure and the excess pyrrole was removed under reduced pressure. The resulting residue was fractionally distilled to give a light yellow oil which solidified in the receiver. Boiling point, 130-135°C (2 mm); yield, 50-60%. Recrystallization from petroleum ether gave large white rhomboid crystals (m.p., 60-61°C; literature, 59°C).

(i) 2,2,7,7,12,12,17,17-Octamethyl-21-aza-22,23,24-trioxaquatar-ene. This compound was prepared by a modification of the procedure reported by Brown and French (69). A solution of 2,2-bis (isopropylolfuryl) propane and 2-furyl-2-pyrrylpropane (0.000172 moles each) in 70 ml of absolute ethanol was cooled in an ice-bath and 0.4 ml of concentrated hydrochloric acid added dropwise over a 15 minute period. Stirring was continued for one hour at 0°C and then two hours at room temperature. The solution turned light yellow and then light brown. It was left standing overnight, then placed in the refrigerator for a few hours, whereupon white crystalline needles formed, m.p., 214-216°C; yield, 70-80%. A second crop of crystals was also obtained by addition of water to the ethanol solution. Elemental analysis gave the following data. Calculated for $C_{28}H_{33}NO_3$: %C, 77.96; %H, 7.66; N, 3.25. Found: %C, 77.70; %H, 7.48; %N, 3.37.

(j) <u>2,2,7,7,12,12,17,17-Octamethyl-21,22-diaza-23,24-dioxaquaterene</u>. The procedure of Brown and French (69) was modified as follows. A solution of 2,2-dipyrryl-propane (0.003 moles), 0.003 moles of 2,2-bis-(5-isopropylol-furyl)propane and 70 ml of absolute ethanol was placed in an erlenmeyer flask, cooled in an ice-bath, and stirred. To this solution, 0.15 ml of concentrated hydrochloric acid was added dropwise over 10 minutes. Stirring was continued for one hour at 0°C and for two hours at room temperature. The reaction mixture was allowed to stand overnight and then placed in a freezer for a few hours to give the first batch of crystals. A second crop of crystals was obtained upon the addition of water to the reaction mixture. The precipitate was coagulated on a hot plate and then recrystallized from benzene to yield white needles, m.p., 254-256°C; yield, 85-95%. Calculated for $C_{28}H_{34}N_2O_2$: %C, 78.14; %H, 7.91; %N, 6.51. Found: %C, 77.82; %H, 7.74; %N, 6.63.

(k) <u>2,2,7,7,12,12,17,17-Octamethyl-21,23-diaza-22,24-dioxaquaterene (69)</u>. To an erlenmeyer flask were added 0.011 moles of 2-furyl-2-pyrryl-propane, 0.052 moles of acetone, and 70 ml of absolute ethanol. The solution was cooled to 0°C and then 2 ml of concentrated hydrochloric acid were added dropwise with stirring over 20 minutes. The solution turned orange and then light red. The cold mixture was stirred for one hour then for two hours at room temperature and was finally heated to 50°C. The mixture was left to stand overnight and then cooled in the refrigerator for a few hours. White crystalline needles formed, m.p. 225-226°C. A second crop of crystals was precipitated by the addition of water to the supernatant solution. The yield was 60-65%. Calculated for $C_{28}H_{34}N_2O_2$: %C, 78.14; %H, 7.91; %N, 6.51. Found: %C, 77.68; %H, 7.90; %N, 6.54.

(ℓ) <u>2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetroxaquaterene</u>. This compound was prepared as outlined by Ackman et al. (68). The method is based on the condensation of acetone with furan in the presence of acid. In the preparation of 2,2-difurylpropane as described earlier, a second fraction from the same distillation was collected at 132-136°C (0.5 mm) and was shown to be 2,2'-isopropylidenebis (5-(dimethylfurfuryl)furan) (68). The product was a viscous, pale yellow oil. The yield of this compound was increased when stirring time was increased by 1.5 hours; yield, 35%.

On further condensation of 2,2-difurylpropane and 2,2'-isopropylindenebis (5-(dimethylfurfuryl)furan) with acetone in the presence of hydrochloric acid, a white granular solid precipitated. Crystallization from benzene yielded white rectangular crystals, m.p., 240-241°C (literature, 243°C (68)). Calculated for $C_{28}H_{32}O_4$: %C, 77.75; %H, 7.46. Found: %C, 77.56; %H, 8.72.

(m) <u>Catalytic Hydrogenation of Quaterene Compounds</u>. Absolute ethanol containing a small amount of Raney nickel catalyst was placed in a glass Parr hydrogenation bomb. The bomb was flushed six times with hydrogen gas and left under pressure (50 p.s.i.) for one hour to pre-hydrogenate the catalyst. The quaterene compound (0.002 moles) was then placed inside the bomb. The bomb was fitted to the Parr low-pressure reaction apparatus, flushed repeatedly with hydrogen gas, pressurized to 50 p.s.i. at 60°C, and then shaken automatically overnight. The apparatus was dismantled and chloroform added to dissolve any insoluble reaction products. The solution was then filtered through a medium porosity sintered-glass frit to remove the catalyst. After removal of the solvent on a rotary evaporator, the residue was recrystallized from aqueous dioxane. The reduction was also attempted with a catalyst consisting of 5% rhodium on alumina, in place of Raney nickel.

The reduction was repeated at much higher pressures, using a high-pressure Parr rocker autoclave type apparatus. The bomb was made of a one-inch thick stainless steel casing and was equipped with a silver disc that could withstand 3000 p.s.i. The procedure was essentially the same as that described above. Raney-nickel was used as the catalyst, and pressures up to 2700 p.s.i. (at 175°C) were used.

C. Solubility of the Quaterenes

A semi-quantitative measurement of the solubility of the quaterene compounds was made in the following solvents: water, acetone, absolute methanol, absolute ethanol, 1,4-dioxane, dimethylsulphoxide, tetrahydrofuran, dimethylformamide, 1,2-dichloroethane, chloroform, diethylether, carbon tetrachloride, benzene, cyclohexane, toluene and aniline. The procedure was as follows: 3 mg of the compound were added to 5 ml of each of the above solvents and the solutions shaken. As the compound dissolved, an additional 3 mg were added and left for four days to equilibrate at room temperature. The solubility data are given under Results and Discussion.

D. Sulphonation of the Quaterenes

Two different methods were used to sulphonate the quaterene compounds. The procedure outlined by Rondestvedt and Bordwell (74) for the sulphonation of styrene by the 1,4-dioxane-SO_3 complex to yield β-styrene-sulphonate, was followed in the sulphonation of the tetra-oxaquaterene. For the mixed quaterenes, the pyridine-SO_3 complex was used as described by A.P. Terent'ev and L.A. Yanovskaya (75) for the sulphonation of 2,5-dimethylpyrrole.

In a one-litre 3-necked flask equipped with a dropping funnel and two ground glass stoppers were placed 120 ml of 1,2-dichloroethane. To this was added dropwise with stirring 7.8 ml (0.185 moles) of SO_3 at a rate of one drop per 5 seconds. The solution was cooled in an ice-bath during the addition and gradually turned borwnish-yellow. The ground glass stoppers were replaced by a thermometer and a drying tube. The sulphur trioxide solution was cooled below -5°C with an ice-salt bath and then 15.8 ml (0.185 moles) of 1,4 dioxane was added with vigorous stirring at a rate such that the temperature did not exceed 5°C. The mixture turned light brown. Tetraoxaquaterene (0.0232 moles) dissolved in 250 ml of 1,2-dichloroethane was added with stirring in 20-ml portions to the suspension of the dioxane-SO_3 complex. The temperature was maintained below 10°C during the hour required for the addition. After the addition of each 20-ml portion, the solution turned dark reddish-brown initially, and then dark green after a few minutes. After addition of the quaterene, stirring was continued for one hour and the mixture was then refluxed for 30 minutes. On cooling, the solution was poured into 500 ml of ice-water and shaken to ensure transfer of any sulphonated material into the aqueous phase. The emulsion was neutralized with sodium hydroxide solution, the layers separated and the aqueous phase extracted with two 250-ml portions of diethyl ether. Evaporation of the combined ether layers did not yield any significant amount of the sulphonated material.

The pyridine-SO_3 complex, first described by Baumgarten (76) was prepared as described by Feiser and Feiser (73). After preparation, the crystalline complex was stored in a desiccator under vacuum until ready for use.

Tetrazaquaterene (0.005 moles), 50 ml of 1,2-dichloroethane and 0.04 moles of the pyridine-SO_3 complex were heated together for 5 hours in a sealed tube placed inside a Parr reaction bomb at 100°C. Extensive charring of the compounds was observed. The solution together with the charred product was neutralized with a dilute solution of sodium hydroxide. The mixture was shaken and left for 24 hours. The aqueous layer was separated and extracted several times with ether. After evaporation of the ether, a residue was obtained, the NMR spectrum of which was recorded in $CDCl_3$. Similarly, the aqueous layer and the 1,2-dichloroethane layer were evaporated and an NMR spectrum of their residues were recorded. No evidence of sulphonation was obtained. The method was repeated but with benzene as a solvent, at 50°C and a 2.5-hour reaction time. Again, sulphonation did not occur.

A final trial was carried out in an atmosphere of nitrogen at room temperature. A suspension of the pyridine-SO_3 complex in 1,2-dichloroethane was placed in a 3-necked flask and stirred. A solution of the tetrazaquaterene in 1,2-dichloroethane was added dropwise and stirred for one hour. The procedure described above was repeated and again the sulphonated quaterene was not obtained.

E. Reactivity of the Ligands with Metal Ions

The general reactivity of the quaterenes toward metal-ions was examined to determine their ability to function as ligands. The reactions were examined in buffers of pH 8-9, and 13-14. The procedures used are given below.

1. Spectrophotometric Studies

(a) Metal-ion Solutions. Stock solutions (approximately 10^{-3}M, in deionized water) were prepared from reagent-grade perchlorate salts of Na(I), Li(I), K(I), Rb(I), Ca(II), Mn(II), Ni(II), Cu(II), Co(II), and from the chloride salts of Ba(II), Cd(II), Mg(II). A Mg(II) solution of the nitrate was also prepared.

(b) Ligand Solutions. Stock solutions of the ligands (10^{-3}M) were prepared in 1,4-dioxane. The ligands were previously dried for one hour at 100°C. Secondary solutions (4×10^{-5}M) of the ligands were also prepared and used in the preparation of the test metal-ion/ligand solutions.

(c) Metal-ion/Ligand Solutions. To a 20-ml vial were added 7.5 ml of ligand solution (4×10^{-5}M) and 2.5 ml of metal-ion solution (10^{-3}M). The vial was capped and shaken to mix the solution. The final concentrations were: for the ligand, 3×10^{-5}M; for the metal ion, 2.5×10^{-4}M; for dioxane, 75% by volume. Blank solutions were prepared containing separately each of the above metal-ions and separately each of the ligands. The absorbance of all solutions was measured using 1.00 cm quartz cells over the wavelength range 200-350 nm. The reference cell contained a 75% dioxane-water solution. For each metal-ion, three spectra were recorded; one for the ligand blank, one for the metal-ion blank, and one for the metal-ion/ligand solution. All ligands studied had an absorption maximum at 224 nm. The pH of the solutions varied from 8 to 9, depending on the metal-ion salt used. Typical spectra are given in Appendix III, Figure 1.

In the pyrrole-containing quaterenes, it was thought that it might be possible to form stable complexes by removal of a proton from the NH group, followed by chelation. With this in mind, the pH of some metal-ion/ligand solutions was adjusted to 13-14, by the addition of 1M tetramethylammonium hydroxide solution. The UV spectra of the solutions were recorded as before. No attempt was made to control the ionic strength of the medium. Typical spectra are shown in Appendix III, Figure 1.

(d) Extraction Studies. The picrate extraction method developed by Pederson (8) to observe complex formation in solution was used in the present study. An aqueous alkaline solution of the metal-ion picrate salt was shaken with a solution of the polyether in $CHCl_3$ and the organic phase subsequently examined for the presence of the metal chelate-picrate complex.

In this work, aqueous solutions were prepared of metal hydroxides and picric acid. Tetramethylammonium hydroxide was added in the cases where the metal hydroxides were not available. The aqueous solutions were 0.1 M in metal hydroxide and 4×10^{-5}M in picrate. A 4×10^{-5}M solution of the ligands in $CHCl_3$ was prepared. Equal volumes (10 ml) of the two solutions were placed in a screw-cap bottle and thoroughly agitated on a Burrel wrist-action shaker for two hours. Usually, the phases separated cleanly on standing. All extractions were done at room temperature (23 ± 2°C). Control experiments were carried out in which the ligand was omitted. The picrate concentration in the $CHCl_3$ phase for both the test and control experiments was determined spectrophotometrically. Typical spectra obtained under the above conditions are given in Appendix III, Figure 2.

The results for the above studies are discussed under Results and Discussion.

2. <u>Proton NMR Studies</u>. Saturated solutions of each ligand in $CDCl_3$ were prepared and their NMR spectra recorded on a T-60 Varian spectrometer. Tetramethylsilane was used as an internal standard. Equimolar quantities of metal salts were then added directly to the tubes, the solutions agitated for 0.5 hours and left overnight to equilibrate. The NMR spectra were again recorded. In addition, to 5 ml of $CDCl_3$ solutions of the ligands (10^{-2}M) were added equimolar quantities of solid metal salts (as perchlorates or nitrates) and the bottle containing the solutions were agitated on the shaker for two weeks. The NMR spectrum of each solution was then recorded.

The results obtained from these foregoing experiments are presented and discussed under Results and Discussion.

III. RESULTS AND DISCUSSIONS

A. Synthesis and Characterization of Ligands

In all, six quaterenes were synthesized. Of these, were three mixed quaterenes, one containing a pyrrole and three furan residues and two isomers (cis and trans) containing two pyrrole and two furan residues. One quaterene contained four pyrrole residues and another four furan residues. The last quaterene was the reduced tetrafuran compound (X). The synthesis of the first four quaterenes was based on the work of Brown and French (69) while that of the tetrafuran compound was based on the procedure of Ackman et al. (68). The synthetic steps are illustrated in Figures 2 and 3.

When the procedures of former workers were followed precisely, low yields of intermediates and of the quaterenes were obtained along with large amounts of tarry, polymeric materials. This problem arises partly because of the susceptibility of the furan to ring-opening and of the pyrrole to polymerization in acid solution. These reactions were minimized and the yields increased in the present work by the addition of HCl as a final rather than an initial reagent. Another modification involved the use of the high dilution technique in certain reactions.

In the previous work, the intermediate and final compounds have not been fully characterized. In the present work, they were further characterized by infrared, proton NMR, and mass spectrometry. The quaterenes were also characterized by elemental analysis.

Discussion of the preparation of the various intermediates and quaterenes follows.

2-Acetylfuran. The synthesis of 2-acetylfuran has been reported previously (71). In the present work, the yield of 70-80% is consistent with that reported in the literature (77%). The melting point of the semicarbazide derivative (148-149°C) is in agreement with the literature value (148-149°C).

The proton NMR spectrum showed a doublet centered at 7.55 ppm, assigned to the α-proton; a doublet centered at 7.17 ppm, assigned to the β-proton adjacent to the substituted α-position; and a quartet centered at 6.52 ppm, assigned to the second β-proton. The singlet at 2.43 ppm is due to the methyl protons. Integration accounted for all the protons in this compound.

In the mass spectrum the parent peak at m/e = 110 and the isotopic peaks are consistent with the formula $C_6H_6O_2$:

	P + 1	P + 2
Calculated for $C_6H_6O_2$:	6.66%	0.59%
Found:	6.81%	0.61%

The infrared spectrum was also consistent with the structure. The main bands at 3120, 2980 and 2934 and 1675 cm^{-1} correspond to aromatic C-H, methyl C-H and carbonyl stretches.

2-Dimethyl-furylcarbinol. When the method of Reichstein et al. (72) was followed closely, exceedingly low yields (about 20%) were obtained, in contrast to the 80% yield reported. Reichstein's method was modified as follows. The CH_3MgI was prepared in a 500-ml flask under nitrogen and a dilute solution of 2-acetylfuran in absolute ether was added to the Grignard reagent, instead of the reverse addition. The use of dilute solutions reduced the violent reaction between the ketone and Grignard.

The steam distillation step was replaced by repeated extraction of the alcohol with ether. Also, the use of CH_3MgI in excess of the ketone eliminated the semicarbazone formed from excess ketone. Yields of 70-80% were obtained with these modifications.

The NMR spectrum showed a doublet centered at 7.27 ppm due to the α-proton; a quartet centered at 6.26 ppm, assigned to the β-proton adjacent to the substituted position; a doublet centered at 6.13 ppm assigned to the second β-proton; a peak at 2.47 ppm attributed to the hydroxyl proton, and a peak at 1.57 ppm due to the six methyl protons. Integration accounted for all the protons.

In the mass spectrum, the parent-ion peak at m/e = 126 is in agreement with the molecular weight and the P + 1 and P + 2 peak intensities are in reasonable agreement with the calculated intensities for $C_7H_{10}O_2$.

	P + 1	P + 2
Calculated $C_7H_{10}O_2$:	7.80	0.66
Found:	8.19	0.90

The infrared spectrum has a broad peak in the O-H stretch region at 3375 cm^{-1}, an aromatic C-H stretch absorption at 3100 cm^{-1}, peaks at 2980 and 2930 cm^{-1} indicative of the methyl groups and a doublet at 1340 and 1365 cm^{-1} indicative of the gem nature of the two methyl groups.

2-Furyl-2-pyrrylpropane. In the method of Brown and French (69), the pyrrole solution was acidified first, prior to the addition of the dimethylfurylcarbinol, resulting in the formation of a large amount of polymerized material. To reduce polymerization of pyrrole, a more dilute reaction solution was used and the HCl was added last and at a slow rate.

The mass spectrum is in agreement with the molecular weight and the isotopic peaks are in reasonable agreement with those calculated for $C_{11}H_{13}NO$.

	P + 1	P + 2
Calculated for $C_{11}H_{13}NO$:	12.52	0.92
Found:	12.82	0.91

The infrared spectrum showed a band at 3500 cm^{-1}, assigned to the N-H group; a band at 3110 cm^{-1} due to the aromatic C-H stretch; bands at 2970 and 2940 cm^{-1} for the methyl groups; and bands at 1380 and 1360 cm^{-1} indicative of a gem arrangement of the methyl groups.

2,2-Difurylpropane. In the method of Ackman et al. (68), HCl was added to a solution of acetone, furan and absolute ethanol. Since furan undergoes ring-opening and polymerization in acid medium, very poor yields (about 5-8%), far below the 20.5% reported, were obtained. A yield of 40% was obtained when the HCl was added very slowly to a mixture of acetone, furan, and absolute ethanol at 0°C. After separation of the phases, $CHCl_3$ was used to extract the organic layer.

The proton NMR spectrum showed a doublet at 7.17 ppm assigned to the α-protons of both furan rings; a quartet at 6.16 ppm due to the β-protons adjacent to substituted position; a doublet at 5.93 ppm attributed to the remaining two β-protons and a singlet at 1.56 ppm due to the methyl protons. Integration accounted for all the protons.

In the mass spectrum, the parent peak at m/e = 176 confirmed the molecular weight and the P + 1 and P + 2 peaks were in reasonable agreement with the calculated intensities for $C_{11}H_{12}O_2$.

	P + 1	P + 2
Calculated for $C_{11}H_{12}O_2$:	12.16	1.08
Found:	13.51	1.25

The infrared spectrum showed an absorption at 3120 cm^{-1} for the aromatic C-H stretch and bands at 2975, 2940, 1380 and 1360 cm^{-1} for the C-H stretching vibration of the methyl groups.

2,2-Bis(5-acetylfuryl)propane. The procedure used was that reported by Brown and French (69). The proton NMR spectrum showed two doublets at 7.08 ppm and 6.23 ppm for the β-protons; a singlet at 2.41 ppm for the methyl of the acetyl groups and a singlet at 1.77 ppm for the remaining two methyl groups.

The parent-ion peak (m/e = 260) confirmed the molecular weight but the P + 1 isotopic peaks was not in agreement with the calculated value.

	P + 1	P + 2
Calculated for $C_{15}H_{16}O_4$:	16.62	7.93
Found:	21.74	6.09

In the infrared spectrum, bands at 2980, 2940, 1380 and 1365 cm^{-1} were assigned to the methyl groups and bands at 3118 and 1675 cm^{-1} were assigned to the aromatic C-H stretch and C=O stretch, respectively.

2,2-Bis(5-isopropylolfuryl)propane. The procedure of Brown and French (69) was found to be unnecessarily complicated and the reported yield of 36% could not be obtained. The method was thus modified.

The first modification involved the use of a small amount of CH_3MgI to consume all of the 2,2-bis (5-acetylfuryl) propane. The second modification involved immersion of the ether extract from the reaction in an acetone dry ice mixture for two days to induce crystallization. The crystals were decanted and the ether extract partially evaporated and chilled again in acetone/dry-ice. This procedure was repeated several times to obtain maximum yield. The combined crystals gave a yield of 40-50%.

The NMR spectrum showed a doublet at 6.14 ppm for the β-protons (on both rings) adjacent to the isopropyl groups; a doublet at 5.95 ppm assigned to the two remaining β-protons; a peak at 2.4 ppm due to the O-H proton and singlets at 1.6 and 1.53 ppm assigned to the propane and isopropanol methyl groups, respectively.

The mass spectrum was consistent with the structure. The parent peak at m/e = 292 confirmed the molecular weight and the isotopic peaks were in reasonable agreement with those calculated for $C_{17}H_{24}O_4$:

	P + 1	P + 2
Calculated for $C_{17}H_{24}O_4$:	18.91	7.59
Found:	19.67	6.55

The infrared spectrum had a broad band at 3400 cm^{-1} for the O-H stretch and a peak at 3110 cm^{-1} due to the aromatic C-H stretch. The peaks at 2980, 2935, 1380 and 1365 cm^{-1} corresponded to the methyl C-H stretch.

2,2-Dipyrrylpropane. To prevent the excessive polymerization of pyrrole, the HCl was added dropwise to the pyrrole-acetone mixture in absolute ethanol. This step together with $CHCl_3$ extraction of the aqueous layer, increased the yield to 50-60%. Brown and French (69) reported a yield of 31%.

The NMR spectrum showed a broad band at 6.98 ppm attributable to the two N-H protons; a quartet at 6.4 ppm due to the two α-protons; another quartet at 6.22 ppm assigned to the two β-protons adjacent to the α-protons; a doublet at 5.94 ppm due to remaining two β-protons and a singlet at 1.47 ppm for the methyl protons. Integration accounted for all the protons.

The parent peak in the mass spectrum at m/e = 174 confirmed the molecular weight of the compound. However, the mass spectrum showed some contamination from 2,5-bis (dimethylfuryl) pyrrole.

In the infrared spectrum, an absorption band at 3400 cm^{-1} indicated the presence of the N-H group and the peak at 3090 cm^{-1} the presence of aromatic C-H bonds. The peaks at 2990, 2910 and 1350 cm^{-1} were attributed to the methyl groups.

The Mixed Quaterenes. Initial attempts to prepare these compounds met with little success. The low yields were at least partly due to the formation of polymeric material which caused the solutions to turn reddish brown in colour. The polymeric material could form either by linear condensation or else by cyclization to give a tetramer analogous to a porphyrinogen (69). Polymerization could be reduced by dilution (74). With this in mind, the molar ratio of reactants to solvents was reduced from 1:48 to 1:700. The results in each case are discussed separately below.

2,2,7,7,12,12,17,17-Octamethyl-21-aza-22,23,24-trioxaquaterene. Using concentrated solutions, Brown and French (69) reported a 13.5% yield but their procedure gave only 7-9% in the present work. The use of dilute solutions, stirring during addition of the HCl, a longer time for reaction and precipitation gave a 70-80% yield.

The NMR spectrum showed a singlet at 5.87 ppm (β-protons of furan); a doublet at 5.63 ppm (β-protons of pyrrole); and peaks at 1.54 and 1.47 ppm from the methyl protons. Integration accounted for all the hydrogens in this compound.

The parent peak in the mass spectrum at m/e = 431 was in agreement with the molecular weight of the compound. The isotopic peaks were in reasonable agreement with those calculated for $C_{28}H_{33}NO_3$:

	P + 1	P + 2
Calculated for $C_{28}H_{33}NO_3$:	31.28	5.87
Found:	32.66	6.00

The infrared spectrum (KBr pellet) gave an absorption at 3500 cm^{-1} assigned to the N-H group; a weak absorption at 3130 cm^{-1} for aromatic C-H and absorptions at 2995, 2945, 1385 and 1365 cm^{-1} assigned to the methyl C-H stretch.

2,2,7,7,12,12,17,17-Octamethyl-21,22-diaza-23,24-dioxaquaterene. The modifications in the preparation of this compound were essentially the same as for the azatrioxaquaterene. The yield was increased from 50% (69% reported) to 85-90%.

In the NMR spectrum, there was a singlet at 6.0 ppm which was attributable to the α-protons of furan and a doublet at 5.92 ppm assigned to β-protons of pyrrole. The peak at 1.53 ppm was ascribed to the methyl groups. A broad weak band at about 7 ppm is likely the N-H resonance which is broadened because of quadrupole relaxation.

The parent peak at m/e = 430 confirmed the molecular weight and the isotopic peaks were in reasonable agreement with those calculated for $C_{28}H_{34}O_2$:

	P + 1	P + 2
Calculated for $C_{28}H_{34}O_2$:	31.64	6.04
Found:	33.04	7.51

The infrared spectrum (KBr pellet) showed absorptions at 3500 cm^{-1} (N-H stretching); 3110 cm^{-1} (aromatic C-H) and 2990, 2960, 1385 and 1365 cm^{-1} (methyl C-H).

2,2,7,7,12,12,17,17-Octamethyl-21,23-diaza-22,24-dioxaquaterene. A 60-65% yield was obtained compared to the 15% yield reported by Brown and French (69).

The NMR spectrum showed a singlet at 6.07 ppm (β-protons of furan); a doublet at 5.86 ppm (β-protons of pyrrole); and a peak at 1.57 ppm (methyl protons).

The parent peak at m/e = 430 was in agreement with the expected molecular weight. The isotopic peaks were in reasonable agreement with those calculated for $C_{28}H_{34}N_2O_2$:

	P + 1	P + 2
Calculated for $C_{28}H_{34}N_2O_2$:	31.64	6.04
Found:	32.50	5.72

In the infrared spectrum (KBr pellet), there were absorption bands at 3400 cm^{-1} (N-H stretch), 3120 cm^{-1} (aromatic C-H) and 2980, 2920, 1385 and 1365 cm^{-1} (methyl groups).

The Unmixed Quaterenes

2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetroxaquaterene. The method used was essentially the same as that reported by Ackman, Brown and Wright (68) except that in the reaction involving 2,2'-propylidenebis (5-(dimethylfurfuryl) furan), hydrogen chloride gas was added only until the dark green colour was observed and not the subsequent pale red colour. It was found that the volume of hydrogen chloride gas passed through the system is a critical factor which determines whether the final product will be the tetroxaquaterene or a high molecular weight polymer. On standing, the mixture turned pale red and the desired compound precipitated as white crystals.

In the NMR spectrum, there was a singlet at 5.91 ppm (β-protons of furan) and a singlet at 1.50 ppm (methyl proton). Integration accounted for all the hydrogens.

The mass spectrum of the compound was consistent with the structure. The parent peak at m/e = 432 confirmed the molecular weight. The isotopic peaks were in reasonable agreement with those calculated for $C_{28}H_{32}O_4$.

	P + 1	P + 2
Calculated for $C_{28}H_{32}O_4$:	30.93	5.71
Found:	33.3	6.05

The infrared spectrum showed a weak absorption of 3100 cm^{-1} (aromatic C-H) and absorptions at 2980, 2960, 1375, and 1360 cm^{-1} for the methyl groups.

<u>2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetrazaquaterene</u>. The compound was first synthesized by Baeyer (77). The structure was later confirmed by Rothemund et al. (78). In the present work, yields of 90-95% were obtained (88% reported). The HCl was added last to the reaction mixture and in dropwise fashion.

The NMR spectrum showed a broad band in the region 7.03 - 6.8 ppm attributable to the N-H protons; a doublet at 5.85 ppm assigned to the β-protons of pyrrole; and a singlet at 1.4 ppm for the methyl protons. Integration accounted for all the hydrogens in this compound.

The parent (m/e = 428) and isotopic peaks in the mass spectrum confirmed the molecular weight.

	P + 1	P + 2
Calculated for $C_{28}H_{36}N_4$:	32.36	6.38
Found:	34.1	5.2

In the infrared spectrum (KBr pellet), there were absorption bands at 3450 cm^{-1} (N-H stretch); at 3100 cm^{-1} (aromatic C-H stretch), and at 2990, 2950, 1385 and 1365 cm^{-1} (methyl groups).

B. Solubility of the Ligands

All five ligands were found to be insoluble in water. Semi-quantitative solubility measurements were made in a number of solvents as described in the Experimental Section. The results of the tests for each reagent are reported in Table VII below. For those solvents miscible with water, the addition of relatively small amounts of water greatly

Table VII. Solubilities (mg/ml) of the Quaterene Compounds in Various Solvents at 23±1°C.

	Dielectric Constant	4-O	1-N	2N-2O (cis)	2N-2O (trans)	4N
cyclohexane	2.05	sp.s*	7.0	7.0	7.0	7.0
dioxane	2.21		7.0	9.0	9.0	16.0
carbon tetrachloride	2.24	5.0	6.0	11.0	11.0	13.0
benzene	2.28	9.0	7.5	7.0	7.0	7.0
toluene	2.38	sp.s.	sp.s.	sp.s.	sp.s.	50.0
chloroform	5.05	sp.s.	sp.s.	13.0	13.0	16.0
tetrahydrofuran	7	sp.s.	sp.s.	5.0	5.0	7.0
1,2-dichloroethane	10.51	sp.s.	s	9.0	9.0	11.0
acetone	21.4	s	s	sp.s.	sp.s.	sp.s.
ethanol	25	s	s	s	s	s
methanol	33.1	s	s	s	s	s
dimethylformamide	36.7	s	s	5.0	5.0	8.5
dimethylsulfoxide	45	s	s	7.0	7.0	8.5
water	80	ins	ins	ins	ins	ins

* sp.s.: sparingly soluble; ins: insoluble; s: soluble but no quantitative data.

reduced the solubility. Solubility differences among the quaterene compounds are marginal with the 4-oxygen quaterene being the least soluble. The solubility is increased with increasing number of nitrogen atoms while there appears to be no consistent correlation with the dielectric constant of the solvent.

The low solubilities of the quaterenes limits their potential analytical usefulness. An attempt was made to increase their solubility in water and other polar solvents by sulphonation. Electrophilic substitution of pyrrole and furan occurs preferentially at the 2-position although the 3-position is attacked when the former is blocked. The placement of at least one sulphonic acid group on each pyrrole or furan ring should be possible.

The procedure used to sulphonate the tetroxaquaterene was one in which styrene has been successfully sulphonated at the β-position (74) using the dioxane-SO_3 adduct. The reaction was carried out under dry conditions to prevent formation of H_2SO_4, which could destroy the tetroxaquaterene and cause polymerization (74). Despite the precautions of controlling the temperature and the moisture, a charred product was obtained with no evidence of sulphonation.

An attempt to sulphonate the tetrazaquaterene was also made using the pyridine SO_3 complex according to the method of Terent'ev and Yanovskaya (75,79). Application of the method to the tetrazaquaterene resulted in excessive charring and some polymerization with no evidence of any sulphonation. The same reaction was repeated using benzene as a solvent at 50°C instead of 1,2-dichloroethane at 100°C, and reducing the reaction time from 5 to 2.5 hours, again with no success. It was thought the reaction conditions were too drastic causing ring cleavage and excessive charring.

When the experiment was repeated at room temperature under a nitrogen atmosphere, some charring still occurred but the major compound isolated was unreacted quaterene.

Pedersen found that the saturated cyclic polyethers, as a group, are much more soluble in all solvents than the corresponding unsaturated compounds. Therefore, another way to increase the solubility of the quaterene compounds would be to reduce them. In addition to enhancing the solubility, the reduction would also increase the basicity of the ring nitrogen and oxygen atoms, thus favouring the formation of complexes. The increased stability could be partly offset by some loss of coplanarity and increased steric hindrance. Molecular models of the quaterene compounds suggested that these effects would not be serious. It was thus decided to attempt to reduce the quaterene compounds. Pyrroles have been reduced to pyrrolidines in glacial acetic acid over 5% rhodium on alumina at 25-50°C under 40-60 p.s.i. of hydrogen (80,81). The pyrrole ring becomes progressively more difficult to hydrogenate (82) with increasing substitution. Raney nickel in absolute ethanol has been used as a catalyst whenever hydrogenation at higher temperatures and pressure is required. The first attempt to reduce the tetrazaquaterene compound was carried out in glacial acetic acid over 5% rhodium on alumina at 60°C under 60 p.s.i. of hydrogen. The NMR spectrum of the recovered material was not any different from that of the original compound. The reaction was then performed under more rigorous conditions, using a rocker-type high-pressure hydrogenation apparatus and a Raney nickel catalyst. The hydrogenation was done in absolute ethanol at 180°C under 2500 p.s.i. of hydrogen. Surprisingly the NMR spectrum again showed that little or no hydrogenation had taken place. The procedure was also tried with the cis-diazadioxaquaterene. Again, no reduction was found to occur.

For the tetroxaquaterene, hydrogenation was successful (at 160°C under 2600 p.s.i. of hydrogen). Recrystallization from absolute ethanol gave white crystalline needles, m.p., 195-7°C. The NMR spectrum taken in $CDCl_3$ (TMS internal standard) showed several kinds of methyl protons between 0.75 and 1.15 ppm. These showed a strong temperature dependence with coalescence occurring at just above 66°C, suggesting the presence of at least one stereoisomer undergoing a conformational change. The spectrum also showed a multiplet between 1.35 ppm and 1.85 ppm assignable to the β-protons. The two kinds of α-protons were represented by two multiplets between 3.15 ppm and 4.45 ppm. Integration accounted for all the hydrogens in this compound (Figure 7, Appendix I).

The parent peak in the mass spectrum at m/e = 448 confirmed the molecular weight of the compound. Elemental analysis gave the following data: calculated for $C_{28}H_{48}O_4$: %C, 75.00; %H, 10.72. Found: %C, 75.08; %H, 10.65.

C. General Reactivity of the Ligands

Although the quaterene compounds have been previously synthesized (68,69), their chelating properties have not been investigated. The only report regarding metal-ion complexation is that of Chastrette and Chastrette (16) in which the reduced form of the tetroxaquaterene was said to complex Li^+ but no other cations. Accordingly, in the present work, a series of qualitative tests were made to investigate more fully the chelating properties of the quaterene compounds.

Table VIII shows the metal ions employed in the tests and their (crystal) ionic radii. For Mg^{+2}, Ba^{+2}, Cd^{+2} and Zn^{+2}, the chloride salts were used. The remaining ions were used as their perchlorate salts.

TABLE VIII. Ionic Radii of Cations (83)

Cation	Radius, A°	Cation	Radius, A°
Li^{+}	0.60	Mn^{+2}	0.80
Na^{+}	0.95	Co^{+2}	0.72
K^{+}	1.33	Ni^{+2}	0.69
Rb^{+}	1.48	Cu^{+2}	0.92
Mg^{+2}	0.65	Zn^{+2}	0.74
Ca^{+2}	0.99	Cd^{+2}	0.97
Ba^{+2}	1.35	Ag^{+}	1.26

Table IX lists the quaterenes and their cavity diameters as estimated by comparison of their Courtauld models with those of cyclic polyethers whose diameters had been estimated previously by Pedersen (8). The diameters correspond to the largest sphere that can pass through the central cavity.

TABLE IX. Estimated Cavity Diameters of Quaterenes

Quaterene	Estimated diameters (A°)
tetrazaquaterene	1.2 - 1.5
cis-diazadioxaquaterene	1.3 - 1.6
trans-diazadioxaquaterene	1.4 - 1.7
monoaza-trioxaquaterene	1.4 - 1.7
tetroxaquaterene	1.4 - 1.7
perhydrotetroxaquaterene	1.4 - 1.7

For the pyrrole containing ligands, the hole size was estimated without the amino hydrogen on the assumption that on complexation, a proton would be released. Based on the estimated cavity sizes, Li^{+}, Mg^{+2}, Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2} would be expected to fit into the hole. In addition, because the hole diameters are not substantially different, any differentiation shown by the quaterenes in their reactions with metal ions would likely best be rationalized on the basis of preference of the ions for the O or N donor atoms.

The various methods that have been used to detect complexation between cyclic polyethers and metal ions were discussed in the INTRODUCTION. In the present study, changes in ultraviolet and proton NMR spectra and the extraction of the picrate ion-pair were used as diagnostic tests. The results of these tests are discussed below.

1. Ultraviolet Spectra

For cyclic polyethers containing a benzo group, Pedersen (8,44) used as evidence of complexation either the appearance of an absorption band about 6 nm to the long wavelength side of the characteristic ligand band at 275 nm (in methanol) or a hypsochromic shift and a changed intensity of the main band.

The ultraviolet spectra of the quaterenes in 75% (v/v) dioxane-water showed a single absorption maximum at about 220 nm with a molar absorptivity of approximately 17,300 cm^{-1} M^{-1}. Figure 1 in Appendix III shows a typical absorption spectrum of a quaterene compound. The perhydrotetroxaquaterene showed similar absorption in the UV and tests of reactivity with this ligand were made by proton NMR. The metal ion was present in about 8-fold excess over the ligand in all these studies.

Comparison of the spectra of the metal-ion/ligand solution, metal-ion solution and ligand solution gave no definite evidence of complexation between any of the ligands and any of the metal ions listed in Table VIII. The key spectra showed no evidence and no change in shape, absorption intensity or band shift (Figure 1, Appendix III).

The tests for reactivity were made at pH 8-9 for all ions. For the alkali metal cations, reactivity tests were also made at pH 13 and in 1M tetramethylammonium hydroxide with the mono, di(trans) and tetraza-quaterenes. The rationale for the high alkalinity was to promote dissociation of a proton from the $\backslash$NH group in the pyrrole quaterenes, thereby aiding in the complexation. The pK_a of pyrrole in water is greater than 14 (17) and thus the percentage of the pyrrole quaterene ligand in dissociated form at pH 14 is likely to be quite small but complexation would shift the equilibrium to favour further dissociation. However, no concrete evidence for coordination was obtained under the above conditions (Figure 1, Appendix III).

2 Solvent Extraction

As mentioned in the INTRODUCTION, extraction into $CHCl_3$ of the polyether complex as the picrate ion-pair is a particularly simple method for the detection of complex formation and has been used extensively by Pedersen (12,44) and Frensdorff (21,27). Their procedure was thought to be a convenient way of comparing the relative complexing powers of the cyclic quaterene compounds for various cations and was used in the present study.

Four quaterene compounds - the monaza, the diaza (trans), the tetrazaquaterene and the reduced form of the tetroxaquaterene - were tested by this method (with the cations Li^+, Na^+, Ca^{+2}, and Mg^{+2}) using $CHCl_3$ as the organic phase. The spectral data (Figure 2, Appendix III) showed no evidence for the extraction of the ion-pair. In addition to the possibility that these compounds may not be good complexing agents, their lack of solubilities in the aqueous phase (and in $CHCl_3$ in the case of the perhydrotetroxa compound) is a factor that might prevent any observable degree of complexation by the extraction technique.

3. <u>Proton Magnetic Resonance</u>

Changes in the proton NMR spectrum of the cyclic polyethers are readily observed upon metal-complex formation. For example, when solid KNO_3 is added to a $CDCl_3$ solution of the [2.2.2]bicyclic diamine (VIII, see INTRODUCTION) in equimolar amounts, a clearly resolved triplet at 2.57 ppm is obtained for the CH_2-N protons. This triplet is shifted about 14 Hz downfield from the corresponding (partially resolved) triplet at 2.77 ppm for the ligand in the absence of KNO_3 (Figure 6, Appendix I). Other metal complexes have been similarly investigated through the use of proton (26, 46) or ^{13}C NMR spectroscopy (21,22,84-86). Similar studies should also be possible with the quaterene compounds.

In this work NMR tests carried out with the di(cis) and tetrazaquaterenes and the tetroxaquaterene (reduced and unreduced form) with $CDCl_3$ as the solvent and 1% tetramethylsilane as an internal standard, gave no positive indications of complexation with any of the ions tested (Li^+, Na^+, Mg^{+2}, Ca^{+2}, Cd^{+2} and Zn^{+2}). Lack of evidence for complexation with Li^+

was particularly surprising since Chastrette and Chastrette (16) had previously reported that the hydrogenated form of the tetroxaquaterene formed a complex with lithium perchlorate in chloroform. In their study, the NMR spectrum of the complexed ligand showed only one peak for all the methyl groups as compared to at least 4 peaks for the uncomplexed form, and one multiplet for the α-protons as compared to two in the free ligand suggesting that on complexation to Li^+, the macrocycle takes on a particular conformation.

As an additional check on the observation of Chastrette and Chastrette (16), chloroform with equimolar amounts of reduced tetroxaquaterene and solid $LiClO_4$ or $NaClO_4$ or $Mg(NO_3)_2$ were placed into three bottles which were then stoppered and agitated for two weeks. The NMR spectra remained unchanged. It was concluded that complexation of the ligand with any of the three salts had not occurred to any significant extent.

In summary, no definitive evidence of complexation between any of the six quaterenes and any of the several metal ions was obtained by the three diagnostic methods. For Li^+, Mg^{+2}, Mn^{+2}, Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2}, this result is surprising since these ions are of suitable size to fit into the quaterene cavities. The result for Li^+ was especially surprising, as mentioned above. No obvious reason can be given for the contradictory results obtained here and those reported by Chastrette and Chastrette (16).

The general lack of reactivity of these compounds must be related to the very weak donor properties of the hetero atoms involved, to the relatively small number of donor atoms and to their lack of coplanarity as illustrated by molecular models. Both furan and pyrrole, from which these macrocyclics are derived, are very weak bases and thus poor ligands.

Apparently, the macrocyclic complexation effect is not sufficient to overcome the inherently poor donor properties of the hetero atoms to the point of promoting appreciable complexation. For ions in solution (as in the spectrophotometric and solvent-extraction experiments), complexation must be sufficiently strong to displace solvent molecules around the ions and to reorganize solvent molecules around the bound ligand. In solvents of high polarity such as water, desolvation of the cation is a seriously inhibiting process to complexation when weakly bonding ligands are involved (the insolubility of the quaterenes in water is an additional important factor). In solvents of low polarity (e.g., $CHCl_3$, CCl_4), in which the inorganic salts are insoluble or only slightly soluble (as in the NMR experiments), complexation by the quaterenes is not strong enough to overcome crystal forces. It is apparent that the quaterenes are too weakly complexing for ions either in solution or in the solid state. Even in strongly basic solution (e.g., 1M tetramethylammonium hydroxide), complexation with the pyrrole-substituted quaterenes was not obtained. Evidently, the solution was not basic enough to produce appreciable amounts of the strongly basic pyrrole anion unit in the macrocycles. The quaterenes thus appear to be very poor complexing agents. In view of their lack of reactivity, the quaterenes investigated in this study obviously have no analytical utility whatsoever.

D. Suggestions for Future Work

The lack of reactivity of the quaterenes towards metal ions is discouraging and no further work with these compounds as ligands is suggested. As an academic curiosity, further study should be given to the

Li^+/perhydrotetroxaquaterene system to determine whether or not reaction occurs. NMR experiments in DMSO-d_6 or CD_3CN, solvents in which $LiClO_4$ is sufficiently soluble, appear promising in this regard.

E. Summary

Six quaterenes have been synthesized by procedures described in the literature. In several instances, modifications which improved the yields were made in the procedures for intermediates and the final compounds. All quaterenes were fully characterized, in contrast to previous work.

The reactivity of the quaterenes towards a number of metal ions was determined by ultraviolet and NMR spectroscopy and by picrate ion-pair solvent extraction. No evidence of reaction was obtained by any of these diagnostic methods. The quaterenes are not suitable as ligands for analytical or other applications involving metal-ion complexation.

IV. APPENDICES

Appendix I. Proton Nuclear Magnetic Resonance Spectra of the Quaterene Compounds.

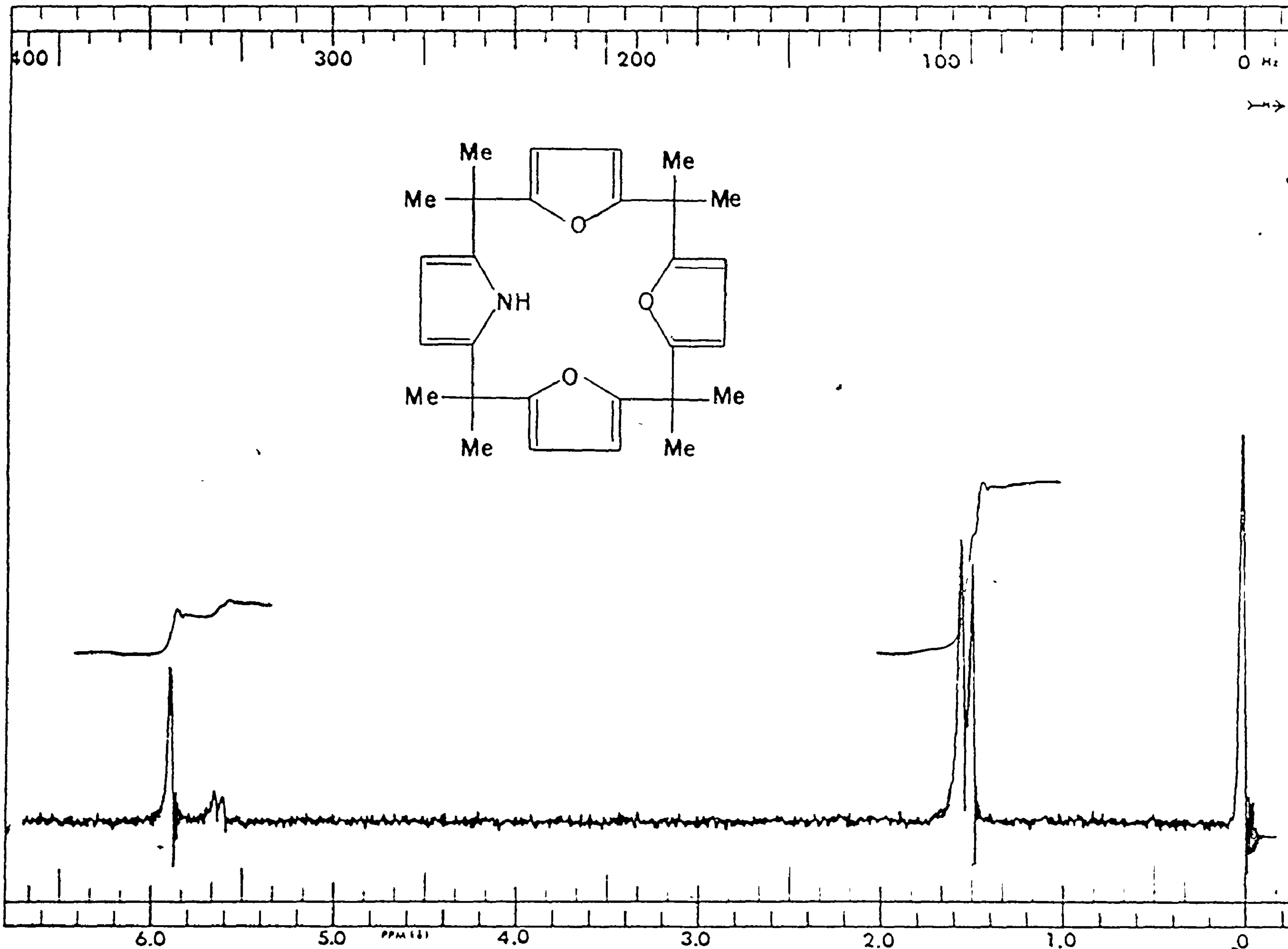


Figure 1. Proton Nuclear Magnetic Resonance Spectrum of Monoaza-trioxaquaterene. Solvent: $CDCl_3$.

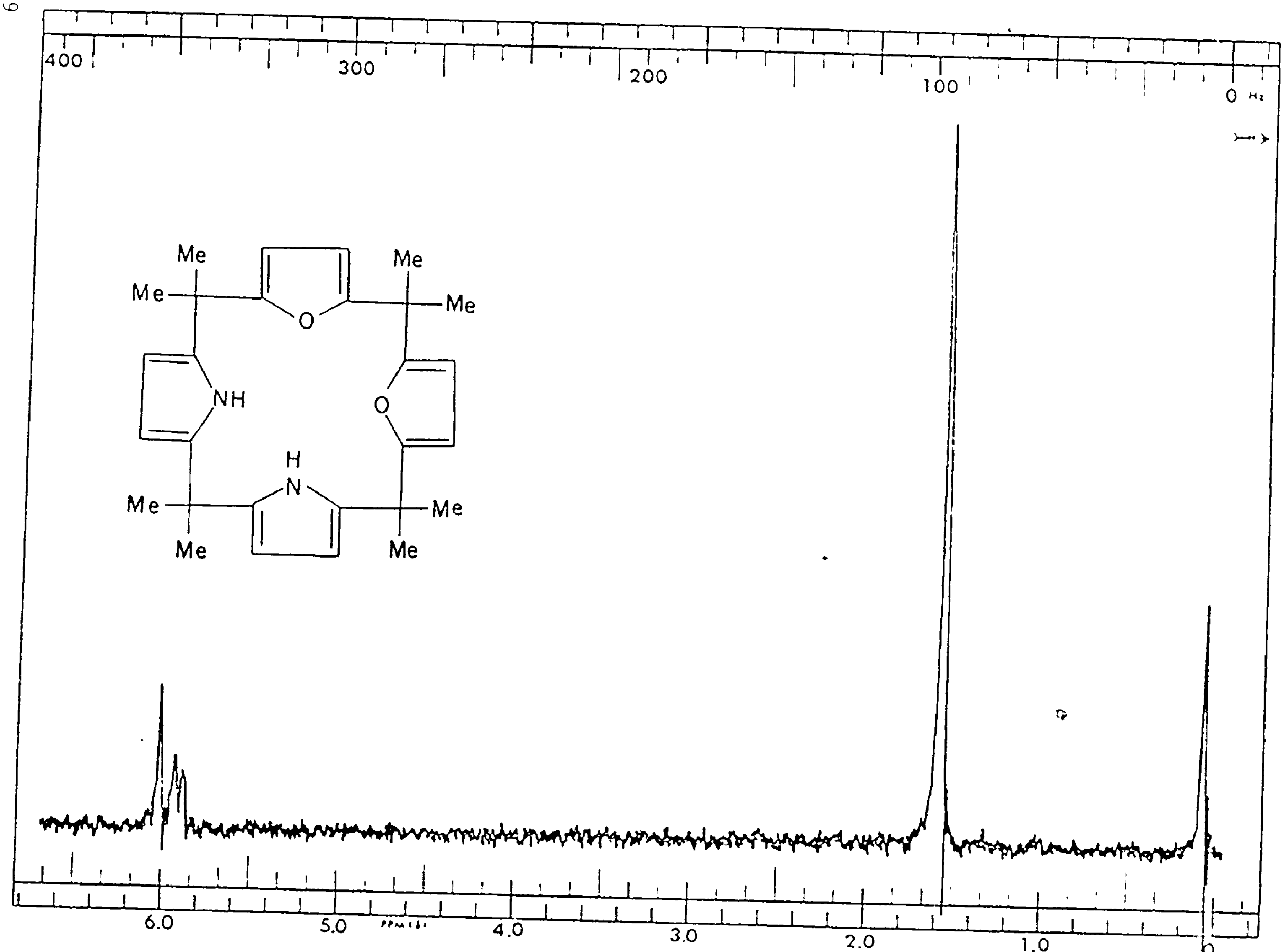


Figure 2. Proton Nuclear Magnetic Resonance Spectrum of cis-Diaza-dioxaquaterene. Solvent: $CDCl_3$.

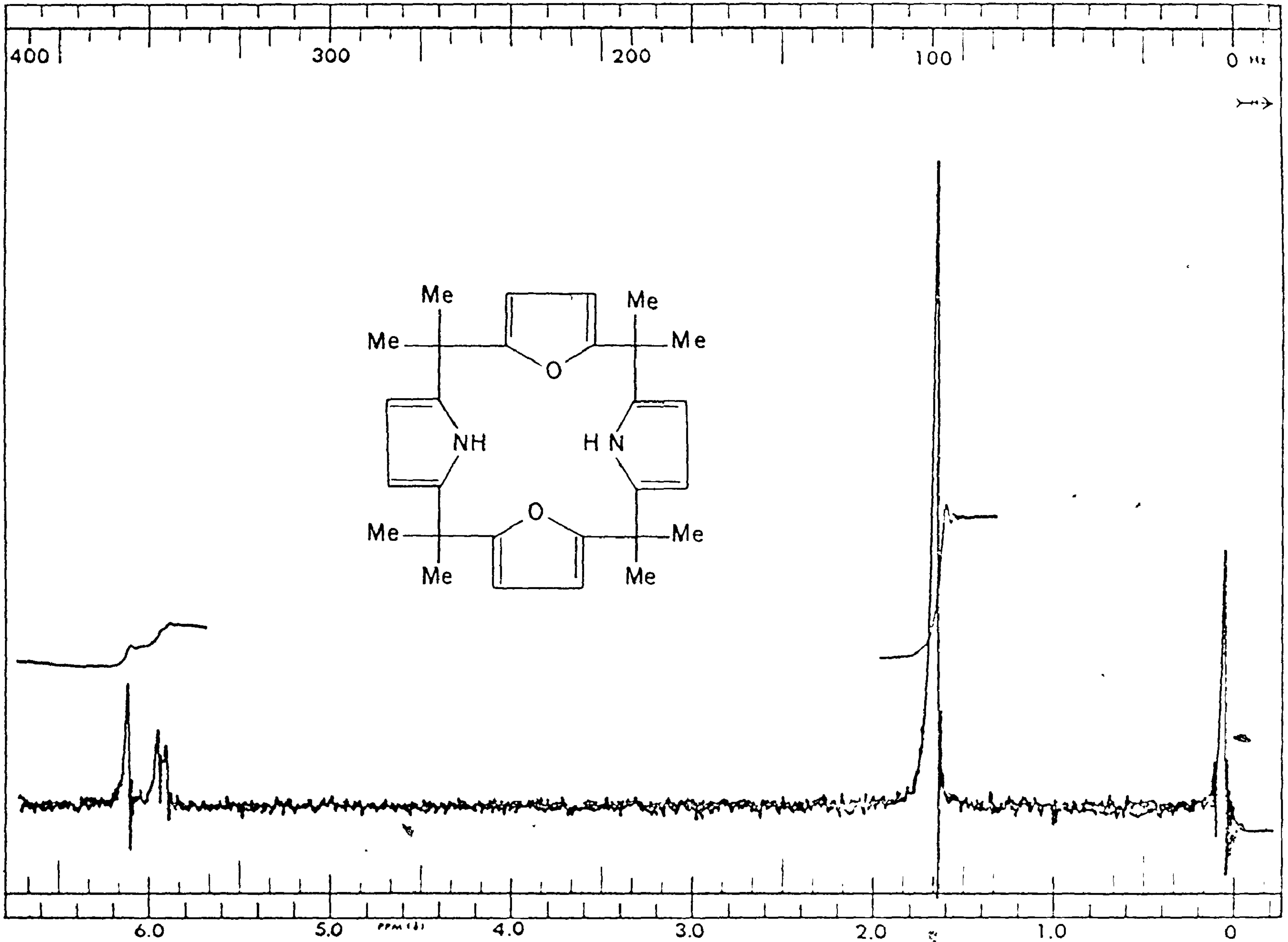


Figure 3. Proton Nuclear Magnetic Resonance Spectrum of trans-Diaza-dioxaquaterene. Solvent: $CDCl_3$.

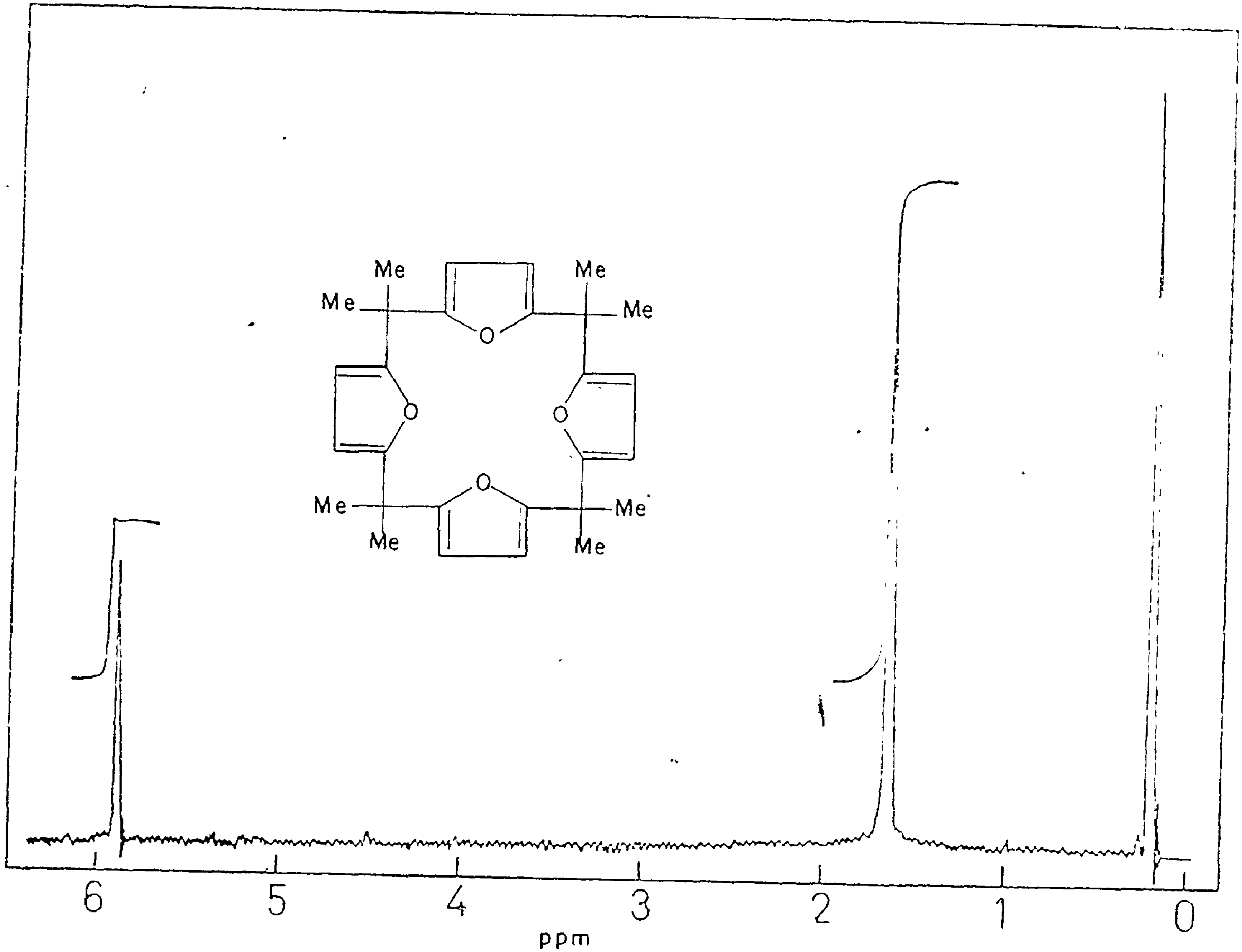


Figure 4. Proton Nuclear Magnetic Resonance Spectrum of Tetroxaquaterene. Solvent: $CDCl_3$.

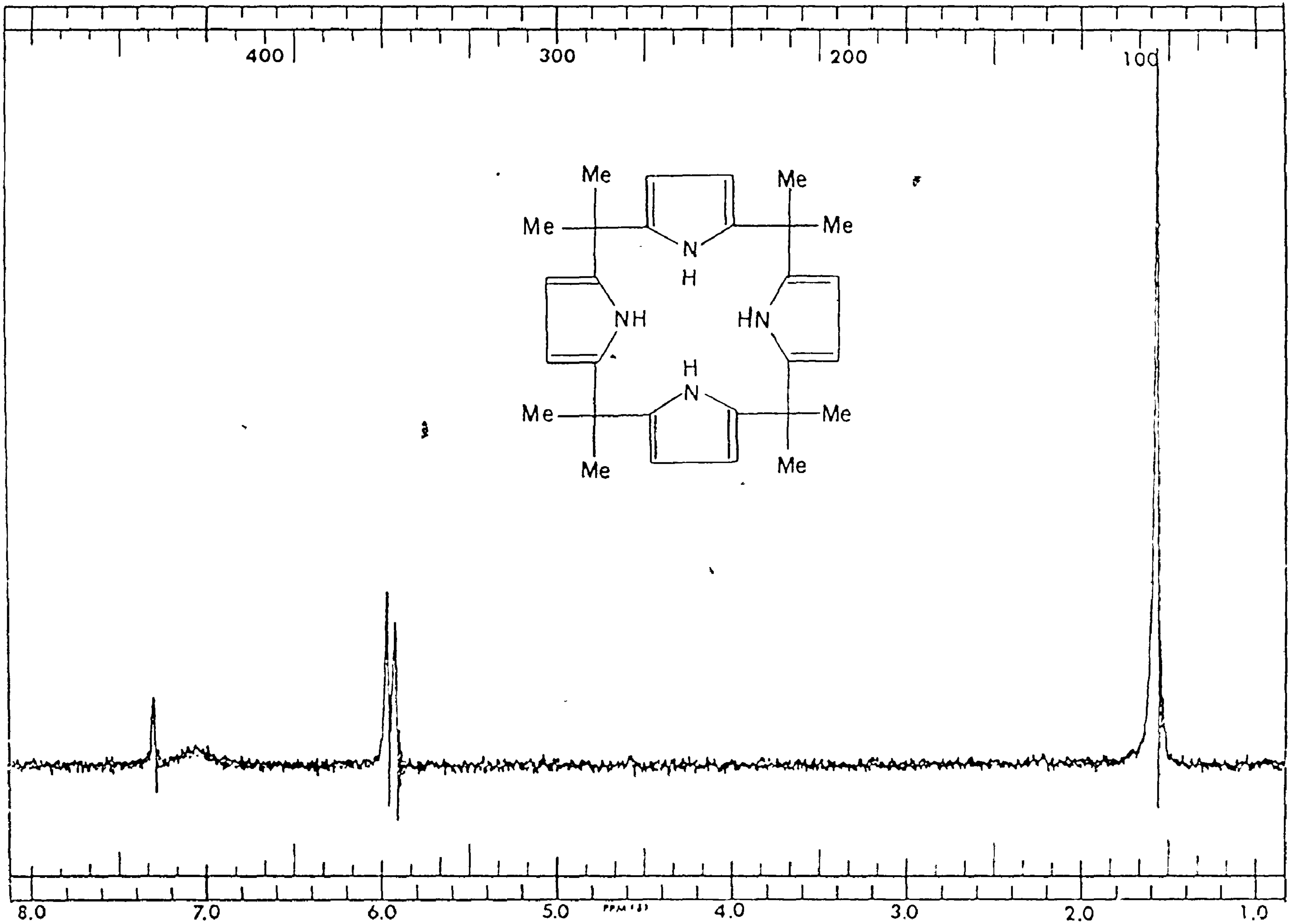


Figure 5. Proton Nuclear Magnetic Resonance Spectrum of Tetrazaquaterene. Solvent: $CDCl_3$.

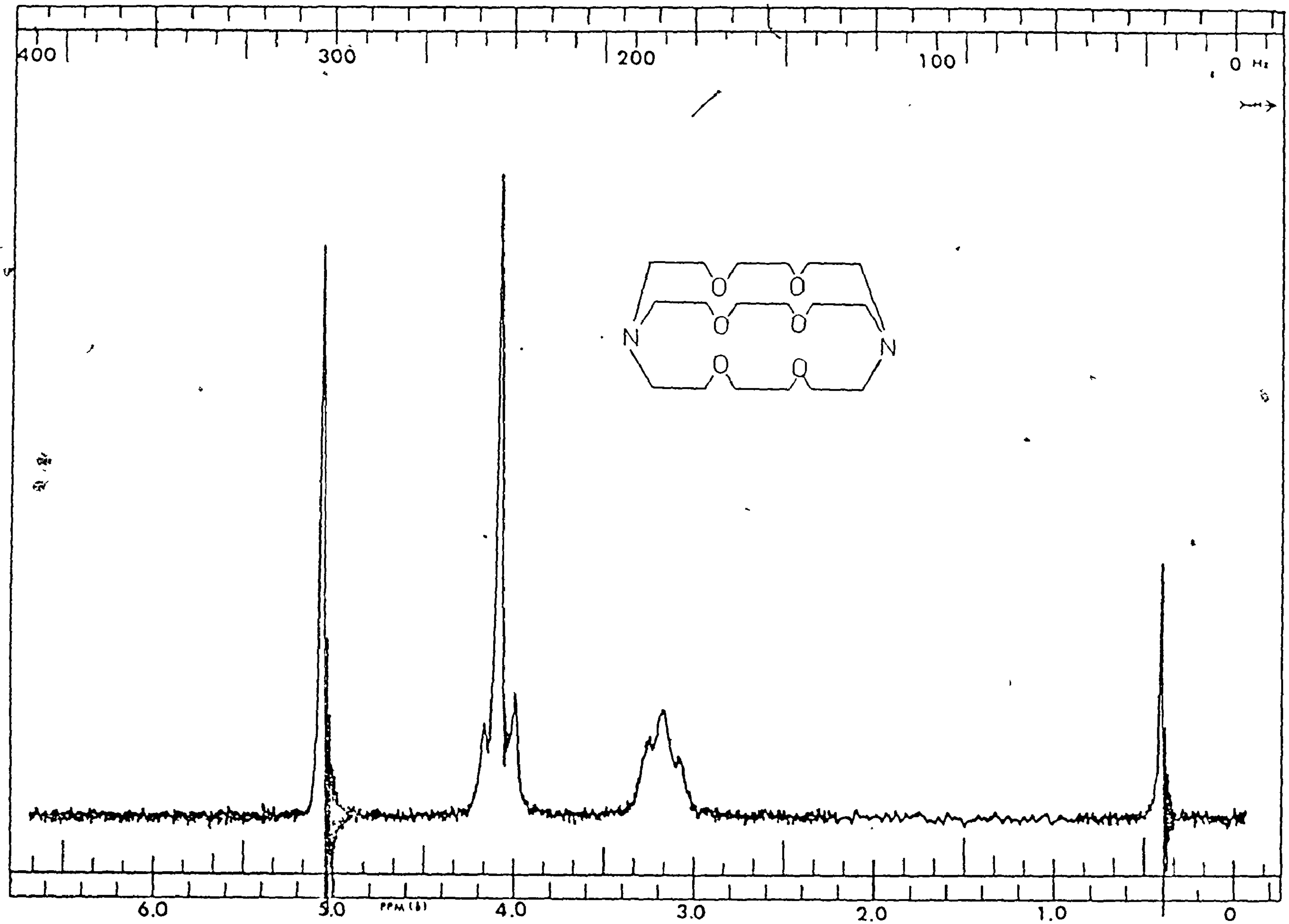


Figure 6(a). Proton Nuclear Magnetic Resonance Spectrum of [2.2.2.] Macrobicyclic diamine. Solvent: TSP.

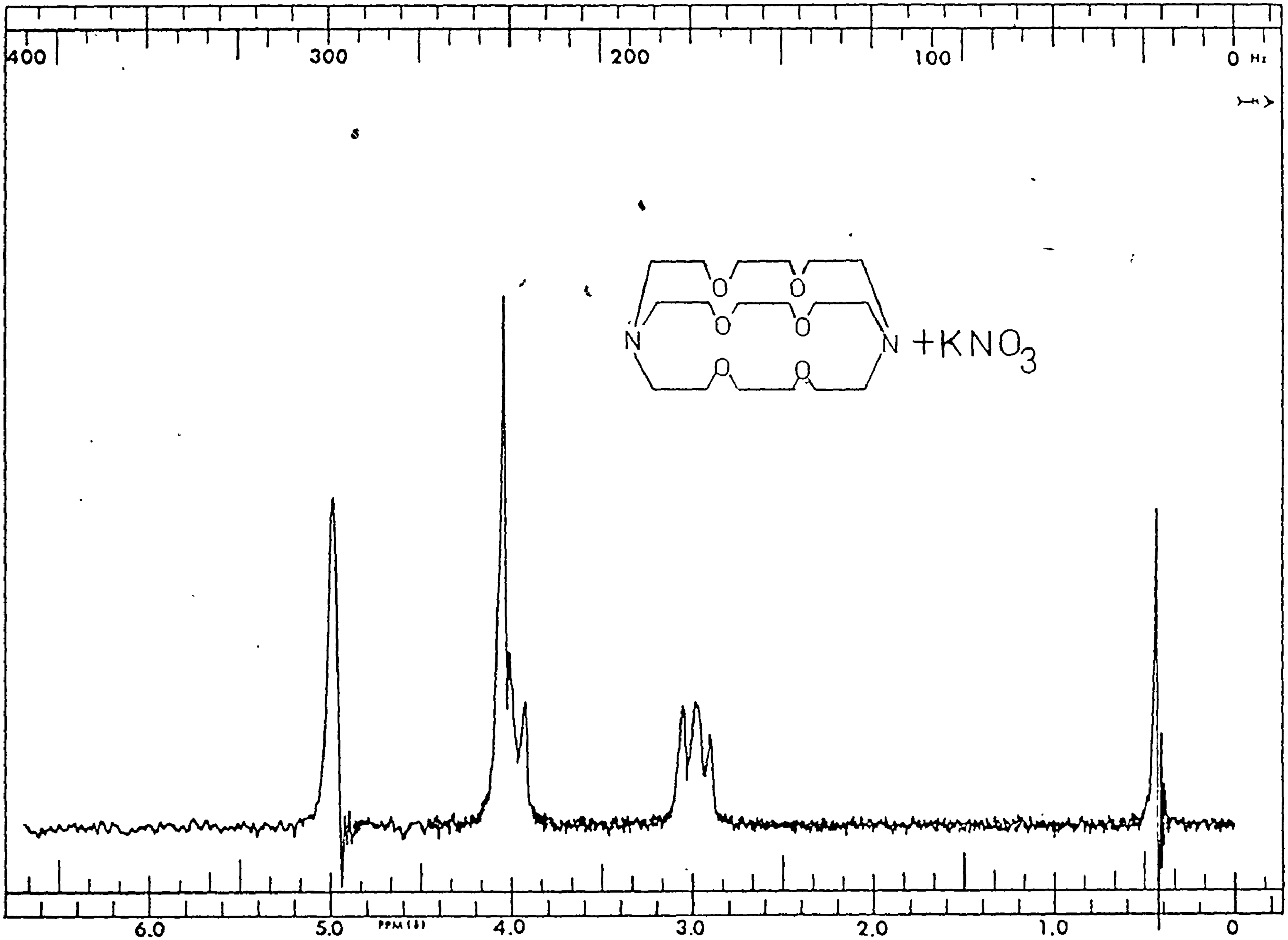


Figure 6(b). Proton Nuclear Magnetic Resonance Spectrum of the KNO_3 Complex of [2.2.2.] Macrobicyclic diamine. Solvent: TSP.

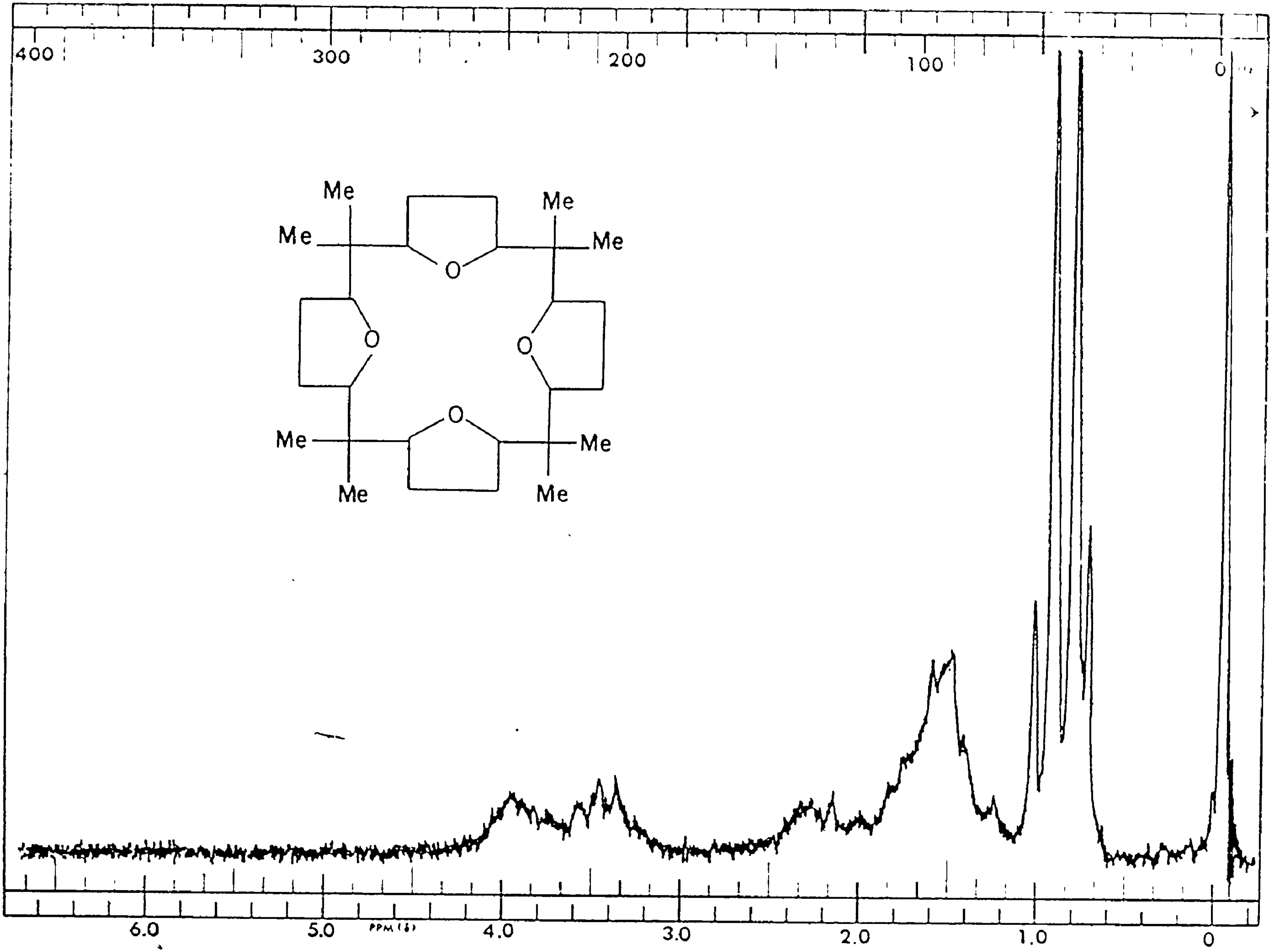


Figure 7. Proton Nuclear Magnetic Resonance Spectrum of the Saturated Form of Tetroxaquaterene. Solvent: $CDCl_3$.

Appendix II. Infrared Spectra of the Quaterene Compounds

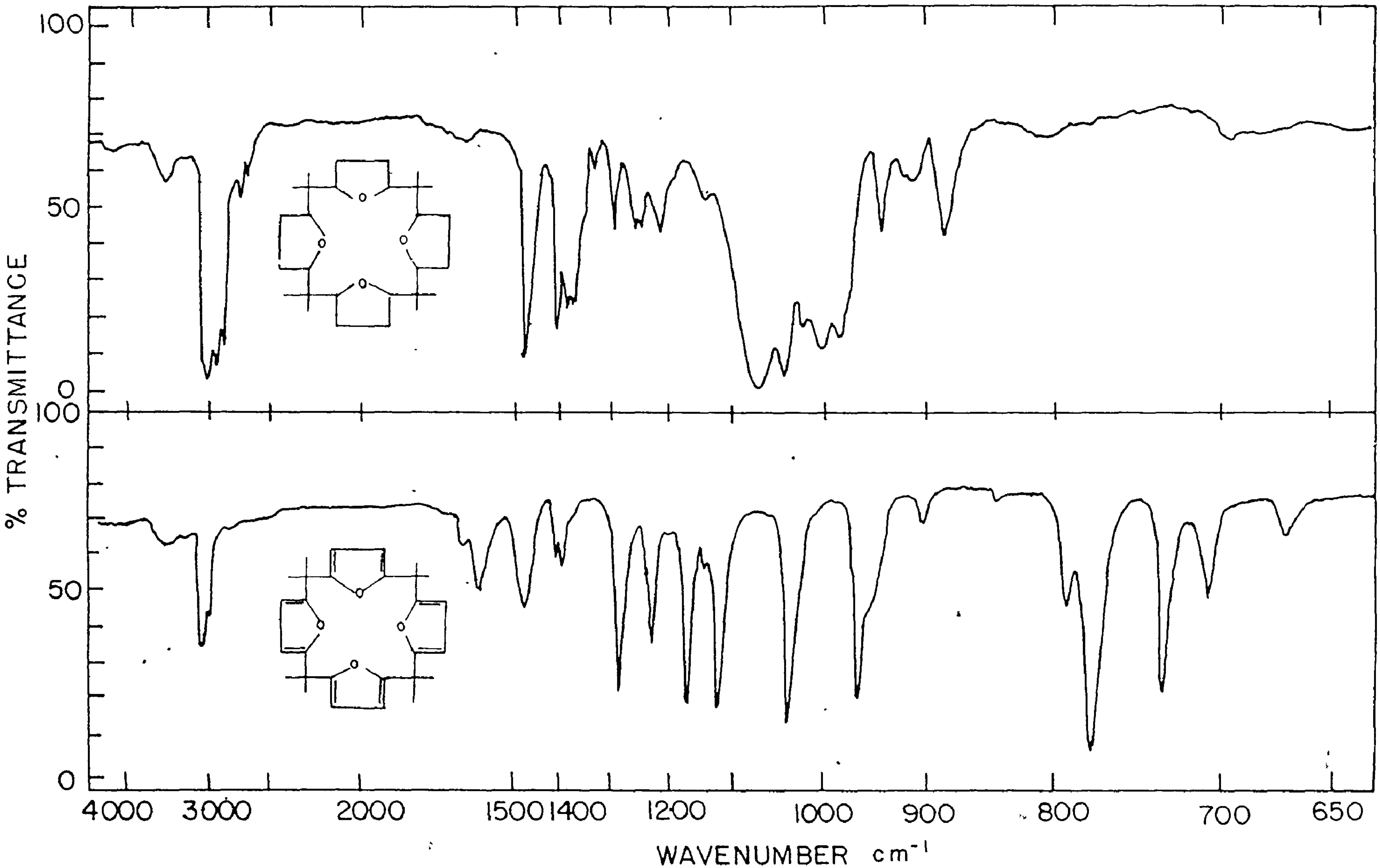


Figure 1. Infrared Spectra (KBr Pellet) of Tetroxaquaterene (bottom) and its Saturated Form (top).

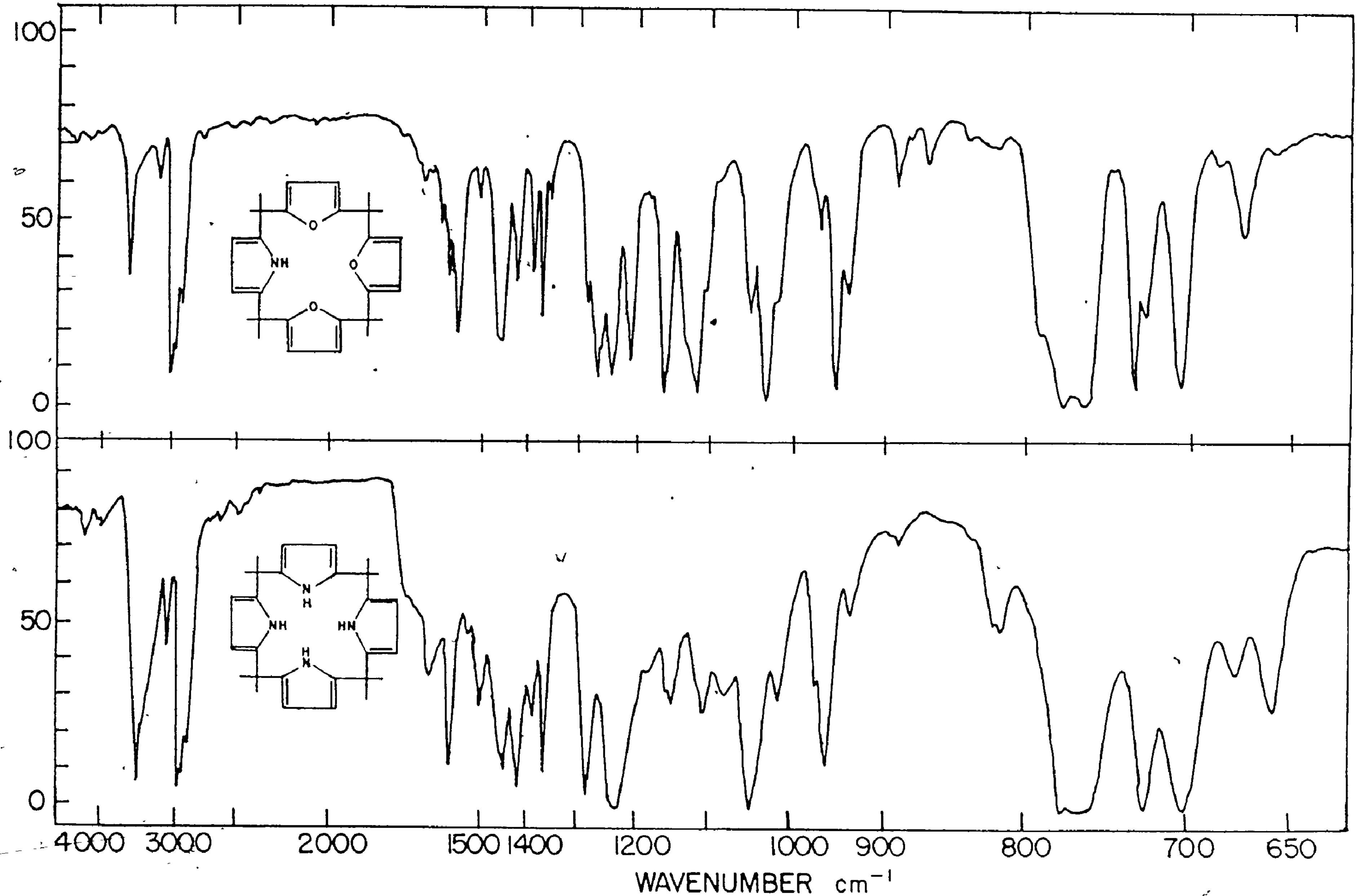


Figure 2. Infrared Spectra (KBr Pellet) of Monoaza-trioxaquaterene (top) and Tetrazaquaterene (bottom).

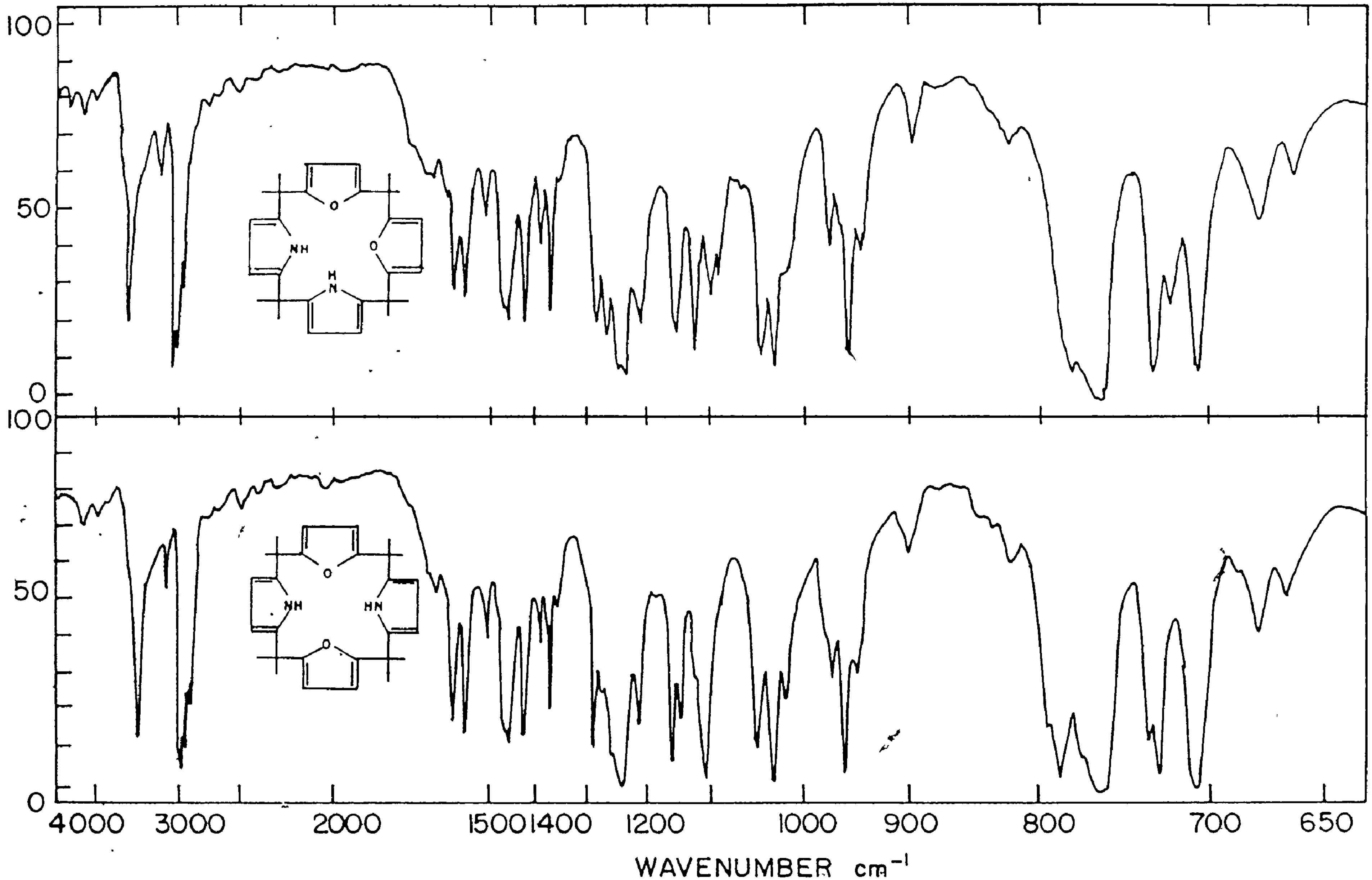


Figure 3. Infrared Spectra (KBr Pellet) of <u>cis</u>-Diaza-dioxaquaterene (top) and <u>trans</u>-Diaza-dioxaquaterene (bottom

Appendix III. Absorption Spectra of Quaterene Ligands and of their Li(I) Complexes.

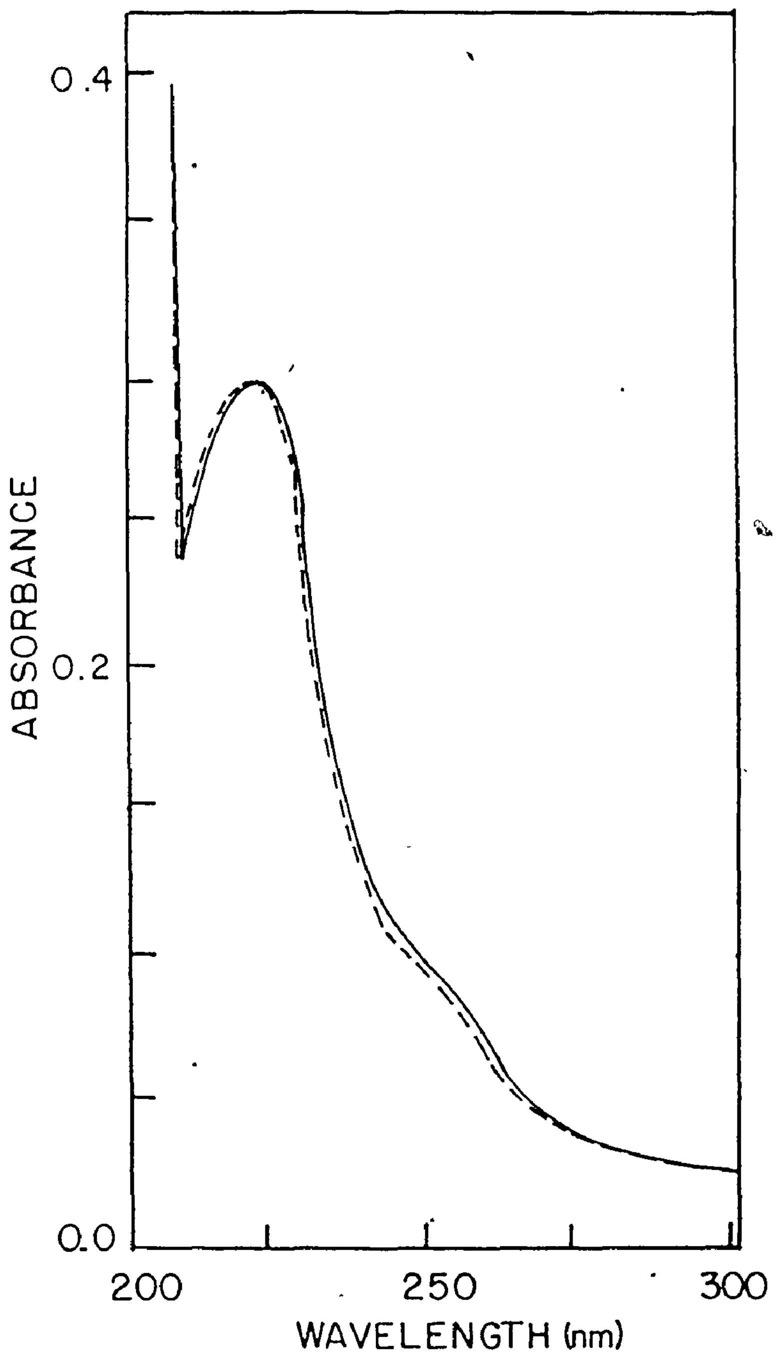


Figure 1. Typical Absorption Spectrum of a Quaterene Compound (3×10^{-5} $\underline{M}$) in 75% V/V Dioxane-Water (Reference: Solvent) (solid line); with $LiClO_4$ Added (2×10^{-4} $\underline{M}$) to Both Sample and Reference (broken line).

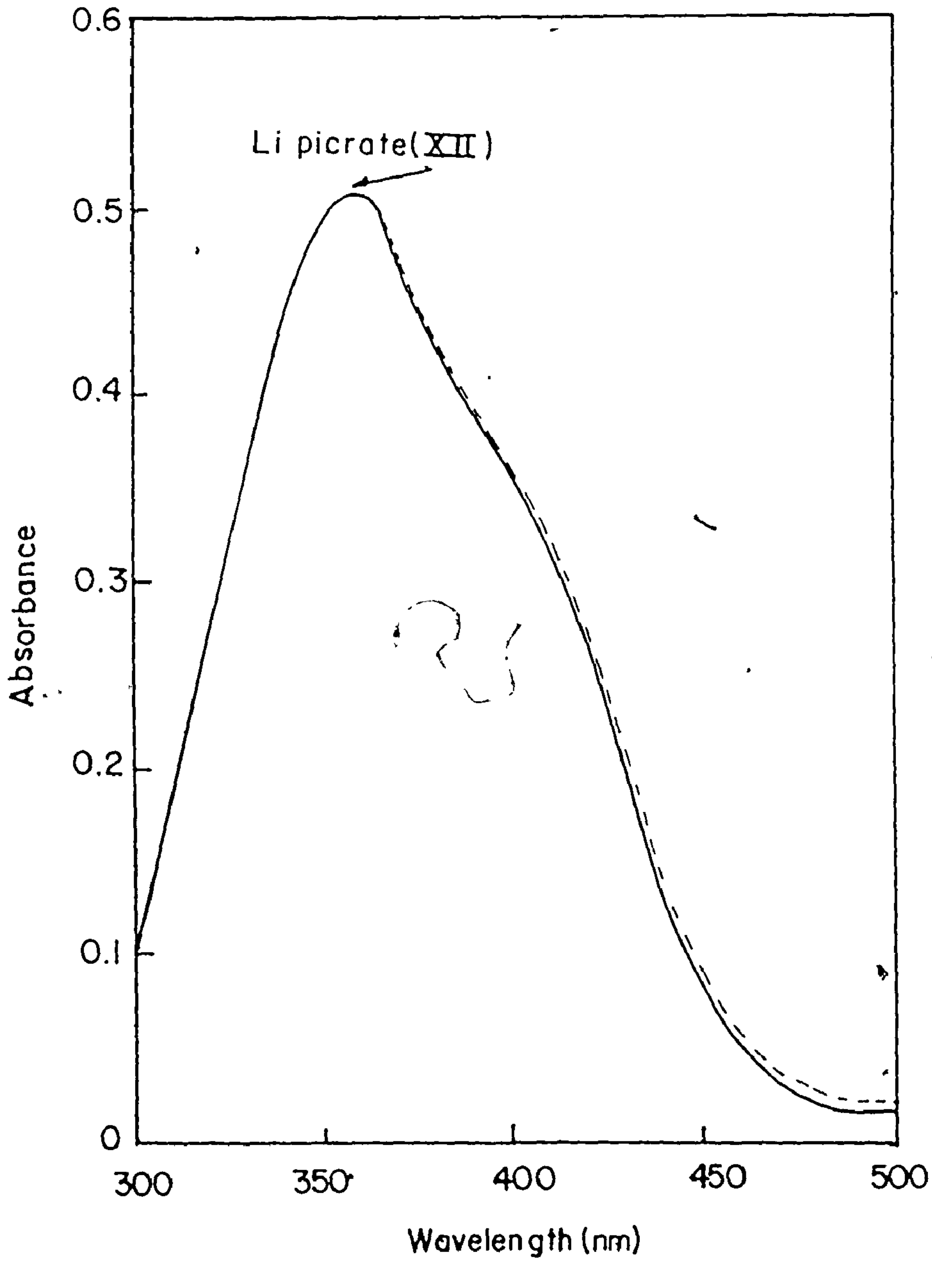


Figure 2. Typical Absorption Spectrum of Picrate Extraction into a Chloroform Solution of Quaterene. Solvent: 50% V/V Chloroform-Water. Concentrations: Metal Hydroxide: 0.1 M; Picric Acid: 4×10^{-5}M; Quaterene: 4×10^{-5}M. Solid Line: Blank; Broken Line: Test.

REFERENCES

1. A. Werner, Z. Anorg. Chem., 3, 267 (1893).
2. L.L. Merritt and J.K. Walker, Ind. Eng. Chem., Anal. Ed., 16, 386 (1944).
3. J.P. Phillips and H.P. Price, J. Amer. Chem. Soc., 73, 4414 (1951).
4. F.J.C. Rossotti in "Modern Coordination Chemistry", edited by J. Lewis and R.G. Wilkins, Interscience, New York, 1960.
5. S. Ahrland, J. Chatt and N.R. Davies, Quart. Rev. (London) 12, 265 (1958).
6. R.J.P. Williams and J.D. Hale, Structure and Bonding, 1, 249 (1966).
7. F. Feigl, Anal. Chem., 21, 1298 (1949).
8. C.J. Pedersen, J. Amer. Chem. Soc., 89, 7017 (1967).
9. Z. Stefanac and W. Simon, Microchem. J., 12, 125 (1967).
10. J.H. Prestegard and S.I. Chan, Biochem., 8, 3921 (1969).
11. idem., J. Amer. Chem. Soc., 92, 4440 (1970).
12. C.J. Pedersen, ibid., 92, 386 (1970).
13. G. Eisenman, S.M. Ciani and G. Szabo, Fed. Proc., 27, 1289 (1968).
14. B.C. Pressman, E.J. Harris, W.S. Jagger and J.H. Johnson, Proc. Nat. Acad. Sci. U.S.A.; 58, 1949 (1967).
15. B.C. Pressman, Fed. Proc., 27, 1283 (1968).
16. M. Chastrette and F. Chastrette, J. Chem. Soc. Chem. Commun., 534 (1973).
17. C.J. Pedersen and H.K. Frensdorff, Angew, Chem. Internat. Ed., 11, 16 (1972).
18. E.J. Corey and G.A. Petersson, J. Amer. Chem. Soc., 94, 460 (1972).
19. C.J. Pedersen, J. Org. Chem., 36, 254 (1971).

20. L. Montillaro, M. Russo, L. Credali and C. DeChecchi, J. Chem. Soc., C, 428 (1966).

21. H.K. Frensdorff, J. Amer. Chem. Soc., 93, 600 (1971).

22. B. Dietrich, J.M. Lehn and J.P. Sauvage, Tetrahedron Letters, 34, 2889 (1969).

23. idem., J. Chem. Soc. Chem. Commun., 1055 (1970).

24. idem., Tetrahedron Letters, 2885 (1969).

25. H.E. Simmon and O.H. Park, J. Amer. Chem. Soc., 90, 2431 (1968).

26. J.M. Lehn, J.P. Sauvage and B. Dietrich, ibid., 92, 2916 (1970).

27. H.K. Frensdorff, ibid., 93, 4684 (1971).

28. G. Klopman, ibid., 90, 223 (1968).

29. P. Schuster and H.W. Preuss, Chem. Phys. Letters, 11, 35 (1971).

30. J.M. Lehn and J.P. Sauvage, J. Chem. Soc. Chem. Commun., 440 (1971).

31. J.J. Christensen, J.O. Hill and R.M. Izatt, Science, 174, 459 (1971).

32. M. Calvin and K.W. Wilson, J. Amer. Chem. Soc., 67, 2003 (1945).

33. R.M. Izatt, D.P. Nelson, J.H. Rytting, J.H. Haymore and J.J. Christensen, ibid., 93, 1619 (1971).

34. A. Lévêque and R. Rosset, Analysis, 2, 218 (1973).

35. W.E. Morf and W. Simon, Helv. Chim. Acta., 54, 794 (1971).

36. S.G.A. McLaughlin, G. Szabo, G. Eisenman and S. Ciani, Biophysical Soc. Abstr., 10, 96a (1970).

37. K.H. Wong, G. Konizer, J. Smid, J. Amer. Chem. Soc., 92, 666 (1970).

38. C.J. Pedersen, ibid., 89, 2495 (1967).

39. idem., ibid., 92, 5226 (1970).

40. D.J. Sam and H.E. Simmons, ibid., 94, 4024 (1972).

41. K.B. Sharpless, R.F. Lauer, O. Repic, A.Y. Teranishi and D.R. Williams, ibid., 93, 3302 (1971).

42. C.M. Starks, ibid., 93, 195 (1971).

43. D.J. Sam and H.E. Simmons, ibid., 94, 4024 (1972).

44. C.J. Pedersen, Fed. Proc., 27, 1305 (1968).

45. G. Eisenman, S. Ciani and G. Szabo, J. Membrane Biol., 1, 294 (1969).

46. D.E. Fenton, M. Mercer, N.S. Poonia and M.R. Truter, J. Chem. Soc. Chem. Commun., 66 (1972).

47. D. Bright and M.R. Truter, J. Chem. Soc. (B), 1543 (1970).

48. idem., Nature, 225, 178 (1970).

49. P.R. Mallison and M.R. Truter, J. Chem. Soc. Perkin Trans. II, 1817 (1972).

50. M.A. Bush and M.R. Truter, J. Chem. Soc. Chem. Commun., 1439 (1970).

51. G.W. Gokel and H.D. Durst, Aldrichimica Acta, 9:1, 3 (1976).

52. C.J. Pedersen, Org. Syn., 52, 66 (1972).

53. M. Mack and H.D. Durst, Department of Chemistry, State University of New York at Buffalo, 1975 (unpublished data).

54. J.S. Valentine and A.B. Curtis, J. Amer. Chem. Soc., 97, 224 (1975).

55. R.A. Johnson and E.G. Nidy, J. Org. Chem., 40, 1680 (1975).

56. C.L. Liotta and H.P. Harris, J. Amer. Chem. Soc., 96, 2250 (1974).

57. C.L. Liotta, H.P. Harris, M. McDermatt, F. Gonzalez and K. Smith, Tetrahedron Letters, 2412 (1974).

58. J.L. Dye, M.G. DeBacker and V.A. Nicely, J. Amer. Chem. Soc., 92, 5226 (1970).

59. "Symposium on Biological and Artficial Membranes", Fed. Proc., 27, 1269 (1968).

60. G. Eisenman, S. Ciani and G. Szabo, J. Membrane Biol., 1, 294 (1969).

61. B.E. Jepson and R. Dewitt, J. Inorg. Nucl. Chem., 38, 1175 (1976)

62. R.B. King and P.R. Heckley, J. Amer. Chem. Soc., 96, 3118 (1974).

63. G.A. Rechnitz and E. Eyal, Anal. Chem., 44, 371 (1972).

64. R.C. Helgeson, J.M. Timko and D.J. Cram, J. Amer. Chem. Soc., 95, 3023 (1973).

65. G.W. Gokel, J.M. Timko and D.J. Cram, J. Chem. Soc. Chem. Commun., 394 (1975).

66. W.D. Curtis, D.A. Laidler, J.F. Stoddard and G.H. Jones, ibid., 833 (1975).

67. J.M. Lehn, Structure and Bonding, 16, 31 (1973).

68. R.G. Ackman, W.H. Brown and G.F. Wright, J. Org. Chem., 20, 1147 (1955).

69. W.H. Brown and W.N. French, Can. J. Chem., 36, 371 (1958).

70. G. Sweifel and H.C. Brown, Org. Reaction, 13, 28 (1963).

71. J.V. Heid and R. Levine, J. Org. Chem., 13, 409 (1948).

72. T. Reichstein, H. Zschokke, R. Gehring and G. Rona, Helv. Chim. Acta., 15, 1118 (1932).

73. L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis", John Wiley and Sons Inc., 1967.

74. C.S. Rondestvedt and F.G. Bordwell, Organic Synthesis, 4, 846 (1963).

75. A.P. Terent'ev and L.A. Yanovskaya, J. Gen. Chem. U.S.S.R., 20, 539 (1950).

76. P. Baumgarten, Chem. Ber., 59, 1166 (1926).

77. A. Baeyer, ibid., 19, 2184 (1886).

78. P. Rothemund and C.L. Gage, J. Amer. Chem. Soc., 77, 3340 (1955).

79. A.P. Terent'ev and L.A. Yanovskaya, J. Gen. Chem. U.S.S.R., 19, 1365 (1949).

80. H. Adins, "Reactions of Hydrogen with Organic Compounds over Copper, Chromium Oxide and Nickel Catalysts", The University of Wisconsin Press, Madison, Wisconsin, 1946, p. 67.

81. C.G. Overberger, L.C. Palmer, B.S. Marks and N.R. Byrd, J. Amer. Chem. Soc., 77, 4100 (1955).

82. F.E. King, J.A. Barltrop and R.J. Wallsy, ibid., 64, 2432 (1947).

83. L. Pauling, "Nature of the Chemical Bond", Cornell University Press, Ithaca, N.Y., 1960.

84. J. Cheney, J.M. Lehn, J.P. Sauvage and M.E. Stubbs, J. Chem. Soc. Chem. Commun., 1100 (1972).

85. J. Cheney and J.M. Lehn, ibid., 487 (1972).

86. J.M. Lehn and F. Montavon, Tetrahedron Letters, 4557 (1972).