Cyclic Polyethers and Their Complexes with Metal Salts

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Abstract: Thirty-three cyclic polyethers, derived from aromatic vicinal diols and containing from 9 to 60 atoms including 3 to 20 oxygen atoms in the ring, have been synthesized. Some of these have been prepared in good yields without the use of a high-dilution technique. Fifteen of the compounds have been catalytically hydrogenated to the corresponding saturated cyclic polyethers. Many of those containing five to ten oxygen atoms form stable complexes with some or all of the cations of: Li, Na, NH_4, RNH_3, K, Rb, Cs, Ag(I), Au(I), Ca, Sr, Ba, Cd, Hg(I), Hg(II), La(III), Tl(I), Ce(III), and Pb(II). Many of these complexes can be isolated in the crystalline form depending on the anion. They appear to be salt-polyether complexes formed by ion-dipole interaction between the cation and the negatively charged oxygen atoms of the polyether ring. The stoichiometry of the complexes is one molecule of polyether per single ion regardless of the valence. Some of the polyethers, by complexing, solubilize inorganic compounds, such as potassium hydroxide and permanganate, in aromatic hydrocarbons.

In a preparation of bis[2-(*o*-hydroxyphenoxy)ethyl] ether by reacting in aqueous 1-butanol bis(2-chloroethyl) ether with the sodium salt of 2-(*o*-hydroxyphenoxy)tetrahydropyran contaminated with some catechol, a very small amount of a white, fibrous, crystalline by-product was obtained. It was found to be 2,3,11,12-dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII), a cyclic polyether capable of forming stable complexes with many salts of the alkali and alkaline earth metals.

A search of the literature disclosed several references to cyclic polyethers containing four or more oxygen atoms in the polyether ring.

Luttringhaus and Ziegler prepared cyclic polyethers derived from resorcinol;[1] and Adams and Whitehill those from hydroquinone.[2] Luttringhaus also synthesized cyclic polyethers derived from hydroquinone, and 1,5- and 2,6-dihydroxynaphthalenes;[3] from 4,4′-dihydroxydiphenyl and 4,4′-dihydroxydiphenylmethane;[4] and from 4,4′-dihydroxydiphenyl ether.[5] Luttringhaus and Sichert-Modrow[6] prepared2, 3,12,13-dibenzo-1,4,11,14-tetraoxacycloeicosa-2,12-diene (XIX) and 2,3,12,13,22,23-tribenzo-1,4,11,14,21,24-hexaoxacyclotriaconta-2,12,22-triene. Ackman, Brown, and Wright[7] obtained 2,2,7,7,12,12,17,17-octamethyl-21,22,-23,24-tetraoxaquaterene by condensing acetone with furan. Stewart, Waddan, and Borrows[8] prepared the cyclic tetramer of ethylene oxide; and Down, Lewis, Moore, and Wilkinson[9,10] synthesized the cyclic tetramer of propylene oxide.

The last authors found that the cyclic tetramer of propylene oxide, like several open-chain polyethers, dissolves very small quantities of potassium and sodium-potassium eutectic to give unstable blue solutions of solvated electrons and solvated cations. The cyclic tetramer was less effective than ethylene glycol dimethyl ether. Lithium, sodium, and calcium failed to give blue solutions.

In none of the references given above is mention made of the formation of stable complexes of the subject compounds with salts of the alkali and alkaline earth elements.

Since the complexing power of XXVIII was unusual, this work was undertaken to investigate this class of compounds. Aromatic vicinal diols were chosen as one of the principal raw materials because the acidic hydroxyl groups are fixed in positions thought to be best for complex formation.

Discussion and Results

Names and Structures of Cyclic Polyethers. The code numbers and the structural formulas of the cyclic polyethers are shown in Figure 1. Although some of the molecules might resemble the drawings, they are not intended to represent their actual configurations. The digits within the diagram indicate the total number of atoms in the polyether ring.

Since many of the names[11] of these polyethers are too cumbersome for repeated use, abbreviated names have been coined for their ready identification. Because of the appearance of its molecular model and its ability to crown the cations, XXVIII, the first cyclic polyether synthesized in this investigation, was called the *crown* and the cyclic polyethers, as a class, the *crown* compounds.

The trivial names are based on this concept. They consist of, in order: (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. The placements of the hydrocarbon rings and the oxygen atoms are as symmetrical as possible in most cases, and

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(1) A. Luttringhaus and K. Ziegler, *Ann.*, **528**, 155, (1937).

(2) R. Adams and L. N. Whitehill, *J. Am. Chem. Soc.*, **63**, 2073 (1941).

(3) A. Luttringhaus, *Ann.*, **528**, 181 (1937).

(4) A. Luttringhaus, *ibid.*, **528**, 211 (1937).

(5) A. Luttringhaus, *ibid.*, **528**, 223 (1937).

(6) A. Luttringhaus and I. Sichert-Modrow, *Makromol. Chem.*, **18–19**, 511 (1956).

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

(8) D. G. Stewart, D. Y. Waddan, and E. T. Borrows, British Patent 785,229 (Oct 23, 1957).

(9) J. L. Down, J. Lewis, B. Moore, and G. W. Wilkinson, *Proc. Chem. Soc.*, 209 (1957).

(10) J. L. Down, J. Lewis, B. Moore, and G. W. Wilkinson, *J. Chem. Soc.*, 3767 (1959).

(11) A more detailed form of this paper (or extended version, or material supplementary to this article) has been deposited as Document number 9583 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington, D. C. 20540. A copy may be secured by citing the document number and by remitting $1.25 for photoprints, or $1.25 for 35-mm microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

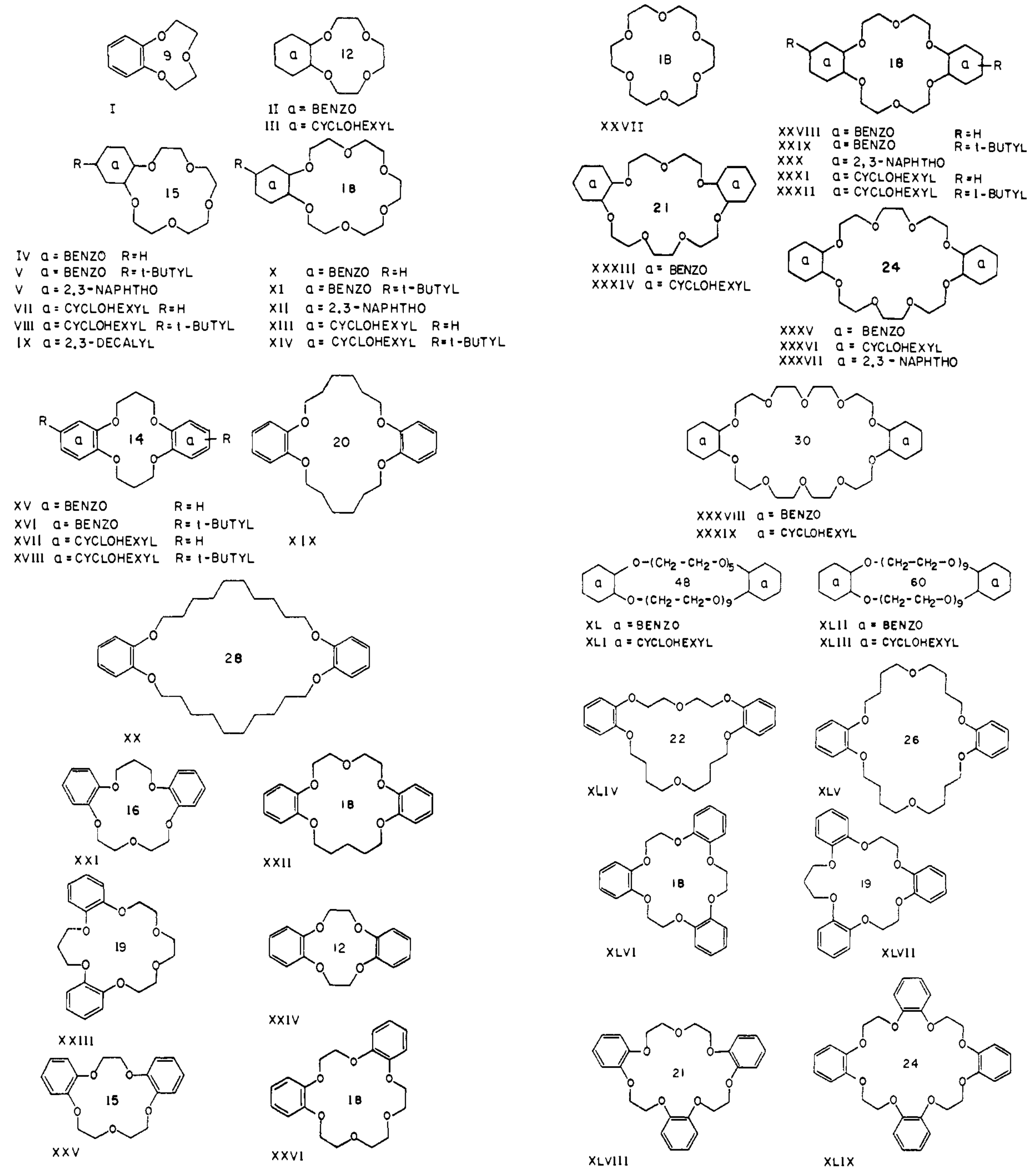


Figure 1. Structural formulas of cyclic polyethers.

the exceptions are indicated by *asym*. 4-*t*-Butyl is abbreviated butyl, and 2,3-naphtho and 2,3-decalyl are abbreviated naphtho and decalyl, respectively. These names will facilitate perusal. The code numbers, however, will be used to ensure correct identification. Some examples of this new nomenclature are given in Table I. When the first number in the name divided by the second equals three, the polyether is a derivative of a cyclic polyethylene oxide.

Methods of Preparation of Cyclic Polyethers. The five different methods used for the preparation of the cyclic polyethers are shown in the following equations where R, S, T, U, and V represent divalent organic groups which may or may not be identical.

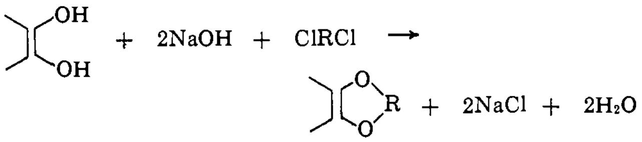
Method Z consists of the hydrogenation of the benzo compounds to the 1,2-cyclohexyl derivatives in *p*-dioxane using ruthenium dioxide catalyst.

Table I. Code Numbers and Trivial Names of Cyclic Polyethers

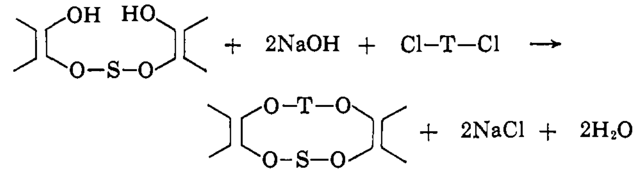
Code	Trivial name
IX	Decalyl-15-crown-5
XV	Dibenzo-14-crown-4
XIX[a]	Dibenzo-20-crown-4
XXI	Dibenzo-16-crown-5
XXII	Dibenzo-18-crown-5
XXIII	*asym*-Dibenzo-19-crown-6
XXVII[b]	18-Crown-6
XXVIII	Dibenzo-18-crown-6
XXXI	Dicyclohexyl-18-crown-6
XLI	*asym*-Dicyclohexyl-48-crown-16
XLIV	*asym*-Dibenzo-22-crown-6
XLV	Dibenzo-26-crown-6

[a] This compound was previously prepared by Luttringhaus and Sichert-Modrow.[6] [b] This compound is not derived from an aromatic vicinal diol, but it is included as an example of an unsubstituted crown compound.

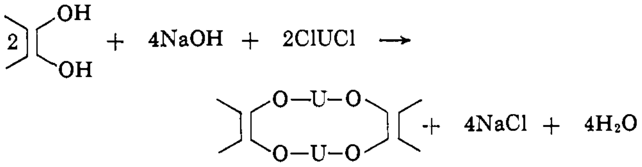
Method V



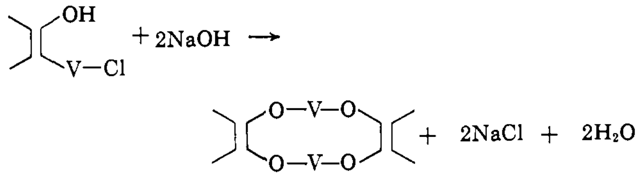
Method W



Method X



Method Y



Method W is the most versatile for the preparation of compounds containing two or more benzo groups. It also gives the highest yields. For example, method W produced dibenzo-14-crown-4 (XV) in a 27% yield; method X, using catechol, 1,3-dibromopropane, and sodium hydroxide, gave an 11% yield of 1,2-trimethylenedioxybenzene but no recoverable amount of XV. Method W gave an 80% yield, and method X a 45% yield of dibenzo-18-crown-6 (XXVIII). In spite of this, the latter is the recommended method for the preparation of XXVIII.

No attempt was made to maximize the yields of the compounds except benzo-15-crown-5 (IV), benzo-18-crown-6 (X), dibenzo-18-crown-6 (XXVIII), and dicyclohexyl-18-crown-6 (XXXI). Many of them were synthesized during the initial stages of the investigation before a good method of recovery had been developed. Since the main object was to obtain the compounds for the determination of their complexing power and not to study synthetic methods, their preparation was not repeated later on. Many of the reported yields, therefore, are too low and are not to be used for an exact comparison of the relative ease of formation of the different ring types. For the same reason details are not given in the Experimental Section for the preparation of all the cyclic polyethers; only the most satisfactory preparations are described. The other compounds should be synthesized by adapting one of the detailed preparations to the method indicated for each in Table II.

It is evident, however, that certain polyether rings are more readily formed than others. The preferred rings are those containing five to six oxygen atoms each separated from the next by two carbon atoms.

The recovery of the aromatic cylic polyethers from the reaction mass is often troublesome especially when the yield is low. The following procedure is generally applicable. Dissolve the reactions products in chloroform and extract with 5% aqueous sodium hydroxide to eliminate phenolic compounds. Remove the solvent and recover the polyether by extracting with a saturated hydrocarbon such as *n*-heptane.

In the preparation of saturated polyethers from the corresponding benzo compounds, method Z, the yields are lowered either by incomplete hydrogenation or the scission of the polyether rings. A study of the catalyst and the reaction conditions will result in better yields. *cis–trans* isomers are obtained in the hydrogenation of the benzo compounds. No attempt was made to separate the isomers but, the mixtures were used in the study of complex formation.

All benzo compounds can be hydrogenated to the corresponding 1,2-cyclohexyl polyether. Some of them were not hydrogenated because the precursors were not available in sufficient quantity, or the products were not expected to be complexing agents.

Identification of Cyclic Polyethers. The proof of the structure of the cyclic polyethers is based on elementary composition, molecular weight, and nmr spectrum. Some of these data are listed in Table III. All nmr spectra obtained in deuteriochloroform are consistent with the proposed structures as shown for some of the aromatic compounds in Table IV. These spectra establish the absence of terminal groups, such as hydroxyl and alkoxy.

Molecular weight distinguishes compounds having the same composition, such as benzo-9-crown-3 (I) and dibenzo-18-crown-6 (XXVIII) and cyclohexyl-15-crown-5 (VII) and dicyclohexyl-30-crown-10 (XXXIX).

Infrared and ultraviolet spectra were also obtained. The former confirm the absence of hydroxyl group, and indicate the presence of ether linkages by strong, broad bands centering near 8.1 (aromatic–O–aliphatic) and 8.85 μ (aliphatic–O–aliphatic).

The ultraviolet spectra of compounds derived from catechol and 4-*t*-butylcatechol have absorption bands (in methanol) at 273–275 and 277–278 mμ, respectively. These bands are characteristic for the two diols and their ethers. The extinction coefficients, ϵ, of the compounds derived from catechol containing one benzo group are 2100–2300, two groups 4400–5200, three groups 6300–7200, and four groups 8400. Those of 4-*t*-butylcatechol derivatives: one group 2700 and two groups 5000–5200.

Dibenzo-18-crown-6 (XXVIII) and dicyclohexyl-18-crown-6 (XXXI) have been selected to represent the aromatic and the saturated cyclic polyethers, respectively, for more detailed treatment. Their nmr and infrared spectra and the ultraviolet spectrum and Courtauld model of XXVIII are shown in Figures 2–9.

Nature of the Complexes and Factors Affecting Their Stability. Many of these cyclic polyethers form complexes with the salts of the elements belonging to the following groups of the periodic table: all in IA and IB; most in IIA; some in IIB; and a few in IIIA, IIIB, and IVB.[12]

These compounds appear to be salt–polyether complexes formed by ion-dipole interaction between the cation and the negatively charged oxygen atoms sym-

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(12) The complexes of the transition metals will be the subject of a separate paper.

Table II. Synthetic Methods for Cyclic Polyethers: Reactants,[a] Solvents, and Yields

Compd	Method	Reactant 1	Reactant 2	Solvent	Yield, %
I	V	Catechol	Bis(2-chloroethyl) ether	Water	5
II	V	Same as I	1,6-Dichloro-3,6-dioxaoctane	Aqueous 1-butanol	4
III	Z	Hydrogenation of II		*p*-Dioxane	48
IV	V	Same as I	1,11-Dichloro-3,6,9-trioxaundecane	1-Butanol	62
V	V	4-*t*-Butylcatechol	Same as IV	1-Butanol	61
VI	V	2,3-Dihydroxynaphthalene	Same as IV	1-Butanol	20
VII	Z	Hydrogenation of IV		*p*-Dioxane	58
VIII	Z	Hydrogenation of V		*p*-Dioxane	17[b]
IX	Z	Hydrogenation of VI		*p*-Dioxane	28
X	V	Same as I	1,14-Dichloro-3,6,9,12-tetraoxatetradecane	1-Butanol	60
XI	V	Same as V	Same as X	1-Butanol	62
XII	V	Same as VI	Same as X	1-Butanol	25
XIII	Z	Hydrogenation of X		*p*-Dioxane	46
XIV	Z	Hydrogenation of XI		*p*-Dioxane	12[b]
XV	W	1,3-Bis(*o*-hydroxyphenoxy)propane	1,3-Dibromopropane	Aqueous 1-butanol	27
XVI	W	1,3-Bis(4′- or 5′-*t*-butyl-2′-hydroxyphenoxy)propane	Same as XV	Aqueous 1-butanol	11
XVII	Z	Hydrogenation of XV		*p*-Dioxane	55
XVIII	Z	Hydrogenation of XVI		*p*-Dioxane	41
XIX	W	1,6-Bis(*o*-hydroxyphenoxy)hexane	1,6-Dibromohexane	Aqueous 1-butanol	4
XX	Y	1-Bromo-10-(*o*-hydroxyphenoxy)decane	1-Bromo-10-(*o*-hydroxyphenoxy)decane	1-Butanol	3
XXI	W	Same as XV	Same as I	Aqueous 1-butanol	18
XXII	W	Bis[2-(*o*-hydroxyphenoxy)-ethyl] ether	1,5-Dibromopentane	Aqueous 1-butanol	28
XXIII	W	1,8-Bis(*o*-hydroxyphenoxy)-3,6-dioxaoctane	Same as XV	1-Butanol	16
XXIV	W	1,2-Bis(*o*-hydroxyphenoxy)ethane	1,2-Dibromomethane	Water	11
XXIV	V	Same as I	*o*-Bis(2-chloroethoxy)benzene	1-Butanol	15
XXV	W	Same as XXIV	Same as I	2-Methoxyethanol	43
XXVI	W	Same as XXIV	Same as II	Aqueous 1-butanol	25
XXVII		Special method (see Experimental Section)		1,2-Dimethoxyethane	2
XXVIII	W	Same as XXII	Same as I	1-Butanol	80
XXVIII	X	Same as I	Same as I	1-Butanol	45
XXIX	W	Bis[2-(4′- or 5′-*t*-butyl-2′-hydroxyphenoxy]ethyl) ether	Same as I	Aqueous 1-butanol	17[b]
XXX	W	Same as VI	Same as I	Aqueous 1-butanol	25
XXXI	Z	Hydrogenation of XXVIII		*p*-Dioxane	45–67
XXXII	Z	Hydrogenation of XXIX		*p*-Dioxane	52
XXXIII	W	Same as XXII	Same as II	1-Butanol	36
XXXIV	Z	Hydrogenation of XXXIII		*p*-Dioxane	50
XXXV	X	Same as I	Same as II	1-Butanol	38
XXXVI	Z	Hydrogenation of XXXV		*p*-Dioxane	63
XXXVII	X	Same as VI	Same as II	1-Butanol	63
XXXVIII	X	Same as I	Same as IV	1-Butanol	*c*
XXXIX	Z	Hydrogenation of XXXVIII		*p*-Dioxane	61
XL	W	1,26-Bis(1-hydroxyphenoxy)-3,6,9,12,15,18,-21,24-octaoxahexacosane	Same as X	1-Butanol	32
XLI	Z	Hydrogenation of XL		*p*-Dioxane	58
XLII	W	Same as XL	1,26-Dichloro-3,6,9,12,15,18,21,24-octaoxahexacosane	1-Butanol	41
XLIII	Z	Hydrogenation of XLII		*p*-Dioxane	45
XLIV	W	Same as XXII	Bis(4-chlorobutyl) ether	Aqueous 1-butanol	9
XLV	X	Same as I	Same as XLIV	2-Methoxyethanol	17
XLVI	W	Same as XXIV	*o*-Bis(2-chloroethoxy)benzene	Aqueous 1-butanol	28
XLVII	W	Same as XV	Same as XLVI	Aqueous 1-butanol	16
XLVIII	W	Same as XXII	Same as XLVI	1-Butanol	19
XLIX	W	1,14-Dihydroxy-1,2,7,8,13,14-tribenzo-3,6,-9,12-tetraoxatetradeca-1,7,13-triene	Same as XLVI	1-Butanol	19
XLIX	X	Same as I	Same as XLVI	1-Butanol	18

[a] Potassium hydroxide was used for the preparation of XXXV, XXXVII, XXXVIII, XL, and XLII; sodium hydroxide for the others. [b] Low yield is due to difficulty in isolating the pure product. [c] A mixture of IV and XXXVIII was obtained in a 51% yield. The yield of XXXVIII was at least 6%.

metrically placed in the polyether ring.[13] The formation of stable ammonium complexes supports this interpretation.

The conditions necessary for the formation and the factors influencing the stability of the complexes include: (1) the relative sizes of the ion and the hole in the polyether ring, (2) the number of oxygen atoms in the polyether ring, (3) the coplanarity of the oxygen atoms, (4) the symmetrical placement of the oxygen atoms, (5) the basicity of the oxygen atoms, (6) steric hindrance in the polyether ring, (7) the tendency of the ion to associate with the solvent, and (8) the electrical charge on the ion.

A stable complex is not formed if the ion is too large

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(13) A helpful discussion on this aspect of the problem with Professor G. W. Watt is gratefully acknowledged.

Table III. Analytical Data and Melting Points

Compd	Formula	Mp, °C[a]	Carbon, %: Found	Carbon, %: Calcd	Hydrogen, %: Found	Hydrogen, %: Calcd	Mol wt[b]: Found	Mol wt[b]: Calcd
I	$C_{10}H_{12}O_3$	67–69	66.6	66.6	6.4	6.7	180	180
II	$C_{12}H_{16}C_4$	44–45.5	64.5	64.3	7.4	7.1	219	224
III	$C_{12}H_{22}O_4$	Below 26	63.0	62.6	9.8	9.6	238	230
IV	$C_{14}H_{20}O_5$	79–79.5	62.7	62.7	7.4	7.5	278	268
V	$C_{18}H_{28}O_5$	43.5–44.5	66.4	66.7	8.9	8.6	320	324
VI	$C_{18}H_{22}O_5$	117–119	67.8	67.9	7.0	6.9	317	318
VII	$C_{14}H_{26}O_5$	Below 26	60.8	61.3	9.4	9.5	262	274
VIII	$C_{18}H_{34}O_5$	Below 26	66.1	65.5	10.6	10.3	329	330
IX	$C_{18}H_{32}O_5$	Below 26	65.4	65.8	9.6	9.8	316	328
X	$C_{16}H_{24}O_6$	43–44	61.3	61.5	7.6	7.7	319	312
XI	$C_{20}H_{32}O_6$	35–37	65.1	65.2	8.7	8.7	363	368
XII	$C_{20}H_{26}O_6$	110–111.5	66.1	66.3	7.2	7.2	349	362
XIII	$C_{16}H_{30}O_6$	Below 26	60.4	60.4	9.5	9.4	314	318
XIV	$C_{20}H_{38}O_6$	Below 26	64.4	64.2	10.5	10.2	354	374
XV	$C_{18}H_{20}O_4$	150–152	71.7	72.0	6.6	6.7	299	300
XVI	$C_{26}H_{36}O_4$	149–152	76.2	75.8	8.7	8.7	433	412
XVII	$C_{18}H_{32}O_4$	153.5–155.5	69.3	69.2	10.3	10.3	. . .	312
XVIII	$C_{26}H_{48}O_4$	A glass at 26°	73.9	73.6	10.4	11.3	420	424
XIX	$C_{24}H_{32}O_4$	139–141	74.6	75.0	7.9	8.3	. . .	384
XX	$C_{32}H_{48}O_4$	137–138.5	77.4	77.4	9.6	9.7	. . .	496
XXI	$C_{19}H_{22}O_5$	117–118	68.9	69.1	6.6	6.8	330	330
XXII	$C_{21}H_{26}O_5$	157–158	69.3	70.4	7.3	7.3	359	358
XXIII	$C_{21}H_{26}O_6$	84.5–86	67.0	67.4	6.9	7.0	387	374
XXIV	$C_{16}H_{16}O_4$	208–209	70.4	70.6	5.6	5.9	. . .	272
XXV	$C_{18}H_{20}O_5$	113.5–115	68.4	68.4	6.3	6.3	328	316
XXVI	$C_{20}H_{24}O_6$	117–118	66.5	66.6	7.0	6.7	360	360
XXVII	$C_{12}H_{24}O_6$	39–40	54.9	54.5	9.4	9.1	299	264
XXVIII	$C_{20}H_{24}O_6$	164	66.3	66.6	6.8	6.7	371	360
XXIX	$C_{28}H_{40}O_6$	135–137	71.2	71.2	8.1	8.5	450	472
XXX	$C_{28}H_{28}O_6$	244–246	72.3	73.0	6.2	6.1	. . .	460
XXXI[c]	$C_{20}H_{36}O_6$	68.5–69.5	64.5	64.5	9.6	9.7	378	372
XXXII	$C_{28}H_{52}O_6$	Below 26	70.1	69.4	10.2	10.8	445	484
XXXIII	$C_{22}H_{28}O_7$	106.5–107.5	65.1	65.4	7.0	6.9	420	404
XXXIV	$C_{22}H_{40}O_7$	Below 26	62.9	63.5	9.6	9.6	402	416
XXXV	$C_{24}H_{32}O_8$	113–114	64.4	64.3	6.9	7.1	453	448
XXXVI	$C_{24}H_{44}O_8$	Below 26	62.8	62.6	9.8	9.6	450	460
XXXVII	$C_{32}H_{36}O_8$	190–191.5	70.2	70.0	6.6	6.6	548	548
XXXVIII	$C_{28}H_{40}O_{10}$	106–107.5	62.7	62.7	7.5	7.5	539	536
XXXIX	$C_{28}H_{52}O_{10}$	Below 26	61.3	61.3	9.7	9.5	520	548
XL	$C_{40}H_{64}O_{16}$	Below 26	60.3	60.0	8.1	8.0	810	800
XLI	$C_{40}H_{76}O_{16}$	Below 26	58.9	59.1	9.5	9.4	. . .	812
XLII	$C_{48}H_{80}O_{20}$	Below 26	58.4	59.0	8.3	8.2	963	976
XLIII	$C_{48}H_{92}O_{20}$	Below 26	57.4	58.3	9.4	9.4	. . .	988
XLIV	$C_{24}H_{32}O_6$	82–83	68.6	69.2	7.5	7.7	441	416
XLV	$C_{28}H_{40}O_6$	125–127	70.3	71.1	8.4	8.5	493	472
XLVI	$C_{24}H_{24}O_6$	190–192	70.9	70.6	5.9	5.9	. . .	408
XLVII	$C_{25}H_{26}O_6$	147–149	71.0	71.1	6.2	6.2	418	422
XLVIII	$C_{26}H_{28}O_7$	98.5–100	68.8	69.0	6.3	6.2	470	452
XLIX	$C_{32}H_{32}O_8$	150–152	70.8	70.6	5.9	5.9	. . .	544

[a] Melting points were taken on a Fisher–Johns apparatus and are uncorrected. The melting point of XXVIII, 164°, however, was obtained by another method and is corrected. This compares with 163–165° on the aluminum block. [b] Molecular weights were determined by the boiling point method using benzene. No value is given in the table when there was not enough material for a determination or it was too insoluble in benzene. [c] The normal sample of XXXI used in the preparation of its salt complexes is a mixture of *cis–trans* isomers and has a melting range lying between 36 and 56°. Fractionation must have occurred in the preparation of the crystals of XXXI whose melting point of 68.5–69.5° is given in Table III (see Experimental Section). All the other hydrogenation products, except XVII and XVIII (a glass) are viscous liquids at room temperature.

to lie in the hole of the polyether ring. The ionic diameters of the complexable cations are listed in Table V, and the estimated sizes of the holes for typical members of the different polyether rings are given in Table VI. The latter, corresponding to the diameters of the largest spheres that can pass through them, were estimated by means of molecular models built with Fisher–Hirschfelder–Taylor atomic models.

A complex is the more stable the greater the number of oxygen atoms, provided the oxygens are coplanar and symmetrically distributed in the polyether ring. An oxygen atom is considered to be coplanar if it lies in the same plane as all the other oxygens in the ring, and the apex of the C–O–C angle is centrally directed in the same plane. Symmetry is at a maximum when all the oxygen atoms are evenly spaced in a circle. When seven or more oxygens 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 apices of the C–O–C angles pointed toward the center of the cylinder. This configuration, termed cylindrically symmetrical, permits the formation of salt complexes. These definitions are used for the comments in Table VI which refer to the oxygen atoms.

The stability of the complex is the higher the more

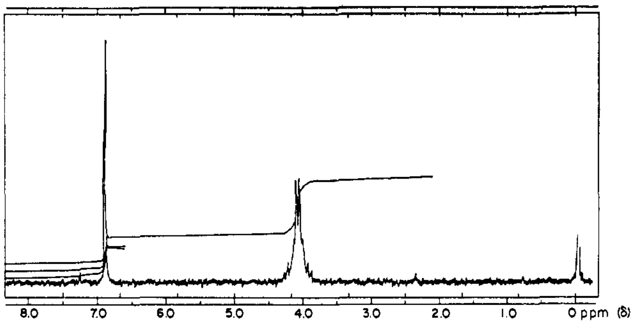

Figure 2. Nmr spectrum of dibenzo-18-crown-6 (XXVII): (upper) multiplet, 4.11 ppm downfield from TMS, area ratio 2.2; (lower) singlet, 6.92 ppm downfield from TMS, area ratio 1.0.

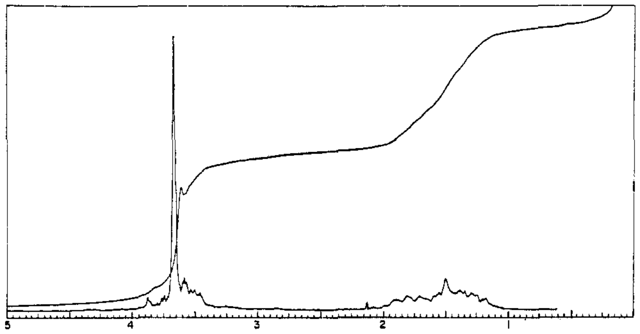

Figure 3. Nmr spectrum of dicyclohexyl-18-crown-6 (XXXI): (upper) multiplet, 1.50 ppm downfield from TMS, area ratio 1.17; (lower) singlet, 3.67 ppm downfield from TMS, area ratio 1.00.

basic the oxygen atoms, one attached to an aromatic carbon being less basic than one attached only to aliphatic carbon atoms.

Steric hindrance in the polyether ring prevents the formation of complexes.

Table IV. Nmr Spectra

Compd	Proton	δ, cps	Rel intens Obsd	Rel intens Theory
I	CH_2-O	∼−230	3.8	4
	CH_2-O	∼−260	4.1	4
	Aromatic	−417	4.0	4
II	CH_2-O	−227	7.9	4
	CH_2-O	∼−227		4
	CH_2-O	−251	4.2	4
	Aromatic	−418	3.8	4
XV	C-CH_2-C	−137	4.4	4
	CH_2-O	−257	7.6	8
	Aromatic	−418	8.0	8
XIX	C-CH_2-C	−100	16.5	16
	CH_2-O	−239	7.7	8
	Aromatic	−413	7.8	8
XXI	C-CH_2-C	−132	2.2	2
	CH_2-O	−235	11.7	8
	CH_2-O	−253		4
	Aromatic	−412	8.1	8
XXII	CH_2-O	−227	7.9	4
	CH_2-O	∼−232		4
	CH_2-O	∼−248	3.8	4
	CH_2-O	−263	4.5	4
	Aromatic	−415	7.8	8
XXVIII	CH_2-O	∼−246	16.6	16
	Aromatic	−413	7.4	8
XXXV	CH_2-O	−232	15.3	8
	CH_2-O	−237		8
	CH_2-O	−247	8.8	8
	Aromatic	−414	7.9	8

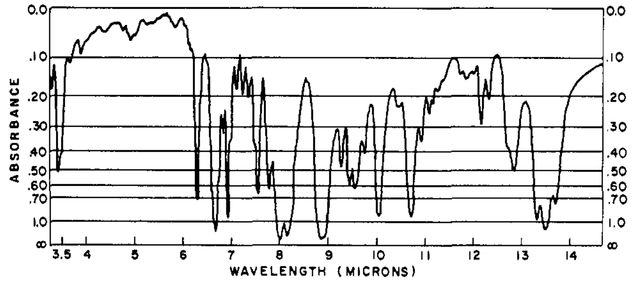

Figure 4. Infrared spectrum of dibenzo-18-crown-6 (XXVIII), KBr pellet.

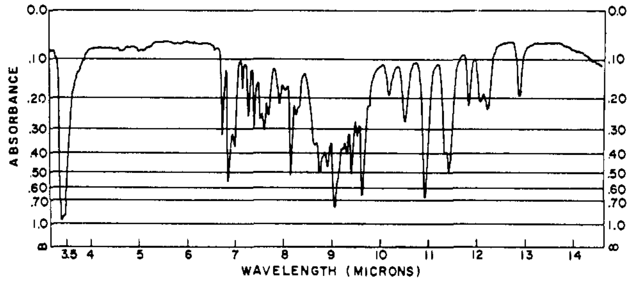

Figure 5. Infrared spectrum of dicyclohexyl-18-crown-6 (XXXI) mp 68.5–69.5°, KBr pellet.

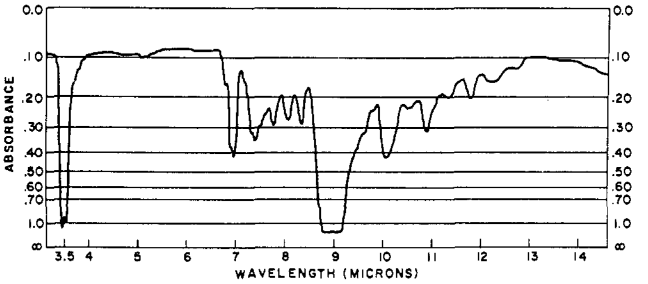

Figure 6. Infrared spectrum of dicyclohexyl-18-crown-6 (XXXI) mixture of isomers, melt smear.

Complexes are formed according to this equation

$$(\text{metal}^{m+})\text{-}n\text{solvent} + \text{polyether} \rightleftharpoons \text{polyether-}(\text{metal}^{m+}) + n\text{solvent}$$

Hence, the formation of the complex of a particular ion will be minimized or prevented if the ion is too strongly associated with the solvent. In a given group of elements, the solvation energy is usually an inverse function of the ionic diameter.

Table V. Ionic Diameters of Cations in Angstrom Units

Group I		Group II		Group III		Group IV	
Li	1.20	Be	0.62				
Na	1.90	Mg	1.30				
K	2.66	Ca	1.98				
Cu(I)	1.92	Zn	1.48				
Rb	2.96	Sr	2.26				
Ag	2.52	Cd	1.94				
Cs	3.34	Ba	2.70	La	2.30		
Au(I)	2.88	Hg(II)	2.20	Tl(I)	2.80	Pb(II)	2.40
Fr	3.52	Ra	2.80				

The influence of the ionic charge has not yet been determined experimentally. The stoichiometry of the

Table VI. Diameters of Holes in Cyclic Polyethers in Angstrom Units

Compound	Diameter	Comments
Dibenzo-12-crown-4 (XXIV)	⩽1.8	Not coplanar
Dibenzo-14-crown-4 (XV)	1.8	Coplanar and symmetrical
Dibenzo-20-crown-4 (XIX)	?	Difficult to estimate
Dibenzo-28-crown-4 (XX)	?	Difficult to estimate
Dibenzo-15-crown-5 (XXV)	2.7	Coplanar and symmetrical
Dibenzo-16-crown-5 (XXI)	2.7	Coplanar and symmetrical
Dibenzo-18-crown-5 (XXII)	3.3	Coplanar and not symmetrical
Dibenzo-18-crown-6 (XXVIII)	4.0	Coplanar and symmetrical
asym-Dibenzo-19-crown-6 (XXIII)	4.0	Coplanar and nearly symmetrical
asym-Dibenzo-22-crown-6 (XLIV)	4.4	Not all coplanar and nearly symmetrical
Dibenzo-26-crown-6 (XLV)	?	Difficult to estimate
Dibenzo-21-crown-7 (XXXIII)	>4	Cylindrically symmetrical
Dibenzo-24-crown-8 (XXXV)	>4	Cylindrically symmetrical
Dibenzo-30-crown-10 (XXXVIII)	>4	Cylindrically symmetrical
asym-Dibenzo-48-crown-16 (XL)	>4	Cylindrically symmetrical
Dibenzo-60-crown-20 (XLII)	>4	Cylindrically symmetrical

complex is one molecule of polyether per single ion regardless of the valence.

X-Ray analysis of crystalline complexes is in progress. Work done so far to determine the nature of the complexes by nmr spectroscopy has provided negative or ambiguous results. Positive conclusions, however, have been drawn from a study of infrared spectra.[14]

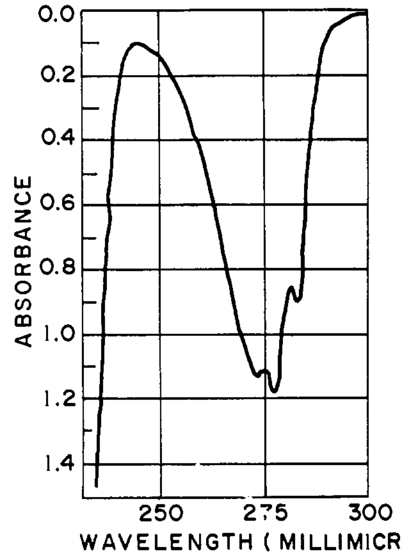

Figure 7. Ultraviolet spectrum of dibenzo-18-crown-6 (XXVIII) in cyclohexane, concentration 0.000255 mole/l., cell path 1 cm; λ_{max} 274 (ϵ 4400), 278 (ϵ 4700), and 283 (ϵ 3600).

The spectrum of the potassium thiocyanate complex of dibenzo-18-crown-6 (XXVIII) is shown in Figure 10. It should be compared to that of XXVIII, Figure 4.

Aside from the thiocyanate band at 4.87 μ, the spectra of XXVIII and its potassium thiocyanate complex differ most strikingly in the 9–14-μ region which contains bands attributable to the wag, twist, and rock modes of vibration of methylene groups.[15] These modes are opposed by the adjoining groups, and changes in the bonding character of these groups will affect the wag, twist, and rock modes of vibration.

The two medium intensity bands of XXVIII at 10.04 and 10.71 μ, which can probably be attributed to either the wag or twist mode of vibration of the methylene groups, are shifted closer together to 10.41 and 10.60 μ and increased in intensity in the spectrum of the complex. This indicates that there is less restriction on the coupling of these vibrational modes in the complex. This decrease in coupling can be accounted for by postulating that the oxygen atoms are showing less effect on these modes because they are bonded to some extent with the potassium ion.

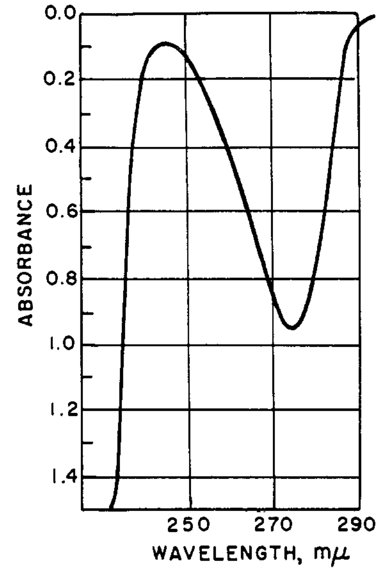

Figure 8. Ultraviolet spectrum of dibenzo-18-crown-6 (XXVIII) in methanol, concentration 0.000183 mole/l., cell path 1 cm; λ_{max} 274 mμ (ϵ 5200).

The significant variation in the aromatic bands between 13 and 14 μ is the shift to shorter wavelengths with complex formation. Since these bands are attributable to the carbon–hydrogen out-of-plane bending mode of vibration,[16] it is apparent that the potassium ion is

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[14] Kindly analyzed by E. G. Brame, Jr., of this laboratory.

[15] N. B. Colthup, L. H. Daly, and S. E. Wiberley, "Introduction to IR and Raman Spectroscopy," Academic Press Inc., New York, N. Y., 1964, pp 195–198.

[16] K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1964, pp 26–27.

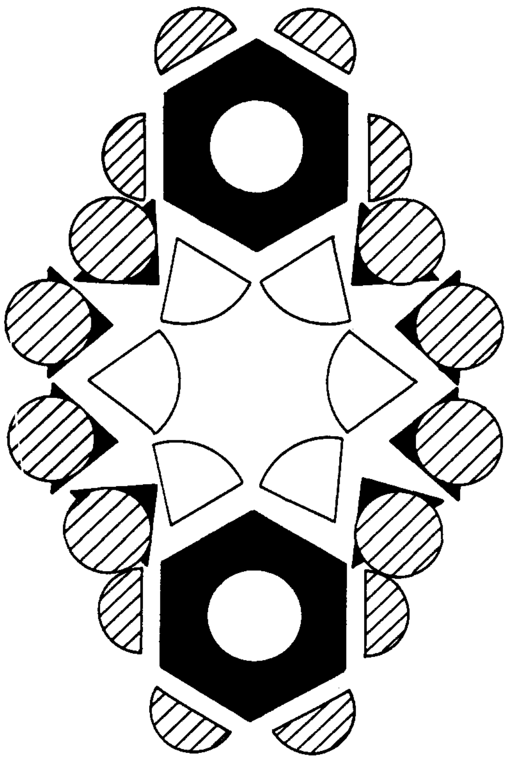

Figure 9. Courtauld model of dibenzo-18-crown-6 (XXVIII).

bonded in such a way as to cause this carbon–hydrogen vibration to be more restricted in the complex.

Formation of Salt Complexes. Three criteria are used for the formation of complexes between the cyclic polyethers and salts: (a) changes in the solubilities of the polyethers and salts in different solvents, (b) characteristic changes in the ultraviolet spectra of the aromatic polyethers, and (c) isolation of the complexes as pure compounds. The most positive test is c but some complexes, although stable in solution in certain solvents, have not yet been successfully isolated. Test a is a general one but it has been applied only to a few of the polyethers. Test b is used most widely because it is the easiest and the most generally applicable, provided the salts themselves do not absorb too strongly in the region of 270–290 mμ.

The statement that a complex is not formed between a salt and a polyether is not a denial of all interaction between the two but that the interaction is too slight to be detected by the particular experimental technique. In the following discussion, the hydroxides are included with the salts.

Solubility Effects. Dibenzo-18-crown-6 (XXVIII) is only slightly soluble in methanol at room temperature, 0.38 g/l. Since it contains no phenolic or other acidic group, it was surprising that its solubility in methanol is greatly increased by the addition of sodium hydroxide. This puzzle was solved by the discovery that most methanol-soluble salts of the alkali and alkaline earth metals have the same effect. Hence, it is not the hydroxyl ion that is responsible for the increased solubility but the cations which operate by complexing with the polyether.

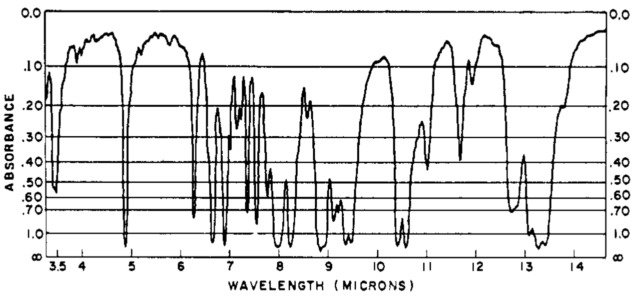

Figure 10. Infrared spectrum of KCNS complex of dibenzo-18-crown-6 (XXVIII), KBr pellet.

The effects of salts on the solubility of XXVIII in methanol are shown in Table VII.[17] The values in the third column are the solubilities of XXVIII in the methanolic salt solutions of the indicated concentrations.

Table VII. Effects of Salts on Solubility of Dibenzo-18-crown-6 (XXVIII) in Methanol at 30°

Salt	Concn of salt, moles/l.	XXVIII dis- solved,[a] moles/l.	XXVIII dis- solved/ mole salt
No salt	...	0.0011	...
Lithium thiocyanate	0.025	0.0008	0.032
Sodium thiocyanate	0.025	0.024	0.96
Ammonium thiocyanate	0.025	0.0033	0.13
Potassium thiocyanate	0.025	0.025	1.00
Potassium fluoride	0.025	0.025	1.00
Potassium adipate	0.025	0.053	2.12
Potassium adipate	0.0125	0.024	1.92
Potassium sulfate	Saturated	0.0012	...
Rubidium thiocyanate	0.025	0.026	1.04
Cesium thiocyanate	0.025	0.030	1.20
Silver nitrate	0.025	0.022	0.88
Cuprous chloride	Saturated	0.0011	...
Magnesium chloride–6 H_2O	0.025	0.0017	0.068
Calcium chloride–2 H_2O	0.025	0.002	0.080
Strontium chloride–6 H_2O	0.025	0.018	0.072
Barium thiocyanate–2 H_2O	0.025	0.027	1.08
Barium chloride–2 H_2O	0.025	0.023	1.92
Zinc chloride	0.025	0.001	0.04
Cadmium chloride–2.5 H_2O	0.025	Nil	Nil
Mercurous nitrate–H_2O	0.025	0.0046	0.18
Mercuric chloride	0.025	Nil	Nil

[a] Corrected for the amount of XXVIII normally soluble in the absence of salts (except the first value).

According to these data, barium and all the alkali metals except lithium form stable complexes with XXVIII. The complexes of silver and strontium are only slightly less stable, but the other metals complex feebly or not at all under these conditions.

The low complexing power of lithium, magnesium, and calcium is probably due to the tendency of these ions to solvate too strongly. Potassium sulfate does not complex because it is too insoluble in methanol; copper(I), zinc, cadmium, and mercuric chlorides do not because they complex more strongly with halide and/or solvent than with the ether.

The solubilities of complexable salts in methanol are increased by XXVIII as shown in Table VIII. The greatest percentage increases tend to occur with salts that are least soluble in methanol in the absence of the polyether.

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(17) The data presented in Tables VII and VIII were obtained by G. T. Perkins of this laboratory.

Table VIII. Effect of Dibenzo-18-crown-6 (XXVIII)[a] on Solubilities of Salts in Methanol at 30°

Salt	Solubility, moles/l. Salt	Solubility, moles/l. Complex	Ratio of solubilities (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
Potassium bromate	0.0017	0.018	11
Potassium nitrate	0.031	0.28	9.0
Potassium chloride	0.057	0.23	4.0

[a] XXVIII present in excess.

The molecular weight of the XXVIII complex of potassium thiocyanate was determined in methanol by ebullioscopy. Three determinations gave values of 234, 238, and 258 g/mole. The average, 243, is not too far from half the molecular weight of the complex, 457, indicating that the complex dissociates in methanol into XXVIII-K$^+$ and -SCN$^-$.

The specific conductivity of 8.8 × 10^{-3} normal potassium hydroxide in methanol at 25° is 8.14 × 10^{-4} mho/cm, and that of the same concentration of XXVIII-KOH complex is 6.75 × 10^{-4}. This decrease in electrical conductivity is typical for sodium, ammonium, and potassium salts, and is probably due to the decrease in the mobility of the cations by complex formation with the large molecule of the polyether.

The effects of alkali metal hydroxides on the solubilities of some other compounds are shown in Table IX. The solubilities of the compounds in methanol or aqueous methanol in the absence of the hydroxides do not exceed 0.001 mole/l. at 26°.

Table IX. Effects of Alkali Metal Hydroxides on Solubilities at 26°

Compound	Solubility, moles/l. Solution A[a]	Solubility, moles/l. Solution B[b]	Solubility, moles/l. Solution C[c]
Dibenzo-14-crown-4 (XV)	>0.009	~0.005	~0.004
Dibenzo-16-crown-5 (XXI)	>0.012	>0.046	...
Dibenzo-15-crown-5 (XXV)	>0.013	>0.035	...
Dibenzo-18-crown-6 (XXVIII)	~0.004	>0.031	>0.045
2,3,7,8-Dibenzo-1,4,6,9-tetraoxacyclodeca-2,7-diene ($C_{14}H_{12}O_4$)	<0.001	<0.001	<0.001
1,1′,4,4′-Bis(trimethylenedioxy)-dibenzene[2] ($C_{18}H_{20}O_4$)	<0.001	<0.001	<0.001
2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetraoxaquaterene[7] ($C_{28}H_{32}O_4$)	<0.001	<0.001	<0.001

[a] Solution A, 58 g of LiOH·H_2O in 1 l. of methanol. [b] Solution B, 214 g of NaOH in 300 ml of water and diluted with 1 l. of methanol. [c] Solution C, 350 g of 85% KOH in 250 ml of water and diluted with 1 l. of methanol.

The solubilities of the last three compounds are not noticeably affected by the hydroxides, although this seems unexpected for the last compound. 2,3,7,8-Dibenzo-1,4,6,9-tetraoxacyclodeca-2,7-diene is a diformal obtained by Gensler and Samour[18] in low yield as a by-product in the synthesis of 1,2-methylenedioxybenzene. 1,1′,4,4′-Bis(trimethylenedioxy)dibenzene is a hydroquinone analog of XV. The solubilities of the cyclic polyethers are increased by the hydroxides but to different degrees. Lithium has a greater effect on dibenzo-14-crown-4 (XV) than sodium or potassium; sodium has a greater effect on dibenzo-16-crown-5 (XXI) and dibenzo-15-crown-5 (XXV) than lithium; and sodium and potassium have greater effects on dibenzo-18-crown-6 (XXVIII) than lithium. This is thought to be due to the different ionic diameters and the different sizes of the holes in the polyethers.

The solubilities of dibenzo-18-crown-6 (XXVIII) and its potassium thiocyanate complex in different solvents are listed in Table X. The values are approximate and were obtained at 26 ± 0.5°.

Table X. Solubilities of Dibenzo-18-crown-6 (XXVIII) and Its KCNS Complex in Different Solvents at 26 ± 0.5°

Solvent	Dielectric constant	Solubilities, moles/l. XXVIII	Solubilities, moles/l. XXVIII-KSCN
Cyclohexane	2.05	0.00067	0.000007
Carbon tetrachloride	2.24	0.005	...
Benzene	2.28	0.018	...
Chloroform	5.05	0.21	0.002
Ethyl acetate	6.4	0.01	...
Tetrahydrofuran	7	0.022	...
1-Butanol	7.8	0.001	...
Pyridine	12.5	0.12	0.13
Acetone	21.4	0.0092	0.014
Ethanol	25	0.00089	...
Methanol	33.1	0.001	0.107
Formic acid	...	1.06	...
Dimethylformamide	36.7	0.056	...
Acetonitrile	38.8	0.079	0.063
Nitromethane	39	0.047	0.063
Dimethyl sulfoxide	45	0.048	>0.27
Water	80	0.00009	[a]

[a] Decomposed by high excess of water.

The solubilities differ widely, those of the complex being more closely related to the dielectric constant of the solvents. Formic acid, chloroform, dichloromethane, and pyridine are outstanding solvents for XXVIII. Ethers are relatively poor solvents, and alcohols and water are very poor solvents. The temperature coefficient of solubility of XXVIII is high, and it can be conveniently crystallized from solvents such as benzene and *p*-dioxane.

The solubilities of the other benzo cyclic polyethers can be roughly correlated to that of XXVIII by means of their melting points. The solubility tends to be lower the higher the melting point. The solubilities of these compounds in aprotic solvents are increased by the presence of *t*-butyl groups. The solubilities of the polyethers are increased in solvents of high dielectric constant and decreased in solvents of low dielectric constant by complex formation.

The saturated cyclic polyethers, as a group, are much more soluble in all solvents than the corresponding benzo compounds. The solubility of a mixture of isomers of dicyclohexyl-18-crown-6 (XXXI) is shown in Table XI. XXXI is more soluble in cold than in hot water due to decreased hydrogen bonding with rising temperature. XXXI and the other saturated polyethers are soluble even in petroleum ether, and very

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(18) W. J. Gensler and C. M. Samour, *J. Org. Chem.*, **18**, 9 (1953).

Table XI. Solubility of Dicyclohexyl-18-crown-6 (XXXI) in Water and Aqueous Solutions

Solvent	Temp, °C	Solubility, moles/l.
Water	26	0.036
	53	0.022
	82	0.010
1 *N* KOH	26	0.89
1 *N* KCl	26	>0.93

Table XII. Solubilization of Salts in Aprotic Solvents by Cyclic Polyethers at 26°

Compound	Salt	Solvent	Method	Solubility, moles/l.
Butylbenzo-15-crown-5 (V)	NaSH	Benzene	2	Solution decomposes with evolution of H_2S
Butylbenzo-18-crown-6 (XI)	$SrCl_2$	Nitromethane	2	>0.2
Bisbutylbenzo-18-crown-6 (XXIX)	KOH	Benzene	2	>0.2
XXIX	$KOC(CH_3)_3$	Benzene	2	>0.02
XXIX	$KMnO_4$	Benzene	2[a]	>0.15
Dicyclohexyl-18-crown-6 (XXXI)	KC_6H_5	Benzene	1	0.2[b]
XXXI	KOH	Toluene	2	0.32
XXXI	KOH	Dimethylformamide	2	>0.3
XXXI	KOH	Dimethyl sulfoxide	2	>0.4
XXXI	CsOH	Benzene	2	0.065
XXXI	$KO{-}C(CH_3)_3$	Benzene	1	0.12
XXXI	KCN	Nitromethane	2	>0.19
XXXI	$KOC(O)C(C_2H_5)H(n\text{-}C_4H_9)$	Benzene	2	>0.1
XXXI	K abietate	Benzene	2	Very soluble
XXXI	$KSC(S)NC_6H_5$	Benzene	2	>0.4
XXXI	$KO_3SC(C_2H_5)H(n\text{-}C_4H_9)$	Benzene	2	>0.2
XXXI	$KOP({=}O)(OC(C_2H_5)H\text{-}n\text{-}C_4H_9)_2$	Benzene	2	>0.6
XXXI	K_3PF_6	*o*-Dichlorobenzene	2	>0.08
XXXI	NaI	Benzene	2	>0.1
XXXI	$KAg(CN)_2$	*o*-Dichlorobenzene	1	0.27
XXXI	$KAgI_2$	*o*-Dichlorobenzene	1	0.17
XXXI	$KAu(CN)_2$	Benzonitrile	1	0.13
XXXI	$K_4Fe(CN)_6$[c]	Nitrobenzene	2	0.022
XXXI	$KMnO_4$	Benzene	1	Intense purple solution which decomposes slowly with formation of MnO_2
XXXI	K_2CoCl_4	Xylene	2	0.021
XXXI	K_2CoCl_4	*o*-Dichlorobenzene	2	0.24
XXXI	K_2PdCl_4	*o*-Dichlorobenzene	1	0.18
XXXI	K_2PtCl_4	*o*-Dichlorobenzene	1	0.047

[a] Acetone was used instead of methanol. The purple solution in benzene gradually decomposes with deposition of MnO_2. [b] Decomposes within hours, probably by attack on the ether linkage. Butyllithium opens the polyether ring of XXVIII to produce a phenoxide group. [c] In this and the following salts the transition elements are in the anions.

soluble in aromatic hydrocarbons and alcohols. The distribution ratio of XXXI between benzene and water is over 170 at 26°.

The saturated cyclic polyethers have the useful property of solubilizing salts in aprotic solvents. Most of the work on solubilization was done with potassium salts and XXXI because they were found to make the most generally satisfactory combination. Some examples are shown in Table XII. The concentrations are not the highest attainable. The solutions were prepared by two methods: (1) the salt was added directly to the solvent containing an equimolar quantity or an excess of the cyclic polyether; and (2) the complex was formed in methanol, freed of solvent under vacuum, dissolved in the final solvent, and filtered through paper. For all practical purposes, the uncomplexed salts may be considered insoluble in the final solvents.

Potassium 2-ethylhexanoate complex of bisbutylbenzo-18-crown-6 (XXIX) is soluble in cyclohexane. The ultraviolet spectrum of this complex in cyclohexane is similar to that of the potassium complex of dibenzo-18-crown-6 (XXVIII) in methanol. Most of the salt complexes, however, are insoluble in saturated aliphatic hydrocarbons. Aromatic, halogenated, and nitro hydrocarbons, nitriles, amides, and dimethyl sulfoxide are much better solvents for the complexes.

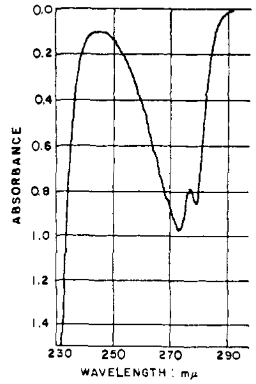


Figure 11. Ultraviolet spectrum of KCNS complex of dibenzo-18-crown-6 (XXVIII) in methanol, concentration 0.000183 mole/l., cell path 1 cm; λ_{max} 273 mμ (ϵ 5300) and 279 (ϵ 4700).

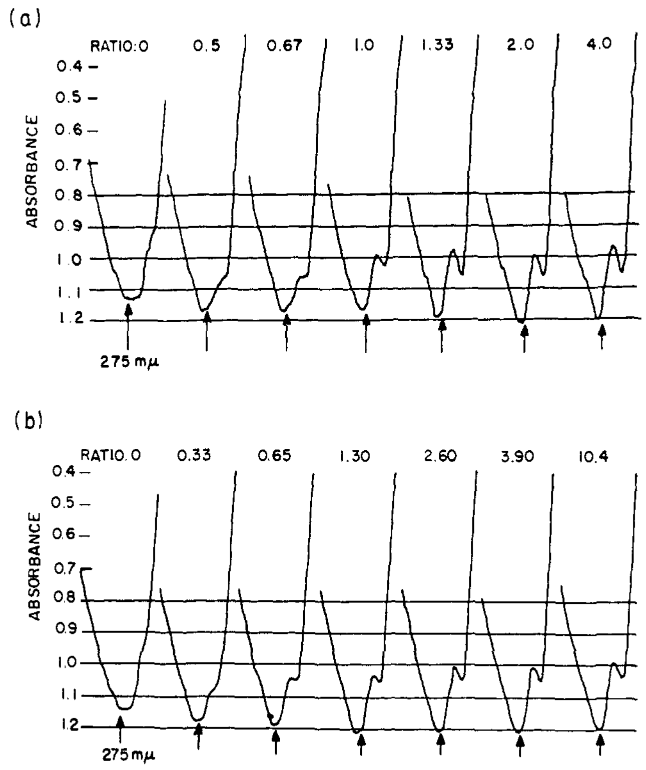


Figure 12. Ultraviolet spectrum of dibenzo-18-crown-6 (XXVIII) in the presence of different proportions: (a) ratio above the curves (moles of KI)/(moles of XXVIII), (b) ratio above the curves (moles of $NaOCH_3$)/(moles of XXVIII); in methanol as solvent; concentration of XXVIII was 0.000214 mole/l.

Not all potassium salts, however, can be solubilized even in the better solvents. Salts of high crystal lattice energy, such as potassium carbonate, acetate, nitrate, phosphate, and fluoride, do not form complexes in aprotic solvents, and neither can these complexes be isolated as solids from protic solvents, such as methanol.

Preliminary experiments suggest that the solubilities in aprotic solvents of the complexes of the saturated polyethers containing six oxygen atoms with a particular potassium salt will be arranged in this ascending order: 18-crown-6 (XXVII), cyclohexyl-18-crown-6 (XIII), butylcyclohexyl-18-crown-6 (XIV), dicyclohexyl-18-crown-6 (XXXI), and bisbutylcyclohexyl-18-crown-6 (XXXII).

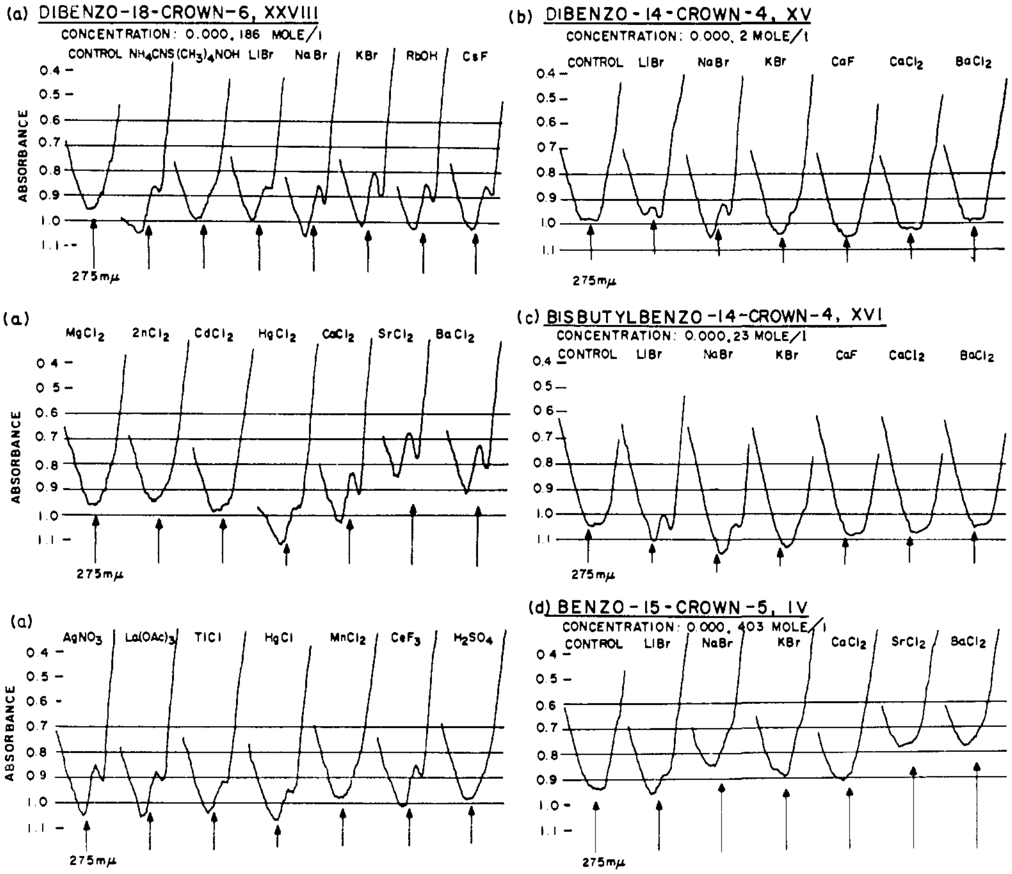
Benzene and toluene solutions of the XXXI complex of potassium hydroxide, due probably to the presence of bare, unsolvated hydroxide anions, can saponify the hindered esters of 2,4,6-trimethylbenzoic acid (see Appendix). These solutions can also be used for acid-base titration in aprotic solvents using, for example (3,-5-di-*t*-butyl-1,4-benzoquinone)-1-(3′,5′-di-*t*-butyl-4′-hydroxyphenyl)methide as indicator (acid or neutral, yellow, basic, purple). When contacted with water, potassium hydroxide is rapidly transferred to the aqueous phase and most of the polyether remains in the hydrocarbon.

Changes in Ultraviolet Spectra. Catechol and its oxygen derivatives in methanol have a single absorption peak in the region of 275 mμ. When a solution of a derivative containing a free hydroxyl group is made alkaline, this peak is shifted to around 291 mμ due to the formation of phenoxide ions. If both hydroxyl groups are blocked as in veratrole, the peak at 275 mμ is not affected by the alkali. All the cyclic polyethers derived from catechol have the characteristic maximum, but the curves for the complexing polyethers are altered in a special manner by the addition of the hydroxides and the soluble salts of complexable metals. This is exemplified by the spectrum of the potassium thiocyanate complex of dibenzo-18-crown-6 (XXVIII) in methanol, Figure 11, which should be compared to that of XXVIII, Figure 8.

The spectrum of the complex shows a second peak about 6 mμ to the longer wavelength side of the major peak. The curves in Figure 12a depict the gradual development of the second peak by the addition of increasing amounts of potassium iodide. The peak is fully formed between (moles of KI)/(moles of XXVIII) ratios of 1.0 and 1.33. This indicates that even at 0.000214 mole/l. in methanol this complex is only slightly dissociated, attesting to its remarkable stability. The curves in Figure 12b show that the XXVIII complex of sodium methoxide is dissociated to a greater extent than the potassium complex, since the second peak is not fully developed until (moles of CH_3ONa)/(moles of XXVIII) equals about 2.3. Aside from this, the second peak for sodium is less pronounced than that for potassium. Hence, there seems to be a connection between the stability of the complexes and the magnitude of the second peak observed in solutions containing the salts in excess.

The spectral evidence is nearly always confirmed by solubility effects and formation of isolable complexes. With very few exceptions, no crystalline complex is obtained from a combination of an aromatic polyether and a salt which shows no interaction by ultraviolet spectroscopy. When a salt has no effect on the spectrum of a polyether in methanol, this salt has no effect on the solubility of the polyether in methanol except, if enough salt is present, to depress it by salting out. Hence, the spectra can be interpreted with more confidence than if they were the only evidence available.

The effects of different salts on the ultraviolet spectrum of dibenzo-18-crown-6 (XXVIII) are shown in Figure 13a. The spectra in Figures 13–16, inclusive, were obtained under these conditions: the solvent was methanol, the salts were present in 50-fold excess, the temperature was 26°, and the cell path was 1 cm. The absorbances are ±0.015, and the arrows point to 275 mμ. The high excess of salt was used so that if com-


(a) DIBENZO-18-CROWN-6, XXVIII

(b) DIBENZO-14-CROWN-4, XV

(c) BISBUTYLBENZO-14-CROWN-4, XVI

(d) BENZO-15-CROWN-5, IV

Figure 13. Effects of salts on ultraviolet spectrum.

plex formation is significant at all, an indication of this should be evident in the spectra.

Note that the salts are of different anions. Anions have pronounced effects in the solubilization of cyclic polyethers and salts, and in the formation of crystalline complexes. They have little effect, however, under the conditions used for obtaining the spectra: very low concentration of polyether and high excess of salt; as long as the salt is soluble in methanol and the anion does not absorb in the region of 275 mμ.

Polyethers containing a ring of six oxygen atoms each separated from the next by two carbon atoms, exemplified by XXVIII, are the strongest and most versatile complexing agents. This is the coplanar, symmetrical polyether ring with the greatest number of oxygen atoms. Its hole diameter of 4 A is large enough to accommodate any unsolvated metal cation. It is noteworthy that the ammonium ion forms a complex. The tetramethylammonium ion with a diameter of about 7 A is too large. Beryllium (not shown), magnesium, zinc, and cadmium, according to spectral data, do not form complexes, probably because they are too strongly solvated or are un-ionized. Thallium(III) has no effect on the spectrum. The complex of lithium is relatively unstable because it is small and solvated. Strontium and barium have a hypsochromic effect and decrease the absorbance by a considerable extent. This might be due to the double charge on their ions. Calcium is too strongly solvated to have such a pronounced effect.

The action of strontium and barium on the spectrum of XXVIII is similar, though greatly reduced, to that of attaching electron-withdrawing groups on the oxygen atoms of catechol. In methanol, catechol has a single peak at 279 mμ with an extinction coefficient of 2600. *o*-Phenylenebis(methane sulfonate) has two peaks: the major one at 263 mμ and another at 270 mμ with extinction coefficients of 300 and 210, respectively.

The spectra of the potassium and barium complexes of XXVIII are quite different. The one can be readily changed into the other by adding an excess of the other salt. This must apply also to all the complexable salts.

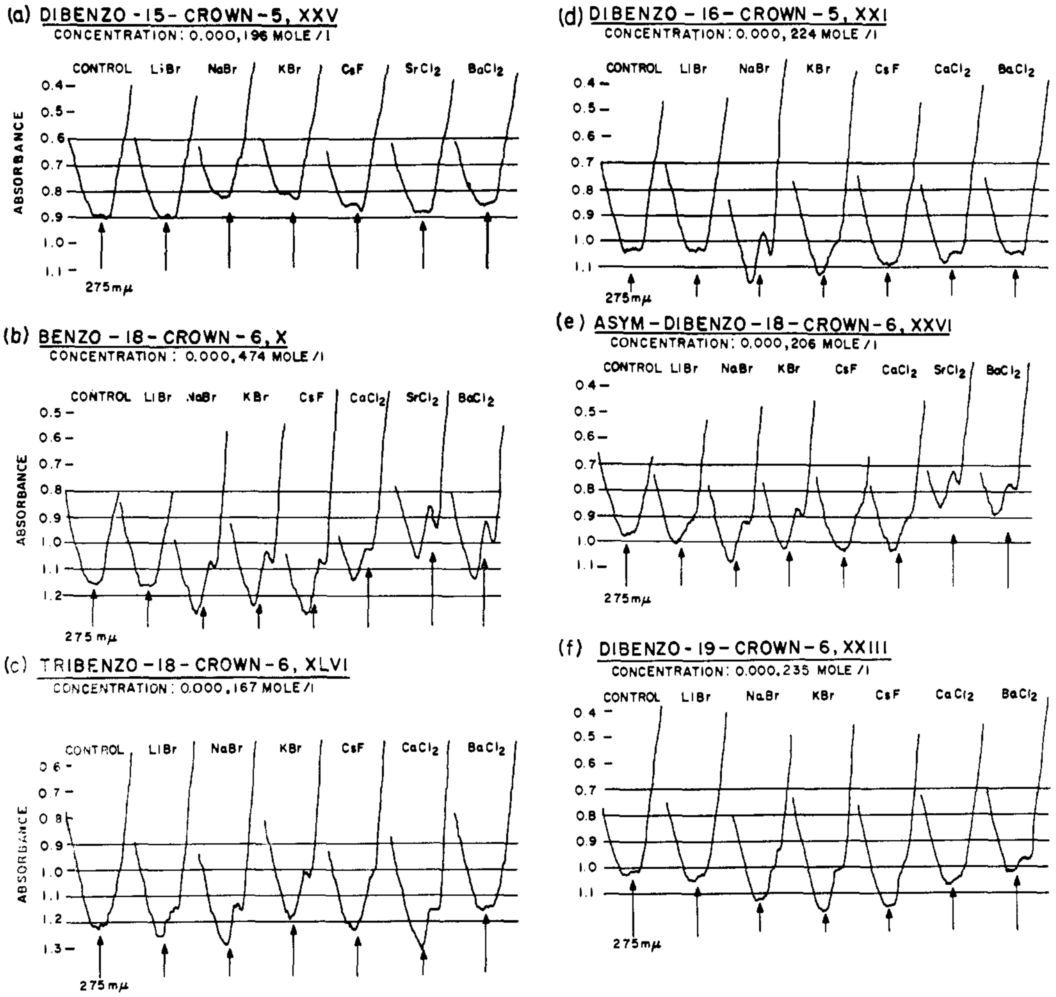
According to their effects on the spectrum of XXVIII in methanol, compounds containing $-NH_3^+$ form complexes but not compounds containing $>NH_2^+$ and $\geqslant NH^+$, as shown in Table XIII. Apparently, $-NH_3^+$ can intrude sufficiently into the polyether ring of XXVIII to affect its spectrum but, due to steric hindrance, $>NH_2^+$ and $\geqslant NH^+$ cannot do so.

The spectra of the ammonium and other salt complexes are not altered by the addition of acids whose anions do not make the cations insoluble in the solvent.

Spectrophotometric evidence was sought for complex formation between cyclic polyethers and hydronium and primary oxonium ions. Only negative results were obtained with XXVIII in methanol, dioxane, and cyclohexane using $H_2O \cdot HCl$, $CH_3OH \cdot HCl$, and $CH_3OH \cdot C_7H_{15}COOH$.

The spectrum of XXVIII in water has a peak at 273.5 mμ and a distinct shoulder at 279 mμ. The shape of the curve is not affected by the addition of hydrochloric acid or a complexable salt.

The spectrum of XXVIII in concentrated sulfuric


(a) DIBENZO - 15 - CROWN - 5, XXV
CONCENTRATION: 0.000,196 MOLE/l

(b) BENZO - 18 - CROWN - 6, X
CONCENTRATION: 0.000,474 MOLE/l

(c) TRIBENZO - 18 - CROWN - 6, XLVI
CONCENTRATION: 0.000,167 MOLE/l

(d) DIBENZO - 16 - CROWN - 5, XXI
CONCENTRATION: 0.000,224 MOLE/l

(e) ASYM - DIBENZO - 18 - CROWN - 6, XXVI
CONCENTRATION: 0.000,206 MOLE/l

(f) DIBENZO - 19 - CROWN - 6, XXIII
CONCENTRATION: 0.000,235 MOLE/l

Figure 14. Effects of salts on ultraviolet spectrum.

acid contains a peak with a blunt tip extending from 277 to 284 mμ with the extinction coefficient decreasing from 8100 to 7900 toward the longer wavelength. The shape of the curve is not changed by the addition of sodium sulfate. Since XXVIII is sulfonated by concentrated sulfuric acid, the changes in the absorption characteristics might be partially due to substitution.

The *t*-butyl group on the benzo ring increases the maximum wavelength by 3–4 mμ, but otherwise causes little change in the spectra of the parent compounds. Hence, except for bisbutylbenzo-14-crown-4 (XVI), the curves for the butyl derivatives are not given.

Salts have no effect on the spectra of the following compounds (their curves are not given) and are presumed not to form any complex: benzo-12-crown-4 (II) and dibenzo-12-crown-4 (XXIV) because the oxygen atoms are not coplanar (the hole is large enough for lithium and sodium); dibenzo-20-crown-4 (XIX) and dibenzo-28-crown-4 (XX) because of steric hindrance by the polymethylene linkages; dibenzo-18-crown-5 (XXII) because of steric hindrance and lack of symmetry (this compound is identical with dibenzo-18-crown-6 (XXVIII) except for the replacement of one of the oxygen atoms by a methylene group); and dibenzo-26-crown-6 (XLV) because of steric hindrance.

The curves for dibenzo-14-crown-4 (XV) are shown in Figure 13b. Lithium and sodium definitely interact with this compound. According to the molecular model, the oxygen atoms of XV can be coplanar, and the hole is large enough for lithium and sodium but not for potassium and the others except the weakly complexing calcium.

The curves for bisbutylbenzo-14-crown-4 (XVI) in Figure 13c are presented to confirm the specific complexing power of this four-oxygen configuration. Potassium appears to have a very slight effect on both XV and XVI, but barium whose size is close to that of potassium causes no change in the spectrum.

The curves for benzo-15-crown-5 (IV), dibenzo-15-crown-5 (XXV), and dibenzo-16-crown-5 (XXI) representing the five-oxygen compounds, Figures 13d, 14a, and 14d, respectively, are indecisive. The changes in shape are slight and complex formation is suggested mainly by a hypsochromic shift and a decrease in absorbance, particularly for IV which contains only one benzo group. XXI has one more methylene group than XXV, yet this variation causes them to interact so differently with sodium.

The spectrum of benzo-18-crown-6 (X), Figure 14b, is affected less by salts than that of dibenzo-18-crown-6 (XXVIII). It might be argued that this is due to the presence of only two aromatic oxygen atoms in X while XXVIII contains four of them, and it is the Ar–O–R that is responsible for the absorption peak. However, the spectrum of *asym*-dibenzo-18-crown-6 (XXVI) with four aromatic oxygen atoms, Figure 14e, and that

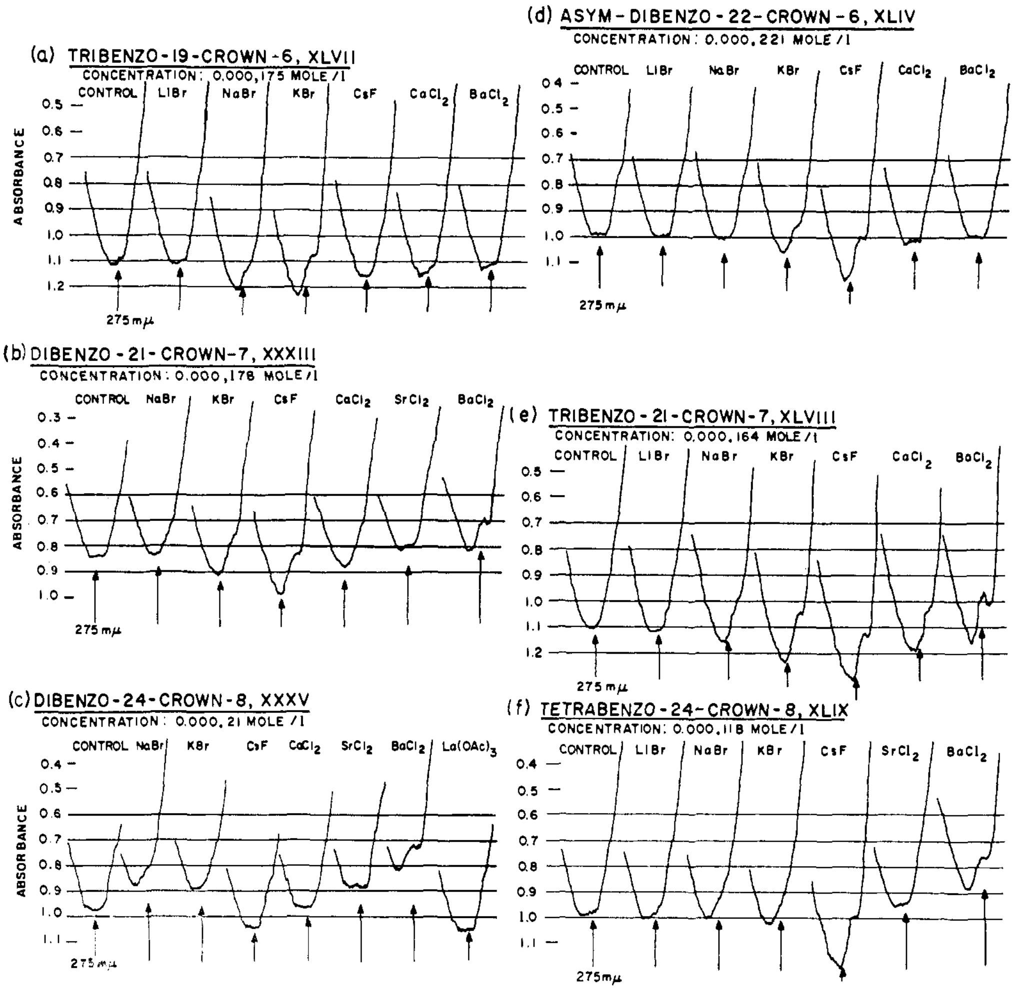


Figure 15. Effects of salts on ultraviolet spectrum.

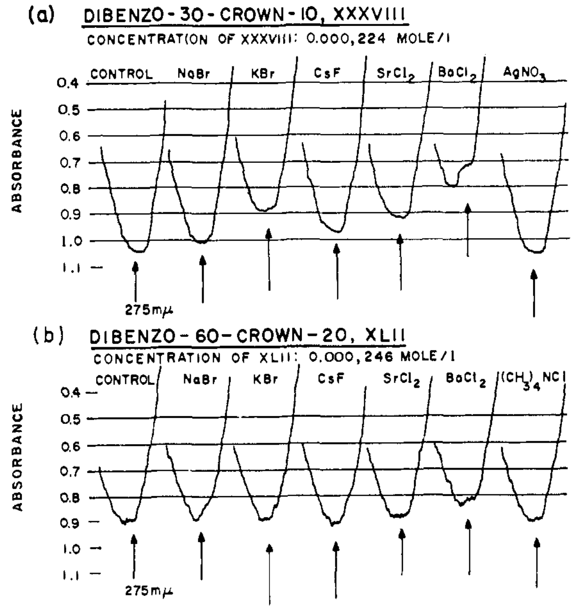


Figure 16. Effects of salts on ultraviolet spectrum.

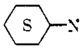
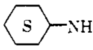
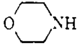
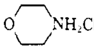
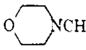
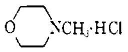
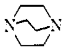
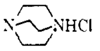
of tribenzo-18-crown-6 (XLVI) with six of them, Figure 14c, are also affected less by salts. It is likely that the relative basicity of the differently linked oxygen atoms, symmetry, and the rigidity of the polyether molecules are involved in these differences.

The complexing power of the six-oxygen compounds is decreased by changing one of the two-carbon links to a three-carbon link. Compare the curves for *asym*-dibenzo-18-crown-6 (XXVI) to those for *asym*-dibenzo-19-crown-6 (XXIII), Figure 14f, and those for tribenzo-18-crown-6 (XLVI) to those for tribenzo-19-crown-6 (XLVII), Figure 15a.

When dibenzo-18-crown-6 (XXVIII) is altered by replacing two of its ethylene links by tetramethylene links, the resulting compound, *asym*-dibenzo-22-crown-6 (XLIV), still possesses some complexing power particularly for potassium and cesium, the larger ions, Figure 15d. Its lack of response to barium is surprising in view of the data in the subsequent figures. Dibenzo-26-crown-6 (XLV) is obtained by replacing all four ethylene links in XXVIII by tetramethylene links, and steric hindrance becomes too great for it to complex any of the metals.

As the polyether ring increases in size beyond 18 atoms including the six oxygen atoms, the complexing power for the smaller ions disappears, and even the power for the larger ions diminishes as shown in Figures 15 and 16. The sole exception is dibenzo-24-crown-8 (XXXV) which complexes with sodium and strontium, Figure 15c. Lithium has no effect on its spectrum (not shown). Cesium and barium, the biggest univalent and divalent ions, interact most strongly with the larger rings, although their effects are scarcely discernible for dibenzo-60-crown-20 (XLII), Figure 16b. The tetra-

Table XIII. Complex Formation between Amino Compounds and Dibenzo-18-crown-6 (XXVIII)[a]

Amino compd	Complex formed
$HONH_3Cl$	Yes
NH_2NH_3OH	No
NH_2NH_3Cl	Yes
$(CH_3)_2CHCH_2NH_2$	No
$(CH_3)_2CHCH_2NH_3Cl$	Yes
$(CH_3)_2CHCH_2CH_2NH_2$	No
$(CH_3)_2CHCH_2CH_2NH_3Cl$	Yes
$(CH_3)_3CNH_2$	No
$(CH_3)_3CNH_3Cl$	Yes
	No
	Yes
$NH_2CH_2CH_2NH_2$	No
$NH_2CH_2CH_2NH_3Cl$	Yes
$(CH_3)_4NOH$	No
$(CH_3)_4NCl$	No
	No
	No
	No
	No
	No
	No
$HOOCCH_2NH_2$	No
$HOOCCH_2NH_3Cl$	Yes
$(NH_2C(=NH_2)NH_2)_2{}^+CO_3$	Yes
$(NH_2C(=NH_2)NH_2)^+ Cl^-$	Yes
$[(CH_3)_2NC(=NH_2)N(CH_3)_2]^+ Cl^-$	No

[a] Solvent, methanol; concentration of XXVIII, 0.00018 to 0.00023 mole/l.; concentration of amino compounds, *ca.* 0.02 mole/l.

methylammonium ion does not complex with XLII even if its ring, if properly arranged, is large enough to accommodate it.

Dicyclohexyl-18-crown-6 (XXXI) does not absorb significantly above 200 mμ, the lower limit for commercial ultraviolet spectrophotometers. Hence, the spectral method of determining complex formation is not directly applicable to this and other saturated polyethers. An indirect method can be used as shown in Figure 17, where the superiority of XXXI over dibenzo-18-crown-6 (XXVIII) as a complexing agent for potassium is demonstrated. Potassium bromide was added dropwise as a 1.05×10^{-3} *M* solution in methanol; hence, the solutions in the cells became progressively more dilute. At the final ratio of 2.24, the concentrations of XXVIII and XXXI were 8.4×10^{-5} *M*. The dilutions were identical for the two sets.

The upper set of curves is a repetition of the set in Figure 12 with some modifications. The second peak for XXVIII is observable as a shoulder at a (moles of KBr)/(moles of XXVIII) ratio of 0.188 in the absence of XXXI. The lower set of curves was obtained in the presence of an equimolar quantity of XXXI, and the second peak is not evident until a ratio of 0.933.

Since XXXI and its potassium complex have no absorption in this region, the only way it can alter the spectrum of the potassium complex of XXVIII is by taking potassium away from the latter. Roughly, at

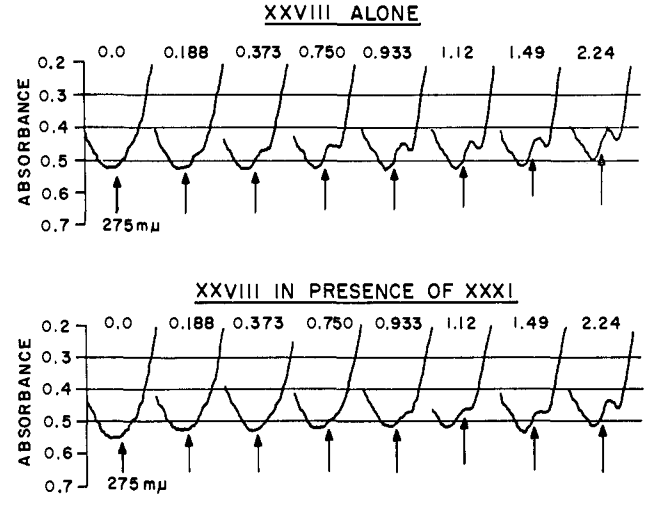


Figure 17. Competition of XXVIII and XXXI for potassium ion: concentration of XXVIII and XXXI, 0.0001 mole/l. The values given above the curves are (moles of KBr)/(moles of XXVIII).

1.0×10^{-4} *M* concentrations of XXVIII and XXXI and 9.3×10^{-5} *M* concentration of potassium bromide, 80% of the potassium is complexed with XXXI.

It has been established by the indirect method that the aromatic polyethers are less effective complexing agents than the corresponding ring-hydrogenated products, due probably to the lower basicity of the oxygen atoms in the former.

The indirect method, however, is troublesome, and the complexation of the saturated polyethers is usually followed by observing the changes in the solubility of the salts.

Isolation of Solid Complexes. Crystalline etherates of the alkali metal salts have not been common heretofore. Cotton and Wilkinson[19] mention two of them: $[Na(CH_3OCH_2CH_2OCH_2CH_2OCH_3)_2][Ta(CO)_6]$ and $[K(CH_3OCH_2CH_2OCH_2CH_2OCH_3)_3][Mo(CO)_5I]$.

Cyclic polyethers of the proper oxygen configuration form solid complexes with many salts of the complexable ions. Crystalline complexes are obtainable if: (1) the crystal lattice energy of the polyether is not too high, (2) the complexing power of the polyether is strong enough, (3) the crystal lattice energy of the salt is not too great, and (4) the solubility of the complexable salt in the polyether or a mutual solvent is appreciable.

The solid complexes of the cyclic polyethers are prepared by one or more of the following methods.

Method 1. One mole of polyether is warmed with thorough mixing with 1 mole of salt. No solvent is used.

Method 2. One mole of polyether and 1 mole of salt are dissolved in a suitable solvent and the solvent removed by evaporation, usually under vacuum.

Method 3. One mole of polyether and 1 mole (or an excess) of salt are dissolved in a minimum quantitiy of hot solvent, and the complex is precipitated by cooling and recovered by filtration.

Method 4. One mole of polyether is heated with 1 mole of (or an excess) of salt in a solvent in which the salt is readily soluble, and the polyether is converted into the crystalline salt complex without the system ever be-

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(19) F. A. Cotton and G. Wilkinson, "Advanced Inorganic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1962, p 318.

Table XIV. Crystalline Salt Complexes of Cyclic Polyethers

	Complex between							Calcd, %				Found, %			
No.	Polyether	Salt	Method	Solvent	Formula	Mol wt	Mp, °C	C	H	N	S	C	H	N	S
1	Benzo-15-crown-5 (IV)	NaI	1	None	$C_{14}H_{20}O_3INa$	418	152.5–156	40.2	4.8	I, 30.4		39.4	5.0	I, 29.4	
2	Butylbenzo-15-crown-5 (V)	LiCNS	3	Methanol	$C_{19}H_{28}NO_5SLi$	389	169–174	58.6	7.2	3.6	8.2	58.8	7.3	3.6	8.1
3	V	NaBr	2	Methanol	$C_{18}H_{28}O_5BrNa$	427	77–84	50.6	6.6	Br, 19.0		49.3	6.7	Br, 18.7	
4	V	NaI	2	Methanol	$C_{18}H_{28}O_5INa$	474	86–134	45.6	5.9	I, 26.8		46.1	6.3	I, 23.1	
5	V	NaCNS	3	Methanol	$C_{19}H_{28}NO_5SNa$	405	163–167	56.3	6.9	3.5	7.9	56.4	6.7	3.5	7.7
6	V	KCNS	2	Methanol	$C_{19}H_{28}NO_5SK$	421	. . .	54.2	6.6	3.3	7.6	58.6	7.2	3.1	7.1
7	Cyclohexyl-15-crown-5 (VII)	NaCNS	2	Methanol	$C_{15}H_{26}NO_5SNa$	355	94-110	50.2	7.5	3.4	8.9	50.7	7.3	3.9	9.0
8	Butylcyclohexyl-15-crown-5 (VIII)	KI	2	Methanol	$C_{18}H_{34}O_5IK$	496	100–133	42.2	6.7	I, 25.0		43.6	6.9	I, 25.6	
9	Benzo-18-crown-6 (X)	KCNS	3	Water	$C_{17}H_{24}NO_6SK$	409	134.5–136.5	49.9	5.9	3.4	7.8	49.4	6.0	3.5	7.9
10	Butylbenzo-18-crown-6 (XI)	KCNS	2	Methanol	$C_{21}H_{32}NO_6SK$	465	134–136	54.2	6.9	3.0	6.9	52.0	6.9	3.3	6.7
11	Cyclohexyl-18-crown-6 (XIII)	NH_4CNS	2	Methanol	$C_{17}H_{34}N_2O_6S$	394	124–147	51.4	8.6	7.0	8.4	51.8	8.6	7.1	8.1
12	XIII	$Ba(CNS)_2$	2	Methanol	$C_{18}H_{30}N_2O_6S_2Ba$	571	282.5	37.6	5.3	4.3	11.2	37.8	5.3	4.9	10.3
13	Butylcyclohexyl-18-crown-6 (XIV)	KI	2	Methanol	$C_{20}H_{38}O_6IK$	540	52–98	44.1	7.0	I, 22.4		44.4	7.0	I, 23.5	
14	Dibenzo-14-crown-4 (XV)	LiCNS	2	Methanol	$C_{19}H_{20}NO_4SLi$	365	300	62.4	5.5	3.8	8.8	. . .	. . .	4.0	8.8
15	Dibenzo-19-crown-6 (XXIII)	KCNS	3	Methanol	$C_{22}H_{26}NO_6SK$	471	160–162	56.0	5.5	3.0	6.8	53.1	5.2	4.0	7.6
16	Dibenzo-18-crown-6 (XXVIII)	HI_3	5	MCW[b]	$C_{20}H_{25}O_6I_3$	742	. . .	32.3	3.4	I, 51.4		23.0	2.7	I, 63.0	
17	XXVIII	LiI_3	5	MCW[b]	$C_{20}H_{24}O_6I_3Li$	748	134–139	32.1	3.2	I, 50.9		32.4	3.4	I, 46.7	
18	XXVIII	NaCNS	3	Methanol	$C_{21}H_{24}NO_6SNa$	441	230–232	57.2	5.4	3.2	7.3	57.1	5.7	4.0	7.1
19	XXVIII	$NaNO_2$	4	1-Butanol	$C_{20}H_{24}NO_8Na$	429	154–157	55.9	5.6	3.3	. . .	54.4	5.7	3.1	. . .
20	XXVIII	KI	2	Methanol	$C_{20}H_{24}O_6IK$	526	232–234	45.6	4.6	I, 24.1		44.5	4.9	I, 23.1	
21	XXVIII	$KI_{1.5}$	5	MCW[b]	$C_{20}H_{24}O_6I_{1.5}K$	589.5	152–153	40.7	4.1	I, 32.3		40.4	4.3	I, 32.2	
22	XXVIII	KI_2	5	MCW[b]	$C_{20}H_{24}O_6I_2K$	653	156–238	36.7	3.7	I, 38.9		36.5	3.7	I, 39.1	
23	XXVIII	KI_3	5	MCW[b]	$C_{20}H_{24}O_6I_3K$	780	258–267 dec	30.8	3.1	I, 48.8		30.6	3.0	I, 48.2	
24	XXVIII	KCNS	3	Methanol	$C_{21}H_{24}NO_6SK$	457	248–249	55.1	5.2	3.1	7.0	55.3	5.3	3.1	6.7
25	XXVIII	K pivalate	2	Methanol	$C_{33}H_{49}O_8K$	612	. . .	64.7	8.0			64.5	7.9	Mol wt, 605	
26	XXVIII	NH_4CNS	4	Methanol	$C_{21}H_{23}N_2O_6S$	436	187–189	57.9	6.4	6.4	7.3	58.0	6.3	6.5	7.2
27	XXVIII	CH_3NH_3CNS	2	Methanol 1-Butanol	$C_{22}H_{30}N_2O_6S$	450	128–155	58.7	6.7	6.2	7.1	59.0	6.8	6.0	6.8
28	XXVIII	RbCNS	3	Methanol	$C_{21}H_{24}NO_6SRb$	504	182–185	50.0	4.8	2.8	6.4	49.5	4.9	2.6	6.2
29	XXVIII	CsCNS	3	Methanol	$C_{21}H_{24}NO_6SCs$	551	Soft at 105	45.8	4.4	2.5	5.8	45.2	4.5	2.5	5.8
30	XXVIII	MgI_6	5	MCW[b]	$C_{20}H_{24}O_6I_6Mg$	1146	145–150 dec	20.9	2.1	I, 67.5 Mg, 2.1		28.9	3.4	I, 50.9 Mg, 0.8	
31	XXVIII	$CaCl_2$	4	1-Butanol	$C_{20}H_{24}O_6Cl_2Ca$	471	Over 300	50.9	5.1	. . .	. . .	47.3	5.6	. . .	. . .
32	XXVIII	$Ba(OH)_2$	2	Methanol	$C_{20}H_{26}O_8Ba$	531	Soft at 180	45.1	4.9	Ba, 25.9		45.2	4.3	Ba, 23.1	
33	XXVIII	BaI_6	5	MCW[b]	$C_{20}H_{24}O_6I_6Ba$	1259	153–159 dec	19.1	1.9	I, 60.5		20.4	2.1	I, 58.0	
34	XXVIII	$Ba(CNS)_2$	4	1-Butanol	$C_{22}H_{24}N_2O_6S_2Ba$	613	Over 360	43.0	3.9	4.6	10.4	45.4[a]	4.1	4.8	8.3
35	XXVIII	$CdCl_2$	4	1-Butanol	$C_{20}H_{24}O_6Cl_2Cd$	543	Over 300	44.2	4.4	. . .	. . .	42.6	4.3	. . .	. . .
36	XXVIII	$HgCl_2$	4	1-Butanol	$C_{20}H_{24}O_6Cl_2Hg$	632	238–249	38.0	3.8	Cl, 11.2		39.9	3.9	Cl, 8.9	
37	XXVIII	PbAc	4	1-Butanol	$C_{24}H_{30}O_{10}Pb$	685	167–198	42.0	4.4	Pb, 30.2		42.3	4.4	Pb, 28.9	
38	Bisbutylbenzo-18-crown-6 (XXIX)	KCNS	3	Methanol	$C_{29}H_{40}NO_6SK$	569	186–189	61.2	7.0	2.5	5.6	58.0	6.7	2.5	5.3
39	Dicyclohexyl-18-crown-6 (XXXI)	KI	2	Methanol	$C_{20}H_{36}O_6IK$	538	123–170	44.6	6.7	I, 23.6		45.5	6.7	I, 23.0	
40	XXXI	KI_3	2	Methanol	$C_{20}H_{36}O_6I_3K$	792	113–157	30.3	4.6	I, 48.1		29.9	4.6	I, 47.9	
41	XXXI	KCNS	2	Methanol	$C_{21}H_{36}NO_6SK$	469	72–122	53.7	7.7	3.0	6.8	52.5	7.8	3.0	6.4
42	XXXI	NH_4CNS	2	Methanol	$C_{21}H_{40}N_2O_6S$	448	107–110	56.3	8.9	6.3	7.1	55.1	8.9	6.1	7.1
43	Dibenzo-24-crown-8 (XXXV)	KCNS	2	Methanol	$C_{25}H_{32}NO_8SK$	545	113–114	55.0	5.9	2.6	5.9	54.2	5.8	2.7	5.8
44	Dibenzo-30-crown-10 (XXXVIII)	KCNS	3	Methanol	$C_{29}H_{40}NO_{10}SK$	633	176–177.5	54.9	6.3	2.2	5.1	54.6	6.5	2.2	4.8

[a] Calculates to XXXI–$BaI_{5.4}$. [b] MCW = methylene chloride–water.

coming a clear solution. The complex is recovered by filtration.

Method 5. One mole of polyether in a water-immiscible solvent is mixed with 1 mole (or an excess) of salt in water. The resulting complex being less soluble in either solvent than the original compounds, separates as crystals.

It is possible that solid products obtained by methods 1 and 2 might be mixtures rather than true complexes. A comparison of the melting points of the polyether and the complex will usually dispel any doubt concerning the nature of the product, since the melting point of an organic compound is not affected by an inorganic salt with which it does not interact.

Some solid complexes of the cyclic polyethers are listed in Table XIV. They are colorless compounds unless the anion is colored. The dibenzo-18-crown-6 complex of hydrogen triiodide (XXVIII–HI_3), no. 16, and (XXVIII–MgI_6), no. 30, are included in spite of their unsatisfactory composition to show that crystalline complexes cannot be obtained from combinations having little or no complexing tendency.

Note that cadmium chloride forms a solid complex, no. 35, although it does not affect the spectrum of XXVIII in methanol, Figure 13a. Attempts to prepare the following solid complexes were unsuccessful: XXVIII–$MgCl_2$, XXVIII–$ZnCl_2$, XXVIII–isobutyl amine hydrochloride, XXVIII–isobutylammonium thiocyanate, and XXVIII–*t*-butylammonium *p*-toluenesulfonate. In general, crystalline complexes have not been obtained with salts of high crystal lattice energy, such as the carbonates, acetates, nitrates, phosphates, and fluorides.

The melting points of the crystalline complexes of the aromatic cyclic polyethers are sharp, but those of the saturated compounds are not because the latter are mixtures of *cis-trans* isomers. The melting point of XXVIII–KCNS is 248–249°, considerably higher than the melting points of the components, 164° for XXVIII and 172° for potassium thiocyanate. This is not always the case, and the complexes melt with the separation of the uncomplexed salts.

Recrystallization of solid complexes from pure solvents is often unsuccessful because: (1) in the case of the aromatic polyethers (high melting points and low solubilities), the uncomplexed polyethers are recovered; and (2) in case of the saturated polyethers (low melting points and high solubilities), the complexes tend to remain in solution and ultimately form glassy products.

Although the thiocyanate complex of dibenzo-18-crown-6 (XXVIII) is stable in water containing excess of the salt, the pure complex is decomposed by water, the rate and extent of decomposition depending on the proportion of water and the temperature. This is true for most of the complexes but there are exceptions. Crystals of the potassium triiodide complexes of XXVIII and XXXI are practically insoluble in water, and they are stable indefinitely in contact with it. The vapor pressure of iodine over solutions and crystals of the triiodide complexes is very much lower than that over the uncomplexed triiodides. Although most of the triiodide complexes melt with decomposition and evolution of iodine vapor, the potassium triiodide complex of dicyclohexyl-18-crown-6 (XXXI) is a clear red-brown liquid above its melting point with no observable vapor of iodine. In many respects, this complex resembles the quaternary ammonium triiodides.

Experimental Section

The following instruments were used: Varian Model A-60 for nmr spectra, Perkin-Elmer Infracord Model 137 for infrared spectra, and Perkin-Elmer ultraviolet-visible spectrophotometer Model 202 for ultraviolet spectra.

All inorganic compounds were reagent grade, and all solvents and available organic materials were commercial products used without purification.

All phenolic reactants (reactant 1 in Table II), except catechol, 4-*t*-butylcatechol, and 2,3-dihydroxynaphthalene, were synthesized by treating 2 moles of the sodium salt of 2-(*o*-hydroxyphenoxy)-tetrahydropyran or of *o*-hydroxyphenoxymethylmethyl ether with 1 mole of the dihalides, and obtaining the free dihydric phenols by acid hydrolysis. Unlike the reactions of 2 moles of the sodium salt of guaiacol with the dihalides which gave the dimethyl ethers of the dihydric phenols in high yields, the above reactions failed to give satisfactory yields and no method worth reporting was developed. 2-(*o*-Hydroxyphenoxy)tetrahydropyran was prepared according to Parham and Anderson.[20]

The dichloro ethers (reactant 2 in Table II), except bis(2-chloroethyl) ether and 1,8-dichloro-3,6-dioxaoctane which are commercially available, were prepared by this general method. The yields were usually good.

A mixture of 430 g (2.2 moles) of tetraethylene glycol, 2000 ml of benzene, and 386 g (4.9 moles) of pyridine was heated to 86° (reflux), and 580 g (4.9 moles) of thionyl chloride was added dropwise with stirring in 3 hr. During this period the reflux temperature of the mixture dropped from 86 to 78°, and a white precipitate was formed. Heating was continued overnight (16 hr) and, after cooling, 50 ml of concentrated hydrochloric acid diluted with 200 ml of water was added dropwise in about 15 min. Benzene was removed from the upper layer containing the product, and the residue (473 g) was distilled from a rotary evaporator at about 95° (0.4 mm). The product, a light yellow liquid, weighed 469 g (yield, 92%) and contained 30.6% Cl (calcd 30.7%), $n^{24}\text{D}$ 1.4618.

Polyethylene glycols, including tetraethylene glycol, are commercial products. Pentaethylene glycol was prepared by reacting 1 mole of 1,8-dichloro-3,6-dioxaoctane with 2 moles of potassium hydroxide in excess ethylene glycol.

The data in Table VII were obtained by shaking an excess of dibenzo-18-crown-6 (XXVIII) with the methanolic salt solutions overnight at 30° and developing the results gravimetrically. The data in Table VIII were obtained by gravimetrically determining the solubilities of the salts in methanol alone and in the presence of excess XXVIII.

Preparation of 2,3-Benzo-1,4,7,10,13-pentaoxacyclopentadeca-2-ene (IV). Method V. A mixture of 110 g (1 mole) of catechol, 1500 ml of 1-butanol, and 85 g (2.13 moles) of sodium hydroxide dissolved in 100 ml of water was stirred for 5 min under nitrogen and treated with 231 g (1 mole) of 1,11-dichloro-3,6,9-trioxaundecane. The mixture was refluxed with good agitation for 30 hr during which time the temperature dropped from 102 to 100°.

The mixture was acidified with 8 ml of concentrated hydrochloric acid, cooled to 30°, and filtered, and the solids were washed with 400 ml of methanol. The filtrate and the washings were combined and evaporated to dryness in a rotary vacuum evaporator. The residue weighing 289 g was extracted continuously with *n*-heptane at 80–90° for about 3 hr and gave 174 g of white flakes containing 95% of the desired compound, yield 62%. Analytically pure compound was obtained by recrystallizing from *n*-heptane.

Preparation of 2,3-(4′-*t*-Butyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2-ene (XI). Method V. A mixture of 9 g (0.0542 mole) of 4-*t*-butylcatechol, 200 ml of 1-butanol, 4.4 g (0.11 mole) of sodium hydroxide in 10 ml of water, and 15 g (0.0546 mole) of 1,14-dichloro-3,6,9,12-tetraoxatetradecane was refluxed under nitrogen with agitation for 23 hr during which time the temperature remained at 105°.

The solution was decanted from the solids and evaporated to dryness in a rotary vacuum evaporator. The residue, 22.3 g, was dissolved in 200 ml of chloroform and washed twice with 250 ml of 1% aqueous sodium hydroxide, dried with anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue, 20.6 g, was distilled from a rotary evaporator at 0.45m m. The viscous, oily

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(20) W. E. Parham and E. L. Anderson, *J. Am. Chem. Soc.*, 70, 4187 (1948).

distillate, 17.3 g, contained 12.3 g of the desired product, yield 62%. The pure product was obtained through its potassium thiocyanate complex and by vacuum distillation. The liquid crystallized on standing at room temperature. Purification by chromatography is probably a better method than by complexation.

Preparation of 2,3,9,10-Dibenzo-1,4,8,11-tetraoxacyclotetradeca-2,9-diene (XV). **Method W.** A mixture of 13 g (0.05 mole) of 1,3-bis(*o*-hydroxyphenoxy)propane, 400 ml of water, 4 g (0.1 mole) of sodium hydroxide, and 10.1 g (0.05 mole) of 1,3-dibromopropane was refluxed under nitrogen with good agitation for 22 hr during which time the temperature rose from 100 to 102°.

The mixture was extracted with 200 ml of chloroform, washed twice with 100 ml of 5% aqueous sodium hydroxide, dried with anhydrous magnesium sulfate, filtered, and evaporated to dryness under vacuum. The residue, 11.8 g of light buff crystals, was recrystallized from methanol and gave 4 g of the desired compound, yield 27%.

An attempt to prepare this compound by method X using catechol, 1,3-dibromopropane, and sodium hydroxide, gave an 11% yield of 1,2-trimethylenedioxybenzene but no recoverable amount of the desired cyclic polyether.

Preparation of 2,3,32,33-Dibenzo-1,4,7,10,13,16,19,22,25,28,31,34,-37,40,43,46,49,52,55,58-eicosaoxacyclohexaconta-2,32-diene (XLII). **Method W.** A mixture of 59.0 g (0.1 mole) of 1,26-bis(*o*-hydroxyphenoxy)-3,6,9,12,15,18,21,24-octaoxahexacosane, 250 ml of 1-butanol, and 13.0 g (0.2 mole) of 85% potassium hydroxide was brought to reflux (temperature, 113.5°) under nitrogen. At this temperature 44.4 g (0.1 mole) of 1,26-dichloro-3,6,9,12,15,18,21,24-octaoxahexacosane dissolved in 60 ml of 1-butanol was added dropwise, and the mixture was refluxed for 28 hr (temperature, 113.5–115.5°). The mixture was cooled, filtered, and evaporated in a vacuum rotary evaporator (100° (0.3 mm)). The brown viscous oil, 107.3 g, was dissolved in chloroform and chromatographed on a 9 × 1.75 in. column of alumina. The crude product, 79.0 g of brown viscous oil, was recovered from the eluate. Its infrared spectrum showed very little OH absorption.

Anal. Calcd: C, 59.0; H, 8.2; mol wt, 976. Found: C, 58.4; H, 8.3; mol wt, 1,009.

The crude product was purified on a 9 × 1.75 in. column of alumina using benzene (*ca.* 150 ml). The OH-free product weighed 38.6 g, yield 41.4%.

Preparation of 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII).[21] **Method W.** A mixture of 29 g (0.1 mole) of bis[2-(*o*-hydroxyphenoxy)ethyl] ether, 320 ml of 1-butanol and 8 g (0.2 mole) of sodium hydroxide dissolved in 20 ml of water was brought to reflux (100.5° temperature) and 14.4 g (0.1 mole) of bis(2-chloroethyl) ether diluted with 20 ml of 1-butanol was added dropwise during the next 20 min. Refluxing was continued 20 hr more.

The mixture was acidified with 2 ml of concentrated hydrochloric acid and most of the 1-butanol was removed by taking off 450 ml of distillate while adding 500 ml of water. The mixture was allowed to cool and settle, filtered, washed with water, and sucked as dry as possible. The precipitate was dispersed in 100 ml of acetone, filtered, and washed with 30 ml of acetone. The precipitate was treated again in the same way and dried.

The white product, 29 g, consisted of nearly pure crystals of the desired compound, yield 80%.

Method X. A mixture of 330 g (3 moles) of catechol, 2000 ml of 1-butanol, and 122 g (3 moles) of sodium hydroxide pellets was refluxed under nitrogen for 30 min to ensure complete dissolution of sodium hydroxide (temperature about 115°). A solution of 222 g (1.55 moles) of bis(2-chloroethyl) ether diluted with 150 ml of 1-butanol was added dropwise over 2 hr, and the mixture was refluxed for 1 hr. The temperature was lowered to 90°, and 122 g of sodium hydroxide pellets was added. Refluxing was continued for 30 min, and 222 g of bis(2-chloroethyl) ether diluted with 150 ml of 1-butanol was added dropwise over 2 hr. Refluxing was continued for 16 hr.

Concentrated hydrochloric acid (21 ml) was slowly added, and then 700 ml of solvent was rapidly removed by distillation. The distillation was continued but the volume in the flask was kept constant by the steady addition of water until the vapor temperature reached 100°, then for 10 min more.

The mixture was filtered, washed with 2000 ml of water, and sucked dry. The solids were dispersed in 1500 ml of acetone, stirred for 30 min, filtered, washed with 500 ml of acetone, and dried in an oven at 100°.

The dry product weighed 240–260 g and melted at 162–164°. The pure product melts at 164° and boils at about 380–384° (769 mm), yield 44–48%.

Note: the acetone filtrate and wash contained about 16 g of the desired product, but its recovery from a single run is not worth the trouble.

Preparation of 2,3,16,17-Dibenzo-1,4,15,18-tetraoxacyclooctacosa-2,16-diene (XX). **Method Y.** A mixture of 28.7 g (0.087 mole) of 1-bromo-10-(*o*-hydroxyphenoxy)decane, 120 ml of 1-butanol, and 3.9 g (0.098 mole) of sodium hydroxide dissolved in 10 ml of water was refluxed under nitrogen with good agitation for 22 hr during which time the temperature rose from 102.5 to 104°.

The mixture was evaporated in a vacuum rotary evaporator. The residue, 28.3 g, was dissolved in 100 ml of warm chloroform, filtered, extracted with 50 ml of 5% aqueous sodium hydroxide, dried with anhydrous magnesium sulfate, and evaporated to dryness. The residue, 22.1 g, was distilled from a rotary evaporator at 0.25 mm using an electric heating mantle. The distillate which solidified, 1.2 g, was dispersed in 30 ml of methanol, filtered, and dried. It was recrystallized from 40 ml of *n*-heptane. The fine white crystals of the desired compound weighed 0.65 g, yield 3%.

Preparation of 2,6,13,17-Tetraoxatricyclo[16.4.0.$0^{7,12}$]docosane (XVII). **Method Z.** A mixture of 1.75 g (0.0058 mole) of 2,3,9,10-dibenzo-1,4,8,11-tetraoxacyclotetradeca-2,9-diene, 100 ml of spectro grade *p*-dioxane, and 0.25 g of ruthenium dioxide was hydrogenated in a 400-ml stainless steel shaker bomb at 100° and 1600 psig for 4 hr with good agitation.

The mixture was filtered and evaporated in a vacuum rotary evaporator. White crystals, 1.6 g, of the crude product were obtained, yield about 88%. The pure product was obtained by crystallization from petroleum ether.

Preparation of 2,5,8,15,18,21-Hexaoxatricyclo[20.4.0.$0^{9,14}$]hexacosane (XXXI). **Method Z.** A mixture of 125 g of dibenzo-18-crown-8, 500 ml of 1-butanol, and 12.5 g of ruthenium catalyst (5% ruthenium on alumina) was hydrogenated in a 1-l. stainless steel bomb at 100° and 1000–1500 psig with very good agitation until the theoretical amount of hydrogen (2.08 moles) had been absorbed. Hydrogenation was continued under these conditions for 30 min more.

The catalyst was removed by filtration, and the solvent was removed under vacuum in a rotary evaporator. The product, a mixture of *cis* and *trans* isomers of the desired compound, solidified on standing at room temperature and had a melting range above 36°. The yield was quantitative except for the loss in handling. If the product was contaminated with small amounts of dibenzo-18-crown-6 or the alcohols resulting from the scission of the polyether ring, it was purified in the following way.

The product (130 g) was dissolved in 400 ml of *n*-heptane and placed on a 2.75 × 8 in. column of acid-washed alumina (100 mesh). It was allowed to drain until the liquid level at the top had reached that of the alumina, then the eluate was made up to 700 ml with fresh *n*-heptane and passed through the column, allowing to drain as much as possible. The elution was continued as long as the infrared spectrum of the eluate showed no OH band. The purified product was recovered by removing the solvent.

Since dicyclohexyl-18-crown-6 is a polyether, it will peroxidize with ultimate scission of the polyether ring. It should be protected, therefore, from the atmosphere particularly at high temperatures. This product possesses some unexpected toxic properties and should be handled with care. For toxicity data see Appendix.

Preparation of 1,4,7,10,13,16-Hexaoxacyclooctadecane (XXVII). **Special Method.** A mixture of 32.5 g (0.108 mole) of 17-chloro-3,6,9,12,15-pentaoxaheptadecanol (hexaethylene glycol monochloride), 700 ml of 1,2-dimethoxyethane, and 14.2 g (0.108 mole) of 90.5% potassium *t*-butoxide was brought to reflux under nitrogen with vigorous agitation. The distillate (200 ml) was removed at 85.5°, and the remainder was refluxed for 23 hr.

The mixture was acidified with 25 ml of concentrated hydrochloric acid, cooled, filtered, and evaporated under vacuum. The residue, 30.2 g, was dissolved in 200 ml of chloroform, filtered, and concentrated. The residue, 25.3 g, was distilled from a rotary evaporator at 0.45 mm. The distillate, 16.3 g, was put on a column of acid-washed alumina and eluted with *n*-heptane to give 0.5 g of colorless, viscous liquid that solidified when contacted with a crystal of sodium chloride. This was the desired product, yield 1.8%. On crystallization from petroleum ether 0.43 g of white crystals was obtained.

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[21] Dibenzo-18-crown-6 (XXVIII) forms a complex with radium bromide in methanol according to spectrophotometric tests made by TRACERLAB, a division of Laboratory for Electronic, Inc.

A preparation was made with sodium hydride instead of potassium *t*-butoxide. The desired product was obtained in 1.8% yield.

Preparation of Crystalline Sodium Iodide Complex of 2,3-Benzo-1,4,7,10,13-pentaoxacyclopentadeca-2-ene (IV). Method 1. A mixture of 2.36 g (0.0088 mole) of benzo-15-crown-5 and 1.32 g (0.0088 mole) of powdered sodium iodide was melted in a beaker. The pasty mixture gradually hardened on the steam bath and became a solid in about 1 hr. The product was broken up into pieces, leached with hot *n*-heptane, and dried, yield nearly 100%. It was evident that the rate of reaction between IV and sodium iodide is much slower in the absence of a suitable solvent such as methanol.

Preparation of Crystalline Methylammonium Thiocyanate Complex of 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII). Method 2. A mixture of 0.9 g (0.01 mole) of methylammonium thiocyanate and 3.6 g (0.01 mole) of dibenzo-18-crown-6 in 70 ml of methanol and 85 ml of 1-butanol was warmed on a steam bath for 30 min. The solvents were removed in a rotary evaporator under high vacuum. The pale pink crystals weighed 3.7 g, yield 100%.

Preparation of Crystalline Potassium Triiodide Complex of 2,5,8,15,18,21-Hexaoxatricyclo[20.4.0.0^{9,14}]hexacosane (XXXI). Method 2. A mixture of 150 ml of methanol, 0.212 g (0.00085 mole) of iodine, and 0.458 g (0.00085 mole) of potassium iodide complex of dicyclohexyl-18-crown-6 was warmed on a steam bath, and the solvent was removed under high vacuum in a rotary evaporator. The product, a dark brown solid, weighed 0.67 g, yield 100%.

The product is soluble in methylene chloride and chloroform; less soluble in *o*-dichlorobenzene and tetrahydrofuran; poorly soluble in carbon tetrachloride; and insoluble in water. Water in contact with a methylene chloride solution of this complex remains colorless indefinitely.

Preparation of Crystalline Potassium Thiocyanate Complex of 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII). Method 3. A mixture of 18 g (0.05 mole) of dibenzo-18-crown-6, 4.9 g (0.0505 mole) of potassium thiocyanate, and 250 ml of methanol was warmed on a steam bath until the mixture became a clear solution. It was treated with 1 g of clarifying charcoal, filtered, and allowed to cool very slowly to room temperature. Ten grams of glistening, long needles (some 2 cm long) of the complex were obtained, yield 44%. The remainder of the complex was recovered by evaporation.

Preparation of Crystalline Ammonium Thiocyanate Complex of 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII). Method 4. A mixture of 1.52 g (0.02 mole) of ammonium thiocyanate, 32 ml of methanol, and 3.6 g (0.01 mole) of dibenzo-18-crown-6 in a fibrous crystalline form was warmed on a steam bath. The fibrous crystals were converted gradually into granular crystals of the complex without the mixture ever becoming a clear solution. The white crystals weighed 4.21 g, yield 96.6%.

Preparation of Crystalline Lead Acetate Complex of 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII). Method 4. A mixture of 2.5 g (0.0069 mole) of dibenzo-18-crown-6, 2.65 g (0.007 mole) of lead acetate trihydrate, and 100 ml of 1-butanol was warmed on a steam bath for 30 min with occasional stirring. The mixture was cooled to room temperature, filtered, washed with 1-butanol, and dried. The product was a white powder and weighed 4.5 g, yield 95%.

Preparation of Crystalline Potassium Polyiodide Complexes of 2,3,11,12-Dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (XXVIII). Method 5. A mixture of 41.3 ml of methylene chloride solution containing 1.27 g (0.005 mole) of iodine, 103 ml of methylene chloride solution containing 7.2 g (0.02 mole) of dibenzo-18-crown-6, and 27 ml of aqueous solution containing 3.32 g (0.02 mole) of potassium iodide was shaken vigorously. Dark, nearly black, shiny crystals were formed. They were filtered, washed with water and methylene chloride, and dried. The product, 5.6 g analyzed as the $KI_{1.5}$ complex of XXVIII, yield 47.5%.

By altering the proportions of the solutions, the KI_2 complex was obtained in 68.9% yield and the KI_3 complex in 95% yield.

Preparation of Toluene Solution of Potassium Hydroxide Complex of 2,5,8,15,18,21-Hexaoxatricyclo[20.4.0.0^{9,14}]hexacosane (XXXI). Dicyclohexyl-18-crown-6 (14.9 g, 0.04 mole) and 2.64 g (0.04 mole) of 85% potassium hydroxide were dissolved in 50 ml of methanol by gently warming on a steam bath. Toluene (100 ml) was added, and all but about 50 ml of solvent was removed on a rotary vacuum evaporator at 100°. Toluene (100 ml) was added again, and the volume was reduced to about 50 ml. The volume was made up to 100 ml with toluene, 1 g of clarifying charcoal was added, and the mixture was allowed to settle overnight under nitrogen at room temperature. It was filtered by gravity through fine paper.

The resulting clear solution (about 94 ml) was 0.3 *N* by direct titration with standard 0.1 *N* aqueous hydrochloric acid. The solution must be protected from the atmosphere to prevent interaction with moisture and carbon dioxide.

It is likely that the solution contained, in addition to unsolvated hydroxyl ions, methoxide ions, methanol, and water. Regardless of its exact composition, this particular solution is meant by the toluene solution of the potassium hydroxide complex of dicyclohexyl-18-crown-6.

Preparation of *o*-Dichlorobenzene Solution of Potassium Palladous Chloride Complex of 2,5,8,15,18,21-Hexaoxatricyclo[20.4.0.0^{9,14}]-hexacosane (XXXI). A mixture of 2.134 g (0.01 mole) of palladous chloride dihydrate, 1.49 g (0.02 mole) of pulverized potassium chloride, 7.44 g (0.02 mole) of dicyclohexyl-18-crown-6, and 56 ml of *o*-dichlorobenzene was kept at room temperature without agitation for 19 days. A dark orange-brown solution containing 1.5% by weight of palladium was obtained. This reaction can be speeded up by stirring and warming.

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Appendix

It has been found that the sterically hindered esters of 2,4,6-trimethylbenzoic acid, although resistant to saponification by potassium hydroxide in hydroxylic solvents, can be saponified by the postassium hydroxide complex of dicyclohexyl-18-crown-6 (XXXI) in aromatic hydrocarbons. The second-order rate constant for the saponification of the methyl ester at 26° is 3.9×10^{-7} l. mole^{-1} sec^{-1}.

The acyl chloride and the esters of 2,4,6-trimethylbenzoic acid were synthesized according to Cohen and Schneider[22] or Newman.[23] The refractive indices of the esters were: methyl 1.5063 at 24.8°, *t*-butyl 1.4900 at 25°, and neopentyl 1.4862 at 24.7°.

Saponification was effected at the reflux with the attendant variations in reaction temperature. A few experiments were run at constant temperature. Saponification was measured by extracting the resulting potassium 2,4,6-trimethylbenzoate with water, acidifying with hydrochloric acid, and determining the free acid gravimetrically. No correction was made for the amount of acid lost in the aqueous filtrate (62 ml for 0.0045 mole of ester). The results are presented in Table XV.

Additional data from no. 1 and 3 gave these second-order rate constants: 1.08×10^{-4} l. mole^{-1} sec^{-1} at $73.8 \pm 0.2°$; and 1.17×10^{-3} at $99.9 \pm 0.1°$. From these values using the Arrhenius equation the activation energy is estimated to be 24 kcal/mole and *A* to be 9.1×10^{10}.

From the identical optical rotation (−49° at 22°) of the original l-menthol and that recovered from its 2,4,6-trimethylbenzoate, it is concluded that the normal acyl–

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(22) S. G. Cohen and A. Schneider, *J. Am. Chem. Soc.*, **63**, 3382 (1941).

(23) M. A. Newman, *ibid.*, **63**, 2431 (1941).

Table XV. Saponification of Esters of 2,4,6-Trimethylbenzoic Acid with Potassium Hydroxide Complex of Dicyclohexyl-18-crown-6

			Concn, M^a				
No.	Solvent	Ester	Ester	Base	Temp, °C	Time, hr	Hydrolyzed, %^{b}
1	Toluene	Methyl	0.122	0.122	73.8 ± 0.2	31	58.4
2	Benzene	Methyl	0.061	0.154	80–80.1	5	39
3	Toluene	Methyl	0.120	0.120	99.9 ± 0.1	2	53.0
4	Toluene	Methyl	0.061	0.154	105–111	5	93
5	Benzene	*t*-Butyl	0.060	0.154	79.6–80.2	5	22
6	Toluene	*t*-Butyl	0.060	0.154	104–111	5	94
7	Benzene	Neopentyl	0.060	0.154	80.3–80.7	5	40

[a] The initial concentration. [b] No saponification measurable by this method occurred when the methyl ester was refluxed at 75.5–77° with excess potassium hydroxide in 1-propanol for 5 hr.

oxygen fission occurs in this saponification. It is likely that the activity of these solutions of the potassium hydroxide complex of XXXI is due to the presence of unsolvated hydroxyl ions which can attack the carbonyl groups of the hindered esters much more readily than the ordinary solvated hydroxyl ions.

Toxicity. Dicyclohexyl-18-crown-6 (XXXI) possesses unusual physiological properties which require care in its handling. It is likely that other cyclic polyethers with similar complexing power are also toxic, and should be handled with equal care.

Oral Toxicity. The approximate lethal dose for XXXI for ingestion by rats was 300 mg/kg. In a 10-day subacute oral test, the compound did not exhibit any cumulative oral toxicity when administered to male rats at a dose level of 60 mg/kg/day. It should be noted that dosage at the ALD level caused death in 11 min, but that a dose of 200 mg/kg was not lethal in 14 days.

Eye Irritation. XXXI produced some generalized corneal injury, some iritic injury, and conjunctivitis when introduced as a 10% solution in propylene glycol. Although tests are not complete, there may be permanent injury to the eye even if the eye is washed after exposure.

Skin Absorption. XXXI is very readily absorbed through the skin of test animals. It caused fatality when absorbed at the level of 130 mg/kg.

Skin Irritation. Primary skin irritation tests run on XXXI indicate the material should be considered a very irritating substance.

Molecular Geometry. V. Evaluation of Functions and Conformations of Medium Rings[1]

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Abstract: Constants in the functions used for the calculation of minimum-energy conformations for *n*-butane and cycloalkanes were varied so as to find the set which best reproduced a dozen items of experimental data (geometry and energies). The resultant best functions were then applied to obtain the geometry and energies of the symmetrical cycloalkane rings.

Calculations aimed at determining the conformational geometry of molecules[3] depend for their validity on the assumptions made and on the functions used to relate geometrical parameters to energy. Assumptions must be made partly because no clear physical mandate exists to guide the choice of selection of certain procedures and partly because the scale of the requisite computations usually demands some simplification even when employing contemporary high-speed computers. The functions used embody a number of constants, values for which are only available by extrapolation from experimental data. However, the experiments commonly either do not measure cases comparable to those on which the functions will be used in calculations or else they are not measurements of the pure, isolated effect for which a constant is required.[6] The calculations, however, allow variations

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(1) Paper IV: J. B. Hendrickson, *J. Am. Chem. Soc.*, **86**, 4854 (1964). Much of the present work was the subject of a lecture by the author at the Conformational Analysis Symposium at the National Meeting of the American Chemical Society, New York, N. Y., Sept 13, 1966. Support of this work by a grant from the National Institutes of Health is gratefully acknowledged, as is the opportunity afforded the author of using the computation facilities at the Massachusetts Institute of Technology (IBM 7094) and Brandeis University (IBM 1620).

(2) Alfred P. Sloan Foundation Fellow, 1962–1966.

(3) A general account of the procedures involved is available in E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, John Wiley and Sons, Inc., New York, N. Y., 1965, Chapter 7-2, which in turn derives largely from the discussions in ref 4 and 5.

(4) F. H. Westheimer in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 12.

(5) J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961).

(6) For example, spectroscopic determination of angle-bending constants must involve some 1–3 nonbonded interactions[7] and nonbonded potential functions are sought in many indirect ways.[3-5]