

from both Ox1 and Ox3 and is spectrally consistent with acetone. The significantly lower intensity from Ox2 could be the result of (1) the higher excited-state energies of acetone leading to poorer competition of the diabatic channel with adiabatic reaction or (2) the lower luminescence quantum yields of acetone or both. To the extent that we have characterized its luminescence, Ox3 behaves like Ox1, as would be expected from their common fragmentation products.

Photochemical Implications. Many photochemical systems are thermally reversible. Some oxetanes thermally revert to the ketone and olefin⁵¹ from which they were photochemically formed. Any process by which a molecule breaks down to give the chemical species from which it was formed is obviously the "reverse" (chemical) of the formation reaction. So in that limited sense, the thermal chemistry of oxetanes can be considered the reverse of photochemical cycloaddition. However, a careful analysis of the reaction mechanism reveals that the photocycloaddition is fundamentally different from the thermal decomposition. There are, for example, many different ways in which excess energy could be partitioned in proceeding from the oxetane to a carbonyl and an olefin. Since the formation of oxetanes by the Paterno-Buchi reaction is diabatic, only those decomposition pathways along which energy partitioning leads to an excited-state carbonyl can be considered the formal reverse. That is, the dissociation of an oxetane is the formal reverse of the Paterno-Buchi reaction if and only if the same (two) energy surfaces are involved in both the formation and dissociation of the oxetane—but traversed in opposite order.

The formal reverse of any diabatic photochemical reaction is difficult to obtain. There are no other reported examples where a diabatic photochemical reaction has been formally reversed.⁵²

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(52) Turro, N. J.; Chow, M. J. *Am. Chem. Soc.* 1979, 101, 1300 is a related example.

Since forward diabatic photochemical reactions return a molecule to the ground-state surface with significant excess vibrational energy, the formal reverse reaction pathway requires the initial production of a highly vibrationally-excited ground-state molecule. IRMP excitation is an ideal method for effecting the instant heating required to access these high-lying vibrational states.

The ability of IRMP excitation to promote otherwise minor or unobservable higher energy pathways has been demonstrated in numerous IRMP photolyses where both competing pathways are ground state (adiabatic) channels. Because up-pumping is faster than reaction until well above the critical energy, the reacting molecules usually have significant amounts of excess internal energy. For example, IRMP excitation of vinyl cyclopropane leads to average internal energies of reacting molecules some 25 kcal/mol above the lowest energy reaction channel.¹⁷

Consequently, reaction channels not prominent during normal pyrolysis compete. The observation we have made, in the oxetane system, that the higher energy channel can be a diabatic version of the principal reaction pathway is an interesting variation on this phenomenon.

While the behavior of these selected oxetanes is unique, we feel it has an additional significance. By establishing a pair of diabatic reactions, one the formal reverse of the other, one presents a system (and more broadly a methodology) for studying surface crossings from either direction. By altering the substituent pattern on the oxetane it will be possible to examine the effects of heavy atoms and radical stabilizing substituents on the efficiency of surface crossing. Preliminary experiments addressing the role of a bi-radical intermediate in the reverse of the Paterno-Buchi reaction have been executed. We believe that the IRMP methodology for studying diabatic chemistry introduced here promises to be a useful tool in mechanistic photochemistry.

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Complexes of Macrocyclic Polyethers and Neutral Guest Molecules: A Systematic Approach to the Complexation of Water Molecules by 2,6-Pyridinium Crown Ethers¹

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Abstract: pK_a determinations of 2,6-pyridinium crown ethers **1** ($n = 0-6$) in four different solvent systems show that the acidity of these ligands strongly depends on ring size and solvent composition. This dependence is explained in terms of a stabilizing, macroring-assisted solvation of the pyridinium moiety, which varies with the ring size. X-ray analyses of the solid complexes of 2,6-pyrido-18-crown-6·H₂O·HClO₄ (1:1:1), 2,6-pyrido-18-crown-6·H₂O·HPic (1:1:1), 2,6-pyrido-21-crown-7·H₂O·HClO₄ (1:1:1), and 2,6-pyrido-24-crown-8·H₂O·HClO₄ (1:2:1) support this interpretation. The 18-membered pyrido crown ether has a structure which is optimally suited to form an encapsulated complex with water. The effect of complexation on the conformation of the macroring was studied by performing an X-ray analysis of the free 2,6-pyrido-18-crown-6. Approximate stability constants of the water complexes in the various solvent systems could be estimated from the pK_a data.

The ability of macrocyclic polyethers ("crown ethers") to form well-defined stoichiometric complexes with a variety of small, cationic guests has received much attention during the last 2

decades. Although a number of complexes between crown ethers and neutral molecules are known,² our understanding of this type

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(1) Part of this work appeared in preliminary form: Grootenhuys, P. D.; van Staveren, C. J.; den Hertog, H. J., Jr.; Reinhoudt, D. N.; Bos, M.; Uiterwijk, J. W. H. M.; Kruijs, L.; Harkema, S. *J. Chem. Soc., Chem. Commun.* 1984, 1412-1413.

of complexes is almost exclusively based on X-ray crystallographic data. All these complexes were obtained more or less by accident, and no information on thermodynamic properties and the nature of the binding was available. We have recently³ developed a method for the determination of association constants of some simple 18-membered crown ethers with several neutral guest molecules by ¹H NMR spectroscopy, and we found that complexes of macrocyclic ligands and neutral guests are weak compared to complexes with charged guests. Larger crown ethers generally show even weaker interactions and smaller association constants.⁴

In relation with the selective complexation of urea,⁵ we are currently studying the possibility of inducing a charge separation in neutral complexes by means of a proton-transfer reaction from host to guest, thus increasing the binding forces between host and guest. In the literature, few examples of such complexes have been reported for amines, viz. the proton transfer from 2,2'-bis-(carboxymethoxymethyl)-1,1'-binaphthyl crown ethers to L-valine,⁶ a crystalline complex of 2-carboxy-1,3-xylyl-18-crown-5 and *tert*-butylamine,⁷ and the formation of an ammonium phenoxide crown ether complex by reacting 2-hydroxy-1,3-xylyl-18-crown-5 and ammonia in methanol.⁸ In an intermolecular reaction, complete proton transfer from a proton-donating group to a proton-accepting guest molecule can theoretically only be achieved if the pK_a value of the base exceeds the pK_a of the acid by 2–3 units. However, Masci⁹ has indicated the possibility that the presence of crown ethers can shift acid–base equilibria by partial complexing of the protonated species.

It is clear that a quantitative knowledge and understanding of the factors determining the acidity of intraannular proton donors are a prerequisite for the rational design of receptor molecules based on this concept. However, systematic studies have not been reported so far. In order to obtain such information, Cram and co-workers have determined the pK_a values of some crown ethers with an intraannular carboxyl group⁷ or pyridyl binding site¹⁰ and of some intramolecular complexes.¹¹ After completion of this work, Browne et al.⁸ reported that phenolic crown ethers show virtually no dependence of the acidity on the ring size, although these authors have studied a relatively small range of ring sizes (15–21 ring atoms). In order to gain further insight into the role of solvent, ring size, and hydrogen bonding, we have studied 2,6-pyrido crown ethers in which the ring size varies from 15 to 33 ring atoms. In macrocyclic polyethers with intraannular proton-donating substituents, the cavity is at least partly filled by the substituent, but in protonated pyrido crown ethers, a large part of the cavity is still available for complexation. Complexes of pyridinium crown ethers with neutral guests would represent a class of crown ether–guest complexes in which the positive charge

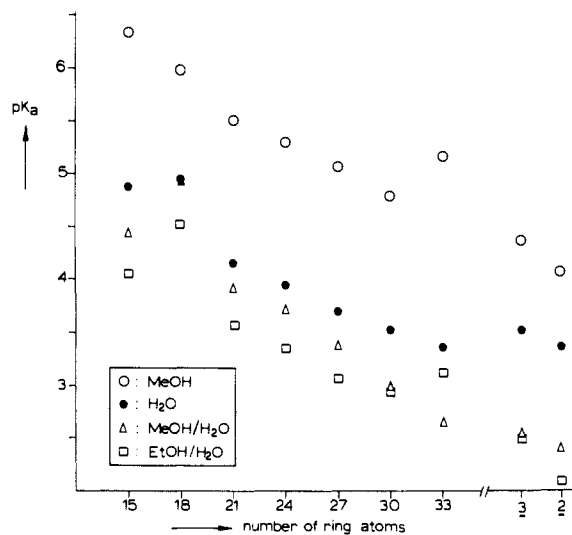
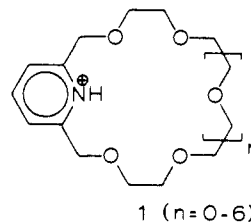


Figure 1. pK_a 's of 2,6-pyridinium crown ethers (1, $n = 0-6$) and open-chain analogues (2, 3) in several solvents (25.0 °C).

is mainly located on the ligand, this in contrast with the conventional type of host–guest complexes in which the guest is positively charged. We are aware of only one example, viz. the aza-18-crown-6·H₂O·HCl (1:1:1) complex that was reported by Gokel and Garcia.¹² Such complexes show some resemblance to the complexes of cationic paracyclophane-type hosts with (preferably) aromatic neutral guest molecules.^{2f} The associative hydrophobic forces in such complexes can in some cases lead to very large stability constants in water up to 10⁷ dm³ mol⁻¹, but in other solvents, the association constants decrease drastically.

In this paper, we report the results of a study on the acidity and complexation properties of 2,6-pyrido crown ethers 1 as a function of ring size and solvent composition.



Results

pK_a Determinations. Apparent pK_a values for 2,6-pyrido crown ethers in several water–alcohol mixtures were determined by potentiometric titrations with hydrogen chloride or perchloric acid. A glass/silver–silver chloride electrode combination was calibrated in carefully prepared buffer solutions, a method to be preferred over the use of pH correction numbers δ .¹³ Thermodynamic pK_a values were calculated iteratively by using activity coefficients. Based on the experimental reproducibility and pK_a determinations of standard substances, we estimate the uncertainties in the pK_a to be ± 0.02 units for water as solvent and ± 0.06 units for the other solvent systems.

The pK_a data depicted in Figure 1 show that the acidity of the pyridinium crown ethers strongly depends on ring size and solvent composition. The conjugate acids of two open-chain model compounds 2 and 3 are included in the figure in order to evaluate the macrocyclic effects.

In water, the pK_a 's of compounds 2 (3.36) and 3 (3.53) are rather low when compared with pyridine (5.23) and 2-(methoxymethyl)pyridine, 4 (4.40).¹⁴ When the Hammett-type

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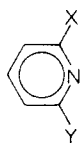
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- 2 X = Y = CH₂OCH₃
 3 X = Y = CH₂OCH₂CH₂OCH₃
 4 X = CH₂OCH₃, Y = H

equation for 2-substituted pyridinium ions ($pK_a = 5.03 - 11.8 \sigma_{meta}$)¹⁵ is used, with $\sigma_{meta} = 0.02$ for an alkoxyethyl group,¹⁶ a pK_a of 4.8 can be calculated for protonated 4. This is much higher than the experimentally obtained value and possibly due to steric effects.¹⁷ In a recent paper, Hopkins et al.¹⁸ conclude that the unusually low basicity of 2,6-di-*tert*-butylpyridine in aqueous solution has to be explained in terms of loss of entropy due to sterically restricted internal rotations in the water complex of the 2,6-di-*tert*-butylpyridinium cation. Similar effects may account for the rather low basicities of 2 and 3.

The pK_a 's of the open-chain model compounds resemble the pK_a 's of the larger macrocycles 1 ($n = 4-6$), showing that macro-ring-assisted solvation is absent. The relatively high basicities of the small macrocycles 1 ($n = 0-3$), in particular the 18-membered ring, point to an extraordinary large stabilization of the protonated species.

In three cases (1, $n = 1-3$), white crystals were formed after the titration experiments and subsequent X-ray crystallographic analyses revealed the complexation of water molecules by the pyridinium crown ethers (see Crystallographic section). Apparently, the complexed water molecules strongly solvate the pyridinium cation by formation of hydrogen bonds with the protonated nitrogen atoms. In the case of 1 ($n = 1$), a very stable complex is formed, causing the extra basicity of this ligand.

It has been shown that in the gas phase, the strongest interaction of the pyridinium cation is with the first solvent molecule.¹⁹ Therefore, the gradual increase in acidity with increasing ring size may be explained by the decreasing solvation of the protonated species by the first solvent (water) molecule because of a decreased "second-sphere" stabilization by the macro-ring oxygen atoms.

Compared with the reference compounds 2 and 3, the pyridino-15-crown-5 is a much stronger base, which means that the protonated form is particularly stabilized. According to Corey-Pauling-Koltun (CPK) model studies, the cavity of the 15-membered cycle is too small to form an encapsulated water complex, but it might be possible that one water molecule accepts a hydrogen bond from the pyridinium moiety and uses one hydrogen atom for a hydrogen bond with a polyether oxygen atom. The remaining hydrogen atom is pointing outside the cavity probably interacting with another solvent molecule.

In order to investigate the effect of different solvents on the acid dissociation equilibria, titrations were carried out in 52.1 wt % MeOH/H₂O.²⁰ Again, an increased acidity of the pyridinium crown ethers with an increasing ring size is observed. The extreme basicity of the 18-membered ring points to the formation of a very stable H₂O complex. The decrease in pK_a relative to 3 and 4 is even more pronounced than in water, which is attributed to the

Table I. Association Constants (dm³ mol⁻¹)^a of 2,6-Pyridinium (15 + 3*n*)-Crown-(5 + *n*) Chloride and Water in Different Solvent Systems at 25.0 °C

<i>n</i>	H ₂ O ^b	MeOH/H ₂ O (52.1%) ^c	EtOH/H ₂ O (85.4%) ^c
1	39	347	263
2	6	33	30
3	4	21	17
4	2	10	9

^a $pK_a(\text{ref}) = pK_a(2)$. ^b Accuracy: $\pm 7\%$. ^c Accuracy: $\pm 22\%$.

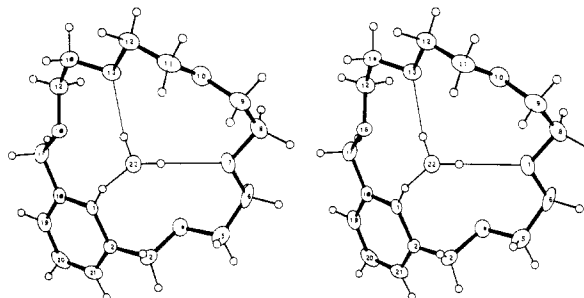


Figure 2. Stereoscopic view of the 2,6-pyridino-18-crown-6-H₂O-HClO₄ (1:1:1) complex (5), showing atom numbering. The perchlorate ion is omitted.

higher stability of the H₂O complex in this less-polar medium. However, it is generally recognized that the interpretation of pK_a data from alcohol-water systems is difficult and complex,²¹ and for a quantitative understanding, more detailed studies would be needed.

In pure methanol, the pK_a data show two striking phenomena: firstly, the extremely enhanced basicity of the 18-membered macrocycle has disappeared; secondly the pK_a value of the 33-membered ligand is relatively large. Apparently, the methanol solvent molecules have taken over the role of water in stabilizing the cation. CPK models indicate an almost perfect match in the complex of the 33-membered macrocycle and two encapsulated methanol molecules. Unfortunately, all our attempts to obtain crystals for an X-ray study failed. It is known from literature that (substituted) pyridines are hydrogen bonded by methanol,²² and Voegtle and co-workers²³ have reported solid complexes of several pyridine-functionalized crown ethers with alcohols.

Surprisingly, the basicity of the pyridino crown ethers in methanol is larger by 1.3–1.5 units when compared with water. In contrast to this, Rochester et al.²⁴ experimentally demonstrated that eq 1 is valid for various substituted pyridines, showing that the pK_a 's

$$pK_a(\text{MeOH}) = pK_a(\text{H}_2\text{O}) + 0.08 \quad (1)$$

of pyridines in H₂O and MeOH are nearly the same. A possible explanation for this solvent effect might be that the hydrogen bonding between the pyridinium hydrogen and the solvent oxygen atom will be stronger in MeOH than in water,^{22b} resulting in a more stable complex.

To investigate the effect of ethanol molecules as pyridinium-stabilizing guest molecules, pK_a values were determined in 85.4 wt % EtOH/H₂O.²⁰ Obviously, the characteristics of both the water and methanol systems are present. The enlarged basicity of the 33-membered cycle indicates that larger alcohols also may be complexed by pyridinium crown ethers. The alkyl chain of the alcohol might partially be outside of the cavity, and the α -

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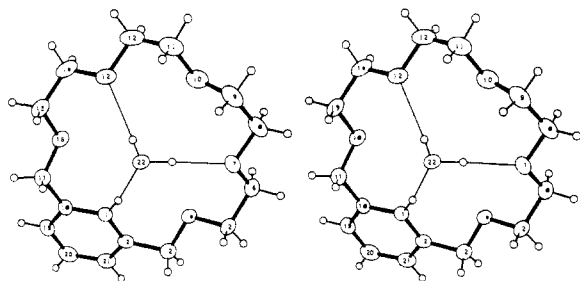


Figure 3. Stereoscopic view of the 2,6-pyrido-18-crown-6-H₂O-HPic (1:1:1) complex (6), showing atom numbering. The picrate ion is omitted.

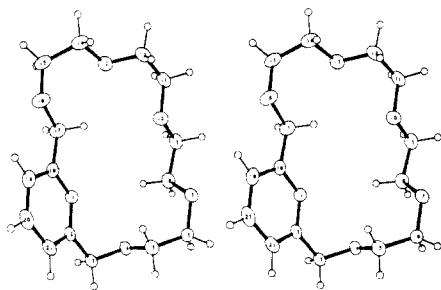


Figure 4. Stereoscopic view of uncomplexed 2,6-pyrido-18-crown-6 (1, $n = 1$), showing atom numbering.

methylene protons may be also weakly hydrogen-bonded.

It is possible to estimate very roughly the stability constants K_s of the H₂O complexes of some pyridinium crown ethers in the different solvent systems. Under the assumption that no H₂O complexes are formed with the unprotonated ligands, one can easily derive that

$$pK_a(\text{exptl}) - pK_a(\text{ref}) = \log K_s \quad (2)$$

in which $pK_a(\text{exptl})$ stands for the experimental pK_a and $pK_a(\text{ref})$ for a reference (model) compound. The results are given in Table I. In water, the stability constants are 5–8 times smaller than in the alcohol–water mixtures. Hitherto thermodynamic data on the complexation of water by crown ethers are not available from the literature for comparison. The K_s values for the protonated 18-membered macrocycle with water in the mixed alcoholic solvents are in between the values reported for the complexation of 18-crown-6 with neutral molecules (e.g., CH₃NO₂)³ and with H₃O⁺ ions.²⁵

X-ray Structures. The structures of the uncomplexed 2,6-pyrido-18-crown-6 (1, $n = 1$), of the 2,6-pyrido-18-crown-6-H₂O-HClO₄ (1:1:1) complex (5), the 2,6-pyrido-18-crown-6-H₂O-HPic (1:1:1) complex (6, HPic = picric acid), the 2,6-pyrido-21-crown-7-H₂O-HClO₄ (1:1:1) complex (7), and the 2,6-pyrido-24-crown-8-H₂O-HClO₄ (1:2:1) complex (8) have been determined by X-ray crystallography. Details of the structure determinations are given in the Experimental Section. Stereoscopic ORTEP²⁶ views of the complexes, including atom numbering, are given in Figures 2–6, using 50% probability ellipsoids for all non-hydrogen atoms. The radii of the hydrogen atoms have been chosen arbitrarily. Positional and thermal parameters of the atoms are available as supplementary material. Torsion angles in the macrorings are given in Table II. Parameters for the hydrogen bonds involving the water molecules are presented in Table III. Although the uncomplexed 2,6-pyrido-18-crown-6 molecule in the solid state as well as the crown ether molecules in the four crystalline complexes mentioned are involved in short intermolecular contacts with other polyether molecules or with anions, no short and almost linear hydrogen bonds like those involving the complexed water molecules exist.

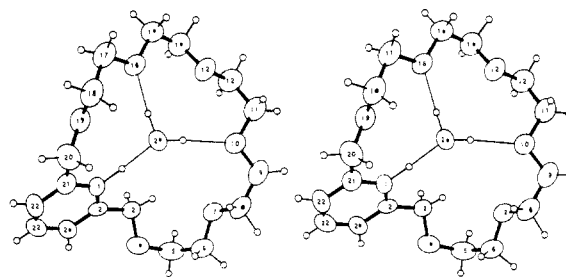


Figure 5. Stereoscopic view of the 2,6-pyrido-21-crown-7-H₂O-HClO₄ (1:1:1) complex (7), showing atom numbering. The perchlorate ion is omitted.

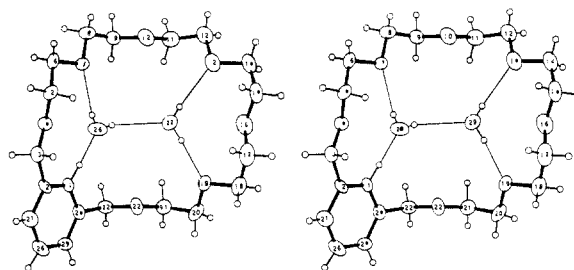


Figure 6. Stereoscopic view of the 2,6-pyrido-24-crown-8-H₂O-HClO₄ (1:2:1) complex (8), showing atom numbering. The perchlorate ion is omitted.

2,6-Pyrido-18-crown-6-H₂O-HClO₄ (1:1:1) Complex (5). The X-ray structure determination reveals a structure in which the crown ether completely encapsulates the water molecule (Figure 2). The crown ether molecule is protonated at the pyrido nitrogen atom. The conformation adopted by the macrocycle can be characterized by the torsion code $ag^+a ag^-a ag^+a ag^-a ag^+a$. Some torsion angles are, however, rather distorted from the ideal values (see Table II). The conformation happens to be the same one as adopted by the macroring in an analogous tetracarboxylic 18-crown-6-H₃O⁺-Cl⁻ (1:1:1) complex,²⁷ in which the guest water molecule is protonated. The conformation resembles the D_{3d} conformation, although more strained, involving an “eclipsed” fragment in both complexes (O15–C16–C17–O18 in the complex with the tetracarboxylic polyether and O16–C17–C18–N1 in 5).

The pyrido hydrogen atom in complex 5 is involved in a N–H···O hydrogen bond to the water molecule, which, in addition, forms two O–H···O hydrogen bonds to next-nearest oxygen atoms of the macrocycle. A similar hydrogen bonding scheme was found in the tetracarboxylic 18-crown-6-H₃O⁺-Cl⁻ (1:1:1) complex, although in this complex all three hydrogen bonds have the guest ion as the donor. The water molecule is positioned above the least-squares plane defined by the 18 macroring atoms, with its hydrogen atoms pointing toward the plane (distances to the plane: 0.93, 0.62, and 0.71 Å, for the oxygen and the hydrogens, respectively).

2,6-Pyrido-18-crown-6-H₂O-HPic (1:1:1) (6). To study the effect of the anion on complexation, the structure of complex 6 was determined. The complexation between the water molecule and the polyether is very similar to the complexation in the analogous perchlorate complex (5; see Figure 3). Nevertheless, the macroring in the picrate complex adopts a conformation different from the one in the perchlorate complex viz. the well-known D_{3d} conformation ($ag^+a ag^-a ag^+a ag^-a ag^+a ag^-a$).

Although the water molecule is again positioned above the least-squares plane defined by the 18 macroring atoms, with its hydrogens pointing toward the plane, it is closer (distances to the plane: 0.64, 0.42, and 0.40 Å for the oxygen and the hydrogens, respectively). This is probably a result of the somewhat larger cavity size of the D_{3d} conformation compared to the “eclipsed” conformation adopted by the macrocycle in the perchlorate complex.

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Table II. Torsion Angles^a (deg) in the Macrocycles of the Compounds^b

1, <i>n</i> = 1		5		6	
N1-C2-C3-O4	44.3 (1)	N1-C2-C3-O4	62.4 (3)	N1-C2-C3-O4	-38.8 (2)
C2-C3-O4-C5	67.0 (1)	C2-C3-O4-C5	177.6 (4)	C2-C3-O4-C5	166.5 (1)
C3-O4-C5-C6	178.2 (1)	C3-O4-C5-C6	158.6 (3)	C3-O4-C5-C6	176.2 (1)
O4-C5-C6-O7	83.7 (1)	O4-C5-C6-O7	-65.7 (4)	O4-C5-C6-O7	67.5 (1)
C5-C6-O7-C8	-70.9 (1)	C5-C6-O7-C8	-158.5 (4)	C5-C6-O7-C8	173.9 (2)
C6-O7-C8-C9	-176.00 (9)	C6-O7-C8-C9	161.8 (4)	C6-O7-C8-C9	171.1 (1)
O7-C8-C9-O10	-73.7 (1)	O7-C8-C9-O10	70.7 (4)	O7-C8-C9-O10	-69.7 (1)
C8-C9-O10-C11	-173.6 (1)	C8-C9-O10-C11	-155.1 (4)	C8-C9-O10-C11	-177.3 (2)
C9-O10-C11-C12	174.2 (1)	C9-O10-C11-C12	175.0 (4)	C9-O10-C11-C12	-168.7 (2)
O10-C11-C12-O13	-67.5 (1)	O10-C11-C12-O13	-57.8 (4)	O10-C11-C12-O13	66.7 (2)
C11-C12-O13-C14	175.4 (1)	C11-C12-O13-C14	-164.5 (4)	C11-C12-O13-C14	171.5 (2)
C12-O13-C14-C15	-163.5 (1)	C12-O13-C14-C15	-170.8 (3)	C12-O13-C14-C15	-174.8 (1)
O13-C14-C15-O16	72.8 (1)	O13-C14-C15-O16	-57.2 (4)	O13-C14-C15-O16	-69.2 (1)
C14-C15-O16-C17	-82.2 (1)	C14-C15-O16-C17	-167.7 (4)	C14-C15-O16-C17	167.1 (2)
C15-O16-C17-C18	-175.64 (9)	C15-O16-C17-C18	-152.2 (3)	C15-O16-C17-C18	-176.0 (1)
O16-C17-C18-N1	-170.8 (1)	O16-C17-C18-N1	7.8 (4)	O16-C17-C18-N1	61.6 (2)
C17-C18-N1-C2	178.5 (1)	C17-C18-N1-C2	178.3 (4)	C17-C18-N1-C2	175.0 (1)
C18-N1-C2-C3	179.0 (1)	C18-N1-C2-C3	-178.8 (4)	C18-N1-C2-C3	-172.6 (2)
7					
N1-C2-C3-O4	137.3 (3)	N1-C2-C3-O4	24.7 (5)		
C2-C3-O4-C5	-168.2 (3)	C2-C3-O4-C5	-157.8 (4)		
C3-O4-C5-C6	70.2 (4)	C3-O4-C5-C6	-170.8 (4)		
O4-C5-C6-O7	-85.2 (3)	O4-C5-C6-O7	-64.4 (4)		
C5-C6-O7-C8	169.5 (4)	C5-C6-O7-C8	-171.8 (5)		
C6-O7-C8-C9	166.3 (3)	C6-O7-C8-C9	-173.6 (4)		
O7-C8-C9-O10	72.4 (3)	O7-C8-C9-O10	-75.0 (5)		
C8-C9-O10-C11	173.3 (4)	C8-C9-O10-C11	-175.1 (5)		
C9-O10-C11-C12	146.0 (4)	C9-O10-C11-C12	174.3 (4)		
O10-C11-C12-O13	72.3 (4)	O10-C11-C12-O13	62.9 (5)		
C11-C12-O13-C14	-174.7 (4)	C11-C12-O13-C14	168.4 (5)		
C12-O13-C14-C15	-178.9 (4)	C12-O13-C14-C15	175.3 (4)		
O13-C14-C15-O16	-55.0 (3)	O13-C14-C15-O16	59.5 (4)		
C14-C15-O16-C17	-176.0 (3)	C14-C15-O16-C17	-174.3 (5)		
C15-O16-C17-C18	-169.0 (3)	C15-O16-C17-C18	-172.6 (5)		
O16-C17-C18-O19	-59.2 (3)	O16-C17-C18-O19	-61.3 (5)		
C17-C18-O19-C20	178.5 (3)	C17-C18-O19-C20	-176.8 (6)		
C18-O19-C20-C21	-167.0 (3)	C18-O19-C20-C21	-174.5 (5)		
O19-C20-C21-N1	53.2 (3)	O19-C20-C21-N1	-68.3 (5)		
C20-C21-N1-C2	178.1 (3)	C20-C21-N1-C2	-169.8 (5)		
C21-N1-C2-C3	-177.6 (3)	C21-N1-C2-C3	170.6 (4)		
		O22-C23-C24-N1	78.5 (5)		
		C23-C24-N1-C2	-174.2 (5)		
		C24-N1-C2-C3	173.3 (4)		

^a Estimated standard deviations given in parentheses in units of the least significant digit. ^b 1, *n* = 1: 2,6-pyrido-18-crown-6. 5: 2,6-pyrido-18-crown-6.H₂O.HClO₄ (1:1:1). 6: 2,6-pyrido-18-crown-6.H₂O.HPic (1:1:1). 7: 2,6-pyrido-21-crown-7.H₂O.HClO₄ (1:1:1). 8: 2,6-pyrido-24-crown-8.H₂O.HClO₄ (1:2:1).

2,6-Pyrido-18-crown-6 (1, *n* = 1). ¹H NMR studies have shown that transannular interactions in crown ethers present in the solid state are reflected in the thermodynamic parameters of complex formation in solution.²⁸ Therefore, we have also determined the structure of the "free" 2,6-pyrido-18-crown-6. Figure 4 shows that the molecule has a structure that is rather different from the structure of the polyether in the two forementioned complexes. The macroring adopts a conformation with torsion code *ag⁺g⁺ag⁺g⁺ag⁺g⁺aaa*, yielding an elongated shape with two hydrogens pointing inward, thereby effectively narrowing the cavity. Although this conformation differs from the one adopted by the uncomplexed 18-crown-6 molecule in the crystalline state,²⁹ it has many common features, including two relatively short intramolecular C-H...O contacts (C8...O4 3.00 Å and C17...O13 2.92 Å; see Figure 4), due to the two *g⁺g⁺* "pseudo-corners" in the macroring.³⁰ Furthermore, these two hydrogen atoms point

more or less to other heteroatoms in the ring, but, contrary to uncomplexed 18-crown-6, the distances are too long to denote these contacts as hydrogen bonds (C8...N1 3.87 Å and C17...O10 3.79 Å).

The pyrido moiety is turned outward, the nitrogen atom thereby being situated within the macrocyclic cavity. From the results of the structure determination (and from CPK models), it is clear that the cavity is too small to yield a conformation with the pyrido moiety turned inward,³¹ as displayed by the uncomplexed 2,6-pyrido-24-crown-8 (1, *n* = 3) molecule in the crystalline state.³²

2,6-Pyrido-21-crown-7.H₂O.HClO₄ (1:1:1) (7). From Figure 5, it is revealed that the crown ether molecule in this complex is too large to encapsulate the water molecule optimally. Consequently, the macroring adopts a conformation (torsion code *g⁺g⁺ag⁺ag⁺ag⁺ag⁺aaa*) with part of the ring turned

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Table III. Hydrogen-Bond Parameters^a involving Water of Complexation for the Compounds^b

donor atom: D	acceptor atom: A	distance D...A, Å	distance H...A, Å	angle D-H...A, deg
5				
N1	O22	2.735 (5)	1.78 (5)	165 (4)
O22	O7	2.899 (5)	2.08 (6)	176 (4)
O22	O13	2.838 (5)	1.97 (6)	171 (5)
6				
N1	O22	2.705 (2)	1.84 (2)	170 (2)
O22	O7	2.854 (2)	1.89 (3)	169 (2)
O22	O13	2.883 (2)	2.14 (2)	171 (2)
7				
N1	O25	2.740 (5)	1.63 (4)	167 (3)
O25	O10	2.933 (4)	2.04 (5)	163 (4)
O25	O16	2.865 (4)	1.90 (7)	155 (5)
8				
N1	O28	2.73 (1)	1.78 (7)	173 (5)
O28	O7	2.880 (8)	2.23 (5)	169 (5)
O28	O29	2.90 (1)	2.32 (8)	162 (9)
O29	O13	2.947 (7)	2.20 (6)	174 (5)
O29	O19	2.846 (8)	2.02 (6)	167 (4)

^aSee footnote a of Table II. ^bSee footnote b of Table II.

outward (O4-C5-C6), thereby mimicking the optimal complementary relationship between the water molecule and the 18-membered macroring as displayed by complexes **5** and **6**. The resulting cavity size is, however, slightly larger, and the water molecule is positioned therefore almost at the center of the macroring (distances to the least-squares plane defined by the macroring atoms: +0.18, +0.45, and -0.24 Å for the oxygen and the hydrogen atoms, respectively).

2,6-Pyrido-24-crown-8-H₂O-HClO₄ (1:2:1) (8). The X-ray structure determination of complex **8** reveals that the 24-membered macroring has the optimal size to encapsulate two water molecules (Figure 6). The polyether adopts a highly symmetrical conformation with approximate *D*_{2d} symmetry (neglecting the pyrido moiety): torsion code *ag⁺a ag⁺a ag⁻a ag⁻a ag⁺a ag⁺a ag⁻a ag⁻a*. The conformation found was predicted to be the conformation with the lowest energy out of thousands of different conformations for 24-membered crown ethers.³⁰

Each water molecule is surrounded by six heteroatoms (see Figure 6) in an almost planar arrangement. Therefore, the environment of each water molecule resembles the environment of the guests in the 18-membered water complexes (**5** and **6**), except that the two ether oxygen atoms, which are "shared" by both water molecules (O10 and O22), are located at a larger distance. Also the orientation of the water molecules relative to the least-squares plane of the macroring atoms is quite similar: the water oxygen atoms are both located at 1.21 Å from this plane at the same side, approximately in line with the hydrogen at O28 pointing toward O29 (at 1.26 Å); the remaining hydrogen atoms all point toward the macroring (distances: 0.95, 0.80, and 0.78 Å).

Discussion

Ring Size. The acidity of 2,6-pyridinium crown ethers in a particular solvent strongly depends on the ring size. Differences of 1.3–1.5 p*K*_a units are observed between 18- and 33-membered macrorings in several solvent systems. X-ray studies revealed the complexation of water molecules in the case of ligand **1** (*n* = 1–3). One water molecule fits very well in the cavity of the 18-membered cycle. The 21-membered ring is obviously too large and only a part of the cavity is used to encapsulate the guest. The cavity of 2,6-pyridinium 24-crown-8 is occupied by two water molecules. Since both substituent effects and intraannular hydrogen bonding are unlikely to account for the decreased acidity, we conclude that the degree of macroring-assisted solvation is responsible for the ring size dependent acidity.

Cram and co-workers⁷ have also reported a ring size dependence for the acidity of 2-carboxyl-1,3-xylyl crown ethers, but they were unable to show special solvation effects due to the inaccuracy of

the p*K*_a-determination method used.

Solvent Interactions. For a particular crown ether, the acidity of the protonated species in different solvents varies approximately by 2 p*K*_a units. Such solvent effect is difficult to rationalize because the observed variation in p*K*_a may result from both different solvation energies of the free macrocycles and of the corresponding protonated species. However, we assume that the interactions between solvent molecules and the charged macrocycles will dominate. Therefore, the different p*K*_a values in water, methanol/water, and ethanol/water will reflect mainly the different solvation of the pyridinium moieties.

The 33-membered ring exhibits a remarkable decreased acidity in methanol which, in analogy with the 18-membered macrocycle, can be explained by the formation of a highly structured methanol-crown ether complex.

Hydrogen Bonding between Water and Crown Ethers. The results of the structure determinations for the four complexes between water and 2,6-pyridinium crown ethers demonstrate that the 18-membered macrocycle is best suited to encapsulate one water molecule. Although the cavity is perhaps slightly too small (as may be seen from the positioning of the water molecule above the plane of the macrocycle), it has the right number and types of heteroatoms for a complementary arrangement of donor and acceptor atoms for hydrogen bonding with a water molecule. The larger 21-membered macrocycle is suited to encapsulate one water molecule almost at the center of the cavity, but the optimal arrangement of heteroatoms is absent, which results in a rather asymmetrical conformation of the macroring. The even larger 24-membered macrocycle is too large to accommodate one water molecule optimally. Instead, it encapsulates two water molecules, creating an "18-membered-like" environment for each water molecule.

The two water molecules in the latter complex form an almost linear water dimer (O...O distance, 2.90 (1) Å; O-H...O angle, 162 (9)°; see Table III), which is very similar to the experimental geometry of the water dimer, as obtained by molecular beam electric resonance spectroscopy³³ (O...O distance, 2.98 (1) Å; O-H...O angle, 179 (6)°). Quantum mechanical calculations^{34,35} show that the linear geometry is preferred over other structures, like cyclic or bifurcated ones. However, whereas both the experimental data³³ and the theoretical investigations^{34,35} are indicative of an arrangement of the dimer, in which the planes of the two molecules are at a right angle to each other, the water molecules in complex **8** are virtually coplanar. The extensive ab initio calculations of Clementi and Habitz³⁵ indicate that although the water dimer interaction energy varies considerably with the type of hydrogen bonding and with the O...O distance, it is relatively insensitive to the acceptor orientation. Therefore, we feel that the structure of the water dimer in complex **8** is a rather stable one.

In all four crystalline complexes investigated, each water molecule shows a similar hydrogen-bond pattern, viz. using both of its hydrogens in almost linear hydrogen bonds to surrounding oxygen atoms and receiving a third strongly linear hydrogen bond from the pyrido nitrogen or another water molecule in a direction in the bisecting plane of the first two hydrogen bonds (i.e., the plane containing the two assumed lone pairs). It is therefore tempting to postulate that this third hydrogen bond is directed preferentially toward a lone pair of the water oxygen atom. To verify this, we examined the geometry of the three involved hydrogen atoms and the water oxygen atom by calculating the distances from these four atoms to the least-squares plane defined by these atoms. The results (in order of oxygen atom, hydrogen atoms at the oxygen involved, and the remaining hydrogen atom) are as follows: 0.23, -0.04, -0.11, -0.08 Å (complex **5**); 0.18, -0.03, -0.06, -0.09 Å (complex **6**); 0.01, -0.00, -0.01, -0.00 Å (complex **7**); 0.14, -0.02, -0.07, -0.04 Å (O28 water molecule

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in complex 8); 0.11, -0.02, -0.04, -0.05 Å (O29 water molecule in complex 8). Although the water molecules complexed with the 18- and 24-membered macrocycles show a significant pyramidal hydrogen-bonding pattern, this is certainly not true for the complex with the 21-membered macrocycle, the four atoms almost lying in the same plane. We therefore conclude that the hydrogen bonds using a water oxygen atom as hydrogen-bond acceptor are not preferentially directed toward a lone pair, although there seems to be a preference for the plane containing the lone pairs. This is in agreement with the results of investigations of N-H...O hydrogen bonds between urea-like guest molecules and crown ether oxygen atoms³⁶ and on several types of hydrogen bonds involving alcohol or ether oxygen atoms as the acceptor.³⁷ The pyramidal hydrogen-bond pattern in complexes 5, 6, and 8 is therefore probably due to the smallness of the macrocyclic cavity.

Comparison with Literature. To date, only a few other X-ray structure determinations involving crown ethers encapsulating water molecules are known to us.

In the monoaza-18-crown-6·H₂O·HCl (1:1:1) complex,¹² the macrocycle is protonated at the nitrogen atom and adopts a *D*_{3d} conformation. One amine hydrogen forms a hydrogen bond to the water molecule, which in addition forms two hydrogen bonds to either oxygen atoms of the macrocyclic ring. The complexation is thus very similar as in the complexes between water and 18-membered pyridinium crown ethers.

The cavity in the 3,3'-(2-hydroxy-1,1'-binaphthyl)-21-crown-5·H₂O (1:1) complex³⁸ is too large to encapsulate the guest molecule optimally. Like in the 2,6-pyrido-21-crown-7·H₂O·HClO₄ (1:1:1) complex discussed above, the macrocycle adopts a conformation with part of the ring turned outward. The part of the macrocycle, which is hydrogen-bonded to the guest, again forms a *D*_{3d}-like environment. Beside the two hydrogen bonds to crown ether oxygen atoms, using the water hydrogens, the guest accepts a third hydrogen bond from one of the two phenol groups.

A similar hydrogen-bonding is observed in the solid state of a 1:1 complex between water and a linear analogue of 18-crown-6: bis[*o*-hydroxyphenoxy]ethoxyethane.³⁹ This podand is folded around the guest, creating a *D*_{3d}-like environment. It donates one strong hydrogen bond to the guest from a phenolic end group and accepts two strong hydrogen bonds from the water molecule. The hydrogen bonds thus formed deviate more from linearity than those in the analogous crown ether complexes, giving rise to the formation of additional (weaker) hydrogen bonds to neighboring polyether oxygen atoms (bifurcated hydrogen bonds).

In a 2:1 complex of water with a 2,6-pyrido-18-crown-6 diester⁴⁰ (the ester functions being located at the carbon atoms nearest to the aromatic ring), only one water molecule is bonded to the crown ether molecule with only one hydrogen bond. The pyrido nitrogen atom is not used for hydrogen bonding. This demonstrates the destabilizing effect of the carbonyl groups on water complexation.

Other X-ray determinations of crown ether/water complexes, reported in the literature, either concern structures for which no hydrogen positions were obtained⁴¹ or structures in which the water molecules are strongly coordinated to other atoms or molecules, in addition to hydrogen-bonding with the crown ether.^{42,2b}

To our knowledge, only one X-ray structure determination of a complex involving a 2,6-pyrido-3*n*-crown-*n* type of macrocycle

has been reported, i.e., the structure of the 1:1 complex of 1 (*n* = 1) with *tert*-butylammonium perchlorate.⁴³ The macrocyclic ring in this complex adopts the familiar *D*_{3d} conformation. The -NH₃⁺ group is located above the macrocyclic ring and forms three hydrogen bonds to next-nearest neighbor heteroatoms of the crown ether molecule (*tripod* arrangement). It resembles therefore the complexation of water with the protonated 2,6-pyrido-18-crown-6. The pyrido nitrogen atom in the former complex is used as a hydrogen bond acceptor, demonstrating the same preference for hydrogen bonds of the pyrido nitrogen over ether oxygen atoms as observed in complexes 5-8, although no proton transfer to the nitrogen atom has taken place.

Conformational Flexibility of the Macroring. The structure determinations of the 2,6-pyrido-18-crown-6·H₂O·HClO₄ (1:1:1) and the 2,6-pyrido-18-crown-6·H₂O·HPic (1:1:1) complexes reveal a slightly different conformation of the macrocyclic ring, despite the fact that both macrocycles are connected in a similar way via three short hydrogen bonds to the same guest and do not form strong hydrogen bonds to other molecules (only very weak "hydrogen bonds" are formed with the anions or other crown ether molecules). This shows that the macrocyclic ring in the complexed state still has a reasonable degree of conformational freedom, which may be influenced by anion choice and crystal packing forces. A similar effect was also observed for the 2,6-pyrido-27-crown-9-guanidinium perchlorate (1:1) and the 2,6-pyrido-27-crown-9-guanidinium thiocyanate·EtOH (2:3:1) complexes.³²

The uncomplexed 2,6-pyrido-18-crown-6 molecule, on the contrary, adopts a completely different conformation in the solid state, with an elongated shape, no appreciable cavity, and two heteroatoms pointing outward. The resultant structure resembles the structures of the uncomplexed 18-crown-6²⁹ and diaza-18-crown-6⁴⁴ molecules in the solid state. It is assumed that uncomplexed crown ethers adopt such conformations rather than more symmetrical "round" conformations with a large cavity and all heteroatoms pointing inward, because the resulting negative potential in the cavity destabilizes such conformations unless compensated by attractive interactions between the host and some guest molecule. Moreover, the van der Waals' forces will always disfavor a large "empty hole" in a molecule.

Conclusions

The results described in this paper reveal that accurate *pK*_a determinations are a useful tool for studying host-guest interactions. It represents the first method to search systematically for complexes of macrocyclic cations with neutral molecules. In our case, the encapsulated species are solvent molecules, but in principle, the method can be extended to solutions containing other neutral guest species that may stabilize the protonated form of a macrocyclic host by a specific inclusion.

Experimental Section

Melting points were determined with a Reichert melting point apparatus and are uncorrected. The ¹H NMR and ¹³C NMR spectra were recorded with a Bruker WP-80 and a N.M.C. 1280 spectrometer, respectively, in CDCl₃ with Me₄Si as an internal standard. Mass spectra were obtained with a Varian Mat 311A. Elemental analyses and titrant standardizations were carried out by the Department of Analytical Chemistry under supervision of W. Lengton.

Materials. All 2,6-pyrido crown ethers (1, *n* = 0-6) were synthesized and purified as described elsewhere.³² In addition to the usual spectroscopic techniques and elemental analysis in the case of solid crown ethers, the purities were checked by potentiometric titration (*vide infra*) and in all cases were found to be better than 99%. The commercially available chemicals, needed for preparing the 52.1 wt % methanol/water,⁴⁵ 85.4 wt % ethanol/water,⁴⁵ and methanol buffers,⁴⁶ were purified according to the recommended procedures. In the case of aqueous titrations, Merck

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Table IV. Data-Collection Parameters of the X-ray Structure Determinations

	compound ^a				
	5	6	1, <i>n</i> = 1	7	8
formula	C ₁₅ H ₂₆ O ₁₀ NCl	C ₂₁ H ₂₈ O ₁₃ N ₄	C ₁₅ H ₂₃ O ₅ N	C ₁₇ H ₃₀ O ₁₁ NCl	C ₁₉ H ₃₆ O ₁₃ NCl
lattice type	monoclinic	monoclinic	monoclinic	triclinic	monoclinic
space group	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 1	<i>P</i> 2 ₁ / <i>n</i>
T, K	168	144	166	222	168
cell dimensions					
<i>a</i> , Å	19.638 (9)	12.531 (7)	10.483 (1)	13.239 (9)	22.553 (3)
<i>b</i> , Å	11.858 (11)	9.076 (3)	16.683 (2)	10.751 (3)	13.706 (1)
<i>c</i> , Å	8.134 (3)	21.859 (7)	9.847 (1)	8.210 (3)	8.387 (1)
α , deg	90.0	90.0	90.0	74.61 (3)	90.0
β , deg	95.05 (2)	94.48 (3)	117.37 (2)	99.37 (6)	100.14 (1)
γ , deg	90.0	90.0	90.0	104.73 (3)	90.0
<i>V</i> , Å ³	1886.79	2478.46	1529.34	1083.91	2552.02
<i>Z</i>	4	4	4	2	4
10 ⁻³ <i>D</i> _c , kg m ⁻³	1.468	1.463	1.295	1.413	1.358
radiation (graphite monochromated)	Mo K α	Mo K α	Mo K α	Mo K α	Mo K α
10 ⁻³ μ , m ⁻¹	0.25	0.11	0.09	0.11	0.21
<i>S</i> -range (<i>S</i> = sin θ / λ), Å ⁻¹	0.07–0.59	0.10–0.59	0.10–0.59	0.07–0.48	0.07–0.48
no. of unique reflections measd	3316	4410	2843	3801	2527
no. of reflections used in refinement	2446	2985	2439	1504	1616
final no. of variables	349	456	283	391	452
final <i>R</i> , %	7.4	3.6	3.7	5.3	5.0
final <i>R</i> _w , %	5.5	3.7	3.5	3.5	6.6

^a See footnote *b* of Table II.

buffers were used. Solvents, prepared from doubly distilled water, methanol, and ethanol (both p.a., Merck), were flushed with nitrogen to remove traces of carbon dioxide.

Titants were prepared by mixing a calculated weight of a stock solution with the alcohol. A stock solution of hydrochloric acid was prepared by diluting an ampule (Merck) with water, after which it was standardized. To pure methanol, a calculated weight of perchloric acid (70%, p.a., Merck) was added.

2,6-Bis(methoxymethyl)pyridine (2).¹⁰ A suspension of 1.00 g (0.02 mol) of NaH (50% in oil) and 50 mL of THF was heated to reflux. Methanol (0.64 g, 0.02 mol) was added in 10 min. Subsequently, a solution of 2.65 g (0.01 mol) of 2,6-bis(bromomethyl)pyridine was added. The mixture was refluxed for an additional 15 min. Residual NaH was decomposed by careful addition of H₂O. The solvent was evaporated in vacuo. The residue was dissolved in CHCl₃ (100 mL) and washed with 3 × 50 mL of water. The organic layer was dried over MgSO₄, concentrated in vacuo, and purified by chromatography (silica, CHCl₃) to give an oil: yield 87%; ¹H NMR (CDCl₃) δ 7.8–7.2 (m, 3 H, ArH), 4.57 (s, 4 H, ArCH₂), 3.47 (s, 6 H, OCH₃); ¹³C NMR δ 157.8 (Ar C-2, C-6), 137.1 (Ar C-4), 119.9 (Ar C-3, C-5), 75.4 (ArCH₂), 58.7 (OCH₃); mass spectrum, *m/e* 168.103 (M⁺; calcd 168.102).

2,6-Bis[(2-methoxyethoxy)methyl]pyridine (3). A suspension of 1.20 g (0.025 mol) of NaH (50% in oil) in 100 mL of THF was heated to reflux. Over a period of 15 min, a solution of 1.52 g (0.02 mol) of 2-methoxyethanol in 50 mL of THF was added. Subsequently, a solution of 2.97 g (0.01 mol) of 2,6-bis(bromomethyl)pyridine in 50 mL of THF was added. The mixture was refluxed for 1 h. NaH was decomposed by careful addition of water. The solvent was evaporated, and the residue was dissolved in CHCl₃, washed with 3 × 50 mL of water, dried over MgSO₄, concentrated in vacuo, and purified by chromatography (silica, CHCl₃), to give a pale-yellow oil: yield 90%; ¹H NMR (CDCl₃) δ 7.8–7.3 (m, 3 H, ArH), 4.67 (s, 4 H, ArCH₂), 3.8–3.3 (m, 8 H, OCH₂CH₂O), 3.40 (s, 6 H, OCH₃); ¹³C NMR δ 157.8 (Ar C-2, C-6), 137.1 (Ar C-4), 119.8 (Ar C-3, C-5), 74.0 (ArCH₂), 71.8 (OCH₂), 70.0 (OCH₂), 58.9 (OCH₃); mass spectrum, *m/e* 224.128 (M⁺; calcd 224.129).

pK_a Measurements. Determinations of the pK_a's⁴⁷ were carried out in nitrogen-flushed solvents in a thermostated titration vessel at 25.0 °C by means of a computerized potentiometric titration device. Detailed information on the apparatus used was described elsewhere.⁴⁸ At least 15 relevant data points within 1 pH unit from the pK_a were used for the calculation of the pK_a with an iterative procedure based on the Newton–Raphson algorithm. Between every (fixed) titrant addition, there was a waiting time of at least 45 s in which the pH did not vary more than 0.02 units. Although the concentrations of the titrands were low

(<0.01 mol dm⁻³), activities were used throughout all calculations. After every third run, the glass/silver–silver chloride electrode combination (Metrohm, Type EA121, 6.0203.000) was calibrated. At least three carefully prepared buffer solutions in the relevant pH section were used. The pK_a determinations were performed at least in duplo and generally showed an excellent agreement.

pK_a Data. The pK_a values for 1, 2, and 3 in H₂O were published previously.¹ The pK_a's in MeOH, 52.1 wt % MeOH/H₂O, and 85.4 wt % EtOH/H₂O, respectively are as follows: 6.33, 4.46, 4.08 (1, *n* = 0); 5.98, 4.94, 4.57 (*n* = 1); 5.51, 3.92, 3.62 (*n* = 2); 5.30, 3.72, 3.39 (*n* = 3); 5.07, 3.38, 3.09 (*n* = 4); 4.80, 2.98, 2.95 (*n* = 5); 5.18, 2.65, 3.17 (*n* = 6); 4.08, 2.40, 2.15 (2); 4.38, 2.55, 2.52 (3).

Crystalline Compounds. The compounds used in the X-ray structure determinations were prepared as follows:

2,6-Pyrido-18-crown-6-H₂O-HClO₄ (1:1:1) (5). To a solution of 0.297 g (1 mmol) of 2,6-pyrido-18-crown-6 in 5 mL of EtOH was added 0.13 g of a 70% solution of HClO₄. The product crystallized immediately and was filtered off: yield 53%; mp 86–88 °C (EtOH); ¹H NMR (CDCl₃) δ 8.6–7.8 (m, 6 H, ArH, H₂O, N-H), 4.93 (s, 4 H, ArCH₂), 3.9–3.6 (m, 16 H, CH₂O); ¹³C NMR δ 152.5 (Ar C-2, C-6), 146.6 (Ar C-4), 125.6 (Ar C-3, C-5), 70.5–68.7 (ArCH₂, CH₂O). Anal. Calcd for C₁₅H₂₆NO₁₀Cl: C, 43.33; H, 6.30; N, 3.37. Found: C, 43.50; H, 6.24; N, 3.61.

2,6-Pyrido-18-crown-6-H₂O-Picric Acid (1:1:1) (6). To a solution of 0.297 g (1 mmol) of 2,6-pyrido-18-crown-6 in 5 mL of EtOH was added a solution of 0.229 g (1 mmol) of picric acid in 5 mL of EtOH and a few drops of water. The solvent was allowed to evaporate slowly, to give the product as yellow crystals: yield 55%; mp 93–96 °C (EtOH); ¹H NMR (CDCl₃) δ 8.79 (s, 2 H, Ar'H), 8.5–7.9 (m, 6 H, ArH, H₂O, NH), 4.93 (s, 4 H, ArCH₂), 4.0–3.4 (m, 16 H, CH₂O); ¹³C NMR δ 162.0 (Ar'C-1), 152.9 (Ar C-2, C-6), 146.0 (Ar C-4), 141.9 (Ar' C-2, C-6), 126.5, 125.3 (Ar, Ar' C-3, C-5), 125.5 (Ar' C-4), 70.6, 70.5, 69.9, 69.7, 69.1 (OCH₂). Anal. Calcd for C₂₁H₂₈N₄O₁₃: C, 46.33; H, 5.18; N, 10.29. Found: C, 46.57; H, 5.13; N, 10.22.

2,6-Pyrido-21-crown-7-H₂O-HClO₄ (1:1:1) (7). To a solution of 1 mmol of 2,6-pyrido-21-crown-7 in 3 mL of water was added 0.5 mL of a 20% solution of HClO₄ in water. The solvent was evaporated to give the product as colorless crystals. The product was purified by titration with chloroform: yield 45%; mp 68–72 °C; ¹H NMR (CDCl₃) δ 8.7–7.8 (m, 3 H, ArH), 7.8–7.3 (br s, 3 H, H₂O, HClO₄), 5.08 (s, 4 H, ArCH₂), 4.0–3.6 (m, 20 H, CH₂O); ¹³C NMR δ 154.2 (Ar C-2, C-6), 144.8 (Ar C-4), 123.9 (Ar C-3, C-5), 70.9–69.3 (ArCH₂, CH₂O). No satisfactory elemental analysis could be obtained due to loss of H₂O. Anal. Calcd for C₁₇H₃₀NO₁₁Cl: C, 44.40; H, 6.58; N, 3.04. Found: C, 44.95; H, 6.88; N, 3.01.

2,6-Pyrido-24-crown-8-H₂O-HClO₄ (1:2:1) (8). To a solution of 1 mmol of 2,6-pyrido-24-crown-8 in 3 mL of water was added 0.5 mL of a 20% solution of HClO₄ in water. The solvent was evaporated to give the product as colorless crystals. The product was purified by titration with chloroform: yield 35%; mp 39–47 °C; ¹H NMR (CDCl₃) δ 8.7–7.9 (m, 3 H, ArH), 5.8 (br s, 5 H, H₂O, HClO₄), 5.08 (s, 4 H, ArCH₂),

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4.1-3.6 (m, 24 H, CH₂O), ¹³C NMR δ 153.6 (Ar C-2, C-6), 146.8 (Ar C-4), 124.4 (Ar C-3, C-5), 70.6-68.5 (ArCH₂, CH₂O). No satisfactory elemental analysis could be obtained due to loss of H₂O. Anal. Calcd for C₁₉H₃₆NO₁₃Cl: C, 43.72; H, 6.95; N, 2.68. Found: C, 43.51; H, 6.40; N, 2.27.

X-ray Diffraction. X-ray measurements were performed on a single-crystal diffractometer (Philips PW1100) using the ω-2θ scanning mode. The most important data-collection parameters are presented in Table IV. Measured intensities were corrected for the decrease in intensity during data collection, using the intensities of three standard reflections measured every hour.

The structures were solved by direct methods⁴⁹ and refined by full-matrix least-squares analysis,⁵⁰ using reflections having an intensity larger than some threshold value ($\sigma(I)$ for uncomplexed 2,6-pyrido-18-crown-6 (1, $n = 1$) and for its complex with perchloric acid and water (5) and $3\sigma(I)$ for the other three water complexes (6-8), $\sigma(I)$ being the estimated standard deviation from counting statistics). All hydrogen atoms in the complexes could unambiguously be located from difference-Fourier maps.

Parameters refined were the overall scale factors, isotropic secondary extinction parameters, positional parameters of all atoms, anisotropic thermal parameters for non-hydrogen atoms, and isotropic thermal parameters for hydrogens. The weight for each reflection was taken to be $w = \{\sigma(F_o) + 0.01|F_o|\}^{-2}$, where $\sigma(F_o)$ is the estimated standard deviation of the observed structure factor (F_o) derived from counting statistics. Scattering factors for non-hydrogen atoms were taken from "International Tables for X-ray Crystallography";⁵¹ for H, the scattering factors of Stewart et al.⁵² were used. No absorption corrections were applied.

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For the crystalline 2,6-pyrido-21-crown-7·H₂O·HClO₄ (1:1:1) complex, a second modification exists at lower temperature (transition temperature 216 ± 2 K). The structure of this complex at 193 K was also solved by using X-ray diffraction.⁵³ The low-temperature modification has a doubled unit cell (with two independent moieties of the compound in the asymmetric unit). The two perchlorate anions in the asymmetric unit have a markedly different orientation. The two independent crown ether-water entities are related by approximate translation symmetry and hardly differ in structure. They also have the same conformation as the higher-temperature modification 7 discussed above.

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Registry No. 1 ($n = 0$), 99747-84-9; 1 ($n = 1$), 64726-19-8; 1 ($n = 2$), 99747-85-0; 1 ($n = 3$), 99747-86-1; 1 ($n = 4$), 99747-87-2; 1 ($n = 5$), 99764-92-8; 1 ($n = 6$), 99747-88-3; 2, 64726-18-7; 3, 99747-89-4; 5, 95731-92-3; 6, 99747-91-8; 7, 99747-92-9; 8, 99747-93-0; 2,6-bis(bromomethyl)pyridine, 7703-74-4.

Supplementary Material Available: Lists of anisotropic thermal parameters for heavy atoms and isotropic thermal parameters for hydrogens and positional parameters for all atoms as well as complete lists of bond lengths, bond angles, and torsional angles (46 pages). Ordering information is given on any current masthead page.

(53) Relevant data-collection parameters of the lower-temperature modification of the crystalline 2,6-pyrido-21-crown-7·H₂O·HClO₄ (1:1:1) complex are as follows: lattice type: triclinic; space group *P*1; $T = 193$ K. Cell dimensions: $a = 15.073$ (4) Å, $b = 14.729$ (3) Å, $c = 11.593$ (3) Å, $\alpha = 114.41$ (1)°, $\beta = 74.07$ (2)°, $\gamma = 111.61$ (2)°; $V = 2156.12$ Å³; $Z = 4$; $D_c = 1.420 \times 10^3$ kg m⁻³; Mo K α radiation; $\mu = 0.11 \times 10^3$ m⁻¹. S -range: 0.10-0.48 Å⁻¹; 7575 reflections measured, of which 3378 with $I > 3\sigma(I)$ were used in the refinement; 780 final variables. Final R and R_w : 3.3 and 3.5%, respectively.

Efficient Catalytic Cleavage of Reactive Phosphates by an *o*-Iodosobenzoate Functionalized Surfactant

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Abstract: 5-(*N*-(*n*-Hexadecyl)-*N,N*-dimethyl-*N*-(β -ethoxy)ammonium)-2-iodosobenzoate, **1c**, cleaved *p*-nitrophenyl diphenyl phosphate (PNPDPP), *p*-nitrophenyl diethyl phosphate (PNPDEP), and *p*-nitrophenyl isobutyl methylphosphonate (PNPIMP) in aqueous cetyltrimethylammonium chloride (CTACl) at pH 8 and 25 °C. With 4×10^{-5} M **1c** in 2×10^{-4} M CTACl, second-order cleavage rate constants (L/(M-s)) were PNPDP, 28 500, PNPDEP, 0.865, and PNPIMP, 215. These represented kinetic advantages of 14 700, 43 600 and 846, respectively, over nonfunctional CTACl-catalyzed cleavages of the substrates. In the presence of excess PNPDP at pH 8, catalyst **1c**/CTACl "turned over" with $k \sim 0.17$ s⁻¹ for the hydrolysis of the putative **1c**-diphenyl phosphate intermediate.

An efficient method of cleavage of reactive phosphates is needed for the decontamination of areas affected by these toxic compounds.¹ The problem has been under attack for more than a decade, with micellar and other aggregated reagents a focus of attention.² Particularly in the pioneering work of Bunton and

his associates, many functional groups have been surveyed for their reactivity toward phosphates, including hydroxide and phenoxide,³ peroxide and hydroperoxide,⁴ fluoride ion,⁵ imidazole and benz-

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