J. Org. Chem. 1991, *56*, 673-677

Hydrolysis of Crown Ether Acetals. Effects of Ring Size and Cation Binding

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Received March 29, 1990

Rates of acid-catalyzed hydrolysis of 8–23-membered ring benzaldehyde, acetophenone, and benzophenone crown ether acetals **2**, **3**, and **4** in 60% dioxane–water (v/v) are dependent upon the ring size as well as the type of acetal. For **2**, rates strongly decrease for the 17-, 20-, and 23-membered rings in the presence of Na^+, Rb^+, and Cs^+, respectively, as well as for the 20-membered ring in the presence of ammonium chloride. Hydrolysis of the 14-membered ring is only slightly influenced by addition of these ions. These retarding effects are appreciably reduced for the series **3** and **4**. These results are explained by a combination of steric effects and selective cation binding by the crown ethers.

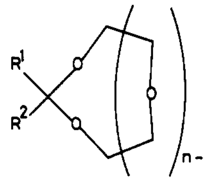
Introduction

Crown ether acetals that contain one or more dioxymethylene units, $-(OCR^1R^2O)-$, in the crown rings are interesting compounds because they should exhibit the properties of both crown ethers[1] and acetals.[1b,2] However, these macrocyclic polyethers have received little attention in contrast to the extensive studies of other crown ethers.[3] Presumably, this is due to a lack of general and useful syntheses for such macrocyclic compounds.[4] Recently, we have found a new redox reaction that provides variously substituted crown ether acetals.[5] These compounds undergo acid-catalyzed hydrolysis, and we have investigated the effects of ring size and substituents on their hydrolysis.[2b]

The cation complexing properties of crown ether acetals have been reported by Gold and Sghibartz who found retardation by added alkali and alkaline earth metal chlorides on the HCl-catalyzed hydrolysis of a series of 2-methyl-substituted crown ether acetals **1**.[1b,2a] We report an extended investigation of the effects of ring size and added metal cations on the hydrolysis of a series of 2-phenyl-, 2-methyl-2-phenyl-, and 2,2-diphenyl-substituted crown ether acetals **2**, **3**, and **4**.

Results and Discussion

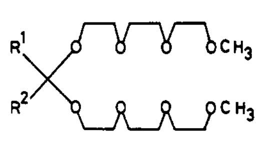
Effects of Ring Size. According to the commonly accepted A-1 mechanism for hydrolysis of simple acetals,[6] the acid-catalyzed hydrolysis of crown ether acetals is expected to proceed through the reaction sequence involving a preequilibrium protonation of the substrate (S), a rate-determining unimolecular decomposition of the resulting conjugated acid (SH^+) to an oxocarbenium ion, and subsequent multistep degradation into the carbonyl compound and oligoethylene glycol with addition of water.



(1-4)a-f

	R^1	R^2
1:	CH_3	H
2:	Ph	H
3:	Ph	CH_3
4:	Ph	Ph

	n
a:	2
b:	3
c:	4
d:	5
e:	6
f:	7



5-7

	R^1	R^2
5:	Ph	H
6:	Ph	CH_3
7:	Ph	Ph

We first studied ring-size effects by using 2-phenyl-, 2-methyl-2-phenyl-, and 2,2-diphenyl-substituted 8–23-membered ring crown ether acetals **2**, **3**, and **4**. HCl-catalyzed hydrolysis was carried out in 60% dioxane–water (v/v) at 30 °C. The second-order rate constants (k_2) are collected in Table I, and log k_2 are plotted against the number (n) of oxyethylene units in Figure 1. Hydrolysis rates are dependent upon the ring size and type of acetal. The most reactive acetophenone crown ether acetals **3** hydrolyze 4–26 and 250–780 times faster than the corresponding benzaldehyde and benzophenone crown ether acetals **2** and **4**, respectively. The substituent effects, which were also found in the hydrolysis of acyclic dimethyl acetals,[2c] can be interpreted in terms of the inductive, resonance, and steric contributions of the substituents on a positively charged transition state.[7]

With respect to ring-size effects, the rates of benzaldehyde crown ether acetals **2** increase with increasing n, reaching a maximum rate at $n = 4$ (14-membered ring), and decrease with further increase of n (Figure 1). This rate profile is almost the same as that of Gold's 2-methyl-substituted acetals **1**,[1b] despite the large difference in reactivity between the two series of acetals. However, replacement of the hydrogen at position 2 of benzaldehyde acetals **2** by a methyl group changes the rate profile, shifting the maximum rate to the 17-membered acetal **3d** and effecting a rate reversal between 11- and 14-membered

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Table I. Second-Order Rate Constants (k_2) for HCl-Catalyzed Hydrolysis of Crown Ether Acetals 2, 3, and 4 in 60% Dioxane–Water (v/v) at 30 °C

	$10k_2/\mathrm{dm^3\ mol^{-1}\ s^{-1}}$					
acetal	$n = 2$	3	4	5	6	7
2	29.8	76.8	148	88.5	68.2	41.7
3	126	990	868	2290	1160	701
4	0.494	2.20	1.54	3.84	1.84	0.887

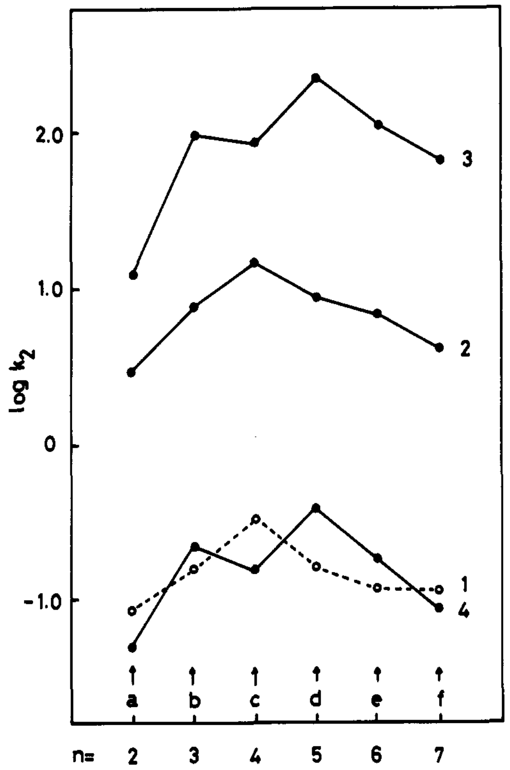
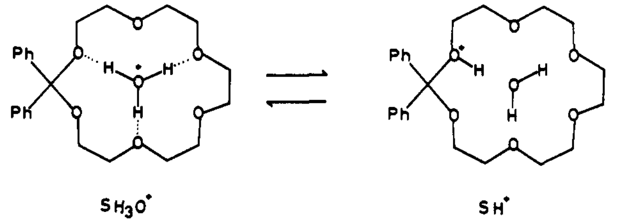


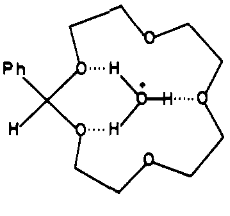
Figure 1. Plots of log k_2 vs ring size of crown ether acetals 1–4. Values of k_2 for acetals 1 were taken from ref 1b (at 25 °C) and those for acetals 2–4 were measured at 30 °C.

ring acetals. The rate profile for acetophenone acetals with the additional small peak at the 11-membered ring is essentially superimposable on that for benzophenone acetals **4**. The actual hydrolysis rates of **4**, however, are reduced by 2.4–2.9 log units because of steric effects. A similar dependence of rate on ring size of **4** has already been found in a more dioxane-rich (80%) medium.[2b] The maximum rate for 17-membered ring **4d** is not ascribed to ring strain because the flexible polyether linkage will release such strain.

We previously attributed the peak rate for 17-membered ring **4d** to formation of a three-hydrogen-bonded complex (SH_3O^+) with a hydronium ion on the basis of the activation parameters of these hydrolyses.[2b] Such a hydronium ion complexed acetal, which may be in rapid equilibrium with the conjugated acid form (SH^+), should enhance the rate by stabilizing the transition state (TS), in light of the close structural resemblance between SH^+ and TS.[6a,c] The reduction of rate in the smaller and larger ring size acetals was therefore accounted for by poor template fit with H_3O^+. Indeed, similar tripod arrangements due to ion–hydrogen bonding have been proposed for the complexation of hydronium ion by 18-crown-6[8] and reported for the crystal structure of hydronium ion complexed with a tetracarboxylic 18-crown-6 ligand.[9]



If the incorporation of hydronium ion is also the reason for the maximum rate for both series of acetaldehyde and benzaldehyde acetals, the one oxyethylene unit shorter 14-membered rings of these monosubstituted acetals should interact more strongly with H_3O^+ than the 17-membered ring acetals. Furthermore, the substituents of the crown ether acetals may exert appreciable steric effects upon their complexation with H_3O^+, as in the usual crown ethers.[8g] We suggest that the possible complex of monosubstituted 14-membered acetals has a triply hydrogen bonded structure ($S'H_3O^+$) constructed by bonding to both the oxygen atoms of acetal function and to the opposite ring oxygen. Molecular models show that the orientations of the sp^3 hybrid lone pairs of acetal oxygen atoms are suitably directed for the formation of a quasi six-membered ring structure. Disubstitution at the acetal carbon atom is likely to disturb such a specific interaction of the acetal function by steric effects and thereby, as the second-best preferable complexation manner, would lead to hydrogen bonding with three alternate oxygens, as formulated for 17-membered **4d**.



$S'H_3O^+$

Another noticeable feature in the rate profiles is the humps for the disubstituted 11-membered ring acetals **3b** and **4b**. Although we have no appropriate explanation for this phenomenon, the enhancement of reactivity may be related to strain in this medium-size ring, which will be strengthened by introduction of substituents. An alternative is a 2:1 sandwich complex (two crown ether acetal molecules and one hydronium ion); 12-crown-4, which contains the same oxygen atoms as the 11-membered acetal, forms a similar complex with $(H_3O^+)(PF_6^-)$ in CH_2Cl_2–Et_2O.[8b] However, this speculation does not explain why monosubstituted 11-membered ring acetals **1b** and **2b** show no indication of 2:1 complexation with hydronium ion. This is presumably a result of increased hydrophilic properties of monosubstituted acetals, so that 2:1 complexes, even if formed in less polar solvent, would tend to more easily dissociate in the present aqueous dioxane than those formed from less hydrophilic disubstituted acetals.

Effects of Cation Binding. Gold et al. explained the retarding effects of alkali and alkaline earth metal chlorides on the hydrolysis of 1 by the basicity-lowering electrostatic influence of the bound metal ion, by which the metal

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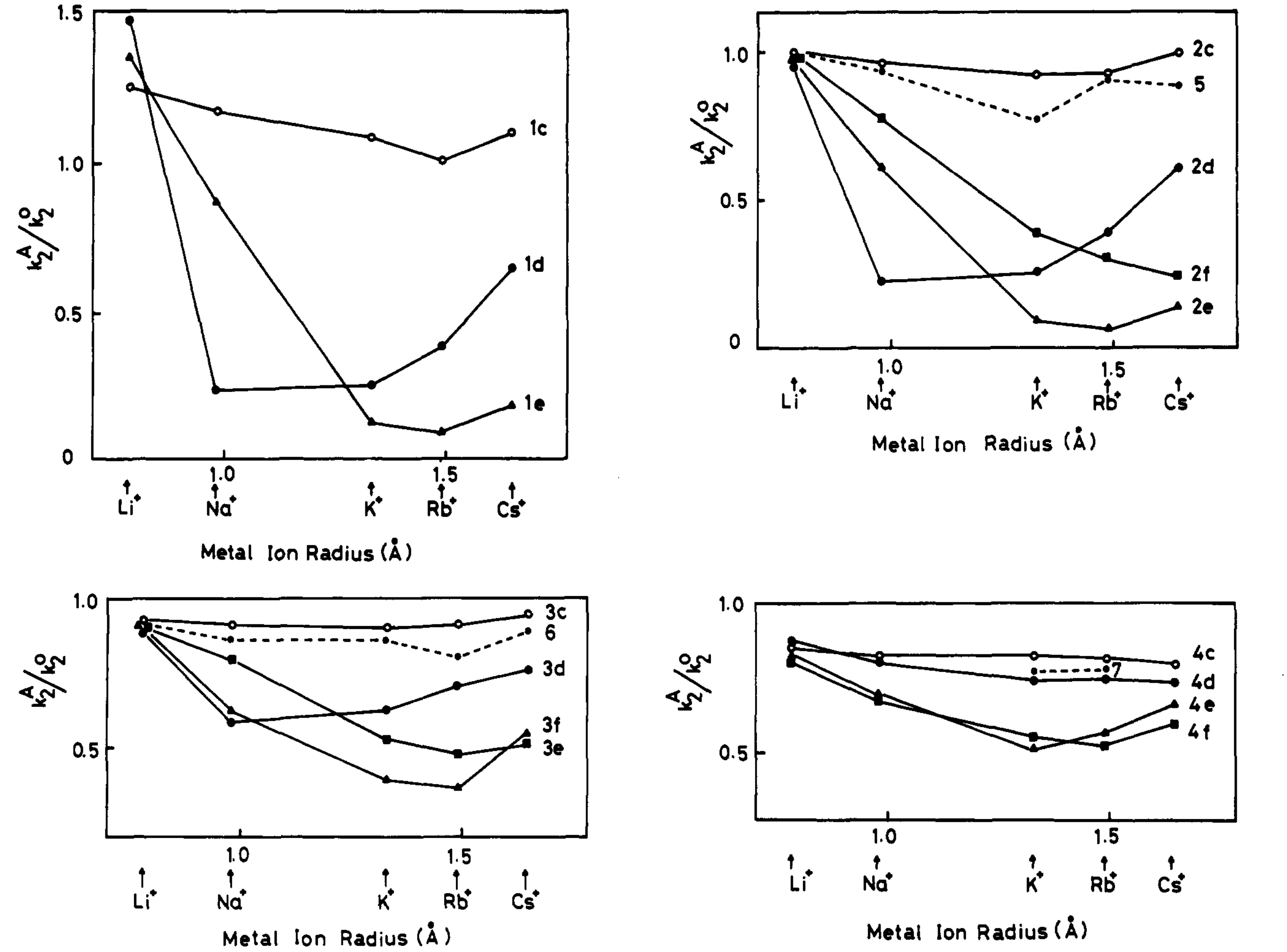

Figure 2. (a) Effects of alkali metal ions on hydrolysis of acetals 1. Plots of k_2^A/k_2^0 vs ion radius. (b) Effects of alkali metal ions on hydrolysis of acetals 2 and 5. Plots of k_2^A/k_2^0 vs ion radius. (c) Effects of alkali metal ions on hydrolysis of acetals 3 and 6: Plots of k_2^A/k_2^0 vs ion radius. (d) Effects of alkali metal ions on hydrolysis of acetals 4 and 7: Plots of k_2^A/k_2^0 vs ion radius.

complexed acetal (SM^{m+}) would be protonated in the first preequilibrium step of hydrolysis[6] to much smaller extent than is the free acetal (S).[1b]

We have extended this hydrolysis study to substituted crown ether acetals 2–4 and to analogous acyclic acetals 5–7. We have chosen 14–23-membered ring acetals, since the smaller ring acetals would not be expected to exhibit such a cation binding.[1b] We used the same concentration (0.25 M) of added alkali metal chlorides and ammonium chloride and the same solvent composition (60% dioxane–water v/v) as those in the previous study.[1b] In general, the initial concentrations of our acetals were <0.01 those of the added salts to permit simple first-order kinetic treatment.

In Figure 2, parts a–d, the effects of alkali metal cations on this hydrolysis are shown by the plots of k_2^A/k_2^0 vs the corresponding cation sizes for each series of acetals together with the results for acetaldehyde acetals. In these plots, k_2^A and k_2^0 are the second-order rate constants for the hydrolysis in the presence or absence of the additives, respectively. The numerical values of k_2^A/k_2^0 are given in the Appendix. As shown in Figure 2, parts a and b, 14–20-membered acetaldehyde and benzaldehyde crown ether acetals have similarly shaped plots, except that, for the former, LiCl-promoted hydrolysis and the 14-membered acetal underwent rate enhancement in the presence of alkali metal chlorides. The increase in rate has been attributed to an electrolyte effect[2a] from the high concentration of alkali metal chlorides (0.25 M). However, we observed rate retardation for each of our 14-membered ring acetals, which was amplified by the increasing bulk of the acetal substituents. Thus 14-membered benzaldehyde acetal **2c** showed little complexing ability toward metal cations probably because of its small ring size. However, introduction of one oxyethylene unit into the crown ring brought about an abrupt reduction of rate for Na^+, though the rates were again raised with increasing cation sizes,[10] $K^+ < Rb^+ < Cs^+$. This effect of Na^+ in 17-membered acetal **2d** became less important for the next 20-membered ring acetal **2e**, but the larger three metal cations caused the most significant drop in rate, giving a shallow valley at Rb^+. For the last 23-membered acetal **2f**, the effects of cations were considerably reduced and the largest, Cs^+, became a bottom cation. Analogous acyclic acetal **5** showed only little cation-selective rate retardation for K^+, despite its containing eight oxygen atoms equal to a 23-membered ring acetal. These findings indicate that complexation of metal cations by acetals having a suitable ring size for guest cations is important for rate retardation of hydrolysis.

Replacement of the hydrogen of acetal **2** by a methyl group resulted in noticeable weakening of the affinity for metal cations as seen in Figure 2c. The 17-membered acetal **3d** apparently became a poor host molecule for cations larger than Li^+. Similarly, the effect of K^+, Rb^+, and Cs^+ on the hydrolysis of 20- and 23-membered acetals **3e** and **3f** was diminished compared to the benzaldehyde

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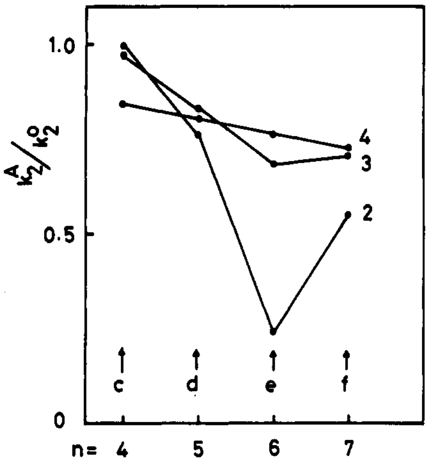

Figure 3. Effects of ammonium ion on hydrolysis of acetals **2**–**4c**–**f**: Plots of k_2^A/k_2^0 vs ring size.

acetals. Although Cs^+ was the most effective cation for the 23-membered benzaldehyde acetal **2f**, Rb^+ was most effective for the corresponding acetophenone acetal **3f**. The plot for acyclic acetal **6** tracked that for the 14-membered acetal **3c** except for a slight downward deviation at Rb^+.

Substitution of two phenyl groups produced further reductions in the contribution of cations to hydrolysis rate as typically represented in the case of 17-membered ring benzophenone acetal **4d**, which gave a monotonic line, as did the 14-membered ring acetal (Figure 2d). Moreover, most of the k_2^A/k_2^0 values of 20-membered acetal **4e** increased to those of 23-membered ring acetal **4f**, accompanied by reversal for the large cations ($Rb^+ \rightarrow K^+$), compared to the corresponding benzaldehyde and acetophenone acetals. The plot for acyclic acetal **7** was located between those of the 14- and 17-membered acetals and showed no indication of cation complexing.

Corresponding experiments with ammonium chloride instead of alkali metal chlorides also revealed rate reduction, especially for benzaldehyde acetals, as found in the plots of k_2^A/k_2^0 vs ring size for each series of acetals (Figure 3). The values of k_2^A/k_2^0 are given in the Appendix. The distinct reduction in rate for 20-membered benzaldehyde acetal **2e** disappeared on replacement of the hydrogen atom at the 2-position by a methyl or phenyl group. The rate retardation may be ascribed to multiple $NH^+\cdots O$ hydrogen bonding between NH_4^+ and the acetal rings in view of the fact that similar host–guest interaction due to ion–hydrogen bonds is well documented for the complexes of ammonium and alkylammonium ions with usual crown ethers.[11] This observation rules out the possibility that complexed NH_4^+ might itself serve as a catalyst like H_3O^+ and thus lead to a rate enhancement. It has been reported that NH_4^+ is bound most strongly by 18-crown-6 among the series of crown ethers ranging from 12-crown-4 to 24-crown-8.[11d] However, the present results indicate that selective binding was attained rather in the 20-membered benzaldehyde acetal with one additional ring oxygen atom. This shift to larger ring size, which is contrast to H_3O^+ mentioned above, seems to be accounted for by larger size of NH_4^+. In fact, X-ray crystallographic analysis shows that pyramidal H_3O^+ is anchored deeper into the cavity of the 18-crown-6 ring than the larger tetrahedral NH_4^+.[9,12]

Table II. Alkali Metal Ion Selectivity for Crown Ether Acetals 2–4c–f and Crown Ethers

	crown ether acetal[a]			
	2	3	4	crown ether[b]
c: 14-crown-5	–	–	–	15-crown-5, K^+
d: 17-crown-6	Na^+	Na^+	–	18-crown-6, K^+
e: 20-crown-7	Rb^+	Rb^+	K^+	21-crown-7, Cs^+
f: 23-crown-8	Cs^+	Rb^+	Rb^+	24-crown-8, Cs^+

[a] Pedersen's abbreviated nomenclature was adopted for the ring moieties of crown ether acetals. [b] Taken from refs 11a and 13.

In Table II are listed cations that selectively cause rate retardation in the hydrolysis of 14–23-membered **2**, **3**, and **4**, together with the cations that selectively bind to 15-crown-5 to 24-crown-8.[11a,13] Our crown ether acetals have a tendency to complex with rather smaller cations than do the corresponding crown ethers with same numbers of ring oxygen atoms. Thus 14-membered crown acetals are all poor ligands for the cations studied here in contrast to 15-crown-5, which preferentially binds K^+. Strong complexation of K^+ is well known for 18-crown-6,[11a,13] but the 17-membered acetals **2d** and **3d** exhibit selectivity for the smaller Na^+. Furthermore, such a selective binding disappeared in diphenyl-substituted acetal **4d** because of the large steric interference. Both 21-crown-7 and 24-crown-8 show selectivity for Cs^+,[11a] whereas, except for 23-membered benzaldehyde acetal **2f**, other 21- and 23-membered acetals selectively bind the smaller cations Rb^+ or K^+. Apparently, these results are in harmony with the prevalent theory[14] that correspondence of ring cavity to cation size,[15] as well as steric effects of ring substituents, are important for the stabilities of complexes.

Experimental Section

IR, NMR, and mass spectra were taken on Perkin-Elmer 983G, Varian EM 390, and Hitachi RMU 6E spectrometers, respectively.

Materials. Dioxane was dried over sodium and distilled. Water was deionized through an ion exchange resin (Millipore Milli-RO 40). All alkali metal chlorides and ammonium chloride were extra pure and were used without further purification. New crown ether acetals **2a**,**b**,**d**–**f** and **3b**,**d**–**f** and open chain analogues **5** and **6** were prepared by the previously reported procedure and were identified by IR, NMR, mass spectra, and elemental analyses (all other acetals **2c**, **3a**,**c**, **4a**–**f**, and **7** are described elsewhere).[2b,5a,5b]

2-Phenyl-1,3,6-trioxacyclooctane (2a): colorless oil; 20% yield; IR (film) 2918, 1141, 1057, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.7–4.1 (m, 8 H, OCH_2CH_2), 5.70 (s, 1 H, methine), 7.2–7.6 (m, 5 H, Ph); MS *m/e* 194 (M^+). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.85; H, 7.15.

2-Phenyl-1,3,6,9-tetraoxacycloundecane (2b): colorless oil; 13% yield; IR (film) 2866, 1122, 1070, 704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.5–3.8 (m, 12 H, OCH_2CH_2), 5.57 (s, 1 H, methine), 7.1–7.5 (m, 5 H, Ph); MS *m/e* 238 (M^+). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.35; H, 7.81.

2-Phenyl-1,3,6,9,12,15-hexaoxacycloheptadecane (2d): colorless oil; 6.5% yield; IR (film) 2870, 1350, 1105, 704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.67 and 3.72 (s + s, 20 H, OCH_2CH_2), 5.68 (s, 1 H, methine), 7.2–7.6 (m, 5 H, Ph); MS *m/e* 326 (M^+). Anal.

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[15] Recently, Gokel et al. have shown that the hole–size relationship fails to explain cation selectivity in flexible macrocycles and lariat ethers; see: *J. Am. Chem. Soc.* **1982**, *104*, 625; **1983**, *105*, 6786; **1985**, *107*, 6659; **1986**, *108*, 4078.

Calcd for $C_{17}H_{26}O_6$: C, 62.56; H, 8.03. Found: C, 62.56; H, 7.97.

2-Phenyl-1,3,6,9,12,15,18-heptaoxacycloeicosane (2e): colorless oil; 7.2% yield; IR (film) 2870, 1351, 1110, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.62 and 3.67 (s + s, 24 H, OCH_2CH_2), 5.58 (s, 1 H, methine), 7.1–7.5 (m, 5 H, Ph); MS *m/e* 370 (M^+). Anal. Calcd for $C_{19}H_{30}O_7$: C, 61.60; H, 8.16. Found: C, 61.65; H, 8.07.

2-Phenyl-1,3,6,9,12,15,18,21-octaoxacyclotricosane (2f): colorless oil; 5.7% yield; IR (film) 2871, 1351, 1107, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.67 and 3.70 (s + s, 28 H, OCH_2CH_2), 5.67 (s, 1 H, methine), 7.2–7.6 (m, 5 H, Ph); MS *m/e* 414 (M^+). Anal. Calcd for $C_{21}H_{34}O_8$: C, 60.85; H, 8.27. Found: C, 61.04; H, 8.23.

2-Methyl-2-phenyl-1,3,6,9-tetraoxacycloundecane (3b): mp 76–77 °C; colorless prisms (from hexane); 15% yield; IR (KBr) 2864, 1299, 1128, 949, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.62 (s, 3 H, CH_3), 3.57 (s, 4 H, OCH_2CH_2), 3.67 (s, 8 H, OCH_2CH_2), 7.2–7.7 (m, 5 H, Ph); MS *m/e* 252 (M^+). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.56; H, 8.01. Found: C, 66.64; H, 7.99.

2-Methyl-2-phenyl-1,3,6,9,12,15-hexaoxacycloheptadecane (3d): colorless oil; 4.3% yield; IR (film) 2870, 1270, 1127, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.55 (s, 3 H, CH_3), 3.5–3.8 (m, 20 H, OCH_2CH_2), 7.2–7.7 (m, 5 H, Ph); MS *m/e* 340 (M^+). Anal. Calcd for $C_{18}H_{28}O_6$: C, 63.51; H, 8.29. Found: C, 63.36; H, 8.30.

2-Methyl-2-phenyl-1,3,6,9,12,15,18-heptaoxacycloeicosane (3e): colorless oil; 3.7% yield; IR (film) 2873, 1269, 1122, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 3 H, CH_3), 3.4–3.8 (m, 24 H, OCH_2CH_2), 7.2–7.6 (m, 5 H, Ph); MS *m/e* 384 (M^+). Anal. Calcd for $C_{29}H_{32}O_7$: C, 62.48; H, 8.39. Found: C, 62.58; H, 8.31.

2-Methyl-2-phenyl-1,3,6,9,12,15,18,21-octaoxacyclotricosane (3f): colorless oil; 3.1% yield; IR (film) 2871, 1269, 1121, 956, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 3 H, CH_3), 3.4–3.8 (m, 28 H, OCH_2CH_2), 7.2–7.7 (m, 5 H, Ph); MS *m/e* 428 (M^+). Anal. Calcd for $C_{22}H_{36}O_8$: C, 61.66; H, 8.47. Found: C, 61.42; H, 8.40.

Benzaldehyde bis(3,6,9-trioxadecyl) acetal (5): colorless oil; 18% yield; IR (film) 2874, 1451, 1109, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.33 (s, 6 H, OCH_3), 3.4–3.7 (m, 24 H, OCH_2CH_2), 5.60 (s, 1 H, methine), 7.2–7.6 (m, 5 H, Ph); MS *m/e* 253 ($M^+ - (OCH_2CH_2)_3OCH_3$). Anal. Calcd for $C_{21}H_{36}O_8$: C, 60.55; H, 8.71. Found: C, 60.24; H, 8.57.

Acetophenone bis(3,6,9-trioxadecyl) acetal (6): colorless oil; 19% yield; IR (film) 2877, 1448, 1110, 704 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.55 (s, 3 H, CH_3), 3.33 (s, 6 H, OCH_3), 3.4–3.7 (m, 24 H, OCH_2CH_2), 7.2–7.7 (m, 5 H, Ph); MS *m/e* 267 ($M^+ - (OCH_2CH_2)_3OCH_3$). Anal. Calcd for $C_{22}H_{38}O_8$: C, 61.37; H, 8.90. Found: C, 61.03; H, 8.87.

Kinetic Measurements. The rates of hydrolysis of crown ether acetals, the initial concentrations of which were controlled below 2.5×10^{-3} mol/dm^3, were measured in 60% dioxane–water (v/v) at HCl concentrations of 5.0×10^{-4} mol/dm^3 for benzaldehyde acetals **2a–f** and **5** and acetophenone acetals **3a–f** and **6** and of 5.0×10^{-3} mol/dm^3 for benzophenone acetals **4a–f** and **7**. The reaction mixtures for kinetic runs were prepared by quickly mixing in a cuvette an appropriate volume of crown ether acetal in dioxane and a requisite volume of aqueous hydrochloric acid with or without a given amount of alkali metal or ammonium chloride. Both the acetal and hydrochloric acid solutions were preheated in the cuvettes at 30 ± 0.1 °C through a constant-temperature cell holder by circulating water from a Haake Model FE constant-temperature circulating bath. The reactions were monitored spectrophotometrically (JASCO UVIDEC 505) by following the absorption (A) of carbonyl products up to 75% completion at 290 nm (ϵ = 1160 in 60% dioxane–water) for **2a–f** and **5**, at 300 nm (ϵ = 167) for **3a–f** and **6**, and at 332 nm (ϵ = 164) for **4a–f** and **7**. Infinity points (A_∞) were taken at more than 10 half-lives. The k_{obsd} values were obtained from the slopes of plots of $\ln [A_\infty - A_t]$ vs time. The second-order rate constants (k_2) were taken by dividing k_{obsd} by the activity of H^+ as described previously.[2c]

Appendix. Effects of Alkali Metal and Ammonium Ions on Hydrolysis of Crown Ether Acetals and Analogous Open Chain Acetals in 60% Dioxane–Water (v/v) at 30 °C[a]

	k_2^A/k_2^0					
acetal	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+
2c	1.00	0.95	0.92	0.93	0.99	0.99
2d	0.95	0.23	0.26	0.39	0.61	0.76
2e	0.98	0.61	0.095	0.066	0.14	0.24
2f	0.99	0.78	0.39	0.31	0.25	0.55
3c	0.92	0.91	0.90	0.91	0.94	0.97
3d	0.89	0.59	0.62	0.70	0.76	0.83
3e	0.91	0.63	0.39	0.37	0.53	0.68
3f	0.91	0.80	0.53	0.48	0.53	0.71
4c	0.85	0.82	0.82	0.82	0.80	0.84
4d	0.86	0.80	0.74	0.75	0.74	0.80
4e	0.83	0.69	0.51	0.56	0.66	0.76
4f	0.80	0.68	0.55	0.52	0.60	0.72
5[b]	1.00	0.93	0.77	0.90	0.88	0.97
6[b]	0.89	0.87	0.86	0.80	0.89	0.92
7[b]	–	–	0.77	0.79	–	0.83

[a] Values of k_2^0 for acetal **2–4** are equal to values of k_2 in Table I.
[b] Values of k_2^0 for acetals **5**, **6**, and **7** are 2.10, 38.7, and 0.0884 dm^3 mol^{-1} s^{-1}, respectively.