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The Ionic Hydrogen Bond. 2. Intramolecular and Partial Bonds. Protonation of Polyethers, Crown Ethers, and Diketones

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Abstract: Intramolecular hydrogen bonding in protonated di-, tri-, and tetraethers, as well as cyclic crown ethers, increases the proton affinities of these compounds vs. comparable monoethers. The enthalpy of the intramolecular hydrogen bond (ΔH°_{HB}) ranges from −7 kcal mol^{-1} in $CH_3O(CH_2)_2OCH_3H^+$ to −25 kcal mol^{-1} in $CH_3(OCH_2)_3OCH_3H^+$ and −20 kcal mol^{-1} in (18-crown-6)H^+. Intramolecular hydrogen bonding also results in significantly negative entropies of protonation (ΔS°_{HB}) from −4 cal mol^{-1} K^{-1} in $CH_3O(CH_2)_2OCH_3H^+$ to −18 cal mol^{-1} K^{-1} in $CH_3(OCH_2CH_2)_3OCH_3H^+$. Small values of ΔH°_{HB} and ΔS°_{HB} in $CH_3O(CH_2)_2OCH_3H^+$, $CH_3COCH_2COCH_3H^+$, and $CH_3COCH_2CH_2COCH_3H^+$ suggest that only a partial hydrogen bond is formed in these ions. Thus, due to the stretched $OH^+\cdots O$ bond and small bond angle, here the "hydrogen bond" may amount only to the electrostatic stabilization of the cis conformation, and rotation about the C–C bond is still allowed, although the barrier is increased by $-\Delta H^\circ_{HB}$. In the larger ions more favorable geometry allows the formation of increasingly optimal hydrogen bonds. Thermochemistry suggests that in $CH_3(OCH_2CH_2)_2OCH_3H^+$ the proton is localized on a terminal $-OCH_3$ group, and hydrogen bonding forms a large ring. Proton shift to the central oxygen atom would be favorable in entropy terms ($\Delta S^\circ_{shift} = 9.5$ cal mol^{-1} K^{-1}), but unfavorable in terms of enthalpy ($\Delta H^\circ_{shift} = 20$ kcal mol^{-1}). In the protonated tetraether $CH_3(OCH_2CH_2)_3OCH_3H^+$ the proton can be stabilized both by location on a central oxygen and formation of a large ring, resulting in the high PA of the tetraether. The stability of the internal hydrogen bond decreases in the order diamines > diethers > diketones. The following are some proton affinities and entropies of protonation (PA, kcal mol^{-1}; ΔS°_{prot}, cal mol^{-1} K^{-1}): $CH_3O(CH_2)_2OCH_3$, 204.7, −4.3; $CH_3O(CH_2)_3OCH_3$, 213.8, −6.0; $CH_3(OCH_2CH_2)_2CH_3$, 218.9, −13.8; $CH_3(OCH_2CH_2)_3OCH_3$, 226.0, −18.6; 12-crown-4, 219.6, −3.2; 18-crown-6, 220.6, −5; $CH_3COCOCH_3$, 194.9, −2.6; $CH_3COCH_2COCH_3$, 207.7, −3.6; $CH_3COCH_2CH_2COCH_3$, 212.4, −7.0; cyclohexanone, 204.0, 0; 1,3-cyclohexanedione, 211.0, 1.4.

A common structural feature of complex organic molecules is the presence of multiple functional groups capable of hydrogen bonding. In such polyfunctional ions a protonated group may interact with an unprotonated group to form an intramolecular hydrogen bond. The intramolecular hydrogen bond then stabilizes the ion, and thereby increases the proton affinity (PA) of the molecule.[1,2] Thus, intramolecular hydrogen bonding stabilizes the protonated ion by up to 20 kcal mol^{-1} in several diamines, triamines, and amino alcohols.[2,3] Similar effects may occur in protonated halogenated amines and diketones.[4]

The formation of intramolecular hydrogen bonds creates constrained structures in the protonated polyfunctional ions. As a result, negative entropy changes up to −20 cal mol^{-1} K^{-1} were observed upon protonation.[2]

Intramolecular hydrogen bonding should be prevalent in polyfunctional ions in the gas phase, and also in protonated polyfunctional macromolecules such as proteins. Nevertheless, the ΔH and ΔS effects of intramolecular hydrogen bonds are available only for ten ions, all but one polyfunctional amines.[2,3] It is clearly desirable that the relationship between molecular structure and the thermochemical effects of intramolecular hydrogen bonding should be further explored.

Polyethers and crown ethers are well known as polydentate complexing agents for inorganic and organic cations. In the present work we shall examine the interaction of polyethers and crown ethers with the smallest cation, i.e., H^+. The effects of interactions between the multiple ether groups in these protonated ions will provide further insight into structure–energy relationships in intramolecular hydrogen bonding. For comparison, several diketones will also be studied.

Experimental Section

The measurements were done on the NBS pulsed high-pressure mass spectrometer. Mixtures of 0.01–1% of ethers and amines in cyclohexane were injected to a heated bulb, and the vapor was allowed to flow into the mass spectrometer ion source. The reaction mixture was ionized by 1000–2000-μs pulses of 500–1000-V electrons. Ion intensities were observed to 1000–2000 μs after the ionizing pulse. The transfer reactions (eq 1) and/or association reactions (eq 2) were observed; also (3) and

$$BH^+ + \text{ether} \rightleftarrows \text{ether}H^+ + B \tag{1}$$

$$BH^+ + \text{ether} \rightleftarrows \text{ether}H^+\cdot B \tag{2}$$

$$BH^+ + B \rightleftarrows BH^+\cdot B \tag{3}$$

$$\text{ether}H^+ + \text{ether} \rightleftarrows \text{ether}H^+\cdot\text{ether} \tag{4}$$

$$\text{ether}H^+ \rightarrow \text{fragment}^+ + N \tag{5}$$

$$\text{fragment}^+ + \text{ether} \rightarrow \text{ether}H^+ + \text{fragment} \tag{6}$$

(4) reached equilibrium during the observed reaction time. At high temperatures, the reaction system is complicated by the pyrolysis reactions (eq 5) and the reaction of the pyrolysis product ions to regenerate the protonated molecular ion (eq 6).

Ion-source temperatures of 420–700 K and pressures of 0.15–1.0 torr were used. Checks were made to ensure that the equilibrium constants were independent of pressure and mixture composition. Conditions were selected to keep cluster ions to less than 50% of total ion intensity to minimize problems resulting from dissociation outside the ion source. To minimize errors due to ion pyrolysis, we avoided conditions where the pyrolysis product amounted to more than 20% of the total ion current.

The chemicals were purchased from commercial sources at stated purities of 98% or higher and used as purchased. A sample of 1,3-dimethoxypropane was donated by Dr. T. Morton. The structures of the compounds used as summarized in Chart I.

Proton Affinities and Entropies of Protonation of Polyethers and Crown Ethers

Proton transfer equilibria (eq 1) between reference compounds and ethers III–XIII were measured as a function of temperature. van't Hoff plots (Figure 1) yield the ΔH and ΔS values shown in Table I. PAs of a given ether, derived from measurements vs. several reference compounds, usually agree within ±1 kcal mol^{-1} and ΔS values within ±2 cal mol^{-1} K^{-1}. The structural changes associated with protonation of the reference compounds should be negligible, except for changes in rotational symmetry. The entropy changes therefore reflect the effects of structural

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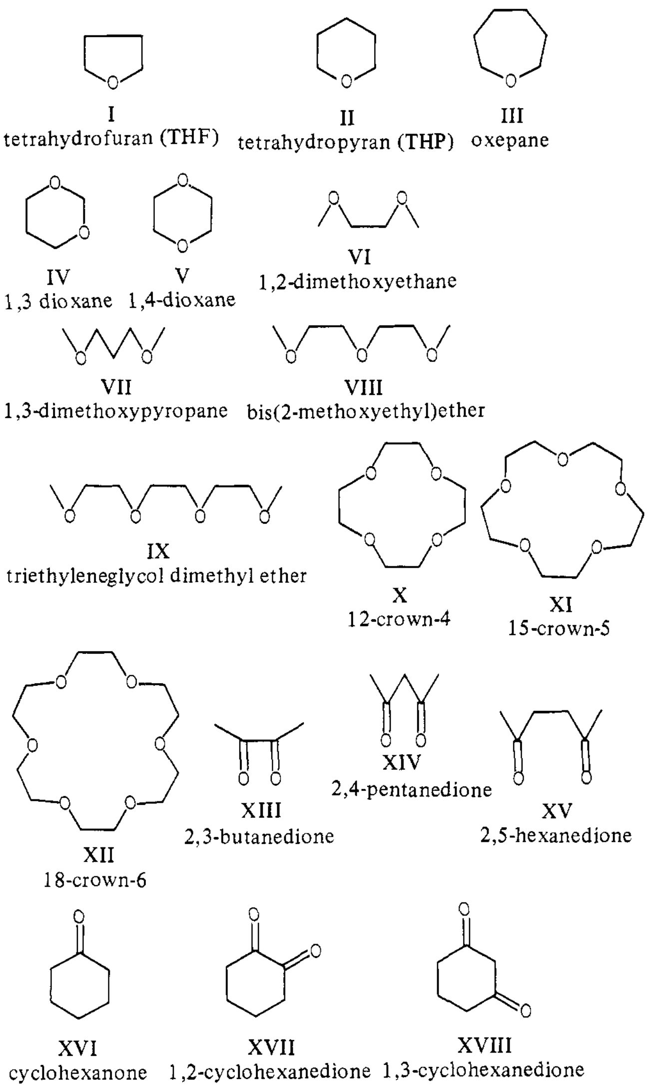
[1] Aue, D. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1973**, *95*, 2699.

[2] Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1973**, *95*, 3504.

[3] Meot-Ner (Mautner), M.; Hamlet, R.; Hunter, E. P.; Field, F. H. *J. Am. Chem. Soc.* **1980**, *102*, 6393.

[4] Aue, D. H.; Bowers, M. T. "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, p 18.

Chart I. The Structures of Molecules Measured in This Work and Some Related Compounds



changes on entropies of protonation of the polyethers.

The temperature ranges of proton-transfer measurements were limited by the decomposition reactions (eq 5) on the upper end and by the clustering reactions (eq 3) on the lower side. In general, the clustering reactions (eq 4) are not significant, except for dimethoxyethane. The absence of clustering of the protonated polyethers results from the fact that intramolecular solvation of the protonated function blocks hydrogen bonding to other molecules. However, the higher polyethers bond strongly to all of the reference ammonium and pyridinium ions. This problem, and increased fragmentation of the larger compounds at high temperatures, limited the range of proton-transfer-equilibrium measurements causing the larger error limits quoted for some compounds. For the largest crown ethers the temperature range of strong clustering and pyrolysis overlap. For this reason we could not perform temperature studies on proton-transfer equilibria of 15-crown-5 and 18-crown-6. Fortunately, these are cyclic compounds and therefore no significant structural entropy changes are expected upon protonation, as is indeed seen in 12-crown-4. In the larger crown ethers we therefore assume that ΔS protonation is similar to but slightly more negative than that for 12-crown-4 and calculate the PA of 15-crown-5 and 18-crown-6 from proton-transfer equilibria at one temperature.

The Contributions of Intramolecular Interactions

In the following discussion, we shall estimate the thermochemistry of the internal hydrogen bond by comparisons between polyfunctional and analogous monofunctional ions. Before proceeding, it should be emphasized that these methods only measure the effects of multiple functional groups in an operational sense, and do not prove that there are indeed hydrogen bonding effects.

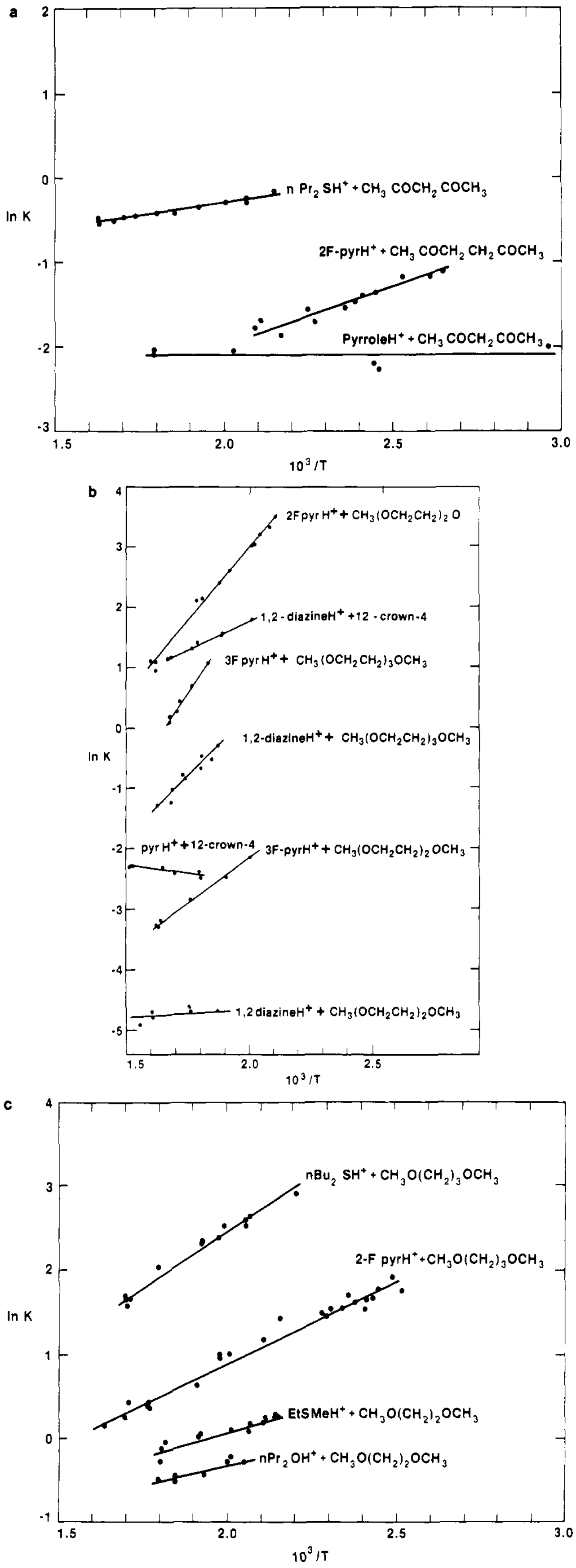


Figure 1. (a–c) van't Hoff plots for proton-transfer reactions ($B_1H^+ + B_2 \rightleftarrows B_2H^+ + B_1$) for reactant pairs B_1H^+ and B as indicated.

Table I. Thermochemistry[a] of Proton-Transfer Equilibria, $B_1H^+ + B_2 \rightleftarrows B_2H^+ + B_1$

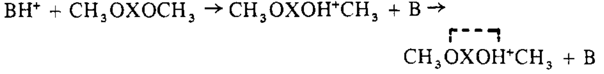
B_1	B_2	$\Delta H°$	$\Delta S°$ [b]	$\Delta G°_{600}$	$PA(B_1)$[c]	$PA(B_2)$	$PA(B_2)$	$\Delta S°_{prot}(B_2)$[b]
THF (I)	oxepane (III)	−2.7	(0)	−2.7	198.9	201.6	202.0	(1.4)
THP (II)		−1.9	(0)	−1.9	199.8	201.7		
EtSMe		0.5	(1.4)	−0.3	203.1	202.6		
THF (I)	1,3-dioxane (IV)	+0.2	(0)	+0.2	199.2	199.0	198.8	(1.4)
Et_2O		+1.4	(0)	+1.4	200.0	198.6		
n-Pr_2O	$CH_3OCH_2CH_2OCH_3$ (VI)	−2.2	−5.0		202.3	204.5	204.7	−4.3
EtSMe		−1.8	−3.6		203.1	204.9		
n-Bu_2S	$CH_3OCH_2CH_2CH_2OCH_3$ (VII)	−5.2	−5.4		208.4	213.6	213.8	−6.0
2-F-pyridine		−3.6	−5.5		210.7	214.3		
3-F-pyridine		+0.8	−7.0		214.2	213.4		
2-F-pyridine	$CH_3(OCH_2CH_2)_2OCH_3$ (VIII)	−8.5	−13.2		210.7	219.2	218.9	−13.8
3-F-pyridine		−5.7	−15.7		214.2	219.9		
1,2-diazine		−1.4	−11.7		216.2	217.6		
3-F-pyridine	$CH_3(OCH_2CH_2)_3OCH_3$ (IX)	−12.2	−20.2		214.2	226.6	226.0	−18.6
1,2-diazine		−9.1	−17.7		216.2	225.3		
1,2-diazine	12-crown-4 (X)	−3.3	−3.1		216.2	219.5	219.6	−3.2
pyridine		+1.2	−2.6		220.8	219.6		
1,2-diazine	15-crown-5 (XI)	−4.2	(−4)	−1.8	216.2	220.4	220.9[d]	
pyridine		−0.5	(−4)	+1.9	220.8	221.3		
1,2-diazine	18-crown-6 (XII)[d]	−3.9	(−5)	−0.9	216.2	220.1	220.6[d]	
pyridine		−0.3	(−5)	+2.7	220.8	221.1		
Me_2CO	$CH_3COCOCH_3$ (XIII)	+1.8	−2.6	+1.6	196.7	194.9	194.9[d]	−2.6
n-Pr_2S	$CH_3COCH_2COCH_3$ (XIV)	−1.2	−3.0		206.6	207.8	207.7	−3.6
pyrrole		+0.1	−4.1		207.6	207.5		
pyrrole	$CH_3COCH_2CH_2COCH_3$ (XV)	−3.9	−5.6		207.6	211.5	212.4	−7.0
2-F-pyridine		−2.6	−8.5		210.7	213.3		
Et_2CO	cyclohexanone (XVI)	−2.5	(0)	−2.5	201.4	203.9	204.0	(0)
EtSMe		−1.0	(0)	−1.0	203.1	204.1		(0)
EtSMe	1,2-cyclohexanedione (XVII)	−1.7	(1.4)	−2.5	203.1	204.8	203.8	(1.4)
n-Pr_2S		−3.8	(0)	−3.8	206.6	202.8		(1.4)
pyrrole	1,3-cyclohexanedione (XVIII)	−2.7	(1.4)	−3.4	207.6	210.3	211.0	(1.4)
2-F-pyridine		−1.0	(1.4)	−1.8	210.7	211.7		(1.4)

[a] ΔH and ΔG and PA values in kcal mol^{-1} (=4.8 kJ mol^{-1}); ΔS in cal mol^{-1} K^{-1} (=4.18 J mol^{-1} K^{-1}). Error estimates from standard deviation of van't Hoff plots, and from agreement between $PA(B_2)$ values determined vs. different bases B_1: ±1 kcal mol^{-1}, ±2 cal mol^{-1} K^{-1}. [b] ΔS protonation defined as the entropy of proton transfer to B_2 from a reference compound B_1, where all entropy terms associated with the formation of the B_1-H^+ and B_2-H^+ cancel, except entropy terms due to overall molecular geometry changes and changes in rotational symmetry numbers (σ). ΔS terms in parentheses are estimated value or values calculated from $\Delta S = R \ln \sigma(B_1H^+)\sigma(B_2)/\sigma(B_2H^+)\sigma(B_1)$. [c] $PA(B_1)$ from ref 5. n-Bu_2S estimated. [d] Because of low volatility of experimental problems, error limits in $\Delta G°$ (proton transfer) ≈ ±2 kcal mol^{-1}.

For example, the increased PAs of polyethers may correlate with the decreased IPs of these compounds, the latter due to through-space oxygen–oxygen orbital interactions. The use of "intramolecular hydrogen bonding" in this work should therefore be interpreted only in the aforesaid operational sense. Nevertheless, we feel that "intramolecular hydrogen bonding" probably corresponds to actual physical $-OH^+\cdots O$ interactions. This is indicated for example by the fact that these internal bonds block the formation of hydrogen-bonded clusters. With these reservations in mind, we shall analyze the experimental data to obtain the enthalpy and entropy contributions of the intramolecular hydrogen bond, i.e., $\Delta H°_{HB}$ and $\Delta S°_{HB}$.

The experimental data show that the PAs of the polyethers range up to 220 kcal mol^{-1}, substantially higher than the largest monoethers such as dipentyl ether (PA = 205 kcal mol^{-1}).[5] Also, the structural entropies of protonation are significantly negative, up to −18 cal mol^{-1} K^{-1} in IX. We shall now examine the intramolecular interactions that are responsible for these values.

In order to identify the thermochemistry of the internal bond, we may *conceptually*[6] break down the protonation process to two steps (reaction 7).[2,3] Step 7a leads to a protonated polyether



$$\mathrm{BH^+ + CH_3OXOCH_3 \xrightarrow{a} CH_3OXOH^+CH_3 + B \xrightarrow{b} CH_3OXOH^+CH_3 + B} \quad (7)$$

without the intramolecular hydrogen bond.[7] Step 7b constitutes the formation of the intramolecular hydrogen bond. Evidently, $\Delta H°_{\text{proton transfer}} = \Delta H°_a + \Delta H°_b = \Delta H°_a + \Delta H°_{HB}$. We measure $\Delta H°_{\text{proton transfer}}$, and we must estimate $\Delta H°_{7a}$ to find $\Delta H°_{HB}$, i.e., the enthalpy of the intramolecular hydrogen bond.

To estimate $\Delta H°_{7a}$, we equate the PAs of the "open" form of polyethers with PAs of monoethers of a comparable polarizability. (Intramolecular ion–dipole interactions are considered part of the hydrogen bonding effect.) Thus, we use the PA of $CH_3OCH_2CH_2CH_3$, i.e., 198 kcal mol^{-1}, as the model [5,8] for the PA of a terminal $CH_3OCH_2CH_2-$ function in a polyether. Similarly, for the central $-CH_2CH_2OCH_2CH_2-$ functions in polyethers and crown ethers, we use the PA of di-n-propyl ether, i.e., 202 kcal mol^{-1}, as a model. In the absence of sufficient data, we do not make corrections for possible non-hydrogen bonding interactions between the oxygen functions.[9] We therefore use eq 8 to calculate $-\Delta H°_{7b} = \Delta H°_{HB}$ for the terminal ether functions[8] in compounds VI–IX and eq 9 for the central functions in VIII–XII.

$$\Delta H°_{HB} = \text{PA(ether)} - 198 \text{ kcal mol}^{-1} \quad (8)$$

$$\Delta H°_{HB} = \text{PA(ether)} - 202 \text{ kcal mol}^{-1} \quad (9)$$

With respect to the ring compounds, we also note by comparing THF (I), THP (II), and oxepane (III) that the PA does not vary significantly with ring size (Table I).

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(5) Proton affinities of all reference compounds from NBS tabulation of proton affinity data (S. G. Lias, private communication). On this scale, $PA(NH_3)$ = 204.9 kcal mol^{-1}.

(6) The two-step mechanism (eq 7) is purely a conceptual tool for thermochemical calculations. Indeed, the formation of the internal hydrogen bond affects the reaction kinetics and therefore it must occur concertedly with proton transfer within the reaction complex (ref 3).

(7) Benson, S. W. "Thermochemical Kinetics"; 2nd ed.; Wiley-Interscience: New York, 1976.

(8) Estimated from the PA of $CH_3OCH_2CH_3$ and the variation of PAs within homologous amine and ether series (ref 6).

(9) A question to this point arises because the PA of 1,4-dioxane (compound V Chart I), where through-bond interactions between the oxygen functions are possible, is lower than the PA of THP (II) by 6 kcal mol^{-1}. To check if this phenomenon is general, we measured the PA of 1,3-dioxane (IV) and found it to be similar to that of THF. Therefore, we conclude that special factors operate in 1,4-dioxane: destabilizing ion–dipole orientation or the increased IP due to degeneracy splitting may be responsible. In fact, however, the dipole orientations in the sterically allowed conformations of $CH_3OCH_2CH_2OCH_2$ are significantly different from those of 1,2-dioxane. In the absence of further data, we cannot apply corrections for through-bond oxygen–oxygen interactions.

Table II. Thermochemical Parameters[a] Related to Intramolecular Hydrogen Bonding

	$-\Delta H^\circ_{HB}$[b]	$-\Delta S^\circ_{HB}$[c]	T_{op},[d] K	ΔH_{BWF}[e]	$-\Delta S^\circ_{HB}/n$[f]
$CH_3COCH_2CH_2COCH_3$ (XV)	6	7.0	860	24	2.3
$CH_3OCH_2CH_2OCH_3$ (VI)	7	4.3	1600	23	1.4
$CH_3OCH_2CH_2CH_2OCH_3$ (VII)	16	6.0	2700	14	1.5
$CH_3(OCH_2CH_2)_2OCH_3$ (VIII)	22	13.8	1600	8	2.3
$CH_3(OCH_2CH_2)_3OCH_3$ (IX)	24	18.6	1300	6	3.1
12-crown-4 (X)	18			12	
15-crown-5 (XI)	19			11	
18-crown-6 (XII)	19			11	
$NH_2CH_2CH_2NH_2$[3]	6.7	8.0	840	17	2.7
$NH_2CH_2CH_2CH_2NH_2$[3]	14.2	14.7	970	9	3.7
$NH_2CH_2CH_2CH_2CH_2NH_2$[3]	17.9	17.1	1100	5	3.4
$HOCH_2CH_2CH_2NH_2$[3]	8.8	11.9	740	8	3.0
$HOCH_2CH_2CH_2CH_2NH_2$[3]	13.7	16.9	810	3	3.4

[a] ΔH in cal mol^{-1} (=4.18 kJ mol^{-1}); ΔS in cal mol^{-1} K^{-1} (=4.18 J K^{-1} mol^{-1}). [b] Calculated from eq 8 and 9. [c] $\Delta S_{HB} = \Delta S_{prot}$ (see Table II). [d] Calculated from eq 10. [e] Calculated from eq 11. [f] n = number of single bonds incorporated into hydrogen-bonded structure (see text). [g] From ref 3.

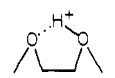
As we noted, ΔS°_{HB}, the entropy change associated with the formation of the internal bond in reaction 7b, is measured by the overall ΔS° of the proton-transfer reaction (except corrections for $\Delta S^\circ_{rot\,sym}$). To evaluate the overall thermal stability of the hydrogen bond, we can define T_{op}, the temperature where the ion population is equally divided between the "bonded" and "open"[10] forms. At T_{op}, $K_{7b} = 1$, i.e., $\Delta G^\circ_{7b} = \Delta H^\circ_{HB} - T_{op}\Delta S^\circ_{HB} = 0$, and therefore

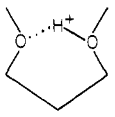
$$T_{op} = \Delta H^\circ_{HB}/\Delta S^\circ_{HB} \qquad (10)$$

The high values of T_{op} (Table II) show that at any temperature where the protonated polyethers are stable against pyrolysis, they will exist in the hydrogen-bonded form.[10]

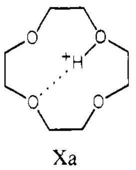
While the internal hydrogen bond is stable, its enthalpy in most cases falls substantially short of the strength of the strong hydrogen bonds observed in dimer ions, $R_2OH^+\cdots OR_2$, where $\Delta H^\circ_{HB} = 30 \pm 2$ kcal mol^{-1}.[13] The intramolecular bond is attenuated due to several bond-weakening factors (BWF):

(a) Unfavorable Geometry. Molecular models show that the $O–H^+\cdots O$ bond angle θ_{HB} is seriously distorted from the optimal 180°, especially in the smaller diethers VI and VII. In VIa, $\theta_{HB} \approx 120°$, and the proton on OH^+, which carries a higher partial positive charge, is removed by ≈1 Å from the van der Waals surface of the other, unprotonated oxygen atom. In VIIa the larger ring permits optimal approach to the $OH^+\cdots O$ distance, but θ_{HB} is still distorted to ≈150°.


VIa


VIIa

However, in the larger ions such as protonated VII and IX, the flexibility of the large ring permits optimal geometry if protonation is on the terminal $-OCH_3$ groups. Optimal hydrogen bonding geometry is available even in the crown ethers, if the interaction is between non-adjacent oxygens such as in Xa. We note that the formation of the internally bonded structure in Xa requires some tightening of the loose 12-membered ring, as evidence by the −3 kcal mol^{-1} K^{-1} structural entropy of protonation.


Xa

(b) Polarization. The protonation of one ether function will alter the charge densities on other ether functions, possibly localizing a fraction of the positive charge on these functions. Partial positive charge on an unprotonated oxygen will then decrease its ability to serve as a lone-pair donor for hydrogen bonding.

(c) Ring Strain. The strain associated with small rings in covalently bonded systems, such as cyclobutane and cyclopentane, is substantial. Similar strain may destabilize the quasi-four-member ring in VIa, and the quasi-five-member ring in VIIa.

The overall bond weakening factor ΔH°_{BWF} can be calculated by comparing the intramolecular hydrogen bond strength ΔH°_{HB} with that of intermolecular dimers such as $(CH_3)_2OH^+\cdot O(CH_3)_2$, where the dissociation energy of the hydrogen bond is 30 ± 2 kcal mol^{-1}. We then find the overall intramolecular bond weakening factor ΔH°_{BWF} (Table II) from (11).

$$\Delta H^\circ_{BWF} = 30 + \Delta H^\circ_{HB} \qquad (11)$$

The unfavorable geometry factors, polarization, and ring strain should be most severe in the smallest ring and decrease with increasing ring size. Indeed, ΔH°_{HB} is especially small in $CH_3OCH_2CH_2OCH_3H^+$, where the charge-donor positive center and the electron-donor negative center are kept separated by the σ-bond skeleton. In this ion, ΔH°_{HB} achieves only 23% of its optimal strength. However, even in VII where optimal distance and in VIII andd X where overall optimal geometry is possible ΔH°_{HB} still reaches only 53%, 73%, and 60% of its optimal value, respectively. Evidently, polarization and strain factors must be significant. Only in the largest ion, IX, does ΔH°_{HB} approach the optimal intermolecular bond strength.

Partial Hydrogen Bonding

The values of ΔH°_{HB} and ΔH°_{BWF} (Table II) show that the strength of the intramolecular bond falls far short of a fully developed intermolecular bond, especially in the smaller compounds. Entropy effects also indicate the formation of only partial intramolecular bonding in the small ions. To quantify the entropy factor, we can compare the present ions with cycloalkanes, where, of course, a fully covalent ring exists. From the entropies of formation of alkanes and cycloalkanes we calculate the entropy of cyclization of C_3–C_8 alkanes per C–C bond that is transformed from an acyclic to a cyclic skeleton. This entropy, given by $\Delta S^\circ_{cyc}/n = [\Delta S_f{}^\circ{}_{298}(c\text{-}C_nH_{2n}) - \Delta S_f{}^\circ{}_{298}(n\text{-}C_nH_{2n+2})]/n$, is constant from C_3 to C_8 alkanes,[2] at $\Delta S^\circ_{cyc} = -2.8 \pm 0.2$ cal mol^{-1} K^{-1}. Interestingly, similar numbers are obtained for ΔS°_{HB} in cyclic structures formed in $NH_2(CH_2)_3NH_3^+$, $NH_2(CH_2)_4NH_3^+$, and $HO(CH_2)_3NH_3^+$. Here $\Delta S^\circ_{HB}/n = -3.7$, -3.4, and -3.0 cal mol^{-1} K^{-1}, respectively (where n is the number of single C–C, C–O, and C–N bonds transformed from an acyclic to a cyclic chain). In contrast, $\Delta S^\circ_{HB}/n$ as listed in Table II is only −1.4 and −1.5 for VI and VII and, even in the large ion vIII, short of the values of −2.8 to −3.1 cal mol^{-1} K^{-1} found in fully formed rings.

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(10) More precisely, the "bonded" or "cyclic" form means the conformation where the stabilizing intramolecular interaction is maximized; the "open" form means the large number of conformations where this interaction is negligible.

(11) Very recent calculations by R. Houriet et al. show that in $H_2NCH_2CH_2NH_3^+$ and $HOCH_2CH_2NH_3^+$ libration to ±30° about the X–C–C–X dihedral angle of 0° has negligible barrier. However, the barrier to a full 180° rotation is 21 kcal mol^{-1} (Houriet, R.; Rufenacht, H.; Carrupt, P. A.; Vogel, P.; Tichy, M. *J. Am. Chem. Soc.*, in press).

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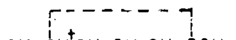
From these observations we conclude that only a partial hydrogen bond is formed in the small protonated polyethers. Similarly, the small entropy changes, in diketones (see below), as well as in the protonated diamine $NH_2CH_2CH_2NH_3^+$, are not consistent with a structure fixed in a "cyclic conformation". Rather, the "cyclic conformation" in these ions may constitute only an energy well with a depth $\Delta H°_{HB}$. The energy barrier to rotation about the C–C bonds away from the most stable conformation will be increased by $\Delta H°_{HB}$. Thus, due to this factor, the energy barrier to rotation about the C–C bond increases from an ethane-like barrier of 3 kcal mol^{-1} in the neutral molecule [7] to about 3 + 7 = 10 kcal mol^{-1} in the protonated ion. This change will decrease the entropies of rotation of the $-CH_2OCH_3$ groups about the C–C bond. The expected magnitude of the change of rotational entropy of the hindered rotor due to the increased barrier[7] is ≈ -3 cal mol^{-1} K^{-1}, close to the experimental value of $\Delta S°_{HB} = -4.3$ cal mol^{-1} K^{-1}. Alternatively, the motion about the C–C bond may be a wide, low-frequency libration.[11]

In the larger ions, an increasing ring size permits a full hydrogen bond to develop, and the magnitude of $\Delta H°_{HB}$ and thus the barrier to rotation away from the hydrogen bonded form increases. The increased rigidity is reflected in the larger $\Delta S°_{HB}/n$ found in VIII and IX.

Intramolecular Bonding in Oxygen vs. Nitrogen Bases

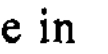
The $-OH^+\cdots O-$ hydrogen bond is stronger than the $-NH^+\cdots N$ bond. Thus, the dimer ions $R_2OH^+\cdots OR_2$ are typically bonded[13] by 30 ± 2 kcal mol^{-1}, while $R_3NH^+\cdots NR_3$ clusters are bonded[2,12] by 23 ± 2 kcal mol^{-1}. By analogy, we expected that intramolecular hydrogen bonding in oxygen compounds would be more efficient than that in nitrogen analogues. However, the experimental results show that $\Delta H°_{HB}$ for protonated diamines and diethers of comparable size is similar in magnitude. Looking at it another way, the bond weakening factor $\Delta H°_{BWF}$ in $CH_3O(CH_2)_2OCH_3H^+$, 23 kcal mol^{-1}, is somewhat larger than that in $NH_2(CH_2)_2NH_3^+$, 17 kcal mol^{-1}, and that in $CH_3O(CH_2)_3OCH_3H^+$, 14 kcal mol^{-1}, is larger than that in $NH_2(CH_2)_3NH_3^+$, 9 kcal mol^{-1}. Also, $-\Delta S°_{HB}/n$ is smaller in diethers and diketones than in diamines of comparable size (Table II).

Since the geometries of the protonated diamines and diethers of the same size are comparable, the geometry and strain factors must be similar. Therefore, other bond weakening factors, such as for example through-bond polarization effects, should be more significant in polyfunctional oxonium than in analogous ammonium ions. Another possibility is that some further tightening of the hydrogen bond in the protonated diethers may lead to larger $\Delta H°_{HB}$ values, but that such change would be prevented by unfavorable entropy effects. For example, if tightening of the structure of



$$CH_3OH^+CH_2CH_2CH_2OCH_3$$

would decrease $\Delta H°_{BWF}$, but increase $-\Delta S°_{HB}/n$ for this ion to values similar to those in

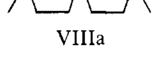


$$H_3N^+CH_2CH_2CH_2NH_2$$

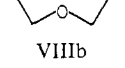
then such a change would increase $\Delta H°_{HB}$ by 5 kcal mol^{-1}, but would cause a negative entropy term of 4 × –2.2 = –8.8 cal mol^{-1} K^{-1}, and thus such a further tightening of the structure would be unfavorable, in terms of $\Delta G°_{500}$, by 3.8 kcal mol^{-1}. In other words, because of the stronger $OH^+\cdots O$ vs. $NH^+\cdots N$ bonds, a loose structure may be favorable, in terms of free energy, in the protonated diethers vs. protonated diamines.

Thermochemistry of Intramolecular Proton Shift

In the protonated triether VIII two intramolecularly bonded structures VIIIa and VIIIb are possible:

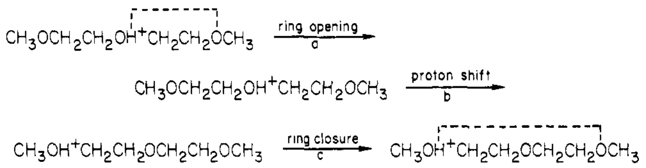


VIIIa



VIIIb

The central oxygen should be the most basic site, since it is bonded to large polarizable groups on both sides. Shift to a terminal oxygen should be endothermic. The shift is facilitated by the geometry of VIIIb which allows the formation of a large ring and optimal geometry for hydrogen bonding. However, the shift is opposed by the large negative $\Delta S°_{HB}$ of the large ring. Experimentally, the large negative $\Delta S°_{HB}$ found in VIII is not compatible with the formation of a small ring such as in VIIIa. Evidently, the large ring is actually formed. The thermochemistry of the proton shift from VIIIa to VIIIb may be estimated by the hypothetical process:



$$CH_3OCH_2CH_2OH^+CH_2CH_2OCH_3 \xrightarrow[a]{\text{ring opening}} CH_3OCH_2CH_2OH^+CH_2CH_2OCH_3 \xrightarrow[b]{\text{proton shift}} CH_3OH^+CH_2CH_2OCH_2CH_2OCH_3 \xrightarrow[c]{\text{ring closure}} CH_3OH^+CH_2CH_2OCH_2CH_2OCH_3 \quad (12)$$

The thermochemistry of the first step may be equated with $\Delta H°_{HB}$ and $\Delta S°_{HB}$ of the small ring in VI. Thus $\Delta H°_{11a} = 7$ kcal mol^{-1} and $\Delta S°_{12a} = 4.3$ cal mol^{-1} K^{-1}. The second step should involve no entropy change, and $\Delta H°_{12b}$ can be estimated by the difference between the PA of $CH_3OC_3H_7$ and that of a large symmetric ether, e.g., $C_4H_9OC_4H_9$, thus $\Delta H°_{12b} = -5$ kcal mol^{-1}. The formation of the large ring in step c is equivalent with the actual $\Delta H°_{HB}$ and $\Delta S°_{HB}$, and therefore $\Delta H°_{12} = -22$ kcal mol^{-1} and $\Delta S°_{12} = -13.8$ cal mol^{-1} K^{-1}. Summing up the thermochemistry of the overall shift, $\Delta H°_{12} = -20$ kcal mol^{-1} and $\Delta S°_{12} = -9.5$ cal mol^{-1} K^{-1}. From $\Delta H°_{12}/\Delta S°_{12}$, the larger ring is more stable up to 2100 K, while the proton would shift to form structure VIIIb above this temperature. However, of course, the ion decomposes much before the proton would shift.

In the tetraether IX an efficient large ring can form even when the proton is located on one of the inner oxygens. The increased PA of the inner oxygen and the stability of the large ring combine here to make this the favorable proton site. The surprisingly large increase in PA from VIII to IX may be in part due to this effect.

PAs and Intramolecular Bonding in Diketones

The protonation thermochemistry of diketones is listed in Table I. To evaluate the effects of intramolecular hydrogen bonding we again compare the PAs of acyclic and cyclic ketones and diketones.

The PA of biacetyl (XIII) is lower than that of a comparable monoketone $CH_3COC_2H_5$, by 3.0 kcal mol^{-1}. The rigid structure of biacetyl would make intramolecular hydrogen bonding highly inefficient; such effect, if any, is overwhelmed by the through-bond inductive effects.

The additional carbonyl oxygen at the 3 position in 1,3-cyclohexanedione increases the PA by a surprisingly large 7 kcal mol^{-1} vs. cyclohexanone. Assuming a similar effect (without hydrogen bonding) in going from a monoketone such as $CH_3COC_2H_5$ to $CH_3COCH_2COCH_3$ (XIV) and $CH_3COCH_2CH_2COCH_3$ (XV), the PAs of these compounds should be ≈ 207 kcal mol^{-1}. The actual PA of XIV is 207.7 kcal mol^{-1}, and thus $\Delta H°_{HB}$ in this ion is negligible. The PA of XV, 212.4 kcal mol^{-1}, indicates $\Delta H°_{HB} = 5$ kcal mol^{-1}. These values are substantially smaller than those in the comparable diethers VI and VII. The entropy effect, $\Delta S°_{HB}$ and $\Delta S°_{HB}/n$, in XV is small and comparable to that in the diethers.

A further complicating factor in evaluating the structural contributions to the PAs of diketones is that some of the neutrals may be present as the enol tautomers, and thus the comparison between the PAs of the different isomers may reflect this factor as well as the structures of the ions.

The small $\Delta H°_{HB}$ and $\Delta S°_{HB}/n$ values in the diketones indicate that, at most, partial hydrogen bonding may apply here. Molecular models show the geometry of $CH_3COH^+CH_2CH_2COCH_3$ to be similar to that of $CH_3OH^+CH_2CH_2OCH_3$, i.e., the hydrogen bond is distended by about 1 Å and the $O-H^+\cdots O$ angle is distorted to about 120°. Again, a full hydrogen bond is probably absent.

Pyrolysis of Protonated Ethers

In the course of the equilibrium measurements, we observed that the protonated polyethers decompose thermally in the general reaction

$$\mathrm{ROCH_2CH_2OH^+R'} \rightarrow \mathrm{ROH^+CH{:}CH_2} + \mathrm{R'OH} \quad (13)$$

In general, the fragment ions protonate the parent polyether, reaction 14. This pattern is consistent with alcohol loss from protonated ethers after chemical ionization.[14] The cycle of reactions 13 and 14 constitutes the proton-catalyzed decomposition of polyethers to olefinic ethers and alcohols.

$$\mathrm{ROH^+CH{:}CH_2} + \mathrm{ROCH_2CH_2R'} \rightarrow \mathrm{ROCH{:}CH_2} + \mathrm{ROCH_2CH_2OH^+R'} \quad (14)$$

For example, in dimethoxyethane we observe a fragment ion at *m/e* 59, probably due to the reaction

$$\mathrm{CH_3OCH_2CH_2OH^+CH_3} \rightarrow \mathrm{CH_3OH^+CH{:}CH_2} + \mathrm{CH_3OH} \quad (15)$$

$$\mathrm{CH_3OH^+CH{:}CH_2} + \mathrm{CH_3OCH_2CH_2OCH_3} \rightarrow \mathrm{CH_3OCH_2CH_2OH^+CH_3} + \mathrm{CH_3OCH{:}CH_2} \quad (16)$$

Since the proton affinity of CH_3OCHCH_2 is lower than that of $CH_3OCH_2CH_2OCH_3$, the fragment ion will protonate the parent molecule, reaction 16. Similarly $CH_3O(CH_2)_3OH^+CH_3$ loses CH_3OH to yield a fragment at *m/e* 73.

The loss of CH_3OH is the major pyrolitic pathway also in the protonated ions of the tri- and tetraethers VIII and IX.

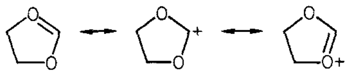
The decomposition reactions are thermally activated. Typical rate constants are in the range 10^2 to $5 \times 10^3\ s^{-1}$ at 600–650 K.

The cyclic crown ethers also pyrolize in the same high-temperature range. The major product ion from the protonated ion of X is at *m/e* 133, presumably the ion $CH_2{:}CHOCH_2CH_2OCH_2CH_2OHH^+$. The corresponding neutral product is $CH_2{:}CHOH$. A decomposition product is also observed at *m/e* 89, due to the loss of $CH_2{:}CHOCH_2CH_2OH$. In general, the protonated crown ethers pyrolyze to a protonated and a neutral olefinic hydroxy ether.

A decomposition product of a different kind was observed in the attempted protonation of $CH_3OCH_2OCH_3$ at 600 K, in 1 torr of H_2O as the carrier gas. Instead of the protonated ion, the carbonium ion $CH_3OCH^+OCH_3$ is formed. Evidently, the protonated ion is unstable under our conditions and loses H_2 to produce the resonance stabilized carbonium ion:

$$\mathrm{CH_3O^+{:}CHOCH_3} \leftrightarrow \mathrm{CH_3OCH{:}O^+CH_3}$$

Similarly, the cyclic diether 1,3-dioxolane at 450 K, in cyclohexane as the carrier gas, yields the ion with *m/e* 73, i.e., $(M - H)^+$, presumably the resonance-stabilized ion XIX. We note however that 1,3-dioxane, which also has the same $-OCH_2O-$ function as dimethoxymethane and 1,3-dioxolane, gives, upon protonation, the MH^+ oxonium rather than the $(M - H)^+$ carbonium ion.

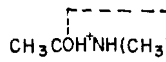


XIX

Conclusions

We observed the relation between molecular structure and intramolecular hydrogen bonding in polyfunctional oxonium ions in terms of the enthalpy (ΔH°_{HB}) and entropy (ΔS°_{HB}) of the internal bond; the thermal stability of the bond as reflected by the bond opening temperature *T*, the bond weakening factor ΔH°_{BWF}, and the entropy of "cyclization" per single C–C, C–O, or C–N bond incorporated into the ring, $\Delta S^\circ_{HB}/n$. We find that in the smallest compounds the "cyclic" structure may amount only to a stabilized cis conformation, while in the largest compounds the hydrogen bond approaches its full intermolecular strength.

Together with previous results, the present data show that intramolecular bonding is prevalent in complex organic ions. Thus, its effects have now been quantitatively determined in protonated diamines,[2] triamines,[3] amino alcohols,[3] polyethers, diketones, as well as radical ions of diphenylalkanes[14] and even of normal alkanes.[14] Recent results show that intramolecular hydrogen bonding also occurs in biological type species such as the protonated alanine derivative



$$\mathrm{CH_3COH^+NH(CH_3)COOCH_3}$$

Here the geometry of the interacting groups is similar to the geometry of adjacent amide links in a peptide, and ΔH°_{HB} contributes 6 kcal mol^{-1} to the stability of this protonated species. Further studies are necessary to generalize the thermochemical effects in compounds with mixed functional groups such as amine halides, peptides, and possibly the intramolecular solvation of ionized functional groups by long alkyl chains.[4]

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Registry No. III, 592-90-5; IV, 505-22-6; VI, 110-71-4; VII, 17081-21-9; VIII, 111-96-6; IX, 112-49-2; X, 294-93-9; XI, 33100-27-5; XII, 17455-13-9; XIII, 431-03-8; XIV, 123-54-6; XV, 110-13-4; XVI, 108-94-1; XVII, 765-87-7; XVIII, 504-02-9.

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