Structure and Energetics of Protonated *ω*-Methoxy Alcohols

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The proton affinity (PA) of a molecule in the gas phase is an expression of its fundamental basicity and is a possible factor controlling the course of many ion−molecule reactions. The formation of an intramolecular hydrogen bond increases the PA value over that of similarly sized monofunctional molecules and the values of $\Delta S°$ are an indication of an intramolecular cyclization which occurs via hydrogen bonding in protonated bifunctional molecules. The first step in exploring these thermochemical properties has been the examination of the experimental proton-transfer equilibria using both ion cyclotron resonance (ICR) and high-pressure mass spectrometric (HPMS) studies. Parallel ab initio molecular orbital (MO) calculations on the protonated species show that the cyclized structures are the most stable species, in agreement with the experimental PA and entropy observations.

Introduction

Hydrogen bonding can greatly influence the structure and the properties of organic compounds. In particular, intramolecular hydrogen bonds are often responsible for determining the predominant conformers in both solution[1] and the gas phase.[2−6] Many organic and enzymatic reactions proceed through protonated intermediates or involve direct hydrogen bonding such as those involving protein or DNA complexes.

The occurrence of such intramolecular solvation in protonated species has been characterized both theoretically and experimentally in a series of studies on the intramolecular hydrogen bonding interactions in gaseous ions of both di- and polyfunctional ions such as diols,[2] diamines,[3−5] diethers,[5,6] diketones,[5,7] amides and amino acid derivatives,[8] or amino alcohols.[4] This paper extends the study to asymmetric bifunctional ions: protonated *ω*-methoxy alcohols. Ethers have been chosen for examination because of the simplicity of their ion chemistry and their volatility.

Although gas-phase structural data are available for neutral 2-methoxyethanol,[9−12] there is a general paucity of information for the other methoxy alcohols, except for a recent microwave spectroscopy study of 3-methoxypropanol.[13] Nevertheless, the presence of an intramolecular hydrogen bond has also been shown in ethylene glycol and 1,2-dimethoxyethane,[14] 1,2-ethanediol, 1,3-propanediol, and 1,4-butanediol, by microwave spectrometry,[15] gas phase electron diffraction,[16] IR,[10] Raman,[17] and NMR[18] spectroscopies, ab initio calculations,[12,19] and molecular mechanics calculations,[12,15,20] and in solution.[1b]

Intramolecular hydrogen bonds in bifunctional organic compounds have been characterized by their thermochemical data since the 1970s. It is has also been acknowledged that such intramolecular bonding can stabilize the protonated form, MH^+, thus increasing the exothermicity of the protonation reaction (eq 1). Such compounds, M, therefore may show an enhanced gas-phase basicity, GB(M), ($-\Delta G_1°$) and a significant increase in the proton affinity ($PA(M) = -\Delta H_1°$) compared to a similarly sized monofunctional molecule.

$$M + H^+ \rightarrow MH^+ \qquad (1)$$

The addition of the proton to a neutral molecule cannot be directly examined, but relative thermochemical data can be obtained from an examination of proton-transfer equilibria between the molecule under study, M, and a number of reference bases, B, as a function of temperature. The equilibrium constant (K_{eq2}) at a given temperature is determined from the ion intensity ratio of the two protonated bases at equilibrium and the partial pressure ratio of the two neutral bases. The standard free energy changes of reaction ($\Delta G_2°$, eq 3) are then obtained directly from the experimentally determined equilibrium constants.

$$BH^+ + M \rightleftharpoons B + MH^+ \qquad (2)$$

$$\Delta G_2° = -RT(K_{eq2}) \qquad (3)$$

The majority of quantitative gas-phase measurements have been determined using either ion cyclotron resonance (ICR) or high-pressure mass spectrometry (HPMS) techniques.[21]

In ICR experiments GB(M) may be determined from equilibrium proton-transfer reactions, usually at a single temperature (320 K). The free energy change for proton transfer is given by $-\Delta G°_2 = GB(M) - GB(B)$, where the reference GB(B) is an established quantity usually anchored to a few primary standards. The determination of proton affinities, however, requires the evaluation of the entropy terms associated with the protonation reaction (eq 1) as described in eqs 4−6.

$$PA(M) = GB(M) - T\Delta S°_1 \qquad (4)$$

$$PA(M) = PA(B) + \Delta G°_2 + T[\Delta S°_{1/2}(B) - \Delta S°_{1/2}(M)] \qquad (5)$$

$$\Delta S°_{1/2}(X) = S_T°(XH^+) - S_T°(X) \qquad (6)$$

Here $\Delta S°_{1/2}(X)$ is the difference in standard entropy between the protonated $S_T°(XH^+)$ and the neutral $S_T°(X)$ species at a

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specified temperature T (eq 6). When experimental values are not available, $\Delta S°_{1/2}(X)$ must be estimated. In many cases, the entropy of XH^+ can be approximated by that of an isoelectronic neutral analogue; for example H_3O^+ may be approximated by NH_3. If the entropies of the neutral base, X, and the isoelectronic neutral analogue of XH^+ are available in the literature, then an estimate for $\Delta S°_{1/2}(X)$ can be attempted in most instances. Sometimes $\Delta S°_{1/2}(X)$ is simply estimated from the change in rotational symmetry numbers (both internal and external) that occur in the protonation process, eq 7.

$$\Delta S°_{1/2}(X) = -R \ln \sigma XH^+/\sigma_X \tag{7}$$

In HPMS experiments[22] both the entropy and enthalpy changes for proton transfer can be determined more effectively and accurately from the variation of the equilibrium constant as a function of temperature. From linear regression of a plot of $\ln K_{eq2}$ vs $1/T$, a van't Hoff plot (eq 8), the slope yields $\Delta H°_2$

$$\ln K_{eq2} = \frac{\Delta H°_2}{RT} - \frac{\Delta S°_2}{R} \tag{8}$$

and the intercept, $\Delta S°_2$. This is inherently more satisfactory than relying on sometimes erroneous $\Delta S°_{1/2}(X)$ estimations. If the PA(B) and $\Delta S°_{1/2}(B)$ have been well-established through an accurately determined proton exchange thermochemical ladder referenced to a few primary standards, then the unknown values are readily established from the equilibrium examined, eqs 9 and 10. In this study the PA(B) and $\Delta S°_{1/2}(B)$ data were

$$PA(M) = PA(B) - \Delta H°_2 \tag{9}$$

$$\Delta S°_{1/2}(M) = \Delta S°{}^{0}_{1/2}(B) + \Delta S°_2 \tag{10}$$

mainly taken from ref 22 and related additional experiments.

The purpose of the present study is the determination of the thermochemistry of gas-phase proton-transfer reactions involving the methoxyalkanes **0**−**4** (**0** = methoxyethane, **1** = 1-methoxypropane, **2** = 1-methoxybutane, **3** = 1-methoxypentane, **4** = 2-methoxypentane) and ω-methoxy alcohols **5**−**10** (**5** = 2-methoxyethanol, **6** = 3-methoxypropanol, **7** = 4-methoxybutanol, **8** = 5-methoxypentanol, **9** = 3-methoxybutanol, **10** = 3-methoxy-3-methylbutanol) using both ICR and HPMS measurements. Our approach involves the experimental determination of $\Delta G°_2$, $\Delta H°_2$, and $\Delta S°_2$. Also, ab initio molecular orbital (MO) calculations were performed to support the experimental conclusions and to gain more detailed structural insight.

Experimental Section

(1) Materials. The compounds (**5**, **7**, **9**) discussed in this study were purchased from Aldrich. Compound **6** was obtained by reduction of methyl 3-methoxypropanoate and compound **8** from 1,5-pentandiol. The remaining ethers (**0**−**4**) were prepared by reaction of the appropriate iodide with the appropriate potassium alkoxide in dimethyl sulfoxide (DMSO) solvent.[23] The structures were confirmed by ^{1}H NMR spectrometry using a Bruker AM 200 instrument and GC/MS on a HP5890 gas chromatograph connected to a HP5972 mass spectrometer.[24] In the former case, where necessary, the compounds were purified by distillation or column chromatography on silica gel (KG 60; 0.063−0.200 mm) with a mixture of petroleum ether/ethyl acetate as eluents.

(2) Apparatus. The gas-phase basicities of the alkyl ethers (**0**−**4**) were measured near room temperature (ca. 320 K) on a Bruker Spectrospin CMS 47X FT-ICR mass spectrometer.[25] The two substances were introduced via a dual inlet system equipped with two separate Balzers-UDV-035 valves controlling the partial pressure of each component. Experiments were performed at a total (indicated) pressure in the range of 5×10^{-8} to 2×10^{-7} mbar. A temperature of 320 K was maintained during all experiments.[26] The ions were produced by "self-chemical ionization"[27] following electron impact inside the ICR cell. It has been demonstrated that after a postionization delay of 4 s all of the ions should be relaxed to thermal energies in the presence of the static pressure of the neutral reactants used. Unwanted ions are then ejected by a combination of chirp and shot radio frequency (rf) pulses, and the remaining MH^+ and/or BH^+ ions are then allowed to react with the neutrals present. In order to check the reversibility of the proton-transfer reactions, three series of experiments were performed where the selected ion was either MH^+ or BH^+, or both. Equilibrium was generally achieved after a delay of 2−10 s. The partial pressure ratio was calculated from ion gauge readings (Balzers-IMR-132). The ion gauge readings have been corrected for the ionization cross-sections of M and B which were estimated from a polarizability/ionization cross-section correlation[28] for M and B.

Pulsed ionization high-pressure mass spectrometer studies were performed on an instrument configured around a VG 70−70 mass spectrometer whose geometry was reversed to provide a B−E instrument. The apparatus and its capabilities have been described in detail previously.[29]

All samples were prepared in a 5 L stainless reservoir and introduced into the high-pressure ion source via an inlet system. Methane was used as the high-pressure bath gas (to 10 Torr) and served as both the inert third body stabilization species and proton-transfer chemical ionization reagent. The partial pressures of the bases in the ion source were in the 0.01−0.1 Torr range. The samples were allowed to mix in the reservoir for at least 30 min before use to ensure complete mixing. The reaction mixture was ionized by 200 μs pulses of 2 keV electrons with a duty cycle of 20−35 ms, depending upon the persistence of the ion intensity profiles. The time evolution of the ion time intensity profiles was monitored for 10−30 ms after the ionizing pulse.

In all cases a wide range of a partial pressure ratios of the two bases under study was employed as a check of the precision and accuracy of the measured equilibrium constants. Ion source pressures ranged from 6 to 10 Torr, and temperatures from 350 to 550 K were used.

(3) Molecular Orbital Calculations. The geometries of ω-methoxy alcohols and their protonated species were optimized by ab initio molecular orbital calculations with the GAUSSIAN 92 suite of programs.[30] Initially these calculations were carried out at the Hartree−Fock (HF) SCF level of theory using the 3-21G basis set, with optimization of all parameters and without any symmetry constraints. All stationary points were characterized as local minima by having no negative eigenvalues in the computed force constant matrix. The optimized HF/3-21G structures are reoptimized at the HF/6-31G* level. In addition, single-point energy calculations were performed at the MP2/6-31G* level[31] to explicitly take into account electron correlation effects, which have a significant effect on the relative energies of intramolecular bonding compounds.[14] Calculations at the HF/6-31G* level proved to be the best compromise between accuracy and tractability.

Most of the GAUSSIAN 92 calculations are performed on an IBM RISC 6000 workstation. However, the larger, time

TABLE 1: Experimental FT-ICR Free Energy Changes (kcal·mol^{-1}) for the Reaction $MH^+ + B \rightleftharpoons BH^+ + M$ (M = Ethers 0−3) and Derived Proton Affinities (kcal·mol^{-1})

M	ref base, B	$\Delta G°_{320}{}^a$	$\Delta S°_{1/2}$			PA(M)				
		ICR	M^b	B^{b,c}	PA(B)^c	ICR^d	av	add^e	PW^f	MP2
0	isopropyl cyanide	0.6	(4.0)^h	0.0	193.5	192.8	193.1	194.0	195.0^l	193.1^g
	acetone	−0.8	(4.0)^h	4.5	193.9	193.3				195.3^h
	methyl acetate	−1.8	(4.0)^h	4.0	195.1	193.3				
	methyl acetate^i	(−1.5)	(4.0)^h	4.0	195.1	193.6				
1	acetone	−0.2	(3.5)^j	4.5	193.9	194.0	195.0	195.5	197.5^g	
	194.3^g									
	ethyl acetate	−2.4	(3.5)^j	4.0	198.2	196.0			196.6^f	
	ethyl acetate^g	(−3.6)	(3.5)^j	4.0	198.2	194.4				
2	ethyl acetate	−0.6	4.0^k	4.0	198.2	197.6	197.6	196.4	198.0^g	
	ethyl ether	−0.5	4.0^k	3.5	198.4	197.7				
3	**2**	0.3	(4.0)^j	4.0	196.4	196.7	197.4	196.6		
	ethyl acetate	−0.9	(4.0)^j	4.0	198.2	197.5				
	3-pentanone	−1.0	(4.0)^j	2.5	199.6	198.1				

[a] ±0.2 kcal·mol^{-1}. [b] Taken from published[22] and additional unpublished data from this laboratory. [c] In cal mol^{-1} K^{-1}. [d] $PA(M) = PA(B) + \Delta G°_{320} + 0.32[\Delta S°_{1/2}(B) - \Delta S°_{1/2}(M)]$. [e] For a $[(n\text{-}C_mH_{2m+1})O(n\text{-}C_nH_{2n+1})]$ type ether: $PA = -8.55(1/m + 1/n) + 206.85$ kcal·mol^{-1} based on unpublished data from this laboratory. [f] Reference 6. The PA value has been reevaluated using the published value for NH_3. [g] MP2 $PA_{320K} = PA_{0K} + 2.5(320R)$: vibrational frequency scaled by 0.89.[34] [h] HF 298K $\Delta S°_{1/2}(\mathbf{0}) = 4.0$ cal mol^{-1} K^{-1} and MP2 298K PA(**0**) = 195.3 kcal·mol^{-1}.[35] [i] Reference 36. [j] Estimates based on HPMS data obtained at this laboratory: methyl ether, $\Delta S°_{1/2} = 4.5$ cal mol^{-1} K^{-1}; ethyl ether, $\Delta S°_{1/2} = 3.5$ cal mol^{-1} K^{-1}; methyl butyl ether, $\Delta S°_{1/2} = 4.0$ cal mol^{-1} K^{-1}; butyl ether, $\Delta S°_{1/2} = 3.0$ cal mol^{-1} K^{-1}. [k] See footnote *j*.

TABLE 2: ICR and PHPMS Results[a]

M	B	ICR results				PHPMS results			
		$\Delta G°_{320}$	$\Delta S°(B)$	PA(B)	$GB_{320}(M)$	$\Delta S°(M)$	PA(M)	$GB_{320}(M)$	$\Delta GB_{320}(M)$
5	diethyl ether	0.4	3.5	198.4	191.6	−2.5	199.8	190.7	0.6
6	pyrrole	2.0	1.0	209.2	203.2	−14.0	213.5	200.7	2.5
7	methylamine	−1.8	−3.0	215.4	204.3	−15.0	219.3	206.2	−1.9
8	dimethylamine	−6.5	−1.5	222.5	207.2	−18.0	219.5	205.3	−1.8

[a] Experimental free energy change (kcal·mol^{-1}) $\Delta G°_{320}$ for the reaction $MH^+ + B \rightleftharpoons BH^+ + M$ (M = ethers **5**−**8**, B are reference bases) and the derived gas-phase basicities GB(M) calculated from PA(M), PA(B), $\Delta S°(M)$, and $\Delta S°(B)$.

intensive MP2/6-31G* level frequency calculations performed on the ω-methoxy alcohols were run on a Cray C98.

Luke[32] and co-workers have presented an extensive examination of the stable conformations of $CH_3CH_2OCH_2CH_2OH$ at different levels of theory and concluded that HF relative conformational energies may be in error by as much as 1.5 kcal·mol^{-1}, even if polarization functions are included in the basis set. Moreover a single-point MP2 calculation produces results that are virtually identical to the MP2=FULL/6-31G* + ZPVE value.

Vibrational analysis has been done in order to deduce both zero-point vibrational energy corrections and absolute entropies at the HF/6-31G* level of theory. The vibrational frequencies were scaled by the empirical factor 0.9 to account for the fact that theoretical harmonic frequencies are too high compared with experimental fundamental frequencies. In this way, the scaled frequencies of cyclized and noncylized conformers of 2-methoxyethanol are in agreement with the infrared studies[1b] (ν_{OH} stretching vibrations). The basis set superposition error (BSSE) was estimated by the Boys−Bernardi counterpoise method.[33]

The theoretical proton affinity, $-PA_{calc}$ (at 1 atm), is defined by eqn 11, where $\Delta E_{el} = E_{MH^+} - E_M$ is the difference in the electronic energy of the protonated base (E_{MH^+}) and neutral base (E_M), ΔE_{vib} is the scaled zero-point vibrational energy difference of the protonated base and neutral base, BSSE is the basis set correction term, $^3/_2(RT)$ is the contribution due to thermal translational energy, and a ΔPV is the work term of RT.

$$-PA_{calc} = \Delta E_{el} + \Delta E_{vib} + BSSE - {}^3/_2(RT) - \Delta PV \quad (11)$$

Results

In the literature, only a few proton affinities of alkyl ethers are known. Dimethyl ether, diethyl ether, butyl methyl ether, and dibutyl ether have been recently studied using the HPMS technique.[22] Their PA values are 189.6, 198.1, 196.4, and 202.4 kcal·mol^{-1}, respectively. Although in many cases the PA's of asymmetric monofunctional ether compounds can be estimated by additivity methods from a few known symmetric ether PA values, investigation of the gas-phase basicities of a number of methyl alkyl ethers, $CH_3O(CH_2)_nCH_3$ ($1 < n < 4$), was also undertaken in order to have as accurate a comparison as possible to the data for the methoxyalkanols.

(1) Thermochemical Data. *(a) Monoether Protonation Thermochemical Data.* In Table 1 are summarized the experimental $\Delta G°_2$ and GB(M) values obtained from ICR experiments. Experimental values for $\Delta S°_{1/2}(B)$ were taken from the published and unpublished data of Szulejko and McMahon.[29] The PA(M) values can be calculated from $\Delta G°_2$, if the value for $\Delta S°_{1/2}(M)$ can be deduced. For the methyl alkyl ethers a $\Delta S°_{1/2}$ of 3 ± 1 cal mol^{-1} K^{-1} has been used, on the basis of recent HPMS data and MO calculations. The derived PA values are summarized in Table 1.

(b) Bifunctional Compound Protonation Thermochemical Data. The basicities of the ω-methoxyalkanols **5**−**8** were determined by ICR at 320 K relative to several reference bases. The data thus obtained are shown in Table 2 together with the HPMS data extrapolated to 320 K.

The temperature dependence of the proton-transfer equilibrium constant for each of the ω-methoxyalkanols **5**−**10** was also examined by HPMS. The temperature ranges of proton-transfer measurements were limited by the dissociation reactions (eq 12) at the upper end and by the clustering reactions (eqs 13 and 14) at the lower end.

At low temperatures, protonated ω-methoxy alcohols MH^+, protonated bases, BH^+, and proton-bound dimers of the ω-methoxy alcohols, M_2H^+, are in the interconnected equilibria

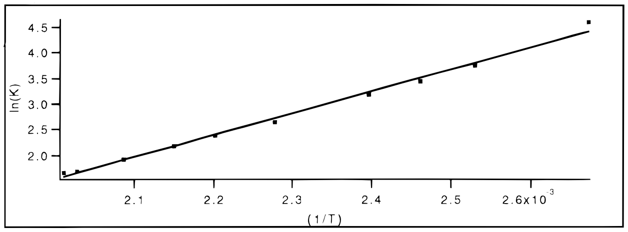


Figure 1. van't Hoff plot concerning the protonated species pyrrole(H$^+$) (m/z = 68) and 3-methoxybutanol(H$^+$) (m/z = 105). Ion source conditions: 206 °C; pyrrole, 0.033%; 3-methoxybutanol, 0.064%; methane, 99.9%; total pressure, 7.9 Torr.

$$M_2H^+ \text{ or } M_2H^+ \rightarrow F^+ + N \qquad N = H_2O,\ CH_3OH,\ \text{or } 2CH_3OH \quad (12)$$

$$MH^+ + B \rightarrow MBH^+ \qquad \text{mixed proton-bound dimer} \quad (13)$$

$$MH^+ + M \rightarrow M_2H^+ \qquad \text{symmetric proton-bound dimer} \quad (14)$$

described by eqs 2, 10, and 11. For example, proton-transfer equilibrium from protonated pyrrole (BH$^+$, m/z = 68) to 3-methoxybutanol (MH$^+$, m/z = 105) is not established until after 1 ms. This implies that thermodynamic data can be obtained for both the proton transfer and association equilibria, eqs 15 and 16, respectively. In all cases, care was taken to

$$\underset{m/z\,=\,68}{BH^+} + M \rightleftharpoons B + \underset{m/z\,=\,105}{MH^+} \quad (15)$$

$$\underset{m/z\,=\,105}{MH^+} + M \rightleftharpoons \underset{m/z\,=\,209}{M_2H^+} \quad (16)$$

ensure that the ion intensity profiles were followed for a reaction time sufficiently long to ensure that equilibrium had been achieved. The van't Hoff plots for this reaction is shown in Figure 1.

Competing side reactions such as protonation followed by loss of methanol or water do not prevent the equilibrium from being achieved. Peaks corresponding to the loss of methanol and water from M_2H^+ (e.g. $[M_2H^+ - H_2O]^+$, $[M_2H^+ - 2H_2O]^+$, and $[M_2H^+ - 2MeOH]^+$ are present in all spectra even when the temperature is below 200 °C. The formation of these unwanted ionic species is not a major problem if the pseudo first order rate constants for the reversible proton transfer reaction under investigation are significantly faster than the unimolecular rate constants for dissociation of either the protonated monomer MH$^+$ or the dimer M_2H^+.

The thermochemical data derived from proton-transfer van't Hoff plots are presented in Table 3b. These data were anchored to the PA scale based on the absolute value of the proton affinity and a 500 K $\Delta S°_{1/2}$ for CO of 141.9 kcal·mol^{-1} and 3.0 cal mol^{-1} K^{-1}, respectively. It should be noted that the equilibrium between open and cyclized intramolecularly hydrogen bonded conformers of the neutral methoxyalkanols should be accounted for in a more detailed analysis of the protonation thermochemical data (see below).

(2) MO Calculations. The gas-phase conformations of neutral and protonated 1,2-1,3-, and 1,4-methoxyalkanols were examined. Ethers are generally considered to be more basic than alcohols[26] of similar size, and therefore the protonation of ω-methoxy alcohols will occur preferentially on the methoxy group oxygen site. Nevertheless the two individual sites of protonation of ω-methoxy alcohols must be considered for the intramolecularly hydrogen bonded conformer.

The nomenclature used for the conformations of the neutral ω-methoxy alcohols depends upon the different axes of internal rotation, as follows:

(a) 2-Methoxyethanol. The first and third letters (lower case) denote the COC_2C_1 and C_2C_1OH torsions as trans (t), gauche (g), or −gauche (g′); the second (capital) letter describes the OC_2C_1O torsion as trans (T) or gauche (G).

(b) 3-Methoxyethanol, 4-Methoxybutanol, and 5-Methoxypentanol. For these others, respectively, four, five, and six letters are necessary to specify the different conformations; those letters have the same meaning as those for *2-methoxyethanol*.

Molecules that do not possess a center of symmetry should have a greater number of unique local minima on the potential energy surface (PES). The conformational surface could be extensively examined by varying the values of the rotatable bonds. If each of these torsion angles is allowed to have an initial value of +60, −60, and +180°, all possible stable conformations should be obtained from a full geometry optimization of the initial structure. For example, in the largest compound in our study, 5-methoxypentanol, there are $3^6 = 729$ starting geometries that would have to considered. Because the goal is not to obtain exhaustive details of the PES, our interest was therefore focused on the cyclized conformers and comparisons were made to previously reported studies.[12−19]

In these four cases, the internal hydrogen bond causes the molecules to fold upon themselves into compact five, six, seven, or eight-membered rings. As already observed, with symmetric compounds this phenomenon occurs in both neutral and protonated forms.

It should be noted that we have observed a trend which has also been described using ab initio calculations for aliphatic ethers[11] and from microwave studies of methoxyethanol and methoxypropanol[13] in which the ω-methoxy group is always in the trans conformation, the energetically most stable form of the neutral.

Protonated systems are more affected than the corresponding neutral molecules by intramolecular hydrogen bonding. Accordingly, the main characteristics of hydrogen bonds involving ionized species are a large H-bond energy and a short H-bond length.

Optimized geometric parameters of neutral and protonated cyclized ω-methoxy alcohols are given in Table 4a, b, respectively. Geometries are shown in Figure 2. In Table 5 the total and relative calculated energies of the most stable conformers are reported with respect to the all trans structure. Calculated enthalpy and entropy at 298 K are also shown.

(3) Neutral Form. *(a) 2-Methoxyethanol (2M).* Two different conformers were investigated, namely, tGg′ (gauche), and tTt (trans). Our calculations show that the gauche conformer, tGg′, with an internal hydrogen bond is the most stable conformation with $HO-C_1-C_2-O = 47.9°$ and $MeO-C-C-O = 56.4°$; the methyl group is oriented about 50° toward the hydroxyl group ($Me-O-C_2-C_1 = 5°$). In the completely relaxed structure, the H-bond length is 2.36 Å. This value compares reasonably well with the H-bond length of 2.3 Å found for 2-methoxyethanol by Buckeley and Brochu.[9]

Optimized geometric parameters could be compared with previous values from microwave studies (45 ± 5, 57 ± 3, and 8 ± 3°).[9] In spite of the low level of the calculations, we obtain a comparable energy of stabilization between the two conformers (tGg′ and tTt) of the 2-methoxyethanol (2.0 kcal·mol^{-1}) as that obtained at the HF/6-31G**/MP2 + BSSE level.[12] Compared with ethylene glycol and other diols or diethers, the internal hydrogen bond is thought to be weaker, but it appears to be the

TABLE 3

(a) Summary of Equilibrium Proton-Transfer Thermochemical Data

B	M	$\Delta H_r^{\circ a}$	$\Delta S_r^{\circ b}$	$\Delta G_{300}{}^a$	$\Delta G_{500}{}^a$	$T_{min}{}^c$	$T_{max}{}^c$
isobutene	*m*-xylene	−0.5	2.8	−1.3	−1.9	119	241
isobutene	*n*-butyl methyl ether (**2**)	−4.7	−1.5	−4.3	−4.1	147	208
isobutene	2-methoxy−1-ethanol (**5**)	−8.1[d]	−8.0[d]	−5.7	−3.4	197	307
m-xylene	*n*-butyl methyl ether (**2**)	−4.1	−3.5	−3.0	−2.3	149	241
methyl acetate	2-methoxy−1-ethanol (**5**)	−4.8[d]	−6.8[d]	−2.8	−0.7	197	307
n-butyl ether	5-nonanone	−1.6	−1.6	−1.1	−0.7	164	251
n-butyl ether	cyclopropyl methyl ketone	−1.9	−2.3	−1.2	−0.7	136	241
5-nonanone	cyclopropyl methyl ketone	−0.3	−0.1	−0.2	−0.2	175	358
pyrrole	3-methoxy−1-propanol (**6**)	−4.3	−14.5	0.0	2.9	115	280
3-methoxy−1-propanol	4-methoxy−1-butanol (**7**)	−5.6	−1.8	−5.0	−4.7	130	249
pyrrole	4-methoxy−1-butanol (**7**)	−10.5	−15.8	−5.8	−2.6	124	267
pyrrole	3-methoxy−1-butanol (**9**)	−8.7	−14.3	−4.3	−0.1	100	224
pyrrole	5-methoxy−1-pentanol (**8**)	−10.2	−19.2	−4.4	−0.6	133	263
pyrrole	3-methoxy−3-methyl-1-butanol (**10**)	−13.3	−19.8	−7.3	−3.4	103	172

(b) Summary of Protonation Thermochemical Data for the Molecules Studied

M	$PA_{exp}{}^a$	$\Delta S^\circ_{1/2}$		M	$PA_{exp}{}^a$	$\Delta S^\circ_{1/2}$	
		expt[b,e]	estd[b,f]			expt[b,e]	estd[b,f]
5	199.8	−2.5	−15	**8**	219.4	−18	−15
6	213.5	−14	−15	**9**	217.9	−12	−15
7	219.4	−15	−23	**10**	222.5	−12	−15

[a] Units: kcal·mol^{-1}. [b] Units: cal mol^{-1} K^{-1}. [c] Units: °C. [d] Reference 29. [e] Absolute 500 K half-reaction entropy change, $\Delta S^\circ_{1/2}(\text{expt}) = S^\circ_{1/2}(BH^+) - S^\circ_{1/2}(B)$ referenced to the 500 K value for CO of 3.0 cal mol^{-1} K^{-1} estimated in ref 29. [f] 298 K, $\Delta S^\circ_{1/2}(\text{estd}) = S^\circ(1\text{-Me}(c\text{-}C_{n+2}H_{2n+1})) - S^\circ_{1/2}(MeO(CH_2)_nOH)$.

TABLE 4: Hydrogen Bond Parameters (Bond Length, Å; Angles, deg) of Neutral Cyclized ω-Methoxy Alcohols and Protonated ω-Methoxy Alcohols[a]

(a) Neutral Cyclized ω-Methoxy Alcohols[b]

		2Mc[d]	3Mc[e]	4Mc	5Mc	[MeOH···OMe$_2$]
a	H*···O[c]	2.36	2.08	1.94	1.93	2.00
c	O···O	2.77	2.84	2.82	2.89	2.93
d	∠O−H···O	105.6	135.3	152.7	152.4	164.8
e	∠O−H,OMe	56.5	73.2	104.7	117.9	173.3

(b) Protonated ω-Methoxy Alcohols[f]

		2MH$^+$c	3MH$^+$c	4MH$^+$c	5MH$^+$c	[MeOH··· H$^+$···OMe$_2$]
a′	H*···O	1.91	1.66	1.53	1.53	1.54
b′	H−OMe	0.97	0.98	1.00	1.00	1.00
c′	O···O	2.49	2.52	2.51	2.53	2.54
d′	∠O−H*···O[b]	116.3	143.5	165.3	170.9	177.6

[a] Optimized parameters at the HF/6-31G* level. [b] ωMc means cyclized ω-methoxy alcohol. [c] H* means the hydrogen involved in the hydrogen bond. [d] Previous work, from microwave study.[9] [e] Previous work, from ab initio study:[13] $a = 2.1$ Å; $b = 2.8$ Å; $d = 138°$; $e = 16°$. [f] ωMH$^+$c means cyclized form of the protonated ω-methoxy alcohol.

key factor determining the relative stability of the molecular conformations observed with microwave spectroscopy.[9]

*(b) 3-Methoxypropanol (**3M**).* Only three of the various possible conformations containing an internal hydrogen bond were investigated, namely, tG′gT, tG′gG, tG′gG′ (gauche), as well to the trans conformer TtTt. The most stable conformer is a chairlike form with the methyl of the methoxy group in an equatorial position (tG′gG) which closely resembles the chair conformation of six-membered rings. The ab initio rotational constants of the cyclized form (6.27, 2.19, 1.75 GHz) are consistent with spectroscopic constants for the 3-methoxypropanol.[13] This MW study reveals the existence of only one conformer in the gas phase.

*(c) 4-Methoxybutanol (**4M**).* It is known that seven-membered rings have their lowest energies in the twist-chair conformation.[37] This is indeed the case for the most stable conformer of compound **7**. The structure of the H-bonded conformers reveals interesting features (Table 4a).

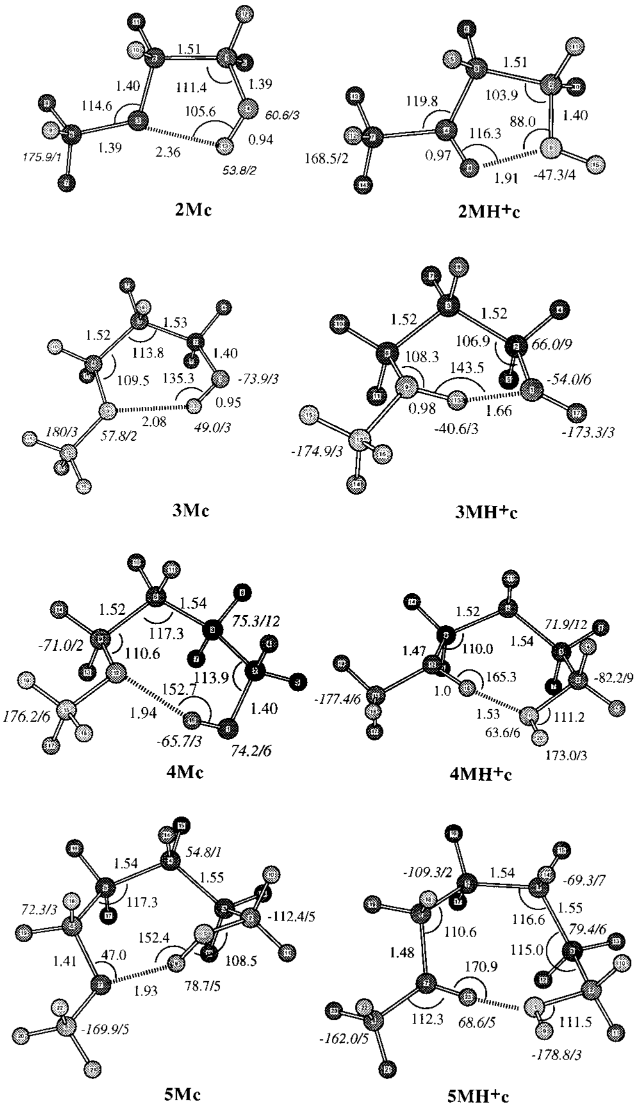
The hydroxyl hydrogen atom is nearly as close as possible to the ether oxygen atom, with the O···H distance shorter than the sum of the van der Waals radii of hydrogen and oxygen (entries a). The O−H···O angles (entry d) increase with the ring size: 105.6, 135.3, 152.7, and 152.4° for the five-, six-, seven-, and eight-membered rings, respectively, while 164.8° would produce an ideal H-bond interaction. The decrease of the torsion value between the O−H and O−Me bonds (entry e) shows that these bonds have become almost parallel, which increases the stabilization due to the bond dipole.

(4) Protonated Species. For the M_cH^+ species, the internal hydrogen bonds are much shorter than those of the corresponding neutrals, M, leading to the stabilization of the chelated structure. Inspection of the protonated 2-methoxyethanol, ($2M_cH^+$) reveals a nondistorted five-membered ring structure of greater stability than the cyclized M_c.

The parameters of the hydrogen bond are listed in Table 4b. The strengthening of the hydrogen bond is reflected in the shortening of the O···H and O···O distances (entries a′,c′ vs a,c, respectively), as well as in the opening of the O−H···O angle (entry d′). The protonation occurs at the oxygen of the methoxy group as shown by the H···O and H−OMe distances (entries a′ and b′). The proton shifts toward midway between the two oxygen atoms in going from $2M_cH^+$ to $5M_cH^+$.

Discussion

To study the influence of a second functional group on the thermochemical properties of a molecule, Kebarle first suggested[3] a comparison of the proton affinities and entropies of protonation of polyfunctional ions with those of model monofunctional molecules. Therefore the PA of the ω-methoxy alcohols (bifunctional compounds) are compared with those for methoxyalkanes (monofunctional compounds) of comparable polarizability (Table 6).



2Mc **2MH+c**

3Mc **3MH+c**

4Mc **4MH+c**

5Mc **5MH+c**

Figure 2. Optimized parameters of neutral and protonated cyclized ω-methoxy alcohols at the HF/6-31G* level of theory. ωMc and ωMH$^+$c mean respectively the cyclized forms of ω-methoxy alcohol and of protonated ω-methoxy alcohol (distances in angstroms; angle values and dihedral angle values in degrees; dihedrals in italic).

It should be noted that the PA's of bifunctional compounds are considerably larger than those of monofunctional homologues. Moreover, as the number of methylene groups increases, the difference between the PA of the bifunctional and monofunctional compounds becomes larger. Such results have also been obtained for symmetric compounds[2−5] (dimethoxy ethers or diamines). Table 7 shows that ours results are consistent with those previously published.

(1) Structure of the Neutral and Protonated Species. A possible explanation for the PA enhancement observed in bifunctional molecules is the stabilization of the protonated form, MH$^+$ by formation of an intramolecular hydrogen bond. Obviously, the flexibility of the long chain allows near-optimum O···H···O distances and dipole alignments to be attained (Table 4b). The energy difference between cyclized and noncyclized forms may be taken as a rough estimate of the internal H-bond energy. It should be noted, however, that other factors are also present which determine the conformations, such as internal dipole interaction and strain energy. MO calculations demonstrate, as shown in Table 5, that the intramolecular hydrogen bond strength can be as great as 25.8 kcal·mol^{-1}. Protonated systems are more affected than the corresponding neutral molecules by intramolecular hydrogen bonding, but the neutral species may also exist as cyclized conformers if the temperature is low enough to offset entropic considerations.

TABLE 5: Total and Relative Calculated Energies (ab Initio MP2 6-31G*//6-31G*) of Neutral and Protonated ω-Methoxy Alcohols

	electronic energy (au)	thermal correction		ΔH$_{oc}$[a]	
		E_{298} (kcal·mol^{-1})	S_{298} (cal mol^{-1} K^{-1})	MH$^+$	M
2Mo	−268.712 123	73.426	79.544		
2Mc	−268.717 582	73.553	78.166		−3.9
2MH^+_o	−269.014 000	81.019	82.484		
2MH^+_c	−269.044 235	81.549	79.094	−19.0	
3Mo	−307.882 158	91.509	87.305		
3Mc	−307.890 381	91.762	84.670		−5.5
3MH^+_o	−308.199 560	99.494	90.343		
3MH^+_c	−308.232 606	99.600	85.360	−21.2	
4Mo	−347.054 038	109.636	94.952		
4Mc	−347.061 908	110.020	91.286		−5.1
4MH^+_o	−347.372 764	117.635	98.054		
4MH^+_c	−347.413 226	117.640	91.459	−25.9	
5Mo	−386.224 202	127.722	99.950		
5Mc	−386.228 970	128.223	97.663		−3.1
5MH^+_o	−386.536 307	135.653	102.673		
5MH^+_c	−386.581 798	135.911	98.283	−25.8	

[a] Derived thermochemical data ($\Delta H°_{ocn}$) concerning equilibrium between the cyclized intramolecularly hydrogen bonded species (M$_c$) and the open *n*-alkane-like uncyclized species (M$_o$) in kilocalories per mole.

Infrared spectroscopic studies conducted on the methoxyalkanols in dilute solutions have examined the equilibrium between the cyclized intramolecularly hydrogen bonded species (M$_{cn}$) and the open *n*-alkane-like uncyclized species (M$_{on}$) as a function of temperature (eq 18). The derived thermochemical data ($\Delta H°_{ocn}$ and $\Delta S°_{ocn}$) are shown in Table 8. The $\Delta H°_{ocn}$ obtained in solution are in excellent agreement with both the present and literature theoretical MO calculated results.[44,45] As can be readily seen (Table 8), only for methoxyethanol can there be significant concentrations of both the open and cyclized conformers over the entire temperature range used in our experiments (320−600 K). For the other methoxyalkanols studied, the open form is favored over the cyclized form due to entropic effects. The protonated methoxyalkanols are assumed to be exclusively in the cyclized form, as the intramolecularly hydrogen bond conformer (M$_c$H$^+$), under our temperature conditions due to the much larger intramolecular hydrogen bond energy involved.

In view of the above arguments, the standard treatment of the temperature dependence of the experimentally obtained equilibrium constants for proton tranfer between a reference base (B) and a methoxyalkanol (M) may be misleading if used to try to determine intramolecular hydrogen bond strengths. The calculation of the experimental equilibrium constant, K_{ex} (eq 17), fails to account for the simultaneous equilibrium which

$$K_{ex} = \frac{[MH^+][B]}{[BH^+][M]} \qquad (17)$$

may occur between the cylized and open forms of the neutral methoxyalkanols, eq 18, with an equilibrium constant, K_{ocn}. If

$$BH^+ + M_{on} \rightleftharpoons BH^+ + M_{cn} \quad \text{equilibrium constant } K_{ocn} \qquad (18)$$

$$BH^+ + M_{cn} \rightleftharpoons M_cH^+ + B \quad \text{equilibrium constant } K_{ccp} \qquad (19)$$

TABLE 6: PA Results for $CH_3O(CH_2)_nCH_3$ and $CH_3O(CH_2)_nOH$ (kcal·mol^{-1})

	$CH_3O(CH_2)_nCH_3$		$CH_3O(CH_2)_nOH$	intramolecular hydrogen bond strength			
n	PA_{mi} ICR[a]	PA_{ma} add[b]	PA_{oc} PHPMS[c]	$IHBS_i$ ICR[d]	$IMBS_a$ add[e]	$IHBS_i$ $IHBS_{EA}$[f]	$IHBS_c$ calc[g]
2	195.0	195.5	201.8	6.8	6.3	24%	5.1
3	197.6	196.4	213.9	16.3	17.4	66%	14.5
4	197.4	196.6	219.8	22.4	23.2	88%	19.2
5	(197.4)	196.9	219.4	22.0	22.5	85%	19.3

[a] See Table 2 for ICR data. [b] The PA for a $(C_mH_{2m+1})O(C_nH_{2n+1})$ type ether using data from our laboratory can be estimated from an additivity scheme as follows: $PA_{ma} = -8.55(1/m + 1/n) + 206.85$ kcal·mol^{-1}. PA data: methyl ether, 189.6 kcal·mol^{-1}; ethyl ether, 198.4 kcal·mol^{-1}; butyl methyl ether, 196.4 kcal·mol^{-1}; butyl ether, 202.4 kcal·mol^{-1}. [c] From Table 3 see also text for details. [d] $IMBS_i = PA_{oc} - PA_{mi} = -\Delta H^\circ_{cycl}$. [e] $IMBS_a = PA_{oc} - PA_{ma} = -\Delta H^\circ_{cycl}$. [f] $100IMBS_a/IHBS_{EA}$ $IHBS_{EA} \approx 26.5$ kcal·mol^{-1} and is the maximum intramolecular hydrogen bond strength. See text for details. [g] $IMBS_c$, theoretically calculated intramolecular hydrogen bond strength.

TABLE 7: Comparison of the Proton Affinities for Bifunctional Compounds $X(CH_2)_nY$ with the Same Carbon Numbers (X, Y = OH, OMe, NH_2) (PA, kcal·mol^{-1})[a]

ref	X	Y	$n = 2$	$n = 3$	$n = 4$	$n = 5$
2	OH	OH	195.4	208.8	218.3	
this work	OH	OMe	198.8	213.5	219.4	219.5
39	OMe	OMe	203.4		222.6	222.6
8			203.3	215.4		
4	OH	NH_2	222.7	232.0	236.3	
4			227.3	236.1	240.3	
3	NH_2	NH_2	232.1	240.3	240.3	

[a] The PA's for the reference base used in ref 26 have been critically reevauated using published[29] and unpublished data from this laboratory.

the equilibrium between cyclized and open forms of the methxoyalkanols is considered, then eqs 20 or 21 may be used

$$K_{ex} = K_{ccp}*(1 + K_{ocn}^{-1})^{-1} \qquad (20)$$

$$K_{ccp} = K_{ex}*(1 + K_{ocn}^{-1}) \qquad (21)$$

to interpret the experimental data. For methoxyethanol, methoxypropanol, and methoxybutanol equilibrium data are available from solution studies and were used to estimate K_{ocn} in the gas phase. This enables K_{ccp} to be evaluated. The thermochemical data thus derived, ΔH°_{ccp}, ΔS°_{ccp}, PA_{cc}, and PA_{oc}, are shown in Table 8, where PA_{cc} and PA_{oc} are the proton affinities of a cyclized and an uncyclized methoxyalkanol, respectively to give a cyclized protomer. Except for methoxyethanol, PA_{oc} and $\Delta S^\circ_{1/2}(M_{oc})$ are very close to PA_{st} and $\Delta S^\circ_{1/2}(M_{st})$ obtained using the results derived directly from a van't Hoff plot. The neglect of the equilibrium between the neutral conformers in the analysis of the thermochemical data for protonation becomes significant only for methoxyethanol. An analysis of data for 1,2-ethanediol shows that this consideration should also be important. In view of this, protonation data available in the literature for diamines and diols may also need to be reevaluated. For comparison, reevaluated literature basicity data are also presented for 1,2 ethanediol in Table 8.

(2) Energetics. Strong H-bond energies have previously been measured for bimolecular complexes involving an $R_2O^+H\cdots OR_2$ interaction.[38] Opening up the O−H···OMe angle toward a value of 180° in the cyclized conformers leads to an increase in the hydrogen bond energy (Table 3b). As the number of methylene groups increases, the optimum angle is more readily attained and approches 177.6°, the angle found theoretically in proton bound dimers. Therefore it is possible to compare the formation of a proton-bridged intramolecular species with the bond formation in a proton-bound dimer.

The strength of the hydrogen bonds in similar molecules should, in principle, increase with a decrease in the strain energy. A comparison of the data in Table 3b and Table 5 reveals that, as a rule, opening up the O−H···OMe angle of the closed conformers leads to an increase in the hydrogen bond energy.

(3) Measured PA. Consideration of the above arguments indicates that the proton affinities determined by ICR at 320 K correspond to a mixture of open and cyclized neutral alkanol conformers. Using the K_{oc} data leads to a prediction of compositions of 90, 35, and 20% of the cyclic conformer for **5**−**7**. The difference between the PA of an open bifunctional molecule, PA_{oc}, and its monofunctional analogue, PA_{mono}, can then be ascribed to the enthalpy change associated with the formation of the intramolecular hydrogen bond during protonation, eq 22. As expected, ΔH°_{cycl} values increase with

$$\Delta H^\circ_{cycl} = PA_{oc} - PA_{mono} \qquad (22)$$

increasing ring size of the protonated conformer. Comparable values for ΔH°_{cycl} are obtained for $n = 4$ and 5, which is consistent with the results obtained from the ab initio calculations. As n increases, the optimized O−H···O angle increases to approach 180° asymptotically and the proton bond length decreases markedly (Table 3b). Interestingly for $n = 3$ and 4 the parameters a′−d′ are very similar, in agreement with their comparable ΔH°_{cycl} values.

The experimentally determined hydrogen bond energy of 26.3 kcal·mol^{-1} for the protonated dimethyl ether···methanol proton-bound dimer $(Me_2O\cdots H^+\cdots HOMe)$[39] might be considered appropriate to use as an estimate for the maximum intramolecular hydrogen bond strength in a strain free protonated methoxyalkanol. It is therefore interesting to note that the values for intramolecular hydrogen bond strength determined in the present work are very close to aproaching this value.

(4) Cyclization Entropy. The entropy changes accompanying proton transfer to the ω-methoxyalcohols decrease with increasing chain length. In Table 9 are listed the differences in the standard entropy values of the protonated and unprotonated forms of the compounds examined ($\Delta S^\circ_{1/2}$). Such large negative entropy changes might then be compared to the entropy difference ΔS°_{cy}, between an alkane and cycloalkane of the same carbon number. The values available from the literature for ΔS°_{cy} are −10.7, −13.4, −21.5, and −20.5 cal mol^{-1} K^{-1} for butane/cyclobutane, pentane/cyclopentane, hexane/cyclohexane, and heptane/cycloheptane couples, respectively. It is readily apparent that all of the HPMS determined entropy changes ($\Delta S^\circ_{1/2}$) for protonation of the ω-methoxy alcohols tend to approch the alkane/cycloalkane ΔS°_{cy} values with increasing chain length: −2.5, −14.0, −15.0, and −18.0 cal mol^{-1} K^{-1} for methoxyethanol, methoxypropanol, methoxybutanol, and methoxypentanol, respectively.

It should also be noted that the rotational energy barriers for the $-CH_2OCH_3$ and $-CH_2CH_2OH$ subgroups differ from the $-CH_2CH_2CH_3$ model subgroups which can make direct entropy

TABLE 8: Equilibrium Data for Cyclized Intramolecularly Hydrogen Bonded (M_c) and Open Conformers (M_o) of Methoxyalkanols Obtained from Dilute Solution Studies and Comparison to MO Calculations. PA(M) and $\Delta S°_{1/2}$(M) for M_o and M_c Conformers Derived from Reanalysis of Experimental van't Hoff Plots with and without the Implicit Incorporation of the Neutral Equilibrium Data

	neutral equilib[a]						PA(M_{**})[c]			$\Delta S°_{1/2}$(M_{**})[c]		
compd	ΔH_{oc}[a,b]	ΔS_{oc}[a,b]	K_{320}	K_{400}	K_{500}	K_{600}	oc	cc	st	oc	cc	st
methoxyethanol (**5**)	−3.6	−6.9	9.0	3.0	1.2	0.65	201.8	198.2	199.8	−5.0	2.0	−2.5
	−3.5[d]											
	−3.9[e]	−1.5[e]					201.8[e]	198.5[e]			1.0[e]	
methoxypropanol (**6**)	−3.6	−12.4	0.55	0.18	0.07	0.04	213.3	208.4	213.5	−14.0	−1.5	−14.0
	−5.5[e]											
methoxybutanol (**7**)	−4.3	−16.3	0.25	0.06	0.02	0.01	218.9	214.3	219.3	−15.5	1.5	−15.0
	−5.1[e]											
methoxypentanol (**8**)	−3.1[e]						219.4	214.9	219.4	−18.5	0.0	−18.0
1,2-ethanediol[f]	−2.8[g]	−2.4[g,h]	24.0	10.0	5.0	3.0	197.4	194.6	195.4	−10.5	−8.0	−8.5

[a] $M_o \rightleftharpoons M_i$(equilibrium). [b] Solution data.[43] [c] ** refers to oc, cc, or st. Where oc or cc denotes protonation on open or cyclized neutral conformers, respectively, to a protonated cyclized conformer and st refers to simple treatment of K_{ex} *vs* 1/*T*. See text. [d] MP2/6-31G* calculation.[44] [e] MP2/6-31G* calculation, present work; see Table 5. [f] HPMS data.[2] [g] MP2/(fu)/6-311*G(2d,p)/MP2(fu)/6-31G**.[45] [h] See footnote e for details on torsional/vibration mode analysis: $\Delta S°_{oi} = S_o$(all conformers) − S°(tGg′ conformer) at 298 K.

TABLE 9: Comparison of $S°$ (cal mol^{-1} K^{-1}) for a Number of Processes between Protonated ω-Methoxyalkanols, Neutral ω-Methoxyalkanols ($M_o \rightarrow M_c$), and Alkane ⇌ Cycloalkane (n-$C_mH_{2m+2} \rightarrow c$-$C_mH_{2m}$) Equilibria

	$S°(n\text{-}C_mH_{2m+2} \rightarrow c\text{-}C_mH_{2m})$			
process[a]	calc[b]	expt[c]	m	$\Delta S°$
$2M_o \rightarrow 2M_c$		−7.0		
$2M_c \rightarrow 2M_cH^+$	0.9	2.0		
$2M_o \rightarrow 2M_cH^+$	−0.5	−5.0	4	−10.7
$2M_oH^+ \rightarrow 2M_cH^+$	−3.4			
$3M_o \rightarrow 3M_c$		−12.5		
$3M_c \rightarrow 3M_cH^+$	0.7	−1.5		
$3M_o \rightarrow 3M_cH^+$	−2.0	−14.0	5	−13.4
$3M_oH^+ \rightarrow 3M_cH^+$	−5.0			
$4M_o \rightarrow 4M_c$		−16.5		
$4M_c \rightarrow 4M_cH^+$	0.2	1.5		
$4M_o \rightarrow 4M_cH^+$	−3.5	−15.0	6	−21.5
$4M_oH^+ \rightarrow 4M_cH^+$	−6.6			
$5M_o \rightarrow 5M_c$		−18.5		
$5M_c \rightarrow 5M_cH^+$	0.6	0.0		
$5M_o \rightarrow 5M_cH^+$	−1.7	−18.5	7	−20.5
$5M_oH^+ \rightarrow 5M_cH^+$	−4.4			

[a] The subscript o or c denotes either an open or a cyclized comformer, respectively. [b] Present work. [c] See also Table 8 and text for details.

TABLE 10: Mean Thermal Energies[a] ($\langle E_{th} \rangle$) and Stabilization Energies[a] of Neutral ($\Delta E_{M_{oc}}$) and Protonated Methoxyalkanols ($\Delta E_{M_{oc}}H^+$) Calculated at the HF/6-31G* Level

T (K)		$2M_c$	$2M_cH^+$	$3M_c$	$3M_cH^+$
300	$\langle E_{th} \rangle$	2.3	3.6	2.9	3.3
500	$\langle E_{th} \rangle$	6.6	7.2	8.6	9.2
	$\Delta E_{M_{oc}}$	3.9 (3.6)[b]		5.5 (3.6)[b]	
	$\Delta E_{M_{oc}}H^+$		18.4 (6.3)[c]		20.2 (17.4)[c]

[a] Units: kcal·mol^{-1}. [b] IR solution study.[43] [c] Experimental value: $PA_{oc} - PA_{mono}$ (see text and Table 6).

comparisons difficult. The HPMS measurements were obtained for temperature above 350 K, which leads to some uncertainty as to whether any free internal rotation takes place for the thermalized neutral and protonated species. Some insight may be gained by comparing 1,2-ethanediol with butane for which gas-phase entropies are known. If there is significant intramolecular hydrogen bonding in 1,2-ethanediol, then its entropy should be lower than that of butane. The actual gas-phase entropies are however 75.6 and 74.1 cal mol^{-1} K^{-1} for 1,2-ethanediol and butane, respectively. Using group equivalent methods to correct the former by substitution of $-CH_3$ groups in butane by −OH gives a S° value of 79.9 cal mol^{-1} K^{-1} derived for 1,2-ethanediol compared to the 75.6 cal mol^{-1} K^{-1} found experimentally. The $\Delta S°_{cy}$ for neutral 1,2-ethanediol may then be estimated as −4.3 cal mol^{-1} K^{-1}. This agrees reasonably well with the theoretical estimate of −2.4 mol^{-1} K^{-1} (Table 8) and would imply a significant hindrance to internal rotations in 1,2-ethanediol. A similar situation may be expected in methoxyethanol for which no gas-phase entropy is readily available. A dilute solution spectroscopic study on methoxyethanol in CCl_4 as a function of temperature has yielded a $\Delta S°_{cy}$ of −6.9 cal mol^{-1} K^{-1} and ΔH_{cy} of 3.6 kcal·mol^{-1} for the formation of an intramolecular hydrogen bond. In the current HPMS temperature range there will be comparable concentrations of both open and cyclized conformers in the ion source. However, thermochemical data obtained from dilute solution studies on methoxypropanol and methoxybutanol would suggest that the open conformer is the major species in the temperature range from 400 to 550 K. The HPMS determined protonation $\Delta S°_{1/2}(M_{oc})$ for 1,2-ethanediol of −10.5 cal mol^{-1} K^{-1} is in agreement with the −10.7 cal mol^{-1} K^{-1} estimated from the butane/cyclobutane couple.

The mean internal energy can be estimated from the Stein and Rabinovith algorithm[40] using the set of scaled 6-31G* vibrational frequencies. Those values are shown Table 10 and were calculated at both 298 and 500 K. The values of the potential energy barrier to the rotation around the C−C bonds are unknown and can only be assigned a lower limit based on the values calculated for the energy of stabilization, Δ*E*, of the cyclized form relative to an all trans conformation. For protonated ω-methoxy alcohol ΔE_{MH^+} are clearly greater than at both 298 and 500 K. However, the mean internal energy of neutrals lies 3 kcal·mol^{-1} above ΔE_M at 500 K, which means than a free internal rotation cannot be ruled out for thermalized neutral ω-methoxy alcohols. Indeed the potential energy barriers to the rotation around the C−C bond of 1,2-ethanediol has been calculated to be 7.2 and 14.3 kcal·mol^{-1} for the protonated 1,2-ethanediol.[41] For the other ω-methoxy alcohols studied, the HPMS protonation entropies, $\Delta S°_{1/2}(M_{st})$, are all very close to values predicted from the alkane/cycloalkane model. This would imply that the larger neutral methoxy alcohols exist primarily as an open uncyclized *n*-alkane-like chain due to a more unfavorable 500 K $\Delta G°_{cycl}$ for cyclization in which the $T\Delta S°_{cy}$ term (6.2−9.5 kcal·mol^{-1}) exceeds the intramolecular hydrogen bond energy of ΔH_{oc} of 4−5 kcal·mol^{-1} (Table 6).

Conclusions

In conclusion it seems reasonable to consider that the protonation reaction involves different stable conformers of neutral molecules and only one protonated cyclized conformer. Using ICR equilibrium measurements, compositions of 90, 35, and 20% of the cyclic conformer for 2-methoxyethanol (**5**), 3-methoxybutanol (**6**), and 4-methoxypentanol (**7**), respectively, can be predicted.

The thermochemical analysis reveals a significant number of vibrational frequencies below 500 cm^{-1}. If these motions are considered to be harmonic torsions, only slight errors in the enthalpies result but seriously overestimated entropy values are obtained. This problem has been investigated by Nagy et al.[42] using both free rotation and hindered rotation models for low-energy torsions in the tTt conformer. They found that the amount of the trans conformer in the gas phase is negligible, with use of either one of the above models and in accord with the present findings.

For the smallest methoxy alcohol, the low-frequency motions account for 90% of the vibrational entropy. In this, the discrepancy between the experimental value and the ab initio value is the greatest.

The mixture of different stable conformers of neutral molecules combined with the errors resulting from low frequency is likely the explanation for the difference between the calculated absolute entropies and the experimental values presented in Table 9.

References and Notes

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