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JMS Letters

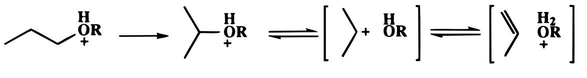
Dear Sir,

Unimolecular Reactions of Protonated Methoxybutanols

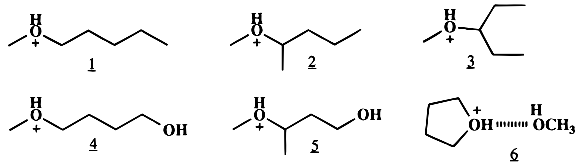
The dissociation of protonated alkyl ethers is preceded by isomerization processes and by H exchange involving the intermediacy of ion–neutral complexes. Depending on the structure of the alkyl chains, the reaction leads to alcohol loss and/or to the formation of a protonated alcohol[1–5] (Scheme 1).

For this reason, the MIKE spectra of isomer protonated methyl pentyl ethers **1**, **2** and **3** are almost identical. In this work, protonated methoxybutanols **4** and **5** (Scheme 2) were studied. It will be shown that replacement of a CH_3 group by a OH group ($1 \rightarrow 4$) completely changes the reaction pathway for the straight-chain analogues. In order to study the unimolecular reactions of ion **4**, the three mechanisms shown in Scheme 3 will be discussed.

The behaviours of metastable ions 4 and 5 are completely different. Whereas the MIKE spectra of ions **1** and **2** are almost identical, those of ions **4** and **5** are significantly different (Fig. 1). The reaction of both ions **4** and **5** leads to water and methanol eliminations but the abundant fragment of *m*/*z*: 63 ($CH_3OH\cdots H^+\cdots OCH_2$) formed when **5** reacts is not observed in the spectrum of ion **4**. Moreover, whereas the dissociation of **5** is preceded by extensive H exchange, no exchange takes place prior to losses of water and methanol in ion **4**. (Spectra obtained in the presence of D_2O: exchange of the hydroxylic hydrogen and protonation by D^+ performed in a CI source of a VG ZAB-2F mass spectrometer; pressure 10^{-5} Torr (1 Torr = 133.3 Pa), temperature 150 °C). Therefore, it is possible to conclude that **4** does not isomerize to **5** and that the reaction of **4**, in contrast to that of **5**, does not occur via the mechanism described for protonated alkyl ethers[1] shown in Scheme 1.



Scheme 1



Scheme 2

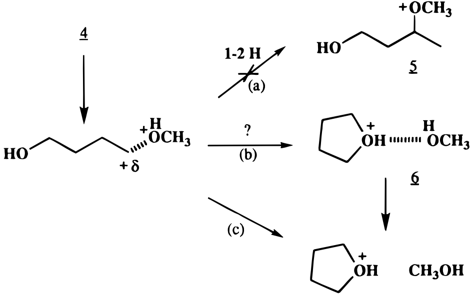
Is ion 6 intermediate in the reaction pathway of 4? An alternative mechanism to form the $[4 - CH_3OH]^+$ fragment ion is shown in Scheme 3. During the stretching of the C—O(H)CH_3 bond, the carbocation thus formed is stabilized by the hydroxyl group to yield the proton-bound dimer **6**.

It has been shown for a long time that the fragmentation in the ion source of protonated butane-1,4-diol[6] and 4-phenoxybutanol[7] yield protonated tetrahydrofuran. In the present case, several results are consistent with the intermediacy of **6** leading to the same fragment ion as follows.

(i) Ion **6** was generated in a chemical ionization ion source by reaction of tetrahydrofuran with methanol in the presence of water (relatively low-pressure chemical ionization conditions: pressure 10^{-5} Torr, temperature 150 °C). In the 2nd FFR, **6** exclusively eliminates methanol. The $[6 - CH_3OH]^+$ and $[4 - CH_3OH]^+$ fragment ions and protonated tetrahydrofuran lead to the same CID spectra.

(ii) Metastable decompositions of both ions **4** and **6** (generated in the ion source as described above) are not preceded by significant H exchange.

(iii) Energetic measurements obtained from equilibrium studies using high-pressure mass spectrometry (HPMS) (ionization source conditions: total pressure 5 Torr with methane as carrier gas; temperature 180–320 °C; for the method, see Refs 8 and 9) indicate that the enhalpies of formation of **4** and **6** are almost the same: on the one hand, the proton affinities (*PA*) of 4-methoxybutanol[9] and 3-methoxybutanol were found to be 219.3 and 218.4 kcal mol^{-1}, respectively, leading to $\Delta H(4) = 48.4$ kcal mol^{-1} and



Scheme 3

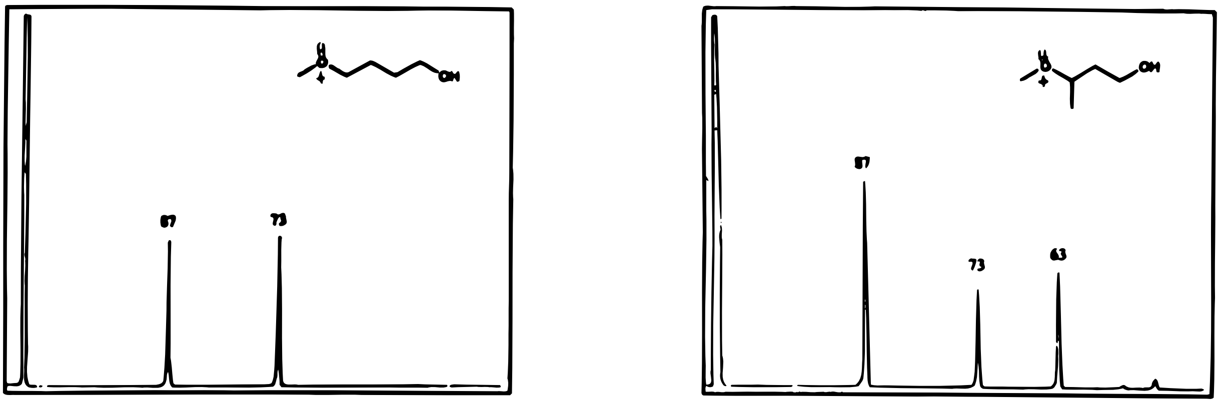


Figure 1. Metastable dissociations of ions **4** and **5** in the second field-free region (FFR) of a VG ZAB-2F mass spectrometer.

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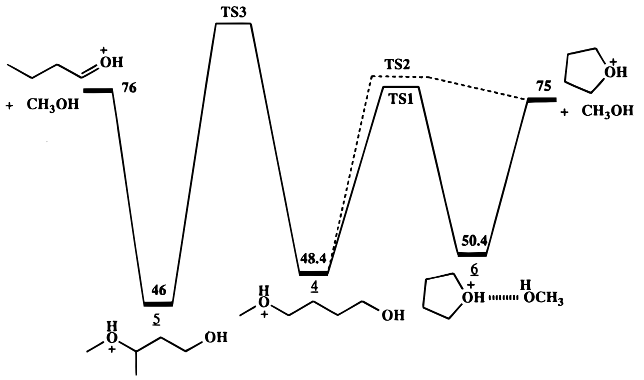

Figure 2. Schematic energy profile for the methanol loss of protonated ions **4**, **5** and **6** (see text).

$\Delta H(\mathbf{5}) = 46$ kcal mol^{-1} (1 kcal = 4.184 kJ). On the other hand, from the enthalpy change ($-\Delta H_{\text{cluster}} = 24.6$ kcal mol^{-1}) associated with the clustering reaction between protonated tetrahydrofuran and methanol, $\Delta H(\mathbf{6})$, was determinated to be 50.4 kcal mol^{-1}. While the formation of protonated tetrahydrofuran as a final product corresponds to a particularly favorable final state,[10] it possesses an energy above those of **4** and **6**.

However, if **6** is intermediate in the reaction of **4**, two other results show that its lifetime is not long. First, the equilibrium reaction of ion **4** with pyrrole shows a straight line in the van't Hoff plot, without any break. The large experimental enthalpy and entropy changes ($\Delta H_r = -10.1$ kcal mol^{-1}, $\Delta S_r = -17$ cal mol^{-1} K^{-1}) characterize a unique covalent structure, **4**. Second, if ion **6** were a long-lived intermediate in the fragmentation of ion **4**, an equilibrium would be observed between [tetrahydrofuran$\cdots H^+ \cdots CH_3OH$], ion **6** and [tetrahydrofuran$\cdots H^+ \cdots CD_3OH$] in the presence of CD_3OH under HPMS conditions. Such equilibrium was not observed.

This indicates that the importance of the intermediate structure **6** is negligible when ion **4** reacts.

The mechanism may be a concerted process leading directly to methanol loss (Fig. 2). The stretching of the H_2C—$O(H)CH_3$ bond can lead to methanol loss via either the transition state TS1 ($\mathbf{4} \rightarrow \mathbf{6} \rightarrow [\mathbf{4} - CH_3OH]^+$) or TS2 ($\mathbf{4} \rightarrow [\mathbf{4} - CH_3OH]^+$) routes (b) and (c) in Scheme 3, respectively. These two transition states may be very close to one another energetically. The stretching of the same bond also may lead to TS3 ($\mathbf{4} \rightarrow \mathbf{5}$), route (a) in Scheme 3. It is known[4, 11] that such processes involving the stretching of a C(primary)—O^+ bond require important energy barriers which can be exemplified by the irreversibility of the isomerization of protonated propyl methyl ether into protonated isopropyl methyl ether.[2–5] Experiments performed in this work indicate that unimolecular reaction of ion **4** is determined by the fact that TS1 and TS2 lie below TS3 in energy. This can be intuitively understood by considering that the reaction $\mathbf{4} \rightarrow [\mathbf{4} - CH_3OH]^+$ corresponds to an intramolecular nucleophilic substitution. However, calculations will be necessary to obtain a better understanding of these processes and establish whether **6** is involved in this concerted elimination.

Yours

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