On the Mechanism of the Ethyl Elimination from the Molecular Ion of 6-Methoxy-1-Hexene

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It is shown by ¹³C and D labelling that the ethyl radical elimination from the molecular ion of 6-methoxy-1-hexene is a very complex process involving at least two different channels. The major channel (80%) is induced by an initial 1,5-hydrogen shift in the molecular ion from C(5) to C(1) leading via a series of steps to methoxycyclohexane, which then undergoes a ring contraction to 2-methyl-1-methoxycyclopentane, being the key intermediate for the ethyl loss. The same key intermediate is formed in the other, minor channel (20%) by ring closure directly following an initial 1,6-hydrogen shift in the molecular ion of 6-methoxy-1-hexene from C(6) to C(1). Collision-induced dissociation experiments on the $[M - ethyl]^+$ ion from 6-methoxy-1-hexene have further established that it has the unique structure of oxygen methyl cationized 2-methylpropen-2-al. This ion is also generated by ethyl loss from the molecular ion of 2-methyl-1-methoxycyclopentane itself, as shown by collision-induced dissociation experiments, thus confirming the key role of the intermediate mentioned.

INTRODUCTION

It has been reported in a previous paper¹ that the molecular ion of methoxycyclohexane eliminates a molecule of methanol via both 1,3- and 1,4-elimination. On the basis of field ionization kinetics measurements and isotopic labelling experiments it has been shown that most of the 1,4-elimination takes place at ion lifetimes $< 10^{-10.1}$ s via the intermediate structure of (double-bond-ionized) 6-methoxy-1-hexene The 1,3-elimination has been proposed to occur via the 1-methoxy-1-hexene structure.

Another decomposition channel of ionized methoxycyclohexane is the elimination of an ethyl radical. However, this process has not been detected for ions with lifetimes $< 10^{-9}$ s. It becomes an important process in the first and second field-free region of the mass spectrometer following both field ionization and electron impact (EI), but because of interference and overlap with signals due to the methanol elimination in some of the D-labelled analogues it was difficult to unravel the mechanism of the ethyl radical elimination. However, for the ethyl loss occurring in the ion source upon EI it could be detected by high-resolution measurements that four hydrogen atoms from the 3(5)-position are largely involved, together with one hydrogen atom from the 2(6)-position, which is in full agreement with the results reported by Klein and Smith.²

The molecular ion of 6-methoxy-1-hexene, the intermediate in the 1,4-elimination of methanol from the molecular ion of methoxycyclohexane, also eliminates an ethyl radical. This process has not been found for ions having lifetimes $< 10^{-9}$ s following field ionization, whereas it is a minor process in the ion source, compared with the loss of a molecule of methanol following EI. In the second field-free region, however, the loss of an ethyl radical becomes five times more abundant than the loss of methanol following EI. This enabled us to study the mechanism of the ethyl loss from ionized 6methoxy-1-hexene in detail, as will be discussed below.

RESULTS AND DISCUSSION

The mass-analysed ion kinetic energy (MIKE) spectrum of the EI-generated molecular ion of 6-methoxy-1hexene (1) shows two intense peaks. The major peak corresponds to loss of an ethyl radical from the molecular ion to give m/z 85 (relative intensity 100%), while the minor peak is due to loss of methanol leading to m/z82 (relative intensity 20%). Small signals (relative intensity 1-2%) have been found for the losses of a methyl radical and a molecule of ethene.

From D labelling in the 4-position of 6-methoxy-1hexene (1f), a compound available from earlier studies,¹ it was evident that the hydrogen atoms of this position are largely retained ($\sim 72\%$) in the eliminated ethyl radical. This observation suggests that the ethyl radical originates from the middle of the alkyl chain.

The following labelled compounds have been studied:

$$H_{2}C = CHCH_{2}CH_{2}CH_{2}CH_{2}CH_{2}OCH_{3}$$

$$H_{2}^{13}C = CHCH_{2}CH_{2}CH_{2}CH_{2}OCH_{3}$$

$$Ia$$

$$H_{2}C = CHCH_{2}CH_{2}^{13}CH_{2}CH_{2}OCH_{3}$$

$$Ib$$

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¹³C Labelling

Table 1 lists the relative intensities of peaks in the MIKE spectra of the ¹³C-labelled analogues of 6-methoxy-1-hexene, corresponding to the channel of ethyl radical loss.

 13 C Labelling in the 5-position (1b) shows that this carbon atom is retained for 57% in the eliminated ethyl group, which means that at some stage of the reaction a ring closed structure has been formed.

¹³C Labelling in the 1-position (1a) shows that the remaining 41% of the eliminated ethyl radical contains a carbon atom from the 1-position. A possible explanation of these results is presented in Scheme 1 (pathway 1). Following a 1,5-hydride shift from C(6) to C(2) in ionized 6-methoxy-1-hexene, ring closure to methoxycyclohexane, ring opening and successive 1,5-hydrogen shift from C(5)[C(1)] to C(1)[C(5)] and 1,4-hydrogen shift from C(2)[C(4)] to C(5)[C(1)], a ring closure to 2methyl-1-methoxycyclopentane can take place (sequence $a' \rightarrow b \rightarrow c \rightarrow d \rightarrow e \rightarrow f \rightarrow g$ in Scheme 1).

From this structure an ethyl radical can be eliminated eventually as shown in Scheme 1 (sequence $g \rightarrow h \rightarrow i$). It should be noted here that the sequence of reactions

Table 1.	Relative intensities ^a concerning the loss molecular ions	of peaks in of an ethyl of 6	the MIKE radical fre -methoxy-1-	spectra om the hexene,	
	$H_2C^1=C^2H-C^3H_2C^4H_2C^5H_2C^6H_2OCH_3$, and its ¹³ C-labelled analogues, following 70 eV EI				

		m/z	
Labelled position	85	86	87
Unlabelled	99	1	
1- ¹³ C	40	58	2
5- ¹³ C	57	41	2
^a Σ 85–87 = 100.			

 $c \rightarrow d \rightarrow e \rightarrow f \rightarrow g \rightarrow h \rightarrow i$ in this scheme is fully analogous to that proposed by Audier et al.³ for the ethyl elimination from the molecular ion of aminocyclohexane on the basis of D labelling experiments. At any rate, the mechanism proposed in Scheme 1 1), $a \to a' \to b \to c \to d \to e \to f \to g \to h \to i$, (pathway would predict a complete equivalence of the carbon atoms of the 1- and 5-position in the ethyl elimination. However, as the data in Table 1 show, there is about 20% preference for retention of the carbon atom from the 5-position in the eliminated ethyl radical. This must imply another mechanism in addition to that given in Scheme 1, which might well be due to a direct ring closure to 2-methyl-1-methoxycyclopentane following a 1,6-hydride shift from C(6) to C(1) in ionized 6methoxy-1-hexene as pictured in Scheme 1, sequence $a \rightarrow a'' \rightarrow j \rightarrow f \rightarrow g$ (pathway 2). The ¹³C labelling results then would indicate that about 80% of the 6-methoxy-1-hexene ions have passed through the methoxycyclohexane structure prior to formation of 2-methyl-1methoxycyclopentane, while the remaining 20% have assumed directly the latter structure prior to the ethyl radical elimination.

Collision-induced dissociation (CID)

The mechanisms presented in Scheme 1 for ethyl loss from the molecular ion of 6-methoxy-1-hexene both lead eventually to the same structure, i.e. ion *i*. In order to establish that the $[M - C_2H_5]^+$ ion has indeed the structure of ion *i*, the method of CID, advanced by McLafferty and his co-workers over many years,^{4,5} has been applied.

Figure 1 shows the CID spectra of the $[M - C_2H_5]^+$ ions from 6-methoxy-1-hexene (1), methoxycyclohexane (2) and 2-methyl-1-methoxycyclopentane (3) and for the purpose of reference the $[M - OCH_3]^+$ ions from 3,3dimethoxy-2-methyl-1-propene (4) and 4,4-dimethoxy-1butene (5).

As can be seen, the CID spectra of 1-4 are very similar, if not identical, whereas the CID spectrum of 5 is slightly different with regard to the peak corresponding to an ion having a m/z 45 value. These observations allow the conclusion that the $[M - C_2H_5]^+$ ions from 6-methoxy-1-hexene have indeed the structure of ion i, as suggested in Scheme 1. Another important observation is that the CID spectrum of the $[M - C_2H_5]^+$ ion 6-methoxy-1-hexene from remains essentially unchanged when the electron energy is varied from 70 eV down to 13 eV (compare Fig. 1(f), which is the CID spectrum following 13 eV EI, with Fig. 1(a) representing the CID spectrum following 70 eV EI). This strongly suggests that the ion structure *i* is unique for the $[M - C_2H_5]^+$ ions from 6-methoxy-1-hexene.

D Labelling

Although the ¹³C labelling and CID results, described above, are highly informative with regard to the occurrence of intermediates in the $[M - C_2H_5]^+$ ion formation and its corresponding structure, respectively, it will be clear that prior to the eventual elimination of



Scheme 1. Mechanism for the loss of an ethyl radical from ionized 6-methoxy-1-hexene proposed on the basis of ¹³C labelling in the 1and 5-position in combination with CID experiments.

the C₂H₅ radical many hydrogen shifts are required following ionization of 6-methoxy-1-hexene. For more detailed mechanistic information than already given in Scheme 1, the deuterated analogues 1c-1j have been studied as well. Table 2 summarizes the relative intensities of the peaks concerning the loss of ethyl in the MIKE spectra of the deuterated analogues 1c-1j. Apart from the hydrogen atoms of the methoxy group which are fully retained in the $[M - ethyl]^+$ ion, the hydrogen atoms of all other positions appear to participate in the ethyl radical elimination. However, the results obtained are not in line with complete randomization of the hydrogens of positions 1 to 6. This is obvious if the per-centages for losses of C_2H_5 , C_2H_4D and $C_2H_3D_2$. from the molecular ions of the $4,4-d_2, 5,5-d_2, 6,6-d_2$ analogues of 6-methoxy-1-hexene to give the ions m/z87, m/z 86 and m/z 85, respectively, are compared with each other (see Table 2). Note, for example, the abundant loss of $C_2H_3D_2$ from the ionized 4,4- d_2 analogue to give m/z 85, which is not observed to such a large extent for the $5,5-d_2$ and $6,6-d_2$ analogues. In that respect the $4,4-d_2$ analogue seems to occupy a special position, as the hydrogen atom of position 4 is also mainly (95%) lost in the methanol elimination channel occurring as the major process in the ion source at 15 eV. It is difficult to account quantitatively for the Dlabel distributions in the eliminated ethyl radicals from the molecular ions of compounds 1c-1j. However, a reasonably qualitative agreement between the observed and predicted D-label distributions in the ethyl radicals is obtained by a mechanistic model in which the following assumptions have been made:

(i) 80% of the molecular ions of 6-methoxy-1-hexene start with a 1,5 hydrogen shift from C(5) to C(1), which after equilibration of positions 1 and 5 in ion a' further undergo successive hydrogen shifts from C(5) to C(1), C(6) to C(2), C(4) to oxygen and C(1) to C(4), followed by ring closure between C(1) and C(6), then complete exchange between the hydrogen atoms of positions 2 and 5 (ion $o \neq i$ ion p) and eventual transfer of the hydrogen atom at oxygen (originally from the 4-position)

Table 2. Relative intensities^{a,b} of peaks in the MIKE spectra concerning the loss of an ethyl radical from the molecular ions of 6-methoxy-1-hexene, H₂C¹=C²H-C³H₂C⁴H₂C⁵H₂C⁶H₂OCH₃ and its D-labelled analogues, following 70 eV E1

Labelled			m/z		
position	85	86	87	88	89
<i>d</i> _o (1)	99 (100)	1 (-)			<u> </u>
1-d ₁ (1c)	32 (42)	67 (58)	1 (-)		
1,1-d ₂ (1d)	13 (18)	37 (48)	49 (34)	1 ()	
2,6,6-d ₃ (1e) ^c		46 (27)	44 (67)	10 (7)	_
4,4-d ₂ (1f)	72 (70)	21 (30)	7 (-)		
4,4,6,6- <i>d</i> ₄ (1g)°		39 (27)	49 (67)	10 (7)	2
5,5-d ₂ (1h)	28 (38)	48 (48)	23 (14)	1 (-)	_
6,6-d ₂ (1i)	2	54 (50)	43 (50)	1 (-)	
$-OCD_3(1j)$			_	99 (100)	1

^a Σ 85–89 = 100.

 $^{\rm b}$ The calculated intensities on the basis of 80% pathway 1 (Schemes 1 and 2) and 20% pathway 2 (Scheme 1) are given in parentheses.

^c Corrected for methanol loss, neglecting an isotope effect.



Figure 1. CID-MIKE spectra of the ions m/z 85 following 70 eV or 13 eV EI from (a) 6-methoxy-1-hexene (at 70 eV); (b) methoxy-cyclohexane; (c) 2-methyl-1-methoxycyclopentane; (d) 3,3-dimethoxy-2-methyl-1-propene; (e) 4,4-dimethoxy-1-butene and (f) 6-methoxy-1-hexene (at 13 eV).

either to C(2) or C(5) (see Scheme 2) to generate the molecular ion of methoxycyclohexane. This ion can eliminate the ethyl radical via pathway 1 as presented in Scheme 1 by the sequence $c \rightarrow d \rightarrow e \rightarrow f \rightarrow g \rightarrow h \rightarrow i$.

(ii) 20% of the molecular ions of 6-methoxy-1-hexene start with a 1,6-hydride shift from C(6) to C(1), followed by ring closure to 2-methyl-1-methoxycyclopentane and elimination of an ethyl radical via pathway 2 (Scheme 1, sequence $g \rightarrow h \rightarrow i$).

Calculations of the D-label distributions in the eliminated ethyl radicals from compounds 1c-1j based upon this model and its assumptions predict the percentages which are given between parentheses in Table 2. As can be seen, these calculated percentages agree rather well with the observed percentages for the variously Dlabelled ethyl radicals lost.

We feel, therefore, quite confident that the mechanistic details, proposed in Schemes 1 and 2 on the basis of



Scheme 2. Elaboration of the sequence of reactions $a' \rightarrow b \rightarrow c$ in Scheme 1 proposed on the basis of D labelling results. NB. Sequence $a' \rightarrow k \rightarrow l$ could also take place as sequence $a' \rightarrow l \rightarrow k$.

the ${}^{13}C$ and D labelling results, are valid for the elimination of ethyl from ionized 6-methoxy-1-hexene.

CONCLUSIONS

The present work, like many other reported investigations, has shown that application of the method of CID is essential in mechanistic studies where the structures of generated product ions must be known. Equally important in such studies is the use of stable isotopic labelling, which can provide a detailed insight into the routes of formation of the product ions, i.e. the dynamics of a fragmentation process, as clearly demonstrated in this paper.

EXPERIMENTAL

All measurements were performed on a reversegeometry VG ZAB-2HF high field mass spectrometer coupled to a VG 11/250 data system (VG Analytical Ltd, Manchester, UK). The operating parameters were: accelerating potential 8 kV, electron energy 13-70 eV, ion repeller 0 V and ion source temperature 150 °C.

The samples were introduced via a heated inlet system at $150 \,^{\circ}$ C. During the high-resolution EI mass spectrometric measurements a resolving power of 25 000 (10% valley definition) was used.

The MIKE data were obtained by varying the electrostatic voltage, the main beam energy being 8 keV.

CID-MIKE spectra were obtained using helium as collision gas at a pressure such that the intensity of the main beam was reduced by 50%.

Preparation of compounds

6-Methoxy-1-hexene (1), 4,4-dideutero-6-methoxy-1-hexene (1f), and methoxycyclohexane (2). These were available from earlier studies.¹ All compounds used were purified by gas chromatography, using a 20% Reoplex 400 column and/or an 0V 17 silicone column. Positions of D and ¹³C labelling were checked by nuclear magnetic resonance (NMR). Since the abundance of the $[M - H]^+$ ion is relatively high, even at low electron energy, percentages of D labelling were measured by NMR. Percentages of ¹³C labelling were measured in the starting material, assuming no loss of label in the last step of the synthesis.

 1^{-13} C-6-Methoxy-1-hexene (1a). This was obtained by reaction of 5-methoxy-1-pentanal⁶ with triphenyl ¹³C-methyl phosphonium iodide⁷ (90% ¹³C).

5-1³C-6-Methoxy-1-hexene (1b). Cyclopropyl methyl bromide was treated with magnesium and ${}^{13}CO_2$ (from Ba ${}^{13}CO_3$) to yield 4-pentenoic- ${}^{13}C$ -acid.⁸ After reduction with LAH and bromination with PBr₃,5- ${}^{13}C$ -5-bromo-1-pentene was obtained. This was treated again with magnesium, then CO₂, reduced with LAH and converted into the methyl ether by established methods¹ (90% ${}^{13}C$).

1,1-Dideutero-6-methoxy-1-hexene (1d). 5-Methoxy-1-pentanal was treated with triphenyl trideuteromethyl phosphonium iodide to yield 1,1-dideutero-6-methoxy-1hexene⁶ (77% D).

2,6,6-Trideutero-6-methoxy-1-hexene (1e). 1,1,5,5-Tetradeuteropentane-1,5-diol⁹ was treated with 1 eq. of sodium methoxide, followed by oxidation with chromium trioxide to yield 1,5,5-trideutero-5-methoxy-1pentanal.⁶ This was converted into 2,6,6-trideutero-6methoxy-1-hexene by a Wittig reaction with triphenyl methyl phosphonium iodide⁷ (>95% D).

5,5-Dideutero-6-methyl-1-hexene (1h). 2,2-Dideutero-1,3dibromopropane⁹ was treated with 1 eq. of sodium methoxide followed by reaction with allylmagnesium bromide to give 5,5-dideutero-6-methoxy-1-hexene¹⁰ (>95% D).

6,6-Dideutero-6-methoxy-1-hexene (1i). 5-Hexenoic acid, obtained by a Grignard reaction of 5-bromo-1-pentene with CO_2 , was reduced with LAD to give 1,1-dideutero-5-hexene-1-ol, which was converted into 6,6-dideutero-6-methoxy-1-hexene by established methods¹ (>95% D).

4,4,6,6-Tetradeutero-6-methoxy-1-hexene (1g). This compound was synthesized as described for 1h, starting with 1,1,3,3-tetradeutero-1,3-dibromopropane⁹ (>95% D).

2-Methyl-1-methoxy-cyclopentane (3). 2-Methylcyclopentanone was reduced with LAH and converted into the methyl ether by established methods. **3,3-Dimethoxy-2-methyl-1-propene** (4). Isobutyraldehyde dimethylacetal was brominated¹¹ and dehydrohalogenated to give 3,3-dimethoxy-2-methyl-1-propene.

4,4-Dimethoxy-1-butene (5). Reaction of allylmagnesium bromide with trimethyl orthoformate gave 4,4dimethoxy-1-butene.12

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