ORGANIC MASS SPECTROMETRY, VOL. 24, 977–983 (1989)

Fragmentation of Acylium Ions from Methyl Levulinate. Isomerization Processes Involving Carbon and Oxygen Atoms of Both Carbonyl Groups

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The fragmentations of the acylium ions $O{=}C^+{-}CH_2{-}CH_2{-}CO_2CH_3$ and $O{=}C^+{-}CH_2{-}CH_2{-}COCH_3$ generated from methyl levulinate are governed extensively by the interaction of the two carbonyl groups. Both species eliminate a molecule of CO unimolecularly and under CID conditions. The results derived from measurements of ^{13}C and ^{18}O labelled precursors, together with kinetic energy release values, have been used to study the mechanisms. In the first of these acylium ions, both carbonyl groups are equivalent; this phenomenon can be the result of a 1,4 methoxy shift. In the second acylium ion, only the oxygen atoms change their positions; this isomerization occurs via the $[M - H]^+$ ion of γ-valerolactone. Some other fragmentation processes also discussed in relation to ^2H labelling are the formation of the $[M - COOCH_3]^+$ ion and the loss of $HCOOCH_3$ in the collision-induced dissociation mass spectra of the first acylium ion, and the formation of the $[CH_3CO]^+$ ion and the loss of H_2O for the second one.

INTRODUCTION

The recent publication of a mass spectrometric study of levulinic acid[1] prompted us to report some of our results concerning the fragmentation of methyl levulinate. To our knowledge, the only previous studies on levulinic esters have been brief studies of the fragmentation of ethyl levulinate by 70 eV electrons, without isotopic labelling.[2,3] Fig. 1(a) shows the 70 eV mass spectrum of methyl levulinate. It is proposed in Ref. 2 that the spectrum is 'virtually free of skeletal rearrangement fragments'. This is confirmed for $[M - CH_3]^+$ and $[M - OCH_3]^+$ ions by isotopic labelling (*vide infra*). In other respects these two even-electron species, 'carbonyl acylium ions', are potentially interesting. Indeed we have recently reported[4] that the smaller members of these series show an unexpected isomerization pathway related to an exchange of the oxygen atoms before fragmentation.

We have studied the structure and fragmentation pathways of metastable $[M - CH_3]^+$ and $[M - OCH_3]^+$ ions (mass-analysed ion kinetic energy (MIKE) spectra) in the 2nd field-free region of a BE mass spectrometer, and of the same ions activated by collisions (MIKE-CID spectra) making use of D, ^{18}O and ^{13}C isotopic labelling. We also determined the values of the kinetic energy release for some metastable transitions. An analogous study of $M^{+\cdot}$ ions is not of interest, as the only abundant fragmentation in these energy ranges is the loss of methanol: specific deuterium labelling shows that this is a specific process with regard to the departing methoxy group, but not with regard to the hydrogen atom lost at the same time.

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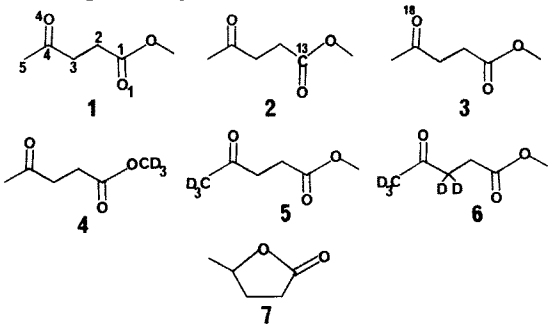
0030–493X/89/110977–07 $05.00

RESULTS AND DISCUSSION

This study relates to the methyl levulinates **1–6**. We also examined the $[M - H]^+$ ions from γ-valerolactone (**7**) because these ions are isomers of the $[M - OCH_3]^+$ ions from **1**.

Looking at the 70 eV mass spectra of **1–3** and **5** (Fig. 1(a)–(d)) it is evident that the only possibilities for loss of CH_3 and OCH_3 are direct cleavages of the C(4)—C(5) bond and the C(1)—OCH_3 bond, respectively. We suppose that the more energetic ions fragmenting in the 2nd field-free region, with or without extra energy, contain the same atoms as these stable ions not fragmenting before detection.



The only major fragmentation process in the MIKE spectrum of $[M - CH_3]^+$ ions is the loss of CO, whereas the collision spectrum shows two other abundant ions: $[COOCH_3]^+$ and, formally, $[M - CH_3$

Received 26 June 1989
Accepted 7 July 1989

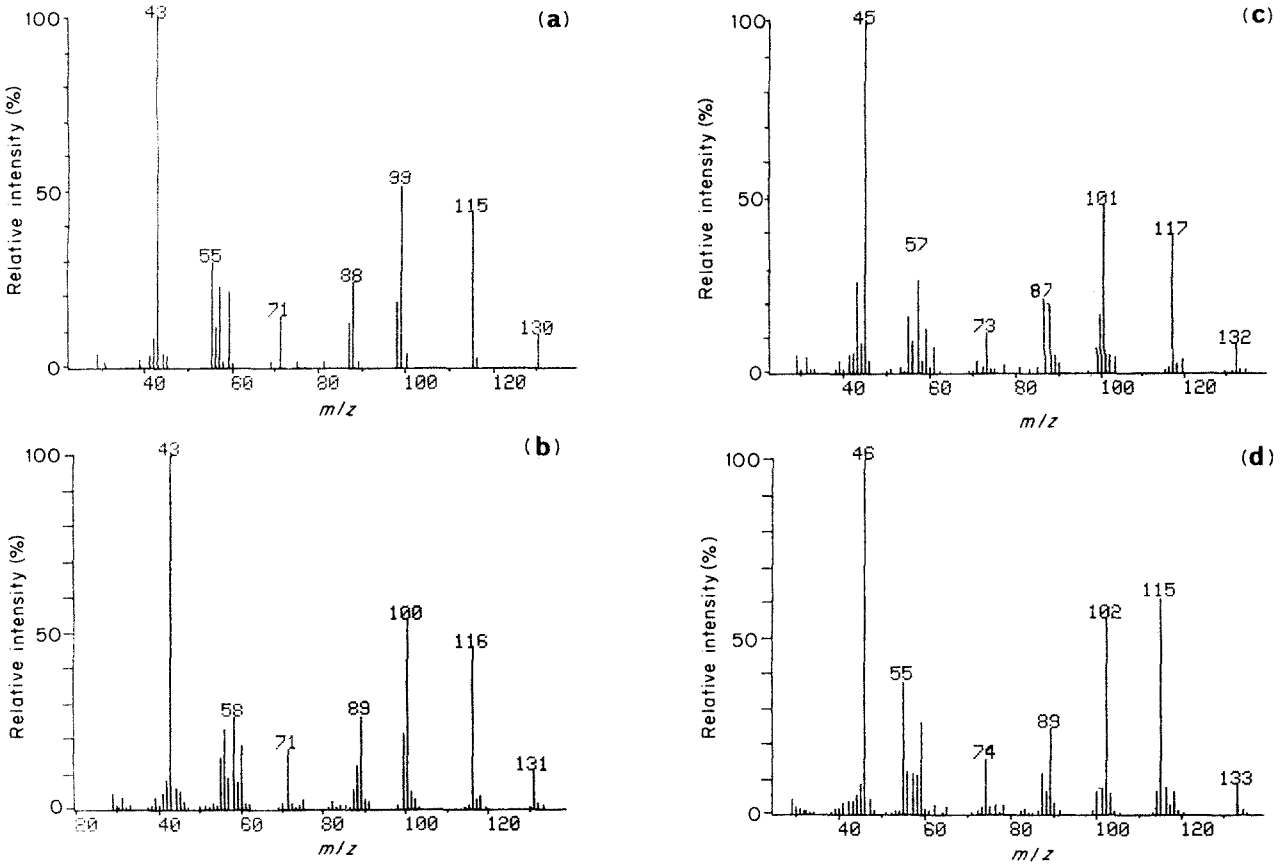


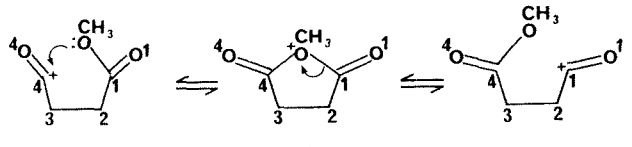
Figure 1. 70 eV Mass spectra of (a) methyl levulinate (**1**); (b) **2**; (c) **3** corrected for 30% of **1**; and (d) **5**.

$-(HCOOCH_3)]^+$. Experimental results for $[M - CH_3]^+$ labelled ions from **2–4** and **6** are reported in Table 1. For $[M - OCH_3]^+$ ions, three fragmentation pathways are of interest in the MIKE mass spectra and MIKE-CID mass spectra: loss of H_2O, loss of CO and formation of $[CH_3CO]^+$ ions. The results for labelled compounds **2**, **3**, **5** and **6** are summarized in Table 2.

FRAGMENTATION OF THE $[M - CH_3]^+$ IONS

Loss of CO

It is seen from Table 1 that the MIKE mass spectra and MIKE-CID mass spectra for ^{13}C and ^{18}O labelled ions are very similar for this process. We can consider, as a first approximation, that C(4) and C(1) on one hand, and O(4) and O(1) on the other hand, are equally involved in this loss. This result leads us to believe that the two carbonyl groups remain intact, and to propose the following mechanism (Scheme 1) which is formally a 1,4-transfer of the methoxy group.



a

Scheme 1

The supposed intermediate structure (*a*) should allow loss of the two carbonyl groups in equal proportion. Unfortunately our attempts to generate *a* by methylation of succinic anhydride in the spectrometer have failed.

Formation of $[COOCH_3]^+$ ions—loss of $HCOOCH_3$

For these two high-energy processes, the MIKE-CID mass spectra of $[M - CH_3]^+$ ions from **4** and **6** (Table 1) show that the methoxy groups are eliminated without any rearrangement. With regard to the carbonyl groups, the data of Table 1 show that the participation of C(1) and O(1) atoms on the one hand, and C(4) and O(4) atoms on the other, are nearly the same. This leads to the conclusion that, as in the case of CO loss, these groups remain intact and are equally involved, at least for the formation of $[COOCH_3]^+$ ions. This equivalence is again explained by the mechanism presented in Scheme 1.

In the case of the $HCOOCH_3$ loss, the elimination of C(4)O(4) is somewhat larger. The mechanism seems to be more complex, since hydrogen transfer is not specific, as can be seen from the spectrum of the $[M - CD_3]^+$ ions from **6**: the hydrogen atoms are transferred from C(2) and C(3) in a 3:2 ratio.

FRAGMENTATION OF $[M - OCH_3]^+$ IONS

Loss of H_2O

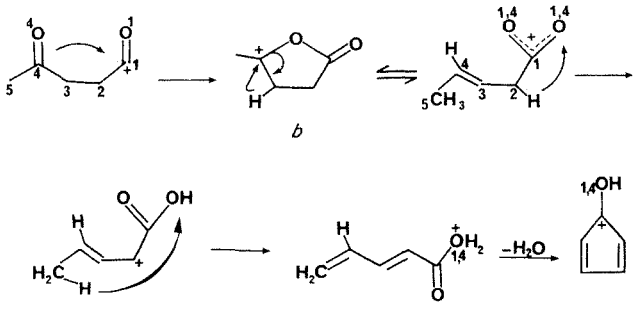
In the MIKE and CID mass spectra the oxygen atom O(1) is eliminated slightly more than the O(4) (as H_2O)

Table 1. MIKE and MIKE-CID fragmentations of $[M - CH_3]^+$ ions from compounds 2–4 and 6. Each set containing ions of the same composition is normalized to 100

		$-CO$ *m/z 88*	$-{}^{13}CO$ *m/z 87*	$[COOCH_3]^+$ *m/z 59*	$[{}^{13}COOCH_3]^+$ *m/z 60*	$-HCOOCH_3$ *m/z 56*	$-H{}^{13}COOCH_3$ *m/z 55*
$[2 - CH_3]^+$ *m/z* 116	MIKE	53[a]	47				
	MIKE-CID	52	48	49	51	54	46
		$-C{}^{18}O$ *m/z 87*	$-CO$ *m/z 89*	$[C{}^{18}OOCH_3]^+$ *m/z 61*	$[COOCH_3]^+$ *m/z 59*	$-HC{}^{18}OOCH_3$ *m/z 55*	$-HCOOCH_3$ *m/z 57*
$[3 - CH_3]^+$ *m/z* 117	MIKE	49	51				
	MIKE-CID	49	51	49	51	53	47
				$[COOCD_3]^+$ *m/z 62*		$-HCOOCD_3$ *m/z 55*	
$[4 - CH_3]^+$ *m/z* 118	MIKE-CID			100		100	
				$[COOCH_3]^+$ *m/z 59*		$-DCOOCH_3$ *m/z 56*	$-HCOOCH_3$ *m/z 57*
$[6 - CD_3]^+$ *m/z* 117	MIKE-CID			100		42	58

[a] Relative abundance, within the set.

(Table 2). A mechanism leading to the H_2O loss and making O(4) and O(1) indistinguishable is proposed in Scheme 2. It involves closing and opening of the cyclic ion *b* (the $[M - H]^+$ ion from γ-valerolactone (**7**)) followed by H transfers. The final state could be the particularly stable cyclopentadienyl ion.



b

Scheme 2

Indeed, $[M - H]^+$ ions from γ-valerolactone exhibit MIKE and CID mass spectra qualitatively comparable with those of $[M - OCH_3]^+$ ions of methyl levulinate. The relative abundances of the ions obtained by collisions, with a 750 V potential applied to the collision cell, are nearly the same, as can be seen from Table 3.

Scheme 2 is corroborated by the origin of the H atoms lost as H_2O, essentially from positions 5 and 2, as can be calculated from the data of Table 2, C(2):C(3):C(5) = 33:4:63. The slight predominance of $H_2O(1)$ loss might be due to the occurrence of an isotope effect of ^{18}O in the hydrogen atom transfers. This is suggested by the values of the kinetic energy release (see Table 4) for the H_2O loss from $[M - H]^+$ ions from γ-valerolactone (structure *b*, Scheme 2), and the H_2O and $H_2{}^{18}O$ losses from $[M - OCH_3]^+$ ions from **3**: 11, 14, and 14 meV, respectively.

Loss of CO

Owing to the lack of resolution for the ^{13}C-labelled compound, we can consider that the participation of C(1) in CO loss is greater than 95%.

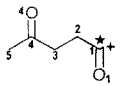
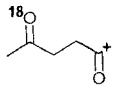
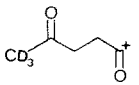
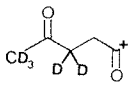
With regard to the oxygen atoms, we see from Table 2 that both oxygen atoms are involved, O(1) being eliminated to a slightly greater extent than O(4). So the major fragments eliminated are C(1)O(1) and C(1)O(4), whilst C(4)O(1) and C(4)O(4) are minor participants. A reasonable set of mechanisms seems to be as follows (Schemes 3 and 4).

(i) The direct breaking of the C(1)—C(2) bond, eliminating C(1)O(1).

(ii) A set of reversible reactions of formation and opening of the cyclic ion *b*, previously proposed for the H_2O loss (Scheme 2). This allows in a first step the exchange of the oxygen atoms between C(1) and C(4), followed by the direct rupture of the C(1)—C(2) bond (Scheme 3).

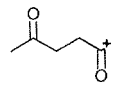
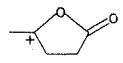
(iii) A 1,4 methyl transfer ($c \rightarrow f$) of low probability, allowing loss of C(4)O(4) by cleavage of the C(3)—C(4) bond (Scheme 4).

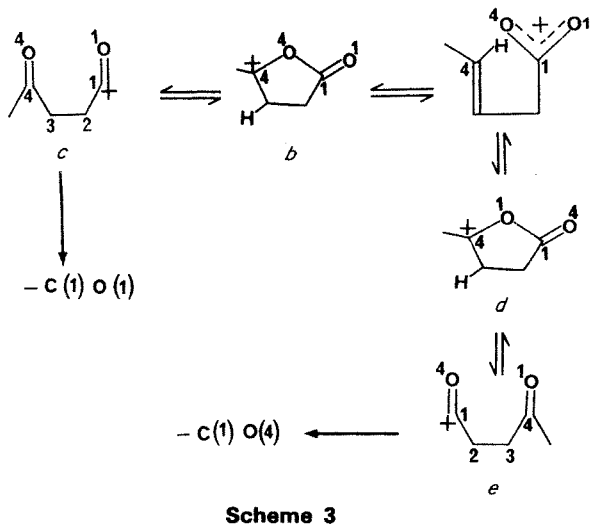
Table 2. MIKE and MIKE-CID fragmentations of $[M - OCH_3]^+$ ions from compounds 2, 3, 5 and 6. Each set containing ions of the same composition is normalized to 100

					−CO *m/z 72*	$-^{13}CO$ *m/z 71*		$[CH_3{}^{13}CO]^+$ *m/z 44*		$[CH_3CO]^+$ *m/z 43*	
$[\mathbf{2} - OCH_3]^+$ *m/z* 100	MIKE				7[a]	93		40		60	
	MIKE-CID				6[a]	94		–		100	
		$-H_2O$ *m/z 83*	$-H_2{}^{18}O$ *m/z 81*		$-C^{18}O$ *m/z 71*	−CO *m/z 73*		$[CH_3CO]^+$ *m/z 43*		$[CH_3C^{18}O]^+$ *m/z 45*	
$[\mathbf{3} - OCH_3]^+$ *m/z* 101	MIKE	53	47		45	55		43		57	
	MIKE-CID	55	45		44	56		42		58	
		$-D_2O$ *m/z 82*	−HDO *m/z 83*	$-H_2O$ *m/z 84*			$[CD_3CO]^+$ *m/z 46*	$[CD_2HCO]^+$ *m/z 45*	$[CDH_2CO]^+$ *m/z 44*	$[CH_3CO]^+$ *m/z 43*	$[CH_2CO]^+$ *m/z 42*
$[\mathbf{5} - OCH_3]^+$ *m/z* 102	MIKE	32	58	10			28	47	21	4	–
	MIKE-CID	32	61	7			69	13	9	–	9
		$-D_2O$ *m/z 84*	−HDO *m/z 85*	$-H_2O$ *m/z 86*			$[CD_3CO]^+$ *m/z 46*		$[CD_2HCO]^+$ *m/z 45*		$[CDH_2CO]^+$ *m/z 44*
$[\mathbf{6} - OCH_3]^+$ *m/z* 104	MIKE	37	57	6			45		48		7
	MIKE-CID	39	56	5			71		20		9

[a] Maximum value, owing to the lack of resolution for the ^{13}C compound.

Table 3. Pure CA spectra of the $[M - OCH_3]^+$ ions from compound 1, and of the $[M - H]^+$ ions (*b*) from compound 7

Compound	*m/z* 81	*m/z* 71	*m/z* 43
 $[1 - OCH_3]^+$	11[a]	22	67
 *b*	11	24	65



Scheme 3

Scheme 4

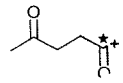
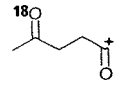
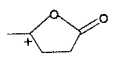
(iv) A 1,4 methyl transfer in *e*, or starting from *f*, the set of processes of Scheme 3, leading to C(4)O(1) loss by cleavage of the C(3)—C(4) bond.

To verify the reactions of Scheme 3, we have measured the kinetic energy release (T) in metastable loss of CO from the $[M - H]^+$ ion *b* from γ-valerolactone (**7**) and the $[M - OCH_3]^+$ ions from **2** and **3**. Both peaks are composite, except for the loss of ^{12}CO from the $[2 - OCH_3]^+$ ions. The T values are reported in Table 4 and are comparable for the two components.

Looking at the curves n(T) *vs.* T for CO loss from $[2 - OCH_3]^+$ (Fig. 2(a)), we note the occurrence of a very weak, narrow component for the ^{13}CO loss. We attribute this weak component, corresponding to a T_p value of 10–20 meV, to the direct cleavage of the C(1)—C(2) bond, giving a slight C(1)O(1) loss, whereas the same cleavage following a number of reversible closings and openings of the ring *b* (Scheme 3) gives rise to C(1)O(1) and C(1)O(4) losses with a T_p value of 240 meV. On the other hand, the absence of a broad component for ^{12}CO loss from the same ion suggests that a C(4)O(1) loss does not occur, but a C(4)O(4) loss does, which implies only a 1,4 methyl shift before C(3)—C(4) bond cleavage.

In the same manner, the T_p value of ~10 meV in the n(T) curve for $C^{18}O$ loss from $[3 - OCH_3]^+$ (Fig. 2(b)) can be ascribed to the C(4)O(4) loss. The narrow component of the n(T) curve for the $C^{16}O$ loss can be assigned to the direct C(1)O(1) loss, as in the case of ^{13}CO loss.

Table 4. Kinetic energy (T_p in meV) released in metastable fragmentations (loss of H_2O, loss of CO, formation of $[CH_3CO]^+$) from $[M - OCH_3]^+$ ions of compounds 2 and 3, and from the $[M - H]^+$ ion *b* from γ-valerolactone (compound 7)

	$-H_2O$		$-CO$		$[CH_3CO]^+$	
			$-CO$	$-^{13}CO$	$[CH_3{}^{13}CO]^+$	$[CH_3CO]^+$
$[2 - OCH_3]^+$			13 –	(~10)[a] 240	12 –	(0–10) 93
	$-H_2O$	$-H_2{}^{18}O$	$-C^{18}O$	$-CO$	$[CH_3CO]^+$	$[CH_3C^{18}O]^+$
$[3 - OCH_3]^+$	14	14	~10 240	~10 240	4 (~80)	57 –
		11		20		8
b		(~110)		230		70

[a] The parentheses indicate a very minor component of the composite peak.

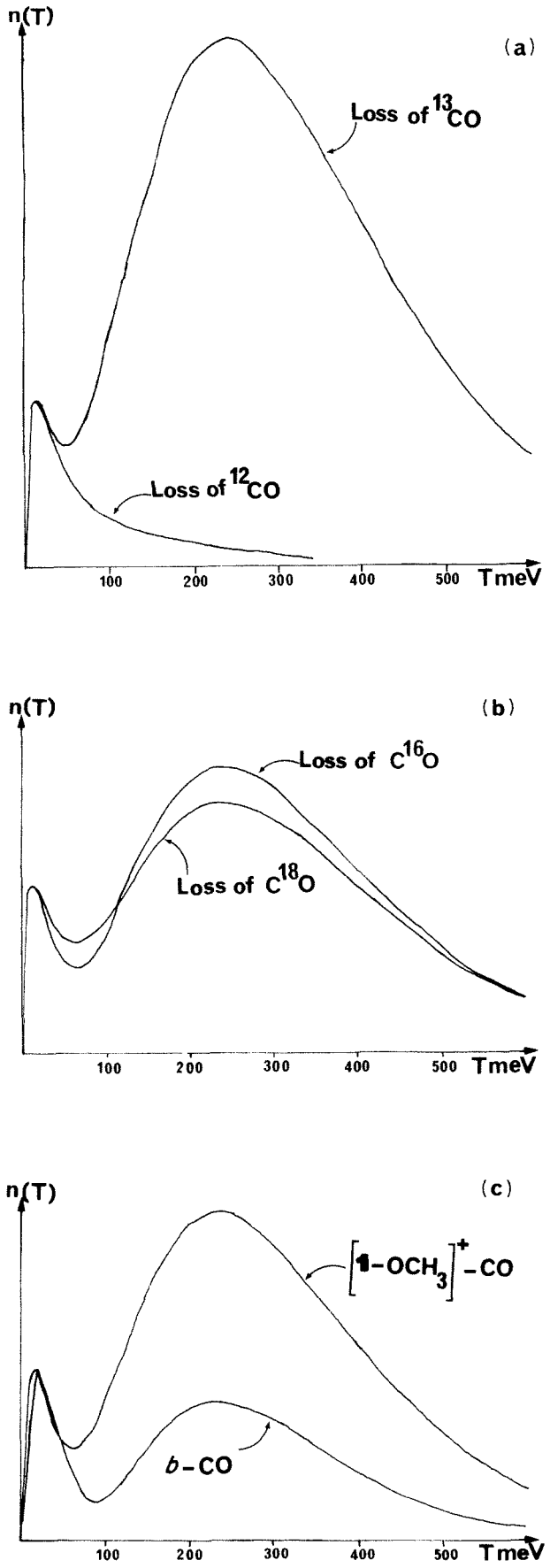


Figure 2. n(*T*) Curves for (a) CO and ^{13}CO losses from $[2-OCH_3]^+$ metastable ions; (b) $C^{18}O$ and CO losses from $[3-OCH_3]^+$ metastable ions; and (c) CO loss from $[1-OCH_3]^+$ and $[7-H]^+$ metastable ions *b*.

For the $[M-H]^+$ ions *b* from γ-valerolactone (7) the same order of magnitude is observed for the T_p values (20 and 230 meV) the first one being of greater weight than for the $[M-OCH_3]^+$ ions from **1** (Fig. 2(c)). In the case of **7** the calculation of the n(*T*) *vs. T* curve is somewhat inaccurate, owing to the very weak abundance of the $[M-H]^+$ ions.

Formation of $[CH_3CO]^+$ ions

The data in Table 2 reveal that the formation of $[CH_3CO]^+$ ions is accompanied by a scrambling of the hydrogen atoms, more pronounced in the MIKE mass spectra. In the collisional mode, a weak $[CD_2CO]^{+\cdot}$ peak can also interfere. Nevertheless, we shall propose, independently of this phenomenon, an interpretation of the results relevant to C and O atoms.

The carbonyl group of the $[CH_3CO]^+$ ions includes the C(1) and C(4) carbon atoms in the ratio 1:3 measured in the MIKE mass spectrum, but only C(4) in CID, as shown in Table 2. The retention ratio of O(1) and O(4) atoms is not appreciably different in MIKE and CID mass spectra.

The CID results suggest the reactions of Scheme 3 as a possible mechanism for the $[CH_3CO]^+$ formation under collisions. Indeed, the breaking of the C(3)—C(4) bond in *c* and *e*, or a concerted process from the corresponding cyclic forms *b* and *d*, would lead to the observed ions, the major participation being that of the original form *c*.

In the low-energy MIKE mass spectrum these two fragmentation processes are in competition with a mechanism involving the C(1) atom, that is to say involving cleavage of the C(1)—C(2) bond. The 1,4 methyl transfer $c \rightarrow f$ (Scheme 4) postulated for the CO loss could be the intermediate step. The values of the kinetic energy release reported in Table 4 support this assumption: a weak kinetic energy release is observed for the formation of $[CH_3{}^{13}CO]^+$ from $[2-OCH_3]^+$ and $[CH_3CO]^+$ from $[3-OCH_3]^+$, attributable to C(1)—C(2) bond cleavage after methyl transfer; a larger kinetic energy release occurs for formation of $[CH_3CO]^+$ from $[2-OCH_3]^+$ and of $[CH_3C^{18}O]^+$ from $[3-OCH_3]^+$, ascribable to C(3)—C(4) bond cleavage after ring closure and opening according to Scheme 3. The corresponding values of kinetic energy release are observed for the two components of the metastable signal of $[CH_3CO]^+$ ions from decomposition of *b*.

CONCLUSIONS

The 70 eV electron impact mass spectra of labelled derivatives of methyl levulinate show that the molecular ion loses CH_3 and OCH_3 as well as CH_3OH without a skeletal rearrangement as previously observed for the ethyl derivative.[2] With regard to the ulterior fragmentation pathways of the $[M-CH_3]^+$ and $[M-OCH_3]^+$ ions (both possessing two carbonyl groups) in the 1st field-free region, ^{13}C labelling of one of these groups and ^{18}O labelling of the other revealed that the apparently simple cleavage reactions (loss of CO, formation

of the acetyl ion and of the methoxycarbonyl ion by α-cleavages) are in fact accompanied by extensive rearrangements.

(i) For the $[M - CH_3]^+$ ions, a 1,4 methoxy shift can account for the quasi-equivalence of the carbonyl groups for all the fragmentation processes.

(ii) For the $[M - OCH_3]^+$ ions, only the oxygen atoms become nearly equivalent. Besides the minor intervention of a 1,4 methyl shift, reversible reactions of closing and opening of a five-membered ring ion, the $[M - H]^+$ ion of γ-valerolactone, explain both the ion abundances and the kinetic energy release values.

This work shows the importance of the use of ^{18}O labelling in addition to ^{13}C labelling in studies of polyoxygenated ions. Other studies related to higher homologues of γ-ketoesters are in progress.

EXPERIMENTAL

The 70 eV mass spectra and the MIKE and MIKE-CID mass spectra were recorded on a VG Micromass ZAB-2F mass spectrometer. The ion source was kept at 150 °C and the accelerating voltage was 8kV. The collision spectra were obtained using helium as target gas.

Methyl levulinate (**1**) and methyl-D_3 levulinate (**4**) were prepared by esterification of levulinic acid by methanol and perdeuteromethanol, respectively.

Methyl 4-oxo-3,3,5,5,5-pentadeuteropentanoate (**6**) was obtained after three exchanges with K_2CO_3 in D_2O.

Methyl 4-oxo-5,5,5-trideuteropentanoate (**5**) was obtained by making use of the reaction of methyl-d_3 cadmium chloride on acid chloride.[5,6] To CD_3MgI obtained from CD_3I (99.3% D) and Mg on a 25 mmol-scale in anhydrous ether (25 cm^3) were added at 0 °C, with strong stirring, 5 g (27 mmol) of finely powdered anhydrous $CdCl_2$. Most of the ether was removed, anhydrous C_6H_6 (20 cm^3) was added, then the remaining ether and some of the C_6H_6 were removed by distillation. After adding a further 20 cm^3 of C_6H_6, 3-methoxycarbonylpropionyl chloride (20 mmol in 10 cm^3 of C_6H_6) was added dropwise at 0 °C. Stirring was continued for several hours at room temperature, then at reflux temperature for one hour. After hydrolysis and ordinary treatments, the methyl levulinate **5** was separated by column chromatography (SE30). The yield was 25%.

Methyl 1-^{13}C-4-oxo-pentanoate (**2**) was prepared in three steps starting from methyl vinyl ketone.

(i) 2-Methyl-2-(β-bromoethyl)-1,3-dioxolane (**8**).[7] To a solution of hydrogen bromide (0.28 mol) in ethylene glycol (30 g) methyl vinyl ketone (0.20 mol) was added dropwise at 0 °C. After stirring for one hour at room temperature, the reaction mixture was extracted with hexane. After the usual treatments of the solution, hexane was removed and distillation of the residue gave 93 mmol of **8** (b.p. 73–74 °C/14 mmHg). The yield was 46%.

(ii) 1-^{13}C-4-dioxolane pentanoic acid. The Grignard reagent from **8** was obtained according to the procedure of Ponaras[8] using a three-fold excess of Mg and a small amount of 1,2-dibromoethane in THF; the temperature was held at 25 °C. The carbonation was performed at −30 °C with $^{13}CO_2$ from $Ba^{13}CO_3$ (99% ^{13}C); excess Mg was eliminated by decantation and after hydrolysis (6N H_2SO_4 in an ice bath) and the usual treatments of the organic layer and removal of solvent, we obtained a crude mixture of 1-^{13}C-4-dioxolane- and 1-^{13}C-4-oxo-pentanoic acid.

(iii) Methyl 1-^{13}C-4-oxo-pentanoate (**2**). The esterification of the crude residue by diazomethane in ether gave a mixture of ketoester and dioxolane-ester which were separated by column chromatography (SE30). The total yield was 25% with regard to $Ba^{13}CO_3$ (the keto:dioxolane ratio was about 2:3).

Methyl 4(^{18}O)-oxopentanoate (**3**) was obtained by cleavage of the dioxolane of methyl levulinate with $H_2{}^{18}O$ (97% ^{18}O) and a small amount of APTS.

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