Functional Group Migration in Ionized Long-Chain Compounds

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Abstract: Many mechanisms have been advanced for the formation of alkyl-radical-loss ions in the mass spectra of fatty acid derivatives. Murphy has shown that these are the dominant products under dissociation conditions of lowest energy. With use of unit resolution spectra measured with low mass discrimination, ^2H and ^{13}C labeling evidence is only consistent with the Longevialle mechanism involving $^\bullet C(OH)OCH_3^+$ migration, with a preference for a 6-membered-ring intermediate (Scheme 1). This mechanism also predicts formation from the linear precursor of a branched product, the protonated 2-alkylpropenoate ion, as confirmed by MS/MS/MS using mass spectra from collisionally activated dissociation of this product. Other alkyl-loss products formed at higher energies appear to be due to this plus competitive mechanisms based on earlier proposals.

Fatty acid esters were the first "large" molecules whose mass spectra were thoroughly studied, with extensive investigations more than 30 years ago by Ryhage, Stenhagen, and co-workers.[1] The electron ionization (EI) behavior of these compounds, detailed by studies in many laboratories,[1–14] has been critical to our current understanding of ion fragmentation mechanisms.[14] For EI (70 eV) of methyl esters (Figure 1a), only methoxy loss[1] clearly occurs by simple bond cleavage; the other dominant fragment ions are (Schemes 1 and 2) from γ-H rearrangement to yield **3**[1,2] (*m/z* 74 for α-unsubstituted) and alkyl-radical loss (*m/z* 87, 101, 115, 129, 143, etc.),[3–14] with the latter series showing a surprising 56-Da periodicity (*m/z* 87, 143, 199, etc.) for unsubstituted compounds, whose CH_2–CH_2 backbone bonds should presumably exhibit nearly identical bond dissociation energies. Although the mechanisms of the first two are well understood,[14] for alkyl loss the products **4**, **5**, **9**, **10**, **12**, and **13** are among those proposed.

Table 1

6′	1c-2-^{13}C	$CH_3O(HO)C^+C^\bullet(CH_2\text{-}\underline{C_2H_4CH_3})CH_2\text{-}\underline{C_{11}H_{23}}$	→	*m/z* 255(10), 144 (9)
	1d-3-^{13}C	" $\quad -\underline{C_{12}H_{25}}$	→	269(10), 144 (9)
6″	1c-2-^{13}C	$CH_3O(HO)C^+C^\bullet(CH_2\text{-}\underline{C_6H_{12}CH_3})CH_2\text{-}\underline{C_7H_{15}}$	→	*m/z* 199 (10′), 200 (9′)
	1d-3-^{13}C	" $\quad -\underline{C_8H_{17}}$	→	213(10′), 200 (9′)
6‴	1c-2-^{13}C	$CH_3O(HO)C^+C^\bullet(CH_2\text{-}\underline{C_{10}H_{20}CH_3})CH_2\text{-}\underline{C_3H_7}$	→	*m/z* 143 (10″), 256 (9″)
	1d-3-^{13}C	" $\quad -\underline{C_4H_9}$	→	157 (10″), 256 (9″)

Clarifying evidence for Scheme 1, an extension of the Longevialle proposal,[10] is presented here.

Deuterium labeling at every carbon atom (and 2- and 3-^{13}C) of methyl octadecanoate (**1c**)[7] led to the conclusion that the alkyl-loss ions "are formed partly by simple cleavage of the chain and partly by expulsion of part of the chain plus one hydrogen atom."[4] Lowering the internal energy of the molecular ions increases the relative amount of alkyl loss.[5] As shown recently by Zirrolli and Murphy,[11] low energy (5 eV) collisionally activated dissociation (CAD, $\sim 10^{-2}$-s lifetime) of **1c** produces a negligible amount of the *m/z* 74 rearrangement product. This is confirmed for higher energy collisions by Harvey[12] and here, and also for spontaneous dissociation of metastable **1a–d** ions (MI spectra; $\sim 10^{-5}$-s lifetime) here and by Gross.[15] Even more dramatically, low energy (5-eV CAD) long lifetime ($\sim 10^{-2}$ s) dissociation[11] of $CD_3(CH_2)_{16}COOCH_3^{\bullet+}$ (**1c**-*18,18,18-d*$_3$) yields nearly equal losses of $CD_3(CH_2)_n^\bullet$ and $CH_3(CH_2)_n^\bullet$ for each value of *n* from 2 to 14, with similar results for **1b**-*1,2,3,4*-$^{13}C_4$. These low-energy alkyl losses are unexpectedly more useful than those of the 70-eV EI spectrum for determining the position of alkyl branching.[11]

The major mechanistic proposals for the lowest energy reactions involve either (Scheme 1) $^\bullet C(OH)OCH_3^+$ group rearrangement (probably through a cyclic intermediate)[10] to form products **9** and **10**[9,10,13,14b] or (Scheme 2) alkyl migration to the carbonyl oxygen to form **12** and **13**.[5,6,8,11,12] Evidence from both tandem mass spectrometry (MS/MS and MS/MS/MS) and higher resolution studies here shows that the former is dominant. This is consistent with recent studies demonstrating functional group migration[9,10,14,16] and clarifies the mechanisms for higher energy dissociations.

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(1) Ryhage, R.; Stenhagen, E. *Ark. Kemi* **1959**, *13*, 523–542; **1959**, *14*, 483–495. Dinh-Nguyen, N.; Ryhage, R.; Stallberg-Stenhagen, S.; Stenhagen, E. *Ark. Kemi* **1961**, *18*, 393–399.

(2) McLafferty, F. W. *Anal. Chem.* **1959**, *31*, 82–87.

(3) Beynon, J. H. *Mass Spectrometry and its Applications to Organic Chemistry*; Elsevier: Amsterdam, 1960; p 382.

(4) Ryhage, R.; Stenhagen, E. In *Mass Spectrometry of Organic Ions*; McLafferty, F. W., Ed.; Academic Press: New York, 1963; pp 399–452.

(5) Spiteller, G.; Spiteller-Friedmann, M.; Houriet, R. *Monatsh. Chem.* **1966**, *97*, 121–128.

(6) Budzikiewicz, H.; Djerrasi, C.; Williams, D. H. *Mass Spectrometry of Organic Compounds*; Holden-Day: San Francisco, 1967; pp 174–183.

(7) Dinh-Nguyen, N. *Ark. Kemi* **1968**, *28*, 289–362.

(8) McCloskey, J. A. *Topics in Lipid Chemistry*; Gunstone, F. D., Ed.; Logos Press: London, 1070; Vol. 1, pp 369–440.

(9) Göksu, E.; Weiske, T.; Halim, H.; Schwarz, H. *J. Am. Chem. Soc.* **1984**, *106*, 1167–1168. Weiske, T.; Halim, H.; Schwarz, H. *Chem. Ber.* **1985**, *118*, 495–509. Weiske, T.; Schwarz, H. *Tetrahedron* **1986**, *42*, 6245. Bouchoux, G. *Mass Spectrom. Rev.* **1988**, *7*, 1–39.

(10) (a) Mollova, N.; Longevialle, P. *J. Am. Soc. Mass Spectrom.* **1990**, *1*, 238–248. (b) Lefèvre, O.; Mollova, N.; Longevialle, P. *Org. Mass Spectrom.* **1992**, *27*, 589–596. (c) Lefèvre, O.; Mollova, N.; Longevialle, P. *Rapid Commun. Mass Spectrom.* **1993**, *7*, 454–459.

(11) Zirrolli, J. A.; Murphy, R. C. *J. Am. Soc. Mass Spectrom.* **1993**, *4*, 223–229.

(12) Harvey, D. J. *Org. Mass Spectrom.* **1993**, *28*, 287–288.

(13) Zirrolli, J. A.; Murphy, R. C. Amer. Soc. Mass Spectrom. Conference, San Francisco, June 1993, paper TP229.

(14) (a) McLafferty, F. W.; Turecek, F. *Interpretation of Mass Spectra*, 4th ed.; University Science Books: Mill Valley, CA, 1993; (b) p 254, (c) p 187.

(15) Gross, M. L., cited in ref 11, and a private communication, May 1993.

(16) Vidavsky, I.; Mandelbaum, A. *Org. Mass Spectrom.* **1992**, *27*, 527–528, 847–849.

0002-7863/94/1516-5865$04.50/0

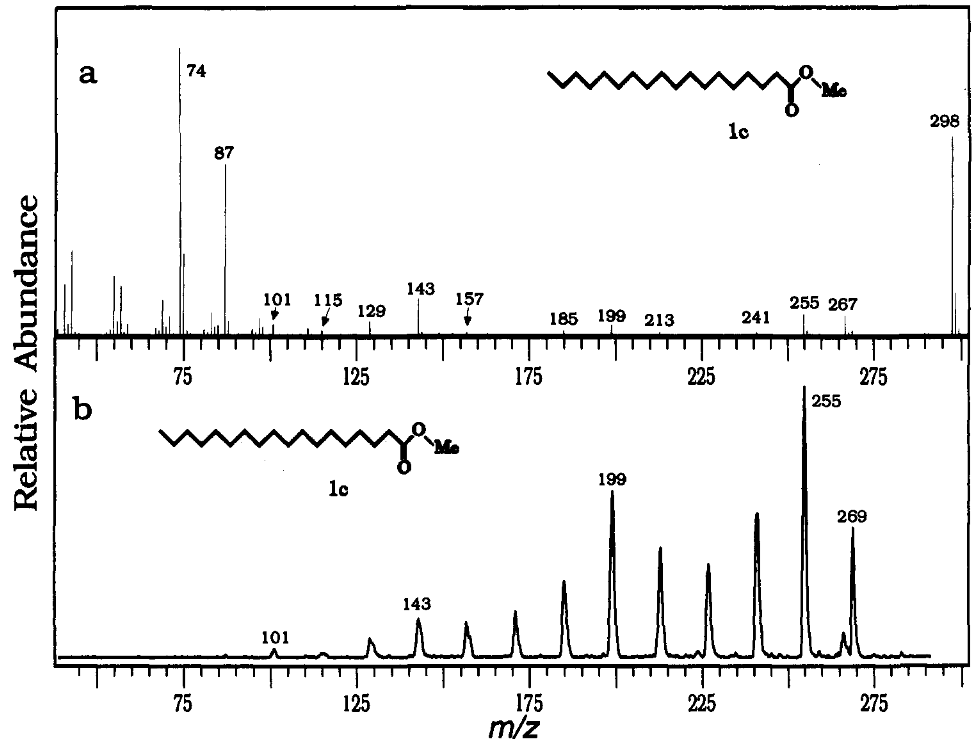

Figure 1. Mass spectra of methyl octandecanoate (**1c**): (a) 70-eV EI; (b) metastable ion (MI) dissociation of $M^{\bullet+}$.

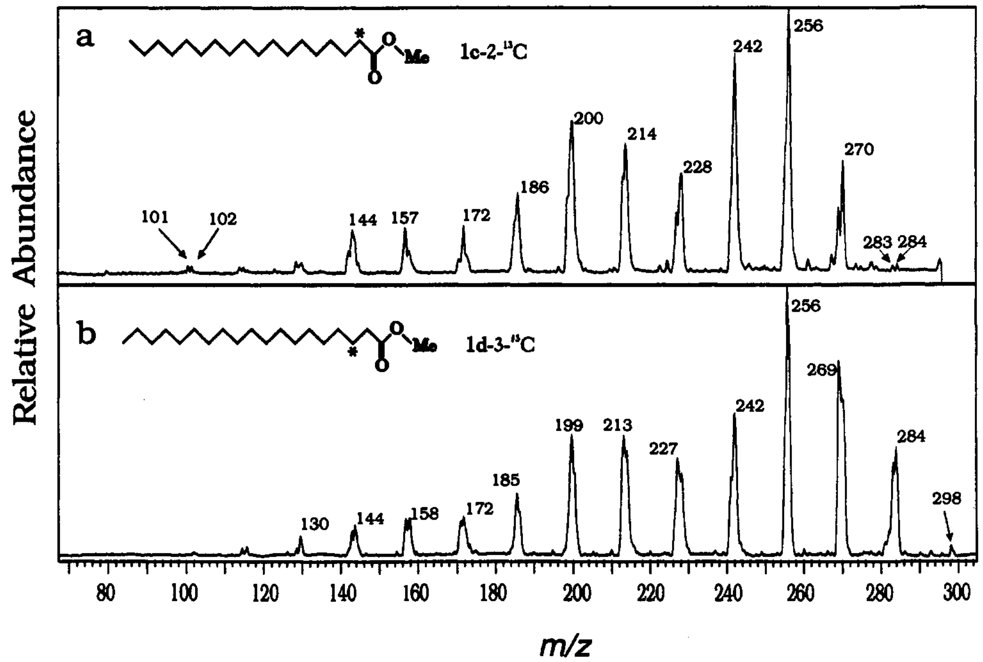

Figure 2. MI mass spectra of $M^{\bullet+}$ from (a) methyl octadecanoate-*2*-^{13}C (**1c**-*2*-^{13}C) and (b) methyl nonadecanoate-*3*-^{13}C (**1d**-*3*-^{13}C).

Experimental Section

Measurements were made with an instrument described previously,[17] using a modified Hitachi RMH-2 double-focusing mass spectrometer (EB) as the first mass analyzer (MS-I) followed by a field-free collision region and an electrostatic analyzer (ESA-II). Electron ionization employed 70-eV electrons, while chemical ionization used ~1 Torr of isobutane, with a 9.8-keV ion acceleration and a 140 °C ion source. In MS/MS experiments, metastable ions selected by MS-I underwent dissociation spontaneously (MI spectra) or by collision (9.8 keV) with He (30% transmission), using ESA-II as MS-II. In MS/MS/MS experiments, a fragment ion, formed by spontaneous dissociation of the molecular ion ($M^{\bullet+}$) in the field free region before ESA-I was selected by adjusting ESA-I and magnet-I, was allowed to undergo collision with He (30% transmission), and the product ions were analyzed by ESA-II as MS-III. Such MS^n spectra were not corrected for the fall-off in multiplier response with decreasing ion mass. After the original submission of this manuscript, the MI spectra of **1c**, **1c**-*2*-^{13}C, and **1d**-*3*-^{13}C (Figure 3a,c,d) and the CAD spectrum of **1c** (Figure 3b) were repeated at unit resolution on the VG-Fisons four-sector instrument at the NSF Midwest Center for Mass Spectrometry, Lincoln, NE.[18] Ion lifetimes in both instruments are $\sim 10^{-5}$ s.

Ethylpropanedioic acid, methyl 2-butenoate, 3-butenoic acid, 4-pentenoic acid, dimethyl propanedioate, methyl propenoate, iodohexane, and iodomethane-^{13}C were purchased from Aldrich (Milwaukee), hexadecanoic acid-*16,16,16*-d_3 and diethyl propanedioate-*2*-^{13}C from Isotec

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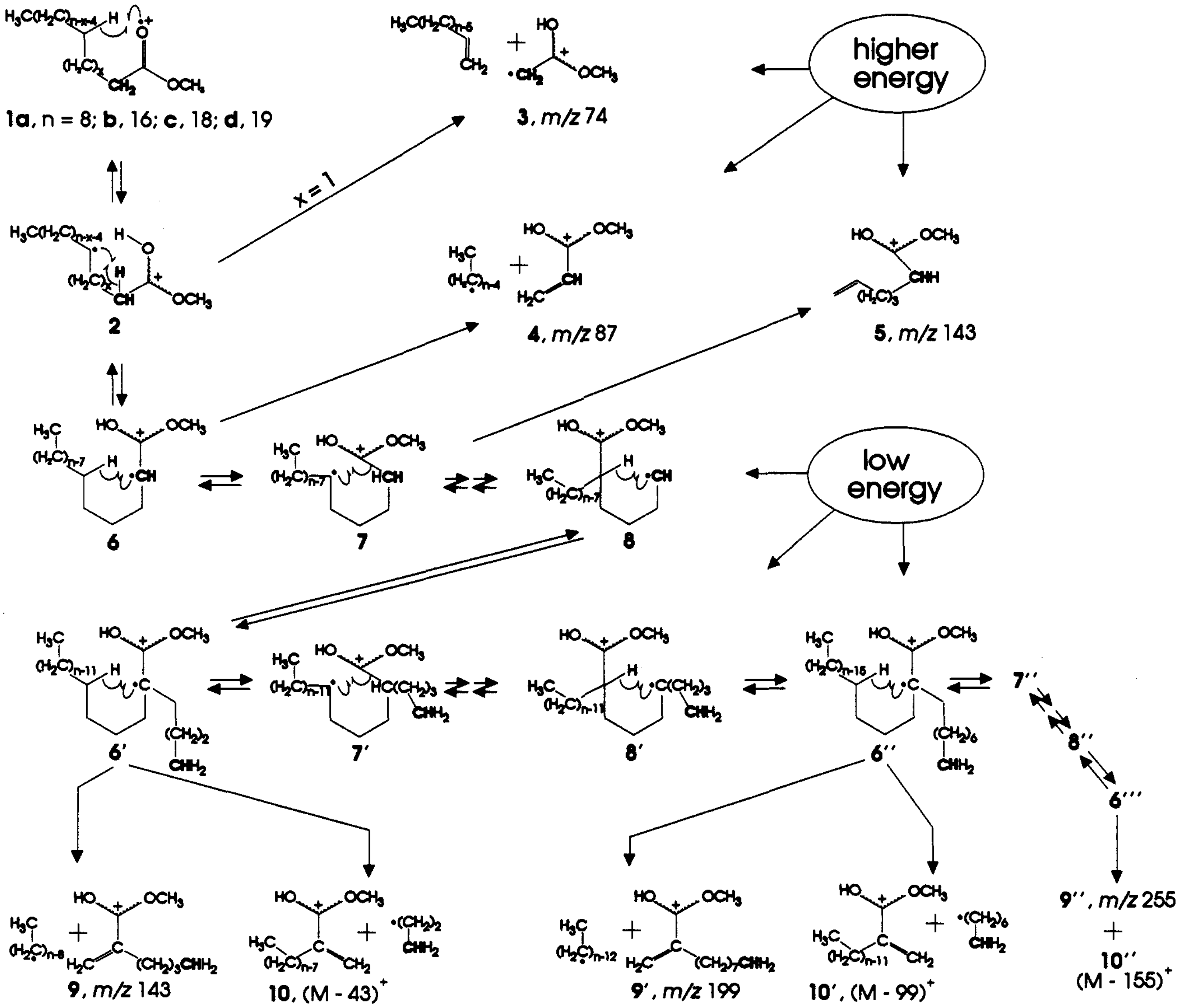
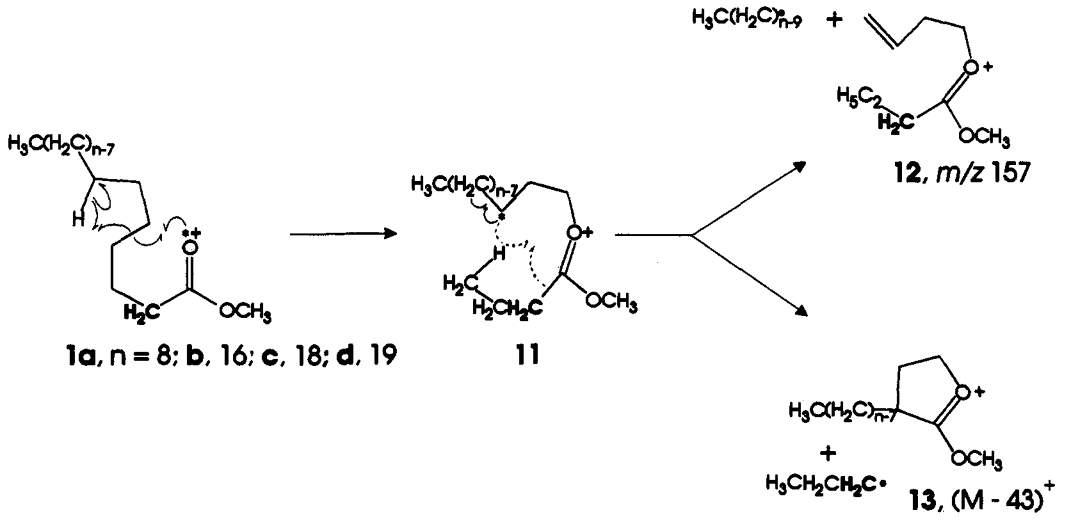
(17) McLafferty, F. W.; Todd, P. J.; McGilvery, D. C.; Baldwin, M. A. *J. Am. Chem. Soc.* **1980**, *102*, 3360–3363. Feng, R.; Wesdemiotis, C.; Baldwin, M. A.; McLafferty, F. W. *Int. J. Mass Spectrom. Ion. Proc.* **1988**, *86*, 95–107.

(18) Gross, M. L.; Cerny, R. L.; Giblin, D. E.; Rempel, D. L.; Macmillan, D. K.; Hu, P.; Holliman, C. L. *Anal. Chim. Acta* **1991**, *250*, 105–130.

Scheme 1



Scheme 2



(Miamisburg, OH), hexadecanoic acid-*7,7,8,8-d*$_4$ from MSD Isotopes (Montreal), and other chemicals from Sigma (St. Louis). Methyl octadecanoate-*2-*^{13}*C* and methyl nonadecanoate-*3-*^{13}*C* were gifts from Prof. Nguyêñ Dinh-Nguyêñ, University of Goteborg, Sweden. The acids were esterified with $MeOH/H_2SO_4/C_2H_4Cl_2$. Methyl-2-ethylpropenoate was prepared from dimethyl ethylpropanedioate.[19] Methyl octanoate-*2-*^{13}*C* was prepared from diethyl propanedioate-*2-*^{13}*C* and iodohexane.[20] Alkylation of diethyl propanedioate with iodomethane-$^{13}C^{21}$ and trans-

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[19] Miller, R. B.; Smith, B. F. *Synth. Commun.* **1973**, *3*, 359–363.

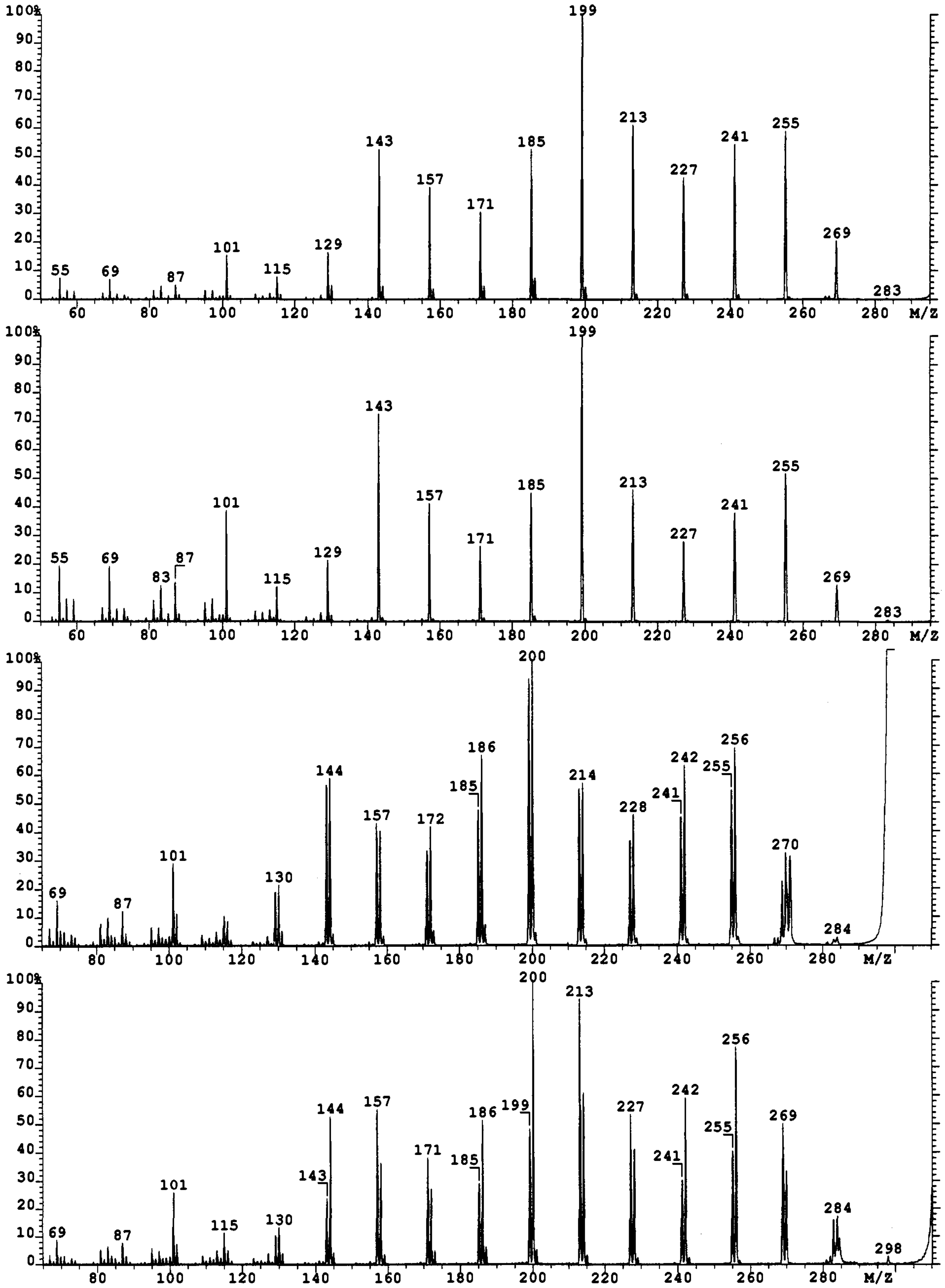

Figure 3. Unit-resolution mass spectra by (a) MI dissociation of **1c**, (b) collisionally-activated dissociation (CAD) of **1c**, (c) MI dissociation of **1c**-*2*-^{13}C, and (d) MI dissociation of **1d**-*3*-^{13}C. The spectra appear in the order a to d from top to bottom.

esterification in methanol gave dimethyl methylpropanedioate-^{13}C, which was converted to methyl 2-methyl-^{13}C-propenoate.[19] All synthetic materials gave satisfactory analyses by GC/MS.

Results and Discussion

Lowest-Energy Alkyl-Radical Loss. Isotopic labeling shows that $^{\bullet}C_3H_7$ loss from **1c** (forming *m/z* 255, Figure 1a) with 70-

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(20) Reid, E. E.; Ruhoff, J. R. *Organic Syntheses*; Wiley: New York, 1943; Collect Vol. II, p 474.

(21) Weiner, N. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 279.

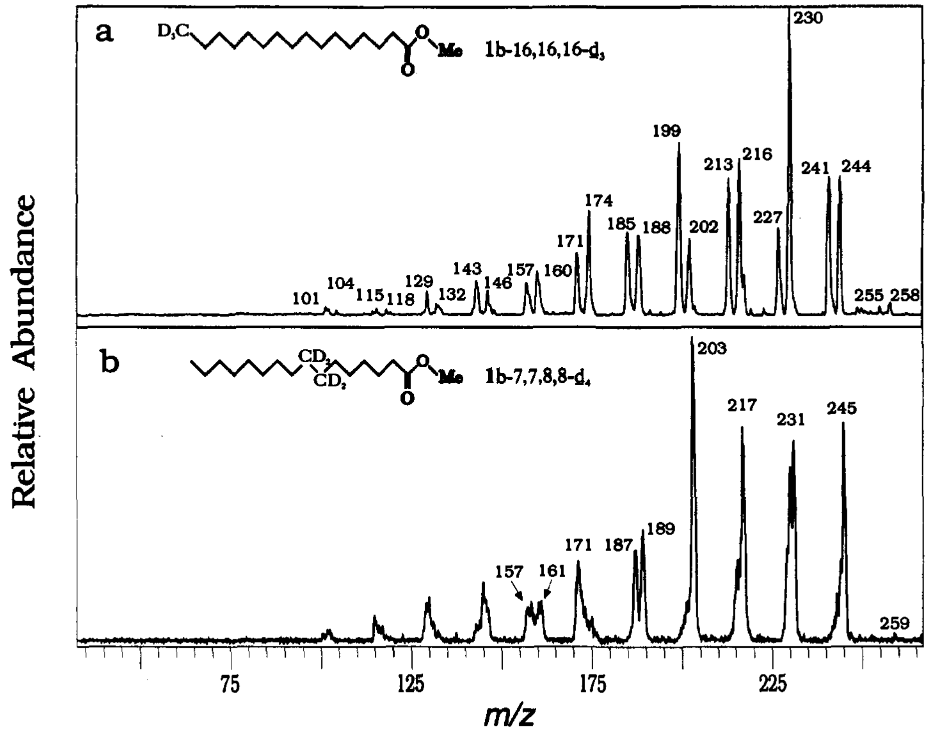

Figure 4. MI mass spectra of $M^{\cdot+}$ from methyl hexadecanoate, (**1b**): (a) *16,16,16-*d_3; (b) *7,7,8,8-*d_4.

eV EI involves mainly carbons 2, 3, and 4.[1,4,7] Early workers[5,6,8] suggested that this occurs (Scheme 2) through displacement formation of a C–O bond (**11**) followed by cyclization to eliminate $^{\bullet}C_3H_7$ (**13**). Extension of this mechanism was first proposed[11,12] to explain the near equivalent losses at low energies of $^{\bullet}C_nH_{2n+1}$ and $^{\bullet}C_nH_{2n-2}D_3$ from **1c**-*18,18,18-*d_3 or of $^{\bullet 12}C_nH_{2n+1}$ and $^{\bullet 12}C_{n-3}{}^{13}C_3H_{2n+1}$ from **1b**-*1,2,3,4-*$^{13}C_4$ to form **12** and **13**. The alternative Longevialle mechanism,[10,13,14b] an extension of that elucidated for butyrates from Schwarz,[9] instead involves (Scheme 1) migration of the $^{\bullet}C(OH)OCH_3{}^+$ group (**7** → **8**) to form **6′**, or **7′** → **8′** to form **6″**, etc.; loss of either alkyl group from **6′**, **6″**, etc. yields a protonated methyl alkylpropenoate ion (**9**, **9′**, **10**, **10′**, etc.) that should be of high stability. The applicability of these mechanisms to the low-energy mass spectra will be considered first.

Dissociation Symmetry. In contrast to Scheme 2, in Scheme 1 the intermediates $CH_3O(HO)C^+C^{\bullet}RR'$ have similar structures (Table 1); for the octadecanoate (**1c**), the intermediate **6″** is symmetrical, and **6′** and **6‴** are identical. When both alkyl groups are larger than ethyl (thus excluding **6**), the activation barriers for the loss of either one to form **9**, **9′**, etc. versus **10**, **10′**, etc. should be nearly equal, predicting a nearly equal probability for losing either alkyl group (those underlined in Table 1). However, in Scheme 2 the intermediate **11** forms **12** and **13** by significantly different pathways, one a simple cleavage and the other a displacement cyclization. The *m*/*z* values of these complementary products can be varied by changing the chain length (*n*) or by isotopic labeling; in this way earlier[10] low-resolution MI spectra (and Figures 1b and 2) give qualitative support to Scheme 1.

This is seen far more clearly, however, in the higher resolution spectra of the ^{13}C-labeled compounds measured on the tandem double-focusing instrument (Figure 3); this instrument was also designed to minimize MS-II mass discrimination (note the more abundant low mass ions in Figure 3 vs Figures 1b and 2). For **1c**-*2-*^{13}C (Table 1), the pathways **6′** → **9** (*m*/*z* 144) vs **6‴** → **10″** (143), **6′** → **10** (255) vs **6‴** → **9″** (256), and **6″** → **9′** (200) vs **6″** → **10′** (199) should form identical products by Scheme 1 except for the ^{13}C label; the observed (Figure 3c) similar abundances of those peak pairs bear this out. Further, the abundances of *m*/*z* 144 and 143 vs 256 and 255 are nearly the same also, as predicted for **6′** (⇄ **6″**) ⇄ **6‴** equilibration prior to dissociation. For the MI spectrum of **1d**-*3-*^{13}C, the **10** products should contain an additional CH_2 group. Thus (Table 1), **9** (*m*/*z* 144) vs **10″** (157), **10** (269) vs **9″** (256), and **9′** (200) vs **10′** (213) should be equivalent, as should **9** (*m*/*z* 144) vs **10** (269) and **9″** (256) vs **10″** (157), as observed. Scheme 2 would produce the data in Figure 3 only by an unusual coincidence.

Other Possible Factors Affecting Product Abundances. The extent of agreement with the Scheme 1 predictions is also consistent with other factors. Mass discrimination in the Nebraska instrument appears to be unimportant; for **1c** (Figure 3a), both **6′** and **6‴** should yield *m*/*z* 143 and 255 (Table 1) in equivalent abundances. Carbon atom scrambling competitive with **6′** ⇄ **6″** ⇄ **6‴** would randomize the ^{13}C atom out of the $^{\bullet}C_3H_7$ lost in **6′** → **10**, consistent with the small increase in *m*/*z* 256 at the expense of *m*/*z* 255 for **1c**-*2-*^{13}C and *m*/*z* 256 at the expense of *m*/*z* 269 in **1d**-3-^{13}C. However, the concomitant decreases in *m*/*z* 144 vs 143 and vs 157, respectively, are not observed, while the 5-eV CAD mass spectrum of **1b**-*1,2,3,4-*$^{13}C_4$ shows only minor ^{13}C-atom scrambling.[11]

Unexplained anomalies are the $(M - 28)^{\cdot+}$ peaks in spectra c and d of Figure 3 of the ^{13}C-labeled compounds. These are **not** present in the unlabeled spectrum of Figure 3a, the spectra of Figures 1, 2, and 4, or the 5-eV CAD spectra.[11] Conceivably, these ions could fragment further to produce additional anomolous ions; if they are structurally similar to the **1c**-*2-*^{13}C and **1c**-*3-*^{13}C molecular ions, they could produce significant peaks from secondary losses of $^{\bullet}C_3H_7$ and $^{\bullet}C_4H_9$, contributing to *m*/*z* 228 and 214 in Figure 3c and *m*/*z* 242 and 228 in Figure 3d.

Product stability should also affect yields. In Figure 3d **6′** → **10** (*m*/*z* 269) involves loss of $^{\bullet}C_3H_7$, while **6‴** → **9″** (256) involves loss of $^{\bullet}C_4H_9$, with the 27 kJ increased stabilization for the latter neutral far greater than that of the extra CH_2 in the **10** vs **9″** ionic products. This rationalizes the extra abundance of *m*/*z* 256 vs 269 in the **1d**-*3-*^{13}C spectrum as compared to that of *m*/*z* 256 vs 255 in Figure 3, spectrum c (Table 1). However, the near-equivalency of the *m*/*z* 255 and 143 abundances from **1c** (Figure 3a, which could also be affected by mass discrimination) argues that the extra stabilization of the C_8H_{16} on the neutral lost in forming *m*/*z* 143 is offset by the corresponding stabilization of *m*/*z* 255 in its formation.

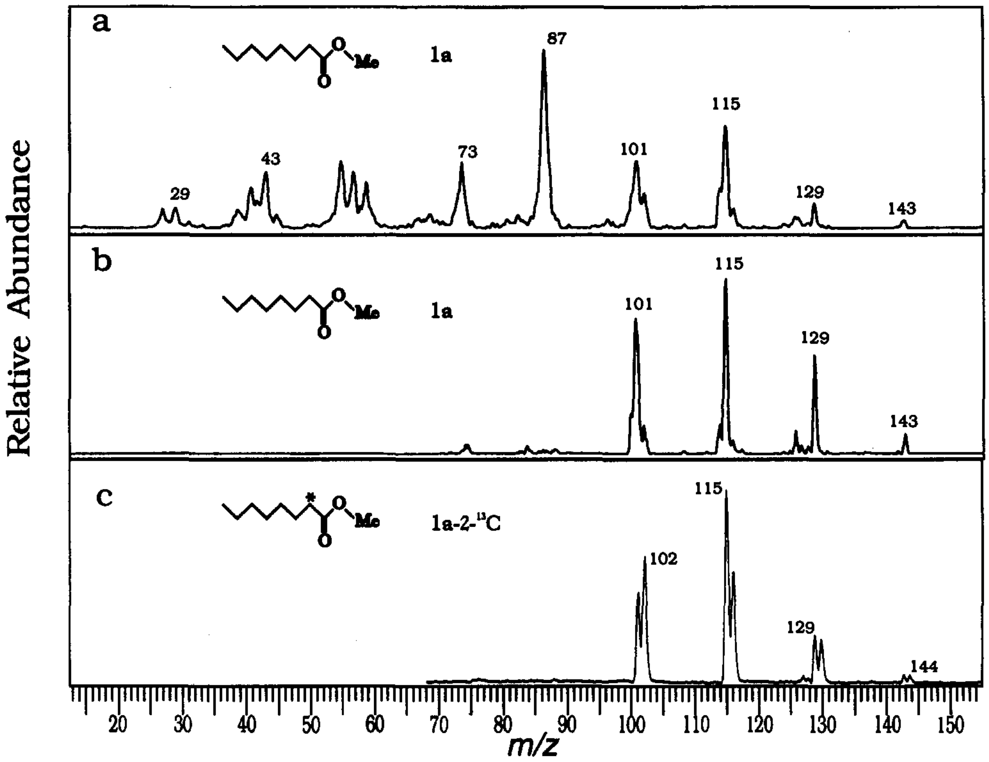

Figure 5. Mass spectra of $M^{•+}$ from methyl octanoate (**1a**): (a) CAD; (b) MI; (c) MI of methyl octanoate-*2*-^{13}C (**1a**-**2**-^{13}C).

The abundances of the unlabeled **1c** spectrum, Figure 3a, display another anomaly, however. Complete equilibration of **6′** ⇄ **6″** ⇄ **6‴** should produce equal amounts of these intermediates if they are of equal stabilities; equal rates of dissociation by Scheme 1 should then produce equal abundances of *m/z* 143, 199, and 255. Possibly the much larger *m/z* 199 arises from a larger equilibrium concentration of the **6″** intermediate, with stabilization of the radical site carbon by two $^•C_8H_{17}$ alkyl groups instead of the $^•C_4H_9$ and $^•C_{12}H_{25}$ groups on the **6′** and **6‴** intermediates.

Cyclic Intermediates. Double sets of arrows are indicated (Scheme 1) for the reversible reaction between the distonic radical ions **7** and **8**, **7′** and **8′**, etc., to reflect the persuasive evidence for a cyclohexane intermediate in these reactions.[10] However, the relative stability of this intermediate is not important to the mechanistic conclusions here.

Other Ring Sizes for $^•C(OH)OCH_3{}^+$ Transfer. Lower abundance peaks also occur in the MI spectra at all masses of the ion series *m/z* 101, 115, 129, etc. (Figure 3a). If one of the $^•C(OH)OCH_3{}^+$ transfers **7** → → **8**, **7′** → → **8′**, or **7″** → → **8″** involves instead a five- (seven)- membered-ring intermediate, for **1c**-*2*-^{13}C the complementary product pairs would be **9**–**10**, *m/z* 130–269 (158–241); **9′**–**10′**, 186–213 (214–185); and **9″**–**10″**, 242–157 (270–129). For **1d**-*3*-^{13}C, these product pairs would be **9**–**10**, *m/z* 130–283 (158–255); **9′**–**10′**, 186–227 (214–199); and **9″**–**10″**, 242–171 (270–143). Spectra c and d in Figure 3 agree quite well with these predictions. Similarly, replacing two of the six-membered-ring rearrangements with two five- (seven-) membered counterparts would account in **1c**-*2*-^{13}C for the peak pairs for **9′**–**10′** at *m/z* 172–227 (228–171) and for **9″**–**10″** at 228–171 (284–115) (Figure 3c), and in **1d**-*3*-^{13}C at respectively *m/z* 172–241 (228–185) and 228–185 (284–129) (Figure 3d). Note that the relative peak abundances are consistent with the reaction rates for the corresponding rearrangements.

Peaks are also present above and below these predicted values that would result from the $^•C(OH)OCH_3{}^+$ rearrangement of Scheme 1 taking place through even smaller cyclic intermediates or a multiplicity of 5- to 7-membered rings. This is confirmed dramatically in Figures 2 and 3c,d with both $^{•13}CH_3$ and $^{•12}CH_3$ losses (*m/z* 283 and 284) from **1c**-*2*-^{13}C, but only $^{•12}CH_3$ loss (*m/z* 298) from **1d**-*3*-^{13}C. Similarly, the spectra of **1c**-*2*-^{13}C and **1d**-*3*-^{13}C in Figure 2 show small peaks at *m/z* 101, 102, 115, and 116, and corresponding peaks are seen in the MI spectrum of **1b**-*16,16,16*-d_3 (*m/z* 101, 104, 115, 118, Figure 4) and the 5-eV CAD spectra[11] of **1c**-*18,18,18*-d_3 (*m/z* 101, 104) and **1b**-*1,2,3,4*-$^{13}C_4$ (*m/z* 102, 105).

H• vs $^•C(OH)OCH_3{}^+$ Rearrangement. As discussed above, equilibration of the key intermediates **6′** ⇄ **6″** ⇄ **6‴** takes place at low energies before their dissociation into the product pairs. However, in the 5-eV CAD spectrum of **1c**-*2,2*-d_2, the ethyl loss peaks are mainly $(M - C_2H_5)^+$, not $(M - C_2H_3D_2)^+$, with $[(M - C_3H_7)^+] > [(M - C_3H_6D)^+] > [(M - C_3H_5D_2)^+]$, *m/z* 101 ≫ 103, and 115 > 116 > 117. As pointed out by Murphy,[11] H rearrangement at C-2 must be far faster than the skeletal reorganization leading to C-2 and/or C-3 loss. In Scheme 1 this would occur by partial equilibration of **1** ⇄ **2** through transition states of varying size.

For H/D scrambling in **1b**-*7,7,8,8*-d_4 (Figure 4b), transfer of a D to oxygen by **1** → **2** requires a low-probability 9- or 10-membered-ring intermediate, but transfer of D to C-2 by **6** → **7** requires only that this reaction instead proceed through a 7- (or 8-) membered-ring intermediate. With back transfer of H by **7** → **6** followed by the normal **6** → **7** → **8** etc. sequence, the predictions for no (one) D atom scrambled from C-7 to C-2 in the major Scheme 1 complementary products are **9**, *m/z* 145 (145), and **10**, *m/z* 231 (230); this D transfer will not affect the masses of the other products (**9′**, 203; **10′**, 171; **9″**, 259; **10″**, 115). From the *m/z* 230 vs 231 abundances, the 7- (and 8-) membered-ring H transfer in **6** → **7** competes effectively with the back transfer of D away from C-2 as shown for **1c**-*2,2*-d_2.[11] Note in Figure 4b that the products **9′** and **10′** formed with one five-membered-ring intermediate in **7** → **8** or **7′** → **8′** should yield *m/z* 189 and 187, respectively, as observed.

Effect of Ion Lifetimes. In the low-energy mass spectrum of **1c** measured by Murphy on a triple-quadrupole instrument (ref 11, Figure 1b), the ion abundances in the series *m/z* 101, 115, 129, etc. increase fairly continuously to *m/z* 199 and then decrease similarly to *m/z* 269, so that *m/z* 227 is actually more abundant than *m/z* 255 and *m/z* 171 more than *m/z* 143; instead, Figure

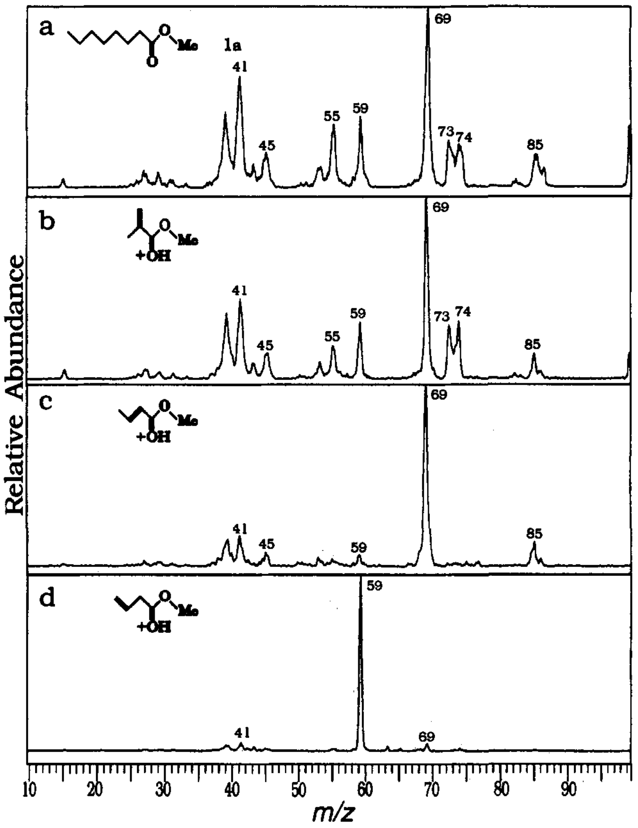

Figure 6. CAD mass spectra of the m/z 101 ion from (a) the MI spectrum of $M^{\bullet+}$ from methyl octanoate (**1a**), (b) MH^+ of methyl 2-methylpropenoate, (c) MH^+ of methyl 2-butenoate, and (d) MH^+ of methyl 3-butenoate.

3a shows m/z 143, 199, and 255 as the most abundant. A major difference is that ion velocities are $\sim 10^{-3}$ as great, and ion lifetimes 10^3 longer, in the quadrupoles vs in our magnetic sector instruments. This apparently provides sufficient time for equilibration through the 5- and 7-membered-ring intermediates, as well as the 6-membered-ring intermediates.[10b] Stabilization of the **6′**, **6″**, etc. ion-radicals $CH_3O(HO)C^+C^{\bullet}RR'$ again appears to be favored by the degree of size equivalence of R and R′.

Murphy has also shown that these low-energy spectra can indicate the position of methyl substitution;[11] for $CH_3(CH_2)_x$-$CH(CH_3)$-$(CH_2)_{n-x-4}COOCH_3$, the abundances of peaks of masses equivalent to $^+(CH_2)_{n-x-4}COOCH_3$ and $^+CH(CH_3)(CH_2)_{n-x-4}COOCH_3$ are substantially increased. Methyl substitution should lower the local bond dissociation energies and enhance formation of **9**, **9′**, **10**, **10′**, etc. The 10^{-2} s ion lifetimes appear advantageous in removing confusion from the 6-membered-ring specificity of the $^{\bullet}C(OH)OCH_3^+$ rearrangements of Scheme 1.

Alkylpropenoate Product. The lowest energy alkyl loss pathway of Scheme 1 is also unique in predicting the protonated 2-alkylpropenoate products **9** and **10**, branched chain products from the dissociation of an unbranched precursor. In order to obtain structural confirmation, CAD spectra[22] were measured for the smallest alkyl-loss ions (m/z 101, 115), for which the number of possible isomers would be minimized. Only smaller esters such as methyl octanoate (**1a**) gave sufficient abundance of the ions for MS/MS/MS measurement. However, the similarity of the 70-eV EI and CAD spectra, and of the ^{13}C-labeling effect on the MI spectra, of the C-8 ester (Figure 5) to those of their longer chain counterparts (Figures 1–3) indicates little dependence of the mechanism on chain length.

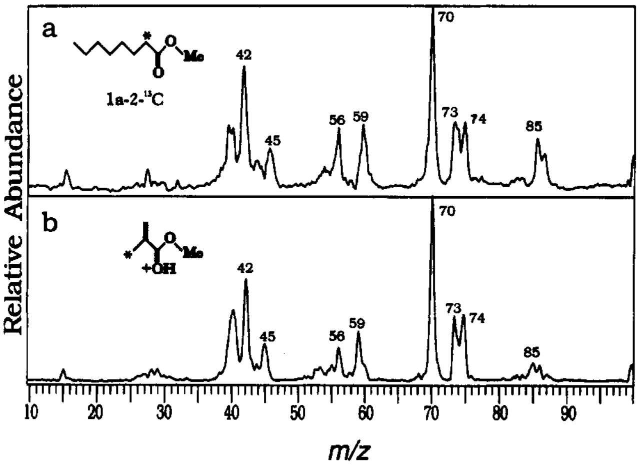

Figure 7. CAD mass spectra of the m/z 102 ion from (a) the MI spectrum of $M^{\bullet+}$ from methyl 2-^{13}C-octanoate (**1a**-*2*-^{13}*C*) and (b) MH^+ from methyl 2-(methyl-^{13}*C*)propenoate.

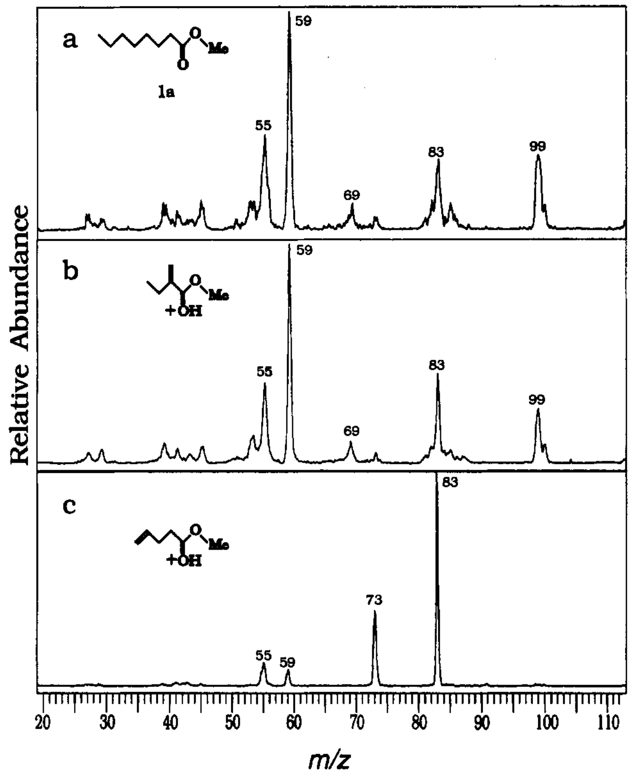

Figure 8. CAD mass spectra of the m/z 115 ion from (a) the MI spectrum of $M^{\bullet+}$ from methyl octanoate (**1a**), (b) MH^+ of methyl 2-methylpropenoate, and (c) MH^+ of methyl 4-pentenoate.

In this MS/MS/MS experiment (Figure 6), the CAD spectrum from dissociating m/z 101 of the MI spectrum from $M^{\bullet+}$ of **1a** compares quite closely with that from the MH^+ ion from chemical ionization of methyl 2-methylpropenoate, with much less resemblance to that of MH^+ from the isomeric methyl 3-methylpropenoate, and very different from that of MH^+ from methyl 3-butenoate. No straightforward way was found to prepare the oxonium reference ion structures similar to **11** and **12** in order to compare their CAD spectra.

Scheme 1 is unusual in predicting that m/z 101 formed from either terminal or interior alkyl loss will have the same protonated 2-methylpropenoate structure. As a separate check on the **9** product structure without **10** present, the CAD spectrum of m/z 102 in the MI spectrum from $M^{\bullet+}$ of **1a**-*2*-^{13}*C* (Figure 7) matches well with that of MH^+ from methyl 2-(methyl-^{13}*C*)propenoate, although it is not clear that any of the major fragmentations delineate the ^{13}C position among the carbons of the isopropenyl

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[22] McLafferty, F. W.; Kornfeld, R.; Haddon, W. F.; Levsen, K.; Sakai, I.; Bente, P. F., III; Tsai, S.-C.; Schuddemage, H. D. R. *J. Am. Chem. Soc.* **1973**, *95*, 3886–3892.

group. Further, the CAD spectrum of m/z 115 isolated from the metastable dissociation of $M^{\bullet+}$ of **1a** (Figure 8) matches that of MH^+ from methyl 2-ethylpropenoate, and not that of MH^+ from methyl 4-pentenoate. Thus a multiplicity of evidence favors Scheme 1, not Scheme 2, for the lowest energy alkyl loss.

Higher-Energy Alkyl Loss. The next most abundant fragment ion in the 70-eV EI mass spectrum of **1c** is m/z 87. The early labeling studies gave convincing evidence[1,4,6] for its formation by the pathway **1** → **2** → **6** → **4**, Scheme 1. Although in the CAD spectrum of **1c** (Figure 3b) this peak is slightly more abundant than in the MI spectrum (Figure 3a), the alkyl-loss ions (m/z 101, 115, etc.) are still dominant. This is further evidence that the equilibration $\mathbf{6'} \rightleftarrows \mathbf{6''} \rightleftarrows \mathbf{6'''}$ etc. has occurred in the 10^{-5} s before CAD. However, in the 70-eV EI spectrum of **1c**, m/z 199 is now less abundant than m/z 143 (Figure 1a), and labeling shows that both m/z 143 and 255 arise mainly from **6′**,[4,7] showing that at these higher energies the $\mathbf{6'} \rightleftarrows \mathbf{6''} \rightleftarrows \mathbf{6'''}$ equilibration is no longer competitive with dissociation. The increased m/z 101 in the 70-eV spectrum and, especially, in the higher-energy CAD spectrum (Figure 3b) could result from further dissociation of the **9**, **10**, **9′**, **10′**, etc. products by olefin loss resulting from H-rearrangement through a 6-membered-ring transition state, presumably forming the protonated methyl 2-methylpropenoate ion identified above from **1a** by MS/MS/MS.

Conclusions

For ion dissociations at lowest energies, the tendency for larger functional groups to rearrange, probably through a cyclic intermediate, has been clearly demonstrated in a number of cases recently, such as migration of $-C(OH)OCH_3$,[9,10] $-CHNH_2$,[10] CO,[14c] and $-OCH_3$.[16] This also appears to be true for $^{\bullet}C(OH)OCH_3^+$ rearrangement in fatty acid esters (Scheme 1), with both the specificity for a 6-membered-ring intermediate and the extent of equilibration depending on the degree of excitation of the dissociating molecular ion. Thus the $\sim 10^{-2}$-s-lifetime spectra show near-equilibration of alkyl-loss product abundances consistent with many $^{\bullet}C(OH)OCH_3^+$ transfers through 5-, 6-, and 7-membered rings, while in the 70-eV spectra this transfer is competitive only to form **6′** through a single 6-membered-ring rearrangement. Understanding these dissociation mechanisms is of particular importance because chain substitution can now direct fragmentation to provide valuable structural information,[11] in contrast to the increasing tendency for structural randomization with lowered dissociation energies found previously for many molecular cation dissociations.[14]

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