ORGANIC MASS SPECTROMETRY, VOL. 22, 421-429 (1987)

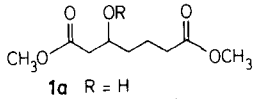
A Mass Spectrometric Study of Dimethyl Ester Trimethylsilyl Ether Derivatives of Some 3-Hydroxydicarboxylic Acids

John S. Svendsen,† Leiv K. Sydnes† and Jon E. Whist‡
University of Tromsø, N-9001 Tromsø, Norway

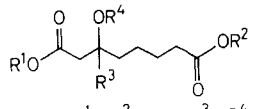
The fragmentation pathways for the dimethyl ester trimethylsilyl ether derivatives of some 3-hydroxydicarboxylic acids have been found by using *B/E* and *B²/E* linked scans and isotope substitution techniques. Most of the fragments are due to ionization at silicon, which induces a fragmentation pattern that intimately reflects the structure of the compounds.

INTRODUCTION

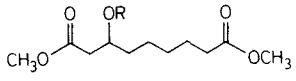
During the metabolism of long-chain dicarboxylic acids in man, 3-hydroxydicarboxylic acids with chain lengths ranging from six to twelve carbon atoms are formed and excreted in the urine.[1-3] The metabolites have been detected by gas chromatography/mass spectrometry (GC/MS) using the highly selective and sensitive multiple ion detection technique. This method, which is used extensively in quantitative analysis, can achieve a selectivity almost as great as that obtained in the full scanning mode by sampling on a great number (>8) of characteristic ions from the compound under investigation. In order to obtain optimal specificity, these ions must be of high abundance (to promote sensitivity) and of high mass (to minimize the possibility of sampling on co-eluting compounds). These conditions are not met by the 3-hydroxydicarboxylic acids, and it is therefore necessary to convert the acids to suitable derivatives prior to GC/MS analysis. The combination of methylating the acid groups and trimethylsilylating the hydroxyl function has so far proven to be the best derivatization procedure for analytical purposes,[1,2] yielding derivatives which have excellent chromatographic properties and whose mass spectra contain ions with high abundance at high masses. In order to establish the connection between the structure and the fragments formed, we have investigated the fragmentation pattern of some 3-hydroxydicarboxylic acids as dimethyl ester trimethylsilyl ether derivatives (**1-4**). The results show that the mass spectra of these derivatives contain fragments which yield valuable structural information.



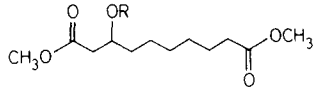
1a R = H
1b R = $Si(CH_3)_3$



2a R^1 = R^2 = CH_3, R^3 = R^4 = H
2b R^1 = R^2 = CH_3, R^3 = H, R^4 = $Si(CH_3)_3$
2c R^1 = CD_3, R^2 = CH_3, R^3 = R^4 = H
2d R^1 = CD_3, R^2 = CH_3, R^3 = H, R^4 = $Si(CH_3)_3$
2e R^1 = CH_3, R^2 = CD_3, R^3 = R^4 = H
2f R^1 = CH_3, R^2 = CD_3, R^3 = H, R^4 = $Si(CH_3)_3$
2g R^1 = R^2 = CH_3, R^3 = D, R^4 = H
2h R^1 = R^2 = CH_3, R^3 = D, R^4 = $Si(CH_3)_3$
2i R^1 = R^2 = CH_3, R^3 = H, R^4 = $Si(CD_3)_3$



3a R = H
3b R = $Si(CH_3)_3$



4a R = H
4b R = $Si(CH_3)_3$

EXPERIMENTAL

Electron impact (EI) mass spectra were recorded on a VG MicroMass 7070H double-focusing mass spectrometer using a direct inlet system (inlet temperature 100-180°C). The ionization energy was 70 eV, except for the low-energy spectra, which were recorded at 10 eV. Metastable transitions were detected by *B/E* and *B²/E* linked scans using a VG linked-scanning unit. Data were acquired and processed on a VG 2050 data system.

^1H NMR (89.55 MHz) and ^{13}C NMR (22.50 MHz) spectra were obtained on a JEOL FX 90 Q spectrometer at 29°C. The ^{13}C NMR C-H decoupling was achieved by a broad-band decoupling pulse at 89.55 MHz.

The infrared spectra were recorded on a Shimadzu IR-435 infrared spectrophotometer as liquid film.

Ozone was prepared with a Fisher Model 501 ozone generator.

† Institute of Mathematical and Physical Sciences, PO Box 953.
‡ Institute of Medical Biology, PO Box 977.

0030-493X/87/070421-09$05.00

Received 16 September 1985
Accepted (revised) 12 January 1987

Synthesis of reference compounds

Methyl 6-oxohexanoate (5). Cyclohexene (8.29 g, 100 mmol) was ozonolysed at −78 °C in methanol/dichloromethane (1:5, 120 cm^3) with some sodium hydrogencarbonate.[4] The solution was filtered and benzene (50 cm^3) was added before the solvents were removed with a rotary evaporator. The resulting clear, viscous oil was dissolved in dichloromethane (50 cm^3) and a mixture of acetic anhydride (20 cm^3) and triethylamine (20 cm^3) was carefully added. This mixture was hydrolysed after 5 h and ether (50 cm^3) was added, the organic phase was then separated and washed with a saturated solution of sodium carbonate until the water phase had become basic. The organic phase was dried (with magnesium sulphate) and evaporated using a rotary evaporator. The resulting oil was distilled (61 °C at 40 Pa) to give **5** (13.1 g, 91%). IR(cm^{-1}): 2925(s), 2845(s), 2700(m), 1730(s), 1435(s), 1360(s), 1010(m). ^{1}H NMR: δ 1.6-1.8(4H, m), 2.1-2.6(4H, m), 3.66 (3H, s), 9.75 (1H, t, J = 1.7 Hz). ^{13}C NMR: δ 21.6, 24.5, 33.8, 43.5, 51.5, 173.6, 201.9. MS (m/z (% RI)): 144(2), 143(3), 113(45), 112(21), 101(45), 95(8), 94(100), 85(16), 84(26), 74(64), 73(11).

Methyl 5-oxopentanoate (6), methyl 7-oxoheptanoate (7) and methyl 8-oxooctanoate (8). These compounds were prepared by similar methods, in yields ranging from 65 to 86%. All compounds gave IR spectra similar to that of compound **5**. ^{1}H NMR: **6**—δ 1.5-1.7(2H, m), 2.2-2.5(4H, m), 3.65(3H, s), 9.75(1H, t, J = 1.7 Hz); **7**—δ 1.4-1.7 (4 H, m), 2.2-2.5(4H, m), 3.67(3H, s), 9.77(1H, t, J = 1.5 Hz); **8**—δ 1.3-1.6(6H, m), 2.1-2.4(4H, m), 3.67 (3H, s), 9.76(1H, t, J = 1.8 Hz). ^{13}C NMR: **6**—δ 17.6, 33.1, 43.0, 51.5, 173.3, 201.5; **7**—δ 21.8, 24.7, 28.7, 33.8, 43.6, 51.4, 173.9, 202.1; **8**—δ 21.5, 24.3, 28.3, 28.4, 33.5, 43.3, 50.9, 173.5, 201.8.

Methyl-d_3 6-oxohexanoate (9). Ozonolysis of cyclohexene was performed as for compound **5**, using methanol-d_4/dichloromethane as solvent. After standard work-up, **9** was purified by distillation (66 °C at 53 Pa) in 87% yield. IR(cm^{-1}): 2830(m), 2700(m), 2240(w), 2190(w), 2080(w), 1720(s), 1085(s). ^{1}H NMR: δ 1.6-1.8(4H, m), 2.1-2.6(4H, m), 9.75(1H, t, J = 1.6 Hz). ^{13}C NMR: δ 21.3, 24.1, 33.4, 43.1, 173.3, 201.4, MS (m/z (% RI)): 147(7), 146(19), 129(14), 117(27), 113(16), 112(14), 111(26), 100(19), 90(40), 77(66).

Methyl-d_3 bromoacetate (10). Bromoacetic acid (27.8 g, 200 mmol) was dissolved in thionyl chloride (25 cm^3) and was occasionally shaken for 2 h. Unreacted thionyl chloride was removed by a stream of dry nitrogen before addition of methanol-d_4 (5 cm^3). After 3 h, the reaction was quenched by addition of water (50 cm^3). The mixture was made slightly basic by adding sodium carbonate before extraction with ether (3 × 50 cm^3). The combined organic phases were dried (with magnesium sulphate), evaporated and distilled (53 °C at 2000 Pa) giving **10** in 95% yield. IR(cm^{-1}): 3005(m), 2850(m), 2250(m), 2180(m), 2080(m), 1730(s), 1400(m), 1300(s). ^{1}H NMR: δ 3.88(2H,s). ^{13}C NMR: δ 26.6, 168.7. MS (m/z (% RI)): 157(22), 155(22), 123(23), 121(23), 113(26), 111(25), 95(46), 93(50), 62(100).

Dimethyl 3-hydroxyoctanedioate (2a). Activated zinc dust (0.65 g, 10 mmol)[5] was suspended in a dry mixture of benzene and ether (5:1, 25 cm^3). A mixture of methyl bromoacetate (1.53 g, 10 mmol) and **5** was then added. The resulting solution was refluxed for 3 h. The reaction was quenched by addition of 10% sulphuric acid (15 cm^3), the layers were separated and the organic phase was washed with dilute sulphuric acid, water and aqueous sodium carbonate before drying (with magnesium sulphate). Compound **2a** was obtained essentially pure in 67% yield by removal of the solvent under reduced pressure. IR(cm^{-1}): 3500(s), 1730(s), 1430(s). ^{1}H NMR: δ 1.2-1.9(6H, m), 2.2-2.6(4H, m), 3.4(1H, s), 3.66(3H, s), 3.70(3H, s), 4.0(1H,m). ^{13}C NMR: δ 24.8, 25.1, 33.7, 34.0, 41.4, 51.4, 51.6, 67.8, 173.8, 174.0

Dimethyl 3-hydroxyheptanedioate (1a), dimethyl 3-hydroxynonanedioate (3a) and dimethyl 3-hydroxydecanedioate (4a). These compounds were prepared in the same way from the corresponding ester aldehyde, giving yields ranging from 54 to 65%. All compounds gave IR spectra similar to that of compound **2a**. ^{1}H NMR: **1a**—δ 1.2-1.7(4H, m), 2.2-2.5(4H, m), 3.4(1H, s), 3.66(3H, s), 3.70(3H, s), 4.0(1H, m); **3a**—δ 1.2-1.8(8H, m), 2.2-2.6(4H, m), 3.66(3H, s), 3.70(3H, m), 4.0(1H, m); **4a**—δ 1.1-1.8(10H, m), 2.2-2.5(4H, m), 2.5(1H, s), 3.64(3H, s), 3.67(3H, m), 4.0(1H, m). ^{13}C NMR: **1a**—δ 18.5, 30.4, 34.0, 41.3, 51.4, 51.7, 67.7, 172.3, 173.2; **3a**—δ 24.6, 24.8, 28.7, 33.7, 36.1, 41.0, 51.1, 51.3, 67.6, 172.9, 173.8; **4a**—δ 24.4, 24.8, 28.7, 33.6, 36.2, 41.0, 50.9, 51.5, 67.5, 172.2, 173.6.

α-Methyl-d_3-ω-methyl 3-hydroxyoctanedioate (2c). The compound was prepared from **10** as described for compound **2a**. The yield was 60%.

ω-Methyl-d_3-α-methyl 3-hydroxyoctanedioate (2e). This was prepared from compound 9 as described for compound **2a**. The yield was 58%.

Dimethyl 3-oxooctanedioate (11). Compound **2a** (0.50 g, 2 mmol) was oxidized by pyridinium chlorochromate[6] (0.65 g, 3 mmol) in dichloromethane (5 cm^3) for 18 h. The black reaction mixture was diluted with dry ether (10 cm^3), and the organic phase was filtered through Florisil. The residue was decanted three times with dry ether before the combined organic phase was evaporated under reduced pressure, giving essentially pure **11** in 75% yield.

Dimethyl 3-deutero-3-hydroxyoctanedioate (2g). Ketodiester **11** (50 mg, 0.2 mmol) was selectively reduced by sodium borodeuteride (0.2 g, 5 mmol) in methanol for 1 h. The reaction mixture was hydrolysed with water (4 cm^3), neutralized with dilute sulphuric acid and extracted with ether (3 × 5 cm^3). The organic phase was dried (with magnesium sulphate) and evaporated under reduced pressure to yield **2g**.

Silylation

The 3-hydroxy diesters were silylated with a mixture of *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) and

1% trimethylsilyl chloride. Unreacted BSTFA was removed by a stream of dry nitrogen, and the corresponding 3-trimethylsiloxy dimethyl esters (compounds **1b**, **2b**, **2d**, **2f**, **2h**, **3b** and **4b**) were immediately analysed on the mass spectrometer. Compound **2a** was in addition silylated with *N,O*-bis(tri(methyl-d_3)silyl)acetamide (d_{18}-BSA), yielding the corresponding trimethylsilyl-d_9 ether derivative **2i**.

RESULTS AND DISCUSSION

The mass spectra of the silylated hydroxy diesters (Fig. 1) all contain a number of peaks due to fragments resulting from the same processes, which are discussed for one compound only, namely, dimethyl 3-trimethylsiloxyoctanedioate (**2b**).

No molecular ion was observed in the mass spectrum of **2b** (Fig. 1). Furthermore, no metastable transition from the molecular ion in the first field-free region (1st FFR) could be detected by B^2/E linked scanning, even with an ionization potential as low as 10 eV. This can be due to low activation energies or high-frequency factors in the primary reactions. In **2b** all primary fragments are due to single-bond cleavages, and high-frequency factors are the most plausible explanation for the efficient processes.

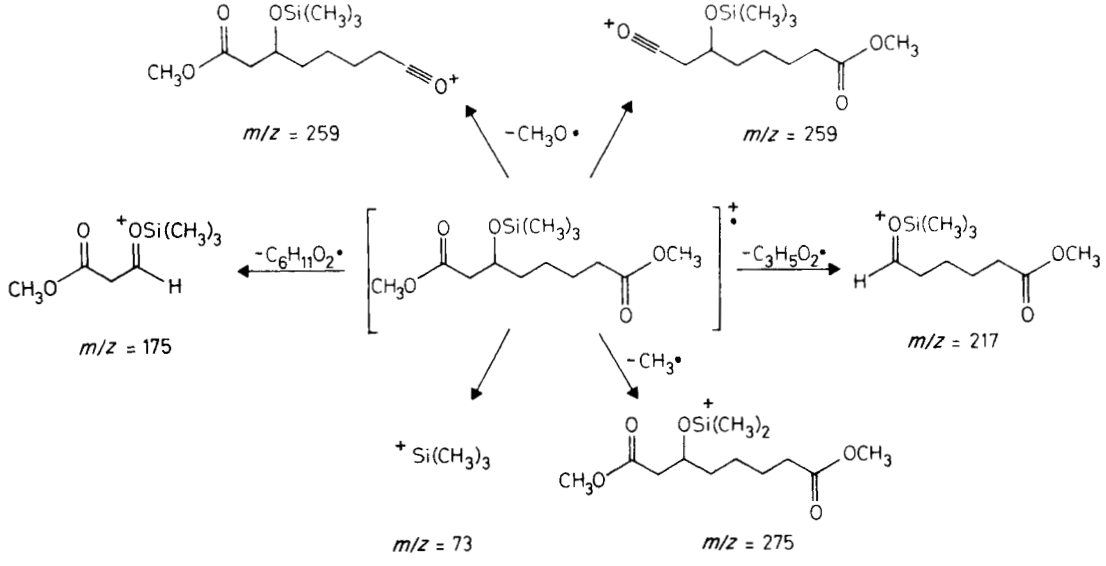
The presence of a number of strongly fragmentation-directing functional groups in the molecule renders a large number of different primary fragmentation processes available to the molecular ion. Typical examples are loss of a methyl radical from the trimethylsilyl (TMS) group to yield m/z 275, loss of a methoxy radical from one of the ester functional groups to give m/z 259 and cleavage on either side of the trimethylsiloxy moiety producing the m/z 217 and 175 fragments, respectively. The base peak at m/z 73, due to the TMS ion, is possibly also the result of a primary reaction. These processes are summarized in Scheme 1.

Formation and fragmentation of m/z 275

The m/z 275 fragment was formed from $M^{+\cdot}$ by expulsion of a methyl radical from the TMS moiety.[7,8] This was borne out by comparing the mass spectrum of **2b** with that of the TMS-d_9 analogue **2i**: the peak corresponding to m/z 275 for **2b** appeared at m/z 281 for **2i**, which shows that the expelled radical contained three deuterium atoms.

The even-electron species m/z 275 is degraded by five different reactions, which are outlined in Scheme 2 and Fig. 2. Both ester groups eliminate methanol with the formation of the m/z 243 ions *a* and *b*. This was established by B/E linked scans of the m/z 278 ion formed from the methyl-d_3 ester **2d** (Fig. 3), which had one metastable transition to m/z 246, corresponding to an elimination of methanol from the ω-ester group, and one transition to m/z 243, with elimination of methanol-d_3 from the α-ester group. Analogous results were obtained with **2f** (Fig. 4).

Another reaction which takes place in both ester groups is a McLafferty rearrangement with formation of m/z 201. B/E linked scans of m/z 278 from **2d** showed loss of a fragment with mass 74 u, corresponding to a rearrangement at the ω-ester group, and a loss of 77 u, corresponding to a rearrangement in the α-ester moiety (Fig. 3). The last important mode of fragmentation from m/z 275 involves loss of ketene affording an ion at m/z 233.[9] This transformation is possibly initiated by a 1,3-hydrogen transfer from C(3) to the silicon atom, thereby producing an electron-deficient centre at C(3) (Scheme 2). The methoxy group from the α-ester function is then transferred to C(3), and a subsequent elimination of ketene occurs to give *c*. The remaining ester function then eliminates methanol to give an m/z 201 ion. In order to clarify the hydrogen-transfer step, compound **2h** was synthesized. No deuterium isotope effect was observed in the mass spectrum of this compound, indicating that the hydrogen transfer is not the rate-limiting step in this process. An analogous ketene elimi-



Scheme 1. Primary fragmentation processes from the molecular ion of compound **2b**.

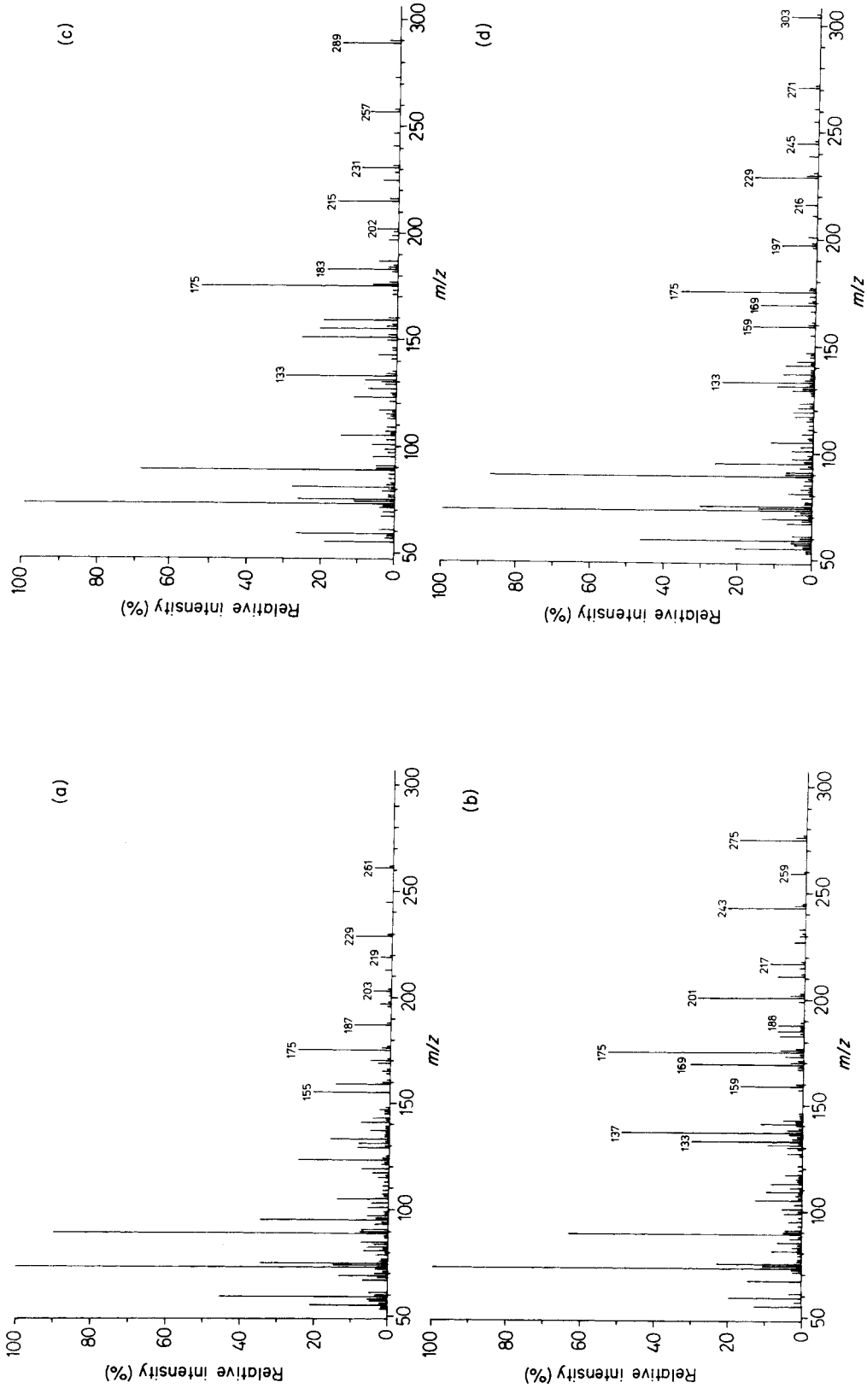
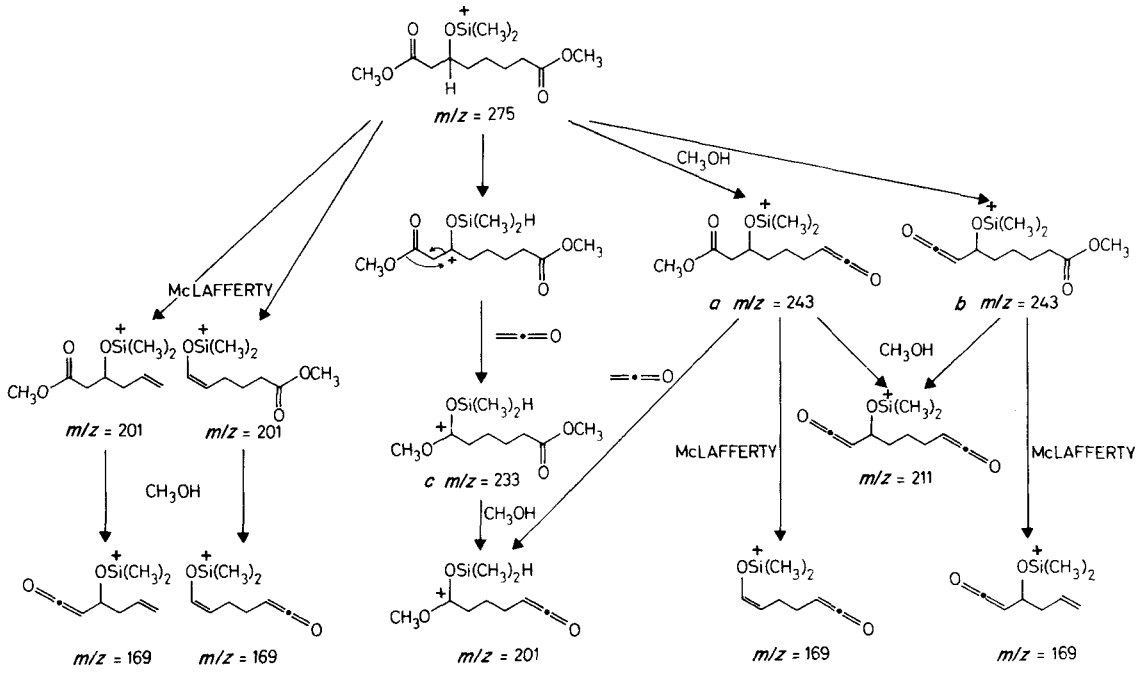


Figure 1. Mass spectra of (a) **1b**, (b) **2b**, (c) **3b** and (d) **4b**.



Scheme 2. Secondary fragmentation reactions from m/z 275.

nation occurs from *a*, producing ion m/z 201, according to a linked scan of *a* and of the corresponding m/z 246 ion formed from **2d**. Interestingly, the other m/z 243 ion formed from **2b**, *i.e. b*, with an ω-ester moiety, does not undergo such a transformation. Both *b* and *a* can eliminate another molecule of methanol yielding an ion at m/z 211 which does not give rise to any metastable transition. The same species also eliminates a fragment with mass 74 u and gives daughter ions at m/z 169, probably by a McLafferty rearrangement which in the 2nd FFR gives a metastable transition at m/z 117.5 (calc. 117.535). The corresponding ions m/z 246 and 243 (from **2d** and **2f**) lose fragments with mass 77 and 74 u, respectively, yielding transitions at m/z 116.1 (calc. 116.102) and 117.5. The m/z 169 ions formed in this manner may equilibrate with the m/z 169 ions formed from m/z 201. In any case, one or several of the m/z 169 ions expel carbon monoxide and form a fragment at m/z 141.

Formation and fragmentation of m/z 217

The m/z 217 fragment conceivably results from an α-cleavage on the α-side of the trimethylsilyloxy moiety together with the elimination of a $CH_3OOCCH_2^{\bullet}$ radical. This hypothesis is supported by isotope substitution experiments. The TMS-d_9 diester **2i** yields an ion at

m/z	Fragment ion
275	$[M-CH_3^{\bullet}]^+$
259	$[M-CH_3O^{\bullet}]^+$
243	$[M-CH_3^{\bullet}-CH_3OH]^+$
233	$[M-CH_3^{\bullet}-C_2H_2O]^+$
227	$[M-CH_3O^{\bullet}-CH_3OH]^+$
217	$[M-CH_3OOCCH_2^{\bullet}]^+$
211	$[M-CH_3^{\bullet}-2\times CH_3OH]^+$
201	$[M-CH_3^{\bullet}-CH_3OOCCH_3]^+$
185	$[M-CH_3OOCCH_2^{\bullet}-CH_3OH]^+$
175	$[CH_3OOCCH_2CHOSi(CH_3)_3]^+$
169	$[C_9H_{13}O_3]^+$
169	$[C_8H_{13}O_2Si]^+$
141	$[C_7H_{13}OSi]^+$
137	$[C_8H_9O_2]^+$
133	$[C_5H_{13}O_2Si]^+$
131	$[C_6H_{15}OSi]^+$
117	$[C_4H_9O_2Si]^+$

Figure 2

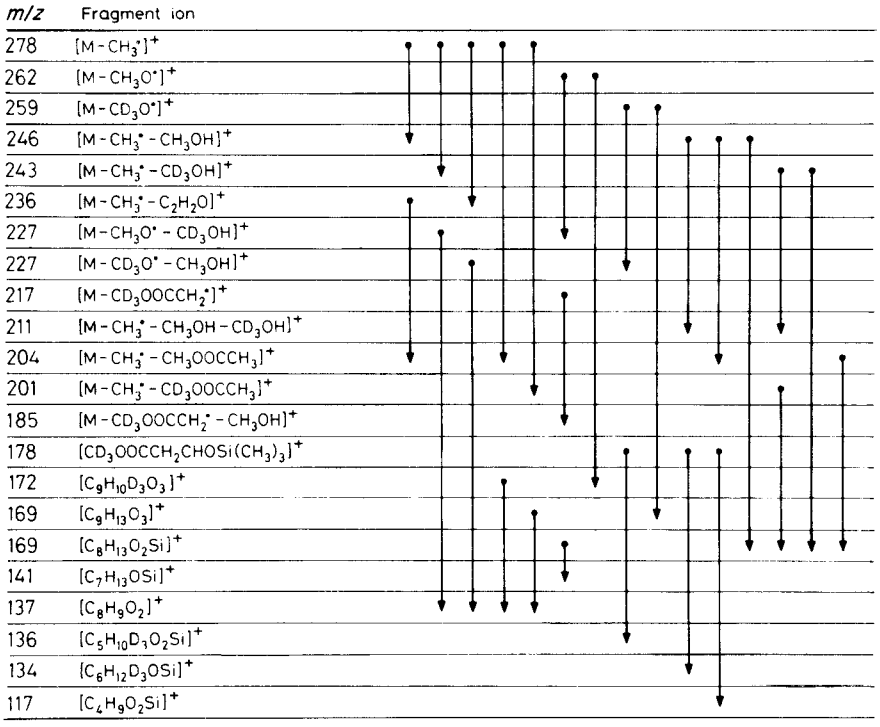


Figure 3

m/z 266 showing that the TMS group is still present, and, furthermore, the α-methyl-d_3 ester derivative **2d** yields m/z 217 while the ω-methyl-d_3 ester **2f** yields m/z 220, indicating a cleavage between the C(2) and C(3) atoms. Only one metastable transition is observed from the m/z 217 ion, namely, methanol elimination from the ω-ester function to m/z 185. This transition is also observed in the 2nd FFR as a broad peak at m/z 157.9 (calc. 157.817).

Formation and fragmentation of m/z 175

Cleavage between C(3) and C(4) in the diester chain of the molecular ion, the other α-cleavage[7,8] available to the trimethylsilyloxy moiety, produces the m/z 175 fragment. Isotopic substitution experiments, analogous to those outlined above, showed that the fragment contained a complete TMS group and the α-ester function. The ion decomposes by three mestable transitions,

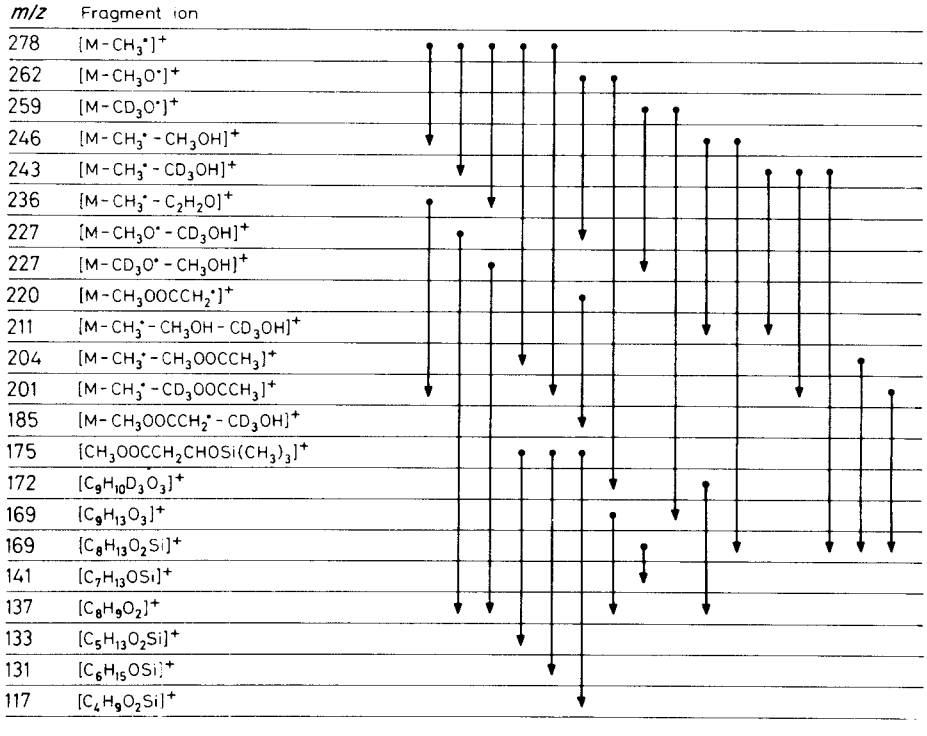
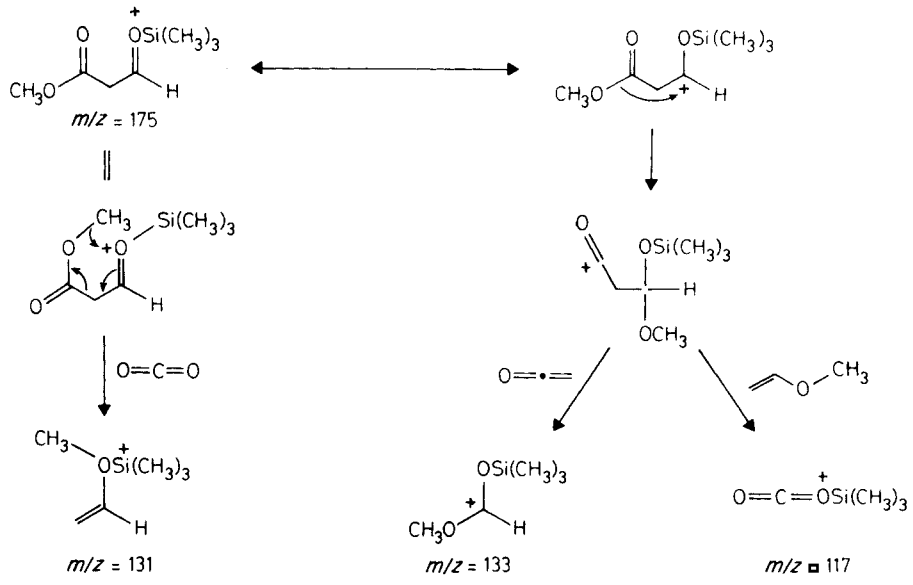


Figure 4



Scheme 3. Secondary fragmentation reactions from *m/z* 175.

shown in Scheme 3. One is a ketene elimination to *m/z* 133, probably by a mechanism similar to that described for the ketene elimination in the *m/z* 275 fragmentation series (Scheme 2). This rearrangement could also be observed in the 2nd FFR as a broad peak at *m/z* 101.1 (calc. 101.080). Another reaction involves a transfer of the ester methyl group on to the oxygen atom in the TMS ether moiety and subsequent elimination of carbon dioxide, creating an ion at *m/z* 131. The third rearrangement, to *m/z* 117, involves loss of methyl vinyl ether. The proposed structure of the *m/z* 117 ion is based on isotopic substitution experiments and high-resolution data, indicating a complete TMS group and an elemental composition of $C_4H_9O_2Si$.

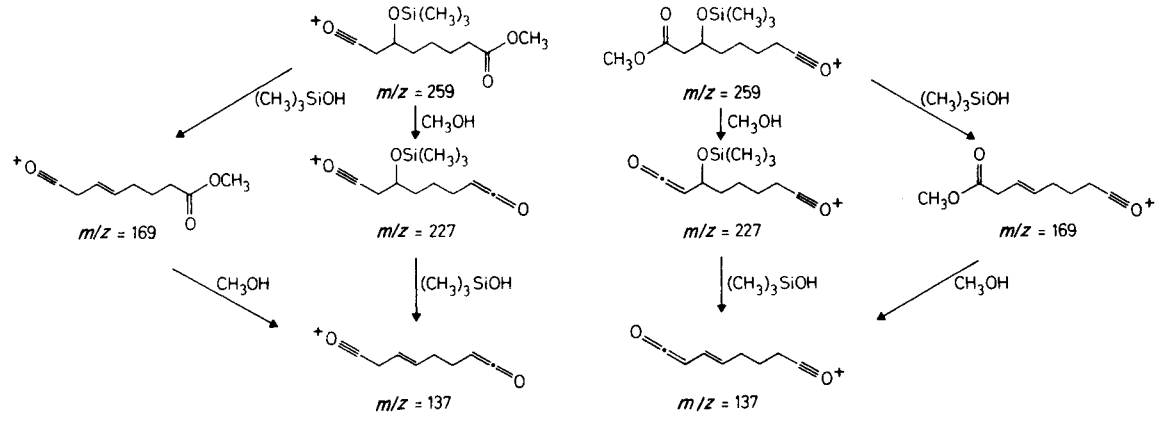
Formation and fragmentation of *m/z* 259

The *m/z* 259 fragments result from a loss of a methoxy radical from the ester groups. This was established by isotopic substitution, observing that compound **2d** lost both methoxy-d_3 and methoxy radicals as a result of cleavage at the α- and ω-ester moiety, respectively (Fig. 3). No fragment due to the typical methanol elimination[9] could be observed. The *m/z* 259 ions eliminated a molecule of methanol to *m/z* 227, or trimethylsilanol to *m/z* 169. The *m/z* 227 and 169 ions could further eliminate trimethylsilanol or methanol, respectively, yielding an ion at *m/z* 137 (Scheme 4). Loss of trimethylsilanol, which is very common in steroidal TMS derivatives,[10,11] was restricted to the *m/z* 259 series.

Fragmentations observed in the other homologues

The mass spectra of compounds **1b**, **2b**, **3b** and **4b** are presented in Fig. 1, and the elemental composition of most of the characteristic fragments are listed in Table 1. These data clearly reveal that a number of the fragments have a mass difference of 14 u as expected for a series of homologues, whereas other ions appear to be common to all compounds. The fragmentation of the compounds is therefore dominated by the same fundamental processes as described for compound **2b**.

However, an important fragmentation pathway from dimethyl 3-trimethylsiloxydecanedioate (**4b**) and



Scheme 4. Secondary fragmentation reactions from *m/z* 259.

Table 1. The characteristic fragment ions of dimethyl 3-trimethylsiloxyalkanedioates 1b, 2b, 3b and 4b[a]

Fragment ion	*m/z* (% relative intensity) 1b	2b	3b	4b
$[M-CH_3^{\bullet}]^+$	261 (5)	275 (5)	289 (16)	303 (7)
$[M-CH_3O^{\bullet}]^+$	245 (2)	259 (1)	273 (1)	
$[M-CH_3^{\bullet}-CH_3OH]^+$	229 (10)	243 (9)	257 (8)	271 (6)
$[M-CH_3^{\bullet}-C_2H_2O]^+$	219 (3)	233 (1)	247 (2)	261 (1)
$[M-CH_3O^{\bullet}-CH_3OH]^+$	213 (2)	227 (2)	241 (2)	
$[M-CH_3OOCCH_2^{\bullet}]^+$	203 (5)	217 (3)	231 (10)	245 (1)
$[M-CH_3^{\bullet}-CH_3OH-CH_3OH]^+$	197 (3)	211 (4)	225 (4)	239 (3)
$[M-CH_3^{\bullet}-CH_3OOCCH_2]^+$	187 (10)	201 (10)	215 (17)	229 (17)
$[M-CH_3OOCCH_2^{\bullet}-CH_3OH]^+$	171 (6)	185 (5)	199 (2)	
$[CH_3OOCCH_2CHOSi(CH_3)_3]^+$	175 (25)	175 (18)	175 (54)	175 (35)
$[M-C_5H_{13}O_3^{\bullet}]^+/[M-C_4H_{13}O_2Si^{\bullet}]^+$[b]	155 (21)	169 (19)	183 (20)	197 (10)
$[M-C_6H_{13}H_4^{\bullet}]^+$	127 (9)	141 (8)	155 (21)	169 (15)
$[M-C_5H_{17}O_3Si^{\bullet}]^+$	123 (25)	137 (24)	151 (27)	165 (12)
$[C_5H_{13}O_2Si]^+$	133 (16)	133 (17)	133 (30)	133 (25)
$[C_6H_{15}OSi]^+$	131 (8)	131 (7)	131 (9)	131 (10)
$[C_4H_9O_2Si]^+$	117 (5)	117 (5)	117 (4)	117 (5)

[a] Fragments with relative intensity lower than 1% are omitted.
[b] The relative intensity unknown (two fragments at the same nominal *m/z* value).

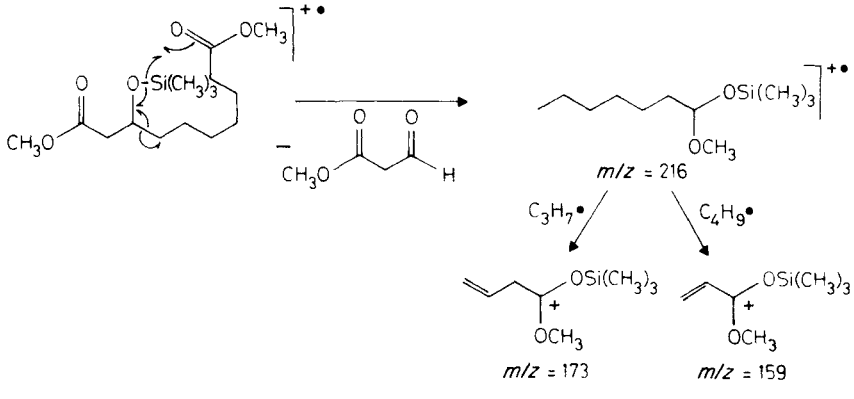
dimethyl 3-trimethylsiloxynonanedioate (**3b**) (Scheme 5) is not observed in the lower homologues **2b** and **1b**. For compound **4b**, this fragmentation series originates from an ion at *m/z* 216, probably formed by a primary process. Isotopic substitution experiments reveal that the *m/z* 216 ion contains a complete TMS group and the ω-terminal methoxy moiety. Together with the elemental composition, $C_{11}H_{24}O_2Si$, this strongly suggests that extensive rearrangement takes place during the formation of this ion. Scheme 5 includes a tentative rationale of the cleavage process. A prerequisite for this transformation is an alkyl chain long enough to allow a macrocyclic transition state with the silicon atom and the ω-carbonyl oxygen atom in proximate positions.[12-14] A bond is formed between these atoms, while the existing silicon-oxygen bond is broken. This cleavage is accompanied by a cleavage between the C(3) and C(4) atoms in the diester alkyl chain affording an ion at *m/z* 216 with the stable methyl TMS acetal cation structure. However, in contrast with the *m/z* 233 ion from the *m/z* 275 series (Scheme 2), the *m/z* 216 ion is a cation radical, which further eliminates propyl and butyl radicals yielding fragments at *m/z* 173 and 159, respectively.

CONCLUDING REMARKS

From the results discussed above, it is evident that EI induced fragmentation of the dimethyl ester TMS ether derivatives of the 3-hydroxydicarboxylic acids is strongly directed by the TMS substituent. The molecular ion undergoes a number of characteristic fragmentation processes, namely, methyl elimination[7,8] and α-cleavages at either side of the trimethylsilyloxy moiety,[7-9,12] yielding mass spectra with useful structural information. Additional information about the structure is obtained from fragments formed from the ester groups. 3-Trimethylsiloxy bis(trimethylsilyl) ester analogues produced mass spectra that were less characteristic and harder to interpret.[1,15]

Acknowledgement

Financial support from the Norwegian Research Council for Science and the Humanities is gratefully acknowledged.



Scheme 5. Formation and degradation of *m/z* 216 from compound **4b**.

REFERENCES

1. J. Greter, S. Lindstedt, H. Seeman and G. Steen, *Clin. Chem.* **26**, 261 (1980).
2. J. S. Svendsen, L. K. Sydnes and J. E. Pettersen, in *Chromatography and Mass Spectrometry in Nutrition Science and Food Safety*, ed. by A. Frigerio and H. Milon, p. 223. Elsevier, Amsterdam (1984).
3. J. S. Svendsen, J. E. Whist and L. K. Sydnes, *J. Chromatogr.* **337**, 9 (1985).
4. S. L. Schreiber, R. E. Claus and J. Reagan, *Tetrahedron Lett.* **23**, 3867 (1982).
5. C. R. Hauser and D. S. Breslow, *Org. Synth. Coll. Vol. III* 408 (1955).
6. E. J. Corey and J. W. Suggs, *Tetrahedron Lett.* 2647 (1975).
7. J. Diekman and C. Djerassi, *J. Org. Chem.* **39**, 1005 (1967).
8. P. Vouros and D. J. Harvey, *J. Chem. Soc., Perkin Trans. 1* 727 (1973).
9. G. Eglinton, D. H. Hunneman and A. McCormic, *Org. Mass Spectrom.* **1**, 593 (1968).
10. I. Björkhem, J. Å. Gustafsson and J. Sjövall, *Org. Mass Spectrom.* **7**, 227 (1973).
11. G. H. W. Brooks, E. C. Horning and J. S. Young, *Lipids* **3**, 391 (1968).
12. W. J. Richter and A. L. Burlingame, *J. Chem. Soc., Chem. Commun.* 1158 (1968).
13. P. Capella and C. M. Zorzut, *Anal. Chem.* **40**, 1458 (1968).
14. G. H. Draffan, R. N. Stillwell and J. A. McCloskey, *Org. Mass Spectrom.* **1**, 669 (1968).
15. T. Niwa, K. Yamada, T. Ohki and H. Furukawa, *J. Chromatogr.* **337**, 1 (1985).