Mass Spectral Studies on Some Naturally Occurring Phloroglucinol Derivatives. Part I. The Mass Spectra of Filicinic Acid and Its Acetyl, Propionyl and Butyryl Derivatives

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The mass spectrometric fragmentation of filicinic acid (I) and its
acetyl, propionyl, and butyryl derivatives (II), (III), (IV) has been
investigated with the aid of high resolution mass spectrometry.

Les fragmentations en spectrométrie de masse de l'acide filicinique
(I), ainsi que celles de ses dérivés acétyle, propionyle et butyryle (II),
(III), (IV), ont été examinées à l'aide de la spectrométrie de masse à
haute résolution.

In connection with our studies of the mass spectral behavior of some
naturally occurring polycyclic phloroglucinol derivatives isolated from
rhizomes of different *Dryopteris* species,[1-3] it was desirable to collect additional
information on the fragmentation of their monocyclic break-down products.
In this paper we describe the mass spectral behavior of filicinic acid (I) and
its acetyl, propionyl, and butyryl derivatives (II), (III), (IV).
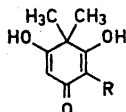
(I)   R = H
(II)   R = CO—CH₃
(III) R = CO—CH₂—CH₃
(IV)   R = CO—CH₂—CH₂—CH₃

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The mass spectra are presented in Figs. 1 – 4 and the results of accurate mass measurements in Table 1.

Considering the mass spectral behavior of filicinic acid (I) and its acyl derivatives (II), (III), and (IV), the existence of several tautomeric forms in the ionisation chamber must be taken into account. That is why, in many fragmentation processes depicted in this paper, there are several ways to describe the fragmentation patterns, of which the most appropriate is to assume that the positive charge is on one of the oxygen atoms or to use the
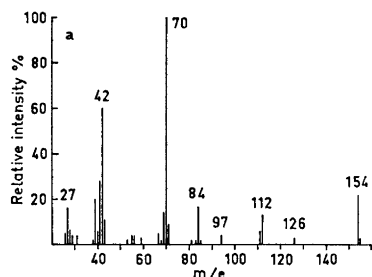

Fig. 1a. Mass spectrum (75 eV) of filicinic acid (I).
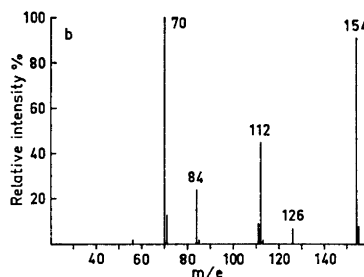

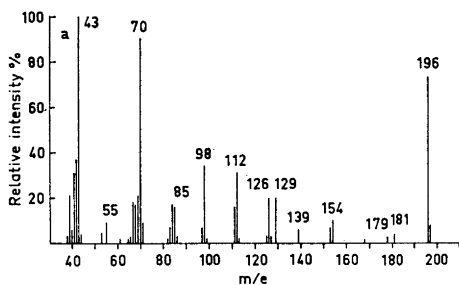Fig. 1b. Mass spectrum (12 eV) of filicinic acid (I).

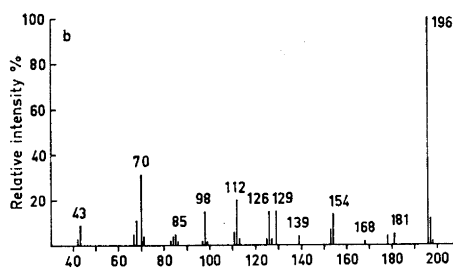Fig. 2a. Mass spectrum (75 eV) of acetyl-filicinic acid (II).

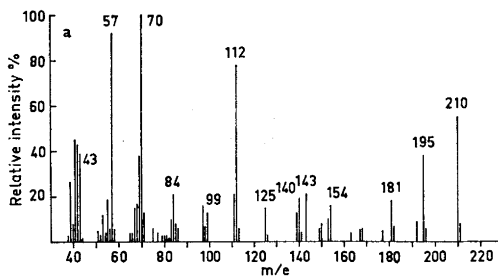Fig. 2b. Mass spectrum (12 eV) of acetyl-filicinic acid (II).

Fig. 3a. Mass spectrum (75 eV) of propionylfilicinic acid (III).
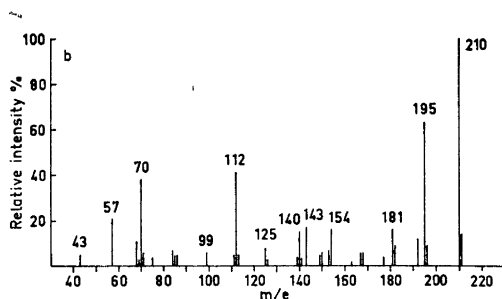
Fig. 3b. Mass spectrum (12 eV) of propionylfilicinic acid (III).
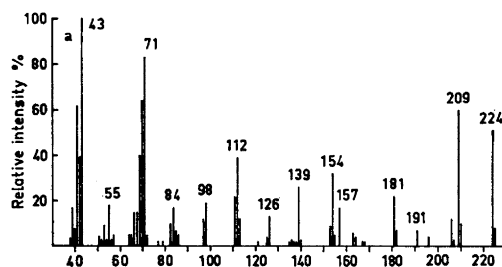
Fig. 4a. Mass spectrum (75 eV) of butyrylfilicinic acid (IV).
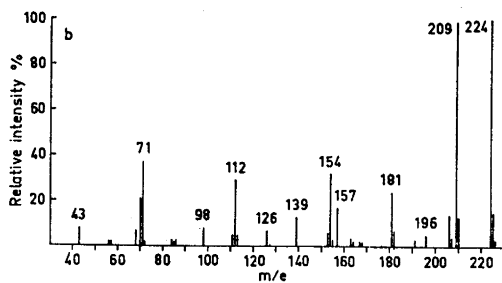
Fig. 4b. Mass spectrum (12 eV) of butyrylfilicinic acid (IV).

retro-Diels-Alder process. However, in many cases both processes may operate simultaneously and a distinction between them, on the basis of the available experimental facts, is not always possible. Despite this, generally only one process is described in connection with the different fragmentation patterns.

In the fragmentation of filicinic acid (I), five main fragmentations of the molecular ion are expected (*cf.* Scheme 1), leading to $M - CO$ $(M - 28)$ (route A), $M - C_2H_2O$ $(M - 42)$ (route B), $M - C_4H_6O$ $(M - 70)$ (route C), $M - C_4H_4O_2$ $(M - 84)$ (route D), and $M - C_6H_8O_2$ $(M - 112)$ (route E).

Table 1. High resolution measurements.

| Ion (m/e)	Elemental composition	I %	II %	III %	IV %
41	C_2HO	10		5	
	C_3H_5	90	q	95	q
42	C_2H_2O	20	20	20	20
	C_3H_6	80	80	80	80
43	C_2H_3O	65	q	80	35
	C_3H_7	35		20	65
55	C_3H_3O	65	75	45	45
	C_4H_7	35	25	55	55
56	C_3H_4O	60			
	C_4H_8	40			
57	C_3H_5O			q	
67	C_4H_3O		25	20	25
	C_5H_7		75	80	75
69	C_3HO_2	60	55	55	45
	C_4H_5O	40	45	45	55
70	C_4H_6O	q	q	q	q
71	C_4H_7O				q
84	$C_4H_4O_2$	q	q	55	95
	C_5H_8O			45	5
85	$C_4H_5O_2$		85		
	C_5H_9O		15		
97	$C_5H_5O_2$	q	q	q	90
	C_6H_9O				10
98	$C_5H_6O_2$		q	q	90
	$C_6H_{10}O$				10
99	$C_5H_7O_2$			q	
111	$C_5H_3O_3$		25	40	25
	$C_6H_7O_2$	q	75	60	75
112	$C_6H_8O_2$	q	q	q	q
113	$C_6H_9O_2$				q
125	$C_6H_5O_3$			30	
	$C_7H_9O_2$			70	
126	$C_6H_6O_3$		70		30
	$C_7H_{10}O_2$	q	30		70
129	$C_5H_5O_4$		q		
139	$C_7H_7O_3$		q		q
140	$C_7H_8O_3$			q	
143	$C_6H_7O_4$			q	
153	$C_8H_9O_3$		q	q	
154	$C_8H_{10}O_3$		q	q	q
157	$C_7H_9O_4$				q
167	$C_8H_7O_4$			20	25
	$C_9H_{11}O_3$			80	75
168	$C_9H_{12}O_3$			q	
181	$C_9H_9O_4$			q	70
	$C_{10}H_{13}O_3$				30
182	$C_9H_{10}O_4$			35	40
	$C_{10}H_{14}O_3$			65	60
196	$C_{10}H_{12}O_4$				q

The relative intensities of the ions presented in the table do not take into account the contribution of isotopic ions. Numerical values are considered accurate to $\pm 5\%$ for peaks in excess of 20 % relative abundance. The symbol q refers to a percentage superior to 95 %.

$C_6H_7O_2$ $C_6H_7O_2$ $C_5H_5O_2$ $\xrightarrow{-CO}$ C_4H_5O
m/e 111   m/e 111   m/e 97   m/e 69

$-CH_3\cdot$ ↑ $-H\cdot$ ↑ $-CH_3\cdot$
m*   m*

$C_7H_{10}O_2$ $C_6H_8O_2$
m/e 126   m/e 112

$-CO$ ↑ $-C_2H_2O$ C_4H_5O $\xrightarrow{-CO}$ C_3H_5
m*   m* $-C_2H_2O$ m/e 69   m/e 41
Route A Route B

                                                          $-H\cdot$

      CH_3 CH_3 Route D C_4H_6O $\xrightarrow[m^*]{-CO}$ C_3H_6
HO   OH $\overline{-C_4H_4O_2}$ m/e 70   m/e 42

        O $-CH_3\cdot$

$C_8H_{10}O_3$ Route C C_2H_3O C_3H_3O
m/e 154   m/e 43   m/e 55
                C_4H_6O
Route E $-\dot{C}_2HO$
       $-C_6H_8O_2$ $C_4H_4O_2$ m* $-CH_3\cdot$ C_3HO_2
                       m/e 84   m/e 69

C_2H_2O
m/e 42 $-CO$ $-C_2H_2O$

                       C_3H_4O C_2H_2O
                       m/e 56   m/e 42

Scheme 1.
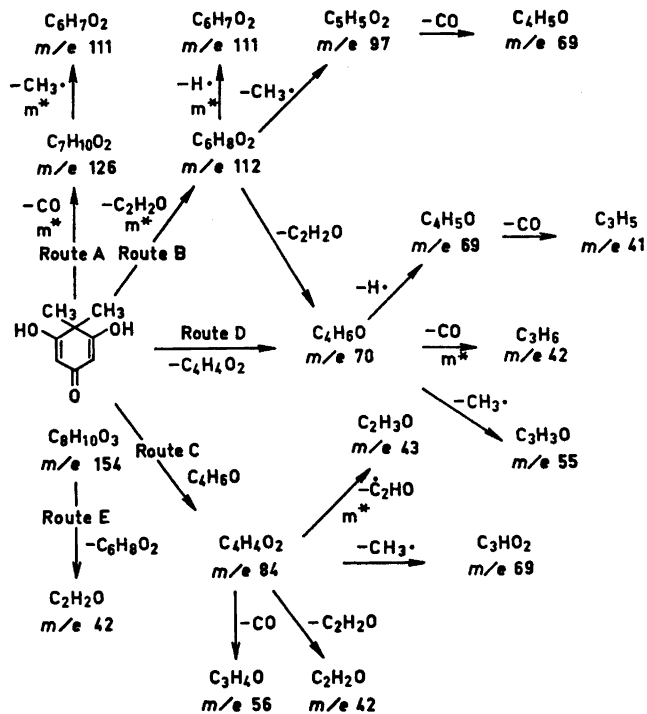
In the case of the acyl derivatives, the 84 of $M-84$ (route D) has to be replaced by $84+42$, $84+56$, and $84+70$ for the acetyl, propionyl, and butyryl derivatives, respectively. As the cleaved part may or may not contain the side chain, it may be expected that the fragmentation of these acyl derivatives will lead, in connection of routes B and E, not only to $M-42$ and $M-112$ ions, but also to $M-(42+42)$, $M-(112+42)$, $M-(42+56)$, *etc.*, ions. Furthermore, the spectra of all acyl derivatives may be expected to contain the elements of the filicinic acid fragmentation pattern because of the following rearrangements.
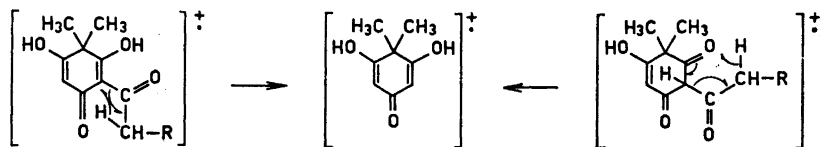
Scheme 1 shows, on the basis of the proposed paths, the fragmentation pattern of filicinic acid (I), considered with the experimental facts. Transitions indicated by an m* are supported by the presence of an appropriate metastable peak.

*Route A.* The formation of the ion $C_7H_{10}O_2^{\cdot+}$ of m/e 126, and the ion $C_6H_7O_2^+$ of m/e 111, may be explained on the basis of the scheme depicted below. These steps are confirmed by the presence of metastable peaks at m/e 103 and 97.8. However, this fragmentation does not seem to play a very important role (*cf.* acyl derivatives). Some of the ions of m/e 111 are produced by a different route (*cf.* route B).
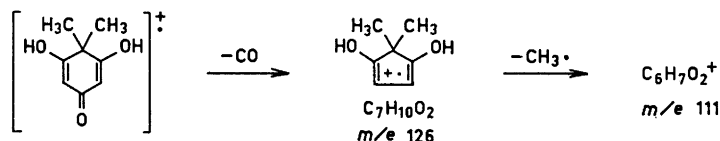
Route B. Since several tautomeric forms of filicinic acid (I) may exist in the ionisation chamber, it is probably best to describe these fragmentations by starting from different forms. The loss of a C_2H_2O unit from the molecular ion, which is confirmed by the presence of a metastable peak at m/e 81.5, leads to the ion $C_6H_8O_2^{\cdot+}$ of m/e 112. Depending on which tautomeric form is in question, further fragmentation may proceed by different routes.

The loss of a hydrogen radical leads to the $C_6H_7O_2^+$ ion (m/e 111) (*cf.* route A). A metastable peak at m/e 110 confirms that this ion is partly derived from the ion of m/e 112.
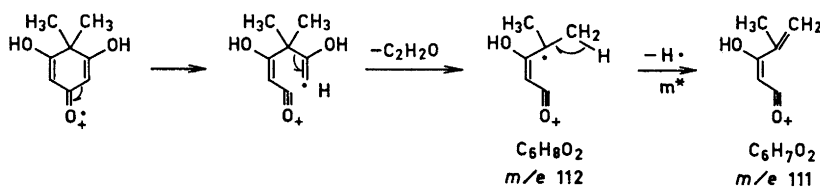
The second process depicts the successive losses of two C_2H_2O units leading to the $C_4H_6O^{\cdot+}$ ion (m/e 70). Further fragmentation of this ion is described in connection with route D.
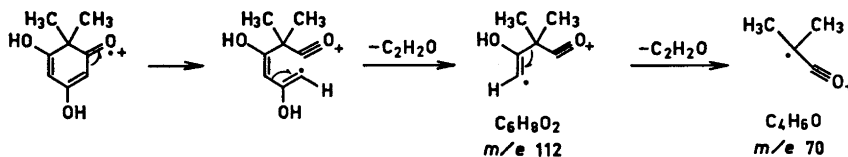
The elimination of a methyl radical from the $C_6H_8O_2^{\cdot+}$ ion leads to the $C_5H_5O_2^+$ ion (m/e 97), from which the $C_4H_5O^+$ ion (m/e 69) is formed by the loss of CO. The $C_4H_5O^+$ ion is formulated as a cyclopropenyl cation derivative which represents a relatively stable 2π-electron aromatic system.[4]
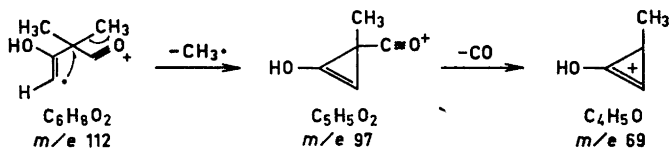

It is noteworthy that there is no loss of CO from the $C_6H_7O_2^+$ ion (no $C_5H_8O^+$ ion present).

Route C. Accurate mass measurement showed that the peak at m/e 84 is a singlet corresponding to $C_4H_4O_2^{\cdot+}$. The spectrum taken at low electron voltage (Fig. 1b) suggests that this ion may be formed directly from the molecular ion. However, there is no metastable peak that supports this proposal. Again, further fragmentations are perhaps best described by assuming that different tautomeric forms of filicinic acid (I) are involved in the formation of the $C_4H_4O_2^{\cdot+}$.

The first process involves the loss of a methyl radical leading to the resonance stabilized $C_3HO_2^+$ ion, which represents 60 % of the total intensity of the peak at m/e 69 (*cf.* route D). Hydrogen transfer obviously occurs in the formation of this ion.
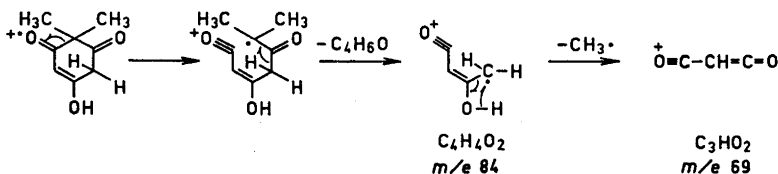
In the second process, the loss of a C_2H_2O unit leads to the $C_2H_2O^{\cdot+}$ radical ion which represents 20 % of the total intensity of the peak at m/e 42. However, this radical ion may also be formed directly from the molecular ion (*cf.* route E).
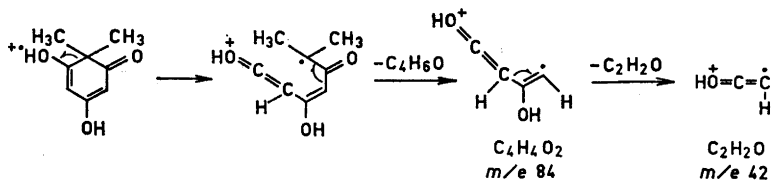
The third process leading to the formation of the $C_2H_3O^+$ ion is best represented by starting with a retro-Diels-Alder process.

$$\left[\underset{OH}{\overset{H_3C\quad CH_3}{\overset{O\quad\quad O}{\bigcirc}}}\right]^{\ddagger} \xrightarrow{-C_4H_6O} \underset{\underset{\underset{m/e\ 84}{C_4H_4O_2}}{HO^{\bullet}_+}}{CH_2=C-CH=C=O} \xrightarrow{-\overset{\bullet}{C_2}HO} \underset{\underset{m/e\ 43}{C_2H_3O}}{CH_2=C=\overset{+}{O}H}$$
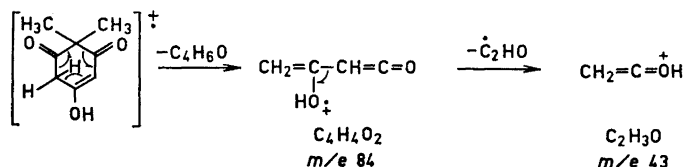
Furthermore, the presence of the $C_3H_4O^{\cdot+}$ ion $(m/e\ 56)$, may be explained by loss of carbon monoxide from the ion of $m/e\ 84$.

Route D. The direct formation of the $C_4H_6O^{\cdot+}$ ion $(m/e\ 70)$ from the molecular ion suggested by the spectrum taken at low electron voltage (Fig. 1b) may be presented in the following manner.

$$\underset{OH}{\overset{H_3C\quad CH_3}{\overset{HO}{\bigcirc}_{\cdot+}^{O}}} \longrightarrow \underset{OH}{\overset{H_3C\quad CH_3}{\overset{HO}{\bigcirc}_{H}^{O_{\cdot}}}} \xrightarrow{-C_4H_4O_2} \underset{\underset{m/e\ 70}{C_4H_6O}}{\overset{H_3C\quad CH_3}{\overset{\bullet}{\underset{O_+}{\diagup}}}}$$

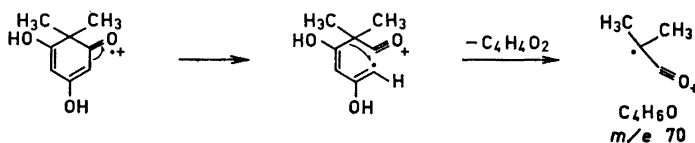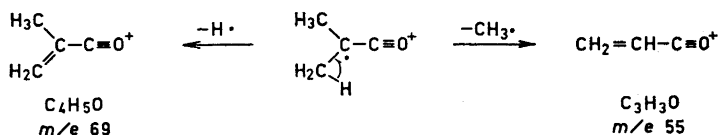The peaks at m/e 69 and 55, which are doublets according to accurate mass measurements, are due, the first one to $C_4H_5O^+$ (40 %) and $C_3HO_2^+$ (60 %), and the second one to $C_3H_3O^+$ (65 %) and $C_4H_7^+$ (35 %). Of these the $C_4H_5O^+$ ion may be derived from the ion of m/e 70 by loss of a hydrogen radical, and the $C_3H_3O^+$ ion by loss of a methyl radical.

$$\underset{\underset{m/e\ 69}{C_4H_5O}}{\overset{H_3C}{\underset{H_2C}{\diagup}}C-C\equiv O^+} \xleftarrow{-H\cdot} \overset{H_3C}{\underset{H_2C\underset{H}{\diagdown}}{\diagup}}C-C\equiv O^+ \xrightarrow{-CH_3\cdot} \underset{\underset{m/e\ 55}{C_3H_3O}}{CH_2=CH-C\equiv O^+}$$

Loss of carbon monoxide from $C_4H_6O^{\cdot+}$, $C_4H_5O^+$, and $C_3H_3O^+$ leads to $C_3H_6^{\cdot+}$ $(m/e\ 42)$, $C_3H_5^+$ $(m/e\ 41)$, and $C_2H_3^+$ $(m/e\ 27)$, respectively.

Route E. The direct formation of the $C_2H_2O^{\cdot+}$ ion $(m/e\ 42)$ from the molecular ion, which is suggested by the spectrum taken at low electron voltage (Fig. 1b), but not confirmed by a metastable peak, may be presented in either or both of the following ways.
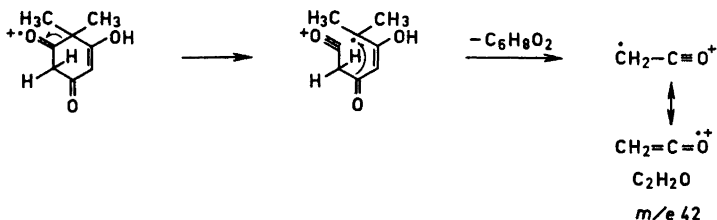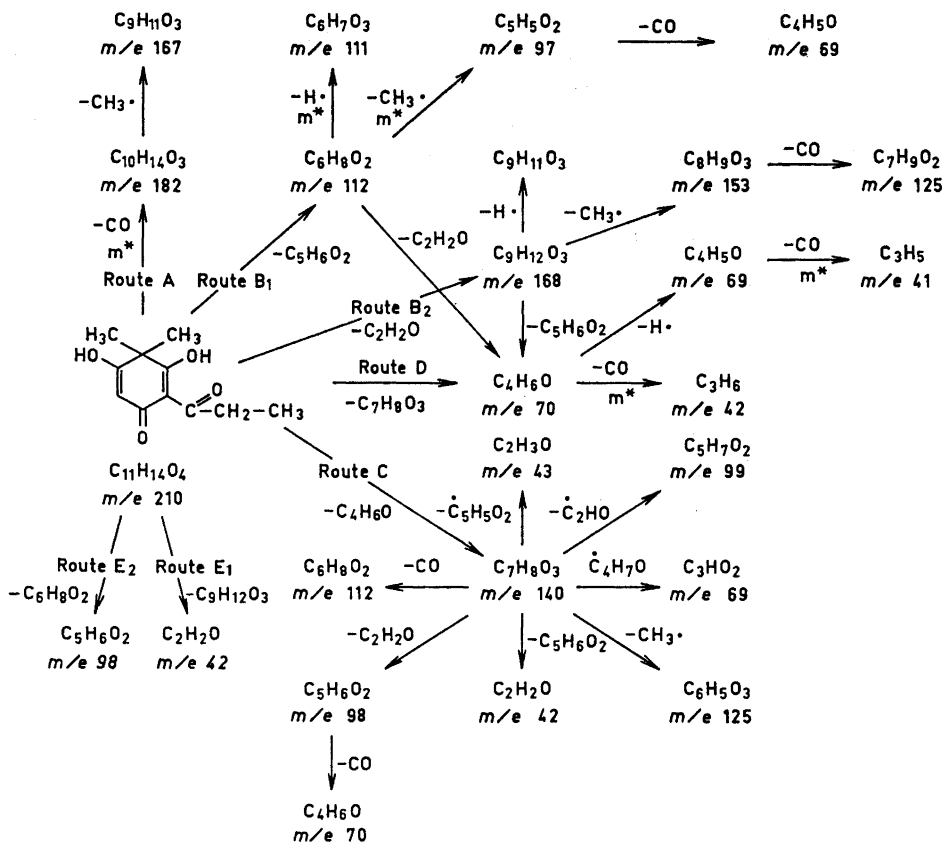
or
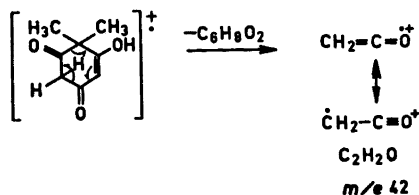
The main fragmentations of the acyl derivatives of filicinic acid are similar to those of filicinic acid (I). Of course, there are additional peaks due to the side chain fragmentations at m/e 181 ($C_9H_9O_4{}^+$) and at m/e 43 ($C_2H_3O^+$), m/e 57 ($C_3H_5O^+$), and m/e 71 ($C_4H_7O^+$) in the spectra of the acetyl, propionyl, and butyryl derivatives, respectively. Loss of carbon monoxide from these ions leads to the $C_8H_9O_3{}^+$ ion (m/e 153), the $CH_3{}^+$ ion (m/e 15), the $C_2H_5{}^+$ ion (m/e 29), and the $C_3H_7{}^+$ ion (m/e 43).

Several peaks due to further fragmentations of the side chains of the ions formed in the fragmentation paths depicted in connection with filicinic acid (I) are also present. Furthermore, McLafferty rearrangement of the side chain in the case of butyrylfilicinic acid (IV) leads to the loss of a C_2H_4 unit from several ions. For example, the $C_5H_6O_2{}^{.+}$ ion at m/e 98, is formed by consecutive losses of C_4H_6O, CO, and C_2H_4 from the molecular ion (cf. route C).

The fact that the spectra of all the acyl derivatives contain elements of the spectrum of filicinic acid (I) may be, at least partly, due to the rearrangements suggested above, which lead to filicinic acid (I).

Scheme 2 shows the fragmentation processes of propionylfilicinic acid (III) which are analogous to those of filicinic acid (I). Transitions indicated by an m* are supported by the presence of an appropriate metastable peak. The experimental results fully agree with the conclusions made above. Routes B and E are each subdivided into two parts (B_1, B_2, and E_1, E_2, respectively) since the fragmentation described in conncetion with filicinic acid (I) may start either from the side of the side chain or from the opposite side. The same situation applies to the fragmentations depicted in route C after the formation of the $C_7H_8O_3{}^{.+}$ ion of m/e 140.

The peak at m/e 111 is a doublet, which according to accurate mass measurements is due to $C_5H_3O_3{}^+$ (40 %) and $C_6H_7O_2{}^+$ (60 %). The $C_5H_3O_3{}^+$ ion (not depicted in Scheme 2) may be derived from the $C_7H_8O_3{}^+$ ion (m/e 140)

$C_9H_{11}O_3$ m/e 167 — $C_6H_7O_3$ m/e 111 — $C_5H_5O_2$ m/e 97 $\xrightarrow{-CO}$ C_4H_5O m/e 69

$-CH_3\cdot$

$-H\cdot$ m^* $-CH_3\cdot$ m^*

$C_{10}H_{14}O_3$ m/e 182 — $C_6H_8O_2$ m/e 112 — $C_9H_{11}O_3$ m/e 153 $\xrightarrow{-CO}$ $C_8H_9O_3$ m/e 153 $\xrightarrow{-CO}$ $C_7H_9O_2$ m/e 125

$-CO$ m^*

$-H\cdot$ $-CH_3\cdot$

Route A   Route B_1 $-C_5H_6O_2$ $-C_2H_2O$ $C_9H_{12}O_3$ m/e 168

C_4H_5O m/e 69 $\xrightarrow{-CO}$ m^* C_3H_5 m/e 41

Route B_2 $-C_2H_2O$

H_3C CH_3 HO OH ... $C-CH_2-CH_3$ ‖ O

$-C_5H_6O_2$ $-H\cdot$

Route D $-C_7H_8O_3$ → C_4H_6O m/e 70 $\xrightarrow{-CO}{m^*}$ C_3H_6 m/e 42

$C_{11}H_{14}O_4$ m/e 210

C_2H_3O m/e 43

$C_5H_7O_2$ m/e 99

Route C $-C_4H_6O$

Route E_2 Route E_1

$-C_6H_8O_2$ $-C_9H_{12}O_3$

$C_6H_8O_2$ m/e 112 $\xleftarrow{-CO}$ $C_7H_8O_3$ m/e 140 $\xrightarrow{\dot{C}_4H_7O}$ C_3HO_2 m/e 69

$-\dot{C}_5H_5O_2$ $-\dot{C}_2HO$

$C_5H_6O_2$ m/e 98 C_2H_2O m/e 42

$-C_2H_2O$ $-C_5H_6O_2$ $-CH_3\cdot$

$C_5H_6O_2$ m/e 98 C_2H_2O m/e 42 $C_6H_5O_3$ m/e 125

$-CO$

C_4H_6O m/e 70

Scheme 2

(route C) by loss of an ethyl radical. The formation of the $C_6H_7O_2{}^+$ ion by loss of a hydrogen radical (route B_1) from the $C_6H_8O_2{}^{\cdot+}$ ion of m/e 112 is confirmed by the presence of a metastable peak at m/e 110.

In connection with the fragmentation of filicinic acid (I), it was pointed out that cleavage of carbon monoxide does not occur from the $C_6H_8O_2{}^{\cdot+}$ ion (m/e 112) (route B). In the case of propionylfilicinic acid (III), the spectrum exhibits a peak at m/e 84 due to the $C_5H_8O^{\cdot+}$ ion. A metastable peak at m/e 63.0 suggests that this ion is formed from the $C_6H_8O_2{}^{\cdot+}$ ion. However, since the peak at m/e 140 is a singlet due to the $C_7H_8O_3{}^{\cdot+}$ ion (cf. route C), an analogous cleavage of carbon monoxide from the $C_9H_{12}O_3{}^{\cdot+}$ ion, which should lead to the $C_8H_{12}O_2{}^{\cdot+}$ ion (m/e 140), does not occur (cf. route B_2). Therefore it appears evident, that the transition from $C_6H_8O_2{}^{\cdot+}$ to $C_5H_8O^{\cdot+}$ does not take place in connection with route B_1 but by some other route, probably route C. A similar situation exists in the fragmentation of butyrylfilicinic acid (IV), where the $C_5H_8O^{\cdot+}$ ion may be formed from the $C_6H_8O_2{}^{\cdot+}$ produced from the molecular

ion by loss of a $C_6H_8O_2$ unit (route E_2). In the case of acetylfilicinic acid (II), for which there are no other fragmentation paths leading to the $C_6H_8O_2 \cdot^+$ ion, the spectrum does not exhibit a peak at m/e 84 corresponding to the $C_5H_8O \cdot^+$ ion, in agreement with the conclusions drawn above.

By a similar reasoning, the $C_7H_{10}O_2 \cdot^+$ ion at m/e 126 in the spectrum of acetylfilicinic acid (II) is considered not to be formed by loss of carbon monoxide from the $C_8H_{10}O_3 \cdot^+$ ion (m/e 154) (corresponding to the $C_9H_{12}O_3 \cdot^+$ ion in the case of propionylfilicinic acid (III) (route B_2)). Its existence is probably due to cleavage of carbon monoxide from filicinic acid (I) (route A) formed in the ionisation chamber as described above.

The spectra of all acyl derivatives of filicinic acid exhibit an interesting peak corresponding to $[M - 67]^+$. The spectra taken at low electron voltage suggest the direct formation of the respective ions from the molecular ions. However, there are no metastable peaks present that would support the origin of these ions from the molecular ions. A $[M - 67]^+$ fragment is not present in the spectrum of filicinic acid (I).

Accurate mass measurement indicated that in the case of propionylfilicinic acid (III) this peak is due to the $C_6H_7O_4^+$ ion (m/e 143). Its formation and further cleavages are explained by the fragmentation paths on p. 3438.

The loss of 15 mass units from the molecular ion in the case of propionyl-filicinic acid (III) resulting in an abundant ion of m/e 195 is mainly due to allylic cleavage in the side chain after a McLafferty rearrangement.
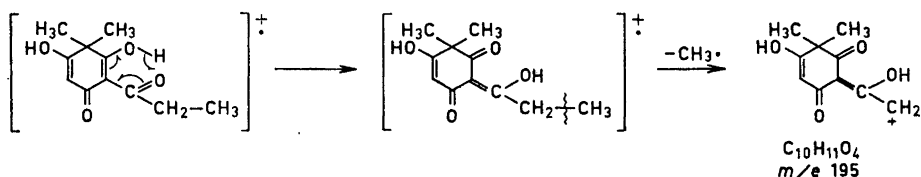
The corresponding loss in the case of butyrylfilicinic acid (IV) leads to an even more abundant ion at m/e 209, which may be explained by two successive McLafferty rearrangements followed by allylic cleavage. The ion thus formed is even more stabilized than the ion in the former case.
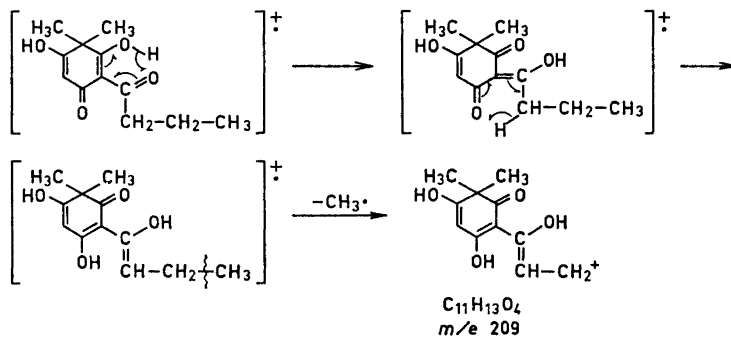
EXPERIMENTAL

Mass spectra were recorded on a Hitachi Perkin-Elmer RMU – 6E double-focusing mass spectrometer using direct sample insertion into the ion source whose temperature was 180° for the compounds (I) and (II) and 130° for the compounds (III) and (IV). Low voltage studies were carried out at 12 eV nominal energy, accuracy ± 1 eV. Exact mass measurements were performed with a resolution of 10 000 (40 % valley definition).

The syntheses of compounds (I), (II), (III), and (IV) have been described previously.[5]

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