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Mass Spectral Studies on Some Naturally Occurring Phloroglucinol Derivatives. Part III.* The Mass Spectra of Some Mono- and Bicyclic Phloroglucinol Derivatives from Rhizomes of Different *Dryopteris* Species

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The mass spectrometric fragmentation of some mono- and bicyclic phloroglucinol derivatives isolated from rhizomes of different *Dryopteris* species, as well as some of their synthetical equivalents have been investigated.

Les fragmentations en spectrométrie de masse de quelques dérivés mono- et bicycliques du phloroglucinol, isolés des rhizomes de différentes espèces de *Dryopteris*, ainsi que celles de quelques uns de leurs équivalents synthétiques, ont été examinées.

Continuing our studies of the mass spectral behavior of naturally occurring phloroglucinol derivatives isolated from rhizomes of different *Dryopteris* species,[1,2] we have investigated the following mono- and bicyclic phloroglucinol compounds (I–XX), utilizing either the natural products or their synthetic equivalents. The compounds investigated may be divided into five groups.

Group 1. Aspidinol (I) (*D. dilatata*),[4] isoaspidinol (II) (synthetic), pseudo-aspidinol (III) (synthetic),[4] desaspidinol (IV) (synthetic), *o*-desaspidinol (V) (synthetic).[3]

Group 2. Phloraspin (VI) (*D. marginalis*),[5] margaspidin (VII) (*D. marginalis*),[5] phloraspidinol (VIII) (synthetic),[6] pseudo-aspidin (IX) (synthetic),[7] methylene-bis-aspidinol (X) (synthetic), methylene-bis-desaspidinol (XI) (synthetic).

Group 3. Albaspidin BB (XII) (*D. spinulosa*),[8] albaspidin PP (XIII) (synthetic),[6] albaspidin AA (XIV) (synthetic).[6]

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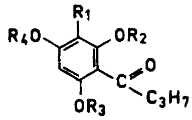
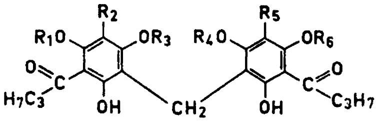
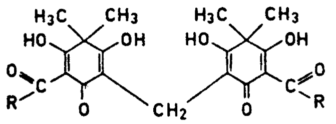
Group 4. Aspidin AB (XV) (*D. intermedia*),[9] aspidin BB (XVI) (*D. intermedia*),[9] flavaspidic acid AP * (XVII) (*D. goldiana*),[10] *para*-aspidin BB (XVIII) (*D. campyloptera*),[11] desaspidin BB (XIX) (*D. assimilis*).[9]
Group 5. Phloropyron (XX) (*D. campyloptera*).[11]

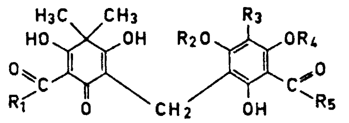




(I) $R_2 = R_3 = H,\ R_1 = R_4 = CH_3$
(II) $R_2 = R_4 = H,\ R_1 = R_3 = CH_3$
(III) $R_3 = R_4 = H,\ R_1 = R_2 = CH_3$
(IV) $R_1 = R_2 = R_3 = H,\ R_4 = CH_3$
(V) $R_1 = R_3 = R_4 = H,\ R_2 = CH_3$

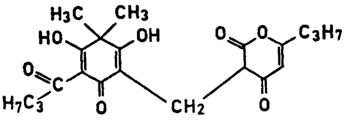
(VI) $R_1 = R_3 = R_5 = R_6 = H,\ R_2 = R_4 = CH_3$
(VII) $R_1 = R_3 = R_6 = H,\ R_2 = R_4 = R_5 = CH_3$
(VIII) $R_1 = R_5 = R_6 = H,\ R_2 = R_3 = R_4 = CH_3$
(IX) $R_3 = R_4 = H,\ R_1 = R_2 = R_5 = R_6 = CH_3$
(X) $R_1 = R_6 = H,\ R_2 = R_3 = R_4 = R_5 = CH_3$
(XI) $R_1 = R_2 = R_5 = R_6 = H,\ R_3 = R_4 = CH_3$





(XII) $R = CH_3 - CH_2 - CH_2$
(XIII) $R = CH_3 - CH_2$
(XIV) $R = CH_3$

(XV) $R_2 = H,\ R_1 = R_3 = R_4 = CH_3,$
$R_5 = CH_3 - CH_2 - CH_2$
(XVI) $R_2 = H,\ R_3 = R_4 = CH_3,$
$R_1 = R_5 = CH_3 - CH_2 - CH_2$
(XVII) $R_2 = R_4 = H,\ R_1 = R_3 = CH_3,$
$R_5 = CH_3 - CH_2$
(XVIII) $R_4 = H,\ R_2 = R_3 = CH_3,$
$R_1 = R_5 = CH_3 - CH_2 - CH_2$
(XIX) $R_3 = R_4 = H,\ R_2 = CH_3,$
$R_1 = R_5 = CH_3 - CH_2 - CH_2$



(XX)

The compounds of the first group (I – V), being simple alkyl aryl ketones, undergo normal α-cleavages without any special mass spectral interest.

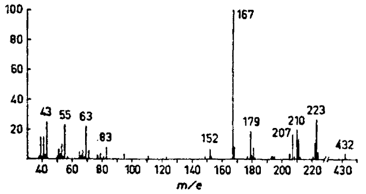


Fig. 1 a. Mass spectrum (75 eV) of phloraspin (VI).

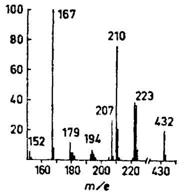


Fig. 1 b. Mass spectrum (12 eV) of phloraspin (VI).

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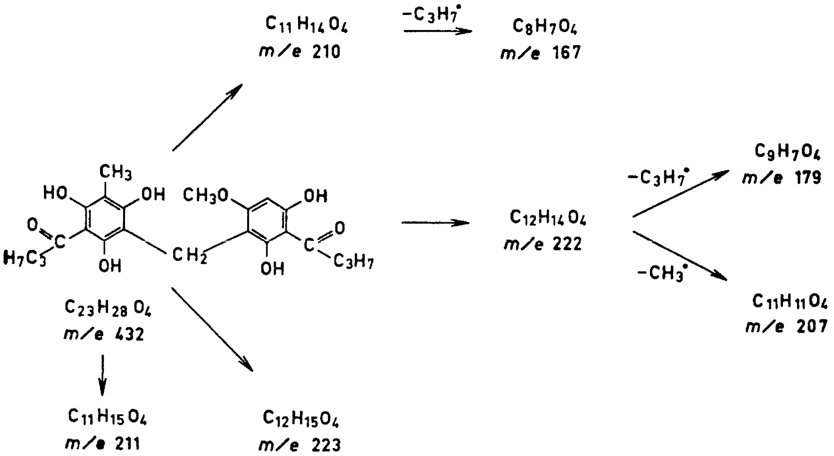
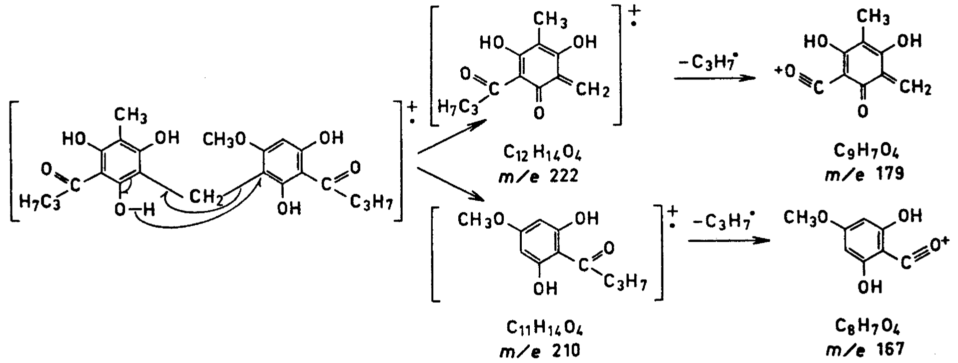
* This flavaspidic acid, isolated from *D. goldiana* (Hook) A. Gray, was previously identified as flavaspidic acid AB.[10] However, the present work shows that it consists mainly of flavaspidic acid AP together with small amounts of the AB homolog. This explains the low melting point reported [10] (102 – 106°C) for the natural product, as compared with that of the synthetic flavaspidic acid AB (210 – 212°C).[12]

The major fragmentations of phloraspin (VI), which represents the group 2 compounds, are shown in Scheme 1.

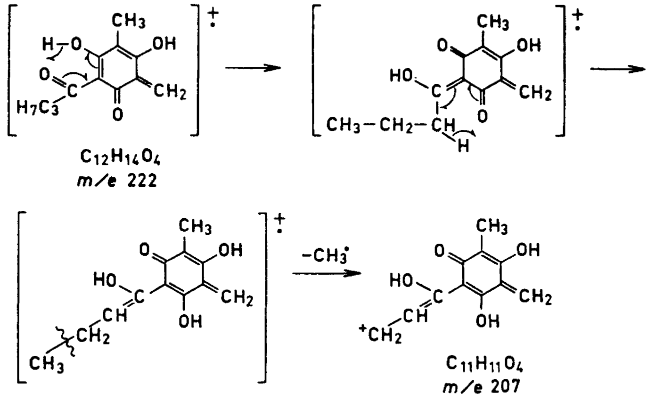


Scheme 1.

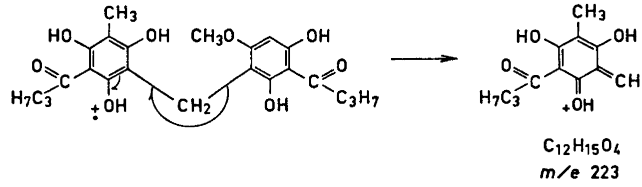
Important peaks occur at m/e 167 (base peak) and at m/e 179. The fragment formation may be formulated by assuming the known [13,14] cleavage with concomitant transfer of a hydrogen atom from a hydroxyl group located *ortho* to the methylene bridge. This leads to the ions at m/e 210 and at m/e 222, which then lose $C_3H_7^•$. Of course, the hydrogen transfer may operate also in the other direction but in this special instance ions of the same elemental composition are formed.



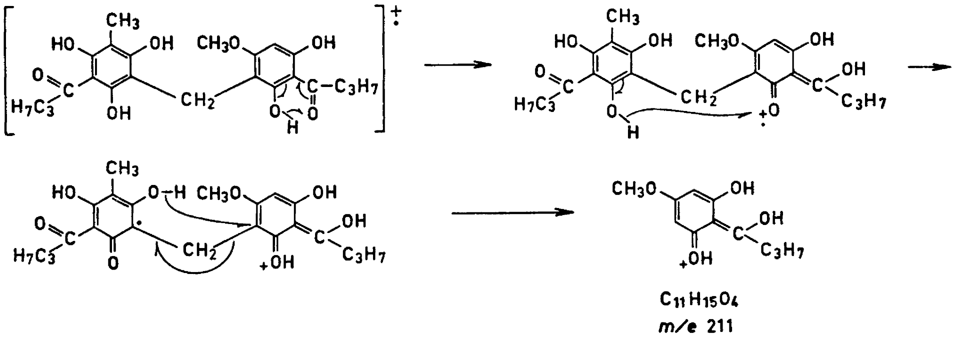
The ion at m/e 207 may arise from the ion at m/e 222 by two successive McLafferty rearrangements, followed by allylic cleavage.



The ion at *m/e* 223 may be assumed to result from a simple cleavage, as formulated below.



The ion at *m/e* 211 is of special interest. Its formation, which necessitates two hydrogen transfer, is perhaps best explained by the following scheme.

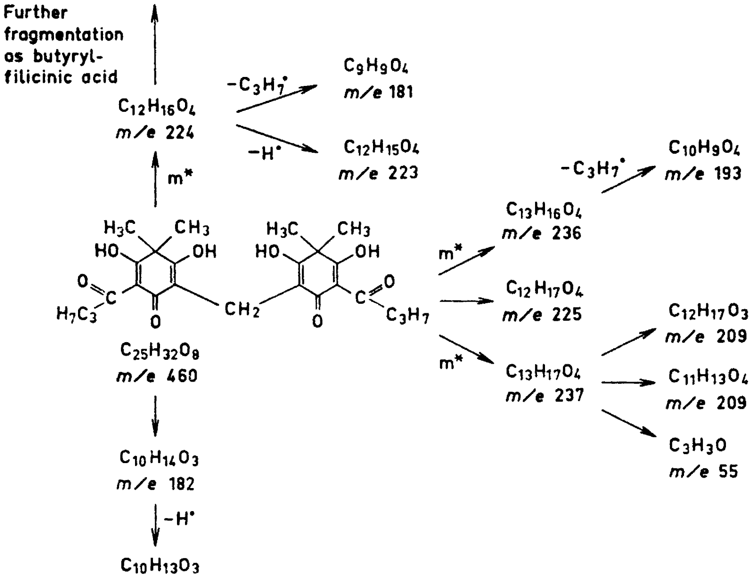


The existence of this ion requires the presence of hydroxyl groups (or similar ones) in the two positions *ortho* to the methylene bridge. This should be useful for structural determinations of compounds of this type.

The mass spectra of the other group 2 compounds presented in Table 1 exhibit fragmentation patterns similar to the pattern of phloraspin (VI).

Table 1. Mass spectra of margaspidin (VII), phloraspidinol (VIII), pseudo-aspidin (IX) methylene-bis-aspidinol (X) and methylene-bis-desaspidinol (XI).

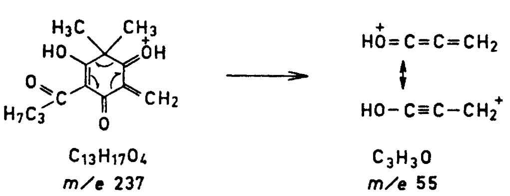
m/e	(VII)	(VIII)	(IX)	(X)	(XI)
39	8	7		8	6
41	9	8	10	12	6
43	15	15	22	18	7
44				8	
53	6	5		5	5
55	13	9	7	8	8
57				8	
58		5			
65	5	5		5	
67	7	5		7	5
69	11	5	6	7	11
71	5		6		
83	9	5	7	5	
117	6				
152	7	6			7
165			5		
166				6	
167	35	25	6		100
168					10
179	18	14	5		21
180	6	6			5
181	100	100	56	100	7
182	12	11	6	11	
187			13		
191			5		
192			6		
193	9	8	60	14	5
194	5		7		5
195				6	
205	6	5			7
206			5		
207	17	20	9	7	23
209			5		
210	11	7			25
211					6
219	5		19	5	
221	8	9	17	16	
222	14	12			16
223	25	16	8		48
224	48	30	13	46	7
225	17	5	70	7	
226			10		
236	7	6	25	16	
237	24	18	100	34	
238			16	7	
417			30		
418			7		
432					8
446	12	5			
460			56	6	
461			17		



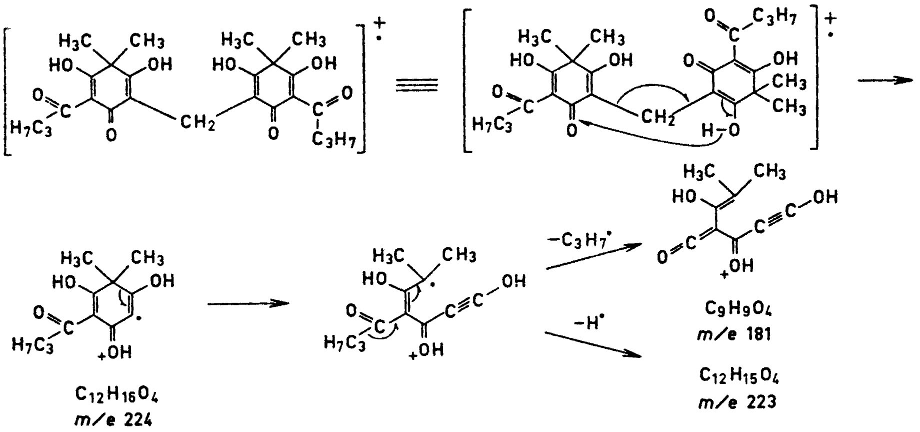
Scheme 2.

Scheme 2 shows the main fragmentation pattern of albaspidin BB (XII), considered with the experimental data.

The simple cleavage of the methylene bridge, which may be formulated in a manner analogous to that depicted in connection with phloraspin (VI), leads to the ion at *m/e* 237. The peak at *m/e* 209, which, according to accurate mass measurements, is a doublet due to $C_{12}H_{17}O_3^+$ (10 %) and $C_{11}H_{13}O_4^+$ (90 %) is regarded as being derived from the ion of *m/e* 237 by losses of carbon monoxide and ethylene, respectively. The formation of the resonance stabilized ion $C_3H_3O^+$ at *m/e* 55 may be formulated as a retro-Diels-Alder cleavage of the ion of *m/e* 237.



The direct formation of the ions of *m/e* 224 and *m/e* 236 from the molecular ion (metastable peaks) results from cleavage of the methylene bridge with transfer of a hydrogen atom from a hydroxyl group *ortho* to the methylene bridge to the other ring. The loss of a propyl radical from the ion of *m/e* 236 gives rise to an important peak at *m/e* 193. Further fragmentation of the ion of *m/e* 224 is similar to that presented for butyrylfilicinic acid.[1] Of special interest is the presence of the characteristic peak at *m/e* 157 (*cf.* part I, compound IV, the $(M-67)^+$ ion) in the spectrum of albaspidin BB (XII), thus strongly suggesting the formation of ionized butyrylfilicinic acid. However, the relative intensities of the peaks below *m/e* 224, compared with that of the peak at *m/e* 224, are smaller in the spectrum of albaspidin BB (XII) than in the spectrum of butyrylfilicinic acid. This seems to indicate that the ion at *m/e* 224 is partly formed by another route. One possible explanation for this, as well as for further fragmentations leading to the ions $C_{12}H_{15}O_4^+$ (*m/e* 223) and $C_9H_9O_4^+$ (*m/e* 181, 55 %), is depicted below.



The formation of the ion of *m/e* 225 directly from the molecular ion, which is supported by the spectrum taken at low electron voltage (Fig. 2 b), obviously involves two hydrogen transfers.

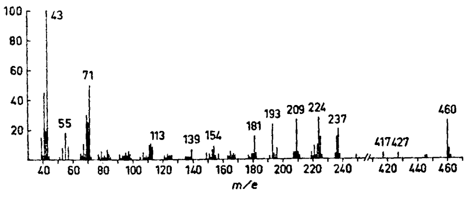


Fig. 2 a. Mass spectrum (75 eV) of albaspidin BB (XII).

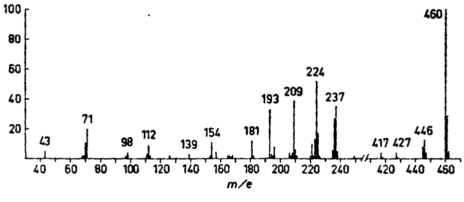
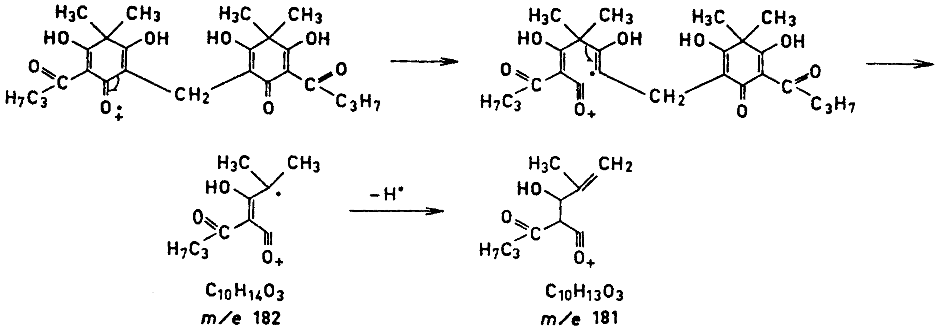


Fig. 2 b. Mass spectrum (12 eV) of albaspidin BB (XII).

The direct formation of the ion $C_{10}H_{14}O_3^{\cdot+}$ (*m/e* 182) from the molecular ion and further loss of a hydrogen radical leading to the ion $C_{10}H_{13}O_3^+$ (*m/e* 181, 45 %) represent a fragmentation mode analogous to that proposed earlier for filicinic acid and its acyl derivatives.[1]



The mass spectra of albaspidin PP (XIII) and albaspidin AA (XIV), (Figs. 3 and 4) exhibit fragmentation patterns similar to that of albaspidin BB (XII).

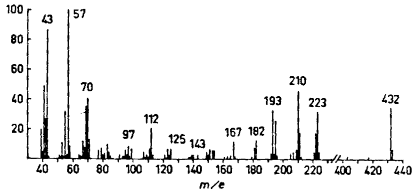


Fig. 3. Mass spectrum (75 eV) of albaspidin PP (XIII).

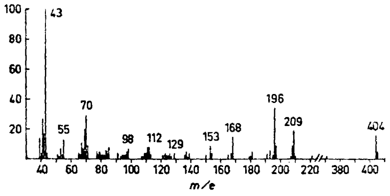
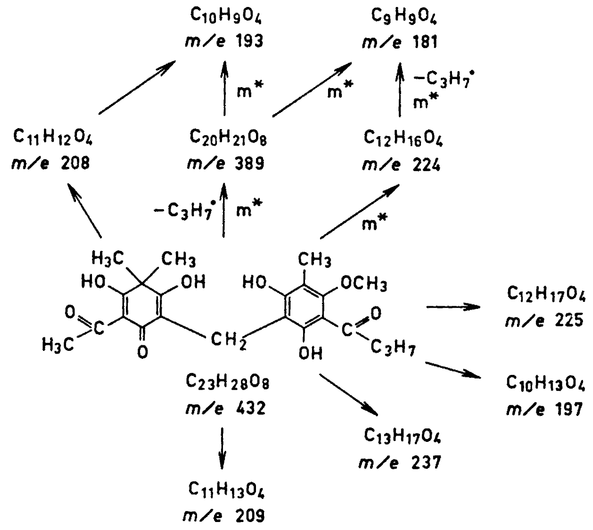


Fig. 4. Mass spectrum (75 eV) of albaspidin AA (XIV).



Scheme 3.

The fragmentation pattern of aspidin AB (Figs. 5 a and b, Scheme 3), which represents group 4 compounds, is largely similar to the patterns of phloraspin (VI) and albaspidin BB (XII). However, the strong tendency of the charge to remain on the aromatic moiety is noteworthy.

The main fragmentations, supported by metastable peaks, seem to be the loss of a propyl radical, leading to the ion of *m/e* 389, followed by a hydrogen transfer with cleavage of the methylene bridge.

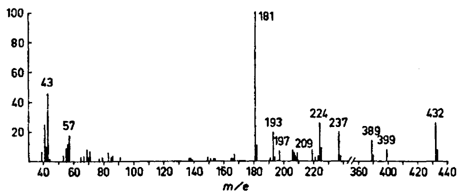


Fig. 5 a. Mass spectrum (75 eV) of aspidin AB (XV).

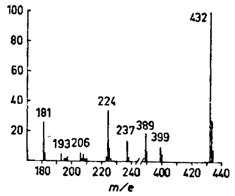


Fig. 5 b. Mass spectrum (12 eV) of aspidin AB (XV).

Of the ions at *m/e* 193 and *m/e* 181 thus formed the latter represents the base peak. A metastable peak indicated that the ion at *m/e* 181 is partly formed by the loss of a propyl radical from the ion of *m/e* 224, which itself is formed from the molecular ion by hydrogen transfer with cleavage of the methylene bridge. A similar, but less pronounced process, where the charge remains on the non-aromatic moiety is responsible for the weak peak at *m/e* 208. Further loss of a methyl radical would lead to the ion of *m/e* 193, which thus may be partly formed by this route.

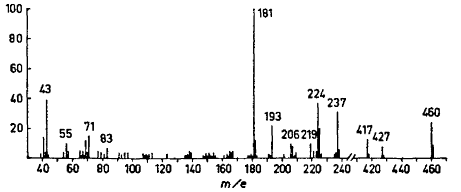


Fig. 6. Mass spectrum (75 eV) of aspidin BB (XVI).

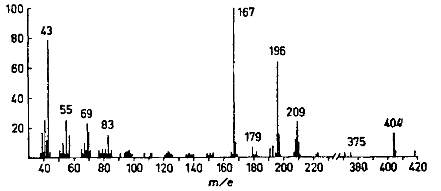


Fig. 7. Mass spectrum (75 eV) of flavaspidic acid AP (XVII).

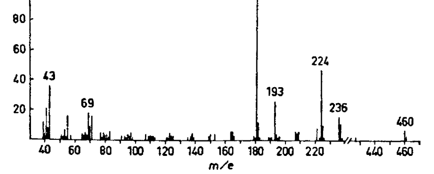


Fig. 8. Mass spectrum (75 eV) of *para*-aspidin BB (XVIII).

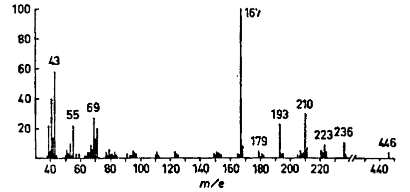


Fig. 9. Mass spectrum (75 eV) of desaspidin BB (XIX).

Furthermore, the double hydrogen transfer, which is similar to that described in connection with phloraspin (VI) and albaspidin BB (XII), seems to be operating in both directions and leads to the ions of *m/e* 225 and *m/e* 197. The formation of the ions of *m/e* 237 and *m/e* 209 results from simple cleavage of the methylene bridge.

The fragmentation of the other group 4 compounds (XVI – XIX) (Figs. 6 – 9) is similar to that of aspidin AB (XV). However, in the case of desaspidin BB (XIX) and *para*-aspidin (XVIII), where one of the two hydroxyl groups of the aromatic ring *ortho* to the methylene bridge is methylated, the double hydrogen transfer does not occur from the aromatic moiety to the filicinic acid moiety. This is seen very clearly in the spectrum of desaspidin BB (XIX), where there is no peak at *m/e* 225. In the case of *para*-aspidin BB (XVIII), the weak peak at *m/e* 225 may arise, except from the isotopic contribution, from the double hydrogen transfer from the filicinic acid moiety to the aromatic moiety.

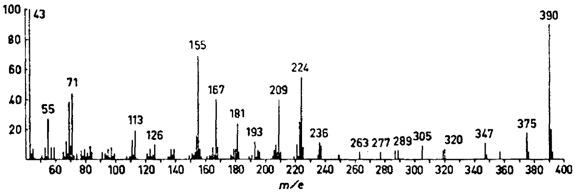


Fig. 10 a. Mass spectrum (75 eV) of phloropyron (XX).

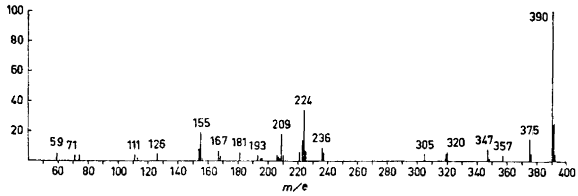
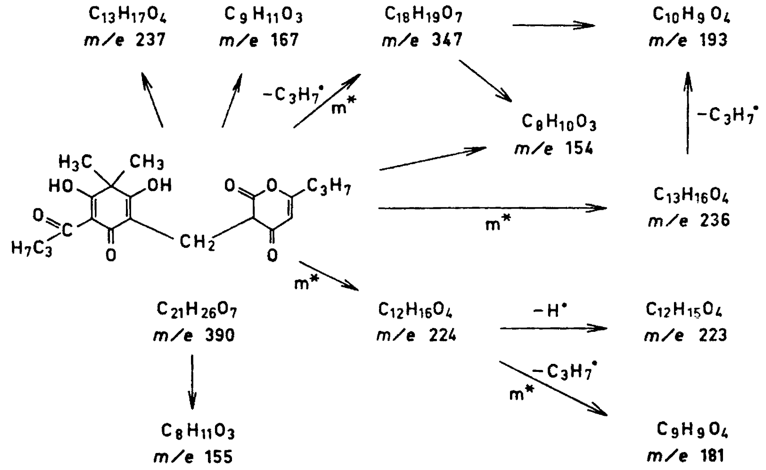


Fig. 10 b. Mass spectrum (12 eV) of phloropyron (XX).

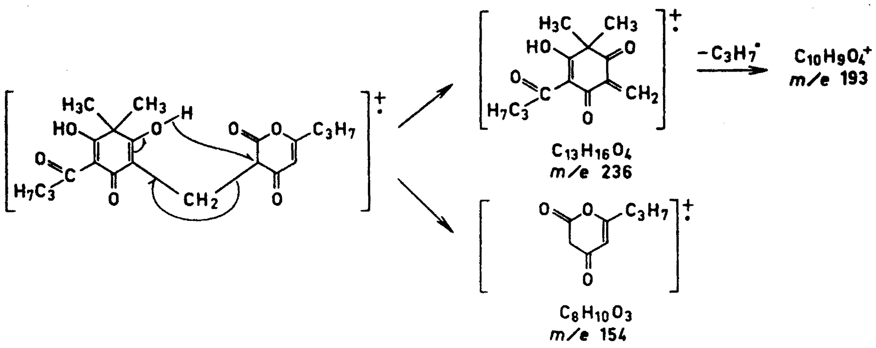
Phloropyron (XX), mass spectra of which are presented in Figs. 10 a and 10 b, shows a fragmentation pattern similar to those of the other bicyclic phloroglucinol derivatives presented above. This is shown in Scheme 4.

The formation of the ions of *m/e* 237 and *m/e* 167 can be ascribed to simple cleavage of the methylene bridge. The main fragmentation pattern seems to result from hydrogen transfer and cleavage of the methylene bridge. When the hydrogen comes from the filicinic acid moiety, it gives rise to the ions of *m/e* 236 and *m/e* 154. Further loss of a propyl radical from the former ion leads to the ion of *m/e* 193. The fact that the spectrum of phloropyron (XX) below *m/e* 154 shows only qualitative resemblance to that of 6-propyl-2,3-di-



Scheme 4.

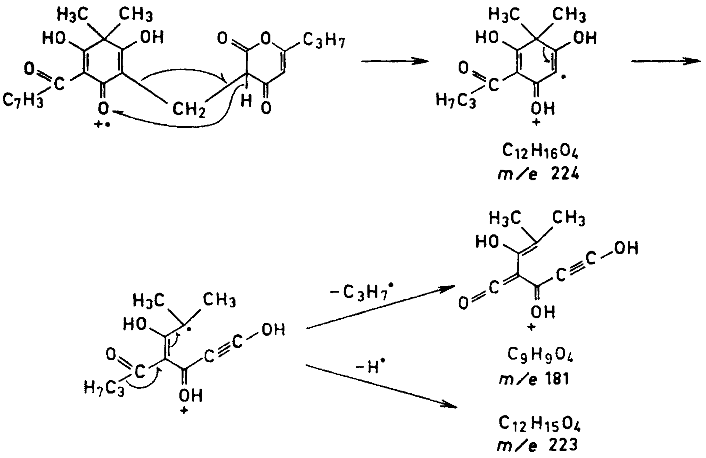
hydropyran-2,4-dione[2] seems to indicate that only part of the ion of *m/e* 154 originating from the dihydropyran moiety is formed as depicted below.



The loss of a propyl radical from the acyl group also takes place directly from the molecular ion leading to the ion of *m/e* 347. Subsequent hydrogen transfer and the cleavage of the methylene bridge give rise to the ions of *m/e* 154 and *m/e* 193.

The hydrogen transfer may also take place from the dihydropyran moiety. In this case, the charge remains mainly on the filicinic acid moiety and an ion of *m/e* 224 is formed. The direct formation of this ion from the molecular ion is supported by a metastable peak and by the spectrum taken at low electron voltage (Fig. 10 b).

The fact that the spectrum of phloropyron (XX) below *m/e* 224 does not greatly resemble that of butyrylfilicinic acid[1] seems to indicate that ionized butyrylfilicinic acid is not present to any appreciable extent in the ionization chamber. Noteworthy the characteristic peak at *m/e* 157 is absent (*cf.* the spectrum of phloraspin (VI)). One possible route to the ion of *m/e* 224 and its further fragmentation are depicted below.



The important peak at *m/e* 155, which according to the high resolution measurements corresponds to the ion $C_8H_{11}O_3^+$, results from double hydrogen transfer from the filicinic acid moiety to the dihydropyran moiety. Its formation may be formulated as in the case of phloraspin (VI).

All spectra described in this paper exhibit additional peaks, which are not discussed here, due to losses of water, carbon monoxide, ethylene, $C_3H_7{\cdot}$, *etc.*, from different ions.

The spectra indicate also that several samples used in this work contained small quantities of homologs of the compounds examined (*cf.* Refs. 8 – 10).

EXPERIMENTAL

The mass spectra of the compounds (VI), ((XII) – (XX)) were recorded on a Hitachi Perkin-Elmer RMU-6E double-focusing mass spectrometer (source temperature 150°), while the spectra of the compounds ((I) – (V)), ((VII) – (XI)) were recorded on a Perkin Elmer 270 mass spectrometer (source temperature 135°) at 75 eV using in all cases a direct sample insertion into the ion source. 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 preparation of the following compounds studied in this work has been described before: aspidinol (I),[3] pseudo-aspidinol (III),[4] desaspidinol (IV),[3] *o*-desaspidinol (V),[3] phloraspidinol (VIII),[6] pseudo-aspidin (IX),[7] albaspidin PP (XIII),[6] albaspidin AA (XIV).[6]

Isoaspidinol (II), m.p. 150 – 152°, was prepared by the standard method [3] from 2,6-dihydroxy-4-methoxy-toluene.

Methylene-bis-aspidinol (X) and methylene-bis-desaspidinol (XI) were prepared by condensing aspidinol (I) and desaspidinol (IV), respectively, with formaldehyde, by the method of Penttilä and Sundman.[15]

The natural products studied in this work were isolated from the following plants: phloraspin (VI) (*D. marginals* (L.) A. Gray),[5] margaspidin (VII) (*D. marginalis* (L.) A. Gray),[5] albaspidin BB (XII) (*D. spinulosa* Watt),[8] aspidin AB (XV) (*D. intermedia* (Muhl.) A. Gray),[9] aspidin BB (XVI) (*D. intermedia* (Muhl.) A. Gray),[9] flavaspidic acid AP (XVII) (*D. goldiana* (Hook) A. Gray),[10] *para*-aspidin BB (XVIII) (*D. campyloptera* Clarkson),[11] desaspidin BB (XIX) (*D. assimilis* S. Walker),[9] phloropyron (XX) (*D. campyloptera* Clarkson).[11]

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