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The Mass Spectra of Oxygen Heterocycles. II.

The Mass Spectra of Some Flavonoids

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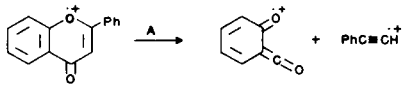
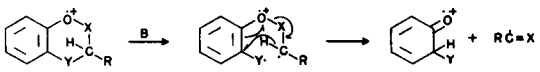
The mass spectra of the flavones apigenin and acacetin have been reported by Wilson and Reed (1) whilst the mass spectrum of flavone itself has been described by Barnes and Occolowitz (2). A discrepancy between the results obtained lies in the importance assumed by breakdown *via* a Diels-Alder reaction (described as mode A in paper I (3) of this series) in the natural products as compared with the parent compound.

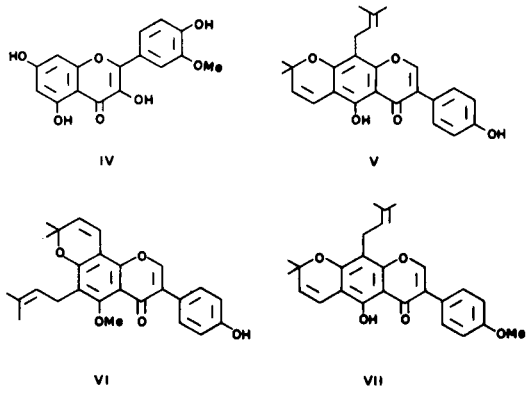


I 100% II 80% III

In the highly oxygenated natural products this fragmentation is minor (15-16% of the molecular ion) whilst in flavone (I) itself, the peak due to species (II) was 80% of the intensity of the molecular ion. Nor are the latter results due to the high inlet temperature used (200-250°) as we have repeated this work using a low temperature probe and obtained substantially the same spectrum. It appears therefore to be dangerous to generalise in this field as oxygenation of the nucleus profoundly affects the breakdown observed. Presumably if the initially produced ion-radical can be stabilised by mesomerism over a number of oxygen atoms, then breakdown by mode A is strongly diminished. In the field of natural products the compounds examined invariably carry hydroxyl, methoxyl or methylenedioxy-groups and it is reasonable to suggest that reverse Diels-Alder reactions of naturally occurring flavones or flavonols will be minor pathways, leading to spectra in which the molecular ion is by far the largest peak. These minor breakdowns, however, may still be of diagnostic value as they frequently represent the only even numbered peaks in their particular region, and hence are readily distinguished. The anomalous case of the isoflavonols has been previously discussed (3). A further generalisation that may be made is that in the case of the reduced flavonoids, in which the heterocyclic ring is no longer aromatic, breakdown by path A and B (illustrated below) will be of great importance leading to clean cut, characteristic spectra.

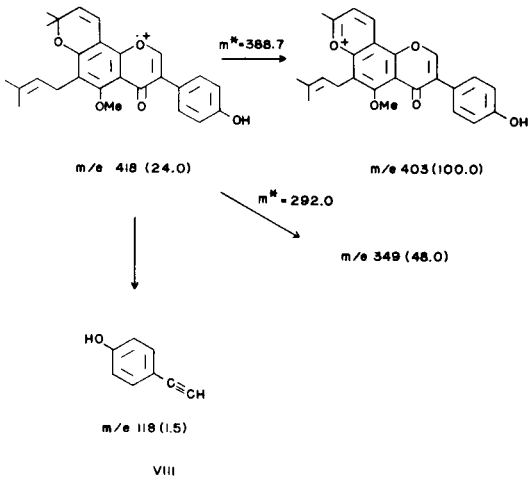


A typical example of a highly stable flavonoid is isorhamnetin (IV), (Fig. 1). Here mode A is minor, and indeed all peaks other than the molecular ion radical are small, often arising by pathways peculiar only to the substance in question. Little structural information may be culled from mass spectra in this series.



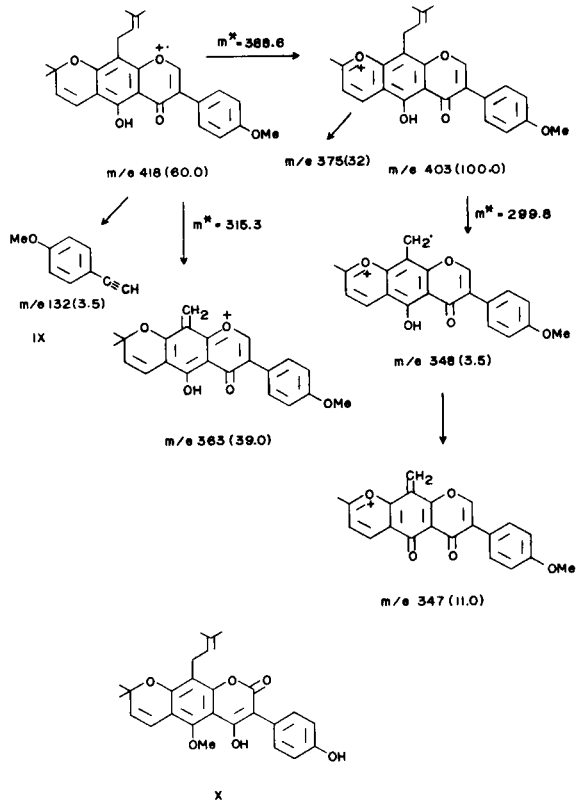
IV V VI VII

The spectrum of the isoflavones scandenone (V) (Fig. 2), scandinone (VI) (Fig. 3), and scandenone-4'-methyl ether (VII) (Fig. 4) also show very little breakdown by route A. Scandenone, in the usual way for 2,2-dimethylchromenes (1,2) loses a methyl group, to give the base peak at m/e 389. Scandinone (VI) does likewise, but also loses C_5H_9 to give an even electron species at m/e 349. It was noticeable that this compound gave a small peak at m/e 118, the only peak at even mass in this region, corresponding to fragment (VIII). Scandenone-4'-methyl ether, on the other hand gave no peak at m/e 118,



VIII

but instead a quite distinct one at m/e 132, corresponding to fragment (IX). The breakdown of this compound is rather different from the preceding one, as the molecular ion stabilises itself by loss of C_4H_7, as shown, as well as by the loss of CH_3. The difference in the mass spectrum between (VI) and (VII) were sufficient to indicate whether the methoxyl group was on ring A or ring B in each compound, at a time when insufficient quantity was in hand to allow n.m.r. spectra or the usual degradations to be carried out.



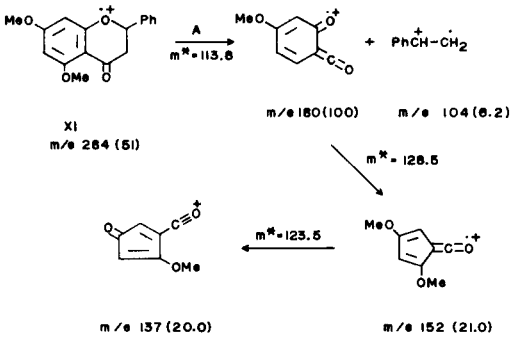
IX

X

The great difference between the isoflavone scandinone (VI) and the corresponding isoflavonol, lonchocarpic acid (X) in which the major breakdown involves the loss of a methyl radical followed by a reverse Diels-Alder reaction (4) once more underlines the high stability of the former class of compounds.

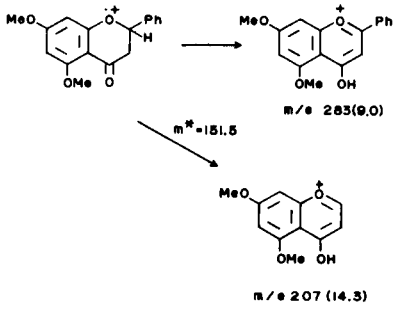
Attention was turned to the reduced flavonoids and two flavanones were examined first. 5,7-Dimethoxyflavanone (XI) (Fig. 5) gave rise to a clean spectrum which may be rationalised as follows.

The major pathway involves breakdown by mode A to give the fragments of m/e 180 and m/e 104, the fragment at m/e 180 containing the two methoxy groups taking most of the charge. This species loses carbon monoxide to give the fragment at m/e 152, the series being terminated by the loss of a methyl radical to give the even electron species at m/e 137.

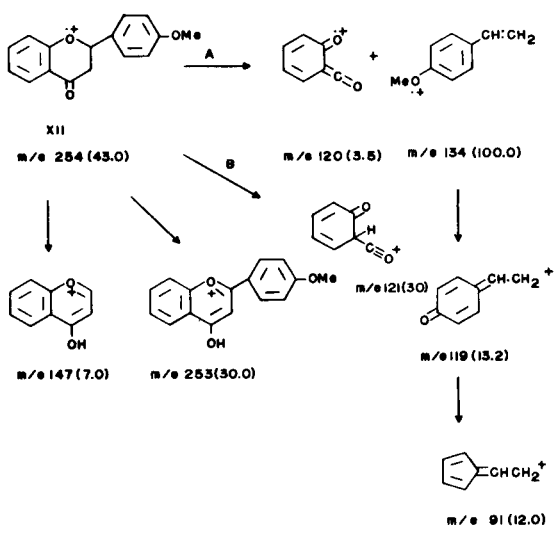


XI

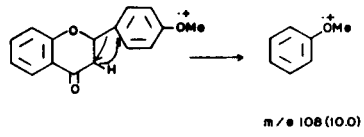
A further method of breakdown, that helps characterise the flavanones is the loss of either a hydrogen atom or an aryl radical from the molecular ion to give even-electron fragments.



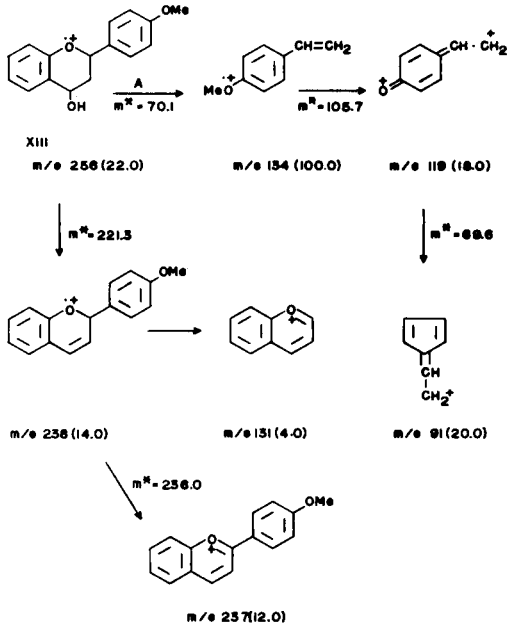
A very similar breakdown pattern is found for 4'-methoxyflavanone (XII) (Fig. 6), once more the fragment with the methoxyl group taking nearly all the charge. Path B is more noticable, the breakdown scheme being as shown below.



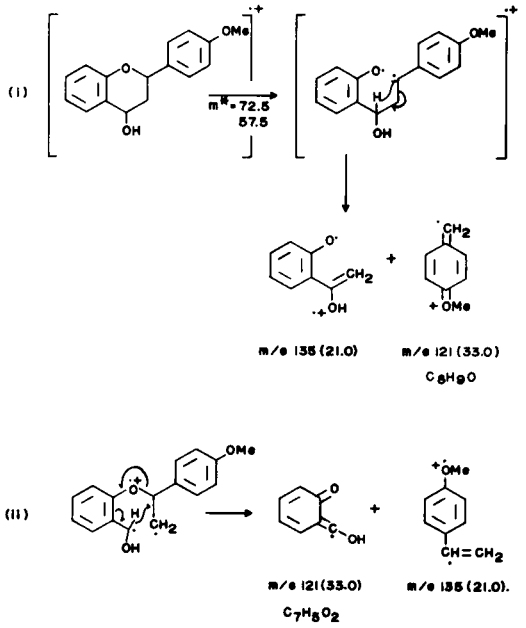
A further peak is at m/e 108, arising from a hydrogen transfer reaction.



The behaviour of flavan-4-ols was next examined. 4'-Methoxyflavan-4-ol (XIII) (Fig. 7) broke down mainly by mode A, but other pathways involving hydrogen transfer reactions were also important. The loss of water, followed by loss of a proton to give the even-electron species at m/e 237 was also clearly distinguishable.

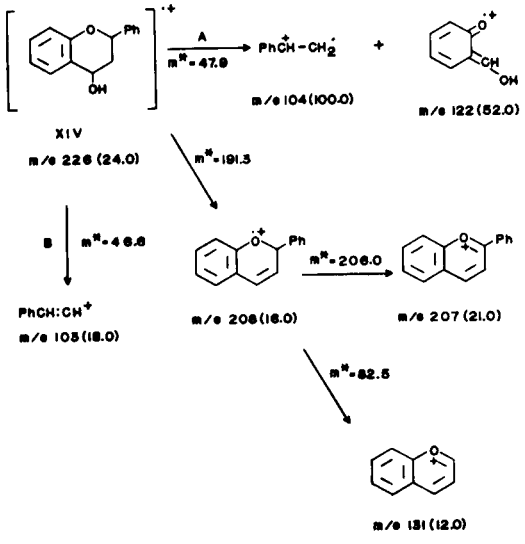


The peak at m/e 121 was of great interest as it could arise in two ways, each path fortuitously giving rise to a peak of equal mass, *i.e.*

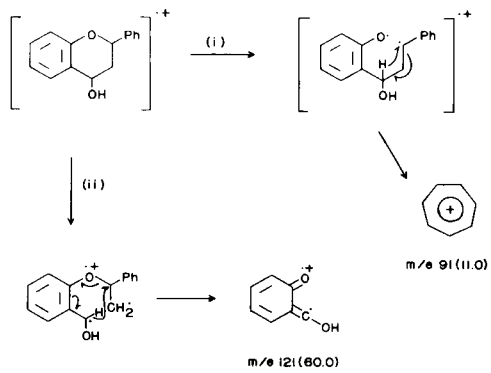


Path (i), which involves the opening of the O-C_2 bond, followed by hydrogen transfer gives a fragment of formula C_8H_9O; path (ii) involving a cleavage of the C_2-C_4 bond gives a fragment of the same mass but of formula $C_7H_5O_2$. Examination at high resolution showed that the peak at m/e 121 was a doublet, made up of two peaks of almost equal height and of mass corresponding precisely to that required from the two possible formulae. Thus both modes (i) and (ii) are operating. The peak at m/e 135 is too large to be merely isotope contribution from m/e 134, and presumably (i) and (ii) also contribute to this peak.

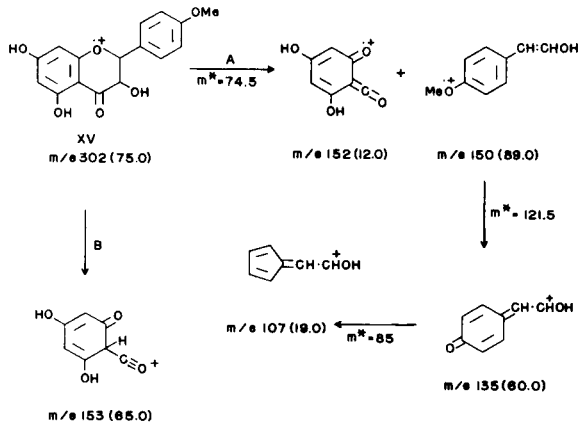
With flavan-4-ol (XIV) (Fig. 8) itself, a similar picture was obtained, although as no methoxyl groups are present the charge is more evenly distributed.



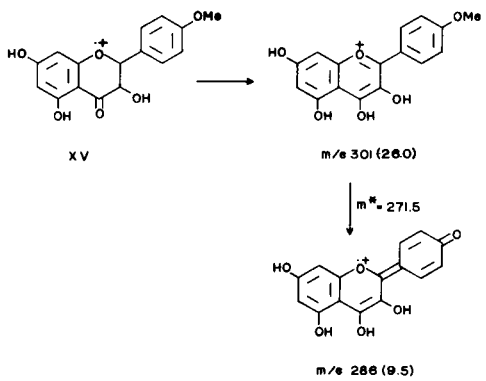
In this case paths (i) and (ii) as shown by compound (XIII) are distinguishable; path (i) leading to a peak at m/e 91 and path (ii) leading to a fragment of m/e 121. Both these fragments are seen clearly in the spectrum.



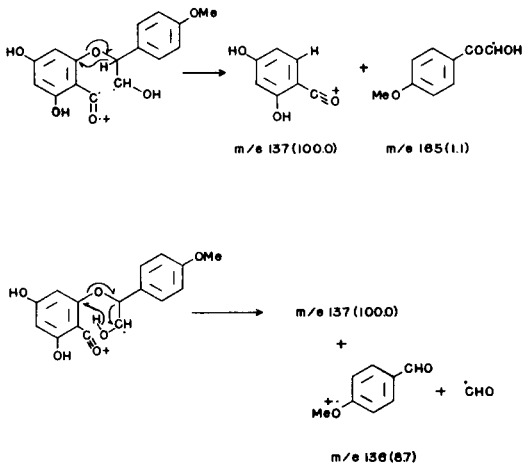
The spectrum of 3,5,7-trihydroxy-4'-methoxyflavan-4-one (XV) (Fig. 9) was of great interest as it was the first reduced flavonoid encountered in which the base peak was neither the molecular ion nor a fragment arising from breakdown by mode A. However this type of breakdown as well as mode B, is found as shown.



The loss of a hydrogen atom followed by the loss of a methyl radical is of importance, but the base peak is found at m/e 137. The metastable peak at

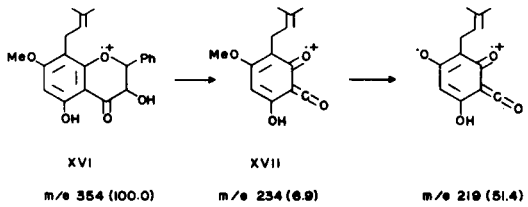


m/e 62.2 indicates that this fragment is formed directly from the molecular ion. Several processes can give rise to this species, but due to the phenolic hydroxyl groups present, deuteration studies were inconclusive. Such studies on related compounds

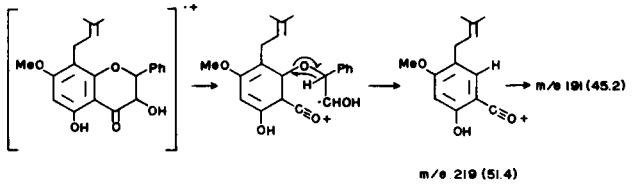


are in hand.

The compound leaserone (XVI) has been examined (1) and the peak at m/e 219 has been attributed to the following sequence.

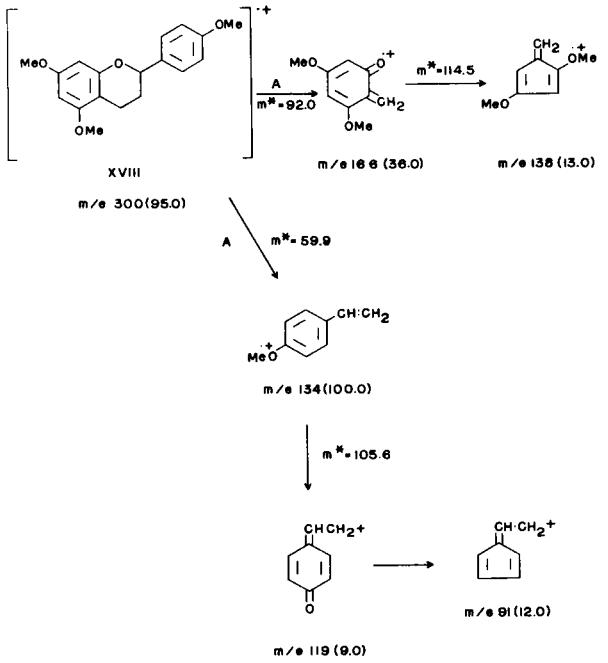


However, we have examined many fragments similar to (XVII), and in no case has the loss of a methyl group been so facile as would be indicated by the relative intensities of the two species. If a mechanism similar to that operating with (XV) were at work here this peak would arise directly from the molecular ion, the high intensity being in line with

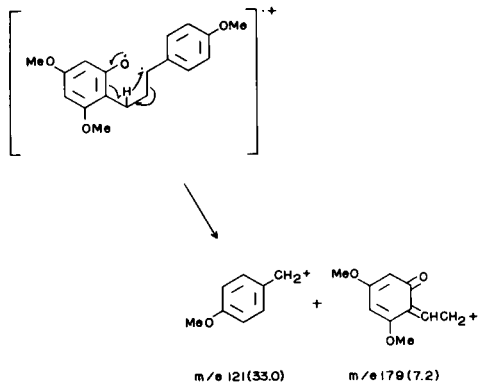


that found by us for (XV). The intense peak at m/e 191 would be produced by the loss of CO from m/e 219. Unfortunately the metastable peaks that could serve to distinguish the various possibilities were not reported for leaserone.

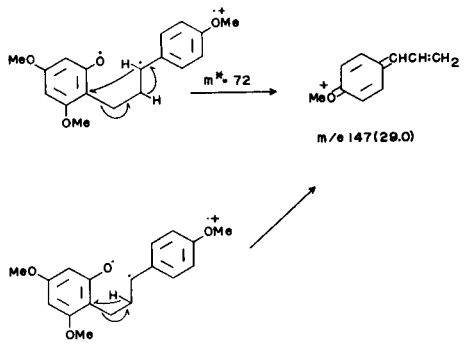
The flavan (XVIII) (Fig. 10) was recently discovered as a natural product (5), mass spectrometry being used by us to help to characterise this substance. Mode A was the major breakdown path.



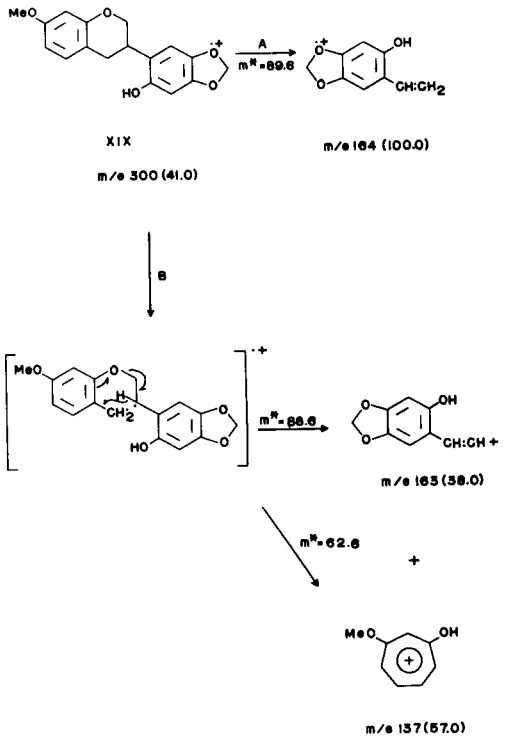
The peak at m/e 121 involves a hydrogen transfer of the type previously met in the flavan-4-ol series. *i.e.*



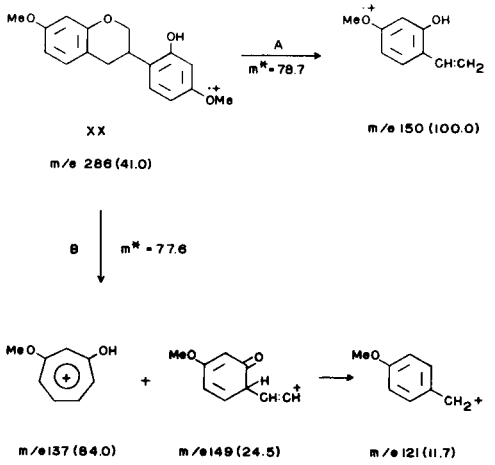
For the peak at m/e 147, more than one mechanism of formation is possible requiring deuteration studies to distinguish between them.



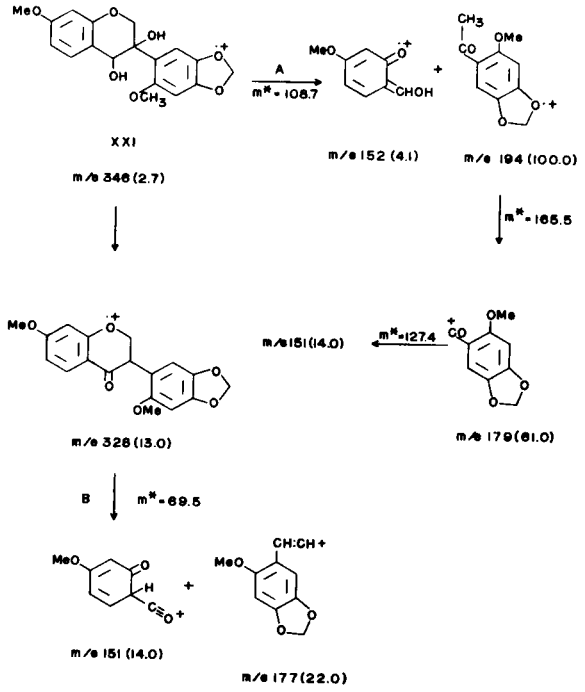
The *iso*flavan (XIX) (Fig. 11), behaves in a similar fashion but a far higher proportion of the fragmentation is channelled *via* mode B. The reason for this is that homolytic fission of the C_3-C_4 bond in an isoflavan gives rise to a diradical in which both electrons are stabilised by mesomerism over an adjacent benzene ring. It is possible that this may serve to distinguish between the flavans and *iso*flavans.



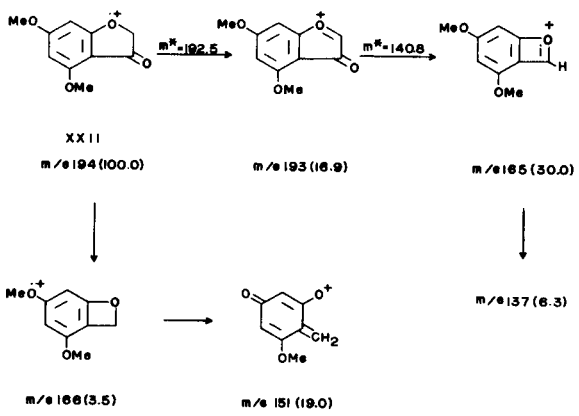
A very similar picture is found for 2'-hydroxy-4',7-dimethoxy*iso*flavan (XX) (Fig. 12), mode B once more competing successfully with mode A in the breakdown process.



The *iso*flavandiol (XXI) (Fig. 13) broke down by mode A as the main pathway. The loss of methyl from the ion of m/e 194 was followed by loss of carbon monoxide. The loss of water between C_3-C_4 gave the species of m/e 328, an *iso*flavanone. This broke down by mode B, as expected to yield the fragments of m/e 151 and m/e 177.

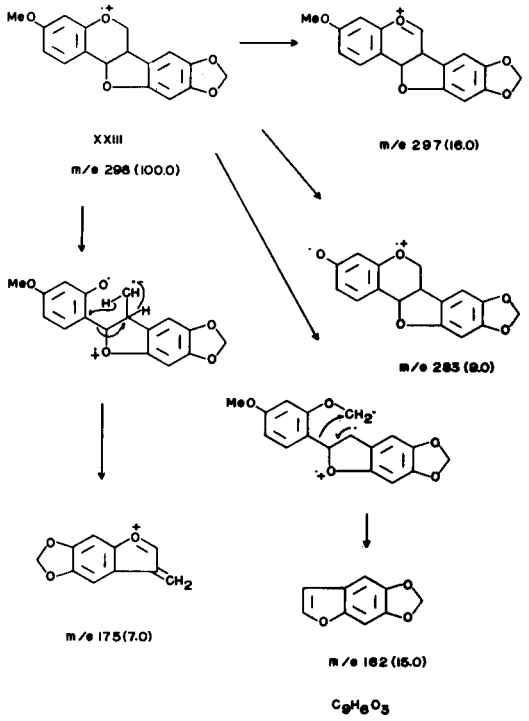


The spectrum of 4,6-dimethoxycoumaran-3-one (XXII) (Fig. 14) was readily interpreted as shown.

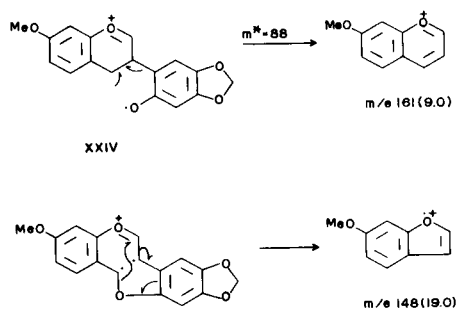


In pterocarpin (XXIII) (Fig. 15), very little breakdown occurs, as the reverse Diels-Alder reaction does not lead to fragmentation. A loss of a hydrogen atom is favoured and peaks appear at m/e 283, 175, 162, 149 and 148. The fragment at m/e 283 is due to the loss of a methyl radical. The peaks at 162, 161 and 148 were mass measured and shown to consist of fragments of formula $C_9H_6O_3$, $C_{10}H_9O_2$ and $C_9H_8O_2$ respectively.

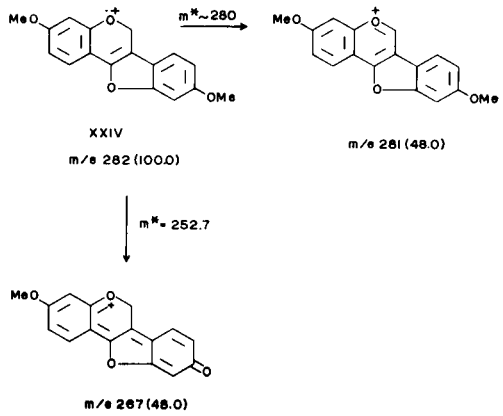
The processes may be rationalised as follows:



The peak at m/e 162 does not contain any indication of a species of formula $C_{10}H_{10}O_2$, the fragment of m/e 161 ($C_{10}H_9O_2$) probably arising from the M-1 ion, as does that at m/e 148.



In line with other chromenes, the loss of a hydrogen atom from anhydrohomopisatin (XXIV) (Fig. 16) was very large, as was the loss of methyl due to the intervention of quinonoid forms. The peak at m/e 141 was a doubly charged molecular ion.



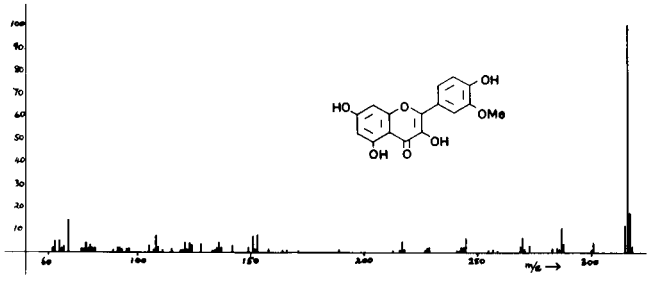


Figure 1

TABLE I

m/e	Intensity	m/e	Intensity	m/e	Intensity
317	17.4	269	6.4	137	2.4
316	100.0	245	2.9	136	4.8
315	12.0	244	2.7	135	2.3
301	4.4	243	2.4	128	4.0
288	4.0	229	2.3	124	3.6
287	10.8	228	2.0	123	4.4
285	2.0	217	5.0	121	4.5
283	2.0	153	8.0	109	2.4
273	3.0	151	7.3	108	7.6
271	2.0				

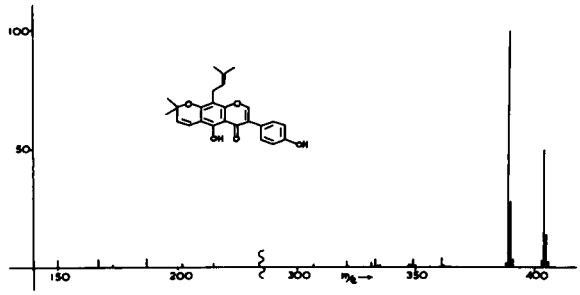


Figure 2

TABLE II

m/e	Intensity	m/e	Intensity	m/e	Intensity
406	2.5	390	28.0	333	3.5
405	14.0	389	100.0	321	2.5
404	50.0	388	2.0	187	3.6
403	3.0	361	4.0	167	3.1
391	3.5	349	3.5		

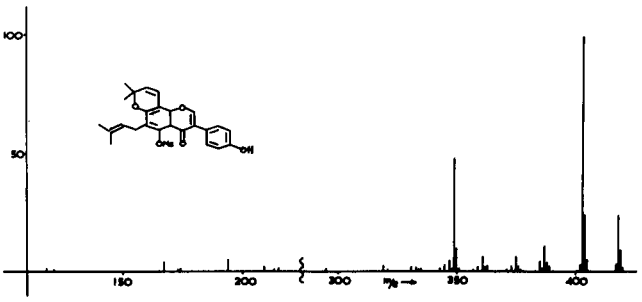


Figure 3

TABLE III

m/e	Intensity	m/e	Intensity	m/e	Intensity
419	9.0	385	4.2	349	48.0
418	24.0	375	6.2	347	5.0
404	24.0	363	3.0	345	3.0
403	100.0	361	6.2	167	4.0
387	11.0	350	10.0	118	1.5

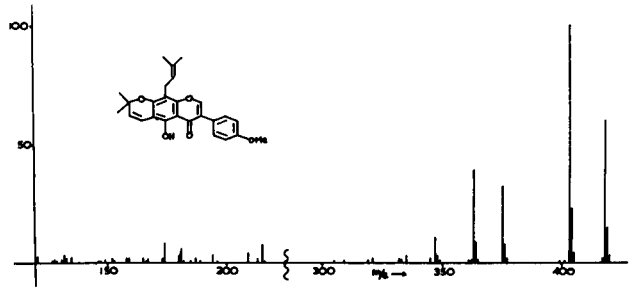


Figure 4

TABLE IV

m/e	Intensity	m/e	Intensity	m/e	Intensity
419	15.0	348	3.5	174	8.5
418	60.0	347	11.0	135	2.5
404	23.0	215	8.0	133	2.0
403	100.0	209	4.5	132	3.5
376	8.0	194	3.5	121	2.5
375	32.0				
364	9.3	181	5.5		
363	39.0	180	3.0		

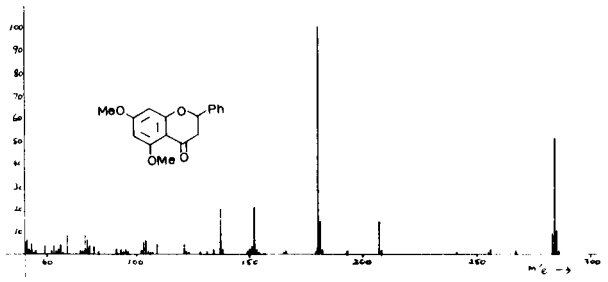


Figure 5

TABLE V

m/e	Intensity	m/e	Intensity	m/e	Intensity
285	10.2	153	2.2	109	4.3
284	51.0	152	21.0	104	6.2
283	9.0	151	3.4	103	5.4
256	2.0	150	2.4	78	6.6
208	2.0	138	2.5	77	8.6
207	14.3	137	20.0	69	8.4
181	14.3	134	2.2		
180	100.0	121	4.2		

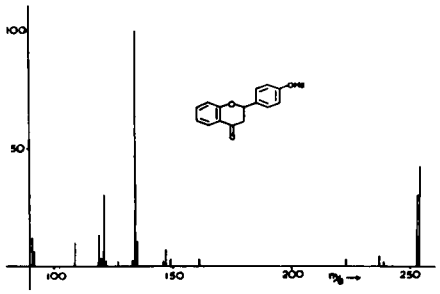


Figure 6

TABLE VI

m/e	Intensity	m/e	Intensity	m/e	Intensity
254	43.0	147	7.0	121	30.3
253	30.0	146	2.0	120	3.5
239	2.2	135	10.6	119	13.2
237	4.6	134	100.0	108	10.0
223	3.2	133	2.7	92	6.2
161	3.0	127	2.0	91	12.0
149	3.1	122	2.2		

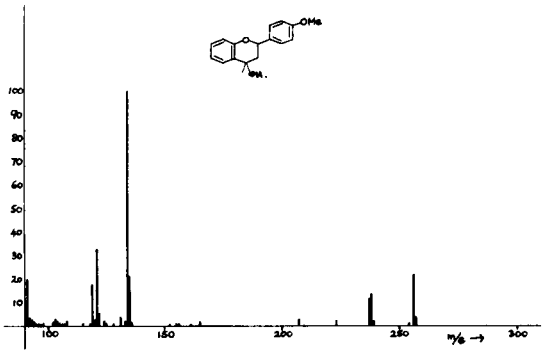


Figure 7

TABLE VII

m/e	Intensity	m/e	Intensity	m/e	Intensity
256	22.0	135	21.0	120	3.0
239	2.6	134	100.0	119	18.0
238	14.0	131	3.9	108	2.5
237	12.0	124	2.4	91	20.0
223	2.6	122	5.8		
207	2.9	121	33.0		

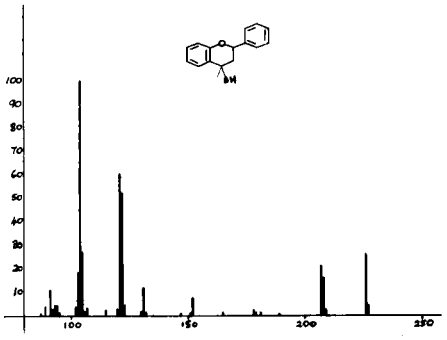


Figure 8

TABLE VIII

m/e	Intensity	m/e	Intensity	m/e	Intensity
226	24	122	52.0	103	17.0
209	2.6	121	60.0	102	3.8
208	16.0	120	3.0	94	4.6
207	21.0	115	2.7	93	4.7
152	7.5	107	3.2	92	27.0
131	12.0	105	27.0	91	11.0
123	4.8	104	100.0		

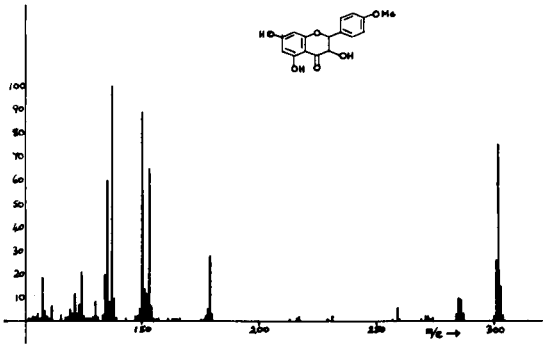


Figure 9

TABLE IX

m/e	Intensity	m/e	Intensity	m/e	Intensity
303	15.0	154	6.6	125	2.7
302	75.0	153	65.0	124	21.0
301	26.0	152	12.0	123	7.5
287	3.3	151	14.0	122	3.1
286	9.5	150	89.0	121	12.0
285	10.0	149	4.4	120	3.6
284	3.1	138	10.0	119	5.0
259	6.0	137	100.0	111	6.6
180	3.2	136	8.7	108	4.6
179	28.0	135	60.0	107	18.5
178	5.6	134	20.0		

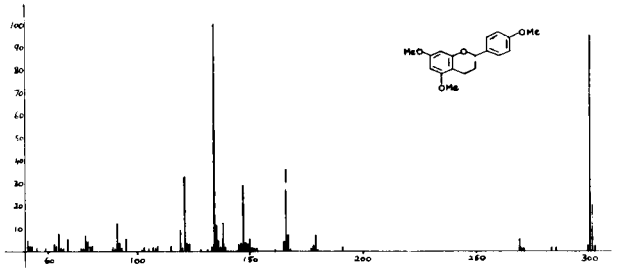


Figure 10

TABLE X

m/e	Intensity	m/e	Intensity	m/e	Intensity
301	20.0	165	4.4	135	11.0
300	95.0	150	5.4	134	100.0
299	2.7	148	3.6	123	3.2
269	5.7	147	29.0	122	3.6
179	7.2	146	3.7	121	33.0
178	3.0	145	3.2	119	9.0
167	7.2	138	12.5	95	6.0
166	36.0	136	5.0	91	12.0

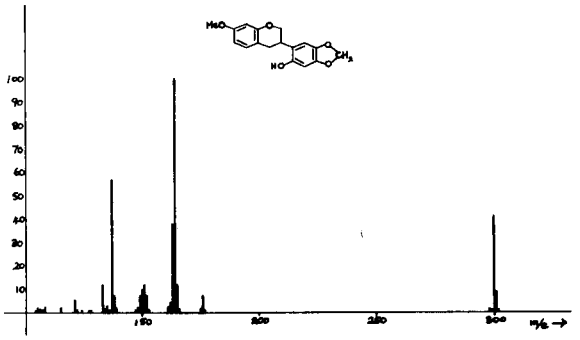


Figure 11

TABLE XI

m/e	Intensity	m/e	Intensity	m/e	Intensity
301	9.0	161	2.8	138	7.6
300	41.0	152	7.6	137	57.0
176	7.5	151	12.0	135	3.1
165	12.0	150	10.0	133	12.0
164	100.0	149	7.5	121	5.7
163	38.0	148	2.5	108	2.6
162	4.6	139	2.3		

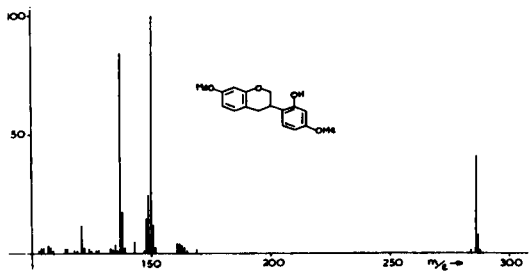


Figure 12

TABLE XII

m/e	Intensity	m/e	Intensity	m/e	Intensity
287	8.0	152	2.5	138	17.5
286	41.0	151	12.0	137	84.0
164	2.5	150	100.0	135	3.5
163	3.3	149	24.5	121	11.7
162	4.0	148	14.5	107	3.3
161	4.2	143	4.8		

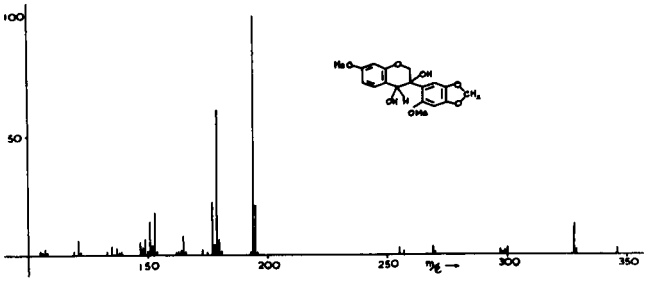


Figure 13

TABLE XIII

m/e	Intensity	m/e	Intensity	m/e	Intensity
346	2.7	180	6.7	149	6.8
328	13.0	179	61.0	148	2.9
300	3.2	178	4.2	147	5.5
297	2.5	177	22.0	137	3.0
269	3.7	165	8.0	135	3.8
255	3.0	153	18.0	121	6.4
195	21.0	152	4.1	107	2.5
194	100.0	151	14.0		

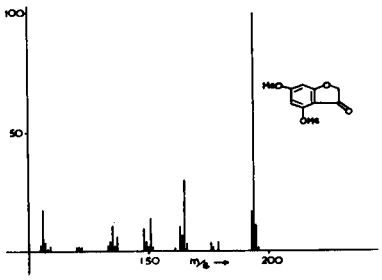


Figure 14

TABLE XIV

m/e	Intensity	m/e	Intensity	m/e	Intensity
195	11.5	165	30.0	137	6.3
194	100.0	164	7.0	135	11.0
193	16.9	163	10.5	134	4.2
179	4.1	151	19.0	107	4.0
176	3.7	149	4.2	106	17.5
166	3.5	148	9.4	105	2.8

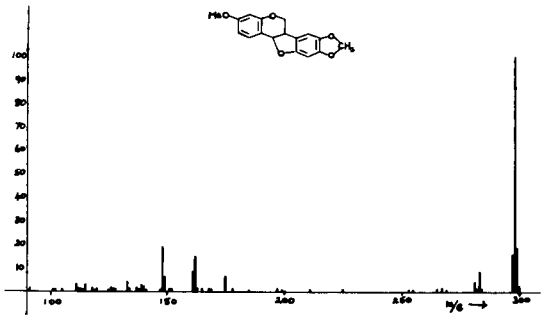


Figure 15

TABLE XV

m/e	Intensity	m/e	Intensity	m/e	Intensity
298	100.0	162	15.0	137	2.0
297	16.0	161	8.8	133	4.5
283	4.5	148	19.0	126	2.0
281	9.0	140	2.8	115	3.4
175	6.6	139	3.2	111	3.6

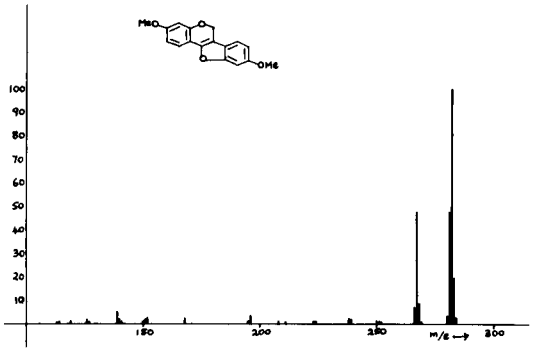


Figure 16

TABLE XVI

m/e	Intensity	m/e	Intensity	m/e	Intensity
283	20.0	267	48.0	168	2.8
282	100.0	266	7.5	152	3.0
281	48.0	239	2.4	141	16.0
280	3.7	238	2.5	139	5.4
268	9.0	196	3.8		

All spectra were taken on an A.E.I., MS9 model mass spectrometer using a direct insertion probe.

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