

The University of Manchester and A. E. I. Ltd.

The Mass Spectra of Oxygen Heterocycles (III) (1,2)

An Examination of Simple Lignans

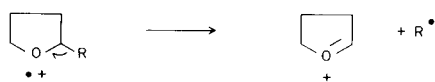
Andrew Pelter, A. P. Stainton and M. Barber

The mass spectra of some simple lignans containing the tetrahydrofuran nucleus have been examined. The fragmentation patterns of various types have been defined and shown not to be sensitive to the stereochemistry of the substituents. Positional isomers however give very different mass spectra.

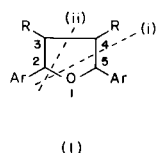
The lignans are a group of naturally occurring substances, of vegetable origin and of varying complexity (3). Many of these compounds contain a tetrahydrofuran nucleus, and the present investigation, initially of the simpler members of this class, was undertaken with two aims. The first was to find out whether the mass spectra were sufficiently meaningful to define the gross structure of these compounds; the second was to investigate whether stereo-isomers gave breakdown patterns sufficiently different to allow the stereochemistry to be clarified.

It rapidly became clear that the mass spectra did define the overall structure but in none of the cases examined by us did stereo-isomerism do more than slightly affect the intensity of some peaks, and that this effect was too slight to be useful.

The mass spectra of tetrahydrofurans have previously been studied (4, 5, 6, 7), the main breakdown being shown to be an α -cleavage, *i.e.*

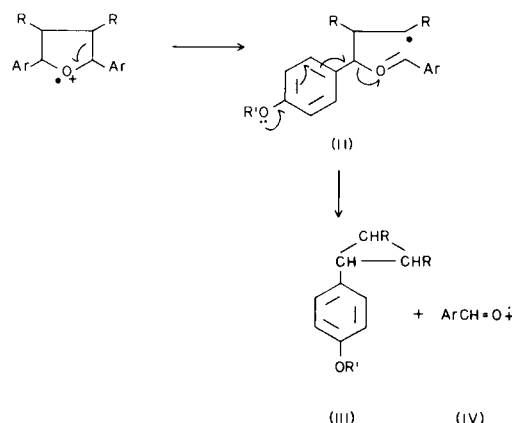


In the case of the lignans this mode of fragmentation, where it can be observed at all, is minor. Instead, with lignans of the general formula (I), the two breakdowns indicated by the dotted lines are the main pathways from the molecular ion. The overlapping degradations are sufficient to define

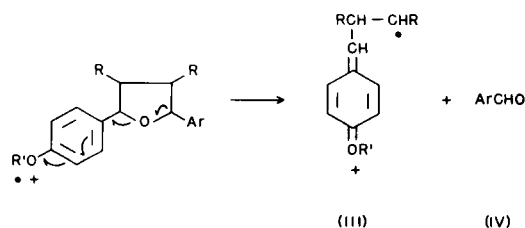


the overall structure of the molecule, though not of course the position of alkoxy groups on the benzene rings, nor the stereochemistry of the molecule.

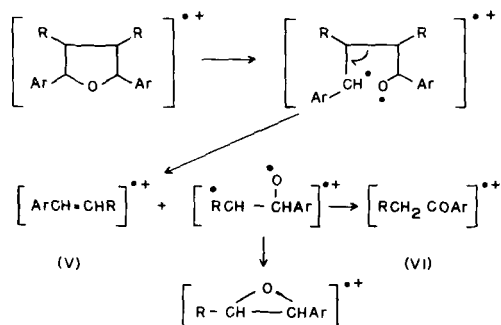
All fragments possible from these breakdowns are seen, though to highly varying degrees and various explanations for them may be put forward. Thus path (i) may be explained as shown below.



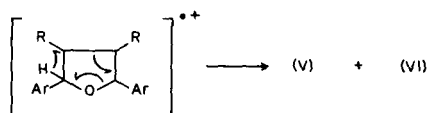
Or ion (III) may be the odd-electron species, either by the movement of two electrons in ion (II) instead of one, or by initial ionisation of the oxygen of an aromatic ether.



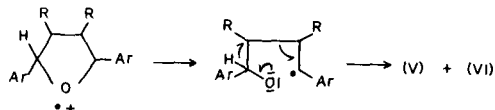
For path (ii) similar mechanisms can be used;



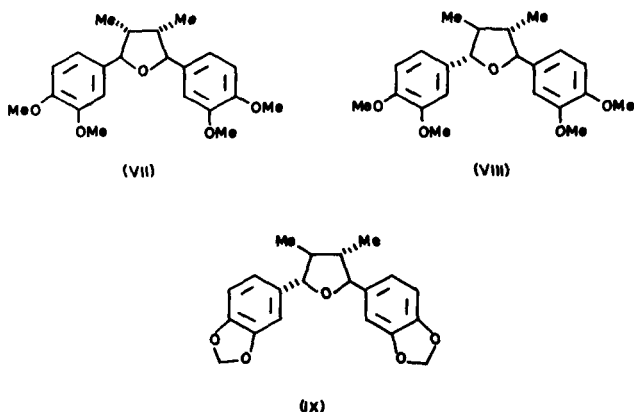
or else a concerted mechanism may be written, or



again ionisation of the ring oxygen may be used.

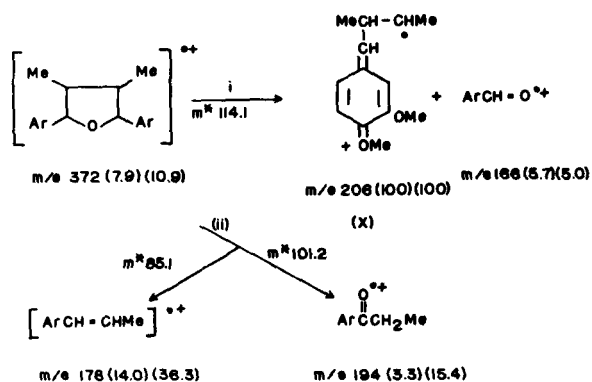


The rest of the spectrum of this type of lignan is provided, in the main, by further breakdown of the ions arising from (i) and (ii). Examples are galgravin (VII) (Fig. 1), galbelgin (VIII) (Fig. 2) and galbacin (IX) (Fig. 3) (3). As can be seen, the spectra of galgravin and galbelgin are extremely similar, all groups of peaks being replicated. In



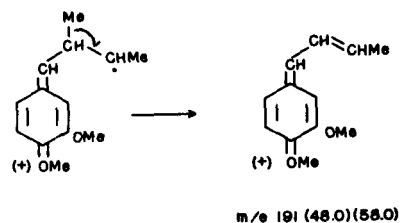
the following discussion of the mass spectra of these two compounds the intensities in the first brackets (1,2) are those of galgravin, in the second those for galbelgin and the metastable ions shown are common to both. The term Ar- stands for a 3,4-dimethoxybenzene nucleus. The stereochemistry is not defined in the formulae.

The base peak arises from path (i), and path (ii) can readily be discerned.

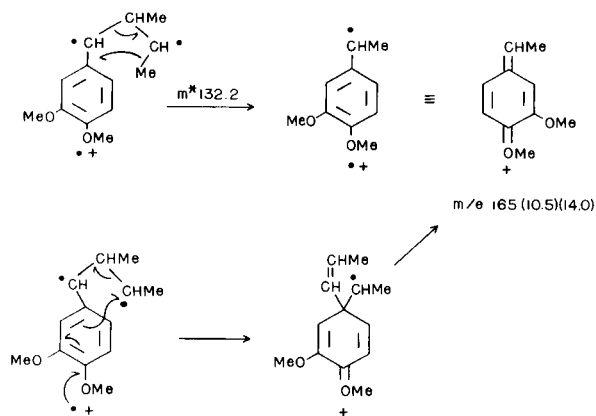


From (X), which may of course exist in many forms, various breakdowns occur.

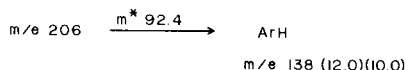
(a) A loss of methyl group is very prominent and, as this loss is also shown by the corresponding ion in galbacin (IX), it must arise from the side chain.



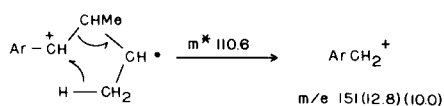
(b) An interesting fragmentation that must involve either an aryl or an alkyl migration is the production of an ion at m/e 165. Accurate mass measurements have shown that this peak is a doublet, represented by $\text{ArC}\equiv\text{O}^+$ (60%) and ArCHMe^+ (40%). The latter ion is defined as arising from (X) by a metastable peak at m/e 132.2.



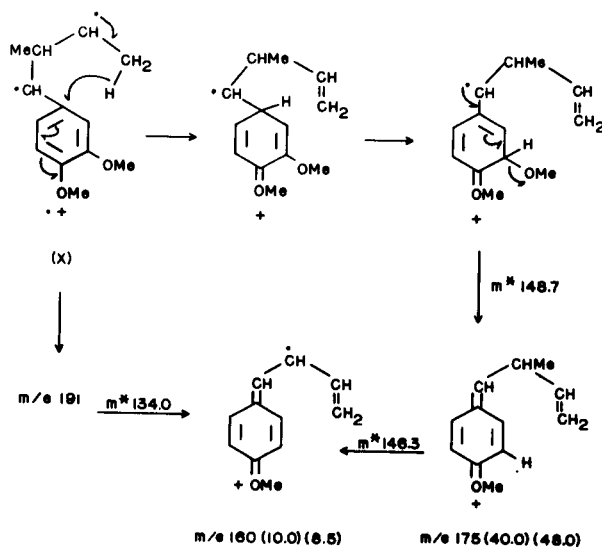
(c) A fragmentation of (X) involves a hydrogen transfer with the production of dimethoxybenzene.



(d) The origin of the ion at $m/e\ 151$ cannot be exactly defined as the metastable peak at 110.6 may be assigned to another transition. However, (X) is the most likely precursor.

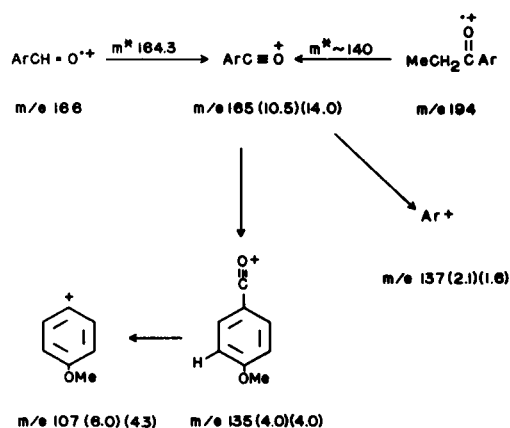


(e) The most striking feature of the breakdown of (X) is the large extent of the loss of a methoxyl group. Both in galgravin and galbelgin this loss produces the third largest peak in the spectrum. In the breakdown of aromatic ethers it is rare (1, 2, 3, 8) for the loss of a methoxyl group, as such, to be more than a minor mode, the case of osthol (8) with an unsaturated side chain being an exception. It is obvious that the side chain of (X) must be intimately involved in the expulsion of the methoxyl radical and in view of the known reluctance of benzyl ions containing methoxyl groups to rearrange to the tropylium form (9), we provisionally formulate this change as follows. Work on model compounds is going forward to attempt to define the mechanism of this breakdown more narrowly.

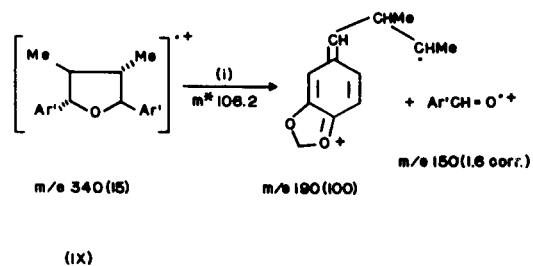


A further loss of methyl from the species at $m/e\ 175$ gives rise to the ion at $m/e\ 160$, the latter also arising from loss of a methoxyl radical from the ion at $m/e\ 191$.

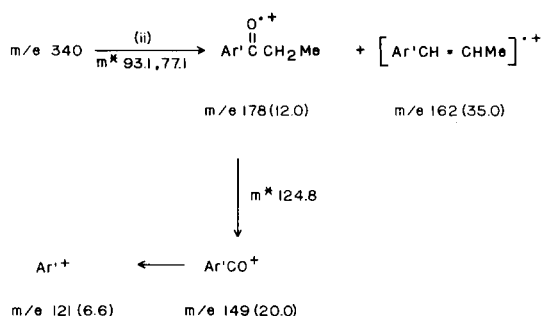
Naturally the aldehyde, mass 166, produced by route (i) will lose a hydrogen atom to give rise to a peak at $m/e\ 165$. This same ion is also produced by fragmentation of the species at $m/e\ 194$, produced by path (ii).



With galbacin (IX), the breakdown pattern is extremely similar to those previously given, once more the base peak being produced *via* path (i). In the following discussion Ar'- stands for 3,4-dimethylenedioxyphenyl.

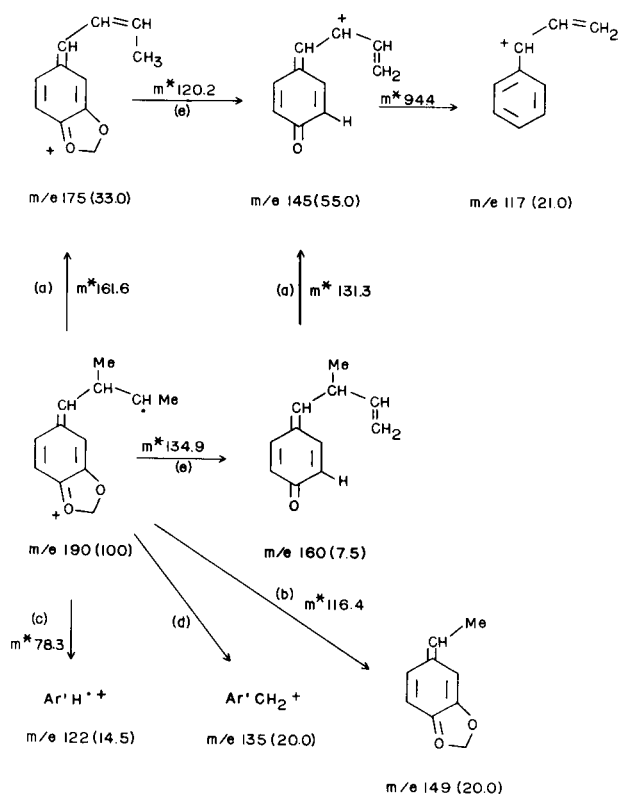


Here route (ii) leads to peaks of rather higher intensity than before, leading to the breakdowns shown.



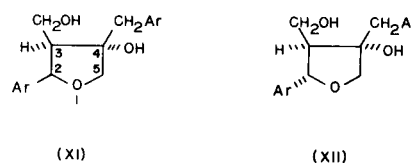
A metastable peak also implicates the aldehyde of mass 150 in the production of the ion at m/e 149, which has been shown to be a doublet made up of $Ar^+C\equiv O^+$ (50%) and Ar^+CHMe (50%).

As with the two lignans already discussed the ion corresponding to the base peak may break down in various ways, by mechanisms similar to those already presented.



In the case of galbacin the loss of formaldehyde from the ions of mass 190 and 175 is taken as formally equivalent to the losses of methoxyl previously commented on.

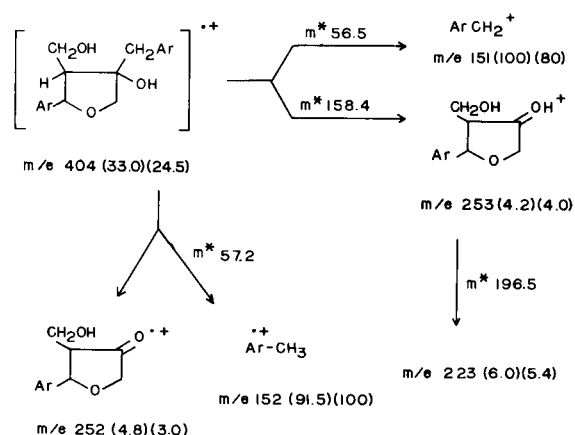
A different type of lignan is found in the stereoisomers dihydrogmelinol (XI) (10) (Fig. 4) and di-O-methylolivil (11) (XII) (Fig. 5). (The term Ar here, as previously, stands for 3,4-dimethoxy-



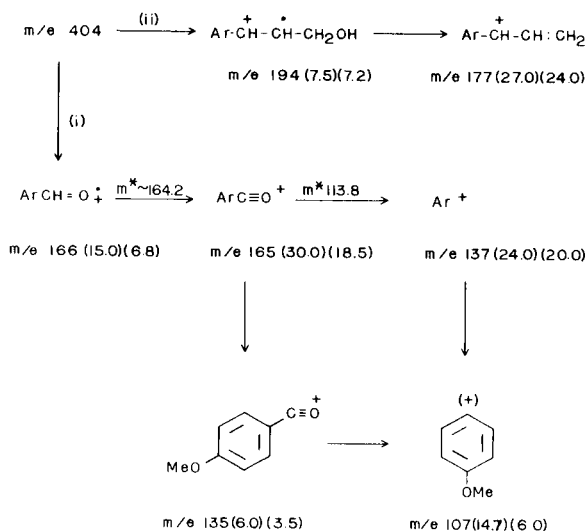
phenyl). α -Cleavage is shown by neither of these compounds, instead pathways differing somewhat from those already observed are seen. Once more the two stereo-isomers give spectra that are extremely similar, and in the ensuing discussion the figures in the first bracket refer to (XI) and in the second to (XII).

The most important breakdown involves displacement of the benzyl side chain on C_4 , either with or without hydrogen transfer.

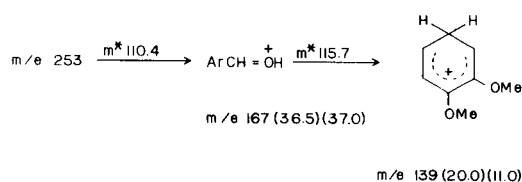
The ion at m/e 253 loses formaldehyde, though the origin of this (there being two reasonable alternatives) is not known.



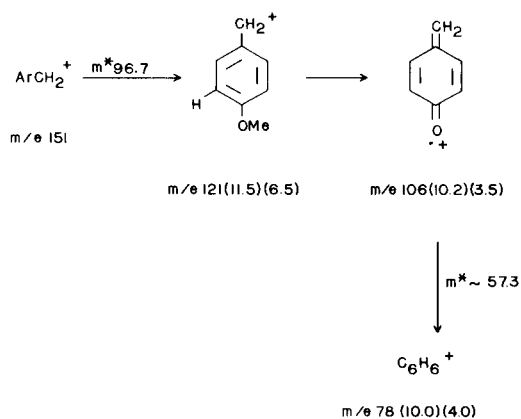
Breakdown by processes equivalent to paths (i) and (ii) are observed also.



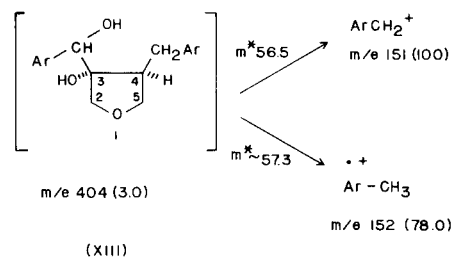
An interesting feature of the spectra of these compounds is the large peak at $m/e\ 167$, corresponding to $\text{ArCH}=\text{OH}^+$. The metastable peak at $m/e\ 110.4$ indicates the ion at $m/e\ 253$ ($m^* 110.3$) as the most likely precursor, though the species at $m/e\ 252$ cannot be completely excluded ($m^* 110.7$). A further loss of carbon monoxide leads to the ion at $m/e\ 109$.



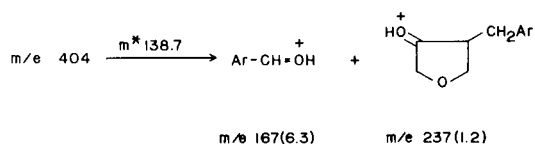
From the benzyl ion at $m/e\ 151$, successive losses of formaldehyde, a methyl radical and carbon monoxide occur, whilst as before a peak at $m/e\ 138$ (8.0) (3.0) occurs, corresponding to ArH^+ .



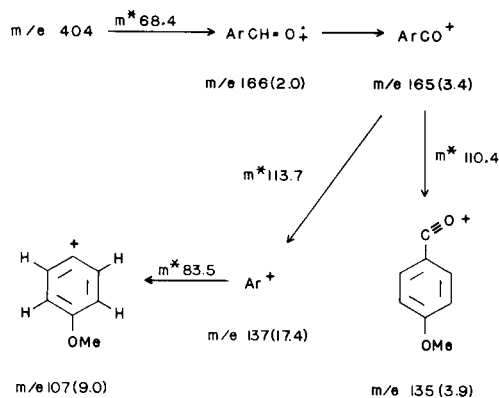
A very different lignan is dihydroneogmelinol (XIII) (Fig. 6), this being a positional isomer of (XI) and (XII), bearing no aryl substituents on either C_2 or C_5 . It gives a relatively simple spectrum, the base peak being formed by cleavage of the benzyl group at C_4 . The same cleavage, with hydrogen transfer is responsible for the second largest peak, and these two ions are by far the most numerous recorded. A



similar breakdown at C_3 occurs to only a minor extent. An analogous process with hydrogen transfer



leads to the following transformations. The other



peak of any note is that due to Ar^+-H , which may arise from either aryl group.

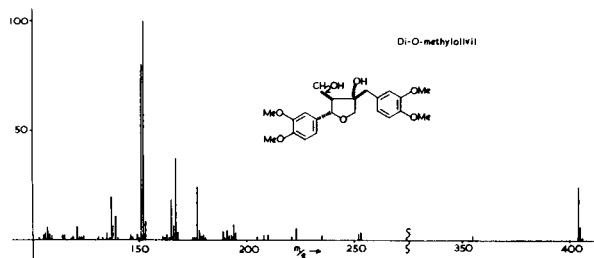


Figure 5

TABLE 5 (Olivil dimethyl ether)

m/e	I	m/e	I	m/e	I	m/e	I	m/e	I
406	1.1	195	3.5	175	1.5	149	2.7	122	1.4
405	6.4	194	7.2	168	3.6	147	1.7	121	6.5
404	24.5	193	2.2	167	37.0	146	2.4	119	2.0
355	2.2	192	2.2	166	6.8	140	1.1	118	1.0
325	1.1	191	4.8	165	18.5	139	11.0	115	2.3
253	4.0	190	1.1	164	1.3	138	6.5	109	2.3
252	3.0	189	4.1	163	2.6	137	20.0	108	2.9
235	2.4	181	1.1	162	1.3	136	1.2	107	6.0
223	5.4	180	2.3	161	1.8	135	3.3	106	3.6
221	1.5	179	2.0	153	8.7	133	1.2	105	2.4
210	2.7	178	4.7	152	100.0	131	1.4	103	1.2
208	2.2	177	24.0	151	80.0	124	2.0		
205	1.6	176	1.4	150	1.1	123	1.7		

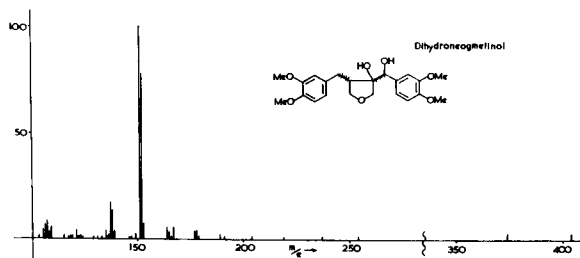


Figure 6

TABLE 6 (Dihydroneogmelinol)

m/e	I	m/e	I	m/e	I	m/e	I
404	3.0	166	2.0	136	2.0	115	1.8
374	3.3	165	3.4	135	3.9	109	5.7
254	1.9	164	5.6	133	1.2	108	3.8
237	1.2	153	7.7	131	1.2	107	9.0
219	1.0	152	78.0	129	1.0	106	7.3
204	1.3	151	100.0	124	1.2	105	4.7
191	1.4	149	2.6	123	1.8	103	1.8
189	2.4	147	1.2	122	1.5		
179	1.6	146	1.0	121	4.6		
178	4.4	139	4.0	119	1.4		
177	4.0	138	14.0	118	1.3		
167	6.3	137	17.4	117	1.2		

All spectra were run on an A.E.I. Ltd. MS9 double-focussing mass spectrometer, using the inlet system previously described (1).

We wish to thank Professor A. J. Birch for the generous provision of samples and Dr. J. Wilson for helpful discussions. One of us (P.S.) thanks the S.R.C. for the provision of a maintenance grant.

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