

# ELECTRON IMPACT STUDIES—XXXVI<sup>1</sup>

## PROXIMITY EFFECTS IN THE MASS SPECTRA OF AROMATIC CARBONYL COMPOUNDS CONTAINING ADJACENT ETHOXYL SUBSTITUENTS—A LABELLING STUDY

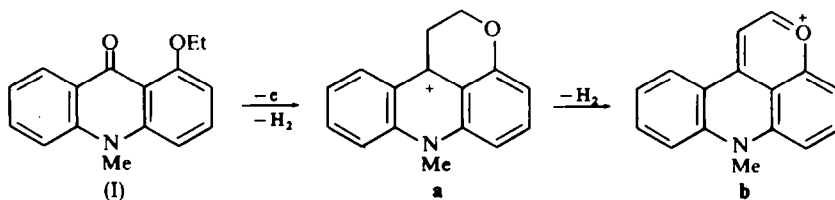
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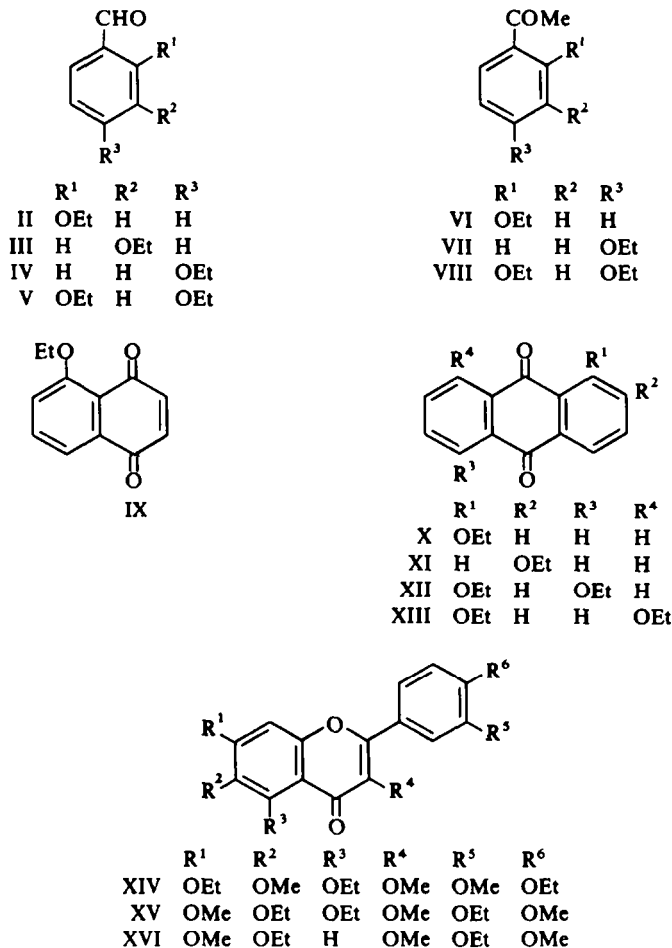
**Abstract**—The mass spectra of aromatic carbonyl compounds with *ortho* or *peri* ethoxyl substituents exhibits M-H<sub>3</sub>O<sup>+</sup> (M-19) peaks. This “proximity-effect” is of diagnostic value and may be used for structure elucidation. The mechanism of the elimination is complex, and has been studied by deuterium and <sup>18</sup>O labelling. The effect is still observed when the size of the *n*-alkoxy group is increased.

DURING an investigation<sup>2</sup> of the mass spectra of acridone alkaloids, it was observed that M-19 peaks were present in the spectra of 1-ethoxyacridones, but were absent when the OEt was not *peri* to the CO group. A concurrent study<sup>3</sup> also showed that the presence of a OMe group next to a CO substituent (of an aromatic system) could be detected by the presence of M-H<sub>2</sub>O fragments. The latter proximity-effect is only diagnostic for simple systems, and cannot be extended to polyoxygenated systems.<sup>3</sup> “*Ortho*-effects”<sup>4</sup> are quite common in aromatic systems and (for example) have been observed in the spectra of *o*-hydroxybenzyl alcohol,<sup>5</sup> *o*-hydroxybenzoic acid,<sup>6</sup> anthranilic acid<sup>7</sup> and *o*-carboxythiophenol<sup>8</sup> where 6-centre transition states are involved. 6-Membered transition states are not always necessary, e.g. the non-concerted eliminations in the spectra of 4-substituted benzo[*c*]cinnolines<sup>9</sup> and the elimination of water from the molecular ion of *o*-methoxybenzoic acid<sup>10</sup> (which probably involves a 7-membered transition state).



It was suggested<sup>2</sup> that the M-19 ion in the mass spectra of 1-ethoxy-acridones is an oxonium cation (b) possibly produced by the process I → b. To extend this project, we have synthesized a series of simple OEt derivatives (II–XIII) in order to determine whether this decomposition process is of diagnostic value. In addition, selected compounds have been labelled isotopically to allow the study of the mechanism of the elimination.

The mass spectra of the benzaldehydes, acetophenones and quinones which contain either *ortho* or *peri* ethoxyl substituents (II, V, VI, VIII, IX, X, XII and XIII), all exhibit M-17, M-18 and M-19 peaks (Table 1). The spectra of the corresponding compounds where the OEt substituent is not adjacent to a CO function (III, IV, VII

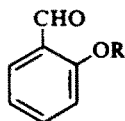


and XI) are completely devoid of M-17, 18 and 19 peaks. The spectra of 4-ethoxybenzaldehyde (IV) and 2-ethoxybenzaldehyde (II), which are reproduced in Figs 1 and 2, illustrate the ease with which the 'proximity-effect' allows the differentiation of the two isomers.

If M-H<sub>3</sub>O<sup>+</sup> ions are to be diagnostic for this substitution pattern, then they must be present in spectra of more complex systems (e.g. natural products) which contain (or which may be modified to) this substitution pattern. The spectra of three OEt derivatives (XIV–XVI) of naturally occurring flavones have been reported,<sup>11</sup> and it can be seen (Table 1) that when an OEt group is present at C-5 (R<sup>3</sup>) that M-17, 18 and 19 ions are present (XIV and XV) whereas the spectrum of XVI has no peaks in this region. It has already been shown<sup>2</sup> that the spectra of 1-ethoxyacridones, but not 4-ethoxyacridones, exhibit pronounced M-17, 18 and 19 peaks. It has therefore been demonstrated that ions resulting from the overall processes M-HO<sup>+</sup>, M-H<sub>2</sub>O and M-H<sub>3</sub>O<sup>+</sup> are of diagnostic value in the spectra of benzaldehydes, acetophenones, quinones, flavones and acridones when *ortho* or *peri* OEt substituents

TABLE 1. RELATIVE ABUNDANCES OF M-17, M-18 AND M-19 IONS IN THE SPECTRA OF (II)-(XVI)

Compound	M-17	M-18	M-19
II	7	11	8
III	0	0	0
IV	0	0	0
V	36	3	2
VI	3	5	2
VII	0	0	0
VIII	17	2	1
IX	4	10	13
X	10	17	20
XI	0	0	0
XII	13	8	3
XIII	1	0.5	0.5
XIV	14	3	7
XV	5	4	3
XVI	0	0	0



- XVII  $n$  C<sub>3</sub>H<sub>7</sub>  
 XVIII *iso* C<sub>3</sub>H<sub>7</sub>  
 XIX  $n$  C<sub>4</sub>H<sub>9</sub>  
 XX *sec* C<sub>4</sub>H<sub>9</sub>  
 XXI CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>

TABLE 2. RELATIVE ABUNDANCES OF M-17, 18 AND 19 IONS IN THE SPECTRA OF XVII-XXI

Compound	M-17	M-18	M-19
II	7	11	8
XVII	5	5	5
XVIII	2	2	1
XIX	1	1	1
XX	1	1	1
XXI	1	1	0

are present. This fragmentation should also occur in other systems containing suitably positioned substituents.

The effect of increasing the size of the alkoxy group can be seen from the abundances (Table 2) of the M-17, 18 and 19 ions in the spectra of the *o*-alkoxybenzaldehydes (XVII-XXI). In general, the abundance of the M-19 ion decreases as the size of the alkyl group increases. This is due to two effects. First, as the size of the alkyl group increases the stability of the oxonium species will decrease because of the possibility of fragmentation through its side chain. Second, the normal fragmentation of the alkoxy substituent is enhanced at the expense of oxonium-ion formation. When a

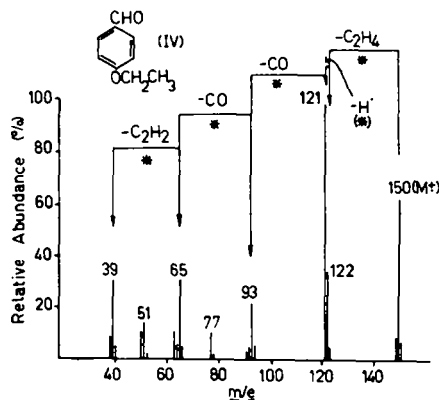


FIG. 1

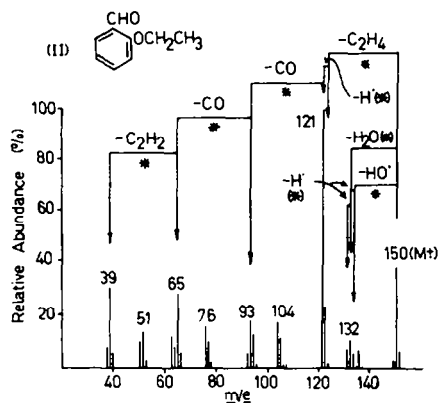


FIG. 2

benzyloxy group is present (as in XXI) the  $M-H_3O^+$  fragmentation no longer occurs.

The  $M-19$  ion is produced by two quite different pathways, viz.,  $M-H_2O-H^+$  and  $M-HO^+-H_2$  (or  $M-HO^+-H^+-H^+$ ). These processes generally occur (to a greater or lesser extent) in all spectra, and are always substantiated by appropriate metastable ions (a metastable ion is indicated in a Figure by an asterisk). The  $M-HO^+-H_2$  process is more pronounced in the spectra of complex systems (e.g. acridones and flavones), whereas in simpler systems (e.g. benzaldehydes, acetophenones and simple quinones) both processes occur with approximately equal probability. In order to see whether the mechanism (I  $\rightarrow$  b) outlined above is feasible, the labelled compounds XXII–XXVII were synthesized and their partial spectra are recorded in Figs 3–5. The compositions of all fragment ions in these partial spectra have been established by exact mass measurement. It should be noted that the maximum resolution [10,000 (40% valley definition)]<sup>12</sup> does not allow the resolution of for example, an  $M-DO^+$  or an  $M-H_2O$  ion. When such a situation occurs, careful consideration of the spectra of labelled and unlabelled compounds, the fragmentation patterns, and the metastable ions generally allows differentiation between two possibilities.

The partial spectra of 1-ethoxyanthraquinone (X and XXII) are recorded in Fig. 3.

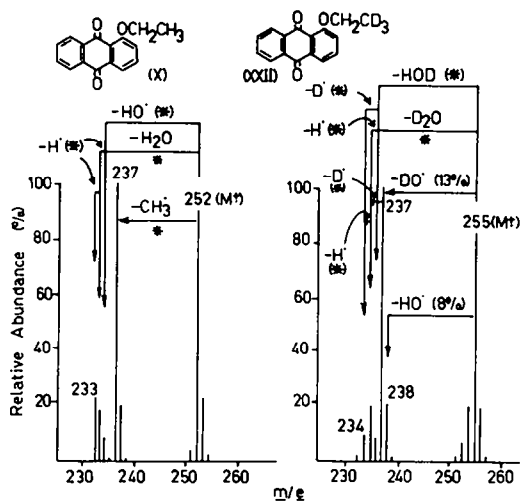


FIG. 3

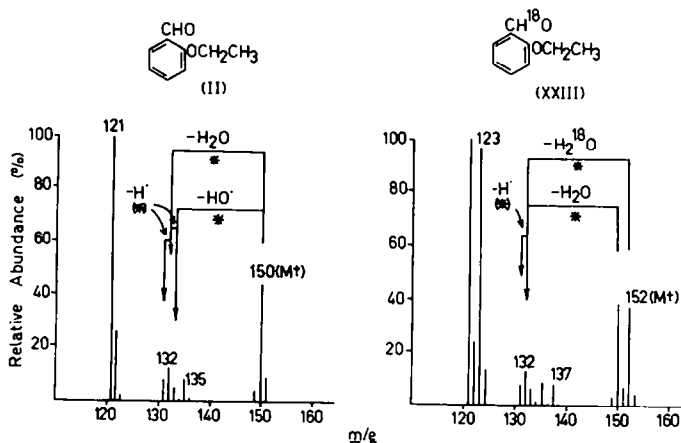


FIG. 4

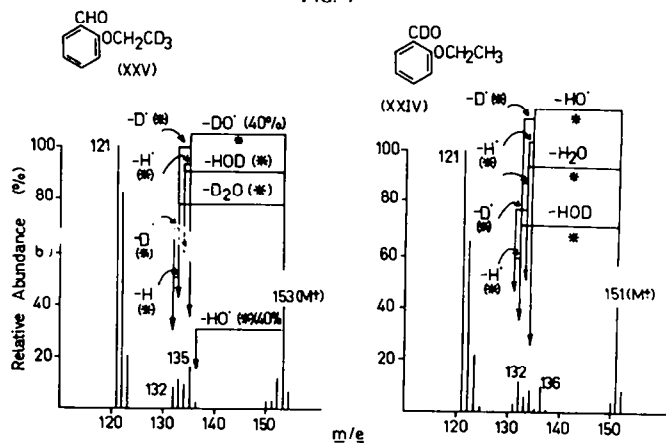
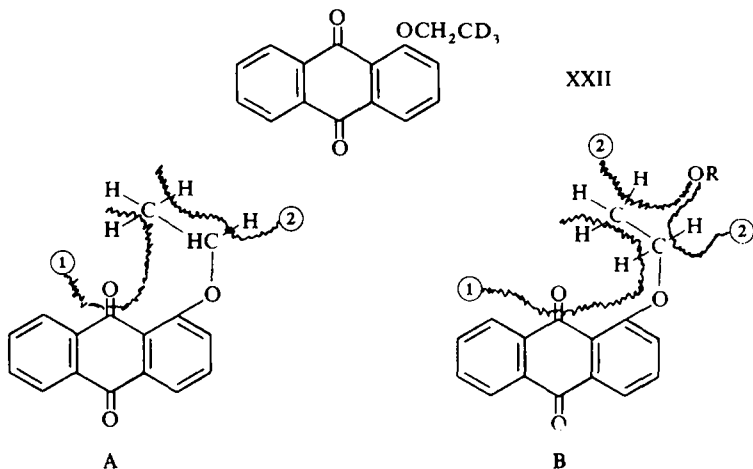
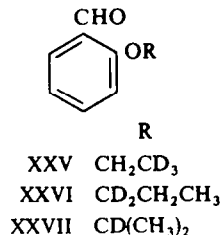
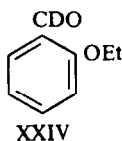
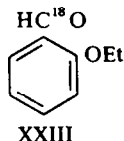


FIG. 5

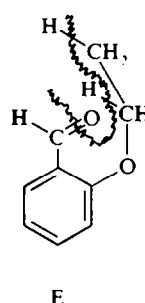
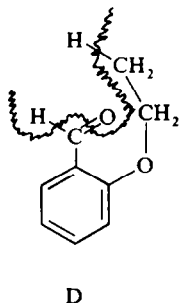
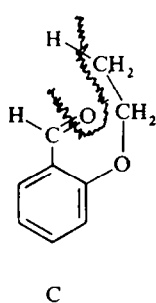


No attempt was made to label the carbonyl oxygens of X with  $^{18}\text{O}$  because of the ambiguity of interpretation of the mass spectrum. However,  $^{18}\text{O}$  labelling of *o*-ethoxybenzaldehyde (II) (see below) shows that the oxygen lost in the M-19 process originates specifically from the CO group (Fig. 4). The spectrum (Fig. 3) of XXII shows the two elimination processes to be complex. High resolution shows that 13% of the M-18 peak corresponds to M-DO' (the complement is M-CD<sub>3</sub>'), and that 8% of the M-17 peak is M-HO'. Comparison of the relative abundances now show that the processes M-DO' and M-HO' occur in the ratio 81:15. Although it is possible to equate the actual relative abundances of the M-17 and M-18 peaks in (XXII), the same approach cannot be used to determine the extent of M-HOD and M-D<sub>2</sub>O fragmentation, because the M-19 and M-20 ions also arise by losses of hydrogen and/or deuterium radicals from the M-17 and M-18 species. In order to rationalize this situation, the ratios of the heights of the metastable peaks for the M-HOD and M-D<sub>2</sub>O processes will be taken to indicate the relative extent to which these processes proceed. It is possible that the fast processes which give rise to these fragment ions in the source may not proceed by the same mechanisms as the slow processes which give rise to the metastable peaks (cf. M-HO' and M-DO' in the spectrum of C<sub>6</sub>H<sub>5</sub>COOD<sup>13,14</sup>). With this limitation in mind, the abundances of the metastable ions for the slow processes M-HOD and M-D<sub>2</sub>O indicate that these processes occur in the ratio 4:1. The major processes occurring in this spectrum are therefore M-HOD—D', M-HOD—H', and M-DO'—H'—D' (or M-DO'—D'—H'). Although there is no evidence to indicate that hydrogen randomization in the ethoxy substituent does not occur prior to the M-19 fragmentation [even though the M-CD<sub>3</sub>' process (in XXII) occurs without deuterium randomization (see Fig. 3), it has recently been shown that different processes from the same molecular ion may occur both with and without hydrogen rearrangement prior to fragmentation<sup>15</sup>], it is considered that the labelling results are consistent with the major fragmentations occurring by the processes outlined in A and B.

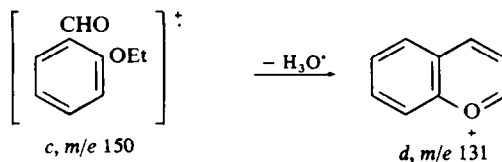
The M-19 process is more complex in the spectrum of 1-ethoxybenzaldehyde (II). The partial spectra of II and the labelled compounds (XXIII-XXV) are recorded



in Figs 4 and 5. The carbonyl oxygen is lost during the elimination process, as evidenced by the spectrum (Fig. 4) of XXIII. The hydrogen of the formyl group is now additionally involved in the elimination. This is analogous to the loss of water from the molecular ion of *o*-methoxybenzaldehyde,<sup>3</sup> which also involves participation of the formyl hydrogen. The spectrum (Fig. 5) of XXV shows that the abundances of ions arising from M-DO<sup>+</sup> and M-HO<sup>+</sup> eliminations occur in the ratio of 7:1. The slow processes M-HOD and M-D<sub>2</sub>O occur in the ratio 5:1 (it is assumed that any M-H<sub>2</sub>O process in this spectrum is minor in comparison with the M-D<sub>2</sub>O loss). The major processes in this spectrum are M-HOD—D<sup>+</sup>, M-HOD—H<sup>+</sup> and M-DO<sup>+</sup>—H<sup>+</sup>—D<sup>+</sup> (or M-DO<sup>+</sup>—D<sup>+</sup>—H<sup>+</sup>). The spectrum (Fig. 5) of XXIV shows the slow processes M-H<sub>2</sub>O/M-HOD in the ratio 2:3. The major processes for XXIV are therefore M-HOD—H<sup>+</sup>, M-H<sub>2</sub>O—H<sup>+</sup> (or D<sup>+</sup>) and M-HO<sup>+</sup>—[(H<sup>+</sup> + H<sup>+</sup>) or (H<sup>+</sup> + D<sup>+</sup>)]. The initial losses in the major processes are outlined in C, D and E. In C, initial loss of HO<sup>+</sup> is followed by loss of two of the remaining five hydrogens, while for D (which is more important than E) initial loss of H<sub>2</sub>O is followed by loss of any one of the four remaining hydrogens.



The spectra of the labelled propyl ethers XXVI and XXVII are consistent with the mechanisms shown in C and D. In both spectra the M-17 ion is more abundant than the M-18 ion, showing that M-HO<sup>+</sup> is more favoured than M-DO<sup>+</sup>. In addition, metastable heights in the spectrum of XXVI show the slow processes M-H<sub>2</sub>O/M-HOD/M-D<sub>2</sub>O to occur in the ratio 4:5:1, while for XXVII the corresponding ratio is 2:1 (M-H<sub>2</sub>O/M-HOD).



The 'kinetic-approach'<sup>16-19</sup> has been applied to the M-18 ion in the spectrum of *o*-methoxybenzaldehyde,<sup>3</sup> and has indicated that the ion may correspond to a benzofuran radical ion. Unfortunately the application of this method to the oxonium species *d* is not practicable, because no fragmentation of *d* (or of its analogues in other spectra) is observed. In the absence of evidence to the contrary, it is argued that oxonium cations are the most plausible representations for the M-19 species in the spectra of aromatic carbonyl compounds with adjacent OEt substituents.

#### EXPERIMENTAL

All spectra were determined with an Hitachi Perkin-Elmer RMU 6D double-focusing mass spectrometer operating a 70 eV. Exact mass measurements were determined at a resolution of 10,000 (40% valley definition)<sup>12</sup> using heptacosafuorotributylamine to provide reference masses.

The unlabelled compounds used for this study were either prepared by standard methods or were available from previous studies.<sup>2, 11</sup>

The labelled compounds (XXII and XXV-XXVII) were prepared by alkylation of the required phenol with the appropriate labelled alkyl iodide.<sup>20</sup> Compound XXIV was prepared by labelling<sup>21</sup> of the propylene-thioacetal followed by hydrolysis with HgO. Treatment of II with H<sub>2</sub><sup>18</sup>O (80% <sup>18</sup>O) in dioxan (containing a trace of trifluoroacetic acid) at room temp for 3 hr produced XXIII with 50% incorporation of <sup>18</sup>O.

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