Tetrahedron, 1963, Vol. 19, pp. 2233 to 2240. Pergamon Press Ltd. Printed in Northern Ireland

MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS—XXXIV[1]

AROMATIC METHYL AND ETHYL ETHERS[2]

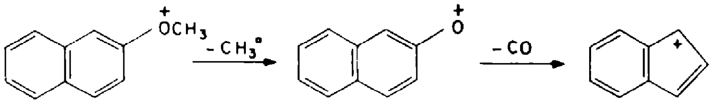
Z. Pelah, J. M. Wilson, M. Ohashi, H. Budzikiewicz and Carl Djerassi
Department of Chemistry, Stanford University, Stanford, California

(*Received* 29 *May* 1963; *in revised form* 8 *July* 1963)

Abstract—The behavior under electron impact of a series of aromatic methoxy and ethoxy compounds has been observed. The more common fragmentation processes are interpreted and in some cases the differences among spectra of positional isomers can be explained.

In an investigation of the mass spectra of some isothiocyanates[3] significant differences were noted among the spectra of the three isomeric methoxybenzyl isothiocyanates. Similar differences have also been noted in the spectra of methyl *o*- and *p*-methoxyphenylacetates.[4] In this article we are reporting the behavior on electron impact of a wider variety of methoxybenzyl and some ethoxybenzyl derivatives as well as of some related naphthalenic ethers.

Although diaryl ethers have been examined by this method,[5] the mass spectra of only a few alkyl aryl ethers have been recorded. McLafferty[6] has observed the elimination of ethylene from phenetole and the fragmentation of β-naphthyl methyl ether has been discussed[7] briefly. The principal process by which it decomposes, as shown below, is completely analogous to that observed for the pyrolytic decomposition of aryl methyl ethers.[8]



Besides exhibiting the above-mentioned ions, the mass spectra of simple aromatic methyl ethers usually have abundant M-31 ions. It has been demonstrated,[9] since completion of our own studies, that such ions are not formed by simple loss of a methoxyl radical, but by the following processes.

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[1] For paper XXXIII see J. M. Wilson, M. Ohashi, H. Budzikiewicz, F. Šantavý and C. Djerassi, *Tetrahedron*, **19**, 2225 (1963) (previous paper).

[2] Financial support was provided by the National Institutes of Health of the U.S. Public Health Service (grants Nos. CRTY-5061 and AM-04257).

[3] A. Kjaer, M. Ohashi, J. M. Wilson and C. Djerassi, *Acta Chem. Scand.* in press.

[4] K. Biemann, *Mass Spectrometry* pp. 307–308 McGraw-Hill, New York (1962).

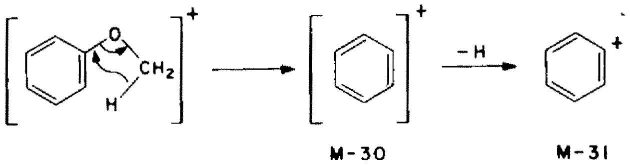
[5] J. M. Wilson, *Experientia* **16**, 403 (1960); R. I. Reed and J. M. Wilson, *Chem. Ind.* 1428 (1962).

[6] F. W. McLafferty, *Analyt. Chem.* **31**, 2072 (1959).

[7] Ref. 4, p. 140.

[8] R. F. Pottie and F. P. Lossing, *J. Amer. Chem. Soc.* **85**, 269 (1963).

[9] C. S. Barnes and J. L. Occolowitz, *Austral. J. Chem.* **16**, 219 (1963).



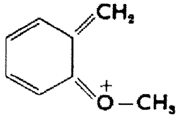
In the spectra of the earlier cited *o*-methoxybenzyl isothiocyanate[3] and methyl *o*-methoxyphenylacetate,[4] the predominant processes were the following:

$$CH_3OC_7H_6R^+ \xrightarrow{-R\cdot} CH_3OC_7H_6^+ \xrightarrow{-CH_2O} C_7H_7^+$$

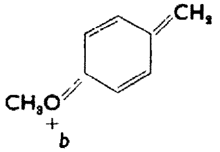
In the mass spectra of several unsubstituted benzyl compounds the $C_7H_7^+$ ion has been found to be the tropylium ion.[10] However recent studies on the mass spectral behavior of substituted benzyl compounds show that the $CH_3OC_7H_6^+$ ions from the methoxybenzyl chlorides probably retain the benzyl type structure.[11]

The same must be true of the methoxybenzyl isothiocyanates,[3] since, if a methoxytropylium ion were formed, it would be the identical one for all three isomers. Thus, contrary to the experimental observation,[3] there should be only minor differences in the spectra, as in the case of the xylenes.[12]

In Fig. 1 are shown the mass spectra of the three isomeric methoxybenzyl bromides. Significant differences can be noted. The *meta* isomer (Fig. 1b) exhibits a very abundant molecular ion; this can be explained most easily in terms of formation of a methoxybenzyl rather than a methoxytropylium ion. The *m*-methoxybenzyl ion (*m*/*e* 121) cannot be stabilized by participation of non-bonding electrons on the ether oxygen so the molecular ion will not decompose so readily. Such stabilization is possible in the case of the *o*- and *p*-isomers with contributions from the quinonoid forms *a* and *b*.

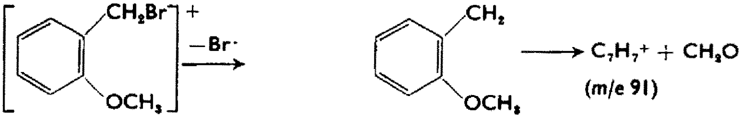


a



b

The outstanding feature of the spectrum (Fig. 1a) of the *ortho* isomer is that the base peak is at *m*/*e* 91 rather than at *m*/*e* 121 as in the other isomers. The presence of a metastable peak at *m*/*e* 68·8 (calcd. *m*/*e* 68·4 for $121^+ \rightarrow 91^+$) confirms that it is formed by the following process.



It is not possible to establish in detail the process by which formaldehyde can be eliminated, but the following mechanisms may be considered:

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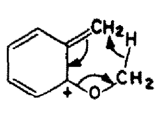
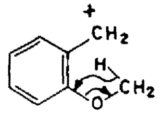
[10] S. Meyerson, P. N. Rylander, E. L. Eliel and J. D. McCollum, *J. Amer. Chem. Soc.* **81**, 2606 (1959) and references cited therein.

[11] J. M. S. Tait, T. W. Shannon and A. G. Harrison, *J. Amer. Chem. Soc.* **84**, 4 (1962).

[12] P. N. Rylander, S. Meyerson and H. M. Grubb, *J. Amer. Chem. Soc.* **79**, 842 (1957).

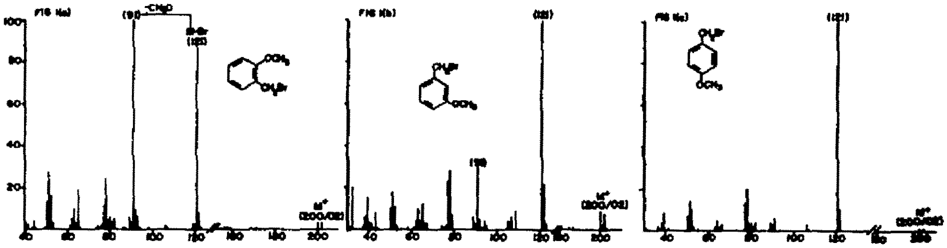


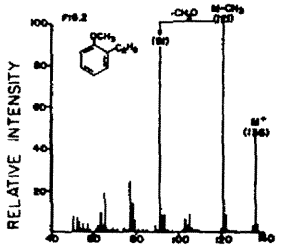
c

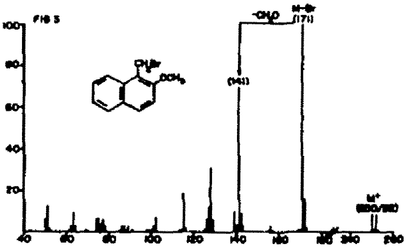


d

If *c* is the mechanism which operates, it is difficult to explain the formation of an abundant *m/e* 91 ion in the spectrum (Fig. 1b) of the *meta* isomer. If *d* is correct, then all three isomers should exhibit these peaks with similar intensities. From the evidence available all that can be stated is that the effectiveness of this process depends upon the proximity of the methoxyl group to the original point of fission.[4] It should be noted that no metastable ion for the transition *m/e* 121 → 91 could be observed in the spectrum of *m*-methoxybenzyl bromide.







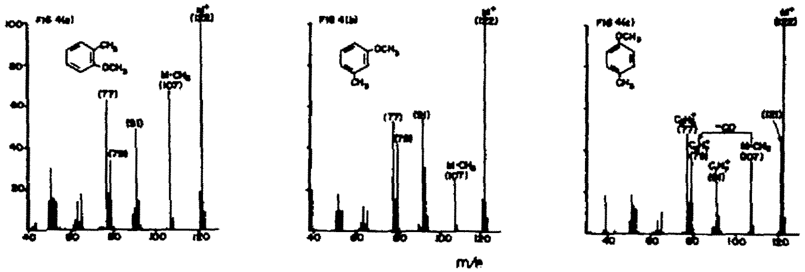


FIG. 1. Mass spectra of *o*-methoxybenzyl bromide (a), *m*-methoxybenzyl bromide (b), *p*-methoxybenzyl bromide (c).

FIG. 2. Mass spectrum of *o*-ethylanisole.

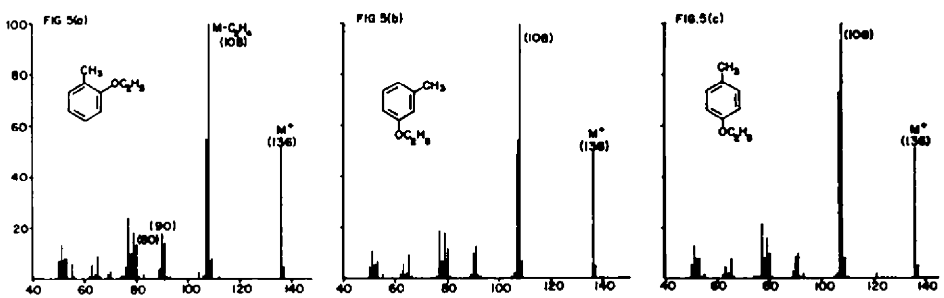
FIG. 3. Mass spectrum of 1-bromomethyl-2-methoxynaphthalene.

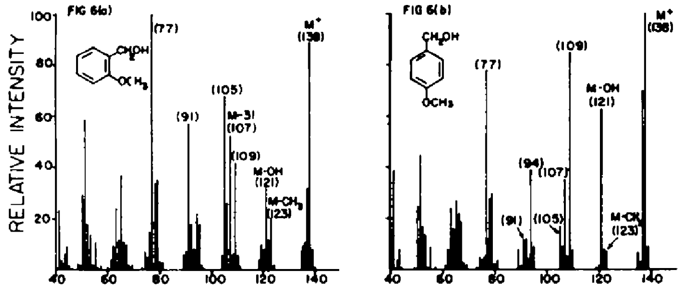
FIG. 4. Mass spectra of *o*-methylanisole (a), *m*-methylanisole (b), *p*-methylanisole (c).

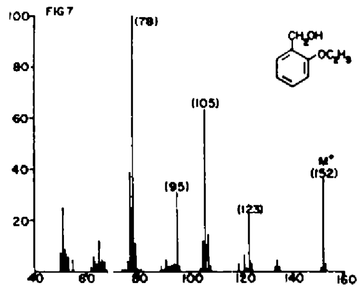
o-Ethylanisole (Fig. 2) shows similar behavior in that the loss of methyl from the ethyl group, as in ethylbenzene,[11] is a favorable cleavage. The resulting ion (*m/e* 121) behaves as do *o*-methoxybenzyl ions from other sources, losing formaldehyde. The ion formed (*m/e* 91) in all cases is probably the tropylium ion, since all unsubstituted

$C_7H_7^+$ ions so far investigated (including that obtained by ionization of benzyl radicals[13]) have proved to be such.

The same behavior is found when other aromatic systems have the necessary structural features. In the spectrum (Fig. 3) of 1-bromomethyl-2-methoxynaphthalene the most intense peak (*m*/*e* 171) is formed by loss of bromide from the molecular ion, but further loss of formaldehyde furnishes an ion of high abundance corresponding in structure to α-naphthylmethyl or benztropylium (*m*/*e* 141).







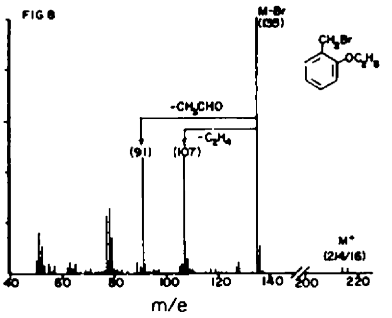


Fig. 5. Mass spectra of *o*-methylphenetole (a), *m*-methylphenetole (b) *p*-methylphenetole (c).

Fig. 6. Mass spectra of *o*-methoxybenzyl alcohol (a), *p*-methoxybenzyl alcohol (b),

Fig. 7. Mass spectrum of *o*-ethoxybenzyl alcohol.

Fig. 8. Mass spectrum of *o*-ethoxybenzyl bromide.

In Fig. 4 are shown the mass spectra of the three isomeric methylanisoles which have already been discussed.[9] The differences here are not so striking as in the case of the benzyl bromides in Fig. 1. In the spectra of all three isomers there is a substantial peak at *m*/*e* 91, which is formed by successive loss of formaldehyde and a

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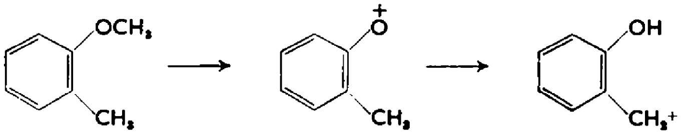
[13] R. F. Pottie and F. P. Lossing, *J. Amer. Chem. Soc.* **83**, 2634 (1961).

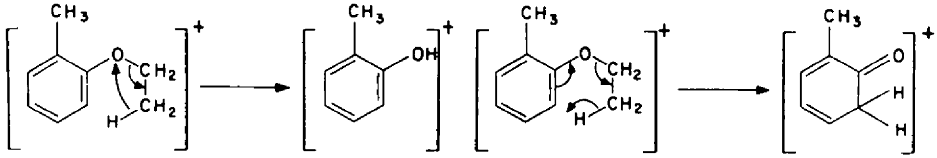
hydrogen atom.[9] A noticeable feature in the spectrum of the *ortho* isomer is the abundance of the M-15 ion which can be stabilized by transfer of a hydrogen atom



from the adjacent methyl group in a manner analogous to the behavior of the pyrrole carboxylic esters.[14]

In Fig. 9 are shown the mass spectra of five isomeric methylmethoxynaphthalenes. All exhibit similar behavior to that observed for the methylanisoles but it is less easy to draw correlations between intensities of peaks and orientation of substituents. It is of interest that there is a substantial difference between the spectra of 1-methyl-2-methoxynaphthalene (Fig. 9a) and 1-methoxy-2-methylnaphthalene (Fig. 9b).

In the spectra (Fig. 5) of the three isomeric methylphenetoles only small differences can be found. In all cases the most intense peak is at *m/e* 108, corresponding to the loss of ethylene[6] from the *o*-ethyl group (see *e* or *f*). The other significant peaks below *m/e* 108 are those which appear also in the mass spectra of the cresols.[15]



e *m/e* 108 *f* *m/e* 108

These peaks have lower intensity relative to *m/e* 108 than the cresol spectra, but relative to each other the intensities are similar to those of the cresol spectra. The intensities are lower, because the cresol ion from methylphenetole will have less excess energy than the ion formed by ionization of cresol. The only ions which show any difference are those at *m/e* 80 formed by loss of carbon monoxide from the cresol ion. In all three cases shown, the *m/e* 80 to *m/e* 79 ratio is greater than in the published[15] cresol spectrum. This suggests that process *f* operates giving the keto form of the cresol ion, as has already been proposed.[6]

In Fig. 6 are reproduced the mass spectra of *o*- and *p*-methoxybenzyl alcohol. The spectra are much more complicated than those of other aromatic compounds, as has already been noted with benzyl alcohol itself.[16,17]

Loss of the hydroxyl group to form the methoxybenzyl ion (*m/e* 121) takes place fairly readily and in the *o*-isomer (Fig. 6a) further expulsion of formaldehyde also occurs with the formation of an ion at *m/e* 91 which is present to only a small extent in the spectrum (Fig. 6b) of the *p*-isomer. The M—CH_3 peak is also more prominent in the spectrum (Fig. 6a) of the *o*-isomer. It is probably stabilized by transfer of one

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[14] H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman and J. M. Wilson, *J. Chem. Soc.* In press.

[15] T. Aczel and H. E. Lumpkin, *Analyt. Chem.* **32**, 1819 (1960).

[16] J. S. Shannon, *Austral. J. Chem.* **15**, 265 (1962).

[17] E. L. Eliel, J. D. McCollum, S. Meyerson and P. N. Rylander, *J. Amer. Chem. Soc.* **83**, 2481 (1961).

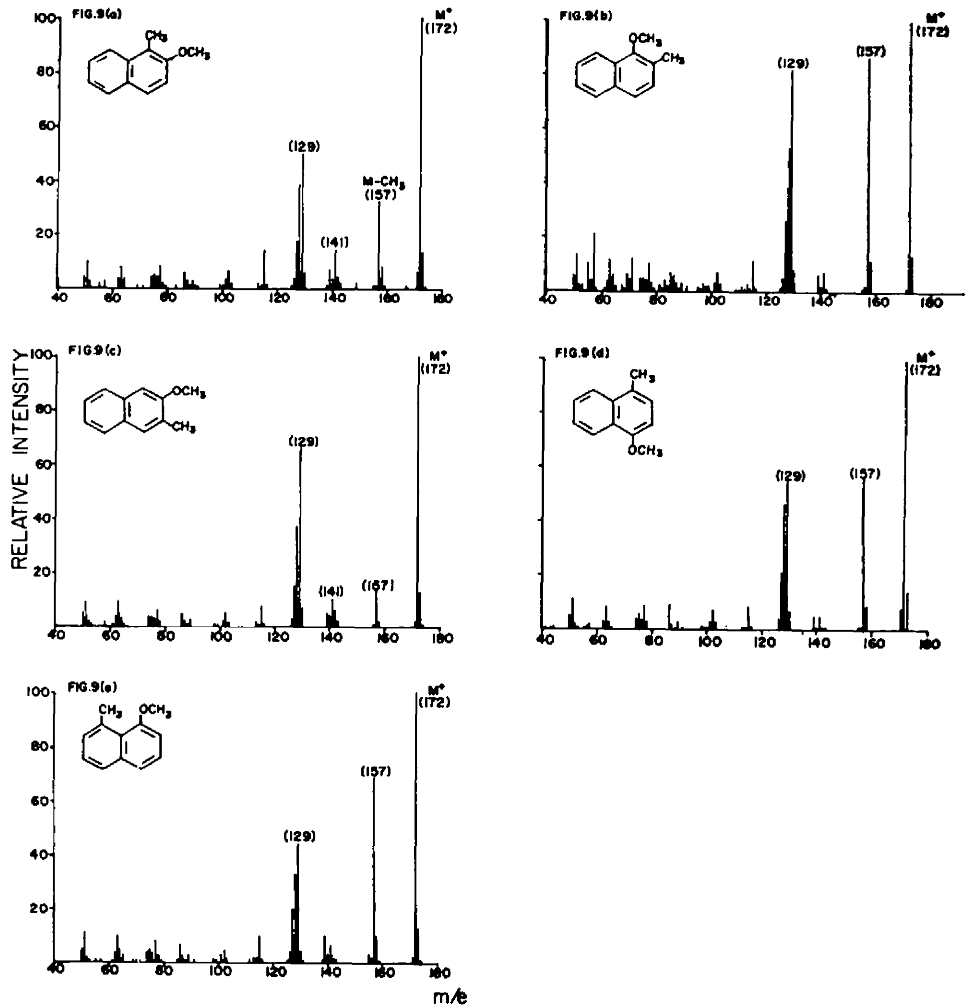
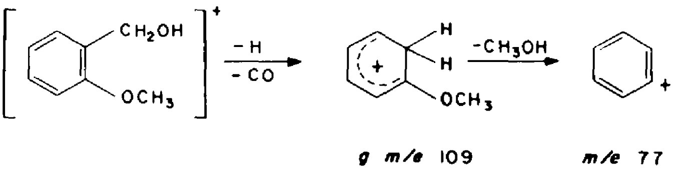


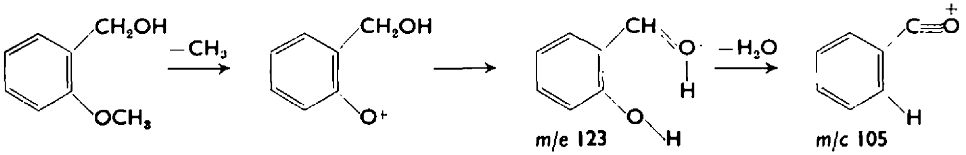
FIG. 9. Mass spectra of 1-methyl-2-methoxynaphthalene (a), 1-methoxy-2-methylnaphthalene (b), 2-methoxy-3-methylnaphthalene (c), 1-methyl-4-methoxynaphthalene (d), 1-methoxy-8-methylnaphthalene (e).

of the α-hydrogen atoms. Both isomers exhibit an abundant ion of *m/e* 109. This is formed by the loss of carbon monoxide and a hydrogen atom from the alcohol group as in the case of benzyl alcohol.[17] If the product is a benzonium ion as has been suggested,[17] it will have structure *g* and can eliminate methanol with formation of the phenyl ion (*m/e* 77).



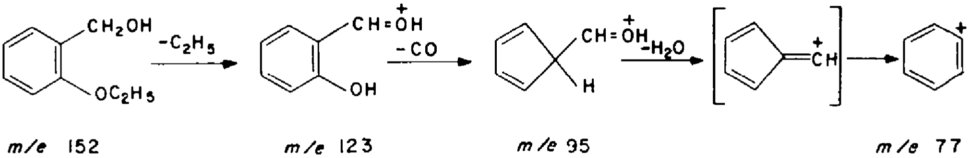
The M-31 (CH_2O + H)[9] peak is present in the spectra of both isomers. It is possible that there are several processes contributing and that either the methoxyl or the hydroxymethyl group are involved. In the spectrum of the α,α-dideuterio analog this peak is mainly split between M-31 and M-32 (the actual values of percentage retention of the label in this ion cannot be calculated because of the presence of adjacent peaks of high intensity). This would suggest that the main process is loss of formaldehyde and a hydrogen, since it has already been demonstrated[17] that the loss of a hydrogen atom from benzyl alcohol occurs randomly from ring- and α-positions.

The peak at *m/e* 105 can be formed in two ways, by loss of a hydrogen molecule from the M-31 ion or by elimination of a molecule of water from the M—CH_3 species. We have been unable to detect any metastable ions associated with its formation. However, there may be an analogy with the formation of the ion of *m/e* 105 in the spectrum[14,17] of benzyl alcohol, which loses a hydrogen molecule and a hydrogen atom almost entirely from the side chain; it is probably the benzoyl ion which is formed. The following scheme seems plausible for the case of the *o*-methoxybenzyl alcohol.

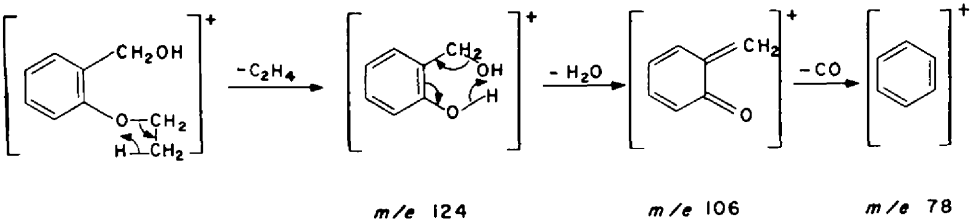


The presence of the same ion to a lesser extent in the spectrum (Fig. 6b) of the *p*-isomer is consistent with the operation of a similar mechanism which will however invoke more extensive hydrogen transfers. That such transfers can take place is demonstrated by the ability of ring and side chain hydrogen atoms to randomize completely in toluene[11] and other aromatic ions.[18]

The spectrum of *o*-ethoxybenzyl alcohol (Fig. 7) is much simpler than that (Fig. 6a) of the analogous methoxy compound. As in the case of the other ethyl ethers, loss of ethylene should be a common process. The resulting ion should be *o*-hydroxybenzyl alcohol, and this molecule is known to have a very small molecular ion peak.[16] The peak at *m/e* 123 is probably formed by loss of the ethyl group, in the same manner as the M-15 peak in the methoxy analog. Consecutive loss of molecules of carbon monoxide and water can take place by the following scheme.



The peaks at *m/e* 106 and 78 are also present in the spectrum of *o*-hydroxybenzyl alcohol, and the following processes have been suggested for their genesis.[16]



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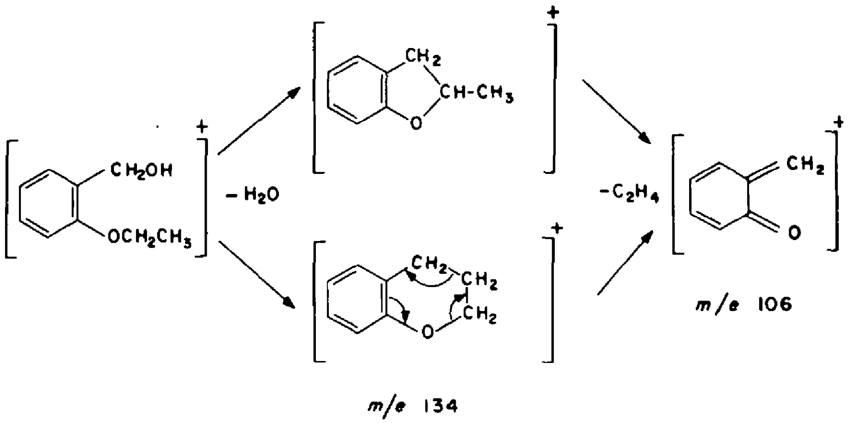
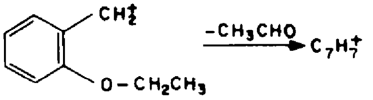
[18] C. G. Macdonald and J. S. Shannon, *Austral. J. Chem.* **15**, 771 (1962).

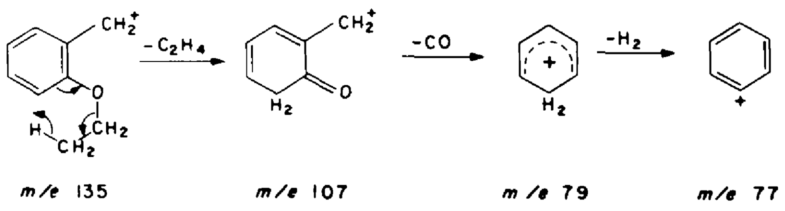
The formation of the *m/e* 106 ion could also take place by initial loss of water followed by elimination of ethylene in a manner similar to the behavior of salicylamide ethyl ether.[19] The fact that this further decomposition does occur suggests that the six-membered intermediate is formed rather than the five-membered ring.



The mass spectrum of *o*-ethoxybenzyl bromide (Fig. 8) can be readily interpreted by analogy to the behavior of the corresponding methoxy compound and the general behavior of aromatic ethyl ethers. The most abundant ion is formed by loss of a bromine atom. This resultant ethoxybenzyl ion can then decompose by two different paths, in both cases by elimination of a neutral molecule. The first occurs by loss of acetaldehyde in a manner entirely analogous to the expulsion of formaldehyde from the methoxybenzyl ion:



Alternatively, elimination of ethylene as in other ethyl ethers can take place followed by loss of carbon monoxide or a formyl radical with formation of benzene-related ions:



EXPERIMENTAL

All spectra were obtained using a C.E.C. 21-103C Mass spectrometer with an ionizing voltage of 70 v. Samples were introduced through a heated inlet system with a reservoir maintained at 200°C. We are indebted to Professors N. P. Buu-Hoi, W. Cocker, R. Huisgen and E. Wenkert for supplying certain samples. The remainder were purified from commercial specimens while d_2-*o*-methoxybenzyl alcohol was obtained in 90% isotopic purity by lithium aluminum deuteride reduction of *o*-methoxybenzoic acid.

[19] G. Spiteller, *Monatsh.* **92**, 1147 (1961).