

A Study of the Fragmentation Processes of Some Benzoxazepines Upon Electron Impact*

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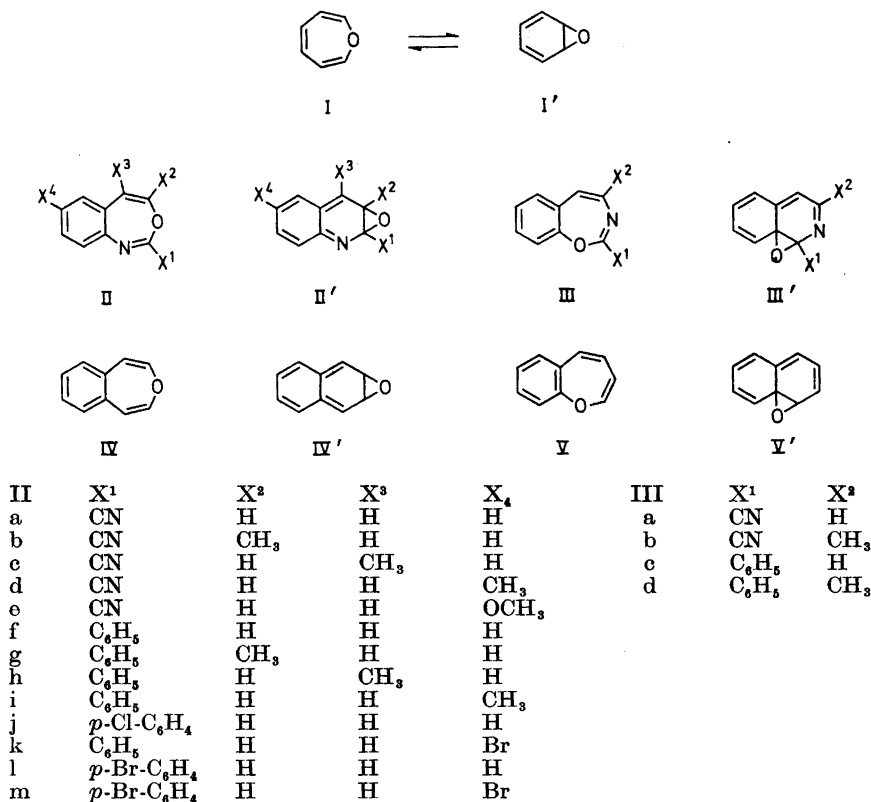
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The mass spectra of a series of benz[d][1,3]oxazepines (II) and benz[f][1,3]oxazepines (III)** have been recorded and mechanistic rationalizations for the origin of the principal peaks are presented. The loss of oxygen ($M-16$) suggests that these compounds may exist in the gas phase in tautomeric equilibrium with their valence isomers (II'), whereas no valence tautomerizations needed to be postulated to rationalize the mass spectra** of four benz[f][1,3]oxazepines (III). The expulsion of carbon monoxide or of ketene in the 4-methyl analogs is a particularly characteristic decomposition mode of such compounds.

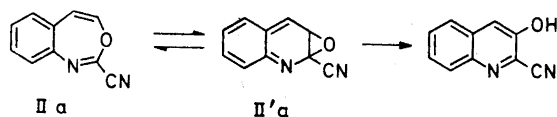
A number of oxazepines (I) have recently been shown² to exist in equilibrium with their valence tautomer benzene oxides (I'). Benz[d][1,3]oxazepines (II) and benz[f][1,3]oxazepines (III) can formally exist as their valence tautomers II' and III', respectively. The benzoxazepines (IV and V) exist preferentially in this form² as no evidence in favor of the naphthalene oxide tautomers (IV' and V') has as yet been reported. Hence it was of some interest to subject a series of benzoxazepines (II-III) to mass spectral scrutiny to clarify the electron impact induced behavior of these new classes of compounds and to observe whether these spectra would show evidence for the existence of the oxide tautomers II' and III' in the gas phase.

* Part CLXII of a series of papers on "Mass Spectrometry in Structural and Stereochemical Problems"; for paper CLXI see L. Tökeš, G. Jones, and C. Djerassi, *J. Am. Chem. Soc.* **90** (1968) 5465.

** A preliminary account of the fragmentation of benz[f][1,3]oxazepines (III) has appeared previously.¹



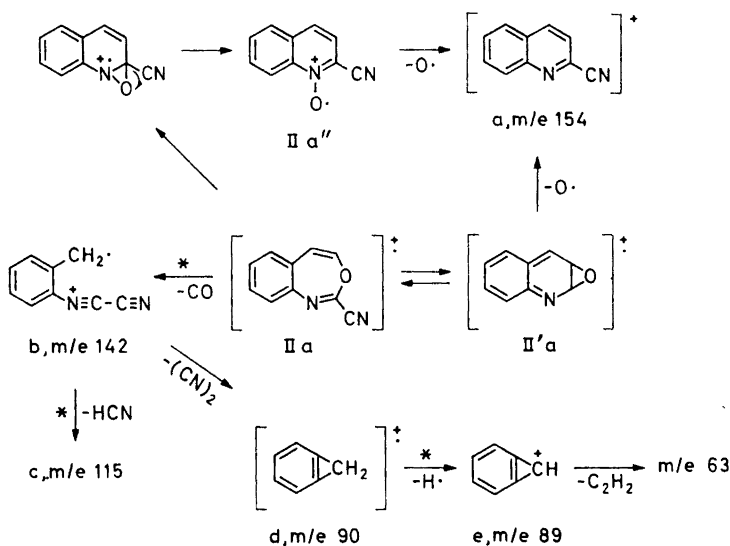
The only chemical evidence for the valence tautomerism in benzoxazepines is the facile rearrangement of some benz[d][1,3]oxazepines (II) to 3-hydroxyquinolines (IV)³ which most probably proceeds through the valence tautomer II'.



DISCUSSION OF MASS SPECTRA

The mass spectrum (Fig. 1) of 2-cyanobenz[d][1,3]oxazepine (IIa) exhibits a conspicuous M-16 ion* and the presence of this fragment (*a*) is perhaps more easily rationalized from the molecular ion of the tautomeric species II'a than from IIa. Loss of oxygen from epoxides by electron impact is not

* In a recent communication⁴ the mass spectrum of IIa was reported. However, under the instrumental conditions employed in that investigation (all glass heated inlet system, temperature not reported) minor peak height differences relative to our spectrum (direct inlet system) were evident and no peak at M-16 was reported in the mass spectrum of IIa.

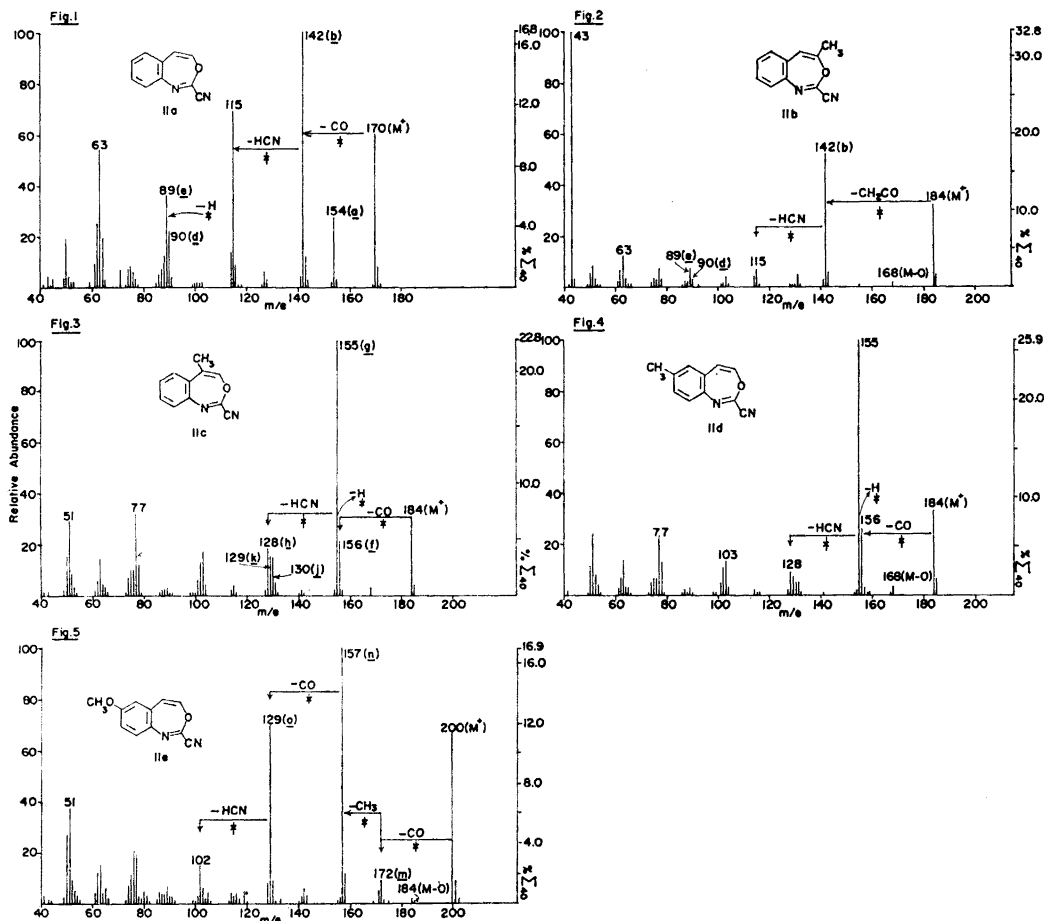


an established mode of fragmentation for simple members of this class⁵ but the formation of the aromatic system of the molecular ion of 2-cyanoquinoline should be an energetically favored process. A second, and more complex mode of formation, for the species *a* in Fig. 1 could involve rearrangement of the molecular ion of IIa to ionized 2-cyanoquinoline *N*-oxide (II'a) (which is the reverse of the photochemical formation of IIa) as *N*-oxides,⁶ and II'a in particular,⁴ are known to readily eliminate oxygen from their molecular ions. It is pertinent to note that at low voltage (12 eV) the ion *a* has been completely removed.

A second mode of fragmentation of the molecular ion of IIa is the expulsion⁴ of carbon monoxide⁷ which can more easily be rationalized mechanistically (formation of *b*)* by invoking participation of the benz[d][1,3]oxazepine molecular ion (IIa). Further expulsion⁷ of HCN from *b* produces the ion of mass 115 while the ion of mass 90 may be *d* due to the loss of (CN)₂ from *b*. The abundant ion at mass 89 (*e*) is formed, at least in part, by the loss of a hydrogen atom⁷ from *d*. At low voltage (12 eV) the only ions observed in the mass spectrum of IIa are *m/e* 142 (33 % relative abundance) *m/e* 115 (1 %) and the molecular ion (100 %).

The mass spectrum (Fig. 2) of 2-cyano-4-methylbenz[d][1,3]oxazepine (IIb) contains an M — oxygen fragment which is less abundant than the corresponding ion in Fig. 1 and its formation may be interpreted by processes analogous to those used for the origin of ion *a*. The principal fragmentation mode of IIb is initiated by the expulsion of ketene⁷ (formation of *b*) and this process is analogous to the ubiquitous loss of carbon monoxide in those benzoxazepines which lack a 4-methyl substituent. Further decomposition of *b* appears to be similar to that encountered in the mass spectrum (Fig. 1) of the lower homolog

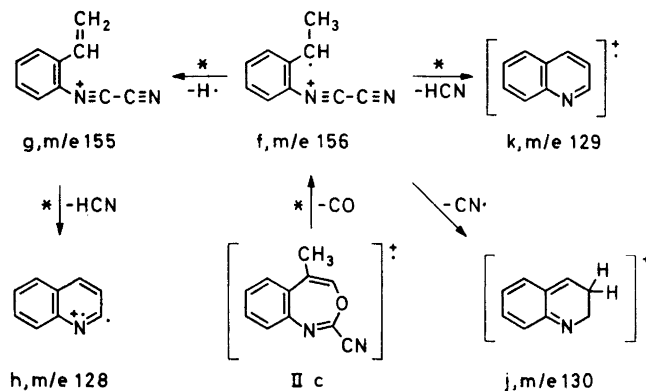
* Species such as *b* may exist in ring expanded forms but for the sake of brevity throughout this paper such ions are formulated in terms of benzylic structures.



Figs. 1—5. Mass spectra of 1 2-cyanobenz[d][1,3]oxazepine (IIa), 2 2-cyano-4-methylbenz[d][1,3]oxazepine (IIb), 3 2-cyano-5-methylbenz[d][1,3]oxazepine (IIc), 4 2-cyano-7-methylbenz[d][1,3]oxazepine (IIId), 5 2-cyano-7-methoxybenz[d][1,3]oxazepine (IIe).

IIa. It is interesting that the base peak in Fig. 2 is located at m/e 43 (CH_3CO^+) but the formation of this fragment must involve a relatively high energy process since it was completely repressed at low (12 eV) ionizing voltage.

Carbon monoxide⁷ and to a lesser extent oxygen is expelled from the molecular ion (see Fig. 3) of 2-cyano-5-methylbenz[d][1,3]oxazepine (IIc). The elimination of carbon monoxide results in the production of a species that formally can be written as *f*, (m/e 156) and this ion then serves as progenitor by the successive loss of a hydrogen radical and then HCN for the ions *g* (m/e 155) and *h* (m/e 128). Although m/e 128 is formulated as a quinoline species it is quite possible that it corresponds to an open chain form. Alterna-

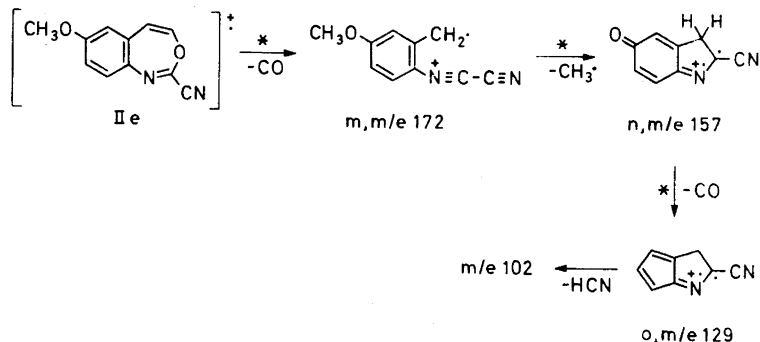


tively *f* may expel a cyanide radical (no metastable ion was observed for this process) to yield *j* (*m/e* 130) or HCN⁷ to afford *k* (*m/e* 129).

Two ions (*m/e* 156 and 155) dominate the mass spectrum (Fig. 4) of 2-cyano-7-methylbenz[d][1,3]oxazepine (II d) and these fragments arise by consecutive loss of carbon monoxide and a hydrogen radical from the molecular ion and mechanistically their origin can be considered similar to *f* and *g*. In fact the mass spectrum of II d is strikingly similar to that of its positional isomer II c such that analogous decomposition processes must occur in both compounds.

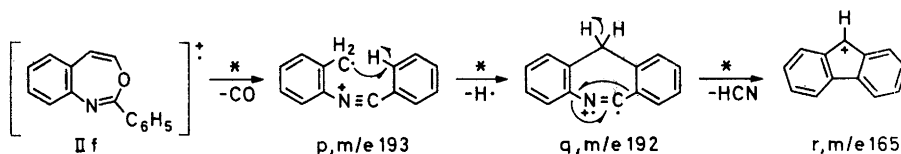
The electron impact induced fragmentation (Fig. 5) of 2-cyano-7-methoxybenz[d][1,3]oxazepine (II e) is dominated by the peaks at *m/e* 157 and 129. The principal modes of fragmentation of this compound can be rationalized by II e \rightarrow *m* (*m/e* 172) \rightarrow *n* (*m/e* 157) \rightarrow *o* (*m/e* 129) \rightarrow *m/e* 102 in which the influence of the 7-methoxy substituent superimposed upon the benz[d][1,3]oxazepine fragmentation is clearly discernible.

The mass spectra of all the 2-phenyl substituted benz[d][1,3]oxazepines examined (II f—m) except II h contain peaks due to the loss of oxygen from the molecular ion and in these instances this ion is much reduced in abundance as compared to their 2-cyano analogs. This possibly represents less valence



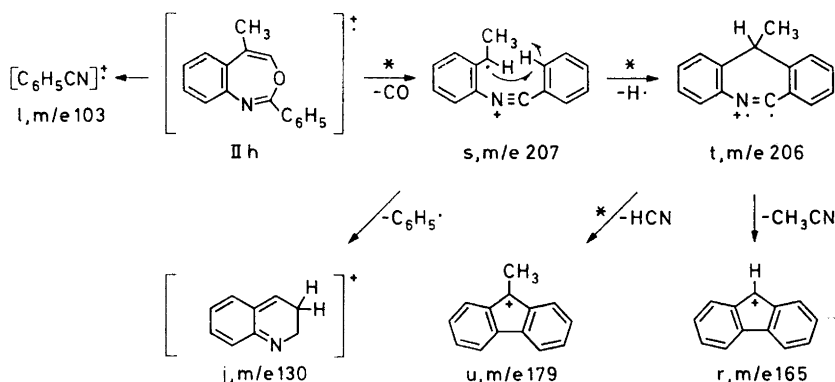
tautomerism (II→II') in the 2-phenyl substituted analogs and is consistent with the observation that these compounds do not rearrange thermally to 3-hydroxyquinolines.³

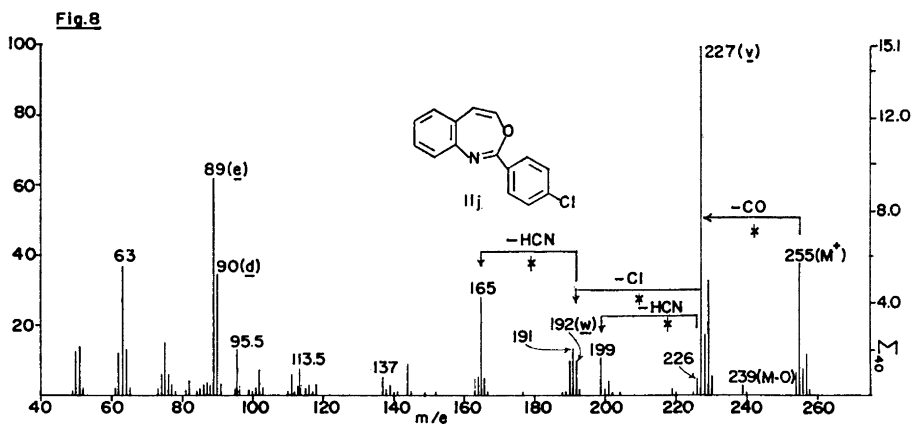
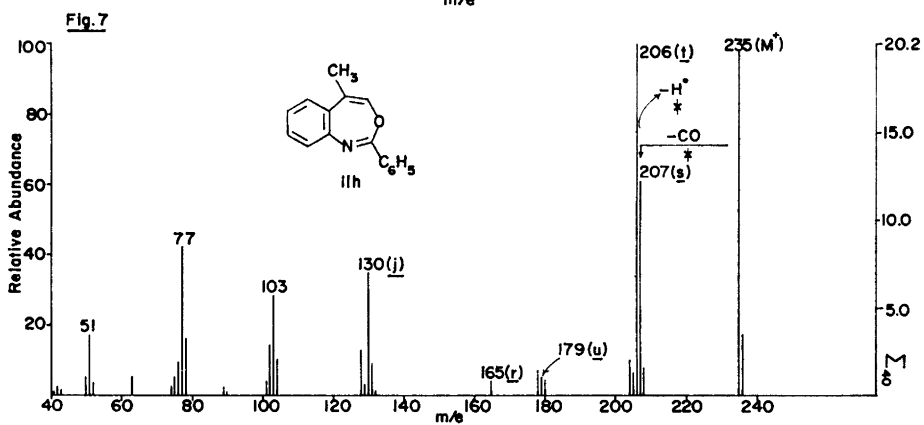
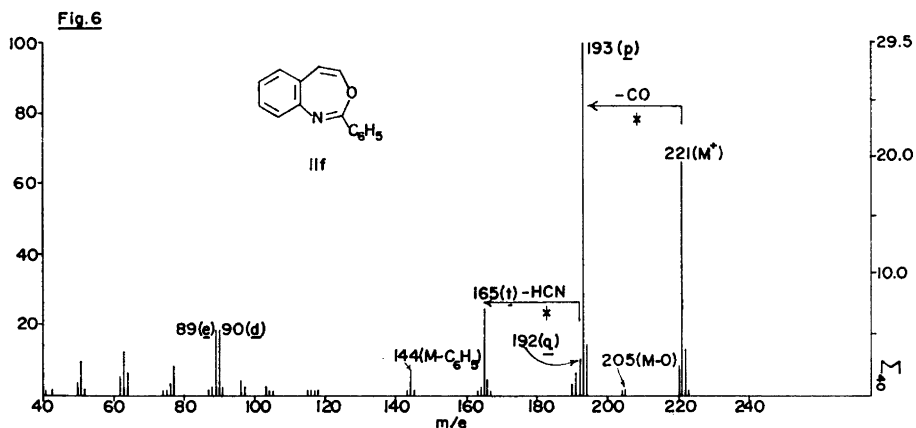
2-Phenylbenz[d][1,3]oxazepine (II_f) upon electron impact (Fig. 6) ejects carbon monoxide⁷ producing a species which can be represented as *p* (*m/e* 193). In marked contrast to the situation prevailing in the mass spectra of the 2-cyano substituted compounds *p* fragments by the expulsion of a hydrogen atom,⁷ which we suggest originates from the *o* position of the 2-phenyl substituent, resulting in the formation of the ion *q* (*m/e* 192) which then eliminated hydrogen cyanide⁷ to yield the stable fluorene ion *r* (*m/e* 165).



As anticipated from a study of the mass spectrum (Fig. 2) of 2-cyano-4-methylbenz[d][1,3]oxazepine (II_b) the spectrum of the corresponding 2-phenyl compound (II_g) displays a prominent loss of ketene rather than of carbon monoxide (production of *p* (*m/e* 193)). Subsequent decomposition of *p* is accomplished by successive elimination of a hydrogen radical⁷ and then hydrogen cyanide⁷ and is thus completely analogous to the situation found for 2-phenylbenz[d][1,3]oxazepine (II_f).

The electron impact induced fragmentation (Fig. 7) of 2-phenyl-5-methylbenz[d][1,3]oxazepine (II_h) can be rationalized by processes similar to those outlined above for II_f. One additional point of interest, however, is that the ion *t* (*m/e* 206) can expel both hydrogen cyanide⁷ and acetonitrile to yield the ions *u* (*m/e* 179) and *r* (*m/e* 165), respectively. Expulsion of a phenyl radical from the species *s* (*m/e* 207) would yield *j* (*m/e* 130) which in turn by ejection of hydrogen cyanide could generate the ion of mass 103 in Fig. 7. However, a more likely genesis of the ion of mass 103 is the direct elimination of benzonitrile as the charged species (*l*) from the molecular ion of II_h and this is



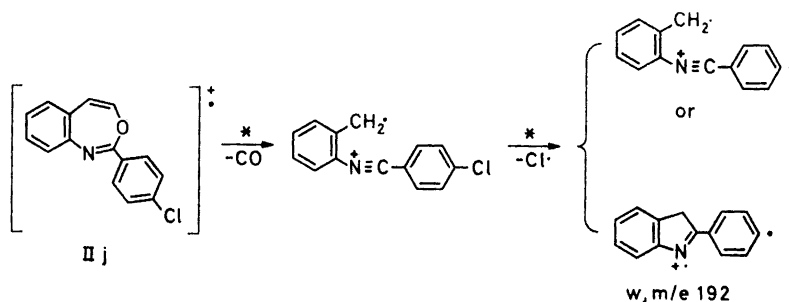


Figs. 6–8. Mass spectra of 6 2-phenylbenz[d][1,3]oxazepine (IIf), 7 2-phenyl-5-methylbenz[d][1,3]oxazepine (IIh), 8 2-(4-chlorophenyl)benz[d][1,3]oxazepine (IIj).

supported by the observation that in the *p*-chloro compound (IIj) an ion is found at m/e 137 which corresponds to ionized *p*-chlorobenzonitrile.

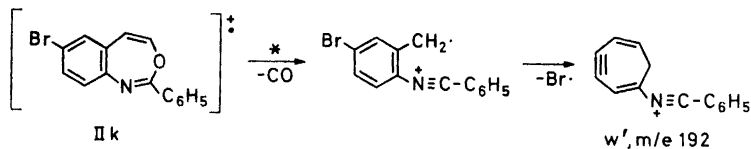
The mass spectrum (not reproduced) of 2-phenyl-7-methylbenz[d][1,3]-oxazepine (IIi) can be rationalized by similar procedures as used with IIh and no detailed discussion of its spectrum is warranted.

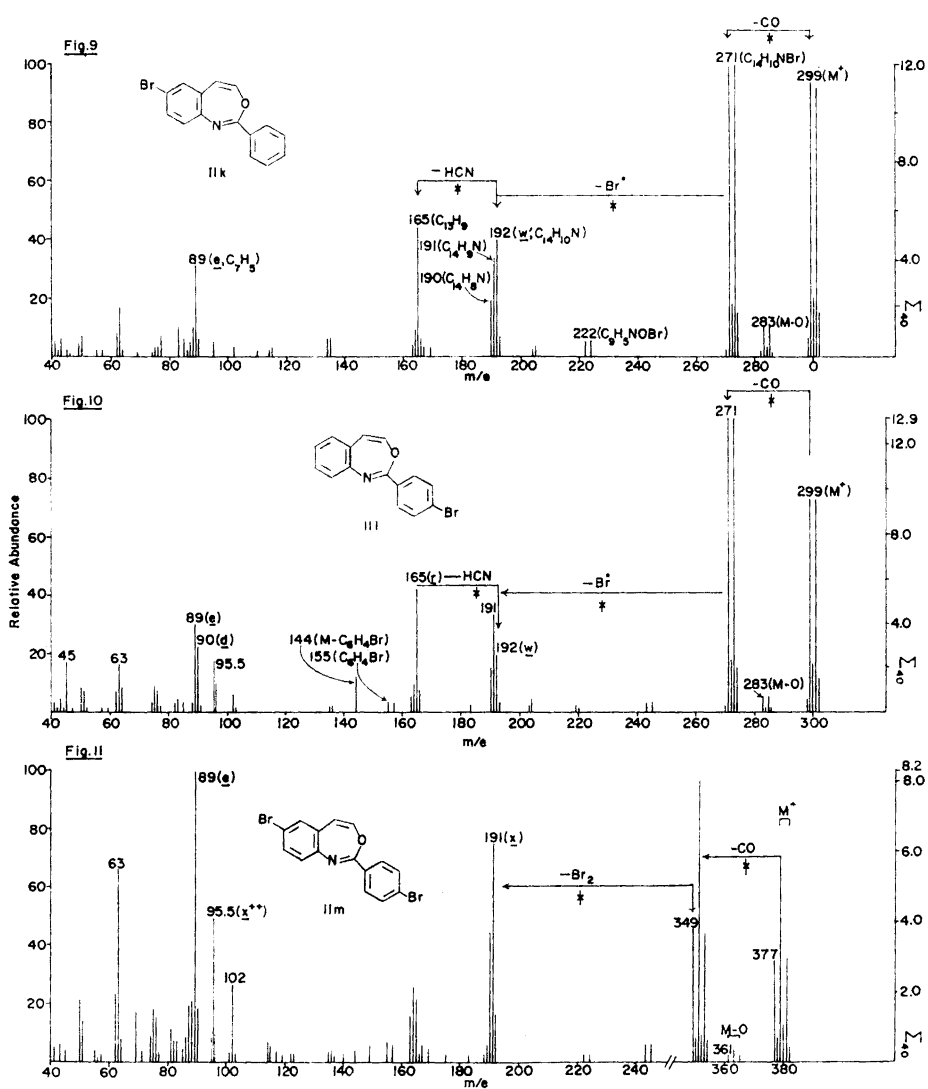
2-(4-Chlorophenyl)benz[d][1,3]oxazepine (IIj) upon electron impact (Fig. 8) exhibits the ubiquitous loss of carbon monoxide⁷ from the molecular ion and we formulate the product as *v* (m/e 227). This ion then expels a chlorine radical⁷ with the formation of *w* (m/e 192) and the subsequent decompositions of *w* parallel those outlined for the ion *q*. Loss of a hydrogen radical followed by hydrogen cyanide from *v* rationalizes the presence of a peak at m/e 199 in Fig. 8 and this ion can be represented as a chloro substituted fluorene molecular ion analogous to the species *r*.



It is surprising that 2-phenyl-7-bromobenz[d][1,3]oxazepine (IIk) and 2-(4-bromophenyl)benz[d][1,3]oxazepine (III) have mass spectra (Figs. 9 and 10) whose fragmentation patterns are very similar. Thus both readily lose carbon monoxide⁷ from their respective molecular ions to generate the base peak in both spectra. Subsequent loss of a bromine radical followed by hydrogen cyanide⁷ generates the peaks at m/e 192 and 165, respectively, in Figs. 9 and 10. In the case of III the ion of mass 192 can be represented by *w* whereas this structure is best amended to the ring expanded form *w'* for IIk. One important difference between Figs. 9 and 10 is the occurrence of an $M-C_6H_5$ ion (m/e 222) in the spectrum of IIk while the spectrum (Fig. 10) of III contains the anticipated $M-C_6H_4Br$ ion (m/e 144).

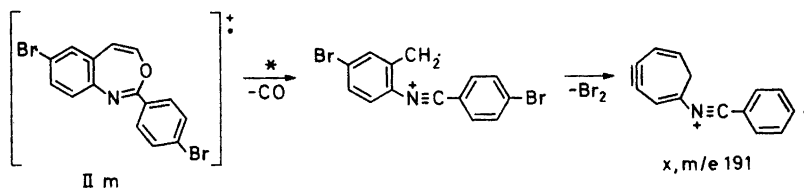
An unusual feature present in the mass spectrum (Fig. 11) of 2-(4-bromophenyl)-7-bromobenz[d][1,3]oxazepine (IIIm) is the possible loss of both bromine atoms in one step⁷ following initial expulsion of carbon monoxide⁷





Figs. 9–11. Mass spectra of 9 2-phenyl-7-bromobenz[d][1,3]oxazepine (IIk), 10 2-(4-bromophenyl)benz[d][1,3]oxazepine (III), 11 2-(4-bromophenyl)-7-bromobenz[d][1,3]oxazepine (IIIm).

from the molecular ion.* This series of events can be formulated in terms of $\text{II}m \rightarrow x$ (m/e 191). It is noteworthy that the majority of the mass spectra of 2-phenyl substituted benz[d][1,3]oxazepines contain prominent peaks at m/e 90 and 89 which could be due to species such as d and e , respectively.



The mass spectra of the four benz[f][1,3]oxazepines (IIIa–d) have been discussed in our previous publication¹ and these compounds fragment in a straightforward manner with no loss of carbon monoxide from their molecular ions and thus this elimination of carbon monoxide upon electron impact can be used to differentiate between benz[f]- and benz[d][1,3]oxazepines. We only wish to focus attention here on the fact that these compounds do not lose oxygen from their molecular ions indicating that no valence tautomerism of these compounds to their benzene oxide analogs ($\text{III} \rightarrow \text{III}'$) needs to be postulated.

EXPERIMENTAL

Low and high resolution mass spectra were obtained by Mr. R. G. Ross of Stanford University with an A. E. I. MS-9 instrument using direct sample insertion into the ion source which was maintained at 180°. Low voltage measurements refer to nominal values only and mass measurements were accurate to within 3 ppm (Fig. 9).

The benz[d][1,3]oxazepines were prepared by the method previously described.⁹ 2-(4-Chlorophenyl)benz[d][1,3]oxazepine: (Found: C 70.55; H 3.94; N 5.44; Cl 13.81. Calc. for $\text{C}_{15}\text{H}_{10}\text{ClNO}$: C 70.45; H 3.94; N 5.47; Cl 13.87). M.p. 85–87°. Yield 90 %.

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* Many instances have been recorded in the literature where the observance of a metastable ion for a particular process has evidently not been associated with a single-step decomposition but rather with a two-step fragmentation process; see Ref. 5, p. 29.

6. Buchardt, O., Duffield, A. M. and Shapiro, R. H. *Tetrahedron* **24** (1968) 3139.
7. The occurrence in this process is supported by the presence of the appropriate metastable peak in the mass spectrum and this is indicated with an asterisk in the degradation schemes.
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