THE STRUCTURAL SIGNIFICANCE OF DOUBLY CHARGED IONS FOUND IN THE MASS SPECTRA OF SOME ORGANIC MOLECULES

by

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B.A., Wesleyan University (1961)

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ABSTRACT

The formation and identification of doubly charged organic ions formed in a mass spectrometer using high resolution mass spectrometric techniques in combination with low resolution mass spectrometric data is discussed.

The fragmentation pattern of doubly charged ions is compared to that of singly charged. The doubly charged ion spectra of various N,N'-alkyl substituted phenylenediamines are compared to their singly charged counterparts. The structural and electronic requirements for the resonance stabilization of doubly charged organic ions were established and it was shown that they can be used to differentiate between certain structural isomers which give practically identical singly charged ions.

A comparison is made of the relative ease of stabilization of doubly charged ions of bicyclic nitrogen and oxygen analogs (quinoxaline, 1,2,3,4-tetrahydroquinoxaline, methylene catechol and catechol polymethylene diethers). Certain unexpected ions in the spectra of catechol polymethylene diether homologs were observed and their possible mechanisms of formation were investigated with the aid of deuterium labeled derivatives. The methods used for the preparation of those compounds not previously reported are discussed.

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Introduction

The majority of ions produced in a mass spectrometer upon electron impact are singly charged. At sufficiently high potentials, however, it is possible to obtain multiply charged ions by removal of two or more electrons from the species undergoing electron bombardment. Multiply charged ions in mass spectra were first observed by W. Bleakney,[1] who determined the minimum ionization potentials of Hg^{+}, Hg^{2+}, Hg^{3+}, Hg^{4+}, and Hg^{5+}. He studied the variation of the fraction of the total number of ions carrying one, two, three, four and five charges as a function of the ionizing voltage, noting e.g. that beyond 150 volts the fraction of the singly charged Hg^{+} ion drops to 78% while that of Hg^{2+} increases to 16%.

At the ionization potentials ordinarily used in mass spectrometers (70e.v.) the intensities of the doubly charged ions formed from monatomic gases seem to be about 20 to 40 per cent those of the corresponding singly charged ions. Ions with a higher charge are formed in only negligible amount.[2] Helium forms multiply charged ions in the smallest abundance as compared to the other monatomic gases, He^{2+} constituting only 1% of all the ions formed at an electron energy of 330 e.v.[2]

The existence of multiply charged ions in the mass spectra of polyatomic molecules was first observed by

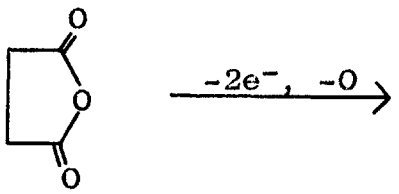
R. Conrad,[3] who reported the formation of doubly charged ions such as CH_3^{++}, $C_2H_2^{++}$, $C_2H_4^{++}$, etc. from hydrocarbons. It was thus proved that doubly charged ions of polyatomic fragments could indeed exist, contrary to views held until then.[4] A fairly detailed study on the doubly charged ions of hydrocarbons has been done by F. Mohler and coworkers.[5] They note that the amount of double ionization which occurs is quite small, the most intense doubly charged peaks usually being less than 1% of the most intense peak in the spectrum. The amount of double ionization in hydrocarbons was found to decrease with the increasing molecular weight of a given type of compound. Of significant importance, however, was their observation that the presence of olefinic bonds enhanced the formation of doubly charged ions, their relative abundance becoming quite significant in aromatic systems.[2]

One of the reasons for the low abundance of doubly charged ions in hydrocarbons has also been attributed to the possibility that doubly charged fragments may decompose to two singly charged ions, the total kinetic energy of which is nearly equal to the Coulomb energy of two ions at a distance equal to the greatest distance between valence electrons in the parent doubly charged ion.[5] Their suggestion was based on the observation of so called "satellite" peaks at the high mass side of the peaks at m/e 14, m/e 15 and m/e 16 corresponding to ions of slightly higher energy. The appearance potential of these "satellite" peaks, which incidentally are of sharply defined energy, was over 30 e.v.

while the main peak was observed around 20 e.v. "Satellite" peaks have also been reported recently[6] for the fragmentation of the doubly charged benzene ion. Metastable peaks were observed corresponding to the dissociation of the doubly charged molecular ion into a CH_3^+ ion and a further ion:

$$C_6H_6^{2+} \longrightarrow CH_3^+ + C_5H_3^+$$

The higher abundance of doubly charged ions in unsaturated or aromatic hydrocarbons, as reported by Mohler et al.,[5] is certainly not surprising since the ionization process here involves the removal of π-electrons which are at a higher energy level than the σ-bonded electrons of hydrocarbons. The presence of heteroatoms such as nitrogen or oxygen in an aromatic system, as expected, greatly enhances the formation of doubly charged ions, since the non-bonding electrons of the heteroatoms are at energy levels comparable to those of the π-electrons. Nevertheless, doubly charged ions have been generally believed to be of lower abundance than the corresponding singly charged. Exceptions noted are the $(M-16)^{++}$ peak in maleic anhydride (I) where the doubly charged fragment (II) is seven times more intense than the corresponding singly charged,[4] this preference being due to stabilization of the two positive charges one on each oxygen atom:



I

$\xrightarrow{-2e^-,\ -O}$

$|\overset{+}{O} \equiv C - CH = CH - C \equiv \overset{+}{O}|$

II

The $(M-2)^{++}$ peak in 2-methyl indole is another example in which the doubly charged fragment is thirteen times more abundant than the corresponding $(M-2)^{+}$.[7]

Metastable peaks which have been attributed to the fragmentation of a doubly charged ion into a second doubly charged ion of lower mass by elimination of a neutral species have been reported. For example, 1,4-di-t-butyl-benzene eliminates C_2H_4, and this process is substantiated by the presence of a metastable peak at m/e 54.5 corresponding to the transition:[8]

$$\underset{160}{C_{12}H_{16}^{++}} \longrightarrow \underset{132}{C_{10}H_{12}^{++}} + \underset{28}{C_2H_4}$$

The mass spectrum of 2-hydroxyanthraquinone has three very intense peaks at m/e 196, 168 and 139 which correspond to successive losses of two CO molecules followed by the loss of a CHO radical. Doubly charged ions are observed corresponding to $(M-CO)^{++}$, $(M-2CO)^{++}$ and $(M-3CO)^{++}$ and the metastable peak at 58.2 corresponds to the transition

$$168^{++} \longrightarrow 140^{++} + 28$$
$$\text{i.e. } (M-2CO)^{++} \longrightarrow (M-3CO)^{++} + CO$$

This already indicates that fragmentation of doubly charged ions may be different from that operating in the case of singly charged ions.[9]

Formation and Identification of Doubly Charged Ions

A doubly charged ion can be formed in one of two ways:[10]

$$AB + e^- \longrightarrow AB^{++} + 3e^-$$

followed by: $AB^{++} \longrightarrow A^{++} + B\cdot$

while the decomposition of a singly charged ion into a doubly charged fragment plus a negative ion cannot necessarily be ruled out:

$$AB^{+} \longrightarrow A^{++} + B^-$$

As the ions formed in the mass spectrometer are collected and recorder according to their mass-to-charge ratio, m/e, particles bearing two positive charges will be recorded at the mass number which corresponds to half their mass. Doubly charged species in a mass spectrum, therefore, can be distinguished and identified by the following three methods:

(1) If a peak is observed at half a mass unit it is due to a doubly charged species of odd mass.

(2) If the integral mass observed cannot be composed of the available elements; e.g. a peak at 47 m.u. in hydrocarbons cannot be due to a singly charged species.

(3) If the doubly charged species is of even mass, it will be observed at an integral mass number, but, if sufficiently abundant, its isotopic peak can be found half a mass unit higher.

The observation of Beynon[9] that doubly and singly charged 2-hydroxyanthraquinone follow a different path of fragmentation, and Meyerson's finding that the identity of the methyl hydrogens is retained in the doubly charged

toluene ion while it is lost in the singly charged toluene ion,[11] make it quite evident that one is dealing with a different kind of excited species in each case. Meyerson calculated the exact abundance of the doubly charged ions based on the height of the isotopic peak half a mass unit higher. This is not necessarily correct, however, since the peak at 1/2 mass can be due to the doubly charged ^{13}C-species as well as a doubly charged ion containing one hydrogen atom more than the ion half a mass lower.

The present study was undertaken in order to explore the structural significance of abundant multiply charged ions as it was expected that these should be just as interpretable as singly charged ions which in the past have been used almost exclusively. Particular emphasis was placed on compounds which could form ions that are able to support two positive charges very well, and thus would lead to pronounced peaks due to these species. If the fragmentation mode leading to the doubly charged species is, in fact, different from the formation of singly charged ions, different -- and complementary -- information should be obtainable from the "doubly charged spectrum" (beyond mere distinction between saturated and highly unsaturated or aromatic systems).

In order to more clearly distinguish the singly charged ions from the multiply charged ones, a more sophisticated approach had to be devised for this differentiation. Accurate mass measurements were used for this purpose based on the mass difference (2.25 m.m.u.) of $(^{12}CH-^{13}C)/2$.

Consider, e.g., the line drawings of the low resolution spectra of ortho, meta and para-N,N'-diethyl phenylenediamines which are given in Figs. 1 (a)-(c). The large number of peaks appearing at half mass unit indicates beyond any doubt the large abundance of doubly charged ions. Consider e.g. the peak at m/e 67.5 in Fig. 1c. This is preceded by a very intense peak at m/e 67 and one would be inclined to say that m/e 67.5 is the isotopic (i.e. ^{13}C containing) peak of m/e 67. This was indeed the assumption made in similar cases by S. Meyerson[8] and by M. Wacks.[12] This is not necessarily true though, as m/e 67.5 could be a mixture of the ^{13}C containing species ($^{13}CC_7H_{10}N_2^{++}$) and the ion of composition $C_8H_{11}N_2^{++}$.* It could, in fact, exclusively be the $C_8H_{11}N_2^{++}$ ion, which would mean that m/e 67 is simply the ion $C_5H_4N^+$. In this specific case, of course, the very low intensity of the m/e 68 peak excludes the presence of any significant abundance of the latter ion and it almost entirely corresponds to the $^{13}C_2C_6H_{10}N_2^{++}$ ion. The differentiation therefore of the singly charged from the doubly charged ions and the calculation of their exact intensities becomes impossible with a conventional focusing mass spectrometer. The mass difference between ^{12}CH and ^{13}C is 4.5 millimass units, which for doubly charged species becomes 2.25 millimass units. At m/e 67.5 a resolving power of 1 part in 30,000 is required. As this resolution was just within the reach of our double focusing mass spectrometer,

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*The symbols of elements refer always to the most abundant stable isotope unless indicated by superscripts.

Figure 1

Mass spectra of

(a) N,N'-diethyl-o-phenylenediamine

(b) N,N'-diethyl-m-phenylenediamine

(c) N,N'-diethyl-p-phenylenediamine

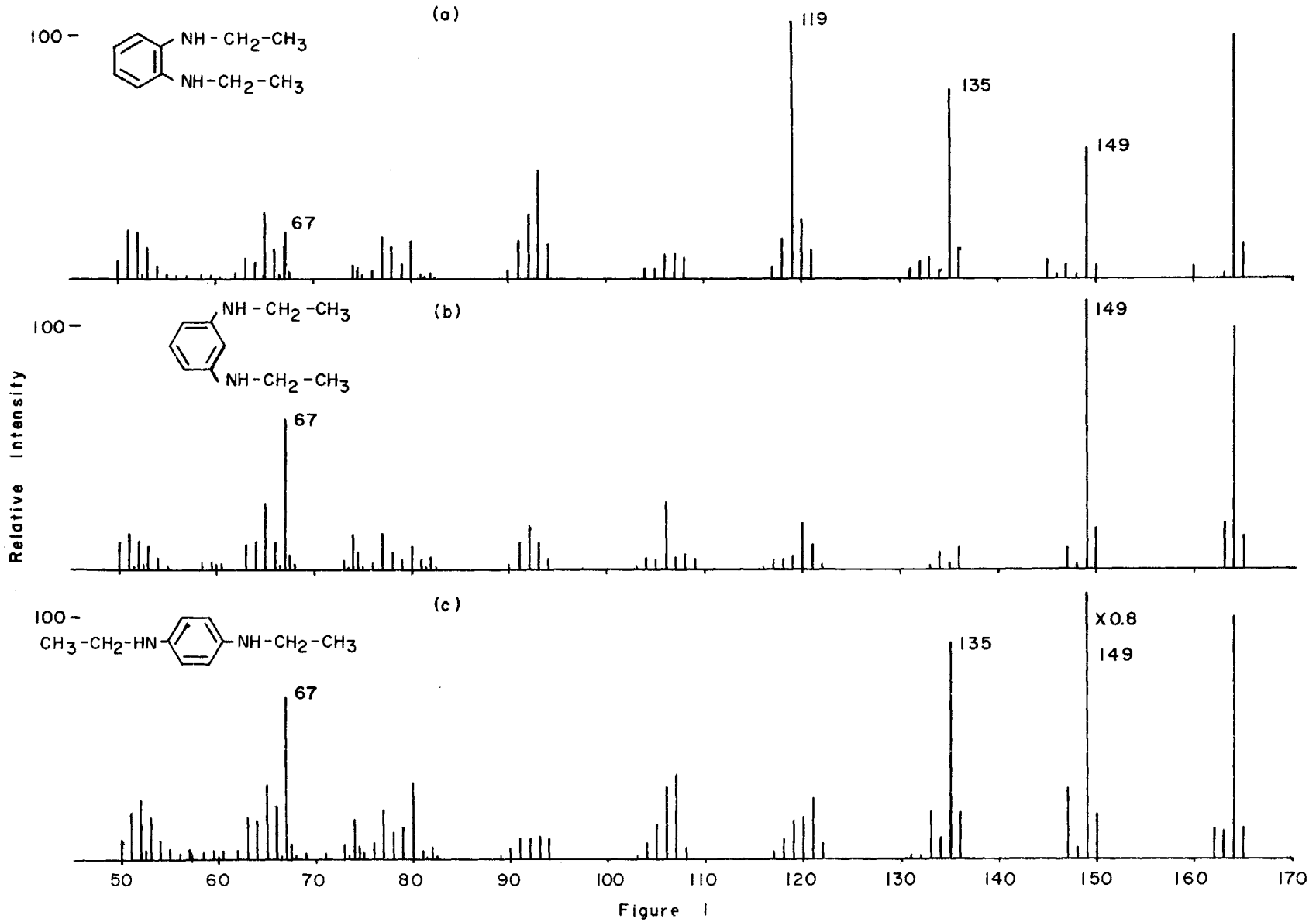
(a)
100 –
NH - CH2-CH3
NH-CH2-CH3
119
135
149
67
(b)
100 –
NH - CH2 -CH3
NH-CH2 -CH3
149
67
(c)
100 –
CH3-CH2-HN
NH-CH2-CH3
135
X0.8
149
67
Relative Intensity
50
60
70
80
90
100
110
120
130
140
150
160
170

Figure 1

compounds were chosen for this investigation whose molecular weight was not much higher than 160, the doubly charged ions of which appeared thus at m/e 80 or below. The elemental composition of each fragment was therefore determined as previously described[13] and its exact intensity was then calculated from the low resolution spectrum.

The identification and calculation of the exact abundance of the doubly charged ion at m/e 67 discussed above or other similar cases is not a very serious problem considering the absence of a peak of significant intensity at m/e 68. A more complicated case is offered by consideration of the fragments at m/e 66, m/e 66.5 and m/e 67 in N,N-dimethyl-N'-ethyl-p-phenylenediamine (E). The low resolution scan of this region (Fig. 2c) shows each peak as a singlet and it is impossible from only that data to determine how much -- if any -- of m/e 66.5 is the ^{13}C-species of the doubly charged ion 132^{++} (m/e 66). The high resolution mass spectrum which was recorded on a photoplate did indeed reveal some very interesting aspects as far as the identity of these fragments is concerned (Fig. 2b)*.

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*It should be noted that there are peaks corresponding to nitrogen-free C_5-ions of relatively high hydrogen content which thus cannot be derived from compound E. They are due to a hydrocarbon background in the instrument. Figure 1 is an excellent example of another aspect of high resolution mass spectra, namely that impurities do not falsify the data as long as the elemental composition of the impurity differs from that of the compound under investigation. The low-resolution spectrometer was checked for the absence of background contributions whenever any of the spectra discussed in this thesis were to be run.

Figure 2

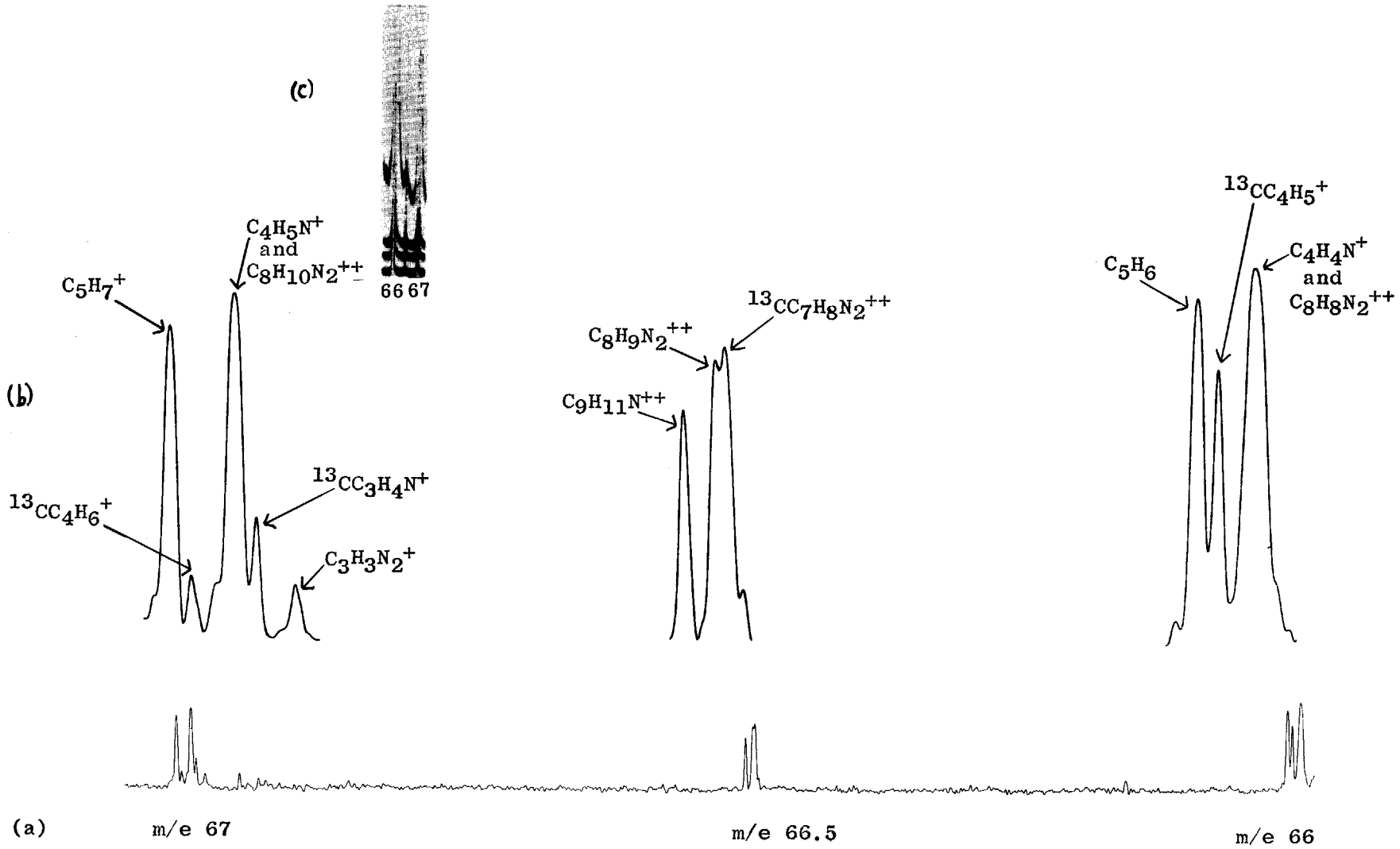
(a) Densitometer scan of the photographically recorded high resolution mass spectra of N,N-dimethyl-N'-ethyl-p-phenylenediamine (E) in the region of m/e 66-67.

(b) Enlargement of portions of (a).

(c) Conventional (low resolution) spectrum of the region of m/e 66-67.

Exact Masses

C_4H_4N	66.0353	(calcd. 66.0353)
$^{13}CC_4H_5$	66.0425	(calcd. 66.0434)
C_5H_6	66.0476	(calcd. 66.0476)
$^{13}CC_7H_8N_2$	66.5370	(calcd. 66.5361)
$C_8H_9N_2$	66.5380	(calcd. 66.5383)
$C_9H_{11}N$	66.5450	(calcd. 66.5440)
$C_3H_3N_2$	67.0345	(calcd. 67.0345)
$^{13}CC_3H_4N$	67.0381	(calcd. 67.0381)
C_4H_5N	67.0429	(calcd. 67.0429)
C_5H_7	67.0548	(calcd. 67.0547)
$^{13}CC_4H_6$	67.0509	(calcd. 67.0509)


(c)
66 67
$C_4H_5N^+$ and $C_8H_{10}N_2^{++}$
$C_5H_7^+$
(b)
$^{13}CC_4H_6^+$
$^{13}CC_3H_4N^+$
$C_3H_3N_2^+$
$C_8H_9N_2^{++}$
$^{13}CC_7H_8N_2^{++}$
$C_9H_{11}N^{++}$
$^{13}CC_4H_5^+$
C_5H_6
$C_4H_4N^+$ and $C_8H_8N_2^{++}$
(a)
m/e 67
m/e 66.5
m/e 66

The peak at m/e 66.5 e.g. was found to be composed of $^{13}CC_7H_8N_2^{++}$, $C_8H_9N_2^{++}$ and $C_9H_{11}N^{++}$, the first ion being the principal component. A densitometer scan of the photoplate between m/e 66 and m/e 67 (Fig. 2a) represents a typical example of the method used for the identification and calculation of the exact abundances of doubly charged ions given in Tables I-XIII and graphically represented in Figs. 2, 5 and 7. The optical densities represented by the curves in Fig. 2 were converted to intensities[24] using calibration data for this emulsion (Ilford Q2) and the exact relative intensity ratios of these three ions was thus obtained and the one of $^{13}CC_7H_8N_2^{++}$ was used for the calculation of the principal ion, in this case $C_8H_8N_2^{++}$. The intensity values are subject to a $\pm$5-10% error. It should be noted that the values given for the intensities of the most important doubly charged ions (e.g. $(M-30)^{++}$ in A,B,C,D,E,F,G, and H, $(M-2)^{++}$ in K,L,M and P) are subject only to a $\pm$1% error as they could be taken from the direct, low resolution scan because the peak at half mass was only one single species (the doubly charged ^{13}C-ion).

The Mass Spectra of Alkyl Substituted Phenylenediamines

It was thought that phenylenediamine derivatives would be most suitable for the study of the significance of doubly charged ions, not only because aromatic compounds have a tendency to form doubly charged ions, but also because nitrogen atoms with adjacent C-C bonds are known to provide a means for stabilizing a positive charge in singly charged ions:

$$R\text{-}\bar{N}H\text{-}CH_2\text{-}CH_3^{+} \longrightarrow R\text{-}\bar{N}H\text{-}CH_2^{+} + CH_3\cdot \leftrightarrow R\text{-}\overset{+}{N}H = CH_2$$

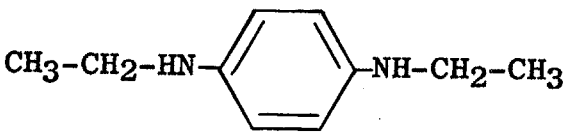
The presence of two such systems within a molecule might thus provide means for the stabilization of two positive charges. Different sets of structural isomers of polyalkyl phenylenediamines were studied in order to evaluate requirements for best stabilization of two positive charges in a molecule and thus the possibility to differentiate among different isomers based entirely on their doubly charged spectrum.

In general mass spectra of positional isomers of alkyl substituted aromatic compounds are very similar and their interpretation in terms of a unique structure is difficult in the absence of an authentic sample. It was hoped that the fragments of isomeric polyalkyl phenylene-diamines may differ in their ability to stabilize two positive charges and thus give rise to appreciable differences in the abundance of doubly charged ions which could be related to the arrangement of the alkyl groups.

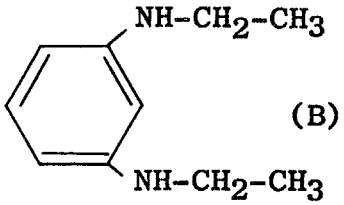
The structural requirements for the formation of doubly charged ions, often in preference over the corresponding singly charged ions, was therefore studied in sets of isomers of compositions $C_{10}H_{16}N_2$, $C_{12}H_{20}N_2$ and $C_8H_{12}N_2$.

Isomers of Composition $C_{10}H_{16}N_2$

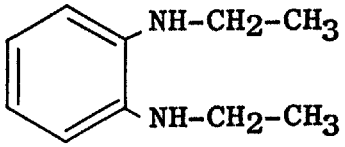
The mass spectra of the three positional isomers N,N'-diethyl-para, meta and ortho-phenylenediamines (A, B and C) and their structural isomers, N,N-diethyl-para-phenylenediamine (D) and N,N-dimethyl-N'-ethyl-para-phenylenediamine (E) are compared in Fig. 3. These drawings represent monoisotopic spectra (i.e. corrected for ^{13}C). Tables I through V give the exact calculated relative intensities and elemental compositions (as determined from their high resolution spectra) for the main singly charged peaks versus their doubly charged counterparts.



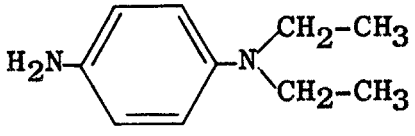
(A)



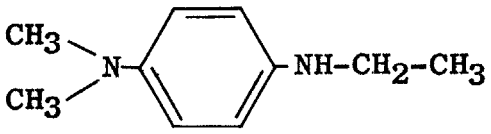
(B)



(C)



(D)



(E)

Figure 3

Monoisotopic mass spectra of isomers (A-E) of composition $C_{10}H_{16}N_2$

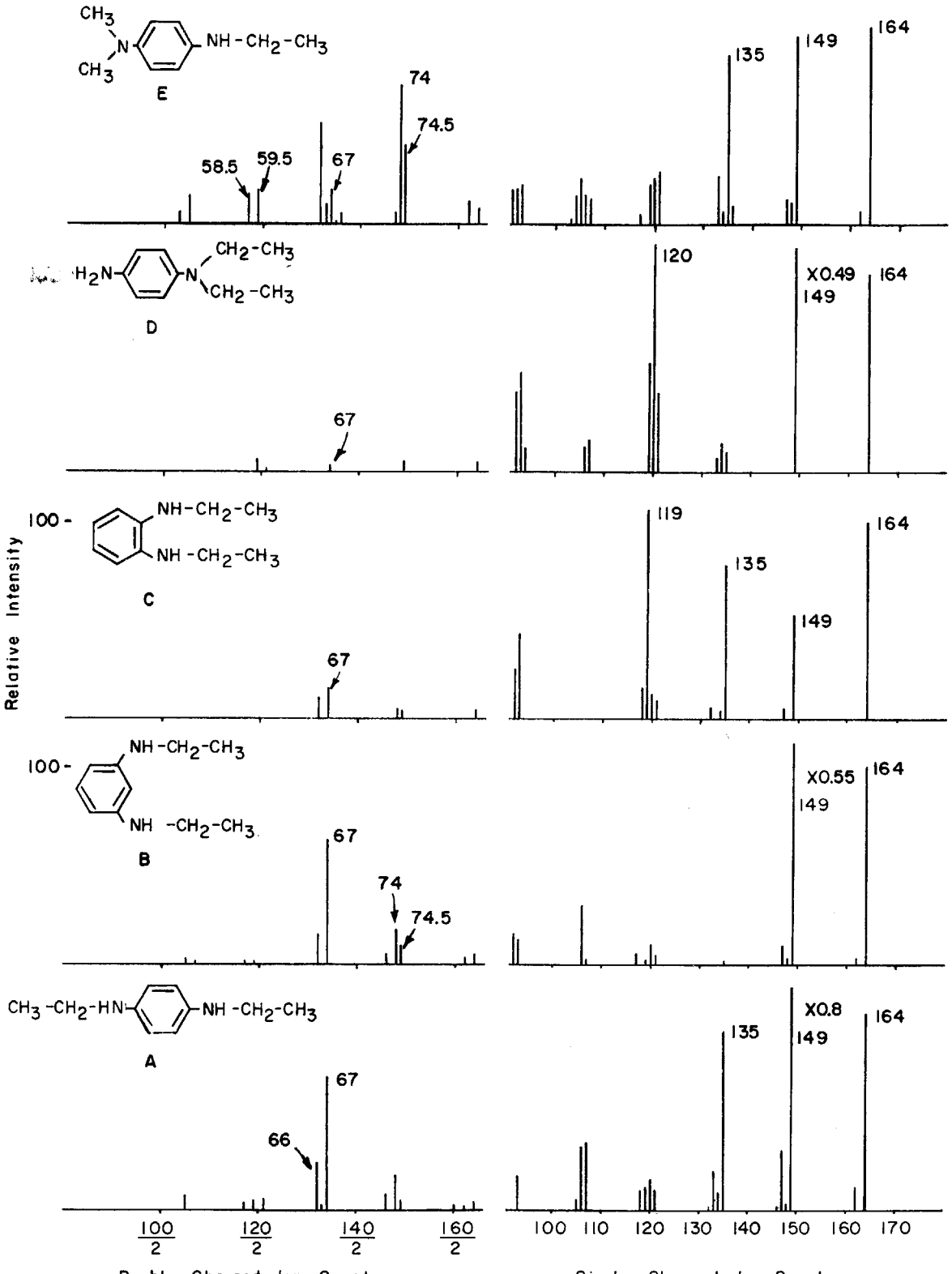

E
74
74.5
58.5
59.5
67
135
149
164
D
120
X0.49
149
164
67
C
100 -
119
135
149
164
67
B
100 -
67
74
74.5
X0.55
149
164
A
66
67
X0.8
135
149
164
Relative Intensity
100/2
120/2
140/2
160/2
100 110 120 130 140 150 160 170
Doubly Charged Ion Spectrum
Singly Charged Ion Spectrum

Figure 3

As shall become clear during the following discussions these spectra consist of three general parts: (1) the higher mass range representing singly charged ions due to loss of parts of the alkyl groups, mainly in the form of H, CH_3, $CH_2{=}CH_2$, NR_1R_2 and various combinations thereof. These fragments are formed by all of the isomers to a variable extent; (2) peaks in the lower mass range due to more drastic fragmentation processes involving cleavage of the aromatic system, resulting in small peaks of low mass; and (3) peaks due to doubly charged ions which thus appear at masses not higher than half the molecular weight.

The line spectra presented in Fig. 3 and similar figures thereafter consist of singly charged ions of the higher mass range as formed by the loss of groups described in (1) above, and of the doubly charged counterparts which appear at M/2 or below as formed in (3). The singly charged ion spectra are given on the right hand side and the doubly charged ion spectra on the left hand side. Peaks due to singly charged ions of mass below M/2 (2) are not shown in these spectra.

It is the first and last group which are most important in our present work and the former shall be discussed first for all the isomers. Having determined all the elemental compositions[13] it is relatively easy to rationalize the fragmentation processes that occur upon electron impact and to draw "structures" for these ions illustrating the possible reasons for the variation in abundance of analogous ions formed from the various isomers.

TABLE I

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N'-Diethyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
164	4.0	100	$C_{10}H_{16}N_2$
162	3.4	13	$C_{10}H_{14}N_2$
160	2.3	<1	$C_{10}H_{12}N_2$
149	4.3	138	$C_9H_{13}N_2$
148	17	2.9	$C_9H_{12}N_2$
147	<1	29	$C_9H_{11}N_2$
146	6.0	<1	$C_9H_{10}N_2$
135	<1	90	$C_8H_{11}N_2$
134	67	7	$C_8H_{10}N_2$
133	5	20	$C_8H_9N_2$
132	24	2	$C_8H_8N_2$
121	3	10	$C_7H_9N_2$
120	<1	15	$C_7H_8N_2$
119	3	12	$C_7H_7N_2$
117	2.5	11	C_8H_7N
105	4	11	C_7H_5N

TABLE II

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N'-Diethyl-m-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
164	5.0	100	$C_{10}H_{16}N_2$
162	1.8	1.5	$C_{10}H_{14}N_2$
149	9.5	185	$C_9H_{13}N_2$
148	17	2.7	$C_9H_{12}N_2$
147	<1	8.5	$C_9H_{11}N_2$
146	5.2	<1	$C_9H_{10}N_2$
135	<1	2	$C_8H_{11}N_2$
134	62.5	4	$C_8H_{10}N_2$
132	14	2	$C_8H_8N_2$
121	1.5	5.5	$C_7H_9N_2$
120	<1	10	$C_7H_8N_2$
119	1.8	4	$C_7H_7N_2$
117	2	5	C_8H_7N
106	<1	32	C_7H_8N
105	2.7	5.0	C_7H_7N
93	<1	12	C_6H_7N
92	<1	15	C_6H_6N
91	<1	12	C_6H_5N

TABLE III

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N'-Diethyl-o-Phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
164	2.0	100	$C_{10}H_{16}N_2$
162	<1	<1	$C_{10}H_{14}N_2$
149	4.0	53	$C_9H_{13}N_2$
148	4.5	<1	$C_9H_{12}N_2$
147	<1	6.0	$C_9H_{11}N_2$
135	<1	77	$C_8H_{11}N_2$
134	15	3.6	$C_8H_{10}N_2$
132	11	5.0	$C_8H_8N_2$
121	<1	9.0	$C_7H_9N_2$
120	<1	24.0	$C_7H_8N_2$
119	<1	105.0	$C_7H_7N_2$
118	<1	16.0	$C_7H_6N_2$
93	<1	44.0	C_6H_7N
92	<1	26.0	C_6H_6N

TABLE IV

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N -Diethyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
164	4.8	100	$C_{10}H_{16}N_2$
149	4.7	230	$C_9H_{13}N_2$
135	<1	11.0	$C_8H_{11}N_2$
134	2.0	15.5	$C_8H_{10}N_2$
133	<1	7.0	$C_8H_9N_2$
121	2.0	42	$C_7H_9N_2$
120	<1	115	$C_7H_8N_2$
119	6.3	56	$C_7H_7N_2$
107	<1	15	C_7H_9N
106	<1	13	C_7H_8N
94	<1	14	C_6H_8N
93	<1	30	C_6H_7N
		20	$C_5H_5N_2$
92	<1	35	C_6H_6N
		8	$C_5H_4N_2$

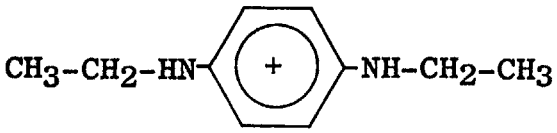
TABLE V

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N-dimethyl-N'-ethyl-p-phenylenediamine

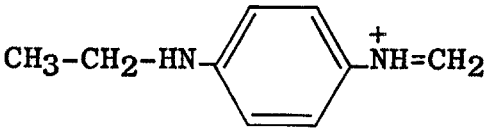
Mass	Doubly Charged	Singly Charged	Composition
164	8.0	100	$C_{10}H_{16}N_2$
162	12.0	7.0	$C_{10}H_{14}N_2$
149	40	96	$C_9H_{13}N_2$
148	70	12	$C_9H_{12}N_2$
147	6.5	13	$C_9H_{11}N_2$
136	6.0	9.0	$C_8H_{12}N_2$
135	<1	86	$C_8H_{11}N_2$
134	16	6.0	$C_8H_{10}N_2$
133	3.3	24	$C_8H_9N_2$
	1.7	<1	$C_9H_{11}N$
132	53	5.0	$C_8H_8N_2$
121	<1	26	$C_8H_{11}N$
120	<1	20	$C_8H_{10}N$
	<1	6	$C_7H_8N_2$
119	6	10	$C_7H_7N_2$
	12	10	C_8H_9N
117	14	4	C_8H_7N
	<1	<1	$C_7H_5N_2$
105	14	23	C_7H_7N
103	6.0	3.0	C_7H_5N

It should be understood that the "structures" drawn in the following for positive ions have by no means the significance which the chemical structures of molecules in the ground state have. They rather represent our opinion which of the atoms of the original molecule are present in the ion in question, arranged in a way that involves the least changes in the bonds originally present and the (intuitively) energetically most favorable arrangement of bonds and positive charge(s).

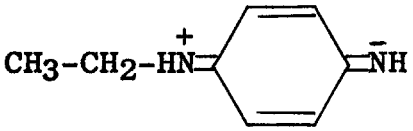
The most important singly charged ions in the <u>para</u> isomer (A) appear at m/e 164, 149, 135, 121 and 107. Species III-VII are proposed for those ions in agreement with their elemental composition. The most striking difference between the singly charged ion spectra of A and B



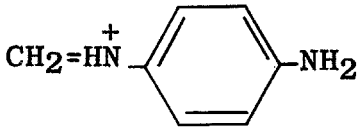
III m/e 164



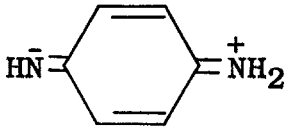
IV m/e 149



V m/e 135

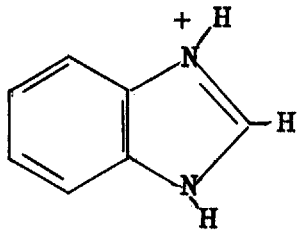


VI m/e 121



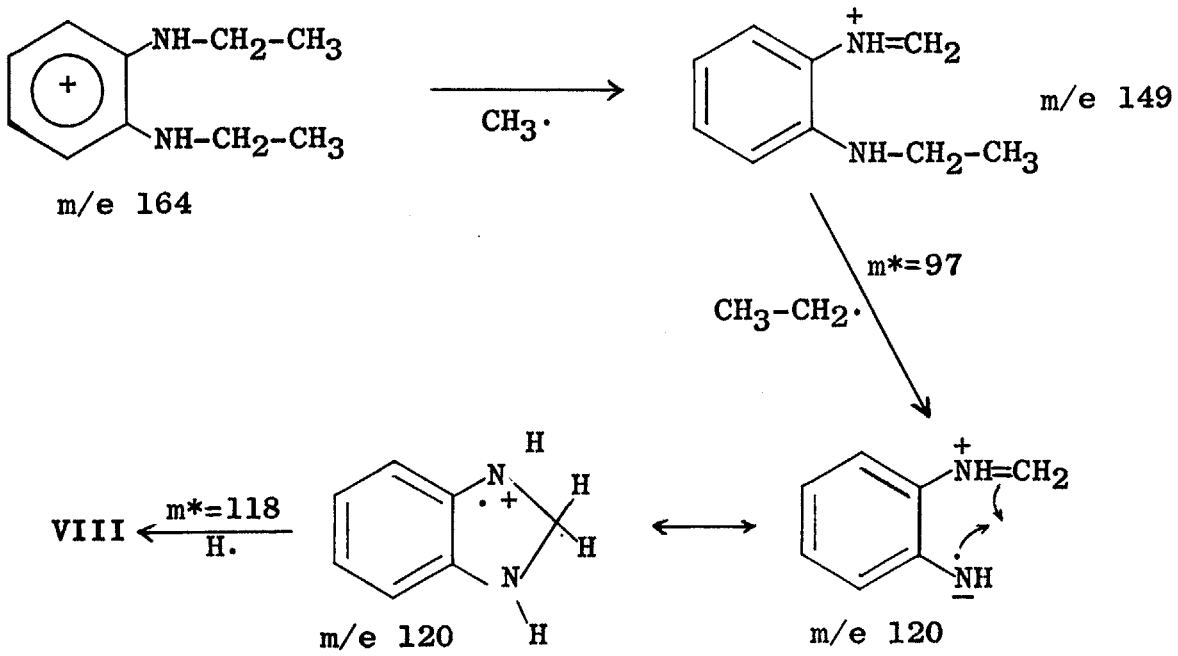
VII m/e 107

is the absence of a peak at m/e 135 $(M-29)^+$. This could be explained by the inability of one nitrogen to stabilize the positive charge of an electron deficient nitrogen atom in the meta position. It is again possible in the ortho isomer (C) which follows the same fragmentation pattern as A, the most abundant singly charged ions being due to M^+, $(M-15)^+$ and $(M-29)^+$. There is, however, a very intense peak (105% of M^+) at m/e 119. The proximity of the amino groups in the ortho position could contribute to the production of the stable ion VIII of a structure similar to the

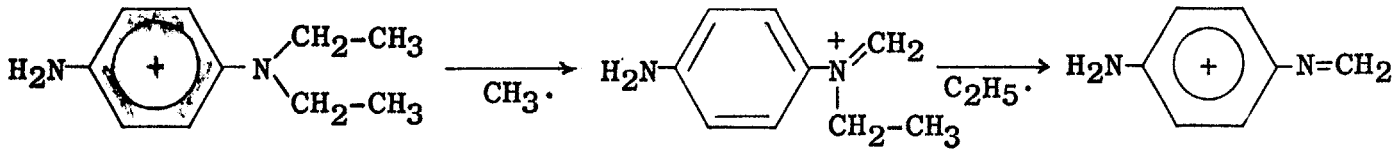


VIII m/e 119

ion at m/e 121 observed in polymethylene catechol diether derivatives (see section on oxygen analogs). This ion (VIII) can be formed in principle by loss of CH_3 and C_2H_6, CH_4 and C_2H_5 or CH_3, C_2H_5 and H. The presence of metastable peaks at m/e 97 (calcd. 96.7) and 118 (calcd. 118) substantiates the last sequence which is at first glance the least likely one, as it involves the loss of three separate radicals ($CH_3\cdot$, $C_2H_5\cdot$, and $H\cdot$). Apparently the product ion VIII has so much resonance energy that the energy required for the cleavage of three bonds and production of three radicals is compensated for.

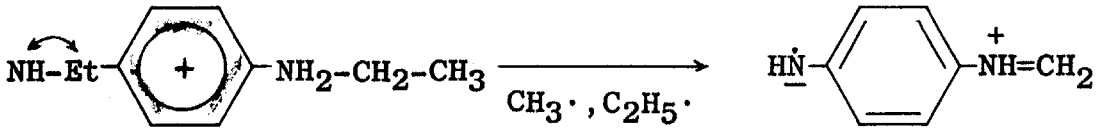


The ion of mass 135 is almost absent in the asymmetrical isomer (D) while it is quite pronounced in A, C and E. It is possible to rationalize this difference not by claiming that the ion is produced by loss of C_2H_5 (which should be able to form an imino quinone-type ion just as well as A does), but by much more favored competing fragmentation processes. As shown in Fig. 3, the mass spectrum of D exhibits a very abundant ion (IX) due to loss of a methyl group (favored both by the steric situation at the highly substituted nitrogen and the increased electron density of this nitrogen caused by the alkyl substituent). Furthermore, loss of the ethyl group from this species (substantiated by a metastable peak at 96.8 for the process $149^+ \rightarrow 120^+ + 29$) leads to the ion X.

(2) 

D^+ IX X

Ion X corresponds to an ionized molecule (para-phenylenediamine monomethine) while the corresponding ion (XI) from A would be an ion radical which may be less favored:



A^+ XI

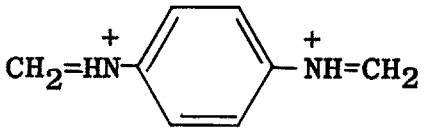
The mass spectrum of the N,N-dimethyl-N'-ethyl isomer E shows in the high mass range merely the expected loss of either CH_3 or C_2H_5. The more significant region containing the doubly charged ions shall be discussed later.

It thus turns out that the mass spectra of the diethyl-derivatives A through D exhibit pronounced differences which can be rationalized (see above) once the spectra have been determined, but which would have been difficult to predict. The spectra of isomers A and E are, however, quite similar in the high mass region as they consist mainly of the intense peaks at M^+, $(M-15)^+$ and $(M-29)^+$ and their intensities are also very similar.

It is this case in which the consideration of the doubly charged ions is most informative as shall be outlined later in this section.

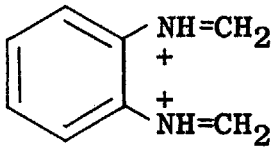
Before turning to this aspect, the doubly charged ions shall be discussed in comparison with the singly charged ones formed from the same compound to illustrate the great difference in the fragmentation modes of the singly charged versus the doubly charged molecular ions.

The doubly charged ion spectra of A and B are practically identical in contrast to their corresponding singly charged ion spectra which differ mainly in the presence of intense peaks at m/e 135 and 107 in A and their absence in B. Of considerable importance in A and B is the high intensity of m/e 67 corresponding to $(M-30)^{++}$, whereas the corresponding singly charged ion of m/e 134 is of very low intensity. The ratio of $(M-30)^{++}$ to $(M-30)^{+}$ in A is 9.6/1. The elimination of two methyl groups from the doubly charged molecular ion produces the stable ion XII. It is of interest to note that the $(M-30)^{++}$ as well as the $(M-16)^{++}$



XII

peaks (m/e 74) in A and B are of almost similar intensities relative to their respective molecular ions. This is in line with the fact that resonance between the two positive centers <u>via</u> the ring cannot play any stabilizing role in either of the two isomers. On the other hand, the intensity of the $(M-30)^{++}$ peak in the <u>ortho</u> isomer C is considerably lower due to the proximity of the two positive charges:

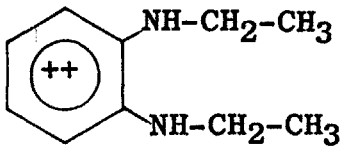


The small increase in the proximity of the two positive centers from A to B could in fact contribute to the slight decrease of the relative abundance of the $(M-30)^{++}$ in B (62.5% of M^+) as compared to A (67% of M^+). The exact relative abundance of all ions are given in Tables I through V.

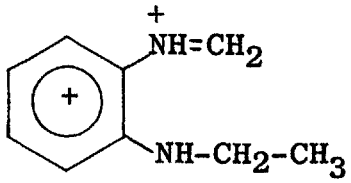
Considering the ortho and meta isomers it can be noticed from Tables III and II that the most abundant doubly charged ions occur at the following m/e values: 82, 81, 80; 74.5, 74, 73; 67, 66.5, 66, 60.5; 59.5 and 58.5. It is evident that these ions appear in "groups of ions" and that in each group one or two ions are the most abundant ones and can, therefore, be considered the most significant ones. Thus we can focus our attention on the ions at m/e 82, 74.5, 74 and 67. The first two and the last happen to be the most hydrogen-rich ions in each of the groups (see Tables II and III), and were attributed to the following doubly charged fragments:*

---

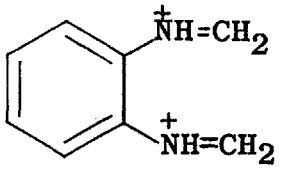
* Whenever one or both of the positive charges can formally be due to removal of one or two electrons from the benzene ring, the hexagon is drawn with a circle and one or two plus-signs in the center. If the positive charges are formally due to an ammonium ion produced by cleavage of the neighboring C-C bond the phenyl ring is drawn as one of the Kekule-forms. This symbolism is chosen for graphic purposes only without implying that the charges are fixed where they are shown.



XIII m/e 82

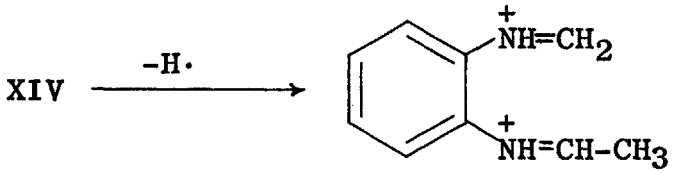


XIV m/e 74.5



XV m/e 67

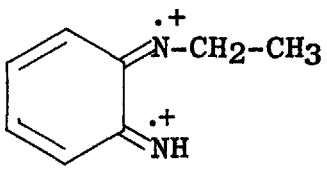
The odd electron ion XIV can further lose one hydrogen atom to produce a more stable fragment XVI corresponding to $(M-16)^{++}$ in which all electrons are paired:



XVI

Similar structures can be written for the analogous fragments formed from A and B.

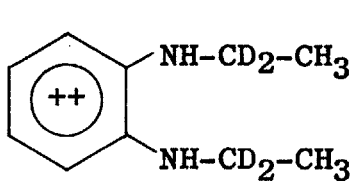
In order to prove that the most abundant doubly charged ion (m/e 67) in these spectra is indeed due to the loss of two methyl groups, and not due to some other species of the same elemental composition as XV (e.g. a fragment such as XVII) the spectra of B and C were compared with those of the



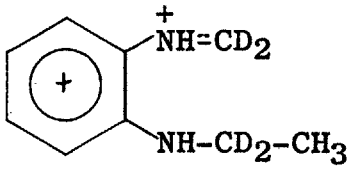
XVII

tetradeuterated isomers obtained on $LiAlD_4$-reduction of the corresponding diacetylphenylenediamines. In these isomers

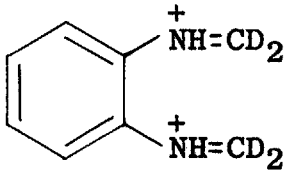
the $-CH_2-CH_3$ groups are thus replaced by $-CD_2-CH_3$ groups. The peak at m/e 67 is indeed shifted to m/e 69 (Figs. 4a, 4b) and so are the other most significant doubly charged peaks to give fragments corresponding to the following possible structures (XIIIa, XIVa and XVa):



XIIIa



XIVa



XVa

The abundances of these labeled fragments -- relative to their corresponding singly charged molecular ions -- are generally the same as those of their unlabeled counterparts. Similar structures can be written for the tetradeuterated meta isomer (Fig. 4a). It should also be noted here that the loss of hydrogen involved in the formation of the $(M-16)^{++}$ ion is not highly specific because the process XIV $\longrightarrow$ XVI would require that the ion formerly at m/e 74 shifts exclusively to m/e 75.5. There is, however, a peak at m/e 76. Writing a structure such as XVI indicates thus only the gross structure but does not mean to indicate precisely from which position the additional hydrogen was lost.

A comparison of the doubly charged ion spectrum of D to those of the symmetric isomers A, B and C indicates their very low abundance in this case. The abundance of the doubly charged molecular ion (m/e 82) is roughly the same as that of

Figure 4

Mass spectra of

(a) Tetradeuterated-N,N'-diethyl-m-phenylenediamine

(b) Tetradeuterated-N,N'-diethyl-o-phenylenediamine

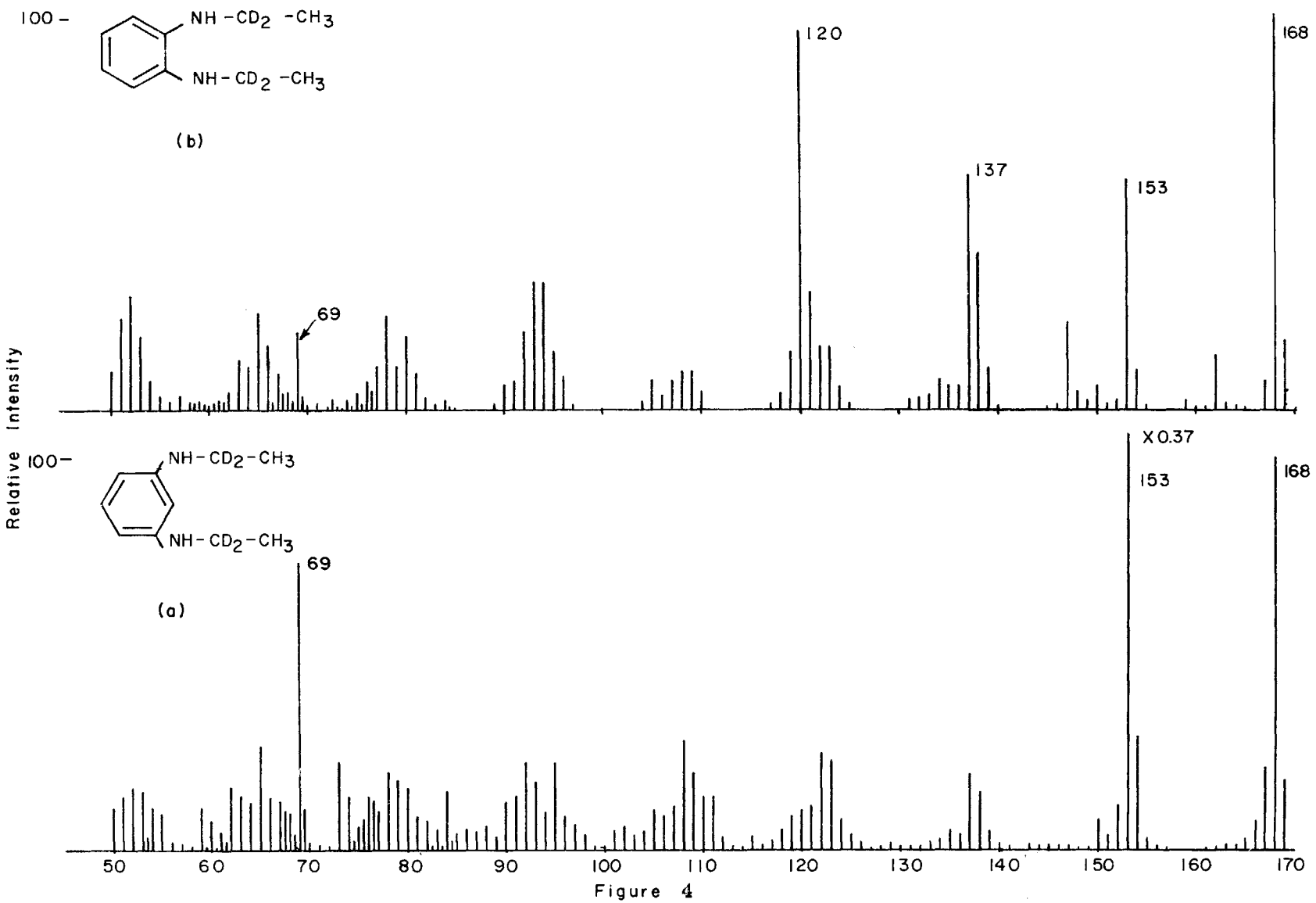
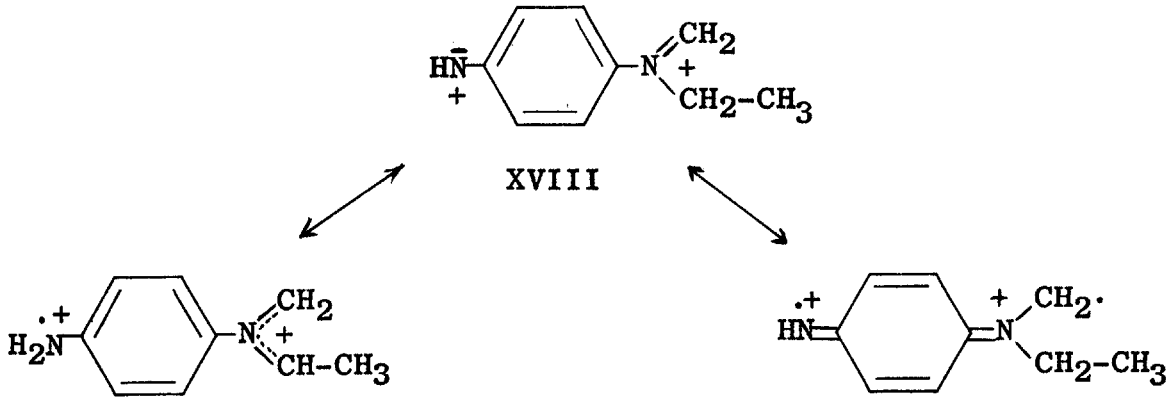

100 –
NH – CD2 – CH3
NH – CD2 – CH3
(b)
120
137
153
168
69
Relative Intensity
100 –
NH – CD2 – CH3
NH – CD2 – CH3
(a)
69
X 0.37
153
168
50
60
70
80
90
100
110
120
130
140
150
160
170

Figure 4

A, B or C relative to their corresponding singly charged molecular ions. The intense peaks, however, observed previously at m/e 74 or m/e 67 are absent in D, because the stabilization of the two positive charges in fragments such as XV or XVI is not as favorably accomplished by only one nitrogen:



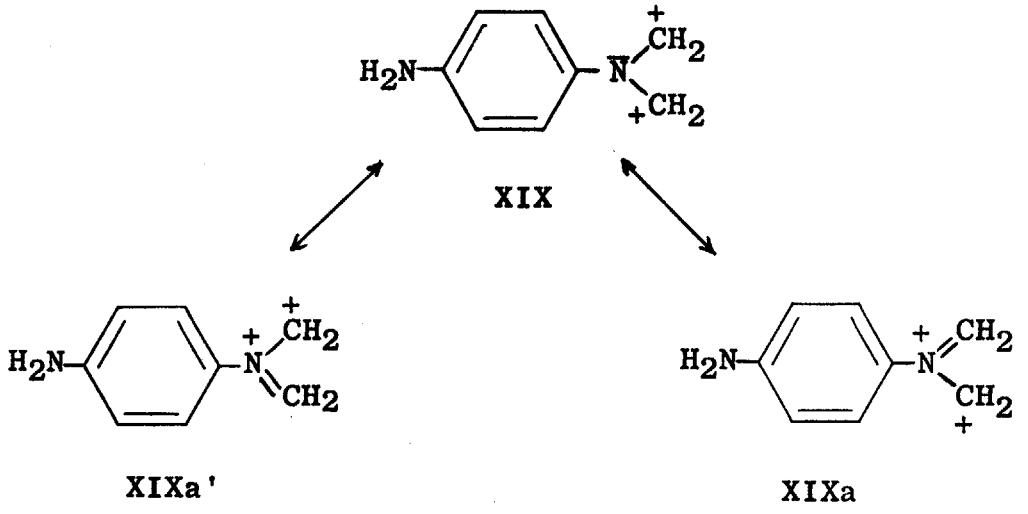
XVIII

XVIIIa'

XVIIIa

The only other way in which a maximum separation of charges can be achieved is by the formation of an unpaired electron species, e.g. (XVIIIa), which would be equally as unfavorable as XVIII.

Most significant is, however, the very low abundance of the $(M-30)^{++}$ ion at m/e 67, which in this case (XIX) would require stabilization of <u>two</u> positive charges by one and the same nitrogen atom which is, of course, impossible in any way analogous to the cases A, B and C discussed earlier.



XIX

XIXa'

XIXa

The close neighborhood of the positive charges, one of them being a carbonium ion (XIXa and XIXa') is detrimental to the stability of the ion. As a consequence, it is only about 1/30 as abundant as in A (relative to the corresponding M^+-ions).

The formation of m/e 67 $(M-30)^{++}$ in A, B and C corresponds to the loss of two methyl groups from the doubly charged molecular ion. The presence of a metastable peak at m/e 60 (calcd. 60.5) corresponding to the process

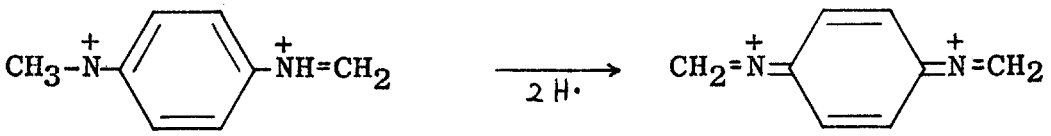
$$\text{m/e } 74.5 \longrightarrow \text{m/e } 67$$

indicates that a large number of $(M-30)^{++}$ ions is formed from the $(M-15)^{++}$ fragment by the further loss of a second methyl group. As a matter of fact there is no evidence of a metastable peak at m/e 55 corresponding to the process

$$\text{m/e } 82 \longrightarrow \text{m/e } 67$$

and it can be assumed that the loss of the two methyl groups proceeds mainly in a stepwise fashion rather than in a one step concerted mechanism.

The differences observed in the case of the N,N-diethyl versus the N,N'-diethyl-p-phenylenediamine clearly indicate the importance of the two different nitrogens in the stabilization of the two positive centers. In view of this fact, it is not surprising that the $(M-30)^{++}$ peak in E is weaker by a factor of 4 than it is in A. This very significant difference can be explained by the fact that the $(M-30)^{++}$ peak in A is due to the loss of two methyl groups, involving the cleavage of two C-C bonds next to nitrogen, whereas in E the same peak, as indicated by the shift of the peak to m/e 68 in the dideuterated isomer, $(CH_3)_2$-N-C_6H_5-NH-CD_2-CH_3, is formed by cleavage of one C-C and one C-N bond leading to an ion (XX) with an electron deficient nitrogen which is much less favorable than ion XII, but then seems to easily lose two hydrogens to give an intense doubly charged ion at m/e 66 (XXa).



XX XXa

On the other hand, the stable $(M-16)^{++}$ ion in E is formed in very high abundance, due to the loss of a methyl group and the elimination of a hydrogen atom upon cleavage of a C-H bond. The shift of this peak from m/e 74 to m/e 75 in the labeled isomer (Fig. 5a) indicates that the above process leads to the formation of the stable fragment XXI. As far as its formation and

Figure 5

Mass Spectra of

(a) N,N-dimethyl-N'-ethyl-p-phenylenediamine

(b) N,N-dimethyl-N'-ethyl-d_2-p-phenylenediamine

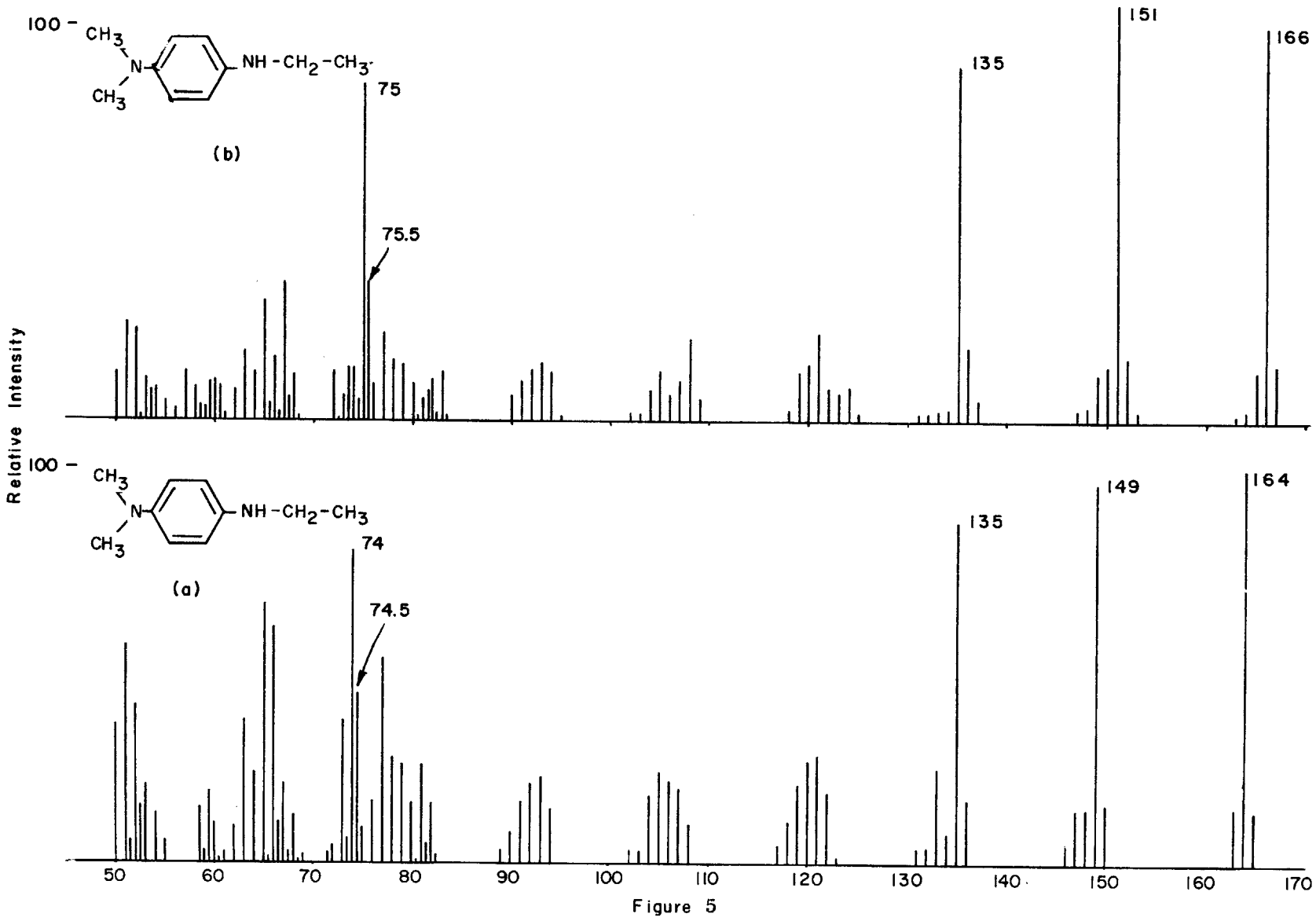
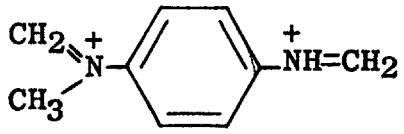

100 -
CH3
N
CH3
NH - CH2 - CH3
(b)
75
75.5
135
151
166
Relative Intensity
100 -
CH3
N
CH3
NH - CH2 - CH3
(a)
74
74.5
135
149
164
50
60
70
80
90
100
110
120
130
140
150
160
170

Figure 5

the stabilization of the positive charges goes, it is analogous to the $(M-30)^{++}$ ion formed from A.



XXI

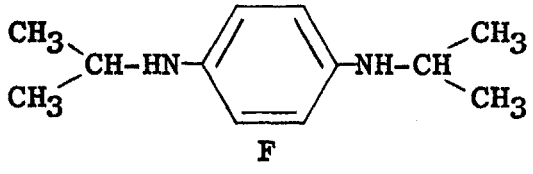
Isomers A and E provide an excellent example in which it is practically impossible to differentiate between two compounds mass spectrometrically (in the absence of the spectra of authentic samples) based on the singly charged ion spectra alone. The doubly charged ion spectra, however, exhibit distinct and easily predictable differences which can be used for the structural differentiation of certain molecular isomers. On the other hand, in the case of isomers A and B the doubly charged ion spectra are essentially identical and the only means for their differentiation is their singly charged ion spectra.

The above data very clearly indicate the difference in the mode of fragmentation of doubly charged and singly charged molecular ions due to the necessity for stabilization of two positive charges in the ions produced from the former which may greatly differ (for the better or worse) from the stabilization of a single positive charge (plus a radical in some cases), in the singly charged ions. These differences are well illustrated by Tables I-V. For example, Table I shows that the singly charged molecular ion of A is quite

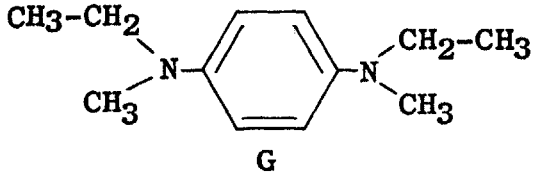
abundant and that it loses quite easily a C_2H_5 group (0.9 times as abundant as the M^+ ion) but that two CH_3 groups are lost with great difficulty (0.07 times as abundant as the M^+ ion). On the other hand, the doubly charged molecular ion is of low abundance and seems to have a much lower tendency to lose a C_2H_5 group (less than 0.25 times as abundant as the M^{++} ion) while the tendency to lose two CH_3 groups is extremely high (17 times the abundance of the M^{++}). Similar comparisons can be made between many pairs of ions listed in the Tables.

Isomers of Composition $C_{12}H_{20}N_2$

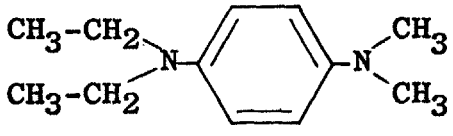
In an effort to assess the general applicability of the conclusions drawn in the foregoing section, the mass spectra of the higher homologs N,N'-diisopropyl-p-phenylenediamine (F), N,N'-dimethyl-N,N'-diethyl-p-phenylenediamine (G), N,N-dimethyl-N',N'-diethyl-p-phenylenediamine (H), and N,N-diethyl-N'-ethyl-p-phenylenediamine (J) were determined. The singly and doubly charged



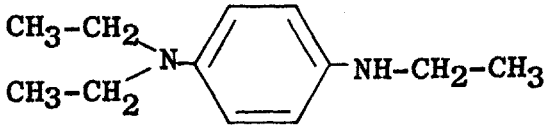
F



G



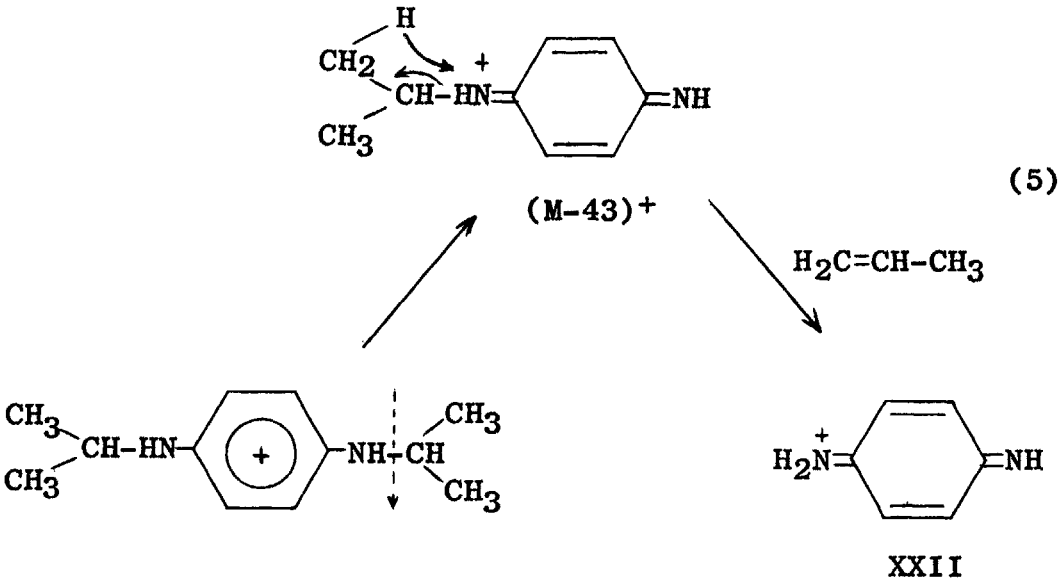
H



J

ion spectra (corrected for ^{13}C contributions) of each isomer are shown in Figs. 6a, b, c and d, respectively. Tables VI, VII, VIII and IX give the elemental compositions of the doubly and singly charged fragments as determined from high resolution spectra along with their respective intensities, calculated from the low resolution spectra (with the aid of abundance ratios taken from the high resolution spectra in the case of multiplets).

The most significant singly charged ions of F occur at m/e 192, 177, 149 and 107. The first three correspond to M^+, $(M-15)^+$ and $(M-43)^+$ respectively. The loss of the isopropyl group $(M-43)^+$ is probably followed by the successive loss of two methyl groups yielding the peaks at m/e 135 and m/e 120. This somewhat unexpected process is supported by the analogous case (loss of C_2H_5, CH_3 and H from (C)) discussed earlier. Finally the peak at m/e 107 which corresponds to $C_6H_7N_2^+$ is formed <u>via</u> process (5) yielding the stable ion XXII.



(5)

XXII

Figure 6

Monoisotopic mass spectra of isomers (F-J) of composition $C_{12}H_{16}N_2$.

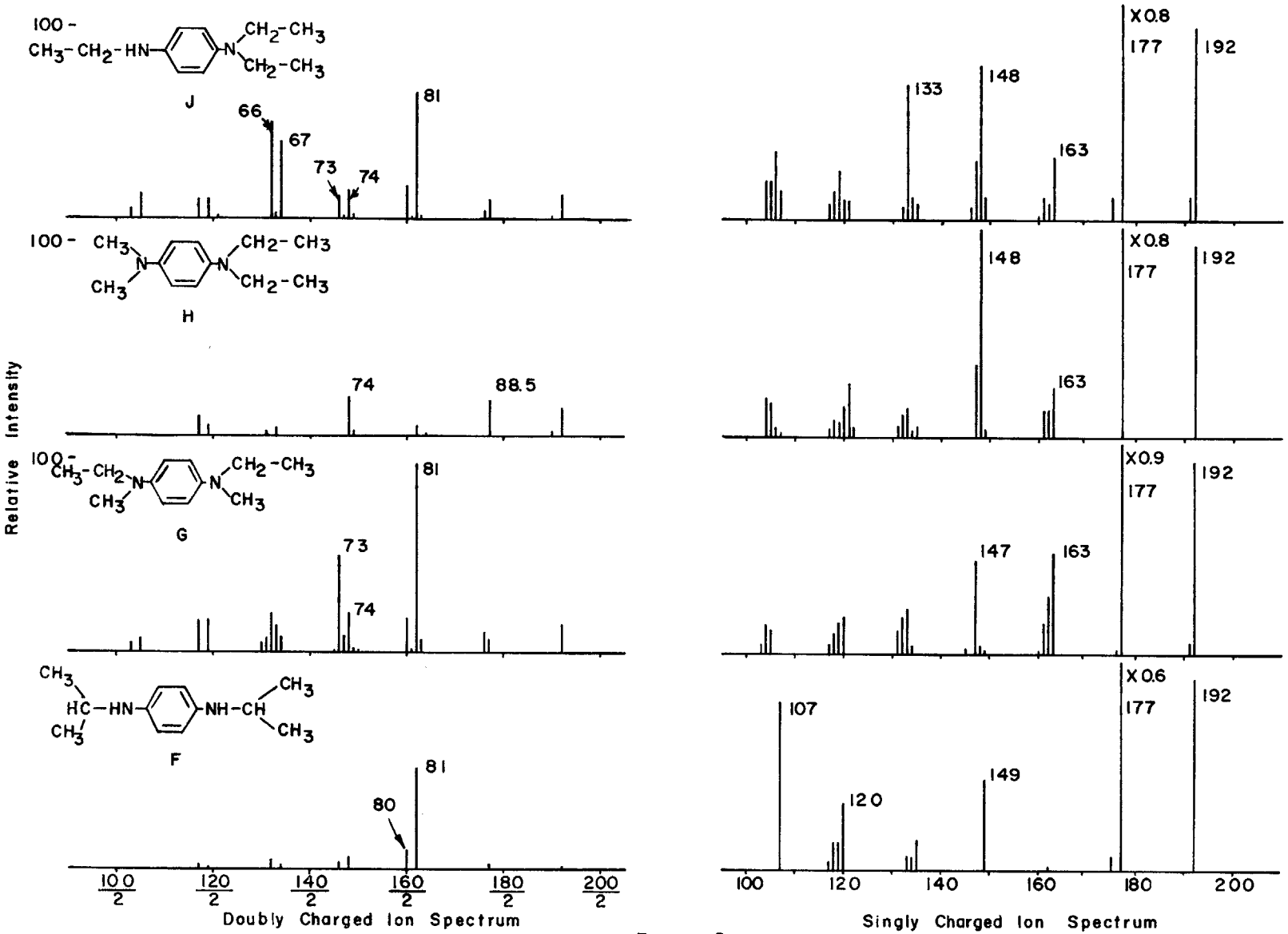

Relative Intensity
100 -
J
66
67
73
74
81
H
74
88.5
G
73
74
81
F
80
81
100/2
120/2
140/2
160/2
180/2
200/2
Doubly Charged Ion Spectrum
X0.8
177
192
133
148
163
X0.8
177
192
148
163
X0.9
177
192
147
163
X0.6
177
192
107
120
149
100
120
140
160
180
200
Singly Charged Ion Spectrum

Figure 6

TABLE VI

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N'-diisopropyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
192	0.4	100	$C_{12}H_{20}N_2$
177	2	188	$C_{11}H_{17}N_2$
162	51	2.5	$C_{10}H_{14}N_2$
160	11	0.7	$C_{10}H_{12}N_2$
148	5.5	2	$C_9H_{12}N_2$
146	4	<1	$C_9H_{10}N_2$
135	<1	12	$C_8H_{11}N_2$
134	2.7	9	$C_8H_{10}N_2$
133	<1	6.0	$C_9H_{11}N$
	<1	4.0	$C_8H_9N_2$
132	5	3	$C_8H_8N_2$
119	<1	9	$C_7H_7N_2$
	<1	4	C_8H_9N
117	2	4	C_8H_7N

TABLE VII

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N'-dimethyl-N,N'-diethyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
192	14	100	$C_{12}H_{20}N_2$
191	<1	6.5	$C_{12}H_{19}N_2$
177	7	123	$C_{11}H_{17}N_2$
176	10	3.0	$C_{11}H_{16}N_2$
163	6	53	$C_{10}H_{15}N_2$
162	97	30	$C_{10}H_{14}N_2$
161	2	16	$C_{10}H_{13}N_2$
160	18	2	$C_{10}H_{12}N_2$
149	2	2	$C_9H_{13}N_2$
	<1	<1	$C_{10}H_{15}N$
148	20	4	$C_9H_{12}N_2$
147	4	73	$C_9H_{11}N_2$
	4	<1	$C_{10}H_{13}N$
146	42	4	$C_9H_{10}N_2$
145	2	3	$C_9H_9N_2$
134	11	4	$C_8H_{10}N_2$
133	5	10.5	$C_8H_9N_2$
	9	10.5	$C_9H_{11}N$

TABLE VII (continued)

Mass	Doubly Charged	Singly Charged	Composition
132	35	17	$C_8H_8N_2$
131	3	8	$C_8H_7N_2$
	6	4	C_9H_9N
130	5	<1	C_9H_8N
120	<1	19	$C_8H_8N_2$
119	17	8.5	C_8H_9N
		8.5	$C_7H_7N_2$
117	16	3	C_8H_7N
		2	$C_7H_5N_2$
105	7	10	C_7H_7N
103	4	2	C_7H_5N

TABLE VIII

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N-dimethyl-N',N'-diethyl-para-phenylenediamine

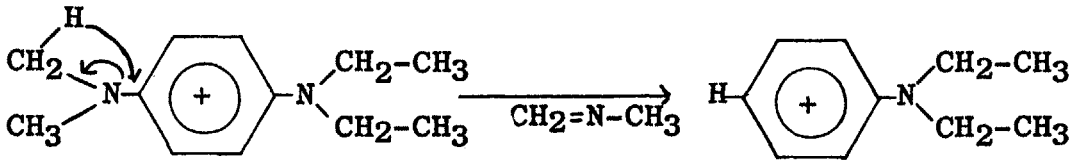
Mass	Doubly Charged	Singly Charged	Composition
192	16	100	$C_{12}H_{20}N_2$
190	2	<1	$C_{12}H_{18}N_2$
177	17	140	$C_{11}H_{17}N_2$
164	1.5	4.0	$C_{10}H_{16}N_2$
163	<1	25	$C_{10}H_{15}N_2$
162	5.0	12	$C_{10}H_{14}N_2$
149	2.0	3.0	$C_9H_{13}N_2$
148	20.0	118	$C_9H_{12}N_2$
147	5.0	18	$C_9H_{11}N_2$
	<1	19	$C_{10}H_{13}N$
133	4.0	15.0	$C_9H_{13}N$
131	2.0	8.0	$C_9H_{11}N$
121	<1	26.0	$C_8H_{11}N$
120	<1	14.0	$C_8H_{10}N$
119	6.0	8.0	C_8H_9N
117	9.0	5.0	C_8H_7N

TABLE IX

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N-diethyl-N'-ethyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
192	13	100	$C_{12}H_{20}N_2$
191	<1	12	$C_{12}H_{19}N_2$
177	10	140	$C_{11}H_{17}N_2$
175	<1	12	$C_{11}H_{15}N_2$
164	<1	<1	$C_{10}H_{16}N_2$
163	<1	34	$C_{10}H_{15}N_2$
162	65	8.5	$C_{10}H_{14}N_2$
161	<1	11	$C_{10}H_{13}N_2$
160	14	2.0	$C_{10}H_{12}N_2$
149	2.0	12	$C_9H_{13}N_2$
148	15	80	$C_9H_{12}N_2$
147	1.0	30	$C_9H_{11}N_2$
146	12	7.0	$C_9H_{10}N_2$
135	<1	8.0	$C_8H_{11}N_2$
134	18	5	$C_8H_{10}N_2$
133	3.0	70.0	$C_8H_9N_2$
132	40	7.0	$C_8H_8N_2$
121	<1	9.7	$C_8H_{11}N$
	<1	1.3	$C_7H_9N_2$
119	10	25	$C_7H_7N_2$
117	10	8.0	C_8H_7N
	<1	<1	$C_7H_5N_2$
105	13	20	C_7H_7N
103	5.0	2.0	C_7H_5N

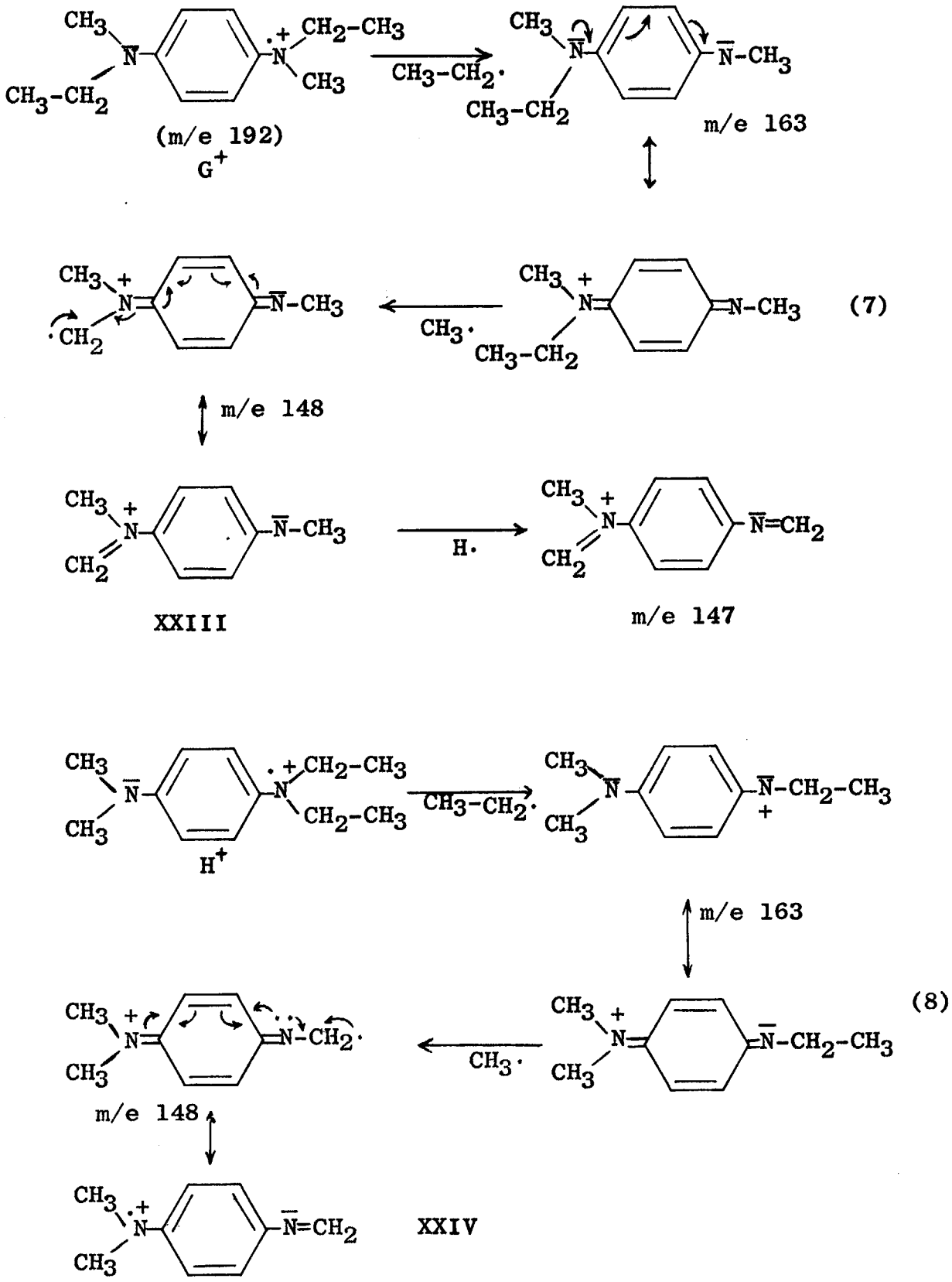
Isomers G and H each have two methyl and two ethyl groups attached to two nitrogen atoms and in each case the peaks at m/e 192, 177 and 163 correspond to M^+, $(M-15)^+$ and $(M-29)^+$ respectively. The most striking difference between the two in the singly charged region is the almost complete absence of m/e 148 in the spectrum of G whereas the peak at m/e 147 is relatively intense. On the other hand the fragment of mass 148 in H is the second most abundant ion in the spectrum and is formed in preference over the fragment of mass 147. The elemental composition of m/e 148 was determined as $C_9H_{12}N_2$ in both G and H while the exact mass of m/e 147 in G was found to correspond to $C_9H_{11}N_2$ and in H m/e 147 consists of $C_9H_{11}N_2$ and $C_{10}H_{13}N$ to approximately equal amounts (see Tables VII and VIII). Process (6) explains the formation of $C_{10}H_{13}N^+$ in H. Processes (7) and (8) can best explain the difference between G and H with regard to the preference of m/e 148



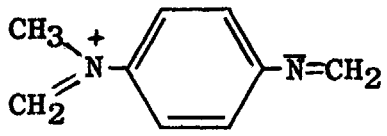
(6)

m/e 147

over m/e 147 in the former and 147 over 148 in the latter. From (7) we can see that compound G after the loss of an ethyl and a methyl group, forms the unstable fragment XXIII with an electron deficient nitrogen. As a result,


(m/e 192)
G+
m/e 163
m/e 148
XXIII
m/e 147
(7)
m/e 163
m/e 148
XXIV
(8)

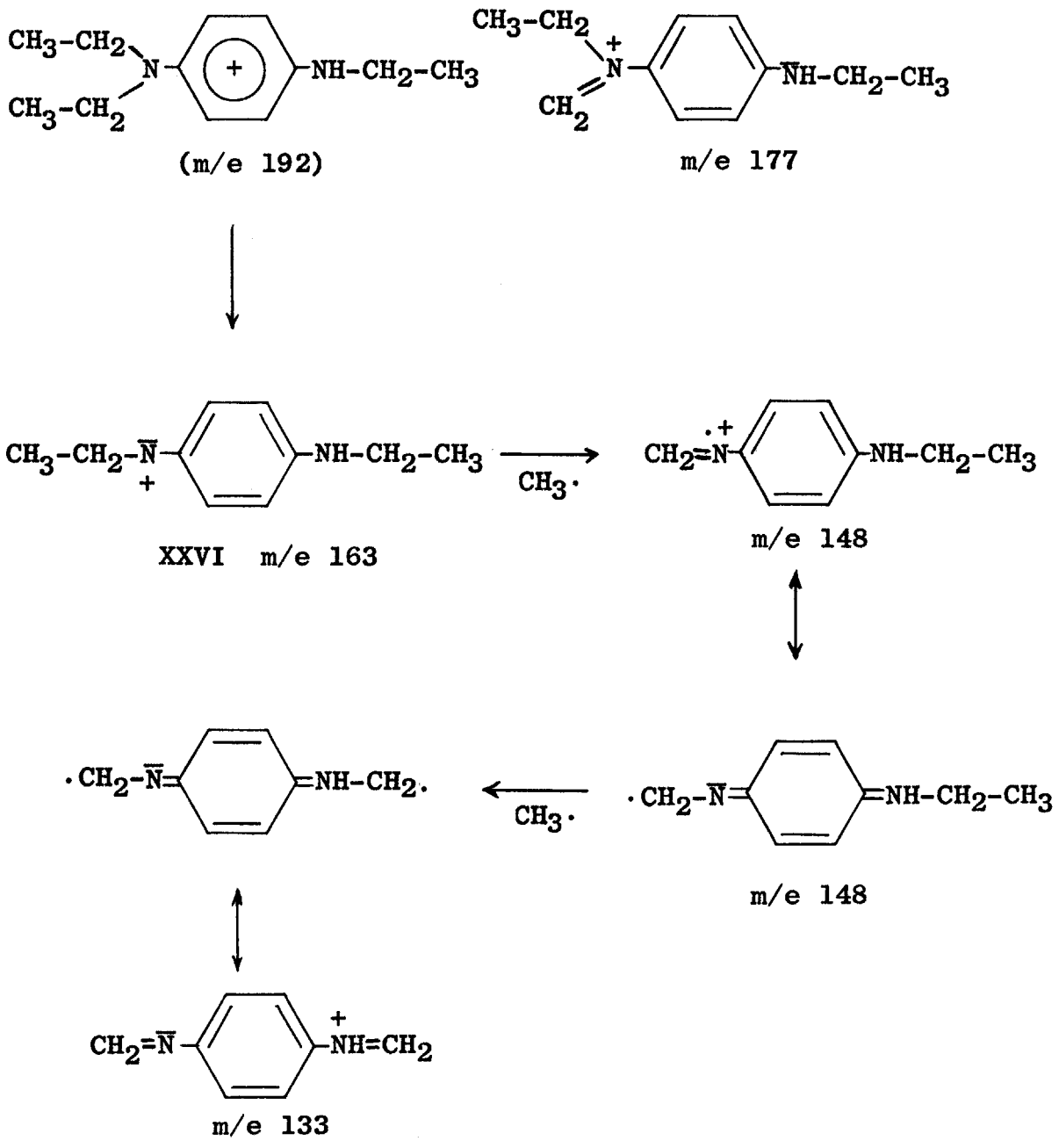
this ion prefers to further lose a hydrogen atom to produce the stable fragment at m/e 147 and hence the almost complete absence of m/e 148 in G. On the other hand, the loss of an ethyl and a methyl group in H leads to the stable molecular ion-type species XXIV and thus the preference of m/e 148 over m/e 147. The fragment $C_9H_{11}N_2$ at m/e 147 is actually present but to a lesser extent. The loss of a hydrogen atom from XXIV produces ion XXV, a relatively stable fragment, more so than XXIII, since all electrons can be considered as paired.



XXV

It should be noted that a similar situation existed in isomers A and D of the $C_{10}H_{16}N_2$ series. In that case, A had an intense $(M-29)^+$ peak whereas D showed higher preference for the formation of the $(M-29-15)^+$ as well as the $(M-29-15-1)^+$ ion.

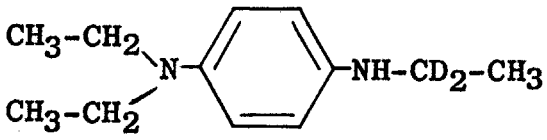
The singly charged ion spectrum of N,N-diethyl-N'-p-phenylenediamine (J) follows the same general pattern of fragmentation as that of H. The intense peaks at m/e 192, 177, 163, 148 and 135 correspond to M^+, $(M-15)^+$, $(M-29)^+$ and $(M-29-15-15)^+$ respectively. The following ions can be written for each of the above fragments:



The high intensity of the peak at m/e 133 in J is the only major difference between H and J in the singly charged region of the spectrum.

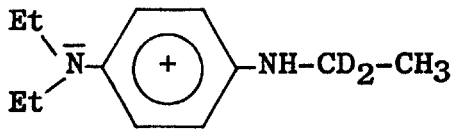
In an attempt to ascertain which of the ethyl groups in J is more preferably retained, the labeled molecule N,N-diethyl-N'-ethyl-d_2-p-phenylenediamine (Ja) was prepared. All major peaks were shifted two mass units

higher (Fig. 7b) which means that the lone ethyl group

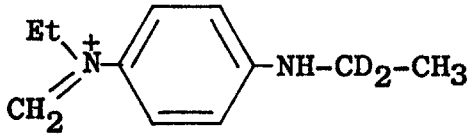


Ja

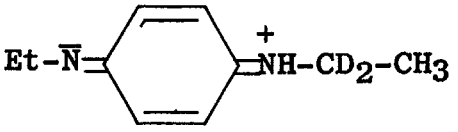
is retained much more readily than either of the two equivalent ethyl groups of the tertiary amino group. The corresponding ions for the main fragments in the labeled molecule are shown below. The considerably higher intensity of m/e 163 is only in part due to the loss of a deuterium or two hydrogens from m/e 165 (corresponding to the peaks at m/e 162 and 161 in the undeuterated species J). The remainder must represent the ion formed by loss of the deuterated ethyl group



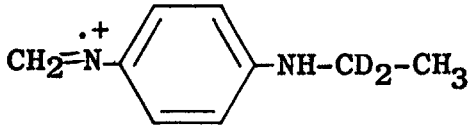
Ja (m/e 194)



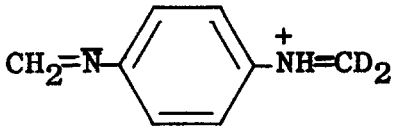
m/e 179



m/e 165



m/e 150



m/e 135

Figure 7

Mass Spectra of

(a) N,N-diethyl-N'-ethyl-p-phenylenediamine

(b) N,N-diethyl-N'-ethyl-d_2-p-phenylenediamine

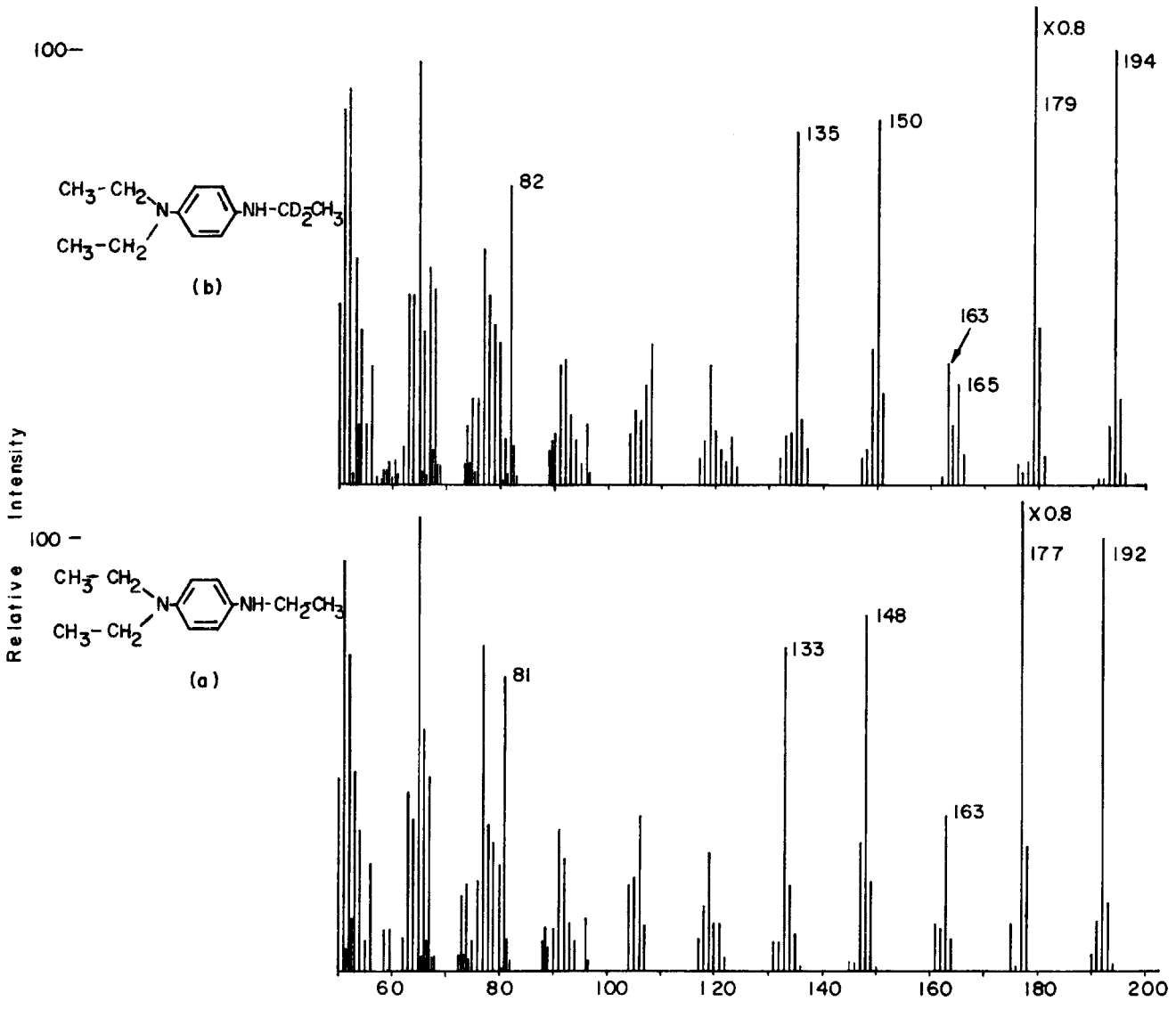
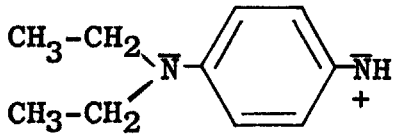

100—
X0.8
194
179
135
150
82
163
165
(b)
Relative Intensity
100 —
X0.8
177
192
148
133
81
163
(a)
60
80
100
120
140
160
180
200

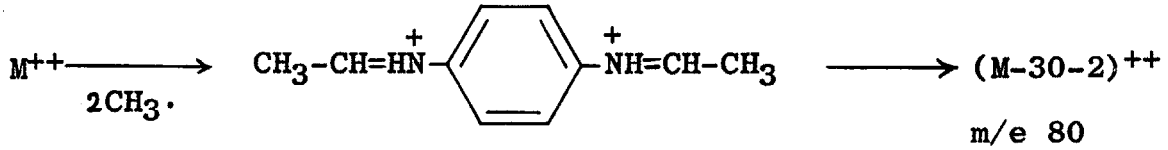
Figure 7

which seems however not to undergo the further fragmentation (loss of two methyl groups) outlined above for the other ion of m/e 163 (XXVI).



XXVIa

The doubly charged ion spectrum of the diisopropyl derivative F follows basically the same pattern of fragmentation as that of the diethyl derivative A. The two main peaks at m/e 81 and m/e 80 correspond to $(M-30)^{++}$ and $(M-32)^{++}$ respectively:

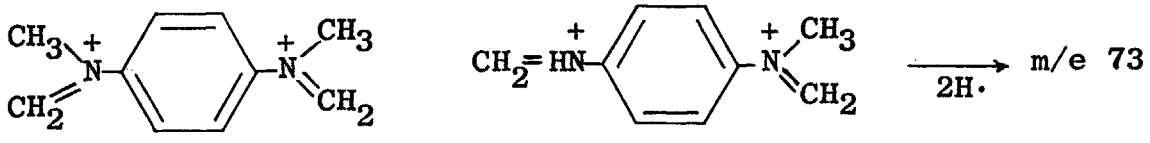


m/e 81

The doubly charged molecular ion is much less abundant than that in A as are all the other doubly charged fragments. The inductive effect of the additional methyl groups increases the stabilization of the $(M-30)^{++}$ ion and therefore it is the only doubly charged fragment, formed in significant abundance. The almost complete absence of the corresponding singly charged ion $(M-30)^{+}$ should be pointed out. The ratio $(M-30)^{++}/(M-30)^{+}$ is approximately 20:1 (see Table VI).

The very high abundance of doubly charged fragments evident in the spectrum of G (Fig. 6b) is to be expected in view of the previous data (Fig. 1a). The elimination of two methyl groups from 192^{++} yields the very stable $(M-30)^{++}$ ion at m/e 81 (XXVIII). Comparison of XXVIII and XII makes it quite evident that the additional methyl group on each of the nitrogens in XXVIII may stabilize that ion further, more so than could the hydrogen atoms in XII. Indeed, the abundance of XXVII is 97% of M^+ while that of XII is 67% of M^+. In other words, the substitution of methyl groups for hydrogens increased the relative abundance of $(M-30)^{++}$ by approximately 30% in terms of the corresponding molecular ion. Possible structures, which are in agreement with their elemental composition, of the most abundant doubly charged ions in G are the following:

XXVII m/e 88.5 m/e 88.0

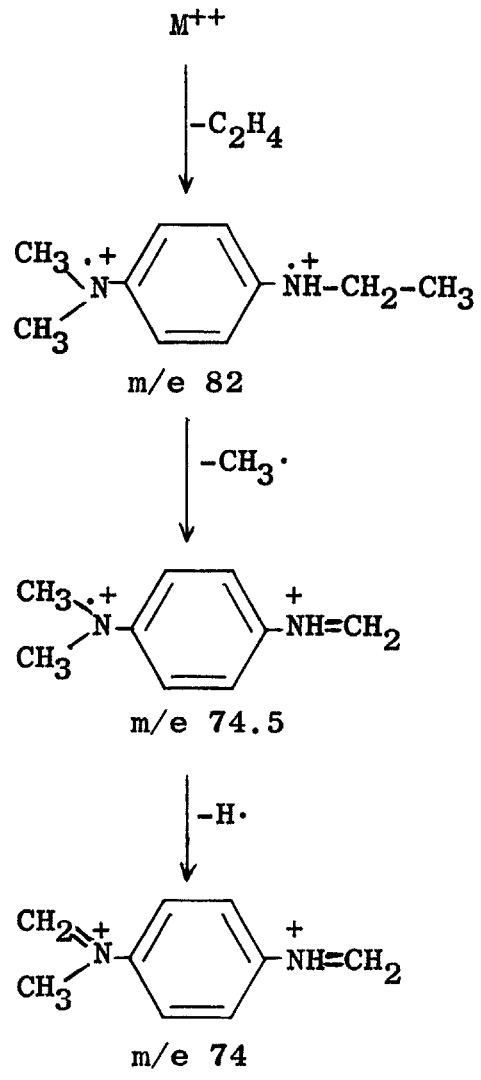


XXVIII m/e 81 m/e 74

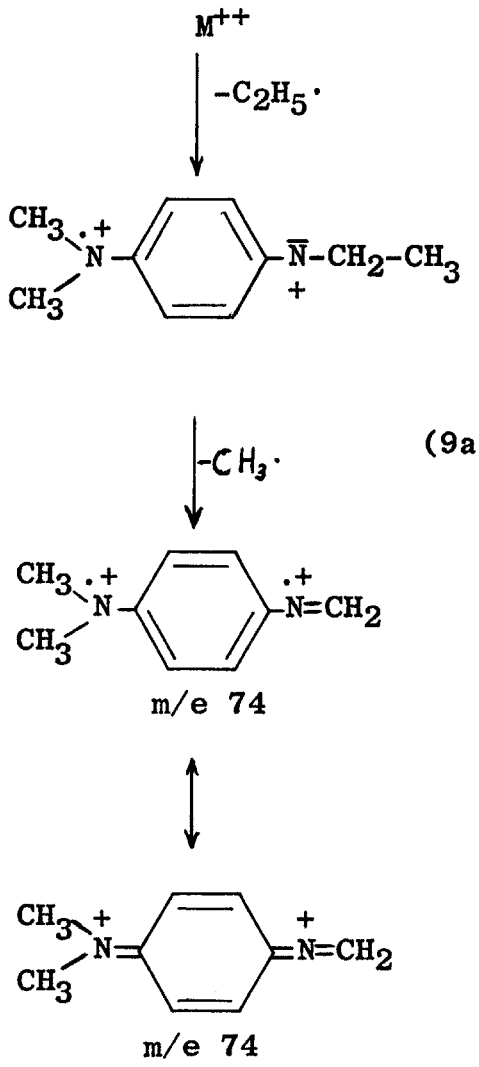
The loss of a methyl group from M^{++} yields the odd-electron fragment XXVII which upon further loss of a hydrogen atom produces the more stable even electron species at m/e 88. Similar factors must govern the preferential formation of m/e 74 over m/e 74.5 and m/e 73 over m/e 73.5. The preference of $(M-30)^{++}$ over $(M-30)^{+}$ has already been pointed out as well as the higher intensity of 148^{++} and 146^{++} compared to 148^{+} and 146^{+}. The doubly charged and singly charged spectra of G are indeed extremely different.

The marked decrease of doubly charged ions in the spectrum of H as compared to G is similar to that of D as compared to A. There is a rather more intense molecular ion (m/e 96) as well as an intense $(M-15)^{++}$ peak, compared to the corresponding peaks in D relative to the respective singly charged molecular ions. The two additional alkyl groups in H could be responsible for this increase in intensity of the above two peaks. The doubly charged ion of m/e 74 can be attributed to a process involving the elimination of ethylene followed by the loss of a methyl group and a hydrogen (9). An alternative process involving the loss of an ethyl group followed by the loss of a methyl group (9a) cannot necessarily be ruled out. Regardless of which is the preferred path for the formation of m/e 74 the fact remains that H has a low abundance of doubly charged ions compared to G. This indicates that certain structural requirements have to be satisfied before a doubly charged ion can be formed in any significant amount. The presence of non-bonding

(9)



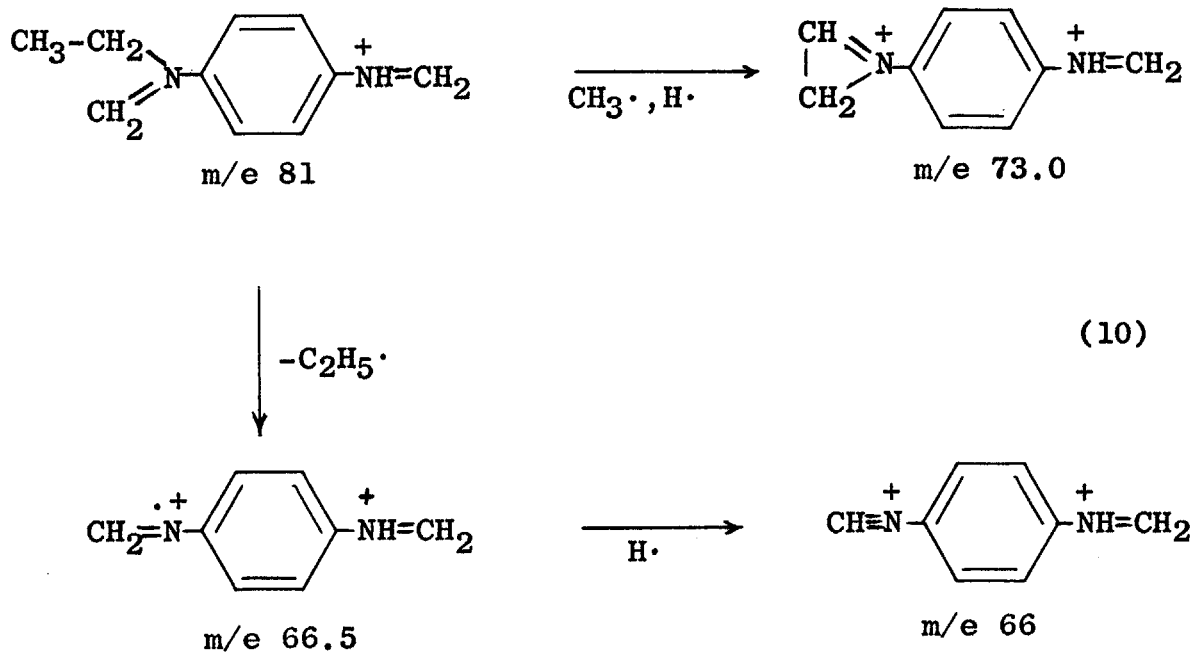
(9a)



electrons in two different positive centers, and the widest possible separation of charges seem to be important factors for the stabilization of a doubly charged ion.

Comparison of the spectrum of H with that of J in which doubly charged ions are remarkably abundant provides good support for these conclusions. The $(M-30)^{++}$ peak is more intense than the $(M-30)^{+}$ by a factor of approximately 8. The shift of this peak from 81 to 82 in the dideuterated molecule (Ja),

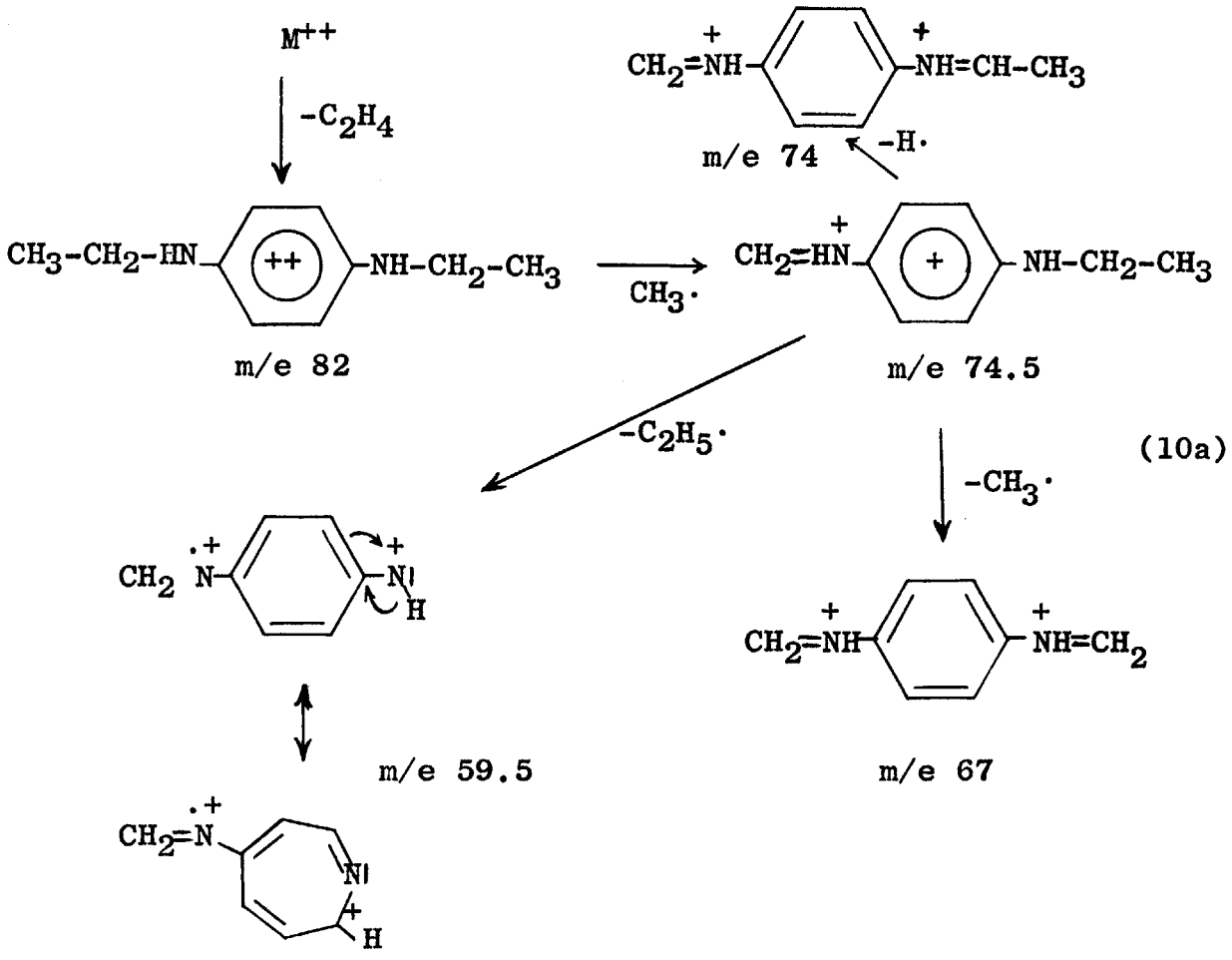
Fig. 7b, indicates that no methylene carbons are involved in the fragmentation that leads to the formation of this ion. The formation of the most intense doubly charged peaks of J can be represented by the following processes:



(10)

An alternative process to (10) would be the elimination of ethylene (10a), followed by a sequence of fragmentation such as that observed in A. The formation of the intense m/e 66 and m/e 73 peaks can certainly be explained by reaction (10).

In the first scheme (10) the odd electron species at m/e 66.5 can readily lose a hydrogen to form the stable fragment at m/e 66. The structure written for m/e 73 in the first scheme (10) possesses maximum separation of charges for best stabilization of the doubly charged fragment and hence its relatively high abundance.



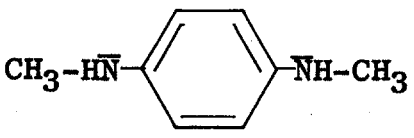
(10a)

It should be noted that the intensity of m/e 82 is very low but this would be in agreement with Fig. 3a (A). The spectrum of A (which is the species formed from J upon elimination of C_2H_4) exhibits also a very small peak at m/e 82 (=164/2) and a very intense one at m/e 67. Similarly the peak at m/e 74 is relatively intense in the spectra of both A and J and all this adds to the credibility of scheme 10a.

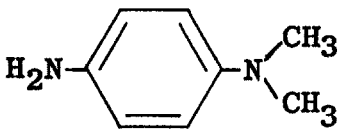
Isomers of Composition $C_8H_{12}N_2$

The formation of XVI, a fragment corresponding to $(M-16)^{++}$ in A, B, and C, involves the loss of a methyl

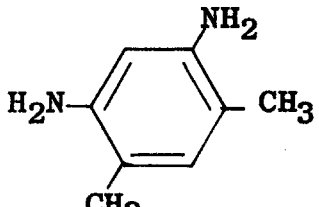
group (to give XXI) followed by loss of a hydrogen. This process is similar to the loss of two methyl groups from XIII to form the stable, even electron fragment XV. The latter proposed structure was verified by deuterium labeling experiments. The substitution of hydrogens for the methyl groups in A, B or C should give rise to a reasonably intense $(M-2)^{++}$ peak if indeed the cleavage of a C-H bond is a likely process. It was felt that this, along with the labeling experiments carried out previously, would provide sufficient evidence for the suggestion of structures such as XXI, etc. The isomers N,N'-dimethyl-p-phenylenediamine (K) and N,N-dimethyl-p-phenylenediamine (L) were therefore investigated. The isomeric 2,4-dimethyl-1,5-phenylenediamine (M) was also included in order to consider the possibility of formation of doubly charged ions in a molecule which has no C-C or C-H bonds adjacent to a nitrogen atom. The singly and doubly charged ion spectra for the above three isomers are given in Fig. 8.



K



L



M

Figure 8

Monoisotopic mass spectra of Isomers (K-M) of Composition $C_8H_{12}N_2$

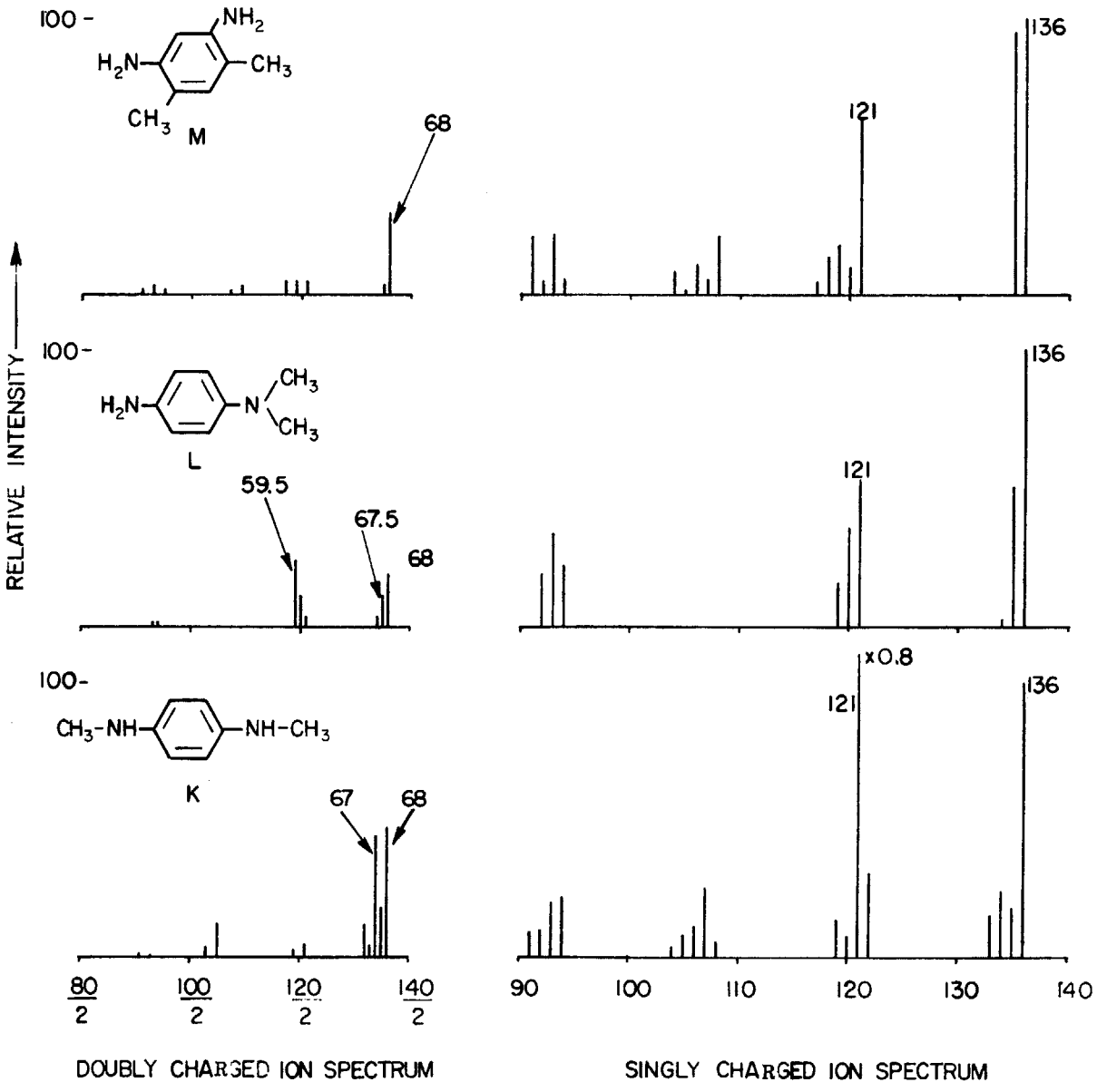
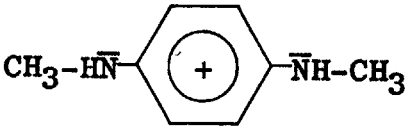
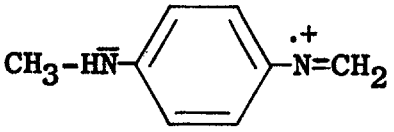

100 -
NH2
H2N
CH3
CH3
M
68
136
121
RELATIVE INTENSITY
100-
H2N
N
CH3
CH3
L
59.5
67.5
68
136
121
100-
CH3-NH
NH-CH3
K
67
68
x0.8
121
136
80/2
100/2
120/2
140/2
90
100
110
120
130
140
DOUBLY CHARGED ION SPECTRUM
SINGLY CHARGED ION SPECTRUM

FIGURE 8

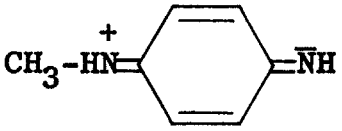
The singly charged ion spectrum of K exhibits four intense peaks at m/e 136, 134, 121 and 107. The following structures are proposed for these ions, in agreement with their elemental composition:



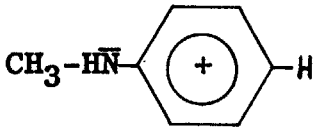
m/e 136



m/e 134

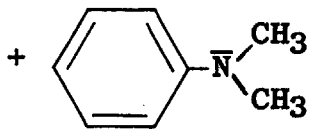


m/e 121



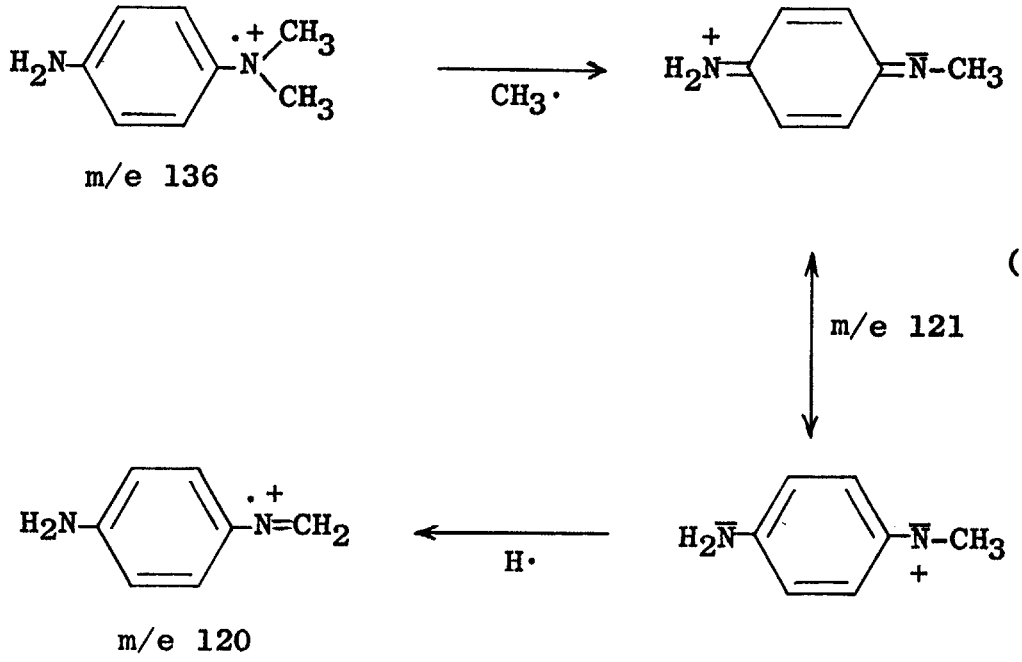
m/e 107

The corresponding asymmetric isomer (L) follows a slightly different pattern of fragmentation in the singly charged region. Its $(M-1)^+$ peak is 2.5 times more intense than that of K, while it has a very small $(M-2)^+$ peak. The peak at m/e 121 in L is also 2.5 times weaker than that in K, but the $(M-16)^+$ peak is quite pronounced. The latter peak, m/e 120, consists of two fragments $C_7H_8N_2^+$ and $C_8H_{10}N^+$ in a roughly 2 to 1 ratio. The $C_8H_{10}N^+$ ion corresponds to the loss of NH_2 (e.g. XXIX).



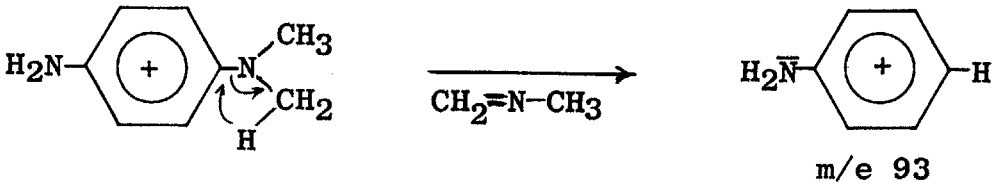
XXIX

The fragment $C_7H_8N_2^+$ can be rationalized by a process such as (11) whereby the loss of a methyl group from the



(11)

molecular ion produces the fragment at m/e 121 which can further lose a hydrogen atom to give the stable molecular ion-type fragment at m/e 120. Process (12) is the most likely path for the formation of m/e 93. Elimination of the neutral methyl methyleneimine molecule makes the



(12)

aniline-ion peak in L quite pronounced, more so than if it were to be formed by loss of a free radical.

TABLE X

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N'-dimethyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
136	47	100	$C_8H_{12}N_2$
135	18	19	$C_8H_{11}N_2$
134	45	24	$C_8H_{10}N_2$
133	5	15	$C_8H_9N_2$
132	12	<1	$C_8H_8N_2$
121	5	135	$C_7H_9N_2$
119	3	14	$C_7H_7N_2$
107	<1	25	C_7H_9N
105	12	8	C_7H_7N
103	4	<1	C_7H_5N
94	<1	22	C_6H_8N
93	<1	16	C_6H_7N
	<1	4	$C_5H_5N_2$
92	<1	9	C_6H_6N
91	1.5	8	C_6H_5N

TABLE XI

Relative Intensities of Selected Peaks in the Mass Spectrum of N,N-dimethyl-p-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
136	19	100	$C_8H_{12}N_2$
135	11	51	$C_8H_{11}N_2$
134	4	3	$C_8H_{10}N_2$
121	3.5	50	$C_7H_9N_2$
120	11	25	$C_7H_8N_2$
	<1	11	$C_8H_{10}N$
119	24	16	$C_7H_7N_2$
117	<1	<1	$*C_7H_5N_2$
	<1	<1	C_8H_7N
94	2.0	22	C_6H_8N
93	2.0	25	C_6H_7N
		9	$C_5H_5N_2$

* Most abundant species.

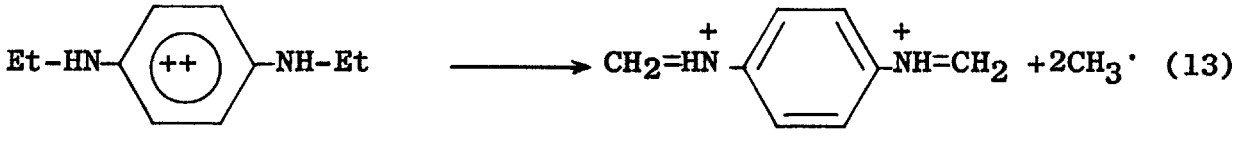
TABLE XII

Relative Intensities of Selected Peaks in the Mass Spectrum of 2,4-dimethyl-1,5-phenylenediamine

Mass	Doubly Charged	Singly Charged	Composition
136	29	100	$C_8H_{12}N_2$
135	3.0	95	$C_8H_{11}N_2$
121	5.0	64	$C_7H_9N_2$
119	2.5	<1	$C_7H_7N_2$
	2.5	18	C_8H_9N
117	5.0	5.0	C_8H_7N
109	3.5	<1	$C_6H_9N_2$
108	2.0	22	$C_6H_8N_2$
107	1.8	7.0	C_6H_7N
95	2.0	4.0	$C_5H_7N_2$
93	3.5	22	C_6H_7N
91	2.0	21	C_6H_5N

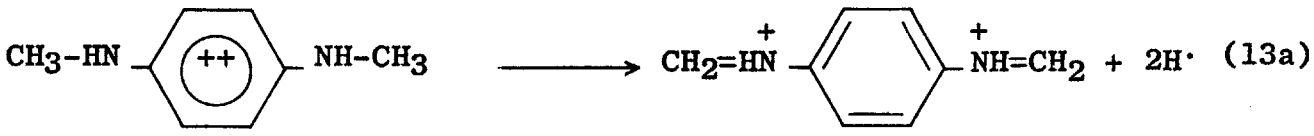
As expected the amount of fragmentation in M is quite low. The molecular ion peak is the most intense one, but the large number of labile hydrogens present makes the $(M-1)^+$ peak almost equally as intense. The loss of a methyl group gives rise to the m/e 121 peak.

The difference in the doubly charged ion spectra of K and L can be compared to that between A and D. Compound K, for instance, has an intense $(M-2)^{++}$ peak at m/e 67 whereas the $(M-2)^{++}$ peak in L is about ten times weaker. This can be compared to the situation in A and D where the $(M-30)^{++}$ ion is thirty times more abundant in the former. The fact that the relative ratio of the $M^{++}/(M-2)^{++}$ in K is almost 1:1 as compared to a 1:15 ratio between $M^{++}/(M-30)^{++}$ in A can be attributed to the higher energy required for the cleavage of a C-H bond than for a C-C bond. Another reason for the difference may be the relative free energy difference between the two processes 13 and 13a which will partly depend on the difference in stability between a methyl and a hydrogen radical. The stepwise loss of two



(13)

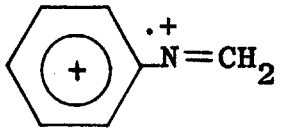
m/e 67



(13a)

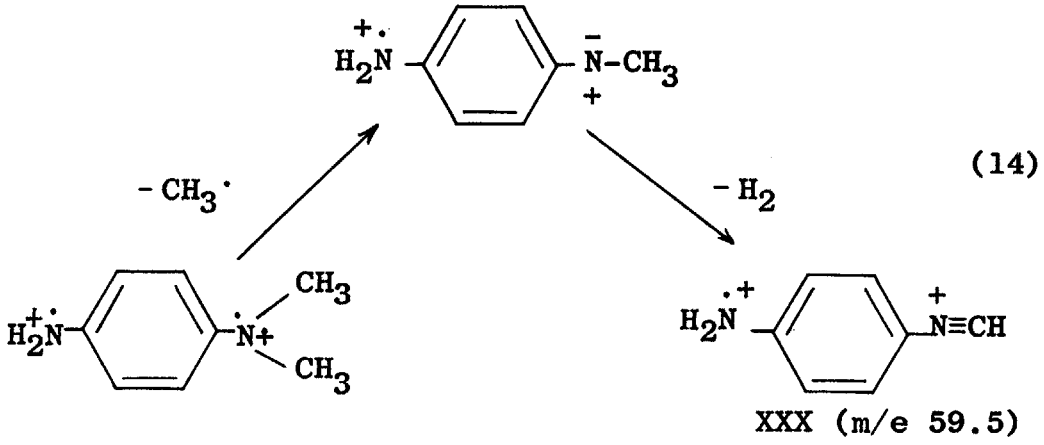
m/e 67

more hydrogens from m/e 67 (13a) gives rise to the peaks at m/e 66.5 and m/e 66. The intense peak at m/e 52.5 was found to correspond to $C_7H_7N^{++}$. A possible structure for that is given below:



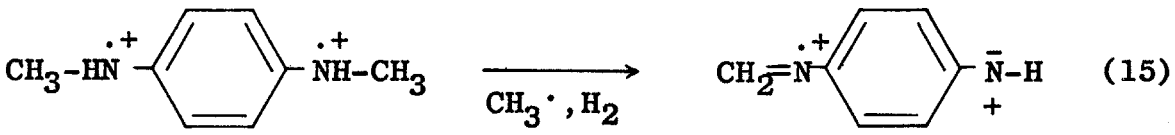
m/e 52.5

The most abundant doubly charged ion of L occurs at m/e 59.5. It is interesting to recall that in N,N-diethyl-p-phenylenediamine (D) m/e 59.5 was also the most intense doubly charged peak. The best rationalization would be process (14) in which a fragment XXX is formed with a maximum



XXX (m/e 59.5)

(14)



(15)

separation of charges. The same process in the case of K would give rise to an ion with electron deficient nitrogens and hence the smaller intensity of the m/e 59.5 peak.

The doubly charged ion spectrum of M has only one peak of importance, that of its molecular ion. As predicted from its structure, this molecule offers no way by which it could form a fragment ion particularly capable of supporting two positive charges.

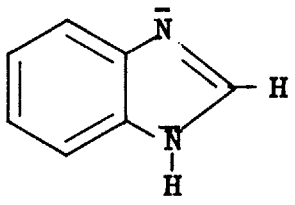
The spectra of all compounds following E were determined after the Faraday detector in the mass spectrometer was replaced by a wien -filter and electron multiplier, a combination which filters out metastable peaks (except apparently when a hydrogen atom loss is involved). There is therefore no evidence of any metastable peaks due to the fragmentation of doubly charged ions in the spectra of compounds following E except for the loss of hydrogen. The formation of fragment XII in K corresponds to the loss of two hydrogen atoms. There is sufficient evidence of a metastable peak at m/e 66.5 corresponding to the process:

$$67.5 \xrightarrow{m^{*}=66.5} 67$$

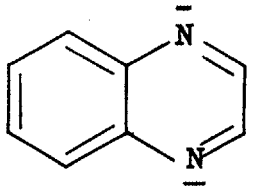
Although the above evidence does not eliminate the possibility of a single step process for the elimination of two hydrogens from m/e 68 (M^{++}), most of the evidence available points towards a stepwise loss of hydrogens or methyl groups from K or A respectively, for the formation of XII.

6π Electron Systems and Stabilization of Doubly Charged Ions

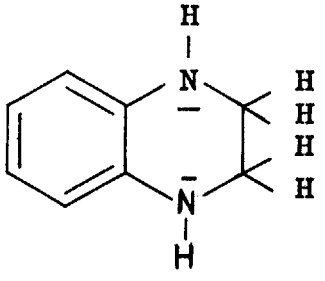
It was found during the study of the N,N' - dialkyl-p- phenylenediamines that the formation of an even electron fragment ion helps stabilize a doubly charged ion. If the electronic conformation of an ion is indeed such an important factor for the best stabilization of a doubly charged species, then it should be expected that the possibility of formation of a stable 6π electron system upon the loss of two electrons as such, or followed by loss of two radicals or a neutral molecule, from an ionized molecule should increase the abundance of the corresponding doubly charged ion at sufficiently high bombarding electron voltages. The following three systems were selected to substantiate the above assumption: β - benzimidazole (N), quinoxaline (O) and 1,2,3,4-tetrahydroquinoxaline (P).



N

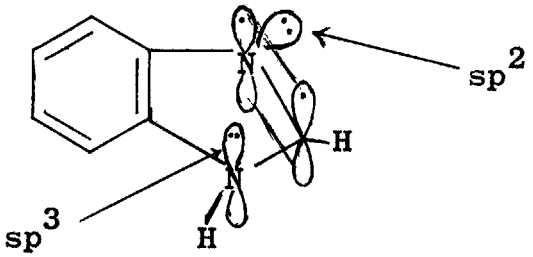


O



P

β-Benzimidazole contains a highly conjugated 6π electron system as evidenced by its resistance to any reduction of the benzimidazole nucleus by reducing agents such as sodium amalgam or zinc+hydrochloric acid.[14] Double ionization of this molecule will probably involve either the loss of 2π electrons and/or the two non-bonding electrons of the sp^2 nitrogen or both. In either



case, however, the 6π system will remain intact because if two π electrons are lost there are two sp^2 electrons available from the nitrogen to participate in ring resonance and hence help stabilize the doubly charged molecular ion. Significant fragmentation of the doubly charged molecular ion is not expected and Fig. 9a does indeed indicate an M^{++} peak of an intensity 15% of M^+ (m/e 59) and the only other intense doubly charged peak observed at m/e 44.5 is less than 3% of M^+. A strong π system therefore enhances the stability of the doubly charged molecular ion.

A similar situation prevails in quinoxaline (O) where the loss of two electrons does not disrupt the 6π system and the doubly charged molecular ion, m/e 65, is quite abundant (37% of M^+). It is important to notice that there is no evidence for appreciable loss of hydrogen or hydrogens to

Figure 9

Mass spectra of

(a) Benzimidazole (N)

(b) Quinoxaline (O)

(c) 1,2,3,4-tetrahydroquinoxaline (P)

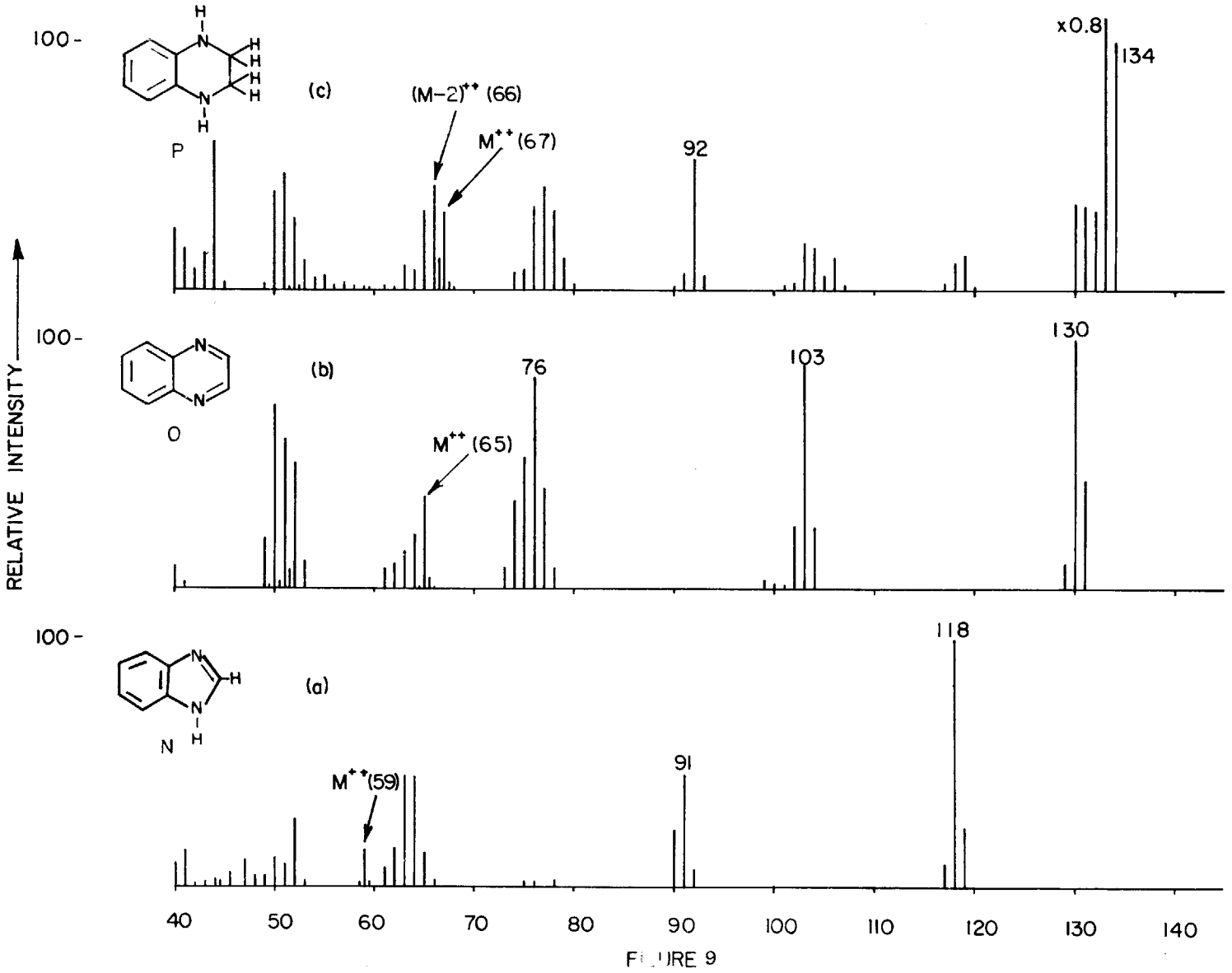
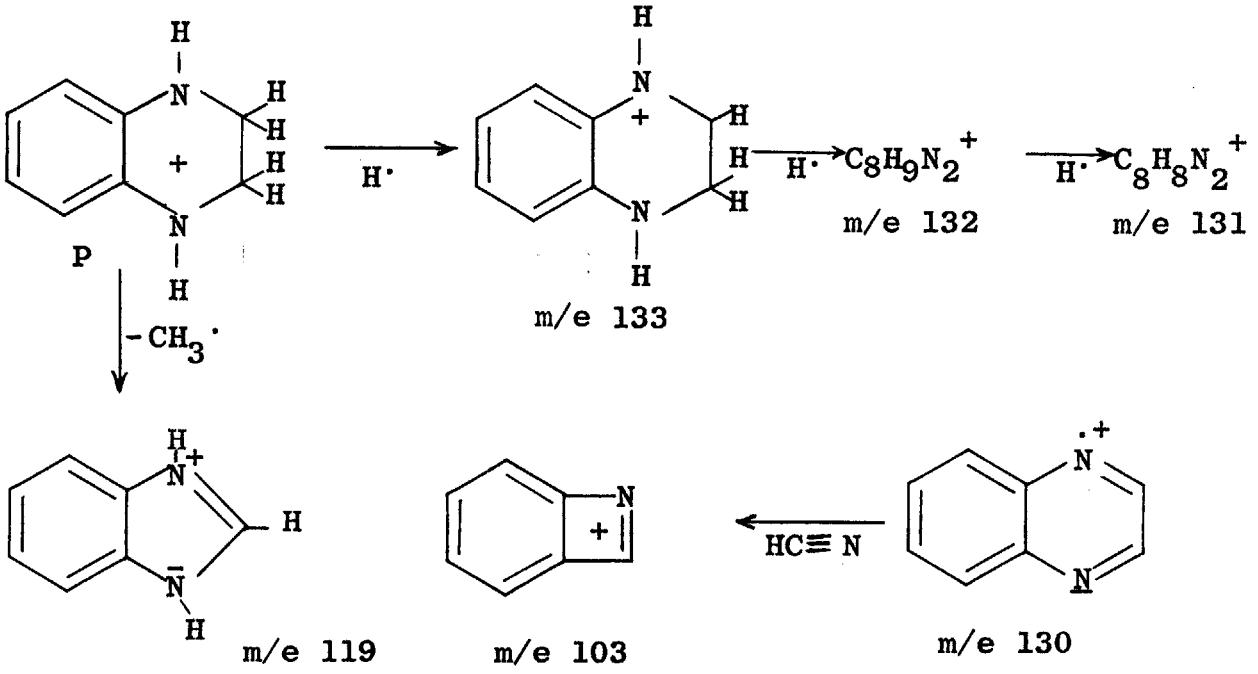

100-
(c)
P
(M-2)++ (66)
M++ (67)
92
x0.8
134
100-
(b)
O
76
M++ (65)
103
130
100-
(a)
N
M++ (59)
91
118
RELATIVE INTENSITY
40
50
60
70
80
90
100
110
120
130
140

FIGURE 9

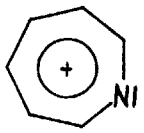
give rise to a peak at $(M-1)^{++}$ or $(M-2)^{++}$.

In line with the mass spectra of heterocyclic compounds containing only one nitrogen atom[7] both N and O exhibit peaks due to the ion $(M-HCN)^{+}$ at m/e 90 and 103, respectively.

The fragmentation pattern of singly charged 1,2,3,4-tetrahydroquinoxaline (P) can be pictured by the formation of the following ions:



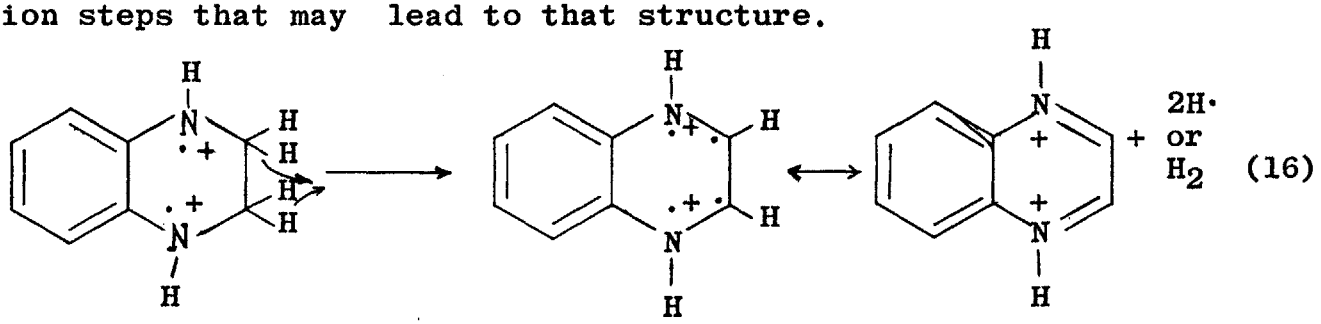
Finally the peak at m/e 92 can be interpreted by the formation of the resonance stabilized azotropylium ion $C_6H_6N^+$. The loss of a methyl group from the molecular



ion (m/e 134) to give the peak at m/e 119 is rather unexpected. This type of fragmentation, however, is

apparently quite common and is found also in the oxygen analog, ethylene catechol diether which forms an abundant ion of mass 121. Details of this process will be discussed later in connection with the fragmentation pattern of polymethylene catechol diethers. It may be also recalled that the same fragment (VIII) was observed in the spectrum of N,N'-diethyl-o-phenylenediamine (C).

The doubly charged molecular ion of P is relatively abundant (21% of M^+) but as might be expected it is significantly less abundant than the M^{++} ion of quinoxaline which is stabilized by the formation of a 6π electron system. As stated previously the doubly charged ion of O does not favor further loss of hydrogens and its $(M-1)^{++}$ and $(M-2)^{++}$ peaks are very weak. The loss, however, of two hydrogens from M^{++} of P (16) would lead to a similarly stable 6π electron system to give $(M-2)^{++}$. The peak indeed at m/e 66 is 39% of M^+ (see Table XIII) or almost twice as intense as its corresponding M^{++} ion. It is obvious that if it is possible for a doubly charged ion to attain a stable electronic conformation then it will undergo the necessary fragmentation steps that may lead to that structure.



(16)

P XXXI

TABLE XIII

Relative Intensities of Selected Peaks in the Mass Spectrum of 1,2,3,4-Tetrahydroquinoxaline

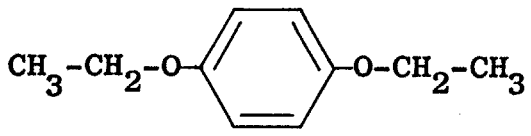
Mass	Doubly Charged	Singly Charged	Composition
134	21	100	$C_8H_{10}N_2$
133	7	135	$C_8H_9N_2$
132	39	33	$C_8H_8N_2$
131	<1	35	$C_8H_7N_2$
130	10	35	$C_8H_6N_2$
105	3.0	10	C_7H_9N
103	1.5	19	C_7H_7N
92	<1	52	C_6H_6N

The $(M-2)^{++}$ ion in P can be compared to the formation of the same ion in N,N'-dimethyl-p-phenylenediamine (K). The loss of two separate atoms in K is the only possible path for the formation of the $(M-2)^{++}$ ion. On the other hand, the proximity of the hydrogens in P makes it plausible that the elimination of a hydrogen molecule instead of two hydrogen atoms may take place. This and the attainment of a stable 6π ring structure may tend to overcome the charge repulsion in P which might arise due to the larger proximity of the positive centers (in analogy to C), and hence the still slightly larger $(M-2)^{++}/M^{++}$ ratio in the spectrum of P as compared with K.

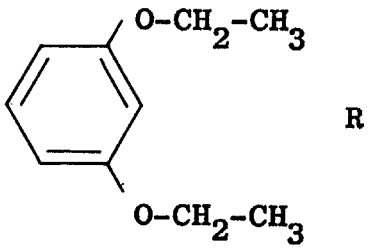
The Mass Spectra of Oxygen Analogs

Isomeric Diethoxy Benzenes

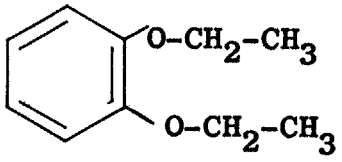
Since the foregoing investigation of mass spectra of isomeric polyalkyl phenylenediamines revealed a significant role of the nitrogen atoms in the formation of doubly charged ions, an effect which was shown to be related to the presence of the free electron pairs on nitrogen, it was thought worthwhile to see to which extent this effect is operating with other hetero atoms. The oxygen analogs of A, B and C, <u>para</u>-, <u>meta</u>- and <u>ortho</u> diethoxy-benzene (Q, R and S) were chosen for this purpose and their mass spectra are shown in Fig. 10.



Q



R

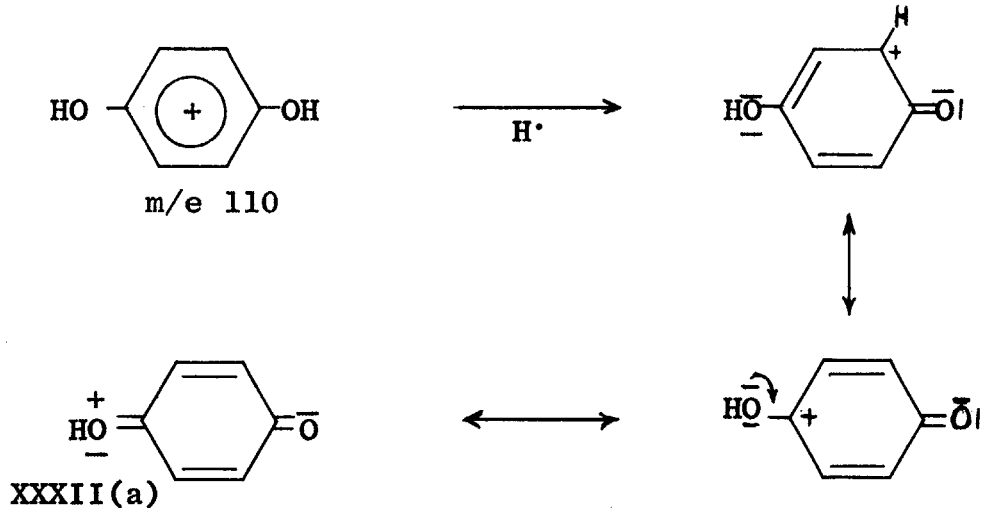


S

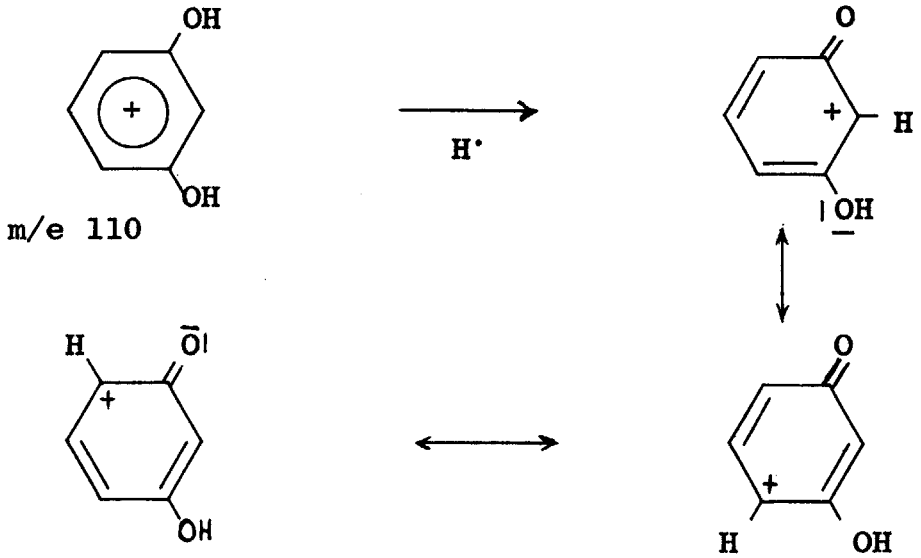
Surprisingly, only traces of doubly charged $(M-30)^{++}$ ions are found in the spectra of these compounds as compared to 67% of M^{+} in A. The total amount of doubly charged

ions is due to the higher electron affinity of oxygen atoms and as a result of that much higher bombarding electron energies would have to be employed if more than one electron is to be removed from the molecule. At bombarding energies of 90 e.v. in fact no significant increase in doubly charged ions was observed.

The singly charged ion spectra of the three diethoxy



(17)



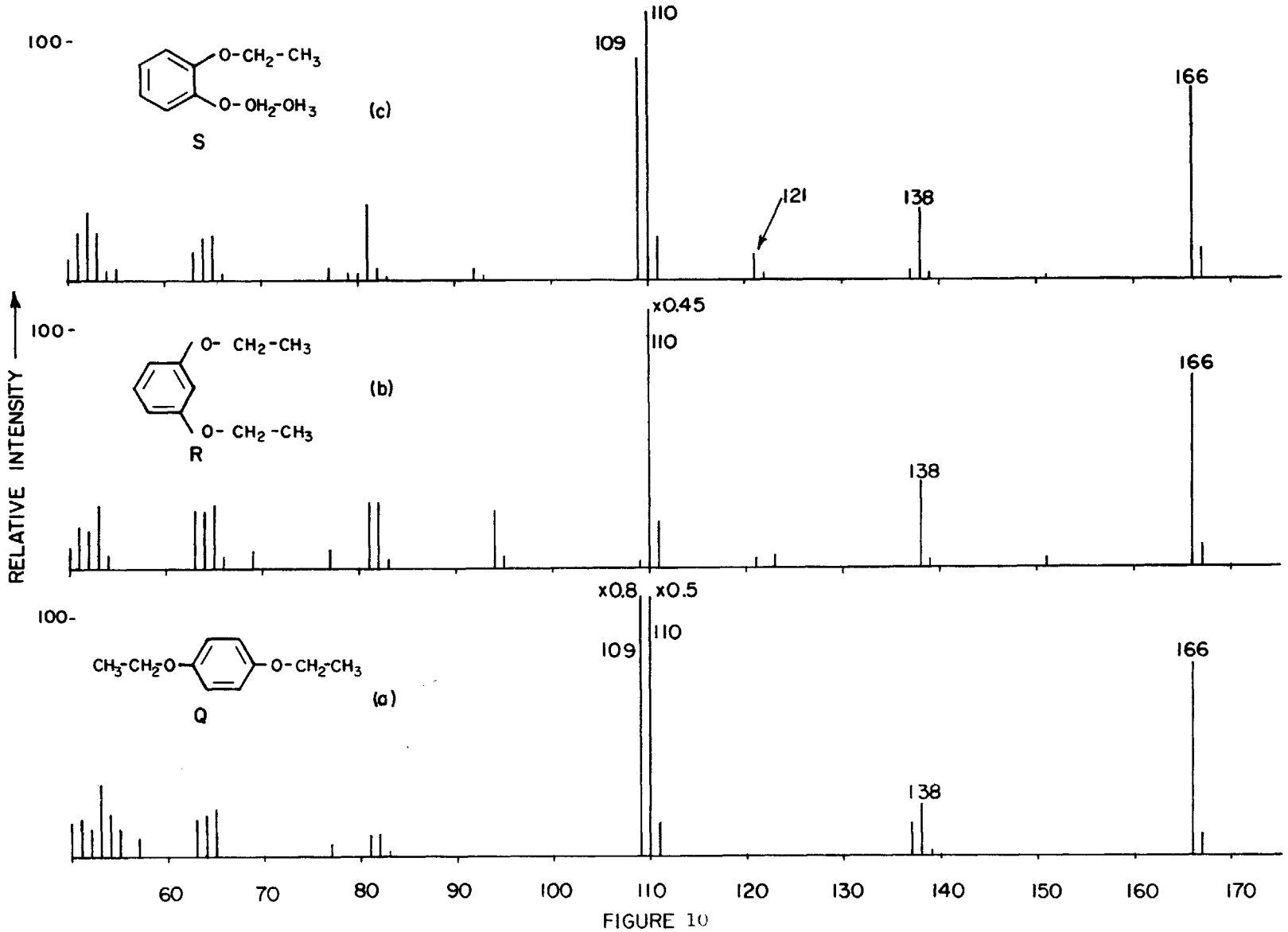
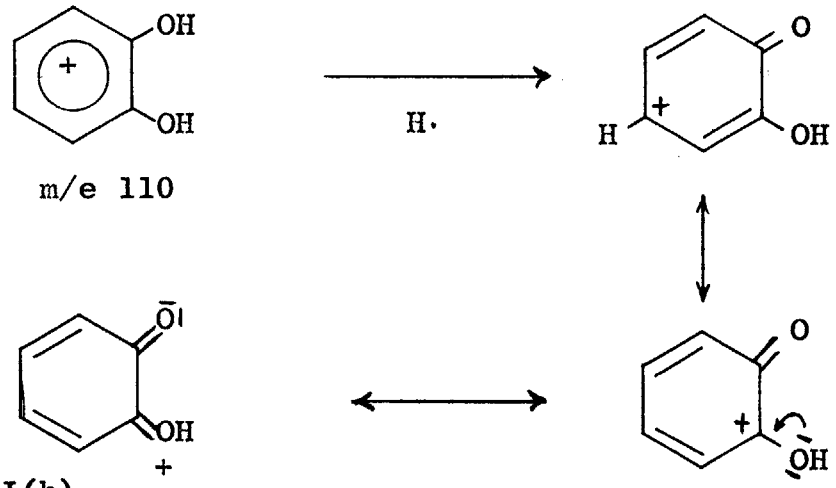

100-
O-CH2-CH3
O-CH2-CH3
S
(c)
109
110
121
138
166
RELATIVE INTENSITY
100-
O- CH2-CH3
O- CH2-CH3
R
(b)
x0.45
110
138
166
100-
CH3-CH2-O
O-CH2-CH3
Q
(a)
x0.8
x0.5
109
110
138
166
60
70
80
90
100
110
120
130
140
150
160
170

FIGURE 10

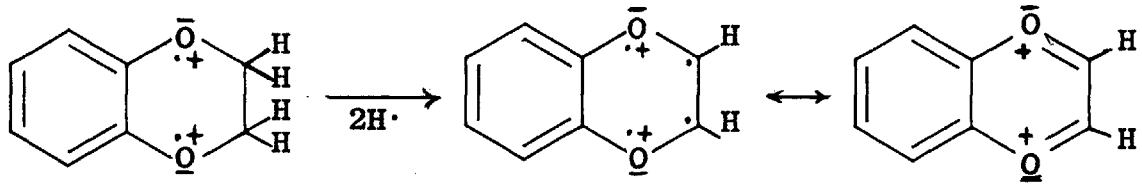


XXXII(b)

isomers are remarkably similar, the main fragments in each case coming from the elimination of two molecules of ethylene from the molecular ion to give catechol cation (m/e 110). Significant is the absence of an ion of mass 109-due to the loss of a hydrogen from catechol ion-in the meta isomer, a very abundant ion in the ortho-and para- structures. The resonance structures in (17) offer the best explanation for this difference. A resonance structure such as XXXII (a) or (b) in which the positive charge density is adjacent to an oxygen cannot be written for the meta isomer. The oxygen electrons in the para and ortho isomers can stabilize the m/e 109 fragment but are not in a position to do so in the meta-diethoxy benzene. Finally the weak peak at m/e 121 in the ortho isomer should be pointed out. This is comparable to the m/e 119 fragment observed in N,N'-diethyl-o-phenylenediamine (C) and 1,2,3,4-tetrahydroquinoxaline (P). It will be discussed in detail in the following section.

Polymethylene Catechol Diether Derivatives

In an attempt to compare the fragmentation pattern of 1,2,3,4-tetrahydroquinoxaline (P) to its oxygen analog, the mass spectrum of ethylene catechol diether (U) was determined. It was expected that the oxygen analog would exhibit a doubly charged $(M-2)^{++}$ ion XXXI(a) corresponding to XXXI, but the amount of m/e 67 formed was less than 1% of M^{+}, while the M^{++} peak at m/e 68 for U is 7% of M^{+}.

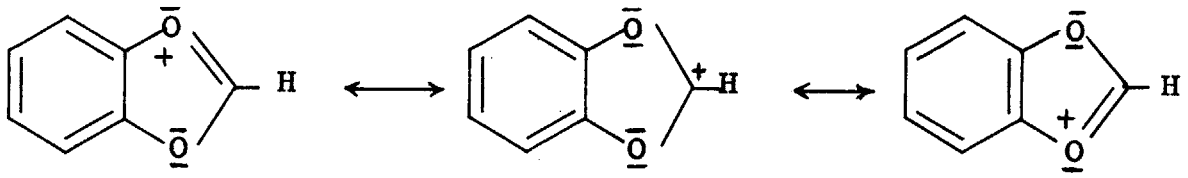


XXXI(a) (16a)

This is significantly less than the amount of double ionization observed in P by a factor of at least 40 in the case of $(M-2)^{++}$ and a factor of 4 in the case of M^{++} in terms of their respective singly charged molecular ions. This certainly corroborates the general observation that oxygen compounds do not stabilize positive charges as well as their nitrogen containing counterparts.

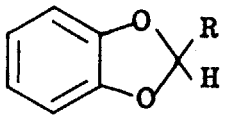
While the oxygen analogs thus exhibit a surprising lack of tendency to form doubly charged ions, a few aspects of the mass spectrum of U indicated the occurence of a number of interesting fragmentation processes. Their further investigation seemed to be of importance not only for the interpretation of the spectra of such compounds but also

for a study of the mechanisms of fragmentation of such cyclic aryl-alkyl ethers. It was noted, for example, that one of the major peaks of the spectrum of U, a compound which does not contain any methyl groups, appears at m/e 121 corresponding to the loss of a CH_3-group from the molecular ion to form the stable fragment $C_7H_5O_2^+$.

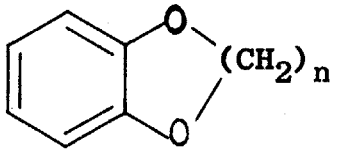


XXXIII m/e 121

Structure XXXIII, an ion in which the positive charge is stabilized by two adjacent oxygens, is suggested. In order to explore the generality of this process, which could conceivably lead to confusion with catechol acetals,

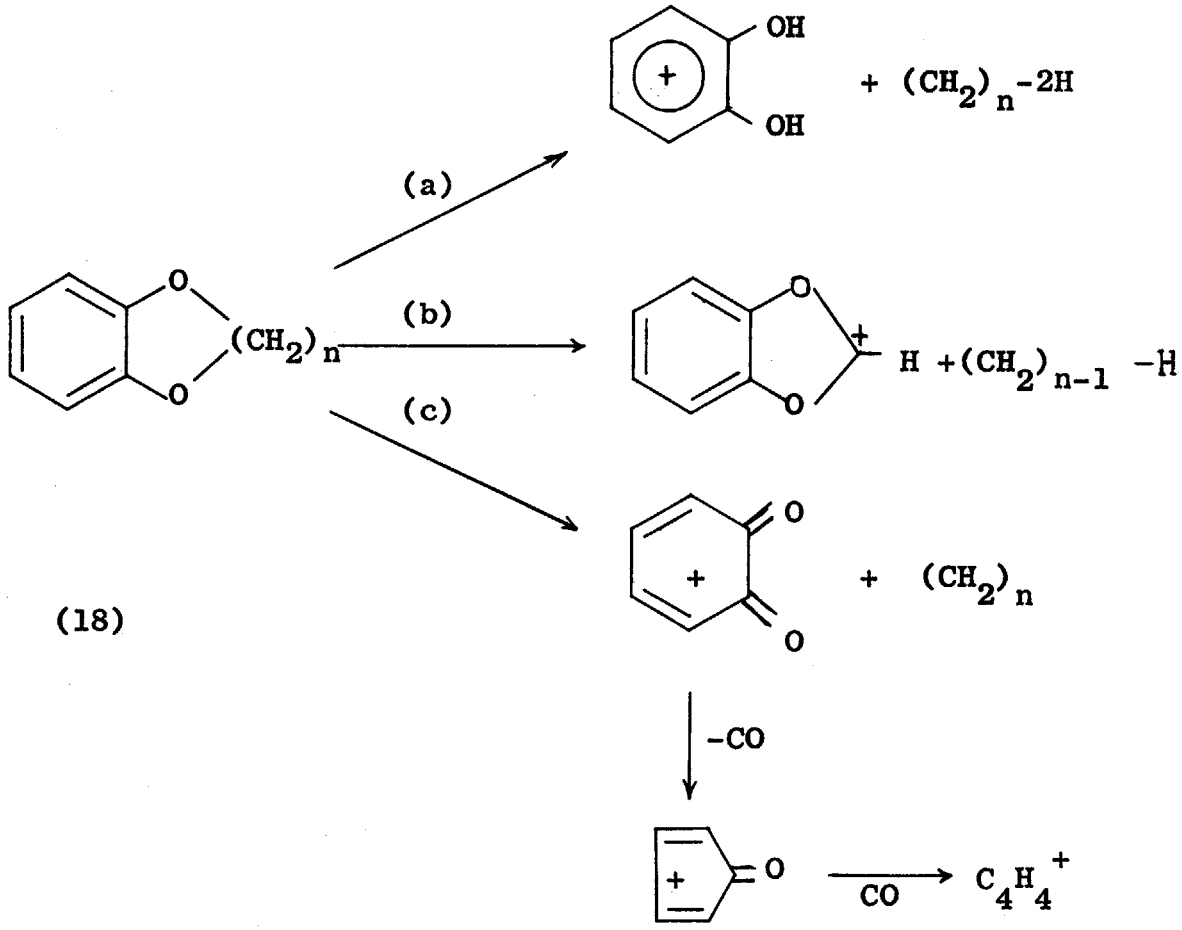


and to elucidate the mechanism of this ring contraction, the homologs T through Y were studied.



T	n=1	W	n=4
U	n=2	Y	n=5
V	n=3		

Three processes seem to be predominant in the fragmentation of these catechol diether ring compounds (Fig.11) and each one seems to depend on the size of the ether ring. Process 18(a) seems to be the predominant one when the ether ring is large. Note, for example, the relative increase of m/e 110 in the sequence U<V<W<Y. On the other hand, the formation of XXXIII (m/e 121) via 18(b) will depend on the proximity of an α-carbon to the second oxygen. The metastable



(18)

peak at m/e 120 in R and W indicates that XXXIII is preceded by m/e 122 (T^+) which subsequently loses a hydrogen radical to give m/e 121. This is quite evident in V and W where the

Figure 11

Mass Spectra of

(a) Catechol methylene diether (T)
(b) Catechol ethylene diether (U)
(c) Catechol trimethylene diether (V)
(d) Catechol tetramethylene diether (W)
(e) Catechol pentamethylene diether (Y)
(f) 2-n-propyl-1,3-benzodioxole (Z)

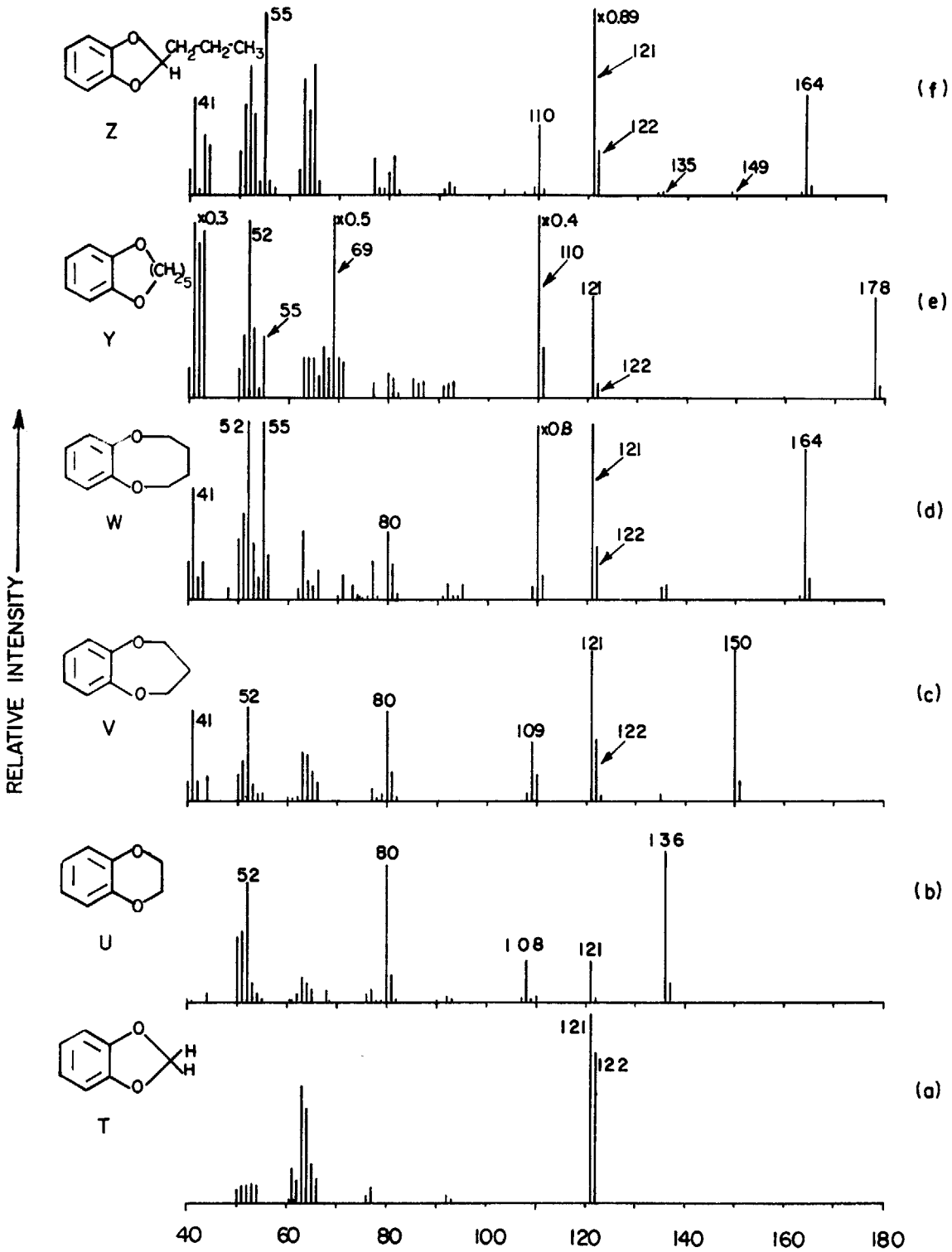
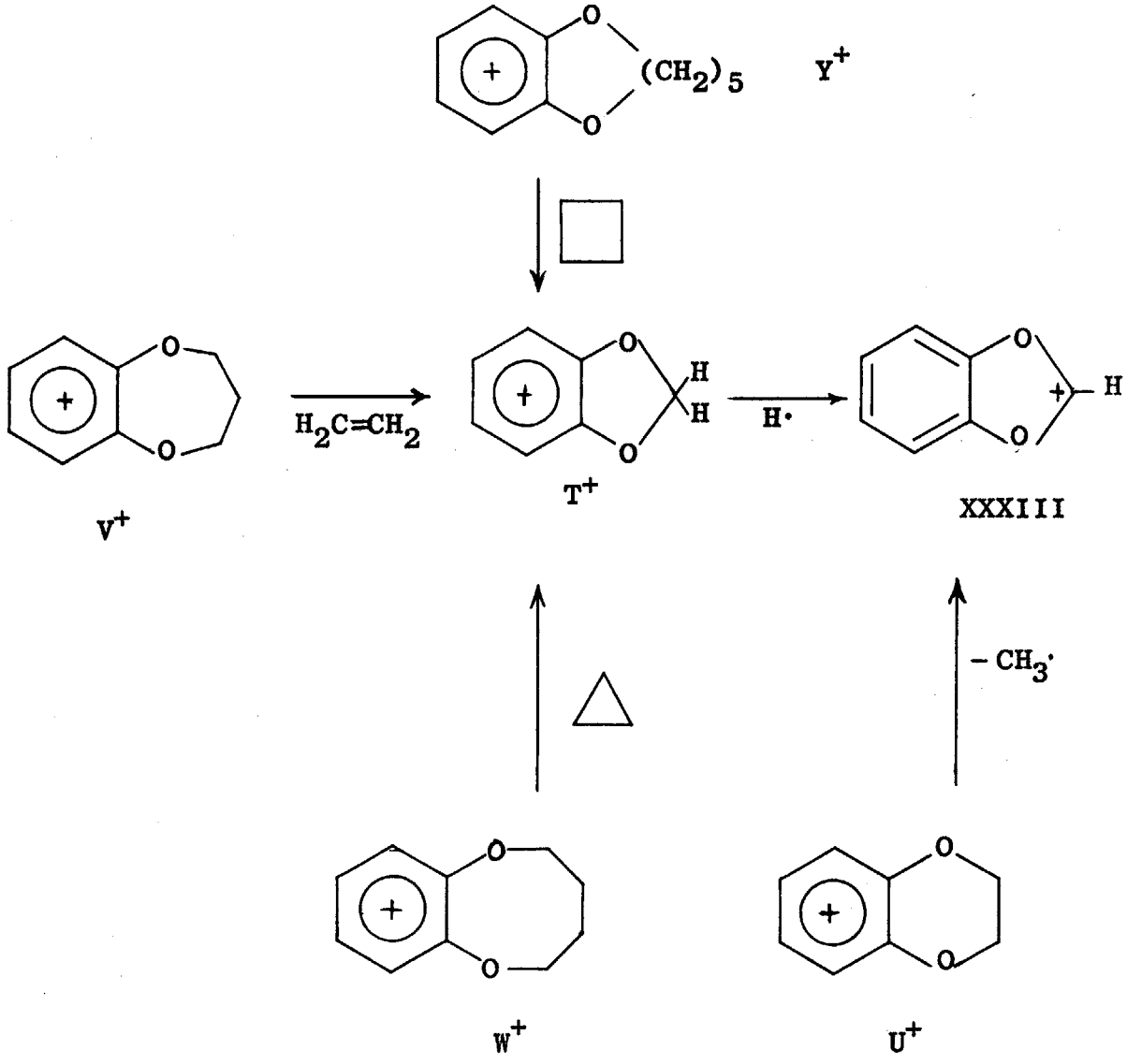

RELATIVE INTENSITY
Z
Y
W
V
U
T
(f)
(e)
(d)
(c)
(b)
(a)
55
x0.89
121
164
41
110
122
135
149
x0.3
52
x0.5
69
x0.4
110
121
178
55
122
52
55
x0.8
121
164
41
80
122
121
150
52
80
41
109
122
136
80
52
108
121
121
122
40
60
80
100
120
140
160
180

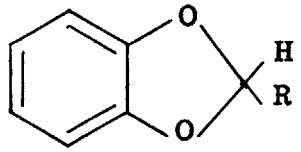
FIGURE 11

intensity of m/e 122 is quite high (much higher than the isotope peak of m/e 121), but as the distance between the α-carbon and the opposite oxygen increases again-e.g. in Y-mass 122 is mainly the isotope peak of m/e 121 and the metastable peak at m/e 120 is hardly detectable. The following scheme indicates the most probable neutral species eliminated prior to the formation of m/e 121 from m/e 122 in the above catechol diether derivatives:



The above scheme quite adequately describes process 18(b) for the catechol diether homologs. Labeling experiments to be discussed later in greater detail, indicate that- at least in the case of W- only the two α-carbons are involved in the formation of the m/e 121 fragment.

The mass spectra of the five compounds T-Y contain features which one might expect from an α-alkyl substituted methylene catechol diether Z(a). Especially the loss of a methyl group from U is certainly quite unusual and it becomes therefore necessary to investigate the possibility

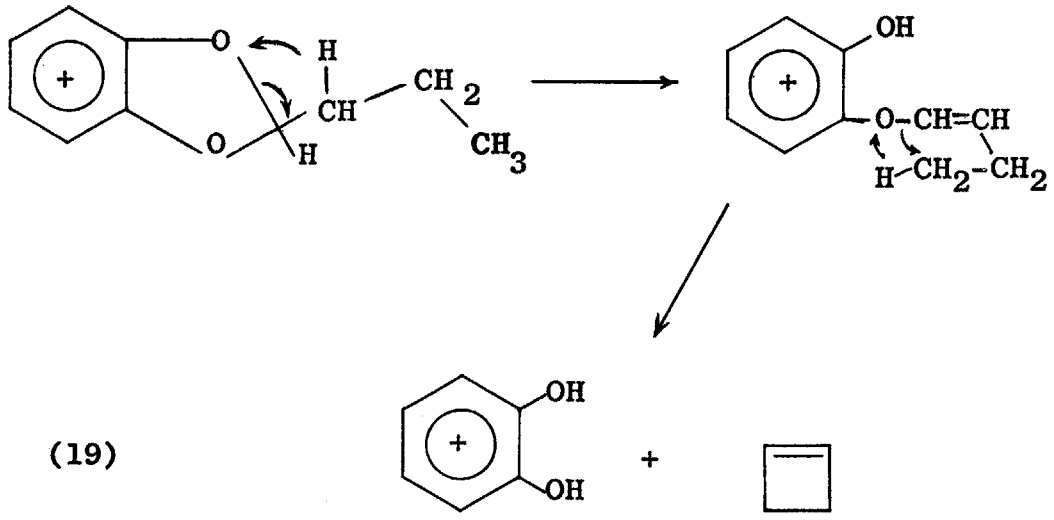


Z(a)

of a molecular rearrangement to form a species of the form of Z(a) upon electron impact. The mass spectrum of 2-n-propyl-1,3-Benzodioxole (Z)-isomer of W-was therefore determined. In contrast to Fig. 11(d) the peak at m/e 121 is the by far most intense one in the spectrum of Z (Fig. 11(f)). In addition the peak at m/e 122 is only 16% (half of which is ^{13}C contribution) of that at m/e 121 as compared to 28.5% in W. These differences express the fact that the $C_7H_5O_2$ ion is formed by simple cleavage of a C-C bond next to two ether oxygens in Z while its formation from W requires rearrangement of bonds prior to loss of hydrogen. The absence of a metastable peak at m/e 120 is a further indication for the formation of m/e 121 <u>via</u> the direct loss of a

n-propyl group. A small amount of $(M-15)^+$ and $(M-29)^+$- m/e 159 and m/e 135 respectively- is observed but the same ions are absent in W. The absence of these peaks in W does not necessarily eliminate the possibility of a rearrangement to Z, but this data in combination with the absence of a metastable peak at m/e 120 and the low abundance of m/e 122 in Z indicate that it is rather unlikely that the formation of the m/e 121 ion in these catechol diether derivatives proceeds <u>via</u> a rearrangement to a structure like Z(a).

The appreciable abundance of the catechol ion (m/e 110) in Z is rather surprising although its formation is by no means impossible. (See e.g. (19)).



(19)

The retention of the positive charge on the hydrocarbon part of the fragment in (19) would account for the intense m/e 55 peak in Z which is also observed in W. The m/e 52

ion corresponds to $C_4H_4^+$ in both cases.

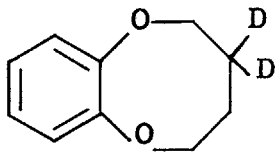
Process 18(c) is quite likely to occur in a retro-Diels Alder type fashion as indicated below, which is

certainly a favorable path for n=0 or n=1. The ortho-quinone cation in U is indeed quite abundant since it was formed by elimination of the neutral ethylene molecule. The stepwise loss of two carbon monoxide molecules from m/e 108 produces the fragments at m/e 80 (cyclopentadienone cation) and m/e 52 $(C_4H_4)^+$ - possibly cyclobutadiene cation or some other highly unsaturated species). Elimination of cyclopropane from V gives again m/e 108, but at this point the molecule has also the tendency to eliminate a stable allyl radical (CH_2=CH-CH_2·) to give a protonated orthoquinone ion (m/e109). In the larger homologs process 18(c) plays no important role and 18(a) and 18(b) become more significant. The possible mechanisms of formation of the m/e 121 and m/e 110 peaks are discussed in the next section of labeled derivatives of W. It should be kept in mind that the intense peaks at m/e 41 in V, m/e 55 and m/e 41 in W and m/e 69, 55 and 41 in Y are all hydrocarbon peaks due to retention of the charge in the hydrocarbon part of the ether ring. It

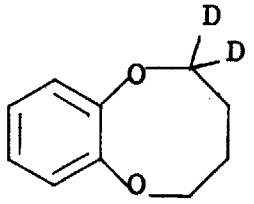
is evident that the cleavage of a C-O bond is involved at some point during the fragmentation-probably the catechol ion formation-of these homologs.

Deuterium Labeled Tetramethylene Catechol Diethers

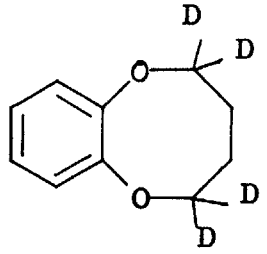
The two most important ions in the spectra of the catechol diether derivatives are undoubtedly those at m/e 110 and at m/e 121. In order to gain a better understanding of the mechanism of their formation it was decided to determine the mass spectra of deuterium labeled tetramethylene catechol diether (W), β-di-D-tetramethylene catechol diether (Wa), α-di-D-tetramethylene catechol diether (Wb) and α,α'-tetra-D-tetramethylene catechol diether (Wc), and compare them with those of the unlabeled molecule W. The compounds were prepared by condensation of the correspondingly labeled diols with catechol.



Wa



Wb



Wc

The formation of the m/e 121 ion (XXXIII) in these catechol diether derivatives is quite likely to involve participation of the α-carbon in a trans-annular fashion[20] preceding or following the cleavage of the opposite C-O bond. This was further proved by the absence of any peak

Figure 12

Mass Spectra of

(a) Catechol tetramethylene diether (W)
(b) β-di-D-Catechol tetramethylene diether (Wa)
(c) α-di-D-Catechol tetramethylene diether (Wb)
(d) α,α'-tetra-D-Catechol tetramethylene diether (Wc)

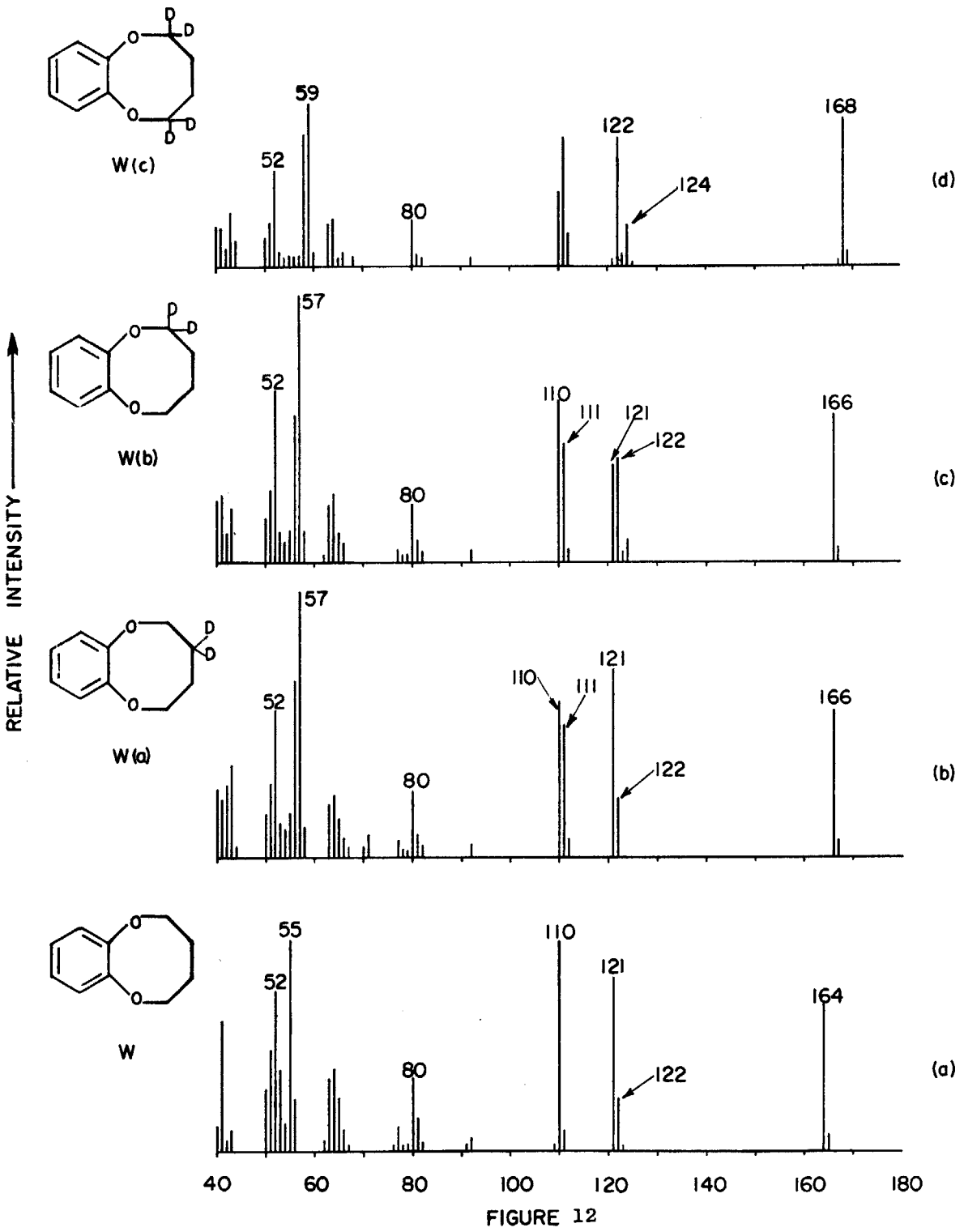
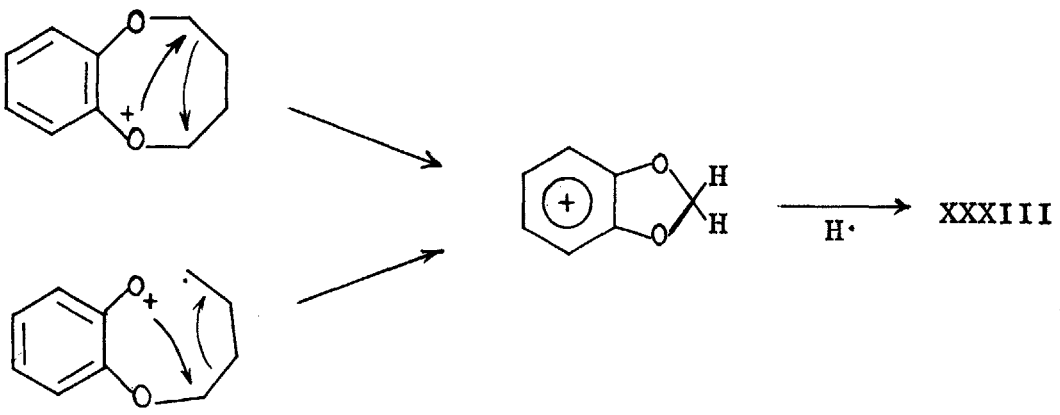

W(c)
59
52
80
122
124
168
(d)
W(b)
57
52
80
110
111
121
122
166
(c)
W(a)
57
52
80
110
111
121
122
166
(b)
W
55
52
80
110
121
122
164
(a)
RELATIVE INTENSITY
40
60
80
100
120
140
160
180

FIGURE 12

at m/e 122 in Wa, and the presence of the m/e 122 and m/e 124 peaks in Wc and the doublet at m/e 121 and m/e 122 in Wb. Careful measurement of the m/e 121 to m/e 122 ratios at various electron energies were made for all four compounds (W,Wa,Wb and Wc) in the presence of an internal



(20)

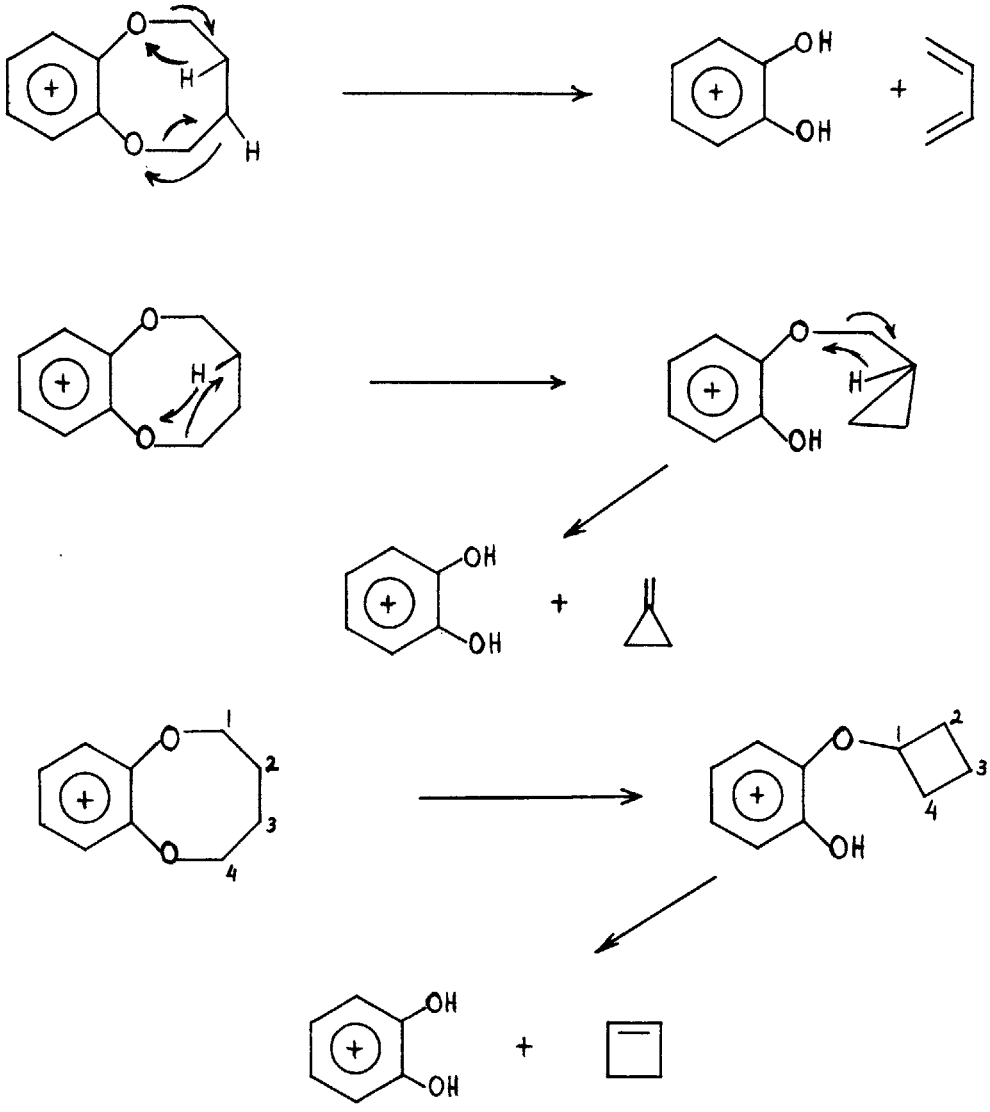
standard (xylene). Tables XIV-XVII give the abundances of the catechol and XXXIII ions relative to their respective molecular ions for compounds W-Wc. The consistency of the ratios of m/e 106 to m/e 105 of xylene is a good means for comparison of the different compounds at the same ionizing voltages.

It is interesting to note that the intensity of the m/e 122 peak in W increases from 28.4% of m/e 121 at the highest voltage (50 e.v.) to 30% of m/e 121 (20 e.v.) up to 56% of m/e 121 (13.5 e.v.). Obviously the energy available in the m/e 122 ion for the removal of the hydrogen atom is insufficient at the lower ionizing voltages. On the other hand, it is interesting to compare the relative ease of loss of deuterium vs. hydrogen in the labeled isomers Wb and Wc.

At the voltage where the $M^+/(M-1)^+$ ratio in xylene is 100:32 the ratio of the intensities of m/e 122/ m/e 121 in W and Wa is 32.4:100 and 30.4:100 respectively, after correction for ^{13}C isotopic contribution. The slight discrepancy may be due to some isotope scrambling in the case of Wa. The ratio, however, of the intensities of m/e 124/ m/e 122 corresponding to the cleavage of a C-D bond to give the deuterated XXXIII ion is 38:100 and 50:100 in Wc and Wb respectively. The preference for retention of deuterium over hydrogen is quite remarkable if it is also borne in mind that the ionizing voltages employed are quite high. This isotopic effect is also quite evident even at a bombarding voltage of 70 e.v. (Fig.12).

Four possibilities were considered for the formation of the catechol cation (m/e 110) in W. Processes 21 (a), (b) and (c) describe three of the possible mechanisms, the fourth one being complete scrambling and statistical distribution of D to form the catechol cation. If the hydrogens then were to retain their positional identity completely the following results would be expected for the three labeled compounds in terms of the mechanisms 21(a),(b),and (c).

For 21(a)	Wa	m/e 110: m/e 111(1:1)
	Wb	m/e 110
	Wc	m/e 110
For 21(b)	Wa	m/e 110: m/e 112 (1:1)
	Wb	m/e 110
	Wc	m/e 110
For 21(c)	Wa	m/e 110: m/e 111 (1:1)
	Wb	m/e 110: m/e 111 (1:3)
	Wc	m/e 110: m/e 112 (1:1)



(a)

(b)

(21)

(c)

A statistical distribution of the deuteriums would give a mixture of:

For Wa and Wb	m/e 110: m/e111: m/e 112 (9:6:1)
For Wc	m/e 110: m/e 111: m/e 112 (1:2:1)

The results (Tables XV-XVII) indicate that for Wa the ratio obtained is 5:4:0.1, for Wb 5:2.75:0.38 and for Wc 2.5: 4.2:1. These ratios are essentially retained throughout the region over which the ionizing voltage was varied.

It is evident that closest approximation of the experimental data with the various possibilities considered is the statistical distribution which, however would involve complete isotope scrambling. Process 21(c) is undoubtedly improbable considering the data for Wc and Wb which are appreciably off the expected values. Process 21(b) is equally as unlikely considering the high abundance of the m/e 111 ion in Wa, and the m/e 112 ion in Wc. Undoubtedly the formation of the catechol cation proceeds via an almost complete hydrogen scrambling with 21(a) being the most likely path as evidenced by the high m/e 111 for Wa and the high m/e 110 peaks in Wb and Wc.

It should be noted that the peak at m/e 55 in W is shifted to m/e 56 and 57 in Wa and in Wb and to m/e 58 and 59 in Wc, indicating that m/e 55 is indeed due to retention of the charge on the hydrocarbon part of the ether ring. On the other hand, there is no mass shift of the peaks at m/e 80 and m/e 52 in any of the labeled isomers, indicating that those peaks were due to cyclopentadiene cation and the $C_4H_4^+$ fragment respectively, thus substantiating the processes suggested in (18).

TABLE XIV

Relative Intensities of Selected Peaks in the Mass Spectrum of Catechol-tetramethylene Diether

E.V.*	Xylene 105	106	110	111	112	121	122	123	164	165
50	67	100	149	13	4	116	33	4	100	12
40	66	100	165	13	2	110	32	4	100	12
30	63	100	154	11	2	100	30	4	100	12
25	61	100	143	10.5	1.5	89	27	3.5	100	12
20	57	100	122	9.0	1.5	65	22	3.0	100	11.5
17	32	100	99	7.0	<1	42	17	2.5	100	11.5
15	14	100	76	6.0	<1	27	12.5	2.0	100	12
13.5	9	100	57	4.5	<1	16	9	<2	100	12
12	3	100	37	3.0	<1	7	5.6	<1	100	12

*Approximate value

TABLE XV

Relative Intensities of Selected Peaks in the Mass Spectrum of α-di-D-Catechol-tetramethylene diether (W(b))

E.V.*			110	111	112	121	122	123	124	164	165	166	167
50			118	74	8.0	72	60	7.0	17	7.5	5.0	100	12
40	45	100	109	68	7.0	68	57	6	13	7.5	5	100	12
30	42	100	102	65	7.0	63	55	6	12	8.0	5.0	100	12
25	39	100	100	63	7.0	57	50	6	12	8.0	5.0	100	12
20	31	100	80	50	5.0	43	37	5	10	8.0	5.0	100	12
17	22	100	61	40	4.0	27	26	4	8	8.0	5.0	100	12
15	14	100	48	30	3.0	18	18	3	6.5	8.0	5.0	100	12
13.5	9	100	36	24	2.4	11	12	1.5	5.0				

*Approximate value

TABLE XVI

Relative Intensities of Selected Peaks in the Mass Spectrum of β-di-D-Catechol-tetramethylene diether (W(a))

E.V.*	105	106	110	111	112	121	122	123	124	164	165	166	167
50	47	100	113	97	8.5	134	43	6.0	1.5	1.0	8.0	100	11.5
40	45	100	107	93	8.0	127	41	5.5	1.5	1.0	8.0	100	11.5
30	41.5	100	101	87	7.0	118	38	5.0	1.5	1.0	8.0	100	11.5
25	39	100	92.5	80	7.0	103	35	5.0	1.5	1.0	8.0	100	11.5
20	31	100	75	65	6.0	73	28	4.0	1.0	1.0	8.0	100	11.5
17	21	100	57	50	4.5	48	21	3.0	1.0	1.0	8.0	100	11.5
15	13.5	100	43	37	3.5	31	15.5	2.5	1.0	1.0	8.0	100	11.5
13.5	8.0	100	30	26.5	2.5	17	11	2.0	<1	1.0	8.0	100	11.5
12	3.5	100	20	17.5	2.0	7.5	7.0	1.5	<1	1.0	8.0	100	11.5
11	2.0	100	15	13	1.5	4.5	5.0	<1	<1	1.0	8.0	100	11.5

*Approximate value

TABLE XVII

Relative Intensities of Selected Peaks in the Mass Spectrum of α,α'-tetra-D-Catechol-tetramethylene diether (W(c))

E.V.*			110	111	112	121	122	123	124	167	168	169
50	47	100	65	113	33	8.0	106	12	33	4.0	100	12
40			64	110	33	7.0	103	9.3	32	4.0	100	12
30	42	100	58	98	30	8.0	90	9	30	4.0	100	12
25			55	93	29	6.5	85	9	28	4.0	100	12
20	33	100	44	77	23	6.0	62	6.5	23.5	4.0	100	12
17	21.5	100		55	15	3	36	4.5	17	4.0	100	12
15	14.5	100	25	44	13	<1	24		13.5	4.0	100	12

*Approximate value

Conclusions

The results obtained from the mass spectra of the nitrogen compounds studied can be summarized as follows:

1. Doubly charged ions do fragment further into another doubly charged ion and a neutral species as evidenced by the presence of metastable peaks corresponding to such a process.

2. A comparison of the doubly and singly charged ion spectra of the same molecule indicates two different patterns of fragmentation and the doubly charged ion spectrum may, in certain cases, permit differentiation between structures not distinguishable on the basis of their singly charged ion spectra.

3. The following factors contribute to the formation and stabilization of doubly charged ions:

   (a) Maximum separation of charges.

   (b) The presence of electrons of higher energy such as non-bonding or π-electrons that can be easily lost upon bombardment, or shared after ionization and cleavage of two bonds providing two $\overset{+}{\text{C}}\text{-}\overset{-}{\text{N}} \leftrightarrow \text{C}=\overset{+}{\text{N}}$ centers.

   (c) The formation of even electron fragment ions.

   (d) The formation, in general, of any kind of electronically stable system, such as a 6π ring system.

4. A doubly charged ion may often be much more abundant than the corresponding singly charged ion of the same mass.

5. The amount of doubly charged ions formed in oxygen compounds is considerably lower than that in oxygen analogs. As a result of that, there is a considerable difference between the doubly charged ion spectrum of an oxygen compound

and that of its nitrogen analog.

There is nothing unusual about point 1, as long as the resulting species are stable, although the possibility of fragmentation of a doubly charged ion into a singly charged positive ion and an anion should perhaps be investigated by a study of negative ions. The difference between a doubly charged ion spectrum from its singly charged counterpart is not unexpected since the excited state of a doubly charged ion is bound to be quite different from that of the corresponding singly charged. This may result in a change of the symmetry properties of an ion as suggested by Meyerson[11] and one is actually dealing with a different type of structure for the singly charged and doubly charged ions. It should be borne in mind that all structures written in preceding paragraphs are convenient ground state formulas for the respective ions, and even though they do not necessarily correspond to reality (see p. 30) they can be used to interpret and/or account for fragmentation patterns.

The maximum separation of charges would tend to decrease the Coulomb repulsion and hence decrease the potential energy of the ion. The presence of non-bonding or π-electrons can help "neutralize" a positive charge by distribution of the charge density over more than one atom. Finally, the formation of even electron ions or stable electron systems in general has been known to increase the stability of singly charged ions, and therefore it is not surprising that similar factors may govern the formation of doubly charged ions. If two competing or consecutive reactions are considered, like for instance, the fragmentations of M^{++} to $(M-1)^{++}$ or $(M-2)^{++}$ in P, the formation

of a more stable transition state in either one of those fragmentations would lead to a more abundant species, as in this case the more abundant $(M-2)^{++}$ ion.

The larger abundance, in many instances, of a doubly charged ion over a correspondingly singly charged of the same mass should not come as a surprise. Consider, e.g., the $(M-30)^{++}$ peak (m/e 81) in N,N'-dimethyl-N,N'-diethyl-p-phenylenediamine (G). The corresponding $(M-30)^{+}$ ion is an odd-electron ion-radical and it is quite plausible the doubly charged even electron ion is better stabilized, the Coulomb repulsion being more than compensated by the coupling of electrons. A comparison could perhaps be made at this point between the absorption spectrum of ethylene[15] and the above phenomenon. It should not be forgotten, of course, that in the excitation of ethylene the excited electrons remain under the influence of the inner electrons while the excited electrons are completely removed upon electron impact in the mass spectrometer. The absorption spectrum of ethylene is expected to show three transitions. The first is a singlet→triplet excitation and hence forbidden. The second is the V←N transition, occurs at 165 mμ and is very intense. It is a $\pi \rightarrow \pi^*$ transition (bonding $\pi \longrightarrow$ antibonding π-orbital). The last is also V←N but as a two electron transition it is forbidden and expected to be weak. However, it has been observed at 200 mμ. One might have expected that excitation of two electrons from ψ_1 to ψ_2 would have required two times as much energy as excitation of one electron rather than much less. Careful MO calculations, including electron correlation (and

configuration interaction) have shown, however, that the wavelength is not unreasonable.[15] The conservation of energy by the coupling of electrons in the formation of doubly charged ions can account for their larger than expected abundance upon ionization in the mass spectrometer just as it does for the lower energy required for the two electron excitation in ethylene.

The $(M-30)^{++}$ peak (m/e 81) in G was studied as a function of ionizing voltage and its intensity compared to that of m/e 162 $(M-30)^{+}$. It was found that the ratio of $(M-30)^{++}/(M-30)^{+}$ rises from 1.73 at 70 e.v.* to 2.5 at 50 e.v. and even at 30 e.v. it remains at 1.78, but declines rapidly at lower potentials until $(M-30)^{++}$ disappears at 20 e.v. This maximum is certainly unusual but it becomes easily explainable when the abundance of $(M-30)^{++}$ is compared to that of $(M-15)^{++}$ or M^{++}. It is found that the trend is exactly the opposite. At potentials over 50 e.v. the further fragmentation of $(M-30)^{++}$ is probably greatly enhanced and therefore its abundance reaches a maximum at about 40-50 e.v. This maximum, however, drops rapidly at lower voltages and the ratio of $(M-30)^{++}/(M-15)^{++}$ becomes smaller until the $(M-30)^{++}$ ion disappears at approximately 22-23 e.v. while the $(M-15)^{++}$ ion still persists, but its abundance gradually drops

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*All e.v. values should be taken as relative rather than absolute.

in favor of the M^{++} ion. The appearance potential in fact of the doubly charged molecular ion (m/e 96) is just below 20 e.v. It is evident that the fragmentation of doubly charged ions proceeds in a fashion similar to that of singly charged ions, namely via the formation of molecular ions (M^{+} and M^{++}, respectively) which then fragment to singly or doubly charged fragments, respectively, in one or more steps. The above mentioned rough appearance potential measurements indicate, for example, the process $M^{++} \longrightarrow (M-15)^{++} \longrightarrow (M-30)^{++}$. As mentioned repeatedly, the possibility of formation of a doubly charged ion from a singly charged by elimination of a negative ion cannot be excluded but seems to be a minor process (if it operates at all) in the cases discussed above.

The higher electronegativity of oxygen vs nitrogen is a major factor for the low abundance of doubly charged ions in the oxygen containing compounds. It is evident that the presence of non-bonding electrons which can then be readily available to "neutralize" the positive charge produced upon electron impact and/or fragmentation is the determining factor in increasing the abundance and stability of doubly charged ions.

The difference in fragmentation between nitrogen and oxygen analogs is not only limited in the doubly charged ion spectrum, but is equally as pronounced in the singly charged region. For example, very little elimination of two ethylene molecules is observed in N,N'-diethyl-o-phenylenediamine (C) to give an o-phenylenediamine ion (m/e 108),

whereas the corresponding process in o-diethoxybenzene (S) produces the catechol cation (m/e 110) which is by far the most abundant ion in its spectrum.

Finally, the spectra of the catechol polymethylene diether homologs are a very good example of the type of apparent contradictions which one often encounters when one attempts to interpret the mass spectra of organic molecules. Misleading conclusions can be reached when the presence of the m/e 121 ion is observed in compounds such as the oxygen analogs (T-W) discussed above, and the loss e.g. of 15 mass units in T may be erroneously attributed to the presence of a methyl group or other corresponding alkyl groups in the higher homologs. Further research in this area would provide sufficient information which could be used to eliminate the possibilities for confusion in the determination of organic molecular structures. The knowledge obtained about the structural requirements for formation of doubly charged ions may also find application in the study of structures of alkaloids.

Experimental

All mass spectra were determined with a CEC-103C mass spectrometer, and the temperature of the inlet system in all cases was between 150-170° C. An electron multiplier system was used for detection in all compounds except for A through E in which a Faraday detector was employed. The energy of the ionizing beam was 70 e.v. unless stated otherwise. The high resolution spectra were obtained with a CEC-110 mass spectrometer employing photoplate recording. The line spectra given in Figs. 3,6, and 8 have been corrected for isotopic contributions and the intensities of the peaks are the ones obtained from the low resolution spectrum after the elemental composition of the ions was determined from the high resolution spectrum.

The spectra of all compounds were run on a sample purified and collected by vapor-phase chromatography. A Wilkens Instruments Aerograph Model No. 1520 was used, equipped with a thermal conductivity detector and 1/4 inch, 20% SE-30 columns. The spectra in Figs. 1(c) and 4(b) are those of the distilled compound before a VPC-pure sample was collected and the 2,3-dimethyl-2,3-dihydroquinoxaline impurity is indicated. The high resolution mass spectra were run on the pure sample using a gas chromatographic column directly attached to the mass spectrometer *via* a pressure reduction unit.[16]

The following compounds used in this work were commercially available:

N,N-diethyl-p-phenylenediamine (D): furnished by Eastman

Organic Chemicals as the dihydrochloride.

N,N'-dimethyl-p-phenylenediamine (K): obtained from Eastman Organic Chemicals as the dioxalate.

N,N-dimethyl-p-phenylenediamine (L): obtained from Eastman Organic Chemicals as the dihydrochloride.

β-Benzimidazole (N) and Quinoxaline (O): obtained from Eastman Organic Chemicals.

The remaining compounds were prepared as follows:

N,N'-diethyl-p-m-and o-phenylenediamines (A), (B) and (C): These were prepared by lithium aluminum hydride reduction of the corresponding N,N'-diacetyl-p-phenylenediamines.

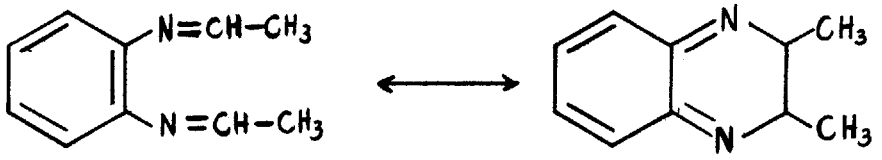
$$CH_3-\overset{O}{\overset{\|}{C}}-HN-C_6H_4-NH-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{LiAlH_4} CH_3CH_2NH-C_6H_4-NHCH_2CH_3$$

The preparation of the diacetyl derivatives is described by Adams and Anderson.[17] Their reduction was carried out as follows:

The N,N'-diacetate (0.25g.) was placed in a soxhlet extractor over a solution of refluxing tetrahydrofuran and lithium aluminum hydride. After 50 hrs. of refluxing sufficient water was slowly added to decompose the slight excess of lithium aluminum hydride. The precipitate of lithium aluminate was filtered off. The filtrate was evaporated at the aspirator vacuum and a brown-black viscous residue remained. This residue was distilled at 120° (bath temperature)/1.2 mmHg for A, 115°/1.5 mmHg for B and 110°/2.5 mmHg for C. In the case of the para isomer the distillate solidified and was recrystallized from petroleum ether. White, needle-shaped crystals were obtained (m.p. 47°). The meta and ortho isomers were colorless liquids at room temperature. The yields were 61% para, 50% meta and 22% ortho.

The preparation of the tetradeuterated isomers of B and C was carried out in the same way. The diacetate (0.25 g.) was placed again in a soxhlet extractor over 200 mgs. lithium aluminum deuteride in 80 ml. refluxing tetrahydrofuran. The yields were approximately the same (48% for meta, 16% for ortho).

It should be noted that the mass spectrum of C (Fig.1(a)) exhibits an intense peak at m/e 160 corresponding to $(M-4)^+$. This was absent in both the para and meta isomers (A and B). This ion is not formed in the mass spectrometer upon electron impact because its abundance relative to the m/e 164 peak- m/e 168 in the labeled molecule (Fig.3(b))- is considerably higher in the spectrum of the tetradeuterated molecule where the reduction was carried out with only 25% excess of reducing agent rather than the 4-fold excess taken when lithium aluminum hydride was used. The formation of a compound resistant to further reduction is quite likely, and the following structure, which is in agreement with a possible intermediate in the reduction reaction is suggested.



N,N-dimethyl-N'-ethyl-p-phenylenediamine (E): The N,N-dimethyl-p-phenylenediamine dihydrochloride (3.50g.) was stirred with acetic anhydride (2.3 ml.) and 50% excess NaOAc in water for 24 hrs. at room temperature. After 24 hrs. 1.64 g. of white N,N-dimethyl-N'-acetyl-p-phenylenediamine (m.p. 130-134°) was precipitated (34% yield). The monoacetate (250 mgs.)

was dissolved in 80 ml. tetrahydrofuran and 200 mg. lithium aluminum hydride. The mixture was heated to reflux for approximately six hours and worked up as described for A. The product (E) was obtained as a light yellow liquid at 120°/1.7 mmHg. (Yield 40%)

The di-deuterated isomer of E was prepared in the same way. The monoacetate (112 mg.) was dissolved in 80 ml. tetrahydrofuran containing lithium aluminum deuteride (160 mg.) and heated to reflux for approximately 50 hrs. The mixture was worked up again as described for A and the pure compound distilled at 75°C/0.15 mmHg. (Yield 43%).

N,N'-di-isopropyl-p-phenylenediamine (F): prepared by the catalytic reduction (Pt/2 atm., room temperature) of para-phenylenediamine and acetone as described by R.T. Major.[18]

N,N'-dimethyl, N,N'-diethyl-p-phenylenediamine (G): N,N'-dimethyl-p-phenylenediamine (1.464 g.) was dissolved in 25 ml. acetic anhydride and refluxed for three hours. The excess acetic anhydride and acetic acid formed were evaporated under reduced pressure to give 2.145 g. of N,N'-dimethyl-N,N'-diacetyl-p-phenylenediamine (Yield 91%).

The above diacetate (o.5 g.) was refluxed for 24 hrs. in 80 ml. tetrahydrofuran containing 0.500 g. lithium aluminum hydride to give G which was distilled at 88°/0.07 mmHg (Yield 46%).

N,N-dimethyl-N',N'-diethyl-p-phenylenediamine (H): N,N-dimethyl-p- phenylenediamine dihydrochloride (4.350 g.) was dissolved in 150 ml. of water, the solution made basic with

NaOH and the free amine base (3.686 g.) extracted with ether. The solvent was evaporated and the product refluxed for 3 hrs. with 20 ml. acetic anhydride. Excess NaOH was then added, the solution cooled in ice, and the N, N-dimethyl-N'-acetyl-p-phenylenediamine crystallized out (m.p. 130-132°, Yield 62.5%).

The acetyl derivative (1.00 g.) was dissolved in 100 ml. tetrahydrofuran, 250 mg. lithium aluminum hydride were added and refluxed for 12 hrs. The product was worked up as before, and collected at 145°/2.1 mm to yield 0.61 g. (66.5%) of N,N-dimethyl-N'-ethyl-p-phenylenediamine (E).

The reduction product E (0.500 g.) was further treated with 15 ml. acetic anhydride to give N, N-dimethyl-N'-ethyl-N'-acetyl-p-phenylenediamine in 92% yield. A portion (0.377 g.) of it was reduced with 200 mgs. of lithium aluminum hydride during 20 hrs. of reflux, and the desired product, H, was isolated (0.2715 g.) in 78% yield (b.p. 100°/0.1 mmHg).

N, N-diethyl-N'-ethyl-p-phenylenediamine (J): N,N-diethyl-p-phenylenediamine (D) was treated with acetic anhydride to give N, N- diethyl-N'-acetyl-p-phenylenediamine. The latter (0.500 g.) in 80 ml. tetrahydrofuran was reacted with lithium aluminum hydride (0.400 g.) for 12 hrs. The product was worked up as described previously and 0.294 g. of J were isolated (85°/0.07 mmHg, Yield 63%).

The dideuterated isomer (Ja) was prepared by reacting 200 mg. of the above diacetyl derivative with 150 mg. lithium

aluminum deuteride in 80 ml. tetrahydrofuran for 48 hrs. The light yellow product was collected at 80°/0.05 mmHg (Yield 59%).

2,4-dimethyl-1,3-phenylenediamine (M): obtained by reduction of 2,4-dimethyl-3-nitroaniline (0.400 g.) with lithium aluminum hydride (o.200 g.) in 80 ml. tetrahydrofuran. After a 5 hr. reflux the excess hydride was decomposed with H_2O and the product (N) extracted from the basic aqueous solution with ether. (Yield 0.31 g., 71%).

1, 2, 3, 4-tetrahydroquinoxaline (P): was prepared by reduction of quinoxaline (O) with Na in ethanol as described by Hinsberg.[19] The reduced compound was sublimed three times (95°/0.03 mmHg) until pure white crystals were obtained (m.p. 94-95°C).

Catechol methylene diether (T).- A solution of 6.6 g. (6.0×10^{-2} moles) catechol in 80 ml. ethanol, in which 2.76 g. of sodium had been dissolved, and 10 g. methylene chloride (1.2×10^{-1} moles) was heated to reflux for 20 hrs.[20] Total of T collected was 0.400 g. (b.p. 40°/3 mmHg). The low yield is probably due to the poorer reactivity of methylene chloride as compared to CH_2Br_2 or CH_2I_2 used in other published procedures.

Catechol ethylene diether (U).- Catechol, 2.75 g., 6.0 g. ethylene bromide, 0.4 g. water and 3.5 g. KOH were heated to 110 in a sealed tube. The diether formed was extracted with ethyl ether and after evaporation of the latter, U was distilled at 55°/0.14 mmHg. (lit. 124°/25 mmHg)[21] Yield 0.646 g.

Catechol tri-,tetra-, and penta-methylene diethers (V, W and Y).- Catechol was reacted with 1,3-dibromopropane, 1,4-dibromobutane and 1,5-dibromopentane respectively in the presence of base, according to a procedure described by K. Ziegler, et. al.[22] The quantities of reactants used were scaled down by a factor of ten. The products were purified by distillation, V (b.p. 65°/0.15 mm), W (b.p. 70°/0.35 mm), Y (b.p. 80°/0.05 mm).

2-n-propyl-1,3-Benzodioxole (Z).- 1,1-dichlorobutane, 3.0 g., and 1.0 g. of pyrocatechol in 20 ml. absolute ethyl alcohol were added to 40 ml. ethanol, in which 1.0 g. of sodium had been dissolved, and heated to reflux for three days. The ethanol and excess 1,1-dichlorobutane were evaporated at 60° under reduced pressure (40-50 mm) and the residue was dissolved in water and extracted with ether. The ether extracts were washed repeatedly with water and 1M NaOH solution to remove the excess catechol and washed again with water. The extracts were dried with $MgSO_4$ and the product was distilled at 90°/1.5 mmHg to give 50 mg. of the Benzodioxole, Z.

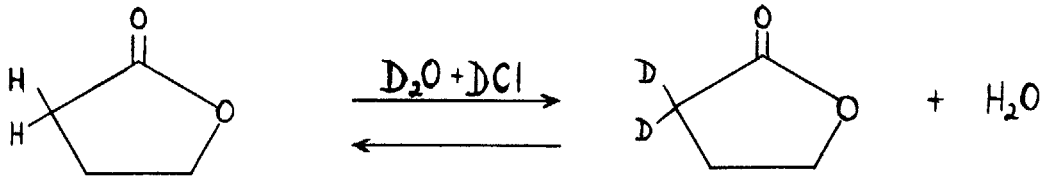
β-di-D-catechol-tetramethylene diether (Wa)- The synthesis of Wa involved the production of 2,2-di-D-1,4-dibromo-butane which was then reacted with catechol in the presence of base.

A stream of nitrogen-dried by passage through H_2SO_4 and $CaCl_2$- was passed over a flask of benzoyl chloride (210 ml.-1.25 moles) to which D_2O (20 g.-1.0 moles) was

slowly added. After initiation of the reaction, the mixture was slowly warmed and finally brought to a very mild reflux

for about fifteen minutes. The DCl produced was carried by the stream of nitrogen into a flask of D_2O (100 g.) cooled in an ice bath. The process was continued under stirring for approximately six hours.

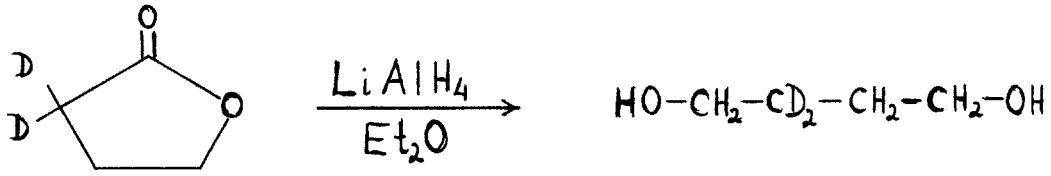
γ-butyrolactone (8.64 g.-1 mole) was dissolved in the D_2O-DCl mixture (50 g.) and the solution was brought under reflux for 48 hrs. The α-hydrogens next to the carbonyl carbon are quite labile and in equilibrium with the large



excess of deuterium ions were slowly exchanged. The same process was repeated with another 5.0 g. of γ-lactone and the whole mixture was extracted with ether in a liquid-liquid extractor. Due to the high solubility of the lactone in water and possible hydrolysis only 9.0 g. lactone (70%) was recovered. The mass spectrum showed 75% dideuterated, 20% monodeuterated and about 5% undeuterated lactone. The partially labeled material was redissolved in 50 g. D_2O-DCl solution and upon addition of 50 g. more D_2O the

solution was heated to reflux for 93 hrs. The material extracted-after three days 6.31 g. were recovered-was over 92% dideuterated and less than 1% undeuterated. The gas chromatogram indicated no detectable impurity to any extent higher than 1%.

The di-D-γ-butyrolactone prepared above was dissolved (1.410 g.) in dry diethyl ether (150 ml.) with 0.40 g. of lithium aluminum hydride and heated to reflux for approximately two hours to assure completion of the reduction.



The diol produced is not very soluble in ether and therefore its complete recovery poses a major problem. At the end of the reduction, ethyl acetate was added to decompose the excess hydride, followed by one or two ml. of water in order to free the reduced product from the basic aluminate complex. The ether was evaporated completely under reduced pressure and excess ethyl acetate was then added to dissolve the diol thus avoiding the extraction of any of the hydroxides present. The ethyl acetate phase was dried with $MgSO_4$ and after evaporation of the solvent the crude diol still containing some residual solvent was obtained.

To the crude diol 7.0 ml. of 48% hydrobromic acid was added and the mixture heated at 140° C in a sealed tube

for a period of 12 hrs. according to a proviously described procedure for the preparation of the unlabeled dibromobutane.[23] The labeled dibromobutane was extracted with ether and distilled at 90°/0.4 mmHg. Yield of labeled dibromide 1.18 g. (37%). The mass spectrum showed only the triplet at m/e 216, 218, 220 in the molecular ion region whereas the unlabeled isomer shows the same triplet at m/e 214, m/e 216, m/e 218 in the same ratios. No other impurities were found by gas chromatography.

Because of the small quantities of labeled materials available and the low yields of the diether, the final steps of the preparation are described in detail. The labeled dibromobutane (2.0 g.) and pyrocatechol (0.5 g.) were dissolved in absolute ethanol (30 ml.) and 1M NaOEt solution (4 ml.) slowly added. After two hours of reflux the ethanol was evaporated and the excess dibromobutane distilled off. The bromoether was then extracted with ether, dissolved in n-AmOH (30 ml.) containing 0.3 g. K_2CO_3 and heated to reflux for 36 hrs. The solution was dissolved in ether and extracted with water and aqueous NaOH to remove all catechol and salts present. A brown residue was left after evaporation of the ether consisting of n-AmOH, a small amount of dibromobutane and the β-di-D-catechol tetramethylene diether (Wa). The bulk of the first two impurities was distilled at a bath temperature of 50°/0.60 mmHg. The final fraction was collected at 90°/0.60 mmHg and the gas chromatogram indicated the presence of a

substantial amount of Wa. The mass spectra shown in Figs. 12(a), (b), (c) and (d) were determined on the pure sample collected after gas chromatography.

α-di-D-Catechol tetramethylene diether (Wb)- The reduction of γ-butyrolactone (2.0 g.) with lithium aluminum deuteride (0.65 g.) in 200 ml. of ether produced 1,1-d_1,d_1-1,4-butanediol which was treated with hydrobromic acid to yield 1,1-d_1,d_1-1,4 dibromodutane (1.37 g., Yield 25%). The reaction mixtures were worked up as described in Wa above. The latter was reacted with catechol to produce Wb as described earlier.

α-,α'-tetra-D-catechol-tetramethylene diether (Wc).- Diethyl succinate (3.48 g.) was dissolved in 20 ml. ethyl ether and added to a solution of 1.0 g. lithium aluminum deuteride in 150 ml. ether. The 1,1,4,4-tetradeuterobutane diol obtained was treated with hydrobromic acid to give 1,1-d_1,d_1-4,4-d_4,d_4-1,4 dibromobutane (1.64 g., Yield 37%). The latter was reacted with catechol in the presence of base to produce Wc. The same procedure was used to work up the reactions as described in the preparation of Wa.

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BIOGRAPHICAL NOTE

Paul Vouros, son of Mr. and Mrs. Christos Vouros, was born on April 1, 1938 in Thessaloniki, Greece. He graduated from Anatolia College in Thessaloniki in June 1957 and was awarded a Fulbright Travel Grant for study in the United States. He was enrolled at Wesleyan University in Middletown, Connecticut on a Foreign Scholar Award in September 1957 and was graduated in June 1961 with a B.A. degree in Chemistry.

The author entered the Graduate School of M.I.T. in September 1961 where he served as a teaching assistant during the years 1961-1963. He was awarded a Moore Fellowship for the academic year 1963-1964 and a research assistantship during 1964-1965. He is a member of the Society of Sigma Xi.