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APPLICATIONS OF ARTIFICIAL INTELLIGENCE FOR CHEMICAL INFERENCE

XIX—COMPUTER GENERATION OF ION STRUCTURES†

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Abstract—The purpose of this paper is to discuss an interactive computer program which can be used to study questions of plausible ion structures. The program can be constrained in a variety of ways by the user, based on information inferred from (i) the structure of the intact molecule which gave rise to the ion, (ii) metastable defocusing experiments to identify progenitors, and (iii) existing knowledge of the fragmentations and rearrangements of related molecules, including deuterium labeled analogs. Implementation of these constraints is discussed primarily with the example of triethylamine, an apparently simple compound whose behavior is examined in detail with the aid of the program because of the complexity of its fragmentation.

KNOWLEDGE of the structures of gaseous ions is fundamental to our understanding of the fragmentations and rearrangements of molecules subsequent to ionization in a mass spectrometer. The processes by which molecules decompose frequently involve highly energetic pathways, placing correlations with known structures of ions near or in the ground state (e.g. solution chemistry) on a largely speculative basis. Yet these correlations have contributed a great deal to our rationalization, if not deeper understanding, of many fragmentation processes. Of more value to a deeper understanding, however, is the knowledge of the actual ion structures. Recent advances in instrumental techniques, e.g. ion cyclotron resonance (i.c.r.)[2] metastable ion analysis,[3] collision-induced metastable ions[4] and field ionization analysis over the course of ion decomposition,[5] have provided a variety of tools for indirect studies of ion structures. From these studies, structural features of ions can be inferred with much more certainty than in the past.

Studies using i.c.r. or metastable ions normally require that two criteria be met. For completeness, one should have available *all* plausible structures for an ion of given composition (empirical formula). This ensures that no reasonable alternatives will be overlooked. For each reasonable alternative, one must have a means of producing the ion in an unambiguous way, so that its behavior under the experimental conditions can be standardized for comparison with unknown ion structures. This requires a search for compounds which on ionization or fragmentation can yield only one reasonable structure for the given decomposition.

Using the structure generator,[6] with constraints ('CONGEN'[1]) where appropriate, we can now explore questions of possible isomeric ion structures. The availability of the program makes it possible to meet the first criterion mentioned in the previous paragraph. The remainder of this report is devoted to a discussion of how the program can be used under constraints inferred from a variety of sources, including the structure of the intact molecule, studies of metastable ions and mass spectra of labeled analogs. The example discussed in most detail is that of ion structures from the

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† See Ref. 1.

fragmentation of triethylamine. We had originally intended this as a simple, illustrative example, but the complexities of its fragmentation demanded a more detailed examination. This example provided ample opportunity to exercise CONGEN based on different constraints; the program's results greatly simplified our consideration of possible structures which might explain the observed data.

Programming details are avoided completely; the algorithm is described elsewhere.[1,6] There exists a mechanism for pursuing examples other than those discussed below (see Experimental).

METHOD

Ions can be treated by CONGEN[1,6] exactly like neutral molecules if we assume, as have other studies,[2–5] that the charge can be localized on a given site in the representation of ion structures. The only difference is that now the properties of some atom or atoms in a structure may be different, i.e. they may be assigned a charge or a radical site. One simply defines a new atom (or atoms) with the specified valence and charge and/or radical site, and generates structures with the new atom (atoms) together with the remaining atoms in the empirical formula. This approach can be used for even or odd electron ions.

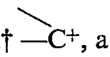
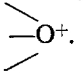
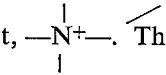
Even electron ions, e.g. $[C_3H_7O]^+$, $[C_2H_6N]^+$, require only a specification of which type of atom will receive the charge and the attendant valence of that atom. A carbon bearing a positive charge is generally formally trivalent,†  $-C^+$, as are oxonium ions,  $-O^+$. Nitronium ions are formally tetravalent,  $-N^+-$. The input to CONGEN for the two example formulae above is summarized in Table 1.

TABLE 1. INPUT TO CONGEN FOR THE EVEN ELECTRON IONS $[C_3H_7O]^+$ AND $[C_2H_6N]^+$ AND THE ODD ELECTRON ION $[C_2H_6O]^{+\cdot}$

Ion	Atom bearing Charge	Atom bearing Radical	Representation of electron deficient species	Generate structures from[a]
$[C_3H_7O]^+$	O	—	$[O]^+$ (valence 3)	$[C_3O^+U_1]$ or $[C_3H_7O^+]$
	C	—	$[C]^+$ (valence 3)	$[C_2C_1{}^+O_1U_0]$ or $[C_2H_7C_1{}^+O]$
$[C_2H_6N]^+$	N	—	$[N]^+$ (valence 4)	$[C_2N_1{}^+U_1]$ or $[C_2H_6N^+]$
	C	—	$[C]^+$ (valence 3)	$[C_1C_1{}^+N_1U_0]$ or $[C_1H_6C^+N]$
$[C_2H_6O]^{+\cdot}$	O	O	$[O]^{+\cdot}$ (valence 2)	$[C_2O_1{}^{+\cdot}U_0]$ or $[C_2H_6O^{+\cdot}]$
	O	C	$[O]^+$ (valence 3) $[C]\cdot$ (valence 3)	$[C_1C_1{}^\cdot O_1{}^+U_0]$ or $[C_1H_6C^\cdot O]$
	C	O	$[C]^+$ (valence 3) $[O]\cdot$ (valence 3)	$[C_1C_1{}^+O_1{}^\cdot U_0]$ or $[C_1H_6C^+O^\cdot]$
	C (same carbon atom)[b]	C	$[C]^{+\cdot}$ (valence 4)	$[C_1C_1{}^{+\cdot}O_1U_0]$ or $[C_1H_6O_1C^{+\cdot}]$

[a] The symbol U represents degree of unsaturation or rings plus multiple bonds.

[b] The additional case, using a trivalent C· and a trivalent $[C]^+$, is not possible for $[C_2H_6O]^{+\cdot}$, but could be utilized for an ion of higher unsaturation, e.g. $[C_2H_4O]^{+\cdot}$.

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† To our knowledge, there have not been reports of $[R_5C]^+$ gaseous ions, where the carbon is formally pentavalent, with the exception of $[H_5C]^+$, which has been known for some time.[7] $[M + H]$ ions of alkanes, formed in a chemical ionization experiment, may formally be viewed as containing a pentavalent $[C]^+$. Such ion structures can, of course, also be studied.

Odd electron ions require specification of both the charge and radical site. Example distributions of the charge and radical among the atoms for the ion $[C_2H_6O]^{+\cdot}$ are given in Table 1. Odd electron ions which are molecular ions are generally represented as having a single atom bearing both charge and radical, usually the atom of lowest ionization potential (see $[O]^{+\cdot}$, Table 1). Other distributions (Table 1) are perhaps less likely, but should at least be remembered when considering energetic fragmentations.

RESULTS AND DISCUSSION

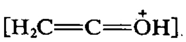
Exhaustive generation

As will be seen from results presented below, exhaustive generation is frequently neither desirable nor necessary. There are many constraints available from a variety of sources on possible structures of ions. Nevertheless, some examples from small empirical formulae are interesting to consider in their entirety, as they serve to illustrate the scope of potential ion structures and to suggest structures which would probably not be considered normally.

The ion $[C_2H_3O]^+$ (*m*/*e* 43) will call to mind generally the acetyl ion $[CH_3—C\equiv O]^+$ (*a*) and this structure is a plausible candidate for $[C_2H_3O]^+$ (*m*/*e* 43) ions from a variety of sources. However, considering structures formally possessing an oxonium ion, there are five possible structures (*a*–*e*). To our knowledge, no systematic study has been undertaken to differentiate among *a*–*e* for $[C_2H_3O]^+$ ions from different oxygen-containing molecules.

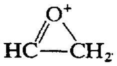
$[CH_3—C\equiv O]^+$

a

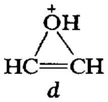


$[H_2C=C=\overset{+}{O}H]$

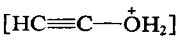
b



c



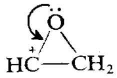
d



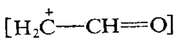
$[HC\equiv C—\overset{+}{O}H_2]$

e

There are five additional structures for $[C_2H_3O]^+$ ions with the positive charge formally on carbon (C^+, *f*–*j*). Of these five, *f*, *h* and *i* are resonance structures of *c*, *a* and *b*, respectively. (CONGEN normally differentiates between resonance forms unless constraints are applied).

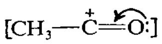


f

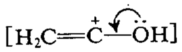


$[H_2\overset{+}{C}—CH=O]$

g



h

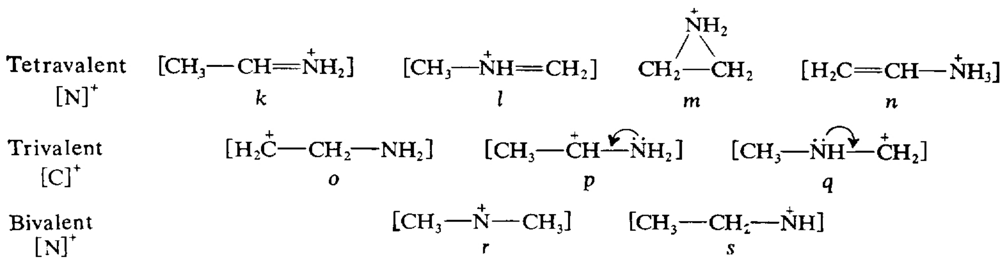


i

$[H\overset{+}{C}=CH—OH]$

j

The ion $[C_2H_6N]^+$ (*m*/*e* 44) (see Table 1) is generally represented as an immonium ion (*k* or *l*). This ion has been subjected to detailed study by the technique of collisional activation.[4b] Possible isomers for $[C_2H_6N]^+$ were presented,[4b] including, in addition to structures arising from the two cases in Table 1, structures with a (formally) bivalent nitrogen atom bearing the positive charge. We obtain from the structure



SCHEME 1.

generator the possibilities *k*–*s* for the three cases summarized in Scheme 1. Structures *m* and *n* represent additional possibilities to those discussed in detail[4b] (*p* and *q* are resonance forms of *k* and *l* respectively), although *n* is mentioned briefly. A similar situation pertains to $[C_3H_8N]^+$ (*m/e* 58) ions which are formally nitronium ions. There are five possibilities stabilized by electron sharing.[4b,8] However, there are eight other ions which are cyclic or bear a carbon–carbon double bond. Several of these are discussed in a subsequent section.

Slightly larger problems quickly become unmanageable without constraints. The number of structural isomers for $[C_nH_{2n+1}O]^+$ and $[C_nH_{2n-1}O]^+$ ions are given in Table 2, considering only oxonium ($[O]^+$, Table 1) ions.

TABLE 2. THE NUMBER OF STRUCTURAL ISOMERS FOR $[C_nH_{2n+1}O]^+$ AND $[C_nH_{2n-1}O]^+$ OXONIUM IONS

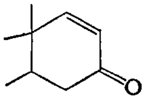
Empirical formula	Number of structural isomers
$[C_3H_7O]^+$	12
$[C_3H_5O]^+$	21
$[C_4H_9O]^+$	35
$[C_4H_7O]^+$	85
$[C_5H_{11}O]^+$	100
$[C_5H_9O]^+$	313

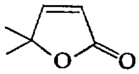
Constrained generation

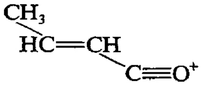
Intuitively, we expect these problems (Table 2) to grow very quickly.[9] With this knowledge, we try to apply as many constraints as possible to focus on the most plausible candidates. Choosing to examine only oxonium or nitronium ions is one such constraint. Although this neglects any carbonium ion structures, it is not unreasonable based on existing knowledge of ion structures.[2–5] Constraints based on ground state chemistry are less tenable. Although some may be valid, there is no clear indication of what to expect from ions of higher internal energy. There are other constraints which are much more reasonable, however, and they are frequently invoked in studies of ion structures.[4] For a known compound, the skeletal constitution of the intact molecule is a powerful constraint on structures of fragment ions if skeletal rearrangements are forbidden, or unlikely. Fragmentation pathways discerned from studies of metastable ions and normal and metastable ion spectra of deuterated derivatives, all tell us more about the fragmentation processes and thus, indirectly, the possible structures of ions which result. Two examples are presented below.

$[C_4H_5O]^+$

The mass spectra of **1**[10] and **2**[11] show large contributions corresponding to *m/e* 69. High resolution spectra show the ion to have the composition $[C_4H_5O]^+$ in both cases. On the basis of this information and additional data obtained from other experiments (e.g. specific deuterium labeling), structure *t* was proposed[10,11] for this ion.

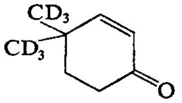

1

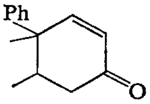

2

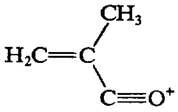

$CH_3-HC=CH-C\equiv O^+$

t

Unconstrained generation yields 116 structures for the oxonium ion $[C_4H_5O]^+$, but this number can be lowered significantly by the use of a few simple constraints.[1] Initial reduction can be accomplished by retaining only those structures which have an intact methyl group. This requirement is at least reasonable in light of the fact that the mass 69 ion, which is thought to originate via a 1,2-alkyl rearrangement,[10] is shifted to *m/e* 72 in the spectrum of **3**. Additionally, **4** shows an intense ion corresponding to phenyl incorporation into the ion of interest (*m/e* 69 → *m/e* 131). Of the 116 structures, only 38 contain at least one methyl group.


3


4


$H_2C=C(CH_3)-C\equiv O^+$

u

Additionally, the mass spectra of both **1** and **2** show a metastable transition corresponding to loss of CO from the $[C_4H_5O]^+$ ion (*m/e* 69 → *m/e* 41). This implies that the ion should contain the unit $[-C\equiv O]^+$. Only two of the 38 remaining structures meet this constraint, namely *t* and *u*. Species *t* is more plausible as it requires only a 1,2 shift for its formation, whereas *u* requires a 1,3 shift. It is pertinent to note that structure *u* had not even been considered in the earlier literature.[10,11]

Note that such a stepwise approach provides a guarantee that no other alternatives are possible under the given constraints (supplied under the control of the chemist).

Triethylamine

A detailed study of the fragmentation of triethylamine (**5**) offers an opportunity to illustrate the use of other simple constraints when considering the possible structures of ions. Surprisingly, the mass spectrum[13] of such a simple tertiary amine does not seem to have been subjected to detailed mechanistic study. Metastable ions formed during fragmentation of $[5]^{+\cdot}$ have been reported.[12]

The low resolution spectrum obtained on our instrument is presented in Fig. 1(a). We have recorded the high resolution spectrum of **5**; all ions of significant abundance above *m/e* 30 contain the nitrogen atom. The INTSUM program[14] has been used to suggest plausible fragmentation processes. Because these processes are represented symbolically, they serve only to suggest the portions of the molecule lost and retained and do not detail the fragmentation. For a more complex example, the INTSUM results represent an important first step to ensure that all possible portions of the molecule which may have given rise to the observed fragment ion have been identified.

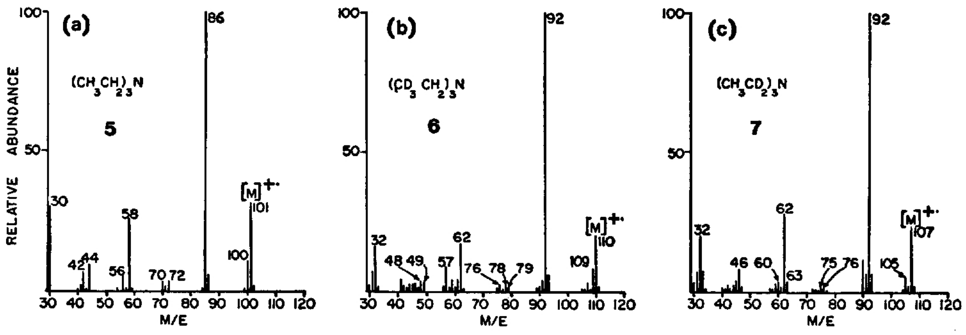
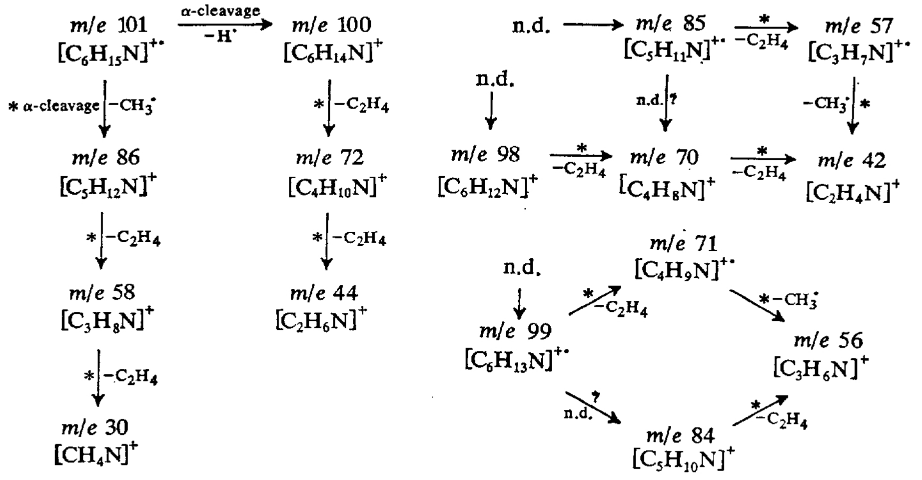


FIG. 1. (a) Low resolution mass spectrum of triethylamine (5); (b) low resolution mass spectrum of 2,2,2,2′,2′,2′,2″,2″,2″-nonadeuteriotriethylamine (6); (c) low resolution mass spectrum of 1,1,1′,1′,1″,1″-hexadeuteriotriethylamine (7).

Levsen and McLafferty[4b] have discussed evidence concerning the absence of skeletal rearrangements in the fragmentation of related amines. They have discussed the structure of the abundant mass 58 ion in the spectrum of **5** and assign to it the structure *v*. A metastable map illustrating detectable precursors (in the first field free region of a double focusing mass spectrometer) for the significant ions above *m*/*e* 30 is presented in Scheme 2. (In Schemes 2–5, an asterisk indicates a transition supported by metastable ions. All detectable precursors for the indicated fragment ion are reported in these Schemes).

$$\underset{[\mathbf{5}]^{+\cdot}}{(CH_3CH_2)_3\overset{+\cdot}{N}} \rightarrow\rightarrow \underset{m/e\ 58\ v}{H_2C{=}\overset{+}{N}H{-}CH_2CH_3}$$



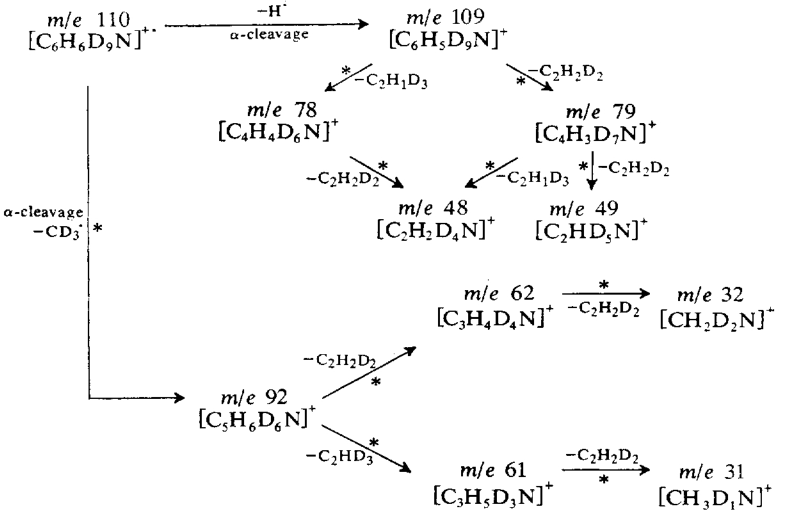
SCHEME 2. Metastable map indicating pathways of fragmentation of $[(CH_3CH_2)_3N]^{+\cdot}$ (**5**).†

† n.d. = not detected.

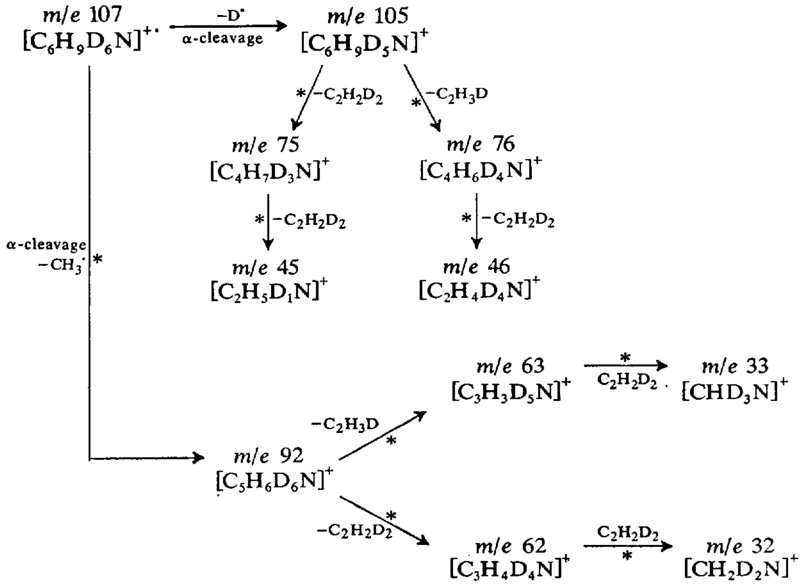
Our results support and extend those presented previously.[12] In addition, we have recorded the mass spectra and obtained data on metastable ions for the two deuterium labeled analogs **6** and **7**. The metastable decompositions for $[6]^{+\cdot}$ and $[7]^{+\cdot}$ relating

$(CD_3CH_2)_3N$ **6** $(CH_3CD_2)_3N$ **7**

to Scheme 2 and the subsequent discussion are presented in Schemes 3 and 4, respectively.



Scheme 3. Metastable map indicating pathways of fragmentation of $[(CD_3CH_2)_3N]^{+\cdot}$ (**6**).



Scheme 4. Metastable map indicating pathways of fragmentation of $[(CH_3CD_2)_3N]^{+\cdot}$ (**7**).

With these data in hand, the possible structures for ions in the spectrum of **5** can be investigated systematically with the aid of the program. As a first assumption, we will restrict our attention to immonium ions, because all ions contain nitrogen and immonium ions are more plausible than alternative primary or secondary carbonium ions. A second assumption is that skeletal rearrangements are forbidden;[4] note that this constraint does not necessarily forbid the formation of cyclic ions which could reopen into formally rearranged species. Results obtained using the constrained structure generator are presented for the ions in Scheme 2. Unless otherwise noted, all fragmentations discussed subsequently are supported by observations of metastable decompositions.

$[C_6H_{15}N]^{+\cdot}$ (*m*/*e* 101). The molecular ion is represented under the above assumptions in the conventional way as $[(CH_3CH_2)_3N]^{+\cdot}$.

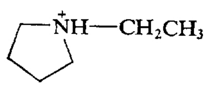
$[C_6H_{14}N]^{+}$ (*m*/*e* 100). The ion of mass 100 represents loss of a hydrogen radical. With no constraints (other than an immonium ion) there are 314 (!) possible structures. The assumption of skeletal integrity and the fact that stepwise loss of two C_2H_4 units must be possible (100 → 72 → 44, Scheme 2) can be partially expressed as a constraint that every candidate must possess (at least) the substructure $C{-}C{-}\overset{+}{N}{-}C{-}C$ and that the nitrogen atom must be (at least) trisubstituted. In addition to the conventional representation of such an ion (*w*), there are five other structures (*x*–*bb*) satisfying these criteria, with unrearranged skeletons. Structures *x*–*bb* would require internal hydrogen rearrangements and/or cyclization of *w* for their formation. There is no evidence that such additional structures (or higher or lower homologs) have ever been considered in the mass spectra of simple amines. Hydrogen rearrangement, coupled with new bond formation, yields *x*, *bb*, *z* and *aa* (paths α, β, γ and δ above), while a more complex process is required for formation of *y*. Data presented below do not differentiate among all these structures. However, we now present evidence for the existence of *bb*.

$[CH_3{-}CH{=}\overset{+}{N}(CH_2CH_3)_2]$

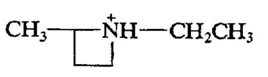
w

$[CH_2{=}CH{-}\overset{+}{N}H(CH_2CH_3)_2]$

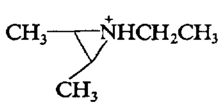
x



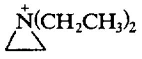
y



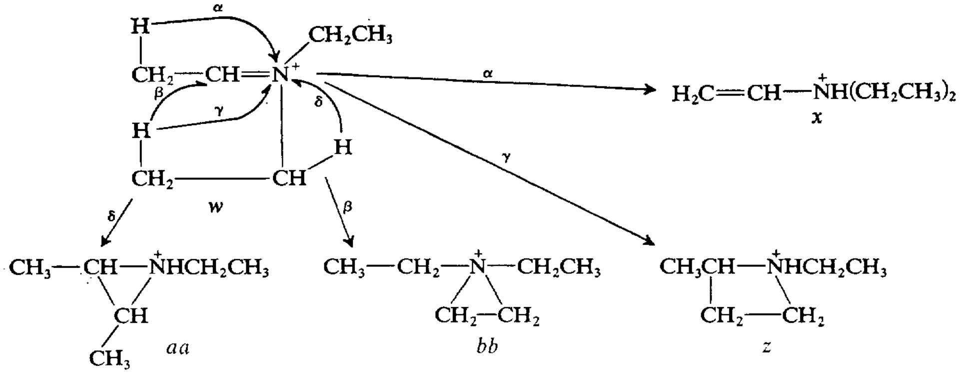
z



aa

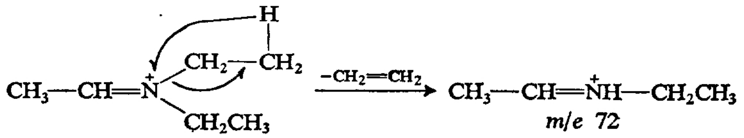


bb



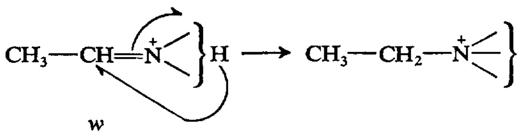
Because the spectra of **6** (Fig. 1(b), loss of H· from $[M]^{+\cdot}$) and **7** (Fig. 1(c), loss of D· from $[M]^{+\cdot}$) support clean loss of an α-hydrogen in **5**, structure *w* is presumed to be formed initially. Rearrangement to other structures (i.e. *x–bb*) is possible, subsequent to formation.

In fact, some rearrangement prior to fragmentation seems to be occurring. The decomposition *m/e* 100 → 72 (Scheme 2) is expected to be a hydrogen rearrangement followed by C—N bond cleavage to yield *cc*.[15] This portrayal predicts that the β-



w *cc*

labeled d_9 analog (**6**) should display a clean loss of 30 a.m.u. (loss of $CH_2{=}CD_2$), as should the α-labeled d_6 analog (**7**). The spectrum of **6** [Fig. 1(b)], however, indicates loss of 30 *and* 31 a.m.u. to *m/e* 79 and 78 (Scheme 3). The spectrum of **7** [Fig. 1(c)] indicates loss of 30 *and* 29 a.m.u. to *m/e* 75 and 76 (Scheme 4). These data indicate some loss of positional identity of the hydrogen/deuterium atoms in a rather specific process. The data for **6** and **7** suggest that one of the hydrogen or deuterium atoms on a carbon beta to the nitrogen atom is, in some ions, transferred to a carbon alpha to the nitrogen prior to decomposition of *m/e* 100 to *m/e* 72. This process can be formally depicted as follows:

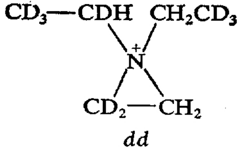


w

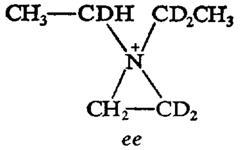
In the case of **6**, a grouping $CD_3{-}CDH{-}\overset{+}{N}{<}$ is observed to be lost as C_2HD_3 indicating transfer of a β-deuterium atom to the α-carbon. In the case of **7**, a similar rearrangement results in a grouping $CH_3{-}CDH{-}\overset{+}{N}{<}$ which can lose C_2H_3D.

These observations, when coupled with the observations of subsequent decomposition of these ions in the *m/e* 70 region to ions in the *m/e* 40 region, supports the existence of a structure other than solely *w* for those ions of $[M]^{+\cdot} - H\cdot$, *m/e* 100, that undergo subsequent decomposition. Considering **5**, *m/e* 72 decomposes via loss of C_2H_4 to *m/e* 44. The d_4 analog (**6**) displays loss of 30 and 31 a.m.u. from *m/e* 79 to yield *m/e* 49 and 48; *m/e* 78 undergoes loss of 30 a.m.u. to *m/e* 48 (Scheme 3); for **7**, the analogous decompositions are *m/e* 76 to *m/e* 46 and *m/e* 75 to *m/e* 45 (Scheme 4).

The only alternative to species *w*, which on rearrangement of *w* undergoes an exchange of α- and β-hydrogen, is *bb*. Rearrangement of the analog of *w* for molecules



dd



ee

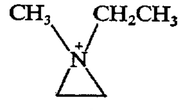
6 and **7** would yield analogs of *bb*, *dd* and *ee*, respectively. These species on subsequent decomposition, could yield the observed shifts discussed above.

$[C_5H_{12}N]^+$ (*m/e* 86). This ion is the alternate α-cleavage product resulting from **5**. All evidence indicates that this ion results from simple loss of a carbon, beta to the nitrogen atom, as a methyl group (see Fig. 1 and Schemes 2–4). This decomposition would yield an ion structure formally represented as *ff*, which is the one conventionally used in the literature. Other plausible structures suggested by CONGEN are homologs of *x–bb*.

Subsequent decomposition of *m/e* 86, however, indicates some rearrangement of *ff* prior to fragmentation. In a situation exactly analogous to that of *m/e* 100 above, two losses of C_2H_4 are suffered by *m/e* 86, to *m/e* 58 and eventually *m/e* 30 (Scheme 2). The spectrum of **6** [Fig. 1(b)] displays losses of 30 ($C_2H_2D_2$) and 31 (C_2HD_3) a.m.u. from *m/e* 92 to *m/e* 62 and 61 followed by loss of $C_2H_2D_2$ to *m/e* 32 and 31 (Scheme 3). The spectrum of **7** [Fig. 1(c)] displays losses from *m/e* 92 to *m/e* 63 ($—C_2H_3D$) and 62 ($—C_2H_2D_2$) followed by loss of $C_2H_2D_2$ to *m/e* 33 and 32, respectively (Scheme 4). Species *gg*, a homolog of *bb*, is again a rearrangement (of *ff*) which makes the necessary α/β-hydrogen exchange. The ion structure *gg*, however, only explains all the data if it can lose two molecules of C_2H_4.

$[H_2C{=}\overset{+}{N}(CH_2CH_3)_2]$

ff



gg

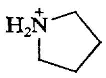
$[C_4H_{10}N]^+$ (*m/e* 72). A precursor of *m/e* 72 is *m/e* 100 (Scheme 2, and above discussion). The shifts of *m/e* 72 in the spectra of **6** and **7** [Figs. 1(b), 1(c)] were also mentioned above. Assuming that C_2H_4 must have been lost as an intact unit from *m/e* 100, there are six structures which maintain structural integrity (*hh–mm*). Species *hh* is the conventional structure expected to represent *m/e* 72. Evidence presented previously in this paper points to *hh* and *ll* as the structures which participate in subsequent decomposition to *m/e* 44. Species *kk* would be expected to decompose analogous to *hh*; however, available data cannot differentiate between them.

$[CH_3{—}CH_2{—}\overset{+}{N}H{=}CH{—}CH_3]$

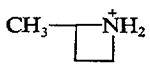
hh

$[CH_3{—}CH_2{—}\overset{+}{N}H_2{—}CH{=}CH_2]$

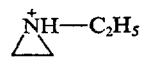
ii



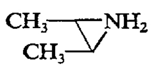
jj



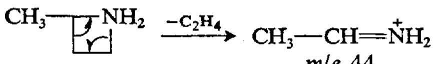
kk



ll



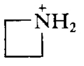
mm

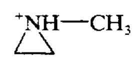


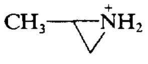
kk

m/e 44

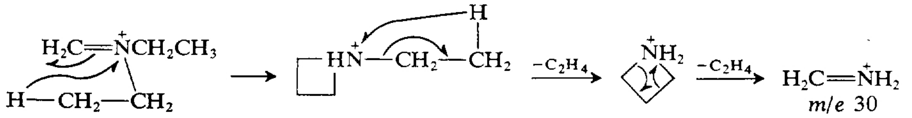
$[C_3H_8N]^+$ (*m/e* 58). Although the subsequent decomposition of *m/e* 58 may indicate that structure *v* is an important contributor to *m/e* 58,[4b] evidence presented above indicates contributions to *m/e* 58 from more complex processes. Thus, it is reasonable to expect some ions of alternative structure to *v*. Those ions which decompose further to m/e 30 (—C_2H_4) must have an intact C—C unit. Plausible structures, in addition to *v*, are *nn–pp*. The peak shifts on the spectra of **6** and **7** discussed


nn


oo


pp

previously are difficult to rationalize solely in terms of a structure *v* which arises from the process m/e 86→ m/e 58 as normally depicted. Although *nn* can be visualized to eliminate C_2H_4, its formation formally involves no hydrogen rearrangements which would allow differentiation between *v* and *nn*. Elimination of C_2H_4 from *gg* would



ff
m/e 86
nn
m/e 58

yield *oo*; this ion may be involved in the abnormal transitions (involving α/β-hydrogen exchange) of m/e 92 → 61 → 31 for **6** and m/e 92 → 63 → 33 for **7**.

$[C_2H_6N]^+$ (m/e 44). Possible structures for $[C_2H_6N]^+$ were presented above (*k–n*), together with a discussion of the precursors for these ions in compounds **5**, **6** and **7**. Although the shifts of m/e 44 of **5** (see Fig. 1) in the spectra of **6** and **7** present a complex pattern, there is evidence for the existence of both *k* and *m*. The former retains one α-carbon and one α-hydrogen (shifts to m/e 45 in **6**, m/e 49 in **7**); the latter retains one α-carbon and two α-hydrogens (shifts to m/e 46 in **6**, m/e 48 in **7**). There is no obvious evidence for the existence of *l*; species *n* cannot be differentiated from *k* if it is a simple rearrangement product of *k*.

Other ions. Other important ions in the spectrum of **5** [Fig. 1(a)] are summarized in Scheme 2. In the subsequent section we discuss briefly some aspects of possible structures of the even electron ions of m/e 70, 56 and 42, each of which formally possesses two degrees of unsaturation.

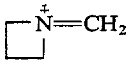
Ion m/e 70, $[C_4H_8N]^+$ has a complex history. The sensitivity of the metastable defocusing technique allows detection of a precursor at m/e 98 in the spectrum of **5** and related precursors in the spectra of **6** and **7**, even though such precursors are insignificant in the normal spectra. The pattern of peak shifts in the spectra of **6** and **7** [Figs. 1(b), 1(c)] indicates a significant amount of hydrogen rearrangement (in **6**, m/e 70 is shifted to m/e 73, 74, 75 and 76; in **7**, m/e 70 is shifted to m/e 72, 73 and 74). Metastable defocusing reveals, however, that these ions decompose further by loss of C_2H_4 in the unlabeled compound (**5**) and by loss of CH_2D_2 in the labeled compounds **6** and **7**. These decompositions yield the complex patterns from m/e 41 to 46 in Fig. 1(b) and m/e 41 to 44 in Fig. 1(c). There is some evidence for transitions involving loss of C_2HD_3 and C_2H_3D also, supporting prior hydrogen/deuterium rearrangements. With the assumption of skeletal integrity and an intact C—C unit (for subsequent loss of C_2H_4), there are 23 possible structures, two with a triple bond, *qq* and *rr*, fourteen with one double bond, e.g. *ss–uu* and seven with no multiple bonds, e.g. *vv*, *ww*. If the loss of C_2H_4 can occur from a species [H_2C=CH—R], then structures such as *xx* and *yy* must also be considered.

$[CH_3—CH_2—\overset{+}{N}H_2—C\equiv CH]$

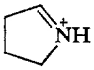
qq

$[CH_3—CH_2—\overset{+}{N}\equiv C—CH_3]$

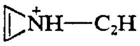
rr



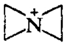
ss



tt



uu



vv

ww

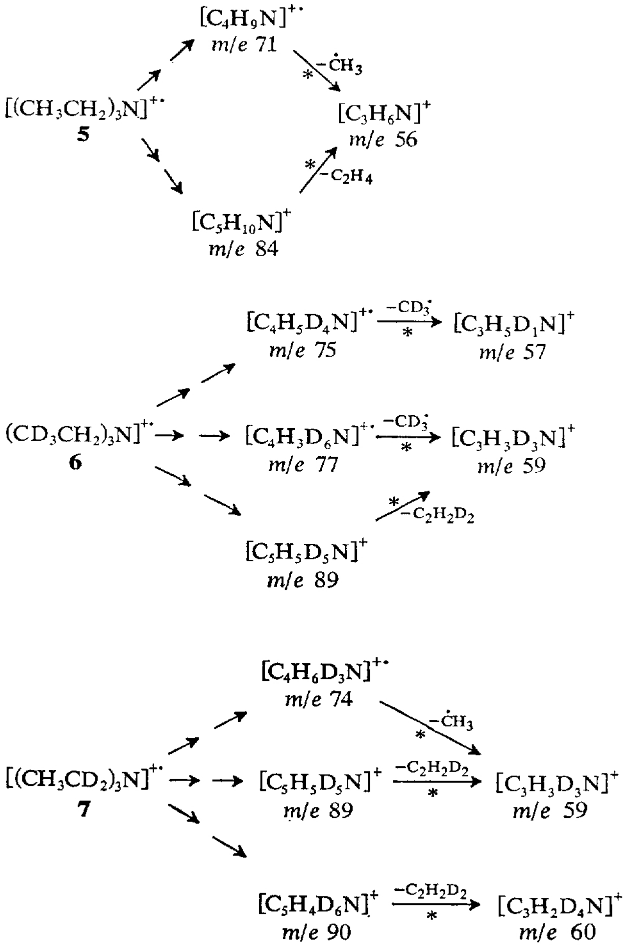
$H_2C=CH\overset{+}{N}H_2—CH=CH_2$

xx

$H_3C—CH=\overset{+}{N}H—CH=CH_2$

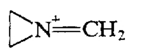
yy

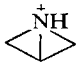
Ion *m/e* 56 $[C_3H_6N]^+$ arises from at least *m/e* 71 and 84 (Scheme 2). There are probably several ion structures involved, as revealed by the peak shifts of *m/e* 56 to *m/e* 57, 58 and 59 in the spectrum of **6** and to *m/e* 59, 60 and 61 in the spectrum of **7**. The observed precursors for these ions are summarized in Scheme 5. These data are



SCHEME 5

evidence for one ion of mass 56 which retains the three α-carbon atoms (shift of *m/e* 56 to 57 in **6**, and to 61 in **7**). This ion has lost one α-hydrogen and gained a β-hydrogen. Structures *zz–ccc* are possible contributors. The ion of mass 59 in both **6** and **7** is


zz

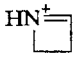

aaa


bbb


ccc

evidence for a structure which has retained two α-carbons and one β-carbon, having exchanged one α-hydrogen for a β-hydrogen. (The occurrence of such exchanges indicates that these ions may have been involved in processes similar to those discussed above in connection with decomposition of *m/e* 100 and 86.) Structures *zz–ccc* could also be involved here; *ddd–fff* represent additional structures. The ions of mass 58 in


ddd


eee

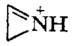
$[CH_3{-}CH{=}\overset{+}{N}{=}CH_2]$
fff

6 and 60 in **7** suggest a third contribution to the mass 56 fragment ion of triethylamine, where two α-carbons and one β-carbon have been retained with no hydrogen/deuterium exchange. The structures mentioned previously (*zz–fff*) would not be differentiated by these data.

Ion *m/e* 42 $[C_2H_4N]^+$ displays complex shifts in the spectra of **6** and **7** [Figs. 1(b), (1c)]. Metastable defocusing does little to point to probable structures for this ion; these ions arise from the complex *m/e* 70's region and result from loss of ethylene with (generally) two deuterium atoms. There is evidence for between zero to four deuterium atoms in the $[C_2H_nD_mN]^+$ ions ($n + m = 4$) for both **6** and **7**. In the absence of additional data, the seven possibilities (*ggg–mmm*) must be considered.

$[H_2C{=}\overset{+}{N}{=}CH_2]$
ggg

$[H_2\overset{+}{N}{=}C{=}CH_2]$
hhh


iii


jjj

$[H_3\overset{+}{N}{-}C{\equiv}CH]$
kkk

$[CH_3{-}C{\equiv}\overset{+}{N}H]$
lll

$[CH_3{-}\overset{+}{N}{\equiv}CH]$
mmm

CONCLUSIONS

We have presented an approach to defining the scope of isomerism of gaseous ions. As we have illustrated with examples, a variety of constraints can be applied to define sets of plausible structures. This information should serve to assist those who are actively engaged in work on determination of the structures of ions, because all alternatives can be determined and examined quickly prior to the more time-consuming aspects of differentiating among the various alternatives. Frequently, a list of ion structures suggests the necessity of certain deuterated analogs which can then be employed to differentiate among various possibilities. The simple example of triethylamine discussed in detail in this paper offers a striking illustration of how many plausible structures have really been ignored in the past and how convenient can be a computer generated list of candidates, generated with appropriate constraints.

In principle, one could envision a system which would determine structural possibilities for an intact molecule based on the possible structures of all the fragment ions observed. In fact, some structure elucidation by mass spectrometry proceeds by this model in instances where knowledge of chemistry and mass spectrometry point to a single structure for an ion or ions representing a significant portion of the molecule. In practice, we do not have sufficient constraints for most problems to avoid having to deal with large numbers of possibilities for every ion, which yields vast numbers of possible structures. Hopefully, the future will bring improved techniques for rapid determination of ion structures. At that time, such a model of structure elucidation would be more amenable to systematic treatment.

EXPERIMENTAL

Mass spectral data were determined on a Varian MAT 711 mass spectrometer. All spectra were recorded at 70 eV ionizing voltage. Data on metastable ions were obtained by analysis of decompositions occurring in the first field free region of this double focusing mass spectrometer. The n.m.r. spectra were obtained on a Varian T-60 spectrometer with deuteriochloroform as the solvent and tetramethylsilane as an internal reference. Preparative g.c. was performed on a Hewlett-Packard 402 gas chromatograph at a temperature of 180 °C using a 6 ft × $\frac{3}{8}$ in. glass column packed with Porapak Q.

Triethylamine (**5**), reagent grade, was further purified by preparative g.c.

1,1,1′,1′,1″,1″.-*Hexadeuteriotriethylamine* (**7**). Ethanol-1,1-d_2 was obtained from the reaction of acetic acid and lithium aluminum deuteride (99 atom % D) according to the method of Friedman and Jurewicz.[16] Ethyl bromide-1,1-d_2 was prepared from the alcohol by the action of hydrobromic + sulfuric acid solution.[17] Overall yield for the two steps from acetic was 60%. The n.m.r. spectrum of the alkyl halide showed no absorption in the region of 3·4 δ, which would correspond to a proton at C-1.

Through a solution of dry ethyl bromide-1,1-d_2 (1 ml, 13 mmol) in 3·5 ml absolute ethanol was bubbled ammonia gas for 5 min, after which the reaction vessel was sealed and allowed to stand for 48 h. Crystals (presumably ammonium bromide[18]) could be seen in the solution after 24 h. Sodium hydroxide (1·5 g) in a minimum of water was added and the resulting solution was extracted with ether. Samples of 1,1,1′,1′,1″,1″-hexadeuteriotriethyl amine were obtained by preparative g.c. of the ether solution.

2,2,2,2′,2′,2′,2″,2″,2″-*Nonadeuteriotriethylamine* (**6**). The reduction of acetic acid-d_4 (99·5% atom D) with lithium aluminum hydride in diglyme[16] gave ethanol-2,2,2-d_3, which was transformed without purification to ethyl bromide-2,2,2-d_3[17] in 63% yield from the starting acid. The n.m.r. spectrum showed no absorption in the region of 1·7 δ, demonstrating the absence of protons at C-2.

The synthesis of the nonadeuteriotriethylamine was accomplished in an analogous fashion to the synthesis of the hexadeuteriotriethylamine presented above. Samples for mass spectral analysis were obtained by preparative g.c.

The CONGEN program is mounted on the Stanford University Medical Experimental (SUMEX) computer facility. It is accessible via a nationwide computer network to an outside community of users, to the limits of available resources. For additional information on access to SUMEX, to CONGEN, or to more details on the structures described in this work, contact the authors, or Professor J. Lederberg, SUMEX, Department of Genetics, Stanford University Medical School, Stanford, Ca 94305, U.S.A.

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