

# Mass Spectrometry in Structural and Stereochemical Problems. LXXI.<sup>1</sup> A Study of the Influence of Different Heteroatoms on the Mass Spectrometric Fragmentation of Five-Membered Heterocycles<sup>2</sup>

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The mass spectra of five-membered saturated heterocycles containing O, S, Se, Te, N, P, Si, and Ge have been measured and the differing modes of fragmentation upon electron impact have been determined from deuterium labeling studies.

A number of publications has appeared from this laboratory on the ability of functional groups to control and direct the mass spectrometric fragmentation of organic molecules,<sup>4</sup> but as yet no study has been undertaken on the ability of different atoms in the same environment to stabilize the positive charge initially formed upon electron impact and thus to direct fragmentation of the molecule. It has been shown that nitrogen is better able to direct the electron-induced fragmentation of  $\beta$ -aminoethanol than does oxygen, as determined by the tenfold intensity of the ion  $\text{CH}_2=\text{NH}_2^+$  ( $m/e$  30) as compared to  $\text{CH}_2=\text{OH}^+$  ( $m/e$  31) in the spectrum of this compound.<sup>5</sup>

The present paper is concerned with the mass spectra of five-membered heterocycles containing atoms from groups IV, V, and VI of the periodic table, with special emphasis on their relative abilities in influencing the fragmentation of each molecule. The five-membered ring system was chosen in preference to larger rings since the latter have more bonds susceptible to cleavage, resulting in more complex spectra. This phenomenon can be readily seen by comparing the mass spectra of pyrrolidine and piperidine and the geneses of the ions in each.<sup>6</sup> Furthermore, five-membered rings seem to be preferred intermediates<sup>7</sup> in certain decomposition reactions of alcohols, thiols, and halides and it was, therefore, of interest to examine related heterocyclic systems.

The mass spectra of some five-membered heterocycles (I) where X corresponds to O, S, Se, Te, N, P,

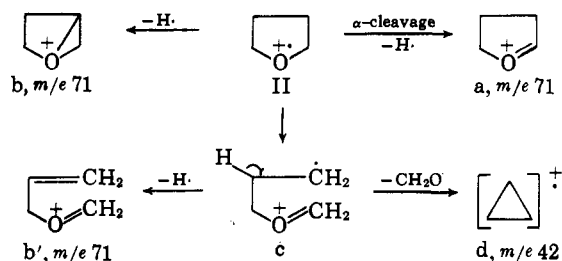
C, Si, and Ge are recorded in Figures 1 to 9, while the spectra of selected deuterated analogs are reproduced in Figures 1a to 9a. In addition, the per cent total ionizations from  $m/e$  40 to the molecular ion are tabulated in Table I for the principal ions of each compound. Since all the heterocycles studied can be synthesized from 1,4-butanediol it was necessary to prepare 1,4-butanediol-1,1,4,4- $d_4$ <sup>8</sup> to specifically label the  $\alpha$  and  $\alpha'$  ring carbon atoms with deuterium. Heterocycles of silicon and germanium were labeled at the heteroatom with deuterium by lithium aluminum deuteride reduction of the corresponding 1,1-dichloro (or diiodo) compounds.



A number of the heteroatoms utilized in this study contain many stable isotopes (Se, Te, Si, and Ge), which complicates recognition of the abundance of ions situated one, two, or three mass units apart in the spectra of these heterocycles. Recourse was taken to programming peak heights<sup>9</sup> obtained directly from hybrid peaks in their mass spectra such that the results from the computer were in the form of a single isotope and  $M - 1$ ,  $M - 2$ , etc., peaks could be immediately recognized (see Figure 9b).

## Mass Spectrometry

*Group VI* ( $X = \text{O}, \text{S}, \text{Se}, \text{and Te}$ ). The mass spectrum of tetrahydrofuran<sup>10</sup> (Figure 1) contains an abundant molecular ion II and an equally intense peak corresponding to an  $M - 1$  species. Deuterium labeling (Figure 1a) established that 70% of the  $M - 1$  species corresponded to loss of an  $\alpha$ -hydrogen atom (a,  $m/e$  71), which requires that the remainder arose



(1) Paper LXX: A. M. Duffield, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 2913 (1965).

(2) We are indebted to the National Institutes of Health of the U. S. Public Health Service (Grants No. GM-11309 and AM-04257) for financial support. The purchase of the Atlas CH-4 mass spectrometer was made possible by the National Aeronautics and Space Administration (Grant No. NsG 81-60).

(3) Postdoctoral Research Fellow 1963-1965.

(4) See, for instance, H. Budzikiewicz, Z. Pelah, and C. Djerassi, *Monatsh.*, **95**, 158 (1964); D. H. Williams, H. Budzikiewicz, Z. Pelah, and C. Djerassi, *ibid.*, **95**, 166 (1964); A. Kjaer, M. Ohashi, J. M. Wilson, and C. Djerassi, *Acta Chem. Scand.*, **17**, 2143 (1963); A. M. Duffield, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 5536 (1964).

(5) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 87.

(6) A. M. Duffield, H. Budzikiewicz, D. H. Williams, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 810 (1965).

(7) See H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, pp. 32, 60, 129.

(8) E. R. Bissell and M. Finger, *J. Org. Chem.*, **24**, 1259 (1959).

(9) We are indebted to Professor J. I. Brauman of Stanford University for the program used which utilized the least-squares technique. The computations were performed on a Burroughs B5000 computer at the Stanford University Computer Center.

(10) "Catalog of Mass Spectral Data," American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburgh, Pa., spectrum no. 780.

Table I<sup>a</sup>

M <sup>+</sup>	13.2	17.8	17.5	21.0	14.0	11.2	14.8	9.4	7.4
M - 1	12.3	5.0	0.9	...	17.4	3.4	...	3.0	3.4
M - 2	...	...	...	...	...	...	...	1.5	6.5
M - CH <sub>3</sub>	...	1.2	...	...	...	1.9	14.3	0.9	...
M - 28 (i, 2-3; ii, 3-4)	...	(i) 7.5, (ii) 22.5	(i) 8.5, (ii) ...	2.2	(i) ... (ii) 40.5	19.0	49.3	48.3	8.7
M - 29	6.6	4.2	2.1	...	8.8	2.9	14.3	4.8	5.2
CH <sub>2</sub> X <sup>b</sup>	...	7.5	12.3	8.0	...	5.3	...	1.9	...
X <sup>+</sup>	...	...	1.0	8.9	...	0.6 <sup>c</sup>	...	3.1 <sup>c</sup>	31.1
XH <sup>+</sup>	...	...	0.7	1.9	...	...	...	4.5 <sup>c</sup>	10.3
(M - CH <sub>2</sub> X) <sup>b</sup>	43.9	0.9	2.7	...	...	1.5	...	1.4	...
C <sub>4</sub> H <sub>7</sub> <sup>+</sup>	...	3.8	34.1	44.6	...	7.6	14.3	4.4	2.5

<sup>a</sup> Table I lists the per cent total ionization from  $m/e$  40 to the molecular ion for each of the principal ions present in the spectra of the compounds discussed in the text. <sup>b</sup> In the case of silicon and germanium X = SiH<sub>2</sub> and GeH<sub>2</sub>, respectively. <sup>c</sup> The values of P<sup>+</sup>, Si<sup>+</sup>, and SiH<sup>+</sup> are calculated from peaks of equal abundance falling in the mass range above  $m/e$  40.

from loss of a  $\beta$ -hydrogen. Mechanistically this portion of the ion yield can be assigned structure b or b' ( $m/e$  71).

The base peak in the spectrum of tetrahydrofuran (Figure 1) occurs at  $m/e$  42 (M - 30) and is quantitatively shifted to  $m/e$  44 in the  $\alpha,\alpha,\alpha',\alpha'$ -tetradeuterio

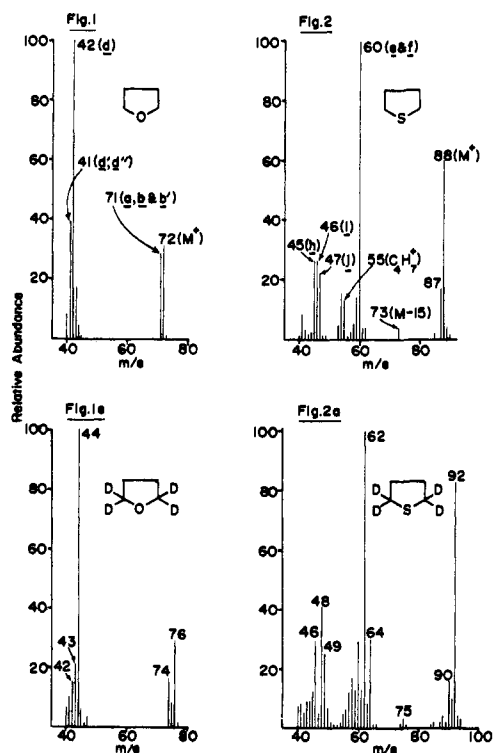


Figure 1. Mass spectrum of tetrahydrofuran.  
Figure 1a. Mass spectrum of tetrahydrofuran- $\alpha,\alpha,\alpha',\alpha'$ -d<sub>4</sub>.  
Figure 2. Mass spectrum of tetrahydrothiophene.  
Figure 2a. Mass spectrum of tetrahydrothiophene- $\alpha,\alpha,\alpha',\alpha'$ -d<sub>4</sub>.

derivative. The neutral eliminated species must correspond to formaldehyde and the charged entity to the cyclopropane ion radical d ( $m/e$  42), which is formed from the  $\alpha$ -cleavage product c of the molecular ion II by heterolysis of the carbon-oxygen bond. The high-resolution mass spectrum of tetrahydrofuran is avail-

able<sup>11</sup> and is in complete agreement with the representation d for the ion of mass 42.

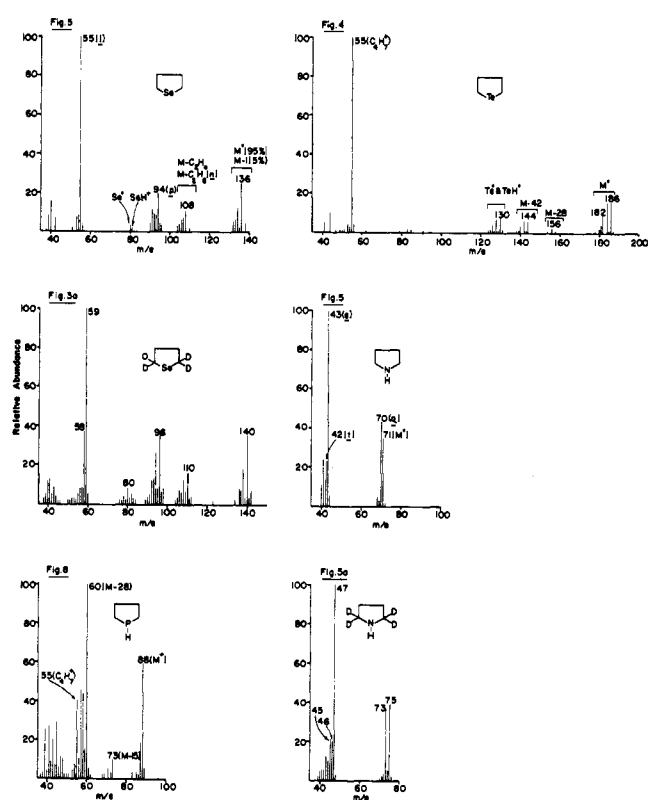


Figure 3. Mass spectrum of tetrahydroseleophene.  
Figure 3a. Mass spectrum of tetrahydroseleophene- $\alpha,\alpha,\alpha',\alpha'$ -d<sub>4</sub>.  
Figure 4. Mass spectrum of tetrahydrotellurophene.  
Figure 5. Mass spectrum of pyrrolidine.  
Figure 5a. Mass spectrum of pyrrolidine- $\alpha,\alpha,\alpha',\alpha'$ -d<sub>4</sub>.  
Figure 6. Mass spectrum of phospholane. (A peak at  $m/e$  62 of 40% relative abundance has been erased, as it was assumed to arise from an impurity.)

High-resolution mass spectrometry<sup>11</sup> established the composition C<sub>3</sub>H<sub>5</sub><sup>+</sup> for the peak at  $m/e$  41 (M - 29) in the spectrum of tetrahydrofuran. This peak was observed to shift to  $m/e$  43 (60%) and  $m/e$  (40%) in

(11) J. H. Beynon in "Advances in Mass Spectrometry," J. D. Waldron, Ed., Pergamon Press Ltd., London, 1959, p. 348.

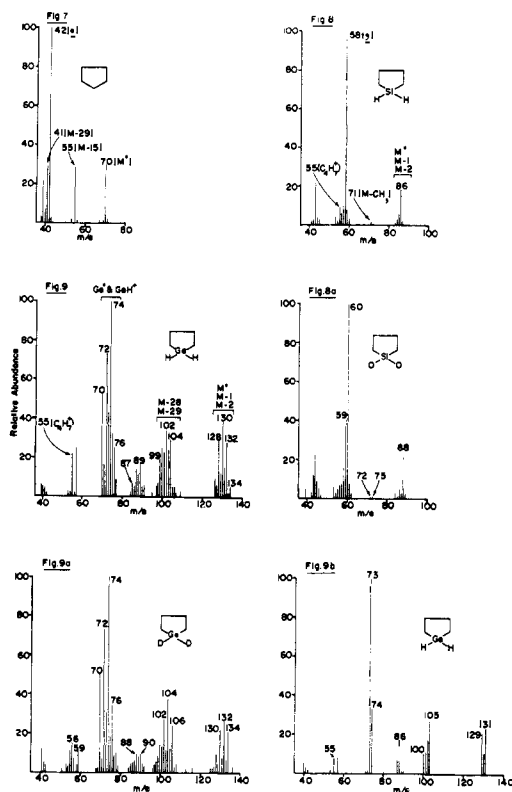
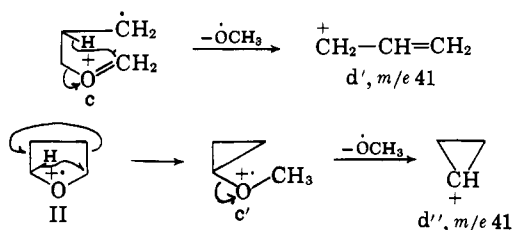


Figure 7. Mass spectrum of cyclopentane.  
 Figure 8. Mass spectrum of silacyclopentane.  
 Figure 8a. Mass spectrum of silacyclopentane-1,1- $d_2$ .  
 Figure 9. Mass spectrum of germacyclopentane.  
 Figure 9a. Mass spectrum of germacyclopentane-1,1- $d_2$ .  
 Figure 9b. Mass spectrum of germacyclopentane normalized for one isotope ( $Ge^{73}$ ) of germanium.

the spectrum of tetrahydrofuran- $\alpha,\alpha,\alpha',\alpha'-d_4$ , and hence two processes must be involved in the formation of this ion. One mode of formation (60%) must involve loss of a  $\beta$ -hydrogen atom and in the  $\alpha$ -cleavage product c of the molecular ion II this can be depicted as hydrogen transfer to carbon with concomitant heterolytic fission of the carbon-oxygen bond and generation of  $d'$  ( $m/e$  41) together with a methoxyl radical. The minor portion (40%) of the ion of mass 41 must involve loss of an  $\alpha$ -hydrogen atom, and this can be depicted as hydrogen transfer in II to yield  $c'$ , which on expulsion of a methoxyl radical would afford  $d''$  ( $m/e$  41), a valence tautomer of  $d'$ .



The mass spectrum of tetrahydrothiophene<sup>12</sup> (Figure 2) contains a more abundant molecular ion (III)<sup>13</sup> and a less abundant  $M - 1$  fragment than does tetrahydrofuran. Deuterium labeling (Figure 2a) showed that the  $M - 1$  species in the spectrum of tetrahydro-

thiophene is formed by two mechanisms, one in which an  $\alpha$ -hydrogen is eliminated (65%) and the other from expulsion of a  $\beta$ -hydrogen atom (35%), and this behavior is completely analogous to that found for tetrahydrofuran.

The base peak in the spectrum of tetrahydrothiophene (Figure 2) occurs at  $m/e$  60 ( $M - 28$ ) and in the  $\alpha,\alpha,\alpha',\alpha'$ -tetradeuterio analog (Figure 2a) this peak is shifted to  $m/e$  64 and  $m/e$  62 to the extent of 25 and 75%. The elimination of ethylene in the genesis of this ion clearly involves loss of one  $\alpha$ - and one  $\beta$ -carbon atom (75%) with the formation of e ( $m/e$  60), while loss of two  $\beta$ -carbon atoms (25%) and generation of f ( $m/e$  60) also contribute to the ion yield. It should be noted that carbon-sulfur bond cleavage with charge retention on sulfur occurs in the genesis of the base peak in the spectrum of tetrahydrothiophene but that carbon-oxygen bond rupture with charge retention on oxygen was absent in the formation of the most intense ion in the fragmentation of tetrahydrofuran. Carbon-heteroatom bond rupture with charge retention on the heteroatom has been found to be more pronounced in the mass spectra of aliphatic thioethers than ethers.<sup>14</sup> The ability of the sulfur atom to compensate for electron deficiency by utilizing electrons from the d-shell may be an explanation for this behavior.



The mass spectrum of tetrahydrothiophene (Figure 2) contains a small peak at  $m/e$  73 corresponding to the loss of a methyl radical, and the preponderant mode of formation (60%) was shown by deuterium labeling (Figure 2a) to involve the expulsion of an  $\alpha$ -methylene group together with a  $\beta$ -hydrogen atom. Smaller contributions to this ion yield involve loss of a  $\beta$ -methylene group plus an  $\alpha$ -hydrogen atom (20%) and an  $\alpha$ -hydrogen atom plus an  $\alpha$ -methylene group (20%).

A peak at  $m/e$  55 ( $M - 33$ ) in the spectrum of tetrahydrothiophene (Figure 2) must correspond to  $C_4H_7^+$  and involve the elimination of a sulfhydryl radical. This ion was completely absent in tetrahydrofuran (Figure 1) but becomes the base peak in the spectra of cyclo-selenobutane and cyclotellurobutane (Figures 3 and 4). It is interesting to note that the elimination of  $CH_2=S$  from tetrahydrothiophene upon electron impact is a minor process ( $m/e$  42 = 3% relative abundance), while expulsion of formaldehyde from tetrahydrofuran generated the base peak of the spectrum (Figure 1).

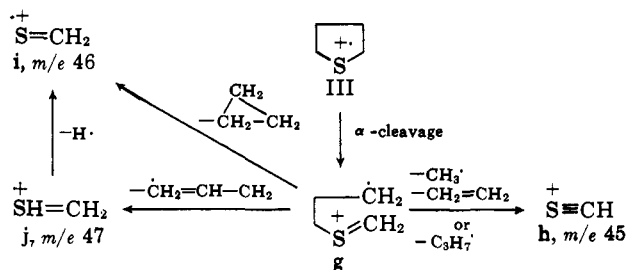
Three peaks of almost identical abundance at  $m/e$  45, 46, and 47 in the spectrum of tetrahydrothiophene (Figure 2) must correspond to  $CHS^+$ ,  $CH_2S^+$ , and  $CH_3S^+$ . In the spectrum (Figure 2a) of the  $\alpha,\alpha,\alpha',\alpha'-d_4$  analog the following peak shifts were noted:  $m/e$  45  $\rightarrow$  46,  $m/e$  46  $\rightarrow$  47,  $m/e$  47  $\rightarrow$  48 (15%) and 49 (85%). These species can be considered as emanating from the molecular ion III.  $\alpha$ -Cleavage would then produce g, which in turn would yield h ( $m/e$  45) via a hydrogen transfer from C-2 with synchronous elimination of a methyl radical and ethylene (or alternatively a propyl radical). Expulsion of cyclopropane from g

(12) Reference 10, spectrum no. 161.

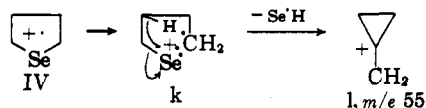
(13) The increased yield of molecular ion in aliphatic thioethers as compared to aliphatic ethers has been noted; see ref. 7, p. 59.

(14) Unpublished results by Shelia Sample and Catherine C. Fenselau of this laboratory.

would generate the odd-electron species *i* (*m/e* 46), while hydrogen transfer from a  $\beta$ -carbon atom to sulfur in *g* would lead to *j* (*m/e* 47). This latter ion eliminates hydrogen to yield *i* (*m/e* 46), as is evidenced<sup>12</sup> by a metastable ion at *m/e* 45 ( $46^2/47 = 45.0$ ), but this does not eliminate the possibility of the process  $g \rightarrow i$  contributing toward the ion yield at *m/e* 46.



A drastic change is encountered on comparison of the mass spectra of tetrahydrothiophene (Figure 2) and tetrahydrosephenone (Figure 3). The base peak in the spectrum of the selenium analog no longer corresponds to the elimination of 28 mass units but to the loss of SeH with the charged species being  $C_4H_7^+$  (*m/e* 55). The genesis of this ion can be envisaged through homolysis of the carbon-selenium bond in the molecular ion IV to yield *k*, which on transfer of a hydrogen atom from the  $\beta$ -carbon atom to selenium and heterolysis of the carbon-selenium bond would yield *l* (*m/e* 55). The spectrum of tetrahydrosephenone- $\alpha,\alpha,\alpha',\alpha'-d_4$  is in agreement with 72% of the ion yield being formed in this manner while the remaining 28% arises from loss of an  $\alpha$ -hydrogen atom and selenium.



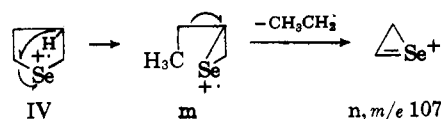
The spectrum of tetrahydrosephenone (Figure 3) contains a strong series of peaks representing the molecular ion IV<sup>15</sup> and shows a small amount ( $\sim 5\%$ ) of an  $M - 1$  species. Deuterium labeling ( $\alpha,\alpha,\alpha',\alpha'-d_4$  derivative) showed this ion to be formed principally from the elimination of a  $\beta$ -hydrogen atom but, due to the low intensity of the  $M - 1$  species, coupled with the presence of the isotope peaks<sup>15</sup> of selenium, small contributions from loss of an  $\alpha$ -hydrogen atom cannot be rigidly excluded. The major  $M - 1$  species presumably arises in a manner similar to that postulated for species *b* or *b'* in the spectrum (Figure 1) of tetrahydrofuran.

No  $M - 15$  species is present in the spectrum (Figure 3) of tetrahydrosephenone, but ions corresponding to  $M - 28$  and  $M - 29$  are discernible. Elimination of ethylene from tetrahydrosephenone is accomplished by loss of one  $\alpha$ - and one  $\beta$ -carbon atom, as is evidenced by a two-mass unit displacement in the spectrum of the  $\alpha,\alpha,\alpha',\alpha'-d_4$  analog, and the genesis of this ion is completely analogous to that of *f* (*m/e* 60) in the spectrum of tetrahydrothiophene. If ethylene is also eliminated from tetrahydrosephenone by the expulsion of two

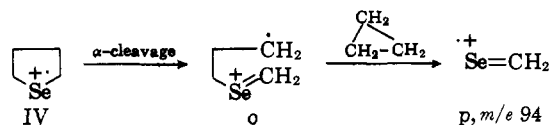
(15) The stable isotopes of selenium are  $Se^{76}$  (9.1%),  $Se^{77}$  (7.5%),  $Se^{78}$  (23.6%),  $Se^{80}$  (50.0%), and  $Se^{82}$  (8.8%). See "Handbook of Chemistry and Physics," 44th Ed., The Chemical Rubber Publishing Co., Cleveland, Ohio, 1962, p. 460.

$\beta$ -carbon atoms then this can represent no more than 10% of the ion yield.

An ion of mass 107 due to the loss of an ethyl radical in the spectrum (Figure 3) of tetrahydrosephenone is preponderantly transferred by two mass units in the spectrum of the  $\alpha,\alpha,\alpha',\alpha'-d_4$  derivative. This is consistent with the expulsion of one  $\beta$ - and one  $\alpha$ -carbon atom together with one hydrogen atom from the second  $\beta$ -carbon. Due to the low abundance of the  $M - 29$  species transfer of hydrogen from an  $\alpha$ -carbon cannot be rigidly excluded but if present it contributes less than 20% to the ion yield. The formation of the  $M - 29$  species can be envisaged as proceeding from the molecular ion of tetrahydrosephenone (IV), which on homolysis of the carbon-selenium bond with synchronous  $\beta$ -hydrogen transfer would yield *m*; expulsion of an ethyl radical would then generate *n* (*m/e* 107).



The group of peaks between *m/e* 90 and *m/e* 96 ( $M - 42$ ) in the spectrum of tetrahydrosephenone corresponds to  $M - 44$  in the  $\alpha,\alpha,\alpha',\alpha'-d_4$  derivative, consistent with the elimination of the elements of cyclopropane according to the sequence  $IV \rightarrow o \rightarrow p$  (*m/e* 94). This mode of formation is identical with that of *d* (*m/e* 42) in tetrahydrofuran except that in the present instance the charge remains with the heteroatom.



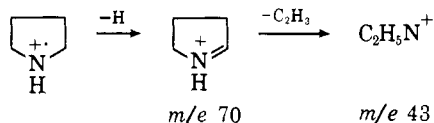
Ions of low abundance corresponding to  $Se^+$  and  $SeH^+$  (displaced to  $SeD$  in the  $\alpha,\alpha,\alpha',\alpha'-d_4$  analog) are barely visible in the spectrum of tetrahydrosephenone (Figure 3).

The base peak in the spectrum of tetrahydrotellurophene (Figure 4) occurs at *m/e* 55 ( $C_4H_7^+$ ) and is somewhat more intense (see Table I) than was found for tetrahydrosephenone. No  $M - CH_3$  ion is present in the spectrum of tetrahydrotellurophene, while  $Te^{+16}$  and  $TeH^+$  constitute more of the total ionization than was observed for the corresponding ions of other atoms of group VI of the periodic table. A weak group of peaks representing an  $M - 28$  ion is also present in the spectrum (Figure 4) of tetrahydrotellurophene, but in the absence of deuterium labeling no conclusions regarding possible modes of formation of this ion can be presented. A second series of peaks between *m/e* 136 and *m/e* 144 ( $M - 42$ ) in the spectrum of the tellurium compound originates from loss of cyclopropane, and a mechanism analogous to that used in the formation of *p* (*m/e* 94) in tetrahydrosephenone can be invoked in this instance.

*Group V (X = N and P).* The modes of formation of the principal ions present in the mass spectrum of

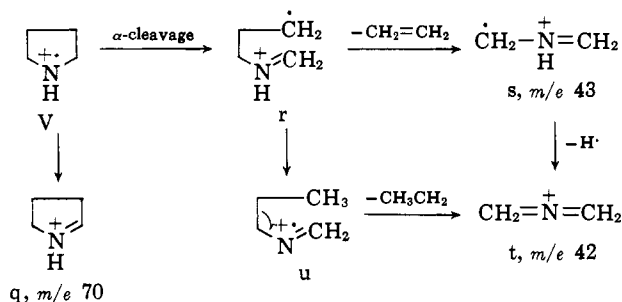
(16) The stable isotopes of tellurium are  $Te^{122}$  (2.5%),  $Te^{124}$  (4.7%),  $Te^{126}$  (18.7%),  $Te^{128}$  (31.8%), and  $Te^{130}$  (34.8%); see ref. 15, p. 475.

pyrrolidine<sup>17</sup> (Figure 5) have been rationalized by deuterium labeling studies.<sup>6</sup> The present investigation utilized pyrrolidine- $\alpha,\alpha,\alpha',\alpha'-d_4$  (rather than the previously studied<sup>6</sup>  $\alpha,\alpha-d_2$  analog) and confirmed the previous conclusion<sup>6</sup> that 94% of the  $M - 1$  species arose from loss of an  $\alpha$ -hydrogen atom with the generation of q ( $m/e$  70). In the spectrum of pyrrolidine (Figure 5) 87% of the base peak ( $m/e$  43) has the composition<sup>17b</sup>  $C_2H_5N^+$  (87%), and this portion is quantitatively shifted to  $m/e$  47 in the spectrum of the tetra-deuterio analog (Figure 5a). The British authors<sup>17b</sup> observed a metastable ion for the transition  $M - 1$  ( $m/e$  70)  $\rightarrow$   $M - 28$  ( $m/e$  43) and formulated this process in the following way. However, since it has



been shown that the  $M - 1$  species is formed by loss of an  $\alpha$ -hydrogen atom (q) and that during the loss of  $C_2H_4$  (28 mass units) all four  $\alpha$ -hydrogen atoms are retained (s), these two species (q and s) cannot be linked together. The observed<sup>17b</sup> metastable ion can, therefore, only be connected with the formation of the minor portion of the  $m/e$  43 peak ( $C_3H_7^+$ , 13%) and its genesis can be explained by expulsion of HCN (27 mass units) from the  $M - 1$  ion (q).

An ion at  $m/e$  42 ( $M - 29$ ) in the spectrum of pyrrolidine (Figure 5) was shown<sup>6</sup> to correspond to the



species t being formed from either of two processes: (i) loss of hydrogen from s ( $m/e$  43) which was substantiated by the recognition of a metastable ion<sup>17</sup> at  $m/e$  41 ( $42^2/43 = 41$ ), and (ii) hydrogen transfer from nitrogen in r to yield u which then eliminates an ethyl radical.

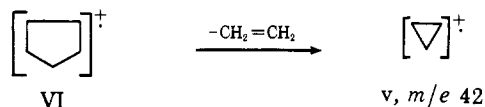
The base peak in the spectrum of phospholane (Figure 6) occurs at  $m/e$  60 ( $M - 28$ ) and in the absence of deuterium labeling no conclusions can be reached regarding the origin of the expelled carbon atoms. The ratio of the relative abundances of  $M^+/(M - 1)$  ions increases substantially in phospholane as compared to pyrrolidine, and a similar increase was observed for the ratio of these ions in tetrahydrothiophene as compared to tetrahydrofuran (see Table I).

The spectrum (Figure 6) of phospholane exhibits a hydrocarbon ion of substantial abundance at  $m/e$  55 ( $C_4H_7^+$ ) which was absent in the spectrum of pyrrolidine, and this is in agreement with the increase in intensity of this ion in the spectra of five-membered

heterocycles on progressing along the series O, S, Se, and Te.

An ion of low abundance at  $m/e$  73 ( $M - 15$ ) in the spectrum of phospholane is due to the expulsion of a methyl radical, and no corresponding loss occurs in the fragmentation of pyrrolidine.

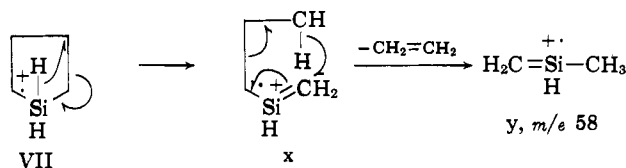
*Group IV (X = C, Si, and Ge).* The mass spectrum (Figure 7) of cyclopentane<sup>18</sup> contains a prominent molecular ion (VI). Loss of a methyl radical from VI generates an abundant ion ( $m/e$  55), while the base peak of the spectrum is formed by loss of ethylene from VI, and this species can be assigned structure v ( $m/e$  42). Elimination of an ethyl radical is also a favored process as is evidenced by the presence of a substantial peak at  $m/e$  41 in the mass spectrum of cyclopentane.



The mass spectrum of silacyclopentane (Figure 8) contains a relatively abundant molecular ion (VII) which may lose one of the hydrogen atoms attached to silicon since the  $M - 1$  ion became an  $M - 2$  species in the spectrum (Figure 8a) of silacyclopentane-1,1- $d_2$ . The spectrum (Figure 8) of the parent heterocycle also exhibits a small  $M - 2$  species.

A small peak at  $m/e$  71 ( $M - 15$ ) in the spectrum (Figure 8) of silacyclopentane was evenly split between  $m/e$  72 and  $m/e$  73 in the spectrum (Figure 8a) of the 1,1- $d_2$  derivative. This result demonstrates that in the genesis of 50% of this ion the eliminated methyl radical obtains a hydrogen atom from silicon.

By far the most dominant peak in the spectrum of silacyclopentane occurs at  $m/e$  58 ( $M - 28$ ) and is displaced to the extent of 67% and 33% to  $m/e$  60 and  $m/e$  59 in the spectrum (Figure 8a) of the 1,1- $d_2$  analog. A mechanism consistent with this result would involve transfer of hydrogen from silicon in the molecular ion VII to a  $\beta$ -carbon atom with synchronous  $\alpha,\beta$ -carbon bond rupture and generation of x. This latter intermediate can by a concerted process eliminate ethylene and transfer hydrogen back to the charged species which may be represented as y ( $m/e$  58). The quantitative figures in the peak shifts of the labeled derivative indicate the absence of any appreciable isotope effect in this hydrogen rearrangement.



The situation becomes completely different in germacyclopentane, since the base peak in its spectrum (Figure 9) is due to  $Ge^+$ <sup>19</sup> while the ion  $GeH^+$  is also prominent and corresponds to the extent of 50% to  $GeD^+$  in the spectrum (Figure 9a) of germacyclopentane-1,1- $d_2$ .

(18) Reference 10, spectrum no. 116.

(19) The stable isotopes of germanium are  $Ge^{70}$  (20.5%),  $Ge^{72}$  (27.4%),  $Ge^{73}$  (7.7%),  $Ge^{74}$  (36.6%), and  $Ge^{76}$  (7.8%); see ref. 15, p. 459.

(17) (a) Reference 10, spectrum no. 1533; (b) R. A. Saunders and A. E. Williams, paper presented at Institute of Petroleum-ASTM Mass Spectrometry Symposium, Paris, 1964.

The molecular ion region of the spectrum (Figure 9) of germacyclopentane is interesting as it shows a molecular ion as well as  $M - 1$  and  $M - 2$  species, the latter being almost as abundant as the molecular ion (particularly obvious in Figure 9b) in the spectrum (Figure 9a) of germacyclopentane-1,1- $d_2$ , the  $M - 1$  ion almost completely (at least 90%) becomes an  $M - 2$  species while the original  $M - 2$  ion is divided evenly between  $M - 2$ ,  $M - 3$ , and  $M - 4$  species.

A group of peaks around  $m/e$  100 in the mass spectrum (Figure 9) of germacyclopentane corresponds to  $M - 28$ ,  $M - 29$ , and  $M - 30$  ions, respectively, while a second series of peaks around  $m/e$  87 belongs to  $M - 43$  and  $M - 44$  ions.

### General Conclusions

All the heterocycles examined exhibit appreciable molecular ions which generally increase in the series O, S, Se, and Te but decrease from N to P and again along the series C, Si, and Ge.

The  $M - 1$  fragments in tetrahydrofuran and tetrahydrothiophene are formed by loss of an  $\alpha$ -hydrogen atom (70 and 65%, respectively), while the selenium analog loses only a  $\beta$ -hydrogen atom. The per cent total ionization (Table I) of the  $M - 1$  species decreases in the series O, S, Se, and Te and again in N to P, while an increase is observed in the order C, Si, and Ge.

The spectra of the silicon and germanium heterocycles are unique among those studied in that they both contain  $M - 2$  ions of appreciable intensity.

The only five-membered heterocycle containing elements of group VI of the periodic table to show an  $M - CH_3$  ion in its mass spectrum was tetrahydrothiophene. This ion was absent in pyrrolidine but was present, although in low yield, in phospholane; from being an abundant fragment in cyclopentane it decreased markedly in the silicon and was absent in the germanium heterocycles.

Ions corresponding to loss of 28 mass units were generally abundant in the spectra of the five-membered heterocycles investigated with the striking exception of tetrahydrofuran. Of the two possible modes of formation (i) loss of one  $\alpha$ - and one  $\beta$ -carbon or (ii) loss of two  $\beta$ -carbon atoms, process ii was favored over i in tetrahydrothiophene by a margin of 3:1, while in the selenium analog only i was observed. In contrast pyrrolidine loses ethylene only *via* process ii. The per cent total ionization corresponding to the  $M - 28$  species decreases in five-membered heterocycles along the series S, Se, Te, and again in N to P and down the series C, Si, and Ge.

The only heterocycle lacking an  $M - 29$  ion in its spectrum was tetrahydrotellurophene and  $\Sigma_{10}$  values for this species decreased in descending the elements of groups VII, VI, and V, respectively, of the periodic table.

Ions corresponding to  $CH_2X^+$  ( $M - C_3H_6$ ) contribute more to the per cent total ionization in the spectrum of tetrahydroselenophene than for the other heterocycles studied (Table I).

The fragments  $X^+$  contribute significantly to  $\Sigma_{40}$  in the spectra of tetrahydrotellurophene and germacyclopentane, and in both these spectra the species  $XH^+$  is also prominent.

Retention of charge by the hydrocarbon portion of the heterocycle with formation of ions of the formula  $(M - CH_2X)^+$  is greatest in the spectrum of tetrahydrofuran and contributes much less to the per cent total ionization of the other heterocycles studied.

The hydrocarbon ion  $C_4H_7^+$  increases in per cent total ionization along the series O, S, Se, and Te, and again in going from N to P, while a decrease is observed in progressing along the series C, Si, and Ge.

### Experimental<sup>20</sup>

*Tetrahydrofuran- $\alpha,\alpha,\alpha',\alpha'-d_4$ .* This compound was prepared from 1,4-butanediol-1,1,4,4- $d_8$  according to the procedure of Reppe<sup>21</sup> and was shown to contain 97%  $d_4$  species (mass spectrometry).

*1,4-Dibromobutane-1,1,4,4- $d_4$ .* The method of Wilson<sup>22</sup> was employed starting with tetrahydrofuran- $\alpha,\alpha,\alpha',\alpha'-d_4$ .

*Tetrahydrothiophene- $\alpha,\alpha,\alpha',\alpha'-d_4$ .* This substance was synthesized from 1,4-dibromobutane-1,1,4,4- $d_4$  (400 mg.) and sodium sulfide (700 mg.) as previously described<sup>23</sup> and purified by preparative vapor phase chromatography using 10% phenyldiethylamine succinate as the stationary phase at 90° and helium pressure of 5 p.s.i. Under these conditions tetrahydrothiophene- $\alpha,\alpha,\alpha',\alpha'-d_4$  (97%  $d_4$  species) had a retention time of 4.5 min.

*Tetrahydroselenophene- $\alpha,\alpha,\alpha',\alpha'-d_4$ .* 1,4-Dibromobutane-1,1,4,4- $d_4$  (1.5 g.) and sodium selenide (2.5 g.) were condensed in water (5 ml.) according to the procedure of Morgan and Burstall<sup>24</sup> and the product was isolated by preparative vapor phase chromatography using 20% polybutylene glycol<sup>25</sup> as the stationary phase at a temperature of 125° and helium pressure of 5 p.s.i. Under these conditions tetrahydroselenophene- $\alpha,\alpha,\alpha',\alpha'-d_4$  (97%  $d_4$  species) had a retention time of 8 min.

*Tetrahydrotellurophene.* This compound was synthesized from tellurium (1.4 g.) and 1,4-diiodobutane (8.5 g.) by a published procedure<sup>26</sup> and isolated by preparative vapor phase chromatography using 15% phenyldiethylamine succinate as the stationary phase at 170° and helium pressure of 8 p.s.i. Tetrahydrotellurophene under these conditions had a retention time of 2.5 min.

*Pyrrolidine- $\alpha,\alpha,\alpha',\alpha'-d_4$ .* Succinimide (210 mg.) was reduced with lithium aluminum deuteride (40 mg.) in ether solution and pyrrolidine- $\alpha,\alpha,\alpha',\alpha'-d_4$  (97%  $d_4$  species, retention time 11 min.) was isolated by preparative vapor phase chromatography using polybutylene glycol<sup>25</sup> as the stationary phase at 60° with a helium pressure of 4 p.s.i.

(20) Mass spectra were obtained with an Atlas CH-4 mass spectrometer using the AN 4 ion source with the source and reservoir thermostated at 60°. The ionizing energy was maintained at 70 e.v. and the ionizing current at 20  $\mu$ a., using a tungsten ribbon filament. Preparative vapor phase chromatography was carried out on a Wilkens Aerograph instrument.

(21) W. Reppe, *Ann.*, **596**, 1 (1955).

(22) C. L. Wilson, *J. Chem. Soc.*, **48** (1945).

(23) C. S. Marvel and W. W. Williams, *J. Am. Chem. Soc.*, **61**, 2714 (1939).

(24) G. T. Morgan and F. H. Burstall, *J. Chem. Soc.*, 1096 (1929).

(25) L. D. Quin, *J. Org. Chem.*, **24**, 911 (1959).

(26) G. T. Morgan and F. H. Burstall, *J. Chem. Soc.*, 180 (1931).

**Phospholane.** This compound<sup>27</sup> was generously supplied by Professor A. B. Burg.

**Silacyclopentane-1,1-*d*<sub>2</sub>.** 1,1-Dichlorosilacyclopentane<sup>28</sup> (150 mg.) in dry ether (25 ml.) was heated under reflux with lithium aluminum deuteride (80 mg.) during 4.5 hr. Excess reagent was destroyed with water and ether was removed through a fractionating column. Preparative vapor phase chromatography using polybutylene glycol<sup>25</sup> as the stationary phase at 54° and a helium pressure of 1.5 p.s.i. yielded sila-

(27) A. B. Burg and P. J. Slota, Jr., *J. Am. Chem. Soc.*, **82**, 2148 (1960).

(28) R. A. Benkeser, R. F. Grossman, and G. M. Stanton, *ibid.*, **84**, 4723 (1962). We wish to thank Professor Benkeser for supplying us with samples of 1,1-dichlorosilacyclopentane and silacyclopentane.

cyclopentane-1,1-*d*<sub>2</sub> (97% *d*<sub>2</sub> species) at a retention time of 9.5 min.

**Germacyclopentane-1,1-*d*<sub>2</sub>.** 1,1-Diiodogermacyclopentane<sup>29</sup> (150 mg.) in dry ether (20 ml.) was reduced with lithium aluminum deuteride (50 mg.) under reflux for 2 hr. The reaction mixture was processed in the usual manner and germacyclopentane-1,1-*d*<sub>2</sub> (97% *d*<sub>2</sub> species) was isolated by preparative vapor phase chromatography using polybutylene glycol<sup>25</sup> as the stationary phase at 66° and helium pressure of 4 p.s.i. (retention time, 6.5 min.).

(29) P. Mazerolles, *Bull. soc. chim. France*, 1907 (1962). We would like to thank Professor Mazerolles for gifts of germacyclopentane and 1,1-diiodogermacyclopentane.

## Mass Spectrometry in Structural and Stereochemical Problems. LXXII.<sup>1</sup> A Study of the Fragmentation Processes of Some Tobacco Alkaloids<sup>2</sup>

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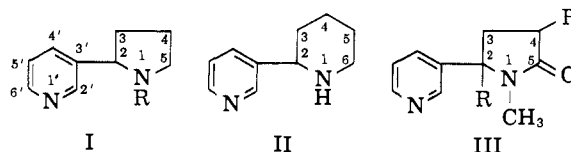
Contribution from the Department of Chemistry, Stanford University, Stanford, California. Received February 20, 1965

*Deuterium labeling studies have made possible mechanistic interpretations for the principal ions formed subsequent to electron impact in nicotine (I, R = CH<sub>3</sub>), nornicotine (I, R = H), and anabasine (II). The product obtained from bromination of nicotine has been shown to possess the geminal dibromolactam structure IV (R = Br) rather than the previously assigned structure III (R = Br). The structure of anabasene has been shown to be VIII rather than VII.*

A recent study of the mass spectrometric fragmentation of some five- and six-membered cyclic amines<sup>4</sup> was undertaken to determine modes of formation of the principal ions formed in this class of compounds subsequent to electron impact. With this information it was hoped to gain some insight into the probable fragmentation behavior of the principal tobacco alkaloids, nicotine (I, R = CH<sub>3</sub>), nornicotine (I, R = H), and anabasine (II), which contain either a five- or a six-membered cyclic amine substituted at C-2 with a β-pyridyl moiety. The mass spectra of nicotine, nornicotine, and anabasine have been discussed<sup>5</sup> and recently new mechanistic interpretations of the more abundant ions have appeared.<sup>6</sup> The present investi-

gation was commenced with a view of testing the validity of these suggestions.<sup>6</sup>

The structure of nicotine (I, R = CH<sub>3</sub>) was suggested by Pinner<sup>7</sup> on the basis of results obtained from studies of the action of bromine on this alkaloid. He was able to obtain a crystalline compound analyzing for C<sub>10</sub>H<sub>10</sub>Br<sub>2</sub>NO to which structure III (R = Br) was assigned on the basis of its conversion to methylamine, oxalic acid, and methyl β-pyridyl ketone on alkaline hydrolytic fission.



The dibromolactam III (R = Br) should offer easy access for the introduction of deuterium into the nicotine molecule.<sup>8</sup> Thus debromination of III (R = Br) with zinc in acetic acid yielded continine (III, R = H) which on lithium aluminum deuteride reduction afforded nicotine-5,5-*d*<sub>2</sub>. Exchange of the hydrogen atoms at C-4 in continine (III, R = H) with potassium carbonate-deuterium oxide<sup>9</sup> followed by lithium aluminum hydride reduction generated nicotine-4,4-*d*<sub>2</sub>. Repetition of the debromination of III (R = Br) with zinc and deuterioacetic acid yielded a product

of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif. 1964, pp. 104-110.

(7) A. Pinner, *Ber.*, **26**, 292 (1893).

(8) For a review of the presently available methods for the introduction of deuterium into organic molecules, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 2.

(9) A. M. Duffield, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 5536 (1964).

(1) Paper LXXI: A. M. Duffield, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 2920 (1965).

(2) We are indebted to the National Institutes of Health of the U. S. Public Health Service for financial support (Grants No. GM-11309 and AM-04257).

(3) Postdoctoral Research Fellow 1963-1965.

(4) A. M. Duffield, H. Budzikiewicz, D. H. Williams, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 810 (1965).

(5) (a) W. F. Kuhn, C. J. Varsel, and W. A. Powell, paper presented at ASTM Committee E-14 Mass Spectrometry Conference, New Orleans, La., June 1962; (b) F. W. McLafferty, *Anal. Chem.*, **28**, 306 (1956).

(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation