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Mass Spectrometry in Structural and Stereochemical Problems. LVIII.[1] A Study of the Fragmentation Processes of Some Lactams[2]

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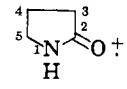
A study of the mass spectra of deuterated analogs of 2-pyrrolidone, N-methyl-2-pyrrolidone, 2-piperidone, and N-methyl-2-piperidone has enabled mechanistic interpretations to be presented for the formation of the principal ions in the spectra of the parent compounds. Deuterium labeling has been particularly effective in determining the site of hydrogen transfer in many of the ions. High-resolution mass spectrometry was also used, mainly to confirm the presence of isobaric ions, whose presence was suggested by the deuterium labeling experiments.

As part of the investigations currently in progress in this laboratory on the ability of functional groups to direct and control mass spectrometric fragmentation of organic compounds,[4] a study of 2-pyrrolidone, 2-piperidone, and their N-methyl analogs has been undertaken as typical representatives of cyclic amides. Deuterium labeling[5] by the following procedures has made possible a mechanistic interpretation[6] of the genesis of the principal fragments in the spectra of these compounds.

Exchange of the hydrogen atoms α to the carbonyl group in the lactams studied was accomplished by refluxing the compound in deuterium oxide containing potassium carbonate. The incorporation of deuterium was found to be directly proportional to the reaction time, 10 days being sufficient to give in excess of 90% d_2 species. Introduction of 2-pyrrolidone and 2-piperidone in deuterium oxide into the inlet system of the mass spectrometer, which had been previously equilibrated with deuterium oxide,[5,7] gave the N-deuterated lactams of 80% d_1 and 86% d_1 species, respectively.

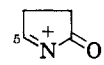
Partial reduction of succinimide with lithium aluminum deuteride afforded 5,5-d_2-2-pyrrolidone, and N-methylation of the unsubstituted lactams using trideuteriomethyl iodide and sodium hydride in tetrahydrofuran gave N-d_3-methyl-2-pyrrolidone and N-d_3-methyl-2-piperidone, each of 92% isotopic purity.

2-Pyrrolidone (Fig. 1).—The base peak in the spectrum of 2-pyrrolidone is the molecular ion m/e 85, which is obtained by removal of a nonbonding electron from either nitrogen or oxygen, and may be represented[6] by Ia and Ib. α-Cleavage to nitrogen, by expulsion of a hydrogen atom from C-5, would be expected to afford the M − 1 fragment Ic and this was confirmed from the spectrum of 5,5-d_2-2-pyrrolidone in which an M−2 ion was encountered to the extent of 85% (Table I).



Ia

Ib

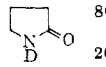
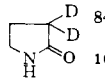
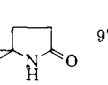


Ic, m/e 84

The fragment of mass 56 (M − 29) in 2-pyrrolidone might arise from any one of three mechanisms.[1,8] The first is cleavage of Ia adjacent to the carbonyl group to afford Id, which by expulsion of the neutral fragment $CH_2{=}NH$ yields the cyclopropanone ion radical Ie. The second mechanism utilizes α-cleavage adjacent to nitrogen with transfer of a hydrogen atom from C-5 and loss of a formyl radical. The third possibility for the genesis of the m/e 56 species is depicted in the sequence Ij → Il, in which the hydrogen atom on nitrogen is transferred to the primary radical with subsequent loss of an ethyl radical.

TABLE I[a]

PRINCIPAL MASS SPECTRAL PEAKS OF 2-PYRROLIDONE AND DEUTERATED ANALOGS

Compound	m/e M+	M−1	M−29	M−43	M−55
	85	84	56	42	30
 80% d_1 20% d_0	86	85 (90%)	57 (30%) 56 (70%)	42 (q)	31 (q)
 84% d_2 16% d_1	87	86 (q)	58 (90%)	44 (q)	31 (80%)
 97% d_2	87	85 (85%)	57 (40%) 56 (60%)	44 (q)	32 (90%)

[a] Tables I–IV show the % shift of the compounds discussed when specifically labeled with deuterium. The symbol (q) refers to a quantitative transfer (*i.e.*, >95%). Sometimes the % shift in a peak is difficult to observe owing to the presence of adjacent ions and in such cases any quantitative information which can be given is quoted. Occasionally blank spaces appear in the tables when no assignment was possible.

The spectrum of N-d_1-2-pyrrolidone indicated (Table I) that at least one of these mechanisms does in fact operate since one-third the ion intensity at m/e 56 is shifted to m/e 57, and hence Ih, the only postulated ion retaining the hydrogen atom attached to nitrogen, must contribute one-third of the total. Discrimination between Ie and Il could be decided easily by high-resolution mass spectrometry[9] which demonstrated that all

(1) Paper LVII: C. Djerassi, *Pure Appl. Chem.*, **9**, 159 (1964).

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

(3) Postdoctoral Research Fellow, 1963–1965.

(4) See, for example, D. H. Williams, H. Budzikiewicz, Z. Pelah, and C. Djerassii, *Monatsh.*, **95**, 166 (1964); H. Budzikiewicz, Z. Pelah, and C. Djerassi, *ibid.*, **95**, 158 (1964); G. von Mutzenbecher, Z. Pelah, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *Steroids*, **2**, 475 (1963); Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Ohashi, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2470 (1963); A. Kjaer, M. Ohashi, J. M. Wilson, and C. Djerassi, *Acta Chem. Scand.*, **17**, 2143 (1963).

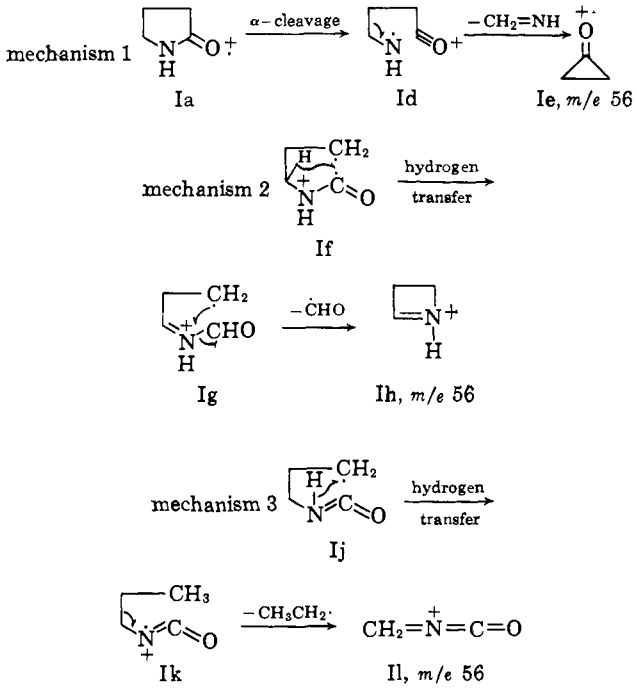
(5) For review of various procedures for the introduction of deuterium into organic molecules, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 2.

(6) Based on principles presented for other organic functional groups in H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964.

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

(8) One-electron shifts are denoted by fishbooks following the convention adopted in ref. 5, p. 2.

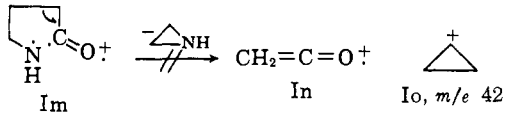
(9) We are indebted to Dr. D. F. Shaw of the University of Liverpool for the high-resolution mass spectrum of 2-pyrrolidone which was determined on an MS-9 mass spectrometer.



three possibilities (Ie, $C_3H_4O^+$, 56.026213), (Ih, $C_3H_6N^+$, 56.050022), and (Il, $C_2H_2NO^+$, 56.013637) contribute in the ratio 6:2:1.

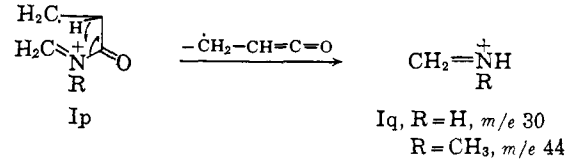
The mass spectrum of 5,5-d_2-2-pyrrolidone should differentiate between Ie, Ih, and Il, since peaks at *m/e* 56, 57, and 58, respectively, should be observed. In point of fact, the low yield of Il (11% as determined from the high-resolution spectrum) coupled with the relatively low abundance of the ion of *m/e* 56 (20% that of the molecular ion), and the presence of adjacent ions made its recognition impossible from deuterium labeling, although the presence of the fragments corresponding to Ie and Ih was clearly visible.

The species corresponding to *m/e* 42 was originally assumed to be ionized ketene In, since it shifted completely to *m/e* 44 in 3,3-d_2-2-pyrrolidone and was unaffected in the N-deuterio compound. Its formation was interpreted in terms of α-cleavage of Ia to afford Im followed by expulsion of the neutral fragment as



ethylenimine. This view, however, was shown to be untenable, since a quantitative shift from *m/e* 42 to 44 was observed (Table I) in the spectrum of 5,5-d_2-2-pyrrolidone. Such a result can be rationalized by representing *m/e* 42 as the cyclopropane ion Io, arising from Ij by heterolysis of the carbon–nitrogen bond, and expulsion of the neutral entity NH=C=O. Full confirmation was provided by high-resolution mass spectrometry[10] which showed *m/e* 42 to consist of $C_3H_6^+$ (96%), $C_2H_2O^+$ (2%), and $C_2H_4N^+$ (2%). High-resolution mass spectrometry[10] established that the ion at mass 41 had the composition C_3H_5.$^+$

The relatively abundant fragment (Fig. 1) at *m/e* 30 (M − 55) in 2-pyrrolidone is shifted (Table I) to *m/e* 31 in the spectra of 3,3-d_2-2-pyrrolidone and N-d_1-2-pyrrolidone, while C-5 and its two hydrogen atoms are implicated in this fragment since *m/e* 30 completely shifts to *m/e* 32 in the 5,5-dideuterio compound. High-resolution mass spectrometry[10] indicated *m/e* 30 to be composed entirely of the CH_4N^+ species, and this result, coupled with the labeling experiments, is consistent with the following mechanism: alternate α-cleavage of the molecular ion Ib affords Ip (R = H), which by hydrogen transfer from C-3 with concomitant nitrogen–carbon bond fission (Ip) leads to ion Iq (*m/e* 30, R = H), and the substituted resonance-stabilized ketene radical.



A β-hydrogen transfer to nitrogen with carbon–nitrogen bond fission was postulated by Gohlke and McLafferty[11] to explain a rearrangement ion found in the spectra of aliphatic amines.[12] This process is responsible for the base peaks in the spectra of N-methyl-2-pyrrolidone, 2-piperidone, and N-methyl-2-piperidone, and has been confirmed in these examples by deuterium labeling (see below).

N-Methyl-2-pyrrolidone (Fig. 2).—The mass spectrum of N-methyl-2-pyrrolidone exhibits a substantial yield of the molecular ion, which we represent by IIa and IIb. The M − 1 fragment in N-d_3-methyl-2-pyrrolidone showed no loss of deuterium, and from analogy with 2-pyrrolidone it may be assigned structure IIc.

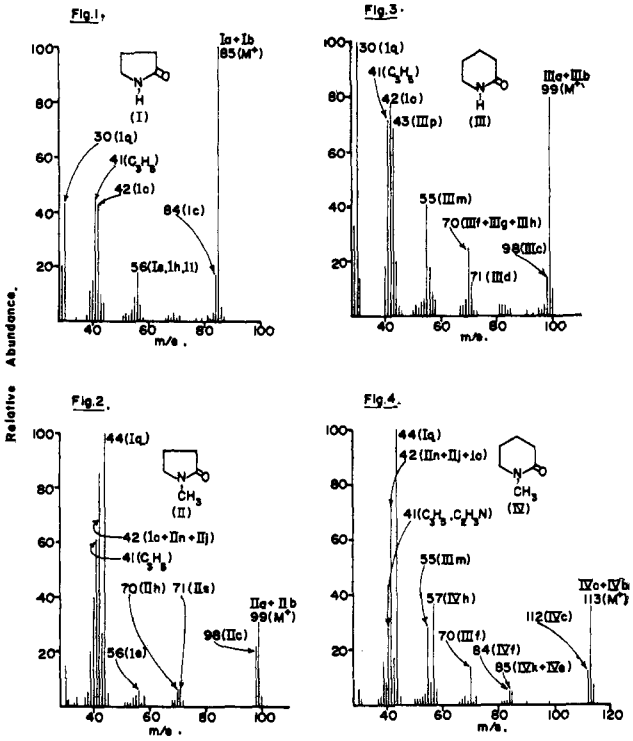


Fig. 1.—Mass spectrum of pyrrolidone (I).
Fig. 2.—Mass spectrum of N-methyl-2-pyrrolidone (II).
Fig. 3.—Mass spectrum of 2-piperidone (III).
Fig. 4.—Mass spectrum of N-methyl-2-piperidone (IV).

(10) Determined by Dr. D. A. Lightner of this laboratory on an MS-9 double focussing mass spectrometer.

(11) R. S. Gohlke and F. W. McLafferty, *Anal. Chem.*, **34**, 1281 (1962).

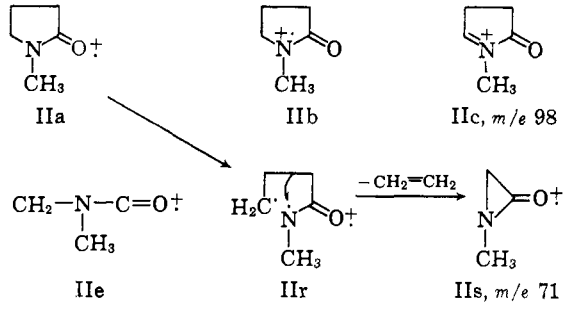
(12) We have recently substantiated this process by deuterium labeling in pyrrolidine, piperidine, and their N-methyl analogs, but in these cases the process was much less favored than in the corresponding lactams.

TABLE II

PRINCIPAL MASS SPECTRAL PEAKS OF N-METHYL-2-PYRROLIDONE AND DEUTERATED ANALOGS

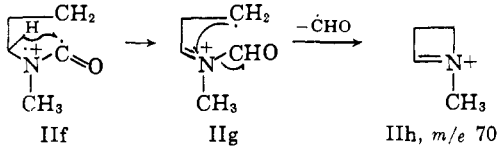
Compound		m/e M+	M−1	M−28	M−29	M−43	M−55	M−57
		99	98	71	70	56	44	42
	95% d_2 5% d_1	101	100 (q)	73 (q)	72 (q)	58 (q)	45 (q)	44 (30%)
	92% d_3	102	101 (q)	74 (q)	73 (q)	56 (q)	47 (q)	42 (40%) 45 (60%)

The ion at *m/e* 71 (M − 28) might arise from loss of either carbon monoxide or ethylene. Deuterium labeling (Table II) established that C-3 with its hydrogen atoms and the N-methyl group are retained. This eliminates representation IIe for *m/e* 71, originating from loss of carbons 3 and 4 as ethylene.



High-resolution mass spectrometry showed the composition of *m/e* 71 to be 88% $C_3H_5NO^+$, 8% $C_4H_7O^+$, and 4% $C_4H_9N^+$. The dominant ion, in view of the deuterium labeling experiments, must correspond to IIs, arising from IIa through cleavage of the N–C-5 bond (IIc) followed by loss of ethylene.

The fragment corresponding to *m/e* 70 (M − 29) is shifted completely (Table II) to *m/e* 72 in the 3,3-dideuterio compound and its production is consistent with the sequence IIf → IIg → IIh (*m/e* 70). The alternative possibility—loss of 29 mass units resulting from expulsion of an ethyl radical— can be rejected since no loss of deuterium was observed from the labeled positions (3,3-d_2 and N-d_3) and such a transfer to either C-4 or C-5 would be required to furnish an ethyl radical.



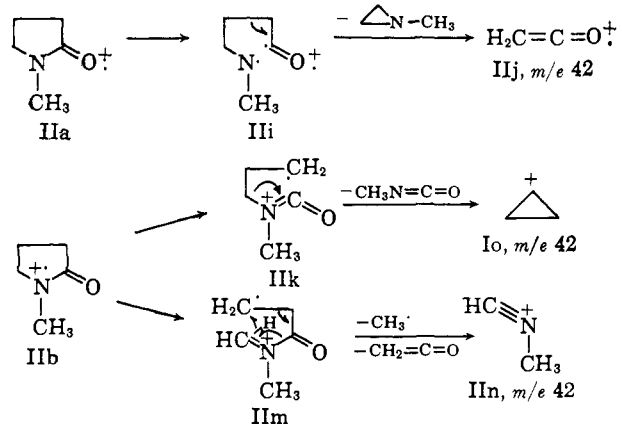
The fragment at *m/e* 56 (M − 43) in N-methyl-2-pyrrolidone is shifted to *m/e* 58 in N-methyl-3,3-d_2-2-pyrrolidone indicating that C-3 and its hydrogen atoms are incorporated in the charge-bearing species. A loss of 46 mass units was observed (Table II) in the spectrum of the N-d_3-methyl compound, which is in accordance with mechanism 1 used above to explain portion Ie of *m/e* 56 in 2-pyrrolidone, except that in the present case the expelled neutral species is $N(CH_3)=CH_2$.

The base peak of the spectrum (Fig. 2) of N-methyl-2-pyrrolidone and N-methyl-2-piperidone (Fig. 4) occurs at *m/e* 44 (M − 55) and is shifted in both cases to *m/e* 45 in the 3,3-dideuterio compound, and to *m/e* 47 in the N-d_3-methyl analog. Its genesis is completely analogous to that of the *m/e* 30 species Iq (R = H) in 2-pyrrolidone, and the ion can be represented as Iq (R = CH_3). High-resolution mass spectrometry confirms this assignment since *m/e* 44 was shown to consist entirely of the $C_2H_6N^+$ species in both N-methyl-2-pyrrolidone and N-methyl-2-piperidone.

The ion intensity at *m/e* 42 (M − 57) is shifted partially (30%) to *m/e* 44 in the spectrum of N-methyl-3,3-d_2-2-pyrrolidone and this amount can be attributed to either of two species. The first possibility arises from expulsion of ionized ketene IIj from IIi, and the second from loss of the stable neutral species $CH_3N=C=O$ from IIk by heterolysis of the nitrogen–carbon single bond and formation of the cyclopropane ion Io.

In the spectrum of N-d_3-methyl-2-pyrrolidone *m/e* 42 was shifted (60%) to *m/e* 45, the remainder being unaffected. Hence 60% of this fragment must retain the N-methyl group, and a mechanism consistent with this observation is loss of a methyl radical and ketene from IIm with formation of IIn.

High-resolution mass spectrometry established the following composition for the *m/e* 42 peak which is consistent with the results obtained from deuterium labeling: 55% $C_2H_4N^+$, 40% $C_3H_6^+$, and 5% $C_2H_2O^+$.



2-Piperidone (Fig. 3).—The mass spectrum of 2-piperidone displays a strong molecular ion (IIIa and IIIb), and a less abundant M − 1 fragment. The latter may be represented as IIIc by analogy to 2-pyrrolidone and by virtue of the fact that the hydrogen atom on nitrogen is retained (Table III) in its formation.

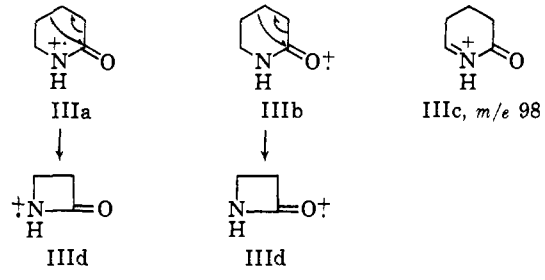
The fragment at *m/e* 71 represents a loss of 28 mass units and its quantitative shift is difficult to determine

TABLE III

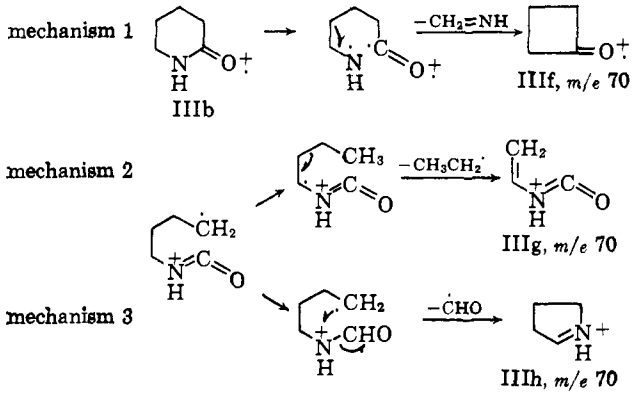
PRINCIPAL MASS SPECTRAL PEAKS OF 2-PIPERIDONE AND DEUTERATED ANALOGS

Compound	m/e							
	M+	M−1	M−28	M−29	M−44	M−56	M−57	M−69
	99	98	71	70	55	43	42	30
 86% d_1 14% d_0	100	99 (90%)	72 71	70 (70%) 71	55 (q)	44 (75%)	42 (90%)	31 (q)
 92% d_2 8% d_1	101	100 (q)	71	72 70 (10%)	56 (q)	45 (90%)	44	31 (q)

with any certainty in 3,3-d_2-2-piperidone, since there is a shift to m/e 72 of twice the abundance of m/e 71 in the unlabeled compound, together with retention of a peak at m/e 71. The m/e 72 peak in the 3,3-dideuterio compound must result, at least in part, from a shift of m/e 70 in the unlabeled compound (see below). Formally, loss of 28 mass units could be attributed to expulsion of either carbon monoxide or ethylene. The former can be excluded since it would require the unobserved movement of m/e 71 to 73 in the 3,3-dideuterio compound. Loss of ethylene involving C-3 (and hence C-4) must occur, and structure IIId arising from either IIIa or IIIb is consistent with the experimental facts.

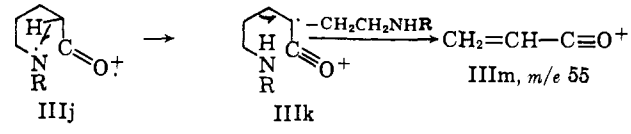


Elimination of 29 mass units and formation of m/e 70 can be envisaged as proceeding through either of three mechanisms which are analogous to those invoked in the genesis of the multiple ions at m/e 56 in the spectrum of 2-pyrrolidone (*vide supra*).

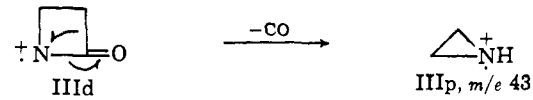


Deuterium labeling (see Table III) limits mechanism 2 (IIIg) to 10% of the total since m/e 70 shifts to the extent of 90% to m/e 72 in the spectrum of 3,3-d_2-2-piperidone. Mechanism 1 (IIIf) is shown to predominate in the formation of m/e 70 because in the spectrum of N-d_1-2-piperidone 70% of this peak is unaffected. Hence those ions retaining the hydrogen atom on nitrogen account for 30% of the total and by difference mechanism 3 (IIIh) contributes 20%. It is interesting to note that in the analogous formation of the multiple ions at m/e 56 in 2-pyrrolidone and at m/e 70 in 2-piperidone, the dominant fragment is derived from ring cleavage α to oxygen with expulsion of the same neutral fragment. High-resolution mass spectrometry established firmly the composition of m/e 70 in 2-piperidone as 84% $C_4H_6O^+$ (IIIf), 14% $C_3H_8N^+$ (IIIh), and 2% $C_3H_4NO^+$ (IIIg).

The fragment at m/e 55 (M − 44) in 2-piperidone is transferred to m/e 56 in the spectrum of the 3,3-dideuterio compound, indicating that only one of the hydrogen atoms on C-3 is incorporated in the charge-bearing fragment. Furthermore, m/e 55 was unchanged in N-d_1-2-piperidone demonstrating that the nitrogen atom was not involved in this ion. This peak also occurs in N-methyl-2-piperidone (transferred to m/e 56 in the 3,3-dideuterio analog and unaffected in the N-d_3-methyl compound—see below), and in both compounds its formation can be ascribed to the following mechanism. Transfer of a C-3 hydrogen atom in IIIj (R = H) would afford IIIk (R = H), homolysis of the 4–5 bond then affording the resonance-stabilized ion IIIm.



Rationalization of the shifts involved in the fragments at m/e 43 and 42 is complicated by the presence of an equally strong m/e 41 ion (see Fig. 3). In 3,3-d_2-2-piperidone 90% of m/e 43 is transferred (Table III) to m/e 45, while in N-d_1-2-piperidone 75% is shifted to m/e 44. A mechanism involving extrusion of carbon monoxide from IIId with generation of the ion IIIp accommodates the deuterium-labeling experiments. High-resolution mass spectrometry confirmed the presence of 80% $C_2H_5N^+$ (IIIp), while $C_2H_3O^+$ (10%) and $C_3H_7^+$ (10%) account for the remainder of this peak.



It is difficult to assign qualitative shifts to the peak at m/e 42 in the deuterated analogs of 2-piperidone owing to the strong adjacent ions (Fig. 3). High-resolution mass spectrometry determined the composition $C_3H_6^+$ (90%) and $C_2H_4N^+$ (10%) for m/e 42, while m/e 41 was shown to consist of $C_3H_5^+$ (95%) and $C_2H_3N^+$ (5%).

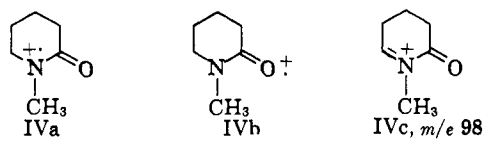
TABLE IV

PRINCIPAL MASS SPECTRAL PEAKS OF N-METHYL-2-PIPERIDONE AND DEUTERATED ANALOGS

Compound	m/e								
	M+	M−1	M−28	M−29	M−43	M−56	M−58	M−69	M−71
	113	112	85	84	70	57	55	44	42
 95% d_2 5% d_1	115	114 (q)	87 (q)	86 (q)	72 (q)	59 (q)	56 (q)	45 (q)	44 (60%)
 92% d_3	116	115 (90%)	88 (q)	87 (q)	73 (q)	60 (q)	55 (q)	47 (q)	42 (60%) 45 (35%)

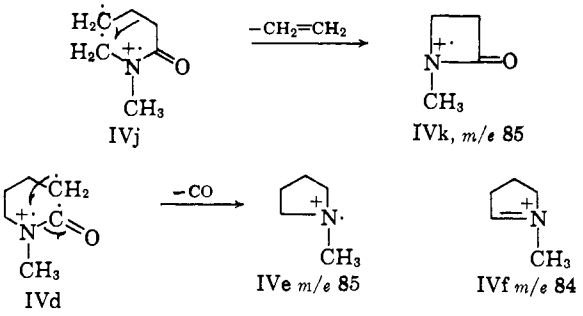
The base peak of the spectrum of 2-piperidone occurs at *m/e* 30 and its formation is shown (Table III) from deuterium labeling to involve transfer of a β-hydrogen with simultaneous carbon–nitrogen bond rupture. Mechanistically its formation is identical with the process used to explain the origin of *m/e* 30 in 2-pyrrolidone (Iq, R = H).

N-Methyl-2-piperidone (Fig. 4).—The mass spectrum of N-methyl-2-piperidone shows a molecular ion IVa and IVb of moderate intensity with a smaller M − 1 fragment. The latter was unaffected in the spectrum of N-d_3-methyl-2-piperidone (Table IV) and by analogy to 2-pyrrolidone it is assigned structure IVc.



A weak peak at *m/e* 85 (M − 28) is shifted to *m/e* 87 and 88 in the spectra of the 3,3-dideuterio and N-d_3-methyl compounds. Formally this loss could be attributed to carbon monoxide or ethylene, and the latter cannot involve C-3.

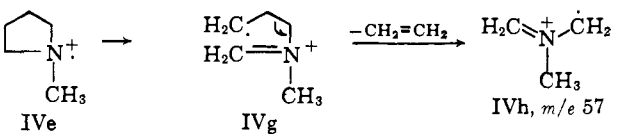
High-resolution mass spectrometry indicated the following composition for *m/e* 85: $C_4H_7NO^+$ (50%), $C_5H_9O^+$ (37%), and $C_5H_{11}N^+$ (13%). α-Cleavage of IVa would yield IVj which could eliminate ethylene to IVk, a structure in agreement with the deuterium labeling and one which accounts for 50% of the peak at *m/e* 85. Loss of carbon monoxide from IVd would yield IVe and account for an additional 13% of this peak.



The ion corresponding to loss of 29 mass units is of equally low abundance (Fig. 4) and might be attributed to expulsion of either an ethyl or formyl radical. No loss of deuterium from the labeled positions was noted and, by analogy to the M − 29 peak in the spectrum (Fig. 2) of N-methyl-2-pyrrolidone (IId → IIg → IIh), it is more likely that a formyl radical is lost with the charged species represented by IVf. This view was substantiated from high-resolution mass spectrometry which showed *m/e* 84 to consist of $C_5H_{10}N^+$ (85%) and $C_4H_6NO^+$ (15%).

The ion at *m/e* 70 (M − 43) is shifted to *m/e* 72 in the 3,3-dideuterio derivative and is unaffected in N-d_3-methyl-2-piperidone. This is consistent with its formulation as the cyclobutanone ion IIIf arising from mechanism 1 in the formation of *m/e* 70 in 2-piperidone, except that in the present case the neutral amine fragment $CH_2{=}NCH_3$ is lost. Loss of 43 mass units could also be attributed to expulsion of a propyl radical, involving carbon atoms 3, 4, and 5 with a hydrogen transferred from the N-methyl group, but this is eliminated from the spectrum of the N-d_3-methyl compound, where no transfer of deuterium was found.

The fragment of mass 57 (M − 56) is shifted completely to *m/e* 59 in N-methyl-3,3-d_2-2-piperidone and to *m/e* 60 in N-d_3-methyl-2-piperidone. A mechanism involving retention of C-3 with its hydrogen atoms and the N-methyl group can be envisaged as proceeding *via* expulsion of carbon monoxide from the molecular ion and formation of IVe. α-Cleavage of IVe would produce IVg, loss of ethylene then affording the resonance-stabilized ion radical IVh. Support for this mechanism was obtained from recognition of a metastable ion in the spectrum of N-methyl-3,3-d_2-2-piperidone at *m/e* 39.9 (calculated for *m/e* 87 → *m/e* 59, 40.1).

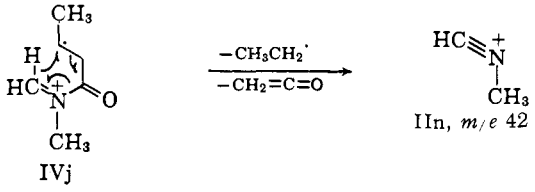


The ion at *m/e* 55 (M − 58) in N-methyl-2-piperidone has its genesis by an identical process as does the ion IIIm of the same mass in 2-piperidone (see above).

The base peak in the spectrum (Fig. 4) of N-methyl-2-piperidone occurs at *m/e* 44 and is shifted to *m/e* 45 in the 3,3-dideuterio analog, and to *m/e* 47 in the N-d_3-methylated compound. Its origin is thus identical with that of *m/e* 44 in N-methyl-2-pyrrolidone (Iq, R = CH_3), except for the nature of the neutral species.

The ion at *m/e* 42 (M − 71) in the spectrum of N-methyl-2-piperidone is transferred to the extent of 60% to *m/e* 44 in the 3,3-dideuterio compound, while 35% of it is shifted to *m/e* 45 in the case of N-d_3-methyl-2-

piperidone. This is qualitatively, although not quantitatively, analogous to the m/e 42 species in N-methyl-2-pyrrolidone (see above). Hence 60% of the peak can be assigned to ionized ketene IIj or cyclopropane ion Io and 35% to IIn. The latter evidently arises from expulsion of an ethyl radical and ketene from IVj.



The high-resolution mass spectrum established the composition of the m/e 42 peak as 38% $C_2H_2O^+$ (IIj), 19% $C_3H_6^+$ (Io), and 43% $C_2H_4N^+$ (IIn), while the ion at mass 41 contained $C_2H_3N^+$ (40%) and $C_3H_5^+$ (60%).

Summary.—All the fragments discussed in the spectra of the four lactams can be interpreted best by assuming the intervention of molecular ions in which a nonbonding electron from either oxygen or nitrogen is removed followed by α-cleavage with and without hydrogen rearrangement: (i) 2-Pyrrolidone and 2-piperidone show strong molecular ions, which are markedly reduced in the corresponding N-methylated compounds. Conversely the ions near mass 40 are more abundant in the N-methylated analogs than in the parent lactams. (ii) Loss of methyl (M − 15) is not a favored process in any of the lactams studied, while loss of 28 mass units is achieved in 2-piperidone and N-methyl-2-pyrrolidone by expulsion of ethylene, whereas in N-methyl-2-piperidone loss of carbon monoxide and CH_2N also contributes. (iii). In 2-pyrrolidone and 2-piperidone the M − 29 species is generated predominantly through elimination of $CH_2{=}NH$ and to a lesser degree of both a formyl and an ethyl radical, while the N-methylated compounds expel a formyl radical. (iv) The two six-membered lactams have an abundant fragment at m/e 55 arising in both cases by an identical process: IIIj → IIIk → IIIm. (v) The base peak in three lactams, 2-piperidone, N-methyl-2-pyrrolidone, and N-methyl-2-piperidone and an abundant ion in 2-pyrrolidone arise from β-hydrogen transfer to nitrogen in the respective molecular ions with concomitant carbon–nitrogen bond fission as depicted in Ip → Iq. (vi) All four lactams have relatively intense m/e 42 peaks which were shown to have a variable composition. This peak consists almost entirely of the cyclopropane ion Io in 2-pyrrolidone and in the N-methyl compound of almost equal amounts of Io and the species IIn. In 2-piperidone, Io was the dominant fragment, while in the N-methylated lactam m/e 42 consisted mainly of ionized ketene IIj plus IIn with a smaller contribution from Io. (vii). The ion at m/e 41 in all four lactams was shown to consist predominantly of the $C_3H_5^+$ species.

Experimental[13]

N-Deuterated Lactams.—The lactam (20 mg.) was shaken with deuterium oxide (0.1 ml.) and the mass spectrum determined.[5,7] The following deuterium incorporations were obtained: N-d_1-2-pyrrolidone, 80% d_1, 20% d_0; N-d_1-2-piperidone, 86% d_1, 14% d_0.

3,3-d_2-Lactams.—The lactam (250 mg.) was heated under reflux in deuterium oxide (2 ml.) containing potassium carbonate (150 mg.) over a period of 10 days. The solution was cooled, lyophilized, and the residue extracted with anhydrous ether. The dideuterio lactams were isolated and distilled *in vacuo*, and the following deuterium incorporations were obtained: 3,3-d_2-2-pyrrolidone (7 days reflux), 84% d_2, 16% d_1; 3,3-d_2-2-piperidone, 93% d_2, 7% d_1; N-methyl-3,3-d_2-2-pyrrolidone, 95% d_2, 5% d_1; N-methyl-3,3-d_2-2-piperidone, 95% d_2, 5% d_1.

5,5-d_2-2-Pyrrolidone.—Succinimide (200 mg.) in anhydrous tetrahydrofuran (10 ml.) was reduced with lithium aluminum deuteride (20 mg.) by heating under reflux for 1 hr. Water (2 drops) was added, the mixture filtered, and the solvent removed on the water bath. Preparative gas phase chromatography using polybutylene glycol[14] as the stationary phase at 145° and a helium pressure of 8 p.s.i. in. gave 5,5-d_2-2-pyrrolidone at a retention time of 21 min., shown by mass spectrometry to contain 97% d_2 species.

N-d_3-Methyl-2-pyrrolidone.—2-Pyrrolidone (100 mg.) in anhydrous tetrahydrofuran (2 ml.) was stirred under a nitrogen atmosphere with sodium hydride (100 mg.) during 30 min. Trideuteriomethyl iodide (0.06 ml.) was added and stirring continued for 2 hr. Ether (10 ml.) was added, the solution filtered, the solvent removed on the water bath, and the product isolated by preparative gas phase chromatography using polybutylene glycol[14] as the stationary phase at 135° and a helium pressure of 8 p.s.i. Under these conditions N-d_3-methyl-2-pyrrolidone had a retention time of 20 min. and was shown by mass spectrometry to contain 92% d_3 species.

N-d_3-Methyl-2-piperidone.—2-Piperidone (100 mg.) was converted into the trideuterio compound using the same conditions as described above. It had a retention time of 30 min. and mass spectrometry showed it to contain 92% d_3 species.

(13) All mass spectra—other than high-resolution spectra[9,10]—were obtained with a Consolidated Electrodynamics Corp. mass spectrometer Model No. 21-103C using an all-glass inlet system heated to 200°. The ionizing energy was maintained at 70 e.v. and the ionizing current at 50 μa. Preparative gas-phase chromatography was conducted on a Wilkins Aerograph instrument.

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