Tetrahedron, Supplement No. 7, pp. 145 to 173. Pergamon Press Ltd. Printed in Northern Ireland

MASS SPECTROMETRY IN STRUCTURAL AND STEREOCHEMICAL PROBLEMS–XCVII[1]

A STUDY OF THE FRAGMENTATION PROCESSES OF OXIMES[2]

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(*Received* 2 *November* 1965)

Abstract—Aliphatic aldoxime and ketoxime spectra are characterized by substantial McLafferty rearrangement peaks, the site specificity of the accompanying hydrogen rearrangements having been demonstrated by deuterium labeling. In contrast to dipropyl ketone, the McLafferty rearrangement of its oxime is accompanied to a small extent by methyl migration. Another diagnostic, though less prevalent process of such oximes is fission of the γ-bond.

Alicyclic ketoximes, such as cyclopentanone and cyclohexanone oxime, yield more complex spectra with many hydrocarbon ions. A characteristic heteroatom fission is the loss of an oxygen atom from the molecular ion—a reaction which is not observed in aliphatic oximes but does occur in aromatic ones such as benzophenone oxime. The previously claimed occurrence of an electron impact-induced Beckmann rearrangement in benzophenone oxime could not be substantiated.

In terms of fragmentation-directing ability, the oxime function does not surpass the carbonyl group as shown by the mass spectra of the oximes of 2-, 3- and 11-keto steroids. Through the aid of several deuterated analogs plausible structures and reaction paths could be presented for several characteristic ions.

INTRODUCTION

AN UNDERSTANDING of the ability of various functional groups to control and direct the mass spectrometric fragmentations of organic molecules is of fundamental importance in the use of this technique for structure elucidation.[4] Previous work has shown, for example, that whereas extensive correlations between the mass spectra and the structures of various steroidal ketones are not possible,[5] the use of the corresponding ethylene ketals or dimethylamino compounds does in fact lead to largely predictable fragmentation patterns.[6] As part of the investigation of a variety of functionally substituted compounds we have examined the mass spectra of oximes. The oxime function, in contrast to the ketal and amino groups noted above, has trigonal hybridization. It was of particular interest, therefore, to determine whether oximes resemble in their fragmentation processes ketones[7] and their azomethine

* This contribution has been dedicated to the memory of Professor H. Stephen.

[1] Paper XCVI, M. Fischer and C. Djerassi, *Chem. Ber.* in press.

[2] Financial assistance by the National Institutes of Health (Grants No. AM-04257 and CA-07195) is gratefully acknowledged.

[3] [a] N.I.H. Special Fellow (1965) while on leave from Emory University, Atlanta, Georgia; [b] Recipient of a NATO postdoctoral fellowship, 1965–1966; [c] National Science Foundation predoctoral fellow, 1963–1965.

[4] See for instance H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, Holden-Day, San Francisco (1964).

[5] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Structure Elucidation of Natural Products by Mass Spectrometry*, Vol. II; chap. 20, Holden-Day, San Francisco (1964).

[6] For review and leading Refs see chap. 18 in Ref. 5.

[7] See chap. 1 in Ref. 4.

derivatives,[1] or whether their spectra become simplified as in amines and ketals because of favored charge stabilization by the new substituent. Oximes, differ from carbonyl compounds and Schiff bases by offering the possibility of stabilization of the initial positive charge by two different heteroatoms. Of additional interest, therefore, was the attempt to determine if any differentiation between the two might be made as a result of their differing abilities to trigger the various fragmentation processes.

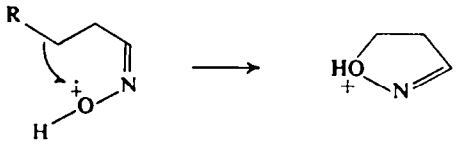
Some work pertaining to this problem has been reported. Harless[8] examined a number of aliphatic oximes and suggested that "the most important feature of these compounds is their tendency to form an ion representing the charged molecule of the lowest member of the family, acetoxime in the case of ketoximes and acetaldoxime in the case of the aldehyde derivatives." As part of another investigation Bose and collaborators[9] reported that the fragmentations of several diaryl and aryl-alkyl ketoximes were complicated by Beckman rearrangements of the molecular ion with the resulting spectra showing the patterns of the corresponding amides. As will be shown in the sequel, substantial modification of both of these views is necessary. There has also appeared recently[10] a report of some of the features of the spectra of *o*-methylated oximes of a number of steroids. In the present paper we shall discuss the mass spectra of simple acyclic and cyclic aliphatic oximes, benzophenone oxime and steroidal ketoximes as typical examples of the various types of oximes which are most likely to be encountered in practice.

Aliphatic aldoximes

Both butyraldehyde oxime (I) (Fig. 1) and valeraldehyde oxime (II) (Fig. 2) show small molecular ions and peaks at M-17 for the loss of a hydroxyl radical. The first major fragment is found in each spectrum at *m/e* 72. This corresponds to the loss of a methyl radical from butyraldehyde oxime and of an ethyl radical from the five-carbon analog. In both cases high resolution measurement verified the expected formulation, $C_3H_6NO^+$. It is clear that these cleavages must result in a species that has some special stability and that they are not the result of simple losses of alkyl fragments. If the latter were the case, then valeraldehyde oxime would also be expected to show a prominent M-15 peak. In fact it is a minor feature of the spectrum (Fig. 2). This special stabilization is then presumably either ring formation between the site of the intially formed ion-radical and the new radical center produced by loss of the alkyl moiety, or due to homoylsis of a tautomeric molecular ion.

The nature of the ring species, if operative, is uncertain. As noted above two heteroatoms are available in oximes for preferred charge localization, and the two possible electron deficient species, *a*, and *b*, for butyraldehyde oxime are in effect interconvertible resonance forms. Considering them separately, however, leads to the formulation of two structures for the *m/e* 72 ion. Loss of a methyl radical from *a* would lead to the protonated isoxazolene *c*, while location of the charge on nitrogen as in *b* would produce the four-membered ring structures, *d*, for this fragment. The same argument holds for the loss of an ethyl radical from *a'* and *b'*.

[8] H. R. Harless, paper presented at ASTM Committee, E-14, *Mass Spectrometry Conference*, Montreal, August (1964).
[9] P. Funke, K. G. Das and A. K. Bose, *J. Amer. Chem. Soc.* **86**, 2527 (1964).
[10] H. Fales and T. Luukkainen, *Analyt. Chem.* **37**, 955 (1965).



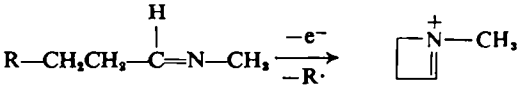
a, R = CH_3 *m/e* 97
a', R = C_2H_5 *m/e* 113

c, *m/e* 72

b, R = CH_3 *m/e* 97
b', R = C_2H_5 *m/e* 113

d, *m/e* 72

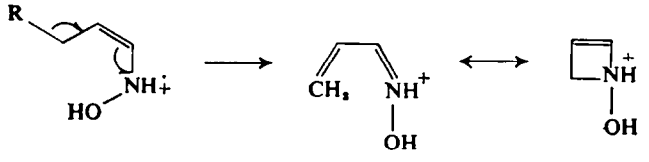
Results from other series of compounds suggest that the latter is the preferred species. The mass spectra of the Schiff bases III and IV show[1] the same type of cleavage as the aldoximes described above leading to a fragment ion at *m/e* 70 which in terms of ring formation can only correspond to the four-membered imine *e*. Ketones also show[11] specific cleavage of the γ-bond since di-n-propyl ketone loses a methyl radical, while di-n-butyl ketone exhibits instead the preferential expulsion of an ethyl radical. It might be noted additionally that in terms of charge stabilization of the product ion, the four-membered ring is preferred on electronic grounds since only in this species is delocalization of the charge possible.



III R = CH_3
IV R = C_2H_5

c, *m/e* 70

An alternative explanation for this fragmentation, however, arises from the possibility of allylic cleavage of the tautomeric molecular ions, *f* and *f'*. The species produced by rupture of the γ-bond in this enoximino form would then be the protonated oxime, *g*. Analogous enol forms and ions could also explain the corresponding cleavages in Schiff bases[1] and ketones.[11]



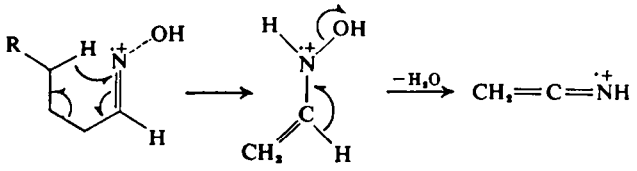
f, R = CH_3 *m/e* 97
f', R = C_2H_5 *m/e* 113

g, *m/e* 72

The base peak in both aldoxime spectra occurs at *m/e* 59. High resolution measurements show it to be the fragment $C_2H_5NO^+$, and in one case, valeraldehyde oxime, its

[11] H. Budzikiewicz, C. Fenselau and C. Djerassi, *Tetrahedron* **22**, 1391 (1966).

direct formation from the molecular ion is substantiated by a metastable ion at *m/e* 34·5 ($59^2/101 = 34·5$). This mode of cleavage is obviously analogous to the well known McLafferty rearrangement[12] of carbonyl compounds and may be represented mechanistically for the two aldoximes as shown below. It is noteworthy that butyraldehyde oxime which must transfer a primary hydrogen in this process does so in contrast to



h, *m/e* 59 *i*, *m/e* 41

the corresponding 2,4-dinitrophenylhydrazone[13] which does not show a similar rearrangement ion. Not until a secondary hydrogen is available as in valeraldehyde 2,4-dinitrophenylhydrazone is the McLafferty rearrangement observed.[13]

Further fragmentation of the ion of mass 59 is evidenced by a metastable peak in the butyraldehyde oxime spectrum at *m/e* 28·5 ($41^2/59 = 28·5$) for the formation of an intense peak at *m/e* 41. High resolution measurements show the latter to be mainly $C_2H_3N^+$, and the pathway $h \rightarrow i$ indicates a plausible mode for its formation. The remaining peaks in both spectra consist for the most part of nitrogen-containing species in which the hydroxyl group has been lost, or of hydrocarbon ions. For example, as determined by high resolution mass spectrometry, only *m/e* 46 (CH_4NO^+) from butyraldehyde oxime retains the oxygen function, while *m/e* 54 and 50% of *m/e* 52 are the species $C_3H_4N^+$ and $C_3H_2N^+$, and *m/e* 56, 55, and the remaining 50% *m/e* 52 are the appropriate hydrocarbons. The same general pattern is seen in the spectrum (Fig. 2) of valeraldehyde oxime.

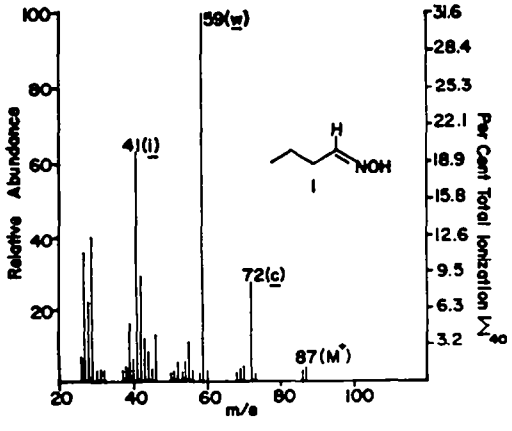


FIG. 1. Mass spectrum of butyraldehyde oxime (heated inlet).

[12] F. W. McLafferty, *Analyt. Chem.* **31**, 82 (1959).
[13] C. Djerassi and S. Sample, *Nature, Lond.* **208**, 1314 (1965).

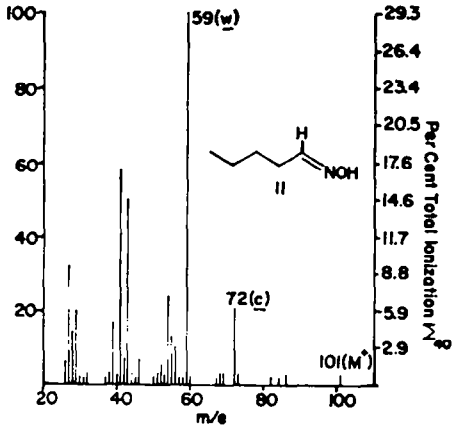
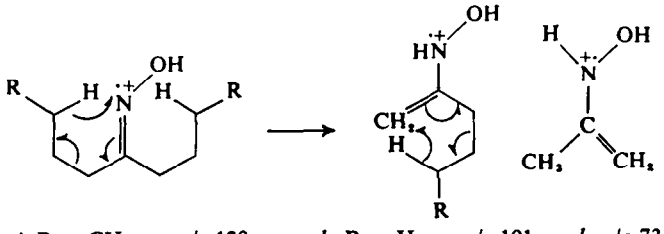


FIG. 2. Mass spectrum of valeraldehyde oxime (heated inlet).

Aliphatic ketoximes

Examination of the spectra of several aliphatic ketoximes and their deuterated derivatives reveals both similarities and significant contrasts to the fragmentations of the corresponding ketones. In terms of total ionization, the electron impact induced dissociation of oximes is more complex than that of the ketones. The base peak (*m/e* 43) of di-n-propyl ketone,[11] for example, constitutes 39% Σ_{40}. In the corresponding oxime (V) spectrum (Fig. 3), however, the base peak (*m/e* 73) amounts only to 24·2% Σ_{40}, and only one other peak in the latter spectrum accounts for more than 10% of the total ionization. The most striking aspect of this spectrum (Fig. 3) and that of the dibutyl analog VI (Fig. 4), is the nature of the base peak, which occurs at *m/e* 73 and which was shown by high resolution measurements to correspond to $C_3H_7NO^+$. This ion must be the oxime equivalent of the *double* McLafferty rearrangement peak (*m/e* 58) of unbranched aliphatic ketones[11,14] and its formation may be represented by the process *j* (or *j'*) → *l*.



j, R = CH_3 *m/e* 129 *k*, R = H *m/e* 101 *l*, *m/e* 73
j, R = CH_3 *m/e* 143 *k'*, R = CH_3 *m/e* 115

This conclusion necessitates the postulation, analogous to the aldoximes, of an initial McLafferty rearrangement of the molecular ion (*j* or *j'*) to an ion (*k* or *k'*) of mass 101 for di-n-propyl ketoxime, and mass 115 for the di-n-butyl compound. Both of these species are found in the appropriate spectra, and from high resolution measurements are found to have the expected molecular compositions, $C_6H_{12}NO^+$ and $C_7H_{14}NO^+$. There are found additionally the appropriate metastable ions for

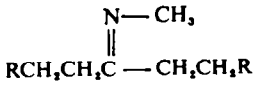
[14] A. G. Sharkey, Jr., J. L. Shultz and R. A. Friedel, *Analyt. Chem.* **28**, 934 (1956).

these transformations (Table 1). Although these ions appear to be produced by the mechanistic pathway of the McLafferty rearrangement, they differ markedly from the equivalent ketone and azomethine fragments in their contribution to the total ionization. The single and double McLafferty peaks in the spectrum of di-n-propyl ketone constitute only 0·5% Σ_{40} and 3·7% Σ_{40} respectively. For di-n-butyl ketone the values are 1·8% Σ_{40} and 18·1% Σ_{40}[11]. For the methyl amine-derived Schiff bases, VII

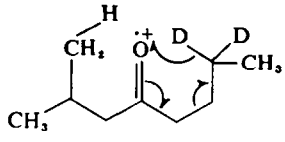
TABLE 1. METASTABLE PEAKS IN MASS SPECTRA OF N-DIPROPYL AND N-DIBUTYL KETONES

	Metastable Peaks (*m/e*)		
	Observed	Calculated	Transition
n-Dipropyl ketone	100·7	100·7	129 → 114
	79·1	79·1	129 → 101
	52·7	52·7	101 → 73
	39·1	39·1	43 → 41
	26·4	26·4	70 → 43
n-Dibutyl ketone	84·2	84·2	157 → 115
	46·3	46·3	115 → 73

and VIII, the contributions of the second McLafferty peaks have been found to be 6·5% Σ_{40} and 22·3% Σ_{40}. As noted previously the double McLafferty rearrangement peaks from the two oximes, the base peaks of the spectra, are 24·2% Σ_{40} and 26·2% Σ_{40}. These striking differences, particularly for the propyl compounds, in the abundance of the rearrangement ions of oximes vis à vis ketones and Schiff bases raises the question of how closely the analogy between the various systems may be drawn.



VII R = CH_3
VIII R = C_6H_5

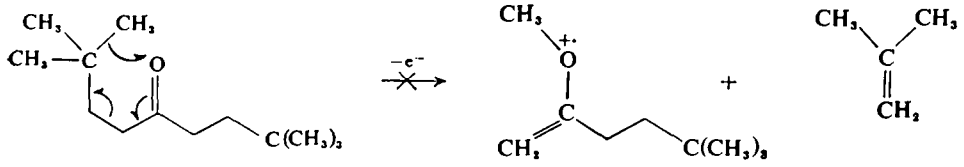


m, m/e 144

The ketone rearrangements have recently been investigated in detail[11] and a marked preference (>10:1) for the transfer of a secondary hydrogen over a primary one has been found. As noted above, transfer of hydrogen from the terminal methyl group of butyraldehyde 2,4-dinitrophenylhydrazone simply does not occur.[13] In contrast to these cases, McLafferty type rearrangements of both aldoximes and ketoximes are the most favored fragmentation processes. Although it is not yet clear why the energetics of this pathway should vary so widely, we have shown that the process is fundamentally the same in oximes as it is in carbonyl compounds,[11] i.e., the single and double McLafferty rearrangements of oximes are for the greatest part site specific for the transfer of a γ-hydrogen.

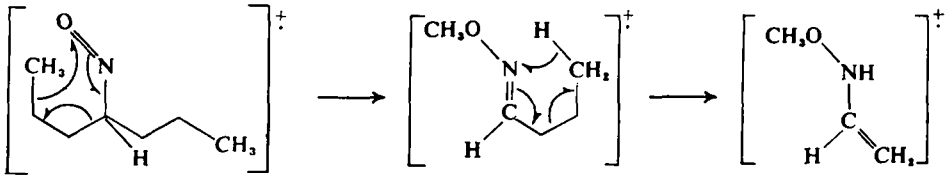
An analysis of the spectrum (Fig. 3) of γ,γ'-d_6-di-n-propyl ketoxime reveals that the first McLafferty rearrangement ion shifts from *m/e* 101 to *m/e* 105 to the extent of 85%. This is attributable to the transfer of one deuterium atom from a γ-position, and a high resolution measurement confirmed the expected composition of the rearrangement ion as $C_5H_7D_4NO^+$. There are also found shifts of the *m/e* 101 peak to *m/e* 104

(9%) corresponding to a non-specific shift of hydrogen from either the α- or β-positions, and at *m/e* 107 (6%) resulting from what is apparently a d_3-methyl shift. For the parent ketone a value of at least 85% γ-site specificity has been found.[11] For the double McLafferty peak of the oxime one finds again a specific γ-deuterium shift of 85% (*m/e* 73 → *m/e* 75), a non-specific shift of 8% (*m/e* 73 → *m/e* 74), and a methyl migration shift of 7% (*m/e* 73 → *m/e* 77), the composition of the latter ion, $C_3H_3D_4O^+$, having been verified by high resolution. Interestingly, methyl migrations do not seem to occur in the fragmentations of the dipropyl and dibutyl ketones[15] or Schiff bases.[1] Neither does one occur with the ketone IX[16] in which such a process might most likely happen since no hydrogens are available for the normal McLafferty rearrangement.



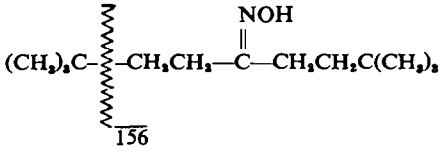
IX

Conceivably the tautomeric possibilities of the oxime system and the availability of more than one site for charge localization may account for the observed methyl migrations as shown below in the overall change from molecular ion to rearrangement ion (n). A normal McLafferty rearrangement of *n* to form *o* would then account for the presence of an apparent methyl migration in the second stage of this fragmentation



n, *m/e* 101 *o*, *m/e* 73

process. In addition this type of rearrangement appears limited to methyl groups as γ,γ′-d_4-di-n-butyl ketoxime shows only γ-deuterium transfer in both the single and double McLafferty rearrangement. Further confirmation of the γ-hydrogen specificity of these rearrangements was provided by the electron impact fragmentation of the fully γ-substituted ketoxime X.[16] This oxime, if it is to undergo β-cleavage with transfer of a hydrogen atom, must clearly deliver the latter from a position other than

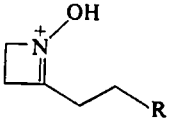


X

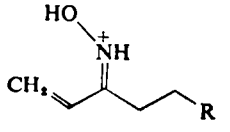
[15] As seen from the spectra of deuterated derivatives published in Ref. 11.
[16] R. R. Arndt and C. Djerassi, *Chem. Commun.* 578 (1965).

a γ- site. In fact no peak appears at either *m/e* 143 or *m/e* 73 for this type of rearrangement ion.

The simple ketoximes are also characterized by the same type of γ-cleavage as found in aldoximes. Di-n-propyl ketoxime accordingly shows a peak at *m/e* 114, for the loss of a methyl radical, and the dibutyl compound a peak at *m/e* 128 for the species corresponding to the loss of an ethyl radical. As before, the compositions of both ions were confirmed by high resolution mass spectrometry. These fragments may be represented structurally as either *p* and *p'* or *q* or *q'* since the species undergoing cleavage may be either the oximino form of the molecular ion or the tautomeric hydroxyenamino form. The *m/e* 128 peak in the dibutyl spectrum (Fig. 4) is shifted to *m/e* 130 in the γ,γ'-d_4-oxime, and the M-15 peak from the dipropyl oxime (Fig. 3) is shifted to *m/e* 117 in the γ,γ'-d_6-analog showing in both cases that the β,γ-bond is broken with the loss of the γ-carbon and any attached substituents. As expected the fully γ-substituted oxime X loses the 57 mass unit t-butyl group by γ-cleavage to produce a fragment at *m/e* 156.

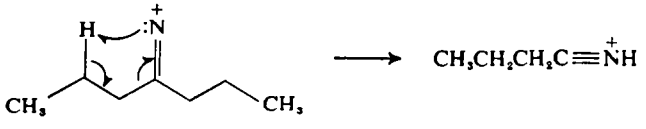


p, R = CH_3 *m/e* 114
p', R = C_2H_5 *m/e* 128



c, R = CH_3 *m/e* 114
q', R = C_2H_5 *m/e* 128

One other aspect of the fragmentation patterns of these two ketoximes which may be noted here is the series of peaks in which the hydroxy group of the oxime is no longer present. For example, in the spectrum (Fig. 3) of the dipropyl ketoxime peaks occur at *m/e* 112 for the ion *r* ($C_7H_{14}N^+$) and at *m/e* 70 for the rearrangement ion *s* ($C_4H_8N^+$). Di-n-butyl ketoxime displays (Fig. 4) peaks at *m/e* 140 ($C_5H_{10}N^+$) and *m/e* 84 for the homologous fragments. The formulations of all of these species were verified by high resolution measurements.



r, *m/e* 112 *s*, *m/e* 70

Before turning our attention to other classes of oximes, some comment is required on the earlier quoted conclusions of Harless.[8] His contention that acyclic aldoximes and ketoximes fragment under electron impact to form ions representing the lowest member of each class (acetaldoxime and acetoxime respectively) is of course, a limited expression of the tendency of these compounds to undergo β-cleavage with accompanying hydrogen migration, i.e., McLafferty rearrangement. For obvious reasons, therefore, methyl sec-butyl ketoxime does not give an *m/e* 73 ion ("acetoxime") according to Harless[8] but does give a peak at *m/e* 87 for the ion produced by a normal McLafferty process.

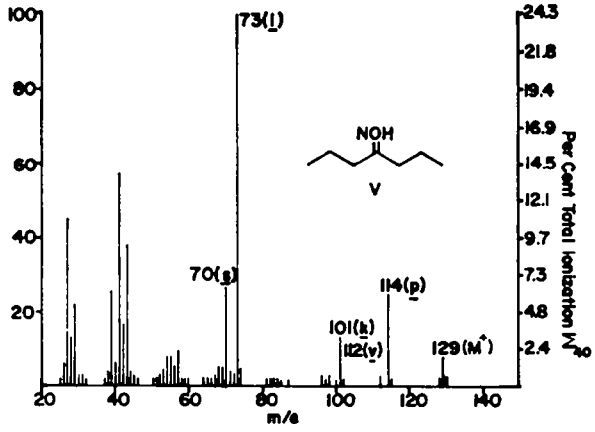


FIG. 3. Mass spectrum of di-n-propyl ketoxime (heated inlet).

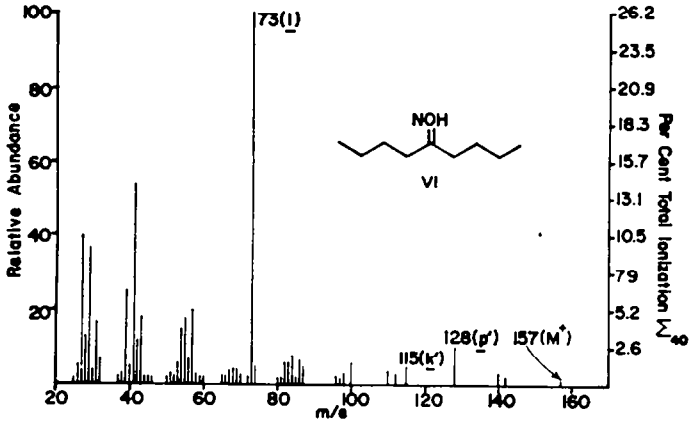


FIG. 4. Mass spectrum of di-n-butyl ketoxime (heated inlet).

Alicyclic ketoximes

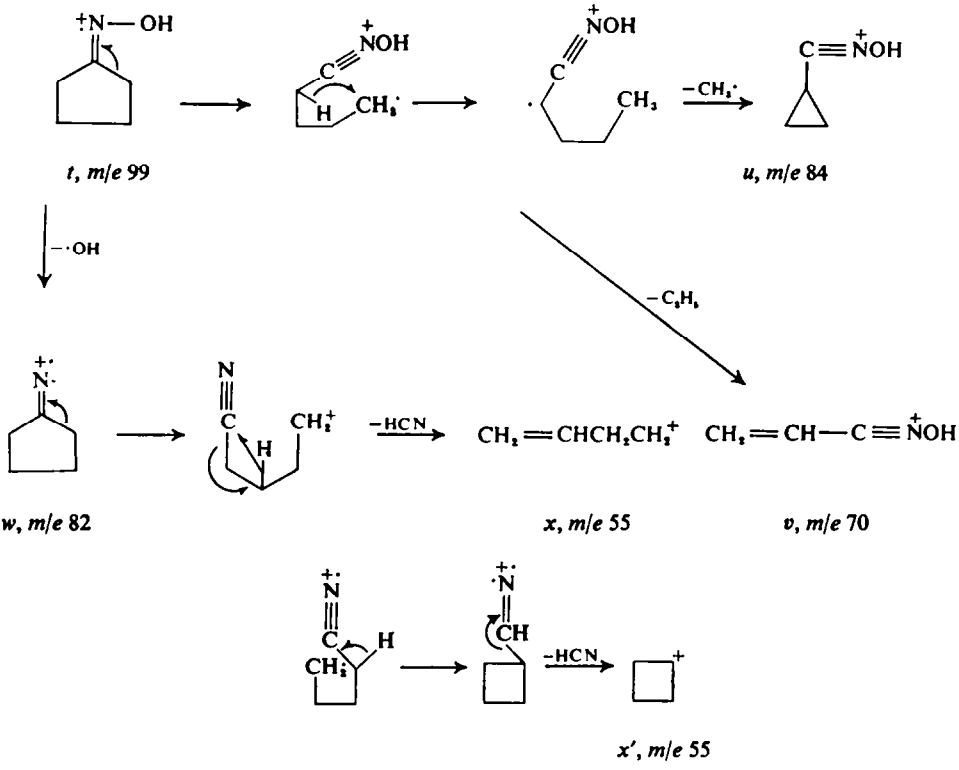
In contrast to the acyclic cases, the cyclic ketoximes appear to undergo some α-cleavage. For example in the spectrum (Fig. 5) of cyclopentanone oxime (XI) the following pathways, supported by the appropriate metastable ions (Table 2) and high resolution measurements (Table 3) account for the appearance of the weak ions of mass 84 and 70 which may be depicted in terms of *u* and *v*. The more abundant peaks in this spectrum (Fig. 5), however, arise from the breaking of heteroatom bonds, followed in many cases by α-fission of the resulting fragments. It is significant that many of the fragment ions consist of hydrocarbons. The base peak (*m/e* 55) 16·4% Σ_{40}, as evidenced by metastable ions (Table 2) and high resolution measurements (Table 3), is formed first by loss of a hydroxyl radical from the molecular ion (*t*) to yield *w* (*m/e* 82: $C_5H_8N^+$). Its formulation as *x* and *x'* ($C_4H_7^+$) requires two successive α-cleavages, the second one with concomitant hydrogen migration. That the migrating hydrogen originates from the α- and β-positions is shown by the shift of the *m/e* 55 peak to *m/e* 58 and 59 in the spectrum of the 2,2,5,5-d_4-oxime. The next lower mass peak, *m/e* 54, is a doublet (Table 3) consisting of 66% $C_3H_4N^+$ and 33% $C_4H_6^+$. A metastable ion (Table 2)

TABLE 2. METASTABLE PEAKS IN MASS SPECTRA OF CYCLOPENTANONE OXIME

Metastable Peaks (*m/e*)		
Observed	Calculated	Transition
78·1	78·1	82 → 80
71·3	71·3	99 → 84
67·9	67·9	99 → 82
66·3	66·3	99 → 81
65·3	65·3	98 → 80
51·1	51·1	55 → 53
49·5	49·5	99 → 70
45·3	45·3	99 → 67
36·9	36·9	82 → 55
35·2	35·1	83 → 54
28·2	28·2	54 → 39
27·7	27·6	67 → 43
25·2	25·1	67 → 41

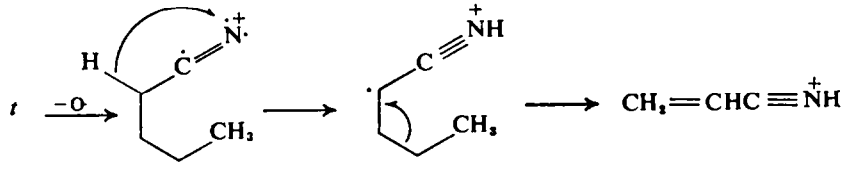
TABLE 3. HIGH RESOLUTION MASS MEASUREMENTS OF SOME CYCLOPENTANONE OXIME IONS

m/e	Composition	%
39	C_3H_3	100
41	C_2H_3N	20
41	C_3H_5	80
42	C_2H_4N	67
42	C_3H_6	33
43	C_2H_5N	33
43	C_3H_7	67
53	C_3H_3N	20
53	C_4H_5	80
54	C_3H_4N	67
54	C_4H_6	33
55	C_4H_7	>90
55	C_3H_5N	<10
67	C_4H_5N	10
67	C_5H_7	90
80	C_5H_6N	100
81	C_5H_7N	100
82	C_5H_8N	100
83	C_5H_9N	100
84	C_4H_6NO	100



t, *m/e* 99 *u*, *m/e* 84 *w*, *m/e* 82 *x*, *m/e* 55 *v*, *m/e* 70 *x'*, *m/e* 55

indicates that at least one of these species is derived from an M-16 ion (discussed below). It would seem likely that the nitrogen-containing portion of the doublet at *m/e* 54 is the progeny of this oxygen-free moiety and a likely pathway for its formation is given in the sequence $t \rightarrow y \rightarrow z$.



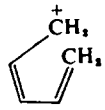
y, *m/e* 83 *z*, *m/e* 54

The peak appearing at *m/e* 67 is also the consequence of heteroatom loss. The species is principally a hydrocarbon (Table 3) and at least in part (Table 2) is produced directly from the molecular ion by the loss of the radical ·NHOH. Examination of the spectrum of the oxime of 2,2,5,5-d_4-cyclopentanone[17] indicates that the hydrogen that is lost from the ring in this fission may come from both the α and β positions since the *m/e* 67 peak is shifted to both *m/e* 70 and *m/e* 71. Although a number of structures, such as *aa* or *bb*, may be written for this ion, their genesis remains mechanistically obscure. Other hetero bond cleavages are seen (Table 3) in the ions of mass

[17] Z. Pelah, M. A. Kielczewski, J. M. Wilson, M. Ohashi, H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.* **85**, 2470 (1963).

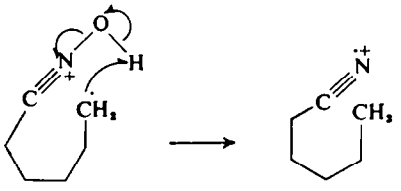
80, 81 and 93. The *m/e* 80 peak is associated (Table 2) with "dehydration" of the M-1 species, while the *m/e* 81 peak arises from the loss of water from the molecular ion. In accord with the high resolution data (Table 3) and the proposed mechanisms only the *m/e* 8/4 peak was shifted in the mass spectrum of the O-d_1-oxime.

aa

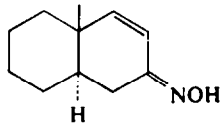


bb

Of particular interest is the *m/e* 83 species which corresponds (Table 3) to the loss of an oxygen atom from the parent ion. The same type of M-16 peak is also found in the spectrum (Fig. 6) of cyclohexanone oxime (XII), in the spectra of steroidal oximes and to an especially marked extent in the unsaturated ketoxime XIII.[18] This oxygen loss is not observed with either the corresponding carbonyl compounds[7] or with the acyclic aliphatic oximes. One possible explanation for this sixteen mass unit loss in cyclic oximes may lie in their capacity for α-cleavage. Since the species formed by such a fission still contains a reactive radical center as in *cc* the ability of the hydroxyl group to undergo an intramolecular hydrogen transfer might account for the overall expulsion of oxygen, as shown below for cyclohexanone oxime. With acyclic oximes α-cleavage results in the complete separation of the radical center thereby preventing

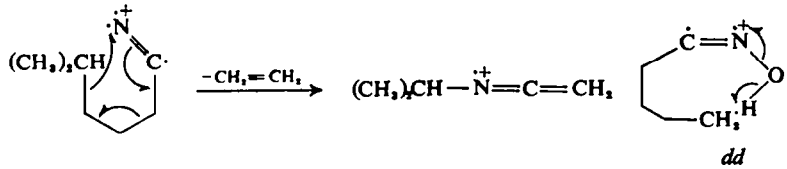


cc



XIII

the ready transfer of a hydrogen. This explanation would appear to founder on a stereochemical reef since the distances in the initial α-cleavage product corresponding to *cc* from cyclopentanone oxime seem too great for transfer of hydrogen. It has been shown,[19] however, that considerable distortion of "normal" sp bond angles occurs in the fragmentations of ions produced by electron bombardment. Isohexyl cyanide, for example, loses carbon atoms three and four with transfer of an isopropyl group through a six-membered transition state as shown below. With the α-cleavage product of cyclopentanone oxime mesomeric contributions from extreme structures such as *dd*



dd

[18] Unpublished results of F. Komitsky of this Laboratory.

[19] R. Beugelmans, D. H. Williams, H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.* **86**, 1386 (1964).

would lead to a bridging of the distance necessary for the hydrogen migration. A variety of other examples in which the linear geometry of other sp hybridized systems is distorted in such rearrangements is also known.[20]

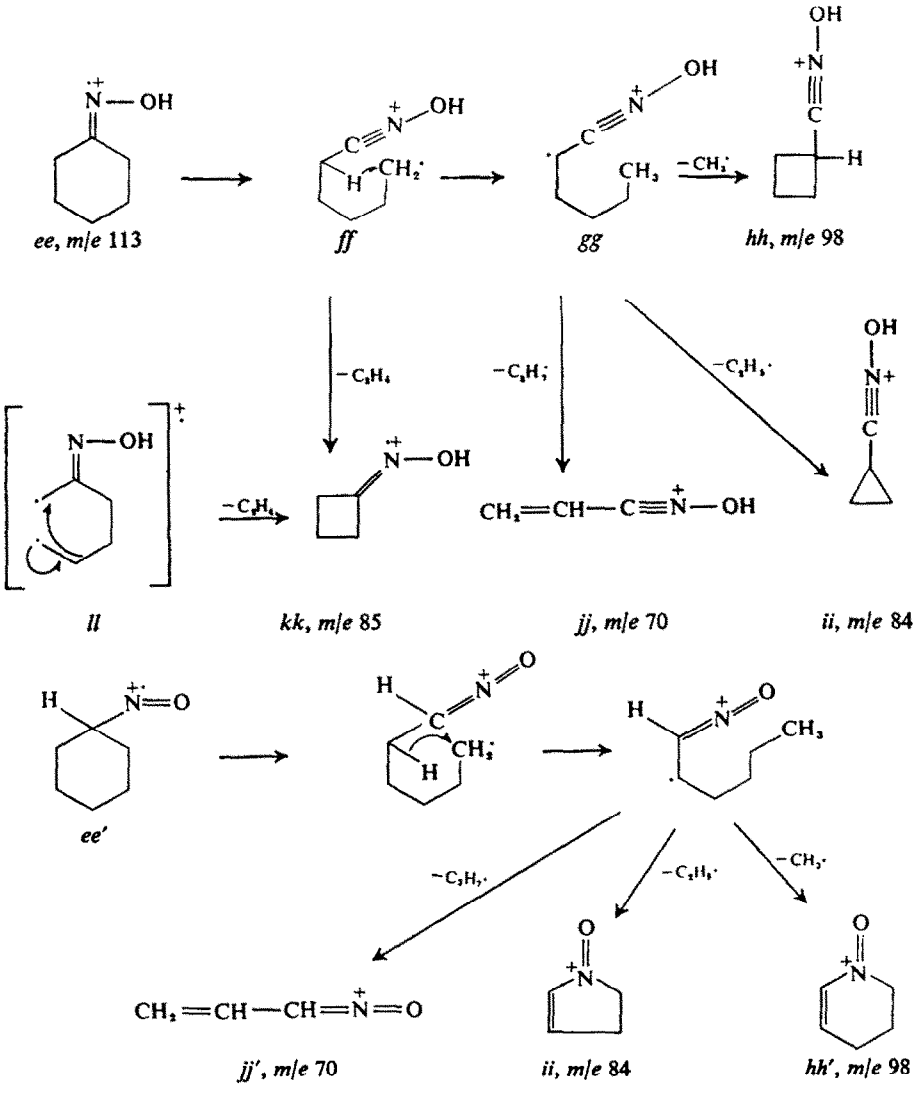
The spectrum (Fig. 6) of cyclohexanone oxime (XII) displays the same general fragmentation pattern as that of cyclopentanone oxime, namely cleavage of hetero bonds and α-cleavage. For instance, there are seen (Table 4) losses from the molecular ion of oxygen, hydroxyl radical and water at *m/e* 97, 96 and 95, and losses of methyl, ethyl, ethylene and propyl groups at *m/e* 98, 84, 85 and 70. A number of pathways may be written for the formation of these ions. Thus, one route involves α-cleavage and rearrangement of the cyclohexanone oxime molecular ion *ee* to form the ion-radical *gg*. This species in turn would lose methyl, ethyl or propyl radicals to

TABLE 4. HIGH RESOLUTION MASS MEASUREMENTS OF SOME CYCLOHEXANONE OXIME IONS

m/e	Composition	%
39	C_3H_3	100
41	C_3H_3N	33
41	C_3H_5	67
42	C_3H_4N	40
42	C_3H_6	60
51	C_3HN	50
51	C_4H_3	50
52	C_3H_3N	75
52	C_4H_4	25
53	C_3H_3N	50
53	C_4H_5	50
54	C_3H_4N	87
54	C_4H_6	13
55	C_4H_7	100
66	C_4H_4N	50
66	C_5H_6	50
67	C_4H_5N	40
67	C_5H_7	60
68	C_4H_6N	50
68	C_5H_8	50
69	C_4H_7N	50
69	C_5H_9	50
72	C_3H_6O	100
77	C_6H_5	100
79	C_6H_7	100
81	C_6H_9	100
82	C_5H_8N	75
82	C_6H_{10}	25
83	C_6H_{11}	100
84	C_4H_6NO	100
85	C_4H_7	100
96	$C_6H_{10}N$	100
97	$C_6H_{11}N$	100
98	C_5H_8NO	100

[20] See chap. 6 in Ref. 4.

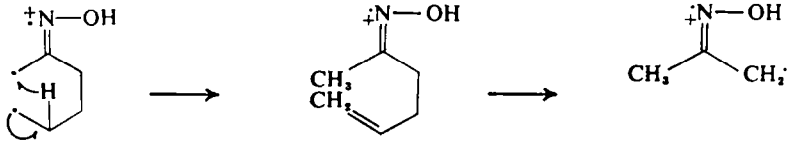
form *hh*, *ii* and *jj*. The intermediate α-fission product *ff* may also eject ethylene to yield *kk* (*m/e* 85). Alternatively, disintegration of the tautomeric nitroso molecular ion *ee'* by loss of the methyl, ethyl and propyl radicals would suggest the formulations, *hh'*, *ii'* and *jj'* for *m/e* 98, 84 and 70. The spectrum (not shown) of 3-d_1-cyclohexanone oxime lends some credence to these postulations. It is observed, for example, that the *m/e* 98 peak ($M-CH_3$) is shifted by the expected one mass unit to *m/e* 99, and the



m/e 84 peak is shifted in part (50% chance of losing the C-3 deuterium) to *m/e* 85. The region of the *m/e* 70 peak is too complex to detect the isotope shift of this peak. An alternative proposal for the formation of the *m/e* 85 peak (loss of ethylene) involves β-cleavage of *ee* to form *ll* which then loses two carbon atoms to yield *kk*. This proposal is experimentally different from the one given above since the ion

produced here would retain all of the original α-hydrogens of the oxime. In contrast, the fragment obtained *via* the route of initial α-cleavage would have lost two of these hydrogens. The spectrum of the oxime of 2,2,6,6-d_4-cyclohexanone shows that both these mechanisms and perhaps still others are operative since the original *m/e* 85 peak appears to be shifted to *m/e* 87, 88 and 89.

The origins of a number of other fragments are also revealed by the spectra of the deuterated derivatives. The ion $C_3H_6NO^+$ (Table 4) of mass 72 in cyclohexanone oxime appears partly at *m/e* 72 and partly at *m/e* 73 in the spectrum of 3-d_1-cyclohexanone oxime. With the 2,2,6,6-d_4 derivative at least part of this fragment occurs at *m/e* 76, a shift of four mass units from the position of the unlabeled fragment. These results are only compatible with β-cleavage of the molecular ion *ee* to yield a species *mm* which transfers hydrogen from either C-3 or C-4 to produce *nn*. Finally, cleavage of the latter yields *oo* as the *m/e* 72 species. Other labeling results which may be noted



mm *nn* *oo*, *m/e* 72

are the partial shift of *m/e* 59 to *m/e* 60 in the spectrum of the 3-d_1 oxime indicative of another non-specific hydrogen rearrangement, and the change in the triumvirate of doublets (Table 4) at *m/e* 52, 53 and 54, which also shift in part one mass unit higher with the same deuterated derivative. It is evident, however, from the high resolution mass measurements (Table 4) of many of the peaks in the cyclohexanone oxime spectrum that the oxime group has only a partial role in triggering the course of the fragmentation. For example, peaks at *m/e* 66–69, and 51–54 are all doublets composed of a hydrocarbon and the isobaric nitrogen-containing species. In addition, *m/e* 55, 77, 79 and 81 are solely hydrocarbons.

The different measuring conditions may have an important influence on the fragmentation of alicyclic oximes.

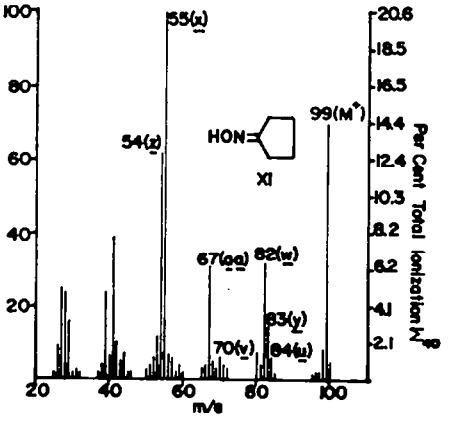


FIG. 5. Mass spectrum of cyclopentanone oxime (heated or direct inlet).

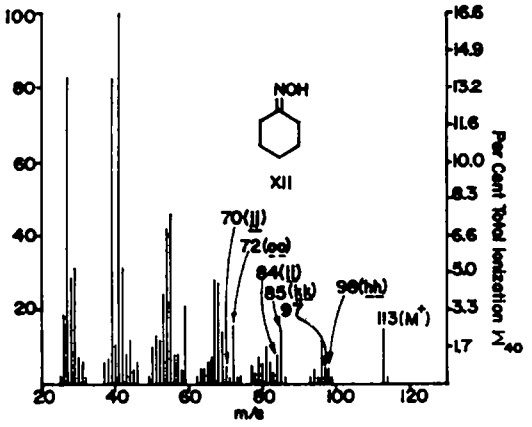
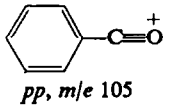


FIG. 6. Mass spectrum of cyclohexanone oxime (heated inlet).

Benzophenone oxime

From the preceding discussion it is clear that virtually the only skeletal rearrangements that occur during the electron impact induced dissociations of oximes are migrations of hydrogen atoms. The only discernible exception to this statement from our work is the previously discussed finding of a minor amount of methyl migration in the single and double McLafferty rearrangements of di-n-propyl ketoxime. Another type of oxime, however, said to undergo deep seated rearrangement in the mass spectrometer ion source is benzophenone oxime (XIV).[9] This rearrangement, a Beckmann type process leading to benzanilide, is claimed to be caused by electron impact and to be a property of the *molecular ion*. Because of the paucity of rearrangements of groups other than hydrogen found in our work on oximes we have reinvestigated this problem.

The spectrum of benzophenone oxime was obtained in two ways; first by direct introduction of the sample into the ion source of an AEI MS-9 mass spectrometer, and second by introduction through an all-glass heated (200°) inlet system of a CEC 21-103C mass spectrometer of the type used in the reported[9] work. Figures 7 and 8 show the spectra obtained by these methods. The occurrence of a Beckmann rearrangement was inferred[9] from the presence of a substantial peak (4% Σ_{40}) at *m/e* 105 which can only have the composition $C_7H_6O^+$ (*pp*). In addition the remainder of the spectrum below *m/e* 105 was said[9] to correspond to that of the rearrangement product, benzanilide. The latter statement is certainly correct since benzanilide (XV) (Fig. 9) shows only two peaks of consequence below *m/e* 105, namely *m/e* 77 and 51; two species to be expected from any simple aromatic compound.[21]



pp, *m/e* 105

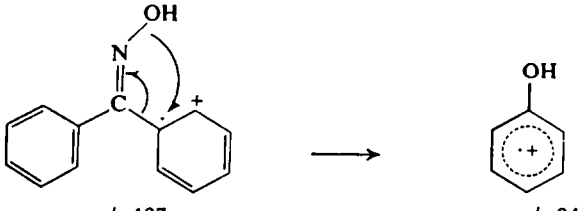
The benzophenone oxime spectra (Figs. 7 and 8) obtained by either insertion method into the ion source do indeed show an ion at *m/e* 105. It is a doublet, half of which in

[21] See chap. 9 in Ref. 4.

the spectrum from direct insertion is the C^{13} isotope peak of *m/e* 104 (as shown by high resolution measurements) and the other half having the composition suggested by the previous authors.[9] This latter species, however, amounts to only 0·5% Σ_{40}. The two peaks found in the benzanilide spectrum are of course also present here, to the extent of 12·5% Σ_{40} (*m/e* 77) and 2·2% Σ_{40} (*m/e* 51). In the benzanilide spectrum the values are 22·8% and 8·3% Σ_{40} respectively, but the *m/e* 105 peak is now the most intense one (41·5% Σ_{40}). The two ions referred to above then clearly cannot come from a rearrangement product such as benzanilide but rather from benzophenone oxime itself.

When the oxime was introduced into the ion source by a heated inlet system quantitative alterations in the resulting spectrum (Fig. 8) were apparent. Although all of the peaks of the previous spectrum were present and no new ones appeared, some intensity relationships were changed. The *m/e* 77 peak is now the base peak, and the *m/e* 104 peak ($C_7H_6N^+$ by high resolution) is considerably diminished in intensity. The species *pp*, however, supposedly derived[9] from benzanilide, has risen in abundance to only 0·7% Σ_{40}. It is clear, therefore, that the molecular ion of benzophenone oxime does not undergo Beckmann rearrangement to any significant extent, and that any of this type of skeletal rearrangement that does occur most probably does so in the inlet system of the spectrometer. The relatively intense *m/e* 105 peak reported earlier[9] probably arises from the presence of a trace of benzophenone itself (which displays in its spectrum predominantly *m/e* 105 and *m/e* 77 peaks), while the material used in our work was scrupulously purified and shown to be homogeneous by thin layer chromatography. In this connection, it should be recalled that benzophenone oxime decomposes rapidly on storage and that freshly prepared material must be employed.

Although the multiple group migrations required by a Beckmann rearrangement do not appear to occur in the electron impact induced fragmentation of benzophenone oxime, there are a number of other rearrangements which are of interest. For example, a hydroxyl group is transferred (*qq* → *rr*) to produce *m/e* 94 ($C_6H_6O^+$) as evidenced by a metastable ion at *m/e* 44·8 ($94^2/197 = 44·8$) and a high resolution mass measurement. The peak at *m/e* 167, *tt*, ($C_{13}H_{11}^+$) may be produced from the tautomeric nitroso



qq, *m/e* 197 *rr*, *m/e* 94

molecular ion *ss* by loss of NO and the peaks at *m/e* 104 (*uu*) and *m/e* 103 (*vv*) may result from the M-16 species (*ww*) by α-cleavage. The loss of oxygen from benzophenone oxime may be readily accounted for by the realization that the aromatic ring may also share in the charge localization as suggested for the genesis of the *m/e* 94 species and as shown below. This factor may also account for the apparent conversion of the ion of mass 104 (*uu*) into the single hydrogen less species *vv*. If *m/e* 104 were instead the tautomeric ion *xx* the loss of a hydrogen atom would seem energetically unlikely since it necessitates a transition from a stable even electron species to an odd-electron one. In the case of the conversion *uu* → *vv*, however, the restoration of the

aromatic π system might easily provide the driving force for the expulsion of a hydrogen atom. Interestingly there is no peak at *m/e* 120 (*yy*) corresponding to simple α-cleavage of the molecular ion. There is, however, a peak at *m/e* 119 which arises by α-cleavage with either hydrogen loss or transfer to form the highly resonance-stabilized radical ion *zz*. The elementary composition of all these ions was established by high resolution mass spectrometry.

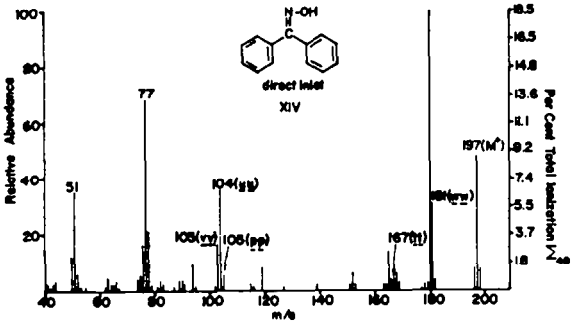


FIG. 7. Mass spectrum of benzophenone oxime (direct inlet).

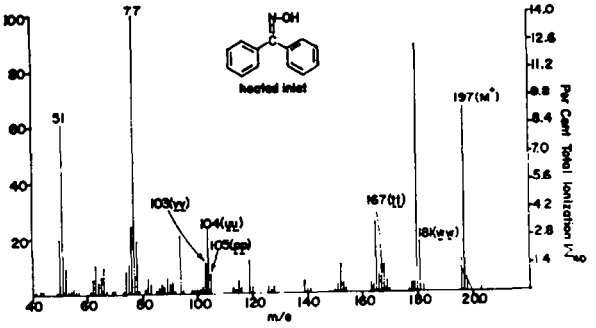


FIG. 8. Mass spectrum of benzophenone oxime (heated inlet in GEC mass spectrometer).

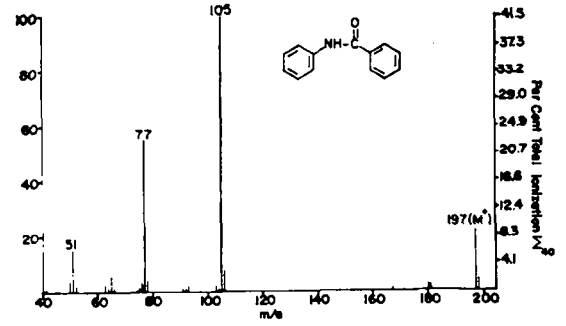
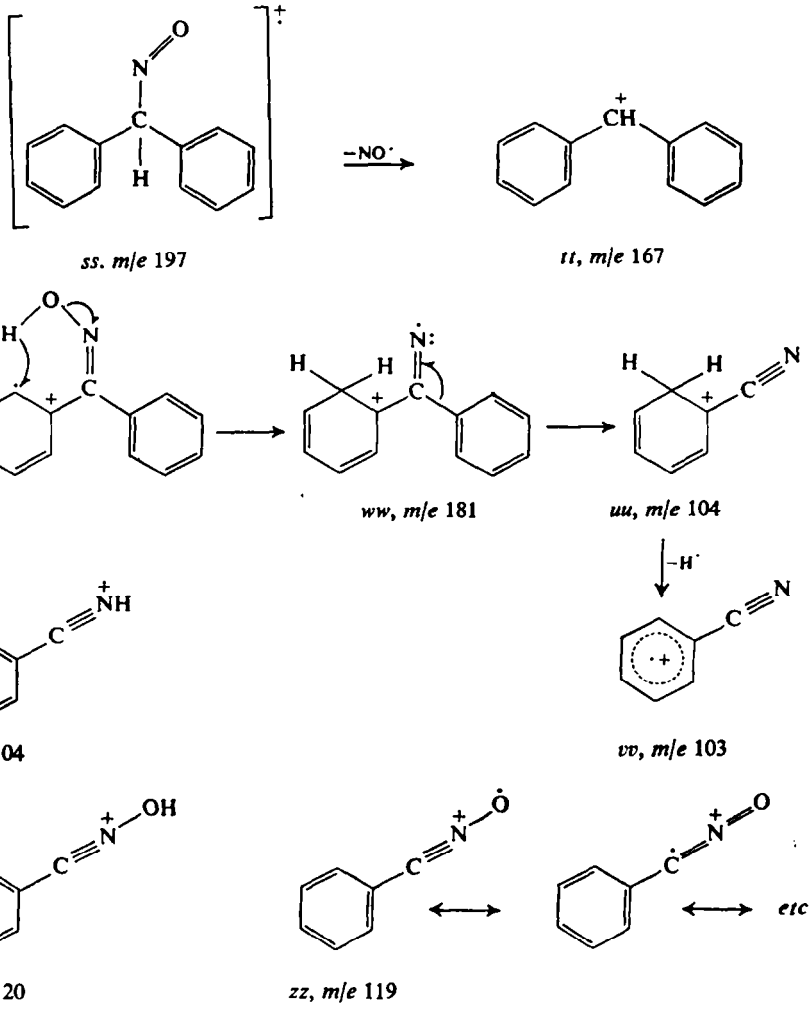


FIG. 9. Mass spectrum of benzanilide (direct inlet).



Steroidal ketoximes

As noted earlier a number of functional groups have been found to strongly direct the fragmentation of the steroid skeleton, while others, particularly the carbonyl group,[5] prove to be poor charge localizing entities. Steroidal oximes would appear to be an attractive class of compounds for mass spectral fragmentation studies since they are readily prepared and they complement the ethylene ketal derivatives[6] of ketones in being formed in the absence of strong acid. However, as shown below the electron impact induced fragmentations of steroidal ketoximes resemble most closely those of the corresponding ketones, and their usefulness in structure determination is limited. We shall discuss here three examples of such compounds where deuterium labeling and/or high resolution mass measurements have been performed: an 11-ketosteroid oxime, the spectrum of which closely resembles that of the 11-ketone,[22]

[22] D. H. Williams, J. M. Wilson, H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.* **85**, 2091 (1963).

and several of 2- and 3-ketoximes which give rise to ions seemingly peculiar to these positional isomers.

5α-*Androstan*-11-*one oxime* (XVI). The spectrum (Fig. 10) of this oxime is dominated by three main sets of peaks. One group, at *m/e* 272, 273 and 274 is due to the usual cyclic ketoxime loss of hydroxyl, oxygen and methyl radicals. The compositions of these ions were determined by high resolution measurements (Table 5); metastable ions (Table 6) were also found for the conversion of the molecular ion to the M-15 and M-17 species.

TABLE 5. HIGH RESOLUTION MASS MEASUREMENTS OF SOME 5α-ANDROSTAN-11-ONE OXIME IONS

m/e	Composition (all 100%)
53	C_4H_5
55	C_4H_7
67	C_5H_7
77	C_6H_5
79	C_6H_7
81	C_6H_9
91	C_7H_7
93	C_7H_9
95	C_7H_{11}
105	C_8H_9
107	C_8H_{11}
109	C_8H_{13}
166	$C_{10}H_{16}NO$
179	$C_{11}H_{17}NO$
192	$C_{12}H_{18}NO$

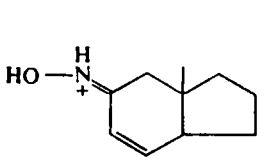
TABLE 6. METASTABLE PEAKS IN MASS SPECTRUM OF 5α-ANDROSTAN-11-ONE OXIME

Metastable Peaks (*m/e*)		
Observed	Calculated	Transition
256·0	256·0	289 → 272
259·8	259·8	289 → 274
127·6	127·6	289 → 192
110·9	110·9	289 → 179
95·3	95·3	289 → 166

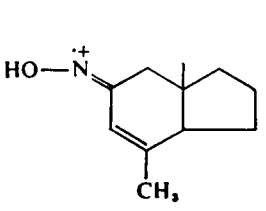
A second important group of peaks is the populous collection ranging from *m/e* 40 to *m/e* 110. High resolution measurements (Table 5) of most of the prominent peaks in this group indicates the virtual predominance of hydrocarbon ions. Indeed, this pattern is seen more or less intensely in the spectra of a variety of androstanone oximes[23] in addition to the ones reported here, and is characteristic of steroids in general. The intensity of these peaks (Fig.10) demonstrates, however, that the oxime group like the carbonyl one[5] competes only poorly with the hydrocarbon skeleton in directing the course of the fragmentation.

[23] Unpublished results of this laboratory.

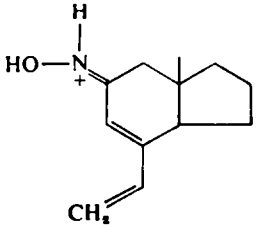
The final group which characterizes this spectrum (Fig. 10) is the one encompassing the peaks at *m/e* 166, 179 and 192. Metastable ions (Table 6) are found for the formation of each of them from the molecular ion. In all three cases high resolution measurements (Table 5) suggest that the ions are merely the oximino analogs of the corresponding species produced in the fission of the 11-ketone,[22] and that they may be represented accordingly as the structures *aaa*, *bbb* and *ccc*. Mechanistic modes for their genesis are also analogous to the pathways suggested for the ions of masses 151, 164 and 177 from the ketone fragmentation.[22] There are, therefore, apart from the standard cyclic ketoxime M-15, 16 and 17 peaks no significant differences between the mass spectra of 5α-androstan-11-one and its oxime derivative.



aaa *m/e* 166



bbb *m/e* 179



ccc *m/e* 192

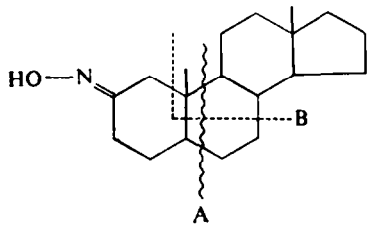
2-*Ketosteroid oximes.* The mass spectral behavior (Fig. 11) of 5α-androstan-2-one oxime (XVII) is characterized in part by the same type of hydrocarbon ion production and loss of methyl, oxygen and hydroxyl groups as described for the 11-ketoxime, but in addition several other fragmentation sub-patterns are found. Two of these, however, the trios of peaks at *m/e* 215, 216 and 217, and *m/e* 255, 256 and 257 are non-specific for the 2-oxime, being found in a variety of isomeric androstanone oximes.[23] Like the ions found in the mass region below 110, these peaks correspond exclusively to hydrocarbon species as shown by high resolution (Table 7) with the

TABLE 7. HIGH RESOLUTION MASS MEASUREMENTS OF SOME 5α-ANDROSTAN-2-ONE OXIME IONS

m/e	Composition	%
124	$C_7H_{10}NO$	100
138	$C_8H_{12}NO$	100
215	$C_{16}H_{23}$	100
216	$C_{16}H_{24}$	100
217	$C_{16}H_{25}$	100
255	$C_{19}H_{27}$	100
256	$C_{19}H_{28}$	50
256	$C_{18}H_{30}N$	50
257	$C_{19}H_{29}$	100

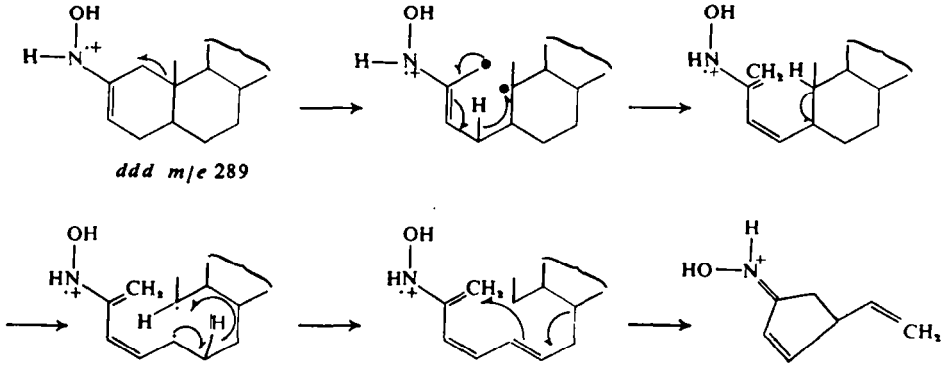
partial exception of *m/e* 256 which is a doublet. The major feature, moreover, of the spectrum of 5α-androstan-2-one itself,[24] the loss of the elements of acetone barely manifests itself in the oxime spectrum (Fig. 11) as a weak peak at *m/e* 216 (M-73).

[24] J. E. Gurst and C. Djerassi, *J. Amer. Chem. Soc.* **86**, 5542 (1964).



XVII

Despite the general structural non-specificity of this spectrum (Fig. 11) there exist two particularly distinctive peaks at *m/e* 124 and *m/e* 138. The same two fragment ions are also found in the spectrum (Fig. 12) of 5α-cholestan-2-one oxime (XVIII) indicating that their occurrence may be useful in structural work on the establishment of a carbonyl grouping at C-2. High resolution measurement (Table 7) of the first of these peaks shows the *m/e* 124 species to have the composition $C_7H_{10}NO^+$. Two sources of the carbon skeleton of this fragment may be visualized. Path A (wavy line in structure XVII) would incorporate all of the carbons of ring A plus the C-19 angular methyl group, while path B (dotted line in structure XVII) would lead to a fragment containing C-1 through C-7. An investigation of the mass spectra of two deuterated 2-ketoximes indicates that path B is the preferred one. The ion of mass 124 of the parent ketone XVII shifts to mass 128 in the spectrum of 1,1,3,3-d_4-5α-androstan-2-one oxime, a result to be expected from either pathway, but it is shifted to mass 125 in the spectrum of 6,6-d_2-5α-androstan-2-one oxime. This result seems incompatible with the formulation of the $C_7H_{10}NO^+$ species as ring A plus C-19. Since one deuterium from C-6 is *incorporated* in the ion such a formulation would require the transfer of two hydrogens to the neutral fragment, as well as the transfer of the deuterium to the ion since the net result must be the loss of one hydrogen from the ionic species. A more reasonable alternative is the formation of the ion from C-1 through C-7 (path B) by a mechanism such as the one shown below. The intervention of the tautomeric molecular ion *ddd* would explain both the cleavage of the 1–10 bond and the ready transfer of hydrogen atoms from C-4 and C-6. Finally cleavage of the 7–8 bond as shown would lead to *eee* as an expression of the *m/e* 124 species.



ddd m/e 289

eee m/e 124

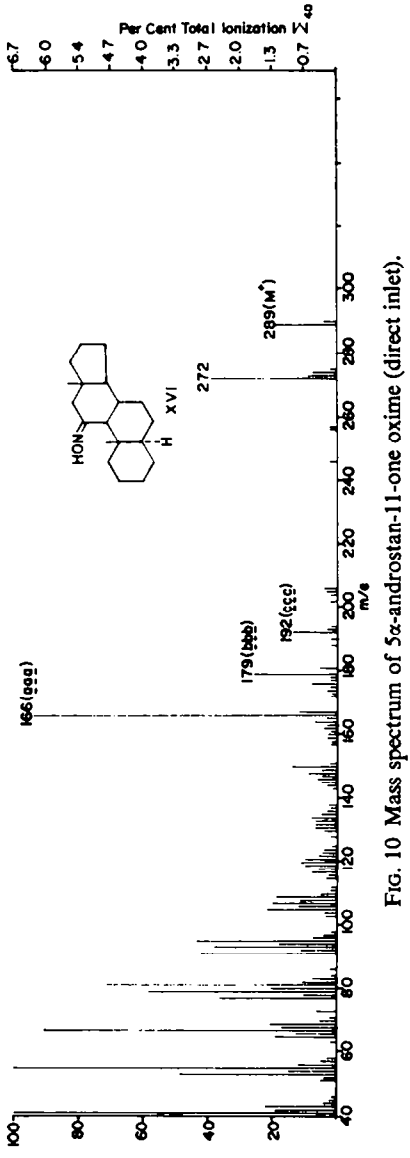
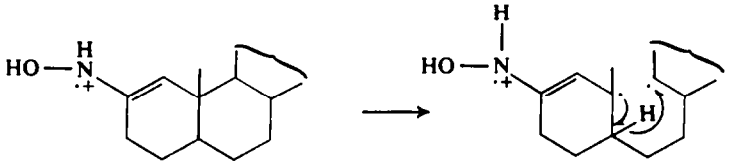
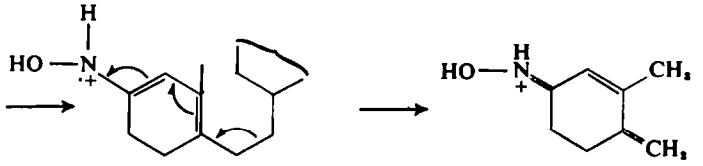


FIG. 10 Mass spectrum of 5α-androstan-11-one oxime (direct inlet).

The *m/e* 138 peak in the spectrum (Fig. 11) of 5α-androstan-2-one oxime (XVII) was shown by a high resolution measurement (Table 7) to have the composition $C_8H_{12}NO^+$. It is shifted to *m/e* 142 in the spectrum of the 1,1,3,3-d_4-ketoxime and to *m/e* 140 in the fragmentation pattern of 6,6-d_2-5α-androstan-2-one oxime. These results suggest that the ion of mass 138 in the undeuterated compound arises from ring A plus C-19 and C-6. A plausible mechanism for its genesis is shown in the sequence *fff* → *ggg*.



fff *m/e* 289



ggg *m/e* 138

3-*Ketoximes.* The oximes of these ketosteroids give rise to one particularly distinctive fragment (*m/e* 112) when subjected to electron bombardment. Before discussing this characteristic fission product a few of the other features of these spectra may be noted.

The spectrum (Fig. 13) of 5α-androstan-3-one oxime (XIX) is interestingly devoid of any intense ions of masses greater than 112. In this respect it does not resemble the spectrum[25] of the parent ketone to any significant extent since the latter shows major peaks at *m/e* 202 and 203 for the loss of ring A. By contrast, another 3-ketoxime, 5α-pregnan-3-one oxime (XX), (Fig. 14) does yield a number of high mass fragments. For example, the peaks at *m/e* 246, 247 and 248 are nitrogen-containing fragments, the compositions of which (Table 8) suggest that ring D and the side chain have been lost.

TABLE 8. HIGH RESOLUTION MASS MEASUREMENTS OF SOME 3-KETOSTEROID OXIME IONS

Compound	*m/e*	Composition (all 100%)
5α-pregnan-3-one oxime	112	$C_6H_{10}NO$
	139	$C_8H_{13}NO$
	178	$C_{11}H_{16}NO$
	246	$C_{16}H_{24}NO$
	247	$C_{16}H_{25}NO$
	248	$C_{16}H_{26}NO$
4,4-dimethyl-5α-cholestan-3-one oxime	140	$C_9H_{14}NO$
	99	C_5H_9NO

[25] R. H. Shapiro, D. H. Williams, H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.* **86**, 2837 (1964).

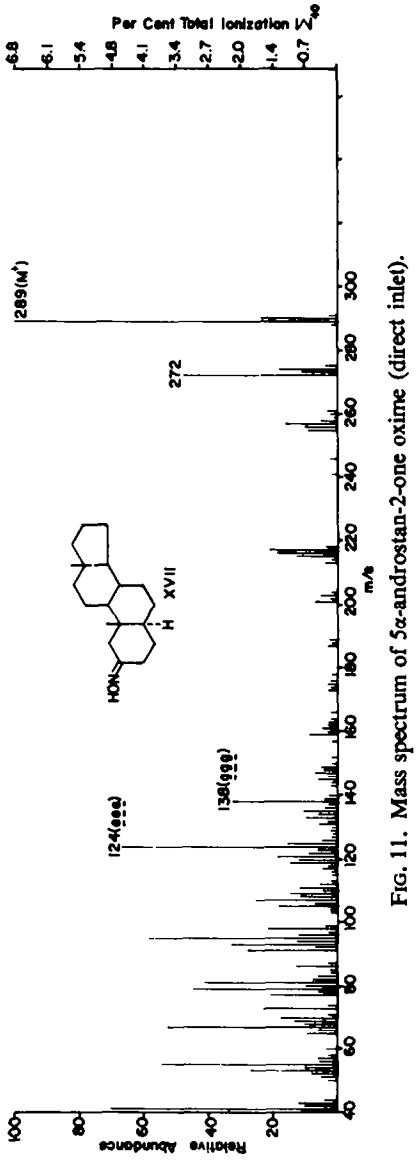
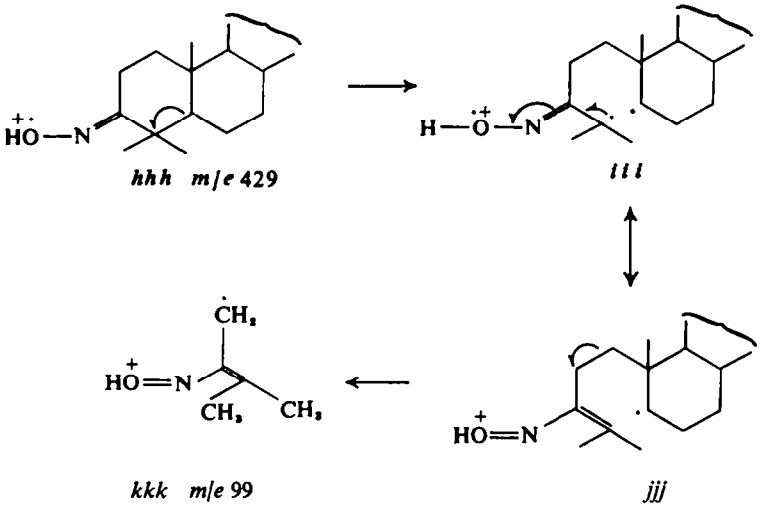


FIG. 11. Mass spectrum of 5α-androstan-2-one oxime (direct inlet).

FIG. 12. Mass spectrum of 5α-cholestan-2-one oxime (direct inlet).

In addition there are two fragments found at *m/e* 139 and *m/e* 178 which are composed (Table 8) of the elements of rings A and B. A third 3-ketoxime, 5α-cholestan-3-one oxime (XXI) provides a spectrum (Fig. 15) which like that of the parent ketone[26] is dominated by the peaks at *m/e* 246 and 247. In the case of both the oxime and the ketone, the functional group has little directive power in the formation of these fragments since they arise by cleavage of ring D and the side chain.

Finally, 4,4-dimethyl-5α-cholestan-3-one oxime (XXII) furnishes a spectrum (Fig. 16) which is characterized by only two intense peaks above mass 90, *m/e* 99 (the base peak) and *m/e* 140. This spectrum, moreover, is quite unlike that of the parent ketone[27] which does not show the equivalents of these ions. The *m/e* 99 peak was shown by a high resolution measurements (Table 8) to be due to the ion $C_5H_9NO^+$. Apparently the combination of the oxime group and the neighboring quaternary *gem*-dimethyl center is responsible for an extremely favorable β-cleavage of the molecular ion *hhh* to form *iii*. The latter in contrast to the equivalent species from β-cleavage of a ketone is stabilized through the contribution of a form such as *jjj*. A final allylic cleavage to form the resonance stabilized ion *kkk* would account for the formation of this *m/e* 99 species.



hhh *m/e* 429 *iii* *kkk* *m/e* 99 *jjj*

The other peak of interest in this spectrum (Fig. 16), *m/e* 140 ($C_8H_{14}NO^+$) (Table 8) is apparently related to the characteristic *m/e* 112 peak which is found in the spectra (Figs. 13, 14 and 15) of the other 3-ketoximes discussed in this paper, since its higher mass is attributable to the substitution of the 30 mass unit *gem*-dimethyl group for two hydrogen atoms. This contention is borne out by high resolution measurement of the *m/e* 112 peak (Table 8) which confirms the composition, $C_6H_{10}NO^+$. The formation of this type of species is clearly a favored fragmentation process of 3-ketoximes, and its importance as a mass spectrometric structural tool is only partly diminished by substitution at C-17 or within ring A. Although C-4 must clearly be incorporated in the ion as noted above, it was necessary to investigate the mass

[26] H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.* **84**, 1430 (1962).
[27] R. H. Shapiro and C. Djerassi, *Tetrahedron* **20**, 1987 (1964).

spectral behavior of a number of deuterated 3-ketoximes to establish the sources of the remaining carbon atoms. The spectra of 5-d_1-, 6,6-d_2- and 7,7-d_2-androstan-3-one oximes reveal that neither C-5, C-6 or C-7 is incorporated in the $C_6H_{10}NO^+$ ion since the *m/e* 112 peak is unshifted in all three cases. In contrast, the spectrum of a 5α-androstan-3-one oxime containing three deuterium atoms distributed between C-2 and C-4 shows a three mass unit shift of the *m/e* 112 peak to *m/e* 115. In addition, the peak is shifted to *m/e* 114 in the spectrum of the oxime of 1α,2α-d_2-5α-androstan-3-one. This labeling evidence indicates that the C_6 fragment encompasses carbon atoms 1, 2, 3, 4, 10 and 19. A possible mechanism for its formation involves cleavage of a molecular ion *lll* to form *mmm*. Ring closure and rearrangement as shown would lead to the species *nnn*, which through rupture of the 5–10 bond would yield the resonance stabilized ion *ooo*.

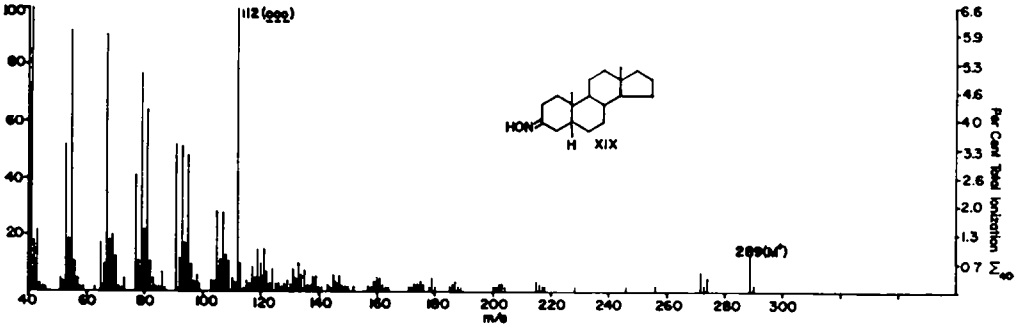
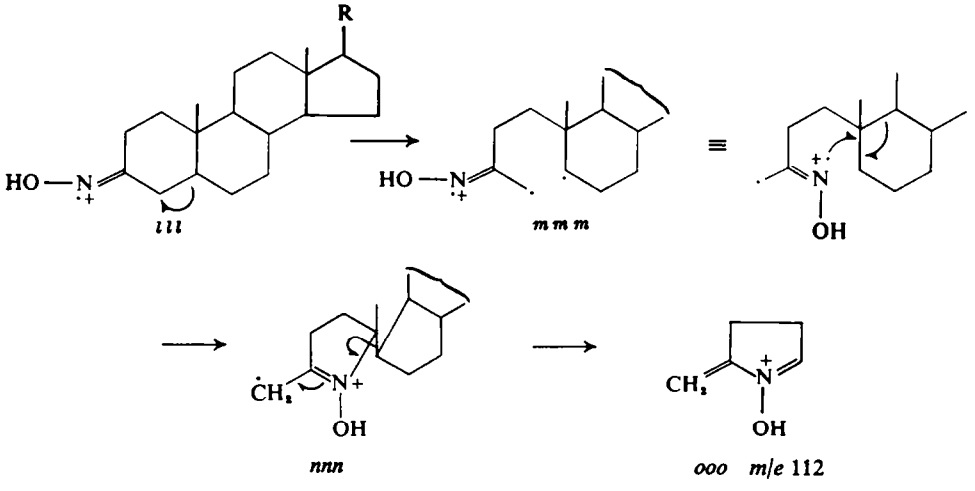


FIG. 13. Mass spectrum of 5α-androstan-3-one oxime (direct inlet).



EXPERIMENTAL

The mass spectra (except for Fig. 8) and high-resolution measurements were determined with an AEI MS-9 mass spectrometer operating with an ionization energy of 70 eV. The temp of the ion source was 200°. Samples were introduced into the source with either a heated inlet system operating at 80° or with a direct insertion probe incorporating a vacuum lock. Particular mention should be made, however, of the effect of experimental conditions on the fragmentations of the two alicyclic ketoximes, cyclopentanone oxime (XI) and cyclohexanone oxime (XII). Both quantitative and qualitative differences in the spectra of these compounds may be produced by varying the instrumental

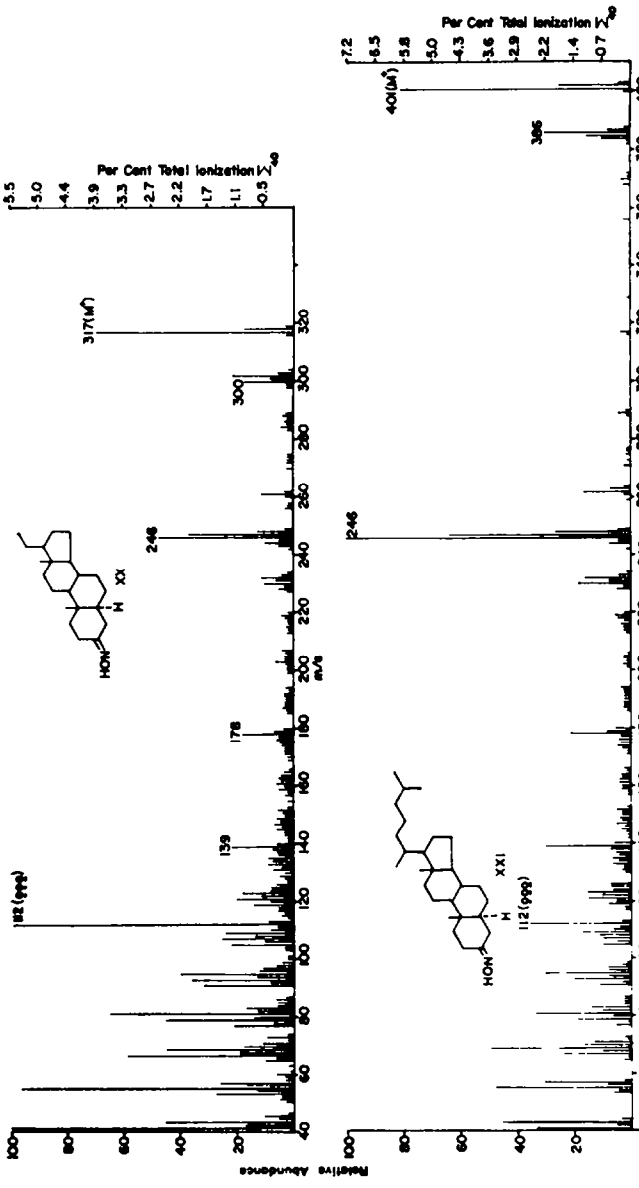


FIG. 14. Mass spectrum of 5α-pregnan-3-one oxime (direct inlet).
FIG. 15. Mass spectrum of 5α-cholestan-3-one oxime (direct inlet).

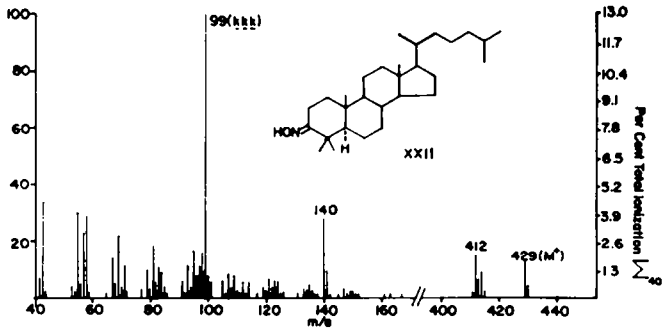


FIG. 16. Mass spectrum of 4,4-dimethyl-5α-cholestan-3-one oxime (direct inlet).

conditions. For example, cyclopentanone oxime yields virtually the same spectrum when introduced into the ion source of the MS-9 with either of the sampling systems noted above, and in the case of the direct insertion method with an ion source temperature of either 100° or 200°. However, when the spectrum of this material was obtained by using the 70° heated inlet system and gas analysis cartridge of an Atlas CH-4 mass spectrometer operating with a source temp of 170°, it showed significant quantitative differences from the spectra described in this report. Typically, the base peak in the spectrum from the Atlas instrument occurs at *m/e* 54, while in the spectrum from the MS-9 the base peak is at *m/e* 55. Qualitatively, even the origins of these ions may differ depending on the instrument or sampling system employed. The spectrum of O-d_1-cyclopentanone oxime shows no substantial shift of the ion of mass 54 to mass 55 when obtained with the MS-9 instrument using any of the sampling methods or source temps described above. In contrast, *m/e* 54 shows a marked shift to *m/e* 55 in the spectrum of the deuterated compound obtained with the Atlas CH-4 spectrometer. This latter observation is in accord with the finding of Aplin[29] that the *m/e* 54 peak is shifted one mass unit when the O-d_1-oxime is introduced into ion source of the MS-9 instrument using a heated gallium inlet system. It was found,[29] moreover, from high-resolution measurements on a sample introduced by this last method that the ion of mass 55 in the spectrum of cyclopentanone oxime itself has the composition $C_3H_6N^+$, while under our experimental conditions this ion corresponds mainly to a hydrocarbon species, $C_4H_7^+$ (Table 3).

In the case of cyclohexanone oxime the method of sample introduction determines at least the quantitative aspects of the spectrum. For example, the pattern obtained, using the heated inlet system of the MS-9, displays as the base peak *m/e* 41 whereas using the direct insertion probe the base peak is the molecular ion.

The oximes were prepared by standard methods[17,28a,b] and their purity checked by either gas chromatography, thin layer chromatography, or a high-resolution measurement of the M-15 peak of the mass spectrum. O-d_1-Cyclopentanone oxime was prepared by refluxing for twenty minutes, a solution of the unlabeled oxime in O-d_1-methanol containing deuterium oxide, followed by sublimation of the deuterated material. The preparations of the labeled aliphatic aldehydes and ketones are given in Ref. 11 and leading references to the preparation of the labeled cyclic and steroidal ketones are given in chap. 1 of Ref. 4, and chap. 20 of Ref. 5.

[28] [a] R. L. Shriner, R. C. Fuson and D. Y. Curtin, *The Systematic Indentification of Organic Compounds* (4th Edition) J. Wiley, New York (1956); [b] A. I. Vogel, *A Text-book of Practical Organic Chemistry*, (3rd Edition) J. Wiley, New York (1962).

[29] R. T. Aplin (Oxford University), private communication.