a lower activation energy and a lower activation entropy (or frequency factor[36]) than the fragmentation to lose methyl.[47] The same conclusion can be established[18] somewhat more securely from, and is implicit in, our discussion of the FIK results (Figures 5 and 6).

It has been common practice among mass spectroscopists to refer to all such H–D rearrangement as we have been discussing as "scrambling." The term "scrambling" seems to hold a mechanistic implication, namely that H and D atoms move and exchange positions in a random manner. This is not the case with the 2-methylpropene ion. We suggest, mainly on the basis of FIK results,[17,18,47-49] that with all functionalized aliphatic ions the predominant reactions leading to H–D randomization are *specific* and *definable hydrogen shifts*. The nature of the shifts will depend very much on the nature of the molecule; *e.g.*, shifts in alkene ions[17,18] bear little relationship to those in ketone ions.[48] In such a situation the term "scrambling" is seriously and objectionably misleading. The mechanistic implication is false and there is the false suggestion of some common characteristics or links among processes which are actually widely disparate. We suggest therefore that the use of the term "scrambling" be discontinued. In those cases where the rearrangements cannot be identified more precisely, it seems sufficient to refer to "rearrangements leading to H–D randomization."

(47) For a discussion of the usefulness of the concepts of energy and entropy of activation in understanding unimolecular reactions of (radical-) cations and in particular FIK results, see P. J. Derrick and A. L. Burlingame, *Accounts Chem. Res.*, in press.

(48) P. J. Derrick, A. M. Falick, A. L. Burlingame, and C. Djerassi, *J. Amer. Chem. Soc.*, **96**, 1054 (1974).

(49) P. J. Derrick, A. M. Falick, and A. L. Burlingame, *J. Chem. Soc., Perkin Trans. 2*, submitted for publication.

Conclusion

The study of this relatively simple system establishes with some degree of certainty that 1,3 allylic hydrogen shifts are facile and rapid unimolecular gas-phase reactions of the 2-methylpropene radical-cation. This is an important result in itself. Moreover, similar 1,3 allylic hydrogen shifts must be expected to occur in other alkene radical-cations. This knowledge will be a considerable asset in unraveling the complexities of the chemistry of such reaction systems. Further FIK experiments are in progress with butenes and other alkenes.

Acknowledgment. We are indebted to the National Science Foundation (Grant GP 38389X) and the National Aeronautics and Space Administration (Grant NGL 05-003-003) for financial support. We thank Miss Rosalynd Jackson for measuring the EI mass spectra.

Mass Spectrometry in Structural and Stereochemical Problems. CCXLIII.[1] Functional Group Interaction. Unusual Fragmentations of Amides as Exemplified by Bipiperidyl Alkaloids[2]

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Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received January 11, 1974*

Abstract: This study deals with the mass spectrometric behavior of the bipiperidyl alkaloids of the 1-acetyl-1,2,3,4-tetrahydro-5-(2-piperidyl)pyridine (ammodendrine) (**1**) type. This alkaloid and its acyl analogs (**10,14-16**) display prominent peaks due to amide bond cleavage and several rearrangement ions. The most unusual fragmentation involves loss of hydroxyl from these molecules, which is unprecedented among amides. Other bipiperidyl alkaloids discussed are *N'*-methylammodendrine (**9**), adenocarpine (**10**), hystrine (**11**), and *N*-acetylhystrine (**12**). The mass spectrum of *N'*-acetylammodendrine (**13**) shows loss of water as its base peak at both 70 and 15 eV. This unexpected reaction as well as the hydroxyl loss and others were investigated using high-resolution mass spectrometry, metastable defocusing, and deuterium labeling. Plausible rationalizations are presented for these reactions which are consistent with all isotopic labeling studies.

In recent years one of the main activities in this laboratory has been the study of the mass spectra of di- and polyfunctional molecules.[3] As the mass spectral fragmentation patterns of monofunctional molecules are well understood, it becomes important to determine the extent to which functional groups within a molecule interact to produce fragmentations not characteristic of either isolated functionality. In this context we now wish to report some unusual results encountered in the mass spectra of some bipiperidyl alkaloids, represented by ammodendrine (**1**).

During the course of an investigation into the alkaloidal constituents of a local plant, *Lupinus formosus*,[4] we isolated a compound of molecular formula

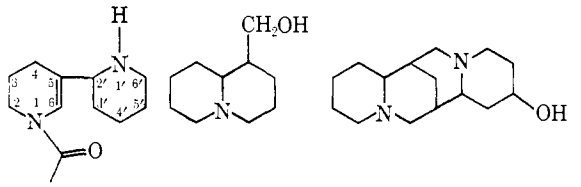
(1) For the preceding paper, see D. H. Smith, C. Djerassi, K. Maurer, and U. Rapp, *J. Amer. Chem. Soc.*, **96**, 3482 (1974).

(2) Financial assistance by the National Institutes of Health (Grant No. AM 04257) is gratefully acknowledged.

(3) See, for example: (a) M. Sheehan, R. Spangler, M. Ikeda, and C. Djerassi, *J. Org. Chem.*, **36**, 1776 (1971), and references cited therein; (b) R. J. Liedtke and C. Djerassi, *J. Org. Chem.*, **37**, 2111 (1972); (c) J. R. Dias and C. Djerassi, *Org. Mass Spectrom.*, **6**, 385 (1972).

(4) W. L. Fitch, P. M. Dolinger, and C. Djerassi, submitted for publication in *J. Org. Chem.*

$C_{12}H_{20}N_2O$. The mass spectrum of this compound showed a significant (25% relative intensity) loss of hydroxyl from the molecular ion at both 70 and 15 eV. Since the comon lupin alkaloids lupinine (**2**) and 13-hydroxysparteine (**3**) show this fragmentation,[5] some

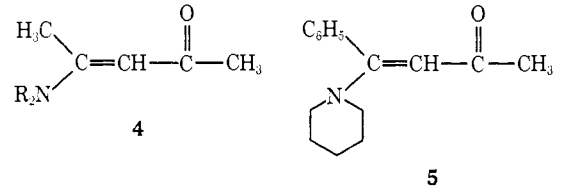


1 2 3

consideration was given initially to variations on these structures. Eventually, however, based on other spectral evidence, the compound was shown to be the well-known[6,7] bipiperidyl alkaloid ammodendrine (**1**), a structural type that had not been encountered hitherto among *Lupinus* species. This initial confusion as well as the uniqueness of the fragmentation led us to a thorough investigation.[8]

The loss of a hydroxyl radical is a fairly rare mass spectral fragmentation process.[9] Special classes of alcohols, such as benzyl alcohols[9] and γ-amino alcohols[10] (including the previously mentioned lupin alkaloids lupinine (**2**)[5] and 13-hydroxysparteine (**3**)[5]), lose a hydroxyl radical to give abundant M − OH ions. However, only two cases of the loss of hydroxyl from carbonyl compounds could be found in the literature.

A series of β-diketone enamines (**4**)[11] lose hydroxyl upon electron impact, especially when the nitrogen is tertiary. Partial deuterium labeling[11] of the enamine (**5**) showed that the expelled hydrogen originates from the piperidine ring, presumably from the α position.



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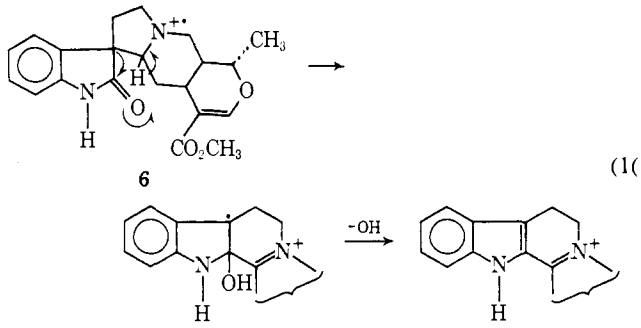
Loss of hydroxyl is also a standard feature of the mass spectra of oxindole alkaloids[12] such as mitraphylline (**6**). Deuterium labeling supports the following pathway (eq 1).



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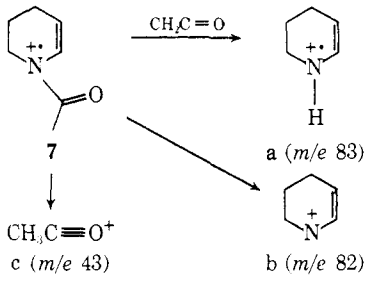
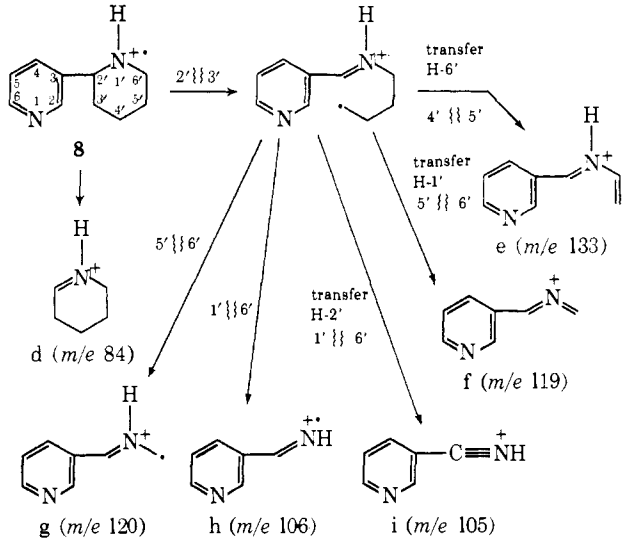
The potential directing power of the ammodendrine functionalities upon electron impact was investigated with the use of model compounds. As a model for the unsaturated amide half of ammodendrine, we recorded the mass spectrum of 1-acetyl-1,2,3,4-tetrahydropyridine (**7**).[13] This molecule shows little fragmentation, 70% of the ion current at 70 eV being represented by the molecular ion and three ions corresponding to the loss of ketene (a) or cleavage of the amide bond with charge retention on either fragment (b,c) (Scheme I). Consequently that portion of the ammodendrine molecule by itself does not satisfy the structural requirements for the unusual M − OH loss.

Scheme I



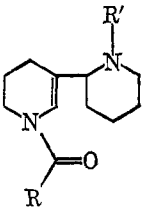
The mass spectra of a large number of 2-substituted piperidines have been reported,[9,14] α cleavage being the predominant process in 2-alkylpiperidines. Another potential model (pyridine rather than tetrahydropyridine substituent) is the tobacco alkaloid anabasine (**8**)[15] whose major presumed fragmentation pathways are summarized in Scheme II. Only limited deuterium

Scheme II



(5) N. Neuner-Jehle, H. Nesvadba, and G. Spiteller, *Monatsh. Chem.*, **95**, 687 (1964).
(6) A. Orechoff and N. Proskurnina, *Chem. Ber.*, **68**, 1807 (1935).
(7) C. Schöpf and F. Braun, *Naturwissenschaften*, **36**, 377 (1949).
(8) The mass spectrum of ammodendrine has been reported, but was not discussed by R. R. Arndt and L. M. DuPlessis, *J. S. Afr. Chem. Inst.*, **21**, 54 (1968).
(9) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.
(10) W. M. Bryant, A. L. Burlingame, H. O. House, C. G. Pitt, and B. A. Tefertiller, *J. Org. Chem.*, **31**, 3120 (1966).
(11) H. J. Jakobsen, S. O. Lawesson, J. T. P. Marshall, G. Schroll, and D. H. Williams, *J. Chem. Soc. B*, 940 (1966).
(12) B. Gilbert, J. A. Brissolese, N. Finch, W. I. Taylor, H. Budzikiewicz, T. M. Wilson, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 1523 (1963).
(13) The mass spectral behavior of this compound has been described recently by H. Schwarz and F. Bohlmann, *Org. Mass Spectrom.*, **7**, 1197 (1973).
(14) Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds," Wiley-Interscience, New York, N. Y., 1971.
(15) A. M. Duffield, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **87**, 2926 (1965).

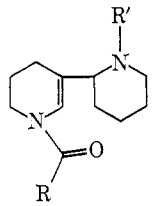
Table I. Abundances of M − 17 Ions in the Mass Spectra of Ammodendrine (1) and Various Analogs

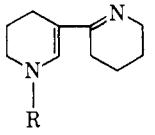


Compound	Mass of ion formed	70 eV: % rel abundance	70 eV: Total ionization (Σ_{40})	15 eV: % rel abundance	15 eV: Total ionization (Σ_{40})
1 (R = CH_3, R′ = H)	191	25	1.4	18	3.8
14 (R = R′ = H)	177	15	1.1	13	2.6
15 (R = C_2H_5, R′ = H)	205	15	0.9	25	3.2
16 (R = Ph, R′ = H)	253	29	2.6	43	4.3
10 (R = PhCHCH, R′ = H)	279	15	1.4	17	4.2
17 (norammodendrine)	177	13	1.1	28	4.5
9 (R = R′ = CH_3)	205	1	0.07	1	0.7

labeling was done in this early study, and the ion structures below represent only the major contribution to each peak.

In order to gain further insight into the unusual M − OH loss of ammodendrine (**1**), the related bipiperidyl alkaloids *N*′-methylammodendrine (**9**), adenocarpine (**10**), hystrine (**11**), and *N*-acetylhystrine (**12**) were examined as well as the simple derivative, *N*′-acetylammodendrine (**13**). The latter's mass spectrum displayed an





9, R = R′ = CH_3

10, R = $C_6H_5CH^+$═CH—; R′ = H

13, R = CH_3; R′ = $COCH_3$

11, R = H

12, R = $COCH_3$

unprecedented M − H_2O peak (base peak) and consequently led to a detailed investigation of this fragmentation as well.

Results and Discussion

Ammodendrine (1). The mass spectrum of ammodendrine is reproduced in Figure 1. At 70 eV the spectrum is fairly complex, with nine peaks of greater than 50% relative abundance. Our attention was centered mainly upon the amide cleavage fragments of mass 43 and 165, and the major rearrangement ions of mass 191, 179, 137, and 136. Some comments on the complex sets of fragments centered around *m/e* 109, 123, and 150 will also be presented. The nature of these fragmentations was investigated by the use of high-resolution mass spectral measurements, metastable defocusing, and the synthesis of deuterium-labeled compounds **1a–g** (Table II).

m/e **191 Peak (M − OH).** Accurate mass measurements showed this peak to be associated solely with the loss of a hydroxyl radical, and a large metastable peak for this process was observed in all spectra. The abundances of this fragmentation in ammodendrine and several related compounds are listed in Table I. As previously mentioned, the monocyclic model 1-acetyl-1,2,3,4-tetrahydropyridine (**7**) does not show an M − OH

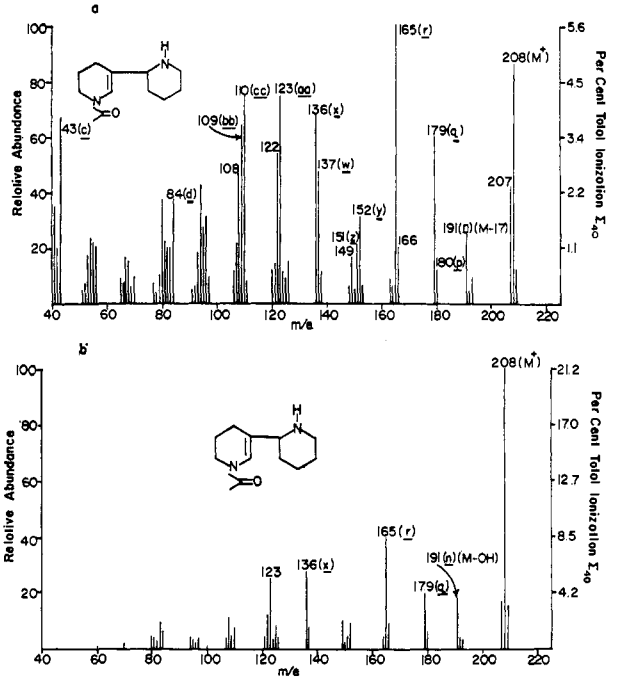
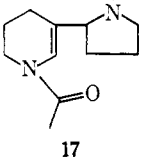


Figure 1. Mass spectrum of ammodendrine (**1**) at (a) 70 eV and (b) 15 eV.

peak. Other analogs of ammodendrine which fail to show this fragment include dihydroammodendrine (1-acetyl-2′,3-bipiperidyl) (**18**) and *N*-acetylhystrine (**12**).



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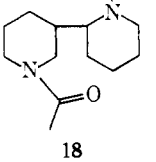

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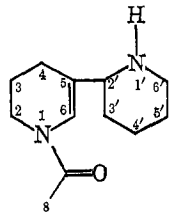
However, the fragment is seen in the mass spectrum of the pyrrolidinyl analog of ammodendrine, norammodendrine (1-acetyl-1,2,3,4-tetrahydro-5-(2-pyrrolidinyl)-pyridine) (**17**). Evidently the M − OH fragmentation is sensitive to changes in either functional group and apparently involves some interaction involving both nitrogen atoms.

Table II. Major Fragment Ions of Ammodendrine (**1**) and Deuterium-Labeled Analogs[a]



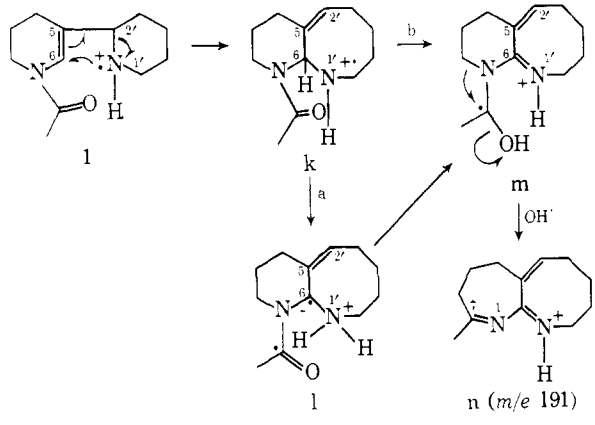
m/e	Origin[b] (% rel abundance)	**1a**-*1′*-d_1	**1b**-*8,8,8*-d_3	**1c**-*2′*-d_1	**1d**-*3′,3′*-d_2	**1e**-*2,2,6′,6′*-d_4	**1f**-*3,3,5′,5′*-d_4	**1g**-*2,2,6,2′,6′,6′*-d_6
191	M − OH (25)	192 (55)	194	192	193	195	195	197 (40)
		191 (45)						196 (60)
179	M − C_2H_5	180 (90)	182	180	181 (5)	183 (35)	183 (70)	185 (30)
	(180 − H) (60)	179 (10)			180 (20)	182 (45)	182 (10)	184 (45)
					179 (75)	181 (20)	181 (20)	183 (25)
166	M − C_3H_6 (11)	167 (5)	169 (5)	167 (5)	167 (75)	170 (10)	169 (75)	172 (5)
165	M − C_3H_7 (25)	166 (65)	168 (15)	166 (85)	166 (5)	169 (75)	168 (5)	171 (80)
	M − C_2H_3O (100)	165 (30)	166 (15)	165 (10)	165 (20)	168 (15)	167 (20)	170 (15)
			165 (65)					
152	M − C_4H_8 (31)	153	155	153	152	154	154	156
137	179 − C_2H_2O (38)	138 (35)	138 (15)	139 (10)	139 (5)	141 (20)	141 (35)	143 (15)
		137 (55)	137 (20)	138 (30)	138 (65)	140 (15)	140 (60)	142 (10)
136	165 − CH_3N (67)	136 (10)	136 (65)	137 (50)	137 (30)	139 (15)	139 (5)	141 (15)
				136 (10)		138 (50)		140 (50)
								139 (10)

[a] All compounds have been corrected to 100% isotopic purity and the shifts were calculated after correcting for natural ^{13}C abundance. Numbers in parentheses are percentages of peak shifts. [b] From high-resolution mass spectral measurements and metastable defocusing.

The results of the deuterium labeling study are summarized in Table II and reveal that the hydrogen lost in the M − OH fragmentation (*m/e* 191 in Figure 1) arises approximately equally from C-6 and N-1′. These results require either a mechanism in which these two hydrogens are equilibrated or else two separate mechanisms, each of them involving loss of a different hydrogen atom.

A rationalization for these results is given in Scheme III. Bond formation between N-1′ and C-6 with concomitant cleavage of the N-1′–C-2′ bond gives ion k, which offers an explanation for the otherwise unlikely loss of the vinylic C-6 proton of ammodendrine (**1**). A 1,2-hydrogen shift from C-6 (path a) gives ion l which can transfer either hydrogen equally (through a six-membered transition state) to give m. Ring enlargement and expulsion of hydroxyl give the stabilized ion n. The labeling results indicate a small but reproducible excess of label lost from C-6 over that lost from nitrogen. This can be rationalized by postulating the existence of a minor pathway (path b) involving C-6 hydrogen transfer directly to oxygen to give ion m.

Scheme III



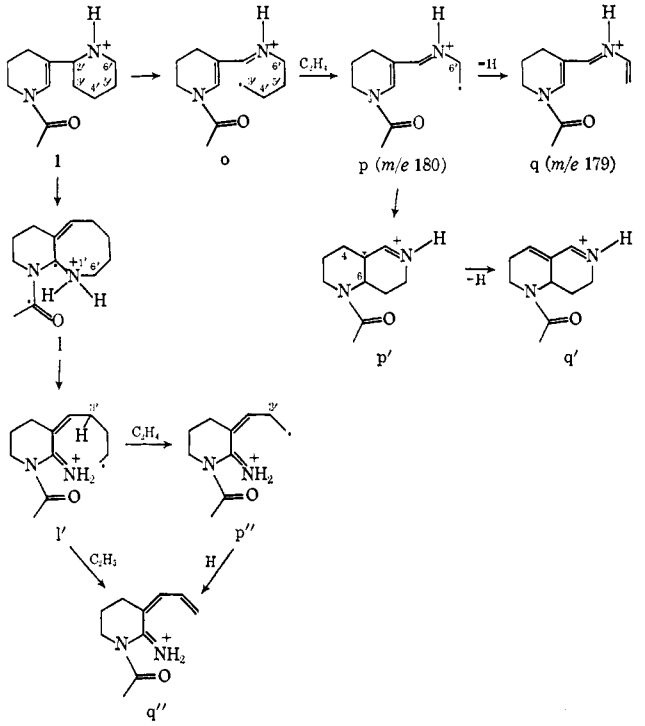
The labeling results (**1a** *vs.* **1g** in Table II, 105%) indicate that the total loss of label is greater than 100%. This can be explained by assuming that the 1,2-hydrogen shift (k → l) of path a is rate determining in which case an isotope effect in the labeled molecule **1g** would favor path b in this molecule and hence actually result in an increased loss of deuterium.

The skeletal rearrangement l → k obviously involves a fortuitous juxtaposition of functional groups and would not necessarily be seen in altered structures. Thus the M − OH loss is greatly reduced (Table I) in *N′*-methylammodendrine (**9**) which is probably not only due to the importance of other pathways but also to the steric bulk of the methyl group which would prevent the formation of an intermediate analogous to k.

m/e **179 Peak.** High-resolution mass spectral measurements and metastable defocusing data indicate that the *m/e* 179 peak arises by loss of C_2H_5 from the molecular ion, as well as by loss of C_2H_4 to give *m/e* 180 followed by loss of hydrogen. Deuterium labeling (Table II) shows that 75% of the C-3′ hydrogen are lost in this process. Since position 2′ is not involved, it follows that carbons 3′ and 4′ are lost in 75% of the fragment. This can be rationalized (Scheme IV) by assuming α cleavage (also favored by allylic activation) to ion o followed by loss of ethylene to give p. Since elimination of one of the C-6′ hydrogens occurs to the extent of 45%, it seems reasonable to visualize 45% of the *m/e* 179 peak in terms of structure q. Although position 4 in the tetrahydropyridine ring was not labeled, we feel that the remainder of the ion involving loss of carbons 3′ and 4′ is best represented as involving ring closure of p to p′, followed by expulsion of a C-4 hydrogen to give q′.

The other large part (*ca.* 25%) of the *m/e* 179 peak involves loss of carbons 5′ and 6′ and one of the C-3′ hydrogens. This can be represented as derived from the rearranged molecular ion l by cleavage of the 1′–6′ bond

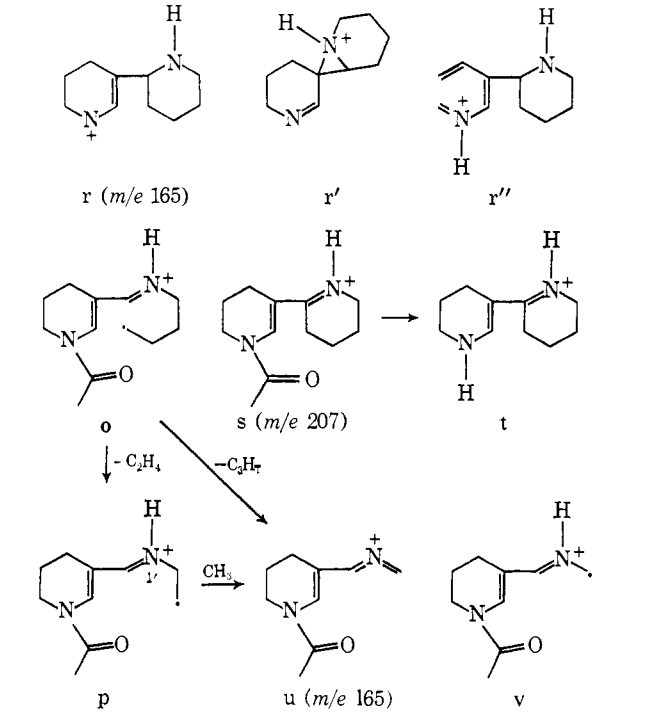
Scheme IV



to give l′, which would then transfer a C-3′ hydrogen to yield, after loss of ethyl, ion q″ (or loss of ethylene to give p″, followed by loss of hydrogen).

m/e **165 Peak.** High-resolution mass spectral measurements show this peak to be associated to the extent of 80% with the loss of C_2H_3O, the remaining 20% being due to elimination of C_3H_7. Metastable defocusing indicates that most of the fragments arise from the molecular ion with small contributions from *m/e* 207 and 180. Deuterium labeling supports the conclusion that most (80–85%) of the oxygen-free ion of mass 165 arises by direct cleavage of the amide bond to give (Scheme V)

Scheme V

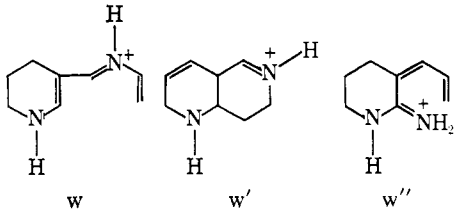


an ion represented as r, r′, or r″. Charge retention on the acyl fragment leads to the abundant ion c of mass 43.

Another 15–20% of the oxygen-free component of the *m/e* 165 peak involves loss of only two of the hydrogens from the acetyl group and thus is best represented in terms of ketene elimination (t) from an M − 1 precursor (s).

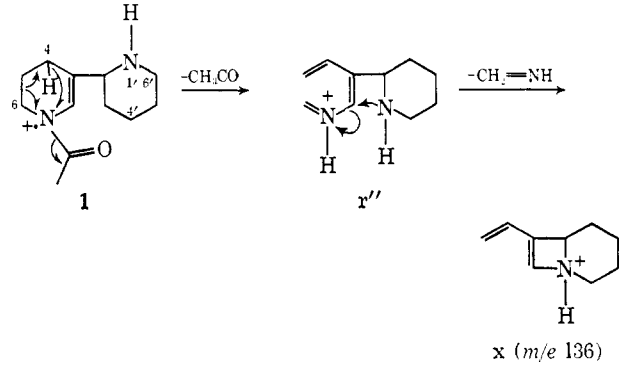
The oxygen-containing ion of mass 165 (involving formal loss of propyl) is best represented as u (analogous to the mass 119 ion of anabasine[15]) derived from o (by 1,6-hydrogen shift from N′ and loss of propyl) or from p (by 1,3-hydrogen shift and loss of methyl). A small *m/e* 166 peak (loss of cyclopropane from the molecular ion) is included in Table II, but is too small for the deuterium labeling to be significant. By analogy to the work[15] on anabasine, this is represented as v. Loss of ketene from the molecular ion to give *m/e* 166 was not detectable.

m/e **137 Peak.** High-resolution mass spectrometry and metastable defocusing indicate this peak to arise by expulsion of ketene from *m/e* 179 or by elimination of ketene from *m/e* 180 followed by loss of hydrogen. Deuterium labeling is complicated by the presence of the large *m/e* 136 peak but indicates a similar labeling pattern as seen for the *m/e* 179 peak. Thus we visualize the mass 137 ion as being composed of roughly equal amounts of w, w′, and w″.



m/e **136 Peak.** According to high-resolution mass spectral measurements and metastable defocusing this significant peak arises by loss of CH_3N from an *m/e* 165 precursor. Deuterium labeling demonstrates that two of the C-2 or C-6′ hydrogens are lost quantitatively, and since the amino proton is retained, the fragment lost must be N-1 and C-2. The source of the third hydrogen was not found and by elimination must be either C-4 or C-4′. Therefore, the mass 136 ion is best represented, as depicted in Scheme VI, as arising by a displacement reaction in ion r″ to give x.

Scheme VI



Other Significant Peaks. The *m/e* 152 peak in the ammodendrine spectrum (Figure 1) involves loss of C_4H_8 from the molecular ion and can be envisaged in terms of cyclobutane elimination from o or ethylene loss

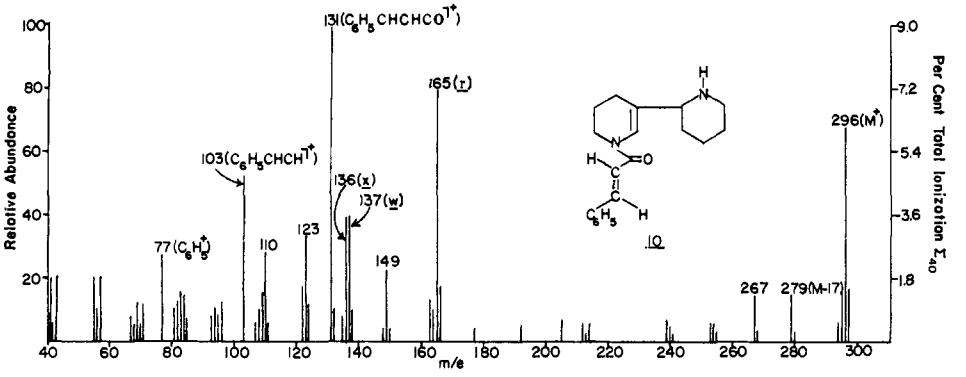


Figure 2. Mass spectrum of adenocarpine (**10**) at 70 eV.

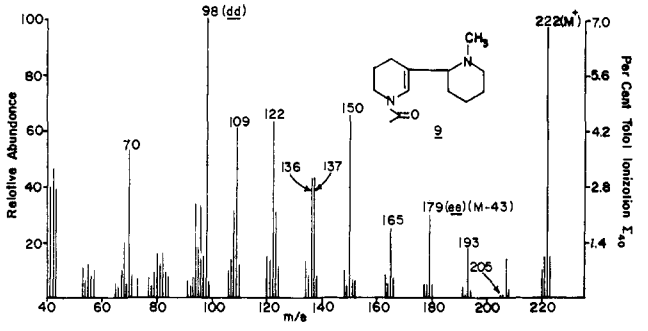


Figure 3. Mass spectrum of *N'*-methylammodendrine (**9**) at 70 eV.

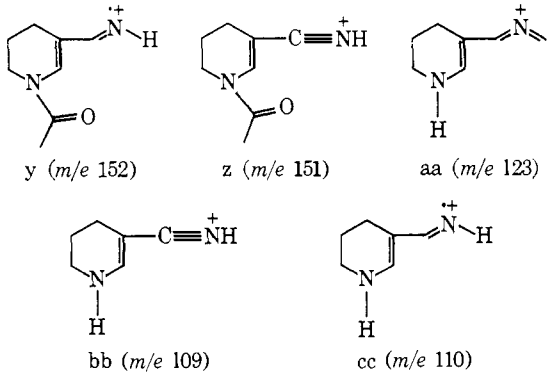
from p, either case giving ion y (analogous to ion h of mass 106 in anabasine,[15] Scheme II).

The *m/e* 151 peak of ammodendrine (**1**) has a composition corresponding to loss of C_4H_9 from the molecular ion. Metastable defocusing data testify to a complex origin for this ion, which arises mainly by loss of hydrogen from *m/e* 152 with small contributions from *m/e* 166, 193, and 207. Deuterium labeling was not conclusive and the ion undoubtedly has several structures. By analogy to anabasine (**8**)[15] one of the contributors can be represented as z.

The small *m/e* 149 peak arises by loss of C_2H_4N from the M − OH precursor (*m/e* 191). The acetyl group is quantitatively lost in this fragment, but the source of the fourth hydrogen atom and which of the two nitrogens is involved could not be determined because of the low intensity of the peak and its surroundings.

The origins of the intense peaks at *m/e* 122 and 123 are complex and impossible to interpret. Deuterium-labeling results are complicated by the presence of peaks at *m/e* 120, 121, 124, and 126. Metastable defocusing indicates multiple origins for both of these ions, *m/e* 122 arising mainly from *m/e* 123, but also from *m/e* 137, 149, 164, and 180. The *m/e* 123 peak arises principally from *m/e* 165 but also from *m/e* 124. High-resolution mass spectrometry indicates 40% of the mass 123 ion to have the composition $C_7H_{11}N_2$, and it seems reasonable to assign structure aa to this portion of *m/e* 123 (derived by loss of ketene from u). The remainder has the isobaric composition $C_8H_{13}N$. The *m/e* 122 peak corresponds in its entirety to $C_8H_{12}N$.

Similar arguments apply to the complex set of peaks which include *m/e* 108, 109, and 110. About 70% of the *m/e* 109 peak has the composition $C_6H_9N_2$ and could arise by loss of ketene from z to give bb. A similar portion of the *m/e* 110 peak is assigned structure cc.



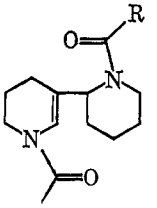
Special note should be made of the low relative abundance of the α cleavage ion d of mass 84 in the mass spectrum (Figure 1) of ammodendrine (**1**).

In summary, two general trends from the mass spectrum of ammodendrine should be noted. First, the presence of two similar fragmentation directing functionalities will give rise to a complex spectrum; second, the interaction of these two functionalities, when properly juxtaposed, can generate several unexpected rearrangement fragmentations which are difficult or impossible to rationalize *ab initio*. However, these are amenable to reasonable interpretation by means of extensive isotopic labeling.

Adenocarpine (10). The mass spectrum of this naturally occurring alkaloid is reproduced in Figure 2. The major peaks in the spectrum are analogous to those of ammodendrine (**1**), *m/e* 279 (M − OH), 267 (M − C_2H_5), 165, 149, 137, 136, 123, and 110. The cinnamoyl fragment (*m/e* 131) is accompanied by two ions derived from it, *m/e* 103 (131 − CO) and *m/e* 77 (103 − C_2H_2). No deuterium labeling was done on adenocarpine, since its mass spectral fragmentation follows the paths established for ammodendrine.

***N'*-Methylammodendrine (9).** The 70-eV mass spectrum of the recently isolated[4] alkaloid *N'*-methylammodendrine (**9**) is depicted in Figure 3. The increased fragmentation directing power of a tertiary amine over a secondary or an amide is well documented.[9] This fact is supported by the mass spectrum of **9**, the base peak of which is the α cleavage ion dd of mass 98 (Σ_{40} 7.0% *vs.* 2.2% for corresponding ion d (*m/e* 84) of ammodendrine). The mass spectral fragmentations of **9** were investigated using high-resolution mass spectrom-

Table III. Abundances of M − 18 Ions in the Mass Spectra of *N'*-Acetylammodendrine and Analogs

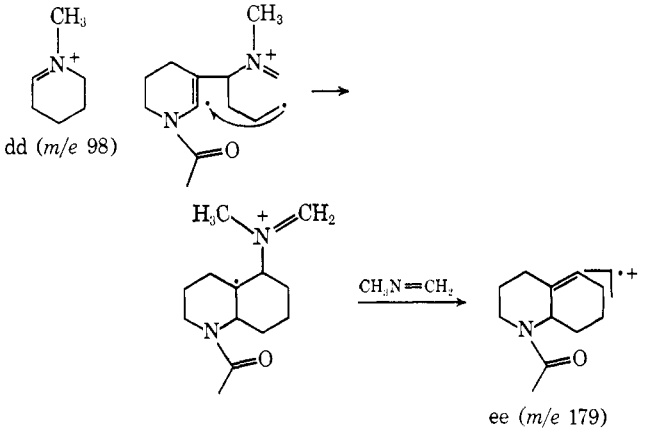


Compound	Mass of ion formed	70 eV		15 eV	
		% rel abundance	Total ionization (Σ_{40})	% rel abundance	Total ionization (Σ_{40})
13 (R = Me)	232	100	8.8	100	22
19 (R = H)	218	100	11.0	100	32
20 (1'-acetylnor-ammodendrine)	218	28	2.4	63	8.8

etry, metastable defocusing, and the synthesis of the deuterium-labeled analog *N'*-methylammodendrine-*7',7',7'-d*$_3$ (**9a**). The spectrum of this labeled analog showed that the *N'*-methyl group is retained in almost every fragment.

The high range peaks of **9** at *m/e* 193 (M − 29), 165 (M − C_4H_9), and 150 (*m/e* 179 − CH_3N) are analogous to those previously discussed for ammodendrine (**1**). The M − OH fragment (*m/e* 205) is very small for reasons previously mentioned. The *m/e* 179 peak (M − 43) is composed of three isobaric components in roughly equal amounts, M − C_3H_7, M − C_2H_3O, and M − C_2H_5N. About 30% of this peak remains at *m/e* 179 in the labeled compound **9a**, thus suggesting ee (Scheme VII) as a plausible formulation for it.

Scheme VII



Other Bipiperidyl Alkaloids. The mass spectrum of hystrine (**11**) has been reported[16] and consists mainly of molecular ion and M − 1 species. The spectrum of its *N*-acetyl derivative **12** is dominated by M^+, M − 43, and *m/e* 43 peaks, which bear almost 50% of the ion current at 70 eV.

During the course of this work, the unnatural bipiperidyls 1-formyl-, 1-propionyl-, and 1-benzoyl-1,2,3,4-tetrahydro-5-(2-piperidyl)pyridines (**14–16**) were synthesized. Their mass spectra were completely analogous to that of ammodendrine and require no further comment. However, acetylation of the other nitrogen atom of ammodendrine resulted in major changes which merited detailed analysis.

(16) E. Steinegger, Ch. Moser, and P. Weber, *Phytochemistry*, 7, 849 (1968).

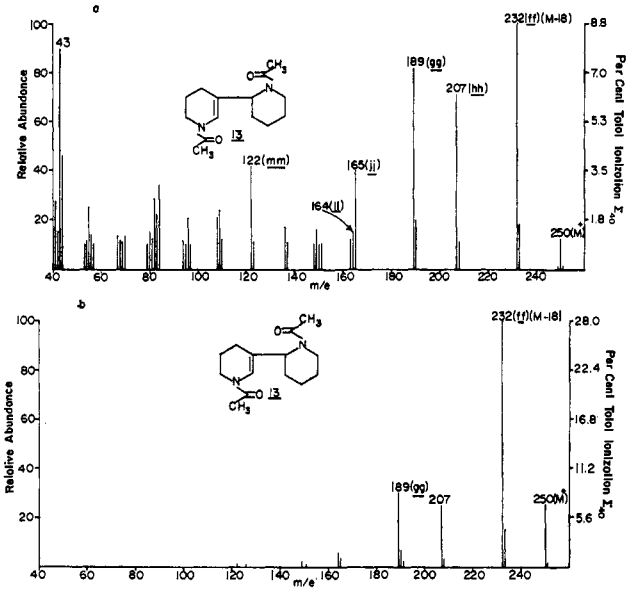
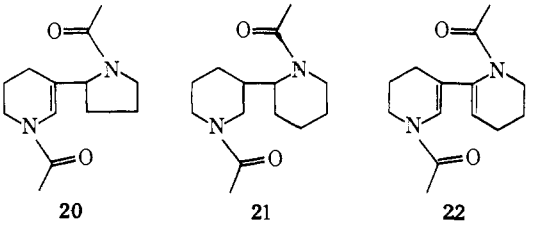


Figure 4. Mass spectrum of *N'*-acetylammodendrine (**13**) at (a) 70 eV and (b) 15 eV.

***N'*-Acetylammodendrine (13).** The most remarkable and unexpected feature associated with simple acetylation is the enormous loss of water (*m/e* 232 in Figure 4) observed at both 70 and 15 eV. This fragmentation was also noted (Table III) in *N'*-formylammodendrine (**19**) and *N'*-acetylnorammodendrine (**20**). However loss of water was absent in the spectra of *N'*-acetyldihydroammodendrine (**21**) and 1,1'-diacetyl-1,2,3,4,1',2',3',4'-octahydro-5,6'-bipyridyl (**22**). Since no precedence for

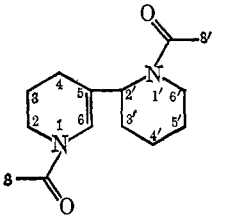


20 **21** **22**

such a fragmentation could be found in the literature, a detailed examination of this behavior was undertaken involving high-resolution mass spectrometry, metastable defocusing, and the synthesis of the deuterium-labeled analogs **13a–g** (Table IV).

The first positions to be labeled in this molecule were synthetically the most readily available ones, namely the

Table IV. Major Fragment Ions of *N'*-Acetylammodendrine (**13**) and Deuterium-Labeled Analogs[a]

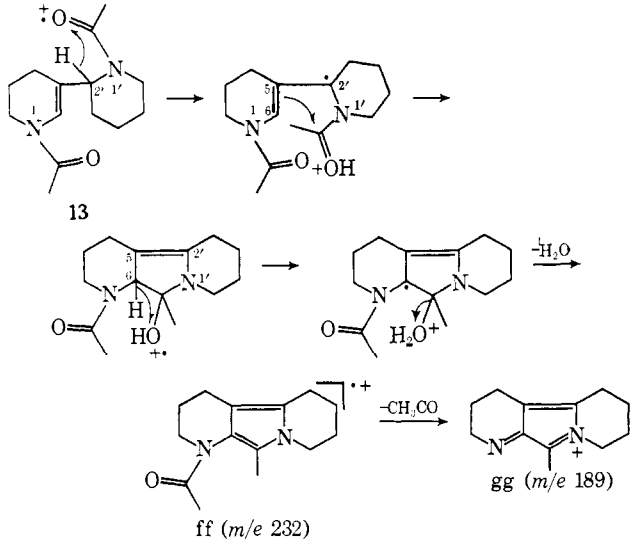


m/e	Origin and % rel abundance	**13a**-2′-d_1	**13b**-8′,8′,8′-d_3	**13c**-8,8,8,8′,-8′,8′-d_6	**13d**-3′,3′-d_2	**13e**-3,3,5′,-5′-d_4	**13f**-2,2,6′,-6′-d_4	**13g**-2,2,6,-2′,6′,6′-d_6
232	M − H_2O (100)	232	235	238	234	236	236	236
207	M − C_2H_3O (71)	208	207 (85) 210 (15)	210	209	211	211	213
189	232 − C_2H_3O (82)	189	192	192	191	193	193	193
165	207 − C_2H_2O (40)	166	165 (80) 166 (20)	166	167	169	169	171
122	164 − C_2H_2O (42)	123	122	123	123	124	124	126
43	C_2H_3O (90)	43	43 (45) 46 (55)	46	43	43	43	43

[a] See footnotes *a* and *b*, Table II.

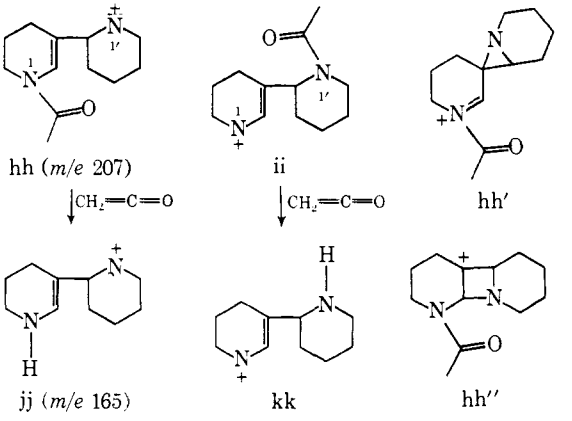
acetyl groups and C-2′. The latter was found (Table IV) to be the source of one of the two hydrogens, which was not too surprising in view of its steric accessibility and allylic activation. The site of the second hydrogen was the vinyl hydrogen at C-6, which was surprising since such hydrogens are rarely involved in rearrangements.[17] The source of the eliminated oxygen atom was deduced with the aid of the *m/e* 189 peak which in turn is derived by loss of acetyl from the M − H_2O ion (*m/e* 232). In the mass spectrum of the analog **13b** labeled in the *N'*-acetyl group, the *m/e* 235 (M − H_2O) peak loses acetyl (43 mass units) to give a labeled *m/e* 192 peak, whereas, in the analog **13c** labeled in both acetyl groups, the *m/e* 238 peak (M − H_2O) loses d_3-acetyl (46 mass units) to give *m/e* 192. Therefore the *N*-acetyl group remains intact in the ion of mass 232 and the oxygen involved is necessarily the one from the *N'*-acetyl group. All of these results are consistent with the sequence summarized in Scheme VIII.

Scheme VIII



The other major peaks in the mass spectrum (Figure 4) of the diacetate **13** are the amide cleavage peaks *m/e* 43 (c) and 207 and the peaks at *m/e* 165 and 122. The deuterium-labeling results (Table IV) indicate that 85% of the *m/e* 207 peak involves loss of the *N'*-acetyl group generating ion hh (Scheme IX), while 15%

Scheme IX

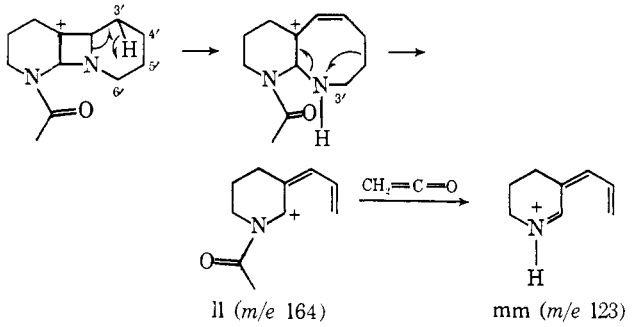


proceeds by elimination of the *N*-acetyl group to give ii. These ions could be stabilized by structures such as hh′ or hh″. The *m/e* 165 peak is formed by loss of ketene from *m/e* 207; both ions hh and ii appear to lose ketene with equal ease, since the deuterium labeling results (Table IV) for *m/e* 165 are consistent with a mixture of 80% jj and 20% kk.

The only other significant peak in the mass spectrum (Figure 4) of **13** is the *m/e* 122 peak of composition $C_8H_{12}N$. Metastable defocusing indicates that this peak arises by loss of ketene from the small *m/e* 164 peak ($C_{10}H_{14}NO$), which in turn arises by loss of C_2H_5N from *m/e* 207 (ii). Although the deuterium labeling was somewhat ambiguous because of its low intensity and the presence of other peaks, the mass 164 ion appears to retain the label from the *N*-acetyl group, and therefore must arise from ion hh. The *m/e* 122 peak is shifted to *m/e* 123 in the spectrum of the 3′,3′-d_2 analog (**13d**), thus implying that one of the 3′ hydrogens is involved in the process leading to *m/e* 164. Carbons 2 and 3 (or 5′ and 6′) are quantitatively expelled in this fragmentation. A possible reaction sequence rationalizing all of the data is summarized in Scheme X.

(17) This would normally imply the intermediacy of a vinyl radical, or the breaking of two bonds to one carbon, a rare process.

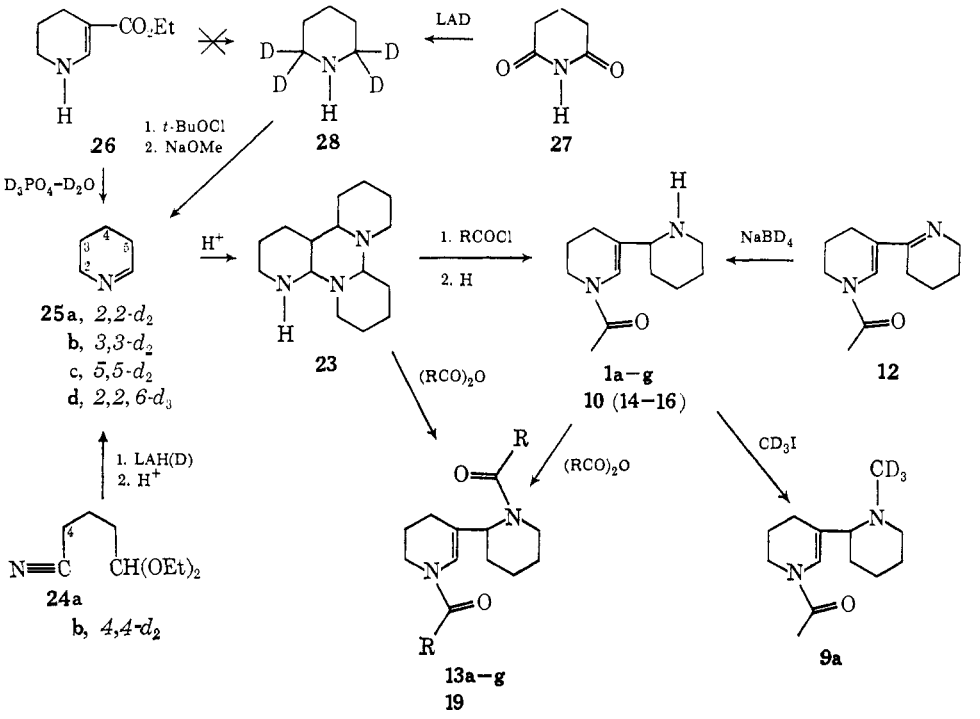
Scheme X



molecules. This *caveat* must be kept in mind when mass spectrometry is used in the structure elucidation of completely new molecules.

Synthesis of Labeled Compounds and Analogs (Scheme XI). Most of the labeled ammodendrines and acyl analogs were prepared by treatment of isotripiperidine (**23**)[18,19] with the appropriate acid chloride, followed by acid-catalyzed decomposition of the intermediate acylisotripiperidine.[20] The labeled isotripiperidines were prepared by various means. Cyanoacetal **24a**[21] on lithium aluminum deuteride reduction and acid work-up[22] gave 2,3,4,5-tetrahydropyridine-*2,2-d*$_2$ (**25a**).

Scheme XI



Summary

This investigation details the potential difficulty which arises at times in interpretating the mass spectra of polyfunctional molecules. For ammodendrine (**1**) and its acyl analogs (**9**, **10**, **14–16**), the spectra contain many peaks explainable on the basis of the separate functionalities. However, the presence of a few unusual rearrangement ions in the high mass range (where the least number of bizarre rearrangements are usually encountered) hindered our structural investigations[4] considerably until other spectral data were considered. In the case of *N'*-acetylammodendrine (**13**), the spectrum is dominated by rearrangement ions and adequate interpretation in the absence of isotopic labeling would be impossible.

These unusual rearrangement reactions are specific to the unique structural features of ammodendrine and *N'*-acetylammodendrine. Excluding the acyl analogs of these molecules, no other molecule to our knowledge exhibits these or similar rearrangements on electron impact.

Perhaps the most significant conclusion to be made from this investigation is a warning. In spite of the extensive investigations of mass spectral fragmentation over the last decade, unexpected rearrangement reactions can still be encountered even in rather simple

This compound exists as a trimer and is easily isomerized to isotripiperidine (**23**) by known methods.[18,19] Prior exchange of the cyanoacetal (**24a**) with $Ca(OD)_2$ in D_2O[23] gave the labeled cyanoacetal **24b**, which on lithium aluminum hydride reduction gave **25b**. Hydrolysis and decarboxylation of ester **26** in dilute D_3PO_4 gave **25c**.[19,24] Lithium aluminum deuteride reduction of glutarimide (**27**) gave piperidine-*2,2,6,6-d*$_4$ (**28**) which was converted to **25d** by known methods.[25] Ammodendrine-*2'-d*$_1$ (**1b**) was prepared by sodium borodeuteride reduction of *N*-acetylhystrine (**12**).

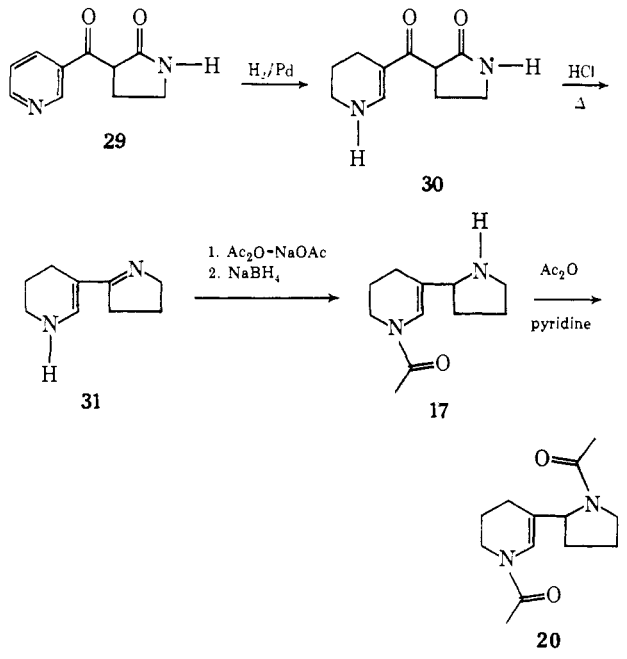
The labeled *N'*-acetylammodendrines (**13c–g**) were synthesized by heating the appropriate isotripiperidine with acetic anhydride.[18] Labeled compounds **13a,b** were prepared from the appropriate ammodendrine and acetic (or acetic-d_6) anhydride. The labeled *N'*-methyl-

(18) C. Schöpf, A. Komsak, F. Braun, F. Jacobi, M. L. Bormuth, M. Bullheimer, and I. Hagel, *Justus Liebigs Ann. Chem.*, **559**, 1 (1948).
(19) F. Haglid, *Acta Chem. Scand.*, **20**, 2896 (1966).
(20) C. Schöpf, F. Braun, and K. Kreibach, *Justus Liebigs Ann. Chem.*, **674**, 87 (1964).
(21) Ajinomoto Co. Inc., British Patent 985, 265; *Chem. Abstr.*, **62**, 16068h (1964).
(22) E. Leete, *J. Amer. Chem. Soc.*, **91**, 1697 (1969).
(23) L. C. Leitch, *Can. J. Chem.*, **35**, 345 (1957).
(24) P. M. Quan and L. D. Quin, *J. Org. Chem.*, **31**, 2487 (1966).
(25) C. Schöpf, German Patent 1,054,088; *Chem. Abstr.*, **55**, 8439g (1961).

ammodendrine (**9a**) was prepared from ammodendrine and methyl-d_3 iodide.[6]

The norammodendrine series of analogs was prepared as shown in Scheme XII. 3-Nicotinoylpyrrolidone

Scheme XII



(**29**)[26] was reduced to the tetrahydro derivative **30**,[27] which on acid-catalyzed rearrangement gave norhystrine (1,2,3,4-tetrahydro-5-(1-pyrrolin-2-yl)pyridine (**31**)).[24] Acetylation and borohydride reduction led to norammodendrine (1-acetyl-1,2,3,4-tetrahydro-5-(2-pyrrolidinyl)pyridine (**17**)) and upon further acetylation to 1-acetyl-1,2,3,4-tetrahydro-5-(1-acetyl-2-pyrrolidinyl)-pyridine (**20**).

Experimental Section

Low-resolution mass spectra were recorded on Atlas CH-4 and AEI MS-9 spectrometers by Messrs. R. Conover and R. Ross. Spectra of compounds run on both of these instruments were essentially identical. High-resolution mass spectra were recorded on a Varian MAT 711 mass spectrometer. Mass measurement accuracies for single scans of a mass spectrum at high resolving power (10,000) are routinely better than 10 ppm with the mass spectrometer and its associated computer system. Compounds were submitted for mass spectral measurement only after purification by vapor phase chromatography (6 ft × 0.25 in., 3% OV-25 on Gas Chrom Q; 3% UCW-98 on Chromosorb W, both columns glass).

Infrared characterization was carried out using a Perkin-Elmer Model 700 spectrophotometer. Nmr spectra were obtained with either a Varian Model T-60 or HA-100 spectrometer, and are recorded in δ values with $CDCl_3$ as solvent unless stated otherwise.

(+)-Ammodendrine (**1**), (+)-*N'*-methylammodendrine (**9**), hystrine (**11**) and *N*-acetylhystrine (**12**) were isolated from *L. formosus*.[4] The following compounds were prepared by known methods: 1-benzoyl-1,2,3,4-tetrahydro-5-(2-piperidyl)pyridine (**16**),[20] (±)-adenocarpine (**10**),[20] dihydroammodendrine (**18**),[7] and 1-acetyl-1,2,3,4-tetrahydropyridine (**7**).[18]

1-Propionyl-1,2,3,4-tetrahydro-5-(2-piperidyl)pyridine (15). Isotripiperidine **23** (130 mg) in 1 ml of ether was treated with propionyl chloride (60 mg) at 0°. After the mixture was stirred for 15 min, 5 drops of 60% $HClO_4$ was added and stirring continued for 1 hr at room temperature. After neutralization (K_2CO_3), extraction (ether), and drying ($MgSO_4$), **15** was obtained as a colorless oil (90 mg, 80%): ir (neat) 1645 cm^{-1}; nmr 1.15 (t, 3 H, H-9), 1.5–2.1 (b, 11 H), 2.52 (t, 1 H, H-2'), 2.68 (q, 2 H, H-8), 3.05 (t, 2 H, H-6'), 3.65 (t, 2 H, H-2), 6.65 and 7.15 (s, 1 H, H-6); M^+ 222.171 by high-resolution mass spectrometry (calcd for $C_{13}H_{22}N_2O$, 222.173).

1-Formyl-1,2,3,4-tetrahydro-5-(2-piperidyl)pyridine (14). This oily substance was prepared in a similar manner from **23** and chloral[28] in 50% yield: ir 1660 cm^{-1}; nmr 1.2–2.3 (b, 11 H), 2.69 (t, 1 H, H-2'), 3.06 (t, 2 H, H-6'), 3.54 (m, 2 H, H-2), 6.52 and 7.05 (s, 1 H, H-6), 7.95 and 8.18 (s, 1 H, H-8); M^+ 194.141 (calcd for $C_{11}H_{18}N_2O$, 194.142).

3-(1,4,5,6-Tetrahydronicotinoyl)pyrrolidone (30). 3-Nicotinoylpyrrolidone (**29**)[26] (1 g) was dissolved in MeOH and hydrogenated over 10% Pd/C (150 mg) at atmospheric pressure and room temperature.[27] After 30 hr the theoretical amount of H_2 had been absorbed. After removal of the catalyst by filtration and the solvent (*in vacuo*), **30** was obtained in quantitative yield as a white solid. Recrystallization from EtOH gave the pure compound: mp 198–199°; ir (KBr) 3300, 1675, 1590 cm^{-1}; nmr (D_2O) 1.72 (m, 2 H, H-5'), 2.15 (m, 4 H, H-4,4'), 3.13 (t, 2 H, H-6'), 3.30 (t, 2 H, H-5), 3.95 (t, 1 H, H-3), and 7.69 (s, 1 H, H-2').

Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.81; H, 7.27; N, 14.40. Found: C, 61.44; H, 7.22; N, 14.20.

1,2,3,4-Tetrahydro-5-(1-pyrrolin-2-yl)pyridine (31). A 1-g sample of **30** was treated under reflux for 3 hr with concentrated HCl (10 ml), cooled, neutralized with K_2CO_3, and diluted with 100 ml of EtOH. After the mixture was stirred at room temperature for 15 min, the precipitated KCl was filtered and the solvent removed *in vacuo*. On standing crude 1,2,3,4-tetrahydro-5-(1-pyrrolin-2-yl)pyridine hydrochloride crystallized (850 mg, 89%). Recrystallization from EtOH–ether gave pure 1,2,3,4-tetrahydro-5-(1-pyrrolin-2-yl)pyridine hydrochloride: mp 167–169°; ir (film) 1590 cm^{-1}; nmr 1.7–2.3 (b, 4 H), 2.46 (t, 2 H, H-4), 2.78 (t, 2 H, H-3'), 3.30 (t, 2 H, H-2), 3.78 (t, 2 H, H-5'), 7.35 (s, 1 H, H-6), and 8.10 (b, 1 H, H-1); M^+ 150.115 (calcd for $C_9H_{14}N_2$, 150.116).

1-Acetyl-1,2,3,4-tetrahydro-5-(2-pyrrolidinyl)pyridine (17). The preceding hydrochloride (130 mg) was stirred at room temperature with anhydrous sodium acetate (60 mg) and acetic anhydride (1 ml) for 1 hr. The acetylated product was not isolated but was directly reduced with excess sodium borohydride in EtOH. After 1-hr reflux, the EtOH was removed *in vacuo;* the residue was dissolved in 10% KOH and extracted with dichloromethane. Drying ($MgSO_4$) and evaporation yielded **17** (70 mg, 52%). Preparative tlc on silica gel developed with ethyl acetate–hexane–diethylamine (7:7:2) yielded the pure compound as a colorless oil: ir (neat) 1640 cm^{-1}; nmr 1.5–2.0 (b, 9 H), 2.05 (s, 3 H, H-8), 3.05 (t, 1 H, H-2'), 3.37 (5, 2 H, H-5'), 3.60 (t, 2 H, H-2), 6.65 and 7.20 (s, 1 H H-6); M^+ 194.142 (calcd for $C_{11}H_{18}N_2O$, 194.142).

1-Acetyl-1,2,3,4-tetrahydro-5-(1-acetylpiperid-2-yl)pyridine, *N'*-Acetylammodendrine (13). A sample (145 mg) of ammodendrine (**1**) was stirred for 1 hr with pyridine (1 ml) and acetic anhydride (1 ml). The mixture was dissolved in ether, washed with 10% KOH, and then 5% HCl, and dried ($MgSO_4$). After removal of the solvent **13** was obtained as a colorless oil: ir (neat) 1640 cm^{-1}; nmr 1.5–2.0 (b, 10 H), 2.08 and 2.11 (s, 6 H, H-8, 8'), 2.8–4.0 (b, 4 H, H-2, 6'), 4.45 and 5.35 (b, 1 H, H-2'), 6.42 and 7.20 (s, 1 H, H-6); M^+ 250.168 (calcd for $C_{14}H_{22}N_2O_2$, 250.169).

1-Acetyl-1,2,3,4-tetrahydro-5-(1-formylpiperid-2-yl)pyridine (19). In a similar manner **1** was formylated with chloral, yield 55% as a colorless oil: ir (neat) 1640 and 1665 cm^{-1}; nmr 1.4–2.0 (b, 10 H), 2.18 (s, 3 H, H-8), 2.7–4.0 (b, 4 H, H-2, 6'), 4.02 and 5.09 (b, 1 H, H-2'), 6.46, 6.56, 7.20, and 7.31 (s, 1 H, H-6), 8.09 and 8.17 (s, 1 H, H-7');[29] M^+ 236.152 (calcd for $C_{13}H_{20}N_2O_2$, 236.152).

1,1'-Diacetyl-2,3'-bipiperidyl (21). Dihydroammodendrine (**18**)[7] was treated as described above to give **21** as a colorless oil: ir (neat) 1640 cm^{-1}; nmr 1.2–2.0 (b, 11 H), 2.10 (2, 6 H, H-8, 8'), 2.5–4.5 (b, complex, 7 H); M^+ 252.184 (calcd for $C_{14}H_{24}N_2O_2$, 252.184).

1-Acetyl-1,2,3,4-tetrahydro-5-(1-acetylpyrrolidin-2-yl)pyridine (20). In a similar manner **17** was acetylated to give **20** as a colorless oil: ir (neat) 1640 cm^{-1}; nmr 1.5–2.0 (b, 8 H), 2.08 and 2.12 (s, 6 H, H-8,7'), 3.2–3.7 (b, 4 H, H-2,6'), 4.0–4.5 (b, 1 H, H-2'),

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(29) Compound **19** shows four peaks for the vinyl hydrogen in the nmr due to restricted rotation about both amide bands. The long range effects of the formyl group are surprising because the corresponding acetyl compound **13** shows only two peaks for the vinyl hydrogen.

6.38 and 7.15 (s, 1 H, H-6); M^+ 236.152 (calcd for $C_{13}H_{20}N_2O_2$, 236.152).

1,1′-Diacetyl-1,2,3,4,1′,2′,3′,4′-octahydro-5,6′-bipyridyl (22). Hystrine hydrochloride (**11**)[4] (125 mg) was refluxed for 1 hr with excess anhydrous sodium acetate and acetic anhydride, 10% KOH was added, and the mixture was extracted with dichloromethane to give **22** as a colorless oil (125 mg, 80%): ir (neat) 1640 cm^{-1}; nmr 1.8–2.2 (b, 8 H), 2.05 (s, 6 H, H-8,8′), 3.69 (t, 4 H, H-2,2′), 5.40 (t, 1 H, H-5′), 6.70 and 7.35 (s, 1 H, H-6); M^+ 248.152 (calcd for $C_{14}H_{20}N_2O_2$, 248.152).

Ammodendrine-*1′*-d_1 (1a). When **1** was slurried with D_2O and the mass spectrum taken, the best incorporation obtained in several attempts was 40% d_1, 60% d_0.

Ammodendrine-*8,8,8*-d_3 (1b). Isotripiperidine (**23**) was treated with acetyl-d_3 chloride as described for the preparation of **15** to give **1b** of 95% isotopic purity.

Ammodendrine-*2′*-d_1 (1c). *N*-Acetylhystrine (**12**)[4] (24 mg) was refluxed with excess sodium borodeuteride for 1 hr in EtOH. The solvent was removed *in vacuo*, 10% KOH was added, and the mixture was extracted with dichloromethane to give **1c** (95% d_1).

Ammodendrine-*2,2,6′,6′*-d_4 (1e). 4-Cyanobutyraldehyde diethyl acetal (**24a**)[21] was refluxed overnight with lithium aluminum deuteride in ether.[22] After careful addition of water, the mixture was filtered and extracted with 10% HCl. This solution, containing 1,2,3,4-tetrahydropyridine-*2,2*-d_2 (**25a**), was neutralized (K_2CO_3), extracted with ether, dried ($MgSO_4$), and evaporated to yield the labeled trimer. Refluxing with piperidine hydrochloride in acetone gave the labeled isotripiperidine. Acetylation and acid treatment as previously described led to **1e** (90% d_4, 10% d_3).

Ammodendrine-*3,3,5′,5′*-d_4 (1f). Calcium metal (2.5 g) was dissolved in heavy water (25 ml) and **24a** (2 g) was added. This was refluxed for 12 hr, cooled, filtered, extracted with ether, dried ($MgSO_4$), and evaporated to give 4-cyanobutyraldehyde-*4,4*-d_2 diethyl acetal (**24b**) (1.7 g, 80% d_2). This was converted to the labeled isotripiperidine and then to **1f** (60% d_4, 30% d_3, 10% d_2).

Ammodendrine-*3′,3′*-d_2 (1d). Ethyl 1,4,5,6-tetrahydronicotinate (**26**)[24] (500 mg) was refluxed under N_2 for 30 min in dilute deuteriophosphoric acid (from P_2O_5 (700 mg) and heavy water (30 ml))[19] After cooling and neutralization (K_2CO_3), the labeled isotripiperidine was extracted with ether and then converted by the standard method to **1d** (70% d_2, 20% d_1, 10% d_0).

Ammodendrine-*2,2,6,2′,6′,6′*-d_6 (1g). Glutarimide (**27**) (Aldrich Chem.) (4 g) was refluxed with lithium aluminum deuteride (1.7 g) for 3 days in tetrahydrofuran. After careful addition of water, the mixture was filtered and distilled to yield piperidine-*2,2,6,6*-d_4 (**28**). This was converted to the labeled isotripiperidine by known procedures.[25] Acetylation gave **1g** (90% d_6, 10% d_5).

***N′*-Methylammodendrine-*7′,7′,7′*-d_3 (9a).** Refluxing of **1** with excess methyl-d_3 iodide in acetone overnight, solution of the precipitated salt in 10% KOH, extraction with dichloromethane, drying ($MgSO_4$), and evaporation gave **9a** of 95% isotopic purity.

Labeled *N′*-Acetylammodendrines (13a–g). The labeled compounds were prepared by two methods. Method A involved acetic anhydride (or acetic-d_6 anhydride)–pyridine acetylation of the appropriately labeled ammodendrine. Method B involved heating the appropriately labeled isotripiperidine (described above) with excess acetic anhydride at 100° for 1 hr. The following list gives the method of preparation and deuterium incorporations for **13a–g**: **13a**, *N′*-acetylammodendrine-*2′*-d_1, method A, 95% d_1; **13b**, *N′*-acetylammodendrine-*8′,8′,8′*-d_3, method A, 90% d_3, 10% d_2; **13c**, *N′*-acetylammodendrine-*8,8,8,8′,8′,8′*-d_6, method A, 85% d_6, 10% d_5, 5% d_4; **13d**, *N′*-acetylammodendrine-*3′,3′*-d_2, method B, 70% d_2, 20% d_1, 10% d_0; **13e**, *N′*-acetylammodendrine-*3,3,5′,5′*-d_4, method B, 60% d_4, 30% d_3, 10% d_2; **13f**, *N′*-acetylammodendrine-*2,2,6′,6′*-d_4, method B, 90% d_4, 10% d_3; **13g**, *N′*-acetylammodendrine-*2,2,6,2′,6′,6′*-d_6, method B, 90% d_6, 10% d_5.

Oxaziridine–Silver Fluoborate Complexes. Site of Complexation by Carbon-13 Nuclear Magnetic Resonance and X-Ray Photoelectron Spectroscopy[1]

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Abstract: Silver fluoborate complexes of a variety of oxaziridines, the first stable complexes of oxaziridines reported, were isolated and found to have the stoichiometry 2(oxaziridine)·$AgBF_4$. In methylene chloride, proton and ^{13}C nmr spectra of oxaziridines showed downfield shifts upon complexation. Comparison of these shifts with those for diethyl ether and triethylamine provides evidence for complexation at nitrogen. X-Ray photoelectron spectroscopy in the solid state also indicates complexation at nitrogen with considerable back-donation from Ag^+ to the oxaziridine, an interpretation supported by MINDO/2 calculations. Complexation with other salts, $AgClO_4$, $AgNO_3$, $LiClO_4$, and $CsClO_4$, is also discussed along with reactivity of the $AgBF_4$ complexes and their importance in mechanistic pathways.

Small ring charged heterocycles,[2] shown to be useful for their biological activity[3] as well as for synthetic intermediates[4] and polymerization catalysts,[5] and metal complexes of some small ring heterocycles[6] have attracted the interest of many researchers in recent years.

Oxaziridines, three-membered ring compounds containing oxygen and nitrogen atoms, are nonbasic compounds,[7] and although SCF–LCAO–MO calculations for protonation of oxaziridines suggest nitrogen to be the most favored position for protonation,[8] mechanisms for acid hydrolysis have been proposed with

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