Mass Spectra of some Aminonaphthyridines and Aminoquinolines (1)

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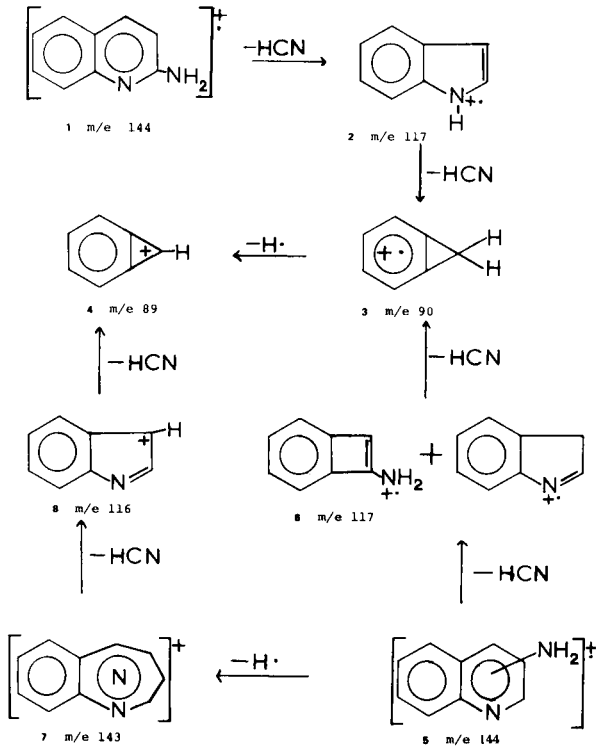
The mass spectra of all the aminoquinolines, the 2-, 3- and 4-amino-1,5-naphthyridines, some amino-1,6-naphthyridines, and two amino-1,8-naphthyridines with methyl substituents are reported. The major fragment in the aminoquinolines is formed by the loss of HCN from the molecular ion. The most abundant fragment in the aminonaphthyridines is formed by the loss of HCN from the molecular ion except in the 2-amino-1,5-naphthyridine isomer. In both 1,8-naphthyridine isomers investigated, the loss of C_2H_2 is an alternate fragmentation pathway of significance. In all of the compounds investigated, the loss of the primary amino group from the molecular ion was found to be an insignificant fragmentation.

Introduction

In the past, we have been concerned with naphthyridine chemistry (2,3) and the chemistry of the aminoquinolines (4,5). Another investigation has been conducted into the fragmentation of the aminocinnolines and related compounds upon electron impact (6). There has been only one report in the literature concerning the mass spectrometric behavior of naphthyridines (7) while several papers have dealt with the quinolines (5,8-16). However, none of these papers have studied the amino compounds. It was now of interest to determine the fragmentation patterns of the aminoquinolines and compare them with the structurally similar aminonaphthyridines.

Scheme I



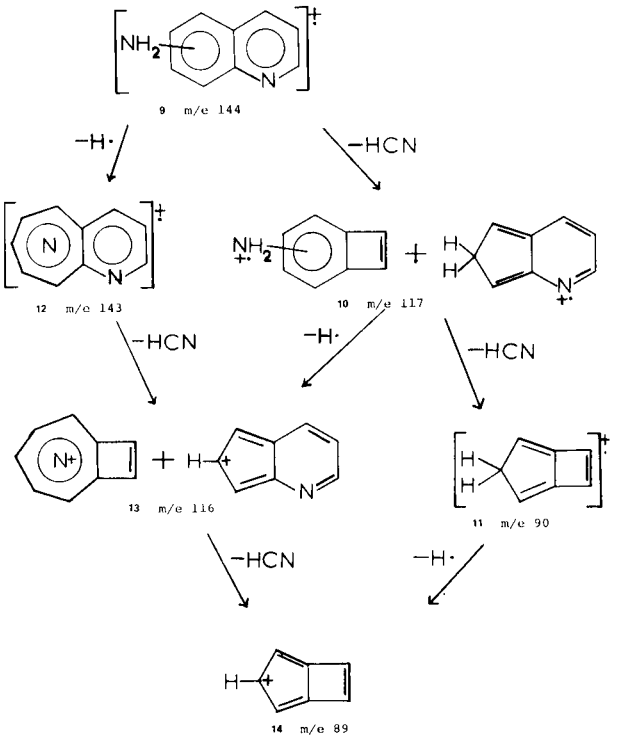
Results and Discussion

Metastable peaks observed in the spectra which correspond to the calculated values are denoted by m*. Bold numbers in parenthesis denote proposed structures which appear in Schemes I-IV.

Aminoquinolines

It can be seen from the mass spectra of the aminoquinolines in Table I that the most abundant fragment ion occurs at m/e 117 (m* 95.1) in all of the isomers. This is due to the loss of 27 mass units as HCN from the parent ion. Upon examination of the 2-isomer (**1**) Scheme I, we see the loss of a second fragment of HCN from the M-27 ion fragment (**2**) to give one at m/e 90 (**3**) (m* 69.2). Then as proposed by Buchardt and coworkers (13) this odd electron ion of mass 90 could lose a hydrogen atom to yield the m/e 89 moiety (**4**). They also noted the appropriate metastable peak in their spectrum, and while we could not detect this metastable peak it can be seen that the only way for 2-aminoquinoline (**1**) to lose two consecutive fragments of HCN is to go through the same indole intermediate ion at m/e 117 (**2**) (or its valence tautomer) which Buchardt *et al.*, have postulated in the fragmentation of quinoline *N*-oxide. There is also a small M-1 peak at m/e 143 due to the loss of a hydrogen atom from the parent ion. The loss of a hydrogen atom and 2 molecules of HCN has been observed in 2-aminopyridine (24). In the 3- and 4- isomers (**5**) the loss of HCN from either m/e 117 ion (**6**) again occurs to give the fragment m/e 90 (**3**) (m* 69.2). Notice that the m/e 90

Scheme II



peak is smaller than the m/e 89 fragment (**4**) in the 3- and 4- isomers. This indicates that some of the m/e 89 fragment must come from another fragmentation pathway. Rinehart and co-workers (17) have shown that one of the fragmentations of the molecular ion of aniline is the loss of a hydrogen atom from the primary amine function followed by ring expansion of the M-1 fragment and finally expulsion of HCN and C_2H_2. We have observed metastable peaks at 94.1 and 68.3 in the spectra of 3- and 4-aminoquinoline which correspond to the loss of two consecutive fragments of HCN from the M-1 ion, m/e 143 (**7**). We would like to suggest that this m/e 143 ion is the parent ion which has first lost a hydrogen atom from the primary amino group and then has undergone ring expansion. The loss of 54 mass units (two HCN fragments from this moiety would indeed lead to (**8**) m/e 116 and finally (**4**) m/e 89. There is another possible structure for ion (**8**) with the positions of the carbon and nitrogen of the double bond in the five membered ring reversed.

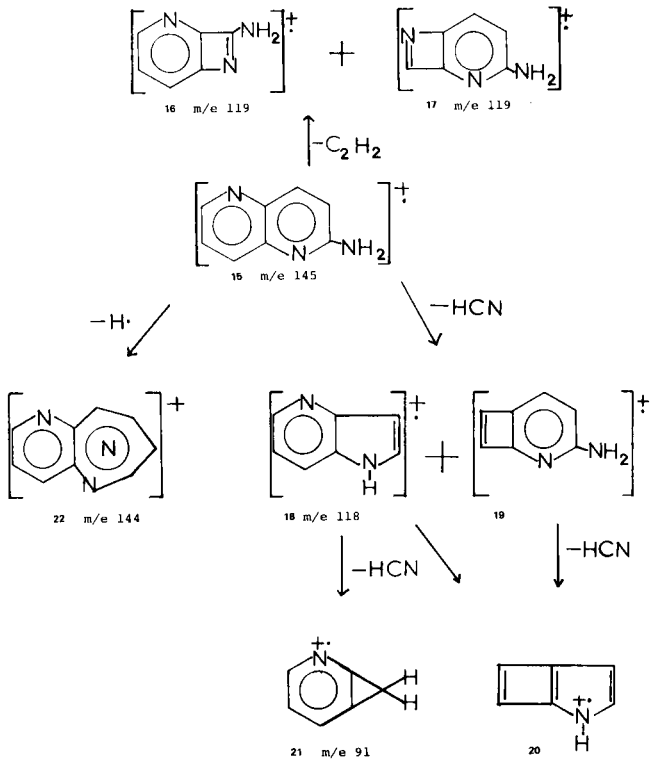
In the 5-, 6-, 7-, and 8-aminoquinoline isomers (**9**) (Scheme II) the expulsion of a second molecule of HCN from the m/e 117 fragment (**10**) to give the m/e 90 (m* 69.25) moiety (**11**) is again noted. As in the 3- and 4-amino isomers, metastable peaks are found in the spectra at 94.1 and 68.3 which correspond to the loss of two consecutive fragments of HCN from the M-1 moiety at m/e 143 (**12**) the ring expanded species. However, note that the abundance of these three fragments at m/e 143 (**12**), 116 (**13**) and 89 (**14**) increases toward the m/e 89 (**14**) fragment in all four amino isomers of the benzenoid ring. This indicates another fragmentation process must contribute to the m/e 116 (**13**) and 89 (**14**) fragments. The loss of a hydrogen atom from the m/e 144 and 90 fragments has been postulated above and it would seem that this process could also occur with the m/e 117 (**10**) fragment to provide an alternate fragmentation pathway to the m/e 116 ion (**13**).

We would like to suggest that a three step fragmentation process, the loss of a hydrogen atom and the loss of two fragments of HCN are responsible for the m/e 89 moiety (**14**). We would like to further suggest that the loss of a hydrogen atom can and does occur as the first, second, or third step in this process and therefore three different fragmentation pathways contribute to the m/e 89 moiety. The peaks at 52, 51, 50, 39, and 38 are typical of pyridine (18) and occur strongly only in the isomers with the amino group on the benzenoid ring.

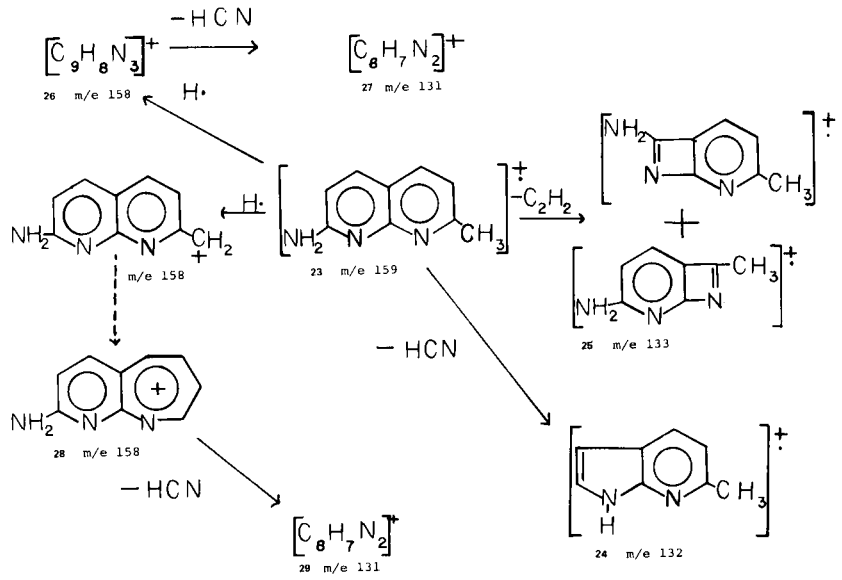
Aminonaphthyridines

When we examine the mass spectra of the aminonaphthyridines in Table II we see that in all of the isomers investigated the loss of HCN from the parent ion is the largest fragmentation, except in the case of 2-amino-1,5-naphthyridine, where the loss of 26 mass units from the

Scheme III



Scheme IV



parent ion predominates. Paudler and Kress (7) have shown that the loss of 26 mass units from methylnaphthyridines occurs when the C-3 and C-4 positions are unsubstituted. They attribute this fragment of 26 mass units of C_2H_2 lost from the C-3 and C-4 positions. The loss of C_2H_2 from the parent ion of 2-amino-1,5-naphthyridine (**15**) (Scheme III) gives a species at m/e 119 (**16**) (m* 97.66). The loss of C_2H_2 could also occur from the unsubstituted ring to yield (**17**). An alternate fragmentation which occurs in 2-amino-1,5-naphthyridine is the loss of two consecutive fragments of HCN from the parent ion to give peaks at m/e 118 (**18**,**19**) (m* 96.0) and m/e 91 (**20**,**21**) (m* 70.2) in the spectra. There is a large M-1 peak in the mass spectrum of 2-amino-1,5-naphthyridine at m/e 144 (**22**), probably the ring expanded species which loses HCN to give a m/e 117 moiety (m* 95.1).

The remaining isomers, 3- and 4-amino-1,5-naphthyridine and 2- and 4-amino-1,6-naphthyridine follow two general fragmentation patterns from the molecular ion. The first path is the consecutive loss of 2 fragments of HCN to give peaks at m/e 118 (m* 96.0) and m/e 91 (m* 70.2). The second pathway is the loss of a hydrogen atom from the primary amino group to yield the ring expanded M-1 species m/e 144 followed by the loss of two consecutive fragments of HCN to yield the ions at m/e 117 (m* 95.1) and m/e 90 (m* 69.2). Perhaps of greater significance here is the fact 2-amino-1,6-naphthyridine does not lose significant amounts of C_2H_2 as the m/e 119 peak is of the same magnitude in all four isomers.

Methylaminonaphthyridines

The mass spectra of two methyl-amino-1,8-naphthyridines are in Table III. In both cases, the largest fragment m/e 132 (**24**) (m* 109.6) is due to the loss of 27 mass units of HCN from the parent ion (**23**). However, in both isomers the M-26 peak at m/e 133 (**25**) (m* 111.2) is quite significant indicating that the loss of C_2H_2 from the parent ion is a second fragmentation pathway of importance. The presence of the methyl groups on the naphthyridine molecule offers an additional fragmentation pathway involving the M-1 peak at m/e 158. We have discussed above the pathway involving loss of a hydrogen radical from the amino function when ring expansion occurs (**26**) followed by expulsion of HCN from the M-1 ion to give a m/e 131 fragment (**27**). Paudler and Kress (7) have postulated that the methylnaphthyridines lose a hydrogen radical from the methyl group and then form a ring expanded species, m/e 158 (**28**) which in turn loses HCN. The loss of HCN from this species would then give an ion at m/e 131 (**29**) (m* 108.6). The m/e 131 peak is probably due to a combination of the two fragmentations from the molecular ion. No evidence indicating any *ortho* effect was present as was observed with 2-amino-6-picoline (24).

Summary

The following general conclusions can now be made:
1) The most abundant fragmentation is the expulsion of HCN from all of the compounds studied with the exception of 2-amino-1,5-naphthyridine.
2) In 2-amino-1,5-naphthyridine the primary fragmentation is the loss of C_2H_2 from the parent ion.
3) In none of the isomers was the loss of $-NH_2$ a significant fragmentation.

4) In all of the amino isomers studied, metastable peaks support the loss of a second fragment of HCN.
5) The methylaminonaphthyridines have four possible fragmentation pathways from the parent ion.

TABLE I

Mass Spectra of Aminoquinolines
Relative Abundances

m/e	2	3	4	5	6	7	8
145	13	13	16	12	11	11	11
144	100	100	100	100	100	100	100
143	5	16	14	9	11	9	7
118	3	3	4	5	5	7	6
117	27	20	20	31	23	62	43
116	8	13	12	16	15	21	14
104	0	1	5	1	1	1	1
90	10	12	9	15	12	17	18
89	8	14	10	22	18	23	20
78	1	1	2	5	3	3	3
76	2	1	3	6	3	5	4
75	2	1	2	5	3	4	3
74	1	1	1	5	3	4	3
72	5	5	6	4	8	9	5
65	1	1	2	6	4	5	5
64	1	1	2	8	6	6	6
63	3	5	4	19	15	18	16
62	1	2	1	10	7	10	8
58.5	3	4	4	3	8	8	6
52	1	1	3	13	9	9	8
51	2	2	2	11	5	10	8
50	1	2	2	10	5	9	7
41	1	1	1	6	5	6	3
39	2	3	2	18	10	12	13
38	1	1	1	11	6	6	7
37	0	0	1	5	3	3	3
28	1	2	2	20	12	11	11
27	0	0	0	5	3	3	3

EXPERIMENTAL

The melting points were determined with a Fisher-Johns block and are corrected. Mass spectra were determined with a Hitachi Perkin-Elmer RMU-6E mass spectrometer with an ionizing potential of 70 eV and an inlet temperature (up to 200°) high enough to obtain sufficient sample for a determination.

The aminoquinolines (19), methyl-amino-1,8-naphthyridines (2) and the 2- and 4-amino-1,5-naphthyridines (20) were prepared as previously described.

The 3-amino-1,5-naphthyridine melted at 148-149° and was prepared from 3-bromo-1,5-naphthyridine by the method of Czuba (21) (m.p. 144-145° uncorrected).

2-amino-1,6-naphthyridine melted at 237-239° and was pre-

TABLE II

Mass Spectra of Aminonaphthyridines
Relative Abundances

m/e	2A-1,5	3A-1,5	4A-1,5	2A-1,6	4A-1,6
146	11	10	12	10	11
145	100	100	100	100	100
144	30	17	5	17	14
119	35	5	5	6	5
118	10	35	32	31	22
117	6	8	5	7	8
105	0	1	3	3	5
91	4	13	9	8	8
90	2	7	4	5	5
79	2	1	5	1	4
72.5	1	4	4	3	7
64	3	7	5	6	7
63	2	10	4	6	9
52	3	5	7	7	11
50	1	3	2	6	5
41	2	4	2	4	5
39	3	6	4	4	5

TABLE III

Mass Spectra of Two
Methyl-amino-1,8-naphthyridines
Relative Abundances

m/e	5Me-2A	7Me-2A
160	18	13
159	100	100
158	25	15
149	6	0
142	0	6
133	15	21
132	42	23
131	18	11
116	11	3
104	8	4
90	4	5
89	5	2
77	6	2
63	6	4
52	5	2
51	5	2
43	6	0
41	7	1
39	7	1

pared from 1,6-naphthyridine by the method of Paudler and Kress (22) (m.p. 238-240°).

Preparation of 4-amino-1,6-naphthyridine

A mixture of 7 g. of phenol, 5 g. of acetamide and 3.53 g. (0.021 mole) of 4-chloro-1,6-naphthyridine (23) was heated slowly while passing a stream of ammonia into the mixture at 120°. The temperature rose quickly to 175° and the mixture was held at 160° for one hour. The solution was cooled to 50° and poured into 20% sodium hydroxide solution and filtered. The basic solution was extracted with ether, the ether dried and evaporated. The crude product was sublimed under vacuum at 220° and was crystallized from water. The yield was 0.63 g. (20.4%) of 4-amino-1,6-naphthyridine and melted at 254° (sealed tube) (uncorrected).

Anal. Calcd. for $C_8H_7N_3$: C, 66.19; H, 4.86. Found: C, 65.90; H, 4.94.

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REFERENCES

(1) Presented in part at the 21st Southeastern Regional Meeting of the American Chemical Society, Richmond, Virginia, November 6, 1969.

(2) E. V. Brown, *J. Org. Chem.*, **30**, 1607 (1965).

(3) E. V. Brown and A. C. Plasz, *ibid.*, **32**, 241 (1967).

(4) E. V. Brown, R. M. Novack, A. A. Hamdan, *ibid.*, **26**, 2831 (1961).

(5) E. V. Brown, *J. Heterocyclic Chem.*, **6**, 571 (1969).

(6) J. R. Elkins and E. V. Brown, *ibid.*, **5**, 639 (1968).

(7) W. W. Paudler and T. J. Kress, *ibid.*, **4**, 547 (1967).

(8) H. Budzikiewicz, C. Djerassi and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, California, 1967, p. 573-580.

(9) S. D. Sample, D. A. Lightner, O. Buchardt and C. Djerassi, *J. Org. Chem.*, **32**, 997 (1967).

(10) P. M. Draper and D. B. Maclean, *Can. J. Chem.*, **46**, 1487 (1968).

(11) D. M. Glugston and D. B. Maclean, *ibid.*, **44**, 781 (1966).

(12) R. T. Coutts, *Can. J. Pharm. Sci.*, **3**, 37 (1968).

(13) O. Buchardt, A. M. Duffield and R. H. Shapiro, *Tetrahedron*, **24**, 3139 (1968).

(14) R. T. Coutts, R. W. Hindmarsh, *Org. Mass. Spectrom.*, **2**, 81 (1969).

(15) T. S. Muraski, C. Djerassi, *J. Org. Chem.*, **33**, 2962 (1968).

(16) F. R. Stermitz, C. C. Wei, *J. Am. Chem Soc.*, **91**, 3103 (1969).

(17) K. L. Rinehart, A. C. Buchholz and G. E. Van Lear, *ibid.*, **90**, 1073 (1968).

(18) Selected Mass Spectral Data, Thermodynamics Research Center Publications, 1966.

(19) E. V. Brown and A. C. Plasz, *J. Heterocyclic Chem.*, **7**, 335 (1970).

(20) E. V. Brown and A. C. Plasz, *ibid.*, submitted for publication, **7**, (1970).

(21) W. Czuba, *Rec. Trav. Chim.*, **82**, 988 (1963).

(22) W. W. Paudler and T. J. Kress, *J. Org. Chem.*, **33**, 1384 (1968).

(23) A. Albert, *J. Chem. Soc.*, 1790 (1960).

(24) G. H. Keller, L. Bauer, C. L. Bell, *J. Heterocyclic Chem.*, **5**, 647 (1968).

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