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# Naphthyridine Chemistry. VIII (1). The Mass Spectra of the 1,X-Naphthyridines and some of their Methyl Derivatives

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The mass spectra of the four parent 1,X-naphthyridines, the 2,3 and 4-monomethyl-1,5-, 1,6-, and 1,8- naphthyridines, seven dimethyl-1,8-naphthyridines, and one trimethyl-1,8-naphthyridine are reported. Evidence for an azatropylium ion intermediate in the fragmentation of the methyl compounds is presented. The fragmentation modes of the naphthyridines are similar to those for the quinolines in addition to several new processes

Recent publications (2-6) have described the mass spectral cleavage patterns of some nitrogen heteroaromatic compounds.

The general conclusion that can be drawn from these publications is that, where structurally possible, the loss of HCN from the molecular ion predominates over all other fragmentation processes.

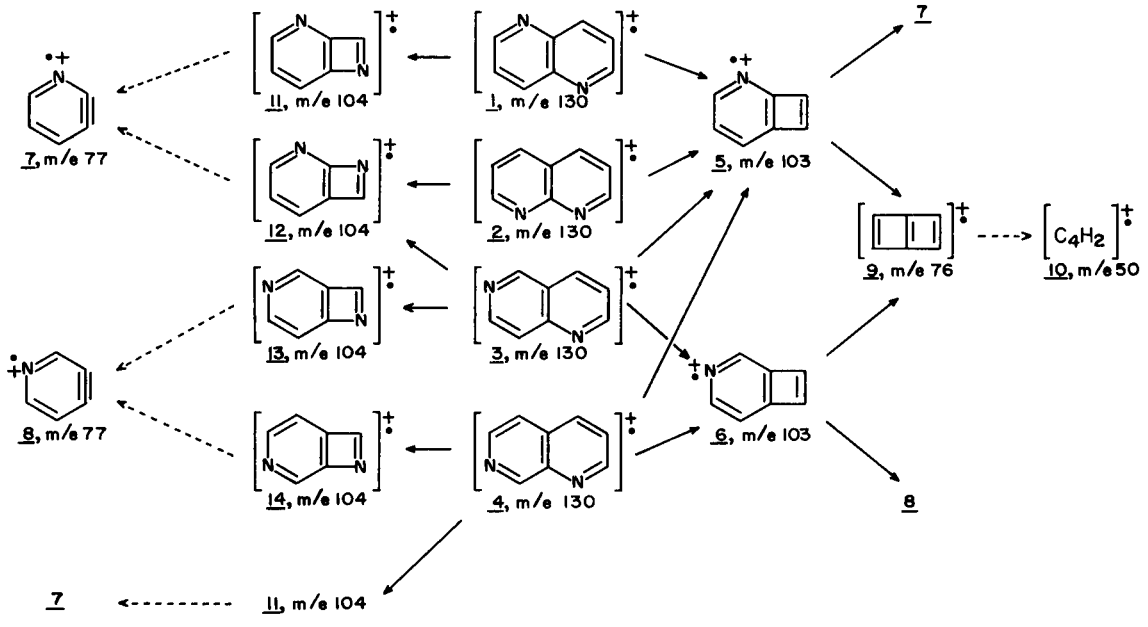
During the past several years we have been concerned with the chemistry of the 1,X-naphthyridine (6-12) and now wish to report on the electron impact caused fragmentations of these compounds.

## Mass Spectra of the 1,X-Naphthyridines.

The most interesting feature of the mass spectra of the 1,5-, 1,6-, 1,7-, and the 1,8-naphthyridines lies in the fact that all four compounds afford essentially the same mass spectra.

The most abundant fragment ion in all of these spectra (*cf.* Fig. 1) is found at m/e 103 and is the ion resulting from the expulsion of HCN from the respective molecular ions. The structure of this ion is unambiguous for the fragment resulting from the symmetrical naphthyridines **1** and **2** and can be assigned structure **5**. The m/e ion resulting

SCHEME I



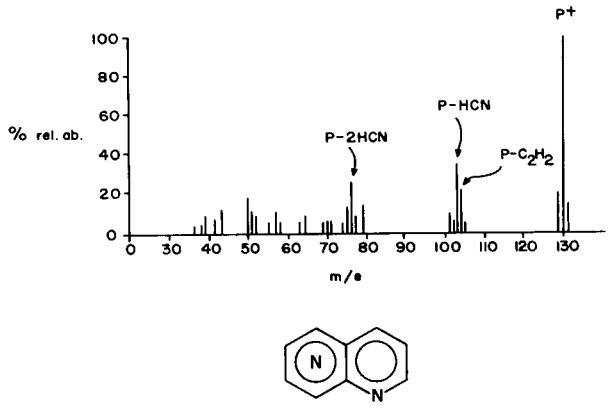



FIGURE 1

from the 1,6- and the 1,7-naphthyridine ion radicals **3** and **4** can arise by expulsion of either one of the nitrogen atoms to yield the ion **5** and/or **6**.

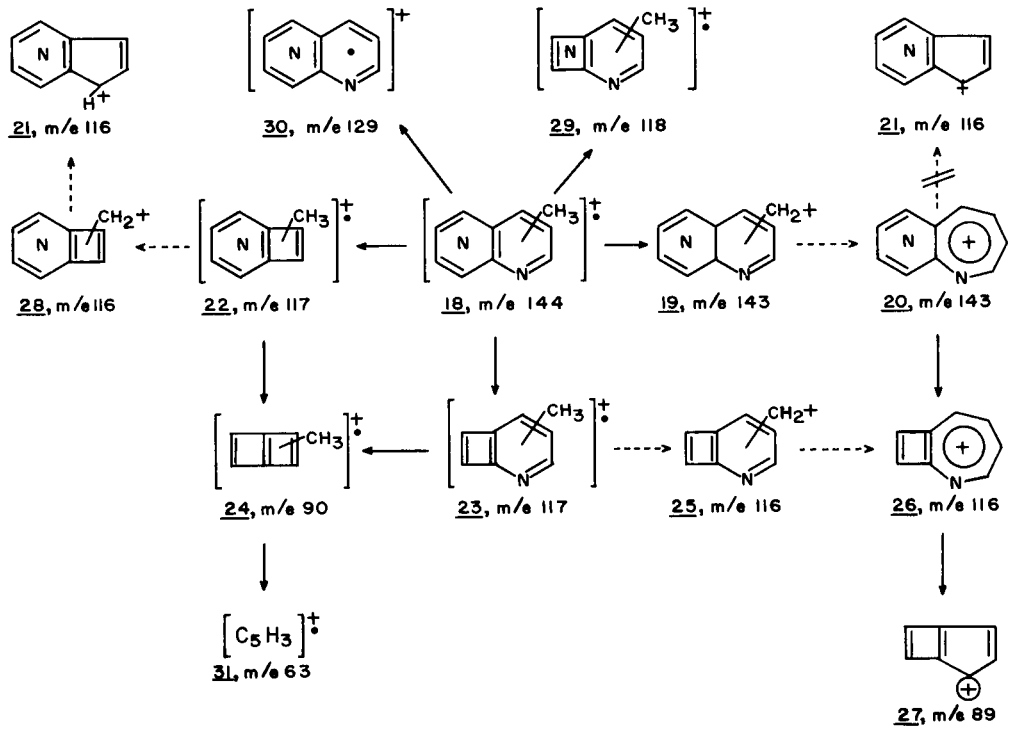
If all of the naphthyridines form the same ion **5** the ratio of the abundancies for the species **9** with respect to species **5** should be the same. On the other hand, if species **6** alone or in conjunction with species **5** is formed, this ratio would be expected to vary from one naphthyridine isomer to another. Table I shows clearly that this ratio is the same for the 1,5-, 1,7-, and 1,8-naphthyridines while it is smaller for the 1,6-isomer. Thus one might suggest that the 1,6-naphthyridine fragments by either forming the ion radical **6** only or along with the ion radical **5**.

As is shown in Scheme 1, the ion radicals **5** and/or **6** lose HCN to afford the species tentatively drawn as structure **9**. The consecutive loss of two molecules of HCN is substantiated by appropriate metastable peaks. The loss of $C_2H_2$ from species **5** and **6** affords the pyridine ion radicals **7** and **8**, respectively. These fragmentations are again substantiated by metastables. The further fragmentations of the bicyclic ion radical **9** by loss of $C_2H_2$ affords a species $C_4H_2^+$ (**10**).

An alternate fragmentation that occurs involves the loss of $C_2H_2$ from the parent ion radical to afford a species at m/e 104. The 1,5- and 1,8-naphthyridines can form the species **11** and **12**, respectively. In the case of 1,6-naphthyridine the two isomeric ion radicals **12** and/or **13** can be formed. Similarly, two alternate isomeric structures (**11** and/or **14**) can be formed from the parent ion of 1,7-naphthyridine. The loss of $C_2H_2$ from the parent ion radicals is substantiated by metastables. The ion radicals **11** and **14** can then lose HCN to afford the pyridyne ion radicals **7** and **8**, as outlined in Scheme 1.

A rather intriguing fragmentation that is observed for all of the parent naphthyridines involves the formation of a species $C_5H_5N^+$ (pyridine ion radical ?) in a direct

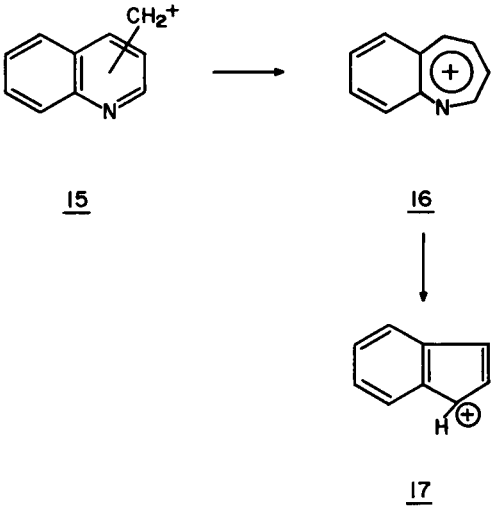
SCHEME 2



process from the parent ion. At this point, no mechanistic considerations are warrented.

Monomethyl Naphthyridines.

The electron impact caused fragmentations of methylquinolines and methylisoquinolines (4) involve mainly the loss of a hydrogen radical followed by the expulsion of HCN from either the benzyl type cation **15** or its ring expanded isomeric structure **16**, to afford species **17**. The



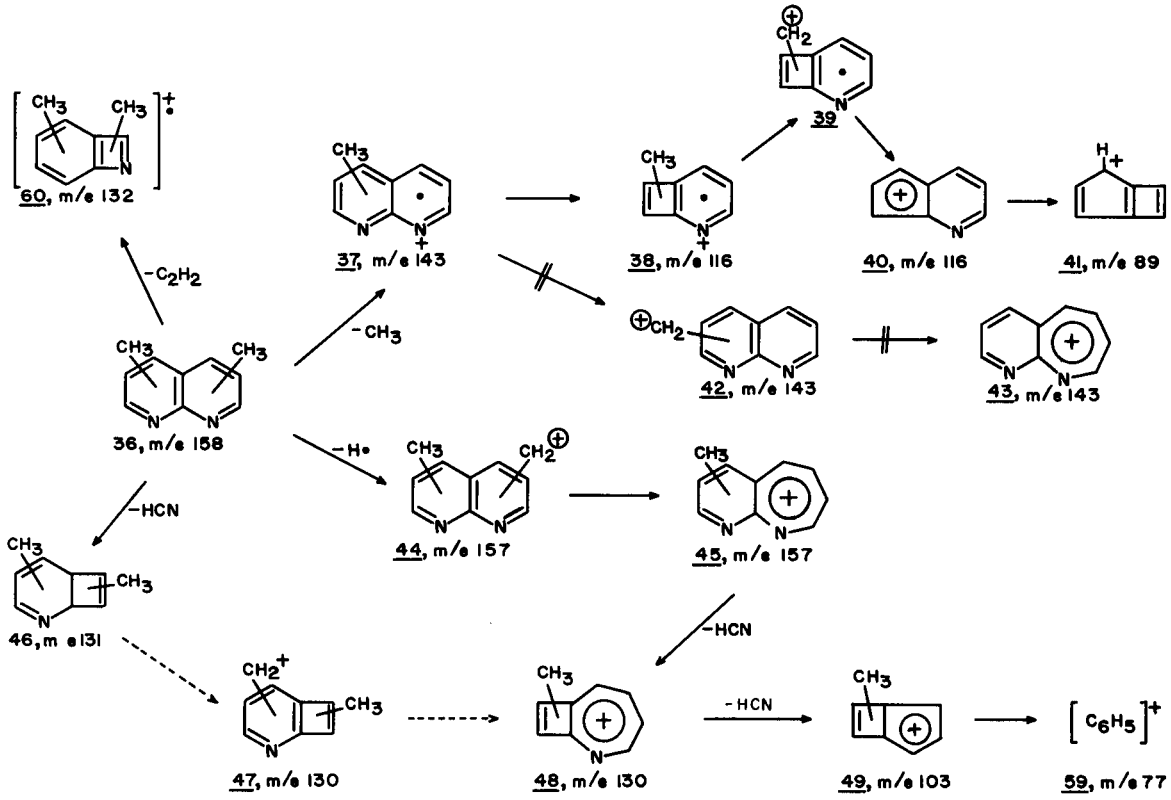
15 16 17

ratio of the abundancies of species **17** to ion **16** (or **15**) has been shown to be constant if the methyl groups are in the hetero ring. A constant but different value is obtained in those compounds where the methyl group is in the benzene ring of the quinolines and isoquinolines. The constancy of these ratios has been utilized to afford proof for the presence of the ring expanded ions.

We have obtained the mass spectra of a large number of methylnaphthyridines and have observed some significant differences between their mass spectral fragmentation patterns and those of the methylquinolines and methylisoquinolines.

The various 2-methyl-1,X-naphthyridines lose, as expected, a hydrogen radical to form the ion **19** (see Scheme 2). Since the ratio of abundancies (see Table III) of the m/e 116 ion to the ion **19** is constant for these compounds, we can again suggest that the m/e 143 species is the ring expanded product of structure **20**. An identical ratio is obtained for the similar ions generated from 3-methyl-1,6-naphthyridine. The remaining 3-methyl and 4-methyl-1,X-naphthyridines do not afford the same ratio value (see Table III). This then implies that the m/e 116 species may arise in these instances by an additional fragmentation. An alternate explanation might be that the ion **19** does not ring expand in these compounds. This explanation does

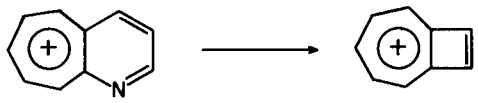
SCHEME 3



not appear tenable in view of the fact that fragments typical of ring expanded products are also observed in these compounds.

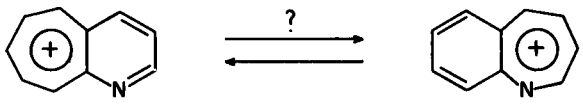
The change in the abundancy ratio of species **26** to **19** (or **20**) is clearly explainable by the observation that the parent ions in the 3-methyl-1,5-, 3-methyl-1,8-, and all of the 4-methyl-1,X-naphthyridines readily lose HCN to form species **22** and/or **23**. Either one of these species can afford a m/e 116 ion (**25**,**26**,**28**, or **21**). Thus, the change in the abundancy ratio, mentioned above, is explainable by the formation of the m/e 116 ions by additional routes.

The ring expanded ion **20** can lose HCN from either the six membered ring or the seven membered ring to afford the identical m/e ions, **21** or **26**, respectively. A differentiation between these two processes appears tentatively possible since it has been reported (4) that the ratio of the abundancies of the quinoline fragments **17** to **16** is 1.28, while the ratio of the species **33** to **32**, resulting from ring expansion from methylquinolines with the methyl group in the benzene ring is 0.32.



**32** **33**

The latter ratio is essentially that for the loss of HCN from species **20** *vs.* the m/e 116 ion. Thus, we can suggest that the fragmentation **20** to **21** is not the preferred process for the loss of HCN from the ring expanded ion **20**. The HCN is consequently expelled from the "neutral" pyridine part of the pyridoazepinium ion **20**. This also has some bearing on the existence or lack thereof of the equilibrium between **34** and **35** which has recently been pro-



**34** **35**

posed to account for the low ratio which has been observed for the abundancy ratio of ions **33** to **32**. If there is any validity to the numerical values of these ratios, which seems certainly feasible, then the suggested possible equilibrium does not exist.

The further fragmentation of species **26** involves the expulsion of HCN to afford the bicyclic ion **27**.

Expulsion of HCN can occur from either the methyl group containing ring or the unsubstituted one to afford species **23** or **22**, respectively. The transformation **18** to **23** is certainly expected to be the preferred one for the various 3-methyl-1,X-nephthyridines in view of the involvment of a secondary radical as compared to a primary one in the conversion of **18** to **22**. Both means of expulsion of HCN from the ion radical **18** appear equally probable for the different 4-methyl-1,X-naphthyridines.

The further fragmentation of the m/e 117 species is outlined in Scheme 2.

The loss of a methyl radical from the parent ions (**18**) becomes significant only in the instances of the 2- and the 4-methyl-1,X-naphthyridines to afford the ion radical **30**.

A process similar to the elimination of HCN from the parent ion involves the loss of $C_2H_2$ to yield the ion radical **29**. This occurs to a minor extent in all of the monomethyl-1,X-naphthyridines investigated.

Dimethyl-1,8-naphthyridines.

The dimethyl-1,8-naphthyridines fragment in a manner analogous to those processes described for the monomethyl-1,X-naphthyridines. Thus, the dimethyl compounds with the methyl groups in the 2- and/or the 4-positions afford the ion radical **37** which can lose HCN after rearrangement to the species **43** via the benzyl type ion **42**. This does not appear to be taking place since the ratio of the intensities of the m/e 116 to m/e 143 peaks are much larger in this series than in the monomethyl compounds.

The loss of a hydrogen to afford the benzyl type cation **44** occurs to a fairly large extent in all of these compounds. The abundancy of the m/e 157 ion is generally independent of the position of the methyl groups. This species then loses, after ring expansion to the ion **45**, HCN in two consecutive steps to afford the ions **48** and **49** respectively.

Similar to the monomethyl-1,X-naphthyridines, the direct loss of HCN from the parent ion occurs most readily in those compounds that do not have a methyl group *ortho* to the nitrogen atom. Where both *ortho* positions are blocked, as is the case in the 2,7-dimethyl and the 2,4,7-trimethyl-1,8-naphthyridines, no direct loss of HCN from the parent ion occurs. The loss of HCN does however occur from the ring expanded ion **45**. This observation further substantiates the existence of the ring expanded azatropylium ions of general structure **20**.

The remaining pathway, the loss of $C_2H_2$ from the parent ion, forming the ion radical **60**, occurs in those instances where the 3- and the 4-positions of the 1,8-naphthyridine nucleus is unsubstituted. Thus, the $C_2H_2$ species that are lost in the 1,X-naphthyridines arise from the $C_3$-$C_4$ atoms and not from the $C_2$-$C_3$ atoms.

The major fragmentation pathways for the various parent and methyl substituted 1,X-naphthyridines can be summarized by the following general statements:

(1) The loss of HCN from either the molecular ion or from the P-1 ring expanded ion in the case of the methyl

TABLE I

Ratio of M-2HCN/M-HCN for the Parent 1,X-Naphthyridines

| Compound | % Relative Abundance M-2HCN m/e 76 | % Relative Abundance M-HCN m/e 103 | M-2HCN/M-HCN m/e 76/103 |
|---|---|---|---|
| 1,5-Naphthyridine | 20 | 12 | 1.05 |
| 1,6-Naphthyridine | 24 | 29 | 0.83 |
| 1,7-Naphthyridine | 25 | 26 | 0.96 |
| 1,8-Naphthyridine | 27 | 26 | 1.04 |

TABLE II

Mass Spectral Data of the 1,X-Naphthyridines

| m/e | 1,5- % rel. abund. | 1,6- % rel. abund. | 1,7- % rel. abund. | 1,8- % rel. abund. |
|---|---|---|---|---|
| 131 | 10 | 12 | 17 | 15 |
| 130 | 100 | 100 | 100 | 100 |
| 129 | 22 | 22 | 21 | 20 |
| 105 | – | – | 5 | – |
| 104 | 20 | 18 | 24 | 19 |
| 103 | 19 | 29 | 26 | 26 |
| 102 | 5 | 5 | 8 | 8 |
| 101 | – | – | 13 | 9 |
| 79 | 15 | 15 | 16 | 14 |
| 77 | 8 | 10 | 10 | 10 |
| 76 | 20 | 24 | 25 | 27 |
| 75 | 10 | 15 | 14 | 11 |
| 74 | 4 | 10 | 6 | 5 |
| 71 | – | – | 5 | – |
| 70 | – | – | 6 | – |
| 69 | – | – | 6 | – |
| 65 | 8 | 9 | 8 | 8 |
| 63 | – | 10 | 5 | 5 |
| 58 | – | – | 5 | – |
| 57 | – | – | 9 | – |
| 55 | – | – | 5 | – |
| 52 | 10 | 10 | 7 | 8 |
| 51 | 11 | 13 | 10 | 10 |
| 50 | 15 | 22 | 20 | 16 |
| 44 | – | 5 | 5 | – |
| 43 | – | 6 | 15 | – |
| 41 | – | – | 8 | – |
| 39 | 19 | 10 | 8 | 9 |
| 38 | 10 | 10 | 5 | 6 |
| 36 | – | – | 6 | 7 |

TABLE III

% Relative Abundance of Peaks Caused by M-H and M-(H+HCN)

| Compound | Fragments of Methyl-1,X-naphthyridines M-H | M-(H+HCN) | M-(H+HCN)/M-H |
|---|---|---|---|
| 2-Methyl-1,5- | 15 | 5 | 0.33 |
| 3-Methyl-1,5- | 35 | 15 | 0.43 |
| 4-Methyl-1,5- | 20 | 8 | 0.40 |
| 2-Methyl-1,6- | 17 | 5 | 0.29 |
| 3-Methyl-1,6- | 35 | 10 | 0.29 |
| 4-Methyl-1,6- | 27 | 7 | 0.26 |
| 2-Methyl-1,8- | 41 | 13 | 0.32 |
| 3-Methyl-1,8- | 18 | 15 | 0.83 |
| 4-Methyl-1,8- | 23 | 14 | 0.61 |

TABLE IV

Mass Spectral Data of the Methyl-1,5-naphthyridines

| m/e | 2-Methyl- % rel. abund. | 3-Methyl- % rel. abund. | 4-Methyl- % rel. abund. |
|---|---|---|---|
| 145 | 11 | 12 | 13 |
| 144 | 100 | 100 | 100 |
| 143 | 15 | 35 | 20 |
| 129 | 13 | – | – |
| 118 | 6 | 16 | 8 |
| 117 | 10 | 30 | 16 |
| 116 | 5 | 15 | 8 |
| 90 | 6 | 22 | 12 |
| 89 | 5 | 22 | 12 |
| 67 | – | 9 | – |
| 65 | – | 8 | 5 |
| 64 | 5 | 9 | 7 |
| 63 | 5 | 16 | 8 |
| 53 | – | 7 | – |
| 52 | 7 | 13 | 7 |
| 51 | 8 | 16 | 10 |
| 50 | 7 | 13 | 7 |
| 39 | 10 | 35 | 12 |

derivatives, is significant in all examples.

(2) The loss of a methyl group is significant only from the 2- and the 4- positions.

(3) The loss of hydrogen from a methyl group occurs in all the methyl compounds.

(4) The loss of $C_2H_2$, from the molecular ion occurs when the C-3 and the C-4 positions are unsubstituted.

(5) The ring expansion of the benzyl type cations seem to occur in these heterocyclic compounds and is analogous to similar observations on the quinolines. These expansions occur regardless of the position of the nitrogen atoms with respect to the methyl group in either ring.

## EXPERIMENTAL

### Materials and Apparatus.

All samples were prepared by previously described procedures (6-12).

Mass spectra were determined on a Hitachi Perkin-Elmer RMU-6E mass spectrometer at an ionizing potential of 80 eV and an ionizing current of 100 uA. Samples were introduced through an all glass inlet system at 200°. Only peaks equal to or greater than 5% of the base peak are reported.

TABLE V

Mass Spectral Data of Some Methyl-1,6-naphthyridines

| m/e | 2-Methyl- % rel. abund. | 3-Methyl- % rel. abund. | 4-Methyl- % rel. abund. |
|---|---|---|---|
| 145 | 12 | 11 | 11 |
| 144 | 100 | 100 | 100 |
| 143 | 17 | 35 | 27 |
| 129 | 13 | – | 43 |
| 118 | 7 | 9 | 8 |
| 117 | 8 | 18 | 12 |
| 116 | 5 | 10 | 7 |
| 103 | – | – | 5 |
| 102 | 6 | – | 11 |
| 91 | – | 8 | 5 |
| 90 | 7 | 24 | 11 |
| 89 | 6 | 21 | 11 |
| 76 | 7 | – | – |
| 75 | 10 | – | – |
| 72 | 5 | – | – |
| 63 | 7 | 22 | – |
| 52 | 5 | 8 | 7 |
| 51 | 8 | 9 | 14 |
| 50 | 11 | 8 | 10 |
| 39 | 7 | 14 | – |

TABLE VI

Mass Spectral Data of the Methyl-1,8-naphthyridines

| m/e | 2-Methyl- % rel. abund. | 3-Methyl- % rel. abund. | 4-Methyl- % rel. abund. |
|---|---|---|---|
| 145 | 11 | 15 | 15 |
| 144 | 100 | 100 | 100 |
| 143 | 41 | 18 | 23 |
| 129 | 10 | – | 7 |
| 118 | 15 | 9 | 8 |
| 117 | 12 | 44 | 25 |
| 116 | 13 | 15 | 14 |
| 91 | – | 5 | 12 |
| 90 | 6 | 31 | 32 |
| 89 | 9 | 24 | 26 |
| 79 | – | 7 | 7 |
| 77 | 6 | 5 | 10 |
| 76 | 13 | 5 | 11 |
| 75 | 6 | 5 | 11 |
| 65 | – | 5 | 10 |
| 64 | 5 | 10 | 15 |
| 63 | 9 | 18 | 23 |
| 62 | – | – | – |
| 52 | 5 | 7 | 11 |
| 51 | 10 | 12 | 24 |
| 50 | 11 | 9 | 15 |
| 39 | 10 | 19 | 32 |

TABLE VII

Mass Spectral Data of Some Methyl-1,8-naphthyridines

| | % Relative Abundance | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| m/e | 2,5- | 2,6- | 2,7- | 3,5- | 3,6- | 4,5- | 2,4- | 2,4,7- |
| 173 | – | – | – | – | – | – | – | 14 |
| 172 | – | – | – | – | – | – | – | 100 |
| 171 | – | – | – | – | – | – | – | 17 |
| 159 | 14 | 14 | 14 | 14 | 14 | 14 | 14 | – |
| 158 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 6 |
| 157 | 17 | 40 | 35 | 20 | 20 | 23 | 23 | 10 |
| 143 | 25 | 7 | 8 | 10 | – | 17 | 23 | – |
| 142 | – | – | – | – | – | – | 11 | – |
| 141 | – | – | – | – | – | – | – | – |
| 132 | 12 | 9 | 12 | 7 | – | – | 6 | – |
| 131 | – | 11 | – | 29 | 32 | 25 | 5 | – |
| 130 | 10 | 19 | 5 | 45 | 51 | 30 | 7 | 7 |
| 118 | 13 | – | – | – | – | – | 5 | – |
| 117 | 5 | – | – | – | – | – | 7 | – |
| 116 | 14 | 6 | 10 | 8 | – | 10 | 9 | – |
| 103 | – | 9 | – | 15 | – | – | – | – |
| 90 | 12 | 7 | 7 | – | 6 | – | 7 | – |
| 89 | 20 | 12 | 14 | 10 | 7 | – | 11 | – |
| 79 | 6 | – | – | – | – | – | 6 | – |
| 78 | 10 | 5 | – | 10 | 10 | – | 6 | – |
| 77 | 15 | 14 | – | 22 | 25 | – | 6 | – |
| 76 | 8 | 5 | – | – | – | – | 5 | – |
| 75 | – | – | – | – | – | – | 5 | – |
| 65 | 10 | 5 | 5 | 11 | 7 | – | 5 | – |
| 64 | 16 | 7 | 6 | 10 | 9 | – | 5 | – |
| 63 | 25 | 13 | 10 | 15 | 15 | – | 10 | – |
| 53 | 10 | – | – | 8 | – | – | – | – |
| 52 | 15 | 9 | 5 | 13 | 10 | – | – | – |
| 51 | 30 | 15 | 8 | 24 | 19 | – | 9 | – |
| 50 | 16 | 10 | 5 | – | 9 | – | 6 | – |
| 39 | 50 | 21 | 12 | 29 | 26 | – | 14 | – |

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