Electron-impact Induced Fragmentation of 2-Substituted Pyridines and Picolines

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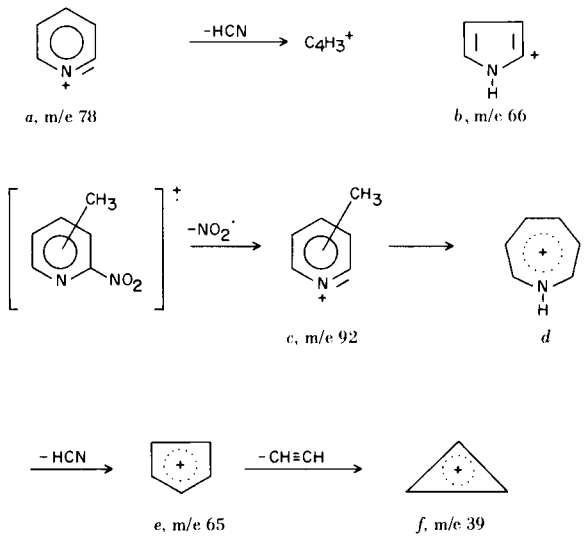
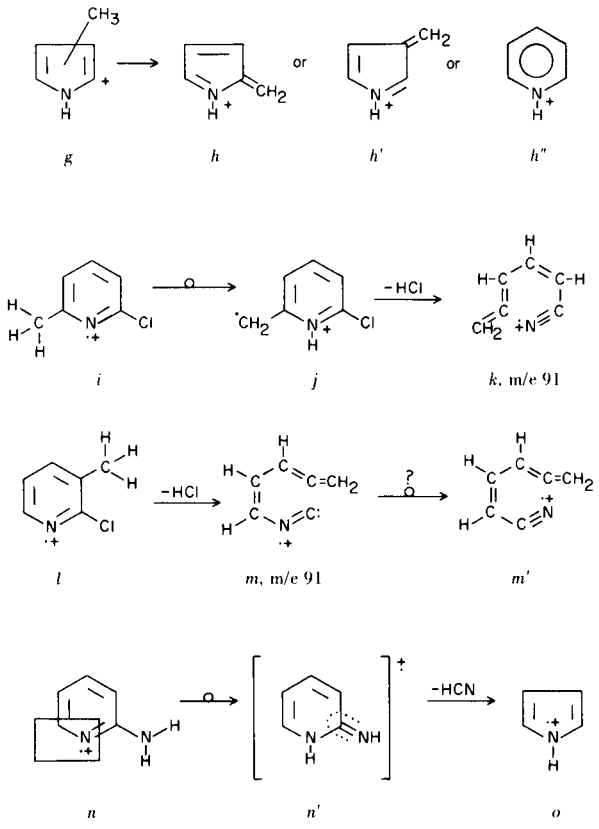
The fragmentation patterns obtained upon electron impact on 2-nitro-, 2-chloro, and 2-aminopyridines, as well as those of the corresponding 3-, 4-, 5- and 6-picolines were examined. There was considerable departure from those patterns reported for the corresponding benzenoid derivatives. Although the molecular ion from 2-nitro-3-picoline did not show fragment ions attributable to an "*ortho*-effect" (unlike *o*-nitrotoluene), those from 2-chloro- and 2-amino-3-picolines did show a loss of HCl and NH_3, respectively. Quite unexpectedly the ions from 2-chloro- and 2-amino-6-picolines also lost HCl and NH_3. Such *meta*-eliminations for the 2-substituted-6-picolines are postulated to be preceeded by either hydrogen or methyl migration. The mass spectra of 2-pyridone, 2-pyridthione and their respective 3-, 4-, 5- and 6-methyl analogs were also studied. The primary fragmentations of the 2-pyridones were as expected from those reported in the literature. The ions from 3- and 6-methyl-2-pyridones lost water also, the former being another example of an "*ortho*-effect" observed in this series. Of the thiones, the fragmentations of 3-methyl-2-pyridthione proved most unique since its molecular ion showed besides the loss of HS, the pronounced elimination of H_2S, the latter presumably due to an "*ortho*-effect." Figures are presented to illustrate the patterns and metastable ions are indicated when found for the transitions discussed.

INTRODUCTION

Fragmentation upon electron impact of pyridine and some substituted derivatives have been reported (2,3). In this study we set out to investigate systematically the mass-spectral fragmentation patterns of a number of 2-substituted pyridines and their four *C*-methyl analogs. Thus, it was possible to contrast the primary fragmentation of a series of the 2-nitro-, 2-chloro- and 2-aminopyridines with that of those of the potentially tautomeric and less aromatic 2-pyridones and 2-pyridthiones. It was of interest to determine if the primary loss was that of the substituent (at C-2) either as a radical or as a neutral molecule - or if it involved ring rupture.

In extending this study from 2-substituted pyridines to the corresponding 3-, 4-, 5- and 6-picolines additional interesting data was obtained. In most instances the fragmentation of the methyl analogs served to substantiate the decompositions proposed for the corresponding 2-substituted pyridines. Thus, in the mass spectral pattern of the picolines, a number of fragment ions with 14 mass units more were found than in similarly constituted 2-substituted pyridine. Furthermore, the presence of a neighboring methyl group in the 2-substituted-3-picolines afforded us the chance to investigate any pronounced "*ortho*-effects" which were so frequently encountered in *o*-substituted benzenes (2). The compounds utilized in this study were purified as described previously





(4) and their 70-eV spectra recorded by means of a Hitachi-Perkin Elmer RMU-6D single-focusing mass spectrometer equipped with a Honeywell 1508 Visicorder. Liquids were usually introduced *via* the liquid sample inlet, solids by means of the direct inlet system.

RESULTS AND DISCUSSION

Figures 1 through 5 show the mass spectra of five 2-substituted pyridines and those of the *C*-methyl derivatives. Known fragmentation pathways, as determined by metastable ions, m*, are marked on the figures by a heavy dot over the appropriate arrow. Not all fragmentation processes will be discussed, since many are predictable from a given parent ion or already discussed in the literature, and only those that are unique or offer an interesting comparison will be mentioned in the discussion.

2-Nitropyridine and 2-Nitropicolines (Figure 1).

The mass spectra of 2-nitropyridine and its *C*-methyl analogs have a small molecular ion peak (0.3 to 2.3% Σ_{29}) and therefore differ considerably in their fragmentation from carbocyclic nitroarenes which usually display a large molecular ion peak (5). 2-Nitropyridine, like nitrobenzene, loses a NO_2 radical upon electron-impact to produce the base peak fragment which accounts for 55.3 percent of the total ion current and corresponds to the pyridyne ion, *a*, at m/e 78. Subsequent elimination of HCN from *a*, leads to a fragment $C_4H_3^+$ at m/e 51 (18.8% Σ_{29}) and is the only other ion in the spectrum to exceed 7% of the total current. Among the less abundant species, however, the absence of a fragment characteristic of aromatic nitro compounds (5) is noted, mainly the M-16 (M-O) fragment ($< 0.1\%$ Σ_{29}).

Another characteristic fragmentation of nitrobenzene involves the consecutive loss of NO and CO from the molecular ion to give the resonance-stabilized cyclopentadienyl carbonium ion, $C_5H_5^+$, *e*, (6). Although such a sequence was noted in the mass spectrum of 2-nitropyridine, (M-NO-CO), the ion, *b*, so produced would not be considered a "favored" species.

The general appearance of the spectra for the four 2-nitropicolines are very similar to each other and to the spectrum of 2-nitropyridine, displaced by 14 mass units (Figure 1). All of the 2-nitropicolines fragment by the same principal routes as mentioned for 2-nitropyridine and differ only in the relative abundance of the fragment ions produced. For example, the M-NO_2 fragment is reduced in the picolines to between 26.8 and 35.6% Σ_{29} and in fact, is no longer the base peak in 2-nitro-5-picoline. This is somewhat surprising since the M-NO_2 fragment at m/e 92, *c*, would correspond to the azatropilium ion, *d*, and should be more stable than the pyridyne ion, *a*, produced above. The difference in abundance is undoubtedly due to the difference in stability between the $C_4H_3^+$ fragment and the $C_5H_5^+$ fragment subsequently produced from this ion by loss of HCN. Also prominent in the 2-nitropicoline spectra is the m/e 39 peak (cyclopropenyl cation, *f*) established by a metastable ion as produced from *e*.

Again, the M-NO-CO fragmentation occurs in the nitropicolines, but no large change in relative abundances is found compared to 2-nitropyridine. This is somewhat surprising since the resultant ion *g*, m/e 80, could easily rearrange to a more stable species like either h,h' or h". In 2-nitro-4-picoline this ion (m/e 80) accounts for 5.7% Σ_{29} but in the other isomers to less than 3% Σ_{29}.

A comparison of the 2-nitropicoline spectra with those of the nitro-toluenes is most interesting since a profound difference is evident between these aromatic nitro compounds (5,6). In addition to the very abundant molecular ions observed for nitrotoluenes, compared to their pyridine analogs, the fragmentation which gives rise to the base peak in the spectrum of *o*-nitrotoluene, M-OH, is completely absent in 2-nitro-3-picoline although the methyl group and nitro group are *ortho* in both compounds as required for this loss to occur. Except for the prominent loss of NO_2, little similarity in fragmentation

is found. In the other nitrotoluenes, the fragmentation parallels the processes found in the 2-nitropicolines except that the characteristic M-O ions are absent (< 0.05% Σ_{29}).

No M-H ion is found in 2-nitropyridines (or the nitrotoluenes) although this ion is present in the other 2-substituted pyridines reported here.

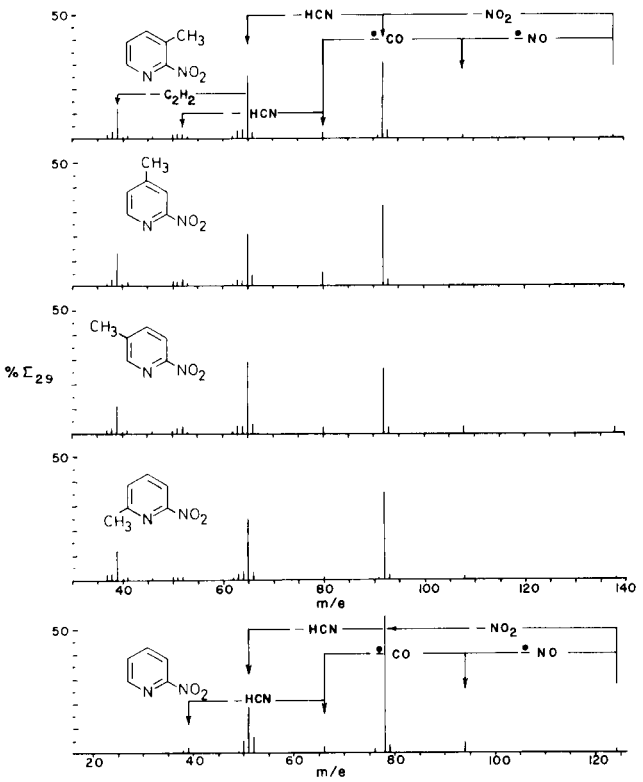


Figure 1. Mass Spectra (70-eV) of 2-Nitropyridines and 2-Nitropicolines.

2-Chloropyridine and 2-Chloropicolines (Figure 2).

The spectrum of 2-chloropyridine exhibits, in addition to a strong molecular ion, only two fragment ions over 8% Σ_{29} and these are due to M-Cl to give the base peak at m/e 78 (30.8% Σ_{29}) followed by the loss of HCN to give the m/e 51 ion, $C_4H_3^+$ (12.8% Σ_{29}). The loss of the substituent followed by the loss of HCN was also the favored fragmentation route in 2-nitropyridine and in this respect the spectra are quite similar. However, the fragmentation of the 2-chloropicolines diverge somewhat from the expected.

Although an anticipated "*ortho*-effect" was notably absent in the 2-nitropicolines, a strong "*ortho*-effect" is observed in 2-chloro-3-picoline where the most abundant fragment ion (18.9% Σ_{29}) at m/e 91 is due to the loss of HCl as established by a metastable peak at m/e 65.3, while in 2-chloro-4-picoline, where the groups are *meta*, the m/e 91 fragment amounts to only 2.5% Σ_{29}. The M-Cl fragment is prominent in all of the 2-chloropicoline spectra and is the most abundant fragment ion in the 3- and 5-picolines.

The most interesting observation in the 2-chloropicoline fragmentation scheme is the major loss of HCl from 2-chloro-6-picoline in which the methyl and chloro groups are *meta* to each other. A metastable peak confirms this loss. Although not proven, it seems logical to assume that the hydrogen in the HCl expelled orginates in the methyl substituents. If this is so, then a hydrogen (or methyl) migration must precede the loss of HCl. For hydrogen migration, a process $i \rightarrow j \rightarrow k$ is feasible. A similar m/e 91 fragment species, *m*, and mechanism can be postulated for the loss of HCl from 2-chloro-3-picoline *via* *1*, without rearrangement however.

The possibility that the HCl loss from either 2-chloro-3- or 6-picolines is thermally induced was eliminated by introducing a sample directly into the ion source with all heaters turned off. In addition, the spectrum obtained at an ionizing voltage of 12-eV contained two predominant ions due to the loss of Cl and HCl, with the latter being

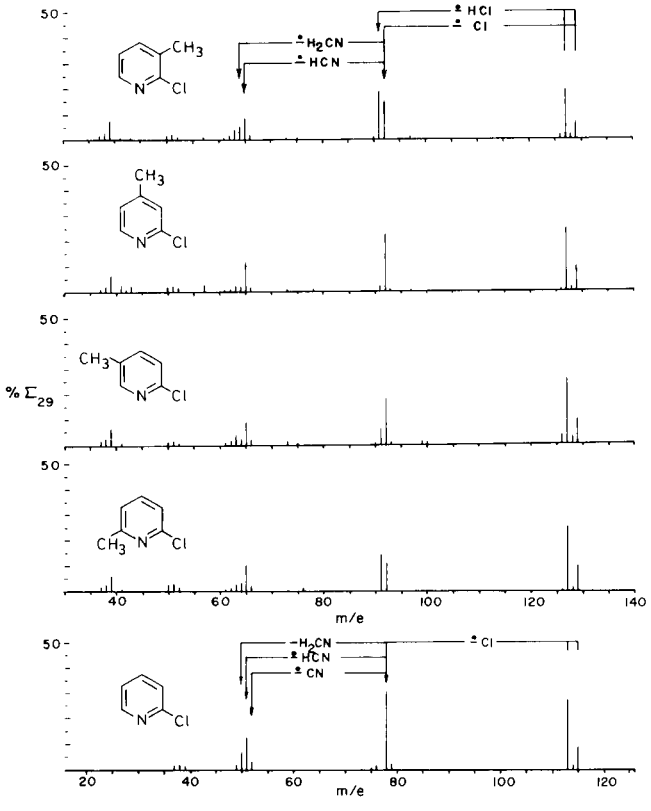


Figure 2. Mass Spectra (70-eV) of 2-Chloropyridines and 2-Chloropicolines.

four times more intense as in the 70-eV spectrum where the two ions are near equal in abundance.

An M-1 fragment ion, although small, is found in the spectrum of the chloropicolines and is largest in the 3- and 5-picolines as expected. It is of interest to note that in the mass spectra of chloroarenes the loss of Cl is more pronounced than that of HCl (7). This is certainly not true in the pyridine series.

2-Aminopyridine and 2-Aminopicolines (Figure 3).

In contrast to the previous pyridines, 2-aminopyridine loses HCN directly from the molecular ion, *n*, which is the the base peak, to produce a pyrrole ion, *o*, which in turn loses 26,27 and 28 mass units assignable to the loss of CN, HCN and H_2CN. The loss of HCN from the molecular ion, *n*, could involve either one of the nitrogen atoms in 2-aminopyridine. It is plausible that the arrangement of $n \rightarrow n'$, (8) precedes the loss of HCN involving the amino nitrogen (dotted lines) to form *o*, or HCN is lost in a

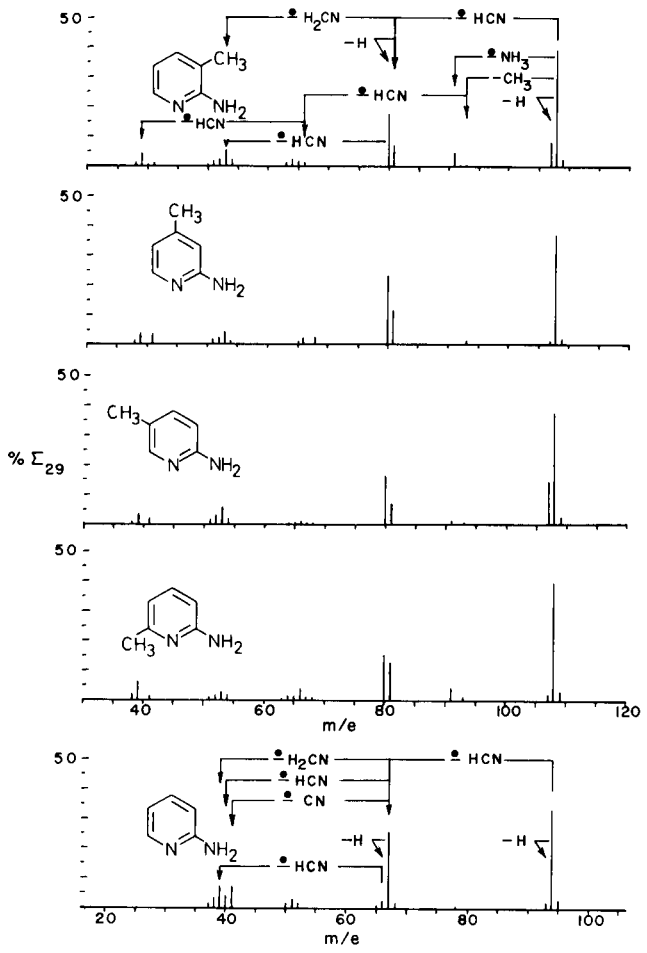


Figure 3. Mass Spectra (70-eV) of 2-Aminopyridine and 2-Aminopicolines.

manner analogous to that from pyridine itself (2,3) (boxed sequence in *n*) but further investigation is essential to settle this problem. It should also be realized that a major fragmentation of the molecular ion of aniline is the loss of HCN (9). In addition, both the molecular ion *n*, and the pyrrole ion, *o*, show a small loss of one mass unit (< 5% Σ_{29}).

The fragmentation of the 2-aminopicolines reveal a large M-1 peak for the 3- and 5-picolines and a loss of one from the ion corresponding to a methyl pyrrole ion (m/e 81). Both of these losses were anticipated. However, the loss of ammonia to give an ion, m/e 91 (4.9% Σ_{29}), in the spectrum of 2-amino-3-picoline was not expected. A weak metastable peak was found to correspond to this fragmentation at m/e 76.7. Again this can be ascribed to an "*ortho*-effect", as previously described for 2-chloro-3-picoline. Even more surprising is the appearance of an ion corresponding to the loss of NH_3 in the spectrum of 2-amino-6-picoline. The loss of ammonia is not common (unlike that of HCl, encountered in some of the chloropicolines), and in 2-amino-6-picoline seemingly less likely since a rearrangement must precede this fragmentation. Direct introduction of a sample of 2-amino-6-picoline into the unheated ion source did not alter the spectrum significantly.

2-Pyridthione and *C*-Methyl-2-pyridthiones (Figure 4).

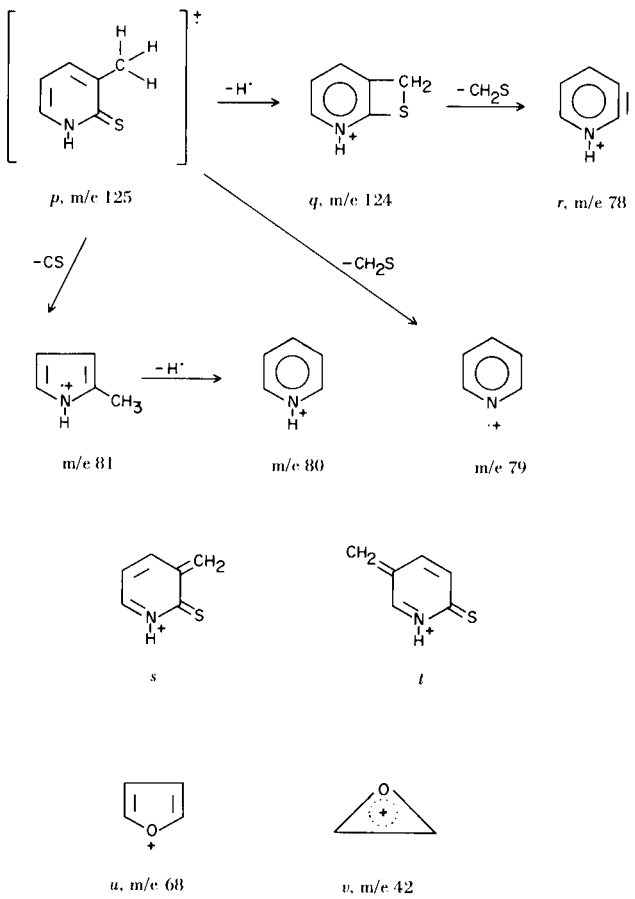
The spectrum of 2-pyridthione and the fragmentation to pyrrole by the loss of carbon monosulfide from the molecular ion has been reported as well as the spectrum of 4- and 6-methyl-2-pyridthione (10). The spectrum of 2-pyridthione obtained under the conditions of this study is reported for comparison with the *C*-methyl derivatives. Of the four *C*-methyl-2-pyridthiones, only the 3-methyl compound shows large differences in fragmentation presumably due to an "*ortho*-effect", the most abundant fragment ion being the M-1 ion, while in the others it is the M-CS-H ion. The large M-1 ion from the molecular ion of 3-methyl-2-pyridthione, *p*, can be rationalized if an even-electron fragment ion of structure *q* is postulated.

In addition, several other unique fragments appear in the 3-methyl-2-pyridthione spectrum. The loss of SH, while prominent in all the thione spectra, is overshadowed by the loss of H_2S from *p*. It is possible to visualize this loss thermally if 3-methyl-2-pyridthione were first pyrolyzed, but at the lowest possible temperatures needed to vaporize all of the *C*-methyl-2-pyridthiones (using the direct inlet system) the expulsion of H_2S took place only from the 3-methyl compound indicating it is an electron-impact induced decomposition. The "*ortho*-effect" producing an ion m/e 91 (M-H_2S) might be expected to be operating in 6-methyl-2-pyridthione by analogy to the

2-chloro and 2-amino-6-picolines described above. However, only a small abundance of this ion species is found in the spectrum (1% Σ_{29}) of the 6-methyl derivative which is still an increase when compared to 0.2% Σ_{29} for the 4- and 5-methyl-2-pyridthiones.

In the low voltage spectra of *p* (12- and 14-eV), the ration of M-SH and M-H_2S was about the same as in the 70-eV spectrum showing that the ion arises more probably directly from *p* rather than by the loss of H from the M-SH ion. Surprising also in the low voltage spectrum is the persistence of the M-S ion which is barely discernible (< 1% Σ_{29}) in the high voltage spectrum. Another unique feature in the region of the spectrum of *p* is the presence of ions at m/e 79 and 78 in addition to those expected at m/e 81 and 80. The former ions would correspond to the loss of CH_2S from the molecular ion, *p* and from the M-1 ion, respectively. This is consistent with the low voltage (12-eV) spectrum in which only the ions at m/e 79 and 81 remain since these are produced directly from the molecular ion. A plausible scheme of the fragmentation of *p* is suggested in Scheme 1.

SCHEME I



Although alternate structures and routes to the fragment ions in Scheme 1 are possible, the ions shown best describe the behavior observed. For example, the m/e 124 ion could be formulated as *s*, but the loss of CH_2S from it would be difficult to explain. By analogy, the molecular ion of 5-methyl-2-pyridthione could give an M-H fragment represented by *t*. Since *p* yields such an intense M-H peak, the bicyclic structure *q*, is preferred.

It should be pointed out that the m/e 78 fragment could be produced by an alternate route and still be consistent with the low voltage spectrum. A loss of H_2 from the even-electron ion m/e 80 could produce this ion. There also appears to be a *weak* metastable ion at m/e 76.0 which could correspond to this process. What makes this process very unlikely is the lack of an m/e 78 fragment ion in the spectrum of other pyridines where an ion at m/e 80 is even more prominent (see following discussion of methyl-2-pyridones).

In contrast to the behavior of the *C*-methyl-2-pyridthiones are the three isomeric thiocresols whose mass spectra do not differ greatly from one another and which have as their main fragmentation the loss of SH (11).

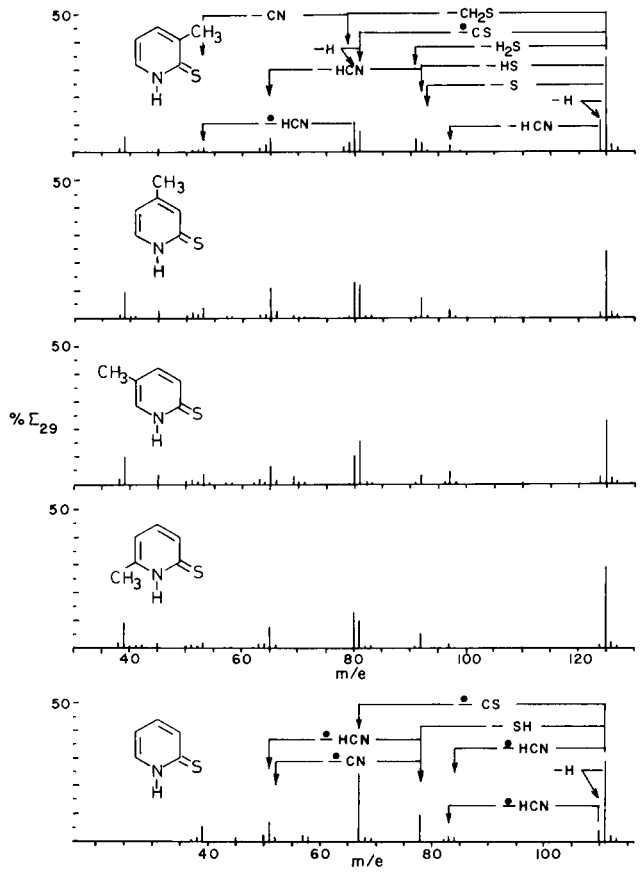


Figure 4. Mass Spectra (70-eV) of 2-Pyridthiones and *C*-Methyl Analogs.

In all of the pyridthione spectra studied, a significant fragment at m/e 45 is present indicating that in addition to CS and CH_2S, CHS (m/e 45) is also a sulfur-bearing fragment in which the positive charge is retained preferentially. The published spectrum of 6-methyl-2-pyridthione (10) appears to contain peaks due to contaminants since large m/e 93 (33.8%) and m/e 76 ions (26.4%) are reported as well as several smaller peaks which this study did not find.

2-Pyridone and *C*-Methyl-2-pyridones (Figure 5).

The electron-bombardment induced fragmentation of 2-pyridone and several derivatives thereof, have been recorded in the literature (10, 12, 13). A common feature is the production of a relatively intense peak due to the expulsion of CO and a similar phenomenon is observed in the molecular ions of 2-quinolones (14, 15). The spectrum of 2-pyridone-^{18}O (16) showed that only two fragment ions, and these in very low abundance, retained the pyridone oxygen, *viz.*, *u* and *v*. The spectrum of 2-pyridone differs from the of 2-pyridthione since it did not possess fragment ions due to either M-1 or M-OH (corresponding to the SH loss) and subsequent fragments derived from such initial decomposition.

With three exceptions the *C*-methyl-2-pyridone spectra were similar. The 3- and 5-methyl compounds gave a significant M-1 fragment (25% Σ_{29}) which was absent in the others. More important was the novel loss of water (M-18) observed for the 3- and 6- methyl-2-pyridones again analogous to the loss of HCl and NH_3 discussed previously. The resulting fragment (m/e 91) was more abundant in the spectrum of the 3-methyl compound and can be attributed to an "*ortho*-effect". As a matter of fact, the loss of water was observed also in the mass spectra of 3-methyl and 3,4-dimethyl-2-quinolones and not in those of 2-quinolone, 1-methyl- and 4-methyl-2-quinolones (15).

In 6-methyl-2-pyridone, a transfer of hydrogen (or methyl) must precede this loss of water as pointed out previously. The 6-methyl compound was also unique in the loss of CH_3 from the molecular ion to show a fragment at m/e 94 followed by the loss of CO from this ion to give a prominent m/e 66 fragment ion (17).

By way of contrast, it is interesting to compare the rate of formation of the fragment ion at m/e 81 in the *C*-methyl-2-pyridones and the corresponding thiones by the loss of CO and CS respectively, with that of the ions at m/e 80 produced by the loss of one mass unit from the ion, m/e 81. In the *C*-methyl-2-pyridthiones, these two fragments are of comparable abundance while in *C*-methyl-2-pyridones the ion at m/e 80 is 2 to 5 times more abundant than the m/e 81 fragment. Since the ion, m/e 81, in both series of compounds is a precursor to the one at m/e 80, the difference in abundances reflects the difference in the rate at which the m/e 81 ion is formed. The conclusion is that CO is expelled from *C*-methyl-2-pyridones at a slower rate than CS is expelled from the corresponding 2-pyridthiones.

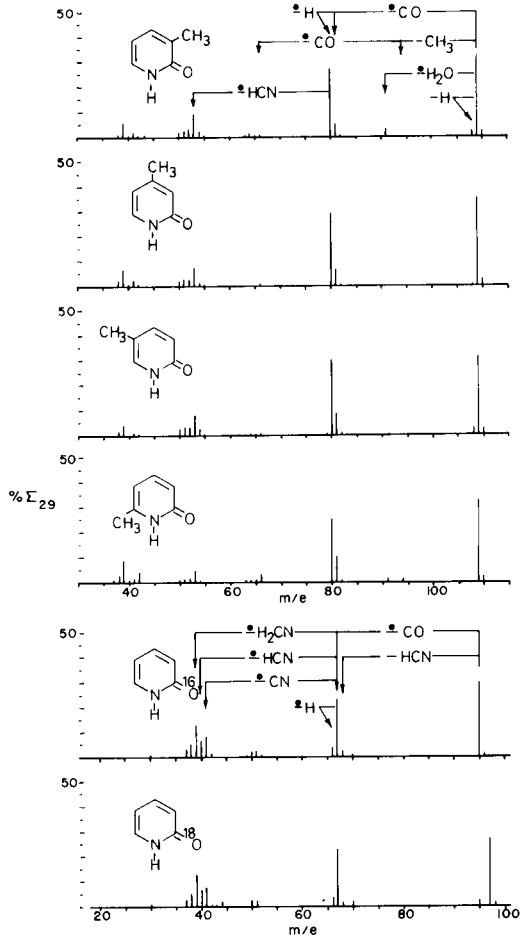


Figure 5. Mass Spectra (70-eV) of 2-Pyridone and *C*-Methyl Analogs.

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