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Mass Spectrometry of Onium Compounds

Part VIII.[1] Dihydrothiazolo[3,2-a]pyridinium Derivatives

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Simple 2-alkylthiopyridinium-3-oxides are volatile in the mass spectrometer. A corresponding *S*-acetic acid was partly decarboxylated to the methio analogue but the major pathway was deacetylation with formation of the corresponding pyrid-2-thione. The latter product was the major component from the HI salts. The acid salts of the analogous dihydrothiazolo[3,2-a]pyridinium-8-oxides behaved differently in that the acid and the betaine were evaporated separately. Betaines without electronegative substituents in the dihydrothiazolo ring are evaporated structurally unchanged. Derivatives with strongly electronegative substituents, or carboxylic acids which are decarboxylated in the instrument, suffer ring opening to the corresponding *N*-vinyl thione prior to evaporation. Intermediate cases can be deduced from the fragmentation patterns.

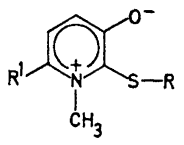
Deuterio derivatives have been prepared for mechanistic studies and pyrolytic products synthesized.

On mass spectrometry *N*-quaternary compounds may undergo structural or electronic rearrangements prior to evaporation. As a continuation of our mass spectrometry studies of pyridinium compounds [1] we now report on dihydrothiazolo[3,2-a]pyridinium-8-oxides.

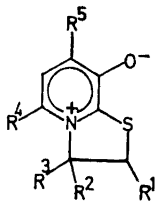
The elementary compositions of the main fragments in selected compounds were determined by high resolution. The fragmentation pathways were confirmed by appropriate metastable peaks and if necessary the metastable defocusing technique was used.[2]

The following compounds are included in this report.

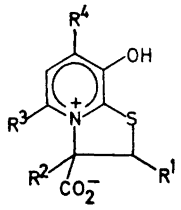
The betaine (I) shows a strong signal corresponding to the molecular ion (*m/e* 183) (Fig. 1) while the acid (II) (Fig. 2) undergoes decarboxylation (*m/e* 169). Compound I can become non-charged by a number of routes. Thus intermolecular proton exchange could occur between the 6-methyl group and the phenolate oxygen (XVIII). The latter should readily interchange its phenolic hydrogen with deuterium. No interchange did take place in a deuterium oxide atmosphere. Formation of the *O*-methyl ether by transalkylation would not seem likely since simple pyridinium-3-oxides evaporate without



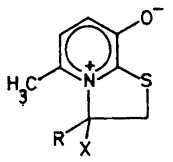
I $R=C_2H_5$, $R^1=CH_3$
Ia $R=C_2H_5$, $R^1=CD_3$
II $R=CH_2CO_2H$, $R^1=CH_3$



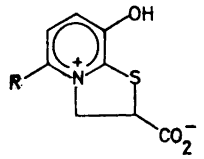
III $R^1=R^2=R^3=H$, $R^4=CH_3$, $R^5=H$
IIIa $R^1=R^2=R^3=H$, $R^4=CD_3$, $R^5=H$
IIIb $R^1=H$, $R^2=R^3=D$, $R^4=CH_3$, $R^5=H$
IIIc $R^1=R^2=R^3=H$, $R^4=CH_3$, $R^5=D$
IV $R^1=CH_3$, $R^2=R^3=H$, $R^4=CH_3$, $R^5=H$
V $R^1=C_6H_5$, $R^2=R^3=H$, $R^4=CH_3$, $R^5=H$
VI $R^1=R^2=R^3=R^4=R^5=H$
VII $R^1=R^2=R^3=H$, $R^4=CH_3$, $R^5=Br$



VIII $R^1=R^2=H$, $R^3=CH_3=R^4=H$
VIIIa $R^1=H$, $R^2=D$, $R^3=CH_3$, $R^4=H$
VIIIb $R^1=H$, $R^2=D$, $R^3=CD_3$, $R^4=H$
IX $R^1=CH_3$, $R^2=H$, $R^3=CH_3$, $R^4=H$
X $R^1=R^2=R^3=R^4=H$
XI $R^1=R^2=H$, $R^3=CH_3$, $R^4=Br$

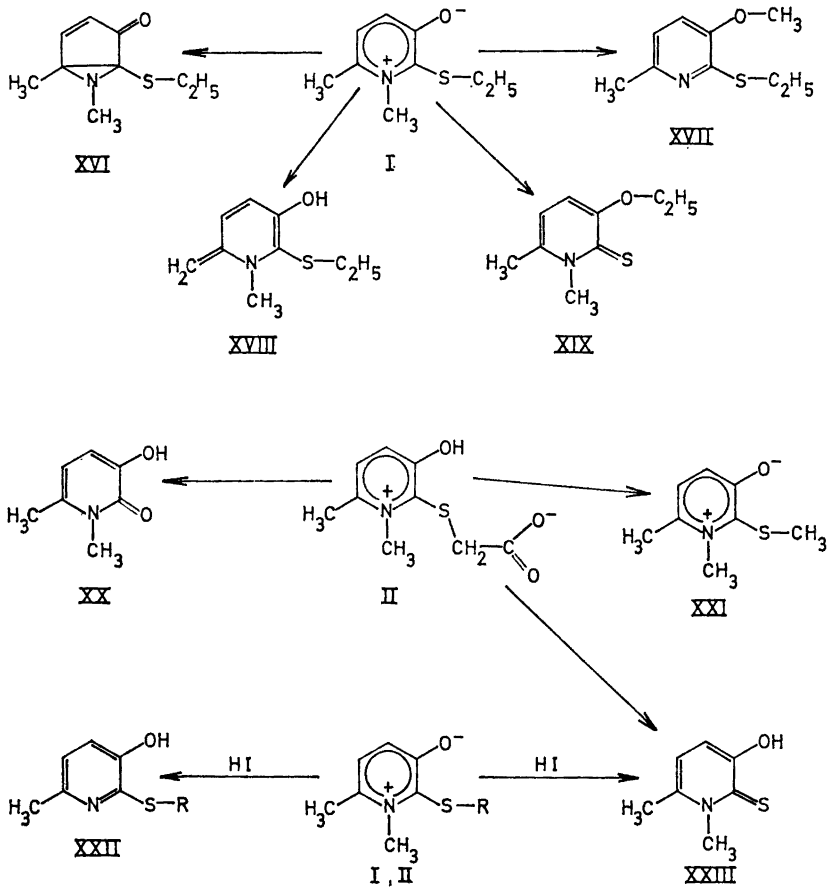


XII X=CN, R=H
XIIa X=CN, R=D
XIII $X=CONH_2$, R=H
XIIIa $X=CONH_2$, R=D



XIV $R=CH_3$
XV R=H

structural changes.[3] More complex pyridinium-oxides give rise to higher molecular weight substances by *O*-alkylation without *N*-dealkylation.[3] No volatile substance with a higher molecular weight was present in this case. Also the ether (XVII) is excluded by the absence of marked $[M-CH_3]$ and $[M-CH_2O]$ fragments characteristic for aryl-methyl ethers.[4] Formation of the thione (XIX) by S–O transethylation can also be ruled out from the fragmentation pattern. The base peak (*m/e* 150) in the spectrum (Fig. 1) is formed by SH expulsion. Loss of the SH radical is characteristic for alkyl-aryl thioethers and is especially strong when the alkyl group is ethyl.[5] Volatile species, however, can arise through thermal excitation leading to electronic rearrangements with the formation of a neutral cyclopentenone structure (XVI). Alternatively the charges in the betaine structure (I) are largely compensated internally through increased delocalization of the negative charge of the oxy-group into the azinium nucleus. No distinction between these pos-

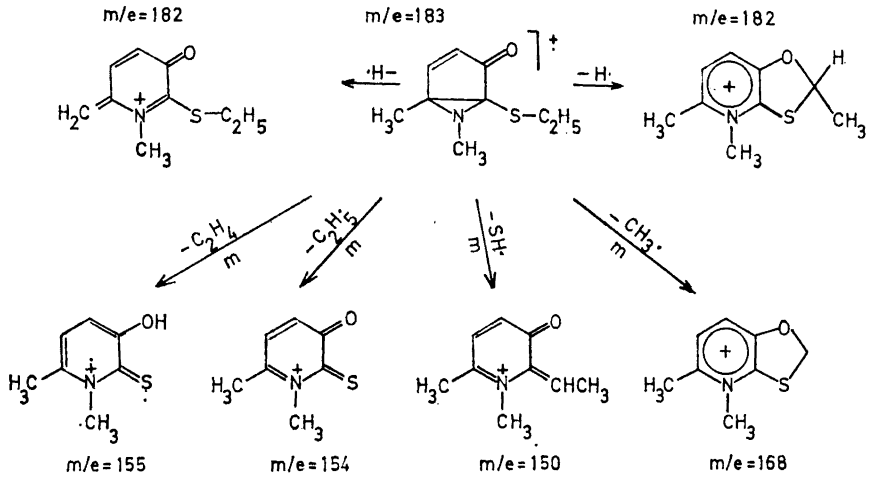


Scheme A.

sibilities is made in the presented work. For illustrative purposes, however, the volatile species from betaines which have not undergone a structural rearrangement are drawn in a cyclopentenone form (*e.g.* XVI).

The acid (II) is partly decarboxylated (XXI) (Fig. 2) before evaporation (*m/e* 169). The spectrum, however, is completely dominated by the fragmentation of the pyrolytically formed thione (XXIII) at *m/e* 155. The *m/e* 139 peak was found by high resolution to have a composition corresponding to the lactam XX. As its intensity is dependent on time and conditions this is also a pyrolysis product.

The base peak (*m/e* 150) in the spectrum (Fig. 1) of the zwitterion (I) is due to SH expulsion from the molecular ion at *m/e* 183 (Scheme 1). The other major fragment is at *m/e* 155 found by high resolution to be a singlet due to $[M-C_2H_4]$. The absence of the expected $[M-CO]$ peak is explained by the McLafferty rearrangement being an energetically highly favoured process.

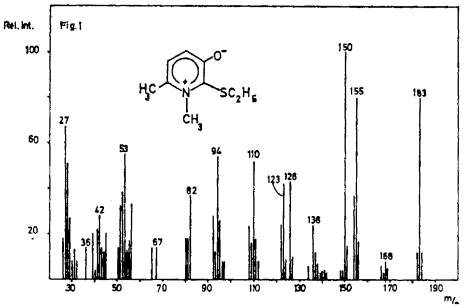


Scheme 1.

Another primary fragmentation process involves thioether α-cleavage with C_2H_5 expulsion (*m/e* 154). Thioether β-cleavage with either hydrogen or methyl radical expulsions contribute to the peaks at *m/e* 182 and *m/e* 168. Expulsion of the pyridyl 6-methyl group as shown by the spectrum of the deuterated analogue (Ia) is unimportant. The *N*-methyl group could contribute to [M − 15] but β-cleavage to sulphur should give the more stable ion. Part of the [M − H] fragment originates from the pyridyl 6-methyl group as seen in the deuterio analogue (Ia).

The hydroiodide salts of I and II have the base peak in the spectrum at *m/e* 155. This peak is mainly due to the *N*-methyl thione (XXIII) formed by preferential pyrolytic attack by the iodide ion on the *S*-alkyl carbon yielding also the corresponding alkyl halide. Thus the intensity of the ethyl iodide signal (*m/e* 156) in the spectrum of I is 80 % of the base peak while that for methyl iodide (*m/e* 142), arisen by *N*-demethylation, is only 7 − 8 %. The molecular ion at *m/e* 169 is very weak. Preferential dealkylation agrees with the low (5 %) intensity of the HI (*m/e* 128) signal and the low intensity (2 %) of the signal (*m/e* 183) corresponding to the molecular weight of the betaine. In the hydroiodide, hydrobromide, and hydrochloride salts of the bicyclic betaine (III), however, no nucleophilic substitution by the anion took place. Instead the phenolic hydrogen was exclusively abstracted and the betaine and the acid were evaporated separately.

For the bicyclic zwitterions the question also arises how these are volatilized. Thus the base peak (*m/e* 167) in the spectrum (Fig. 3) of 5-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide (III) corresponds to the molecular weight. The stability of this ion is further demonstrated by its appearance as a doubly charged ion at *m/e* 83.5. Several ways are open for the betaine (III) to become covalent prior to evaporation (Scheme B) similar to those discussed for I.


Rel. int.
Fig. 1
100
60
20
27
36
42
53
67
82
94
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123
126
138
150
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166
183
30
50
70
90
110
130
150
170
190
m/e

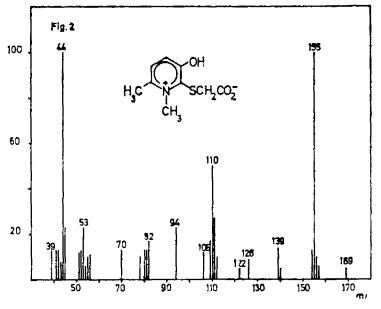
Fig. 2
100
60
20
44
53
70
92
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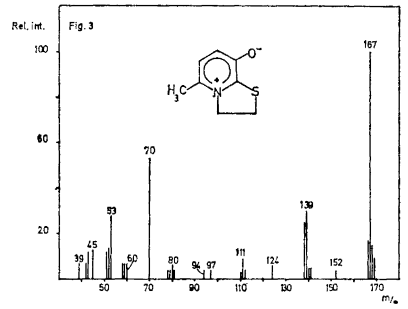
105
110
122
126
138
155
169
50
70
90
110
130
150
170
m/e


Rel. int.
Fig. 3
100
60
20
39
45
53
60
70
80
94
97
111
124
139
152
167
50
70
90
110
130
150
170
m/e

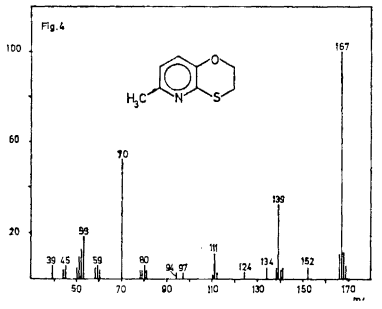
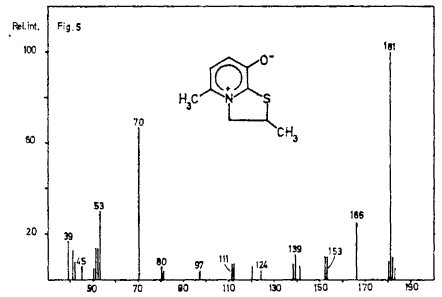


Fig. 4
100
60
20
39
45
56
59
70
80
94
97
111
124
134
139
152
167
50
70
90
110
130
150
170
m/e


Rel. int.
Fig. 5
100
60
20
39
45
53
70
80
97
111
124
139
153
166
181
50
70
90
110
130
150
170
190

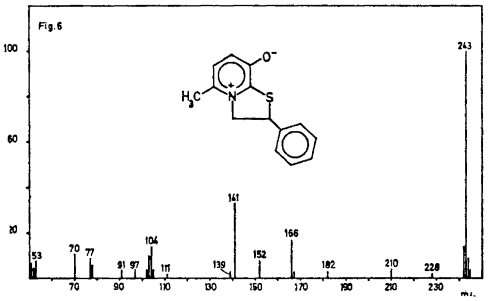
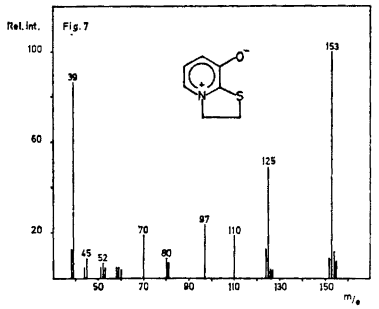


Fig. 6
100
60
20
53
70
77
91
97
104
111
139
141
152
166
182
210
228
243
70
90
110
130
150
170
190
210
230
m/e


Rel. int.
Fig. 7
100
60
20
39
45
52
70
80
97
110
125
153
50
70
90
110
130
150
m/e

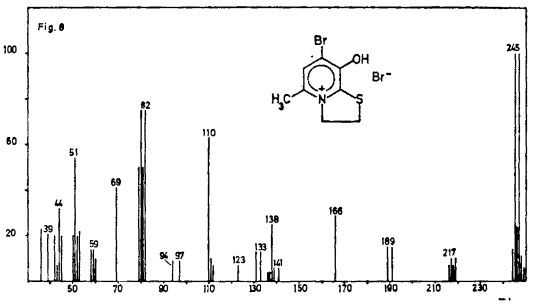
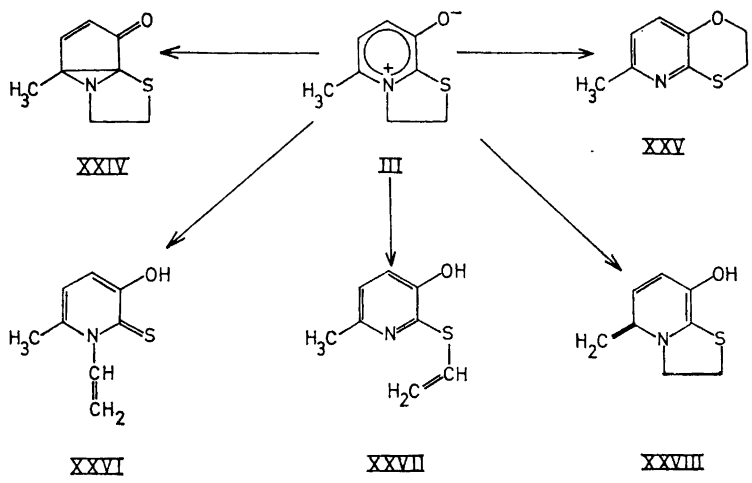


Fig. 8
100
60
20
39
44
51
59
69
82
94
97
110
123
133
138
141
166
189
217
245
50
70
90
110
130
150
170
190
210
230
m/e



Scheme B.

Pyrolytic formation of structures XXVI – XXVIII would be evident from mixed deuterium studies since these molecules must be formed by intermolecular prototropic shifts. No hydrogen-deuterium exchange should occur in the formation of XXIV and XXV. Experimentally a homogeneous mixture of III and its 5-trideuteriomethyl analogue (IIIa) gave the respective molecular ions at *m/e* 167 and *m/e* 170 with little variation in the intensities of the relatively weak *m/e* 168 and *m/e* 169 peaks. The contribution of XXVIII to the molecules in the gaseous phase is therefore very small. Any involvement of the 5-methyl group in the evaporation process would also seem excluded since the 5-desmethyl analogue (VI) behaves in the same way. In a similar experiment with the 3-dideuterio analogue (IIIb) any significant contribution from XXVI could be excluded. This is further supported by the behaviour of the acid analogue (VIII). The latter is evaporated, as shown below, by decarboxylation and opening of the thiazolo ring. A significant difference in the spectrum (Fig. 9) is the much decreased intensity of the [M – 28] peak which arises mainly through C_2H_4 expulsion. High resolution of this peak in the spectrum of III shows that the peak is due to [M – CO] and [M – C_2H_4] in the ratio 1:1. Finally on indirect insertion of III into the instrument, when the temperature needed to give a sufficient vapour pressure is 310°, the spectrum obtained is largely that from the acid (VIII) which shows that these conditions lead to opening of the ring.

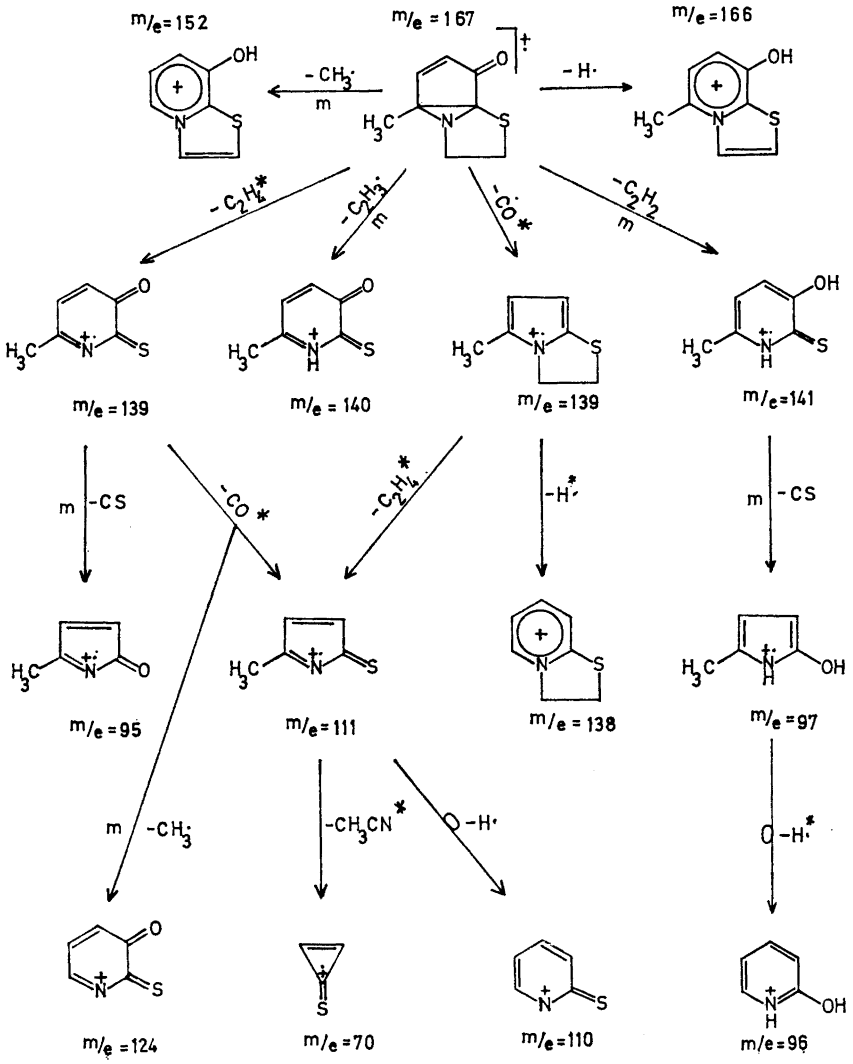
Structure XXVII would seem unlikely for the gaseous species from III, since other *S*-vinyl ethers show a different fragmentation pattern.[6] Further evidence against XXVI – XXVIII is the failure to increase the [M + 1] peak through rapid phenolic proton exchange on saturating the instrument with deuterium oxide.

The presence of XXV, formed in a multistep process, would seem unlikely from the fragmentation pattern. Thus the initial fragment is formed by loss

of 28 mass units, the peak being due to $[M-CO]$ and $[M-C_2H_4]$ in the ratio 1:1. It is difficult, however, to see why initial CO expulsion should be a major fragmentation from XXV. The latter compound was therefore synthesized [7] and found by preliminary examination to give a spectrum (Fig. 4) very much the same as III. However, the $[M-C_2H_4]/[M-CO]$ ratio was now found to be 4:1. Another significant difference in the spectrum is the near absence of the $[M-CHO]$ fragment (*m/e* 138) which is marked in the case of III.

From the above data is concluded that the betaine (III) is evaporated structurally unchanged. The valence isomeric structure (XXIV) is used to describe the observed volatility.

The major fragmentations are given in Scheme 2.



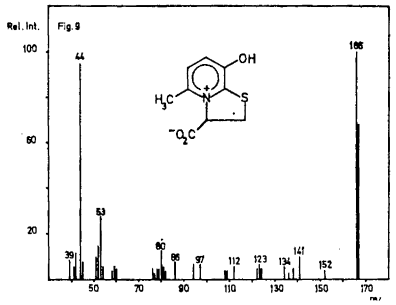
Scheme 2.

The molecular ion at *m/e* 167 is the base peak. Expulsion of the 5-methyl group results in a 5 % intensity fragment (*m/e* 152). Hydrogen expulsion gives a 15 – 20 % intensity peak. The hydrogen does not come from the methyl group since the 5-trideuterio-methyl derivative (IIIa) does not give any [M – 2] peak. The 3-dideuterio derivative (IIIb) gives signals both at [M – 1] and [M – 2] and therefore the hydrogen radical is expelled from either of the thiazolo carbons. In the 2-methyl derivative (IV) the [M – CH_3] peak is much increased as compared to III and is largely due to methyl radical expulsion from the thiazolo ring (Fig. 5). The [M – 1] peak in this compound has reduced intensity. In the 7-deuterio analogue (IIIc) all the fragments above 50 mass units are found at one mass unit higher than for III. Thus the *m/e* 70 fragment from III is found exclusively at *m/e* 71 in the spectrum of IIIc. Therefore this fragment arises from carbons 6, 7, and 9, and the hydrogens on carbon 6 and 7. The *m/e* 70 peak is strong also in the spectra of the 2-methyl (IV) (Fig. 5) and the 5-desmethyl (VI) (Fig. 7) derivatives. In the case of III the *m/e* 70 fragment is formed from the molecular ion by C_2H_4 (*m/e* 139) and CO (*m/e* 111) expulsions in either order followed by loss of CH_3CN. In the 5-desmethyl derivatives (VI) (Fig. 7) these fragments are 14 mass units lower and the *m/e* 70 fragment arises by HCN expulsion. In the 2-methyl derivative (IV) loss of propene from the molecular ion (*m/e* 181) leads to *m/e* 139 in the same way as loss of ethylene from III, but loss of CO now gives the ion at *m/e* 153. Both *m/e* 139 and *m/e* 153 lead to *m/e* 111 and further to *m/e* 70.

The 7-bromo (VII) derivative fragments very much like III and therefore appears to evaporate structurally unchanged (Fig. 8). Thus the molecular ion at *m/e* 245 can expel a hydrogen (*m/e* 244), or either CO or C_2H_4 to *m/e* 217 followed by C_2H_4 or CO respectively (*m/e* 189). [M – CO] also expels a hydrogen (*m/e* 216). Alternatively the bromine is expelled first (*m/e* 166) followed by both CO and C_2H_4 (*m/e* 138 and *m/e* 110). The latter ion loses acetonitrile to *m/e* 69 which corresponds to the *m/e* 70 peak in the spectrum of III.

The 2-phenyl derivative (V) is also volatile. The molecular ion (Fig. 6) is by far the strongest peak (*m/e* 243). The weak fragmentation follows the usual pattern with hydrogen (*m/e* 242) and phenyl radical (*m/e* 166) expulsions. The [M – 28] fragments are unusually weak while phenylacetylene elimination from the thiazolo ring to give *m/e* 141 is highly favoured. The latter fragment is also formed from any ring opened product as discussed below.

The 3-carboxy derivative (VIII) readily suffers decarboxylation due to the activating effect of the quaternary nitrogen. Thus in the mass spectrometer the observed molecular ion (*m/e* 167) is that of the decarboxylated material. But the spectrum of VIII is different from that of III which excludes a simple decarboxylation. The decarboxylation was therefore run on a preparative scale by heating the acid at 180° at 10^{-1} torr. The UV spectra with maxima at 390, 285 and 231 mμ (NaOH/EtOH) and at 373, 273 and 223 mμ (HCl/EtOH) suggest a *N*-vinylthione formulation (XXVI) for this product.[6,8] In the NMR spectrum in $CDCl_3$ there is one 1-proton quartet at 3.1 τ and two 1-proton quartets at 4.3 and 4.7 τ. The coupling constant between the protons at 3.1 and 4.3 τ is 8 cps and therefore these protons are *cis*. The *trans* coupling between the protons at 3.1 and 4.7 τ is 16 cps. The coupling between the terminal protons is 1.5 cps. In the deuterated acids (VIIIa and VIIIb) pyrolyzed as


Rel. Int.
Fig. 9
100
60
20
44
53
166
39
80
86
97
112
123
134
141
152
50
70
90
110
130
150
170
m/e

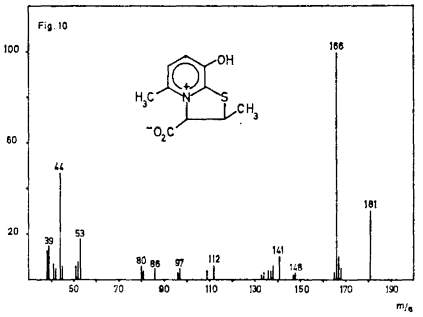
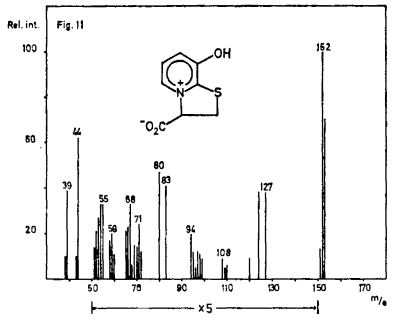


Fig. 10
100
60
20
44
53
166
181
39
80
86
97
112
141
148
50
70
90
110
130
150
170
190
m/e


Rel. int.
Fig. 11
100
60
20
44
39
55
68
71
58
80
83
94
108
127
152
50
70
90
110
130
150
170
m/e
x5

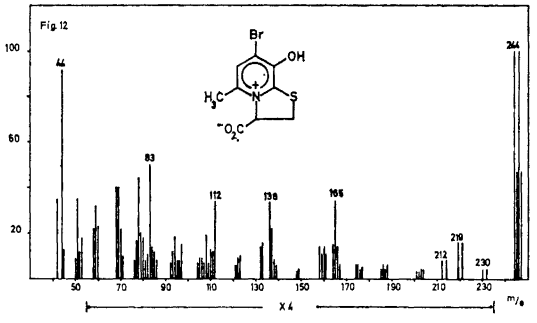
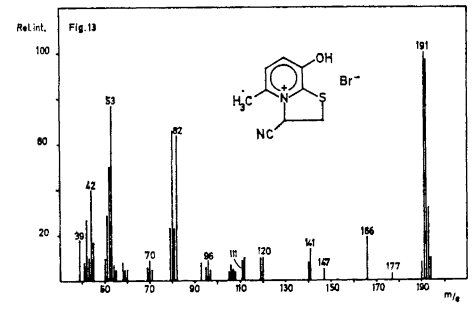


Fig. 12
100
60
20
44
83
112
138
166
212
219
230
244
50
70
90
110
130
150
170
190
210
230
m/e
x4


Rel. int.
Fig. 13
100
60
20
53
42
39
82
70
96
111
120
141
147
166
177
191
60
70
90
110
130
150
170
190
m/e

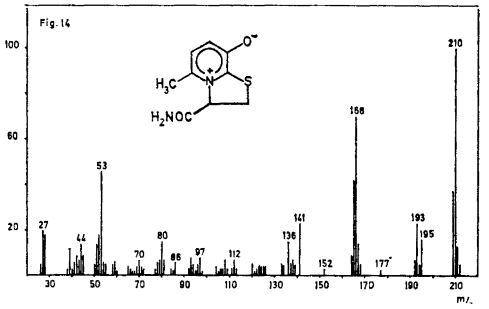


Fig. 14
100
60
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27
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80
86
97
112
136
141
152
166
177
193
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210
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50
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130
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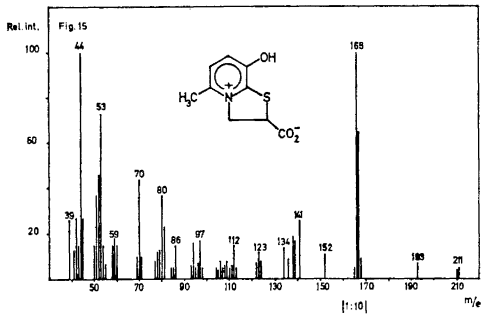
170
190
210
m/e


Rel. int.
Fig. 15
100
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44
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39
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86
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112
123
134
141
152
168
183
211
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70
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110
130
150
170
190
210
m/e

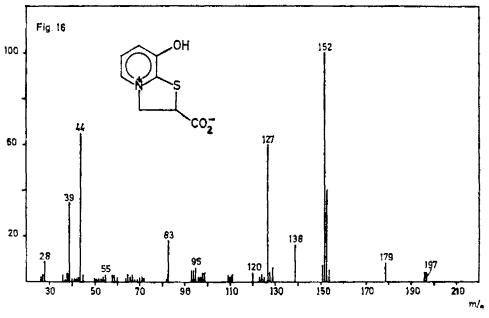
Fig. 16
100
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44
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28
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63
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120
127
138
152
179
197
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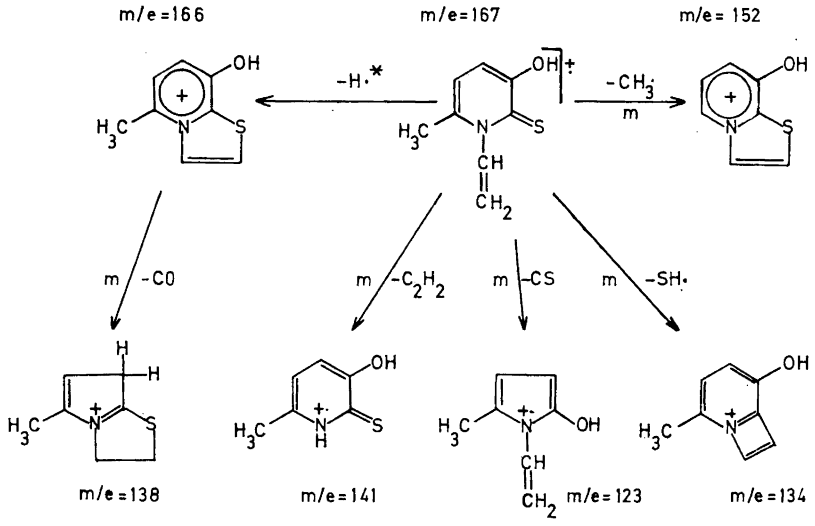
110
130
150
170
190
210
m/e

above, the quartet at 3.1 τ was absent with the two remaining protons at 4.3 and 4.7 τ with coupling constant $J = 1.5$ cps.

Since both protons in the deuterated analogue from the NMR evidence cited is on the same vinyl carbon the *S*-vinyl structure (XXVII) is excluded.

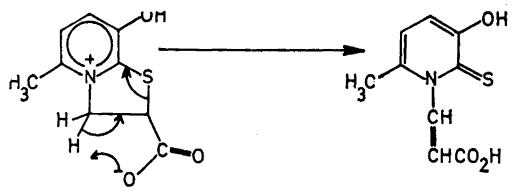
The base peak in the spectrum (Fig. 9) is at *m/e* 166 due to [M − H]. It will be recalled that the relative intensity of the [M − H] peak in the spectrum of III is about 15 % which shows that we have different species in the gas phase. The 3-deuterio derivative (VIIIa) retains its deuterium in this process as does the trideuterio methyl acid (VIIIb) and therefore the hydrogen is expelled from the original 2-position. This point is clearly demonstrated for the 2-methyl derivative (IX) where methyl radical expulsion from the molecular ion (*m/e* 181) leads to the by far strongest peak (*m/e* 166) in the spectrum (Fig. 10) while the [M − H] peak is very weak. Also the higher stability of the methyl radical compared to hydrogen is seen in the much increased [M − CH_3]/[M] compared to [M − H]/[M] ratios in IX and VIII, respectively (Figs. 9 and 10). The stability of the ion formed from the molecular ion by initial radical expulsion is such that secondary fragmentations are of little importance. This is best explained by the formation of an aromatic structure such as a thiazolo-pyridine.



Scheme 3.

The 5-desmethyl derivative (X) gives the same type of spectrum (Fig. 11). A bromine in the pyridine ring (XI) does not affect the initial fragmentation (Fig. 12). The base peak (*m/e* 244) is due to [M − H]. The bromine can be expelled initially to *m/e* 166 which loses H (*m/e* 165) and fragments further in the established way. Alternatively the bromine is retained and the molecular ion expels the usual groups.

From the fragmentation pattern it now should be possible to distinguish between those compounds which evaporate without ring opening, illustrated by compound III, and those which suffer ring opening, illustrated by compound VIII. The [M−CO] fragment characteristic for III is practically absent in VIII. Noticeable is also the much reduced intensity of the *m/e* 70 peak. Removal of the thiazolo ring to the thione (*m/e* 141) by acetylenic expulsion is much more important for VIII. The most important and characteristic fragmentation of VIII, however, is the initial expulsion of a radical in the 2-position. The other compounds are classified on the bases of these differences. Thus the isomeric 2-carboxylic acid (XIV) and the 5-desmethyl derivative (XV) appear to evaporate largely without decarboxylation (Figs. 15 and 16).

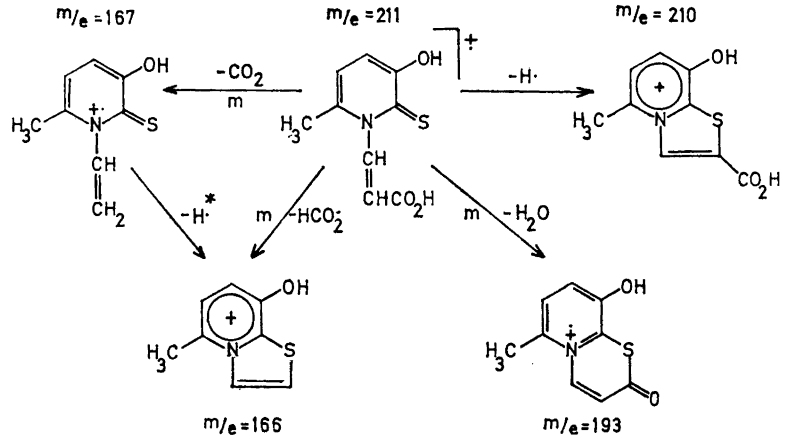


XIV XXIX

Scheme C.

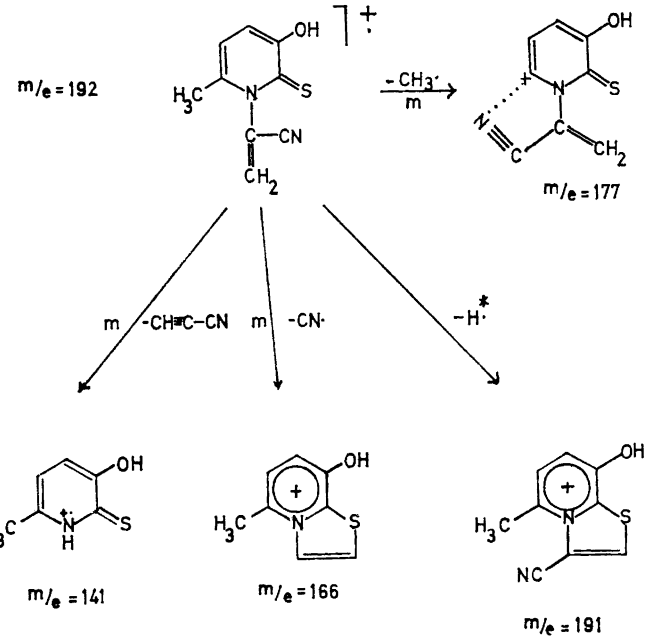
The base peak for the acid is at *m/e* 166 [M−CO_2H] with the [M−CO_2] peak somewhat less intense. The intensity of the molecular ion (*m/e* 211) in the ordinary spectrum is only about 1−2 % but is increased to 35 % in the 16 eV spectrum. The intensity of the [M−H_2O] peak (*m/e* 193) is also much increased at 16 eV. Since the major pathway seems to go through the *m/e* 166 fragment the weak secondary fragmentations are very much the same as for the 3-carboxy derivative (VIII). The relative intensity of the [M−CO_2H] fragment for the 5-desmethyl derivative (XV) is considerably higher and the *m/e* 70 peak is absent, which suggests complete ring opening before evaporation. Among the less intense secondary fragments of VIII is the thione at *m/e* 141 which is nearly absent in the spectrum of III. In the 5-desmethyl derivative (XV) this corresponds to the relative intense fragment at *m/e* 127. We therefore conclude that XIV is largely ring opened, presumably by an intramolecular Hofmann elimination, before evaporation. There are, however, fragments present in the spectrum which suggest that some of the material is evaporated structurally unchanged. Scheme 4 is suggested for the primary fragmentations.

The 3-nitrile (XII) and the amide (XIII) could be expected to evaporate in a valence isomeric cyclopentenone form as suggested for III. The fragmentation of the nitrile (XII), however, is different from that of III and similar to that of VIII (Fig. 13). Thus the base peak (*m/e* 191) is due to the [M−1] fragment. Another primary fragmentation is the expulsion of CN to give the *m/e* 166 peak. Both these species fragment further to the characteristic *m/e* 141 fragment. The species *m/e* 139, 111, and 70, which would be expected important for a valence isomeric structure, are very weak. This fragmentation



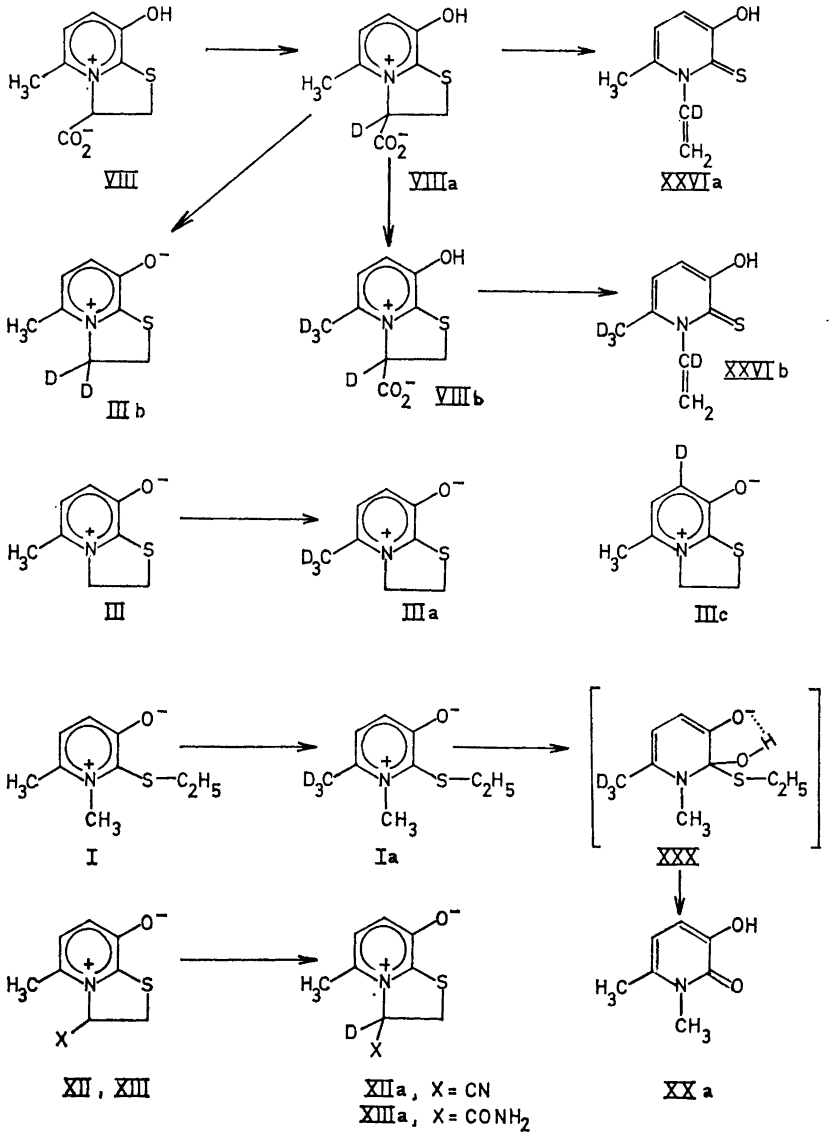
Scheme 4.

pattern leads us to conclude that the nitrile is ring opened prior to evaporation. That this compound should ring open is readily understood since the proton on the 3-carbon is very acidic due to the quaternary nitrogen and the electronegative nitrile group. Ring opening is also suggested by the observation that the 3-deuterated analogue in the instrument partly exchanged the deuterium with hydrogen but this argument is only valid if one can assume the phenolic but not the methine deuterium to be exchangeable with the hydrogen in the water vapour in the instrument.



Scheme 5.

The spectrum of the amide (XIII) is more complex. The methine proton in this compound will be less acidic than in the nitrile (XII) and therefore a carbanion intermediate is less stabilized which again decreases the ring opening tendency. The spectrum obtained is very sensitive to recording conditions and is best interpreted as arising from the ring-opened product admixed with the parent pyridinium compound (Fig. 14).



Scheme D.

A number of deuterated compounds were prepared for this study. It has previously been reported that the methine proton on the highly activated 3-position in the acid VIII is rapidly exchanged with deuterium in weak NaOD.[9] Preparatively this was done in N NaOD in the cold (VIIIa). The rate and degree of deuterium exchange was conveniently followed by NMR. Deuteration in the pyridyl methyl group (VIIIb), in addition to the 3-position, was achieved by heating in 2 N NaOD. Similarly, heating the descarboxy derivative (III) in N NaOH gave the trideuteriomethyl analogue (IIIa). NMR showed practically no exchange of protons in the 3-position under these conditions. When the simple pyridinium derivative (I), however, was treated as above, sulphur displacement took place with formation of *N*-methyl-2-pyridone (XX). The product was readily identified by NMR and MS. The sulphur displacement probably involves pseudobase formation followed by thiol expulsion as indicated (XXX). Selective deuteration in the pyridyl 6-methyl group was achieved by allowing I to stand in 0.5 N NaOD in the cold for a few days.

Previously we have reported that moistened DMSO is a good decarboxylating agent for the acid (III).[10] Heating the 3-deuterio acid (VIIIa) in DMSO moistened with deuterium oxide led to the desired 3-dideuterio derivative (IIIb). Decarboxylation of the acid (VIII) under these conditions gave an isotopically impure product. Pyrolysis of the deuterated acids (VIIIa and VIIIb) furnished *N*-vinyl derivatives deuterated on the α-carbon (XXVIa and XXVIb). The methine proton in the amide (XIII) was exchanged rapidly in cold dilute alkali. But the pyridyl methyl group in this molecule is highly activated and is readily deuterated. Selective deuteration in the 3-position takes place in weakly acidic deuterium oxide. The nitrile, which in weakly alkaline solution is rapidly hydrolyzed to the amide, is also best deuterated in acid solution. Deuteration in the pyridyl nucleus (IIIc) was simply achieved by reduction of the corresponding bromo derivative (VII) with zinc in deuterioacetic acid.

EXPERIMENTAL

The mass spectra were recorded on an AEI 902 mass spectrometer. The compounds were introduced directly into the ionization chamber. The source temperature was 230°, the electron energy 70 eV and the ionizing current 100 A.

The syntheses of compounds I–II;[8] III–VI, VIII–X, XII–XIII; [11,12] VII and XI;[13] XIV and XV;[11] have recently been described.

2-Ethio-1-methyl-6-trideuteriomethylpyridinium-3-oxide (Ia). 1,6-Dimethyl-2-ethiopyridinium-3-oxide (0.55 g, 0.003 mol) was dissolved in 0.8 N NaOD (3.5 ml) and the solution left in the cold. NMR showed that the 6-methyl group was completely deuterated after 1 week. The neutralized solution was passed through a column of Amberlite IR 120 in the acid form and the betaine eluted with 0.1 N ammonia. Evaporation left the deuterated material; yield 0.50 g (83 %).

3-Hydroxy-1-methyl-6-trideuteriomethylpyrid-2-one (XXa). 1,6-Dimethyl-2-ethiopyridinium-3-oxide (0.55 g, 0.003 mol) in 2 N NaOD (10 ml) was heated at 100° for 3 h. The cold solution was neutralized, extracted with chloroform and the chloroform extracts washed and dried before evaporation. The solid residue, after recrystallization from dilute ethanol, had m.p. 199–200°; yield 0.35 g (84 %).

The same reaction in NaOH gave the non-deuterated material, *viz.*, *1,6-dimethyl-3-hydroxypyrid-2-one.* (Found: C 60.05; H 6.34; N 9.82. Calc. for $C_7H_9NO_2$: C 60.42; H 6.45; N 10.01.)

3-Deuterio-8-hydroxy-5-methyldihydrothiazolo[3,2-a]pyridinium-3-carboxylate (VIIIa). A solution of the parent compound (VIII; 0.50 g, 0.0024 mol) in N NaOD (5 ml) was left

in the cold for 1 h. NMR at this time showed complete exchange at the C-3 carbon. The C-2 hydrogens appeared as a quartet centered at 6.1 τ (J_{gem} 12 cps). No measurable deuterium exchange had occurred in the 5-methyl group (7.55 τ). The solution was neutralized, passed over a column of Amberlite IR 120 in the acid form, the title compound eluted with 0.1 N ammonia and obtained as a solid by evaporation; yield 0.40 g (80 %). NMR showed no loss of deuterium after the ammonia eluation.

3-Deuterio-8-hydroxy-5-trideuteriomethyldihydrothiazolo[3,2-a]pyridinium-3-carboxylate (VIIIb). The parent compound (VIII) was deuterated by heating in 2 N NaOD at 85° for 2 h. The progress of the deuteration was followed by NMR. The methylene protons in the 2-position were hardly affected under these conditions. The title compound was isolated in 80 % yield by using the above work up procedure.

3-Cyano-3-deuterio-6-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide (XIIa) and *3-carbamoyl-3-deuterio-6-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide (XIIIa)* were prepared by keeping solutions of the respective parent compound hydrobromides (100 mg) in D_2O (1 ml), pH about 3, at 80° for 12 h. Neutralization of the cold solutions precipitated the deuterio derivatives.

5-Trideuteriomethyldihydrothiazolo[3,2-a]pyridinium-8-oxide (IIIa). The parent compound (III; 0.85 g, 0.005 mol) in N NaOD (10 ml) was heated at 90°. NMR showed that deuteration of the methyl group was complete after 1 h while the 3-position was hardly affected. The title compound slowly crystallized out from the neutralized solution yield 0.65 g (76 %). NMR in TFA: Triplets centered at 6.2 τ ($S-CH_2$) and 4.9 τ ($=\overset{+}{N}-CH_2$).

3-Dideuterio-6-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide (IIIb). 3-Deuterio-8-hydroxy-5-methyldihydrothiazolo[3,2-a]pyridinium-3-carboxylate (50 mg, 2.4×10^{-4} mol) dissolved in DMSO-d_6 (1 ml) to which had been added 3 – 4 drops of D_2O was heated at 120° for 3 h when the CO_2 evolution had ceased. The solution was then evaporated and the title compound made to crystallize by the addition of a little water. NMR in TFA: Singlet at 6.2 τ ($S-CH_2$).

7-Deuterio-5-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide (IIIc). Zinc powder (0.15 g, 2.3×10^{-3} mol) was added to a solution of 7-bromo-5-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide hydrobromide [0.20 g, 6×10^{-4} mol) in deuterioacetic acid (10 ml). After stirring for 3 h in the cold chromatography showed the reaction to be finished. The reaction mixture was filtered, the filtrate evaporated, the residue dissolved in water, the solution passed through a column of Amberlite IR 120 in the acid form and the title compound eluted with N ammonia and isolated by evaporation; yield 0.08 g (48 %).

3-Hydroxy-6-methyl-1-vinylpyrid-2-thione (XXVI). 8-Hydroxy-5-methyldihydrothiazolo[3,2-a]pyridinium-3-carboxylate (1.05 g, 0.005 mol) was heated at 180° and 10^{-1} torr using a "coldfinger". The yellow sublimate, after recrystallization from dilute ethanol, had m.p. 115°; yield 0.60 g (72 %). (Found: C 57.46; H 5.36; N 8.24. Calc. for C_8H_9NOS: C 57.46; H 5.42; N 8.38.) UV maxima in 0.1 N HCl in EtOH: 373 mμ (log ε 4.05), 273 mμ (2.85), 223 mμ (3.93). In 0.1 N NaOH in EtOH: 390 mμ (log ε 3.95), 285 mμ (3.85), 231 mμ (3.80).

1-(1-Deuteriovinyl)-3-hydroxy-6-methylpyrid-2-thione (XXVIa) and *1-(1-deuteriovinyl)-3-hydroxy-6-trideuteriomethylpyrid-2-thione (XXVIb)* were prepared as the parent compound (XXVI) by pyrolysis as above from the respective deuterated acids (VIIIa and VIIIb).

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