ACTA CHEMICA SCANDINAVICA 25 (1971) 2954–2964

Mass Spectrometry of Onium Compounds

Part VII.[1] Thiazolo[3,2-a]pyridinium-8-oxides

KJELL RAGNAR REISTAD and KJELL UNDHEIM

Department of Chemistry, University of Oslo, Oslo 3, Norway

Evidence is presented that thiazolo[3,2-a]pyridinium-8-oxides are evaporated in the mass spectrometer without any prior chemical rearrangement.

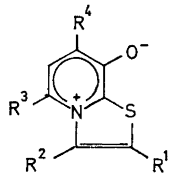
The molecular ion is highly stable and fragments by primary CO expulsion. In 5-methyl derivatives the initial fragmentations are M−H−CO or M−CO−H expulsions. Secondary fragmentations are weak.

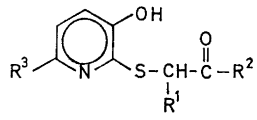
The fragmentation of corresponding α-formyl or keto pyridyl sulphides occurs primarily in the *S*-sidechain through McLafferty rearrangements or γ-cleavages.

N-Quaternary salts are not volatile due to strong intermolecular electrostatic forces, but must undergo chemical[2,3] or electronic rearrangement with charge neutralisation prior to evaporation. We now report on the behaviour of thiazolo[3,2-a]pyridinium betaines in the mass spectrometer.

The composition of the peaks discussed has been determined by high resolution. Metastable transitions, if not present in the ordinary spectrum, have been measured by the special defocusing technique. [7] The latter transitions are marked by "m". The compounds included in this work are shown on p. 2955.

Simple *N*-alkylpyridinium-3-oxides give signals on mass spectrometry corresponding to the molecular weights.[4] Our interpretation is that a non-charged valence isomer may be formed prior to evaporation. A such electronic rearrangement now appears to be supported by the behaviour of the bicyclic thiazolo[3,2-a]pyridinium-8-oxides in the mass spectrometer. On direct introduction into the ionization chamber of the instrument these substances give a peak for the molecular weight of the sample. This is the base peak in the spectrum, or has an intensity close to the base peak. Indirect insertion, however, leads to the formation of pyrolysis products. The difference in behaviour is due to the higher temperature needed in the indirect insertion technique to give a sample pressure of about 10^{-2} torr, as compared to about 10^{-6} torr in the ionization chamber. The experimental findings may seem best explained by thermally induced electronic rearrangements of the bicyclic

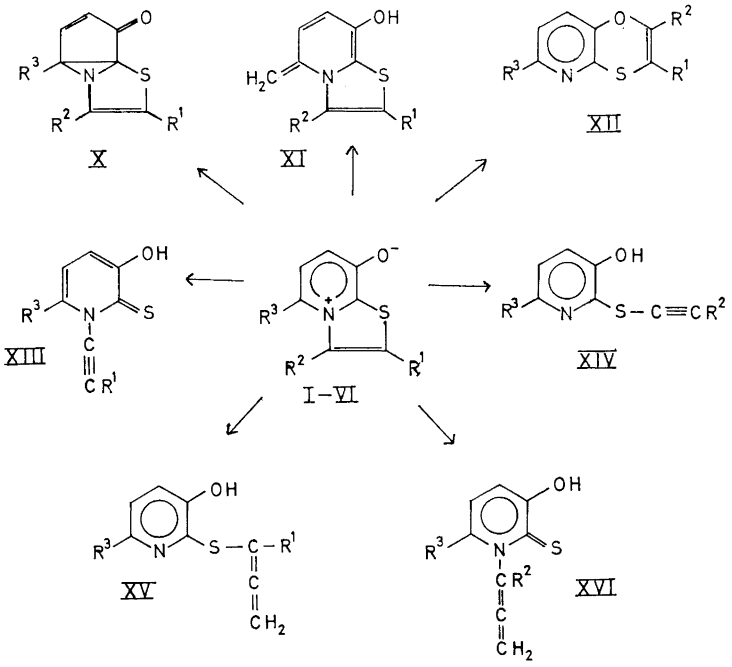




I $R^1=H$, $R^2=CH_3$, $R^3=R^4=H$
Ia $R^1=D$, $R^2=CH_3$, $R^3=R^4=H$
Ib $R^1=H$, $R^2=CH_3$, $R^3=R^4=D$
II $R^1=R^2=H$, $R^3=CH_3$, $R^4=H$
IIa $R^1=R^2=D$, $R^3=CH_3$, $R^4=H$
III $R^1=CH_3$, $R^2=H$, $R^3=CH_3$, $R^4=H$
IIIa $R^1=CH_3$, $R^2=D$, $R^3=CH_3$, $R^4=H$
IIIb $R^1=CH_3$, $R^2=H$, $R^3=CH_3$, $R^4=D$
IIIc $R^1=CD_3$, $R^2=D$, $R^3=CD_3$, $R^4=H$
IV $R^1=H$, $R^2=R^3=CH_3$, $R^4=H$
IVa $R^1=D$, $R^2=R^3=CH_3$, $R^4=H$
IVb $R^1=H$, $R^2=R^3=CH_3$, $R^4=D$
V $R^1=H$, $R^2=R^3=CH_3$, $R^4=Br$
VI $R^1=H$, $R^2=CH_3$, $R^3=R^4=Br$

VII $R^1=H$, $R^2=CH_3$, $R^3=H$
VIII $R^1=H$, $R^2=R^3=CH_3$
IX $R^1=CH_3$, $R^2=H$, $R^3=CH_3$

betaines to covalent cyclopentenones (X) before evaporation. The electron induced fragmentation also seems to support this postulate. Thus the most important diagnostic fragmentations are CO expulsion or hydrogen expulsion, followed by CO. The primary CO losses are in agreement with a ketonic structure (X).



The above tentative interpretations involving a covalent isomer do not exclude the possibility that the gaseous species, in the absence of a chemical rearrangement, have a betaine like structure. In the latter case the charges in the betaine are largely compensated internally through increased delocalisation of the negative charge of the oxy-group into the azinium nucleus made possible through thermal excitation. No clear distinction between these possibilities can be made in this work. For illustrative purposes, however, the volatile species are drawn in the cyclopentenone form.

Possible chemical rearrangements are shown on p. 2955.

The bicyclic 6-membered ring structure (XII) should not exhibit CO expulsion as a primary strong fragment and is therefore discarded. Its formation also seems unlikely since it would involve intermolecular ring opening at the nitrogen by some nucleophile and recyclisation over the oxygen. Allene formation (XV and XVI) by intermolecular proton abstraction from the 2- and 3-methyl derivatives (I, III – VI) (Fig. 3) would seem possible, but the fragmentation of II (Fig. 2) which lacks a 2- or 3-methyl group, is not different and this pathway therefore is unlikely. Proton abstraction from the 5-methyl group would be possible (XI), but the 5-desmethyl derivative (I) (Fig. 1) gives

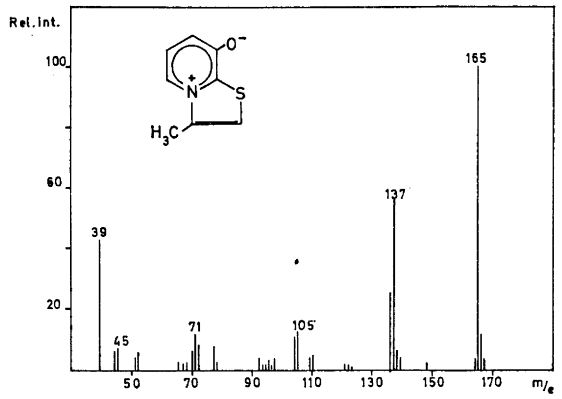


Fig. 1.

the same mass spectrum which therefore excludes this possibility. If opening of the thiazolo ring were to occur the acetylene formed would depend on whether the substituent is on the 2-carbon (XIII) or the 3-carbon (XIV). That no difference is seen in the fragmentation pattern can of course be due to primary recyclisation from either of the structures on electron impact. This possibility could be excluded by deuteration experiments, and this also applies to the other decyclisation reactions and to the prototropic shift which leads to XI. These processes all take place by intermolecular proton transfer to the phenolate oxygen. Therefore, a homogeneous mixture of the 2,5-dimethyl derivative (III) and its heptadeuterio analogue (IIIc) was studied (Fig. 3, Scheme 1). The spectrum showed the molecular ion of the deuterio derivative at *m/e* 186, with a much weaker signal (10 %) at *m/e* 185, while the non-

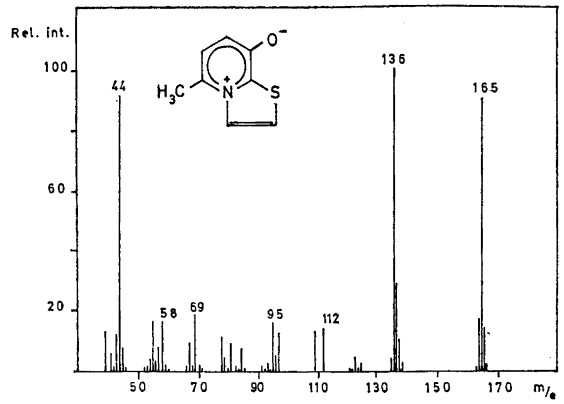


Fig. 2.

deuterated compound (III) had its molecular ion at *m/e* 179,with apparently no deuterium uptake. For ring opening reactions or the formation of XI the peaks at *m/e* 179 and *m/e* 180 should both be present, but with the latter of somewhat lower intensity due to hydrogen deuterium exchange in the instrument. The loss of deuterium in IIIc was investigated using the 3-deuterio derivative (IIIa). It was found that at 270° it gradually exchanged deuterium with hydrogen, but at 250° no such exchange took place. The thermally induced deuterium exchange at this high temperature is not surprising in view of the ease with which the thiazole protons are exchanged in the presence of a

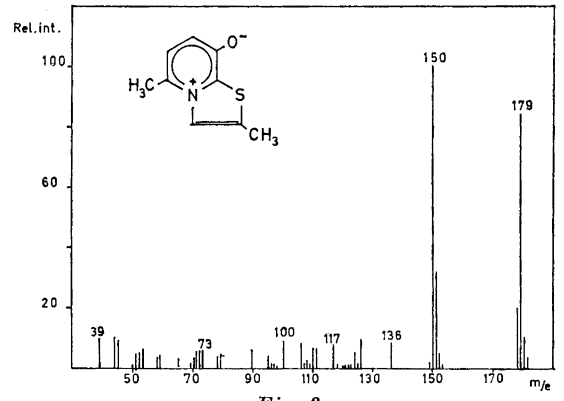
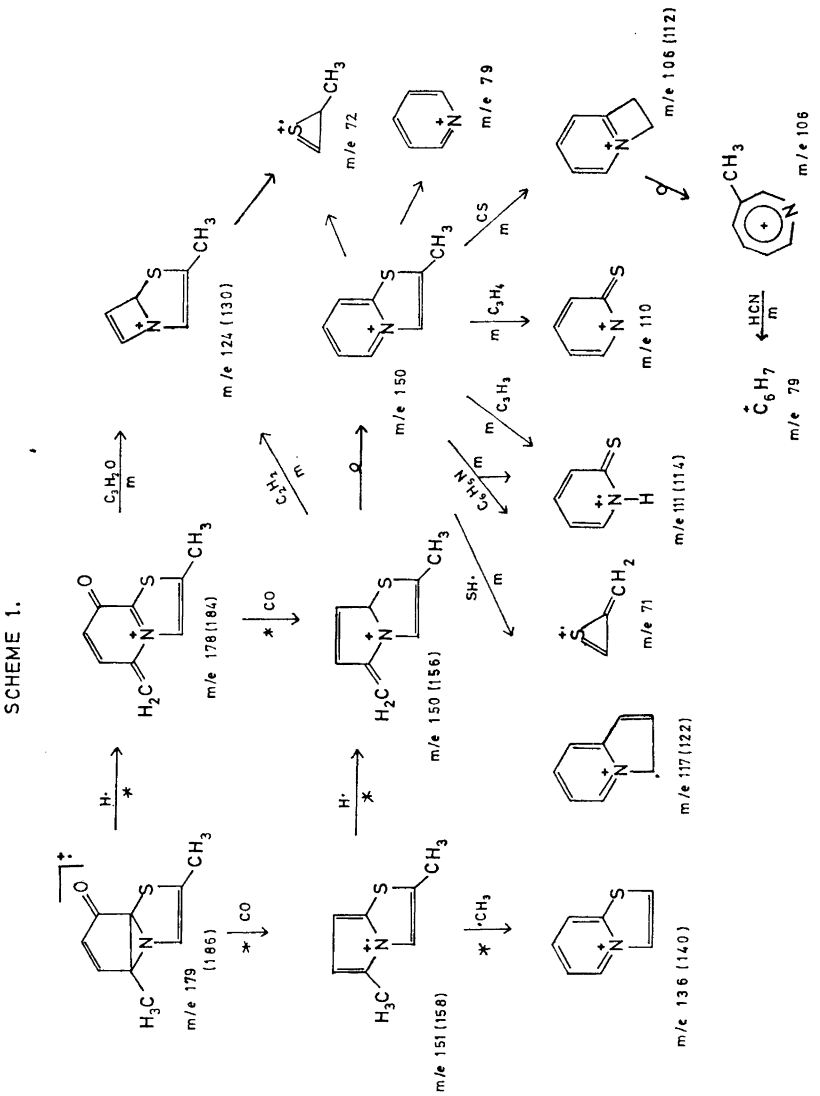


Fig. 3.

base.[8] The base in this case is the phenolate oxygen. The instrument was then saturated with deuterium oxide and the spectra of III run at 230°, at 240°, and rapidly at 270°. No deuterium was incorporated. Corresponding experiments with IV and IVa gave the same answers. We therefore conclude that the thiazolo-pyridinium betaines largely evaporate without chemical rearrangements.

SCHEME 1.



The spectra are characterized by a strong molecular ion and the fragments (M − CO) and (M − CHO), and in the 5-methyl derivatives also (M − H). There is no metastable peak for the direct expulsion of CHO, so this fragment is formed from either (M − H) or from (M − CO) by CO or by hydrogen expulsion, respectively. There are metastables for these transitions in the ordinary spectrum. Further fragmentations are of little importance, and the low energy spectra show practically only the (M − 28) and (M − 29) fragments.

The more detailed fragmentation pattern for the 5-methyl derivatives will be discussed for the 2,5-dimethyl derivative (III) (Scheme 1, Fig. 3), whose spectrum is practically the same as that for the 3,5-dimethyl analogue (IV) (Fig. 4). The (M − H) species arise by hydrogen expulsion from the 5-methyl

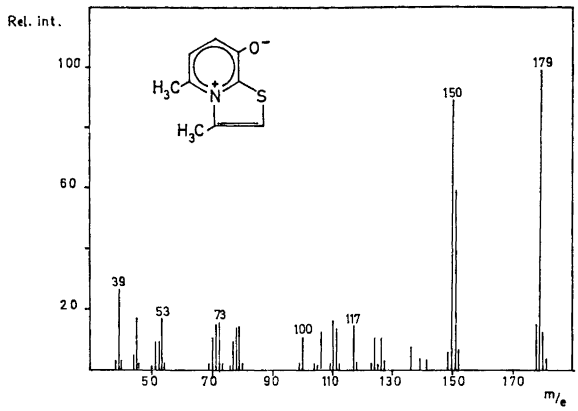


Fig. 4.

group as seen by loss of 2 mass units in the 5-trideuteriomethyl analogue (IIIc), the retention of deuterium in IIa, IIIa, and IVa, as well as the absence of the (M − 1) fragment in the 3-methyl-5-desmethyl analogue (I) (Fig. 1). The preferred hydrogen expulsion from the (M − CO) fragment is also from the 5-methyl group. This follows from the mass of this fragment from the various deuterio analogues and the relative low intensity of the (M − CHO) fragment compared to the (M − CO) fragment in the 3-methyl-5-desmethyl analogue (I). In the 5-methyl derivatives the (M − CHO) is the stronger peak which shows that hydrogen expulsion is a favoured process compared to methyl radical expulsion which gives a very weak signal at *m/e* 136. The (M − CHO) species can fragment further by loss of SH to *m/e* 117. In the deuterio analogue (IIIc), this fragment is at *m/e* 122, so the SH proton in this case probably comes from the 2-methyl group. The 3-deuterio analogue (IIIa) has this fragment at *m/e* 118. The (M − CHO) ion also expels CS (*m/e* 106), followed by loss of HCN (*m/e* 79). The carbons in the thiazolo ring are lost either as methylacetylene (*m/e* 110) or as a methylacetylene radical (*m/e* 111). The peak at *m/e* 71 is due to pyridine elimination from (M − CHO). Another pathway from the latter is C_2H_2 expulsion (*m/e* 124). The *m/e* 124 species are also formed by expulsion of C_3H_2O from (M − H). In the deuterated derivative (IIIc) this fragment is at *m/e* 130 so that the two hydrogen lost are the pyridyl hydrogens. This fragment, as well as the (M − CHO) fragment, can give rise to *m/e* 72. The signals at *m/e* 77, 53, and 39 arise from benzene type fragments.

The initial fragmentation of the 5-methyl derivative (II), without 2- and 3-substituents, is the same (Fig. 2). The base peak is the (M − CHO) fragment at *m/e* 136. The relative intensities of the secondary fragments vary, however,

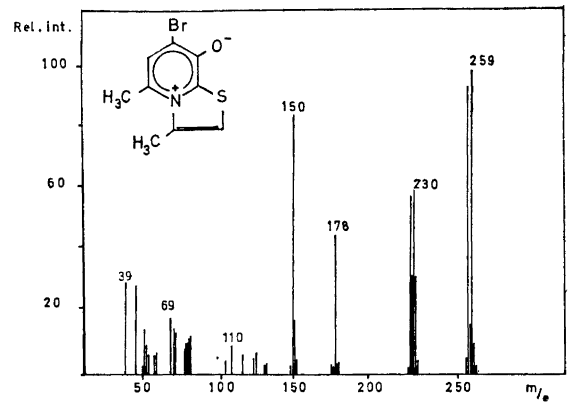


Fig. 5.

since the stabilities of the various species will be different with and without a methyl group. Like the parent compound (IV), the 7-bromo derivative (Fig. 5) has the molecular ion at *m/e* 257 as the base peak. The same initial fragments (M−H) and (M−CO) are found at *m/e* 256 and *m/e* 229. The latter again expels hydrogen (*m/e* 228). In competition with these processes, direct loss of bromine from the molecular ion occurs, to give *m/e* 178, and the latter then goes on to expel CO (*m/e* 150), followed by hydrogen (*m/e* 149). The latter fragments are also formed by Br expulsion from the (M−CO) and (M−CHO) ions.

The spectrum of the 5-desmethyl derivative (I) (Fig. 1) is simplified because of the absence of the (M−H) species. In this spectrum the molecular ion (*m/e* 165) is by far the most stable. It fragments by CO expulsion (*m/e* 137), but this species shows less tendency to expel a hydrogen radical (*m/e* 136) in agreement with the postulated hydrogen expulsion from a 5-methyl group with stabilization through rearrangement to a pyridinium structure which is not possible in this case. The 5,7-dibromo derivative (VI) Fig. 6)

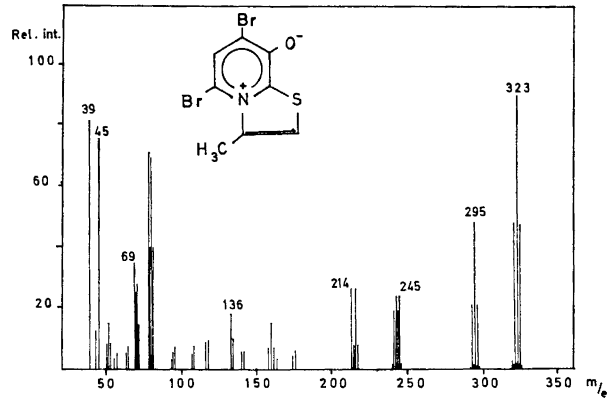
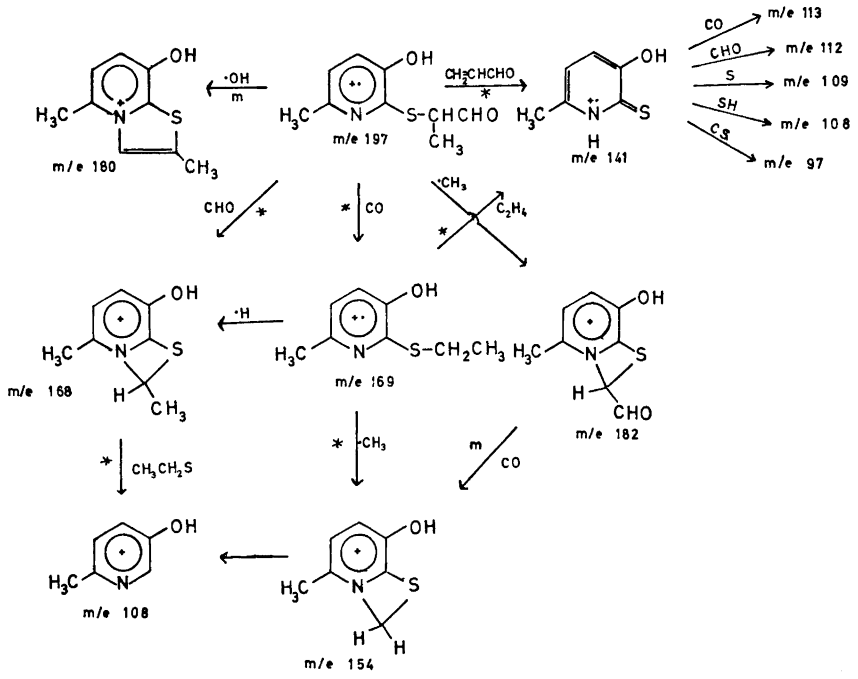


Fig. 6.

behaves in the same way. The base peak is the molecular ion at *m/e* 323. This either loses CO (*m/e* 295) or Br (*m/e* 244). The former loses Br while the latter loses CO to give *m/e* 214. The (M – Br – CO) species can either expel the last bromine (*m/e* 135) or retain the bromine, and as usual expel the 2,3-carbons of the thiazole as methylacetylene (*m/e* 174).

SCHEME 2.



The carbonyl derivatives (VII – IX) were included in this study to see if any cyclodehydration occurs in the mass spectrometer as found for corresponding carboxylic acids.[6] In this case, however, there is no (M – 18) peak so no thermal cyclodehydration occurs. The spectrum of the aldehyde (IX) (Fig. 8), however, has a weak fragment (M – OH) at *m/e* 180 which corresponds to electronically induced cyclisation to the thiazolo structure (Scheme 2). The base peak in this spectrum arises by a McLafferty rearrangement and expulsion of acrolein (*m/e* 141). Such processes are known to occur in 2- alkylpyridines with γ-hydrogens.[9] The intensity of the thione in this spectrum is such that the lower region of the spectrum is dominated by its fragments which arise by the following expulsions: SH (*m/e* 108), S (*m/e* 109), CS (*m/e* 97), CO (*m/e* 113), and CHO (*m/e* 112).[10] The *m/e* 169 fragment is due to (M – CO). The CO group comes from the formyl group since the corresponding fragment is absent in the spectra of the ketones (VII, VIII) and in 2-alkylthio-3-hy-

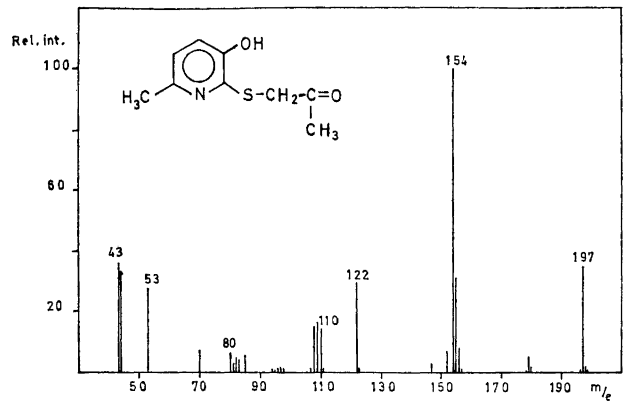


Fig. 7.

droxypyridines.[10] The (M − CO) species fragment further, either by a McLafferty rearrangement to *m/e* 141 with expulsion of ethylene or γ-cleavages to *m/e* 154 with methyl radical expulsion, or by hydrogen expulsion to *m/e* 168. The latter species are also formed directly from the molecular ion by

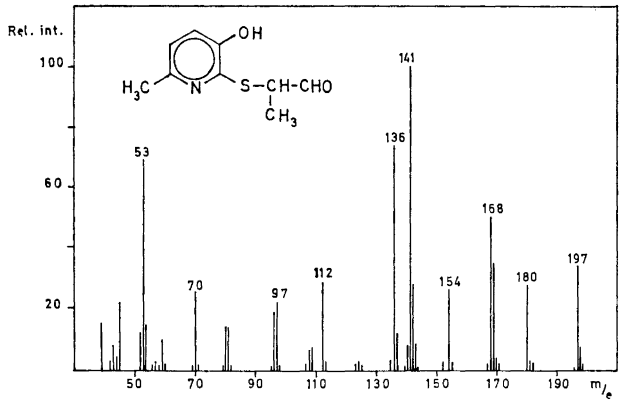


Fig. 8.

γ-cleavage of the formyl group. γ-Cleavage with methyl expulsion should give *m/e* 182. This peak is hardly noticeable in the spectrum, but these species are formed since there is a well defined metastable for CO elimination to *m/e* 154. The third possibility, *viz.*, hydrogen expulsion to *m/e* 196, is not seen. This is understandable in terms of the relative stabilities of the expelled hydrogen and methyl radicals, and by the destabilizing effect by the formyl group on the ion formed. The γ-cleavage, however, is important for formyl radical expulsion.

In the aldehyde McLafferty rearrangement will compete with γ-cleavage, but in the isomeric ketone (VIII) (Fig. 7) the McLafferty rearrangement is not possible and γ-cleavage will dominate. Thus expulsion of the acetyl group gives the base peak at m/e 154. No significant (M−H) peak due to γ-cleavage of hydrogen is seen, the main reason being the destabilizing effect of the car-

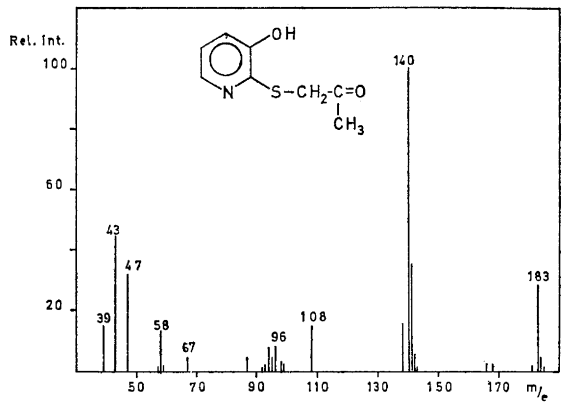


Fig. 9.

bonyl group on the positive ion formed. A competitive but less favourable fragmentation of the ketone is ketene expulsion to m/e 155. This ion fragments further as the corresponding *S*-methyl derivative where the dominating fragment is due to SH expulsion (m/e 122).

The pyridyl methyl group does not noticeably affect the primary fragmentation. Thus the 6-desmethyl derivative (VII) exhibits a very similar mass spectrum with the main fragments displaced 14 units towards lower mass range.

EXPERIMENTAL

The mass spectra were recorded on an AEI MS 902 double focusing mass spectrometer. The source temperature was kept at about 250°. All compounds were introduced directly into the source. The electron energy was 70 eV and ionizing current 100 μA.

The preparation of the compounds used is described elsewhere,[8] except for *3-deuterio-2,5-hexadeuteriodimethylthiazolo[3,2-a]pyridinium-8-oxides* (IIIc), which was prepared from the parent compound (III) by heating in N NaOD at 100° for 4 h. The compound was isolated as previously described for the other deuterio analogues.[8]

REFERENCES

1. Undheim, K. and Hvistendahl, G. *Org. Mass Spectrom.* **5** (1971) 325.
2. Undheim, K. and Hvistendahl, G. *Org. Mass Spectrom.* **3** (1970) 1423.
3. Hvistendahl, G., Undheim, K. and Bremer, J. *Org. Mass Spectrom.* **3** (1970) 1433.
4. Grønneberg, T. and Undheim, K. *Acta Chem. Scand.* **25** (1971) 2807.
5. Undheim, K., Thorstad, O. and Hvistendahl, G. *Org. Mass Spectrom.* **5** (1971) 73.

6. Undheim, K., Fjeldstad, P. E. and Tveita, P. O. *Acta Chem. Scand.* **25** (1971) 2943.
7. Jennings, K. R. *J. Chem. Phys.* **43** (1965) 4176.
8. Undheim, K. and Reistad, K. R. *Acta Chem. Scand.* **24** (1970) 2956.
9. Lawrence, R. and Waight, E. S. *J. Chem. Soc.* **B 1968** 1.
10. Undheim, K. and Hurum, T. *Acta Chem. Scand. In press.*

Received December 28, 1970.