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Mass Spectrometry of Onium Compounds

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

KJELL UNDHEIM, PER EINAR FJELDSTAD and PER OLAV TVEITA

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

Thiazolo[3,2-a]pyridinium-3-oxides in the mass spectrometer are readily volatile. The gaseous species are either the mesoion itself or its isomeric ketene. The most characteristic electron induced fragmentations are CO and CHO expulsions from the thiazolo moiety. The corresponding α-(2-pyridylthio)carboxylic acids are either evaporated intact, thermally cyclodehydrated or decarboxylated, depending on the influence of the substituents on the relative chemical stabilities and volatilities. The gaseous phase composition is also very much dependent on the conditions used for recording the spectra. The electron induced fragmentation patterns are discussed.

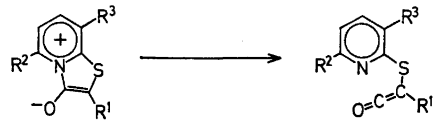
Pyridinium-3-oxides and thiazolo[3,2-a]pyridinium-8-oxides undergo valence isomerism or a partial internal charge neutralisation prior to evaporation in the mass spectrometer.[2,3] In thiazolo[3,2-a]pyridinium-3-oxides another electronic rearrangement becomes possible, *viz.* over the thiazolo oxygen with formation of a ketene. In agreement with this postulate, the thiazolo[3,2-a]pyridinium-3-oxides on mass spectrometry give a peak corresponding to the molecular weight of the substance. The molecular ion is also the base peak or has an intensity close to that of the base peak in the spectrum unless the molecule contains a substituent which is initially very easily eliminated. Indirect insertion of the substances also leads to spectra which are qualitatively the same as by direct insertion despite the higher temperature needed by the indirect technique to reach the required vapour pressure.

The observed molecular ion can arise from a valence isomeric ketene as discussed above, as well as from the betaine itself made volatile through partial internal charge compensation by thermal excitation. For the hydroxy pyridines (I, II, IV) a reactive ketene intermediate could cyclise over the pyridyl oxygen. No clear distinction between these possibilities can be made at present. The fragmentations, however, appear to follow the same pattern and the ketene formulation for the gaseous species is therefore used to illustrate the volatility. For the same reason the ketene formulation is used in the frag-

mentation schemes while the zwitterionic structure is reproduced on the spectra.

The thiazolo-pyridinium compounds were introduced either as betaines or as salts with strong acids. The salts in the instrument are dissociated, and the components evaporated separately to furnish the spectrum of the betaine with the superimposed spectrum of the acid.

The compositions of the peaks discussed have been determined by high resolution. The metastable transitions, where not present in the ordinary spectrum, have been measured by the special defocusing technique [4] and are marked "m". The following compounds were investigated:



I-VII Ia-VIIa

I	$R^1=R^2=H$, $R^3=OH$
II	$R^1=CH_3$, $R^2=H$, $R^3=OH$
III	$R^1=CH_3$, $R^2=H$, $R^3=H$
IV	$R^1=C_6H_5$, $R^2=H$, $R^3=OH$
V	$R^1=C_6H_5$, $R^2=H$, $R^3=H$
VI	$R^1=C_6H_5$, $R^2=H$, $R^3=OCOCH_3$
VII	$R^1=C_6H_5$, $R^2=CH_3$, $R^3=OCOCH_3$

The results will be discussed in terms of compound II (Scheme 1, Fig. 2). The major initial fragmentations of the compounds I – V are expulsions of CO and CHO from the molecular ion which is the base peak in the spectra. The loss of CO is verified by strong metastables while CHO expulsion does not always show a metastable peak in the ordinary spectrum. Compound I, which carries no substituent in the 2-position, has no metastable peak for

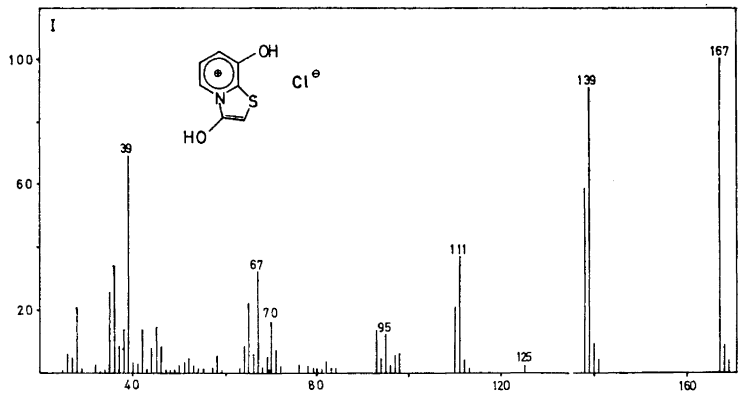


Fig. 1.

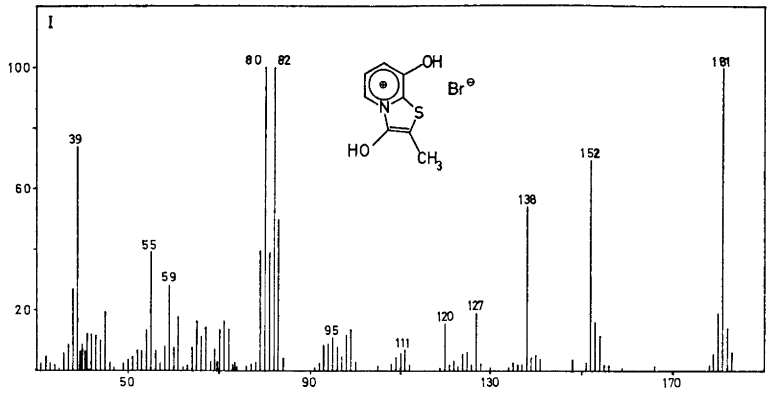
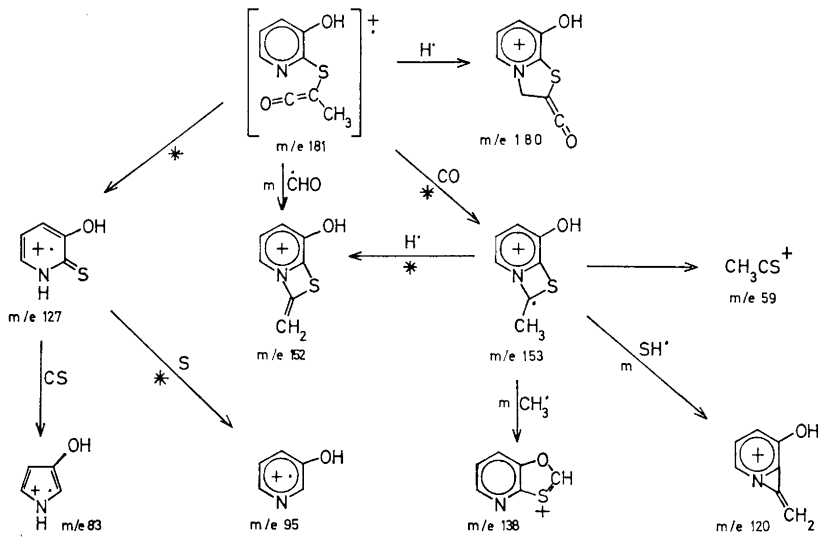


Fig. 2.

direct CHO loss. After CO loss, however, the (M − CO) species go on to expel a hydrogen radical to the (M − 29) ions. For compound II, metastable peaks also show that the (M − 29) fragment at *m/e* 152 is formed by H-expulsion from (M − CO), and the *m/e* 138 fragment by a competing methyl radical

Scheme 1



expulsion. The other major fragmentation of (M − CO) is SH expulsion to *m/e* 120. Another important fragment in the spectrum is found at *m/e* 127. In the corresponding 8-desoxy derivative (III) this peak is at *m/e* 111 (Fig. 3) and is practically missing for the other derivatives. A McLafferty rearrange-

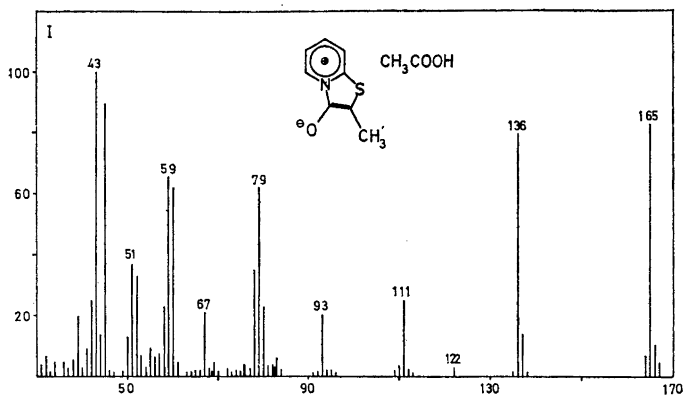


Fig. 3.

ment would seem a likely explanation, but no metastable for this transition was found, and the respective fragments show variable intensities so that their genesis must at least in part be pyrolytic. In both the 2-methyl derivatives (II, III), there is a signal at (M − H) absent in the spectra of the desmethyl analogues. The hydrogen radical therefore is expelled from the 2-methyl group.

The stability of the (M − CO) and (M − CHO) species from the various compounds is such that they often give rise to fairly strong doubly charged species.

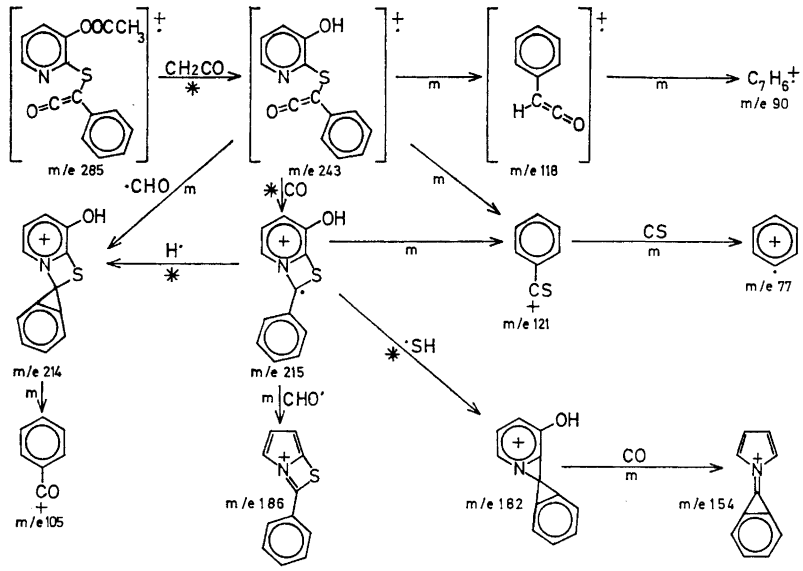
The major fragmentation route for pyridinium-3-oxides [2] and thiazolo[3,2-a]pyridinium-8-oxides [3] is CO expulsion from the pyridine ring, a process which is also important in simple 3-hydroxypyridines.[5] CO expulsion from the pyridine ring in I, II, and IV, however, must be small since the relative intensities of these fragments in the 8-desoxy derivatives (III, V) are not markedly reduced. Therefore, the primary carbonyl fragments must come from the thiazolo moiety.

The more important fragments from the (M − CO) species at *m/e* 139 for compound I (Fig. 1) arise by the usual H expulsion (*m/e* 138) or by CO expulsion to *m/e* 111 which further expels a hydrogen to *m/e* 110. Alternatively the (M − CO) species loses CS to give *m/e* 95 which fragments further to *m/e* 67 by CO expulsion.

The thiolactam at *m/e* 111, formed by expulsion of the side chain from III (Fig. 3), can lose either S or CS to give the ions *m/e* 79 and *m/e* 67. The (M − CO) species at *m/e* 137 expels either the hydrogen radical (*m/e* 136) or the methyl radical (*m/e* 122). The strong signal at *m/e* 59 is due to $CH_3-C\equiv\overset{+}{S}$ arisen by pyridyl expulsion. The charge may also remain on the aromatic ring (*m/e* 78), while thioketene expulsion gives pyridine (*m/e* 79). The other major fragment from M − CO is due to CS expulsion (*m/e* 93).

The relative intensities of the molecular ion peak for the 8-acetoxy derivatives (VI, VII) are 30 − 40 % (Figs. 5 and 6). The fragmentation patterns for both compounds are very similar, the methyl homologue having the

Scheme 2



pyridyl residues displaced 14 units towards higher mass numbers. The fragmentation is discussed in terms of compound VI (Scheme 2). The base peak is at *m/e* 121, and is due to the phenylthioacylium ion. This is also the base peak in all 2-aryl derivatives (IV – VII). The intensity of the corresponding methylthioacylium ion (*m/e* 59) from compounds II and III (Figs. 2 and 3) is much less due to decreased stabilization.

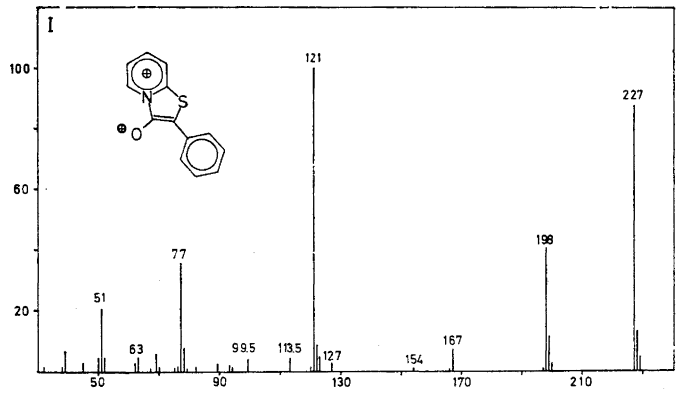


Fig. 4.

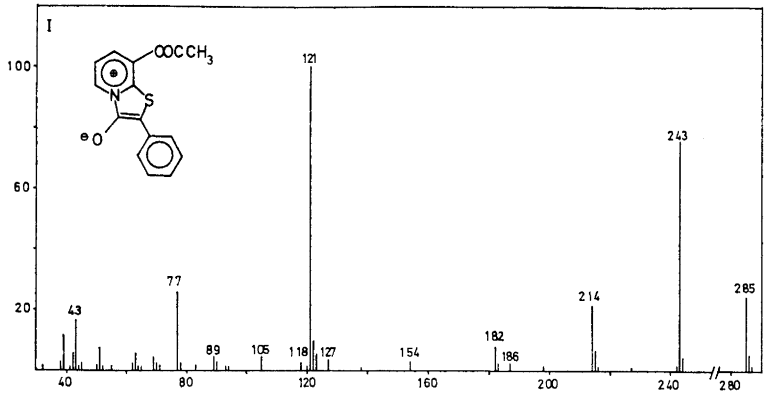


Fig. 5.

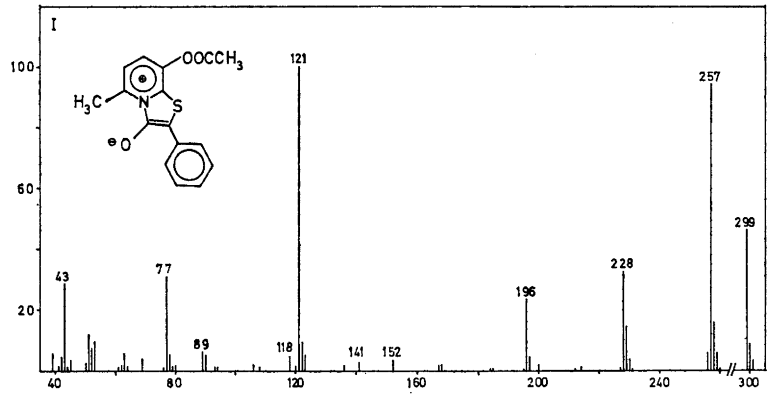


Fig. 6.

The molecular ion (*m/e* 285) fragments almost exclusively by ketene expulsion from the acetate group to the corresponding hydroxy analogue, *m/e* 243. This transition has a strong metastable peak in the ordinary spectrum. The dominating influence of this pathway on the fragmentation patterns is also evident from the spectrum of the 8-hydroxy analogue (IV). The spectrum of the latter is practically identical with the spectrum of VI from *m/e* 243 towards lower mass units. Therefore, the spectrum of IV is not reproduced. The *m/e* 243 ion loses CO or CHO as usual, to give *m/e* 215 or *m/e* 214. Again, the former expels a hydrogen to *m/e* 214. Phenyl radical expulsion is hardly noticeable (*m/e* 138), but is slightly more important in the methyl homologue (*m/e* 152). The most important fragmentation, however, is the generation of the phenylthioacylium ion at *m/e* 121. By the special defocusing technique it was also found that the latter is formed directly from the *m/e* 243 species.

Other important fragmentations are SH expulsion to *m/e* 182, followed by CO loss to *m/e* 154 or formyl expulsion to *m/e* 186.

The base peak in the spectrum (Fig. 4) of the simple 2-aryl derivative (V) is due to the phenylthioacylium ion at *m/e* 121. There are metastable peaks for direct generation from the molecular ion (*m/e* 227) or from the (M−CO) species at *m/e* 199. The *m/e* 198 peak is due to CHO expulsion from the molecular ion and hydrogen expulsion from (M−CO). Phenyl expulsion from the latter gives rise to a weak signal at *m/e* 122. The charge in this cleavage could also have been retained on the phenyl group, but the major origin of the *m/e* 77 peak is CS expulsion from the *m/e* 121 species as shown by a strong metastable. The (M−CO) fragment can also expel S to give *m/e* 167 as shown by an appropriate metastable.

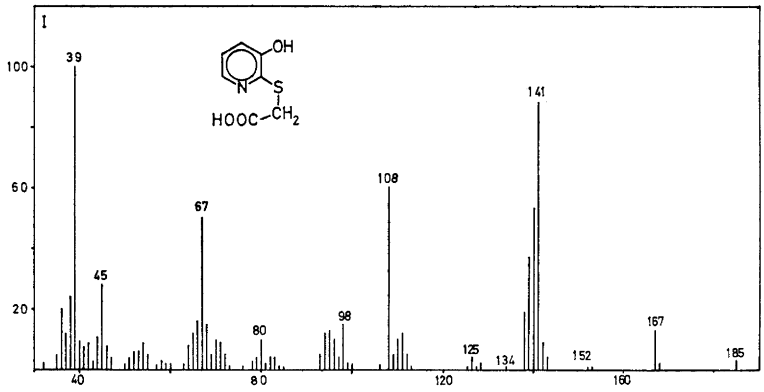


Fig. 7.

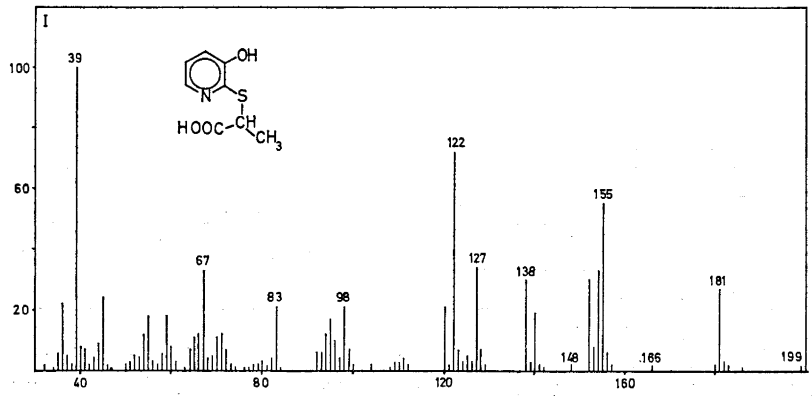
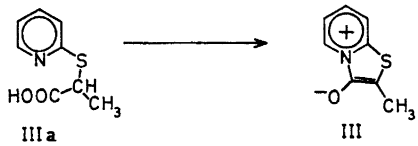


Fig. 8.

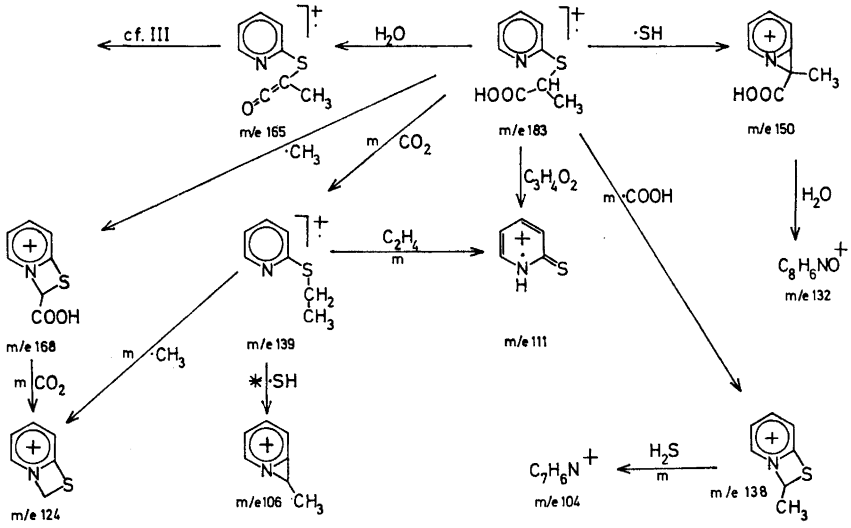
The compounds used in this study are obtained by cyclisation of the corresponding acids, illustrated with the cyclodehydration of IIIa to III.[6]



IIIa III

It was conceivable that cyclodehydration would also occur in the instrument before evaporation, and therefore, a few of the precursor acids were studied.

Scheme 3



The acid IIIa (Fig. 9, Scheme 3) illustrates the behaviour of the acid precursors for the bicylic structures I–III. The intensity of the molecular ion amounts to a few per cent. The peak corresponding to $(M-H_2O)$ shows variable intensity (10–30 %). No metastable peak was found for water expulsion which therefore appears to be largely a pyrolytic process. In the analogous aldehyde and ketones a cyclodehydration process in the instrument is hardly noticeable.[3]

The electron induced fragmentation follows an understandable pattern. Hydroxyl group expulsion gives a weak peak at *m/e* 166. γ-Cleavage with CO_2H expulsion results in the base peak (*m/e* 138). γ-Cleavage with methyl radical expulsion is much less favourable due to the destabilizing effect of the carboxyl group on the cation (*m/e* 168) formed, while hydrogen expulsion is hardly seen. SH expulsion (*m/e* 150) is less important again, because of the destabilizing effect of the carboxyl group on the cation formed. For comparison,

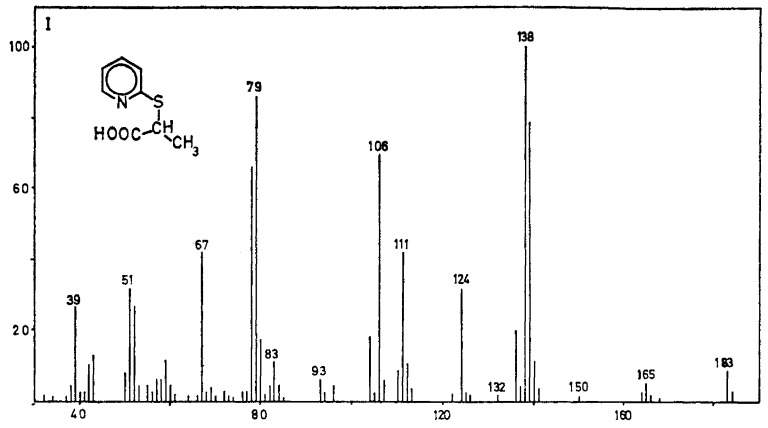
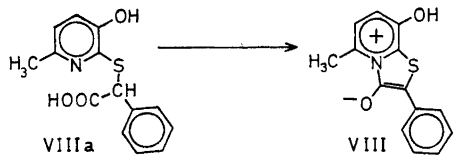


Fig. 9.

the $(M-CO_2)$ species at *m/e* 139 have as a major fragmentation route SH expulsion (*m/e* 106). Other important fragments from the $(M-CO_2)$ species are at *m/e* 124 due to the normal methyl expulsion, and at *m/e* 111 due to ethylene loss. The thione corresponding to *m/e* 111 is also formed directly from the molecular ion by acrylic acid expulsion.

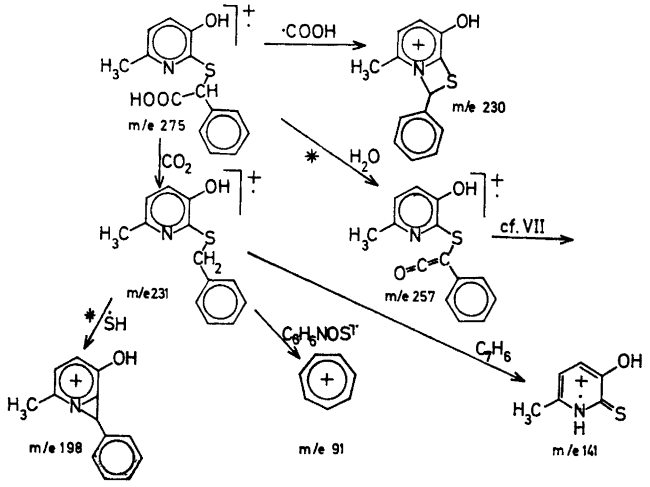
The spectra from the acids after indirect insertion, which requires a higher temperature for evaporation, corresponded closely to those of the bicyclic thiazolo-pyridinium oxides. The 3-desoxy acid (IIIa), however, due to increased volatility, gives a spectrum which is best interpreted as arising from a gaseous mixture of III and IIIa in the ratio 5:2.

The aryl precursor acids without the 6-pyridylmethyl group are so readily cyclised that they in the mass spectrometer would behave as the corresponding bicyclic compounds. The 6-methyl group in the acid introduces *peri* interaction between the 3-oxide group and the 5-methyl group in the bicyclic structure (VIII) which makes cyclisation less favourable.[6]



By direct insertion of the acid VIIIa, thermal dehydration to *m/e* 257 occurs to a large extent (Fig. 10, Scheme 4). In this case, however, the $(M-H_2O)$ species are also formed by an electron induced pathway, as seen by an appropriate metastable. Pyrolytic decarboxylation is important due to aryl stabilization of the intermediate in the decarboxylation. The spectrum

Scheme 4



obtained is best interpreted as arising from a mixture of the acid, the product from cyclodehydration, and the *S*-benzylpyridine from decarboxylation. On indirect insertion decarboxylation is the major pyrolytic pathway. The benzyl group gives rise to the tropylium ion (*m/e* 91) as parent peak in both spectra.

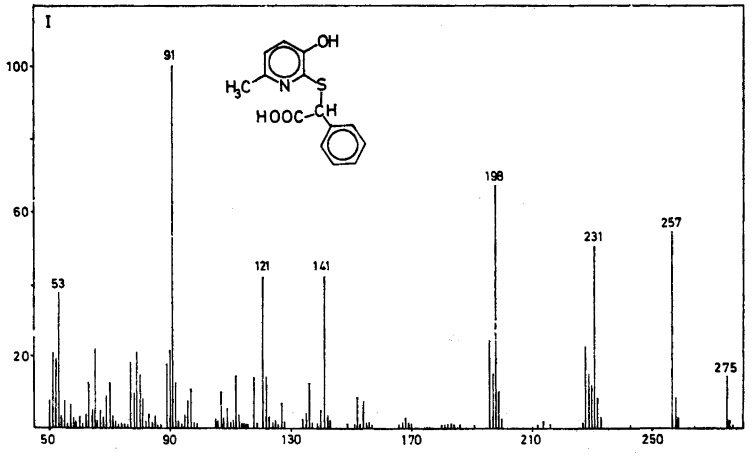


Fig. 10.

EXPERIMENTAL

The mass spectra were recorded on an AEI MS 902 double focusing mass spectrometer. For direct introduction into the source, the source temperature was 230 – 240°, the electron energy 70 eV and the ionizing current 100 μA. For indirect introduction, the heated glass inlet system was kept at 310 – 320°, and the source temperature at 230°.

The compounds used were prepared as previously described.[6]

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