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Electron Impact Induced Fragmentations of Some 2,2-disubstituted 1,3-oxathiolanes

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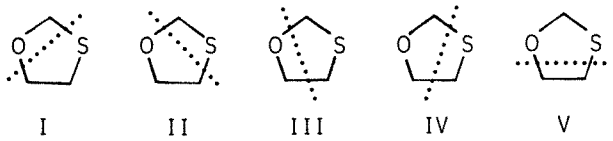
The electron impact induced fragmentations of nine 2,2-disubstituted 1,3-oxathiolanes have been studied by means of exact mass measurement and metastable ion analysis. The ring cleavage almost always takes place so that the C(2)—S and C(5)—O bonds are broken, leading to the most stable products. The nature of the substituents determines the primary fragmentations of molecular ions. Ring cleavage is important only if both substituents are alkyl groups or if the carbon attaching to the ring has an alkyl character. The loss of the substituent becomes the most favourable process if it is attached to the ring through the electron-deficient carbon atom.

INTRODUCTION

Intense fragment ion peaks resulting from cleavages α to the acetal oxygen atoms are characteristic of the mass spectra of 1,2-dioxolanes, the ring cleavage having only a minor role.[1–4] In the case of the 2,2-dialkyl 1,3-dioxolanes, the loss of the larger alkyl group gives rise to the base peak of the spectrum.[2,3] Substituents in which a functional group is not situated in the carbon atom attaching to the ring do not alter this relationship.[4] The ability of the 1,3-dioxolane ring to stabilize a positive charge has made it an important derivative for mass spectrometric studies of steroids.[5–7] The 1,3-oxathiolane ring seems not to have this ability,[5,7] which may be one of the reasons why this ring system is not so widely studied.

The fragmentation of 1,3-oxathiolane mainly gives rise to sulphur-containing fragment ions due to their greater stability as presented by Conde-Caprace and Collin.[8] Alkyl substituents in ring position 2 slightly increase the proportion of oxygen-containing fragment ions.[9,10] According to Pasto,[9] there occur only two significant primary fragmentations of the ring system (types I and II) from five possibilities, giving rise to ions $[C_2H_4S]^{+\cdot}$ and $[CHS]^+$, respectively. The above-mentioned studies, however, have been limited to the oxathiolane itself or its simple alkyl derivatives. In connection with other studies, we have synthesized some 2,2-disubstituted 1,3-oxathiolanes. In order to find out the effect of a substituent containing a functional group on the fragmentation of the 1,3-oxathiolane ring under electron impact, we have



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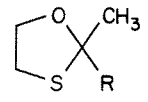

	R
1	CH_3
2	CH_2CH_3
3	CH_2COOCH_3
4	$CH_2COOCH_2CH_3$
5	$COCH_3$
6	$CH(OH)CH_3$
7	$COOCH_2CH_3$
8	$CH_2C_6H_5$
9	C_6H_5

carried out a detailed investigation of the fragmentation characteristics of the compounds listed above. Exact mass measurement, used to determine the elemental composition of all the principal fragments considered, and metastable ion analysis confirm all the reaction paths deduced.

RESULTS AND DISCUSSION

The 70-eV mass spectra of the compounds studied are presented in Fig. 1 and Table 1. All the compounds show a molecular ion peak, although some of them are fairly weak. The compounds studied can be divided into three groups on the basis of their different fragmentation patterns.

Compounds 1–4

These compounds contain only alkyl substituents or substituents where the functional group is not situated

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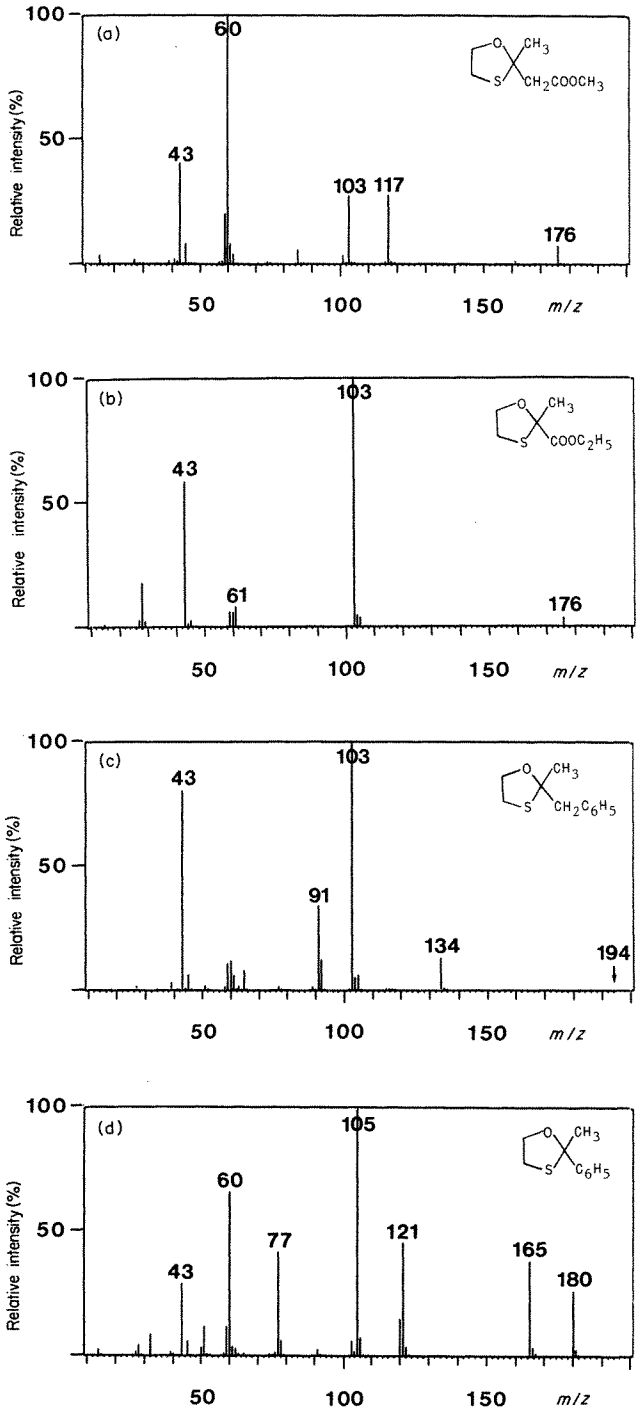


Figure 1. The 70 eV mass spectra of (a) 2-methyl-1,3-oxathiolane-2-acetic acid methyl ester (**3**), (b) 2-methyl-1,3-oxathiolane-2-carboxylic acid ethyl ester (**7**), (c) 2-methyl-2-benzyl-1,3-oxathiolane (**8**) and (d) 2-methyl-2-phenyl-1,3-oxathiolane (**9**).

in the carbon atom attaching to the ring. As an example, we consider compound **3**. The main fragmentation routes of this compound are given in Scheme 1. There exist two primary ring cleavage reactions, both being type I. The first type I cleavage (IA) is a simple cleavage and gives rise to the sulphur-containing ion *c*, which represents the base peak in the spectrum of **3** as well as in the spectrum of the other compounds in this group (Table 1). The

Table 1. The 70 eV mass spectra of compounds 1, 2 and 4–6 (*m/z* (rel. abund.))

2,2-Dimethyl-1,3-oxathiolane (1)

26(2), 27(5), 31(2), 39(3), 41(4), 42(2), 43(38), 45(18), 46(2), 55(2), 58(11), 59(33), 60(100), 61(9), 62(5), 103(6), 118(34).

2-Ethyl-2-methyl-1,3-oxathiolane (2)

15(3), 26(3), 27(13), 39(3), 41(4), 42(3), 43(95), 45(23), 55(8), 57(19), 58(8), 59(36), 60(100), 61(14), 62(5), 72(17), 73(11), 103(57), 104(3), 105(3), 117(4), 132(15).

2-Methyl-1,3-oxathiolane-2-acetic acid ethyl ester (4)

27(5), 29(9), 41(3), 42(2), 43(45), 44(2), 45(8), 58(4), 59(14), 60(100), 61(11), 62(5), 85(11), 88(4), 102(2), 103(41), 104(2), 105(2), 130(6), 131(32), 132(2), 190(7).

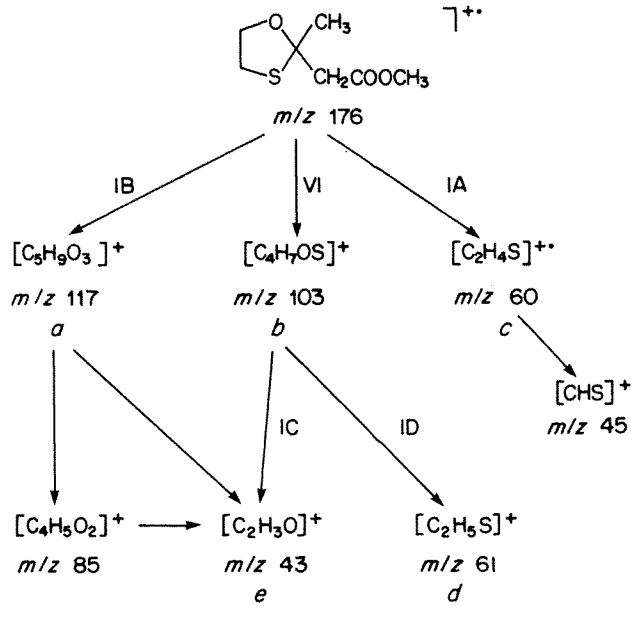
2-(1-Oxoethyl)-2-methyl-1,3-oxathiolane (5)

15(4), 27(2), 42(2), 43(100), 44(3), 45(4), 58(2), 59(7), 60(5), 61(15), 103(85), 104(5), 105(4), 146(0.3).

2-(1-Hydroxyethyl)-2-methyl-1,3-oxathiolane (6)

14(5), 15(2), 16(2), 17(22), 27(4), 29(4), 40(6), 43(68), 44(3), 45(18), 59(8), 60(8), 61(20), 68(2), 88(2), 103(100), 104(6), 105(5), 112(2), 148(5).

second type I cleavage (IB) takes place with proton abstraction, forming ion *a*. The bias of this reaction towards compound **3** is probably due to the position of the carbonyl group in the side-chain; it can easily take a proton from ring carbon 4 or 5 through a tight activated complex. This reaction shows all the features typical of a low-energy rearrangement reaction.[11] It gives rise to an unusually strong metastable transition. Furthermore, the intensity of the peak at *m/z* 117 increases with decreasing electron energy (8.9 and 28.8% of the total ion current at 70 eV and 16 eV, respectively).

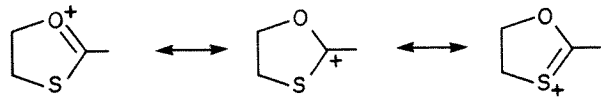


Scheme 1

The third important primary fragmentation is the α-cleavage of the larger substituent, giving rise to ion *b*. This decomposes further with two type I reactions (IC and ID). The loss of a methyl group also occurs to a minor extent, but a metastable transition for this process could not be observed; this is the opposite of what happens with the 2,2-disubstituted 1,3-dioxolanes.[3] The almost total absence of fragments typical of an ester group in the molecule is also significant.

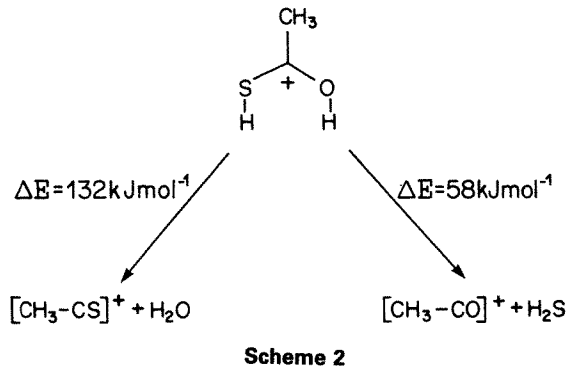
Compounds **3** and **4** behave identically, as in principle do compounds **1** and **2**. A type IB cleavage like that with **3** and **4** is, however, not possible with compounds **1** and **2**. Formally similar fragments representing type I cleavage with proton abstraction can, however, be observed in the spectra of **1** and **2**, although they are not as important as with the esters **3** and **4**. This fragmentation mode must involve proton abstraction to the ring oxygen. A related process does not occur with unsubstituted 1,3-oxathiolane[8,9] but electron-releasing alkyl groups probably stabilize the cations so formed and enable this reaction to take place with **1** and **2**.

As is apparent from the above discussion, the only significant ring cleavages observed are type I cleavages. As an example, ion *b* could be expected to decompose equally as well with type I as type II cleavages. The only observed metastable transitions



b

are, however, type I reactions (IC and ID), forming ions *e* (*m/z* 43) and *d* (*m/z* 61). The former is direct ring cleavage with preferential charge retention on the oxygen fragment. The latter proceeds with proton abstraction, the charge remaining with the sulphur fragment. The formation of *e* gives rise to a much more intense metastable transition, as does the formation of *d*, indicating a lower critical energy for reaction IC than for reaction ID.[11] On the other hand, in the spectrum of **3** there are peaks at *m/z* 59 and *m/z* 45, which could represent type II cleavages of ion *b*. However, these cleavages are, energetically, clearly less favourable than type I cleavages, because no metastable transition can be seen for them. These fragment ions are present in the collisionally induced dissociation (CID) spectrum of *b*, thus they may occur in the ion source to some extent. Type I cleavage was also found to be energetically more favoured (by *c.* 74 mol^{-1}) than type II cleavage, based on quantum chemical study (Scheme 2).[12] These calculations were carried out using the GAUSSIAN 82 program of Pople *et al*; complete geometry optimization was performed using analytical gradients at the 6–31G* level.[13]



Scheme 2

Compounds 5–8

The mass spectra of these compounds are very simple. The only common primary fragmentation giving rise to metastable transition is the loss of the larger substituent. This loss represents the α-cleavage with respect to three different functional groups and leads to the formation of more stable radicals,[14] as in case of compounds **1–4**. The attachment of an electron-deficient carbon atom to ring carbon 2 thus has a very dramatic influence, as can be seen by comparing, for example, the mass spectra of compounds **4** and **7** (Fig. 1(a) and (b)). The formation of ion *b* (*m/z* 103) occurs in both cases but it is a much more important reaction with **7** than with **4**. On the other hand, the α-cleavage with respect to the carbonyl group in **4** can hardly be seen at all.

The energetic preference for the loss of the larger substituent as a consequence of the α-cleavage with respect to the three functional groups also appears as the absence of a metastable transition for the primary ring cleavage of type IA in this group of compounds. Compound **5**, however, shows a low-energy primary ring cleavage, which is formally a type ID reaction, giving rise to an ion of *m/z* 61. This is the only observed primary cleavage of this type and is probably due to the favourable position of the methyl hydrogens in the acetyl group related to the ring sulphur.

There also occurs another unusual primary ring cleavage in this group of compounds. Namely, compound **8** (Fig. 1(c)) decomposes through a type I reaction forming a radical cation $[C_9H_{10}O]^{+\cdot}$ at *m/z* 134. This is the only case when there exists a type I primary ring cleavage without proton abstraction, along with charge retention on the oxygen fragment at the same time. The ion formed at *m/z* 134 could have the same structure as the molecular ion of 1-phenyl-2-propanone (**10**). The structures of these two ions have been studied by comparing their CID spectra, which show remarkable differences (Table 2). The biggest difference appears to be the lack of a metastable transition for the formation of the *m/z* 91 ion from the molecular ion of **10**. If this is taken into account, the differences are still larger than the precision of the method with our instrument (better than 10%). This indicates that there must be some kind of difference between the compared structures. According to the Cram rule, one of the most probable conformations for compound **8** could be the one where the phenyl group is situated near the ring oxygen. This makes some kind of interaction possible

Table 2. The CID spectra of the m/z 134 ions generated from 2-benzyl-2-methyl-1,3-oxathiolane (8) and 1-phenyl-2-propanone (10). The intensities were normalized so that the total abundance in each spectrum = 100

m/z	8	10	m/z	8	10
38	1.3	0.3	76	1.1	0.3
39	4.6	3.5	77	6.0	4.5
41	1.1	1.3	78	2.8	1.4
43	[a]	[a]	79	2.7	1.8
44	4.9	3.9	89	7.4	4.0
45	1.6	—	90	6.6	4.3
50	2.5	1.6	91	[a]	39.6
51	5.6	4.4	92	[a]	[a]
52	1.7	1.6	93	[a]	[a]
55	0.7	—	102	0.3	—
57	0.3	—	103	2.6	1.8
59	0.3	—	104	1.0	0.3
60	1.4	—	105	7.2	4.4
61	0.8	0.3	106	0.4	—
62	1.2	1.3	115	1.8	0.3
63	4.8	3.0	116	0.3	—
64	2.4	1.0	117	—	0.3
65	10.5	8.4	118	7.2	5.9
66	0.9	0.3	119	[a]	[a]
69	2.3	—	131	2.5	—
74	0.6	—	132	[a]	[a]
75	0.6	—	133	[a]	[a]

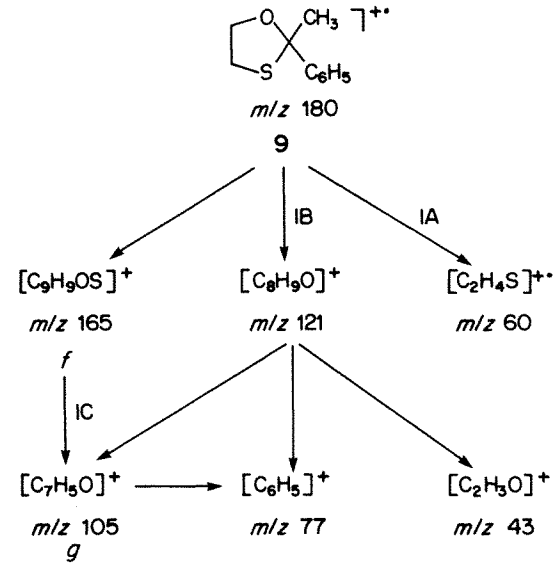
[a] Peaks excluded because they gave rise to metastable transitions.

between the oxygen and the phenyl carbon atom when the m/z 134 ion is formed, possibly giving extra stabilization to the ion. Due to the larger flexibility of the smaller ketone molecule, it is improbable that the same kind of bond is formed with it or at least with all the molecules.

In connection with these compounds, the lack of reactions typical of the functional group of the substituent should also be taken into account. For example, compound **6** does not eliminate water through a mass spectrometric process. There exists a weak peak in the spectrum of this compound for the loss of water, but it is probably due to thermal or catalytic decomposition because the abundance of this peak varied during the measurements depending on the condition of the mass spectrometer; also, there is no metastable transition for this process.

Compound 9

The main fragmentation routes for compound **9** are presented in Scheme 3. Here, as distinct from all the other compounds studied, the loss of the methyl group is the most important primary reaction. This is due to the phenyl group attaching to the ring, which can cause a resonance stabilization for the ion formed (*f*). This ion decomposes further through type IC reaction to the benzoyl ion *g*, which gives rise to the base peak in the spectrum (Fig. 1(d)). Here, again, the related thiobenzoyl ion (m/z 121) is not formed to any significant extent in the ion source because $[C_8H_9O]^+$ (m/z 121) is formed through formal type IB fragmentation directly from the molecular ion.



Scheme 3

CONCLUSIONS

The nature of the substituent greatly affects the primary fragmentation of 2,2-disubstituted 1,3-oxathiolanes. In contrast to the behaviour of the 1,3-dioxolanes, the ring cleavage itself is important when the substituents are both alkyl groups or the carbon attaching to the ring has an alkyl character. Only type I ring cleavage occurs to any significant extent, leading to the most stable products. The charge tends to remain with the sulphur-containing fragments in the case of alkyl substitution. 2,2-Disubstitution, however, clearly increases the amount of oxygen-containing fragments, as compared to unsubstituted 1,3-oxathiolane. Since these primary fragments are usually formed with proton abstraction, the likelihood of their formation is greatly increased when there is a suitably situated heteroatom in the side-chain.

When the substituent is attached to the ring through the electron-deficient carbon atom, its loss becomes the most favourable reaction.

Fragmentations typical of the functional group of the substituent are not observed to any significant extent.

EXPERIMENTAL

The mass spectra were recorded on a Jeol JMS-D300 mass spectrometer equipped with a Jeol JMA-2000H data system. Typical source conditions were: temperature 170 °C, electron energy 70 eV, accelerating voltage 3 kV, and ionization current 300 μA. The samples were introduced through a heated inlet system at 90 °C or an attached Carlo Erba Fractovap gas chromatograph. The mass spectra using either of the introduction procedures showed no discernible differences. The resolution of the instrument was 500

in the low resolution measurements, except for linked scans where the nominal resolution was 1000. The compositions of all the principal fragment ions were verified with exact mass measurements at a resolving power of *c.* 5000 using the data system. Fragmentation reactions (metastable transitions) occurring in the first field-free region between the ion source and the electric sector were examined using linked scans at constant B/E and B^2/E. CID spectra were measured relatively, leading helium into this field-free region so that transmission of the main beam was 30%. When the quantitative CID measurements were made, the operating conditions were kept carefully constant throughout the measurements.

Compounds **1–5** and **7–9** were synthesized by refluxing, in a Dean-Stark water separator, an equivalent amount of the corresponding ketone and 2-mercaptoethanol in benzene containing a crystal of *p*-toluenesulphonic acid as described by Eliel *et al.*[15] Alcohol **6** was prepared with sodium borohydride reduction from the corresponding ketone (**5**). Purification was carried out using preparative gas/liquid chromatography (GLC) and an FFAP column. The structure and purity of the compounds were checked by GLC and ^{13}C-NMR (nuclear magnetic resonance).

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