Mass Spectral Fragmentation of Thioesters

1—Identification of Low Energy, Slow Processes

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A variety of thiol and thion esters, including acetates and benzoates with *n*-butyl and β-phenethyl alkyl groups, have been studied by electron impact mass spectrometry. Several rearrangement ions were documented and their persistence in low voltage and field ion spectra demonstrated. Among the significant ions found in the rich thion spectra, the most general requires O to S rearrangement of the alkyl group and subsequent cleavage to yield acyl ions (CH_3CO or PhCO). This process is more important in longer chain compounds than in the methyl and ethyl homologues studied previously.

INTRODUCTION

Early in the development of field ionization (FI) mass spectrometry, esters were shown to be capable of relatively rapid rearrangements of the McLafferty type.[1,2] More recently, the technique known as field ionization kinetics (FIK), which yields a form of time-resolved FI mass spectrum, has been applied to a variety of compounds including ketones,[3] aldehydes[4] and olefins.[5] Although these studies have yielded a good deal of useful information, in several instances the fragment ions are of rather low abundance.

Our interest in a molecular system which might be expected to yield an FI spectrum rich in rearrangement ions led us to consider sulfur analogues of esters. Widespread exploitation for synthetic purposes[6] of various related sulfur-containing compounds adds a measure of utility to further study of their mass spectral behaviour.

We present here a selection of mass spectral results for a variety of monothioester analogues, both thiol and thion isomers, under electron impact (EI) and FI conditions. At this survey stage, high resolution and metastable measurements were used to document the major decomposition pathways in EI spectra, while low voltage and FI measurements were used to identify low energy processes of potential interest for more detailed study by FIK. Comparisons with earlier EI studies, which concentrated on lower homologues of the compounds studied in this work, are included in the discussion of our results.

Thiol esters	Thion esters
$CH_3C(=O)-S-R$	$CH_3C(=S)-O-R$
$PhC(=O)-S-R$	$PhC(=S)-O-R$
$CH_3C(=O)-S-CH_2CH_2Ph$	$CH_3C(=S)-O-CH_2CH_2Ph$
$PhC(=O)-S-CH_2CH_2Ph$	$PhC(=S)-O-CH_2CH_2Ph$

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The compounds studied are summarized above, where *R* represents a range of alkyl groups from C-3 to C-6.

RESULTS AND DISCUSSION

Thiol and thion analogues of several acetates were studied. In Table 1 and elsewhere presentation of complete mass spectra is limited to the *n*-butyl member of the series.

Our thiol EI spectra are similar to mass spectra published previously by McFadden[7] except for a generally lower level of fragmentation (e.g. our $[M]^{+\cdot}$ for *n*-butyl acetate of 28% vs 16%). Previous work on alkyl thionacetates appears to have been limited to methyl and ethyl esters,[8,9] compounds whose alkyl portions are too short to allow ready transfer of β-hydrogen and other potentially interesting processes. For example, in addition to $[M]^{+\cdot}$, ethyl thionacetate gave only cleavages to $[CH_3CS]^+$ and $[CH_3CH_2O]^+$; rearrangements to $[CH_3CO]^+$, $[CH_3CH_2S]^+$, $[M-SH]^+$; and the single McLafferty rearrangement product $[CH_3COSH]^{+\cdot}$. In agreement with previous reports,[9] our thion spectra are generally richer than those of the thiols in major peaks. This is exemplified by the *n*-butyl esters where the relatively intense thion $[M]^{+\cdot}$ (93%) carries less than 15% of the total ion current, a proportion comparable with that found for the thiol, although $[M]^{+\cdot}$ is only 28% of the base peak for the latter. A number of ions are worthy of specific comment, for the insight they offer into the processes at work in these compounds and the related benzoates and β-phenethyl compounds to be discussed below.

m/z 99

Loss of SH from the molecular ion has been reported at about the 1% level for thiolacetates,[7] and up to 10% for thionacetates.[9] We also found this process to be more important for the *n*-butyl thionacetate (2.4 vs 0.2%) and the thionbenzoate (see below).

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Table 1. EI mass spectra of thiol and thion analogues of *n*-butyl acetate

$CH_3C(=X)-Y-CH_2CH_2CH_2CH_3$ (M = 132)

m/z	Thiol (X = O, Y = S)	Thion (X = S, Y = O)
132 $[M]^{+\cdot}$	27.8	93.4
99 $[M-SH]^+$	0.2	2.4
89 $[n\text{-BuS}]^+$	1.5	3.2
88 $[n\text{-BuS–H}]^{+\cdot}$	1.1	2.1
77 $[CH_3C(OH)SH]^+$	3.5	84.3
76 $[CH_3C(OH)S]^{+\cdot}$	2.4	28.0
73	0.3	2.2
72 $[M-CH_2CH_2S]^{+\cdot}$	5.8	1.2
60 $[CH_3CSH]^{+\cdot}$	0.4	10.2
59 $[CH_3CS]^+$	0.7	43.6
57 $[n\text{-Bu}]^+$	1.6	34.9
56 $[n\text{-Bu–H}]^{+\cdot}$	11.8	100
55 $[n\text{-Bu–2H}]^+$	3.1	17.3
47 $[CH_2SH]^+$	2.7	1.8
43 $[CH_3CO]^+$	100	77.6

m/z 88[*M*-CH_3COH]$^{+\cdot}$

This minor peak has been reported[7] in thiolacetates (2–10% of base peak), and was found in the present work in the *n*-butyl and *n*-propyl thions as well. The most reasonable assignment in the thiol case is $[C_4H_9S\text{-H}]^{+\cdot}$ (cyclic?) and this same composition is not unlikely for the thions, considering the other evidence for O to S rearrangement of the alkyl group.

m/z 77, 76

These ions arise from the double and single McLafferty rearrangements respectively. Distribution of the charge between the acid fragment and the olefin portion *m/z* 55, 56 will be discussed below.

m/z 59

This ion is assigned to $[CH_3CS]^+$, thioacetyl. It is accompanied by an ion *m/z* 60, which has no oxygen counterpart. It was noted also, that the charged acid fragments $[CH_3C(SH)O]^{+\cdot}$ and $[CH_3C(SH)OH]^+$, *m/z* 76, 77 show a similar preference for the extra hydrogen in the thion.

m/z 57

Cleavage of the alkyl group is not important for the thiols, but becomes significant with the higher alkylthions. This ion is also found in the FI spectrum of *n*-butyl thionacetate.

m/z 56, 55

These ions are complementary to *m/z* 76, 77 and represent charge location on the alkyl fragment following McLafferty rearrangement. For both the thiol and thion, most of the charge is located on the olefin fragment in the single rearrangement. This rearrangement is considerably more important in the thion (*c.* 25% of ionization vs 10%), a result which, if the normal 6-membered ring transfer of β-hydrogen to ionized carbonyl (thiocarbonyl here) obtains, may reflect the ease of ionization at sulfur.

m/z 43

Finding the acetyl ion to be the base peak in thiolacetates is not surprising;[7] likewise, the importance of this ion in methyl and ethyl thionacetates has been discussed previously.[9] The explanation for the latter lies in the prior migration of the alkyl group from O to S, a process which is known to occur in the structurally analogous phosphonothioates.[10] That the *m/z* 43 ion found here is not $[C_3H_7]^+$ may be inferred from its presence as base peak in the ethyl thionacetate spectrum. The ratio of $[CH_3CO]^+/[CH_3CS]^+$ in thionacetates increases from 0.4 to 2.0 when the alkyl group is changed from methyl to ethyl;[9] in the present work this ratio ranges from 1.8 (*n*-butyl) to 2.0–2.7 (*n*-propyl, *n*-pentyl). Aside from *m/z* 57 already mentioned, the *m/z* 43 ion is the only fragment found consistently in the FI spectra of thioacetates. Insofar as $[CH_3CS]^+$ is absent from the FI spectrum of *n*-butyl thionacetate, the ratio $[CH_3CO]^+/[CH_3CS]^+$ is meaningless.

Mass spectra of thiol and thion analogues of *n*-butyl benzoate are presented in Table 2 as illustrative of our results with these higher alkyl esters (*n*-propyl through *n*-hexyl). In many respects these results parallel those reported previously for methyl and ethyl[7,9] as well as those for the acetates just discussed. Thus, the thion spectra show richer fragmentation, substantial loss of SH from $[M]^{+\cdot}$, more charged acid products from single and double McLafferty rearrangements (*m/z* 138, 139), less $[M\text{-}60]^{+\cdot}$ (*m/z* 134 for these examples), large thiobenzoyl peaks (*m/z* 121) accompanied by a hydrogen transfer peak (*m/z* 122), and as base peak, the benzoyl ion formed after O to S rearrangement of the alkyl group. The thiol spectra also have *m/z* 105 as base peak, arising from simple

Table 2. Mass spectra of thiol and thion analogues of *n*-butyl benzoate

$PhC(=X)-Y-CH_2CH_2CH_2CH_3$ (M = 194)

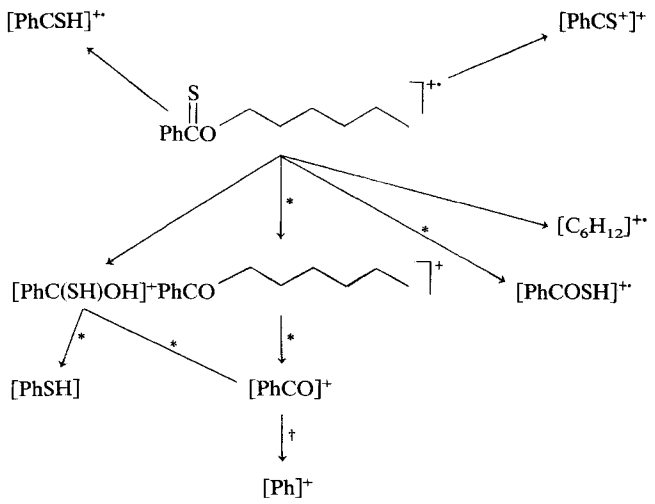
m/z	Thiol (X = O, Y = S)	Thion (X = S, Y = O)
194 $[M]^{+\cdot}$	9.3	30.6
161 $[M-SH]^+$	0.5	7.9
139 $[PhC(SH)OH]^+$	4.2	36.8
138 $[PhC(SH)O]^{+\cdot}$	0.9	8.2
134 $[M-CH_2CH_2S]^{+\cdot}$	3.3	0.2
122 $[PhCSH]^{+\cdot}$	1.5	9.5
121 $[PhCS]^+$	0.5	34.6
110 $[PhSH]^{+\cdot}$	0.5	1.4
109 $[PhS]^+$	0.5	1.2
105 $[PhCO]^+$	100	100
77 $[Ph]^+$	23.2	22.2
56 $[n\text{-Bu–H}]^{+\cdot}$	0.5	5.5

cleavage. The most obvious difference between the thioacetate and thiobenzoate spectra is the much reduced intensity of m/z 56 in the latter. This result appears to be in keeping with Stevenson's Rule; that is, the expected lower ionization potential of thiobenzoic acid compared with thioacetic acid allows more effective competition with the complementary (C_4H_8) for the charge.

The enhanced ratio of O to S rearrangement of the alkyl portion with increasing size is quite marked for the thionbenzoates. Thus, the reported[9] spectra for methyl and ethyl esters show $[PhCO]^+/[PhCS]^+$ values of 0.05 and 0.48 respectively. We have found that for n-propyl through n-hexyl esters this ratio is 3–4. Indeed, among the numerous minor peaks found in the FI spectra of thionbenzoates, m/z 105 which we assign to $[PhCO]^+$ is present at the 1–2% level. For thiols the reverse process, that is, S to O rearrangement followed by cleavage, is trivial (1%) regardless of alkyl group length.(It was pointed out by a referee that the O to S rearrangement observed in thions may have some precedent in earlier work by Bowie *et al.* although migration to a singly bonded S as seen in that work would have somewhat different thermochemical results.)

Some indication of the low energy, slow processes in the EI fragmentation of n-butyl thionbenzoate was found in low voltage spectra taken at nominal voltages between 10 and 30 eV. At 20 eV $[M]^{+\cdot}$ becomes the base peak; m/z 139 (double McLafferty product), 74%; m/z 161 $[M–SH]^+$, 19%; the ratio m/z 122/m/z 121 approaches unity; and m/z 56 persists, 4%. These ions, plus m/z 88 (cyclic $[C_4H_8S]^{+\cdot}$?) which appears at 15 eV and below, are being sought in FI defocusing experiments.

Additional information about the sequence of formation of the major ions from thionbenzoates was obtained from a study of the metastable ions, summarized in Scheme 1.



† Metastable reported previously for lower homologue.[9]

Scheme 1. Fragmentation of n-hexyl thionbenzoate.

Thioesters related to β-phenethyl acetate and benzoate should be fertile ground for study of McLafferty rearrangements because of the ease of formation of the styrene ion. This expectation is borne out by the data in Table 3. Three of the four compounds show styrene ions as the base peak (about 50% of total ionization) and even the thiolbenzoate shows this ion at 54.6% (23% of total ion current). There are several other ions derived from the β-phenyl group, presumably a result of electron deficiency in this region of the molecular ion. Thus m/z 91 is significant, particularly where the acid moiety in the molecule is acetate. The ion m/z 105 may likewise be assigned unambiguously to cleavage of the alkyl chain in the acetates. However, for the thiolbenzoate, high resolution measurements show that 94% of this peak corresponds to the

Table 3. Mass spectra of thiol and thion analogues of β-phenethyl acetates and benzoates

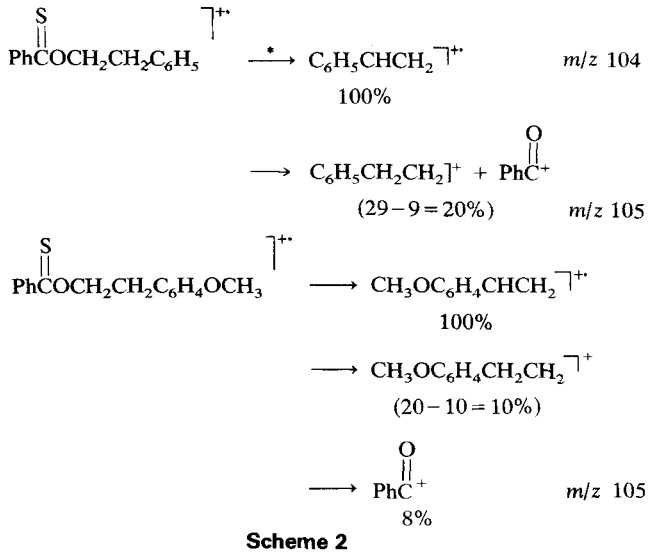
X ‖ RC—Y—CH_2CH_2Ph	-----Acetate(R = CH_3, M = 180)-----		-----Benzoate(R = Ph, M = 242)-------	
	Thiol (X = O, Y = S)	Thion (X = S, Y = O)	Thiol (X = O, Y = S)	Thion (X = S, Y = O)
m/z				
242/180 $[M]^{+\cdot}$	13.5	1.2	4.6	1.3
142	0.5	0.2	3.6	0.1
138 $[PhC(OH)S]^{+\cdot}$	1.0	0.1	4.4	0.1
137	1.2	0.1	1.0	0.1
135	1.4	0.2	1.3	0.1
122	0.5	0.3	0.2	1.0 $[PhCSH]^{+\cdot}$
121	0.5	0.4	0.4	7.9 $[PhCS]^+$
105	13.5 $[PhCH_2CH_2]^+$	37.2 $[PhCH_2CH_2]^+$	100 $[PhCO]^+$[a]	29.4[b]
104 $[PhCHCH_2]^{+\cdot}$	100	100	51.3	100
103	4.6	9.7	2.8	5.7
91 $[PhCH_2]^+$	32.6	12.8	4.9	1.8
89	3.0	1.1		0.3
79	2.8	8.6	1.3	4.3
78	6.1	5.7	4.2	4.3
77 $[Ph]^+$	9.3	11.4	27.6	14.1
59	1.5	7.6		
43 $[CH_3CO]^+$	38.3	3.7		

[a] High resolution measurements show that this ion is 94% $[PhCO]^+$ (see text).
[b] Experiments with the p-methoxy derivative suggest that this ion is a mixture of $[PhCO]^+$ and $[PhCH_2CH_2]^+$ (see text).

benzoyl ion. The phenyl ion, *m/z* 77, presents a more difficult problem since its origin from the benzoates can be determined only by means of a labelling experiment. Following Ohno,[9] the ion *m/z* 122 in thionbenzoate is assigned to $[PhCSH]^{+\cdot}$. The minor peak at *m/z* 122 in thiolbenzoate has been shown by high resolution to be $[PhCOOH]^{+\cdot}$ and is thus assumed to arise from an impurity.

Further insight into the processes generating ions *m/z* 104, 105 from β-phenethyl thionbenzoates was obtained from measurements on the *p*-methoxy-β-phenethyl analogue.

As shown in Scheme 2, the *p*-methoxy compound gives roughly equal amounts of benzoyl ion and substituted β-phenethyl cleavage ion (8% vs 10% after allowance is made for the isotope contribution to the latter). The mixture of cleavage ions in the unsubstituted thionbenzoate may well contain a larger proportion of benzoyl ions, but resolution of the doublet was not attempted because of the overlap from the ^{13}C isotope peak of the styrene ion.



Scheme 2

EXPERIMENTAL

Mass spectra were recorded on a Varian MAT CH5 DF spectrometer interfaced to an INCOS Model 2000 data system. Ion source temperature was 200–250 °C for EI and 50–70 °C for FI measurements. Separate tests at other source temperatures failed to show any evidence of thermal decomposition of the samples prior to ionization. Spectra were normally recorded at a nominal resolution of 1500 in both EI and FI modes. Calibration of the mass scale was carried out with perfluorokerosene in the EI mode, in the case of high resolution measurements (nominal 10 000) on the same day as the measurements. Metastable ion measurements were generally made by scanning the accelerating voltage at a fixed ESA voltage. Precursor ions (m_1) are then calculated from $m_2 \times V_0/V$ where m_2 is a daughter ion, V_0 is the initial accelerating voltage which passes m_2, and V is the accelerating voltage which passes the parent ion, m_1. In some instances the DADI technique [12] was also used.

Alkyl thiolacetates were prepared by the method of Wenzel and Reid.[13]

Alkyl thiolacetates were prepared by a modification of the procedure of Pratt and Reid:[14] to mercaptan (0.05 mol) in 20 cm^3 concentrated sodium hydroxide solution was added benzoic anhydride (0.06 mol) with stirring. After 0.25 h, the mixture was poured into water, the organic layer separated, and the aqueous layer extracted with ether (3×50 cm^3). The combined organic layers were washed with water, 10% hydrochloric acid, sodium bicarbonate solution, and finally water again. The dried extracts were distilled to yield the products.

Thion esters were prepared by bubbling hydrogen sulfide through a stirred suspension of the appropriate imidate hydrochloride[15] in dry pyridine for 9 h.[16]. Thionesters were purified by column chromatography. The purity of all esters prepared was checked by nuclear magnetic resonance (NMR), infrared spectroscopy (IR) and mass spectrometry (MS).

Thiolacetates

n-propyl, b.p. 140 °C (Lit.[13] 139.8 °C).
n-butyl, b.p. 159–161 °C (Lit.[13] 163.4 °C).
n-pentyl, b.p. 90 °C/30 mm (Lit.[13] 185.1 °C).
β-phenethyl, b.p. 130 °C/11 mm (Lit.[15] 135–138 °C/14 mm).

Thiolbenzoates

n-propyl, b.p. 130 °C/15 mm (Lit.[14] 144 °C/13 mm).
n-butyl, b.p. 160 °C/22 mm (Lit.[17] 160 °C/23 mm).
n-pentyl, b.p. 130 °C/1.2 mm (Lit.[18] 105–106 °C/3 mm).

Thionacetates

n-propyl, b.p. 126–129 °C (Lit.[19] 125–130 °C).
n-butyl, b.p. 145–148 °C (Lit.[19] 146–149 °C).
n-pentyl, b.p. 73 °C/55 mm (Lit.[19] 72–74 °C/55 mm).

Thionbenzoates

n-propyl, b.p. 122 °C/8 mm (Lit.[19] 127–132 °C/29 °C mm).
n-butyl, b.p. 138 °C/7 mm (Lit.[17] 160 °C/23 mm).
β-phenethyl, b.p. 114 °C/0.2 mm (Lit.[20] 116–118 °C/0.1 mm).
p-methoxyphenethyl m.p. 83 °C (Lit.[20] 78–81 °C).

n-Pentyl thionbenzoate

An orange liquid, was prepared as described above, b.p. 128 °C/3.4 mm. (Found: C, 69.3; H, 7.7; S, 15.4 $C_{12}H_{16}OS$ requires C, 69.2; H, 7.7; S, 15.4).
IR: $\nu(CHCl_3)$, 3100, 3020, 1290, 1270 cm^{-1}.
NMR: $\delta(CDCl_3)$, 8.2–7.35 (5H, m); 4.7 (2H, t); 2.1 (6H, m); 1.95 (3H, m).
MS: *m/z* 208 (24), 121 (30), 105 (100), 103 (1.3), 77 (20), 71 (6.2).

Isopentyl thionbenzoate

An orange liquid, was prepared as described above, b.p. 129–130 °C/3.4 mm. (Found C, 69.4; H, 7.8; S, 15.4. $C_{12}H_{16}OS$ requires C, 69.2; H, 7.7; S, 15.4). IR: $\nu(CHCl_3)$, 3080, 3010, 1310, 1295 cm^{-1}. NMR: $\delta(CDCl_3)$ 8.25–7.5 (5H, m); 4.72 (2H, t); 1.82 (3H, m); 2.0 (6H, d). MS: *m/z* 208 (21), 121 (45), 105 (100), 103 (6.5), 77 (33), 71 (16).

β-phenethyl thionacetate

An orange liquid, was prepared as described above, b.p. 98 °C/1.8 mm. (Found: C, 66.5; H, 6.8; S, 17.8. $C_{10}H_{12}OS$ requires C, 66.6; H, 6.7; S, 17.8). IR: $\nu(CHCl_3)$, 3100, 3040, 1370, 1295 cm^{-1}. NMR: $\delta(CDCl_3)$, 7.15 (5H, s); 4.6 (2H, t); 3.0 (2H, t); 2.5 (3H, s). MS: *m/z* 180 (10), 105 (37), 104 (100), 59 (7.6).

β-phenethyl thiolbenzoate

Was prepared as described above, b.p. 176–178°C/1.16 mm. (Found: C, 75.0; H, 6.0; S, 11.0. $C_{15}H_{14}OS$ requires C, 74.4; H, 5.8; S, 13.2. IR: $\nu(CHCl_3)$, 3075, 3055, 1660 cm^{-1}. NMR: $\delta(CDCl_3)$, 7.85–7.35 (5H, m); 7.2 (5H, s); 3.16 (2H, m); 2.75 (2H, m). MS: *m/z* 242 (17), 105 (100), 104 (51), 77 (28).

n-Hexyl thiolbenzoate

Was synthesized as described above, b.p. 156°C/1.8 mm. (Found: C, 70.3; H, 8.1; S, 13.9. $C_{13}H_{18}OS$ requires C, 70.2; H, 8.2; S, 14.4). IR: $\nu(CHCl_3)$, 3090, 3020, 1665 cm^{-1}. NMR: $\delta(CDCl_3)$, 7.9–7.4 (5H, m); 4.7 (2H, t); 1.8–1.2 (8H, bm); 0.98 (3H, t). MS: *m/z* 222 (6.4), 117 (0.5), 105 (100), 85 (0.3), 77 (21).

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