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# MASS SPECTRA OF BIS-1,3-DITHIOLANES AND BIS-1,3-DITHIANES

## FRAGMENTATION MECHANISMS AND DEUTERIUM ISOTOPE EFFECTS[1]

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Abstract—The mass spectra of bis-1,3-dithiolanes and bis-1,3-dithianes show that three major fragmentation reactions are induced upon electron-impact. In addition to the expected α-cleavage, two ring cleavages occur with concomitant hydrogen migration. A deuterium isotope effect was observed for one of the ring cleavage reactions as well as for the α-cleavage process. The isotope effect data shed some light on the mechanisms of the cleavage reactions.

## INTRODUCTION

THE results of several investigations have shown that high molecular weight aldehydes and ketones behave rather unpredictably upon electron-impact[2a] and therefore derivatives of these carbonyl compounds were sought for the purpose of obtaining structural information by mass spectrometry. Of the readily prepared carbonyl compound derivatives, the type which has been shown to be best suited for mass spectral analysis are ketals (or acetals) and thioketals (or thioacetals).[2b, 3] Although molecular ions are not always discernible in the mass spectra of these compounds, molecular weights can usually be determined from the spectra of the parent carbonyl compounds. The derivatives undergo specific fragmentation reactions which frequently yield information concerning the substitution pattern in the carbonyl compound.

The electron-impact induced fragmentation reactions of thioacetals and thioketals have been the subject of a few investigations,[2, 4] and like aliphatic thioethers[5] the most abundant ions result from α-cleavage. Fragmentation reactions of ethylene thioketals in the steroid series[3] have been shown to follow the same α-cleavage route as the corresponding ethylene ketals, but the diagnostically significant peaks in the spectra of the sulfur derivatives are of much lower relative intensity and therefore these derivatives were deemed less desirable for structural work than the oxygen analogs.[2b] In the sugar series[6] several thioketals and thioacetals were prepared to increase volatility and again α-cleavage was the dominant feature in the mass spectra.

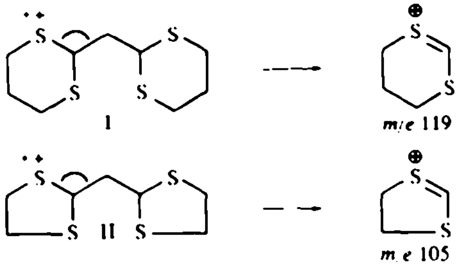
We became interested in the mass spectra of bis-thioacetals and related systems when we observed that the bis-trimethylene thioacetal of malonaldehyde (I), which gives an intense molecular ion, decomposed to three major fragment ions upon electron impact. In addition to the expected α-cleavage, two fragmentation reactions which involve a specific hydrogen transfer occur. Through the use of labeled compounds, a deuterium isotope effect was observed for the expulsion of $C_3H_7S_2\cdot$(Type II-cleavage), whereas no isotope effect was detected for the expulsion of $C_3H_7S\cdot$(Type

I-cleavage). In addition, a surprisingly high secondary isotope effect associated with α-cleavage was observed.

## RESULTS AND DISCUSSION

The mass spectrum of malonaldehyde bis-trimethylene thioacetal (I) is dominated by four peaks in the high mass range appearing at *m/e* 252 ($M^{+\cdot}$, $C_9H_{16}S_4$), *m/e* 177 ($C_6H_9S_3$), *m/e* 145 ($C_6H_9S_2$) and *m/e* 119 ($C_4H_7S_2$).[*] The corresponding ethylene thioacetal II behaves analogously upon electron impact giving ions appearing at *m/e* 244 ($M^{+\cdot}$, $C_7H_{12}S_4$), *m/e* 163 ($C_5H_7S_3$), *m/e* 131 ($C_5H_7S_2$) and *m/e* 105 ($C_3H_5S_2$). The occurrence of a strong metastable ion at *m/e* 83·4 in the spectrum of I indicates that the mass 145 ion is generated, at least in part, from the molecular ion ($145^2/252 = 83{\cdot}4$). Similarly, the molecular ion of II decomposes directly to the mass 131 ion as indicated by a metastable ion at *m/e* 76·6 ($131^2/224 = 76{\cdot}6$). These fragment ions could also be partly produced from the $C_6H_9S_3^+$ and $C_5H_7S_3^+$ ions, respectively, by the expulsion of a sulfur atom. Although no metastable ions were detected for the production of the mass 119 ion from I or the mass 105 ion from II, these species are believed to be generated by simple α-cleavage from the molecular ion in view of the literature precedents.[2b]

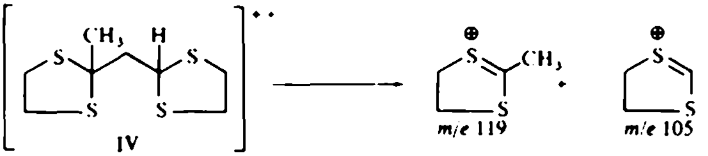
*α-Cleavage.* Since the thioacetals I and II are symmetrical, α-cleavage on either side of the central methylene group leads to the same ions at *m/e* 119 and *m/e* 105, respectively.



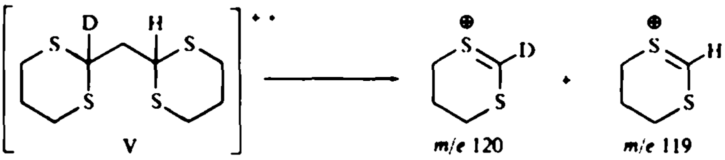
We have prepared three unsymmetrical analogs (III, IV and V) of these thioacetals and all behave in the same fashion upon electron-impact. It is interesting to note, however, that in the mass spectra of compounds III and IV cleavage of the least substituted bond is favored (Table 1). In addition, loss of a Me radical from the molecular ion of III or IV was not detected in either spectrum. Also of interest is the relative abundances of the mass 119 and 120 ions in the spectrum of the monodeutero derivative V. After correcting for the natural heavy isotope contamination, the ratio of *m/e* 120 to *m/e* 119 is 0·91, i.e. a secondary isotope effect of this magnitude discriminates against α-cleavage on the side of the molecule containing the deuterium atom. This ratio is invariant at varied ionizing voltages (Table 2). This secondary deuterium isotope effect is of about the same order of magnitude as the primary deuterium isotope effect determined in the McLafferty rearrangement of esters and some related compounds.[7]

[*] Peak assignments are based on exact mass measurements, kindly carried out by Dr. Alan Duffield of Stanford University on an AEI MS9 mass spectrometer

III

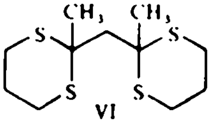


IV

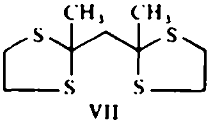


V

The symmetrical thioketals VI and VII gave single α-cleavage ions recorded at *m/e* 133 and *m/e* 119, respectively.



VI



VII

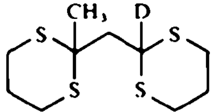
TABLE 1 PRINCIPAL PEAKS IN THE MASS SPECTRA OF BISTHIOACETALS AND BISTHIOKETALS AT 70 eV

| Compound | α-cleavage | Type I-cleavage | Type II-cleavage |
|---|---|---|---|
| I | *m/e* 119 (80%) | *m/e* 177 (15%) | *m/e* 145 (100%) |
| II | *m/e* 105 (100%) | *m/e* 163 (14%) | *m/e* 131 (82%) |
| III | *m/e* 119 (100%) | *m/e* 191 (29%) | *m/e* 159 (67%) |
| | *m/e* 133 (63%) | | |
| IV | *m/e* 105 (74%) | *m/e* 177 (18%) | *m/e* 145 (100%) |
| | *m/e* 119 (71%) | | |
| V | *m/e* 119 (64%) | *m/e* 177 (13%) | *m/e* 145 (79%) |
| | *m/e* 120 (58%) | *m/e* 178 (13%) | *m/e* 146 (94%) |
| VI | *m/e* 133 (100%) | | |
| VII | *m/e* 119 (100%) | · | — |
| VIII | *m/e* 120 (100%) | *m/e* 191 (40%) | *m/e* 159 (95%) |
| | *m/e* 133 (97%) | | |

*Type I cleavage– -Expulsion of* $C_3H_7S\cdot$ *and* $C_2H_5S\cdot$. All of the trimethylene thioacetals having a hydrogen atom attached to C-1 in one or both rings (i.e. I, III and V) undergo expulsion of $C_3H_7S\cdot$ upon electron impact. Correspondingly, the thioacetals prepared from ethanedithiol (II and IV) expel $C_2H_5S\cdot$. The bisthioketals (VI and VII) do not undergo an analogous fragmentation reaction.

This reaction involves a specific hydrogen migration from C-1 to the incipient expelled neutral fragment. This point was proved by comparing the mass spectrum of compound III with that of its monodeutero derivative VIII. Both compounds gave rise to the same unlabeled fragment ion at *m/e* 191, i.e. the deuterium atom was lost with the neutral species.

Benzaldehyde trimethylene thioacetal (IXa),[8] its monodeutero derivative X[8] and the trimethylene thioacetal of propionaldehyde all expel $C_3H_7S\cdot$ upon electron-impact. Therefore it is concluded that the hydrogen migrates to the proximal ring.



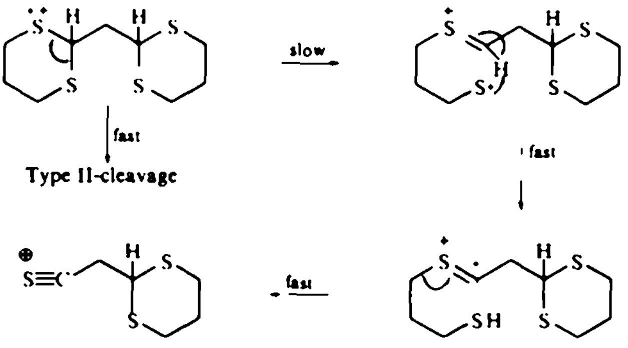
VIII

IX, R = H
X, R = D

The labeled parent compound V gave a pair of peaks at *m/e* 177 and *m/e* 178 as expected and after correcting for natural heavy isotope contamination these peaks were found to be of equal intensity; therefore no primary isotope effect was evident in this reaction even at lower voltages (Table 2). This result can be interpreted to mean that the cleavage of the C—H bond occurs after the rate determining step of the fragmentation reaction. Moreover this overall reaction occurs to a smaller extent (i.e. slower or possibly by faster secondary decomposition) than the Type II-cleavage, which does involve an isotope effect. The following mechanistic scheme is consistent with these results.

TABLE 2. VARIATION OF MASS SPECTRUM OF V WITH IONIZING VOLTAGE

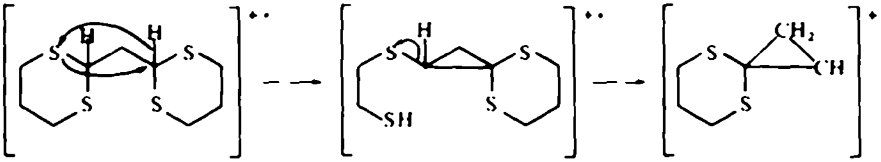
| Peak | 70 eV ($M^+$ = 42%) | 20 eV ($M^+$ = 44%) | 12 eV ($M^+$ = 60%) |
|---|---|---|---|
| *m/e* 119 | 64 | 46 | 14 |
| *m/e* 120 | 58 | 42 | 12·5 |
| *m/e* 145 | 79 | 71 | 61 |
| *m/e* 146 | 94 | 95 | 96 |
| *m/e* 177 | 13 | 11 | 5 |
| *m/e* 178 | 13 | 11 | 5 |



*Type* II *cleavage—Expulsion of* $C_3H_7S_2\cdot$ *and* $C_2H_5S_2\cdot$. The generation of the M-107 ($C_3H_7S_2\cdot$) fragment ion from I and III and the M-93 ($C_2H_5S_2\cdot$) ion from II and IV constitutes the most or second most important electron-impact reaction that these compounds undergo. Again as with the Type I cleavage, this reaction does not occur with the thioketals VI and VII. An appropriate metastable ion in each spectrum indicated that the fragmentation reaction proceeds, at least in part, in one step from the molecular ion.

The methylated labeled derivative VIII undergoes this reaction with the complete loss of deuterium with the neutral fragment. The labeled parent compound V loses hydrogen in preference to deuterium as evidenced by the relative intensities of the *m/e* 145 and *m/e* 146 ions. At 70 eV the ratio of *m/e* 145 to *m/e* 146 was 0·84; therefore the discrimination against deuterium transfer is of this magnitude. This primary isotope effect was extremely dependent on the ionizing voltage; as the voltage was lowered the discrimination against deuterium increased (Table 2). Thus the reaction became more selective as less energy was transferred to the molecular ion. This behavior might have been predicted for primary isotope effects and in fact two previous voltage dependent isotope effects have been reported.[9, 10]

Benzaldehyde trimethylene thioacetal (IX), its monodeutero derivative X and the thioacetals of propionaldehyde undergo this process to only a very small extent (3% of the base peak) and therefore it is concluded that the hydrogen is transferred to the distal ring in the Type II cleavage of the bis-thioacetals. The voltage dependent isotope effect is consistent with the following two step mechanism in which the first step leading to the rearranged molecular ion is the slower one.



*Low voltage results.* Table 2 shows the results of lowering the voltage from 70 eV to 12 eV on the spectrum of the labeled derivative V. It is clear that the process which requires the least energy is the Type II cleavage, whereas the α-cleavage is most affected by lowering the voltage. This result is somewhat surprising in view of the fact that the former reaction requires a rearrangement and the dissociation of at least three chemical bonds, while α-cleavage necessitates the rupture of only one bond.

## EXPERIMENTAL

Mass spectra were obtained by Mr. J. R. Sadecky on a CEC 21-103-C mass spectrometer equipped with an all-glass heated inlet system maintained at 150°. All of the compounds were shown to be stable toward these conditions since they were purified by distillation or sublimation under even more vigorous conditions. M.ps are uncorrected. The IR spectra were measured on a Perkin-Elmer Model 137 instrument and the NMR spectra on a Varian A-60 instrument. Chemical shifts are given in ppm from TMS as internal standard.

*General procedure for the preparation of thioketals and thioacetals.* The β-dicarbonyl compounds or dimethyl acetal derivatives in 0·5M benzene soln were heated under reflux with 2 equivs 1,2-ethanedithiol or 1,3-propanedithiol and 1 mg/mmole *p*-toluene-sulfonic acid as catalyst. The solns were heated for 24 to 48 hr, using a Dean Stark trap to collect and remove water and/or MeOH as formed. The cooled solns were washed with ice-cold $NaHCO_3$ aq and dried over $Na_2SO_4$. The benzene was evaporated under reduced press leaving crystalline or readily crystallized crude products. The products were purified by recrystallization. Samples for spectral analysis were further purified by sublimation.

The anticipated structures were corroborated by IR and NMR spectra and by the mass spectrometrically determined molecular weights.

*Malonaldehyde* bis-*ethylenethioacetal* was obtained in 97% yield from the reaction of malonaldehyde bis-dimethylacetal with 1,2-ethanedithiol. The product was recrystallized from $CH_2Cl_2$-hexane giving colorless crystals. A sublimed sample had m.p. 71–74°; $\nu_{\max}^{\text{Nujol}}$ 1425, 1275, 1225, 965 and 862 $cm^{-1}$; NMR ($CDCl_3$) 2·35 (2H, triplet, $J = 7$ c/s), 3·35 (8H, singlet) and 4·68 ppm (2H, triplet, $J = 7$ c/s); and M.W. 224.

*Malonaldehyde* bis-*trimethylene thioacetal* was obtained in quantitative yield from the reaction of malonaldehyde bis-dimethylacetal with 1,3-propanedithiol. Recrystallization from EtOAc afforded large, colorless crystals. A sublimed sample had m.p. 110–114°; $\nu_{\max}^{\text{Nujol}}$ 1425, 1278, 1250, 910, 872 and 728 $cm^{-1}$; NMR ($CDCl_3$) 2·2 (6H, broad multiplet), 2·90 (8H, unsym. triplet), and 4·32 ppm (2H, triplet, $J = 7·5$ c/s); and M.W. 252.

*Acetylacetaldehyde ethylenethioacetal ethylenethioketal* was obtained in 94% yield from the reaction of acetylacetaldehyde dimethylacetal with 1,2-ethanedithiol. The product was purified by distillation (140° bath at 0·05 mm) and recrystallization of the crystalline distillate from $CH_2Cl_2$–hexane. The purified product had m.p. 30–32°; $\nu_{\max}^{\text{Nujol}}$ 1425, 1280, 1070, 976 and 855 $cm^{-1}$; NMR ($CCl_4$) 1·77 (3H, singlet), 2·47 (2H, doublet, $J = 6$ c/s), 3·14 (4H, broad singlet), 3·30 (4H, singlet) and 4·57 ppm (1H, triplet, $J = 6$ c/s); and M.W. 238.

*Acetylacetaldehyde trimethylenethioacetal trimethylenethioketal* was obtained in 94% yield from the reaction of acetylacetaldehyde dimethylacetal with 1,3-propanedithiol. The product was recrystallized from $CH_2Cl_2$–hexane. A sublimed sample had m.p. 76–77°; $\nu_{\max}^{\text{Nujol}}$ 1420, 1275, 1180, 907 and 868 $cm^{-1}$; NMR ($CCl_4$) 1·55 (3H, singlet), 2·0 (4H, broad multiplet), 2·20 (2H, doublet, $J = 5$ c/s), 2·8 (8H, broad multiplet), and 4·09 ppm (1H, triplet, $J = 5$ c/s); and M.W. 266.

2,4-*Pentanedione bis-ethylenethioketal* was obtained in 84% yield from the reaction of 2,4-pentanedione with 1,2-ethanedithiol. The product was recrystallized from $CH_2Cl_2$–hexane. A sublimed sample had m.p. 57–58°; $\nu_{\max}^{\text{Nujol}}$ 1425, 1280, 1110, 1085, 1052 and 858 $cm^{-1}$; NMR ($CCl_4$) 1·88 (6H, singlet), 2·82 (2H, singlet), and 3·29 ppm (8H, singlet); and M.W. 252.

2,4-*Pentanedione bis-trimethylenethioketal* was obtained in 70% yield from the reaction of 2,4-pentanedione with 1,3-propanedithiol. The crude product slowly formed large, colorless crystals which had m.p. 73–74°; $\nu_{\max}^{\text{Nujol}}$ 1420, 1278, 1110, 1085, 910 and 876 $cm^{-1}$; NMR ($CDCl_3$) 2·00 (10H, singlet plus multiplet), and 2·90 ppm (10H, singlet plus unsym. triplet); and M.W. 270.

*Monodeuteration and methylation of malonaldehyde bis-trimethylenethioacetal.* THF (20 ml) was distilled from LAH into a dry, 3-neck flask under dry $N_2$. A sublimed sample of the bis-thioacetal (504 mg, 2 mmoles) was added and the resulting soln cooled in a dry ice–$CCl_4$ bath. The stirred soln was treated with 2 ml 1·7M n-BuLi in hexane and allowed to warm to 18° during 4 hr. A 2 ml aliquot of the yellow soln of the monoanion[*] was pipetted into 1 ml $D_2O$. The resulting mixture was diluted with $CH_2Cl_2$, dried with $MgSO_4$ and the solvents evaporated to give 45 mg crystalline product. After sublimation, the NMR ($CDCl_3$) spectrum of this substance showed a triplet at 4·32 ppm which integrated for one hydrogen, the 6H multiplet at 2·2 ppm could now be analyzed as a quintet (with additional fine splitting) and a doublet ($J = 7·5$ cps). The mass spectrum indicated a molecular weight of 253 and complete monodeuteration.

The remainder of the anion soln was treated with MeI (1·5 ml) giving, after workup, the same product obtained in the condensation of acetylacetaldehyde dimethylacetal with two moles of 1,3-propanedithiol.

*Deuteration of acetylacetaldehyde trimethylenethioacetal trimethylenethioketal.* The thioacetal anion (2 mmoles) was generated by the procedure described above. Quenching with $D_2O$ afforded 458 mg (86%) of crystalline product. The mass spectrum indicated a molecular weight of 267 and 20% (mono) deuteration.

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[*] We have been unable to detect the highly desirable dianion.

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