Synthesis of Sulfur-Containing Derivatives from Olefinic Fatty Esters

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ABSTRACT

The reaction of 3-mercaptopropan-1,2-diol with methyl 10-undecenoate (**Ib**) yielded three products, methyl 11-(3′-mercaptopropan-1′,2′-diacetoxy) undecanoate (**II**, 48.9%), methyl 11-(1′-oxapropan-2′-acetoxy-3′-mercaptoacetyl) undecanoate (**III**, 27.4%) and methyl 10-(3′-mercaptopropan-1′-acetoxy-2′-ol) undecanoate (**IV**, 23.0%) along with hydrolyzed starting material (**Ia**, 5.4%). The same reaction with methyl 9-octadecenoate (**Vb**) gave an isomeric product, 9(10)-(3′-mercaptopropan-1′-acetoxy-2′-ol) octadecanoic acid (**VI**, 78.5%) and oleic acid (**Va**, 21.4%). Reaction with *trans*-2-octadecenoic acid (**VII**) afforded 2(3)-(3′-mercaptopropan-1′-acetoxy-2′-ol) octadecanoic acid (**VIII**, 85.7%).

INTRODUCTION

The addition of sulfur and/or sulfur-containing reagents to unsaturated oils is frequently used in the production of commercial materials suitable as lubricant additives, plasticizers and rubber-like products. Recently, some thioethers have been synthesized and tested for antiinflammatory, neurotropic, bactericidal, fungicidal, anticholesteremic and hypolipemic activities (1–3). A few thioethers have also been reported as tranquilizers (4).

The addition of mercaptans (mercaptoacetic acid and thiols) to olefin is a well known reaction which generally proceeds by a free radical mechanism (5–10). In view of the abovementioned importance of thioethers, we have synthesized thioethers by the reaction of 3-mercaptopropan-1,2-diol with terminal, internal and α,β-unsaturated fatty esters in the presence of acetic acid and boron trifluoride (BF_3)-etherate as catalyst (11).

EXPERIMENTAL PROCEDURES

All melting points are uncorrected. Infrared (IR) spectra were obtained with a Perkin-Elmer 621 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were run in $CDCl_3$ on a Varian A60 spectrometer with tetramethylsilane (TMS) as the internal standard. Mass spectra were measured with AEI MS-30 and Kratos MS-45 spectrometers with a digital PD PB/1 data interface system. Thin layer chromatographic (TLC) plates were coated with silica gel. The spots were visualized by charring after spraying with a 20% aqueous solution of perchloric acid.

MATERIALS AND METHODS

Trans-2-octadecenoic acid, **VII** (mp 58–59 C) was prepared from stearic acid by the procedure of Palameta and Prostenik (12). The 2-enoic structure of this acid as well as its geometry was established by IR, NMR and mass spectrometry (13). The methyl esters of 10-undecenoic acid (**Ia**) and oleic acid (**Va**) were prepared by reaction with methanolic sulfuric acid (0.25 M).

Reaction of 3-Mercaptopropan-1,2-diol with Ib

Methyl 10-undecenoate, **Ib** (1.98 g, 10 mmol) in glacial acetic acid (20 mL) was reacted with 3-mercaptopropan-1,2-diol (1.08 g, 10 mmol) in the presence of few drops of BF_3-etherate catalyst at room temperature. The reaction was completed in ca. 35 min as shown by TLC. The reaction mixture was poured in water, extracted with ether, and the ether extract washed successively with sodium bicarbonate (5%) to remove catalyst and finally with water. The ethereal layer was dried over anhydrous sodium sulfate and evaporation of ether yielded a viscous oil (1.85 g) showing four distinct spots on TLC (petroleum ether/ether/acetic acid, 80:20:1, v/v).

The reaction mixture was chromatographed over Silica Gel G (35 g) column using petroleum ether/ether as eluant. Fractions of 15 mL were collected. Elution with petroleum ether/ether (97:3, v/v) gave hydrolyzed starting material, **Ia** (0.10 g, ca. 5.4%) as a colorless liquid. Further elution with petroleum ether/ether (92:8, v/v) yielded the major product, methyl 11-(3′-mercaptopropan-1′,2′-diacetoxy) undecanoate, **II** (0.8 g, ca. 48.9%). It resisted all attempts of crystallization. Analysis: calc. for $C_{19}H_{34}O_6S$: C, 58.46; H, 8.72. Found: C, 58.22; H, 8.51%.

Elution with petroleum ether/ether (88:12, v/v) gave methyl 11-(1′-oxapropan-2′-acetoxy-3′-mercaptoacetyl) undecanoate, **III** (0.5 g, ca. 27.4%) as a colorless liquid. Analysis: calc. for $C_{19}H_{34}O_6S$: C, 58.46; H, 8.72. Found: C, 58.37; H, 8.63%.

Elution with petroleum ether/ether (71:29, v/v) afforded methyl 10-(3′-mercaptopropan-1′-acetoxy-2′-ol) undecanoate, **IV** (0.42 g, ca. 23.0%) as a viscous liquid product. Analysis: calc. for $C_{17}H_{32}O_5S$: C, 58.62; H, 9.19. Found: C, 58.46; H, 9.07%.

Reaction of 3-Mercaptopropan-1,2-diol with Vb

A similar reaction of methyl *cis*-9-octadecenoate, **Vb** (1.48 g, 5 mmol) in acetic acid (15 mL) with 3-mercaptopropan-1,2-diol (0.54 g, 5 mmol) in the presence of BF_3-etherate was completed in 30 min at room temperature. Final work-up yielded an oily substance (1.42 g), which showed two distinct spots on TLC. The reaction mixture was chromatographed over Silica Gel G (30 g) column using petroleum ether/ether. Elution with petroleum ether/ether (97:3, v/v) gave hydrolyzed starting material, oleic acid, **Va** (0.3 g, ca. 21.4%).

Elution with petroleum ether/ether (75:25, v/v) afforded the isomeric product, 9(10)-(3′-mercaptopropan-1′-acetoxy-2′-ol) octadecanoic acid, **VI** (1.1 g, ca. 78.5%) as a viscous liquid, which resisted all attempts of crystallization. Analysis: calc. for $C_{23}H_{44}O_5S$: C, 63.88; H, 10.17. Found: C, 63.59; H, 10.03%.

Reaction of 3-Mercaptopropan-1,2-diol with VII

The reaction of *trans*-2-octadecenoic acid, **VII** (1.41 g, 5 mmol) with 3-mercaptopropan-1,2-diol (0.54 g, 5 mmol) in acetic acid (15 mL) and BF_3-etherate did not take place at room temperature as described above. On heating the reaction mixture at 120 C for 1 hr, a product of low R_f value was observed on TLC along with starting material. The usual work-up yielded a viscous oil (1.40 g), which was chromatographed over Silica Gel G (28 g) column. Elution with petroleum ether/ether gave compound **VII** (0.19 g, ca. 13.5%). Elution with petroleum ether/ether (73:27, v/v)

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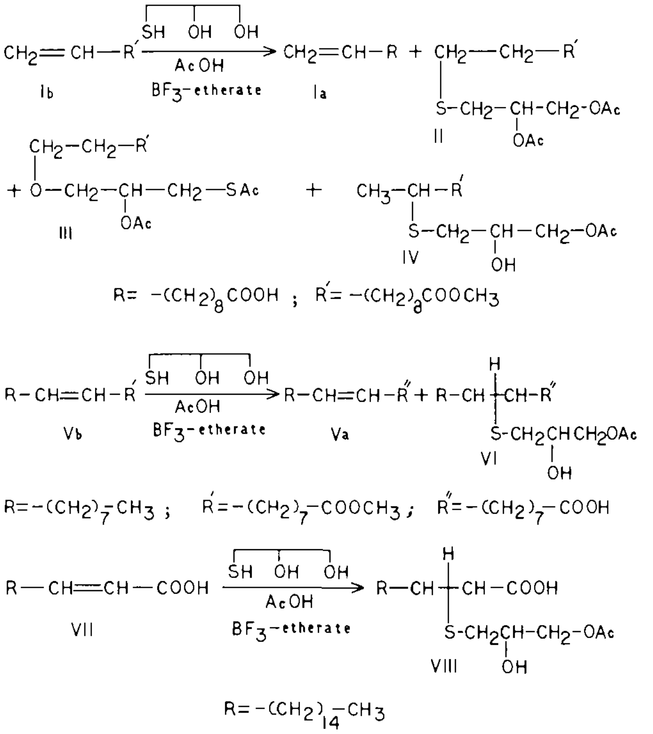
gave semisolid 2(3)-(3′-mercaptopropan-1′-acetoxy-2′-ol) octadecanoic acid, **VIII** (1.2 g, ca. 85.7%). Analysis: calc. for $C_{23}H_{44}O_5S$: C, 63.88; H, 10.17. Found: C, 63.41; H, 10.07%.



SCHEME 1

RESULTS AND DISCUSSION

The reaction of methyl 10-undecenoate (**Ib**) with 3-mercaptopropan-1,2-diol gave three products, **II**, **III** and **IV** (Scheme 1) which were characterized by combustion and spectroscopic data.

Compound **II** analyzed for $C_{19}H_{34}O_6S$. Its IR spectrum displayed bands at 1750 ($OC\underline{O}CH_3$), 1735 ($\underline{CO}OCH_3$), 1440 (CH_2–S deformation), 1235 (CH_2–S wagging), 1220 (acetate), 1090 and 1040 cm^{-1} (C–O). The presence of acetate group suggested that primary and secondary hydroxy functions had been derivatized to the corresponding acetate in the presence of acetic acid and BF_3-etherate. The NMR spectrum of **II** gave further support to the assigned structure, in that it gave signals at δ 5.15 m (1H, $C\underline{H}$–OAc), 4.22 d (2H, $C\underline{H}_2$–OAc), 2.65 m (4H, $C\underline{H}_2$–S–$C\underline{H}_2$), and 2.15 s (6H, 2 × $OCOC\underline{H}_3$). The larger yield of this product is probably related to the fact that sulfur has a greater tendency to increase its covalency than oxygen. That is why the attack of SH is preferred in comparison to OH. The structure of **II** was further substantiated by its mass spectral analysis (Fig. 1), which showed molecular ion peak at m/e 390 ($C_{19}H_{31}O_5S$). The genesis of structure-revealing fragment ions supports the structure of linear product, methyl 11-(3′-mercaptopropan-1′,2′-diacetoxy) undecanoate, **II**, assigned on the basis of chemical analysis, IR and NMR spectral values.

Compound **III** analyzed for $C_{19}H_{34}O_6S$. Its IR spectrum had bands at 1750 ($OC\underline{O}CH_3$), 1740 ($SC\underline{O}CH_3$), 1730 ($\underline{CO}OCH_3$), 1430 (CH_2–S deformation), 1230 (acetate and CH_2–S wagging), 1070 and 1035 cm^{-1} (C–O). NMR spectrum of **III** had signals at δ 5.13 m (1H, $C\underline{H}$–OAc), 4.12 m (4H, $C\underline{H}_2$–O–$C\underline{H}_2$), 2.70 d (2H, ($C\underline{H}_2$–SAc), 2.3 t (2H, $C\underline{H}_2$–$COOCH_3$), 2.18 s (6H, $SOC\underline{H}_3$ and $OCOC\underline{H}_3$) and 1.25 br, s (chain–$C\underline{H}_2$). From these data, **III** was formulated as methyl 11-(1′-oxapropan-2′-acetoxy-3′-mercaptoacetyl) undecanoate. This product is obtained by the addition of reagent from the hydroxy function side, which is less preferred. Therefore, the yield of compound **III** is lower than that of **II**.

Its mass spectrum was quite consistent with the structure of **III**, and showed molecular ion peak at m/e 390 ($C_{19}H_{34}O_6S$) followed by other salient peaks. The genesis of diagnostic fragment ions is shown in Figure 2.

The elemental analysis of minor product **IV** corresponded to molecular formula $C_{17}H_{32}O_5S$. The IR spectrum of **IV** had bands at 3320 (CH–O$\underline{H}$), 1745 ($OC\underline{O}CH_3$), 1735 ($\underline{CO}OCH_3$), 1435 (CH_2–S deformation), 1370 (CH_3 stretching), 1240 (CH_2–S wagging), 1225 (acetate) and 1030 cm^{-1} (C–O). The NMR peaks observed were at δ 4.68 (1H, CH–O$\underline{H}$, disappeared on D_2O shaking), 4.1 d (2H, $C\underline{H}_2$–OAc), 3.7 m (1H, $C\underline{H}$–OH, merged with ester protons), 3.65 s (3H, $COOC\underline{H}_3$), 2.58 m (3H, $C\underline{H}$–S–$C\underline{H}_2$), 2.7 t (2H, $C\underline{H}_2$–$COOCH_3$), 2.05 s (3H, $OCOC\underline{H}_3$), 1.25 br, s (chain–$C\underline{H}_2$) and 0.90 d (3H, CH–$C\underline{H}_3$). All these data led to the conclusion that compound **IV** was methyl 10-(3′-mercaptopropan-1′-acetoxy-2′-ol) undecanoate.

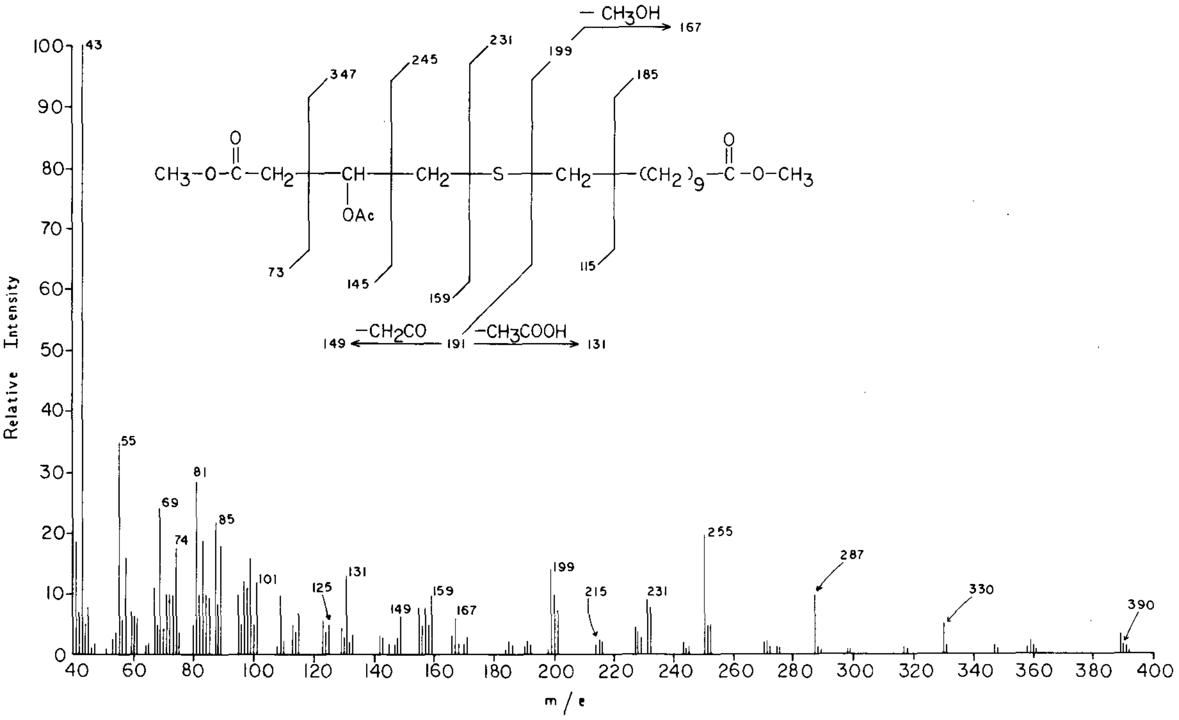
The structure of this branched product, **IV**, was further confirmed by its mass spectrum. It gave the molecular ion peaks at m/e 348 ($C_{17}H_{32}O_5S$) followed by other salient peaks. The structure-identifying fragment ions are shown in Figure 3.

A similar reaction with methyl oleate (**Vb**) yielded the product **VI** as an isomeric mixture, along with oleic acid (**Va**). Compound **VI** analyzed for $C_{23}H_{44}O_5S$. The IR spectrum of **VI** showed bands at 3360 ($COO\underline{H}$ and CH–O$\underline{H}$), 1750 ($OC\underline{O}CH_3$), 1710 ($\underline{CO}OH$), 1230 (acetate) and 1025 cm^{-1} (C–O). The NMR spectrum of **VI** had signals at δ 5.9 (1H, CH–O$\underline{H}$, disappeared on D_2O exchange), 4.0 d (2H, $C\underline{H}_2$–OAc), 3.75 m (1H, $C\underline{H}$–OH), 2.7 m (3H, $C\underline{H}$–S–$C\underline{H}_2$), 2.05 s (3H, $OCOC\underline{H}_3$) as well as other peaks expected for fatty acids. The disappearance of an ester peak at δ 3.65 showed that the ester function is hydrolyzed to the carboxylic group. On the basis of these data, **VI** was formulated as 9(10)-(3′-mercaptopropan-1′-acetoxy-2′-ol) octadecanoic acid.

A similar reaction was conducted with *trans*-2-octadecenoic acid (**VII**) to give the isomeric addition product **VIII**. Microanalysis of this product gave composition as $C_{23}H_{44}O_5S$ with characteristic IR bands at 3380–3430 ($COO\underline{H}$ and CH–O$\underline{H}$), 1745 ($OC\underline{O}CH_3$), 1710 ($\underline{CO}OH$), 1230 (acetate), 1080 and 1040 cm^{-1} (C–O). The NMR spectrum of **VII** was devoid of any signal for vinylic protons and exhibited peaks at δ 5.0 br, s (1H, CH–O$\underline{H}$, removed on addition of D_2O); 4.1 d (2H, $C\underline{H}_2$–OAc), 3.72 m (1H, $C\underline{H}$–OH), 2.9 m (3H, $C\underline{H}$–S–$C\underline{H}_2$), 2.3 m (2H, $C\underline{H}_2$–COOH), 2.1 s (3H, $OCOC\underline{H}_3$) and other usual peaks of fatty acids. From these data, **VIII** was characterized as 2(3)-(3′-mercaptopropan-1′-acetoxy-2′-ol) octadecanoic acid.

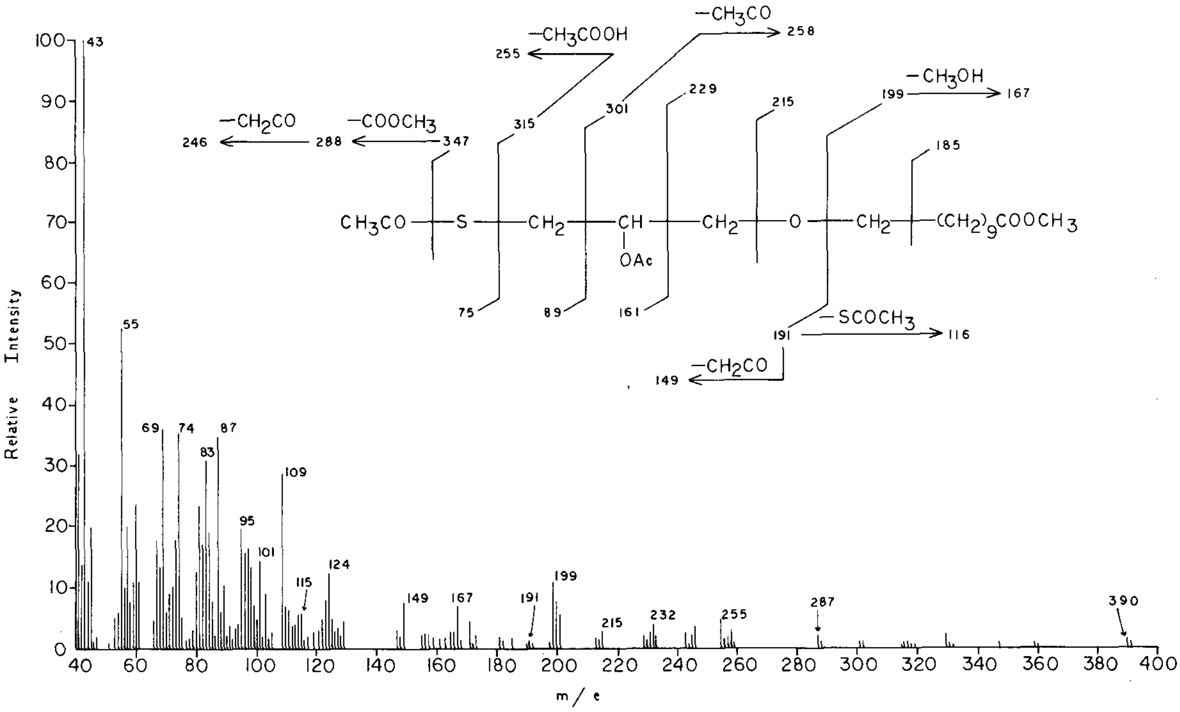
The above structure of **VIII** was further supported by its mass spectrum. It gave molecular ion peak at m/e 432 ($C_{23}H_{44}O_5S$) followed by other expected peaks. The mass spectral fragmentation pattern of **VIII** is shown in Fig. 4. The fragment ions m/e 59, 207 and 221 clearly established the fact that the compound **VIII** is an isomeric mixture.

From the foregoing discussion, it can be summarized that the results are in agreement with the earlier observations except the one where the addition took place according to Markownikoff's rule.



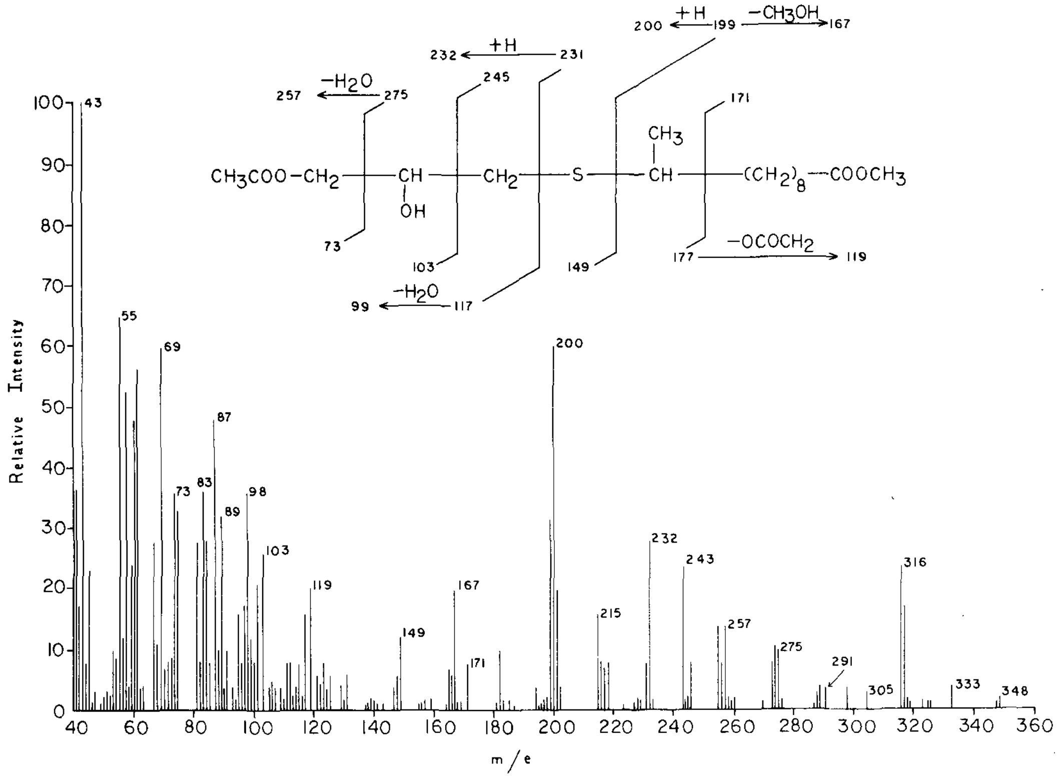
m/e 390 (M$^{+\cdot}$), (M+1, M+2), 359 (M−OCH$_3$), 347 (M−CH$_3$CO), 331 (M−OCOCH$_3$ or 359−CO), 317 (331−CH$_2$), 257 (317−CH$_3$COOH), 74 (McLafferty ion), and 43 (CH$_3$CO, base peak).

FIG. 1. Mass spectrum of II.



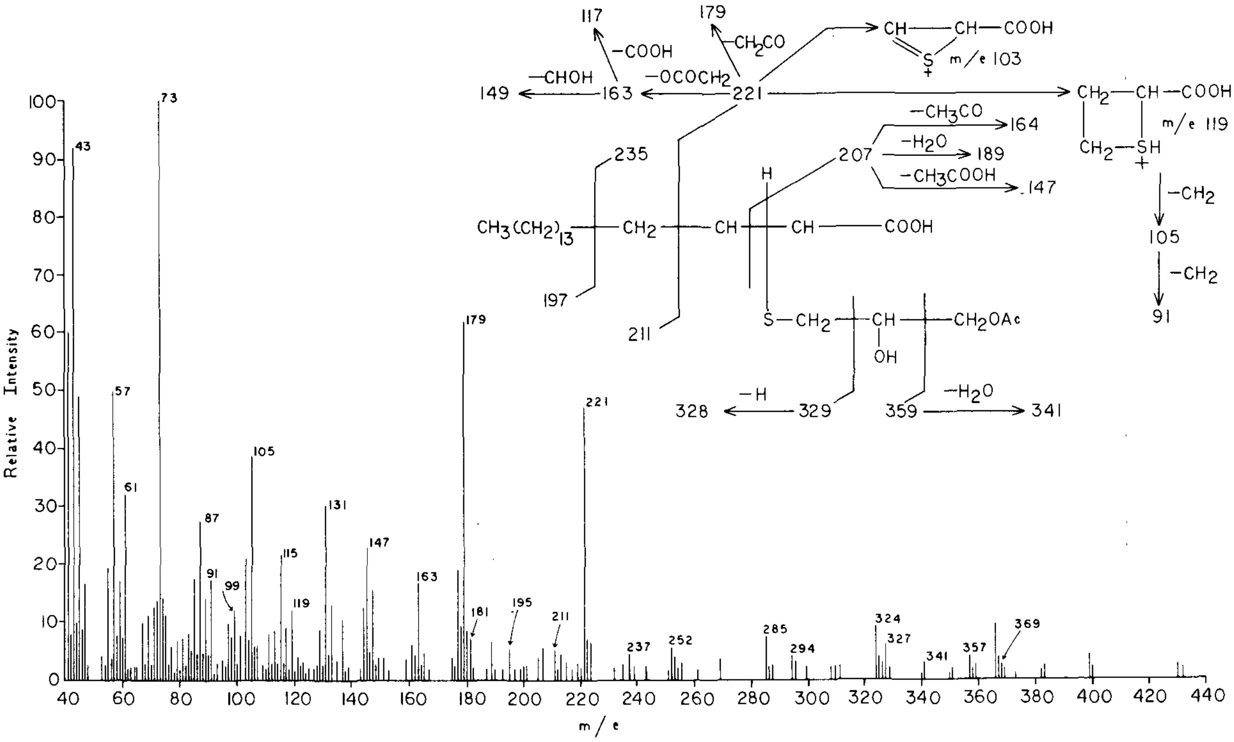
m/e 390 (M^{+}), (M+1), 347 (M−CH$_3$CO), 331 (M−OCOCH$_3$ or M−COOCH$_3$), 330 (331−H), 317 (331−CH$_2$), 287 (330−CH$_3$CO), 232 (246−CH$_2$), and 43 (CH$_3$CO, base peak).

FIG. 2. Mass spectrum of III.



m/e 348 (M^{+}), (M+1), 333 (M−CH$_3$), 316 (M−CH$_3$OH), 305 (M−CH$_3$CO), 289 (M−OCOCH$_3$ or M−COOCH$_3$), 275 (289−CH$_2$), 218 (275−COOCH$_3$), and 43 (CH$_3$CO, base peak).

FIG. 3. Mass spectrum of IV.



m/e 432 (M^{+}), (M+1), 399 (M−SH), 382 (399−OH), 369 (383−CH$_2$), 327 (369−CH$_2$CO), 324 (369−COOH), 294 (369−CH$_3$COOCH$_3$), 221 (235−CH$_2$), 131 (164−SH), 73 (CH$_2$OCOCH$_3$, base peak), 59 (CH$_2$COOH), and 43 (CH$_3$CO).

FIG. 4. Mass spectrum of VIII.

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