☘Synthesis of Sulfur Heterocycles from α, β-Unsaturated Carbonyl Fatty Acid Esters

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ABSTRACT

Alkyl chain substituted oxathiolanes from allylic oxo are described. Reaction of methyl 4-oxo-*trans*-2-hexadecenoate (I) with β-mercaptoethanol yields methyl 4-oxathiolane-*trans*-2-hexadecenoate (II), methyl 4-oxathiolane-2(3)-($\underline{S}$-β-mercaptoethyl acetate) hexadecanoate (III) and methyl 4-oxathiolane-2(3)-($\underline{S}$-β-mercaptoethanol)hexadecanoate (IV).

INTRODUCTION

Mercaptans of higher molecular weight are of industrial importance. Some thioethers are successfully tested for bactericidal, fungicidal (1) and hypolipemic activities (2) and biological activity of oxathiolanes are known in the literature. With the view of introducing these 2 functionalities in the fatty acid chain, an attempt has been made to carry out the reaction of methyl 4-oxo-*trans*-2-hexadecenoate with β-mercaptoethanol using the method adopted by Fieser (3). This communication reports the preparation and characterization of new derivatives containing both the oxathiolane and thioether moieties.

EXPERIMENTAL PROCEDURES

Infrared (IR) spectra were obtained with a Perkin-Elmer 621 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian A60 spectrometer; chemical shifts were measured in relation to tetramethylsilane (TMS) in ∂ (ppm). The samples were run as 10% solution in CCl_4. The abbreviations s, m, d, t and br, stand for singlet, multiplet, doublet, triplet and broad. Mass spectra (MS) was measured with an AEIMS-902 mass spectrometer.

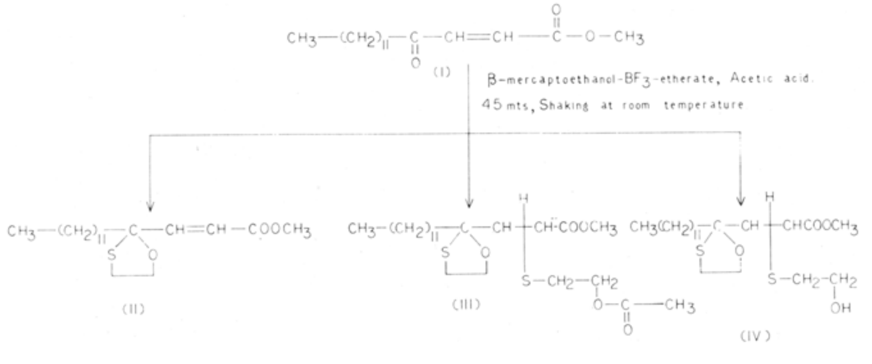
Analytical thin layer chromatography (TLC) was done on glass plates (20 × 5 cm) with a layer of silica gel G (0.25 mm thickness). Mixtures of petroleum ether/diethyl ether/acetic acid (70:30:1, v/v/v) were used as developing solvents. Components were made visible on TLC plates by spraying with an aqueous solution (20%) of perchloric acid and heating at 120 C.

Compound I was synthesized and characterized by the method we had adopted earlier (4).

Reaction of I with an Excess of β-Mercaptoethanol

A solution of methyl 4-oxo-*trans*-2-hexadecenoate (I) (2 g) in acetic acid (30 mL), β-mercaptoethanol (8 mL) and boron trifluoride-etherate (16 mL) was stirred at room temperature for 50 min following the procedure of Fieser (3). Progress of the reaction was monitored by TLC. At the end of the reaction, solvent was removed under reduced pressure. The residue was extracted with ether, washed with a 5% solution of sodium bicarbonate and dried over anhydrous Na_2SO_4. After evaporation of solvent, 1.9 g of liquid was obtained, which was chromatographed over silica gel (40 g) and provided 3 products (Scheme 1). Elution with petroleum ether/diethyl ether (94:6, v/v) gave compound II; yield is 10.4%. (Found: C, 66.57; H, 10.0; calculated for $C_{19}H_{34}O_3S$: C, 66.62; H, 10.0%), IR(neat): 1730-($\underline{CO}OCH_3$), 1650, 980 (*trans*-olefin), 1440(S-CH_2 def.), 1200, 1220, 1280 (S-CH_2 wag.), 1120 (C-O stretch.), 1020, 1040 cm^{-1}(oxathiolane or hemithioketal group); NMR-(CCl_4): ∂ 6.82 d(1H, C$\underline{H}$=CH-$COOCH_3$, J=14Hz), 5.82 d(1H, CH=C$\underline{H}$-$COOCH_3$, J=14Hz), 3.9-4.3 m(2H, protons α to oxygen in oxathiolane ring), 3.75 s(3H, COOC$\underline{H}_3$), 2.78-2.98(2H, protons α to sulfur in oxathiolane ring), 1.8 m (protons α to oxathiolane ring), 1.25 br,s(chain-C$\underline{H}_2$), 0.88 t (3H, terminal CH_3); mass: $M^{+\cdot}$ 342 (Fig. 1). Further elution with petroleum ether/ diethyl ether (90:10, v/v) gave compound III; yield is 48%. (Found: C, 59.6; H, 9.14; calculated for $C_{23}H_{42}O_5S_2$: C, 59.70; H, 9.14%). IR-(nujol): 1740 br(O$\underline{CO}CH_3$, $\underline{CO}OCH_3$), 1435 (S-CH_2 def.), 1270 (CH_3COO), 1250(S-CH_2 wag.), 1110 (C-O stretch.), 1020 cm^{-1}(oxathiolane ring); NMR (CCl_4): ∂ 4.42-3.91 m(4H, two protons α to oxygen in oxathiolane ring, C$\underline{H}_2$-O-$COCH_3$), 3.65, 3.62 s(3H, COOC$\underline{H}_3$), 3.18-2.52 m (5H, 2 protons α to sulfur in oxathiolane ring, C$\underline{H}$-S-C$\underline{H}_2$), 2.46 m (α to ester carbonyl), 2.02 s (OCOC$\underline{H}_3$), 1.8 m(protons α to oxathiolane ring), 1.5 br,s(chain-C$\underline{H}_2$), 0.85 t(3H, terminal CH_3); mass: $M^{+\cdot}$ 462 (Fig. 2). Final elution with petroleum ether/diethyl ether (85:15, v/v) gave compound IV; yield is 38.1%. (Found: C, 59.89; H, 9.59; calculated for $C_{21}H_{40}O_4S_2$: C, 59.95; H, 9.58%). IR(Nujol): 3400 (OH), 1740-($\underline{CO}OCH_3$), 1410(S-CH_2 def.), 1250(S-CH_2 wag.), 1125-(C-O stretch.) and 1020 cm^{-1} (oxathiolane ring); NMR-(CCl_4): ∂ 4.32-3.92 m(411, 2 protons α to oxygen in

SCHEME 1



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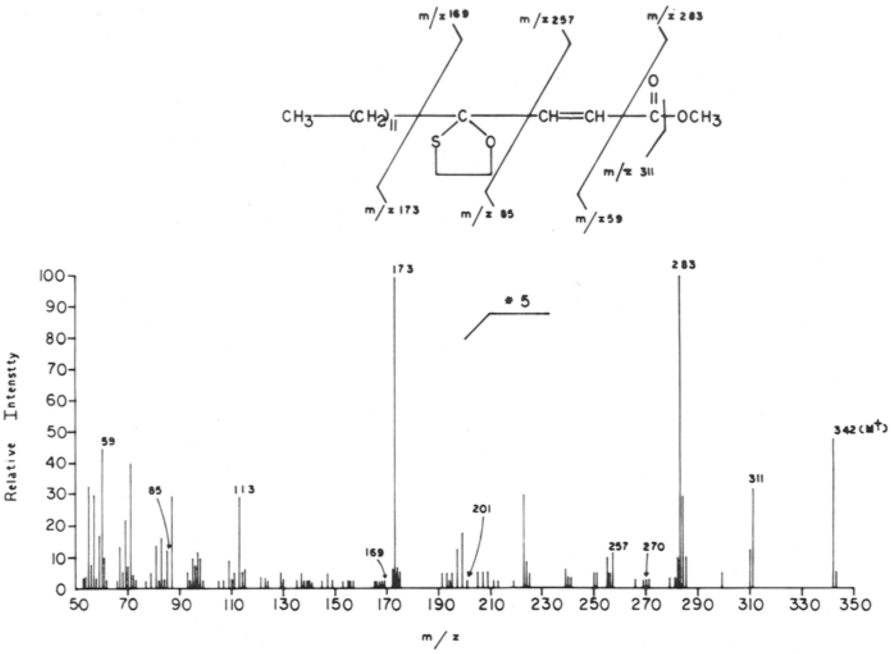


FIG. 1. MS of Methyl 4-oxathiolane-*trans*-2-hexadecenoate.

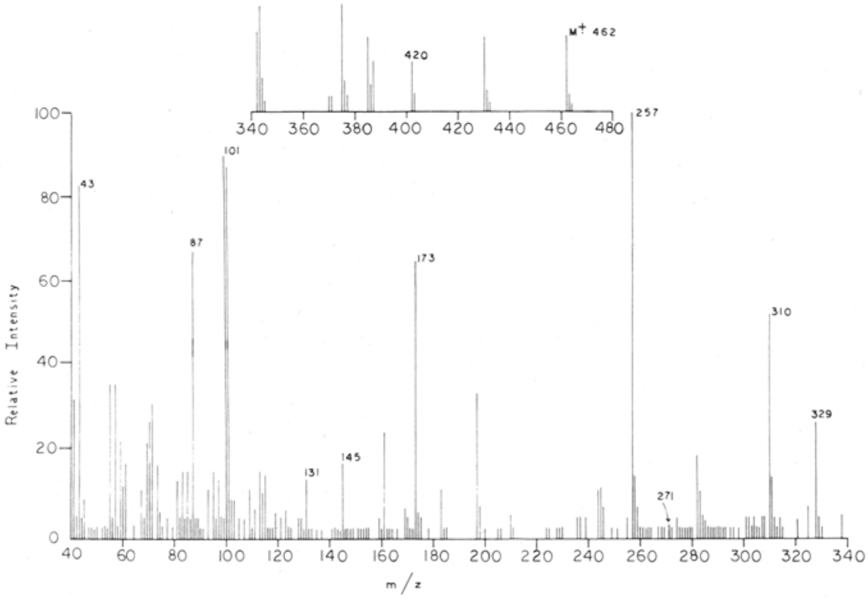


FIG. 2. MS of methyl 4-oxathiolane-2(3)-(*S*-β-mercaptoethyl acetate) hexadecanoate.

oxathiolane ring, -C$\underline{H}_2$-OH), 3.9 br,s(1H, O$\underline{H}$, D_2O exchangeable), 3.7, 3.68 s (3H, COOC$\underline{H}_3$), 3.45-2.72 m(5H, 2 protons α to sulfur in oxathiolane ring, -C$\underline{H}$-S-C$\underline{H}_2$), 2.83 m(protons α to ester carbonyl), 1.72 m(prontons α to oxathiolane ring), 1.25 br, s(chain-C$\underline{H}_2$-), 0.82 t(3H, terminal CH_3), mass: $M^{+\cdot}$ 420 (Fig. 3).

RESULTS AND DISCUSSION

Elemental analysis of compound II corresponded to the formula $C_{19}H_{34}O_3S$. Illustration of IR bands at 1650 and 980 cm^{-1} indicates that the *trans* double bond remained unaffected and diagnostic bands at 1020 and 1040 cm^{-1} supported the formation of oxathiolane(hemithioketal) grouping at the site of 4-oxo. Conclusive support in favor of methyl 4-oxathiolane-*trans*-2-hexadecenoate (II) has come from its NMR spectrum. Signals at ∂ 5.82 d(J=14) and ∂ 6.82 d(J=14Hz) for 1 proton each are assigned to α,β-unsaturated protons. The J value confirms a *trans*-unsaturation. Downfield appearance of 2 multiplets at ∂ 3.9-4.3 and ∂ 2.78-2.98 integrating for 2 protons each are ascribable to the protons α to oxygen and sulfur in the oxathiolane ring, respectively. MS of compound II showed $M^{+\cdot}$ 342. Few important fragmentations are shown in Figure 1.

Compound III was found to have a composition, $C_{23}H_{42}O_5S_2$, consistent with methyl 4-oxathiolane-2(3)-(*S*-β-mercaptoethyl acetate) hexadecanoate. IR showed characteristic bands at 1270 and 1020 cm^{-1} for acetate and oxathiolane moieties in the molecule. Disappearance of IR bands at 1640 and 970 cm^{-1} and vinylic protons indicate the consumption of the double bond and formation of thioether at the very site. Appearance of a 5-proton multiplet at ∂ 3.18-2.52 indicates that the attack of mercapto-

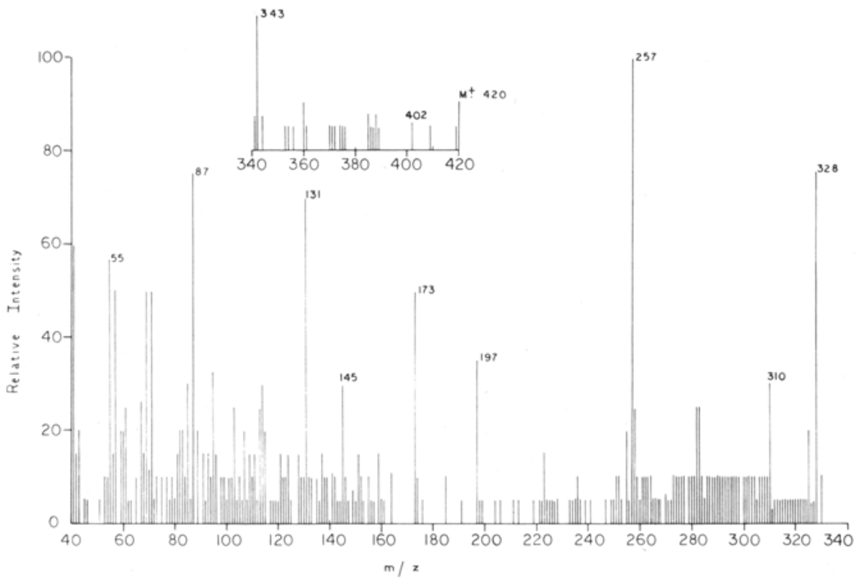
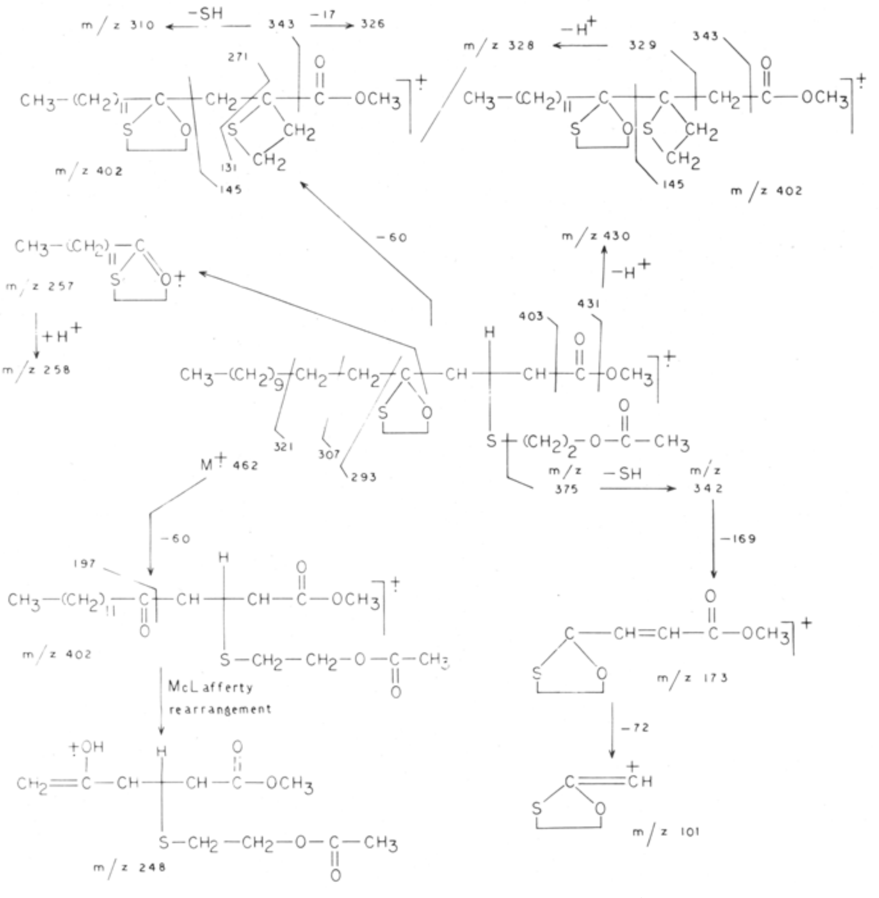


FIG. 3. MS of methyl 4-oxathiolane-2(3)(*S*-β-mercaptoethanol) hexadecanoate.

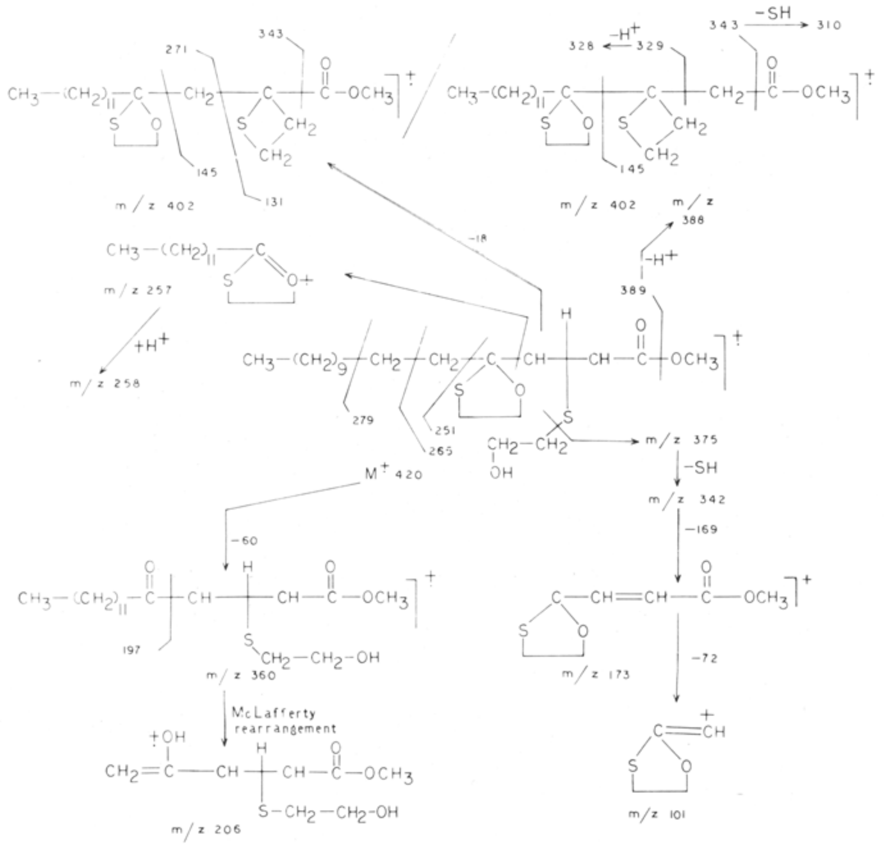
SCHEME 2



ethanol is through sulfur not through oxygen, otherwise its integration would have been 1 proton less and integration at signal ∂ 4.42-3.91 would have shown 5 protons instead of 4. The 2 sharp singlets of equal intensities at ∂ 3.65 and 3.62 for ester protons indicate the formation of an isomeric mixture of thioethers in almost equal amount on the α- as well as the β-carbon. A sharp singlet of 3 protons at ∂ 2.02 supports the acetylation of the hydroxy group. The mass of compound III ($M^{+\cdot}$ 462) shows important fragment ions m/z 402, 375, 342, 329 and 131 (Scheme 2), which confirms the formation of an isomeric mixture as well as the attack through sulfur instead of through oxygen. NMR and MS confirm that the attack on the double bond proceeds via sulfur, which is a better nucleophile than oxygen (5).

Compound IV was analyzed for $C_{21}H_{40}O_4S_2$. IR of the compound methyl 4-oxathiolane-2(3)-(*S*-β-mercaptoethanol) hexadecanoate (IV) showed usual bands along with a broad band for hydroxy grouping at 3400 cm^{-1}, which indicates

SCHEME 3



nonconversion of hydroxy into acetate. The previous situation applies here also as far as the formation of an isomeric mixture of thioethers and the attack of sulfure are concerned. The mass spectrum (M^{+} 420) confirms the existence of an isomeric mixture and attack through sulfur by fragment ions m/z 402, 375, 342, 329 and 131 (Scheme 3).

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REFERENCES

1. Zirnigibl, L., J. Fischer and K. Thiele, Chem. Abstr. 88:89673j (1978).
2. Victor, L., and L. Louis, Chem. Abstr. 88:50510d (1978).
3. Cavill, G.W.K., and D.H. Soloman, J. Chem. Soc. 3943 (1954).
4. Mustafa, J., M.S. Ahmad, Jr., A. Rauf and S.M. Osman, JAOCS 61:555 (1984).
5. Husain, S.R., F. Ahmad and M. Ahmad, JAOCS 60:1340 (1983).

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