

Studies on Organo Sulfur Compound. V.¹⁾ The Reaction of 4-Alkylidene-1,3-oxathiolane-2-thiones and Metal Xanthate

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In the reaction of α -acetylenic alcohol and carbon disulfide, three compounds (4-alkylidene-1,3-oxathiolane-2-thione, -1,3-dithiolane-2-thione and -1,3-oxathiolane-2-one) were obtained.^{3,4)}

In this paper it became clear that the formation of two compounds (V and VI) of them was due to the reaction of sodium α -acetylenyl xanthate (III) and IV by using 3-phenyl-2-propyn-1-ol.

New 4-alkylidene-1,3-dithiolane-2-thiones (XXIV and XXVI) were easily prepared from 4-alkylidene-1,3-oxathiolane-2-thiones (XXIII and XXV) and commercially available potassium xanthate.

In the previous papers^{3,4)} the authors reported that the syntheses of 4-alkylidene-1,3-oxathiolane-2-thiones (IV) were achieved by hydrolytic intramolecular cyclization of sodium α -acetylenic xanthates prepared from α -acetylenic alcohols and carbon disulfide, and in these reactions, besides IV, corresponding 1,3-dithiolane-2-thiones (V) and 1,3-oxathiolane-2-ones (VI) were occasionally formed.

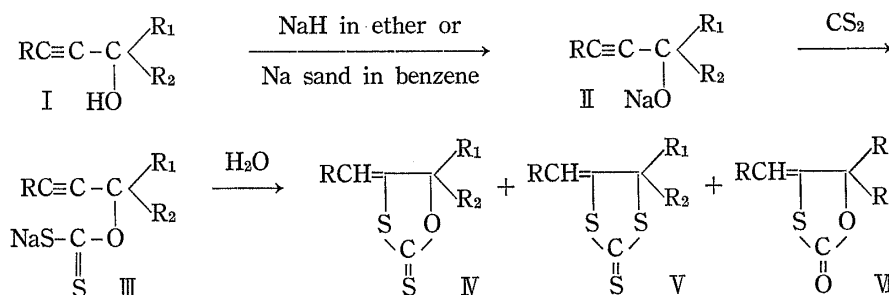


Chart 1

The formation of IV was comprehensible but those of the other cyclic compounds (V and VI) were yet in question, so we wished to elucidate the mechanism of the formation of 4-alkylidene-1,3-dithiolane-2-thiones (V) and to know the condition under which such cyclic trithiocarbonates were obtained in good yield. We had made a detailed investigation for the formation of 4-benzylidene-1,3-dithiolane (XII): 3-phenyl-2-propyn-1-ol (X) was more conveniently chosen as the resulting dithiolanethione (XII) and oxathiolanethione (XIII) were both well defined crystalline compounds having sharp melting points and under a strict condition 4-benzylidene-1,3-oxathiolane-2-thione was obtained in almost quantitative yield.

On the syntheses of 1,3-oxathiolane-2-thiones (IV) a large excess of carbon disulfide was generally used. If the excess of carbon disulfide were responsible for production of the cyclic trithiocarbonate (V), the following mechanism (Chart 2) might be postulated to account for

- 1) Part IV: K. Tomita and M. Nagano, *Chem. Pharm. Bull.* (Tokyo), **16**, 1911 (1968).
- 2) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
- 3) K. Tomita, M. Nagano, and H. Oka, *Chem. Pharm. Bull.* (Tokyo), **16**, 910 (1968).
- 4) K. Tomita and M. Nagano, *Chem. Pharm. Bull.* (Tokyo), **16**, 1324 (1968).

the formation of V. But this assumption was denied from the experiment. Isolated sodium 3-phenyl-2-propynyl xanthate (XI) was treated with a large excess carbon disulfide to afford only 4-benzylidene-1,3-oxathiolane-2-thione (XIII), and no expected 4-benzylidene-1,3-dithiolane-2-thione (XII) could be isolated.

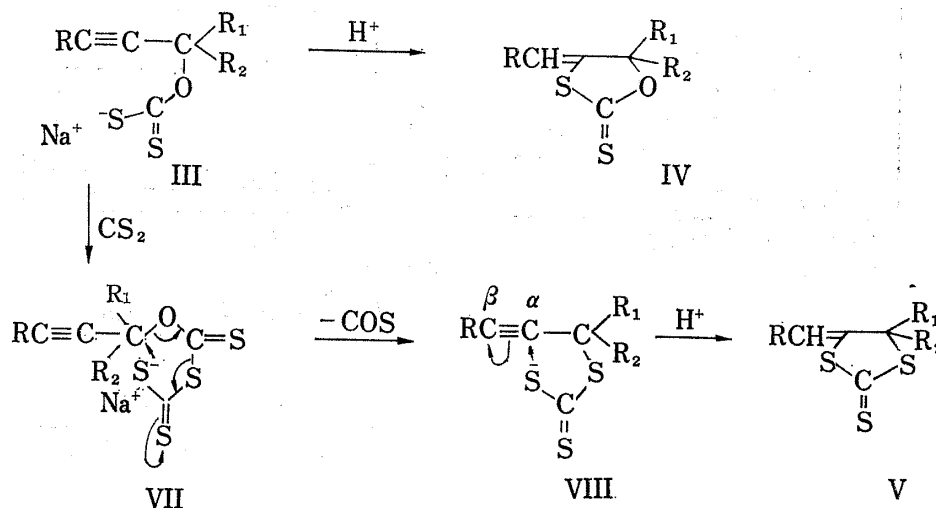
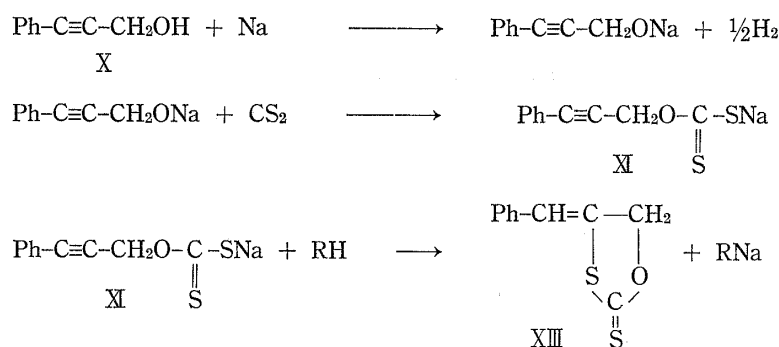


Chart 2

A convenient explanation of the formation of 4-benzylidene-1,3-oxathiolane-2-thione is provided by the following equations.



If the starting alcohol were an available proton source (RH), this cyclization should be proceeded in the presence of catalytic amount of sodium. When about one third equivalent of sodium hydride to 3-phenyl-2-propyn-1-ol was used in this reaction, the reaction produced a mixture of the expected compound (XIII) in minor and unexpected one (XII) in major.

It was assumed that 4-benzylidene-1,3-oxathiolane-2-thione (XIII) was the precursor of 4-benzylidene-1,3-dithiolane-2-thione (XII), and the former was reacted with some coexisting reagent to afford XII. Attempts to synthesize XII by the reaction of XIII with carbon disulfide in the presence of sodium hydride, or XIII with sodium alcoholate, were failed, but the desired compound (XII) was obtained by adding absolute ethanol to the former reaction mixture. Under this reaction condition sodium O-ethyl xanthate should be formed. The reaction of XIII with potassium O-ethyl xanthate also formed XII and the precipitated salts were treated with methyl iodide to give S-methyl-O-ethyl thiolcarbonate besides S-methyl-O-ethyl xanthate. This reaction was extended to other 4-alkylidene-1,3-oxathiolane-2-thiones (XX, XXIII and XXV) to afford corresponding cyclic trithiocarbonates (XXI, XXIV and XXVI), however, in the case of XX, the rearranged isomer (XXII) was obtained rather than XXI which was easily rearranged into the former with base.³⁾

When the sodium alcoholate prepared from 3-phenyl-2-propyn-1-ol and a half equivalent of sodium sand was treated with a large excess of carbon disulfide, only XII was obtained in

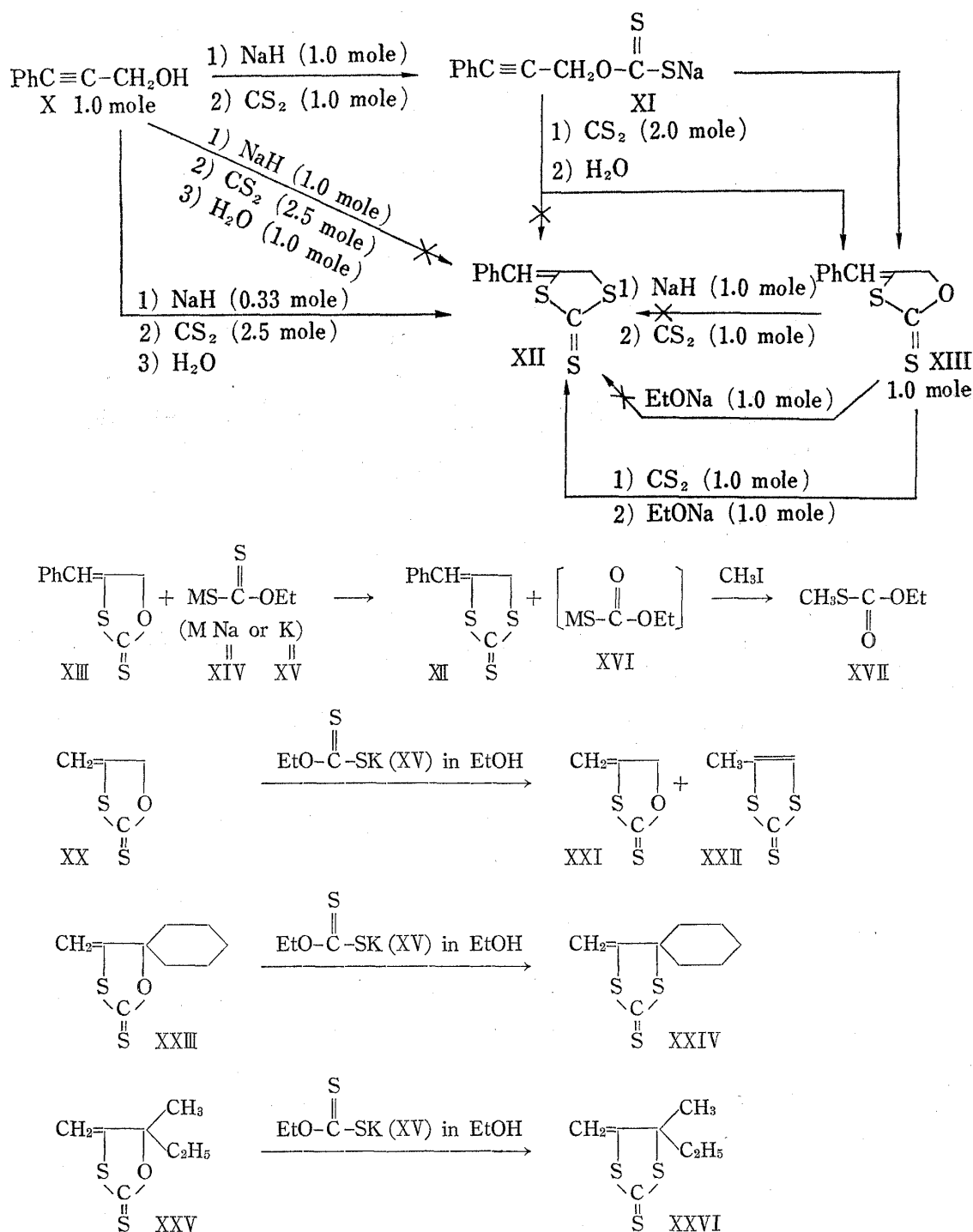
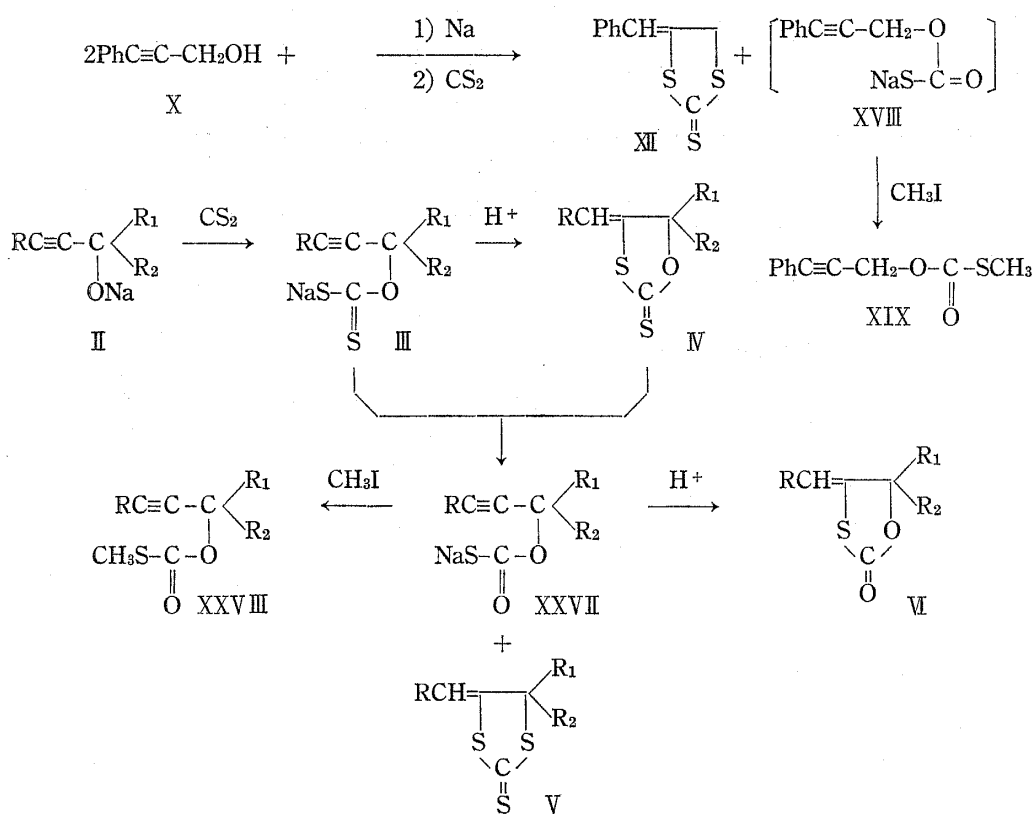


Chart 3

almost quantitative yield to sodium sand, and S-methyl-O-3-phenyl-2-propyn-1-yl thiol carbonate (XIX) was isolated from precipitated salts after treatment with methyl iodide.

The formation of V was attributed to the replacement of oxygen of IV with sulfur of metal xanthogenate, which was converted into the corresponding metal thiolcarbonate and sometimes it cyclized into 4-alkylidene-1,3-oxathiolan-2-ones (VI). The following processes (Chart 4) could be accounted for all of the products from the reaction of sodium α -acetylenic alcoholate with carbon disulfide. In the next paper we will report a detailed investigation on the reaction by using ^{35}S -labelled compound.



Experimental⁵⁾

Reaction of 3-Phenyl-2-propyn-1-ol (X) with an Excess of Carbon Disulfide and Sodium Hydride—

To a suspension of alcoholate prepared from 3-phenyl-2-propyn-1-ol (X) (6.6 g) and sodium hydride (0.05 mole)⁶⁾ in dry ether (100 ml) freshly distilled carbon disulfide (9.5 g) was added dropwise under ice cooling, and after stirring for 6 hr at room temperature, the reaction mixture was poured into ice water (100 ml), ethereal layer was separated and aqueous layer was extracted with benzene. The combined extracts were washed with H₂O, and dried over anhyd. Na₂SO₄. After removal of solvent, a solid residue was recrystallized from benzene to afford 4-benzylidene-1,3-oxathiolane-2-thione (XIII) (7.8 g), which was coincided with the authentic sample.³⁾

Reaction of 4-Benzylidene-1,3-oxathiolane-2-thione (XIII) with Carbon Disulfide and Sodium Hydride—

To benzene (100 ml) solution of XIII (2.1 g) sodium hydride (0.01 mole) and carbon disulfide (1.5 g) were added under ice water-cooling, and after stirring for 6 hr at room temperature, insoluble solid was filtered off and the solid was washed with benzene. Combined filtrates were washed with H₂O and satd. NaCl solution and dried over anhyd. Na₂SO₄. After removal of solvent, a solid residue was recrystallized from benzene to afford 1.8 g of XIII.

Reaction of 4-Benzylidene-1,3-oxathiolane-2-thione (XIII) and Sodium Ethoxide—To a solution of the sodium alcoholate prepared from sodium (0.12 g) and absolute EtOH (50 ml) a solution of XIII (1.04 g) in xylene (10 ml) was added and after refluxing for 30 minutes, solvent was evaporated under reduced pressure. Ice water (100 ml) was added to the residue and the mixture was extracted with benzene and CHCl₃. Combined extracts were washed with H₂O and satd. NaCl solution, and dried over anhyd. Na₂SO₄. After removal of solvent, only 0.3 g of a colorless amorphous powder, mp 153° (decomp.), was obtained.

Reaction of 3-Phenyl-2-propyn-1-ol (X) with an Excess of Carbon Disulfide and One-Third Equivalent of Sodium Hydride—To a suspension of sodium alcoholate prepared from 3-phenyl-2-propyn-1-ol (X) (6.6 g) and sodium hydride (0.0166 mole) in dry ether carbon disulfide (9.5 g) was added dropwise under ice water-cooling, and after stirring for 6 hr at room temperature, the reaction mixture was poured into ice water (200 ml). Organic layer was separated, aqueous layer was extracted with benzene, and combined

5) All boiling points were uncorrected. The NMR spectra were recorded on Varian A-60 in tetrachloromethane containing tetramethylsilane as internal standard.

6) Wakō Pure Chemical Industries, LTD. NaH: ca. 50% (in oil).

extracts were washed with H_2O and satd. NaCl solution and dried over anhyd. Na_2SO_4 . After removal of solvent under reduced pressure, a yellow residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (4:1) afforded XIII (0.59 g) and 4-benzylidene-1,3-dithiolane-2-thione (XII) (1.85 g). These two compounds were coincided with authentic samples.³⁾

Reaction of 4-Benzylidene-1,3-oxathiolane-2-thione (XIII) with Carbon Disulfide and Sodium Ethoxides—To the alcoholate solution prepared from sodium (0.12 g) and absolute EtOH (50 ml), carbon disulfide (0.8 g) and XIII (2.1 g) were added, and after stirring for 1 hr at room temperature and for 2 hr at 45–50°. After removal of EtOH under reduced pressure, a yellow residue was poured into ice water (100 ml), extracted with benzene, combined extracts were washed with H_2O and satd. NaCl solution, and dried over anhyd. Na_2SO_4 . After removal of benzene, a yellow residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (4:1) afforded XIII (0.9 g) and XII (0.69 g).

Reaction of 3-Phenyl-2-propyn-1-ol (X) with an Excess of Carbon Disulfide and a Half Equivalent of Sodium—To a suspension of sodium sand (0.2 g) in xylene (60 ml), X (2.64 g) was added dropwise at room temperature, stirred at 40–50° until a grain of sodium disappeared, and carbon disulfide (1.9 g) was added dropwise under ice water-cooling. After stirring for 3 hr at 40°, an insoluble salt was filtered off and washed with ether. Filtrate was washed with H_2O and satd. NaCl solution and dried over anhyd. Na_2SO_4 . After removal of solvent under reduced pressure, a yellow residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene afforded 2.2 g of XII (Yield: 98%). To a suspension of the separated salt in ether (100 ml) methyl iodide was added and refluxed for 6 hr. An insoluble salt was filtered off, and the filtrate was washed with H_2O and dried over anhyd. Na_2SO_4 . After removal of ether, an oily residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (1:1) afforded 0.3 g of S-methyl-O-3-phenyl-2-propynyl thiolcarbonate (XIX) as a colorless oil, bp 140° (0.2 mmHg). *Anal.* Calcd. for $\text{C}_{11}\text{H}_{10}\text{O}_2\text{S}$ (XIX): C, 64.05; H, 5.23; S, 15.54. Found: C, 63.70; H, 5.05; S, 15.40. IR $\nu_{\text{max}}^{\text{liquid}}$ cm^{-1} : 2220 ($-\text{C}\equiv\text{C}-$), 1720 ($-\text{C}=\text{O}$), 1135 ($-\text{C}-\text{O}-$). NMR (in CCl_4) τ ($J=\text{cps}$): 2.42–2.90 (5H, m.), 5.02 (2H, s.), 7.67 (3H, s.).

Reaction of 4-Benzylidene-1,3-oxathiolane-2-thione (XIII) with Potassium Ethyl Xanthate (XV)—To a suspension of commercially available potassium ethyl xanthate (XV) (0.73 g) in dry EtOH (10 ml), a solution of XIII (1.04 g) in xylene (30 ml) was added, and stirred for 2 hr at 40–50°. After removal of solvent under reduced pressure, dry ether (200 ml) was added to the residue and an insoluble salt was filtered off. The filtrate was washed with H_2O and dried over anhyd. Na_2SO_4 . After removal of ether, an oily residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (1:1) afforded 0.40 g of XIII and 0.48 g of XII. Furthermore, to a suspension of the separated salt in ether (100 ml), methyl iodide (1.0 g) was added and refluxed for 6 hr. After an insoluble salt was filtered off, the filtrate was washed with H_2O and dried over anhyd. Na_2SO_4 . After removal of ether, an oily residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (9:1) afforded two compounds. One of them was S-methyl-O-ethyl xanthate (0.22 g) as a pale yellow oil, bp 70° (20 mmHg). *Anal.* Calcd. for $\text{C}_4\text{H}_8\text{OS}_2$: C, 35.26; H, 5.99; S, 47.07. Found: C, 35.32; H, 6.30; S, 46.57. IR $\nu_{\text{max}}^{\text{liquid}}$ cm^{-1} : 1218, 1050 ($-\text{O}-\text{CS}-\text{S}-$). Another was S-methyl-O-ethylthiolcarbonate (XVII) (0.12 g) as a colorless oil, bp 65° (50 mmHg). *Anal.* Calcd. for $\text{C}_4\text{H}_8\text{O}_2\text{S}$ (XVII): C, 39.97; H, 6.71; S, 26.64. Found: C, 40.23; H, 6.92; S, 26.17. IR $\nu_{\text{max}}^{\text{liquid}}$ cm^{-1} : 1715, 1145 ($-\text{O}-\text{CO}-\text{S}-$).

Reaction of 4-Methylidene-1,3-oxathiolane-2-thione (XX) with Potassium Ethyl Xanthate (XV)—To a suspension of potassium ethyl xanthate (XV) (1.5 g) in EtOH (60 ml), XX (1.32 g) was added and stirred for 1 hr at 40°. EtOH was evaporated under reduced pressure, the residue was poured into ice water (100 ml) and extracted with ether. The ethereal layer was washed with H_2O and dried over anhyd. Na_2SO_4 . After removal of ether, a yellow oily residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (4:1) afforded 1.6 g of 4-methyl-1,3-dithiole-2-thione (XXII) and 0.1 g of 4-methylidene-1,3-dithiolane-2-thione (XXI). These two compounds (XXI and XXII) were coincided with authentic samples.³⁾

Reaction of 4-Methylidene-1-oxa-3-thio-spiro[4,5]decan-2-thione (XXIII) and Potassium Ethyl Xanthate (XV)—To a suspension of potassium ethylxanthate (XV) (0.15 g) in EtOH (50 ml), XXIII (0.27 g) was added and stirred for 1 hr at 40°. EtOH was evaporated under reduced pressure, the residue was poured into ice water (100 ml) and extracted with ether. The ethereal layer was washed with H_2O and dried over anhyd. Na_2SO_4 . After removal of ether, a yellow oily residue was chromatographed over silica gel column. Elution with *n*-hexane-benzene (4:1) afforded 0.15 g of 4-methylidene-1,3-dithio-spiro[4,5]decan-2-thione (XXIV) as a yellow oil, bp 85–90° (0.1 mmHg). *Anal.* Calcd. for $\text{C}_9\text{H}_{12}\text{S}_3$ (XXIV): C, 49.95; H, 5.58; S, 44.45. Found: C, 49.66; H, 5.44; S, 44.80. IR $\nu_{\text{max}}^{\text{liquid}}$ cm^{-1} : 1613 ($-\text{C}=\text{C}-$), 1070 ($-\text{S}-\text{CS}-\text{S}-$), 877 ($\text{CH}_2=$). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (log ϵ): 328 (4.24). NMR (in CCl_4) τ ($J=\text{cps}$): 8.95–7.5 (10H, m.), 5.09 (1H, d., $J=1.4$), 4.93 (1H, d., $J=1.4$).

Reaction of 4-Methylidene-5-methyl-5-ethyl-1,3-oxathiolane-2-thione (XXV) with Potassium Ethyl Xanthate (XV)—To a suspension of potassium ethyl xanthate (XV) (0.16 g) in EtOH (50 ml), XXV (0.18 g) was added and stirred for 1 hr at 40°. EtOH was evaporated under reduced pressure, a yellow residue was poured into ice water (100 ml) and extracted with ether. The ethereal layer was washed with H_2O and dried over anhyd. Na_2SO_4 . After removal of ether, a yellow oily residue was chromatographed

over silica gel column. Elution with *n*-hexane-benzene (4:1) afforded 0.11 g of 4-methyldene-5-methyl-5-ethyl-1,3-dithiolane-2-thione (XXVI) as a yellow oil, bp 135—130° (0.35 mmHg). *Anal.* Calcd. for $C_7H_{10}S_2$ (XXVI): C, 44.16; H, 5.29; S, 50.53. Found: C, 44.16; H, 5.31; S, 49.92. IR ν_{\max}^{EtOH} cm^{-1} : 1610 ($-C=C-$), 1070 ($-S-CS-S-$), 887 ($CH_2=$). UV λ_{\max}^{EtOH} $m\mu$ ($\log \epsilon$): 308 (3.62), 327 (4.15). NMR (in CCl_4) τ ($J=cps$): 8.88 (3H, t., $J=7.0$), 8.30 (3H, s.), 8.02 (2H, q., $J=7.0$), 4.75 (2H, s.).

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