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# Studies on Organo Sulfur Compounds. VII.[1] The Reaction Mechanism of 4-Benzylidene-1,3-oxathiolane-2-thione and Metal Xanthates

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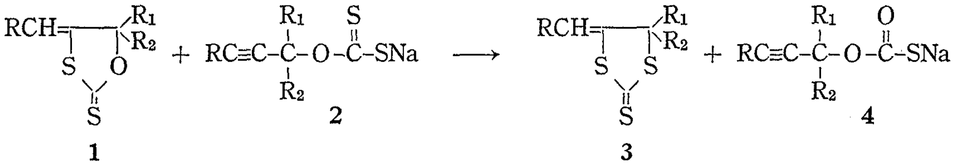
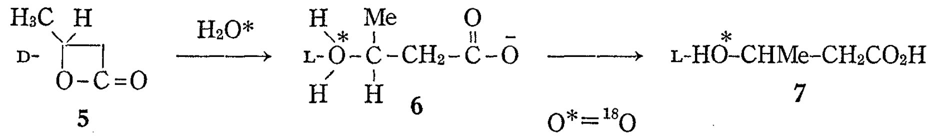
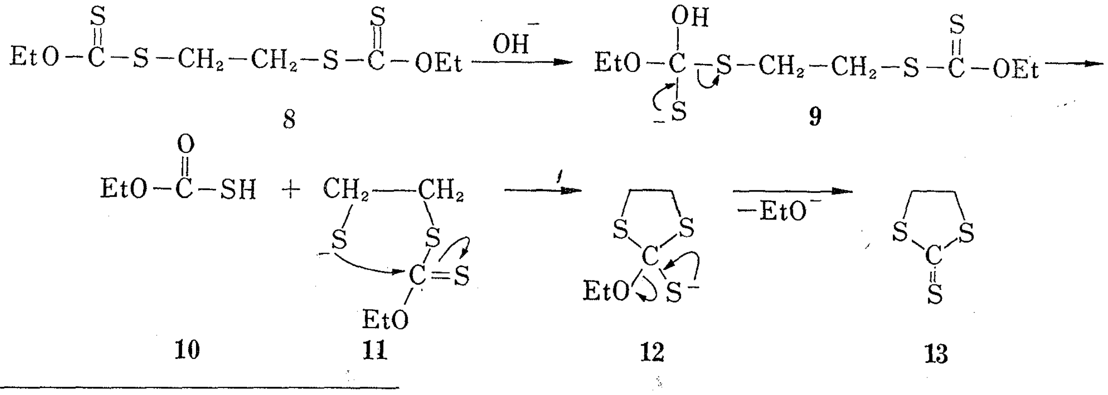
The mechanism of the formation of 4-benzylidene-1,3-dithiolane-2-thione (**19**) in the reaction of 4-benzylidene-1,3-oxathiolane-2-thione (**14**) with sodium ethyl xanthate (**15**) became clear by the measurement of the radioactivity of $^{35}$S-4-benzylidene-1,3-dithiolane-2-thione (**32**), which was synthesized by the treatment of **14** with $^{35}$S-sodium ethyl xanthate (**29**), and that of $^{35}$S-4-benzylidene-1,3-dithiolane-2-one (**38**) which was obtained by the oxidation of **32** with mercuric acetate.

In the previous paper[3] 4-alkylidene-1,3-dithiolane-2-thione (**3**) was reported as being prepared by the reaction of 4-alkylidene-1,3-oxathiolane-2-thione (**1**) and sodium α-acetylenyl xanthate (**2**). However, details of the reaction mechanism, that the sodium xanthate (**2**) will attack any site of **1** and consequently **3** will be formed by any process, remained to be clarified. In this paper, we wish to report in detail the reaction of 4-benzylidene-1,3-oxathiolane-2-thione (**14**) and labeled $^{35}$S-sodium ethyl xanthate (**29**).



Olson and Miller[4] reported the basic hydrolysis mechanism of β-butyrolactone to be a $B_{AL}2$ type fission[5] from the results of the treatment of optically active D-β-butyrolactone (**5**)





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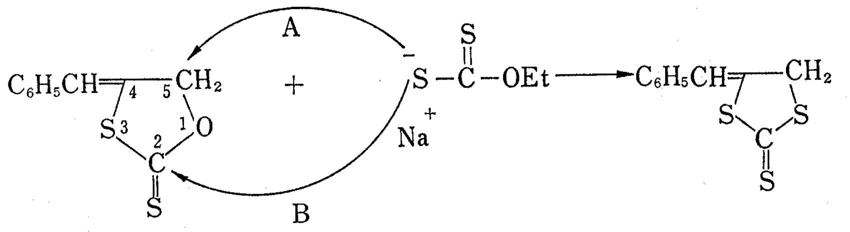
[1] Part VI: K. Tomita and M. Nagano, *Chem. Pharm. Bull.* (Tokyo), **20**, 2302 (1972).
[2] Location: *Hiromachi, Shinagawa-ku, Tokyo.*
[3] K. Tomita and M. Nagano, *Chem. Pharm. Bull.* (Tokyo), **17**, 2442 (1969).
[4] A.R. Olson and R.J. Miller, *J. Am. Chem. Soc.*, **60**, 2678 (1938).
[5] $B_{AL}2$=Bimolecular alkyl-oxygen bond fission by a base. Edwin. S. Gould, "Mechanism and Structure in Organic Chemistry," 1959, pp. 344—345.

with $H_2{}^{18}O$. Frasseti[6] reported that a xanthate (**8**) on the treatment with alkali afforded a cyclic trithio compound (**13**), and explained the mechanism of its formation, wherein the hydroxide anion would attack one of the two thiocarbonyl carbons of **8** to form an intermediate **9** which could cyclize intramolecularly to afford **13**.

In the formation reaction of 4-benzylidene-1,3-dithiolane-2-thione (**19**), two possible positions, where 4-benzylidene-1,3-oxathiolane-2-thione (**14**) may be attacked by sodium ethyl xanthate (**15**), are considered, namely C-5 and C-2. In course A, **14** reacts with **15** to afford **17** which may cyclize intramolecularly to form **19** (Chart 1). In course B, **14** is cleaved with **15** to afford **21** or **22**, respectively *via* course B-a or course B-b. The former course (B-a) is that **21** transforms to **23** from which ethyl alcohol may be eliminated to form a seven membered ring compound (**24**) followed by elimination of oxygen carbonsulfide to yield **19**. The latter course (B-b) is that **22** undergoes intramolecular cyclization to form an intermediate (**25**) to furnish (**19**): Three pathways may be considered for this latter transformation, namely B-b-i, B-b-ii, and B-b-iii. Course B-b-i is that ethyl alcohol is eliminated from **25** to form **24** followed by liberation of oxygen carbonsulfide to yield **19**. Elimination of the thiolcarbonate anion (**28**) results in the formation of **19** *via* course B-b-ii or B-b-iii. All the possible processes of the transformation of **14** into **19** considered herein are illustrated in Chart 1.



**14** **15** **19**

The use of labeled $^{35}S$-sodium xanthate (**29**) in the reaction of 4-benzylidene-1,3-oxathiolane-2-thione (**14**) and sodium xanthate (**15**) seemed to be one of the best methods for elucidating the reaction mechanism in the formation of 4-benzylidene-1,3-dithiolane-2-thione (**19**). It would be expected that $^{35}S$-4-benzylidene-1,3-dithiolane-2-thione (**30**) arising *via* course A would have the same radioactivity as that of $^{35}S$-S-methyl-O-ethyl xanthate (**33**) which may be obtained by the reaction of $^{35}S$-sodium xanthate (**29**) and the methyl halide. On the other hand, radioactive compounds (**31** and **32**) formed *via* course B should have one-half the radioactivity of **33** (Chart 2).

The radioactive 4-benzylidene-1,3-dithiolane-2-thione (X), which was synthesized by the treatment of **14** with $^{35}S$-sodium ethyl xanthate (**29**), had about one-half the radioactivity (3.66 mC/m mole) of $^{35}S$-S-methyl-O-ethyl xanthate (**33**) (7.97 mC/m mole) which was prepared as a standard radioactive compound from **29** and methyl iodide. From these data, the compound (X) was regarded as $^{35}S$-4-benzylidene-1,3-dithiolane-2-thione (**31** or **32**), and consequently the process for the formation of **19** *via* course A was eliminated.

The conversion of the thiocarbonyl sulfur of **19** into another function seemed to be a good method for determining the structure of the radioactive trithio compound (X) as being either **31** or **32**.

Several methods for substituting the thiocarbonyl sulfur of **19** by a reagent such as bromine, dimethyl sulfate, hydroxyl amine or phenylhydrazine, were undertaken, but the ex-

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6) P. Frasseti, *Chem. Ber.*, **38**, 483 (1950).

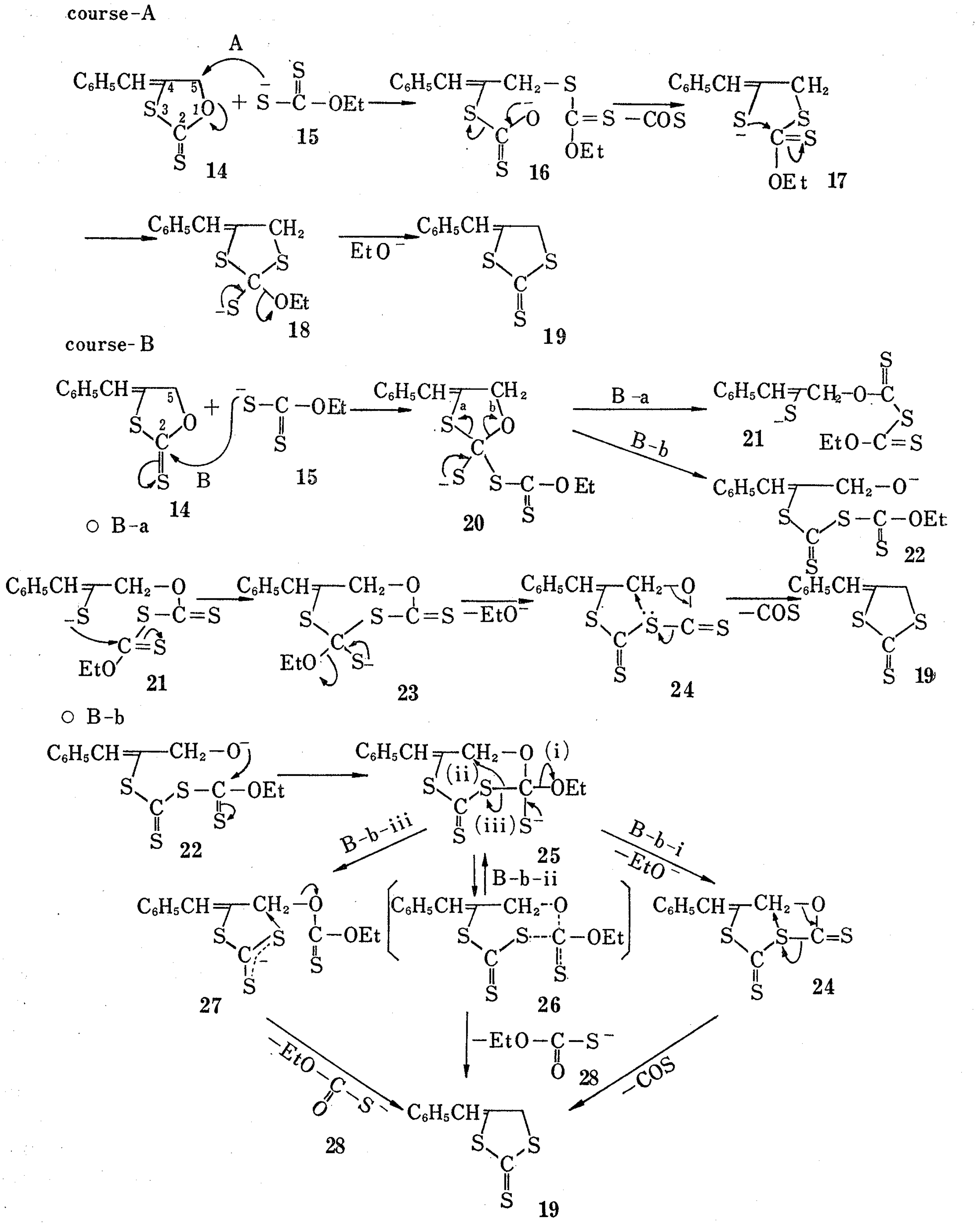

Chart 1

pected products (**34, 36** and **37**) could not be obtained[7-9] (Chart 3). However, by the method of F. Challenger, *et al.*,[10] 4-benzylidene-1,3-dithiolane-2-one (**35**) could be prepared by the

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7) R. Mayer and K. Schäfer, *J. Prak. Chem.*, **26**, 279 (1964).
8) R.S. Spindt, D.R. Stevens, and W.E. Baldwin, *J. Am. Chem. Soc.*, **73**, 3693 (1951).
9) A. Lüttinghaus, H.R. König, and B. Bottcher, *Ann.*, **560**, 201 (1948).
10) F. Challenger, E.A. Mason, E.C. Haldworth, and R. Emmot, *J. Chem. Soc.*, **1953**, 298.

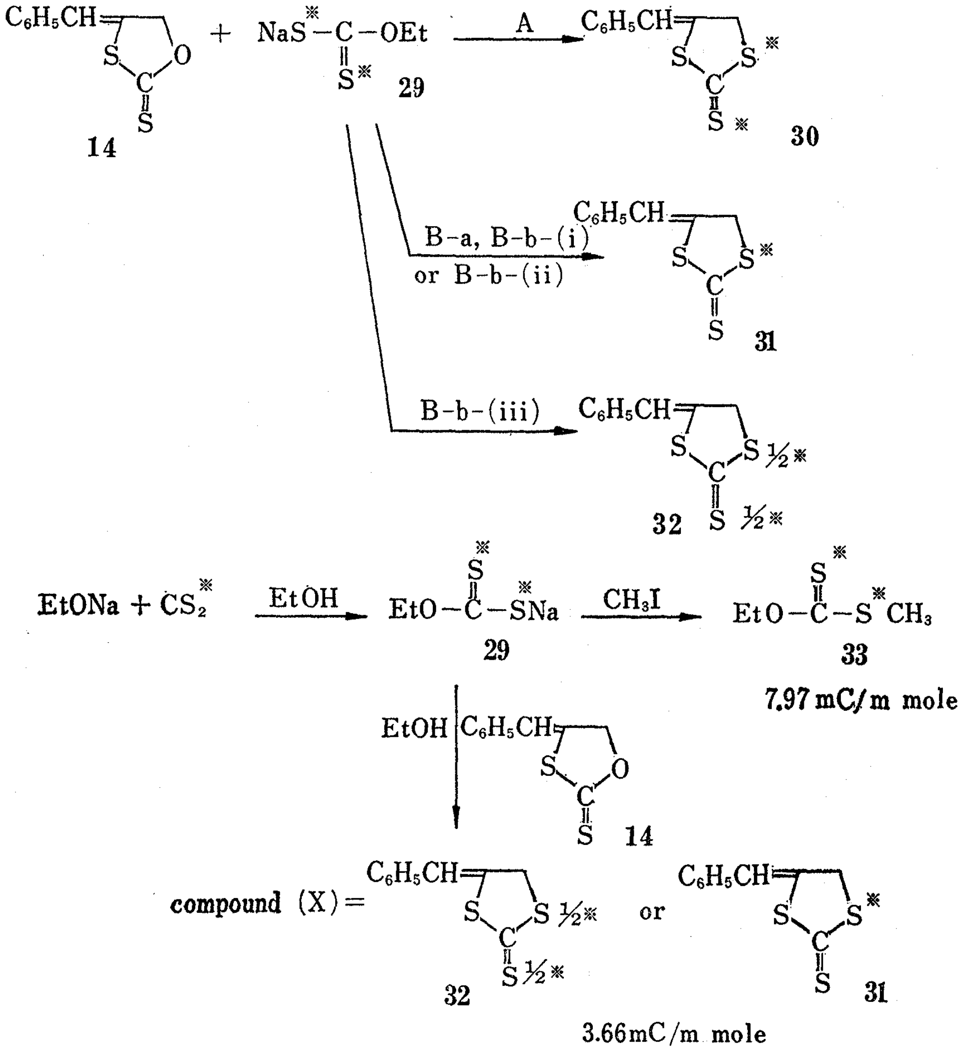

Chart 2

oxidation of **19** with mercuric acetate. The structure of **35** was determined on the basis of analytical and spectral data. Characteristic infrared absorption bands were observed at 1625 cm$^{-1}$ for a carbon-carbon double bond, and 1753, 1667, and 875 cm$^{-1}$ for a dithiol carbonate group (-S-CO-S-). Further confirmation of the structure was obtained from the nuclear magnetic resonance (NMR) spectrum which showed a doublet at 5.55 $\tau$ for two equivalent protons with coupling constants of 1.8 cps, a triplet at 3.24 $\tau$ for a methyne proton with coupling constants of 1.8 cps, and a singlet at 2.72 $\tau$ corresponding to aromatic five protons.

Under the same reaction conditions as those in the case of **19**, the radioactive trithio compound (X) was treated with mercuric acetate to afford $^{35}$S-4-benzylidene-1,3-dithiolane-2-one (**38**) whose infrared spectrum and melting point agreed with those of **35**. The radioactivity (1.45 mC/m mole) of **35** was about one-half that (2.76 mC/m mole) of (X), and accordingly the compound (X) was regarded as the radioactive compound (**32**).

From these experiments, it became clear that 4-benzylidene-1,3-dithiolane-2-thione (**19**) was consequently formed through course B-b-iii in the reaction of 4-benzylidene-1,3-oxathiolane-2-thione (**14**) with sodium xanthate (**15**).

On the basis of these results, the pathway for the transformation of 4-alkylidene-1,3-oxathiolane-2-thione (**1**) to 4-alkylidene-1,3-dithiolane-2-thione (**3**) is shown schematically in Chart 4.

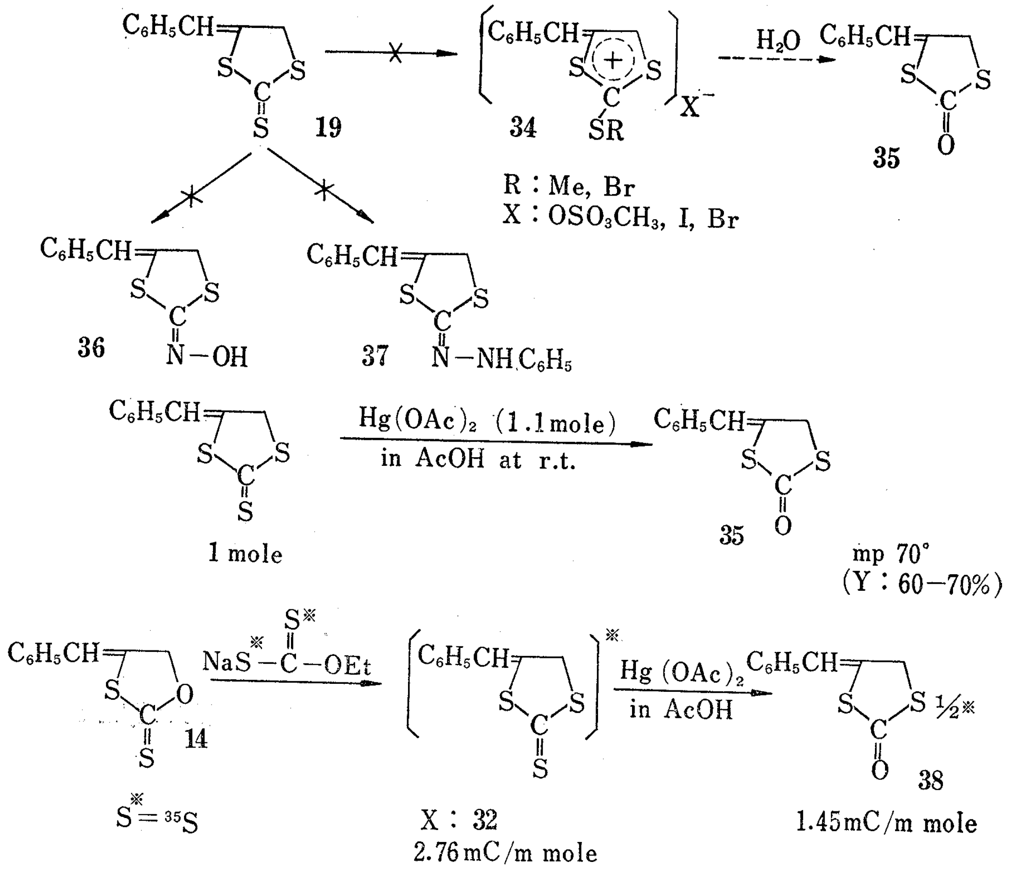

Chart 3

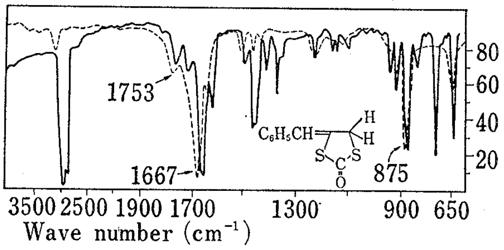

Fig. 1. Infrared Spectrum of 4-Benzylidene-1,3-dithiolane-2-one (35) (——Nujol, ------$CHCl_3$)

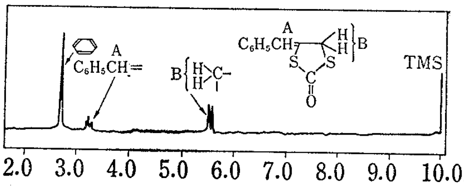

Fig. 2. NMR Spectrum of 4-Benzylidene-1,3-dithiolane-2-one (35) (in $CDCl_3$)

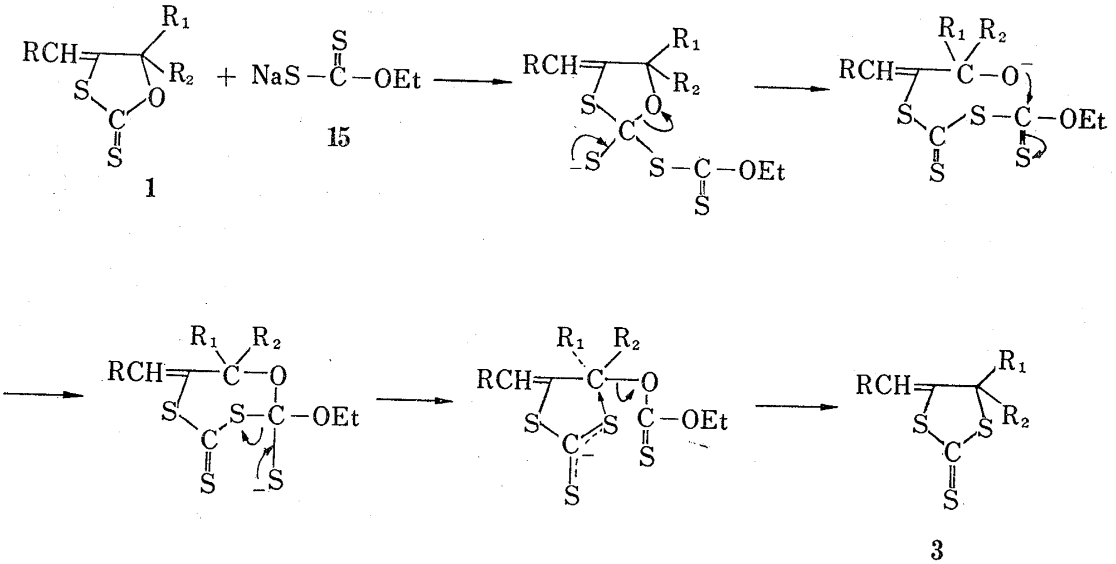

Chart 4

## Experimental[11,12]

**Synthesis of $^{35}$S-S-Methyl-O-ethyl Xanthate** (33)——To the solution of $^{35}$S-carbon disulfide (1.85 mg) and cold carbon disulfide (1.75 g) in EtOH (35 ml), potassium hydroxide (1.0 g) was added and stirred for 3 hr at 0° to give the suspension (A) of $^{35}$S-sodium ethyl xanthate (29).

To 10 ml of A, methyl iodide (2.5 g) was added at room temperature, refluxed for 6 hr, and EtOH was carefully evaporated under reduced pressure. The residue was extracted with ether (100 ml × 3), ethereal layer was washed with satd. NaCl solution, and dried over anhyd. $Na_2SO_4$. After removal of ether, the oily residue was chromatographed over silica gel. Elution with *n*-hexane–benzene (9:1) afforded 0.5 g of $^{35}$S-S-methyl-O-ethyl xanthate (33) as a pale yellow oil. The infrared spectrum of compound (33) was coincided with that of S-methyl-O-ethyl xanthate which was prepared from commercial potassium ethyl xanthate and methyl iodide.

**Synthesis of $^{35}$S-4-Benzylidene-1,3-dithiolane-2-thione** (32)——To 25 ml of the suspension (A), 4-benzylidene-1,3-oxathiolane-2-thione (**14**) was added, stirred for 2 hr at 60°, and EtOH was removed under reduced pressure. To the residue ice water (100 ml) was added, extracted with ether (100 ml × 3), ethereal layer was washed with satd. NaCl solution, and dried over anhyd. $Na_2SO_4$. After removal of ether, a yellow solid residue was chromatographed over silica gel. Elution with *n*-hexane–benzene (4:1) afforded $^{35}$S-4-benzylidene-1,3-dithiolane-2-thione as yellow crystals, whose infrared spectrum was coincided with that of compound (**19**). The radioactive counts of compound (32) and compound (33) were measured at the same time by Liquid Scintillation Counter. The counts of compound (32) were 3.66 mC/m mole and those of compound (33) were 7.97 mC/m mole.[13]

**Reaction of 4-Benzylidene-1,3-dithiolane-2-thione** (19) **with Hydroxyl Amine or Phenyl Hydrazine**——To compound (**19**) (2.24 g) in EtOH (50 ml), $NH_2OH \cdot HCl$ (0.69 g) and $K_2CO_3$ (1.08 g) were added at room temperature and refluxed for 2 hr. After removal of EtOH, ice water was added to the oily residue and was extracted with $CHCl_3$, combined extracts were washed with $H_2O$, and dried over anhyd. $Na_2SO_4$. After removal of $CHCl_3$, a gummy residue could not purified by distillation or silica gel chromatogram. In the reaction of compound (**19**) (2.24 g) and phenyl hydrazine (1.3 g) under the same reaction condition as those of hydroxyl amine, an unknown gummy product was obtained and it could not be purified.

**Reaction of 4-Benzylidene-1,3-dithiolane-2-thione** (19) **with Dimethyl Sulfate or Bromine**——To compound (**19**) (2.24 g) in $CHCl_3$ (100 ml), dimethyl sulfate (1.5 g) or bromine (1.6 g) was added under ice-cooling, and stirred for 6 hr at room temperature. After removal of $CHCl_3$ under reduced pressure, in the former case compound (**19**) (2.0 g) was recovered and in the latter case an brown gummy substance was obtained, but it was decomposed in air and could not be purified.

**Synthesis of 4-Benzylidene-1,3-dithiolane-2-one** (35)——To the solution of **19** (0.33 g) in $CHCl_3$ (30 ml), mercuric acetate (0.5 g) in AcOH was added dropwise at room temperature and stirred for 1 hr. An insoluble substance was filtered off and was washed with water, the filtered organic layer was separated and aqueous layer was succeedingly extracted with $CHCl_3$ (100 ml × 2). Combined extracts were washed with $NaHCO_3$ solution, $H_2O$ and satd. NaCl solution, and dried over anhyd. $Na_2SO_4$. After removal of $CHCl_3$ under reduced pressure, an oily residue was chromatographed over silica gel. Elution with *n*-hexane–benzene (3:2) afforded 0.22 g of compound (35) as colorless crystals, mp 70°. *Anal.* Calcd. for $C_{10}H_8OS_2$: C, 57.69;

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11) The nuclear magnetic resonance spectra were recorded on Varian A-60 in deuteriochloroform containing tetramethyl silane as internal standard.

12) AMERSHAM Co. (England). Weit: 1.85 mg. Specific Activity: 52.3 mC/m mole. Total Activity: 1.3 mC.

13) 1) The construction of Scintillator: ppo (8 g) + dimethyl POPOP (200 ml) + toluene (200 ml) + dioxane (800 ml); 2) The measurements of radioactive counts of compound (32 and 33): To 0.1 ml of the solution of compound (32) (0.87 mg) dissolved in dioxane (10 ml), 15 ml of the Scintillator and 0.1 ml of $^{14}$C-toluene ($4.37 \times 10^4$ dpm), which was the standard radioactive substance, were added, and then the radioactive counts of the mixture were measured by Liquid Scintillation Counter. Also, the radioactive counts of compound (33) (1.423 mg) in dioxane (10 ml) were measured at the same time under the same conditions as those of compound (32). 3) The radioactive counts of compound (33 and 32) for 5 minutes.

| | $^{14}$C-toluene + (33) | 33 | Back ground | $^{14}$C-toluene + (32) | 32 | Back ground |
|---|---|---|---|---|---|---|
| 1 | 167438 | 11256 | 161 | 195049 | 33813 | 182 |
| 2 | 167028 | 11407 | 163 | 195573 | 33877 | 175 |
| 3 | 167277 | 10977 | 175 | 195573 | 34002 | 188 |

H, 3.87; S, 30.80. Found: C, 57.49; H, 3.98; S, 30.40. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm$^{-1}$: 1625 (-C≡C-), 1735, 1667 and 875 (-S-CO-S-). UV $\lambda_{\max}^{\mathrm{EtOH}}$ m$\mu$(log $\varepsilon$): 275 (3.50). NMR (in $CDCl_3$) $\tau$ ($J$=cps): 5.55 (2H, d, $J$=1.8), 3.24 (1H, t, $J$=1.8), 2.72 (5H, s).

**Synthesis of $^{35}$S-4-Benzylidene-1,3-dithiolane-2-one** (38)——To compound (32) in $CHCl_3$ (30 ml), mercuric acetate (0.5 g) in AcOH (10 ml) was added at room temperature, additionally stirred for 2 hr, an insoluble salt was filtered off and was washed with $H_2O$. The filtered organic layer was separated and aqueous layer was succeedingly extracted with $CHCl_3$ (100 ml × 2). Combined extracts were washed with cold $NaHCO_3$ solution, $H_2O$ and satd. NaCl solution, and dried over anhyd. $Na_2SO_4$. After removal of $CHCl_3$ under reduced pressure, an oily residue as chromatographed over silica gel to afford compound (38) whose infraed spectrum was coincided with that of compound (35). The radioactive counts of compound (38) and compound (32) were measured by Liquid Scintillation Counter. The radioactive counts of compound (38) were 1.45 mC/m mole and those of compound (32) were 2.76 mC/m mole.[14]

**Acknowledgement** We are grateful to Dr. G. Kuwata, manager of this laboratories. We are also indebted to the members of the Section of Physical Chemistry for the elemental analyses and determination of absorption spectra.

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[14] The measurements of radioactive counts of compound (38) and (32): To 0.1 ml of compound (38) (0.176 mg) in dioxane (10 ml), 15 ml of the Scintillator and 0.1 ml of $^{14}$C-toluene were added, and then the radioactive counts of the mixture were measured by Liquid Scintillation Counter. Also the counts of the previously prepared solution of compound (32) were measured at the same time; 2) Radioactive counts of compound (38 and 32) for 5 minutes.

| | $^{14}$C-toluene+(38) | 38 | Back ground | $^{14}$C-toluene+(32) | 32 | Back ground |
|---|---|---|---|---|---|---|
| 1 | 150526 | 8735 | 161 | 160180 | 9196 | 152 |
| 2 | 149660 | 8759 | 165 | 160624 | 9231 | 174 |
| 3 | 150131 | 8836 | 156 | 161144 | 9155 | 175 |
| 4 | 150320 | 8780 | 171 | 161141 | 9154 | 160 |