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Studies on Organo Sulfur Compound. I. The Reaction of Prim. α-Acetylenic Alcohols and Carbon Disulfide

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The reaction of sodium alcoholates of prim. α–acetylenic alcohols and carbon disulfide in an aprotic solvent gave new heterocyclic compounds, 4–alkylidene–1,3–oxathiolane–2–thiones and 4–alkylidene–1,3–dithiolane–2–thiones.

There are many reports concerning the intramolecular cyclization reactions of compounds having both a carbon–carbon triple bond and a nucleophilic radical. Many chemists have reported that propargyl urethanes and propargyl ureas prepared from propargyl alcohols and propargyl amines with isocyanates smoothly are converted to 4–methylidene–2–imidazolidinones and 4–methylidene–2–oxazolidinones in the presence of basic catalysts.[2–4] Furthermore, it is well known that alcohols and amines are treated with carbon disulfide to produce corresponding xanthogenates and dithiocarbamates, respectively. Batty[5] intended to prepare a dithiocarbamate from 3–isopropylamino–1–butyne and carbon disulfide, he could not isolate the expected dithiocarbamate, but only a thiazoline derivative by intramolecular –SH addition to the triple bond. From these facts, it should be considered that α–acetylenic alcohols react with carbon disulfide to afford the corresponding xanthogenic acids or their cyclization products. Nevertheless, we found no report on this reaction except two Belgian patents.[6,7] The present paper describes on the reaction of some prim. α–acetylenic alcohols and carbon disufide.

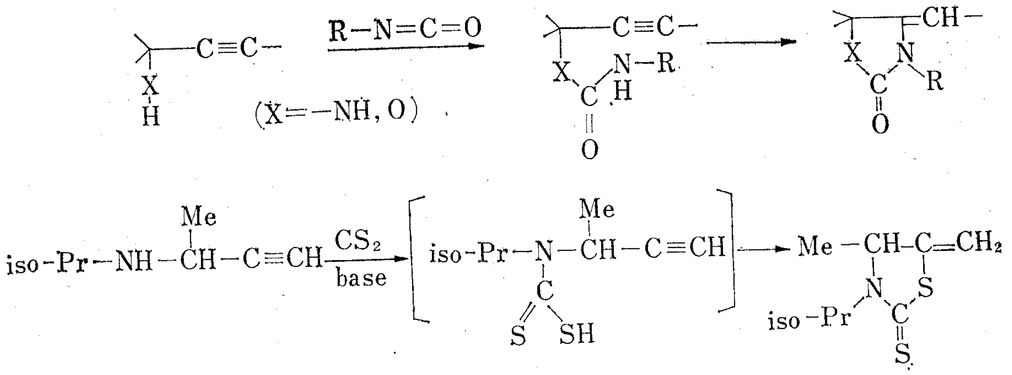

Chart 1

A Belgian patent[6] has shown that 1,3–oxathiole–2–thiones are prepared by the reaction of carbon disulfide and prim.α–acetylenic alcohols in the presence of an alkali hydroxide. Under the same condition, we attempted to prepare a 4–benzyl–1,3–oxathiole–2–thione (VII) from

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1) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
2) N. Shacht and J.J. Bagnell, Jr., *J. Org. Chem.*, **28**, 991 (1963).
3) K. Sisido, K. Hukuoka, M. Tuda, and H. Nozaki, *J. Org. Chem.*, **27**, 2663 (1962).
4) N.R. Easton, D.R. Cassady, and R.D. Dillard, *J. Org. Chem.*, **27**, 2927 (1962).
5) W. Batty and B.C.L. Weedon, *J. Chem. Soc.*, **1949**, 786.
6) Berg. Patent 648453 (May 31, 1963).
7) Berg. Patent 648456 (May 31, 1963).

3-phenyl-2-propyn-1-ol (I) and carbon disulfide in dimethylformamide, in the presence of equimolar amounts of potassium hydroxide, but neither the expected compound (VII) nor the other isomeric compounds could be isolated. Carbon disulfide was treated with the alcoholate (II) prepared from sodium hydride and small excess of 3-phenyl-2-propyn-1-ol (I) in dry ether and then the reaction mixture was hydrolyzed to afford pale yellow crystals (A) in 98.5% yield, being accompanied with yellow crystals (B) in 1.0% yield. The analytical data of the former compound agreed with the addition compound of alcohol (I) and carbon disulfide in equimolecular proportion. The compound was devoid of significant infrared absorption bands at 3600—3200 and 2200—2000 cm^{-1} regions, but showed characteristic absorption bands for double bond at 1625 and for the xanthate group at 1214 and 1052 cm^{-1}. From these results, it was evident that the intramolecular cyclization of the intermediate, 3-phenyl-2-propyn-1-yl xanthogenic acid (III:X=H), had taken place to afford certain cyclic xanthate having a double bond. The three most probable structures (IV, VI, VII) could be considered for the cyclic xanthate.

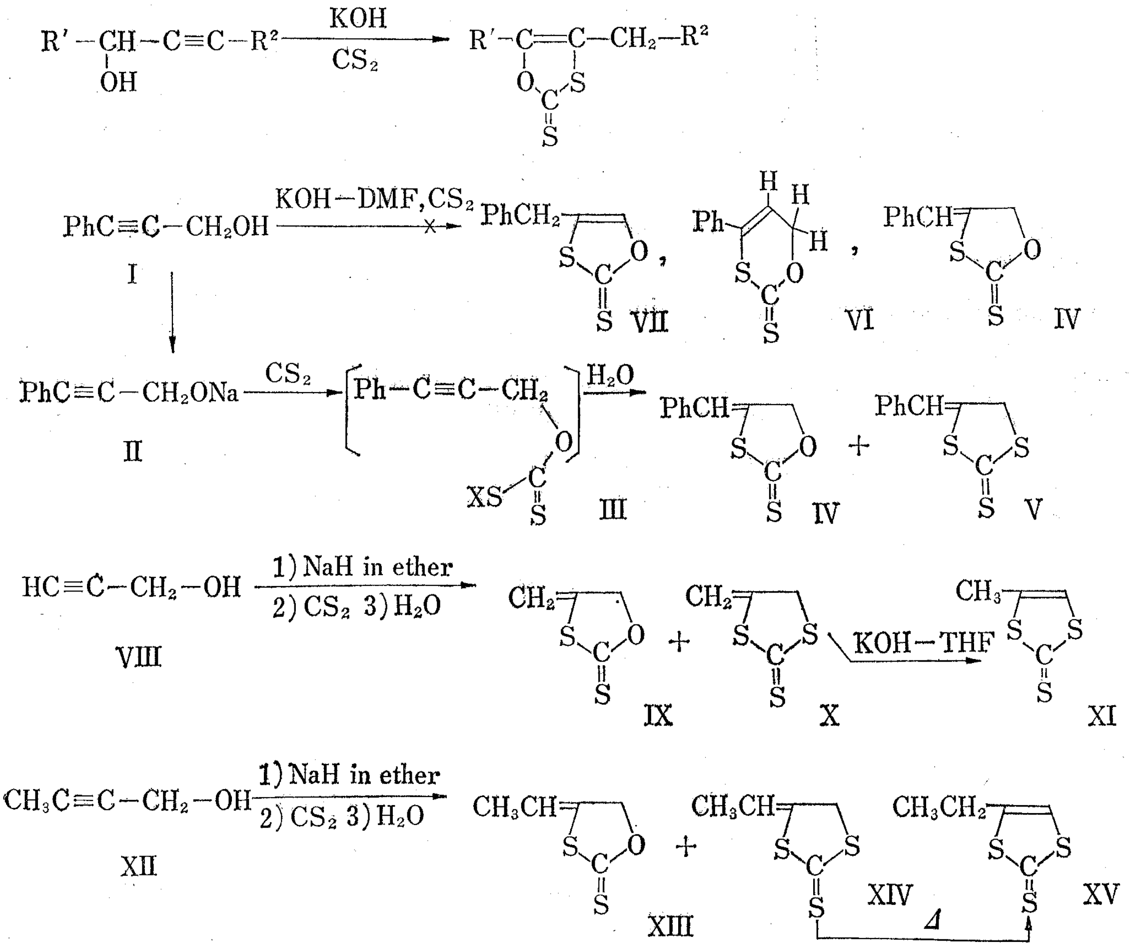


Chart 2

The NMR spectrum of the compound afforded an evidence supporting the structure IV. The spectrum showed, in addition to peaks for the aromatic hydrogens, a doublet at 5.62 and a triplet at 6.58 ppm with an intensity ratio of 2 to 1, and with a coupling constant of 2.0 cps which was much closer to that expected for 1,3-hydrogens of $-\overset{3}{C}H=\overset{2}{C}-\overset{1}{C}H_2-$ system in IV and VII rather than for 1,2-hydrogens of $-\overset{3}{C}=\overset{2}{C}H-\overset{1}{C}H_2-$ system in VI. The signals of benzyl-

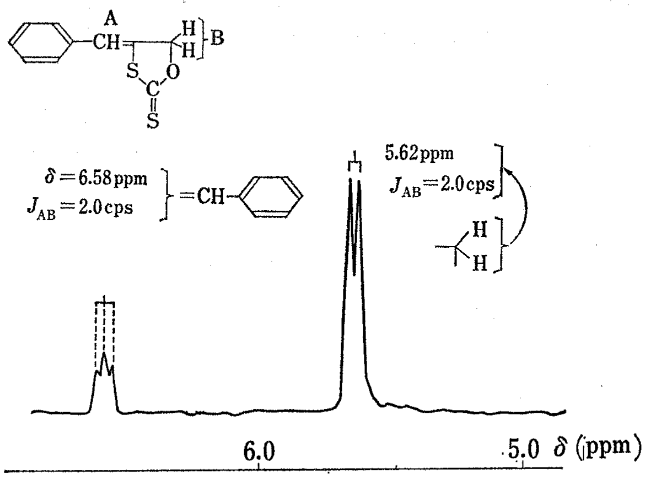
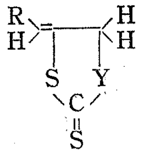


Fig.1. NMR Spectrum of 4-Benzylidene-1,3-oxathiolane-2-thione

methylene in structure VII generally appeared at 3.3—4.3 ppm.[8] Therefore, a signal centered at 5.62 ppm was better assigned for the methylene of 4-benzylidene-1,3-oxathiolane-2-thione (IV) than that of 4-benzyl-1,3-oxathiole-2-thione (VII).

The structure of compound B was assigned as 4-benzylidene-1,3-dithiolane-2-thione (V) on the basis of analytical and infrared data. Characteristic infrared absorption bands were observed at 1615 (C=C) and 1065 cm^{-1}(-S-CS-S-), but no bands characterized for carbon-carbon triple bond and hydroxy group could be observed. Further confirmation of the structure was obtained from its NMR spectrum, which showed a doublet for the methylene (CH_2-S-) at 4.80 ppm and a triplet for the methyne (PhCH=) at 6.77 ppm, and with coupling constant of 1.9 cps. The former appeared at so far high field that of the methylene hydrogen (CH_2-O-) of the compound IV.

Table I. NMR Spectra of 4-Alkylidene-1,3-oxathiolane-2-thiones and 4-Alkylidene-1,3-dithiolane-2-thoines



Comp. No.	R	Y	δ=ppm, J=cps A H(R)C=	 B H(R)C=	 C -$\underline{CH_2}$-O-	 D -$\underline{CH_2}$-S-
X	H	S	5.26 (d.t.) $J_{AB}=2.0$ (d.) $J_{AD}=2.0$ (t.)	5.43 (d.t.) $J_{AB}=2.0$ (d.) $J_{BD}=2.0$ (t.)		4.58 (t.) $J_{AD}=2.0$ (d.) $J_{BD}=2.0$ (d.)
XIV	Me	S	5.82 (q.t.) $J_{AB}=7.0$ (q.) $J_{AD}=1.8$ (t.)	1.77 (d.t.) $J_{AB}=7.0$ (d.) $J_{BD}=1.8$ (t.)		4.58 (d.q.) $J_{AD}=1.8$ (d.) $J_{BD}=1.8$ (q.)
V	Ph	S	6.77 (t.) $J_{AD}=1.9$	7.12—7.18 (m.)		4.80 (d.) $J_{AD}=1.9$
IX	H	O	5.32 (d.t.) $J_{AB}=2.5$ (d.) $J_{AC}=2.5$ (t.)	5.50 (d.t.) $J_{AB}=2.5$ (d.) $J_{BC}=2.5$ (t.)	5.58 (t.) $J_{AC}=2.5$ (d.) $J_{BC}=2.5$ (d.)	
XIII	Me	O	5.65 (q.t.) $J_{AB}=7.0$ (q.) $J_{AC}=2.0$ (t.)	1.77 (d.t.) $J_{AB}=7.0$ (d.) $J_{BC}=2.0$ (t.)	5.37 (d.q.) $J_{AC}=2.0$ (d.) $J_{BC}=2.0$ (q.)	
IV	Ph	O	6.58 (t.) $J_{AC}=2.0$	7.02—7.69 (m.)	5.61 (d.) $J_{AC}=2.0$	

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[8] In Varian's NMR spectra catalog, chemical shifts (ppm) for benzyl-methylenes of the following compounds have been shown indene (3.33), eugenol (3.30), dibenzylketone (3.70), diphenan (3.97), 2-benzylpyridine (4.18) and α-(3,5-dimethyl-4-hydroxybenzyl)-naphthalene (4.27).

In place of 3-phenyl-2-propyn-1-ol (I), propargyl alcohol (VIII) was treated with carbon disulfide under the same condition to give two main products after silica-gel chromatography. They were identified as 4-methylidene-1,3-oxathiolane-2-thione (IX) and 4-methylidene-1,3-dithiolane-2-thione (X) on the basis of elemental and spectral analyses. The presence of methylidene group in IX and X was established by their infrared absorption spectra appeared at 875 and 872 cm^{-1}, respectively. Accurate evidence of the position of the double bond was obtained from their NMR spectra, which displayed a triplet (at 5.58 ppm in IX and at 4.58 ppm in X) and two multiplets (at 5.52 and 5.50 ppm in IX, and at 5.26 and 5.43 ppm in X), with an intensity ratio of 2 to 1, respectively.

The cyclic trithiocarbonate (X) was readily rearranged to the isomeric trithiocarbonate (XI) in good yield by treatment with potassium hydroxide in tetrahydrofuran at room temperature. The compound showed infrared absorption bands at 1648 and 1070 cm^{-1} due to double bond and trithiocarbonate group, but no band attributed to methylidene (CH_2=) was observed. The structure was finally proved by the NMR spectrum which showed a doublet centered at 2.34 ppm for a methyl group and a quartet centered at 6.70 ppm for a vinyl proton with a coupling constant of 1.3 cps.

In the case of 2-butyn-1-ol (XII), 4-ethylidene-1,3-oxathiolane-2-thione (XIII) was obtained. The structure of the cyclic xanthate was assigned on the basis of analytical and spectral data. The reaction afforded, in addition, considerable amounts of two other products, namely, 4-ethylidene-1,3-dithiolane-2-thione (XIV) and 4-ethyl-1,3-dithiole-2-thione (XV). The structures of the both isomeric trithiocarbonates were confirmed from infrared and NMR spectral analyses, similar to the foregoing cases, and the facts that the trithiocarbonate (XIV) was readily rearranged to the isomer (XV) at the vacuum distillation temperature (see Experiment).

Alkylidene dithiolane-2-thiones were rearranged to the corresponding dithiole-2-thiones except 4-benzylidene-1,3-dithiolane-2-thione. When the rearrangement of 4-alkylidene-1,3-oxathiolane-2-thiones was attempted under various condition, the expected 4-alkyl-1,3-oxathiole-2-thiones described as 1-oxa-3-thiacyclopent-4-ene-2-thiones in the Belgian patent[6] were not obtained, but only the starting materials were recovered.

Experimental[9]

Preparing or Refining of Starting Materials——3-Phenyl-2-propyn-1-ol (bp 100—103° (5 mmHg)) was prepared from phenyl ethynyl magnesium bromide and formaldehyde,[10] and 2-butyn-1-ol (bp 62—65° (28 mmHg)) was obtained from 1,3-dichloro-2-butene.[11]

Commercially available 2-propyn-1-ol (bp 56—57° (75 mmHg)) and carbon disulfide were purified by distillation.

Commercially available sodium hydride[12] was used as 50% contents.

Above mentioned three alcohols were identified by NMR and infrared spectra, and elemental analysis.

Reaction of 3-Phenyl-2-propyn-1-ol (I) and Carbon Disulfide——To suspension of NaH (0.05 mole) in anhyd. ether (100 ml), 3-phenyl-2-propyne-1-ol (I) (7.25 g) was added dropwise under ice-salt cooling and stirred continuously at room temperature, until no bubbles were recognized when a drop of the reaction mixture was added into EtOH. To the reaction mixture freshly distilled carbon disulfide (4.2 g) was added under ice cooling, and after stirring for 3 hr at room temperature. The reaction mixture was poured into ice water (100 ml), precipitated solid (8.5 g) was collected by filtration and recrystallized from benzene to afford 4-benzylidene-1,3-oxathiolane-2-thione (IV) as pale yellow crystals of mp 133—134°. *Anal.* Calcd. for $C_{10}H_8OS_2$ (IV): C, 57.69; H, 3.87; S, 30.80. Found: C, 57.73; H, 3.86; S, 30.58. IR ν_{max}^{Nujol} cm^{-1}: 1625 (-C=C-),

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[9] All boiling points were uncorrected. The NMR spectra were recorded on Varian A-60 in deuteriochloroform or tetrachloromethane containing tetramethylsilane as internal standard. The appeared data of the 4-alkylidene-1,3-oxathiolane-2-thiones and -1,3-dithiolane-2-thiones were summarized in Table.

[10] T.Y. Lai, *Bull. Soc. Chim. France*, 3, 1093 (1963).

[11] Org. Synthesis, Collective volume IV. p. 128.

[12] Wakō Pure Chemical Industries, LTD. NaH: *ca.* 50% (in oil).

1214, 1052 (–S–CS–O–). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 262 (4.20), 291 (4.20). From filtrate organic layer was separated and aqueous layer was extracted with benzene. Combined extracts were washed successively with H_2O and satd. NaCl solution and dried over anhyd. Na_2SO_4. Solvents were evaporated under reduced pressure and the residue was chromatographed over silica gel (Cica: 100 mesh). Elution with *n*–hexane–benzene (4:1) afforded two crystalline substances. One of them was recrystallized from benzene to give 1.75 g of plae yellow crystals (IV), mp 133—134°. Total yield of IV was 98.5%. The other was recrystallized from *n*–hexane to give 0.06 g (Yield: 1.0%) of 4–benzylidene–1,3–dithiolane–2–thione (V) as yellow crystals, mp 119.5—121°. *Anal.* Calcd. for $C_{10}H_8S_3$ (V): C, 53.53; H, 3.59; S, 42.87. Found: C, 53.56; H, 3.76; S, 42.41. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1615 (–C=C–), 1067 (–S–CS–S–). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 264 (4.04), 310.3 (4.17), 344 (4.02).

Reaction of Propargly Alcohol (VIII) with Carbon Disulfide——By the same method as the case of 3–phenyl–2–propyn–1–ol, propargyl alcohol (VIII) (3.02 g) was treated with NaH (0.05 mole) and carbon disulfide (4.2 g) in ether (100 ml), the reaction mixture was poured into ice water, organic layer was separated and aqueous layer was extracted with ether. Combined extracts were washed with H_2O and satd. NaCl solution, and dried over anhyd. Na_2SO_4 and ether was evaporated under reduced pressure. The resulting oil was chromatographed (silica gel). Elution with *n*–hexane–benzene (4:1) afforded the following two substances: (1) 2.9 g of 4–methylidene–1,3–oxathiolane–2–thione (IX) as a pale yellow oil, bp 81° (3 mmHg) (Yield. 44.5%). *Anal.* Calcd. for $C_4H_4OS_2$ (IX): C, 36.34; H, 3.05; S, 48.51. Found: C, 36.43; H, 3.13; S, 48.49. IR $\nu_{\max}^{\text{Liquid}}$ cm^{-1}: 1630 (–C=C–), 1208, 1048 (–S–CS–O–), 875 (H_2C=). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 228 (3.69), 291.5 (3.89). (2) 0.85 g of 4–methylidene–1,3–dithiolane–2–thione (X) as a yellow oil, bp 100° (3 mmHg) (Yield: 23.6%). *Anal.* Calcd. for $C_4H_4S_3$ (X): C, 32.39; H, 2.72; S, 64.86. Found: C, 32.76; H, 2.54; S, 64.04. IR $\nu_{\max}^{\text{Liquid}}$ cm^{-1}: 1615 (–C=C–), 1065 (–S–CS–S–), 872 (H_2C=). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 230 (3.76), 320 (4.03).

Rearrangement of X to 4-Methyl-1,3-dithiole-2-thione (XI)——Mixture of 4–methylidene–1,3–dithiolane–2–thione (X) (0.02 g) and KOH (0.02 g) in THF (20 ml) and EtOH (10 ml) was stirred for 1 hr at room temperature, and after removal of solvent under reduced pressure at room temperature the resulting yellow oil was poured into ice water (50 ml), extracted with ether, etheral layer was washed with satd. NaCl solution and dried over anhyd. Na_2SO_4. After removal of ether yellow oily residue was chromatographed. Elution with *n*–hexane–benzene (4:1) gave 0.015 g of a yellow oil (XI), bp 100° (3 mmHg) (Yield: 75%). *Anal.* Calcd. for $C_4H_4S_3$ (XI): C, 32.39; H, 2.72; S, 68.86. Found; C, 32.47; H, 2.49; S, 64.69. IR $\nu_{\max}^{\text{Liquid}}$ cm^{-1}: 1630 (–C=C–), 1055 (–S–CS–S–). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 233.5 (3.50), 370.5 (4.10). NMR (in CCl_4) τ (J=cps): 7.66 (3H, d., J=1.3), 3.3 (1H, q., J=1.3).

Reaction of 2-Butyn-1-ol (XII) with Carbon Disulfide——2–Butyn–1–ol (XII) (3.85 g) was recated with NaH (0.05 mole) and carbon disulfide (4.5 g) in ether (100 ml), and the reaction mixture was poured into ice water, organic layer was separated and aqueous layer was extracted with ether. Combined extracts were washed with H_2O and satd. NaCl solution, and dried over anhyd. Na_2SO_4 and ether was evaporated. The residue was chromatographed (silica gel). Elution with *n*–hexane–benzene (4:1) afforded two substances. One of them was 4–ethylidene–1,3–oxathiolane–2–thione (XIII) as a pale yellow oil, bp 75—80° (2 mmHg), 1.83 g (Yield: 24%). *Anal.* Calcd. for $C_5H_6OS_2$ (XIII): C, 41.07; H, 4.31; S, 43.85. Found: C, 41.53; H, 4.13; S, 43.72. IR $\nu_{\max}^{\text{Liquid}}$ cm^{-1}: 1655 (–C=C–), 1205, 1048 (–S–CS–O–). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 246.5 (3.83), 297.5 (4.07). The other was 4–ethylidene–1,3–dithiolane–2–thione (XIV) as a yellow oil, 1.42 g (Yield: 35%). *Anal.* Calcd. for $C_5H_6S_3$ (XIV): C, 37.00; H, 3.72; S, 59.27. Found: C, 37.26; H, 3.90; S, 58.95. IR $\nu_{\max}^{\text{Liquid}}$ cm^{-1}: 1648 (–C=C–), 1070 (–S–CS–S–). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 233.15 (3.78), 315 (4.09). When compound XIV was distilled at 110—115° (bath temp.) under 0.05 mmHg, a part of XIV rearranged to 4–ethyl–1,3–dithiole–2–thione (XV). *Anal.* Calcd. for $C_5H_6S_3$ (XV): C, 37.00; H, 3.72; S, 59.27. Found: C, 37.29; H, 3.84; S, 59.38. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1660 (–C=C–), 1058 (–S–CS–S–). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (log ε): 234 (3.88), 362 (4.20). NMR (in $CDCl_3$) τ (J=cps): 3.28 (1H, t., J=1.2), 8.74 (3H, t., J=7.0), 7.23 [2H, q., d., J_1=7.0 (q.), J_2=1.2 (d.)].

Reaction of 3-Phenyl-2-propyn-1-ol (I) with Potassium Hydroxide and Carbon Disulfide——To a suspension of KOH (2.8 g)in DMF (20 ml) was added dropwise a mixture of 3–phenyl–2–propyn–1–ol (6.6 g), carbon disulfide (4.5 g) and DMF (30 ml). The temperature was kept at 5° under ice cooling. After the addition was complete the mixture was stirred for 3 hr. The reaction mixture was poured into ice water (60 ml), neutralized with cold dil. H_2SO_4, and then extracted with methylene chloride (3 × 50 ml), organic layers were washed with H_2O and dried over anhyd. Na_2SO_4. The solvent was distilled off and a gummy residue was chromatographed (*n*–hexane–benzene), but no pure substance could be isolated.

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