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Studies on Acetylenic Compounds. XLVI.[1] The Reactions of Acetylenic Compounds with Thiourea or Ammonium Dithiocarbamate

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Treatment of ethyl propiolate (I) with thiourea or ammonium dithiocarbamate under neutral conditions gave diethyl *cis–cis–β,β′*–thioacrylate (II), stereospecifically. Analogously II was obtained from ethyl *cis–β*–chloroacrylate and the same reagents. II was easily converted to *trans–trans*–II(XII) by heating or irradiation. On the other hand, the reactions of *β*–substituted acetylenic acid esters (XVII a—f) with thiourea afforded the corresponding 1,3–thiazine derivatives (XVIII a—f), unexpectedly. The reactions of propiolonitrile (XX), tetrolonitrile (XXIII) and phenylpropiolonitrile (XXV) with thiourea or ammonium dithiocarbamate afforded *cis–cis–β,β′*–thioacrylonitrile (XXI), *cis–cis–β,β′*–thiocrotononitrile (XXIV) and *cis–cis–β,β′*–thiocinnamonitrile (XXVI), respectively.

Although many reports concerning the addition reactions of acetylenic acid esters have been accumulated, relatively few of the reactions with sulfur– and nitrogen–containing compounds, such as thiourea, ammonium dithiocarbamate and thiosemicarbazide *etc.*, have so far been explored. Ruhemann, *et al.*[3] have reported that the reaction of ethyl phenylpropiolate with thiourea in the presence of sodium ethoxide yields benzalthiohydantoin, while Yokoyama, *et al.*[4] have obtained 2–amino–6–phenyl–4*H*–1,3–thiazin–4–one by the same reaction without base. Mushkalo[5] has obtained thiazolidines by the condensation reactions of dimethyl acetylenedicarboxylate with substituted thioureas. Warrener, *et al.*[6] and Garraway[7] have synthesized 1,3–thiazine derivatives from propiolic acid and dithiocarbamic acid under the acidic conditions. These reactions have mostly been carried out under either acidic or basic conditions and the cyclized products (1,3–thiazine, thiazolidine, and thiohydantoin) have been obtained.

In this paper the authors wish to report the reactions of acetylenic acid ester derivatives, their corresponding potential Michael acceptors,[8] *i.e.* *β*–haloacrylic acid ester, and acetylenic nitrile derivatives with thiourea or ammonium dithiocarbamate in neutral conditions.

When ethyl propiolate (I) was refluxed with thiourea or ammonium dithiocarbamate in ethanol, a common crystalline substance (II) of mp 99—101° was obtained in 87.3 and 28.5% yield, respectively, whose elemental analysis corresponded to $C_{10}H_{14}S$. This compound, II, no longer showed infrared absorption maximum at 2100 cm^{-1} region for triple bond. The ultraviolet absorption spectrum showed a maximum at 303 mμ (ε=26300). The nuclear magnetic resonance spectrum in hexadeuterodimethyl sulfoxide showed the AB type quartet at 6.2 and 7.7 ppm (J_{AB}=10 cps) due to olefinic protons having *cis* configuration, the triplet at 1.2 ppm, and the quartet at 4.17 ppm due to the ethyl ester group. From these results, II was not a cyclized product, but evidently diethyl *cis–cis–β,β′*–thioacrylate.

1) Part XLV: J. Ide and Y. Kishida, *Chem. Pharm. Bull.* (Tokyo), **16**, 784 (1968).
2) Location: *Hiromachi, Shinagawa–ku, Tokyo.*
3) S. Ruhemann and H.E. Stapleton, *J. Chem. Soc.*, **77**, 239 (1900).
4) A. Yokoyama and H. Tanaka, *Chem. Pharm. Bull.* (Tokyo), **10**, 19 (1962), **12**, 683 (1964).
5) L.K. Mushkalo and G. Ya. Yangul, *Ukr. Khim. Zh.*, **21**, 732 (1955) [*C.A.*, **50**, 16751*a* (1956)].
6) R.N. Warrener and E.N. Cain, *Chem. & Ind.* (London), **1964**, 1989.
7) J.L. Garraway, *J. Chem. Soc.*, **1962**, 4077.
8) H.O. House, W.F. Roelofs, and B.M. Trost, *J. Org. Chem.*, **31**, 646 (1966).

The formation of II from I is thought to proceed with the reaction mechanisms shown in Chart 1. In the case of the reaction of I with ammonium dithiocarbamate, ammonium thiocyanate was obtained together with II, however, the reaction with thiourea, cyanamide or O–ethyl urea were not detectable.[9]

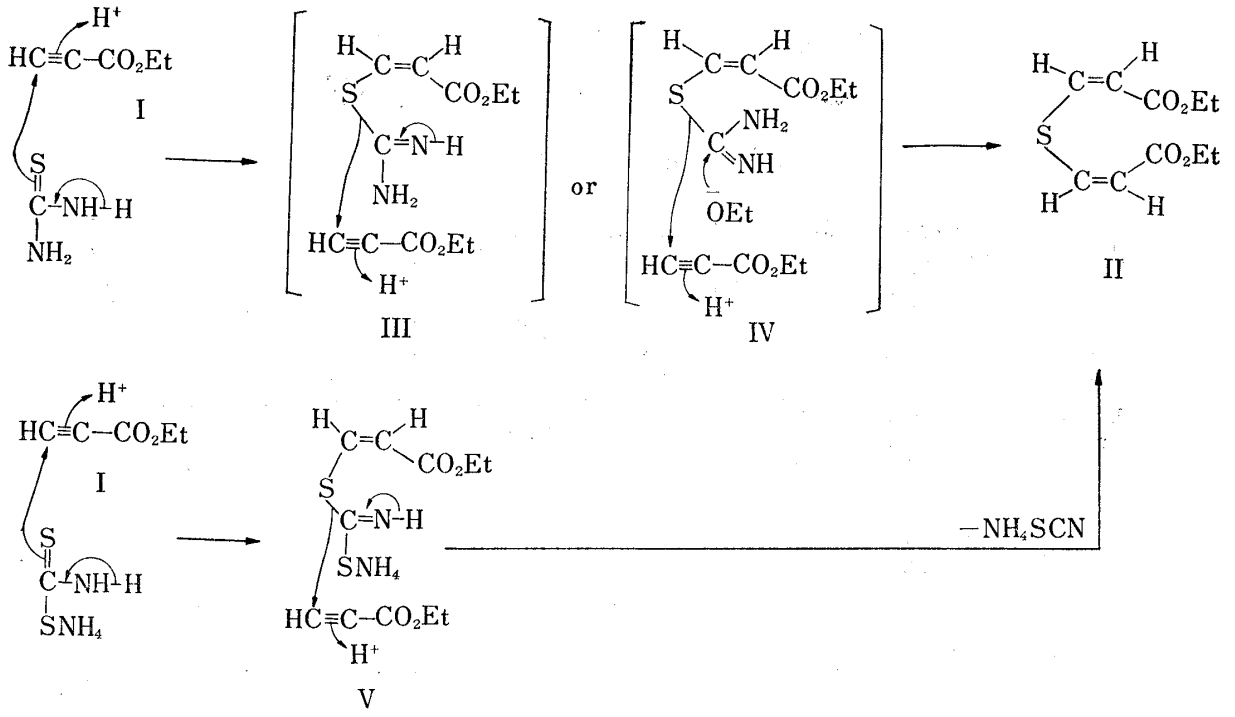


Chart 1

On the other hand, when ethyl *cis*–β–chloroacylate (VI) was treated with thiourea or ammonium dithiocarbamate, the same crystalline product was obtained in 46.3 and 44% yield, respectively, as in the reaction of I with the same reagents. The plausible reaction mechanism for the formation of II from VI is thought as shown in Chart 2, wherein the addition of the nucleophile is followed by loss of chloride ion, just as proposed by Jones, *et al.*[10] in the similar reactions. It can proceed with either synchronous way or the formation of an intermediate adduct. The activated complex may be represented by [A] in Chart 2. By losing chloride ion, the complex can return to its original configuration. Moreover, many reports have been described[11–17] that this type of the reactions proceed largely with retention of the original geometric configuration. The second stage (VII, VIII→IX and X→XI) would

9) Recently J.W. Lown and J.C.N. Ma [*Can. J. Chem.*, **45**, 939, 953 (1967)] have reported independently the syntheses of 1,3–thiazine derivatives and the addition reaction of 1–acetylthiosemicarbazone to methyl propiolate to give dimethyl β,β'–thioacrylate. The reaction mechanism, they proposed, contained the step of attacking of methoxy anion (type IV in Chart 1). According to this mechanism, 1–acetyl–O–methylsemicarbazone or its degradation products (*i.e.* 1–acetyl–2–carbohydroxyhydrazine, acetylhydrazine) should be obtained. However, in our reactions with ammonium dithiocarbamate, ammonium thiocyanate was obtained as shown in Chart 1. From this, it is reasonable to consider that a second stage of the reaction path would proceed with loss of a proton attached to the imino group (type III in Chart 1) rather than with an attack of ethoxy anion.

10) D.E. Jones, R.O. Morris, C.A. Vernon, and R.F.M. White, *J. Chem. Soc.*, **1960**, 2349.

11) W. Autenrith, *Chem. Ber.*, **29**, 1639 (1896).

12) H. Scheiber and J. Vors, *Chem. Ber.*, **53**, 379 (1920).

13) Montanari, *Bull. Sic. Fac. Chim. Ind.*, **31**, 16 (1958).

14) Modena, *Ric. Sci.*, **28**, 341 (1958).

15) Moioli and Modena, *Gazz. Chim. Ital.*, **89**, 854 (1959).

16) Modena and Todesco, *Gazz. Chim. Ital.*, **89**, 856 (1959).

17) Modena, Todesco, and Tanti, *Gazz. Chim. Ital.*, **89**, 878 (1959).

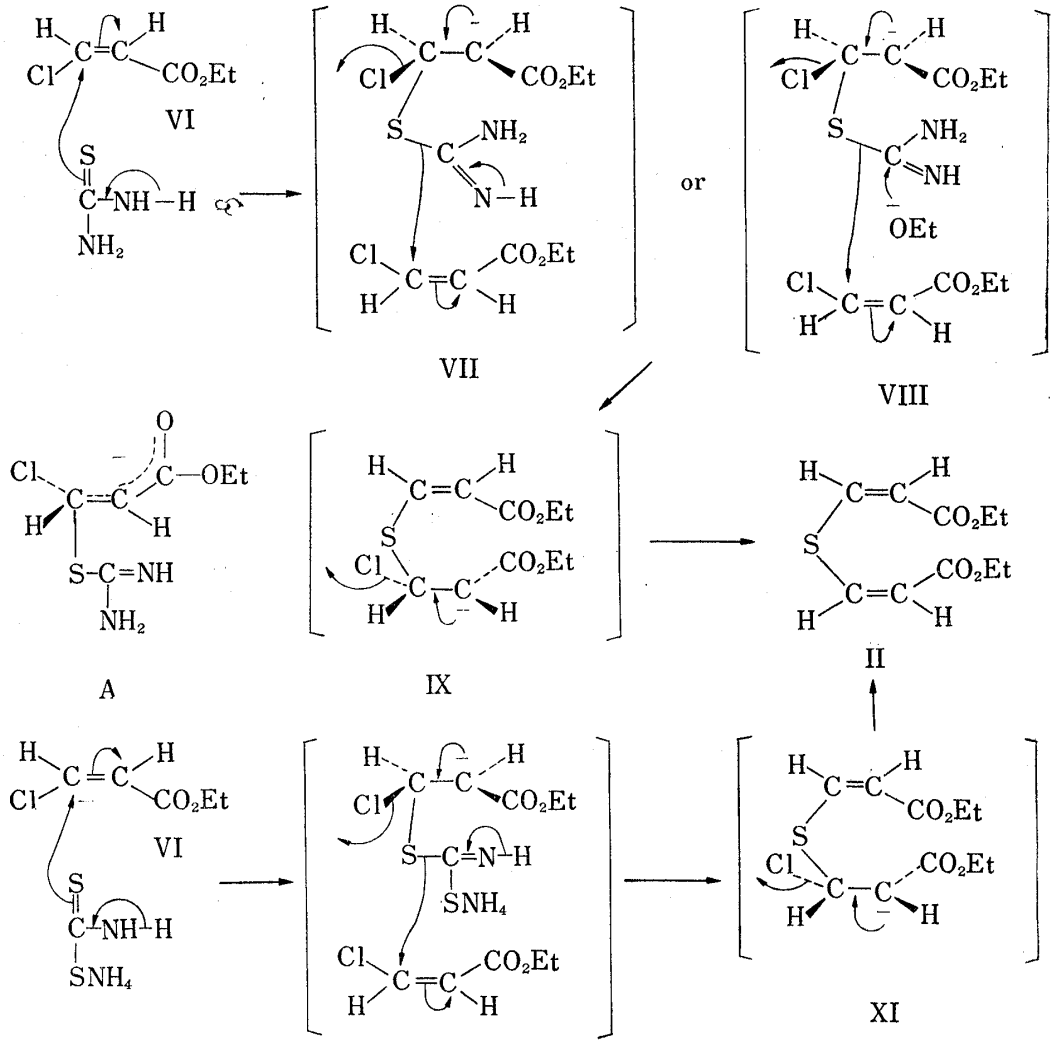


Chart 2

proceed similarly to the first stage (VI→VII, VIII and VI→X) with retention of the geometric configuration.

When diethyl *cis–cis–β,β′*–thioacrylate, II, was heated at 150° under reduced pressure (100 mmHg) or irradiated (Hanovia, high pressure lamp, 450 W), it was easily converted to diethyl *trans-trans-β,β′*-thioacrylate(XII) as the main product. In this case, a mixture of *cis–cis*, *trans–trans*, and *cis–trans* was obtained as by–products (Chart 3).

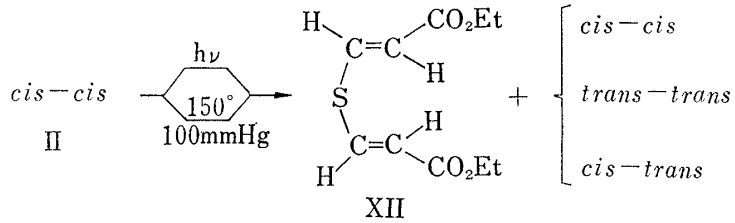


Chart 3

The configuration of this compound, XII, is thought to be *trans–trans*, because the nuclear magnetic resonance spectrum of XII in hexadeuterodimethyl sulfoxide showed the AB type quartet at 6.18 and 7.94 ppm due to olefinic protons with the coupling constant $J_{AB}=15$ cps. The ultraviolet absorption maximum showed 300 mμ ($\varepsilon=25500$).

Similarly, the authors expected to obtain diethyl *β,β′*–substituted thioacrylate (XIII) on the reaction of substituted propiolic acid esters with thiourea or ammonium dithiocarbamate.

However, contrary to our expectation, treatment of ethyl tetrolate (XIV) with thiourea in ethanol under the same conditions as described above afforded a thiazine compound (XV)

melted at 209—211° in 50% yield. The infrared absorption spectrum showed the bands at 1645, 1680 cm^{-1} due to the amide group and the imino group, respectively. The analytical data agreed with the empirical formula of $C_5H_6ON_2S$. This substance could not be dissolved in any solvent, even in hydrochloric acid. Refluxing of the compound, XV, with conc-hydrochloric acid—ethanol, afforded a crystalline substance (XVI), mp 177—180°, which had the constitution, $C_5H_5O_2NS$. The infrared absorption spectrum showed the existence of an imide group (1680, 1665 cm^{-1}) in the compound. The nuclear magnetic resonance spectrum of XVI in hexadeuterodimethyl sulfoxide showed the doublet peak at 2.25 ppm (J=1.1 cps) due to the vinyl methyl group and a quartet peak at 6.4 ppm (J=1.1 cps) assigned to the vinyl proton. From these results, XV was assigned to 2,3-dihydro-2-imino-4-oxo-6-methyl-4*H*-1,3-thiazine, and for the hydrolysis product, XVI, 2,3-dihydro-2,4-dioxo-6-methyl-4*H*-1,3-thiazine.

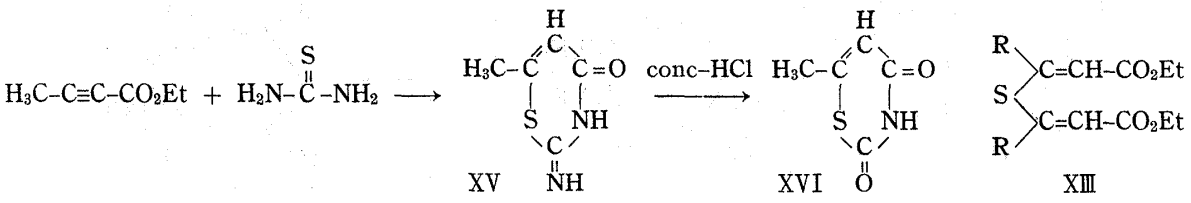
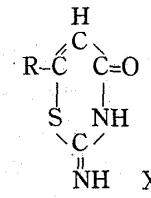


Chart 4

Similarly, other substituted acetylenic acid esters (XVII a—f) were treated with thiourea under the same conditions as described above to yield 2,3-dihydro-2-imino-4-oxo-6-substituted-4*H*-1,3-thiazine (XVIII a—f), respectively, and subsequent hydrolyses gave 2,3-dihydro-2,4-dioxo-6-substituted-4*H*-1,3-thiazine (XIX a—f), respectively (Table I, Table II).

Expecting the same results as in the derivatives of acetylenic acid esters, propiolonitrile (XX) was treated with thiourea or ammonium dithiocarbamate in ethnaol. In this case a crystalline substance (XXI) of mp 142—142.5° was obtained in 60 and 21% yield, respectively, based on the precursor, propiolamide which had been dehydrated with phosphorous pentoxide to the starting propiolonitrile. The elemental analysis of this substance agreed with the formula $C_6H_4N_2S$. The infrared absorption spectrum still showed nitrile group (2210 cm^{-1}). The nuclear magnetic resonance spectrum in deuterochloroform showed only the AB type

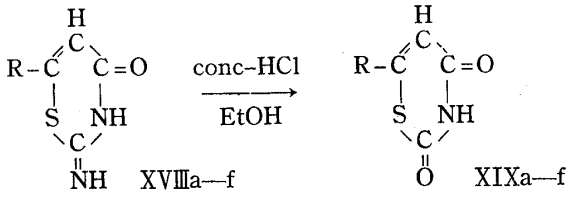
Table I. $R-C\equiv C-CO_2R' + H_2N-C(=S)-NH_2 \longrightarrow$ XVIIIa—f



	R	R′	mp (°C)	Yield (%)	NMR[a] Chemical shift H-5 (ppm)
a.[4,c]	ph-	Et	208—210	67	6.8 (s)
b.	*p*-CH_3-C_6H_4	Et	226—228	52.7	6.7 (s)
c.	*p*-CH_3O-C_6H_4	Et	226—229	40.6	6.65(s)
d.	*p*-Cl-C_6H_4-	Et	266—270	58.3	6.7 (s)
e.	*o*-Cl-C_6H_4-	Et	213—215	41.7	6.35(s)
f.	MeO_2C-	Me	245 (decomp.)	88.8	6.8 (s)

a) NMR spectra were taken on Varian A-60 spectrometer with Me_4Si as the internal standard.
b) s=singlet
c) Yokoyama, *et al.* have reported that the compound obtained in this reaction is 2-amino-6-phenyl-4*H*-1,3-thiazine-4-one.

TABLE II.



	R	mp (°C)	Yield (%)	NMR[a] Chemical shift H-5 (ppm)
a.	ph-	242—243	88.8	6.85(s)[b]
b.	*p*-CH_3-C_6H_4	241—244	81.8	6.70(s)
c.	*p*-CH_3O-C_6H_4-	233—235	90.0	6.80(s)
d.	*p*-Cl-C_6H_4-	248—251	90.0	6.80(s)
e.	*o*-Cl-C_6H_4-	148—151	75.0	6.60(s)
f.	MeO_2C- (HO_2C-=XIX)	236—241	85.8	6.75(s)

a, b) similar to those in the case of Table I

quartet at 6.00 and 7.75 ppm (J_{AB}=10 cps) due to olefinic protons having *cis* configuration. From these results the compound, XXI, was assigned to *cis-cis-β,β'*-thioacrylonitrile.

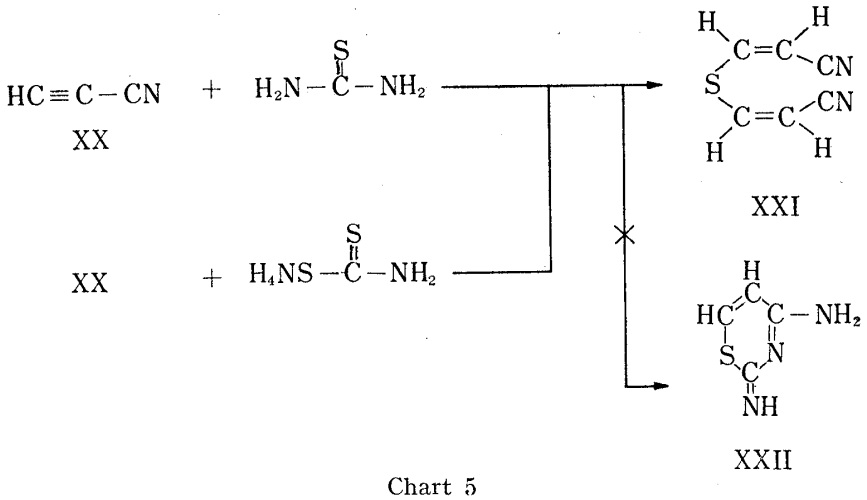


Chart 5

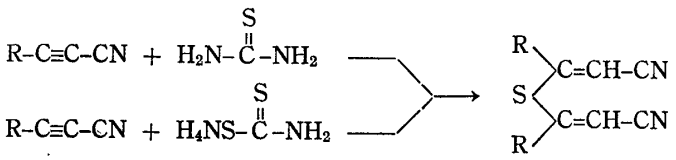
Similarly, the reaction of tetrolonitrile (XXIII) with thiourea or ammonium dithiocarbamate gave *β,β'*-thiocrotononitrile (XXIV), mp 119—121°, in 80 and 20% yield, respectively, and of phenyl propiolonitrile (XXV) gave *β,β'*-thiocinnamonitrile (XXVI), mp 175—176°, in 83.3 and 50% yield, respectively. The physical data and yields are summarized in Table III.

Although there is no decisive evidence about the configurations of the compounds, XXIV (R=CH_3) and XXVI (R=Ph),from their physical data, these would have *cis* configuration by analogy with the propiolonitrile case.

The same compound, XXVI, was also obtained[18] in 60% yield from *β*-bromocinnamonitrile (XXVII),[19] which had been prepared by the addition of cyanogen bromide to phenylacetylene, and thiourea under the same conditions as described above.

18) Unpublished data from our laboratory.
19) I. Iwai, T. Iwashige, Y. Yura, N. Nakamura, and K. Shinozaki, *Chem. Pharm. Bull.* (Tokyo), **12**, 1446 (1966).

TABLE III.



	R	mp (°C)	Yield (%) with thiourea	Yield (%) with ammonium dithiocarbamate	NMR[a,b] Chemical shift (ppm)
XXI	H	142—142.5	60	21	6.0(d), 7.95(d) (J=10 cps)
XXIV	CH_3	119—121	80	20	2.2(d), 6.15(q) (J=2 cps)
XXVI	Ph	176—168	83.3	50	6.3(s), 7.3(m)

a) As the internal standard, tetramethylsilane was used in $CDCl_3$
b) s=singlet, d=doublet, q=quartet, m=multiplet

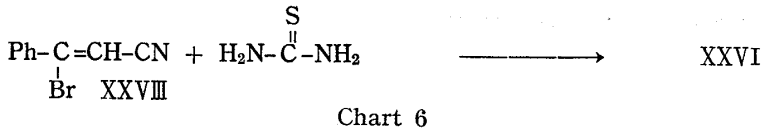


Chart 6

The reaction forming these β,β'-thioacrylonitrile derivatives would proceed with just the same behavior as in the reaction using ethyl propiolate.

It is very difficult to explain the different results of the formations of thiazine and *cis–cis*-β,β'-thioether derivatives. However, it is clear that the reactions of propiolic acid ester (with the exception of β-substituted ester derivatives), β-haloacrylic acid ester and all propiolonitrile derivatives with thiourea or ammonium dithiocarbamate, are very convenient for stereospecific syntheses of *cis–cis*-thioether derivatives.

Experimental[20]

Diethyl *cis-cis*-β,β'-thioacrylate (II)——a) From ethyl propiolate and thiourea: A mixture of ethyl propiolate (2.94 g, 0.03 mole), thiourea (2.3 g, 0.03 mole) and 99% EtOH (15 ml) was heated on steam bath for 3 hr. After cooling, the solvent was evaporated under reduced pressure and H_2O and AcOEt were added to the residue. The aqueous layer was extracted with AcOEt and the combined extracts were washed with H_2O three times, dried over Na_2SO_4 and evaporated under reduced pressure to give a crystalline substance (3.0 g). Recrystallization from ether gave diethyl *cis–cis*-β,β'-thioacrylate (II) as white needles of mp 99—101°. UV λ_{max} mμ (ε): 303 (26300). *Anal.* Calcd. for $C_{10}H_{14}S$: C, 52.15; H, 6.09; S, 13.91. Found: C, 52.15; H, 6.23; S, 13.65.

b) From ethyl propiolate and ammonium dithiocarbamate: To ammonium dithiocarbamate in EtOH prepared from 15% NH_3 in EtOH (10 ml) and CS_2 (3.92 g, 0.04 mole) was added dropwise ethyl propiolate (3.92 g, 0.04 mole) in EtOH (15 ml) under controlling the temperature at 20—30° with stirring. The reaction mixture was stirred overnight at room temperature. Then, EtOH was evaporated under reduced pressure and the residue was dissolved in H_2O and AcOEt, and the AcOEt layer was separated, the aqueous layer was extracted with AcOEt. The combined extracts were washed with H_2O three times, dried over Na_2SO_4 and evaporated to give a crystalline substance (1.2 g). Recrystallization from ether gave diethyl *cis–cis*-β,β'-thioacrylate (II) of mp 99—101°, which showed no depression in mp on admixture with a product from a), and the infrared spectrum was superimposable on that of a product from a). The aqueous layer was evaporated under reduced pressure at 40—50°, and the residue was washed with ether. Recrystallization from EtOH gave ammonium thiocyanate (1.1 g) of mp 149—150°, whose infrared spectrum was superimposable on that of an authentic sample.

20) All melting points are uncorrected. UV spectra were taken in EtOH. NMR spectra were recorded on Varian A-60 spectrometer.

c) From ethyl *cis*-β-chloroacrylate and thiourea: A suspension of ethyl *cis*-β-chloroacrylate (2.0 g, 0.015 mole) and thiourea (2.3 g, 0.03 mole) in 99% EtOH (10 ml) was heated on steam bath for 3 hr. After cooling, the reaction mixture was evaporated under reduced pressure and the residue was dissolved in H_2O and AcOEt, and the AcOEt layer was separated. The aqueous layer was extracted with AcOEt and the combined extracts were washed with H_2O three times, dried over Na_2SO_4 and evaporated. The crystalline residue (0.8 g) was recrystallized from ether to afford II of mp 99—101°. The infrared spectrum was superimposable on that of a product from a) or b).

d) From ethyl *cis*-β-chloroacrylate and ammonium dithiocarbamate: To ammonium dithiocarbamate in EtOH prepared from 15% NH_3 in EtOH (5 ml) and CS_2 (1.52 g) was added dropwise ethyl *cis*-β-chloroacrylate (2.7 g, 0.02 mole) in EtOH (10 ml) at room temperature. The reaction mixture was stirred overnight at room temperature and then evaporated under reduced pressure to give a crystalline substance (1.0 g). Recrystallization from ether afforded II of mp 99—101°. The infrared spectrum was superimposable on that of a products from a), b), or c).

Diethyl *trans-trans-β,β'*-Thioacrylate (XII) and *trans-trans*, *cis-cis*, and *cis-trans* Mixture——a) By heating: Diethyl *cis-cis*-β,β'-thioacrylate (II) (0.5 g) was heated at 150° under 100 mmHg for 8 hr. After cooling, the crystalline substnace was recrystallized from ether–hexane to afford colorless needles of diethyl *trans-trans*-β,β'-thioacrylate (XII) (0.33 g), mp 54—57°. UV λ_{max} mμ (ε): 300 (25500). *Anal.* Calcd. for $C_{10}H_{14}S$: C, 52.15; H, 6.09; S, 13.91. Found: C, 52.11; H, 6.21; S, 13.84.

The mother liquor of the first recrystallization was concentrated to afford a crystalline substance, which was recrystallized from ether–hexane several times to afford colorless prisms of *cis-cis*, *trans-trans* and *cis-trans* mixture (*ca.* 1:1:1) (0.07 g), mp 66—67°. The nuclear magnetic resonance spectrum in $(CD_3)_2SO$ showed the three AB type quartets at 5.15, 7.17 ppm (J_{AB}=10 cps), 5.98, 7.20 ppm (J_{AB}=10 cps) and 6.10, 7.70 ppm (J=15 cps) due to olefinic protons and the three triplet peaks at 1.26, 1.28 and 1.30 ppm and the three quartets at 4.18°, 4.20 and 4.22 ppm due to the ethyl ester groups. *Anal.* Calcd. for $C_{10}H_{14}S$: C, 52.15; H, 6.09; S, 13.91. Found: C, 52.01; H, 6.01; N, 13.82.

b) By irradiation: A mixture of diethyl *cis-cis*-β,β'-thioacrylate (II) (0.5 g) and THF (150 ml) was irradiated (Hanovia, high pressure lamp, 450 W) for 7 hr. During the reaction, the UV spectra were being checked every 1 hr. The solvent was evaporated to give a crystalline substance. Recrystallization from ether–hexane gave diethyl *trans-trans*-β,β'-thioacrylate (XII) (0.2 g), mp 55—57°. The infrared spectrum was superimposable on that of the product from a). The residue was recrystallized from ether–hexane several times to afford white prisms (0.205 g) of *cis-cis*, *trans-trans* and *cis-trans* mixture (*ca.* 1:1:1), mp 66—67°.

General Procedure for the Synthesis of 2,3-Dihydro-2-imino-4-oxo-4*H*-1,3-thiazine——A suspension of acetylenic acid ester (1.0 mole) and thiourea (1.0 mole) in 150 ml of EtOH was refluxed for 2—3 hr. After cooling, a crystalline substance separated was collected by filtration, and the filtrate was concentrated under reduced pressure to leave a solid. The combined crystalline substance was washed with H_2O, a small amount of EtOH and ether, and dried *in vacuo* to give 2,3-dihydro-2-imino-4-oxo-4*H*-1,3-thiazine derivatives. Recrystallization from a suitable solvent gave a sample.

2,3-Dihydro-4-oxo-6-methyl-4*H*-1,3-thiazine (XV)——The reaction from ethyl tetrolate (1.12 g, 0.01 mole), thiourea (0.76 g, 0.01 mole) and 15 ml of EtOH gave a crystalline substance (0.7 g), mp 209—211° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3320, 3120 (NH), 1680 (–C=N–), 1640 (–CONH–). UV λ_{max} mμ (ε): 226 (17400), 248.5 (14400). *Anal.* Calcd. for $C_5H_6ON_2S$: C, 42.27; H, 4.23; N, 19.72; S, 22.53. Found: C, 42.34; H, 4.39; N, 19.48; S, 22.41.

2,3-Dihydro-2-imino-4-oxo-6-phenyl-4*H*-1,3-thiazine (XVIIIa)——The reaction from ethyl phenylpropiolate (5.2 g, 0.03 mole), thiourea (2.28 g, 0.03 mole) and 50 ml of EtOH gave a colorless solid, mp 208—210°. IR ν_{max}^{Nujol} cm^{-1}: 3350, 3130 (–NH–), 1640 (–C=N), 1615, 1505 (–CONH–). UV λ_{max} mμ (ε): 246 (18100). *Anal.* Calcd. for $C_{10}H_8ON_2S$: C, 58.82; H, 3.92; N, 13.72; S, 15.68. Found: C, 58.74; H, 3.99; N, 13.85; S, 15.66.

2,3-Dihydro-2-imino-4-oxo-6-(*p*-methylphenyl)-4*H*-1,3-thiazine (XVIIIb)——The reaction from ethyl *p*-methylphenylpropiolate (3.76 g, 0.02 mole), thiourea (1.52 g, 0.02 mole) and EtOH (25 ml) gave 2.3 g of a colorless solid, mp 226—228°. IR ν_{max}^{Nujol} cm^{-1}: 3330, 3130 (–NH–), 1640 (–C=N), 1625, 1530 (–CONH–). UV λ_{max} mμ (ε): 254 (16800), 297 (11600). *Anal.* Calcd. for $C_{11}H_{10}ON_2S$: C, 60.55; H, 4.59; N, 12.84; S, 4.68. Found: C, 60.45; H, 4.71; N, 12.81; S, 14.68.

2,3-Dihydro-2-imino-4-oxo-6-(*p*-methoxyphenyl)-4*H*-1,3-thiazine (XVIIIc)——The reaction from ethyl *p*-methoxyphenylpropiolate (4.1 g, 0.02 mole), thiourea (1.52 g, 0.02 mole) and EtOH (40 ml) gave a colorless solid (1.9 g), mp 226—229°. IR ν_{max}^{Nujol} cm^{-1}: 3330, 3130 (–NH–), 1645 (–C=N–), 1615, 1540 (–CONH–). UV λ_{max} mμ (ε): 220 (24100), 258 (12000), 310.5 (14700). *Anal.* Calcd. for $C_{11}H_{10}O_2N_2S$: C, 56.41; H, 4.27; N, 11.96; S, 13.67. Found: C, 56.30; H, 4.46; N, 11.87; S, 13.52.

2,3-Dihydro-2-imino-4-oxo-6-(*p*-chlorophenyl)-4*H*-1,3-thiazine (XVIIId)——The reaction from ethyl *p*-chlorophenylpropiolate (1.05 g, 0.005 mole), thiourea (0.38 g, 0.005 mole) and EtOH (15 ml) gave a pale

21) I. Iwai and N. Nakamura, *Chem. Pharm. Bull.* (Tokyo), **14**, 1277 (1966).

yellow crystals (0.7 g), mp 266—270°. IR ν_{max}^{Nujol} cm^{-1}: 3330, 3180 (–NH–), 1660 (–C=N–), 1625, 1530 (–CONH–). UV λ_{max} mμ (ε): 253 (18000), 294 (10600). *Anal.* Calcd. for $C_{10}H_7ON_2SCl$: C, 50.31; H, 2.93; N, 11.74; S, 13.41; Cl, 14.88. Found: C, 50.21; H, 3.10; N, 11.71; S, 13.33; Cl, 14.97.

2,3-Dihydro-2-imino-4-oxo-6-(*o*-chlorophenyl)-4*H*-1,3-thiazine (XVIIIe)——The reaction from ethyl *o*-chlorophenylpropiolate (1.05 g, 0.005 mole), thiourea (0.38 g, 0.005 mole) and 15 ml of EtOH gave a colorless solid (0.5 g), mp 213—215°. IR ν_{max}^{Nujol} cm^{-1}: 3330, 3180 (–NH–), 1650 (–C=N), 1640, 1530 (–CONH–). UV λ_{max} mμ (ε): 249 (shoulder) (14000). *Anal.* Calcd. for $C_{10}HCl_7ON_2SCl$:C, 50.31; H, 2.93; N, 11.74; S, 13.41; Cl, 14.88. Found: C, 50.34; H, 3.08; N, 11.74; S, 13.37.

2,3-Dihydro-2-imino-4-oxo-6-carbomethoxy-4*H*-1,3-thiazine (XVIIIf)——To a suspension of thiourea (1.52 g, 0.02 mole) in EtOH was added dropwise dimethyl acetylenedicarboxylate (2.84 g, 0.02 mole) in EtOH (5 ml) maintaining the temperature at 20—25° with vigorous stirring. The stirring was continued for 5 hr at 30°. The crystalline substance separated was collected by filtration, washed with H_2O and ether to give a colorless solid (3.3 g), mp 245° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3320, 3130 (–NH–), 1720 (–CO_2Et), 1680, 1555 (–CONH–). UV λ_{max} mμ (ε): 278.5 (15000), 316 (6400). *Anal.* Calcd. for $C_6H_6O_3N_2S$: C, 38.71; H, 3.23; N, 15.05; S, 17.20. Found: C, 38.71; H, 3.46; N, 14.77; S, 17.05.

General Procedure for the Synthesis of 2,3-dihydro-2,4-dioxo-4*H*-1,3-thiazine (XVI and XIX a—f)——A suspension of 2,3-dihydro-2-imino-4-oxo-4*H*-1,3-thiazine (1 g), conc-HCl (20 ml) in EtOH (10 ml) was refluxed for 2—3 hr. After cooling, the crystalline substance was collected by filtration, and the organic solvent was removed under reduced pressure to leave a solid. The combined crystalline substance was washed with a small amount of H_2O and ether to give 2,3-dihydro-2,4-dioxo-4*H*-1,3-thiazine. Recrystallization from a suitable solvent gave a sample.

2,3-Dihydro-2,4-dioxo-6-methyl-4*H*-1,3-thiazine (XVI)——A suspension of 2,3-dihydro-2-imino-4-oxo-6-methyl-4*H*-1,3-thiazine (XV) (2.0 g, 0.014 mole), conc-HCl (30 ml) in EtOH (15 ml) was refluxed for 2 hr. The solvent was evaporated under reduced pressure to give a crystalline substance (0.7 g). Recrystallization from H_2O afforded colorless needles, mp 175—183°. IR ν_{max}^{Nujol} cm^{-1}: 1680, 1655 (–CONHCO–). UV λ_{max} mμ (ε): 220 (7400), 268 (6900). *Anal.* Calcd. for $C_5H_5O_2NS$: C, 41.95; H, 3.50; N, 9.80; S, 22.37. Found: C, 41.78; H, 3.81; N, 10.03; S, 22.21.

2,3-Dihydro-2,4-dioxo-6-phenyl-4*H*-1,3-thiazine (XIXa)——The reaction from 2,3-dihydro-2-imino-4-oxo-6-phenyl-4*H*-1,3-thiazine (XVIIIa) (1.0 g, 0.005 mole), conc-HCl (10 ml) and EtOH (5 ml) gave a colorless solid (0.9 g), mp 242—243°. IR ν_{max}^{Nujol} cm^{-1}: 1700, 1625 (–CONHCO–). UV λ_{max} mμ (ε): 222 (11800), 255 (10300), 290 (10970). *Anal.* Calcd. for $C_{10}H_7O_2NS$: C, 58.33; H, 3.41; N, 6.87; S, 15.61. Found: C, 58.86; H, 3.39; N, 6.86; S, 15.68.

2,3-Dihydro-2,4-dioxo-6-(*p*-methylphenyl)-4*H*-1,3-thiazine (XIXb)——The reaction from 2,3-dihydro-2-imino-4-oxo-6-(*p*-methylphenyl)-4*H*-1,3-thiazine (XVIIIb) (1.1 g, 0.005 mole), conc-HCl (20 ml) and EtOH (10 ml) gave a colorless solid (0.9 g), mp 241—244°. IR ν_{max}^{Nujol} cm^{-1}: 1695, 1675 (–CONHCO–). UV λ_{max} mμ (ε): 224 (12500), 268 (11000), 296 (13500).

2,3-Dihydro-2,4-dioxo-6-(*p*-methoxyphenyl)-4*H*-1,3-thiazine (XIXc)——The reaction from 2,3-dihydro-2-imino-4-oxo-6-(*p*-methoxyphenyl)-4*H*-1,3-thiazine (XVIIIc) (1.0 g, 0.005 mole), conc-HCl (20 ml) and EtOH (10 ml) gave a colorless solid (0.9 g), mp 233—235°. IR ν_{max}^{Nujol} cm^{-1}: 1680, 1575 (–CONHCO–). UV λ_{max} mμ (ε): 222 (13900), 311 (17300). *Anal.* Calcd. for $C_{11}H_9O_2NS$: C, 56.17; H, 3.81; N, 5.96; S, 13.61. Found: C, 56.12; H, 3.81; N, 5.95; S 13.40.

2,3-Dihydro-2,4-dioxo-6-(*p*-chlorophenyl)-4*H*-1,3-thiazine (XIXd)——The reaction from 2,3-dihydro-2-imino-4-oxo-6-(*p*-chlorophenyl)-4*H*-1,3-thiazine (XVIIId) (1.0 g), conc-HCl (20 ml) and EtOH (10 ml) gave a colorless solid (0.9 g), mp 248—251°. IR ν_{max}^{Nujol} cm^{-1}: 1690, 1670, 1560. UV λ_{max} mμ (ε): 232 (shoulder) (11600), 264 (11700), 291 (11700). *Anal.* Calcd. for $C_{10}H_6O_2NSCl$: C, 50.10; H, 2.50; N, 5.84; S, 13.36; Cl, 14.82. Found: C, 49.94; H, 2.57; N, 6.12; S, 13.26; Cl, 15.10.

2,3-Dihydro-2,4-dioxo-6-(*o*-chlorophenly)-4*H*-1,3-thiazine (XIXe)——The reaction from 2,3-dihydro-2-imino-4-oxo-6-(*o*-chlorophenyl)-4*H*-1,3-thiazine (XVIIIe) (0.4 g), conc-HCl (10 ml) and EtOH (5 ml) gave a crystalline substance (0.3 g), mp 148—151°. IR ν_{max}^{Nujol} cm^{-1}: 1680, 1665, 1588. UV λ_{max} mμ (ε): 229.5 (shoulder) (12200), 277 (9000). *Anal.* Calcd. for $C_{10}H_6O_2NSCl$: C, 50.10; H, 2.50; N, 5.84; S, 13.36; Cl, 14.82. Found: C, 50.05; H, 2.69; N, 5.72; S, 13.35; Cl, 15.02.

2,3-Dihydro-2,4-dioxo-4*H*-1,3-thiazine-6-carboxylic Acid (XIXf)——The reaction from 2,3-dihydro-2-imino-4-oxo-6-carbomethoxy-4*H*-1,3-thiazine (XVIII–f) (1.9 g, 0.01 mole), conc-HCl (30 ml) and EtOH (10 ml) gave a crystalline substance. Recrystallization from EtOH gave colorless needles (1.63 g), mp 236—241°. IR ν_{max}^{Nujol} cm^{-1}: 2800—2500, 1760 (–CO_2H), 1715, 1660, 1610. UV λ_{max} mμ (ε): 238 (4500), 300 (6000). *Anal.* Calcd. for $C_5H_3O_4NS$: C, 34.68; H, 1.73; N, 8.09; S, 18.39. Found: C, 34.53; H, 1.89; N, 7.96; S, 18.39.

***cis-cis*-β,β′-Thioacrylonitrile (XXI)**——a) From propiolonitrile and thiourea: Propiolonitrile, prepared from propiolamide (3.5 g, 0.05 mole), P_2O_5 (5.5 g) and sea sand (5.5 g), was dissolved in 10 ml of EtOH and mixed with thiourea (4.4 g, 0.058 mole) in 50% EtOH under controlling the temperature at 10—15°. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated *in vacuo* and the crystalline residue was recrystallized from EtOH to afford colorless needles, mp 142—142.5° (1.8 g).

IR ν_{max}^{Nujol} cm^{-1}: 2210 (-C≡N), UV λ_{max} $m\mu$ (ε): 285 (21200). *Anal.* Calcd. for $C_6H_4N_2S$: C, 52.94; H, 2.99; N, 20.59; S, 23.53. Found: C, 52.79; H, 3.08; N, 20.70; S, 23.54.

b) From propiolonitrile and ammonium dithiocarbamate: Propiolonitrile, prepared from propiolamide (3.5 g, 0.05 mole), P_2O_5 (5.5 g) and sea sand (5.5 g), was dissolved in 10 ml of EtOH and mixed with a solution of ammonium dithiocarbamate (5.6 g) in 20 ml of 50% EtOH under controlling the temperature at 15—20°. The reaction mixture was stirred at room temperature for 1 hr. The crystalline substance was collected by filtration and recrystallized from EtOH to afford colorless needles, mp 142—142.5° (0.605 g), which showed no depression in mp on admixture with the product from a), and the infrared spectrum was superimposable on that of a product from a).

β,β′-Thiocrotononitrile (XXIV)——a) From tetrolonitrile and thiourea: A suspension of tetrolonitrile[21] (0.65 g) and thiourea (0.76 g) in 15 ml of EtOH was refluxed for 2 hr. After cooling, the solvent was evaporated *in vacuo* and the resulting crystalline substance was recrystallized from EtOH to give colorless prisms (0.6 g), mp 119—121°. UV λ_{max} $m\mu$ (ε): 268.5 (7600), 295 (6800). IR ν_{max}^{Nujol} cm^{-1}: 2210 (-C≡N). *Anal.* Calcd. for $C_8H_8N_2S$: C, 58.53; H, 4.91; N, 17.07; S, 19.49. Found: C, 58.57; H, 5.23; N, 17.07; S, 19.55.

b) From tetrolonitrile and ammonium dithiocarbamate: A suspension of tetrolonitrile (0.65 g), ammonium dithiocarbamate (1.1 g) in EtOH (15 ml) was refluxed for 2 hr. After cooling, the solvent was evaporated *in vacuo*, and the resulting crystalline substance was washed with H_2O and a small amount of ether. Recrystallization from EtOH to afford colorless prisms (0.15 g), mp 119—120°. The infrared spectrum was superimposable on that of a product from a).

β,β′-Thiocinnamonitrile (XXVI)——a) From phenylpropiolonitrile and thiourea: A suspension of phenylpropiolonitrile (0.64 g, 0.005 mole) and thiourea (0.38 g) in EtOH (10 ml) was refluxed for 2 hr. After cooling, the crystalline substance was collected by filtration and recrystallized from EtOH to give white needles (0.6 g), mp 176—178°. IR ν_{max}^{Nujol} cm^{-1}: 2215 (-C≡N). UV λ_{max} $m\mu$ (ε): 276 (19700), 319 (11800). *Anal.* Calcd. for $C_{18}H_{12}N_2S$: C, 75.00; H, 4.18; N, 9.73; S, 11.12. Found: C, 74.68; H, 4.44; N, 9.76; S, 11.12.

b) From phenylpropiolonitrile and ammonium dithiocarbamate: A suspension of phenylpropiolonitrile (2.5 g), ammonium dithiocarbamate (2.2 g) in 30 ml of EtOH was refluxed for 30 minutes. After cooling, EtOH was evaporated *in vacuo* at 30—40°, and the crystalline residue was washed with H_2O. Recrystallization from EtOH afforded 1.4 g of white needles, mp 176—178°. The infrared spectrum was superimposable on that of a product from a).