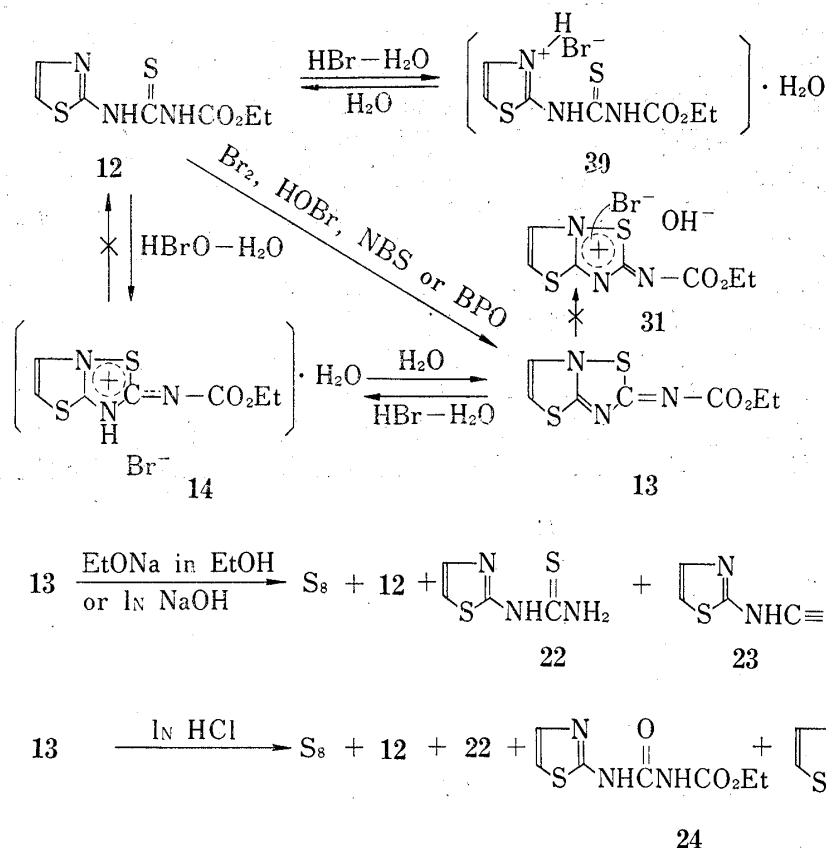


(9), which was obtained by the addition reaction of 2-amino-5-bromothiazole (10) to ethyl isocyanate (11), by treatment with hydrogen peroxide.

N-Ethoxycarbonyl-N'-(2-thiazolyl) thiourea¹⁰ (12) was reacted with bromine in acetic acid, and the reaction solution was neutralized with ammonia water to give 2-ethoxycarbonyliminothiazolo[3,2-*b*]thiadiazoline (13). When 12 was treated with bromine in chloroform, the resulting solid was recrystallized to afford 2-ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline hydrobromide monohydrate (14).

The structures of 13 and 14 are discussed in detail in this paper. The molecular formula of 13 was expressed as $C_7H_7O_2N_3S_2$ by the elemental analysis and the mass spectrum: $M^+=229$, and the infrared (IR) spectrum showed a strong peak at 1580 cm^{-1} , but no absorption band appeared in the range of $1800\text{ to }1600\text{ cm}^{-1}$. The nuclear magnetic resonance (NMR) spectrum consisted of a triplet at $\delta 1.29$ due to three methyl

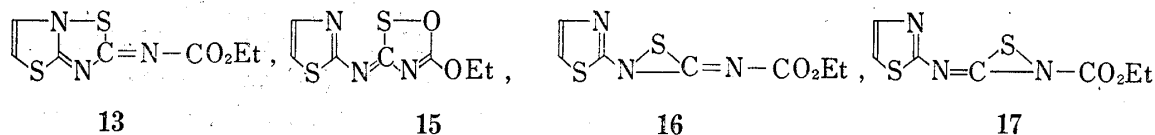


protons ($J=7.0\text{ Hz}$), a quartet at $\delta 4.27$ due to two methylene protons ($J=7.0\text{ Hz}$) and a pair of doublets at $\delta 7.55$ and 8.18 corresponding to two ring protons ($J=4.8\text{ Hz}$). In the ultraviolet (UV) spectrum, the absorption maximum at $308\text{ m}\mu$ shifted to $295\text{ m}\mu$ on the addition of hydrochloric acid. These data suggested that the structure of 13 may be one

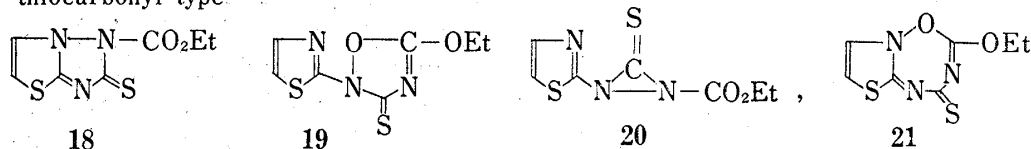
10) M. Nagano, J. Tobitsuka, T. Matsui, and K. Oyamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 2618 (1972).

of the eight structures which comprise four sulfide types (**13**, **15**, **16** and **17**) and four thiocarbonyl types (**18**, **19**, **20** and **21**). To confirm the structure of **13** as belonging to either of

sulfide type

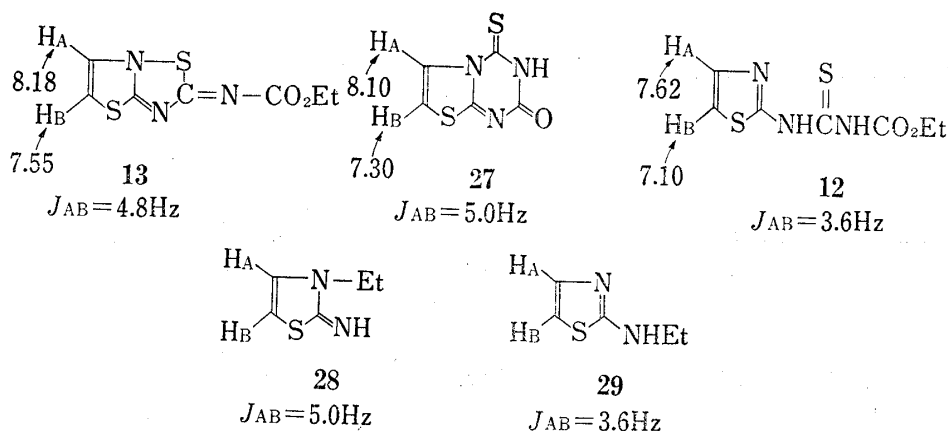


thiocarbonyl type



these two types, **13** was allowed to hydrolyze in the presence of a base and an acid. The compound (**13**) was treated with sodium ethoxide in ethyl alcohol or 1*N* sodium hydroxide to afford sulfur, **12**, *N*-(2-thiazolyl)thiourea (**22**) and 2-cyanaminothiazole (**23**). These products were confirmed on the basis of the elemental analyses and spectral data. Among these reaction products, **22** was also obtained in a good yield by treatment of **12** with 1*N* sodium hydroxide under the same reaction conditions as those mentioned above. The formation of **12** in the reaction of **13** with a base suggests that **13** has a certain oxidative power. The compound (**13**) was reacted with equimolecular amounts of phenylhydrazine to give **12** in 93% yield.

A solution of **13** in acetone containing 1*N* hydrochloric acid was refluxed for 2 hr to afford sulfur, **12**, **22**, *N*-ethoxycarbonyl-*N'*-(2-thiazolyl)urea (**24**), 2-aminothiazole (**25**) and *N*-2-thiazolylurea (**26**). Among these products, **25** or **26** was obtained in a good yield by the hydrolysis of **12** or **23** with 1*N* hydrochloric acid, respectively, under the same reaction conditions as those in the case of **13**. These experiments make it clear that **13** doesn't correspond to a thiocarbonyl type, but to a sulfide type. In order to determine the structure of **13** corresponding to one of the four structures (**13**, **15**, **16** and **17**), the chemical shifts and the coupling constants of the two ring protons of **13** were compared with those of the two ring protons of other model compounds, namely thiazolo[3,2-*a*]-*s*-triazine-4-thio-2-one (**27**; δ 8.10 and 7.30, $J_{AB}=5.0$ Hz),¹⁰ **12** (δ 7.62 and 7.10, $J_{AB}=3.6$ Hz), 3-ethyl-2-iminothiazoline (**28**; $J_{AB}=5.0$ Hz)¹¹ and 2-(ethylamino)thiazole (**29**; $J_{AB}=3.6$ Hz).¹² The high resolution technique for the mass



spectrum of **13** shows that the peaks at m/e 229 ($C_7H_7O_2N_3S_2$, mol.wt.,obs.=228.993, mol.wt.,calc.=228.998), m/e 185 ($C_5H_3ON_3S_2$, mol.wt.,obs.=184.972, mol.wt.,calc.=184.972),

11) J. Drucy, *J. Helv. Chim. Acta*, **24E**, 226 (1941).

12) I.A. Kaye and C.L. Parris, *J. Org. Chem.*, **17**, 737 (1952).

m/e 184 ($C_5H_2ON_3S_2$, mol.wt.,obs.=183.964, mol. wt.,calc.=183.964), m/e 157 ($C_4H_3N_3S_2$, mol.wt.,obs.=156.977, mol.wt.,calc.=156.977), m/e 152 ($C_5H_2ON_3S$, mol.wt.,obs.=151.990, mol.wt.,calc.=151.992), m/e 142 ($C_4H_2N_2S$, mol.wt.,obs.=141.964, mol.wt.,calc.=141.966), m/e 130 ($C_3H_2N_2S_2$, mol.wt.,obs.=129.966, mol.wt.,calc.=129.966), m/e 125 ($C_4H_3N_3S$, mol.wt.,obs.=125.005, mol.wt.,calc.=125.005), m/e 115 (C_3HNS_2 , mol.wt.,obs.=114.951, mol.wt.,calc.=114.955) and m/e 104 ($C_2H_2NS_2$, mol.wt.,obs.=103.967, mol.wt.,calc.=103.963) correspond to the fragments of the structures in Fig. 1. From these facts, the most suitable

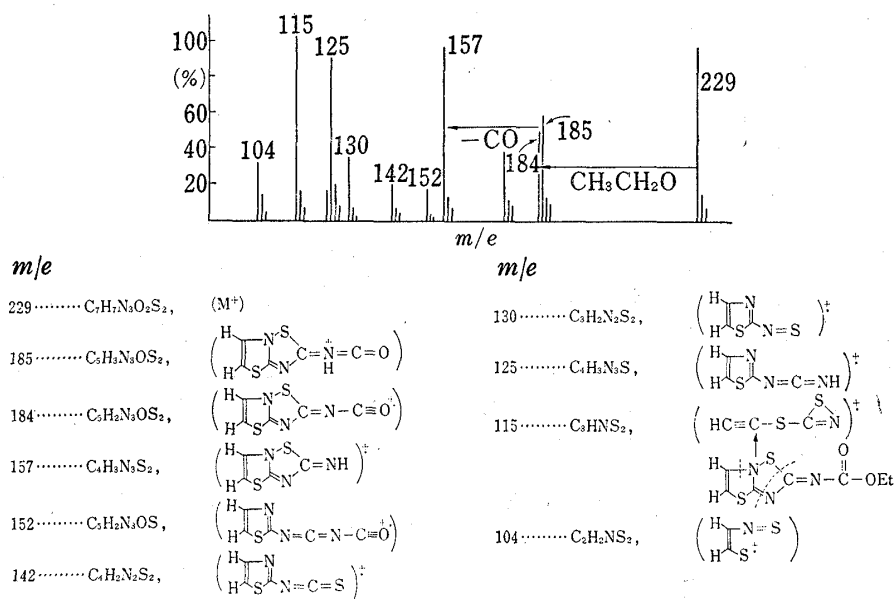


Fig. 1. Mass Spectrum of 2-Ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (**13**)

structure representing **13** would be 2-ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline. The compound (**13**) was also easily prepared by using other oxidants, such as hypobromous acid (HBrO), N-bromosuccinimide (NBS) and benzoyl peroxide, instead bromine. However, in the reaction of **12** with hydrogen peroxide (H_2O_2), **13** could not be obtained, but only **24** was isolated in a good yield. The yields of **13** in the reaction of **12** with various oxidants are summarized in Table I.

TABLE I. Yields of 2-Ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (**13**) in the Reaction of **12** with some Oxidants

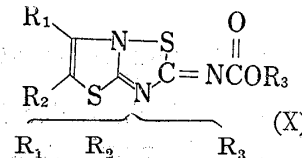
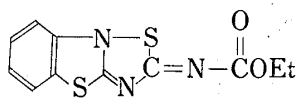
Oxid. reagents	Solvents	Yield (%)
Br_2	AcOH	65 (%)
Br_2	$CHCl_3$	90 (%)
HBrO	$CHCl_3$	83 (%)
NBS	EtOH	79 (%)
BPO	dichloroethane	88 (%)
H_2O_2 (30%)	AcOH	not isolated

but **13** was recovered unchanged. Furthermore, the IR spectrum of N-ethoxycarbonyl-N'-(2-thiazolyl)thiourea hydrobromide monohydrate (**30**), which was obtained by treatment of **12** with 48% hydrobromic acid, was different from that of **14**. From these facts, the compound (**14**) was regarded as the hydrobromide of **13**, namely 2-ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline hydrobromide monohydrate. It is very interesting that the IR ab-

sorption band of the carbonyl bond of **13** appears at 1580 cm^{-1} and that of **14**, which is formed by the protonation of **13**, appears in a normal absorption range (1680 cm^{-1}). If the structure of **13** has a nonbonded resonance structure (**32**) in a fairly high extent, the difference between the IR spectrum of **13** and that of **14** could be reasonably explained.

Some other N-alkoxycarbonyl-N'-(2-thiazolyl)thioureas were allowed to react with bromine under same reaction conditions as those in the case of **12** to give the corresponding thiazolothiadiazoline derivatives in good yields. The yields of 2-alkoxycarbonylimino-thiazolo[3,2-*b*]thiadiazolines (X) are summarized in Table II.

TABLE II. Yields of 2-Alkoxycarbonylimino-thiazolo[3,2-*b*]thiadiazolines (X)

Compd. No.	 R_1 R_2 R_3			mp ($^{\circ}\text{C}$)	Yield (%)
34	H	H	Me	167—168	91
13	H	H	Et	165—166	90
36	H	H	<i>n</i> -Pr	139—141	93
38	H	H	<i>iso</i> -Pr	156—158	91
40	H	H	<i>t</i> -Bu	120—122	92
42	H	H	<i>iso</i> -Bu	125—126	93
44	H	Me	Et	181—183	91
46	H	Et	Et	175—177	92
48	H	<i>n</i> -Pr	Et	172—174	91
50	H	<i>n</i> -Bu	Et	168—170	92
52	H	Br	Et	194—196	88
54	Me	H	Et	187	87
56	Ph	H	Et	210—212	67
58				205—207	87

Experimental¹³⁾

Synthesis of N-Ethyl-N'-(2-thiazolyl)thiourea (7)—The mixtures of 2-aminothiazole (**25**; 30.0 g) and ethyl isothiocyanate (22.5 g) in AcOEt (200 ml) were refluxed for 2 days, and the precipitated crystals were

13) All melting points were uncorrected. NMR spectra were obtained in the specified solvents on a Varian A-60 spectrometer with tetramethyl silane as an internal standard. Mass spectra were determined on a JEOL-JMS-OISG spectrometer.

collected on a glass filter and recrystallized from benzene to give 25.0 g of N-ethyl-N'-(2-thiazolyl)thiourea (7), colorless needles, mp 136—137°. *Anal.* Calcd. for $C_6H_9N_3S_2$: C, 38.50; H, 4.80; N, 22.45; S, 34.20. Found: C, 38.10; H, 4.71; N, 22.10; S, 34.11. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3160 and 3120 (>NH). NMR (DMSO- d_6) δ (J =Hz): 1.08 (3H, t, J =7.0), 5.23 for two methylene protons ($-\text{NH}-\text{CH}_2-\text{CH}_3$, d, q, $J_1=5.0$, $J_2=7.0$), 7.06 (1H, d, J =3.8), 7.40 (1H, d, J =3.8), *ca.* 0.44 (2H, broad).

Reaction of N-Ethyl-N'-(2-thiazolyl)thiourea (7) with Bromine—To a solution of 7 (5.6 g) in CHCl_3 (450 ml), bromine (5.1 g) in CHCl_3 (50 ml) was added dropwise at room temperature, and then the reaction solution was stirred for 1 hr at room temperature followed by refluxing for 1 hr. After removal of CHCl_3 , the residue was poured into ice water and neutralized with ammonia water. The precipitate was recrystallized from benzene to afford 3.5 g of N-ethyl-N'-(5-bromothiazole-2-yl)thiourea (8) as colorless needles, mp 162—163°. *Anal.* Calcd. for $C_6H_8N_3S_2\text{Br}$: C, 27.07; H, 3.02; N, 15.78; S, 24.09; Br, 30.02. Found: C, 27.22; H, 2.96; N, 15.60; S, 24.36; Br, 30.11. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3330 and 3220 (>NH). NMR (DMSO- d_6) δ (J =Hz): 1.12 (3H, t, J =7.0), 3.51 for two methylene protons ($-\text{NH}-\text{CH}_2-\text{CH}_3$, d, q, $J_1=4.5$, $J_2=7.0$), 7.46 (1H, s), *ca.* 8.43 (1H, broad), *ca.* 11.52 (1H, broad).

Oxidation of N-Ethyl-N'-(5-bromothiazol-2-yl)thiourea (8) with Hydrogen Peroxides—To a solution of 8 (0.27 g) in AcOH (20 ml), 30% H_2O_2 (10 ml) was added dropwise at a range of 5 to 10°, and the reaction mixture was poured into ice water (150 ml), and the precipitate was collected on a glass filter and dried to be recrystallized from AcOEt to afford 0.12 g of N-ethyl-N'-(5-bromothiazol-2-yl)urea (9), colorless needles, mp 197—199° (decomp.). *Anal.* Calcd. for $C_6H_9ON_3S\text{Br}$: C, 28.81; H, 3.22; N, 16.79; S, 12.81; Br, 31.94. Found: C, 28.86; H, 3.26; N, 16.42; S, 12.67; Br, 32.13. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3230, 3165 and 3110 (>NH). NMR (DMSO- d_6) δ (J =Hz): 1.10 (3H, t, J =7.0), 3.16 for two methylene protons ($-\text{NH}-\text{CH}_2-\text{CH}_3$, d, q, $J_1=4.5$, $J_2=7.0$), 7.32 (1H, s), *ca.* 6.46 (1H, broad), *ca.* 10.54 (1H, broad).

Synthesis of N-Ethyl-N'-(5-bromothiazol-2-yl)urea (9)—The mixtures of 2-amino-5-bromothiazole (10: 1.70 g) and ethyl isocyanate (11: 1.0 g) in acetone (50 ml) were refluxed for four days, and after removal of acetone, the resulting residue was eluted with AcOEt-benzene on silica gel to give 1.04 g of N-ethyl-N'-(5-bromothiazol-2-yl)urea (9).

Reaction of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) with Bromine—a) To a solution of 12 (2.31 g) in acetic acid (30 ml), bromine (1.68 g) in acetic acid (10 ml) was added dropwise at 10°, and the reaction solution was stirred for 1 hr at room temperature and subsequently poured into ice water (500 ml). After the aqueous solution was neutralized with ammonia water, the resulting solid was recrystallized from ethyl alcohol to afford 1.50 g of 2-ethoxycarbonyl-thiazolo[3,2-*b*]thiazoline (13), colorless needles, 168—169°(decomp.). *Anal.* Calcd. for $C_7H_7O_2N_3S_2$: C, 36.69; H, 3.08; N, 18.34; S, 27.92. Found: C, 36.29; H, 3.01; N, 18.41; S, 28.03. UV $\lambda_{\max}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 308 (17000).

b) To a solution of 12 (2.31 g) in CHCl_3 (250 ml), bromine (1.68 g) was added at room temperature, and the reaction mixture were stirred for 1 hr at room temperature followed by refluxing for 1 hr. After removal of CHCl_3 , the resulting solid was recrystallized from EtOH to give 1.58 g of 2-ethoxycarbonyliminothiazolo[3,2-*b*]thiadiazoline hydrobromide monohydrate (14), colorless prisms, mp 137—139° (decomp.). *Anal.* Calcd. for $C_7H_{10}O_3N_3S_2\text{Br}$: C, 25.61; H, 3.07; N, 12.80; S, 19.53; Br, 24.34. Found: C, 25.73; H, 3.20; N, 12.80; S, 19.69; Br, 24.74.

Reaction of 2-Ethoxycarbonyl-thiazolo[3,2-*b*]thiadiazoline (13) with Sodium Ethoxide—To a solution of 2.31 g of 13 in 50 ml of EtOH, ethanolic sodium ethoxide, which was prepared from Na (0.3 g) and EtOH (50 ml), was added under ice cooling, and the reaction mixture was stirred for 4 hr at room temperature, and after removal of EtOH under reduced pressure, the residue was poured into ice water (100 ml) and neutralized with 1N HCl. The reaction products were extracted with CHCl_3 (200 ml), and the CHCl_3 layer was washed with H_2O , dried over anhyd. Na_2SO_4 , and after removal of drying agent and solvent, the residue was eluted with AcOEt-benzene on silica gel to afford 0.12 g of sulfur, 1.2 g of 12, 0.1 g of 22 and 0.5 g of 23. N-(2-Thiazolyl)thiourea (22), colorless needles from AcOEt, mp 186—188°. *Anal.* Calcd. for $C_4H_5N_3S_2$: C, 30.19; H, 3.17; N, 26.41; S, 40.23. Found: C, 30.37; H, 3.21; N, 26.18; S, 40.15. Mass Spectrum: $M^+=159$. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 3350, 3270, 3170 and 1608 (>NH and $-\text{NH}_2$). NMR (DMSO- d_6) δ (J =Hz): 7.14 (1H, d, J =4.0), 7.46 (1H, d, J =4.0), *ca.* 8.76 (2H, broad), *ca.* 10.60 (1H, broad). 2-Cyanaminothiazole (13), colorless needles from AcOEt-benzene, mp 146—148° (decomp.). *Anal.* Calcd. for $C_4H_5N_3S$: C, 38.40; H, 2.42; N, 33.60; S, 25.58. Found: C, 38.26; H, 2.67; N, 32.24; S, 25.13. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 31.00 (>NH). NMR (DMSO- d_6) δ (J =Hz): 6.78 (1H, d, J =4.0), 7.24 (1H, d, J =4.0), *ca.* 13.30 (1H, broad). UV $\lambda_{\max}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 230 (2300), 284 (13400).

Reaction of 2-Ethoxycarbonyl-thiazolo[3,2-*b*]thiadiazoline (13) with Sodium Hydroxide—A suspension of 2.29 g of 13 in 50 ml of 1N NaOH solution was stirred for 4 hr at room temperature followed by neutralizing with 1N HCl, and the reaction mixtures were extracted with CHCl_3 . The CHCl_3 layer was washed with H_2O and dried over anhyd. Na_2SO_4 , and after removal of drying agent and solvent, the residue was chromatographed on silica gel (AcOEt-benzene) to afford 0.08 g of sulfur, 0.11 g of 12, 0.93 g of 22 and 0.42 g of 23.

Reaction of 1-Ethoxycarbonyl-3-(2-thiazolyl)thiourea (12) with Sodium Hydroxide—A suspension of 12 (2.31 g) in 1N NaOH solution (50 ml) was stirred for 4 hr at room temperature and neutralized with 1N HCl. The precipitate was collected on a glass filter followed by washing with H_2O to give 1.47 g of 22.

Reaction of 2-Ethoxycarbonyl-thiazolo[3,2-*b*]thiadiazoline (13) with Phenylhydrazine—After a mixture of 13 (2.29 g) and phenylhydrazine (1.10 g) in EtOH (100 ml) was stirred for 3 hr, EtOH was evaporated under reduced pressure, and the residual solid was washed with ethyl ether to afford 2.15 g of 12.

Reaction of 2-Ethoxycarbonylimino-thiazolo[3,2-*b*]thiazoline (13) with Hydrochloric Acid—A suspension of 2.29 g of 13 in 60 ml of 1N HCl solution was refluxed for 3 hr and neutralized with sodium carbonate, and H₂O was evaporated under reduced pressure. The resulting residue was chromatographed on silica gel (AcOEt–benzene) to afford 0.14 g of sulfur, 0.735 g of 12, 0.123 g of N-ethoxycarbonyl-N'-(2-thiazolyl)urea (24),¹⁴ 0.136 g of 22, 0.257 g of 2-aminothiazole (25) and 0.375 g of 26. N-(2-Thiazolyl)urea (26), colorless needles from AcOEt, mp 203° (decomp.). *Anal.* Calcd. for C₄H₈ON₂S: C, 33.57; H, 3.52; N, 29.37; S, 22.36. Found: C, 33.28; H, 3.55; N, 28.96; S, 22.33. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3490, 3320, 3260 and 3180 (>NH and –NH₂), 1720 (>C=O). NMR (DMSO-*d*₆) δ (J=Hz): ca. 6.36 (2H, broad), 7.04 (1H, d, J=4.0), ca. 7.36 (1H, d, J=4.0), ca. 10.40 (1H, broad).

Reaction of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) with Hydrochloric Acid—A suspension of 0.23 g of 12 in 20 ml of 1N HCl solution was refluxed for 3 hr and neutralized with Na₂CO₃, and H₂O was evaporated under reduced pressure. The residue was dried and chromatographed on silica gel (benzene–AcOEt) to afford 0.10 g of sulfur and 0.04 g of Sulfur 2-aminothiazole (25).

Reaction of 2-Cyanaminothiazole (23) with Hydrochloric Acid—A suspension of 0.125 g of 23 in 10 ml of 1N HCl solution was refluxed for 3 hr and neutralized with Na₂CO₃, and H₂O was evaporated under reduced pressure. The residue was dried and chromatographed on silica gel (AcOEt) to afford 0.123 g of N-(2-thiazolyl)urea (26).

Reaction of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) with Hypobromous Acid (HBrO)—To a solution of 2.31 g of 12 in CHCl₃ (300 ml), HBrO–H₂O, which was prepared from HgO (yellow, 3.0 g) and 3% Br₂–H₂O (3.0 g), was added dropwise under ice cooling and further, the reaction solution was stirred for 1 hr at same temperature. After removal of CHCl₃ under reduced pressure below 20°, the resulting residue was poured into H₂O (200 ml) and the precipitate was collected on a glass filter and dried in a vacuum to afford 1.80 g of 2-ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (13).

Reaction of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) with Benzoyl Peroxide (BPO)—To a solution of 2.31 g of 12 in dichloroethane (200 ml), 2.90 g of BPO was added under ice cooling, and the reaction solution was stirred for 3 hr at room temperature, and after removal of solvent, the resulting residue was washed with ether and benzene to give 2.06 g of 2-ethoxycarbonyliminothiazolo[3,2-*b*]thiadiazoline (13).

Reaction of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) with N-Bromosuccinimide (NBS)—To a solution of 2.31 g of 12 in EtOH (100 ml), 2.14 g of NBS was added under ice cooling, and after removal of EtOH under reduced pressure, the residue was washed with ether and dissolved in CHCl₃ (200 ml). The CHCl₃ layer was washed with H₂O and dried over anhyd. Na₂SO₄, and CHCl₃ was removed to afford 1.83 g of 2-ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (13).

Reaction of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) with Hydrogen Peroxide (H₂O₂)—To a solution of 2.31 g of 12 in AcOH (50 ml), 30% H₂O₂ (10 ml) was added dropwise at a range of 10 to 15°, and the reaction mixture was poured into ice water (200 ml) and neutralized followed by extracting with CHCl₃ (200 ml). The CHCl₃ layer was washed with H₂O and dried over anhyd. Na₂SO₄, and after removal of drying agent and solvent, the resulting solid was recrystallized to afford 1.63 g of N-ethoxycarbonyl-N'-(2-thiazolyl)urea (24).

Synthesis of N-Ethoxycarbonyl-N'-(2-thiazolyl)thiourea Hydrobromide Monohydrate (30)—A mixture of 2.31 g of N-ethoxycarbonyl-N'-(2-thiazolyl)thiourea (12) and 5 ml of 48% HBr–H₂O in acetone (5 ml) was stirred for 2 hr at room temperature, and after removal of acetone and H₂O under reduced pressure at 20°, the resulting residue was recrystallized from EtOH–benzene to give N-ethoxycarbonyl-N'-(2-thiazolyl)thiourea hydrobromide monohydrate (30), prisms, mp 139–140° (decomp.), 2.8 g. *Anal.* Calcd. for C₇H₁₂O₃N₃S₂Br: C, 25.45; H, 3.66; N, 12.72; S, 19.41; Br, 24.19. Found: C, 25.63; H, 3.75; N, 12.68; S, 19.58; Br, 24.23. IR $\nu_{\max}^{\text{Nujol}}$ cm⁻¹: 3380 and 1625 for absorption bands of a latticewater, 3140 (>NH), 1738 and 1280 (>C(O)–O–). 1.65 g of 30 was suspended in 100 ml of H₂O, and the suspension was stirred for 1 hr at room temperature, and the deposited crystals were collected on a glass filter and dried in a vacuum to afford 1.06 g of 12.

Synthesis of 2-Ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline Hydrobromide Monohydrate (14)—The mixture of 2.29 g of 2-ethoxycarbonylimino[3,2-*b*]thiadiazoline (13) and 5 ml of 48% HBr–H₂O in acetone (100 ml) was stirred for 1 hr at room temperature, and after removal of acetone and H₂O, the resulting residue was recrystallized from EtOH to afford 2.88 g of 2-ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline hydrobromide monohydrate*. *2.38 g of 14 was suspended in 100 ml of H₂O, and stirred for 1 hr, and an insoluble solid was collected on a glass filter and washed with H₂O and dried to give 2.08 g of 13.

Reaction of 2-Ethoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (13) with Hypobromous Acid (HBrO)—To a solution of 2.29 g of 13 in CHCl₃ (300 ml) HBrO–H₂O, which was prepared from HgO (yellow, 3.0 g) and 3% Br₂–H₂O (3.0 g), was added dropwise under ice cooling and the mixture was stirred for 1 hr. After

removal of CHCl_3 under reduced pressure at 20° , the resulting residue was recrystallized from EtOH to give 1.82 g of 13.

General Method for the Reaction of N-Alkoxy carbonyl-N'-(2-thiazolyl)thioureas (A) with Bromine—To a solution of N-alkoxy carbonyl-N'-(2-thiazolyl)thioureas (A; 0.01 mole) in CHCl_3 (250 ml), bromine (0.0105 mole) in CHCl_3 (50 ml) was added dropwise at room temperature, and the reaction mixture was stirred for 1 hr at room temperature followed by refluxing for 1 hr. After removal of solvent, the resulting solid was washed with water until the pH value of the washings became to 6. The neutral substances were recrystallized from a suitable solvent to give 2-alkoxy carbonylimino-thiazolo[3,2-*b*]thiadiazolines (X).

Reaction of N-Methoxycarbonyl-N'-(2-thiazolyl)thiourea (33) with Bromine—2.17 g of 33 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to afford 1.95 g of 2-methoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (34), colorless needles from AcOEt, mp $167\text{--}168^\circ$ (decomp.). *Anal.* Calcd. for $\text{C}_6\text{H}_5\text{O}_2\text{N}_3\text{S}_2$: C, 33.48; H, 2.34; N, 19.52; S, 29.79. Found: C, 33.79; H, 2.50; N, 19.29; S, 29.74. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1585, 1292 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 252 (3000), 308 (22400). NMR ($\text{DMSO}-d_6$) δ ($J=\text{Hz}$): 3.02 (3H, s), 7.56 (1H, d, $J=4.8$), 8.19 (1H, d, $J=4.8$).

Reaction of N-*n*-Propoxycarbonyl-N'-(2-thiazolyl)thiourea (35) with Bromine—2.45 g of 35 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to afford 2.30 g of 2-*n*-propoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (36), colorless needles from benzene, mp $139\text{--}141^\circ$ (decomp.). *Anal.* Calcd. for $\text{C}_8\text{H}_9\text{O}_2\text{N}_3\text{S}_2$: C, 39.49; H, 3.73; N, 17.27; S, 26.36. Found: C, 39.43; H, 3.72; N, 17.29; S, 26.37. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1588 and 1288 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 251 (3000), 308 (23000). NMR [$(\text{CD}_3)_2\text{CO}$] δ ($J=\text{Hz}$): 0.98 (3H, t, $J=6.5$), 1.68 (2H, t, q, $J_1=J_2=6.5$), 4.23 (2H, t, $J=6.5$), 7.52 (1H, d, $J=4.8$), 8.10 (1H, d, $J=4.8$).

Reaction of N-iso-Propoxycarbonyl-N'-(2-thiazolyl)thiourea (37) with Bromine—2.45 g of 37 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to give 2.24 g of 2-iso-propoxy carbonylimino-thiazolo[3,2-*b*]thiadiazoline (38), colorless needles from benzene, mp $156\text{--}158^\circ$ (decomp.). *Anal.* Calcd. for $\text{C}_8\text{H}_9\text{O}_2\text{N}_3\text{S}_2$: C, 39.49; H, 3.73; N, 17.27; S, 26.36. Found: C, 39.42; H, 3.91; N, 17.12; S, 26.11. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1580 and 1300 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 251 (2900), 308 (23000). NMR [$(\text{CD}_3)_2\text{CO}$] δ ($J=\text{Hz}$): 1.32 (6H, d, $J=6.6$), 5.08 (1H, q, q, $J_1=J_2=6.6$), 7.48 (1H, d, $J=4.8$), 8.05 (1H, d, $J=4.8$).

Reaction of N-*n*-Butoxycarbonyl-N'-(2-thiazolyl)thiourea (39) with Bromine—2.59 g of 39 was reacted with 1.70 g of bromine by the general method to give 2.36 g of 2-*n*-butoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (40), colorless needles from isopropyl ether, mp $120\text{--}122^\circ$. *Anal.* Calcd. for $\text{C}_9\text{H}_{11}\text{O}_2\text{N}_3\text{S}_2$: C, 42.00; H, 4.31; N, 16.33; S, 24.92. Found: C, 41.68; H, 4.19; N, 16.43; S, 25.15. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1580 and 1290 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 252 (2900), 308 (22900). NMR (CDCl_3) δ ($J=\text{Hz}$): 0.96 (3H, t, $J=6.5$), 1.12–2.22 (4H, m), 4.35 (2H, t, $J=6.5$), 7.18 (1H, d, $J=4.8$), 7.72 (1H, d, $J=4.8$).

Reaction of N-iso-Butoxycarbonyl-N'-(2-thiazolyl)thiourea (41) with Bromine—2.59 g of 41 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) to give 2.40 g of 2-iso-butoxycarbonylimino-thiazolo[3,2-*b*]thiadiazoline (42), pale yellow needles from isopropylether, mp $125\text{--}126^\circ$. *Anal.* Calcd. for $\text{C}_9\text{H}_{11}\text{O}_2\text{N}_3\text{S}_2$: C, 42.00; H, 4.31; N, 16.33; S, 24.92. Found: C, 41.82; H, 4.54; N, 16.14; S, 24.73. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1590 and 1290 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 251 (2900), 308 (22400). NMR [$(\text{CD}_3)_2\text{CO}$] δ ($J=\text{Hz}$): 0.99 (6H, d, $J=6.5$), 2.09 (1H, q, q, t, $J_1=J_2=J_3=6.5$), 4.07 (2H, d, $J=6.5$), 7.53 (1H, d, $J=4.5$), 8.09 (1H, d, $J=4.5$).

Reaction of N-Ethoxycarbonyl-N'-(5-methylthiazol-2-yl)thiourea (43) with Bromine—2.45 g of 43 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) to give 2.22 g of 2-ethoxycarbonylimino-5-methylthiazolo[3,2-*b*]thiadiazoline (44), colorless needles from benzene, mp $181\text{--}183^\circ$ (decomp.). *Anal.* Calcd. for $\text{C}_8\text{H}_9\text{O}_2\text{N}_3\text{S}_2$: C, 39.49; H, 3.73; N, 17.27; S, 26.36. Found: C, 39.91; H, 3.66; N, 17.27; S, 26.32. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1592 and 1270 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 251 (3300), 312 (22600). NMR (DMF) δ ($J=\text{Hz}$): 1.32 (3H, t, $J=7.0$), 2.55 (3H, d, $J=2.0$), 4.31 (2H, q, $J=7.0$), 1.98 (1H, q, $J=2.0$).

Reaction of N-Ethoxycarbonyl-N'-(5-ethylthiazol-2-yl)thiourea (45) with Bromine—2.59 g of 45 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to afford 2.37 g of 2-ethoxycarbonylimino-5-ethylthiazolo[3,2-*b*]thiadiazoline (46), colorless needles from benzene, mp $175\text{--}177^\circ$ (decomp.). *Anal.* Calcd. for $\text{C}_9\text{H}_{11}\text{O}_2\text{N}_3\text{S}_2$: C, 42.00; H, 4.31; N, 16.33; S, 24.92. Found: C, 41.92; H, 4.58; N, 16.38; S, 24.90. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1590 and 1280 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 251 (3300), 312.3 (23000). NMR (CDCl_3) δ ($J=\text{Hz}$): 1.15 (3H, t, $J=7.0$), 1.18 (3H, t, $J=7.0$), 2.84 (2H, q, d, $J_1=7.0$, $J_2=2.0$), 4.38 (2H, q, $J=7.0$), 7.35 (1H, t, $J=2.0$).

Reaction of N-Ethoxycarbonyl-N'-(5-*n*-propylthiazol-2-yl)thiourea (47) with Bromine—2.73 g of 47 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) to give 2.46 g of 2-ethoxycarbonylimino-5-*n*-propylthiazolo[3,2-*b*]thiadiazoline (48), colorless needles from benzene, mp $172\text{--}174^\circ$. *Anal.* Calcd. for $\text{C}_{10}\text{H}_{13}\text{O}_2\text{N}_3\text{S}_2$: C, 44.26; H, 4.83; N, 15.49; S, 23.63. Found: C, 44.62; H, 4.81; N, 15.67; S, 23.53. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1590 and 1285 (–C(O)–O–). UV $\lambda_{\text{max}}^{\text{EtOH}}$ $\text{m}\mu$ (ϵ): 251 (3500), 312.3 (23900). NMR (CDCl_3) δ ($J=\text{Hz}$): 1.03 (3H, t, $J=7.0$), 1.38 (3H, t, $J=7.0$), 1.75 (2H, q, t, $J_1=J_2=7.0$), 2.78 (2H, t, d, $J_1=7.0$, $J_2=1.0$), 4.39 (2H, q, $J=7.0$), 7.35 (1H, t, $J=1.0$).

Reaction of N-Ethoxycarbonyl-N'-(5-*n*-butylthiazol-2-yl)thiourea (49) with Bromine—2.87 g of 49 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to give 2.62 g of 2-ethoxycarbonylimino-5-*n*-butylthiazolo[3,2-*b*]thiadiazoline (50), colorless plates from benzene-*n*-hexane, mp 168--

170°. *Anal.* Calcd. for $C_{11}H_{15}O_2N_3S_2$: C, 46.29; H, 5.30; N, 14.73; S, 22.47. Found: C, 45.86; H, 5.40; N, 14.78; S, 22.55. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1590 ($>C=O$). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (ϵ): 251 (4200), 314 (23400). NMR (CDCl_3) δ ($J=\text{Hz}$): 0.97 (3H, t, $J=6.0$), 1.38 (3H, t, $J=7.0$), 1.11–2.02 (4H, m), 2.80 (2H, t, d, $J_1=7.0$, $J_2=1.0$), 4.39 (2H, q, $J=7.0$), 7.33 (1H, t, $J=1.0$).

Reaction of N-Ethoxycarbonyl-N'-(5-bromothiazol-2-yl)thiourea (51) with Bromine—3.10 g of 51 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to give 2.72 g of 2-ethoxycarbonylimino-5-bromo-thiazolo[3,2-*b*]thiadiazoline (52), colorless needles from acetone, mp 194–196°. *Anal.* Calcd. for $C_7H_6O_2N_3S_2Br$: C, 27.28; H, 1.96; N, 13.64; S, 20.81; Br, 25.93. Found: C, 27.29; H, 1.81; N, 13.81; S, 20.64; Br, 25.70. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1582 and 1275 ($-C(O)-O-$). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (ϵ): 250 (4000), 316 (24700). NMR (CDCl_3) δ ($J=\text{Hz}$): 1.40 (3H, t, $J=7.0$), 4.42 (2H, q, $J=7.0$), 7.64 (1H, s).

Reaction of N-Ethoxycarbonyl-N'-(4-methylthiazol-2-yl)thiourea (53) with Bromine—2.45 g of 53 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to give 2.15 g of 2-ethoxycarbonyl-6-methyl-thiazolo[3,2-*b*]thiadiazoline (54), colorless needles from benzene, mp 187° (decomp.). *Anal.* Calcd. for $C_8H_9O_2N_3S_2$: C, 39.49; H, 3.73; N, 17.27; S, 26.36. Found: C, 39.45; H, 3.86; N, 17.18; S, 26.13. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1590 and 1285 ($-C(O)-O-$). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (ϵ): 254 (2500), 311 (22400). NMR (CDCl_3) δ ($J=\text{Hz}$): 1.39 (3H, t, $J=7.0$), 2.48 (3H, d, $J=1.0$), 4.39 (2H, q, $J=7.0$), 6.69 (1H, q, $J=1.0$).

Reaction of N-Ethoxycarbonyl-N'-(4-phenylthiazol-2-yl)thiourea (55) with Bromine—3.07 g of 55 was reacted with 1.70 g of bromine in CHCl_3 (300 ml) by the general method to afford 2.04 g of 2-ethoxycarbonyl-6-phenyl-thiazolo[3,2-*b*]thiadiazoline (56), colorless needles from AcOEt , mp 210–212° (decomp.). *Anal.* Calcd. for $C_{13}H_{11}O_2N_3S_2$: C, 51.15; H, 3.63; N, 13.77; S, 20.96. Found: C, 51.05; H, 3.51; N, 13.77; S, 20.93. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1580 and 1300 ($-C(O)-O-$). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (ϵ): 258 (10200), 316 (20300).

Reaction of N-Ethoxycarbonyl-N'-(2-benzothiazolyl)thiourea (57) with Bromine—3.87 g of 57 was reacted with 1.70 g of bromine by the general method to give 2.44 g of 2-ethoxycarbonylimino-benzothiazolo[3,2-*b*]thiadiazoline (58), colorless plates from acetone, mp 205–207° (decomp.). *Anal.* Calcd. for $C_{11}H_9O_2N_3S_2$: C, 47.32; H, 3.25; N, 15.05; S, 22.92. Found: C, 46.72; H, 2.87; N, 14.94; S, 22.52. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1} : 1590 and 1285 ($-C(O)-O$). UV $\lambda_{\max}^{\text{EtOH}}$ $m\mu$ (ϵ): 252 (7000, sh.), 261.5 (12500), 280 (3600, sh.), 290 (5100, sh.), 322 (26900). NMR (CDCl_3) δ ($J=\text{Hz}$): 1.42 (3H, t, $J=7.0$), 4.43 (2H, q, $J=7.0$), 7.24–8.02 (4H, m).