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Studies on Organic Sulfur Compounds. XI.[1] Synthesis of 2-Alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones[2]

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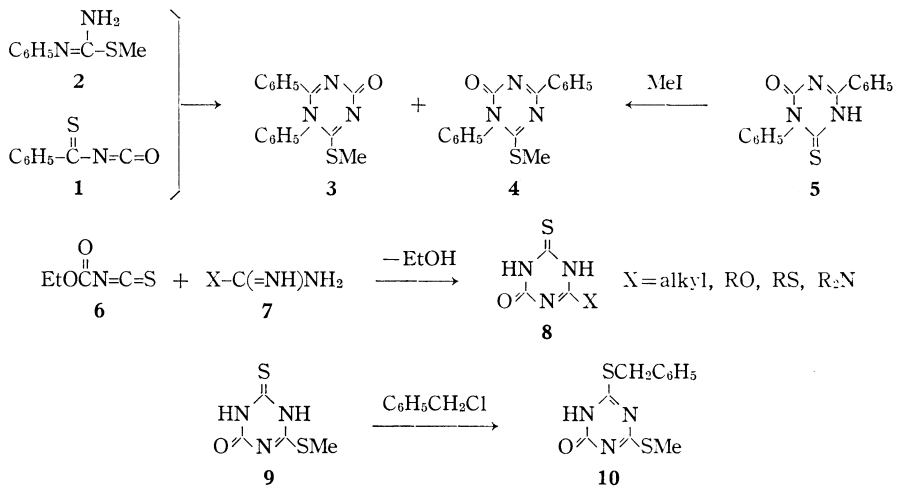
1-Alkoxycarbonyl-3-(2-thiazolyl)thioureas (A) were reacted with alkyl halides in the presence of potassium carbonate to afford 1(H)-alkoxycarbonyl-2-alkyl-3-(2-thiazolyl)-isothioureas (D), 1-alkoxycarbonyl-2-alkyl-3-(3-alkylthiazolin-2-ylidene)isothioureas (E) and 2-alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones (C). However, the rate of this reaction and the yields of the products were dependent on the kinds of alkyl halide and thiazolyl thioureas (A). The cyclization products (C) were obtained in a good yield by the thermal treatment of the compounds (E).

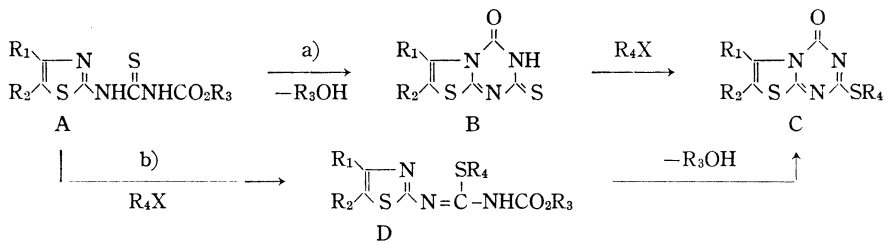
There are a few reports concerning thiazolo[3,2-*a*]-*s*-triazine-2,4-dione derivatives,[4-6] but neither thiazolo[3,2-*a*]-*s*-triazine-2-thio-4-ones (B) nor 2-alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones (C) are known in the literature. However, the synthetic methods of some mono cyclic *s*-triazine-thio-ones have been published. For example, Goerdeler and Neuffer[7] have reported that the reaction of thiobenzoyl isocyanate (**1**) and isothiourea (**2**) affords two structural isomers (**3** and **4**), and that **4** is also prepared by methylation of **5** with methyl halide. Furthermore, it has been recently reported that *s*-triazine-4-thio-2-ones (**8**) are formed by treatment of ethoxycarbonyl isothiocyanate (**6**) with amidines or amidinoids (**7**), and also



1) Part X: M. Nagano, T. Matsui, J. Tobitsuka, and K. Oyamada, *Chem. Pharm. Bull.* (Tokyo), **21**, 62 (1973).
2) This was presented at 3rd International Congress of Heterocyclic Chemistry, Sendai, August 1971. Preliminaly Report pp. 392—395.
3) Location: *Hiromachi, Shinagawa-ku, Tokyo.*
4) U.V. Gizychi and G. Oertel, *Angew. Chem.* (Int. Engl. Edit), **7**, 380 (1968).
5) U.V. Gizychi and G. Oertel, *Angew. Chem.* (Int. Engl. Edif) **7**, 381 (1968).
6) R. Richter and H. Ulrich, *Chem. Ber.*, **1970**, 103.
7) J. Goerdeler and J. Neuffer, *Tetrahedron Letters*, **1967**, 2791.

S-benzyl-triazine-2-one (**10**) is obtained by benzylation of **9** with benzyl chloride.[8] We now wish to describe the synthesis of a new class of 2-alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones (C).

1-Alkoxycarbonyl-3-(2-thiazolyl)thioureas (A)[9,10] were regarded as the most suitable precursors leading to the title compounds (C), and subsequently two synthetic routes (a and b) were examined: a) Thermal cyclization of thiazolyl thioureas (A) to thiazolo[3,2-*a*]-*s*-triazine-2-thio-4-ones (B) followed by alkylation to (C). b) Alkylation of the same thiazolyl thioureas (A) to (D) followed by thermal or alkali-treatment to form (C).



Route a——1-Ethoxycarbonyl-3-(2-thiazolyl)thiourea (**11**) was heated at 180—190° for 30 minutes on an oil-bath to give thiazolo[3,2-*a*]-*s*-triazine-2-thio-4-one (**12**)[9] in 25% yield, which was successfully treated with ethyl bromide in the presence of triethyl amine to produce (**13**) in 65% yield. The assignment of the structure of **13** as a thiazolo[3,2-*a*]-*s*-triazine derivative was on the basis of the elemental analysis and spectral data. The infrared (IR) spectrum of **13** showed a band at 1685 cm^{-1} for a ring carbonyl group, and the nuclear magnetic resonance (NMR) spectrum showed a triplet at 8.64 τ for three methyl protons ($-SCH_2\underline{CH_3}$, J=7.0 Hz), a quartet at 6.85 τ for two methylene protons ($-S\underline{CH_2}CH_3$, J=7.0 Hz), and two doublets at 2.34 and 1.98 τ assignable to two ring protons (J=5.0 Hz). For further confirmation, this compound was treated with one normal sodium hydroxide to afford 2-N-cyanoaminothiazole (**14**). From these data, the structure of **13** was determined as 2-ethylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one. However, it was rather difficult to obtain **12** in a good yield by the thermal decomposition of **11**. Therefore, thermal cyclization of thiazolyl thioureas (A) seemed not to be a practical method for preparing various thiazolo-[3,2-*a*]-*s*-triazine-2-thio-4-ones (B).

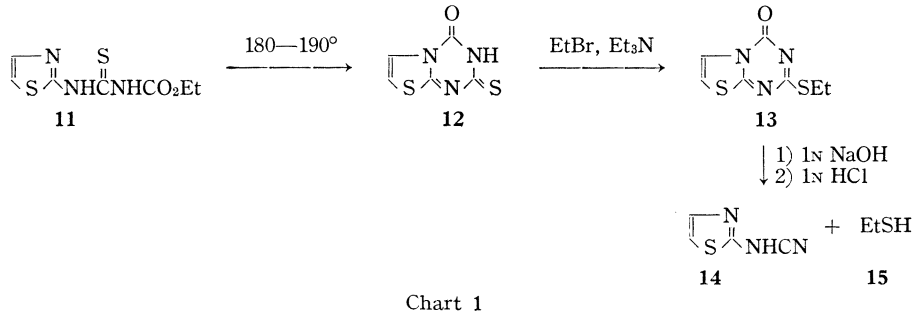


Chart 1

Route b——A mixture of the compound (**11**: 0.01 mole), ethyl iodide (0.02 mole) and potassium carbonate (0.012 mole) in acetone (200 ml) was stirred at room temperature for three days, and the reaction mixture was chromatographed over silica gel to afford four pro-

8) J. Goerdeler and J. Neuffer, *Chem. Ber.*, **104**, 1606 (1971).
9) M. Nagano, J. Tobitsuka, T. Matsui and K, Oyamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 2168 (1972).
10) M. Nagano, T. Matsui, J. Tobitska and K. Oyamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 2626 (1972).

ducts (**16**, **17**, **13**, and **11**). Compound (**16**) was assigned as 1(H)-ethoxycarbonyl-2-ethyl-3-(2-thiazolyl)isothiourea by its hydrolysis with one normal hydrogen chloride to 1-ethoxycarbonyl-3-(2-thiazolyl)urea (**18**), which was also obtained by the oxidation of the compound (**11**) with mercuric acetate; and by the comparison of its spectral data with those of 1-ethoxycarbonyl-3-ethyl-2-methyl-3-(2-thiazolyl)isothiourea (**23**). This substance (**23**) could be prepared by the methylation of 1(H)-ethoxycarbonyl-3-ethyl-3-(2-thiazolyl)thiourea (**20**) obtained by the reaction of 2-ethylaminothiazole (**19**)[11] and ethoxycarbonyl isothiocyanate (**6**). The IR absorption bands of the carbonyl groups (>C=O) of **16** and **23** appeared at 1750 cm^{-1} and 1688 cm^{-1}, respectively, and their ultraviolet (UV) spectra showed absorption maximums at 315 mμ (ε=20600) and 295 mμ (ε=11600), respectively. Compound (**17**) was hydrolyzed with one normal hydrogen chloride to give 1(H)-ethoxycarbonyl-3-(3-ethylthiazolin-2-ylidene)urea (**28**), and furthermore, **17** could be also prepared by the ethylation of 1(H)-ethoxycarbonyl-3-(3-ethylthiazolin-2-ylidene)thiourea (**26**) which was synthesized by the reaction of ethoxycarbonyl isothiocyanate (**6**) and 3-ethyl-2-iminothiazoline (**25**).[12] From the above experiments and on the basis of the analytical data, compound (**17**) was assigned as 1-ethoxycarbonyl-2-ethyl-3-(3-ethylthiazolin-2-ylidene)isothiourea.

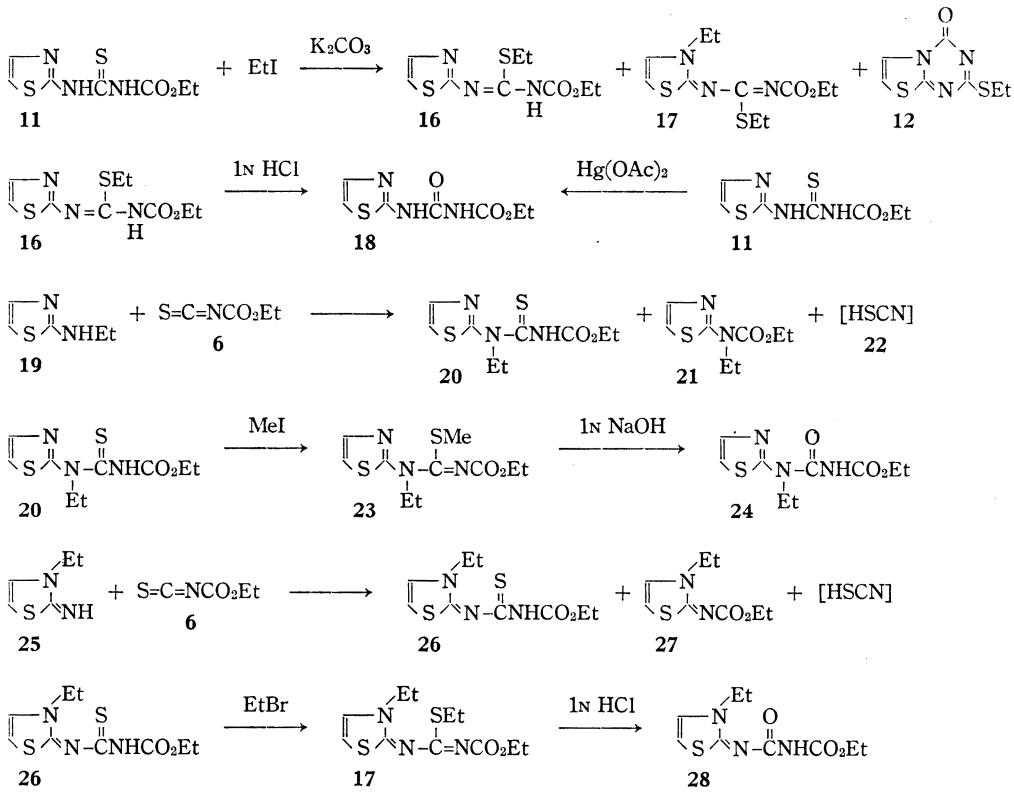
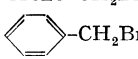
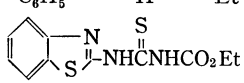


Chart 2

Other 1-alkoxycarbonyl-3-(2-thiazolyl)thioureas (A) were treated with alkyl halides under the same reaction conditions as those employed in the ethylation of **11**. Isopropyl iodide and isobutyl bromide reacted slowly with **11**, and in the case of tertiary butyl bromide this

11) I.A. Kaye and C.L. Parris, *J. Org. Chem.*, **17**, 737 (1952).
12) J. Drucy, *J. Helv. Chim. Acta*, **1941**, 24E, 226.

TABLE I. Isolated Yields of 1(H)-Alkoxycarbonyl-2-alkyl-3-(2-thiazolyl)isothioureas(D), 1-Alkoxycarbonyl-2-alkyl-3-(3-alkylthiazolin-2-ylidene)isothioureas (E) and 2-Alkylthio-thiazolo[3,2-*a*]-*s*-triazines (C)

A				R_4X	D		E		C		Recov. Comp. (A)
R_1	R_2	R_3	Comp. (No)								
H	H	Me	**29**	MeI	78.7 (%)	**30**	10.3 (%)	**31**	8.2 (%)	**32**	not isolated
H	H	Et	**11**	MeI	75.8	**33**	15.1	**34**	6.9	**32**	not isolated
H	H	*n*-Pr	**35**	MeI	74.4	**36**	19.8	**37**	3.5	**32**	not isolated
H	H	iso-Pr	**38**	MeI	77.5	**39**	19.2	**40**	1.6	**32**	not isolated
H	H	*n*-Bu	**41**	MeI	68.7	**42**	18.2	**43**	7.3	**32**	not isolated
H	H	iso-Bu	**44**	MeI	65.2	**45**	21.4	**46**	7.8	**32**	not isolated
H	H	Et	**11**	EtI	72.4	**16**	10.6	**17**	6.9	**13**	6.3 (%)
H	H	Et	**11**	*n*-PrI	68.8	**47**	10.6	**48**	5.7	**49**	12.6
H	H	Et	**11**	iso-PrI	20.8	**50**	6.7	**51**	6.8	**52**	59.2
H	H	Et	**11**	*n*-BuI	60.5	**53**	11.9	**54**	7.3	**55**	14.8
H	H	Et	**11**	iso-BuBr	25.4	**56**	not isolated		8.1	**57**	63.5
H	H	Et	**11**	*t*-BuBr	not isolated		not isolated		not isolated		96.3
H	H	Et	**11**	CH_2=CH-CH_2Br	74.5	**58**	15.6	**59**	3.2	**60**	4.4
H	H	Et	**11**	HC≡C-CH_2Br	75.9	**61**	11.8	**62**	8.9	**63**	0.5
H	H	Et	**11**	 -CH_2Br	82.6	**64**	10.1	**65**	5.8	**66**	5.8
H	Me	Et	**67**	MeI	71.5	**68**	20.3	**69**	5.6	**70**	not isolated
H	Et	Et	**71**	MeI	72.5	**72**	18.8	**73**	5.1	**74**	not isolated
H	*n*-Pr	Et	**75**	MeI	71.8	**76**	20.3	**77**	5.4	**78**	not isolated
H	*n*-Bu	Et	**77**	MeI	71.5	**80**	19.7	**81**	3.7	**82**	not isolated
H	C_6H_5	Et	**83**	MeI	56.2	**84**	32.3	**85**	3.2	**86**	5.6 (%)
H	Br	Et	**87**	MeI	57.7	**88**	20.2	**89**	not isolated		15.7
Me	H	Et	**90**	MeI	76.2	**91**	16.8	**92**	not isolated		not isolated
C_6H_5	H	Et	**93**	MeI	90.8	**94**	7.6	**95**	not isolated		not isolated
			**96**	MeI	78.9	**97**	6.6	**98**	not isolated		10.8 (%)

reaction was negligible due to steric factors. In the alkylations of 5-bromo-, 4-methyl, 4-phenyl-, and benzothiazolyl thioureas (**87**, **90**, **93**, and **96**), the cyclization products (**99**, **100**, **101**, and **102**) could not be obtained. It seemed that in the case of **87** the S-methyl compound (**88**) could not be cyclized to the compound (**99**) because of election deficiency of the 3-nitrogen of the thiazole ring; and in the cases of **90** and **93**, the isothioureas (**91** and **94**) were not convertable to compounds (**100** and **101**) owing to the steric effect of the substituent groups at the 4-position of the thiazole ring. However in the case of **96**, it is still uncertain why the isothiourea (**97**) did not undergo an intramolecular cyclization to give the corresponding cyclic product (**102**). However, in almost cases of the reactions of thioureas (A) with halides, 1(H)-alkoxycarbonyl-2-alkyl-3-(2-thiazolyl)thioureas (D), 1-alkoxycarbonyl-2-alkyl-3-(3-alkylthiazolin-2-ylidene)isothioureas (E) and 2-alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones (C) were obtained. The products and their yields are summarized in Table I.

Finally, we examined the cyclization methods for preparing 2-ethylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**13**) from 1-ethoxycarbonyl-3-(2-thiazolyl)isothiourea (**16**). One method was to treat 0.01 mole of **16** with 10 ml of one normal sodium carbonate at room temperature for two days, and another was to heat **16** at 160—170° for fifteen minutes on an oil-bath.

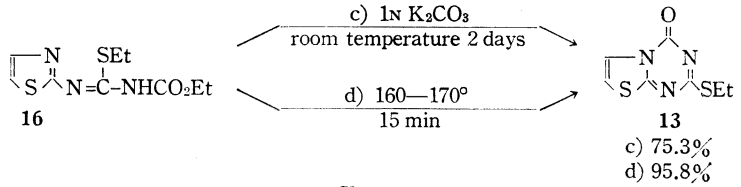
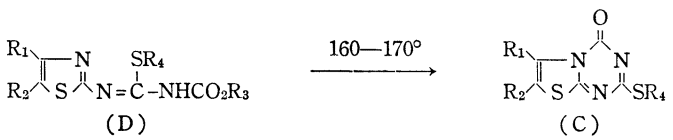


Chart 3

Table II. Yields of 2-Alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones (C)



(D) (C)

30	**32**: 98.3 (%)
33	**32**: 95.8 (%)
36	**32**: 96.1 (%)
39	**32**: 94.7 (%)
42	**32**: 96.4 (%)
45	**32**: 93.8 (%)
16	**13**: 95.2 (%)
47	**49**: 94.8 (%)
50	**52**: 93.7 (%)
53	**55**: 94.4 (%)
56	**57**: 91.2 (%)
58	**60**: 96.3 (%)
61	**63**: 97.6 (%)
64	**66**: 94.8 (%)
68	**70**: 95.2 (%)
72	**74**: 95.6 (%)
76	**75**: 94.1 (%)
80	**82**: 93.8 (%)
84	**86**: 92.6 (%)
88	**99**: 92.3 (%)
91	**100**: 91.8 (%)
94	**101**: 84.2 (%)
97	**102**: 94.4 (%)

Compound (**13**) was obtained in the former case in 75.3% and in the latter case in 95.8% yield, respectively. Other 1(H)-alkoxycarbonyl-2-alkyl-3-(2-thiazolyl)isothioureas (D) could be cyclized to 2-alkylthio-thiazolo[3,2-*a*]-*s*-triazine-4-ones (C) in a good yield under similar thermal conditions. The cyclization products (C) and their yields are summarized in Table 2.

Experimental[13)]

Synthesis of 2-Ethylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (13) *via* Course a——2.31 g of 1-ethoxycarbonyl-3-(2-thiazolyl)thiourea (**11**) was heated at 180—190° for 30 minutes on an oil-bath in nitrogen atmosphere to give 0.47 g of thiazolo[3,2-*a*]-*s*-triazine-2-thio-4-one (**12**) as crude crystals, whose IR spectrum agreed with that of an authentic sample,[9)] and then the compound (**12**) was solved in 50 ml of acetone involving 0.6 g of triethyl amine. To the solution 0.6 g of ethyl bromide was added dropwise at room temperature, refluxed for 5 hr, and the solvent was removed under reduced pressure. The residual solid was solved in $CHCl_3$ (100 ml), washed with H_2O, and dried over anhyd. Na_2SO_4. After removal of dring agent and solvent the residue was recrystallized from aceton to afford 0.35 g of **13** as a colorless needls of mp 144—145°. Mass Spectrum *m/e*: M^+=213. *Anal.* Calcd. for $C_7H_7ON_3S_2$: C, 39.23; H, 3.30; N, 19.67; S, 29.96. Found: C, 39.44; H, 3.31; N, 19.72; S, 30.02. IR ν_{max}^{Nujol} cm^{-1}: 1685 (>C=O). NMR (DMF)τ(J=Hz): 8.64 (3H, t, J=7.0), 6.85 (2H, q, J=7.0), 2.38 (1H, d, J=5.0), 1.98 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 247 (4900), 270 (7900), 309 (18500), 318 (18300). *A mixture of 0.19 g of **13**, 5 ml of 1N NaOH and 20 ml of acetone was stirred for 5 hr at room temperature. After acetone was removed under reduced pressure, the residue was neutralized with 1N HCl, and was extracted with 50 ml $CHCl_3$, and $CHCl_3$ layer was washed with H_2O and dried over anhyd. Na_2SO_4. After removal of drying agent and solvent, the residual solid was resrystallized from benzene to give 0.052 g of 2-N-cyanothiazole (**14**) as colorless needles of mp 146—147°. *Anal.* Calcd. for $C_4H_3N_3S$: C, 38.40; H, 2.42; N, 33.60; S, 25.58. Found: C, 38.26; H, 2.67; N, 33.24; S, 25.13, IR ν_{max}^{Nujol} cm^{-1}: 3100 (>NH), 2220 (–C≡N). NMR (DMSO-d_6)τ(J=Hz): 9.22 (1H, d, J=4.0), 2.76 (1H, d, J=4.0), *ca.* −3.30 (1H).

General Method for Reactions of 1-Alkoxycarbonyl-3-(2-thiazolyl)thioureas (A) and Alkyl Halides——A suspension of 0.01 mole of A, 0.012 mole of alkyl halides and 0.012 mole of potassium carbonate in 100 ml of acetone was stirred at room temperature for 3 days. After removal of acetone under reduced pressure below 30°, 200 ml of ethyl ether was added to the residue, and an inorganic salt was filtered off, and the filtrate was washed with H_2O, dried over anhyd. Na_2SO_3. After removal of ether, the residue was chromatographed over sllica gel and the isolated compounds were refined by distillation or recrystallization.

Reaction of 1-Methoxycarbonyl-3-(2-thiazolyl)thyourea (29) and Methyl Iodide——2.17 g of **29** was reacted with 1.54 g of methyl iodide by the general method to give three products (**30, 31** and **32**). 1(H)-Methoxycarbonyl-2-methyl-3-(2-thiazolyl)isothiourea (**30**), 1.82 g, colorless needles from *n*-hexane-benzene, mp 118—120°. *Anal.* Calcd. for $C_7H_9O_2N_3S_2$: C, 36.37; H, 3.92; N, 18.18; S, 27.68. Found: C, 36.39; H, 3.63; N, 18.06; S, 27.53. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1775 and 1736 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 7.50 (3H, s), 6.18 (3H, s), 3.04 (1H, d, J=4.0), 2.53 (1H, d, J=4.0), *ca.* −2.96 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 242 (6700), 315 (21100). 1-Methoxycarbonyl-2-methyl-3-(3-methylthiazolin-2-ylidene)isothiourea (**31**), 0.25 g, colorless needles from acetone, mp 199—201°. *Anal.* Calcd. for $C_8H_{11}O_2N_3S_2$: C, 39.19; H, 4.52; N, 17.14; S, 26.10. Found: C, 39.22; H, 4.28; N, 16.93; S, 25.91. IR ν_{max}^{Nujol} cm^{-1}: 1665 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 7.48 (3H, s), 7.25 (3H, s), 6.18 (3H, s), 3.28 (1H, d, J=5.0), 2.97 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3000), 279.5 (7000), 331 (22300). 2-Methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**32**), 0.158 g, colorless needles from acetone, mp 202—203°. Mass Spectrum *m/e*: M^+=199. *Anal.* Calcd. for $C_6H_5ON_3S_2$: C, 36.17; H, 2.53; N, 21.09; S, 32.19. Found: C, 36.23; H, 2.65; N, 21.25; S, 32.12. IR ν_{max}^{Nujol} cm^{-1}: 1690 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 7.41 (3H, s), 3.07 (1H, d, J=5.0), 2.31 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 225.5 (9400), 245 (7200), 268 (8000), 308.3 (19300), 316 (19200).

Reaction of 1-Ethoxycarbonyl-3-(2-thiazolyl)thiourea (11) and Methyl Iodide——2.31 g of **11** was reacted with 1.7 g of methyl iodide by the general method, to afford (**33**), (**34**) and 0.131 g of **32**. 1(H)-Ethoxycarbonyl-2-methyl-3-(2-thiazolyl)isothiourea (**33**), 1.85 g, colorless needles from *n*-hexane-benzene, mp 96—97°. *Anal.* Calcd. for $C_8H_{11}O_2N_3S_2$: C, 39.19; H, 4.52; N, 17.14; S, 26.10. Found: C, 39.66; H, 4.68; N, 17.52; S, 25.90. IR ν_{max}^{Nujol} cm^{-1}; 3180 (>NH), 1742 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.67 (3H, t, J=7.0), 7.56 (3H, s), 5.70 (2H, q, J=7.0), 2.98 (1H, d, J=3.7), 2.48 (1H, d, J=3.7), *ca.* −2.90 (1H, broad). 1-Ethoxycarbonyl-2-methy-3-(3-methylthiazolin-2-ylidene)isothiourea (**34**), 0.39 g, colorless needles from benzene, mp 116—117°. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.70; H, 5.06; N, 16.21; S, 24.68. Found: C, 41.95; H, 5.23; N, 16.23; S, 24.42. IR ν_{max}^{Nujol} cm^{-1}: 1660 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.64 (3H, t, J=7.0), 8.49 (3H, s), 6.25 (3H, s), 5.72 (2H, q, J=7.0), 3.28 (1H, d, J=5.0), 2.94 (1H, d, J=5.0). UV

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

$\lambda_{max}^{dioxane}$ mμ (ε): 246.5 (1900), 280 (7200), 332 (23100).

Reaction of 1-Propoxycarbonyl-3-(2-thiazolyl)thiourea (35) and Methyl Iodide——2.45 g of **35** was reacted with 1.7 g of methyl iodide by the general method to afford **36**, **37** and 0.07 g of **32**. 2-Methyl-1(H)-*n*-propoxycarbonyl-3-(2-thiazolyl)isothiourea (**36**), 1.592 g, colorless needles from pet. ether, mp 73—74°. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.70; H, 5.06; N, 16.21; S, 24.68. Found: C, 41.75; H, 5.20; N, 16.30; S, 24.53. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1742 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.02 (3H, t, J=7.0), 8.25 (2H, q, t, J_1=J_2=7.0), 7.55 (3H, s), 5.80 (2H, t, J=7.0), 3.01 (1H, d, J=4.0), 2.48 (1H, d, J=4.0), *ca.* −2.88 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 243 (6800), 312.7 (21400). 2-Methyl-3-(3-methylthiazolin-2-ylidene)-1-*n*-propoxycarbonyl isothiourea (**37**), 0.54 g, mp 113—114°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 44.11; H, 5.31; N, 51.26; S, 23.38. IR ν_{max}^{Nujol} cm^{-1}: 1655 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.04 (3H, t, J=7.0), 8.25 (2H, q, t, J_1=J_2=7.0), 7.50 (3H, s), 7.25 (3H, s), 5.85 (2H, t, J=7.0), 3.30 (1H, d, J=5.0), 2.98 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (2100), 280 (7100), 331 (22600).

Reaction of 1-Isopropoxycarbonyl-3-(2-thiazolyl)thiourea (38) and Methyl Iodide——2.45 g of 1-isopropoxycarbonyl-3-(2-thiazolyl)thiourea (**38**) was reacted with 1.54 g of methyl iodide to afford **39**, **40** and 0.032 g of **32**. 2-Methyl-1(H)-isopropoxycarbonyl-3-(2-thiazolyl)isothiourea (**39**), 2.01 g, colorless needles from *n*-hexane–benzene, mp 88.5—89.5°. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.70; H, 5.06; N, 16.21; S, 24.68. Found: C, 41.79; H, 4.78; N, 16.36; S, 24.77. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1738 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.68 (6H, d, J=7.0), 7.56 (3H, s), 4.95 (1H, q, q, J_1=J_2=7.0), 3.06 (1H, d, J=3.8), 2.50 (1H, d, J=3.8), *ca.* −2.75 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 242 (6000), 314 (20900). 2-Methyl-3-(3-methylthiazolin-2-ylidene)-1-isopropoxycarbonyl isothiourea (**40**), 0.524 g, colorless needles from *n*-hexane–benzene, mp 163—165°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 48.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 44.16; H, 5.39; N, 15.58; S, 23.57. IR ν_{max}^{Nujol} cm^{-1}: 1648 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (6H, d, J=7.0), 7.50 (3H, s), 7.26 (3H, s), 4.96 (1H, q, q, J_1=J_2=7.0), 3.31 (1H, d, J=5.0), 3.00 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3500), 280 (8100), 330 (24900).

Reaction of 1-*n*-Butoxycarbonyl-3-(2-thiazolyl)thiourea (41) and Methyl Iodide——2.59 g of **41** was reacted with 1.7 g of methyl iodide by the general method to afford **42**, **43** and 0.145 g of **32**. 1(H)-*n*-Butoxycarbonyl-2-methyl-3-(2-thiazolyl)isothiourea (**42**), 1.88 g, colorless needles from pet. ether, mp 31—32°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 43.77; H, 5.63; N, 15.53; S, 23.62. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1748 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.05 (3H, t, J=6.5), 8.90—8.02 (4H, m), 7.58 (3H, s), 5.78 (2H, t, J=7.0), 3.05 (1H, d, J=3.8), 2.54 (1H, d, J=3.8), *ca.* −2.85 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 242 (6400), 314 (20700). 1-*n*-Butoxycarbonyl-2-methyl-3-(3-methylthiazolin-2-ylidene)isothiourea (**43**), 0.522 g, colorless needles from *n*-hexane–benzene, mp 113—114°. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.99; H, 5.97; N, 14.63; S, 22.28. Found: C, 46.22; H, 5.80; N, 14.54; S, 22.41. IR ν_{max}^{Nujol} cm^{-1}: 1670 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.04 (3H, t, J=6.0), 8.87—7.98 (4H, m), 7.63 (3H, s), 6.25 (3H, s), 5.80 (2H, t, J=7.0), 3.32 (1H, d, J=5.0), 2.96 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (2100), 279 (7500), 331 (23300).

Reaction of Isobutoxycarbonyl-3-(2-thiazolyl)thiourea (44) and Methyl Iodide——2.59 g of **44** was reacted with 1.7 g of methyl iodide to afford **45**, **46** and 0.155 g of **32**. 1(H)-Isobutoxycarbonyl-2-methyl-3-(2-thiazolyl)isothiourea (**45**), 1.78 g, colorless needles from *n*-hexane–benzene, mp 53—55°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 43.68; H, 5.48; N, 15.62; S, 23.34. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1755 and 1740 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.04 (6H, d, J=7.0), 8.64—7.66 (1H, m), 7.50 (3H, s), 6.00 (2H, d, J=7.0), 3.03 (1H, d, J=3.8), 2.50 (1H, d, J=3.8), *ca.* −2.88 (1H, broad). UV λ_{max}^{EtOH} mμ (ε): 242 (4500), 314 (22000). 1-Isobutoxycarbonyl-2-methyl-3-(3-methylthiazolin-2-ylidene)-isothiourea (**46**), 0.615 g, colorless needles from *n*-hexane–benzene, mp 139—141°. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.99; H, 5.99; N, 14.63; S, 22.28. Found: C, 46.29; H, 5.62; N, 14.81; S, 22.16. IR ν_{max}^{Nujol} cm^{-1}: 1656 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.04 (6H, d, J=7.0), 8.48—7.60 (1H, m), 7.50 (3H, s), 6.25 (3H, s), 6.03 (2H, d, J=7.0), 3.30 (1H, d, J=5.0), 2.99 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3500), 280 (7900), 330 (24300).

Reaction of 1-Ethoxycarbonyl-3-(2-thiazolyl)thiourea (11) and Ethyl Iodide——2.31 g of **11** was reacted with 3.14 g of ethyl iodide to give **16**, **17**, 0.197 g of **13** and 0.146 g of **11**. 1(H)-Ethoxycarbonyl-2-ethyl-3-(2-thiazolyl)isothiourea (**16**), 1.80 g, pale yellow oil, bp 140—145° at 0.3 mmHg, n_D^{22} 1.6041. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.70; H, 5.06; N, 16.21; S, 24.69. Found: C, 41.62; H, 5.20; N, 16.16; S, 24.28. IR ν_{max}^{liquid} cm^{-1}: 3200 (>NH), 1750 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.44 (6H, t, J=7.1), 6.92 (2H, q, J=7.1), 5.72 (2H, q, J=7.1), 3.04 (1H, d, J=3.6), 2.50 (1H, d, J=3.6), *ca.* −2.82 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 242 (3800), 315 (20600). 1-Ethoxycarbonyl-2-ethyl-3-(3-ethylthiazolin-2-ylidene)isothiourea (**17**), 0.304 g, colorless needles from *n*-hexane–benzene, mp 86—87°. Mass Spectrum *m/e*: M$^+$=287. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.99; H, 5.97; N, 14.63; S, 22.28. Found: C, 45.59; H, 5.83; N, 14.24; S, 22.03. IR ν_{max}^{Nujol} cm^{-1}: 1660 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.68 (3H, t, J=7.0), 8.64 (3H, t, J=7.0), 8.58 (3H, t, J=7.0), 6.88 (2H, q, J=7.0), 5.77 (4H, q, J=7.0), 3.30 (1H, d, J=5.0), 2.92 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 280 (7000), 331 (22700).

Hydrolysis of 1(H)-Ethoxycarbonyl-2-ethyl-3-(2-thiazolyl)isothiourea (16) with 1N HCl——A suspension of 2.59 g of **16** in 20 ml of 1N HCl was refluxed for 30 minutes, poured into 200 ml of ice-water, and neutralized with potassium carbonate. A precipitate was separated from the solution by filtration, washed

with H_2O, and dried in vacuum, and recrystallized from acetone to afford 1.88 g of 1-ethoxycarbonyl-3-(2-thiazolyl)urea (**18**)* as colorless needles of mp 157—158°. *Anal.* Calcd. for $C_7H_7O_3N_3S$: C, 39.07; H, 4.22; N, 19.53; S, 14.87. Found: C, 39.04; H, 4.23; N, 19.69; S, 14.90. Mass Spectrum *m/e*: M^+=215. IR ν_{max}^{Nujol} cm^{-1}: 3250, 1730 and 1710 (-NHCNHC-). NMR ($CDCl_3$)τ(J=Hz): 8.66 (3H, t, J=7.0), 5.70 (2H, q, J=7.0), 3.17 (1H, d, J=3.8), 2.52 (1H, d, J=3.8), *ca.* 1.44 (1H, broad), *ca.* −1.12 (1H, braod). UV λ_{max}^{EtOH} mμ (ε): 262 (11500). *1.65 g of this compound (**18**) was also obtained by the oxidation of 2.31 g of **11** with 3.5 g of mercuric acetate in 200 ml of $CHCl_3$ at room temperature.

Reaction of 2-Ethylaminothiazole (19)[11] and Ethoxycarbonyl Isothiocyanate (6)——To a solution of 1.28 g of **19** in 50 ml of ethyl acetate, 1.45 g of **6** was added dropwise at room temperature, refluxed for 2 hr, and then the solvent was removed under reduced pressure. The resulting residue was chromatographed over silica gel to give **20**, **21** and 0.48 g of **19**. 1(H)-Ethoxycarbonyl-3-ethyl-3-(2-thiazolyl)thiourea (**20**), 0.85 g, pale yellow needles from *n*-hexane–benzene, mp 65—66°. Mass Spectrum: *m/e*: M^+=259. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.70; H, 5.06; N, 16.21; S, 24.69. Found: C, 41.78; H, 5.03; N, 16.23; S, 24.81. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1770 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.64 (3H, t, J=7.0), 8.57 (3H, t, J=7.0), 5.68 (2H, q, J=7.0), 5.23 (2H, q, J=7.0), 2.85 (1H, d, J=3.5), 2.44 (1H, d, J=3.5), *ca.* −3.80 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 264 (7500), 315 (18500). N-Ethoxycarbonyl-2-ethylaminothiazole (**21**), 0.27 g, colorless oil, bp 110—115° at 0.4 mmHg (bath. temp.). *Anal.* Calcd. for $C_8H_{12}O_2N_2S$: C, 47.99; H, 6.04; N, 13.99; S, 15.98. Found: C, 48.26; H, 6.36; N, 13.84; S, 15.84. IR $\nu_{max}^{Liq.}$ cm^{-1}: 1710 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.68 (3H, t, J=7.0), 8.61 (3H, t, J=7.0), 5.76 (2H, q, J=7.0), 5.61 (2H, q, J=7.0), 3.04 (1H, d, J=3.5), 2.55 (1H, d, J=3.5). UV λ_{max}^{EtOH} mμ (ε): 259 (9400).

Reaction of 1(H)-Ethoxycarbonyl-3-ethyl-3-(2-thiazolyl)thiourea (20) and Methyl Iodide——A suspension of 1.3 g of **20**, 0.8 g of methyl iodide and 0.7 g of potassium carbonate in 50 ml of acetone was stirred for 2 days at room temperature. After removal of an insoluble salt and solvent, the resulting residue was poured into 100 ml of ice–water, neutralized with 3.5% HCl, and extracted with ether. Ethereal layer was washed with H_2O, and dried over anhyd. Na_2SO_4. After removal of ether, the resulting solid was recrystallized from *n*-hexane–benzene to afford 1.15 g of 1(H)-ethoxycarbonyl-3-ethyl-2-methyl-3-(2-thiazolyl)-isothiourea (**23**) as colorless needles of mp 58—59°. Mass Spectrum *m/e*: M^+=273. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 44.13; H, 5.56; N, 15.54; S, 23.01. NMR ($CDCl_3$) τ(J=Hz): 8.63 (3H, t, J=7.0), 8.58 (3H, t, J=7.0), 7.46 (3H, s), 5.70 (2H, q, J=7.0), 5.48 (2H, q, J=7.0), 2.96 (1H, d, J=3.5), 2.47 (1H, d, J=3.5).

Hydrolysis of 23 with Aqueous NaOH——A suspension of 0.68 g of **23** in 5 ml of 1N NaOH was stirred for a period of 30 min, poured into 50 ml of ice–water, neutralized with 1N HCl, and extracted with 50 ml of $CHCl_3$, $CHCl_3$ layer was washed with H_2O, dried over anhy. Na_2SO_4, and then after removal of drying agent and solvent, the resulting solid was recrystallized from *n*-hexane–benzene to afford 0.52 g of 1(H)-ethoxycarbonyl-3-ethyl-3-(2-thiazolyl)urea (**24**) as colorless needles of mp 91—93°. *Anal.* Calcd. for $C_9H_{13}O_3N_3S$: C, 44.44; H, 5.39; N, 17.28; S, 13.15. Found: C, 44.67; H, 5.32; N, 17.22; S, 13.47. IR ν_{max}^{Nujol} cm^{-1}: 3100, 1785 and 1698 (-C(O)NHC(O)-O-). NMR ($CDCl_3$)τ(J=Hz): 8.67 (6H, t, J=7.0), 5.96 (2H, q, J=7.0), 5.70 (2H, q, J=7.0), 2.99 (1H, d, J=3.5), 2.56 (1H, d, J=3.5), *ca.* −2.35 (1H, broad). UV λ_{max}^{EtOH} mμ (ε): 267 (12700).

Reaction of 3-Ethyl-2-iminothiazoline (25)[12] and 6——To a solution on 1.28 g of **25** in 50 ml of ethyl acetate, 1.45 g of **6** was added at room temperature, refluxed for 2 hr, and then solvent was removed under reduced pressure. The residue was chromatographed over silicagel column to afford two products (**26** and **27**). 1-Ethoxycarbonyl-3-(3-ethylthiazolin-2-ylidene)thiourea (**26**), 2.25 g, pale yellow needles from benzene, mp 130—132°. Mass Spectrum *m/e*: M^+=259. *Anal.* Calcd. for $C_9H_{12}O_2N_3S$: C, 41.70; H, 5.06; N, 16.21; S, 24.64. Found: C, 41.51; H, 4.95; N, 16.02; S, 24.81. NMR ($CDCl_3$)τ(J=Hz): 8.68 (3H, t, J=7.0), 8.51 (3H, t, J=7.0), 5.72 (2H, q, J=7.0), 5.60 (2H, q, J=7.0), 3.16 (1H, d, J=4.6), 2.75 (1H, d, J=4.6), *ca.* −1.84 (1H, broad). UV λ_{max}^{EtOH} mμ (ε): 279 (11200), 347 (17900). 2-Ethoxycarbonylimino-3-ethylthiazoline (**27**), 0.08 g, colorless needles from *n*-hexane–benzene, mp 65—67°. *Anal.* Calcd. for $C_8H_{12}O_2N_2S$: C, 47.99; H, 6.04; N, 13.99; S, 15.98. Found: C, 48.26; H, 6.35; N, 14.17; S, 16.15. IR ν_{max}^{Nujol} cm^{-1}: 1650 (>C=O), 1640 (>C=C- or >C=N-). NMR ($CDCl_3$)τ(J=Hz): 8.64 (3H, t, J=7.0), 8.51 (2H, q, J=7.0), 5.70 (2H, q, J=7.0), 3.37 (1H, d, J=5.0), 3.03 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 233 (2400), 284 (14700).

Synthesis of 17 by the Reaction of 26 with Ethyl Bromide——To a solution of 2.59 g of **26** in 30 ml of DMF, 0.7 g of CH_3ONa and 1.2 g of ethyl bromide were added, stirred at room temperature for 5 hr, and then the reaction mixture was poured into 200 ml of H_2O, and extracted with 100 ml of $CHCl_3$. $CHCl_3$ layer was washed with H_2O, and dried over anhyd. Na_2SO_4. After removal of drying agent and solvent, the resulting solid was recrystallized from *n*-hexane–benzene to give 2.42 g of **17**.

Hydrolysis of 17 with Aqueous HCl——A suspension of 0.29 g of **17** in 5 ml of 1N HCl was refluxed for a period of 5 minutes, neutralized with K_2CO_3, and extracted with 20 ml of $CHCl_3$. $CHCl_3$ layer was washed with H_2O, and dried over anhyd. Na_2SO_4. After removal of drying agent and solvent, the resulting solid was recrystallized from benzene to afford 0.182 g of 1-ethoxycarbonyl-3-(3-ethylthiazolin-2-ylidene)urea (**28**) as colorless needles of mp 101—102°. *Anal.* Calcd. for $C_9H_{13}O_2N_3S$: C, 44.81; H, 4.60; N, 17.42; S,

13.27. Found: C, 44.76; H, 4.57; N, 17.63; S, 13.20. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3220, 1770 and 1720 [-C(O)NHC(O)-], 1650 (>C=N- or -C=C<). NMR ($CDCl_3$)τ(J=Hz): 8.70 (3H, t, J=7.0), 8.42 (3H, t, J=7.0), 5.87 (2H, q, J=7.0), 5.72 (2H, q, J=7.0), 3.48 (1H, d, J=4.8), 6.51 (1H, d, J=4.8), *ca.* 2.44 (1H, broad). UV λ_{max}^{EtOH} mμ (ε): 235 (3400), 295 (21500).

Reaction of 11 and *n*-Propyl Iodide——2.31 g of **11** was reacted with 2.40 g of *n*-propyl iodide by the general method to give **47**, **48**, **49** and 0.291 g of **11**. 1(H)-Ethoxycarbonyl-2-*n*-propyl-3-(2-thiazolyl)-isothiourea (**47**), 1.88 g, colorless needles from *n*-hexane–benzene, mp 45—46°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 43.51; H, 5.88; N, 15.54; S, 23.14. IR ν_{max}^{Nujol} cm^{-1}: 3200 (>NH), 1750 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.96 (3H, t, J=6.8), 8.65 (3H, t, J=7.0), 8.24 (2H, q, t, J_1=6.8, J_2=7.0), 6.94 (2H, t, J=7.0), 5.69 (2H, q, J=7.0), 3.03 (1H, d, J=4.0), 2.50 (1H, d, J=4.0), *ca.* −2.89 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 243 (7000), 315 (20900). 1-Ethoxycarbonyl-2-*n*-propyl-3-(3-*n*-propylthiazolin-2-ylidene)isothiourea (**48**), 0.334 g, colorleds needles from *n*-hexane–benzene, mp 90—91°. *Anal.* Calcd, for $C_{13}H_{21}O_2N_3S_2$: C, 49.51; H, 6.71; N, 13.33; S, 20.30. Found: C, 49.73; H, 6.87; N, 13.10; S, 19.97. IR ν_{max}^{Nujol} cm^{-1}: 1660 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.05 (3H, t, J=6.5), 8.96 (3H, t, J=6.5), 8.65 (3H, t, J=7.0), 8.24 (4H, q, t, J_1=6.5, J_2=7.0), 6.90 (2H, t, J=7.0), 5.85 (2H, t, J=7.0), 5.75 (2H, d, J=7.0), 3.30 (1H, d, J=5.0), 2.95 (1H, d, J=5.0). *n*-Propylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**49**), 0.128 g, colorless needles from *n*-hexane–benzene, mp 121—122°. Mass Spectrum *m/e*: M$^+$=227. *Anal.* Calcd. for $C_8H_9ON_3S_2$: C, 42.29; H, 3.99; N, 18.50; S, 28.14. Found: C, 42.14; H, 4.08; N, 11.15; S, 27.80. IR ν_{max}^{Nujol} cm^{-1}: 1705 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.95 (3H, t, J=6.5), 8.29 (2H, q, t, J_1=6.5, J_2=7.0), 6.82 (2H, t, J=7.0), 2.89 (1H, d, J=5.0), 2.09 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 226 (10000), 245.5 (7200), 270 (8600), 310 (20400), 317 (20400).

Reaction of 11 and Isopropyl Iodide——2.31 g of **11** was reacted with 2.04 g of isopropyl iodide by the general method to give **50**, **51**, **52** and 1.368 g of **11**. 1(H)-Ethoxycarbonyl-2-isopropyl-3-(2-thiazolyl)-isothiourea (**50**), 0.6 g, colorless needles from *n*-hexane–benzene, mp 60—61°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 43.69; H, 5.38; N, 15.28; S, 23.08. IR ν_{max}^{Nujol} cm^{-1}: 2150 (>NH), 1750 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 8.60 (6H, d, J=7.0), 6.00 (1H, q, q, J_1=J_2=7.0), 5.70 (2H, q, J=7.0), 3.04 (1H, d, J=4.0), 3.50 (1H, d, J=4.0), *ca.* −2.84 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 243 (6200), 325 (20400). 1-Ethoxycarbonyl-2-isopropyl-3-(3-isopropylthiazolin-2-ylidene)isothiourea (**51**), colorless needles from *n*-hexane-benzene, mp 105—106°. *Anal.* Calcd. for $C_{13}H_{21}O_2N_3S_2$: C, 49.51; H, 6.71; N, 13.33; S, 20.30. Found: C, 49.85; H, 6.55; N, 13.37; S, 20.03. IR ν_{max}^{Nujol} cm^{-1}: 1658 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.68 (3H, t, J=7.0), 8.61 (3H, d, J=7.0), 8.51 (3H, d, J=7.0), 6.00 (1H, q, q, J_1=J_2=7.0), 5.79 (2H, q, J=7.0), 4.70 (1H, q, q, J_1=J_2=7.0), 3.06 (1H, d, J=5.0), 2.82 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 244 (3600), 280 (7600), 331 (22700). 2-Isopropylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**52**), 0.159 g, colorless needles from *n*-hexane–benzene, mp 146—148°. Mass Spectrum *m/e*: M$^+$=227. *Anal.* Calcd. for $C_8H_9ON_3S_2$: C, 42.29; H, 3.99; N, 18.50; S, 28.14. Found: C, 42.56; H, 4.10; N, 18.23; S, 28.11. IR ν_{max}^{Nujol} cm^{-1}: 1710 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 7.10 (6H, d, J=7.0), 1.92 (1H, q, q, J_1=J_2=7.0), 2.91 (1H, d, J=5.0), 2.10 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 226 (10200), 246 (7500), 270 (8900), 310 (21000), 317 (21000).

Reaction of 11 and *n*-Butyl Iodide——2.31 g of **11** was reacted with 2.21 g of *n*-butyl iodide by the general method to give **53**, **54**, **55** and 0.342 g of **11**. 2-*n*-Butyl-1(H)-ethoxycarbonyl-3-(2-thiazolyl)isothiourea (**53**), 1.74 g, colorless needles from *n*-hexane–benzene, mp 51—53°. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.99; H, 5.97; N, 14.63; S, 22.27. Found: C, 46.49; H, 5.94; N, 14.37; S, 21.90. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1747 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.15 (3H, t, J=6.5), 8.85—7.94 (4H, m), 8.65 (3H, t, J=7.0), 6.90 (2H, t, J=6.5), 5.70 (2H, q, J=7.0), 3.02 (1H, d, J=4.0), 2.49 (1H, d, J=4.0), *ca.* −2.89 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 243 (7000), 315 (20400). 2-*n*-Butyl-3-(3-*n*-butylthiazolin-2-ylidene)-1-ethoxycarbonyl isothiourea (**54**), 0.41 g, colorless needles from *n*-hexane–branzene, mp 97—99°. *Anal.* Calcd. for $C_{15}H_{25}O_2N_3S_2$: C, 52.47; H, 7.34; N, 12.24; S, 18.64. Found: C, 52.47; H, 7.48; N, 12.50; S, 18.41. NMR ($CDCl_3$)τ(J=Hz): 9.06 (3H, t, J=6.5), 9.03 (3H, t, J=6.5), 8.84—7.86 (8H, m), 8.62 (3H, t, J=7.0), 6.85 (2H, t, J=7.0), 5.80 (2H, t, J=7.0), 5.70 (2H, q, J=7.0), 3.29 (1H, d, J=5.0), 2.95 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3700), 281 (8100), 331.6 (23600). 2-*n*-Butylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**55**), 0.176 g, colorless needles from isopropyl ether, mp 114—115°. Mass Spectrum *m/e*: M$^+$=241. *Anal.* Calcd. for $C_9H_{11}ON_3S_2$: C, 44.81; H, 4.60; N, 17.42; S, 26.58. Found: C, 44.95; H, 4.64; N, 17.18; S, 26.45. IR ν_{max}^{Nujol} cm^{-1}: 1708 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.05 (3H, t, J=6.0), 8.88—7.99 (4H, m), 6.80 (2H, t, J=7.0), 2.99 (1H, d, J=5.0), 2.11 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 226 (10500), 246 (7500), 270 (9000), 310.5 (21700), 318 (21700).

Reaction of 11 and Isobutyl Bromide——2.31 g of **11** was reacted with 1.65 g of isobutyl bromide by the general method to give **50**, **51** and 1.47 g of **11**. 1(H)-Ethoxycarbonyl-2-isobutyl-3-(2-thiazolyl)isothiourea (**56**), 0.73 g, colorless needles from *n*-hexane–benzene, mp 46—48°. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.99; H, 5.97; N, 14.63; S, 22.28. Found: C, 45.99; H, 5.83; N, 14.82; S, 22.28. IR ν_{max}^{Nujol} cm^{-1}: 2200 (>NH), 1742 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.93 (6H, d, J=7.0), 8.75 (3H, t, J=7.0), 7.92 (1H, q, q, t, J_1=J_2=J_3=7.0), 6.98 (2H, d, J=7.0), 5.68 (2H, q, J=7.0), 3.02 (1H, d, J=4.0), 2.46 (1H, d, J=4.0), *ca.* −2.80 (1H, m). UV $\lambda_{max}^{Dioxane}$ mμ (ε): 243 (7200), 315 (21500). 2-Isobutylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**57**), 0.195 g, colorless needles from isopropyl ether, mp 113—114°. *Anal.* Calcd. for C_9H_{11}-

ON_3S_2: C, 44.81; H, 4.60; N, 17.42; S, 26.58. Found: C, 44.74; H, 4.69; N, 16.99; S, 26.54. Mass Spectrum *m/e*: M^+=241. IR ν_{max}^{Nujol} cm^{-1}: 1750 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.09 (6H, d, J=6.5), 8.43—7.63 (1H, m), 6.87 (2H, d, J=6.5), 2.98 (1H, d, J=5.0), 2.12 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 226 (10100), 246 (7100), 270 (8500), 311 (20800), 317 (20900).

Reaction of 11 and *t*-Butyl Bromide——2.31 g of **11** was reacted with 1.65 g of *t*-butyl bromide in acetone involving 1.54 g of potassium carbonate by the general method, and then after removal of solvent and inorganic compound, the residual solid was chromatographed over silica gel column to give 2.25 g of **11**.

Reaction of 11 and Allyl Bromide——2.31 g of **11** was reacted with 1.46 g of allyl bromide by the general method to give **58**, **59**, **60** and 0.101 g of **11**. 1(H)-Ethoxycarbonyl-2-(2-propen-1-yl)-3-(2-thiazolyl)isothiourea (**58**). 2.02 g, colorless needles from *n*-hexane–benzene, mp 49—50°. *Anal.* Calcd. for $C_{10}H_{13}O_2N_3S_2$: C, 44.28; H, 4.83; N, 15.49; S, 23.26. Found: C, 44.68; H, 4.97; N, 15.26; S, 23.21. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1748 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.64 (3H, t, J=7.0), 6.24 (2H, d, t, J_1=6.5, J_2=1.0), 5.70 (2H, q, J=7.0), 5.01—3.68 (3H, m), 3.00 (1H, d, J=3.5), 2.47 (1H, d, J=3.5), *ca.* −2.89 (1H, m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 243 (6600), 314 (20200). 1-Ethoxycarbonyl-2-(2-propen-1-yl)-3-[3-(2-propen-1-yl)thiazolin-2-ylidene]isothiourea (**59**), 0.517 g, colorless needles from *n*-hexane–benzene, mp 112—113°. *Anal.* Calcd. for $C_{13}H_{17}O_2N_3S_2$: C, 50.16; H, 5.50; N, 13.50; S, 23.89. Found: C, 50.37; H, 5.74; N, 13.49; S, 23.59. IR ν_{max}^{Nujol} cm^{-1}: 8.64 (3H, t, J=7.0), 7.16 (2H, d, t, J_1=6.5, J_2=1.0), 5.72 (2H, q, J=7.0), 5.15 (2H, d, t, J_1=6.5, J_2=1.0), 5.05—3.52 (6H, m), 3.26 (1H, d, J=5.0), 2.93 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3100), 280 (7700), 333 (23100). 2-(2-Propen-1-yl)thio-thiazole[3,2-*a*]-*s*-triazine-4-one (**60**), 0.072 g, colorless needles from ethyl acetate, mp 138—140°. *Anal.* Calcd. for $C_8H_7ON_3S_2$: C, 42.84; H, 2.70; N, 18.74; S, 28.42. Found: C, 42.69; H, 2.67; N, 18.89; S, 28.60. IR ν_{max}^{Nujol} cm^{-1}: 1690 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 6.14 (2H, d, t, J_1=6.5, J_2=1.0), 5.00—3.65 (3H, m), 2.94 (1H, d, J=5.0), 2.10 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 224.5 (10600), 245.5 (7600), 269 (8900), 310 (21000), 317 (21000).

Reaction of 11 and Propargyl Bromide——2.31 g of **11** was reacted with 1.43 g of propargyl bromide by the general method to give **61**, **62**, **63** and 0.015 g of **11**. 1(H)-Ethoxycarbonyl-2-(2-propyn-1-yl)-3-(2-thiazolyl)isothiourea (**61**), 1.97 g, colorless needles from benzene, mp 106—108°. *Anal.* Calcd. for $C_{10}H_{11}O_2N_3S_2$: C, 44.61; H, 4.12; N, 15.61; S, 23.44. Found: C, 44.93; H, 4.21; N, 15.70; S, 23.37. IR ν_{max}^{Nujol} cm^{-1}: 3300 (–C≡CH), 3180 (>NH), 2100 (–C≡C–), 1740 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.84 (1H, t, J=2.3), 6.16 (2H, d, J=2.3), 5.70 (2H, q, J=7.0), 2.98 (1H, d, J=3.2), 2.46 (1H, d, J=3.2), *ca.* −2.90 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 238 (6900), 313 (20300). 1-Ethoxycarbonyl-2-(2-propyn-1-yl)-3-(2-propyn-1-yl)thiazolin-2-ylidene isothiourea (**62**), 0.362 g, colorless needles from benzene, 147—149°. *Anal.* Calcd. for $C_{13}H_{13}O_2N_3S_2$: C, 50.81; H, 4.26; N, 13.68; S, 20.85. Found: C, 51.03; H, 4.24; N, 13.51; S, 20.79. IR ν_{max}^{Nujol} cm^{-1}: 3270 (–C≡CH), 2100 (–C≡C–), 1655 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.85 (1H, t, J=2.5), 7.46 (1H, t, J=2.5), 6.15 (2H, d, J=2.3), 5.74 (2H, q, J=7.0), 4.94 (2H, d, J=2.5), 3.22 (1H, d, J=5.0), 2.67 (1H, d, J=5.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 243 (4000), 276 (7500), 333 (23600). 2-(2-Propyn-1-yl)thio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**63**), 0.199 g, colorless needles from ethyl acetate, mp 175—176°. Mass Spectrum *m/e*: M^+=223. *Anal.* Calcd. for $C_8H_5ON_3S_2$: C, 43.06; H, 2.26; N, 18.23; S, 28.74. Found: C, 42.77; H, 2.09; N, 18.82; S, 29.20. IR ν_{max}^{Nujol} cm^{-1}: 3260 (HC≡C–), 2100 (–C≡C–), 1700 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 6.90 (1H, t, J=2.1), 6.05 (2H, d, J=2.1), 2.48 (1H, d, J=5.0), 2.05 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 224.5 (8600), 265 (8600), 310 (19800), 318.5 (shoulder).

Reaction of 11 and Benzyl Bromide——2.31 g of **11** was reacted with 2.05 g of benzyl bromide by the general method to give **64**, **65**, **66** and 0.134 g of **11**. 2-Benzyl-1(H)-ethoxycarbonyl-3-(2-thiazolyl)isothiourea (**64**), 3.22 g, colorless needles from benzene, mp 108—110°. *Anal.* Calcd. for $C_{14}H_{15}O_2N_3S$: C, 52.23; H, 4.71; N, 13.08; S, 19.92. Found: C, 52.21; H, 4.62; N, 12.76; S, 19.60. IR ν_{max}^{Nujol} cm^{-1}: 1748 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.69 (3H, t, J=7.0), 5.75 (2H, q, J=7.0), 5.70 (2H, s), 3.02 (1H, d, J=3.2), *ca.* 2.64 for five aromatic protons (m), 2.50 (1H, d, J=3.2), *ca.* −2.88 (1H, m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (7300), 315 (20300). 2-Benzyl-3-(3-benzylthiazolin-2-ylidene)-1-ethoxycarbonyl isothiourea (**65**), 0.445 g, colorless needles from benzene, mp 134—135°. *Anal.* Calcd. for $C_{21}H_{21}O_2N_3S_2$: C, 61.31; H, 5.15; N, 10.21; S, 15.55. Found: C, 60.96; H, 5.13; N, 10.14; S, 15.44. IR ν_{max}^{Nujol} cm^{-1}: 1675 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.68 (3H, t, J=7.0), 5.75 (2H, q, J=7.0), 5.68 (2H, s), 4.69 (2H, s), 3.34 (1H, d, J=5.0), 3.04 (1H, d, J=5.0), 2.99—2.49 for the aromatic protons (m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 281 (8600), 411 (23800). 2-Benzylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**66**), 0.16 g, colorless needles from ethyl acetate, mp 136—137°. *Anal.* Calcd. for $C_{12}H_9ON_3S_2$: C, 52.37; H, 3.30; N, 15.27; S, 23.30. Found: C, 52.04; H, 3.33; N, 15.56; S, 23.27. IR ν_{max}^{Nujol} cm^{-1}: 1707 and 1685 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 5.56 (2H, s), 3.04 (1H, d, J=5.0), 2.90—2.44 for five aromatic protons (m), 2.14 (1H, d, J=5.0). UV λ_{max}^{EtOH} mμ (ε): 270 (8800), 310.5 (21900), 318 (21900).

Reaction of 1-Ethoxycarbonyl-3-(5-methylthiazol-2-yl)thiourea (67) and Methyl Iodide——2.45 g of **67** was reacted with 1.7 g of methyl iodide by the general method to afford three products (**68**, **69** and **70**). 1(H)-Ethoxycarbonyl-2-methyl-3-(5-methylthiazol-2-yl)isothiourea (**68**), 1.85 g, colorless needles from *n*-hexane–benzene, mp 80—81°. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.68; H, 5.05; N, 16.20; S, 24.73. Found: C, 41.83; H, 5.42; N, 15.93; S, 24.45. IR ν_{max}^{Nujol} cm^{-1}: 1752 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.58 (3H, d, J=1.0), 5.70 (2H, q, J=7.0), 2.85 (1H, q, J=1.0), *ca.* −2.84 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 241.5 (6400), 319 (21100). 1-Ethoxycarbonyl-2-methyl-3-(3,5-dimethyl-thiazolin-2-ylidene)-

isothiourea (**69**), 0.553 g, colorless needles from benzene, mp 128.5—129.5°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.46. Found: C, 43.86; H, 5.48; N, 15.20; S, 23.14. IR ν_{max}^{Nujol} cm^{-1}: 1652 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.74 (3H, d, J=1.8), 7.50 (3H, s), 6.32 (3H, s), 5.75 (2H, q, J=7.0), 3.30 (1H, q, J=1.8). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3000), 279.5 (7000), 331 (22300). 7-Methyl-2-methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**70**), 0.119 g, colorless needles from benzene, mp 173—175°. *Anal.* Calcd. for $C_7H_7ON_3S_2$: C, 39.44; H, 3.31; N, 19.72; S, 30.20. Found: C, 39.30; H, 3.07; N, 14.49; S, 29.86. IR ν_{max}^{Nujol} cm^{-1}: 1685 (>C=O). NMR (DMF)τ(J=Hz): 7.50 (3H, s), 7.48 (3H, d, J=1.2), 2.22 (1H, q, J=1.2). UV λ_{max}^{EtOH} mμ (ε): 246 (7200), 267 (8300), 314 (20200), 320 (shoulder).

Reaction of 1-Ethoxycarbonyl-3-(5-ethylthiazol-2-yl)thiourea (71) and Methyl Iodide——2.59 g of **71** was reacted with 1.7 g of methyl iodide to afford three products (**72**, **73** and **74**). 1(H)-Ethoxycarbonyl-3-(5-ethylthiazol-2-yl)-2-methyl isothiourea (**72**), 2.73 g, colorless needles from *n*-hexane–benzene, mp 52—53°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.42. Found: C, 44.01; H, 5.79; N, 15.41; S, 23.40. IR ν_{max}^{Nujol} cm^{-1}: 3200 (>NH), 1750 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.70 (3H, t, J=7.0), 8.66 (3H, t, J=7.0), 7.57 (3H, s), 7.31 (2H, q, d, J_1=7.0, J_2=1.0), 5.72 (2H, q, J=7.0), 2.84 (1H, t, J=1.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 242 (6900), 329.6 (21900). 1-Ethoxycarbonyl-2-methyl-3-(5-ethyl-3-methylthiazolin-2-ylidene)isothiourea (**73**), 0.54 g, colorless needles from benzene, mp 129—130°. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.97; H, 5.96; N, 14.62; S, 22.31. Found: C, 46.31; H, 6.33; N, 15.03; S, 21.91. IR ν_{max}^{Nujol} cm^{-1}: 1670 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.71 (3H, t, J=7.0), 8.64 (3H, t, J=7.0), 7.50 (3H, s), 7.33 (2H, q, d, J_1=7.0, J_2=1.2), 6.31 (3H, s), 5.73 (2H, q, J=7.0), 3.28 (1H, t, J=1.2). UV $\lambda_{max}^{dioxane}$ mμ (ε): 245 (3900), 278 (7200), 337 (24100). 7-Ethyl-2-methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**74**), 0.116 g, colorless needles from benzene, mp 135—137°. *Anal.* Calcd. for $C_8H_9ON_3S_2$: C, 42.29; H, 3.99; N, 18.50; S, 28.17. Found: C, 42.37; H, 3.72; N, 18.34; S, 28.15. IR ν_{max}^{Nujol} cm^{-1}: 1702 (>C=O). NMR ($CDCl_3$)τ (J=Hz): 8.64 (3H, t, J=7.2), 7.44 (3H, s), 7.19 (2H, q, d, J_1=7.2, J_2=1.5), 2.41 (1H, t, J=1.5). UV λ_{max}^{EtOH} mμ (ε): 246 (7000), 267 (8100), 314 (20000), 322 (shoulder).

Reaction of 1-Ethoxycarbonyl-3-(5-*n*-propylthiazol-2-yl)thiourea (75) and Methyl Iodide——2.73 g of **75** was reacted with 1.7 g of methyl iodide by the general method to afford three products (**76**, **77** and **78**). 1(H)-Ethoxycarbonyl-2-methyl-3-(5-*n*-propylthioazol-2-yl)isothiourea (**76**), 2.06 g, colorless needles from *n*-hexane–benzene, mp 65.5—67°. *Anal.* Calcd. for $C_{11}H_{17}O_2N_3S_2$: C, 45.99; H, 5.97; N, 14.73; S, 22.28. Found: C, 46.07; H, 5.94; N, 14.93; S, 22.35. IR ν_{max}^{Nujol} cm^{-1}: 3200 (>NH), 1743 (>C=O). NMR ($CDCl_3$)τ (J=Hz): 9.11 (3H, t, J=7.0), 8.66 (3H, t, J=7.0), 8.44 (2H, q, t, J_1=J_2=7.0), 7.57 (3H, s), 7.26 (2H, t, d, J_1=7.0, J_2=1.0), 5.72 (2H, q, J=7.0), 2.84 (1H, t, J=1.0), *ca.* −2.89 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 240 (8000), 319.2 (22800). 1-Ethoxycarbonyl-2-methyl-3-(3-methyl-5-*n*-propylthiazolin-2-ylidene)isothiourea (**77**), 0.61 g, colorless needles from *n*-hexane–benzene, mp 97—98.5°. *Anal.* Calcd. for $C_{12}H_{19}O_2N_3S_2$: C, 47.83; H, 6.30; N, 13.95; S, 21.22. Found: C, 48.15; H, 6.76; N, 14.26; S, 21.28. IR ν_{max}^{Nujol} cm^{-1}: 1670 (>C=O), 1608 (>C=C– or >C=N–). NMR ($CDCl_3$) (J=Hz): 9.02 (3H, t, J=7.0), 8.64 (3H, t, J=7.0), 8.45 (2H, q, t, J_1=J_2=7.0), 7.51 (3H, s), 7.38 (2H, t, d, J_1=7.0, J_2=1.0), 6.30 (3H, s), 5.73 (2H, q, J=7.0), 3.28 (1H, t, J=1.0). UV $\lambda_{max}^{Dioxane}$ mμ (ε): 245 (4000), 279 (7400), 338 (24400). 2-Methylthio-7-*n*-propylthiazolo[3,2-*a*]-*s*-triazine-4-one (**78**), 0.13 g, colorless needles from benzene, mp 86—88°. *Anal.* Calcd. for $C_9H_{11}O_2N_3S_2$: C, 44.81; H, 4.60; N, 17.42; S, 26.53. Found: C, 44.54; H, 4.42; N, 17.06; S, 26.52. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.97 (3H, t, J=6.5), 8.18 (2H, q, t, J_1=6.5, J_2=7.0), 7.43 (3H, s), 7.25 (2H, t, d, J_1=7.0, J_2=1.5), 2.42 (1H, t, J=1.5). UV λ_{max}^{EtOH} mμ (ε): 246 (5400), 268 (8400), 313 (21100), 322 (shoulder).

Reaction of 3-(5-*n*-Butylthiazol-2-yl)-1-ethoxycarbonyl Thiourea (79) and Methyl Iodide——2.87 g of **79** was reacted with 1.7 g of methyl iodide by the general method to afford three products (**80**, **81** and **82**). 3-(5-*n*-Butylthiazol-2-yl)-1(H)-ethoxycarbonyl-2-methyl isothiourea (**80**), 2.15 g, colorless needles from pet. ether, mp 31.3—32.5°. *Anal.* Calcd. for $C_{12}H_{19}O_2N_3S_2$: C, 47.83; H, 6.36; N, 13.96; S, 21.24. Found: C, 47.45; H, 6.09; N, 13.71; S, 20.77. IR ν_{max}^{Nujol} cm^{-1}: 3200 (>NH), 1752 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.06 (3H, t, J=6.5), 8.87—8.00 (4H, m), 8.68 (3H, t, J=7.0), 7.56 (3H, s), 7.23 (2H, t, d, J_1=7.0, J_2=1.0), 5.70 (2H, q, J=7.0), 2.82 (1H, t, J=1.0), *ca.* −2.88 (1H, broad). UV $\lambda_{max}^{Dioxane}$ mμ (ε): 242 (5900), 320 (22000), 3-(5-*n*-Butyl-3-methylthiazolin-2-ylidene)-1-ethoxycarbonyl-2-methyl isothiourea (**81**), 0.615 g, colorless needles from benzene, mp 81—82.5°. *Anal.* Calcd. for $C_{12}H_{19}O_2N_3S_2$: C, 47.83; H, 6.36; N, 13.95; S, 21.24. Found: C, 47.45; H, 6.09; N, 13.71; S, 20.77. IR ν_{max}^{Nujol} cm^{-1}: 1650 (>C=O), 1605 (>C=C< or >C=N–). NMR ($CDCl_3$)τ(J=Hz): 9.05 (3H, t, J=6.5), 8.86—8.15 (4H, m), 8.75 (3H, t, J=7.0), 7.50 (3H, s), 7.30 (2H, t, d, J_1=7.0, J_2=1.2), 6.30 (3H, s), 5.72 (2H, q, J=7.0), 3.29 (1H, t, J=1.2). UV $\lambda_{max}^{Dioxane}$ mμ (ε): 245 (4300), 279 (7000), 337 (22600). 7-*n*-Butyl-2-methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**82**), 0.095 g, colorless needles from benzene, mp 84—85°. *Anal.* Calcd. for $C_{10}H_{13}ON_3S_2$: C, 47.06; H, 5.13; N, 16.47; S, 25.03. Found: C, 46.86; H, 4.95; N, 16.18; S, 25.26. IR ν_{max}^{Nujol} cm^{-1}: 1703 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 9.03 (3H, t, J=6.5), 8.85—7.83 (4H, m), 7.43 (3H, s), 7.23 (2H, t, d, J_1=7.0, J_2=1.2), 2.43 (1H, t, J=1.2). UV λ_{max}^{EtOH} mμ (ε): 246 (7000), 267 (8100), 315 (20400), 322 (shoulder).

Reaction of 1-Ethoxycarbonyl-3-(5-phenylthiazol-2-yl)thiourea (83) and Methyl Iodide——3.07 g of **83** was reacted with 1.7 g of methyl iodide by the general method to give **84**, **85**, **86** and 0.172 g of **83**. 1(H)-Ethoxycarbonyl-2-methyl-3-(5-phenglthiazol-2-yl)isothiourea (**84**), 2.08 g, colorless needles from benzene, mp 122—124°. *Anal.* Calcd. for $C_{14}H_{15}O_2N_3S_2$: C, 52.23; H, 4.71; N, 13.08; S, 19.92. Found: C, 51.97;

H, 4.60; N, 13.09; S, 19.53. IR ν_{max}^{Nujol} cm^{-1}: 3200 (>NH), 1748 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.54 (3H, s), 5.70 (2H, q, J=7.0), 2.76—2.36 (5H, m), 2.31 (1H, s), *ca.* −2.63 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε): 345 (20900). 1-Ethoxycarbonyl-2-methyl-3-(3-methyl-5-phenylthiazolin-2-ylidene)isothiourea (**85**), 1.08 g, colorless needles from benzene, mp 167—169°. *Anal.* Calcd. for $C_{15}H_{17}O_2N_3S_2$: C, 53.73; H, 5.11; N, 12.53; S, 19.08. Found: C, 53.47; H, 4.80; N, 12.28; S, 20.26. IR ν_{max}^{Nujol} cm^{-1}: 1662 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.64 (3H, t, J=7.0), 7.54 (3H, s), 6.28 (3H, s), 5.72 (2H, q, J=7.0), 2.86 (1H, s), 2.78—2.34 (5H, m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 279 (12900). 2-Methylthio-7-phenylthiazolo[3,2-*a*]-*s*-triazine-4-one (**86**), 0.107 g, colorless needles from acetone, mp 240—242°. *Anal.* Calcd. for $C_{12}H_9ON_3S_2$: C, 52.37; H, 3.30; N, 15.27; S, 23.25. Found: C, 52.74; H, 3.13; N, 15.16; S, 23.44. IR ν_{max}^{Nujol} cm^{-1}: 1700 (>C=O). NMR (DMF) τ: 8.48 (3H, s), 2.55—1.88 (5H, m), 1.53 (1H, s). UV λ_{max}^{EtOH} mμ (ε): 279 (11100), 296 (8500), 332 (29400).

Reaction of 3-(5-Bromothiazol-2-yl)-1-ethoxycarbonyl Thiourea (87) and Methyl Iodide——3.1 g of **87** was reacted with 1.7 g of methyl iodide by the general method to give **88**, **89**, and 0.487 g of **87**. 3-(5-Bromothiazol-2-yl)-1(H)-ethoxycarbonyl-2-methyl isothiourea (**88**), 1.881 g, colorless needles from benzene, mp 92—94°. *Anal.* Calcd. for $C_8H_{12}O_2N_3S_3Br$: C, 29.63; H, 3.11; N, 12.96; S, 19.78; Br, 24.65. Found: C, 29.53; H, 2.81; N, 12.85; S, 19.88; Br, 25.04. αR ν_{max}^{Nujol} cm^{-1}: 3150 (>NH), 1743 (>C=O). NMR ($CDCl_3$) τ(J=Hz): 8.68 (3H, t, J=7.0), 2.42 (3H, s), 5.70 (2H, q, J=7.0), 2.60 (1H, s), *ca.* −2.46 (1H, broad). UV $\lambda_{max}^{dioxane}$ mμ (ε)α: 246 (6200), 324 (24100). 3-(5-Bromo-3-methylthiazolin-2-ylidene)-1-ethoxycarbonyl-2-methyl isothiourea (**89**), 0.685 g, colorless needles from benzene, mp 147—149°. *Anal.* Calcd. for $C_9H_{12}O_2N_3S_2Br$: C, 31.96; H, 3.58; N, 12.42; S, 18.96; Br, 23.63. Found: C, 32.04; H, 3.28; N, 12.53; S, 19.10; Br, 23.81. IR ν_{max}^{Nujol} cm^{-1}: 1655 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.62 (3H, t, J=7.0), 7.50 (3H, s), 6.28 (3H, s), 5.73 (2H, q, J=7.0), 2.99 (1H, s), UV $\lambda_{max}^{dioxane}$ mμ (ε): 282 (7600), 338 (23800).

Reaction of 1-Ethoxycarbonyl-3-(4-methylthiazol-2-yl)thiourea (90) and Methyl Iodide——2.45 g of **90** was reacted with 1.7 g of methyl iodide by the general method to afford two products (**91** and **92**). 1(H)-Ethoxycarbonyl-2-methyl-3-(4-methylthiazol-2-yl)isothiourea (**91**), 1.97 g, colorless needles from *n*-hexane–benzene, mp 123—124°. *Anal.* Calcd. for $C_9H_{13}O_2N_3S_2$: C, 41.70; H, 5.06; N, 16.21; S, 24.68. Found: C, 41.80; H, 5.25; N, 16.37; S, 24.59. IR ν_{max}^{Nujol} cm^{-1}: 3170 (>NH), 1735 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.63 (3H, d, J=1.0), 7.58 (3H, s), 5.70 (2H, q, J=7.0), 3.56 (1H, q, J=1.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 240 (6200), 319 (19800). 1-Ethoxycarbonyl-2-methyl-3-(3,4-dimethylthiazolin-2-ylidene)isothiourea (**92**), 0.46 g, colorless needles from benzene, mp 172—173°. *Anal.* Calcd. for $C_{10}H_{15}O_2N_3S_2$: C, 43.95; H, 5.53; N, 15.38; S, 23.08. Found: C, 44.24; H, 5.77; N, 15.46; S, 23.03. IR ν_{max}^{Nujol} cm^{-1}: 1650 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.65 (3H, t, J=7.0), 7.66 (3H, d, J=1.0), 7.50 (3H, s), 6.32 (3H, s), 5.74 (2H, q, J=7.0), 3.63 (1H, q, J=1.0). UV $\lambda_{max}^{dioxane}$ mμ (ε): 279 (7000), 335 (221000).

Reaction of 1(H)-Ethoxycarbonyl-3-(4-phenylthiazol-2-yl)thiourea (93) and Methyl Iodide—— 3.07 g of **93** was reacted with 1.7 g of methyl iodide by the general method to afford two products (**94** and **95**). 1(H)-Ethoxycarbonyl-2-methyl-3-(4-phenylthiazol-2-yl)isothiourea (**94**), 2.91 g, colorless needles from benzene, mp 126—128°. *Anal.* Calcd. for $C_{11}H_{15}O_2N_3S_2$: C, 52.33; H, 4.71; N, 13.08; S, 19.92. Found: C, 52.48; H, 4.83; N, 13.03; S, 19.93. IR ν_{max}^{Nujol} cm^{-1}: 3200 (>NH), 1748 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.62 (3H, t, J=7.0), 7.54 (3H, s), 5.71 (2H, q, J=7.0), 2.80 (1H, s), 2.74—1.98 (5H, m), *ca.* −3.34 (1H, broad). UV $\lambda_{max}^{Dioxane}$ mμ (ε): 221.5 (18400), 261.5 (18400), 288 (12500), 333 (17000). 1-Ethoxycarbonyl-2-methyl-3-(3-methyl-4-phenylthiazolin-2-ylidene)isothiourea (**95**), 0.254 g, colorless needles from benzene, mp 148—150°. *Anal.* Calcd. for $C_{15}H_{17}O_2N_3S_2$: C, 53.73; H, 5.11; N, 12.53; S, 19.08. Found: C, 54.15; H, 5.15; N, 12.16; S, 18.87. IR ν_{max}^{Nujol} cm^{-1}: 1665 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.67 (3H, t, J=7.0), 7.47 (3H, s), 6.37 (3H, s), 5.74 (2H, q, J=7.0), 3.43 (1H, s), 2.79—2.33 (5H, m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 279 (7200), 336.2 (24800).

Reaction of 3-(2-Benzothiazolyl)-1-ethoxycarbonyl Thiourea (96) and Methyl Iodide——2.81 g of **96** was reacted with 1.7 g of methyl iodide by the general method to give **97**, **98** and 0.304 g of **96**. 3-(2-Benzothiazolyl)-1(H)-ethoxycarbonyl-2-methyl isothiourea (**97**), 2.34 g, colorless needles from benzene, mp 140—142°. *Anal.* Calcd. for $C_{12}H_{13}O_2N_3S_2$: C, 48.81; H, 4.44; N, 14.23; S, 21.67. Found: C, 48.84; H, 4.48; N, 14.05; S, 21.44. IR ν_{max}^{Nujol} cm^{-1}: 3180 (>NH), 1742 (>C=O). NMR ($CDCl_3$) τ(J=Hz): 8.42 (3H, t, J=7.0), 7.51 (3H, s), 5.64 (2H, q, J=7.0), 2.85—2.03 (4H, m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 228 (18000), 253.5 (11900), 262.6 (9600), 326 (27700), 338 (shoulder). 1-Ethoxycarbonyl-2-methyl-3-(3-methyl-benzothiazolin-2-ylidene)isothiourea (**98**), 0.203 g, colorless needles from benzene, mp 156—157°. *Anal.* Calcd. for $C_{13}H_{15}O_2N_3S_2$: C, 50.48; H, 4.89; N, 13.59; S, 20.69. Found: C, 50.75; H, 4.91; N, 13.69; S, 20.66. IR ν_{max}^{Nujol} cm^{-1}: 1670 (>C=O). NMR ($CDCl_3$)τ(J=Hz): 8.62 (3H, t, J=7.0), 7.45 (3H, s), 6.15 (3H, s), 5.70 (2H, q, J=7.0), 2.91—2.23 (4H, m). UV $\lambda_{max}^{dioxane}$ mμ (ε): 224 (9900), 237 (shoulder), 279 (9400), 293.5 (8900), 338 (35000).

Cyclization Reaction of 1(H)-Ethoxycarbonyl-2-ethyl-3-(2-thiazolyl)isothiourea (16) by Using a Base (c-Course)——A suspention of 2.59 g of **16** in 10 ml of 1N K_2CO_3 was stirred at room temperature for 2 days, was neutralized with 3.5% HCl, and then the precipitate was separated from the solution by filtration, was washed with H_2O, and dried *in vacuo*. The solid was recrystallized from benzene to give 1.61 g of 2-ethylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**13**).

General Method for Peparation of 2-Alkylthio-thiazolo[3,2,*a*]-*s*-triazine-4-ones (C) by a Thermal Treatment——1(H)-Alkoxycarbonyl-2-alkyl-3-(2-thiazolyl)isothioureas (D: 0.01 mole) were heated at 160—170° for a period of 15 min under reduced pressure (80 mmHg) on an oil-bath, and the resulting solid was

recrystallized from a suitable solvent.

Synthesis of 7-Bromo-2-methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (99)——3.24 g of **88** was cyclized to **99** by the thermal treatment. 7-Bromo-2-methylthio-thioaolo[3,2-*a*]-*s*-triazine-4-one (**99**), 2.57 g, colorless needles from acetone, mp 216—217°. *Anal.* Calcd. for $C_6H_4ON_3S_2Br$: C, 25.91; H, 1.45; N, 15.11; S, 23.05; Br, 28.73. Found: C, 26.05; H, 1.28; N, 15.02; S, 22.87 Br, 29.19. IR ν_{max}^{Nujol} cm^{-1}: 1700 (>C=O). NMR (DMF)τ: 7.46 (3H, s), 1.76 (1H, s). UV λ_{max}^{EtOH} mμ (ε): 271 (8300), 316 (20300), 324 (shoulder).

Synthesis of 6-Methyl-2-methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (100)——2.59 g of **91** was cyclized to **100** by the thermal treatment. 6-Methyl-2-methylthio-thiazolo[3,2-*a*]-*s*-triazine-4-one (**100**), 1.96 g, colorless needles from benzene, mp 220—222°. *Anal.* Calcd. for $C_7H_7ON_3S_2$: C, 39.49; H, 3.31; N, 19.72; S, 30.02. Found: C, 39.68; H, 2.94; N, 19.75; S, 29.95. IR ν_{max}^{Nujol} cm^{-1}: 1706 and 1680 for one carbonyl group. NMR (DMF)τ(J=Hz): 8.45 (3H, s), 7.30 (3H, d, J=1.5), 2.88 (1H, q, J=1.5). UV λ_{max}^{EtOH} mμ (ε): 225 (9600), 250 (8400), 267 (8700), 320 (18400).

Synthesis of 2-Methylthio-6-phenylthiazolo[3,2-*a*]-*s*-triazine-4-one (101)——3.21 g of **94** was cyclized to **101** by the thermal treatment. 2-Methylthio-6-phenylthiazolo[3,2-*a*]-*s*-triazine-4-one (**101**), 3.21 g, mp 215—217°. *Anal.* Calcd. for $C_{12}H_9ON_3S_2$: C, 52.37; H, 3.30 N, 15.27; S, 23.25. Found: C, 52.24; H, 3.17; N, 15.15; S, 23.16. IR ν_{max}^{Nujol} cm^{-1}: 1702 (>C=O). NMR (DMF)τ: 7.44 (3H, s), 2.75—2.50 for five phenyl protons and one ring proton. UV λ_{max}^{EtOH} mμ (ε): 260 (17800), 323 (18200).

Synthesis of 2-Methylthio-benzothiazolo[3,2-*a*]-*s*-triazine-4-one (102)——2.95 g of **97** was cyclized to **102** by the thermal treatment. 2-Methylthio-benzothiazolo[3,2-*a*]-*s*-triazine-4-one (**102**), 2.342 g, colorless needles from acetone, mp 235—237°. *Anal.* Calcd. for $C_{10}H_7ON_3S_2$: C, 48.20; H, 2.83; N, 16.86; S, 25.69. Found: C, 48.54; H, 2.54; N, 17.01; S, 25.81. IR ν_{max}^{Nujol} cm^{-1}: 1730 (>C=O). NMR (DMF)τ: 8.41 (3H, s), 2.50—1.04 (4H, m). UV λ_{max}^{EtOH} mμ (ε): 226.5 (21200), 276 (11000), 316 (22900), 326 (24800).

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