Reactions of 1,3-Thiazine-2,6-dithiones. Part 7 [1]. Formation Reactions of 3-Thioureidocinnamthioamides, 3-[Bis(alkylthio)methyleneamino]- and 3-[Bis(alkoxy)methyleneamino]-dithiocinnamic Acid Esters by the Thiazine Ring Opening Reactions with primary Amines, Thiols, and Alcohols. Recyclizing Reactions of the Acyclic Thioamides and the Alkyl Dithiocinnamates and Some Related Compounds

Tatsuo Yamamoto and Motomu Muraoka*

Department of Chemistry, Faculty of Science, Josai University, 1-1, Keyaki-Dai, Sakado, Saitama 350-02, Japan

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2-Alkylamino- and 2-arylamino-1,3-thiazine-6-thiones **3** were synthesized by the reactions of 1,3-thiazine-2,6-dithiones **1** or 2-methylthio-1,3-thiazine-6-thiones **2** with aliphatic or aromatic primary amines. 3-(3-Alkylthioureido)cinnamthioamides **4** were formed on treatment of compounds **3** with primary amines. The same compounds **4** formed pyrimidine-2,4-dithiones **5** and primary amines by acid-catalyzed intramolecular cyclization and the primary amines and compounds **5** gave compounds **4** quantitatively (*vice versa*). Further, treatment of compounds **4** (R^3 = butyl, pentyl, hexyl) with hydrochloric acid or thermolysis of **4** gave rise to 2-alkylimino-6-amino-1,3-thiazine-5-(*N*-alkyl)carbothioamides **6** accompanied by compounds **5**. Compounds **3**, when allowed to react with the amines in aqueous ethanol gave 3-alkyl-2-alkylaminopyrimidine-6-thiones **8** in addition to compounds **4** by two types of reactions occuring simultaneously.

On the other hand, compounds **2**, when treated with thiols and alcohols instead of primary amines in the presence of alkyl iodide, yielded alkyl 3-[bis(alkylthio)methyleneamino]dithiocinnamates **11** and alkyl 3-[bis(methoxy)methyleneamino]dithiocinnamates **14** respectively.

The mechanisms of the formation of these cyclic and acyclic compounds here obtained are also discussed in some detail.

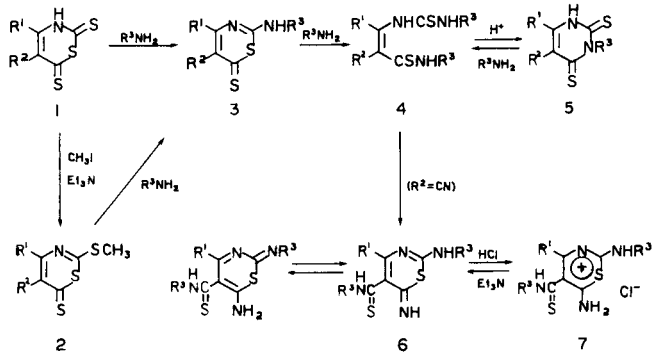
J. Heterocyclic Chem., **25**, 835 (1988).

We have reported the synthesis of heterocyclic and fused heterocyclic compounds [2-4] by the several types of reactions of reactive 1,3-thiazine-2,6-dithiones bearing an electron-withdrawing group at the 5-position with various types of amino compounds. We have also reported that the thiazinedithiones **1** react with enaminonitriles and enaminosulfones to give pyrimidine-4-thiones [5] and 4-mercaptopyridines or 4-thiopyridones [6] respectively by taking two different reaction courses depending upon the solvent used for the reaction.

An additional case of versatile reactivity of the 1,3-thiazine-2,6-dithiones was reductive alkylation of the thiazinedithiones by the reaction with thiolate anions to give 2-alkylthio-2,3-dihydro-1,3-thiazine-6-thiones [1].

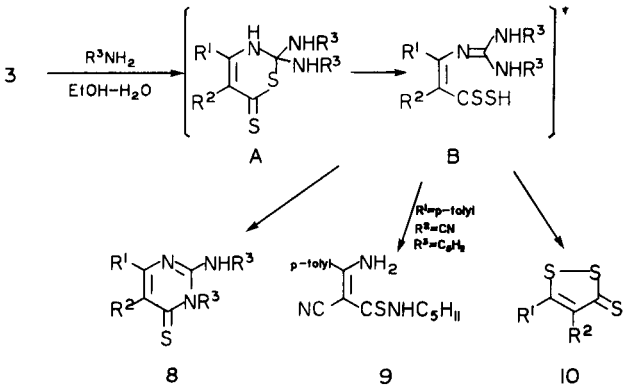
In view of the fact that primary diamines such as ethylenediamine, trimethylenediamine, and *o*-phenylenediamine, when allowed to react with 1,3-thiazine-2,6-dithiones using ethanol as the solvent, lead to very smooth reactions to give several nitrogen-containing fused ring compounds in high yields, we thought that 2 molar equivalents of primary amine, on treatment with the thiazinedithiones under the same reaction conditions as the diamines or secondary amines, would give 2-amino-1,3-thiazine-6-thiones **3** together with 2-alkyl- or 2-arylaminopyrimidine-2,4-dithiones **8**. Unexpectedly however, in spite of repeated attempts, the anticipated products were never obtained, but only intractable tarry material.

When we resumed the study of this reaction, we performed the reaction using 50% aqueous alcohol as the solvent and first obtained a mixture of several products by adding water to the reaction mixture, from which on separation by column chromatography, 3-(3-alkylthioureido)-*N*-alkylcinnamthioamides **4**, pyrimidine-2,4-dithiones **5**, and, in some cases, 2-alkylimino-6-amino-1,3-thiazine-5-carbothioamides **6** and 3-aminocinnamthioamide **9** were separated. The same reaction mixture, when



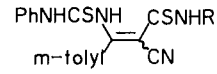
Scheme I

treated with dilute hydrochloric acid followed by extraction with ether, did not give compounds **4** but afforded two other types of compounds, 2-aminopyrimidine-4-thione derivatives **8** and 1,2-dithiole-3-thiones **10** in addition to these compounds **5**, **7** (hydrochloride of **6**), and **9** (see Scheme 1 and 2). Aniline and toluidines, in this reaction, gave 2-arylamino-1,3-thiazine-6-thiones **3** as the sole products and never gave any products corresponding to compounds **4**, **5**, **6**, or **8** because further reaction of compounds **3** with arylamines did not take place owing to the weak nucleophilicity of these arylamines.



Scheme 2 *Proposed mechanism

2-Arylamino-1,3-thiazine-6-thiones, for example **3j** (R^3 = phenyl), however, also reacted with alkylamines such as propyl- and *t*-butylamine to form the corresponding 3-(3-phenylthioureido)-*N*-alkylcinnamthioamides **4m,n** in quantitative yields. On the contrary, 2-pentylaminothiazinethione **3g**, although highly reactive to lower amines, did not react with *t*-butylamine due, probably, to steric



4m R=C_3H_7
4n R=t-C_4H_9

Block 1

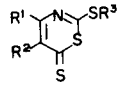
hindrance between *t*-butyl- and pentyl groups. In addition, we found that 2-methylthio-1,3-thiazine-6-thiones **2**, which were obtained by methylation of the thiazinedithiones with methyl iodide in the usual manner, reacted cleanly with any primary amines to give 2-alkyl- and 2-arylamino-1,3-thiazine-6-thiones **3** quantitatively. Further, it became obvious that compounds **3** are important intermediates for the formation of all other compounds here obtained.

We now report the results of the reaction of 1,3-thiazine-2,6-dithiones and their 2-alkylthio derivatives **2** with primary amines and the further reaction of 2-alkylamino-1,3-thiazine-6-thiones **3** with primary alkyl amines. We also report the reaction of compounds **2** with thiols and alcohols instead of the amines in presence of alkyl iodide.

The simplest reaction of primary amines with the 5-cyanothiazinedithiones **1** was that giving 2-cyano-3-(3-alkylthioureido)cinnamthioamides **4a-f** in very high yields when **1** was treated with an excess of lower alkyl amines such as aqueous methyl-, ethyl- and propylamine. Isopropyl- and *sec*-butylamine in the same reaction, however, never produced compounds **4** but gave corresponding compounds **3** exclusively. Hexylamine, in the reaction with

Table 1

2-Alkylthio-1,3-thiazine-6-thiones **2a-f**

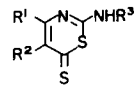


Compound	R^1	R^2	R^3	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N
2a	*p*-tolyl	CN	Me	90	188-189	$C_{13}H_{10}N_2S_3$	53.80	3.48	9.65
							53.85	3.43	9.61
2b	*m*-tolyl	CN	Me	98	173-174	$C_{13}H_{10}N_2S_3$	53.80	3.48	9.65
							53.69	3.53	9.83
2c	Ph	SO_2Ph	Me	96	170-174 [b]	$C_{17}H_{13}NO_2S_4$	52.15	3.35	3.58
							52.33	3.30	3.66
2d	*m*-tolyl	SO_2Me	Me	100	151-152	$C_{13}H_{13}NO_2S_4$	45.46	3.80	4.08
							45.35	3.75	3.86
2e	Ph	SO_2Me	Me	91	176-177	$C_{12}H_{11}NO_2S_4$	43.75	3.26	4.25
							44.07	3.26	4.65
2f	Ph	SO_2Me	Et	44	143	$C_{13}H_{13}NO_2S_4$	45.46	3.80	4.08
							45.23	3.77	3.96

[a] Solvent for recrystallization: benzene-hexane for **2a-e**; dichloromethane-hexane for **2f**. [b] Lit [1] 167-172°.

Table 2

2-Alkylamino- and 2-Arylamino-1,3-thiazine-6-thiones **3a-q**



Compound	R^1	R^2	R^3	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N
3a [b]	*p*-tolyl	CN	Pr	41 [c]	209-210 (EtOH-hexane)	$C_{15}H_{15}N_3S_2$	59.77 59.59	5.02 4.96	13.94 13.74
3b [d]	*p*-tolyl	CN	*i*-Pr	71 [e] 99 [c]	237-238 (iso-PrOH)	$C_{15}H_{15}N_3S_2$	59.77 59.99	5.02 5.23	13.94 14.20
3c [f]	*m*-tolyl	CN	*i*-Pr	62 [e] 82 [c]	184-184.5 (iso-PrOH)	$C_{15}H_{15}N_3S_2$	59.77 59.52	5.02 4.85	13.94 13.65
3d	*p*-tolyl	CN	Bu	51 [c]	195-196 (EtOH-hexane)	$C_{16}H_{17}N_3S_2$	60.92 61.18	5.43 5.48	13.32 13.25
3e	*p*-tolyl	CN	*s*-Bu	40 [e]	186-187 (Benzene)	$C_{16}H_{17}N_3S_2$	60.92 60.76	5.43 5.30	13.32 13.24
3f	*m*-tolyl	CN	*s*-Bu	35 [e]	137-138 (Benzene)	$C_{16}H_{17}N_3S_2$	60.92 61.19	5.43 5.35	13.32 13.37
3g	*p*-tolyl	CN	Pe	44 [c]	179-180 (EtOH-hexane)	$C_{17}H_{19}N_3S_2$	61.97 61.96	5.82 5.89	12.75 12.41
3h	*m*-tolyl	CN	Pe	82 [c]	131-132 (EtOH-hexane)	$C_{17}H_{19}N_3S_2$	61.97 61.92	5.82 5.91	12.75 12.51
3i [g]	*p*-tolyl	CN	Ph	41 [e] 95 [c]	275-277 (EtOH)	$C_{18}H_{13}N_3S_2$	64.26 64.26	3.91 3.87	12.53 12.75
3j	*m*-tolyl	CN	Ph	33 [e] 98 [c]	222 (EtOH)	$C_{18}H_{13}N_3S_2$	64.26 64.22	3.91 4.01	12.53 12.53
3k [h]	*p*-tolyl	CN	*m*-tolyl	90 [c]	274-276 (EtOH-hexane)	$C_{19}H_{15}N_3S_2$	65.29 65.54	4.33 4.37	12.03 11.77
3l	*m*-tolyl	CN	*m*-tolyl	95 [c]	242 (iso-PrOH)	$C_{19}H_{15}N_3S_2$	65.29 65.22	4.33 4.48	12.03 11.91
3m [i]	*p*-tolyl	CN	*p*-tolyl	92 [c]	259-260 (EtOH-hexane)	$C_{19}H_{15}N_3S_2$	65.29 65.00	4.33 4.56	12.03 11.89
3n	*m*-tolyl	CN	*p*-tolyl	98 [c]	254-255 (EtOH)	$C_{19}H_{15}N_3S_2$	65.29 65.46	4.33 4.61	12.03 11.73
3o	*m*-tolyl	SO_2Me	Ph	99 [e]	214-215 dec (THF-hexane)	$C_{18}H_{16}N_2O_2S_3$	55.64 55.34	4.15 4.39	7.13 7.46
3p	*m*-tolyl	SO_2Me	*m*-tolyl	98 [e]	220 dec (THF-hexane)	$C_{19}H_{18}N_2O_2S_3$	56.68 56.78	4.51 4.58	6.96 6.82
3q	*m*-tolyl	SO_2Me	*p*-tolyl	91 [e]	203-205 dec (THF-hexane)	$C_{19}H_{18}N_2O_2S_3$	56.68 56.81	4.51 4.59	6.96 6.69

[a] Solvent for recrystallization in parentheses. [b] ^{1}H nmr (deuteriochloroform): 7.86 (d, 1H, J = 8 Hz), 7.78 (d, 1H, J = 8 Hz), 7.00 br (s, 0.5H), 6.48 br (s, 0.5H), 3.65 (d, t, 1H, J = 5 and 7 Hz), 3.32 (t, 1H, J = 7 Hz), 2.42 (s, 3H), 1.04 (t, 1.5H, J = 7 Hz), 1.00 ppm (t, 1.5H, J = 7 Hz). [c] Procedure A. [d] ^{1}H nmr (hexadeuterioacetone): 9.3 br (s, 0.1H), 8.86 br (s, 0.9H), 7.86 (d, 1.8H, J = 8 Hz), 7.75 (d, 0.2H, J = 8 Hz), 7.34 (d, 2H, J = 8 Hz), 4.63 (sept, 0.9H, J = 7 Hz), 3.99 (m, 0.1H), 2.42 (s, 3H), 1.41 (d, 0.6H, J = 7 Hz), 1.33 ppm (d, 5.4H, J = 7 Hz). [e] Procedure B. [f] ^{1}H nmr (hexadeuterioacetone): 9.5 br (s, 0.2H), 9.05 (s, 0.8H), 7.73 (m, 2H), 7.43 (m, 2H), 4.63 (sept, 0.8H, J = 7 Hz), 4.01 (sept, 0.2H, J = 7 Hz), 2.43 (s, 2.4H), 2.40 (s, 0.6H), 1.42 (d, 1.2H, J = 7 Hz), 1.33 ppm (d, 4.8H, J = 7 Hz). [g] ^{1}H nmr (hexadeuteriodimethylsulfoxide): 11.80 br (s, 1H), 7.0-8.0 (m, 9H), 2.40 ppm (s, 3H). [h] ^{1}H nmr (heptadeuteriodimethylformamide): 7.0-8.0 (m, 8H), 2.43 (s, 3H), 2.27 ppm (s, 3H). [i] ^{1}H nmr (heptadeuteriodimethylformamide): 12.10 br (s, 1H), 7.0-8.0 (m, 8H), 2.43 (s, 3H), 2.32 ppm (s, 3H).

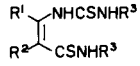
the same **1** (R^1 = *p*- and *m*-tolyl, R^2 = CN), yielded only **6e,f** which were isolated as their hydrochlorides. Aniline and toluidines, when conducted with the thiazine-dithiones (R^1 = aryl, R^2 = CN and SO_2CH_3) in 50% aqueous alcohol, gave compounds **3** in quantitative to medium yields. The formation of **3** by the reaction between **1** and primary amines was limited to only a few cases and the yields were medium to low.

When compounds **3a-d,g,h,j**, prepared by the reaction of the corresponding **2** with each amine, were each treated with neat primary alkylamine, 3-(3-alkylthioureido)cinnamthioamides **4** were formed. Subsequent treatment of compounds **4** with hydrochloric acid, converted them into pyrimidine-2,4-dithiones **5** quantitatively.

Compounds **5n-q** were also obtained but not an intermediate compound such as compounds **3** and **4** could be obtained.

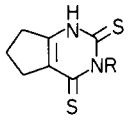
Table 3

3-(3-Alkylthioureido)-*N*-alkylcinnamthioamides **4a-k**



Compound	R^1	R^2	R^3	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N	S
4a	*p*-tolyl	CN	Me	85 [b]	>300	$C_{14}H_{16}N_4S_2$	55.23	5.30	18.40	21.06
				29 [c]			55.20	5.44	18.31	21.30
4b	*m*-tolyl	CN	Me	90 [b]	214-216	$C_{14}H_{16}N_4S_2$	55.23	5.30	18.40	21.06
							55.52	5.17	18.13	21.30
4c	*p*-tolyl	CN	Et	35 [b]	278-281	$C_{16}H_{20}N_4S_2$	57.80	6.06	16.85	19.29
				59 [c]			57.83	5.97	16.55	19.55
4d	*m*-tolyl	CN	Et	86 [b]	214-216	$C_{16}H_{20}N_4S_2$	57.80	6.06	16.85	19.29
							57.63	5.84	16.59	19.39
4e	*p*-tolyl	CN	Pr	95 [b]	236-241	$C_{18}H_{24}N_4S_2$	59.96	6.71	15.54	17.79
				91 [c]			59.66	6.50	15.48	18.00
4f	*m*-tolyl	CN	Pr	85 [b]	220-222	$C_{18}H_{24}N_4S_2$	59.96	6.71	15.54	17.79
							59.77	6.54	15.28	17.95
4g	*m*-tolyl	CN	*i*-Pr	77 [d]	144-145	$C_{18}H_{24}N_4S_2$	59.96	6.71	15.54	17.79
							59.95	6.79	15.31	17.88
4h	*p*-tolyl	CN	Bu	35 [d]	227-231	$C_{20}H_{28}N_4S_2$	61.82	7.27	14.42	16.49
				89 [c]			61.53	7.09	14.31	16.73
4i	*m*-tolyl	CN	Bu	82 [d]	229-231	$C_{20}H_{28}N_4S_2$	61.82	7.27	14.42	16.49
							61.81	7.39	14.32	16.72
4j	*p*-tolyl	CN	Pe	60 [d]	119-121	$C_{22}H_{32}N_4S_2$	63.42	7.74	13.45	15.39
				97 [c]			63.42	7.57	13.50	15.20
4k	*m*-tolyl	CN	Pe	60 [d]	218-222	$C_{22}H_{32}N_4S_2$	63.42	7.74	13.45	15.39
							63.43	7.89	13.36	15.22

[a] Solvent for recrystallization: ethanol for **4a-d**; dichloromethane-hexane for **4e-k**. [b] Method A. [c] Method C. [d] Method B.



5n R=CH_3

5o R=C_2H_5

5p R=C_3H_7

5q R=C_4H_9

Block 2

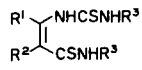
It is very interesting that whereas compounds **4** whose R^3 substituents are lower alkyl groups such as methyl, ethyl, and propyl, gave, on treatment with hydrochloric acid, pyrimidine derivatives **5** as the sole products, those compounds **4** bearing higher alkyl groups as R^3 substituents gave compounds **6** in addition to compounds **5**. Only compound **4j** gave **6c** in nearly quantitative yields when heated at 70° in ethanol requiring no acid catalyst. The same compound **4j**, however, when treated with hydrochloric acid in ethanol at 70°, gave pyrimidine derivative **5i** exclusively in quantitative yield and none of compound **6c** was obtained. In contrast, the reaction of hexylamine differed from those of lower alkyl amines in this reaction gave neither compounds **3**, **4**, nor **5**, but merely yielded compounds **6**.

Leistner and co-workers [7], in the study of the reaction of trithioisatoic anhydride and hexahydro-3,1-benzothiazine-2,4(4*H*)-dithione with various reagents, synthesized 2-anilino-3-phenyl-4-thioxohexahydroquinazoline from the benzothiazinedithione and aniline. They postulated an intermediate similar to compounds **4** for the formation of the quinazoline derivative which corresponds to compounds **8**, though they could not isolate the intermediate. Furthermore, the pyrimidines **5**, when treated with an amine at room temperature, reverted into compounds **4** quantitatively and never gave compounds **8**, which were obtained in low yields only when either the thiazinedithiones or 2-alkylaminothiazinethiones **3** were allowed to react with an excess of amine in 50% ethanol. Use of an organic solvent and a high amine concentration converted compounds **3** to compounds **4**. The best procedure for the formation of **4** is, accordingly, to dissolve compounds **3** in the neat amine.

It may be reasonable to consider that such a marked difference in the course of the reaction of compounds **3**

Table 4

Spectral Properties of Compounds **4a-k**



Compound	UV & Visible λ max (EtOH) (log ε), nm	^{1}H NMR (CD_3COCD_3) (δ, ppm)
4a	282 (4.50) 309 (4.38) 390 (4.05)	7.71 (d, 2H, J = 8 Hz), 7.32 (d, 2H, J = 8 Hz), 4.21 (s, 3H), 3.38 (s, 2.7H), 2.67 (s, 0.3H), 2.40 (s, 3H), 3.15 br (s, 3H)
4b	284 (4.42) 315 (4.31) 395 (4.02)	7.56 (m, 5H), 7.34 (m, 2H), 4.22 (s, 3H), 3.33 (s, 2H), 2.64 (s, 0.3H), 2.56 (s, 0.7H), 2.39 (s, 3H)
4c	284 (4.51) 314 (4.38) 396 (4.11)	7.68 (d, 2H, J = 8 Hz), 7.30 (d, 2H, J = 8 Hz), 5.18 (q, 2H, J = 7 Hz), 3.77 (q, 1.3H, J = 7 Hz), 3.30 br (s, 3H), 3.09 (q, 0.7H, J = 7 Hz), 2.39 (s, 3H), 1.40 (t, 3H, J = 7 Hz), 1.29 (t, 2H, J = 7 Hz), 1.21 (t, 1H, J = 7 Hz)
4d	282 (4.51) 311 (4.41) 390 (4.11)	7.54 (m, 2H), 7.33 (m, 2H), 5.20 (q, 2H, J = 7 Hz), 3.75 (q, 1H, J = 7 Hz), 3.38 (q, 0.3H, J = 7 Hz), 3.05 q, 0.7H, J = 7 Hz), 1.40 (t, 3H, J = 1.28 (t, 1.5H, J = 7 Hz), 1.20 (t, 0.5H, J = 7 Hz), 1.19 (t, 1H, J = 7 Hz)
4e [a]	285 (4.50) 313 (4.36) 396 (4.04)	7.66 (d, 2H, J = 8 Hz), 7.28 (d, 2H, J = 8 Hz), 4.94 (t, 2H, J = 7 Hz), 3.56 (t, 1.4H, J = 7 Hz), 2.72 (t, 1.4H, J = 7 Hz), 2.73 (s, 3H), 1.85 (sext, 2H, J = 7 Hz), 1.64 (sext, 0.6H, J = 7 Hz), 1.53 (sext, 1.4H, J = 7 Hz), 0.90 (t, 3H, J = 7 Hz), 0.88 (t, 3H, J = 7 Hz)
4f	282 (4.44) 315 (4.33) 395 (4.04)	7.66 (m, 2H), 7.35 (m, 3H), 5.03 (t, 2H, J = 7 Hz), 3.68 (t, 1.5H, J = 7 Hz), 3.27 (t, 0.1H, J = 7 Hz), 2.98 (t, 0.4H, J = 7 Hz), 2.39 (s, 3H), 1.97 (m, 2H), 1.74 (m, 2H), 0.94 (t, 3H, J = 7 Hz)
4g [b]	243 (4.32) 314 (4.11) 358 (4.10)	8.46 br (s, 1H), 7.53 br (s, 2H), 7.4 (m, 4H), 4.73 (d, sept, 1H, J = 5 and 6 Hz), 4.10 (d, sept, 1H, J = 5 and 6 Hz), 2.40 (s, 3H), 1.34 (d, 6H, J = 6 Hz), 0.84 (d, 6H, J = 6 Hz)
4h	286 (4.50) 314 (4.35) 396 (4.04)	7.67 (d, 2H, J = 8 Hz), 7.29 (d, 2H, J = 8 Hz), 5.10 (m, 2H), 3.68 (t, 2H, J = 7 Hz), 3.39 (s, 3H), 1.92 (m, 2H), 1.39 (m, 4H), 0.94 (t, 3H, J = 7 Hz), 0.88 (t, 2H, J = 7 Hz), 0.83 (t, 1H, J = 7 Hz)
4i	284 (4.45) 315 (4.35) 395 (4.06)	7.54 (m, 2H), 7.34 (m, 2H), 5.10 (m, 2H), 3.66 (t, 2H, J = 7 Hz), 2.39 (s, 3H), 1.92 (m, 2H), 1.62 (m, 2H), 1.37 (m, 4H), 0.98 (t, 3H, J = 7 Hz), 0.88 (t, 2H, J = 7 Hz), 0.83 (t, 1H, J = 7 Hz)

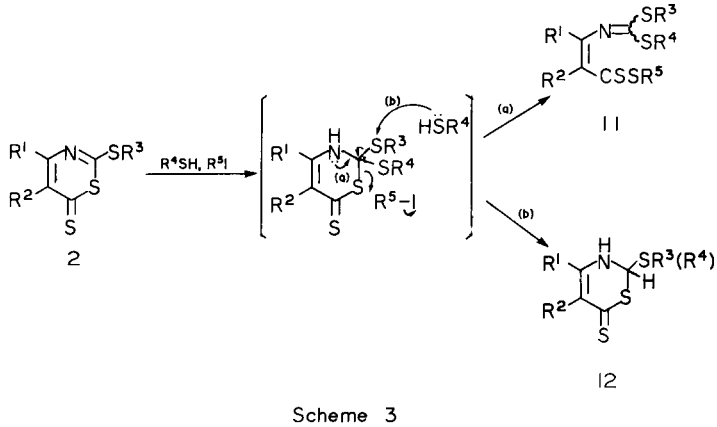
Table 4 (continued)

Compound	UV & Visible λ max (EtOH) (log ε), nm	^{1}H NMR (CD_3COCD_3) (δ, ppm)
4j	286 (4.49) 310 (4.35) 396 (4.03)	9.40 br (s, 1H), 7.71 (d, 2H, J = 8 Hz), 7.22 (d, 2H, J = 8 Hz), 4.70 br (s, 2H), 3.46 (m, 2H), 2.36 (s, 3H), 1.88 (m, 2H), 1.39 (m, 6H), 1.12 (m, 2H), 0.80 (m, 5H), 0.78 (t, 3H, J = 7 Hz)
4k	284 (4.46) 314 (4.35) 395 (4.07)	7.53 (m, 2H), 7.33 (m, 2H), 5.09 (m, 2H), 3.65 (t, 2H, J = 7 Hz), 2.39 (s, 3H), 1.95 (m, 2H), 1.65 (m, 2H), 1.35 (m, 8H), 0.94 (t, 3H, J = 7 Hz), 0.86 (m, 3H)

[a] Hexadeuteriodimethylsulfoxide used for nmr. [b] Only compound **4g** showed abnormal λ max because no geometrical isomerization arose.

depending upon the solvent employed is due, on one hand, to the change in the most reactive position: the 2-position in compounds **1** and **2** into the 6-position in compounds **3**. On the other hand, solvation of the reactive position by polar solvent such as water is also concerned in the reaction course. Thus, it is suggested that when the reaction of **3** with an amine is performed in 50% alcohol, the amine adds, predominantly, to C=N double bond to give pyrimidine derivatives **8** *via* intermediate B formed by ring opening of the precursor A (see Scheme 2) and by-products **9** and **10** are also produced through further reaction of the intermediate B with the amine employed or hydrogen sulfide respectively. In contrast, compounds **3**, when dissolved in neat amine or in the aqueous solution of high amine concentration, will first undergo the addition of the amine to C=S double bond and subsequent ring opening reaction with another mole of the amine will produce compounds **4**.

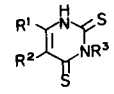
We next focused upon other reactions of 2-alkylthio-5-



Scheme 3

Table 5

3-Alkylpyrimidine-2,4-dithiones **5a-m**

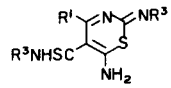


Compound	R^1	R^2	R^3	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N
5a	*p*-tolyl	CN	Me	93 [b]	236 (EtOH)	$C_{13}H_{11}N_3S_2$	57.12 57.20	4.06 4.09	15.37 15.35
5b	*m*-tolyl	CN	Me	98 [b]	240-242 (EtOH-hexane)	$C_{13}H_{11}N_3S_2$	57.12 57.40	4.06 4.15	15.37 15.10
5c	*p*-tolyl	CN	Et	100 [b]	198-199 (EtOH-hexane)	$C_{14}H_{13}N_3S_2$	58.68 58.68	4.56 4.70	14.62 14.92
5d	*m*-tolyl	CN	Et	87 [b]	282-283 [c] (EtOH-hexane)	$C_{14}H_{13}N_3S_2$	58.68 58.97	4.56 4.69	14.62 14.53
5e	*p*-tolyl	CN	Pr	98 [b]	192 (EtOH)	$C_{15}H_{15}N_3S_2$	59.77 60.06	5.02 5.21	13.94 13.71
5f	*m*-tolyl	CN	Pr	99 [b]	239-240 (EtOH)	$C_{15}H_{15}N_3S_2$	59.77 60.07	5.02 4.97	13.94 13.68
5g	*p*-tolyl	CN	Bu	57 [b]	155-156 (EtOH)	$C_{16}H_{17}N_3S_2$	60.92 60.83	5.43 5.37	13.32 13.09
5h	*m*-tolyl	CN	Bu	28 [b]	222.5 (EtOH)	$C_{16}H_{17}N_3S_2$	60.92 60.63	5.43 5.48	13.32 13.13
5i	*p*-tolyl	CN	Pe	93 [b]	207-208 (EtOH-hexane)	$C_{17}H_{19}N_3S_2$	61.97 62.08	5.82 5.77	12.76 12.82
5j	*m*-tolyl	CN	Pe	18 [b]	149 (Etoh-hexane)	$C_{17}H_{19}N_3S_2$	61.97 62.10	5.82 5.90	12.76 12.55
5k	Ph	SO_2Ph	Me	67 [d]	246-247 (Dioxane-H_2O)	$C_{17}H_{14}N_2O_2S_3$	54.52 54.24	3.77 3.69	7.47 7.30
5l	*m*-tolyl	SO_2Me	Et	58 [d]	229-230 (BuOH)	$C_{14}H_{16}N_2O_2S_3$	49.38 49.60	4.74 4.69	8.22 8.50
5m	*m*-tolyl	SO_2Me	Bu	29 [d]	168.5 (MeOH)	$C_{16}H_{20}N_2O_2S_3$	52.15 51.89	5.47 5.67	7.60 7.31

[a] Solvent for recrystallization in parentheses. [b] Method A. [c] In sealed tube. [d] Method B.

Table 6

6-Amino-2-alkylimino-1,3-thiazine-5-(*N*-alkyl)carbothioamides **6a-f**

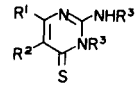


Compound	R^1	R^3	Yield (%)	Mp [a] (°C)	UV & Visible λ max (EtOH) (log ε), nm	Molecular Formula	Analyses % Calcd./Found C	H	N
6a	*m*-tolyl	Bu	38	144-146	279 (4.34) 380 (3.99)	$C_{20}H_{28}N_4S_2$	61.83 61.94	7.25 7.27	14.42 14.18
6b	*p*-tolyl	Bu	22	145-146	284 (4.40) 380 (4.00)	$C_{20}H_{28}N_4S_2$	61.83 61.94	7.25 7.27	14.42 14.18
6c	*m*-tolyl	Pe	63	217-218	280 (4.41) 380 (4.01)	$C_{22}H_{32}N_4S_2$	63.42 63.24	7.74 7.98	13.45 13.11
6d	*p*-tolyl	Pe	88	138-139	283 (4.51) 380 (4.03)	$C_{22}H_{32}N_4S_2$	63.42 63.61	7.72 7.96	13.45 13.17
6e	*p*-tolyl	hexyl	37	178-179	282 (4.33) 381 (3.93)	$C_{24}H_{36}N_4S_2$	64.82 64.56	8.16 7.94	12.60 12.47
6f	*m*-tolyl	hexyl	35	122-123	280 (4.36) 380 (4.01)	$C_{24}H_{36}N_4S_2$	64.82 64.58	8.16 7.94	12.60 12.47

[a] Solvent for recrystallization: acetone-water for **6a,b,e**; ethanol-water for **6c,d,f**.

Table 7

3-Alkyl-2-alkylaminopyrimidine-4-thiones **8a-e**

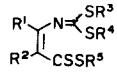


Compound	R^1	R^2	R^3	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N
8a	*p*-tolyl	CN	Pe	26	192-193 (EtOH-hexane)	$C_{22}H_{30}N_4S$	69.07 68.80	7.91 7.68	14.65 14.37
8b	*m*-tolyl	CN	Pe	20	155-157 (Cyclohexane)	$C_{22}H_{30}N_4S$	69.07 68.70	7.91 7.91	14.65 14.96
8c	Ph	SO_2Ph	Me	33	292-293 (DMF-water)	$C_{18}H_{17}N_3O_2S_2$	58.20 58.02	4.61 4.55	11.32 11.04
8d	*m*-tolyl	SO_2Me	Me	29	>300 (DMF-water)	$C_{14}H_{17}N_3O_2S_2$	51.99 52.07	5.30 5.30	12.99 12.93
8e	*m*-tolyl	SO_2Me	Bu	16	168-168.5 (DMF-water)	$C_{17}H_{23}N_3O_2S_2$	58.93 58.87	7.17 6.99	10.31 10.13

[a] Solvent for recrystallization in parentheses.

Table 8

3-[Bis(alkylthio)methyleneamino]dithiocinnamic Acid Esters **11a-i**



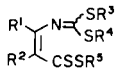
Compound	R^1	R^2	R^3	R^4	R^5	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N
11a	Ph	SO_2Me	Me	Me	Me	32	131-132	$C_{14}H_{17}NO_2S_5$	42.94 42.67	4.38 4.25	3.58 3.58
11b	Ph	SO_2Me	Me	Me	Et	69	108-109	$C_{15}H_{19}NO_2S_5$	44.41 44.17	4.72 4.61	3.45 3.36
11c	Ph	SO_2Me	Me	Et	Me	60	112-116	$C_{15}H_{19}NO_2S_5$	44.41 44.34	4.72 4.45	3.45 3.37
11d	Ph	SO_2Ph	Me	Me	Me	64	109	$C_{19}H_{19}NO_2S_5$	50.30 50.12	4.12 4.17	3.09 3.00
11e	Ph	SO_2Ph	Me	Me	Et	68	92-92.5	$C_{20}H_{21}NO_2S_5$	51.36 51.38	4.52 4.69	2.99 2.81
11f	Ph	SO_2Ph	Me	Et	Me	78	78	$C_{20}H_{21}NO_2S_5$	51.36 51.30	4.52 4.33	2.99 2.99
11g	*m*-tolyl	SO_2Me	Me	Me	Me	51	98-100	$C_{15}H_{19}NO_2S_5$	44.41 44.39	4.72 4.62	3.45 3.38
11h	*m*-tolyl	SO_2Me	Me	Me	Et	60	124	$C_{16}H_{21}NO_2S_5$	45.79 45.60	5.04 4.95	3.34 3.36
11i	*m*-tolyl	SO_2Me	Me	Et	Me	41	92-93	$C_{16}H_{21}NO_2S_5$	45.79 45.53	5.04 4.83	3.34 3.29

[a] Ethanol used for recrystallization.

methylsulfonylthiazine-6-thiones **2** with thiols or alcohols expecting the same type thiazine ring opening reactions as those for primary amines to occur. In our previous paper, we reported the reductive *S*-alkylation reaction of compounds **1** with thiolates [1]. Very interestingly, compounds **1** and thiolate anions, in the presence of alkyl halides such as methyl or ethyl iodide, took another reaction course giving 3-[bis(alkylthio)methyleneamino]dithiocinnamates **11** as sole products in moderate yields. None of reductively *S*-alkylated compounds were obtained except in one case (a trace of compound **12**, see Scheme 3).

Table 9

Spectral Properties of Compounds **11a-i**

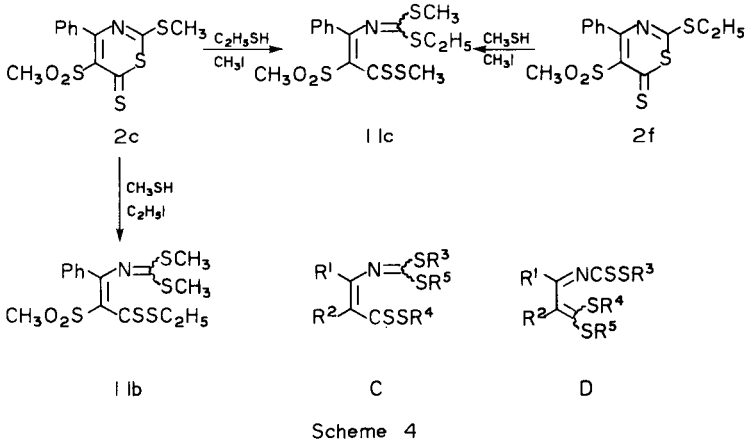


Compound	UV & Visible λ max (EtOH) (log ε), nm	^{1}H NMR ($CDCl_3$) (δ, ppm)
11a	230 (4.14) 256 (4.15) 321 (3.86)	7.2-7.6 (m, 5H), 3.27 (s, 1H), 3.19 (s, 2H), 2.70 (s, 3H), 2.53 (s, 3H), 2.31 (s, 3H)
11b	232 (4.15) 261 (4.20) 323 (3.82)	7.2-7.6 (m, 5H), 3.25 (q, 2H, J = 7 Hz), 3.24 (s, 3H), 2.70 (s, 1H), 2.53 (s, 2H), 2.31 (s, 3H), 1.48 (t, 3H, J = 7 Hz)
11c	259 (4.10) 323 (3.74)	7.2-7.7 (m, 5H), 3.28 (s, 1.5H), 3.20 (s, 1.5H), 3.12 (q, 1H, J = 7 Hz), 2.90 (q, 1H, J = 7 Hz), 2.70 (s, 1.5H), 2.52 (s, 1.5H), 2.31 (s, 3H), 1.28 (m, 3H)
11d	228 (4.30) 261 (4.16) 323 (3.88)	7.1-8.2 (m, 10H), 2.54 (s, 3H), 2.29 (s, 3H), 2.25 (s, 3H)
11e	228 (4.22) 266 (4.02) 332 (3.72) 366 (3.53)	7.2-8.2 (m, 10H), 3.71 (q, 1.3H, J = 7 Hz), 3.02 (q, 0.7H, J = 7 Hz), 2.28 (s, 2H), 2.25 (s, 2H), 1.56 (s, 1H), 1.52 (s, 1H), 1.24 (t, 1H, J = 7 Hz), 1.15 (t, 2H, J = 7 Hz)
11f	229 (4.23) 263 (4.13) 324 (3.86)	
11g	262 (4.19) 323 (3.85)	7.1-7.5 (m, 4H), 3.28 (s, 1H), 3.19 (s, 2H), 2.72 (s, 2H), 2.55 (s, 2H), 2.39 (s, 1H), 2.32 (s, 4H)
11h	262 (4.18) 323 (3.82)	7.1-7.5 (m, 4H), 3.23 (q, 2H, J = 7 Hz), 3.22 (s, 3H), 2.55 (s, 1H), 2.39 (s, 3H), 2.32 (s, 5H), 1.50 (t, 3H, J = 7 Hz)
11i	262 (4.14) 323 (3.82)	7.0-7.5 (m, 4H), 3.27 (q, 1H, J = 7 Hz), 3.20 (s, 3H), 2.89 (q, 1H, J = 7 Hz), 2.72 (s, 1.5H), 2.54 (s, 1.5H), 2.39 (s, 3H), 2.32 (s, 3H), 1.28 (m, 3H)

In this reaction, alkyl halide plays a role alkylating the dithiocarboxylate formed transiently on opening of the thiazine ring. The suggested mechanism in Scheme 3 was confirmed by the following experiments; when a mixture of compound **2c** (R^1 = Ph, R^2 = SO_2CH_3, R^3 = CH_3) and methyl iodide was treated with an excess of ethanethiolate, corresponding dithiocinnamic acid methyl ester **11c** was obtained. Moreover, the same methyl dithiocinnamate **11c** was also prepared when compound **2f** (R^1 = Ph, R^2 = SO_2CH_3, R^3 = C_2H_5) was conducted with methyl iodide and methanethiolate. On the other hand, compound **2c**, when mixed with ethyl iodide and methanethiolate, gave compound **11b** (R^3 = R^4 = CH_3, R^5 = C_2H_5). These results support the proposed mechanism (Sheme 4) for the formation of compounds **11** and hence, both isomeric structures, **C** and **D**, were ruled out.

The thiazinedithiones bearing cyano group at 5-position were resistant to undergo this reaction under any reaction conditions.

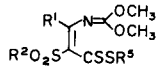
Towards the thiazinedithiones, alcohols have shown no reactivity even in the presence of triethylamine. In fact, we have often made use of alcohols as excellent solvents for reactions of the title compounds. 2-Methylthio-1,3-thiazine-6-thione **2c**, however, when dissolved in methanol in the presence of triethylamine, produced brownish powder-like product **13** (11%). On the other hand, all the compounds **2**, when dissolved in methanol containing an alkyl halide under similar reaction conditions, always produced red crystals **14a-e** together with compounds **11** in almost equal molar ratio. These results seem to prove that an intermediate **13** is first formed and liberated methanethiol reacts exclusively with compound **2** very quickly to yield compounds **11a,b,d,e,h** respectively. 3-[Bis(methoxy)-methyleneamino]dithiocinnamic acid esters **14a-e** are formed by the slow reaction of compounds **13** and methanol (see Scheme 5). Compound **14a** was also obtained in 31% yield when compound **13** was dissolved again in methanol containing methyl iodide and triethylamine.



Scheme 4

Table 10

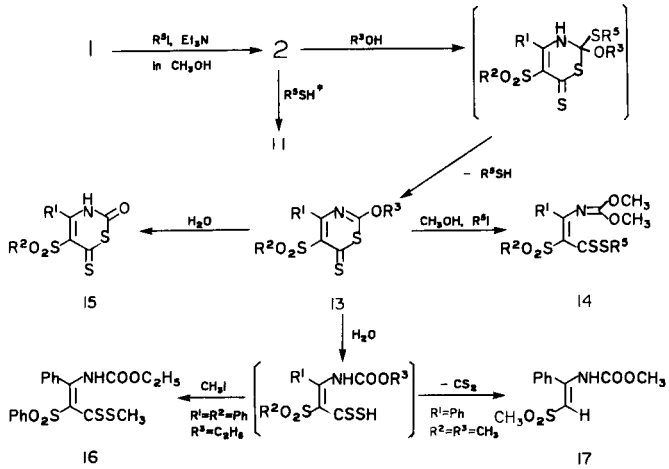
Alkyl 3-[Bis(methoxy)methyleneamino]dithiocinnamates **14a-e**



Compound	R^1	R^2	R^5	Yield (%)	Mp [a] (°C)	Molecular Formula	Analyses % Calcd./Found C	H	N	S
14a	Ph	Me	Me	11	128.5	$C_{14}H_{17}NO_4S_3$	46.78	4.71	3.90	26.74
							46.53	4.71	3.85	26.83
14b	Ph	Me	Et	21	113.5-114	$C_{15}H_{19}NO_4S_3$	48.23	5.13	3.75	25.75
							47.98	4.88	3.73	25.92
14c	Ph	Ph	Me	23	150-151	$C_{19}H_{19}NO_4S_3$	54.13	4.55	3.32	22.82
							54.00	4.35	3.28	23.11
14d	Ph	Ph	Et	41	146.5-147	$C_{20}H_{21}NO_4S_3$	55.14	4.86	3.24	22.09
							54.87	4.63	3.14	22.33
14e	*m*-tolyl	Me	Et	22	168.5	$C_{16}H_{21}NO_4S_3$	49.58	5.46	3.62	23.38
							49.32	5.21	3.47	23.55

[a] Solvent for recrystallization: ethanol for **14a,b,d,e**; methanol for **14c**.

In addition to these compounds **11** and **14**, 6-thioxothiazin-2-one **15**, methyl 3-ethoxycarbonylaminodithiocinnamate **16**, and methyl *N*-(2-methylsulfonyl-1-phenyl)-vinyl carbamate **17** were also isolated in low yields respectively. These by-products **15**, **16**, and **17** arise by hydrolysis by trace of water in the solvent.



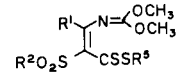
Scheme 5 * Liberated one

5-Cyanothiazinedithiones did not readily undergo this reaction. 2-Methylthiocyclopenta[*d*][1,3]thiazine-4-thione was too unstable to be isolated and could not be used in those reactions mentioned above.

All the compounds isolated here, including compounds **2**, had satisfactory microanalyses. All the proposed structures for compounds **2-17** were based upon the elemental analyses and nmr, ir, uv-vis., and partly mass spectra as well as chemical reactions.

Table 11

Spectral Properties of Compounds **14a-e**



Compound	UV & Visible λ max (EtOH) (log ε), nm	^{1}H NMR ($CDCl_3$) (δ, ppm)
14a	231 (4.43)	7.2-7.6 (m, 4H), 3.85 (s, 6H), 3.31
	253 (4.32)	(s, 3H), 2.51 (s, 3H)
	324 (4.10)	
	505 (2.47)	
14b	247 (4.13)	7.49 (d, 2H, J = 8 Hz), 7.25 (m,
	328 (4.03)	3H), 3.84 (s, 6H), 3.30 (s, 3H), 3.10
	505 (2.05)	(q, 2H, J = 7 Hz), 1.09 (t, 3H, J =
		7 Hz)
14c	249 (4.08)	8.14 (d, 2H, J = 6 Hz), 7.1-7.6
	329 (4.00)	(m, 8H), 3.61 (s, 6H), 2.51 (s, 3H)
	505 (2.44)	
14d	250 (4.23)	8.13 (d, 2H, J = 8 Hz), 7.1-7.6 (m,
	326 (4.08)	8H), 3.61 (s, 6H), 3.09 (q, 2H, J =
	505 (2.44)	7 Hz), 1.08 (t, 3H, J = 7 Hz)
14e	250 (4.13)	7.0-7.4 (m, 4H), 3.85 (s, 6H), 3.29 (s,
	330 (4.03)	3H), 3.10 (q, 2H, J = 7 Hz), 2.29
	505 (2.25)	(s, 3H), 1.10 (t, 3H, J = 7 Hz)

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were determined on a Nippon-Bunko IRA-302 infrared spectrophotometer. The ^{1}H- and ^{13}C-nmr spectra were recorded on a JEOL-JNM-GX 270 spectrometer with TMS as internal standard. The electronic absorption spectra were measured with a Hitachi 557 double wavelength double beam spectrophotometer. Mass spectra were determined with a JEOL JMS-DX 300 mass spectrometer. 1,3-Thiazine-2,6-dithiones were prepared by the published literature procedures [8-10].

2-Alkylthio-1,3-thiazine-6-thiones **2**

These compounds were prepared by a literature procedure [1] using tetrahydrofuran as solvent instead of ethanol.

Physical properties of compounds **2a-f** are shown in Table 1.

2-Alkylamino- and 2-Arylamino-1,3-thiazine-6-thiones **3**.

(Procedure A).

To an ethanolic solution (5 ml) containing 3% amine, was suspended 2-methylthio-1,3-thiazine-6-thione **2** (1 mmole). The mixture was warmed at 70° for 3 minutes and kept standing at room temperature for 4 hours. Hexane (20 ml) was added to the reaction mixture and the resulting precipitates were collected, dried, and recrystallized.

(Procedure B).

A mixture of a 1,3-thiazine-2,6-dithione (1 mmole), an amine (1.5 mmoles), ethanol (4 ml), and water (4 ml) was shaken mechanically at room temperature for 2 hours. Water was added and the solid which separated was collected and recrystallized.

Yields, mps, solvent for recrystallization, electronic spectra, and elemental analyses of compounds **3** are listed in Table 2 and representative ^{1}H nmr spectral data are shown in the footnotes of Table 2.

3-(3-Alkylthioureido)-*N*-alkylcinnamthioamides **4**.

Method A.

To a solution of 5-cyano-4-aryl-1,3-thiazine-2,6-dithione (1 mmole) in ethanol (4 ml), an amine [11] (5 mmoles) was added. After 3 hours, water (5 ml) was added to the reaction mixture and the resulting yellow solid product was collected, dried, and recrystallized.

Method B.

5-Cyano-2-alkylamino-4-aryl-1,3-thiazine-6-thione **3** (1 mmole) was dissolved in each amine (0.5 ml) and to this, hexane (10 ml) was added. The solid which precipitated was collected, washed with hexane, and recrystallized to give each corresponding 5-cyano-3-(3-alkylthioureido)-*N*-alkylcinnamthioamides **4g-k**.

Method C.

Each alkylamine (7.5 mmoles) was added to an ethanolic solution of 5-cyano-3-alkyl-6-arylpyrimidine-2,4-dithione **5** (1 mmole) and kept standing for a few minutes. The mixture was evaporated to dryness *in vacuo* and recrystallized.

Compounds **4a,c,e,h,j** were obtained by method C as well as method A. Quantitative yields were attained when neat amine was employed.

2-Cyano-3-(3-phenylthioureido)-*N*-propyl-(3'-methyl)cinnamthioamide (**4m**).

Compound **4m** was synthesized by method B mentioned above (93%), mp 135-140° (ethanol-hexane); uv-vis (ethanol): λ max (log ε) 264 (4.33), 306 sh (4.21), 426 nm (4.02); ir (potassium bromide): 3040, 2960, 2880, 2200, 1560, 1510, 1380, 1305, 1260, 930, 760 cm^{-1}.

Anal. Calcd. for $C_{21}H_{22}N_4S_2$: C, 63.93; H, 5.62; N, 14.20. Found: C, 64.00; H, 5.58; N, 14.16.

2-Cyano-3-(3-phenylthioureido)-*N*-*t*-butyl-(3'-methyl)cinnamthioamide (**4n**).

Compound **4n** was prepared similarly to compound **4m** (96%), mp 220-221° (acetone-hexane); uv-vis (ethanol): λ max (log ε) 264 (4.33), 306 sh (4.21), 426 nm (4.01); ir (potassium bromide): 3120, 3050, 2970, 2200, 1575, 1510, 1480, 1370, 1300, 1260, 1210, 1130, 930, 730, 690 cm^{-1}.

Anal. Calcd. for $C_{22}H_{24}N_4S_3$: C, 64.67; H, 5.89; N, 13.70. Found: C, 64.76; H, 5.89; N, 13.67.

Yields, solvent for recrystallization, mps, and elemental analyses of compounds **4a-l** are listed in Table 3 and electronic and ^{1}H nmr spectral data are provided in Table 4.

3-Alkylpyrimidine-2,4-dithiones **5**.

Method A.

A suspension of each compound **4** (1 mmole) in ethanol (4 ml) was made acid (*p*H *ca.* 1) by adding 2*M*-hydrochloric acid and then water (10 ml) was added. Pale yellow powder-like crystals were precipitated instantaneously, which were collected, washed with water, dried, and recrystallized. Compounds **5a-j** were prepared by this Method.

Method B.

To a suspension of each 1,3-thiazine-2,6-dithione (1 mmole) in 50% ethanol, each amine (1 ml) was added and the mixture was heated at 70° for 5 hours. The mixture was cooled to 0° and acidified with 2*M*-hydrochloric acid. The resulting solid product which separated was collected, washed with water, dried, and recrystallized. Compounds **5k-m** were prepared by this method B. Yields, solvent for recrystallization, mps, electronic spectral data and elemental analyses are shown in Table 5.

Compounds **5n-q** were also synthesized according to the method B using 1,5,6,7-tetrahydrocyclopenta[*d*][1,3]thiazine-2,4-dithione [8] as the starting material.

3-Methyl-3,5,6,7-tetrahydrocyclopenta[*e*]pyrimidine-2,4-(1*H*)-dithiones (**5n**).

This compound was obtained in a yield of 25%, mp >280° (2-butanone); uv-vis (ethanol): λ max (log ε) 296 (4.26), 360 nm (4.07); ir (potassium bromide): 3200, 3120, 3030, 2975, 2900, 1635, 1570, 1450, 1430, 1405, 1275, 1260, 1070 cm^{-1}.

Anal. Calcd. for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.09; N, 14.13. Found: C, 48.69; H, 5.01; N, 14.04.

3-Ethyl-3,5,6,7-tetrahydrocyclopenta[*e*]pyrimidine-2,4(1*H*)-dithione (**5o**).

This compound was obtained in a yield of 67%, mp 200-201° (benzene-hexane); uv-vis (ethanol): λ max (log ε) 297 (4.44), 360 nm (4.05); ir (potassium bromide): 3200, 3140, 3020, 2950, 1630, 1560, 1445, 1330, 1260, 1240, 1215, 1080 cm^{-1}.

Anal. Calcd. for $C_9H_{12}N_2S_2$: C, 50.91; H, 5.70; N, 13.19. Found: C, 50.93; H, 5.59; N, 13.22.

3-Propyl-3,5,6,7-tetrahydrocyclopenta[*e*]pyrimidine-2,4(1*H*)-dithione (**5p**).

This compound was obtained in a yield of 87%, mp 189-190° (hexane); uv-vis (ethanol): λ max (log ε) 290 (4.39), 361 nm (4.03); ir (potassium bromide): 3200, 3140, 3020, 2960, 1645, 1550, 1450, 1365, 1330, 1260, 1235, 1200, 1100 cm^{-1}.

Anal. Calcd. for $C_{10}H_{16}N_2S_2$: C, 53.06; H, 6.24; N, 12.37. Found: C, 53.26; H, 5.98; N, 12.47.

3-Butyl-3,5,6,7-tetrahydrocyclopenta[*e*]pyrimidine-2,4(1*H*)-dithione (**5q**).

This compound was obtained in a yield of 72%; mp 213-214° (benzene-hexane); uv-vis (ethanol): λ max (log ε) 298 (4.37), 361 nm (4.03); ir (potassium bromide): 3180, 3120, 3020, 2960, 1620, 1550, 1440, 1365, 1330, 1300, 1260, 1200, 1100 cm^{-1}.

Anal. Calcd. for $C_{11}H_{16}N_2S_2$: C, 54.96; H, 6.71; N, 11.65. Found: C, 54.73; H, 6.92; N, 11.71.

6-Amino-2-butylimino-4-(*m*-tolyl)-1,3-thiazine-5-(*N*-butyl)carbothioamide (**6a**).

A suspension of compound **4i** (0.194 g, 0.500 mmole) in ethanol (2 ml) was acidified to *p*H *ca.* 1 with 2*M*-hydrochloric acid and to this, water (10 ml) and ether (10 ml) were added. On allowing the mixture to stand for 1 hour at 0°, a white solid product **7** and the hydrochloride of **6a** precipitated, which was collected and suspended again in ethanol. Triethylamine (0.05 g, 0.5 mmole) and water (10 ml) were added in turn and the resulting solid was collected, dried, and recrystallized; ^{1}H nmr (hexadeuterioacetone): 7.5 (m, 4H), 4.69 (s, 2H), 3.45 (m, 2H), 2.92 br (s, 3H), 2.34 (s, 3H), 1.85 (m, 2H), 1.44 (m, 2H), 1.25 (m, 2H), 0.97 (t, 3H), 0.94 (m, 2H, 0.72 ppm (t, 3H); ^{13}C nmr (hexadeuteriacetone): 186.0, 173.0, 153.7, 149.5, 137.0, 129.8, 128.9, 127.8, 125.6, 112.2, 48.8, 44.9, 28.3, 26.4, 20.7, 19.4, 18.9, 13.5 ppm.

6-Amino-2-butylamino-4-(*m*-tolyl)-5-butyl(thiocarbamoyl)-1,3-thiazinium Chloride (**7**).

Compound **7**, the hydrochloride of compound **6a**, was purified as only one case of these hydrochlorides of compounds **6a-f**, mp 153-154°

(ethanol-hexane); ^{1}H nmr (hexadeuteriodimethylsulfoxide): 7.55 (s, 4H), 5.64 br (s, 4H), 4.06 (t, 2H, J = 7 Hz), 3.19 (t, 2H, J = 7 Hz), 2.41 (s, 3H), 1.71 (quint, 2H, J = 7 Hz), 1.55 (quint, 2H, J = 7 Hz), 1.35 (m, 3H), 0.94 (t, 3H, J = 7 Hz), 0.89 ppm (t, 3H, J = 7 Hz); ^{13}C nmr (hexadeuteriodimethylsulfoxide): 179.9, 163.0, 155.9, 149.3, 139.1, 133.8, 129.6, 128.7, 125.7, 100.6, 56.0, 49.5, 42.3, 28.9, 20.9, 19.6, 13.4 ppm.

Anal. Calcd. for $C_{20}H_{29}ClN_4S_2$: C, 56.51; H, 6.88; N, 13.18. Found: C, 56.82; H, 7.12; N, 12.99.

Other hydrochlorides of **6b-f** were directly converted into compounds **6b-f** without purification. Compounds **6b,c** were also prepared by similar procedure to that for the synthesis of compound **6a**.

6-Amino-2-pentylimino-4-(*p*-tolyl)-1,3-thiazine-5-(*N*-pentyl)carbothioamide (**6d**).

An ethanolic solution (3 ml) of compound **4j** (0.15 g, 0.36 mmole) was heated at 70° for 1 hour. Water (5 ml) was added to the solution and the solid which separated was collected, dried, and recrystallized; ^{1}H nmr (hexadeuteriodimethylsulfoxide) 7.88 br (s, 2H), 7.58 (d, 2H, J = 8 Hz), 7.18 (d, 2H, J = 8 Hz), 4.57 br (s, 1H), 2.31 (s, 3H), 1.71 (m, 2H), 1.36 ppm (m, 4H); ^{13}C nmr (hexadeuterioacetone): 191.2, 177.8, 156.8, 153.6, 139.2, 134.8, 128.3, 128.1, 108.7, 48.6, 45.2, 28.3, 28.0, 25.8, 24.5, 21.8, 20.8, 13.8, 13.6 ppm.

6-Amino-2-hexylimino-4-(*p*-tolyl)-1,3-thiazine-5-(*N*-hexyl)carbothioamide (**6e**).

The molar ratio of reactants and the reaction conditions were simlar to those of procedure A for compounds **3**. The reaction mixture to which ether and 2*M*-hydrochloric acid were added, was allowed to stand for 1 hour. The white crystalline solid which separated as hydrochloride of **6e** was treated with triethylamine and resulting pale yellow solid was collected, washed with water, dried, and recrystallized from acetone-water; ^{1}H nmr (hexadeuteriodimethylsulfoxide): 10.34 br (s, 1H), 7.91 br (s, 2H), 7.58 (d, 2H, J = 8 Hz), 7.17 (d, 2H, J = 8 Hz), 4.58 (m, 2H), 3.34 (m, 4H), 2.31 (s, 3H), 1.70 (m, 2H), 1.33 (m, 6H), 1.16 (m, 6H), 0.84 ppm (m, 6H).

Compound **6f** was also obtained by a similar procedure to that for the preparation of compound **6e**.

Physical properties of compounds **6** are provided in Table 6.

5-Cyano-3-pentyl-2-pentylamino-6-(*p*-tolyl)pyrimidine-4-thione (**8a**).

A mixture of 5-cyano-2-pentylamino-4-(*p*-tolyl)-1,3-thiazine-6-thione (**3g**) (23 mg, 0.07 mmole), pentylamine (61 mg, 0.7 mmole), ethanol (1 ml), and water (1 ml) was allowed to stand at room temperature for 1 hour. Ether and 2*M*-hydrochloric acid were added to this reaction mixture and filtered. The ethereal layer was dried and evaporated to dryness. The residue was chromatographed (silica gel 60, 400 mesh; 20 x 1.0 cm) with benzene to give pure compound **8a** (7 mg, 26%) (See also Table 7). Compound **5i** was also obtained in 41% yield along with compound **8a**.

Reaction of 5-Cyano-4-(*m*-tolyl)-1,3-thiazine-2,6-dithione with Pentylamine in 50% Ethanol. Isolation of Compounds **5i, 6c·HCl, 8b,** and **10a**.

A mixture of 5-cyano-4-(*m*-tolyl)-1,3-thiazine-2,6-dithione (0.276 g, 1 mmole), pentylamine (0.87 g, 10 mmoles), ethanol (4 ml), and water (4 ml) was kept standing at room temperature for 2 hours. The mixture, after ether and 2*M*-hydrochloric acid were added, was shaken mechanically for 1 hour. The resulting solid product (hydrochloride of compound **6c**, yield 43%) was filtered off. The ethereal layer was dried and the ether was removed under diminished pressure to give solid matter, which was chromatographed over silica gel 60 (Merck 230-400 mesh, benzene) to separate compounds **5j** (25%), 4-cyano-5-(*m*-tolyl)-1,2-dithiole-3-thione (**10a**) (2%), mp 183° (Lit [12] 183°), and 5-cyano-3-pentyl-2-pentylamino-6-(*m*-tolyl)pyrimidine-4-thione (**8b**, 20%).

3-Methyl-2-methylamino-5-methylsulfonyl-6-(*m*-tolyl)pyrimidine-4-thione (**8c**).

A solution of 4-phenyl-5-phenylsulfonyl-1,3-thiazine-2,6-dithione (0.77 g, 1 mmole) in 5% methylamine (5 ml) was allowed to stand at room temperature for 3 hours. The solid which separated was collected, dried, and recrystallized.

Compounds **8d,e** were also prepared similarly to the preparation of compound **8c** and the mother liquors, when acidified (*p*H *ca.* 1) with 2*M*-hydrochloric acid, gave compounds **5k** (40%) and **5m** (27%). Yields, mps, and elemental analyses of compounds **8a-e** are shown in Table 7.

3-Amino-2-cyano-*N*-pentyl-(4'-methyl)cinnamthioamide (**9**).

The molar ratio of reactants, reaction conditions, and work up procedure were similar to those for the preparation of compound **8b**, yield 7%, mp 144.5°; ir (potassium bromide): 3320, 3030, 2950, 2920, 2860, 2190, 1600, 1515, 1500, 1480, 1420, 1260, 1225, 955, 830 cm^{-1}; uv (ethanol): λ max (log ε) 233 sh (4.27), 285 (4.14), 3.24 nm, (4.20); ^{1}H-nmr (deuteriochloroform): 12.13 br (s, 1H), 7.51 br (s, 1H), 7.45 (d, 2H, J = 8 Hz), 7.29 (d, 2H, J = 8 Hz), 5.80 br (s, 1H), 3.70 (dt, 2H, J = 5 and 7 Hz), 2.41 (s, 3H), 1.69 (t, 2H, J = 7 Hz), 1.38 (m, 4H), 0.92 ppm (t, 3H, J = 7 Hz).

Anal. Calcd. for $C_{16}H_{21}N_3S$: C, 66.87; H, 7.37; N, 14.62; S, 11.14. Found: C, 66.69; H, 7.17; N, 14.48; S, 11.40.

Compound **9** was accompanied by compounds **5i** (14%), **6d·HCl** (39%), **8a** (10%), and 4-Cyano-5-(*p*-tolyl)-1,2-dithiole-3-thione (**10b**) (2%), mp 210.5° (Lit [12] 210.5°).

3-[Bis(alkylthio)methyleneamino]dithiocinnamates **11**.

A mixture of 6-methylsulfonyl-2-methylthio-4-phenyl-1,3-thiazine-6-thione (0.329 g, 1 mmole), methyl iodide (0.426 g, 3 mmoles), 15% sodium methanethiolate (2.8 ml, 2 mmoles), triethylamine (0.303 g, 3 mmoles), and tetrahydrofuran (10 ml) was refluxed at 75° for 6 hours and cooled. Water (20 ml) and ether (50 ml) were added to the reaction mixture and the aqueous layer was extracted with ether. The combined ether extracts were washed with 2*M*-hydrochloric acid and then with water, dried, and evaporated *in vacuo*. The residual material was washed with ethanol and recrystallized from hot ethanol to give methyl 3-[bis(methylthio)methyleneamino]-2-methylsulfonyldithiocinnamate (**11a**) as pale yellow crystals; ms: 391 (M$^+$, 2), 344 (M$^+$-47, 81), 312 (M$^+$-79, 25), 145 (Ph-C≡C-C≡S$^+$, 100).

Yields, mps, solvent for recrystallization, and elemental analyses of compounds **11a-i** are listed in Table 8 and spectral data are listed in Table 9.

2-Methoxy-5-methylsulfonyl-4-phenyl-1,3-thiazine-6-thione (**13**).

5-Methylsulfonyl-2-methylthio-4-phenyl-1,3-thiazine-6-thione (**2e**) (0.493 g, 1.5 mmoles) and triethylamine (0.303 g, 3.0 mmoles) were dissolved in a mixed solvent of methanol (10 ml)-tetrahydrofuran (2 ml) and allowed to stand for 24 hours. Water was added to the mixture and the aqueous layer was washed with ether and then acidified (*p*H *ca.* 1) and extracted with ether. The ethereal layer was dried, evaporated, and a small quantity of ethanol was added to the residue. The resulting brown powder-like product was collected (0.13 g, 27%) and recrystallized from acetone-water, mp 161°; ir (potassium bromide): 3000, 2950, 2930, 1600, 1530, 1450, 1430, 1380, 1310, 1230, 1135, 1105, 1030, 1020 cm^{-1}; uv-vis (ethanol): λ max (log ε): 247 (4.00), 317 (3.86), 333 (3.87), 352 (3.86), 430 sh nm (3.39); ms: 313 (M$^+$, 42), 282 (M$^+$-31, 2), 234 (M$^+$-79, 100).

Anal. Calcd. for $C_{12}H_{11}NO_3S_3$: C, 45.98; H, 3.54; N, 4.47; S, 30.68. Found: C, 46.02; H, 3.72; N, 4.52; S, 30.65.

Methyl 3-[Bis(methoxy)methyleneamino]-2-methylsulfonyldithiocinnamate (**14a**).

To a mixture of 5-methylsulfonyl-4-phenyl-1,3-thiazine-2,6-dithione (3.15 g, 10 mmoles), triethylamine (2.0 g, 20 mmoles), and methanol (50 ml), was added methyl iodide (7.10 g, 50 mmoles) dropwise at 0° and then shaken mechanically at room temperature for 1 hour. Water (100 ml) and ether (100 ml) were added to the reaction mixture. The ethereal layer was washed with 2*M*-hydrochloric acid and then with water and kept standing for 1 hour at 0°. The organic layer, after the removal of brown crystals (**2c**, 10%) which precipitated from the layer, was dried and evaporated. The residual material was dissolved in a small amount of methanol and allowed to stand for a few minutes. The resulting red crystals were col-

lected, washed with a small quantity of ethanol, and recrystallized. Compound **11a** was also obtained from the mother liquor (19%).

Compounds **14b-e** were prepared similarly. Yields, mps, solvent for recrystallization, and elemental analyses of compounds **14a-e** are provided in Table 10 and the ^{1}H nmr and electronic spectral data are provided in Table 11.

Reaction of Compound **13** with Methanol. Formation of Compound **14a**.

A mixture of 2-methoxy-5-methylsulfonyl-4-phenyl-1,3-thiazine-6-thione (**13**) (0.130 g, 0.4 mmole), triethylamine (0.050 g, 0.5 mmole), methyl iodide (0.142 g, 1.0 mmole), and methanol (2 ml) was kept standing for 2 hours and to the reaction mixture was added water (5 ml) and ether (10 ml). The organic layer was washed once with 2*M*-hydrochloric acid, once with water, dried over magnesium sulfate, and evaporated *in vacuo* to give compound **14a** in 31% yield.

The ir spectrum was identical with that of the compound prepared from corresponding compound **1** and methanol/methyl iodide by the above procedure.

4-Phenyl-5-phenylsulfonyl-6-thioxo-1,3-thiazin-2-one (**15**).

A solution of 2-methylthio-4-phenyl-5-phenylsulfonyl-1,3-thiazine-6-thione (**2d**, 0.782 g, 2.0 mmoles) in methanol (15 ml) containing triethylamine (0.404 g, 4.0 mmoles) was heated at 70° for 2 hours and to this was added ether (50 ml) and water (30 ml). The aqueous layer, after being washed with ether and the ether remaining being removed under diminished pressure, was acidified with 2*M*-hydrochloric acid (*p*H *ca.* 1) to give brown precipitates which were collected, washed with water, and dried. Recrystallization from acetone-water gave brown crystals, yield 15%, mp 188-189°; ir (potassium bromide): 3140, 1700, 1600, 1525, 1460, 1330, 1305, 1250, 1150, 1110, 1080, 1020 cm^{-1}; uv-vis (ethanol): λ max (log ε) 310 (4.17), 408 sh (3.51), 470 sh nm (3.16).

Anal. Calcd. for $C_{16}H_{11}NO_3S_3$: C, 53.17; H, 3.07; N, 3.88; S, 26.61. Found: C, 52.90; H, 3.07; N, 3.61; S, 26.72.

The ethereal layer was washed once with 2*M*-hydrochloric acid and once with water, dried, and evaporated. The resulting oil was dissolved in a small amount of ethanol to separate yellow crystals, which were collected, washed with ethanol and recrystallized from hot ethanol to give 2-methylthio-4-phenyl-5-phenylsulfonyl-2,3-dihydro-1,3-thiazine-6-thione (**12**) (10%), mp 204-205° (Lit [1] 204-205°).

Methyl 3-Ethoxycarbonylamino-2-phenylsulfonyldithiocinnamate (**16**).

The molar ratio of reactants, conditions, and work up procedure were similar to those of compound **14a** except for the use of ethanol as the solvent. Recrystallization from hot ethanol gave yellow crystals of compound **16** (25%), mp 135-136°; ir (potassium bromide): 3340, 2970, 2920, 1760, 1580, 1560, 1475, 1440, 1340, 1300, 1200, 1140, 1075, 1060, 1020 cm^{-1}; ^{1}H nmr (deuteriochloroform): 9.73 br (s, 1H), 7.0-8.2 (m, 10H), 4.04 (q, 2H, J = 7 Hz), 2.36 (s, 3H), 1.19 ppm (t, 3H, J = 7 Hz); ^{13}C nmr (deuteriochloroform): 221.2, 151.8, 147.3, 140.5, 133.9, 133.4, 129.9, 128.9, 128.4, 127.7, 62.3, 21.3, 14.2 ppm.

Anal. Calcd. for $C_{19}H_{19}NO_4S_3$: C, 54.14; H, 4.54; N, 3.32; S, 22.82. Found: C, 54.31; H, 4.50; N, 3.01; S, 22.55.

Methyl *N*-(2-Methylsulfonyl-1-phenyl)vinyl Carbamate (**17**).

Compound **17** was prepared similarly to the synthesis of compound **13** with the exception that the reaction temperature and time were 65° and 3 hours respectively. Recrystallization from hot ethanol gave white crystals of compound **17** (32%), mp 129-130°; ir (potassium bromide): 3300, 1725, 1605, 1490, 1440, 1290, 1230, 1215, 1110, 1035 cm^{-1}; uv (ethanol): λ max (log ε) 264 nm (4.19); ^{1}H nmr (deuteriochloroform): 9.18 br (s, 1H), 7.4 (m, 5H), 5.53 (s, 1H), 3.65 (s, 3H), 3.05 ppm (s, 3H); ^{13}C nmr (deuteriochloroform): 152.6, 151.4, 134.5, 130.5, 128.4, 127.3, 107.6, 53.0, 44.3 ppm.

Anal. Calcd. for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49. Found: C, 51.62; H, 4.83; N, 5.38.

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