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Synthesis and Reactions of Heterocyclic Dithiocarbamates

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(Alkylthio)thiocarbonylimino-1-methyl-1,2-dihydropyridine derivatives (**3a**—**e**) were prepared by the reaction of 2-amino-1-methylpyridinium iodide (**1a**—**c** or **d**) with carbon disulfide in the presence of sodium hydride and subsequent methylation with dimethyl sulfate in good yields. Similarly, 1-methyl-4-(methylthio)thiocarbonyl-1,4-dihydropyridine (**3i**), 1-methyl-2-(methylthio)thiocarbonyl-1,2-dihydrothiazole (**3g**), and 1-methyl-2-(methylthio)thiocarbonyl-1,2-dihydrobenzothiazole (**3h**) were synthesized by the reaction of the corresponding 2-imino- and 4-imino-N-methyl heterocyclic compounds with carbon disulfide.

The reaction of **3a**—**e** with dimethyl acetylenedicarboxylate afforded the 2- or 4-[1,2-bis(methoxycarbonyl)-2-thioxoethylidene]-1,2- or 1,4-dihydropyridine derivatives (**8a**—**d**). The reaction of **3i** with dimethyl acetylenedicarboxylate (2 mol) gave cyclobuta[*b*]azocine (**9**). The reaction of **3h** with dimethyl acetylenedicarboxylate afforded 2,3-dihydrobenzothiazole-2-spiro-2′-(2H-pyrrole) (**10**).

2-[N-bis(methylthio)methylene]amino-N-methylpyridinium and benzothiazolium iodide (**11b**, **c**), which were prepared by the methylation of **3a** and **h** with methyl iodide, reacted with nucleophiles to yield the corresponding products substituted on one or two methylthio groups.

Keywords——heterocyclic dithiocarbamate; Diels-Alder reaction; 1,4-cycloaddition reaction; 1,2-dihydropyridine; thiocarbonyl; imidazoline

We reported previously that the reaction of heterocyclic enamine derivatives with carbon disulfide in the presence of a base gave the corresponding enaminodithiocarboxylates, which are very useful synthetic intermediates for the synthesis of heterocyclic compounds.[2] For example, enaminodithiocarboxylates react with amines to give the corresponding thioamide derivatives in good yields, and also react with dienophiles, such as dimethyl acetylenedicarboxylate (DMAD), to yield 1,4-cycloaddition products.[2c]

The present paper deals with the synthesis and reactions of heterocyclic dithiocarbamates.

Synthesis of Alkyl Dithiocarbamates

The reaction of 2-amino-1-methylpyridinium iodide (**1a**) with carbon disulfide in the presence of sodium hydride in tetrahydrofuran (THF) under reflux gave the sodium dithio-

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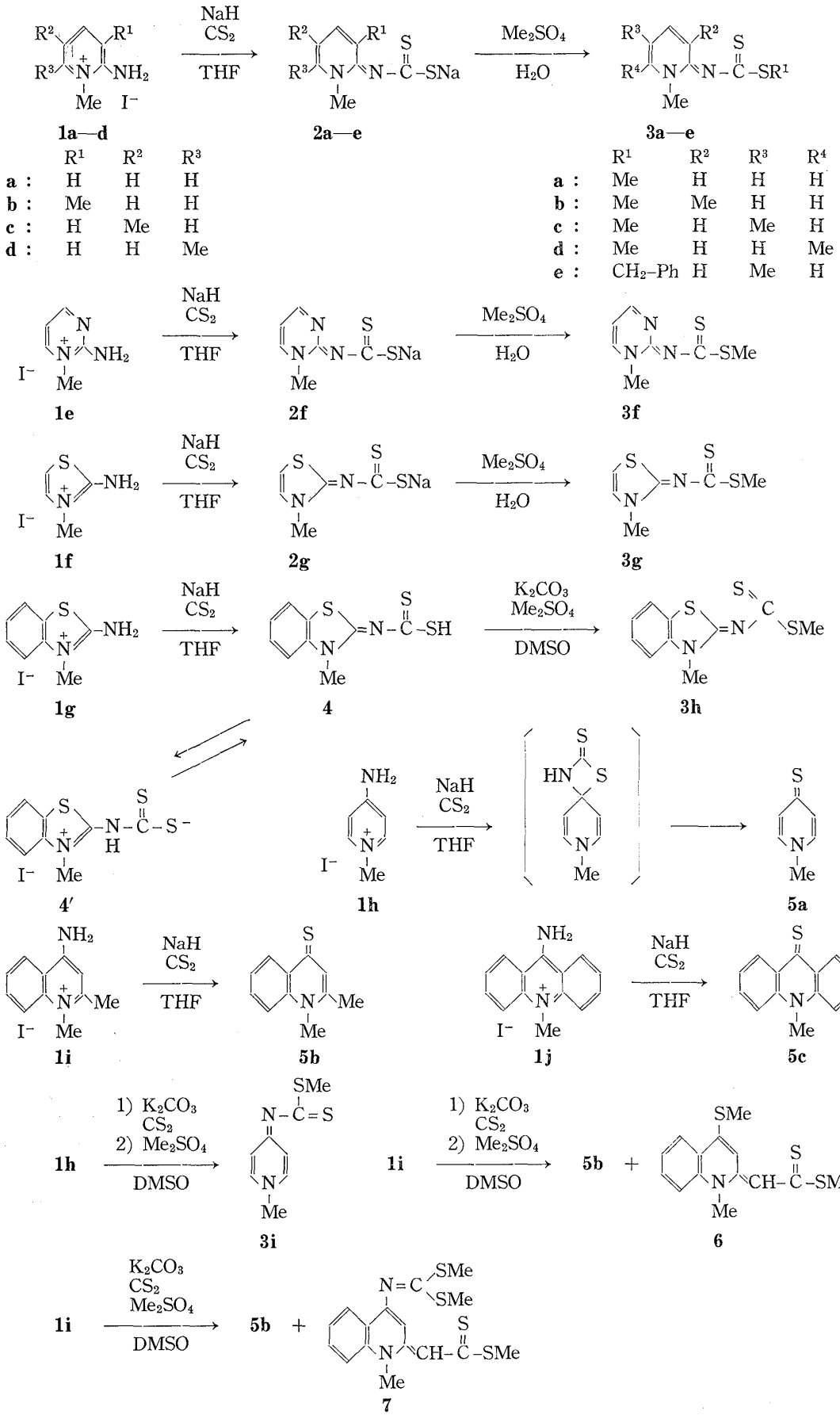


Chart 1

carbamate (**2a**), which was methylated with dimethyl sulfate to afford 1-methyl-2-(methylthio)thiocarbonylimino-1,2-dihydropyridine (**3a**). Using the same method, other dithiocarbamates (**3b**—**d**) were prepared from the corresponding 2-amino-1-methylpyridinium iodide derivatives (**1b**—**d**) in good yields. With benzyl chloride instead of dimethyl sulfate as the alkylating reagent in the reaction of **1c** with carbon disulfide, 2-(benzylthio)thiocarbonylimino-1,5-dimethyl-1,2-dihydropyridine (**3e**) was obtained. Similarly, other heterocyclic dithiocarbamates (**3f, g**) were prepared by the reaction of 2-amino-1-methylpyridinium iodide (**1e**) and 2-amino-3-methylthiazolium iodide (**1f**) with carbon disulfide in good yields. The reaction of 2-amino-3-methylbenzothiazolium iodide (**1g**) with carbon disulfide under similar reaction conditions afforded the stable dithiocarboxylic acid derivative (**4**). It is interesting that compound **4** is stable and shows no acid character, presumably because of the betaine structure **4′**. Methylation of **4** with dimethyl sulfate in the presence of potassium carbonate in dimethyl sulfoxide (DMSO) yielded the desired methyl dithiocarbamate (**3h**).

When 4-amino-1-methylpyridinium iodide (**1h**) was reacted with carbon disulfide in a similar manner, 1-methyl-4-thioxo-1,4-dihydropyridine (**5a**) was obtained in 50% yield. In a similar manner, the reaction of 4-amino-1,2-dimethylquinolinium iodide (**1i**) and 9-amino-10-methylacridinium iodide (**1j**) with carbon disulfide also gave thioxo derivatives (**5b** and **c**).[3] Since the desired corresponding dithiocarbamates were not obtained under these reaction conditions, the following conditions were examined. The use of potassium carbonate and DMSO instead of sodium hydride and THF gave the desired dithiocarbamate, 1-methyl-4-(methylthio)thiocarbonylimino-1,4-dihydropyridine (**3i**). However, the reaction of **1i** with carbon disulfide under similar conditions gave two products, **5b** and 1-methyl-4-methylthio-2-(methylthio)thiocarbonylmethylene-1,2-dihydroquinoline (**6**), in 5 and 20% yields, respectively. On the other hand, when a mixture of carbon disulfide and dimethyl sulfate in DMSO was added to a solution of **1i** and potassium carbonate in DMSO, **5b** and **7** were obtained **7** and 35% yields, respectively. The formation of **7** can be regarded as a result of attack of the dithiocarbamate anion because of the preferential methylation of the dithiocarbamic acid group by dimethyl sulfate co-existing in the reaction mixture. Compounds **6** and **7** were identified from their spectral data and elemental analyses. (see "Experimental")

1,4-Cycloaddition Reaction

Conjugated dienes and their heteroanalogs have been thoroughly investigated in organic chemistry. However, few studies have been reported on diheterodienes having a thiocarbonyl group and a carbon-nitrogen double bond.[4] The methyl dithiocarbamate derivatives described above have a conjugated diheterodiene system.

Reaction of **3a** with DMAD gave yellow needles of mp 217—218° (dec.). This compound, **8a**, was found to be 1-methyl-2-[1,2-bis(methoxycarbonyl)-2-thioxoethylidene)-1,2-dihydropyridine on the basis of infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR) and mass spectral data, and elemental analysis. In a similar manner, treatment of other methyl dithiocarbamate derivatives (**3b**—**e**) with DMAD afforded the corresponding 2-(2-thioxoethylidene)-1,2- or 1,4-dihydropyridine derivatives (**8b**—**e**), accompanied by the elimination of methylthiocyanate, in fairly good yields. However, the reaction of **3f** with DMAD did not occur under similar conditions. To investigate the reaction mechanism, the reaction of **3e** with DMAD was examined under similar conditions, and two products, **8c** and benzylthiocyanate, were obtained. This benzylthiocyanate was identical with the original sample.[5]

3) *a*) K. Gleu and R. Schaarschmidt, *Chem. Ber.*, **72**, 1246 (1939); *b*) E. Campaigne, R.E. Cline, and C.E. Kaslow, *J. Org. Chem.*, **15**, 600 (1950).

4) *a*) J.C. Meslin and H. Quiniou, *Synthesis*, **1974**, 298; *b*) J.C. Mesilin and H. Quiniou, *Tetrahedron*, **31**, 3055 (1975); *c*) K. Burger, J. Albanbauer, and W. Foag, *Angew. Chem.*, **87**, 816 (1975); *d*) K. Burger, R. Ottlinger, and J. Albanbauer, *Chem. Ber.*, **110**, 2114 (1977); *e*) R. Okazaki, M. O-oka, and N. Inamoto, *J. Chem. Soc. Chem. Commun.*, **1976**, 562.

5) G.A. Barbalia, *Chem. Ber.* **5** 687 (1872).

When a solution of **3i** and 2 molar equivalents DMAD in dimethylformamide was stirred at room temperature for 72 hr, white needles of mp 183—184° were obtained. On the basis of IR, UV, NMR, and mass spectral data and elemental analysis, this compound was assigned as 1,6,6a,8a-tetrahydro-1′,2′,3,4,7,8-hexakis(methoxycarbonyl)-1-methyl-6-(2-thioxoethylidene)-cyclobuta[*b*]azocine (**9**).

The reactions of **3h** with DMAD at 150° for 5 hr afforded 3-methyl-2,3-dihydrobenzothiazole-2-spiro-2′-[3′,4′-(methoxycarbonyl)-5′-methylthio-2*H*-pyrrole] (**10**). This reaction did not give the 1,4-cycloaddition product at room temperature. It has been reported that the analogous 1,4-cycloaddition reaction of an enaminodithiocarboxylate with DMAD gave the corresponding spiro(benzothiazolinecyclopentadiene) derivative by mono-desulfurization.[2c]

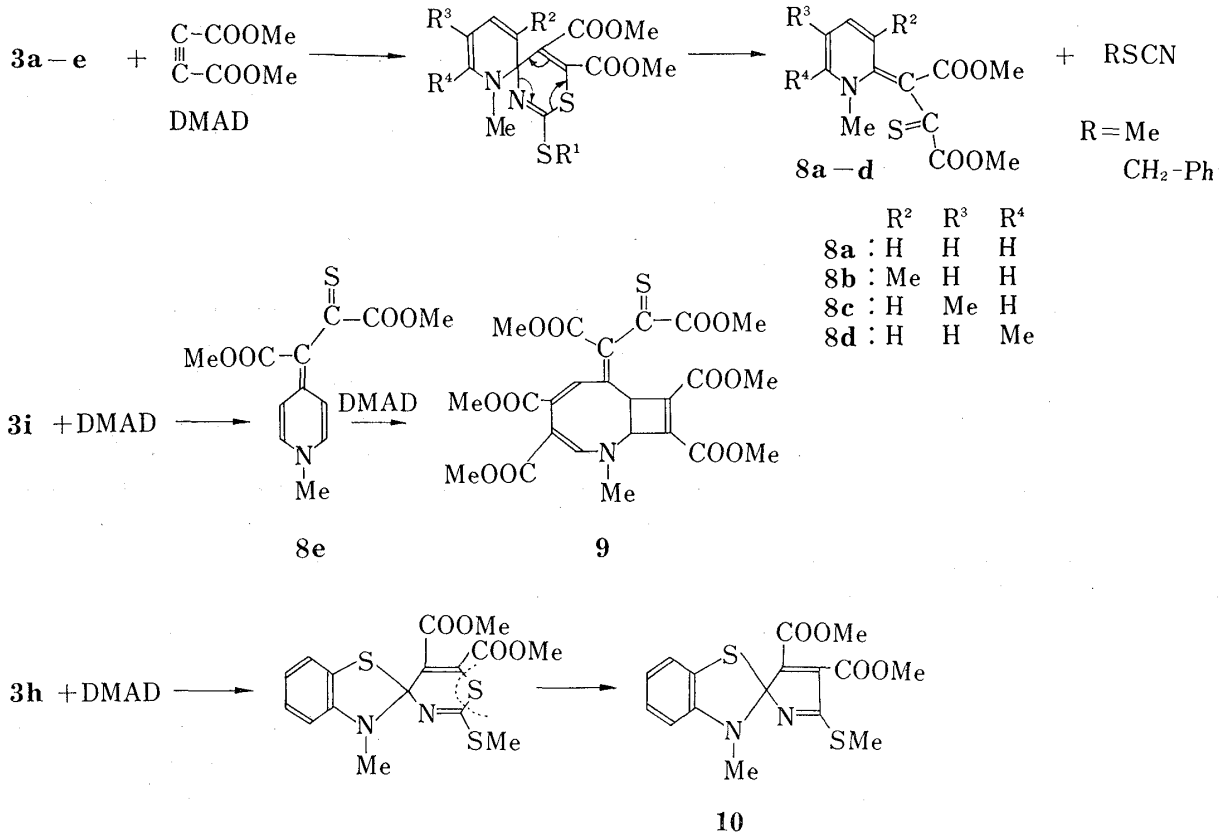


Chart 2

Methylation and the Reactions of Methyl Dithiocarbamates

The treatment of **3a** with methyl iodide gave 1-methyl-2-[N-bis(methylthio)methylene]-aminopyridinium iodide (**11a**) in 90% yield. In a similar manner, 1-methyl-2-[N-bis(methylthio)methylene]aminobenzothiazolium iodide (**11c**) was readily obtained from **3f** and **h**, in 97 and 95% yields, respectively. Compound **11c** was easily hydrolyzed in methanol on heating to give the thioamide (**12**). The chemical reactivity of the methylthio group of **11a**, **b**, and **c** can be investigated by reacting **11** with amines or active methylene compounds.

The reaction of **11a** with morpholine gave the dimorpholine derivative (**13**). However, **11c** reacted with morpholine to afford the amide derivative (**14**), which was also obtained by the reaction of **12** with morpholine. The reaction of **11a** with hydrazine hydrate in ethanol gave the dihydrazone derivative (**15a**). In the same way, **11c** reacted with hydrazine hydrate to give **15b**. In a similar manner, the reaction of **11a** with ethylenediamine or ethanolamine under reflux in methanol gave the corresponding imidazoline (**16a**) and oxazoline (**16b**) derivatives in good yields. The reaction of **11b** and **c** with these amines also afforded the corresponding **16c**—**e** in good yields.

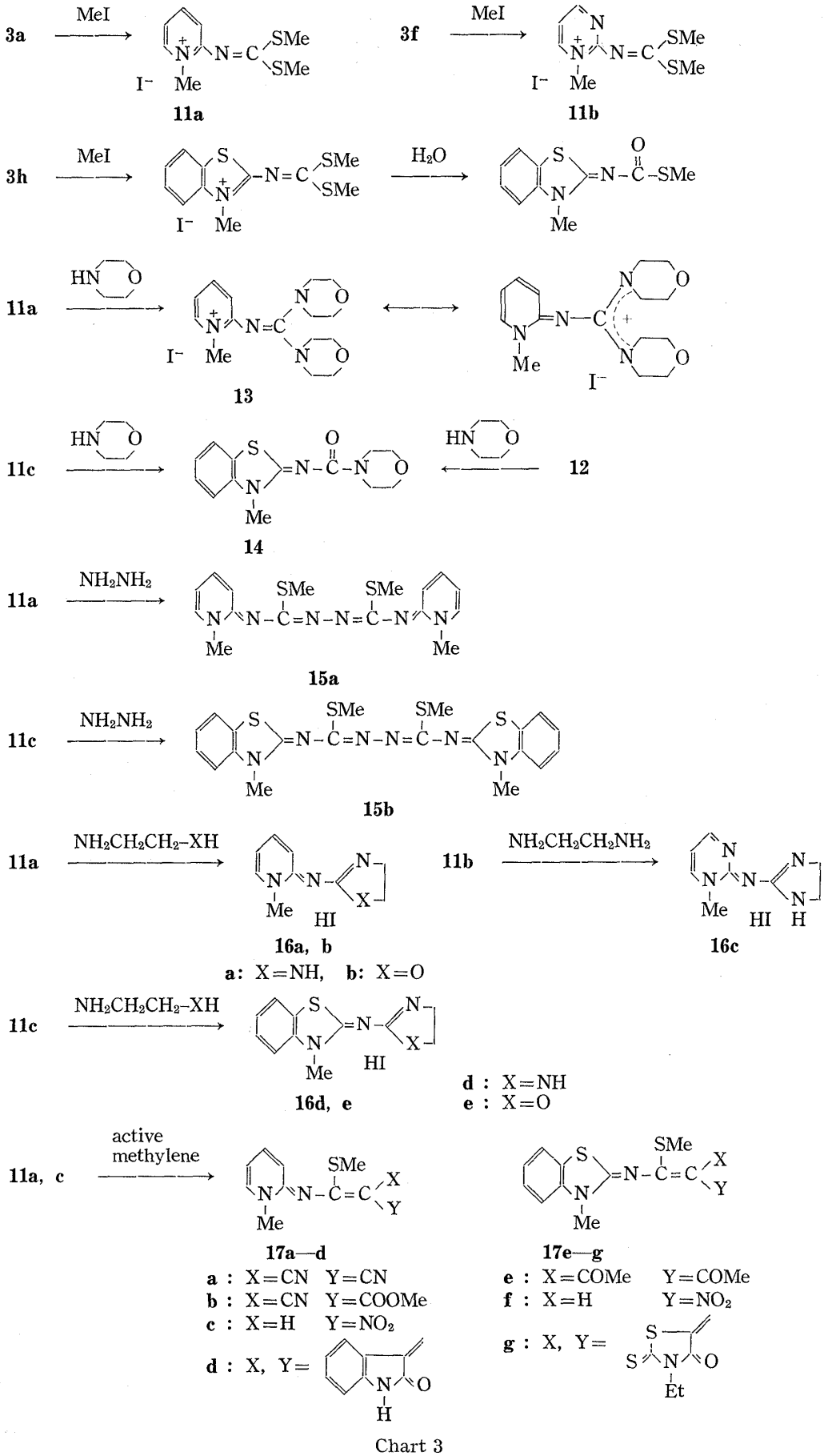


Chart 3

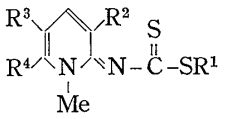
Compounds **11a** and **c** readily reacted with active methylene compounds (malononitrile, methyl cyanoacetate, nitromethane, oxindole, acetylacetone, rhodanine) to give the corresponding methylthiosubstituted products (**17a—g**) in good yields.

Experimental

All melting points were determined in a capillary tube and are uncorrected. IR spectra were recorded in KBr pellets on a Jasco IRA-2 spectrometer, UV absorption spectra were determined on a Hitachi EP-S2 spectrometer in 95% EtOH, and NMR spectra were obtained using a JNM-PS-100 (100 MHz) spectrometer with tetramethylsilane as an internal standard, unless otherwise indicated. Mass spectra were recorded on a JEOL JMS-01SG double-focus mass spectrometer.

2-(Alkylthio)thiocarbonylimino-1-methyl-1,2-dihydropyridines (3a—e)——Sodium hydride (1.5 g of a 50% mineral oil dispersion, 0.03 mol) was freed from mineral oil by washing and decanting three times with petroleum ether (bp 40—60°). Next, 100 ml of THF was added to the resulting gray solid, and 0.01 mol of 2-amino-1-methylpyridinium iodide (**1a—c** or **d**) and 0.02 mol of CS_2 were added together. The mixture was heated to reflux with rapid evolution of hydrogen at first. After 1.5—2 hr, THF and the excess CS_2 were removed by evaporation to give a yellow solid. The solid was added to 100 ml of H_2O and stirring was until all of the solid was dissolved, then 1.3 g of Me_2SO_4 or 1.3 g of benzylchloride (for **3e** from **1c**) was slowly added dropwise to the solution with stirring at room temperature. After 1 hr, the precipitate was collected,

TABLE I.



	R^1	R^2	R^3	R^4	Yield (%)	mp (C°)	Appearance (Recrystal. solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N	S
3a	Me	H	H	H	85	115	Pale yellow needles (MeOH)	$C_8H_{10}N_2S_2$	48.45 (48.03	5.08 5.07	14.13 14.06	32.34 32.32)
3b	Me	Me	H	H	67	189	Colorless needles (MeOH)	$C_9H_{12}N_2S_2$	50.91 (50.56	5.70 5.72	13.19 13.09	30.20 30.38)
3c	Me	H	Me	H	80	119	Pale yellow prisms (MeOH)	$C_9H_{12}N_2S_2$	50.91 (50.87	5.70 5.71	13.19 13.31	30.20 30.45)
3d	Me	H	H	Me	50	146	Pale yellow needles (MeOH)	$C_9H_{12}N_2S_2$	50.91 (50.80	5.70 5.88	13.19 13.22	30.20 30.32)
3e	CH_2Ph	H	Me	H	65	121	Pale yellow needles (MeOH)	$C_{15}H_{16}N_2S_2$	62.46 (62.15	5.59 5.56	9.71 9.65	22.23 22.01)

	NMR ($CDCl_3$) δ	UV λ_{max}^{EtOH} nm (log ε)
3a	2.36 (3H, s, S–Me), 3.84 (3H, s, N–Me), 6.84 (1H, t, J=7 Hz, 4-H) 7.68—7.88 (2H, m, 3,5-H), 8.39 (1H, d, J=7 Hz, 6-H)	220(3.96) 308(3.98) 374(4.07)
3b	2.19 (3H, s, 3-Me), 2.31 (3H, s, S–Me), 3.95 (3H, s, N–Me) 7.11 (1H, dd, J=7, 7.5 Hz, 5-H) 7.85 (1H, d, J=7.5 Hz, 4-H), 7.97 (1H, d, J=7 Hz, 6-H)	220(4.08) 240(4.00) 300(3.98)
3c	2.28 (3H, s, 5-Me), 2.50 (3H, s, S–Me), 3.86 (3H, s, N–Me) 7.70 (1H, dd, J=1, 9 Hz, 4-H), 7.76 (1H, d, J=1 Hz, 6-H) 8.72 (1H, d, J=9 Hz, 3-H)	220(4.05) 306(4.00)
3d	2.32 (3H, s, S–Me), 2.60 (3H, s, 6-Me), 3.84 (3H, s, N–Me) 6.81 (1H, d, J=7 Hz, 5-H), 7.68 (1H, dd, J=7, 8 Hz, 4-H), 8.12 (1H, d, J=8 Hz, 3-H)	220(4.02) 308(3.95) 374(4.08)
3e	2.26 (3H, s, 5-Me), 3.70 (3H, s, N–Me), 4.36 (2H, s, S–CH_2–) 7.20—7.70 (7H, m, 3,6-H, Ph), 8.26 (1H, d, J=7 Hz, 4-H)	220(4.16) 308(3.91) 370(4.06)

washed with H_2O, and recrystallized from MeOH or acetone to give the corresponding dithiocarbamate derivative (**3a**—**d** or **e**).

1-Methyl-2-(methylthio)thiocarbonylimino-1,2-dihydropyrimidine (**3f**)——This compound was obtained from **1e** by the procedure described for **3a**, and was purified by recrystallization from MeOH to give yellow needles, mp 135°, in 55% yield. *Anal.* Calcd. for $C_7H_9N_3S_2$: C, 42.18; H, 4.55; N, 21.09; S, 32.18. Found: C, 41.89; H, 4.60; N, 21.21; S, 32.42. UV λ_{max}^{EtOH} nm (log ε): 220 (3.96), 256 (3.92), 310 (4.13). IR ν_{max}^{KBr} cm^{-1}: 1620, 1548, 1500, 1455, 1430, 1402. NMR ($CDCl_3$) δ: 2.60 (3H, s, S–Me), 3.66 (3H, s, N–Me), 6.50 (1H, dd, J=2, 4 Hz, 4-H), 7.84 (1H, dd, J=2, 6 Hz, 6-H), 8.64 (1H, dd, J=2, 4 Hz, 3-H).

3-Methyl-2-(methylthio)thiocarbonylimino-2,3-dihydrothiazole (**3g**)——This compound was obtained from **1f** by the procedure described for **3a**, and was purified by recrystallized from MeOH to give yellow needles, mp 165°, in 85% yield. *Anal.* Calcd. for $C_6H_8N_2S_3$: C, 35.27; H, 3.95; N, 13.71; S, 47.07. Found: C, 35.28; H, 3.94; N, 13.88; S, 47.52. UV λ_{max}^{EtOH} nm (log ε): 221 (4.30), 314 (4.00), 359 (4.31). NMR ($CDCl_3$) δ: 2.64 (3H, s, S–Me), 3.86 (3H, s, N–Me), 6.78 (1H, d, J=5 Hz, 5-H), 7.14 (1H, d, J=5 Hz, 4-H). IR ν_{max}^{KBr} cm^{-1}: 1550, 1480, 1400, 1360, 1250.

3-Methyl-2-imino-2,3-dihydrobenzothiazole N-Dithiocarboxylic Acid (**4**)——Free sodium hydride was prepared by the method described above. THF (100 ml) was added to the resulting gray solid, then 0.01 mol of **1g** and 0.02 mol of CS_2 were added together. The mixture was heated to reflux for 1.5—2 hr. THF and the excess CS_2 were then removed by evaporation to give a yellow solid. The solid was added to 200 ml of H_2O and the whole was stirred for 1 hr. The resulting yellow precipitate was collected by filtration, washed with H_2O, and recrystallized from acetone to give **4**, yellow needles, mp 300°, in 92% yield. *Anal.* Calcd. for $C_9H_8N_2S_3$: C, 44.97; H, 3.35; N, 11.66; S, 40.02. Found: C, 44.98; H, 3.27; N, 11.45; S, 40.29. IR ν_{max}^{KBr} cm^{-1}: 1715, 1660, 1495, 1425, 1235, 1200.

3-Methyl-2-(methylthio)thiocarbonylimino-2,3-dihydrobenzothiazole (**3h**)——a) Me_2SO_4 (1.5 g) was slowly added dropwise to a solution of 2.5 g of **4** and 2 g of K_2CO_3 in 50 ml of DMSO at room temperature. After 2 hr, the reaction mixture was poured into 100 ml of ice-water. The yellow precipitate was collected by filtration, washed with H_2O, and recrystallized from acetone to give yellow needles, mp 142°, in 93% yield.

b) To a solution of 0.01 mol of **1g** in 30 ml of DMSO, 0.04 mol of CS_2 and 0.04 mol of K_2CO_3 were added together. The mixture was stirred for 15—20 min at room temperature. The color of the solvent became red. The reaction mixture was poured into 200 ml of ice-water, and the precipitate was collected by filtration, washed with H_2O, then recrystallized from acetone to give yellow needles, mp 142°, in 72% yield. *Anal.* Calcd. for $C_{10}H_{10}N_2S_3$: C, 47.21; H, 3.96; N, 11.01; S, 37.81. Found: C, 47.23; H, 4.06; N, 11.07; S, 37.65. UV ν_{max}^{KBr} cm^{-1}: 1490, 1460, 1400, 1350, 1270, 1225. NMR ($CDCl_3$) δ: 2.60 (3H, s, S–Me).

Thioxo Derivatives (**5a—c**)——Free sodium hydride was prepared by the method described above. THF (50 ml) was added to the resulting gray solid, then 0.01 mol of **1**(**h**—**j**) and 0.02 mol of CS_2 were added together. The mixture was heated to reflux for 1.5—2 hr. THF and excess CS_2 were removed by evaporation to give a yellow solid. The solid was added to 100 ml of H_2O and stirring was continued for 1 hr. The resulting yellow precipitate was collected by filtration, washed with H_2O, and recrystallized from MeOH to give **5a**—**c**. **5a**: mp 150°, Yield 50%, yellow needles. *Anal.* Calcd. for C_6H_7NS: C, 57.56; H, 5.46; N, 11.19; S, 25.61. Found: C, 57.40; H, 5.50; N, 11.00; S, 25.49. **5b**: mp 266°, Yield 75%, red needles. *Anal.* Calcd. for $C_{14}H_{11}NS$: C, 74.63; H, 4.92; N, 6.22; S, 14.23. Found: C, 74.42; H, 4.83; N, 5.99; S, 14.21. **5c**: mp 224°, yield 20%, red needles. *Anal.* Calcd. for $C_{11}H_{11}NS$: C, 69.80; H, 5.86; N, 7.40; S, 16.94. Found: C, 69.58; H, 5.84; N, 7.18; S, 16.91.

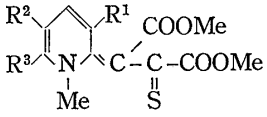
1-Methyl-4-(methylthio)thiocarbonylimino-1,4-dihydropyridine (**3i**)——K_2CO_3 (7 g) was sdded slowly with stirring to a solution of 2.38 g of **1h** and 1.5 g of CS_2 in 50 ml of DMSO, while the temperature of the mixture was maintained at 5—10°. The mixture was stirred at 10° for 1 hr, and 1.5 g of Me_2SO_4 was added dropwise with cooling over a period of 20 min. The mixture was stirred for 2 hr, then poured into 300 ml of ice-water. The reaction mixture was extracted with $CHCl_3$, then the extract was dried over Na_2SO_4 and concentrated. The residue was recrystallized from MeOH to give yellow needles, mp 149—150°, in 40% yield. *Anal.* Calcd. for $C_8H_{10}N_2S_2$: C, 48.45; H, 5.08; N, 14.13; S, 32.34. Found: C, 48.61; H, 5.19; N, 14.11; S, 31.94. IR ν_{max}^{KBr} cm^{-1}: 1625, 1490, 1430, 1360, 1260, 1230. UV λ_{max}^{EtOH} nm (log ε): 220 (4.18), 318 (4.01), 384 (4.23). NMR (CF_3COOH) δ: 2.64 (3H, s, S–Me), 4.20 (3H, s, N–Me), 8.16 (2H, d, J=7 Hz, 3 and 5-H), 8.76 (2H, d, J=7 Hz, 2 and 6-H).

1-Methyl-4-methylthio-2-(methylthio)thiocarbonylmethylene-1,2-dihydroquinoline (**6**)——K_2CO_3 (7 g) was added to a solution of 3 g of **1i**, 3 g of CS_2, and 1.9 g of Me_2SO_4 in 50 ml of DMSO with stirring at room temperature. The initially pale yellow solution slowly became red. After stirring for 1 hr, the reaction mixture was poured into 200 ml of ice-water. The precipitate was collected by filtration, washed with H_2O, and recrystallized from MeOH to give the thioxo derivative, **5b**, mp 266°, in 20% yield. The filtrate was extracted with $CHCl_3$. The organic extracts were washed with H_2O and dried over Na_2SO_4. Removal of the solvent under reduced presure left a residue, which was chromatographed over Al_2O_3 with benzene to afford red needles, mp 211°, in 20% yield. This compound was recrystallized from benzene. *Anal.* Calcd. for $C_{14}H_{15}NS_3$: C, 57.30; H, 5.15; N, 4.77; S 32.78. Found: C, 57.58; H, 5.11; N, 4.63; S, 32.80. IR ν_{max}^{KBr} cm^{-1}: 1590, 1545, 1480, 1280. UV λ_{max}^{EtOH} nm: 233, 346, 495; λ_{max}^{EtOH} nm: 296, 395. NMR ($CDCl_3$) δ: 2.66 (6H, s, S–Me), 3.69 (3H, s, N–Me), 6.54 (1H, s, =CH), 7.24—7.92 (4H, m, aromatic H), 10.10 (1H, s, 3-H).

1-Methyl-4-[N-bis(methylthio)methylene]amino-2-(methylthio)thiocarbonylmethylene-1,2-dihydroquinoline (7)——K_2CO_3 (7 g) was added to a solution of 3 g of **1i**, 3 g of CS_2, and 3.8 g of Me_2SO_4 in 50 ml of DMSO with stirring at room temperature. The initially oily yellow solution slowly became red. After stirring for 1 hr, the reaction mixture was poured into 200 ml of ice-water. The precipitate was collected by the filtration, washed with H_2O, and recrystallized from MeOH to give the thioxo derivative, **5b**, in 7% yield. The filtrate was extracted with $CHCl_3$. The organic extracts were washed with H_2O and dried over Na_2SO_4. Removal of the solvent under reduced pressure left a residue, which was chromatographed over Al_2O_3 with benzene to afford red needles, mp 198°, in 35% yield. This compound was recrystallized from acetone. *Anal.* Calcd. for $C_{16}H_{18}N_2S_4$: C, 52.42; H, 4.95; N, 7.65; S, 34.98. Found: C, 52.58; H, 4.93; N, 7.41; S, 35.20. IR ν_{max}^{KBr} cm^{-1}: 1600, 1550, 1480, 1420, 1275, 1200, 1170, 920, 860. UV λ_{max}^{EtOH} nm: 236, 346, 500; λ_{max}^{EtOH} nm: 300, 405. NMR ($CDCl_3$) δ: 2.60 (6H, s, 2×S–Me), 2.68 (3H, s, S–Me), 3.78 (3H, s, N–Me), 6.68 (1H, s, =CH–), 7.40—7.80 (4H, m, aromatic H), 9.60 (1H, s, 3-H).

1-Methyl-2-[1,2-bis(methoxycarbonyl)-2-thioxoethylidene]-1,2-dihydropyridine (8a—e)——A solution of 0.01 mol of **3a—c** or **d** and 0.015 mol of DMAD in 50—80 ml of dioxane was stirred for 2—4 hr at room temperature. The precipitate was collected by filtration and recrystallized from methanol to give **8a—c** or **d**. The filtrate was concentrated and the residue was recrystallized from MeOH to give **8a—c** or **d** in 2—3% yield. When the benzylthio derivative, **3e**, was reacted with DMAD in dioxane, benzylthiocyanate was obtained. After this reaction, the removal of dioxane gave a dark residue which was chromatographed over Al_2O_3 with benzene to give benzylthiocyanate, mp 43°.

TABLE II.



	R¹	R²	R³	Yield (%)	mp (°C)	Appearance (Recrystal. solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N	S
8a	H	H	H	80	217—218	Yellow needles (MeOH)	$C_{12}H_{13}NO_4S$	53.92 (53.78	4.90 4.77	5.24 5.11	12.00 11.92)
8b	Me	H	H	50	214—215	Yellow needles (MeOH)	$C_{13}H_{15}NO_4S$	55.50 (55.11	5.37 5.28	4.98 4.99	11.40 11.29)
8c	H	Me	H	98	230—232	Yellow needles (MeOH)	$C_{13}H_{15}NO_4S$	55.50 (55.51	5.37 5.36	4.98 4.72	11.40 11.33)
8d	H	H	Me	70	239—240	Pale yellow needles (MeOH)	$C_{13}H_{15}NO_4S$	55.50 (55.15	5.37 5.57	4.98 4.84	11.40 11.83)

	NMR ($(CD_3)SO$) δ	IR ν_{max}^{KBr} cm^{-1} (C=O)	UV λ_{max}^{EtOH} nm (log ε)
8a	3.45 (3H, s, O–Me), 3.64 (3H, s, O–Me), 4.10 (3H, s, N–Me), 7.86 (1H, d, J=7 Hz, 3-H), 7.90 (1H, t, J=7 Hz, 5-H), 8.44 (1H, t, J=7 Hz, 4-H), 8.97 (1H, d, J=6 Hz, 6-H)	1670 1720	220(3.82) 264(3.81) 332(4.26)
8b	2.24 (3H, s, 3-Me), 3.42 (3H, s, O–Me), 3.62 (3H, s, O–Me), 4.03 (3H, s, N–Me), 7.79 (1H, t, J=7 Hz, 5-H), 8.32 (1H, d, J=7 Hz, 4-H), 8.81 (1H, d, J=7 Hz,6-H)	1660 1725	220(3.94) 272(3.89) 334(4.33)
8c	2.28 (3H, s, 5-Me), 3.44 (3H, s, O–Me), 3.64 (3H, s, O–Me), 7.76 (1H, d, J=8 Hz, 3-H), 8.30 (1H, dd, J=1, 8 Hz, 4-H), 8.90 (1H, d, J=1 Hz, 6-H)	1660 1710	220(4.03) 272(3.87) 332(4.28)
8d	2.82 (3H, s, 6-Me), 3.47 (3H, s, O–Me), 3.67 (3H, s, O–Me), 4.00 (3H, s, O–Me), 7.75 (1H, dd, J=1, 7 Hz, 5-H), 7.88 (1H, dd, J=1, 8 Hz, 3-H), 8.34 (1H,dd, J=7.5, 8 Hz, 4-H)	1660 1730	220(3.80) 272(3.92) 330(4.28)

1,6,6a,8a-Tetrahydro-1′,2′,3,4,7,8-hexakis(methoxycarbonyl)-1-methyl-6-(2-thioxoethylidene)cyclobuta[*b*]azocine (9)——A solution of 0.01 mol of **3i** and 0.03 mol of DMAD in 30 ml of DMF was stirred for 72 hr at room temperature. After the removal of DMF, the resulting dark red oil was chromatographed over Al_2O_3 (benzene: acetone 50: 1) to give a crystalline product. This product was recrystallized from MeOH to give colorless needles, mp 183—184°, in 40% yield. *Anal.* Calcd. for $C_{24}H_{25}NO_{12}S$: C, 52.27; H, 4.57; N,

2.54; S, 5.80. Found: C, 52.14; H, 4.56; N, 2.31; S, 5.58. IR ν_{max}^{KBr} cm^{-1}: 1708, 1728—1742. UV λ_{max}^{EtOH} nm (log ε): 220 (4.54), 298 (3.80). NMR ($CDCl_3$) δ: 3.12 (1H, d, J=6 Hz, 6a-H), 3.76 (3H, s, O–Me), 3.84 (6H, s, 2×OMe), 3.88 (6H, s, 2×OMe), 4.05 (1H, d, J=6 Hz, 8a–H), 5.90 (1H, d, J=1 Hz, 2-H). MS m/e: 551 (M^+).

3-Methyl-2,3-dihydrobenzothiazole-2-spiro-2′-[3′,4′-bis(methoxycarbonyl)-5′-methylthio-2H-pyrrole] (10)——A solution of 0.001 mol of **3h** and 0.002 mol of DMAD was heated at 150° for 5 hr. After cooling, 5 ml of MeOH was added to the reaction mixture and the was collected by filtration, washed with a small amount of MeOH, and recrystallized from acetone to give yellow crystals, mp 245°, in 30% yield. *Anal.* Calcd. for $C_{16}H_{16}N_2O_4S_2$: C, 52.73; H, 4.43; N, 7.69; S, 17.59. Found: C, 52.55; H, 4.32; N, 7.56; S, 17.60. IR ν_{max}^{KBr} cm^{-1}: 1670, 1750. UV λ_{max}^{EtOH} nm (log ε): 220 (4.23), 254 (4.33), 286 (4.42), 300 (4.27), 405 (3.78). NMR (C_5H_5N) δ: 2.60 (3H, s, S–Me), 3.32 (3H, s, O–Me), 3.62 (3H, s, O–Me).

1-Methyl-2-[N-bis(methylthio)methylene]aminopyridinium Iodide (11a)——A solution of 1.98 g of **3a** and 2 ml of MeI in 50 ml of acetone was heated to reflux for 1 hr. After cooling, the precipitate was collected by filtration and recrystallized from MeOH to give colorless needles, mp 120—122°, in 90% yield. *Anal.* Calcd. for $C_9H_{13}IN_2S_2$: C, 31.78; H, 3.85; N, 8.24; S, 18.82. Found: C, 32.07; H, 3.83; N, 8.12; S 19.18. IR ν_{max}^{KBr} cm^{-1}: 1620, 1530, 1420, 1300, 1250. UV λ_{max}^{EtOH} nm (log ε): 220 (4.30), 325 (3.99). NMR (CF_3COOH) δ: 2.74 (6H, s, S–Me).

1-Methyl-2-[N-bis(methylthio)methylene]aminopyrimidinium Iodide (11b)——A solution of 2 g of **3f** and 2 ml of MeI in 50 ml of THF was allowed to stand for 24 hr. The resulting crystals were recrystallized from MeOH to give **11b**, mp 208°, in 95% yield. *Anal.* Calcd. for $C_8H_{12}IN_3S_2$: C, 28.16; H, 3.55; N, 12.32; S, 18.76. Found: C, 28.18; H, 3.49; N, 12.44; S, 19.49. IR ν_{max}^{KBr} cm^{-1}: 1590, 1470, 1390, 1265. UV λ_{max}^{EtOH} nm (log ε): 300 (4.12), 338 (4.30). NMR (CF_3COOH) δ: 2.81 (6H, s, S–Me), 4.20 (3H, s, N–Me), 7.47 (1H, dd, J=5, 7 Hz, 5-H), 8.78 (1H, dd, J=2, 7 Hz, 4 or 6-H), 9.14 (1H, dd, J=2, 5 Hz, 4 or 6-H).

3-Methyl-2-[N-bis(methylthio)methylene]aminobenzothiazolium Iodide (11c)——This compound was also obtained from **3h** by the procedure described for **11a**: yellow needles, mp 127—130°, yield 95%. *Anal.* Calcd. for $C_{11}H_{13}IN_2S_3$: C, 33.35; H, 3.31; N, 7.67; S, 24.23. Found: C, 33.11; H, 3.22; N, 7.68; S, 24.00. UV λ_{max}^{EtOH} nm (log ε): 220 (4.61), 280 (3.90), 288 (3.92), 306 (4.05), 320 (3.74), 370 (3.86). NMR (CF_3COOH) δ: 2.80 (6H, s, S–Me).

3-Methyl-2-[N-(methylthio)carbonyl]imino-2,3-dihydrobenzothiazole (12)——A solution of 3.95 g of **11c** and 0.5 ml of H_2O in 50 ml of MeOH was refluxed on a boiling water bath for 3 hr. After removal of the solvent, the residue was recrystallized from MeOH to give yellow needles, mp 172—173°, in 95% yield. *Anal.* Calcd. for $C_{10}H_{10}N_2OS_2$: C, 50.39; H, 4.23; N, 11.76; S, 26.91. Found: C, 50.20; H, 4.10; N, 11.90; S, 26.48. IR ν_{max}^{KBr} cm^{-1}: 1600, 1495, 1455, 1400, 1340, 1170. UV λ_{max}^{EtOH} nm (log ε): 283 (3.68), 319 (4.55). NMR ($CDCl_3$) δ: 2.40 (3H, s, S–Me), 3.80 (3H, s, N–Me), 7.24—7.72 (4H, m, aromatic H).

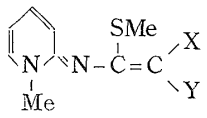
1-Methyl-2-(N-dimorpholinomethylene)aminopyridinium Iodide (13)——A mixture of 1.7 g of **11a** and 1.5 g of morpholine was heated at 130° for 10 min. After cooling, 30 ml of acetone was added to the reaction mixture, and the whole was allowed to stand for 2 hr. The precipitate was collected by filtration, washed with ether, and recrystallized from MeOH to give colorless needles, mp 222°, in 80% yield. *Anal.* Calcd. for $C_{15}H_{23}IN_4O_2$: C, 43.06; H, 5.54; N, 13.39. Found: C, 42.82; H, 5.59; N, 13.15. IR ν_{max}^{KBr} cm^{-1}: 1620, 1500, 1430. UV λ_{max}^{EtOH} nm (log ε): 278 (4.08), 327 (4.23).

3-Methyl-2-(morpholinocarbonyl)imino-2,3-dihydrobenzothiazole (14)——a) A mixture of 2 g of **11c** and 1.5 g of morpholine was heated at 100° for 30 min. After cooling 5 ml of MeOH was added to the

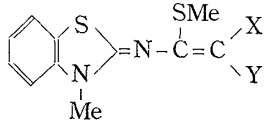
Table III

	X	mp (°C)	Yield (%)	Appearance (Recrystal. solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR ν_{max}^{KBr} cm^{-1} (NH)	UV λ_{max}^{EtOH} nm (log ε)
16a	NH	176—177	90	Colorless needles (MeOH+MeCOOEt)	$C_9H_{12}N_4\cdot HI$	35.54 (35.78	4.31 4.22	18.42 18.60)	3200	220(4.28) 272(4.17) 330(4.11)
16b	O	156—158	93	Colorless needles (MeOH+MeCOOEt)	$C_9H_{11}N_3O\cdot HI$	35.42 (35.27	3.96 3.99	13.77 13.83)		220(4.23) 262(4.18) 320(4.24)
16c	NH	283—284	95	Colorless needles (MeOH)	$C_8H_{11}N_5\cdot HI$	31.48 (31.63	3.96 4.02	22.95 23.30)	3210	220(4.22) 268(4.53)
16d	NH	253—254	65	Colorless needles (MeOH)	$C_{11}H_{12}N_4S\cdot HI$	36.68 (36.52	3.64 3.68	15.56 15.59)	3320	220(4.56) 310(4.40)
16e	O	214	85	Pale yellow needles (MeOH)	$C_{11}H_{11}N_3OS\cdot HI$	36.57 (31.63	3.34 4.02	11.63 23.30)		220(4.52) 257(3.90) 304(4.17)

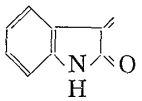
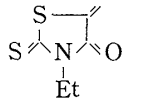
TABLE IV.



17a—d



17e—g

	X	Y	Yield (%)	mp (C°)	Appearance (Recrystal. solvent)	Formula	Analysis (%) Calcd. (Found) C	H	N	S	NMR δ Ⓓ: $(CD_3)_2SO$ Ⓒ: $CDCl_3$ Ⓣ: CF_3COOH	IR ν_{max}^{KBr} cm^{-1}	UV λ_{max}^{EtOH} nm (log ε)
17a	CN	CN	70	163—165	Yellow needles (MeOH)	$C_{11}H_{10}N_4S$	57.37 (57.37	4.38 4.27	24.33 24.55	13.92 13.95)	Ⓓ 2.28 (3H, s, S–Me)	2190 (CN)	220(3.85) 243(3.87) 308(4.08) 376(4.24)
17b	CN	COOMe	90	154—156	Pale yellow crystals (MeOH)	$C_{12}H_{13}N_3O_2S$	54.74 (54.61	4.98 4.95	15.96 15.85	12.18 12.06)	Ⓒ 2.28 (3H, s, S–Me) 3.70 (3H, s, O–Me)	2190 (CN) 1670 (CO)	220(4.14) 259(4.04) 310(4.19) 374(4.30)
17c	H	NO_2	55	187—188	Yellow needles (acetone)	$C_9H_{11}N_3O_2S$	47.99 (47.90	4.92 4.98	18.65 18.40	14.23 14.19)	Ⓣ 2.60 (3H, s, S–Me)	1505 (NO_2) 1350 (NO_2)	220(4.01) 233(4.22) 260(4.01) 340(4.08) 420(4.35)
17d			85	>280	Yellow crystals (MeOH)	$C_{16}H_{15}N_3OS$	64.62 (64.72	5.08 5.05	14.13 13.94	10.78 10.80)	Ⓣ 2.46 (3H, s, S–Me)	3100 (NH) 1645 (CO)	220( )[a] 258( ) 280( ) 354( ) 384( )
17e	COMe	COMe	87	156—157	Pale yellow crystals (MeOH)	$C_{15}H_{16}N_2O_2S_2$	56.22 (56.06	5.03 5.15	8.74 8.71	20.01 20.66)	Ⓒ 2.15 (3H, s, S–Me) 2.28 (6H, s, S–Me)	1680 (CO) 1625 (CO)	220(4.52) 264(4.19) 302(4.15) 322(4.12)
17f	H	NO_2	65	176—178	Yellow needles (acetone)	$C_{11}H_{11}N_3O_2S_2$	46.96 (47.02	3.94 3.88	14.94 14.97	22.79 22.73)	Ⓒ 2.30 (3H, s, S–Me)	1520 (NO_2) 1369 (NO_2)	220( )[a] 271( ) 351( ) 412( )
17g			50	143	Yellow needles (MeOH)	$C_{15}H_{15}N_3OS_4$	47.21 (47.05	3.91 4.14	11.01 11.07	33.62 33.78)	Ⓒ 2.36 (3H, s, S–Me)	1680 (CO)	220(4.75) 275(4.22) 291(4.22) 413(4.47)

a) Concentrations could not be determined because of insufficient solubility.

reaction mixture and the whole was allowed to stand for 1 hr. The precipitate was collected by filtration, washed with ether, and recrystallized from MeOH to give colorless needles, mp 181°, in 70% yield.

b) A solution of 1.2 g of **12** and 0.7 g of morpholine was heated in a boiling water bath. After removal of the solvent, the residue was recrystallized from MeOH to give colorless needles, mp 181°, in 97% yield. *Anal.* Calcd. for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15; S, 11.56. Found: C, 56.30; H, 5.45; N, 15.29; S, 11.46. IR ν_{max}^{KBr} cm^{-1}: 1600, 1530, 1400, 1265, 1208. UV λ_{max}^{EtOH} nm (log ε): 279 (4.08), 305 (4.45), 310 (4.57).

The Reaction of 11a and 11c with Hydrazine Hydrate——A mixture of 0.01 mol of **11a** or **11c** and 3 ml of hydrazine hydrate was heated at 130° for 30 min. After cooling, 10 ml of MeOH was added to the reaction mixture. The precipitate was collected by filtration, washed with MeOH, and recrystallized from benzene+DMF. **15a**: yellow crystals, mp 262°, Yield 70%. *Anal.* Calcd. for $C_{16}H_{20}N_6S_2$: C, 53.31; H, 5.59; N, 23.13; S, 17.79. Found: C, 53.17; H, 5.59; N, 23.47; S, 17.75. MS *m/e*: 360 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1635, 1535, 1510, 1370. UV λ_{max}^{EtOH} nm: 260, 305, 364; λ_{max}^{EtOH} nm: 285, 326. **15b**: pale yellow needles, mp 270°. Yield 87%. *Anal.* Calcd. for $C_{20}H_{20}N_6S_4$: C, 50.82; H, 4.27; N, 17.78; S, 27.13. Found: C, 50.70; H, 4.35; N, 17.70; S, 26.92. MS *m/e*: 472 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1580, 1550, 1520, 1460, 1395, 1225. UV λ_{max}^{EtOH} nm: 235, 295, 390; λ_{max}^{EtOH} nm: 250, 300. NMR (CF_3COOH) δ: 2.90 (6H, s, 2×S–Me), 4.08 (6H, s, 2×N–Me).

Reaction of 11a—c with Ethylenediamine and Ethanolamine——A solution of 0.001 mol of **11**(**a**, **b** or **c**) and 0.012 mol of amine (ethylenediamine or ethanolamine) in 50 ml of EtOH was heated under reflux for 2 hr. After removal of the solvent, the residue was recrystallized from EtOH to give the corresponding imidazoline (**16a**, **c**, **d**) and oxazoline (**16b**, **e**) derivatives.

Reaction of 11a and 11b with Active Methylene Compounds——Compound **11**(**a** or **c**) (0.01 mol) was added to a solution of 0.011 mol of an active methylene compound (malononitrile, methyl cyanoacetate, oxindole, acetylacetone, nitromethane, or rhodanine) and 0.03 mol of K_2CO_3 in 30 ml of DMSO with stirring at room temperature for 3 hr. The color of the reaction mixture became reddish-brown. The mixture was poured into ice-water and acidified with 10% HCl solution. The precipitate was collected by filtration, washed with H_2O, and recrystallized from MeOH to give the corresponding products substituted in the methylthio group. The results are shown in Table IV.