Synthesis and Cyclization Reaction of 2-(Hydroxyimino)alkyl *N,N*-Dialkyldithiocarbamates, *S*-[2-(Hydroxyimino)alkyl] *O*-Methyl Dithiocarbonate, and Alkyl 2-(Hydroxyimino)alkyl Trithiocarbonates

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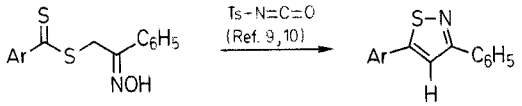
2-(Hydroxyimino)alkyl dialkyldithiocarbamates and alkyl 2-(hydroxyimino)alkyl trithiocarbonates react with tosyl isocyanate as dehydrating agent to give bis(4-isothiazolyl) disulfides in moderate yields. However, treatment of *S*-[2-(hydroxyimino)phenylethyl] O-methyl dithiocarbonate with tosyl isocyanate affords a novel heterocycle 3-phenyl-4*H*-1,5,2-oxathiazine-6-thione, in 49% yield.

The isothiazole (1,2-thiazole) nucleus may be built up in numerous ways, one of the best methods for the synthesis of this heterocycle involving S–N bond formation of a suitable S–C–C–C–N unit. However, the preparation of the starting materials required for this synthesis may be rather tedious and/or difficult.[1,2]

In connection with our efforts to develop new synthetic applications of dithiocarboxylic acid derivatives,[3-8] we have described a novel reaction of 2-(hydroxyimino)alkyl arenecarbodithioates with a dehydrating agent, tosyl isocyanate, which gave 3,5-disubstituted isothiazoles.[9,10] In this reaction, the starting materials contain the S–C–S–C–C–N unit and the arenecarbodithioate moiety serves as a source of the C–S moiety of the isothiazole ring. Because of its general applicability and of the ready availavility of the starting materials, this method seems to be superior over the previously reported methods.

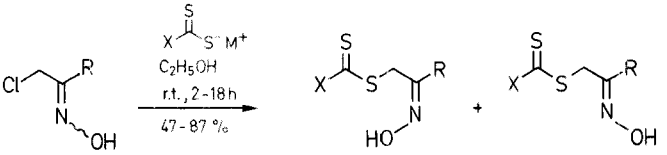


Ts = *p*-$CH_3C_6H_4SO_2$

We now report the extension of this reaction type to analogous oximes, such as 2-(hydroxyimino)alkyl *N,N*-dialkyldithiocarbamates (**2a–f**), alkyl 2-(hydroxyimino)alkyl trithiocarbonates (**2h, i**), and *S*-(2-hydroxyimino-2-phenylethyl) *O*-methyl dithiocarbonate (**2g**) to give bis(4-isothiazolyl) disulfides **3a–f, h, i**, isothiazoles **5h, i**, or 3-phenyl-4*H*-1,5,2-oxathiazine-6-thione (**4g**), respectively.

The 2-(hydroxyimino)alkyl *N,N*-dialkyldithiocarbamates **2a–f** were prepared in moderate to high yields by treatment of sodium *N,N*-dimethyldithiocarbamate or dialkylammonium *N,N*-dialkyldithiocarbamates with 1-chloro-2-(hydroxyimino)-2-phenylethane (ω-chloroacetophenone oxime), 1-chloro-2-(hydroxyimino)propane, or 1-chloro-2-(hydroxyimino) ethane[11] (chloroacetaldehyde oxime) in ethanol at room temperature. *S*-[2-(Hydroxyimino)-2-phenylethyl] *O*-methyl dithiocarbonate (**2g**) and the alkyl 2-(hydroxyimino)-2-phenylethyl trithiocarbonates (**2h, i**) were similarly prepared from sodium *O*-methyl dithiocarbonate or sodium alkyl trithiocarbonates by reaction with 1-chloro-2-(hydroxyimino)-2-phenylethane.

The oximes **2a–e, h, i** were obtained as mixtures of the *syn* and *anti* isomers; the isomer ratios were determined from the ^{1}H-NMR spectra which showed the signal of the methylene protons α to the oxime moiety of the *anti* isomer as a singlet at higher field than that of the *syn* isomer.[12] The following reactions with tosyl isocyanate (a typical procedure is given for **2a**) were carried out without further purification of the oximes.



M = Na, R_2NH_2

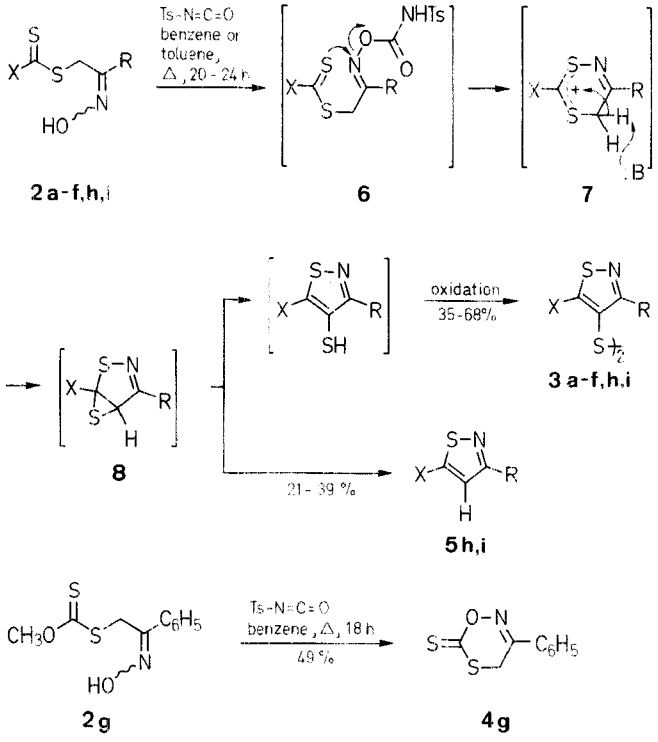
2	X	R	2	X	R
a	$(CH_3)_2N$	C_6H_5	**e**	$(CH_3)_2N$	CH_3
b	$(C_2H_5)_2N$	C_6H_5	**f**	$(CH_3)_2N$	H
c		C_6H_5	**g**	CH_3O	C_6H_5
d		C_6H_5	**h**	C_2H_5S	C_6H_5
			i	*i*-C_3H_7S	C_6H_5

Scheme A

The reactions of the other 2-(hydroxyimino)alkyl *N,N*-dialkyldithiocarbamates **2b–f** with tosyl isocyanate gave similar results. The reactions of alkyl 2-(hydroxyimino)alkyl trithiocarbonates **2h, i** with tosyl isocyanate were carried out similarly in boiling toluene to give the disulfides **3h, i** together with considerable amounts of isothiazoles **5h, i**. In contrast, the reaction of *S*-[2-(hydroxyimino)-2-phenylethyl] *O*-methyl dithiocarbonate (**2g**) with tosyl isocyanate gave an intramolecular

substitution product, the 4*H*-1,5,2-oxathiazine-6-thione **4g**, without formation of the disulfide **3g** or the isothiazole **5g**. In all cases, Beckmann rearrangement products such as amides were not detected.

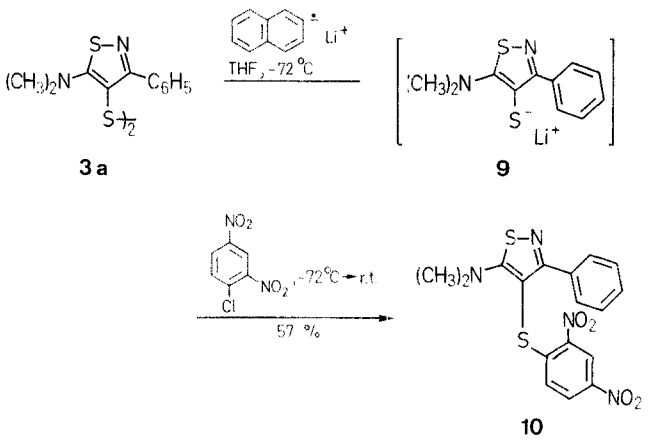
The reaction seems to be proceed as illustrated in Scheme **B**. At first, the hydroxy group of the oxime **2** reacts with tosyl isocyanate to form the intermediate **6** which undergoes intramolecular cyclocondensation to give the 1^+-1,3,4-dithiazinium ion **7**; proton abstraction at C-6 then results in the formation of the bicyclic heterocycle **8** which upon cleavage of the episulfide followed by oxidation gives the bis(4-isothiazolyl) disulfide **3**. The isothiazole **5** may be formed by sulfur extrusion from **8**.[14] Electron donation from the hetero atom seems to be a driving force for this reaction.



Scheme **B**

The structural assignment of the bis(4-isothiazolyl) disulfides **3** was performed on the basis of element analysis, mass, ^{1}H-NMR and ^{13}C-NMR spectra. For example, the mass spectrum of **3a** showed a parent ion (M^+) at $m/e = 470$ and a fragment ion at $m/e = 235$; the latter is assumed to be formed by cleavage of the $S-S$ bond. The ^{1}H-NMR spectrum showed a singlet peak at $\delta = 3.08$ ppm due to methyl protons and multiplet peaks at $\delta = 7.3-7.5$ ppm due to aromatic protons. The ^{13}C-NMR spectrum showed three characteristic signals of the isothiazole ring at $\delta = 178.3$, 172.1, and 101.5 ppm[15,16,17] four aromatic carbon signals at $\delta = 136.2$, 129.2, 128.2, and 127.6 ppm, and a methyl signal at $\delta = 43.3$ ppm and thus clearly suggested the symmetrical structure **3a**.

The disulfide moiety of **3a** was further ascertained by the reaction with lithium naphthalenide.[18] Treatment of **3a** with two molecular equivalents of lithium naphthalenide in tetrahydrofuran at −72 °C under an argon atmosphere gave a pale brown solution of lithium 5-(dimethylamino)-3-phenyl-isothiazole-4-thiolate (**9**). The solution was quenched by addition of an equimolecular amount of 1-chloro-2,4-dinitrobenzene to afford a 57% yield of 5-(dimethylamino)-4-(2,4-dinitrophenylthio)-3-phenylisothiazole (**10**; Scheme **C**) as orange crystals.



Scheme **C**

Melting points were determined using a Yanagimoto melting point apparatus and are uncorrected. Microanalyses were performed by Elemental Analysis Center of Osaka University and Kyoto University. Mass spectra were recorded on a Hitachi RMU-6M mass spectrometer at an ionizing voltage of 20 eV. High-resolution mass spectra were recorded on a JEOL DX-300 mass spectrometer at an ionizing voltage of 20 eV. The IR spectra were measured on a JASCO grating IR spectrometer IR-G. The ^{1}H-NMR spectra were recorded on Hitachi R-24 (60 MHz), Hitachi R-22 (90 MHz), and JEOL-JNM-GX 270 (270 MHz) instruments. ^{13}C-NMR spectra were recorded on a JEOL-JNM-GX 270 (64.5 MHz) instrument.

2-Hydroxyimino-2-phenylethyl *N,N*-Dimethyldithiocarbamate (2a); Typical Procedure:

A mixture of ω-chloroacetophenone oxime (**1**; R = C_6H_5; 510 mg, 3.0 mmol) and sodium *N,N*-dimethyldithiocarbamate (540 mg, 3.0 mmol) in ethanol (150 ml) is stirred for 18 h at room temperature. The solvent is then removed and the residue is extracted with dichloromethane (80 ml). The extract is washed with water (5 × 100 ml) and dried with sodium sulfate. Removal of the solvent followed by recrystallization from dichloromethane/hexane (1:2) gives a mixture of *syn*- and *anti*-2-hydroxyimino-2-phenylethyl *N,N*-dimethyldithiocarbamate (**2a**) as colorless needles; yield: 490 mg (64%; *syn*-**2a**/*anti*-**2a** = 9:1); m.p. 113–114 °C.

$C_{11}H_{14}N_2OS_2$	calc.	C 51.94	H 5.55	N 11.01
(256.4)	found	51.88	5.49	11.00

***S*-(2-Hydroxyimino-2-phenylethyl) *O*-Methyl Dithiocarbonate (2g):**

A mixture of sodium *O*-methyl dithiocarbonate (660 mg, 5.0 mmol) and ω-chloroacetophenone oxime (**1**, R = C_6H_5; 845 mg, 5.0 mmol) in ethanol (80 ml) is stirred at room temperature for 2 h. The solvent is then removed and the residue is extracted with ether (60 ml), washed with water (3 × 50 ml), and dried with sodium sulfate. Removal of the solvent gives the oxime **2g** as colorless needles; yield: 1.052 g (87%). Pure **2g** is obtained by recrystallization from hexane; m.p. 61–63 °C.

$C_{10}H_{11}NO_2S_2$	calc.	C 49.77	H 4.59	N 5.80
(241.3)	found	49.74	4.57	5.94

Ethyl 2-Hydroxyimino-2-phenylethyl Trithiocarbonate (2h); Typical Procedure:

To a solution of ω-chloroacetophenone oxime (**1**, R = C_6H_5; 848 mg, 5.0 mmol) in ethanol (40 ml) is added to a solution of potassium ethyl trithiocarbonate (885 mg, 5.0 mmol) in ethanol (40 ml). The mixture is stirred for 2 h at room temperature. The solvent is then removed and the residue is extracted with dichloromethane (60 ml), washed with water (3 × 50 ml), and dried with sodium sulfate. Removal of the solvent gives a mixture of *syn*- and *anti*-2-hydroxyimino-2-phenylethyl ethyl trithiocarbonate (**2h**) as yellow needles; yield: 432 mg (69%; syn-**2h**/*anti*-**2h** = 1:20). Recrystallization from hexane/dichloromethane (4:1) gives pure sample; m.p. 64–66 °C.

$C_{11}H_{13}NOS_3$	calc.	C 48.68	H 4.87	N 5.16
(271.4)	found	48.72	4.77	5.19

Bis[5-dimethylamino-3-phenyl-4-isothiazolyl] Disulfide (3a); Typical Procedure:

A mixture of 2-hydroxyimino-2-phenylethyl *N,N*-dimethyldithiocarbamate (**2a**; 510 mg, 2.0 mmol) and tosyl isocyanate (0.56 ml,

788 mg, 4 mmol) in benzene (60 ml) is refluxed for 24 h under argon. The solvent is then removed and the residue is column-chromatographed on silica gel (dichloromethane/hexane 7:1 as eluent) followed by preparative TLC (dichloromethane/hexane 20:1) to give crude **3a** as yellow crystals; yield: 216 mg (46%). Recrystallization from ethyl acetate/hexane (1:2) gives pure **3a**; m.p. 152–154°C.

$C_{22}H_{22}N_4S_4$	calc.	C 56.14	H 4.71	N 11.90	S 27.95
(470.7)	found	55.96	4.63	11.68	27.73

3-Phenyl-6-thioxo-4*H*-1,5,2-oxathiazine (4g):
A mixture of *S*-(2-hydroxyimino-2-phenylethyl) *O*-methyl dithiocarbonate (**2g**; 121 mg, 0.5 mmol) and tosyl isocyanate (0.14 ml, 197 mg, 1.0 mmol) in benzene (20 ml) is refluxed for 18 h under argon. The solvent is then removed and the residue is column-chromatographed on silica gel (dichloromethane/hexane 1:1 as eluent) followed by preparative TLC (dichloromethane/hexane 1:1 as eluent: $R_f = 0.36$) to give product **4g** as yellow needles; yield: 51 mg (49%). Pure **4g** is obtained by recrystallization from dichloromethane/hexane; m.p. 81–83°C.

$C_9H_7NOS_2$	calc.	C 51.65	H 3.37	N 6.65
(209.3)	found	51.84	3.33	6.69

Bis[5-ethylthio-3-phenyl-4-isothiazolyl] Disulfide (3h) and 5-(Ethylthio)-3-phenylisothiazole (5h); Typical Procedure:
A mixture of ethyl 2-hydroxyimino-2-phenyl trithiocarbonate (**2h**; 135 mg, 0.5 mmol) and tosyl isocyanate (0.14 ml, 197 mg, 1.0 mmol) in toluene (20 ml) is refluxed for 20 h under argon. The solvent is then removed and the residue column-chromatographed on silica gel (dichloromethane/hexane, 1:1 as eluent), and further purified by preparative TLC on silica gel (hexane/ethyl acetate 10:1 as eluent) to give the disulfide **3h** as a yellow oil; yield: 44 mg (35%); R_f: 0.30.

$C_{22}H_{20}N_2S_6$	calc.	C 52.35	H 3.99	N 5.55
(504.8)	found	52.05	3.95	5.21

In addition, the isothiazole **5h** is obtained as an orange-yellow oil; yield: 23 mg (21%); R_f: 0.66.

$C_{11}H_{11}NS_2$	calc.	C 59.69	H 5.01	N 6.33
(221.3)	found	59.44	5.21	6.06

5-Dimethylamino-4-(2,4-dinitrophenylthio)-3-phenylisothiazole (10):
To a stirred solution of disulfide **3a** (47 mg, 0.1 mmol) in dry tetrahydrofuran (4 ml) at −72°C under argon is added dropwise a 0.51 molar solution of lithium naphthalenide in tetrahydrofuran (0.44 ml,

Table 1. 2-(Hydroxyimino)alkyl Dialkyldithiocarbamates (**2a–f**), *S*-(2-Hydroxyimino-2-phenylethyl) *O*-Methyl Dithiocarbonate (**2g**), and Alkyl 2-(Hydroxyimino)alkyl Trithiocarbonates (**2h, i**) Prepared

Product	Yield (%)[a]	m.p. (°C)	Molecular Formula[b]	MS (20 eV) *m/e* (M^+)	IR (KBr) ν (cm^{-1})	UV λ_{max} (nm) (log ε)	^{1}H-NMR ($CDCl_3$) δ (ppm)
2a	64[c]	112–113 (CH_2Cl_2/hexane)	$C_{11}H_{14}N_2OS_2$ (254.4)	254	1490 N–(C=S)	(ethanol): 251 (4.25); 271 sh (4.14)	3.46 (br, 6H, $2CH_3$); 4.55 (s, 2H, CH_{2anti}); 4.75 (s, 2H, CH_{2syn}); 7.2–7.8 (m, $5H_{arom}$); 9.2–9.4 (br, 1H, OH)
2b	58[d]	100–101 (CH_2Cl_2/hexane)	$C_{13}H_{18}N_2OS_2$ (282.4)	282	3300 (OH); 1490 N–(C=S)	(ethanol): 250 (4.31); 271 sh (4.16)	1.24 (t, 6H, $2CH_3$); 3.4–4.3 (br, 4H, $2CH_2$); 4.52 (s, 2H, CH_{2anti}); 4.73 (s, 2H, CH_{2syn}); 7.7–8.4 (m, $5H_{arom}$); 8.4–8.7 (br, 1H, OH)
2c	70[d]	133–134 (CH_2Cl_2/hexane)	$C_{13}H_{16}N_2OS_2$ (280.4)	280	1650 (C=N); 1474 N–(C=S)	(ethanol): 250 (4.33); 273 sh (4.17)	1.8–2.2 (m, $4H_{pyrrolidine}$); 3.4–4.2 (m, $4H_{pyrrolidine}$); 4.55 (s, 2H, CH_{2anti}); 4.80 (s, 2H, CH_{2syn}); 7.2–7.9 (m, $5H_{arom}$); 9.3–9.7 (br, 1H, OH)
2d	79[d]	140–141 (CH_2Cl_2/hexane)	$C_{14}H_{18}N_2OS_2$ (294.4)	294	3300 (OH); 1480 N–(C=S)	(ethanol): 253 (4.35); 273 sh (4.20)	1.5–1.9 (m, $6H_{piperidine}$); 3.7–4.5 (m, $4H_{piperidine}$); 4.60 (s, 2H, CH_{2anti}); 4.80 (s, 2H, CH_{2syn}); 7.3–8.0 (m, $5H_{arom}$); 9.2–9.6 (br., 1H, OH)
2e	47[c]	95–96 (CH_2Cl_2/hexane)	$C_6H_{12}N_2OS_2$ (192.3)	192	1510 N–(C=S)	(ethanol): 253 (3.98); 279 (4.04)	1.98 (s, 3H, CH_3); 3.2–3.8 (br, 6H, $2CH_3$); 4.29 (s, 2H, CH_{2anti}); 4.38 (s, 2H, CH_{2syn}); 9.2–9.7 (br., 1H, OH)
2f	68[c]	109–110 (CH_2Cl_2/hexane)	$C_5H_{10}N_2OS_2$ (178.3)	178	1665 (C=N); 1485 N–(C=S)	(ethanol): 246 (3.95); 276 (3.96)	3.2–3.7 (m, 6H, $2CH_3$); 4.18 (d, 2H, CH_2); 7.3 (br, 1H, CH); 7.5–8.0 (br., 1H, OH)[e]
2g	87	119–121 (CH_2Cl_2/hexane)	$C_{10}H_{11}NO_2S_2$ (241.3)	241	3250 (OH); 1670 (C=N)	(CH_2Cl_2): 277 (4.09)	4.14 (s, 3H, CH_3); 4.32 (s, 2H, CH_2); 7.2–7.8 (m, $5H_{arom}$); 8.1–8.9 (br, 1H, OH)
2h	75	92–94 (hexane)	$C_{11}H_{13}NOS_3$ (271.4)	271	3250 (OH); 1050 (C=S)	(CH_2Cl_2): 308 (4.29); 429 (1.86)	1.30, 1.33 (2t, 3H, CH_3); 3.34, 3.37 (2q, 2H, CH_2); 4.52 (s, 2H, CH_{2anti}); 4.75 (s, 2H, CH_{2syn}); 7.2–7.6 (m, $5H_{arom}$); 8.2–8.6 (br, 1H, OH)
2i	71	90–92 (hexane)	$C_{12}H_{15}NOS_3$ (285.4)	285	3250 (OH); 1050 (C=S)	(CH_2Cl_2): 308 (4.39); 429 (1.76)	1.36, 1.38 (2d, 6H, $2CH_3$); 4.16 (m, 1H, CH); 4.47 (s, 2H, CH_{2anti}); 4.73 (s, 2H, CH_{2syn}); 7.2–7.6 (m, $5H_{arom}$); 8.6–8.9 (br, 1H, OH)

[a] Yields of a mixture of *syn* and *anti* isomers: Ratio **2a–d** *syn*/*anti* = 9:1, **2e** *syn*/*anti* = 3:7, **2f, g** *anti* isomer only, **2h, i** *syn*/*anti* = 2:8.

[b] Satisfactory microanalyses obtained: C ±0.12, H ±0.16, N ±0.19, S ±0.29.

[c] Sodium dimethyldithiocarbamate was used.

[d] The corresponding dialkylammonium salt was used.

[e] Addition of a few drops of D_2O shows the formation of a mixture of *syn* and *anti* isomers (1:1); δ = 3.2–3.7 (m, 6H, $2CH_3$); 4.16 (d, 2H, CH_{2anti}); 4.24 (d, CH_{2syn}); 6.70 (t, 1H, CH_{syn}); 7.54 ppm (t, CH_{anti}).

Table 2. Reaction of Compounds **2a–i** with Tosyl Isocyanate

Reactant	Product	Yield[a] (%)	m.p. (°C)	Molecular Formula[b]	MS (20 eV) *m/e*	UV λ_{max} (nm) (log ε)	^{1}H-NMR ($CDCl_3$) δ (ppm)
2a	**3a**	46	154–155 (ethyl acetate/hexane)	$C_{22}H_{22}N_4S_4$ (470.7)	470 (M^+), 235 ($M^+/2$)	(ethanol): 297 (3.96); 348 sh (3.44)	3.08 (s, 12H, $4CH_3$); 7.3–7.5 (m, $10H_{arom}$)
2b	**3b**	38	97–99 (CH_2Cl_2/hexane)	$C_{26}H_{30}N_4S_4$ (526.8)	526 (M^+), 263 ($M^+/2$)	(ethanol): 298 (4.09); 340 sh (3.70)	1.22 (t, 12H, $4CH_3$); 3.5 (br, 8H, $4CH_2$); 7.3–7.4 (m, $10H_{arom}$)
2c	**3c**	68	203–204 (ethyl acetate/hexane)	$C_{26}H_{26}N_4S_4$ (522.8)	522 (M^+), 261 ($M^+/2$)	(ethanol): 297 (3.99); 347sh (3.37)	1.9 (m, $8H_{pyrrolidine}$); 3.3 (m, $8H_{pyrrolidine}$); 7.1–7.6 (m, $10H_{arom}$)
2d	**3d**	46	133–134 (hexane)	$C_{28}H_{30}N_4S_4$ (550.8)	550 (M^+), 275 ($M^+/2$)	(ethanol): 301 (3.96); 335 sh (3.60)	1.6 (m, $12H_{piperidine}$); 3.4 (m, $8H_{piperidine}$); 7.3–7.4 (m, $10H_{arom}$)
2e	**3e**	44	189–192 (ethanol)	$C_{12}H_{18}N_4S_4$[c] (346.5)	346 (M^+), 173 ($M^+/2$)	(ethanol): 282 (4.08); 318 sh (3.58)	2.31 (s, 6H, $2CH_3$); 3.05 (s, 12H, $4CH_3$)
2f	**3f**	36	109–111 (ethanol)	$C_{10}H_{14}N_4S_4$ (318.5)	318 (M^+), 159 ($M^+/2$)	(ethanol): 285 (4.09); 315 sh (3.70)	3.09 (s, 12H, $4CH_3$); 7.94 (s, $2H_{ring}$)
2g	**4g**	49	81–83 (CH_2Cl_2/hexane)	$C_9H_7NOS_2$ (209.3)	209 (M^+)	(CH_2Cl_2): 258 (4.06); 295 (4.02)	4.27 (s, 2H, CH_2); 7.5–8.0 (m, $5H_{arom}$)
2h	**3h**	35	yellow oil	$C_{22}H_{20}N_2S_6$ (504.8)	504 (M^+), 252 ($M^+/2$)	(CH_2Cl_2): 252 (4.49); 289 sh (4.30)	1.41 (t, 6H, $2CH_3$); 2.96 (q, 4H, $2CH_2$); 7.2–7.7 (m, $10H_{arom}$)
	5h	21	orange oil	$C_{11}H_{11}NS_2$ (221.3)	221 (M^+)	(CH_2Cl_2): 275 (4.20)	1.38 (t, 3H, CH_3); 2.99 (q, 2H, CH_2); 7.2–8.1 (m, $6H_{ring+arom}$)
2i	**3i**	40	yellow oil	$C_{24}H_{24}N_2S_6$[d] (532.8)	532 (M^+), 266 ($M^+/2$)	(CH_2Cl_2): 248 (4.36); 290 sh (4.14)	1.39 (d, 12H, $4CH_3$); 3.36 (sept, 2H, 2CH); 7.2–7.9 (m, $10H_{arom}$)
	5i	39	orange oil	$C_{12}H_{13}NS_2$ (235.4)	235 (M^+)	(CH_2Cl_2): 274 (4.20)	1.38 (d, 6H, $2CH_3$); 3.38 (sept, 1H, CH); 7.1–8.1 (m, $6H_{ring+arom}$)

[a] Yield of isolated product.
[b] Satisfactory microanalyses obtained: C ±0.30, H ±0.29, N ±0.34, S ±0.22. Exception **3b**, C +0.48.
[c] Exact Mass: calc. *m/e* = 346.041, found *m/e* = 346.040. (JEOL JMS DX-300 at Kyushu Institute of Technology).
[d] Exact Mass: calc. *m/e* = 532.026, found *m/e* = 532.023 (as in c).

Table 3. ^{13}C-NMR-Spectral Data ($CDCl_3$) of Some Compounds **3** and **5**

Compound	δ (ppm)	
	C-Atoms of Isothiazole Ring	Other C-Atoms
3a	178.3, 172.2, 101.5	136.2, 129.2, 128.2, 127.6 (phenyl); 43.3 (CH_3)
3b	176.2, 172.2, 100.4	136.6, 129.3, 128.2, 127.6 (phenyl); 47.6, 12.4 (C_2H_5)
3d	179.4, 171.7, 104.1	136.2, 129.2, 128.2, 127.6 (phenyl); 51.8, 25.2, 23.8 (piperidine)
3e	177.2, 171.8, ?[a]	43.3, 19.7 (CH_3)
3h	172.4, 169.6, 122.0	134.4, 128.9, 128.7, 127.9 (phenyl); 28.7, 14.1 (C_2H_5)
5h	167.8, 162.4, 121.1	134.6, 129.3, 128.8, 126.8 (phenyl); 30.8, 14.6 (C_2H_5)

[a] Not observed, probably because of low concentration.

0.22 mmol). The mixture is stirred for 15 min. Then, 1-chloro-2,4-dinitrobenzene (41 mg, 0.2 mmol) is added and the mixture is stirred for 5 min at −72 °C and for additional 1 h at room temperature. Removal of the solvent followed by preparative TLC on silica gel (dichloromethane/hexane 10:1 as eluent) gives the isothiazole **10**; yield: 23 mg (57%); R_f: 0.53; m.p. 179–181 °C.

$C_{17}H_{14}N_4O_4S_2$ (402.4) calc. C 50.74 H 3.51 N 13.92
found 50.43 3.46 13.66

MS (20 eV): *m/e* = 402 (M^+).

IR (KBr): ν = 1590, 1528 cm^{-1} (NO_2).

^{1}H-NMR ($CDCl_3$): δ = 3.24 (s, 6H, $2CH_3$); 7.18 (d, *J* = 9.2 Hz, $1H_{arom}$); 7.2–7.5 (m, 5H, C_6H_5); 8.22 (dd, *J* = 9.2 Hz, 2.6 Hz, $1H_{arom}$); 9.03 ppm (d, *J* = 2.6 Hz, $1H_{arom}$).

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(19) *Note added in proof:* The failure of **2g** in intramolecular cyclocondensation reaction may be attributable to the low nucleophilicity of thiocarbonyl sulfur, since the energy of the nonbonding orbital is lowered by the interaction with the σ* orbital of the O–CH_3 bond.