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Author	山本, 有一(Yamamoto, Yuichi) 与田, 玲子(Yoda, Reiko)
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Studies on Thiazole and Thiazoline Derivatives (XVII)
Methylation of N-Alkyl (or N, N-dialkyl)-N'-(2-thiazolyl)
thiourea derivatives.¹⁾

YUICHI YAMAMOTO and REIKO YODA

山本有一, 与田玲子

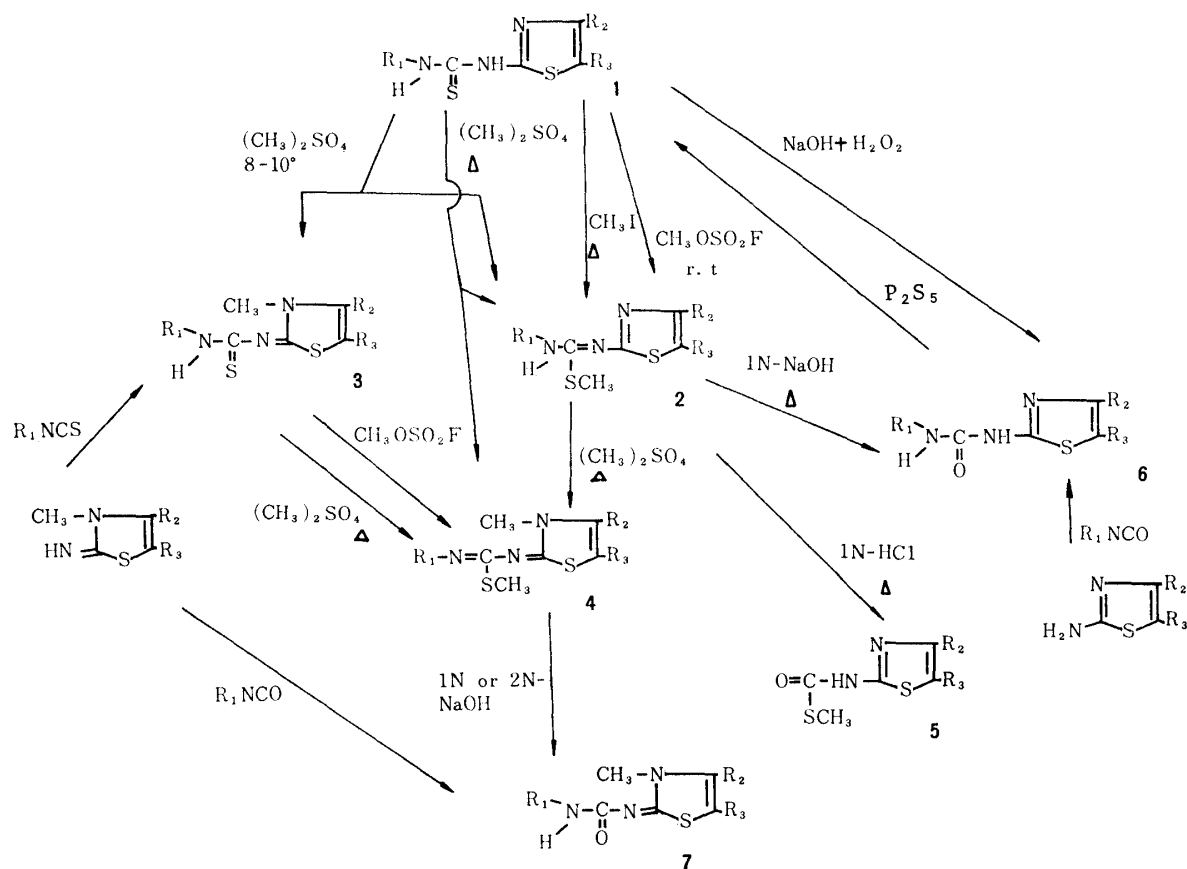
(Received October 1, 1979)

As shown in Scheme 1 and 2, methylation of title compounds was examined by various kinds of methyl agents. S-methyl derivatives and ring N-methyl derivatives as mono-methyl substituent and ring N,S-dimethyl derivatives as di-methyl substituents were obtained and the structure of these compounds was identified by NMR, Mass, IR, elemental analysis, and the hydrolyzed products of their methyl derivatives. Among them, we found that when S-methyl derivatives, N,N-dimethyl-N'-(4-methyl (or 4,5-dimethyl)thiazole)-S-methylisothiourea, were heated at 155—160°, ring N-methyl derivatives, N,N-dimethyl-N'-(3,4-dimethyl (or 3,4,5-trimethyl)thiazole-2-ylidene) thiourea were obtained. A detailed methyl rearrangement will be reported elsewhere at a later date.

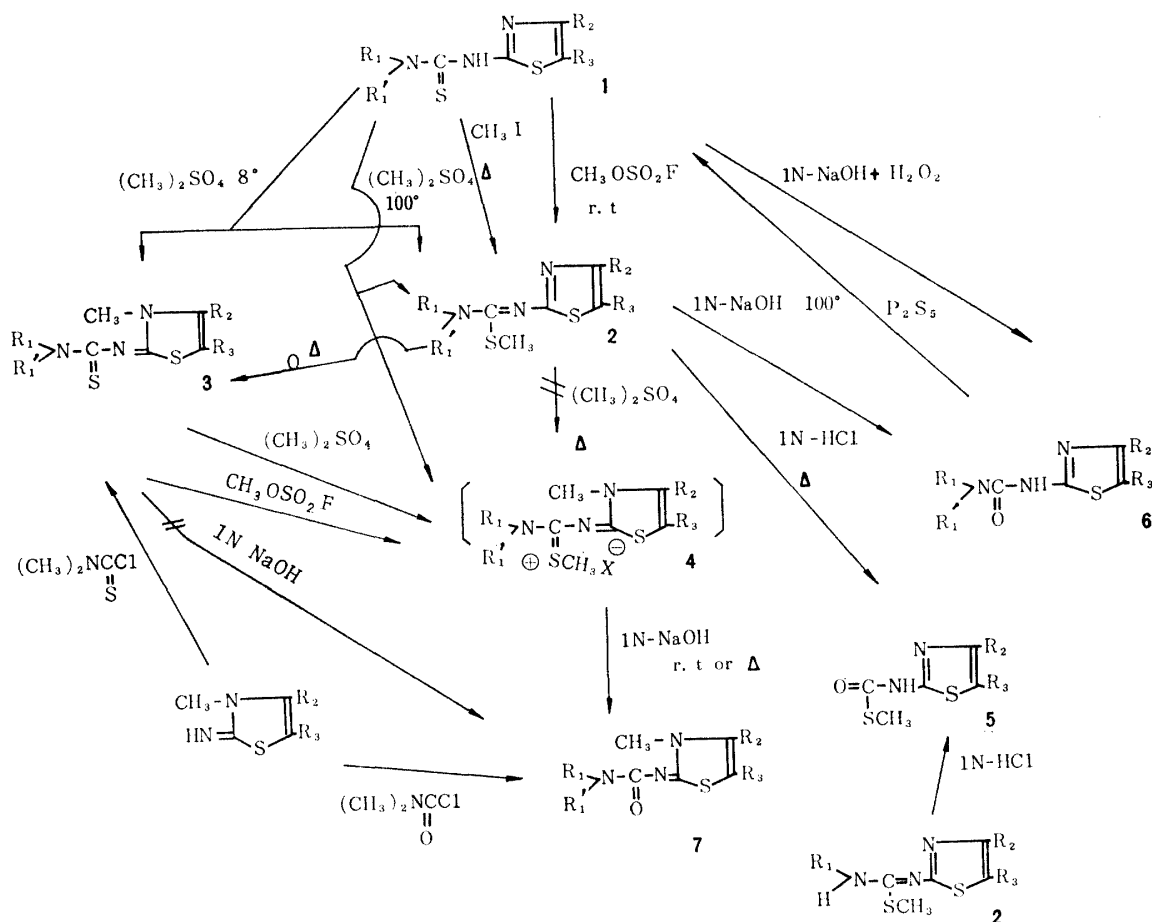
For many years we have synthesized ureido and thioureido derivatives of thiazoles, thiazolines and oxazolines, and studied relationships between their biological activities and structures, as well as their chelate formation with metallic ions such as Pd²⁺, Cu²⁺, Hg²⁺, Au³⁺ etc²⁾. Thioureido derivatives exhibited effectively biological activity, but showed an oral toxicity in rat. This communication describes methylation of thioureido thiazole derivatives as shown in Scheme 1, 2 and Table I. The effects depending upon the reaction conditions with various methyl agents such as (CH₃)₂SO₄, CH₃OSO₂F (magic methyl) and CH₃I were examined and identified the structure of their products. In the case of N-Alkylthioureidothiazoles, **1a** to **1e**, possible positions of methylation are four as marked→(arrow) in Scheme 3 and N,N-dialkylthioureidothiazoles, **1f**, **1g**, are two. On the other hand dimethyl-substituents of compounds **1** may be also considered for methylation.

To a solution of **1a** in 2N-NaOH solution was added an equivalent of (CH₃)₂SO₄ (or molar ratio of 1:2), the mixture was left at 8—10° for several hours. The resulting yellow precipitate was filtered and neutralized with NaHCO₃ solution to afford free base

- 1) Y. Yamamoto and R. Yoda, S-methylation were presented at the 98 Annual Meeting of the Yakugakukai April 4 (1978) (preprints 283p, 1978)
- 2) Y. Yamamoto, K. Horiuchi, R. Yoda, K. Kubo, and Y. Murakami, Kyoritsu Yakka Daigaku Kenkyu Nempo (abbreviated hereafter: Kyoyaku nempo) **18**, **64** (1973), **CA 80**, 140793n (1974). Y. Yagi, K. Horiuchi, R. Yoda, Y. Yamamoto, and Y. Murakami, Nippon Kagaku Kaishi, 831 (1975), **CA 83**, 125678x (1975).

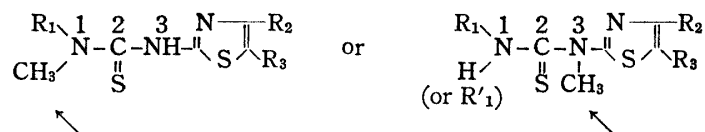


(mp 42—102°) which had a widely distributed melting point. On the TLC (solvent: ether) of raw products with 42—102°, two spots appeared showing *R_f*-values 0.75 and 0.29 and these data suggested the mixture of two derivatives. For the purpose of characterization, the crude products were separated by an ethanol-soluble product having *R_f* value of 0.75 and the other one as ethanol-insoluble product having *R_f*-value of 0.29. Based on spectroscopic data the former was identified N-methyl-N'-(2-thiazolyl)-S-methylisothiourea, **2a**, (S-methyl derivatives) and the latter, N-methyl-N'-(3-methyl-4-thiazolyl-2-ylidene)thiourea, **3a**, (ring N-methyl derivatives). Thermal reaction of **1a** with an equivalent of (CH₃)₂SO₄ in the absence of solvents gave S-methyl derivative **2a** and N-methyl-N'-(3-methyl-4-thiazolin-2-ylidene)-S-methylisothiourea (ring N,S-dimethyl derivative) **4a**. Methyl group was introduced to both sulfur of thiocarbonyl group and nitrogen at the 3 position of thiazole ring. Only trace amounts of ring N-methyl derivative **3a** was observed on TLC. Mono-methyl substituents, S-methyl or ring N-methyl derivatives, were furthermore reacted with various kinds of methyl agents to afford ring N,S-dimethyl derivatives. Compounds **4** were given high yields.



Scheme 2

On the other hand we expected methylation of 1-nitrogen and 3-nitrogen of thioureido group, isomeric to each other, as shown below (marked→). However these methylated

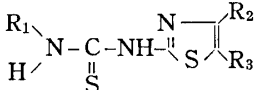
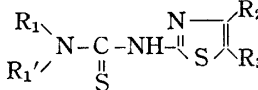
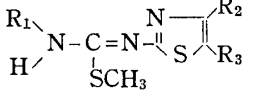
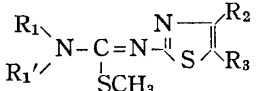
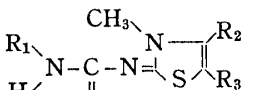
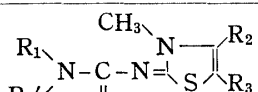
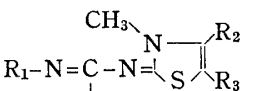
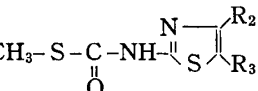


products were not obtained, these compounds had already reported *via* another route.^{3,6} Next, an equimolar mixture of compound 1 and CH₃OSO₂F (or a small excess of CH₃OSO₂F) was stirred at room temperature for several days and resulting precipitate was collected. After neutralization of 1N-NaOH solution, white crystals of S-methyl derivatives were afforded.

In order to confirm structures of S-methyl derivatives, 2 were hydrolyzed with 1N-NaOH solution at *ca.* 100° and was given white crystals which showed at 1680 cm⁻¹ for a strong

- 3) Y. Yamamoto, H. Nakamura, R. Yoda, M. Inoue, and S. Kato, *Kyoyaku nempo*, **12**, 116 (1967), *CA* **69**, 96554g (1968). R. Yoda and Y. Yamamoto, *ibid.* **18**, 37 (1973), *CA* **81**, 77824b (1974). Y. Yamamoto, R. Yoda, and K. Sekine, *Chem. Letters*, 1299 (1977).

Table I Substituents of thioureidothiazole derivatives.

structures	compd. No.	substituents	ref.	UV λ_{max} 2-PrOH nm ($\epsilon \times 10^{-3}$)
	1a	$R_1 = \text{CH}_3, R_2 = R_3 = \text{H}$	3)	254.5 (10.4) 289 (20.4)
	1b	$R_1 = R_2 = \text{CH}_3, R_3 = \text{H}$	3)	255 (8.9) 292.5 (19.7)
	1c	$R_1 = \text{C}_2\text{H}_5, R_2 = \text{CH}_3, R_3 = \text{H}$	mp 242 (dioxane)	258 (9.9) 294 (19.6)
	1d	$R_1 = (\text{CH}_3)_2\text{H}, R_2 = \text{CH}_3, R_3 = \text{H}$	mp 171.5 (EtOH)	259 (9.9) 294.5 (18.5)
	1e	$R_1 = R_2 = R_3 = \text{CH}_3$	mp 207 (EtOH)	256 (8.2) 298 (18.0)
	1f	$R_1 = R_1' = R_2 = \text{CH}_3, R_3 = \text{H}$	3)	293 (7.9) 329 (15.4)
	1g	$R_1 = R_1' = R_2 = R_3 = \text{CH}_3$	3)	289 (8.1) 332 (15.7)
	2a	$R_1 = \text{CH}_3, R_2 = R_3 = \text{H}$		
	2b	$R_1 = R_2 = \text{CH}_3, R_3 = \text{H}$		
	2c	$R_1 = \text{C}_2\text{H}_5, R_2 = \text{CH}_3, R_3 = \text{H}$		
	2d	$R_1 = (\text{CH}_3)_2\text{CH}, R_2 = \text{CH}_3, R_3 = \text{H}$		
	2e	$R_1 = R_2 = R_3 = \text{CH}_3$		
	2f	$R_1 = R_1' = R_2 = \text{CH}_3, R_3 = \text{H}$		
	2g	$R_1 = R_1' = R_2 = R_3 = \text{CH}_3$		
	3a	$R_1 = \text{CH}_3, R_2 = R_3 = \text{H}$		
	3b	$R_1 = \text{C}_2\text{H}_5, R_2 = R_3 = \text{H}$		
	3c	$R_1 = (\text{CH}_3)_2\text{CH}, R_2 = R_3 = \text{H}$		
	3d	$R_1 = R_2 = \text{CH}_3, R_3 = \text{H}$	4)	
	3e	$R_1 = \text{C}_2\text{H}_5, R_2 = \text{CH}_3, R_3 = \text{H}$	4)	
	3f	$R_1 = (\text{CH}_3)_2\text{CH}, R_2 = \text{CH}_3, R_3 = \text{H}$	4)	
	3g	$R_1 = R_2 = R_3 = \text{CH}_3$		
	3h	$R_1 = R_1' = R_2 = \text{CH}_3, R_3 = \text{H}$		
	3i	$R_1 = R_1' = R_2 = R_3 = \text{CH}_3$		
	4a	$R_1 = \text{CH}_3, R_2 = R_3 = \text{H}$		
	4b	$R_1 = R_2 = \text{CH}_3, R_3 = \text{H}$		
	4c	$R_1 = \text{C}_2\text{H}_5, R_2 = \text{CH}_3, R_3 = \text{H}$		
	4d	$R_1 = (\text{CH}_3)_2\text{CH}, R_2 = \text{CH}_3, R_3 = \text{H}$		
	4e	$R_1 = R_2 = R_3 = \text{CH}_3$		
	5a	$R_2 = R_3 = \text{H}$		
	5b	$R_2 = \text{CH}_3, R_3 = \text{H}$		
	5c	$R_2 = R_3 = \text{CH}_3$		

amide vibration in IR spectra. These hydrolyzed products were identical with the known N-Alkyl-N'-(2-thiazolyl)ureido derivatives, **6**.⁵⁾ Thiourea derivatives **1** was oxidized with H₂O₂ in 1N-NaOH solution to give also compounds **6**. Then, in order to confirm structures of ring N,S-dimethyl derivatives, **4** were also hydrolyzed by the same treatment as just above mentioned. These hydrolyzed products were identical with the known N-Alkyl-N'-(3-methylthiazol-2-ylidene)ureido derivatives **7**.⁴⁾ In connection with elimination of SCH₃ group T.A. Briody *et al.* reported recently that elimination-addition mechanism was due to the base catalyzed conversion of S-Alkylisothiureas to ureas.⁷⁾

On heating of S-methyl derivative **2a** with 1N-HCl solution at around 100°, a HCl-salt was afforded which was neutralized to yield a free base as white crystals with mp 170—174°. It showed a molecular ion peak at *m/e* 174 (Relative intensity: 40%) and a fragment peak at *m/e* 126 (49%) which was corresponding to [M⁺-CH₃SH] and at *m/e* 100 (63%) corresponding to 2-aminothiazole cation. In the 100 MHz NMR spectrum (CDCl₃) it showed signals at δ 2.48 (s, 3H, CH₃), δ 7.58 and δ 6.89 (m, 1H, CH, 4 and 5 position of thiazole ring, respectively) and δ 13.16 (broad, 1H, NH, disappeared after D₂O exchange). Compound with mp 170—174° was identified as 2-(methylthiocarbonyl)-aminothiazole **5a** by above mentioned data and elemental analysis. Compound **5a** in the mixture of DMSO-*d*₆ and D₂O was heated at 100° for deuteration. The deuterated compound **5a** showed a molecular ion peak at *m/e* 175 and then a base peak at *m/e* 101

probably for $\text{D}-\text{N}(\text{H})-\text{N}(\text{S})=\text{C}=\text{N}^{\oplus}$.

Methylation of N,N-dimethyl thioureido derivatives, **1f** and **1g**, was also examined by the same manners as shown in Scheme 2. However ring N,S-dimethyl derivatives **4** were not isolated as intermediates. After stirring the mixture of **3h** and methyl agents at room temperature, red oily material obtained was neutralized with 1N-NaOH solution and **7e** with mp 154° was obtained. Compound **7e** was synthesized independently by the reaction of 2-imino-4-methyl-4-thiazoline with N,N-dimethylcarbamoyl chloride. IR and NMR data of this compound agreed with those of **7e** with mp 154°. These data may be explained that, on the first stage ring N,S-dimethyl derivative of **3h** was obtained as HSO₃F salt and then, S-methyl group of this salt was hydrolyzed with 1N-NaOH solution. On the other hand in similar conditions, the reaction of **3h** in 1N-NaOH solution did not give the expected product for **7e**, the compound **3h** being recovered essentially unreacted. Compound **2a** was irradiated at 150° for 17 hr by ultraviolet ray 253 nm, but did not changed.

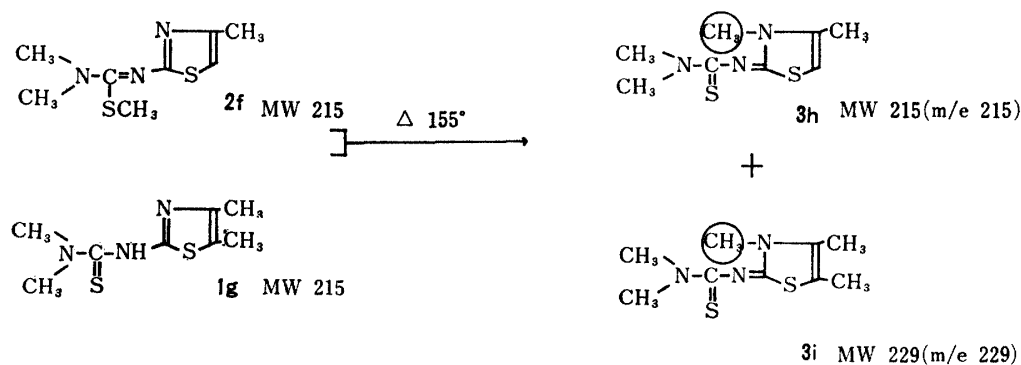
4) Y. Yamamoto, R. Yoda, S. Koda, M. Matsumura, K. Sekine, and Y. Yoshida, *Kyoyaku nempo*, **20**, 57 (1975), *ibid.* **21**, 145 (1976).

5) Y. Yamamoto, H. Nakamura, R. Yoda, N. Kaneko, and R. Usuba, *Kyoyaku nempo*, **11** 42 (1966), *CA68*, 105071f (1968).

6) Y. Yamamoto, R. Yoda, and C. Tamura, *Chem. Letters*, 1147 (1975).

7) T.A. Briody, A.F. Hegarty and F.L. Scott, *Tetrahedron*, **33**, 1469 (1977).

However **2a** was heated at 150° for 140 hr in pyridine to afford only trace amount of ring N,S-dimethyl derivative which was observed on TLC. Its formation of this dimethyl derivative may be explained that after being eliminated of methyl group of S-methyl derivatives, this eliminated methyl group was transferred to nitrogen at the 3-position of a thiazole ring of S-methyl derivative and the resulting N,S-dimethyl derivative was obtained. In the case of N,N-dimethylthioureidothiazole **1f**, after methylation with $\text{CH}_3\text{OSO}_2\text{F}$ by the same manner a raw product was neutralized saturated NaHCO_3 solution and extracted with CHCl_3 . The solvent was removed under reduced pressure and the residual oily material was distilled *in vacuo* (**2f**, bp 154°/0.35 mmHg). S-methyl derivative **2f** was heated at 155° without the addition of solvent and a raw product was purified by silica-gel chromatography using acetone- CHCl_3 (1:2). Treatment with decolorizing carbon, yellow needles with mp 204° were afforded. After treatment as described above, **2g** gave also pale-yellow crystals having mp 224° (EtOH). These compounds were synthesized independently by the reaction of 2-imino-3,4-dimethyl(or 3,4,5-trimethyl)thiazole with N,N-dimethylthiocarbamoylchloride or **4** with $(\text{CH}_3)_2\text{SO}_4$. IR, UV, NMR and mixed mp determination of these compounds agreed with those of the compounds having mp 204° and 224°, respectively. Therefore the structure of compound having of mp 204° was identified as N,N-dimethyl-N'-(3,4-dimethyl-4-thiazolin-2-ylidene)thiourea **3h** and mp 224°, N,N-dimethyl-N'-(3,4,5-trimethyl-4-thiazolin-2-ylidene)thiourea **3i**. We found these were isomeric products which were formed by easy rearrangement of methyl group of isothiourea **2f** or **2g**. In order to clarify whether this transfer mechanism of methyl group was caused either intramolecular rearrangement or intermolecular one, cross reaction was carried out as shown in Scheme 4. Cross reaction products of yellow needles in the Mass spectrum showed a molecular ion peak at m/e 229 which was m/e 14 more than that of starting materials having m/e 215 as shown in Fig. 2. However it was difficult to isolate each of cross products as usual manners.

Scheme 4 Cross reaction of **2f** and **1g**.

UV absorption curves

Comparing with starting materials (thioureido derivatives) S-methyl derivatives indi-

cated blue shifts of about 20–30 nm in the first absorption maximum and red shifts of about 15 nm in the second absorption maximum were observed as shown in Table I, II, and Fig. 1. On the other hand ring N-methyl derivatives showed red shifts of *Ca.* 30 nm both in the first and second absorption maximum, but the ring N,S-dimethyl derivatives indicated that blue shifts of 10 nm in the first absorption maximum and red shifts of 16–20 nm in the second absorption maximum. In the case of S-methyl derivatives of N,N-dimethylthioureido it indicated larger red shifts of 40–67 nm in the first absorption maximum and no change or red shifts of 10 nm in the second absorption maximum.

Mass

Thioureido derivatives **1** (starting materials) showed those own characteristic fragment peaks of $[M^+-RNH]$, $[M^+-RN]$ and $[M^+-SH]$. S-methyl derivatives showed a stable base peak corresponding to $[M^+-CH_3S]$ and no fragment peaks of $[M^+-RNH]$ and $[M^+-RN]$ as mentioned above. N,N-dimethylthioureido derivatives, **2f** and **2g** exhibited a molecular ion at m/e 215 (base), 229 (86%), respectively, and had at m/e 168 (98%), 182 (base) for $[M^+-CH_3S]$, respectively. Ring N-methyl derivatives **3h** and **3i** had a base peak at m/e 171, 185 for $[M^+-(CH_3)_2N]$, at m/e 182 (31%), 196 (6%) for $[M^+-SH]$ and both had a peak at m/e 88 for $(CH_3)_2N^+CS$ which was a characteristic one for N,N-dimethylthioureido derivatives.

Table II-A Physical properties of compounds **2**.

Comp. No.	mp (recryst. solvent)	Formula (MW)	Anal. Calcd. (found)			UV 2-PrOH max nm ($\epsilon \times 10^{-3}$)
			C	H	N	
2a	48~9 (EtOH)	$C_6H_9N_3S_2$ 187.287	38.48	4.84	22.44	226.0 (6.0)
			(38.65)	4.67	22.14)	305.5(18.0)
2b	69~70 (EtOH+H ₂ O)	$C_7H_{11}N_3S_2$ 201.314	41.76	5.51	20.87	231.5 (6.9)
			(41.59)	5.45	20.62)	309.5(17.1)
2c	158~9 * (EtOH+H ₂ O)	$C_8H_{13}N_3S_2$ 215.341	37.83	3.63	18.91	230sh (6.8)
			(37.89)	3.57	18.88)	308 (17.6)
2d	40 (EtOH+H ₂ O)	$C_9H_{15}N_3S_2$ 229.368	47.13	6.59	18.32	236.0 (6.3)
			(48.25)	6.92	16.92)	311.0(17.7)
2e	52 (EtOH)	$C_8H_{13}N_3S_2$ 215.341	44.62	6.09	19.51	215sh (7.1)
			(44.65)	6.15	19.41)	310.0(19.2)
2f	126 * (EtOH+H ₂ O)	$C_8H_{13}N_3S_2$ 215.341	37.83	3.63	18.91	245.0 (8.1)
			(37.61)	3.50	18.20)	316.5 (7.2)
2g	103~4 * (EtOH+H ₂ O)	$C_9H_{15}N_3S_2$ 229.368				246.0 (7.6)
						330.0 (7.1)

* Picrate, sh (shoulder)

Table II-B Physical properties of compounds 3.

Comp. No.	mp (recryst. solvent)	Formula (MW)	Anal. Calcd. (found)			UV 2-PrOH max nm($\epsilon \times 10^{-3}$)
			C	H	N	
3a	154~6 (EtOH)	C ₈ H ₉ N ₃ S ₂ 187.287	38.48	4.84	22.44	287.0(8.0) 323.5(16.0)
			(38.52)	(4.69)	(22.41)	
3b	112~4 (EtOH)	C ₇ H ₁₁ N ₃ S ₂ 201.314	41.76	5.51	20.87	291.0(8.7) 323.0(16.2)
			(41.74)	(5.53)	(20.84)	
3c	137~8 (EtOH)	C ₈ H ₁₃ N ₃ S ₂ 215.341	44.62	6.09	19.51	290.5(10.2) 324.0(17.5)
			(44.71)	(6.26)	(19.58)	
3d	215 (EtOH)	C ₇ H ₁₁ N ₃ S ₂ 201.314	41.76	5.51	20.87	290.0(6.8) 326.0(15.4)
			(42.24)	(5.30)	(20.93)	
3e	213 (EtOH)	C ₈ H ₁₃ N ₃ S ₂ 215.341	44.62	6.09	19.51	291 (10.0) 327 (18.5)
			(44.81)	(5.95)	(19.63)	
3f	181 (EtOH)	C ₉ H ₁₅ N ₃ S ₂ 229.368	47.13	6.59	18.32	290.0(9.3) 327.5(18.5)
			(47.08)	(6.51)	(18.53)	
3g	232 (CHCl ₃)	C ₈ H ₁₁ N ₃ S ₂ 215.341	44.62	6.09	19.51	284.0(5.0) 331.0(16.6)
			(44.61)	(6.11)	(19.58)	
3h	204~6 (EtOH)	C ₈ H ₁₁ N ₃ S ₂ 215.341	44.62	6.09	19.51	295sh(9.5) 327 (17.7)
			(44.62)	(6.07)	(19.23)	
3i	224~6 (EtOH)	C ₉ H ₁₅ N ₃ S ₂ 229.368	47.13	6.59		291.5(8.5) 332.5(17.4)
			(47.36)	(6.83)		

NMR (in CDCl₃ solvent)

S-methyl derivatives **2a**, **b**, **e** exhibited SCH₃ signal at about δ 2.43—2.47 which were a sharp singlet. On the other hand N,S-dimethyl derivatives **4a-c** exhibited SCH₃ signal at δ 2.49—2.53 which were observed at some lower field than that of S-methyl derivatives and a signal due to N-CH₃ at the 3-position of thiazole ring was observed a sharp singlet at δ 3.43—3.57.

Further investigation on mechanism is now in progress.

We are grateful to Miss Tomoko Takahashi for Mass, and Miss Midori Yamazaki and Michiko Yoshida for their assistance in experimental works. We also wish to acknowledge the staff of Department of Physical Chemistry for elemental analysis and the staff of Department of Pharmacology for screening tests, the Central Research Laboratories, Sankyo CO., Ltd..

Table II-C Physical properties of compounds 4 and 5.

Comp. No.	mp (recryst. solvent)	Formula (MW)	Anal. Calcd. (found)				UV 2-PrOH max nm($\epsilon \times 10^{-3}$)
			C	H	N	S	
4a	87~9 (EtOH+H ₂ O)	C ₇ H ₁₁ N ₃ S ₂ 201.314	41.76 (41.57)	5.51 5.30	20.90 20.89	246.0(6.5) 307.0(14.0)	
4b	122 (EtOH+H ₂ O)	C ₈ H ₁₃ N ₃ S ₂ 215.341	44.62 (44.55)	6.09 6.76	19.51 19.38	244.0(5.4) 313.0(12.1)	
4c	105~6 (EtOH+H ₂ O)	C ₉ H ₁₅ N ₃ S ₂ 229.368	47.13 (47.11)	6.59 6.59	18.32 18.28	244.0(5.6) 312.0(13.5)	
4d	115 (EtOH+H ₂ O)	C ₁₀ H ₁₇ N ₃ S ₂ 243.395	49.35 (49.39)	7.04 6.99	17.26 17.55	243.0(5.2) 359 (13.5)	
4e	201 (CHCl ₃)	C ₉ H ₁₅ N ₃ S ₂ 229.368	47.13 (47.05)	6.59 6.84	18.32 18.26	240.0(5.4) 316.0(12.7)	
5a	170~4 (EtOH)	C ₅ H ₈ N ₂ OS ₂ 174.244	34.47 (34.48)	3.47 3.45	16.08 15.94	36.80 35.75	270.5(15.9) 310sh(1.0)
5b	166~7 (EtOH+H ₂ O)	C ₆ H ₈ N ₂ OS ₂ 188.271	38.28 (38.10)	4.28 4.80	14.88 14.75	34.06 33.89	276 (11.3) 320sh(1.0)
5c	163 (<i>n</i> -hexane)	C ₇ H ₁₀ N ₂ OS ₂ 202.298	41.56 (41.70)	4.98 5.20	13.85		283.0(11.4) 320sh(2.5)

Table II-D Physical properties of compounds 6e and 7.

Comp. No.	mp (recryst. solvent)	Formula (MW)	Anal. Calcd. (found)			UV 2-PrOH max nm($\epsilon \times 10^{-3}$)
			C	H	N	
6e	103 (cyclohexane)	C ₇ H ₁₁ N ₃ OS 185.249	45.39 (45.89)	5.99 6.12	22.68	265.0(8.5) 297.0(3.7)
7a	92~3 (toluene)	C ₆ H ₉ N ₃ OS 171.22	42.09 (42.15)	5.30 5.19	24.54 24.26	241.0(3.0) 289.0(11.9)
7b	189~90 (H ₂ O)	C ₇ H ₁₁ N ₃ OS 185.249	45.39 (45.23)	5.99 5.94	22.68 22.21	237.0(3.4) 293.0(16.4)
7c	121 (H ₂ O)	C ₈ H ₁₁ N ₃ OS 199.276	48.22 (48.14)	6.58 6.49	21.09 20.92	239.0(3.4) 292.0(17.3)
7d	95 (H ₂ O)	C ₉ H ₁₃ N ₃ OS 213.303	50.68 (49.42)	7.09 7.08	19.70 16.50	240.5(2.4) 292.5(11.8)
7e	154 (<i>n</i> -hexane)	C ₈ H ₁₃ N ₃ OS 199.276	48.22 (48.26)	6.58 6.59	21.09 20.93	226.5(4.6) 295.0(18.0)

Table III-A Mass spectra data of compounds 2 and 3. m/e (Relative Intensity : %)

2a	187(22, M ⁺), 140(base, M ⁺ -SCH ₃), 125(5), 113(28), 100(3), 99(6), 86(6), 74(14)
2b	201(76, M ⁺), 154(base, M ⁺ -SCH ₃), 127(49), 114(5), 113(8), 99(12), 88(15), 74(27)
2c	215(66, M ⁺), 168(base, M ⁺ -SCH ₃), 140(base), 113(21), 74(19), 72(21), 71(23)
2e	215(32, M ⁺), 168(base, M ⁺ -SCH ₃), 141(13), 127(4), 100(4), 86(7), 85(7), 74(5)
2f	215(base, M ⁺), 168(98, M ⁺ -SCH ₃), 153(64), 145(23), 88(23), 83(33), 73(11), 72(22), 71(18)
2g	229(86, M ⁺), 182(base, M ⁺ -SCH ₃), 167(43), 159(20), 149(8), 128(2), 127(3), 126(6), 86(17), 83(21)
3g	215(92, M ⁺), 185(base, M ⁺ -CH ₃ NH), 182(77, M ⁺ -SH), 153(38), 141(29), 127(33), 114(12), 99(11), 85(27)
3h	215(90, M ⁺), 182(M ⁺ -SH), 171(base, M ⁺ -(CH ₃) ₂ N), 139(26), 113(19), 88(27), 73(20), 72(15), 71(9)
3i	229(62, M ⁺), 196(9, M ⁺ -SH), 185(base, M ⁺ -(CH ₃) ₂ N), 153(19), 128(2), 127(11), 88(16), 86(6)

Table III-B Mass spectra data of compounds 4, 5, 6e and 7e.

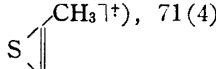
4a	201(7, M ⁺), 154(base, M ⁺ -SCH ₃), 139(7), 99(8), 86(5), 73(7), 72(5)
4b	215(33, M ⁺), 170(23), 169(35), 168(base, M ⁺ -SCH ₃), 153(30), 113(12), 88(27), 82(14), 73(24), 72(28)
4c	229(12, M ⁺), 182(base, M ⁺ -SCH ₃), 154(71), 139(9), 113(6), 82(7), 74(11), 73(8)
4d	243(11, M ⁺), 196(48, M ⁺ -SCH ₃), 154(base), 140(5), 74(8), 73(7)
4e	229(70, M ⁺), 182(base, M ⁺ -SCH ₃), 167(57), 155(3), 152(7), 141(16), 127(24), 88(50), 86(36), 85(56)
5a	174(30, M ⁺), 146(20), 126(49, M ⁺ -CH ₃ SH), 100(63), 99(11), 86(5), 75(base, CH ₃ SCO ⁺), 58(86)
5b	188(base, M ⁺), 173(17, M ⁺ -CH ₃), 160(38), 141(18), 140(50), 127(4), 114(91), 88(18), 86(12), 75(89, CH ₃ SCO ⁺)
5c	202(base, M ⁺), 174(15), 154(40, M ⁺ -CH ₃ SH), 128(54), 100(6), 86(17), 85(44), 75(38, CH ₃ SCO ⁺), 72(2), 71(16)
6e	185(42, M ⁺), 141(26, M ⁺ -(CH ₃) ₂ N), 114(4), 72(base, ) ⁺ , 71(4)
7e	199(22), 156(8), 155(base, M ⁺ -(CH ₃) ₂ N), 72(13)

Table N-A NMR spectra data by JNM-NH 100(100 Hz).

Compd. No. (solvent)	SCH_3	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H} \end{array}$	$\begin{array}{c} \text{CH}_3\text{CH}_2 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H} \end{array}$	$\begin{array}{c} \text{CH}_3\text{CH}_2 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H} \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{N} \end{array}$	$\begin{array}{c} \text{H} \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H} \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H} \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{N} \\ \diagup \\ \text{H} \end{array}$	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{C} \\ \diagup \\ \text{CH}_3 \end{array}$	NH
2a (CDCl ₃)	2.47 (s, 3H)	3.00 (d, J=5.0, 3H)					7.21, 6.67 (d, 1H), (d, 1H)				9.87 (b, 1H)
2b (CDCl ₃)	2.45 (s, 3H)	3.03 (d, J=5.0, 3H)						2.26 (b, J=1.0, 3H)	6.27 (1H)		10.16 (b, 1H)
2c (CDCl ₃)	2.45 (s, 3H)		1.27 (t, J=7.0, 3H)	3.24~ 3.45 (m, 2H)				2.26 (d, J=1.0, 3H)	6.24 (d, J=1.0, 1H)		10.26 (b, 1H)
2e (CDCl ₃)	2.43 (s, 3H)	2.99 (d, J=5.0, 3H)								2.14, 2.20 (s, 3H), (s, 3H)	10.07 (b, 1H)
2f (CDCl ₃)	2.16 (s, 3H)				3.14 (s, 6H)			2.26 (d, J=1.0, 3H)	6.28 (d, J=1.0, 1H)		
2g (CDCl ₃)	2.18 (*)				3.18 (s, 6H)					2.24~2.54 (m*, 9H)	
3h (CDCl ₃)					3.28~ 3.48 (6H)	3.55 (s, 3H)		2.26 (d, J=1.0, 3H)	6.08 (1H)		
3i (CDCl ₃)					3.22~ 3.46 (b, 6H)	3.52 (s, 3H)				2.13 (s, 6H)	
6e (CDCl ₃)					2.95 (s, 6H)			2.20 (d, J=1.0, 3H)	6.31 (d, J=1.0, 1H)		8.70~ 9.10 (b, 1H)
7e (CDCl ₃)					3.08 (s, 6H)	3.49 (s, 3H)		2.19 (d, J=1.0, 3H)	5.98 (d, J=1.0, 1H)		

Table IV-B NMR spectra data.

Compd. No. (solvent)	SCH_3	$\text{CH}_3\text{N}=\text{}$	$\text{CH}_3\text{CH}_2\text{-N}=\text{}$	$\text{CH}_3\text{CH}_2\text{-N}=\text{}$	$\text{CH}_3\text{N}=\text{}$	$\text{N}=\text{CH}_2$	$\text{N}=\text{CHCH}_3$	$\text{N}=\text{CHCH}_3$	$\text{CH}_2=\text{C}(\text{CH}_3)_2$	NH
4a (CDCl ₃)	2.53 (s, 3H)	3.08 (s, 3H)			3.57 (s, 3H)	6.35, 6.80 (d, J=4.5, 1H) (")				
" (DMSO-d ₆)	2.48 (s, 3H)	3.10 (s, 3H)			3.56 (s, 3H)	6.43, 7.11 (d, J=4.5, 1H) (")				
4b (CDCl ₃)	2.50 (s, 3H)	3.18 (s, 3H)			3.47 (s, 3H)		2.18 (d, J=1.0, 3H)	5.85 (1H)		
" (DMSO-d ₆)	2.44 (solvent overlap)	3.04 (s, 3H)			3.44 (s, 3H)		2.18 (d, J=1.0, 3H)	6.12 (1H)		
4c (CDCl ₃)	2.49 (s, 3H)		1.28 (t, J=7.0, 3H)	*	*3.30~3.47 (m, 5H)		2.19 (d, J=1.0, 3H)	5.87 (1H)		
" (DMSO-d ₆)	2.45 (solvent overlap)		1.21 (t, J=7.0, 3H)		3.48 (s, 3H)		2.21 (d, J=1.0, 3H)	6.14 (1H)		
4e (DMSO-d ₆ + CDCl ₃)	2.41 (s, 3H)	3.03 (s, 3H)			3.43 (s, 3H)				2.07 (6H)	
5a (CDCl ₃)	2.48 (s, 3H)					6.89, 7.58 (m, 1H) (")				13.16 (b, 1H)
5b (CDCl ₃)	2.40 (3H)						6.40 (1H)	2.38 (3H)		13.5 (b, 1H)
5c (CDCl ₃)	2.44 (3H)								2.28 (6H)	

Table V-A IR spectra of compounds 2. (KBr disk, cm^{-1})

com- pounds	-3000	3000 -1800	1800 -1600	-1500	-1400	-1300	-1200	-1000	-800	-600	-400
2a	3100w	2925w		1580vs 1575vs 1562vs 1545sh	1485m 1440 s 1428 s	1370m 1320m	1205m	1160w 1130m 1070m 1040w	870m	710m	595sh 525sh
2b	3180m 3100m	2910m		1580vs 1570vs 1540sh 1525m 1510sh	1430vs	1380vs 1320m 1300m	1280m 1205 s	1150m 1125 s 1058m 1050m 1000w	980w 860m 853m 810w	740m 730m 710 s 635m	520w
2d				1580br 1545vs 1530 s 1510 s	1470 s 1445vs 1420 s	1390m 1370m 1350m 1335m 1328sh 1308 s	1275m 1200m	1170m 1155m 1130vs 1060sh	990m 970m 950sh 930sh 900w 880w 860m 805w	730w 720w 700 s 675sh 640m 615w	560w 550w 470w
2e		2910m 2850m		1573vs 1559vs 1539sh 1520sh 1505 w	1495w 1489w 1462m 1438 s 1424 s	1381m 1372 s 1369sh 1338m 1313m	1290m 1268m 1203m	1173m 1139m	1092w 1048m 969w 893w 808w	737w 711m 681m 638w 621w 609w	528w 514w

abbreviation : vs (very strong), s (strong), m (medium), w (weak), sh (shoulder), br (broad).

Table V-B IR spectra of compounds 4. (KBr disk, cm^{-1})

com- pounds	-3000	-1800	-1600	-1500	-1400	-1300	-1200	-1000	-800	-600	-400
4a	3095m	2900m		1570sh	1410m	1390 s	1265 w	1100m	955m	770m	530 w
	3060m	2830m		1560 s		1365m	1240m	1045m	853w	725 w	502 w
		2315m		1515vs		1350m	1215m	1025m	823 w	685m	
				1505vs						650 w	
										630m	
										610m	
4b	3100 w	2910 w	1650 w	1570 s	1475sh	1380vs	1290 w	1170 w	970 w	753 w	553 w
		2830 w		1560 s	1435m	1360m	1265 w	1110 w	890m	720 w	535 w
				1540sh	1410 s	1340m	1245 w	1070m	830 w	705m	450 w
				1505vs		1315m	1220 s	1040 w	810sh	690 w	
								1020m		650 w	
								1005sh			
4c	3105 w	2970 w	1600 w	1553 s	1430m	1385 w	1283 w	1176 w	936m	746 w	550 w
		2915 w		1528vs	1414m	1372 w	1265 w	1100 w	880 w	720 w	533 w
		2858 w				1351m	1239 w	1069 w	828 w	709 w	447 w
		2815 w				1335m	1210m	1036m		690 w	
									642 w		
4d	3095 w	2960m	1600 w	1568vs	1468 w	1391 w	1291 w	1180 w	974m	740 w	565 w
		2923 w		1520vs	1451 w	1378 w	1245 w	1158 w	900m	721 w	553 w
		2845 w			1434 w	1365m	1218m	1142m	858 w	692 w	538 w
					1420m	1349m		1119 w	830 w	649 w	478 w
						1332m		1060 w			
								1008 w			
4e		2980 w	1634 w	1563vs	1472sh	1381vs	1290 m	1196 w	958 w	767 m	558 w
		2950 w		1503vs	1463sh	1358vs	1262 w	1111m	879 s	678 w	551 w
		2915m			1455m	1312sh	1242vs	1062 s		648 w	523 w
		2840m			1435m			1020m		618 w	517 w
		2320m			1414vs						460 w

Table V-C IR spectra of compounds **3**, **5**, **6e** and **7e**. (KBr disk, cm^{-1})

com- pounds	-3000	-1800	-1600	-1500	-1400	-1300	-1200	-1000	-800	-600	-400
3g	3230vs 3010m	2925m 2900m 2825w	1630 w	1562 w 1543sh 1525vs 1512vs 1502vs	1466 s 1450 s 1410 s	1388vs 1375 s 1350 s 1328m	1298sh 1283m 1235vs 1215m 1203sh	1138m 1052w 1025w	956 w 884m	706 w 650 w	562 w 531 w 468 w
3h	3070m	2590m		1596m 1524vs	1418m	1378vs 1358vs 1300m	1287vs 1217 m	1132m 1115m 1110m 1050m	920m 879m 823 w	735 w 649w 632 w	594 w 540 w 512 w 454 w
3i		2900m	1632 w	1548sh 1528sh 1510vs 1505vs	1498vs 1478vs 1458sh 1412m	1370vs 1347vs 1310 s	1290 s 1237 m	1128m 1105m 1095m 1045 w	989 w 920m 871m 842 w	765 w 635 w	558 w
5a	3160m	2925m 2850m 2700m 2325m	1675vs 1654m	1585 s 1560m 1540m	1490 w 1440m 1420 w	1375 w 1320m	1282vs 1230 w	1165vs 1075 w 1060m	970 w 895m 870 w 815 w	770m 718 w 710 w 700m 690 w 655m 615m	520 w
5b	3400m 3100 s	2999m 2895 s	1664 s	1530vs	1431m	1376m 1306vs	1258vs 1150vs	1006m	974m 885 s 850m	740m 727m 663m 633m	
5c	3110m 3000m	2905m	1665 s	1565m 1545vs 1528vs 1509sh	1435m	1300m	1273 s 1255 s 1225m	1172sh 1150vs	980br 895m 870m	690 w 655 w 605 w	
6e	3140br	2905br	1689vs 1665vs 1650vs 1644vs	1562vs 1547vs 1530vs 1500vs	1485sh 1439vs 1405 s	1360vs 1307vs	1290vs 1265vs	1171vs 1145 s 1138 s 1065m 1040m	970m 885 s 842m	770m 740m 718 s 705sh 685m 620m	
7e	3070m	2900m	1665 w 1640 w	1590vs 1545m 1530 s	1483 s 1458m 1430m 1415 s	1390vs 1370vs	1275m 1265m 1208 s	1190 s 1050m 1025m	905m 830 w 815 w	770m 710 w 635 w	540 w 465 w

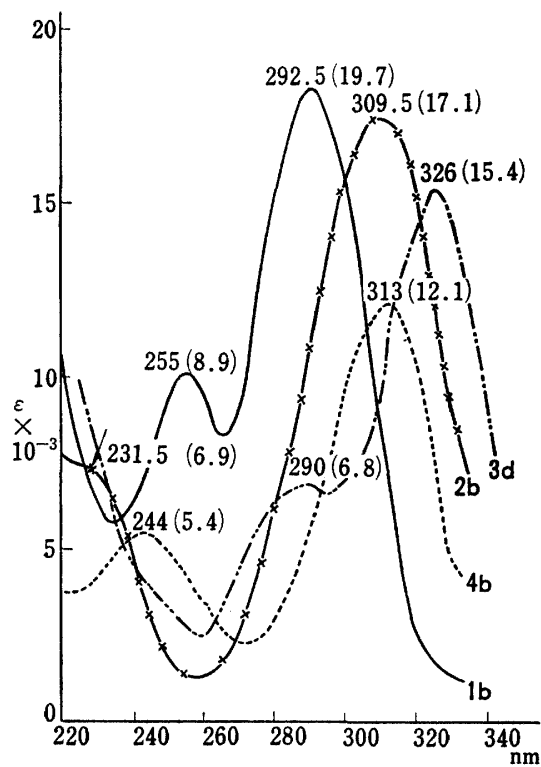


Fig. 1 UV Absorption Spectra of 1b, 2b, 3d, and 4b in 2-PrOH.

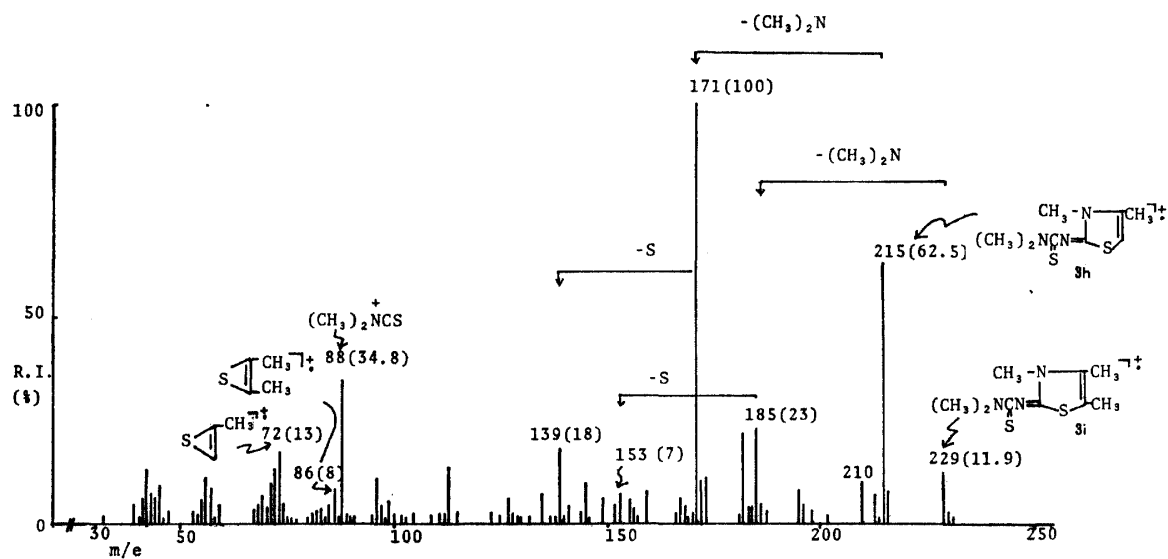


Fig. 2 Mass spectra of cross products 3h and 3i.

Experimental

Melting points were taken on a Yanako micro melting-point apparatus and are uncorrected. Infrared spectra were obtained with a Hitachi EPI-G3 spectrometer, ultraviolet spectra, with a Shimadzu double beam spectrophotometer UV-200s and nuclear magnetic resonance spectra with a Nihon Denshi JNM-NH 100 [100 MHz] with tetramethylsilane (TMS) as internal standard. Chemical shift are expressed in δ (ppm). The coupling constants (J) is expressed in Hz. Abbreviation: s: singlet, d: doublet, q: quartet, m: multiplet, b: broad.

Typical procedures for these reaction were as follows.

2a and **3a**: To a solution of **1a** (0.8 g) in 2N-NaOH solution (26 ml), was added $(\text{CH}_3)_2\text{SO}_4$ (0.58 g) at 10° under stirring. Stirring was continued for 20 min. The resulting yellow-pale crystals were collected and yielded 0.4 g, mp $42\text{--}102^\circ$. These raw products were isolated as an ethanol-soluble product and an ethanol-insoluble product. The former was identified compound **2a**, mp $48\text{--}49^\circ$ (from EtOH), the latter compound **3a**, mp $156\text{--}158^\circ$ (from EtOH). When the molar ratio of 1:2 (**1a**: $(\text{CH}_3)_2\text{SO}_4$) was examined by the same manner, raw products having mp $42\text{--}102^\circ$ yielded 1.5 g.

3a and **4a**: An equimolar of **1a** (0.5 g) and $(\text{CH}_3)_2\text{SO}_4$ (0.35 g) was heated at 90° for 20 min. The white precipitate was filtered, identified as compound **3a** having *Rf*-value 0.49 (ether). Neutralization of filtrate with 2N-NaOH solution **4a** having *Rf*-value 0.49 (ether) yielded. When the molar ratio of 1:2 (**1a**: $(\text{CH}_3)_2\text{SO}_4$) was heated at 94° for 15 min, the mixture of **3a** and **4a** also were yielded by the same treatment as just above mentioned.

2a: To a solution of **1a** (0.9 g) in CHCl_3 (65 ml), was added $\text{CH}_3\text{OSO}_2\text{F}$ (1.17 g) at room temperature. After stirring for 4.5 hr, the white-yellow precipitate having mp 145° was collected (0.45 g), carefully neutralized with 2N-NaOH solution. S-methyl derivative **2a** was obtained as white crystals. TLC (ether): *Rf*-value 0.76.

4a: To a solution of **2a** (0.4 g) in CHCl_3 (5 ml), was added $\text{CH}_3\text{OSO}_2\text{F}$ (0.24 g) at room temperature. After stirring for 3 hr, the white precipitate (raw mp 171°) was collected. The raw product was dissolved in H_2O and made alkaline with 4% NaOH solution. Recrystallization from EtOH+ H_2O solution gave compound **4a**, mp 90° .

4a: To a solution of **3a** (0.7 g) in CHCl_3 (20 ml), was added $\text{CH}_3\text{OSO}_2\text{F}$ (0.42 g) at room temperature. After stirring for 6 hr, the white crystals (mp $137\text{--}138^\circ$) was collected and made alkaline with 2N-NaOH solution. Recrystallization from EtOH+ H_2O solution gave compound **4a**, mp $89\text{--}90^\circ$. TLC (ether): *Rf*-value 0.09 (salt), 0.17 (free).

4a: The mixture of compound **2a** (0.3 g) and $(\text{CH}_3)_2\text{SO}_4$ (0.23 g) was heated at 100° for 5–10 min. The crude product was made alkaline with 4% NaOH solution and white crystals were collected to get **4a**.

4a: The mixture of compound **3a** (0.49 g) and $(\text{CH}_3)_2\text{SO}_4$ (0.5 g) were heated at 60° for 2–3 min. After treatment as described above, compound **4a** having mp $90\text{--}91^\circ$ was

obtained.

6a: A solution of compound **2a** (0.3 g) in 1N-NaOH solution (14 ml) was heated at 60° for 1 hr. The yellow oily materials was neutralized with 1N-HCl solution. Then unreacted **2a** was filtered off and the filtrate was extracted with CHCl₃. After evaporation of solvent, compound **6a** was recrystallized from 2-PrOH, mp 214—218°. TLC (ether): *Rf*-value 0.11.

6a: To a solution of **1a** (0.3 g) in 1N-NaOH (10 ml), was added H₂O₂ (3 ml) at 8°. After standing for 30 min, the white crystals were collected, and recrystallized from 2-PrOH to get **6a** (mp 212—214°) 0.17 g which gave a negative chelate formation with Cu²⁺ ion.

7a: A solution of compound **4a** (0.28 g) in 2N-NaOH solution (10 ml) was heated at 100° for 1 hr. The reaction mixture was neutralized with 1N-HCl solution and extracted with CHCl₃. After evaporation of solvent, the yellow crystals were recrystallized from toluene to get **7a**, mp 94—96° (0.15 g).

7a: To a solution of **3a** (0.1 g) in the mixture of H₂O (0.6 ml), EtOH (4 ml) and 0.5 N-NaOH (0.4 ml), was added H₂O₂ (1 ml) at room temperature. The reaction mixture was neutralized with 2N-NaOH solution and extracted with CHCl₃. The raw product was recrystallized from toluene to get **7a**, mp 93—94° (0.07 g).

5a: A solution of compound **2a** (1.53 g) in 1N-HCl solution (7 ml) was heated at 160° for 1.5 hr. The raw product was recrystallized from EtOH to get **5a**, mp 179—180° (0.57 g).

2c: To a solution of **1c** (1 g) in EtOH (25 ml), was added CH₃I (2.8 g). The reaction mixture was heated at 67° for 3 hr. After removal of the solvent, the crude product (HI salt) was dissolved in H₂O, neutralized with NaHCO₃ solution extracted with CHCl₃ and dried over Na₂SO₄. The solvent was evaporated under reduced pressure to give yellow oily materials which gave a negative chelate formation with Cu²⁺ ion. TLC (ether): *Rf*-value 0.65, (acetone: CHCl₃=1: 2): *Rf*-value 0.65. Picrate: mp 158—159° (from EtOH+H₂O).

2f: To a solution of **1f** (3.0 g) in CHCl₃ (200 ml), was added CH₃OSO₂F (5.1 g)(bp₉₈ 34—35°) at room temperature. After stirring for 3 days red oily materials were dissolved in H₂O, neutralized with saturated NaHCO₃ solution and extracted with CHCl₃. After evaporation of CHCl₃, raw product of 2.7 g yielded. Picrate: mp 126°.

3h: To a solution of 2-imino-3,4-dimethyl-4-thiazoline (8.52 g) in dry acetone (40 ml), was added N,N-dimethylthiocarbamoyl chloride (7.52 g) in dry acetone (20 ml) at room temperature and stirred for 2 days. The raw product was collected, washed with H₂O and was recrystallized with EtOH, mp 206—207°. TLC (acetone: CHCl₃=1: 2): *Rf*-value 0.73.

7e: The raw oily material **2f** from **1f** and (CH₃)₂SO₄ in 1N-NaOH solution (10 ml) was heated at 120° for 2 hr. The precipitate was collected and recrystallized from *n*-hexane

to get **7e**, mp 147—149°. TLC (ether): *R_f*-value 0.23.

7e: An equimolar mixture of 2-imino-3,4-dimethyl-4-thiazoline (1.94 g) in dry ether (60 ml), and N,N-dimethylcarbamoyl chloride (1.61 g) in dry ether (20 ml) stirred at room temperature for 15.5 hr. The reaction mixture was filtered, the filtrate was evaporated and washed with water. The white raw product was recrystallized from *n*-hexane to get **7e**, mp 149—151°. TLC (ether): *R_f*-value 0.23.

5b: The oily material **2f** (0.4 g) in 10% HCl solution (6 ml) was heated at 50—55° for 1 hr. The reaction mixture was neutralized with 1N-NaOH solution and recrystallized from EtOH to get **5b**, mp 161—163°.

3h: To a solution of **1f** (2.01 g) in 2N-NaOH solution (65 ml), was added (CH₃)₂SO₄ (1.26 g) at 9°. The reaction mixture was stirred for 1 hr. The yellow precipitate was filtered. On the TLC (acetone :CHCl₃=1:2) two spots were appeared at the position of *R_f*-values 0.66 and 0.47. The raw product (0.925 g) was recrystallized from ethanol to yield, ring N-methyl derivative **3h**, mp 202.5°. A trace amount of S-methyl derivative **2f** having *R_f*-value 0.47 g yielded. The filtrate was adjusted pH 4 with 10% HCl solution and the resulting product was identical with **1f** of starting material, which gave a positive chelate formation with Cu²⁺ ion.

7e: To a solution of **3h** (0.4 g) in CHCl₃ (20 ml), was added CH₃OSO₂F (0.64 g) and stirred at room temperature for 2 days. The red oily materials was neutralized with 1N-NaOH solution to give white crystals **7e**, mp 150° (from *n*-hexane). TLC (acetone:CHCl₃=1:2): *R_f*-value 0.54.

3h: Compound **2f** was heated at 155—165° for 14 hr. On the TLC the raw product showed two spots having *R_f*-values 0.55 and 0.39 (ether). The raw cross product was purified by silica-gel column chromatography using acetone-CHCl₃ (1:2) as a eluent. The eluate was evaporated under reduced pressure, and treated with an activated charcoal in EtOH to give compound **3h**, mp 204—205° (12 mg).

Cross reaction of **2f** and **1g**

The mixture of **2f** (300 mg) and **1g** (150 mg) was heated at 145° for 1.5 hr. The raw cross product was purified by silica-gel column chromatography using acetone-CHCl₃ (1:2) as a eluent. The eluate was evaporated and the yellow precipitate was examined on Mass. As shown in Fig. 2, its Mass data showed a molecular ion peak at *m/e* 229 corresponding to compound **3i** having molecular weight 229.