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Studies on Azole Compounds. VI.[1] Reactions of 2,4- and 2,5-Disubstituted Thiazole *N*-Oxides with Aryl Isocyanates

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The reactions of 2,4- (Ia—d) and 2,5-disubstituted thiazole 3-oxides (Ie—f) with aryl isocyanates (II) were studied. While the reactions of Ia—d with II proceeded smoothly to give bis(5-imidazolyl) disulfides (IV), those of Ie—f with II did not take place. The structures of IV were deduced from their chemical behavior and spectral data. The reaction mechanism of Ia—d with II is discussed.

Keywords——2,4-disubstituted thiazole 3-oxides; 2,5-disubstituted thiazole 3-oxides; bis(5-imidazolyl) disulfides; imidazoles; ring transformation; MS; UV

In the preceding papers of this series[1] it has been shown that oxazole 3-oxides react easily with phenyl isocyanate to give imidazole derivatives, and in this reaction the 2-position of oxazole 3-oxides is extraordinarily sensitive to nucleophilic reagents, even when the 2-position is occupied by a substituent. In the case of the reaction of 4-methyloxazole 3-oxides with phenyl isocyanate, 4-exomethylene derivatives were obtained,[2] while in the case of 4-phenyloxazole 3-oxides we observed the formation of bicyclic compounds,[1] *i.e.*, totally different results from those with 4-methyloxazole 3-oxides (Chart 1).

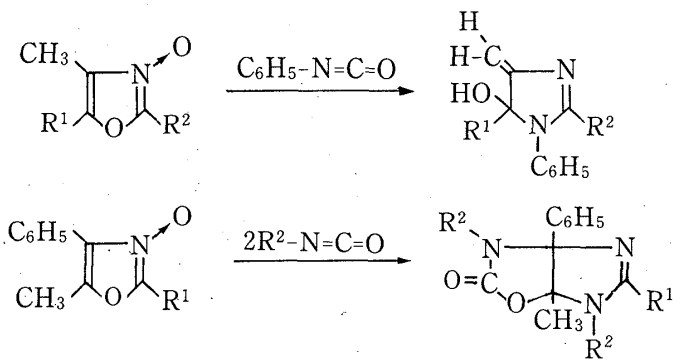
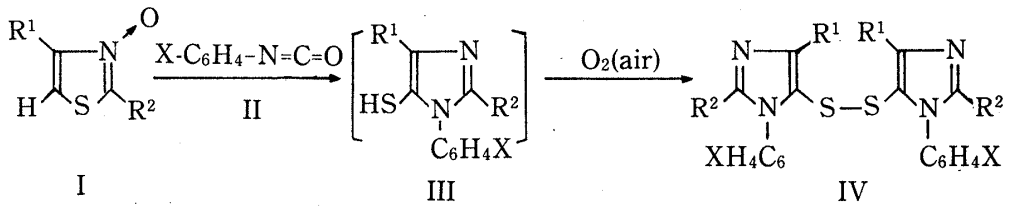


Chart 1

As a further extension of our studies on the reaction of azole *N*-oxides with aryl isocyanates, the present investigation was carried out to examine the chemical behavior of 2,4- and 2,5-disubstituted thiazole 3-oxides under treatment with aryl isocyanates.

Both 4-methyl- and 4-phenylthiazole 3-oxides react with aryl isocyanates to give bis(5-imidazolyl) disulfides. The results obtained are shown in Chart 2.

Addition of phenyl isocyanate (IIa) to a chloroform solution of 4-methyl-2-phenylthiazole 3-oxide (Ia) at room temperature and further refluxing of the mixture for 3 h gave a yellow crystalline substance $C_{32}H_{26}N_4S_2$ (IVaa). Refluxing of compound IVaa with Raney Ni in ethanol[3] gave a desulfurized product $C_{16}H_{14}N_2$ (Vaa). When IVaa was treated with triisopropylphosphite, the S–S bond of IVaa was cleaved[4] and a compound $C_{19}H_{20}N_2S$ (VIaa), which has an isopropyl group, was obtained. On reduction[5] of IVaa with $LiAlH_4$ under an N_2 atmosphere, the S–S bond of IVaa was apparently cleaved, because the yellow color of the

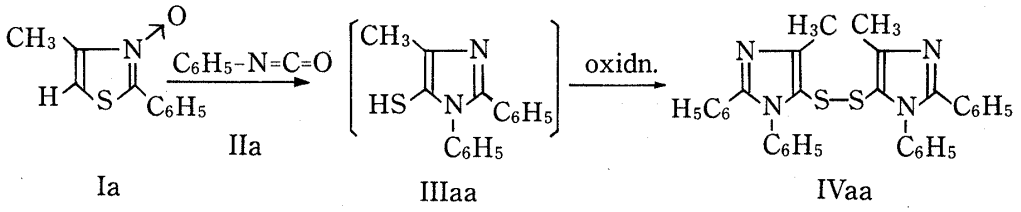


Ia : $R^1=CH_3$, $R^2=C_6H_5$
Ib : $R^1=C_6H_5$, $R^2=CH_3$
Ic : $R^1=p$-ClC_6H_4, $R^2=CH_3$
Id : $R^1=p$-BrC_6H_4, $R^2=CH_3$

IIa : X=H
IIb : X=*o*-Cl
IIc : X=*p*-Cl
IId : X=*o*-Br
IIe : X=*p*-Br

IVaa : $R^1=CH_3$, $R^2=C_6H_5$, X=H
IVab : $R^1=CH_3$, $R^2=C_6H_5$, X=*o*-Cl
IVac : $R^1=CH_3$, $R^2=C_6H_5$, X=*p*-Cl
IVad : $R^1=CH_3$, $R^2=C_6H_5$, X=*o*-Br
IVae : $R^1=CH_3$, $R^2=C_6H_5$, X=*p*-Br
IVba : $R^1=C_6H_5$, $R^2=CH_3$, X=H
IVbb : $R^1=C_6H_5$, $R^2=CH_3$, X=*o*-Cl
IVbc : $R^1=C_6H_5$, $R^2=CH_3$, X=*p*-Cl
IVbd : $R^1=C_6H_5$, $R^2=CH_3$, X=*o*-Br
IVca : $R^1=p$-ClC_6H_4, $R^2=CH_3$, X=H
IVda : $R^1=p$-BrC_6H_4, $R^2=CH_3$, X=H

Chart 2



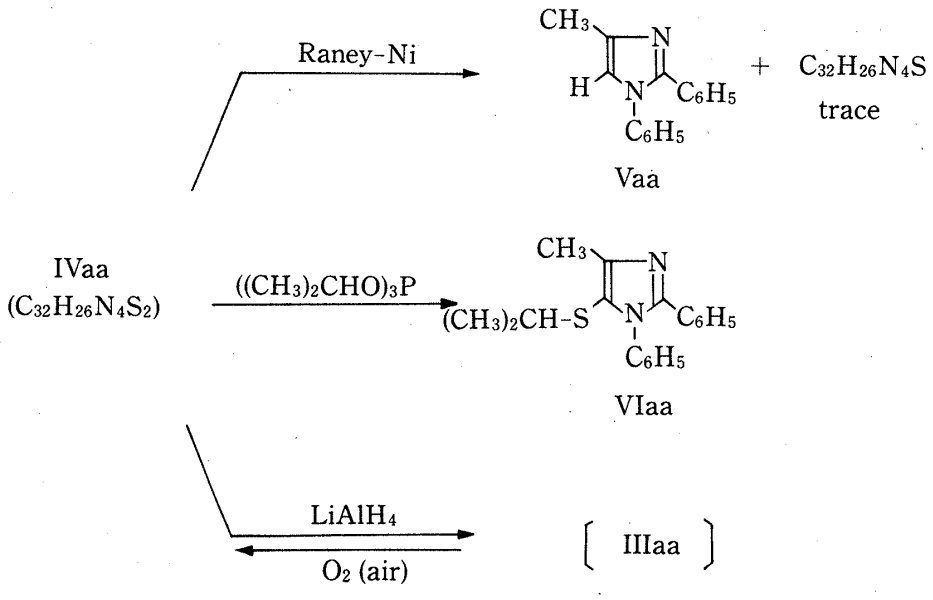


Chart 3

solution disappeared. However, a yellow color reappeared on the addition of water in order to decompose the excess $LiAlH_4$. The experimental results described above are shown in Chart 3.

On the other hand, as shown in Chart 4, the reaction of 5-substituted thiazole *N*-oxides with aryl isocyanates did not proceed and almost all the starting *N*-oxides were recovered together with very small amounts of the corresponding deoxygenated thiazoles.

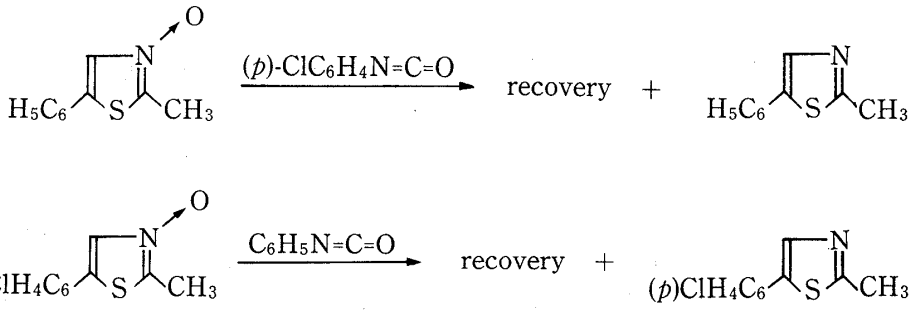


Chart 4

As shown in Fig. 1, in the UV spectrum of IVaa the new absorption maximum appears at longer wavelength in comparison with that of the starting thiazole *N*-oxide. This indicates that the basic skeleton of thiazole *N*-oxide was changed and the conjugated system lengthened. In the spectra of Vaa and VIaa no absorption maxima at longer wavelengths similar to that of IVaa are observed. Their absorption intensities are less than that of IVaa and these two absorption spectra are very similar to that of 1,2-diphenyl-4,5-dimethylimidazole.[2)]

In the IR spectrum of IVaa, the absorption band of the S–S bond is too weak to identify, and it is also difficult to identify the absorption band of the C–S bond, owing to overlapping with that of out-of-plane bending of the hydrogen of the aromatic nucleus.

Compound IVaa has no SH group, because no absorption band in the range of 2550—2600 cm^{-1} is observed. Compound VIaa shows the characteristic bands of an isopropyl group (doublet in *gem*-dimethyl groups (1381, 1376 cm^{-1}); skeletal vibrations (1180, 1155 cm^{-1})).

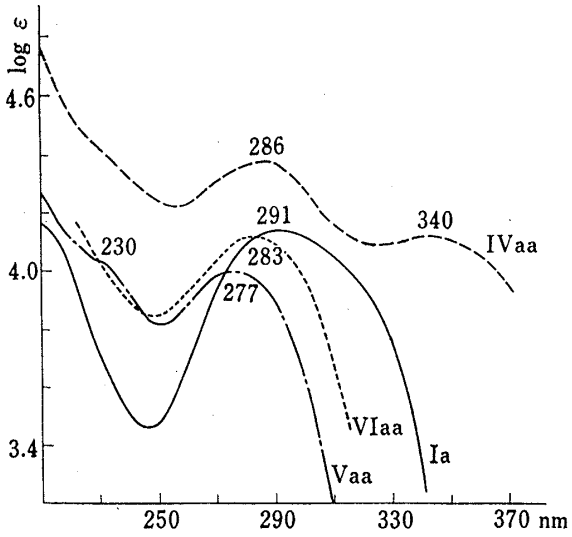
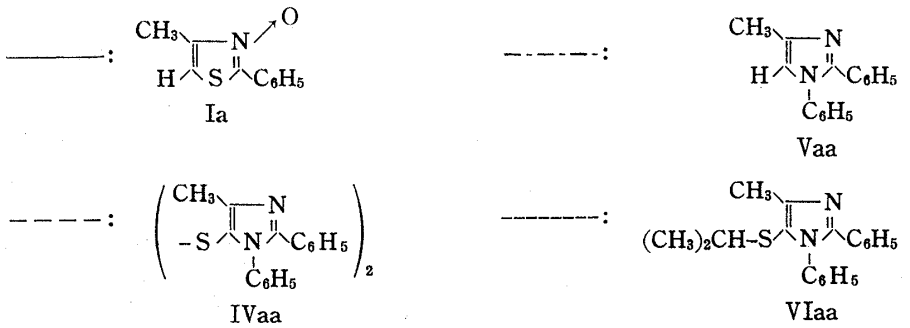


Fig. 1. UV Spectra of Ia, IVaa, Vaa, and VIaa in EtOH



In the mass spectrum (MS) (Fig. 2) obtained by the field desorption (FD) method the molecular ion of IVaa was observed at *m/e* 530. The main fragment ions of IVaa are as follows: *m/e* 530 (M^+), 498, 266, 265, 233, 180, 162, 130, 121, 104 and 103. The *m/e* 498 ion is formed by the loss of one sulfur atom from the molecular ion. The intense *m/e* 265 peak is $M^+/2$, and the *m/e* 266 peak is $M^+/2+1$. The fragment ion 233 is produced by the elimination of one sulfur atom from the *m/e* 265 fragment, and the *m/e* 162 peak should arise from the *m/e* 265 fragment by elimination of benzonitrile (metastable peak at *m/e* 99.03). Therefore, this spectrum indicates that compound IVaa has a symmetrical structure with respect to the S–S bond. The peak at *m/e* 180 ($C_6H_5\overset{+}{N}{\equiv}CC_6H_5$) shows that the nitrogen of phenyl isocyanate was bound to the 2-position of the starting thiazole ring. The MS of Vaa shows peaks at the following mass numbers: *m/e* 234 (M^+), 193, 180, 165 and 130. The ion at *m/e* 193 is produced by the elimination of acetonitrile from the molecular ion, and that at *m/e* 180 is also observed as in the case of the MS of IVaa. The main peaks of the MS of VIaa are as follows: *m/e* 308 (M^+), 293, 266, 265, 233, 180, 162, 130, 121, 104 and 103. This spectrum is very similar to that of IVaa except for the molecular and the *m/e* 293 ions. Both the *m/e* 266 (metastable peak at *m/e* 229.73) and 265 ions should arise from the molecular ion from which propene and isopropyl radical are eliminated, respectively. The *m/e* 233 and 162 (metastable peak at the *m/e* 99.03) fragments are produced by the loss of a sulfur atom and benzonitrile from *m/e* 265, respectively.

The ^{1}H-NMR spectra of IVaa, Vaa and VIaa are shown in Fig. 3. The spectrum of IVaa also indicates, like its MS, that compound IVaa has a symmetrical structure with respect to the S–S bond. This spectrum did not change on the addition of D_2O, *i.e.* there is no SH group in IVaa. The spectrum of Vaa, which is the desulfurization product from compound IVaa

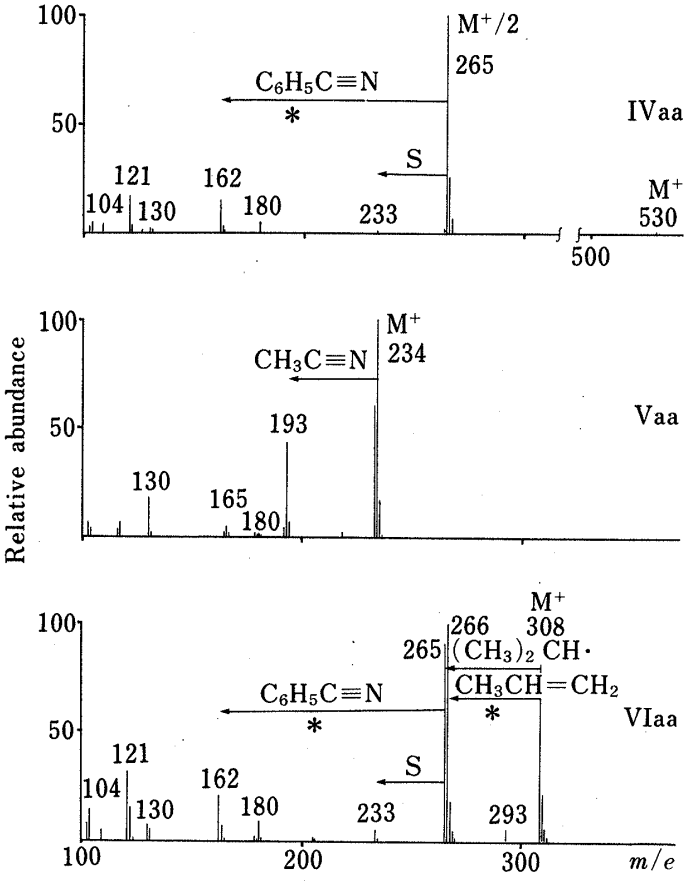


Fig. 2. MS of IVaa, Vaa, and VIaa

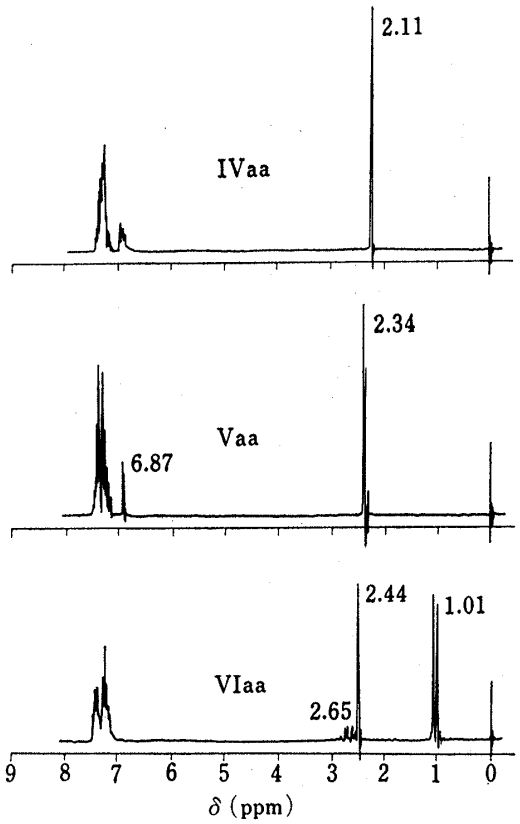


Fig. 3. ^{1}H-NMR Spectra of IVaa, Vaa, and VIaa in $CDCl_3$ at 90 MHz

with Raney Ni, shows a signal at δ 6.87, ascribable to the proton on the 5-position of the imidazole ring. The spectrum of VIaa shows the characteristic signals of an isopropyl group.

On the basis of the chemical behavior and the spectral data described above, it is concluded that compounds IVaa, Vaa and VIaa are bis(1,2-diphenyl-4-methylimidazol-5-yl) disulfide, 1,2-diphenyl-4-methylimidazole and 1,2-diphenyl-5-isopropylthio-4-methylimidazole, respectively. As already shown in Chart 2, besides the reaction of Ia with IIa, the reactions of 2,4-

Table I-1. Mass Spectral Data for IV

Compd. No.		$M^{+a)}$	M^+-S	M^+-X	$M^+/2+H$ (A)	(A)	(A)–S	(A)–X (B)	(A)–R^2CN	(B)–C_6H_5CN	$XC_6H_4\overset{+}{N}\equiv CR^2$	R^1–(+)N–R^2
IVab	*m/e*	598	566	563	300	299	267	264	196	161	214	130
	Rel. Ab.$^{b)}$		≪1	≪1	29	100	1	71	2	20	8	1
IVac	*m/e*	598	566	563	300	299	267	264	196	161	214	130
	Rel. Ab.$^{b)}$		≪1	≪1	100	31	9	27	7	9	15	8
IVad	*m/e*	686	654	607	344	343	311	264		161	258	130
	Rel. Ab.$^{b)}$		≪1	≪1	<1	2	≪1	100		43	≪1	≪1
IVae	*m/e*	686	654		344	343	311	264	240	161	258	130
	Rel. Ab.$^{b)}$		≪1		24	32	2	22	3	16	5	12

a) Molecular ions were observed by the FD method.
b) Rel. Ab.=relative abundance.

Table I-2. Mass Spectral Data for IV

Compd. No.		$M^{+a)}$	M^+-S	M^+-X	$M^+/2+H$ (A)	(A)	(A)–S	(A)–X (B)	(A)–R^2CN	(B)–C_6H_5CN	$XC_6H_4\overset{+}{N}\equiv CR^2$	R^1–(+)N–R^2
IVba	*m/e*	530	498		266	265	233		224	161	118	130
	Rel. Ab.$^{b)}$		≪1		49	50	1		100	1	17	3
IVbb	*m/e*	598			300	299	267	264	258	161	152	130
	Rel. Ab.$^{b)}$				31	93	1	15	100	1	7	1
IVbc	*m/e*	598	566		300	299	267	264	258	161	152	130
	Rel. Ab.$^{b)}$		≪1		45	100	1	3	95	1	12	1
IVbd	*m/e*	686		607	344	343	311	264	302	161	196	130
	Rel. Ab.$^{b)}$			≪1	12	15	<1	100	8	<1	<1	<1
IVca	*m/e*	598	566		300	299	267	264	258	161	118	164
	Rel. Ab.$^{b)}$		≪1		34	100	<1	37	80	3	8	<1
IVda	*m/e*	686	654		344	343	311	264	302	161	118	208
	Rel. Ab.$^{b)}$		≪1		58	17	1	100	7	3	9	2

a) Molecular ions were observed by the FD method.
b) Rel. Ab.=relative abundance.

Table II. Mass Spectral Data for V

Compd. No.		M^+	M^+-CH_3CN (C)	M^+-X (D)	(C)–X	$C_{13}H_9^+$	$M^+-C_6H_5CN-H$	(D)–C_6H_5CN	$XC_6H_4\overset{+}{N}\equiv CR^2$	R^1–(+)N–H
Vab	*m/e*	268	227	233	192	165	164		214	
	Rel. Ab.$^{a)}$	100	20	72	25	24	7		≪1	
Vad	*m/e*	312	271	233	192	165		130	258	
	Rel. Ab.$^{a)}$	8	1	30	24	2		2	≪1	
Vae	*m/e*	312	271	233	192	165		130	258	
	Rel. Ab.$^{a)}$	12	2	25	28	6		3	≪1	
Vba	*m/e*	234	193			165	130		118	116
	Rel. Ab.$^{a)}$	100	14			18	24		1	17
Vbb	*m/e*	268	227	233	192	165	164		152	116
	Rel. Ab.$^{a)}$	100	10	6	12	34	19		3	17
Vca	*m/e*	268	227	233	192	165	164		118	150
	Rel. Ab.$^{a)}$	75	14	3	7	33	8		10	26

a) Rel. Ab.=relative abundance.

Table III. Mass Spectral Data for VI

Compd. No.		M^+	M^+-CH_3	$M^+-CH_2(CH_3)_2CH$	$M^+-CH_3(CH_3)_2CH\cdot$ (D)	(D)–S	(D)–Cl	(D)–R^2CN (E)	$XC_6H_4\overset{+}{N}\equiv CR^2$	R^1–(N)–R^2	(E)–Cl
VIab	*m/e*	342	327	300	299	267	264	196	214	130	161
	Rel. Ab.[a]	87	≪1	100	55	5	40	3	7	4	7
VIac	*m/e*	342	327	300	299	267	264	196	214	130	161
	Rel. Ab.[a]	77	4	100	55	4	35	8	31	8	11
VIba	*m/e*	308	293	266	265	233		224	118	130	
	Rel. Ab.[a]	97	3	100	28	3		55	22	3	
VIbb	*m/e*	342	327	300	299	267	264	258	152	130	223
	Rel. Ab.[a]	100	1	14	3	1	5	8	3	2	14
VIbc	*m/e*	342	327	300	299	267	264	258	152	130	223
	Rel. Ab.[a]	100	3	91	25	2	1	33	16	3	45
VIca	*m/e*	342	327	300	299	267	264	258	118	165	223
	Rel. Ab.[a]	86	3	100	18	2	18	32	14	12	19

a) Rel. Ab.=relative abundance.

disubstituted thiazole 3-oxides (Ib—d) with aryl isocyanates (IIb—e) were examined, and these results are the same as that of the reaction of Ia with IIa. The MS data for the corresponding IV, V and VI derivatives are shown in Tables I—III.

From the results described above, all the reactions presented in this paper are considered to proceed according to the following scheme (Chart 5). In the initial step of the reaction, the reaction proceeds in a manner similar to that of oxazole *N*-oxide with aryl isocyanate.[1,2] At first, the addition of the isocyanate to the thiazole *N*-oxide to give an intermediate bicyclic compound occurs, and carbon dioxide is eliminated to give the intermediate III. It may be considered that the intermediate III dimerizes into IV due to oxidation with either air[6] or thiazole *N*-oxide[7] in the reaction mixture. Taking into account the chemical behavior in the post-treatment of the reduction of IV with $LiAlH_4$ already described above, it is presumed that the dimerization is due to air oxidation.

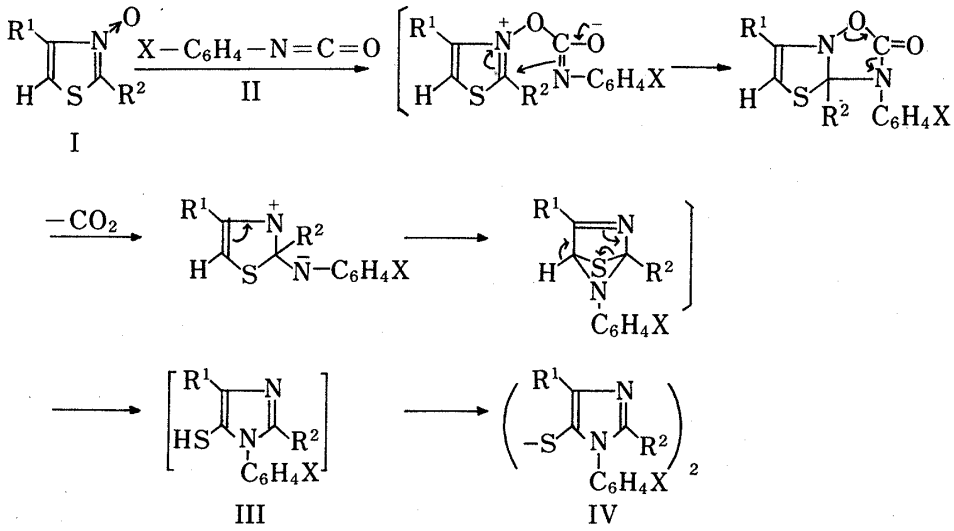


Chart 5

As already described, 2,4-disubstituted thiazole 3-oxides reacted smoothly with aryl isocyanates (II), but the reaction of 2,5-disubstituted thiazole 3-oxides with II did not proceed and the starting *N*-oxides were recovered. An investigation of this difference between the reactivity of 2,4- and 2,5-disubstituted thiazole *N*-oxides is in progress.

Experimental

All melting points are uncorrected. UV spectra were measured on a Hitachi 556 double-wavelength spectrophotometer, IR spectra on a Hitachi 295 infrared spectrophotometer, ^{1}H-NMR spectra on JNM C-60-H and Hitachi R22 with tetramethylsilane as an internal standard, and mass spectra on JEOL JMS-01SG and JMS-D300 spectrometers.

Preparation of 2,4-Disubstituted Thiazole 3-Oxides (I)[8]

General Procedure——To a solution of maleic anhydride (30 g) in $CHCl_3$ (60 ml), 30% H_2O_2 (12 g) was added dropwise with stirring under ice-cooling. The mixture was stirred for 2 h under the same conditions, then a thiazole (0.021 mol) was added and the mixture was stirred for a further 1 h. The resulting mixture was allowed to stand for 5 d in the refrigerator. The reaction mixture was made slightly alkaline with conc. ammonia water under ice-cooling, then extracted with $CHCl_3$. The $CHCl_3$ extract was dried over anhyd. K_2CO_3 and $CHCl_3$ was removed by evaporation. The residue was chromatographed over silica gel (Merck Kieselgel 60, 70—230 mesh) with $CHCl_3$ or $CHCl_3$–MeOH (10: 1), and recrystallized from acetone to give thiazole 3-oxides (Ia—d).

4-Methyl-2-phenylthiazole 3-Oxide (Ia)——Colorless prisms, mp 122—124°C, 38% yield. *Anal.* Calcd for $C_{10}H_9NOS$: C, 62.82; H, 4.75; N, 7.33. Found: C, 63.00; H, 4.67; N, 7.09. IR ν_{max}^{KBr}cm^{-1}: 1283 (N→O).

2-Methyl-4-phenylthiazole 3-Oxide (Ib)——Colorless prisms, mp 133—134°C, 15% yield. *Anal.* Calcd for $C_{10}H_9NOS$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.96; H, 4.71; N, 7.12. IR ν_{max}^{KBr} cm^{-1}: 1295 (N→O).

4-(*p*-Chlorophenyl)-2-methylthiazole 3-Oxide (Ic)——Colorless needles, mp 156—157°C, 18% yield. *Anal.* Calcd for $C_{10}H_8ClNOS$: C, 53.21; H, 3.57; N, 6.21. Found: C, 53.42; H, 3.55; N, 6.09. IR ν_{max}^{KBr} cm^{-1}: 1299 (N→O).

4-(*p*-Bromophenyl)-2-methylthiazole 3-Oxide (Id)——Colorless leaflets, mp 150—151°C, 18% yield. *Anal.* Calcd for $C_{10}H_8BrNOS$: C, 44.46; H, 2.98; N, 5.19. Found: C, 44.28; H, 2.78; N, 4.71. IR ν_{max}^{KBr} cm^{-1}: 1296 (N→O).

Reaction of 2,4-Disubstituted Thiazole 3-Oxides (I) with Aryl Isocyanates (II)

General Procedure——An aryl isocyanate (II) (0.011 mol) was added at room temperature to a solution of a thiazole 3-oxide (I) (0.01 mol) in $CHCl_3$ (10 ml), and the reaction mixture was refluxed for 2 h. The solvent was removed, and the residue was chromatographed over silica gel with $CHCl_3$, followed by ether. The substance eluted with $CHCl_3$ was recrystallized to give a small amount of the corresponding deoxygenated thiazole. The main product, a disulfide (IV), was eluted with ether as a bright yellow crystalline solid, and recrystallized from an appropriate solvent. A small amount of *N*-oxide was recovered from the final eluate.

Disulfide (IVaa)——Yellow prisms (from acetone), mp 184—185°C, 33% yield. *Anal.* Calcd for $C_{32}H_{26}N_4S_2$: C, 72.44; H, 4.94; N, 10.56. Found: C, 72.60; H, 4.92; N, 10.56. UV λ_{max}^{EtOH} nm (log ε): 286 (4.08), 340 (3.82). NMR $\delta_{ppm}^{CDCl_3}$: 2.11 (6H, s, CH_3), 6.83—7.02 (4H, m, phenyl-H), 7.16—7.42 (16H, m, phenyl-H).

Disulfide (IVab)——Yellow needles (from acetone), mp 210°C (dec.), 38% yield. *Anal.* Calcd for $C_{32}H_{24}Cl_2N_4S_2$: C, 64.10; H, 4.03; N, 9.35. Found: C, 63.84; H, 3.92; N, 9.33.

Disulfide (IVac)——Yellow prisms (from ether), mp 168—169°C, 30% yield. *Anal.* Calcd for $C_{32}H_{24}Cl_2N_4S_2$: C, 64.10; H, 4.03; N, 9.35. Found: C, 64.10; H, 3.98; N, 9.43. UV λ_{max}^{EtOH} nm (log ε): 222.5 (sh., 4.60), 282.5 (4.32), 339 (4.09). NMR $\delta_{ppm}^{CDCl_3}$: 2.18 (6H, s, CH_3), 6.85 (4H, d, J=7.7 Hz, phenyl-H), 7.26 (4H, d, J=7.7 Hz, phenyl-H), 7.29 (10H, s, phenyl-H).

Disulfide (IVad)——Yellow needles (from EtOH), mp 237°C (dec.), 35% yield. *Anal.* Calcd for $C_{32}H_{24}Br_2N_4S_2$: C, 55.82; H, 3.51; N, 8.14. Found: C, 55.59; H, 3.43; N, 7.88.

Disulfide (IVae)——Yellow prisms (from acetone), mp 171—173°C, 36% yield. *Anal.* Calcd for $C_{32}H_{24}Br_2N_4S_2$: C, 55.82; H, 3.51; N, 8.14. Found: C, 55.83; H, 3.38; N, 7.85. UV λ_{max}^{EtOH} nm (log ε): 225 (sh., 4.59), 284 (4.31), 340 (4.09). NMR $\delta_{ppm}^{CDCl_3}$: 2.17 (6H, s, CH_3), 6.78 (4H, d, J=7.7 Hz, phenyl-H), 7.27 (10H, s, phenyl-H), 7.43 (4H, d, J=7.7 Hz, phenyl-H).

Disulfide (IVba)——Yellow needles (from acetone), mp 200—201°C, 46% yield. *Anal.* Calcd for $C_{32}H_{26}N_4S_2$: C, 72.44; H, 4.94; N, 10.56. Found: C, 72.38; H, 4.95; N, 10.54. UV λ_{max}^{EtOH} nm (log ε): 242.5 (4.54), 270 (sh., 4.24), 304 (3.87), 350 (sh., 3.78). NMR $\delta_{ppm}^{CDCl_3}$: 2.04 (6H, s, CH_3), 6.75—7.09 (4H, m, phenyl-H), 7.22—7.51 (12H, m, phenyl-H), 7.60—7.93 (4H, m, phenyl-H).

Disulfide (IVbb)——Yellow prisms (from ether), mp 166—167°C, 28% yield. *Anal.* Calcd for $C_{32}H_{24}Cl_2N_4S_2$: C, 64.10; H, 4.03; N, 9.35. Found: C, 64.08; H, 3.95; N, 9.27.

Disulfide (IVbc)——Yellow prisms (from ether), mp 197—198°C, 35% yield. *Anal.* Calcd for $C_{32}H_{24}Cl_2N_4S_2$: C, 64.10; H, 4.03; N, 9.35. Found: C, 64.07; H, 3.92; N, 9.28. UV λ_{max}^{EtOH} nm (log ε): 220 (sh., 4.61), 242.5 (4.51), 350 (sh., 3.88), 355 (sh., 3.73). NMR $\delta_{ppm}^{CDCl_3}$: 2.22 (6H, s, CH_3), 6.67—7.04 (4H, m, phenyl-H), 7.27—7.49 (10H, m, phenyl-H), 7.49—7.82 (4H, m, phenyl-H).

Disulfide (IVbd)——Yellow prisms (from acetone), mp 179—180°C, 38% yield. *Anal.* Calcd for $C_{32}H_{24}Br_2N_4S_2$: C, 55.82; H, 3.51; N, 8.14. Found: C, 55.92; H, 3.37; N, 7.83.

Disulfide (IVca)——Yellow prisms (from acetone), mp 184—185°C, 29% yield. *Anal.* Calcd for $C_{32}H_{24}Cl_2N_4S_2$: C, 64.10; H, 4.03; N, 9.35. Found: C, 64.16; H, 4.09; N, 9.08. UV λ_{max}^{EtOH} nm (log ε): 250 (4.26), 280 (sh., 4.30), 350 (3.50). NMR $\delta_{ppm}^{CDCl_3}$: 2.12 (6H, s, CH_3), 6.78—7.14 (4H, m, phenyl-H), 7.21—7.86 (14H, m, phenyl-H).

Disulfide (IVda)——Yellow prisms (from acetone), mp 192—193°C, 32% yield. *Anal.* Calcd for $C_{32}H_{24}Br_2N_4S_2$: C, 55.82; H, 3.51; N, 8.14. Found: C, 55.54; H, 3.38; N, 7.70. UV λ_{max}^{EtOH} nm (log ε): 252.5 (4.54), 275 (sh., 4.36), 315 (sh., 3.91), 350 (sh., 3.78). NMR $\delta_{ppm}^{CDCl_3}$: 2.09 (6H, s, CH_3), 6.96 (4H, broad s, phenyl-H), 7.33—7.76 (14H, m, phenyl-H).

Desulfurization of Disulfides (IV) by Raney Ni

General Procedure——Raney Ni (2.5 g) was added to a solution of a disulfide (IV) (0.5 g) in EtOH (20 ml), and the solution was refluxed for 7 h. The Raney Ni was filtered off, EtOH was removed, and the residue, an imidazole derivative (V), was recrystallized from an appropriate solvent.

Imidazole (Vaa)——Colorless prisms (from petr. ether), mp 90—91°C, 64% yield. *Anal.* Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.43; H, 6.07; N, 11.85. UV λ_{max}^{EtOH} nm (log ε): 230 (4.04), 277 (4.00). NMR $\delta_{ppm}^{CDCl_3}$: 2.34 (3H, d, J=1.0 Hz, CH_3), 6.87 (1H, q, J=1.0 Hz, C_5–H), 7.1—7.55 (10H, m, phenyl-H).

Imidazole (Vab)——Colorless scales (from ether–petr. ether), mp 87—88.5°C, 37% yield. *Anal.* Calcd for $C_{16}H_{13}ClN_2$: C, 71.50; H, 4.87; N, 10.43. Found: C, 71.59; H, 4.76; N, 10.23. UV λ_{max}^{EtOH} nm (log ε): 273.5 (4.04). NMR $\delta_{ppm}^{CDCl_3}$: 2.36 (3H, d, J=1.0 Hz, CH_3), 6.78 (1H, q, J=1.0 Hz, C_5–H), 7.06—7.56 (9H, m, phenyl-H).

Imidazole (Vad)——Colorless prisms (from petr. ether), mp 87—88°C, 40% yield. *Anal.* Calcd for $C_{16}H_{13}BrN_2$: C, 61.39; H, 4.19; N, 8.95. Found: C, 61.50; H, 4.21; N, 9.03. UV λ_{max}^{EtOH} nm (log ε): 276 (4.14). NMR $\delta_{ppm}^{CDCl_3}$: 2.33 (3H, d, J=1.0 Hz, CH_3), 6.86 (1H, q, J=1.0 Hz, C_5–H), 7.09—7.44 (9H, m, phenyl-H).

Imidazole (Vae)——Colorless prisms (from ether–petr. ether), mp 89—90°C, 42% yield. *Anal.* Calcd for $C_{16}H_{13}BrN_2$: C, 61.39; H, 4.19; N, 8.95. Found: C, 61.62; H, 4.31; N, 9.08. UV λ_{max}^{EtOH} nm (log ε): 276.5 (4.13). NMR $\delta_{ppm}^{CDCl_3}$: 2.34 (3H, d, J=1.0 Hz, CH_3), 6.87 (1H, q, J=1.0 Hz, C_5–H), 7.11—7.44 (9H, m, phenyl-H).

Imidazole (Vba)——Colorless scales (from petr. ether), mp 70—71°C, 61% yield. *Anal.* Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.05; H, 5.80; N, 11.88. UV λ_{max}^{EtOH} nm (log ε): 220 (sh., 4.21), 263.5 (4.25). NMR $\delta_{ppm}^{CDCl_3}$: 2.4 (3H, s, CH_3), 7.12—7.99 (11H, m, C_5–H, phenyl-H).

Imidazole (Vbb)——Colorless prisms (from petr. ether), mp 119—120°C, 51% yield. *Anal.* Calcd for $C_{16}H_{13}ClN_2$: C, 71.50; H, 4.87; N, 10.43. Found: C, 71.58; H, 4.83; N, 10.37. UV λ_{max}^{EtOH} nm (log ε): 262.5 (4.25). NMR $\delta_{ppm}^{CDCl_3}$: 2.27 (3H, s, CH_3), 7.22—7.87 (10H, m, C_5–H, phenyl-H).

Imidazole (Vca)——Colorless plates (from petr. ether), mp 125—126°C, 68% yield. *Anal.* Calcd for $C_{16}H_{13}ClN_2$: C, 71.50; H, 4.87; N, 10.43. Found: C, 71.52; H, 4.81; N, 10.50. UV λ_{max}^{EtOH} nm (log ε): 220 (sh., 4.27), 274 (4.39). NMR $\delta_{ppm}^{CDCl_3}$: 2.38 (3H, s, CH_3), 7.22—7.80 (10H, m, C_5–H, phenyl-H).

S-S Bond Cleavage Reaction of Disulfides (IV) by Triisopropylphosphite

General Procedure——Triisopropylphosphite (2 g) was added to a solution of a disulfide (IV) (0.5 g) in $CHCl_3$ (10 ml), and the solution was refluxed for 7 h. After $CHCl_3$ had been removed by evaporation, the residue was chromatographed over silica gel with ether–petr. ether to give a 5-isopropylthioimidazole derivative (VI).

5-Isopropylthioimidazole (VIaa)——Colorless needles (from petr. ether), mp 98—99.5°C, 30% yield. *Anal.* Calcd for $C_{19}H_{20}N_2S$: C, 73.98; H, 6.54; N, 9.08. Found: C, 73.60; H, 6.39; N, 8.91. UV λ_{max}^{EtOH} nm (log ε): 283 (4.13). NMR $\delta_{ppm}^{CDCl_3}$: 1.01 (6H, d, J=6.5 Hz, CH_3), 2.44 (3H, s, CH_3), 2.65 (1H, sept, J=6.5 Hz, >CH–), 7.07—7.49 (10H, m, phenyl-H).

5-Isopropylthioimidazole (VIab)——Colorless prisms (from petr. ether), mp 127—129°C, 39% yield. *Anal.* Calcd for $C_{19}H_{19}ClN_2S$: C, 66.55; H, 5.58; N, 8.17. Found: C, 66.81; H, 5.57; N, 8.11. UV λ_{max}^{EtOH} nm (log ε): 280 (4.16). NMR $\delta_{ppm}^{CDCl_3}$: 1.06 (6H, d, J=6.5 Hz, CH_3), 2.45 (3H, s, CH_3), 2.72 (1H, sept, J=6.5 Hz, >CH–), 7.09—7.51 (9H, m, phenyl-H).

5-Isopropylthioimidazole (VIac)——Colorless needles (from petr. ether), mp 98°C, 25% yield. *Anal.* Calcd for $C_{19}H_{19}ClN_2S$: C, 66.55; H, 5.58; N, 8.17. Found: C, 66.84; H, 5.16; N, 7.98. UV λ_{max}^{EtOH} nm (log ε): 223 (sh., 4.33), 282 (4.13). NMR $\delta_{ppm}^{CDCl_3}$: 1.03 (6H, d, J=6.5 Hz, CH_3), 2.43 (3H, s, CH_3), 2.65 (1H, sept, J=6.5 Hz, >CH–), 7.03—7.49 (9H, m, phenyl-H).

5-Isopropylthioimidazole (VIba)——Colorless prisms (from petr. ether), mp 67°C, 49% yield. *Anal.* Calcd for $C_{19}H_{20}N_2O$: C, 73.98; H, 6.54; N, 9.08. Found: C, 73.89; H, 6.57; N, 8.80. UV λ_{max}^{EtOH} nm (log ε): 248 (4.03), 276 (4.02). NMR $\delta_{ppm}^{CDCl_3}$: 0.93 (6H, d, J=6.5 Hz, CH_3), 2.3 (3H, s, CH_3), 2.73 (1H, sept, J=6.5 Hz, >CH–), 7.11—7.58 (8H, m, phenyl-H), 8.08—8.27 (2H, m, phenyl-H).

5-Isopropylthioimidazole (VIbb)——Colorless prisms (from petr. ether), mp 120°C, 38% yield. *Anal.* Calcd for $C_{19}H_{19}ClN_2S$: C, 66.55; H, 5.58; N, 8.17. Found: C, 66.46; H, 5.56; N, 8.13. UV λ_{max}^{EtOH} nm (log ε): 247.5 (4.04); 274.5 (4.06). NMR $\delta_{ppm}^{CDCl_3}$: 1.0 (6H, d, J=6.5 Hz, CH_3), 2.27 (3H, s, CH_3), 2.81 (1H, sept, J=6.5 Hz, >CH–), 7.24—7.68 (7H, m, phenyl-H), 8.18—8.33 (2H, m, phenyl-H).

5-Isopropylthioimidazole (VIbc)——Colorless plates (petr. ether), mp 107—108°C, 36% yield. *Anal.* Calcd for $C_{19}H_{19}ClN_2S$: C, 66.55; H, 5.58; N, 8.17. Found: C, 66.30; H, 5.60; N, 8.13. UV λ_{max}^{EtOH} nm (log ε): 245 (sh., 4.13), 276 (4.07). NMR $\delta_{ppm}^{CDCl_3}$: 0.91 (6H, d, J=6.5 Hz, CH_3), 2.28 (3H, s, CH_3), 2.72 (1H, sept, J=6.5 Hz, >CH–), 7.11—7.56 (7H, m, phenyl-H), 8.10—8.26 (2H, m, phenyl-H).

5-Isopropylthioimidazole (VIca)——Colorless prisms (petr. ether), mp 96°C, 35% yield. *Anal.* Calcd

for $C_{19}H_{19}ClN_2S$: C, 66.55; H, 5.58; H, 8.17. Found: C, 66.23; H, 5.46; N, 8.05. UV λ_{max}^{EtOH} nm (log ε): 252 (4.09), 283 (4.15). NMR $\delta_{ppm}^{CDCl_3}$: 0.93 (6H, d, J=6.5 Hz, CH_3), 2.30 (3H, s, CH_3), 2.73 (1H, sept, J=6.5 Hz, >CH–), 7.18—7.63 (7H, m, phenyl-H), 8.07—8.30 (2H, m, phenyl-H).

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