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Studies on Fungicides. XXIV.[1] Reaction of 5-Methoxycarbonylmethylidene-2-thioxo(or oxo)-4-thiazolidones with *o*-Aminobenzenethiol and Other Thiols

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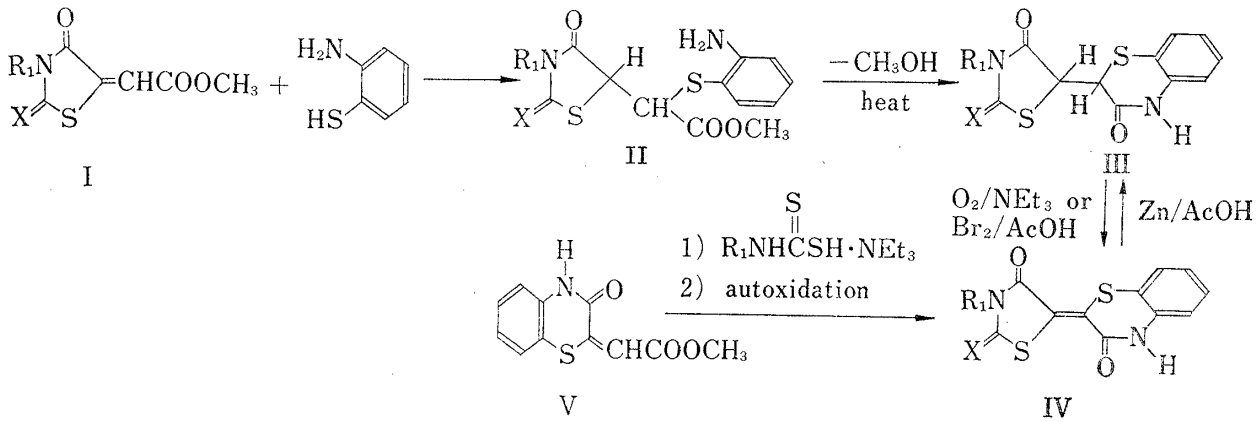
By a novel addition reaction of *o*-aminobenzenethiol to 5-methoxycarbonylmethylidene-2-thioxo(or oxo)-4-thiazolidones (I) were obtained 5-(3-oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-2-thioxo(or oxo)-4-thiazolidones (III).

I was also found to reat with thiols to afford 1 : 1 adducts (II and VI) in the presence of a catalytic amount of triethylamine. Thermal cyclization of the adducts (II) to III was observed. The adducts (VI) were proved to dissociate into I and thiols when heated above their melting points or dissolved in acetone or ethanol.

Oxidation of III and VI gave the dehydro-compounds (IV and VIII), respectively.

In the preceeding paper[1] was described a novel synthesis of a variety of 5,5′-bi-4-thiazolidones by the reaction of 5-methoxycarbonylmethylidene-4-thiazolidones (I) with dithiocarbamates. This prompted the author to synthesize new 5-(3-oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-2-thioxo(oxo or imino)-4-thiazolidones (III) by addition of *o*-aminobenzenethiol to the 4-thiazolidones (I).

Nucleophilic addition of thiols to activated double bonds is well reported in the literature.[3] *o*-Aminobenzenethiol reacts with ethyl maleate or fumarate and cinnamic acid to afford ethyl 3-oxo-2,3-dihydro-4H-1,4-benzothiazine-2-acetate[3d] and 2-phenyl-2,3-dihydro-1,5-benzothiazepin-4-(5H)-one,[3a] respectively.



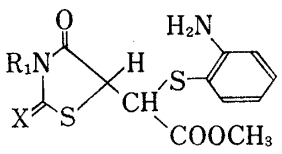
a: $R_1=CH_3$, X=S b: $R_1=PhCH_2$, X=S c: $R_1=CH_3$, X=O

Chart 1

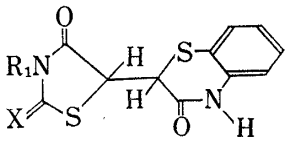
The 4-thiazolidones (I; X=S or O) were found to react readily with *o*-aminobenzenethiol to give a novel type of bi-heterocyclic compounds, 5-(3-oxo-2,3-dihydro-4H-1,4-benzothiazin-

1) Part XXIII: H. Nagase, *Chem. Pharm. Bull.* (Tokyo), **21**, 1132 (1973).
2) Location: *Higashiyodogawa-ku, Osaka.*
3) *e.g. a*) W.H. Mills and J.B. Whitworth, *J. Chem. Soc.*, **1927**, 2738; *b*) A. Mustafa, W. Asher, and M.E. E-D Sobhy, *J. Am. Chem. Soc.*, **82**, 2597 (1960); *c*) C.F.H. Allen and W.J. Humphlett, *Can. J. Chem.*, **44**, 2315 (1966); *d*) S.M. Kalbag, N.D. Nair, P. Ragagopalan, and C.N. Jalaty, *Tetrahedron*, **23**, 1911 (1967).

TABLE I. 5-(α-*o*-Aminophenylthio-methoxycarbonylmethyl)-2-thioxo(or oxo)-4-thiazolidones (IIa, b, c) and 5-(3-Oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-2-thioxo(or oxo)-4-thiazolidones (IIIa,b, c)



II

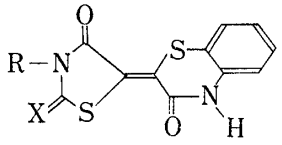


III

Compd. No.	R_1	X	mp (°C)	Appearance (recrystn. solvent)	Method[a] (% yield)	Formula	Analysis (%) Found (Calcd.) C	H	N
IIa	CH_3	S	77— 79	pale yellow powder	A (76.5)	$C_{13}H_{14}O_3N_2S_3$	45.50 (45.62)	3.97 (4.12)	8.36 (8.19)
IIb	$C_6H_5CH_2$	S	74	pale yellow powder	A (59.5)	$C_{19}H_{18}O_3N_2S_3$	55.20 (54.55)	4.17 (4.34)	6.90 (6.70)
IIc	CH_3	O	113—117	colorless powder	B (61.7)	$C_{13}H_{14}O_4N_2S_2$	47.80 (47.85)	4.20 (4.33)	8.46 (8.59)
IIIa	CH_3	S	240—242	pale yellow leaflets (EtOH)	C (84.8) D (81.0) E (40.0)	$C_{12}H_{10}O_2N_2S_3$	46.55 (46.46)	3.06 (3.25)	9.15 (9.03)
IIIb	$C_6H_5CH_2$	S	208—209	pale yellow powder (MeOH)	C (80.0) D (77.7) E (63.4)	$C_{13}H_{14}O_2N_2S_3$	55.89 (55.96)	3.52 (3.65)	7.23 (7.25)
IIIc	CH_3	O	190—191	colorless powder (acetone)	C (27.4) D (47.6) E (38.5)	$C_{12}H_{10}O_3N_2S_2$	48.92 (48.98)	3.44 (3.43)	9.39 (9.52)

a) See the experimental section.

TABLE II. 5-(3-Oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-$\Delta^{2',5}$-2-thioxo(or oxo)-4-thiazolidones (IV)



IV

Compd. No.	R	X	mp (°C)	Appearance	Method[a] (%yield)	Formula	Analysis (%) Found (Cacld.) C	H	N
IVa	CH_3	S	350	red yellow leaflets	G (37.1) H (62.5)	$C_{12}H_8O_2N_2S_3$	46.43 (46.76)	2.34 (2.62)	8.74 (9.09)
IVb	$C_6H_5CH_2$	S	330—332	red yellow leaflets	F (44.6) G (38.5) H (51.1)	$C_{18}H_{12}O_2N_2S_3$	55.82 (56.25)	2.93 (3.15)	7.42 (7.29)
IVc	CH_3	O	350	yellow needles	H (41.9)	$C_{11}H_6O_3N_2S_2$	49.56 (49.32)	2.64 (2.76)	9.60 (9.59)

a) See the experimental section.

2-yl)-2-thioxo-(or oxo)-4-thiazolidones (III), on heating in methanol. 2-Methylimino-3-methyl-5-methoxycarbonylmethylidene-4-thiazolidone (I; R_1=CH_3, X=NCH_3) failed to react with *o*-aminobenzenethiol under similar conditions. The expected intermediate compounds (II) were isolated when the reaction was carried out in the presence of a catalytic amount

of triethylamine. IIa, b, c gave the cyclized products (IIIa, b, c) on heating in methanol.

The structures of II and III are substantiated by the ultraviolet (UV) and nuclear magnetic resonance (NMR) spectra summarized in Table III. The UV spectra of IIa and IIIa,

TABLE III. NMR and UV Spectra of 5-(α-*o*-Aminophenylthio-methoxycarbonylmethyl)-2-thioxo(or oxo)-4-thiazolidone (IIa, b, c) and 5-(3-Oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-2-thioxo(or oxo)-4-thiazolidone (IIIa, b, c)

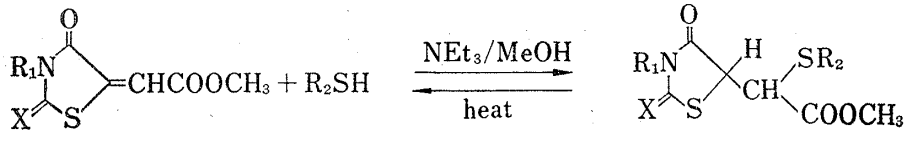
Compd. No.	R_1	X	NMR spectra (δ ppm) H_A[a)]	H_B[a)]	J_{AB} (Hz)	R_1	NH_2 (or NH)	OCH_3	Solvent	UV spectra $\lambda_{max}^{n\text{-hexane}}$ (nm) (log ε)		
IIa	CH_3	S	4.73	4.36	4.0	3.36	4.16	3.74	$CDCl_3$	257 (3.99)	295 (4.37)	348 (3.70)
			5.05	4.38	4.0	3.35		3.70	d_6-acetone			
			4.71	4.54	5.0	3.28		3.70				
IIb	$C_6H_5CH_2$	S	4.68	4.27	4.0	5.16 (CH_2)	3.85	3.70	$CDCl_3$			
IIc	CH_3	O	5.18	4.29	3.5	3.00	4.98	3.65	d_6-DMSO			
			5.04	4.37	4.0	3.07		3.69	d_6-acetone			
			4.82	4.57	5.0	3.07		3.69				
IIIa	CH_3	S	5.30	4.54	4.0	3.31	10.87		d_6-DMSO	237 (4.36)	255 (4.24)	297 (4.24)
			5.00	4.64	5.0	3.25	10.80					
IIIb	$C_6H_5CH_2$	S	5.48	4.61	4.0	5.17	10.91		d_6-DMSO	237 (4.35)	256 (4.29)	295 (4.29)
			5.24	4.79	5.0	5.12	10.91					
IIIc	CH_3	O	5.28	4.55	3.5	3.03	10.87		d_6-DMSO	238 (4.34)	282 (3.45)	
			5.00	4.65	5.0	2.97	10.78					

a) H_A is the methyne proton of the 4-thiazolidone ring and H_B is that of 2,3-dihydro-4H-1,4-benzothiazine ring.

b show the characteristic absorptions of 2-thioxo-4-thiazolidones in the region of 255 nm and 295 nm. In the NMR spectra of II and III appear the absorptions of the vicinal methyne protons in the region of δ 4.2—5.3 as a pair of doublets or as two sets of a pair of doublets. This proves that II and III are the mixtures of the diastereomers.

In an attempt to synthesize IIIb alternatively 2-methoxycarbonylmethylidene-3-oxo-2,3-dihydro-4H-1,4-benzothiazine (V)[3d)] was reacted with triethylammonium benzyldithiocarbamate in dimethylformamide. The product was proved to have the empirical formula of $C_{18}H_{12}O_2N_2S_3$ and gave IIIb on reduction with zinc in acetic acid. The results described above show that the structure of the product should be 3-benzyl-5-(3-oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-$\Delta^{2',5}$-2-thioxo-4-thiazolidone (IVb). IVa, b were obtained from IIIa, b on autoxidation in the presence of catalytic amount of triethylamine. Although IIIc failed to be autoxidized to IVc under similar conditions, the oxidation was effected by heating with an equivalent amount of bromine in acetic acid. It is reasonably considered that 2,3-dihydro-4H-1,4-benzothiazine (V) reacts with benzyldithiocarbamate initially to give IIIb, which then is autoxidized to IVb in the presence of triethylamine.

The results described above stimulated the author to investigate further the addition of other thiols to the 4-thiazolidones (I). Thiols such as *p*-chloro(bromo or methyl)-benzene-

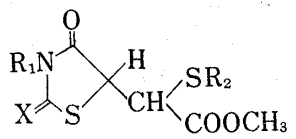


I VI

a : $R_1=CH_3$, X=S, b : $R_1=C_6H_5CH_2$, X=S
c : $R_1=CH_3$, X=O, d : $R=C_2H_5$, X=S

Chart 2

TABLE IV. 2-Thioxo(or oxo)-4-thiazolidones (VI)



Compd. No.	R_1	R_2	X	mp (°C)	Appearance (recrystn. solvent)	Method[a] (% yield)	Formula	Analysis (%) Found (Calcd.) C	H	N
VIa	CH_3	$COCH_3$	S	131—136	pale yellow powder	J (90.0)	$C_9H_{11}O_4NS_3$	36.77 (36.84)	3.68 (3.78)	4.84 (4.78)
VIb	CH_3	4-Cl-C_6H_4	S	103—105	pale yellow powder (*n*-hexane)	I (88.6)	$C_{13}H_{12}O_3ClNS_3$	43.04 (43.14)	3.20 (3.34)	3.65 (3.87)
VIc	C_2H_5	4-Br-C_6H_4	S	126—127	pale yellow needles (*n*-hexane)	I (65.0)	$C_{14}H_{14}O_3BrNS_3$	40.11 (40.00)	3.29 (3.36)	3.55 (3.33)
VId	$C_6H_5CH_2$	$COCH_3$	S	113—118	pale yellow powder	J (84.0)	$C_{15}H_{15}O_4NS_3$	48.90 (48.78)	4.16 (4.09)	3.91 (3.79)
VIe	$C_6H_5CH_2$	$C_6H_5CH_2$	S	118—120	pale yellow needles (AcOH)	I (41.7)	$C_{20}H_{19}O_3NS_3$	57.33 (57.55)	4.71 (4.59)	3.54 (3.36)
VIf	$C_6H_5CH_2$	4-Cl-C_6H_4	S	110—112	pale yellow powder (AcOH)	I (93.3)	$C_{19}H_{16}O_3ClNS_3$	51.90 (52.10)	3.51 (3.68)	2.97 (3.20)
VIg	$C_6H_5CH_2$	4-CH_3-C_6H_4	S	107—110	pale yellow powder (AcOH)	I (68.6)	$C_{20}H_{19}O_3NS_3$	57.50 (57.55)	4.66 (4.59)	3.48 (3.36)
VIh	CH_3	$COCH_3$	O	110—111	pale yellow powder	J (54.1)	$C_9H_{11}O_5NS_2$	38.98 (38.97)	3.95 (4.00)	4.76 (5.05)
VIi	CH_3	4-Cl-C_6H_4	O	75—84	colorless powder	I (26.1)	$C_{13}H_{12}O_4ClNS_2$	45.17 (45.15)	3.31 (3.50)	4.26 (4.05)

a) See the experimental section.

TABLE V. NMR and UV Spectra of 2-Thioxo(or oxo)-4-thiazolidones (VI)

Compd. No.	R_1	R_2	X	NMR spectra (δ ppm) H_A[a]	H_B[a]	J_{AB} (Hz)	R_1	R_2	OCH_3	Solvent[b]	UV spectra $\lambda_{max}^{n\text{-hexane}}$ (nm) (log ε)		
VIa	CH_3	$COCH_3$	S	5.18	4.79	4.0	3.36	2.38 (CH_3)	3.76	CH			
VIb	CH_3	4-Cl-C_6H_4	S	4.76	4.36	4.0	3.40		3.78	CH	230 (4.15)	258 (4.14)	292 (4.27)
				5.12	4.54	4.0	3.36		3.76	AC			
				4.71	4.75	5.0	3.36		3.76				
VIc	CH_3	4-Br-C_6H_4	S	4.74	4.39	4.0			3.77	CH			
VId	$C_6H_5CH_2$	$COCH_3$	S	5.21	4.75	3.5	5.13 (CH_2)	2.17 (CH_3)	3.70	CH		260 (4.02)	293 (4.19)
VIe	$C_6H_5CH_2$	$C_6H_5CH_2$	S	4.58	3.96	4.0	5.13 (CH_2)		3.70	CH			
VIf	$C_6H_5CH_2$	4-Cl-C_6H_4	S	4.70	4.32	4.0	5.22 (CH_2)		3.77	CH	230.5 (4.14)	259 (4.06)	295 (4.21)
VIg	$C_6H_5CH_2$	4-CH_3-C_6H_4	S	4.65	4.26	4.0	5.18 (CH_2)		3.72	CH		259 (4.06)	295 (4.23)
VIh	CH_3	$COCH_3$	O	5.19	5.09	3.5	2.96	2.40 (CH_3)	3.68	DM	258 (4.06)	291 (4.20)	346 (3.01)
VIi	CH_3	4-Cl-C_6H_4	O	4.74	4.36	4.0	3.12		3.76	CH			

a) H_A is the methyne proton of the ring and H_B is that of the side chain.
b) CH: $CDCl_3$, AC: d_6-acetone, DM: d_6-DMSO

thiols, α-toluenethiol or thiolacetic acid reacted with the 4-thiazolidones (I) to afford 1:1 adducts (VI) only when a catalytic amount of triethylamine was present. The results are summarized in Table IV. 2-Methylimino-3-methyl-5-methoxycarbonylmethylidene-4-thiazolidone (I; $R_1=CH_3$, $X=NCH_3$), however, failed to react with *p*-chlorobenzenethiol under similar conditions.

The structures of the adducts (VI) are identified by the UV and NMR spectra summarized in Table V. The UV spectra of VIb, d, f, g show the typical absorption bands of 2-thioxo-4-thiazolidones in the region of 260 nm and 295 nm. The NMR spectra of VI exhibit the absorptions of the vicinal methyne protons in the region of δ 4.2—5.2. The absorptions for VIb appear as a pair of doublets in deuterochloroform, while they appear as two sets of a pair of doublets in deuteroacetone. This indicates that the adducts (VI) are the mixtures of the diastereomers due to the vicinal asymmetric centers.

During the NMR examination of VIb in deuteroacetone partial dissociation of VIb into Ia and *p*-chlorobenzenethiol was revealed by the appearance of the peak at δ 6.78 due to the vinyl proton of Ia. Further evidence for the dissociation of VIb was given by the fact that the UV spectrum of VIb in ethanol was identical with that of Ia. VIb was found to dissociate completely to Ia and *p*-chlorobenzenethiol when heated above its melting point (103—105°) for a short time or by removal of the solvent from its acetone solution. Similar dissociations of VIa, e, i were observed in their UV spectra in ethanol. The results described above indicate that the addition of thiols to the 4-thiazolidones (I) is a reversible reaction and requires a base such as triethylamine as a catalyst.

Oxidation of VI is rather complicated than that of III. Although VIb, f failed to be autoxidized in the presence of triethylamine, they reacted with bromine to give the monobromides (VIIa, b), which were not isolated because of their instabilities. In the NMR spectrum of crude VIIa appears an absorption of a methyne proton at δ 4.6 as a singlet which is in a higher field than that of the ring of VIb and in a lower field than that of the side chain of VIb. This indicates that the methyne proton of the ring of VIb is substituted by bromine. The decomposition of VII proceeded in different ways depending on the reaction conditions. Thermal decomposition of the crude VIIa in acetic acid gave Ia and bis-*p*-chlorophenyldisulfide. When the crude VIIa was treated with triethylamine was obtained 5-(α-*p*-chloro-

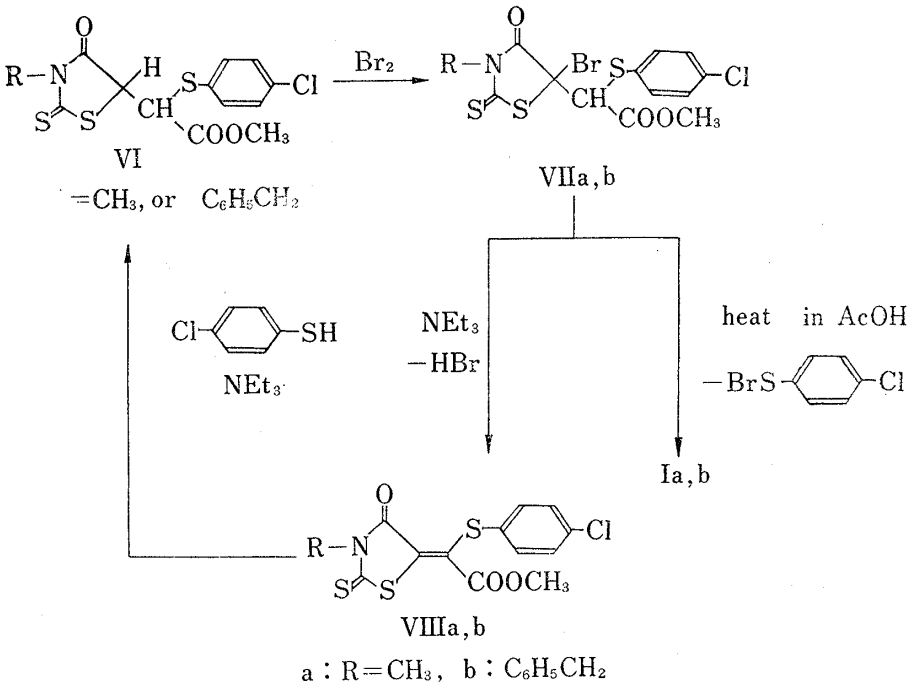
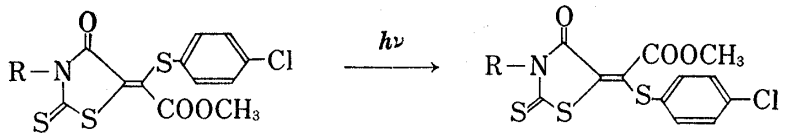


Chart 3

phenylthio-methoxycarbonylmethylidene)-2-thioxo-4-thiazolidone (VIIIa). In the same way was also obtained VIIIb. The structure of VIIIa, b was elucidated by the fact that VIIIb was reduced with *p*-chlorobenzenethiol to give VIf.

As for the geometry of IV and VIII their infrared (IR) spectra were investigated. Irradiation of the chloroform solution of IV and VIII with a 470 W incandescent bulb caused changes of carbonyl absorption bands in the IR spectra similar to those obtained with thioindigo,[4] thiopheneindigo,[5] bithiolanylidene[5] and $\Delta^{5,5'}$-birhodanines.[1] This implies that IV and VIII should have the *trans* geometry shown in Charts 1 and 3. The unstable *cis* isomers formed on irradiation of the chloroform solutions of IV were not isolated. On the other hand the *cis* isomers of VIII were found to be stable and obtained on removal of the solvent after irradiation of their chloroform solutions. The *cis* isomers (IX) were not converted to VIII on heating above their melting points.



VIIIa, b IXa, b

Chart 4

TABLE VI. 5-(*p*-Chlorophenylthio-methoxycarbonylmethylidene)-2-thioxo-4-thiazolidones (VIII and IX) and Their IR Spectra

Compd. No.	R	mp (°C)	Appearance (recrystn. solvent)	Formula	Analysis (%) Found (Calcd.) C	H	N	IR Spectra νCO in $CHCl_3$ (cm^{-1})
VIIIa	CH_3	125—127	red needles (MeOH)	$C_{13}H_{10}O_3NS_3Cl$	42.94 (43.38)	2.53 (2.80)	3.77 (3.89)	1705, 1700
VIIIb	$C_6H_5CH_2$	108—110	red needles (EtOH)	$C_{19}H_{14}O_3NS_3Cl$	52.08 (52.34)	3.33 (3.24)	3.55 (3.21)	1705, 1700
IXa	CH_3	175—177	yellow needles ($CHCl_3$)	$C_{13}H_{10}O_3NS_3Cl$	43.43 (43.38)	2.67 (2.80)	3.85 (3.89)	1740, 1715
IXb	$C_6H_5CH_2$	168—169	yellow needles (*n*-hexane)	$C_{19}H_{14}O_3NS_3Cl$	52.45 (52.34)	3.11 (3.24)	3.21 (3.21)	1740, 1715

Experimental

All melting points are uncorrected. IR spectra were recorded on a Hitachi EPI-S2 spectrometer. UV spectra were determined on a Hitachi EPF-2 spectrometer. NMR spectra were measured with a Varian A-60 spectrometer using tetramethylsilane as internal reference.

General Procedure for the Preparation of 5-(α-*o*-Aminophenylthio-methoxycarbonylmethyl)-2-thioxo-(or oxo)-4-thiazolidones (II)——Method A: A mixture of Ia (2.2 g, 10.1 mM), *o*-aminobenzenethiol (2.0 g, 16.0 mM) and triethylamine (0.025 ml) in methanol (50 ml) was refluxed for 1 min and condensed *in vacuo*. The residual oily matter was dissolved into ether (10 ml) and diluted with *n*-hexane until the mixture became turbid. After standing overnight the separated crystals were collected and washed with *n*-hexane to give 2.6 g (76.5%) of IIa, mp 77—79°. Analytical data are given in Table I.

Method B: A mixture of Ic (2.0 g, 9.9 mM), *o*-aminobenzenethiol (1.7 g, 13.6 mM) and triethylamine (0.025 ml) in methanol (30 ml) was refluxed for 20 min and condensed *in vacuo*. The residual oily matter was dissolved into benzene (20 ml). After cooling the separated crystals were collected and washed with

4) J. Winstein and G.M. Nyman, *J. Am. Chem. Soc.*, **78**, 2387 (1956).
5) H. Hermann and W. Luttke, *Chem. Ber.*, **101**, 1715 (1968).

n-hexane to give 2.0 g (61.7%) of IIc, mp 113—117°. Analytical data are given in Table I.

General Procedure for the Preparation of 5-(3-Oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-2-thioxo-(or oxo)-4-thiazolidones (III)——Method C: A mixture of Ib (1.4 g, 4.78 mM), *o*-aminobenzenethiol (0.7 g, 5.60 mM) in methanol (30 ml) was refluxed for 5 min. After cooling the separated crystals were collected and washed with small amount of cooled methanol to give 1.5 g (80.0%) of IIIb, mp 203—205°. After recrystallization from methanol it melts at 208—209°. Analytical data are given in Table I.

Method D: A solution of IIb (2.1 g, 5.0 mM) in ethanol (20 ml) was refluxed for 15 min. After cooling the separated crystals were collected and washed with ethanol to give 1.5 g (77.7%) of IIIb, mp 204—208°. After recrystallization from methanol it melts at 208—209°.

Method E: To a suspension of IVa (0.1 g, 0.325 mM) in acetic acid (50 ml) was added zinc dust (3 g) in small portions under reflux. The resulting pale yellow solution was filtered hot in order to remove the solid matters. The filtrate was diluted with water (50 ml) and allowed to stand overnight. The separated crystals were collected and washed with water to give 0.04 g (40.0%) of IIIa, mp 239—241°.

General Procedure for the Preparation of 5-(3-Oxo-2,3-dihydro-4H-1,4-benzothiazin-2-yl)-$\Delta^{2',5}$-2-thioxo(or oxo)-4-thiazolidones (IV)——Method F: A mixture of V (0.5 g, 2.20 mM) and triethylammonium benzyldithiocarbamate (0.7 g, 2.47 mM) in DMF (10 ml) was heated on a boiling water bath for 1 hr and allowed to stand overnight. To the mixture was added water. The separated solids were collected and washed with acetone to give 0.3 g (44.6%) of IVb, mp 330—332°. Analytical data are given in Table II.

Method G: A mixture of IIIb (0.39 g, 1.01 mM) and triethylamine (0.05 ml) in DMF (5 ml) was stirred at room temperature for 24 hr. The separated crystals were collected and washed with acetone to give 0.15 g (38.5%) of IVb, mp 330—332°.

Method H: To a solution of bromine (1.3 g, 8.12 mM) in acetic acid (20 ml) was added IIIa (2.4 g, 7.75 mM). The mixture was heated on a boiling water bath for 10 min. The separated crystals were collected and washed with water and then with acetone to give 1.5 g (62.5%) of IVa, mp 350°. Analytical data are given in Table II.

General Procedure for the Reaction of 2-Thioxo(or oxo)-4-thiazolidone (I) with Thiols——Method I: A mixture of Ib (1.0 g, 3.4 mM), *p*-chlorobenzenethiol (1.0 g, 70 mM) and triethylamine (0.05 ml) in ethanol (20 ml) was heated under reflux for 5 min. After cooling the separated crystals were collected and washed with ethanol to give 1.4 g (93.3%) of VIf, mp 108—110°. After recrystallization from acetic acid it melts at 110—112°. Analytical data are given in Table IV.

Method J: A mixture of Ib (2.93 g, 10 mM), thiolacetic acid (1.0 g, 13 mM) and triethylamine (0.025 ml) in acetone (15 ml) was heated under reflux for 30 min. After cooling the separated crystals were collected and washed with water and then with ether to give 3.1 g (84.0%) of VId, mp 113—118°. Analytical data are given in Table IV.

Preparation of VIIIa——a) Bromination of VIb: To a solution of VIb (3.6 g, 9.9 mM) in $CHCl_3$ (50 ml) was added dropwise bromine (1.6 g, 10.0 mM) in $CHCl_3$ (10 ml) at room temperature. After removal of the solvent *in vacuo* the residual oil was triturated with MeOH (30 ml). The yellow crystals were collected and washed with small amount of MeOH to give 2.4 g of crystals, mp 64—87°. The crystals were proved to be composed of Ia and VIIa in the molar ratio of 7: 5 by the NMR spectrum. NMR spectrum ($CDCl_3$): 3.53 (singlet, CH_3N), 3.87 (singlet, CH_3O), and 4.60 (singlet, CH) for VIIa and 3.49 (singlet, CH_3N), 3.87 (singlet, CH_3O) and 6.84 (singlet, =CH) for Ia.

b) Decomposition of VIIa in Acetic Acid: After bromination of VIb as described in a), the residual oil was dissolved in acetic acid (30 ml). The solution was heated under reflux for 10 min and diluted with water. After cooling the separated crystals were collected and washed with water and then with ether to give 1.5 g (88.7%) of Ia. When the ether extract was condensed to dryness colorless leaflets (0.4 g) of bis-*p*-chlorophenyldisulfide, mp 70—73°, was obtained.

c) Reaction of VIIa with Triethylamine: After bromination of IIb as described in a), the residual oil was dissolved into MeOH (30 ml). To the cooled solution was added dropwise NEt_3 (1.0 g, 10 mM) and then conc. HCl (20 ml). The mixture was heated on a water bath for a short time. After cooling the separated crystals were collected and washed with H_2O to give 2.9 g of red brown crystals, mp 86—94°. The crystals were proved to be a mixture of Ia and VIIIa in the molar ratio of 7: 6 by the NMR spectrum. The mixture was separated by column-chromatography with silica gel and $CHCl_3$. The separated red crystals were recrystallized from MeOH to give 0.6 g (16.6%) of VIIIa, mp 125—127°. Analytical and IR spectral data are given in Table VI.

Preparation of VIIIb——To a cooled stirred solution of bromine (0.16 g, 1.00 mM) in $CHCl_3$ (10 ml) was added VIf (0.40 g, 0.91 mM). After removal of the solvent *in vacuo* NEt_3 (0.1 g, 1.0 mM) in $CHCl_3$ (5 ml) was added to the residual oil. The separated $NEt_3 \cdot HBr$ was filtered and washed with $CHCl_3$. The combined filtrate and washings were condensed *in vacuo*. The residual oil was triturated with a small amount of ether to give 0.2 g of red brown crystals. The crystals were proved to be a mixture of Ib and IIIVb in the molar ratio of 1: 1 by the NMR spectrum. The mixture was separated by column-chromatography with silica gel and $CHCl_3$. The separated red crystals were recrystallized from EtOH to give VIIIb, mp 108—110°. Analytical and IR spectral data are given in Table VI.

Isomerization of VIIIa, b to IXa, b——A solution of VIIIa (0.36 g, 1.0 mM) in $CHCl_3$ (15 ml) was irradiated with a 470 W incandescent bulb for 20 min. The resulting yellow solution was condensed *in vacuo* to give 0.30 g (83.3%) of IXa, mp 175—177°. Analytical and IR spectral data are given in Table VI.

In the same way IXb was derived from VIIIb in 80.0% yield. Analytical and IR spectral data are given in Table VI.

Reduction of VIIIb to IIf——A solution of VIIIb (90 mg, 0.207 mM), *p*-chlorobenzenethiol (100 mg, 0.692 mM) and NEt_3 (0.05 ml) in EtOH (5 ml) was heated under reflux for 2 min. After removal of the solvent *in vacuo* the residual oil was triturated with hot *n*-hexane to give 60 mg (66.6%) of IIf, mp 105—108°. After recrystallization from AcOH it melts at 110—112°.

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