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Studies on Fungicides. XXIII.[1] Addition of Dithiocarbamates and Thiolcarbamates to 2-Thioxo-, 2-Oxo- and 2-Imino-5-methoxycarbonylmethylidene-4-thiazolidones

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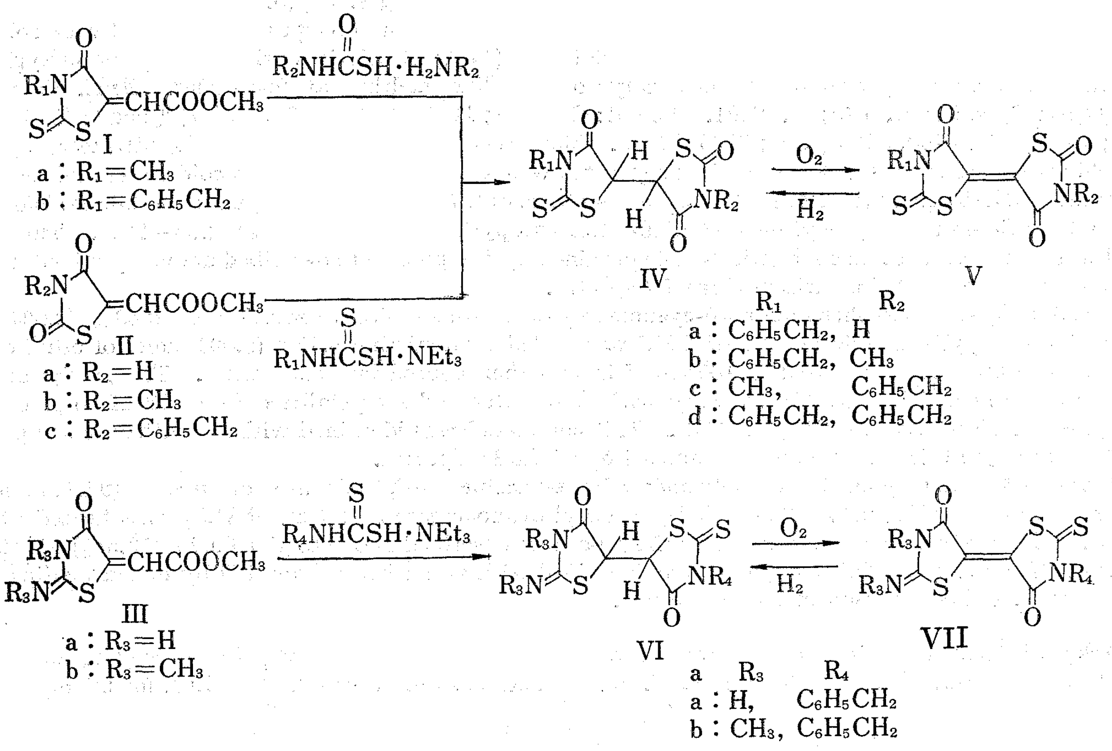
The addition of dithiocarbamates to double bonds is not well known in the literature. Thus only a few papers which are concerned with the addition of dithiocarbamates to α,β-unsaturated carbonyl compounds[3] have been published. In our previous papers[4] the addition of dithiocarbamates to maleic acid and its derivatives has been widely investigated. Furthermore, the addition of dithiocarbamates to 2-thioxo-5-methoxycarbonylmethylidene-4-thiazolidones (I) has been reported.[1]

The high reactivity of the double bonds of 2-thioxo-5-methoxycarbonylmethylidene-4-thiazolidones (I) to dithiocarbamates prompted the author to investigate further the addition reaction of dithiocarbamates and thiolcarbamates to 2-oxo- and 2-imino-5-methoxycarbonylmethylidene-4-thiazolidones (II and III).



Chart

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[1] Part XXII: H. Nagase, *Chem. Pharm. Bull.* (Tokyo), **21**, 279 (1973).
[2] Location: *Higashiyodogawa-ku, Osaka.*
[3] C.M. Buess, *J. Am. Chem. Soc.*, **77**, 6613 (1955); J.L. Garraway, *J. Chem. Soc.*, **1964**, 4004.
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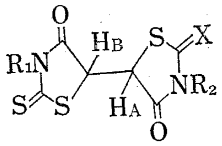
2-Oxo- and 2-imono-5-methoxycarbonylmethylidene-4-thiazolidones (II and III)[5] were found to be less reactive to dithiocarbamates than 2-thioxo-5-methoxycarbonylmethylidene-4-thiazolidones (I). Thus IIa, b, c, and IIIa,b reacted with dithiocarbamates only by heating in acetone or dimethylformamide to give 2-thioxo-2′-oxo-Δ5,5′-bi-4-thiazolidones (V) and 2-thioxo-2′-imino-Δ5,5′-bi-4-thiazolidones (VII), respectively.

In the above reaction the addition of dithiocarbamates to II and III was followed by cyclization to 5,5′-bi-4-thiazolidones (IV and VI), which were further autoxydized in the presence of triethylamine to Δ5,5′-bi-4-thiazolidones (V and VII), respectively, as shown in the Chart.

Because of the ease of oxidation IV and VI could not be isolated from the reaction mixture. But they were obtained by hydrogenation of V and VII with zinc in acetic acid.

Table I. Spectral Data of 5,5′-bi-4-Thiazolidones (IV, VI)



Compd. No.	R_1	R_2	X	UV spectra λ_{max}^{EtOH} (nm) (log ε)	IR spectra ν_{max}^{Nujol} (cm^{-1})	NMR spectra (δ ppm) (J Hz)					
						H_A	H_B	(J_{AB})	R_1	R_2	Solvent
IVa	$C_6H_5CH_2$	H	O	262 295 (4.03) (4.19)	1760 1730 1715—1700 (broad)	5.39	5.54	(4.0)	5.08 (CH_2)	12.4 (NH) (broad)	d_6-DMSO
IVc	CH_3	$C_6H_5CH_2$	O		1745,1720 1690	4.81	4.88	(3.5)	3.41	4.75 (CH_2)	$CDCl_3$
IVd	$C_6H_5CH_2$	$C_6H_5CH_2$	O	260 295 (4.00) (4.13)	1755,1735 1680	4.75			5.14 (CH_2) (q, $J=14.0$)	4.75 (CH_2)	$CDCl_3$
VIb	$C_6H_5CH_2$	CH_3	CH_3N	264 295 (4.35) (4.26)	1750,1740	4.63	4.78	(3.0)	5.16 (CH_2) (q, $J=14.0$)	3.22	$CDCl_3$

The structures of IV and VI have been substantiated by the ultraviolet (UV), infrared (IR), and nuclear magnetic resonance (NMR) spectra. The UV spectra of IV and VI showed characteristic absorption bands for 2-thioxo-4-thiazolidones in the region of 260 nm and 295 nm. The IR spectra showed the non-conjugated carbonyl bands in the region of 1700—1760 cm^{-1}. In the NMR spectra the absorptions of 5,5′-protons appeared in the region of δ 4.6—5.5.

The addition reaction of thiolcarbamates to 2-thioxo-5-methoxycarbonylmethylidene-4-thiazolidones (I), then, investigated. The addition took place on heating in methanol to give Δ5,5′-bi-4-thiazolidones (Vb,c,d) as shown in the Chart. 2-Oxo- and 2-imino-5-methoxycarbonylmethylidene-4-thiazolidones (II and III), however, failed to react with thiolcarbamates under similar conditions.

Irradiation of the chloroform solution of Δ5,5′-bi-4-thiazolidones (V and VII) caused changes of carbonyl absorption bands in IR spectra similar to those obtained with thioindigo,[6] thiopheneindigo[7] and bithiolanylidene.[7] This indicates that V and VII may have the geometry shown in the, Chart.

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5) H. Nagase *Chem. Pharm. Bull.* (Tokyo), **21**, 270 (1973).
6) J. Winstein and G.M. Nyman, *J. Am. Chem. Soc.*, **78**, 2387 (1956).
7) H. Hermann and W. Luttke, *Chem. Ber.*, **101**, 1715 (1968).

Experimental

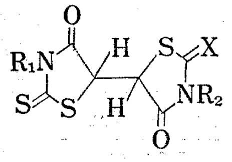
All melting points are uncorrected. IR spectra were recorded on a Hitachi EPI-S2 spectrometer in nujol mull. UV spectra were measured with a Hitachi EPF-2 spectrometer. NMR spectra were obtained with a Varian A-60 spectrometer using tetramethylsilane as internal reference.

3-Benzyl-2-thioxo-2′-oxo-Δ5,5′-bi-4-thiazolidone (Va) Method A——A solution of IIa (1.8 g, 9.82 mM) and triethylammonium N-benzyldithiocarbamate (2.9 g, 10.2 mM) in acetone (20 ml) was stirred for 1.5 hr at room temp. After standing over night the mixture was refluxed for 5 min. After cooling the mixture was acidified with conc. HCl (1 ml) and then diluted with water to give 1.6 g (49.4%) of Va. Recrystallization from aqueous acetone gave 1.2 g of Va, mp 249—251°. Analytical data are listed in Table II.

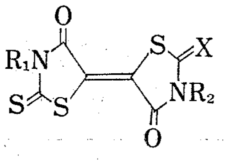
2-Thioxo-2′-imino-Δ5,5′-bi-4-thiazolidone (VIIa) Method B——A mixture of IIIa (1.5 g, 8.06 mM) and triethylammonium N-benzyldithiocarbamate (3.0 g, 10.6 mM) in DMF (20 ml) was heated at 80° under stirring for 30 min. After cooling the mixture was diluted with water (150 ml). The separated resinous matter was recrystallized from ethanol to give 1.0 g (37.0%) of VIIa, mp 290°. Analytical data are listed in Table II.

3′-Methyl-2-thioxo-2′-methylimino-Δ5,5′-bi-4-thiazolidone (VIIb). Method C——A mixture of IIIb (1.1 g, 5.15 mM) and triethylammonium N-benzyldithiocarbamate (1.6 g, 5.63 mM) in DMF (20 ml) was heated at 80° under stirring for 5 min. After cooling the mixture was diluted with water to give a red brown

Table II. 5,5′-Bi-4-thiazolidones (IV, VI) and Δ5,5′-Bi-4-thiazolidones (V, VII)



IV or VI



V or VII

Compod. No.	R_1	R_2	X	mp (°C)	Appearance (Recrystn. solvent)	Method (% yield)	Formula	Analysis (%) Found (Calcd.)		
								C	H	N
IVa	$C_6H_5CH_2$	H	O	57— 60	pale yellow powder (acetone)	E (60.0)	$C_{13}H_{10}O_3N_2S_3$	46.13 (46.12)	3.18 (2.98)	8.03 (8.28)
IVc	CH_3	$C_6H_5CH_2$	O	101—102	pale yellow powder (C_6H_6)	E (50.0)	$C_{14}H_{12}O_3N_2S_3$	47.67 (47.73)	3.12 (3.43)	7.75 (7.95)
IVd	$C_6H_5CH_2$	$C_6H_5CH_2$	O	120—122	pale yellow needles (C_6H_6)	E (75.0)	$C_{20}H_{16}O_3N_2S_3$	56.22 (56.08)	3.68 (3.77)	6.42 (6.54)
VIb	$C_6H_5CH_2$	CH_3	CH_3N	147—148	pale yellow powder (acetone)	E (63.1)	$C_{15}H_{15}O_2N_3S_3$	49.56 (49.32)	4.27 (4.14)	11.18 (11.50)
Va	$C_6H_5CH_2$	H	O	249—251	yellow powder (acetone)	A (37.1)	$C_{13}H_{10}O_3N_2S_3$	46.11 (46.44)	2.53 (2.40)	8.29 (8.33)
Vb	$C_6H_5CH_2$	CH_3	O	199—220	yellow powder (acetone)	A (49.1) D (25.0)	$C_{14}H_{10}O_3N_2S_3$	47.82 (48.01)	2.70 (2.88)	8.09 (8.00)
Vc	CH_3	$C_6H_5CH_2$	O	210	yellow needles (AcOH)	A (61.4) D (41.3)	$C_{14}H_{10}O_3N_2S_3$	48.08 (48.01)	2.77 (2.88)	8.00 (8.00)
Vd	$C_6H_5CH_2$	$C_6H_5CH_2$	O	272	brown leaflets (AcOH)	A (51.7) D (32.2)	$C_{20}H_{14}O_3N_2S_3$	56.56 (56.34)	3.57 (3.33)	7.08 (6.57)
VIIa	$C_6H_5CH_2$	H	NH	290	brown powder (EtOH)	B (37.0)	$C_{13}H_9O_2N_3S_3$	46.54 (46.57)	2.49 (2.71)	12.20 (12.54)
VIIb	$C_6H_5CH_2$	CH_3	CH_3N	189—190	red needles (acetone)	C (42.6)	$C_{15}H_{13}O_2N_3S_3$	49.46 (49.59)	3.55 (3.61)	11.56 (11.57)

resinous matter. Recrystallization from aqueous acetone gave 1.3 g of red crystals, mp 115—130°, which were identified as a mixture of VIb and VIIb by thin-layer chromatography. The solution of the crystals and triethylamine (0.05 ml) in acetone (20 ml) was stirred for 2 hr at room temp. The separated red crystals were collected and washed with acetone to give 0.8 g (42.6%) of VIIb, mp 189—190°. Analytical data are listed in Table II.

Reaction of Ib with Benzylammonium N-Benzylthiolcarbamate. Method D——A mixture of Ib (1.4 g, 4.78 mM) and benzylammonium N-benzylthiolcarbamate (2.0 g, 7.30 mM) in methanol (40 ml) was heated under reflux for 1 min and left standing for 1 hr at room temperature. The separated crystals were collected and washed with methanol to give 0.5 g (32.2%) of Vd, mp 254—270°. On recrystallization from acetic acid it melts at 270°. Analytical data are listed in Table II.

General Procedure for Hydrogenation of V and VII. Method E——To a solution of Vd (0.85 g, 2.0 mM) in acetic acid (30 ml) was added zinc dust (1.0 g) in small portions under reflux. The pale yellow solution was filtered hot in order to remove solid matters. The filtrate was diluted with water. The separated crystals were collected and washed with water to give 0.63 g (75.0%) of IVd, mp 115—120°. Recrystallization from benzene gave 0.45 g of IVd, mp 120—122°. Analytical data are listed in Table II.

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Stereochemical Studies. XXII.[1] Thermal Rearrangement of *S*(−)-1-Phenylethyl Isocyanide[2]

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As a possible reverse reaction of the well-known Hofmann, Curtius, and Schmidt rearrangements,[4,5] the authors paid attention to the thermal rearrangement[6] of isocyanide (I) to cyanide (II) by way of a cyclic transition state such as III. However, since only one report[6a] concerned with the thermal reaction of optically active and simple open chain compound in which *S*(+)-2-butyl isocyanide was converted to *S*(+)-2-butyl cyanide with 87% retention of configuration, we also undertook the thermal rearrangement of *S*(−)-1-phenylethyl isocyanide (*S*(−)-IV) carrying a simple structure similar to *S*(+)-2-butyl isocyanide, to explore the general applicability of this novel rearrangement to synthetic organic chemistry.

Preliminary experiments carried out with racemic compounds were described in detail in experimental part.

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