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Studies on Fungicides. XXII.[1] Reaction of Dimethyl Acetylenedicarboxylate with Dithiocarbamates, Thiolcarbamates, Thiosemicarbazides and Thiosemicarbazones

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Dimethyl acetylenedicarboxylate was found to react readily with dithiocarbamates, thiolcarbamates, thiosemicarbazides and thiosemicarbazones to give 4-thiazolidones (I, IV, V, VI and VII). The exodouble bond of 4-thiazolidones (I) was highly reactive to dithiocarbamates to give 2,2′-dithioxo-5,5′-bi-4-thiazolidones (II), which were autoxydized to 2,2′-dithioxo-Δ5,5′-bi-4-thiazolidones (III) in the presence of catalytic amount of amines.

The high reactivity of dimethyl acetylenedicarboxylate (DMAD) to thioureas[1] stimulated the author to investigate the reactions of DMAD with dithiocarbamate, thiolcarbamates, thiosemicarbazides, and thiosemicarbazones.

Reaction of Dimethyl Acetylenedicarboxylate with Dithiocarbamates

Dithiocarbamates react with some acetylenic compounds such as propiolic acid,[3] ethyl propiolate,[4,5] cyanoacetylene[4,5] and β-hydroxymethylpropiolate[6] in various ways to give *cis*-β-thiocarbamoylthio-acrylic acids, diethyl *cis*,*cis*-β,β'-bithioacrylate, *cis*,*cis*-β,β'-bithioacrylonitrile and 3,4-dihydro-6-hydroxymethyl-2-thioxo-4-oxo-2*H*-1,3-thiazine, respectively.

Although DMAD reacts readily with dithiocarbamates in methanol at room temperature, the course of the reaction was found to be markedly influenced by the reaction conditions. When DMAD was added to the methanolic solution of ammonium N-benzyldithiocarbamate, red crystals were obtained as a result of the reaction of DMAD with two equivalents of N-benzyldithiocarbamates. The product was identified with 3,3′-dibenzyl-2,2′-

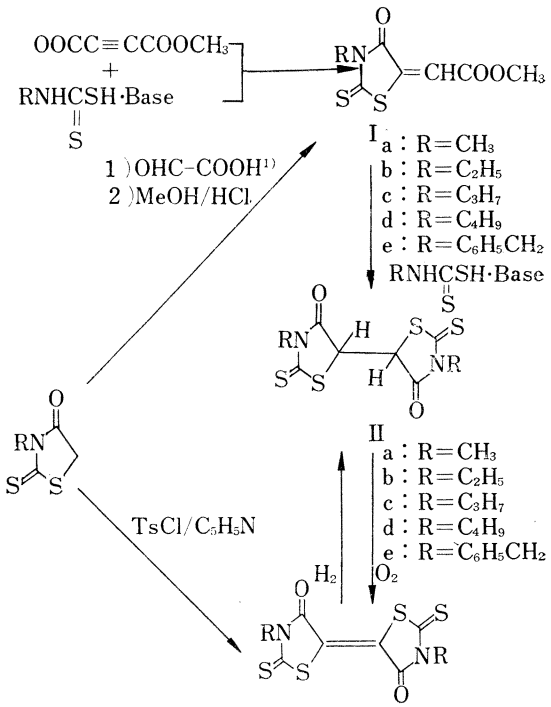


Chart 1

1) Part XXI: H. Nagase, *Chem. Pharm. Bull.* (Tokyo), **21**, 279 (1973).
2) Location: *Higashiyodogawa-ku, Osaka.*
3) J.L. Garraway, *J. Chem. Soc.*, **1962**, 4077.
4) Y. Kishida and A. Terada, *Chem. Pharm. Bull.* (Tokyo), **16**, 1351 (1968).
5) E.N. Cain and R.N. Warrener, *Aust. J. Chem.*, **23**, 51 (1970).
6) R.N. Warrener and E.N. Cain, *Aust. J. Chem.*, **23**, 785 (1971).

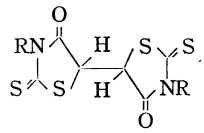
dithioxo-⊿5,5′-bi-4-thiazolidone (IIIe) synthesized unambiguously by self-condensation of 3-benzyl-2-thioxo-4-thiazolidone according to Nederlof's method.[7] Alternative synthesis of IIIe by the reaction of N-benzyldithiocarbamate with dibromosuccinic acid or dimethyl dibromosuccinate further confirmed the identity.

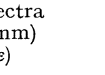
On the other hand, when ammonium N-benzyldithiocarbamate was added slowly to the methanolic solution of small excess amount of DMAD, yellow crystals were formed. The yellow crystals were changed to the red crystals described above by the addition of excess N-benzyldithiocarbamate. The yellow crystals were identified with the authentic 3-benzyl-5-methoxycarbonylmethylidene-2-thioxo-4-thiazolidone (Ie).[1]

In the same manner, Ia,b,c,d, and IIIa,b,c,d were obtained from the reaction of DMAD with alkylammonium N-alkyldithiocarbamates. Ia was identified with the authentic 3-methyl-5-methoxycarbonylmethylidene-2-thioxo-4-thiazolidone.[1]

2,2′-Dithioxo-⊿5,5′-bi-4-thiazolidones (IIIa,b,c,d,e) were hydrogenated with zinc dust in acetic acid or with *p*-chlorobenzenethiol to give the corresponding 2,2′-dithioxo-5,5′-bi-4-thiazolidones (IIa,b,c,d,e) as were observed with other 2,2′-dithioxo-⊿5,5′-bi-4-thiazolidones.[7] The infrared (IR) spectrum of II reveals the non-conjugated carbonyl bands at 1720—1730 cm^{-1}. The ultraviolet (UV) spectrum of II shows characteristic absorptions in the region of 260 nm and 295 nm. In the nuclear magnetic resonance (NMR) spectrum of II, the protons at the 5- and 5′-positions appear as a sharp singlet equivalent to two protons. These 2,2′-dithioxo-5,5′-bi-4-thiazolidones (II) were proved to be readily autoxidized to 2,2′-dithioxo-5,5′-bi-4-thiazolidones (III) in the presence of catalytic amount of triethylamine.

TABLE I. UV, IR and NMR Spectra of 2,2′-Dithioxo-5,5′-bi-4-thiazolidones (II)



Comp. No.	R	UV spectra λ_{max}^{EtOH} (nm) (log ε)		IR spectra ν_{max}^{Nujol} (cm^{-1})	NMR spectra (δ ppm)	
						solvent
IIa	CH_3	258 (4.25)	295 (4.38)	1720	5.38	d_6-DMSO
IIb	C_2H_5	260 (4.25)	296 (4.39)	1730, 1720	4.95	$CDCl_3+d_6$-DMSO
IIc	C_3H_7			1730, 1720	4.87	$CDCl_3$
IId	C_4H_9			1730, 1720	4.84	$CDCl_3$
IIe	$C_6H_5CH_2$	262 (4.24)	299 (4.36)	1730, 1720	4.92	$CDCl_3$

The above results suggest that the reaction of DMAD with dithiocarbamates gives 4-thiazolidones (I) and that dithiocarbamates react readily with I to give 2,2′-dithioxo-5,5′-bi-4-thiazolidones (II), which are authoxidized to 2,2′-dithioxo-⊿5,5′-bi-4-thiazolidones (III) in the presence of amines, as shown in Chart 1. This was supported by the fact that 4-thiazolidones (I), 2,2′-dithioxo-5,5′-bi-4-thiazolidones (II) and 2,2′-dithioxo-⊿5,5′-bi-4-thiazolidones (III) were detected in the reaction mixtures by thin-layer chromatography (TLC) in the earlier stage of the reaction, when DMAD was added to the methanolic solution of dithiocarbamates.

Reaction of Dimethyl Acetylenedicarboxylate with Thiolcarbamates

DMAD reacted with methylammonium N-methylthiolcarbamate in methanol at room temperature to give 3-methyl-5-methoxycarbonylmethylidene-2,4-dioxothiazolidine (IVa). IVa failed to reat further with thiolcarbamates.

7) A. Nederlof, *Rec. Trav. Chim.*, **82**, 75 (1963).

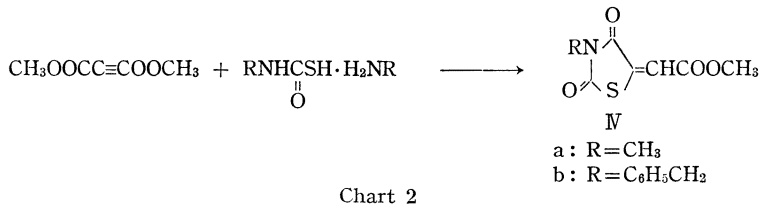
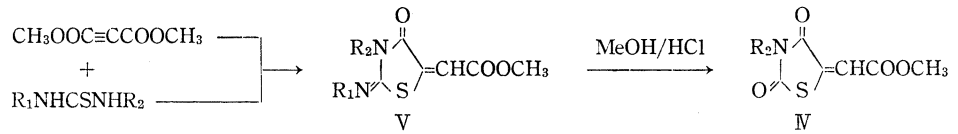


Chart 2

In the same way, IVb was obtained from DMAD and benzylammonium N-benzylthiolcarbamate. 2,4-Dioxo-thiazolidines (IVa,b) were identified with the authentic samples.[1]

Reaction of Dimethyl Acetylenedicarboxylate with Thiosemicarbazides and Acetone Thiosemicarbazones

As for the reaction of thiosemicarbazides with acetylenic compounds, Lown, *et al.*[8] reported that the reaction of DMAD with 4-methyl(allyl or phenyl)-thiosemicarbazides gave 3,4-dihydro-2*H*-1,3-thiazines.



a: $R_1=(CH_3)_2C=N$, $R_2=H$
b: $R_1=(CH_3)_2C=N$, $R_2=CH_3$
c: $R_1=C_6H_5$, $R_2=NH_2$

c: $R_2=H$
d: $R_2=NH_2$

Chart 3

The reaction of DMAD with thiosemicarbazides and acetone thiosemicarbazones, however, were proved to give 4-thiazolidones (V) by chemical evidence as Charts 3 and 4 show.

DMAD reacted readily with 4-phenylthiosemicarbazide, acetone thiosemicarbazone and acetone 4-methylthiosemicarbazone to give 4-thiazolidones (Va,b,c), respectively. Va was hydrolyzed with methanolic hydrogen chloride to give the compound identified by the authentic 2,4-dioxothiazolidine (IVc).[1] Vb was identified with the specimen prepared by the conventional methylation of Va. Vc was hydrolyzed with methanolic hydrogen chloride to give the 2,4-dioxothiazolidine (IVd), which gave the known compound IVc[1] by the reaction with nitrous acid.

From the reaction of DMAD with 4-methylthiosemicarbazide, the main product (A), mp 178—179° and the minor product (B), mp 170—172° were obtained. The compound (A) reacted with acetone to give 2-methylimino-3-isopropylideneamino-5-methoxymethylidene-4-thiazolidone (VIII), the structureal isomer of Vb. The structure of the compound (A), therefore, was determined as 2-methylimino-3-amino-5-methoxycarbonylmethylidene-4-thiazolidone (VII). Reaction of VII with DMAD gave a mixture of the 1:1 adducts; amino-maleate (*cis*-IX) and amino-fumarate (*trans*-IX) in the ratio of 3:4 by the NMR spectrum. In the NMR spectrum, the signal due to NH of *trans*-IX is shifted to a lower field than that of *cis*-IX because of hydrogen bonding between NH and the ester carbonyl group. Futhermore, the vinyl proton of amino-fumarate moiety of *trans*-IX appears at a lower field (δ 5.48) than that of amino-maleate moiety of *cis*-IX, which is consistent with the NMR spectra of the related compounds.[9]

The compound (B) was found to be formed by the reaction of DMAD with two equivalents of 4-methylthiosemicarbazide by the elemental analysis. However, since the compound

8) J.W. Lown and J.C.N. Ma, *Can. J. Chem.*, **45**, 953 (1967).
9) R. Huisgen, K. Herbig, A. Siegle, and H. Hubner, *Chem. Ber.*, **99**, 2526 (1966); E.C. Taylor and N.D. Heindel, *J. Org. Chem.*, **32**, 3339 (1967); N.D. Heindel, I.S. Bechara, T.F. Lembe, and V.B. Fish, *ibid.*, **32**, 4155 (1967); S. Toppet, E. van Look, F. Lábbé, and S. Smets, *Chem. & Ind.*, **1971**, 703.

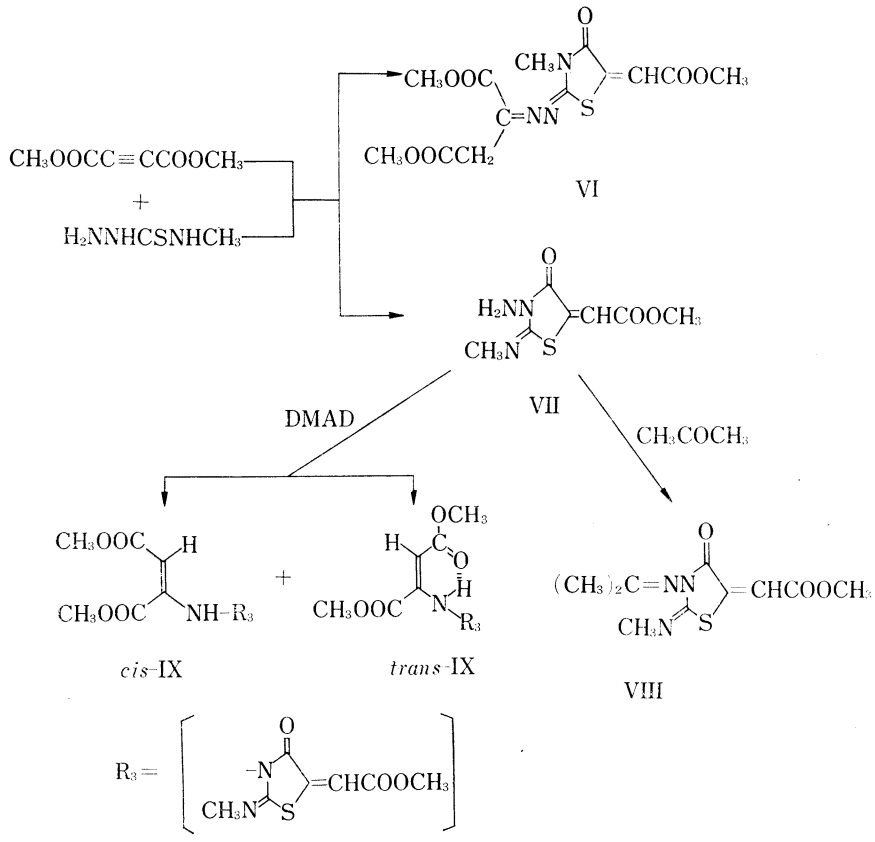


Chart 4

(B) was not identical with both isomeric IX in all respects, it is obvious that the compound (B) dose not arise from the reaction of VII with DMAD. Taking into consideration that DMAD reacts[8,10] with hydrazines and semicarbazides to give hydrazones and semicarbazones of dimethyl oxaloacetate, respectively, it is likely that DMAD might react with 4-methylthiosemicarbazide to afford both the 4-thiazolidone (VII) and 4-methylthiosemicarbazone of dimethyl oxaloacetate, and the latter might then react further with DMAD to give the 4-thiazolidone (VI). The NMR spectrum of the compound (B) was in good consistence with that expected for VI.

Experimental

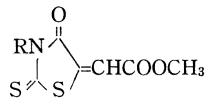
All melting points are uncorrected. IR spectra were recorded on a Hitachi EPI-S2 spectrometer in nujcl mulls. UV spectra were measured with a Hitachi EPF-2 spectrometer. NMR spectra were obtained with a Varian A-60 spectrometer. Chemical shifts are recorded in δ units using tetramethylsilane as internal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

General Procedure for the Preparation of 5-Methoxycarbonylmethylidene-2-thioxo-4-thiazolidines (I) (Method A)——To a stirred solution of DMAD (0.7 g, 4.93 mM) in cooled methanol (20 ml) was added ammonium N-benzyldithiocarbamate (0.9 g, 4.50 mM) in small portions over a period of 1 min. After addition, conc. HCl (1 ml) was added to the mixture. After stirring for 1 hr, the separated yellow crystals were collected and washed with small amount of methanol. The crude product (0.7 g) was extracted with hot acetone (20 ml). The residual red crystals (0.02 g, mp 270°) was identified with IIIe. Removal of the solvent from the acetone extract gave 0.65 g (49.3%) of Ie as yellow needles, mp 147—148° (lit.[1] mp 147—149°).

10) N.D. Heindel, P.D. Kinnewell, and M. Pfau, *J. Org. Chem.*, **35**, 81 (1970).

In the same manner, Ia,b,c,d were obtained by the reaction of DMAD with alkylammonium N-alkyldithiocarbamates. The results are summarized in Table II.

Table II. 5-Methoxycarbonylmethylidene-2-thioxo-4-thiazolidone (I)

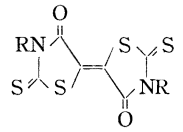


Comp. No.	R	mp (°C)	Appearance (recrystn. solvent)	Method (% yield)	Formula	Analysis (%) Calcd. (Found) C	H	N
Ia	CH_3	120—121[a]	yellow needles (AcOH)	A (38.0)				
Ib	C_2H_5	85— 87	yellow needles (AcON)	A (45.0)	$C_8H_9O_3NS_2$	41.56 (41.50)	3.92 (3.86)	6.06 (6.22)
Ic	C_3H_7	105—107	yellow needles (AcOH)	A (51.7)	$C_9H_{11}O_3NS_2$	44.08 (44.07)	4.52 (4.45)	5.71 (5.88)
Id	C_4H_9	90— 91	yellow plates (AcOH)	A (50.5)	$C_{10}H_{13}O_3NS_2$	46.33 (46.48)	5.06 (5.01)	5.40 (5.32)
Ie	$PhCH_2$	147—149[b]	yellow needles (EtOH)	A (49.3)				

a) lit.[1] mp 120—121° *b*) lit.[1] mp 147—149°

General Procedure for the Preparation of 2,2′-Dithioxo-Δ5,5′-bi-4-thiazolidones (III) (Method B)——To a stirred solution of ammonium N-benzyldithiocarbamate (2.0 g, 10.0 mM) in cooled methanol (20 ml), was added DMAD (1.45 g, 10.2 mM) dropwise over a period of 5 min. After stirring for 8 hr at room temperature, the separated red crystals were collected and washed with methanol to give 1.7 g (79.0%) of IIIe, mp 250°. After recrystallization from dioxane, it melts at 270°. The results are summarized in Table III.

Table III. 2,2′-Dithioxo-Δ5,5′-bi-4-thiazolidones (III)



Compd. No.	R	mp (°C)	Appearance (recrystn. solvent)	Method (% yield)	Formula	Analysis (%) Calcd. (Found) C	H	N
IIIa	CH_3	317	red brown powder (HOAc)	B (65.0)	$C_8H_6O_2N_2S_4$	33.12 (33.06)	2.08 (2.16)	9.66 (9.64)
IIIb	C_2H_5	246—247[a]	orange plates (HOAc)	B (73.1)	$C_{10}H_{10}O_2N_2S_4$	37.74 (37.89)	3.17 (3.07)	8.80 (8.80)
IIIc	C_3H_7	196—199	orange plates (HOAc)	B (68.0)	$C_{12}H_{14}O_2N_2S_4$	41.62 (41.33)	4.08 (4.08)	8.09 (8.08)
IIId	C_4H_9	190—191	orange plates (HOAc)	B (56.0)	$C_{14}H_{18}O_2N_2S_4$	44.92 (44.67)	4.85 (4.93)	7.48 (7.45)
IIIe	$C_6H_5CH_2$	270	orange powder (dioxane)	B (79.0)	$C_{20}H_{14}O_2N_2S_4$	54.30 (54.11)	3.19 (3.22)	6.33 (6.38)

a) lit.[7] mp 252—252.5°

Self-condensation of 3-Benzyl-2-thioxo-4-thiazolidone——3-Benzyl-2-thioxo-4-thiazolidone (4.4 g, 20.0 mM) and tosyl chloride (11 g) were dissolved into pyridine (10 ml). The mixture was heated for 20 min on a boiling water bath. After cooling, the separated crystals were collected and washed with acetone to give 2.4 g (54.5%) of IIIe, mp 250°. After recrystallization from dioxane, it melts at 270°.

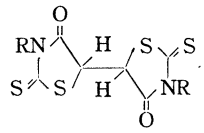
Reaction of *dl*-Dibromosuccinic Acid with Triethylammonium N-Benzyldithiocarbamate——To a stirred solution of *dl*-dibromosuccinic acid (5.5 g, 20.0 mM) in aqueous Na_2CO_3 (2 g of Na_2CO_3 in 30 ml of water), was added triethylammonium N-benzyldithiocarbamate (6 g, 21.1 mM) in small portions. After stirring for 20 min, 10% HCl (4 ml) was added to the mixture. Small amount of dark green precipitate was removed by filtration. The filtrate was allowed to stand overnight. The separated red brown crystals were collected and washed with acetone to give 1.0 g (11.4%) of IIIe, mp 248°. After recrystallization from dioxane, it melts at 270°.

Reaction of Dimethyl *meso*-Dibromosuccinate with Triethylammonium N-Benzyldithiocarbamate——To a stirred solution of dimethyl *meso*-dibromosuccinate (1.5 g, 4.09 mM) in methanol (20 ml) was added triethylammonium N-benzyldithiocarbamate (2.9 g, 10.2 mM). The mixture was refluxed for 20 min. After cooling, the separated crystals were collected and washed with water and then with acetone to give 0.8 g (36.1%) of IIIe, mp 250°. After recrystallization from dioxane it melts at 270°.

General Procedure of Hydrogenation of 2,2′-Dithioxo-Δ5,5′-bi-4-thiazolidones (III)——a) Method C: To the solution of IIIe (0.7 g, 1.59 mM) in acetic acid (30 ml) was added Zn dust (0.6 g) in small portions under reflux. The yellow colored 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 0.4 g (57.2%) of IIe, mp 143—146°. Recrystallization from acetone–water gave 0.25 g of IIe, mp 178—179°. Analytical data are given in Table IV.

b) Method D: To the mixture of IIIe (2.1 g, 4.75 mM) and *p*-chlorobenzenethiol (3.4 g, 23.6 mM) in acetone (30 ml) was added triethylamine (0.05 ml). The mixture was refluxed for 10 min, and condensed *in vacuo* to give an oily matter, which was extracted with hot *n*-hexane (100 ml) to give 1.9 g (90.5%) of IIe, mp 178—179°. The *n*-hexane extract was condensed *in vacuo* to give an oily matter, which was dissolved into benzene (100 ml). The benzene layer was washed with 10% aqueous NaOH and then with water and dried over anhydrous Na_2SO_4. Removal of the slovent gave 1.2 g (88.0%) of di-*p*-chlorophenyldisulfide, mp 68—70°. The results are summarized in Table IV.

TABLE IV. 2,2′-Dithioxo-5,5′-bi-4-thiazolidones (II)



Compd. No.	R	mp (°C)	Appearance (recrystn. solvent)	Method (% yield)	Formula	Analysis (%) Calcd. (Found) C	H	N
IIa	CH_3	217—218	yellow powder (EtOH)	C (51.0)	$C_8H_8O_2N_2S_4$	32.86 (33.31)	2.76 (2.87)	9.58 (9.69)
IIb	C_2H_5	155—157[a]	yellow granules (EtOH)	C (60.0)	$C_{10}H_{12}O_2N_2S_4$	37.51 (37.77)	3.78 (3.84)	8.75 (8.77)
IIc	C_3H_7	120—121	yelllw leaflets (acetone)	C (50.0)	$C_{12}H_{16}O_2N_2S_4$	41.38 (41.70)	4.63 (4.82)	8.04 (7.95)
IId	C_4H_5	83— 84	yellow leaflets (EtOH)	C (40.0)	$C_{14}H_{20}O_2N_2S_4$	44.68 (44.60)	5.36 (5.37)	7.44 (7.32)
IIe	$C_6H_5CH_2$	160—161	yellow leaflets (acetone)	C (57.2) D (90.5)	$C_{20}H_{16}O_2N_2S_4$	54.06 (54.13)	3.63 (3.50)	6.31 (6.31)

a) lit.[7] mp 155—157°

Oxydation of 3,3′-Dibenzyl-2,2′-dithioxo-5,5′-bi-4-thiazolidone (IIe)——To the solution of IIc (0.1 g) in acetone (15 ml) was added triethylamine (0.05 ml) and stirred for 48 hr at room temperature. The separated crystals were collected and washed with acetone to give 0.7 g of IIIe, mp 165—170°.

General Procedure for the Reaction of DMAD with Thiolcarbamates——To the cooled solution of DMAD (1.2 g, 8.46 mM) in methanol (15 ml) was added methylammonium N-methylthiolcarbamate (0.6 g, 4.91 mM) over a period of 1 min. After stirring for 30 min the separated crystals were collected and washed with small amount of cooled methanol to give 0.45 g (45.4%) of IVa, mp 112—113°, which was identical with the authentic sample[1] by comparison of the IR spectra.

In the same manner, IVb was obtained in 63.8% yield with mp 141—142° and identified with the authentic sample.[1]

2-Isopropylidenehydrazono-5-methoxycarbonylmethylidene-4-thiazolidone (Va)——To the stirred solution of acetone thiosemicarbazone (1.3 g, 10 mM) in acetone (20 ml) was added DMAD (1.5 g, 10.6 mM) dropwise at room temperature. The mixture was refluxed for 20 min to give yellow needles (0.7 g, mp 131—132°). Condensation of the filtrate gave an additional crop (0.4 g, mp 130—132°). The combined crops were recrystallized from methanol to give 0.8 g of yellow needles, mp 131—132°. *Anal.* Calcd. for $C_9H_{11}O_3N_3S$ (Va): C, 44.81; H, 4.60; N, 17.42. Found: C, 45.00; H, 4.62; N, 17.45. IR (cm^{-1}): 3150 (NH), 1710 (CO). NMR (d_6-DMSO): 12.5 (broad, NH), 6.63 (singlet, >=<H), 3.80 (singlet, OCH_3) and 2.04 (singlet, $CH_3 \times 2$).

2-Isopropylidenehydrazono-3-methyl-5-methoxycarbonylmethylidene-4-thiazolidone (Vb)——a) The solution of Va (0.20 g, 0.834 mM), K_2CO_3 (60 mg, 0.435 mM) and methyl iodide (0.12 g, 0.845 mM) in DMF (3 ml) was heated on a boiling water bath for 30 min and diluted with water to give 0.15 g (70.4%) of Vb as pale yellow needles, mp 173—175°. Recrystallization from acetone gave 0.1 g of pale yellow needles, mp 176—177°. *Anal.* Calcd. for $C_{10}H_{13}O_3N_3S$ (Vb): C, 47.06; H, 5.13; N, 16.47. Found: C, 47.04; H, 4.90; N, 16.18. IR (cm^{-1}): 1720 (CO), 1700 (CO). NMR (d_6-DMSO): 6.68 (singlet, >=<H), 3.77 (singlet, OCH_3), 3.26 (singlet, NCH_3), 2.06 (singlet, CH_3) and 2.04 (singlet, CH_3).

b) The solution of 4-methylthiosemicarbazide (0.1 g, 0.952 mM) in acetone (10 ml) was refluxed for 10 min. To the cooled mixture, was added DMAD (0.14 g, 0.986 mM) in acetone (10 ml) dropwise. The mixture was refluxed for 5 min and condensed *in vacuo* to give a solid mass, which was recrystallized from methanol to give 0.07 g (28.8%) of Vb, mp 176—177°. The mother liquor was diluted with water to give an additional crop of Vb (0.07 g, mp 172—175°). Both crops indicate one spot on TLC.

2-Phenylimino-3-amino-5-methoxycarbonylmethylidene-4-thiazolidone (Vc)——To the stirred solution of 4-phenylthiosemicarbazide (1.67 g, 10.0 mM) in methanol (50 ml) was added DMAD (1.50 g, 10.6 mM) at room temperature. After an additional stirring for 1 hr, the separated crystals were collected and washed with methanol to give 1.6 g (58.2%) of Vc, mp 159—160°. *Anal.* Calcd. for $C_{12}H_{11}O_3N_3$ (Vc): C, 51.99; H, 4.00; N, 15.16. Found: C, 51.98; H, 3.78; N, 14.92. IR (cm^{-1}): 3300 (NH), 3150 (NH), 1735 (CO), 1695 (CO), 1650 (NH_2). NMR (d_6-DMSO): 7.5—7.0 (arom.), 6.89 (singlet, >=<H), 5.18 (broad, NH_2) and 3.77 (singlet, OCH_3).

Reaction of DMAD with 4-Methylthiosemicarbazide——To the stirred solution of 4-methylthiosemicarbazide (1.67 g, 10.0 mM) in methanol (50 ml) was added DMAD (1.50 g, 10.6 mM) dropwise at room temperature. After an additional stirring for 1 hr, the separated crystals were collected and washed with small amount of methanol to give 1.5 g of yellow needles, mp 178—179°. Recrystallization from methanol gave 1.0 g of yellow needles, mp 179—180°. *Anal.* Calcd. for $C_7H_9O_3N_3S$ (VII): C, 39.07; H, 4.23; N, 19.53. Found: C, 39.12; H, 4.18; N, 19.96. IR (cm^{-1}): 3300 (NH), 3200 (NH), 1740 (CO), 1690 (CO), 1665 (NH_2). NMR (d_6-DMSO): 6.76 (singlet, >=<H), 5.10 (braod, NH_2), 3.78 (singlet, OCH_3), and 3.24 (singlet, NCH_3). From the mother liquor was obtained 0.2 g of pale yellow needles, mp 171—172°. Recrystallization from methanol gave 0.15 g of pale yellow needles, mp 171—172°. *Anal.* Calcd. for $C_{13}H_{15}O_3N_3S$ (VI): C, 43.70: H, 4.23; N, 11.76. Found: C, 43.43; H, 4.14; N, 11.67. IR (cm^{-1}): 1730, 1720 and 1700 (CO's). NMR (d_6-DMSO): 6.82 (singlet, >=<H), 3.87 (singlet, $OCH_3 \times 2$), 3.84 (singlet, CH_2), 3.64 (singlet, OCH_3) and 3.32 (singlet, NCH_3).

2-Methylimino-3-isopropylideneamino-5-methoxycarbonylmethylidene-4-thiazolidone (VIII)——The solution of VII (0.10 g, 0.46 mM) in acetone (30 ml) was refluxed for 8 hr and condensed *in vacuo*. The residual oily matter was dissolved into small amount of ether and allowed to stand until crystals separated. The crystals were collected and recrystallized from methanol to give 0.03 g (25.2%) of VIII as pale yellow needles, mp 120—122°. *Anal.* Calcd. for $C_{10}H_{13}O_3N_3S$ (VIII): C, 47.06; H, 5.13; N, 16.46. Found: C, 46.82; H, 5.15; N, 16.44. IR (cm^{-1}): 1730 and 1710 (CO's). NMR (d_6-DMSO): 6.75 (singlet, >=<H), 3.80 (singlet, OCH_3), 3.21 (singlet, NCH_3), 2.19 (singlet, CH_3) and 1.83 (singlet, CH_3).

Reaction of VII with DMAD——The solution of VII (0.2 g, 0.93 mM) and DMAD (0.15 g, 1.43 mM) in methanol (20 ml) was refluxed for 20 min and condensed *in vacuo*. The residue was washed with *n*-hexane to give 0.2 g of pale yellow powder, mp 126—131°. The yellow powder was subjected to the elemental analysis without further purification and assigned as a mixture of *cis*-IX and *trans*-IX in the ratio of 3: 4 by the NMR spectrum. *Anal.* Calcd. for $C_{13}H_{15}O_3N_3S$: C, 43.70; H, 4.23; N, 11.76. Found: C, 43.56; H, 3.95; N, 11.76. NMR ($CDCl_3$): 9.60 (singlet, NH), 6.84 (singlet, >=<H), 4.76 (singlet, >=<H), 3.84 (singlet, OCH_3), 3.70 (singlet, OCH_3), and 3.18 (OCH_3) for *cis*-IX; 10.00 (NH), 6.84 (singlet, >=<H), 5.48 (singlet, >=<H), 3.84 (singlet, OCH_3), 3.82 (singlet, NCH_3), 3.54 (singlet, OCH_3) and 3.24 (singlet, NCH_3) for *trans*-IX.

Hydrolysis of Vc——The solution of Vc (0.30 g, 1.08 mM) in methanol (20 ml) was saturated with HCl and refluxed for 1 hr. Removal of the solvent gave a solid mass, which was washed with water and recrystallized from methanol to give 0.10 g (45.7%) of IVd as pale yellow powder, mp 171—172°.

Hydrolysis of Va——The solution of Va (1.8 g, 7.50 mM) in methanol (10 ml) was saturated with HCl

and refluxed for 2 hr. Removal of the solvent gave a solid mass, which was washed with water to give 1.0 g of colorless crystals, mp 158—164°. Recrystallization from acetone gave 0.5 g of IVc, mp 164—165°. IVc was identified with the authentic sample.[1]

Reaction of IVd with Nitrous Acid——The solution of IVd (0.18 g, 0.89 mM) in methanol (5 ml) was saturated with HCl. To the mixture was added Na_2NO_2 (0.30 g, 4.35 mM). The mixture was refluxed for 15 min and diluted with water to give 0.06 g (35.9%) of IVc as pale yellow crystals, mp 163—165°. Recrystallization from acetone gave colorless crystals, mp 164—165°, which was identified with IVc obtained above.

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