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Synthesis of Ethyl 2-Thioxo (and 2-Methylene)thiazoline-4-acetates

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Reaction of ethyl 4-chloro (and 4-bromo) acetoacetate (**1** and **2**) with ammonium benzyldithiocarbamate gave ethyl 3-benzyl-4-hydroxy-2-thioxothiazolidine-4-acetate (**3a**), which was treated with 10% hydrochloric acid to afford ethyl 3-benzyl-2-thioxo-4-thiazoline-4-acetate (**4a**). Reaction of **1** (and **2**) with *N*-substituted dithiocarbamates prepared from carbon disulfide and amines, followed by treatment with 10% hydrochloric acid gave the corresponding 4-thiazolines **4a**—**e**.

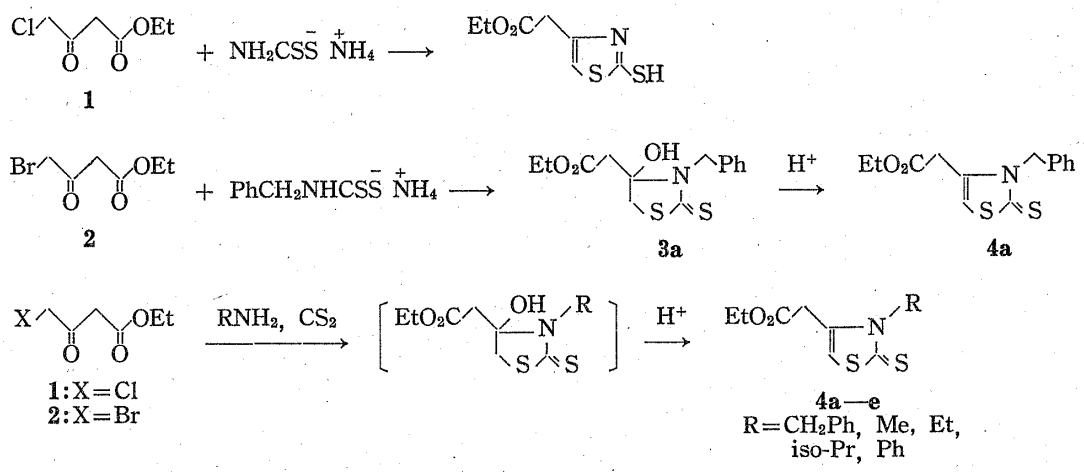
Reaction of **1** (and **2**) with thioacetanilide derivatives prepared from phenyl isothiocyanate and active methylene compounds such as ethyl cyanoacetate, malononitrile, ethyl malonate, and cyanoacetamide in the presence of sodium ethoxide gave 2-substituted 4-hydroxythiazolidines **9a**—**c** and thiophene derivative **10**. Treatment of **9a**—**c** with acid gave 4-thiazolines **8a**—**c**, which were also prepared from compound **4e**, ethyl iodide, and active methylene compounds.

Keywords——ethyl 4-haloacetoacetate; dithiocarbamates; phenyl isothiocyanate; 4-thiazolidineacetates; 4-thiazoline-4-acetates; 2-thiophenepropionates

It was reported that ethyl 4-chloroacetoacetate (**1**) reacts with ammonium dithiocarbamate to give ethyl 2-mercaptothiazole-4-acetate.[1] In the present paper we wish to report the reaction of ethyl 4-haloacetoacetate (**1** and **2**), which can be readily prepared from diketene, with *N*-substituted dithiocarbamates and with phenyl isothiocyanate in the presence of active methylene compounds.

When ethyl 4-bromoacetoacetate (**2**) was allowed to react with ammonium benzyldithiocarbamate, ethyl 3-benzyl-4-hydroxy-2-thioxothiazolidine-4-acetate (**3a**) was obtained in 74% yield. Elemental analysis and spectroscopic data were consistent with this structure as detailed in the experimental section. Treatment of compound **3a** with 10% hydrochloric acid in ethanol afforded ethyl 3-benzyl-2-thioxo-4-thiazoline-4-acetate (**4a**) in 87% yield.

Similarly, the reaction of **1** (and **2**) with *N*-substituted dithiocarbamates prepared from carbon disulfide and amines such as benzylamine, methylamine, ethylamine, isopropylamine,



4a: R=CH_2Ph, **4b**: R=Me, **4c**: R=Et, **4d**: R=iso-Pr, **4e**: R=Ph

Chart 1

and aniline, followed by treatment with 10% hydrochloric acid gave the corresponding 4-thiazolines **4a**—**e** in 47—72% yields.

Hirai *et al.*[2] reported that the reaction of 2-alkylthio-2-thiazolines **5** with active methylene compounds gave 2-substituted thiazolidines **6**. We investigated the reaction of ethyl 3-phenyl-2-thioxo-4-thiazoline-4-acetate (**4e**) with active methylene compounds. Thus, compound **4e** was treated with ethyl iodide to afford the 2-ethylthiothiazolium iodide **7**, which was allowed to react with active methylene compounds such as ethyl cyanoacetate, malononitrile, and ethyl malonate in the presence of triethylamine to give the corresponding 2-substituted 4-thiazolines **8a**, **8b**, and **8c** in 56, 45, and 44% yields, respectively.

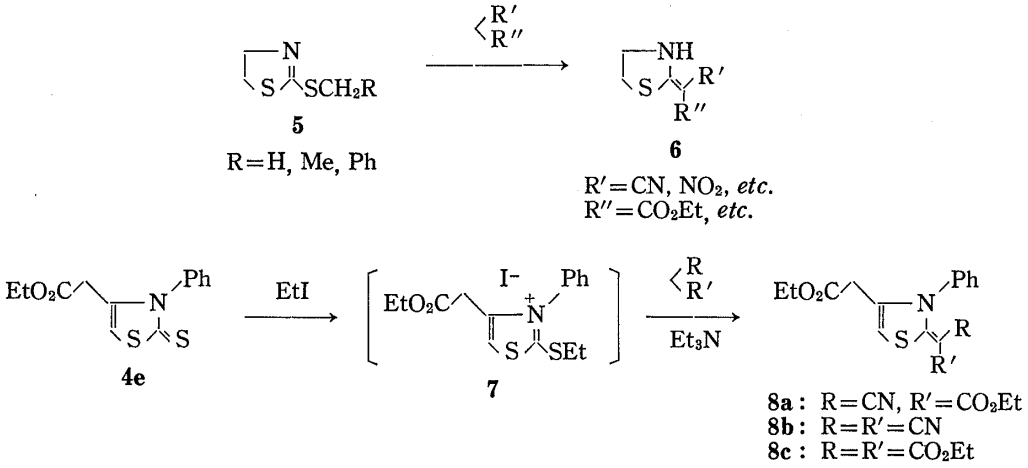


Chart 2

Attempts were made to prepare the 2-methylene-4-thiazolines **8a**—**c** from ethyl 4-haloacetoacetate (**1** and **2**) directly. Phenyl isothiocyanate was allowed to react with ethyl cyanoacetate in the presence of sodium ethoxide, and the resulting mixture was subsequently treated with **1** (and **2**) to give ethyl 2-cyano(ethoxycarbonyl)methylene-4-hydroxy-3-phenylthiazolidine-4-acetate (**9a**) in 66—70% yields. Similarly, the reaction of **1** (and **2**) with phenyl isothiocyanate and active methylene compounds such as malononitrile and ethyl malonate in the presence of sodium ethoxide gave the corresponding 2-substituted thiazolidines **9b** and **9c**.

Treatment of compounds **9a**, **9b**, and **9c** with 10% hydrochloric acid or *p*-toluenesulfonic acid afforded the corresponding 4-thiazolines **8a**, **8b**, and **8c** in good yields.

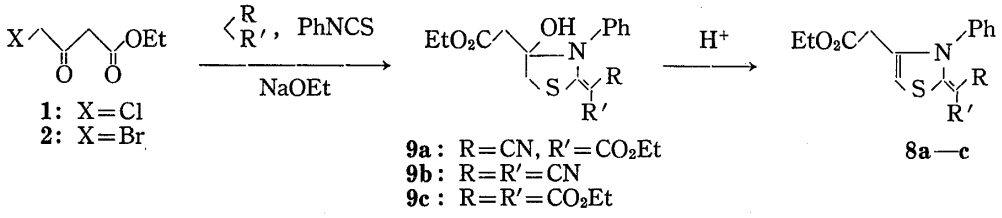


Chart 3

On the other hand, the reaction of **1** (and **2**) with phenyl isothiocyanate and cyanoacetamide in the presence of sodium ethoxide gave ethyl 3-amino-5-anilino-4-carbamoylthiophene-2-(3-oxo)propionate (**10**). Elemental analysis and spectroscopic data were consistent with this structure as detailed in the experimental section.

When compound **2** was allowed to react with phenyl isothiocyanate and malononitrile in the presence of excess sodium ethoxide, compound **9b** and thiophene derivative **11** were obtained in 12 and 30% yields, respectively. Treatment of **9b** with sodium ethoxide afforded

11 in 42% yield. However, similar treatment of **9a** with sodium ethoxide did not give the corresponding thiophene derivative.

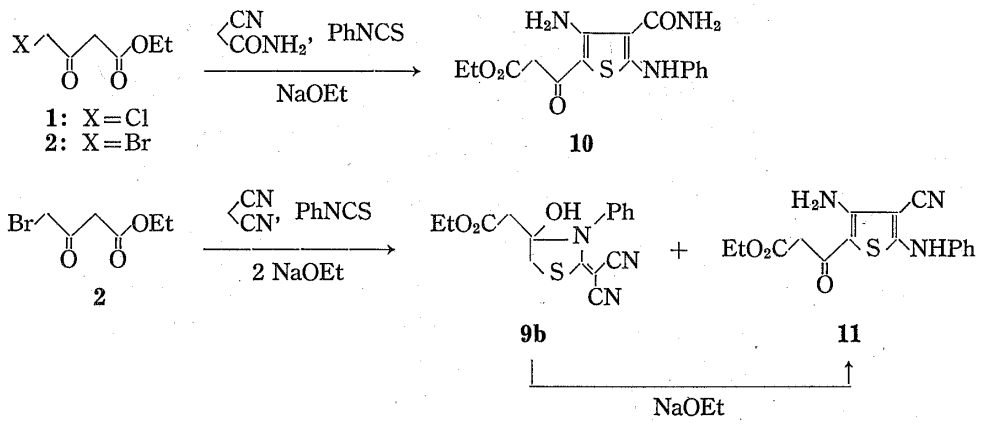


Chart 4

Although the details of the mechanism of the formation of compounds **9a—c**, **10**, and **11** are not clear at present, a likely pathway is as follows. The reaction of phenyl isothiocyanate with active methylene compounds gives a thioacetanilide intermediate **A**, which reacts with ethyl 4-haloacetoacetate to yield an intermediate **B**. Ring closure of **B** would give rise to compounds **9a—c**. The cyclization of an intermediate **C**, which is formed from **B** in the presence of an ethoxide anion, results in the formation of **10** or **11**.

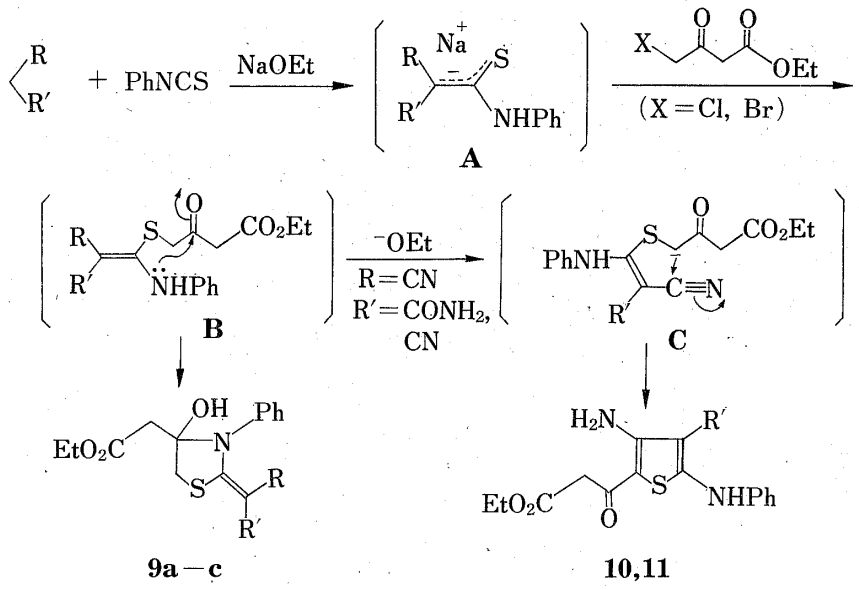


Chart 5

Experimental

Melting points and boiling points are uncorrected. Infrared (IR) spectra were taken on JASCO IR-S and JASCO A-102 spectrophotometers. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on JEOL JNM-PMX 60 and Hitachi R-20 instruments using tetramethylsilane or 3-(trimethylsilyl)propanesulfonic acid sodium salt as an internal standard.

Ethyl 3-Benzyl-4-hydroxy-2-thioxothiazolidine-4-acetate (3a)——a) A solution of ethyl 4-bromoacetoacetate (2) (2.1 g, 0.01 mol) in ethanol (5 ml) was added dropwise to a suspension of ammonium benzyldithiocarbamate (2.0 g, 0.01 mol) in ethanol (5 ml) under stirring at 0—10°C. The mixture was stirred at

room temperature for 1.5 h. Separated crystals were collected and recrystallized from hexane–benzene (1: 1) to give the product **3a** as colorless prisms, mp 108—109°C. Yield, 2.3 g (74%). *Anal.* Calcd for $C_{14}H_{17}NO_3S_2$: C, 54.00; H, 5.50; N, 4.50; S, 20.59. Found: C, 54.18; H, 5.75; N, 4.43; S, 20.49. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1725, 1710. ^{1}H-NMR (DMSO-d_6) δ: 1.21 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.78 (2H, s, CH_2CO), 3.45, 3.95 (2H, ABq, J=12.6 Hz, CH_2S), 3.93 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.77, 5.17 (2H, ABq, J=16 Hz, $NC\underline{H}_2$-Ph), 7.15—7.50 (5H, m, Ph), 7.46 (1H, s, OH).

b) Carbon disulfide (1.4 ml, 0.023 mol) was added dropwise to a solution of benzylamine (4.3 g, 0.04 mol) in ethanol (10 ml) under stirring at 0—10°C. The mixture was stirred at room temperature for 1.5 h. A solution of ethyl 4-chloroacetoacetate (**1**) (3.3 g, 0.02 mol) or **2** (4.2 g, 0.02 mol) in ethanol (10 ml) was added dropwise to the mixture under stirring at 0—10°C. The reaction mixture was worked up as described in the above run (method a), and crystals thus obtained were recrystallized from hexane–benzene (1: 1) to afford compound **3a**. Yield, 5.2 g (83%) (from **1**), 4.5 g (72%) (from **2**).

Ethyl 3-Benzyl-2-thioxo-4-thiazoline-4-acetate (4a)——A mixture of **3a** (3.1 g, 0.01 mol) and 10% hydrochloric acid (1 ml) in ethanol (10 ml) was refluxed for 1 h. The reaction mixture was cooled. Separated crystals were collected and recrystallized from hexane–benzene (1: 1) to give the product **4a** as colorless needles, mp 83—84°C. Yield, 2.55 g (87%). Elemental analyses, IR and ^{1}H-NMR spectral data are listed in Table I.

Ethyl 3-Substituted 2-Thioxo-4-thiazoline-4-acetate (4b—e): General Procedure——In the procedure given for **3a** (method b), **1** (3.3 g, 0.02 mol) or **2** (4.2 g, 0.02 mol) was allowed to react with carbon disulfide (1.4 ml, 0.023 mol) and primary amines (0.04 mol) such as methylamine, ethylamine, isopropylamine, and aniline. The reaction mixture was concentrated *in vacuo*, and the residue was extracted with chloroform (20 ml×3). After removal of chloroform by evaporation, the residual oil was added to a solution of 10% hydrochloric acid (1 ml) in ethanol (10 ml). The mixture was refluxed for 1 h, and then concentrated *in vacuo*. The residue was purified by recrystallization or distillation to afford compounds **4b—e**. Elemental analyses, IR and ^{1}H-NMR spectral data are listed in Table I.

Ethyl 3-Methyl-2-thioxo-4-thiazoline-4-acetate (4b)——Following the general procedure described above, methylamine (40% aqueous solution, 3.2 g) was treated with carbon disulfide, and the mixture was allowed to react with **1** (or **2**) to give the product **4b** as colorless needles (recrystallized from hexane–benzene (1: 2)), mp 81—82°C. Yield, 3.0 g (69%) (from **1**), 2.8 g (65%) (from **2**).

Ethyl 3-Ethyl-2-thioxo-4-thiazoline-4-acetate (4c)——Following the general procedure described above, ethylamine (70% aqueous solution, 2.6 g) was treated with carbon disulfide, and the mixture was allowed to react with **1** (or **2**) to give the product **4c** as colorless needles (recrystallized from ether), mp 55—56°C. Yield, 2.8 g (61%) (from **1** or **2**).

Ethyl 3-Isopropyl-2-thioxo-4-thiazoline-4-acetate (4d)——Following the general procedure described above, isopropylamine (2.4 g) was treated with carbon disulfide, and the mixture was allowed to react with **1** (or **2**) to give the product **4d** as a yellow oil, bp 146—150°C (0.3 mmHg). Yield, 2.4 g (49%) (from **1**), 2.3 g (47%) (from **2**).

Ethyl 3-Phenyl-2-thioxo-4-thiazoline-4-acetate (4e)——Following the general procedure described above, aniline (3.7 g) was treated with carbon disulfide, and the mixture was allowed to react with **1** (or **2**) to give the product **4e** as colorless needles (recrystallized from hexane–benzene (1: 2)), mp 122—123°C. Yield, 3.8 g (68%) (from **1**), 3.4 g (61%) (from **2**).

Ethyl 2-Cyano(ethoxycarbonyl)methylene-3-phenyl-4-thiazoline-4-acetate (8a)——a) A mixture of **4e** (1.4 g, 5 mmol) and ethyl iodide (0.8 g, 5 mmol) in absolute ethanol (30 ml) was refluxed for 5 h. A solution of ethyl cyanoacetate (0.6 g, 5 mmol) and triethylamine (1.0 g, 0.01 mol) in absolute ethanol (10 ml) was added to the mixture. After being refluxed for 2 h, the reaction mixture was concentrated *in vacuo*. The residue was extracted with chloroform (50 ml). The chloroform extract was washed with 10% sodium hydroxide (20 ml×3). The chloroform layer was dried over sodium sulfate and concentrated *in vacuo*. The residue was subjected to silica gel (40 g) column chromatography using chloroform as an eluent to afford the product **8a** as colorless prisms (recrystallized from benzene), mp 177—178°C. Yield, 1.0 g (56%). Elemental analyses, IR and ^{1}H-NMR spectral data are listed in Table II.

b) A suspension of **9a** (3.8 g, 0.01 mol) in 10% hydrochloric acid (20 ml) was heated at 70—80°C for 1 h. Precipitates were collected and purified by recrystallization from benzene to give compound **8a**. Yield, 3.3 g (91%).

Ethyl 2-Dicyanomethylene-3-phenyl-4-thiazoline-4-acetate (8b)——a) In the procedure given for **8a** (method a), the reaction of **4e** (1.4 g, 5 mmol) with ethyl iodide (0.8 g, 5 mmol), malononitrile (0.35 g, 5 mmol), and triethylamine (1.0 g, 0.01 mol) afforded the product **8b** as colorless prisms (recrystallized from ethyl acetate), mp 193—194°C. Yield, 0.7 g (45%). Elemental analyses, IR and ^{1}H-NMR spectral data are listed in Table II.

b) A mixture of **9b** (3.3 g, 0.01 mol) and 10% hydrochloric acid (1 ml) in ethanol (10 ml) was refluxed for 2 h. The reaction mixture was cooled. Separated crystals were collected and recrystallized from ethyl acetate to give compound **8b**. Yield, 2.6 g (83%).

Ethyl 2-Diethoxycarbonylmethylene-3-phenyl-4-thiazoline-4-acetate (8c)——a) In the procedure given for **8a** (method a), the reaction of **4e** (1.4 g, 5 mmol) with ethyl iodide (0.8 g, 5 mmol), ethyl malonate (0.8 g,

Table I

	R	Formula	Analysis (%) Calcd (Found) C	H	N	S	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
4a	CH_2Ph	$C_{14}H_{15}NO_2S_2$	57.31 (57.07)	5.15 (5.17)	4.77 (4.72)	21.85 (21.95)	1740 1595	1.23 (3H, t, J=7 Hz), 3.42 (2H, s), 4.10 (2H,q, J=7 Hz), 5.57 (2H, s), 6.53 (1H, s), 6.95—7.50 (5H, m)
4b	Me	$C_8H_{11}NO_2S_2$	44.22 (44.01)	5.10 (5.03)	6.45 (6.57)	29.51 (29.18)	1740 1590	1.30 (3H, t, J=7 Hz), 3.63 (5H, s), 4.22 (2H, q, J=7 Hz), 6.51 (1H, s)
4c	Et	$C_9H_{13}NO_2S_2$	46.74 (46.44)	5.66 (5.80)	6.06 (5.89)	27.72 (27.54)	1740 1585	1.29 (3H, t, J=7 Hz), 1.31 (3H, t, J=7 Hz), 3.64 (2H, s), 4.22 (2H, q, J=7 Hz), 4.25 (2H, q, J=7 Hz), 6.55 (1H, s)
4d	iso-Pr	$C_{10}H_{15}NO_2S_2$	48.95 (49.00)	6.16 (6.34)	5.71 (5.57)	26.13 (25.96)	1740 1585	1.29 (3H, t, J=7 Hz), 1.62 (6H, d, J=7 Hz), 3.71 (2H, s) 4.22 (2H, q, J=7 Hz), 5.10—6.00 (1H, br), 6.46 (1H, s)
4e	Ph	$C_{13}H_{13}NO_2S_2$	55.89 (55.82)	4.69 (4.62)	5.01 (5.03)	22.96 (22.62)	1735 1595	1.14 (3H, t, J=7 Hz), 3.30 (2H, s), 4.04 (2H, q, J=7 Hz), 6.62 (1H, s), 7.10—7.70 (5H, m)

Table II

	R	R′	Formula	Analysis (%) Calcd (Found) C	H	N	S	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
8a	CN	CO_2Et	$C_{18}H_{18}N_2O_4S$	60.32 (60.27	5.06 5.10	7.82 7.79	8.94 8.83)	2200 1730 1650	1.14 (3H, t, J=7 Hz), 1.26 (3H, t, J=7 Hz), 3.27 (2H, s), 3.99 (2H, q, J=7 Hz), 4.22 (2H, q, J=7 Hz), 6.72 (1H, s), 7.15—7.75 (5H, m)
8b	CN	CN	$C_{16}H_{13}N_3O_2S$	61.72 (61.65	4.21 4.15	13.50 13.44	10.30 10.59)	2220 2200 1735	1.10 (3H, t, J=7 Hz), 3.47 (2H s), 4.00 (2H, q, J=7 Hz), 7.15 (1H, s), 7.40—7.75 (5H, m)[a]
8c	CO_2Et	CO_2Et	$C_{20}H_{23}NO_6S$	59.25 (59.10	5.69 5.82	3.45 3.56	7.91 7.73)	1730 1700 1640	1.13 (9H, t, J=7 Hz), 3.23 (2H, s), 3.80 (4H, q, J=7 Hz), 3.97 (2H, q, J=7 Hz), 6.52 (2H, s), 7.10—7.70 (5H, m)

a) Measured in CD_3COCD_3.

5 mmol), and triethylamine (1.0 g, 0.01 mol) afforded the product **8c** as colorless needles (recrystallized from petroleum ether–ether (2: 1)), mp 65—66°C. Yield, 0.9 g (44%). Elemental analyses, IR and ^{1}H-NMR spectral data are listed in Table II.

b) A mixture of **9c** (4.2 g, 0.01 mol) and *p*-toluenesulfonic acid (0.1 g) in benzene (30 ml) was refluxed for 2 h. The reaction mixture was concentrated *in vacuo*. The residue was subjected to silica gel (60 g) column chromatography using chloroform as an eluent to give compound **8c**. Yield, 3.4 g (84%).

Ethyl 2-Substituted 4-Hydroxy-3-phenylthiazolidine-4-acetate (9a—c): General Procedure——A solution of phenyl isothiocyanate (2.7 g, 0.02 mol) in absolute ethanol (5 ml) was added dropwise to a solution of the sodium salt of active methylene compounds (0.02 mol) such as ethyl cyanoacetate, malononitrile, and ethyl malonate in absolute ethanol (30 ml) under stirring at 0—10°C. The mixture was stirred at room temperature for 1.5 h. A solution of **1** (3.3 g, 0.02 mol) or **2** (4.2 g, 0.02 mol) in absolute ethanol (10 ml) was added dropwise to the mixture under stirring at 0—10°C. The mixture was stirred at room temperature for 1.5 h, and then concentrated *in vacuo*. The residue was extracted with chloroform (20 ml×3). After removal of chloroform by evaporation, the oily residue was purified by recrystallization or column chromatography

to afford compounds **9a**—**c**. Elemental analyses, IR and ^{1}H-NMR spectral data are listed in Table III.

Ethyl 2-Cyano(ethoxycarbonyl)methylene-4-hydroxy-3-phenylthiazolidine-4-acetate (9a)——Following the general procedure described above, a mixture of ethyl cyanoacetate (2.3 g, 0.02 mol), phenyl isothiocyanate, **1** (or **2**), and sodium ethoxide (prepared from sodium, 0.46 g, 0.02 g atom) was worked up to give an oily residue, which was crystallized by rubbing with a glass rod in hexane. Crystals thus obtained were recrystallized from benzene to give the product **9a** as colorless needles, mp 113—115°C. Yield, 5.0 g (66%) (from **1**), 5.3 g (70%) (from **2**).

Ethyl 2-Dicyanomethylene-4-hydroxy-3-phenylthiazolidine-4-acetate (9b)——Following the general procedure described above, a mixture of malononitrile (1.3 g, 0.02 mol), phenyl isothiocyanate, **1** (or **2**), and sodium ethoxide (prepared from sodium, 0.46 g, 0.02 g atom) was worked up to give an oily residue, which was subjected to silica gel (60 g) column chromatography using chloroform as an eluent to give the product **9b** as a red oil. Yield, 4.4 g (67%) (from **1**), 4.7 g (71%) (from **2**).

Ethyl 2-Diethoxycarbonylmethylene-4-hydroxy-3-phenylthiazolidine-4-acetate (9c)——Following the general procedure described above, a mixture of ethyl malonate (3.2 g, 0.02 mol), phenyl isothiocyanate, **1** (or **2**), and sodium ethoxide (prepared from sodium, 0.46 g, 0.02 g atom) was worked up to give an oily residue, which was crystallized by rubbing with a glass rod in hexane. Crystals thus obtained were recrystallized from hexane–benzene (1: 1) to give the product **9c** as colorless prisms, mp 104—105°C. Yield, 5.2 g (61%) (from **1**), 5.1 g (60%) (from **2**).

Table III

	R	R′	Formula	Analysis (%) Calcd (Found) C	H	N	S	IR $\nu_{max}^{CHCl_3}$ cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
9a	CN	CO_2Et	$C_{18}H_{20}N_2O_5S$	57.43 (57.55)	5.36 (5.40)	7.44 (7.54)	8.52 (8.61)	3350, 2220, 1725, 1710, 1675	1.18 (3H, t, J=7 Hz), 1.23 (3H, t, J=7 Hz), 2.69 (2H, s,) 3.35, 3.59 (2H, ABq, J=12 Hz), 4.05 (2H, q, J=7 Hz), 4.17 (2H, q, J=7 Hz), 5.28 (1H s), 6.90—7.70 (5H, m)
9b	CN	CN	$C_{16}H_{15}N_3O_3S$	58.35 (58.03)	4.59 (4.67)	12.76 (12.36)	9.73 (9.45)	3350, 2220, 1730, 1715	1.18 (3H, t, J=7 Hz), 2.68 (2H, s), 3.55, 3.85 (2H, ABq, J=12 Hz), 4.04 (2H, q, J=7 Hz), 5.69 (1H, s), 7.05—7.75 (5H, m)
9c	CO_2Et	CO_2Et	$C_{20}H_{25}NO_7S$	56.73 (56.62)	5.95 (6.13)	3.31 (3.26)	7.57 (7.55)	3350, 1720, 1710, 1670	1.05 (6H, t, J=7 Hz), 1.17 (3H, t, J=7 Hz), 2.70 (2H, s), 3.39, 3.81 (2H, ABq, J=12 Hz), 3.67 (4H, q, J=7 Hz), 4.04 (2H, q, J=7 Hz), 5.87 (1H, s), 7.10—7.70 (5H, m)[a]

a) Measured in CD_3COCD_3.

Ethyl 3-Amino-5-anilino-4-carbamoylthiophene-2-(3-oxo)propionate (10)——Following the method described in the general procedure for **9**, a mixture of cyanoacetamide (1.7 g, 0.02 mol), phenyl isothiocyanate, **1** (or **2**), and sodium ethoxide (prepared from sodium, 0.46 g, 0.02 g atom) was worked up to give a residue, which was subjected to silica gel (60 g) column chromatography using ethyl acetate as an eluent to afford the product **10** as plates (recrystallized from ethyl acetate), mp 174—175°C (dec.). Yield, 2.4 g (35%) (from **1**), 2.6 g (37%) (from **2**). *Anal.* Calcd for $C_{16}H_{17}N_3O_4S$: C, 55.32; H, 4.93; N, 12.10; S, 9.23. Found: C, 55.23; H, 4.96; N, 11.93; S, 8.95. IR ν_{max}^{Nujol} cm^{-1}: 3450, 3250, 3200—3100, 1735, 1720, 1650. ^{1}H-NMR (DMSO-d_6) δ: 1.18 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.47 (2H, s, CH_2CO), 4.08 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.90—7.60 (7H, m, $CONH_2$ and Ph), 7.50—7.90 (2H, br, 3-NH_2), 10.10—10.50 (1H, br, N$\underline{H}$Ph).

Ethyl 3-Amino-5-anilino-4-cyanothiophene-2-(3-oxo)propionate (11)——a) As described in the general procedure for **9**, a mixture of malononitrile (1.3 g, 0.02 mol), phenyl isothiocyanate, **2**, and sodium ethoxide (prepared from sodium, 0.92 g, 0.04 g atom) was stirred at 0°C for 30 min. The mixture was neutralized with 10% hydrochloric acid. Precipitates were collected by suction and purified by recrystallization from benzene to give the product **11** as plates, mp 182—183°C (dec.), 1.3 g. *Anal.* Calcd for $C_{16}H_{15}N_3O_3S$: C, 58.35; H, 4.59; N, 12.76; S, 9.73. Found: C, 58.15; H, 4.46; N, 12.59; S, 10.04. IR ν_{max}^{Nujol} cm^{-1}: 3400, 3300, 3250, 3200, 2225, 1740, 1730. ^{1}H-NMR (DMSO-d_6) δ: 1.18 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.48 (2H, s, CH_2CO), 4.12 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.05—7.60 (5H, m, Ph), 7.50—8.00 (2H, br, NH_2), 10.45—10.65 (1H, br, N$\underline{H}$Ph). The filtrate was concentrated *in vacuo*, and the residue was subjected to silica gel (60 g) column

chromatography. Elution with chloroform gave compound **9b**. Yield, 0.8 g (12%). Subsequent elution with chloroform gave compound **11**, 0.7 g. Total yield of **11**, 2.0 g (30%).

b) A mixture of **9b** (3.3 g, 0.01 mol) and sodium ethoxide (prepared from sodium, 0.23 g, 0.01 g atom) in absolute ethanol (20 ml) was stirred at 0°C for 30 min. The reaction mixture was worked up as described in the above run (method a) to give the product **11**. Yield, 1.4 g (42%).

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References

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