

Scheme 2.

TABLE 1. PROPERTIES OF ARYLIDENE *N,N*-DIALKYL-*N*-THIOCARBAMOYL THIOCYANOACETAMIDES (3)

Product R=R'	R''	Reaction time (hr)	Mp (°C)	Yield (%)	Formula	Analysis (%)				SH str. (cm ⁻¹)	SCN str. (cm ⁻¹)	C=O str. (cm ⁻¹)	C=N str. (cm ⁻¹)	C=C str. (cm ⁻¹)
						C	H	N	S					
a	CH ₃	H	2	185—186	65	C ₁₃ H ₁₃ ON ₃ S	53.48 (53.61)	4.44 (4.50)	14.35 (14.43)	21.90 (21.90)	2550 w	2050 s	1740 s	1600 s
b	CH ₃	<i>p</i> -CH ₃	1.5	172—173	53	C ₁₄ H ₁₅ ON ₃ S ₂	55.24 (55.08)	4.90 (4.95)	13.89 (13.77)	21.00 (20.96)	2550 w	2050 s	1750 s	1640 a 1610 sh
c	CH ₃	<i>o</i> -OCH ₃	1.5	196—197	47	C ₁₄ H ₁₅ O ₂ N ₃ S ₂	52.38 (52.33)	4.76 (4.71)	13.10 (13.08)	19.28 (19.22)	2600 w	2050 s	1740 a	1600 s
d	CH ₃	<i>p</i> -OCH ₃	2	180—181	43	C ₁₄ H ₁₅ O ₂ N ₃ S ₂	52.42 (52.33)	4.55 (4.71)	13.50 (13.08)	19.34 (19.22)	2600 w	2050 s	1740 s	1600 s
e	CH ₃	<i>p</i> -N(CH ₃) ₂	2	236—237	56	C ₁₅ H ₁₈ ON ₄ S ₂	53.90 (53.88)	5.48 (5.43)	16.72 (16.76)	19.18 (19.14)	2550 w	2050 s	1730 s	1630 a 1600 s
f	CH ₃	<i>o</i> -OH	2	210—211	46	C ₁₃ H ₁₃ O ₂ N ₃ S ₂	51.00 (50.81)	4.52 (4.26)	13.71 (13.68)	21.01 (20.82)	2600 w	2050 s	1730 s	1620 m 1590 s
g	CH ₃	<i>p</i> -OH	2	219—221 ^{a)}	39	C ₁₃ H ₁₃ O ₂ N ₃ S ₂	51.16 (50.81)	4.30 (4.26)	13.74 (13.68)	20.89 (20.82)	2600 sh	2050 s	1730 s	1640 s 1600 s
h	C ₂ H ₅	H	2	169—170	62	C ₁₅ H ₁₇ ON ₃ S ₂	56.82 (56.42)	5.40 (5.37)	13.20 (13.16)	20.10 (20.04)	2600 w	2050 s	1720 s	1620 sh 1600 s
i	C ₂ H ₅	<i>p</i> -CH ₃	2	157—158	65	C ₁₆ H ₁₉ ON ₃ S ₂	57.67 (57.65)	5.78 (5.75)	12.64 (12.61)	19.15 (19.19)	2600 w	2050 s	1720 s	1640 s 1590 s
j	C ₂ H ₅	<i>o</i> -OCH ₃	1.5	164—165	59	C ₁₆ H ₁₉ O ₂ N ₃ S ₂	55.09 (55.01)	5.50 (5.48)	12.10 (12.03)	18.45 (18.32)	2600 w	2050 s	1720 s	1640 s 1590 s
k	C ₂ H ₅	<i>p</i> -OCH ₃	1.5	174—175	45	C ₁₆ H ₁₉ O ₂ N ₃ S ₂	55.29 (55.01)	5.48 (5.48)	12.22 (12.03)	18.49 (18.32)	2600 w	2050 s	1740 s	1650 s 1610 m
l	C ₂ H ₅	<i>p</i> -N(CH ₃) ₂	2	201—202	45	C ₁₇ H ₂₂ ON ₄ S ₂	56.39 (56.34)	6.18 (6.12)	15.41 (15.46)	17.61 (17.66)	2600 w	2050 s	1720 s	1640 s 1590 s
m	C ₂ H ₅	<i>o</i> -OH	2	137—138	48	C ₁₅ H ₁₇ O ₂ N ₃ S ₂	53.61 (53.73)	5.23 (5.11)	12.86 (12.53)	19.15 (19.08)	2550 w	2050 s	1730 s	1620 s 1590 s
n	C ₂ H ₅	<i>p</i> -OH	2	98—99	49	C ₁₅ H ₁₇ O ₂ N ₃ S ₂	53.78 (53.73)	5.32 (5.11)	12.49 (12.53)	19.28 (19.08)	2550 w	2050 s	1730 s	1630 s 1590 s

a) Decomp. All IR spectra were measured in KBr pellets.

cianoacetamide (**2**), which subsequently condenses with aromatic aldehyde to give **3**.

Support for this may be supplied by the fact that the ester **1** reacted easily with *N,N'*-dialkylthiourea to give the amide **2**, and that the amide **2** thus isolated condensed with an aromatic aldehyde in the presence of *N,N'*-dialkylthiourea as a basic catalyst to give the product **3**. In contrast with the above reaction, when thiourea was used instead of *N,N'*-dialkylthiourea, the reaction of the ester **1** with benzaldehyde led to the formation of 5-benzylidene-2-imino-4-thiazolidinone (**5a**).³⁾

The reaction of ester **1** with benzaldehyde in the presence of *N*-methylthiourea afforded 5-benzylidene-3-methylthiazolidine-2,4-dione (**6a**).³⁾ This compound is considered to be produced by the hydrolysis of 5-benzylidene-2-imino-3-methylthiazolidin-4-one (**5b**), which may be formed as an intermediate. Compound **6a** was obtained by the hydrolysis of the **3a** product with hydrochloric acid-ethanol. In addition, the reaction of the ester **1** with *N*-methylthiourea gave the corresponding amide (**2a**) ($R=CH_3$, $R=H$), but not 2-imino- or oxothiazolidinone. On the other hand, the treatment of **3a** with potassium carbonate or fluoride gave 5-benzylidene-2-methylimino-3-methyl-4-thiazolidinone (**5c**), which was identical with the authentic sample prepared by the alternative synthesis from benzaldehyde and 2-methylimino-3-methyl-4-thiazolidinone.⁴⁾ Furthermore, this compound (**5c**) was also obtained by the reaction of the amide **2b** ($R=R'=CH_3$) with benzaldehyde in the presence of potassium carbonate or fluoride. These facts suggest that, in the reaction of the amide **2** with aromatic aldehyde, the formation of a 4-thiazolidinone ring occurs after the condensation between the amide **2** and aromatic aldehyde has taken place. It is interesting that the ring closure of **3** might occur with the elimination of hydrogen thiocyanide, as is shown in Scheme 2.

Experimental

All the melting points are uncorrected. The IR spectra were recorded with a Shimadzu IR-27G spectrometer. The NMR spectra obtained on a Nihondenshi JNM-C-60 high-resolution NMR spectrometer (60 MHz). Tetramethylsilane was used as the internal standard. The chemical shifts of the protons are presented in terms of δ values.

*General Procedure for the Reaction of Ethyl Thiocynoacetate. (1) With Aromatic Aldehyde in the Presence of *N,N'*-Dialkylthiourea:* A mixture of the ester **1** (0.02 mol), an aldehyde (0.02 mol), and an *N,N'*-dialkylthiourea (0.02 mol) in ethanol (20 ml) was refluxed for a suitable period. After the reaction mixture had then been cooled, the resulting precipitates were filtered and washed with water. They were recrystallized from ethanol to give arylidene *N,N'*-dialkyl-*N*-thiocarbamoyl thiocynoacetamide (**3**). The results are summarized in Table 1.

*The Reaction of Ethyl Thiocynoacetate (1) with Benzaldehyde in the Presence of *N*-Methylthiourea.* A mixture of the ester **1** (0.02 mol), benzaldehyde (0.02 mol), and *N*-methyl-

thiourea (0.02 mol) in ethanol (20 ml) was refluxed for 5 hr. After cooling, the resulting precipitate was filtered and washed with water. Recrystallization from ethanol gave 5-benzylidene-3-methylthiazolidine-2,4-dione (**6a**); yield, 48%; mp 133–134°C (lit.³⁾ 134–135°C).

The Reaction of Ethyl Thiocynoacetate (1) with Benzaldehyde in the Presence of Thiourea. A mixture of the ester **1** (0.02 mol), benzaldehyde (0.02 mol), and thiourea (0.02 mol) in ethanol (20 ml) was refluxed for 3 hr. A crystalline precipitate was deposited during the reaction; this was collected on a filter and washed with ethanol. Recrystallization from dimethyl sulfoxide gave 5-benzylidene-2-imino-4-thiazolidinone (**5a**); yield, 37%; decomp. 282–284°C (lit.³⁾ decomp. 282–284°C).

*The Reaction of Ethyl Thiocynoacetate (1) with *N*-Methylthiourea.* The ester **1** (0.02 mol) was added, drop by drop at approximately 60°C, to a mechanically-stirred solution of *N*-methylthiourea (0.02 mol) in 20 ml of ethanol. Stirring was continued for 3 hr. After the solvent had then been removed with a vacuum evaporator, the residue was allowed to stand overnight. The precipitate which thus formed was separated by filtration, washed with water, and recrystallized to give *N*-methyl-*N*-thiocarbamoyl thiocynoacetamide (**2a**); yield, 25%; decomp. 175–178°C.

IR (KBr): near 3300 (NH), near 2500 (SH), 2050 (SCN), 1670 (C=O), 1650 (C=N) cm^{-1} .

Found: C, 31.71; H, 3.69; N, 21.43; S, 33.81%. Calcd for $C_5H_7ON_2S_2$: C, 31.75; H, 3.73; N, 22.22; S, 33.83%.

*The Reaction of Ethyl Thiocynoacetate (1) with *N,N*-Dimethylthiourea.* A mixture of the ester **1** (0.02 mol) and *N,N*-dimethylthiourea (0.02 mol) in ethanol (20 ml) was refluxed for 2 hr. The resulting precipitate was collected on a filter and washed with water. Recrystallization from ethanol gave *N,N*-dimethyl-*N*-thiocarbamoyl thiocynoacetamide (**2b**); yield, 68%; mp 174–175°C.

IR (KBr): near 2550 (SH), 2050 (SCN), 1750 (C=O), 1640 (C=N) cm^{-1} .

Found: C, 35.51; H, 4.50; N, 20.89; S, 31.67%. Calcd for $C_6H_9ON_2S_2$: C, 35.47; H, 4.47; N, 20.69; S, 31.50%.

*The Reaction of Ethyl Thiocynoacetate (1) with *N,N'*-Diethylthiourea.* A solution which contained the ester **1** (0.02 mol) and *N,N'*-diethylthiourea (0.02 mol) in ethanol (20 ml) was refluxed for 4 hr. After the solvent had then been removed with a vacuum evaporator, the residue was allowed to stand for several days. The crystalline matter thus formed was collected, washed with water, and air-dried. Recrystallization from ethanol-water gave *N,N'*-diethyl-*N*-thiocarbamoyl thiocynoacetamide (**2c**); yield, 21%; mp 96–97°C.

Found: C, 41.52; H, 5.66; N, 18.31; S, 27.73%. Calcd for $C_8H_{13}ON_2S_2$: C, 41.56; H, 5.67; N, 18.18; S, 27.73%.

The Reaction of Ethyl Thiocynoacetate (1) with Thiourea. Thiourea (0.02 mol) was stirred in ethanol (20 ml) at approximately 60°C; the stirring was then continued until the thiourea was completely dissolved. To a stirred alcoholic solution there was then added, drop by drop, the ester **1** (0.02 mol) over a 0.5-hr period. After this addition, stirring was continued for an additional 4 hr, and then the reaction mixture was allowed to stand for several hours. The crystalline matter thus formed was collected and washed with ethanol. Recrystallization from acetic acid gave 2-imino-4-thiazolidinone; yield, 19%; decomp. 232–235°C (lit.⁵⁾ 233–238°C).

3) S. Kambe, T. Hayashi, H. Yasuda, and A. Sakurai, *Nippon Kagaku Zasshi*, **92**, 867 (1971).

4) R. Andreasch, *Monatsh. Chem.*, **39**, 417 (1918).

5) H. R. Snyder and E. X. Werber, "Organic Syntheses" Vol. 27, p. 71 (1947).

The Reaction of N,N'-Dimethyl-N-thiocarbamoyl Thiocyanacetamide (2b) with Benzaldehyde in the Presence of N,N'-Dimethylthiourea.

A solution of the amide **2b** (0.01 mol) benzaldehyde (0.01 mol), and *N,N'*-dimethylthiourea (0.0025 mol) in ethanol (30 ml) was refluxed for 4 hr. After cooling, a crystalline matter separated; this was recrystallized from ethanol to afford benzylidene *N,N'*-dimethyl-*N*-thiocarbamoyl thiocyanacetamide (**3a**); yield, 65%.

The Reaction of N,N'-Dimethyl-N-thiocarbamoyl Thiocyanacetamide (2b) with Benzaldehyde in the Presence of Potassium Carbonate or Fluoride.

To a solution of the (**2b**) amide (0.01 mol) and benzaldehyde (0.01 mol) in ethanol (20 ml), potassium carbonate or fluoride (0.01 mol) was added, after which the mixture was refluxed for a suitable period. After standing overnight, the resulting precipitate was collected on a filter and washed with water. Recrystallization from ethanol gave 5-benzylidene-2-methylimino-3-methyl-4-thiazolidinone (**5c**); mp 109–110°C.

When potassium carbonate was used as the catalyst, the reaction time was 2 hr and the yield was 54%.

When potassium was used as the catalyst, the reaction time was 7 hr and the yield was 58%.

IR (Nujol): 1750 (C=O), 1660 (C=N), 1620 (C=C) cm^{-1} .

NMR (DMSO- d_6): δ 3.20, 3.40 (CH_3), 6.05 (C_6H_5), 6.15 (=CH) ppm.

Found: C, 61.89; H, 5.20; N, 12.04; S, 13.74%. Calcd for $\text{C}_{12}\text{H}_{12}\text{ON}_2\text{S}$: C, 62.06; H, 5.21; N, 12.06; S, 13.77%.

The Reaction of Benzylidene N,N'-Dimethyl-N-thiocarbamoyl Thiocyanacetamide (3a) in the Presence of Potassium Carbonate or Fluoride.

A mixture of the amide **3a** (0.01 mol) in ethanol (20 ml) containing potassium carbonate or fluoride (0.01 mol) was refluxed for a suitable period. After the mixture had then stood overnight, the precipitate formed was separated by filtration, washed with water, and recrystallized from ethanol to afford 5-benzylidene-2-methylimino-3-

methyl-4-thiazolidinone (**5c**).

When potassium carbonate was used as the catalyst, the reaction time was 2 hr and the yield was 56%.

When potassium fluoride was used as the catalyst, the reaction time was 6 hr and the yield was 58%.

The Hydrolysis of Benzylidene N,N'-Dimethyl-N-thiocarbamoyl Thiocyanacetamide (3a).

To a solution containing concentrated hydrochloric acid (10 ml) and ethanol (10 ml), we added the amide **3a** (0.01 mol), and then the mixture was refluxed for 6 hr. After cooling, the reaction mixture was poured onto cracked ice. The crystalline matter thus formed was collected, washed with water, and air-dried. Recrystallization from ethanol gave 5-benzylidene-3-methylthiazolidin-2,4-dione (**6a**); yield, 52%; mp 133–134°C (lit.³) 134–135°C).

The Hydrolysis of 5-Benzylidene-2-methylimino-3-methyl-4-thiazolidinone.

The procedure used was essentially the same as that described above; yield, 53%; mp 133–134°C.

The Reaction of 2-Methylimino-3-methyl-4-thiazolidinone with Benzaldehyde.

2-Methylimino-3-methyl-4-thiazolidinone was prepared according to the procedure described in the literature.⁴

A mixture of 2-methylimino-3-methyl-4-thiazolidinone (0.01 mol) and benzaldehyde (0.01 mol) in ethanol (10 ml) containing potassium acetate (0.01 mol) was refluxed for 4 hr. After the solvent had been removed, the residue was allowed to stand overnight. The resulting crystals were collected on a filter. Recrystallization from ethanol gave 5-benzylidene-2-methylimino-3-methyl-4-thiazolidinone (**5c**); yield, 56%; mp 109–110°C.

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