BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 2926—2928 (1973)

Thiocyanoacetate. V. Reaction of Thiocyanoacetic Esters with Aromatic Aldehydes in the Presence of Potassium Acetate[1]

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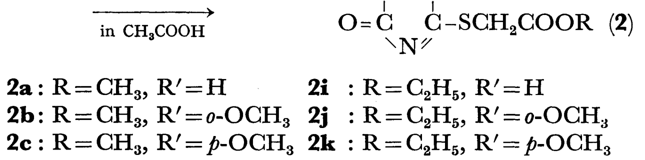
(Received October 21, 1972)

In the course of studies on the reaction of thiocyanoacetic ester (**1**) with aldehydes, it was found that the base as a catalyst might have some distinct effect on the nature of the reaction.[1,2] For the confirmation the author has investigated the effects of potassium acetate–acetic acid system on the reaction course.



$2\,NCS\text{-}CH_2COOR$ (**1**) + $R'\text{-}C_6H_4CHO$

1a: $R = CH_3$ **1b**: $R = C_2H_5$

$\xrightarrow[\text{in } CH_3COOH]{CH_3COOK}$ $R'\text{-}C_6H_4\text{-}CH{=}C{-}S$, $O{=}C$, $C\text{-}SCH_2COOR$, N (**2**)

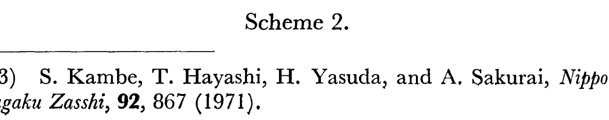
2a: $R = CH_3$, $R' = H$
2b: $R = CH_3$, $R' = o\text{-}OCH_3$
2c: $R = CH_3$, $R' = p\text{-}OCH_3$
2d: $R = CH_3$, $R' = o\text{-}Cl$
2e: $R = CH_3$, $R' = p\text{-}Cl$
2f: $R = CH_3$, $R' = m\text{-}NO_2$
2g: $R = CH_3$, $R' = p\text{-}OH$
2h: $R = CH_3$, $R' = p\text{-}CH_3$
2i: $R = C_2H_5$, $R' = H$
2j: $R = C_2H_5$, $R' = o\text{-}OCH_3$
2k: $R = C_2H_5$, $R' = p\text{-}OCH_3$
2l: $R = C_2H_5$, $R' = o\text{-}Cl$
2m: $R = C_2H_5$, $R' = p\text{-}Cl$
2n: $R = C_2H_5$, $R' = m\text{-}NO_2$
2o: $R = C_2H_5$, $R' = p\text{-}OH$
2p: $R = C_2H_5$, $R' = p\text{-}CH_3$

Scheme 1.

The reaction of **1** with aromatic aldehydes was carried out in an acetic acid containing potassium acetate, direct synthesis of 1,3-oxathiolan-2-one derivatives being expected.

However, an unexpected acid-unstable crystalline product was obtained upon the treatment of **1b** with benzaldehyde in acetic acid containing potassium acetate. The structure of 5-benzylidene-2-ethoxycarbonylmethylthio-1,3-thiazolin-4-one (**2i**) was indicated by elemental analysis, IR, NMR, and mass spectra. **2i** was identical with an authentic sample prepared from 5-benzylidene-1,3-thiazolidine-2-thione-4-one (**3**) and ethyl chloroacetate with sodium ethoxide in ethanol.

On the other hand, **2i** is readily hydrolyzed with hydrochloric acid to yield 5-benzylidene-1,3-thiazolidine-2,4-dione (**4**).[3] Furthermore, **1b** reacted easily with ethyl thioglycollate (**5**) in acetic acid containing potassium acetate to give 2-ethoxycarbonylmethylthio-1,3-thiazolin-4-one (**6**), which gave **2i** in the reaction



$C_6H_5\text{-}CH{=}C{-}S$, $O{=}C$, $C{=}S$, N, H (**3**) + $CH_2COOC_2H_5$, Cl $\xrightarrow{C_2H_5ONa}$ **2i**

Scheme 2.

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[1] Part IV of this series: S. Kambe and T. Hayashi, This Bulletin, **45**, 3192 (1972).

[2] S. Kambe, T. Hayashi, H. Yasuda, and H. Midorikawa, *ibid.*, **44**, 1357 (1971).

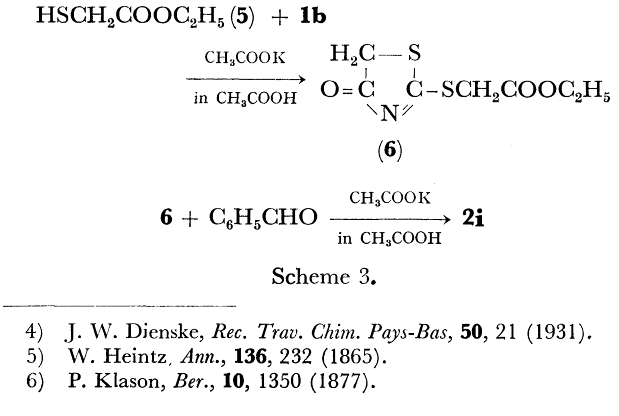
[3] S. Kambe, T. Hayashi, H. Yasuda, and A. Sakurai, *Nippon Kagaku Zasshi*, **92**, 867 (1971).

Table 1. Properties and analyses of product **2**

Product 2	Reac. time (hr)	Yield (%)	Mp °C	Formula	Analysis (%) Found (Calcd) C	H	N	S	IR spectrum (cm^{-1}) ester C=O	ring C=O	C=N	C=C
a	5	54	139—140	$C_{13}H_{11}O_3NS_2$	53.24	3.77	4.45	21.69	1750	1710	1610	1600
					(53.24)	(3.78)	(4.78)	(21.82)	s	s	m	w
b	7	41	147—149	$C_{14}H_{13}O_4NS_2$	52.31	4.42	4.38	19.82	1740	1690	1590	1550
					(52.02)	(4.05)	(4.33)	(19.79)	s	s	s	w
c	6	38	162—163	$C_{14}H_{13}O_4NS_2$	52.21	4.19	4.35	19.82	1740	1700	1590	1560
					(52.02)	(4.05)	(4.33)	(19.79)	s	s	s	w
d	5	31	151—152	$C_{13}H_{10}O_3NS_2Cl$	47.91	3.10	4.30	19.62	1740	1700	1600	1580
					(47.60)	(3.05)	(4.27)	(19.53)	s	s	m	w
e	4	28	156—157	$C_{13}H_{10}O_3NS_2Cl$	47.71	3.09	4.31	19.82	1740	1700	1610	1590
					(47.60)	(3.05)	(4.27)	(19.53)	s	s	m	w
f	7	33	152—153	$C_{13}H_{10}O_5N_2S_2$	46.24	2.80	8.31	19.18	1740	1710	1600	1570
					(46.12)	(2.95)	(8.27)	(18.90)	s	s	m	w
g	6	22	199—201	$C_{13}H_{11}O_4NS_2$	50.50	3.62	4.60	20.72	1740	1700	1600	1580
					(50.49)	(3.59)	(4.53)	(20.69)	s	s	m	w
h	7	43	164—166	$C_{14}H_{13}O_3NS_2$	54.87	4.32	4.61	20.78	1740	1700	1600	1570
					(54.72)	(4.26)	(4.56)	(20.82)	s	s	m	sh
i	6	52	138—139	$C_{14}H_{13}O_3NS_2$	54.68	4.25	4.62	21.20	1730	1700	1600	1570
					(54.72)	(4.26)	(4.56)	(20.82)	s	sh	m	w
j	5	43	127—128	$C_{15}H_{15}O_4NS_2$	53.51	4.50	4.20	19.01	1740	1690	1590	1570
					(53.41)	(4.48)	(4.15)	(18.97)	s	s	m	sh
k	6	50	130—131	$C_{15}H_{15}O_4NS_2$	53.52	4.49	3.99	18.69	1730	1700	1600	1570
					(53.41)	(4.48)	(4.15)	(18.97)	s	s	s	w
l	6	45	158—159	$C_{14}H_{12}O_3NS_2Cl$	49.09	3.56	4.07	21.62	1740	1700	1600	1580
					(49.15)	(3.51)	(4.09)	(21.82)	s	s	s	w
m	6	42	153—154	$C_{14}H_{12}O_3NS_2Cl$	49.13	3.51	4.17	21.99	1730	1710	1600	1590
					(49.15)	(3.51)	(4.09)	(21.82)	s	s	m	m
n	5	40	138—139	$C_{14}H_{12}O_5N_2S_2$	47.75	3.49	8.00	18.24	1730	1710	1610	1570
					(47.73)	(3.43)	(7.95)	(18.16)	s	s	m	sh
o	5	30	203—204	$C_{14}H_{13}O_4NS_2$	52.45	4.36	4.41	19.81	1740	1710	1610	1570
					(52.02)	(4.05)	(4.33)	(19.79)	s	s	m	w
p	5	45	163—164	$C_{15}H_{15}O_3NS_2$	56.05	4.72	4.36	19.52	1740	1700	1600	1570
					(56.07)	(4.71)	(4.36)	(19.92)	s	s	s	sh

with benzaldehyde in acetic acid containing potassium acetate.

1,3-Thiazolin-4-one derivatives (**2**) could be obtained by the reaction of **1** with other aldehydes. The results are summarized in Table 1. **1** might be led to mercaptoacetate (**5**) in the presence of potassium acetate, since thiocyanates are converted into mercaptanes when treated with basic reagents.[4] The reaction of **1b** with benzaldehyde in acetic acid without using potassium acetate gave only product **4** in poor yield. Heintz[5] and Klason[6] reported that 1,3-thiazolidine-2,4-dione was obtained when **1** was treated with acid.



Scheme 3.

Accordingly, it seems that **1b** was hydrolyzed with acetic acid, yielding the 1,3-thiazolidine-2,4-dione which is then condensed with benzaldehyde to give **4**. A reaction pathway is postulated in Scheme 4.

$$\mathbf{1} \xrightarrow{CH_3COOK} \mathbf{5} \xrightarrow{(1)} \mathbf{6} \xrightarrow{R'\text{-}C_6H_4CHO} \mathbf{2}$$

Scheme 4.

Experimental

All the melting points are uncorrected. IR spectra were measured with a Shimadzu IR-27G spectrophotometer in KBr pellets. NMR spectra were determined in DMSO-d_6 with a JEOLCO JNM-C-60 high-resolution NMR spectrometer (60 MHz), using tetramethylsilane as an internal standard. Mass spectra were measured with a JMS-O1S instrument operating at 75 eV.

Reaction of Thiocyanoacetate Ester (1) with Aromatic Aldehyde. Procedure. A mixture of **1** (0.04 mol), aromatic aldehyde (0.02 mol) and potassium acetate (2 g) in acetic acid (15 ml) was stirred at 90—100 °C,[7] and then poured into crushed ice with vigorous stirring. The resulting precipitates were collected, washed with ether and recrystallized from ethanol. The yield and properties are summarized in Table 1. NMR (δ): **2a**; 4.00 (OCH_3), 4.50 (SCH_2), 7.55 (C_6H_5), and 8.30

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[4] J. W. Dienske, *Rec. Trav. Chim. Pays-Bas*, **50**, 21 (1931).

[5] W. Heintz, *Ann.*, **136**, 232 (1865).

[6] P. Klason, *Ber.*, **10**, 1350 (1877).

[7] Reaction times in each case are indicated in Table 1.

(=CH). **2i**; 1.40 (CH_3), 4.50 (OCH_2), 4.60 (SCH_2), 6.50 (C_6H_5), and 8.45 (=CH). MS spectrum: **2i** (relative abundance); *m/e* 307 (87), 262 (24), 234 (11), 188 (8), 161 (39), 133 (100), and 101 (30). NMR and MS data of other compounds are deleted.

Reaction of 5-Benzylidene-1,3-thiazolidine-2-thione-4-one (3) with Ethyl Chloroacetate. To a solution of **3** (0.01 mol) in absolute ethanol (30 ml) containing metallic sodium (0.3 g) was added ethyl chloroacetate (0.01 mol), and the solution was stirred for 15 hr under gentle reflux. The sodium chloride thus precipitated was then filtered out. After the filtrate had been left to stand overnight, crystalline matter was separated which was collected and washed with water. Recrystallization from ethanol gave **2i**; yield 23%, mp 138—139 °C. Unreacted **3** was recovered from the filtrate of **2i**.

Reaction of Ethyl Thiocyanoacetate (1b) with Ethyl Thioglycollate (5). To a mixture of **1b** (0.02 mol) and potassium acetate (0.02 mol) in acetic acid (15 ml) was added dropwise **5** (0.02 mol) with stirring. The raection temperature was maintained at 25—30 °C. After completion of addition, stirring was continued for 10 hr. The reaction mixture was poured into water with vigorous stirring. The resulting precipitate was filtered and washed with ether. Recrystallization from CCl_4 gave **6**; yield 60%; mp 78—79 °C. IR (cm^{-1}): 1750 (O–C=O) and 1700 (C=O). NMR (δ): 1.35 (CH_3), 4.40 (OCH_2), 4.45 (ring CH_2), and 4.60 (SCH_2). Found: C, 38.11; H, 4.06; N, 6.39; S, 29.20%. Calcd for $C_7H_9O_3S_2N$: C, 38.36; H, 4.14; N, 6.39; S, 29.20%.

Reaction of 2-Ethoxycarbonylmethylthio-1,3-thiazolin-4-one (6) with Benzaldehyde. A solution of **6** (5 mmol) and benzaldehyde (5 mmol) in acetic acid (10 ml) containing potassium acetate (5 mmol) was refluxed for 2 hr. After cooling, the solution was poured into water and allowed to stand for several hours. The solid product (**2i**) precipitated was recrystallized from ethanol; yield 48%, mp 138—139 °C.

Hydrolysis of **2i**. To ethanol (5 ml) containing concd. hydrochloric acid (15 ml) was added **2i** (5 mmol). The mixture was refluxed for 2 hr and then cooled to room temperature. Deposited solid product (**4**) was recrystallized from ethanol; yield 32%; mp 239—240 °C (lit,[3] 239—240 °C).

Reaction of Ethyl Thiocyanoacetate (1b) with Benzaldehyde in Acetic Acid. A solution of **1b** and benzaldehyde in acetic acid (10 ml) was refluxed for 15 hr. The reaction mixture, on cooling, was poured onto cracked ice. The crystalline matter thus formed was collected and washed with ether. Recrystallization from ethanol gave **4**; yield 0.5%; mp 239—240 °C.

The author wishes to express his thanks to Dr. Hiroshi Midorikawa, Dr. Heinosuke Yasuda, and Mr. Toshio Hayashi for their helpful discussions and encouragement. Thanks are also due to Dr. Haruo Homma and his staff for the microanalyses.