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Thiocyanoacetate. III. The Synthesis of 2-Hydrazono-4-thiazolidinone Derivatives[1]

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Although a number of papers[2-6] have been published concerning the syntheses of 2-hydrazono-4-thiazolidinone derivatives, no syntheses using ethyl thiocyanoacetate (**1**) as the starting material have been reported. We wish now to report a convenient synthesis of 2-arylidenehydrazono-4-thiazolidinones from **1**, arylideneazines (**2**), and hydrazine hydrate (**3**).

The reaction was performed by refluxing a mixture of **1**, **2**, and **3** (molar ratio 2: 1: 1) in ethanol containing a small amount of acetic acid. For example, the reaction of **1** with **2a** and **3** afforded a pale yellow solid melting at 254—5°C, which was identified as 2-benzylidenehydrazono-4-thiazolidinone (**4a**). The structure of **4a** was inferred from the results of elementary analysis and of spectral studies. The IR spectrum of **4a** revealed the presence of NH (3025 cm^{-1}), C=O (1713 cm^{-1}), and C=N (1645 cm^{-1}) bands. The NMR spectrum showed the NH proton signal at δ 12.1, the CH_2 at 3.9, the =CH at 8.4, and the C_6H_5 at 7.5 ppm. For the structual confirmation of **4a**, an authentic sample was prepared by the treatment of ethyl chloroacetate with benzaldehyde thiosemicarbazone according to the method in the literature.[5] These products were proved to be identical by a mixed-melting-point determination and by IR and NMR spectral studies. On the other hand, the reaction of **1** with **2a** and **3** (molar ratio 1: 1: 1) in acetic acid gave a product which was identified as 5- benzylidene-2-benzylidenehydrazono-4-thiazolidinone (**5a**). The NMR spectrum of **5a** lacked the CH_2 proton signal and showed the =CH proton as a doublet (δ 8.4 and 8.5 ppm). **5a** was hydrolyzed by hydrochloric acid to

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[1] Part II of this series: S. Kambe, T. Hayashi, H. Yasuda, and A. Sakurai, *Nippon Kagaku Zasshi*, **92**, 867 (1971).

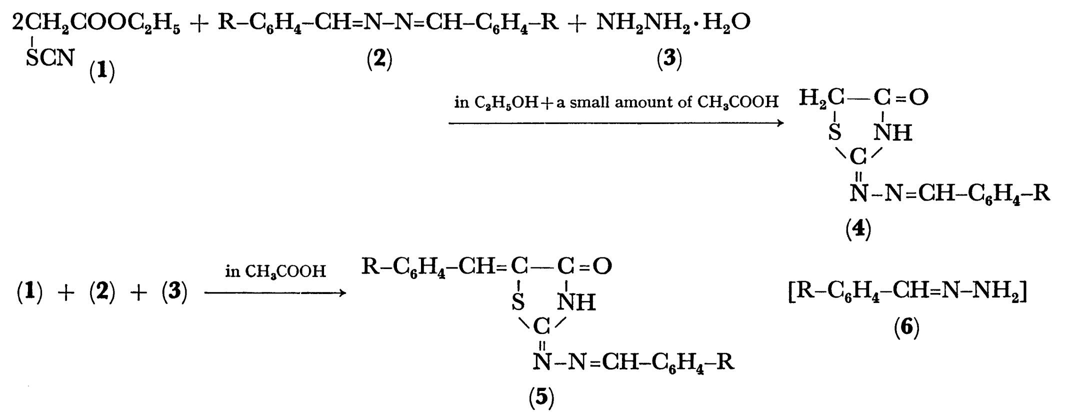
[2] F. J. Wilson and R. Burns, *J. Chem. Soc.*, **121**, 870 (1922).

[3] F. J. Wilson and R. Burns, *ibid.*, **123**, 799 (1923).

[4] P. Chabrier and E. Cattelain, *Bull. Soc. Chem. Fr.*, **17**, 48 (1950).

[5] H. Taniyama, B. Yasui, and T. Imamura, *Yakugaku Zasshi*, **75**, 8 (1955).

[6] H. Taniyama and T. Yusa, *ibid.*, **75**, 11 (1955).



a, R=H **b**, R=*p*-$N(CH_3)_2$ **c**, R=*o*-Cl **d**, R=*p*-Cl **e**, R=*p*-CH_3 **f**, R=*p*-OCH_3 **g**, R=*o*-OH

Scheme 1

give 5-benzylidene-2,4-thiazolinedione, whose IR spectrum showed a carbonyl stretching band as a doublet (1670 and 1740 cm^{-1}). A similar conversion has been reported in the case of 2-isopropylidenehydrazone-4-thiazolidinone.[2] Furthermore, **5a** was also obtained by the reaction of **1** with benzaldehyde acethylhydrazone in acetic acid. However, when **2 g** was employed as the azine reactant, the reaction did not lead to the formation of the corresponding product (**5 g**), but to **4 g**.

A plausible reaction sequence is illustrated in Scheme 1. Presumably, the reaction proceeds through the intermediary of the hydrazone (**6**), which subsequently condenses with **1** to give **4**. The product, **5**, may be formed by the further condensation of **4** with aromatic aldehyde.

Table 1. 2-Arylidenehydrazono-4-thiazolidinones (**4**)

Product	Reac. time (hr)	Yield (%)	Mp °C	Formula	Analysis (%) Found (Calcd)			
					C	H	N	S
4a	2	66	254—255[b]	$C_{10}H_9ON_3S$	55.18 (54.79)	4.03 (4.14)	20.01 (19.17)	14.56 (14.59)
4b	3	52	255—256	$C_{12}H_{14}ON_4S$	55.12 (54.95)	5.28 (5.38)	21.48 (21.37)	12.38 (12.20)
4c	3.5	54	221—222	$C_{10}H_8ON_3SCl$	47.35 (47.33)	3.26 (3.15)	16.72 (16.56)	12.91 (12.62)
4d	4	56	280—282	$C_{10}H_8ON_3SCl$	47.48 (47.33)	3.21 (3.15)	16.62 (16.56)	12.79 (12.62)
4e	3	59	254—255	$C_{11}H_{11}ON_3S$	56.88 (56.65)	4.63 (4.75)	18.03 (18.02)	13.58 (13.72)
4f	2	62	252—253	$C_{11}H_{11}O_2N_3S$	53.04 (53.01)	4.27 (4.45)	16.06 (16.86)	12.32 (12.84)
4g[a]	5	49	307—309[c]	$C_{10}H_9O_2N_3S$	51.19 (51.06)	3.85 (3.86)	17.97 (17.87)	13.86 (13.60)

a) Reac. solv.: CH_3COOH, Crystn. solv.: $(CH_3)_2SO$

b) Lit,[5] 256°C c) Lit,[5] 315°C

Table 2. 5-Arylidene-2-arylidenehydrazono-4-thiazolidinones (**5**)

Product	Reac. time (hr)	Yield (%)	Mp °C	Formula	Analysis (%) Found (Calcd)			
					C	H	N	S
5a	6	32	288—290	$C_{17}H_{13}ON_3S$	66.03 (66.44)	4.17 (4.26)	13.50 (13.68)	10.26 (10.43)
5b	5	25	305—307	$C_{21}H_{23}ON_5S$	64.82 (64.11)	5.90 (5.87)	17.65 (17.80)	8.19 (8.13)
5c	6	28	301—304	$C_{17}H_{11}ON_3SCl$	57.28 (57.08)	2.78 (2.73)	10.49 (10.51)	8.08 (8.01)
5d	8	20	275—277	$C_{17}H_{11}ON_3SCl$	57.10 (57.08)	2.69 (2.73)	10.53 (10.51)	8.04 (8.01)
5e	11	23	269—270	$C_{19}H_{17}ON_3S$	68.09 (68.05)	5.14 (5.11)	12.59 (12.53)	9.56 (9.54)
5f	15	18	254—255	$C_{19}H_{17}O_3N_3S$	62.53 (62.12)	4.79 (4.66)	11.39 (11.44)	8.79 (8.71)

a) Lit,[5] 291—292°C

Experimental[7]

2-Arylidenehydrazono-4-thiazolidinones (4). General Procedure. A mixture of **1** (0.02 mol), **2** (0.01 mol), and **3** (0.01 mol) in ethanol (10 m*l*) containing acetic acid (1 m*l*) was refluxed for a suitable period. Crystalline precipitates were formed during the reaction; these were collected on the filter and washed with ethanol. Recrystallization from acetic acid gave **4**. The results are summarized in Table 1.

5-Arylidene-2-arylidenehydrazone-4-thiazolidinones (5). General Procedure. To a mixture of **2** (0.01 mol) and **3** (0.01 mol) in acetic acid (10 m*l*), we added **1** (0.01 mol), and then the mixture was refluxed for a suitable period. The resulting precipitates were filtered and washed with ethanol. Recrystallization from dimethyl sulfoxide gave **5**. The results are summarized in Table 2.

5-Benzylidene-2-benzylidenehydrazono-4-thiazolidinone (5a) from 1 and Benzaldehyde Acetylhydrazone. A mixture of **1** (0.01 mol) and benzaldehyde acetylhydrazone (0.02 mol) in acetic acid (10 m*l*) was refluxed for 14 hr. The resulting precipitate was collected on a filter, washed with ethanol, and recrystallized from dimethyl sulfoxide. Yield, 14%.

The Hydrolysis of ***5a***. To a solution containing concentrated hydrochloric acid (10 m*l*) and ethanol (10 m*l*), we added **5a** (0.01 mol), and then the mixture was heated for 15 hr. After being cooled, the reaction mixture was poured onto cracked ice. The crystalline matter thus formed was collected, washed with water, and air-dried. Recrystallization from acetic acid gave 5-benzylidene-2,4-thiazolidinones; mp 239—40°C; yield, 26%. IR (cm^{-1}): 3150 (NH), 1740 and 1690 (C=O), 1610 (C=C). NMR (δ): 7.50 (C_6H_5), 8.10 (=CH), 9.55 (NH).

Found: C, 58.65; H, 3.56; N, 6.75; S, 15.54%. Calcd for $C_{10}H_7O_2NS$: C, 58.54; H, 3.44; N, 6.83; S, 15.82%.

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[7] All the melting points are uncorrected. The IR spectra were measured with a Shimadzu IR-27G spectrophotometer in Nujol mulls. The NMR spectra were determined in trifluoroacetic acid with a Nihondenshi JNM-C-60 high-resolution NMR spectrometer (60 MHz), using tetramethylsilane as the internal standard. The chemical shifts of the protons are presented in terms of δ values.