Novel Heterocyclization of 4-Phenylthiosemicarbazones and Related Compounds with Chlorocarbonylsulfenyl Chloride

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Chlorocarbonylsulfenyl chloride was allowed to react with 1-alkylidene-4-phenylthiosemicarbazones in the presence of triethylamine to give 1,2,4-triazolines, whereas with 1-arylidene-4-phenylthiosemicarbazones to afford 1,2,4-dithiazolidines. Treatment of diarylidenethiocarbohydrazides and diarylidenaminoguanidines with chlorocarbonylsulfenyl chloride under similar conditions gave 1,2,4-dithiazolidines and 1,2,4-thiadiazolidines, respectively.

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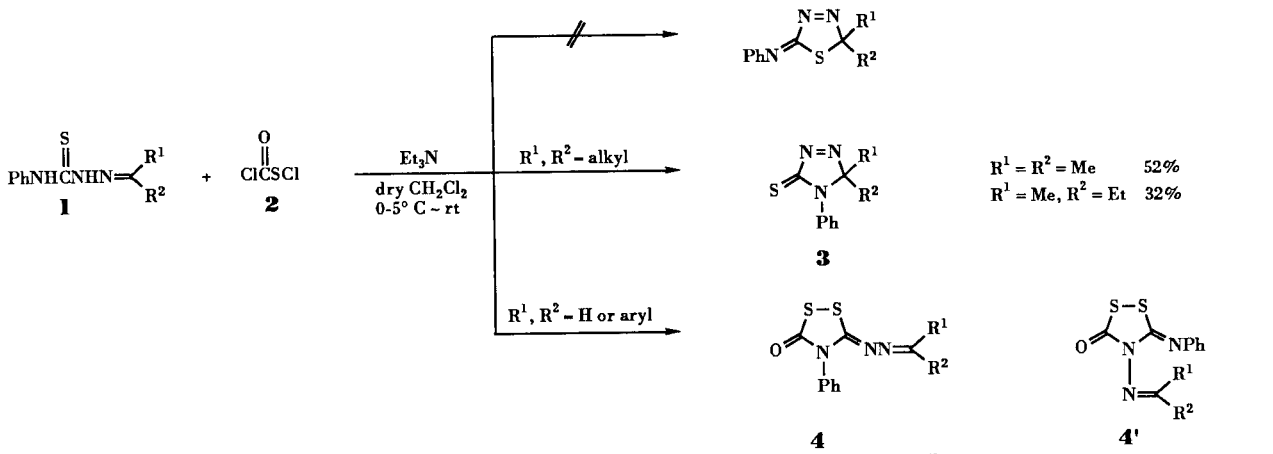
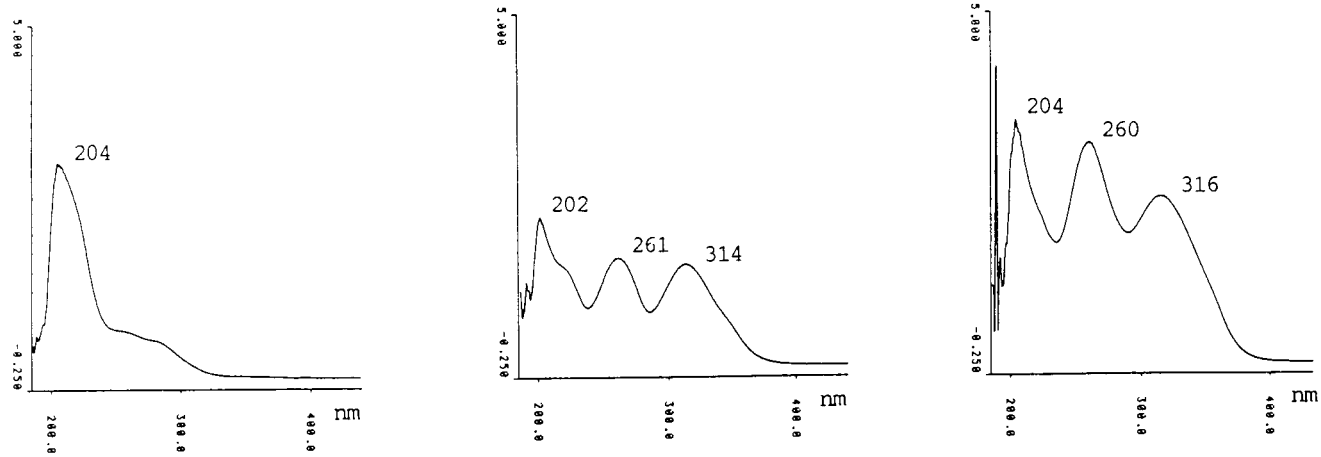
Chlorocarbonylsulfenyl chloride, a bifunctional electrophile, is a useful reagent for the construction of a variety of heterocycles containing a sulfur. Several cyclization reactions using this reagent have hitherto been reported to give thiazolines [1], thiadiazolines [2], dithiazolines [3], oxathiazoles [4], dithiadiazoles [5], and thiatriazepine [6].

By the way, it is reported that interesting heterocyclization of thiosemicarbazones with chlorocarbonyl isocyanate

Scheme 1





Product (R^1 = H, R^2 = Ph)

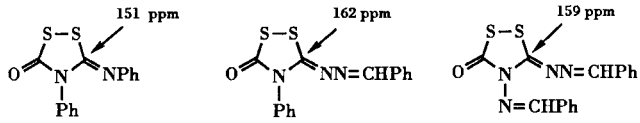
	λ (nm)	ε max (x 10^4)
5	204	3.02
4a	314	1.37
	261	1.47
	202	2.07
6a	316	2.32
	260	3.10
	204	3.42

Figure 1 The uv spectra [ε max (x 10^4)] of the product (R^1 = H, R^2 = Ph) and the related compounds **5** and **6a**.

provided triazolothiadiazoles [7]. Chlorocarbonylsulfenyl chloride is also expected to behave analogously toward thiosemicarbazones to give thiadiazoles. We report here a new heterocyclization of chlorocarbonylsulfenyl chloride (**2**) with thiosemicarbazones **1**. The reaction was carried out by adding **2** into the stirred solution of **1** in the presence of a base at 0-5° under a nitrogen atmosphere, followed by stirring for 12 hours at room temperature to provide unexpectedly 1,2,4-triazolines **3** and 1,2,4-dithiazolidines **4** in low yields (Scheme 1). The results are summarized in Table I.

The structure of the product **3** (R^1, R^2 = alkyl) was confirmed by direct comparison with the authentic sample prepared from **1** (R^1 = R^2 = alkyl) and chlorosulfonyl isocyanate [8]. On the other hand, the structure of the product **4** (R^1, R^2 = H or aryl) was assigned by spectral data and elemental analysis. The ir spectra showed the carbonyl absorption, and the ms spectra exhibited the molecular ion peak corresponding to the assigned structure. However, these data could not be distinguished from another possible isomeric structure **4'**. In order to discriminate between these structures **4** and **4'**, the uv spectra of the product **4a** (R^1 = H, R^2 = phenyl) was compared with those of the analogous functional compounds **5** and **6a** (Figure 1).

The uv spectrum of **4a** showed a pattern similar to that of **6a**, but a quite different spectral pattern from that of **5** as shown in Figure 1. The peaks at 316 nm and 260 nm in the uv spectrum of **6a** are assignable to be due to >C=N-N=CHPh moiety. The product which possesses the peaks at 314 nm and 261 nm is, therefore, more reasonable to be assigned to structure **4a**.



5 **4a** **6a**

Figure 2 The ^{13}C-nmr chemical shift of the carbon atoms at the position of compounds **5**, **4a**, **6a**.

Furthermore, the ^{13}C-nmr also provided the validity of **4a**. In the ^{13}C-nmr spectra of **5**, **4a**, and **6a**, the signals of each carbon atom at the 5-position were observed at 151 ppm,

Scheme 2

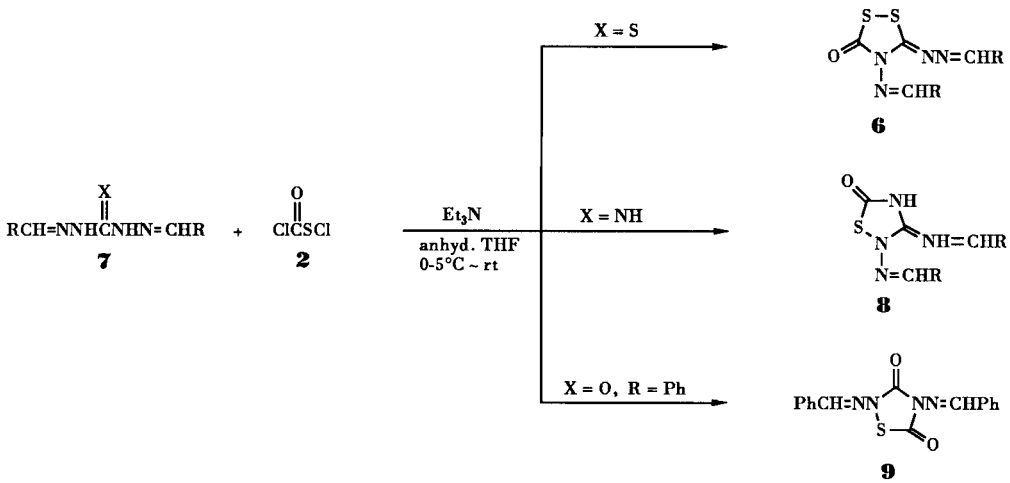


Table I

5-Arylidenehydrazono-4-phenyl-1,2,4-dithiazolidin-3-ones **4** and 4-Phenyl-5-phenylimino-1,2,4-dithiazolidin-3-one (**5**)

Entry	R^1	R^2	Mp (°C)	Yield (%)	IR (cm^{-1}) C=O	MS (m/z) (M^+)	^{1}H-NMR (δ) (deuteriochloroform)	Molecular Formula	Analysis (%) Cacld.(Found) C	H	N
4a	H	phenyl	168-169	25	1690	313	7.01-7.86 (m, 10H, Ph x 2) 8.25 (s, 1H, CH)	$C_{15}H_{11}N_3OS_2$	57.49 (57.41)	3.54 (3.54)	13.41 (13.64)
4b	H	2-furyl	165-166	10	1690	303	6.21-7.68 (m, 8H, ArH) 8.08 (s, 1H, CH)	$C_{13}H_9N_3O_2S_2$	51.47 (51.29)	2.99 (3.09)	13.85 (13.73)
4c	phenyl	phenyl	151-152	75	1695	389	6.97-7.80 (m, 15H, Ph x 3)	$C_{21}H_{15}N_3OS_2$	64.76 (64.90)	3.88 (3.94)	10.79 (10.79)
5	–	–	122-123	65	1715 1695	286	6.65-7.68 (m, 10H, Ph x 2)	$C_{14}H_{10}N_2OS_2$	58.72 (58.94)	3.52 (3.58)	9.78 (9.68)

Table II

4-Arylidenamino-5-arylidenehydrazono-1,2,4-dithiazolidin-3-ones **6**

Entry 6	R	Mp (°C)	Yield (%)	IR (cm^{-1}) C=O	MS (m/z) (M+)	^{1}H-NMR (δ) (DMSO-d_6)	Molecular Formula	Analysis (%) Cacld.(Found) C	H	N
a	phenyl	163-164	91	1680	340	7.27-8.05 (m, 10H, Ph x 2), 8.48 (s, 1H, CH), 8.94 (s, 1H, CH)	$C_{16}H_{12}N_4OS_2$	56.45 (56.21)	3.55 (3.40)	16.46 (16.61)
b	2-furyl	157-158	50	1660	320	6.56-8.20 (m, 6H, ArH), 8.41 (s, 1H, CH), 8.88 (s, 1H, CH)	$C_{12}H_8N_4O_3S_2$	44.99 (44.83)	2.52 (2.49)	17.49 (17.29)
c	2-thienyl	163-164	69	1670	352	6.98-8.08 (m, 6H, ArH), 8.73 (s, 1H, CH), 9.17 (s, 1H, CH)	$C_{12}H_8N_4OS_2$	40.89 (41.36)	2.89 (2.42)	15.90 (15.98)
d	2-pyridyl	150-151	54	1710	342	7.29-8.90 (m, 8H, ArH), 8.49 (s, 1H, CH), 9.15 (s, 1H, CH)	$C_{14}H_{10}N_6OS_2$	49.11 (49.25)	2.94 (2.87)	24.55 (24.60)
e	3-pyridyl	170-171	55	1690	342	7.38-9.14 (m, 8H, ArH), 8.67 (s, 1H, CH), 9.21 (s, 1H, CH)	$C_{14}H_{10}N_6OS_2$	49.11 (49.22)	2.94 (2.68)	24.55 (24.49)

Table III

2-Arylidenamino-3-arylidenehydrazono-1,2,4-thiadiazolidin-5-ones **8** and 2,4-Dibenzylidenamino-1,2,4-thiadiazolidine-3,5-dione (**9**)

Entry	R	Mp (°C)	Yield (%)	IR (cm^{-1}) C=O	MS (m/z) (M+)	^{1}H-NMR (δ) (DMSO-d_6)	Molecular Formula	Analysis (%) Cacld.(Found) C	H	N
8a	phenyl	190-191	60	1690	323	7.17-7.98 (m, 10H, Ph x 2), 8.17 (s, 1H, CH), 8.93 (s, 1H, NH) 9.79 (s, 1H, CH)	$C_{16}H_{13}N_5OS$	59.43 (59.67)	4.05 (4.01)	21.66 (21.67)
8b	2-furyl	225-226	30	1690	303	6.62-8.10 (m, 7H, ArH and CH), 6.90 (s, 1H, NH), 9.38 (s, 1H, CH)	$C_{12}H_9N_5O_3S$	47.52 (47.73)	2.99 (3.06)	23.09 (22.90)
8c	2-thienyl	157-158	55	1680	335	7.00-8.11 (m, 6H, ArH), 8.65(s, 1H, CH), 9.56 (s, 1H, CH) 10.83 (s, 1H, NH)	$C_{12}H_9N_5OS_3$	42.97 (43.09)	2.71 (2.90)	20.88 (20.59)
9	–	157-158	48	1770 1695	324	7.25-8.03 (m, 11H, Ph x 2 and CH), 9.23 (s, 1H, CH)	$C_{16}H_{12}N_4O_2S$	59.25 (59.03)	3.73 (3.69)	17.27 (17.07)

162 ppm, and 159 ppm, respectively. The approximate value with **6a** supports the assigned structure **4a** (Figure 2).

The reaction of dihydrazones **7** with **2** was also examined. The reaction was successfully carried out by adding **2** into the stirred suspension of **7** in the presence of triethylamine, followed by stirring for 12 hours at room temperature to provide 4-arylidenamino-5-arylidenehydrazono-1,2,4-dithiazolidin-3-ones **6**, 2-arylidenamino-3-arylidenehydrazono-1,2,4-thiadiazolidin-5-ones **8**, and 2,4-dibenzylidenamino-1,2,4-thiadiazolidine-3,5-dione (**9**). The results were summarized in Tables II and III. The structures of **6**, **8**, and **9** were established by ir, ^{1}H-nmr, and mass spectral data and elemental analysis.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. The ir spectra were recorded with a JASCO A-100 grating infrared spectrophotometer. The ^{1}H-nmr and ^{13}C-nmr spectra were determined with a HITACHI R-600 ^{1}HFT-nmr (60 MHz), a JEOL JNM-Gx400 (400 MHz) spectrometers. Mass spectra were measured with a JEOL JMS-Dx303 HF mass spectrometer.

5,5-Dialkyl-1-phenyl-Δ^3-1,3,4-triazoline-2-thiones **3**, 5-Arylidenehydrazono-4-phenyl-1,2,4-dithiazolidin-3-ones **4**.

Into a solution of 1-alkylidene-4-phenylthiosemicarbazides (5 mmoles) or 1-arylidene-4-phenylthiosemicarbazides (5 mmoles) in dry dichloromethane (30 ml) was added triethylamine (10 mmoles, 1.4 ml) at room temperature under a nitrogen atmosphere. After half an hour, chlorocarbonylsulfenyl chloride (**2**) (5 mmoles, 0.42 ml) was added dropwise into the stirred solution at 0-5°. Then the reaction mixture was stirred for 12 hours at room temperature. The solution was evaporated to dryness under reduced pressure, and the residue was added to tetrahydrofuran (30 ml). The separated white solid (triethylamine hydrochloride) was filtered off, and the filtrate was condensed under vacuum. The residue then column chromatographed (silica gel, with dichloromethane as eluent). Evaporation of the solvent afforded the pure compounds, **3** or **4**. Analytical samples were recrystallized from ethanol.

4-Phenyl-5-phenylimino-1,2,4-dithiazolidin-3-one (**5**).

To a solution of diphenylthiourea (5 mmoles, 1.1 g) in dry dichloromethane (30 ml) was added triethylamine (10 mmoles, 1.4 ml) at room temperature under a nitrogen atmosphere. After half

an hour, chlorocarbonylsulfenyl chloride (**2**) (5 mmoles, 0.42 ml) was added dropwise to the stirred solution at 0-5°. Then the reaction mixture was allowed to stir at room temperature for an additional 12 hours. The solution was evaporated *in vacuo*, and the residue was added to tetrahydrofuran (30 ml). The separated white solid (triethylamine hydrochloride) was filtered off, and the filtrate was condensed under vacuum. The residue was then column chromatographed (silica gel, with dichloromethane as eluent). Evaporation of the solvent afforded the pure compound **5** (0.93 g). An analytical sample was recrystallized from ethanol.

Dihydrazones **7**.

These compounds were prepared from thiocarbohydrazide, diaminoguanidine, carbohydrazide and aldehydes according to the method of Beyer [9] and Ried [10].

4-Arylidenamino-5-arylidenehydrazono-1,2,4-dithiazolidin-3-ones **6**, 2-Arylidenamino-3-arylidenehydrazono-1,2,4-thiadiazolidin-5-ones **8**, 2,4-Dibenzylidenamino-1,2,4-thiadiazolidine-3,5-dione (**9**).

To a suspension of 1,5-diarylidenethiocarbohydrazides (3 mmoles), 1,3-diarylidenaminoguanidines (3 mmoles) or 1,5-dibenzylidenecarbohydrazide (3 mmoles, 0.80 g) in anhydrous tetrahydrofuran (30 ml) was added triethylamine (6 mmoles, 0.84 ml) at room temperature under a nitrogen atmosphere. After half an hour, chlorocarbonylsulfenyl chloride (**2**) (3 mmoles, 0.25 ml) was added dropwise to the stirred suspension at 0-5°. The reaction mixture was stirred for 12 hours at room temperature. The separated white precipitates (triethylamine hydrochloride) were filtered off, the filtrate was condensed under vacuum, and the residue was column chromatographed (silica gel, with dichloromethane as eluent). Evaporation of the solvent afforded the pure compounds **6**, **8**, or **9**, respectively. Analytical samples were recrystallized from ethanol.

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