upon standing. Recrystallization from ethyl acetate gave 0.42 g (39%) of 2-methylamino-1,3,4-thiadiazole (**4a**), mp 65° (lit.[9] mp 65–66°).

B. Ethyl Formate 4-Methylthiosemicarbazone (3, R = CH_3; R′ = C_2H_5).—The above reaction was repeated but the period of heating was 1 hr. At this time, the reaction flask was cooled in an acetone–Dry Ice bath and a white, crystalline product was obtained. Recrystallization from ethyl acetate gave 1.5 g (93.3%) of ethyl formate 4-methylthiosemicarbazone (**3**, R = CH_3; R′ = C_2H_5): mp 100–101°; ir ($CHCl_3$) 3375, 1645, 1550, 1180 cm^{-1}; nmr ($CDCl_3$) δ 1.6 (t, 3 H), 3.5 (d, 3 H), 4.45 (q, 2 H), 6.8 (s, 1 H), 7.6 (broad signal, 1 H), 9.2 (broad signal, 1 H).

Anal. Calcd for $C_5H_{11}N_3OS$: C, 37.25; H, 6.88; N, 26.06; S, 19.89. Found: C, 37.44; H, 7.05; N, 26.10; S, 20.09.

This compound (1.6 g, 10 mmol) was heated (neat) at 190° for 5 min. The resultant oil was dissolved in hot absolute ethanol and, upon cooling, 0.32 g (27.8%) of **5a** was obtained, mp 166–167°. The filtrate was evaporated *in vacuo* and the product was distilled to give 0.28 g (24.3%) of **4a** as an oil which crystallized upon standing, mp 63–64°. Similar yields of both products were obtained when ethanol was used as a reaction solvent, with and without acid catalyst. In these cases, the reaction mixture was refluxed for 20 hr.

C. 2-Methylamino-1,3,4-thiadiazole (4a).—Triethyl orthoformate (3.0 g, 20 mmol) and **2a** (1.0 g, 10 mmol) were added to absolute ethanol (10 ml). Concentrated hydrochloric acid (0.05 ml) was added and the suspension was stirred until solution was complete (1 hr). After the solution had been refluxed for 1 hr, the solvent was evaporated *in vacuo* and the crystalline product was dissolved in chloroform (10 ml). This solution was filtered and the filtrate was evaporated *in vacuo*. Recrystallization of the residue from ethyl acetate gave 1.65 g (72%) of **4a** as white needles, mp 66–67°.

The 2-alkylamino-1,3,4-thiadiazoles **4b–f** were prepared in the same manner as **4a**, part C, using 10 mmol of 4-alkylthiosemicarbazide, 20 mmol of triethyl orthoformate, and 0.05 ml of concentrated HCl.

2-*n*-Propylamino-1,3,4-thiadiazole (4c).—The product **4c** was obtained as low-melting white crystals, mp 37–40°. Distillation, bp 136–138° (0.3 mm), gave a sample which melted at 42–43°: nmr ($CDCl_3$) δ 1.01 (t, 3 H), 1.76 (m, 2 H), 3.36 (t, 2 H), 7.33 (broad s, 1 H), 8.50 (s, 1 H); ir (neat) 3226 and 1530 cm^{-1}; hydrochloride salt mp 127–128°.

Anal. Calcd for $C_5H_9N_3S \cdot HCl$: C, 33.43; H, 5.61; N, 23.39; S, 17.85; Cl, 19.73. Found: C, 33.58; H, 5.57; N, 23.43; S, 17.92; Cl, 19.66.

2-*tert*-Octylamino-1,3,4-thiadiazole (4e).—The product **4e** was recrystallized from ethyl acetate: mp 127–128°; ir ($CHCl_3$) 3400, 1570 cm^{-1}; nmr ($CDCl_3$) δ 1.0 (s, 9 H), 1.6 (s, 6 H), 1.8 (s, 2 H), 6.9 (broad signal, 1 H), 8.55 (s, 1 H).

Anal. Calcd for $C_{10}H_{19}N_3S$: C, 56.30; H, 8.98; N, 19.70; S, 15.03. Found: C, 56.28; H, 8.84; N, 19.60; S, 14.96.

2-(1-Adamantylamino)-1,3,4-thiadiazole (4f).—The product **4f** was recrystallized from ethanol: mp 155–155.5°; ir ($CHCl_3$) 1570 cm^{-1}; nmr (DMSO-d_6) δ 1.6–2.2 (m), 8.95 (s, 1 H).

Anal. Calcd for $C_{12}H_{17}N_3S$: C, 61.24; H, 7.28; N, 17.85; S, 13.62. Found: C, 61.52; H, 7.41; N, 17.94; S, 13.69.

2-Methylamino-5-methyl-1,3,4-thiadiazole (6).—A mixture of 4-methylthiosemicarbazide (0.79 g, 7.5 mmol), triethyl orthoacetate (2.43 g, 15 mmol), and 0.05 ml of concentrated hydrochloric acid in ethanol (10 ml) was stirred at room temperature for 1 hr. The resulting clear solution was refluxed for 1 hr and the solvent was removed *in vacuo*. Recrystallization of the residue from ethyl acetate gave 0.75 g (78.1%) of **6** as white crystals, mp 111–112° (lit.[10] mp 112°).

Registry No.—**1**, 26907-35-7; **2a**, 6610-29-3; **2b**, 13431-34-0; **2c**, 13431-35-1; **2d**, 13431-41-9; **2e**, 41593-77-5; **2f**, 21126-27-2; **3** (R = CH_3; R′ = C_2H_5), 21304-97-2; **4a**, 38490-45-8; **4b**, 13275-68-8; **4c**, 41593-82-2; **4c** HCl, 41593-83-3; **4d**, 23289-12-5; **4e**, 41593-85-5; **4f**, 41593-86-6; **5a**, 24854-43-1; **5b**, 32362-78-0; **5c**, 41593-89-9; **5d**, 32362-84-8; **5e**, 41593-91-3; **6**, 38917-35-0; 2-amino-1,3,4-thiadiazole, 4005-51-0; trimethyl orthoformate, 149-73-5; *tert*-octyl isothiocyanate, 17701-76-7; triethyl orthoformate, 122-51-0.

(9) G. Werber and F. Massio, *Ann. Chim. (Rome)*, **51**, 944 (1961); *Chem. Abstr.*, **56**, 7305 (1962).

(10) C. Pulvermacher, *Chem. Ber.*, **27**, 613 (1894).

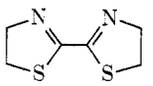
A Facile Synthesis of 2,2′-Bi-2-thiazolines and -thiazines

DONALD A. TOMALIA* AND J. N. PAIGE

E. C. Britton Research Laboratory, The Dow Chemical Company, Midland, Michigan 48640

Received April 18, 1973

The first reports of the synthesis of 2,2′-bi-2-thiazolines appeared in 1954. In that year, two groups[1,2] discovered independently that the parent compound **1** could be prepared in poor to modest yield by the reaction of cyanogen with 2-mercaptoethylamine. Subsequent work by Woodburn, *et al.*,[3] has shown that **1** can also be prepared in very good yield by the reaction of dibutyloxamidine 2HCl with 2-mercaptoethylamine HCl. Preparation of its six-membered analogs, **2**,



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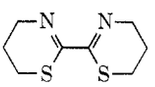


2

however, has been hindered in that necessary precursors were not readily available. To date, the synthesis of 2,2′-bi-2-thiazine, **2**, or its homologs has not yet been reported.

We wish to describe a general and facile synthesis of **1**, **2**, and their homologs based on the readily available precursors: dithiooxamide (rubeanic acid) and amino alcohols. Heterocycles **1** and **2** are of interest in that they have been found to form dications bearing charge on mutually attached carbon atoms when allowed to react with acylating agents[4a] or Brønsted acids.

The synthetic route involved stirring appropriate amino alcohols with dithiooxamide at room temperature until ammonia evolution ceased, using modified Wallach reaction conditions.[4b] Reaction of the resulting *N,N′*-bis(hydroxyalkyl)dithiooxamide with thionyl chloride produced the corresponding bithiazolinium or -thiazinium dications (**1′–4′**) in good to excellent yield. The free bases (**1–4**) were liberated by treatment with sodium bicarbonate since stronger bases generally led to hydrolysis products. (See Scheme I.)

The dications could be stored for several days under anhydrous conditions; however, exposure to moisture led to unidentified hydrolysis products. Samples of the free bases appeared to have long-term stability. The latter compounds were characterized by ir and nmr analyses as well as by elemental analyses.

Dication **5**, as well as its oxygen analog **6**, were of particular interest in that there are relatively few examples of dications bearing positive charges on mutually attached carbon atoms reported in the literature.[5] Dications **5** and **6** were prepared by addition of **1** or 2,2′-bi-2-oxazoline to neat FSO_3H. The proton chemical shift assignments for protons a and b were based

(1) R. Kuhn and F. Drawert, *Justus Liebigs Ann. Chem.*, **590**, 55 (1954).

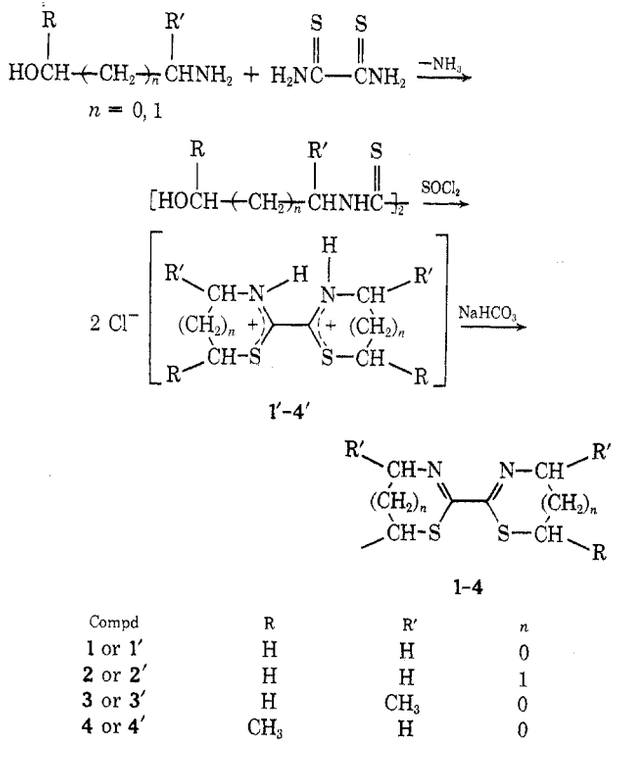
(2) H. M. Woodburn and B. G. Pautler, *J. Org. Chem.*, **19**, 863 (1954).

(3) H. M. Woodburn and W. E. Hoffman, *J. Org. Chem.*, **23**, 262 (1958).

(4) (a) D. A. Tomalia, to be published; (b) O. Wallach, *Justus Liebigs Ann. Chem.*, **262**, 357 (1891).

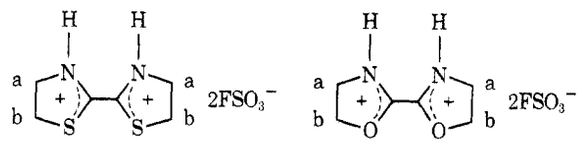
(5) C. U. Pittman, Jr., S. P. McManus, and J. W. Larsen, *Chem. Rev.*, **72**, 376 (1972).

SCHEME I



Compd	R	R′	n
1 or 1′	H	H	0
2 or 2′	H	H	1
3 or 3′	H	CH_3	0
4 or 4′	CH_3	H	0

on observations made by Weinberger, *et al.*,[6] wherein they noted that methylene protons on carbon attached to the nitrogen in monothiazolines or oxazolines were always at a higher field than those attached to the sulfur or oxygen atom. Previous attempts to prepare the related bis-2,2′-1,3-dioxolenium dication, **7** (n = 0),

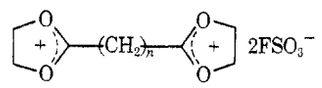


5

a, 4.15 (t)
b, 4.78 (t)
(a:b = 1:1)

6

a, 4.64 (t)
b, 5.60 (t)
(a:b = 1:1)



7

were unsuccessful although the bis-2,2′-methylene-1,3-dioxolenium dication **7** (n = 1) was prepared and characterized by nmr spectroscopy.[7,8]

Experimental Section

Nmr spectra were obtained with a Varian A-60 spectrometer. Chemical shifts are reported as δ (parts per million) relative to tetramethylsilane (TMS) or tetramethylammonium tetrafluoroborate (TMA·BF_4). The TMA·BF_4 signal is assumed to be at 3.10 ppm, relative to TMS.[9] Ir spectra were scanned on a Perkin-Elmer 337 spectrometer. Melting points were determined in a capillary and are uncorrected unless otherwise noted.

Dithiooxamide (rubeanic acid) and N,N'-bis(2-hydroxyethyl)-dithiooxamide were available from Mallinckrodt Chemical Co.

2,2′-Bi-2-thiazoline (1).—To a stirred suspension of N,N'-bis-(2-hydroxyethyl)dithiooxamide (104 g, 0.5 mol) in 600 ml of toluene was added a total of 238 g (2.0 mol) of thionyl chloride in two equal portions. After addition of a second portion (119 g) a strong exothermic reaction accompanied by a considerable amount of frothing was observed. A maximum temperature of 55° was attained. After the temperature subsided, the reaction mixture was maintained at 45° for 1.5 hr while stirring. The resulting insoluble, mustard yellow salt was filtered off, slurried with n-hexane, and refiltered. After drying, the product weighed 121.7 g (99%) and had a melting point of 140–143° (decomposed to orange oil). The infrared spectrum displayed a broad band centered at ~2220 cm^{-1} (–N=C–) and a medium-intensity band at 1780 cm^{-1} which is characteristic for the thiazolinium ring. An nmr spectrum in DMSO-d_6 consisted of two triplets at 4.44 and 3.40 ppm in a ratio of 1:1.

2,2′-Bi-2-thiazolinium dihydrochloride (100 g, 0.41 mol) was added in small portions to a stirred solution of sodium bicarbonate (31 g, 0.41 mol) in 300 ml of water. A grayish-brown precipitate fell out of solution upon neutralization. The precipitate was filtered, washed with two 25-ml portions of water, and dried in a vacuum oven at 60–80°. The gray-brown, powdery product weighed 56.5 g (79.5%) and melted at 124–128° (lit. mp 127–129°).

This material was not very soluble in most common organic solvents. It did dissolve in liquid sulfur dioxide, giving an nmr spectrum (–25°) consisting of triplets at 4.42 (–SCH_2–) and 3.46 ppm (=NCH_2–) in a ratio of 1:1.

2,2′-Bi-2-thiazine (2).—N,N'-Bis(3-hydroxypropyl)dithiooxamide was prepared by a method similar to that of Jacob and Herman.[9] A mixture of 3-aminopropanol (50 g, 0.66 mol) and dithiooxamide (40 g, 0.33 mol) in 160 ml of absolute ethanol was stirred at room temperature for 16 hr, during which time the reaction became nearly homogeneous. The dark brown solution was filtered and the filtrate was concentrated to a semisolid state. Trituration with water gave a gold-colored solid weighing 47.1 g (60%) which melted at 69–72°. This material was used without further purification for the next step.

To a stirred slurry of N,N'-bis(3-hydroxypropyl)dithiooxamide (35.4 g, 0.15 mol) in 200 ml of toluene was added 71.5 g (0.6 mol) of thionyl chloride in two equal increaments over a period of 1.5 hr. A gummy solid appeared as the reaction mixture turned dark. A maximum temperature of 43° was noted during this exothermic reaction. After addition was complete, the reaction temperature was maintained at 45–50° for 2 hr. The beige-colored product which formed was filtered, washed with toluene, and found to weigh 37.1 g (91%). The dication melted at 138–140° and was liberated as the free base without further purification.

A 27.3-g (0.1 mol) sample of the dication intermediate was added in small increments to a stirred solution of sodium bicarbonate (18.6 g, 0.22 mol) in 200 ml of water. The beige-colored product was filtered and found to weigh 21 g (100%). Recrystallization from carbon tetrachloride gave a cream-colored material melting at 161.5–163°. *Anal.* Calcd: C, 48.0; H, 6.00; N, 14.0; S, 32.0. Found: C, 48.0; H, 5.89; N, 13.8; S, 31.9.

The nmr spectrum of **2** in $CDCl_3$ consisted of triplets at 3.87 (–SCH_2–) and 3.03 ppm (=NCH_2–) as well as a pentet at 1.87 ppm (–CCH_2C–).

4,4′-Dimethyl-2,2′-bi-2-thiazoline (3).—A mixture of *l*-2-amino-1-propanol (10 g, 0.133 mol) and dithiooxamide (8 g, 0.066 mol) was stirred at room temperature for 19 hr. The dark solution was concentrated to a dark-brown semisolid. Trituration with water gave 7.6 g (49%) of a dark-brown powder, mp 113–118°.

To a stirred mixture of 7.5 g (0.032 mol) of N,N'-bis(2-hydroxy-1-methylethyl)dithiooxamide in 50 ml of toluene was added 16 g (0.13 mol) of thionyl chloride in four equal portions over a 1.5-hr period. The reaction mixture was then heated at 45–50° for 2 hr. Filtration yielded 6.5 g (75%) of the dication as a gold-colored powder, mp 100–105°.

Neutralization of the dication with a solution of sodium bicarbonate (4.2 g, 0.05 mol) in 50 ml of water gave a beige-colored product which was recrystallized from hexane to give 2.3 g (49%) of a light yellow material which melted at 73–74°. *Anal.* Calcd: C, 48.0; H, 6.00; N, 14.0; S, 32.0. Found: C, 47.96; H, 6.00; N, 14.0; S, not determined.

5,5′-Dimethyl-2,2′-bi-2-thiazoline (4).—A mixture of dithiooxamide (40 g, 0.33 mol) and 1-amino-2-propanol (50 g, 0.66 mol) in 300 ml of ethanol was stirred at room temperature until

(6) M. A. Weinberger and R. Greenhalgh, *Can. J. Chem.*, **41**, 1038 (1963).
(7) H. Hart and D. A. Tomalia, *Tetrahedron Lett.*, **No. 15**, 1347 (1967).
(8) D. A. Tomalia, Ph.D. Thesis, Michigan State University, 1968.
(9) W. A. Jacob and M. A. Herman, *Anal. Chim. Acta*, **33**, 229 (1965).

ammonia evolution ceased (~5 days). A small amount of solid, which formed during that time, was filtered and the filtrate was reduced to a dark-brown, gummy semisolid by removing solvent under vacuum. This material was stirred with 600 ml of water for 4 hr and filtered to give 33.4 g (43%) of a yellow powder, mp 95–100° (lit.[10] mp 98–101°).

A mixture of *N,N'*-bis(2-hydroxypropyl)dithiooxamide (113.5 g, 0.48 mol) in toluene (575 ml) was treated with four 60-g portions of thionyl chloride over a period of 1.5 hr. The reaction mixture was then heated at 45–50° for 1.5 hr, after which the resulting gold-colored dication was filtered and found to weigh 66.9 g (51%), mp 118–131°.

Neutralization of the dication (66.9 g) with a solution of sodium bicarbonate (42.5 g, 0.5 mol) in 450 ml of water gave 49 g (100%) of a dark-brown solid. Recrystallization from *n*-hexane yielded a cream-colored powder, mp 92–93.5°. *Anal.* Calcd: C, 48.0; H, 6.00; N, 14.0; S, 32.0. Found: C, 48.2; H, 6.22; N, 13.9; S, 31.9.

The nmr spectrum ($CDCl_3$) consisted of a complex multiplet at 4.75–3.80 ppm ($-CH_2CH-$) and a doublet centered at 1.38 ppm (CH_3-).

Registry No.—**1**, 41601-87-0; **1'** $2Cl^-$, 41601-88-1; **2**, 41601-89-2; **2'** $2Cl^-$, 41601-90-5; **3**, 41601-91-6; **3'** $2Cl^-$, 41601-92-7; **4**, 41601-93-8; **4'** $2Cl^-$, 41601-88-1; *N,N'*-bis(2-hydroxyethyl)-dithiooxamide, 120-86-5; *N,N'*-bis(2-hydroxypropyl)dithiooxamide, 3815-26-7; *l*-2-amino-1-propanol, 35320-23-1; *N,N'*-bis-(2-hydroxy-1-methylethyl)dithiooxamide, 41601-97-2; 1-amino-2-propanol, 78-96-6; dithiooxamide, 79-40-3.

(10) R. N. Hurd, G. DeLaMater, G. C. McElheny, R. J. Turner, and V. H. Wallingford, *J. Org. Chem.*, **26**, 3980 (1961).

Thioimidates and Ketene Mercaptals from Ketenimines

MARVIN W. BARKER,* SUSAN C. LAUDERDALE,[1] AND JOSEPH R. WEST

Department of Chemistry, Mississippi State University, Mississippi State, Mississippi 39762

Received April 2, 1973

The addition of mercaptans to such heterocumulenes as ketenes, isocyanates, and carbodiimides has been found to occur smoothly and in good yield to produce thio esters,[2] thiocarbamates,[3] and S-substituted isothioureas,[4] respectively. As a continuation of a study of the chemistry of ketenimines[5] and mercaptan addition to heterocumulenes, we have investigated the reactions of mercaptans and ketenimines.

When diphenylketene-*N*-(*p*-bromophenyl)imine (**1a**) is treated with excess thiophenol at the temperature of refluxing benzene, the corresponding thioimidate (**2**) is formed in 72% yield (eq 1). Other *N*-aryl ketenimines behave similarly to produce thioimidates in yields of 44–90%. Structure assignments were based on ir data (loss of the ketenimine absorption at 2000 cm^{-1} and appearance of the imine absorption at approximately 1640 cm^{-1}), nmr data (absorption for the benzhydryl proton at δ 5 ppm), and elemental analyses. All thioimidates produced from thiophenol were crystalline solids and were easily purified. Aliphatic mercaptans as represented by the ethyl and *n*-propyl substituents also add to ketenimines to yield crystalline thioimidates in good yields (Table I).

$$\underset{\mathbf{1a}}{Ph_2C{=}C{=}NAr} + RSH \xrightarrow{80^\circ} \underset{\mathbf{2a}}{Ph_2CHC(SR){=}NAr} \quad (1)$$

(1) NDEA Predoctoral Fellow, 1969–1972.
(2) P. J. Lillford and D. P. N. Satchell, *J. Chem. Soc. B*, 1303 (1970).
(3) S. Ozaki, *Chem. Rev.*, **72**, 457 (1972).
(4) P. Schlack and G. Keil, *Justus Liebigs Ann. Chem.*, **661**, 164 (1963); M. Busch, G. Blume, and E. Pungs, *J. Prakt. Chem.*, **79**, 513 (1909).
(5) For previous reports see M. W. Barker and R. H. Jones, *J. Heterocycl. Chem.*, **9**, 555 (1972); M. W. Barker and J. D. Rosamond, *ibid.*, **9**, 1147 (1972); M. W. Barker, L. L. Combs, and J. T. Gill, *ibid.*, **9**, 77 (1972); and references cited therein.

TABLE I
THIOIMIDATES FROM KETENIMINES[a]

$$Ph_2C{=}C{=}NAr + RSH \longrightarrow Ph_2CHC(SR){=}NAr$$

Sample	Ar	R	Yield of **2**, %	Mp, °C
a	*p*-Bromophenyl	Phenyl	72	92–93
b	*m*-Bromophenyl	Phenyl	60	82.5–83
c	*p*-Chlorophenyl	Phenyl	73	83.5–84.0
d	*m*-Chlorophenyl	Phenyl	44	75.0–75.5
e	Phenyl	Phenyl	45	80.0–81.0
f	*p*-Tolyl	Phenyl	64	85–85.5
g	*p*-Anisyl	Phenyl	81	106.5–107.5
h	*p*-Fluorophenyl	Phenyl	61	91.5–92.5
i	*p*-Bromophenyl	Ethyl	71	95–95.5
j	*p*-Bromophenyl	*n*-Propyl	90	88.5–89.0

[a] Satisfactory analytical data (±0.4% for C, H, and N) were reported for all thioimidates listed in this table: Ed.

Although these reactions were first performed with irradiation and presumed to occur by radical addition, it was subsequently found that light is not needed. Furthermore, the same products are obtained in comparable yields if the sodium salt of the mercaptans is employed.

When **1a** was treated with excess thiophenol at 169° (refluxing thiophenol), rather than 80°, no thioimidate was found. Instead, aniline hydrobromide precipitate from solution and work-up of the reaction mixture yielded only diphenylketene diphenylmercaptal[6] (**3**) (eq 2). This reaction is apparently an acid-catalyzed

$$\underset{\mathbf{1a}}{Ph_2C{=}C{=}N{-}C_6H_4{-}Br} + PhSH \xrightarrow{169^\circ} PhNH_2{\cdot}HBr + \underset{\mathbf{3}}{Ph_2C{=}C(SPh)_2} \quad (2)$$

process and the HBr catalyst is produced through a hydrogenolysis reaction of the aryl bromide of **1a**. To test this hypothesis, **1e** was treated with excess thiophenol at 169° with the addition of HCl; **3** was obtained from the reaction in 68% yield. Table II con-

TABLE II
KETENE MERCAPTALS FROM KETENIMINES

$$Ph_2C{=}C{=}N{-}C_6H_4{-}X + PhSH \xrightarrow{HCl} X{-}C_6H_4{-}NH_2{\cdot}HCl + Ph_2C{=}C(SPh)_2$$

X	Yield, %
H	67.7
p-Cl	52
m-Cl	64
p-CH_3	42.5
p-OCH_3	42.5

(6) A. Schonberg and L. V. Vargha, *Justus Liebigs Ann. Chem.*, **483**, 176 (1930).