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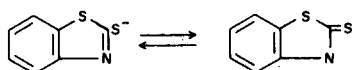
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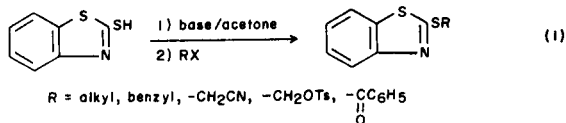
Attempts to thermally rearrange 2-benzothiazolythioacetonitrile (**1**) to the titled compound **8** failed. The reaction of 3-chloromethyl-2-benzothiazolinethione with potassium cyanide in dimethylformamide (DMF) or dimethylsulfoxide (DMSO) at 25-30° afforded **8** in 98% yield. Whereas replacing the DMF or DMSO solvent with acetone furnished the unexpected sulfide **9** in 92% yield. Substituting 3-chloromethyl-2-benzoxazolinethione as the electrophile in the same reaction gave the sulfide **10** in 95% yield. Possible mechanisms and supporting nmr data are discussed.

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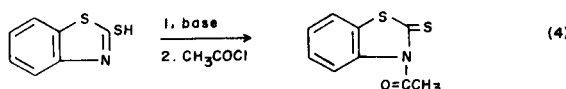
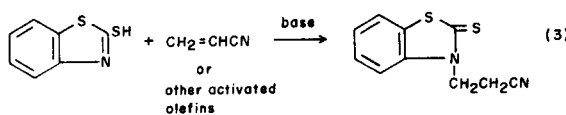
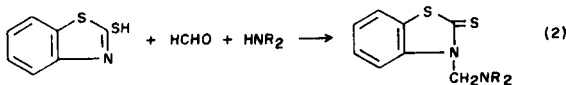
Due to the ambident nature of 2-mercaptobenzothiazole anion that in nucleophilic displacement reactions under



basic conditions either the *N* or *S*-substituted products are possible. However, almost exclusively under a variety of reaction conditions, the *S*-substituted products are obtained. For example in the following alkylation reaction afforded *S*-substituted compounds:



Examples where *N*-substituted products are obtained are shown below:

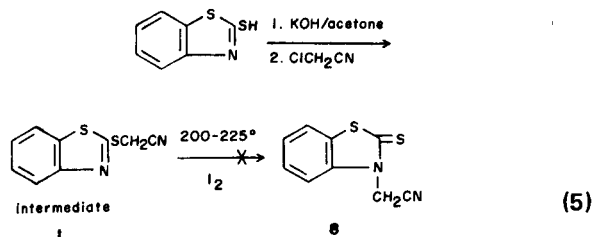


The propensity for nitrogen rather than sulfur alkylation and acylation reactions has previously been studied by Halasa [2].

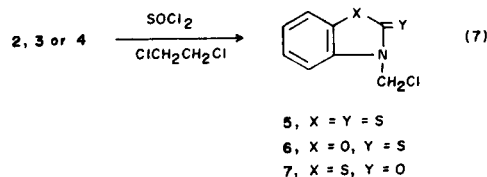
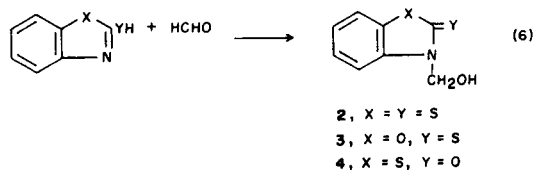
The object of the present investigation was to prepare 2-thioxo-3-benzothiazolineacetonitrile (**8**) and related compounds.

As noted in reaction 1, the treatment of 2-mercaptobenzothiazole with chloroacetonitrile under basic conditions

afforded the *S*-substituted product, 2-benzothiazolythioacetonitrile (**1**). Based on our reported studies [3] concerning the thermal rearrangement of 2-methylthiobenzothiazole to 3-methyl-2-benzothiazolethione, we attempted the isomerization of this intermediate to **8**. Our efforts failed for under the thermal conditions **1** decomposed.



The reaction of the appropriate benzothiazole with formaldehyde in methyl alcohol afforded 3-(hydroxymethyl)-2-benzothiazolinethione (**2**), 3-(hydroxymethyl)-2-benzoxazolinethione (**3**) or 3-(hydroxymethyl)-2-benzothiazolinone (**4**) in excellent yields. The treatment of **2**, **3** or **4** with excess thionyl chloride in ethylene dichloride furnished the intermediates 3-(chloromethyl)-2-benzothiazolinethione (**5**), 3-(chloromethyl)-2-benzoxazolinethione (**6**) or 3-(chloromethyl)-2-benzothiazolinone (**7**). Chien-Pen Lo [4] reported



the synthesis of **4** and **7** but gave no details for the preparation of **2**, **3**, **5** and **6**. Moreover, by substituting *meta*-

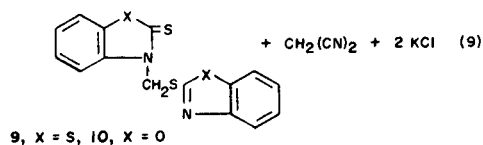
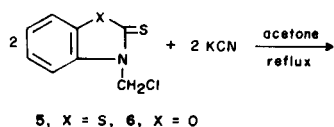
*nol for ethanol*, reducing the reaction time from 3 to 1 hour, elimination of potassium carbonate and the addition of water at the end of the reflux period until cloudiness appeared, we were able to increase the yield of **4** from 65 to 92%.

The reaction of **5** with potassium cyanide in dimethylformamide or dimethylsulfoxide at 25-30° for 3 days afforded **8** in 98% yield.

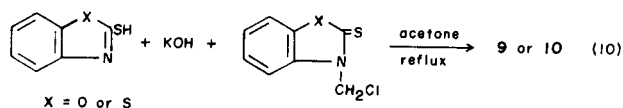


It is noteworthy to contrast the chemical shift for the methylene protons in **1** and **8**. The SCH<sub>2</sub>CN in **1** appeared at  $\delta$  4.68, whereas the NCH<sub>2</sub>CN in **8** was found at  $\delta$  5.61. The large downfield shift in **8** is due to the deshielding effect of the thiocarbonyl group. The same effect has been observed with 2-(methylthio)benzothiazole ( $\delta$  SCH<sub>3</sub> = 2.75) and its rearranged product, 3-methylbenzothiazoline-2-thione ( $\delta$  NCH<sub>3</sub> = 3.80) [3a,8].

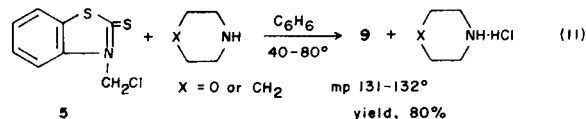
However, when the solvent in reaction **8** was replaced with acetone the desired product **8** was not obtained but instead gave the unexpected 3-[(2-benzothiazolyl)thiomethyl]-2(3*H*)-benzothiazolethione (**9**) in 92% yield. Replacing the electrophile with **6** in the same reaction afforded 3-[(2-benzoxazolyl)thiomethyl]-2(3*H*)-benzoxazolethione (**10**) in 95% yield.



Proof of structure of **9** and **10** in reaction 9 was established by reactions **10** and **11**.

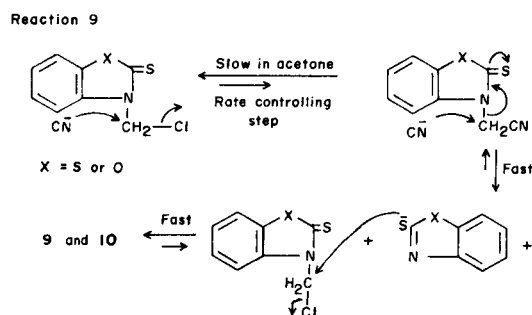
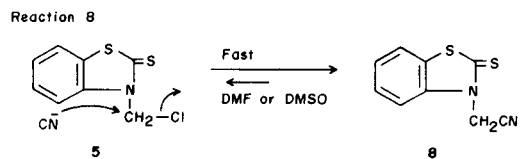


Compound **9** was first prepared by Kolosova and Stavrovskays [5] by the reaction of **5** with piperidine or morpholine.



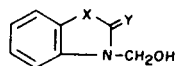
A mixture melting point of **9** derived by reactions 9, 10 or 11 was not depressed and the nmr spectra of all three samples were superimposable.

The following mechanisms are offered to explain the formation of different products in reactions 8 and 9.



The reaction of **7** with potassium cyanide in three different solvents (acetone, dimethylformamide or acetonitrile) was studied in order to determine whether or not the normal or unexpected products formed. As noted in Table 3, only the expected 2-oxo-3-benzothiazolineacetonitrile (**11**) was obtained.

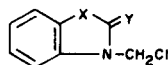
Table 1



No.	X	Y	Mp °C	% Yield	Empirical formula	% C		% H		% N		% S	
						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
2	S	S	126-128	99	C <sub>8</sub> H <sub>7</sub> NOS <sub>2</sub>	48.71	48.55	3.58	3.62	7.10	7.12	32.51	32.60
3	O	S	129-130	90	C <sub>8</sub> H <sub>7</sub> NO <sub>2</sub> S	53.02	53.12	3.89	3.92	7.73	7.73	17.69	17.63
4	S	O	101-103 [a]	92	C <sub>8</sub> H <sub>7</sub> NO <sub>2</sub> S	53.02	53.19	3.89	3.92	7.73	7.70	17.69	17.78

[a] Ref 4 reported mp 93-97° and a 65% yield was obtained.

Table 2



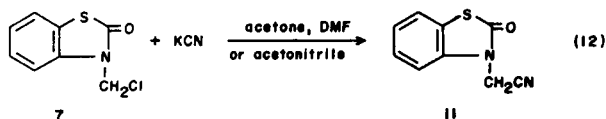
No	X	Y	Mp °C	% Yield	NMR, $\delta$ , ppm Deuteriochloroform-TMS	Empirical formula	% C		% H		% N		% S	
							Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
5	S	S	127-128 [a]	95	6.05 (s, 2, -NCH <sub>2</sub> ), 7.10-7.60 (m, 4, ArH)	C <sub>8</sub> H <sub>6</sub> CINS <sub>2</sub>	44.54	44.42	2.80	2.86	6.49	6.50	29.73	29.76
6	O	S	149-150	97	6.00 (s, 2, -NCH <sub>2</sub> ), 7.10-7.60 (m, 4, ArH)	C <sub>8</sub> H <sub>6</sub> CINOS	48.13	48.32	3.03	3.15	7.02	7.10	16.06	16.32
7	S	O	103-104 [b,c]	98	5.70 (s, 2, -NCH <sub>2</sub> ), 7.00-7.60 (m, 4, ArH)	C <sub>8</sub> H <sub>6</sub> CINOS	48.13	48.02	3.03	3.06	7.02	7.02	16.06	16.02

[a] Recrystallization from ethylene dichloride. [b] Recrystallization from carbon tetrachloride. [c] Ref 4 reported mp 97-99° and no mention of % yield obtained.

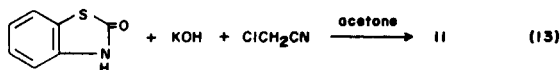
Table 3

No	Reaction		Mp °C	% Yield	NMR, $\delta$ , ppm Deuteriochloroform-TMS	Empirical formula	% C		% H		% N		% S	
	Solvent	Temp °C					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
11	acetone	56-58	132-133 [a]	91	4.85 (s, 2, CH <sub>2</sub> CN), 7.00-7.70 (m, 4, ArH)	C <sub>8</sub> H <sub>6</sub> N <sub>2</sub> OS	56.83	56.68	3.18	3.21	14.73	14.60	16.86	17.07
11	DMF	80-90	134-135 [a]	87	4.85 (s, 2, CH <sub>2</sub> CN), 7.00-7.70 (m, 4, ArH)	C <sub>8</sub> H <sub>6</sub> N <sub>2</sub> OS	56.83	56.55	3.18	3.20	14.73	14.50	16.86	16.93
11	aceto- nitrile	80-82	134-135 [a]	90	4.85 (s, 2, CH <sub>2</sub> CN), 7.00-7.70 (m, 4, ArH)	C <sub>8</sub> H <sub>6</sub> N <sub>2</sub> OS	56.83	56.51	3.18	3.15	14.73	14.67	16.86	16.91

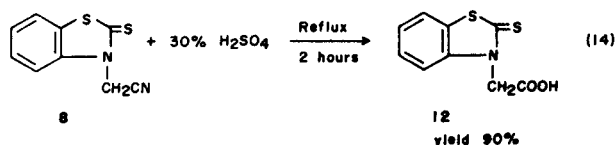
[a] Recrystallization from isopropyl alcohol.



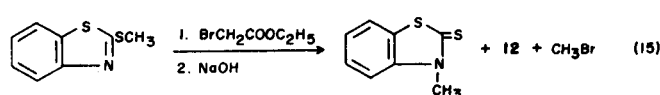
Proof of structure was afforded by the synthesis of **11** by the following conventional method [6]:



Further proof for the proposed structure **8** was obtained by the following reaction:



Chen [7] reported the synthesis of 2-thioxo-(3H)-benzothiazoline-3-acetic acid (**12**) in 36% yield by the reaction of 2-(methylthio)benzothiazole with ethyl bromoacetate at 150-155° followed by the saponification of the ester with sodium hydroxide.



A mixture melting point of **12** derived by reactions 14 and 15 was not depressed and their nmr spectra were identical.

## EXPERIMENTAL

The nmr spectra were obtained with a Varian T-60 nmr spectrometer. The chemical shifts are reported in  $\delta$ , using tetramethylsilane as reference. All melting points were taken upon a Fisher-Johns block and are uncorrected.

### 2-Benzothiazolythioacetonitrile (1).

To a stirred solution containing 34 g (0.2 mole) of 2-mercaptobenzothiazole, 13.2 (0.2 mole) of 85% potassium hydroxide and 500 ml of water, 15.2 g (0.2 mole) of chloroacetonitrile was added in one portion. After stirring at 25-30° for 3 hours, the solid was collected by filtration, washed with water until neutral and air-dried at 25-30°. The crude **1**, mp 77-79°, was obtained in 95% yield. After recrystallization from methyl alcohol it melted at 81-82°; nmr (deuteriodimethylsulfoxide):  $\delta$  4.68 (s, 2, -CH<sub>2</sub>CN), 7.20-8.30 (m, 4, ArH).

Anal. Calcd. for C<sub>8</sub>H<sub>6</sub>N<sub>2</sub>S<sub>2</sub>: C, 52.40; H, 2.93; N, 13.58; S, 31.09. Found: C, 52.50; H, 2.97; N, 13.51; S, 31.38.

### Attempted Isomerization of 1.

A stirred solution containing 20.7 g (0.1 mole) of **1** and two crystals of

iodine was heated 200-225° for 5 hours. At the end of the heating period the hot liquid was poured into a Pyrex dish and allowed to stand overnight. Since the resulting black tarry semi-solid could not be purified by recrystallization, it was concluded that under the thermal conditions 1 decomposed.

3-(Hydroxymethyl)-2-benzothiazolinethione (2), 3-(Hydroxymethyl)-2-benzoxazolinethione (3) and 3-(Hydroxymethyl)-2-benzothiazolinone (4).

A stirred slurry containing 0.2 mole of 2-mercaptobenzothiazole, 2-mercaptobenzothiazole, 2-mercaptobenzoxazole or 2-hydroxybenzothiazole, 32 ml of 37% aqueous formaldehyde and 40 ml of methyl alcohol was heated at reflux for 1 hour. For 4 only at reflux water (75 ml) was added until cloudiness appeared. The resultant solution was allowed to cool to room temperature and then stirred at 0-10° for 30 minutes. The solid was collected by filtration and air-dried at 25-30°. The data are summarized in Table 1.

3-(Chloromethyl)-2-benzothiazolinethione (5), 3-(Chloromethyl)-2-benzoxazolinethione (6) and 3-(Chloromethyl)-2-benzothiazolinone (7).

To a stirred slurry containing 0.5 mole of 2, 3 or 4 in 500 ml of ethylene dichloride, 89.3 g (0.75 mole) of thionyl chloride was added in one portion. The stirred reaction mixture was heated at reflux for 2 hours. The excess thionyl chloride and solvent were removed *in vacuo* at a maximum temperature of 70° at 1-2 mm. The data are listed in Table 2.

2-Thioxo-3-benzothiazolineacetonitrile (8).

To a stirred slurry containing 71.6 g (1.1 moles) of potassium cyanide, 1 liter of dimethylformamide (DMF) or dimethylsulfoxide (DMSO) and 90 ml of water, 215.8 g (1.0 mole) of 5 was added in one portion. After stirring for 25 minutes a temperature rise from 20° to 40° was noted. After cooling to 25°, the reaction mixture was stirred at 25-30° for 3 days. After the addition of 2 liters of water, stirring was continued at 25-30° for 1 hour. The solid was collected by filtration, washed with water until neutral to litmus and air-dried at 50°. The crude 8, mp 168-170°, was obtained in 98% yield. After recrystallization from toluene it melted at 179-180°; nmr (deuteriodimethylsulfoxide):  $\delta$  5.61 (s, 2, -CH<sub>2</sub>CN), 7.04-7.84 (m, 4, ArH).

Anal. Calcd. for C<sub>9</sub>H<sub>8</sub>N<sub>2</sub>S<sub>2</sub>: C, 52.40; H, 2.93; N, 13.58; S, 31.09. Found: C, 52.53; H, 2.96; N, 13.48; S, 31.00.

3-[(2-Benzothiazolyl)thiomethyl]-2(3H)-benzothiazolethione (9) and 3-[(2-Benzoxazolyl)thiomethyl]-2(3H)-benzoxazolethione (10).

Method 1.

A stirred slurry containing 0.1 mole of 5 or 6, 7.2 g (0.11 mole) of potassium cyanide and 150 ml of acetone was heated at reflux for 24 hours. After cooling to 5°, 800 g of ice water was added and stirring continued at 0-10° for 1 hour. The solid was collected by filtration, washed with water until neutral to litmus and air-dried at 25-30°. Crude 9, mp 106-108°, and 10, mp 133-135°, were obtained in 92% and 95% yields, respectively. After recrystallization from toluene 9 and 10 melted at 130-131° and 152-153°, respectively; nmr for 9 (deuteriochloroform):  $\delta$  6.30 (s, 2, -NCH<sub>2</sub>S-), 7.00-8.10 (m, 8, 2 ArH); nmr for 10 (deuteriochloroform):  $\delta$  6.10 (s, 2, -NCH<sub>2</sub>S-), 7.04-7.90 (m, 8, 2 ArH).

Anal. Calcd. for 9 C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>S<sub>4</sub>: C, 51.99; H, 2.91; N, 8.08; S, 37.01. Found: C, 52.09; H, 2.96; N, 7.97; S, 36.80.

Anal. Calcd. for 10 C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub>: C, 57.31; H, 3.21; N, 8.91; S, 20.40. Found: C, 57.01; H, 3.27; N, 8.68; S, 20.65.

Method 2.

A stirred solution containing 0.1 mole of 2-mercaptobenzothiazole or 2-mercaptobenzoxazole, 6.6 g (0.1 mole) of 85% potassium hydroxide in 200 ml of acetone and 10 ml of water 0.1 mole of 5 or 6 was added in one portion. The stirred reaction mixture was heated at reflux for 24 hours. The remainder of the procedure was identical as described in Method 1. Crude 9, mp 122-124° and 10, mp 147-149°, were obtained in 81 and

89% yields, respectively. After recrystallization from toluene 9 and 10 melted at 131-132° and 152-153°, respectively. A mixture melting point with 9 or 10 obtained by Method 1 was not depressed and the nmr spectra of each pair were identical.

Anal. Calcd. for 9 C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>S<sub>4</sub>: C, 51.99; H, 2.91; N, 8.08; S, 37.01. Found: C, 52.14; H, 2.96; N, 8.01; S, 36.81.

Anal. Calcd. for 10 C<sub>15</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub>: C, 57.31; H, 3.21; N, 8.91; S, 20.40. Found: C, 57.34; H, 3.23; N, 8.91; S, 20.47.

2-Oxo-3-benzothiazolineacetonitrile (11). Method 1.

A stirred slurry containing 20 g (0.1 mole) of 7, 7.2 g (0.11 mole) of potassium cyanide and 150 ml of acetone, dimethylformamide or acetonitrile was heated at the temperature specified in Table 3 for 24 hours. After cooling to 5°, 800 g of ice water was added and stirring continued at 0-10° for 1 hour. The solid was collected by filtration, washed with water until neutral to litmus and air-dried at 25-30°. The data are summarized in Table 3.

Conventional Method.

The reaction of 2-benzothiazoline, 85% potassium hydroxide and chloroacetonitrile in refluxing acetone furnished 11, mp 134-135°, in 95% yield [6]. A mixture melting point with 11 obtained by method 1 was not depressed and the nmr spectra of the two samples were identical.

2-Thioxo-(3H)-benzothiazole-3-acetic acid (12). Method A.

A stirred slurry containing 10.3 g (0.05 mole) of 8 and 150 ml of 30% sulfuric acid (by volume) was heated at reflux for 2 hours. After cooling to 25°, 800 g of ice water was added and stirring continued at 25-30° for 30 minutes. The solid was collected by filtration, washed with water until neutral to litmus and air-dried at 25-30°. The crude 12, mp 187-189°, was obtained in 90% yield. After recrystallization from 1,2-dichloroethane it melted at 192-193°; nmr (deuteriodimethylsulfoxide):  $\delta$  5.15 (s, 2, -NCH<sub>2</sub>CO<sub>2</sub>), 6.00 (s, 1, -COOH), 7.02-7.80 (m, 4, ArH).

Anal. Calcd. for C<sub>9</sub>H<sub>8</sub>NO<sub>2</sub>S<sub>2</sub>: C, 47.98; H, 3.13; N, 6.22; S, 28.46. Found: C, 47.73; H, 3.16; N, 6.30; S, 28.57.

Method B.

Compound 12, mp 192-193°, was obtained in 36% yield by the procedure described by Chen [7]. A mixture melting point with 12 obtained by Method A was not depressed and the nmr spectra of the two samples were identical.

## REFERENCES AND NOTES

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