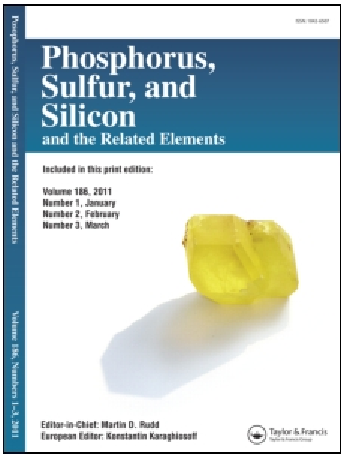

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John J. D'amico[a]; Frederic G. Bollinger[a]; William E. Dahl[a]
[a] Research Department, Monsanto Agricultural Products Company, St. Louis, Missouri

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A NEW ROUTE TO 2H-(1,2,4)TRIAZINO(3,4b)BENZOTHIAZOLE-3(4H)-ONE[1] (4)

JOHN J. D'AMICO, FREDERIC G. BOLLINGER and WILLIAM E. DAHL

Monsanto Agricultural Products Company, Research Department, 800 N. Lindbergh Boulevard, St. Louis, Missouri 63167

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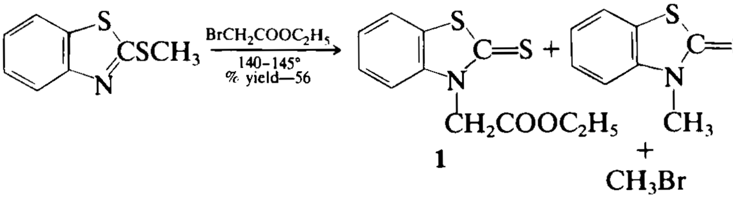
The reaction of 3-(carbethoxymethyl)benzothiazoline-2-thione (**1**) with excess hydrazine in an aqueous medium at 25–30° or 95–100°C afforded the hydrazide (**3**) in 99% yield and the titled heterocyclic compound (**4**) in 63% yield, respectively. Under the same reaction conditions and replacing the above electrophile with 3-(carbethoxymethyl)-2-benzothiazoline furnished the hydrazide (**5**) in 45% yield and a 6% yield of **5** plus a high yield of a resinous mixture, respectively. Possible mechanism and supporting NMR and mass spectral data are discussed.

The synthesis of fused rings containing the benzothiazolyl and benzimidazolyl or other heterocyclic moieties received comparatively little attention until 1948 when several publications appeared.[2–8]

In this communication we wish to report a new route to 2H-(1,2,4)triazino(3,4b)benzothiazole-3(4H)-one (**4**).

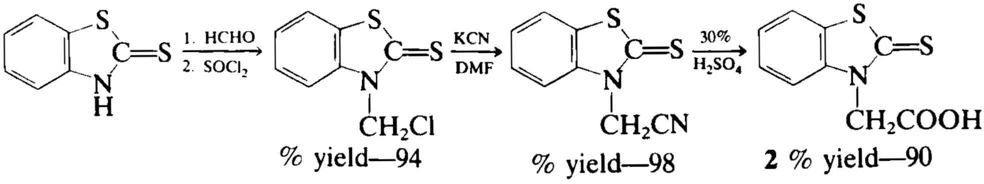
The key intermediate 3-(carbethoxymethyl)-benzothiazoline-2-thione (**1**) was first prepared by Chen[9] by the reaction of 2-(methylthio)benzothiazole with ethyl bromoacetate at 140–145°C.

Method A



(1)

Recently, we reported[10] the synthesis of 2-thioxo-3(3H)-benzothiazoline-3-acetic acid (**2**) in an overall yield of 83% by the following reactions:



(2)

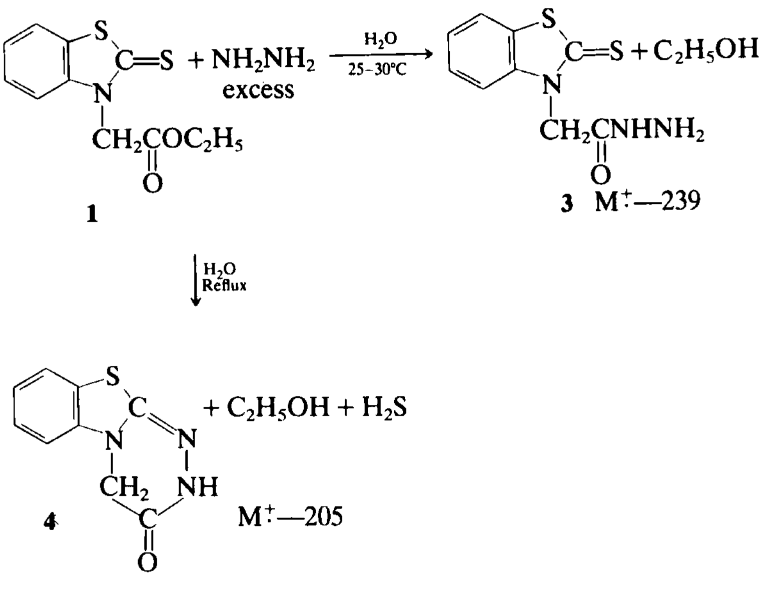
The treatment of **2** with ethanol and boron trifluoride ether complex provided a new route to **1** in 94% yield.

Method B

$$\mathbf{2} + C_2H_5OH \xrightarrow{BF_3\cdot O(C_2H_5)_2} \mathbf{1} \quad \%\ \text{yield—94} \qquad (3)$$

A mixture melting point of **1** derived by methods *A* and *B* (reactions 1 and 3) was not depressed and nmr spectra of samples from both methods were identical.

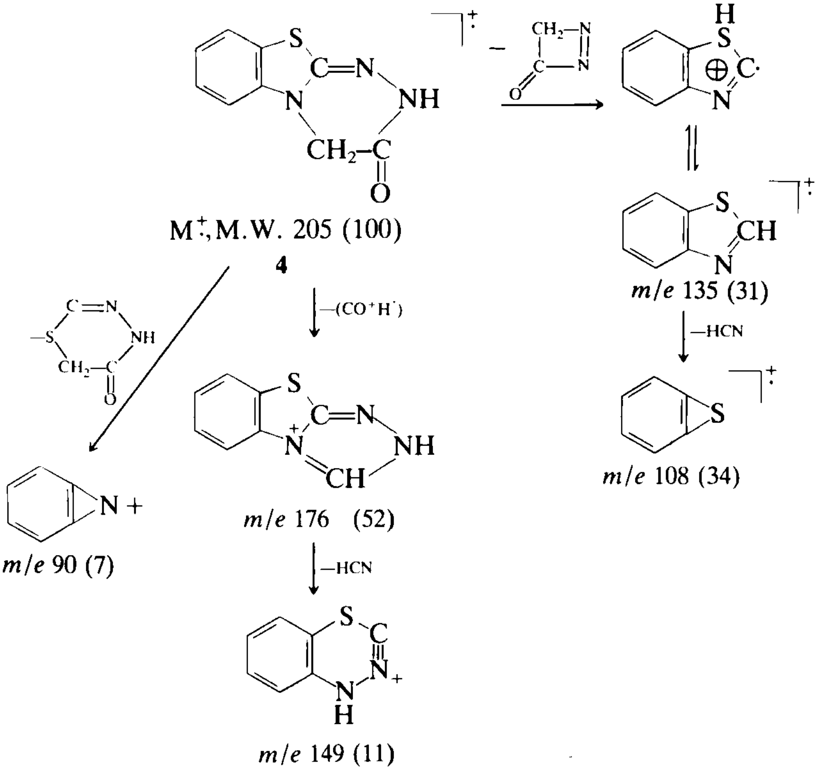
The reaction of **1** with excess hydrazine in an aqueous medium at 25–30°C for several days afforded 2-thioxo-(3H)-benzothiazoline-3-acetic acid hydrazide (**3**) in 99% yield. However, heating the same reactants in the same solvent at reflux for 3 hours furnished a new route to **4**.



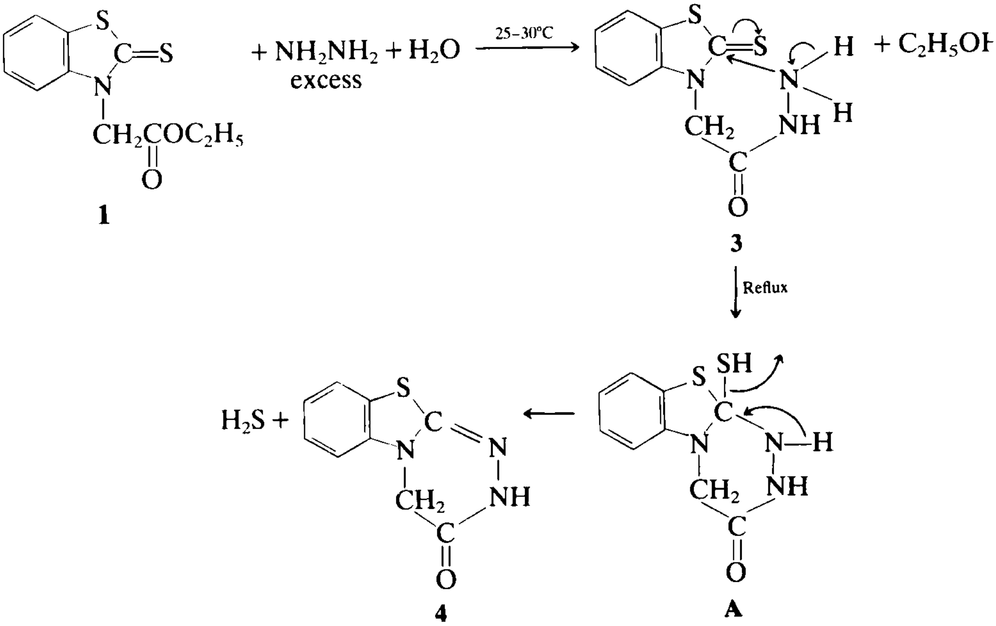
(4)

The analysis, NMR and mass spectral data were in complete agreement for the proposed structures **3** and **4**. The electron impact and isobutane chemical ionization mass spectra for **4** furnished the molecular weight data in the form of M^{+} 205 and $(M + 1)^{+}$ 206, respectively. Furthermore, the fragmentation pathway of **4** (SCHEME 1) is consistent with the proposed structure **4**. The proposed mechanism for reaction 4 is depicted in SCHEME 2. Evidence for the liberation of hydrogen sulfide in reaction 4 was obtained by the formation of lead sulfide when the gas was allowed to bubble through an aqueous solution of lead acetate. The identification of liberated hydrogen sulfide lends support for the proposed mechanism.

However, **4** was first synthesized by Allen and Van Allen[2] in 1948 by the

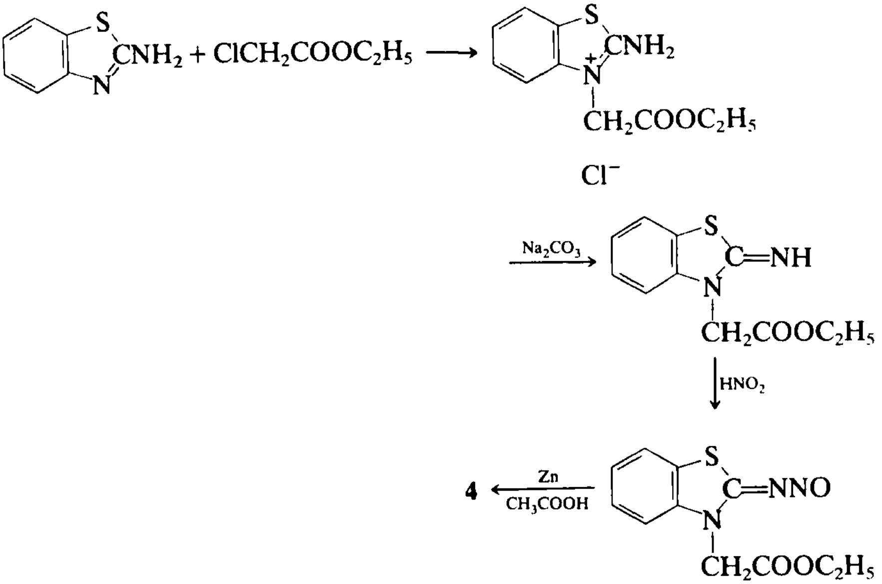


SCHEME 1



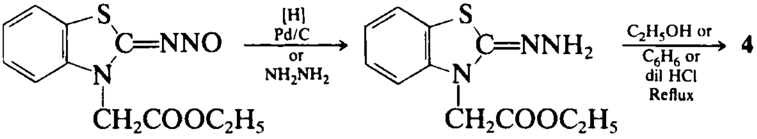
SCHEME 2

following route:

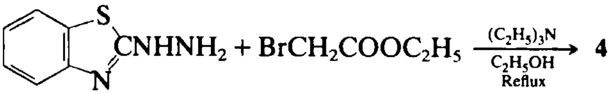


(5)

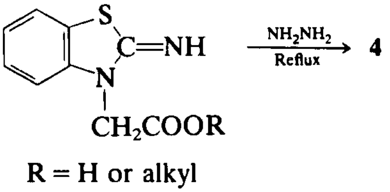
In 1968 Paolini[6] reported the following additional methods for the synthesis of **4**.



(6)

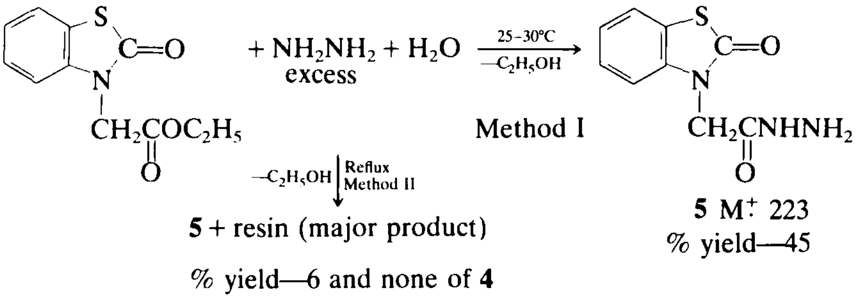


(7)



(8)

It was anticipated that the reaction of 3-(carbethoxymethyl)-2-benzothiazoline[11] with excess hydrazine in refluxing water would have afforded another route to **4**. However, this was not the case for, under reflux temperatures, a very low yield (6%) of 2-oxo-(3H)benzothiazoline-3-acetic acid hydrazide (**5**)[12] and a high yield of a resinous mixture were obtained. It has been reported that under some conditions, resins are obtained in place of a simple hydrazide.[13] The same reaction at 25–30°C afforded **5** in 45% yield free of the resin.



(6)

Proof of structure for **5** was based on analysis, NMR and mass spectral data.

EXPERIMENTAL SECTION

NMR spectra were obtained with a Varian T-60 NMR spectrometer. The chemical shifts are reported in δ, using tetramethyl-silane as reference. All melting points were taken upon a Fisher–Johns block and are uncorrected. The electron impact mass spectra were determined with a Varian-MAT CH-7A mass spectrometer operating at an ionizing potential of 70 eV using the direct insertion probe technique with a source temperature of 250°C. This instrument was operated in the CIMS mode to obtain the chemical ionization mass spectrum for **4**.

3-(Carbethoxymethyl)benzothiazoline-2-thione (**1**)

Method A—**1** was prepared in 56% yield according to the procedure described by Chen.[9]

Method B—To a stirred solution containing 45.2 g (0.2 mol) of **2**[10] in 600 mL of ethanol, 142 g (1.0 mol) of boron trifluoride ether complex was added in one portion. An exothermic reaction set in causing a temperature rise from 22 to 40°. The stirred solution was heated at reflux for 24 hours and then cooled to 0°. After cooling, 1400 mL of 10% aqueous sodium bicarbonate was slowly added (foaming) at 0–10° until pH 8 was obtained. After stirring at 0–10° for 1 hour, the solid was collected by filtration, washed with water until neutral and air-dried at 25–30°. **1**, m.p. 99–100°, was obtained in 94% yield. After recrystallization from ethnaol **1** melted at 101–102°; NMR ($CDCl_3$) δ 1.30 (t, 3, —$CH_2\underline{CH_3}$); 4.25 (q, 2, —$\underline{CH_2}CH_3$); 5.20 (s, 2, —NCH_2); 7.02–7.79 (m, 4, ArH).

Anal. Calcd for $C_{11}H_{11}NO_2S_2$: C, 52.15; H, 4.38; N, 5.53; S, 25.31. Found: C, 51.98; H, 4.39; N, 5.52; S, 25.50. A mixture melting point with **1** obtained by method *A* was not depressed and the nmr spectra of the two samples were identical.

2-Thioxo-(3H)-benzothiazoline-3-acetic acid hydrazide (**3**). A stirred charge containing 38 g (0.15 mol) of 3-(carbethoxymethyl)benzothiazoline-2-thione (**1**), 33.8 g (1.0 mol) of 95% hydrazine and 300 mL of water was stirred at 25–30° for 6 days. After the addition of 1 liter of water, stirring was continued at 25–30° for 10 minutes. The solid was collected by filtration, washed with 500 mL of water and air-dried at 25–30°. Crude **3**, m.p. 214–5°, was obtained in 99% yield. After recrystallization from methanol **3** melted at 222–3°; NMR ($Me_2SO\text{-}d_6$) δ 4.15 (s, 2, —$NH\underline{NH_2}$); 5.05 (s, 2, —NCH_2CO—); 7.05–7.85 (m, 4, ArH); 9.35 (s, 1, —CONH—). Electron impact mass spectrum m/e (rel. intensity) 239 (17) M^{+} 208 (100), 180 (82), 167 (9), 148 (9) 136 (39), 109 (14), and 77 (33).

Anal. Calcd for $C_9H_9N_3OS_2$: C, 45.17; H, 3.79; N, 17.56; S, 26.80. Found: C, 45.20; H, 3.80; N, 17.55; S, 26.76.

2H-(1,2,4)Triazino(3,4-b)benzothiazol-3 (4H)-one (**4**). A stirred charge containing 17.8 g (0.07 mol) of 3-(carbethoxymethyl) benzothiazoline-2-thione, **1**, 33.8 g (1.0 mol) of 95% hydrazine and 100 mL of water was heated at reflux for 3 hours and thereafter at 25–30°C for 24 hours. After the addition of 500 mL of water stirring was continued at 25–30°C for 10 minutes. The solid was collected by filtration, washed with 300 mL of water and air-dried at 25–30°C. Crude **4**, m.p. 259–60°C, was obtained in 63% yield. The melting point of **4** remained unchanged after recrystallization from dimethylformamide; a mixture melting point with an authentic sample[6] was not depressed. NMR ($Me_2SO\text{-}d_6$) δ 4.30 (s, 2, —NCH_2CO—), 6.65–7.60 (m, 4, ArH); 10.60 (br s, 1, —CONH—). Electron impact mass spectrum m/e (rel intensity) 205 (100) M^{+}, 176 (52), 149 (11), 135 (31), 108 (34) and 90 (7); isobutane chemical isoization mass spectrum m/e 206 $(M + 1)^{+}$.

Anal. Calcd for $C_9H_7N_3OS$; C, 52.67; H, 3.44; N, 20.47; S, 15.62. Found: C, 52.64; H, 3.44; N, 20.48; S, 15.58.

2-Oxo-(3H)-benzothiazoline-3-acetic acid hydrazide (**5**)
Method I (25–30°C)—A stirred charge containing 11.9 g (0.05 mol) of 3-(carbethoxymethyl)-2-benzothiazoline,[11] 33.8 g (1.0 mol) of 95% hydrazine and 100 mL of water was stirred at 25–30°C for six days. After the addition of 500 mL of water, stirring was continued at 25–30°C for 10 minutes. The solid was collected by filtration, washed with 200 mL of water and air-dried at 25–30°C. Crude **5**, mp 211–2°C, was obtained in 45% yield. After recrystallization from acetonitrile, **5** melted at 213–4°C; NMR (Me_2SO-d_6) δ 4.28 (s, 2, —$NH\underline{NH_2}$); 4.53 (s, 2, —NCH_2CO—); 7.0–7.8 (m, 4, ArH); 9.45 (s, 1, —CONH—). Electron impact mass spectrum m/e (rel intensity) 223 (22) M^{+}, 192 (48), 164 (52), 136 (100), 109 (50), 82 (6), 77 (11) and 69 (24).

Anal. Calcd for $C_9H_9N_3O_2S$: C, 48.42; H, 4.06; N, 18.82; S, 14.36. Found: C, 48.34; H, 4.05; N, 18.83; S, 14.27.

Method II—The charge and procedure were identical as in method I except the stirred reactants were heated at reflux for 3 hours and thereafter at 25–30°C for 24 hours. After the addition of 500 mL of water stirring was continued at 25–30°C for 3 hours. Since none of the expected precipitate formed, most of the water and excess hydrazine were removed *in vacuo* at a maximum temperature of 50°C at 10–12 mm. The resinous residue was extracted twice with 100 mL of toluene in order to remove more water. Final traces of water were removed by heating the glassy residue (24.1 g) *in vacuo* at a maximum temperature of 50°C at 1–2 mm. The cooled resinous mixture (17.4 g) was covered with 100 mL of ethyl ether and 100 mL of ethyl acetate and allowed to stand overnight in a sealed flask. Two crops of solids were isolated by filtration. The first crop, an impurity, was discarded. Upon evaporation of some of the solvents during filtration a second crop appeared. Recrystallization of crop 2 from ethyl alcohol furnished **5**, mp 211–2°C, in 6% yield. A mixture melting point with **5** obtained from method I was not depressed and the NMR spectra of the two were identical. The residue (12.5 g) was again heated *in vacuo* at a maximum temperature of 50°C at 1–2 mm. Upon standing the amber viscous oil (10.4 g) decomposed with the evolution of gases to give a resinous mixture which was insoluble in water, ethyl ether, heptane, chloroform and ethyl acetate.

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