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A Simple New Synthesis of Thiobisamines[1]

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N,*N*′-Thiobisamines, R_2NSNR_2 (1), are an interesting class of compounds that have found use both in the vulcanization of rubber[2] and in certain synthetic sequences in organic sulfur chemistry.[3,4]

Several methods have been used to prepare thiobisamines. The classical method is reaction of an amine with sulfur dichloride.[5] A variant using $R_2NSi(CH_3)_3$ in place of the amine is reported[6] to give significantly better yields of 1. A second general route[7] to thiobisamines from amines utilizes *N*,*N*′-thiobisphthalimide[8] as the source of the sulfur.

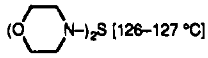
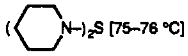
We now report a third method for preparation of thiobisamines that has the virtue of unusual simplicity in terms of reagents required and experimental procedure and affords 1 in good yield. We find that when bromine is added to a stirred suspension of sodium thiosulfate and a solution of the amine in either methylene chloride, pentane, or hexane the reaction shown in eq 1 takes place, and after

$$6R_2NH + Na_2S_2O_3{\cdot}5H_2O + 2Br_2 \xrightarrow{5\text{–}10\ {}^\circ C} \underset{1}{R_2NSNR_2} + Na_2SO_4 + 4R_2NH_2{}^+Br^- \quad (1)$$

filtration to remove sodium sulfate and the amine hydrobromide, evaporation of the reaction solvent affords the thiobisamine. Table I summarizes the experimental results with different amines.

Initially, we assumed that formation of 1 took place by oxidation of thiosulfate to tetrathionate by bromine ($2S_2O_3{}^{2-} + Br_2 \rightarrow S_4O_6{}^{2-} + 2Br^-$) followed by nucleophilic attack of the amine on a dicoordinate sulfur in tetrathionate[9] ($R_2NH + S_4O_6{}^{2-} \rightarrow R_2NSSO_3{}^- + S_2O_3{}^{2-} + H^+$) and reaction of a second mole of amine with $R_2NSSO_3{}^-$ ($R_2NH + R_2NSSO_3{}^- \rightarrow R_2NSNR_2 + HSO_3{}^-$). However, the fact that stirring a suspension of sodium tetrathionate ($Na_2S_4O_6{\cdot}2H_2O$) with a solution of the amine in either pentane or CH_2Cl_2 led to the formation of 1 in only very low (5–10%) yield suggests this is *not* the operative pathway. So too does the fact that addition of bromine to a stirred suspension of sodium thiosulfate and only the solvent is not accompanied by prompt discharge of the bromine color (in contrast to the behavior when the amine is also present).

Table I. Formation of *N*,*N*′-Thiobisamines by Reaction of Amines with Sodium Thiosulfate and Bromine[a]

amine	solvent	product [mp] or (bp)	yield[b] (%)
morpholine	CH_2Cl_2	 [126–127 °C]	83
piperidine	hexane	 [75–76 °C]	62
Et_2NH	hexane	$(Et_2N)_2S$ (80–81 °C (11 mm))	61
Me_2NH	pentane	$(Me_2N)_2S$ (58 °C (55 mm))	67

[a] Reaction carried out by adding bromine to a stirred suspension of sodium thiosulfate and a solution of the amine in the solvent indicated. [b] Yields are for pure 1 after recrystallization or distillation. Yields of 1 before purification were 90–100%.

For that reason we believe the most likely route for the formation of 1 in eq 1 is the sequence of reactions shown in eq 2. In eq 2 the amine is first oxidized to the *N*-

$$2R_2NH + Br_2 \rightarrow R_2NBr + R_2NH_2{}^+Br^- \quad (2a)$$

$$R_2NBr + S_2O_3{}^{2-} \rightarrow R_2NSSO_3{}^- + Br^- \quad (2b)$$

$$R_2NH + R_2NSSO_3{}^- \rightarrow R_2NSNR_2 + H^+ + SO_3{}^{2-} \quad (2c)$$

$$HSO_3{}^- + Br_2 + H_2O \rightarrow HSO_4{}^- + 2H^+ + 2Br^- \quad (2d)$$

bromoamine (R_2NBr),[10] which then reacts with thiosulfate (eq 2b) to give $R_2NSSO_3{}^-$. Whether this reaction occurs by nucleophilic displacement at N by $S_2O_3{}^{2-}$, or alternatively, by a displacement at the halogen to afford $BrSSO_3{}^-$ ($R_2NH_2{}^+ + R_2NBr + S_2O_3{}^{2-} \rightarrow R_2NH + R_2NH + BrSSO_3{}^-$) followed by reaction of $BrSSO_3{}^-$ with the amine ($R_2NH + BrSSO_3{}^- \rightarrow R_2NSSO_3{}^- + Br^-$) is not certain, given the varying claims in the literature regarding the course of nucleophilic displacement reactions of *N*-haloamines.[11,12] Once formed, $R_2NSSO_3{}^-$ reacts (eq 2c) with amine to give 1 and sulfite ion. In the final step (eq 2d), sulfite is oxidized to sulfate by a second mole of bromine. The molecule of water needed for eq 2d is furnished by the water of hydration present in $Na_2S_2O_3{\cdot}5H_2O$.

The simplicity of procedure and reagents make eq 1 a good method to prepare a thiobisamine. Yields are comparable to those obtained (50–88%) in the other procedures[6,7] mentioned earlier.

A number of oxidizing agents were tried as possible substitutes for bromine. None of compound 1 was formed with sodium bromate, sodium iodate, sodium persulfate, or hydrogen peroxide. However, when sodium periodate was used with morpholine in a two-phase system (water–methylene chloride) 1 was formed in moderate yield (47%). In this case we believe that the first step is the oxidation of thiosulfate to tetrathionate in the aqueous phase by periodate, followed by reaction of morpholine with tetrathionate, also in the aqueous phase, since when tetrathionate was allowed to react with morpholine in the same two-phase system 1 was formed in 75% yield. The two-phase solvent system is less convenient to use than the procedure employing bromine and either hexane or methylene chloride. It is also not applicable for the synthesis of Et_2NSNEt_2 or Me_2SNSMe_2, since these two

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thiobisamines are more sensitive to the presence of water than the thiobisamine from morpholine.

Experimental Section

Preparation of 1 from Bromine, Thiosulfate, and an Amine. With piperidine or morpholine, a solution of 3.2 g (20 mmol) of bromine in 10 mL of methylene chloride (or hexane) was added slowly at 5–10 °C to a stirred suspension of 2.48 g (10 mmol) of sodium thiosulfate pentahydrate in a solution containing 75 mmol of the amine in 50 mL of CH_2Cl_2 (or hexane). In the case of diethylamine or dimethylamine, where the product thiobisamines are liquids rather than solids, the reaction was carried out using the same procedure, but on a larger scale: 16.0 g (100 mmol) of bromine in 50 mL of solvent; 12.4 g (50 mmol) of $Na_2S_2O_3 \cdot 5H_2O$; and ~350 mmol of amine in 500 mL of solvent. The reaction mixture was allowed to warm to room temperature, stirred for several hours, and filtered (removing the sodium sulfate and amine hydrobromide that had separated), and the organic solvent was evaporated under reduced pressure to leave crude thiobisamine. This material was then purified as outlined below.

4,4′-Thiobismorpholine (1a). Recrystallization of the residue from methanol gave 1.7 g (83%) of **1a**, mp 126–127 °C (lit.[13] mp 125–126 °C); ^1H NMR ($CDCl_3$) δ 3.64 (m, 8 H), 3.28 (m, 8 H).

Thiobispiperidine (1b). Recrystallization from methanol gave 1.25 g (62%) of **1b**, mp 75–76 °C (lit.[5b] mp 74 °C, lit.[14] mp 76–77 °C); ^1H NMR ($CDCl_3$) δ 3.26 (m, 8 H), 1.53 (m, 12 H).

Thiobis(diethylamine) (1c). Distillation of the residue under reduced pressure gave 5.32 g (61%) of **1c** as a colorless liquid, bp 80–81 °C (11 mm) (lit.[5a] bp 87–87.5 °C (19 mm), lit.[15] bp 39–40 °C (4 mm); ^1H NMR ($CDCl_3$) δ 3.06 (q, J = 7 Hz, 8 H), 1.14 (t, J = 7 Hz, 12 H).

Thiobis(dimethylamine) (1d). Distillation of the residue under reduced pressure gave 4.02 g (67%) of **1d** (bp 58 °C (55 mm)) as a colorless liquid that crystallized on cooling to a low-melting solid, mp 20–23 °C (lit.[13] mp 20 °C, lit.[14] mp 22–23 °C); ^1H NMR ($CDCl_3$) δ 3.01 (s).

Reaction of Morpholine with Sodium Tetrathionate. In Methylene Chloride. Sodium tetrathionate dihydrate (3.06 g, 10 mmol) was added to a solution of 4.36 g (50 mmol) of morpholine in 50 mL of CH_2Cl_2, and the suspension was stirred for 6 h at room temperature. The mixture was filtered, and the CH_2Cl_2 was removed under reduced pressure. To the residue, which was a colorless oil, was added 15 mL of pentane, and the 4,4′-thiobismorpholine (**1a**) that precipitated was filtered off and washed with a little pentane to give 0.23 g (11%) of **1a**, mp 126 °C.

In Water–Methylene Chloride. Sodium tetrathionate (3.06 g, 10 mmol) in 20 mL of water and 3.48 g (40 mmol) of morpholine in 20 mL of CH_2Cl_2 were stirred for 6 h at room temperature. The organic layer was dried, and the solvent was evaporated. Recrystallization of the residue from methanol gave 1.53 g (75%) of **1a**, mp 127 °C.

Formation of 1a Using Sodium Periodate as the Oxidizing Agent. A solution of sodium periodate (4.26 g, 20 mmol) in 10 mL of water was added slowly to a stirred mixture of 2.48 g (10 mmol) of sodium thiosulfate pentahydrate, 0.2 g (0.54 mmol) of tetrabutylammonium iodide in 15 mL of water, and 2.0 g (23 mmol) of morpholine in 30 mL of CH_2Cl_2. The reaction mixture was stirred for 8 h at room temperature. The mixture was then filtered, and the CH_2Cl_2 layer was dried (Na_2SO_4) and evaporated under reduced pressure to give a crystalline residue that was washed with a little pentane (to remove excess morpholine) and then recrystallized from methanol giving 0.96 g (47%) of **1a**, mp 124–126 °C.

Registry No. 1a, 5038-11-9; **1b**, 25116-80-7; **1c**, 3768-61-4; **1d**, 2129-20-6; Et_2NH, 109-89-7; Me_2NH, 124-40-3; morpholine, 110-91-8; piperidine, 110-89-4; bromine, 7726-95-6; sodium thiosulfate, 7772-98-7; sodium tetrathionate, 10101-86-7; sodium periodate, 7790-28-5.

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Additions and Corrections

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Eietsu Hasegawa,* Kenyuki Ishiyama, Takaaki Horaguchi, and Takahachi Shimizu. Exploratory Study on Photoinduced Single Electron Transfer Reactions of α,β-Epoxy Ketones with Amines.

Page 1632, Scheme I. ICS should be ISC.

Page 1632, ref 16a. ΔG values should be −13 to −14 kcal/mol.

Page 1632, ref 17. The scan rate of cyclic voltammetry should be 200 mV/s.

Page 1634, ref 28. The last sentence should read "When excess TEA is present in the reaction solution, BDMAP$^{\bullet+}$ could be reduced to BDMAP by SET from TEA although this process is somewhat endothermic."

James A. Marshall* and William J. DuBay. A Novel Synthesis of Furans by Base-Catalyzed Isomerization of Alkynyloxiranes.

Page 1685. A highly relevant paper by Arens and co-workers (Rompers, J. A.; Hoff, S.; Montijn, P. P.; Brandsma, L.; Arens, J. R. *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 1445) describing the base-catalyzed conversion of 2-methoxy-2,3,4-pentatrienols to furans should be included with ref 3. We thank Professor R. L. Danheiser (MIT) for calling this paper to our attention.