A Simple New Synthesis of Thiobisamines

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N,N'-Thiobisamines, R2NSNR2 (1), are an interesting class of compounds that have found use both in the vulcanization of rubber and in certain synthetic sequences in organic sulfur chemistry. Several methods have been used to prepare thiobisamines. The classical method is reaction of an amine with sulfur dichloride. A variant using R2NSi(CH3)3 in place of the amine is reported to give significantly better yields of 1. A second general route to thiobisamines from amines utilizes N,N'-thiobisphthalimides 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 the solvent the reaction solvent affords 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 tetraiodionate by bromine (2S2O32- + Br2 → S4O62- + 2Br-) followed by nucleophilic attack of the amine on a diconordinate sulfur in tetraiodionate (R2NH + S4O62- → R2NSSO3- + S4O62- + H+) and reaction of a second mole of amine with R2NSSO3- (R2NH + R2NSSO3- → R2NSNR2 + HSO3-). However, the fact that stirring a suspension of sodium tetrathiionate (Na2S2O3·2H2O) with a solution of the amine in either pentane or CH2Cl2 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).

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-2R2NH + Br2 → R2NBr + R2NH2+Br- (2a)

R2NBr + S2O32- → R2NSSO3- + Br- (2b)

R2NH + R2NSSO3- → R2NSNR2 + H+ + SO32- (2c)

bromoamine (R2NBr), which then reacts with thiosulfate (eq 2b) to give R2NSSO3-. Whether this reaction occurs by nucleophlic displacement at N by S2O32-, or alternatively, by a displacement at the halogen to afford BrSSO3- (R2NH2+Br- + S2O32- → R2NBr + S2O32- + R2NH + Br2) followed by reaction of BrSSO3- with the amine (R2NH + BrSSO3- → R2NSSO3- + Br-) is not certain, given the varying claims in the literature regarding the course of nucleophile displacement reactions of N-haloamines. Once formed, R2NSSO3- 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 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 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 tetraiodionate in the aqueous phase by periodate, followed by reaction of morpholine with tetraiodionate, also in the aqueous phase, when tetraiodionate 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 Et4NSN3 or Me8NSNMe8, since these two

Table I. Formation of N,N'-Thiobisamines by Reaction of Amines with Sodium Thiosulfate and Bromine*

<table>
<thead>
<tr>
<th>amine</th>
<th>solvent</th>
<th>product [mp or (bp)]</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>morpholine</td>
<td>CH2Cl2</td>
<td>4R2NSSO3-</td>
<td>83</td>
</tr>
<tr>
<td>piperidine</td>
<td>hexane</td>
<td>4R2NSSO3-</td>
<td>62</td>
</tr>
<tr>
<td>Et4NH</td>
<td>hexane (Et4N)S</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Me2NH</td>
<td>pentane (Me2N)S</td>
<td>67</td>
<td></td>
</tr>
</tbody>
</table>

*Reaction carried out by adding bromine to a stirred suspension of sodium thiosulfate and a solution of the amine in the solvent indicated. **Yields are for pure 1 after recrystallization or distillation. Yields of 1 before purification were 50-100%.

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(9) Foss, O. Acta Chem. Scand. 1968, 12, 969.

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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 CH₂Cl₂ (or hexane). In the case of diethylamine or dimethylamine, where the product thiobisamine is a colorless liquid that crystallized on cooling to a low-melting solid, mp 20–23 °C (lit.13 mp 20–23 °C, lit.14 mp 22–23 °C); 1H NMR (CDCl₃) δ 3.01 (s).

Reactions of Morpholine with Sodium Tetrathionate. 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 CH₂Cl₂, and the suspension was stirred for 6 h at room temperature. The mixture was filtered, and the CH₂Cl₂ 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 CH₂Cl₂ 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.

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 (CDCl₃) δ 3.64 (m, 8 H), 3.28 (m, 8 H). Thiobis(piperidine) (1b). Recrystallization from methanol gave 1.25 g (62%) of 1b, mp 75–76 °C (lit.14 mp 74 °C, lit.15 mp 75–77 °C); 1H NMR (CDCl₃) δ 3.26 (m, 8 H), 1.53 (m, 12 H).

Thiobis(dimethylamine) (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.16 bp 87–87.5 °C (19 mm), lit.17 bp 39–40 °C (4 mm); 1H NMR (CDCl₃) δ 3.06 (q, J = 7 Hz, 8 H), 1.14 (t, J = 7 Hz, 12 H).

Additions and Corrections

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Page 5034, 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** could be reduced to BDMAP by SET from TBA although this process is somewhat endothermic.”


Page 1895. A highly relevant paper by Arens and co-workers (Rompera, J. A.; Hoff, S.; Montijn, P. P.; Brandsma, L.; Arens, J. R. Récl. 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.