Synthesis and Reaction of Triaminosulfoxonium Salts

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Synopsis. Triaminosulfoxonium salts were synthesized by the oxidation of triaminosulfonium salts with sodium perbenzoate. The reaction of these salts with nucleophiles was carried out.

Heteroatom substituted sulfoxonium salts are interesting compounds for their anomalous reactivity.[1] Monoaminosulfoxonium salts were prepared by Johnson and Schroek, which acted as good methylene transfer agents.[2] Previously, we synthesized diaminosulfoxonium salts and examined their reactivities.[3] However, to our knowledge, there is no report on the synthesis of triaminosulfoxonium salts (CA Index name; (triamide)-oxosulfur(1+) salts). Recently, we proposed an excellent method for the preparation of sulfoxonium salts from the corresponding sulfonium salts.[4] We also described the general synthesis of triaminosulfonium salts (**1**) by the reaction of thiobisamines with *N*-chlorobenzotriazole followed by the addition of secondary amines.[5] These findings prompted us to investigate the direct formation of triaminosulfoxonium salts (**2**) from **1** by oxidation reaction. In this paper, we would like to report a convenient synthesis of **2**.

Results and Discussion

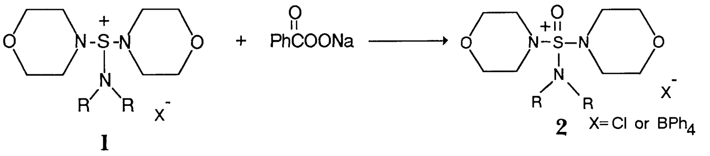
Triaminosulfonium salts were prepared from 4,4′-thiodimorpholine with *N*-chlorobenzotriazole followed by the addition of secondary amines as mentioned before.[5] Treatment of trimorpholinosulfonium chlorides (CA Index name; tris(morpholino-N^4)sulfur(1+) chloride) with 3 equiv of sodium perbenzoate in water afforded a pale yellow solution of trimorpholinosulfoxonium chloride (**2a**). Other triaminosulfonium chlorides (**1b**—**f**) were also oxidized under similar conditions. The triaminosulfoxonium chlorides obtained from **1b**—**f** were very hygroscopic, which were, therefore, isolated by transferring into the corresponding tetraphenylborates (**2b**—**f**). These results are summarized in Table 1. When equal amount of sodium perbenzoate was used, only 30 % of **1** were oxidized. Generally, more than 3 equiv of perbenzoate was required for improving the yields of **2**. However, dimethylaminodimorpholinosulfonium chloride (**1g**) could not be oxidized under these conditions. Even if 10 equiv of sodium perbenzoate was used, **1g** could not be oxidized. It is interesting that relatively hindered sulfonium salts (**1a**, **1b**, and **1e**) could be easily oxidized under these conditions.

The ^{1}H NMR spectra of **2** clearly show that sulfur bears a high degree of positive charge which significantly deshields the *N*-methylene protons, thereby shifting the signals downfield to 3.5 ppm around. The *N*-methylene protons of ethyldimorpholinosulfonium tetrafluoroborate were observed at 3.2 ppm.[6] The downfield shift of *N*-methylene protons is characteristic of triaminosulfoxonium salts compared to triaminosulfonium salts. The ^{13}C NMR spectrum of **2c** also shows that the *N*-methylene carbons are shifted to downfields (**1c**; 46.4 and 49.3 ppm→**2c**; 46.9 and 49.8 ppm).

Previously, Noyori and co-workers reported the formation and reaction of tris(diethylamino)sulfonium difluorotrimethylsiliconate with enol silyl ethers to give the corresponding sulfonium enolates and which

Table 1. Preparation of Aminodimorpholinosulfoxonium Salts (**2**)

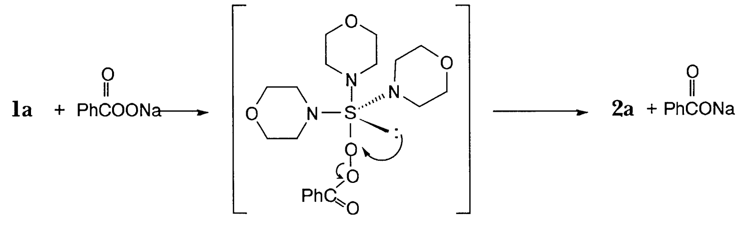
Aminodimorpholinosulfonium Salt **1**		Aminodimorpholinosulfoxonium Salt **2**			
		2	Yield/%	X$^-$	Mp/°C
1a	R,R=$-CH_2CH_2OCH_2CH_2-$	**2a**	63	Cl	91—93
1b	R,R=$-CH_2(CH_2)_3CH_2-$	**2b**	66	BPh_4	212—213
1c	R,R=$-CH_2(CH_2)_2CH_2-$	**2c**	58	BPh_4	196—197
1d	R,R=Et	**2d**	54	BPh_4	185—186
1e	R,R=$(CH_3)_2CH-$	**2e**	58	BPh_4	185—187



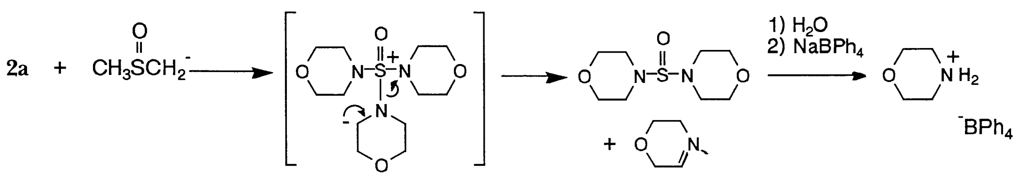
Scheme 1.

Table 2. NMR Methylene Signals of Salts **1** and **2**

	Sulfonium Salt **1**				Sulfoxonium Salt **2**		
	Solvent	*N*-CH_2	*O*-CH_2		Solvent	*N*-CH_2	*O*-CH_2
1a	D_2O	3.16—3.42	3.63—3.90	**2a**	D_2O	3.37—3.61	3.67—3.88
1a	CD_3COCD_3	3.25—3.49	3.63—3.90	**2a**	CD_3COCD_3	3.60—3.80	3.80—4.00
1a	CD_3SOCD_3	3.20—3.49	3.60—3.87	**2a**	CD_3SOCD_3	3.48—3.55	3.73—3.80
1b	CD_3SOCD_3	3.13—3.35	3.65—3.74	**2b**	CD_3SOCD_3	3.45—3.54	3.72—3.80
1c	CD_3SOCD_3	3.20—3.44	3.62—3.74	**2c**	CD_3SOCD_3	3.50—3.58	3.70—3.77
1d	CD_3SOCD_3	3.10—3.23	3.66—3.78	**2d**	CD_3SOCD_3	3.40—3.52	3.67—3.80



Scheme 2.



Scheme 3.

did not form covalent sulfuranes.[7] In contrast to their results, we found that triaminosulfonium salts were easily oxidized by attack of the perbenzoate anion. The difference in the reactivity might be owing to the leaving ability of the benzoate anion. The oxidation of sulfonium salt with sodium perbenzoate in aqueous solution may proceed via an S-O sulfurane intermediate to afford a sulfoxonium salt by nucleophilic attack of perbenzoate anion on the cationic sulfur atom of the sulfonium salt as show in Sheme 2.

Then, we studied the reactivity of these sulfoxonium salts. We first tried the reaction of sulfoxonium chloride **2a** with 1-cyclohexenyl silyl ether in THF. However, no reaction was observed and **2a** was recovered almost quantitatively. The reaction of **2a** with other nucleophiles such as butyllithium (room temperature), sodium phenoxide (60 °C), and CH_3SOCH_2Na (120 °C) also gave the same results. We then compared the reactivity of sulfoxonium salts with those of sulfonium salts. The reaction of **1a** with CH_3SOCH_2Na at 100 °C recovered the starting salts in 85% yield. A similar result was obtained by use of **2a**. However, treatment of **2a** with CH_3SOCH_2Na followed by the addition of sodium tetraphenylborate at 150 °C gave morpholinium tetraphenylborate in 66% yield. The reaction is accounted for by the abstraction of α-proton of morpholino group with CH_3SOCH_2Na to afford 5,6-dihydro-2*H*-1,4-oxazine and 4,4′-sulfinyldimorpholine which degradates into morpholinium salt as shown in scheme 3. A similar result is reported by Richards and Tarbel in the reaction of ethyldimorpholinosulfonium salt with butyllithium.[6]

Another heteroatom-substituted sulfoxonium salts, aryloxysulfoxonium salts, have different reactivity toward nucleophiles. Whiting reported that the reaction of aminodiaryloxysulfoxonium salts with primary amines afforded the corresponding sulfoximides in good yields.[8] Still also reported that aryloxydimethylsulfoxonium salts reacted with $NaBH_4$ to afford dimethyl sulfoxide.[9] We also tried the reaction of **2a** with $NaBH_4$ in methanol. However, starting **2a** was recovered almost quantitatively. Thus, triaminosulfoxonium salts were found to react only under drastic conditions as mentioned above and to be quite stable compounds.

In conclusion, triaminosulfoxonium salts were prepared by oxidation of corresponding triaminosulfonium salts. These salts are very stable toward nucleophiles.

Experimental

Melting points were determined on a Shibata-Büchi Model 510 and uncorrected. ^1H NMR spectra were measured on a JEOL PMX 60 spectrometer using TMS as internal standard.

Preparation of Trimorpholinosulfoxonium Chloride (2a). To a solution of sodium perbenzoate (4.8 g, 30 mmol) in water (50 cm^3) was added a solution of trimorpholinosulfonium chloride (**1a**) (3.3 g, 10 mm ol) in water (25 cm^3) at room temperature. After stirring for 12 h, the resulting suspension was filtered off. The water of filtrate was evaporated to give pale yellow crystals, which were recrystallized from methanol to give trimorpholinosulfoxonium chloride (**2a**) (1.9 g, 5.6 mmol) in 56% yield; mp 91—93 °C. Elemental analysis was carried out after converting this chloride salt into the corresponding tetraphenylborate salt. Anal. Calcd for $C_{36}H_{44}BN_3O_4S$: C, 69.11; H, 7.09; N, 6.71%. Found: C, 68.68; H, 7.14; N, 6.52%.

Preparation of 2b. To a solution of sodium perbenzoate (4.8 g, 30 mmol) in water (50 ml) was added a solution of dimorpholinopiperidinosulfonium chloride (3.3 g, 10 mmol) in water (25 cm^3) at room temperature. After stirring for 12 h, the resulting suspension was filtered off. To this filtrate was added a solution of sodium tetraphenylborate (3.4 g, 10 mmol) in water (25 cm^3). Immediately, colorless fine crystals of **2b** were precipitated. Crude **2b** was collected by filtration and recrystallized from methanol to give colorless crystals (4.2 g, 6.6 mmol, 66%); Anal. Calcd for $C_{37}H_{46}BN_3O_3S$: C, 71.26; H, 7.43; N, 6.77%. Found: C, 71.75; H, 7.01; N, 6.95%.

Compounds **2c**, **2d**, and **2e** were prepared in a similar manner.

2c; (3.5 g, 5.8 mmol, 58%); Anal. Calcd for $C_{36}H_{44}BN_3O_3S$: C, 70.93; H, 7.27; N, 6.89%. Found: C; 70.63; H, 7.51; N, 6.59%.

2d; (3.4 g, 5.4 mmol, 54%); mp 207—208 °C; Anal. Calcd for $C_{36}H_{44}BN_4O_3S$: C, 69.33; H, 7.11%. Found: C, 69.47; H, 7.28%.

2e; (3.8 g, 5.8 mmol, 58%); mp 228—229 °C; Anal. Calcd for $C_{38}H_{52}BN_3O_4S$: C, 69.39; H, 7.97; N, 6.39%. Found: C, 69.05; H, 7.65; N, 6.62%.

Reaction of Trimorpholinosulfonium Chloride (1a) with CH_3SOCH_2Na. Sodium hydride (0.50 g, 5.3 mmol, 50% dispersion) was washed with dry hexane (10 cm^3) for three times. Dimethyl sulfoxide (10 cm^3) was added at 60 °C for 1 h and trimorpholinosulfonium chloride (**1a**) (1.6 g, 5 mmol) was added in one portion to this solution. After stirring at 160 °C for 16 h, the reaction mixture was poured into water (100 cm^3) and a solution of sodium tetraphenylborate (1.7 g, 5 mmol) was added to this solution. Pale yellow crystals were precipitated and collected by filtration. Recrystallization from MeOH/ether afforded colorless crystals of morpholinium salts (1.2 g, 3 mmol, 60%); mp 159—161 °C.

Reaction of Trimorpholinosulfoxonium Chloride (2a) with CH_3SOCH_2Na. Sodium hydride (0.50 g, 5.3 mmol, 50% dispersion) was washed with dry hexane (10 cm^3) for three times. Dimethyl sulfoxide (10 cm^3) was added and warmed up to 60 °C for 1 h. Trimorpholinosulfoxonium chloride (**2a**) (1.7 g, 5 mmol) was added in one portion to this solution. After stirring at 150 °C for 16 h, the reaction mixture was poured into water (100 cm^3) and a solution of sodium tetraphenylborate (1.7 g, 5 mmol) was added to this solution. Pale yellow crystals were precipitated and collected by filtration. Recrystallization from MeOH/ether afforded colorless crystals of morpholinium salts (1.3 g, 3.3 mmol, 66%); mp 159—161 °C.

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