S-Aryl *N*,*N*-dialkylamidothiosulfates, a novel class of sulfenic acid derivatives

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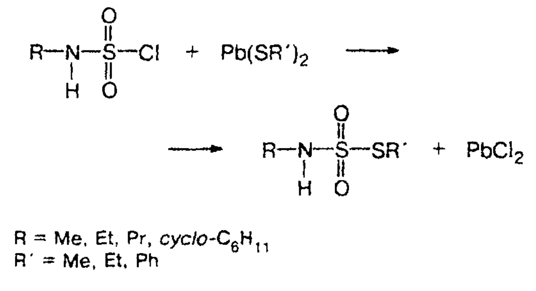
A method for the synthesis of *S*-aryl *N*,*N*-dialkylamidothiosulfates, a novel class of sulfenic acid derivatives, was proposed. The method is based on the reaction of arenesulfenyl chlorides with *N*,*N*-dialkylamidosulfinic acids or with secondary amines in liquid SO_2 in the presence of triethylamine. In the presence of halogen-containing Lewis acids, *S*-aryl *N*,*N*-dialkylamidothiosulfates add to the C=C bonds to give aryl β-haloalkyl sulfides.

Key words: *S*-aryl *N*,*N*-dialkylamidothiosulfates, sulfenylation, sulfenyl chlorides, amidosulfinic acids.

Although free sulfenic acids (R—S—OH) are unstable and not widely used themselves for synthetic purposes, their numerous derivatives (sulfenyl halides, sulfenamides, sulfenates, and thiosulfonates) have been long known as valuable organic reagents (*e.g.*, see a series of reviews[1–3]). However, such derivatives of sulfenic acids as *S*-aryl- and *S*-alkyl amidothiosulfates are currently represented only by *N*-monoalkylsulfamides obtained in the reaction of amidosulfonyl chloride with lead arene- or alkanethiolate (Scheme 1).[4] However, this reaction is not convenient for practical use because of the instability of the resulting *N*-(monoalkyl)amidothiosulfates and the necessity of preparing lead thiolates.

Scheme 1

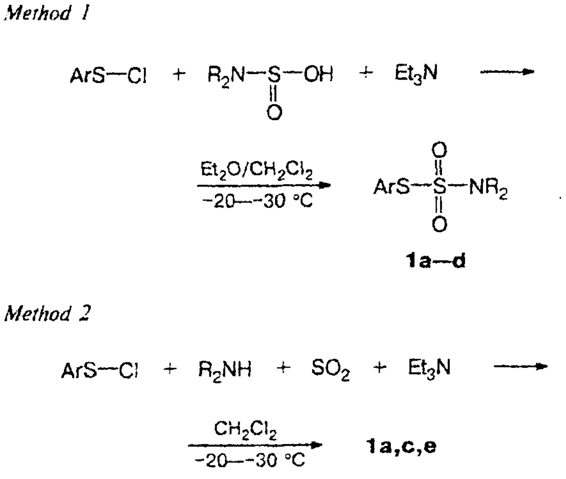


We synthesized *S*-aryl *N*,*N*-dialkylamidothiosulfates by the reaction of arenesulfenyl chloride with *N*,*N*-dialkylamidosulfinic acid in the presence of a tertiary amine as an acceptor of HCl (Scheme 2). *N*,*N*-Dialkylamidosulfinic acids can be either preliminarily prepared (method *1*) or generated *in situ* from the corresponding dialkylamine and SO_2 (method *2*).

The resulting compounds are presented in Table 1.

The solid reaction products are rather stable and can be stored at room temperature for several weeks without apparent decomposition. In polar solvent (methanol or chloroform), they completely transform into diaryl disulfides at room temperature within a few days or, when refluxed, over 2—3 h, for example:

Scheme 2



$$\mathbf{1b} \xrightarrow{\text{MeOH or CHCl}_3} (2\text{-NO}_2\text{C}_6\text{H}_4)_2\text{S}_2\,.$$

(98%)

Studying the reaction of *S*-aryl amidothiosulfates with alkenes revealed that additional activation is needed for the addition of the electrophile to the C=C bond. In the presence of Lewis acids (zinc chloride or aluminum bromide), *S*-aryl amidothiosulfates function as electrophilic sulfenylating reagents. In both cases, the halide ion of the Lewis acid is a nucleophile in the final stage of the addition, and the reaction yields aryl β-haloalkyl sulfides (Scheme 3).

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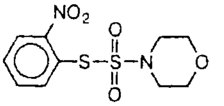
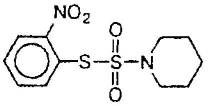
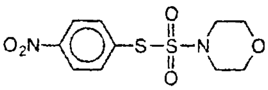
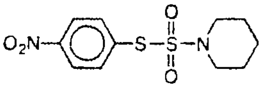
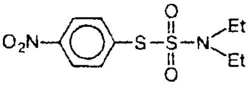
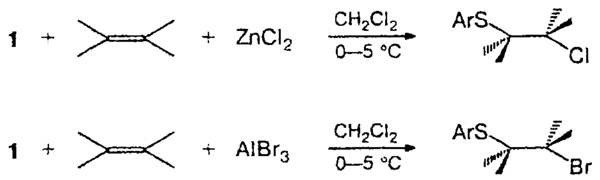
Table 1. *S*-Aryl *N*,*N*-dialkylamidothiosulfates

Product		Obtained by method	Yield (%)
	(**1a**)	*1*	56
		2	20
	(**1b**)	*1*	44
	(**1c**)	*1*	48
		2	20
	(**1d**)	*1*	35
	(**1e**)	*2*	26

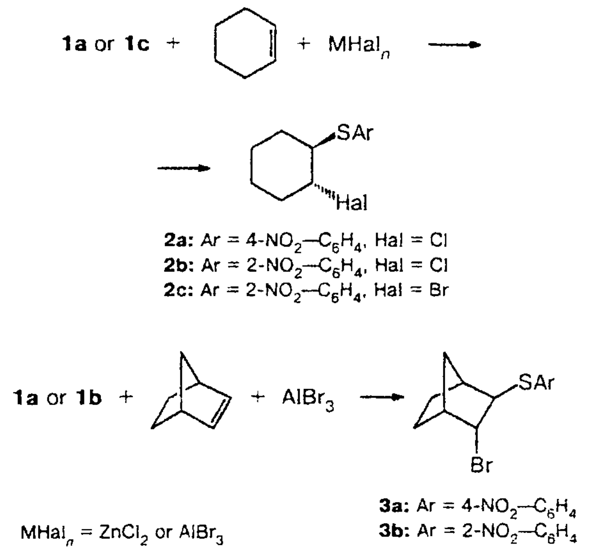
Scheme 3



Thus, in the presence of metal halides, *S*-aryl amidothiosulfates react with olefins like arenesulfenyl halides.

Compounds **1a** and **1c** react with cyclohexene or norbornene (Scheme 4) to give products of *trans*-addition,* which supports the electrophilic character of the process. However, the reaction with norbornene does not result in skeletal rearrangement, suggesting a low effective electrophilicity of these compounds as sulfenylating reagents.

Scheme 4



2a: Ar = 4-NO$_2$—C$_6$H$_4$, Hal = Cl
2b: Ar = 2-NO$_2$—C$_6$H$_4$, Hal = Cl
2c: Ar = 2-NO$_2$—C$_6$H$_4$, Hal = Br

MHal$_n$ = ZnCl$_2$ or AlBr$_3$

3a: Ar = 4-NO$_2$—C$_6$H$_4$
3b: Ar = 2-NO$_2$—C$_6$H$_4$

We thus found a convenient method for the synthesis of a novel class of sulfenic acid derivatives, namely, *S*-aryl *N*,*N*-dialkylamidothiosulfates, in which the S^{II} atom is an electrophilic center.

Experimental

The purity of the reaction products was checked by TLC on Silufol plates in the ethyl acetate—light petroleum (1 : 3) system. ^{1}H NMR spectra were recorded on a Varian VXR-400 instrument (400 MHz) with Me$_4$Si as the internal standard.

Synthesis of *S*-aryl amidothiosulfates (general procedure). Method *1* (from arenesulfenyl chlorides and *N*,*N*-dialkylamidosulfinic acids). Et$_3$N (10 mmol) was added to a suspension of *N*,*N*-dialkylamidosulfinic acid (prepared from the corresponding secondary amine and SO$_2$ in anhydrous ether[6]) (10 mmol) in 100 mL of anhydrous ether at −20 to −30 °C. A solution of arenesulfenyl chloride (10 mmol) in 10 mL of anhydrous CH$_2$Cl$_2$ was then slowly added dropwise with stirring at the same temperature. The reaction mixture was warmed to room temperature in 1 h, whereupon amine hydrochloride was filtered off. The solvent was removed *in vacuo*, and the residue was purified by chromatography on silica gel in ethyl acetate—light petroleum (1 : 3) to give a product in the form of a yellow crystalline substance or yellow oil.

Method *2* (from arenesulfenyl chlorides, secondary amines, and sulfur dioxide). SO$_2$ (8—10 mL) was condensed in a round-bottomed flask cooled to −20 to −30 °C. Et$_3$N (10 mmol) was slowly added dropwise with stirring at the same temperature followed by a secondary amine (10 mmol). After the reaction mixture solidified, a solution of arenesulfenyl chloride in 8—10 mL of anhydrous CH$_2$Cl$_2$ was added dropwise. The reaction mixture was warmed to room temperature, washed twice with water, and dried with Na$_2$SO$_4$. Further work-up was carried out as in method *1*.

***S*-(2-Nitrophenyl) morpholidothiosulfate (1a)**, m.p. 90 °C, R_f 0.65. ^{1}H NMR (CDCl$_3$), δ: 2.91 (m, 4 H, CH$_2$N); 3.72 (m, 4 H, CH$_2$O); 7.38 (m, 1 H); 7.56 (m, 1 H); 7.83 (dd, 1 H, J_1 = 8.7 Hz, J_2 = 1.5 Hz); 8.32 (dd, 1 H, J_1 = 8.7 Hz, J_2 = 1.5 Hz).

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* In the case of cyclohexene, this is confirmed by coincidence of the melting point and ^{1}H NMR spectrum of the addition product of **1c** in the presence of ZnCl$_2$ with those for the compounds described earlier.[5] In the case of norbornene, the fact that the protons at the substituents are *trans* follows directly from their coupling constants ($J_{2,3}$ ≈ 4—5 Hz; see Experimental).

Found (%): C, 39.60; H, 4.05; N, 9.02. $C_{10}H_{12}N_2O_5S_2$. Calculated (%): C, 39.47; H, 3.97; N, 9.20.

***S*-(2-Nitrophenyl) piperididothiosulfate (1b)**, yellow oil, R_f 0.83. ^{1}H NMR ($CDCl_3$), δ: 2.31 (m, 6 H, CH_2); 3.88 (m, 4 H, CH_2N); 7.32 (m, 1 H); 7.56 (m, 1 H); 7.88 (dd, 1 H, J_1 = 8.7 Hz, J_2 = 1.5 Hz); 8.36 (dd, 1 H, J_1 = 8.7 Hz, J_2 = 1.5 Hz). Found (%): C, 43.33; H, 4.90; N, 9.02. $C_{11}H_{14}N_2O_4S_2$. Calculated (%): C, 43.70; H, 4.67; N, 9.26.

***S*-(4-Nitrophenyl) morpholidothiosulfate (1c)**, m.p. 72—74 °C, R_f 0.62. ^{1}H NMR ($CDCl_3$), δ: 3.08 (m, 4 H, CH_2N); 3.78 (m, 4 H, CH_2O); 7.96 (d, 2 H, J = 8.8 Hz); 8.38 (dd, 2 H, J = 8.8 Hz). Found (%): C, 38.90; H, 4.03; N, 9.36. $C_{10}H_{12}N_2O_5S_2$. Calculated (%): C, 39.47; H, 3.97; N, 9.20.

***S*-(4-Nitrophenyl) piperididothiosulfate (1d)**, m.p. 109 °C, R_f 0.90. ^{1}H NMR ($CDCl_3$), δ: 2.30 (m, 6 H, CH_2); 3.83 (m, 4 H, CH_2N); 7.90 (d, 2 H, J = 8.8 Hz); 8.41 (d, 2 H, J = 8.8 Hz). Found (%): C, 43.08; H, 4.13; N, 8.83. $C_{11}H_{14}N_2O_4S_2$. Calculated (%): C, 43.70; H, 4.67; N, 9.26.

***S*-(4-Nitrophenyl) *N,N*-diethylamidothiosulfate (1e)**, m.p. 79—80 °C, R_f 0.61. ^{1}H NMR ($CDCl_3$), δ: 1.32 (t, 3 H, CH_3); 3.58 (q, 2 H, CH_2N); 7.94 (d, 1 H, J = 8.8 Hz); 8.27 (d, 1 H, J = 8.8 Hz). Found (%): C, 41.63; H, 4.92; N, 9.50; S, 20.98. $C_{10}H_{14}N_2O_4S_2$. Calculated (%): C, 41.36; H, 4.86; N, 9.65; S, 22.09.

Reactions of *S*-aryl amidothiosulfates with olefins in the presence of metal halides (general procedure). $ZnCl_2$ (1 mmol) (in the synthesis of chlorides) or $AlBr_3$ (1 mmol) (in the synthesis of bromides) was added to a mixture of *S*-aryl amidothiosulfate (0.21 g, 1 mmol) and an olefin (0.15 mmol) in anhydrous CH_2Cl_2 at 0—5 °C. The reaction mixture was stirred until the *S*-aryl amidothiosulfate disappeared (monitoring by TLC). The solvent was removed *in vacuo*, and the residue was chromatographed on silica gel in ethyl acetate—light petroleum (1 : 3).

***trans*-1-Chloro-2-(4-nitrophenylthio)cyclohexane (2a).** Yield 21%, m.p. 68—69 °C (*cf.* Ref. 5: m.p. 66 °C), R_f 0.61. ^{1}H NMR ($CDCl_3$), δ: 1.37—2.50 (m, 8 H); 3.62 (m, 1 H, HCS); 4.00 (m, 1 H, HCCl); 7.34 (d, 2 H, H arom, J = 8.8 Hz); 8.02 (d, 2 H, H arom, J = 8.8 Hz).

***trans*-1-Chloro-2-(2-nitrophenylthio)cyclohexane (2b).** Yield 28%, m.p. 99—100 °C, R_f 0.60. ^{1}H NMR ($CDCl_3$), δ: 2.50—1.20 (m, 8 H); 3.75 (m, 1 H, HCS); 4.40 (m, 1 H, HCCl); 7.30 (m, 1 H); 7.43 (m, 1 H); 7.58 (m, 1 H); 8.08 (m, 1 H). Found (%): C, 53.34; H, 4.89; N, 5.12. $C_{12}H_{14}ClNO_2S$. Calculated (%): C, 53.04; H, 5.19; N, 5.15.

***trans*-1-Bromo-2-(2-nitrophenylthio)cyclohexane (2c).** Yield 38%, yellow oil, R_f 0.65. ^{1}H NMR ($CDCl_3$), δ: 2.50—1.20 (m, 8 H); 3.75 (m, 1 H, HCBr); 4.40 (m, 1 H, HCS); 7.30 (m, 1 H); 7.43 (m, 1 H); 7.58 (m, 1 H); 8.08 (m, 1 H). Found (%): C, 45.53; H, 3.98; N, 4.00. $C_{12}H_{14}BrNO_2S$. Calculated (%): C, 45.58; H, 4.46; N, 4.43.

***endo*-2-Bromo-*exo*-3-(4-nitrophenylthio)bicyclo[2.2.1]heptane (3a).** Yield 32%, yellow oil, R_f 0.64. ^{1}H NMR ($CDCl_3$), δ: 1.14—2.30 (m, 6 H); 2.40 (m, 1 H); 2.46 (m, 1 H); 3.24 (dd, 1 H, HCS, J_1 = 5.0 Hz, J_2 = 1.8 Hz); 3.95 (dd, 1 H, HCBr, J_1 = 5.0 Hz, J_2 = 3.8 Hz); 7.20 (d, 2 H, J = 8.8 Hz); 8.01 (d, 2 H, J = 8.8 Hz). Found (%): C, 47.78; H, 4.33; N, 4.24. $C_{13}H_{14}BrNO_2S$. Calculated: C, 47.56; H, 4.30; N, 4.27.

***endo*-2-Bromo-*exo*-3-(2-nitrophenylthio)bicyclo[2.2.1]heptane (3b).** Yield 77%, yellow oil, R_f 0.73. ^{1}H NMR ($CDCl_3$), δ: 2.37—1.10 (m, 6 H); 2.48 (m, 1 H); 2.60 (m, 1 H); 3.15 (dd, 1 H, HCS, J_1 = 4.2 Hz, J_2 = 2.3 Hz); 4.05 (dd, 1 H, HCBr, J_1 = 4.2 Hz, J_2 = 2.8 Hz); 7.50—7.05 (m, 3 H); 8.10 (d, 1 H, J = 7.5 Hz). Found (%): C, 48.00; H, 4.29; N, 3.99. $C_{13}H_{14}BrNO_2S$. Calculated (%): C, 47.56; H, 4.30; N, 4.27.

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