Sulfenylation reactions activated by thionyl and sulfuryl chlorides

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Reactions of *N*-(4-nitrophenylthio)morpholine, *N,N'*-thiobismorpholine, and *N,N'*-dithiobismorpholine with thionyl chloride or sulfuryl chloride at −40 °C afford electrophilic chlorosulfenylating reagents, which add to the C=C bond of norbornene in high yields. Semiempirical quantum-chemical calculations and comparison of the relative reactivity of the sulfenylating complexes formed upon activation of arenesulfenamides by sulfur and phosphorus oxohalides were performed. The mechanism of the reactions is discussed.

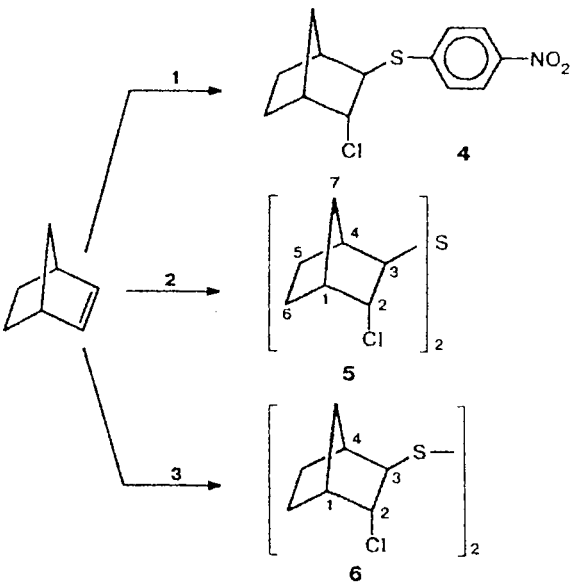
Key words: sulfenylation, arenesulfenamides, thiobisamines, dithiobisamines, thionyl chloride, sulfuryl chloride.

We have established previously that phosphorus oxotrichloride and oxotribromide as Lewis acids can activate electrophilic addition of organosulfur compounds containing S—N bonds (arenesulfenamides,[1] thiobisamines,[2] and dithiobisamines[3,4]) to the C=C bonds. These reactions afford the corresponding aryl (β-haloalkyl) sulfides (if arenesulfenylamides are used as sulfenylating reagents) or di(β-haloalkyl) sulfides and disulfides (in the case of thio- or dithiobisamines) in high yields.

We assumed that similar products would be formed when $SOCl_2$ or SO_2Cl_2 are used for the activation of electrophilic addition. In fact, the reaction of *N*-(4-nitrophenylthio)morpholine (**1**), *N,N'*-thiobismorpholine (**2**), or *N,N'*-dithiobismorpholine (**3**) with norbornene in the presence of $SOCl_2$ or SO_2Cl_2 gives the corresponding chlorosulfenylation products **4**—**6** in high yields (Scheme 1).

Dichlorosulfides **5** were isolated as a mixture of two diastereomeric forms, which differ in configuration of substituents at the C(2) and C(3) atoms; the ratio of DL- and *meso*-configurations was 3 : 2 according to the data of ^1H and ^{13}C NMR spectroscopy (similarly to the addition of SCl_2).[5] The multiplicity of signals and spin-spin coupling constants for both isomers are the same, which makes it difficult to assign signals in the NMR spectra. For exact assignment, we oxidized compounds **5** to the corresponding sulfoxides.* Dichlorodisulfides **6** are formed as a mixture of four diastereomeric forms.[4] Note that in the case of sulfenylation with thio- and dithiobisamines, both S—N bonds of the reagent are activated, and possible products of activation of only one S—N bond (to form β-chloroalkanesulfenamide or *N*-(β-chloroalkyldithio)amine, respectively) are not detected even when a twofold excess of the sulfenylating reagent with respect to the olefin is used in the reaction. In these cases, compounds **5** and **6** were obtained in lower yields (Table 1) as the reaction products.

Scheme 1



Based on the known data on intermediates of nucleophilic substitution by the amino group in dialkyl phosphonates $RPO(OR'_2)$ and phosphonic acid dihalides $RPOHal_2$ under the action of primary,[6,7] secondary,[8] and tertiary[8] amines, we assume that aminosulfonium salts of type **7** are formed (Scheme 2) in reactions of

* A mixture of enantiomeric sulfoxides is formed from the *meso*-form, whereas the oxidation of a mixture of D- and L-enantiomers results in the formation of only one sulfoxide (for details, see Ref. 2).

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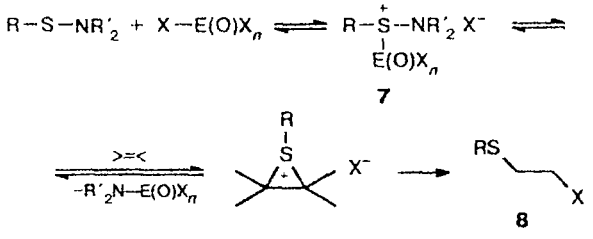
Table 1. Yields of products of norbornene sulfenylation (%)

Sulfenylating reagent	Promotor	
	$SOCl_2$	SO_2Cl_2
$4\text{-}NO_2C_6H_4SN(CH_2CH_2)_2O$ (1)	82	55
$S[N(CH_2CH_2)_2O]_2$ (2)	99	45
$S_2[N(CH_2CH_2)_2O]_2$ (3)	99	80

derivatives of sulfenic acid ($RS-NR'_2$, where R = Ar, $NAlk_2$, and $SNAlk_2$; R′ = Alk) with sulfur- or phosphorus-containing Lewis acids EO_nHal_m (E = S or P; n = 1 or 2; m = 2 or 3). This salt participates later in the electrophilic sulfenylation of the C=C bond resulting in β-haloalkyl sulfide **8** and sulfuric, sulfurous, or phosphoric chloroamidites.

Scheme 2



R = Ar, $NAlk_2$, $SNAlk_2$
R′ = Alk
X = Hal
E = S, P

We compared the sulfenylating reagents obtained upon the activation of sulfenamide **1** with thionyl chloride and phosphorus oxochloride and oxobromide on the basis of the results of the quantum-chemical semiempirical AM1 calculations of intermediates **7**. The results obtained were analyzed taking into account three parameters: the energy and form of the lowest unoccupied molecular orbital (LUMO) of the electrophilic reagent and the charge distribution on the atoms.

The analysis of the shape of the LUMO shows that in all cases of activation, in cation **7** it is mainly localized on the sulfenyl sulfur atom, and its energy, as expected, is substantially lower than that of the LUMO of nonactivated sulfenamide (Table 2). Correspondingly, the value of the energy gap between the LUMO of the electrophilic reagent and the highest occupied molecular orbital (HOMO) of the olefin is also decreased (for norbornene, the energy of the HOMO is equal to −9.58 eV). It can be expected that the reaction of the cation of type **7** with the olefin occurs as an orbital-controlled process (the value of the energy gap between the interacting orbitals varies from 2.73 eV for the $POBr_3$-activated reaction to 4.33 eV for the SO_2Cl_2-activated reaction). Then the rate of the $SOCl_2$- or

Table 2. Energies of frontier orbitals and charges on the sulfur atom of sulfenamide **1** and sulfenylating reagents of type **7** (see Scheme 2)

Reagent	ε(LUMO)	Δε[a]	q(S)	Yield of sulfenylation product (%)
	eV			
1	−0.32	—	—	0
1–$SOCl_2$	−6.01	3.57	0.364	82
1–SO_2Cl_2	−5.25	4.33	0.948	55
1–$POCl_3$[b]	−5.86	3.72	0.472	65
1–$POBr_3$[b]	−6.85	2.73	0.463	95

[a] Energy gap between LUMO of the reagent and HOMO of norbornene.
[b] See Ref. 9.

$POBr_3$-activated sulfenylation reactions are the highest, and the rate of the SO_2Cl_2-activated reaction is the lowest. The experimental results on the yield of the sulfenylation product confirm this conclusion (see Table 1): higher yield of halosulfides is observed when thionyl chloride is used, and lower yield is observed for activation with sulfuryl chloride. In the latter case, where the sulfenylation reaction occurs more slowly, the contribution of the concominant chlorination reaction becomes substantial (in this case, this reaction gives *syn-exo*-2,7-dichloronorbornane, isolated as a by-product in a yield up to 38%). Therefore, the assumption that the structure of the sulfenylating reagent in the activation with thionyl and sulfuryl chlorides is close to that of type **7** cation seems to be substantiated.

Thus, we have shown that thionyl and sulfuryl chlorides, being Lewis acids, as well as the analogous phosphorus-containing oxohalides, activate electrophilic addition of arenesulfenamides, thiobisamines, and dithiobisamines to alkenes. According to the quantum-chemical calculations and experimental results, $SOCl_2$ is preferable for use as a sulfenylation promotor.

Experimental

^1H NMR spectra were recorded on Varian VXR-400 (400 MHz) and Tesla BS-467 (60 MHz) instruments; ^{13}C NMR spectra were obtained on a Varian VXR-400 (100 MHz) instrument. *N*-(4-Nitrophenylthio)morpholine, *N,N′*-thiobismorpholine, and *N,N′*-dithiobismorpholine were synthesized according to the described procedures.[10–12]

Sulfenylation of norbornene (general procedure). A solution of $SOCl_2$ or SO_2Cl_2 (2 mmol) in anhydrous CH_2Cl_2 was added with stirring at −40 °C to a solution of sulfenamide **1** (2 mmol) or thio- or dithiobisamine **2** or **3** (1 mmol) in the same solvent (20 mL). After stirring at this temperature for 10 min, a solution of a 1.5-fold excess of the olefin in CH_2Cl_2 was added. After 0.5 h, the temperature of the reaction mixture was gradually increased to room temperature, and the mixture was filtered through a silica gel layer (h = 5 cm). Then the solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel using an ethyl acetate–light petroleum (1 : 3) mixture as the eluent.

(*endo*-2-Chloroborn-*exo*-3-yl) 4-nitrophenyl sulfide (4). R_f 0.78. ^{1}H NMR (60 MHz, CCl_4), δ: 1.1—2.6 (m, 8 H); 3.15 (m, 1 H, HCS); 3.95 (m, 1 H, HCCl); 7.25 (d, 2 H arom., J = 9.0 Hz); 8.05 (d, 2 H arom., J = 9.0 Hz). Found (%): C, 55.57; H, 5.06; N, 5.00. $C_{13}H_{14}ClNO_2S$. Calculated (%): C, 55.02; H, 4.97; N, 4.94.

Di(*endo*-2-chloronorborn-*exo*-3-yl) sulfide (5). R_f 0.68. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.20—1.72 (m, 4 H, 2 HC(5), 2 HC(6)); 1.38 and 1.39 (both m, 1 H, HC(7)); 1.67 and 1.74 (both m, 1 H, HC(7)); 2.20 and 2.25 (both d, 1 H, HC(4), J = 4.2 Hz); 2.40 and 2.42 (both t, 1 H, HC(1), J = 4.2 Hz); 2.61 and 2.68 (both dd, 1 H, HCS, J_1 = 2.7 Hz, J_2 = 4.2 Hz); 3.90 and 3.91 (both dt, 1 H, HCCl, J_1 = 1.9 Hz, J_2 = 4.1 Hz). ^{13}C NMR, δ: 21.42 and 21.47 (C(5)); 28.86 and 28.88 (C(6)); 35.68 and 35.78 (C(7)); 42.96 and 44.33 (C(4)); 43.82 and 44.08 (C(1)); 55.22 and 57.74 (CS); 68.12 and 68.48 (2 C, CCl). Found (%): C, 57.18; H, 6.77. $C_{14}H_{20}Cl_2S$. Calculated (%): C, 57.73; H, 6.92.

Di(*endo*-2-chloronorborn-*exo*-3-yl) sulfide (6). R_f 0.93. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.20—1.80 (m, 5 H, 2 HC(5), 2 HC(6), HC(7)); 1.95 (m, 1 H, HC(7)); 2.21, 2.28, 2.30, and 2.31 (all d, 1 H, HC(4), J = 4.1 Hz); 2.41, 2.44, 2.47, and 2.48 (all t, 2 H, HC(1), J = 4.1 Hz); 2.64, 2.71, 2.83, and 2.86 (all dd, 2 H, HCS, J_1 = 2.8 Hz, J_2 = 4.1 Hz); 3.95, 4.00, 4.10, and 4.18 (all dt, 2 H, HCCl, J_1 = 1.9 Hz, J_2 = 4.1 Hz). Found (%): C, 51.78; H, 6.23. $C_{14}H_{20}Cl_2S_2$. Calculated (%): C, 52.01; H, 6.23.

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References

1. E. K. Beloglazkina, V. S. Tyurin, I. D. Titanyuk, and N. V. Zyk, *Dokl. Akad. Nauk*, 1995, **344**, 487 [*Dokl. Chem.*, 1995 (Engl. Transl.)].
2. N. V. Zyk, S. Z. Vatsadze, E. K. Beloglazkina, Yu. A. Dubinskaya, and N. S. Zefirov, *Dokl. Akad. Nauk*, 1997, **357**, 209 [*Dokl. Chem.*, 1997 (Engl. Transl.)].
3. E. K. Beloglazkina and N. V. Zyk, *Izv. Akad. Nauk. Ser. Khim.*, 1995, 1846 [*Russ. Chem. Bull.*, 1995, **44**, 1775 (Engl. Transl.)].
4. N. V. Zyk, E. K. Beloglazkina, and N. S. Zefirov, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 2522 [*Russ. Chem. Bull.*, 1996, **47**, 2393 (Engl. Transl.)].
5. G. A. Tolstikov, *Sulfur Reports*, 1983, **3**, 39.
6. I. Granoth, Y. Segall, D. Waisbort, E. Shirin, and H. Leader, *J. Am. Chem. Soc.*, 1980, **102**, 4523.
7. R. F. Hudson and R. Greenhalgh, *J. Chem. Soc., B*, 1969, 325.
8. R. L. Wintermyer, L. L. Szafraniec, and H. R. Bradford, *J. Org. Chem.*, 1972, **37**, 2355.
9. V. S. Tyurin, Ph. D. (Chem.) Thesis, Department of Chemistry, M. V. Lomonosov Moscow State University, Moscow, 1996, 172 pp. (in Russian).
10. J. H. Billman and E. J. O'Mahony, *J. Am. Chem. Soc.*, 1939, **61**, 2340.
11. E. S. Blake, *J. Am. Chem. Soc.*, 1943, **65**, 1267.
12. C. E. Hatch, *J. Org. Chem.*, 1978, **43**, 3953.

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