Reactions of sulfites with secondary amines
1. Diphenyl and alkyl phenyl sulfites

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The interaction of diethylamine and morpholine with diphenyl, methyl phenyl, ethyl phenyl, and isopropyl phenyl sulfites was studied. It was established that two reactions, substitution and alkylation, can occur in parallel. Diphenyl sulfites react with amines to give only substitution products, while other sulfites react with substitution at the sulfur atom and with alkylation of the amines.

Key words: sulfites, complex, sulfur dioxide, secondary amines.

It is known[1] that dialkyl sulfites can alkylate primary and tertiary aromatic amines. Some aliphatic tertiary amines catalyze the rearrangement of dialkyl sulfites into alkyl sulfonates.[2] Literature data on reactions of secondary amines with dialkyl or diaryl sulfites are absent.

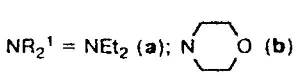
Hence, the present work is devoted to a study of reactions of diethylamine and morpholine with diphenyl sulfite **1a** and alkyl phenyl sulfites **1b—d**, the influence of the nature of the alkoxy substituent at the sulfur atom and temperature on the direction of the reaction, and the use of these reactions for the synthesis of amido sulfites **2** and sulfurous amides **3**.

$$\underset{\mathbf{1}}{(RO)_2S{=}O} \xrightarrow{HNR_2{}^1} \underset{\mathbf{2}}{ROS(O)NR_2{}^1} + \underset{\mathbf{3}}{(R_2{}^1N)_2S{=}O} + ROH$$

As a rule, compounds **3** are obtained by the method proposed by Michaelis,[3] and compounds **2** can be obtained according to other procedures,[4—6] whose disadvantage is the presence of amine hydrochloride in the final products.

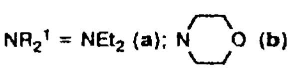
We found that diphenyl sulfite **1a** reacts exothermally with equimolar amounts of diethylamine or morpholine to give phenyl sulfamidites **2a,b** and phenol.

$$\underset{\mathbf{1a}}{(PhO)_2SO} + HNR_2{}^1 \longrightarrow \underset{\mathbf{2a,b}}{PhOS(O)NR_2{}^1} + PhOH$$



When the secondary amine is taken in excess, the other phenoxy group is also substituted to give amides **3a,b**.

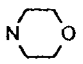
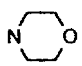
$$\mathbf{1a} + 2HNR_2{}^1 \longrightarrow \underset{\mathbf{3a,b}}{(R_2{}^1N)_2S{=}O} + 2\,PhOH$$



Compounds **2a,b** and **3a,b** were isolated by fractional distillation and characterized by ^{1}H NMR and IR spectroscopy. Their structures were confirmed by data from elemental analysis and independent synthesis.

It was expected that if one phenoxy group in diphenyl sulfite **1a** is replaced by the alkoxy group (—OMe (**1b**); —OEt (**1c**); and —OPr^i (**1d**)), the reaction with diethylamine and morpholine would lead to the substitution for either the alkoxy group or the phenoxy group or both of them. However, only the substitution products of the phenoxy group were isolated and characterized.

$$\underset{\mathbf{1b-d}}{PhO\overset{}{\underset{\underset{O}{\|}}{S}}OR^2} + HNR_2{}^1 \longrightarrow \underset{\mathbf{2c-g}}{R_2{}^1N\underset{\underset{O}{\|}}{S}OR^2} + PhOH$$

2	c	d	e	f	g
$NR_2{}^1$	NEt_2		NEt_2		NEt_2
R^2	Me	Me	Et	Et	Pr^i

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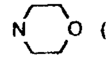
It should be noted that the yields of compounds **2e—g** do not exceed 45—65%. Conducting the reaction in an excess of the secondary amine also does not result in the substitution of the alkoxy group in the sulfite. On fractional distillation of the reaction mixture *in vacuo*, complexes of the secondary amines with sulfur dioxide **4a,b** were isolated and characterized by ^{1}H NMR and IR spectroscopy as well as by comparison of their properties with those of compounds obtained by independent synthesis.

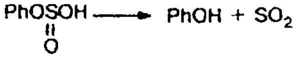
$$SO_2 + HNR_2{}^1 \longrightarrow \underset{\textbf{4a,b}}{HNR_2{}^1 \cdot SO_2}$$

$NR_2{}^1 = NEt_2$ (**a**);



(**b**)

We relate the formation of such complexes to the alkylating properties of the sulfite.[1] The alkylation of a molecule of the secondary amine with the sulfite results in the formation of a tertiary amine, and the decomposition of unstable phenyl hydrogen sulfite **5** is accompanied by evolution of SO_2 and phenol.[7—9]



$$Ph\!O\underset{\underset{O}{\|}}{S}OH \longrightarrow PhOH + SO_2$$

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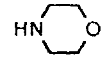
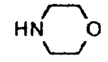
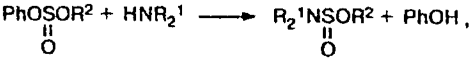
The reaction of sulfur dioxide with the secondary amines occurs sufficiently fast. This process has been described in the literature.[10—14] Note that the higher the alkylating properties of alkyl phenyl sulfites **1b—d** the lower the yield of the substitution product in its reaction with secondary amines (Table 1).

Table 1. The characteristics of reaction products

Sulfite	Amine	Reaction time/h	Products	Yield (%)	B.p./°C (*p*/Torr)
1a	$HN(C_2H_5)_2$	1.0	**2a**	85	84—86 (0.03)
1a		1.0	**2b**	73	112—114 (0.06)
1b	$HN(C_2H_5)_2$	1.5	**2c**	45	73—75 (10)
			4a	51	32—35 (10)
1b		1.5	**2d**	43	93—95 (10)
			4b	54	40—42 (10)
1c	$HN(C_2H_5)_2$	4.0	**2e**	53	81—82 (10)
			4a	45	32—35 (10)
1c		4.5	**2f**	50	114—116 (10)
			4b	42	40—42 (10)
1d	$HN(C_2H_5)_2$	6.0	**2g**	65	85—87 (10)
			4a	27	32—35 (10)

The reaction of **1b** with diethylamine resulted in the alkylation product, diethyl methyl amine, which was isolated and characterized by ^{1}H NMR spectroscopy. The general scheme of reaction of secondary amines with alkyl phenyl sulfite can be presented as two reactions occurring in parallel, the nature of the substituent determining which pathway is predominant.



$$Ph\!O\underset{\underset{O}{\|}}{S}OR^2 + HNR_2{}^1 \longrightarrow R_2{}^1N\underset{\underset{O}{\|}}{S}OR^2 + PhOH, \quad (1)$$

$$Ph\!O\underset{\underset{O}{\|}}{S}OR^2 + HNR_2{}^1 \longrightarrow Ph\!O\underset{\underset{O}{\|}}{S}OH + R^2NR_2{}^1, \quad (2)$$

5

R^2 = Me; Et; Pr^i

The use of a more than twofold excess of a secondary amine only slightly increases the yield of the substitution products **2c—g**.

The effect of temperature on the yield (%) of products **2c** and **4a** in the reaction of sulfite **1b** with diethylamine is presented below:

T/°C	**2c**	**4a**	*T*/°C	**2c**	**4a**
20	43	53	40	32	65
25	45	52	50	27	71
30	41	55			

As the temperature increases, the yield of the substitution product decreases, while that of the complex of secondary amine increases, which attests to the occurrence of reaction (2).

Thus, the reactions of sulfites **4b—d** with diethylamine and morpholine result in both the substitution of the amino group for the phenoxy group and the alkylation of the amine.

Experimental

^{1}H NMR spectra were recorded on a Varian-T 60 instrument (CCl_4, tetramethylsilane was used as the internal standard). IR spectra were recorded on a UR-20 infrared spectrometer (thin layer). Reactions were carried out in anhydrous ether or acetonitrile. Sulfites **1a—d** were obtained according to the known procedures.[15,16]

Reaction of diphenyl sulfite 1a with diethylamine. *A.* Diethylamine (4.7 g, 0.064 mol) was added with vigorous stirring to a solution of sulfite **1a** (15 g, 0.064 mol) in 45 mL of ether. The reaction mixture was stirred at a temperature no higher than 30 °C for 1 h. After the solvent was removed under reduced pressure, the residue was fractionated *in vacuo*. Redistillation of the fraction with b.p. 76—78 °C (0.015 Torr) yielded phenyl diethylsulfamidite (**2a**) (11.5 g, 85%), b.p. 84—86 °C (0.03 Torr), n_D^{20} 1.5319. Found (%): C, 56.21; H, 6.99; N, 6.52; S, 14.93. $C_{10}H_{15}NO_2S$. Calculated (%): C, 56.34; H, 7.04; N, 6.56; S, 15.01. ^{1}H NMR, δ: 1.27 (t, 3 H, CH_3, J = 7 Hz); 4.27 (q, 2 H, CH_2, J = 7.5 Hz); 7.15 (m, 5 H, C_6H_5).

IR (KBr), ν/cm^{-1}: 642 (S—N); 900, 930 (N—C); 1145 (S—O).

B. Diethylamine (8.4 g, 0.115 mol) in 40 mL of ether was added with stirring to a solution of sulfite **1a** (10.8 g, 0.046 mol) in 45 mL of ether. The reaction mixture was kept at a temperature no higher than 30—35 °C for ~1 h, whereupon it turned dark. The solvent and the nonconsumed amine were removed under reduced pressure, and the residue was twice fractionated *in vacuo* to yield *N,N′*-sulfinylbis(diethylamine) **3a** (2.77 g, 32%), b.p. 108—110 °C (20 Torr) (see Ref. 3). ^{1}H NMR, δ: 1.23 (t, 3 H, CH$_3$, J = 7 Hz); 3.24 (q, 2 H, CH$_2$, J = 7.5 Hz). IR (KBr), ν/cm^{-1}: 650 (S—N); 920, 880 (N—C); 1120 (S—O).

Reaction of sulfite 1a with morpholine. Morpholine (3.3 g, 0.038 mol) in 20 mL of acetonitrile was added with vigorous stirring to a solution of sulfite **1a** (8.9 g, 0.038 mol) in 50 mL of acetonitrile at 18—20 °C. After 1 h, the solvent was removed under reduced pressure (10 Torr), and the residue was twice fractionated *in vacuo* to give phenyl sulfomorpholidite **2b** (6.3 g, 73%), b.p. 112—114 °C (10 Torr), n_D^{20} 1.5497. Found (%): C, 52.63; H, 5.71; N, 6.09; S, 14.01. $C_{10}H_{13}NO_3S$. Calculated (%): C, 52.80; H, 5.72; N, 6.16; S, 14.09. ^{1}H NMR, δ: 3.18 (m, 4 H, N(CH$_2$)$_2$); 3.67 (m, 4 H, O(CH$_2$)$_2$); 7.35 (m, 5 H, C$_6$H$_5$).

Reaction of sulfite 1b with diethylamine. Diethylamine (4.2 g, 0.058 mol) in 20 mL of ether was added with vigorous stirring to a solution of sulfite **1b** (10 g, 0.058 mol) in 50 mL of ether at 23—25 °C. The reaction mixture was kept for 1.5 h, and then low-boiling products were removed under reduced pressure. The residue was fractionated *in vacuo*. Two main fractions were collected: (1) b.p. 30—38 °C and (2) b.p. 70—76 °C (10 Torr). Re-distillation of fraction (1) yielded the complex of diethylamine with SO$_2$ (**4a**, 4.06 g, 51%), b.p. 32—35 °C (10 Torr), n_D^{20} 1.4628 (see Ref. 11). ^{1}H NMR, δ: 1.33 (t, 6 H, CH$_3$, J = 7 Hz); 2.97 (q, 4 H, CH$_2$N, J = 7.5 Hz). Re-distillation of fraction (2) yielded methyl diethylsulfamidite **2c** (3.95 g, 45%), b.p. 73—75 °C (10 Torr), n_D^{20} 1.4453. ^{1}H NMR, δ: 1.55 (t, 6 H, CH$_3$); 3.35 (s, 3 H, OCH$_3$); 3.63 (m, 4 H, CH$_2$N). The low-boiling products were fractionated over metallic Na in a Widmer column. The fraction with b.p. 61—63 °C was collected. According to ^{1}H NMR data, it is a mixture of HNEt$_2$ and MeNEt$_2$. ^{1}H NMR, δ: 0.83—1.27 (m, CH$_3$CH$_2$N); 2.15 (s, CH$_3$N); 2.30 (q, HN$\underline{CH_2}$CH$_3$); 2.60 (q, CH$_3$N$\underline{CH_2}$CH$_3$).

Reactions of sulfites **1b,c** with morpholine and sulfites **1c,d** with diethylamine were carried out analogously. The independent synthesis of compounds **2a—g** and **3a,b** was carried out according to the known procedures.[3—5,15]

Synthesis of a complex of diethylamine with SO$_2$ (4a). SO$_2$ was bubbled with cooling through a solution of diethylamine (10 g, 0.137 mol) in 30 mL of anhydrous ether until pH ~4 was attained. Fractional distillation *in vacuo* yielded the complex of diethylamine with SO$_2$ (**4a**) (17.45 g, 93%), b.p. 32—34 °C (10 Torr), n_D^{20} 1.4631. ^{1}H NMR, δ: 1.35 (t, 6 H, CH$_3$); 3.15 (q, 4 H, CH$_2$N). Found (%): C, 35.58; H, 7.98; N, 10.28; S, 23.07. $C_4H_{11}NO_2S$. Calculated (%): C, 35.04; H, 8.03; N, 10.22; S, 23.95. The complex decomposes on storage.

Complex of SO$_2$ with morpholine **4b** was obtained analogously, yield 87%, b.p. 41—42 °C (10 Torr), n_D^{20} 1.5107. Found (%): C, 32.01; H, 6.14; N, 9.13; S, 21.09. $C_4H_9NO_3S$. Calculated (%): C, 31.79; H, 5.96; N, 9.27; S, 21.19.

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