Nitro derivatives of cyclic sulfoximides of the 1,2-benzoisothiazole series

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Nitro derivatives of 1-R-1,2-benzoisothiazol-3-one 1-oxide were synthesized by the reactions of 2-alkyl(phenyl)thio-4-nitro- and 4,6-dinitro-2-(phenylthio)benzamides with chlorine in 60% acetic acid. Analogous reactions of 2-(*n*-butylthio)-4-nitro- and 2-(*tert*-butylthio)-4-nitrobenzamides with chlorine afforded 2-butyl- and 2-H-1,2-benzoisothiazol-3-one 1-oxides, respectively. The proposed reaction mechanism includes the formation and subsequent transformations of *S*-alkyl-*S*-aryl- and *S*,*S*-diarylchlorosulfonium chlorides.

Key words: 1,2-benzoisothiazol-3-one 1-oxide, 1-R-1,2-benzoisothiazol-3-one 1-oxide, alkanethiols, thiophenol, 2,4-dinitrobenzamides, 2,4,6-trinitrobenzamides.

Cyclic sulfoximides, particularly 1,2-benzoisothiazole derivatives, possess various types of biological activity[1] such as antisecretory,[2] antihypertensive,[3] and antispasmodic[4] and can also reduce the sugar level in blood.[4] Such compounds are most commonly synthesized by reactions of *ortho*-(alkylsulfinyl)benzoates with HN_3.[1,5—7] However, this technique is inconvenient for laboratory practice because of the risk of explosions. Nitro-1,2-benzoisothiazole sulfoximides remain unknown so far.

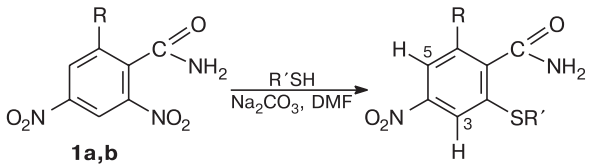
Recently, we have developed a selective synthesis of 2-R-6-nitro- and 2-R-4,6-dinitro-1,2-benzoisothiazol-3-one 1-oxides from the corresponding nitro derivatives of *N*-R-2-(benzylthio)benzamide and chlorine in aqueous organic solvents.[8] One could assume that analogous reactions with 2-RS-benzamides containing no easily leaving benzyl group would proceed with retention of the C—S bond, yielding 1,2-benzoisothiazole sulfoximides.

To verify this assumption, the oxidative chlorination of 2-RS-4-nitro- and 2-RS-4,6-dinitrobenzamides bearing S-alkyl and S-phenyl substituents was studied.

The starting benzamides **2a—h** were prepared by reactions of 2,4-dinitro- and 2,4,6-trinitrobenzamides (**1a,b**) with the corresponding thiols in DMF in the presence of Na_2CO_3.[9] The reactions are regioselective; the reaction products recrystallized from Pr^iOH are individual 2-RS-nitrobenzamides **2a—h** (^1H NMR data) (Scheme 1).

It turned out that the oxidative chlorination of compounds **2a—h** affords structurally different products, depending on the nature of the substituent at the S atom and the number of nitro groups. Thus 2-alkylthio- (R′ ≠ Bu)

Scheme 1



1a,b **2a—h**

1: R = H (**a**), NO_2 (**b**)

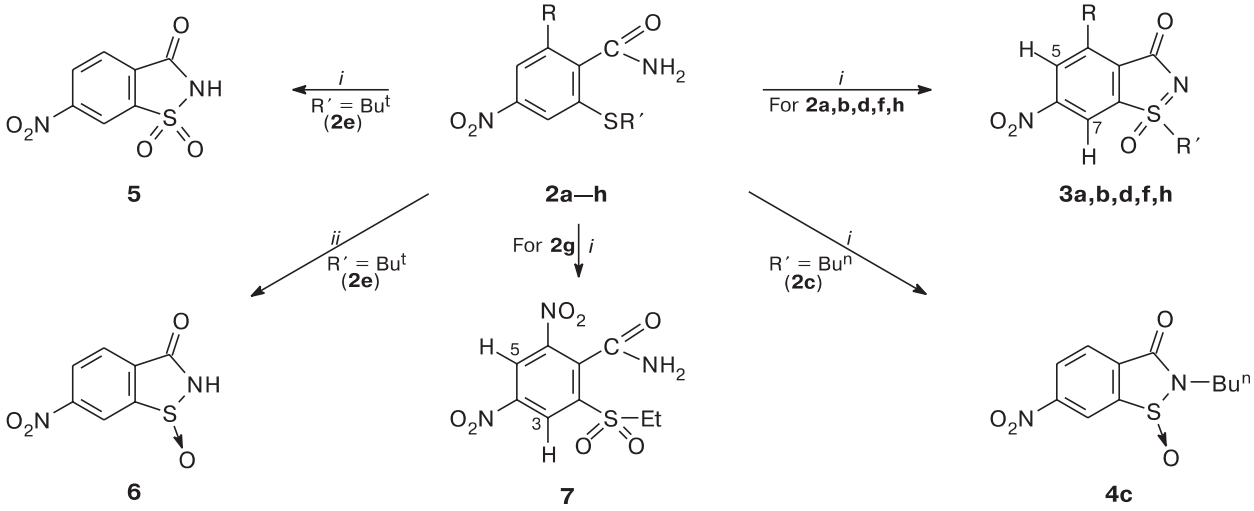
2	R	R′	**2**	R	R′
a	H	Et	**e**	H	Bu^t
b	H	Pr^n	**f**	H	Ph
c	H	Bu^n	**g**	NO_2	Et
d	H	n-C_8H_{17}	**h**	NO_2	Ph

and 2-phenylthio-4-nitrobenzamides **2a,b,d,f**, as well as 4,6-dinitro-2-phenylthiobenzamide (**2h**), react with chlorine in 60% AcOH without cleavage of the C—S bond to give the corresponding 1-R′-1,2-benzoisothiazol-3-one 1-oxides **3a,b,d,f,h** in 60—74% yields as the only reaction products. Chlorination of 2-(*n*-butylthio)-4-nitrobenzamide (**2c**) under the above conditions is accompanied by migration of the Bu^n group from the sulfur atom to the N atom, affording 2-(*n*-butyl)-6-nitro-1,2-benzoisothiazol-3-one 1-oxide (**4c**) in 72% yield. The major products of the reactions of 2-(*tert*-butylthio)-4-nitrobenzamide (**2e**) with chlorine in 60% AcOH and in aqueous CH_2Cl_2 (water content is ~5%) are 6-nitro-1,2-benzoisothiazol-3-one 1,1-dioxide (**5**) and 6-nitro-1,2-benzoisothiazol-3-one 1-oxide (**6**) in 36 and 34% yields, respectively. Finally, chlorination of 2-(ethylthio)-4,6-dinitrobenzamide (**2g**) in 60% AcOH gives sulfone **7** containing no isothiazole ring (Scheme 2).

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1426—1431, August, 2002.

1066-5285/02/5108-1549 $27.00

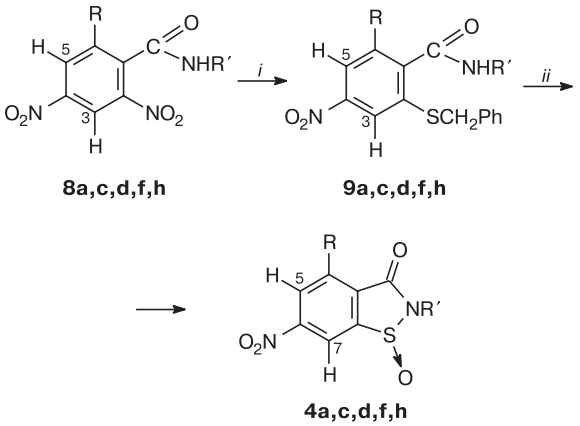
Scheme 2



Reagents and conditions: *i*. Cl_2, 60% AcOH; *ii*. Cl_2, CH_2Cl_2—H_2O (5%).
Note. Substituents R and R′ in compounds **3a,b,d,f,h** and **4c** correspond to those for compounds **2** in Scheme 1.

The compounds obtained were characterized by IR and ^{1}H NMR spectra and elemental analysis data (Tables 1—3). The structures of sulfoximides **3a,b,d,f,h** and oxide **4c** were determined by comparing their physicochemical and spectral data with those of 2-R′-1,2-benzoisothiazol-3-one 1-oxides **4a,c,d,f,h** (Scheme 3) synthesized from 2-(benzylthio)benzamides **9a,c,d,f,h** according to the known procedure.[8]

Scheme 3



Reagents and conditions: *i*. $PhCH_2SH$—K_2CO_3, DMF. *ii*. Cl_2, CH_2Cl_2—H_2O (5%).
Note. Substituents R and R′ in compounds **4**, **8**, and **9** correspond to those for compounds **2** in Scheme 1.

Compounds **3a,d,f,h** differ from isomeric isothiazoslones **4a,d,f,h** in melting points and retention factors R_f (Tables 2, 3). The IR spectra of 1-R′-6-nitro-1,2-benzoisothiazol-3-one 1-oxides **3a,b,d,f,h** show less intense CO absorption bands compared to those for 2-R′-6-nitro-1,2-benzoisothiazol-3-one 1-oxides **4a,c,d,f,h**; in addition, these bands appear in the range of longer wavelengths (~1600 versus 1645—1715 cm^{-1}), which is characteristic of cyclic sulfimides.[1] In the ^{1}H NMR spectra of compounds **3a,b,d**, signals for the methylene protons are shifted upfield (δ ~3.50) relative to analogous signals for products **4a,c,d** (δ 3.70—3.95), which is usually observed while comparing N—CH_2- and S—CH_2-containing compounds.[10] Note that the N–CH_2 protons in 2-R′-1,2-benzoisothiazol-3-one 1-oxides **4a,c,d** are magnetically nonequivalent, whereas those in 1-R′-1,2-benzoisothiazol-3-one 1-oxides **3a,b,d** have the same chemical shifts, probably because of a lower barrier to the inversion of the S atom in compounds **3a,b,d** with the ylide structure.[11] The methylene protons in 1-R′-isomers **3** are spatially closer to the annelated aromatic ring than those in 2-R′-isomers **4**; this was confirmed by the nuclear Overhauser effect for the CH_2 and H(7) protons in compound **3a**, which did not occur in compound **4a**.

The product of oxidative chlorination of 2-(*n*-butylthio)-4-nitrobenzamide (**2c**) proved to be identical with compound **4c** obtained independently from **9c**, and isothiazolones **5** and **6** are identical to authentic samples synthesized according to the known method.[8]

Apparently, the oxidative chlorination of 2-R′S-benzamides **2a—h** proceeds through the formation of chlorosulfonium chlorides **10**, whose subsequent reaction pathways depend on the nature of substituents R and R′ (Scheme 4). For R′ = Alk (R′ ≠ Bu) and R′ = Ph, chlorides **10** are probably hydrolyzed with water con-

Table 1. Yields, melting points, and elemental analysis data for compounds **2a—h**, **3a,b,d,f,h**, **4a,c,d,f,h**, **8a,c,d,f**, and **9a,c,d,f**

Compound	Yield (%)	M.p./°C	Found / Calculated (%)				Molecular formula
			C	H	N	S	
2a	90	193—197	47.92	4.40	12.53	14.02	$C_9H_{10}N_2O_3S$
			47.78	4.45	12.38	14.17	
2b	80	178—180	50.27	4.97	11.40	13.15	$C_{10}H_{12}N_2O_3S$
			49.99	5.03	11.66	13.34	
2c	80	137—141	52.10	5.68	10.88	12.30	$C_{11}H_{14}N_2O_3S$
			51.95	5.55	11.02	12.61	
2d	76	121—125	58.29	7.00	8.89	9.98	$C_{15}H_{22}N_2O_3S$
			58.04	7.14	9.02	10.33	
2e	62	154—158	52.16	5.49	10.79	12.47	$C_{11}H_{14}N_2O_3S$
			51.95	5.55	11.02	12.61	
2f	72	195—197	57.26	3.80	10.10	11.43	$C_{13}H_{10}N_2O_3S$
			56.93	3.67	10.21	11.69	
2g	75	171—178	40.03	3.41	15.21	11.71	$C_9H_9N_3O_5S$
			39.85	3.34	15.49	11.82	
2h	64	238—243	48.99	2.75	13.13	9.88	$C_{13}H_9N_3O_5S$
			48.90	2.84	13.16	10.04	
3a	68	152—154	44.85	3.26	11.39	13.40	$C_9H_8N_2O_4S$
			45.00	3.36	11.66	13.35	
3b	79	119—121	47.01	4.05	11.26	12.79	$C_{10}H_{10}N_2O_4S$
			47.24	3.96	11.02	12.61	
3d	65	100—102	55.38	6.14	8.82	10.27	$C_{15}H_{20}N_2O_4S$
			55.54	6.21	8.64	9.88	
3f	71	144—147	54.20	2.88	9.60	10.95	$C_{13}H_8N_2O_4S$
			54.16	2.80	9.72	11.12	
3h	69	160—162	47.00	2.21	12.75	9.84	$C_{13}H_7N_3O_6S$
			46.85	2.12	12.61	9.62	
4a	84	172—176	45.15	3.20	11.83	13.13	$C_9H_8N_2O_4S$
			45.00	3.36	11.66	13.35	
4c	72	113—115	49.42	4.40	10.28	12.14	$C_{11}H_{12}N_2O_4S$
			49.25	4.51	10.44	11.95	
4d	61	58—60	55.76	6.32	8.63	10.05	$C_{15}H_{20}N_2O_4S$
			55.54	6.21	8.64	9.88	
4f	68	211—213	54.46	2.93	9.55	10.97	$C_{13}H_8N_2O_4S$
			54.16	2.80	9.72	11.12	
4h	74	235—240	46.94	2.08	12.77	9.45	$C_{13}H_7N_3O_6S$
			46.85	2.12	12.61	9.62	
8a	54	198—200	45.27	3.71	17.39	—	$C_9H_9N_3O_5$
			45.19	3.79	17.57		
8c	83	122—125	49.60	5.02	15.61	—	$C_{11}H_{13}N_3O_5$
			49.44	4.90	15.72		
8d	69	107—110	55.98	6.63	12.84	—	$C_{15}H_{21}N_3O_5$
			55.72	6.55	13.00		
8f	75	195—199	54.30	3.25	14.83	—	$C_{13}H_9N_3O_5$
			54.36	3.16	14.63		
9a	72	168—170	61.02	5.01	9.10	9.89	$C_{16}H_{16}N_2O_3S$
			60.74	5.10	8.85	10.13	
9c	82	133—135	62.93	5.92	8.00	9.52	$C_{18}H_{20}N_2O_3S$
			62.77	5.85	8.13	9.31	
9d	74	110—112	66.16	6.94	6.75	7.73	$C_{22}H_{28}N_2O_3S$
			65.97	7.05	6.99	8.00	
9f	78	155—158	66.21	4.55	7.47	9.04	$C_{20}H_{16}N_2O_3S$
			65.92	4.43	7.69	8.80	

Table 2. ^{1}H NMR spectra of nitrobenzamides **2a—h**, **8a,c,d,f**, and **9a,c,d,f**

Compound	δ (*J*/Hz)
2a	1.31 (t, 3 H, $CH_2C\underline{H}_3$, J = 5.0); 3.02 (q, 2 H, $C\underline{H}_2CH_3$, J = 8.0); 7.62 (d, 1 H, H(6), J = 6.0); 7.63, 7.96 (both s, 1 H each, NH); 8.00 (d, 1 H, H(5), J = 6.0); 8.08 (s, 1 H, H(3))
2b	1.07 (t, 3 H, $CH_2CH_2C\underline{H}_3$, J = 2.0); 1.32 (q, 2 H, $CH_2C\underline{H}_2CH_3$, J = 6.5); 3.05 (q, 2 H, $C\underline{H}_2CH_2CH_3$, J = 8.0); 7.59 (br.s, 1 H, NH); 7.67 (d, 1 H, H(6), J = 4.5); 7.72 (br.s, 1 H, NH); 7.94 (d, 1 H, H(5), J = 4.5); 8.08 (s, 1 H, H(3))
2c	0.88 (t, 3 H, $CH_2CH_2CH_2C\underline{H}_3$, J = 6.0); 1.30—1.43 (m, 2 H, $CH_2CH_2C\underline{H}_2CH_3$); 1.58—1.71 (m, 2 H, $CH_2C\underline{H}_2CH_2CH_3$); 3.05 (t, 2 H, $C\underline{H}_2CH_2CH_2CH_3$, J = 6.5); 7.61 (br.s, 1 H, NH); 7.62 (d, 1 H, H(6), J = 6.0); 7.79 (br.s, 1 H, NH); 7.89 (d, 1 H, H(5), J = 6.0); 7.92 (s, 1 H, H(3))
2d	0.88 (t, 3 H, $(CH_2)_7C\underline{H}_3$, J = 3.5); 1.31 (br.s, 8 H, $(CH_2)_3(C\underline{H}_2)_4CH_3$); 1.46 (m, 2 H, $(CH_2)_2C\underline{H}_2(CH_2)_4CH_3$); 1.68 (m, 2 H, $CH_2C\underline{H}_2CH_2(CH_2)_4CH_3$); 2.98 (t, 2 H, $C\underline{H}_2(CH_2)_2(CH_2)_4CH_3$, J = 7.0); 7.44 (br.s, 1 H, NH); 7.67 (d, 1 H, H(6), J = 9.0); 7.81 (br.s, 1 H, NH); 7.97 (d, 1 H, H(5), J = 9.0); 8.03 (s, 1 H, H(3))
2e	1.28 (s, 9 H, $C(C\underline{H}_3)_3$); 7.64 (d, 1 H, H(6), J = 7.5); 7.67, 7.79 (both br.s, 1 H each, NH); 7.85 (d, 1 H, H(5), J = 7.5); 7.92 (s, 1 H, H(3))
2f	7.58 (m, 5 H, Ph); 7.78 (d, 1 H, H(6), J = 8.5); 7.86 (s, 1 H, H(3)); 8.05 (d, 1 H, H(5), J = 8.5); 8.28 (br.s, 2 H, NH_2)
2g	1.31 (t, 3 H, $CH_2C\underline{H}_3$, J = 5.0); 3.19 (q, 2 H, $C\underline{H}_2CH_3$, J = 5.5); 7.88, 8.06 (both s, 1 H each, NH_2); 8.33 (s, 1 H, H(5)); 8.54 (s, 1 H, H(3))
2h	7.42—7.62 (m, 5 H, Ph); 7.78 (s, 1 H, NH); 7.87 (s, 1 H, H(5)); 8.07 (s, 1 H, NH); 8.54 (s, 1 H, H(3))
8a	1.18 (t, 3 H, $CH_2C\underline{H}_3$, J = 2.0); 3.31 (quint, 2 H, $C\underline{H}_2CH_3$, J = 3.5); 7.83 (d, 1 H, H(6), J = 5.5); 8.56 (d, 1 H, H(5), J = 5.5); 8.73 (s, 1 H, H(3)); 8.75 (br.s, 1 H, NH)
8c	0.96 (t, 3 H, $CH_2CH_2CH_2C\underline{H}_3$, J = 8.5); 1.42 (q, 2 H, $CH_2CH_2C\underline{H}_2CH_3$, J = 8.5); 1.56 (q, 2 H, $CH_2C\underline{H}_2CH_2CH_3$, J = 8.5); 3.29 (q, 2 H, $C\underline{H}_2CH_2CH_2CH_3$, J = 7.5); 7.82 (d, 1 H, H(6), J = 7.5); 8.58 (d, 1 H, H(5), J = 7.5); 8.60 (s, 1 H, H(3)); 8.73 (br.s, 1 H, NH)
8d	0.88 (t, 3 H, $(CH_2)_7C\underline{H}_3$, J = 3.5); 1.22—1.41 (m, 10 H, $CH_2CH_2(C\underline{H}_2)_5CH_3$); 1.56 (q, 2 H, $CH_2C\underline{H}_2(CH_2)_5CH_3$, J = 7.5); 3.26 (q, 2 H, $C\underline{H}_2CH_2(CH_2)_5CH_3$, J = 7.5); 7.82 (d, 1 H, H(6), J = 9.5); 8.58 (d, 1 H, H(5), J = 9.5); 8.72 (s, 1 H, H(3)); 8.75 (br.s, 1 H, NH)
8f	7.11 (d, 1 H, *p*-H (Ph), J = 7.0); 7.33 (t, 2 H, *m*-H (Ph), J = 7.0); 7.62 (d, 2 H, *o*-H (Ph), J = 7.5); 8.03 (d, 1 H, H(6), J = 9.0); 8.67 (d, 1 H, H(5), J = 9.0); 8.82 (s, 1 H, H(3)); 10.70 (br.s, 1 H, NH)
9a	1.15 (t, 3 H, $CH_2C\underline{H}_3$, J = 3.5); 3.28 (quint, 2 H, $C\underline{H}_2CH_3$, J = 10.0); 4.29 (s, 2 H, CH_2); 7.24 (d, 1 H, *p*-H (Ph), J = 2.5); 7.32 (t, 2 H, *m*-H (Ph), J = 6.5); 7.39 (d, 2 H, *o*-H (Ph), J = 5.5); 7.59 (d, 1 H, H(6), J = 6.5); 8.00 (d, 1 H, H(5), J = 6.5); 8.12 (s, 1 H, H(3)); 8.42 (br.s, 1 H, NH)
9c	0.91 (t, 3 H, $CH_2CH_2CH_2C\underline{H}_3$, J = 7.0); 1.40 (q, 2 H, $CH_2CH_2C\underline{H}_2CH_3$, J = 4.5); 1.56 (q, 2 H, $CH_2C\underline{H}_2CH_2CH_3$, J = 6.5); 3.28 (q, 2 H, $C\underline{H}_2CH_2CH_2CH_3$, J = 2.0); 4.25 (s, 2 H, CH_2); 7.21 (d, 1 H, *p*-H (Ph), J = 3.5); 7.28 (t, 2 H, *m*-H (Ph), J = 7.5); 7.38 (d, 2 H, *o*-H (Ph), J = 7.5); 7.56 (d, 1 H, H(6), J = 9.5); 7.97 (d, 1 H, H(5), J = 9.5); 8.09 (s, 1 H, H(3)); 8.24 (br.s, 1 H, NH)
9d	0.62 (t, 3 H, $(CH_2)_7C\underline{H}_3$, J = 4.5); 1.20—1.42 (m, 10 H, $CH_2CH_2(C\underline{H}_2)_5CH_3$); 1.52 (q, 2 H, $CH_2C\underline{H}_2(CH_2)_5CH_3$, J = 6.5); 3.21 (q, 2 H, $C\underline{H}_2CH_2(CH_2)_5CH_3$, J = 6.5); 4.06 (s, 2 H, CH_2); 7.25 (d, 1 H, *p*-H (Ph), J = 5.5); 7.29 (t, 2 H, *m*-H (Ph), J = 7.5); 7.39 (d, 2 H, *o*-H (Ph), J = 5.0); 7.56 (d, 1 H, H(6), J = 5.0); 7.99 (d, 1 H, H(5), J = 5.0); 8.12 (s, 1 H, H(3)); 8.38 (br.s, 1 H, NH)
9f	4.32 (s, 2 H, CH_2); 7.05—7.49 (m, 10 H, 2 Ph); 7.78 (d, 1 H, H(6), J = 9.0); 8.09 (d, 1 H, H(5), J = 9.0); 8.19 (s, 1 H, H(3)); 10.42 (br.s, 1 H, NH)

tained in the solvent into *S*-oxides **11**. The latter are either oxidized into sulfone **7** (R = NO_2, R′ = Et) or chlorinated at the carbamoyl N atom to give *N*-chloroamines **12**, which undergo cyclization into sulfoximides **3a,b,d,f,h** according to the known scheme.[12] The formation of intermediate *S*-oxides **11** was confirmed by the synthesis of compound **11a** from amide **2a** and MCPBA followed by its conversion into sulfoximide **3a** under the action of Cl_2 in 60% AcOH. Unlike *S*-oxide **11a**, sulfone **13** obtained by oxidation of amide **2a** with an excess of MCPBA does not yield sulfoximide **3a** upon chlorination under these conditions.

Presumably, the direction of the reactions of *S*-oxides **11** with chlorine depends on the relative nucleophilicity of the N and S atoms. Thus for R = H, the more nucleophilic N atom is chlorinated to give compounds **3a,b,d,f**; for R = NO_2 and R′ = Alk, chlorination of the S atom yields sulfone **7**.

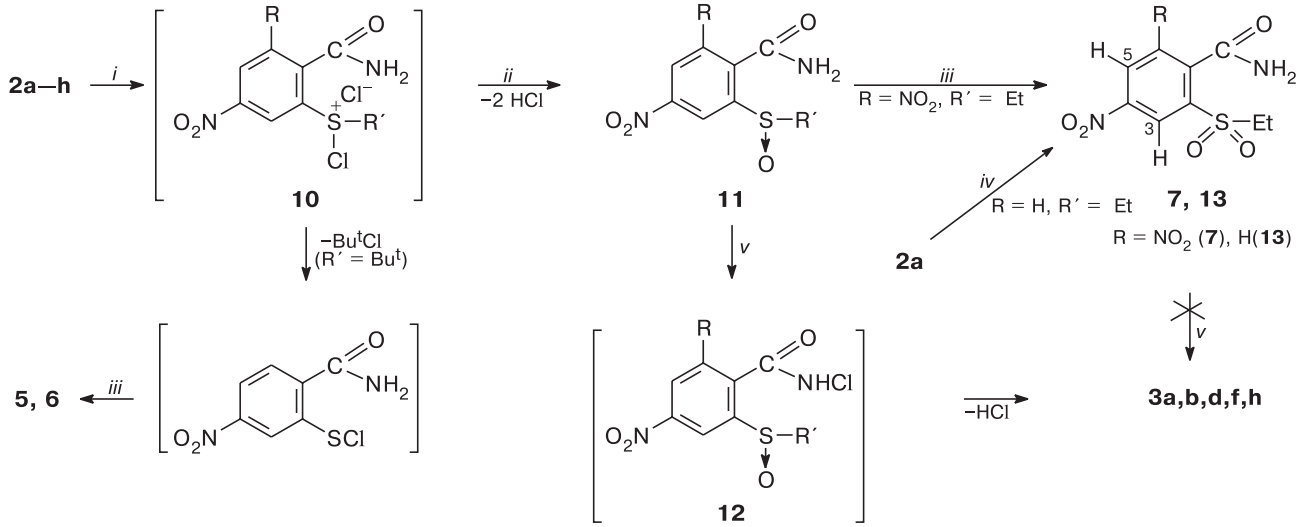
(*tert*-Butyl) chlorosulfonium chloride (**10e**) containing the easily leaving Bu^t group seems to eliminate *tert*-butyl chloride,[13] giving products **5** and **6** according to the known scheme.[8]

The available data are insufficient to explain the S→N migration of the Bu^n group in the reaction of com-

Table 3. Retention factors (R_f), IR, and ^{1}H NMR data for the nitro derivatives of 1-R′-1,2-benzoisothiazol-3-one 1-oxides **3a,b,d,f,h** and 2-R′-1,2-benzoisothiazol-3-one 1-oxides **4a,c,d,f,h**

Compound	R_f	IR, ν/cm^{-1}			δ (*J*/Hz)
		C=O	S=O (s)	NO_2 (s)	
3a	0.38	1600 w	1140	1360	1.29 (t, 3 H, $CH_2C\underline{H}_3$, J = 2.0); 3.53 (q, 2 H, $C\underline{H}_2CH_3$, J = 2.5);
			1160	1540	8.44 (d, 1 H, H(4), J = 7.5); 8.69 (d, 1 H, H(5), J = 7.5); 8.75 (s, 1 H, H(7))
3b	0.36	1600 w	1130	1350	1.08 (t, 3 H, $CH_2CH_2C\underline{H}_3$, J = 1.5); 1.78 (m, 2 H, $CH_2C\underline{H}_2CH_3$);
			1150	1540	3.49 (t, 2 H, $C\underline{H}_2CH_2CH_3$, J = 6.5); 8.42 (d, 1 H, H(4), J = 9.0);
					8.71 (d, 1 H, H(5), J = 9.0); 8.75 (s, 1 H, H(7))
3d	0.44	1600 w	1120	1345	0.88 (t, 3 H, $(CH_2)_7C\underline{H}_3$, J = 1.5); 1.27 (br.s, 8 H, $(CH_2)_3(C\underline{H}_2)_4CH_3$);
			1155	1540	1.46 (br.s, 2 H, $(CH_2)_2C\underline{H}_2(CH_2)_4CH_3$); 1.73 (br.s, 2 H, $CH_2C\underline{H}_2CH_2(CH_2)_4CH_3$);
					3.47 (t, 2 H, $C\underline{H}_2(CH_2)_6CH_3$, J = 2.5); 8.42 (d, 1 H, H(4), J = 6.0);
					8.64 (d, 1 H, H(5), J = 6.0); 8.68 (s, 1 H, H(7))
3f	0.31	1610 w	1140	1360	7.67—7.89 (m, 3 H, *p*-H + *m*-H (Ph)); 8.11 (d, 2 H, *o*-H (Ph), J = 10.0);
			1170	1540	8.43 (d, 1 H, H(4), J = 8.5); 8.69 (d, 1 H, H(5), J = 8.5); 8.91 (s, 1 H, H(7))
3h	0.31	1610 w	1135	1355	7.75 (t, 2 H, *m*-H (Ph), J = 7.5); 7.93 (d, 1 H, *p*-H (Ph), J = 8.0);
			1165	1540	8.23 (d, 2 H, *o*-H (Ph), J = 7.5); 9.21 (s, 1 H, H(5)); 9.49 (s, 1 H, H(7))
4a	0.18	1645 s	1135	1350	1.36 (t, 3 H, $CH_2C\underline{H}_3$, J = 4.0); 3.83 (dt, 1 H, CH_2, J_1 = 6.5, J_2 = 5.0);
			1155	1540	3.93 (dt, 1 H, CH_2, J_1 = 6.5, J_2 = 5.0); 8.18 (d, 1 H, H(4), J = 3.5);
					8.62 (d, 1 H, H(5), J = 3.5); 9.08 (s, 1 H, H(7))
4c	0.19	1645 s	1140	1350	0.93 (t, 3 H, $CH_2CH_2CH_2C\underline{H}_3$, J = 4.0); 1.48 (q, 2 H, $CH_2CH_2C\underline{H}_2CH_3$, J = 5.0);
			1150	1540	1.72 (q, 2 H, $CH_2C\underline{H}_2CH_2CH_3$, J = 5.0); 3.78 (dt, 1 H, CH_2, J_1 = 6.0, J_2 = 7.0);
					3.84 (dt, 1 H, CH_2, J_1 = 6.0, J_2 = 7.0); 8.20 (d, 1 H, H(4), J = 8.0);
					8.66 (d, 1 H, H(5), J = 8.0); 9.08 (s, 1 H, H(7))
4d	0.22	1645 s	1130	1345	0.86 (t, 3 H, $(CH_2)_7C\underline{H}_3$, J = 3.5); 1.21—1.42 (m, 10 H, $CH_2CH_2(C\underline{H}_2)_5CH_3$);
			1150	1540	1.68—1.80 (m, 2 H, $CH_2C\underline{H}_2(CH_2)_5CH_3$); 3.74 (dt, 1 H, CH_2, J_1 = 5.0, J_2 = 5.5);
					3.85 (dt, 1 H, CH_2, J_1 = 5.0, J_2 = 5.5); 8.18 (d, 1 H, H(4), J = 7.5);
					8.61 (d, 1 H, H(5), J = 7.5); 9.08 (s, 1 H, H(7))
4f	0.18	1700 s	1120	1540	7.48—7.62 (m, 5 H, Ph); 8.25 (d, 1 H, H(6), J = 4.5); 8.65 (d, 1 H, H(5), J = 4.5);
			1170	1350	9.18 (s, 1 H, H(7))
4h	0.16	1715 s	1105	1350	7.50—7.69 (m, 5 H, Ph); 9.15 (s, 1 H, H(5));
			1150	1560	9.47 (s, 1 H, H(7))

Scheme 4



Reagents and conditions: *i*. Cl_2. *ii*. H_2O. *iii*. Cl_2—H_2O. *iv*. MCPBA, CH_2Cl_2. *v*. Cl_2, AcOH—H_2O.

pound **2c** with chlorine in 60% AcOH, which affords 2-(*n*-butyl)-6-nitro-1,2-benzoisothiazol-3-one 1-oxide (**4c**).

Hence, a detailed study of the reactions of nitro derivatives of 2-alkylthio- and 2-phenylthiobenzamides with chlorine in aqueous organic solvents made it possible to develop the new convenient synthesis of cyclic sulfoximides of the 1,2-benzoisothiazole series.

Experimental

^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 MHz) in DMSO-d_6 with Me_4Si as the internal standard. Thin-layer chromatography was carried out on Silpearl UV-250 silica gel in CCl_4—acetone (4 : 1).

4,6-Dinitro- and 2,4,6-trinitrobenzamides were prepared according to the known procedure.[14] *N*-Phenyl-2,4,6-trinitrobenzamide **8h** and *N*-phenyl-2-benzylthio-4,6-dinitrobenzamide **9h** were synthesized as described in Ref. 9.

2-Alkylthio(arylthio)-4-nitro- and -4,6-dinitrobenzamides 2a—h and 9a,c,d,f (general procedure). A corresponding thiol (2.2 mmol) and Na_2CO_3 (0.24 g, 2.2 mmol) were added successively to a solution of amide **1a,b** or **8a,c,d,f** (2 mmol) in DMF (8 mL). The reaction mixture was stirred at 20 °C for 5—8 h (in the case of thiophenol, the reaction was carried out in an atmosphere of nitrogen) until the starting amide was completely consumed (TLC) and then acidified with 0.05 *M* HCl (15 mL). The precipitate that formed was filtered off, washed with water (2×5 mL), dried in air, and recrystallized from Pr^{i}OH. The yields, melting points, and elemental analysis data for the compounds obtained are given in Table 1. Their ^{1}H NMR spectra are presented in Table 2.

1-Alkyl(aryl)-4-nitro- and 4,6-dinitro-1-phenyl-1,2-benzoisothiazol-3-one 1-oxides 3a,b,d,f,h (general procedure). Gaseous chlorine was passed at 20 °C for 10 min through a solution of an amide (**2a,b,d,f,h** or **11a**) (2 mmol) in 60% AcOH (7 mL), and the reaction mixture was stirred for 10 min. The solvent and the excess of chlorine were removed *in vacuo*. Cold Pr^{i}OH (3—5 mL) was added, and the precipitate that formed was filtered off, dried in air, and recrystallized from Pr^{i}OH. The yields, melting points, and elemental analysis data for compounds **3a,b,d,f,h** are given in Table 1. Their retention factors, ^{1}H NMR and IR spectra are presented in Table 3.

2-Alkyl(aryl)-4-nitro- and 4,6-dinitro-2-phenyl-1,2-benzoisothiazol-3-one 1-oxides 4a,c,d,f,h (general procedure). Gaseous chlorine was passed at 20 °C for 10 min through a solution of an amide (**9a,c,d,f,h**) (2 mmol) in a mixture of CH_2Cl_2 (10 mL) and water (0.5 mL), and the reaction mixture was stirred for 15 min. The solvent and the excess of chlorine were removed *in vacuo*. Cold Pr^{i}OH (3—5 mL) was added, and the precipitate that formed was filtered off, dried in air, and recrystallized from Pr^{i}OH. The yields, melting points, and elemental analysis data for compounds **4a,c,d,f,h** are given in Table 1. Their retention factors, ^{1}H NMR and IR spectra are presented in Table 3.

6-Nitro-1,2-benzoisothiazol-3-one 1,1-dioxide (5). Gaseous chlorine was passed for 15 min through a vigorously stirred solution of amide **2e** (0.51 g, 2 mmol) in 60% AcOH (7 mL). The reaction mixture was stirred at ~20 °C for 25 min, and the solvent was removed *in vacuo*. Cold Pr^{i}OH was added, and the precipitate that formed was filtered off, dried in air, and recrystallized from Pr^{i}OH to give dioxide **5** (0.15 g, 36%), m.p. 281—282 °C (*cf.* Ref. 8: m.p. 281—283 °C).

6-Nitro-1,2-benzoisothiazol-3-one 1-oxide (6). Gaseous chlorine was passed for 20 min through a solution of amide **2e** (0.51 g, 2 mmol) in a mixture of CH_2Cl_2 (10 mL) and water (0.5 mL). The reaction mixture was stirred at ~20 °C for 15 min, and the solvent was removed *in vacuo*. Cold Pr^{i}OH was added, and the precipitate that formed was filtered off, dried in air, and recrystallized from Pr^{i}OH to give oxide **6** (0.14 g, 34%), m.p. 244—247 °C (*cf.* Ref. 8: m.p. 244—247 °C).

2-Ethylsulfonyl-4,6-dinitrobenzamide (7). Gaseous chlorine was passed at 20 °C for 10 min through a solution of amide **2g** (0.54 g, 2 mmol) in 60% AcOH (7 mL). The reaction mixture was stirred for 15 min. The solvent and the excess of chlorine were removed *in vacuo*. The resulting oil was treated with cold Pr^{i}OH, and the precipitate that formed was filtered off, dried in air, and recrystallized from Pr^{i}OH to give compound **7** (0.45 g, 70%), m.p. 175—178 °C. Found (%): C, 35.47; H, 3.03; N, 13.74, S, 10.46. $C_9H_9N_3O_7S$. Calculated (%): C, 35.65; H, 2.99; N, 13.86; S, 10.57. ^{1}H NMR, δ: 1.29 (t, 3 H, C$\underline{H}_3$CH$_2$, J = 7.5 Hz); 3.63 (q, 2 H, CH$_3$C$\underline{H}_2$, J = 7.5 Hz); 7.96, 8.24 (both br.s, 1 H each, NH); 8.88 (s, 1 H, H(3)); 9.09 (s, 1 H, H(5)).

***N*-Alkyl(aryl)-2,4-dinitrobenzamides 8a,c,d,f (general procedure).** Thionyl chloride (0.44 mL, 0.72 g, 6 mmol) and DMF (one to two drops) were added to a suspension of 2,4-dinitrobenzoic acid (0.42 g, 1.98 mmol) in anhydrous benzene (5 mL), and the reaction mixture was refluxed for 3 h. The solvent and the excess of $SOCl_2$ were removed at a reduced pressure. Anhydrous benzene (3—4 mL) was added, and the solvent was removed again. The 2,4-dinitrobenzoyl chloride obtained was dissolved in anhydrous benzene (5 mL) and stirred at 15 °C while gradually adding an amine (4.2 mmol) (for **8d,f**) or an amine hydrochloride (2.1 mmol) and aqueous Na_2CO_3 (0.44 g, 4.2 mmol) (for **8a,c**). The reaction mixture was stirred at 5 °C for 30 min. The precipitate that formed was filtered off, washed with distilled water (2×2 mL), dried in air, and recrystallized from Pr^{i}OH—acetone. The characteristics of compounds **8a,c,d,f** are given in Tables 1 and 2.

2-Ethylsulfinyl-4-nitrobenzamide (11a). A mixture of 60% MCPBA (0.54 g, 2 mmol) and amide **2a** (0.45 g, 2 mmol) in CH_2Cl_2 (7 mL) was stirred at −70 °C for 4 h. The precipitate that formed was filtered off, and the organic layer was washed with water (4×5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo*; the residue was triturated with cold hexane and crystallized from Pr^{i}OH to give compound **11a** (0.26 g, 50%), m.p. 140—142 °C. Found (%): C, 44.78; H, 4.31; N, 11.35; S, 13.11. $C_9H_{10}N_2O_4S$. Calculated (%): C, 44.62; H, 4.16; N, 11.56; S, 13.24. ^{1}H NMR, δ: 1.21 (t, 3 H, C$\underline{H}_3$CH$_2$, J = 6.5 Hz); 2.75, 3.29 (both m, 1 H each, CH$_2$); 7.78 (s, 1 H, NH); 8.18 (d, 1 H, H(6), J = 6.0 Hz); 8.38 (s, 1 H, NH); 8.41 (d, 1 H, H(5), J = 6.0 Hz); 8.76 (s, 1 H, H(3)).

2-Ethylsulfonyl-4-nitrobenzamide (13). A mixture of 60% MCPBA (1.08 g, 4 mmol) and amide **2a** (0.45 g, 2 mmol) in CH_2Cl_2 (7 mL) was stirred at 20 °C for 4 h. The precipitate that formed was filtered off, and the organic layer was washed with water (4×5 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo*; the residue was triturated with cold hexane and crystallized from Pr^{i}OH to give compound **13**

(0.33 g, 61%), m.p. 152—155 °C. Found (%): C, 41.75; H, 3.98; N, 10.98; S, 12.62. $C_9H_{10}N_2O_5S$. Calculated (%): C, 41.86; H, 3.90; N, 10.85; S, 12.42. ^{1}H NMR, δ: 1.36 (t, 3 H, $C\underline{H}_3CH_2$, J = 6.5 Hz); 3.82 (q, 2 H, $CH_3C\underline{H}_2$, J = 7.0 Hz); 7.78 (s, 1 H, NH); 8.18 (d, 1 H, H(6), J = 6.0 Hz); 8.38 (s, 1 H, NH); 8.41 (d, 1 H, H(5), J = 6.0 Hz); 8.76 (s, 1 H, H(3)).

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Received December 13, 2001;
in revised form March 11, 2002