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Reactions of *N*-(2,2-Dichloro-2-phenylethylidene)arenesulfonamides with Aromatic and Heterocyclic Compounds

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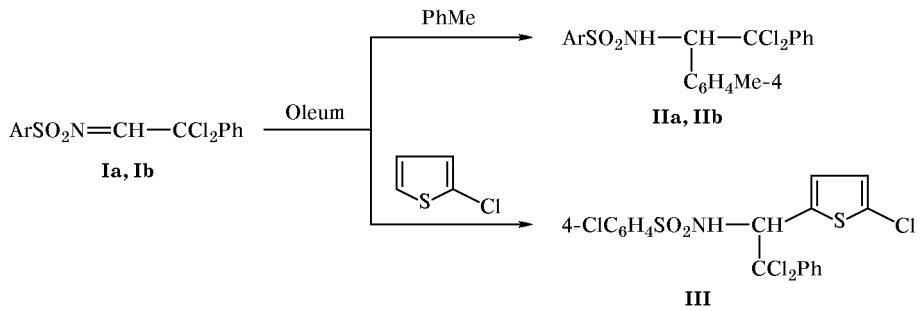
Abstract—Benzene, toluene, and 2-chlorothiophene regioselectively react with *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides in the presence of oleum to give *N*-[1-aryl(or hetaryl)-2,2-dichloro-2-phenylethyl]arenesulfonamides. Analogous *C*-amidoalkylation products are formed by the action of *N*-(2,2-dichloro-1-hydroxy-2-phenylethyl)- and *N*-(1-arylsulfonylamino-2,2-dichloro-2-phenylethyl)arenesulfonamides on toluene and 2-chlorothiophene in concentrated sulfuric acid.

As shown previously [1–3], reactions of *N*,*N*-dichloroarenesulfonamides with phenylacetylene follow a radical mechanism and result in formation of *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides **I**. In continuation of our systematic studies on the reactivity of the CH=N group attached to strong electron-acceptor fragments [4, 5], we examined the behavior of *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides **I** in C-amidoalkylation of aromatic and heteroaromatic compounds with the goal of obtaining *N*-polychloroethylsulfonamides having an aromatic substituent in the α-position with respect to the nitrogen atom. The synthesis of *N*-(1-arylpolychloroethyl)-sulfonamides seemed to be important, for the hydrolysis of *N*-(1-aryl-2,2,2-trichloroethyl)amides is known to involve the halogen atoms while the concurrent hydrolytic cleavage of the C–N bond occurs to a lesser extent [6, 7]. This opens the possibility for synthesis of N-substituted 1-aminocarbonyl compounds and their derivatives on the basis of *N*-dichloroethylamides.

The reaction of amide **Ia** with anisole was shown [8] to occur in the presence of boron trifluoride–diethyl ether complex. However, we failed to effect an analogous reaction with benzene and its alkyl and halogen derivatives in the presence of Lewis acids. We found that toluene, as well as 2-chlorothiophene, readily reacts with *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides **I** in the presence of oleum. The reactions were carried out with excess aromatic substrate under vigorous stirring without heating; the process was complete in 2–3 h, and the products

Scheme 1.



I, **II**, Ar = Ph (**a**), 4-ClC_6H_4 (**b**).

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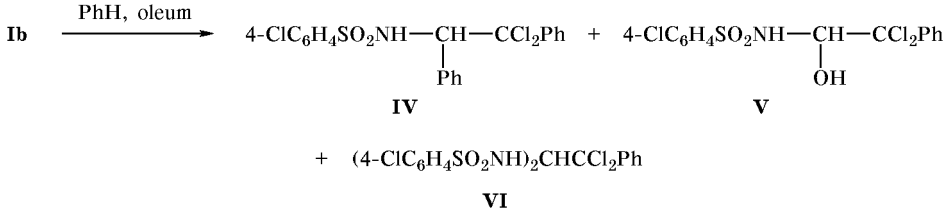
Scheme 2.



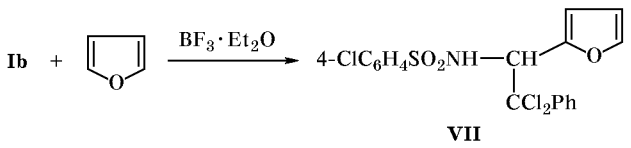
were *N*-(1-aryl-2,2-dichloro-2-phenylethyl)arenesulfonamides **II** and **III** which were formed in good yields (Scheme 1, Table 1). It should be emphasized that the reaction is regioselective: only 4-substituted benzene derivatives **IIa** and **IIb** and 2,5-disubstituted thiophene derivative **III** are formed (Table 2).

Amides **I** reacted with benzene in the presence of oleum in a more complicated manner. ^{1}H NMR study of the reaction mixture obtained from compound **Ib** showed the formation of C-amidoalkylation product **IV**. In addition, *N*-(2,2-dichloro-1-hydroxy-2-phenylethyl)-4-chlorobenzenesulfonamide (**V**) and 1,1-dichloro-2,2-bis(4-chlorophenylsulfonylamino)-1-phenylethane (**VI**) were formed, the latter being the major product (Scheme 2). Unlike *N*-(2,2,2-trichloroethylidene)arenesulfonamides which readily react with both benzene and chlorobenzene [9], amides **I** failed to react with chlorobenzene. Under more severe conditions (heating for 10 h at 50°C in the presence of excess oleum) the mixture underwent tarring.

We previously found [10] that *N*-(2,2,2-trichloroethylidene)arenesulfonamides are capable of reacting with 1,8-bis(dimethylamino)naphthalene without a catalyst to give C-amidoalkylation products. We did not succeed in obtaining the corresponding products by reactions of 1,8-bis(dimethylamino)naphthalene with amides **I** despite prolonged keeping (20 days) of the reaction mixture.

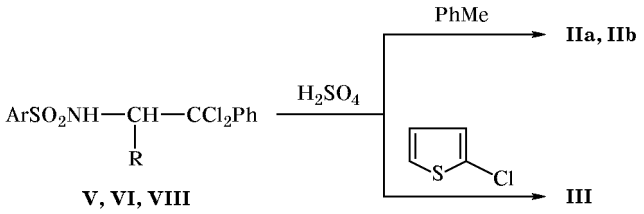
Amide **Ib** was brought into reaction with furan in the presence of boron trifluoride–ether complex. The reaction was carried out in carbon tetrachloride using a small excess of furan. As a result, *N*-[2,2-dichloro-1-(2-furyl)-2-(4-chlorophenyl)ethyl]-4-chlorobenzenesulfonamide (**VII**) was obtained (Scheme 3). No reaction occurred in the absence of a catalyst, in contrast to the known [11] reaction of *N*-(2,2,2-trichloroethylidene)arenesulfonamides with furan. The yield of **VII** can be increased by heating the mixture for 24 h at 40–50°C.

Scheme 3.



C-Amidoalkylation products **II** and **III** were also synthesized by the action of *N*-(2,2-dichloro-1-hydroxy-2-phenylethyl)arenesulfonamides **V** and **VIII** and 1,1-dichloro-2,2-bis(4-chlorophenylsulfonylamino)-1-phenylethane (**VI**) on toluene and 2-chlorothiophene in the presence of concentrated sulfuric acid (Scheme 4). The highest yields of compounds **IIa** and **IIb** were obtained when the aromatic substrate was used as solvent. With equimolar amounts of the reactants in carbon tetrachloride or chloroform amide **V** is converted into bis-amide **VI**.

Scheme 4.



VIII, R = OH, Ar = Ph.

Reactions of **V** with benzene and chlorobenzene in the presence of concentrated sulfuric acid gave no corresponding C-amidoalkylation products, but amide **V** was converted into 1,1-dichloro-2,2-bis(4-chlorophenylsulfonylamino)-1-phenylethane (**VI**). By special experiments we showed that compound **VI** itself reacts neither with benzene nor with chlorobenzene. Presumably, bis-amide **VI** is formed as a result of condensation of **V** with 4-chlorobenzenesulfonamide which is formed from **V** in acid medium. The formation of structures like **VI** was also noted in [12] where we studied the amidoalkylating activity of *N*-(2,2,2-trichloroethyl)arenesulfonamides having a readily departing group in the α-position with respect to the nitrogen atom [12].

The structure of products **II**–**IV** and **VII** was confirmed by elemental analysis and IR and ^{1}H NMR

Table 1. Yields, melting points, and elemental analyses of compounds **II**, **III**, and **V**–**VIII**

Comp. no.	Yield, % (method)	mp, °C	Found, %				Formula	Calculated, %			
			C	Cl	N	S		C	Cl	N	S
IIa	91 (*a*), 93 (*b*)	206–208	59.83	16.67	3.10	7.43	$C_{21}H_{19}Cl_2NO_2S$	60.00	16.87	3.33	7.63
IIb	95 (*a*), 87 (*b*), 63 (*c*)	225–227	55.19	23.06	2.59	6.79	$C_{21}H_{18}Cl_3NO_2S$	55.46	23.39	3.08	7.05
III	73 (*a*), 68 (*b*), 58 (*c*)	179–180	44.62	30.99	2.80	12.99	$C_{18}H_{13}Cl_4NO_2S_2$	44.93	29.47	2.91	13.32
V	100	123–125	44.01	27.50	3.43	8.83	$C_{14}H_{12}Cl_3NO_3S$	44.17	27.94	3.68	8.42
VI	21 (*a*), 76 (*b*)	218–220	43.21	25.05	4.88	11.71	$C_{20}H_{16}Cl_4N_2O_4S_2$	43.48	25.34	5.07	11.59
VII	58	151–153	50.53	23.50	3.39	7.23	$C_{18}H_{14}Cl_3NO_3S$	50.19	24.69	3.25	7.44
VIII	99	127–129[a]	48.32	20.41	3.92	9.37	$C_{14}H_{13}Cl_2NO_3S$	48.57	20.48	4.05	9.26

[a] Published data [2]: mp 126–127°C.

Table 2. IR and ^{1}H NMR spectra of compounds **II**, **III**, and **V**–**VIII**

Comp. no.	IR spectrum, ν, cm^{-1}			^{1}H NMR spectrum (DMSO-d_6), δ, ppm			J_{NHCH}, Hz
	NH	SO_2	other bands	CH	NH	H_{arom}	
IIa[a]	3270	1320, 1180	2950–2850 (C−H_{aliph}), 1450 (C=C_{arom})	5.36 d	9.03 d	6.77; 7.03 (*AA′BB′*, 4-MeC_6H_4); 7.27–7.70 m	10.8
IIb[a]	3270	1330, 1160	2950–2850 (C−H_{aliph}), 1480 (C=C_{arom})	5.20 d	8.85 d	6.72; 6.91 (*AA′BB′*, 4-MeC_6H_4); 7.16; 7.52 (*AA′BB′*, 4-ClC_6H_4); 7.31–7.62 m (H_{arom})	10.4
IIc	3280	1320, 1170	1480 (C=C_{arom})	5.35 d	9.01 d	6.96–7.57 m	10.0
III	3250	1330, 1170	1440 (C=C_{arom})	5.47 d	9.04 d	6.64 d, 6.68 d (2-thienyl); 7.38–7.70 m	10.2
V	3190[b] 3260	1330, 1160	3520, 3430 (OH)[b]; 1450 (C=C_{arom})	5.44 d	8.56 d	7.52–7.82 m	9.7
VI	3280	1340, 1160	1480 (C=C_{arom})	5.73 t	9.01 d	7.25–7.60 m	9.2
VII	3230	1360, 1180	1440 (C=C_{arom})	5.23 d	8.93 d	6.10–6.18 m (2-furyl); 7.23–7.62 m	10.3
VIII	3280	1340, 1170	3490 (OH), 1450 (C=C_{arom})	5.42 d	8.52 d	7.55–7.73 m	9.0

[a] δ(CH_3), ppm: 2.11 s (**IIa**), 2.10 s (**IIb**).

[b] Doublet bands are likely to result from the existence of two stable conformers.

spectroscopy (Tables 1, 2). Their IR spectra contained absorption bands typical of NH and SO_2 groups, aromatic C=C bonds, and alkyl C–H bonds. In the ^{1}H NMR spectra of **II**–**IV** and **VII** we observed signals from protons of aromatic and heteroaromatic rings and characteristic doublet signals from the NHCH fragment. The aromatic proton signals of toluene derivatives **IIa** and **IIb** form an *AA′BB′* spin system, which indicates that the substitution occurred at the *para*-position. The signals from the thienyl ring protons in **III** correspond to the 2,5-substitution pattern. Likewise, the ^{1}H NMR spectrum of **VII** is consistent with the presence of 2-furyl substituent (Table 2). The NHCH group in amide **V** gives rise to two doublets in the ^{1}H NMR spectrum, but the CH signal is located in a weaker field than those of compounds **II** and **IV** (Table 2); this may be due to effect of the hydroxy group oxygen atom in the α-position. The NHCHNH fragment of **VI** appears in the spectrum as a doublet (NH) and a triplet at δ 5.73 ppm (CH); the doublet being twice as intense as the triplet. Thus the ^{1}H NMR spectrum of a mixture of products **IV**, **V**, and **VI** can readily be interpreted.

Compounds **II**–**IV** and **VII** are colorless or slightly colored crystalline substances with a specific odor. They are soluble in DMSO, acetone, and aromatic hydrocarbons and insoluble in water.

Our results indicate a weaker C-amidoalkylating activity of *N*-(2,2-dichloro-2-phenylethylidene)arenesulfonamides and their derivatives, as compared to *N*-(2,2,2-trichloroethylidene) analogs.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker DPX-400 instrument at 400 MHz from 5–10 wt % solutions in DMSO-d_6 containing HMDS as internal reference. The IR spectra were obtained on a Specord 75IR spectrometer in KBr.

***N*-[2,2-Dichloro-1-(4-methylphenyl)-2-phenylethyl]benzenesulfonamide (IIa).** *a.* A mixture of 3.28 g (0.01 mol) of amide **Ia** [2], 5 ml of toluene, and 0.5 ml of oleum (~20% of SO_3) was vigorously stirred for 3 h. Water, 5 ml, was added, and the undissolved material was filtered off, dried, and recrystallized from acetone–carbon tetrachloride (1 : 1).

b. A mixture of 3.46 g (0.01 mol) of amide **VIII** [2], 5 ml of toluene, and 2 ml of concentrated sulfuric acid was vigorously stirred for 3 h. The mixture was then treated as described above in *a*.

***N*-[2,2-Dichloro-1-(4-methylphenyl)-2-phenylethyl]-4-chlorobenzenesulfonamide (IIb).** *a.* Compound **IIb** was synthesized as described above for **IIa** (method *a*) from 3.62 g (0.01 mol) of amide **Ib** [1] and toluene in the presence of oleum.

b. The procedure was similar to that described above for compound **IIa** (method *b*); 3.81 g (0.01 mol) of amide **V** and 5 ml of toluene were taken.

c. A mixture of 2.27 g (0.005 mol) of compound **VI**, 5 ml of toluene, and 1–1.5 ml of concentrated sulfuric acid was vigorously stirred for 5 h. Excess toluene was distilled off under reduced pressure, and the residue was washed first with 30% aqueous ammonia and then with water until neutral reaction. The undissolved material was recrystallized from benzene.

***N*-[2,2-Dichloro-1-(5-chloro-2-thienyl)-2-phenylethyl]-4-chlorobenzenesulfonamide (III).** *a.* Amide **III** was synthesized as described above for **IIa** (method *a*) from 3.62 g (0.01 mol) of amide **Ib** [1] and 5 ml of 2-chlorothiophene in the presence of oleum.

b. Amide **III** was synthesized as described above for **IIa** (method *b*) from 3.81 g (0.01 mol) of amide **V** and 5 ml of 2-chlorothiophene in the presence of concentrated sulfuric acid.

c. Amide **III** was synthesized as described above for compound **IIb** (method *c*) from 2.27 g (0.005 mol) of amide **VI** and 5 ml of 2-chlorothiophene in the presence of 1–1.5 ml of concentrated sulfuric acid.

***N*-(2,2-Dichloro-1,2-diphenylethyl)-4-chlorobenzenesulfonamide (IV).** A mixture of 3.62 g (0.01 mol) of amide **Ib**, 5 ml of benzene, and 0.5 ml of oleum was stirred for 5 h and was then treated as described for compound **IIa** (method *a*). According to the ^{1}H NMR data, the mixture contained 22% of amide **IV**, 10% of hydroxyethylamide **V**, and 68% of diamide **VI**. ^{1}H NMR spectrum, δ, ppm: amide **IV**: 5.34 d (CH, J_{NHCH} = 9.31 Hz), 9.01 d (NH); **V**: 5.42 d (CH, J_{NHCH} = 9.36 Hz), 8.57 d (NH); **VI**: 5.73 t (CH, J_{NHCH} = 9.43 Hz), 9.01 d (NH). Signals from aromatic protons were difficult to assign.

***N*-(2,2-Dichloro-1-hydroxy-2-phenylethyl)-4-chlorobenzenesulfonamide (V).** A mixture of 3.62 g (0.01 mol) of amide **Ib** [1] and 5 ml of water was vigorously stirred and was then left to stand for 20 h. The undissolved material was filtered off and dried.

1,1-Dichloro-2,2-bis(4-chlorophenylsulfonylamino)-1-phenylethane (VI). *a.* Compound **VI** was obtained by the procedure reported in [2] as a by-product of the reaction of 7.82 g (0.03 mol) of *N*,*N*,4-trichlorobenzenesulfonamide and 4 ml (~0.04 mol) of phenylacetylene.

b. A mixture of 3.81 g (0.01 mol) of amide **V**, 1 ml of concentrated sulfuric acid, and 5 ml of

benzene, chlorobenzene, or chloroform was vigorously stirred for 5 h. Water, 5 ml, was added, and the precipitate was filtered off, dried under reduced pressure, and recrystallized from benzene.

***N*-[2,2-Dichloro-1-(2-furyl)-2-phenylethyl]-4-chlorobenzenesulfonamide (VII).** A mixture of 3.62 g (0.01 mol) of amide **Ib**, 1.2 ml (~0.02 mol) of furan, 5 ml of carbon tetrachloride, and 1 drop of freshly distilled boron trifluoride–ether complex was thoroughly stirred and was kept for 5 h at 40–50°C and for 20 h at –5°C. The precipitate of amide **VII** was filtered off and recrystallized from benzene.

***N*-(2,2-Dichloro-1-hydroxy-2-phenylethyl)benzenesulfonamide (VIII)** was synthesized by treatment with water of 3.28 g (0.01 mol) of amide **Ia**, following the procedure reported in [2].

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