Russian Journal of Organic Chemistry, Vol. 37, No. 1, 2001, pp. 96–100. Translated from Zhurnal Organicheskoi Khimii, Vol. 37, No. 1, 2001, pp. 106–110.

Alkylation of Phenols with *N*-(2,2,2-Trichloroethylidene)- and *N*-(2,2,2-Trichloroethyl)arenesulfonamides

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Received February 8, 2000

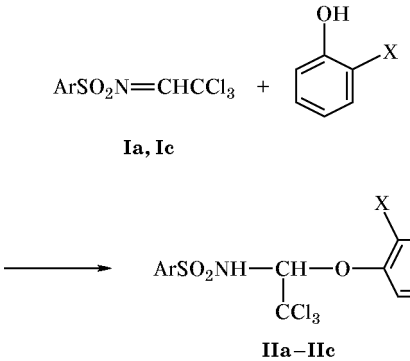
Abstract—*N*-(2,2,2-Trichloroethylidene)- and *N*-(2,2,2-trichloroethyl)arenesulfonamides react with phenol, 2-chlorophenol, and 2-methylphenol in the presence of oleum or sulfuric acid to give the corresponding 4-(2,2,2-trichloro-1-arylsulfonylaminoethyl)phenols in good yields.

We previously showed that reactions of *N*-(2,2,2-trichloroethylidene)arenesulfonamides with aromatic and some heterocyclic compounds in the presence of oleum lead to formation of 1-arylsulfonylaminoethyl-substituted arenes and hetarenes in up to 90% yield [1]. *N*-(Tri- and dichloroethyl)arenesulfonamides with functional substituents in position *1* of the *N*-ethyl group are efficient C-amidoethylating agents for aromatic compounds in the presence of sulfuric acid [2–4]. In the present communication we report on the results of our study of the reaction of *N*-(2,2,2-trichloroethylidene)arenesulfonamides **Ia**–**Ic** and *N*-(2,2,2-trichloroethyl)arenesulfonamides **II** with phenol, 2-chlorophenol, and 2-methylphenol in the presence of oleum and sulfuric acid.

N-(2,2,2-Trichloroethylidene)benzenesulfonamide **Ia** is known to react with phenol in the absence of a catalyst to give product of phenol addition at the activated CH=N bond, *N*-(2,2,2-trichloro-1-phenoxyethyl)benzenesulfonamide (**IIa**) [5]. By analogous reactions of *N*-(2,2,2-trichloroethylidene)-4-chlorobenzenesulfonamide (**Ic**) with phenol and 2-methylphenol we obtained addition products **IIb** and **IIc** (Scheme 1).

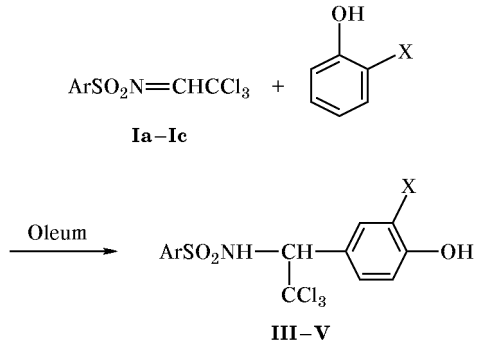
We have found that reactions of *N*-(2,2,2-trichloroethylidene)arenesulfonamides **Ia**–**Ic** with 2-chloro- and 2-methylphenols in the presence of oleum result in formation of previously unknown 4-substituted phenol derivatives, *N*-[2,2,2-trichloro-1-(4-hydroxyphenyl)ethyl]arenesulfonamides **III**–**V** (Scheme 2).

Scheme 1.



II, Ar = C_6H_5, X = H (**a**); Ar = 4-ClC_6H_4, X = H (**b**); Ar = 4-ClC_6H_4, X = CH_3 (**c**).

Scheme 2.



I, Ar = C_6H_5 (**a**), 4-$CH_3C_6H_4$ (**b**), 4-ClC_6H_4 (**c**); **III**, Ar = C_6H_5, X = H; **IV**, Ar = 4-$CH_3C_6H_4$, X = H; **V**, Ar = 4-ClC_6H_4, X = H (**a**), CH_3 (**b**), Cl (**c**).

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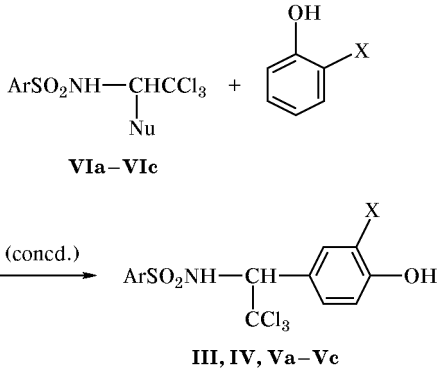
Table 1. Yields, melting points, and elemental analyses of compounds **IIb**, **IIc**, **III**, **IV**, and **Va**–**Vc**

Comp. no.	Yield, %	mp, °C	Found, %					Formula	Calculated, %				
			C	H	Cl	N	S		C	H	Cl	N	S
IIb	88	116–118	40.80	2.65	34.25	3.32	7.74	$C_{14}H_{11}Cl_4NO_3S$	40.51	2.67	34.16	3.37	7.72
IIc	90	118–122	42.22	3.03	33.29	3.21	7.42	$C_{15}H_{13}Cl_4NO_3S$	41.98	3.05	33.05	3.26	7.47
III	69	226–230	44.12	3.16	27.84	3.65	8.44	$C_{14}H_{12}Cl_3NO_3S$	44.17	3.18	27.94	3.68	8.42
IV	68	208–210	45.55	3.54	26.88	3.57	8.15	$C_{15}H_{14}Cl_3NO_3S$	45.65	3.58	26.95	3.55	8.12
Va	72[a], 94[b]	174–177	40.86	2.69	34.24	3.39	7.78	$C_{14}H_{11}Cl_4NO_3S$	40.51	2.67	34.16	3.37	7.72
Vb	74[a], 82[b]	182–185	42.12	3.06	33.17	3.22	7.44	$C_{15}H_{13}Cl_4NO_3S$	41.98	3.05	33.05	3.26	7.47
Vc	74[a], 82[b]	163–166	37.23	2.14	39.13	3.06	7.10	$C_{14}H_{10}Cl_5NO_3S$	37.40	2.24	39.43	3.12	7.13

[a] Method *A*.
[b] Method *B*.

We also examined reactions of phenol, 2-chlorophenol, and 2-methylphenol with *N*-(2,2,2-trichloroethyl)arenesulfonamides **VIa**–**VIc** containing a readily departing group in the α-position with respect to the nitrogen atom. The reactions were carried out in the presence of concentrated sulfuric acid, and they led to formation of the corresponding 4-(1-arylsulfonylamino-2,2,2-trichloroethyl)phenols **III**–**V** (Scheme 3).

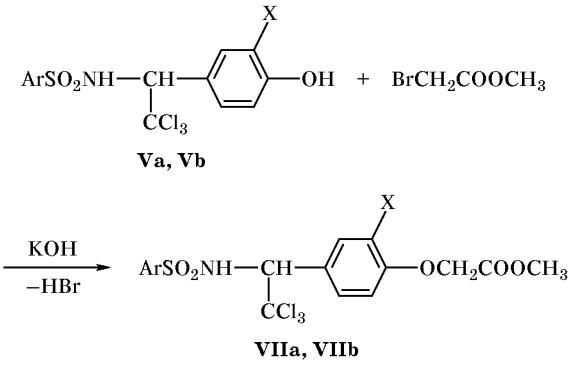
Scheme 3.



III, Ar = C_6H_5, X = H; **IV**, Ar = 4-$CH_3C_6H_4$, X = H; **V**, Ar = 4-ClC_6H_4, X = H (**a**), CH_3 (**b**), Cl (**c**); **VI**, Nu = HO (**a**), MeO (**b**), 4-$ClC_6H_4SO_2NH$ (**c**).

It should be noted that *meta*- and *para*-substituted chloro- and methylphenols reacted neither with Schiff bases **I** nor with *N*-(2,2,2-trichloroethyl)arenesulfonamides **VI**, presumably for steric reasons. Benzenethiol also failed to form C-alkylation products with compounds **I** and **VI** under the above conditions. Instead, its oxidation to diphenyl disulfide and sulfonation of both benzenethiol and diphenyl disulfide occurred. The resulting sulfo derivatives were also inactive as substrates for C-alkylation.

Scheme 4.



VII, Ar = 4-ClC_6H_4, X = H (**a**), CH_3 (**b**).

Compounds **II**–**V** are colorless crystalline substances with an odor typical of trichloroacetaldehyde derivatives. They are readily soluble in alcohols, acetone, and DMSO, sparingly soluble in diethyl ether, chloroform, and hydrocarbons, and insoluble in water. Their structure was proved by the IR and ^1H NMR spectra, elemental analyses (Tables 1, 2), and chemical transformations. 4-Substituted phenols **Va** and **Vb** were brought into reaction with methyl bromoacetate, which afforded methyl 4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenoxyacetates **VIIa** and **VIIb** (Scheme 4). Products **VIIa** and **VIIb** were identical to those obtained

by us previously [6] by reaction of *N*-(2,2,2-trichloroethylidene)-4-chlorobenzenesulfonamide with methyl phenoxyacetates [6].

The IR spectra of compounds **IIa**–**IIc** contain bands belonging to stretching vibrations of the SO_2 and NH groups and aromatic C=C and C−H bonds (Table 2). Substituted phenols **III**–**V** showed in the IR spectra absorption band of the hydroxy group, and the NH band was observed at higher frequencies. In the ^{1}H NMR spectra of 2,2,2-trichloro-1-aroxyethylamides **IIb** and **IIc** and *N*-(2,2,2-trichloro-1-phenoxyethyl)benzenesulfonamide (**IIa**) (which were not given in [5]) we observed signals from aromatic protons and doublet signals from the NH and CH protons with a coupling constant *J* of 9.2 Hz (Table 2). The ^{1}H NMR spectra of substituted phenols **III**–**V** contained analogous signals (Table 2) with the difference that the NH and CH doublets had a coupling constant of 10.5 Hz and were displaced upfield by 0.6–1 ppm relative to the corresponding signals of **IIa**–**IIc**.

We can conclude that, depending on the conditions, reactions of *N*-(2,2,2-trichloroethylidene)arenesulfonamides with phenols yield either 1-arylsulfonylamino-2,2,2-trichloro-1-phenoxyethanes or 4-(1-arylsulfonylamino-2,2,2-trichloroethyl)phenols. The addition of phenol and 2-methylphenol to *N*-(2,2,2-trichloroethylidene)arenesulfonamides occurs in the absence of a catalyst and is accompanied by heat evolution. By contrast, reactions of *N*-(2,2,2-trichloroethylidene)-arenesulfonamides with phenol, 2-chlorophenol, and 2-methylphenol in the presence of oleum yield only the corresponding 4-(2,2,2-trichloro-1-arylsulfonylaminoethyl)phenols. Similar products are formed by reaction of phenols with *N*-[2,2,2-trichloro-1-hydroxy-(methoxy or 4-chlorophenylsulfonylamino)ethyl]-arenesulfonamides in the presence of sulfuric acid.

EXPERIMENTAL

The IR spectra were recorded on a Specord IR-75 spectrometer in KBr. The ^{1}H NMR spectra were obtained on a Jeol FX-90Q instrument (90 MHz) in DMSO-d_6 using TMS as internal reference.

***N*-(2,2,2-Trichloro-1-phenoxyethyl)benzenesulfonamide (IIa)** was synthesized by the procedure reported in [5].

***N*-(2,2,2-Trichloroethylidene)benzenesulfonamide (Ia).** A mixture of 2.26 g (0.01 mol) of *N*,*N*-dichlorobenzenesulfonamide and 15 ml of trichloroethylene was heated for 8 h at 87–89°C under dry argon until vigorous evolution of chlorine ceased (starch–iodine test). Excess trichloroethylene was removed under reduced pressure (5–6 mm, 18–20°C), and the residue was washed with dry petroleum ether and dried. Yield 2.78 g (97%) [7, 8].

***N*-(2,2,2-Trichloroethylidene)-4-methylbenzenesulfonamide (Ib)** was obtained in a similar way from 2.4 g (0.01 mol) of *N*,*N*-dichloro-4-methylbenzenesulfonamide and 15 ml of trichloroethylene. Yield 2.85 g (95%) [7, 8].

***N*-(2,2,2-Trichloroethylidene)-4-chlorobenzenesulfonamide (Ic)** was synthesized in a similar way from 2.56 g (0.01 mol) of *N*,*N*,4-trichlorobenzenesulfonamide and 15 ml of trichloroethylene. Yield 3.12 g (97%) [7, 8].

***N*-(2,2,2-Trichloro-1-phenoxyethyl)-4-chlorobenzenesulfonamide (IIb).** To a solution of Schiff base **Ic** in trichloroethylene, prepared from 2.56 g (0.01 mol) of *N*,*N*,4-trichlorobenzenesulfonamide by the procedure described above, we added with stirring 0.94 g (0.01 mol) of phenol. The mixture spontaneously warmed up to 32°C and was stirred for 1.5–2 h at room temperature. Excess trichloroethylene was removed under reduced pressure, and the precipitate was separated, washed with hexane–diethyl ether, and dried in air. Yield 3.64 g.

***N*-[2,2,2-Trichloro-1-(2-methylphenoxy)ethyl]-4-chlorobenzenesulfonamide (IIc)** was synthesized in a similar way from 1.08 g (0.01 mol) of 2-methylphenol and a solution of Schiff base **Ic** in trichloroethylene, which was prepared from 2.56 g (0.01 mol) of *N*,*N*,4-trichlorobenzenesulfonamide. Yield 3.86 g.

4-(2,2,2-Trichloro-1-phenylsulfonylaminoethyl)-phenol (III). *Method A.* To a solution of 2.86 g (0.01 mol) of *N*-(2,2,2-trichloroethylidene)benzenesulfonamide (**Ia**) in 10 ml of dry benzene we added dropwise 1 ml of oleum while stirring under argon. After 5 min, 1.88 g (0.02 mol) of phenol was added on cooling with water to 15–20°C. The mixture spontaneously warmed up and turned brown (the original mixture was light brown). After 15 min, the mixture was allowed to warm up to room temperature and was stirred for 3 h. The product was filtered off, washed with water (3 × 20 ml) and diethyl ether (3 × 10 ml), and dried in air. Yield 2.63 g.

4-[2,2,2-Trichloro-1-(4-methylphenylsulfonylamino)ethyl]phenol (IV) was synthesized in a similar way from 3.0 g (0.01 mol) of *N*-(2,2,2-trichloroethylidene)-4-methylbenzenesulfonamide (**Ib**) and 1.88 g (0.02 mol) of phenol. Yield 2.70 g.

4-[2,2,2-Trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Va) was synthesized in a similar way from 3.21 g (0.01 mol) of *N*-(2,2,2-trichloroethylidene)-4-chlorobenzenesulfonamide (**Ic**) and 1.88 g (0.02 mol) of phenol. Yield 3.02 g.

Table 2. IR and ^{1}H NMR spectra of compounds **IIa**–**IIc**, **III**, **IV**, and **Va**–**Vc**

Comp. no.	IR spectrum, ν, cm^{-1}						^{1}H NMR spectrum, δ, ppm (J, Hz)			
	SO_2	$C=C_{arom}$	$C-H_{aliph}$	$C-H_{arom}$	NH	OH	$CHCCl_3$	$ArSO_2$	ArO	NH
IIa	1180, 1340	1450, 1490, 1500	2990	3080	3240	–	5.91 d (9.2)	7.69 m	7.24 m	9.92 d (9.2)
IIb	1170, 1330	1450, 1500, 1600	2980	3080	3250	–	5.45 d (9.2)	7.38, 7.58 (*AA′BB′*)	7.28 m	9.78 d (9.2)
IIc[a]	1170, 1340	1430, 1480, 1590	2990	3090	3240	–	5.46 d (9.3)	7.90, 8.00 (*AA′BB′*)	7.44 m	9.77 d (9.3)
III	1165, 1325	1440, 1490, 1590	2990	3090	3290	3420	5.01 d (10.4)	7.55 d (*ortho*), 7.25 t (*meta*), 7.40 t (*para*)	6.50, 7.10 (*AA′BB′*)	8.85 d (10.4)
IV[a]	1170, 1330	1430, 1490, 1600	2980	3085	3290	3430	4.98 d (10.4)	7.25, 7.45 (*AA′BB′*)	6.50, 7.10 (*AA′BB′*)	8.85 d (10.4)
Va	1160, 1325	1445, 1480, 1605	2875, 2950	3090	3280	3420	5.04 d (10.3)	7.33, 7.57 (*AA′BB′*)	6.50, 7.21 (*AA′BB′*)	9.10 d (10.3)
Vb[b]	1160, 1325	1420, 1515, 1610	2850, 2920	3090	3280	3480	5.08 d (10.4)	7.34, 7.52 (*AA′BB′*)	7.11 s, 7.12 d, 6.63 d	7.85 d (10.4)
Vc	1150, 1320	1440, 1505, 1600	2860, 2955	3080	3280	3480	5.15 d (10.4)	7.36, 7.62 (*AA′BB′*)	6.74 d, 7.19 d, 7.40 s	9.13 d (10.4)

[a] $\delta(CH_3)$, ppm: **IIc**: 2.06 s; **IV**: 2.25 s.

[b] The ^{1}H NMR spectrum was recorded in $CDCl_3$, $\delta(CH_3)$ 2.06 ppm.

2-Methyl-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vb) was synthesized in a similar way from 3.21 g (0.01 mol) of *N*-(2,2,2-trichloroethylidene)-4-chlorobenzenesulfonamide (**Ic**) and 2.16 g (0.02 mol) of 2-methylphenol. Yield 3.18 g.

2-Chloro-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vc) was synthesized in a similar way from 3.21 g (0.01 mol) of *N*-(2,2,2-trichloroethylidene)-4-chlorobenzenesulfonamide (**Ic**) and 2.56 g (0.02 mol) of 2-chlorophenol. Yield 3.34 g.

4-[2,2,2-Trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Va). *Method B.* Concentrated sulfuric acid, 3 ml, was added dropwise with stirring to a mixture of 3.39 g (0.01 mol) of *N*-(2,2,2-trichloro-1-hydroxyethyl)-4-chlorobenzenesulfonamide (**VIa**) and 10 ml of dry chloroform. After 5 min, 1.88 g (0.02 mol) of phenol was added on cooling to 15–20°C. The mixture warmed up and turned brown (from light yellow). After 15 min, the mixture was allowed to warm up to room temperature and was stirred for 3 h. The product was filtered off, washed with water (3 × 20 ml) and diethyl ether (3 × 10 ml), and dried in air. Yield 3.9 g (94%).

2-Methyl-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vb) was synthesized in a similar way from 3.39 g (0.01 mol) of *N*-(2,2,2-trichloro-1-hydroxyethyl)-4-chlorobenzenesulfonamide (**VIa**) and 2.16 g (0.02 mol) of 2-methylphenol. Yield 3.51 g (82%).

2-Chloro-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vc) was synthesized in a similar way from 3.39 g (0.01 mol) of *N*-(2,2,2-trichloro-1-hydroxyethyl)-4-chlorobenzenesulfonamide (**VIa**) and 2.56 g (0.02 mol) of 2-chlorophenol. Yield 3.63 g (81%).

4-[2,2,2-Trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Va) was synthesized in a similar way from 3.53 g (0.01 mol) of *N*-(2,2,2-trichloro-1-

methoxyethyl)-4-chlorobenzenesulfonamide (**VIb**) and 1.88 g (0.02 mol) of phenol. Yield 3.9 g (94%).

2-Methyl-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vb) was synthesized in a similar way from 3.53 g (0.01 mol) of *N*-(2,2,2-trichloro-1-methoxyethyl)-4-chlorobenzenesulfonamide (**VIb**) and 2.16 g (0.02 mol) of 2-methylphenol. Yields 3.43 g (80%).

2-Chloro-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vc) was synthesized in a similar way from 3.53 g (0.01 mol) of *N*-(2,2,2-trichloro-1-methoxyethyl)-4-chlorobenzenesulfonamide (**VIb**) and 2.56 g (0.02 mol) of 2-chlorophenol. Yield 3.68 g (82%).

4-[2,2,2-Trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Va) was synthesized in a similar way from 5.12 g (0.01 mol) of 1,1-bis(4-chlorophenylsulfonylamino)-2,2,2-trichloroethane (**VIc**) and 1.88 g (0.02 mol) of phenol. Yield 2.56 g (62%).

2-Methyl-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vb) was synthesized in a similar way from 5.12 g (0.01 mol) of 1,1-bis-(4-chlorophenylsulfonylamino)-2,2,2-trichloroethane (**VIc**) and 2.16 g (0.02 mol) of 2-methylphenol. Yield 2.57 g (60%).

2-Chloro-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenol (Vc) was synthesized in a similar way from 5.12 g (0.01 mol) of 1,1-bis-(4-chlorophenylsulfonylamino)-2,2,2-trichloroethane (**VIc**) and 2.56 g (0.02 mol) of 2-chlorophenol. Yield 2.83 g (63%).

Methyl 4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]phenoxyacetate (VIIa). Potassium hydroxide, 0.73 g (0.013 mol), was dissolved by stirring in 20 ml of methanol, and 4.15 g (0.01 mol) of 4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)-ethyl]phenol (**Va**). The mixture was heated to 100°C, and 1.84 g (0.012 mol) of methyl bromoacetate was added dropwise. After 2 h, the mixture was cooled to 20°C, excess methanol and methyl bromoacetate were removed under reduced pressure, and the product was washed with diethyl ether and dried in air. Yield 4.67 g (96%).

Methyl 4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)ethyl]-2-methylphenoxyacetate (VIIb) was synthesized in a similar way from 0.73 g (0.013 mol) of KOH, 4.29 g (0.01 mol) of 2-methyl-4-[2,2,2-trichloro-1-(4-chlorophenylsulfonylamino)-ethyl]phenol (**Vb**) and 1.84 g (0.012 mol) of methyl bromoacetate. Yield 4.86 g (97%).

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