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Anisole Alkylation with *N*-Arenesulfonylimines of Dichloro(phenyl)acetaldehyde and Derivatives Thereof

T. I. Drozdova and A. N. Mirskova

Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, Irkutsk, 664033 Russia

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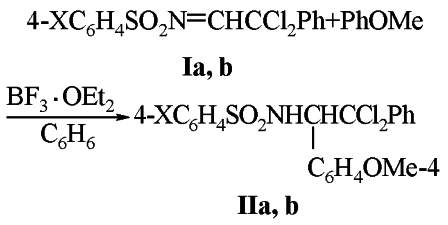
Abstract—*N*-[1-4-Methoxyphenyl-2-phenyl-2,2-dichloroethyl]arenesulfonamides are formed in reaction of *N*-(2-phenyl-2,2-dichloroethylidene)-4-chlorobenzenesulfonamide and *N*-(2-phenyl-2,2-dichloroethylidene)-4-methylbenzenesulfonamide with anisole catalyzed by boron trifluoride etherate, and in reaction of anisole with 1,1-di(arenesulfonamido)-2-phenyl-2,2,-dichloroethanes in the presence of concentrated sulfuric acid.

The prospects of *N*-sulfonylimines of chloral and dichloroacetic anhydride in C-amidoalkylation of aromatic and heterocyclic compounds were discussed in review [1]. Yet the amidoalkylating activity of *N*-sulfonylimines from dichloro(phenyl)acetaldehyde is poorly understood: a single example is described, that of reaction between the dichloro(phenyl)acetaldehyde *N*-sulfonylimine with anisole [2].

In extension of our studies on amidoalkylating activity of *N*-arenesulfonylimines of polyhaloaldehydes and their derivatives we investigated the anisole C-amidoalkylation with imines of dichloro(phenyl)acetaldehyde and looked for amidoalkylating agents among the derivatives thereof.

We established that the reaction of *N*-(2-phenyl-2,2-dichloroethylidene)-4-chlorobenzenesulfonamide and *N*-(2-phenyl-2,2-dichloroethylidene)-4-methylbenzenesulfonamide (**Ia, b**) with anisole occurred at heating in benzene in the presence of boron trifluoride etherate furnishing *N*-[1-4-methoxyphenyl-2-phenyl-2,2-dichloroethyl]-4-chlorobenzene- (**IIa**) and -4-methylbenzenesulfonamides (**IIb**) in up to 67% yield.

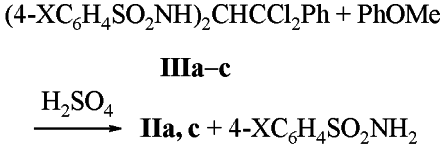


X = Cl (**a**), Me (**b**).

The yield of reaction products **IIa, b** depends on reaction time and temperature. For instance, the reaction at room temperature (18–20°C) within 20–25 h does not afford the C-amidoalkylation products in a notable yield (5–7%). The heating to 65–70°C accelerates the process, and the yield of compounds **IIa, b** in reaction of imines **Ia, b** with anisole amounts to 12–15% in 2–3 h, to 40–46% in 6–8 h, and to 62–67% in 10–14 h. Still longer heating (16–18 h) results in decreased yield for tarring occurs that hampers the isolation of compounds **IIa, b**.

In [3–5] was reported on application as amidoalkylating agents of 2,2,2-trichloroethylarenesulfonamides containing functional groups in position 1, $ArSO_2NHCH–(Nu)CCl_3$ [Nu = OH, OEt, OC(O)Me, $NHSO_2Ar$]. These compounds in the presence of concn. H_2SO_4 reacted with benzene, toluene, phenol, 2-chlorothiophenol, anisole, naphthalene to afford amidoalkylation products. Yet the 1-functionalized derivatives of dichloro(phenyl)acetaldehyde, $ArSO_2NHCH(Nu)CCl_2Ph$, prepared by reaction of *N*,*N*-dichloroarenesulfonamides with phenylacetylene and by nucleophilic addition at the azomethine bond in the *N*-arenesulfonylimines [6] were not tested before in the C-amidoalkylation.

1,1-Di(arenesulfonamido)-2-phenyl-2,2-dichloroethanes (**IIIa–c**) react with anisole in the presence of concn. sulfuric acid at 0–5°C affording C-amidoalkylation products **IIa–c** and arenesulfonamides **IVa–c**.



X = Cl (**a**), Me (**b**), H (**c**).

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We found that the duration of the reaction effected the yield of products **IIa–c**. For instance, in 6 h alongside the C-amidoalkylation products **IIa–c** (yield 58%) were obtained arenesulfonamides **IVa–c** (yield 28–31%) and initial unreacted compounds **IIIa–c**. When the reaction was carried out for 11–12 h the yield of anisole derivatives **IIa–c** grew to 71–75%. We did not found any notable dependence of the reaction products yield on the character of substituent in the *para*-position of the arylsulfonyl group in the initial amides **IIIa–c**.

Compounds **IIa–c** at room temperature are stable against acid hydrolysis. However the heating over 30°C in acidic medium results in hydrolysis of these compounds to arenesulfonamides **IVa–c**.

Lightly colored crystalline compounds **IIa–c** are well soluble in dimethyl sulfoxide, acetone, sparingly soluble in tetrachloromethane, chloroform, ethyl ether, benzene, and insoluble in water. The composition and structure of compounds **IIa, b** were proved by elemental analysis, NMR and IR spectra.

In the IR spectra of compounds **IIa, b** are present the absorption bands of the stretching and bending vibrations of bonds in the regions 3260–3265 (NH), 1165–1170, 1340 (O=S=O), 3060–3080 (=CH), 1480, 1500 (C=C), 2820, 2940 (C–H), 790–810 (C–Cl) cm^{-1}, and no bands of the initial amidoalkylating agents are observed.

The high regioselectivity of the reaction was revealed by ^{1}H NMR spectroscopy. In the ^{1}H NMR spectrum of compounds **IIa–c** recorded in DMSO-d_6 were observed doublets at 8.65 and 8.80 ppm (NH), and 5.12 and 5.16 ppm (CH) with a characteristic coupling constant $^3J_{NH-CH}$ 10 Hz. The benzene ring multiplets appear at 7.35–7.60 ppm, those from the protons in the arene rings of the arenesulfonyl groups [7.26 d and 7.43 d (^3J 8.4 Hz)] and from the protons of the anisole ring [6.51 d and 6.91 d (^3J)] correspond to a $A_2ß_2$ spin system. This splitting of proton signals evidences formation of *para*-substituted reaction products. No reaction occurs at the *ortho*- and *meta*-positions in anisole as shows the lack of the corresponding signals in the ^{1}H NMR spectra. The signal of methyl group attached to anisole ring appears downfield (3.46 ppm) with respect to the signal of methyl protons belonging to the aromatic ring in compound **IIb** (3.32 ppm, s).

In the ^{13}C NMR spectrum of compound **IIa** recorded in DMSO-d_6 are observed signals of carbon nuclei at 95.67 (CCl_2) and 55.19 (CH) ppm. The signals of carbon atoms from the aromatic fragments of the compounds are located between 112.64 (*4* position of the anisole ring) and 158.90 ppm (*4* position in the arenesulfonyl group). The spectral characteristics of compound **IIc** are identical to the data obtained in the study of products in the reaction between dichloro(phenyl)acetaldehyde *N*-benzenesulfonylimine (**Ia, b**) with anisole [6].

The formation of arenesulfonamides **IVa–c** in the course of the reaction was proved by IR spectroscopy. In the IR spectra of the compounds are present the absorption bands in the regions 3230 and 3240 (NH_2), 1170, 1340 (O=S=O), 1480 (C=C arom), 3080 cm^{-1} (=CH arom), and in the ^{1}H NMR spectra (DMSO-d_6) appear signals 7.46 s (NH_2), 7.69 d and 7.82 d (Ar–H), identical to those characteristic of authentic arenesulfonamides **IVb, c**. The melting points of the compounds also are consistent with the data of the authentic substances. The ^{13}C NMR spectrum of compound **IVb** (DMSO-d_6) contains the signals of carbon atoms of the benzene ring at 143.06 (C^4), 136.69 (C^3), 129.15 (C^2), 127.72 ppm (C^1).

Thus *N*-[1-(4-methoxyphenyl)-2-phenyl-2,2-dichloroethyl]arenesulfonamides (**IIa–c**) can originate depending on the reaction conditions not only from dichloro(phenyl)acetaldehyde *N*-arenesulfonylimines (**Ia, b**) but also from the derivatives thereof, 1,1-di(arenesulfonamido)-2-phenyl-2,2-dichloroethanes (**IIIa–c**).

EXPERIMENTAL

IR spectra were registered on spectrophotometer UR-20 from KBr pellets in 400-4000 cm^{-1} region. ^{1}H NMR spectra were recorded on spectrometer Jeol FX-90Q (90 MHz) in DMSO-d_6, internal reference HMDS.

***N*-(2-Phenyl-2,2-dichloroethylidene)arenesulfonamides (Ia, b)** were synthesized by procedure [6, 7].

1,1-Di(arenesulfonamido)-2-phenyl-2,2-dichloroethanes (IIIa–c) were obtained by reaction of *N*,*N*-dichloroarenesulfonamides with phenylacetylene along procedure described before [6].

***N*-[1-(4-Methoxyphenyl)-2-phenyl-2,2-dichloroethyl]parachlorophenylsulfonamide (IIa).** (a) To a solution of 7.3 g of compound Ia in anhydrous benzene was added 2–4 drops of boron trifluoride etherate and 2 ml of anisole. The mixture was heated for 14 h to 65–70°C. The precipitated crystals of the product were filtered off, washed with chloroform, and dried. We obtained 6.3 g (67%) of compound **IIa**, mp 185–186°C.

(b) To 1.1 g of compound **IIIb** was added excess anisole (7.5 ml) and 2.5 ml of concn. sulfuric acid. The reaction mixture was maintained for 11–12 h at 0–5°C while vigorous stirring. On completing the reaction the mixture was diluted with cold water and neutralized with a water solution of sodium carbonate. The insoluble reaction product was filtered off, washed with water till neutral, and dried in vacuum-desiccator over P_2O_5. We obtained 0.75 g (75%) slightly colored crystalline compound, mp 185–186°C. Found, %: C 53.18; H 3.67; Cl 21.97; N 2.67; S 6.74. $C_{21}H_{18}Cl_3NO_3S$. Calculated, %: C 53.58; H 3.85; Cl 22.59; N 2.98; S 6.81.

***N*-[1-(4-Methoxyphenyl)-2-phenyl-2,2-dichloroethyl]paramethylphenylsulfonamide (IIb)** was prepared along procedure *a* from 6.8 g of amidoalkylating agent **Ib** in amount of 5.5 g (62%), mp 181–183°C, and along procedure *b* (amindoalkylating agent **IIIb**) in amount 0.67 g (72%), mp181–183°C. Found, %: C 57.98; H 4.67; Cl 15.18; N 2.87; S 6.98. $C_{22}H_{21}Cl_2NO_3S$. Calculated, %: C 58.67; H 4.70; Cl 15.74; N 3.11; S 7.12.

***N*-[1-(4-Methoxyphenyl)-2-phenyl-2,2-dichloroethyl]benzenesulfonamide (IIc)** was prepared along procedure *b* from compound **IIIc** in amount 0.6 g (71%). Found, %: C 57.33; H 4.32; Cl 16.11; N 3.19; S 7.13. $C_{21}H_{19}Cl_2NO_3S$. Calculated, %: C 57.80; H 4.39; Cl 16.25; N 3.21; S 7.35.

Arenesulfonamides **IVa, b** were separated from the reaction mixture at treating with acid the filtrate obtained by procedure b; the melting points were consistent with the published data [8].

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