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New Approach to the Preparation of *p*-(1-Cyanoethyl)arenesulfonamides by Reaction of Arylsulfonyl Imines of Polychloroacetaldehydes with Acetone Cyanohydrin

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Abstract—Reaction of *N*-(2,2,2-trichloroethylidene)- or *N*-(1-phenyl-2,2-dichloroethylidene)arenesulfonamides with acetone cyanohydrin in acetone in the presence of potassium carbonate led to the formation of *N*-(2,2,2-trichloro-1-cyanoethyl)- or *N*-(2-phenyl-2,2-dichloro-1-cyanoethyl)arenesulfonamides.

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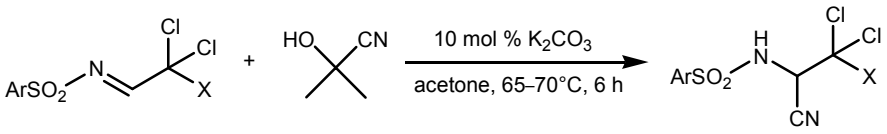
Arylsulfonyl imines of polyhaloaldehydes are valuable reagents for preparation of a wide range of amides derivatives and sulfonamides [1, 2]. The high electrophilicity of the azomethine group in this type imines originating from the effect of strong electron-acceptor sulfonyl and polyhalomethyl groups makes it possible to carry out the addition to the imines of O-, N-, S-, P-, C-nucleophiles [1, 2] affording functionalized sulfonamides which in their turn may be utilized in the synthesis of heterocyclic derivatives [1–7], aminocarbonyl compounds [8], biologically active amino acids [9].

Sulfonyl imines of polyhaloaldehydes were not practically investigated in reactions resulting in the corresponding sulfonylamino-substituted nitriles. In [10] a reaction was described between hydrogen cyanide and arylsulfonyl imines of chloral in the presence of trimethylamine leading to the formation of *N*-(2,2-dichloro-1-cyanovinyl)arenesulfonamides. Similar transformations of chloral *N*-acyl imines were described in more detail; obtained *N*-(2,2,2-trichloro-1-cyanoethyl)amides are valuable reagents for the synthesis of functionalized amide derivatives, in particular, of the heterocyclic structure [11–13]. Aminonitriles are well known key intermediates in the process of Strecker amino acid synthesis [14].

The accessible specimens of activated highly electrophilic sulfonyl imines, *N*-(2,2,2-trichloroethylidene)- and *N*-(2-phenyl-2,2-dichloroethylidene)-arenesulfonamides **1** and **2**, were prepared by radical reactions of *N*,*N*-dichloroarenesulfonamides with trichloroethylene or phenylacetylene [15, 16]. We carried out the cyanation of imines **1a–1c** and **2a–2c** using acetone cyanohydrin as a precursor of the cyanide anion in contrast to the above mentioned procedures that applied sodium cyanide [11] or hydrogen cyanide [10]. In the laboratory practice acetone cyanohydrin due to lower toxicity and higher

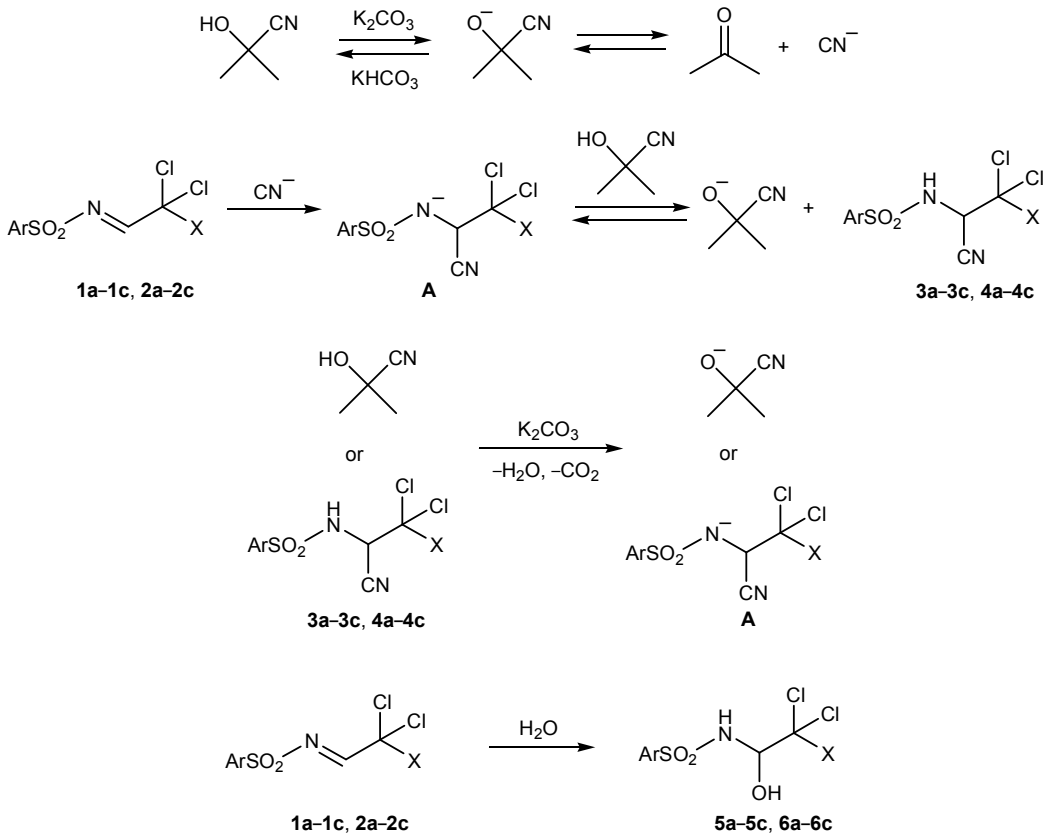
Scheme 1.



1a–1c, **2a–2c** **3a–3c**, **4a–4c**

X = Cl (**1**, **3**), Ph (**2**, **4**); Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**).

Scheme 2.



X = Cl (**1**, **3**, **5**), Ph (**2**, **4**, **6**); Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**).

accessibility is more feasible than sodium or hydrogen cyanide.

The reaction of sulfonyl imines **1a–1c** and **2a–2c** with acetone cyanohydrin led to the formation of *N*-(2,2,2-trichloro-1-cyanoethyl)- and *N*-(2-phenyl-2,2-dichloro-1-cyanoethyl)arenesulfonamides **3a–3c** and **4a–4c** in the presence of potassium carbonate in acetone as the optimum solvent (Scheme 1).

In the absence of potassium carbonate the reaction proceeds insufficiently effectively, yet this reagent used in amount exceeding 10–15 mol % caused the decrease in the yield of cyano derivatives **3** and **4** due to an intensive formation of the corresponding hemiaminals, *N*-(1-hydroxyethyl)sulfonamides **5** and **6**.

Apparently some potassium carbonate is necessary to generate cyanide ions from acetone cyanohydrin. As a result of cyanide ions addition to the azomethine group of highly electrophilic imines **1** and **2** the corresponding *N*-(polychlorocyanoethyl)amidyl ions **A** are formed which react with acetone cyanohydrin giving compounds **3** and **4** and favoring further generation of cyanide anions (Scheme 2). At a large amount of potassium carbonate it reacts with sufficiently acidic hydroxy and sulfonamide groups of acetone cyanohydrin and sulfonamides **3** and **4** providing carbonic acid that decomposes in carbon dioxide and water, and the latter in its turn extremely easily reacts with the activated azomethine group of initial imines **1** and **2** giving hemiaminals **5** and **6** as side products (Scheme 2).

The formation of cyano-substituted sulfonamides **3a–3c** and **4a–4c** was proved by NMR spectra and confirmed by IR spectra and elemental analysis. IR spectra of compounds **3** and **4** contain absorption bands of C≡N, SO_2, NH groups. In the ^1H NMR spectra of sulfonamides **3** and **4** along with the signals of the protons of aromatic rings doublets are observed corresponding to the fragment NHCH, *J* 9–10 Hz. The ^{13}C NMR spectra contain the signals of carbon atoms of the aromatic rings, of C≡N group, of trichloromethyl or phenyldichloromethyl groups, and also of methine group.

Hemiaminals **5** and **6** are thoroughly studied compounds [17–19]. The side process affording these compounds was unambiguously proved by the comparison of their NMR and IR spectra with the spectra of authentic samples.

N-(2,2,2-Trichloro-1-cyanoethyl)- and *N*-(2-phenyl-2,2-dichloro-1-cyanoethyl)arenesulfonamides are promising reagents for further transformations involving the polychloroethyl and cyano groups.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Bruker IFS-25, ^{1}H, ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-400 (operating frequencies 400.13 and 100.62 MHz respectively) in DMSO-d_6. Imines **1** and **2** were prepared by procedures [15, 16].

***N*-(2,2,2-Trichloro-1-cyanoethyl)benzenesulfonamide (3a).** A mixture of 0.49 g (1.7 mmol) of *N*-(2,2,2-trichloroethylidene)benzenesulfonamide **1a**, 0.015 g (7 mol %) of K_2CO_3, 3 mL of 50% acetone solution of acetone cyanohydrin, and 5 mL of acetone was stirred under an argon atmosphere at 65–70°C for 6 h. The reaction mixture was diluted with 20 mL of water, the precipitate was filtered off, dried, and recrystallized from benzene. Yield 0.52 g (97%), colorless crystals, mp 107–109°C. IR spectrum (KBr), ν, cm^{-1}: 3247 (N–H), 2221 (C≡N), 1340, 1169 (SO_2). ^{1}H NMR spectrum, δ, ppm: 5.74 d (1H, CH, ^3J 9.78 Hz), 7.30, 7.46, 7.75 m (5H$_{arom}$), 9.37 d (1H, NH, ^3J 9.78 Hz). ^{13}C NMR spectrum, δ, ppm: 60.69 (CH), 96.38 (CCl_3), 113.91 (CN), 126.94, 129.31, 133.44, 139.79 (C_6H_5). Found, %: C 34.69; H 2.34; N 8.82; S 10.08. $C_9H_7Cl_3N_2O_2S$. Calculated, %: C 34.47; H 2.25; N 8.93; S 10.22.

4-Methyl-*N*-(2,2,2-trichloro-1-cyanoethyl)benzenesulfonamide (3b) was prepared similarly from 0.5 g (1.66 mmol) of 4-methyl-*N*-(2,2,2-trichloroethylidene)-benzenesulfonamide **1b**. Yield 0.38 g (70%), white powder, mp 112–115°C. IR spectrum (KBr), ν, cm^{-1}: 3227 (N–H), 2229 (C≡N), 1339, 1166 (SO_2). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 5.95 d (1H, CH, ^3J 9.29 Hz), 7.35–7.45 m (2H, 4-MeC_6H_4), 7.74–7.82 m (2H, 4-MeC_6H_4), 9.90 d (1H, NH, ^3J 9.29 Hz). ^{13}C NMR spectrum, δ, ppm: 20.95 (Me), 60.31 (CH), 95.63 (CCl_3), 112.89 (CN), 126.68, 129.24, 132.54, 138.78 (4-MeC_6H_4). Found, %: C 34.08; H 3.19; N 8.25; S 9.18. $C_{10}H_9Cl_3N_2O_2S$. Calculated, %: C 36.66; H 2.77; N 8.55; S 9.79.

***N*-(2,2,2-Trichloro-1-cyanoethyl)-4-chlorobenzenesulfonamide (3c)** was prepared similarly from 2 g (6.2 mmol) of *N*-(2,2,2-trichloroethylidene)-4-chlorobenzenesulfonamide **1c**, 0.060 g (7 mol %) of K_2CO_3 and 8 mL of 50% acetone solution of acetone cyanohydrin. Yield 1.78 g (83%), white crystalline powder, mp 127–130°C. IR spectrum (KBr), ν, cm^{-1}: 3230 (N–H), 2263 (C≡N), 1348, 1159 (SO_2). ^{1}H NMR spectrum, δ, ppm: 6.03 d (1H, CH, ^3J 9.22 Hz), 7.69–7.81 m (2H, 4-ClC_6H_4), 7.96–8.04 m (2H, 4-ClC_6H_4), 10.11 d (1H, NH, ^3J 9.22 Hz). ^{13}C NMR spectrum, δ, ppm: 60.62 (CH), 96.22 (CCl_3), 113.87 (CN), 128.79, 129.02, 129.46, 138.56 (4-ClC_6H_4). Found, %: C 29.98; H 2.28; N 8.36; S 9.68. $C_9H_6Cl_4N_2O_2S$. Calculated, %: C 31.06; H 1.74; N 8.05; S 9.21.

***N*-(2-Phenyl-2,2-dichloro-1-cyanoethyl)benzenesulfonamide (4a)** was prepared similarly from 0.551 g (1.6 mmol) of *N*-(2-phenyl-2,2-dichloroethylidene)-benzenesulfonamide **2a**, 0.016 g (7 mol %) of K_2CO_3 and 3 mL of 50% acetone solution of acetone cyanohydrin. Yield 0.369 g (63%), white crystalline powder, mp 137–139°C. IR spectrum (KBr), ν, cm^{-1}: 3218 (N–H), 2262 (C≡N), 1355, 1171 (SO_2). ^{1}H NMR spectrum, δ, ppm: 5.78 d (1H, CH, ^3J 10.04 Hz), 7.43–7.49 m (2H$_{arom}$), 7.52–7.63 m (3H$_{arom}$), 7.63–7.73 m (2H$_{arom}$), 7.73–7.91 m (3H$_{arom}$), 9.47 d (1H, NH, ^3J 10.04 Hz). ^{13}C NMR spectrum, δ, ppm: 58.60 (CH), 90.22 (CCl_2), 115.05 (CN), 126.91, 127.42, 128.40, 129.16, 130.26, 133.20, 136.90, 139.69 (Ar). Found, %: C 51.12; H 3.66; N 8.12; S 9.55. $C_{15}H_{12}Cl_2N_2O_2S$. Calculated, %: C 50.72; H 3.41; N 7.89; S 9.03.

4-Methyl-*N*-(2-phenyl-2,2-dichloro-1-cyanoethyl)benzenesulfonamide (4b) was prepared similarly from 0.5 g (1.4 mmol) of 4-methyl-*N*-(2-phenyl-2,2-dichloroethylidene)benzenesulfonamide **2b**, 0.015 g (7 mol %) of K_2CO_3, and 3 mL of 50% acetone solution of acetone cyanohydrin. Yield 0.46 g (83%), white crystalline powder, mp 73–75°C. IR spectrum (KBr), ν, cm^{-1}: 3227 (N–H), 2226 (C≡N), 1352, 1173 (SO_2). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 5.74 d (1H, CH, ^3J 9.78 Hz), 7.31–7.51 m (6H$_{arom}$), 7.63–7.90 m (3H$_{arom}$), 9.39 d (1H, NH, ^3J 9.78 Hz). ^{13}C NMR spectrum, δ, ppm: 21.01 (Me), 58.56 (CH), 90.23 (CCl_2), 115.11 (CN), 126.94, 127.38, 128.29, 128.35, 129.52, 130.16, 136.90, 143.50 (Ar). Found, %: C 53.28; H 3.55; N 8.22; S 8.61. $C_{16}H_{14}Cl_2N_2O_2S$. Calculated, %: C 52.04; H 3.82; N 7.59; S 8.68.

***N*-(2-Phenyl-2,2-dichloro-1-cyanoethyl)-4-chlorobenzene-sulfonamide (4c)** was prepared similarly from 0.5 g (1.3 mmol) of *N*-(2-phenyl-2,2-dichloroethyl)-4-chlorobenzenesulfonamide **2c**, 0.015 g (7 mol %) of K_2CO_3, and 4 mL of 50% acetone solution of acetone cyanohydrin. Yield 0.52 g (97%), white crystalline powder, mp 163–165°C. IR spectrum (KBr), ν, cm^{-1}: 3232 (N–H), 2232 (C≡N), 1354, 1173 (SO_2). ^{1}H NMR spectrum, δ, ppm: 5.83 d (1H, CH, ^3J 9.98 Hz), 7.41–7.49 m ($3H_{arom}$), 7.64–7.68 m ($2H_{arom}$), 7.73–7.80 m ($2H_{arom}$), 7.83–7.86 m ($2H_{arom}$), 9.58 d (1H, NH, ^3J 9.98 Hz). ^{13}C NMR spectrum, δ, ppm: 58.50 (CH), 90.05 (CCl_2), 115.05 (CN), 127.35, 128.35, 128.91, 129.25, 130.19, 136.79, 138.09, 138.43 (Ar). Found, %: C 47.03; H 3.03; N 6.89; S 8.01. $C_{15}H_{11}Cl_3N_2O_2S$. Calculated, %: C 46.23; H 2.85; N 7.19; S 8.23.

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