Synthesis of *N*-arylsulfonylimidazolidine-4-ones from *N*-(2,2,2-trichloroethylidene)arenesulfonamides and monochloroacetamide

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Dedicated to Academician Boris A. Trofimov on his 65th birthday with heartiest wishes

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Abstract

The reaction of N-(2,2,2-trichloroethylidene)arenesulfonamides with monochloroacetamide involves nucleophilic addition to the C=N bond of the imine function, to give N-(arenesulfonamido-2,2,2-trichloroethyl)chloroacetamides. The latter, in the presence of bases, undergo intramolecular cyclization to give imidazole derivatives.

Keywords: Chloralimines, chloroacetamide, arenesulfonamides, imidazolidine-4-ones, synthesis

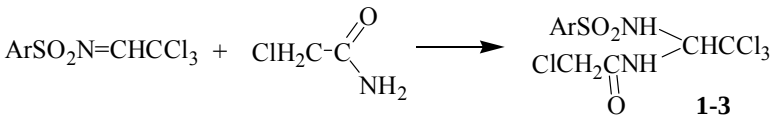
Introduction

We have reported that the products of the reaction of N-(2,2,2-trichloroethylidene)arenesulfonamides with ethylenechlorohydrin,[1] ethylene glycol, mercaptoethanol[2] as well as hydroxyacetic and mercaptoacetic[3] acids were successfully used in the synthesis of heterocyclic compounds of the oxazole- and thiazole series. The addition reactions of the amides of halocarboxylic acids with N-functionally substituted imines of polyhaloaldehydes should result in products which would be promising for the synthesis of heterocyclic compounds, but have not been studied yet, although the interaction of many amides with N-functionally substituted imines of polyhaloaldehydes have been studied in detail.[4] Investigation of the reactions of chloral arenesulfonylimines with monochloroacetamide seems to be important because it should give route for synthesizing new heterocyclic derivatives of N-arylsulfonyl- substituted imidazoles.

Results and Discussion

Chemistry

It was found that N-(2,2,2-trichloroethylidene)arenesulfonamides reacted with the amide of monochloroacetic acid amide to give the products of nucleophilic addition to the C=N bond. As expected, chloroacetamide shows lower reactivity in its reactions with chloral arenesulfonylimines than do the other amides of carboxylic acids which have been studied in similar processes.[4] This can be explained by the electron-accepting effect of the halogen atom. We have defined conditions for the reaction, which result in good yields of the addition products **1–3** (Scheme 1).

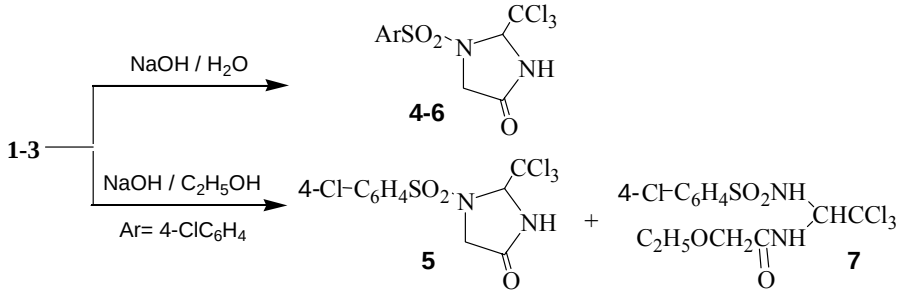


Ar= Ph (**1**), 4-ClC_6H_4 (**2**), 4-MeC_6H_4 (**3**)

Scheme 1

The behavior of the synthesized diamides **1–3** under conditions leading to their cyclization involving NH and CH_2Cl groups has been studied.

It was found that the diamides **1–3,** under the influence of aqueous or alcoholic alkalis, underwent an intramolecular cyclization to give the imidazolidine-4-one derivatives **4–6.** Alcohol and alkali promoted a side process of substitution of the chlorine atom in the chloroacetamide fragment by an alkoxy group, and the compound **7** was formed (Scheme 2).



Ar= Ph (**4**), 4-ClC_6H_4 (**5**), 4-MeC_6H_4 (**6**)

Scheme 2

The compounds **1–6** were colorless crystalline products, soluble in acetone and DMSO and insoluble in aliphatic hydrocarbons and water.

NMR and IR data

The structure of the diamides **1–3** was confirmed by spectroscopic data (Tables 1–3). In the ^1H NMR spectra, proton signals of both the substituted aromatic ring and of the -NH-CH-NH- fragment were

observed. The latter fragment presented as low-field doublets of the NH group and a triplet of the CH-group. The non-equivalent protons of the CH_2Cl fragment appeared as an AB-system. In the ^{13}C- NMR spectra of diamides **1—3, the** signals were assigned to the carbonyl group, aromatic ring, CCl_3, CH_2Cl and CH groups.

Table 1. ^1H NMR data of **1–7** (acetone-d_6): δ_H [ppm] and coupling constants [Hz]

	CH_3	CH_2-AB system (J_{A-B})	CH	NH	Ar
1	-	3.79; 3.90 (12.0)	6.13 t	7.67 d, 7.88 d	5H, 7.58 – 7.87 m (Ph)
2	-	3.79; 3.91 (14.4)	6.08 t	7.72 d, 7.94 d	4H, 7.53, 7.84 (AA'BB', 4-Cl-C_6H_4)
3	2.41 s	3.78; 3.87 (14.4)	6.07 t	7.71 d, 7.96 d	4H, 7.45, 7.71 (AA'BB', 4-MeC_6H_4)
4	-	3.84; 4.04 (16.8)	5.98 s	8.80 br. S	5H, 7.67 – 8.06 m (Ph)
5	-	3.85; 4.02 (16.0)	5.97 s	8.77 br. s	4H, 7.71, 8.09 (AA'BB', 4-ClC_6H_4)
6	2.44 s	3.82; 4.01 (17.2)	5.94 s	8.71 br. s	4H, 7.48, 7.95 (AA'BB', 4-MeC_6H_4)
7*	1.13 t	3.81; 3.52 (15.6)	6.05 t	7.45 d	4H, 7.47 ,7.82 (AA'BB', 4-ClC_6H_4)

* OCH_2 3.34 q.

Table 2. ^{13}C NMR data of **1–5** (acetone-d_6): δ_H [ppm]

	C=0	Ar	CCl_3	CH	CH_2
1	166.15	130.96, 129.27, 129.00, 127.32	102.50	72.16	42.71
2	165.22	138.83, 138.88, 128.13, 128.43	99.40	71.27	41.30
3*	146.41	144.78, 138.71, 130.44, 128.10	102.63	71.27	42.63
4	170.42	136.41, 134.21, 129.72, 128.13	102.14	81.13	49.62
5	171.04	139.67, 134.26, 130.32, 130.00	101.98	80.83	49.78

* CH_3 21.45.

The protons of the 1H NMR spectra of the cyclic compounds **4–6** appeared as broad singlets of the NH group at low field, signals of the aromatic ring, and a singlet for the methane proton (Table 1). Unlike the acyclic products **1–3,** splitting of the methane proton signal by the NH-proton was not observed, which could be explained by the presence of the enol form of imidazolidones **4–6** in the solution. The non-equivalent protons of the methylene group were appeared as dd. In the ^{13}C NMR spectra of the compounds **4, 5** (Table 2) signals of the carbon atom of carbonyl group, aromatic rings, CCl_3 group, and CH and CH_2 fragments were presented. The signals were slightly shifted towards high field in comparison with the same signals of the acyclic products **1–3**.

The compound **7** was isolated as a mixture with the compound **5;** however, its structure was unambiguously confirmed by ^1H NMR data. In the spectra of the precipitate prepared by treatment of diamide **2** with alcoholic alkali, proton signals corresponding to the cyclic derivative **5** were present, but the triplet and quartet could be assigned to the ethoxy group as well as the proton signals of the aromatic rings and multiplets of NH, CH and CH_2-groups, whose shifts differed from the shifts of diamide **2** and compound **5** (Table 1).

As Table 3 illustrates, the IR spectra of the compounds **1–3** and **4–6** confirmed their structures. The low values of νNH, νC=O, as well as their doublet form, could be explained by both intramolecular- (compounds **1–3**) and intermolecular hydrogen bonding in the crystalline state.

Table 3. Infrared spectral data (cm^{-1}) for the main groups in compounds **1–6** in KBr

	ν_{NH}	ν_{CH}	$\nu_{C=O}$	$\nu_{C=C}$ aromatic	$\delta_{C(O)NH}$	ν^{as}_{SO2}, ν^{s}_{SO2}	$\nu_{heterocycle}$	$\nu_{Caryl-S}$	ν_{S-N}
1	3280	2950	1680	1585	1520 s	1336	–	1080	897
	3230		1710 sh	1575		1165		1090	920 sh
				1480					
2	3300	2960	1660	1585	1530 s	1336	–	1087	910
	3260		1700 sh	1575		1170		1078	920 sh
				1477					
3	3280	2950	1660	1598	1518 s	1330	–	1060	875
	3220		1680	1590		1150		1090	890 sh
				1490					
4	3200	2950	1720	1582	1430	1370	1350	1085	940
	br		1740	1575		1175	1210		
				1477			1122		
							1005		
5	3200	2960	1705	1587	1440	1372	1358	1082	960
	br		1750	1570		1172	1200		
				1480			1118		
							1030		
6	3200	2960	1718	1590	1440	1365	1357	1080	940
	br		1750	1490		1172	1210		
				1430			1090		
							1038		

The carbonyl absorption bands of the cyclic products **4–6** were shifted to high frequency, in accord with ref. 5, so the vibration frequencies were increased while the valence angles decreased in systems such as C-CO-C when 5-membered cycles were formed. The formation of cyclic products **4–6** was also confirmed by the presence of νSO_2 high-frequency bands, (especially for asymmetric vibration), which could be assigned to the inductive effect of the 5-membered N-containing heterocycles.[6,7] A series of absorption bands of 5-membered cycle skeleton in the 1350–1005 cm^{-1} region, which was not observed in spectra of acyclic compounds,[8] was indicative of the formation of the saturated heterocycles **4–6**. Absorption bands of the CONH "Amide II" fragment in the 1520–1540 cm^{-1} region are typical for acyclic N-substituted amides, while these vibration bands in 5-membered lactams were shifted to lower frequency. Indeed, these bands for the compounds **4–6** were observed in the 1430–1440 cm^{-1} region. We intend to study further the stereochemical properties, electronic structure, types of hydrogen bonds, donor-acceptor interactions of the compounds obtained, and analyze the comparative characteristics of cyclic and acyclic compounds.

Conclusions

The synthesis of N-(1-arylsulfonamido-2,2,2-trichloroethyl)chloroacetamides was carried out by the reaction of N-(2,2,2-trichloroethylidene)arenesulfonamides with monochloroacetamide. The possibility of preparation of imidazolidine-4-one derivatives from the diamides of such type were shown.

Experimental Section

General Procedures. IR spectra of the compounds **1–6** were recorded on a SPECORD IR 75 spectrometer in KBr, with resolution of 1 cm^{-1} from 1700–500 cm^{-1} and 2 cm^{-1} in the νNH region. ^{1}H- and ^{13}C NMR spectra were recorded on a Bruker DPX-400 instrument (400 and 100.6 MHz respectively) in organic solvents (acetone-d_6) with HMDS as internal standard, concentration 5–10%.

Addition of chloroacetamide to trichloroethylidenearenesulfonamides

A solution of N-(2,2,2-trichloroethylidene)arenesulfonamides (0.01 mol) was prepared by the reaction of N,N-dichloroarenesulfonamides and trichloroethylene.[1] Chloroacetamide (0.93 g, 0.01 mol) was added to the solution and the mixture was heated at reflux for 5 h under an inert gas flow. After cooling, the precipitate was filtered off, to give products **1–3**.

***N*-(1-Benzenesulfonamido-2,2,2-trichloroethyl)chloroacetamide (1).** Yield 92%, m.p. 200^{0}C (EtOH). Anal. Calcd. for $C_{10}H_{10}Cl_4N_2O_3S$: C 31.66; H 2.37; Cl 37.46; N 7.38; S 8.40; Found: C 31.75; H 3.16; Cl 37.85; N 7.55; S 8.65%.

***N*-[1-(4-Chlorobenzene)sulfonamido-2,2,2-trichloroethyl]chloroacetamide (2).** Yield 90%, m.p. 228-230 ^{0}C (acetone). Anal. Calcd. for $C_{10}H_9Cl_5N_2O_3S$: C 28.88; H 2.19; Cl 42.52; N 6.56; S 7.57. Found: C 28.98; H 2.27; Cl 42.76; N 6.89; S 7.73%.

***N*-[1-(4-Methylbenzene)sulfonamido-2,2,2-trichloroethyl]chloroacetamide (3).** Yield 73%, m.p. 185 ^{0}C (acetone). Anal. Calcd. for $C_{11}H_{12}Cl_4N_2O_3S$: C 33.52; H 3.07; Cl 35.98; N 7.11, S 8.48. Found: C 32.54; H 3.13; Cl 35.55; N 6.89; S 8.46%.

Synthesis of 1-arylsulfonyl-2-trichloromethylimidazolidine-4-ones

Sodium hydroxide (0.80 g, 0.02 mol) diluted in water (10 ml) was added to the products **1-3** (0.01 mol). The mixture was heated at reflux for 2 h. The precipitate was filtered off to give 74–88% products **4–6**.

1-Benzenesulfonyl-2-trichloromethylimidazolidine-4-one (4). Yield 86%, m.p. 246–248 ^{0}C (acetone). Anal. Calcd. for $C_{10}H_8Cl_3N_2O_3S$: C 35.06; H 2.35; Cl 31.04; N 8.18; S 9.36. Found: C 35.10; H 2.74; Cl 31.81; N 8.25; S 9.66%.

1-(4-Chlorobenzene)sulfonyl-2-trichloromethylimidazolidine-4-one (5). Yield 73%, m.p. 236–237 ^{0}C (acetone). Anal. Calcd. for $C_{10}H_7Cl_4N_2O_3S$: C 31.77; H 1.87; Cl 37.61; N 7.43; S 8.50. Found: C 31.54; H 1.98; Cl 37.40; N 7.51; S 8.86%.
1-(4-Methylbenzene)sulfonyl-2-trichloromethylimidazolidine-4-one (6). Yield 71%, m.p. 280–281 ^{0}C (acetone). Anal. Calcd. For $C_{11}H_{10}Cl_3N_2O_3S$: C 37.05; H 2.83; Cl 29.82; N 7.86; S 8.99. Found: C 37.31; H 2.29; Cl 28.64; N 7.82; S 9.52%.

Synthesis of *N*-[1-(4-chlorobenzenesulfonamido)-2,2,2-trichloroethyl]ethoxyacetamide (7). Sodium hydroxide (0.40 g, 0.01 mol), compound (**2**) (2.07 g, 0.005 mol) and ethyl alcohol (10 ml) were heated at reflux for 2 h. According to ^{1}H NMR data (Table 1) the precipitate consisted of a mixture of compound (**5**) (52%, 48% yield) and (**7**) (48%, 35% yield).

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