

A novel regiospecific cascade synthesis of sulfonamide derivatives from *N*-(2-polychloroethyl)sulfonamides via chloroaziridine intermediates in the presence of mercaptoethanol

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Abstract *N*-(1-Aryl-2-polychloroethyl)arenesulfonamides obtained on the basis of *N,N*-dichlorosulfoamides and polychloroethenes or phenylacetylene undergo a reaction cascade in the presence of mercaptoethanol. The reaction cascade opens a new route to the series of cyclic or open-chain sulfonamide derivatives. The process includes cyclization to aziridine intermediates, their further recyclization, and isomerization to imidoylechlorides or chloroimines, followed by substitution or reduction under the action of mercaptoethanol or hydrolysis. The final sulfonamide structures depend on the starting *N*-(polychloroethyl)sulfonamides. *N*-(2,2-Dichloroethyl)sulfonamides were transformed into sulfonamide-containing 1,4-oxathians while *N*-(2,2,2-trichloroethyl)sulfonamides were converted to *N*-(2-arylacetyl)arenesulfonamides. *N*-(2-Phenyl-2,2-dichloroethyl)sulfonamides form enamide derivatives that were transformed into aromatic ketones.

Keywords Sulfonamides · Aziridines · Imidoylechlorides · Chloroimines · 1,4-Oxathianes · Ketones · Cascade reactions

Introduction

The importance of sulfonamide compounds for modern medicine and agriculture can hardly be overestimated. Many

antimicrobial and antibiotic drugs [1,2], anticonvulsants, and diuretics [1–3], analgetics and antimigraine remedies [3] were designed on the basis of sulfonamide derivatives. Furthermore, they form powerful inhibitors of proteases [3], carbonic anhydrase [4], COX-2 [5], caspase [6], as well as osteogenic agents [7], and antitumor drugs [8]. Some sulfonamides also exhibit a herbicidal activity [9]. Amides of sulfonic acids are used in organic syntheses to obtain dendrimers [10], heterocyclic compounds [11], and ligands for catalysts of asymmetrical reactions [12,13]. They can also be used as reagents for solid-phase [14] and multi-component [15] reactions. A sulfonamide fragment can be regarded as a protected amino group, and so, when appropriate, it is used for such purpose in organic synthesis [16]. There are also some chemical sensors of sulfonamide nature [17]. Sulfonamide systems are of particular theoretical interest in quantum chemistry [18] and other theoretical studies [19].

The remarkable practical significance of sulfonamide compounds encouraged us to develop new methods for their preparation. The state-of-the-art methods are based on the reactions of amines with sulphonic acids or their derivatives with a general formula RSO_2X where the leaving group X is a halogen atom [11], a hydroxyl group [20], or a triazole fragment [21]. Radical-based transformations of pentafluorophenylvinyl sulfonate resulting in sulfonamides are also known [22]. A promising way to sulfonamidic systems is a direct catalytic sulfonamidation of alkenes, ethers, and benzyl systems [23–25]. Addition of nucleophiles to the azomethyne group of *N*-sulfonylimines [26–28] is another approach to sulfonamides.

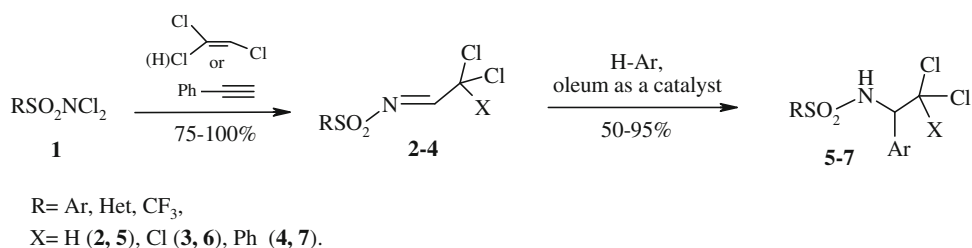
We developed a new route to functionalized sulfonamide derivatives on the basis of *N*-sulfonylpolyhaloaldehydes.

We reported earlier [26] that a series of sulfonylimines of polychloro(bromo)acetaldehydes are accessible through the radical reactions of *N,N*-dichlorosulfonamides **1** with

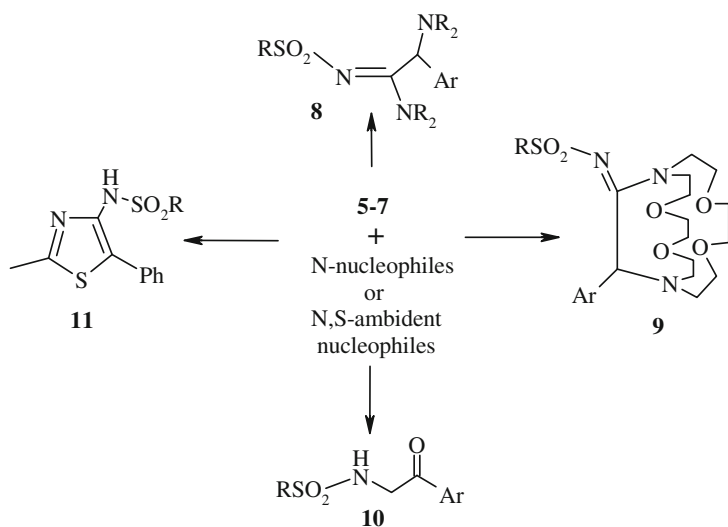
4th International Conference on Multi-Component Reactions and Related Chemistry, Russia, Ekaterinburg, 2009.

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Scheme 1 Synthesis of *N*-sulfonylpolychloroaldimines **2–4** and *N*-(2-polychloroethyl)sulfonamides **5–7** [29,30,32]



Scheme 2 Synthesis of sulfonamide derivatives from polychloroethylsulfonamides **5–7** and *N*- or *N,S*-nucleophiles



1,2-polyhaloethenes or phenylacetylene (Scheme 1). The advantage of this route to chloroimines **2–4** when compared to other methods is that this is a simple one-step procedure characterized by high or quantitative yields. Owing to the high electrophilicity of *N*-sulfonylpolyhaloaldimines **2–4** as a result of strong electron-withdrawing substituents, these compounds have been used as key reagents for synthesis of *N*-(1-aryl-2-polyhaloethyl)sulfonamides of the types **5–7** [26,29–32] (Scheme 1).

Polychloroethylamides **5–7** were applied to produce biologically active *N*-protected amino acids [33]. In addition, the compounds **5–7** can undergo a cascade of reactions in aprotic bipolar media in the presence of inorganic bases to give acyclic and heterocyclic sulfonamides [34–37] that some times cannot be obtained by the other methods. For instance, the reaction of **5–7** in the presence of *N*- or *N,S*-ambident nucleophiles allows for the synthesis of amidine derivatives **8**, diaza-18-crown-6 derivatives **9**, amidoketones **10**, and thiazoles **11**. It is noteworthy that all of them contain the sulfonamide fragments in their structures (Scheme 2) [34–37].

The reaction cascade that polychloroethylamides **5–7** go through includes the formation of aziridines **A1–A3**, and their recyclization to intermediates **B1–B3** that finally transform into polyfunctionalized derivatives of sulfonamides when exposed to a nucleophile (Scheme 3).

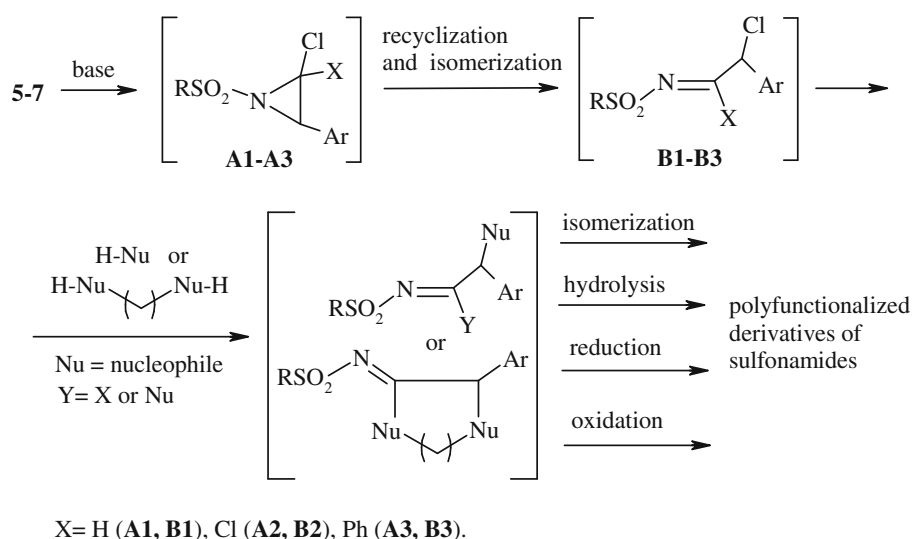
Results and discussion

The final products of the cascade reactions with mercaptoethanol strongly depend on the structures of the starting reagents (e.g., **5a–d**, **6a–c**, **7a–c**). Thus, the reaction of dichloroethylamides **5a–d** results in 2-arenesulfonamido-3-aryl(hetaryl)-1,4-oxathianes **12a–d** while polyhaloethylamides **6a–c**, **7a–c** give no products containing the mercaptoethanol fragment in their structures (Scheme 4).

It has been shown that the cascade transformations of polychloroethylamides **5–7** include the formation of chloroaziridines **A1–A3** followed by their recyclization and rearrangement of a chlorine atom with the formation of various chloroimines **B1–B3** as intermediates which defines the subsequent interaction.

Chloroimines **B1** lead to oxathianes **12a–d** through the substitution of chlorine atom with the sulfanyl group of mercaptoethanol (formation of **C1**) and further intramolecular heterocyclization by the addition of hydroxyl group of **C1** to the azomethine moiety.

The moderate yields of oxathianes **12** could be explained by the side processes of hydration, hydrolysis, or resinification of the potential hydrolysis products. The hydrolysis is possible due to the formation of water during the neutralization of sodium carbonate by starting sulfonamides **5** which are strong *N*–H acids.

Scheme 3 Reaction cascade of polychloroethylsulfonamides **5–7**

By the use of various solvents, it has been shown that the DMF medium is the most favorable for the formation of the compounds **12**. Their yields are lower in DMSO that is apparently due to the redox processes involving the solvent, like those in the reaction of the trichloroethylamides **6** with secondary amines [34]. The reaction does not occur either in aqueous DMF, acetone, diethyl ether or in aliphatic, aromatic, and halogen containing hydrocarbons.

The use of potassium carbonate instead of sodium carbonate makes no changes in the process while the use of alkali metal hydroxides instead of carbonates as well as heating of the reaction mixture leads to a considerable resinification.

The trichloroethylamides **6a–d** do not react with mercaptoethanol at room temperature. However, they form *N*-sulfonylarylacetamides **13a–d** when heated to 100 °C for 1.5–2 h.

Previously, we reported in the short communication [38] on the syntheses of imides of the type **13** by the reaction of compounds **6** with propanethiol and mercaptoethanol. In this article, we expand the range of compounds **13** to corroborate universal character of the reaction of various aromatically substituted trichloroethylamides with thiols and, therewith, to visualize the dependence of the cascade transformations upon the structures of polychloroethylamides **5–7**.

The general mechanism of this cascade transformation is as follows (Scheme 4): heating the trichloroethylamides **6a–d** leads to the dichloroaziridine intermediates **A2**, with the latter subsequently undergoing recyclization to imidoylchlorides **B2** which are further hydrolyzed at imidoylchloride fragment (formation of **C2**) and reduced at the chloromethylene groups. Mercaptoethanol acts as a reduction agent and is transformed into corresponding disulfide which can be detected by NMR spectroscopy.

Phenyldichloroethylamides **7a–c** form the aromatic ketone **15** as the final product when heated in the presence of

mercaptoethanol. We suppose that the reaction proceeds via chloroaziridines **A3** and enamides **14** (tautomers of intermediate **B3**) which are hydrolyzed to eliminate arenesulfonamides and produce the intermediate chloroketone **C3** followed by reduction with mercaptoethanol.

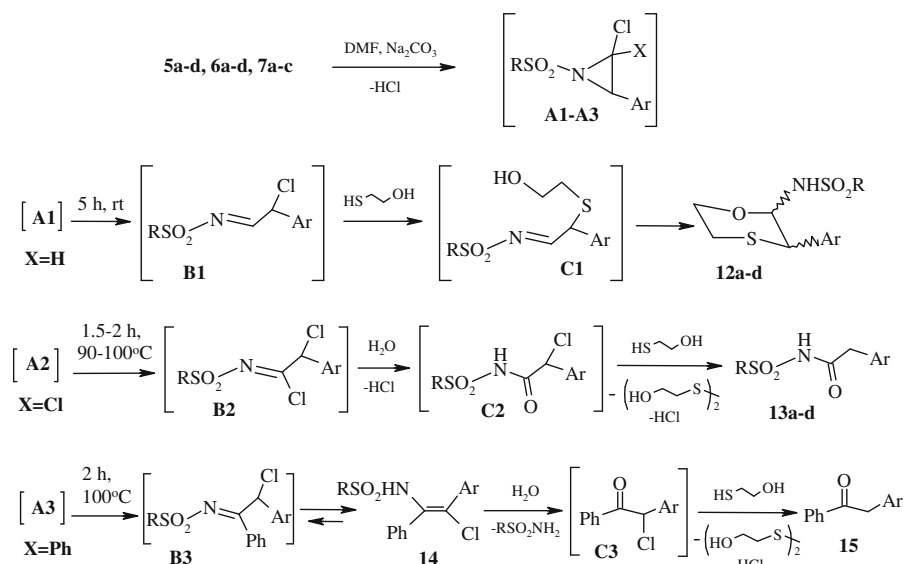
We carried out the target synthesis of 1-arenesulfonamido-2-(4-methoxyphenyl)-1-phenyl-2-chloroethene **14**. In our earlier short report [39], we did not discuss the formation of enamide **14** from chloroaziridine due to the wrong supposition that it was an ordinary dehydrochlorination of phenyldichloroethylamide **7b** to 1-arenesulfonamido-1-(4-methoxyphenyl)-2-phenyl-2-chloroethene isomer. Thus, in this study, the structure of the compound **14** has been rigorously proved for the first time.

The structures of the compounds obtained are confirmed by IR, mass spectra, ^1H , and ^{13}C NMR data. The ^1H and ^{13}C NMR signals of the compounds **12–15** are assigned using the ^{13}C -JMOD, ^{13}C -HSQC, ^{13}C -HMBC, and NOESY experiments. Configurations of the oxathiane derivatives **12a–d** are determined based on the ^1H - ^1H and ^{13}C - ^1H spin-spin coupling constants.

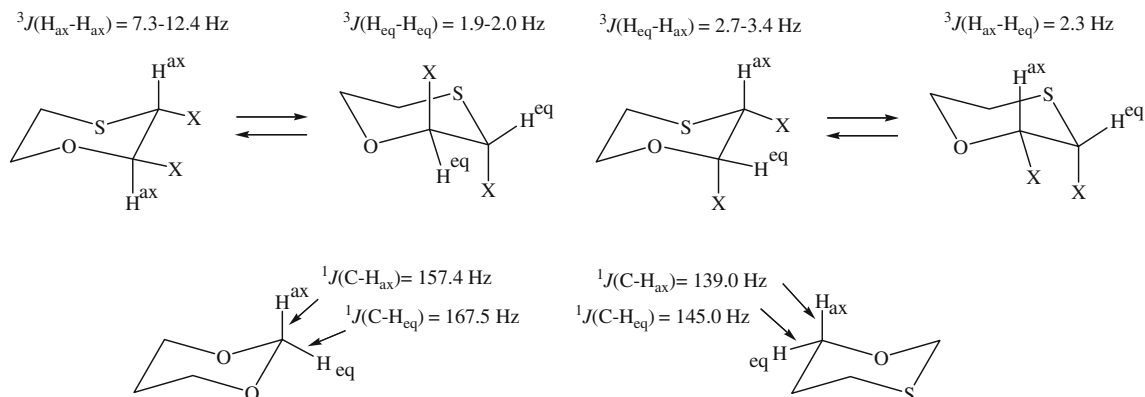
Spin-spin coupling constants involving two diaxial vicinal hydrogen atoms $^3J(\text{H}_{\text{ax}}-\text{H}_{\text{ax}})$ in the 1,4-oxathiane cycles are known to be of 7.3–12.4 Hz which is 4–6 times higher than in the case of other configurations [40], as shown in the Scheme 5. It is known also that for dioxanes and oxatians, the $^1J(\text{C}-\text{H}_{\text{eq}})$ values in α -position to the oxygen atom are 6–10 Hz more as compared to $^1J(\text{C}-\text{H}_{\text{ax}})$ due to the anomeric effect [41]. The comparison of the measured values of $^3J(\text{H}-\text{H})$ and $^1J(\text{C}-\text{H})$ given in Table 1 with the data given in [40,41] allows one to make a conclusion about the configurations of the oxathianes **12a–d**.

In order to confirm the structure of enamide **14**, we used the HMBC ^1H - ^{13}C technique. Besides, according to NOESY, there is no dipole-dipole interaction between

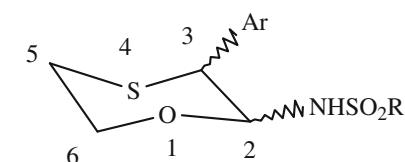
Scheme 4 Reaction of polychloroethylamides **5–7** with mercaptoethanol



Starting compd.				Product	Isolated yield, %
No	R	Ar	X		
5a	Ph	Ph	H	12a	37
5b	4-ClC ₆ H ₄	4-CH ₃ C ₆ H ₄	H	12b	43
5c	4-ClC ₆ H ₄	4-CH ₃ OC ₆ H ₄	H	12c	41
5d	4-ClC ₆ H ₄	5-Cl-2-thienyl	H	12d	39
6a	4-ClC ₆ H ₄	4-ClC ₆ H ₄	Cl	13a	51
6b	4-ClC ₆ H ₄	4-CH ₃ C ₆ H ₄	Cl	13b	49
6c	4-ClC ₆ H ₄	4-CH ₃ OC ₆ H ₄	Cl	13c	43
6d	4-ClC ₆ H ₄	1-naphthyl	Cl	13d	45
7b	4-ClC ₆ H ₄	4-CH ₃ OC ₆ H ₄	Ph	14	54
7a	Ph	4-CH ₃ OC ₆ H ₄	Ph	15	65
7b	4-ClC ₆ H ₄	4-CH ₃ OC ₆ H ₄	Ph	15	67
7c	4-CH ₃ C ₆ H ₄	4-CH ₃ OC ₆ H ₄	Ph	15	45



Scheme 5 Spin–spin coupling constants in oxathianes and dioxanes [40,41]

Table 1 Structures of **12a–d** (10% solution in CDCl₃) according to values of C²–H and H²–H³ spin–spin coupling constants

Cmpd.	R	Ar	¹ J(C ² –H) Hz		¹ J(H ² –H ³) Hz		Molar ratio (%)
12a	Ph	Ph	161.4	ax	7.6	ax–ax	100
12b	4-ClC ₆ H ₄	4-CH ₃ C ₆ H ₄	159.9	ax	8.2	ax–ax	66
			167.3	eq	2.9	eq–ax	34
12c	4-ClC ₆ H ₄	4-CH ₃ OC ₆ H ₄	159.9	ax	8.3	ax–ax	100
12d	4-ClC ₆ H ₄	5-Cl-2-thienyl	159.7	ax	6.4	ax–ax	38
			163.9	eq	2.7	eq–ax	62

protons of the anisole moiety and the benzene ring that points to the *trans*-position of these aromatic fragments.

Experimental section

The compounds **5a–d**, **6a–c**, **7a–c** have been obtained by C-amidoalkylation of the aromatics with arylsulfonylimines **2–4** [29,30,32]. The ¹H and ¹³C NMR spectra have been recorded on a Bruker DPX-400 spectrometer at 400.61 and 100.13 MHz, respectively. Chemical shifts (δ) in ppm are reported with use of TMS as internal NMR standard. Mass spectra have been recorded on a GCMS QP 5050A mass spectrometer operating at an ionization potential of 70 eV. IR spectra have been recorded on a Bruker IFS-25 spectrometer.

General procedure for the synthesis of

N-(3-aryl-1,4-oxathiane-2-yl)arenesulfonamides **12**

A mixture of *N*-(1-aryl-2,2-dichloroethyl)arenesulfonamide **5a–d** (0.95 g, 2.5 mmol), 2-mercaptoethanol (0.59 g, 7.5 mmol), and sodium carbonate Na₂CO₃ (1.59 g, 15 mmol) in 5 ml of DMF was stirred for 5 h. Then, the product **12** was precipitated by adding 30 mL of water, additionally reprecipitated from acetone solution to water, filtered off, dried, and rapidly washed with cold diethyl ether (5–10 mL) to give oxathianes **12a–d** as a colorless solid.

N-(3-Phenyl-1,4-oxathiane-2-yl)benzenesulfonamide **12a**

m.p. 133–135 °C. IR (KBr): 3277, 1332, 1161 cm^{−1}. ¹H NMR (400.61 MHz, CDCl₃) δ (ppm): 2.44, 2.83 (m, 2H, CH₂–S), 3.74 (d, ³J_{aa} = 7.6 Hz, 1H, CH–S), 3.89, 4.10 (m, 2H, CH₂–O), 5.18 (dd, ³J_{NH–CH} = 9.1 Hz, ³J_{aa} = 7.6 Hz, 1H, CH–O), 5.22 (d, ³J_{NH–CH} = 9.1 Hz, 1H, NH), 7.37–7.65 (m, 10H, 2C₆H₅). ¹³C NMR (100.13 MHz, CDCl₃) δ (ppm): 28.5 (CH₂–S), 47.6 (CH–S), 68.3 (CH₂–O), 85.0

(CH–O), 127.5, 128.6, 128.8, 129.3, 129.4, 133.1, 137.21, 140.9 (C_{arom}). Anal. Calcd for C₁₆H₁₇NO₃S₂: C, 57.29; H, 5.11; N, 4.18; S, 19.12. Found: C, 57.31; H, 5.09; N, 4.25; S, 19.18.

N-[3-(4-Methylphenyl)-1,4-oxathiane-2-yl]-4-chlorobenzenesulfonamide **12b**

IR (KBr): 3260, 1334, 1162 cm^{−1}. ¹H NMR (400.61 MHz, CDCl₃) for the major isomer δ (ppm): 2.33 (s, 3H, CH₃), 2.41, 2.88 (m, 2H, CH₂–S), 3.69 (d, ³J_{aa} = 8.2 Hz, 1H, CH–S), 3.92, 4.17 (m, 2H, CH₂–O), 5.08 (dd, ³J_{NH–CH} = 8.5 Hz, ³J_{aa} = 8.2 Hz, 1H, CH–O), 5.38 (d, ³J_{NH–CH} = 8.5 Hz, 1H, NH), 7.02, 7.11 (AA' BB', 4H, C₆H₄), 7.32, 7.56 (AA' BB', 4H, C₆H₄); for the minor isomer δ (ppm): 2.34 (s, 3H, CH₃), 2.54, 2.96 (m, 2H, CH₂–S), 3.76, 3.89 (m, 2H, CH₂–O), 4.27 (d, ³J_{ea} = 2.9 Hz, 1H, CH–S), 5.27 (dd, ³J_{NH–CH} = 9.2 Hz, ³J_{ae} = 2.9 Hz, 1H, CH–O), 6.06 (d, ³J_{NH–CH} = 9.2 Hz, 1H, NH), 6.90, 6.96 (AA' BB', 4H, C₆H₄), 7.21, 7.45 (AA' BB', 4H, C₆H₄). ¹³C NMR (100.13 MHz, CDCl₃) for the major isomer δ (ppm): 21.2 (CH₃), 27.9 (CH₂–S), 47.5 (CH–S), 68.6 (CH₂–O), 85.6 (CH–O), 128.1, 128.5, 129.0, 129.6, 133.4, 138.2, 138.9, 139.5 (C_{arom}); for the minor isomer δ (ppm): 21.1 (CH₃), 27.7 (CH₂–S), 47.5 (CH–S), 60.4 (CH₂–O), 80.9 (CH–O), 127.3, 128.3, 129.0, 129.5, 133.1, 138.1, 138.8, 139.2 (C_{arom}). MS (IE, 70eV): *m/z* = 382 (*M*⁺, 1), 164 (10), 136 (100), 111 (16), 91 (15), 44 (30). Anal. Calcd for C₁₇H₁₈NO₃S₂Cl: C, 53.19; H, 4.73; Cl, 9.23; N, 3.65; S, 16.70. Found: C, 53.23; H, 4.70; Cl, 9.29; N, 3.62; S, 16.77.

N-[3-(4-Methoxyphenyl)-1,4-oxathiane-2-yl]-4-chlorobenzenesulfonamide **12c**

m.p. 137–139 °C. IR (KBr): 3262, 1334, 1162 cm^{−1}. ¹H NMR (400.61 MHz, CDCl₃) δ (ppm): 2.25, 2.72 (m, 2H,

CH₂-S), 3.54 (d, $^3J_{\text{aa}} = 8.3$ Hz, 1H, CH-S), 3.64 (s, 3H, CH₃), 3.76, 4.01 (m, 2H, CH₂-O), 4.90 (dd, $^3J_{\text{NH-CH}} = 8.9$ Hz, $^3J_{\text{aa}} = 8.3$ Hz, 1H, CH-O), 5.32 (d, $^3J_{\text{NH-CH}} = 8.9$ Hz, 1H, NH), 6.58, 6.99 (AA'BB', 4H, C₆H₄), 7.17, 7.40 (AA'BB', 4H, C₆H₄). ¹³C NMR (100.13 MHz, CDCl₃) δ (ppm): 27.9 (CH₂-S), 47.1 (CH-S), 55.2 (CH₃), 68.5 (CH₂-O), 85.8 (CH-O), 114.1, 128.4, 128.5, 128.9, 129.3, 138.8, 139.5, 159.4 (C_{arom}). Anal. Calcd for C₁₇H₁₈NO₄S₂Cl: C, 51.06; H, 4.54; Cl, 8.87; N, 3.50; S, 16.03. Found: C, 51.01; H, 4.51; Cl, 8.95; N, 3.57; S, 16.15.

N-[3-(5-Chloro-2-thienyl)-1,4-oxathiane-2-yl]-4-chlorobenzenesulfonamide **12d**

IR (KBr): 3272, 1341, 1163 cm⁻¹. ¹H NMR (400.61 MHz, CDCl₃) for the major isomer δ (ppm): 2.70 (m, 2H, CH₂-S), 3.77 (m, 2H, CH₂-O), 4.27 (d, $^3J_{\text{ea}} = 2.7$ Hz, 1H, CH-S), 5.34 (dd, $^3J_{\text{NH-CH}} = 9.9$ Hz, $^3J_{\text{ae}} = 2.7$ Hz, 1H, CH-O), 5.75 (d, $^3J_{\text{NH-CH}} = 9.9$ Hz, 1H, NH), 6.72 (m, 2H, thienyl), 7.42, 7.72 (AA'BB', 4H, C₆H₄); for the minor isomer δ (ppm): 2.63 (m, 2H, CH₂-S), 3.90 (d, $^3J_{\text{aa}} = 6.4$ Hz, 1H, CH-S), 3.95 (m, 2H, CH₂-O), 5.11 (dd, $^3J_{\text{NH-CH}} = 9.5$ Hz, $^3J_{\text{aa}} = 6.4$ Hz, 1H, CH-O), 5.73 (d, $^3J_{\text{NH-CH}} = 9.5$ Hz, 1H, NH), 6.78 (m, 2H, thienyl), 7.46, 7.75 (AA'BB', 4H, C₆H₄). ¹³C NMR (100.13 MHz, CDCl₃) for the major isomer δ (ppm): 26.1 (CH₂-S), 42.6 (CH-S), 64.1 (CH₂-O), 81.6 (CH-O), 128.6, 129.3, 138.7, 139.3 (C_{arom}), 125.8, 126.2, 126.5, 136.3 (C_{thienyl}); for the minor isomer δ (ppm): 26.4 (CH₂-S), 42.6 (CH-S), 65.4 (CH₂-O), 83.5 (CH-O), 128.5, 129.4, 138.6, 139.0 (C_{arom}), 125.5, 126.0, 126.3, 136.0 (C_{thienyl}). Anal. Calcd for C₁₄H₁₃NO₃S₃Cl₂: C, 40.98; H, 3.19; Cl, 17.28; N, 3.41; S, 23.44. Found: C, 41.05; H, 3.15; Cl, 17.35; N, 3.38; S, 23.51.

General experimental procedure for the preparation of *N*-arylacetyl-4-chlorobenzenesulfonamides **13**

A mixture of *N*-(1-aryl-2,2,2-trichloethyl)-1-chlorobenzene-sulfonamide **6a–d** (5 mmol), sodium carbonate (20 mmol), and mercaptoethanol (1.56 g, 20 mmol) in 15 ml of DMF was stirred for 1 h at 100 °C. The reaction mass was cooled, mixed with 50 mL of water, and filtered out. The filtrate was acidified with 5% hydrochloric acid to pH = 7 and kept until a precipitate of compound **13** was formed. The precipitate was separated, dried, rinsed out with 5 ml of cold diethyl ether, and recrystallized from hexane.

N-[(4-Chlorophenyl)sulfonyl]-2-(4-chlorophenyl)acetamide **13a**

m.p. 206–208 °C. IR (KBr): 3100, 1690, 1360, 1170 cm⁻¹. ¹H NMR (400.61 MHz, DMSO-d₆) δ (ppm): 3.58 (s, 2H,

CH₂), 7.17, 7.33 (AA'BB', 4H, C₆H₄), 7.68, 7.89 (AA'BB', 4H, C₆H₄), 12.45 (br s, 1H, NH). ¹³C NMR (100.13 MHz, DMSO-d₆) δ (ppm): 41.4 (CH₂), 128.5, 129.6, 129.8, 131.5, 131.9, 132.9, 138.1, 138.9 (C_{arom}), 169.6 (C=O). Anal. Calcd for C₁₄H₁₁NO₃SCl₂: C, 48.85; H, 3.22; Cl, 20.60; N, 4.07; S, 9.31. Found: C, 48.90; H, 3.25; Cl, 20.68; N, 4.15; S, 9.22.

N-[(4-Chlorophenyl)sulfonyl]-2-(4-methylphenyl)acetamide **13b**

m.p. 155–160 °C. IR (KBr): 3100, 1680, 1350, 1160 cm⁻¹. ¹H NMR (400.61 MHz, CDCl₃) δ (ppm): 2.39 (s, 3H, CH₃), 3.59 (s, 2H, CH₂), 7.07, 7.17 (AA'BB', 4H, C₆H₄), 7.53, 7.98 (AA'BB', 4H, C₆H₄), 8.14 (br s, 1H, NH). ¹³C NMR (100.13 MHz, CDCl₃) δ (ppm): 21.1 (CH₃), 43.3 (CH₂), 127.9, 129.0, 129.6, 129.7, 130.0, 138.2, 138.7, 140.6 (C_{arom}), 167.9 (C=O). Anal. Calcd for C₁₅H₁₄NO₃SCl: C, 55.64; H, 4.36; Cl, 10.95; N, 4.33; S, 9.90. Found: C, 55.69; H, 4.35; Cl, 10.93; N, 4.34; S, 9.92.

N-[(4-Chlorophenyl)sulfonyl]-2-(4-methoxyphenyl)acetamide **13c**

m.p. 137–140 °C. IR (KBr): 3150, 1680, 1365, 1170 cm⁻¹. ¹H NMR (400.61 MHz, CDCl₃) δ (ppm): 3.53 (s, 2H, CH₂), 3.80 (s, 3H, CH₃), 6.85, 7.06 (AA'BB', 4H, C₆H₄), 7.49, 7.94 (AA'BB', 4H, C₆H₄), 8.55 (br s, 1H, NH). ¹³C NMR (100.13 MHz, CDCl₃) δ (ppm): 42.3 (CH₂), 54.9 (CH₃), 114.3, 123.6, 128.9, 129.5, 130.1, 136.3, 140.4, 159.0 (C_{arom}), 168.7 (C=O). Anal. Calcd for C₁₅H₁₄NO₄SCl: C, 53.02; H, 4.15; Cl, 10.43; N, 4.12; S, 9.44. Found: C, 52.96; H, 4.11; Cl, 10.48; N, 4.17; S, 9.52.

N-[(4-Chlorophenyl)sulfonyl]-2-(1-naphthyl)acetamide **13d**

m.p. 151–155 °C. IR (KBr): 3150, 1680, 1365, 1170 cm⁻¹. ¹H NMR (400.61 MHz, DMSO-d₆) δ (ppm): 4.06 (s, 2H, CH₂), 7.67, 7.91 (AA'BB', 4H, C₆H₄), 7.33–7.90 (m, 7H, 1-naphthyl). ¹³C NMR (100.13 MHz, DMSO-d₆) δ (ppm): 39.2 (CH₂), 123.6, 125.4, 125.7, 126.1, 127.6, 128.1, 128.4, 129.2, 129.5, 130.4, 131.6, 133.3, 137.9, 138.6 (C_{arom}), 169.6 (C=O). Anal. Calcd for C₁₈H₁₄NO₃SCl: C, 60.08; H, 3.92; Cl, 9.85; N, 3.89; S, 8.91. Found: C, 60.03; H, 3.88; Cl, 9.90; N, 3.84; S, 8.97.

1-(4-Chlorobenzene)sulfonamido-2-(4-methoxyphenyl)-1-phenyl-2-chloroethene **14**

A mixture of *N*-(1-(4-methoxyphenyl)-2-phenyl-2-dichloroethyl)-4-chlorobenzenesulfonamide **7b** (2.35 g, 5 mmol) and sodium carbonate (1.60 g, 15 mmol) in 10 mL of DMF

was stirred for 10 min at room temperature. Then the product **14** was precipitated by addition of water (10 mL) and 5% hydrochloric acid to pH = 7, separated, dried and recrystallized from chloroform.

m.p. 131–132 °C. IR (KBr): 1155, 1330, 1570, 1600, 2920–2960, 3030–3090, 3250. ¹H NMR (400.61 MHz, DMSO-d₆) δ(ppm): 3.70 (s, 3H, OMe), 6.60, 6.98 (AA'BB', 4H, C₆H₄), 7.00–7.10 (m, 5H, Ph), 7.37, 7.53 (AA'BB', 4H, C₆H₄), 9.18 (s, 1H, NH). ¹³C NMR (100.13 MHz, DMSO-d₆) δ (ppm): 55.14 (OMe), 113.66, 121.18, 131.04, 159.06 (OC₆H₄), 126.67 (=C–Cl), 127.73, 127.97, 130.15, 135.44 (Ph), 128.38, 129.00, 131.82, 140.03 (ClC₆H₄), 139.94 (=C–NH). Anal. Calcd for C₂₁H₁₇Cl₂NO₃S: C, 58.07; H, 3.95; Cl, 16.33; N, 3.22; S, 7.38. Found: C, 58.01; H, 3.92; Cl, 16.38; N, 3.30; S, 7.45.

2-(4-Methoxyphenyl)-1-phenylethane-1-on **15**

A mixture of *N*-(1-(4-methoxyphenyl)-2-phenyl-2,2-dichloroethyl) benzenesulfonamide **7a** (0.87 g, 2 mmol), mercaptoethanol (0.78 g, 10 mmol) and sodium carbonate (1.06 g, 10 mmol) in DMF (10 mL) was stirred for 1 h at 100 °C. Then, the products of the reaction were precipitated by addition of water (10 mL) and 5% hydrochloric acid to attain pH = 7. After separating and drying, the precipitate was boiled with hexane (50 mL). The compound **15** was isolated from the hexane solution on cooling as a colorless solid and additionally recrystallized from hexane. In the similar way, the ketone **15** was obtained from *N*-(1-(4-methoxyphenyl)-2-phenyl-2,2-dichloroethyl)-4-chlorobenzenesulfonamide **7b** or from *N*-(1-(4-methoxyphenyl)-2-phenyl-2,2-dichloroethyl)-4-toluenesulfonamide **3c**.

m.p. 98–100 °C. IR (KBr): 1585–1612, 1690, 2833–3056 cm⁻¹. ¹H NMR (400.61 MHz, DMSO-d₆) δ (ppm): 3.71 (s, 3H, OMe), 4.30 (s, 2H, CH₂), 6.86, 7.18 (AA'BB', 4H, 4 – MeOC₆H₄), 7.50–8.04 (m, 5H, Ph). ¹³C NMR (100.13 MHz, DMSO-d₆) δ (ppm): 43.81 (CH₂), 54.95 (OMe), 113.78, 126.85, 130.59, 157.94 (OC₆H₄), 128.35, 128.68, 133.13, 136.32 (Ph), 197.91 (C=O). MS (70 eV): m/z = 226 (M⁺, 29), 121 (97), 105 (100), 91 (12), 77 (84), 65 (6), 51 (40). Anal. Calcd for C₁₅H₁₄O₂: C, 79.62; H, 6.24. Found: C, 79.58; H, 6.22.

Conclusions

Thus, the reaction of *N*-(2-polychloroethyl)sulfonamides with mercaptoethanol has a cascade mechanism and results in the formation of sulfonamido-substituted 1,4-oxathianes, *N*-sulfonylarylacetamides or aromatic ketones depending on the structures of the starting reagents.

The new route to unknown oxathiane derivatives **12** offers obvious advantages over the cited methods. Thus, this new

process is based on the available and inexpensive starting reagents (dichloroamides, polyhaloethenes, etc). The process is simple and is realized in three stages. The first and the second stages (the syntheses of sulfonylimines **2** and dichloroethylamides **5**) are optimized as a *one-pot* reaction [29,30]. The third one (the formation of oxathianes **12** from compounds **5**) is a multipositional chemoselective cascade under mild conditions.

It is expected that the involvement of mercaptoethanol homologs into the reaction gives the access to a larger number of sulfonamide-substituted oxathiane systems. We find it evident that the other known approaches to sulfonamides [11–25] are less preferable for the synthesis of sulfonamides of the type **12** as the methods [11–25] adopted in those cases are non-selective and require unavailable starting reagents.

It is noteworthy that 1,4-oxathiane compounds are of interest as promising antitumor drugs [42], starting reagents for the preparation of natural molecules [43], fluorophores [44], and complexes of the “guest–host” type [45]. Compounds of the types **13** and **15** can be obtained by other methods, and their formation through the new cascade reactions are of great fundamental interest.

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