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Novel convenient approach to 1,4,2-benzodithiazine-1,1-dioxides and 1,2,3-benzoxathiazine-2,2-dioxides

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to Professor György Keglevich on the occasion of his 65th birthday

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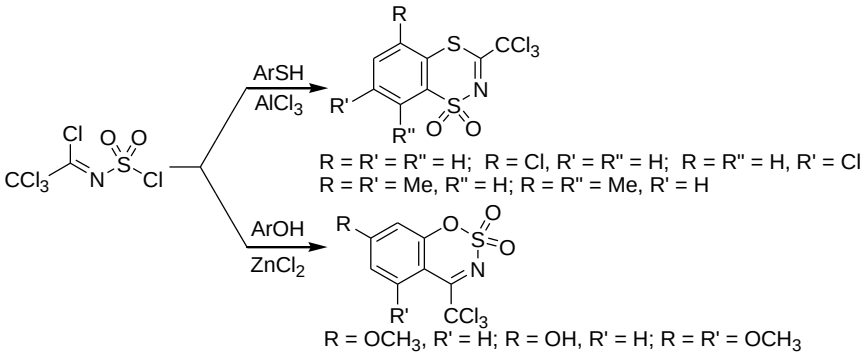
Abstract

A new effective method for the construction of 1,4,2-benzodithiazine and 1,2,3-benzoxathiazine scaffolds, based on the use of easily accessible *N*-chlorosulfonyltrichloroacetimidoyl chloride, has been developed. Reactions of thiophenols involved an initial nucleophilic substitution at the imine carbon atom with a thiol sulfur atom, followed by intramolecular sulfonylation of the benzene ring. Phenols exhibit opposite regioselectivity and react by electrophilic imidoylation of the ortho-carbon atom of the benzene ring (C-C bond formation) and sulfonation of the phenol oxygen atom. Synthesized 1,4,2-benzodithiazine-1,1-dioxides exhibit growth-stimulating activity on monocotyledonous winter wheat "Bezosta" and dicotyledonous plants *Barbarea arcuate*.



Keywords: 1,4,2-Benzodithiazine-1,1-dioxides, 1,2,3-benzoxathiazine-2,2-dioxides, imidoyl chlorides, sulfonyl chlorides, phenols, thiophenols, heterocyclization reactions

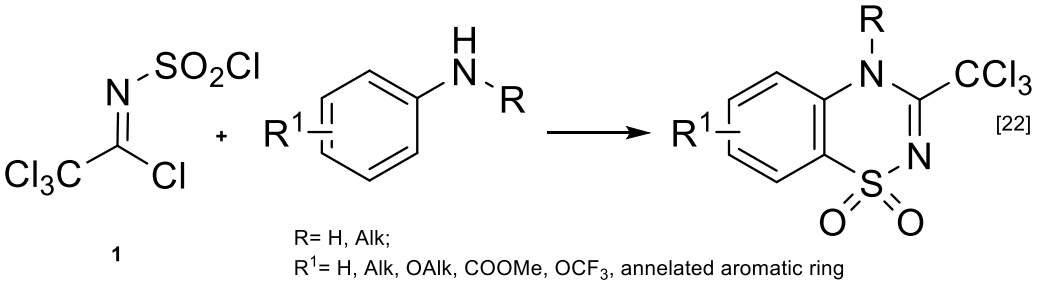
Introduction

Nitrogen heterocycles are among the most commonly present ring structures in marketed drugs. Compounds with a cyclic *N*-sulfonylamide fragment are of particular interest as they are often found in natural compounds, exhibit different biological activities, and can also be used as scaffolds for further modifications and synthesis of compounds for various purposes, for example, as ligands for asymmetric synthesis and chiral auxiliaries.[1-4] The presence of the endocyclic C=NSO_2 fragment offers additional possibilities connected with the use of activated C=N bonds in cycloaddition[5] and addition reactions,[6,7] e.g., enantioselective preparation of biorelevant cyclic aminophosphonic acid derivatives.[7,8] Recent extensive studies of derivatives incorporating a 1,4,2-benzodithiazine-1,1-dioxide moiety have revealed among them anti-HIV agents,[9] potent KATP channel openers,[10] compounds with antitumor[11] and significant cytotoxic activities against ovarian (OVCAR-3) and breast (MDA-MB-468) cancers as well as a good selectivity toward prostate (DU-145), colon (SW-620) and renal (TK-10) cancer cell lines.[12,13]

1,2,3-Benzoxathiazine-2,2-dioxides were prepared by reactions of 2-acylated phenols with chlorosulfonyl isothiocyanate[14], sulfamoyl chloride[15,16] or sulfamide[17] (O-C-C-C + S-N cyclizations). Known methods for the synthesis of 1,4,2-benzodithiazine-1,1-dioxides are based on reactions of 2-halogenosulfonamides with isothiocyanates,[18] dithiocarbamates[10] (N–S–C–C + C-S cyclizations) or [2+2]-cycloaddition of S-aryldithiocarbamates with chlorosulfonyl isothiocyanate followed by C-arylsulfonylation (S-C-C + C-N-S cyclizations),[19] and reactions of 2-mercaptoarylsulfonamides with dialkyl carbonates or phenacyl bromides (S-C-C-S-N + C cyclization).[20,21] All of them have some limitations and drawbacks connected with accessibility of starting compounds, substrate scope, severe reactions conditions, practicability, yields, etc. Thus, it would be useful to expand the range of available synthetic methods for the construction of such biorelevant heterocyclic systems.

Results and Discussion

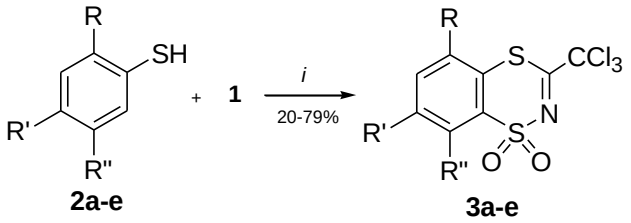
Previously, we have elaborated a convenient method for novel C-N-S-bi-electrophilic reagent, *N*-chlorosulfonyltrichloroacetimidoyl chloride **1**, and demonstrated its utility for the construction of 6-, 7-, and 8-numbered nitrogen heterocycles incorporating endocyclic sulfonamide fragment.[22,23] Specifically, **1** reacts with primary and secondary arylamines to afford derivatives of 1,2,4-benzothiadiazine 1,1-dioxides[22] (Scheme 1).



Scheme 1. Synthesis of 1,2,4-benzothiadiazine 1,1-dioxides.

The reaction involves initial nucleophilic attack of the amine nitrogen on the imine carbon atom of **1**, followed by Friedel-Crafts type sulfonylation of the aromatic ring. The regiospecific nature of the reaction is

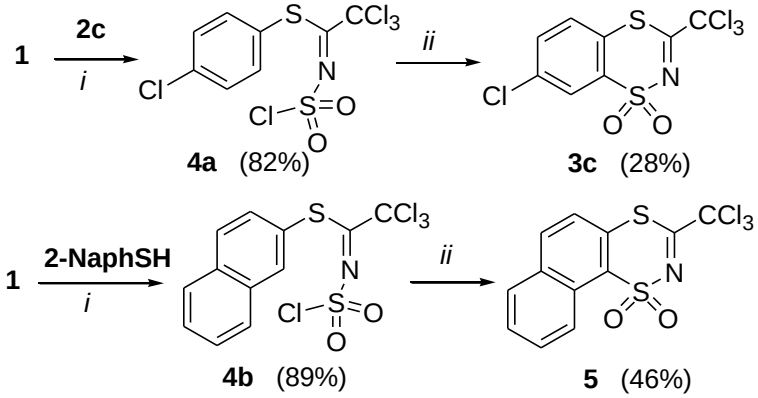
due to the fact that the C-electrophilic center in the bielectrophile **1** is activated by electron-withdrawing CCl_3 and SO_2Cl groups, and is significantly more reactive than the S-electrophilic center. We expected that reactions of thiophenols and phenols, as potential S-C-C and O-C-C binucleophiles, with C-N-S bielectrophile **1** could be used for creation of oxathiazine or dithiazine rings. Indeed, it was found that thiophenols **2a**-**d** reacted regioselectively with imidoyl chloride **1** with the formation of 1,4,2-benzodithiazine-1,1-dioxides **3a-e** (Scheme 2).



2a, 3a: R = R' = R" = H (79%)
2b, 3b: R = Cl, R' = R" = H (25%)
2c, 3c: R = R" = H, R' = Cl (20%)
2d, 3d: R = R' = Me, R" = H (73%)
2e, 3e: R = R" = Me, R' = H (78%)

Scheme 2. One-pot synthesis of 1,4,2-benzodithiazine-1,1-dioxides **3a-d.** *Reagents and conditions*: (*i*) dichloroetane, r.t., 4 h; $AlCl_3$, reflux, 18 h.

The heterocyclization proceeds in two steps. The first step, nucleophilic substitution at the imine carbon atom of **1** proceeds easily at room temperature to afford in high yields stable imidates **4** (Scheme 3).



Scheme 3. Heterocyclization of N-chlorosulfonylthioimidates **4a,b**. *Reagents and conditions*: *i*) CH_2Cl_2, r.t., 4 h; *ii*) $AlCl_3$, dichloroethane, reflux 18 h.

Intramolecular Friedel-Crafts type sulfonylation in thioimidates **4** takes place only in the presence of Lewis acid. Reduced yields of **3b,c** in Scheme 1 are caused most likely by deactivating effect of electron withdrawing chlorine atom, disposed in meta position respective to the C-nucleophilic site of benzene ring, at the sulfonylation step. Heterocyclization of **1** with 2-naphthalenethiol proceeds by the same scheme, intramolecular sulfonylation occurs at the C-1 atom of the naphthalene ring affording **5** (Scheme 3). Molecular structure of 3-(trichloromethyl)naphtho[2,1-e][1,4,2]dithiazine-1,1-dioxide **5** was unambiguously proved by X-ray crystallographic analysis (Figure 1).

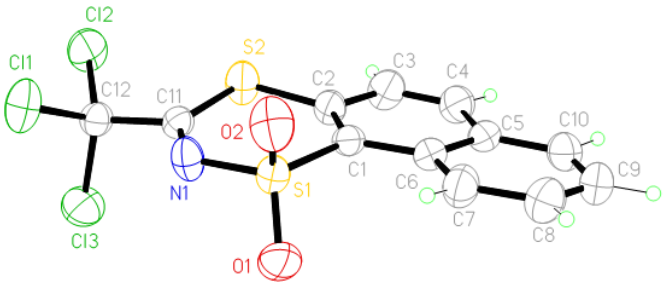
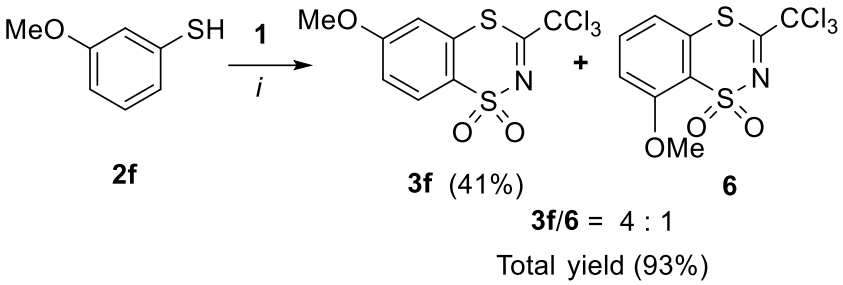


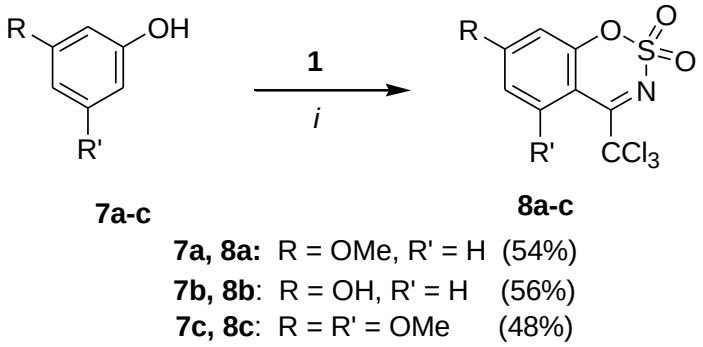
Figure 1. Molecular structure of compound **5** including thermal displacement ellipses with 50% probability.

Both possible isomers, **3f** and **6** (**3f**/**6** 4:1), are formed in reaction of unsymmetrical bielectrophile, 3-methoxythiophenol **1f**, with imidoyl chloride **1** (Scheme 4). Preferential formation of 6-methoxy isomer **3f** is explained by steric reasons. It should be noted that, in this case, the weak Lewis acid $ZnCl_2$ should be used due to the strong electron-donating effect of the methoxy group. The application of $AlCl_3$ leads to tarring.



Scheme 4. Regiochemistry of heterocyclization of imidoyl chloride **1** with 3-methoxythiophenol **2f**. *Reagents and conditions*: *i*) ZnCl2, dichloroethane, reflux 8 h.

Next, the reactions of imidoyl chloride **1** with phenols were studied. It was found that heterocyclization with phenols **7a-c** proceeds regioselectively and leads to respective 1,2,3-benzoxathiazine-2,2-dioxides **8a-c** (Scheme 5).



Scheme 5. One-pot synthesis of 1,2,3-benzoxathiazine-2,2-dioxides **8a-c**. *Reagents and conditions*: *i*) dichloroethane, r.t., 1 h; $ZnCl_2$, dichloroethane, reflux 24 h.

Thus, regiochemistry of reactions of the unsymmetrical bielectrophilic reagent **1** with phenols is opposite to that with thiophenols. The difference can be explained in the framework of Pearson concept: soft

electrophilic imine carbon atom of **1** interacts with soft C-2 nucleophilic center of **7** rather than with hard oxygen nucleophilic center. In addition, in phenols **7a-c**, carbon atoms undergoing electrophilic attack have increased nucleophilicity as a result of the matched influence of the electron donating substituents R, R' and ortho-hydroxy group.

The structure of 5,7-dimethoxy-4-(trichloromethyl)-1,2,3-benzoxathiazine-2,2-dioxide **8c** was confirmed by X-ray crystallographic analysis (Figure 2).

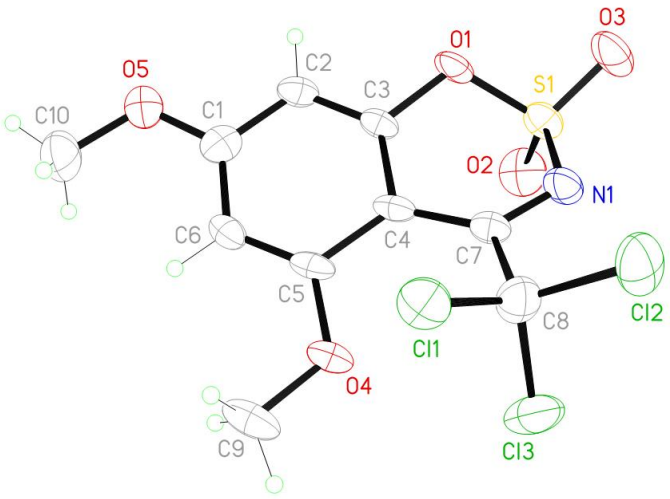
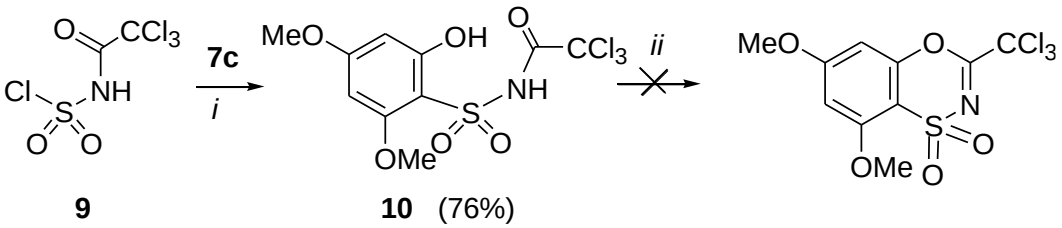


Figure 2. Molecular structure of the compound **8c** including thermal displacement ellipses with 50% probability.

We checked the possibility of obtaining isomeric 4,1,2-benzoxathiazine-1,1-dioxide by an alternative route (Scheme 6). When 3,5-dimethoxyphenol **7c** was reacted with trichloroacetylsulfamoyl chloride **9**, it underwent regioselective sulfamoylation to afford the *N*-arylsulfonyl trichloroacetamide derivative **10**. However, attempts to convert **10** into **11** using various condensing agents failed (Scheme 6).



9 **10** (76%)

Scheme 6. Regioselective sulfamoylation of 3,5-dimethoxyphenol **7c**. *Reagents and conditions*: *i*) dichloroethane, reflux 6 h; *ii*) PPA, toluene, reflux 8 h *or* $POCl_3$, reflux 3 h *or* Me_3SiCl, reflux 3 h.

The structure of compound **10** was confirmed by X-ray crystallographic analysis (Figure 3).

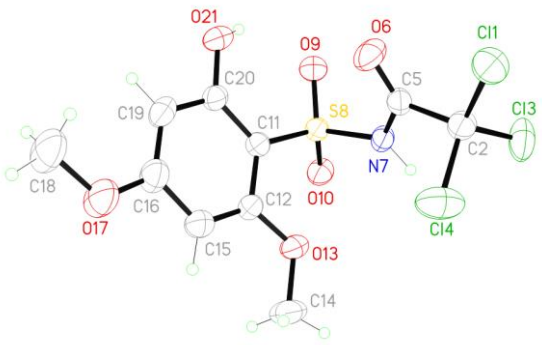


Figure 3. Molecular structure of N-(2-hydroxy-4,6-dimethoxyphenyl)sulfonyl-2,2,2-trichloroacetamide **10** including thermal displacement ellipses with 50% probability.

***Study of growth-regulating activity*.**

1,4,2-Benzodithiazine-1,1-dioxides **3b,e,f** were investigated as growth regulators. The experiments were performed on model monocotyledonous plants of winter wheat "Bezosta" and dicotyledonous plants of *Barbarea arcuata*. The data (Table 1, Supplementary Material) indicate that 1,4,2-benzodithiazines are powerful stimulators of root growth in monocotyledonous and especially dicotyledonous plants. Even at lower concentrations, they are 10-40% more effective than Ivin and Notriol, reference compounds widely used in Ukrainian agriculture. Importantly, benzodithiazine-1,1-dioxides are low-toxicity compounds. The experimentally-determined acute toxicity (LD_{50}) of compounds **3b,f** (2000 mg/kg) is in the same range as for the reference compounds Ivin and Notriol (1700 and 2950 mg/kg, respectively). Thus, 1,4,2-benzodithiazine-1,1-dioxide derivatives are promising for the development of novel, effective plant-growth regulators.

Conclusions

A convenient synthetic method for biorelevant 1,4,2-benzodithiazine-1,1-dioxides and 1,2,3-benzoxathiazine-2,2-dioxides has been developed based on reactions of *N*-chlorosulfonyl trichloroacetimidoyl chloride with thiophenols and phenols. The thiophenols and phenols reveal opposite regioselectivity in reactions with this unsymmetrical bielectrophile. Several 1,4,2-Benzodithiazine-1,1-dioxides exhibit growth-stimulating activity on monocotyledonous winter wheat "Bezosta" and dicotyledonous plants *Barbarea arcuate*.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were acquired on a Varian VXR 300, Varian VXR 400 and Bruker Avance DRX 500. Elemental analysis was carried out in the analytical laboratory of the Institute of Organic Chemistry, NAS of Ukraine. Melting points were determined by capillary method. All crystallographic measurements were performed on a Bruker Smart Apex II diffractometer operating in the ω scans mode. Full crystallographic details for compounds **5**, **8c**, **10** have been deposited at Cambridge Crystallographic Data Centre (CCDC). Any request to the CCDC for these materials should quote the full literature citation and reference numbers CCDC 2127303 (**5**), CCDC 2127304 (**8c**) and CCDC 2127305 (**10**).

General procedure for one-pot synthesis of compounds (3a-e). A solution of the appropriate aryl thiol (**2**) (5 mmol) in anhydrous dichloroethane (20 mL) was added at room temperature to a vigorously stirred solution of 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (**1**) (1.4 g, 5 mmol) in anhydrous dichloroethane (50 mL). The mixture was stirred for 4h. The resulting solution was treated with $AlCl_3$ (1 g, 7.5 mmol) and heated at reflux for 18 h. The solvent was removed under vacuum, the residue was treated with cold water (300 mL), the precipitate was filtered off, washed with water (5×50 mL), a 20% solution of methanol (10 mL), and air-dried.

3-(Trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3a). The title compound was prepared from thiophenol (**2a**) (0.52 g, 4.7 mmol), 2,2,2-trichloro-*N*-(chlorosulfonyl)acetimidoyl chloride (1.31 g, 4.7 mmol). Yield 1.18 g (79%), colorless solid, mp 118-119 °C (CCl_4). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.28 td, (*J* 7.6 Hz, *J* 1.2 Hz) 1H (H6), 7.38 td, (*J* 7.6 Hz, *J* 1.2 Hz) 1H (H7), 7.45 dd, (*J* 7.6 Hz, *J* 1.2 Hz) 1H (H5), 8.01 dd, (*J* 7.6 Hz, *J* 1.2 Hz) 1H (H8). ^{13}C-NMR (DMSO-d_6, 125 MHz) δ 96.0, 127.1, 125.4, 128.6, 132.8, 134.5, 141.8, 161.2. Anal. calcd for $C_8H_4Cl_3NO_2S_2$, %: C 30.35; H 1.27; S 20.26; Cl 33.59. Found, %: C 30.27; H 1.21; S 20.49; Cl 33.72.

5-Chloro-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3b). The title compound was prepared from 2-chlorothiophenol (**2b**) (0.42 g, 2.9 mmol), 2,2,2-trichloro-*N*-(chlorosulfonyl)acetimidoyl chloride (0.81 g, 2.9 mmol). Yield 0.25 g (25%), yellowish solid, mp 152-153 °C (benzene-acetone (20:1)). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.69 t, (*J* 7.9 Hz) 1H (H7), 7.80 dd, (*J* 7.9 Hz, *J* 1.3 Hz) 1H (H6), 8.18 dd, (*J* 7.9 Hz, J 1.3 Hz) 1H (H8). ^{13}C-NMR (DMSO-d_6, 125 MHz) δ 96.9, 126.5, 128.7, 129.9, 132.5, 133.6, 141.1, 162.9. Anal. calcd for $C_3H_3Cl_4NO_2S_2$, %: C 27.37; H 0.86; S 18.27; Cl 40.40. Found, %: C 27.09; H 1.01; S 18.39; Cl 40.37.

7-Chloro-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3c). The title compound was prepared from 4-chlorothiophenol (**2c**) (0.75 g, 5.2 mmol), 2,2,2-trichloro-*N*-(chlorosulfonyl)acetimidoyl chloride (1.45 g, 5.2 mmol). Yield 0.37 g (20%), cream powder, mp 235-237°C (dec.) (benzene-acetone (20:1)). ^{1}H-NMR ($CDCl_3$+DMSO-d_6 (20:1), 300 MHz) δ 7.48 dd, (*J* 8.6 Hz, J 2.3 Hz) 1H (H5), 7.76 d, (*J* 8.6 Hz) 1H (H6), 8.15 d, (*J* 2.3 Hz) 1H (H8). ^{13}C-NMR (DMSO-d_6, 125 MHz) δ 97.1, 128.2, 129.8, 131.2, 131.7, 133.6, 142.4, 164.2. Anal. calcd for $C_3H_3Cl_4NO_2S_2$, %: C 27.37; H 0.86; S 18.27; Cl 40.40. Found, %: C 27.02; H 0.78; S 18.13; Cl 40.22.

5,7-Dimethyl-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3d). The title compound was prepared from 2,4-dimethylthiophenol (**2d**) (0.51 g, 3.7 mmol), 2,2,2-trichloro-*N*-(chlorosulfonyl)acetimidoyl chloride (1.05 g, 3.7 mmol). Yield 1.27g (73%), colorless crystals, mp 142 °C (benzene). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.47 s, 3H, (CH_3), 2.49 s, 3H, (CH_3), 7.39 s, 1H (H6), 7.91 s, 1H (H8). ^{13}C -NMR ($CDCl_3$, 300 MHz) δ 19.3, 21.3, 95.0, 124.1, 124.8, 127.0, 135.9, 136.8, 141.3, 173.0. Anal. calcd for $C_{10}H_8Cl_3NO_2S_2$, %: C 34.85; H 2.34; S 18.61; Cl 30.86. Found, %: C 34.66; H 2.25; S 18.74; Cl 30.91.

5,8-Dimethyl-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3e). The title compound was prepared from 2,5-dimethylthiophenol (**2e**) (0.65 g, 4.7 mmol), 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (1.31 g, 4.7 mmol). Yield 1.26 g (78%), colorless crystals, mp 183 °C (benzene). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.47 s, 3H, (5-CH_3), 2.79 s, 3H, (8-CH_3), 7.36 d, (*J* 7.8 Hz) 1H (H6), 7.40 d, (*J* 7.8 Hz) 1H (H7). ^{13}C-NMR ($CDCl_3$+DMSO-d_6 (20:1), 300 MHz) δ 20.7, 22.6, 95.5, 133.4, 133.8, 133.8, 135.3, 139.9, 143.9, 168.4. Anal. calcd for $C_{10}H_8Cl_3NO_2S_2$, %: C 34.85; H 2.34; S 18.61; Cl 30.86. Found, %: C 34.71; H 2.42; S 18.66; Cl 30.82.

General procedure for the synthesis of compounds (4a,b). A solution of the appropriate arene thiol (**2**) (5 mmol) in anhydrous CH_2Cl_2 (20 mL) was added at room temperature to a vigorously stirred solution of 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (**1**) (1.4 g, 5 mmol) in anhydrous CH_2Cl_2 (30 mL), the mixture was stirred for 4h. The solvent was evaporated to dryness under vacuum, the residue was treated with pentane (50 mL), the precipitate was filtered off. The product was recrystallized from hexane.

4-Chlorophenyl 2,2,2-trichloro-*N*-(chlorosulfonyl)ethanimidothioate (4a). The title compound was prepared from 4-chlorothiophenol (**2c**) (1.27 g, 8.8 mmol), 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (2.46

g, 8.8 mmol). Yield 2.8 g (82%), orange powder, mp 73-75 °C. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.41 d, 2H (*J* 9.5 Hz), 7.54 d, 2H (*J* 9.5 Hz). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 95.8, 124.4, 130.1, 137, 138.7, 177.6. Anal. calcd for $C_8H_4Cl_5NO_2S_2$, %: C 24.80; H 1.04; S 16.55; Cl 45.74. Found, %: C 24.68; H 0.92; S 16.13; Cl 45.54.

2-Naphthyl 2,2,2-trichloro-*N*-(chlorosulfonyl)ethanimidothioate (4b). The title compound was prepared from 2-thionaphtol (0.77 g, 4.8 mmol), 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (1.34 g, 4.8 mmol). Yield 1.72 g (89%), orange powder, mp 119-120 °C. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.55-7.63 m, 3H, 7.85-7.89 m, 3H, 8.17 d, 1H (*J* 1.4 Hz). ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 94.5, 123.1, 127.5, 128.0, 128.4, 128.7, 129.7, 130.4, 133.2, 134.2, 137.1, 178.3. Anal. calcd for $C_{12}H_7Cl_4NO_2S_2$, %: C 35.75; H 1.75; S 15.91; Cl 35.18. Found, %: C 35.47; H 1.89; S 15.63; Cl 34.94.

General procedure for the synthesis of compounds (3c), (5) from thioimidates (4a,b). A solution of 4-chlorophenyl 2,2,2-trichloro-N-(chlorosulfonyl)ethanimidothioate (**4a**) (0.39 g, 1 mmol) or 2-naphthyl 2,2,2-trichloro-N-(chlorosulfonyl)ethanimidothioate (**4b**) (0.4 g, 1 mmol) in anhydrous dichloroethane (30 mL) was treated with $AlCl_3$ (0.5 g, 3.8 mmol), the obtained mixture was heated at reflux for 18 h. The solvent was removed under vacuum, the residue was treated with cold water (100 mL), the precipitate was filtered off, washed with water (5×30 mL) and air-dried.

7-Chloro-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3c). Yield 0.1g (28%), cream powder, mp 235-237°C (dec.) (benzene-acetone (20:1)).

3-(Trichloromethyl)naphtho[2,1-*e*][1,4,2]dithiazine-1,1-dioxide (5). Yield 0.17 g (46%), yellowish crystals, mp 166-167°C (benzene). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.42 d, (*J* 8.7 Hz) 1H (H6), 7.72-7.75 m, 1H (H8), 7.82-7.83 m, 1H (H9), 7.96 d, (*J* 8.1 Hz) 1H (H7), 8.1 d, (*J* 8.7 Hz) 1H (H5), 9.09 d, (*J* 8.1 Hz) 1H (H10). ^{13}C-NMR (DMSO-d_6, 125 MHz) δ 97.4, 121.7, 124.0, 124.2, 126.7, 127.8, 128.7, 129.7, 129.9, 130.3, 134.3, 169.7. Anal. calcd for $C_{12}H_6Cl_3NO_2S_2$, %: C 39.31; H 1.65; S 17.49; Cl 29.01. Found, %: C 39.23; H 1.62; S 17.76; Cl 28.82.

6-Methoxy-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide (3f). A solution of 3-methoxythiophenol (**2f**) (0.47 g, 3.4 mmol) in anhydrous dichloroethane (20 mL) was added at room temperature to vigorously stirred solution of 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (**1**) (0.95 g, 3.4 mmol) in anhydrous dichloroethane (20 mL), the mixture was stirred for 3 h. The obtained solution was treated with $ZnCl_2$ (1 g, 7.4 mmol) and heated at reflux for 8 h. The solvent was removed under vacuum, the residue was treated with cold water (200 mL), the precipitate was filtered off, washed with water (5×30 mL), 10% solution of methanol (5 mL) and air-dried. Total yield of isomers (**3f**) and (**6**) 1.1 g (93%), **3f** / **6** ~ 4:1. **8-Methoxy-3-(trichloromethyl)-1,4,2-benzodithiazine-1,1-dioxide** (**6**) ^{1}H-NMR (CDCl3, 400 MHz) δ 4.06 s, 3H, (CH_3), 6.99 d, (*J* 8.6 Hz) 1H (H5), 7.14 d, (*J* 8.6 Hz) 1H, (H7), 7.57 t, (*J* 8.6 Hz) 1H, (H6). Compound (**3f**) was separated by crystalization from heptane–benzene (10:1). Yield 0.48 g (41%), (colorless crystals) mp 169-170 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.95 s, 3H, (CH_3), 6.82 d, (*J* 2.4 Hz) 1H (H5), 6.91 dd, (*J* 9.3 Hz, J 2.4 Hz) 1H, (H7), 8.35 d, (*J* 9.3 Hz) 1H, (H8). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.7, 93.7, 103.9, 104.5, 113.4, 132.0, 157.8, 167.2, 167.8. Anal. calcd for $C_9H_6Cl_3NO_3S_2$, %: C 31.18; H 1.74; S 18.50; Cl 30.68. Found, %: C 31.02; H 1.95; S 18.55; Cl 30.60.

General procedure for the synthesis of compounds (8a-c). A solution of the appropriate phenol (**7**) (5 mmol) in anhydrous dichloroethane (20 mL) was added at room temperature to a vigorously stirred solution of 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (**1**) (1.4 g, 5 mmol) in anhydrous dichloroethane (50 mL), the mixture was stirred for 1h. The obtained solution was treated with anhydrous $ZnCl_2$ (1 g, 7.4 mmol) and heated at reflux for 24 h. The solvent was removed under vacuum, the residue was treated with cold water (100 mL), the precipitate was filtered off, washed with water (5×30 mL) and air-dried.

7-Methoxy-4-(trichloromethyl)-1,2,3-benzoxathiazine-2,2-dioxide (8a). The title compound was prepared from 3-methoxyphenol (**7a**) (0.68 g, 5.5 mmol), 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (1.54 g, 5.5 mmol). Yield 0.98 g (54%), (colorless crystals) mp 119 °C (benzene). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.95 s, 3H,

(OCH_3), 6.83 d, (*J* 2.4 Hz) 1H (H5), 6.92 dd, (*J* 9.3 Hz, J 2.4 Hz) 1H (H7), 8.36 d, (*J* 9.3 Hz) 1H (H8). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 56.7, 93.7, 103.9, 104.5, 113.3, 132.0, 157.8, 167.3, 167.8. Anal. calcd for $C_9H_6Cl_3NO_4S$, %: C 32.70; H 1.83; S 9.70; Cl 32.17. Found, %: C 32.59; H 1.98; S 9.74; Cl 31.76.

7-Hydroxy-4-(trichloromethyl)-1,2,3-benzoxathiazine-2,2-dioxide (8b). The title compound was prepared from resorcinol (**7b**) (0.7 g, 6.4 mmol), 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (1.79 g, 6.4 mmol). Yield 1.13 g (56%), colorless crystals, mp 144 °C (benzene). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.80 d, (J 2.0 Hz) 1H (H5), 6.85 dd, (J 9.5 Hz, J 2.0 Hz) 1H (H7), 8.26 d, (J 9.5 Hz) 1H (H8), 11.30 s, 1H (OH). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 93.8, 103.7, 106.1, 114.4, 132.4, 157.7, 166.2, 168.1. Anal. calcd for $C_8H_4Cl_3NO_4S$, %: C 30.35; H 1.27; S 10.13; Cl 33.60. Found, %: C 30.14; H 1.32; S 10.19; Cl 33.45.

5,7-Dimethoxy-4-(trichloromethyl)-1,2,3-benzoxathiazine-2,2-dioxide (8c). The title compound was prepared from 3,5-dimethoxyphenol (**7c**) (0.89 g, 5.8 mmol), 2,2,2-trichloro-N-(chlorosulfonyl)acetimidoyl chloride (1.62 g, 5.8 mmol). Yield 1 g (48%), (colorless crystals) mp 158 °C (benzene). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 3.91 s, 3H, (OCH_3), 3.93 s, 3H, (OCH_3), 6.35 d, (*J* 2.3 Hz) 1H (H5), 6.49 d, (*J* 2.3 Hz) 1H (H7). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.7, 56.5, 95.4, 96.6, 97.1, 100.1, 157.7, 160.1, 168.8, 170.8. Anal. calcd for $C_{10}H_8Cl_3NO_5S$, %: C 33.31; H 2.24; S 8.89; Cl 29.49. Found, %: C 33.17; H 2.13; S 8.67; Cl 29.52.

***N*-(2-Hydroxy-4,6-dimethoxyphenyl)sulfonyl-2,2,2-trichloroacetamide** (**10**). A solution 3,5-dimethoxyphenol (**7c**) (0.49 g, 3.2 mmol) and trichloroacetylsulfamoyl chloride (**1**) (0.83 g, 3.2 mmol) in anhydrous dichloroethane (40 mL) was heated at reflux for 6 h. The solvent was removed under vacuum, the residue was treated with cold water (100 mL), the precipitate was filtered off, washed with water (5×30 mL) and air-dried. Yield 0.92 g (76%), colorless crystals, mp 172-173 °C (toluene). ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 3.83 s, 3H, (OCH_3), 3.88 s, 3H, (OCH_3), 6.02 d, (*J* 2.4 Hz) 1H, 6.18 d, (*J* 2.4 Hz) 1H, 9.52 br, 1H, (OH+NH). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.8, 56.5, 90.9, 92.4, 94.5, 100.3, 158.6, 159.4, 161.6, 167.0. Anal. calcd for $C_{10}H_{10}Cl_3NO_6S$, %: C 31.72; H 2.66; S 8.47; Cl 28.09. Found, %: C 31.53; H 2.51; S 8.26; Cl 27.83.

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Supplementary Material

Crystallographic data for compounds **5**, **8c**, **10** and description of growth-regulating assay studies are presented in the Supplementary Material file associated with this article.

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