Concise Synthesis and Displacement Reactions of Model 3-(Alkylthio)-6-chloro- and 2,6-Dichlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-Dioxides

Rajab Abu-El-Halawa[a], Mohanad Masad[a], Yaser Bathich[a], Mahmoud Al-Refai[a], Mohammad M. Ibrahim[a], Mustafa M. El-Abadelah[b], and Wolfgang Voelter[c]

[a] Chemistry Department, Faculty of Science, Al al-Bayt University, Mafraq, Jordan
[b] Chemistry Department, Faculty of Science, The University of Jordan, Amman, Jordan
[c] Interfakultäres Institut für Biochemie, Universität Tübingen, Hoppe-Seyler-Straße 4, 72076 Tübingen, Germany

Reprint requests to Prof. Dr. R. Abu-El-Halawa. E-mail: halawarajab@yahoo.com

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Dedicated to Professor Johannes C. Jochims

A series of 3-(alkylthio)-6-chlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxides (**7a** – **e**) were prepared *via* interaction of deprotonated 2,5-dichlorothiophene-3-sulfonamide with carbon disulfide under reflux, followed by alkylation with alkyl halides. Employment of dimethyl sulfate afforded the isomeric 2-methyl-3-thione derivative **8** together with the expected 3-(methylthio) derivative **7a** in a molar ratio of 1 : 4. Treatment of **7a** or **10** with ethylamine, aniline or *p*-chloroaniline produced the corresponding *N*-ethyl- (or *N*-phenyl)-6-chlorothieno[2,3-*e*][1,4,2]dithiazine-3-amine 1,1-dioxides **3a** – **c**. Likewise, interaction of **7a** with methylhydrazine (or phenylhydrazine) gave the respective 3-(1-methylhydrazinyl or 2-phenylhydrazinyl) 1,1-dioxides **9a**, **b**. Desulfonation of 6-chloro-3-(methylthio)thieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxide (**7a**) with sulfuryl chloride produced 3,6-dichlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxide (**10**). The latter compound was used as a substrate for the preparation of *N*-alkyl- (or aryl)-6-chlorothieno[2,3-*e*][1,4,2]dithiazin-3-amine 1,1-dioxides **3a** – **c** representing a new approach for the synthesis of similar derivatives. Compounds **7a** – **e** showed modest to low antibacterial activity against *E. coli* and *S. aureus.*

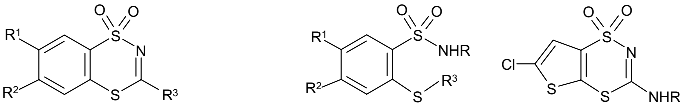
Key words: 2,5-Dichlorothiophene-3-sulfonamide, Cyclization with Carbon Disulfide, Thieno[2,3-*e*][1,4,2]dithiazine 1,1-Dioxides, S_N-Ar Reactions

Introduction

Several 1,4,2-benzodithiazine 1,1-dioxides **1** have been prepared and have shown interesting pharmacological activities [1]. Examples include compounds **1a** [2] and **1b** [3] that exhibit antihypertensive and diuretic activities, while **1c** [4] exhibits moderate anticancer activity (Fig. 1). The 1,4,2-benzodithiazine ring system is currently utilized in the preparation of new *S*,*N*-disubstituted 2-mercaptobenzenesulfonamides (**2**) that are used for the treatment of cancer [5, 6a] and HIV [6] infections.

Quite recently, we have reported [7] on the synthesis of *N*-(alkyl/aryl)thieno[2,3-*e*][1,4,2]dithiazin-3-amine 1,1-dioxides (**3**; *vide infra*), bioisosteres of 1,4,2-benzodithiazine 1,1-dioxides (such as **1a**).

We thought it would be worthwhile to explore a synthetic route towards a new set of 3-alkylthio-6-chlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxides (**7a** – **7e**) as depicted in Scheme 1. The latter compounds would also be useful substrates for the synthesis of *N*-(substituted) 6-chlorothieno[2,3-*e*][1,4,2]dithiazin-3-hydrazine 1,1-dioxides (**9a**, **b**; Scheme 2) as well as



1 **2** **3**

1a ($R^1 = CO_2H$; R^2 = H, Cl; R^3 = NHAr)
1b ($R^1 = CO_2H$; R^2 = Cl; R^3 = SMe)
1c (R^1 = Cl; R^2 =Me; R^3 = NHNHR)

Fig 1.

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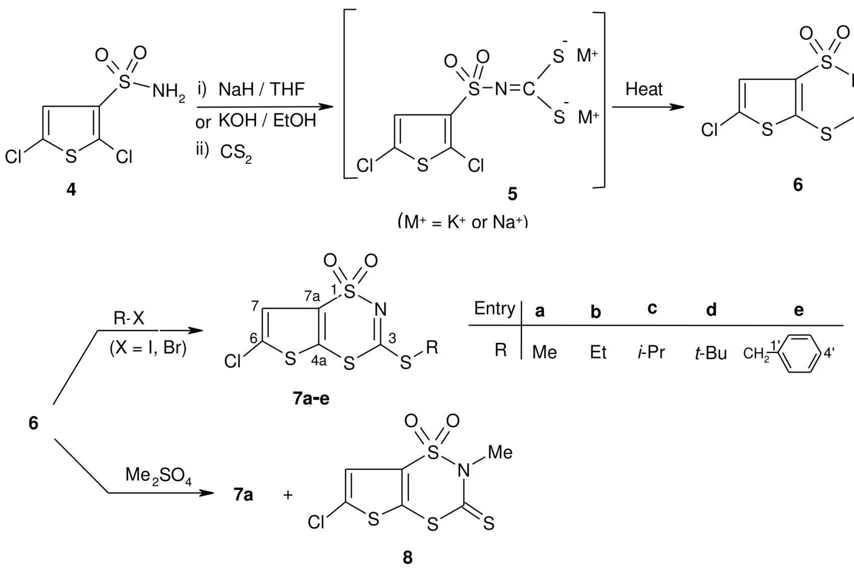


Scheme 1.

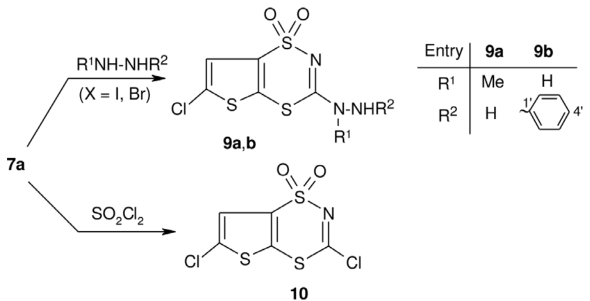
N-(substituted) 6-chlorothieno[2,3-*e*][1,4,2]dithiazin-3-amine 1,1-dioxides (**3a, b**) as illustrated in Scheme 3.

Results and Discussion

In the present work, a new selected set of 3-alkylthio-6-chlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxides (**7a** – **e**) were synthesized utilizing 2,5-dichlorothiophene-3-sulfonamide (**4**). The latter substrate was prepared according to a reported procedure [8] that involves the reaction of 2,5-dichlorothiophene with chlorosulfonic acid, followed by treatment of the resulting 2,5-dichlorothiophene-3-sulfonyl chloride with excess concentrated aqueous ammonium hydroxide. Deprotonation of **4** with sodium hydride in dry DMF (or potassium hydroxide in absolute ethanol) gave the sulfonamide anion which reacts with carbon disulfide in the presence of excess NaH (or KOH) to deliver the intermediate **5**. Upon heating, the latter underwent intramolecular cyclization to produce the cyclic sodium (or potassium) salt **6** (Scheme 1), desired for further derivatization.

The intermediate salt (**6**, M = NH_4^+) was characterized as its ammonium salt, (obtained upon treatment of **6** with ammonium chloride), the structure of which has been confirmed by single-crystal X-ray diffraction analysis [9].

Treatment of **6** with excess alkyl halides yielded the corresponding 3-(*S*-alkyl) derivatives **7a** – **e**. However, treatment of **6** with excess dimethyl sulfate afforded a separable mixture of 3-(*S*-methyl) (**7a**) and 2-(*N*-methyl) (**8**) derivatives in a 4 : 1 molar ratio (Scheme 1).



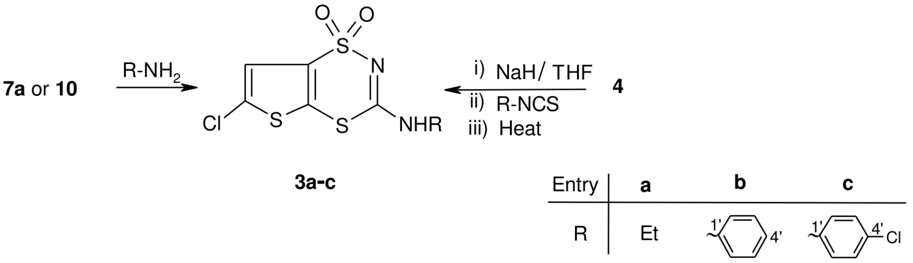
Scheme 2.

The reaction of methylhydrazine or phenylhydrazine with **7a** gave the corresponding 6-chloro-3-(1-methyl or 2-phenylhydrazinyl)thieno[2,3-e][1,4,2]-dithiazine 1,1-dioxides (**9a, b**) (Scheme 2).

Desulfonation of **7a** with sulfuryl chloride produced 3,6-dichlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxide (**10**) (Scheme 2).

Compounds **7** and **10**, incorporating a good leaving groups at C-3, were used for the preparation of 3-alkyl- (or aryl)amino-6-chlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxides **3a** – **c**. This represents a new approach for the synthesis of this class of derivatives (Scheme 3). The latter compounds were identical with authentic samples previously prepared by another route involving direct interaction of deprotenated **4** with the appropriate ethyl or phenyl isothiocyanate [7] (Scheme 3).

Elemental analyses and spectral (MS and NMR) data of the new compounds **7** – **10**, given in the Experimental Part, are in accordance with the assigned



Scheme 3.

structures. Thus, the MS spectra display the correct molecular ions as suggested by their molecular formulas. The isotopic cluster in the molecular ion region of the prepared compounds **7** – **9** (M and M+2, with relative intensities 3 : 1) is in accordance with the presence of only one chlorine atom, while the isotopic cluster in the molecular ion region of **10** (M, M+2 and M+4 with relative intensities 9 : 6 : 1) is in agreement with the presence of two chlorine atoms. The EI fragmentation of **7a** – **e** proceeds *via* elimination of an alkyl thiocyanate fragment (R-SCN) from the molecular ion leading to the formation of the respective ion with $m/z = 212$. The latter ion suffers consecutive extrusion of SO_2, chlorine atom and CS with ultimate production of ions with $m/z = 148$, $m/z = 113$, and $m/z = 69$, respectively.

The ^1H and ^{13}C NMR spectral data of the dithiazines **7** – **10** are in agreement with the proposed structures. Thus, the thieno proton 7-H resonates as a singlet around δ = 7.3 – 7.7 ppm. The exchangeable hydrazino-NH protons' signals of **9a**, **b** appear in the region 7.6 – 9.6 ppm. Signal assignments to the different alkyl and aryl protons in compounds **7a** – **e** are straightforward. Compounds **7a** and **8** are differentiated by their *N*-CH_3 and *S*-CH_3 resonances in the ^1H and ^{13}C NMR spectra, with singlet signals appearing at 2.74 (16.7) and 3.60 (35.3) ppm, respectively. DEPT experiments were used to differentiate between the different primary, secondary and tertiary carbon atoms.

Antibacterial activity

Compounds **3a** – **c** and **7a** – **e** were tested *in vitro* in aqueous DMSO solutions against Gram-negative *Escherichia. coli.* ATCC 8739 and Gram-positive *Staphylococcus aureus* ATCC 6538 bacterial species using ciprofloxacin as reference. The antibacterial activity was evaluated by the minimal inhibitory concentration (MIC) technique. Compounds **7a** – **e** exhibit moderate to low level of antibacterial activity (MIC 32 – 128 μg mL^{-1}) against *E. coli.* and *S. aureus*. However, compounds **3a** – **c** did not show any significant antibacterial activity.

Experimental Section

2,5-dichlorothiophene was purchased from Acros. The alkyl halides and hydrazines used in this study were purchased from Fluka. Melting points were determined on an Electrothermal-9002 apparatus. IR spectra were obtained from KBr discs on a Nicolet Impact-400 FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV-300 ultrashield instrument. Chemical shifts are expressed in ppm with reference to TMS as internal standard. Electron impact mass spectra (EIMS) were taken with a Shimadzo QP instrument at 70 eV and at an ion source temperature of 250 °C. High-resolution mass spectra (HRMS) were measured using the electrospray ion trap (ESI) technique by collision-induced dissociation on a Bruker APEX-4 (7 Tesla) instrument. The samples were dissolved in acetonitrile, diluted in spray solution (methanol-water 1 : 1 v/v + 0.1 % formic acid) and infused using a syringe pump with a flow rate of 2 μL min^{-1}. External calibration was conducted using arginine cluster in a mass range of m/z = 175 – 871. For analyses, all new compounds were further purified on preparative TLC silica-gel plates using chloroform as eluent. Elemental analyses were carried out at Al al-Bayt University (Jordan), and the results were found to be in good agreement (±0.4 %) with the calculated values.

Antibacterial tests

The MICs were determined by the conventional agar dilution procedures according to the method of Mueller-Hinton. Stock solutions (1000 μg mL^{-1}) of the test compounds were prepared with DMSO. Serial dilutions were then made to obtain test concentrations in the range 128 – 0.5 μg mL^{-1}. The agar plates were inoculated with approximately 10^5 CFU per spot. The agar plates were then incubated at 37 °C for 18 h. The MICs were taken as the lowest concentration of the test compounds that inhibits visible growth.

*2,5-Dichlorothiophene-3-sulfonamide (**4**)*

This compound was prepared *via* interaction of 2,5-dichlorothiophene-3-sulfonyl chloride with excess NH_4OH

(28 %) at 100 °C for 30 min according to a reported procedure [8]. The required 2,5-dichlorothiophene-3-sulfonyl chloride was, in turn, obtained by the reaction of 2,5-dichlorothiophene with excess chlorosulfonic acid at 100 – 110 °C for 2 h, by following a literature method [8].

*Sodium/potassium 6-chlorothieno[2,3-e][1,4,2]dithiazine-3-thiolate 1,1-dioxide (**6**)*

Method a): A suspension of sodium hydride (60 % dispersion in mineral oil, 0.17 g, 5 mmol) in dry DMF (20 mL) was added to a stirred solution of 2,5-dichlorothiophene-3-sulfonamide (**4**) (1.0 g, 4.4 mmol) dissolved in DMF (10 mL). The resulting mixture was stirred for 15 min at r. t., followed by dropwise addition of CS_2 (0.35 g, 4.6 mmol). The whole reaction mixture was stirred over night at r. t., and then used immediately for the next alkylation step.

Method b): Sulfonamide **4** (3.0 g, 13 mmol) was added to a stirred solution of KOH (2.8 g, 52 mmol) in absolute ethanol (40 mL), and the resulting mixture was warmed (40 °C) for 30 min. Carbon disulfide (5 mL) was then added dropwise, and the mixture was further refluxed for 12 h. The yellow precipitate of potassium-salt **6**, formed in the cooled reaction mixture, was collected under suction, washed with diethyl ether (2 × 20 mL), dried and then used for the following alkylation step as shown below.

*3-(Alkylthio)-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxides (**7a – e**)*

General procedure

An excess of the appropriate alkyl halide (MeI, EtI, *t*-BuBr, *i*-PrBr or BnBr) (30 mmol) was added to the sodium/potassium salt **6** (10 mmol) in DMF (20 mL), and the reaction mixture was refluxed for 2 h, then diluted with H_2O (20 mL) and extracted with diethyl ether (3 × 10 mL). The combined ether extracts were washed with water (2 × 10 mL) and dried over sodium sulfate; evaporation of ether and excess alkyl halide gave the respective title compounds as solid or oily residues. Upon washing with hexane, the desired compounds formed. Further purification was done using silica gel TLC plates (UV active, 245 nm) and chloroform as the eluent. Accordingly, the following compounds were prepared:

*3-(Methylthio)-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**7a**)*

Pale-yellow solid, m. p. 180 – 181 °C, 55 % yield. – IR (KBr) ν = 3100, 2910 (C-H), 1580 (C=N), 1180 (SO_2) cm^{-1}. – ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.77 (s, 1H, 7-H), 2.71 (s, 3H, CH_3). – ^{13}C NMR (75 MHz, [D_6]-DMSO): δ = 178.0, 133.1, 132.0, 128.8 (C_q-3, 4a, 6, 7a), 122.5 (CH-7), 16.8 (CH_3). – MS (EI, 70 eV): m/z (%) = 285 (20) $[M]^+$, 286 (3) $[M+1]^+$, 287 (10) $[M+2]^+$, 212 (75), 148 (82), 113 (25), 69 (100). – Anal. for $C_6H_4ClNO_2S_4$ (285.81): calcd. C 25.21, H 1.41, N 4.90, S 44.87; found C 24.98, H 1.21, N 4.77, S 44.62.

*3-(Ethylthio)-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**7b**)*

Colorless solid, m. p. 145 – 146 °C, 57 % yield. – ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.77 (s, 1H, 7-H), 1.35 (t, J = 7.4 Hz, 3H, CH_3), 3.28 (q, J = 7.4 Hz, 2H, CH_2). – ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 177.1, 133.2, 132.1, 128.8 (Cq-3, 4a, 6, 7a), 122.8 (CH-7), 29.0 (SCH_2), 16.8 (CH_3). – MS (EI, 70 eV): m/z (%) = 297 (10) $[M]^+$, 298 (5) $[M+1]^+$, 299 (6) $[M+2]^+$, 212 (20), 148 (25), 113 (31), 69 (100). – Anal. for $C_7H_6ClNO_2S_4$ (299.84): calcd. C 28.04, H 2.02, N 4.67, S 42.77; found C 28.43, H 2.22, N 4.96, S 42.57.

*3-(i-Propylthio)-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**7c**)*

Yellow oily residue, 40 % yield. – ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.76 (s, 1H, 7-H), 3.95 – 4.19 (m, 1H, CH), 1.45 (d, J = 6.6 Hz, 6H, CH_3-C-CH_3). – ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 176.4, 133.3, 132.1, 128.7 (C_q-3, 4a, 6, 7a), 122.8 (CH-7), 41.6 (SCH), 22.3 (CH_3). – HRMS ((+)-ESI): m/z = 313.9205 (calcd. 313.9218 for $C_8H_9ClNO_2S_4$, $[M+H]^+$). – Anal. for $C_8H_8ClNO_2S_4$ (313.87): calcd. C 30.61, H 2.57, N 4.46, S 40.86; found C 30.42, H 2.70, N 4.29, S 41.13.

*3-(t-Butylthio)-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**7d**)*

Yellow oily residue, 37 % yield. – ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.76 (s, 1H, 7-H), 1.24 (s, 9H, C-$(CH_3)_3$). – ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 162.7, 140.6, 127.3, 126.2 (C_q-3, 4a, 6, 7a), 122.8 (CH-7), 41.6 (SCH), 22.3 (CH_3). – HRMS ((+)-ESI): m/z= 327.9348 (calcd. 327.9361 for $C_9H_{11}ClNO_2S_4$, $[M+H]^+$). – Anal. for $C_9H_{10}ClNO_2S_4$ (327.89): calcd. C 32.97, H 3.07, N 4.27, S 39.12; found C 33.03, H 3.19, N 4.57, S 39.36.

*3-(Benzylthio)-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**7e**)*

Colorless solid, m. p. 195 – 196 °C, 48 % yield. – ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 7.77 (s, 1H, 7-H), 7.43 (d, J = 6.9 Hz, 2H, arom.), 7.35 (t, J = 5.7 Hz, 2H, arom.), 7.30 (t, J = 5.7 Hz, 1H, arom.), 4.69 (s, 2H, CH_2). – ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 176.3, 135.6, 129.1, 129.0, 128.8 (C_q-3, 4a, 6, 7a, arom.), 129.7, 129.1, 128.4 (CH-arom.), 122.8 (CH-7), 37.9 (SCH_2). – HRMS ((+)-ESI): m/z = 316.9201 (calcd. 361.9205 for $C_{12}H_9ClNO_2S_4$, $[M+H]^+$). –

Anal. for $C_{12}H_8ClNO_2S_4$ (361.91): calcd. C 39.83, H 2.23, N 3.87, S 35.44; found C 39.90, H 2.09, N 4.11, S 35.08.

*3-Methylthio-6-chlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**7a**), and 2-methyl-6-chlorothieno[2,3-e][1,4,2]dithiazine-3(2H)-thione 1,1-dioxide (**8**)*

Potassium salt **6** (3.1 g, 10 mmol) was refluxed with dimethyl sulfate (15 mL) for 30 min. Chloroform (150 mL) was added, the organic layer was washed with water (2 × 50 mL) and dried. Thin-layer chromatography showed that the product is a mixture of **7a** and **8** which were separated by thick-layer chromatography using TLC silica gel glass plates and eluting with chloroform. Herein **7a** has R_f value of 0.67, while that of **8** is 0.84. Both compounds were recrystallized from chloroform/petroleum ether (b. p. 40 – 60 °C).

*Compound **8**:* pale-yellow, m. p. 118 – 120 °C, 28 % yield. – IR (KBr): ν = 3100, 2935 (C-H), 1335 (C=S), 1185 (SO_2) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 3.60 (s, CH_3N), 7.31 (s, 7-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.3 (CH_3N), 126.9 (C-7), 127.7 (C-4a), 132.9, 134.4 (C-7a, C-6a), 190.7 (C_3=S). – MS (EI, 70 eV): m/z (%) = 285 (7) $[M]^+$, 242 (3), 212 (53), 151 (12), 148 (58), 116 (100), 81 (25), 69 (95). – Anal. for $C_6H_4ClNO_2S_4$ (285.81): calcd. C 25.21, H 1.41, N 4.90, S 44.87; found C 25.29, H 1.32, N 4.73, S 44.69.

*6-Chloro-3-(N-substituted hydrazinyl)thieno[2,3-e][1,4,2]-dithiazin 1,1-dioxides **9a, b***

A mixture of compound **7a** (3.0 g, 10 mmol) and methylhydrazine (or phenylhydrazine) (50 mmol) was refluxed for 18 h. Upon cooling, the precipitated product was filtered, washed with 50 % aqueous methanol (2 × 30 mL) and dried.

*6-Chloro-3-(1-methylhydrazinyl)thieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**9a**)*

Pale-yellow solid, m. p. 163 – 165 °C, 57 % yield. – IR (KBr): ν = 3310, 3230 (br, NH_2), 3085, 2940 (C-H), 1575 (C=N), 1160 (SO_2) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 3.42 (s, CH_3N), 7.21 (s, 7-H), 7.82 (br s, NH_2-N). – MS (EI, 70 eV): m/z (%) = 283 (7) $[M]^+$, 268 (16), 234 (35), 232 (100), 212 (28), 148 (35), 116 (21), 81 (30), 69 (42). – Anal. for $C_6H_6ClN_3O_2S_3$ (283.78): calcd. C 25.40, H 2.13, N 14.18, S 33.90; found C 25.24, H 2.02, N 14.37, S 33.74.

*6-Chloro-3-(2-phenylhydrazinyl)thieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**9b**)*

Pale-yellow solid, m. p. 245 – 247 °C, 63 % yield. – IR (KBr): ν = 3480 (br, N-H), 3110, 3080 (C-H), 1595 (C=N), 1175 (SO_2) cm^{-1}. – ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 7.15 (s, 1H, 7-H), 7.28 – 7.72 (m, 7-H, Ph-H+N*H*-N*H*). – MS (EI, 70 eV): m/z (%) = 345 (3) $[M]^+$, 268 (16), 234 (76), 232 (100), 212 (45), 186 (27), 148 (33), 116 (28). – Anal. for $C_{11}H_8ClN_3O_2S_3$ (345.85): calcd. C 38.20, H 2.33, N 12.15, S 27.81; found C 38.06, H 2.25, N 12.12, S 27.68.

*3,6-Dichlorothieno[2,3-e][1,4,2]dithiazine 1,1-dioxide (**10**)*

Sulfuryl chloride (0.40 g, 3 mmol) was added portionwise to 3-methylthio-6-chlorothieno[2,3-e][1,4,2]dithiazine-1,1-dioxide (**7a**) (1.8 mmol, 0.51 g). The mixture was then refluxed for 3 h at 50 °C. The excess amount of sulfuryl chloride was removed by vacuum filtration, and the residue was washed with diisopropyl ether. Pale-yellow solid, m. p. 179 – 181 °C, 77 % yield. – ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 7.31 (s, 1H, 7-H). – ^{13}C NMR (75 MHz, $[D_6]$DMSO): δ = 142.8, 137.3, 129.7, 128.7 (C_q-3, 4a, 6, 7a), 122.7 (CH-7). – MS (EI, 70 eV): m/z (%) = 273 (28) $[M]^+$, 274 (3) $[M+1]^+$, 275 (21) $[M+2]^+$, 212 (96), 148 (100), 113 (21), 69 (85). – Anal. for $C_5HCl_2NO_2S_3$ (274.17): calcd. C 21.90, H 0.37, N 5.11, S 35.09; found C 21.98, H 0.35, N 4.98, S 35.22.

*N-Substituted-6-chlorothieno[2,3-e][1,4,2]dithiazin-3-amine 1,1-dioxides **3a – c***

*General procedure utilizing **7a***

A mixture of compound **7a** (1.50 g, 5 mmol) and the particular amine (25 mmol) was refluxed for 18 h. Upon cooling, the precipitated product was filtered, washed with 50 % aqueous methanol (2 × 30 mL) and dried.

*General procedure utilizing **10***

To a solution of 3,6-dichlorothieno[2,3-*e*][1,4,2]dithiazine 1,1-dioxide (**10**) (0.11 g, 0.4 mmol) in dioxane (20 mL) was added dropwise the particular amine (0.4 mmol). The reaction mixture was stirred at r. t. for 2 h, followed by reflux for 4 h. Thereafter, potassium hydrogencarbonate (5 mL, 1 M) was added and the mixture stirred for 1 h at r. t. The resulting solid product was filtered and recrystallized from a mixture of chloroform-petroleum ether (6 : 1, v/v).

*6-Chloro-N-ethylthieno[2,3-e][1,4,2]dithiazin-3-amine 1,1-dioxide (**3a**)*

Colorless solid, m. p. 180 – 182 °C (lit. [7]: 180 – 182 °C), 63 % yield.

*6-Chloro-N-phenylthieno[2,3-e][1,4,2]dithiazin-3-amine 1,1-dioxide (**3b**)*

Colorless solid, m. p. 242 – 244 °C (lit. [7]: 243 – 245 °C), 78 % yield.

*6-Chloro-N-(p-chlorophenyl)thieno[2,3-e][1,4,2]dithiazin-3-amine 1,1-dioxide (**3c**)*

Colorless solid, m. p. 162 – 164 °C, 83 % yield. – ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 11.50 (s, 1H, NH), 7.63 (s, 1H, 7-H), 7.68 (d, J = 8.9 Hz, 2H, arom.), 7.54 (d, J = 8.9 Hz, 2H, arom.). – ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 158.8, 137.0, 131.5, 130.9, 130.8, 130.1 (C$_q$-3, 4a, 6, 7a, arom.), 122.8 (CH-7), 129.6, 123.9 (CH-arom.). – HRMS ((+)-ESI): m/z = 364.9035 (calcd. 364.9047 for $C_{11}H_7Cl_2N_2O_2S_3$, [M+H]$^+$). – Anal. for $C_{11}H_6Cl_2N_2O_2S_3$ (365.28): calcd. C 36.17, H 1.66, N 7.67, S 26.33; found C 36.34, H 1.93, N 7.82, S 26.76.

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