

Synthesis of bis-thiazoles, bis-pyrazoles, bis-hydrazonates, and bis-triazolothiadiazoles based on bis-hydrazoneoyl and bis-hydrazones

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Abstract: A facile synthesis of bis-thiazoles, bis-pyrazoles, and bis-hydrazonates from the reaction of bis-hydrazoneoyl dichlorides with different moieties is described. Bis-triazolothiadiazoles were synthesized via oxidative cyclization of bis-hydrazones. Structures of the final product were elucidated by elemental analyses and spectral data.

Key words: Bis-hydrazoneoyl, bis-thiazoles, bis-pyrazoles, bis-hydrazonates, bis-hydrazones

1. Introduction

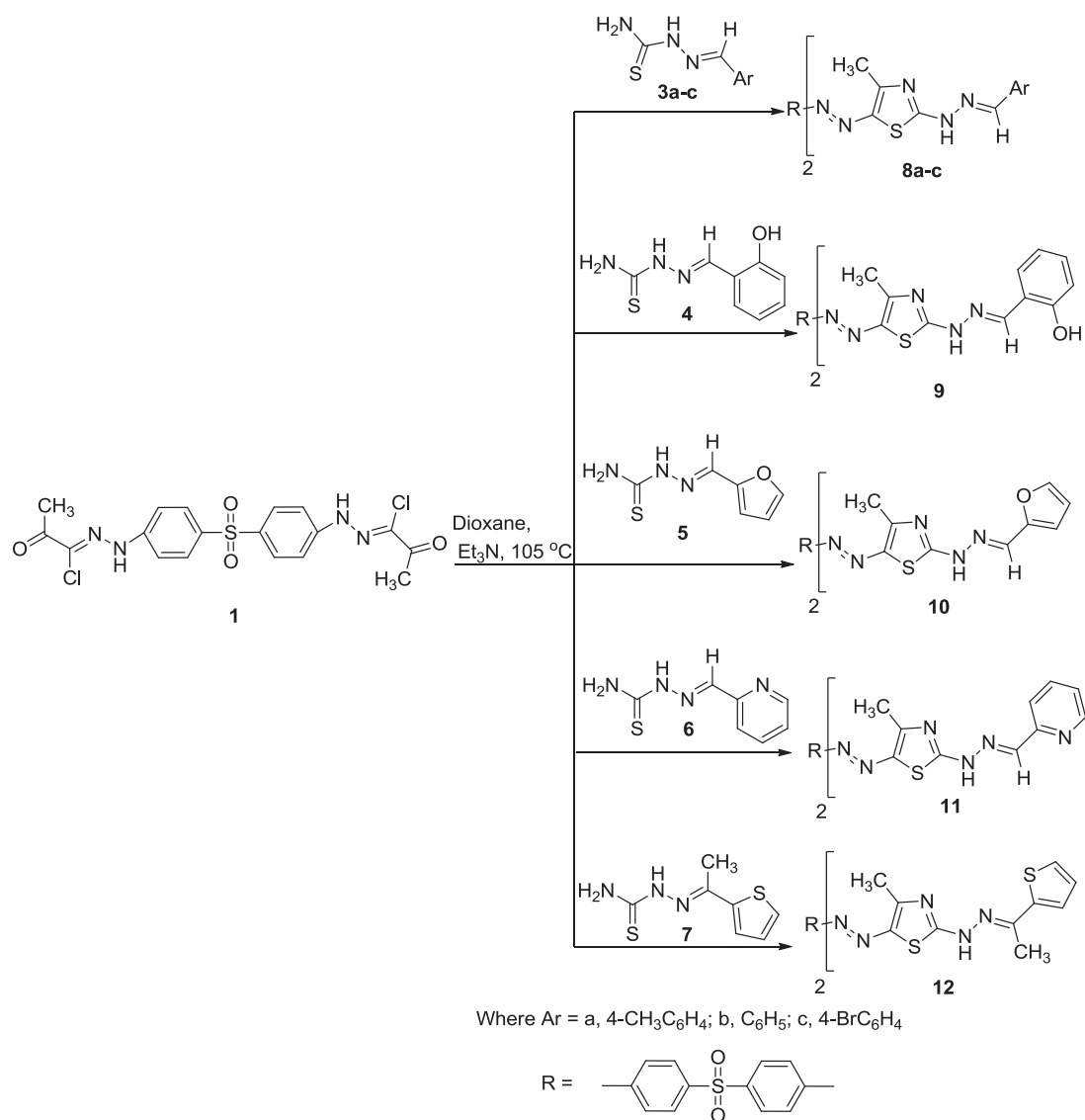
The interest in the chemistry of hydrazoneoyl halides is a consequence of the fact that they undergo a wide variety of reactions.^{1,2} Thiazole compounds can be prepared from hydrazoneoyl halides, which act as antibacterial,³ antifungal,⁴ anti-inflammatory,⁵ and anthelmintic agents.⁶ In addition, hydrazoneoyl halides are useful precursors of nitrilimines, which can undergo 1,3-dipolar cycloaddition reactions used for both academic and industrial purposes.⁷ Moreover, hydrazoneoyl halides can be used to prepare pyrazoles with a broad spectrum of important biological and pharmaceutical activities such as antimicrobial, antihypertensive, antitumor, anti-inflammatory, antidepressant, and anticonvulsant activities.⁸⁻⁹ In addition, hydrazoneoyl halides have proved to be useful synthons for various hydrazone and thiohydrazone esters.¹⁰

Efficient syntheses of new bis-thiazoles, bis-pyrazoles, bis-hydrazonates, and triazolothiadiazoles are reported.

2. Results and discussion

Bis-hydrazoneoyl chlorides are highly versatile reagents and useful building blocks for the synthesis of bis-heterocyclic rings.¹¹ The target compounds **8–17** were synthesized in two steps. In the first step, the thiosemicarbazones **3–7**¹² were prepared by condensing equimolar amounts of substituted aldehyde with thiosemicarbazide. In the second step, reaction of bis-hydrazoneoyl chlorides **1** and **2**¹³ with thiosemicarbazone **3–7** in dioxane in the presence of triethylamine under heating afforded in each case only one product, as examined by TLC. The reaction provided the desired products in excellent yields. The final products were established by elemental analyses and spectroscopic data. The mass spectra of the products revealed in each case a molecular ion peak in agreement with the molecular formula for each compound. The IR spectra showed the absence of the C=O absorption bands present in the starting bis-hydrazoneoyl chlorides **1** and **2** as depicted in Schemes 1 and 2.

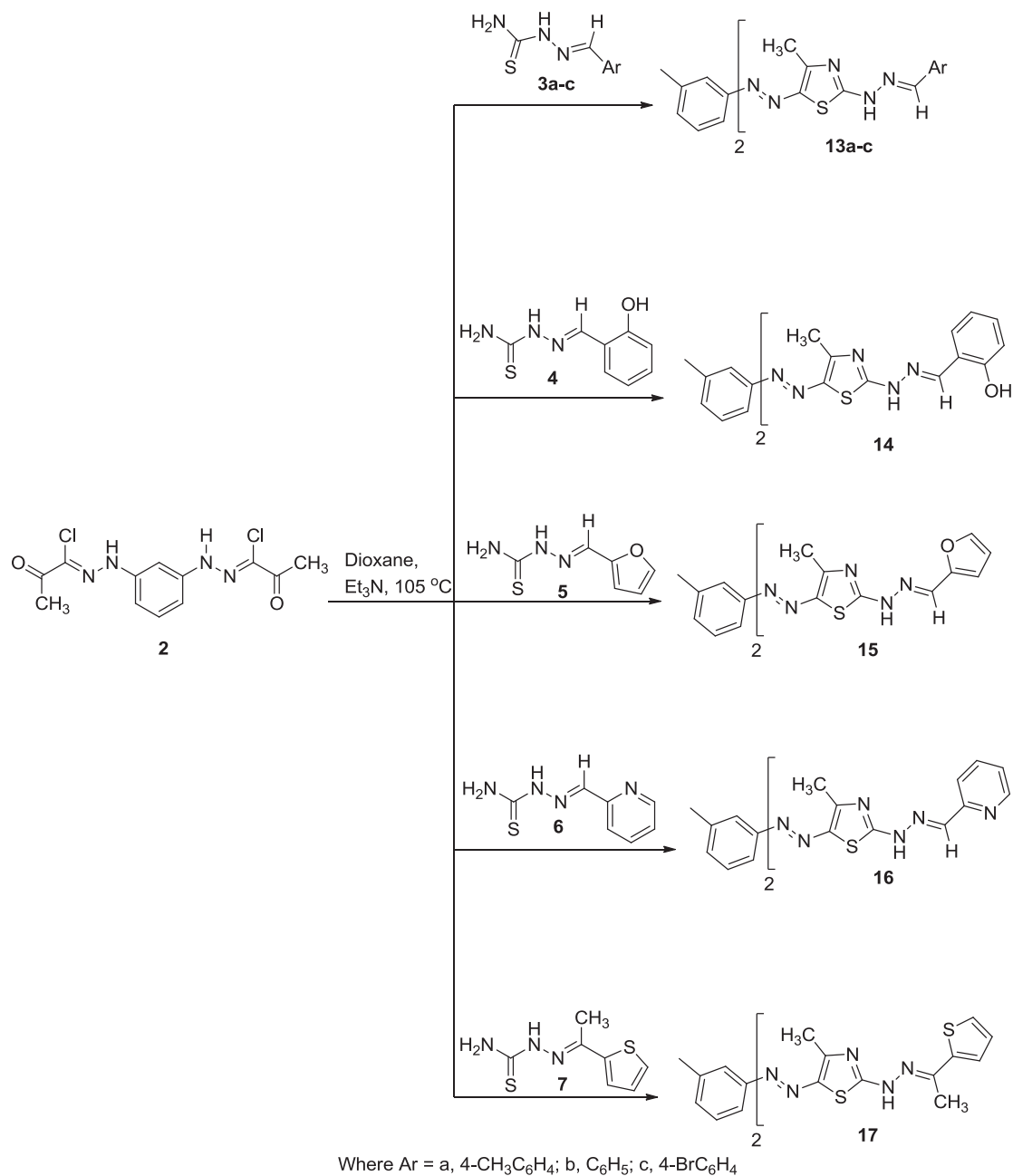
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Scheme 1. Synthesis of bis-thiazole derivatives **8–12**.

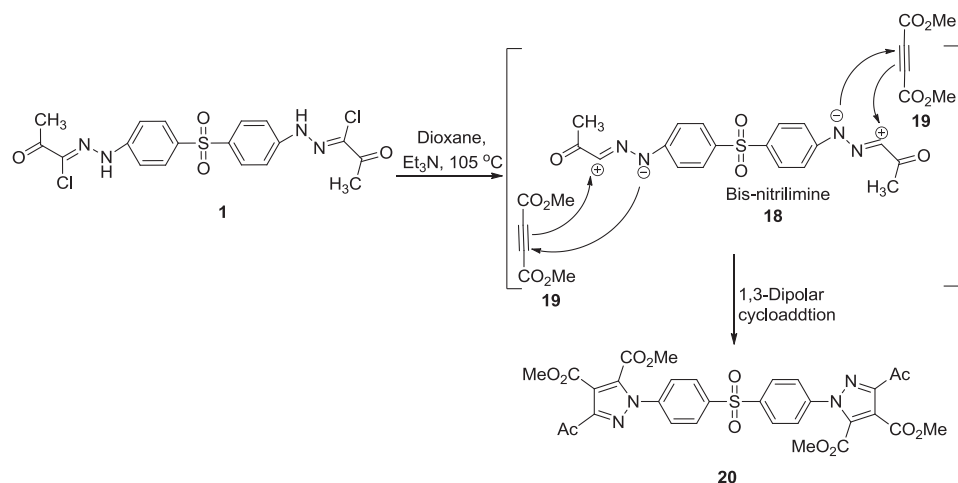
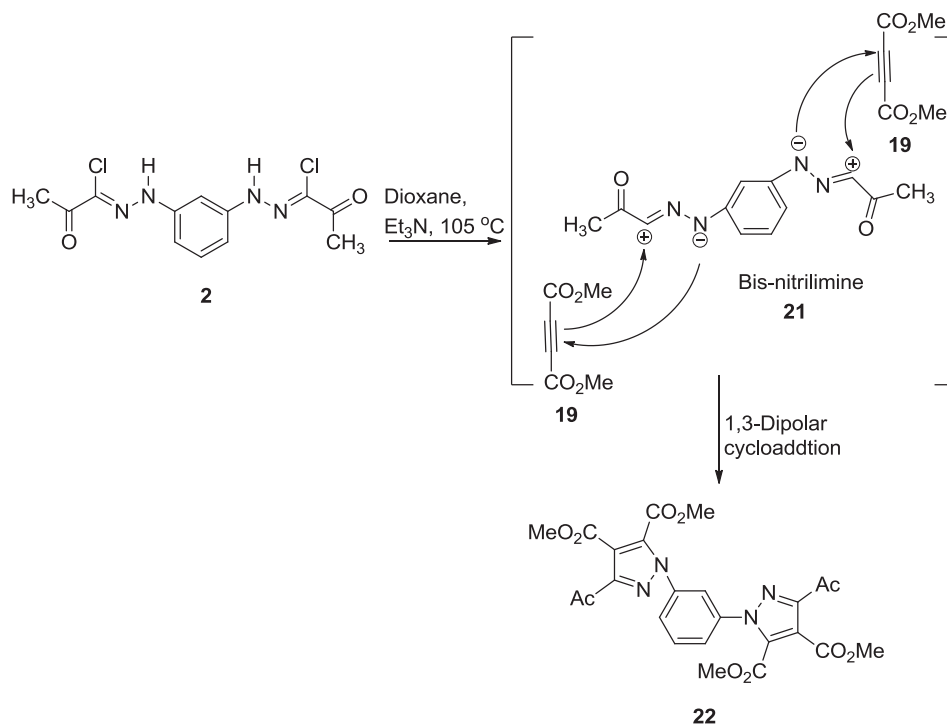
1,3-Dipolar cycloadditions reactions are important and versatile for constructing five-membered rings including pyrazoles.^{11,14} Reaction of bis-hydrazonoyl chlorides **1** and **2** with dimethyl acetylenedicarboxylate **19** in dioxane and in the presence of triethylamine each gave one isolated product, **20** and **22**, respectively (Schemes 3 and 4). In the presence of base bis-hydrazonoyl chlorides **1** and **2** convert into bis-nitrilimines **18** or **21**, respectively. This undergoes cycloadditions with dipolarophiles such as dimethyl acetylenedicarboxylate **19** to give pyrazoles. The isolated final products **20** and **22** gave satisfactory elemental analyses and spectroscopic data (IR, NMR, and MS) consistent with their assigned structures. The IR spectra of the products **20** and **22** showed no NH absorption band.

Previously, the synthesis of arylhydrazonates by reaction of phenols with hydrazonoyl halides was reported.¹⁵ Treatment of bis-hydrazonoyl dichlorides **1** and **2** with 4-bromophenol **23** in NaOMe at room temperature gave the final products **24** and **25**, respectively (Scheme 5). ¹³C NMR spectra for **25** could not be recorded owing to the poor solubility of the products in the available NMR solvents.



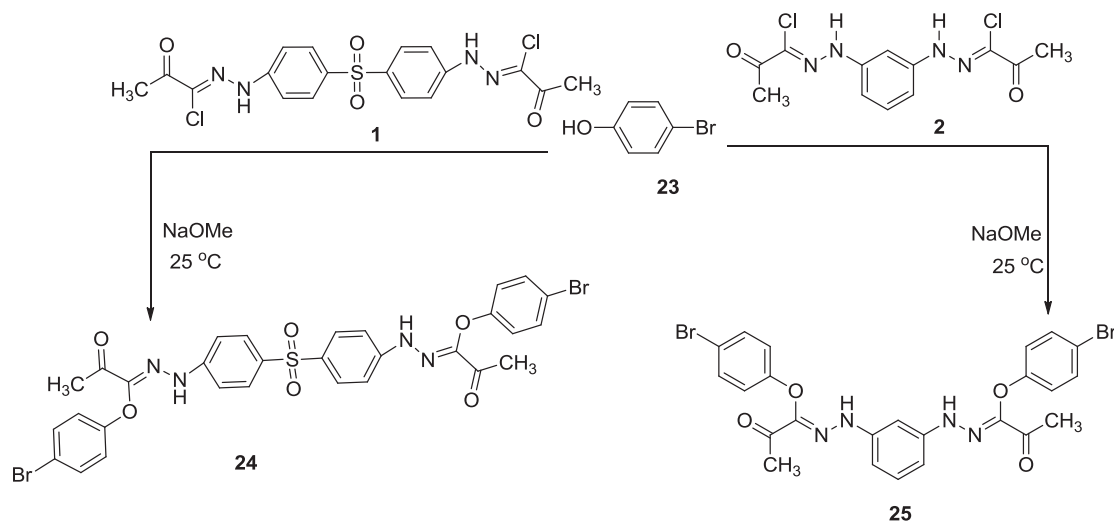
Scheme 2. Synthesis of bis-thiazole derivatives **13**–**17**.

Reaction of bis-hydrazones **27a–c** with two equivalent amounts of ferric chloride in ethanol for 30 min gave crystalline products **29a–c**. The compounds **29a–c** were elucidated by elemental analyses and spectral data. Elemental analyses and mass spectra revealed that the isolated products had four hydrogens fewer than the respective bis-hydrazones **27a–c**.¹⁶ The ¹H NMR spectra showed the absence of both methine (–N=CH–) and hydrazone (–NHN=C) protons. Formation of the final products **29a–c** was suggested to proceed by oxidative cyclizations via the formation of the respective bis-nitrilimine **28**, which underwent in situ 1,5-electrocyclization to give **29a–c** as depicted in Scheme 6.

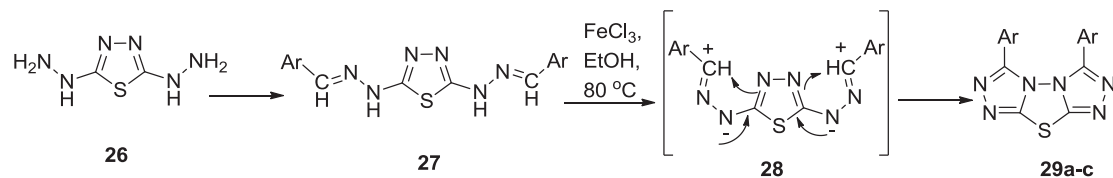
Scheme 3. Synthesis of bis-pyrazole **20**.Scheme 4. Synthesis of bis-pyrazole **22**.

3. Experimental section

All the chemicals were purchased from Aldrich and Fluka and used without further purification. Melting points were measured on an electrothermal Gallenkamp melting point apparatus and are uncorrected. The ^1H and ^{13}C NMR spectra were recorded in $\text{DMSO}-d_6$ with tetramethylsilane (TMS) as an internal standard using a 300 MHz Varian Gemini spectrometer. The IR spectra were measured on Fourier Transform and Pye Unicam Infrared spectrophotometers using potassium bromide wafers. Mass spectra were recorded on a GCMS-QP 1000 EX spectrometer at an ionizing potential of 70 eV. Elemental microanalyses were carried out at the



Scheme 5. Synthesis of thiohydrazone derivatives **24** and **25**.



Ar : a, 4-CH₃C₆H₄; b, C₆H₅; c, 4-ClC₆H₄

Scheme 6. Synthesis of bis-triazolo[3,4-*b*]thiadiazole derivatives **29a-c**.

Microanalytical Laboratory of Cairo University, Giza, Egypt. The identification of compounds from different experiments was secured by mixed mp and superimposable IR spectra.

3.1. General procedure for the synthesis of 8–17

A mixture of the appropriate bis-hydrazonoyl chlorides **1** or **2** (5 mmol), the appropriate thiosemicarbazone derivatives **3–7** (10 mmol), and triethylamine (1 g, 1.5 mL, 10 mmol) in dioxane (20 mL) was heated under reflux for 3 h and then left to cool. The solid precipitated was collected, washed with water, dried, and finally crystallized from DMF/MeOH to give the final products **8–17**.

3.1.1. 5,5'-(4,4'-Diphenylsulphone-4,4'-diyl)-bis-((2-(*p*-methylbenzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (8a)

Brown solid; Yield (89%); mp: 252 °C. IR (KBr): ν_{max} 3219 (NH) cm⁻¹. ¹H NMR (DMSO-*d*₆): 2.38 (s, 6H, 2CH₃), 2.57 (s, 6H, 2CH₃), 7.39–7.88 (m, 16H, ArH), 8.67 (s, 2H, N=CH), and 10.96 (s, 2H, NH), ¹³C NMR (DMSO-*d*₆): at 16.82, 21.62, 115.20, 129.45, 130.01, 130.45, 132.42, 136.2, 140.06, 141.91, 142.02, 143.18, 160.12, and 171.82 ppm. MS *m/z* (%): 732 (M⁺, 42). Analysis Calcd for C₃₆H₃₂N₁₀O₂S₂ (732.19): C, 59.00; H, 4.40; N, 19.11; Found: C, 59.03; H, 4.39; N, 19.14%.

3.1.2. 5,5'-(4,4'-Diphenylsulphone-4,4'-diyl)-bis-((2-(benzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (8b)

Red solid; Yield (89%); mp: 250 °C. IR (KBr): ν_{max} 3222 (NH), 1595 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.56 (s, 6H, 2CH₃), 7.45–7.86 (m, 18H, ArH), 8.65 (s, 2H, N=CH), and 10.97 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 16.59, 114.42, 128.42, 128.91, 128.99, 131.75, 133.70, 134.41, 140.90, 147.39, 160.82, 172.66, and 178.89 ppm. MS m/z (%): 704 (M⁺, 82). Analysis Calcd for C₃₄H₂₈N₁₀O₂S₃ (704.16): C, 57.94; H, 4.00; N, 19.87; Found: C, 57.91; H, 4.01; N, 19.85%.

3.1.3. 5,5'-(4,4'-Diphenylsulphone-4,4'-diyl)-bis-((2-(p-bromobenzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (8c).

Red orange solid; Yield (89%); mp: >300 °C. IR (KBr): ν_{max} 3228 (NH) cm^{-1} . ^1H NMR (DMSO- d_6): 2.58 (s, 6H, 2CH₃) 7.45–7.86 (m, 16H, ArH), 8.66 (s, 2H, N=CH), and 10.98 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 112.02, 127.15, 128.24, 129.21, 132.02, 132.97, 135.62, 141.28, 143.54, 149.01, 153.37, 161.82, and 173.04 ppm. MS m/z (%): 862 (M⁺, 91). Analysis Calcd for C₃₄H₂₆Br₂N₁₀O₂S₃ (862.64): C, 47.34; H, 3.04; N, 16.24; Found: C, 47.31; H, 3.02; N, 16.27%.

3.1.4. 5,5'-(4,4'-Diphenylsulphone-4,4'-diyl)-bis-((2-(o-hydroxybenzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (9)

Red orange solid; Yield (89%); mp: >300 °C. IR (KBr): ν_{max} 3425 (OH), 3205 (NH) cm^{-1} . ^1H NMR (DMSO- d_6): 2.57 (s, 6H, 2CH₃), 6.91–7.89 (m, 16H, ArH), 8.87 (s, 2H, N=CH), 10.75 (s, 2H, OH), and 10.97 (s, 2H, NH). ^{13}C NMR (DMSO- d_6): 16.62, 114.50, 116.69, 118.75, 119.69, 128.94, 129.99, 133.48, 134.22, 140.17, 146.53, 147.32, 158.59, 160.55, 171.74, and 178.88 ppm. MS m/z (%): 736 (M⁺, 74). Analysis Calcd for C₃₄H₂₈N₁₀O₄S₃ (736.15): C, 55.42; H, 3.83; N, 19.01; Found: C, 55.42; H, 3.89; N, 19.02%.

3.1.5. 5,5'-(4,4'-Diphenylsulphone-4,4'-diyl)-bis-((2-(furylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (10)

Black green solid; Yield (78%); mp >300 °C. IR (KBr): ν_{max} 3179 (NH) cm^{-1} . ^1H NMR (DMSO- d_6): 2.58 (s, 6H, 2CH₃), 6.87–7.98 (m, 18H, ArH, Furan-H), 8.71 (s, 2H, N=CH), and 10.88 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 16.79, 113.77, 115.47, 126.88, 128.14, 132.32, 143.25, 145.65, 146.61, 148.97, 158.52, 164.27, and 170.01 ppm. MS m/z (%): 684 (M⁺, 54). Analysis Calcd for C₃₀H₂₄N₁₀O₄S₃ (684.77): C, 52.62; H, 3.53; N, 20.45; Found: C, 52.65; H, 3.57; N, 20.49%.

3.1.6. 5,5'-(4,4'-Diphenylsulphone-4,4'-diyl)-bis-((2-(pyridylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (11)

Red brown solid; Yield (89%); mp: 280 °C. IR (KBr): ν_{max} 3246 (NH) cm^{-1} . ^1H NMR (DMSO- d_6): 2.59 (s, 6H, 2CH₃), 7.01–7.99 (m, 16H, ArH, Pyridine-H), 8.74 (s, 2H, N=CH), and 10.76 (s, 2H, NH) ppm; m/z (%): 706 (M⁺, 69). Analysis Calcd for C₃₂H₂₆N₁₂O₂S₃ (706.15): C, 54.38; H, 3.71; N, 23.78; Found: C, 54.41; H, 3.74; N, 23.74%.

3.1.7. 5,5'-((Sulfonylbis(4,1-phenylene))bis(diazene-2,1-diyl))bis(4-methyl-2-(2-(1-(thiophen-2-yl)ethylidene)hydrazinyl)thiazole) (12)

Red solid; Yield (83%); mp: 240 °C. IR (KBr): ν_{max} 3206 (NH), 1592 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.23 (s, 6H, 2CH₃), 2.58 (s, 6H, 2CH₃), 7.11–8.19 (m, 14H, ArH, Thiophene-H), and 10.91 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 15.98, 16.81, 114.2, 125.91, 127.78, 129.28, 129.45, 130.29, 134.90, 143.37, 146.59, 162.04, 169.61, and 177.88 ppm. MS m/z (%): 744 (M⁺, 75); Anal. Calcd for C₃₂H₂₈N₁₀O₂S₅ (744.96): C, 51.59; H, 3.79; N, 18.80; Found: C, 51.59; H, 3.76; N, 18.83%.

3.1.8. 5,5'-(Phenyl-1,3-diyl)-bis-((2-(p-methylbenzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (13a)

Red solid; Yield (68%); mp: 178 °C. IR (KBr): ν_{max} 3154 (NH), 1595 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.38 (s, 6H, 2CH₃), 2.50 (s, 6H, 2CH₃), 7.14–7.81 (m, 12H, ArH), 8.52 (s, 2H, N=CH), and 10.68 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 18.02, 21.60, 113.89, 125.97, 126.86, 127.46, 129.38, 130.44, 132.15, 133.91, 144.12, 150.14, 160.71, and 167.13 ppm. MS m/z (%): 592 (M⁺, 90). Analysis Calcd for C₃₀H₂₈N₁₀S₂ (592.74): C, 60.79; H, 4.76; N, 23.63; Found: C, 60.75; H, 4.79; N, 23.61%.

3.1.9. 5,5'-(Phenyl-1,3-diyl)-bis-((2-(benzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (13b)

Red solid; Yield (91%); mp: 200 °C. IR (KBr): ν_{max} 3165 (NH), 1608 (C=N) cm^{-1} . ^1H NMR (DMSO- d_6): 2.51 (s, 6H, 2CH₃) 7.03–7.84 (m, 14H, ArH), 8.55 (s, 2H, N=CH), and 10.86 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 21.01, 112.19, 115.38, 126.27, 127.24, 128.62, 129.99, 130.62, 131.24, 138.23, 139.32, 149.63, and 166.62 ppm; m/z (%): 564 (M⁺, 29). Analysis Calcd for C₂₈H₂₄N₁₀S₂ (564.69): C, 59.56; H, 4.28; N, 24.80; Found: C, 59.52; H, 4.27; N, 24.83%.

3.1.10. 5,5'-(Phenyl-1,3-diyl)-bis-((2-(p-bromobenzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (13c)

Red solid; Yield (88%); mp: >300 °C. IR (KBr): ν_{max} 3194 (NH), 1593 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.64 (s, 6H, 2CH₃), 7.23–7.95 (m, 12H, ArH), 8.71 (s, 2H, N=CH), and 10.98 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 20.06, 112.01, 113.65, 126.45, 127.32, 128.61, 129.84, 132.70, 138.66, 142.12, 143.06, 151.64, and 167.11 ppm. MS m/z (%): 722 (M⁺, 27). Analysis Calcd for C₂₈H₂₂Br₂N₁₀S₂ (722.48): C, 46.55; H, 3.07; N, 19.39; Found: C, 46.51; H, 3.04; N, 19.41%.

3.1.11. 5,5'-(Phenyl-1,3-diyl)-bis-((2-(o-hydroxybenzylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (14)

Red brown solid; Yield (75%); mp: >300 °C. IR (KBr): ν_{max} 3433 (OH), 3182 (NH), 1609 (C=N) cm^{-1} . ^1H NMR (DMSO- d_6): 2.66 (s, 6H, 2CH₃), 7.43–7.96 (m, 12H, ArH), 8.81 (s, 2H, N=CH), 10.77 (s, 2H, NH), and 10.97 (s, 2H, NH) ppm. MS m/z (%): 596 (M⁺, 88). Analysis Calcd for C₂₈H₂₄N₁₀O₂S₂ (596.69): C, 56.36; H, 4.05; N, 23.47; Found: C, 56.39; H, 4.03; N, 23.49%.

3.1.12. 5,5'-(Phenyl-1,3-diyl)-bis-((2-(furylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (15)

Deep green solid; Yield (63%); mp: >300 °C. IR (KBr): ν_{max} 3198 (NH), 1613 (C=N) cm^{-1} . ^1H NMR (DMSO- d_6): 2.71 (s, 6H, 2CH₃), 6.84–8.02 (m, 10H, ArH), 8.73 (s, 2H, N=CH), and 10.88 (s, 2H, NH) ppm. MS m/z (%): 544 (M⁺, 19). Analysis Calcd for C₂₄H₂₀N₁₀O₂S₂ (544.61): C, 52.93; H, 3.70; N, 25.72; Found: C, 52.95; H, 3.72; N, 25.75%.

3.1.13. 5,5'-(Phenyl-1,3-diyl)-bis-((2-(pyridylidenehydrazino)-4-methyl-5-azo-1,3-thiazole) (16)

Red brown solid; Yield (79%); mp: >300 °C. IR (KBr): ν_{max} 3181 (NH), 1603 (C=N) cm^{-1} ; ^1H NMR (DMSO- d_6): 2.78 (s, 6H, 2CH₃), 6.78–7.99 (m, 12H, ArH), 8.75 (s, 2H, N=CH), and 10.86 (s, 2H, NH) ppm. MS m/z (%) = 566 (M⁺, 22). Analysis Calcd for C₂₆H₂₂N₁₂S₂ (566.66): C, 55.11; H, 3.91; N, 29.66; Found: C, 55.14; H, 3.93; N, 29.68%.

3.1.14. 1,3-Bis((4-methyl-2-(2-(1-(thiophen-2-yl)ethylidene)hydrazinyl)thiazol-5-yl)diazenyl)benzene (17)

Red solid; Yield (91%); mp: 185 °C. IR (KBr): ν_{max} 3177 (NH), 1596 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.25 (s, 6H, 2CH₃), 2.74 (s, 6H, 2CH₃), 6.99–8.01 (m, 10H, ArH), and 10.97 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 16.73, 21.59, 114.18, 123.87, 127.25, 128.45, 128.72, 130.49, 132.46, 134.32, 142.32, 157.23, 159.84, and 171.24 ppm. MS m/z (%): 604 (M⁺, 88). Analysis Calcd for C₂₆H₂₄N₁₀S₄ (604.8): C, 51.63; H, 4.00; N, 23.16; Found: C, 51.65; H, 4.03; N, 23.19%.

3.2. General procedure for the synthesis of 20 and 22

A mixture of bis-hydrazoyl halides **1** or **2** (5 mmol) and dimethyl acetylenedicarboxylate **19** (1.42 mL, 10 mmol) in dioxane (20 mL) and triethylamine (1 g, 1.5 mL, 10 mmol) was boiled under reflux for 4 h. The reaction mixture was then poured into ice-cold hydrochloric acid with stirring. The solid that precipitated was collected. The resulting solid, which formed after cooling, was collected and crystallized from DMF/EtOH to give **20** and **22** elucidated by elemental spectral analyses.

3.2.1. Tetramethyl-1,1'-(sulfonylbis(4,1-phenylene))bis(3-acetyl-1H-pyrazole-4,5-dicarboxylates) (20).

Brown solid; Yield (65%); mp: 173 °C. IR (KBr): ν_{max} 1741, 1661 (C=O), 1597 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.49 (s, 6H, CH₃), 3.88 (s, 6H, CO₂CH₃), 4.08 (s, 6H, CO₂CH₃), 7.02–8.23 (m, 8H, ArH), ^{13}C NMR (DMSO- d_6): at 26.62, 52.15, 53.64, 122.65, 127.69, 128.24, 138.06, 139.28, 145.68, 152.02, 160.01, 163.25, and 195.27 ppm. MS m/z (%): 666 (M⁺, 17). Analysis Calcd for C₃₀H₂₆N₄O₁₂S (666.60): C, 54.05; H, 3.93; N, 8.40; Found: C, 54.02; H, 3.95; N, 8.44%.

3.2.2. Tetramethyl-1,1'-(1,3-phenylene)bis(3-acetyl-1H-pyrazole-4,5-dicarboxylates) (22)

Brown solid; Yield (54%); mp 120 °C. IR: ν_{max} 1739, 1671 (C=O), 1594 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): 2.52 (s, 6H, CH₃), 3.93 (s, 6H, CO₂CH₃), 4.15 (s, 6H, CO₂CH₃), 7.36–8.02 (m, 4H, ArH), ^{13}C NMR (DMSO- d_6): at 26.74, 52.98, 53.31, 107.69, 124.93, 128.07, 130.29, 138.09, 140.68, 148.71, 158.69, 163.76, and

192.31 ppm; m/z (%): 526 (M^+ , 23); Anal. Calcd for $C_{24}H_{22}N_4O_{10}$ (526.50): C, 54.75; H, 4.21; N, 10.64; Found: C, 54.79; H, 4.24; N, 10.61%.

3.3. Synthesis of thiohydrazone derivatives **24** and **25**

A mixture of bis-hydrazone dichlorides **1** or **2** (5 mmol) and 4-bromophenol **23** (1.881 g, 11 mmol) in NaOMe (20 mL, 11 mmol) was stirred at room temperature for 30 h. The solid that precipitated was collected. The resulting solids filtered, washed with water, and recrystallized from DMF/MeOH.

3.3.1. N,N'-(Sulfonyl)-bis-(1,4-phenylene)-bis-(4-bromophenyl-2-oxopropanehydrazone) (**24**)

Black green solid; Yield (83%); mp: >300 °C. IR (KBr): ν_{max} 3228 (NH), 1661 (C=O), 1591 (C=C) cm^{-1} . 1H NMR (DMSO- d_6): 2.49 (s, 6H, 2CH₃), 7.21–8.18 (m, 16H, ArH), 9.64 (s, 2H, NH), ^{13}C NMR (DMSO- d_6): at 26.70, 96.76, 119.01, 126.67, 128.81, 129.21, 129.64, 141.03, 142.17, 163.58, and 208.11 ppm. MS m/z (%): 728 (M^+ , 19). Analysis Calcd for $C_{30}H_{24}Br_2N_4O_6S$ (728.40): C, 49.47; H, 3.32; N, 7.69; Found: C, 49.49; H, 3.35; N, 7.72%.

3.3.2. N,N'-(1,3-Phenylene)-bis-(4-bromophenyl-2-oxopropanehydrazone) (**25**)

Red brown solid; Yield (72%); mp: >300 °C. IR (KBr): 3194 (NH), 1672 (C=O), 1603 (C=N) cm^{-1} . 1H NMR (DMSO- d_6): 2.50 (s, 6H, 2CH₃), 7.41–7.99 (m, 12H, ArH), 9.73 (s, 2H, NH) ppm. MS m/z (%): 588 (M^+ , 18). Analysis Calcd for $C_{24}H_{20}Br_2N_4O_4$ (588.2): C, 49.00; H, 3.43; N, 9.52; Found: C, 49.03; H, 3.46; N, 9.49%.

3.4. Synthesis of bis-triazolo[3,4-b]thiadiazole (**29a–c**)

To a solution of the bis-hydrazones **27** (2.5 mmol) in ethanol (40 mL) was added a solution of iron(III) chloride (5 mL, 2 M). The reaction mixture was heated at reflux for 30 min and then left to stir overnight at room temperature. The excess solvent was distilled under reduced pressure and the solid residue left was collected and washed with water several times, dried, and finally crystallized from methanol to give the respective compounds **29a–c**.

3.4.1. 3,6-Di(4-methylphenyl)-bis-triazolo[3,4-b]thiadiazole (**29a**)

Brown solid, Yield (65%); mp: 225 °C. IR (KBr): ν_{max} 1604 (C=N) cm^{-1} . 1H NMR (DMSO- d_6): δ 2.38 (s, 6H, 2CH₃), 7.11–8.05 (4d, J8 Hz, 8H, ArH), ^{13}C NMR (DMSO- d_6): at 21.16, 128.14, 129.49, 129.74, 130.74, 143.34, and 162.01 ppm. MS m/z (%): 346 (M^+ , 46). Analysis Calcd for $C_{18}H_{14}N_6S$ (346.41): C, 62.41; H, 4.07; N, 24.26. Found: C, 62.39; H, 4.06; N, 24.21%.

3.4.2. 3,6-Di(diphenyl)-bis-triazolo[3,4-b]thiadiazole (**29b**)

Red brown solid, Yield (72%); mp: 199 °C. IR (KBr): ν_{max} 1602 (C=N) cm^{-1} . 1H NMR (DMSO- d_6): δ 7.38–8.01 (m, 10H, ArH), ^{13}C NMR (DMSO- d_6): at 128.46, 128.87, 129.46, 132.80, 144.12, and 163.24 ppm; m/z (%): 318 (M^+ , 31). Analysis Calcd for $C_{16}H_{10}N_6S$ (318.07): C, 60.36; H, 3.17; N, 26.40. Found: C, 60.34; H, 3.21; N, 26.42%.

3.4.3. 3,6-Di(4-chlorophenyl)-bis-triazolo[3,4-b]thiadiazole (29c)

Yellow brown solid, Yield (86%); mp: 207 °C. IR (KBr): ν_{max} 1593 (C=C) cm^{-1} . ^1H NMR (DMSO- d_6): δ 7.24–8.13 (m, 8H, ArH), ^{13}C NMR (DMSO- d_6): at 128.68, 128.45, 129.94, 134.97, 152.14, and 168.01 ppm. MS m/z (%): 385 (M^+ , 43). Analysis Calcd for $\text{C}_{16}\text{H}_8\text{Cl}_2\text{N}_6\text{S}$ (385.99): C, 49.63; H, 2.08; N, 21.70. Found: C, 49.65; H, 2.11; N, 21.68%.

4. Conclusion

In summary, thiazoles derivatives were prepared from thiosemicarbazone with α -halocarbonyl hydrazonoyl. The synthesis of pyrazoles was achieved by reaction of dimethyl acetylenedicarboxylate with bis-hydrazonoyl chlorides. Thiohydrazonates **24** and **25** were also prepared via reaction of 4-bromophenol with bis-hydrazonoyl chlorides. In addition, bis-triazolothiadiazoles were synthesized via oxidative cyclization of bis-hydrazones.

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