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A simple green synthesis of (*Z*)-5-arylmethylene-4-thioxothiazolidines and thiopyrano[2,3-*d*]thiazolidine-2-thiones in PEG-400 under catalyst-free conditions

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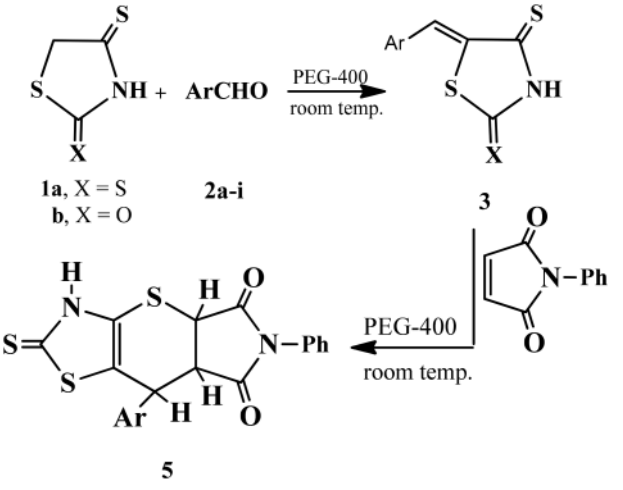
An improved Knoevenagel condensation of various aromatic aldehydes with thiazolidine-2,4-dithione and with 4-thioxothiazolidin-4-one can be achieved at room temperature in polyethylene glycol-400 without catalyst to afford (*Z*)-5-arylmethylene-4-thioxothiazolidine derivatives **3a**–**3o**. Also, the [4+2] cyloaddition reaction of **3a**–**3g** with *N*-phenylmaleimide **4** gave the cycloadducts **5a**–**5g** under the same reactions conditions. The structure of all the newly synthesized compounds was established on the basis of the elemental analysis and spectral data. This process is a simple, efficient, economical, and environmentally benign compared to classical reactions.



Keywords: 5(*Z*)-arylmethylene-4-thioxothiazolidines; 4-thioxothiazolidines; aromatic aldehydes; thiopyrano[2,3-*d*]thiazolidine-2-thiones; PEG-400, solvent-free

1. Introduction

Thiazolidine-2,4-dithione (thiorhodanine) and its derivatives are used in coordination chemistry for the determination and detection of certain metal ions.[1–4] In addition, 4-thioxothiazolidin-2-one (isorhodanine) and its derivatives exhibit a broad spectrum of biological activities such

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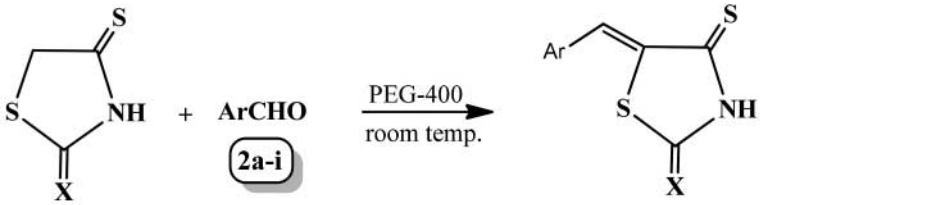
as antimicrobial, cyctotoxic,[5] anticancer, and antiangiogenic effects.[6–8] Moreover, fused heterocycles containing the 2-thioxothiazolidin-4-one or thiazolidin-4-one moiety were found to be important in the field of medicinal chemistry for their anticancer,[9–13] antitubercular, antioxidant,[14] and antimalarial agents.[15] Green chemistry focuses on research that attempts to reduce or eliminate the negative environmental impacts. Among the aims of green chemistry, Ref. [16] is to prevent wastes and generate substances with little or no toxicity to humans and the environment and maximize atom economy. Recently, liquid polymers or low-melting polymers have emerged as alternative green reaction media with unique properties such as stability, commercial availability, non-volatility, immiscibility with a number of organic solvents, and recyclability.[17,18] Polyethylene glycol (PEG) solvent is preferred over other polymers because its inexpensive, completely non-halogenated, easily degradable, and of low toxicity.[19–22] Based on the broad range of biological effects of 5-arylmethylene-4-thioxo-thiazolidinones and their fused thiopyrano[2,3-*d*]thiazoles, our ongoing research aims to develop more simple, more efficient, and environmentally benign methods of synthesizing these compounds that useful in the drug discovery processes.[23–30] Herein we wish to report a simple approach for the preparation of 5-arylidene-4-thioxothiazolidine derivatives and fused thiopyrano[2,3-*d*]thiazolidine-2-thiones at room temperature in PEG-400 without a catalyst.

2. Results and discussion

Knoevenagel condensation is between aromatic aldehydes and thiazolidine-2,4-dithione (thiorhodanine) is known to be carried out in glacial acetic acid in the presence of anhydrous sodium acetate.[31] Also, a series of 5-benzylidene thiorhodanines were obtained by the reaction of 5-benzylidene rhodanines with phosphorus pentasulfide in dioxane.[32] The condensation between 4-thioxothiazolidin-2-one and *p*-dimethylaminobenzaldehyde was carried out in methanol.[33] Another common condensation carried out is glacial acetic acid containing anhydrous sodium acetate,[34–36] and ammonia with amines.[37] Thus, in this paper, we reinvestigate the condensation of 4-thioxothiazolidines **1a,b** with various aromatic aldehydes **2a**–**2i** in PEG-400 under stirring at room temperature without a catalyst to afford the highly colored 5-arylmethylene-2-thioxothiazolidine derivatives **3a**–**o** in high yield. The structure of the isolated products **3a**–**o** was deduced from elemental analysis and spectral data (see Section 4 and Scheme 1). For example, the IR spectrum of **3k** taken as a typical example from the prepared series that showed absorption bands at ν_{max} 3161 and 1686 cm^{-1} due to the NH and carbonyl groups, respectively. Its ^1H NMR spectrum revealed two singlet signals at $\delta = 3.84$ and 8.06 due to methoxy and vinylic protons, respectively, in addition to a D_2O-exchangeable signal at 13.78 ppm due to the NH proton together with other expected signals. Mass spectrum as well as elemental analyses are in agreement with structure **3k**. All the derivatives prepared in this study were obtained exclusively in *Z*-isomer as confirmed by the spectral data. The ^1H NMR spectra of compound **3k** showed that the most characteristic olefinic proton =CH was deshielded more (8.06 ppm) as expected by its *Z*-isomer, compared to the slightly shielded protons of the *E*-isomer (6.0–6.50 ppm).[38]

The reactions of 5-arylidene-1,3-thiazolidine-2,4-dithiones with dimethyl acetylenedicarboxylate, maleic anhydride, arylmaleimide, and acrylonitrile in acetic acid have been reported to yield thiopyrano[2,3-*d*]thiazolidine-2-thione derivatives.[25,39–41] We reinvestigated the *hetero*-Diels–Alder reaction of deeply colored 5-arylidene-thiazolidine-2,4-dithiones **3a**–**3g** with *N*-phenylmaleimide, in PEG-400 under stirring at room temperature a green method to afford in each case one product as evidenced by TLC. The colorless products obtained were identified as 1 : 1 adducts **5**. The assigned structure for products **5a**–**5g** was established on the basis of the



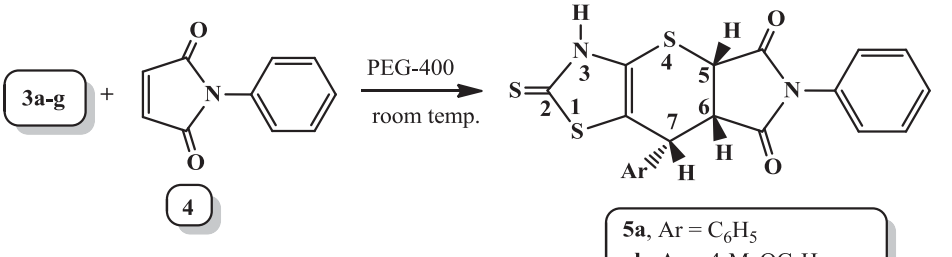
1a, X = S
b, X = O

2a, Ar = C_6H_5
b, Ar = 4-$MeOC_6H_4$
c, Ar = 4-ClC_6H_4
d, Ar = 4-$EtOC_6H_4$
e, Ar = 3,4-$(CH_2)O_2C_6H_3$
f, Ar = 2-furyl
g, Ar = 2-thienyl
h, Ar = 2,4-$(MeO)_2C_6H_3$
i, Ar = 2,4,5-$(MeO)_3C_6H_2$

3a, X = S, Ar = C_6H_5
b, X= S, Ar = 4-$MeOC_6H_4$
c, X = S, Ar = 4-ClC_6H_4
d, X = S, Ar = 4-$EtOC_6H_4$
e, X = S, Ar = 3,4-$(CH_2)O_2C_6H_3$
f, X= S, Ar = 2-furyl
g, X = S, Ar = 2-thienyl
h, X = S, Ar = 2,4-$(MeO)_2C_6H_3$
i, X = S, Ar = 2,4,5-$(MeO)_3C_6H_2$
j, X = O, Ar = C_6H_5
k, X= O, Ar = 4-$MeOC_6H_4$
l, X = O Ar = 4-ClC_6H_4
m, X = O, Ar = 3,4-$(CH_2)O_2C_6H_3$
n, X= O, Ar = 2-furyl
o, X = O, Ar = 2-thienyl

Scheme 1. Reaction of **1a,b** with **2a**–**2i**.

elemental analysis and spectral data. For example, the IR spectrum of **5c** showed an absorption band at ν_{max} 3083 due to the NH group, 1782 and 1722 corresponding to carbonyl groups (imide, CO). Its ^{1}H NMR spectrum revealed to a doublet of doublet at 4.0–4.05 ppm with J values 6.0 and 8.7 Hz corresponding to H-6, a doublet signal at 4.73 ppm with J value = 6 Hz attributed to H-5 and a doublet signal at 5.31 ppm with J value = 8.7 Hz attributed to H-7, beside the other expected signals due to vinylic and NH protons. On the basis of the coupling constant, the *cis*-configuration



5a, Ar = C_6H_5
b, Ar = 4-$MeOC_6H_4$
c, Ar = 4-ClC_6H_4
d, Ar = 4-$EtOC_6H_4$
e, Ar = 3,4-$(CH_2)O_2C_6H_3$
f, Ar = 2-furyl
g, Ar = 2-thienyl

Scheme 2. Reaction of **3a**–**3g** with *N*-phenylmaleimide.

[42] was assigned to the cycloadduct **5c**. The ^{1}H NMR spectra showed that only one stereoisomer was present for all products **5a**–**5g**, indicating that the reaction is stereoselective. Based on the elemental analyses and spectral data, structures **5a**–**5g** were assigned to these adducts (cf. Scheme 2 and exp.).

3. Conclusion

The method reported here describes the synthesis of 5(*Z*)-arylmethylene-4-thioxothiazolidines **3a**–**3o** in PEG which took place at room temperature. Furthermore, the reaction of **3a**–**3g** with *N*-phenylmaleimide **4** underwent 4+2-cycloaddition reaction to give 1 : 1 cycloadducts **5a**–**5g** under the same reaction conditions. The method is simple and effective in terms of short reaction time and only one product is formed. It is also consistent with the green chemistry approach since it does not need heating or microwave irradiation. It occurs at room temperature without a catalyst.

4. Experimental

All melting points were determined on an Electrothermal (9100) apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a Perkin Elmer 1430 spectrophotometer. ^{1}H NMR spectra were recorded in deuterated dimethylsulfoxide at 300 MHz on a Varian Gemini NMR spectrometer using tetramethylsilane as internal reference and results are expressed as δ values. ^{13}C NMR spectra were recorded in dimethylsulfoxide (DMSO-d_6) at 75.46 MHz on a Varian Mercury VXR-300 NMR spectrometer using tetramethylsilane as internal reference and results are expressed as δ values. Mass spectra were taken on a Shimadzu GCMS-QP 1000 Ex mass spectrometer at 70 eV. Elemental analyses were carried out at the Microanalysis Center of Cairo University.

*Preparation of thiazolidine-2,4-dithione **1a***. A mixture of 2-thioxo-4-thiazolidinone (0.09 mol) and 9 g of phosphorus pentsulfide was refluxed for 10–15 min in 90 ml dry dioxane, then added 2 g active charcoal and 4 g zinc dust. The whole mixture was refluxed again for 1–2 min, after which it filtered off. The dioxane was distilled under reduced pressure to give yellowish-orange crystals of mp. 80°C of **1a**.[43]

*Preparation of 4-thioxo-2-thiazolidinon **1b***. A mixture of 2,4-thiazolidinedione (0.25 mol) and 20 g of phosphorus pentsulfide was refluxed for 3 h in 200 ml dry dioxane. The mixture was filtered off. The dioxane was distilled under reduced pressure to give pale yellow crystals of mp. 160°C of **1b**.[44]

4.1. *Preparation of (Z)-5-arylmethylene-4-thioxo-thiazolidine derivatives 3a–3o*

General procedure: To each of **1a,b** (0.005 mol) in 5 ml of PEG-400, add 0.005 mol of the appropriate aldehyde. The mixture was stirred at room temperature till precipitation (TLC). The mixture was poured into water, filtered, washed with water, and crystallized from a mixture of ethanol and dioxane.

4.1.1. *(Z)-5-Phenylmethylene-2,4-thiazolidinedithione (**3a**)*

Brown crystals, yield 0.93 g (64%), mp. 196°C [lit. 198°C]; ν_{max}/cm^{-1} (KBr) 3060 (NH); ^{1}H NMR (DMSO-d_6) δ = 7.35 (s, 1H, CH), 7.44–7.65 (m, 5H, Ar), 9.11 (s, 1H, NH); m/z = 237.36.

Anal. Calcd. $C_{10}H_7NS_3$: C, 50.60; H, 2.97; N, 5.90; S, 40.53. Found: C, 50.42; H, 2.80; N, 5.68; S, 40.78.

4.1.2. *(Z)-5-(4-Methoxyphenyl)methylene-2,4-thiazolidinedithione (**3b**)*

Deep red crystals, yield 1.06 g (80%), mp. 212°C [lit. 208°C]; ν_{max}/cm^{-1} (KBr) 3057 (NH); ^1H NMR (DMSO-d_6) $\delta = 3.73$ (s, 1H, OCH_3), 7.43 (s, 1H, CH), 7.58 (d, 2H, $J = 8.1$ Hz, Ar.), 7.70 (d, 2H, $J = 8.2$ Hz, Ar), 9.16 (s, 1H, NH); $m/z = 267.30$. Anal. Calcd. $C_{11}H_9NOS_3$: C, 49.41; H, 3.39; N, 5.24; S, 35.98. Found: C, 49.59; H, 3.21; N, 5.48; S, 35.80.

4.1.3. *(Z)-5-(4-Chlorophenyl)methylene-2,4-thiazolidinedithione (**3c**)*

Yellow crystals, yield 1.11 g (82%), mp. 217°C; ν_{max}/cm^{-1} (KBr) 3113; ^1H NMR (DMSO-d_6) $\delta = 7.45$ (s, 1H, CH), 7.58 (d, 2H, $J = 8.1$ Hz, Ar.), 7.70 (d, 2H, $J = 8.2$ Hz, Ar.), 9.18 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) $\delta = 128.1, 128.8, 130.8, 133.7, 134.2, 144.1, 195.3, 198.4$. $m/z = 271.81$. Anal. Calcd. $C_{10}H_6NS_3$: C, 44.19; H, 2.22; Cl, 13.04; N, 5.15; S, 35.39. Found: C, 44.40; H, 2.40; N, 5.30; S, 35.20.

4.1.4. *(Z)-5-(4-Ethoxyphenyl)methylene-2,4-thiazolidinedithione (**3d**)*

Brown crystals, yield 0.98 g (71%), mp. 196°C; ν_{max}/cm^{-1} (KBr) 3107 (NH); ^1H NMR (DMSO-d_6) $\delta = 1.33$ (t, 3H, $J = 6.2$ Hz, CH_3), 4.34 (q, 2H, $J = 6.3$ Hz, CH_2), 7.44 (s, 1H, CH), 7.25 (d, 2H, $J = 8.1$ Hz, Ar.), 7.70 (d, 2H, $J = 8.2$ Hz, Ar.), 9.11 (s, 1H, NH); $m/z = 281.42$. Anal. Calcd. $C_{12}H_{11}NOS_3$: C, 51.22; H, 3.94; N, 4.98; S, 34.18. Found: C, 51.70; H, 3.76; N, 6.13; S, 27.20.

4.1.5. *(Z)-5-(Benzo[d][1,3]dioxol-5-ylmethylene)thiazolidine-2,4-dithione (**3e**)*

Brown crystals, yield 1.2 g (86%), mp. 230°C; ν_{max}/cm^{-1} (KBr) 3120 (NH); ^1H NMR (DMSO-d_6) $\delta = 6.21$ (s, 2H, CH_2), 6.88 (d, 1H, $J = 9$ Hz, Ar.), 7.17–7.35 (m, 3H, Ar and CH), 9.11 (s, 1H, NH); $m/z = 280.10$. Anal. Calcd. $C_{11}H_7NO_2S_3$: C, 46.95; H, 2.51; N, 4.98; S, 34.19. Found: C, 46.76; H, 2.69; N, 4.74; S, 34.38.

4.1.6. *(Z)-5-(Furan-2-ylmethylene)thiazolidine-2,4-dithione (**3f**)*

Brown crystals, yield 0.79 g (71%), mp. 187°C; ν_{max}/cm^{-1} (KBr) 3079 (NH); ^1H NMR (DMSO-d_6) $\delta = 6.65$ (s, 1H, CH), 7.14 (m, 1H, furan), 7.28 (d, 1H, $J = 8.1$ Hz, furan.), 9.11 (s, 1H, NH); $m/z = 227.33$. Anal. Calcd. $C_8H_5NOS_3$: C, 42.27; H, 2.22; N, 6.16; S, 42.32. Found: C, 42.10; H, 2.42; N, 6.40; S, 42.50.

4.1.7. *(Z)-5-(Thiophen-2-ylmethylene)thiazolidine-2,4-dithione (**3g**)*

Brown crystals, yield 0.87 g (72%), mp. 245°C [lit. 240°C],[24] ν_{max}/cm^{-1} (KBr) 3080 (NH); ^1H NMR (DMSO-d_6) $\delta = 6.71$ (s, 1H, CH), 7.15 (d, 1H, $J = 8.2$ Hz, thiophene), 7.27 (m, 1H, thiophene), 7.97 (d, 1H, $J = 8.2$ Hz, thiophene), 11.31 (s, 1H, NH); $m/z = 243.39$. Anal. Calcd. $C_{10}H_7NO_2S_2$: C, 39.48; H, 2.07; N, 5.75; S, 52.70. Found: C, 39.29; H, 2.26; N, 5.98; S, 52.88.

4.1.8. *(Z)-5-(2,4-Dimethoxybenzylidene)thiazolidine-2,4-dithione (**3h**)*

Brown crystals, yield 1.24 g (85%), mp. 255°C; ν_{max}/cm^{-1} (KBr) 3117 (NH); ^{1}H NMR (DMSO-d_6) $\delta = 3.86$ (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.63 (s, 1H, Ar.), 6.72 (d, 1H, $J = 8.7$ Hz, Ar.), 7.40 (d, 2H, $J = 8.4$ Hz, Ar.), 8.14 (s, 1H, CH), 10.17 (s, 1H, NH); $m/z = 297.42$. Anal. Calcd. $C_{12}H_{11}NO_2S_3$: C, 48.46; H, 3.73; N, 4.71; S, 32.34. Found: C, 48.64; H, 3.92; N, 4.95; S, 32.52.

4.1.9. *(Z)-5-(2,4,5-Timethoxybenzylidene)thiazolidine-2,4-dithione (**3i**)*

Brown crystals, yield 1.36 g (84%), mp. 285°C; ν_{max}/cm^{-1} (KBr) 3126 (NH); ^{1}H NMR (DMSO-d_6) $\delta = 3.70$ (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 6.45 (s, 1H, Ar.), 7.27 (s, 1H, Ar.), 7.51 (s, 1H, CH), 11.51 (s, 1H, NH); $m/z = 327.44$. Anal. Calcd. $C_{13}H_{13}NO_3S_3$: C, 47.68; H, 4.0; N, 4.28; S, 29.38. Found: C, 47.85; H, 4.19; N, 4.52; S, 29.20.

4.1.10. *(Z)-5-Phenylmethylene-4-thioxothiazolidin-2-one (**3j**)*

Brown crystals, yield 0.93 g (86%), mp. 190°C; ν_{max}/cm^{-1} (KBr) 3148 (NH) and 1684 (CO); ^{1}H NMR (DMSO-d_6) $\delta = 7.38$–7.75 (m, 6H, Ar and CH), 12.14 (s, 1H, NH); $m/z = 221.30$. Anal. Calcd. $C_{10}H_7NOS_2$: C, 54.27; H, 3.19; N, 6.33; S, 28.98. Found: C, 54.44; H, 3.0; N, 6.56; S, 28.80.

4.1.11. *(Z)-5-(4-Methoxybenzylidene)-4-thioxothiazolidin-2-one (**3k**)*

Pink crystals, yield 0.93 g (86%), mp. 251°C; ν_{max}/cm^{-1} (KBr) 3161 (NH) and 1689 (CO); ^{1}H NMR (DMSO-d_6) $\delta = 3.84$ (s, 3H, OCH_3), 7.08 (d, 2H, $J = 8.7$ Hz, Ar.), 7.63 (d, 2H, $J = 8.7$ Hz, Ar.), 8.06 (s, 1H, CH), 13.78 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) $\delta = 54.3$, 113.6, 128.1, 129.8, 132.1, 143.7, 158.4, 196.2, 168.7. $m/z = 251.32$. Anal. Calcd. $C_{11}H_9NO_2S_2$: C, 52.57; H, 3.61; N, 5.57; S, 25.52. Found: C, 52.40; H, 3.79; N, 5.80; S, 25.70.

4.1.12. *(Z)-5-(4-Chlorobenzylidene)-4-thioxothiazolidin-2-one (**3l**)*

Orange crystals, yield 0.93 g (86%), mp. 195°C; ν_{max}/cm^{-1} (KBr) 3185 (NH) and 1688 (CO); ^{1}H NMR (DMSO-d_6) $\delta = 7.68$ (d, 2H, $J = 8.1$ Hz, Ar.), 7.73 (s, 1H, CH), 8.10 (d, 2H, $J = 8.2$ Hz, Ar.), 13.66 (s, 1H, NH); $m/z = 255.74$. Anal. Calcd. $C_{10}H_6ClNOS_2$: C, 46.96; H, 2.36; Cl, 13.86; N, 5.48; S, 25.08. Found: C, 46.72; H, 2.53; N, 5.24; S, 25.27.

4.1.13. *(Z)-5-(Benzo[d][1,3]dioxol-5-ylmethylene)-4-thioxothiazolidin-2-one (**3m**)*

Brown crystals, yield 0.93 g (86%), mp. 275°C; ν_{max}/cm^{-1} (KBr) 3172 (NH) and 1687 (CO); ^{1}H NMR (DMSO-d_6) $\delta = 6.22$ (s, 2H, CH_2), 6.88–7.34 (m, 4H, Ar and CH), 12.34 (s, 1H, NH); $m/z = 265.31$. Anal. Calcd. $C_{11}H_7NO_3S_2$: C, 49.80; H, 2.66; N, 5.28; S, 24.17. Found: C, 49.61; H, 2.83; N, 5.52; S, 24.0.

4.1.14. *(Z)-5-(Furan-2-ylmethylene)-4-thioxothiazolidin-2-one (**3n**)*

Brown crystals, yield 0.93 g (86%), mp. 225°C; ν_{max}/cm^{-1} (KBr) 3164 (NH) and 1689 (CO); ^{1}H NMR (DMSO-d_6) $\delta = 6.63$ (m, 1H, furan H), 7.25 (d, 1H, $J = 8.1$ Hz, furan), 7.67 (s, 1H, CH),

8.0 (d, 1H, $J = 8.2$ Hz, furan), 12.10 (s, 1H, NH); $m/z = 237.30$. Anal. Calcd. $C_8H_5NO_2S_2$: C, 45.48; H, 2.39; N, 6.63; S, 30.36. Found: C, 45.66; H, 2.57; N, 6.87; S, 30.55.

4.1.15. *(Z)-5-(Thiophen-2-ylmethylene)-4-thioxothiazolidin-2-one (**3o**)*

Brown crystals, yield 0.93 g (86%), mp. 217°C; ν_{max}/cm^{-1} (KBr) 3170 (NH) and 1684 (CO); ^{1}H NMR (DMSO-d_6) $\delta = 7.14$ (d, 1H, $J = 8.2$ Hz, thiophen H), 7.32 (s, 1H, CH), 7.46 (m, 1H, thiophen), 7.89 (d, 1H, $J = 8.1$ Hz, Ar.), 12.01 (s, 1H, NH); $m/z = 227.33$. Anal. Calcd. $C_8H_5NOS_3$: C, 42.27; H, 2.22; N, 6.16; S, 42.32. Found: C, 42.46; H, 2.40; N, 6.40; S, 42.15.

4.2. *Preparation of 7-Aryl-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimides 5a–5g*

General procedure: To each of **3a**–**3h** (0.01 mol) in 5 ml of PEG-400, add 0.01 mol of *N*-phenylmaleimide. The mixture was stirred at room temperature until the color changed to violet. The mixture was poured into water, filtered off, and crystallized from a mixture of ethanol and dioxane.

4.2.1. *7-Phenyl-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide (**5a**)*

Pale brown crystals, yield 0.32 g (80%), mp. 266°C [lit. 250°C] [37] ν_{max}/cm^{-1} (KBr) 3097 (NH), 1780, 1718 (imide CO); ^{1}H NMR (DMSO-d_6) $\delta = 3.83$–3.88 (dd, 1H, $J = 6.3$, 8.7 Hz, H-6), 4.86 (d, 1H, $J = 6$ Hz, H-5), 4.97 (d, 1H, $J = 9$ Hz, H-7), 7.0–7.42 (m, 10H, Ar.), 13.62 (s, 1H, NH); $m/z = 410.53$. Anal. Calcd. $C_{20}H_{14}N_2O_2S_3$: C, 58.51; H, 3.44; N, 6.82; S, 23.43. Found: C, 58.70; H, 3.61; N, 7.06; S, 23.25.

4.2.2. *7-(4-Methoxyphenyl)-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide (**5b**)*

Pale violet crystals, yield 0.35 g (81%), mp. 252°C [lit. 240°C](*37*); ν_{max}/cm^{-1} (KBr) 3078 (NH), 1784 and 1718 (imide CO); ^{1}H NMR (DMSO-d_6) $\delta = 4.07$–4.11 (dd, 1H, $J = 6.3$, 8.7 Hz, H-6), 4.64 (d, 1H, $J = 6.3$ Hz, H-5), 5.40 (d, 1H, $J = 8.7$ Hz, H-7), 6.68–7.46 (m, 9H, Ar.), 13.76 (s, 1H, NH); $m/z = 440.56$. Anal. Calcd. $C_{21}H_{16}N_2O_3S_3$: C, 57.25; H, 3.66; N, 6.36; S, 21.83.

4.2.3. *7-(4-Chlorophenyl)-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide (**5c**)*

Brownish white crystals, yield 0.35 g (79%), mp. 273°C; ν_{max}/cm^{-1} (KBr) 3083 (NH), 1782 and 1722 (imide CO); ^{1}H NMR (DMSO-d_6) $\delta = 4.0$–4.05 (dd, 1H, $J = 6$, 8.7 Hz, H-6), 4.73 (d, 1H, $J = 6$ Hz, H-5), 5.31 (d, 1H, $J = 8.7$ Hz, H-7), 6.62–6.85 (m, 2H, Ar.), 7.31–7.44 (m, 7H, Ar.), 13.81 (s, 1H, NH); ^{13}C NMR (DMSO-d_6) $\delta = 34.2$, 40.3, 47.1, 89.7, 127.8, 128.7, 129.5, 129.8, 130.3, 132.5, 133.2, 139.1, 158.3, 173.2, 178.0, 190.2. $m/z = 444.98$. Anal. Calcd. $C_{20}H_{13}ClN_2O_2S_3$: C, 53.98; H, 2.94; Cl, 7.97; N, 6.30; S, 21.62. Found: C, 53.80; H, 2.75; N, 6.54; S, 21.44.

4.2.4. *7-(4-Ethoxyphenyl)-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide **(5d)***

Pale violet crystals, yield 0.34 g (75%), mp. 235°C; ν_{max}/cm^{-1} (KBr) 3077 (NH), 1784 and 1721 (imide CO); ^{1}H NMR (DMSO-d_6) $\delta = 1.27$ (t, 3H, $J = 6.7$ Hz, CH_3), 4.04–4.11(dd, 1H, $J = 6$, 8.7 Hz, H-6), 4.23 (q, 2H, $J = 6.3$ Hz, CH_2), 4.68 (d, 1H, $J = 6$ Hz, H-5), 5.30 (d, 1H, $J = 9$ Hz, H-7), 6.81–7.42 (m, 9H, Ar.), 13.76 (s, 1H, NH); $m/z = 454.58$. Anal. Calcd. $C_{22}H_{18}N_2O_3S_3$: C, 58.13; H, 3.99; N, 6.16; S, 21.16. Found: C, 58.41; H, 3.79; N, 6.40; S, 21.34.

4.2.5. *7-(Benzo[d][1,3]dioxo)-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide **(5e)***

Pale violet crystals, yield 0.37 g (82%), mp. 248°C; ν_{max}/cm^{-1} (KBr) 3086 (NH), 1780 and 1720 (imide CO); ^{1}H NMR (DMSO-d_6) 4.10–4.15 (dd, 1H, $J = 6$, 9 Hz, H-6), 4.78 (d, 1H, $J = 6$ Hz, H-5), 5.38 (d, 1H, $J = 9$ Hz, H-7), 6.23 (s, 2H, CH_2), 6.76–7.68 (m, 8H, Ar.), 13.84 (s, 1H, NH); $m/z = 454.54$. Anal. Calcd. $C_{21}H_{14}N_2O_4S_3$: C, 55.49; H, 3.18; N, 6.16; S, 21.16. Found: C, 55.31; H, 3.29; N, 6.40; S, 21.34.

4.2.6. *7-(Furan-2yl)-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide **(5f)***

Pale brown crystals, yield 0.3 g (76%), mp. 224°C; ν_{max}/cm^{-1} (KBr) 3069 (NH), 1780 and 1719 (imide CO); ^{1}H NMR (DMSO-d_6) $\delta = 3.98$–4.01 (dd, 1H, $J = 6$, 8.7 Hz, H-6), 4.71 (d, 1H, $J = 5.7$ Hz, H-5), 5.28 (d, 1H, $J = 9.3$ Hz, H-7), 6.13 (d, 1H, $J = 6.6$ Hz, furan), 6.34 (m, 1H, furan), 7.28–7.68 (m, 5H, Ar.), 8.11 (d, 1H, $J = 6$ Hz, furan), 13.81 (s, 1H, NH).^{13}C NMR (DMSO-d_6) $\delta = 35.1$, 37.2, 44.1, 89.5, 106.3, 113.1, 128.1, 128.8, 129.2, 133.1, 143.3, 152.2, 157.1, 172.9, 177.8, 189.4. $m/z = 400.49$. Anal. Calcd. $C_{18}H_{12}N_2O_3S_3$: C, 53.98; H, 3.02; N, 6.99; S, 24.02. Found: C, 53.79; H, 3.20; N, 6.76; S, 24.20.

4.2.7. *7-(Thiophen-2-yl)-5,6-bis-hydroxycarbonyl-tetrahydrothiopyrano-7H[2,3-d]thiazole-2-thione-N-phenylimide **(5g)***

Pale brown crystals, yield 0.32 g (78%), mp. 178°C [lit. 175°C](*24*); ν_{max}/cm^{-1} (KBr) 3210 (NH), 1780 and 1754 (imide CO); ^{1}H NMR (DMSO-d_6) $\delta = 3.88$–3.86 (d, 1H, $J = 6$, 9 Hz, H-6), 4.74 (d, 1H, $J = 6$ Hz, H-5), 5.18 (d, 1H, $J = 9$ Hz, H-7), 6.78 (d, 1H, $J = 7.5$ Hz, thiophene), 6.94 (m, 1H, thiophene), 7.21–7.58 (m, 6H, Ar and thiophene), 13.78 (s, 1H, NH); $m/z = 416.56$. Anal. Calcd. $C_{18}H_{12}N_2O_2S_4$: C, 51.90; H, 2.90; N, 6.72; S, 30.79. Found: C, 51.73; H, 3.08; N, 6.96; S, 30.60.

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