

Catalyst Free Synthesis of Pyridine-2,6-bis(2-bromo-propane-1,3-dione) and Pyrdine-2,6-bis(*N*-arylthiazoline-2-thiones)

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Abstract

We have described herein a catalyst-free preparation method of pyridine-2,6-bis(*N*-alkylthiazoline-2-thiones) (4a-i) by the reaction of primary amines, CS₂, and pyridine-2,6-bis(2-bromo-1,3-dicarbonyl) derivatives (2a-c) in water. Also, we have described a catalyst free, green chemistry protocols to monobromination of pyridine-2,6-bis(2-bromo-1,3-dicarbonyl) derivatives with high yield, using NBS as a brominating agent, that led to eco-friendly isolation and purification procedures. Furthermore, we have studied the reactivity of pyridine-2,6-bis(2-bromo-1-methyl-propane-1,3-dione) (2a) towards thiourea to afford 2,6-bis(5-benzoyl-2-aminothiazol-4-yl)pyridine (9).

Keywords

N-Alkylthiazoline-2-Thiones, Catalyst-Free Reactions, Monobromination, 2,6-Disubstituted Pyridine

1. Introduction

α -Bromo-1,3-dicarbonyl compounds are highly useful synthetic intermediates in organic synthesis [1] [2]. Many reports researched the bromination of 1,3-diketones and β -keto esters using different reagents such molecular bromine, potassium bromide, sodium hypobromite, and CuBr that are hazardous chemicals and lead to complicated work-up methods [3]-[6]. The other challenge for using these reagents is the selectivity of monobromination toward 1,3 diketones and β -keto esters because these reagents in many cases lead to a mixture of mono and di-brominated products [7] [8]. On the other hand, *N*-bromosuccinimide is a superior brominating reagent,

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inexpensive, easy to handle and can be used in solvent free and eco-friendly organic syntheses [9]. Thus, we have reported herein solvent and catalyst free strategy as an important alternative to the use of organic solvents in selective monobromination of 1,3-diketones and β -keto esters using NBS as brominating agent and comparing with that obtained from monobromination in diethyl ether as a solvent and $\text{CH}_3\text{COONH}_4$ as a catalyst.

Thiazoline-2-thiones derivatives have found a wide range of applications in many fields, such as diffusion transfer colour photographic materials, agriculture, molecular conductors and as powerful ligands [10] [11]. Also, they applied in medicinal chemistry as they have hypoglycemic, anti-inflammatory and antineoplastic activities [12]. There are many recorded protocols for the synthesis of *N*-substituted thiazoline-2-thiones. For example, they can be prepared by the reaction of α -haloketones with alkyl ammonium dithiocarbamates in the presence of acid [13] or from three component one pot synthesis (carbon disulfide, amines, and ethyl 3-bromo-2-oxopropionate) in the presence of anhydrous potassium phosphate in DMF [14].

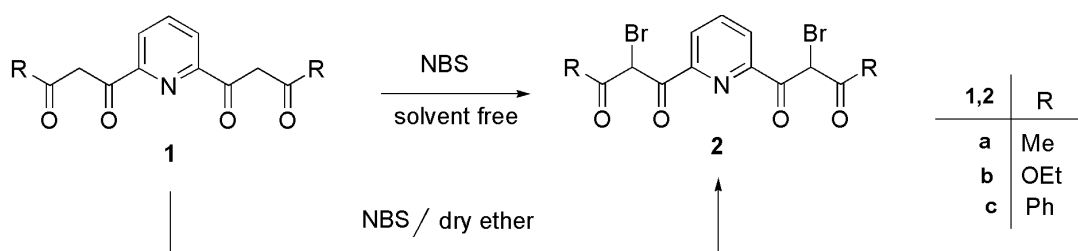
In view of these observations and our interest in the synthesis of biologically target pyridine-2,6-bis(functionalized heterocycles) [15]-[21], we describe herein a catalyst-free, three component one pot synthesis for new class of 2,6-bis(5-substituted-3-aryl-2-thiothiazol-4-yl)pyridine (**4a-i**) by reaction of primary amines, carbon disulfide, and 2-chloro-1,3-dicarbonyl compounds in water. This protocol and the work-up procedure were facile and we have obtained pure target compounds containing several potential centres for further modification.

2. Results and Discussion

Firstly, We have prepared the bis(β -diketone) compounds: pyridine-2,6-bis(1-methyl-propane-1,3-dione) (**1a**), pyridine-2,6-bis(1-ethoxycarbonyl-propane-1,3-dione) (**1b**) and pyridine-2,6-bis(1-phenyl-propane-1,3-dione) (**1c**), by *Claisen* condensation of ethyl pyridine-2,6-dicarboxylate ester with the appropriate ketone using our procedure to synthesize pyridine-2,6-bis-(3-oxopropanenitrile) [21] with excellent yields [91% (**1a**), 93% (**1b**), 89% (**1c**)] that are more than the reported methods [22]. To apply green chemistry protocols in the synthesis of mono-brominated-1,3-dicarbonyl compounds followed by environmentally friendly isolation and purification procedures, we have used NBS as a brominating agent by taking the advantages of the high solubility of succinimide in water.

A mixture of pyridine-2,6-bis(propane-1,3-dione) derivatives (**1a-c**) and NBS was triturated in a porcelain mortar at room temperature for 30 min. After grinding in mortar pestle the color of the reaction mixture gradually changed from pale yellow color to deep yellow-brown color. By addition of few amounts of water to the mixture then lifted for 3 h, resulted in formation of yellow paste for each derivative. The past of each product was washed with water many times and the solid products were separated by decantation to afford the corresponding, monobrominated product (**2a-c**) with good yields, on the basis of the elemental analysis spectral data. The ^1H NMR spectra of the isolated products (**2a-c**) revealed, in each case a singlet signal at the region of δ 6.00 - 6.31 which indicates the presence of the aliphatic CH.

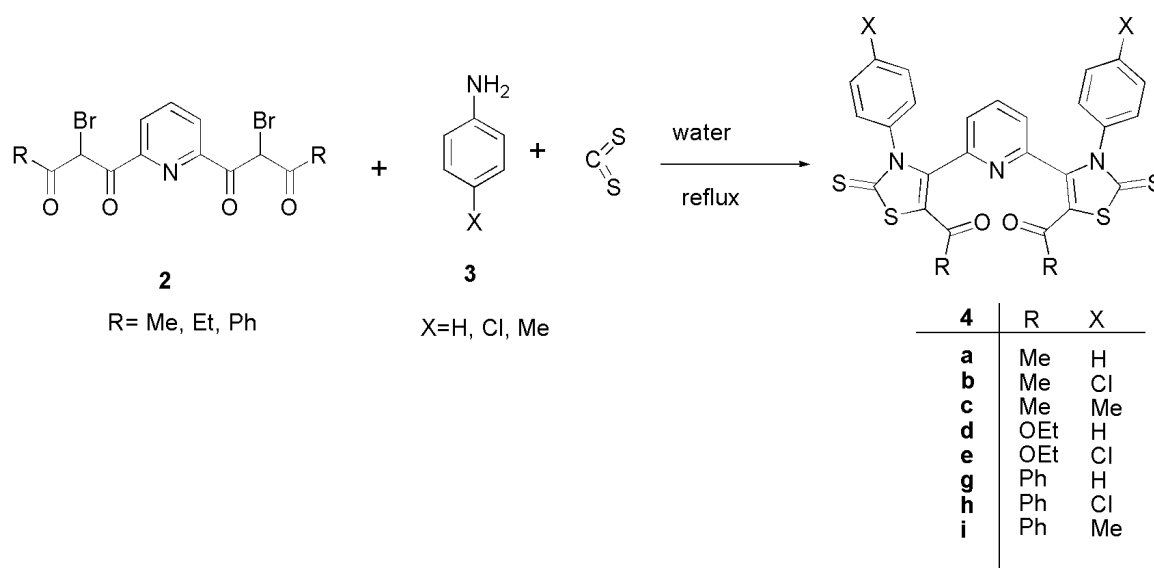
Scheme 1



Treatment of the appropriate freshly prepared pyridine-2,6-bis(2-bromo-1,3-dicarbonyl) compounds (**2a-c**) with the appropriate primary amines (**3a-c**) and carbon disulfide in water, under refluxed temperature, afforded the corresponding 2,6-bis(5-substituted-3-aryl-2-thiothiazol-4-yl)pyridine (**4a-i**) in high yields. The structures of the isolated solid products (**4a-i**) were confirmed on the bases of elemental analysis and spectral data as presented in the experimental part. The Mass spectra of the synthesized compounds, showed the molecular ion peaks at the appropriate m/z values. Also, IR spectra of each product represent the presence of carbonyl group and are in agreement with the proposed structures. The ^1H NMR spectrum of compound (**4c**) as an example

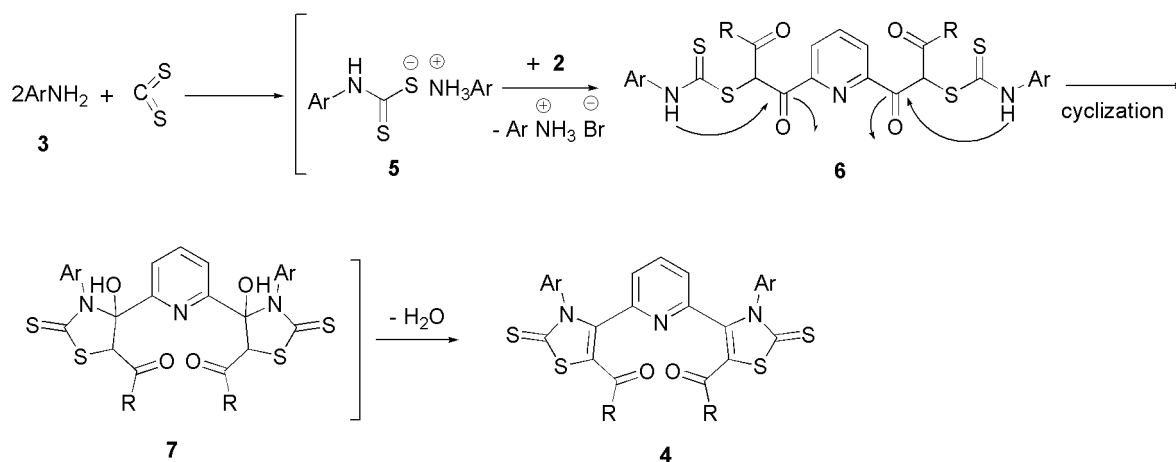
revealed two singlet signals at 2.13 and 2.28 corresponding to (acetyl and p-touyl) methyl groups, respectively.

Scheme 2



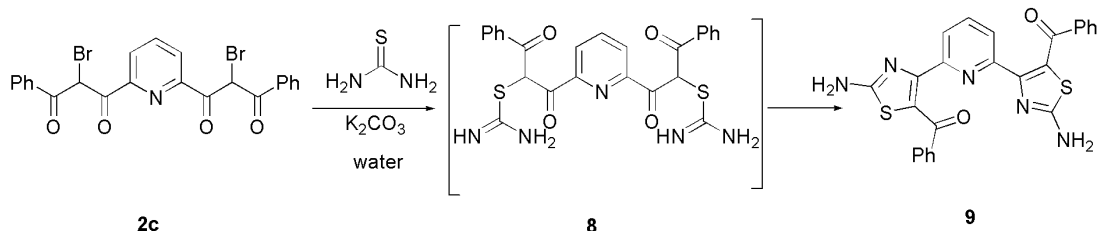
The formation of the synthesized series (**4a-i**) could be explained and assumed to proceed by a sequence as presented in Scheme 3. Firstly, reaction of aniline derivatives with Carbon disulfide to afford aryl ammonium dithiocarbamate salt **5**, followed by addition to pyridine-2,6-bis(2-bromo-1,3-dicarbonyl) (**2**) derivatives to generate acyclic dithiocarbamate derivatives **6**. Subsequent cyclization yields 4-hydroxythiazoline-2-thiones **7** followed by elimination of water to afford pyridine-2,6-bis(*N*-arylthiazoline-2-thiones) **4** (Scheme 3).

Scheme 3



Also, we have studied The behavior of pyridine-2,6-bis(2-bromo-1-methyl-propane-1,3-dione) (**2a**) towards thiourea. Thus, treatment of compound **2a** with thiourea in refluxing water, in the presence of a catalytic potassium carbonate, afforded 2,6-bis(5-benzoyl-2-aminothiazol-4-yl)pyridine (**9**) on the basis of its elemental analysis and spectral data. The IR spectrum of the later compound revealed presence of two absorption bands at the region 3309 - 3127 corresponding to NH_2 groups in addition to absorption band at 1720 corresponding to carbonyl group. The ^1H NMR of compound **9** revealed broad singlet D_2O exchangeable singlet signal at δ 4.45 corresponding to amino groups, The mass spectrum of the same product showed a peak at m/z 327 corresponding to its molecular ion (Scheme 4).

Scheme 4



3. Conclusion

We have described herein a convenient route for the synthesis of monobrominated derivatives: pyridine-2,6-bis(2-bromo-1,3-dicarbonyl) (**2a-c**) with high yield using NBS as a brominating agent. Also, we have described a catalyst-free for the preparations of *N*-arylthiazoline-2-thiones (**4a-i**) by the reaction of primary amines, CS₂, and 2-bromo-1,3-dicarbonyl compounds (**2a-c**) in water. The catalyst-free and green procedure for the preparation of *N*-arylthiazoline-2-thiones (**4a-i**) can be considered as an alternative method for the preparation of this type of compounds.

4. Experimental

General: All melting points were measured on a Gallenkamp melting point apparatus (Weiss Gallenkamp, London, UK). The infrared spectra were recorded in potassium bromide disks on a Pye-Unicam SP 3300 and Shimadzu FT IR 8101 PC infrared spectrophotometers (Pye-Unicam Ltd. Cambridge, England and Shimadzu, Tokyo, Japan, respectively). The NMR spectra were recorded on a Varian Mercury VX-300 NMR spectrometer (Varian, Palo Alto, CA, USA). ¹H spectra were run at 300 MHz and ¹³C spectra were run at 75.46 MHz in deuterated chloroform (CDCl₃) or dimethyl sulfoxide (DMSO-*d*₆). Chemical shifts are given in parts per million and were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer (Shimadzu) at 70 eV. Elemental analyses were carried out at the Micro analytical Centre of Cairo University, Giza, Egypt and recorded on Elementar-Vario EL (Germany) automatic analyzer. We have prepared The bis(β -diketone) compounds, pyridine-2,6-bis(1-methyl-propane-1,3-dione) (**1a**), pyridine-2,6-bis(1-ethoxycarbonyl-propane-1,3-dione) (**1b**) and pyridine-2,6-bis(1-phenyl-propane-1,3-dione) (**1c**), by *Claisen* condensation of ethyl pyridine-2,6-dicarboxylate ester with the appropriate ketone (acetone, ethyl acetate and acetophenone), respectively in dry toluene, using NaH as a base at room temperature, and the experimental data of the products as that as reported in the given references [22].

4.1. General Procedure for the Preparation of Pyridine-2,6-bis(2-bromo-propane-1,3-dione) Derivatives (**2a-c**)

Method A: In a porcelain mortar a mixture of the appropriate pyridine-2,6-bis(propane-1,3-dione) derivatives (**1a-c**) (4 mmol) (**1a**, 0.98 g), (**1b**, 1.23 g) and (**1c**, 1.48 g) and *N*-bromosuccinimide (1.42 g, 8 mmol) was triturated at room temperature for 30 min. Few amounts of water was then added to the resulting mixture and lifted at room temperature for 3 h, to form yellow paste for each derivatives. The past of each products was washed with water many times and the solid product was separated by decantation, to afford the corresponding, monobrominated products (**2a-c**) with yields (1.47 g, 91%; 1.73 g, 93% and 2.01 g, 95%), respectively without further purifications.

Method B: To a stirred solution of the appropriate pyridine-2,6-bis(1,3-dicarbonyl) derivative (**1a-c**) (4 mmol) (**1a**, 0.96 g), (**1b**, 1.23 g) and (**1c**, 1.48 g) and *N*-bromosuccinimide (1.42 g, 8 mmol) in diethyl ether (5 mL) was added 0.2 g ammonium acetate gradually. The reaction mixture was stirred at room temperature for 8 - 14 h then filtered off. The resulting solution was washed with water three times and the organic layer was separated and dried over sodium sulphate. The resulting solution was evaporated under reduced pressure to afford the corresponding pyridine-2,6-bis(2-bromo-propane-1,3-dione) derivatives (**2a-c**) with yields (1.16 g, 74%; 1.50 g, 81% and 1.58 g, 75%), respectively.

1) Pyridine-2,6-bis(2-bromo-1-methyl-propane-1,3-dione) (**2a**)

Brown powder; mp: 60 - 62. IR (KBr, cm⁻¹): ν_{\max} 2923, 1688, 1664, 1592, 1411, 1290. ¹H NMR (CDCl₃): δ 2.12 (s, 6H, 2CH₃), 6.11 (s, 2H, 2CH), 8.12 - 8.39 (m, 3H, pyridine-H). ¹³C NMR (CDCl₃): δ 23.5 (CH₃), 62.23 (CH-aliphatic), 121.36 (CH), 138.12 (CH), 148.03 (C), 181.11 (C=O). 191.22 (C=O). MS *m/z* (%): 407 (M⁺ + 2)

(7), 405 [M⁺] (12), Analysis Calcd. for C₁₃H₁₁Br₂NO₄ (405.04): C, 38.55; H, 2.74; N, 3.46. Found: C, 38.62; H, 2.65; N, 3.41.

2) Pyridine-2,6-bis(2-bromo-1-ethoxymethyl-propane-1,3-dione) (2b)

Yellow powder; mp: 55 - 56. IR (KBr, cm⁻¹): ν_{\max} 3050, 2980, 1735, 1668. ¹H NMR (CDCl₃): δ 1.20 (t, 6H, 2CH₃, *J* = 7.3 Hz), 4.01 (q, 4H, 2CH₂, *J* = 7.3 Hz), 6.04 (s, 2H, 2CH), 8.31 - 8.39 (m, 3H, pyridine-H). MS *m/z* (%): 467 (M⁺ + 2) (5), 465 [M⁺] (7), Analysis Calcd. for C₁₅H₁₅Br₂NO₆ (465.09): C, 38.74; H, 3.25, N, 3.01. Found: C, 38.57; H, 3.35, N, 3.11.

3) Pyridine-2,6-bis(2-bromo-1-phenyl-propane-1,3-dione) (2c)

Brown powder; mp: 110°C - 111°C. IR (KBr, cm⁻¹): ν_{\max} 2924, 1710, 1595, 1450, 1307, 1282, 716. ¹H NMR (DMSO-*d*₆): δ 6.13 (s, 2H, 2CH), 7.31 - 7.45 (m, 10H, Ar-H), 7.58 - 8.32 (m, 3H, pyridine-H). ¹³C NMR (DMSO-*d*₆): δ 66.23 (CH-aliphatic), 120.76 (CH), 127.05 (CH), 128.13 (CH), 128.61 (CH), 129.42 (CH), 130.18 (CH), 138.12 (CH), 140.21 (C), 148.03 (C), 167.22, 187.11 (C=O). MS *m/z* (%): 531(M⁺ + 2) (3), 529 [M⁺] (2), 450 (10), 370 (12), 305 (8), 266 (9), 105 (100), 76 (41). Analysis Calcd. for C₂₃H₁₅Br₂NO₄ (529.18): C, 52.20; H, 2.86; N, 2.65. Found: 52.31; H, 2.72; N, 2.53.

4.2. General Procedure for the Preparations of 2,6-Bis(5-substituted-3-phenyl-2-thiothiazol-4-yl)pyridine (4a-i)

To a cold stirred suspension of the appropriate amine (**3a-e**) (2 mmol) and (0.46 g, 6 mmol) carbon disulphide in 10 mL water, was added slowly pyridine-2,6-bis(2-bromo-propane-1,3-dione) derivative (**2a-c**) (1 mmol) (**2a**, 0.4 g), (**2b**, 0.46 g) and (**2c**, 0.53 g). The reaction mixture was stirred under reflux temperature for 6 - 10 h. the reaction mixture was then treated with 5 mL of saturated sodium bicarbonate solution. The precipitate products were filtered off, washed with water, dried, to afford the corresponding thiazole derivatives (**4a-i**).

1) 2,6-Bis(5-acetyl-3-phenyl-2-thiothiazol-4-yl)pyridine (4a)

Yield (0.45 g, 83%); yellow crystals (EtOH); mp: 201°C - 203°C. IR (KBr, cm⁻¹): ν_{\max} 3061, 1675, 1585, 1547, 1315. ¹H NMR (DMSO-*d*₆): δ 2.51 (s, 6H, 2CH₃), 7.01 - 7.39 (m, 10H, Ar-H), 7.45 - 8.11 (m, 3H, pyridine-H). ¹³C NMR (DMSO-*d*₆): δ 25.55 (CH₃), 108.12 (C), 122.76 (CH), 123.13 (CH), 125.13 (CH), 126.9 (CH), 127.11 (CH), 130.83 (C), 134.13 (C), 135.12 (CH), 155.11 (C), 180.33 (C=S), 192.22 (C=O). MS *m/z* (%): 546 [M⁺] (3). Analysis Calcd. for C₂₇H₁₉N₃O₂S₄ (545.72): C, 59.42; H, 3.51; N, 7.70. Found: C, 59.32; H, 3.62; N, 7.63.

2) 2,6-Bis(5-acetyl-3(4-chlorophenyl)-2-thiothiazol-4-yl)pyridine (4b)

Yield (0.51 g, 83%); Pale yellow crystals (EtOH); mp: 187°C - 188°C. IR (KBr, cm⁻¹): ν_{\max} 3016, 1686 1593, 1538, 1485, 1319, and 1089. ¹H NMR (CDCl₃): δ 2.42 (s, 6H, 2CH₃), 6.55 - 7.22 (m, 8H, Ar-H), 7.65 - 8.0 (m, 3H, pyridine-H). MS *m/z* (%): 615 (5), 614 [M⁺] (5), 368 (10), 295 (14), 261 (8), 206 (9), 169 (44), 127 (100), 111 (25), 75 (35). Analysis Calcd for C₂₇H₁₇Cl₂N₃O₂S₄ (614.61): C, 52.76; H, 2.79; N, 6.84. Found: C, 52.81; H, 2.85; N, 6.78.

3) 2,6-Bis(5-acetyl-3(4-methylphenyl)-2-thiothiazol-4-yl)pyridine (4c)

Yield (0.45 g, 78%); yellow crystals (EtOH); mp: 170°C - 172°C. IR (KBr, cm⁻¹): ν_{\max} 2923, 1688, 1590, 1550, 1318, 1099. ¹H NMR (DMSO-*d*₆): δ 2.13(s, 6H, 2CH₃), 2.28 (s, 6H, 2CH₃), 7.02 - 7.26 (m, 8H, Ar-H), 7.33 - 8.01 (m, 3H, pyridine-H). ¹³C NMR (DMSO-*d*₆): δ 21.18, 21.55, (2CH₃), 110.42 (C), 122.76 (CH), 124.48 (CH), 126.90 (CH), 127.81 (CH), 130.83 (C), 133.43 (C), 136.48 (CH), 155.11 (C), 161.12 (C), 179.63 (C=S), 189.22 (C=O). MS *m/z* (%): 573 [M⁺] (5), 551 (6), 359 (7), 256 (21), 222 (51), 149 (52) 106 (100), 77 (64). Analysis Calcd for C₂₉H₂₃N₃O₂S₄ (573.77): C, 60.71; H, 4.04; N, 7.32. Found: C, 60.79; H, 4.14; N, 7.22.

4) 2,6-Bis(5-ethoxymethyl-3-phenyl-2-thiothiazol-4-yl)pyridine (4d)

Yield (0.51 g, 84%); yellow crystals (EtOH); 148 - 149 mp: °C. IR (KBr, cm⁻¹): ν_{\max} 2924, 1703, 1613, 1593, 1307, 1233, ¹H NMR (CDCl₃): δ 1.18 (t, 6H, 2CH₃, *J* = 7.4), 4.24 (q, 4H, 2CH₂, *J* = 7.4), 6.95 - 7.33 (m, 10H, ArH's), 7.36 - 8.01 (m, 3H, pyridine-H). ¹³C NMR (CDCl₃): δ 14.18 (CH₃), 61.16 (CH₂), 110.01 (C), 119.75 (CH), 126.11 (CH), 127.66 (CH), 128.07 (CH), 129.35 (CH), 130 (C), 154.06 (C), 158.14 (C), 163.76 (C=O), 182.63 (C=S). MS *m/z* (%): 605 [M⁺] (31), 563 (21), 517 (25), 444 (52), 300 (45), 120 (95), 77 (100). Analysis Calcd for C₂₉H₂₃N₃O₄S₄ (605.77): C, 57.50; H, 3.83; N, 6.94. Found: C, 57.43; H, 3.95; N, 6.82.

5) 2,6-Bis(5-ethoxymethyl-3(4-chlorophenyl)-2-thiothiazol-4-yl) pyridine (4e)

Yield (0.5 g, 74%); pale yellow crystals (EtOH); mp: 210°C - 212°C. IR (KBr, cm⁻¹): ν_{\max} 2924, 1725, 1615, 1589, 1541, 1484, 1397, 1311, 1240, 1139. ¹H NMR (DMSO-*d*₆): δ 1.21 (t, 6H, 2CH₃, *J* = 7.3), 4.21 (q, 4H,

2CH₂, $J = 7.3$), 6.94 - 7.31 (m, 8H, ArH's), 7.33 - 8.05 (m, 3H, pyridine- H). ¹³C NMR (DMSO-*d*₆): δ 13.96 (CH₃), 61.15 (CH₂), 110.53 (C), 121.15 (CH), 126.27 (CH), 127.66 (CH), 128.70 (CH), 129.56 (CH), 130.84 (C), 138.87 (C), 154.66 (C), 158.15 (C), 163.76 (C=O), 181.01 (C=S). MS m/z (%): 674 [M⁺] (2), 649 (5), 572 (66), 506 (15), 431 (11), 214 (100), 150 (35), 111 (10), 77 (47). Analysis Calcd for C₂₉H₂₁Cl₂N₃O₄S₄ (674.66): C, 51.63; H, 3.14; N, 6.23. Found: C, 51.69; H, 3.21; N, 6.27.

6) 2,6-Bis(5-benzoyl-3-phenyl-2-thiothiazol-4-yl)pyridine (4g)

Yield (0.59 g, 88%), yellow crystals (EtOH); mp: 191°C - 193°C. IR (KBr, cm⁻¹): ν_{\max} 1721, 1616, 1579, 1322, 1125. ¹H NMR (DMSO-*d*₆): δ 6.75 - 7.33 (m, 20H, Ar-H), 7.45 - 8.01 (m, 3H, pyridine-H). ¹³C NMR (DMSO-*d*₆): δ 120.13 (C), 123.21 (CH), 123.71 (CH₃), 127.85 (CH), 128.73 (CH), 129.12 (CH), 129.59 (CH), 132.33 (CH), 135.22 (C), 136.29 (C), 152.23 (C), 180.21 (C=O), 181.01 (C=S). MS m/z (%): 669 [M⁺] (5), 665 (75), 589 (75), 547 (62), 347 (100), 295 (87), 154 (50), 114 (100), 79 (35). Analysis Calcd for C₃₇H₂₃N₃O₂S₄ (669.86): C, 66.34; H, 3.46; N, 6.27. Found: C, 66.12; H, 3.33; N, 6.21.

7) 2,6-Bis(5-benzoyl-3(4-chlorophenyl)-2-thiothiazol-4-yl) pyridine (4h)

Yield (0.61 g, 82%), yellow crystals (EtOH); mp: 210°C - 212°C. IR (KBr, cm⁻¹): ν_{\max} 1721, ¹H NMR (DMSO-*d*₆): δ 6.66 - 7.31 (m, 18H, Ar-H), 7.55 - 7.89 (m, 3H, pyridine-H). MS m/z (%): 739 [M⁺] (2), 705 (2), 648 (2), 572 (54), 214 (100), 150 (16), 111 (45), 77 (15). Analysis Calcd for C₃₇H₂₁Cl₂N₃O₂S₄ (738.75): C, 60.16; H, 2.87; N, 5.69. Found: C, 60.21 H, 2.91; N, 5.60.

8) 2,6-Bis(5-benzoyl-3(4-methylphenyl)-2-thiothiazol-4-yl)pyridine (4i)

Yield (0.61 g, 85%); yellow crystals (EtOH); mp: 180°C - 181°C. IR (KBr, cm⁻¹): ν_{\max} 2934, 1733, 1595, 1552, 1505, 1244, 1136. ¹H NMR (DMSO-*d*₆): δ 2.27 (s, 6H, 2CH₃), 6.94 - 7.39 (m, 18H, Ar-H), 7.43 - 8.01 (m, 3H, pyridine-H). ¹³C NMR (DMSO-*d*₆): δ 19.96 (CH₃), 115.03 (C), 123.24 (CH), 124.31 (CH), 125.11 (CH), 127.85 (CH), 128.24 (CH), 129.42 (CH), 129.79 (CH), 133.35 (CH), 136.74 (C), 136.90 (C), 151.23 (C), 159.11 (C), 179.62 (C=O), 182.11 (C=S). MS m/z (%): 697 [M⁺] (3), 576 (5), 370 (10), 297 (8), 256 (30), 221 (23), 115 (2), 105 (100), 91 (75), 76 (73), 75 (76). Analysis Calcd for C₃₉H₂₇N₃O₂S₄ (697.91): C, 67.12; H, 3.90; N, 6.02. Found: C, 67.32; H, 3.81; N, 6.12.

9) 2,6-Bis(5-benzoyl-2-aminothiazol-4-yl)pyridine (9)

To a mixture of pyridine-2,6-bis(2-bromo-1-methyl-propane-1,3-dione) (**2c**) (0.53 g, 1 mmol) and thiourea (0.15 g, 2 mmol) in 10 mL water, 0.2g of potassium carbonate was then added. The reaction mixture was refluxed with stirring for 5 h, and then cooled to room temperature. The precipitate product was filtered off, washed with water and dried, to afford 2,6-bis(5-benzoyl-2-aminothiazol-4-yl)pyridine (**9**) Yield (0.31 g, 65%, yellow solid (EtOH); mp: 93°C - 94°C. IR (KBr) cm⁻¹: ν_{\max} 3309, 3127, 1720, 1616, 1250, 1295. ¹H NMR (CDCl₃): δ 4.45 (s, 4H, 2NH₂, 2NH D₂O-exchangeable), 6.91 - 7.36 (m, 10H, Ar-H), 7.83 - 8.01 (m, 3H, pyridine-H). ¹³C NMR (CDCl₃): δ 109.11 (C), 120.31 (CH), 127.7 (CH), 127.9 (CH), 128.9 (CH), 135.11 (C), 137.11 (CH), 153.11 (C), 161.11 (C), 188.12 (C=O). MS m/z (%): 483 [M⁺] (2), 353 (70), 324 (30), 281 (19), 249 (26), 203 (18), 177 (40), 133 (43), 105 (100), 77 (99). Analysis for C₂₅H₁₇N₅O₂S₂ (483.56) Calcd: C, 62.09; H, 3.54; N, 14.48. Found: C, 62.15; H, 3.57; N, 14.62.

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