Synthesis of some Heterocyclic Compound Using α,β-unsaturated Ketones

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ABSTRACT

Objective: This study aimed to the synthesis fused pyridine due to the importance of these heterocycles both from chemical and biological points of view. Method: Pyridine derivatives 1a,b and 2a,b have been utilized for the synthesis of various fused pyridine through different chemical reactions to yield thieno [4,5-c]pyridine 6a,b, 7a,b, 8a,b, pyrido [2',3';2,3]thieno [4,5-d] pyrimidine 9a,b, 2,2'-bis-(3-cyano-4,6-diarylpyridyl)disulfide 10a,b, pyrido [4,5-b] pyrimidine 12a,b, [1,2,4]Triazolo [4,5-a]pyridine 13a,b, tetrazolo [4,5-a] pyridine 14a,b, bis(4,6-diaryl-3-cyanopyridine-2-yl)sulfide 15a,b, pyrido [2,3-b] Pyridine 16a,b, 17a,b, 18a,b and thieno [2,3-b]-1,8-naphthyridine 19a,b, 20a,b derivatives. Pyrido [2,3-d] pyrimidinone derivatives 21a,b were used as starting material for synthesis thiazolo [3,2-a]pyrido [2,3-d] Pyrimidine 23a,b, 24b, 25b, 26a, 29a, thiazin [2,3-a]pyrido [2,3-d] pyrimidinone 28a,b and isoxazolo [5,4,4,5] thiazolo [3,2-a] pyrido [2,3-d] pyrimidinone derivatives 27a. The structures of the synthesized compounds were confirmed by IR, 1H and 13C NMR, elemental analysis and mass spectra data. Conclusion: All structures of synthesized compounds agree with spectral data and elemental analysis.

Keywords: Pyrido [2',3';2,3]thieno [4,5-d] pyrimidinone.

INTRODUCTION

During the last two decades, a large number of substituted pyridines have been reported to have several biological activities1. Fused pyridines comprise a very interesting class of compounds because of their significant and versatile biological and pharmacological activities such as anticonvulsant, antiproliferative, antiviral and antimicrobial2-14.

MATERIALS AND METHODS

Chemistry

Melting points were taken on Gallen Kamp Melting apparatus and were uncorrected. Infrared spectra were obtained on Nexus 470-670 - 870.13C- and 1H-NMR run on JEOL-400 MHZ in DMSO-d6.

The mass spectra were recorded on Ms-S988 operating at 70 ev and the elemental analyses were determined at the Micro analytical center, Cairo University, Egypt.

3-Cyano-4,6-(di-2-thienyl)-pyridine-2(1H)-thione 1a; 3-cyano-4,6-(di-2-furyl)-pyridine-2-(1H)-thione 1,b.

Method A

A mixture of α,β-unsaturated ketones (10 mmol) and cyanothioacetamide (10 mmol) in ethanol (50 ml) in presence of few drops of piperidine was refluxed for 4h. The reaction mixture was poured onto cold water and neutralized with HCl (10%). The solid obtained was filtered and crystallized from proper solvent.

Compound 1a crystallized from dioxane, m.p. 98-100 °C; 80% yield

Anal. calcd. for C14H14N2S2: C, 56.00; H, 2.66; N, 9.33; S, 32.00. Found: C, 56.02; H, 2.20; N, 9.50, S, 31.90. IR (cm\(^{-1}\)): 3369 (NH); 3060 (CH–Ar), 3060 (CH–Ar).
2206(C=Н), 1623 (C=N), 1566 (C=S); 1H-NMR (DMSO-d6, δppm): 6.68 (s, 1H, C3-H pyridine), 7.68-7.95 (m, 6H, two thiophene ring) 8.12 (s, 1H, NH); m/z = 300 (100%).

Compound 1b crystallized from methanol and dimethyl formamide mixture; m.p. 60-62°C; 60% yield.

Method B
A mixture of 2a,b (0.01 mol) and phosphorous penta sulfide in pyridine was heated under reflux for 4h, poured onto cold water. The solid obtained was filtered and no m.p. depression was observed for a mixture of this product with a genuine sample 1a,b.

3- Cyano-4,6-diaryl-2-pyridone 2a,b
Method A
A mixture of α-β-unsaturated ketones (1 mmole) ethyl cyanoacetate (1 mmol) and ammonium acetate (8 mmol) in ethanol (50 ml) was refluxed for 4 h, poured onto cold water the solid obtained was filtered and recrystallized from ethanol.

Compound 2a

Compound 2b: m.p. 310-312°C; 83% yield. Anal. calcd. for C14H12N2O2S: C, 66.66; H, 3.17; N, 11.11. Found: C, 66.43; H, 311; N, 11.00. IR cm⁻¹: 3116 (NH), 3030(CH–Ar), 2217(C=N), 1682 (C=O), 1H-NMR (DMSO-d6, δppm): 6.85 (d, 1H, furan, J=3.7 Hz) 7.10(s, 1H, C3-H–pyridinone) 7.67, 8.12 (2d, 2H, furan, J= 4.4 Hz) 12.68 (S, 1H, NH, exchangeable with D2O).

Method B
A solution of (3 mmole) of chromium trioxide in 5 ml of water was added to a suspension of (0.5 mmole) of disulfide 10a,b in 40 ml of acetic acid, and the mixture was refluxed for 3 h. It was then cooled and diluted with water and the precipitate was separated to give 0.12 g (43%) of pyridine 2a,b with no melting point depression was observed for a mixture of this product with a genuine sample.

3-Cyan-4,6-diaryl-2-cyanomethyl-mercaptopyridine 3a,b
3-cyano-4,6-diaryl-carbomethoxy methyl thiopyridine 4a,b, 3-cyano-4,6-diaryl-2-ethyl mercaptopyridine 5a,b.

A sample of a 10% solution of potassium hydroxide (10 ml) was added to a suspension of (10 mmol) of pyridine-2-thione 1a,b in (30 ml) of DMF, after which a solution of (10 mmol) of chloroacetanilide or chloromethyl acetate or ethyl iodide in (5 ml) of DMF was added drop wise. After 30 min. the reaction mixture was diluted with water and the precipitate was removed by filtration. The temperature of the reaction mixture during the experiment should be maintained at no higher than 15-20°C and recrystallization from ethanol.

Compound 3a: m.p. 206-208°C; 70% yield. Anal. calcd. for C16H16N4S2: C, 56.63; H, 2.65; N, 12.38; S, 28.31. Found: C, 56.40; H, 2.10; N, 12.00, S, 27.90. IR cm⁻¹: 3030(CH–Ar), 2855(CH-aliph), 2200 (2(C=N),1600(C=N),1H-NMR (DMSO-d6, δppm): 4.97 (s, 2H, CH2), 7.30-7.90 (m, 6H, two thiophene), 7.95 (s, 1H, C3-H–pyridine). 13C-NMR (δppm): 54.01 (–CH2–) 124.12, 126.40 127.06, 151.15 (CH–Ar).

Compound 3b: m.p. 220-222 °C; 80% yield. Anal. calcd. for C16H16N4S2: C, 56.54; H, 2.93; N, 13.68, S, 10.42. Found: C, 62.11; H, 2.73; N, 13.00, S, 9.98. IR (cm⁻¹): 3055 (CH–Ar), 2900(CH-aliph), 2210(2C=N) 1605(C=N), 1H-NMR (DMSO-d6, δppm): 4.29 (s, 2H, CH2), 7.22 (s, 1H, C3–pyridine), 7.50-8.00 (m, 6H, two furan).

Compound 4a: m.p. 120-122 °C; 70% yield. Anal. calcd. for C16H16N4S2: C, 54.83; H, 3.22; N, 7.52; S, 25.30. Found: C, 54.61; H, 3.00; N, 6.90; S, 25.60. IR (cm⁻¹): 3080 (CH–Ar), 2942(CH-aliph), 2207(C=N) 1751 (C=O-ester), 1628 (C=N). 1H-NMR (DMSO-d6, δppm): 32.39 (s, 3H, CH3), 4.22 (s, 2H, CH2), 7.33-7.79 (m, 6H, two thiophene), 8.15 (s, 1H, C–H–pyridine); 13C-NMR (δ ppm) (CH3), 53.04 (-CH2-); 116.49 (C=N), 129.60-154.3 (CH–Ar), 169.25 (C=O).

Compound 4b: m.p. 135-137 °C; 75% yield. Anal. calcd. for C16H16N4S2: C, 60.00, H, 3.52; N, 8.23; S, 9.41. Found: C, 60.17; H, 3.22; N, 8.00; S, 8.82. IR (cm⁻¹): 3070 (CH–Ar), 2800 (CH-aliph), 2200(C=N) 1725 (C=O), 1620 (C=N). 1H-NMR (DMSO-d6, δppm): 1.87 (s, 3H, CH3), 2.50 (s, 2H, CH2), 6.99-8.08 (m, 6H, two furan), 8.18 (s, 1H, C3–H–pyridine).

Compound 5a: m.p. 92-94°C; 70% yield. Anal. calcd. for C15H14N2O4S: C, 58.53, H, 3.65; N, 8.53; S, 29.26. Found: C, 58.21; H, 3.20; N, 7.99; S, 29.20. IR (cm⁻¹): 3080 (CH–Ar), 2983-2913 (CH–aliph), 2213(C=N) 1625 (C=N). 1H-NMR (DMSO-d6, δppm): 1.41 (t, 3H, CH3, J=7.4Hz) 4.03(q, 2H, CH2, J= 8.0 Hz), 7.20-7.90 (m, 7H, 6H-two thiophene and C3-H, pyridine).

Compound 5b: m.p. 105-107°C; 6% yield. Anal. calcd. for C15H14N2O4S: C, 64.86, H, 4.05; N, 9.45; S, 10.81. Found: C, 64.40 H, 4.00; N, 9.00; S, 10.50.
3- Amino-2-cyano-4,6-diaryl-thieno[2,3-b] pyridine 6a,b, 3-amino-2-carbomethoxy-4,6-diaryl-thieno[2,3-b] pyridine 7a,b, 3-amino-2-methyl-4,6-diaryl-thieno[2,3-b] pyridine 8a,b.

A sample of a 10% solution of sodium methoxide was added to a suspension of (5 mmol) of cyanomethyl mercaptopyridine 3a,b, 4a,b, and 5a,b in (20 ml) of ethanol and the mixture was heated on a water bath for 1 h. The precipitate was removed by filtration, wash with water and recrystallized from proper solvent.

**Compound 6a:** Crystallized from ethanol; m.p. 235-237°C; 50% yield. Anal. calcd. for C_{16}H_{10}N_{3}S: C, 56.63; H, 2.65; N, 12.38; S, 28.31. Found: C, 56.32; H, 2.10; N, 11.90; S, 27.81. IR (cm⁻¹): 3457, 3331 (NH₂), 3088 (CH–Ar), 2190 (C≡N) 1624 (C=N), 1600(C=C). ¹H-NMR (DMSO-d₆, δppm): 5.92 (s, 2H, NH₂), 7.45-8.10 (m, 7H, two thiophene and C₃–H–pyridine); m/z = 339 (100%).

**Compound 6b:** Crystallized from ethanol DMF mixture (2:1); m.p. > 360°C; 50% yield; Anal. calcd. for C_{16}H_{10}N_{3}O_{2}S: C, 62.54; H, 2.93; N, 13.68; S, 10.92. Found: C, 62.00; H, 2.22; N, 13.77; S, 10.99.

**Compound 7a:** Crystallized from (methanol + DMF) mixture (2:1); m.p. 205-207°C; 90% yield. Anal. calcd. for C_{17}H_{12}N_{2}O_{2}S: C, 54.83, H, 3.22; N, 7.52; S, 25.80. Found: C, 54.66; H, 3.19; N, 7.00; S, 25.89. IR (cm⁻¹): 3377, 3297 (NH₂), 3062 (CH=aliph.), 2930 (CH=aliph.) 1680 (C=O), 1630 (C=C), 1616 (C=C). ¹H-NMR (DMSO-d₆, δppm): 3.78 (s, 3H, CH₃), 4.09 (s, 2H, NH₂), 6.71-7.92 (m, 6H, two thiophene) 8.00 (s, 1H, C₃–H–pyridine) ¹³C (δppm): 28.09 (CH₃), 163.68 (C=O), 119.93–152.69 (CH–Ar).

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Compound 7b: Crystallized from DMF; m.p. >360°C; 80% yield. Anal. calcd. for C₁₁H₂₉N₂O₅S: C, 60.00; H, 3.52; N, 8.23; S, 9.41. Found: C, 60.20; H, 3.31; N, 8.20; S, 9.99. IR (cm⁻¹): 3473, 3342 (NH₂), 3100 (CH−Ar), 29347 (CH−aliph.). 1667 (C=O), 1625 (C=N), 1600(C=C). 1H-NMR (DMSO-d₆, δ ppm): 3.81 (s, 3H, CH₃), 4.16 (s, 2H, NH₂), 6.84 (s, 1H C₃=−pyridine), 7.60−8.09 (m, 6H, two furan).

Compound 8a: Crystallized from Dioxane cyclohexane mixture (2:1); m.p. >360°C; 90% yield. Anal. calcd. for C₁₆H₂₉N₂O₅S: C, 58.53; H, 3.65; N, 8.53; S, 29.26. IR (cm⁻¹): 3400, 3280 (NH₂), 3039 (CH−Ar), 2912 (CH−aliph.), 1603 (C=C), 1595 (C=C). 1H-NMR (DMSO-d₆, δ ppm): 2.08 (s, 3H, CH₃), 4.07 (s, 2H, NH₂), 6.77(s, 1H, C₃−pyridine), 7.37−8.08 (m, 6H, two thiophene); m/z = 328 (102%).

Compound 8b: Crystallized from dioxane m.p. 190−192°C; 85% yield. Anal. calcd. for C₁₆H₂₉N₂O₅S: C, 64.86; H, 4.05; N, 9.45; S, 10.81. Found: C, 64.81; H, 4.00; N, 8.83; S, 10.00. IR (cm⁻¹): 3400, 3280 (NH₂), 3039 (CH−Ar), 2912 (CH−aliph.) 1603 (C=N), 1595 (C=C). 1H-NMR (DMSO-d₆, δ ppm): 1.69 (s, 3H, CH₃), 4.43 (s, 2H, NH₂), 7.40 (s, 1H, C₃−pyridine), 7.44−7.63 (m, 6H, two furan).

8−Amino-2,4-diarylpyridinoid[2,3' & 2,3] thieno [4,5-d] pyrimidin 9a,b.

Compound 3a,b: Crystallize from DMF and methanol mixture (2:1); m.p. >360°C; 75% yield. Anal. Calcd. For C₁₁H₁₀N₂O₂S: C, 55.73; H, 2.73; N, 15.30; S, 26.22. Found: C, 55.71; H, 2.70; N, 15.38; S, 26.28. IR (cm⁻¹): 3475, 3339 (NH₂). 3090 (CH−Ar), 2920 (CH−aliph.), 1610 (C=N), 1594 (C=C). 1H-NMR (DMSO-d₆, δ ppm): 4.41 (s, 2H, NH₂), 6.54 (s, 1H, C₃−pyridine), 7.26−8.03 (m, 6H, two thiophene); 8.45 (s, 1H, C₂−pyrimidin).

Compound 9b: Crystallized from DMF and methanol mixture (2:1); m.p. >360°C; 65% yield. Anal. Calcd. For C₁₁H₁₀N₂O₂S: C, 61.07; H, 2.99; N, 16.76; S, 9.58. Found: C, 61.22; H, 2.70; N, 16.66. S, 8.80 IR (cm⁻¹): 3400, 3310 (NH₂), 3050 (CH−Ar), 2940 (CH−aliph.), 1615 (C=N), 1600 (C=C).

2,2′-Bis(3-cyano-4,6-diarylpyridyl) disulfide 10a,b

A (10 ml) sample of 10% solution of iodine in methanol was added with vigorous stirring to a solution of (4 mmole) of pyridine-2-thione 1a,b (15 ml) of 1N NaOH solution, and the resulting precipitate was washed with ethanol and crystallized from a proper solvent.

Compound 10a: Crystallized from ethanol. m.p. 160−162°C; 80% yield. Anal. calcd. for C₂₈H₂₄N₄S₆: C, 56.00; H, 2.34; N, 9.36; S, 32.80 IR (cm⁻¹): 3090(CH−Ar), 2222 (C=N), 1639 (C≡N).

2-Chloro-3-cyano-4,6-diaryl pyridine 11a,b

Solution of the cyanopyridine derivatives 2a,b (29.4 mmol) in phosphoryl chlorides (100 ml) and triethylamine (4.3 ml) was heating under reflux for 4 h. After cooling the mixture was stirred onto ice/water (500 ml) and stirred further until the brown oil was changed to solid. The mixture was filtered by suction after 12 h standing.

Compound11a: Crystallize from dioxane, m.p. 308−310°C, yield 90%. Anal. calcd. for C₈H₆ClN₂S₂: C, 55.53; H, 2.31; N, 9.25; S, 21.15 Cl, 11.73. Found: C, 55.31; H, 2.10; N, 8.80; S, 20.87, Cl, 11.00. IR (cm⁻¹): 3096 (CH=Ar); 2214 (C≡N). 1H-NMR: δ 7.28 (s, 1H, C₃ − pyridine); 7.26, 7.23 (2d, 2H, two thiophene, J = 4.5 Hz), 7.90, 8.00 (2d, 2H, two thiophene, J = 4.4 Hz), 8.07, 8.08 (2d, 2H, two thiophene, J = 3.8 Hz).

Compound 11b: Crystallized from ethanol, m.p. 160−162°C yield 80%. Anal. calcd. for C₄H₈ClN₂O₂: C, 62.10; H, 2.58; Cl, 13.12. N, 10.35. Found: C, 62.00, H, 2.10; Cl, 13.18 N, 10.00. IR (cm⁻¹): 3090 (CH=Ar); 2210 (C≡N). 1H-NMR: δ 6.75, 6.76 (2d, 2H, two furan ring) J = 5.5 Hz); 6.83, 6.85 (2d, 2H, two furan ring, J = 5.9 Hz), 7.00 (s, 1H, C₃−pyridine) 7.37, 7.64 (2d, 2H, two furan ring, J = 3.6 Hz).

2,8-Diamino-5,7-diaryl-pyrimido [4,5-b] pyridine 12a,b.

Compounds 11a,b (0.043 mol) was heated under reflux with guanidine base in ethanol for 8 h. Guanidine base was prepared by treating a solution of (0.045 mol) of guanidine hydrochloride in 80 ml of warm, dry ethanol with 2.0 g. of sodium in 55 ml of dry ethanol and removing the NaCl by filtration. The reaction mixture was then chilled and the product was collected.

Compound 12a: Crystallized from ethanol, m.p. >360°C; 50%. Yield Anal. calcd. for C₁₅H₁₁N₂S₂: C, 55.38; H, 3.38; N, 21.53. S, 19.69. Found: C, 55.31; H, 3.11, N, 21.10; S, 19.13. IR (cm⁻¹): 3467, 3419, 3310 (2NH₂), 3080 (CH=Ar); 1633 (C≡N). 1H-NMR: δ 4.34, 5.60 (2s, 4H, 2NH₂), 6.61 (s, 1H, C₃−pyridine) 8.61−7.42 (m, 6H, thiophene ring).
Compound 12b crystallized from DMF; m.p. 340-342°C; 65% yield Anal. calcd. for C₁₃H₁₁N₅O₄: C, 61.43; H, 3.75; N; 23.89. Found: C, 61.10; H, 3.22; N, 22.13. IR(cm⁻¹): 3410, 3318, 3120 (2NH₂), 3035 (CH₆Ar.), 1620 (C=N) ¹H-NMR: δ 5.02, 5.08 (2s, 4H, 2NH₂); 6.81 (s, 1H, C₃-H pyridine); 7.90-6.68 (m, 6H, furan ring).

5,7-diary-8-cyano-1,2,4- triazolo [4,5-a] pyridine 13a,b.
A mixture of 11a,b(0.01 mol) and semicarbazide hydrochloride (0.012 mol) in ethanol (25 ml) was treated with a few drops of cone HC1 and refluxed for 8h. The solid obtained was filtered and recrystallized from ethanol.

Compound 13a;m.p. 278-280°C; 90% yield. Anal. calcd. for C₁₅H₁₃N₅O₂S: C, 55.55; H, 2.46; N, 17.28; S, 19.75. Found : C, 55.50; H, 2.00; N, 17.88; S, 19.90. IR(cm⁻¹): 3336 (NH); 3115 (CH₆Ar); 2217(C=O); 1727 (C≡O); 1630(C≡N).¹H-NMR: δ 6.57 (s,1H,C₃-H Pyridine); 7.36-7.28 (m, 2H, two thiophene ring); 7.91 (d, 2H, thiophene ring J= 5.0 Hz); 8.84, 8.26 (2d, 2H, two thiophene ring, J= 4.9 Hz); 9.96 (br.s, 1H, NH ex changeable with D₂O).

Compound 13b;m.p. 248-250°C; 90% yield. Anal. calcd. for C₁₅H₁₃N₅O₂S: C, 61.64; H, 2.73; N, 19.17. Found: C, 61.42; H, 2.30; N, 18.88. IR (cm⁻¹): 3200 (NH); 3087 (CH₆Ar); 2217 (C≡O), 1710 (C≡O); 1640 (C≡N).¹H-NMR: δ 6.32 (s, 1H, C₃-H pyridine), 7.95-6.82 (m, 6H, two furan ring); 10.12 (br.s, 1H, NH exchangeable with D₂O).

5,7-diary-8-cyano tetrazolo [4,5-a] pyridine 14a,b.
A mixture of 11a,b(0.01 mol) in DMF (20ml) and sodium Azide (0.01 mol) was stirred for 30 h, dilute with water and neutralized with HCl. The solid obtained upon dilution with water was filtered off and recrystallized from ethanol.

Compound 14a: m.p.>360°C; 54% yield. Anal. calcd. for C₁₇H₁₅N₃S: C, 54.36; H, 2.26; N, 22.65; S, 20.71. Found: C, 54.12; H, 2.21; N, 22.13; S, 20.00. IR (cm⁻¹): 3100 (CH Ar); 2200 (C≡N); 1640 (C≡N).¹H-NMR: δ 6.62 (s, 1H, C₃-H pyridine ring), 8.01-6.95 (m, 6H, two thiophene rings)

Compound 14b: m.p.>360°C; 40% yield. Anal. calcd. for C₁₇H₁₅N₃S: C, 60.64; H, 2.52; N, 25.27. Found: C,60.51; H,2.20; N, 25.00. IR (cm⁻¹): 3125 (CH Ar); 2195 (C≡N); 1600 (C≡N).¹H-NMR : δ 6.18 (1H, C₃-H Pyridine); 7.35 - 6.68 (m, 6H, two furan rings). Mass spectra of 14b: showed a molecular ion peak at m/z = 277 (5.03%)

Bis (4,6-diary-3-cyano pyridine-2-yl) sulfide 15a,b.
A mixture of 11a,b(0.01 mol) in 20 ml of 25% aqueous NaOH and 3-cyano pyridine -2-thione (0.01 mol) was heated for 2 h. The reaction mixture was cooled, dilute with water and neutralized with dilute acetic acid the solid obtained was filtered.

Compound 15a crystallized from ethanol, m.p.245°C; 90% yield. Anal. calcd. for C₂₉H₁₄N₅S₅: C, 59.36; H, 2.47; N, 9.89; S, 28.26. Found: C, 59.13; H, 2.44; N, 9.41; S, 27.89.IR (cm⁻¹): 3100 (CH Ar.); 2195 (2C≡N), 1632 (C≡N).¹H-NMR: δ 6.68 (s, 1H, C₃-H pyridine), 7.70-7.09 (m, 12H, four thiophene rings); m/z = 566 (5.03%

 Compound 15b crystallized from DMF and MeOH; m.p.>360°C; 95% yield. Anal. calcd. for C₂₉H₁₄N₅S₅: C, 66.93; H, 2.78; N, 11.15 ; S, 6.37. Found: C, 66.71; H, 2.13; N, 11.20; S, 5.84. IR (cm⁻¹): 3070 (CH Ar.); 2215 (C≡N); 1635 (CN).¹H-NMR: δ 6.80 (s, 1H, C₃-H pyridine ring), 7.80-6.90 (m, 12H, four furan rings).

4-Amino 5,7-diary-3-cyano pyrido [2,3-b] pyridine-2 (IH) thione 16a,b.
A mixture of 11a,b(0.01 mol) and cyanothioacetamide (0.01 mol) in pyridine (35ml) was refluxed for 4 h. Poured onto cold water and neutralized with dilute HCl (10%) the solid obtained was filtered and collected.

Compound 16a crystallized from toluene, m.p.> 360°C; 98% yield. Anal. Calcd. For C₁₇H₁₄N₅O₂S: C, 55.73; H, 2.73; N, 15.30; S, 26.22. Found: C, 55.51; H, 2.70; N, 15.47; S, 26.00. IR (cm⁻¹): 3473, 3375 (NH₂); 3142 (NH); 3095 (CH Ar.); 2215 (C≡N).¹H-NMR: δ 5.20 (s, 2H, NH₂), 7.23 (s, 1H, C₃-H pyridine); 7.32-7.24 (m, 4H, two thiophene rings); 7.95-7.85 (2d, 2H, two thiophene ring, J= 4.6 Hz); 8.01 (s, 1H, NH).

Compound 16b crystallized from dioxane and ethanol; m.p.> 360; 50% yield. Anal. calcd. for C₁₇H₁₄N₅O₂S: C, 61.07; H, 2.99; N, 16.76 ; S, 9.58. Found: C, 61.50; H, 2.80; N, 16.11 ; S, 9.99. IR (cm⁻¹): 3420, 3370 (NH₂); 3280 (NH), 3090 (CH Ar.) 2209 (C≡N).¹H-NMR: δ 4.80 (s, 2H, NH₂); 3.80 (s, 1H, C₃-H pyridine), 6.90-7.88 (m, 6H, two furan rings); 9.00 (S,1H, NH).

4-Amino-5,7-diaryl-3-cyano-2-(carbonylethoxymethylthio pyrido) pyrido [2,3-b] pyridine 17a,b.
A mixture of 16a,b(0.01 mol) and α-halo carbonyl compound (chloroethylacetoacetate or chloroacetamide) (0.1 mol) in ethanol (30 ml) in presence of anhydrous sodium acetate (5 g) was refluxed for 2 h. And poured onto cold water. The solid obtained was filtered off and crystallized from ethanol. Compound 17a: m.p. 310-312°C; 60% yield. Anal. calcd. for C₂₁H₁₆O₂N₅S: C, 55.75; H, 3.53; N, 12.38; S,21.23. Found: C, 55.51; H, 3.51; N, 11.98; S, 20.77. IR (cm⁻¹): 3331, 3130 (NH₂), 3100 (CH Ar.),

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Scheme 2

2980 –2920 (CH-aliph.), 2218 (C=O ester), 1732 (C=N). \(^1^H\)-NMR: \(\delta\) 1.42 (t, 3H, CH\(_2\)CH\(_3\), \(J=7.1\) Hz), 2.50 (s, 2H, CH\(_2\)); 3.94 (s, 2H, NH\(_2\)); 4.55 (q, 2H, CH\(_2\)CH\(_3\), \(J=7.2\) Hz); 7.99 - 7.25 (m, 7H, two thiophene rings and C\(_3\)-H pyridine).

**Compound 17b**: m.p. 170-172°C; 50% yield. Anal. calcd. for C\(_{21}\)H\(_{16}\)N\(_4\)O\(_4\): C, 60.00; H, 3.80; N, 13.33; S, 7.61. Found: C, 60.00; H, 3.59; N, 13.00; S, 7.00. IR (cm\(^{-1}\)): 3400; 3250 (NH\(_2\)); 3080 (CH-Aliph), 2950-2920 (CH-aliph.), 2209 (C=O ester); 1629 (C=N). \(^1^H\)-NMR: \(\delta\) 1.40 (t, 3H, CH\(_2\)CH\(_3\), \(J=7.2\) Hz), 2.50 (s, 2H, CH\(_2\)); 4.55 (q, 2H, CH\(_2\)CH\(_3\), \(J=7.1\) Hz); 6.62 (s, 1H, C\(_3\)-H, pyridine ring); 6.62 (s, 1H, C\(_3\)-H, pyridine ring); 6.85 (s, 2H, NH\(_2\)); 8.09 - 7.08 (m, 6H, two furan rings).

**Compound 18a**: m.p. 330-332°C; 55 yield. Anal. calcd. for C\(_{19}\)H\(_{13}\)N\(_5\)O\(_3\): C, 53.90, H, 3.07; N,
Compound 18b: m.p. 240-242°C; 60% yield. Anal. calcd. for C_{19}H_{18}N_{5}O_{2}S_{3}: C, 58.31; H, 3.32; N, 17.90; S, 8.18. Found: C, 58.00; H, 3.30; N, 17.11; S, 8.10. IR (cm\(^{-1}\)): 3420, 3289, 3223, 3149 (2NH\(_{2}\)), 3036 (CH-Aliph.).

3,4-diamino-5,7-dihydro-2-thioxopyridine [2,3-b] - (1,8) - naphthyridine 19'a,b, 3,4-diamino-5,7-dihydro-2-carboxamide thieno [2,3-b]-(1,8) - naphthyridine 20a,b

A sample of compounds (17, 18)a,b (0.5 g) in (25 ml) ethanolic sodium ethoxide solution was refluxed for 1h. The solid product separated from the hot mixture was filtered and crystallized from Dioxane. Compound 19a: m.p. 210-212°C; 40% yield. Anal. calcd. for C_{21}H_{16}N_{2}O_{2}S: C, 57.75; H, 3.53; N, 12.83; S, 21.23. Found: C, 55.91; H, 3.11; N, 12.00; S, 20.91. IR (cm\(^{-1}\)): 3414, 3300, 3186 (2NH\(_{2}\)), 3050 (CH-Aliph.).

Compound 20b: m.p. 322-324°C; 60% yield Anal. calcd. for, C_{19}H_{18}N_{5}O_{2}S: C, 58.31; H, 3.32; N, 17.90; S, 8.18. Found: C, 58.00; H, 3.30; N, 16.99; S, 8.00. IR (cm\(^{-1}\)): 3455, 3353, 3240 (2NH\(_{2}\)), 3025 (CH-Aliph.).

5-(4-chlorophenyl)-2,3-dihydro-7-(2-thienyl)-2-thioxopyrido[2,3-d]pyrimidine-4(1H)-one 21a, 7-(4-bromophenyl)-2,3-dihydro-5-(2-furyl)-2-thioxopyrido[2,3-d]pyrimidine 4(1H)-one 21b

A mixture of \(\alpha,\beta\)-unsaturated ketones (10 mmol) and 6-amino-2,3-dihydro-2-thioxo-4 (1H) pyrimidinone (10 mmol) in DMF (50 ml) was refluxed for 8h. The solid obtained was filtered and recrystallized.

Compound 21a: Crystallized from benzene; m.p. 340-342°C; 90% yield. Anal. calcd. for C_{21}H_{18}N_{5}O_{2}S: C, 54.91; H, 2.69; N, 11.30; S, 17.22. Found: C, 54.31; H, 2.10; 11.10; S, 16.73. IR (cm\(^{-1}\)): 3410, (NH); 3050 (CH-Aliph.); 1700 (C=O), 1633 (C=N). 1H-NMR (DMSO-d_{6} ppm) 7.72 (t, 1H, thiophene, J\(=8.6\) Hz), 7.43 (d, 2H, C_{5}-HcO-H, 4-Cl phenyl, J\(=4.1\) Hz), 7.63 (s, 1H, C_{3}-H pyridine), 7.72-0.80 (2d, 2H, thiophene, J\(=4.5\) Hz), 8.44 (d, 2H, C_{5}-H, C_{3}-H, 4-Cl phenyl, J\(=4.8\) Hz), 8.35, 8.56 (2s, 2H, 2NH).

Compound 21b: Crystallized from dioxane; m.p. 300-302°C; 85% yield. Anal. Calcd. for C_{21}H_{18}Cl_{2}N_{5}O_{2}SBr: C, 51.01; H, 2.50; N, 10.50; S, 8.00. Found: C, 52.10; H, 2.10; N, 10.30; S, 7.81. IR (cm\(^{-1}\)): 3433, (NH); 3098 (CH-Aliph.); 1693 (C=O), 1630 (C=N).

2-(Acetylcetonethio)-5-(4-chlorophenyl)-7-(2-thienyl)-3H, 4H-pyrido[2,3-d] pyrimidine-4-one 22a.

A sample of a 10% solution of potassium hydroxide (10 ml) was added to a suspension of (10 mmol) of compound 21a,b (in 50 ml) of ethanol after which a solution of (12mmol) chloroacetylacetone was refluxed for 5 h poured onto cold water. The solid obtained was filtered and crystallized from proper solvent.

Compound 22a: Crystallized from dioxane; m.p. 310-312 °C; 75 % yield; Anal. calcd. for C_{22}H_{25}N_{5}O_{2}S: C, 56.23; H, 3.40; N, 8.94; S, 13.63. Found: C, 56.00; H, 3.30; N, 9.00; S, 12.85. IR (cm\(^{-1}\)): 3200, (NH); 3090 (CH-Aliph.); 2900 (CH-Aliphatic), 1707 (C=O), 1620 (C=N). 1H-NMR (DMSO-d_{6} ppm) 1.86, 1.90 (3s,6H, 2CH_{3}), 3.68 (s, 1H, SCH).
7.20 (d, 2H, C2-H, C3-H-4-Cl-phenyl, J=7.0 Hz), 7.49, 7.82 (2d, 2H, thiophene, J=4.4 Hz), 7.62 (s, 1H, C3-H-pyridine), 8.05 (d,1H, thiophene, J=4.4 Hz), 8.05 (d,1H,thiophene, J=4.0 Hz), 11.65 (s, 1H, NH): 13C-NMR (δ ppm): 20.67; 20.01 (2CH3), 105.86 (–SCH), 175.86 (C=O), 190.00, 196.00 (2C=O), (136.00 - 155.04) (CH-Ar).

**Compound 22b**: Crystalized from ethanol; m.p. 190-192°C; 70% yield: Anal. calc'd for C22H16N2O2SBr: C, 53.02; H, 3.21; N, 8.43; S, 6.42. Found: C, 52.93; H, 3.14; N, 7.81; S, 6.20. IR (cm⁻¹): 3310, (NH); 3085 (CH-Aliph.), 1700 (C=O), 1666 (C=O), 1640 (C=N). 1H-NMR (DMSO-d6– δ ppm) 1.80, 1.95 (2s, 6H, CH3), 4.40 (s, 1H, SCH), 7.30 (d, 2H, C2-H, C6-H-4-Br-phenyl, J=7.5 Hz), 7.48 (2d, 2H, C3-H,C2-H 4-Br-phenyl, J=7.5 Hz), 7.20, 7.34 (2d, 2H, furan, J= 3.8 Hz), 12.30 (s, 1H, NH).

2-Acetyl-6-(chlorophenyl)-3-methyl-8-(2-thiényl)-5H-thiazolo[3,2-a]pyrido[2,3-d] pyrimidine-5-one 23a

A mixture of 22a,b(10 mmole) and mixture of acetic anhydride & pyridine [2:1] was refluxed for 4 h, poured onto cold water (100 ml). The solid obtained was filtered and crystalized from ethanol.

**Compound 23a**: m.p.>360 °C; 50% yield: Anal. Calc'd for C23H12N2O2SBr: C, 58.47; H, 3.10; N, 9.30; S, 14.17. Found: C, 58.60; H, 3.00; N, 9.10; S, 13.90. IR (cm⁻¹): 3080, (CH--Ar); 2950 (CH-Aliph.), 1711 (C=O), 1658 (C=O), 1589 (C=N). 1H-NMR (DMSO-d6– δ ppm) 2.43 (s, 3H, CH3), 2.66 (s, 3H, COCH3), 7.19 (d, 2H, C2=H, C6=H-4Cl-phenyl, J=8.0 Hz), 7.38 (s, 1H, C1=H-pyridine), 7.42, (t, 1H, thiophene, J=5.5 Hz), 7.77, 7.99 (2d, 2H, thiophene, J=4.2 Hz); 13C-NMR (δ ppm): 21.31 (CH3) 28.07 (CH3), 161.78 (C=O,128.09-155.08 (CH--Ar)).

**Compound 23b**: m.p.>360 °C; 55% yield: Anal. Calc'd for C23H12N2O2SBr: C, 55.01; H, 2.91; N, 8.75; S, 6.66. Found: C, 55.60; H, 2.51; N, 8.33; S, 5.98

2-(3-(2-thényl)-2-propenoyl)-8-(4-bromophenyl)-6-(2-furyl)-3-methyl-5H-thiazolo [3,2-a] pyrido [2,3-d] pyrimidine-5-one 24b

To a solution of compound 23b(0.01 mol) and thiophen-carboxaldehyde (0.01 mol) in absolute ethanol in presence of a catalytic amount of piperidine (1 drop) was heated under reflux for 2h. The reaction mixture was filtered and the obtained precipitate dried and crystallized from petroleum ether.

**Compound 24b**: m.p. 205-207°C; 50% yield: Anal. calc'd for C28H22N2O2SBr: C, 56.45; H, 2.78; N, 7.31; S, 11.14. Found: C, 56.00; H, 2.70; N, 7.30; S, 10.60. IR (cm⁻¹): 3088, (CH--Ar); 2920 (CH-Aliph.), 1710 (C=O), 1680 (C=O). 1H-NMR (DMSO-d6– δ ppm) 2.30 (s, 3H, CH3), 6.11 (s, 1H, C5=H, pyridine). 6.96 (d, 1H, CH=CH2=8.8 Hz) 7.22 (d, 1H, HC=CH, J=8.8 Hz) 7.22 (d, 1H, HC=CH, J= 8.5 Hz) 7.29 (d, 2H, C3=H, C6=H-4-Br-phenyl, J= 8.0 Hz), 7.55 (d, 2H, C2=H-C2=H, J= 8.0 Hz),7.34-7.37 (m, 6H, thiophene and furan).

2-(4-(2-thényl)-4,5-dihydro-2-phenyl-pyrimidine-6-y1)-8-(4-bromophenyl)-6-(2-furyl-3-methyl-5H-thiazolo[3,2-a] pyrido [2,3-d] pyridine-5-one 25b

A mixture of compound 24b (0.01 mol) and benzamidine hydrochloride (0.01 mol) in pyridine (20 ml) was refluxed for 6 h, then cooled and obtained precipitate crystallized from ethanol; m.p.> 360°C 40% yield. Anal. Calc'd for C30H22N2O2SBr: C, 60.36; H, 3.25; N, 10.35; S, 9.46. Found: C, 60.00; H, 3.10; N, 9.85; S, 9.11. IR (cm⁻¹): 3314, (NH); 3063 (CH-Ar), 2956 (CH-Aliph.), 1683 (C=O). 1H-NMR (DMSO-d6– δ ppm) 2.50 (s, 3H, CH3); 7.63 (d, 1H, C3=H-pyridine; 7.77 Hz), 7.77 (d, 2H, C2=H-pyridine, J=7.7 Hz) 8.40-8.99 (m, 11H, Ar--H), 9.33 (s, 1H, NH).

6-(4-chlorophenyl)-2-furylethylene-8-(2-thényl)-2,3,4,5-tetrahydro-thiazolo[3,2-a]pyrido[2,3-d]pyrimidine-3,5-dione 26a

**Method A**

A mixture of compound 21a (10 mmol), 2-furaldehyde (10 mmol) and chloroacetic acid (10 mmol) in (30 ml) glacial acetic acid, (10 ml) acetic anhydride containing anhydrous sodium acetate (1.64 g) was heated under reflux for 4h. The solid product obtained after pouring onto cold water were filtered and then crystallized from proper solvent.

**Method B (step 1)**

6-(4-chlorophenyl)-2,3-dihydro-8-(2-thényl)-5H-thiazolo[3,2-a]pyrido[2,3-d]pyrimidine 3,5-dione 29a

A mixture of compound 21a (10 mmol), and chloroacetic (10 mmol) in (30 ml) glacial acetic acid, (10 ml) acetic anhydride containing anhydrous sodium acetate (1.64 g) was heated under reflux for 3 h the solid product obtained, after pouring onto cold water were filtered and then crystallized.

**Step-2:**

A mixture of compound 29a (10 mmol) and 2-furaldehyde (10 mmol) in (30 ml) glacial acetic acid (10 ml) acetic anhydride containing anhydrous sodium acetate (1.64 g) was heated under reflux for 4h, the solid product obtained, after pouring onto cold water were filtered and then crystallized from proper solvent.

**Compound 26a**: Crystallized from methanol, dioxane mixture (2:1); m.p 300-302°C; 60% yield. Anal. calc'd for C32H22N2O2S2Cl: C, 58.83; H, 2.45; N, 8.58; S, 13.07. Found: C, 58.31; H, 2.01; N, 7.91; S, 12.63. IR (cm⁻¹): 3094 (CH-Ar), 1700 (C=O), 1687
(C=O) 1H-NMR (DMSO-d$_6$– δppm) 6.33 (s, 1H, C$_5$–H– pyridine), 6.82 (s, 1H, HC–Cl), 7.83 (d, 2H, C$_2$–H, C$_6$–H, 4–Cl phenyl, J=4.9 Hz), 7.21, 7.52 (m, 6H, 3H, thiophene and 3H furan), 8.08(d, 2H, C$_3$–H, C$_5$–H, 4–Cl phenyl, J=4.9 Hz); 13C-NMR (δppm): 118.03 (d=CH), 159.12, 175.94 (2 C=O, 110.03-155 (CH–Ar.).

**Compound 29a**: Crystallized from ethanol; m.p. 270-272°C; 50% yield. Anal. calcd. for C$_9$H$_8$(a$_2$O$_2$S)$_2$Cl: C; 55.40; H; 2.43; N; 10.20; S; 15.55. Found: C; 55.00, H; 2.22; N, 9.99%; S; 16.63. IR (cm$^{-1}$): 3008 (CH–Ar), 1701 (C=O), 1680 (C=O) 1H-NMR (DMSO-d$_6$– δppm): 2.78 (s, 2H, CH$_2$), 1.74-7.61 (m, 3H, thiophene), 7.19 (s, 1H, C$_3$–H, pyridine), 7.79 (d, 2H, C$_2$–H, C$_6$–H 4–Cl phenyl, J=5.2 Hz), 8.03 (d, 2H, C$_5$–H, C$_4$–H, 4–Cl phenyl, J=4.8 Hz).

9-(4-Chlorophenyl)-3-(2-furyl)-2,3-dihydro-7-(2-thienyl)-isoxazo[5',4' & 4,5] thiazolo[3,2-a] pyrido[2,3-d] pyrimidine-10 (10H)-one 27a

A mixture of compound 26a (10 mmol) and hydroxyl amine hydrochloride (10 mmol) in (30 ml) glacial acetic acid containing anhydrous sodium acetate (1.64 g) was heated under reflux 6h. the solid product obtained after pouring onto cold water and then crystallized from methanol & DMF mixture (2:1); m.p. > 360°C; 65% yield. Anal. Calcd. For C$_8$H$_7$(a$_2$O$_2$S)$_2$Cl: C; 57.08; H; 2.57; N; 11.10; S; 12.68. Found: C; 56.50, H; 2.00; N; 10.23; S; 12.31. IR (cm$^{-1}$): 3426 (NH), 3088 (CH–Ar), 1715 (C=O), 1592 (C–C). 1H-NMR (DMSO-d$_6$– δppm) 6.85 (s, 1H, C$_5$–H, pyridine), 7.21 (br.s, 1H, C$_3$–H, isoxazde, 7.45-7.85 (m 10H, 3H-thiophene, 3H-furan and 4H-4Cl-phenyl), 8.05 (s, 1H, NH); m/z = 504 (1.02%).

7-(4-chlorophenyl)-4-(4-dimethylaminophenyl)-2-phenyl-9-(2-thienyl)-11H-thiazine [3,2-a] pyrido[2,3-d] pyrimidine-6-one 28a

9-(4-bromophenyl)-7-(2-furyl)-4-(4-dimethylaminophenyl)-2-phenyl-11H-thiazine [3,2-a] pyrido[2,3-d]pyrimidine-6-one 28b

A mixture of compound 21a,b (0.01 mol) and 2-arylcyxmina-monitriles (0.01 mol) in (100 ml) ethyl alcohol containing (1 ml) triethylamine was refluxed for 6 h. The solid product obtained after pouring onto cold water were filtered and crystallized from ethanol.

**Compound 28a**: m.p. 160-162°C; 60% yield. Anal. calcd. for C$_8$H$_7$(a$_2$O$_2$S)$_2$Cl: C; 66.71; H; 3.81; N; 11.11; S; 10.16. Found: C; 66.62; H; 3.81; N; 10.91; S; 10.00. IR (cm$^{-1}$): 3030 (CH–Ar), 2920 (CH–aliph., 2201(C=O), 1654 (C=O), 1609 (C=O) 1H-NMR (DMSO-d$_6$– δ ppm) 3.08, 3.12 (s, 6H, 2CH$_3$), 6.70 (d, 1H, C$_4$–H, thiazine, J=8.4 Hz), 6.99 (s, 1H, C$_5$–H, pyridine), 7.19, 7.28 (m, 9H, phenyl rings), 7.49 (d, 2H, C$_2$–H), C$_7$–H, C$_6$–H, 4-Cl, phenyl, J=6.9 Hz), 7.83 (d, 2H, C$_3$–H, C$_8$–H 4–Cl phenyl, J= 6.9 Hz), 7.94, 7.98, 8.00 (3s, 3H, thiophene).

**Compound 28b**: m.p. 120-122°C; 70% yield. Anal. calcd. for C$_8$H$_7$(a$_2$O$_2$S)$_2$Br: C; 63.83; H; 3.64; N; 10.63 S; 4.86. Found: C; 63.32; H; 3.24; N; 10.00; S; 4.07. 1H-NMR (δ ppm) 21.47 (2 CH$_3$), 68.50 (–CH), 119 (C=N), 158 (C=O), 129.78-151.77 (CH–Ar.). IR (cm$^{-1}$): 3081 (CH–Ar.), 2923 (CH–aliph., 2200 (C=N), 1701 (C=O), 1603 (C=C) 1H-NMR (DMSO-d$_6$– δ ppm) 3.04, 3.09 (2s, 6H, 2CH$_3$), 6.84 (d, 1H, C$_5$–H, thiazine, J=9.1 Hz), 7.52 (s, 1H, C$_3$–H, pyridine), 7.55 (d, 2H, C$_2$–H, C$_6$–H, 4-Br-phenyl, J=7.7 Hz), 7.74(d,2H,C$_3$–H,C$_5$–H,4-Br-phenyl, J=7.7 Hz) 7.62-7.74 (m, 9H, two phenyl), 7.95, 7.97, 8.00 (3g, 3H, furan).

**RESULTS AND DISCUSSION**

Chemistry

Pyridine-2-thiones 1a,b are readily alkylated in presence of bases at the sulfur atom to give alky mercapto pyridine 3a,b, 4a,b and 5a,b, these reaction product formed via the loss of hydrogen halide and IR showed the bands for CN and product formed via the loss of hydrogen halide.

**Compound 28a** was cyclized in sodium methoxide to afford the corresponding thieno [2,3-b] pyridine derivatives 6a,b, 7a,b and 8a,b, respectively. The IR spectra, showed the absence of the CN group and instead the bands of the newly born NH$_2$ group were detected. Their 1H-NMR revealed no signals of –CH$_2$R protons while the NH$_2$ protons were detected. Based on both IR and 1H-NMR spectral data it could be concluded that both the –CH$_2$R protons and CN group were involved in cyclization step.

Compounds 3a,b were also characterized by conversion to 8-amino-2,4-diarylpyrido [2'3':2,3] thieno [4,5-d] pyrimidines 9a,b by heating with formamide.

In solutions under the influence of air oxygen pyridine-2-thiones 1a,b undergo further oxidation to the corresponding 2,2'-bis(3-cyano-4,6-diarylpyridyl) disulfides 10a,b. Disulfides were obtained by oxidation of thiones 1a,b with a 10% solution of iodine in ethanol. Molecular ions (M$^+$) of the corresponding dimers are recorded in the mass spectra of disulfides 10a,b, while signals of protons of the NH group are absent the 1H-NMR spectra. The corresponding 2-pyridone 2a,b is formed by further oxidation of disulfide 10a,b with chomonic anhydride.

Chlorination of cyanopyridone derivatives 2a,b with phosphorly chloride similar to earlier results gave only poor of impure chlorination products. The addition of triethylamine to phosphorly chloride reagent, however, accelerated the reaction speed and afforded 2-chloro-3-cyano-4, 6-diaryl pyridine 11a,b after 4 h in good yield.

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Compounds 11a,b with a vicinal chlorocyno groups was envisaged as a potential starting material for the synthesis of fused heterocycle systems. Thus treatment of 11a,b with guanidine hydrochloride in sodium ethoxide yielded 2,8-diamino-5,7-diarylpyrimido [4,5-b] pyridine. The reaction of 2a,b with sodium azide in DMF afforded 5,7-diaryl-8-cyano teterazolo [4,5-a] pyridine 14a,b in satisfactory yields. Like similar heterocyclic azides having the azido group attached to the cyclic carbon atom adjacent to an annular nitrogen, it may exist as a true tetrazolo [4,5-a] pyridine 14a,b, through

\[ \text{Scheme 3} \]

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intermediate 2-Azido-3-cyano pyridine derivative 14'a,b were formed at the first step in this reaction and the intra molecular cyclizations of 14'a,b, 14a,b occurred immediately. A study of Azido-tetrazolo isomerization is reported in the literature14. We were not able to find any vibration band of the Azido group of 2-azido-3-cyano pyridine derivatives in the IR spectrum of 14a,b. This observation showed that the tetrazole ring in 14a,b is relatively stable. Treatment of 11a,b with cyano pyridine-2-thione derivative yielded the Bis (4,6-diaryl-3-cyano pyridine-2-yl) sulfide 15a,b. Reaction of 2a,b with cyanothioacetamid in pyridine gave 4-amino-5,7-diaryl-3-cyano pyrido[2,3-b] pyridine-2 (H) thione 16a,b. The latter compound were used as a key intermediate to produce other heterocycle ring thus, reaction of 16a,b with α- halo compounds (e.g. ethylchloroacetate, chloroacetamide) in alcoholic solution of anhydrous sodium acetate yield the substituted thio intermediate 17a,b, 18a,b respectively, which upon treatment with sodium ethoxide produce the thieno [2,3-b] 1,8-naphthyridine derivatives (19, 20)a,b.

Compound 21a,b reacted with α-chloroacetyl acetone in DMF to afford the 2-S-alkylated derivatives 22a,b.

The structure 22a,b was established based on elemental analysis, IR and 1H-NMR spectral data. Compound 22a,b were cyclized in acetic anhydride containing the catalytic amount of pyridine (1 ml) to afford the corresponding 6-(2-furyl)-3-methyl-5H-thiazolo [3,2-a] pyrido[2,3-d] pyrimidine-5-one 23a,b. The IR spectra of each of 23a,b showed the absence of the (NH) group and 1H-NMR revealed no signals of – SCH– proton. A further elucidation of 23a,b structures were given from their reaction with thiophen-carboxaldehyde. The reaction product was formulated as 2-(3-(2-thiobenzo-2-propano)-8-(4-bromophenyl)-6-(2-furyl)-3-methyl-5-H-thiazolo[3,2-a] pyrido[2,3-d] pyrimidine-5-one (24b).

It remarkable to report here that compound 25b obtained by reaction with benzamide hydrochloride with compound 24b in pyridine. The IR and 1H NMR spectral data of 25b was found to be in a good agreement with the assigned structure (see experimental).

The synthetic potential of 21a was demonstrated via their reactions with chloroaacetic acid, 2-furaldehyde in acetic acid and in presence acetic anhydride to afford the corresponding thiadiazolo[3,2-a] pyrido[2,3-d] pyrimidinone derivative 26a. It remarkable to report here compound 26a obtained by another method (see experimental) was identical in all aspects (m.p., 1H NMR and elemental analysis).

Compound 26a was reacted with hydroxylamine hydrochloride in glacial acetic acid in presence of anhydrous sodium acetate to give tetracyclic product 27a. The IR, 1H-NMR and mass spectral data of 27a was found to be in a good agreement with the assigned structure (see experimental). In addition compounds 21a,b upon heating under reflux with 2-arylcinnamamide in ethanol to furnish the target thiazine [2,3-a] pyrido [2,3-d] pyrimidinone derivatives 28a,b. The IR spectra of these reaction products showed the bands corresponded to CN group. Moreover, their mass spectra gave m/z = 629 and 658 which corresponded to the exact molecular weight of the molecular formula C15H12N6O2SBr and C15H12N6O2SBr of the assigned structures.

CONCLUSION

New series of thieno [4,5-c] pyridine 6a,b,7a,b,8a,b,9a,b pyrido [2',3',2,3] thieno[4,5-d] pyrimidine 9a,b, 2,2'-bis-(3-cyano-4,6-diaryl) pyridyl disulfide 10a,b, pyrido[4,5-b] pyrimidine 12a,b, Triazolo [4,5-a] pyridine 13a,b, tetracolo [4,5-a] pyridine 14a,b, bis(4,6-diaryl-3-cyanopyridine-2-yl) sulfide 15a,b, pyrido [2,3-b] Pyridine 16a,b,17a,b,18a,b and thieno [2,3-b] 1,8-naphthyridine 19a,b,20a,b derivatives. Pyrido [2,3-d] pyrimidinone derivatives 21a,b were used as starting material for synthesis thiazolo [3,2-a] pyrido [2,3-d] Pyrimidine 23a,b,24a,25,b,26a,29a, thiazin [2,3-a] pyrido [2,3-d] pyrimidinone 28a,b and isoxazolo [5’,4’,5] thiazolo [3,2-a] pyrido [2,3-d] pyrimidinone derivatives 27a. The structures of the synthesized compounds were confirmed by IR, 1H- and 13C-NMR, elemental analysis and mass spectra data.

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Conflict of Interest

The authors declare that they do not have any conflict of interest.

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