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

Aisha .Y. Hassan[1]*, Hanan A. Al-Ghulikah[2]

[1]*Chemistry Department, Faculty of Science, Girl's Branch, Al-Azhar University, Nasr City, Cairo, Egypt*
[2]*Chemistry Department, College of Science, Princess Nora Bint Abdul-Rahman University, Riyadh, Saudi Arabia*

***Corresponding author:** Aisha .Y. Hassan, Chemistry Department, Faculty of Science, Girl's Branch, Al-Azhar University, Nasr City, Cairo, Egypt. Tel.: +201007587847*
E-mail address: helali_aisha@yahoo.com

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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,^{1}H and^{13}C 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] pyrimidine*.

INTRODUCTION

During the last two decades, a large number of substituted pyridines have been reported to have several biological activities[1]. 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 antimicrobial[2-14].

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.^{13}C- and^{1}H-NMR run on JEOL-400 MHZ in DMSO-d_6.

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

3-Cyano-4,6-(di-2-thienyl)-pyridine-2(1H)-thione1a ; 3-cyano-4,6-(di-2-furyl)-pyridine-2-(1H)-thione1,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 $C_{14}H_8N_2S_3$: 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),

2206(C≡N), 1623 (C=N), 1566 (C=S); ^{1}H-NMR (DMSO-d_6, δppm): 6.68 (s, 1H, C_3–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.

Anal. calcd. for $C_{14}H_8N_2O_2S$: C, 62.68; H, 2.98; N, 10.44, S, 11.94. Found: C, 62.28; H, 2.90; N, 10.20, S, 11.02. IR cm^{-1}: 3310 (NH), 3050(CH–Ar), 2211(C≡N), 1610 (C=N), 1550 (C=S); ^{1}H-NMR (DMSO-d_6, δppm): 7.12 (s, 1H, C_3–H pyridine), 7.25-7.40 (m, 6H, two thiophene ring).

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 genuise 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[15]

Compound 2b:m.p. 310-312°C; 83% yield. Anal calcd. for $C_{14}H_8N_2O_3$: 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), ^{1}H-NMR (DMSO-d_6, δppm): 6.85 (d, 1H, furan, J=3.7 Hz 7.10(s, H, C_3–H–pyridinone) 7.67, 8.12 (2d, 2H, furan, J= 4.4 Hz) 12.68 (S, 1H, NH, exchangeable with D_2O).

Method B

A solution of (3.0 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 dilute 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 genuise 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 $1_{a,b}$in (30 ml) of DMF, after which a solution of (10 mmol) of chloroacetonitrile 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 $C_{16}H_9N_3S_3$: 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).^{1}H-NMR (DMSO-d_6, δppm): 4.97 (s, 2H, CH_2), 7.30-7.90 (m, 6H, two thiophene), 7.95 (s, 1H, C_3–H–pyridine). ^{13}C-NMR (δppm): 54.01 (–CH_2) 124.12, 126.40 127.069-151.15 (CH–Ar)

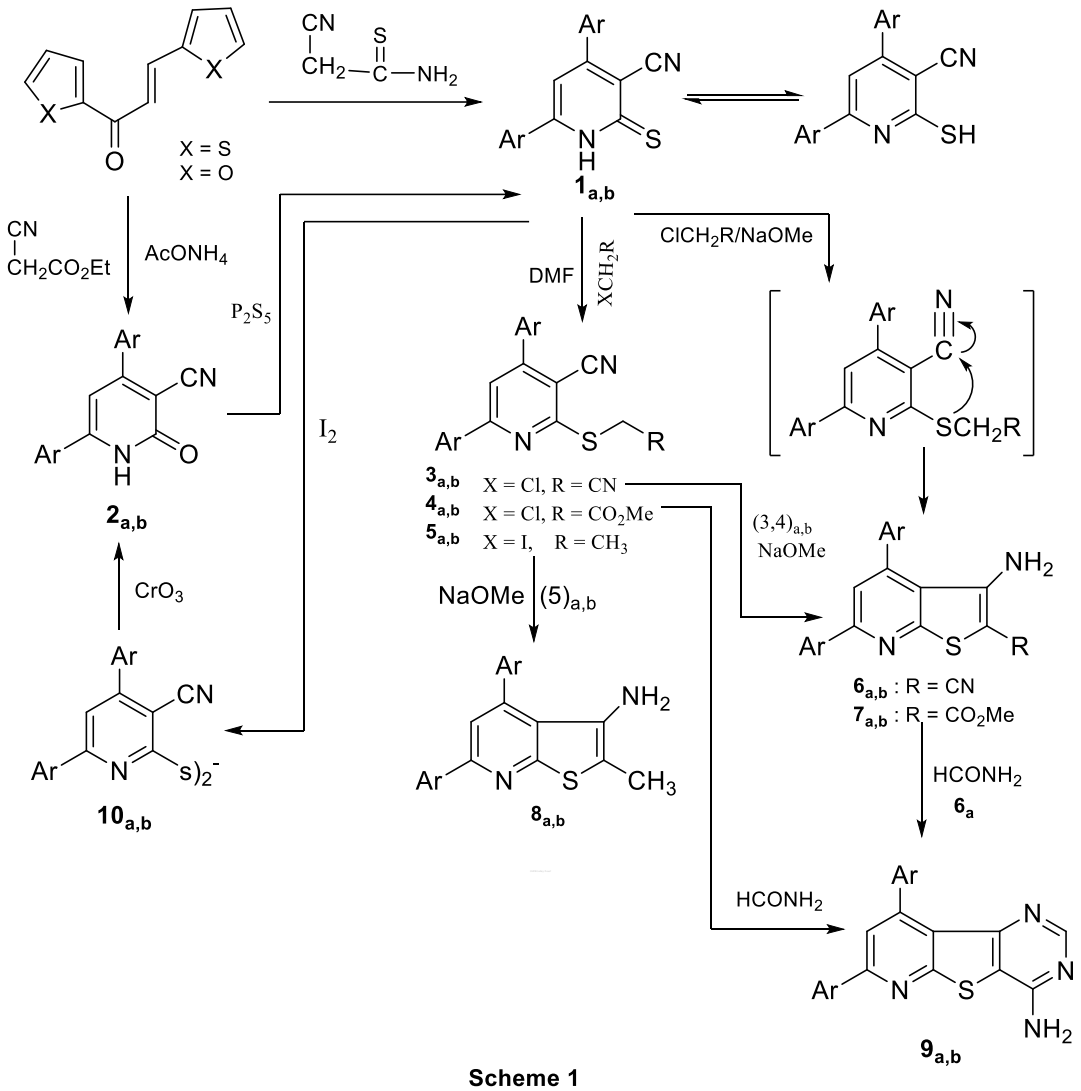
Compound 3b: m.p. 220-222 °C; 80% yield. Anal. calcd. for $C_{16}H_9N_3O_2S$: C, 62.54; H, 2.93; N, 13.68, S, 10.42. Found: C, 62.11; H, 2.73; N, 13.00, S, 9.98. IR (cm^{-1}): 3055 (CH–Ar), 2900(CH–aliph), 2210(2C≡N) 1605 (C=N), ^{1}H-NMR (DMSO-d_6, δppm): 4.29 (s, 2H, CH_2), 7.22 (s, 1H, C_3–pyridine), 7.50-8.00 (m, 6H, two furan).

Compound 4a: m.p. 120-122 °C; 70% yield . Anal. calcd. for $C_{17}H_{12}N_2O_2S_3$: 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). ^{1}H-NMR (DMSO-d_6, δppm): 32.3,9 (s, 3H, CH_3), 4.22 (s, 2H, CH_2), 7.33-7.99 (m, 6H, two thiophene), 8.15 (s, 1H, C–H, pyridine); ^{13}C-NMR (δ ppm) (CH_3), 53.04 (–CH_2); 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 $C_{17}H_{12}N_2O_4S$: 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). ^{1}H-NMR (DMSO-d_6, δppm): 1.87 (s, 3H, CH_3), 2.50 (s, 2H, CH_2), 6.99-8.09 (m, 6H, two furan), 8.18 (s, 1H, C_3–H, pyridine).

Compound 5a: m.p. 92-94°C; 70% yield; Anal. Cacld for $C_{16}H_{12}N_2O_2S$: 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). ^{1}H-NMR (DMSO-d_6, δppm): 1.41 (t, 3H, CH_3, *J=7*.4Hz) 4.03(q, 2H, CH_2, *J=8.0* Hz), 7.20-7.90 (m, 7H, 6H-two thiophene and C_3-H, pyridine)

Compound 5b: m.p. 105-107°C; 6% yield; Anal. calcd. For $C_{16}H_{12}N_2O_2S$: 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.



Scheme 1

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 for1h. 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 $C_{16}H_9N_3S_3$: 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 (NH_2), 3088 (CH–Ar), 2190 (C≡N) 1624 (C=N), 1600(C=C). ^{1}H-NMR (DMSO-d_6, δppm): 5.92 (s, 2H, NH_2), 7.45-8.10(m, 7H, two thiophene and C_3–H–pyridine); m/z = 339 (100%).

Compound 6b: Crystallized from ethanol DMF mixture (2:1); m.p.>360°C; 50% yield; Anal. calcd. for $C_{16}H_9N_3O_2S$: 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 $C_{17}H_{12}N_2O_2S_3$: 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 (NH_2), 3062 (CH–Ar), 2930 (CH=aliph.) 1680 (C=O), 1630 (C=C), 1616 (C=C). ^{1}H-NMR (DMSO-d_6, δppm): 3.78(s, 3H, CH_3), 4.09(s, 2H, NH_2), 6.71-7.92 (m, 6H, two thiophene), 8.00 (s, 1H, C_3–H–pyridine) ^{13}C (δppm): 28.09 (CH_3), 163.68 (C=O), 119.93–152.69 (CH–Ar).

Compound 7b: Crystallized from DMF; m.p.>360°C; 80% yield. Anal. calcd. for $C_{17}H_{12}N_2O_4S$: 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 (NH_2), 3100 (CH–Ar), 29347 (CH=aliph.) 1667 (C=O), 1625 (C=N), 1600(C=C). ^{1}H-NMR (DMSO-d_6, δppm): 3.81 (s, 3H, CH_3), 4.16 (s, 2H, NH_2), 6.84 (s, 1H C_3–H–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 $C_{16}H_{12}N_2S$: C, 58.53; H, 3.65; N, 8.53; S, 29.26. IR (cm^{-1}): 3400, 3280 (NH_2), 3039 (CH–Ar), 2912 (CH–aliph.), 1603 (C=N), 1595 (C=C), ^{1}H-NMR (DMSO-d_6, δppm): 2.08 (s, 3H, CH_3), 4.07 (s, 2H, NH_2), 6.77(s, 1H, C_3–H, pyridine), 7.37-8.08 (m, 6H, two thiophene); m/z = 328 (1.02%).

Compound 8b: Crystallized from dioxane m.p. 190-192°C; 85% yield. Anal. calcd. for $C_{16}H_{12}N_2O_2S$: 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 (NH_2), 3039 (CH–Ar), 2912 (CH=aliph.) 1603 (C=N), 1595 (C=C), ^{1}H-NMR (DMSO-d_6, δppm): 1.69 (s, 3H, CH_3), 4.43 (s, 2H, NH_2), 7.40 (s, 1H, C_3–H, pyridine), 7.44-7.63 (m, 6H, two furan).

8- Amino-2,4-diarylpyrido[2',3' & 2,3] thieno [4,5-*d*] pyrimidine 9a,b.

Compound 3a,bin (5 ml) of formamide was heated for 1 h in a flask equipped with an air condenser. The precipitate was removed by filtration and recrystallized from DMF compound **9a**: m.p> 360°C; 75% yield. Anal. Calcd. For $C_{17}H_{10}N_4S_3$: 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 (NH_2), 3090 (CH–Ar), 2920 (CH–aliph.), 1610 (C=N), 1594 (C=C), ^{1}H-NMR (DMSO-d_6, δppm): 4.41 (s, 2H, NH_2, 6.54 (s, 1H, C_3–H, pyridine), 7.26-8.03 (m, 6H, two thiophene); 8.45 (s, 1H, C2–H–pyrimidine).

Compound 9b: Crystallized from DMF and methanol mixture (2:1);m.p.>360°C; 65% yield. Anal calcd. for $C_{17}H_{10}N_4O_2S$: 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 (NH_2), 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**in (15 ml) of 1N NaOH solution, and the resulting precipitate was washed with ethanol and crystallized from proper solvent.

Compound 10a: Crystallized from ethanol. m.p. 160-162°C; 80% yield. Anal. calcd. for $C_{28}H_{14}N_4S_6$: C, 56.00; H, 2.34; N, 9.36; S, 32.80 IR (cm^{-1}): 3090(CH–Ar), 2222 (C≡N), 1639 (C=N). ^{1}HNMR DMSO-d_6, δppm): 7.20-7.82 (m, 12H, –fourthiophene), 8.09, 8.58 (2s, 2H, C_3–H, two pyridine), ^{13}C, (δppm): 126.56, 126.13 (2C≡N), 128.59-152.87 (CH–Ar).

Compound 10b: Crystallized dioxane; m.p.> 360°C; 90% yield. Anal. calcd. for $C_{28}H_{14}N_4O_4S_2$: C, 62.92; H, 2.62; N, 10.48; S, 11.98. Found: C, 62.22; H, 2.61; N, 9.98; S, 11.00. IR (cm^{-1}): 3042 (CH–Ar), 2210 (C≡N), 1620 (C=N). ^{1}HNMR (DMSO-d_6, δppm): 7.00-7.86 (m, 12H, four furan) 7.65-8.08 (2s, 2H, C_3–H, two pyridine).

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

Solution of the cyanopyridone derivatives **2$_{a,b}$**(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 stirring 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 $C_{14}H_7ClN_2S_2$: 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 (CHAr.); 2214 (C≡N).^{1}H-NMR: δ 7.28 (s, 1H, C_3 - H, 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 $C_{14}H_7ClN_2O_2$: 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). ^{1}H-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, C_3 -H, 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 $C_{15}H_{11}N_5S_2$: 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 ($2NH_2$), 3080 (CH Ar.); 1633 (C=N) ^{1}H-NMR: δ 4.34, 5.60 (2s, 4H, $2NH_2$), 6.61 (s, 1H, C_3- H-Pyridine); 8.61-7.42 (m, 6H, thiophene ring).

Compound 12b crystallized from DMF; m.p. 340-342°C; 65% yield Anal: calcd. for $C_{l5}H_{11}N_5O_2$: 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 ($2NH_2$), 3035 (CH-Ar.), 1620 (C=N) ^{1}H-NMR: δ 5.02, 5.08 (2s, 4H, $2NH_2$); 6.81 (s, 1H, C_3-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 $C_{15}H_8N_4OS_2$: 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 (CHAr); 2217(C≡N), 1727 (C=O); 1630(C=N).^{1}H-NMR:δ 6.57 (s,1H,C_3-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 exchangeable with D_2O)

Compound 13b;m.p. 248-250C; 90% yield. Anal, calcd. for $C_{15}H_8N_4O_3$: 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 (CHAr); 2217 (C≡N), 1710 (C≡O); 1640 (C=N).^{1}H-NMR: δ 6.32 (s, 1H, C_3-H pyridine), 7.95-6.82 (m, 6H, two furan ring); 10.12 (br. S, 1H, NH ex changeable with D_2O).

5,7-diaryl-8-cyano teterazolo [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 HC1. 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 $C_{14}H_7N_5S_2$: 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). ^{1}H-NMR: 6.62 (s, 1H, C_3-H pyridine ring), 8.01-6.95 (m, 6H, two thiophene rings)

Compound **14b**: m.p.>360°C; 40% yield. Anal. calcd. for $C_{14}H_7N_5O_2$: C, 60.64; H, 2.52; N, 25.27. Found: C,60.51; H,2.20; N, 25.00. IR (cm^{-1}): 3125 (CHAr.) ; 2195 (C≡N); 1600 (C=N). ^{1}H-NMR : δ 6.18 (s, 1H, C_3- 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-diaryl-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.240°C; 90% yield. Anal. calcd. for $C_{28}H_{14}N_4S_5$: 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). ^{1}H-NMR: δ 6.68 (s, 1H, C_3-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 $C_{28}H_{14}N_4O_4S$: 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). ^{1}H-NMR: δ 6.80 (s, IH, C_3-H, pyridine ring), 7.80-6.90 (m, 12H, four furan rings).

4-Amino 5,7-diaryl-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 HC1 (10%) the solid obtained was filtered and collected.

Compound16a crystallized from toluene, m.p.> 360°C; 98% yield. Anal. Calcd. For $C_{17}H_{10}N_4S_3$: 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 (NH_2); 3142 (NH); 3095 (CH-Ar.); 2213 (C≡N). ^{1}H-NMR: δ 5.20 (s, 2H, NH_2), 7.23 (s, IH, C_3-H pyridine); 7.32-7.24 (m, 4H, two thiophene ring); 7.95-7.85 (2d, 2H, two thiophene ring, *J= 4.6* Hz); 8.01 (s, IH, NH).

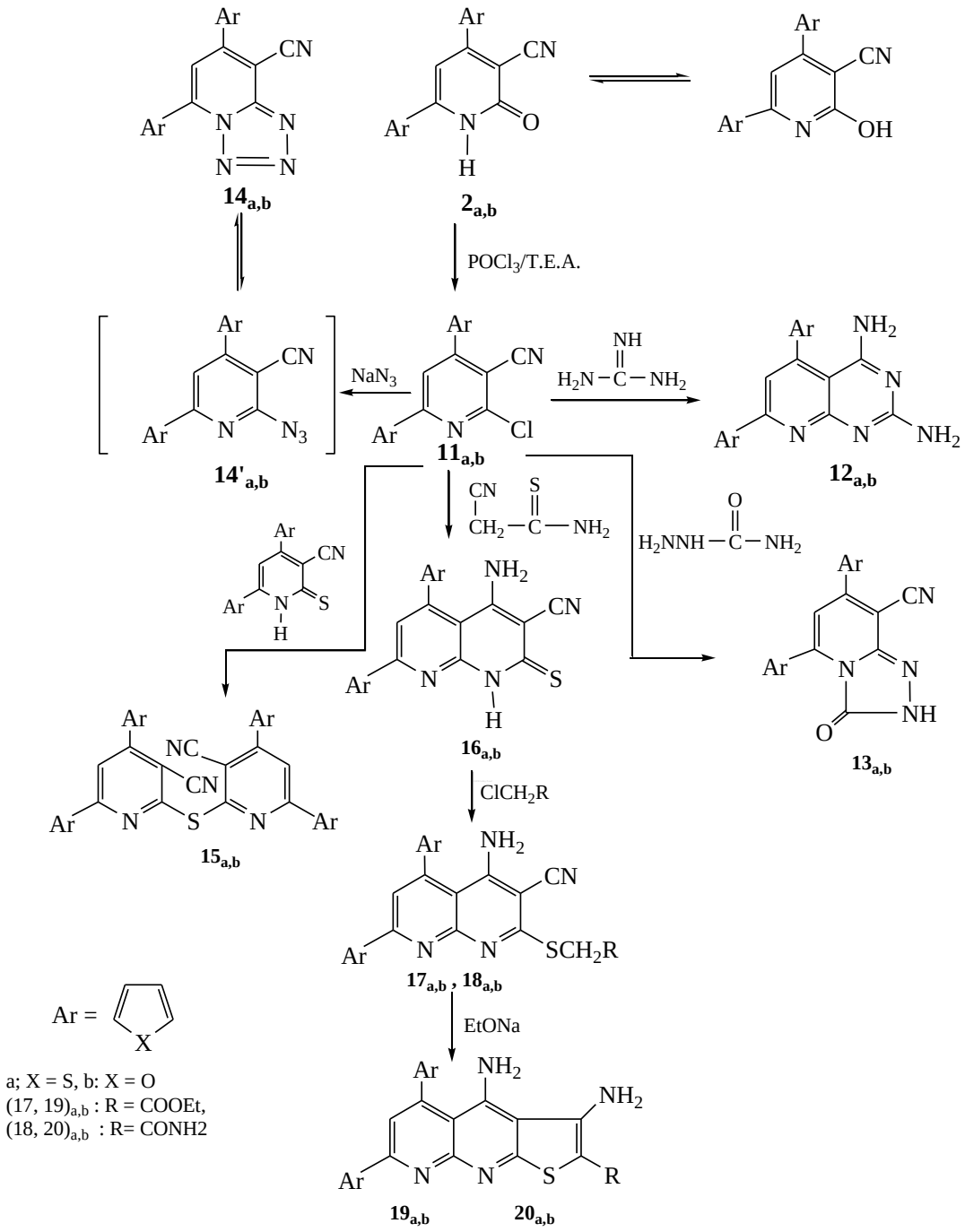
Compound16b crystallized from dioxane and ethanol; m.p.> 360; 50% yield. Anal. calcd. for $C_{17}H_{10}N_4O_2S$: C, 61.07; H, 2.99; N, 16.76 ; S , 9.58. Found: C, 61.50; H, 2.80; N, 16.1 1; S, 9.99. IR (cm^{-1}): 3420, 3370 (NH_2); 3280 (NH), 3090 (CH Ar.) 2209 (C≡N). ^{1}H-NMR: δ 4.80 (s, 2H, NH_2); 6.68 (s, IH, C_3-H, pyridine), 6.90-7.88 (m, 6H, two furan rings); 9.00 (S,IH, NH).

4-Amino-5,7-diaryI-3-cyano-2-(carbonylethoxymethylthio pyrido) [2,3-*b*] pyridine 17a,b.

4-Ammo -5,7-diaryl-3-cyano-2-(acetamidthio) pyrido [2, 3-*b*] pyridine 18a,b.

A mixture of **16a,b**(0.1 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 $C_{21}H_{16}N_4O_2S_3$: 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 (NH_2), 3100 (CH Ar.),



Scheme 2

2980 -2920 (CH-aliph.), 2218 (C≡N), 1732 (C=O ester), 1596 (C=N). ^{1}H-NMR: δ 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 $C_{21}H_{16}N_4O_4$ S: 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-Ar), 2950 - 2920 (CH-aliph.), 2209 (C≡N), 1700 (C=O ester); 1629 (C=N). ^{1}H-NMR: δ 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); 6.85 (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 $C_{19}H_{13}N_5OS_3$: C, 53.90, H, 3.07; N,

16.54 ; S, 22.69. Found: C, 53.70; H, 3.00; N, 16.12; S, 21.90. IR (cm^{-1}): 3484; 3265 ($2NH_2$); 3097 (CH-Ar.); 2924 (CH-aliph.); 2204 (C≡N), 1640 (O = C-NH_2), 1600 (C=N) ^{1}H-NMR: δ 2.49 (s, 2H, CH_2); 5.60 (s, 2H, NH_2), 6.00 (br.s, 2H,NH_2), 7.99-7.26 (m, 7H, two thiophene ring and C3- H, pyridine). ^{13}C-NMR: δ 58.04 (CH_2); 123.93 (C≡N); 170.27 (C=O), 116.15-150.65 (CH–Ar.)

Compound18b; m.p. 240-242°C; 60% yield. Anal. calcd. for $C_{19}H_{13}N_5O_3S$: C, 58.31; H, 3.32; N, 17.90; S, 8.18. Found: C, 58.00; H, 3.30; N, 17.11; S, 8.00. IR (cm^{-1}): 3420, 3289, 3223, 3149 ($2NH_2$), 3036 (CH-Ar.); 2915 (CH-aliph.), 2200 (C≡N); 1685 (O=C-NH_2); 1603 (C=N). ^{1}H-NMR: δ 3.76 (s, 2H, CH_2); 4.38 (s, 2H, NH2), 4.90 (s, 2H, O=C-NH_2), 7.00 (s, 1H, C_3-H-pyridine ring) 7.98-7.21 (m, 6H, two furan rings).

3,4-diamino- 5,7- diary-2-(carbonyl ethoxythieno [2,3 - *b*] - (1,8) - naphthyridine 19a,b, 3, 4-diamino-5,7-diaryl-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 $C_{21}H_{16}N_4O_2S_3$: C, 55.75; H, 3.53; N, 12.38;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-Ar.); 2900 (CH-aliph.); 1717 (C=O ester); 1594 (C=C). ^{1}H-NMR: δ 1.29 (t, 3H, CH_2 CH_3, J= 7.1 Hz); 3.79 (s, 2H, NH_2); 4.27 (q, 2H, CH_2 CH_3, *J=7.1* Hz) 6.10(s,2H, NH_2); 7.32-7.20 (2t , 2H, two thiophene rings, *J=5.3* Hz) 7.45 (d, 1H, thiophene ring J= 3.6 Hz); 7.93-7.77 (2d, 2H, thiophene rings, *J=5.1* Hz), 7.87 (s, IH, C_3-H pyridine ring); 8.06 (d, 2H, thiophene ring, *J=3.8* Hz). ^{13}C-NMR: δ14.25 (CH_3); 60.78 (CH_2); 166.43 (C=O); 121.91; 123.80; 128.31; 129.32 ; 130.00 (121.91-160.15) (CH–Ar).

Compound19b :m.p. 285-287°C; 50% yield. Anal. calcd. for. $C_{21}H_{16}N_4O_4S$: C, 60.00; H, 3.80; N, 13.33; S,7.61. Found: C, 60.20; H, 3.25; N, 13.11, S, 7.90. IR(cm^{-1}): 3415, 3300, 3200 ($2NH_2$), 3050 (CH-Ar.); 2899 (CH-aliph.); 1715 (C=O ester); 1625 (C=C). ^{1}H- NMR: δ 1.40 (t, 3H, CH_2 CH_3 , J = 7.2 Hz), 4.53 (q, 2H, CH_2 CH_3, *J=7.0* Hz), 6.94, 7.08 (2s, 4H, NH_2). 7.35 8.12 (m, 6H, two furan); 7.72 (s, IH, C_3-H pyridine).

Compound 20a: m.p. 320-322°C; 55, yield. Anal. calcd. for: $C_{19}H_{13}N_5OS_3$: C, 53.90; H, 3.07, N, 16.54; S, 22.69. Found: C, 53.40, H, 3.00; N, 16.00, S, 22.80. IR (cm^{-1}): 3400, 3315, 3230 ($3NH_2$), 3050 (CH–Ar.); 1700 (O=C-NH_2); 1637(C=C). ^{1}H-NMR: δ 4.22, 5.82, 6.40 (3s,6H, $3NH_2$); 8.62-7.90 (m, 7H, two thiophene ring and pyridine H)

Compound20b: m.p. 322-324°C; 60% yield Anal. calcd. for, $C_{19}H_{13}N_5O_3S$; C, 58.31; H, 3.32; N, 17.90; S, 8.18. Found: C, 58.00; H, 3.00; N, 16.99; S, 8.00. IR (cm^{-1}): 3455, 3353, 3240 ($3NH_2$); 3025 (CH-Ar); 1695 (O=C-NH_2); 1600 (C=C). ^{1}H-NMR: δ 3.44 (s, 2H, NH_2), 3.85 (s, 2H, NH_2); 6.07 (br. s, 2H,-O=C–NH_2), 6.93, 7.10, 7.27 (3s, 3H, furan ring); 7.95 (s, IH, C_3-H, Pyridine); 8.25, 8.66, 9.00 (3s; 3H; furan ring).

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 α,β-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. And calcd. For $C_{17}H_{10}N_3OS_2Cl$; 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–Ar); 1700 (C=O), 1633 (C=N). ^{1}H-NMR (DMSO-d_6– δppm) 7.22 (t, 1H, thiophene, *J=8.6* Hz), 7.43 (d, 2H, C_2–H,C_6-H,, 4-Cl phenyl, *J=4.1* Hz), 7.63 (s, 1H, C_3–H, pyridine), 7.75-8.08 (2d, 2H, thiophene, *J=4.5* Hz), 8.84 (d, 2H, C_3–H, C_5–H, 4–Cl phenyl, *J=4.8* Hz), 8.35, 8.36 (2s, 2H, 2NH).

Compound 21b: Crystallized from dioxane; m.p. 300-302°C; 85% yield. Anal. Calcd for $C_{17}H_{10}N_3O_2SBr$: 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–Ar); 1693 (C=O), 1630 (C=N). ^{1}H-NMR (DMSO-d_6–δppm) 6.37 (br, s,1H, C_3–H–pyridine), 6.96, 7.56 (2d, 2H, furan, *J=4.2* Hz), 7.73 (t, 1H, furan, *J=5.1* Hz), 7.77, 8.17 (2d, 4H, 4-Br-phenyl, J= 8.5 Hz) 12.51, 13.08 (2s, 2H, 2NH)

2- (Acetylacetonethio)-5-(4-chlorophenyl)-7-(2-thienyl)-3H, 4H-pyrido[2,3,-*d*] pyrimidine-4-one 22a. 2- (Acetylacetonethio)-7-(4-bromophenyl)-5-(2-furyl)-3H, 4H-pyrido[2,3,-*d*] pyrimidine-4-one 22b.

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 crystallozed from proper solvent.

Compound 22a: Crystallized from dioxane; m.p. 310-312 °C; 75 % yield; Anal. calcd. for $C_{22}H_{16}N_3O_2SCl$: 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–Ar); 2900 (CH-aliphatic), 1707 (C=O), 1620 (C=N). ^{1}H-NMR (DMSO-d_6– δ ppm) 1.86, 1.90 (2s,6H, $2CH_3$), 3.68 (s, 1H, SCH),

7.20 (d, 2H, C_2–H, C_5–H,4-Cl–phyenyl, *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); ^{13}C-NMR (δ ppm): 20.67; 20.01 ($2CH_3$), 105.86 (–SCH), 175.86 (C=O), 190.00 , 196.00 (2C=O), (136.00 - 155.04) (CH–Ar).

Compound 22b : Crystallized from ethanol; m.p. 190-192°C; 70% yield; Anal. calcd for $C_{22}H_{16}N_3O_4SBr$: 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–Ar); 2850 (CH-aliph.), 1700 (C=O), 1666 (C=O), 1640 (C=N). ^{1}H-NMR (DMSO-d_6– δppm) 1.80, 1.95 (2s, 6H, $2CH_3$), 4.40 (s, 1H, SCH), 7.30 (d, 2H, C_2–H, C_6–H,4-Br–phenyl, *J=7.5* Hz), 7.48 (2d, 2H, C_3–H,C_4-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-thienyl)-5-H-thiazolo[3,2-*a*]pyrido[2,3-*d*] pyrimidine-5-one 23a, 2-acetyl-8-(bromophenyl)-6-(2-furyl)-3-methyl-5H-thiazolo[3,2-*a*] pyrido[2,3-*d*] pyrimidin-5-one 23b

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 crystallized from ethanol.

Compound 23a:m.p.>360 °C; 50% yield; Anal. Calcd for $C_{22}H_{14}N_3O_2S_2Cl$: 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). ^{1}H-NMR (DMSO-d_6– δppm) 2.43 (s, 3H, CH_3), 2.66 (s, 3H, $COCH_3$), 7.19 (d, 2H, C_2–H, C_6–H,4-Cl–phenyl, *J=8.0* Hz), 7.38 (s, 1H, C_3–H, pyridine), 7.42, (t, 1H, thiophene, *J=5.5* Hz), 7.77, 7.99 (2d, 2H, thiophene, *J=4.2* Hz); ^{13}C-NMR (δppm): 21.31 (CH_3) 28.07 (CH_3), 161.78 (C=O, 128.09-155.08 (CH–Ar.).

Compound 23b:m.p.>360 °C; 55% yield; Anal. Calcd for $C_{22}H_{14}N_3O_3SBr$: 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-thienyl)-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. calcd for $C_{27}H_{16}N_3O_3S_2Br$: 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). ^{1}H-NMR (DMSO-d_6– δ ppm) 2.30 (s, 3H, CH_3), 6.11 (s, 1H, C_3–H, pyridine). 6.96 (d, 1H, $CH=CH_2$ *J=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, C_2–H, C_6–H, 4-Br, phenyl *J= 8.0* Hz), 7.55 (d, 2H, C_3–H, C_5–H, 4–Br, phenyl, *J= 8.0* Hz), 7.34-7.37 (m, 6H, thiohephene and furan).

2-(4-(2-thienyl)-4,5-dihydro-2-phenyl-pyrimidine-6-yl)-8- (4-bromo-phenyl)-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°Cl 40% yield. Anal. calcd for $C_{34}H_{22}N_5O_2S_2Br$: 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). ^{1}H-NMR (DMSO-d_6– δppm) 2.50 (s, 3H, CH_3); 7.63 (d, 1H, C_3–H, pyrimidine; 7.7 Hz), 7.73 (d, 2H, C_4–H pyrimidine, *J=7.7* Hz) 8.40-8.99 (m, 11H, Ar–H), 9.33 (s, 1H, NH).

6-(4-chlorophenyl)-2-furylmethylene-8-(2-thienyl)-2,3,4,5-tetrahydro-thiazolo[3,2-*a*]pyrido[2,3-*d*] pyrimidinine-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 (1.64g) 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-thienyl)-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. calcd for $C_{24}H_{12}N_3O_3S_2Cl$: 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) ^{1}H-NMR (DMSO-d_6– δppm) 6.33 (s, 1H, C_3–H–pyridine), 6.82 (s, 1H, HC=C), 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, C3–H, C5–H, 4-Cl phenyl, *J=4.9* Hz); ^{13}C-NMR (δppm): 118.03 (=CH), 159.12, 175.94 (2 C=O, 118.03-155 (CH–Ar.).

Compound 29a:Crystallized from ethanol; m.p. 270-272°C; 50% yield. Anal. calcd. for $C_{19}H_{10}N_3O_2S_2Cl$: 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) ^{1}H-NMR (DMSO-d_6– δppm) 2.87 (s, 2H, CH_2), 7.14-7.61 (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_3–H, C_5–H, 4-Cl phenyl, *J=4.8* Hz).

9-(4-Chlorophenyl)-3-(2-furyl)-2,3-dihydro-7-(2-thienyl)-isoxazolo [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 $C_{24}H_{13}N_4O_3S_2Cl$: 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). ^{1}H-NMR (DMSO-d_6– δppm) 6.85 (s, 1H, C_3–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 [2,3-*a*] pyrido[2,3-*d*] pyrimidine-6-one 28a

9-(4-bromophenyl)-7-(2-furyl)-4-(4-dimethylaminophenyl)-2-phenyl-11H-thiazine [2,3-*a*] pyrido[2,3-*d*]pyrimidine-6-one28b

A mixture of compound **21a,b**(0.01 mol) and 2-aroylcinna-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 $C_{35}H_{24}N_5OS_2Cl$: 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≡N), 1654 (C=O), 1609 (C=C) ^{1}H-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_3–H, pyridine), 7.19, 7.28 (m, 9H, phenyl rings), 7.49 (d, 2H, C_2–H) , C_2–H, C_6–H, 4-Cl, phenyl, *J=6.9* Hz), 7.83 (d, 2H, C_3–H, C_5–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 $C_{35}H_{24}N_5O_2S_2Br$: 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. ^{13}C-NMR (δ ppm) 40.17 (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) ^{1}H-NMR (DMSO-d_6– δ ppm) 3.04, 3.09 (2s, 6H, 2CH_3), 6.84 (d, 1H, C_4–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,C3-H,C5-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

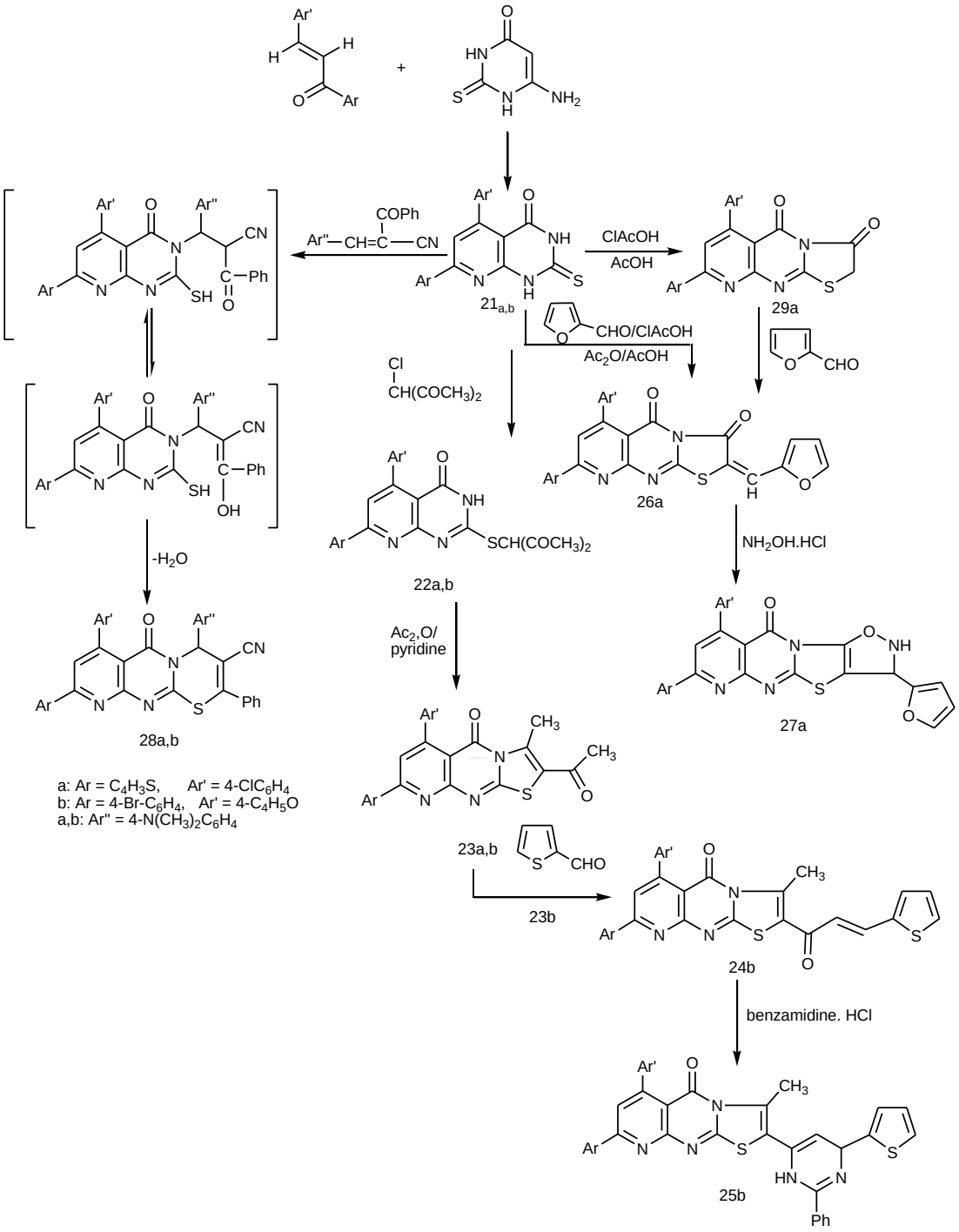
Chemistry

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 ^{1}H-NMR spectra revealed the signals corresponded to –CH_2R. Compound **3a,b, 4a,b and 5a,b** were 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 ^{1}H-NMR revealed no signals of –CH_2R protons while the NH_2.protons were detected. Based on both IR and ^{1}H-NMR spectral data it could be concluded that both the –CH_2R 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 ^{1}H-NMR spectra. The corresponding 2-pyridone **2a,b** is formed by further oxidation of disulfide **10a,b** with chromic anhydride.

Chlorination of cyanopyridone derivatives **2a,b** with phosphoryl chloride similar to earlier results gave only poor of impure chlorination products. The addition of triethylamine to phosphoryl 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.



Scheme 3

Compounds **11a,b**with a vicinal chlorocyano groups was envisaged as a potential starting material for the synthesis of fused heterocycle systemes. Thus treatment of **11a,b** with guanidine hydrochloride in sodium ethoxide yielded 2,8-diamino-5,7- diaryl-pyrimido [4, 5-*b*] pyridine **12a,b.** 8-Cyano -1, 2, 4-triazolo [4,5-*a*] pyridine derivatives **13a,b**was obtained by treatment of **2a,b** with semicarbazide hydrochloride. 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

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**to**14a,b**occurred immediately. A study of Azido-teterazolo isomerization is reported in the literature[14]. 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 (lH) 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 ^{1}H-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 ^{1}H-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-thienyl)-2-propenoyl)-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 benzamidine hydrochloride with compound **24b** in pyridine. The IR and^{1}H 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 chloroacetic acid,2- furaldehyde in acetic acid and in presence acetic anhydride to afford the corresponding thiazolo[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.,^{1}HNMR and elemental analysis).

Compound **26a** was reacted with hydroxylamine hydrochloride in glacial acetic acid in presence of anhydrous sodium acetate to give tetracylic product **27a.** The IR, ^{1}H-NMRand 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-aroylcinnamonitriles 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 $C_{35}H_{24}N_5OS_2Cl$ and $C_{35}H_{24}N_5O_2SBr$ of the assigned structures.

CONCLUSION

New series of 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**. 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, ^{1}H- and ^{13}C-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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