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Synthesis of some new of thieno[2,3-*b*]pyridines, pyrazolo[1,5-*a*]pyrimidine, [1,2,4]triazolo[1,5-*a*]pyrimidine, pyrazolo[5,1-*c*]triazine and pyrimido[1,2-*a*]benzimidazole derivatives containing pyridine moiety

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ABSTRACT

Pyrazolo[1,5-*a*]pyrimidine, [1,2,4]triazolo[1,5-*a*]pyrimidine and pyrimido[1,2-*a*] benzimidazole derivatives were synthesized by reaction of sodium salt of 3-hydroxy-(1-pyridin-2-yl)prop-2-en-1-one or sodium salt of 3-hydroxy-1-(pyridin-3-yl)prop-2-en-1-one with different heterocyclic amines in piperidenium acetate. Also, 3-amino-6-(2-pyridyl)thieno[2,3-*b*]pyridine derivatives were synthesized via reaction of pyridine-2-thione with various halogenated compounds. The structures of the newly synthesized compounds were confirmed by elemental analysis, spectral data, X-ray and alternative synthetic routes whenever possible.

1. Introduction

Pyridine derivatives are widely applied in medicine and agriculture, for example, used as anticancer [1], anti-hypertension [2] and antifungal [3], pesticides [4], herbicides [4], plant growth reagents [4] etc. Several thieno[2,3-*b*]pyridine derivatives are known to possess antibacterial [5], antihypertensive [6] and gonadotropinreleasing hormone antagonizing [7,8] activity. Pyridothienopyrimidine derivatives have found applications as analgesics, antipyretics [9] and anti-inflammatories [10]. Moreover, some pyridothienotriazines are known to exhibit antianaphylactic [11] and antiallergic activity [12]. In view of these facts and as a continuation of our previous work [13,14-19], we report herein the synthesis of new compounds bearing both pyridine, thienopyrimidine, pyrazolo[1,5-*a*]pyrimidine, [1,2,4]triazolo[1,5-*a*]pyrimidine and pyrimido[1,2-*a*]benzimidazole with the objective of obtaining new biologically active compounds.

2. Experimental

2.1. Instrumentation

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian Gemini 300 MHz spectrometer and chemical shifts are expressed as δ ppm using TMS as an internal reference. Mass spectra were recorded on a GC-MS QP 1000 EX Shimadzu. Elemental analyses were carried out at the Microanalytical Center of Cairo University. X-ray single crystals analysis was obtained from the National Research Centre-Dokki, Cairo, Egypt.

2.2. Synthesis of sodium salt of 3-hydroxy-1-(pyridin-2-yl)prop-2-en-1-one (2) and *sodium salt of 3-hydroxy-1-(pyridin-3-yl)prop-2-en-1-one* (15)

In a three-necked flask (250 mL) sodium methoxide (0.054 g, 10 mmol) and ether (20 mL) were poured over through separating funnel the appropriate of 2-acetylpyridine (**1**) or 3-acetylpyridine (1.2 g, 10 mmol) with ethyl formate (0.74 g, 10 mmol) with efficient stirring. The solid product was collected and used directly in the reactions.

2.3. Synthesis of 2-(2-(3-cyano-6-(pyridin-2-yl)pyridin-2-yl)disulfanyl)-6-(pyridin-2-yl)pyridine-3-carbonitrile (3), *1,2-dihydro-2-oxo-6-(pyridin-3-yl)pyridine-3-carbonitrile* (16), *2-mercapto-6-(pyridin-3-yl)pyridine-3-carbonitrile* (17), *pyrazolo[1,5-a]pyrimidines* (9, 12, 23, 24), [1,2,4]triazolo[1,5-*a*]pyrimidines (13, 25), *and hydropyrimidino[1,2-a]benzimidazoles* (14, 26)

Method A: A solution of the appropriate of **2** or **6,** (10 mmol), the appropriate cyanoacetamide, cynothioacetamide, 3-amino-4-phenylepyrazole, 3-amino-4-cyanopyrazole, 3-amino-1,2,4-triazole, 2-aminobenzimidazole (10 mmol) and

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piperidine acetate (1 mL) in water (3 mL) was refluxed for 10 minutes. Acetic acid (1.5 mL) was added to the hot solution. The solid product was filtered off and recrystallized from the proper solvent to give products **3**, **9**, **12-14**, **16**, **17** and **23-26** (Scheme 1-4).

Method B: An equimolar amount of 3-dimethylamino-1-pyridin-2-ylpropenone (**11**) (5 mmol), the appropriate 3-amino-4-phenylpyrazole, 3-amino-4-cyanopyrazole, 3-amino-1,2,4-triazole, 2-aminobenzimidazole, and ammonium acetate (5 mmol) in acetic acid (10 mL) was heated under reflux for 4 hrs. The resulting solid was collected and recrystallized from the proper solvent gave products **9**, **13** and **14**.

Method C: An equimolar amount of *N,N*-dimethyl-*N'*-(4-phenyl-1*H*-pyrazol-5-yl)formamidine (**10**) and appropriate 2-acetylpyridine or 3-acetylpyridine (5 mmol) in ethanol (10 mL) was heated under reflux for 3 hrs. The resulting solid was collected and recrystallized from the proper solvent gave products **9** and **23**, respectively.

2-(2-(3-cyano-6-(pyridin-2-yl)pyridin-2-yl)disulfanyl)-6-(pyridin-2-yl)pyridine-3-carbonitrile (**3**): Pale yellow crystals from ethanol. Yield: 73%. M.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3054 (CH, aromatic), 2219 (CN). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.44 (t, 2H), 7.48 (t, 2H), 8.05 (d, 2H), 8.45 (d, 4H), 8.66 (d, 2H). MS (*m/z, %*): 425 (0.6, M+1), 424 (1.7%, M), 215 (6.0%), 214 (16.5%), 213 (100%, 0.5), 212 (25.7%), 169 (49.2%), 79 (10%), 78 (33.5%). Anal. calcd. for $C_{22}H_{12}N_6S_2$ (424.51): C, 62.25; H, 2.85; N, 19.80; S, 15.11. Found: C, 62.32; H, 2.72; N, 19.70; S, 15.21%.

3-Phenyl-5-(pyridin-2-yl)pyrazolo[1,5-a]pyrimidine (**9**): Yellow crystals from EtOH. Yield: 70%. M.p.: 220-222 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic), 1633 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.91 (d, 2H), 7.27 (d, 1H), 7.55-7.75 (m, 5H), 8.15 (d, 1H), 8.72 (d, 1H), 8.92 (d, 2H). MS (*m/z*, %): 273 (1.8, M+1), 223 (10), 222 (15), 195 (10), 146 (15), 117 (26), 78 (100). Anal. calcd. for $C_{17}H_{12}N_4$ (272.3): C, 74.98; H, 4.44; N, 20.58. Found: C, 75.18; H, 4.23; N, 20.62%.

5-(Pyridin-2-yl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile (**12**): Yellow crystals from EtOH. Yield: 76%. M.p.: 215-217 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic), 2219 (CN), 1623 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.18 (t, 1H), 7.77 (d, 1H), 7.92 (t, 1H), 8.41 (d, 1H), 8.72 (d, 1H), 9.23 (s, 1H), 9.84 (d, 1H). Anal. calcd. for $C_{12}H_7N_5$ (221.22): C, 65.15; H, 3.19; N, 31.66. Found: C, 65.25; H, 3.27; N, 31.78%.

5-(Pyridin-2-yl)-[1,2,4]triazolo[1,5-a]pyrimidine (**13**): Light brown crystals from EtOH. Yield: 76%. M.p.: 225-227 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic), 1618 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.29 (t, 1H), 7.41 (d, 1H), 7.95 (t, 1H), 8.41 (s, 1H), 8.70 (d, 1H), 8.87 (d, 1H), 9.54 (d, 1H). Anal. calcd. for $C_{10}H_7N_5$ (197.2): C, 60.91; H, 3.58; N, 35.51. Found: C, 61.11; H, 3.82; N, 35.71%.

2-(2-Pyridyl)-4a-hydropyrimidino[1,2-a]benzimidazole (**14**): Yellow crystals from EtOH. Yield: 76%. M.p.: 230-233 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic), 1624 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.27 (t, 1H), 7.40-7.58 (m, 2H), 7.91-8.00 (d, 2H), 8.41 (d, 1H), 8.66 (d, 2H), 8.87 (d, 1H), 9.12 (d, 1H). Anal. calcd. for $C_{15}H_{10}N_4$ (246.27): C, 73.16; H, 4.09; N, 22.75. Found: C, 73.26; H, 3.79; N, 22.58%.

1,2-Dihydro-2-oxo-6-(pyridin-3-yl)pyridine-3-carbonitrile (**16**): Pale yellow crystals from DMF. Yield: 70%. M.p.: > 300 °C. FT-IR (KBr, cm^{-1}): 3350 (NH), 3043 (CH, aromatic), 2210 (CN), 1680 (CO), 1622 (C=N). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.88 (t, 1H), 7.53 (t, 1H), 8.25 (d, 1H), 8.69 (d, 1H), 8.70 (d, 1H), 8.99 (d, 1H), 9.05 (s, br., 1H, NH). Anal. calcd. for $C_{11}H_7N_3O$ (197.19): C, 67.00; H, 3.58; N, 21.31. Found: 67.14; H, 3.65; N, 21.11%.

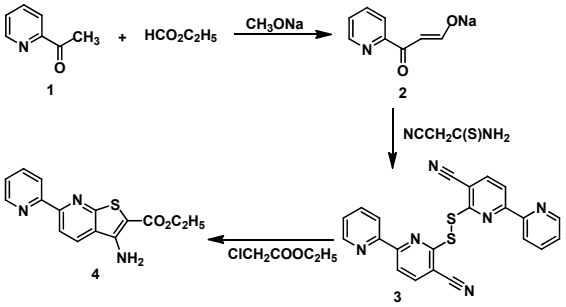
2-Mercapto-6-(pyridin-3-yl)pyridine-3-carbonitrile (**17**): Pale yellow crystals from ethanol. Yield: 73%. M.p.: 230-232 °C. FT-IR (KBr, cm^{-1}): 3013 (CH, aromatic), 2217 (CN). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.14 (t, 1H), 7.56 (t, 1H), 8.17 (d, 1H), 8.73 (d, 1H), 8.92 (d, 2H), 14.25 (s, br., 1H, SH). MS (*m/z*, %): 425 (0.6, M+1), 424 (1.7, M), 215 (6.0), 214 (16.5), 213 (100, 0.5), 212 (25.7), 169 (49.2), 79 (10%), 78 (33.5). Anal. calcd. for $C_{11}H_7N_3S$ (213.26): C, 61.95; H, 3.31; N, 19.70; S, 15.03. Found: C, 62.12; H, 3.22; N, 19.80; S, 15.11%.

3-Phenyl-5-(pyridin-3-yl)pyrazolo[1,5-a]pyrimidine (**23**): Yellow crystals from EtOH. Yield: 65%. M.p.: 120-122 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.09 (t, 2H), 7.47 (t, 1H), 7.77 (d, 2H), 7.90 (t, 1H), 8.15 (d, 1H), 8.41 (t, 2H), 8.73 (t, 2H), 9.12 (d, 1H). MS (*m/z*, %): 274 (2.19), 273 (18.5), 272 (100.0). Anal. calcd. for $C_{17}H_{12}N_4$ (272.3): C, 74.98; H, 4.44; N, 20.58. Found: C, 74.78; H, 4.32; N, 20.42%.

5-(Pyridin-3-yl)pyrazolo[1,5-a]pyrimidine-3-carbonitrile (**24**): Colorless crystals from EtOH. Yield: 76%. M.p.: 240-242 °C. FT-IR (KBr, cm^{-1}): 3043, (CH, aromatic), 2219 (CN), 1628 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 6.98 (d, 1H), 7.27 (t, 1H), 7.48-7.56 (m, 1H), 8.41 (d, 1H), 8.72 (d, 1H), 9.23 (s, 1H), 9.84 (d, 1H). MS (m/z, %): 221 (90, M+1), 194 (10), 168 (8.2), 142 (14), 88 (22.4), 87 (13.3), 66 (15.3), 53 (24.5), 52 (62), 51 (98). Anal. calcd. for $C_{12}H_7N_5$ (221.22): C, 65.15; H, 3.19; N, 31.66. Found: C, 65.04; H, 3.35; N, 31.82%.

5-(Pyridin-3-yl)-[1,2,4]triazolo[1,5-a]pyrimidine (**25**): Colorless crystals from EtOH. Yield: 76%. M.p.: 230-233 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic), 1622 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.27 (t, 1H), 7.40 (d, 1H), 7.55 (s, 1H), 8.41 (s, 1H), 8.66-8.75 (m, 1H), 9.12 (d, 1H), 9.27 (s, 1H). Anal. calcd. for $C_{10}H_7N_5$ (197.2): C, 60.91; H, 3.58; N, 35.51. Found: C, 61.01; H, 3.62; N, 35.61%.

2-(3-Pyridyl)-4a-hydropyrimidino[1,2-a]benzimidazole (**26**): Yellow crystals from EtOH. Yield: 76%. M.p.: 310-312 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, aromatic), 1626 (C=N). ^1H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.27 (t, 1H), 7.42-7.58 (m, 2H), 7.91-8.00 (d, 2H), 8.41 (d, 1H), 8.66 (d, 2H), 8.87 (d, 1H), 9.14 (d, 1H). Anal. calcd. for $C_{15}H_{10}N_4$ (246.27): C, 73.16; H, 4.09; N, 22.75. Found: C, 73.05; H, 4.19; N, 22.89%.

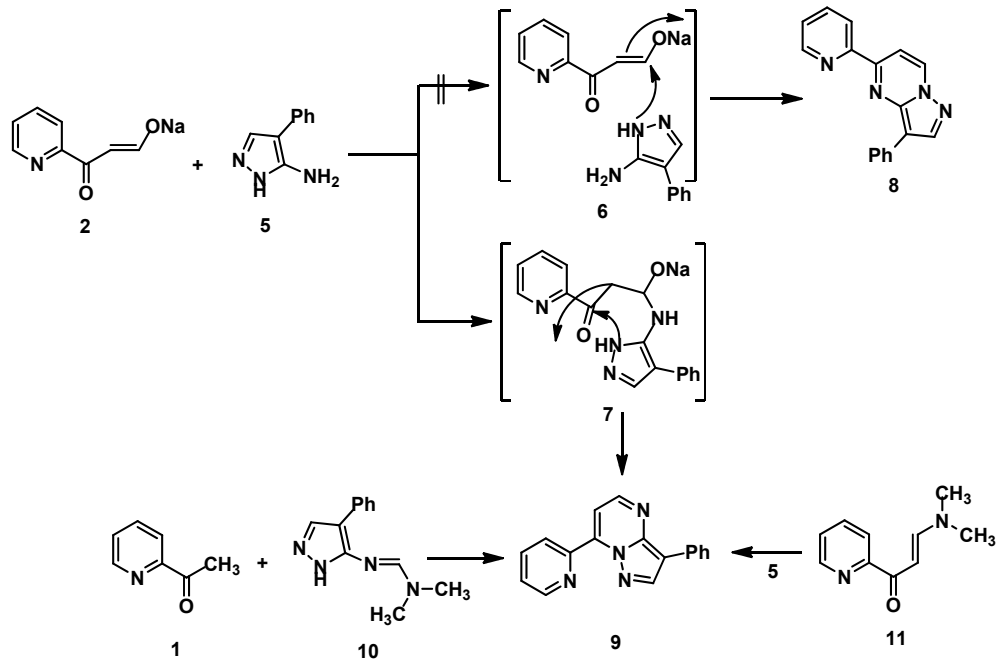


Scheme 1

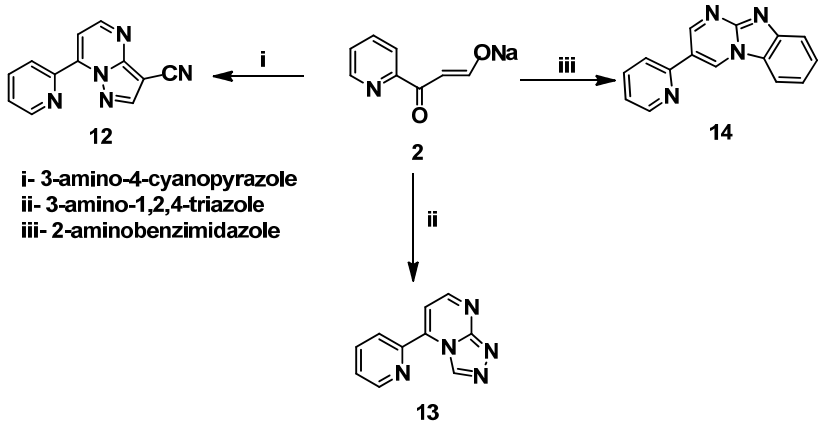
2.4. Synthesis of ethyl 3-amino-6-(2-pyridyl)thieno[2,3-b]pyridine-2-carboxylate (**4**)*, ethyl 3-amino-6-(3-pyridyl)thieno[2,3-b]pyridine-2-carboxylate* (**18**)*, 3-amino-6-(3-pyridyl)thieno[2,3-b]pyridine-2-ylphenylketone* (**19**)*, 3-amino-6-(3-pyridyl)thieno[2,3-b]pyridine-2-carbonitrile* (**20**) *and 2-methylthio-6-(3-pyridyl)pyridine-3-carbonitrile* (**21**)

A mixture of the appropriate **3** and **7** (2.13 g, 10 mmole) and potassium hydroxide (0.56 g, 10 mmole) in *N,N*-dimethylformamide (20 mL) was stirred for 2 hrs at room temperature. Each of ethyl chloroacetate, ω-bromoacetophenonem, chloroacetonitrile and iodomethane (10 mmole each) was added and stirring was continued for 2 hrs. The resulting solid was collected and recrystallized from the proper solvent to give **4**, **9-12**, respectively.

Ethyl 3-amino-6-(pyridin-2-yl)thieno[2,3-b]pyridine-2-carboxylate (**4**): Pale yellow crystals from Dioxane. Yield: 85%. M.p.: 277-280 °C. FT-IR (KBr, cm^{-1}): 3280, 3204 (NH_2), 3077 (CH, Aromatic), 1715 (CO), 1617 (C=N).



Scheme 2



Scheme 3

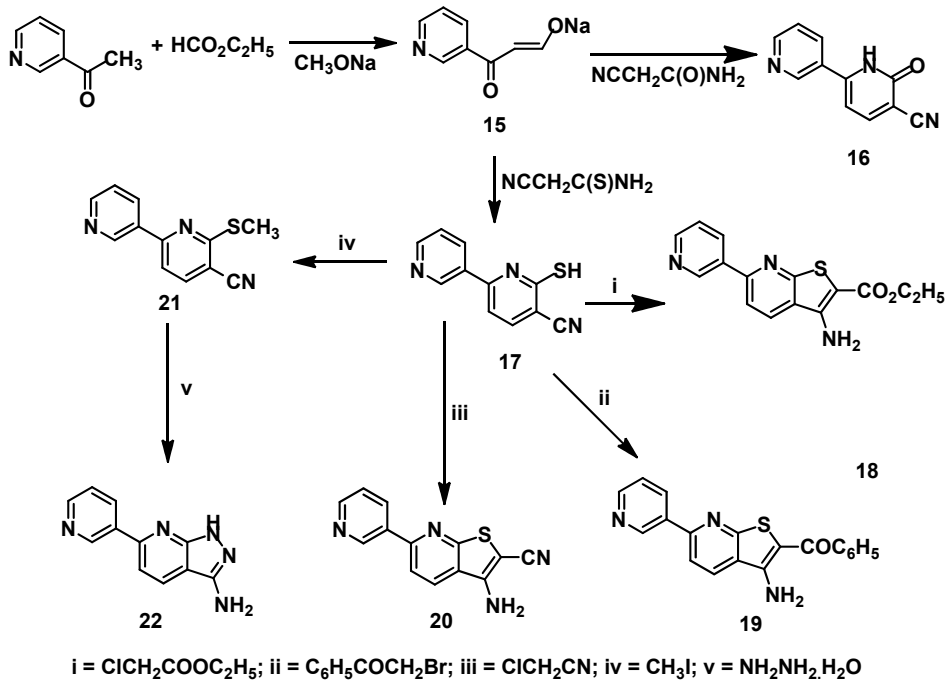
^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.27 (t, 3H, CH_2CH_3), 4.23 (q, 2H, CH_2CH_3), 6.82 (s, br, 2H, NH_2), 7.30 (t, 1H), 7.96 (d, 1H), 8.02 (t, 1H), 8.19 (d, 1H), 8.66 (d, 1H), 8.87 (d, 1H). Anal. calcd. for $C_{15}H_{13}N_3O_2S$ (299.35): C, 60.18; H, 4.38; N, 14.04; S, 10.71. Found: C, 60.00; H, 4.45; N, 14.17; S, 10.94%.

Ethyl 3-amino-6-(pyridin-3-yl)thieno[2,3-b]pyridine-2-carboxylate (**18**): Colorless crystals from Dioxane. Yield: 85%. M.p.: 270-272 °C. FT-IR (KBr, cm^{-1}): 3320, 3180 (NH_2), 3043 (CH, aromatic), 1715 (CO), 1622 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 1.27 (t, 3H, CH_2CH_3), 4.23 (q, 2H, CH_2CH_3), 6.82 (s, br, 2H, NH_2), 7.30 (t, 1H), 7.96 (d, 1H), 8.02 (t, 1H), 8.19 (d, 1H), 8.66 (d, 1H), 8.87 (d, 1H). Anal. calcd. for $C_{15}H_{13}N_3O_2S$ (299.35): C, 60.18; H, 4.38; N, 14.04; S, 10.71. Found: C, 60.00; H, 4.45; N, 14.17; S, 10.94%.

(3-Amino-6-(pyridin-3-yl)thieno[2,3-b]pyridin-2-yl)(phenyl) methanone (**19**): Colorless crystals from EtOH. Yield: 78%. M.p.: 210-212 °C. FT-IR (KBr, cm^{-1}): 3360, 3180 (NH_2), 3043 (CH, aromatic), 1700 (CO), 1622 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 7.01 (s, br, 2H, NH_2), 7.27-7.55 (m, 6H), 7.80 (d, 1H), 8.30 (t, 1H), 8.12 (d, 1H), 8.45 (d, 1H), 9.13 (d, 1H). Anal. calcd. for $C_{19}H_{13}N_3OS$ (331.40), C, 68.86; H, 3.95; N, 12.68; S, 9.68. Found C, 68.65; H, 4.13; N, 12.74; S, 9.53%.

3-Amino-6-(pyridin-3-yl)thieno[2,3-b]pyridine-2-carbonitrile (**20**): Colorless crystals from dioxane. Yield: 71%. M.p.: 280-282 °C. FT-IR (KBr, cm^{-1}): 3320, 3180 (NH_2), 3043 (CH, aromatic), 2148 (CN), 1623 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.92 (s, br, 2H, NH_2), 7.31 (t, 1H), 7.78 (d, 1H), 8.21 (d, 1H), 8.82 (d, 1H), 8.96 (d, 1H), 9.23 (d, 1H). Anal. calcd. for $C_{13}H_8N_4S$ (252.30), C, 61.89; H, 3.20; N, 22.21; S, 12.71. Found: C, 62.00; H, 3.33; N, 22.12; S, 12.93%.

2-(Methylthio)-6-(pyridin-3-yl)pyridine-3-carbonitrile (**21**): Colorless crystals from dioxane. Yield: 71%. M.p.: 280-282 °C. FT-IR (KBr, cm^{-1}): 3053 (CH, aromatic), 2210 (CN), 1627 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6, δ, ppm): 2.45 (s, 3H, SCH_3), 7.43 (t, 1H), 7.53 (t, 1H), 7.91 (d, 1H), 8.38 (d, 1H), 8.74 (d, 1H), 9.31 (d, 1H). Anal. calcd. for $C_{12}H_9N_3S$ (227.28): C, 63.41; H, 3.99; N, 18.49; S, 14.11. Found: C, 63.31; H, 4.12; N, 18.35; S, 14.00%.



Scheme 4

2.5. 6-(Pyridin-3-yl)-1H-pyrazolo[3,4-b]pyridin-3-amine (22)

A mixture of compound **12** (2.27 g, 10 mmole) and hydrazine hydrate (4 ml, 99 %) in absolute ethanol (20 mL) for 2 hrs was heated under reflux. The reaction mixture was cooled, and the resulting solid was collected and washed with ethanol/water and recrystallized from water to give **13**. Colorless crystals from water. Yield: 77%. M.p.: 105-106 °C. FT-IR (KBr, cm^{-1}): 3043 (CH, Aromatic), 3350, 2316, 2189 (NH, NH_2), 1627 (C=N). ^1H NMR (300 MHz, DMSO-d_6, δ, ppm): 6.52 (s, br., 3H, NH and NH_2), 7.26 (t, 1H), 7.35 (d, 1H), 8.45 (d, 1H), 8.64 (d, 1H), 8.87 (d, 1H), 9.63 (d, 1H). Anal. calcd. for $C_{11}H_9N_5$ (211.22): C, 62.55; H, 4.29; N, 33.16. Found: C, 62.35; H, 4.12; N, 33.32%.

3. Results and discussion

2-Acetylpyridine reacted with ethyl formate in dry ether containing sodium methoxide to give sodium salt of 3-hydroxy-1-(pyridin-2-yl)prop-2-en-1-one (**2**). Structure **2** was confirmed by chemical transformation. Thus, treatment of cynothioacetamide with **2** in piperidenium acetate gave 2-(2-(3-cyano-6-(pyridin-2-yl)pyridin-2-yl)disulfanyl)-6-(pyridin-2-yl)pyridine-3-carbonitrile (**3**) based on elemental analysis and spectral data. ^1H NMR spectrum showed signals at δ = 7.44 (t), 7.48 (m), 8.05 (d), 8.45 (d), 8.66 (d) as ratio 1: 1: 1 2: 1. IR spectrum revealed band at 3054 (CH, aromatic), 2219 (CN) group and its mass spectrum showed peak at m/z = 425 (0.6, M+1), 424 (1.7%, M), 215 (6.0%), 214 (16.5%), 213 (100%, 0.5), 212 (25.7%), 169 (49.2%), 79 (10%), 78 (33.5%) and X-ray single crystal showed in Figure 1.

Compound **3** reacted with ethyl chloroacetate in *N,N*-dimethylformamide in presence of potassium hydroxides to give ethyl 3-amino-6-(2-pyridyl)thieno[2,3-*b*]pyridine-2-carboxylate (**4**) (Scheme 1). Structure **4** was confirmed by elemental analysis and spectral data.

Also, treatment of **2** with 3-amino-4-phenylpyrazole in piperidenium acetate yielded 3-phenyl-7-(pyridin-2-yl)pyrazolo[1,5-a]pyrimidine (**9**) (Scheme 2). Structure of **9** was established on the basis of their elemental analysis, spectral data and alternative synthetic routes. ^1H NMR spectrum of **9** revealed signals at δ = 6.88 (d, 2H, *J* = 8 Hz, ArH's), 7.38 (d, 1H, *J* = 8 Hz, ArH), 7.56-7.65 (m, 4H, ArH's), 7.88 (m, 1H, ArH), 8.21 (s, 1H, pyrazole H-5), 8.62 (d, 1H, *J* = 8 Hz, ArH's), 8.75 (d, 1H, *J* = 8 Hz, ArH's), 8.93 (s, 1H, pyrimidine H-4). Thus, treatment of 3-(dimethylamino)-1-(pyridin-2-yl)prop-2-en-1-one (**11**) with 3-amino-4-phenylpyrazole in boiling ethanol gave product identical in all respects (M.p., mixed m.p., and spectra) with **9**. More evidence on the formation of **9** was carried out by boiling of *N,N*-dimethyl-*N'*-(4-phenyl-1*H*-pyrazol-5-yl)formamidine (**10**) with 2-acetylpyridine gave product identical in all aspects (M.p., mixed m.p. and spectra) with **9**.

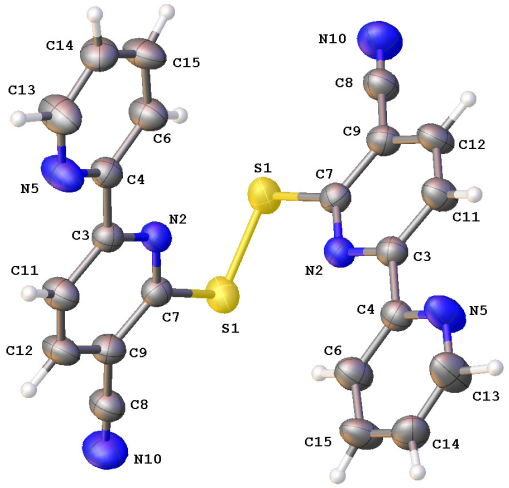
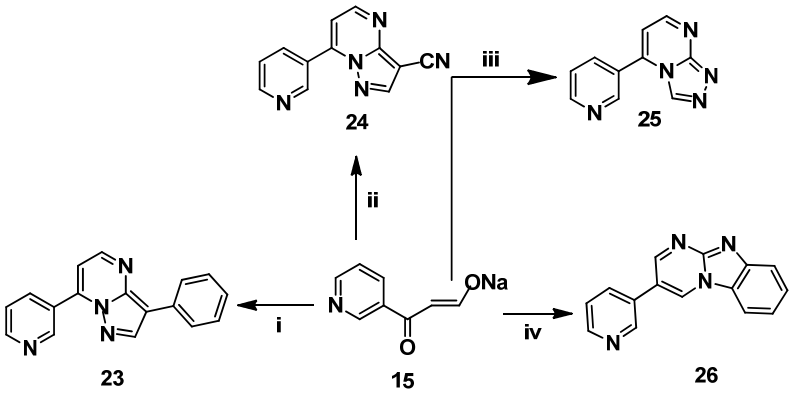


Figure 1. Molecular structure of 2-(2-(3-cyano-6-(pyridin-2-yl)pyridin-2-yl)disulfanyl)-6-(pyridin-2-yl)pyridine-3-carbonitrile (**3**) showing the atom numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.



i- 3-amino-4-phenylpyrazole; ii- 3-amino-4-cyanopyrazole
iii- 3-amino-1,2,4-triazole; iv- 2-aminobenzimidazole

Scheme 5

Analogously, compound **2** reacted with the appropriate 3-amino-4-cyanopyrazole, 3-aminotriazole or 2-aminobenzimidazole gave 5-(pyridin-2-yl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**12**), 5-(pyridin-2-yl)-[1,2,4]triazolo[1,5-*a*] pyrimidine (**13**) and 2-(2-pyridyl)-4*a*-hydropyrimidino[1,2-*a*] benzimidazole (**14**), respectively (Scheme 3).

Meanwhile, sodium salt of 3-hydroxy-1-(pyridin-3-yl)prop-2-en-1-one (**15**), which prepared from 3-acetylpyridine and ethyl formate in sodium methoxide solution, reacted with each of cyanoacetamide and cynothioacetamide to give and 1,2-dihydro-2-oxo-6-(pyridin-3-yl)pyridine-3-carbonitrile (**16**) and 2-mercapto-6-(pyridin-3-yl)pyridine-3-carbonitrile (**17**), respectively (Scheme 4).

Compounds **16** and **17** were confirmed by elemental analysis, spectral data and chemical transformation. Thus, ^{1}H NMR spectrum of **17** showed δ = 5.92 (s, 1H, SH), 7.01-7.08 (d, 1H), 7.86-7.90 (m, 1H), 8.00-8.04 (m, 1H), 8.29-8.33 (d, 1H), 8.72-8.76 (d, 1H), 9.26-9.26 (d, 1H) ppm. Its IR spectrum revealed bands at 2217 (CN group).

On the other hand, treatment of **17** with each of ethyl chloroaceate, ω-bromo acetophenone, chloroacetonitrile or iodomethane afforded ethyl 3-amino-6-(pyridin-3-yl)thieno [2,3-*b*]pyridine-2-carboxylate (**18**), (3-amino-6-(pyridin-3-yl)thieno[2,3-*b*]pyridin-2-yl)(phenyl)methanone (**19**), 3-amino-6-(pyridin-3-yl)thieno[2,3-*b*]pyridine-2-carbonitrile (**20**) and 2-(methylthio)-6-(pyridin-3-yl)pyridine-3-carbonitrile (**21**), respectively. Compound **21** could be proved via the evolution of methanethiol when treated with hydrazine hydrate, forming the sulfur free 6-(pyridin-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridin-3-amine (**22**).

Finally, treatment of **15** with appropriate 3-amino-4-phenylpyrazole, 3-amino-4-cyanopyrazole, 3-amino-1,3,4-triazole or 2-aminobenzimidazole in piperidenium acetate yielded 3-phenyl-5-(pyridin-3-yl)pyrazolo[1,5-*a*]pyrimidine (**23)**, 5-(pyridin-3-yl)pyrazolo[1,5-*a*]pyrimidine-3-carbonitrile (**24**), 5-(pyridin-3-yl)-[1,2,4]triazolo[1,5-*a*]pyrimidine (**25**), and 2-(3-pyridyl)-4a-hydropyrimidino[1,2-*a*]benzimidazole (**26**), respectively (Scheme 5).

4. Conclusion

The present study demonstrates the synthesis of 3-amino-6-(2-pyridyl)thieno[2,3-*b*]pyridine derivatives were synthesized *via* reaction of pyridine-2-thione**.** Also, pyrazolo[1,5-*a*] pyrimidine, [1,2,4]triazolo[1,5-*a*]pyrimidine and pyrimido [1,2-*a*]benzimidazole were synthesized by reaction of sodium salt of 3-hydroxy-(1-pyridin-2-yl)prop-2-en-1-one or sodium salt of 3-hydroxy-1-(pyridin-3-yl)prop-2-en-1-one with different heterocyclic amines in piperidenium acetate.

Supplementary material

CCDC-828284 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

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