o-Aminonitrile in Heterocylic Chemistry: Synthesis of Thienopyridine, Pyridothienopyrimidine, Pyridothieno[1,2,4]triazolopyrimidine, Pyridothienopyridine Derivatives

Ali K. K. El-Louh

Department of Chemistry, Faculty of Science, Al-Azhar University-Gaza, Gaza, Palestine.

E-mail: akklouh@yahoo.com

Received 28/01/2008 *Accepted* 19/02/2008

Abstract: *Reaction of thienopyridine derivatives **1a,b** with triethyl orthoformate gave 3-(ethoxymethyleneamino)thienopyridine-2-carbonitrile derivatives **2a,b**. Compounds **2a,b** were reacted with hydrazine hydrate to give pyrido-theinopyrimidine derivatives **3a,b**, which were reacted with triethyl orthoformate, acetyl chloride and diethyl oxalate to give pyridothieno[1,2,4]triazolopyrimidine derivatives **(4-6)**. Pyridothieno-pyrimidine **(7-12)** and pyridothieno-pyridine **(13, 14)** were synthesized. Diazotization of **1a,b** followed by coupling with ethyl cyanoacetate and malononitrile gave hydrazono derivatives **(16, 17)** which were cyclized with hydrazine hydrate and hydroxylamine hydrochloride to afford pyrazole derivatives **(18, 19)** and isoxazole derivatives **20a,b,** respectively. All newly synthesized structures were established via elemental analysis and spectral data.*

Keywords: *o-Aminonitrile, thienopyridine, pyridothienopyrimidine, pyridothieno[1,2,4]-triazolopyrimidine, pyridothienopyridine.*

Introduction

o-Aminonitriles are versatile reagents to synthesis of several heterocyclic derivatives[1-6]. In continuation of our pervious work in the synthesis of thienopyridine, pyridothienopyrimidine derivatives of expected biological activities[7-11], the formation of o-aminonitrile function at 3-aminothieno-pyridine-2-carbonitrile **1a,b**[8] drew interest to the synthesis of several thienopyridine and annulated thienopyridine derivatives. Many thienopyridines have been evaluated pharmacologically and have been found to show activity against, for example, diabetes mellitus[12-14], as analgesics and anti-inflammatories[15-17], sedatives[14], anticoagulants[17], anti-artherosscl-erotics[18], and as

gonaodotropin releasing hormone antagonists[19,20]. Moreover the pyridothienopyrimidines showed analgesic[21,22], antipyretic[23], anti-inflammatories[24], antianaphylactic [25,26], and antimicrobial[27,28] activities.

Results And Discussion

It has been found that condensation of thieno[2,3-b]pyridine-2-carbonitrile derivative **1a**[8] with triethyl orthoformate in the presence of acetic anhydride afforded a product of molecular formula $C_{24}H_{17}N_3O_3S$ *via* loss of two molecules of ethanol. The IR spectrum of this reaction product showed the disappearance of the characteristic absorption bands of NH_2 group and the appearance of characteristic absorption bands at 2217 and 1629 cm^{-1} attributed to cyano and C=N groups. The presence of ethoxymethylene group in this product was detected in the ^1H NMR spectrum which revealed a triplet signal at δ = 1.01 ppm (CH_3) a quartet signal at δ = 4.11 ppm (CH_2) and a singlet signal at δ = 1.01 ppm (CH=N). Based on the above data, and elemental analysis, the reaction product could be formulated as 3-(ethoxymethyleneamino)thieno[2,3-b]pyridine-2-carbonitrile derivative **2a**. In a similar manner, thieno[2,3-b]pyridine-2-carbonitrile derivative **(1b)**[8] reacted with triethyl orthoformate at the same reaction conditions to give 3-(ethoxymethyleneamino)-thieno[2,3-b]pyridine-2-carbonitrile derivative **2b**, whose structure was elucidated on the basis of elemental analysis and spectral data (cf. Scheme 1 and Experimental part).

Furthermore the structure of compounds **2a,b** were also, confirmed *via* their cyclization with hydrazine hydrate in boiling ethanol to afford pyrido[3',2':4,5]thieno[3,2-d]pyrimidine derivatives **3a,b** with elimination of ethanol followed by cyclization *via* addition of NH proton to nitrile group. The IR spectra of **3a,b** were found entirely free from the absorption band of cyano group, and instead the newly born amino and imino groups were detected in each case. The ^1H NMR spectra were found in a good agreement with the assigned structure. The mass spectra of **3a,b** were agreed with the suggested molecular weights (cf. Scheme 1 and Experimental part).

The presence and the reactivity of amino and imino groups in compounds 3a,b were investigated by their reactions with different reagents. Thus, it has been found that each of **3a,b** reacted with triethyl orthoformate, acetyl chloride and diethyl oxalate to give the

corresponding pyrido[3',2':4,5]thieno[3,2-d][1,2,4]triazolo[5,1-f]pyrimidine derivatives **(4-6)** respectively. The structure of compounds **(4-6)** was confirmed based on elemental analysis and spectral data. Thus, the IR spectrum of **6a** as an example showed the presence of ester CO absorption band at 1718 cm^{-1}. ^1H NMR spectrum revealed triplet signal at δ = 1.11 ppm and a quartet signal at δ = 4.10 ppm in addition to the other protons. Its ^{13}C NMR spectrum revealed the signals of CO (169.24), CH_2 (60.22) and CH_3 (14.5) which confirmed the presence of $COOCH_2CH_3$ group. Moreover the mass spectra of **4a, 5a** and **6a** as typical examples m/z = 423, 437 and 495 which agreed with molecular formulas $C_{23}H_{13}N_5O_2S$, $C_{24}H_{15}N_5O_2S$ and $C_{26}H_{17}N_5O_4S$ of the assigned structures (see Scheme 1 and Experimental part). The imines **3a,b** were subjected to *Dimorth rearrangement* [6] by heating with aqueous KOH solution to afford 4-hydrazinopyridothienopyrimidine derivatives **7a,b**, this reaction gave good evidence on the assignment of structure **3a,b**. The IR spectrum of **7b** as an example showed strong absorption bands at 3425, 3358 and 3224 cm^{-1} corresponded to NH_2 and NH groups. The NH_2, NH protons were detected from ^1H NMR spectrum of **7b** at δ = 5.4 (s), δ = 7.94 (s) which lost by addition of D_2O. The structure of **7a,b** were elucidated on the basis of elemental analysis and spectral data (cf. Scheme 1 and Experimental part).

The synthetic potential of **1a,b** was further demonstrated *via* their reactions with carbon disulfide to yield pyrido[3',2'-4,5]thieno[3,2-d]pyrimidine-2,4-dithione derivatives **8a,b**. The IR spectrum of **8b** showed the absorption bands corresponded to two NH groups at 3324, 3231 cm^{-1}. The ^1H NMR spectrum of **8b** as an example indicated two broad singlet signals at δ = 9.34 and δ = 9.92 ppm corresponded to two NH groups. Moreover the mass spectra of compounds **8a,b** were compatible with the assigned structure (see scheme 2 and experimental part).

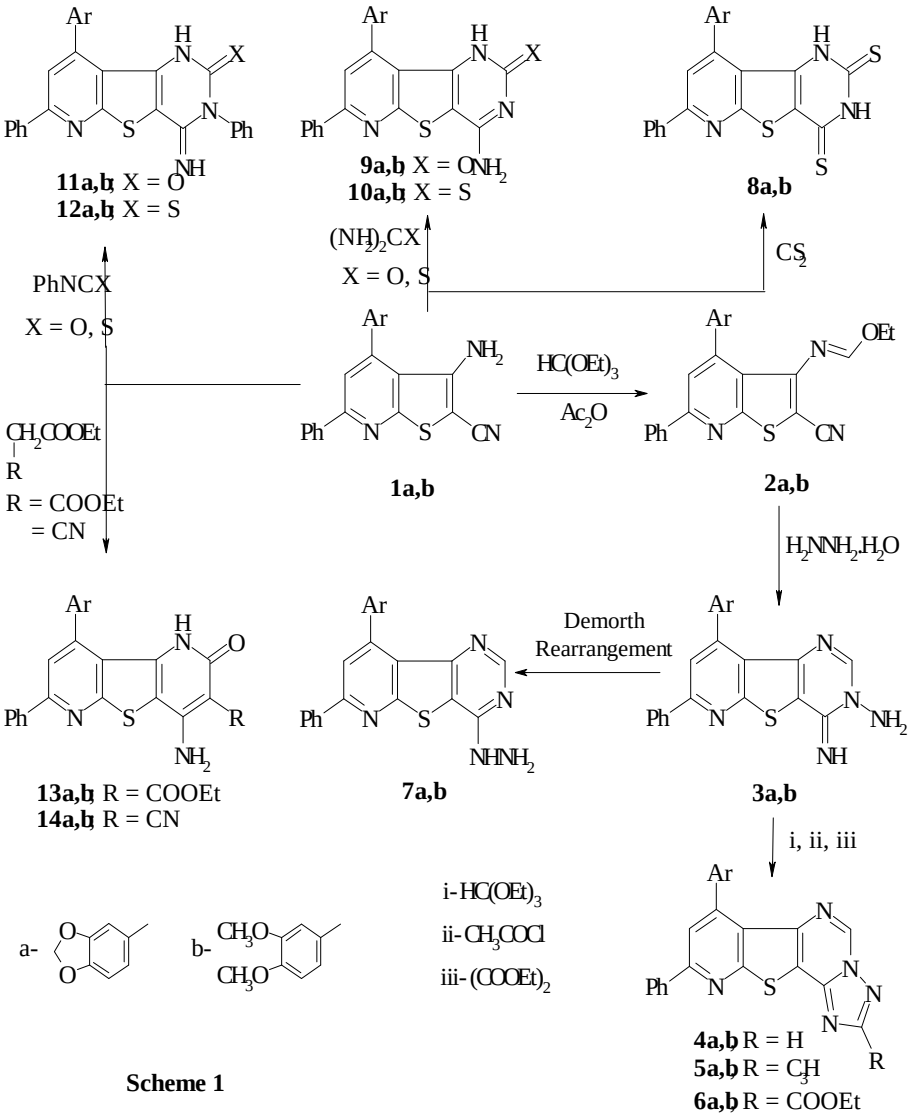
Work was also extended to shed more light on the reactivity and synthetic potential of o-aminonitrile function in **1a,b**. Thus, compounds **1a,b** reacted with urea to give a reaction product formed *via* elimination of NH_3 molecule with cyclization through addition of NH_2 protons to the nitrile group. The IR spectra of these reaction products showed the characteristic bands of NH_2, NH and amidic CO groups and the disappearance of CN group absorption band. ^1H NMR spectra revealed the signals of NH_2 and NH protons. By considering

the above data in addition to elemental analysis and mass spectra, these reaction products could be formulated as 1,2-dihydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine-2-one derivatives **9a,b** (cf. Scheme 2 and Experimental part). Under similar experimental conditions **1a,b** were reacted with thiourea to give 1,2-dihydropyrido[3',2'-4,5]thieno[3,2-d]pyrimidine-2-thione derivatives **10a,b**. The structure of compounds **10a,b** were established based on elemental analysis and spectral data (cf. Scheme 2 and Experimental part).

The 1,2,3,4-tetrahydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine derivatives **11a,b** and **12a,b** were synthesized *via* the reaction of compounds **1a,b** with phenyl isocyanate and phenyl isothiocyanate in refluxing ethanol. The IR spectrum of **11a** as an example gave absorption bands for (two NH) and amidic CO groups. ^{1}H NMR spectrum of **11b** revealed the two singlet signals at δ = 8.82 and δ = 9.69 ppm corresponded to two NH groups. Moreover, the mass spectra of both **11a** and **12a** as selective examples gave m/z = 490 and 506 which represented molecular weights of the molecular formulas $C_{28}H_{18}N_4O_3S$ and $C_{28}H_{18}N_4O_2S_2$ of the assigned structure.

The synthetic potential of **1a,b** was demonstrated *via* their reaction with diethyl malonate in refluxing acetic acid and ammonium acetate to give ethyl 4-amino-1,2-dihydropyrido-[3',2':4,5]thieno[3,2-b]pyridine-3-carboxylate derivatives **13a,b**. The IR spectra of the latter compounds showed the absorption bands corresponded to NH_2, NH, amidic CO and ester CO function groups. The ^{1}H NMR spectrum of **13b** as an example revealed singlet signal at δ = 10.12, singlet signal δ = 5.71, quartet signal δ = 4.02 and triplet signal δ = 1.01 ppm corresponded to NH_2, NH, ester (CH_2) and ester (CH_3) ester respectively in addition to the other protons. ^{13}C NMR spectrum of **13b** revealed the presence of ester CO (167.2), amidic CO (163.4), ester CH_2 (61.2) and ester CH_3 (13.8) ppm in addition to other carbon atoms. The mass spectra of **13a,b** were strongly compatible with the assigned structure. Similarly compounds **1a,b** reacted with ethyl cyanoacetate at same reaction condition to yield 4-amino-1,2-dihydropyrido[3',2':4,5]thieno[3,2-b]pyridine-3-carbonitrile derivatives **14a,b**. The structure of the latter compounds was

established based on elemental analysis and spectral data (cf. Scheme 2 and Experimental part).



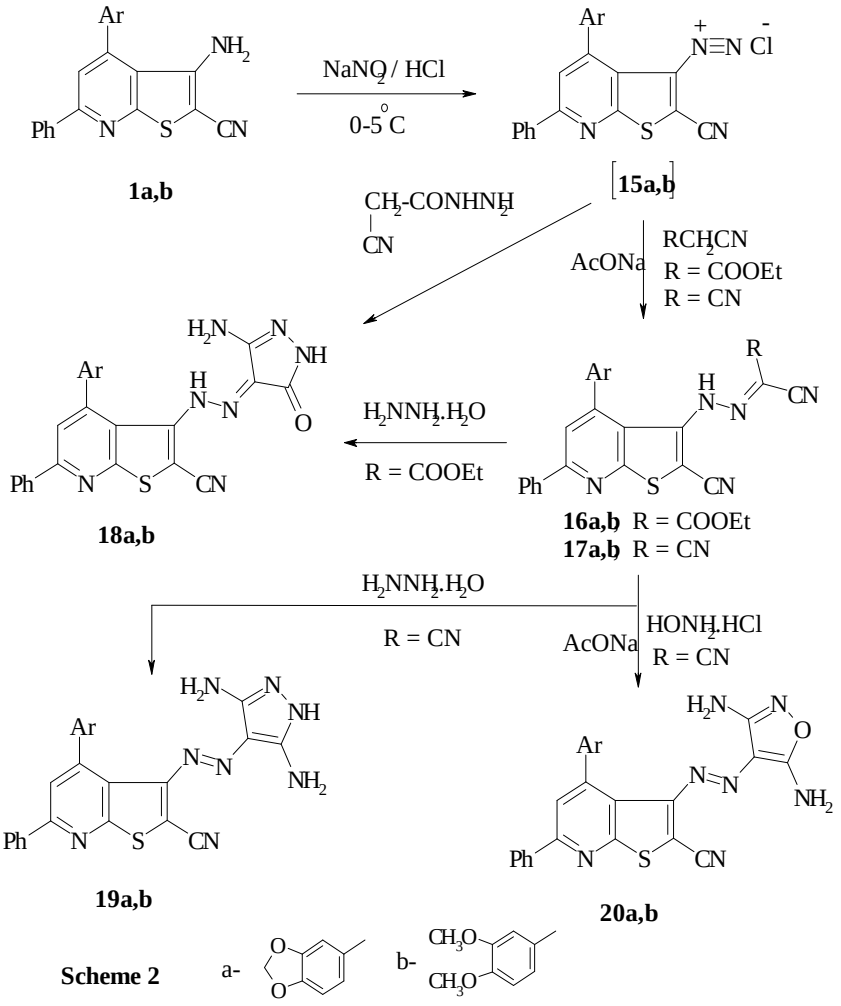
Scheme 1

Diazotization of compounds **1a,b** with sodium nitrite and hydrochloric acid gave non-isolable diazonium salt **15a,b** which coupled with each of ethyl cyanoacetate and malononitrile in the

presence of sodium acetate to afford the corresponding hydrazono derivatives **16a,b** and **17a,b** respectively (see Scheme 2). The IR spectrum of **16a** as an example showed the absorption bands for NH, two CN and ester CO at 3328, 2224, 2212 and 1719 cm^{-1} respectively. Its ^1H NMR revealed the singlet signal at δ = 11.03 ppm corresponded to NH proton and expected signals of protons of ester group in addition to other protons. Furthermore the structure of compounds **16a,b** and **17a,b** was achieved based on elemental analysis and spectral data (see Experimental part).

Hydrazono derivatives **16a,b** and **17a,b** were cyclized with hydrazine hydrate in boiling ethanol to afford the expected 3-(3-amino-5-oxo-1,5-dihydropyrazol-4-ylidene)hydrazinothieno[2,3-b]pyridine-2-carbonitrile derivatives **18a,b** and 3-(3,5-diamino-1H-pyrazol-4-yl)diazothieno[2,3-b]pyridine-2-carbonitrile derivatives **19a,b** (cf. Scheme 2). The structures of the newly synthesized compounds **18a,b** and **19a,b** were confirmed on the bases of elemental analysis and spectral data (see Experimental part). The IR spectrum of **18a** as an example showed characteristic absorption bands due to NH_2, two NH, CN and amidic CO. The ^1H NMR spectrum of **18a** revealed three singlet signals at δ = 5.6, δ = 10.34 and δ = 11.16 ppm corresponding to NH_2 and two NH groups respectively (D_2O exchangeable). Moreover the mass spectra of **18a** gave m/z = 481 that corresponded to the molecular weight of the molecular formula $C_{24}H_{15}N_7O_3S$ of the assigned structure (cf. Scheme 2 and Experimental part). A good evidence for structure **18a,b** came from its synthesis through another route *via* coupling diazonium salts **15a,b** with cyanoacetic acid hydrazide in boiling ethanol. Compounds **18a,b** prepared *via* the two routes were found to be identical in all aspects (mp, mixed mp, analytical and spectral data).

Hydrazono derivatives **17a,b** were cyclized with hydroxylamine hydrochloride in the presence of sodium acetate to give the expected 3-(3,5-diamino-5-oxoisoxazol-4-yl)diazothieno[2,3-b]pyridine-2-carbonitrile derivatives **20a,b**. The structure of the newly synthesized compounds **20a,b** was confirmed based on elemental analysis and spectral data (cf. Scheme 2 and Experimental part).



Experimental

All melting points were measured on a Gallenkamp melting point apparatus are uncorrected. IR spectra (KBr discs) were recorded on Bruker Vector 22 and Perkin-Elmer FT-IR type 4 spectrophotometers. ^{1}H NMR and ^{13}C NMR spectra were determined on a Varian Gemini-300 MHz spectrometer using DMSO-d6 as a solvent and TMS as an internal standard. Mass spectra were measured on Hewlett-Packard GC-MS type 5988 using inlet at 70eV. Microanalyses were performed by the Micro Analytical Center of Cairo University, Giza, Egypt.

The starting 3-aminothienopyridine-2-carbonitrile derivatives **1a,b** were synthesized according to the literature procedures as previously described [8]. In all ^{1}H NMR * = Lost after D_2O exchange.

Synthesis of 2a,b:

A solution of **1a,b** (10 mmol) in acetic anhydride (30 ml) was treated with triethyl orthoformate (25 mmol). The reaction mixture was heated under reflux for 4 hours and then cooled. The solid product obtained was filtered off, and recrystallized from ethanol to give **2a,b**.

*4-(Benzo-1,3-dioxol-5-yl)-3-ethoxymethyleneamino-6-phenylthieno[2,3-b]-pyridine-2-carbonitrile **2a**:* white solid (66%), mp 186 ^{o}C; IR ν max cm^{-1}: 2217 (CN) and 1629 (C=N); ^{1}H NMR δ (ppm): 1.01 (t, J = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 4.11 (q, J = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 6.12 (s, 2H, OCH_2O), 6.86-7.85 (m, 8H, ArH's), 8.21 (s, 1H, pyridine H) and 8.45 (s, 1H, CH=N); MS: m/z = 427. Anal. for $C_{24}H_{17}N_3O_3S$ (427.49): Calcd. (Found) C 67.43 (67.49), H 4.01 (3.82), N 9.83 (9.99).

*4-(3,4-Dimethylphenyl)-3-ethoxymethyleneamino-6-phenylthieno[2,3-b]pyridine-2-carbonitrile **2b**:* white solid (58%), mp 206 ^{o}C; IR ν max cm^{-1}: 2229 (CN) and 1624 (C=N); ^{1}H NMR δ (ppm): 1.12 (t, J = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 3.76, 3.81 (two s, 6H, two OCH_3), 4.14 (q, J = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 6.87-7.62 (m, 8H, ArH's), 8.03 (s, 1H, pyridine H) and 8.38 (s, 1H, CH=N); Anal. for $C_{25}H_{21}N_3O_3S$ (443.53): Calcd. (Found) C 67.70 (67.64), H 4.77 (4.62), N 9.64 (9.67).

Synthesis of 3a,b:

To a well stirred cold solution of compounds **2a,b** (10 mmol) in ethanol (15 mL), 99 % hydrazine hydrate (3 mL) was added dropwise, then the mixture was stirred at room temperature for 6 hours and left overnight. The solid that precipitated was filtered off, washed with cold ethanol and purified by recrystallization from dioxane to give compounds **3a,b**.

*3-Amino-9-(benzo-1,3-dioxol-5-yl)-4-imino-7-phenyl-3,4-dihydropyrido[3',2':4,5]-thieno[3,2-d]pyrimidine **3a**:* white solid (84%), mp 274 ^{o}C; IR ν max cm^{-1}: 3418, 3342, 3215 (NH_2, NH) and 1618 (C=N); ^{1}H NMR δ (ppm): 6.11 (s, 2H, OCH_2O), 5.37 (s, 2H, NH_2^*), 6.96-7.95

(m, 8H, ArH's), 8.17 (s, 1H, pyridine H), 8.35 (s, 1H, pyrimidine H) and 8.94 (s, 1H, NH^*); MS: m/z = 413. Anal. for $C_{22}H_{15}N_5O_2S$ (413.46): Calcd. (Found) C 63.91 (63.73), H 3.66 (3.81), N 16.94 (16.77).

*3-Amino-4-imino-9-(3,4-dimethylphenyl)-7-phenyl-3,4-dihydropyrido [3',2':4,5]-thieno[3,2-d]pyrimidine **3b**:* white solid (91%), mp 244 ^oC; IR ν max cm^{-1}: 3394, 3325, 3205 (NH_2, NH) and 1614 (C=N); ^1H NMR δ (ppm): 3.78, 3.83 (two s, 6H, two OCH_3), 5.72 (s, 2H, NH_2^*), 6.89-8.02 (m, 8H, ArH's), 8.22 (s, 1H, pyridine H), 8.29 (s, 1H, pyrimidine H) and 8.71 (s, 1H, NH^*); MS: m/z = 429. Anal. for $C_{23}H_{19}N_5O_2S$ (429.50): Calcd. (Found) C 64.32 (64.48), H 4.46 (4.22), N 16.31 (16.56).

Synthesis of 4a,b:

A solution of compounds **3a,b** (10 mmol) in triethyl orthoformate (25 mmol) was refluxed for 1-2 hours and left overnight. The precipitated product was collected by filtration and recrystallized from ethanol-chloroform mixture to give compounds **4a,b**.

*7-(Benzo-1,3-dioxol-5-yl)-9-phenylpyrido[3',2':4,5]thieno[3,2-d][1,2,4] triazolo[5,1-f]-pyrimidine **4a**:* white needles (71%), mp 298 ^oC; IR ν max cm^{-1}: 2975 (stretching CH); MS: m/z = 423. Anal. for $C_{23}H_{13}N_5O_2S$ (423.46): Calcd. (Found) C 65.24 (65.35), H 3.09 (3.01), N 16.549 (16.26).

*7-(3,4-Dimethylphenyl)-9-phenylpyrido[3',2':4,5]thieno[3,2-d][1,2,4] triazolo[5,1-f]pyrimidine **4b**:* yellowish white solid (64%), mp >300 ^oC; IR ν max cm^{-1}: 2975 (stretching CH); Anal. for $C_{24}H_{17}N_5O_2S$ (439.50): Calcd. (Found) C 65.59 (65.51), H 3.90 (3.72), N 15.93 (16.12).

Synthesis 5a,b:

To a solution of compounds **3a,b** (20 mmol) in dry benzene (30 mL) acetyl chloride (20 mmol) was added dropwise with stirring. The reaction mixture was refluxed for 4 hours and after cooling poured into ice-cold water (50 mL). The precipitated product was collected by filtration and recrystallized from dioxane to give compounds **5a,b**.

*7-(Benzo-1,3-dioxol-5-yl)-2-methyl-9-phenylpyrido[3',2':4,5]thieno[3,2-d][1,2,4]triazolo[5,1-f]pyrimidine **5a**:* yellow solid (59%), mp 264 ^{o}C; IR ν max cm^{-1}: 2975 (stretching CH); ^{1}H NMR δ (ppm): 2.97 (s, 3H, CH_3), 6.10 (s, 2H, OCH_2O), 6.96-8.01 (m, 8H, ArH's), 8.18 (s, 1H, pyridine H) and 8.40 (s, 1H, pyrimidine H); MS: m/z = 437. Anal. for $C_{24}H_{15}N_5O_2S$ (437.48): Calcd. (Found) C 65.89 (65.71), H 3.46 (3.22), N 16.01 (16.22).

*7-(3,4-Dimethylphenyl)-2-methyl-9-phenylpyrido[3',2':4,5]thieno[3,2-d][1,2,4]triazolo[5,1-f]-pyrimidine **5b**:* white solid (57%), mp >300 ^{o}C; IR ν max cm^{-1}: 2982 (stretching CH); ^{1}H NMR δ (ppm): 2.89 (s, 3H, CH_3), 3.76, 3.81 (two s, 6H, two OCH_3), 6.92-8.09 (m, 8H, ArH's) , 8.18 (s, 1H, pyridine H) and 8.37 (s, 1H, pyrimidine H); Anal. for $C_{25}H_{19}N_5O_2S$ (453.53): Calcd. (Found) C 66.21 (66.10), H 4.22 (4.34), N 15.44 (15.12).

Synthesis of 6a,b:

A mixture of compounds **3a,b** (10 mmol) and diethyl oxalate (10 mmol) in absolute ethanol (20 mL) was refluxed for for 6 hours. On cooling, the precipitated product was collected by filtration and recrystallized from dioxane to give compounds **6a,b**.

*Ethyl 7-(benzo-1,3-dioxol-5-yl)-9-phenylpyrido[3',2':4,5]thieno[3,2-d][1,2,4]triazolo[5,1-f]-pyrimidine-2-carboxylate **6a**:* yellow crystal (61%), mp 286 ^{o}C; IR ν max cm^{-1}: 2975 (stretching CH), 1718 (ester CO); ^{1}H NMR δ (ppm): 1.11 (t, J = 7.2 Hz, 3H, $COOCH_2\mathbf{CH_3}$), 4.10 (q, J = 7.2 Hz, 2H, $COO\mathbf{CH_2}CH_3$), 6.12 (s, 2H, OCH_2O), 6.93-8.12 (m, 8H, ArH's), 8.25 (s, 1H, pyridine H) and 8.47 (s, 1H, pyrimidine H); ^{13}C NMR δ (ppm): 169.24 (ester CO), 163.12, 161.25, 159.01, 158.75, 158.01, 149.58, 148.71, 148.13, 147.26, 146.52, 141.27, 139.14, 137.86, 137.31, 129.54, 129.12, 127.34, 119.46, 116.34, 115.22, 107.55, 106.35 (22 aromatic carbons), 101.46 (OCH_2O), 60.22 (ester CH_2) and 14.61 (ester CH_3); MS: m/z = 495. Anal. for $C_{26}H_{17}N_5O_4S$ (495.52): Calcd. (Found) C 63.02 (63.30), H 3.46 (3.20), N 14.13 (14.25).

*Ethyl 7-(3,4-dimethoxyphenyl)-9-phenylpyrido[3',2':4,5]thieno[3,2-d][1,2,4]triazolo[5,1-f]-pyrimidine-2-carboxylate **6b**:* yellow crystal (58%), mp 296 ^{o}C; IR ν max cm^{-1}: 2971 (stretching CH), 1724 (ester

CO); ^{1}H NMR δ (ppm): 1.05 (t, J = 7.2 Hz, 3H, $COOCH_2\mathbf{CH_3}$), 3.72, 3.83 (two s, 6H, two OCH_3), 4.20 (q, J = 7.2 Hz, 2H, $COO\mathbf{CH_2}CH_3$), 6.87-7.95 (m, 8H, ArH's), 8.22 (s, 1H, pyridine H) and 8.42 (s, 1H, pyrimidine H); Anal. for $C_{27}H_{21}N_5O_4S$ (511.13): Calcd. (Found) C 63.39 (63.29), H 4.14 (3.58), N 13.69 (13.28).

Synthesis of 7a,b:

A mixture of compounds **3a,b,** ethanol (20 mL) and 10% KOH (5 mL) was refluxed for 2-3 hours. After cooling, the reaction mixture was poured into (50 mL) ice-cold water with stirring. The product was precipitated, collected by filtration and recrystallized from ethanol to give compounds **7a,b**.

*7-(Benzo-1,3-dioxol-5-yl)-4-hydrazino-9-phenylpyrido[3',2':4,5]thieno [3,2-d]pyrimidine **7a**:* 61%; yellow solid (63%), mp > 300^{o}C; IR ν max cm^{-1}: 3425, 3358, 3224 (NH_2, NH); ^{1}H NMR δ (ppm): 5.38 (s, 2H , NH_2^*) 6.12 (s, 2H, OCH_2O), 6.93-8.12 (m, 9H, NH^* and ArH's), 8.30 (s , 1H, pyridine H) and 8.40 (s , 1H, pyrimidine H); MS: m/z = 413. Anal. for $C_{22}H_{15}N_5O_2S$ (413.46): Calcd. (Found) C 63.91 (63.79), H 3.66 (3.81), N 16.94 (16.68).

*7-(3,4-Dimethylphenyl)-4-hydrazino-9-phenylpyrido[3',2':4,5]thieno [3,2-d]pyrimidine **7b**:* yellow solid (54%), mp >300 ^{o}C; IR ν max cm^{-1}: 3412, 3357, 3211 (NH_2, NH); ^{1}H NMR δ (ppm): 3.76, 3.88 (two s, 6H, two OCH_3), 5.62 (s, 2H, NH_2^*), 6.76-8.09 (m, 9H, NH^*, ArH's), 8.26 (s, 1H, pyridine H) and 8.46 (s, 1H, pyrimidine H); MS: m/z = 429. Anal. for $C_{23}H_{19}N_5O_2S$ (429.50): Calcd. (Found) C 64.32 (64.29), H 4.46 (4.61), N 16.31 (16.20).

Synthesis of 8a,b.

To a solution of 1**a,b** (10 mmol) in DMF (20 mL), carbon disulfide (15 mmol) and (10 mL) sodium methoxide (prepared from 0.59 g of sodium metal and 30 mL methanol) were added. The mixture was refluxed for 8-10 hours, and then poured into ice cold water. A solution of sodium hydroxide (10 mL, 1M) was added to it and left overnight. The solution was filtered and acidified with dilute acetic acid to give a yellow precipitate. It was collected, washed with dilute acetic acid, dried and recrystallized from ethanol to give compounds **8a,b**.

9-(Benzo-1,3-dioxol-5-yl)-7-phenyl-1,2,3,4-tetrahydropyrido[3',2':4,5] thieno[3,2-d]pyrimidine-2,4-dithione ***8a****:* yellow needle crystals (48%), mp 278 ^{o}C; IR ν max cm^{-1}: 3372, 3297 (two NH); ^{1}H NMR δ (ppm): 6.13 (s, 2H, OCH_2O), 6.94-7.98 (m, 8H, ArH's), 8.32 (s, 1H, pyridine H), 9.12 (s, 1H, NH*) and 9.74 (s, 1H, NH*); MS: m/z = 447. Anal. for $C_{22}H_{13}N_3O_2S_3$ (447.56): Calcd. (Found) C 59.04 (59.11), H 2.93 (2.75), N 9.39 (9.10).

9-(3,4-Dimethoxyphenyl)-7-phenyl-1,2,3,4-tetrahydropyrido[3',2':4,5] thieno-[3,2-d]-pyrimidine-2,4-dithione ***8b****:* yellow crystals (51%), mp 296 ^{o}C; IR ν max cm^{-1}: 3324, 3231 (two NH); ^{1}H NMR δ (ppm): 3.76, 3.83 (two s, 6H, two OCH_3), 6.83-7.97 (m, 8H, ArH's), 8.25 (s, 1H, pyridine H), 9.34 (s, 1H, NH*) and 9.92 (s, 1H, NH*); MS: m/z = 463. Anal. for $C_{23}H_{17}N_3O_2S_3$ (463.60): Calcd. (Found) C 59.59 (59.71), H 3.70 (3.56), N 9.06 (9.16).

Synthesis of (9,10):

A mixture of **1a,b** (10 mmol) and urea or thiourea (10 mmol) in absolute ethanol (30 mL) containing sodium ethoxide (10 mmol) was refluxed for 6-8 hours. The reaction mixture was left to cool at room temperature, then poured into ice-cold water (50 mL) and acidifed with dilute HCl, the separated product was filtered off recrystallized from dioxane to afford **9,10** respectively.

4-Amino-9-(benzo-1,3-dioxol-5-yl)-7-phenyl-1,2-dihydropyrido[3',2':4,5]thieno[3,2-d]-pyrimidine-2-one ***9a****:* yellow solid (52%), mp > 300 ^{o}C; IR ν max cm^{-1}: 3432, 3374 3229 (NH_2, NH), 1679 (amidic CO); ^{1}H NMR δ (ppm): 6.10 (s, 2H, OCH_2O), 6.95-7.99 (m, 8H, ArH's), 8.12 (s, 2H, NH_2^{*}), 8.32 (s, 1H, pyridine H) and 10.42 (s, 1H, NH*); MS: m/z = 414. Anal. for $C_{22}H_{14}N_4O_3S$ (414.45): Calcd. (Found) C 63.76 (63.59), H 3.40 (3.31), N 13.52 (13.66).

4-Amino-9-(3,4-dimethylphenyl)-7-phenyl-1,2-dihydropyrido[3',2':4,5] thieno[3,2-d]-pyrimidine-2-one ***9b****:* white solid (60%), mp >300 ^{o}C; IR ν max cm^{-1}: 3421, 3356, 3258 (NH_2, NH), 1668 (amidic CO); ^{1}H NMR δ (ppm): 3.79, 3.83 (two s, 6H, two OCH_3), 6.93-7.90 (m, 8H, ArH's), 8.17 (s, 2H, NH_2^{*}) 8.28 (s, 1H, pyridine H) and 11.21 (s, 1H,

NH*); MS: m/z = 430. Anal. for $C_{23}H_{18}N_4O_3S$ (430.49): Calcd. (Found) C 64.17 (64.32), H 4.21 (4.02), N 13.01 (12.89).

4-Amino-9-(benzo-1,3-dioxol-5-yl)-7-phenyl-1,2-dihydropyrido[3',2':4,5]thieno[3,2-d]-pyrimidine-2-thione ***10a****:* yellow solid (47%), mp 288 ^oC; IR ν max cm^{-1}: 3401, 3374, 3168 (NH_2, NH); ^1H NMR δ (ppm): 6.10 (s, 2H, OCH_2O), 6.96-7.95 (m, 8H, ArH's), 8.19 (s, 2H, NH_2*), 8.26 (s, 1H, pyridine H) and 11.06 (s, 1H, NH*); MS: m/z = 430. Anal. for $C_{22}H_{14}N_4O_2S_2$ (430.51): Calcd. (Found) C 61.38 (61.28), H 3.28 (2.95), N 13.01 (12.87).

4-Amino-9-(3,4-dimethoxyphenyl)-7-phenyl-1,2-dihydropyrido[3',2':4,5] thieno[3,2-d]-pyrimidine-2-thione ***10b****:* pale yellow solid (56%), mp >300 ^oC; IR ν max cm^{-1}: 3416, 3326, 3154 (NH_2, NH); ^1H NMR δ (ppm): 3.77, 3.83 (two s, 6H, two OCH_3), 6.81-7.95 (m, 8H, ArH's), 8.09 (s, 2H, NH_2*) 8.24 (s, 1H, pyridine H) and 11.21 (s, 1H, NH*); MS: m/z = 446. Anal. for $C_{23}H_{18}N_4O_2S_2$ (446.55): Calcd. (Found) C 61.86 (61.59), H 4.06 (3.87), N 12.55 (12.77).

Synthesis of (11,12):

A mixture of **1a,b** (10 mmol) and phenylisocyanate or phenylisothiocyanate (10 mmol) in dry pyridine (20 mL) was refluxed for 6 hours. The reaction mixture was cooled and poured into ice-water (50 mL) and neutralized with diluted HCl. The solid product so formed was collected by filtration and recrystallized from ethanol to give compounds **(11,12)** respectively.

9-(Benzo-1,3-dioxol-5-yl)-4-imino-3,7-diphenyl-1,2,3,4-tetrahydropyrido [3',2':4,5]thieno[3,2-d]pyrimidine-2-one ***11a****:* yellow solid (68%), mp 278 ^oC; IR ν max cm^{-1}: 3378, 3313 (two NH), 1675 (amidic CO); ^1H NMR δ (ppm): 6.12 (s, 2H, OCH_2O), 6.96-7.95 (m, 13H, ArH's), 8.32 (s, 1H, pyridine H), 8.82 (s, 1H, NH*) and 9.64 (s, 1H, NH*); MS: m/z = 490. Anal. for $C_{28}H_{18}N_4O_3S$ (490.54): Calcd. (Found) C 68.56 (68.64), H 3.70 (3.43), N 11.42 (11.52).

9-(3,4-Dimethylphenyl)-4-imino-3,7-diphenyl-1,2,3,4-tetrahydropyrido [3',2':4,5]thieno[3,2-d]-pyrimidine-2-one ***11b****:* pale yellow solid (72%), mp 286 ^oC; IR ν max cm^{-1}: 3395, 3328 (two NH), (amidic CO); ^1H NMR δ (ppm): 3.75, 3.80 (two s, 6H, two OCH_3), 6.89-8.02

(m, 13H, ArH's), 8.31 (s, 1H, pyridine H), 8.82 (s, 1H, NH^*) and 9.69 (s, 1H, NH^*); Anal. for $C_{29}H_{22}N_4O_3S$ (506.59): Calcd. (Found) C 68.76 (68.71), H 4.38 (4.05), N 11.06 (10.89).

9-(Benzo-1,3-dioxol-5-yl)-4-imino-3,7-diphenyl-1,2,3,4-tetrahydropyrido [3',2':4,5]thieno[3,2-d]pyrimidine-2-thione ***12a****:* yellowish white solid (76%), mp 266 ^oC; IR ν max cm^{-1} : 3396, 3324 (two NH); ^1H NMR δ (ppm): 6.10 (s, 2H, OCH_2O), 6.96-7.95 (m, 13H, ArH's), 8.28 (s, 1H, pyridine H), 8.82 (s, 1H, NH^*) and 9.64 (s, 1H, NH^*); MS: m/z = 506. Anal. for $C_{28}H_{18}N_4O_2S_2$ (506.61): Calcd. (Found) C 66.38 (66.28), H 3.58 (3.25), N 11.06 (11.34).

9-(3,4-Dimethoxyphenyl)-4-imino-3,7-diphenyl-1,2,3,4-tetrahydropyrido [3',2':4,5]thieno[3,2-d]pyrimidine-2-thione ***12b****:* pale yellow solid (67%), mp > 300 ^oC; IR ν max cm^{-1}: 3392, 3321 (two NH); ^1H NMR δ (ppm): 3.77, 3.83 (two s, 6H, two OCH_3), 6.78-7.84 (m, 13H, ArH's), 8.45 (s, 1H, pyridine H), 8.96 (s, 1H, NH^*) and 10.41 (s, 1H, NH^*); Anal. for $C_{29}H_{22}N_4O_2S_2$ (522.65): Calcd. (Found) C 66.65 (66.51), H 4.24 (406), N 10.72 (10.42).

Synthesis of (13, 14):

A mixture of **1a,b** (10 mmol), diethyl malonate or ethyl cyanoacetate (10 mmol), ammonium acetate (3 g) and acetic acid (10 mL) was heated with stirring in oil bath for 2 hours, left to cool and then triturated with ethanol. The solid products thus formed was collected by filtration and recrystallized from ethanol to give compounds **(13,14)** respectively.

Ethyl 4-amino-9-(benzo-1,3-dioxol-5-yl)-2-oxo-7-phenyl-1,2-dihydropyrido[3',2':4,5]thieno-[3,2-b]pyridine-3-carboxylate ***13a****:* yellow solid (54%), mp 296 ^oC; IR ν max cm^{-1}: 3412, 3324, 3215 (NH_2, NH), 1711 (ester CO) and 1659 (amidic CO); ^1H NMR δ (ppm): 1.04 (t, J = 7.2 Hz, 3H, $COOCH_2\mathbf{CH_3}$), 4.12 (t, J = 7.2 Hz, 2H, $COO\mathbf{CH_2}CH_3$), 5.80 (s, 2H, NH_2^*), 6.12 (s, 2H, OCH_2O), 6.91-7.86 (m, 8H, ArH's), 8.21 (s, 1H, pyridine H) and 8.82 (s, 1H, NH^*); MS: m/z = 485. Anal. for $C_{26}H_{19}N_3O_5S$ (485.52): Calcd. (Found) C 64.32 (64.36), H 3.94 (3.72), N 8.65 (8.52).

Ethyl 4-amino-9-(3,4-dimethylphenyl)-2-oxo-7-phenyl-1,2-dihydropyrido[3',2':4,5]thieno[3,2-b]pyridine-3-carboxylate ***13b****:*

orange solid (59%), mp > 300 ^{o}C; IR ν max cm^{-1}: 3432, 3316, 3214 (NH_2, NH), 1710 (ester CO) and 1648 (amidic CO); ^{1}H NMR δ (ppm): 1.05 (t, 3H, $COOCH_2\mathbf{CH_3}$), 3.78, 3.85 (two s, 6H, two OCH_3), 4.02 (t, 2H, $COO\mathbf{CH_2}CH_3$), 5.71 (s, 2H, NH_2^*), 6.74-7.67 (m, 8H, ArH's), 8.25 (s, 1H, pyridine H) and 8.73 (s, 1H, NH^*); ^{13}C NMR δ (ppm): 167.32 (ester CO), 163.51 (amidic CO), 162.34, 161.42, 159.29, 158.56, 157.24, 150.87, 149.61, 148.14, 147.36, 146.43, 141.34, 139.04, 137.56, 137.03, 129.47, 129.25, 127.11, 118.87, 116.48, 115.34, 107.65 (21 aromatic carbons), 60.14 (ester CH_2), 55.87, 55.79 (two OCH_3), and 14.54 (ester CH_3); MS: m/z = 501. Anal. for $C_{27}H_{23}N_3O_5S$ (501.57): Calcd. (Found) C 64.66 (64.47), H 4.62 (4.35), N 8.38 (8.15).

4-Amino-9-(benzo-1,3-dioxol-5-yl)-2-oxo-7-phenyl-1,2-dihydropyrido [3',2':4,5]thieno[3,2-b]-pyridine-3-carbonitrile ***14a****:* yellowish white solid (72%), mp > 300 ^{o}C; IR ν max cm^{-1}: 3415, 3396, 3233 (NH_2, NH), 2220 (CN) and 1640 (amidic CO); ^{1}H NMR δ (ppm): 5.62 (s, 2H, NH_2^*), 6.10 (s, 2H, OCH_2O), 6.81-7.84 (m, 8H, ArH's), 8.16 (s, 1H, pyridine H) and 9.02 (s, 1H, NH^*); MS: m/z = 438. Anal. for $C_{24}H_{14}N_4O_3S$ (438.47): Calcd. (Found) C 65.75 (65.91), H 3.22 (3.51), N 12.78 (12.52).

4-Amino-9-(3,4-dimethoxyphenyl)-2-oxo-7-phenyl-1,2-dihydropyrido [3',2':4,5]thieno[3,2-b]-pyridine-3-carbonitrile ***14b****:* pale yellow solid (61%), mp 294 ^{o}C; IR ν max cm^{-1}: 3421, 3321, 3216 (NH_2, NH), 2218 (CN) and 1637 (amidic CO); ^{1}H NMR δ (ppm): 3.76, 3.85 (two s, 6H, two OCH_3), 5.43 (s, 1H, NH^*), 6.75-7.80 (m, 13H, ArH's), 8.21 (s, 1H, pyridine H) and 8.91 (s, 1H, NH^*); MS: m/z = 454. Anal. for $C_{25}H_{18}N_4O_3S$ (454.51): Calcd. (Found) C 66.07 (65.87), H 3.99 (4.14), N 12.33 (12.22).

Diazotization of 3-aminothieno[2,3-b]pyridine-2-carbonitriles 1a,b:

A mixture of **1a,b** (10 mmol) in concentrated HCl (3 mL) was cooled to 0 - 5 °C under ice, and cooled sodium nitrite solution (1.5 g in 10 mL of water) was added to it dropwise during 15 minutes. The reaction mixture was then stirred for 30 minutes to give non-isolable diazonium salts **15a,b** which were used in the next step.

Coupling of diazonium salts 15a,b with active methylene compounds:

(Method A for synthesis of compounds 18a,b)

To an ice-cold mixture of each of active methylene compounds (10 mmol) (ethyl cyanoacetate, malononitrile and cyanoacetic acid hydrazide and anhydrous sodium acetate (50 mmol) in ethanol (50 mL) was added dropwise with stirring a solution of diazonium salts (10 mmol) (**15a,b**) over 15 minutes. The stirring was continued for 30 minutes and the reaction mixture then left for 2-3 hours at room temperature. The solid products thus formed was collected by filtration and recrystallized from ethanol to give compounds (**16-18)** respectively.

Ethyl 2-{[4-(benzo-1,3-dioxol-5-yl)-2-cyano-6-phenylthieno[2,3-b]pyridin-3-yl]hydrazono}-2-cyanoacetate ***16a****:* yellow solid (82 %), mp 242 ^{o}C; IR ν max cm^{-1}: 3328 (NH), 2221, 2212 (two CN) and 1719 (ester CO); ^{1}H NMR δ (ppm): 1.04 (t, J = 7.2 Hz, 3H, $COOCH_2\mathbf{CH_3}$), 4.12 (t, J = 7.2 Hz, 2H, $COO\mathbf{CH_2}CH_3$), 6.12 (s, 2H, OCH_2O), 6.91-7.86 (m, 8H, ArH's), 8.27 (s, 1H, pyridine H) and 11.03 (s, 1H, NH*); MS: m/z = 495. Anal. for $C_{26}H_{17}N_5O_4S$ (495.52): Calcd. (Found) C 63.02 (63.22), H 3.46 (3.15), N 14.13 (13.79).

Ethyl 2-{[4-(3,4-dimethoxyphenyl)-2-cyano-6-phenylthieno[2,3-b]pyridin-3-yl]-hydrazono}-2-cyanoacetate ***16b****:* orange solid (75 %), mp 268 ^{o}C; IR ν max cm^{-1}: 3289 (NH), 2223, 2217 (two CN) and 1722 (ester CO); ^{1}H NMR δ (ppm): 1.01 (t, J = 7.2 Hz, 3H, $COOCH_2\mathbf{CH_3}$), 3.75, 3.83 (two s, 6H, two OCH_3), 4.09 (t, J = 7.2 Hz, 2H, $COO\mathbf{CH_2}CH_3$), 6.84-7.79 (m, 8H, ArH's), 8.37 (s, 1H, pyridine H) and 11.23 (s, 1H, NH*); MS: m/z = 511. Anal. for $C_{27}H_{21}N_5O_4S$ (511.56): Calcd. (Found) C 63.39 (63.11), H 4.14 (3.89), N 13.69 (13.51).

2-{[4-(Benzo-1,3-dioxol-5-yl)-2-cyano-6-phenylthieno[2,3-b]pyridin-3-yl]-hydrazono}-malononitrile ***17a****:* yellow solid (62%), mp 258 ^{o}C; IR ν max cm^{-1}: 3314 (NH) and 2226, 2218 (three CN); ^{1}H NMR δ (ppm): 6.11 (s, 2H, OCH_2O), 6.91-7.86 (m, 8H, ArH's), 8.23 (s, 1H, pyridine H) and 10.98 (s, 1H, NH*); MS: m/z = 448. Anal. for $C_{24}H_{12}N_6O_2S$ (448.47): Calcd. (Found) C 64.28 (64.61), H 2.70 (2.93), N 18.74 (18.56).

*2-{[2-Cyano-4-(3,4-dimethylphenyl)-6-phenylthieno[2,3-b]pyridin-3-yl]hydrazono}-malononitrile **17b**:* yellow solid (59%), mp 266 ^{o}C; IR ν max cm^{-1}: 3321 (NH) and 2223, 2214 (three CN); ^{1}H NMR δ (ppm): 3.78, 3.85 (two s, 6H, two OCH_3), 6.76-7.77 (m, 8H, ArH's), 8.30 (s, 1H, pyridine H) and 11.21 (s, 1H, NH*); MS: m/z = 464. Anal. for $C_{25}H_{16}N_6O_2S$ (464.51): Calcd. (Found) C 64.64 (64.75), H 3.47 (3.46), N 18.09 (18.21).

Reactions of 16a,b and 17a,b with hydrazine hydrate: (Method B for synthesis of compounds 18a,b)

A mixture of each of compounds **16, 17** (10 mmol), hydrazine hydrate (10 mmol) in ethanol (30 mL) was heated under reflux for 2-3 hours. The solvent was concentrated and the reaction mixture was allowed to cool. The solid products thus formed was collected by filtration and recrystallized from ethanol to give compounds **18-19** respectively.

*3-(3-Amino-5-oxo-1,5-dihydropyrazol-4-ylidene)hydrazino-4-(benzo-1,3-dioxol-5-yl)-6-phenylthieno[2,3-b]pyridine-2-carbonitrile **18a**:* yellow solid (65%), mp 284 ^{o}C; IR ν max cm^{-1}: 3412, 3354, 3178 (NH_2, two NH), 2217 (CN) and 1654 (amidic CO); ^{1}H NMR δ (ppm): 5.70 (s, 2H, NH_2^{*}), 6.09 (s, 2H, OCH_2O), 6.91-7.86 (m, 8H, ArH's), 8.29 (s, 1H, pyridine H), 10.34 (s, 1H, NH*) and 11.16 (s, 1H, NH*); MS: m/z = 481. Anal. for $C_{24}H_{15}N_7O_3S$ (481.50): Calcd. (Found) C 59.87 (59.93), H 3.14 (3.01), N 20.36 (20.51).

*3-(3-Amino-5-oxo-1,5-dihydropyrazol-4-ylidene)hydrazino-4-(3,4-dimethyl-phenyl)-6-phenyl-thieno[2,3-b]pyridine-2-carbonitrile **18b**:* orange solid (59%), mp 278 ^{o}C; IR ν max cm^{-1}: 3432, 3297, 3205 (NH_2, two NH), 2225 (CN) and 1643 (amidic CO); ^{1}H NMR δ (ppm): 3.71, 3.80 (two s, 6H, two OCH_3), 5.75 (s, 2H, NH_2^{*}), 6.72-7.81 (m, 8H, ArH's), 8.34 (s, 1H, pyridine H), 10.65 (s, 1H, NH*) and 11.35 (s, 1H, NH*). Anal. for $C_{25}H_{19}N_7O_3S$ (497.54): Calcd. (Found) C 60.35 (60.25), H 3.85 (3.58), N 19.71 (19.54).

*4-(Benzo-1,3-dioxol-5-yl)-3-(3,5-diamino-1H-pyrazol-4-yl)diazo-6-phenylthieno-[2,3-b]-pyridine-2-carbonitrile **19a**:* yellow solid (59%), mp 277 ^{o}C; IR ν max cm^{-1}: 3412, 3324, 3258, 3215 (two NH_2, NH)

and 2224 (CN); ^{1}H NMR δ (ppm): 5.42, 5.85 (two s, 4H, two NH_2^*), 6.12 (s, 2H, OCH_2O), 6.91-7.86 (m, 8H, ArH's), 8.32 (s, 1H, pyridine H) and 10.21 (s, 1H, NH^*); MS: m/z = 480. Anal. for $C_{24}H_{16}N_8O_2S$ (480.51): Calcd. (Found) C 59.99 (60.12), H 3.36 (3.24), N 23.32 (23.06).

3-(3,5-Diamino-1H-pyrazol-4-yl)diazo-4-(3,4-dimethylphenyl)-6-phenylthieno[2,3-b]-pyridine-2-carbonitrile ***19b****:* orange solid (66%), mp 294 ^{o}C; IR ν max cm^{-1}: 3432, 3316, 3259, 3214 (two NH_2, NH) and 22218 (CN); ^{1}H NMR δ (ppm): 3.78, 3.85 (two s, 6H, two OCH_3), 5.24, 5.78 (two s, 4H, two NH_2^*), 6.89-7.97 (m, 8H, ArH's), 8.37 (s, 1H, pyridine H) and 10.65 (s, 1H, NH^*); Anal. for $C_{25}H_{20}N_8O_2S$ (496.55): Calcd. (Found) C 60.47 (60.60), H 4.06 (4.03), N 22.57 (22.43).

Reactions of 17a,b with hydroxylamine hydrochloride:

A mixture of **17a,b** (10 mmol), hydroxylamine hydrochloride (10 mmol) and sodium acetate (20 mmol) in ethanol (30 mL) was heated under reflux for 2 hours. The solvent was concentrated and the reaction mixture was allowed to cool. The solid products thus formed was collected by filtration and recrystallized from ethanol to give compounds **20a,b**.

4-(Benzo-1,3-dioxol-5-yl)-3-(3,5-diamino-5-oxo-isoxazol-4-yl)diazo-6-phenyl-thieno[2,3-b]-pyridine-2-carbonitrile ***20a****:* yellow solid (54%), mp 284 ^{o}C; IR ν max cm^{-1}: 3412, 3324, 3215 (two NH_2) and 2218 (CN); ^{1}H NMR δ (ppm): 4.15 (t, 2H, COO**CH_2**CH_3), 5.55, 5.89 (two s, 4H, two NH_2^*), 6.10 (s, 2H, OCH_2O), 6.91-7.86 (m, 8H, ArH's) and 8.27 (s, 1H, pyridine H); MS: m/z = 481. Anal. for $C_{24}H_{15}N_7O_3S$ (481.50): Calcd. (Found) C 59.87 (59.66), H 3.14 (3.40), N 20.36 (20.56).

3-(3,5-Diamino-5-oxo-isoxazol-4-yl)diazo-4-(3,4-dimethylphenyl)-6-phenyl-thieno[2,3-b]-pyridine-2-carbonitrile ***20b****:* orange solid (51%), mp 266 ^{o}C; IR ν max cm^{-1} : 3432, 3316, 3214 (two NH_2) and 2229 (CN); ^{1}H NMR δ (ppm): 3.78, 3.85 (two s, 6H, two OCH_3), 5.34, 5.81 (two s, 4H, two NH_2^*), 6.89-7.97 (m, 8H, ArH's) and 8.31 (s, 1H, pyridine H); MS: m/z = 497. Anal. for $C_{25}H_{19}N_7O_3S$ (497.54): Calcd. (Found) C 60.35 (60.39), H 3.85 (3.65), N 19.71 (19.59).

References

1. Y. M. Elkholy, M. A. Morsy; *Molecules*, **2006**, 11, 890.
2. S. A. El-Assiery, G. H. Sayed, A. Fouda; *Acta Pharm.*, **2004**, 54, 143.
3. A. M. M. El-Saghier; *Molecules*, **2002**, 7, 756.
4. A. M. El-Agrody, M. S. Abd El-Latif, N. A. El-Hady, A. H. Fakery, A. H. Bedair; *Molecules*, **2001**, 6, 519.
5. E. I. Al-Afaleq, S. A. Abubshait; *Molecules*, **2001**, 6, 621.
6. T. T. Raj. S. Y. Ambekar; *J. Indian Chem. Soc.*, **1990**, 67, 260.
7. A. K. K. El-Louh, N. M. Abunada, S. M. El-Abbady, M. J. El-Shobaki; *Asian Journal of Chemistry*, **2007**, 19, 1283.
8. A. K. K. El-Louh, N. M. Abunada, N. J. Khudeir; *J. Al-Azhar University-Gaza (Natural Science)*, **2006**, 8, 13.
9. F. A. Attaby, S. M. Eldin, M. A. A. Elneairy, A. K. K. El-Louh; *Phosphorous, Sulfur and Silicon and Related Elements*, **2004**, 179, 2205.
10. M. A. A. Elneairy, S. M. Eldin, F. A. Attaby, A. K. K. El-Louh; *Phosphorous, Sulfur, and Silicon and Related Elements*, **2000**, 167, 289.
11. F. A. Attaby, L. A. Ibrahim, S. M. Eldin, A. K. K. El-Louh; *Phosphorous, Sulfur and Silicon and Related Elements*, **1992**, 73, 127.
12. A. Mongevega, I. Aldama, M. M. Robbani, E. Fernandez-Alvarez; *J. Heterocycl. Chem.*, **1980**, 17, 77.
13. J. H. Bellary, V. V. Badiger; *Indian J. Chem.*, **1981**, 20B, 654.
14. K. C. Joshi, P. Chand; *J. Heterocycl.*, **1980**, 17, 1783.
15. M. S. K. Yossef, Kh. M. Hssan, F. M. Atta, M. S. Abbady; *J. Heterocycl. Chem.*, **1984**, 21, 1565.
16. K. T. Pottus, S. Husain; *J. Org. Chem.*, **1971**, 36, 10.
17. P. K. Bridson, R. A. Davis, L. S. Renner; *J. Heterocycl. Chem.*, **1985**, 22, 753.
18. Y. Saito, M. Yasushi, M. Sakoshita, K. Toyda, T. Shibazalti; *European Patent Appl.*, **1993**, 535,548; C. A. **1993**, 119, 117112.
19. S. Furuya, N. Takeru, H. Matsumoto; *Jpn Kokai Tokkyo Koho JP 09 169 766*, **1997**; C. A. **1997**, 127, 176416.

20. S. Furuya, N. Choho, N. Suzuki, T. Imada; *PCT Int. Appl. WO 000 00 493* **2000**, C. A., **2000**, 132, 64179.
21. M. A. M. Gad-Elkareem, A. M. Abdel-Fattah, M. A. A. Elneairy; *Phosphorus, Sulfur, and Silicon*, **2006**, 181, 891.
22. C. G. Dave, P. R. Shah, A. B. Shah, K. C. Dave, V. J. Patel; *J. Indian Chem. Soc.*, **1989**, 66, 48.
23. E. Bousquent, G. Romero, F. Guerrera, A. Caruso, M. A. Roxas; *Farmaco Ed. Sci.*, **1985**, 40, 869.
24. S. Leistner, G. Wagner, M. Guestschaeo, E. Glusa; *Pharmazie,* **1986**, 41, 54.
25. G. Wagner, S. Leistner, H. Vieweg, U. Krasselt, J. Prantz; *Pharmazie,* **1993**, 48, 342.
26. N. Boehm, U. Krasselt, S. Leistner, G. Wagner; *Pharmazie,* **1992**, 47, 897.
27. A. E. Abdel-Rahman, E. A. Bakhite, E. A. Al-Taifi; *J. Chin. Chem. Soc.*, **2002**, 49, 223.
28. A. M. Hussein, F. A. Abu-Shanab, E. A. Ishak; *Phosphorus, Sulfur, and Silicon*, **2000**, 159, 55.