Synthesis of Some Aryl Thienopyridine, Pyridothienopyrimidine, and Pyridothienotriazolopyrimidine Derivatives

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Abstract: Synthesis of 2-thioxopyridine-3-carbonitriles **3a-d** and their reaction with chloroacetonitrile **4a** or chloroacetamide **4b** afforded pyridin-2-ylthioacetonitriles **5a-d** and pyridin-2-ylthioacetamides **6a-d**, respectively, which on cyclization gave the corresponding 3-aminothienopyridine derivatives **7a-d** and **8a-d**. Reaction of triethyl orthoformate in acetic anhydride gave with **7a-d** 3-ethoxymethylenethienopyridine derivatives **9a-d** which on their reaction with hydrazine hydrate yielded 3-amino-4-imino-3,4-dihydropyridothienopyrimidine derivatives **10a-d**. Reaction of triethyl orthoformate with **10a-d** produced pyridothienotriazolopyrimidine derivatives **11a-d**, where Dimroth rearrangement yielded 4-hydrazinopyridothienopyrimidine derivatives **12a-d**. On the other hand reaction of **8a-d** with triethyl orthoformate in acetic anhydride gave pyridothienopyrimidine-4-one derivatives **13a-d**, which on their chlorination produced 4-chloropyridothienopyrimidine derivatives **14a-d**, and treatment with hydrazine hydrate authenticated **12a-d**. Reaction of compounds **8a-d** with nitrous acid afforded 3,4-dihydropyridothienotriazin-4-ones **15a**,**b**,**d**. Compounds **12a-d** reacted with benzaldehyde, diethylmalonate, and acetylacetone, to give 4-benzylidinehydrazinopyridopyrimidines **16a-d**, ethyl 1,2,4-triazolopyridothienopyrimidin-3-ylacetates **17a-d**, and 4-(3,5-dimethylpyrazolo)pyridothienopyrimidines **18a-d**, respectively.

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1. Introduction

Several thienopyridines have been synthesized and their pharmaceutical medicinal activities evaluated and used as diabetes mellitus,[1-3] analgesics and anti-inflammatories,[4-6] sedatives,[3] anticoagulants,[6] anti-artherossclerotics,[7] and gonaodotropin releasing hormone antagonists.[8,9] Moreover the pyridothienopyrimidines showed analgesic,[10,11] antipyretic,[12] anti-inflammatories,[13] antianaphylactic,[14,15] and antimicrobial [16,17] activities.

In our previous work to synthesize some thienopyridine and pyridothienopyrimidine derivatives,[18-23] the formation of o-aminonitrile[24-29] in 3-aminothienopyridine-2-carbonitrile derivatives **7-8**, which is expected to have biological activities, attracted us to extend this work and synthesize more new thienopyridine, pyridothienopyrimidine and annulated thienopyridine derivatives.

2. Experimental

All melting points are uncorrected and measured on a Gallenkamp apparatus. IR spectra were recorded on a Pye Unicam SP 3-300 and a Shimadzu FT IR 8101 PC IR spectrophotometer (KBr pellets). ^{1}H and ^{13}C-NMR spectra were recorded on a Varian Mercury VX-300 MHz NMR spectrometer in DMSO-d_6 solution using TMS as an internal reference. Electron impact mass spectra were obtained with a 70 eV Shimadzu GCMS-QP 1000 EX spectrometer also elemental analyses were carried out in Micro Analytical Center, Cairo University, Giza, Egypt.

A mixture of (0.01 mol) cyanothioacetamide[30-32] **1** and, -unsaturated carbonyl compounds[33] (**2a-d**); (E)-3-(benzo[d][1,3]dioxol-5-yl)-1-(naphthalen-1-yl)prop-2-en-1-one **2a**, (E)-3-(benzo[d][1,3]dioxol-5-yl)-1-(naphthalen-2-yl)prop-2-en-1-one **2b**, (E)-3-(3,4-dimethoxyphenyl)-1-(naphthalen-1-yl)prop-2-en-1-one **2c**, or (E)-3-(3,4-dimethoxyphenyl)-1-(naphthalen-2-yl)prop-2-en-1-one **2d**, was refluxed in absolute ethanol (25 mL) containing (0.3 mL) piperidine for 5-6 hrs. The reaction mixture was concentrated and cooled to give products which on filtration and crystallization from the appropriate solvent gave 2-thioxo-1,2-dihydropyridine-3-carbonitrile derivatives **3a-d**, respectively.

To a stirred mixture of **3a-d** (0.01 mol) and sodium methoxide (0.01 mol) in methanol (30 mL), chloroacetonitrile **4a** or chloroacetamide **4b** (0.01 mol) was added portion wise. The stirring was continued for 2-3 hrs at room temperature. The product formed was filtered, washed with cold

ethanol and crystallized from the proper solvent to give 3-cyanopyridin-2-ylthioacetonitriles **5a-d** or 3-cyanopyridine-2-ylthioacetamide derivatives **6a-d**, respectively.

Cyclization of **5a-d** and **6a-d** (0.01 mol) by their reflux with 10% KOH solution for 2 hrs followed by cooling and acidification with HCl gave the corresponding 3-aminothieno[2,3-b]pyridine **7a-d** and **8a-d**, respectively which were crystallized from the suitable solvent.

A solution of **7a-d** (0.01 mol) was refluxed with triethyl orthoformate (0.02 mol) in acetic anhydride (30 mL) for 4 hrs. The reaction mixture was cooled, the product obtained filtered, washed and crystallized from the proper solvent, to give 3-(ethoxymethyleneamino)thieno[2,3-b]pyridine derivatives **9a-d** respectively.

To a stirred cold solution of compounds **9a-d** (0.01 mol) in (20 mL) ethanol, (3 mL) of 99% hydrazine hydrate was added drop wise. The reaction mixture was continuously stirred at room temperature for 6 hrs and left overnight. The solids precipitated was filtered, washed with cold ethanol and purified by crystallization from the proper solvent to give the corresponding 3-amino-4-imino-3,4-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine **10a-d**, respectively.

A solution of **10a-d** (0.01 mol) in triethyl orthoformate (0.025 mol) was refluxed for 1-2 hrs and left overnight. The precipitated product was collected by filtration and crystallized from the proper solvent to give pyrido[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[5,1-*f*]pyrimidine derivatives **11a-d**, respectively.

Treatment of **10a-d** (0.01 mol) by their reflux with 10% KOH solution for 2 hrs followed by cooling and acidification with HCl gave the corresponding 4-hydrazinopyridothienopyrimidine **12a-d**, respectively due to Dimroth rearrangement**.** The products were crystallized from the suitable solvent.

Reaction of **8a-d** (0.01 mol) with triethyl orthoformate (0.02 mol) in acetic anhydride (30 mL) for 4 hrs, followed by cooling the reaction mixture filtration of the product, and crystallization from the proper solvent gave pyridothienopyrimidine-4-one derivatives **13a-d**, respectively.

Chlorination of **13a-d** (0.01 mol) took place by its heating under reflux with $POCl_3$ (15 mL) for 4 hrs. The reaction mixture was cooled then poured with vigorous stirring on ice-cold water. The products formed were filtered, and crystallized from the proper solvent to give 4-chloropyridothienopyrimidine derivatives **14a-d**, respectively.

Reflux of **14a-d** (0.01 mol) with 3 mL hydrazine hydrate in 30 mL ethanol for 2-3 hrs gave after cooling the corresponding compounds **12a-d**, respectively.

Sodium nitrite solution (12 mL, 10%,) was added to a solution of **8a**,**b**,**d** (0.01mol) in conc. H_2SO_4 (5 mL) and glacial CH_3COOH (5 mL) at 0 °C over 5 min with stirring. The precipitated solids were filtered and crystallized from the proper solvent to give 3,4-dihydropyrido[3',2':4,5]thieno[3.2-*d*][1,2,3]triazin-4-one derivatives **15a**,**b**,**d**, respectively.

A mixture of **12a-d** (0.01 mol) and benzaldehyde (0.01 mol) in absolute ethanol (25 mL) was refluxed for 3 hrs. The solid that precipitated on cooling was collected and crystallized from the proper solvent to give 4-benzylidinehydrazinopyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine derivatives **16a-d**, respectively.

Reaction of **12a-d** (0.01 mol) with diethyl malonate (15 mL) in presence of few drops of acetic acid under reflux for 2 hrs gave an oily product which was triturated with ethanol (20 mL) to form white solid. The products were crystallized from the proper solvents to give the corresponding ethyl 1,2,4-triazolo[4",3"-*c*]pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-3-ylacetate **17a-d**, respectively.

A mixture of **12a-d** (0.01 mol) and acetyl acetone (5 mL) were heated under reflux for 4 hrs. The reaction products were solidified by their triturated with ethanol. The products were crystallized from the proper solvent to give 4-(3,5-dimethylpyrazolo)pyrido[3',2':4,5]thieno[3, 2-*d*]pyrimidine derivatives, **18a-d**, respectively.

4-(Benzo-1,3-dioxol-5-yl)-6-(1-naphthyl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile (3a): Crystallized from ethanol as orange solid (58%), mp 274 °C. IR: ν (cm-1) = 3349 (NH) and 2217 (CN). 1H-NMR: δ (ppm) = 6.11 (s, 2H, OCH_2O), 6.96 - 7.91 (m, 11H, Ar-H), 13.21 (br., 1H, NH). 13C-NMR: δ (ppm) = 176.1 (C=S), 161.6, 159.8, 157.5, 154.8, 154.3, 152.7, 151.5, 151.0, 149.7, 148.3, 147.3, 146.6, 145.3, 141.6, 137.1, 126.7, 120.3, 117.3, 114.2, 109.6, 108.5 (Ar-C, CN), 101.2 (OCH_2O). MS: m/z = 382. Analysis for $C_{23}H_{14}N_2O_2S$ (382.44): Calcd. (Found) = C 72.23 (71.39), H 3.69 (3.82), N 7.32 (7.25), S 8.38 (8.12).

4-(Benzo-1,3-dioxol-5-yl)-6-(2-naphthyl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile (3b): Crystallized from ethanol as yellow solid (74%), mp 256 °C. IR: ν (cm^{-1}) = 3351 (NH) and 2224 (CN). ^{1}H-NMR: δ (ppm) = 6.15 (s, 2H, OCH_2O), 6.86-7.98 (m, 11H, Ar-H), 13.11 (br., 1H, NH). MS: m/z = 382. Analysis for $C_{23}H_{14}N_2O_2S$ (382.44): Calcd. (Found) = C 72.23 (72.41), H 3.69 (3.79), N 7.33 (7.42), S 8.38 (8.17).

4-(3,4-Dimethoxyphenyl)-6-(1-naphthyl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile (3c): Crystallized from ethanol as orange solid (52%), mp 268 °C. IR: ν (cm^{-1}) = 3321 (NH) and 2218 (CN). ^{1}H-NMR: δ (ppm) = 3.72, 3.84 (2 s, 6H, 2 × OCH_3), 6.79-7.90 (m, 11H, Ar-H), 13.74 (br., 1H, NH). MS: m/z = 398. Analysis for $C_{24}H_{18}N_2O_2S$ (398.49): Calcd. (Found) = C 72.23 (71.39), H 3.69 (3.82), N 7.33 (7.25), S 8.05 (8.25).

4-(3,4-Dimethoxyphenyl)-6-(2-naphthyl)-2-thioxo-1,2-dihydropyridine-3-carbonitrile (3d): Crystallized from ethanol as orange solid (54%), mp 286 °C. IR: ν (cm^{-1}) = 3372 (NH) and 2222 (CN). ^{1}H-NMR: δ (ppm) = 3.72, 3.84 (2 s, 6H, 2 × OCH_3), 6.72-7.93 (m, 11H, Ar-H), 13.61 (br., 1H, NH). MS: m/z = 398. Analysis for $C_{24}H_{18}N_2O_2S$ (398.49): Calcd. (Found) = C 72.23 (71.38), H 3.69 (3.58), N 7.32 (7.25), S 8.05 (7.89).

[4-(Benzo-1,3-dioxol-5-yl)-3-cyano-6-(1-naphthyl)pyridin-2-yl]thioacetonitrile (5a): Crystallized from ethanol as yellow solid (86%), mp 166 °C. IR: ν (cm^{-1}) = 2222, 2216 (2 × CN). ^{1}H-NMR: δ (ppm) = 3.92 (s, 2H, SCH_2) 6.15 (s, 2H, OCH_2O), 6.92-8.01 (m, 11H, ArH's). ^{13}C-NMR: δ (ppm) = 160.3, 158.6, 157.7, 156.2, 154.3, 153.1, 152.6, 152.0, 149.3, 148.5, 147.1, 146.2, 145.5, 142.3, 139.3, 127.6, 120.3, 119.1, 116.4, 115.2, 110.5, 108.6 (Ar-C, CN), 101.1 (OCH_2O), 33.95 (SCH_2). MS: m/z = 421. Analysis for $C_{25}H_{15}N_3O_2S$ (421.47): Calcd. (Found) = C 71.24 (71.02), H 3.59 (3.42), N 9.97 (9.74), S 7.61 (7.34).

[4-(Benzo-1,3-dioxol-5-yl)-3-cyano-6-(2-naphthyl)pyridin-2-yl]thioacetonitrile (5b): Crystallized from ethanol as yellow solid (81%), mp 184 °C. IR: ν (cm^{-1}) = 2223, 2218 (2 × CN). ^{1}H-NMR: δ (ppm) = 3.90 (s, 2H, SCH_2), 6.12 (s, 2H, OCH_2O), 6.90-8.05 (m, 11H, Ar-H). MS: m/z = 421. Analysis for $C_{25}H_{15}N_3O_2S$ (421.48): Calcd. (Found) = C 71.24 (71.41), H 3.59 (3.67), N 9.97 (9.79), S 7.61 (7.55).

[3-Cyano-4-(3,4-dimethoxyphenyl)-6-(1-naphthyl)pyridin-2-yl]thioacetonitrile (5c): Crystallized from dioxane as orange solid (81%), mp 172 °C. IR: ν (cm^{-1}) = 2221, 2214 (2 × CN). ^{1}H-NMR: δ (ppm) = 3.73, 3.87 (2 s, 6H, 2 × OCH_3), 3.97 (s, 2H, SCH_2), 6.79-7.90 (m, 11H, Ar-H). MS: m/z = 437. Analysis for $C_{26}H_{19}N_3O_2S$ (437.52): Calcd. (Found) = C 71.38 (71.35), H 4.38 (4.57), N 9.60 (9.54), S 7.33 (7.08).

[3-Cyano-4-(3,4-dimethoxyphenyl)-6-(2-naphthyl)pyridin-2-yl]thioacetonitrile (5d): Crystallized from dioxane as orange solid (77%), mp 186 °C. IR: ν (cm^{-1}) = 2223, 2217 (2 × CN). ^{1}H-NMR: δ (ppm) = 3.71, 3.85 (2 s, 6H, 2 × OCH_3), 3.98 (s, 2H, SCH_2), 6.99-7.98 (m, 11H, Ar-H). MS: m/z = 437. Analysis for $C_{26}H_{19}N_3O_2S$ (437.52): Calcd. (Found) = C 71.38 (71.41), H 4.38 (4.22), N 9.60 (9.64), S 7.33 (7.12).

[4-(Benzo-1,3-dioxol-5-yl)-3-cyano-6-(1-naphthyl)pyridin-2-yl]thioacetamide (6a): Crystallized from ethanol as yellow solid (57%), mp 176 °C. IR: ν (cm^{-1}) = 3412, 3247, (NH_2), 2221 (CN), 1663 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.87 (s, 2H, SCH_2), 6.11 (s, 2H, OCH_2O), 6.34 (br., 2H, NH_2), 6.95-8.11 (m, 11H, Ar-H). MS: m/z = 439. Analysis for $C_{25}H_{17}N_3O_3S$ (439.49): Calcd. (Found) = C 68.32 (68.12), H 3.90 (3.88), N 9.56 (9.66), S 7.30 (7.02).

2-{[4-(Benzo-1,3-dioxol-5-yl)-3-cyano-6-(2-naphthyl)pyridin-2-yl]thio}acetamide (6b): Crystallized from ethanol as yellow solid (69%), mp 182 °C. IR: ν (cm^{-1}) = 3421, 3265 (NH_2), 2219 (CN), 1668 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.93 (s, 2H, SCH_2), 6.13 (s, 2H, OCH_2O), 6.44 (br., 2H, NH_2), 6.86-8.00 (m, 11H, Ar-H). MS: m/z = 439. Analysis for $C_{25}H_{17}N_3O_3S$ (439.49): Calcd. (Found) = C 68.32 (68.45), H 3.90 (3.83), N 9.56 (9.81), S 7.30 (7.10).

[3-Cyano-4-(3,4-dimethoxyphenyl)-6-(1-naphthyl)pyridin-2-yl]thioacetamide (6c): Crystallized from ethanol as yellow solid (81%), mp 172 °C. IR: ν (cm^{-1}) = 3411, 3298 (NH_2), 2216 (CN), 1665 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.71, 3.85 (2 s, 6H, 2 ×OCH_3), 3.94 (s, 2H, SCH_2), 6.37 (br., 2H, NH_2), 6.79-7.90 (m, 11H, Ar-H). MS: m/z = 455. Analysis for $C_{26}H_{21}N_3O_3S$ (455.54): Calcd. (Found) = C 68.55 (68.66), H 4.65 (4.57), N 9.22 (9.01), S 7.04 (7.33).

[3-Cyano-4-(3,4-dimethoxyphenyl)-6-(2-naphthyl)pyridin-2-yl]thioacetamide (6d): Crystallized from ethanol as yellow solid (88%), mp 184 °C. IR: ν (cm^{-1}) = 3441, 3335 (NH_2), 2220 (CN), 1662 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.72, 3.86 (2 s, 6H, 2 × OCH_3), 3.98 (s, 2H, SCH_2), 6.52 (br., 2H, NH_2), 6.79-7.90 (m, 11H, Ar-H). MS: m/z = 455. Analysis for $C_{26}H_{21}N_3O_3S$ (455.53): Calcd. (Found) C = 68.55 (68.54), H 4.65 (4.54), N 9.22 (9.36), S 7.04 (7.32).

3-Amino-4-(benzo-1,3-dioxol-5-yl)-6-(1-naphthyl)thieno[2,3-*b*]pyridine-2-carbonitrile (7a): Crystallized from ethanol as orange solid (57%), mp 274 °C. IR: ν (cm^{-1}) = 3428, 3187 (NH_2), 2218 (CN). ^{1}H-NMR: δ (ppm) = 6.67 (br., 2H, NH_2), 6.14 (s, 2H, OCH_2O), 6.86-7.97 (m, 11H, Ar-H). MS:

m/z = 421. Analysis for $C_{25}H_{15}N_3O_2S$ (421.48): Calcd. (Found) = C 71.24 (71.07), H 3.59 (3.81), N 9.97 (10.2), S 7.61 (7.35).

3-Amino-4-(benzo-1,3-dioxol-5-yl)-6-(2-naphthyl)thieno[2,3-*b*]pyridine-2-carbonitrile (7b): Crystallized from ethanol as yellow solid (91%), mp 246 °C. IR: ν (cm^{-1}) = 3421, 3175 (NH_2), 2220 (CN). ^{1}H-NMR: δ (ppm) = 5.57 (br., 2H, NH_2), 6.12 (s, 2H, OCH_2O), 6.88-8.59 (m, 11H, Ar-H). MS: m/z = 421. Analysis for $C_{25}H_{15}N_3O_2S$ (421.48): Calcd. (Found) = C 71.24 (71.32), H 3.59 (3.93), N 9.97 (9.75), S 7.61 (7.88).

3-Amino-4-(3,4-dimethoxyphenyl)-6-(1-naphthyl)thieno[2,3-*b*]pyridine-2-carbonitrile (7c): Crystallized from ethanol-acetic acid mixture (4:1) as yellow solid (57%), mp 262 °C. IR: ν (cm^{-1}) = 3415, 3347 (NH_2), 2221 (CN). ^{1}H-NMR: δ (ppm) = 3.71, 3.85 (2 s, 6H, 2 × OCH_3), 5.83 (br., 2H, NH_2), 6.99-8.01 (m, 11H, Ar-H). MS: m/z = 437. Analysis for $C_{26}H_{19}N_3O_2S$ (437.52): Calcd. (Found) = C 71.38 (71.22), H 4.38 (4.40), N 9.60 (9.74), S 7.33 (7.11).

3-Amino-4-(3,4-dimethoxyphenyl)-6-(2-naphthyl)thieno[2,3-*b*]pyridine-2-carbonitrile (7d): Crystallized from ethanol-acetic acid mixture (4-1) as yellow solid (90%), mp 274 °C. IR: ν (cm^{-1}) = 3421, 3344 (NH_2), 2220 (CN). ^{1}H-NMR: δ (ppm) = 3.72, 3.87 (2 s, 6H, 2 × OCH_3), 5.92 (br., 2H, NH_2), 6.87-8.00 (m, 11H, Ar-H). MS: m/z = 437. Analysis for $C_{26}H_{19}N_3O_2S$ (437.52): Calcd. (Found) = C 71.38 (71.28), H 4.38 (4.27), N 9.60 (9.55), S 7.33 (7.04).

3-Amino-4-(benzo-1,3-dioxol-5-yl)-6-(1-naphthyl)thieno[2,3-*b*]pyridine-2-carboxamide (8a): Crystallized from dioxane as yellow solid (74%), mp 258 °C. IR: ν (cm^{-1}) = 3428, 3356, 3267, 3187 (2 ×NH_2), 1668 (amidic CO). ^{1}H-NMR: δ (ppm) = 5.87 (br., 2H, NH_2), 6.14 (s, 2H, OCH_2O), 6.89-7.99 (m, 11H, Ar-H), 8.51 (br., 2H, NH_2). MS: m/z = 439. Analysis for $C_{25}H_{17}N_3O_3S$ (439.50): Calcd. (Found) = C 68.32 (68.51), H 3.90 (3.80), N 9.56 (9.67), S 7.30 (7.14).

3-Amino-4-(benzo-1,3-dioxol-5-yl)-6-(2-naphthyl)thieno[2,3-*b*]pyridine-2-carboxamide (8b): Crystallized from dioxane as yellow solid (76%), mp 232 °C. IR: ν (cm^{-1}) = 3415, 3347, 3252, 3133 (2 × NH_2), 1661 (amidic CO). ^{1}H-NMR: δ (ppm) = 5.63 (br., 2H, NH_2), 6.11 (s, 2H, OCH_2O), 6.92-8.02 (m, 11H, Ar-H), 8.82 (br., 2H, NH_2). MS: m/z = 439. Analysis for $C_{25}H_{17}N_3O_3S$ (439.49): Calcd. (Found) = C 68.32 (68.42), H 3.90 (3.96), N 9.56 (9.49), S 7.30 (7.11).

3-Amino-4-(3,4-dimethoxyphenyl)-6-(1-naphthyl)thieno[2,3-*b*]pyridine-2-carboxamide (8c): Crystallized from ethanol as yellow solid (79%), mp 244 °C. IR: ν (cm^{-1}) = 3412, 3345, 3298, 3189 (2 × NH_2), 1664 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.72, 3.86 (2 s, 6H, 2 × OCH_3), 5.19, 6.37 (two br., 4H, two NH_2), 6.94-7.98 (m, 11H, Ar-H). MS: m/z = 455. Analysis for $C_{26}H_{21}N_3O_3S$ (455.54): Calcd. (Found) = C 68.55 (68.46), H 4.65 (4.62), N 9.22 (9.14), S 7.04 (7.26).

3-Amino-4-(3,4-dimethoxyphenyl)-6-(2-naphthyl)thieno[2,3-b]pyridine-2-carboxamide (8d): Crystallized from dioxane as yellow solid (82%), mp 264 °C. IR: ν (cm^{-1}) = 3423, 3364, 3254, 3171 (2 × NH_2), 1663 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.72, 3.85 (2 s, 6H, 2 × OCH_3), 5.25, 6.44 (two br., 4H, two NH_2), 6.95-8.02 (m, 11H, Ar-H). MS: m/z = 455. Analysis for $C_{26}H_{21}N_3O_3S$ (455.54): Calcd. (Found) = C 68.55 (68.64), H 4.65 (4.43), N 9.22 (9.49), S 7.04 (7.24).

Ethyl [4-(1,3-benzodioxo-5-yl)-2-cyano-6-(1-naphthyl)thieno[2,3-*b*]pyridin-3-yl]imidoformate (9a): Crystallized from ethanol as white solid (56%), mp 186 °C. IR: ν (cm^{-1}) = 2221 (CN). ^{1}H-NMR: δ (ppm) = 1.12 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 3.94 (q, *J* = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 6.10 (s, 2H, OCH_2O), 6.85-8.01 (m, 11H, Ar-H), 8.21 (s, 1H, CH=N). MS: m/z = 477. Analysis for $C_{28}H_{19}N_3O_3S$ (477.55): Calcd. (Found) = C 70.42 (70.31), H 4.01 (4.11), N 8.80 (8.68), S 6.71 (6.62).

Ethyl [4-(1,3-benzodioxo-5-yl)-2-cyano-6-(2-naphthyl)thieno[2,3-*b*]pyridin-3-yl]imidoformate (9b): Crystallized from ethanol as white solid (63%), mp 170 °C. IR: ν (cm^{-1}): 2219 (CN). ^{1}H-NMR: δ (ppm) = 1.04 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 4.04 (q, *J* = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 6.13 (s, 2H, OCH_2O), 6.92-8.02 (m, 11H, Ar-H), 8.22 (s, 1H, CH=N). MS: m/z = 477. Analysis for $C_{28}H_{19}N_3O_3S$ (477.55): Calcd. (Found) = C 70.43 (70.35), H 4.01 (4.06), N 8.80 (8.99), S 6.71 (6.59).

Ethyl [4-(3,4-dimethoxyphenyl -5-yl)-2-cyano-6-(1-naphthyl)thieno[2,3-*b*]pyridin-3-yl]imidoformate (9c): Crystallized from ethanol as white solid (78%), mp 164 °C. IR: ν (cm^{-1}) = 2217 (CN). ^{1}H-NMR: δ (ppm) = 1.01 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 3.74, 3.88 (2 s, 6H, 2 × OCH_3), 4.00 (q, *J* = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 6.87-8.00 (m, 11H, Ar-H), 8.19 (s, 1H, CH=N). MS: m/z = 493. Analysis for $C_{29}H_{23}N_3O_3S$ (493.59): Calcd. (Found) = C 70.57 (70.37), H 4.70 (4.87), N 8.51 (8.44), S 6.50 (6.29).

Ethyl [4-(3,4-dimethoxyphenyl -5-yl)-2-cyano-6-(2-naphthyl)thieno[2,3-*b*]pyridin-3-

yl]imidoformate (9d): Crystallized from ethanol as white solid (78%), mp 164 °C. IR: ν (cm^{-1}) = 2219 (CN). ^{1}H-NMR: δ (ppm) = 1.02 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathbf{CH_3}$), 3.73, 3.88 (2 s, 6H, 2 × OCH_3), 4.10 (q, J = 7.2 Hz, 2H, $O\mathbf{CH_2}CH_3$), 6.90-8.03 (m, 11H, ArH's), 8.24 (s, 1H, CH=N). MS: m/z = 493. Analysis for $C_{29}H_{23}N_3O_3S$ (493.59): Calcd. (Found) = C 70.57 (70.59), H 4.70 (4.94), N 8.51 (8.61), S 6.50 (6.53).

3-Amino-4-imino-9-(benzo-1,3-dioxol-5-yl)-7-(1-naphthyl)-3,4-dihydropyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine (10a): Crystallized from dioxane as white solid (84%), mp 274 °C. IR: ν (cm^{-1}) = 3394, 3325, 3025 (NH_2, NH), 1614 (C=N). ^{1}H-NMR: δ (ppm) = 5.72 (s, 2H, NH_2), 6.12 (s, 2H, OCH_2O), 6.89-8.02 (m, 11H, Ar-H), 8.29 (s, 1H, pyrimidine CH), 8.71 (br., 1H, NH). MS: m/z = 463. Analysis for $C_{26}H_{17}N_5O_2S$ (463.51): Calcd. (Found) = C 67.37 (67.41), H 3.70 (3.60), N 15.11 (15.24), S 6.92 (6.86).

3-Amino-4-imino-9-(benzo-1,3-dioxol-5-yl)-7-(2-naphthyl)-3,4-dihydropyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine (10b): Crystallized from dioxane as white solid (91%), mp 244 °C. IR: ν (cm^{-1}) = 3422, 3325, 3232 (NH_2, NH), 1617 (C=N). ^{1}H-NMR: δ (ppm) = 5.63 (s, 2H, NH_2), 6.11 (s, 2H, OCH_2O), 6.95-8.11 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH), 8.87 (br., 1H, NH). MS: m/z = 463. Analysis for $C_{26}H_{17}N_5O_2S$ (463.52): Calcd. (Found) = C 67.37 (67.28), H 3.70 (3.81), N 15.11 (15.19), S 6.92 (6.87).

3-Amino-4-imino-9-(3,4-dimethoxyphenyl)-7-(1-naphthyl)-3,4-dihydropyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine (10c): Crystallized from dioxane as pale yellow solid (74%), mp 296 °C. IR: ν (cm^{-1}) = 3412, 3354, 3064 (NH_2, NH), 1619 (C=N). ^{1}H-NMR: δ (ppm) = 3.72, 3.84 (2 s, 6H, 2 × OCH_3), 6.95-8.10 (m, 11H, Ar-H), 8.37 (s, 1H, pyrimidine CH), 8.76 (br., 1H, NH). MS: m/z = 479. Analysis for $C_{27}H_{21}N_5O_2S$ (479.56): Calcd. (Found) = C 67.62 (67.65), H 4.41 (4.32), N 14.60 (14.56), S 6.69 (6.59).

3-Amino-4-imino-9-(3,4-dimethoxyphenyl)-7-(2-naphthyl)-3,4-dihydropyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidine (10d): Crystallized from dioxane as pale yellow solid (76%), mp > 300 °C. IR: ν (cm^{-1}) = 3417, 3323, 3054 (NH_2, NH), 1616 (C=N). ^{1}H-NMR: δ (ppm) = 3.73, 3.87 (2 s, 6H, 2 × OCH_3), 6.94-8.12 (m, 11H, Ar-H), 8.35 (s, 1H, pyrimidine CH), 8.89 (br., 1H, NH). MS: m/z = 479. Analysis for $C_{27}H_{21}N_5O_2S$ (479.56): Calcd. (Found) = C 67.62 (67.65), H 4.41 (4.32), N 14.60 (14.56), S 6.69 (6.59).

7-(Benzo-1,3-dioxol-5-yl)-9-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*][1,2,4]-triazolo[5,1-*f*]pyrimidine (11a): Crystallized from dioxane as white solid (84%), mp 274 °C. IR: ν (cm^{-1}) = 3025 (aromatic CH), 2943, 2867 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 6.13 (s, 2H, OCH_2O), 6.93-7.89 (m, 11H, Ar-H), 8.27 (s, 1H, triazole CH), 8.32 (s, 1H, pyrimidine CH). MS: m/z = 473. Analysis for $C_{27}H_{15}N_5O_2S$ (473.52): Calcd. (Found) = C 68.49 (68.65), H 3.19 (3.21), N 14.79 (14.84), S 6.77 (6.87).

7-(Benzo-1,3-dioxol-5-yl)-9-(2-naphthyl)pyrido[3',2';4,5]thieno[3,2-*d*][1,2,4]-triazolo[5,1-*f*]pyrimidine (11b): Crystallized from dioxane as white solid (91%), mp 244 °C. IR: ν (cm^{-1}) = 3036 (aromatic CH), 2923, 2821 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 6.10 (s, 2H, OCH_2O), 6.92-8.01 (m, 11H, Ar-H), 8.25 (s, 1H, triazole CH), 8.35 (s, 1H, pyrimidine CH). MS: m/z = 473. Analysis for $C_{27}H_{15}N_5O_2S$ (473.52): Calcd. (Found) = C 68.49 (solid 68.36), H 3.19 (3.25), N 14.79 (14.84), S 6.77 (6.89).

7-(3,4-Dimethoxyphenyl)-9-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*][1,2,4]-triazolo[5,1-*f*]pyrimidine (11c): Crystallized from dioxane as pale yellow solid (77%), mp 296 °C. IR: ν (cm^{-1}) = 3019 (aromatic CH), 2915, 2794 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 3.71, 3.83 (2 s, 6H, 2 × OCH_3), 6.96-8.02 (m, 11H, Ar-H), 8.29 (s, 1H, triazole CH), 8.38 (s, 1H, pyrimidine CH). MS: m/z = 489. Analysis for $C_{28}H_{19}N_5O_2S$ (489.56): Calcd. (Found) = C 68.70 (68.78), H 3.91 (4.11), N 14.31 (14.57), S 6.55 (6.64).

7-(3,4-Dimethoxyphenyl)-9-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*][1,2,4]-triazolo[5,1-*f*]pyrimidine (11d): Crystallized from dioxane as white solid (79%), mp > 300 °C. IR: ν (cm^{-1}) = 3032 (aromatic CH), 2924, 2787 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 3.72, 3.85 (2 s, 6H, 2 × OCH_3), 6.99-8.00 (m, 11H, Ar-H), 8.27 (s, 1H, triazole CH), 8.32 (s, 1H, pyrimidine CH). MS: m/z = 489. Analysis for $C_{28}H_{19}N_5O_2S$ (489.56): Calcd. (Found) = C 68.70 (68.81), H 3.91 (3.98), N 14.31 (14.43), S 6.55 (6.34).

9-(Benzo-1,3-dioxol-5-yl)-4-hydrazino-7-(1-naphthyl)pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidine (12a): Crystallized from dioxane as white solid (87%), mp 282 °C. IR: ν (cm^{-1}) = 3423, 3364, 3254 (NH, NH_2). ^{1}H-NMR: δ (ppm) = 5.14 (br., 2H, NH_2), 6.12 (s, 2H, OCH_2O), 6.96-8.01 (m, 11H, Ar-H), 8.32

(s, 1H, pyrimidine CH), 9.10 (br., 1H, NH). MS: m/z = 463. Analysis for $C_{26}H_{17}N_5O_2S$ (463.52): Calcd. (Found) = C 67.37 (67.24), H 3.70 (3.66), N 15.11 (15.31), S 6.92 (6.68).

9-(Benzo-1,3-dioxol-5-yl)-4-hydrazino-7-(2-naphthyl)pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidine (12b): Crystallized from dioxane as white solid (92%), mp 296 °C. IR: ν (cm^{-1}) = 3423, 3364, 3254 (NH, NH_2). ^{1}H-NMR: δ (ppm) = 5.14 (br., 2H, NH_2), 6.12 (s, 2H, OCH_2O), 6.96-8.01 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH), 9.10 (br., 1H, NH). MS: m/z = 463. Analysis for $C_{26}H_{17}N_5O_2S$ (463.52): Calcd. (Found) = C 67.37 (67.28), H 3.70 (3.81), N 15.11 (15.29), S 6.92 (6.66).

9-(3,4-Dimethoxyphenyl)-4-hydrazino-7-(1-naphthyl)pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidine (12c): Crystallized from ethanol as white solid (92%), mp 296 °C. IR: ν (cm^{-1}) = 3417, 3334, 3224 (NH, NH_2). ^{1}H-NMR: δ (ppm) = 3.74, 3.88 (2 s, 6H, 2 × OCH_3), 4.94 (br., 2H, NH_2), 6.98-8.04 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH), 9.31 (br., 1H, NH). MS: m/z = 479. Analysis for $C_{27}H_{21}N_5O_2S$ (479.56): Calcd. (Found) = C 67.62 (67.87), H 4.41 (4.45), N 14.60 (14.53), S 6.69 (6.88).

9-(3,4-Dimethoxyphenyl)-4-hydrazino-7-(1-naphthyl)pyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidine (12d): Crystallized from ethanol as white solid (92%), mp 296°C. IR: ν (cm^{-1}) = 3417, 3334, 3224 (NH, NH_2). ^{1}H-NMR: δ (ppm) = 3.74, 3.88 (2 s, 6H, 2 × OCH_3), 4.94 (br., 2H, NH_2), 6.98-8.04 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH), 9.31 (br., 1H, NH). MS: m/z = 479. Analysis for $C_{27}H_{21}N_5O_2S$ (479.56): Calcd. (Found) = C 67.62 (67.87), H 4.41 (4.45), N 14.60 (14.53), S 6.69 (6.88).

9-(Benzo-1,3-dioxol-5-yl)-7-(1-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidine-4-one (13a): Crystallized from acetic acid as white solid (59%), mp > 300 °C. IR: ν (cm^{-1}) = 3216 (NH), 1660 (amidic CO). ^{1}H-NMR: δ (ppm) = 6.10 (s, 2H, OCH_2O), 6.90-7.99 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH), 12.3 (br., 1H, NH). MS: m/z = 449. Analysis for $C_{26}H_{15}N_3O_3S$ (499.49): Calcd. (Found) = C 69.48 (69.43), H 3.36 (3.51), N 9.35 (9.44), S 7.13 (7.24).

9-(Benzo-1,3-dioxol-5-yl)-7-(2-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidine-4-one (13b): Crystallized from acetic acid as white solid (69%), mp > 300 °C. IR: ν (cm^{-1}) = 3224 (NH), 1662 (amidic CO). ^{1}H-NMR: δ (ppm) = 6.11 (s, 2H, OCH_2O), 6.95-7.98 (m, 11H, Ar-H), 8.34 (s, 1H, pyrimidine CH), 12.5 (br., 1H, NH). MS: m/z = 449. Analysis for $C_{26}H_{15}N_3O_3S$ (499.49): Calcd. (Found) = C 69.48 (69.25), H 3.36 (3.21), N 9.35 (9.54), S 7.13 (7.00).

9-(3,4-Dimethoxyphenyl)-7-(1-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine-4-one (13c): Crystallized from acetic acid as white solid (78%), mp 298 °C. IR: ν (cm^{-1}) = 3214 (NH), 1667 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.71, 3.83 (2 s, 6H, 2 × OCH_3), 6.91-8.01 (m, 11H, Ar-H), 8.31 (s, 1H, pyrimidine CH), 11.3 (br., 1H, NH). MS: m/z = 465. Analysis for $C_{27}H_{19}N_3O_3S$ (465.53): Calcd. (Found) = C 69.66 (69.59), H 4.11 (4.15), N 9.03 (8.89), S 6.89 (6.69).

9-(3,4-Dimethoxyphenyl)-7-(2-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine-4-one (13d): Crystallized from acetic acid as white solid (78%), mp 298 °C. IR: ν (cm^{-1}) = 3214 (NH), 1667 (amidic CO). ^{1}H-NMR: δ (ppm) = 3.71, 3.83 (2 s, 6H, 2 × OCH_3), 6.91-8.01 (m, 11H, Ar-H), 8.31 (s, 1H, pyrimidine CH), 11.3 (br., 1H, NH). MS: m/z = 465. Analysis for $C_{27}H_{19}N_3O_3S$ (465.53): Calcd. (Found) = C 69.66 (69.59), H 4.11 (4.15), N 9.03 (8.89), S 6.89 (6.69).

9-(Benzo-1,3-dioxol-5-yl)-4-chloro-7-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*] pyrimidine (14a): Crystallized from dioxane as white solid (71%), mp 208 °C. IR: ν (cm^{-1}) = 3032 (aromatic CH), 2911, 2801 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 6.10 (s, 2H, OCH_2O), 6.79-795 (m, 11H, Ar-H), 8.30 (s, 1H, pyrimidine CH). MS: m/z = 467.5. Analysis for $C_{26}H_{14}N_3O_2SCl$ (467.94): Calcd. (Found) = C 66.74 (66.79), H 3.02 (3.12), N 8.98 (8.84), S 6.85 (6.94).

9-(Benzo-1,3-dioxol-5-yl)-4-chloro-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*] pyrimidine (14b): Crystallized from dioxane as white solid (83%), mp 192 °C. IR: ν (cm^{-1}) = 3047 (aromatic CH), 2924, 2824 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 6.11 (s, 2H, OCH_2O), 6.84-7.94 (m, 11H, Ar-H), 8.31 (s, 1H, pyrimidine CH). MS: m/z = 467.5. Analysis for $C_{26}H_{14}N_3O_2SCl$ (467.94): Calcd. (Found) = C 66.74 (66.88), H 3.02 (3.21), N 8.98 (8.74), S 6.85 (6.79).

4-Chloro-9-(3,4-dimethoxyphenyl)-7-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*]-pyrimidine (14c): Crystallized from dioxane as white solid (77%), mp 188°C. IR: ν (cm^{-1}) = 3027 (aromatic CH), 2922, 2815 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 3.73, 3.84 (2 s, 6H, 2 × OCH_3), 6.92-8.01 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH). MS: m/z = 483.5. Analysis for $C_{28}H_{18}N_3O_2SCl$ (483.98): Calcd.

(Found) = C 67.01 (67.21), H 3.75 (3.68), N 8.68 (8.79), S 6.63 (6.47).

4-Chloro-9-(3,4-dimethoxyphenyl)-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*]-pyrimidine (14d): Crystallized from dioxane as white solid (79%), mp 202°C. IR: ν (cm^{-1}) = 3025 (aromatic CH), 2917, 2811 (aliphatic CH). ^{1}H-NMR: δ (ppm) = 3.72, 3.84 (2 s, 6H, 2 × OCH_3), 6.97-8.00 (m, 11H, Ar-H), 8.30 (s, 1H, pyrimidine CH). MS: m/z = 483.5. Analysis for $C_{28}H_{18}N_3O_2SCl$ (483.98): Calcd. (Found) = C 67.01 (67.13), H 3.75 (3.60), N 8.68 (8.57), S 6.63 (6.77).

9-(Benzo-1,3-dioxol-5-yl)-7-(1-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno-[3,2-*d*][1,2,3]triazin-4-one (15a): Crystallized from dioxane as white solid (67%), mp 272 °C. IR: ν (cm^{-1}) = 3247 (NH), 1659 (amidic CO). ^{1}H-NMR: δ (ppm) = 6.13 (s, 2H, OCH_2O), 6.89 - 7.98 (m, 11H, Ar-H), 8.29 (s, 1H, pyrimidine CH), 9.31 (br., 1H, NH). MS: m/z = 450. Analysis for $C_{25}H_{14}N_4O_3S$ (450.48): Calcd. (Found) = C 66.66 (66.77), H 3.13 (3.23), N 12.44 (12.45), S 7.12 (7.34).

9-(Benzo-1,3-dioxol-5-yl)-7-(2-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno-[3,2-*d*][1,2,3]triazin-4-one (15b): Crystallized from dioxane as white solid (86%), mp 254 °C. IR: ν (cm^{-1}) = 3237 (NH), 1662 (amidic CO). ^{1}H-NMR: δ (ppm) = 6.12 (s, 2H, OCH_2O), 6.91 - 7.99 (m, 11H, Ar-H), 8.33 (s, 1H, pyrimidine CH), 9.24 (br., 1H, NH). MS: m/z = 450. Analysis for $C_{25}H_{14}N_4O_3S$ (450.48): Calcd. (Found) = C 66.66 (66.56), H 3.13 (3.03), N 12.44 (12.34), S 7.12 (7.01).

9-(3,4-Dimethoxyphenyl)-7-(2-naphthyl)-3,4-dihydropyrido[3',2':4,5]thieno-[3,2-*d*][1,2,3]triazin-4-one (15d): Crystallized from dioxane as white solid (68%), mp 286°C. IR: ν (cm^{-1}) = 3274 (NH), 1664 (amidic CO). ^{1}H-NMR δ (ppm): 3.71, 3.82 (2 s, 6H, 2 × OCH_3), 6.98-8.00 (m, 11H, Ar-H), 8.32 (s, 1H, pyrimidine CH). MS: m/z = 466. Analysis for $C_{26}H_{18}N_4O_3S$ (466.52): Calcd. (Found) = C 66.94 (66.88), H 3.89 (3.64), N 12.01 (12.34), S 6.87 (6.73).

9-(Benzo-1,3-dioxol-5-yl)-4-benzylidenehydrazino-7-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (16a): Crystallized from dioxane as white solid (64%), mp 286 °C. IR: ν (cm^{-1}) = 3305 (NH), 1646 (C=N). ^{1}H-NMR: δ (ppm) = 6.13 (s, 2H, OCH_2O), 6.87-8.04 (m, 16H, Ar-H), 8.19 (s, 1H, CH=N), 8.29 (s, 1H, pyrimidine CH). MS: m/z = 551. Analysis for $C_{33}H_{21}N_5O_2S$ (551.63): Calcd. (Found) = C 71.85 (71.67), H 3.84 (3.67), N 12.70 (12.81), S 5.81 (5.88).

9-(Benzo-1,3-dioxol-5-yl)-4-benzylidenehydrazino-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (16b): Crystallized from dioxane as white solid (73%), mp 262 °C. IR: ν (cm^{-1}) = 3248 (NH), 1646 (C=N). ^{1}H-NMR: δ (ppm) = 6.12 (s, 2H, OCH_2O), 6.91 - 8.06 (m, 16H, Ar-H), 8.17 (s, 1H, CH=N), 8.31 (s, 1H, pyrimidine CH). MS: m/z = 551. Analysis for $C_{33}H_{21}N_5O_2S$ (551.63): Calcd. (Found) = C 71.85 (71.91), H 3.84 (3.94), N 12.70 (12.64), S 5.81 (5.87).

4-Benzylidenehydrazino-9-(3,4-dimethoxyphenyl)-7-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (16c): Crystallized from dioxane as white solid (77%), mp 274 °C. IR: ν (cm^{-1}) = 3274 (NH), 1652 (C=N). ^{1}H-NMR: δ (ppm) = 3.72, 3.83 (2 s, 6H, 2 × OCH_3), 6.95-8.00 (m, 16H, Ar-H), 8.18 (s, 1H, CH=N), 8.27 (s, 1H, pyrimidine CH). MS: m/z = 567. Analysis for $C_{34}H_{25}N_5O_2S$ (567.67): Calcd. (Found) = C 71.94 (71.87), H 4.44 (4.45), N 12.34 (12.24), S 5.65 (5.39).

4-Benzylidenehydrazino-9-(3,4-dimethoxyphenyl)-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (16d): Crystallized from dioxane as white solid (69%), mp 258 °C. IR: ν (cm^{-1}) = 3265 (NH), 1651 (C=N). ^{1}H-NMR: δ (ppm) = 3.73, 3.85 (2 s, 6H, 2 × OCH_3), 6.96-8.02 (m, 16H, Ar-H), 8.16 (s, 1H, CH=N), 8.30 (s, 1H, pyrimidine CH). MS: m/z = 567. Analysis for $C_{34}H_{25}N_5O_2S$ (567.67): Calcd. (Found) = C 71.94 (71.98), H 4.44 (4.38), N 12.34 (12.51), S 5.65 (5.47).

Ethyl 7-(benzo-1,3-dioxol-5-yl)-9-(1-naphthyl)-1,2,4-triazolo[4'',3''-*c*]pyrido-[3',2':4,5]thieno[3,2-*d*]pyrimidin-3-ylacetate (17a): Crystallized from dioxane as white solid (56%), mp 192 °C. IR: ν (cm^{-1}) = 1728 (ester CO). ^{1}H-NMR: δ (ppm) = 1.02 (t, 3H, ester CH_3), 3.98 (s, 2H, CH_2), 4.12 (q, 2H, ester CH_2), 6.11 (s, 2H, OCH_2O), 6.81-8.04 (m, 11H, Ar-H), 8.30 (s, 1H, pyrimidine CH). MS: m/z = 559. Analysis for $C_{31}H_{21}N_5O_4S$ (559.61): Calcd. (Found) = C 66.54 (66.51), H 3.78 (3.68), N 12.51 (12.72), S 5.73 (5.47).

Ethyl 7-(benzo-1,3-dioxol-5-yl)-9-(2-naphthyl)-1,2,4-triazolo[4'',3''-*c*]pyrido-[3',2':4,5]thieno[3,2-d]pyrimidin-3-ylacetate (17b): Crystallized from dioxane as white solid (76%), mp 212 °C. IR: ν (cm^{-1}) = 1723 (ester CO). ^{1}H-NMR: δ (ppm) = 1.04 (t, 3H, ester CH_3), 4.02 (s, 2H, CH_2), 4.11 (q, 2H, ester CH_2), 6.13 (s, 2H, OCH_2O), 6.89-8.02 (m, 11H, Ar-H), 8.31 (s, 1H, pyrimidine CH). MS: m/z = 559. Analysis for $C_{31}H_{21}N_5O_4S$ (559.61): Calcd. (Found) = C 66.54 (66.62), H 3.78 (3.73), N 12.51 (12.77), S 5.73 (5.58).

Ethyl 7-(3,4-dimethoxyphenyl)-9-(1-naphthyl)-1,2,4-triazolo[4'',3''-*c*]pyrido-[3',2':4,5]thieno[3,2-d]pyrimidin-3-ylacetate (17c): Crystallized from dioxane as white solid (66%), mp 178 °C. IR: ν (cm^{-1}) = 1723 (ester CO). ^{1}H-NMR: δ (ppm) = 9.99 (t, 3H, ester CH_3), 3.73, 3.86 (2 s, 6H, 2 × OCH_3), 4.01 (s, 2H, CH_2), 4.09 (q, 2H, ester CH_2), 6.84-8.03 (m, 11H, Ar-H), 8.26 (s, 1H, pyrimidine CH). MS: m/z = 575. Analysis for $C_{32}H_{25}N_5O_4S$ (575.65): Calcd. (Found) = C 66.77 (66.68), H 4.38 (4.46), N 12.17 (12.01), S 5.57 (5.42).

Ethyl 7-(3,4-dimethoxyphenyl)-9-(2-naphthyl)-1,2,4-triazolo[4'',3''-c]pyrido-[3',2':4,5]thieno[3,2-d]pyrimidin-3-ylacetate (17d): Crystallized from dioxane as white solid (66%), mp 178 °C. IR: ν (cm^{-1}) = 1723 (ester CO). ^{1}H-NMR: δ (ppm) = 101 (t, 3H, ester CH_3), 3.72, 3.85 (2 s, 6H, 2 × OCH_3), 4.02 (s, 2H, CH_2), 4.10 (q, 2H, ester CH_2), 6.79-8.01 (m, 11H, Ar-H), 8.31 (s, 1H, pyrimidine CH). MS: m/z = 575. Analysis for $C_{32}H_{25}N_5O_4S$ (575.65): Calcd. (Found) = C 66.77 (66.84), H 4.38 (4.27), N 12.17 (12.33), S 5.57 (5.39).

9-(Benzo-1,3-dioxol-5-yl)-4-(3,5-dimethylpyrazolo)-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (18a): Crystallized from dioxane as white solid (72%), mp 242 °C. IR: ν (cm^{-1}) = 3047 (aromatic CH), 2914, 2794 (aliphatic CH), 1654 (C=N). ^{1}H-NMR: δ (ppm) = 2.41, 2.83 (2 s, 6H, 2 × CH_3 at pyrazole ring), 6.11 (s, 2H, OCH_2O), 6.59 (s, 1H, pyrazole CH), 6.92-8.03 (m, 11H, Ar-H), 8.27 (s, 1H, pyrimidine CH). MS: m/z = 527. Analysis for $C_{31}H_{21}N_5O_2S$ (527.61): Calcd. (Found) = C 70.57 (70.43), H 4.01 (4.02), N 13.27 (13.52), S 6.08 (6.24).

9-(Benzo-1,3-dioxol-5-yl)-4-(3,5-dimethylpyrazolo)-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (18b): Crystallized from dioxane as white solid (83%), mp 248 °C. IR: ν (cm^{-1}) = 3031 (aromatic CH), 2924, 2793 (aliphatic CH), 1652 (C=N). ^{1}H-NMR: δ (ppm) = 2.44, 2.82 (2 s, 6H, 2 × CH_3 at pyrazole ring), 6.12 (s, 2H, OCH_2O), 6.61 (s, 1H, pyrazole CH), 6.90-8.01 (m, 11H, Ar-H), 8.28 (s, 1H, pyrimidine CH). MS: m/z = 527. Analysis for $C_{31}H_{21}N_5O_2S$ (527.61): Calcd. (Found) = C 70.57 (70.61), H 4.01 (4.04), N 13.27 (13.33), S 6.08 (6.11).

9-(3,4-Dimethoxyphenyl)-4-(3,5-dimethylpyrazolo)-7-(1-naphthyl)pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (18c): Crystallized from dioxane as white solid (83%), mp 248 °C. IR: ν (cm^{-1}) = 3027 (aromatic CH), 2917, 2789 (aliphatic CH), 1654 (C=N). ^{1}H-NMR: δ (ppm) = 2.43, 2.84 (2 s, 6H, two CH_3 at pyrazole ring), 3.77, 3.84 (2 s, 6H, 2 × OCH_3), 6.60 (s, 1H, pyrazole CH), 6.88-8.02 (m, 11H, Ar-H), 8.25 (s, 1H, pyrimidine CH). MS: m/z = 543. Analysis for $C_{32}H_{25}N_5O_2S$ (543.65): Calcd. (Found) = C 70.70 (70.68), H 4.61 (4.57), N 12.88 (12.82), S 5.90 (5.84).

9-(3,4-Dimethoxyphenyl)-4-(3,5-dimethylpyrazolo)-7-(2-naphthyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidine (18d): Crystallized from dioxane as white solid (77%), mp 262 °C. IR: ν (cm^{-1}) = 3028 (aromatic CH), 2922, 2787 (aliphatic CH), 1653 (C=N). ^{1}H-NMR: δ (ppm) = 2.41, 2.78 (2 s, 6H, 2 × CH_3 at pyrazole ring), 3.76, 3.82 (2 s, 6H, 2 × OCH_3), 6.62 (s, 1H, pyrazole CH), 6.87-8.02 (m, 11H, Ar-H), 8.27 (s, 1H, pyrimidine CH). MS: m/z = 543. Analysis for $C_{32}H_{25}N_5O_2S$ (543.65): Calcd. (Found) = C 70.70 (70.74), H 4.61 (4.66), N 12.88 (12.71), S 5.90 (5.88).

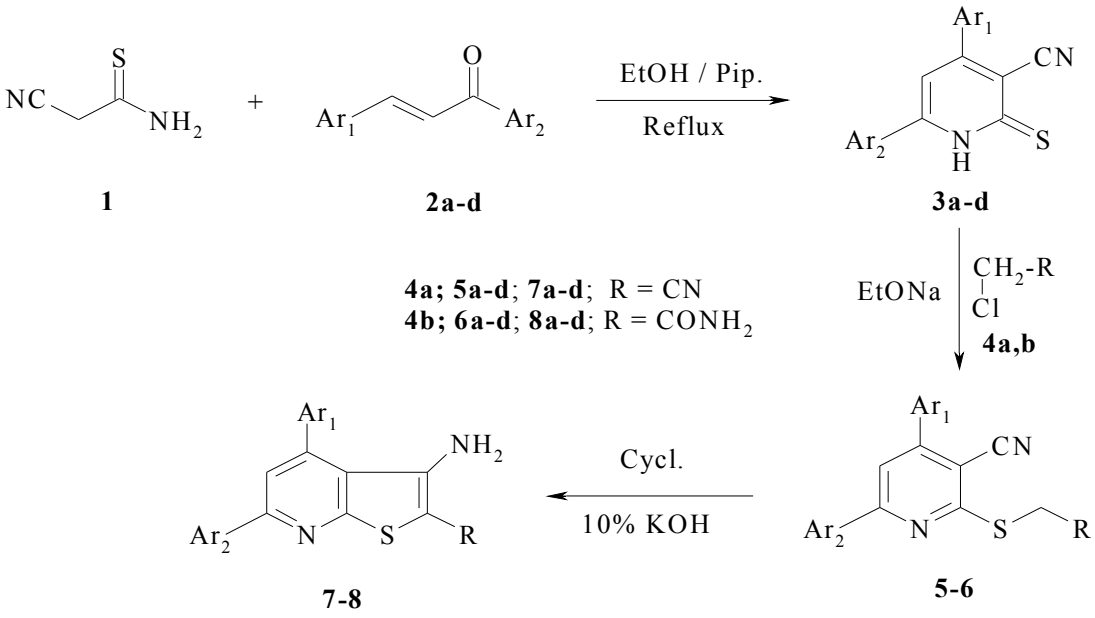
3. Results and discussion

The results obtained showed that reaction of cyanothioacetamide **1** with α,β-unsaturated carbonyl compounds **2a-d** afforded 2-thioxo-1,2-dihydropyridine-3-carbonitrile **3a-d**. Structure of compounds **3a-d** has been elucidated from their spectral data, elemental analysis, and chemical reactions. Their IR spectra showed absorption bands at 3321-3372, and 2217-2224 cm^{-1}, characteristic for NH and CN groups, respectively. Moreover, upon their reaction with chloroacetonitrile **4a** or chloroacetamide **4b**, 3-cyanopyridin-2-ylthioacetonitriles **5a-d** and 3-cyanopyridine-2-ylthioacetamides **6a-d** were formed, respectively. Also, cyclization of compounds **5-6** with ethanolic 10% KOH ascertained their structure, where an addition of methylene protons to cyano group took place, to give 3-aminothieno[2,3-b]pyridine derivatives **7-8**, respectively (Scheme I).

Condensation of compounds **7a-d** with triethyl orthoformate in acetic anhydride gave 3-(ethoxymethyleneamino)thieno[2,3-b]pyridine derivatives **9a-d** which on their treatment with hydrazine hydrate produced 3-amino-4-imino-3,4-dihydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine derivatives **10a-d**. The presence of amino and imino groups in **10a-d** was confirmed by their reaction with triethyl orthoformate to give pyrido[3',2':4,5]thieno[3,2-d][1,2,4]triazolo[5,1-f]pyrimidine derivatives **11a-d**. Also the structure of compounds **10a-d** was substantiated by their heating with aqueous KOH solution where Dimroth rearrangement took place to give 4-hydrazinopyridothienopyrimidines **12a-d**. However, the condensation of compounds **8a-d** with triethyl orthoformate in acetic anhydride gave

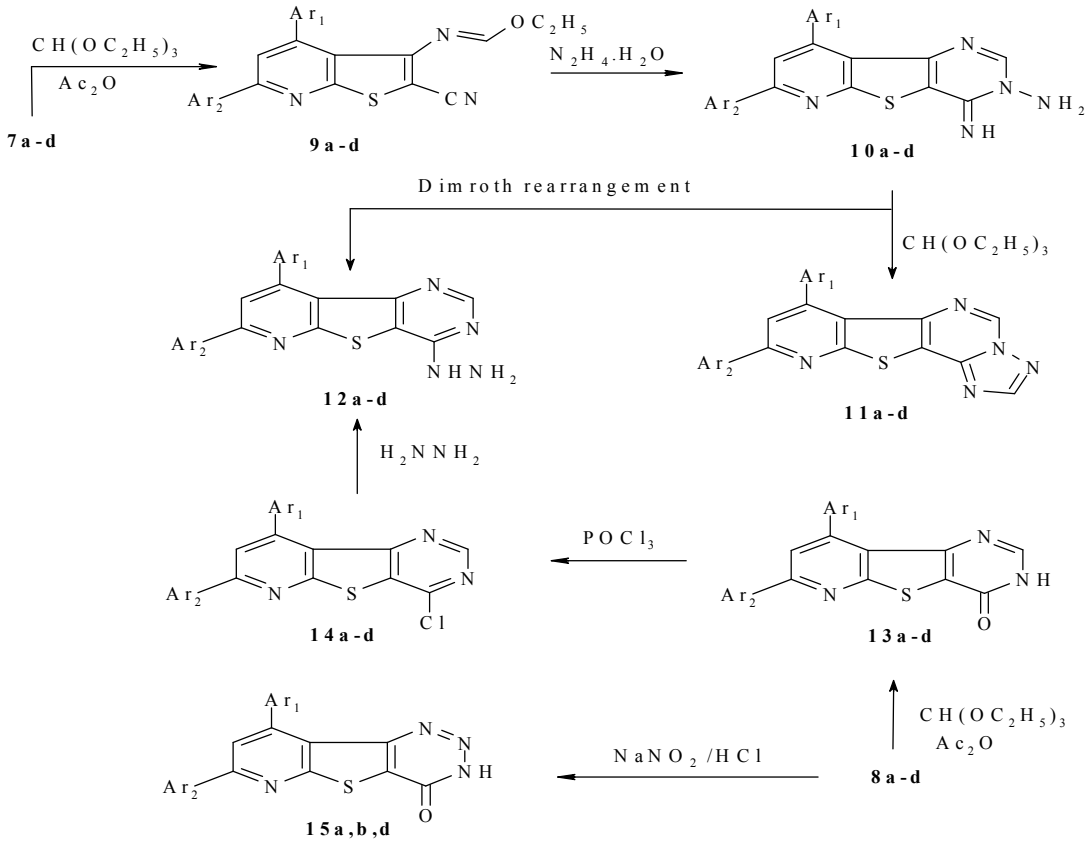
pyridothienopyrimidine-4-one derivatives **13a-d**. Chlorination of them with $POCl_3$ afforded 4-chloropyridothienopyrimidine derivatives **14a-d** which on their reaction with hydrazine hydrates authenticated derivatives **12a-d**. The structure of compounds **13** and **14** was confirmed by their IR spectra where they showed bands at 3214-3224 and 1660-1667 Cm^{-1} characteristic for NH and CO amidic group, respectively. Structure of compounds **8a-d** has been confirmed by their nitrosation with nitrous acid where they gave only 3,4-dihydropyrido[3',2':4,5]thieno[3,2-d][1,2,3]triazin-4-one derivatives **15a**,**b**,**d**. All trials carried out to synthesize derivative **15c** were failed. Structures of the products were ascertained by their IR spectra where they showed bands at 3237-3274 and 1659-1664 cm-1 characteristic for NH and CO amidic group, respectively (Scheme II).

The presence of hydrazino group in compounds **12a-d** was ascertained by its condensation with benzaldehyde, diethyl malonate, and acetylacetone to give 4-benzylidenehydrazinopyrido[3',2': 4,5]thieno[3,2-d]pyrimidine **16a-d**, ethyl 1,2,4-triazolo[4",3"-c]pyrido[3',2': 4,5]thieno[3,2-d]pyrimidin-3-ylacetate **17a-d** and 4-(3,5-dimethylpyrazolo)pyrido[3',2': 4,5]thieno[3,2-d]pyrimidine **18a-d**, respectively (Scheme III).



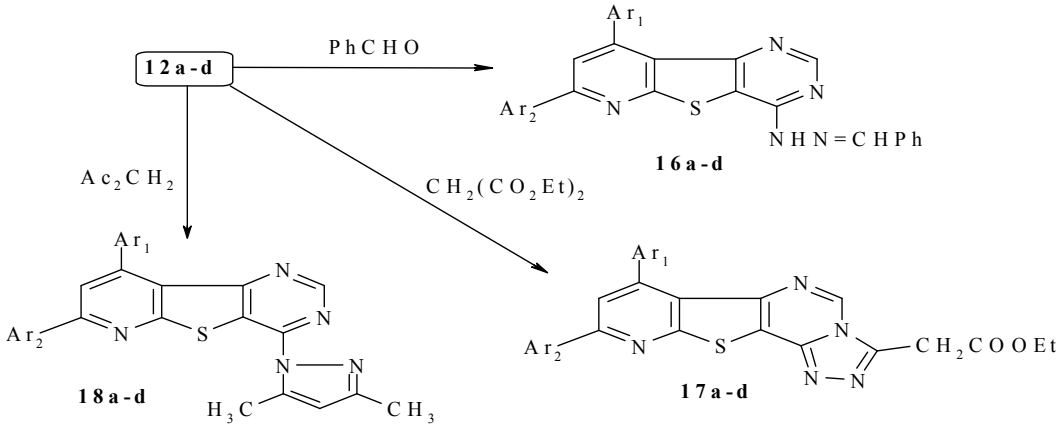
2-8	a	b	c	d
Ar_1	3,4-$(CH_2O_2)C_6H_3$	3,4-$(CH_2O_2)C_6H_3$	3,4$(CH_3O)_2C_6H_3$	3,4$(CH_3O)_2C_6H_3$
Ar_2	α-naphthyl	β-naphthyl	α-naphthyl	β-naphthyl

Scheme I



9-15	a	b	c	d
Ar_1	3,4-$(CH_2O_2)C_6H_3$	3,4-$(CH_2O_2)C_6H_3$	3,4$(CH_3O)_2C_6H_3$	3,4$(CH_3O)_2C_6H_3$
Ar_2	α-naphthyl	β-naphthyl	α-naphthyl	β-naphthyl

Scheme II



16-18	a	b	c	d
Ar_1	3,4-$(CH_2O_2)C_6H_3$	3,4-$(CH_2O_2)C_6H_3$	3,4$(CH_3O)_2C_6H_3$	3,4$(CH_3O)_2C_6H_3$
Ar_2	α-naphthyl	β-naphthyl	α-naphthyl	β-naphthyl

Scheme III

Conclusion

The achieved derivatives of thienopyridine, pyridothienopyrimidine, and pyridothienotriazolopyrimidines that are expected to have pharmaceutical, medicinal, and biological activities, have been synthesized and their structures confirmed by their spectral data, elemental analyses, and with some chemical reactions.

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