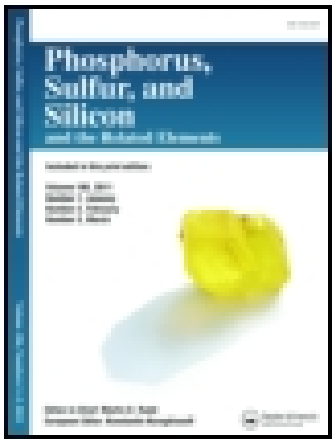

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SYNTHESIS OF SOME NEW FUSED AZINES OF EXPECTED BIO-RESPONSES

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SYNTHESIS OF SOME NEW FUSED AZINES OF EXPECTED BIO-RESPONSES

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*4-Anisy1–5,6-polymethylene-3-cyanopyridine-2(1*H*)-thiones **1** were reacted with chloroacetonitrile in alcoholic KOH to give theino[2,3-*b*]pyridine derivatives **2**. Enaminonitriles **2** were reacted with each of HCOOH, formamide/HCOOH/DMF mixture and cyanamide/HCl to give **3**, **4**, and **5**, respectively, whereas boiling **2** in a proper solvent and basic catalyst with each of CS_2 and thiourea yielded **6** and **7** respcetively. On the other hand, fused pyridine derivatives **8**, **9**, and **10** were obtained by refluxing **2** with each of malononitrile, ethy1 cyanoacetate, and benzalmalononitrile in alcoholic triethylamine mixture. Also, fused pyrazoles and benzo-1,4-diazepines **12** and **14** were synthesized.*

Keywords: B-enaminonitriles; pyridothienopyridines; pyridothienopyrimdines; thienobenzodiazepines; thienopyridines

Thieno[2,3-*b*]pyridine derivatives have been of recent interest because of their broad spectrum of biological activities. Such a ring system is reported to have bactericidal activities,[1] antiviral activities,[2] antianaphylactics, antiinflammatories, and antihypertensive properties.[3] It is also useful as an allergy inhibitor,[4] cardiovascular agent,[5–7] antiAIDS,[8,9] potential drug, and chemical and pharmaceutical intermediate.[10] Prompted by the aforesaid biological and medicinal activities and in connection with our synthetic program[11,12] aimed at the synthesis of several polyfunctionally substituted thieno[2,3-*b*]pyridine, thieno[3,2-*d*]pyrimidine derivatives and other heteroannulated ring systems related to thieno[2,3-*b*]pyridine of expected biological activity, samples of differently substituted thieno[2,3-*b*]pyridine and thieno[3,2-*d*]pyrimidine derivatives were synthesized.

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RESULTS AND DISCUSSION

The reaction of the recently prepared 4-anisyl-5,6-polymethylene-3-cyanopyridine-2-(1*H*)thiones **1a,b**[13] with chloroacetonitrile in alcoholic KOH seems to be a facile convenient route for synthesis of 3-amino-4-(*p*-anisyl)-5,6-polymethylenethieno[2,3-*b*]pyridine-2-carbonitriles **2a,b**. This reaction proceeds as the reported ones of haloesters, haloketones, and haloamides with pyridine-2(1*H*)thiones.[14] Both elemental and spectral data of **2a,b** were inconsistent with the assigned structure (cf. Experimental).

Compounds **2a,b** as a typical enaminonitriles can be used as a strategic starting material for the synthesis of different fused hetercycles. Thus, compounds **2a,b** reacted with formic acid on heating several hours, to yield 9-(*p*-anisyl)-3,4-dihydro-4-oxo-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidines **3a,b**.

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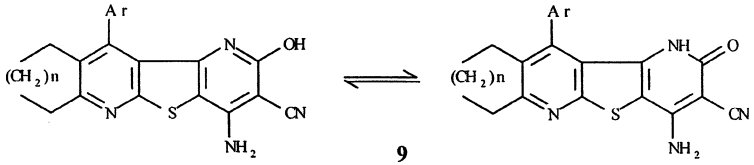
Refluxing each of the compounds **2a,b** in formamide/formic acid/DMF mixture for 10 h gave the expected single product which can be formulated as 4-amino-9-(*p*-anisyl)-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidines **4a,b**. These reactions were shown in our previous work on 3-aminothiazolo[3,2-*a*]pyrimidine-2-carbonitrile derivatives.[15,16] Also, compounds **2a,b** reacted with cyanamide/HCl in dioxane by heating under reflux for 24 h to give 9-(*p*-anisyl)-2,4-diamino-7,8-polymethylenepyrido[3′,2′:4,5]thieno-[3,2-*d*]pyrimidines **5a,b.** In addition, refluxing of **2a,b** with carbon disulphide in dry pyridine gave 9-(*p*-anisyl)-2,4-disulphanyl-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidines **6a,b**. On the other hand, treatment of **2a,b** with thiourea in dioxane and triethylamine as a basic catalyst yielded the expected single product that can be formulated as 4-amino-9-(*p*-anisyl)-2-sulphanyl-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidine **7a,b**. Comparison of the IR spectra of **2a,b**, which contains a characteristic absorption bands for stretching vibration of the conjugated nitrile group in the 2200 cm^{-1} region with that of structures **3–7**, reveals the disappearance of this CN absorption band.

When solutions of **2a,b** in ethanol containing triethylamine were heated under reflux for 24 h with malononitrile, the corresponding 9-(*p*-anisyl)-2,4-diamino-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*b*]-pyridine-3-carbonitrile **8a,b** were formed. Similary, the reaction of **2a,b** with ethyl cyanoacetate gave 4-amino-9-(*p*-anisyl)-1,2-dihydro-2-oxo-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine-3-carbonitriles **9a,b**. Also, compounds **2a,b** underwent Micheal-type addition to α-cyanocinnamonitrile in refluxing pyridine followed by cyclization to furnish finally the corresponding 4-amino-9-(*p*-anisyl)-2-phenyl-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine-3-carbonitrile **10a,b**. Assignment of structures **8–10** were confirmed on the basis of their correct elemental analysis as well as compatible spectral data.



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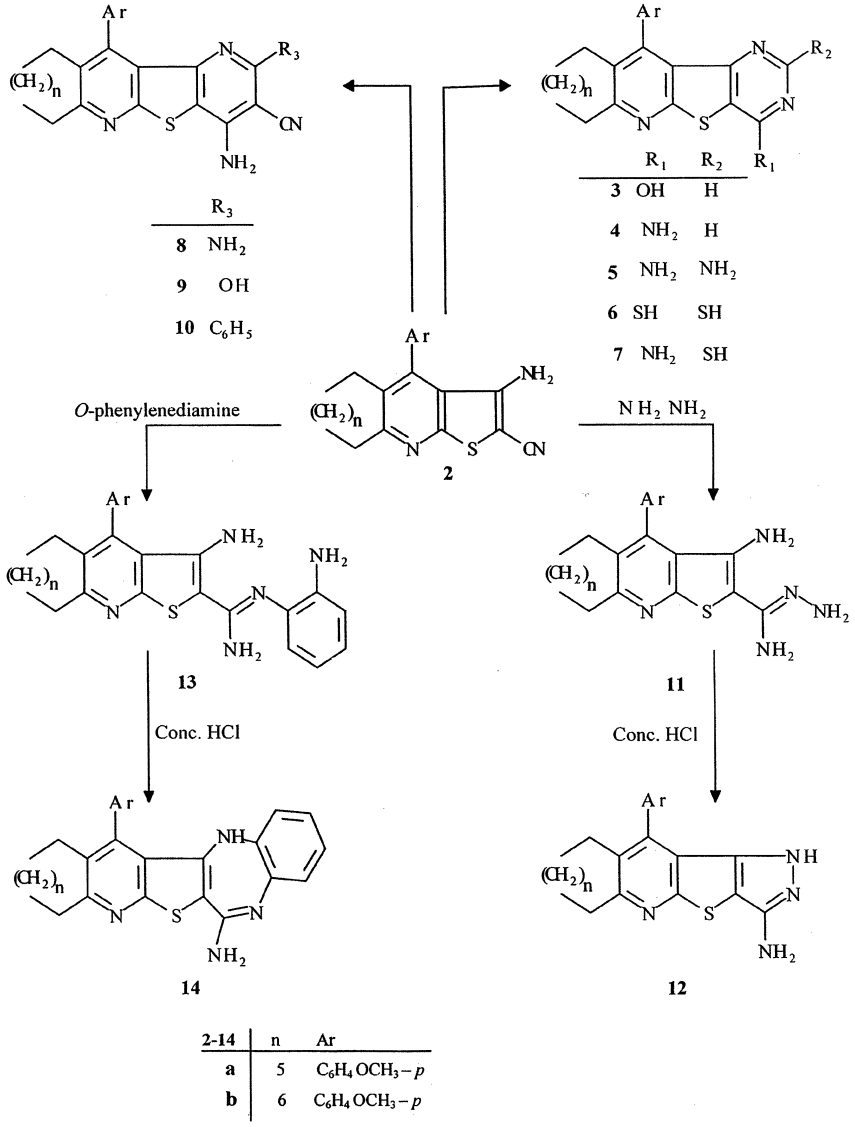
Furthermore, fused pyrazoles and benzo-1,4-diazepines **12** and **14** were synthesized using **2a,b** and bifunctionally amino compounds. Thus, compounds **2a,b** reacted with hydrazine hydrate in boiling absolute ethanol in presence of triethylamine as a basic catalyst, to give the isolated intermediates 3-aminothieno[2,3-*b*]pyridine-3-amidine derivatives **11a,b**. Heating of the amidine derivatives **11a,b** under reflux for 5 h in dioxane in the presence of conc. HCl afforded the corresponding 3-amino-8-(*p*-anisyl)-6,7-polymethylene-1H-pyrazolo[3′,4′:4,5]thieno[2,3-*b*]pyridines **12a,b.** Similarly, compounds **2a,b** reacted with *o*-phenylenediamine to afford the isolated intermediates 3-aminothieno[2,3-*b*]pyridine-3-amidine derivatives **13a,b**, which upon heating under reflux in dioxane in presence of conc. HCl for 5 h, yielded 6-amino-11-(*p*-anisyl)-12H-9,10-polymethylenepyrido[3′,4′:4,5]thieno[2,3-*b*]benzo-1,4-diazepines **14a,b**.

EXPERIMENTAL

All melting points are uncorrected and were determined on an electric melting point (Gallenkamp) apparatus. IR spectra were recorded (KBr) on a Pye Unicam SP-1000 Spectrophotometer. ^{1}H NMR spectra were recorded on a Varian ^{1}H-Gemini 200 MHz and/or Jeol JNM-EX 270 MHz Spectrometers and chemical shifts are expressed in δ (ppm)



using TMS as internal reference. Mass spectra were recorded on a GCMS-QP 1000 EX mass Spectrometer operating at 70 eV. Microanalytical data were obtained from the Microanalytical Center at Cairo University.

3-Amino-4-(*p*-anisyl)-5,6-polymethylenethieno[2,3-b]pyridine-2-carbonitriles 2a,b

Chloroacetonitrile (0.76 g, 0.01 mmol) was added to a solution of the appropriate 3-cyanopyridine-2(1*H*)-thiones **1a,b** (0.01 mmol) in ethanol (50 ml) containing potassium hydroxide (1.1 g, 0.02 mmol, disolved in 5 ml water) and the reaction mixture was refluxed for 3 h. The reaction mixture was cooled at room temperature and poured gradually with stirring onto crused ice and neutralized with dilute HCl (pH = 7). The formed solid product, in each cuse, was filtered off and crystallized from the proper solvent.

(2a)- yield 82%, m.p. = 185°C (EtOH), IR spectrum ν (cm^{-1}): 3314, 3210 (NH_2), 2939 (CH-aliphatic) and 2203 (CN). The ^1H NMR spectrum ($CDCl_3$) δ (ppm) = 1.8–2.1 (m, 6H, 3 CH_2), 3.9 (s, 3H, OCH_3) and 7.1–7.8 (m, 6H, aromatic protons +NH_2). Found C 67.1, H 4.8, N 13.1 and S 10.1. Calculated for $C_{18}H_{15}N_3OS$ (321.38), C 67.27, H 4.71, N 13.08 and S 9.98. MS: m/z = 321, 25.6%.

(2b)- yield 86%, m.p. = 197–200°C (EtOH), IR spectrum ν (cm^{-1}): 3317, 3210 (NH_2), 2942 (CH-aliphatic) and 2209 (CN). Found C 67.9, H 5.4, N 12.3 and S 9.5. Calculated for $C_{19}H_{17}N_3OS$ (335.41), C 68.03, H 5.11, N 12.53 and S 9.56. MS: m/z = 336.15, 16.64%.

9-(p-Anisyl)-3,4-dihydro-4-oxo-7,8-polymethylenepyrido-[3′,2′:4,5]-thieno[3,2-*d*]pyrimidines 3a,b

Each of **2a,b** (0.005 mmol) was heated under reflux in formic acid (30 ml, 85%) for 10 h. The reaction mixture was then left aside to cool at room temperature and poured onto cold water. The solid product so formed, in each case, was filtered off and crystallized from the proper solvent.

(3a)- yield 67%, m.p. = 275°C (dil. DMF), IR spectrum ν (cm^{-1}): 3320, 3215 (NH and/or OH), 2941 (CH-aliphatic) and weak band at 1724 (CO). ^1H NMR spectrum (acetone-d_6) δ (ppm) = 2.0–2.28 (m, 6H, 3 CH_2), 3.9 (s, 3H, OCH_3), 4.34 (s, 1H, OH), 5.1 (s, 1H, pyrimidine H-2) and 7.13–7.53 (m, 4H, aromatic protons). Found C 64.3, H 4.5, N 12.3 and S 9.1. Calculated for $C_{19}H_{15}N_3O_2S$ (349.39), C 65.31, H 4.33, N 12.03 and S 9.17. MS: m/z = 349.3, 16.4%.

(3b)- yield 65%, m.p. = 230°C (dioxane), IR spectrum ν (cm^{-1}): 3340, 3250 (NH and/or OH), 2941 (CH-aliphatic) and weak band at 1708 (CO). Found C 65.7, H 4.8, N 11.2 and S 9.1. Calculated for $C_{20}H_{17}N_3O_2S$ (363.42), C 66.09, H 4.72, N 11.56 and S 8.82.

4-Amino-9-(*p*-anisyl)-7,8-polymethylenepyrido[3′,2′:4,5]-thieno[3,2-*d*]pyrimidines 4a,b

Each of **2a,b** (0.005 mmol) was heated under reflux in a ternary mixture of formic acid (5 ml, 85%), formamide (5 ml), and dimethyl-formamide (5 ml), for 10 h. The reaction mixture was then cooled at room temperature, poured onto cold water whereby, the solid product so formed, in each case, was filtered off, and crystallized from the proper solvent.

(4a)- yield 80%, m.p. = 287°C (acetonitrile), IR spectrum ν (cm^{-1}): 3450 (NH_2), 2950 (CH-aliphatic). ^1H NMR spectrum (DMSO-d_6) δ (ppm) = 2.04–2.51 (m, 6H, $3CH_2$), 3.36 (s, 2H, NH_2, D_2O exchangable), 3.87 (s, 3H, OCH_3), 5.38 (s, 1H, pyrimidine H-2) and 7.16–7.54 (2d, 4H, aromatic protons) Found C 65.1, H 4.6, N 16.2 and S 9.2. Calculated for $C_{19}H_{16}N_4OS$ (348.40), C 65.50, H 4.63, N 16.08 and S 9.20. MS: m/z = 348.1, 18.2%.

(4b)- yield 72%, m.p. = 258°C (acetonitrile), IR spectrum ν (cm^{-1}): 3450 (NH_2), 2955 (CH-aliphatic). Found C 65.7, H 5.1, N 15.1 and S 9.0. Calculated for $C_{20}H_{18}N_4OS$ (362.43), C 66.27, H 5.0, N 15.46 and S 8.85. MS: m/z = 362, 42.4%.

9-(*p*-Anisyl)-2,4-diamino-7,8-polymethylenepyrido-[3′,2′:4,5]thieno[3,2-*d*]pyrimidines 5a,b

Cyanamide (0.42 g, 0.01 mmol) was added to each solution of **2a,b** (0.01 mmol) in dioxane (50 ml) containing a few drops of conc. HCl, and the reaction mixture was heated under reflux for 24 h. The reaction mixture was then cooled at room temperature, poured onto cold water whereby the formed solid produc, in each case, was filtered off and crystallized from the proper solvent.

(5a)- yield 57%, m.p. = 200°C (dil. DMF), IR spectrum ν (cm^{-1}): 3600–3300 (NH_2) and 2940 (CH-aliphatic). Found C 62.5, H 4.5, N 18.9 and S 8.6. Calculated for $C_{19}H_{17}N_5OS$ (363.43), C 62.78, H 4.72, N 19.27 and S 8.82. MS: m/z = 363.3, 22.4%.

(5b)- yield 63%, m.p. = 198–200°C (dil. DMF), IR spectrum ν (cm^{-1}): 3600–3400 (NH_2) and 2950 (CH-aliphatic). ^1H NMR spectrum (acetone-d_6) δ (ppm) = 2.02–2.68 (m, 8H, 4 CH_2), 3.96 (s, 3H, OCH_3), 7.16–7.46 (m, 4H, aromatic protons) and 8.03, 8.18 (d, 4H, $2NH_2$). Found C 63.4, H 5.1, N 19.0 and S 8.8. Calculated for $C_{20}H_{19}N_5OS$ (377.46), C 63.63, H 5.07, N 18.55 and S 8.49.

9-(*p*-Anisyl)-2,4-disulphanyl-7,8-polymethylenepyrido-[3′,2′:4,5]thieno[3,2-*d*]pyrimidines 6a,b

A mixture of each of **2a,b** (0.01 mmol) and carbon disulphide (0.03 mmol) in dry pyridine (50 ml) was boiled under reflux for 8 h. The

reaction mixture was cooled and then poured onto cold water containing few drops of conc. HCl for neutralization. The formed solid product, in each case, was filtered off and crystallized from the proper solvent.

(6a)- yield 85%, m.p. = 297°C (dioxane), IR spectrum ν (cm^{-1}): 3450 (NH), 2930 (CH-aliphatic) and 1190 (C=S). Found C 57.9, H 3.7, N 10.7 and S 24.1. Calculated for $C_{19}H_{15}N_3OS_3$ (397.52), C 57.4, H 3.8, N 10.57 and S 24.19.

(6b)- yield 80%, m.p. = 285°C (dioxane), IR spectrum ν (cm^{-1}): 3500 (NH), 2950 (CH-aliphatic) and 1190 (C=S). ^{1}H NMR spectrum (acetone-d_6) δ (ppm) = 2.0–2.5 (m, 8H, 4 CH_2), 3.9 (s, 3H, OCH_3), 7.12–7.32 (m, 4H, aromatic protons) and 8.51–8.68 (d, 2H, 2NH). Found C 58.2, H 4.3, N 10.2 and S 23.1. Calculated for $C_{20}H_{17}N_3OS_3$ (411.55), C 58.36, H 4.16, N 10.21 and S 23.37.

4-Amino-9-(*p*-anisyl)-2-sulphanyl-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*d*]pyrimidines 7a,b

Thiourea (0.75 g, 0.01 mmol) was added to a solution of each of **2a,b** (0.01 mmol) in dry dioxane (60 ml) containing triethylamine (0.01 mmol) and the reaction mixture was heated under reflux for 10 h. The reaction mixture was cooled at room temperature and poured onto crused ice containing few drops of dil. HCl. The formed solid product, in each case, was filtered off and crystallized from the proper solvent.

(7a)- yield 78%, m.p. = 218–220°C (EtOH), IR spectrum ν (cm^{-1}): 3443 (NH_2), 2926 (CH-aliphatic) and 1177 (C=S). The ^{1}H NMR ($CDCl_3$) at δ (ppm) = 1.9–2.18 (m, 6H, 3CH_2), 3.9 (s, 3H, OCH_3), 7.0–7.5 (m, 4H, aromatic protons), 8.7 (s, 2H, NH_2) and 9.9 (s, 1H, NH). Found C 62.3, H 4.2, N 15.1 and S 17.1. Calculated for $C_{19}H_{16}N_4OS_2$ (364.46), C 62.6, H 4.43, N 15.37 and S 17.58. MS: m/z = 364.2, 18.4%.

(7b)- yield 75%, m.p. = 235°C (EtOH), IR spectrum ν (cm^{-1}): 3450, 3350 (NH_2), 2960 (CH-aliphatic) and 1208 (C=S). Found C 63.2, H 4.9, N 14.7 and S 16.9. Calculated for $C_{20}H_{18}N_4OS_2$ (378.5), C 63.46, H 4.8, N 14.8 and S 16.9.

9-(*p*-Anisyl)-2,4-diamino-7,8-polymethylenepyrido-[3′2′:4,5]thieno[3,2-*b*]pyridine-3-carboniriles 8a,b

Each of **2a,b** (0.01 mmol) was added to a solution of malononitrile (0.66 g, 0.01 mmol) in absolute ethanol (50 ml) containing a catalytic amount of triethylamine (3 drops). The reaction mixture was heated under reflux for 12 h, cooled at room temperature, poured onto cold water and neutralized with few drops of dil. HCl. The formed solid product, in each case, was filtered off and crystallized from the proper solvent.

(8a)- yield 68%, m.p. = 265°C (acetonitrile), IR spectrum ν (cm^{-1}): 3450, 3350 (NH_2), 2960 (CH-aliphatic) and 2200 (CN). ^1H NMR spectrum (DMSO-d_6) δ (ppm) = 2.02–2.25 (m, 6H, 3 CH_2), 3.9 (s, 3H, OCH_3), 7.19–7.42 (m, 4H, aromatic protons), 9.61 (s, 2H, NH_2) and 10.73 (s, 2H, NH_2). Found C 64.8, H 4.3, N 17.9 and S 8.4. Calculated for $C_{21}H_{17}N_5OS$ (387.45), C 65.1, H 4.42, N 18.08 and S 8.28. MS: $m/z = 387.2$, 19.2%.

(8b)- yield 75%, m.p. = 238–240°C (acetonitrile), IR spectrum ν (cm^{-1}): 3500, 3350 (NH_2), 2950 (CH-aliphatic) and 2200 (CN). Found C 65.5, H 4.8, N 17.3 and S 8.1. Calculated for $C_{22}H_{19}N_5OS$ (401.47), C 65.81, H 4.77, N 17.45 and S 7.99.

4-Amino-9-(*p*-anisyl)-1,2-dihydro-2-oxo-7,8-polymethylenepyrido[3′,2′:4,5]thieno[3,2-*b*]pyridine-3-carbonitriles 9a,b

Each of **2a,b** (0.01 mmol) was added to a solution of ethyl cyanoacetate (0.01 mmol) in absolute ethanol (50 ml) containing a catalytic amount of triethylamine (3 drops) and the reaction mixture was heated under reflux for 12 h. The reaction mixture was cooled at room temperature poured onto cold water and neutralized with few drops of dil. HCl. The formed solid product, in each case, was filtered off and crystallized from the proper solvent.

(9a)- yield 80%, m.p. = 275°C (dil. DMF), IR spectrum ν (cm^{-1}): 3310, 3200 (NH_2), 2950 (CH-aliphatic), 2210 (CN) and 1680 (C=O). Found C 64.8, H 4.2, N 14.5 and S 8.3. Calculated for $C_{21}H_{16}N_4O_2S$ (388.43), C 64.93, H 4.15, N 14.43 and S 8.25. MS: $m/z = 388.2$, 16.4%.

(9b)- yield 80%, m.p. = 287–290°C (dil. DMF), IR spectrum ν (cm^{-1}): 3500, 3350 (NH_2), 2970 (CH-aliphatic), 2220 (CN) and 1680 (C=O). ^1H NMR spectrum (DMSO-d_6) δ (ppm) = 2.03–2.62 (m, 8H, 4 CH_2), 3.81 (s, 3H, OCH_3), 5.62 (s, 2H, NH_2), 7.1–7.4 (m, 4H, aromatic protons) and 9.18 (s, 1H, NH). Found C 65.6, H 4.5, N 13.8 and S 7.9. Calculated for $C_{22}H_{18}N_4O_2S$ (402.46), C 65.65, H 4.50, N 13.92 and S 7.97.

4-Amino-9-(*p*-anisyl)-2-phenyl-7,8-polymethylenepyrido-[3′,2′:4,5]thieno[3,2-*b*]pyridine-3-carbonitriles 10a,b

Benzalmalononitrile (1.55 g, 0.01 mmol) was added to a solution of each of **2a,b** (0.01 mmol) in dry pyridine (50 ml) and the reaction mixture was heated under reflux for 8 h. After complete reflux and cooling at room temperature, the reaction mixture was then poured onto crushed ice and neutralized with dil. HCl, whereby the solid precipitate so formed, in each case, was filtered off and crystallized from ethanol.

(10a)- yield 65%, m.p. = 247°C, IR spectrum ν (cm^{-1}): 3450, 3350 (NH_2), 2950 (CH-aliphatic) and 2215 (CN). Found C 71.9, H 4.5, N 12.5 and S 7.4. Calculated for $C_{27}H_{20}N_4OS$ (448.52), C 72.3, H 4.5, N 12.5 and S 7.15. MS: $m/z = 448.4$, 21.2%.

(10b)- yield 63%, m.p. = 233°C, IR spectrum ν (cm^{-1}): 3450, 3350 cm^{-1} (NH_2), 2960 cm^{-1} (CH-aliphatic) and 2200 cm^{-1} (CN). Found C 72.5, H 4.8, N 12.0 and S 7.0. Calculated for $C_{28}H_{22}N_4OS$ (462.55), C 72.7, H 4.79, N 12.14 and S 6.93. MS: $m/z = 462.5$, 30%.

3-Amino-4-(*p*-anisyl)-5,6-polymethylenethieno[2,3-*b*]pyridine-3-(N-amino)amidines 11a,b

Hydrazine hydrate (0.01 mmol) was added to a solution of **2a,b** (0.01 mmol) in absolute ethanol (50 ml) containing a catalytic amount of triethylamine (3 drops) and the reaction mixture was heated under reflux for 5 h. The reaction mixture was cooled at room temperature, poured into cold water and neutralized with few drops of dil. HCl. The formed solid product in each case, was filtered off and crystallized from ethanol.

(11a)- yield 70%, m.p. = 195°C, IR spectrum ν (cm^{-1}): 3500–3380 (NH_2), 2950 and 2940 cm^{-1} (CH-aliphatic). Found C 61.2, H 5.2, N 19.5 and S 9.3. Calculated for $C_{18}H_{19}N_5OS$ (353.44), C 61.16, H 5.41, N 19.82 and S 9.09. MS: $m/z = 353.2$, 8.97%.

(11b)- yield 72%, m.p. = 206°C, IR spectrum ν (cm^{-1}): 3485–3370 (NH_2), 2950 and 2936 cm^{-1} (CH-aliphatic). Found C 62.0, H 5.5, N 19.0 and S 8.6. Calculated for $C_{19}H_{21}N_5OS$ (367.47), C 62.10, H 5.75, N 19.06 and S 8.72%.

3-Amino-8-(*p*-anisyl)-6,7-polymethylene-1*H*-pyrazolo-[3′,4′:4,5]thieno[2,3-b]pyridines 12a,b

Solutions of each of **11a,b** (0.01 mmol) in dioxane (50 ml) containing conc. HCl (10 drops) was heated under reflux for 6 h. The reaction mixture was then left aside to cool at room temperature and poured onto cold water, whereby the formed solid product, in each case, was filtered off and crystallized from the proper solvent.

(12a)- yield 40%, m.p. = 187°C (EtOH), IR spectrum ν (cm^{-1}): 3480, 3320 (NH, NH_2) and 2950 (CH-aliphatic). ^1H NMR spectrum (DMSO) δ (ppm) = 2.3–2.6 (m, 6H, 3 CH_2), 3.9 (s, 3H, OCH_3), 5.3 (s, 2H, NH_2, D_2O exchangable), 7.0–7.5 (2d, 4H, aromatic protons) and 8.4 (s, 1H, NH, D_2O exchangable). MS: $m/z = 336.4$, 16.64%. Found C 64.3, H 4.9, N 16.5 and S 9.6. Calculated for $C_{18}H_{16}N_4OS$ (336.41), C 64.26, H 4.76, N 16.65 and S 9.53.

(12b)- yield 45%, m.p. = 200°C (EtOH), IR spectrum ν (cm^{-1}): 3450, 3350 (NH, NH_2), 2980 (CH-aliphatic). Found C 65.40, H 5.2, N 16.1 and S 9.2. Calculated for $C_{19}H_{18}N_4OS$ (350.43), C 65.12, H 5.18, N 15.99 and S 9.15.

3-Amino-4-(*p*-anisyl)-5,6-polymethylenethieno[2,3-b]-pyridine-3-(*o*-aminophenyl)amidines 13a,b

o-Phenylenediamine (1.1 g, 0.01 mmol) was added to a solution of each of **2a,b** (0.01 mmol) in dry dioxane (40 ml) containing a catalytic amount of triethylamine (3 drops) and the reaction mixture was then heated under reflux for 5 h. After complet reflux and cooling at room temperature, the reaction mixture was poured into cold water and neutralized with dil. HCl. The formed solid product, in each case, was filtered off and crystallized from ethanol.

(13a)- yield 65%, m.p. = 218–220°C, IR spectrum ν (cm^{-1}): 3409, 3385 (NH_2) and 2929 (CH-aliphatic). Found C 66.8, H 5.1, N 15.9 and S 7.4. Calculated for $C_{24}H_{23}N_5OS$ (429.54), C 67.1, H 5.4, N 16.31 and S 7.46. MS: $m/z = 429.5$, 22.4%.

(13b)- yield 67%, m.p. = 226-8°C, IR spectrum ν (cm^{-1}): 3400, 3380 (NH_2) and 2936 (CH-aliphatic). Found C 67.5, H 5.4, N 15.7, S 7.0. Calculated for $C_{25}H_{25}N_5OS$ (443.57), C 67.69, H 5.68, N 15.78, S 7.23. MS: $m/z = 443.4$, 22.4%.

6-Amino-11-(*p*-anisyl)-12*H*-9,10-polymethylenepyrido-[3′,2′:4,5]thieno[3,2-*b*]benzo[1,4]diazepines 14a,b

Each solution of **13a,b** (0.01 mmol) in dry dioxane (60 ml) containing a few drops of conc. HCl was heated under reflux for 6 h. The reaction mixture was then cooled at room temperature and poured onto crushed ice. The formed solid product, in each case, was filtered off and crystallized from the proper solvent.

(14a)- yield 50%, m.p. = 240°C (dioxane), IR spectrum ν (cm^{-1}): 3350, 3280 (NH, NH_2) and 2933 (CH-aliphatic). The ^1H NMR spectrum (DMSO-d_6) δ (ppm) = 2.2–2.6 (m, 6H, 3 CH_2), 3.8 (s, 3H, OCH_3), 4.2 (s, 2H, NH_2, D_2O exchangable), 7.0–7.6 (m, 8H, aromatic protons) and 8.1 (s, 1H, NH, D_2O exchangable). Found C 69.5, H 4.8, N 13.3 and S 7.7. Calculated for $C_{24}H_{20}N_4OS$ (412.5), C 69.88, H 4.89, N 13.58 and S 7.77. MS: $m/z = 412.15$, 18.18%.

(14b)- yield 55%, m.p. = 263°C (dioxane), IR spectrum ν (cm^{-1}): 3350, 3250 (NH, NH_2) and 2928 (CH-aliphatic). Found C 69.9, H 5.1, N 12.7 and S 7.3. Calculated for $C_{25}H_{22}N_4OS$ (426.53), C 70.39, H 5.2, N 13.14 and S 7.40.

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