Hala M. Refat* and Khaled S. Mohamed

Efficient and convenient synthesis of pyrido [2,1-*b*]benzothiazole, pyrimidopyrido[2,1-*b*] benzothiazole and benzothiazolo[3,2-*a*][1,8] naphthyridine derivatives

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Abstract: New 3-aryl-pyrido[2,1-*b*][1,3]benzothiazole derivatives **2a**–**e** were synthesized in excellent yields *via* the reaction of benzothiazoleacetonitrile (**1**) with different aromatic aldehydes. The treatment of 2-(benzo[*d*]thiazol-2-yl)-3-(pyridin-4-yl)acrylonitrile (**6**) with malononitrile afforded 1-amino-3-(pyridin-4-yl)-3*H*-pyrido[2,1-*b*][1,3]benzothiazole-2,4-dicarbonitrile (**7**), which was allowed to react with a variety of reagents to provide pyrimido[5′,4′:5,6]pyrido[2,1-*b*][1,3]benzothiazole **8**, **9** and [1,3]benzothiazolo[3,2-*a*][1,8] naphthyridine **10**, **15** derivatives. All synthesized products were confirmed by elemental analysis, IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectral data.

Keywords: benzothiazoleacetonitrile; pyrido[2,1-*b*][1,3] benzothiazole; pyrimidopyrido [2,1-*b*][1,3]benzothiazole.

Introduction

Benzothiazole derivatives have been important heterocycles for many years because of their broad bioactivities, including antimicrobial [1–5], anticancer [6–11], anthelmintic [12], anticonvulsant [13], and antidiabetic [14] activities. They also serve as intermediates for dyes [15]. In addition, some fused pyridopyrimidine derivatives are biologically active [16–18].

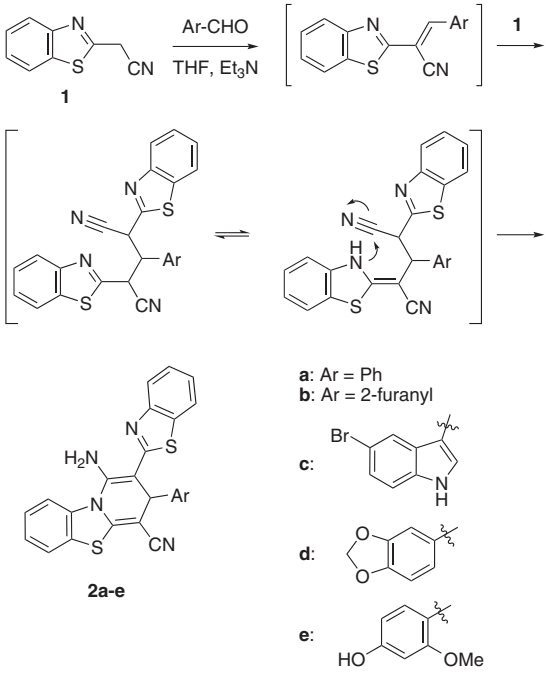
In a similar way, 1,8-naphthyridine derivatives have received attention recently, primarily because this ring system is present in many compounds isolated from natural sources. They exhibit various biological activities [19], such as antibacterial [20, 21], antitumor [22], and antiplatelet [23, 24] activities. Furthermore, various substituted benzothiazoles such as 2-aryl benzothiazoles have received much attention because of their unique structures and uses as radioactive amyloid imagining agents [25] and anticancer agents [26]. In continuation of our interest in the synthesis of heterocycles containing a benzothiazole moiety [27–30], we report herein a facile route to several new benzothiazole-fused heterocyclic systems. We present efficient synthesis of novel pyrido[2,1-*b*][1,3] benzothiazole, pyrimidopyrido[2,1-*b*][1,3]benzothiazole, and benzothiazolo[3,2-*a*][1,8] naphthyridine derivatives.

***Corresponding author: Hala M. Refat,** Faculty of Science, Department of Chemistry, Suez Canal University, Al-Arish 45511, Egypt, e-mail: halamorefat@yahoo.com
Khaled S. Mohamed: Higher Institute for Engineering and Technology, Engineering Chemistry Department, New Damietta 34518, Egypt

Results and discussion

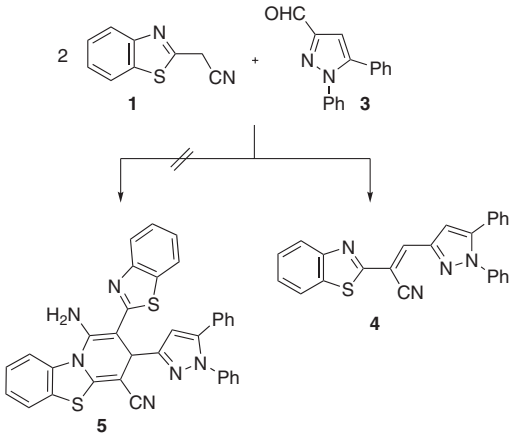
As shown in Scheme 1, condensation of compound **1** with benzaldehyde, furfural, 5-bromo-1*H*-indole-3-carbaldehyde, piperonal, or 4-hydroxy-2-methoxybenzaldehyde in refluxing THF containing a catalytic amount of TEA furnished the corresponding 1-amino-3-aryl-2-(2-benzothiazolyl)-3*H*-pyrido[2,1-*b*][1,3]benzothiazole-4-carbonitrile derivatives **2a**–**e**. The assignments of structures **2a**–**e** were supported by their elemental analyses and spectral data. The ^{1}H NMR spectra of structures **2a**–**e** show two singlets at δ 4.60–4.82 and 8.10–8.90 ppm for C_3-H and NH_2 protons, respectively. In addition, the ^{1}H-NMR spectrum of compound **2c** shows a singlet at δ 10.95 ppm assignable to the NH proton of the indole group. Also, compound **2d** showed a signal at δ 6.10 ppm assignable to the methylene group. Compound **2e** exhibits singlets at δ 3.80 and 10.10 assignable to the OMe and OH protons, respectively. Mass spectra of **2a**–**e** contain the molecular ion peak for each compound.

In contrast to the above-mentioned reaction, the treatment of compound **1** with 1,5-diphenyl-1*H*-pyrazole-3-carbaldehyde (**3**) in THF in the presence of a catalytic amount of TEA furnished 2-(benzo[*d*]thiazol-2-yl)-

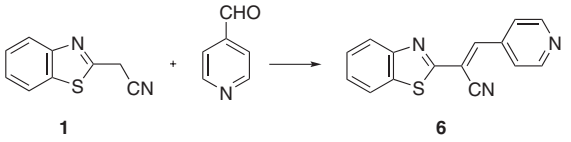


Scheme 1

3-(1,5-diphenyl-1*H*-pyrazol-3-yl)acrylonitrile (**4**) rather than the expected product **5** (Scheme 2). The IR spectrum of **4** shows the absence of NH_2 absorption band, but the absorption band at 2198 cm^{-1} corresponding to a CN group is seen clearly. The structure of **4** is consistent with the ^1H NMR spectrum, which shows the absence of any D_2O exchangeable signal. There is a precedence in the literature for this outcome, in which the condensation between **1** and isonicotinaldehyde in boiling THF containing a catalytic amount of TEA afforded the (*E*)-2-(benzo[*d*]thiazol-2-yl)-3-(pyridin-4-yl)acrylonitrile (**6**) [31] (Scheme 3). Heating under reflux of compound **6** with malononitrile in ethanol in the presence of a catalytic amount of TEA afforded



Scheme 2

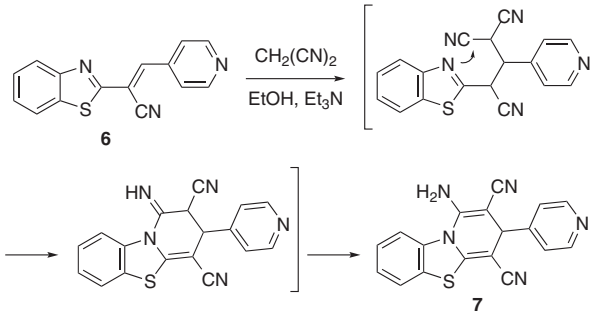


Scheme 3

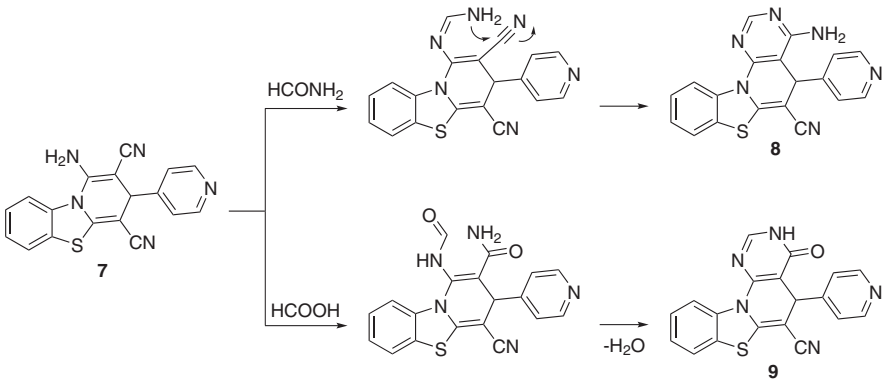
1-amino-3-(pyridin-4-yl)-3*H*-pyrido[2,1-*b*][1,3]benzothiazole-2,4-dicarbonitrile (**7**) [32] (Scheme 4). The IR spectrum of **7** displays stretching vibration bands at 3363, 3243, 2208, and 2191 cm^{-1} corresponding to NH_2 and two CN groups, respectively. Its ^1H NMR spectrum reveals the presence of signals at δ 4.71 and 6.52 ppm assignable to the C_3-H and NH_2 protons, respectively. The mass spectrum shows the molecular ion peak at *m*/*z* 329 (M^+, 49%), corresponding to the molecular formula $C_{18}H_{11}N_5S$.

Compound **7** was utilized as a starting material for preparation of a wide variety of fused heterocyclic compounds. Thus, heating of compound **7** with formamide afforded 4-amino-5-(pyridin-4-yl)-5*H*-pyrimido[5′,4′:5,6]pyrido[2,1-*b*][1,3]benzothiazole-6-carbonitrile (**8**). Similarly, a cyclocondensation of compound **7** with hot formic acid afforded 4-oxo-5-(pyridin-4-yl)-3,5-dihydropyrimido[5′,4′:5,6]pyrido[2,1-*b*][1,3]benzothiazole-6-carbonitrile (**9**) (Scheme 5). The IR spectrum of compound **9** displays stretching vibration bands at 3284, 2195, and 1645 cm^{-1} corresponding to NH, CN, and C=O groups, respectively. Its ^1H NMR spectrum reveals the presence of three singlet signals at δ 4.71, 8.68, and 11.23 ppm assignable to the respective protons C_5-H, C_2-H, and NH protons. The mass spectrum shows the molecular ion peak at *m*/*z* 357 (M^+, 25%) corresponding to the molecular formula $C_{19}H_{11}N_5OS$. Compound **9** is apparently formed by partial nitrile hydrolysis, amine formylation, and cyclodehydration.

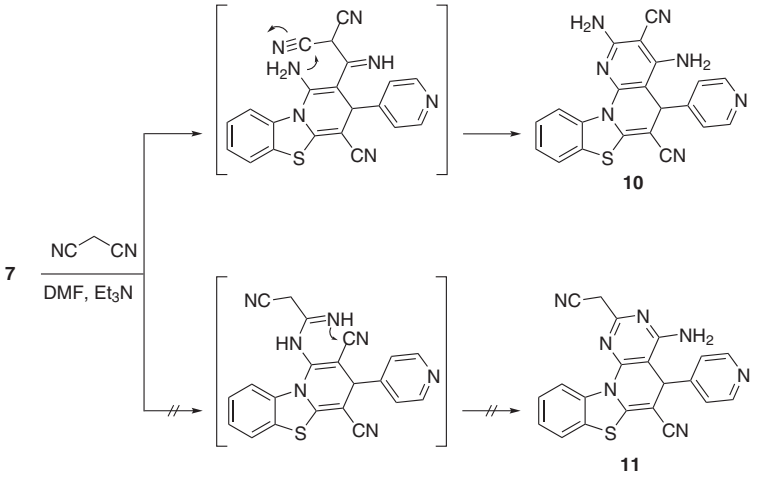
Compound **7** can be transformed into a number of derivatives. For example, heating compound **7** with malononitrile in DMF and a catalytic amount of TEA under reflux conditions afforded 2,4-diamino-5-(pyridin-4-yl)-5*H*-[1,3]benzothiazolo[3,2-*a*][1,8]naphthyridine-3,6-dicarbonitrile



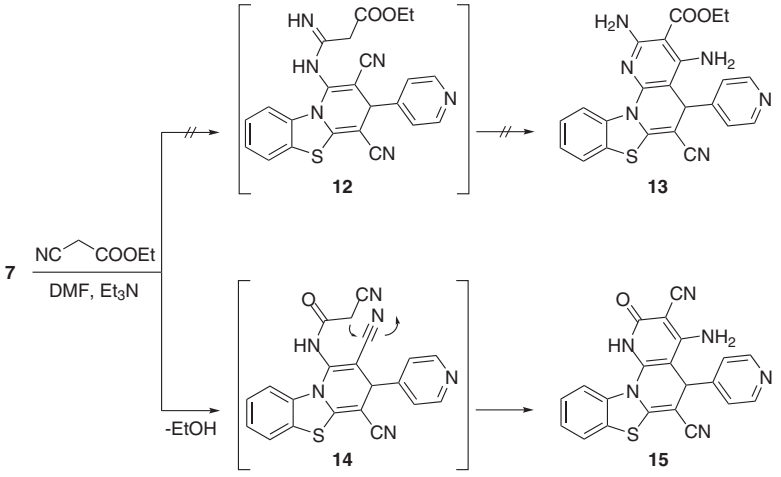
Scheme 4



Scheme 5



Scheme 6



Scheme 7

(**10**) rather than the analog **11**, in line with the reported results [33] (Scheme 6). The IR spectrum of compound **10** shows the presence of signals for two NH_2 groups around 3405–3313 cm^{-1} and two cyano groups at 2205 and 2199 cm^{-1}. The ^1H NMR spectrum of compound **10** shows a singlet at δ 4.73 assignable to C_5-H, two singlets (D_2O exchangeable)

at 6.52 and 8.25 ppm assignable to two NH_2 groups and no signal in the region of 3–4 ppm for a methylene group. Also, ^{13}C NMR spectrum reveals only one signal in the region of 20–60 ppm because of C_5, which is consistent with the given structure **10**.

By contrast, the treatment of **7** with ethyl cyanoacetate in boiling DMF containing a catalytic amount of TEA afforded the dicarbonitrile **15** rather than its analog **13** (Scheme 7).

The structure of **15** was confirmed on the basis of IR, ^1H NMR, ^{13}C NMR, and MS data. The mass spectrum shows the molecular ion peak at *m*/*z* 396 (M^+, 100%), which is consistent with the proposed structure, whereas the absence of a triplet-quartet pattern in the ^1H NMR spectrum confirms elimination of the ethoxy group during the reaction.

Conclusions

A convenient and efficient one-pot synthesis of substituted pyrido[2,1-*b*][1,3]benzothiazoles based on reaction of benzothiazoleacetonitrile with different aromatic aldehydes has been developed. Pyrido[2,1-*b*]benzothiazole derivative **7** was used as a key precursor for synthesis of novel pyrimidopyrido[2,1-*b*][1,3]benzothiazole and [1,3] benzothiazolo [3,2-*a*][1,8]naphthyridine derivatives.

Experimental

Melting points were measured with a Gallenkamp apparatus and are uncorrected. IR spectra were recorded in KBr discs on a Mattson 5000 FTIR spectrophotometer at Microanalytical Unit, Faculty of Science, Mansoura University. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on Bruker WP AC 300 instrument in DMSO-d_6. Electron-impact mass spectra were determined on Finnigan Incos 500 at 70 eV. Elemental analyses were carried out at the Microanalytical Centre, Faculty of Science, Cairo University.

General procedure for the synthesis of 1-amino-3-aryl-2-(2-benzothiazolyl)-3*H*-pyrido[2,1-*b*][1,3]benzothiazole-4-carbonitriles 2a–e

A mixture of 2-cyanomethylbenzothiazole (**1**, 1.74 g, 0.01 mol), an aromatic aldehyde (0.005 mol) in THF (15 mL) and Et_3N (a few drops), was heated under reflux for 6–8 h (TLC monitored). After cooling, the resultant precipitate was isolated by suction, washed with EtOH (5 mL), and then crystallized from THF/EtOH (1:1) to afford compound 2a–e.

1-Amino-2-(2-benzothiazolyl)-3-phenyl-3*H*-pyrido[2,1-*b*][1,3] benzothiazole-4-carbonitrile (2a) Yellow crystals; yield 85%; mp 221–223°C; IR: ν 3354, 3321 (NH_2), 2195 cm^{-1} (CN); ^1H NMR: δ 4.82 (s, 1H, CH), 7.20–8.10 (m, 13H, Ar-H), 8.40 (s, 2H, NH_2); ^{13}C NMR: δ 32.1, 60.5, 86.4, 117.5, 120.1, 121.5 (2C), 122.3 (2C), 124.4 (2C), 126.6 (3C), 127.5 (2C), 128.6 (2C), 136.4, 145.3 (2C), 150.5, 153.3, 160.2, 162.3; MS: *m*/*z* 436 (M^+, 23%). Anal. Calcd for $C_{25}H_{16}N_4S_2$ (436.55): C, 68.78; H, 3.69; N, 12.83. Found: C, 68.72; H, 3.71; N, 12.80.

1-Amino-2-(2-benzothiazolyl)-3-(2-furyl)-3*H*-pyrido[2,1-*b*][1,3] benzothiazole-4-carbonitrile (2b) Yellow crystals; yield 79%; mp 183–185°C; IR: ν 3356, 3330 (NH_2), 2198 cm^{-1} (CN); ^1H NMR: δ 4.64 (s, 1H, CH), 6.19 (m, 1H, C_4-H of furan), 6.38 (d, 1H, C_3-H of furan), 7.20–8.10 (m, 10H, Ar-H), 8.40 (s, 2H, NH_2); ^{13}C NMR: δ 27.6, 62.4, 86.5, 108.8, 110.7, 117.5, 120.2, 121.3 (2C), 122.4 (3C), 124.2, 126.5 (2C), 136.4, 140.2, 145.4, 150.5, 152.5, 153.4, 160.2, 162.4; MS: *m*/*z* 426 (M^+, 56%). Anal. Calcd for $C_{23}H_{14}N_4OS_2$ (426.51): C, 64.77; H, 3.31; N, 13.14. Found: C, 67.73; H, 3.33; N, 13.18.

1-Amino-2-(2-benzothiazolyl)-3-(5-bromo-1*H*-3-indolyl)--3H-pyrido[2,1-*b*][1,3]benzothiazole-4-carbonitrile (2c) Yellow crystals; yield 64%; mp>300°C; IR: ν 3387, 3334 (NH_2), 3188 (NH), 2200 cm^{-1} (CN); ^1H NMR: δ 4.76 (s, 1H, CH), 7.20–8.10 (m, 12H, Ar-H), 8.90 (s, 2H, NH_2), 10.95 (s, 1H, NH); ^{13}C NMR: δ 31.8, 61.5, 86.6, 106.4, 114.4, 116.3, 117.4, 120.2, 121.1 (3C), 122.3 (2C), 124.6 (4C), 126.4 (2C), 130.2, 136.6 (2C), 145.4, 150.2, 153.5, 160.3, 162.2; MS: *m*/*z* 554 (M^+, 33%). Anal. Calcd for $C_{27}H_{16}BrN_5S_2$ (554.48): C, 58.49; H, 2.91; N, 12.63. Found: C, 58.44; H, 2.89; N, 12.66.

1-Amino-2-(2-benzothiazolyl)-3-(benzo[*d*][1,3]dioxol-5-yl)-3*H*-pyrido[2,1-b][1,3] benzothiazole-4-carbonitrile (2d) Yellow crystals; yield 71%; mp 215–217°C; IR: ν 3410, 3385 (NH_2), 2208 cm^{-1} (CN); ^1H NMR: δ 4.60 (s, 1H, CH), 6.10 (s, 2H, CH_2), 7.20–8.10 (m, 11H, Ar-H) 8.44 (s, 2H, NH_2); ^{13}C NMR: δ 33.3, 61.4, 86.5, 101.4, 110.5, 113.5, 117.6, 120.2, 121.3 (2C), 122.4 (2C), 124.5 (3C), 126.7 (2C), 136.4 (2C), 145.8 (3C), 150.3, 153.8, 160.2, 162.3; MS: *m*/*z* 480 (M^+, 27%). Anal. Calcd for $C_{26}H_{16}N_4O_2S_2$ (480.56): C, 64.98; H, 3.36; N, 11.66. Found: C, 65.01; H, 3.39; N, 11.69.

1-Amino-2-(2-benzothiazolyl)-3-(4-hydroxy-2-methoxyphenyl)-3*H*-pyrido[2,1-*b*][1,3] benzothiazole-4-carbonitrile (2e) Yellow crystals; yield 62%; mp 180–182°C; IR: ν br 3400–3300 (NH_2 and OH), 2220 cm^{-1} (CN); ^1H NMR: δ 3.80 (s, 3H, OCH_3), 4.60 (s, 1H, CH), 7.20–8.10 (m, 11H, Ar-H), 8.10 (s, 2H, NH_2), 10.10 (br s, 1H, OH); ^{13}C NMR: δ 31.5, 56.4, 61.2, 86.4, 102.4, 110.2, 113.6, 117.5, 120.3, 121.3 (2C), 122.5, 124.6 (3C), 126.7 (2C), 131.5, 136.2, 145.6, 150.3, 153.7, 155.8, 159.5, 160.5, 162.3; MS: *m*/*z* 482 (M^+, 36%). Anal. Calcd for $C_{26}H_{18}N_4O_2S_2$ (482.58): C, 64.71; H, 3.76; N, 11.61. Found: C, 64.70; H, 3.79; N, 11.64.

Synthesis of 2-(benzo[*d*]thiazol-2-yl)-3-(1,5-diphenyl-1*H*-pyrazol-3-yl)acrylonitrile (4) A mixture of 2-cyanomethylbenzothiazole (**1**, 1.74 g, 0.01 mol), 1,5-diphenyl-1*H*-pyrazole-3-carbaldehyde (**3**, 2.48 g, 0.01 mol), and Et_3N (a few drops) in THF (15 mL) was heated under reflux for 8 h. After cooling, the resultant precipitate was isolated by suction, washed with EtOH (5 mL), and then crystallized from THF/EtOH (1:1) to afford compound **4:** Yellow crystals; yield 68%; mp 220–222°C; IR: ν 2198 cm^{-1} (CN); ^1H NMR: δ 7.10–8.20 (m, 14H, Ar-H), 7.19 (s, 1H, C_4-H of pyrazole), 8.17 (s, 1H, olefinic); ^{13}C NMR: δ 110.5, 112.5, 117.5, 120.5, 121.4, 122.5, 124.5 (2C), 126.2 (2C), 128.3 (3C), 130.2 (4C), 133.4 (2C), 139.8, 141.2, 143.3, 145.5, 156.5, 162.6; MS: *m*/*z* 404 (M^+, 35%). Anal. Calcd for $C_{25}H_{16}N_4S$ (404.49): C, 74.24; H, 3.99; N, 13.85. Found: C, 74.28; H, 3.99; N, 13.82.

Synthesis of (E)-2-(benzo[*d*]thiazol-2-yl)-3-(pyridin-4-yl)acrylonitrile (6) A solution of compound **1** (1.74 g, 0.01 mol) and isonicotinaldehyde (1.07 g, 0.01 mol) in THF (10 mL) containing three drops of Et_3N was heated under reflux for approximately 4 h, with progress monitored by TLC. The solid product **6** formed upon cooling was filtered off, dried, and crystallized from EtOH: Yellow crystals; yield 88%; mp 195–196°C; IR: ν 2215 cm^{-1} (CN); ^1H NMR: δ 7.41 (d, 2H, J = 7.60 Hz, C_3-H, C_5-H of pyridine), 7.55 (m, 2H, C_5-H and C_6-H of benzothiazole), 7.95 (dd, 1H, J = 7.40 Hz and 1.50 Hz, C_7-H of benzothiazole), 8.20 (s, 1H, vinylic H), 8.23 (dd, 1H, J = 7.50 Hz and 1.50 Hz, C_4-H of benzothiazole), 8.66 (d, 2H, J = 7.80 Hz, C_2-H, C_6-H of pyridine); ^{13}C NMR: δ 113.2, 117.8, 121.4, 122.0, 123.7 (3C), 126.1, 133.3, 144.9 (3C), 152.6, 153.8, 162.2; MS: m/z 263 (M^+, 52%). Anal. Calcd for $C_{15}H_9N_3S$ (263.32): C, 68.42; H, 3.45; N, 15.96. Found C, 68.40; H, 3.49; N, 16.01.

Synthesis of 1-amino-3-(pyridin-4-yl)-3*H*-pyrido[2,1-*b*][1,3]benzothiazole-2,4-dicarbonitrile (7) A mixture of compound **6** (2.62 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mol) in absolute EtOH (10 mL) containing Et_3N (3 drops) was heated under reflux for 4 h and then allowed to cool. The precipitated product was filtered off, washed with EtOH, and crystallized from EtOH to afford compound **7**: Yellow crystals; yield 95%; mp 263–264°C; IR: ν 3363, 3243 (NH_2), 2208 and 2191 (two CN), 1618, 1490 cm^{-1}, aromatic; ^1H NMR: δ 4.71 (s, 1H, C_3-H), 6.52 (s, 2H, NH_2), 7.12 (dd, 1H, J = 7.70 Hz and 1.50 Hz, C_4-H of benzothiazole), 7.27 (d, 2H, J = 7.70 Hz, C_3-H, C_5-H of pyridine), 7.38 (m, 2H, C_5-H and C_6-H of benzothiazole), 7.70 (dd, 1H, J = 7.50 and 1.50 Hz, C_7-H of benzothiazole), 8.59 (d, 2H, J = 7.80 Hz, C_2-H, C_6-H of pyridine); ^{13}C NMR: δ 30.9, 62.5, 67.8, 117.5 (2C), 120.3, 121.0, 122.8 (3C), 124.4, 126.6, 145.7, 148.5 (2C), 151.2, 162.5, 164.5; MS: m/z 329 (M^+, 49%). Anal. Calcd for $C_{18}H_{11}N_5S$ (329.38): C, 65.64; H, 3.37; N, 21.26. Found C, 65.69; H, 3.45; N, 21.35.

Synthesis of 4-amino-5-(pyridin-4-yl)-5*H*-pyrimido[5′,4′:5,6]pyrido[2,1-*b*][1,3]benzothiazole-6-carbonitrile (8) A solution of compound **7** (3.29 g, 0.01 mol) in (5 mL) of formamide (0.45 g, 0.01 mol) was refluxed for 12 h, and then allowed to cool. The precipitate that formed was filtered off and crystallized from DMF to give compound **8**: Black crystals; yield 29%; mp>350°C; IR: ν 3398, 3312 (NH_2) and 2198 cm^{-1} (CN); ^1H NMR: δ 4.76 (s, 1H, C_5-H), 6.56 (s, 2H, NH_2), 7.15 (dd, 1H, J = 7.40 Hz and 1.50 Hz, C_{11}-H), 7.21 (d, 2H, J = 7.60 Hz, C_3-H, C_5-H of pyridine), 7.30–7.40 (m, 2H, C_9-H and C_{10}-H), 7.81 (dd, 1H, J = 7.50 Hz and 1.50 Hz, C_8-H), 7.92 (s, 1H, C_2-H), 8.56 (d, 2H, J = 7.80 Hz, C_2-H, C_6-H of pyridine); ^{13}C NMR: δ 27.2, 61.4, 106.0, 117.8, 120.3, 121.7, 122.8, 124.4 (3C), 126.5, 145.6 (2C), 148.6 (2C), 155.4, 156.5, 162.2, 163.6; MS: m/z 356 (M^+, 25%). Anal. Calcd for $C_{19}H_{12}N_6S$ (356.41): C, 64.03; H, 3.39; N, 23.58. Found C, 64.12; H, 3.47; N, 23.50.

Synthesis of 4-oxo-5-(pyridin-4-yl)-3,5-dihydro-pyrimido[5′,4′:5,6]pyrido[2,1-b][1,3]benzothiazole-6-carbonitrile (9) A mixture of compound **7** (3.29 g, 0.01 mol) and formic acid (15 mL, 88%) was heated under reflux for 16 h and then allowed to cool. The precipitate that formed was filtered off and crystallized from DMF to give compound **9**: Pink crystals; yield 35%; mp 320–322°C; IR: ν 3284 (NH), 2195 (CN), and 1645 cm^{-1} (C=O);^1H NMR: δ 4.71 (s, 1H, C_5-H), 7.15 (dd, 1H, J = 7.40 Hz and 1.50 Hz, C_{11}-H), 7.21 (d, 2H, J = 7.70 Hz, C_3-H, C_5-H of pyridine), 7.30–7.40 (m, 2H, C_9-H and C_{10}-H), 7.78 (dd, 1H, J = 7.60 Hz and 1.40 Hz, C_8-H), 8.56 (d, 2H, J = 7.80 Hz, C_2-H, C_6-H of pyridine), 8.68 (s, 1H, C_2-H), 11.23 (s, 1H, NH); ^{13}C NMR: δ 29.5, 61.7, 102.7, 117.4, 120.2, 121.3, 122.6, 123.6 (3C), 126.5, 145.6, 146.7, 148.5 (2C), 150.4, 153.8, 162.3, 165.3; MS: m/z 357 (M^+, 25%). Anal. Calcd for $C_{19}H_{11}N_5OS$ (357.39): C, 63.85; H, 3.10; N, 19.60. Found C, 63.80; H, 3.18; N, 19.68.

Synthesis of 2,4-diamino-5-(pyridin-4-yl)-5*H*-[1,3]benzothiazolo[3,2-*a*][1,8]naphthyridine-3,6-dicarbonitrile (10) A mixture of compound **7** (3.29 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mL) in DMF (10 mL) containing a few drops of Et_3N was heated under reflux for 8 h and then allowed to cool. The precipitate that formed was filtered off and crystallized from DMF to give compound **10**: Black crystals; yield 29%; mp>350°C; IR ν cm^{-1}: 3405–3313 (2 NH_2) and 2205, 2199 cm^{-1} (2 CN); ^1H NMR: δ 4.73 (s, 1H, C_5-H), 6.52 (s, 2H, NH_2), 7.18 (dd, 1H, J = 7.50 Hz and 1.50 Hz, C_{11}-H), 7.23 (d, 2H, J = 7.70 Hz, C_3-H, C_5-H of pyridine), 7.35–7.48 (m, 2H, C_9-H and C_{10}-H), 7.89 (dd, 1H, J = 7.50 Hz and 1.50 Hz, C_8-H), 8.25 (s, 2H, NH_2), 8.59 (d, 2H, J = 7.70 Hz, C_2-H, C_6-H of pyridine); ^{13}C NMR: δ 27.0, 58.4, 61.6, 101.4, 115.3, 117.5, 120.3, 121.7, 122.5, 124.4 (3C), 126.5, 145.2, 146.1, 148.4 (2C), 153.9, 162.2 (2C), 163.5; MS: m/z 395 (M^+, 100%). Anal. Calcd for $C_{21}H_{13}N_7S$ (395.44): C, 63.78; H, 3.31; N, 24.79. Found C, 63.85; H, 3.40; N, 24.70.

Synthesis of 4-amino-2-oxo-5-(pyridin-4-yl)-1,5-dihydro-2H-[1,3]benzothiazolo[3,2-a][1,8]naphthyridine-3,6-dicarbonitrile (15) A solution of compound **7** (3.29 g, 0.01 mol) in DMF (10 mL) containing ethyl cyanoacetate (1.13 g, 0.01 mL) and Et_3N (4 drops) was heated under reflux for 8 h and then allowed to cool. The precipitate that formed was filtered off and crystallized from DMF to give compound **15**: Black crystals; yield 29%; mp 195–197°C; IR: ν 3430, 3329 (NH_2), 3298 (NH), 2202, 2193 (2CN), and 1644 cm^{-1} (C=O); ^1H NMR: δ 4.73 (s, 1H, CH), 6.42 (s, 2H, NH_2), 7.09 (dd, 1H, J = 7.50 Hz and 1.5 Hz, C_{11}-H), 7.25 (d, 2H, J = 7.7 Hz, C_3-H, C_5-H of pyridine), 7.30–7.40 (m, 2H, C_9-H and C_{10}-H), 7.80 (dd, 1H, J = 7.50 Hz and 1.50 Hz, C_8-H), 8.55 (d, 2H, J = 7.7 Hz, C_2-H, C_6-H of pyridine), 11.45 (s, 1H, NH); ^{13}C NMR: δ 28.3, 58.9, 61.2, 102.1, 115.5, 117.6, 120.1, 121.4, 122.6, 123.5 (3C), 126.4, 136.8, 145.5, 146.7, 148.3 (2C), 162.3, 163.4, 165.4; MS: m/z 396 (M^+, 100%). Anal. Calcd for $C_{21}H_{12}N_6OS$ (396.43): C, 63.63; H, 3.05; N, 21.20. Found: C, 63.55; H, 3.13; N, 21.28.

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