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SYNTHESIS OF A NOVEL TETRACYCLIC PYRIDO[3',2':4,5]THIENO[3,2-*b*]INDOLE SYSTEM

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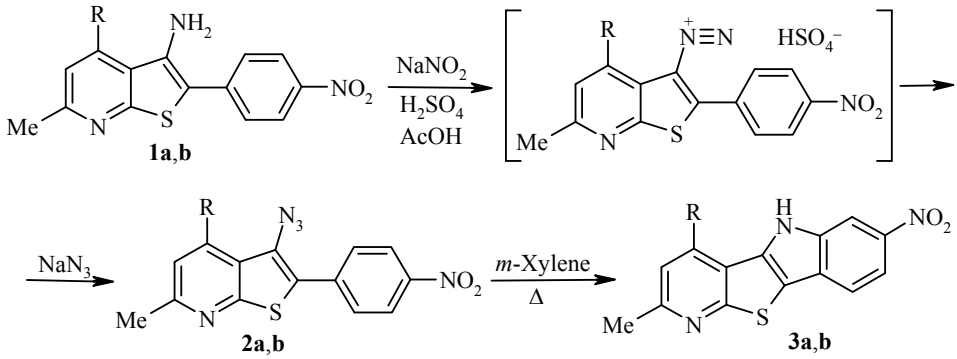
The thermal decomposition of aromatic azides is one of the widely used methods in organic synthesis for the formation of pyrrole-containing condensed systems. This method has been used for the preparation of such heterocyclic systems as indolopyridocarbazolones [1], carbazoles [2], indoloisoquinolines [3], including the alkaloids cryptotackieine and cryptosanguinolentine [4, 5], pyrazino[3,4]indoles [6, 7], pyrimidino[5,4-*b*]indolones [8], dinitroindoles [9] and furopyrroles [10, 11], benzothienoindoles [12], and thieno- and pyrrolo-containing β-carboline analogs [13].

Within the framework of studying the synthetic potential of 3-aminothieno[2,3-*b*]pyridine derivatives, we report in this work the results of the synthesis of the novel tetracyclic pyrido[3',2':4,5]thieno[3,2-*b*]indole system *via* thermolysis of 2-aryl-3-azidothieno[2,3-*b*]pyridines.

The 3-azido-2-(4-nitrophenyl)thienopyridines **2a**,**b** were prepared from the corresponding amines **1a**,**b** in 92 and 90% yield by the successive reactions given below.



a R = Me, **b** R = H

The thermal decomposition of azides **2a**,**b** was carried out by refluxing their solutions in *m*-xylene for 0.5-1.0 h. The yields of products **3a**,**b** were 85 and 81%, respectively.

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IR spectra were recorded on a Perkin-Elmer Spectrum II instrument using an ATR accessory. The ^{1}H and ^{13}C NMR spectra were recorded on Agilent 400-MR (400 and 100 MHz, respectively) and Bruker AM-300 (300 and 75 MHz, respectively) instruments using DMSO-d_6 with TMS as internal standard. Mass spectra were recorded on a Kratos MS-30 instrument using EI ionization (70 eV). Melting points were determined on a Stuart SMP 30 instrument and were not corrected. TLC was performed on Silufol UV-254 and Sorbfil plates (Sorbpolymer Co. Ltd.) using PhMe–EtOH (20:3) as eluent and visualized using iodine and bromine vapors.

The starting 3-aminothienopyridines **1a**,**b** were prepared *via* the reaction of the corresponding 3-cyanopyridine-2-thiones with 4-nitrobenzyl bromide in the presence of aqueous KOH solution using the method reported in [14].

4,6-Dimethyl-2-(4-nitrophenyl)thieno[2,3-*b*]pyridin-3-amine (1a). Yield 93%. Red-orange needles. Mp 222-224°C. IR spectrum, ν, cm^{-1}: 3473, 3440, 3362, 3340, 1584, 1544, 1521, 1502, 1448, 1433, 1382, 1329, 1311, 1261, 1185, 1106, 1069, 1030, 967, 847, 750. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 2.52 (3H, s, CH_3); 2.77 (3H, s, CH_3); 5.42 (2H, br. s, NH_2); 6.99 (1H, s, H-5); 7.78 (2H, d, *J* = 9.0, H-2,6 Ar); 8.26 (2H, d, *J* = 9.0, H-3,5 Ar). Mass spectrum, *m/z* (I_{rel}, %): 301 $[M+2H]^+$ (12), 300 $[M+H]^+$ (17), 299 $[M]^+$ (100), 282 (8), 269 (9), 253 (13), 220 (6), 205 (11), 177 (6), 132 (7), 107 (7), 78 (5), 59 (8), 43 (12). Found, %: C 60.23; H 4.28; N 14.01. $C_{15}H_{13}N_3O_2S$. Calculated, %: C 60.19; H 4.38; N 14.04.

6-Methyl-2-(4-nitrophenyl)thieno[2,3-*b*]pyridin-3-amine (1b). Yield 89%. Bright-orange powder. Mp 229-231°C. IR spectrum, ν, cm^{-1}: 3318, 3231, 1629, 1589, 1566, 1529, 1500, 1391, 1326, 1285, 1258, 1186, 1105, 1062, 952, 849, 821, 750. ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 2.53 (3H, s, CH_3); 6.19 (2H, br. s, NH_2); 7.22 (1H, d, *J* = 8.3, H-5); 7.74 (2H, d, *J* = 9.0, H-2,6 Ar); 8.14 (2H, d, *J* = 9.0, H-3,5 Ar); 8.29 (1H, d, *J* = 8.3, H-4). Mass spectrum, *m/z* (I_{rel}, %): 286 $[M+H]^+$ (18), 285 $[M]^+$ (100), 255 (5), 239 (7), 238 (4), 224 (8), 206 (6), 195 (5), 121 (9), 119 (8), 105 (5), 91 (5), 77 (7), 69 (10). Found, %: C 58.88; H 3.78; N 14.75. $C_{14}H_{11}N_3O_2S$. Calculated, %: C 58.93; H 3.89; N 14.73.

Synthesis of 3-Azidothieno[2,3-*b*]pyridines 2a,b (General Method). Conc. H_2SO_4 (1 ml, 17 mmol) was added with stirring to a solution of the 3-aminothienopyridine **1a**,**b** (33 mmol) in glacial acetic acid (100 ml). The mixture obtained was cooled to +12°C, and a solution of $NaNO_2$ (3.5 g, 50 mmol) in water (3 ml) was added. The mixture was stirred for 15 min, the excess $NaNO_2$ was neutralized using urea, and a solution of NaN_3 (3.3 g, 50 mmol) in water (3 ml) was added. After 15 min, the mixture was poured into water (300 ml). The precipitated crystals were separated by filtration, thoroughly washed with water, and dried in a vacuum desiccator. The synthesized azides **2a**,**b** are unstable materials and their characterization by ^{1}H NMR spectroscopy and elemental analysis was hindered by decomposition. The thermolysis stage of the obtained azides **2a**,**b** was carried out immediately following their preparation without additional purification.

3-Azido-4,6-dimethyl-2-(4-nitrophenyl)thieno[2,3-*b*]pyridine (2a). Yield 9.87 g (92%). Red powder. Mp 157-159°C (decomp.). IR spectrum, ν, cm^{-1}: 2109, 1592, 1521, 1374, 1341, 1318, 1267, 1200, 1108, 1023, 1008, 962, 856, 842, 749, 694.

3-Azido-6-methyl-2-(4-nitrophenyl)thieno[2,3-*b*]pyridine (2b). Yield 9.23 g (90%). Red crystals. Mp 151-152°C (decomp.). IR spectrum, ν, cm^{-1}: 2115, 1589, 1575, 1556, 1504, 1477, 1438, 1372, 1340, 1256, 1227, 1154, 1117, 1105, 1034, 939, 855, 844, 818, 751.

Thermolysis of Compounds 2a,b (General Method). A solution of azide **2a**,**b** (30 mmol) in anhydrous *m*-xylene (100 ml) was refluxed for 0.5-1.0 h until full conversion of the starting compound. The reaction mixture was evaporated at reduced pressure to one third volume and left to crystallize. The precipitated crystals were separated by filtration, washed with petroleum ether, and recrystallized from DMF to give compounds **3a**,**b**.

2,4-Dimethyl-7-nitro-5*H*-pyrido[3',2':4,5]thieno[3,2-*b*]indole (3a). Yield 7.58 g (85%). Red needles. Mp 322-323°C. IR spectrum, ν, cm^{-1}: 3599, 3331, 1645, 1612, 1548, 1507, 1479, 1436, 1378, 1337, 1311, 1296, 1239, 1191, 1065, 883, 808, 749, 730. ^{1}H NMR spectrum (400 MHz), δ, ppm (*J*, Hz): 2.56 (3H, s, CH_3); 2.83 (3H, s, CH_3); 7.18 (1H, s, H-3); 7.91 (1H, d, ^3J = 9.1, H-9), 8.00 (1H, dd, ^3J = 9.1, ^4J = 2.0, H-8), 8.46 (1H, d, *J* = 2.0, H-6); 12.22 (1H, br. s, NH). ^{13}C NMR spectrum (100 MHz), δ, ppm: 19.9; 24.2; 109.4; 112.1; 119.1;

119.2; 121.4; 126.3; 139.4; 139.7; 141.7; 143.4; 156.8; 164.4. Mass spectrum, *m/z* (I_{rel}, %): 299 $[M+2H]^+$ (12), 298 $[M+H]^+$ (25), 297 (100) $[M]^+$, 267 (96), 252 (18), 251 (91), 250 (30), 249 (11), 239 (11), 235 (12), 224 (18), 211 (11), 209 (18), 178 (10), 164 (20), 139 (11), 119 (11), 101 (16), 98 (12), 91 (25), 77 (12), 76 (15), 75 (13), 69 (30), 65 (10), 63 (34), 51 (24), 45 (20), 43 (57), 42 (27), 41 (23). Found, %: C 60.71; H 3.62; N 14.07. $C_{15}H_{11}N_3O_2S$. Calculated, %: C 60.59; H 3.73; N 14.13.

2-Methyl-7-nitro-5*H*-pyrido[3',2':4,5]thieno[3,2-*b*]indole (3b). Yield 6.88 g (81%). Bright-orange needles. Mp 331-332°C. IR spectrum, ν, cm^{-1}: 3605, 3318, 1654, 1616, 1577, 1566, 1499, 1474, 1444, 1381, 1326, 1306, 1289, 1159, 1065, 997, 934, 875, 808, 748. ^{1}H NMR spectrum (300 MHz), δ, ppm (*J*, Hz): 2.62 (3H, s, CH_3); 7.37 (1H, d, *J* = 8.1, H-3); 7.91 (1H, d, *J* = 9.4, H-9); 7.96 (1H, dd, ^3J = 9.4, ^4J = 2.1, H-8), 8.32 (1H, d, *J* = 8.1, H-4); 8.43 (1H, d, *J* = 2.1, H-6); 12.37 (1H, br. s, NH). ^{13}C NMR spectrum (75 MHz), δ, ppm: 24.4, 109.3, 112.3, 115.1, 118.8, 119.4, 120.3, 126.8, 129.4, 138.1, 139.7, 143.5, 157.0, 161.5. Mass spectrum, *m/z* (I_{rel}, %): 284 $[M+H]^+$ (16), 283 $[M]^+$ (100), 253 (30), 238 (11), 237 (62), 210 (5), 118 (6), 105 (8), 91 (8), 69 (12), 63 (6), 44 (24), 40 (7). Found, %: C 59.54; H 3.13; N 14.77. $C_{14}H_9N_3O_2S$. Calculated, %: C 59.35; H 3.20; N 14.83.

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