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PASE facile and efficient multicomponent approach to the new type of 5-C-substituted 2,4-diamino-5*H*-chromeno[2,3-*b*]pyridine scaffold

Michail N. Elinson, Anatoly N. Vereshchagin, Yuliya E. Anisina, Alexander S. Goloveshkin, Ivan E. Ushakov and Mikhail P. Egorov

All melting points were measured with a Gallenkamp melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM-300 (300 and 75 MHz, respectively) at ambient temperature in DMSO-d_6 solutions. Chemical shift values are given in δ scale relative to Me_4Si. IR spectra were registered with a Bruker ALPHA-T FT-IR spectrometer in KBr pellets. Mass-spectra (EI = 70 eV) were obtained directly with a Finningan MAT INCOS 50 spectrometer. Salicylaldehydes were used as purchased. 2-Aminoprop-1-ene-1,1,3-tricarbonitrile was prepared from malononitrile by a known procedure [S1].

Powder X-ray Diffraction (XRD)

The powder pattern of **2a** was measured on Bruker D8 Advance Vario diffractometer with LynxEye detector and Ge (111) monochromator, $\lambda(CuK\alpha_1)$ = 1.54060 Å, θ/2θ scan from 6.0° to 90°, step size 0.009169°, in transmission mode, with the sample deposited between Mylar films. The pattern was indexed using SVD-Index [S2] as implemented in TOPAS 4.2 software [S3]. The model for the solution and refinement was prepared basing on a PBE/L2 [S4] calculation of **2a** using PRIRODA software [S5]. The solution were obtained using the Parallel Tempering method as implemented in FOX [S6] and Rietveld refined in TOPAS 4.2. The structure was refined using soft (parabolic) restraints; distribution of the deviations of the bond lengths from restrained values (Δd) contained no outliers, indicating a consistent structural model according to reported [S7] approach. By variation of individual bond restraints until they produced outliers we estimated the average half uncertainty window for the refinement as HUW = 0.070(25) Å [S8].

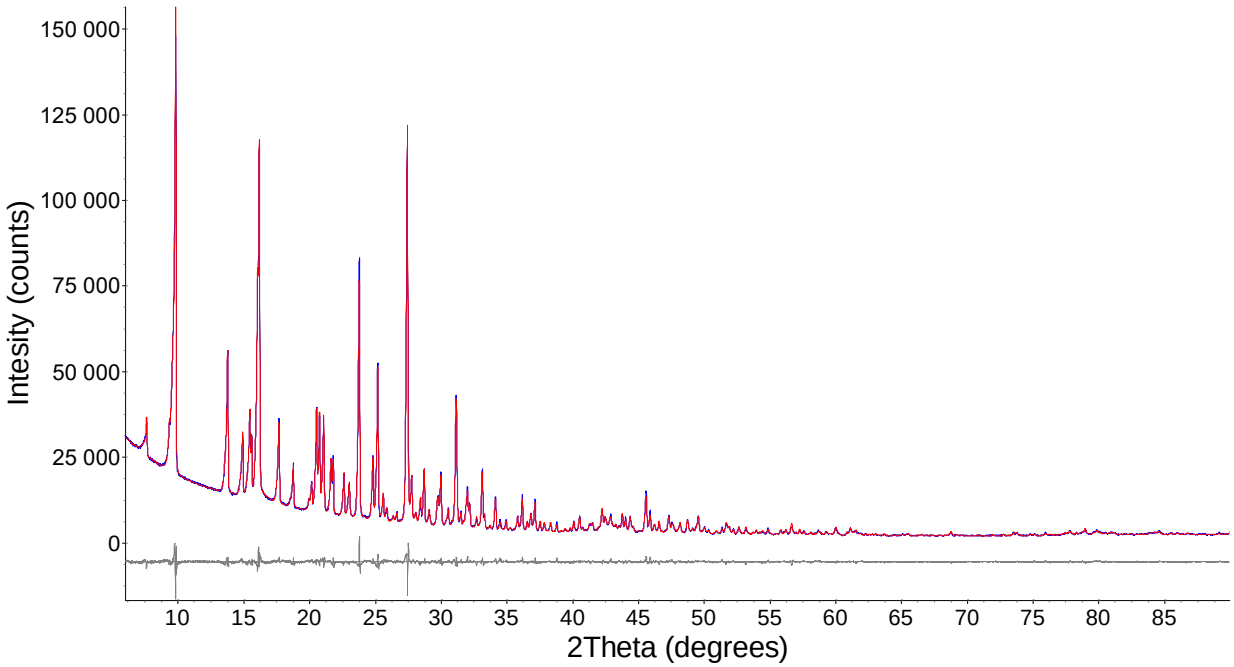

Figure S1 The experimental and calculated powder patterns for **2a** at K1=44 and their difference.

General procedures

Triethylamine (0.3 mmol) was added to a stirred solution of salicylaldehyde **1** (3 mmol), 2-aminoprop-1-ene-1,1,3-tricarbonitrile (3 mmol, 0.396 g) and 3-methyl-2-pyrazolin-5-one (3 mmol, 0.294 g) in *n*-PrOH (2 ml) at ambient temperature. Then, resulting mixture was refluxed for 1 h. After the reaction was finished, the reaction mixture was transferred on filter, washed with methanol (2 x 3 ml) and dried to isolate pure compound **2**. In some cases additional crystallization from DMSO was needed.

2,4-Diamino-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (**2a**)

White solid; 0.98 g (98%); mp: 338-339 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.64 (s, 3H, CH_3), 4.93 (s, 1H, CH), 6.23 (s, 2H, NH_2), 6.40 (s, 2H, NH_2), 7.02-7.15 (m, 3H, Ar), 7.18-7.28 (m, 1H, Ar), 10.88 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.7, 27.0, 70.8, 89.6, 105.6, 115.8, 116.4, 123.7, 123.9, 127.7, 129.4, 137.8, 149.9, 156.8, 158.4, 159.1, 159.2 ppm; IR (KBr) ν = 3402, 3185, 2202, 1641, 1600, 1566, 1488, 1395, 1259, 1063 cm^{-1}; MS (m/z, relative intensity %): 334 [M^{+}] (35), 301 (3), 237 (100), 195 (15), 171 (32), 128 (3), 98 (65), 79 (34), 52 (18), 39 (24); Anal. calcd for $C_{17}H_{14}N_6O_2$: C, 61.07; H, 4.22; N, 25.14. Found C, 60.89; H, 4.15; N, 25.08%.

Crystal Data for **2a** $C_{17}H_{14}N_6O_2$ (M =334.34 g mol^{-1}): triclinic, space group P-1 (no. 2), a = 6.47435(7) Å, b = 10.13429(13) Å, c = 13.01634(14) Å, α = 117.0736(9)°, β = 95.5182(8)°, γ = 82.7553(6)°, V = 753.659(16) Å^3, Z = 2, T = 298 K, μ(CuKα~1~) = 0.844 mm^{-1}, *Dcalc* = 1.473 g cm^{-3}, At average Δd of 0.010 Å (K_1=44) the refinement converged to

R_P/R_P'/R_{WP}/R_{WP}'/R_{Bragg} values of 2.345/6.921/3.364/7.543/1.143 % with R_{exp}/R_{exp}' of 1.098/2.461 %, GOF=3.065 (Figure S1). The crystallographic data for **2a** were deposited in CCDC, ref. code 1821376.

2,4-Diamino-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-7-methyl-5*H*-chromeno[2,3-*b*]-pyridine-3-carbonitrile (2b)

Yellow solid; 0.99 g (94%); mp: 348-349 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.63 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 4.86 (s, 1H, CH), 6.19 (s, 2H, NH_2), 6.38 (s, 2H, NH_2), 6.88 (d, 1H, J = 1.4 *Hz*, Ar), 6.94 (d, 1H, J = 8.1 *Hz*, Ar), 7.03 (dd, 1H, J_1 = 8.1 *Hz*, J_2 = 1.4 *Hz*, Ar), 10.91 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.7, 20.2, 27.0, 70.6, 89.5, 105.6, 115.6, 116.4, 123.2, 128.3, 129.3, 132.8, 137.7, 147.9, 156.7, 158.4, 159.0, 159.2 ppm; IR (KBr) ν = 3414, 3190, 2197, 1637, 1597, 1568, 1482, 1394, 1261, 1222 cm^{-1}; MS (m/z, relative intensity %): 348 [M$^+$] (43), 333 (14), 274 (5), 251 (100), 185 (14), 142 (7), 98 (26), 67 (16), 44 (23), 28 (30); Anal. calcd for $C_{18}H_{16}N_6O_2$: C, 62.06; H, 4.63; N, 24.12. Found C, 61.93; H, 4.57; N, 24.03%.

2,4-Diamino-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-9-methoxy-5*H*-chromeno[2,3-*b*]-pyridine-3-carbonitrile (2c)

Yellowish solid; 0.98 g (90%); mp 338-339 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.65 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.89 (s, 1H, CH), 6.18 (s, 2H, NH_2), 6.38 (s, 2H, NH_2), 6.65 (d, 1H, J = 7.3 Hz, Ar), 6.89 (d, 1H, J = 8.1 Hz, Ar), 6.98 (dd, 1H, J_1 = 7.3 Hz, J_2 = 8.1 Hz, Ar), 10.84 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.7, 27.2, 55.8, 70.8, 89.5, 105.4, 110.2, 116.4, 120.5, 123.5, 124.3, 137.8, 139.6, 147.0, 156.7, 158.3, 159.0, 159.2 ppm; IR (KBr) ν = 3398, 3258, 2199, 1627, 1600, 1568, 1483, 1400, 1229, 1096 cm^{-1}; MS (m/z, relative intensity %): 364 [M$^+$] (29), 333 (11), 267 (100), 224 (22), 201 (6), 182(4), 98 (48), 79 (26), 52 (15), 39 (18); Anal. calcd for $C_{18}H_{16}N_6O_3$: C, 59.34; H, 4.43; N, 23.07. Found C, 59.27; H, 4.37; N, 23.01%.

2,4-Diamino-8-hydroxy-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (2d)

Orange solid; 0.95 g (89%); mp: 302-303 °C (decomp.); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.63 (s, 3H, CH_3), 4.78 (s, 1H, CH), 6.19 (s, 2H, NH_2), 6.35 (s, 2H, NH_2), 6.42 (d, 1H, J = 1.5 *Hz*, Ar), 6.49 (dd, 1H, J_1 = 8.5 *Hz*, J_2 = 1.5 *Hz*, Ar), 6.87 (d, 1H, J = 8.5 *Hz*, Ar), 9.55 (s, 1H, OH), 10.85 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.7, 26.4, 70.6, 89.9, 101.8, 105.8, 111.9, 114.0, 116.4, 129.9, 137.7, 150.5, 156.7 (2C), 158.3, 159.0, 159.1 ppm; IR (KBr) ν

= 3355, 3200, 2197, 1630, 1612, 1568, 1486, 1397, 1178, 1065 cm^{-1}; MS (m/z, relative intensity %): 350 [M^+] (6), 333 (3), 317 (5), 253 (15), 182 (3), 109 (6), 98 (21), 67 (16), 39 (56), 29 (100); Anal. calcd for $C_{17}H_{14}N_6O_3$: C, 58.28; H, 4.03; N, 23.99. Found C, 58.12; H, 4.09; N, 23.87%.

2,4-Diamino-7-bromo-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (2e)

White solid; 0.84 g (68%); mp: 350-351 °C (decomp.); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.68 (s, 3H, CH_3), 4.96 (s, 1H, CH), 6.17 (s, 2H, NH_2), 6.45 (s, 2H, NH_2), 7.06 (d, 1H, *J* = 8.8 *Hz*, Ar), 7.24 (d, 1H, *J* = 2.2 *Hz*, Ar), 7.40 (dd, 1H, J_1 = 8.8 *Hz*, J_2 = 2.2 *Hz*, Ar), 10.86 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.7, 27.0, 70.9, 88.8, 105.1, 115.1, 116.3, 118.3, 126.3, 130.6, 131.5, 137.5, 149.2, 156.7, 158.0, 158.8, 159.3 ppm; IR (KBr) ν = 3417, 3192, 2199, 1634, 1595, 1563, 1479, 1393, 1258, 1063 cm^{-1}; MS (m/z, relative intensity %): 414 [M^+] (43, ^{81}Br), 412 [M^+] (44, ^{79}Br), 370 (8, ^{81}Br), 368 (7, ^{79}Br), 317 (98, ^{81}Br), 315 (100, ^{79}Br), 289 (5, ^{81}Br), 287 (5, ^{79}Br), 236 (17), 182 (3), 143 (6), 98 (40), 79 (59), 39 (27); Anal. calcd for $C_{17}H_{13}BrN_6O_2$: C, 49.41; H, 3.17; Br, 19,34%; N, 20.34. Found C, 49.32; H, Br, 19.43%; 3.09; N, 20.23%.

2,4-Diamino-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-7-nitro-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (2f)

Yellowish solid; 0.72 g (63%); mp: 311-312 °C (decomp.); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.72 (s, 3H, CH_3), 5.10 (s, 1H, CH), 6.25 (s, 2H, NH_2), 6.55 (s, 2H, NH_2), 7.32 (d, 1H, *J* = 8.8 *Hz*, Ar), 7.98 (d, 1H, *J* = 1.9 *Hz*, Ar), 7.98 (dd, 1H, J_1 = 8.8 *Hz*, J_2 = 1.9 *Hz*, Ar), 10.91 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.8, 27.0, 71.4, 88.4, 104.9, 116.1, 117.4, 123.6, 125.2 (2C), 137.6, 143.3, 154.6, 156.8, 157.5, 158.9, 159.4 ppm; IR (KBr) ν = 3422, 3197, 2200, 1637, 1603, 1567, 1529, 1482, 1394, 1254 cm^{-1}; MS (m/z, relative intensity %): 379 [M^+] (9), 332 (3), 282 (31), 236 (23), 230 (2), 150 (2), 98 (100), 79 (43), 39 (48), 29 (36); Anal. calcd for $C_{17}H_{13}N_7O_4$: C, 53.83; H, 3.45; N, 25.85. Found: C, 53.78; H, 3.49; N, 25.73%.

2,4-Diamino-7,9-dichloro-5-(5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)-5*H*-chromeno[2,3-*b*]pyridine-3-carbonitrile (2g)

Yellowish solid; 0.78 g (64%); mp: 345-346 °C (decomp.); ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.69 (s, 3H, CH_3), 4.97 (s, 1H, CH), 6.18 (s, 2H, NH_2), 6.54 (s, 2H, NH_2), 7.04 (d, 1H, *J* = 2.2 *Hz*, Ar), 7.51 (d, 1H, *J* = 2.2 *Hz*, Ar), 10.80 (br s, 2H, NH+OH) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 9.8, 27.5, 71.3, 88.6, 104.6, 116.1, 121.1, 127.1, 127.4, 127.6 (2C), 137.5, 144.9, 156.8, 157.6, 158.9, 159.4 ppm; IR (KBr) ν = 3349, 3195, 2211, 1630, 1592, 1566, 1462, 1390, 1250, 1063 cm^{-1}; MS (m/z, relative intensity %): 406 [M^+] (6, ^{37}Cl, ^{37}Cl), 404 [M^+] (42, ^{37}Cl,

^{35}Cl), 402 [M^{+}] (62, ^{35}Cl, ^{35}Cl), 371 (4, ^{37}Cl, ^{37}Cl), 369 (11, ^{37}Cl, ^{35}Cl), 367 (17, ^{35}Cl, ^{35}Cl), 309 (14, ^{37}Cl, ^{37}Cl), 307 (65, ^{37}Cl, ^{35}Cl), 305 (100, ^{35}Cl, ^{35}Cl), 291 (6), 215 (5), 177 (2), 146 (2), 98 (20), 79 (15), 67 (14); Anal. calcd for $C_{17}H_{12}Cl_2N_6O_2$: C, 50.64; H, 3.00; Cl, 17.58%; N, 20.84. Found C, 50.53; H, 3.08; Cl, 17.45%; N, 20.72%.

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