

Supplementary Material

A simple and efficient synthesis of novel pyranothiadiazolopyrimidine derivatives by three component reactions in solvent-free conditions

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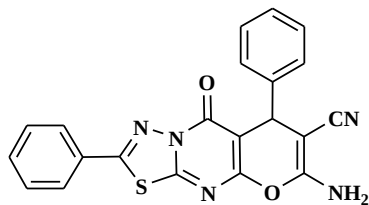
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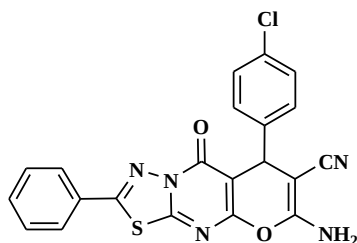
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6-amino-9-oxo-2,8-diphenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4a): Yellow powder; yield:



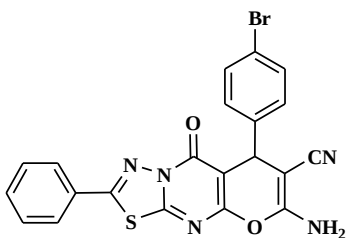
0.32 g (80%); m.p. 276-278 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3444, 3336 (NH_2), 2191 ($\text{C}\equiv\text{N}$), 1700 ($\text{C}=\text{O}$), 1655 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 4.59 (s, 1H, CH), 7.25-7.36 (m, 7H, Ar-H and NH_2), 7.61-7.70 (m, 3H, Ar-H), 7.96 (d, J = 1.8 Hz, 1H, Ar-H), 7.98 (d, J = 1.8 Hz, 1H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 37.52, 57.68, 98.64, 119.99, 127.39, 127.86, 127.97, 128.48, 128.83, 130.19, 133.49, 144.25, 156.07, 158.15, 159.12, 159.52, 161.28 ppm; EI-MS: m/z (%) 399 (2, M^+), 329 (68), 319 (91), 261 (80), 202 (42), 176 (60), 153 (100), 126 (92), 103 (98), 66 (97), 39 (94); Anal. Calcd for $\text{C}_{21}\text{H}_{13}\text{N}_5\text{O}_2\text{S}$ (399.43): C, 63.15; H, 3.28; N, 17.53. Found: C, 63.38; H, 3.17; N, 17.75.

6-amino-8-(4-chlorophenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4b):



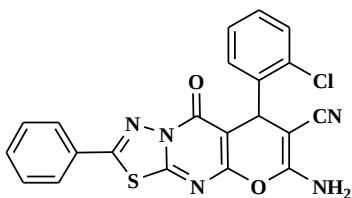
Yellow powder; yield: 0.36 g (84%); m.p. 265-267 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3318, 3284 (NH_2), 2197 ($\text{C}\equiv\text{N}$), 1711 ($\text{C}=\text{O}$), 1660 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 4.62 (s, 1H, CH), 7.32 (d, J = 9.0 Hz, 4H, Ar-H and NH_2), 7.40 (d, J = 9.0 Hz, 2H, Ar-H), 7.61-7.73 (m, 3H, Ar-H), 7.95-7.98 (m, 2H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 37.03, 57.19, 98.14, 119.83, 127.85, 128.44, 128.75, 129.96, 130.20, 131.95, 133.51, 143.20, 156.06, 158.11, 159.16, 159.49, 161.44 ppm; EI-MS: m/z (%) 434 (7, M^+), 365 (33), 319 (73), 295 (69), 202 (41), 187 (74), 152 (72), 103 (71), 66 (77), 44 (76); Anal. Calcd for $\text{C}_{21}\text{H}_{12}\text{ClN}_5\text{O}_2\text{S}$ (433.87): C, 58.13; H, 2.79; N, 16.14. Found: C, 58.33; H, 2.67; N, 16.25.

6-amino-8-(4-bromophenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4c):



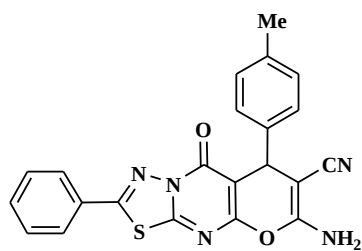
Yellow powder; yield: 0.41 g (86%); m.p. 263-265 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3317, 3286 (NH_2), 2195 ($\text{C}\equiv\text{N}$), 1699 ($\text{C}=\text{O}$), 1658 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 4.60 (s, 1H, CH), 7.25-7.28 (m, 2H, Ar-H), 7.33 (brs, 2H, NH_2), 7.52 (d, J = 2.1 Hz, 1H, Ar-H), 7.54 (d, J = 1.8 Hz, 1H, Ar-H), 7.61-7.72 (m, 3H, Ar-H), 7.95-7.98 (m, 2H, ArH) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 37.11, 57.10, 98.07, 119.84, 120.46, 127.85, 128.42, 130.19, 130.34, 131.67, 133.52, 143.62, 156.05, 158.10, 159.15, 159.48, 161.43 ppm; EI-MS: m/z (%) 478 (8, M^+), 411 (51), 329 (54), 319 (100), 202 (39), 152 (42), 120 (75), 103 (49), 77 (53), 66 (99), 29 (98); Anal. Calcd for $\text{C}_{21}\text{H}_{12}\text{BrN}_5\text{O}_2\text{S}$ (478.32): C, 52.73; H, 2.53; N, 14.64. Found: C, 52.88; H, 2.77; N, 14.35.

6-amino-8-(2-chlorophenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4d): white



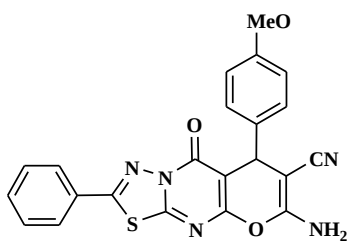
powder; yield: 0.37 g (85%); m.p. 281-283 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3418, 3328 (NH_2), 2195 ($\text{C}\equiv\text{N}$), 1687 ($\text{C}=\text{O}$), 1666 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 5.07 (s, 1H, CH), 7.26-7.30 (m, 5H, NH_2 , Ar-H), 7.40-7.43 (m, 1H, Ar-H), 7.59-7.71 (m, 3H, Ar-H), 7.92 (d, J = 1.5 Hz, 1H, Ar-H), 7.95 (d, J = 1.2 Hz, 1H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 39.89, 61.06, 102.39, 124.28, 132.56, 132.71, 133.15, 133.79, 134.68, 134.92, 135.88, 137.63, 138.24, 145.86, 160.59, 163.29, 163.94, 164.28, 166.15 ppm; EI-MS: m/z (%) 434 (3, M^+), 397 (48), 329 (99), 319 (92), 228 (82), 152 (58), 135 (89), 121 (93), 77 (94), 66 (100), 29 (95); Anal. Calcd for $\text{C}_{21}\text{H}_{12}\text{ClN}_5\text{O}_2\text{S}$ (433.87): C, 58.13; H, 2.79; N, 16.14. Found: C, 58.22; H, 2.87; N, 16.35.

6-amino-9-oxo-2-phenyl-8-(p-tolyl)-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4e): white powder;



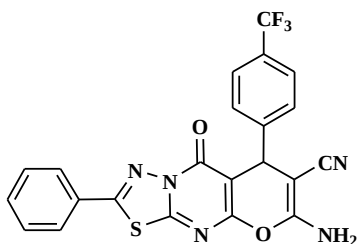
yield: 0.33 g (80%); m.p. 265-267 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3321, 3291 (NH_2), 2196 ($\text{C}\equiv\text{N}$), 1712 ($\text{C}=\text{O}$), 1662 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 2.32 (s, 3H, CH_3), 4.58 (s, 1H, CH), 7.15-7.22 (m, 4H, Ar-H), 7.29 (brs, 2H, NH_2), 7.65-7.74 (m, 3H, Ar-H), 7.99 (d, $J = 1.8$ Hz, 1H, Ar-H), 8.02 (d, $J = 1.5$ Hz, 1H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 21.09, 37.14, 57.86, 98.83, 119.98, 127.86, 128.49, 129.34, 130.17, 133.46, 136.51, 141.31, 156.03, 158.05, 159.08, 159.43, 159.47, 161.13 ppm; EI-MS: m/z (%) 413 (19, M^+), 343 (30), 329 (78), 319 (94), 275 (70), 202 (45), 167 (95), 140 (91), 115 (93), 77 (92), 66 (100), 39 (90); Anal. Calcd for $\text{C}_{22}\text{H}_{15}\text{N}_5\text{O}_2\text{S}$ (413.45): C, 63.91; H, 3.66; N, 16.94. Found: C, 64.11; H, 3.74; N, 17.14.

6-amino-8-(4-methoxyphenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4f):



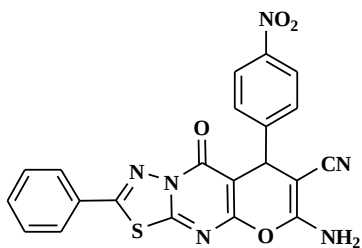
white powder; yield: 0.26 g (60%); m.p. 247-249 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3323, 3290 (NH_2), 2197 ($\text{C}\equiv\text{N}$), 1712 ($\text{C}=\text{O}$), 1663 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 3.74 (s, 3H, CH_3), 4.54 (s, 1H, CH), 6.88 (d, $J = 2.1$ Hz, 1H, Ar-H), 6.90 (d, $J = 2.1$ Hz, 1H, Ar-H), 7.19-7.24 (m, 4H, Ar-H and NH_2), 7.61-7.72 (m, 3H, Ar-H), 7.95 (d, $J = 1.8$ Hz, 1H, Ar-H), 7.97 (d, $J = 2.1$ Hz, 1H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 36.74, 55.56, 57.92, 98.95, 114.17, 120.05, 127.84, 128.48, 129.06, 130.18, 133.48, 136.35, 156.04, 157.93, 158.70, 159.07, 159.41, 161.07 ppm; EI-MS: m/z (%) 429 (5, M^+), 358 (19), 319 (16), 290 (43), 202 (30), 183 (50), 120 (63), 77 (45), 66 (100), 29 (68); Anal. Calcd for $\text{C}_{21}\text{H}_{12}\text{N}_5\text{O}_2\text{S}$ (398.42): C, 63.31; H, 3.04; N, 17.58. Found: C, 63.38; H, 3.13; N, 17.36.

6-amino-9-oxo-2-phenyl-8-(4-(trifluoromethyl)phenyl)-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4g):



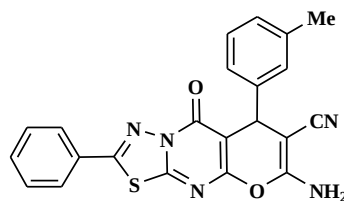
white powder; yield: 0.37 g (78%); m.p. 279-281 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3317, 3286 (NH_2), 2197 ($\text{C}\equiv\text{N}$), 1711 ($\text{C}=\text{O}$), 1660 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 4.73 (s, 1H, CH), 7.39 (brs, 2H, NH_2), 7.52 (s, 1H, Ar-H), 7.55 (s, 1H, Ar-H), 7.61-7.73 (m, 5H, Ar-H), 7.95 (d, $J = 1.8$ Hz, 1H, Ar-H), 7.98 (d, $J = 1.5$ Hz, 1H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 37.52, 56.89, 97.83, 119.71, 125.72, 125.78, 126.55, 127.86, 128.43, 128.98, 130.19, 133.51, 148.77, 156.08, 158.23, 159.21, 159.58, 161.62 ppm; EI-MS: m/z (%) 467 (15, M^+), 319 (100), 220 (40), 120 (42), 102 (55), 66 (35), 29 (37); Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{F}_3\text{N}_5\text{O}_2\text{S}$ (467.42): C, 56.53; H, 2.59; N, 14.98. Found: C, 56.36; H, 2.63; N, 15.23.

6-amino-8-(4-nitrophenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4h): white



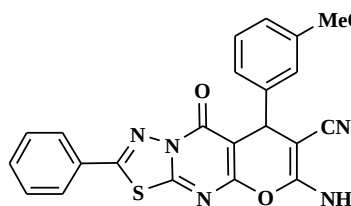
powder; yield: 0.39 g (88%); m.p. 276-278 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3326, 3292 (NH_2), 2193 ($\text{C}\equiv\text{N}$), 1705 ($\text{C}=\text{O}$), 1662 ($\text{C}=\text{N}$), 1527, 1351 (NO_2); ^1H NMR (300.13 MHz, $\text{DMSO}-d_6$): δ 4.82 (s, 1H, CH), 7.46 (brs, 2H, NH_2), 7.61-7.74 (m, 5H, Ar-H), 7.94 (d, $J = 1.8$ Hz, 1H, Ar-H), 7.99 (d, $J = 1.8$ Hz, 1H, Ar-H), 8.22-8.25 (m, 2H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, $\text{DMSO}-d_6$): δ 37.50, 56.46, 97.44, 119.62, 124.07, 127.84, 128.37, 129.50, 130.18, 133.53, 146.96, 151.65, 156.06, 158.27, 159.29, 159.59, 161.75 ppm; EI-MS: m/z (%) 444 (5, M^+), 442 (17), 376 (48), 356 (47), 318 (78), 305 (35), 242 (27), 197 (81), 175 (85), 103 (79), 65 (100), 39 (80); Anal. Calcd for $\text{C}_{21}\text{H}_{12}\text{N}_6\text{O}_4\text{S}$ (444.42): C, 56.75; H, 2.72; N, 18.91. Found: C, 56.49; H, 2.91; N, 19.17.

6-amino-9-oxo-2-phenyl-8-(m-tolyl)-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4i): white powder;



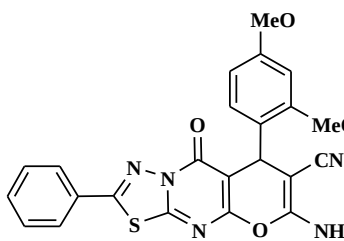
yield: 0.28 g (68%); m.p. 263-265 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3323, 3291 (NH_2), 2196 ($\text{C}\equiv\text{N}$), 1712 ($\text{C}=\text{O}$), 1662 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 4.58 (s, 1H, CH), 7.15-7.22 (m, 4H, Ar-H), 7.29 (brs, 2H, NH_2), 7.65-7.77 (m, 3H, Ar-H), 7.99-8.02 (m, 2H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, DMSO-d_6): δ 21.09, 37.14, 57.86, 98.82, 119.98, 127.86, 128.50, 129.34, 130.18, 133.47, 136.51, 141.31, 156.03, 158.06, 159.08, 159.47, 161.14 ppm; EI-MS: m/z (%) 413 (8, M^+), 409 (45), 341 (83), 317 (92), 273 (90), 241 (37), 201 (82), 166 (99), 120 (91), 76 (88), 65 (100), 39 (89); Anal. Calcd for $\text{C}_{22}\text{H}_{15}\text{N}_5\text{O}_2\text{S}$ (413.45): C, 63.91; H, 3.66; N, 16.94. Found: C, 63.78; H, 3.77; N, 17.21.

6-amino-8-(3-methoxyphenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4j):



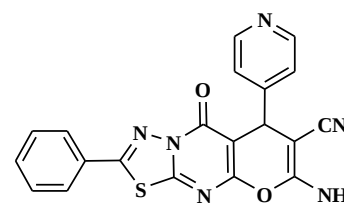
Yellow powder; yield: 0.27 g (63%); m.p. 256-258 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3353, 3317 (NH_2), 2195 ($\text{C}\equiv\text{N}$), 1694 ($\text{C}=\text{O}$), 1656 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, DMSO-d_6): δ 3.79 (s, 3H, CH_3), 4.61 (s, 1H, CH), 6.85-6.89 (m, 3H, Ar-H), 7.26-7.32 (m, 3H, NH_2 , Ar-H), 7.65-7.74 (m, 3H, Ar-H), 7.99-8.02 (m, 2H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, DMSO-d_6): δ 37.42, 55.46, 57.57, 98.51, 112.28, 114.18, 119.96, 120.10, 127.85, 128.48, 129.95, 130.19, 133.48, 145.81, 156.08, 158.17, 159.11, 159.55, 159.68, 161.29 ppm; EI-MS: m/z (%) 429 (10, M^+), 360 (39), 329 (20), 319 (82), 291 (65), 243 (32), 202 (55), 183 (98), 120 (95), 103 (76), 77 (85), 66 (99), 51 (43), 39 (94), 29 (100); Anal. Calcd for $\text{C}_{21}\text{H}_{12}\text{N}_5\text{O}_2\text{S}$ (398.42): C, 63.31; H, 3.04; N, 17.58. Found: C, 63.45; H, 3.18; N, 17.39.

6-amino-8-(2,4-dimethoxyphenyl)-9-oxo-2-phenyl-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4k):



white powder; yield: 0.38 g (83%); m.p. 259-261 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3398, 3305 (NH_2), 2202 ($\text{C}\equiv\text{N}$), 1690 ($\text{C}=\text{O}$), 1669 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, DMSO-d_6): δ 3.75 (s, 6H, 2CH_3), 4.73 (s, 1H, CH), 6.44-6.48 (m, 1H, Ar-H), 6.56 (d, $J = 2.4$ Hz, 1H, Ar-H), 7.00-7.06 (m, 3H, Ar-H, NH_2), 7.60-7.72 (m, 3H, Ar-H), 7.94-7.97 (m, 2H, Ar-H) ppm; ^{13}C NMR (75.46 MHz, DMSO-d_6): δ 32.58, 55.64, 56.23, 56.99, 98.18, 99.40, 105.24, 120.24, 124.16, 127.83, 128.53, 128.67, 130.17, 133.43, 155.91, 158.61, 158.72, 158.91, 159.85, 160.06, 160.64 ppm; EI-MS: m/z (%) 362 (15), 360 (68), 291 (32), 258 (69), 213 (98), 185 (70), 170 (67), 148 (86), 121 (92), 77 (88), 66 (100), 39 (91); Anal. Calcd for $\text{C}_{21}\text{H}_{11}\text{N}_5\text{O}_2\text{S}$ (397.41): C, 63.47; H, 2.79; N, 17.62. Found: C, 63.58; H, 2.62; N, 17.86.

6-amino-9-oxo-2-phenyl-8-(pyridin-4-yl)-8H,9H-pyrano[2,3-d][1,3,4]thiadiazolo[3,2-a]pyrimidine-7-carbonitrile (4l): Yellow



powder; yield: 0.34 g (85%); m.p. 267-269 °C; IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3322, 3289 (NH_2), 2196 ($\text{C}\equiv\text{N}$), 1712 ($\text{C}=\text{O}$), 1663 ($\text{C}=\text{N}$); ^1H NMR (300.13 MHz, DMSO-d_6): δ 4.64 (s, 1H, CH), 7.32 (d, $J = 6.0$ Hz, 2H, Ar-H), 7.41 (s, 2H, Ar-H), 7.61-7.72 (m, 3H, Ar-H), 7.97 (d, $J = 6.0$ Hz, 2H, Ar-H), 8.54 (brs, 2H, NH_2) ppm; ^{13}C NMR (75.46 MHz, DMSO-d_6): δ 37.02, 56.18, 97.10, 119.65, 123.31, 127.86, 128.40, 130.20, 133.53, 150.09, 152.57, 156.09, 158.44, 159.26, 159.69, 161.76 ppm; EI-MS: m/z (%) 397 ([1, $\text{M}-3$] $^+$), 372 (2), 331 (20), 318 (66), 242 (25), 202 (46), 175 (53), 154 (86), 120 (80), 103 (100), 66 (97), 51 (70), 39 (50), 28 (89); Anal. Calcd for $\text{C}_{20}\text{H}_{12}\text{N}_6\text{O}_2\text{S}$ (400.41): C, 59.99; H, 3.02; N, 20.99. Found: C, 60.17; H, 3.15; N, 21.11.

