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Highly efficient one-pot cascade cyclization of 3-(5-hydroxy-3-methylpyrazol-4-yl)-3-arylpropionitriles into spirocyclopropyl pyrazolones

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(2*R, 3*S**) 4-Methyl-7-oxo-2-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2a)** White solid; 1.04 g (83%); mp: 194–195 °C; [found C 67.23, H 4.17, N 22.25; $C_{14}H_{10}N_4O$ requires C 67.19, H 4.03, N 22.39]; ν_{max} (KBr): 3427, 3244, 2976, 2243, 1724, 1579, 1498, 1449, 1388, 1263 cm^{-1}; MS, m/z (%): 250 ($[M]^+$, 25), 195 (3), 185 (11), 166 (15), 148 (10), 144 (12), 119 (15), 109 (19), 92 (63), 91 (100); δ_H (300 MHz, DMSO-d_6) 1.55 (s, 3H, CH_3), 3.98 (s, 1H, CH), 7.43-7.49 (m, 5H, Ar), 11.96 (s, 1H, NH); δ_C (75 MHz, DMSO-d_6): 16.3, 18.6, 42.0, 42.7, 110.9, 111.4, 127.7, 129.0 (2C), 129.4, 129.7 (2C), 150.2, 168.6.

(2*R, 3*S**) 4-Methyl-7-oxo-2-(4-methylphenyl)-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2b)** White solid; 1.06 g (80%); mp: 210–212 °C; [found C 68.05, H 4.42, N 21.15; $C_{15}H_{12}N_4O$ requires C 68.17, H 4.58, N 21.20]; ν_{max} (KBr): 3357, 2980, 2259, 1745, 1581, 1514, 1378, 1339, 1253, 1185 cm^{-1}; MS, m/z (%): 264 ($[M]^+$, 79), 236 (7), 200 (25), 180 (37), 165 (23), 140 (17), 128 (18), 109 (42), 91 (100), 57 (83); δ_H (300 MHz, DMSO-d_6) 1.57 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 3.90 (s, 1H, CH), 7.23 (d, J = 7.9 Hz, 2H, Ar), 7.35 (d, J = 7.9 Hz, 2H, Ar), 11.95 (s, 1H, NHδ_C (75 MHz, DMSO-d_6) 16.3, 18.6, 20.8, 41.9, 42.8, 110.9, 111.4, 124.7, 129.5 (2C), 129.6 (2C), 139.0, 150.3, 168.6.

(*2R*, 3S) 2-(4-*tert*-Buthylphenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2c)** White solid; 1.10 g (72%); mp: 205–207 °C; [found C 70.39, H 5.83, N 18.17; $C_{18}H_{18}N_4O$ requires C 70.57, H 5.92, N 18.29]; ν_{max}(KBr): 3459, 3104, 2966, 2254, 1717, 1589, 1391, 1308, 1268, 1203 cm^{-1}; MS, m/z (%): 306 ($[M]^+$, 100), 291 (79), 263 (12), 242 (27), 227 (65), 207 (41), 185 (35), 152 (19), 118 (23); δ_H (300 MHz, DMSO-d_6) 1.28 (s, 9H, *t*-Bu), 1.55 (s, 3H, CH_3), 3.92 (s, 1H, CH), 7.38 (d, J = 8.2 Hz, 2H, Ar), 7.47 (d, J = 8.2 Hz, 2H, Ar), 11.95 (s, 1H, NH); δ_C (75 MHz, DMSO-d_6) 16.3, 18.5, 30.9 (3C), 34.4, 41.7, 56.0, 110.9, 111.5, 125.6 (2C), 129.3, 129.4 (2C), 150.3, 152.0, 168.6.

(*2R*, 3S) 2-(4-Methoxyphenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2d)** White solid; 0.95 g (68%); mp: 188–190 °C; [found C 64.40, H 4.17, N 19.81; $C_{15}H_{12}N_4O_2$ requires C 64.28, H 4.32, N 19.99]; ν_{max} (KBr): 3203, 2843, 2255, 1724, 1704, 1612, 1516, 1389, 1252, 1027 cm^{-1}; MS, m/*z* (%): 280 ($[M]^+$, 15), 237 (7), 216 (9), 215 (11), 153 (21), 92 (57), 91 (100), 84 (31), 57 (57), 55 (63); δ_H (300 MHz, DMSO-d_6) 1.58 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 3.85 (s, 1H, CH), 7.01 (d, *J* = 8.4 Hz, 2H, Ar), 7.40 (d, *J* = 8.4 Hz, 2H, Ar), 11.94 (s, 1H, NH); δ_C (75 MHz, DMSO-d_6) 16.3, 18.8, 41.7, 42.9, 55.3, 110.9, 111.5, 114.3 (2C), 119.3, 131.1 (2C), 150.3, 159.9, 168.6.

2-(4-Chlorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2e) White solid; 1.09 g (77%); a mixture of diastereisomers; diastereomeric ratio 3:1; mp: 184–185 °C (Lit.[1] mp 184–185 °C); δ_H (300 MHz, DMSO-d_6) major diastereoisomer 1.57 (s, 3H, CH_3), 3.95 (s, 1H, CH), 7.51-7.58 (m, 4H, Ar), 11.96 (s, 1H, NH); minor diastereoisomer 2.13 (s, 3H, CH_3), 4.75 (s, 1H, CH), 7.38-7.47 (m, 4H, Ar), 11.76 (s, 1H, NH).

2-(3-Bromophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2f) White solid; 1.41 g (85%); a mixture of diastereisomers; diastereomeric ratio 3:2; mp: 214–215 °C (Lit.[1] mp 213–214 °C); δ_H (300 MHz, DMSO-d_6) major diastereoisomer 1.57 (s, 3H, CH_3), 3.97 (s, 1H, CH), 7.39-7.44 (m, 1H, Ar), 7.52 (d, *J* = 7.7 Hz, 1H, Ar), 7.66 (d, *J* = 7.7 Hz, 1H, Ar), 7.87 (s, 1H, Ar), 11.96 (s, 1H, NH); minor diastereoisomer 2.13 (s, 3H, CH_3), 4.74 (s, 1H, CH), 7.32-7.38 (m, 2H, Ar), 7.49-7.51 (m, 1H, Ar), 7.58 (d, *J* = 7.5 Hz, 1H, Ar), 11.77 (s, 1H, NH).

2-(4-Fluorophenyl)-4-methyl-7-oxo-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2g) White solid; 1.30 g (97%); as a mixture of diastereisomers; diastereomeric ratio 3:1; mp: 185–187 °C (Lit.[1] mp 184–186 °C); δ_H (300 MHz, DMSO-d_6) major diastereoisomer 1.57 (s, 3H, CH_3), 3.92 (s, 1H, CH), 7.30 (t, *J* = 8.7 Hz, 2H, Ar), 7.57 (dd, J_1 = 5.6 Hz, J_2 = 2.6 Hz, 2H, Ar), 11.95 (s, 1H, NH); minor diastereoisomer 2.14 (s, 3H, CH_3), 4.71 (s, 1H, CH), 7.21 (t, *J* = 8.9 Hz, 2H, Ar), 7.42 (dd, J_1 = 5.6 Hz, J_2 = 2.7 Hz, 2H, Ar), 11.76 (s, 1H, NH).

Methyl (*1S*, 2R*, 3R)-1-cyano-4-methyl-7-oxo-2-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1-carboxylate (2h)** White solid; 0.98 g (69%); mp: 171–172 °C (Lit.[1] mp 170–171 °C); δ_H (300 MHz, DMSO-d_6) 1.51 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 3.93 (s, 1H, CH), 7.42-7.46 (m, 5H, Ar), 11.87 (s, 1H, NH).

Methyl (*1S*, 2R*, 3R) 2-(4-chlorophenyl)-1-cyano-4-methyl-7-oxo-5,6-diaza-spiro[2.4]hept-4-ene-1-carboxylate (2i)** White solid; 1.13 g (71%); mp: 148–149 °C (Lit.[1] mp 148–149 °C); δ_H (300 MHz, DMSO-d_6) 1.90 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 4.44 (s, 1H, CH), 7.34 (d, J = 8.4 Hz, 2H, Ar), 7.44 (d, J = 8.4 Hz, 2H, Ar), 11.70 (s, 1H, NH).

4-Methyl-7-oxo-2,6-diphenyl-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbonitrile (2j) White solid; 1.25 g (77%); a mixture of diastereisomers; diastereomeric ratio 4:1; mp: 189–191 °C (Lit.[1] mp 188–189 °C); δ_H (300 MHz, DMSO-d_6) major diastereoisomer 1.71 (s, 3H, CH_3), 4.20 (s, 1H, CH), 7.21-7.60 (m, 8H, Ar), 7.95 (d, J = 7.9 Hz, 2H, Ar); minor diastereoisomer 2.35 (s, 3H, CH_3), 4.94 (s, 1H, CH), 7.19-7.60 (m, 8H, Ar), 7.85 (d, J = 8.0 Hz, 2H, Ar).

2-(3-Bromophenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1,1-dicarbo-nitrile (2k) White solid; 1.80 g (89%); a mixture of two diastereisomers; diastereomeric ratio 4:1; mp: 198–200 °C; [found C 59.09; H 3.27; Br 19.59; N 13.75. $C_{20}H_{13}BrN_4O$ requires C 59.28; H 3.23; Br 19.72; N 13.83]; ν_{max} (KBr): 3059, 3015, 2249, 1726, 1595, 1499, 1372, 1330, 1325, 757 cm^{-1}; MS, m/*z* (%):406 ([M^+], 95), 404 ([M^+], 100), 342 (55), 340 (63), 186 (20), 185 (37), 165 (21), 153 (33), 119 (25), 91 (63), 77 (79); δ_H (300 MHz, DMSO-d_6) major diastereoisomer: 1.74 (c, 3H, CH_3), 4.18 (c, 1H, CH), 7.39-7.62 (м, 5H, Ar), 7.83-7.93 (m, 3H, Ar), 8.03 (c, 1H, Ar); minor diastereoisomer: 2.33 (c, 3H, CH_3), 4.94 (c, 1H, CH), 7.20-7.42 (м, 6H, Ar), 7.68 (d, J = 7.5 Hz, 2H, Ar), 7.96 (c, 1H, Ar); δ_C (75 MHz, DMSO-d_6): major diastereisomer: 16.6, 20.3, 41.8, 44.8, 110.9, 111.6, 118.5 (2C), 122.1, 125.6, 129.2 (2C), 129.4, 130.7, 131.9, 132.6, 133.1, 151.5, 163.4, 165.2; minor diastereoisomer: 14.4, 21.2, 41.9, 44.9, 109.5, 113.1, 118.4 (2C), 121.6, 125.3, 129.3 (2C), 129.5, 131.2, 132.2, 132.8, 134.3, 154.0, 163.9, 165.9.

(*2R*, 3S)-2-(4-*t*-Butylphenyl)-4-methyl-7-oxo-6-phenyl-5,6-diazaspiro[2.4]hept-4-ene-1,1-di-carbonitrile (2l)** White solid; 1.44 g (75%); mp: 191–193 °C; [found C 75.45; H 5.75; N 14.58. $C_{24}H_{22}N_4O$ requires C 75.37; H 5.80; N 14.65]; ν_{max} (KBr): 2964, 2869, 2251, 1719, 1597, 1502, 1374, 1328, 756 cm^{-1}; MS, m/*z* (%): 382 ([M^+], 100), 368 (3), 318 (1), 207 (8), 185 (10); δ_H (300 MHz, DMSO-d_6): 1.29 (c, 9H, CH_3), 1.72 (c, 3H, CH_3), 4.15 (c, 1H, CH), 7.35-7.55 (м, 5H, Ar), 7.85 (д, J = 8.0 Hz, 2H, Ar), 7.95 (д, J = 7.9 Hz, 2H, Ar); δ_C (75 MHz, DMSO-d_6): 16.6, 20.2, 31.3 (3C), 34.8, 40.9, 44.8, 111.2, 111.7, 118.6, 120.2, 125.0, 125.9 (2C), 129.3 (2C), 129.8 (2C), 138.1 (2C), 151.5, 152.4, 165.4.

References

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