

Regioselective synthesis of substituted isoxazolo[5,4-*d*]pyrimidines

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Experimental

3-Methylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3a: 72 %; m.p.: 220–222 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 2.5 (s, 3H, Me), 8.1 (s, 1H, C6-H), 12.7 (br. s, 1H, NH). Found (%): C, 47.96; H, 3.86; N, 28.12. Calc. for C₆H₅N₃O₂ (%): C, 47.69; H, 3.33; N, 27.81.

3,6-Dimethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3c: 64 %; m.p.: 245–247 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 2.41 (s, 3H, Me), 2.44 (s, 3H, Me), 12.77 (br. s, 1H, NH). Found (%): C, 52.12; H, 4.76; N, 25.32. Calc. for C₇H₇N₃O₂ (%): C, 50.91; H, 4.27; N, 25.44.

3-Ethyl-6-methylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3d: 63 %; m.p.: 199–201 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 1.2 (t, *J* = 7.4 Hz, 3H, Me), 2.3 (s, 3H, Me), 2.8 (q, *J* = 7.4 Hz, 2H, CH₂), 12.8 (br. s, 1H, NH). Found (%): C, 53.87; H, 4.95; N, 23.71. Calc. for C₈H₉N₃O₂ (%): C, 53.63; H, 5.06; N, 23.45.

3-(4-Fluorophenyl)isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3g: 95 %; m.p.: 252–254 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 7.42 (t, *J* = 8.8 Hz, 2H, Ar-H), 8.32 (dd, *J* = 8.8 Hz, *J* = 5.4 Hz, 2H, Ar-H), 8.57 (s, 1H, C6-H), 12.51 (br. s, 1H, NH). Found (%): C, 57.12; H, 2.71; N, 8.15. Calc. for C₁₁H₆FN₃O₂ (%): C, 57.15; H, 2.62; N, 8.22.

3-(4-Methoxyphenyl)isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3i: 80 %; m.p.: 222–223 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 3.8 (s, 3H, OMe), 7.1 (d, *J* = 9.0 Hz, 2H, Ar-H), 8.24 (d, *J* = 9.0 Hz, 2H, Ar-H), 8.39 (s, 1H, C6-H), 13.1 (br. s, 1H, NH). Found (%): C, 59.54; H, 3.47; N, 17.31. Calc. for C₁₂H₉N₃O₃ (%): C, 59.26; H, 3.73; N, 17.28.

3-(3-Fluorophenyl)isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3j: 77 %; m.p.: 244–246 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 7.41 (s, 1H, Ar-H), 7.61 (d, *J* = 7.2 Hz, 1H, Ar-H), 8.11 (dd, *J* = 7.2 Hz, *J* = 7.4 Hz 1H, Ar-H), 8.25 (d, *J* = 7.4 Hz, 1H, Ar-H), 8.49 (s, 1H, C6-H); 13.1 (br. s, 1H, NH). Found (%): C, 57.25; H, 2.44; N, 18.09. Calc. for C₁₁H₆FN₃O₂ (%): C, 57.15; H, 2.62; N, 18.18.

3-(3-Chlorophenyl)-6-ethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one 3k: 78%; m.p.: 277–279 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 1.24 (t, *J* = 7.5 Hz, 3H, Me), 2.72 (q, *J* = 7.5 Hz,

2H, CH₂), 7.52-7.64 (m, 2H, Ar-H), 8.21 (dd, $J = 7.3$ Hz, $J = 1.1$ Hz, 1H, Ar-H), 8.39 (s, 1H, Ar-H), 12.93 (br. s, 1H, NH). Found (%): C, 56.71; H, 3.68; Cl, 12.90; N, 15.23. Calc. for C₁₃H₁₀ClN₃O₂ (%): C, 56.64; H, 3.66; Cl, 12.86; N, 15.24.

Methyl (3-methyl-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl)acetate 5a: 90 %; m.p.: 161-163 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 2.5 (s, 3H, Me), 3.75 (s, 3H, OMe), 4.83 (s, 2H, NCH₂), 8.58 (s, 1H, C6-H). Found (%): C, 48.47; H, 4.01; N, 18.95. Calc. for C₉H₉N₃O₄ (%): C, 48.43; H, 4.06; N, 18.83.

Methyl [3-(4-fluorophenyl)-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl]acetate 5g: 95 %; m.p.: 175-177 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 3.75 (s, 3H, OMe), 4.9 (s, 2H, NCH₂), 7.4 (t, $J = 7.5$ Hz, 2H, Ar-H), 8.8 (d, $J = 7.5$ Hz, 2H, Ar-H), 8.86 (s, 1H, C6-H). Found (%): C, 55.49; H, 3.28; N, 13.91. Calc. for C₁₄H₁₀FN₃O₄ (%): C, 55.45; H, 3.32; N, 13.86.

Methyl [3-(4-methoxyphenyl)-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl]acetate 5h: 96 %; m.p.: 150-152 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 3.75 (s, 3H, OMe), 3.84 (s, 3H, OMe), 4.80 (s, 2H, NCH₂), 7.10 (d, $J = 8.9$ Hz, 2H, Ar-H), 8.30 (d, $J = 8.9$ Hz, 2H, Ar-H), 8.53 (s, 1H, C6-H). Found (%): C, 57.19; H, 4.11; N, 13.24. Calc. for C₁₅H₁₁N₃O₅ (%): C, 57.14; H, 4.16; N, 13.33.

Methyl [3-(3-fluorophenyl)-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl]acetate 5j: 91 %; m.p.: 136-138 °C; ¹H NMR (DMSO+CCl₄, 400 MHz) δ 3.74 (s, 3H, OMe), 4.95 (s, 2H, NCH₂), 7.42-7.48 (m, 1H, Ar-H), 7.58-7.64 (m, 1H, Ar-H), 7.9-8.3 (m, 2H, Ar-H), 8.81 (s, 1H, C6-H). Found (%): C, 55.42; H, 3.34; N, 13.92. Calc. for C₁₄H₁₀FN₃O₄ (%): C, 55.45; H, 3.32; N, 13.86.