

One-pot three-component synthesis of 3-cyano-4-methyl-2,6-dioxopyridine amino enones

Julia S. Oshega, Boris V. Paponov, Irina V. Omelchenko and Oleg V. Shishkin

Melting points were determined on a Kofler apparatus. The ^1H NMR spectra were recorded at 200 MHz on a Varian Mercury VX-200 spectrometer with TMS as an internal standard in $[\text{}^2\text{H}_6]\text{DMSO}$. Mass spectra were taken on a Finnigan MAT 4651P instrument (EI, 70 eV). TLC was used to monitor the reactions and control the purity of products on Silufol UV-254; eluents, toluene–ethyl acetate (1:1) and pure chloroform; visualized under UV light or in iodine camera.

Data for compounds **4b-j**.

4b. Yield 96%. Yellow solid, mp 280-282 °C. MS (EI, 70 eV) m/z 267 (M^+); ^1H NMR (200 MHz, DMSO-D_6) δ ppm: 2.30 (s, 3H, Me); 2.51 (s, 3H, Me); 7.25 (d, 2H, ArH, J 7.9 Hz); 7.50 (d, 2H, ArH, J 7.9 Hz); 8.54 (d, 1H, CH, J 12.8 Hz); 11.48 (s, 1H, NH); 12.98 (d, 1H, NH, J 12.8 Hz). Found (%): C, 67.39; H, 4.89; N, 15.68. Calcd. for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_2$ (%): C, 67.40; H, 4.90; N, 15.72.

4c. Yield 91%. Yellow solid, mp 316-318 °C. MS (EI, 70 eV) m/z 287 (M^+); ^1H NMR (200 MHz, DMSO-D_6) δ ppm: 2.54 (s, 3H, Me); 7.30 (t, 1H, ArH, J 8.2 Hz); 7.49 (t, 1H, ArH, J 7.9 Hz); 7.61 (d, 1H, ArH, J 7.9 Hz); 8.04 (d, ArH, J 8.2 Hz); 8.68 (d, 1H, CH, J 12.5 Hz); 11.64 (s, 1H, NH); 13.44 (d, 1H, NH, J 12.5 Hz). Found (%): C, 58.42; H, 3.49; N, 14.63. Calcd. for $\text{C}_{14}\text{H}_{10}\text{ClN}_3\text{O}_2$ (%): C, 58.45; H, 3.50; N, 14.61.

4d. Yield 96%. Yellow solid, mp 290-292 °C. MS (EI, 70 eV) m/z 332 (M^+); ^1H NMR (200 MHz, DMSO-D_6) δ ppm: 2.52 (s, 3H, Me); 7.66 (d, 2H, ArH, J 9.5 Hz); 7.66 (d, 2H, ArH, J 9.5 Hz); 8.53 (d, 1H, CH, J 12.8 Hz); 11.52 (s, 1H, NH); 12.89 (d, 1H, NH, J 12.8 Hz). Found (%): C, 50.62; H, 3.04; N, 12.62. Calcd. for $\text{C}_{14}\text{H}_{10}\text{BrN}_3\text{O}_2$ (%): C, 50.62; H, 3.03; N, 12.65.

4e. Yield 92%. Orange solid, mp 317-319 °C. MS (EI, 70 eV) m/z 298 (M^+); ^1H NMR (200 MHz, DMSO-D_6) δ ppm: 2.51 (s, 3H, Me); 7.88 (d, 2H, ArH, J 8.9 Hz); 8.30 (d, 2H, ArH, J 8.9 Hz); 8.62 (d, 1H, CH, J 12.8 Hz); 11.65 (s, 1H, NH); 13.95 (d, 1H, NH, J 12.8 Hz). Found (%): C, 56.35; H, 3.36; N, 18.81. Calcd. for $\text{C}_{14}\text{H}_{10}\text{N}_4\text{O}_4$ (%): C, 56.38; H, 3.38; N, 18.79.

4f. Yield 96%. Yellow solid, mp 288-290 °C. MS (EI, 70 eV) m/z 297 (M^+); ^1H NMR (200 MHz, DMSO-D_6) δ ppm: 2.54 (s, 3H, Me); 7.72 (d, 2H, ArH, J 8.9 Hz); 7.98 (d, 2H, ArH, J 8.9 Hz); 8.62 (d, 1H, CH, J 12.8 Hz); 11.59 (s, 1H, NH); 12.98 (d, 1H, NH, J 12.8 Hz). Found (%): C, 60.57; H, 3.76; N, 14.11. Calcd. for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_4$ (%): C, 60.61; H, 3.73; N, 14.14.

4g. Yield 92%. Yellow solid, mp 315-317 °C. MS (EI, 70 eV) m/z 332 (M^+); ^1H NMR (200 MHz, DMSO-D_6) δ ppm: 2.51 (s, 3H, Me); 6.69 (d, 1H, ArH, J 8.5 Hz); 6.97 (s, 1H, ArH); 6.99 (d, 1H, ArH, J 8.5 Hz); 7.23 (t, 1H, ArH, J 8.5 Hz); 8.50 (d, 1H, CH, J 12.8 Hz); 9.86 (s,

1H, OH); 11.51 (s, 1H, NH); 12.90 (d, 1H, NH, *J* 12.8 Hz). Found (%): C, 62.43; H, 4.11; N, 15.61. Calcd. for C₁₄H₁₁N₃O₃ (%):C, 62.45; H, 4.12; N, 15.61.

4h. Yield 91%. Yellow solid, mp 304-306°C. MS (EI, 70 eV) *m/z* 297 (M⁺); ¹H NMR (200 MHz, DMSO-D₆) δ ppm: 2.54 (s, 3H, Me); 7.42 (s, 2H, NH₂); 7.78 (d, 2H, ArH, *J* 8.9 Hz); 7.86 (d, 2H, ArH, *J* 8.9 Hz); 8.61 (d, 1H, CH, *J* 12.5 Hz); 11.6 (s, 1H, NH); 12.95 (d, 1H, NH, *J* 12.5 Hz). Found (%): C, 50.59; H, 3.66; N, 16.85. Calcd. for C₁₄H₁₂N₄O₄S (%):C, 50.60; H, 3.64; N, 16.86.

4i. Yield 93%. Yellow solid, mp 282-284°C. MS (EI, 70 eV) *m/z* 374 (M⁺); ¹H NMR (200 MHz, DMSO-D₆) δ ppm: 2.53 (s, 3H, Me); 6.71 (brs, 4H, NH, NH₂); 7.71 (d, 2H, ArH, *J* 8.9 Hz); 7.8 (d, 2H, ArH, *J* 8.9 Hz); 8.59 (d, 1H, CH, *J* 12.5 Hz); 11.57 (s, 1H, NH); 12.93 (d, 1H, NH, *J* 12.5 Hz). Found (%): C, 48.10; H, 3.76; N, 22.44. Calcd. for C₁₅H₁₄N₆O₄S (%):C, 48.12; H, 3.77; N, 22.45.

4j. Yield 95%. Orange solid, mp 292-294°C. MS (EI, 70 eV) *m/z* 254 (M⁺); ¹H NMR (200 MHz, DMSO-D₆) δ ppm: 2.51 (s, 3H, Me); 2.51 (s, 3H, Me); 7.30 (t, 1H, ArH, *J* 5.2 Hz); 7.64 (d, 1H, ArH, *J* 8.2 Hz); 7.92 (t, 1H, ArH, *J* 8.2 Hz); 8.46 (d, 1H, ArH, *J* 5.2 Hz); 8.97 (d, 1H, CH, *J* 12.5 Hz); 11.6 (s, 1H, NH); 12.76 (d, 1H, NH, *J* 12.5 Hz). Found (%): C, 61.40; H, 3.92; N, 22.01. Calcd. for C₁₃H₁₀N₄O₂ (%):C, 61.41; H, 3.96; N, 22.04.

Table 1. Bond lengths for **4d**.

Atom	Atom	Length/E	Atom	Atom	Length/E
Br1	C12	1.889(4)	Br1A	C12A	1.897(5)
O1	C1	1.239(4)	O1A	C1A	1.227(5)
O2	C2	1.223(5)	O2A	C2A	1.216(5)
O4	C15	1.212(6)	N1A	C8A	1.324(4)
N1	C8	1.321(4)	N1A	C9A	1.414(5)
N1	C9	1.419(5)	N2A	C1A	1.388(5)
N2	C1	1.370(5)	N2A	C2A	1.376(5)
N2	C2	1.374(5)	N3A	C6A	1.136(5)
N3	C6	1.138(5)	C1A	C5A	1.462(6)
N4	C15	1.307(6)	C2A	C3A	1.461(6)
N4	C16	1.421(7)	C3A	C4A	1.366(6)
N4	C17	1.445(7)	C3A	C6A	1.446(6)
C1	C5	1.461(6)	C4A	C5A	1.421(5)
C2	C3	1.451(6)	C4A	C7A	1.507(6)
C3	C4	1.371(6)	C5A	C8A	1.403(6)
C3	C6	1.441(6)	C9A	C10A	1.388(6)
C4	C5	1.424(5)	C9A	C14A	1.369(5)
C4	C7	1.511(6)	C10A	C11A	1.377(5)
C5	C8	1.385(5)	C11A	C12A	1.370(6)
C9	C10	1.384(6)	C12A	C13A	1.368(6)

C9	C14	1.379(5)	C13A	C14A	1.393(6)
C10	C11	1.382(5)	O4A	C15A	1.207(6)
C11	C12	1.374(6)	N4A	C15A	1.326(7)
C12	C13	1.380(6)	N4A	C16A	1.432(7)
C13	C14	1.373(6)	N4A	C17A	1.445(6)

Table 2. Bond Angles for **4d**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C8	N1	C9	128.4(4)	C8A	N1A	C9A	128.8(4)
C1	N2	C2	126.8(4)	C2A	N2A	C1A	127.7(4)
C15	N4	C16	118.9(6)	O1A	C1A	N2A	119.5(5)
C15	N4	C17	123.9(7)	O1A	C1A	C5A	125.1(4)
C16	N4	C17	117.0(6)	N2A	C1A	C5A	115.4(4)
O1	C1	N2	119.2(5)	O2A	C2A	N2A	121.6(5)
O1	C1	C5	124.2(4)	O2A	C2A	C3A	124.5(4)
N2	C1	C5	116.6(4)	N2A	C2A	C3A	113.8(4)
O2	C2	N2	121.1(5)	C4A	C3A	C2A	123.6(4)
O2	C2	C3	124.2(4)	C4A	C3A	C6A	122.5(5)
N2	C2	C3	114.7(4)	C6A	C3A	C2A	113.9(4)
C4	C3	C2	123.2(4)	C3A	C4A	C5A	119.0(5)
C4	C3	C6	121.8(5)	C3A	C4A	C7A	120.3(4)
C6	C3	C2	115.0(4)	C5A	C4A	C7A	120.7(4)
C3	C4	C5	119.0(5)	C4A	C5A	C1A	120.4(4)
C3	C4	C7	120.4(4)	C8A	C5A	C1A	117.9(4)
C5	C4	C7	120.6(4)	C8A	C5A	C4A	121.7(5)
C4	C5	C1	119.6(4)	N3A	C6A	C3A	179.0(7)
C8	C5	C1	119.2(4)	N1A	C8A	C5A	124.4(5)
C8	C5	C4	121.2(5)	C10A	C9A	N1A	122.2(4)
N3	C6	C3	178.6(7)	C14A	C9A	N1A	117.5(5)
N1	C8	C5	124.3(4)	C14A	C9A	C10A	120.3(5)
C10	C9	N1	122.6(4)	C11A	C10A	C9A	119.7(4)
C14	C9	N1	117.3(5)	C12A	C11A	C10A	119.5(5)
C14	C9	C10	120.1(5)	C11A	C12A	Br1A	120.0(4)
C11	C10	C9	119.0(4)	C13A	C12A	Br1A	118.4(4)
C12	C11	C10	120.4(5)	C13A	C12A	C11A	121.5(5)
C11	C12	Br1	120.1(4)	C12A	C13A	C14A	119.1(5)
C11	C12	C13	120.5(5)	C9A	C14A	C13A	119.9(5)
C13	C12	Br1	119.3(4)	C15A	N4A	C16A	119.9(6)
C14	C13	C12	119.1(4)	C15A	N4A	C17A	122.5(6)
C13	C14	C9	120.8(5)	C16A	N4A	C17A	117.4(6)

O4 C15 N4 127.6(7) O4A C15A N4A 126.5(7)

Table 3. Torsion Angles for **4d**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Br1	C12	C13	C14	-179.0(4)	Br1A	C12A	C13A	C14A	-179.8(3)
O1	C1	C5	C4	177.7(4)	O1A	C1A	C5A	C4A	-179.8(4)
O1	C1	C5	C8	0.2(8)	O1A	C1A	C5A	C8A	-0.7(7)
O2	C2	C3	C4	-178.7(5)	O2A	C2A	C3A	C4A	-177.5(5)
O2	C2	C3	C6	-0.7(8)	O2A	C2A	C3A	C6A	2.9(8)
N1	C9	C10	C11	-178.8(4)	N1A	C9A	C10A	C11A	179.8(4)
N1	C9	C14	C13	179.2(5)	N1A	C9A	C14A	C13A	-179.8(4)
N2	C1	C5	C4	-1.6(7)	N2A	C1A	C5A	C4A	-0.3(7)
N2	C1	C5	C8	-179.1(4)	N2A	C1A	C5A	C8A	178.7(4)
N2	C2	C3	C4	1.3(7)	N2A	C2A	C3A	C4A	0.9(7)
N2	C2	C3	C6	179.3(4)	N2A	C2A	C3A	C6A	-178.7(4)
C1	N2	C2	O2	176.2(5)	C1A	N2A	C2A	O2A	176.0(5)
C1	N2	C2	C3	-3.8(7)	C1A	N2A	C2A	C3A	-2.5(7)
C1	C5	C8	N1	0.1(7)	C1A	C5A	C8A	N1A	1.2(7)
C2	N2	C1	O1	-175.4(4)	C2A	N2A	C1A	O1A	-178.3(4)
C2	N2	C1	C5	4.0(7)	C2A	N2A	C1A	C5A	2.2(7)
C2	C3	C4	C5	0.7(8)	C2A	C3A	C4A	C5A	0.6(8)
C2	C3	C4	C7	178.5(5)	C2A	C3A	C4A	C7A	-178.8(5)
C2	C3	C6	N3	-136(28)	C2A	C3A	C6A	N3A	-98(36)
C3	C4	C5	C1	-0.5(7)	C3A	C4A	C5A	C1A	-0.9(7)
C3	C4	C5	C8	176.9(5)	C3A	C4A	C5A	C8A	-179.9(5)
C4	C3	C6	N3	42(29)	C4A	C3A	C6A	N3A	82(36)
C4	C5	C8	N1	-177.4(4)	C4A	C5A	C8A	N1A	-179.8(4)
C6	C3	C4	C5	-177.2(5)	C6A	C3A	C4A	C5A	-179.8(5)
C6	C3	C4	C7	0.6(8)	C6A	C3A	C4A	C7A	0.8(8)
C7	C4	C5	C1	-178.3(5)	C7A	C4A	C5A	C1A	178.5(5)
C7	C4	C5	C8	-0.9(7)	C7A	C4A	C5A	C8A	-0.5(7)
C8	N1	C9	C10	9.1(8)	C8A	N1A	C9A	C10A	7.8(8)
C8	N1	C9	C14	-170.0(5)	C8A	N1A	C9A	C14A	-173.3(5)
C9	N1	C8	C5	176.7(5)	C9A	N1A	C8A	C5A	178.2(5)
C9	C10	C11	C12	-0.1(8)	C9A	C10A	C11A	C12A	-1.0(8)
C10	C9	C14	C13	0.1(8)	C10A	C9A	C14A	C13A	-0.9(7)

C10	C11	C12	Br1	179.4(4)	C10A	C11A	C12A	Br1A	179.8(4)
C10	C11	C12	C13	-0.6(8)	C10A	C11A	C12A	C13A	1.0(8)
C11	C12	C13	C14	1.0(8)	C11A	C12A	C13A	C14A	-1.0(8)
C12	C13	C14	C9	-0.7(8)	C12A	C13A	C14A	C9A	0.9(8)
C14	C9	C10	C11	0.4(8)	C14A	C9A	C10A	C11A	0.9(8)
C16	N4	C15	O4	-0.8(9)	C16A	N4A	C15A	O4A	0.0(9)
C17	N4	C15	O4	-175.4(6)	C17A	N4A	C15A	O4A	-175.1(5)