Formal [4+2] annulation of Enaminones and Cyanomethyl sulfur ylide: One-pot Access to Polysubstituted Pyridin-2(1H)-ones

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I. General information

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. \(^1\)H NMR and \(^13\)C NMR spectra were recorded at 25 °C at 300 MHz, 400 MHz and 100 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded on FTIR-spectrophotometer in the range of 400-4000 cm\(^{-1}\). All melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected.

II. Synthesis and analytical data of compounds 3

Typical procedure for the synthesis of substituted pyridin-2(1H)-ones 3a-3m and 3o-3q (3a as an example): The sulfur ylide was prepared by adding Cs\(_2\)CO\(_3\) (3.0 mmol) in one portion into a solution of sulfonium bromide salt 1a (1.2 mmol) in DMSO (4.0 mL) under stirring for 15 min at room temperature. To the above sulfur ylide was then added 2a (1.0 mmol), which was heated to 100 °C and stirred for 1.5 h. After the reaction was completed, the resulting mixture was poured into saturated aqueous NaCl (100 mL), which was extracted with dichloromethane (3×30 mL). The combined organic phase was washed with water, dried over anhydrous MgSO\(_4\), filtered, and evaporated in vacuo. The crude product was purified by flash silica gel chromatography to give 3a as a yellow solid (85%).

Typical procedure for the synthesis of 3n: The sulfur ylide was prepared by adding Cs\(_2\)CO\(_3\) (3.0 mmol) in one portion into a solution of sulfonium bromide salt 1b (1.2 mmol) in DMSO (4.0 mL) at room temperature under stirring for 15 min under nitrogen. To the above sulfur ylide was then added 2b (1.0 mmol), which was heated to 100 °C and stirred for 2.0 h under nitrogen. After the reaction was completed, the resulting mixture was poured into saturated aqueous NaCl (100 mL), which was extracted with dichloromethane (3×30 mL). The combined organic phase was washed with water, dried over anhydrous MgSO\(_4\), filtered, and evaporated in vacuo. The crude product was purified by flash silica gel chromatography to give 3m as a white solid.

Analytical data of compounds 3

(3a) Yellow solid, m.p. 218-219 °C; \(^1\)H-NMR (300 MHz, DMSO) \(\delta\) 2.23 (s, 3H), 2.36 (s, 3H), 7.03 (s, 2H), 7.27 (d, \(J = 7.2\) Hz, 2H), 7.50-7.60 (m, 3H), 8.20 (s, 1H); \(^13\)C-NMR (100 MHz, DMSO):\(\delta\) 20.5, 31.5, 94.5, 112.1, 129.8, 130.4, 131.3, 137.1, 151.7, 158.8, 162.1, 194.3; IR (KBr): \(\nu\) = 3445, 3059, 2920, 1676, 1584, 1545, 1489, 1459, 1367, 1334, 1262 cm\(^{-1}\); Anal. Calcd for C\(_{14}\)H\(_{14}\)N\(_2\)O\(_2\)S: C, 61.29; H, 5.14; N, 10.21. Found: C, 61.04; H, 5.06; N, 10.36.
(3b) Light yellow solid, m.p. 190-191 °C; \( ^1H\text{-NMR} \) (300 MHz, DMSO):\( \delta \) 2.22 (s, 3H), 2.35 (s, 3H), 7.38 (s, 2H), 7.44-7.47 (m, 1H), 7.52-7.58 (m, 2H), 7.69-7.72 (m, 1H), 8.21 (s, 1H); \( ^{13}C\text{-NMR} \) (100 MHz, DMSO):\( \delta \) 19.8, 30.7, 93.8, 111.0, 129.5, 131.1, 131.4, 131.7, 132.2, 134.0, 151.4, 157.8, 160.6, 193.5; \( \text{IR} \) (KBr): \( \nu \) = 3383, 3164, 2918, 1672, 1633, 1600, 1542, 1493, 1475, 1369, 1338, 1279 cm\(^{-1}\); **Anal. Calcd** for C\(_{14}\)H\(_{13}\)ClN\(_2\)O\(_2\): C, 54.46; H, 4.24; N, 9.07. Found: C, 54.62; H, 4.30; N, 9.21. **HRMS** (ESI) m/z calculated for C\(_{14}\)H\(_{13}\)ClN\(_2\)O\(_2\) [M + Na]\(^+\) : 331.0284. Found: 331.0276.

(3c) Light yellow solid, m.p. 149-151 °C; \( ^1H\text{-NMR} \) (300 MHz, DMSO):\( \delta \) 1.98 (s, 3H), 2.22 (s, 3H), 2.35 (s, 3H), 7.04 (s, 2H), 7.17 (d, \( J = 6.9 \) Hz, 1H), 7.37-7.44 (m, 3H), 8.21 (s, 1H); \( ^{13}C\text{-NMR} \) (100 MHz, DMSO):\( \delta \) 17.2, 19.8, 30.8, 93.7, 111.4, 128.3, 129.0, 130.0, 132.0, 135.5, 135.8, 151.1, 157.7, 160.8, 193.7; \( \text{IR} \) (KBr): \( \nu \) = 3389, 3165, 2915, 1666, 1636, 1593, 1544, 1491, 1369, 1340, 1267 cm\(^{-1}\); **Anal. Calcd** for C\(_{15}\)H\(_{16}\)N\(_2\)O\(_2\): C, 62.48; H, 5.59; N, 9.71. Found: C, 62.75; H, 5.65; N, 9.52.

(3d) Light yellow solid, m.p. 219-222 °C; \( ^1H\text{-NMR} \) (300 MHz, DMSO):\( \delta \) 2.21 (s, 3H), 2.34 (s, 3H), 3.74 (s, 3H), 7.07 (m, 2H), 7.09-7.12 (m, 1H), 7.18-7.25 (m, 2H), 7.47-7.52 (m, 1H), 8.18 (s, 1H); \( ^{13}C\text{-NMR} \) (100 MHz, DMSO):\( \delta \) 19.8, 30.7, 96.2, 93.5, 111.2, 113.6, 121.9, 124.4, 130.3, 131.4, 151.1, 155.2, 158.2, 160.9, 193.6; \( \text{IR} \) (KBr): \( \nu \) = 3376, 3163, 2916, 1670, 1630, 1597, 1543, 1503, 1368, 1343, 1255 cm\(^{-1}\); **Anal. Calcd** for C\(_{15}\)H\(_{16}\)N\(_2\)O\(_3\): C, 59.19; H, 5.30; N, 9.20. Found: C, 59.44; H, 5.20; N, 9.01.
(3e) Yellow solid, m.p. 215-216 °C; \(^1\)H-NMR (300 MHz, DMSO):\(\delta\) 2.22 (s, 3H), 2.35 (s, 3H), 2.38 (s, 3H), 7.01 (s, 2H), 7.05-7.10 (m, 2H), 7.32 (d, \(J = 7.5\) Hz, 1H), 7.46 (t, \(J = 7.5\) Hz, 1H), 8.20 (s, 1H); \(^1^3\)C-NMR (100 MHz, DMSO):\(\delta\) 19.8, 21.3, 30.8, 93.7, 111.4, 125.9, 129.4, 130.4(2), 136.3, 140.2, 150.9, 158.1, 161.3, 193.7; IR (KBr): \(\nu\) = 3436, 3166, 2922, 1587, 1543, 1489, 1455, 1366, 1338, 1267 \(\text{cm}^{-1}\); **Anal. Calcd** for C\(_{13}\)H\(_{16}\)N\(_2\)O\(_3\): C, 62.48; H, 5.59; N, 9.71. Found: C, 62.29; H, 5.49; N, 9.51.

(3f) Yellow solid, m.p. 238-240 °C; \(^1\)H-NMR (300 MHz, DMSO):\(\delta\) 2.21 (s, 3H), 2.35 (s, 3H), 3.83 (s, 3H), 7.04 (s, 2H), 7.08 (d, \(J = 8.7\) Hz, 2H), 7.18 (d, \(J = 8.4\) Hz, 2H), 8.18 (s, 1H); \(^1^3\)C-NMR (100 MHz, DMSO):\(\delta\) 19.7, 30.6, 55.8, 93.5, 111.5, 115.8, 128.8, 130.1, 150.8, 158.4, 160.6, 161.4, 193.6; IR (KBr): \(\nu\) = 3442, 3171, 2908, 1651, 1599, 1543, 1552, 1504, 1362, 1337, 1267 \(\text{cm}^{-1}\); **Anal. Calcd** for C\(_{15}\)H\(_{16}\)N\(_2\)O\(_3\): C, 59.19; H, 5.30; N, 9.20. Found: C, 59.47; H, 5.19; N, 9.34.

Crystal data for 3f: C\(_{15}\)H\(_{16}\)N\(_2\)O\(_3\), white crystal, \(M = 304.36\), orthorhombic, p c c n, \(a =18.861(15)\) Å, \(b = 9.284(8)\) Å, \(c = 16.581(14)\) Å, \(\alpha = 90.00^\circ\), \(\beta = 90.00^\circ\), \(\gamma = 90.00^\circ\), \(V = 2903.5(4)\) Å\(^3\), \(Z = 8\), \(T = 293\) K, \(F_{000} = 1280.0\), \(F_{000}^\prime = 1281.54\), \(R = 0.0458\) (2001), \(wR2 = 0.1181\) (2579). CCDC deposition number: 1013387. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/conts/retrieving.html](http://www.ccdc.cam.ac.uk/conts/retrieving.html) (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (0)1223 762911; or [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).

(3g) Yellow solid, m.p. 254-256 °C; \(^1\)H-NMR (300 MHz, DMSO):\(\delta\) 2.22 (s, 3H), 2.35 (s, 3H), 7.26 (s, 2H), 7.31 (d, \(J = 8.4\) Hz, 2H), 7.60 (d, \(J = 8.4\) Hz, 2H), 8.20 (s, 1H); \(^1^3\)C-NMR (100 MHz, DMSO):\(\delta\) 19.8, 30.8, 94.0, 111.1, 130.7, 131.2, 134.4, 135.5, 151.1, 158.2, 161.3, 193.5; IR (KBr): \(\nu\) = 3420, 2921, 1696, 1608, 1582, 1542, 1503, 1463, 1277 \(\text{cm}^{-1}\); **Anal. Calcd** for C\(_{14}\)H\(_{15}\)ClN\(_2\)O\(_3\): C, 54.46; H, 4.24; N, 9.07. Found: C, 54.19; H, 4.34; N, 9.22.

(3h) Yellow solid, m.p. 168-170 °C; \(^1\)H-NMR (300 MHz, DMSO):\(\delta\) 1.94 (s, 3H), 2.21 (s, 3H), 2.36 (s, 6H), 7.04 (s, 2H), 7.07 (s, 1H), 7.17 (d, \(J = 8.1\) Hz, 1H), 7.26 (s, 1H), 8.21 (s, 1H); \(^1^3\)C-NMR (100 MHz,

(3i) Yellow solid, m.p. 188-189 °C; ¹H-NMR (300 MHz, DMSO): δ 2.19 (s, 3H), 2.42 (s, 3H), 5.36 (s, 2H), 7.13 (d, J = 7.2 Hz, 2H), 7.25-7.27 (m, 1H), 7.31-7.35 (m, 2H), 7.80 (s, 2H), 8.16 (s, 1H); ¹³C-NMR (100 MHz, DMSO): δ 19.7, 30.9, 44.9, 94.3, 110.7, 126.8, 127.4, 128.9, 136.2, 150.2, 157.8, 161.0, 194.0; IR (KBr): ν = 3401, 3171, 2921, 1655, 1543, 1456, 1365, 1247 cm⁻¹; Anal. Calcd for C₁₅H₁₆N₂O₂: C, 62.48; H, 5.59; N, 9.71. Found: C, 62.70; H, 5.66; N, 9.54.

(3j) Yellow solid, m.p. 248-249 °C; ¹H-NMR (300 MHz, DMSO): δ 2.26 (s, 3H), 7.00 (m, 2H), 7.27 (t, J = 7.8 Hz, 2H), 7.35-7.37 (m, 2H), 7.57-7.63 (m, 6H), 8.41 (s, 1H), 11.47 (s, 1H); ¹³C-NMR (100 MHz, DMSO): δ 19.6, 94.4, 104.5, 119.6, 123.3, 129.0, 129.3, 130.0, 130.7, 136.0, 139.6, 151.0, 157.0, 162.3, 162.8; IR (KBr): ν = 3316, 3024, 2913, 1669, 1583, 1539, 1482, 1441, 1359, 1254 cm⁻¹; Anal. Calcd for C₁₉H₁₇N₅O₂S: C, 64.94; H, 4.88; N, 11.96. Found: C, 64.74; H, 4.94; N, 11.79.

(3k) Yellow solid, m.p. 223-225 °C; ¹H-NMR (400 MHz, DMSO): δ 2.25 (s, 3H), 6.95 (s, 2H), 7.28 (d, J = 7.6 Hz, 2H), 7.29-7.34 (m, 2H), 7.42 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 7.2 Hz, 1H), 7.51-7.56 (m, 4H), 8.02 (s, 1H); ¹³C-NMR (100 MHz, DMSO): δ 19.8, 92.8, 111.8, 128.0, 128.9, 129.1, 129.7, 130.6, 131.3, 136.4, 140.5, 152.4, 157.9, 160.3, 192.5; Anal. Calcd for C₁₉H₁₆N₂O₂: C, 67.84; H, 4.79; N, 8.33. Found: C, 64.60; H, 4.83; N, 8.46.
(3l) Yellow solid, m.p. 258-259 °C; $^1$H-NMR (300 MHz, DMSO):$\delta$ 1.19 (t, $J = 7.2$ Hz, 3H), 2.20 (s, 3H), 3.82 (s, 3H), 4.05-4.12 (q, $J = 7.2$ Hz, 2H), 6.86 (s, 2H), 7.07 (d, $J = 9.0$ Hz, 2H), 7.13 (d, $J = 9.0$ Hz, 2H), 8.15 (s, 1H); $^{13}$C-NMR (100 MHz, DMSO):$\delta$ 14.9, 19.8, 55.8, 59.5, 91.3, 102.4, 115.8, 128.9, 130.2, 152.7, 158.1, 159.1, 160.0, 164.9; Anal. Caled for C$_{16}$H$_{18}$N$_2$O$_4$: S, 57.47; H, 5.43; N, 8.38. Found: C, 57.73; H, 5.35; N, 8.22.

(3m) Yellow solid, m.p. 219-220 °C; $^1$H-NMR (400 MHz, DMSO):$\delta$ 1.20 (t, $J = 7.2$ Hz, 3H), 2.21 (s, 3H), 2.40 (s, 3H), 4.07-4.12 (q, $J = 7.2$ Hz, 2H), 6.81 (s, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 8.17 (s, 1H); $^{13}$C-NMR (100 MHz, DMSO):$\delta$ 14.9, 19.8, 21.3, 59.5, 91.3, 102.5, 128.7, 131.1, 133.8, 139.0, 152.7, 157.8, 158.9, 164.9; Anal. Caled for C$_{16}$H$_{18}$N$_2$O$_4$: S, 60.36; H, 5.70; N, 8.80. Found: C, 60.06; H, 5.81; N, 8.92.

(3n) White solid, m.p. 182-183 °C; $^1$H-NMR (400 MHz, DMSO):$\delta$ 1.51 (t, $J = 7.2$ Hz, 3H), 2.35 (s, 3H), 2.61 (q, $J = 7.2$ Hz, 2H), 7.32 (s, 2H), 7.45-7.48 (d, $J = 6.8$ Hz, 1H), 7.51-7.57 (m, 2H), 7.69-7.71 (d, $J = 6.8$ Hz, 1H), 8.18 (s, 1H); $^{13}$C-NMR (100 MHz, DMSO):$\delta$ 14.7, 29.7, 30.7, 91.3, 111.0, 129.5, 131.1, 131.4, 131.7, 132.1, 134.0, 152.3, 158.4, 160.6, 193.5; IR (KBr): $\nu$ = 3164, 2947, 1682, 1611, 1543, 1509, 1475, 1366, 1336, 1249 cm$^{-1}$; Anal. Caled for C$_{15}$H$_{15}$ClN$_2$O$_2$: S, 55.81; H, 4.68; N, 8.68. Found: C, 55.50; H, 4.60; N, 8.80.

(3o) Yellow solid, m.p. 235-237 °C; $^1$H-NMR (400 MHz, DMSO):$\delta$ 2.23 (s, 3H), 7.10 (s, 2H), 7.29 (d, $J = 7.2$ Hz, 2H), 7.53-7.60 (m, 3H), 8.00 (s, 1H); $^{13}$C-NMR (100 MHz, DMSO):$\delta$ 19.7, 85.0, 93.3, 118.5, 128.9, 130.1, 130.7, 135.6, 153.4, 157.8, 160.6; IR (KBr): $\nu$ = 3399, 3175, 2916, 2204, 1649, 1601, 1559, 1511, 1455, 1356, 1279 cm$^{-1}$; Anal. Caled for C$_{13}$H$_{11}$N$_3$O$_3$: S, 60.68; H, 4.31; N, 16.33. Found: C, 60.40; H, 4.38; N, 16.21. HRMS (ESI) m/z calculated for C$_{13}$H$_{11}$N$_3$O$_3$ [M + Na]$^+$: 280.0521. Found: 280.0583.
(3p) Light yellow solid, m.p. 252-255 °C; $^1$H-NMR (300 MHz, DMSO):$\delta$ 2.22 (s, 3H), 7.32 (s, 2H), 7.33 (d, $J = 8.7$ Hz, 2H), 7.60 (d, $J = 8.4$ Hz, 2H), 7.99 (s, 1H); $^{13}$C-NMR (100 MHz, DMSO):$\delta$ 19.7, 84.7, 93.5, 118.5, 130.8, 131.0, 134.6, 134.7, 153.5, 157.8, 160.6; IR (KBr): $\nu$ = 3405, 3178, 2921, 2206, 1646, 1602, 1557, 1508, 1277 cm$^{-1}$; Anal. Calcd for C$_{13}$H$_{10}$ClN$_3$OS: C, 53.52; H, 3.45; N, 14.40. Found: C, 53.20; H, 3.40; N, 14.22.

(3q) Yellow solid, m.p. 254-257 °C; $^1$H-NMR (300 MHz, DMSO):$\delta$ 2.21 (s, 3H), 3.82 (s, 3H), 7.08-7.12 (m, 4H), 7.18 (d, $J = 7.5$ Hz, 2H), 7.97 (s, 1H); $^{13}$C-NMR (100 MHz, DMSO):$\delta$ 19.7, 55.8, 84.9, 93.1, 115.9, 118.6, 128.0, 130.0, 153.2, 158.2, 160.3, 160.8; IR (KBr): $\nu$ = 3403, 3168, 2913, 2201, 1646, 1601, 1558, 1510, 1248 cm$^{-1}$; Anal. Calcd for C$_{14}$H$_{13}$N$_3$O$_2$S: C, 58.52; H, 4.56; N, 14.62. Found: C, 58.75; H, 4.49; N, 14.43.
III. NMR spectra copes

3a
3n

[Chemical Structures and Spectra]