Supporting Information

Facile Synthesis of Cyanofurans via Michael-Addition/Cyclization of Ene-Yne-Ketones with Trimethylsilyl Cyanide

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A. General Methods

$^1$H and $^{13}$C NMR spectra were recorded using a Bruker DRX-400 spectrometer using CDCl$_3$ as solvent. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. Mass spectra were recorded on a Thermo Scientific ISQ gas chromatograph-mass spectrometer. The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Bruker TENSOR 27 spectrometer. Melting points were determined with a Büchi Melting Point B-545 instrument.

B. General Procedure for the Preparation of 1 and 3

**General Procedure for the Preparation of 1**

To a 25 mL round bottom flask, the mixture of 1,3-diketones S1 (5 mmol), AcOH (0.2 equiv), piperidine (0.1 equiv) and dry MgSO$_4$ (1 equiv) was added to a solution of propiolaldehyde S2 (1.2 equiv) in toluene. The reaction was carried out at 40 °C stirring for 4 h and monitored by TLC. After the completion of the reaction, the reaction mixture was filtered through celite and removal of the solvent by rotary evaporation to give the crude product. The ene-yne-ketones 1 was purified by chromatography on silica gel with the appropriate mixture of PE and EA in 60-90% yields (Z/E mixture, 1x was isolated in 42% yield).

**General Procedure for the Preparation of 3**

In a test tube, a mixture of ene-yne-ketone 1 (0.4 mmol), trimethylsilyl cyanide 2 (0.6 mmol) and KF (0.6 mmol) was stirred in DMF (2 mL). Then H$_2$O (2.0 mmol) was added by using a microliter syringe. The mixture was allowed to stir at room temperature for 6 h. After completion of the reaction (monitored by
TLC), water (10 mL) was added to the reaction mixture, and the resulting mixture was extracted with ethyl acetate. The combined organic layers were then dried over MgSO₄, filtered, and then concentrated in vacuo. The residue was purified by flash chromatography on silica gel to give products 3.

C. Optimization of the Reaction Conditions

Table S1. Screening of the Amount of Water for Reaction

<table>
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<th>Entry</th>
<th>n (equiv)</th>
<th>Yield of 3a (%)</th>
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<tr>
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</table>

*a Reaction conditions: All reactions were performed with 1a (0.1 mmol), 2 (0.15 mmol), KF (0.15 mmol) and 1.0 mL DMF at room temperature for 6 h unless otherwise noted. b Yields were analyzed by GC-MS using n-dodecane as an internal standard.*
D. Analytical data

4-Acetyl-2-benzyl-5-methylfuran-3-carbonitrile (3a)
Yellow solid (87.1 mg, 91%) mp 60.2-61.0 °C; IR (KBr): 2922, 2230, 1675, 1244 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.37-7.24 (m, 5H), 4.09 (s, 2H), 2.54 (d, J = 1.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 191.7, 162.2, 158.7, 135.0, 128.9, 128.6, 127.4, 120.9, 113.6, 93.9, 33.5, 29.8, 14.3; MS (EI, 70 eV) m/z: 239.24, 224.21, 196.21, 91.18; HRMS ESI (m/z): calcd for C₁₅H₁₃NNaO₂ [M + Na]⁺: 262.0838, found: 262.0837.

2-Benzyl-5-ethyl-4-propionylfuran-3-carbonitrile (3b)
Yellow oil (93.0 mg, 87%); IR (KBr): 2974, 2231, 1680, 929 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.31 (m, 2H), 7.29-7.25 (m, 3H), 4.11 (s, 2H), 2.93 (dq, J = 19.5, 7.3 Hz, 4H), 1.19 (dt, J = 12.5, 7.3 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 194.9, 163.5, 162.2, 135.1, 128.9, 128.6, 127.4, 119.7, 113.9, 93.6, 35.2, 33.6, 21.6, 11.7, 7.5; MS (EI, 70 eV) m/z: 267.30, 238.25, 182.22, 91.14; HRMS ESI (m/z): calcd for C₁₇H₁₇NNaO₂ [M + Na]⁺: 290.1151, found: 290.1153.

4-Acetyl-2-benzyl-5-phenylfuran-3-carbonitrile and 4-Benzoyl-2-benzyl-5-methylfuran-3-carbonitrile (3c and 3c’)
Yellow oil (101.2 mg, 84%); IR (KBr): 3052, 2232, 1662, 703 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.81-7.26 (m, 10H), 4.17 (d, J = 25.4 Hz, 2H), 2.37 (d, J = 49.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 192.0, 188.9, 163.1, 162.3, 157.4, 156.6, 137.4, 135.0, 134.8, 133.3, 130.6, 129.1, 128.9, 128.9, 128.9, 128.6, 128.6, 128.5, 128.5, 128.2, 127.4, 127.3, 95.4, 95.3, 33.6, 33.5, 29.9, 13.9; MS (EI, 70 eV) m/z: 301.30, 286.27, 105.16, 77.16; HRMS ESI (m/z): calcd for C₂₀H₁₅NNaO₂ [M + Na]⁺: 324.0995, found: 324.0998.

4-Benzoyl-2-benzyl-5-phenylfuran-3-carbonitrile (3d)
Yellow solid (119.2 mg, 82%), mp 105.6-106.6 °C; IR (KBr): 2995, 2231, 1763, 1240 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.79 (dd, \(J = 8.3, 1.2\) Hz, 2H), 7.53-7.48 (m, 1H), 7.43 (dd, \(J = 8.1, 1.5\) Hz, 2H), 7.38-7.21 (m, 10H), 4.24 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 189.2, 162.7, 154.7, 136.3, 134.9, 133.8, 129.8, 129.8, 129.0, 128.8, 128.6, 128.5, 127.9, 127.5, 127.5, 120.3, 112.2, 97.2, 33.8; MS (EI, 70 eV) \(m/z\): 363.37, 286.30, 105.16, 77.18; HRMS ESI (m/z): calcd for C\(_{25}\)H\(_{17}\)NNaO\(_2\) [M + Na]\(^+\): 386.1151, found: 386.1150.

**2-Benzyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-carbonitrile (3e)**

Brown oil (86.0 mg, 77%); IR (KBr): 2951, 2234, 1682, 1042 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.29 (dt, \(J = 15.0, 7.0\) Hz, 5H), 4.11 (d, \(J = 7.2\) Hz, 2H), 2.69 (d, \(J = 7.1\) Hz, 2H), 2.37 (d, \(J = 7.1\) Hz, 2H), 1.12 (d, \(J = 7.1\) Hz, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 191.1, 165.6, 164.2, 134.9, 129.0, 128.7, 127.5, 118.8, 112.2, 91.4, 51.7, 37.0, 35.1, 33.7, 28.5; MS (EI, 70 eV) \(m/z\): 279.33, 223.25, 195.25, 91.18; HRMS ESI (m/z): calcd for C\(_{18}\)H\(_{17}\)NNaO\(_2\) [M + Na]\(^+\): 302.1151, found: 302.1153.

**Ethyl 5-Benzyl-4-cyano-2-methylfuran-3-carboxylate (3f)**

Yellow oil (97.1 mg, 90%); IR (KBr): 2984, 2235, 1718, 1090 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.35-7.24 (m, 5H), 4.34 (q, \(J = 7.1\) Hz, 2H), 4.08 (s, 2H), 2.53 (s, 3H), 1.38 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 162.0, 161.6, 159.5, 135.2, 128.9, 128.6, 127.3, 131.3, 112.9, 94.9, 61.0, 33.5, 14.0, 13.5; MS (EI, 70 eV) \(m/z\): 269.69, 240.23, 223.23, 195.23; HRMS ESI (m/z): calcd for C\(_{16}\)H\(_{15}\)NNaO\(_3\) [M + Na]\(^+\): 292.0944, found: 292.0943.

**Ethyl 5-Benzyl-4-cyano-2-ethylfuran-3-carboxylate (3g)**

Yellow oil (96.3 mg, 85%); IR (KBr): 2981, 2236, 1720, 1099 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.36-7.24 (m, 5H), 4.34 (q, \(J = 7.1\) Hz, 2H), 4.09 (s, 2H), 2.97 (q, \(J = 7.6\) Hz, 2H), 1.38 (t, \(J = 7.1\) Hz, 3H), 1.21 (t, \(J = 7.6\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 164.2, 161.9, 161.5, 135.2, 128.8, 128.5,
Ethyl 5-Benzyl-4-cyano-2-propylfuran-3-carboxylate (3h)

Yellow oil (92.8 mg, 78%); IR (KBr): 2966, 2236, 1719, 1101 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42-7.18 (m, 5H), 4.34 (q, $J$ = 7.1 Hz, 2H), 4.09 (s, 2H), 3.01-2.83 (m, 2H), 1.74-1.56 (m, 2H), 1.38 (t, $J$ = 7.1 Hz, 3H), 0.91 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 163.3, 161.9, 161.5, 135.2, 128.8, 128.5, 127.2, 112.9, 112.9, 94.8, 60.9, 33.5, 29.1, 21.1, 13.9, 13.5; MS (EI, 70 eV) m/z: 297.29, 268.25, 190.20, 127.2, 112.9, 94.8; HRMS ESI (m/z): calcd for C$_{18}$H$_{17}$NNaO$_3$ [M + Na]$^+$: 306.1101, found: 306.1101.

Ethyl 5-Benzyl-4-cyano-2-cyclopropylfuran-3-carboxylate (3i)

Yellow solid (92.1 mg, 78%), mp 76.3-77.6 °C; IR (KBr): 2990, 2235, 1716, 1052 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37-7.17 (m, 5H), 4.35 (q, $J$ = 7.1 Hz, 2H), 4.03 (s, 2H), 2.82-2.66 (m, 1H), 1.39 (t, $J$ = 7.1 Hz, 3H), 1.09-0.97 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 163.6, 161.9, 160.5, 135.1, 128.4, 127.2, 112.8, 95.1, 60.9, 33.3, 14.0, 9.0, 8.9; MS (EI, 70 eV) m/z: 295.31, 249.27, 144.18, 91.16; HRMS ESI (m/z): calcd for C$_{18}$H$_{17}$NNaO$_3$ [M + Na]$^+$: 318.1102, found: 318.1101.

Ethyl 5-Benzyl-4-cyano-2-phenylfuran-3-carboxylate (3j)

Yellow solid (123.3 mg, 93%), mp 76.9-77.6 °C; IR (KBr): 2984, 2236, 2721, 1095 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.85 (dd, $J$ = 6.6, 3.0 Hz, 2H), 7.46-7.37 (m, 3H), 7.37-7.19 (m, 5H), 4.34 (q, $J$ = 7.1 Hz, 2H), 4.15 (s, 2H), 1.36 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 162.5, 161.0, 157.3, 134.8, 130.2, 128.8, 128.5, 128.4, 128.0, 127.8, 127.2, 113.0, 112.6, 96.7, 61.3, 33.4, 13.7; MS (EI, 70 eV) m/z: 331.32, 302.25, 286.27, 105.14; HRMS ESI (m/z): calcd for C$_{21}$H$_{17}$NNaO$_3$ [M + Na]$^+$: 354.1102, found: 354.1102.

Ethyl 5-Benzyl-4-cyano-2-(4-fluorophenyl)furan-3-carboxylate (3k)

White solid (122.9 mg, 88%), mp 114.9-115.6 °C; IR (KBr): 2987, 2235, 1718, 1224 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.85 (dd, $J$ = 6.6, 3.0 Hz, 2H), 7.46-7.37 (m, 3H), 7.37-7.19 (m, 5H), 4.34 (q, $J$ = 7.1 Hz, 2H), 4.15 (s, 2H), 1.36 (t, $J$ = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 162.6, 161.0, 157.3, 134.8, 130.2, 128.8, 128.5, 128.4, 128.0, 127.8, 127.2, 113.0, 112.6, 96.7, 61.3, 33.4, 13.7; MS (EI, 70 eV) m/z: 331.32, 302.25, 286.27, 105.14; HRMS ESI (m/z): calcd for C$_{21}$H$_{17}$NNaO$_3$ [M + Na]$^+$: 354.1102, found: 354.1102.
MHz, CDCl$_3$) δ 7.99-7.86 (m, 2H), 7.40-7.26 (m, 5H), 7.15-7.08 (m, 2H), 4.37 (q, $J = 7.1$ Hz, 2H), 4.20 (s, 2H), 1.40 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 163.7 ($J = 250.5$ Hz), 162.6, 161.1, 156.6, 134.9, 130.8 ($J = 8.6$ Hz), 128.9, 128.6, 127.4, 124.1 ($J = 3.4$ Hz), 115.3 ($J = 21.9$ Hz), 112.9, 112.7, 96.8, 61.6, 33.6, 13.8; $^{19}$F NMR (CDCl$_3$) δ ppm 108.8; MS (EI, 70 eV) $m/z$: 349.28, 320.21, 304.25, 123.15; HRMS ESI (m/z): calcd for C$_{21}$H$_{16}$FNNaO$_3$ [M + Na]$^+$: 372.1006, found: 372.1006.

**Ethyl 5-Benzyl-4-cyano-2-(4-methoxyphenyl)furan-3-carboxylate (3l)**

Yellow solid (109.9 mg, 76%); mp 77.1-78.2 °C; IR (KBr): 2979, 2234, 1717, 1240 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.85 (d, $J = 9.0$ Hz, 2H), 7.37-7.24 (m, 5H), 6.93 (d, $J = 9.0$ Hz, 2H), 4.35 (q, $J = 7.1$ Hz, 2H), 4.16 (s, 2H), 3.82 (s, 3H), 1.38 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 162.0, 161.3, 161.1, 157.8, 135.1, 130.2, 128.9, 128.6, 127.3, 120.4, 113.6, 113.0, 111.6, 96.7, 61.33, 55.3, 33.6, 13.9; MS (EI, 70 eV) $m/z$: 361.36, 333.32, 316.31, 135.18; HRMS ESI (m/z): calcd for C$_{22}$H$_{19}$NNaO$_4$ [M + Na]$^+$: 384.1206, found: 384.1204.

**Ethyl 5-Benzyl-4-cyano-2-(o-tolyl)furan-3-carboxylate (3m)**

Yellow oil (113.3mg, 82%); IR (KBr): 2982, 2236, 1721, 1096 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.65 (d, $J = 7.3$ Hz, 2H), 7.35-7.21 (m, 7H), 4.34 (q, $J = 7.1$ Hz, 2H), 4.16 (s, 2H), 2.37 (s, 3H), 1.36 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 162.4, 161.1, 157.6, 137.8, 134.9, 131.0, 129.0, 128.8, 128.5, 128.0, 127.7, 127.3, 125.7, 112.9, 112.7, 96.8, 61.3, 33.5, 21.3, 13.8; MS (EI, 70 eV) $m/z$: 345.35, 316.28, 119.17, 91.18; HRMS ESI (m/z): calcd for C$_{22}$H$_{19}$NNaO$_4$ [M + Na]$^+$: 368.1257, found: 368.1258.

**Ethyl 5-Benzyl-4-cyano-2-(pyridin-2-yl)furan-3-carboxylate (3n)**

Brown oil (90.4 mg, 68%); IR (KBr): 2984, 2236, 1722, 1234 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.79-8.68 (m, 1H), 8.01 (dt, $J = 8.0, 1.0$ Hz, 1H), 7.77 (td, 13.8 Hz, 1H), 7.58-7.49 (m, 3H), 7.43-7.35 (m, 2H), 4.34 (q, $J = 7.1$ Hz, 2H), 4.16 (s, 2H), 3.82 (s, 3H), 1.36 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ ppm 162.4, 161.1, 157.8, 137.8, 134.9, 131.0, 129.0, 128.8, 128.5, 128.0, 127.7, 127.3, 125.7, 112.9, 112.7, 96.8, 61.3, 33.5, 21.3, 13.8; MS (EI, 70 eV) $m/z$: 345.35, 316.28, 119.17, 91.18; HRMS ESI (m/z): calcd for C$_{22}$H$_{19}$NNaO$_4$ [M + Na]$^+$: 368.1257, found: 368.1258.
Ethyl 5-Benzyl-4-cyano-[2,2'-bifuran]-3-carboxylate (3o)

Brown solid (97.7 mg, 76%), mp 99.2-100.3 °C; IR (KBr): 2987, 2237, 1759, 1240 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.62-7.50 (m, 2H), 7.37-7.30 (m, 4H), 7.29-7.23 (m, 1H), 6.53 (dd, J = 3.6, 1.8 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 4.17 (s, 2H), 1.41 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 162.4, 160.5, 158.9, 135.3, 128.8, 128.6, 127.2, 114.2, 113.0, 95.1, 82.3, 33.5, 28.0, 13.4; MS (EI, 70 eV) m/z: 321.26, 276.23, 219.21, 91.18; HRMS ESI (m/z): calcd for C₁₉H₁₅NNaO₄ [M + Na]⁺: 344.0893, found: 344.0890.

tert-Butyl 5-Benzyl-4-cyano-2-methylfuran-3-carboxylate (3p)

Yellow oil (93.9 mg, 79%); IR (KBr): 2982, 2236, 1713, 1243 cm⁻¹; ¹H NMR NMR (400 MHz, CDCl₃) δ 7.37-7.21 (m, 5H), 4.07 (s, 2H), 2.51 (s, 3H), 1.58 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 161.6, 160.8, 158.9, 135.3, 128.8, 128.6, 127.2, 114.2, 113.0, 95.1, 82.3, 33.5, 28.0, 13.4; MS (EI, 70 eV) m/z: 297.29, 241.22, 224.23, 195.21; HRMS ESI (m/z): calcd for C₁₈H₁₉NNaO₃ [M + Na]⁺: 320.1257, found: 320.1253.

Benzyl 5-Benzyl-4-cyano-2-methylfuran-3-carboxylate (3q)

Yellow oil (120.6 mg, 91%); IR (KBr): 2934, 2235, 1719, 1240 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.53-7.42 (m, 2H), 7.41-7.18 (m, 8H), 5.34 (s, 2H), 4.07 (s, 2H), 2.52 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ ppm 162.1, 161.4, 159.9, 135.4, 135.1, 128.9, 128.6, 128.9, 128.3, 128.3, 127.4, 113.0, 112.9, 94.9, 66.6, 33.5, 13.7; MS (EI, 70 eV) m/z: 331.33, 224.22, 107.20, 91.18; HRMS ESI (m/z): calcd for C₂₁H₁₇NNaO₃ [M + Na]⁺: 354.1101, found: 354.1100.
Allyl 5-Benzyl-4-cyano-2-methylfuran-3-carboxylate (3r)  
Yellow oil (90.0 mg, 80%); IR (KBr): 2932, 2236, 1720, 1093 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.30 (ddd, \(J\) = 10.5, 8.1, 5.9 Hz, 5H), 6.09-5.91 (m, 1H), 5.45 (dd, \(J\) = 17.2, 1.5 Hz, 1H), 5.29 (dd, \(J\) = 10.5, 1.3 Hz, 1H), 4.79 (dt, \(J\) = 5.6, 1.4 Hz, 2H), 4.08 (s, 2H), 2.54 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 162.1, 161.3, 159.8, 135.1, 131.5, 128.9, 128.6, 127.3, 118.6, 112.9, 112.8, 94.8, 65.5, 33.5, 13.6; MS (EI, 70 eV) \(m/z\): 281.27, 240.25, 224.23, 91.17; HRMS ESI (m/z): calcd for C\(_{17}\)H\(_{15}\)NNaO\(_3\) [M + Na]^+: 304.0944, found: 304.0940.

5-Benzyl-4-cyano-\(N,\)\(N\),2-trimethylfuran-3-carboxamide (3s)  
Brown oil (65.5 mg, 61%); IR (KBr): 2925, 2231, 1635, 1062 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.36-7.26 (m, 5H), 4.07 (s, 2H), 3.07 (s, 6H), 2.31 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 163.2, 161.7, 152.8, 135.2, 128.9, 128.7, 127.4, 116.8, 113.0, 94.3, 38.6, 33.7, 12.7; MS (EI, 70 eV) \(m/z\): 268.30, 224.24, 182.22, 91.17; HRMS ESI (m/z): calcd for C\(_{16}\)H\(_{16}\)N\(_2\)NaO\(_2\) [M + Na]^+: 291.1104, found: 291.1102.

4-Acetyl-5-methyl-2-pentylfuran-3-carbonitrile (3t)  
Brown oil (56.1 mg, 64%); IR (KBr): 2941, 2231, 1680, 1411 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.74 (t, \(J\) = 7.5 Hz, 2H), 2.51 (d, \(J\) = 9.2 Hz, 6H), 1.73-1.60 (m, 2H), 1.36-1.24 (m, 4H), 0.87 (t, \(J\) = 7.0 Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 191.9, 164.6, 158.0, 120.7, 113.8, 93.2, 30.9, 29.7, 27.2, 27.1, 22.0, 14.2, 13.7; MS (EI, 70 eV) \(m/z\): 219.28, 204.23, 182.22, 91.17; HRMS ESI (m/z): calcd for C\(_{13}\)H\(_{15}\)NNaO\(_2\) [M + Na]^+: 242.1151, found: 242.1152.

4-Acetyl-2-(4-methoxybenzyl)-5-methylfuran-3-carbonitrile (3u)  
Yellow oil (82.9 mg, 77%); IR (KBr): 2929, 2231, 1676, 1248 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.24-7.15 (m, 2H), 6.90-6.83 (m, 2H), 4.03 (s, 2H), 3.78
(s, 3H), 2.53 (d, J = 2.9 Hz, 6H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 191.8, 162.8, 158.9, 158.7, 128.7, 127.0, 120.9, 114.3, 113.7, 93.6, 55.2, 32.7, 29.8, 14.3; MS (EI, 70 eV) \(m/z\): 269.29, 254.26, 226.27, 108.18; HRMS ESI (m/z): calcd for C\(_{16}\)H\(_{15}\)NNaO\(_3\) [M + Na\(^+\)]: 292.0944, found: 292.0944.

4-Acetyl-2-(2-chlorobenzyl)-5-methylfuran-3-carbonitrile (3v)

White solid (87.4 mg, 80%), mp 97.5-98.0 °C; IR (KBr): 2988, 2231, 1675, 1243 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.45-7.35 (m, 1H), 7.30-7.23 (m, 3H), 4.25 (s, 2H), 2.62-2.48 (m, 6H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 191.8, 160.5, 158.9, 134.1, 132.6, 130.9, 129.8, 129.0, 127.2, 121.0, 113.3, 94.7, 31.4, 29.8, 14.4; MS (EI, 70 eV) \(m/z\): 273.24, 258.21, 238.29, 216.29; HRMS ESI (m/z): calcd for C\(_{15}\)H\(_{12}\)NClNaO\(_2\) [M + Na\(^+\)]: 296.0449, found: 296.0448.

4-Acetyl-5-methyl-2-(3-methylbenzyl)furan-3-carbonitrile (3w)

White solid (83.1 mg, 82%), mp 76.2-77.4 °C; IR (KBr): 2923, 2231, 1677, 1083 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.26 (dd, \(J = 14.8, 7.0\) Hz, 1H), 7.11 (t, \(J = 6.9\) Hz, 3H), 4.08 (s, 2H), 2.57 (d, \(J = 4.3\) Hz, 6H), 2.37 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 191.9, 162.4, 158.8, 138.7, 134.9, 129.3, 128.8, 128.2, 125.6, 120.9, 113.7, 33.5, 29.8, 21.3, 14.4; MS (EI, 70 eV) \(m/z\): 253.29, 238.26, 210.26, 161.17; HRMS ESI (m/z): calcd for C\(_{16}\)H\(_{15}\)NNaO\(_2\) [M + Na\(^+\)]: 276.0995, found: 276.0997.

2-Benzyl-5-phenylfuran-3,4-dicarbonitrile (3x)

White solid (60.3 mg, 53%), mp 122.3-124.3 °C; IR (KBr): 2920, 2230, 2762, 1242 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.98-7.87 (m, 2H), 7.52-7.47 (m, 3H), 7.35 (dt, \(J = 11.8, 8.1\) Hz, 5H), 4.20 (s, 2H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) ppm 162.8, 159.9, 134.0, 131.4, 129.3, 129.2, 128.7, 127.9, 126.3, 125.7, 111.7, 110.4, 97.5, 92.5, 33.9; MS (EI, 70 eV) \(m/z\): 284.30, 225.30, 105.18, 77.18; HRMS ESI (m/z):
cald for $\text{C}_{19}\text{H}_{12}\text{N}_{2}\text{NaO} [\text{M + Na}]^+$: 307.0842, found: 307.0843.

6-Benzyl-3,4-dimethylfuro[3,4-c]furan-1(3H)-imine (4)

Yellow oil (33.4 mg, 69%); IR (KBr): 2921, 2230, 1579, 1075, 710 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39-7.15 (m, 5H), 4.84 (q, $J = 6.6$ Hz, 1H), 4.03 (s, 2H), 2.58 (s, 1H), 2.24 (s, 3H), 1.53 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 161.7, 147.9, 135.8, 128.7, 128.7, 127.1, 123.4, 114.0, 93.3, 62.4, 33.7, 23.5, 11.8; MS (EI, 70 eV) $m/z$: 241.27, 226.25, 148.16, 91.17; HRMS ESI (m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{NNaO}_2 [\text{M + Na}]^+$: 264.0995, found: 264.0998.

4-Amino-5-benzyl-7-cyclopropylfuro[3,4-d]pyridazin-1-ol (5)

Yellow solid (28.1 mg, 45%), mp 268.3-269.5 ºC; IR (KBr): 3320, 2232, 1598, 1049, 714 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.25 (m, 3H), 7.20 (d, $J = 7.0$ Hz, 2H), 3.79 (d, $J = 192.0$ Hz, 4H), 2.76-2.62 (m, 1H), 1.26 (s, 1H), 1.09-0.91 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 161.5, 160.9, 151.7, 146.3, 134.9, 128.9, 128.5, 127.5, 113.4, 92.8, 33.7, 9.0, 8.7; MS (EI, 70 eV) $m/z$: 281.28, 250.26, 180.22, 91.18; HRMS ESI (m/z): calcd for $\text{C}_{16}\text{H}_{16}\text{N}_{3}\text{O}_2 [\text{M + H}]^+$: 282.1237, found: 282.1241.

Ethyl 5-Benzyl-4-carbamoyl-2-cyclopropylfuran-3-carboxylate (6)

White solid (45.1 mg, 72%), mp 128.0-128.9 ºC; IR (KBr): 3320, 1664, 1413, 1086, 700 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.17 (s, 1H), 7.25 (d, $J = 4.4$ Hz, 4H), 7.18 (d, $J = 8.7$, 4.2 Hz, 1H), 5.72 (s, 1H), 4.50-4.23 (m, 4H), 2.68-2.49 (m, 1H), 1.37 (t, $J = 7.1$ Hz, 3H), 1.09-0.87 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 166.1, 164.9, 162.7, 158.6, 137.6, 128.8, 128.3, 126.3, 115.0, 110.6, 61.2, 33.5, 14.1, 9.9, 8.6; MS (EI, 70 eV) $m/z$: 313.29, 296.29, 250.23, 222.23; HRMS ESI (m/z): calcd for $\text{C}_{18}\text{H}_{19}\text{NNaO}_4 [\text{M + Na}]^+$: 336.1206, found: 336.1210.
4-Oxo-2-phenylpentanenitrile (8)

Yellow oil (58.2 mg, 84%); IR (KBr): 3027, 2932, 2235, 1715, 1362 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40-7.30 (m, 5H), 4.34 (dd, $J = 7.9$, 6.1 Hz, 1H), 3.07 (ddd, $J = 24.1$, 18.0, 7.0 Hz, 2H), 2.17 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 203.0, 135.0, 129.2, 128.3, 127.3, 120.3, 48.7, 31.5, 29.9; MS (EI, 70 eV) m/z: 173.25, 130.19, 103.19, 77.18; HRMS ESI (m/z): calcd for C$_{11}$H$_{11}$NNaO [M + Na]$^+$: 196.0733, found: 196.0731.

D$_1$-3a

Yellow oil (75.0 mg, 78%); IR (KBr): 2923, 2231, 1675, 1410 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ ppm 7.42-7.21 (m, 5H), 4.09 (d, $J = 6.8$ Hz, 1.15H), 2.54 (d, $J = 3.8$ Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ ppm 191.8, 162.3, 158.8, 135.0 ($J = 3.9$ Hz), 128.9, 128.6, 127.4, 120.9, 113.9, 93.9 ($J = 1.1$ Hz), 33.6, 29.8, 14.4; MS (EI, 70 eV) m/z: 240.29, 225.26, 197.24, 92.26; HRMS ESI (m/z): calcd for C$_{15}$H$_{12}$DNNaO$_2$ [M + Na]$^+$: 263.0901, found: 263.0896.

E. NMR Spectra

3a
3b
3c
3e
3h

S19
3r

S29
3v

S33
3w