Electronic Supplementary Information

Concise synthesis of rare pyrido[1,2-a]pyrimidin-2-ones and related nitrogen-rich bicyclic scaffolds with a ring-junction nitrogen

T. A. Alanine, W. R. J. D. Galloway, S. Bartlett, J. J. Ciardiello, T. M. McGuire, and D. R. Spring

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, CB2 1EW, UK.
Email: spring@ch.cam.ac.uk; Fax: +44 (0)1223-336362
AstraZeneca UK Ltd., Alderly Park, Macclesfield, Chesire, SK10, UK.

Table of contents:

General experimental details .......................................................................................... 3
General methods ............................................................................................................ 6
   General method 1: Acylation of aminoazines ............................................................ 6
   General method 2: Cyclisation of heterocyclic amides ............................................. 6
Experimental details and NMR spectra ......................................................................... 7
   N-(2-Pyridyl)but-2-ynamide (25) ........................................................................... 7
   N-(4-(trifluoromethyl)pyridin-2-yl)but-2-ynamide (43) ............................................ 9
   N-(4-ethylpyridin-2-yl)but-2-ynamide (44) .......................................................... 11
   N-(4-Bromopyridin-2-yl)but-2-ynamide (45) ......................................................... 13
   N-(4-cyanopyridin-2-yl)but-2-ynamide (46) ............................................................ 15
   N-(4-chloropyridin-2-yl)but-2-ynamide (47) ............................................................ 17
   N-(4-methylpyridin-2-yl)but-2-ynamide (48) .......................................................... 19
   N-(4-phenylpyridin-2-yl)but-2-ynamide (49) .......................................................... 21
   Ethyl 2-((but-2-ynamido)isonicotinate (50) ............................................................ 23
   N-(4-Methoxypyridin-2-yl)but-2-ynamide (51) ....................................................... 25
   N-(6-Methoxypyrazin-3-yl)but-2-ynamide (52) ...................................................... 27
   N-(Pyrazin-2-yl)but-2-ynamide (53) ..................................................................... 30
   N-(6-Chloropyrazin-2-yl)but-2-ynamide (54) ............................................................ 32
   N-(6-Methoxypyrimidin-4-yl)but-2-ynamide (55) ....................................................... 34
   N-(5-Bromopyrimidin-2-yl)but-2-ynamide (56) ...................................................... 36
   N-(Quinolin-2-yl)but-2-ynamide (57) .................................................................... 39
   N-(4,6-bis(ethylthio)pyrimidin-2-yl)but-2-ynamide (58) ........................................ 41
   9-(Benzyloxy)-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (62) ............................... 43
   4-Methyl-2H-pyrimido[1,2-a]pyrimidin-2-one (63) ............................................... 46
   9-ETHOXY-4-ethyl-2H-pyrido[1,2-a]pyrimidin-2-one (64) ....................................... 48
   4-(Trifluoromethyl)-2H-pyrido[1,2-a]pyrimidin-2-one (66) ..................................... 50
   4-Methyl-2H-pyrido[1,2-a]pyrimidin-2-one (67) .................................................... 53
   4-Methyl-8-(trifluoromethyl)-2H-pyrido[1,2-a]pyrimidin-2-one (68) ....................... 55
8-Ethyl-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (69) ........................................ 58
8-Bromo-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (70) ........................................ 60
4-Methyl-2-oxo-2H-pyrido[1,2-a]pyrimidine-8-carbonitrile (71) .............................. 63
8-Chloro-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (72) ........................................ 65
4,8-Dimethyl-2H-pyrido[1,2-a]pyrimidin-2-one (73) .............................................. 68
4-Methyl-8-phenyl-2H-pyrido[1,2-a]pyrimidin-2-one (74) ........................................ 70
Ethyl 4-methyl-2-oxo-2H-pyrido[1,2-a]pyrimidine-8-carboxylate (75) ....................... 72
8-Methoxy-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (76) ..................................... 75
7-Methoxy-4-methyl-2H-pyrimido[1,2-b]pyridazin-2-one (77) ................................. 77
4-Methyl-2H-pyrazino[1,2-a]pyrimidin-2-one (78) .................................................... 79
8-Methoxy-4-methyl-2H-pyrimido[1,6-a]pyrimidin-2-one (79) ................................. 81
1-Methyl-3H-pyrimido[1,2-a]quinolin-3-one (80) ...................................................... 83
References .................................................................................................................... 85
**General experimental details**

All non-aqueous reactions were performed under a constant stream of dry nitrogen using oven-dried glassware. Standard practices were employed when handling moisture and air-sensitive materials.

Room temperature (r.t.) refers to ambient temperature. All temperatures below 0 °C are those of the external baths. Temperatures of 0 °C were maintained using an ice-water bath. Temperatures below 0 °C were maintained using an acetone-cardice bath (-78 °C) or acetonitrile-cardice (-40 °C).

All reagents and solvents were used as received unless otherwise stated. Toluene was distilled from calcium hydride. Tetrahydrofuran was dried over sodium metal wire and distilled from a mixture of lithium aluminium hydride and calcium hydride with triphenylmethane as indicator. Petroleum ether was distilled before use. n-Butyllithium in hexanes and LDA (2.0 M in THF/heptane/ethylbenzene) (Aldrich) were titrated with N-benzylbenzamide before use. Sodium hydride was used without hexane washes. Magnesium turnings were used for the preparation of all Grignard reagents.

Yields refer to chromatographically and spectroscopically pure compounds (purity of at least 95%) unless otherwise stated, in which case corrected with respect to percentage weight purity (in cases where a purity is stated). Where possible, reactions were monitored by thin layer chromatography (TLC) performed on commercially prepared glass plates pre-coated with Merck silica gel 60 F254 or aluminium oxide 60 F254. Visualisation was by the quenching of UV fluorescence ($\nu_{\text{max}} = 254$ nm) or by staining with potassium permanganate or by liquid chromatography mass spectrometry (LC-MS) using a Waters Micromass ZQ spectrometer. Retention factors ($R_f$) are quoted to 0.01.

Flash column chromatography was carried out using slurry-packed Merck 9385 Kieselgel 60 SiO$_2$ (230-400 mesh) under a positive pressure of compressed air, or Combiflash Companion automated purification columns (GRADE silica columns).
Melting points were obtained on a Buchi B-545 melting point apparatus and are uncorrected.

Infrared spectra were recorded on a Perkin-Elmer Spectrum One spectrometer with internal referencing. Selected absorption maxima (vmax) are reported in wavenumbers (cm\(^{-1}\)) with the following abbreviations: w, weak; med, medium; str, strong; br, broad.

Proton magnetic resonance spectra were recorded using an internal deuterium lock at ambient probe temperatures (unless otherwise stated) on the following instruments: Bruker DPX-400 (400 MHz), Bruker Avance 400 QNP (400 MHz) and Bruker Avance 500 Cryo Ultrashield (500 MHz). Chemical shifts (δ\(_H\)) are quoted in ppm, to the nearest 0.01 ppm, and are referenced to the residual non-deuterated solvent peak. Coupling constants (J) are reported in Hertz (Hz) to the nearest 0.1 Hz. Data are reported as follows: chemical shift, integration, multiplicity (br = broad; s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; or as a combination of these), coupling constant(s) and assignment. The numbering/lettering on selected structures does not follow the IUPAC naming system and is used for the assignment of the \(^1\)H NMR and \(^13\)C NMR spectra. Proton assignments were determined either on the basis of unambiguous chemical shift, coupling pattern, by patterns observed in 2D experiments (\(^1\)H-\(^1\)H COSY, HMBC and HMQC) or by analogy to fully interpreted spectra for related compounds.

Carbon magnetic resonance spectra were recorded by broadband proton spin decoupling at ambient probe temperatures using an internal deuterium lock on the following instruments: Bruker DPX-400 (100 MHz), Bruker Avance 400 QNP (100 MHz) and Bruker Avance 500 Cryo Ultrashield (125 MHz). Chemical shifts (δ\(_C\)) are quoted in ppm, to the nearest 0.1 ppm, and are referenced to the residual non-deuterated solvent peak. Assignment was based on chemical shift, DEPT editing and where appropriate, HMQC and HMBC experiments or by analogy to fully interpreted spectra of related compounds.
Fluorine magnetic resonance spectra were recorded on a Bruker DPX-400 (162 MHz) instrument. Chemical shifts ($\delta F$) are quoted in ppm to the nearest 0.1 ppm and are referenced to CFCl$_3$.

High resolution mass spectrometry (HRMS) measurements were recorded on a Bruker Bioapex 4.7e FTICR or a Micromass LCT Premier spectrometer or a Waters Xevo G2 Qtof spectrometer. Mass values are quoted within the error limits of ± 5 ppm mass units. ToF ES+ or FTMS ESI+ refers to the mass ionisation technique.

Microwave reactions were carried out in a CEM Discover Microwave or in a Biotage Initiator Classic.

LC-MS chromatographs were recorded on an HP/Agilent MSD LC-MS APCI 120-1000 full gradient ACq T = 1 min 1 µL. Retention times are reported to the nearest 0.1 min. Preparative HPLC chromatography was carried out on a Dionex Ultimate 3000 loaded with a Reprosil Chiral NR 250 x 4.6 mm column, eluting with an isocratic 40-60% EtOH/heptane (with 0.01 mol/L NH$_4$OAc) over 60 mins or on a Reprosil Chiral NR 250 x 30 mm column, eluting with a 1.60 mL of the same conditions as above or on a Phenomenex Gemini-NX axia Prep C18 OBD column, 5µ silica, 30 mm diameter, 100 mm length, using decreasingly polar mixtures of water (containing 1% NH$_3$) and MeCN as eluents. Retention times are reported to the nearest 0.01 min.
**General methods**

**General method 1: Acylation of aminoazines**

To a stirred solution of aminoazine (1 eq.) in anhydrous THF (reaction molarity of approx. 0.25 M) at -78 °C was added dropwise the solution of lithium base (2.1 eq.). The reaction was left to stir at -78 °C for 30 mins. The electrophile (1.2 eq.) was then added at -78 °C, and the reaction was left to warm to room temperature over 1 hour. The reaction was then quenched with AcOH (approx.1 mL) and diluted with CH₂Cl₂ (approx. 20 mL) and water (approx. 20 mL). The organic layer was separated and the aqueous layer was washed with CH₂Cl₂ (3 x 20 mL). The combined organic layers were then dried (MgSO₄) and the solvent removed under reduced pressure at low temperature (<25 °C) to yield the crude product which was purified by column chromatography. Note – for highest and most reproducible yields reaction and purification should be carried out within six hours.

**General method 2: Cyclisation of heterocyclic amides**

A stirred solution of heterocyclic ynone in DMSO was heated to 85 or 100 °C until TLC/LC-MS showed complete consumption of starting material (see manuscript for times and temperatures). The solvent was then removed under a stream of N₂ gas overnight and the residue purified by column chromatography or preparative HPLC if required.
Experimental details and NMR spectra

N-(2-Pyridyl)but-2-ynamide (25)

Prepared according to General Method 1 from 2-aminopyridine 23 (0.14 g, 1.43 mmol) nBuLi (1.88 mL, 3.00 mmol) and ethyl 2-butynoate 24 (0.20 mL, 1.72 mmol). The crude product was purified by Combiflash Companion (SiO₂, 20 g, 0-50% EtOAc in heptane) to yield a yellow solid (0.10 g, 0.63 mmol, 44%). Rᵣ = 0.26 (1:1 heptane: EtOAc). Mpt (CH₂Cl₂): 130-131 °C. IR νₘₐₓ/cm⁻¹ (neat): 2956 (m, br, C-H/N-H), 2236 (med, C≡C), 1665 (str, C=O), 1581 (str, C=C), 1534 (str, C=C), 1437 (str, C=C). ¹H NMR (500 MHz, CDCl₃): δ_H 9.15 (1H, br s, H5), δ_H 8.32 (1H, dd, J = 4.9, 0.9 Hz, H1), δ_H 8.17 (1H, d, J = 8.4 Hz, H4), δ_H 7.70 (1H, ddd, J = 8.4, 7.5, 1.9 Hz, H3), δ_H 7.03 (1H, ddd, J = 7.3, 5.0, 0.9 Hz, H2), δ_H 1.99 (3H, s, H6). ¹³C NMR (125 MHz, CDCl₃): δ_c 151.3 (C5), δ_c 151.2 (C6), δ_c 147.8 (C1), δ_c 138.6 (C3), δ_c 119.9 (C2), δ_c 114.8 (C4), δ_c 85.5 (C7), δ_c 75.3 (C8), δ_c 3.8 (C9). HRMS (TOF ES+) m/z found [M+H]^+ 161.0716, C₈H₉N₂O⁺ required 161.0715, Δ ppm = 0.6 ppm.
\[N-(4-(\text{trifluoromethyl)}\text{pyridin-2-yl})\text{but-2-ynamide} \ (43)\]

Prepared according to General Method 1 from 2-amino-4-(trifluoromethyl)pyridine 27 (0.10 g, 0.62 mmol), \(n\)BuLi (1.30 mmol) and ethyl 2-butynoate 24 (0.09 mL, 0.74 mmol). The crude product was purified by column chromatography (SiO\(_2\), 20 g, 4:1 then 7:3 40-60 petroleum ether: EtOAc) to yield a beige solid (0.11 g, 0.50 mmol, 82\%). \(R_f = 0.60\) (1:1 40-60 petroleum ether: EtOAc). Mpt (CH\(_2\)Cl\(_2\)): darkens \(>120^\circ\)C, melts 129-131 \(^\circ\)C. IR \(\nu_{\max}/\text{cm}^{-1}\) (neat): 3165 (w, N-H/C-H), 3125 (w, C-H), 2979 (w, C-H), 2241 (med, C=C), 1679 (med, C=O), 1670 (med, C=O), 1618 (w), 1579 (str, C=C), 1529 (str, C=C/C=N), 1467 (w), 1420 (str), 1336 (str), 1309 (w), 1291 (med), 1275 (str), 1230 (str), 1165 (str), 1127 (str), 1087 (str), 1068 (str). \(^1H\) NMR (500 MHz, d\(^6\)-DMSO): \(\delta_H\) 11.55 (1H, s, H4), \(\delta_H\) 8.60 (1H, d, \(J = 5.1\) Hz, H1), \(\delta_H\) 8.26 (1H, app s, H3), \(\delta_H\) 7.48 (1H, dd, \(J = 5.1, 0.9\) Hz, H2), \(\delta_H\) 2.04 (3H, s, H5). \(^{13}C\) NMR (125 MHz, d\(^6\)-DMSO): \(\delta_C\) 152.5 (C5), \(\delta_C\) 151.8 (C7), \(\delta_C\) 150.2 (C1), \(\delta_C\) 138.4 (q, \(^2J_{C,F} = 33\) Hz, C3), \(\delta_C\) 122.8 (q, \(^1J_{C,F} = 273\) Hz, C6), \(\delta_C\) 115.3 (d, \(^3J_{C,F} = 3\) Hz, C2), \(\delta_C\) 109.6 (\(^3J_{C,F} = 4\) Hz, C4), \(\delta_C\) 87.0 (C8), \(\delta_C\) 75.3 (C9), \(\delta_C\) 3.5 (C10). \(^19\)F NMR (162 MHz, d\(^6\)-DMSO): \(\delta_F\) -63.91 (s, CF\(_3\)). HRMS (FTMS ESI+) \(m/z\) found [M+H]\(^+\) 229.0579, \(C_{10}H_8ON_2F_3\)\(^+\) required 229.0579, \(\Delta\) ppm = -2.1 ppm.
$^1$H NMR

$^{13}$C NMR
\(\text{N-(4-ethylpyridin-2-yl)but-2-ynamide (44)}\)

Prepared according to General Method 1 from 2-amino-4-ethylpyridine 28 (0.30 g, 2.46 mmol), \(n\)BuLi (5.16 mmol) and ethyl 2-butynoate 24 (0.34 mL, 2.95 mmol). The crude product was purified by column chromatography (SiO\(_2\), 20 g, 7:3 40-60 petroleum ether: EtOAc) to yield a yellow solid (0.20 g, 90% purity, 0.98 mmol, 40%). \(R_f = 0.50\) (1:1 40-60 petroleum ether: EtOAc). Mpt (CH\(_2\)Cl\(_2\)): 112-114 °C. IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (neat): 3100 (w, N-H/C-H), 3031 (w, C-H), 2972 (w, C-H), 2938 (w, C-H), 2781 (w), 2243 (w, C=C), 2228 (w, C=C), 1695 (w), 1660 (str, C=O), 1610 (med, C=C), 1565 (str, C=C), 1530 (str, C=C/C=N), 1466 (w), 1453 (w), 1416 (str), 1377 (w), 1296 (med), 1284 (w), 1270 (med), 1251 (str), 1164 (med), 1122 (w), 1071 (w), 1061 (w), 1001 (w). \(^1\)H NMR (500 MHz, d\(_6\)-DMSO): \(\delta_H\) 10.94 (1H, s, H4), \(\delta_H\) 8.18 (1H, d, \(J = 5.0\) Hz, H1), \(\delta_H\) 7.82 (1H, app s, H3), \(\delta_H\) 6.98 (1H, dd, \(J = 5.0, 1.5\) Hz, H2), \(\delta_H\) 2.59 (2H, q, \(J = 7.5\) Hz, H6), \(\delta_H\) 2.01 (3H, s, H5), \(\delta_H\) 1.15 (3H, t, \(J = 7.5\) Hz, H7). \(^{13}\)C NMR (125 MHz, d\(_6\)-DMSO): \(\delta_C\) 154.8 (C3), \(\delta_C\) 151.7 (C8), \(\delta_C\) 151.3 (C5), \(\delta_C\) 147.9 (C1), \(\delta_C\) 119.8 (C2), \(\delta_C\) 113.8 (C4), 85.6 (C9), \(\delta_C\) 75.6 (C10), \(\delta_C\) 27.8 (C6), \(\delta_C\) 14.4 (C7), \(\delta_C\) 3.4 (C11). HRMS (TOF ES\(^+\)) \(m/z\) found [M+H\(^+\)] 189.1030, C\(_{11}\)H\(_{13}\)ON\(_2\)\(^+\) required 189.1028, \(\Delta\) ppm = 1.1 ppm.
$^1$H NMR

$^{13}$C NMR
$N$-(4-Bromopyridin-2-yl)but-2-ynamide (45)

Prepared according to General Method 1 from 2-amino-4-bromopyridine 29 (1 g, 5.78 mmol), LDA (12.14 mmol) and ethyl 2-butynoate 24 (0.808 mL, 6.94 mmol). The crude product was purified by column chromatography (SiO$_2$, 0 to 30% EtOAc in heptane) to yield a yellow solid (0.698 g, 51%). This can be titurated with heptane if required. $R_f = 0.65$ (1:1 40-60 petroleum ether: EtOAc). Mpt (CH$_2$Cl$_2$): darkens >160 °C, melts 227-230 °C. IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3199 (w, C-H/N-H), 3147 (w, C-H/N-H), 3052 (w, C-H), 3010 (w, C-H), 2236 (med, C=C), 1659 (str, C=O), 1571 (str, C=C), 1511 (str, C=C), 1455 (w), 1419 (w), 1402 (str), 1290 (med), 1271 (str), 1251 (med), 1224 (med), 1122 (w), 1093 (med), 1066 (med), 1026 (w). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta$H 11.31 (1H, s, H4), $\delta$H 8.24 (1H, d, $J = 5.3$ Hz, H1), $\delta$H 8.21 (1H, d, $J = 1.2$ Hz, H3), $\delta$H 7.40 (1H, dd, $J = 5.3$, 1.8 Hz, H2), $\delta$H 2.05 (3H, s, H5). $^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta$C 152.4 (C5), $\delta$C 151.6 (C6), $\delta$C 149.5 (C1), $\delta$C 133.1 (C3), $\delta$C 122.9 (C2), $\delta$C 117.0 (C4), 86.8 (C7), $\delta$C 75.3 (C8), $\delta$C 3.5 (C9). HRMS (TOF ES+) $m/z$ found [M+H]$^+$ 238.9825, C$_9$H$_8$ON$_2$$^{79}$Br$^+$ required 238.9820, $\Delta$ ppm = 2.1 ppm.
$^1$H NMR

$^{13}$C NMR
N-(4-cyanopyridin-2-yl)but-2-yname (46)

Prepared according to General Method 1 from 2-amino-4-cyanopyridine 30 (0.10 g, 0.84 mmol), LDA (1.76 mmol) and ethyl 2-butynoate 24 (0.12 mL, 1.01 mmol). The crude product was purified by column chromatography (SiO₂, 20 g, 7:3 40-60 petroleum ether: EtOAc) to yield a yellow solid (0.06 g, 0.30 mmol, 36%). Rₚ = 0.35 (1:1 40-60 petroleum ether: EtOAc). Mpt (CH₂Cl₂): darkens >140 °C, decom. >297 °C. IR ν max/cm⁻¹ (neat): 3075 (w, br), 2230 (med, C≡C/C≡N), 1676 (str, C=O), 1600 (w, C=C), 1559 (str, C=C), 1521 (med, C=C), 1420 (str, C=C/C=N), 1293 (w), 1262 (str), 1231 (med), 1150 (med), 1067 (med). ¹H NMR (500 MHz, d₆-DMSO): δH 11.53 (1H, s, H4), δH 8.57 (1H, dd, J = 5.0, 0.3 Hz, H1), δH 8.24 (1H, s, H3), δH 7.57 (1H, dd, J = 5.0, 1.4 Hz, H2), δH 2.04 (3H, s, H5). ¹³C NMR (125 MHz, d₆-DMSO): δC 152.1 (C7), δC 151.7 (C5), δC 149.9 (C1), δC 121.4 (C2), δC 121.0 (C3), δC 116.9 (C6), δC 116.1 (C4), δC 87.2 (C8), δC 75.2 (C9), δC 3.5 (C10). HRMS (FTMS ESI+) m/z found [M+H]⁺ 186.0658, C₁₀H₈O₃N⁺ required 186.0658, Δ ppm = -1.98 ppm.

¹H NMR
$^{13}$C NMR
**N-(4-chloropyridin-2-yl)but-2-ynamide (47)**

Prepared according to General Method 1 from 2-amino-4-chloropyridine 31 (1.00 g, 7.78 mmol), LDA (16.33 mmol) and ethyl 2-butyroate 24 (1.09 mL, 9.33 mmol). The crude product was purified by Combiflash Companion (SiO$_2$, 50 g, 0-100% EtOAc in heptane) to yield a cream solid (0.88 g, 4.52 mmol, 58%). $R_f = 0.18$ (3:1 heptane: EtOAc). Mpt (CH$_2$Cl$_2$): decomp 150-165 °C. IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 2983 (w, br, N-H/C-H), 2326 (w, br, C≡C), 2232 (med, C≡C), 1664 (str, C=O), 1575 (str, C=C), 1522 (str, C=C/C=N), 1406 (str), 1274 (str), 1230 (med), 1098 (med), 1071 (med). $^1$H NMR (400 MHz, d$_6$-DMSO): $\delta_H$ 11.31 (1H, s, H4), $\delta_H$ 8.32 (1H, d, $J = 5.4$ Hz, H1), $\delta_H$ 8.05 (1H, d, $J = 2.0$ Hz, H3), $\delta_H$ 7.27 (1H, dd, $J = 5.4$, 1.9 Hz, H2), $\delta_H$ 2.04 (3H, s, H5). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta_C$ 152.7 (C5), $\delta_C$ 151.6 (C6), $\delta_C$ 149.6 (C1), $\delta_C$ 144.1 (C3), $\delta_C$ 120.0 (C2), $\delta_C$ 114.1 (C4), $\delta_C$ 86.8 (C7), $\delta_C$ 75.4 (C8), $\delta_C$ 3.9 (C9). HRMS (TOF ES+) $m/z$ found [M+H]$^+$ 195.0329, C$_9$H$_8$N$_2$O$_3$Cl$^+$ required 195.0325, $\Delta$ ppm = 2.1 ppm.
**N-(4-methylpyridin-2-yl)but-2-yname (48)**

Prepared according to General Method 1 from 2-amino-4-methylpyridine 32 (1.004 g, 9.28 mmol), $n$BuLi (19.50 mmol) and ethyl 2-butynoate 24 (1.299 mL, 11.14 mmol). The crude product was purified by column chromatography (SiO$_2$, elution gradient 0 to 30% EtOAc in heptane) to yield a yellow solid. This was triturated with heptane to yield a yellow powder (0.624g, 39%). $R_f = 0.35$ (1:1 40-60 petroleum ether: EtOAc). Mpt (CH$_2$Cl$_2$): darkens >120 °C, melts 220-225 °C. IR $\nu_{\text{max/cm}}^{-1}$ (neat): 3114 (w, N-H/C-H), 2959 (w, C-H), 2917 (w, C-H), 1662 (str, C=O), 1612 (str, C=C), 1571 (str, C=C), 1533 (str, C=C/C=N), 1470 (med), 1410 (str), 1293 (str), 1284 (med), 1267 (str), 1259 (str), 1236 (str), 1166 (med), 1122 (w), 1074 (w), 1023 (w), 1000 (w). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta_H$ 10.93 (1H, s, H4), $\delta_H$ 8.16-8.14 (1H, m, H1), $\delta_H$ 7.79 (1H, s, H3), $\delta_H$ 7.95-6.94 (1H, m, H2), $\delta_H$ 2.28 (3H, s, H5), $\delta_H$ 2.01 (3H, s, H6). $^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta_C$ 151.5 (C7), $\delta_C$ 151.3 (C5), $\delta_C$ 149.0 (C3), $\delta_C$ 147.8 (C1), $\delta_C$ 121.0 (C2), $\delta_C$ 115.0 (C4), $\delta_C$ 85.7 (C8), $\delta_C$ 75.6 (C9), $\delta_C$ 20.9 (C6), $\delta_C$ 3.4 (C10). HRMS (FTMS ESI+) $m/z$ found [M+H]$^+$ 175.0859, C$_{10}$H$_{11}$ON$_2^+$ required 175.0866, $\Delta$ ppm = -0.1 ppm.
*N*-\((4\text{-phenylpyridin-2-yl})\)but-2-ynamide (49)

Prepared according to General Method 1 from 2-amino-4-phenylpyridine 33 (0.15 g, 0.88 mmol), \(n\)BuLi (1.85 mmol) and ethyl 2-butynoate 24 (0.12 mL, 1.06 mmol). The crude product was purified by column chromatography (SiO\(_2\), 20 g, 3:2 40-60 petroleum ether: EtOAc) to yield a pale yellow solid (0.07 g, 0.28 mmol, 32\%). \(R_f = 0.57\) (1:1 40-60 petroleum ether: EtOAc). Mpt (CH\(_2\)Cl\(_2\)): darkens >142 °C, melts 210-213 °C. IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (neat): 2979 (w, br), 2357 (w, C≡C), 2343 (w, C≡C), 2229 (w, C≡C), 1663 (str, C=O), 1605 (med, C=C), 1557 (str, C=C), 1530 (med), 1493 (w), 1463 (w), 1448 (w), 1408 (str), 1318 (w), 1282 (w), 1264 (str), 1230 (med), 1074 (med). \(^1\)H NMR (500 MHz, d\(_6\)-DMSO): \(\delta_H\) 11.16 (1H, s, H4), \(\delta_H\) 8.39 (1H, app dd, \(J = 5.2, 0.6\) Hz, H1), \(\delta_H\) 8.28-8.26 (1H, m, H3), \(\delta_H\) 7.74-7.71 (2H, m, H6+H10), \(\delta_H\) 7.57-7.47 (3H, m, H7+H8+H9), \(\delta_H\) 7.45 (1H, dd, \(J = 5.2, 0.6\) Hz, H2), \(\delta_H\) 2.03 (3H, s, H5). \(^{13}\)C NMR (125 MHz, d\(_6\)-DMSO): \(\delta_C\) 167.5 (C12), \(\delta_C\) 152.4 (C5), \(\delta_C\) 149.4 (C3), \(\delta_C\) 148.8 (C1), \(\delta_C\) 137.5 (C6), \(\delta_C\) 129.4 (C8+C10), \(\delta_C\) 127.1 (C9), \(\delta_C\) 126.9 (C7+C11), \(\delta_C\) 117.8 (C2), \(\delta_C\) 111.9 (C4), \(\delta_C\) 86.0 (C13), \(\delta_C\) 75.6 (C14), \(\delta_C\) 3.5 (C15). HRMS (TOF ES+) \(m/z\) found [M+H]\(^+\) 237.1026, C\(_{15}\)H\(_{13}\)ON\(_2\)\(^+\) required 237.1028, \(\Delta \text{ppm} = -0.8\) ppm.
"$^1$H NMR

$^{13}$C NMR
Ethyl 2-(but-2-ynamido)isonicotinate (50)

Prepared according to General Method 1 from 2-amino-isonicotinic acid ethyl ester 34 (0.10 g, 0.60 mmol), LDA (1.26 mmol) and ethyl 2-butynoate 24 (0.08 mL, 0.72 mmol). The crude product was purified by column chromatography (SiO₂, 20 g, 3:2 40-60 petroleum ether: EtOAc) to yield a yellow solid (0.04 g, 0.18 mmol, 30%). Rᵣ = 0.44 (1:1 40-60 petroleum ether: EtOAc). Mpt (CH₂Cl₂): phase change >117 °C, melts 124-125 °C. IR νmax/cm⁻¹ (neat): 3161 (w, N-H), 3127 (w, C-H/N-H), 2980 (w, C-H), 2357 (w, C=C), 1722 (str, C=O), 1665 (str, C=O), 1608 (w), 1572 (str, C=C), 1530 (str, C=C), 1461 (w), 1407 (str), 1369 (w), 1303 (w), 1270 (str, C-O), 1232 (str), 1215 (str), 1173 (w), 1121 (w), 1071 (med), 1016 (med).¹H NMR (500 MHz, d⁶-DMSO): δH 11.36 (1H, s, H4), δH 8.53 (1H, app dd, J = 5.1, 0.8 Hz, H1), δH 8.47 (1H, app s, H3), δH 7.56 (1H, dd, J = 5.1, 1.5 Hz, H2), δH 4.36 (2H, q, J = 7.1 Hz, H6), δH 2.05 (3H, s, H5), δH 1.33 (3H, t, J = 7.1 Hz, H7).¹³C NMR (125 MHz, d⁶-DMSO): δC 164.5 (C10), δC 152.5 (C5), δC 151.5 (C6), δC 149.3 (C1), δC 139.2 (C3), δC 118.7 (C2), δC 113.4 (C4), 86.5 (C7), δC 75.4 (C8), δC 61.7 (C11), δC 14.1 (C12), δC 3.5 (C9). HRMS (TOF ES+) m/z found [M+H]⁺ 233.0936, C₁₂H₁₃O₃N₂⁺ required 233.0926, Δ ppm = 4.3 ppm.
$^{1}H$ NMR

$^{13}C$ NMR
**N-(4-Methoxypyridin-2-yl)but-2-ynamide (51)**

Prepared according to General Method 1 from 2-amino-4-methoxypyridine 35 (0.30 g, 2.42 mmol), "BuLi (5.07 mmol) and ethyl 2-butynoate 24 (0.34 mL, 2.90 mmol). The crude product was purified by column chromatography (SiO₂, 20 g, 3:2 then 1:1 40-60 petroleum ether: EtOAc) to yield a beige solid (0.15 g, 0.81 mmol, 34%). R₆ = 0.28 (1:1 40-60 petroleum ether: EtOAc). Mpt (CH₂Cl₂): darkens >140 °C, melts 149-150 °C. IR νₘₐₓ/cm⁻¹ (neat): 3117 (w, N-H/C-H), 2980 (w, C-H), 2230 (w, C≡C), 1655 (str, C=O), 1577 (str, C=C), 1533 (str, C=C), 1472 (w), 1452 (med), 1426 (med), 1311 (med), 1297 (w), 1279 (str), 1250 (str), 1196 (str), 1164 (str), 1133 (w), 1046 (str).¹H NMR (500 MHz, d⁶-DMSO): δ₁H 10.99 (1H, s, H₄), δ₁H 8.12 (1H, d, J = 5.8 Hz, H₁), δ₁H 7.56 (1H, app s, H₃), δ₁H 6.72 (1H, dd, J = 5.8, 2.4 Hz, H₂), δ₁H 3.78 (3H, s, H₆), δ₁H 2.01 (3H, s, H₅).¹³C NMR (125 MHz, d⁶-DMSO): δ₁C 167.1 (C₃), δ₁C 153.4 (C₅), δ₁C 151.8 (C₇), δ₁C 149.6 (C₁), δ₁C 107.2 (C₂), δ₁C 100.4 (C₄), δ₁C 86.2 (C₈), δ₁C 76.0 (C₉), δ₁C 55.8 (C₆), δ₁C 3.8 (C₁₀). HRMS (FTMS ESI+) m/z found [M+H]⁺ 191.0824, C₁₀H₁₁O₂N₂⁺ required 191.0815, Δ ppm = 4.8 ppm.
$^1$H NMR

$^{13}$C NMR
N-(6-Methoxypyridazin-3-yl)but-2-ynamide (52)

Prepared according to General Method 1 from 6-methoxypyridazin-3-amine 36 (150 mg, 1.20 mmol), nBuLi (2.52 mmol) and ethyl 2-butyrate 24 (0.168 mL, 1.44 mmol). Note – solvent should be evaporated at ambient temperature to avoid cyclisation. The crude product was purified by column chromatography (SiO2, elution gradient 0 to 50% EtOAc in heptane) to yield an off-white solid solid (150 mg, 60%). Rf = 0.23 (1:1 EtOAc: heptane). Mpt (CH2Cl2): decomp. >110 °C. IR νmax/cm⁻¹ (neat): 3038 (m), 2942 (w, C-H), 2238 (w, C≡C), 1645 (str, C=O), 1603 (w), 1562 (w), 1504 (str), 1457 (med), 1408 (w), 1392 (str), 1340 (w), 1321 (w), 1305 (str), 1269 (med), 1251 (med), 1227 (med), 1210 (str), 1139 (w), 1112 (w), 1071 (w), 1051 (w), 1006 (str). ¹H NMR (400 MHz, d⁶-DMSO): δH 11.41 (1H, s, H3), δH 8.07 (1H, d, J = 9.5 Hz, H2), δH 7.22 (1H, d, J = 9.5 Hz, H1), δH 3.98 (3H, s, H5), δH 2.03 (3H, s, H4). ¹³C NMR (100 MHz, d⁶-DMSO): δC 167.3, 151.4, 150.1, 135.2, 123.7, 118.6, 113.6, 54.9, 54.3, 17.4, 3.3. HRMS (TOF ES+) m/z found [M+H]+ 192.0776, C₉H₁₀N₃O₂⁺ required 192.0773, Δ ppm = 1.6 ppm.
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N-(Pyrazin-2-yl)but-2-ynamide (53)

Prepared according to General Method 1 from aminopyrazine 37 (0.10 g, 1.05 mmol), n-BuLi (2.21 mmol) and ethyl 2-butynoate 24 (0.15 mL, 1.26 mmol). The crude product was purified by CombiFlash Companion (SiO$_2$, 12 g, 0-50% EtOAc in heptane) to yield a white solid (0.13 g, 0.79 mmol, 75%). R$_f$ = 0.27 (1:1 heptane: EtOAc). Mpt (H$_2$O/MeCN): decom. >150 °C. IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3210 (med, br, N-H/C-H), 2238 (med, C≡C), 1667 (str, C=O), 1594 (w), 1551 (w), 1528 (w), 1488 (med, C=N), 1417 (str), 1344 (med), 1296 (w), 1257 (med), 1199 (med), 1143 (w), 1120 (med), 1077 (w), 1049 (w), 1013 (w). $^1$H NMR (400 MHz, d$_6$-DMSO): $\delta$H 11.35 (1H, s, H4), $\delta$H 9.19 (1H, s, H3), $\delta$H 8.41 (1H, s, H1 or H2), $\delta$H 8.38 (1H, s, H1 or H2), $\delta$H 2.06 (3H, s, H5). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta$C 151.2 (C4 or C5), $\delta$C 147.8 (C4 or C5), $\delta$C 142.6 (C1 or C2), $\delta$C 140.1 (C1 or C2), $\delta$C 137.0 (C3), $\delta$C 87.0 (C6), $\delta$C 75.0 (C7), $\delta$C 3.3 (C8). HRMS (TOF ES$^+$) m/z found [M+H]$^+$ 162.0672, C$_8$H$_8$N$_3$O$^+$ required 162.0667, $\Delta$ ppm = 3.1 ppm.
Prepared according to General Method 1 from 2-amino-6-chloropyrazine 38 (0.19 g, 1.43 mmol), LDA (3.00 mmol) and ethyl 2-butyrate 24 (0.20 mL, 1.72 mmol). The crude product was purified by Combiflash Companion (SiO<sub>2</sub>, 12 g, 0-50% EtOAc in heptane) to yield orange flakes (0.12 g, 0.59 mmol, 41%). R<sub>f</sub> = 0.71 (1:1 heptane: EtOAc). Mpt (H<sub>2</sub>O/MeCN): phase change >150 °C, then melted 185-187 °C. IR ν<sub>max</sub>/cm<sup>-1</sup> (neat): 3207 (med, N-H), 2968 (med, C-H), 2236 (med, C≡C), 1668 (str, C=O), 1582 (w), 1556 (w), 1527 (w), 1486 (w), 1416 (str), 1398 (str), 1344 (med), 1297 (w), 1258 (med), 1198 (med), 1145 (w), 1120 (med), 1077 (w), 1047 (w), 1003 (w). <sup>1</sup>H NMR (400 MHz, d<sub>6</sub>-DMSO): δ<sub>H</sub> 11.63 (1H, s, H3), δ<sub>H</sub> 9.17 (1H, s, H2), δ<sub>H</sub> 8.49 (1H, s, H1), δ<sub>H</sub> 2.06 (3H, s, H4). <sup>13</sup>C NMR (100 MHz, d<sub>6</sub>-DMSO): δ<sub>C</sub> 151.1 (C4 or C5), δ<sub>C</sub> 147.5 (C4 or C5), δ<sub>C</sub> 145.4 (C1), δ<sub>C</sub> 138.6 (C3), δ<sub>C</sub> 134.7 (C2), δ<sub>C</sub> 87.7 (C6), δ<sub>C</sub> 74.8 (C7), δ<sub>C</sub> 3.3 (C8). HRMS (TOF ES+) m/z found [M+H]<sup>+</sup> 196.0279, C<sub>8</sub>H<sub>7</sub>N<sub>3</sub>O<sup>15</sup>Cl<sup>+</sup> required 196.0278, Δ ppm = 0.5 ppm.
$^1$H NMR

$^{13}$C NMR
**N-(6-Methoxypyrimidin-4-yl)but-2-ynamide (55)**

Prepared according to General Method 1 from 6-methoxypyrimidin-4-amine (0.30 g, 2.40 mmol), nBuLi (5.03 mmol) and ethyl 2-butynoate (0.34 mL, 2.88 mmol). The crude product was purified by column chromatography (SiO$_2$, 30 g, 7:3 40-60 petroleum ether: EtOAc) to yield a pale brown solid (0.24 g, 1.36 mmol, 53%). R$_f$ = 0.47 (1:1 40-60 petroleum ether: EtOAc). Mpt (CH$_2$Cl$_2$): darkens $>170$ °C, decomp. $>220$ °C. IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3362 (w, br, N-H), 3203 (w, N-H), 3004 (w, C-H), 2228 (w, C≡C), 1677 (str, C=O), 1603 (med, C=C), 1570 (str, C=C), 1511 (str), 1482 (str, C=C/C=N), 1397 (str, C-O), 1329 (w), 1301 (w), 1262 (str), 1226 (med), 1193 (str), 1170 (med), 1073 (w), 1036 (med). $^1$H NMR (400 MHz, d$_6$-DMSO): $\delta_H$ 11.41 (1H, s, H3), $\delta_H$ 8.54 (1H, s, H2), $\delta_H$ 7.32 (1H, s, H1), $\delta_H$ 3.90 (3H, s, H5), $\delta_H$ 2.05 (3H, s, H4). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta_C$ 170.2 (C3), $\delta_C$ 157.9 (C1), $\delta_C$ 157.5 (C4), $\delta_C$ 151.8 (C5), $\delta_C$ 94.6 (C2), $\delta_C$ 87.1 (C6), $\delta_C$ 74.9 (C7), $\delta_C$ 53.8 (C9), $\delta_C$ 3.5 (C8). HRMS (FTMS ESI+) m/z found [M+H]$^+$ 192.0766, $\text{C}_9\text{H}_{16}\text{O}_2\text{N}_3^+$ required 192.0768, $\Delta$ ppm = -0.9 ppm.

$^1$H NMR
$^{13}$C NMR
Prepared according to General Method 1 from 2-amino-5-bromopyrimidine 40 (0.10 g, 0.58 mmol), \(^{n}\text{BuLi}\) (1.21 mmol) and ethyl 2-butyrate 24 (0.08 mL, 0.69 mmol). The crude product was purified by column chromatography (SiO\(_2\), 20 g, 1:1 40-60 petroleum ether: EtOAc) to yield a beige solid wax (0.09 g, 94% purity with CH\(_2\)Cl\(_2\), 0.33 mmol, 58%). Further purification by preparative HPLC yielded spectroscopically pure material. R\(_f\) = 0.41 (1:1 40-60 petroleum ether: EtOAc). Mpt (CH\(_2\)Cl\(_2\)): darkens >130-147 °C, melts 152-155 °C. IR \(\nu_{\text{max}}/\text{cm}^{-1}\) (neat): 3220 (w, N-H), 3151 (w, C-H/N-H), 3071 (w, C-H), 2915 (w, C-H), 2227 (w, C=C), 1684 (str, C=O), 1583 (med, C=C), 1560 (med, C=C), 1491 (str, C=C/C=N), 1455 (w), 1428 (str), 1373 (str), 1329 (med), 1266 (med), 1234 (str), 1167 (med), 1124 (med), 1067 (med), 1025 (w), 1007 (w). \(^1\text{H NMR}\) (500 MHz, d\(^6\)-DMSO): \(\delta_H\) 11.35 (1H, s, H3), \(\delta_H\) 8.81 (2H, s, H1+H2), \(\delta_H\) 2.02 (3H, s, H4). \(^{13}\text{C NMR}\) (125 MHz, d\(^6\)-DMSO): \(\delta_C\) 158.8 (C2+C4), \(\delta_C\) 155.8 (C1), \(\delta_C\) 150.6 (C5), \(\delta_C\) 113.9 (C3), \(\delta_C\) 87.2 (C6), \(\delta_C\) 75.5 (C7), \(\delta_C\) 3.5 (C8). HRMS (TOF ES\(^+\)) \(\text{m/z}\) found [M+H]\(^+\) 239.9768, C\(_8\)H\(_7\)ON\(_3\)\(^79\)Br\(^-\) required 239.9772, \(\Delta\) ppm = -1.7 ppm.
This report was created by ACD/NMR Processor Academic Edition. For more information go to www.acdlabs.com/nmrproc/
$^{13}$C NMR
**N-(Quinolin-2-yl)but-2-ynamide (57)**

Prepared according to General Method 1 from 2-aminoquinoline 41 (0.21 g, 1.43 mmol), LDA (3.00 mmol) and ethyl 2-butyanoate 24 (0.20 mL, 1.72 mmol). The crude product was purified by Combiflash Companion (SiO₂, 12 g, 0-25% EtOAc in heptane) to yield an ochre solid (0.22 g, 1.06 mmol, 74%). RF = 0.50 (1:1 EtOAc: heptane). Mpt (CH₂Cl₂): phase change >100 °C then melted 157-159 °C. IR νmax/cm⁻¹ (neat): 3127 (w) 2941 (w, br, C-H), 2238 (w, C≡C), 1671 (str, C=O), 1618 (w), 1594 (str, C=C), 1577 (str, C=C), 1548 (w), 1526 (med), 1499 (str), 1425 (str), 1381 (w), 1320 (str), 1291 (str), 1264 (str), 1249 (str), 1237 (str), 1157 (w), 1146 (w), 1121 (str), 1087 (w), 1017 (w). ¹H NMR (400 MHz, d₆-DMSO): δH 11.31 (1H, s, H7), δH 8.35 (1H, d, J = 9.0 Hz, H2), δH 8.14 (1H, d, J = 9.0 Hz, H1), δH 7.92 (1H, dd, J = 8.1, 1.1 Hz, H3 or H6), δH 7.83-7.81 (1H, m, H3 or H6), δH 7.72 (1H, ddd, J = 8.4, 6.9, 1.5 Hz, H5), δH 7.51 (1H, ddd, J = 8.1, 6.9, 1.2, H4), δH 2.05 (3H, s, H8). ¹³C NMR (100 MHz, d₆-DMSO): δC 151.9 (C1 or C10), δC 151.1 (C1 or C10), δC 146.4 (C3), δC 138.4 (C9), δC 130.2 (C7), δC 127.9 (C5 or C8), δC 127.3 (C5 or C8), δC 125.9 (C4), δC 125.4 (C6), δC 115.1 (C2), δC 86.5 (C11), δC 75.7 (C12), δC 3.5 (C13). HRMS (FTMS ESI⁺) m/z found [M+H]⁺ 211.0859, C₁₃H₁₁N₂O⁺ required 211.0866, Δ ppm = -3.1 ppm.
**N-(4,6-bis(ethylthio)pyrimidin-2-yl)but-2-ynamide (58)**

Prepared according to General Method 1 from 2-amino-4,6-bis(ethylthio)pyrimidine 42 (0.31 g, 1.43 mmol), LDA (3.00 mmol) and ethyl 2-butynoate 24 (0.20 mL, 1.72 mmol). The crude product was purified by Combiflash Companion (SiO$_2$, 24 g, 0-50% EtOAc in heptane) to yield a red gum (0.12 g, 0.44 mmol, 31%). $R_f = 0.28$ (3:1 heptane: EtOAc). IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3284 (w), 3181 (w), 3100 (w), 3036 (w), 2966 (w, C-H), 2925 (w, C-H), 2864 (w, C-H), 2236 (med, C≡C), 1650 (str, C=O), 1554 (str, C=C), 1515 (str, C=C), 1494 (str, C=C), 1454 (w), 1427 (med), 1398 (w), 1377 (w), 1341 (str), 1330 (str), 1261 (str), 1229 (str), 1109 (str), 1082 (str), 1002 (w). $^1$H NMR (400 MHz, d$_6$-DMSO): $\delta_H$ 10.97 (1H, s, H2), $\delta_H$ 6.97 (1H, s, H1), $\delta_H$ 3.15 (4H, q, $J = 7.3$ Hz, H4+H6), $\delta_H$ 2.04 (3H, s, H3), $\delta_H$ 1.29 (6H, t, $J = 7.3$ Hz, H5+H7). $^{13}$C NMR (100 MHz, d$_6$-DMSO): $\delta_C$ 168.9 (C2+C4), $\delta_C$ 155.4 (C1), $\delta_C$ 150.9 (C5), $\delta_C$ 109.7 (C3), $\delta_C$ 87.9 (C6), $\delta_C$ 75.6 (C7), $\delta_C$ 23.1 (C9+C11), $\delta_C$ 14.4 (C10+C12), $\delta_C$ 3.5 (C8). HRMS (TOF ES$^+$) m/z found [M+H]$^+$ 282.0740, C$_{12}$H$_{16}$ON$_3$S$_2$$^+$ required 282.0735, $\Delta$ ppm = 1.8 ppm.
$^1$H NMR

$^{13}$C NMR
9-(Benzyloxy)-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (62)

Prepared according to General Method 1 from 2-amino-3-benzyloxypyridine 59 (700 mg, 3.50 mmol), nBuLi (7.34 mmol) and ethyl 2-butynoate 24 (0.489 mL, 4.20 mmol). The crude product was purified by column chromatography (SiO₂, elution gradient 0 to 100% EtOAc in heptane, followed by a second column, elution gradient 0 to 10% MeOH in CH₂Cl₂) to yield a sticky cream foam (320 mg, 34%). Rₜ = 0.58 (8:2 CH₂Cl₂:MeOH). IR ν max/cm⁻¹ (neat): 3479 (w), 3347 (w), 3262 (w), 3085 (w), 3034 (w, C-H), 2916 (w, C-H), 2871 (w, C-H), 1640 (str, C=O), 1588 (w), 1560 (str), 1470 (str), 1451 (str), 1435 (str), 1392 (med), 1374 (str), 1290 (w), 1268 (str), 1218 (w), 1198 (med), 1163 (str), 1098 (w), 1041 (med), 1015 (str). ¹H NMR (400 MHz, d₆-DMSO): δ ᵃ 7.94-7.79 (1H, m, H2), δ ᵃ 7.56-7.45 (2H, m, H7+H11), δ ᵃ 7.45-7.39 (2H, m), δ ᵃ 7.39-7.33 (1H, m), δ ᵃ 7.23-7.09 (1H, m), δ ᵃ 6.87 (1H, t, J = 7.4 Hz), δ ᵃ 6.47-6.34 (1H, m), δ ᵃ 5.21 (2H, s, H6), δ ᵃ 2.51 (3H, s, H5). ¹³C NMR (100 MHz, d₆-DMSO): δ c 168.8, 148.1, 146.9, 146.6, 136.1, 128.4, 128.1, 127.9, 121.9, 115.2, 112.4, 111.4, 70.3, 18.9. HRMS (TOF ES⁺) m/z found [M+H]⁺ 267.1135, C₁₆H₁₅N₂O₂⁺ required 267.1134, Δ ppm = 0.4 ppm.
4-Methyl-2H-pyrimido[1,2-a]pyrimidin-2-one (63)

Prepared according to General Method 1 from 2-aminopyrimidine 60 (0.14 g, 1.43 mmol), LDA (3.00 mmol) and ethyl 2-butynoate 24 (0.20 mL, 1.72 mmol). The crude product was purified by Combiflash Companion (SiO₂, 12 g, EtOAc) to yield an orange solid (0.04 g, 0.25 mmol, 17%). Rₜ = 0.12 (EtOAc). Mpt (CH₂Cl₂): 159-162 °C. IR νmax/cm⁻¹ (neat): 3105 (w, C-H), 3074 (w, C-H), 3012 (w, C-H), 2917 (w, C-H), 1683 (str, C=O), 1627 (med, C=O), 1565 (med, C=C), 1529 (str, C=C), 1461 (str), 1402 (str), 1352 (str), 1260 (w), 1235 (med), 1199 (w), 1188 (w), 1168 (med), 1125 (med), 1074 (w), 1042 (w), 1025 (w). ¹H NMR (400 MHz, d⁶-DMSO): δH 9.21 (1H, dd, J = 7.0, 2.3 Hz, H2 or H4), δH 9.12 (1H, dd, J = 3.9, 2.3 Hz, H2 or H4), δH 7.37 (1H, dd, J = 7.0, 3.9 Hz, H3), δH 6.37 (1H, s, H1), δH 2.41 (3H, s, H5). ¹³C NMR (100 MHz, d⁶-DMSO): δC 167.3 (C1 or C7), δC 163.3 (C4), δC 157.4 (C1 or C7), δC 151.2 (C3), δC 136.6 (C6), δC 112.4 (C5), δC 102.9 (C2), δC 24.6 (C8). HRMS (TOF ES+) m/z found [M+H]⁺ 162.0673, C₈H₈N₃O⁺ required 162.0667, Δ ppm = 3.7 ppm.
$^1$H NMR

$^{13}$C NMR
9-Ethoxy-4-methyl-2H-pyrazino[1,2-a]pyrimidin-2-one (64)

Prepared according to General Method 1 from 2-amino-3-ethoxypyrazine 61 (0.14 g, 1.43 mmol), LDA (3.00 mmol) and ethyl 2-butynoate 24 (0.20 mL, 1.72 mmol). The crude product was purified by Combiflash Companion (SiO₂, 12 g, 0-50% EtOAc in heptane) to yield a pale yellow solid (0.11 g, 0.54 mmol, 38%). R_f = 0.17 (9:1 CH₂Cl₂: MeOH). Mpt (H₂O/MeCN): 213-214 °C. IR νmax/cm⁻¹ (neat): 3126 (w, C-H), 2997 (w, C-H), 1646 (str, C=O), 1592 (str, C=C), 1541 (str, C=C), 1476 (str), 1432 (w), 1406 (w), 1393 (med), 1369 (str), 1326 (str), 1303 (w), 1272 (w), 1245 (w), 1216 (w), 1201 (w), 1184 (str), 1139 (w), 1041 (med), 1021 (med). ¹H NMR (400 MHz, d⁶-DMSO): δ_H 7.73 (1H, d, J = 5.0 Hz, H2), δ_H 7.38 (1H, d, J = 5.0 Hz, H3), δ_H 6.47 (1H, d, J = 0.9 Hz, H1), δ_H 4.44 (2H, q, J = 7.1 Hz, H5), δ_H 1.41 (3H, t, J = 7.1 Hz, H6). H4 obscured by DMSO signal. ¹³C NMR (100 MHz, d⁶-DMSO): δ_C 167.7 (C6), δ_C 155.8 (C1), δ_C 147.3 (C3), δ_C 140.3 (C7), δ_C 124.2 (C5), δ_C 116.5 (C2), δ_C 115.2 (C4), δ_C 63.5 (C9), δ_C 18.2 (C8), δ_C 14.2 (C10). HRMS (FTMS ESI⁺) m/z found [M+H]⁺ 206.0938, C₁₀H₁₂N₂O₂⁺ required 206.0930, Δ ppm = 3.9 ppm and [M+Na]⁺ 228.0758, C₁₀H₁₁N₃O₂Na⁺ required 228.0749, Δ ppm = 3.9 ppm.
$^1$H NMR

$^{13}$C NMR
4-(Trifluoromethyl)-2H-pyrido[1,2-a]pyrimidin-2-one (66)

Prepared according to General Method 1 from 2-aminopyridine 23 (0.10 g, 1.06 mmol), nBuLi (2.23 mmol) and ethyl 4,4,4-trifluoromethylpropynoate 65 (0.18 mL, 1.28 mmol). The crude product was purified by column chromatography (SiO$_2$, 20 g, 3:1 40-60 petroleum ether: EtOAc) to yield a yellow wax (0.10 g, 96% purity with 2-aminopyridine, 0.42 mmol, 40%). $R_f = 0.32$ (3:1 40-60 petroleum ether: EtOAc). IR $\nu_{max}$/cm$^{-1}$ (neat): 3066 (w, C-H), 2924 (w, C-H), 1700 (str, C=O), 1638 (med, C=C), 1576 (w), 1534 (w), 1483 (str), 1456 (str), 1437 (med), 1365 (w), 1284 (str), 1252 (w), 1173 (str), 1098 (str), 1020 (w). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta_H$ 9.06-9.04 (1H, m, H2), $\delta_H$ 8.14 (1H, ddd, $J = 8.6, 6.8, 1.6$ Hz, H4), $\delta_H$ 7.89 (1H, d, $J = 8.8$ Hz, H5), $\delta_H$ 7.53 (1H, app dt, $J = 1.3, 7.0$ Hz, H3), $\delta_H$ 6.84 (1H, s, H1). $^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta_C$ 157.4 (C1), $\delta_C$ 151.7 (C8), $\delta_C$ 151.0 (q, $^2$J$_{C-F} = 34$ Hz, C3), $\delta_C$ 139.4 (C6), $\delta_C$ 127.7 (C4), $\delta_C$ 126.4 (C7), $\delta_C$ 120.9 (q, $^1$J$_{C-F} = 276$ Hz, C9), $\delta_C$ 118.1 (C5), $\delta_C$ 100.1 (C2). $^{19}$F NMR (162 MHz, d$_6$-DMSO): $\delta_F$ -68.66. HRMS (FTMS ESI$^+$) $m/z$ found [M+H]$^+$ 215.0417, C$_9$H$_6$ON$_2$F$_3^+$ required 215.0427, $\Delta$ ppm = -4.5 ppm. Data consistent with literature values.$^2$
$^1$H NMR

$^{13}$C NMR
$^{19}$F NMR
4-Methyl-2H-pyrido[1,2-a]pyrimidin-2-one (67)

Prepared according to General Method 2 from 25. The crude product was purified by column chromatography (SiO₂, 20 g, 93:7 CH₂Cl₂: MeOH) to yield a yellow solid (85%). R_f = 0.26 (9:1 CH₂Cl₂: MeOH). Mpt (CH₂Cl₂): >195 °C (decomp) (Lit 120-120.5 °C). IR ν_max/cm⁻¹ (neat): 1661 (str, C=O), 1645 (med, C=C/C=O), 1595 (str, C=C), 1547 (med, C=C), 1466 (str, C=C). ^1H NMR (500 MHz, CDCl₃): δ_H 7.82 (1H, d, J = 7.2 Hz, H6), δ_H 7.54-7.50 (1H, m, H4), δ_H 7.39-7.35 (1H, m, H3), δ_H 6.83 (1H, app td, J = 7.0, 2.5 Hz, H5), δ_H 6.49 (1H, d, J = 0.6 Hz, H1), δ_H 2.54 (3H, d, J = 0.7 Hz, H2). ^13C NMR (125 MHz, CDCl₃): δ_C 168.3 (C1), δ_C 152.5 (C9), δ_C 144.4 (C3), δ_C 135.3 (C7), δ_C 127.7 (C5), δ_C 125.8 (C8), δ_C 116.9 (C2), δ_C 113.1 (C6), δ_C 19.1 (C4). HRMS (TOF ES+) m/z found [M+H]^+ 161.0708, C₉H₈N₂O⁺ required 161.0715, Δ ppm = -0.4 ppm. Data consistent with literature values.³
$^1$H NMR

$^{13}$C NMR
4-Methyl-8-(trifluoromethyl)-2H-pyrido[1,2-a]pyrimidin-2-one (68)

Prepared according to General Method 2 from 43. The crude product was purified by column chromatography (SiO$_2$, 10 g, 100:0, 95:5 then 9:1 CH$_2$Cl$_2$: MeOH) to yield an ochre solid (quantitative). R$_f$ = 0.23 (9:1 CH$_2$Cl$_2$: MeOH). Mpt (CH$_2$Cl$_2$): darkens >200 °C, melts 274-275 °C. IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3063 (w, C-H), 1653 (str, C=O), 1614 (str, C=C), 1553 (w, C=C), 1474 (str, C=C/C=O), 1445 (med), 1392 (med), 1359 (str), 1301 (str, C-O), 1287 (str), 1243 (med), 1175 (med), 1159 (str), 1129 (str), 1077 (str), 1050 (w), 1026 (str). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta$H 8.40 (1H, d, $J = 7.5$ Hz, H2), $\delta$H 7.58-7.55 (1H, m, H4), $\delta$H 7.17 (1H, dd, $J = 7.5$, 2.2 Hz, H3), $\delta$H 6.48 (1H, d, $J = 0.6$ Hz, H1), $\delta$H 2.55 (3H, d, $J = 0.5$ Hz, H5). $^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta$C 167.2 (C1), $\delta$C 151.2 (C8), $\delta$C 147.2 (C3), $\delta$C 135.2 (q, $^2$J$_{C-F} = 34$ Hz, C6), $\delta$C 133.2 (C4), $\delta$C 122.1 (q, $^1$J$_{C-F} = 273.6$ Hz, C10), $\delta$C 121.8 (d, $^3$J$_{C-F} = 4.6$ Hz, C7), $\delta$C 116.0 (C2), $\delta$C 106.8 (d, $^3$J$_{C-F} = 1.5$ Hz, C5), $\delta$C 18.5 (C9). $^{19}$F NMR (376 MHz, d$_6$-DMSO): $\delta$F -65.72 (CF$_3$). HRMS (FTMS ESI+) $m/z$ found [M+H]$^+$ 229.0576, C$_{10}$H$_8$ON$_2$F$_3$+ required 229.0583, $\Delta$ ppm = -3.3 ppm.
$^1$H NMR

$^{13}$C NMR
$^{19}$F NMR
8-Ethyl-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (69)

Prepared according to General Method 2 from 44. The crude product was purified by column chromatography (SiO$_2$, 30 g, 19:1 CH$_2$Cl$_2$: MeOH) to yield a yellow wax (quantitative). R$_f$ = 0.57 (9:1 CH$_2$Cl$_2$: MeOH). IR $\nu_{max}$/cm$^{-1}$ (neat): 3494 (w, br), 3082 (w, C-H), 1642 (str, C=O), 1591 (str, C=C), 1546 (w), 1479 (w), 1456 (str, C=C/C=N), 1440 (str), 1389 (str), 1365 (med), 1315 (w), 1283 (str), 1250 (med), 1200 (med), 1165 (med), 1138 (w), 1062 (w), 1051 (w), 1034 (w), 1006 (w). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta_H$ 8.14 (1H, d, J = 7.3 Hz, H2), $\delta_H$ 6.97-6.96 (1H, m, H4), $\delta_H$ 6.89 (1H, dd, J = 7.3, 2.0 Hz, H3), $\delta_H$ 6.31 (1H, d, J = 0.8 Hz, H1), $\delta_H$ 2.65 (2H, dq, J = 0.6, 7.5 Hz, H6), $\delta_H$ 2.50 (3H, d, J = 0.8 Hz, H5), $\delta_H$ 1.20 (3H, t, J = 7.5 Hz, H7).

$^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta_C$ 167.5 (C1), $\delta_C$ 153.3 (C6), $\delta_C$ 152.1 (C8), $\delta_C$ 145.8 (C3), $\delta_C$ 129.9 (C4), $\delta_C$ 119.9 (C7), $\delta_C$ 115.0 (C2), $\delta_C$ 114.1 (C5), $\delta_C$ 27.4 (C10), $\delta_C$ 18.4 (C9), $\delta_C$ 13.4 (C11). HRMS (TOF ES+) m/z found [M+H]$^+$ 189.1019, C$_{11}$H$_{13}$ON$_2$$^+$ required 189.1028, $\Delta$ ppm = -4.8 ppm.
$^1$H NMR

$^{13}$C NMR
8-Bromo-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (70)

Prepared according to General Method 2 from 45. The crude product was purified by column chromatography (SiO$_2$, 30 g, 1:0, 97:3, then 19:1 CH$_2$Cl$_2$: MeOH) to yield a brown wax (0.09g, 89% purity with 45 and methanol, 1.33 mmol, 19%). Further purification by preparative HPLC yielded spectroscopically pure material. $R_f$ = 0.42 (9:1 CH$_2$Cl$_2$: MeOH). IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3360 (w, br), 3045 (w, C-H), 3001 (w, C-H), 1724 (med), 1652 (str, C=O), 1574 (str, C=C), 1534 (w, C=C), 1456 (str, C=C/C=N), 1372 (str), 1354 (str), 1311 (w), 1285 (str), 1257 (w), 1193 (med), 1164 (w), 1104 (w), 1078 (w), 1057 (w), 1024 (med). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta_H$ 8.12 (1H, d, $J = 7.6$ Hz, H2), $\delta_H$ 7.45 (1H, d, $J = 2.2$ Hz, H4), $\delta_H$ 7.11 (1H, dd, $J = 7.6$, 2.3 Hz, H3), $\delta_H$ 6.36 (1H, s, H1), H5 obscured by DMSO signal. $^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta_C$ 167.2 (C1), $\delta_C$ 151.8 (C8), $\delta_C$ 146.7 (C3), $\delta_C$ 131.6 (C4), $\delta_C$ 130.9 (C6), $\delta_C$ 124.9 (C7), $\delta_C$ 115.8 (C5), $\delta_C$ 115.4 (C2), $\delta_C$ 18.4 (C9). HRMS (FTMS ESI+) m/z found [M+H]$^+ 238.9805$, C$_9$H$_8$ON$_2$ Br$^+$ required 238.9815, $\Delta$ ppm = -4.1 ppm.
$^{1}$H NMR

$^{13}$C NMR
4-Methyl-2-oxo-2H-pyrido[1,2-a]pyrimidine-8-carbonitrile (71)

Prepared according to General Method 2 from 46. The crude product was purified by column chromatography (SiO₂, 30 g, 19:1 CH₂Cl₂: MeOH) to yield a yellow wax (61%). Rₖ = 0.46 (9:1 CH₂Cl₂: MeOH). Mpt (CH₂Cl₂): phase change >240 °C, melts 299-301 °C. IR ν_{max}/cm⁻¹ (neat): 3068 (w, C-H), 3040 (w, C-H), 2926 (w, C-H), 2237 (w, C≡C), 1685 (w), 1655 (med), 1642 (med, C=O), 1598 (str, C=C), 1532 (w), 1466 (str, C=N/C=C), 1399 (med), 1366 (med), 1291 (med), 1251 (w), 1206 (med), 1170 (w), 1064 (str), 1031 (med). ¹H NMR (500 MHz, d⁶-DMSO): δ_H 8.35 (1H, d, J = 7.1 Hz, H2), δ_H 7.85 (1H, app dd, J = 2.0, 0.7 Hz, H4), δ_H 7.20 (1H, dd, J = 7.4, 2.0 Hz, H3), δ_H 6.46 (1H, d, J = 0.8 Hz, H1), δ_H 2.52 (3H, d, J = 0.7 Hz, H5). ¹³C NMR (125 MHz, d⁶-DMSO): δ_C 167.1 (C1), δ_C 150.8 (C8), δ_C 147.3 (C3), δ_C 132.4 (C4), δ_C 130.8 (C7), δ_C 118.9 (C6), δ_C 116.1 (C2), δ_C 116.0 (C10), δ_C 111.1 (C5), δ_C 18.4 (C9). HRMS (FTMS ESI+) m/z found [M+H]^+ 186.0656, C_{10}H_{8}ON_3^+ required 186.0662, Δ ppm = -0.2 ppm.
$^1$H NMR

$^{13}$C NMR
8-Chloro-4-methyl-2\textit{H}-pyrido[1,2-a]pyrimidin-2-one (72)

Prepared according to General Method 2 from 47. The crude product was purified by Combiflash Companion (SiO\textsubscript{2}, 12 g, 0-10\% MeOH in CH\textsubscript{2}Cl\textsubscript{2}) to yield a pink solid (5.44 g, 87\% purity, 24.33 mmol, 80\%). Further purification by preparative HPLC yielded spectroscopically pure material. R\textsubscript{f} = 0.23 (9:1 CH\textsubscript{2}Cl\textsubscript{2}: MeOH). Mpt (CH\textsubscript{2}Cl\textsubscript{2}/MeOH): phase change >165 °C, melts >300 °C. IR \textit{v}\textsubscript{max}/cm\textsuperscript{-1} (neat): 3072 (w, C-H), 1640 (str, C=O), 1601 (str, C=C), 1540 (w), 1520 (w), 1464 (str, C=C/C=N), 1391 (str), 1372 (med), 1286 (str), 1251 (w), 1193 (med), 1166 (w), 1089 (w), 1065 (w), 1026 (w). \textsuperscript{1}H NMR (400 MHz, d\textsuperscript{6}-DMSO): \textit{\delta}\textsubscript{H} 8.23 (1H, d, \textit{J} = 7.7 Hz, H2), \textit{\delta}\textsubscript{H} 7.30 (1H, d, \textit{J} = 2.3 Hz, H4), \textit{\delta}\textsubscript{H} 7.03 (1H, dd, \textit{J} = 7.6, 2.4 Hz, H3), \textit{\delta}\textsubscript{H} 6.36 (1H, s, H1), H5 obscured by DMSO signal. \textsuperscript{13}C NMR (100 MHz, d\textsuperscript{6}-DMSO): \textit{\delta}\textsubscript{C} 167.0 (C1), \textit{\delta}\textsubscript{C} 151.7 (C8), \textit{\delta}\textsubscript{C} 146.4 (C3), \textit{\delta}\textsubscript{C} 141.6 (C6), \textit{\delta}\textsubscript{C} 131.9 (C4), \textit{\delta}\textsubscript{C} 121.3 (C7), \textit{\delta}\textsubscript{C} 115.1 (C2), \textit{\delta}\textsubscript{C} 113.2 (C5), \textit{\delta}\textsubscript{C} 18.3 (C9). HRMS (TOF ES+) \textit{m/z} found [M+H]\textsuperscript{+} 195.0333, C\textsubscript{9}H\textsubscript{8}N\textsubscript{2}O\textsuperscript{35}Cl\textsuperscript{+} required 195.0325, \Delta ppm = 4.1 ppm.
$^{13}$C NMR
Prepared according to General Method 2 from 18. The crude product was purified by Combiflash Companion (SiO$_2$, 24 g, 0-10% MeOH/CH$_2$Cl$_2$) to yield a white solid (53%). R$_f$ = 0.26 (9:1 CH$_2$Cl$_2$: MeOH). Mpt (CH$_2$Cl$_2$): phase change >180 °C, melts 230-232 °C. IR $\nu_{\text{max}}$/cm$^{-1}$ (neat): 3233 (w, br, C-H), 3045 (w, C-H), 2955 (w, C-H), 1646 (str, C=O), 1592 (str, C=C), 1543 (w), 1466 (str, C=N/C=C), 1395 (str, C=C/C=N), 1372 (str), 1292 (med), 1253 (med), 1206 (med), 1175 (w), 1067 (str), 1043 (w). $^1$H NMR (500 MHz, d$_6$-DMSO): $\delta$$_H$ 8.10 (1H, d, $J = 7.3$ Hz, H2), $\delta$$_H$ 6.97 (1H, s, H4), $\delta$$_H$ 6.82 (1H, dd, $J = 7.3, 1.9$ Hz, H3), $\delta$$_H$ 6.28 (1H, s, H1), $\delta$$_H$ 2.33 (3H, s, H6). H5 obscured by DMSO signal. $^{13}$C NMR (125 MHz, d$_6$-DMSO): $\delta$$_C$ 167.5 (C1), $\delta$$_C$ 152.0 (C8), $\delta$$_C$ 148.0 (C6), $\delta$$_C$ 146.1 (C3), $\delta$$_C$ 129.6 (C4), $\delta$$_C$ 121.3 (C7), $\delta$$_C$ 115.2 (C2 or C5), $\delta$$_C$ 115.0 (C2 or C5), $\delta$$_C$ 20.7 (C10), $\delta$$_C$ 18.4 (C9). HRMS (FTMS ESI+): m/z found [M+H]$^+$ 175.0861, C$_{10}$H$_{11}$O$_2$N$_2$+ required 175.0866, $\Delta$ ppm = -2.6 ppm.
$^1$H NMR

$^{13}$C NMR
4-Methyl-8-phenyl-2H-pyrido[1,2-a]pyrimidin-2-one (74)

Prepared according to General Method 2 from 49. The crude product was purified by column chromatography (SiO₂, 30 g, 19:1 CH₂Cl₂: MeOH) to yield a beige solid (94%). Rᵣ = 0.49 (9:1 CH₂Cl₂: MeOH). Mpt (CH₂Cl₂): 189-192 °C. IR νmax/cm⁻¹ (neat): 3062 (w, br, C-H), 2923 (w, C-H), 2853 (w, C-H), 1708 (w), 1639 (str, C=O), 1576 (med, C=C), 1505 (w), 1449 (w), 1435 (w), 1393 (med), 1370 (med), 1256 (med), 1238 (med), 1191 (med), 1175 (med), 1073 (w), 1032 (w), 1017 (w). ¹H NMR (500 MHz, d⁶-DMSO): δH 8.50 (1H, d, J = 7.5 Hz, H2), δH 7.95-7.88 (2H, m, H6+H10), δH 7.60-7.52 (3H, m, H7+H8+H9), δH 7.49 (1H, d, J = 2.0 Hz, H4), δH 7.37 (1H, dd, J = 7.5, 2.2 Hz, H3), δH 6.37 (1H, d, J = 0.8 Hz, H1), δH 2.56 (3H, d, J = 0.5 Hz, H5). ¹³C NMR (125 MHz, d⁶-DMSO): δC 167.4 (C1), δC 152.3 (C8), δC 146.6 (C6), δC 146.2 (C3), δC 135.2 (C10), δC 130.7 (C4), δC 130.2 (C13), δC 129.3 (C12+C14), δC 127.0 (C11+C15), δC 118.9 (C7), δC 115.2 (C2), δC 111.2 (C5), δC 18.3 (C9). HRMS (TOF ES+) m/z found [M+H]⁺ 237.1019, C₁₅H₁₃ON₂⁺ required 237.1028, Δ ppm = -3.8 ppm.
$^1$H NMR

$^{13}$C NMR
Ethyl 4-methyl-2-oxo-2H-pyrido[1,2-a]pyrimidine-8-carboxylate (75)

Prepared according to General Method 2 from 50. The crude product was purified by column chromatography (SiO₂, 30 g, 19:1 CH₂Cl₂: MeOH) to yield a pale yellow solid (0.30 g, 88% purity, 1.15 mmol, 87%). Further purification by preparative HPLC yielded spectroscopically pure material. Rf = 0.43 (9:1 CH₂Cl₂: MeOH). Mpt (CH₂Cl₂): darkens >170 °C, decomp, >210 °C. IR νmax/cm⁻¹ (neat): 3330 (w, br), 3098 (w, C-H), 2911 (w, C-H), 2927 (w, C-H), 2870 (w, C-H), 1724 (med, C=O), 1660 (str, C=O), 1640 (str, C=O), 1619 (str, C=C), 1546 (w), 1471 (str, C=C/C=N), 1438 (med, C=C/C=N), 1392 (med), 1365 (med), 1344 (w), 1271 (med), 1258 (med), 1232 (str, C-O), 1188 (w), 1148 (med), 1100 (med), 1057 (w), 1031 (w), 1012 (med).¹H NMR (500 MHz, d₆-DMSO): δH 8.30 (1H, d, J = 7.4 Hz, H2), δH 7.58 (1H, app dd, J = 2.0, 0.5 Hz, H4), δH 7.18 (1H, dd, J = 7.4, 2.0 Hz, H3), δH 6.43 (1H, d, J = 0.7 Hz, H1), δH 4.36 (2H, q, J = 7.1 Hz, H6), δH 2.52 (3H, d, J = 0.7 Hz, H5), δH 1.34 (3H, t, J = 7.1 Hz, H7).¹³C NMR (125 MHz, d₆-DMSO): δC 167.3 (C1), δC 163.3 (C10), δC 151.8 (C8), δC 147.0 (C3), δC 136.5 (C6), δC 131.7 (C4), δC 125.4 (C7), δC 115.9 (C2), δC 109.9 (C5), δC 62.2 (C11), δC 18.5 (C9), δC 14.0 (C12). HRMS (FTMS ESI+) m/z found [M+H]^+ 233.0911, C₁₂H₁₃O₃N₂⁺ required 233.0921, Δ ppm = -0.1 ppm.
8-Methoxy-4-methyl-2H-pyrido[1,2-a]pyrimidin-2-one (76)

Prepared according to General Method 2 from 51. The crude product was purified by column chromatography (SiO₂, 30 g, 92:8 CH₂Cl₂: MeOH) to yield a beige solid (quantitative). Rₚ = 0.42 (9:1 CH₂Cl₂: MeOH). Mpt (CH₂Cl₂): darkens >180 °C, melts 201-203 °C. IR ν max/cm⁻¹ (neat): 3488 (w), 3082 (w, C-H), 1642 (str, C=O), 1579 (str, C=C), 1555 (med, C=C), 1456 (str, C=C/C=N), 1445 (str, C=C/C=N), 1395 (str), 1362 (str), 1261 (str), 1223 (str), 1198 (med), 1184 (med), 1152 (w), 1071 (w), 1057 (w), 1006 (med). ¹H NMR (400 MHz, d⁶-DMSO): δH 8.10 (1H, d, J = 8.0 Hz, H2), δH 6.67 (1H, dd, J = 8.0, 3.2 Hz, H3), δH 6.51 (1H, d, J = 3.2 Hz, H4), δH 6.20 (1H, d, J = 0.8 Hz, H1), δH 3.90 (3H, s, H6), δH 2.46 (3H, d, J = 0.8 Hz, H5). ¹³C NMR (100 MHz, d⁶-DMSO): δC 167.4 (C1), δC 164.2 (C6), δC 154.2 (C8), δC 145.8 (C3), δC 131.6 (C4), δC 113.8 (C2), δC 107.2 (C5), δC 99.4 (C7), δC 56.5 (C10), δC 18.5 (C9).

HRMS (FTMS ESI+) m/z found [M+H]⁺ 191.0814, C₁₀H₁₁O₂N₂⁺ required 191.0815, Δ ppm = -0.4 ppm.
7-Methoxy-4-methyl-2H-pyrimido[1,2-b]pyridazin-2-one (77)

Prepared according to General Method 2 from 52. The crude product was purified by column chromatography (SiO₂, 10 g, 19:1 CH₂Cl₂: MeOH) to yield an off-white solid (85%). R_f = 0.38 (9:1 CH₂Cl₂: MeOH). Mpt (CH₂Cl₂): phase change >170-220 °C then melt/decomposition >255 °C. IR νmax/cm⁻¹ (neat): 3284 (w), 3181 (w), 3100 (w), 3036 (w), 2966 (w, C-H), 2925 (w, C-H), 2864 (w, C-H), 2236 (med, C=O), 1650 (str, C=O), 1554 (str, C=C), 1515 (str, C=C), 1494 (str, C=C), 1454 (w), 1427 (med), 1398 (w), 1377 (w), 1341 (str), 1330 (str), 1261 (str), 1229 (str), 1109 (str), 1082 (str), 1002 (w). ¹H NMR (400 MHz, d⁶-DMSO): δ_H 7.57 (1H, d, J = 8.6 Hz, H2), δ_H 7.39 (1H, d, J = 8.6 Hz, H3), δ_H 6.34 (1H, s, H1), δ_H 3.97 (3H, s, H5), δ_H 2.50 (3H, s, H4).

¹³C NMR (100 MHz, d⁶-DMSO): δ_C 167.5 (C4), δ_C 157.0 (C1), δ_C 150.1 (C3 or C7), δ_C 150.0 (C3 or C7), δ_C 135.6 (C5), δ_C 123.9 (C6), δ_C 113.7 (C2), δ_C 54.8 (C8), δ_C 17.4 (C9). HRMS (FTMS ESI+) m/z found [M+H]^+ 192.0780, C₉H₁₀N₃O₂⁺ required 192.0773, Δ ppm = 3.6 ppm.
4-Methyl-2H-pyrazino[1,2-a]pyrimidin-2-one (78)

Prepared according to General Method 2 from 53. The crude product was purified by Combiflash Companon (SiO₂, 12 g, 0-10% MeOH in CH₂Cl₂) to yield a light brown solid (quantitative). Rₖ = 0.06 (9:1 CH₂Cl₂: MeOH). Mpt (H₂O/MeCN): decomp. >165 °C. IR νmax/cm⁻¹ (neat): 3127 (w, C-H), 3038 (w, C-H), 1651 (str, C=O), 1607 (str), 1513 (str), 1485 (str), 1448 (w), 1408 (w), 1395 (str), 1371 (med), 1312 (w), 1279 (med), 1250 (w), 1239 (w), 1191 (med), 1109 (w), 1062 (med), 1042 (w). ¹H NMR (400 MHz, d⁶-DMSO): δH 8.66 (1H, d, J = 1.2 Hz, H4), δH 8.11 (1H, dd, J = 4.9, 1.2 Hz, H3), δH 7.88 (1H, d, J = 4.9 Hz, H2), δH 6.53 (1H, d, J = 1.0 Hz, H1), H5 obscured by DMSO signal. ¹³C NMR (100 MHz, d⁶-DMSO): δC 167.6 (C1), δC 151.1 (C6), δC 146.4 (C3), δC 145.1 (C7), δC 128.2 (C5), δC 120.8 (C4), δC 116.8 (C2), δC 17.3 (C8). HRMS (FTMS ESI+) m/z found [M+H]+ 162.0657, C₇H₆N₃O⁺ required 162.0662, Δ ppm = -3.9 ppm.
$^1$H NMR

$^{13}$C NMR
8-Methoxy-4-methyl-2\textit{H}-pyrimido[1,6-\textit{a}]pyrimidin-2-one (79)

Prepared according to General Method 2 from 55. The crude product was spectroscopically pure and used without further purification as a yellow solid (quantitative). R\textsubscript{f} = 0.23 (1:1 40-60 petroleum ether: EtOAc). Mpt (CH\textsubscript{2}Cl\textsubscript{2}): 183-185 °C. IR \(v\text{max/cm}^{-1}\) (neat): 3057 (w, C-H), 1691 (str, C=O), 1618 (str), 1573 (str, C=C/C=N), 1546 (w), 1463 (str), 1394 (str), 1288 (w), 1244 (str), 1231 (str, C-O), 1195 (w), 1177 (w), 1158 (med), 1093 (str), 1011 (med). \(^1\)H NMR (400 MHz, d\textsuperscript{6}-DMSO): \(\delta\)H 9.45 (1H, s, H2), \(\delta\)H 6.75 (1H, s, H3), \(\delta\)H 6.13 (1H, s, H1), \(\delta\)H 3.99 (3H, s, H5), \(\delta\)H 2.30 (3H, s, H4). \(^{13}\)C NMR (100 MHz, d\textsuperscript{6}-DMSO): \(\delta\)C 167.7 (C5), \(\delta\)C 166.6 (C1), \(\delta\)C 156.7 (C3), \(\delta\)C 153.1 (C7), \(\delta\)C 143.5 (C4), \(\delta\)C 101.6 (C2), \(\delta\)C 94.5 (C6), \(\delta\)C 56.2 (C9), \(\delta\)C 24.5 (C8). HRMS (TOF ES\textsuperscript{+}) \(m/z\) found [M+H]\textsuperscript{+} 192.0780, C\textsubscript{9}H\textsubscript{10}O\textsubscript{2}N\textsubscript{3}\textsuperscript{+} required 192.0773, \(\Delta\) ppm = -3.6 ppm.
$^1$H NMR

$^{13}$C NMR
1-Methyl-3H-pyrimido[1,2-a]quinolin-3-one (80)

Prepared according to General Method 2 from 57. The crude product was purified by column chromatography (SiO₂, 20 g, 97:3 then 19:1 CH₂Cl₂: MeOH) to yield a brown wax (50%). R<sub>f</sub> = 0.76 (9:1 CH₂Cl₂: MeOH). IR ν<sub>max</sub>/cm<sup>-1</sup> (neat): 3390 (w, br, C-H), 3053 (w, C-H), 2980 (w, C-H), 1628 (str, C=O), 1598 (str, C=C), 1561 (w), 1516 (str, C=C), 1470 (med), 1441 (str), 1407 (med), 1389 (med), 1369 (med), 1291 (w), 1262 (w), 1219 (w), 1188 (w), 1164 (w), 1138 (w), 1049 (w), 1025 (w), 1006 (w). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ<sub>H</sub> 7.72-7.66 (3H, m, H2+H5+H6), δ<sub>H</sub> 7.56 (1H, ddd, J = 8.7, 7.3, 1.5 Hz, H3), δ<sub>H</sub> 7.47 (1H, app td, J = 7.3, 0.9 Hz, H4), δ<sub>H</sub> 7.11 (1H, d, J = 9.3 Hz, H7), δ<sub>H</sub> 6.31 (1H, d, J = 0.7 Hz, H1), δ<sub>H</sub> 2.68 (3H, d, J = 0.6 Hz, H8). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ<sub>C</sub> 168.2 (C1), δ<sub>C</sub> 153.1 (C12), δ<sub>C</sub> 147.7 (C3), δ<sub>C</sub> 136.2 (C10), δ<sub>C</sub> 134.4 (C4), δ<sub>C</sub> 129.0 (C8), δ<sub>C</sub> 128.9 (C6), δ<sub>C</sub> 126.4 (C7), δ<sub>C</sub> 125.0 (C9), δ<sub>C</sub> 124.4 (C11), δ<sub>C</sub> 120.7 (C5), δ<sub>C</sub> 115.8 (C2), δ<sub>C</sub> 23.1 (C13). HRMS (TOF ES+) m/z found [M+H]<sup>+</sup> 211.0879, C<sub>13</sub>H<sub>11</sub>ON<sub>2</sub><sup>+</sup> required 211.0871, Δ ppm = 3.8 ppm.
$^1$H NMR

$^{13}$C NMR
References

