Supplementary Data

Experimental

Materials and methods

1,8-Naphthyrdine-2,7-dicarbonyl dichloride was prepared by literature methods from 1,8-naphthyridine-2,7-dicarboxylic acid.[1]

Commercially available compounds were obtained from Sigma Aldrich or Fisher and, unless specified, all reagents and solvents were reagent grade or better and were used as supplied without further purification.

Melting points (Mp) were measured using a Gallenkamp melting point apparatus and are uncorrected.

Electrospray (ES) mass spectra were recorded using a Micromass Platform II single quadrapole mass spectrometer using either Methanol or Acetonitrile. High resolution spectra were collected by the Mass Spectrometry Service, School of Chemistry, University of Southampton using a Bruker Apex III FT-ICR mass spectrometer fitted with an Apollo electrospray ionisation source.

Nuclear magnetic resonance (NMR) spectra were collected using either a Bruker AV300 spectrometer, or a Bruker DPX400 spectrometer; operating at 300 or 400 MHz respectively for ^{1}H NMR experiments and at 75 MHz or 100 MHz respectively for ^{13}C and Dept-135 NMR experiments. ^{13}C spectra were collected fully decoupled. ACD Labs software was used to process and analyse the spectral data. Chemical Shifts are given in ppm. Multiplicities are denoted as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet.

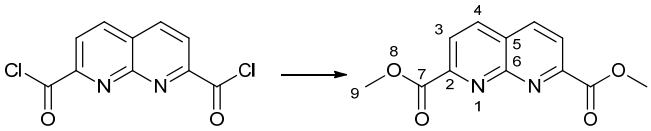
Infrared (IR) spectra were collected on a Nicolet 380 FT-IR spectrometer with a SmartOrbit Golden Gate Attenuated Total Reflection (ATR) attachment.

UV-visible spectra were collected using a Shimadzu UV-1601 UV-visible spectrophotometer running UVPC version 3.5.

Single crystal X-ray diffraction data (for **3a**, **3b** and **3d**) was collected using either a Bruker-Nonius Kappa CCD or Bruker-Nonius Apex II CCD detector. X-rays were generated using a Bruker-Nonius FR591 rotating anode X-ray generator using a molybdenum target Data was

processed using COLLECT,[2] Denzo,[3] DirAX,[4] HKL,[3] SADABS[5] and XPREP[6] software applications. The data for **3c** was collected at Station 9.8 at Daresbury SRS using Bruker SMART APEX2[7]detector at a wavelength λ = 0.6939Å and was processed using SAINT.[8] The structures were solved and refined using the SHELX-97[9] and WinGX[10] software packages, including PLATON.[11] The Crystallographic Information Files (CIFs) were edited in EnCIFer[12] and graphical visualisation was carried out in Mercury[13] and CrystalExplorer.[14]

Dimethyl-1,8-naphthyridine-2,7-dicarboxylate (3a)

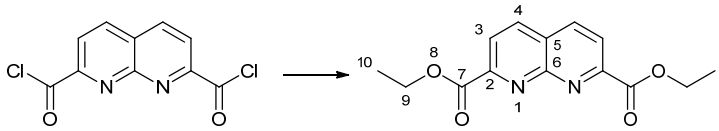


3a

1,8-naphthyridine-2,7-dicarbonyl dichloride (0.200 g, 0.78 mmol) was dissolved in methanol (10 mL). This was stirred for 5 minutes before the addition of triethylamine (0.17 mL, 1.64 mmol) resulted in the solution turning purple with a small amount of off white precipitate. The reaction mixture was left for a further 24 h, during which time the purple colour had disappeared, before the solvent was removed *in vacuo* to give an off white solid (114.6 mg, 60% crude)

Recrystallisation by vapour diffusion of diethyl ether into dichloromethane yielded crystals of x-ray crystallography quality (66 mg, 34 %). Mp: 214 - 215 °C (lit[15] 215 - 217 °C). IR (solid state) ν/cm^{-1} 3019 (w, C-H), 2963 (w, C-H), 2847 (w, C-H), 1704 (s, C=O), 1604 (m, aromatic C-C), 1556 (m, aromatic C-N), 1537 (m, aromatic C-C). IR (solution state in DCM) ν/cm^{-1} 1727 (C=O) 1651, 1634. δ_H (300 MHz; $CDCl_3$) 4.05 (6H, s, H-12), 8.34 (2H, d, *J* = 8.5 Hz, H-3), 8.43 (2H, d, *J* = 8.5 Hz, H-4), δ_c (75 MHz; $CDCl_3$) 53.1 (C-9), 123.2 (C-3), 125.3 (C-5), 138.3 (C-4), 152.0 (C-2), 154.2 (C-6), 165.3 (C-7). LR-MS (ES $^+$): *m/z* 247 (31 %, $[M+H]^+$), 269 (10, $[M+Na]^+$), 301 (23, $M+Na+MeOH]^+$), 515 (100, $[2M+Na]^+$). HR-MS $C_{12}H_{10}N_2O_4Na_1$ requires 269.0533 found 269.0536

Diethyl-1,8-naphthyridine-2,7-dicarboxylate (3b)

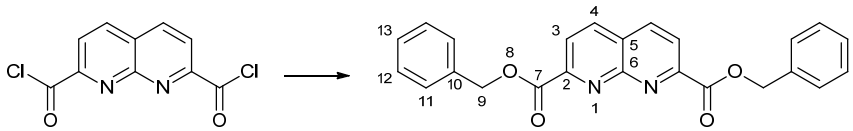


3b

1,8-naphthyridine-2,7-dicarbonyl dichloride (0.200 g, 0.78 mmol) was dissolved in ethanol (20 mL). This was stirred for 5 minutes before the addition of triethylamine (0.17 mL, 1.64 mmol) gave a red solution which turned slowly purple. The reaction mixture was left for a further 24 h, during which time the purple colour disappeared, before the solvent was removed *in vacuo* to give an off white solid (161.8 mg, 75% crude)

Recrystallisation by vapour diffusion of diethyl ether into dichloromethane yielded crystals of x-ray crystallography quality (78.1 mg, 36 %). Mp: 149 - 150 °C. IR ν/cm^{-1} 3048 (w, C-H), 2991 (w, C-H), 2961 (w, C-H), 2945 (w, C-H), 2904 (w, C-H), 1736 (s, C=O), 1598 (m, aromatic C-C), 1556 (m, aromatic C-C), 1532 (m, aromatic C-N), 1477 (m, aromatic C-C). IR (solution state in DCM) ν/cm^{-1} 1747 (C=O), 1722 (C=O). δ_H (300 MHz; $CDCl_3$) 1.50 (6H, t, *J* = 7.2 Hz, H-10), 4.56 (4H, q, *J* = 7.2 Hz, H-9), 8.36 (2H, d, *J* = 8.4 Hz, H-3), 8.43 (2H, d, *J* = 8.4 Hz, H-4). δ_c (75 MHz; $CDCl_3$) 14.3 (C-10), 62.4 (C-9, 123.3 (C-3), 125.3 (C-5), 138.2 (C-4), 152.4 (C-2), 154.3 (C-6), 164.9 (C-7). MS (ES $^+$): *m/z* 275 (24%, $[M+H]^+$), 297 (4, $[M+Na]^+$), 329 (20, $[M+Na+MeOH]^+$), 549 (14, $[2M+H]^+$), 571 (100, $[2M+Na]^+$). HR-MS $C_{14}H_{14}N_2O_4Na_1$ requires 297.0846 found 297.0847

Dibenzyl-1,8-naphthyridine-2,7-dicarboxylate (3c)

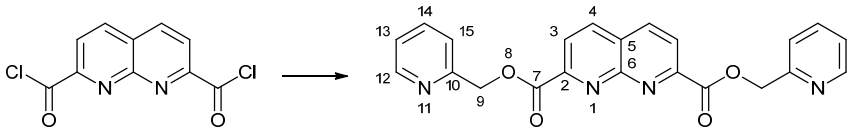


3c

1,8-Naphthyridine-2,7-dicarbonyl dichloride (0.50 g, 1.96 mmol) was dissolved in dichloromethane (50 mL), benzyl alcohol (0.45 ml, 4.31 mmol) was then added followed by triethylamine (0.60 mL, 4.31 mmol) which gave a blue solution. The reaction mixture was left to stir overnight. The following day the reaction mixture was washed with water (3x50 mL) followed by brine (50 mL). The remaining organic residue was dried with magnesium

carbonate and then reduced *in vacuo* yielding a grey solid (0.518 g, 66%). This was recrystallised using a mixed solvent system of dichloromethane : diethyl ether to yield a grey crystalline material (252.4 mg, 32 %). Mp: 214 - 216 °C. IR ν/cm^{-1} 3050 (C-H), 3035 (C-H), 3006 (C-H), 2943 (C-H), 2888 (C-H), 1748 (C=O), 1598 (aromatic C-C), 1536 (aromatic C-N), 1496 (aromatic C-C). IR (solution state in DCM) ν/cm^{-1} 1748 (C=O) 1723 (C=O). δ_H (300 MHz, $CDCl_3$) 5.53 (4H, s, H-7), 7.32 – 7.43 (6H, m, H-10 & H-11), 7.53 (4H, d, *J*=6.6 Hz, H-9), 8.35 (2H, d, *J*=8.4 Hz, H-3), 8.41 (2H, d, *J*=8.4 Hz, H-4). δ_C (75 MHz, $CDCl_3$) 68.0 (C-9), 123.5 (C-3), 125.4 (C-5), 128.5 (C-11), 128.6 (C-12), 128.7 (C-13), 135.3 (C-10) 138.2 (C-4), 152.3 (C-2), 154.3 (C-6), 164.8 (C-7). M/S (ES^+) m/z 399 (8 %, $[M+H]^+$), 417 (21, $[M+NH_4]^+$), 463 (26, $[M+Na+MeCN]^+$), 501 (43, $[M+NH_4+2MeCN]^+$), 815 (20, $[2M+NH_4]^+$), 820 (26, $[2M+Na]^+$). HR-MS $C_{24}H_{18}N_2O_4Na_1$ requires 421.1159 found 421.1165

Bis-(pyridin-2-ylmethyl)-1,8-naphthyridine-2,7-dicarboxylate (3d)

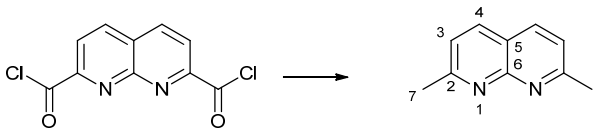


3d

1,8-Naphthyridine-2,7-dicarbonyl dichloride (0.5 g, 1.96 mmol) was dissolved in dichloromethane (50 mL), 2-(hydroxymethyl)pyridine (0.42 ml, 4.31 mmol) was then added, turning the solution green and a white precipitate formed, followed by triethylamine (0.60 mL, 4.31 mmol) which dissolved the precipitate. The reaction mixture was left to stir overnight. The following day the reaction mixture was washed with water (3x50 mL) followed by brine (50 mL). The remaining organic residue was dried with magnesium carbonate and then reduced *in vacuo.* This yielded a grey solid. This was recrystallised using a mixed solvent system of dichloromethane : diethyl ether to yield a slightly blue tinged white powder (388.6 mg, 49 %). Mp: 208 - 211 °C. IR ν/cm^{-1} 3050 (N-H), 3007 (C-H), 2931 (C-H), 1749 (C=O), 1592 (aromatic C-C), 1571 (aromatic C-C), 1558 (aromatic C-N), 1537 (aromatic C-N), 1478 (aromatic C-C). IR (solution state in DCM) ν/cm^{-1} 1749 (C=O), 1727.7 (C=O). δ_H (400 Mhz, $CDCl_3$) 5.64 (4H, s, H-9), 7.24 (2H, dd, *J*=7.0, 5.0Hz, H-13), 7.57 (2H, d, *J*=8.0 Hz, H-15), 7.71 (2H, td, *J*=7.7, 1.8 Hz, H-14), 8.40 (2H, d, *J*=8.5 Hz, H-3), 8.46 (2H, d, *J*=8.5 Hz, H-4), 8.61 (2H, d, *J*=4.5 Hz, H-12). δ_C (100 Mhz, $CDCl_3$) 68.3 (C-9), 122.0 (C-13), 123.0 (C-15), 123.7 (C-3), 125.6 (C-5), 136.8 (C-14), 138.4 (C-4), 149.4 (C-12), 152.1 (C-10),

154.4 (C-6), 155.3 (C-2), 164.6 (C-7). M/S (ESI (MeCN)) m/z 402 (29, $[M+H]^+$), 465 (20 %, $[M+H]^+$), 802 (11, $[2M+H]^+$), 824 (11, $[2M+Na]^+$). HR-MS $C_{22}H_{16}N_4O_4$ requires 401.1244 found 401.1237

2,7-Dimethyl-1,8-naphthyridine[1] (4)



4

5-Chloro-2,7-dimethyl-1,8-naphthyridine (1.695 g, 8.80 mmol) was dissolved in methanol and ammonium formate (1.714 g, 27.1 mmol) was then added. The mixture was left under a nitrogen gas flow for 15 mins to purge the reaction prior to the addition of Pd on carbon (5%, 0.7g). Progress of the reaction was monitored by TLC and appeared to have gone to completion after ca. 4 hours. The catalyst was then filtered off and the filtrate was concentrated *in vacuo*. The residues were taken up in DCM (100 mL) and the solution was then washed with water (3 x 50 mL), dried with magnesium sulphate. The solvent was removed *in vacuo* yielding a slightly yellowed solid (1.056 g, 97 %). Mp: 186 - 187 °C (lit.[1] 193 - 194 °C). IR ν/cm^{-1} 3053 (w, C-H), 3001 (w, C-H), 2918 (w, C-H), 2853 (w, C-H), 1603 (s, aromatic C-C), 1538 (s, aromatic C-N), 1508 (s, aromatic C-C). IR (solution state in DCM) ν/cm^{-1} 1607 (C=O). δ_H (300 MHz, $CDCl_3$) 2.78 (6H, s, H-7), 7.30 (2H, d, J=8.3 Hz, H-3), 8.01 (2H, d, J=8.3 Hz, H-4). δc (75 MHz, $CDCl_3$) 25.5 (C-7), 118.6 (C-5), 122.0 (C-3), 136.4 (C-4), 155.6 (C-6), 162.6 (C-2). M/S (ES $^+$) 159 (37%, $[M+H]^+$), 181 (62, $[M+Na]^+$), 213 (4, $[M+Na+MeOH]^+$), 339 (100, $[2M+Na]^+$).

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