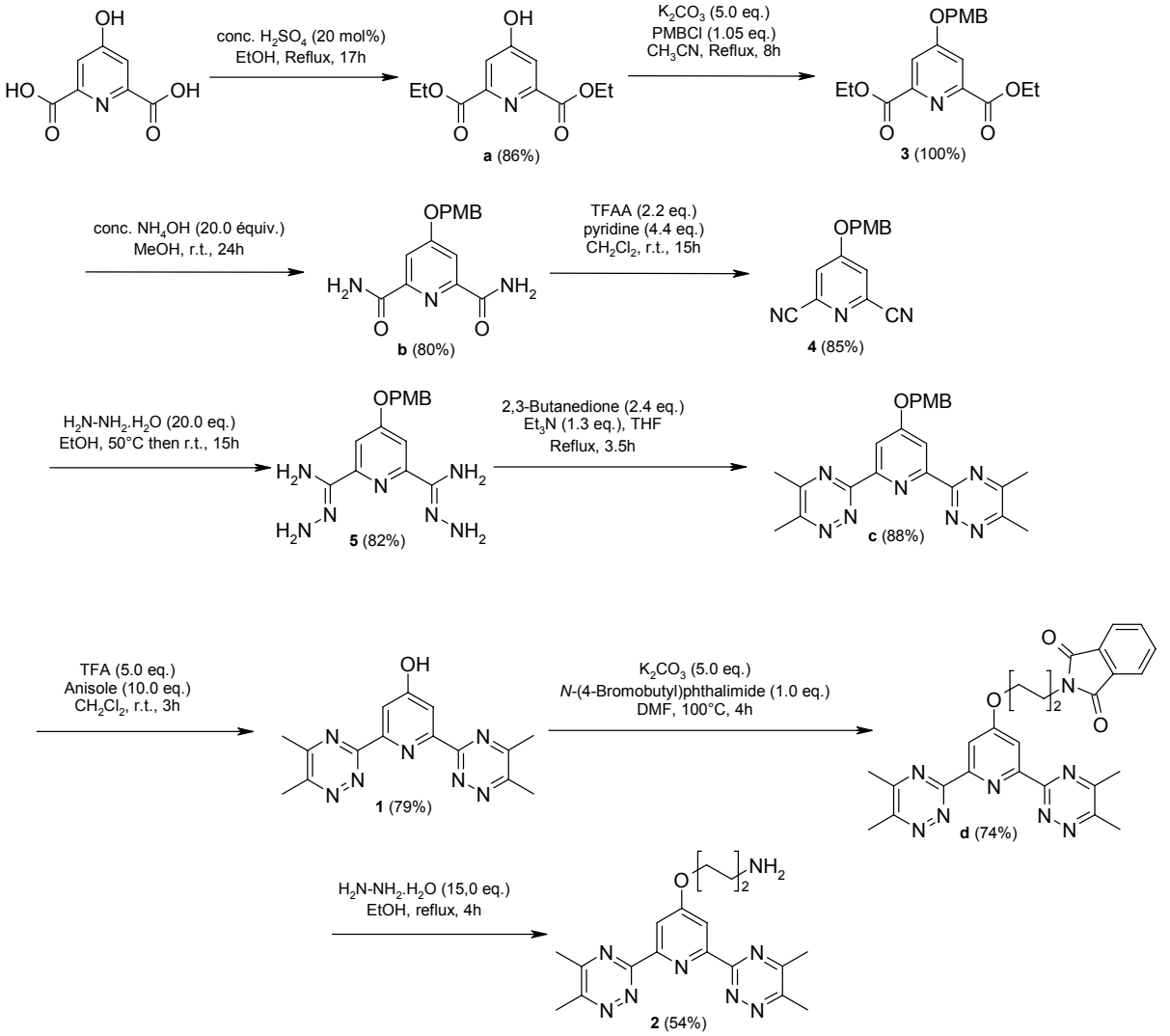
Supplementary information

All commercial solvents (analytical grade) were used without any further purification. Anhydrous dichloromethane was obtained by distillation from calcium hydride prior to use. Chelidamic acid monohydrate and the other reagents were purchased either from Aldrich or from Acros and used as received. Reactions were monitored by thin layer chromatography using 0.25 mm E. Merck silica gel coated glass plates (60 F_{254}) using UV light to visualize the course of reaction. Flash column chromatography was performed using E. Merck silica gel (60, particle size 0.040-0.070 mm). Chemical yields refer to pure isolated substances. ^{1}H and ^{13}C NMR spectra were recorded using a Bruker Avance DPX 250 spectrometer. Chemical shifts are reported in ppm either from tetramethylsilane as internal standard when using $CDCl_3$ or from the solvent residual peak when using DMSO-d_6. The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. ESI-MS spectra were recorded using a Perkin Elmer Sciex API 300 spectrometer. IR spectra were obtained from a Thermo Nicolet 6700 spectrometer. Melting points were measured in a capillary tube with a Büchi apparatus and were not corrected. HRMS (ESI-TOF) was performed on a Micromass LC TOF spectrometer.



Synthesis of diethyl 4-(4-methoxybenzyloxy)pyridine-2,6-dicarboxylate (3)

*Diethyl 4-hydroxypyridine-2,6-dicarboxylate (**a**):* To a suspension of commercially available chelidamic acid monohydrate (10.6 g, 52.8 mmol) in EtOH (350 mL) was added dropwise 95% H_2SO_4 (566 µL, 10.1 mmol, 20 mol%) and the mixture was refluxed during 17 hours. The reaction was then allowed to cool to room temperature and the solvent was evaporated under reduced pressure. To the resulting residue were added water (200 mL) and EtOAc (450 mL). The organic phase was collected, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography on silica gel (CH_2Cl_2/MeOH; 98:2 then 95:5) afforded diethyl 4-hydroxypyridine-2,6-dicarboxylate (10.9 g, 86%) as a white solid; mp 121-122 °C (Lit. 120-121 °C)[1]; MS (Ionspray®): m/z 240.0 $[M+H]^+$; ^{1}H NMR (250 MHz, DMSO-d_6) δ (ppm): 7.57 (s, 2 H), 4.35 (q, *J* = 7.0 Hz, 4 H), 1.33 (t, *J* = 7.0 Hz , 6 H);

[1] Markees, D.G. *J. Org. Chem.* **1964**, *29*, 3120-3121.

^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 166.0, 164.3, 149.9, 115.2, 61.4, 14.1; IR: ν_{max} 2985, 1738, 1722, 1603, 1458, 1332, 1228, 999, 791 cm^{-1}.

*Diethyl 4-(4-methoxybenzyloxy)pyridine-2,6-dicarboxylate (**3**):* To a solution of diethyl 4-hydroxypyridine-2,6-dicarboxylate (3.1 g, 12.5 mmol) in CH_3CN p.a. (150 mL) were added K_2CO_3 (8.7 g, 62.9 mmol, 5.0 eq.), *p*-methoxybenzyl chloride (1.8 mL, 13.2 mmol, 1.05 eq.) and the resulting mixture was refluxed under vigorous stirring during 8 hours. After cooling to room temperature water was added to the reaction until complete dissolution of the salts. CH_3CN was then evaporated under reduced pressure and the remaining aqueous phase was extracted with CH_2Cl_2 (3 x 100 mL). The combined collected organic phases were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The remaining residue was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH; 98:2 then 95:5 (v:v)) to afford quantitatively **3** (4.64 g) as a white solid; mp 81 °C; MS (Ionspray®): m/z 360.0 $[M+H]^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.85 (s, 2 H), 7.37 (d, *J* = 8.4 Hz, 2 H), 6.94 (d, *J* = 8.4 Hz, 2 H), 5.15 (s, 2 H), 4.47 (q, *J* = 7.2 Hz, 4 H), 3.83 (s, 3 H), 1.45 (t, *J* = 7.2 Hz, 6 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 166.8, 164.9, 160.1, 150.3, 129.7, 126.9, 114.8, 114.4, 70.8, 62.5, 55.5, 14.4; IR: ν_{max} 1733, 1720, 1593, 1519, 1335, 1250, 1227, 1098, 1024 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{21}NO_6Na$ ($M+Na^+$) 382.1267, found 382.1256.

Synthesis of 2,6-dicyano-4-(4-methoxybenzyloxy)pyridine (4)

*4-(4-methoxybenzyloxy)pyridine-2,6-dicarboxamide (**b**):* To a solution of compound **3** (3.79 g, 10.6 mmol) in MeOH p.a. (30 mL) was added dropwise conc. NH_4OH (30 mL, 0.2 mol, 20.0 eq.) and the resulting mixture was vigorously stirred at room temperature during 24 hours. The white precipitate formed was filtrated on Büchner, washed with ice-cooled water and dried under vacuum over P_2O_5 to give 4-(4-methoxybenzyloxy)pyridine-2,6-dicarboxamide (2.53 g, 80%) as a white solid; mp 240-241°C; MS (Ionspray®): m/z 302.0 $[M+H]^+$; ^{1}H NMR (250 MHz, DMSO-d_6) δ (ppm): 8.83 (br s, 2H), 7.71 (s, 4 H), 7.41 (d, *J* = 8.5 Hz, 2 H), 6.96 (d, *J* = 8.5 Hz, 2 H), 5.26 (s, 2 H), 3.76 (s, 3 H); ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 166.9, 165.2, 159.3, 151.2, 129.7, 127.7, 114.0, 110.5, 69.7, 55.2; IR: ν_{max} 3315, 1684, 1665, 1581, 1516, 1434, 1377, 1245, 1106, 1015 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{15}N_3O_4Na$ ($M+Na^+$) 324.0960, found 324.0968.

*2,6-Dicyano-4-(4-methoxybenzyloxy)pyridine (**4**):* Under argon atmosphere, to a suspension of 4-(4-methoxybenzyloxy)pyridine-2,6-dicarboxamide (1.0 g, 3.3 mmol) in anhydrous CH_2Cl_2 (125 mL) at r.t. were added pyridine (1.2 mL, 14.8 mmol, 4.5 eq.) and, slowly, TFAA (1.1 mL, 7.9 mmol, 2.4 eq.). After stirring the resulting mixture at room temperature during 18 hours, water (75 mL) was added. The organic phase was collected and the aqueous one was extracted with CH_2Cl_2 (50 mL). The combined organic phases were dried over anhydrous $MgSO_4$, concentrated under reduced pressure and the residue obtained was purified by flash chromatography on silica gel (CH_2Cl_2 + 0.1% MeOH) to afford compound **4** (749 mg, 85%) as a white solid; mp 145 °C; MS (Ionspray®): m/z 266.0 $[M+H]^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 7.41 (s, 2 H), 7.32 (d, *J* = 8.8 Hz, 2 H), 6.95 (d, *J* = 8.8 Hz, 2 H), 5.15 (s, 2 H), 3.84 (s, 3 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 166.1, 160.5, 136.3, 129.7, 125.3, 118.6, 115.7, 114.7, 71.8, 55.5; IR: ν_{max} 1593, 1516, 1341, 1249, 1153, 1037, 1018, 879, 816 cm^{-1}.

*Synthesis of (4-methoxybenzyloxy)pyridine-2,6-biscarbamidrazone (**5**):* To a solution of compound **4** (1.6 g, 6.2 mmol) in EtOH (100 mL) at 50°C was added dropwise hydrated hydrazine (10 mL, 0.2 mol, 33.3 eq.). After cooling to room temperature, the reaction mixture was stirred during 48 hours. The resulting precipitate was filtrated on Büchner, washed with a minimum of EtOH and dried under vacuum to afford the pyridine derivative **5** (1.7 g, 82%) as a pale yellow solid; mp 174-176 °C; MS (Ionspray®): m/z 330.5 $[M+H]^+$; ^{1}H NMR (250 MHz, DMSO-d_6) δ (ppm): 7.40 (s, 2 H), 7.36 (d, *J* = 8.5 Hz, 2 H), 6.94 (d, *J* = 8.5 Hz, 2 H), 6.01 (br s, 4 H), 5.20 (br s, 4 H), 5.10 (s, 2 H), 3.75 (s, 3 H); ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 164.4, 159.1, 152.2, 143.4, 129.4, 128.2, 113.9, 104.5, 68.9, 55.1; IR: ν_{max} 3413, 3315, 1587, 1516, 1435, 1374, 1247, 1110, 1029, 1019, 857, 835 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{20}N_7O_2$ ($M+H^+$) 330.1678, found 330.1683.

Synthesis of 2,6-bis(5,6-dimethyl-1,2,4-triazin-3-yl)-4-hydroxypyridine (1)

*2,6-Bis(5,6-dimethyl-1,2,4-triazin-3-yl)-4-(p-methoxybenzyloxy)pyridine (**c**):* To a suspension of compound **5** (1.9 g, 5.9 mmol) in THF (40 mL) were added dropwise triethylamine (1.1 mL, 7.8 mmol, 1.3 eq.) and 2,3-butanedione (2.1 mL, 24.0 mmol, 4.1 eq.). The resulting yellow solution was refluxed under vigorous stirring during 3.5 hours. After cooling to room temperature the precipitate was filtrated on Büchner, washed with THF and Et_2O and finally dried under vacuum to give the 2,6-bis-(5,6-dimethyl-1,2,4-triazin-3-yl)-4-(*p*-

methoxybenzyloxy)-pyridine (2.2 g, 88%) as a pale yellow solid; mp 182-185 °C; MS (Ionspray®): m/z 430.5 $[M+H]^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.41 (s, 2 H), 7.43 (d, *J* = 8.7 Hz, 2 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 5.27 (s, 2 H), 3.83 (s, 3 H), 2.78 (s, 6 H), 2.71 (s, 6 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 167.0, 161.4, 160.0, 159.8, 157.4, 155.2, 129.7, 127.5, 114.3, 112.3, 70.5, 55.5, 22.1, 19.8; IR: ν_{max} 1598, 1517, 1385, 1248, 1132, 1017 cm^{-1}; HRMS (ESI) calcd for $C_{23}H_{24}N_7O_2$ $(M+H^+)$ 430.1991, found 430.1991.

*2,6-Bis(5,6-dimethyl-1,2,4-triazin-3-yl)-4-hydroxypyridine (**1**):* To a solution of 2,6-bis-(5,6-dimethyl-1,2,4-triazin-3-yl)-4-(*p*-methoxybenzyloxy)pyridine (241 mg, 0.6 mmol) and anisole (610 µL, 5.6 mmol, 10.0 eq.) in CH_2Cl_2 p.a. (10 mL) at room temperature was added TFA (210 µL, 2.8 mmol, 5.0 eq.). The reaction mixture was vigorously stirred at room temperature during 4 hours. The reaction was then diluted with CH_2Cl_2 (10 mL) and water (15 mL) was added under vigorous stirring. The resulting yellow-coloured insoluble products were filtrated on Büchner and washed with CH_2Cl_2 (20 mL). The aqueous phase was extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were dried on anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting oil was dissolved in THF (4 mL) and Et_2O (10 mL) was added. The resulting precipitate was filtrated, washed with Et_2O and dried under vacuum to afford compound **1** (137 mg, 79%) as a pale yellow solid; mp 237-238 °C; MS (Ionspray®): m/z 308.0 $[M-H]^-$; ^{1}H NMR (250 MHz, DMSO-d_6) δ (ppm): 7.78 (s, 2 H), 2.71 (s, 6 H), 2.64 (s, 6 H); ^{13}C NMR (62.5 MHz, DMSO-d_6) δ (ppm): 160.1, 157.9, 113.1, 21.7, 19.3, carbon signals corresponding to $C_{2(pyridine)}$/$C_{6(pyridine)}$, $C_{4(pyridine)}$ and $C_{3(triazines)}$ were not observed; IR: ν_{max} 3443, 1533, 1508, 1394, 983 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{16}N_7O$ $(M+H^+)$ 310.1416, found 310.1426.

Synthesis of 4-(4-aminobut-1-yloxy)-2,6-bis(5,6-dimethyl-1,2,4-triazin-3-yl)pyridine (5):

*2,6-Bis(5,6-dimethyl-1,2,4-triazin-3-yl)-4-[4-(phthalimid-N-yl)-but-1-yloxy]pyridine (**d**):* To a solution of 4-hydroxy-BTP **1** (293 mg, 0.95 mmol) in DMF p.a. (35 mL) were added potassium carbonate (655 mg, 4.7 mmol, 5.0 eq.) and *N*-(4-bromobutyl)phthalimide (267 mg, 0.95 mmol, 1.0 eq.). The reaction mixture was then vigorously stirred at 100°C during 4 hours. After cooling to room temperature the solvent was evaporated under reduced pressure. The resulting residue was triturated in CH_2Cl_2, filtrated on Büchner and the insoluble products were washed abundantly with CH_2Cl_2. The combined organic phases were concentrated under reduced pressure and the remaining residue was purified by flash chromatography on silica

gel (CH_2Cl_2/MeOH/Et_3N; 95:4:1 (v:v:v)) to afford 2,6-bis-(5,6-dimethyl-1,2,4-triazin-3-yl)-4-[4-(phthalimid-*N*-yl)-but-1-yloxy]pyridine (360 mg, 74%) as a yellow solid; mp 113-114 °C; MS (Ionspray®): m/z 511.5 $[M+H]^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.31 (s, 2 H), 7.86 (dd, *J* = 3.1 Hz, *J* = 5.5 Hz, 2 H), 7.72 (dd, *J* = 3.1 Hz, *J* = 5.5 Hz, 2 H), 4.30 (br s, 2 H), 3.82 (br s, 2 H), 2.78 (s, 6 H), 2.72 (s, 6 H), 1.96 (br s, 4 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 168.6, 167.1, 161.3, 159.8, 157.4, 155.0, 134.1, 132.2, 123.4, 112.0, 68.1, 37.6, 26.5, 25.4, 22.0, 19.8; IR: ν_{max} 1708, 1533, 1395, 1044, 725 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{27}N_8O_3$ $(M+H^+)$ 511.2206, found 511.2206.

*4-(4-Aminobut-1-yloxy)-2,6-bis(5,6-dimethyl-1,2,4-triazin-3-yl)pyridine (**2**):* A solution of 2,6-bis-(5,6-dimethyl-1,2,4-triazin-3-yl)-4-[4-(phthalimid-*N*-yl)-but-1-yloxy]pyridine (360 mg, 0.7 mmol) and hydrated hydrazine (510 µL, 10.5 mmol, 15.0 eq.) in EtOH (25 mL) was refluxed overnight under stirring. After cooling to room temperature, the precipitate formed was filtrated on Büchner and washed with CH_2Cl_2 (15 mL). The combined organic phases were evaporated under reduced pressure and the remaining residue was triturated in CH_2Cl_2. The insoluble products were filtrated on Büchner. The filtrate was concentrated to 10 mL and was washed with a 1N aqueous HCl solution (4 x 6 mL). The combined aqueous phases were basified to pH = 11 with a 10N aqueous NaOH solution. The mixture was then cooled to 5 °C with an ice-bath and the resulting precipitate was filtrated, washed with H_2O (5 mL), THF (5 mL) and Et_2O (5 mL). The solid was dried under vacuum to afford the amino-BTP **2** (143 mg, 54%) as a yellow solid [Note: when no precipitate appeared, the following purification was undertaken: the aqueous phase was concentrated under reduced pressure and the remaining residue was purified by flash chromatography on silica gel (CH_2Cl_2/MeOH/Et_3N; 85:10:5 (v:v:v)] mp 93-95 °C; MS (Ionspray®): m/z 381.5 $[M+H]^+$; ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.33 (s, 2 H), 4.29 (t, *J* = 6.5 Hz, 2 H), 2.82 (t, *J* = 7.1 Hz, 2 H), 2.78 (s, 6 H), 2.72 (s, 6 H), 1.96 (dt, *J* = 6.3 Hz, *J* = 6.5 Hz, 2H), 1.69 (dt, *J* = 6.3 Hz, *J* = 7.1 Hz, 2 H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 167.3, 161.3, 159.8, 157.4, 155.1, 112.0, 68.7, 42.0, 30.3, 26.5, 22.0, 19.8; IR: ν_{max} 2928, 1591, 1521, 1423, 1383, 1350, 1032, 743 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{25}N_8O$ $(M+H^+)$ 381.2151, found 381.2132.