Synthesis and Reactivity of Triazaphenanthrenes

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A) General information

Unless otherwise indicated, all reactions were carried out with magnetic stirring. If required, flame dried glassware was used under an argon atmosphere. Syringes needed to transfer reagents and solvents were purged with argon prior to use.

Reactions were monitored by gas chromatography (GC and GC-MS) or thin layer chromatography (TLC). TLC was performed with aluminium plates coated with SiO$_2$ (Merck 60, F-254) and visualized by UV detection.

Purification via column chromatography was performed using Merck silica gel 60 (40 – 63 mm 230-400 mesh ASTM from Merck), or using preparative high performance liquid chromatography (HPLC).

THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. Acetonitrile and diisopropylamine were distilled from CaH$_2$ under nitrogen. HPLC grade quality DMF and analytical grade CHCl$_3$ were used.

Melting points were measured using a Büchi B-540 apparatus and are uncorrected. NMR spectra were recorded in CDCl$_3$ or DMSO-d$_6$ and chemical shifts (δ) are reported in parts per million (ppm).

Mass spectra and high resolution mass spectra (HRMS) were recorded using electrospray ionization (ESI) except where otherwise noted. GCs were recorded on machines of the type Hewlett-Packard 6890 (Hewlett Packard, 5 % phenylmethylpolysiloxane; length: 15 m, diameter: 0.25 mm; film thickness: 0.25 mm).
B) Starting material synthesis

Starting materials 9a-b, as well as trichloroisocyanuric acid, potassium phthalimide and chloranil are commercially available reagents and were used without further purification.

\(i\)-PrMgCl·LiCl was purchased as a solution in THF from Rockrood Lithium and titrated against iodine prior to use.\(^1\)

\(n\)-BuLi was purchased as a solution in hexane from Rockwood Lithium and titrated against \(i\)-PrOH in the presence of 1,10-phenanthroline.\(^2\)

Preparation of ZnCl\(_2\) (1 M solution in THF):
A dry and argon flushed 250 mL Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with ZnCl\(_2\) (13.6 g, 100 mmol). The salt was heated to 140 °C under high vacuum for 4 h. After cooling to 25 °C, dry THF (100 mL) was added and stirring was continued until the salt was dissolved (4 h).

1. Synthesis of 3-iodo-2-methylpyridine (8a)

A dry, argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with LiCl (128 mg, 1.5 equiv) and heated with a heat gun under high vacuum (5 min). After cooling to room temperature, magnesium turnings (122 mg, 2.5 equiv) were added, followed by THF (2 mL). The magnesium was activated using 1,2-dibromoethane (5 mol%) and TMSCl (5 mol%). Then, ZnCl\(_2\)-solution (2.2 mL, 1.1 equiv, 1 M in THF) was added followed by 3-bromo-2-methylpyridine (344 mg, 1.0 equiv). The reaction mixture was stirred at 25 °C until GC-analysis of hydrolyzed reaction aliquot showed full consumption of the starting material (12 h). To the reaction mixture was added dropwise an iodine solution in THF (1.01 g, 2.0 equiv, 1 M in THF) at 0 °C and stirred for 1 h at 25 °C. The suspension was then quenched with a saturated aqueous solution of Na\(_2\)S\(_2\)O\(_3\) and extracted with EtOAc (3x). The organic layer was dried with MgSO\(_4\), filtered, and concentrated in vacuo to obtain the crude compound. Flash column chromatography (DCM) furnished 8a as yellow solid (267 mg, 61%).

\textbf{m.p.:} 169.1 - 170.3 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\)/ppm: 8.44 (d, \(J = 4.78\) Hz, 1 H), 8.05 (d, \(J = 7.88\) Hz, 1 H), 6.82 (dd, \(J = 7.78, 4.75\) Hz, 1 H), 2.74 (s, 3 H).

\(^1\) Krasovskiy, A.; Knochel, P. \textit{Synthesis} 2006, 2006, 0890.

\(^2\) Lin, H.-S.; Paquette, A. \textit{Synth. Commun.}, 1994, 24, 2503.
**1H NMR (400 MHz, CDCl₃)** δ/ppm: 7.95 (d, J = 8.19 Hz, 1 H), 6.89 (d, J = 8.21 Hz, 1 H), 2.70 (s, 3 H).

**13C NMR (101 MHz, CDCl₃)** δ/ppm: 161.3, 150.5, 148.7, 123.1, 93.8, 28.8.

**MS (70 eV, EI) m/z (%):** 254 (28), 253 (100), 126 (48), 91 (24), 90 (29), 85 (28), 71 (37), 57 (73), 55 (29), 43 (45), 41 (22).

**IR ATR ν (cm⁻¹):** 3096, 3048, 2998, 2952, 2920, 1556, 1538, 1432, 1412, 1380, 1206, 1146, 1012, 974, 876, 814, 724, 684.

**HRMS (EI) for C₆H₅ClIN (252.9155) [M]+:** 252.9154.

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2. **Synthesis of 6-chloro-3-iodo-2-methylpyridine (8b)**

A dry, argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with n-BuMgCl (7.15 mL, 0.5 equiv, 0.5 M in THF) in 10 mL THF and n-BuLi (8.2 mL, 1.0 equiv, 2.44 M) was added at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and added dropwise to a solution of 6-chloro-3-bromo-2-methylpyridine (4.13 g, 1.0 equiv) in 8 mL THF at 0 °C. After 15 min, GC-analysis of hydrolyzed reaction aliquot showed full consumption of the starting material. An iodine solution in THF (10.1 g, 2 equiv) was added to the reaction mixture at 0 °C and stirred 30 min. The suspension was then quenched with a saturated aqueous solution of Na₂S₂O₃ and extracted with EtOAc. The organic layer was dried with MgSO₄, filtered, and concentrated in vacuo to obtain the crude compound. Flash column chromatography (DCM) furnished 8a as yellow oil (4.49 g, 89%).
C) General procedures

Typical procedure for the preparation of pyridyl-zinc reagents (TP1):
A dry, argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with the neat pyridyl bromide (1.0 equiv) in THF (0.5 mL/mmol). i-PrMgCl-LiCl (1.1 equiv, 1.25 M in THF) was added dropwise to the starting material solution in THF at 0 °C and the reaction mixture was stirred at 0 °C until GC-analysis of iodinated reaction aliquot showed full consumption of the starting material. ZnCl₂ in THF (1.2 equiv, 1 M) was then added dropwise to the Grignard reagent at 0 °C and the solution was stirred 30 min for transmetallation. The obtained organozinc reagents were then directly used in Negishi cross-couplings (see TP2 and TP3).

Typical procedure for the Pd(PPh₃)₄-catalyzed Negishi cross-coupling (TP2):
A dry, argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with the pyridyl iodide (0.9 equiv) and Pd(PPh₃)₄ (2 mol%). THF was added (1 mL/mmol) and the suspension was stirred 15 min at 25 °C. The desired freshly prepared zinc reagent in THF was added dropwise to the reaction mixture at 25 °C and the mixture was then stirred for the given time at 50 °C. The reaction mixture was quenched with sat. NaCl solution and extracted with EtOAc (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was purified by flash column chromatography to give the analytically pure product.

Typical procedure for the Pd(OAc)₂/SPhos-catalyzed Negishi cross-coupling (TP3):
A dry, argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with the pyridyl iodide (0.9 equiv), Pd(OAc)₂ (2 mol%) and SPhos³ (4 mol%). THF was added (1 mL/mmol) and the suspension was stirred 15 min at 25 °C. The desired freshly prepared zinc reagent in THF was added dropwise to the reaction mixture at 25 °C and the mixture was then stirred for the given time at 50 °C. The reaction mixture was quenched with sat. NaCl solution and extracted with EtOAc (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was purified by flash column chromatography to give the analytically pure product.

Typical procedure for the chlorination using trichloroisocyanuric acid (TP4):
A round-bottom flask was charged with the picolyl-derivative (1.0 equiv) and benzamide (0.03 equiv) in chloroform (3 mL/mmol) at 25 °C. Trichloroisocyanuric acid (0.54 equiv) was added portionwise

³ 2-Dicyclohexylphosphino-2’,6’-dimethoxybiphenyl; See: Bruno, N. C.; Tudge, M. T.; Buchwald, S. L. Chem. Sci. 2013, 4, 916.
to this solution at 25 °C. The reaction mixture was then stirred and heated to reflux until GC-MS analysis of a reaction aliquot showed full consumption of the starting material. After cooling to room temperature, water was added to the reaction mixture and the solution was neutralized with sat. NaHCO₃ and extracted with DCM (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was purified by flash column chromatography to give the analytically pure product.

**Typical procedure for the chlorination via deprotonation by LDA and TMSCl trapping (TP5):**

A dry, argon flushed Schlenk-flask equipped with a magnetic stirring bar and a septum was charged with a solution of lithium diisopropylamide (1.2 equiv, 0.5 M in THF) and was cooled to -78 °C. A solution of the desired picolyl-derivative (1.0 equiv) in THF (8 mL/mmol) was added dropwise to the cooled solution. This solution was stirred for 2 h at -78°C and TMSCl (1.3 equiv) was added to the rapidly stirred lithium reagent and let warm up to 25 °C overnight (12 h). Sat. aq. NaHCO₃ was added to the reaction mixture and the aqueous phase was extracted with EtOAc (3x). The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The resulting oil containing the product and ca. 10% of the bis(trimethylsilylmethyl) compound was dried on the high vacuum line and used in the next step without further purification.

Hexachloroethane (2 equiv) and finely ground and dried CsF (2 equiv) were placed in a round-bottom flask equipped with a stirring bar, a septum and purged with argon. A solution of the freshly synthesized (trimethylsilyl)methyl-derivative (1.0 equiv) in dry MeCN (2 mL/mmol) was added to the flask and the mixture was stirred and heated to reflux for 3 h. Sat. NaCl was poured to the reaction mixture and extracted with EtOAc (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was purified by flash column chromatography to give the analytically pure product.

**Typical procedure for the Gabriel substitution of chloromethyl-derivatives (TP6):**

A round-bottom-flask was equipped with the chloromethyl-derivative (1.0 equiv) in DMF (2 mL/mmol) and potassium phthalimide (1.2 equiv) was added at 25 °C. The reaction mixture was stirred and warmed up to 100 °C until TLC-monitoring showed full consumption of the starting material. Water was added to the solution and the aqueous phase was extracted with EtOAc (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was purified by flash column chromatography to give the analytically pure product.
Typical procedure for the Manske-Ing phthalimide deprotection (TP7):

A round-bottom-flask was equipped with the phthalimide-derivative (1.0 equiv) in abs. EtOH (15 mL/mmol). To the suspension was added hydrazine hydrate (3 equiv) at 25 °C and the reaction mixture was heated to reflux for 2 h. After cooling down to 25 °C, 2N HCl was added carefully (2 mL/mmol) and the suspension was brought to reflux for 5 min, until the precipitate dissolves. The solution was cooled down to 25 °C and sat. NaHCO₃ was added dropwise until neutralization. EtOH was evaporated in vacuo and the aqueous phase was extracted with DCM (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was used without further purification.

Typical procedure for the aromatization with chloranil (TP8):

The crude dihydroazaphenanthrene (1.0 equiv) obtained by TP7 was charged in a round-bottom flask and dissolved in DMF (3 mL/mmol) at 25 °C. Chloranil (1.2 equiv) was added portionwise and the reaction mixture was stirred 2 h at 25 °C until TLC monitoring showed full consumption of the starting material. Water was added to the suspension and the aqueous phase was extracted with DCM (3x). The combined organic phases were dried over MgSO₄ and concentrated in vacuo. The crude residue obtained was purified by flash column chromatography to give the analytically pure product.

Typical procedure for the preparation of organolithium reagents (TP9):

Solutions of lithium reagents were freshly prepared and titrated against i-PrOH with 1,10-phenanthroline as indicator: Phenyllithium 14a and (4-methoxyphenyl)lithium 14b were prepared by addition of Li granulas (2.0 equiv) to the corresponding iodides (1.0 equiv) in diethyl ether (0.5 M) at 0 °C and obtained as reddish ca. 0.5 M solutions after 30 min stirring. (4-(trifluoromethyl)phenyl)lithium 14c and (3-fluorophenyl)lithium 14d were obtained as colored solutions (ca. 0.6-0.9 M) according to a literature procedure by adding t-BuLi solution (2.0 equiv.) to the corresponding iodides (1.0 equiv.) in diethyl ether (1.0 M) at -78 °C and stirring for 30 min.⁴ Heteroaryl α-lithiated reagents 14e-h were prepared by adding n-BuLi solution (1.05 equiv.) to the heteroaryl compounds (1.0 equiv.) in THF (1.0 M) at -78 °C and stirring for 30 min, followed by 1 h at -10 °C and 5 min at 25 °C. Titration indicated a 0.5-0.9 M concentration of these reagents. (1-ethoxyvinyl)lithium 14i was prepared according to a literature procedure⁵ and obtained as ca. 0.6 M solution in THF/hexanes.

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⁴ Enders, D.; Chelain, E.; Raabe, G. B. Soc. Chim. Fr. 1997, 134, 299.
⁵ Baldwin, J. E.; Hoefle, G. A.; Lever, O. W. Jr. J. Am. Chem. Soc. 1974, 96, 7126.
Typical procedure for the addition of organolithiums and rearomatization (TP10):

Pyrido[3,2-f][1,7]naphthyridine (4a, 18 mg, 0.1 mmol, 1.0 equiv) was dissolved in 1 mL dry THF under an argon atmosphere. Brief heating was applied to ensure that all material was dissolved. The solution was then cooled to -60 °C in a dry ice/acetone bath. The organolithium solution was cooled to -60 °C prior to addition or -40 °C, if precipitation was observed at -60 °C. The precooled solution of organolithium compound (14, 0.15 mmol, 1.5 equiv.) was then added dropwise via syringe to 4a and the mixture was stirred for 30 min at -60 °C. The dry ice cooling was subsequently changed to an ice bath (0 °C) and stirring was continued for 5 min. Subsequently, 3 mL of sat. aq. NH₄Cl solution was added to quench the reaction. The organic phase was separated, and the aqueous phase was extracted with EtOAc (3x). The combined organic layers were dried over MgSO₄ and solvents were removed in vacuo. The solid residues were dissolved in 2 mL DMF and chloranil (30 mg, 0.12 mmol, 1.2 equiv) was added. The mixture was stirred overnight at room temperature in an open flask before water (10 mL) and ca. 200 mg LiCl were added. The mixture was extracted with EtOAc (5x). After removal of the solvent in vacuo, the analytically pure product of type 4d-m was obtained after flash column chromatography (silica gel, EtOAc + 5% NEt₃).
D) Compounds synthesized according to the general procedures

1. Synthesis of 2-chloro-2'-methyl-3,3'-bipyridine (6a)

According to TP2, the substituted bipyridine 6a was synthesized from the Negishi cross-coupling of 7a (1 mmol, preparation according to TP1) with 8a (0.9 equiv) in the presence of 2 mol% Pd(PPh₃)₄ at 50 °C for 1 h. Flash column chromatography (i-hexane/ethyl acetate 8:2 + 2% NEt₃) furnished 6a as yellow oil (171 mg, 93%).

H NMR (400 MHz, CDCl₃) δ/ppm: 8.53 (dd, J = 4.89, 1.75 Hz, 1 H), 8.41 (dd, J = 4.80, 1.98 Hz, 1 H), 7.56 (dd, J = 7.49, 1.97 Hz, 1 H), 7.43 (dd, J = 7.70, 1.79 Hz, 1 H), 7.31 (dd, J = 7.50, 4.81 Hz, 1 H), 7.19 (dd, J = 7.64, 4.90 Hz, 1 H), 2.33 (s, 3 H).

C NMR (101 MHz, CDCl₃) δ/ppm: 156.3, 150.4, 149.3 (2C), 139.6, 137.2, 135.0, 132.5, 122.6, 121.0, 23.0.

MS (70 eV, EI) m/z (%): 206 (29), 204 (100), 169 (79), 168 (57), 167 (12).

IR ATR ν (cm⁻¹): 3046, 2956, 2924, 2856, 1732, 1568, 1556, 1432, 1392, 1190, 1162, 1126, 1096, 1070, 1062, 1000, 802, 758, 752, 736, 722, 676.

HRMS (EI) for C₁₁H₉ClN₂ (204.0454) [M]+: 204.0446.

2. Synthesis of 2,5-dichloro-2'-methyl-3,3'-bipyridine (6b)

According to TP3, the substituted bipyridine 6b was synthesized from the Negishi cross-coupling of 7b (1 mmol, preparation according to TP1) with 8a (0.9 equiv) in the presence of 2 mol% Pd(OAc)₂ and 4 mol% SPhos at 50 °C for 5 h. Flash column chromatography (i-hexane/ethyl acetate 9:1 + 2% NEt₃) furnished 6a as yellow oil (86 mg, 40%).

H NMR (400 MHz, CDCl₃) δ/ppm: 8.60 (dd, J = 4.90, 1.76 Hz, 1 H), 8.42 (d, J = 2.58 Hz, 1 H), 7.60 (d, J = 2.58 Hz, 1 H), 7.46 (dd, J = 7.71, 1.78 Hz, 1 H), 7.24 (dd, J = 7.70, 4.85 Hz, 1 H), 2.40 (s, 3 H).

C NMR (101 MHz, CDCl₃) δ/ppm: 156.2, 149.8, 148.5, 148.0, 139.1, 137.2, 136.0, 131.4, 131.0, 121.1, 23.1.

MS (70 eV, EI) m/z (%): 240 (73), 238 (100), 203 (66), 168 (78), 57 (46).
IR ATR \(\nu\) (cm\(^{-1}\)): 3050, 2924, 2854, 1566, 1430, 1402, 1388, 1278, 1214, 1124, 1088, 1016, 912, 822, 810, 744, 694, 678.

HRMS (EI) for \(C_{11}H_8Cl_2N_2\) (238.0065) \([M]^+\): 238.0065.

3. Synthesis of 2',6-dichloro-2-methyl-3,3'-bipyridine (6c)

According to TP2, the substituted bipyridine 6c was synthesized from the Negishi cross-coupling of 7a (1 mmol, preparation according to TP1) with 8b (0.9 equiv) in the presence of 2 mol\% Pd(PPh\(_3\))\(_4\) at 50 °C for 2 h. Flash column chromatography (i-hexane/ethyl acetate 8:2 + 2\% NEt\(_3\)) furnished 6c as yellow solid (147 mg, 68%).

\(m.p.:\) 73.8 - 75.4 °C.

\(^1H\) NMR (400 MHz, CDCl\(_3\)) \(\delta/\text{ppm}:\) 8.49 (dd, \(J = 4.83, 1.95\) Hz, 1 H), 7.58 (dd, \(J = 7.51, 1.97\) Hz, 1 H), 7.44 (d, \(J = 8.03\) Hz, 1 H), 7.37 (dd, \(J = 7.52, 4.80\) Hz, 1 H), 7.26 – 7.29 (m, 1 H), 2.36 (s, 3 H).

\(^{13}C\) NMR (101 MHz, CDCl\(_3\)) \(\delta/\text{ppm}:\) 157.5, 150.7, 150.5, 149.8, 140.0, 139.7, 133.9, 131.3, 122.7, 121.6, 22.8.

MS (70 eV, EI) m/z (%): 240 (45), 238 (67), 167 (50), 71 (44), 57 (70), 43 (100).

IR ATR \(\nu\) (cm\(^{-1}\))): 3066, 2924, 1556, 1398, 1384, 1150, 1126, 1090, 850, 810, 760, 752, 692.

HRMS (EI) for \(C_{11}H_8Cl_2N_2\) (238.0065) \([M]^+\): 238.0049.

4. Synthesis of 2-chloro-2'-/(chloromethyl)-3,3'-bipyridine (10a)

According to TP4, the substituted chloromethyl-bipyridine 10a was synthesized from 6a (1 mmol) with trichloroisocyanuric acid (0.53 equiv) in the presence of benzamide (0.03 equiv) at reflux for 4 h. Flash column chromatography (i-hexane/ethyl acetate 8:2 + 2\% NEt\(_3\)) furnished 10a as yellow oil (194 mg, 81%).

\(^1H\) NMR (800 MHz, CDCl\(_3\)) \(\delta/\text{ppm}:\) 8.70 (dd, \(J = 4.81, 1.73\) Hz, 1 H), 8.50 (dd, \(J = 4.85, 1.95\) Hz, 1 H), 7.74 (dd, \(J = 7.47, 1.94\) Hz, 1 H), 7.58 (dd, \(J = 7.74, 1.74\) Hz, 1 H), 7.37 – 7.40 (m, 2 H), 4.59 (d, \(J = 11.30\) Hz, 1 H), 4.39 (d, \(J = 11.34\) Hz, 1 H).

\(^{13}C\) NMR (201 MHz, CDCl\(_3\)) \(\delta/\text{ppm}:\) 154.2, 150.2, 150.2, 150.0, 140.2, 138.5, 133.2, 133.0, 123.4, 122.6, 45.1.
MS (70 eV, EI) m/z (%): 240 (56), 238 (82), 203 (50), 168 (59), 167 (100), 140 (20), 43 (53).

IR ATR v (cm⁻¹): 3052, 2253, 1558, 1437, 1427, 1393, 1265, 1130, 1116, 1092, 999, 903, 802, 723.
3050, 2924, 2854, 1566, 1440, 1430, 1402, 1388, 1214, 1124, 1088, 1016, 912, 822, 810, 790, 744, 694, 678.

HRMS (EI) for C₁₁H₈Cl₂N₂ (238.0065) [M⁺]: 238.0058.

5. Synthesis of 2,5-dichloro-2'-((chloromethyl)-3,3'-bipyridine (10b)

According to TP4, the substituted chloromethyl-bipyridine 10b was synthesized from 6b (1 mmol) with trichloroisocyanuric acid (0.53 equiv) in the presence of benzamide (0.03 equiv) at reflux for 12 h. Flash column chromatography (i-hexane/ethyl acetate 9:1 + 2% NEt₃) furnished 10b as yellow oil (213 mg, 78%).

¹H NMR (400 MHz, CDCl₃) δ/ppm: 8.66 (dd, J = 4.78, 1.73 Hz, 1 H), 8.40 (d, J = 2.64 Hz, 1 H), 7.71 (d, J = 2.62 Hz, 1 H), 7.54 (dd, J = 7.73, 1.72 Hz, 1 H), 7.35 (dd, J = 7.75, 4.79 Hz, 1 H), 4.55 (d, J = 11.29 Hz, 1 H), 4.36 (d, J = 11.31 Hz, 1 H).

¹³C NMR (101 MHz, CDCl₃) δ/ppm: 153.9, 150.4, 148.4, 148.0, 139.5, 138.3, 134.0, 131.7, 130.9, 123.4, 44.9.

MS (70 eV, EI) m/z (%): 276 (23), 274 (62), 272 (63), 237 (38), 203 (45), 202 (83), 201 (83), 97 (31), 71 (42), 57 (55), 43 (45), 43 (100).

IR ATR v (cm⁻¹): 3050, 2924, 2854, 1566, 1440, 1430, 1402, 1388, 1214, 1124, 1088, 1016, 912, 822, 810, 790, 744, 694, 678.

HRMS (EI) for C₁₁H₈Cl₂N₂ (271.9675) [M⁺]: 271.9671.

6. Synthesis of 2',6-dichloro-2-((chloromethyl)-3,3'-bipyridine (10c)

According to TP5, the substituted (trimethylsilyl)methyl-derivative 10a was synthesized from 6c (1 mmol) after deprotonation with LDA (1.2 equiv), followed by trapping with TMSCl (1.3 equiv). The desired chloromethyl-bipyridine 10c was then obtained from the reaction of 10a with CsF
(2 equiv) and C₂Cl₆ (2 equiv) at reflux for 3 h. Flash column chromatography (DCM) furnished 10e as beige powder (168 mg, 62% over these two steps).

**m.p.:** 79.6 - 81.2 °C.

$^1$H NMR (400 MHz, CDCl₃) δ/ppm: 8.47 (dd, $J = 4.79$, 1.94 Hz, 1 H), 7.72 (dd, $J = 7.52$, 1.92 Hz, 1 H), 7.36 – 7.40 (m, 2 H), 4.48 (d, $J = 11.20$ Hz, 1 H), 4.29 (d, $J = 11.22$ Hz, 1 H).

$^{13}$C NMR (101 MHz, CDCl₃) δ/ppm: 154.7, 151.3, 150.2, 150.0, 141.2, 140.1, 131.9, 131.8, 124.3, 122.6, 44.2.

**MS (70 eV, EI) m/z (%):** 276 (29), 274 (52), 272 (60), 237 (36), 202 (47), 201 (100), 85 (21), 71 (35), 66 (43), 57 (50), 44 (84).

**IR ATR ν (cm⁻¹):** 3050, 2924, 1570, 1552, 1432, 1396, 1380, 1126, 1116, 1082, 750, 710, 696.

**HRMS (EI) for C₁₁H₇Cl₃N₂ (271.9675) [M]+:** 271.9664.

7. Synthesis of 2-((2'UchloroU[3,3'Ubipyridin]U2Uyl)methyl)isoindolineU1,3Udione (12a)

According to TP6, the substituted phthalimide derivative 12a was synthesized from 10a (1 mmol) with potassium phthalimide (1.2 equiv) at 100 °C for 2 h. Flash column chromatography (i-hexane/ethyl acetate 7:3 + 2% NEt₃) furnished 12a as white solid (283 mg, 81%).

**m.p.:** 166.9 - 168.9 °C.

$^1$H NMR (400 MHz, CDCl₃) δ/ppm: 8.55 (dd, $J = 4.79$, 1.70 Hz, 1 H), 8.50 (dd, $J = 4.78$, 1.95 Hz, 1 H), 7.82 – 7.86 (m, 3 H), 4.59 (d, $J = 15.87$ Hz, 1 H), 7.71 (dd, $J = 5.49$, 3.05 Hz, 2 H), 7.52 (dd, $J = 7.70$, 1.70 Hz, 1 H), 7.41 (dd, $J = 7.53$, 4.79 Hz, 1 H), 7.27 – 7.30 (m, 1 H), 5.02 (d, $J = 15.89$ Hz, 1 H).

$^{13}$C NMR (101 MHz, CDCl₃) δ/ppm: 168.3 (2C), 152.6, 150.8, 149.9 (2C), 140.1, 137.7, 134.1 (2C), 133.7, 132.4 (2C), 131.9, 123.5 (2C), 122.8, 122.4, 40.9.

**MS (70 eV, EI) m/z (%):** 351 (10), 349 (28), 315 (20), 314 (100), 304 (11), 167 (36), 160 (17), 104 (12), 77 (11), 76 (12).

**IR ATR ν (cm⁻¹):** 3050, 2924, 2854, 1718, 1674, 1430, 1418, 1390, 1354, 1320, 1192, 1126, 1112, 1086, 1068, 1060, 998, 952, 942, 810, 798, 750, 736, 724, 710, 694, 684.

**HRMS (EI) for C₁₉H₁₂Cl₂N₂O₂ (349.0618) [M]+:** 349.0613.

8. Synthesis of 2-((2',5'UdichloroU[3,3'Ubipyridin]U2Uyl)methyl)isoindolineU1,3Udione (12b)
According to TP6, the substituted phthalimide derivative **12b** was synthesized from **10b** (1 mmol) with potassium phthalimide (1.2 equiv) at 100 °C for 2 h. Flash column chromatography (i-hexane/ethyl acetate 7:3 + 2% NEt₃) furnished **12b** as white solid (265 mg, 69%).

**m.p.:** 151.2 - 153.7 °C.

**1H NMR (400 MHz, CDCl₃)** δ/ppm: 8.50 (dd, J = 4.83, 1.72 Hz, 1 H), 8.37 (d, J = 2.58 Hz, 1 H), 7.75 – 7.79 (m, 3 H), 7.63 – 7.66 (m, 2 H), 7.44 (dd, J = 7.71, 1.71 Hz, 1 H), 7.19 – 7.24 (m, 1 H), 4.94 (d, J = 15.84 Hz, 1 H), 4.54 (d, J = 15.85 Hz, 1 H).

**13C NMR (101 MHz, CDCl₃)** δ/ppm: 168.1 (2C), 152.6, 150.2, 148.6, 148.4, 139.5, 137.6, 134.6, 134.1 (2C), 132.3 (2C), 131.2, 130.6, 123.5, 122.5 (2C), 41.0.

**MS (70 eV, EI) m/z (%):** 385 (11), 383 (17), 385 (11), 383 (17), 350 (33), 349 (21), 348 (100), 203 (12), 201 (39), 160 (28), 104 (18), 77 (15), 76 (18).

**IR ATR ν (cm⁻¹):** 3048, 1710, 1392, 1016, 734, 724, 714.

**HRMS (EI)** for C₁₉H₁₁Cl₂N₃O₂ (383.0228) [M⁺]: 383.0212.

9. Synthesis of 2-((2',6-dichloro-[3,3'-bipyridin]-2-yl)methyl)isoindoline-1,3-dione (**12c**)

According to TP6, the substituted phthalimide derivative **12c** was synthesized from **10c** (1 mmol) with potassium phthalimide (1.2 equiv) at 100 °C for 4 h. Flash column chromatography (i-hexane/ethyl acetate 7:3 + 2% NEt₃) furnished **12c** as white solid (353 mg, 92%).

**m.p.:** 186.1 - 189.4 °C.

**1H NMR (800 MHz, CDCl₃)** δ/ppm: 8.48 (dd, J = 4.78, 1.96 Hz, 1 H), 7.80 – 7.84 (m, 3 H), 7.72 (dd, J = 5.49, 3.01 Hz, 2 H), 7.48 (d, J = 7.99 Hz, 1 H), 7.39 (dd, J = 7.50, 4.78 Hz, 1 H), 7.31 (d, J = 8.00 Hz, 1 H), 4.96 (dd, J = 16.09, 0.72 Hz, 1 H), 4.55 (d, J = 16.08 Hz, 1 H).

**13C NMR (201 MHz, CDCl₃)** δ/ppm: 168.1 (2C), 153.7, 151.7, 150.8, 150.3, 140.6, 140.2, 134.3 (2C), 132.7, 132.4 (2C), 130.8, 123.7 (2C), 123.5, 123.0, 40.8.
MS (70 eV, EI) m/z (%): 385 (12), 383 (17), 385 (12), 383 (17), 350 (31), 349 (20), 348 (100), 201 (37), 160 (26), 104 (18), 77 (12), 76 (16).

IR ATR ν (cm⁻¹): 2959, 2922, 2850, 1768, 1713, 1555, 1419, 1389, 1109, 1082, 995, 947, 812, 728, 714, 698.

HRMS (EI) for C₁₉H₁₁Cl₂N₃O₂ (383.0228) [M⁺]: 383.0217.

10. Synthesis of pyrido[3,2-f][1,7]naphthyridine (4a)

According to TP7, the substituted phthalimide derivative 12a (1 mmol) reacted with NH₂NH₂·H₂O (3 equiv) in EtOH at reflux for 2 h, leading to the dihydroazaphenanthrene 12a. After acidic work-up and neutralization, the crude intermediate 12a was aromatized with chloranil (1.2 equiv) at 25 °C for 2 h, as specified in TP8. Flash column chromatography (EtOAc + 2% NEt₃) furnished 4a as beige powder (155 mg, 86% over these two steps).

m.p.: 230.1 - 232.3 °C.

¹H NMR (800 MHz, CDCl₃) δ/ppm: 9.79 (s, 1 H), 9.18 (dd, J = 4.26, 1.86 Hz, 1 H), 9.15 (dd, J = 4.25, 1.56 Hz, 1 H), 8.89 − 8.93 (m, 2 H), 7.84 (dd, J = 8.33, 4.25 Hz, 1 H), 7.70 (dd, J = 8.08, 4.29 Hz, 1 H).

¹³C NMR (201 MHz, CDCl₃) δ/ppm: 158.9, 153.9, 152.6, 152.1, 142.2, 132.0, 130.5, 128.4, 126.0, 123.1, 118.4.

MS (70 eV, EI) m/z (%): 182 (15), 181 (100), 180 (26), 97 (15), 85 (16), 83 (15), 71 (21), 57 (34), 43 (79).

IR ATR ν (cm⁻¹): 3054, 3006, 2922, 2852, 1744, 1602, 1572, 1440, 1370, 1350, 1316, 1160, 896, 786, 746, 710.

HRMS (EI) for C₁₁H₇N₃ (181.0640) [M⁺]: 181.0633.

11. Synthesis of 2-chloropyrido[3,2-f][1,7]naphthyridine (4b)

According to TP7, the substituted phthalimide derivative 12b (1 mmol) reacted with NH₂NH₂·H₂O (3 equiv) in EtOH at reflux for 2 h, leading to the dihydroazaphenanthrene 12b. After acidic work-up and neutralization, the crude intermediate 12b was aromatized with chloranil (1.2 equiv) at 25 °C for
2 h, as specified in TP8. Flash column chromatography (EtOAc + 2% NEt₃) furnished 4b as beige/light pink powder (161 mg, 75% over these two steps).

**m.p.:** decomposition starts at 276.3 °C.

**¹H NMR (800 MHz, DMSO-d₆) δ/ppm:** 9.66 (d, J = 0.80 Hz, 1 H), 9.54 (d, J = 2.56 Hz, 1 H), 9.40 – 9.43 (m, 1 H), 9.21 (dd, J = 4.26, 1.51 Hz, 1 H), 9.13 (d, J = 2.52 Hz, 1 H), 8.05 (dd, J = 8.34, 4.26 Hz, 1 H).

**¹³C NMR (201 MHz, DMSO-d₆) δ/ppm:** 158.1, 152.7, 151.1, 150.6, 141.3, 132.3, 132.1, 129.8, 126.6, 119.2.

**MS (70 eV, EI) m/z (%):** 217 (31), 216 (13), 215 (100), 180 (34), 153 (12).

**IR ATR ν (cm⁻¹):** 3064, 2946, 2924, 2854, 1600, 1568, 1464, 1450, 1366, 1330, 1234, 1120, 948, 900, 878, 826, 796, 742, 726.

**HRMS (EI) for C₁₁H₆ClN₃ (215.0250) [M⁺]:** 215.0243.

12. Synthesis of 8-chloropyrido[3,2-f][1,7]naphthyridine (4c)

According to TP7, the substituted phthalimide derivative 12c (1 mmol) reacted with NH₂NH₂·H₂O (3 equiv) in EtOH at reflux for 2 h, leading to the dihydroazaphenanthrene 12c. After acidic work-up and neutralization, the crude intermediate 12c was aromatized with chloranil (1.2 equiv) at 25 °C for 2 h, as specified in TP8. Flash column chromatography (EtOAc + 2% NEt₃) furnished 4c as beige solid (191 mg, 89% over these two steps).

**m.p.:** decomposition starts at 226.8 °C.

**¹H NMR (800 MHz, DMSO-d₆) δ/ppm:** 9.58 (d, J = 0.76 Hz, 1 H), 9.39 – 9.43 (m, 1 H), 9.34 (dd, J = 8.21, 1.82 Hz, 1 H), 9.15 (dd, J = 4.28, 1.80 Hz, 1 H), 8.13 (d, J = 8.64 Hz, 1 H), 7.87 (dd, J = 8.11, 4.26 Hz, 1 H).

**¹³C NMR (201 MHz, DMSO-d₆) δ/ppm:** 156.3, 152.9, 152.7, 151.9, 141.0, 135.8, 133.6, 127.6, 127.4, 123.6, 117.8.

**MS (70 eV, EI) m/z (%):** 217 (36), 215 (100), 180 (39), 153 (11), 84 (54), 66 (56), 46 (13).

**IR ATR ν (cm⁻¹):** 3483, 2249, 2124, 1997, 1622, 1438, 1222, 1053, 1024, 1005, 820, 757.

**HRMS (EI) for C₁₁H₆ClN₃ (215.0250) [M⁺]:** 215.0242.

13. Synthesis of 6-phenylpyrido[3,2-f][1,7]naphthyridine (4d)
According to TP10, the substituted azaphenanthrene derivative 4d was obtained from 4a (0.1 mmol) via addition of the organolithium reagent 14a (0.52 M in diethyl ether, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt₃) furnished 4d as colorless solid (24 mg, 93%).

m.p.: 217 - 218 °C.

^1H NMR (200 MHz, CDCl₃) δ/ppm: 9.25 – 9.09 (m, 2H), 8.93 (dd, J = 13.8, 8.3 Hz, 2H), 8.39-8.20 (m, 2H), 7.82 (dd, J = 8.3, 4.3 Hz, 1H), 7.66 (dd, J = 8.0, 4.4 Hz, 1H), 7.62 – 7.49 (m, 3H).

^13C NMR (100 MHz, CDCl₃) δ/ppm: 164.0, 153.1, 152.6, 150.9, 141.1, 138.1, 131.8 (2C), 131.4, 130.6, 129.8, 129.2, 127.9 (2C), 125.2, 122.4, 118.1.

MS (70 eV, EI) m/z (%): 258 (25), 257 (100), 129 (10), 84 (12).

IR ATR ν (cm⁻¹): 3060, 2927, 2360, 2231, 1712, 1556, 1514, 1452, 1434, 1356, 1260, 905, 793, 710, 693, 686.

HRMS (EI) for C₁₇H₁₁N₃ (257.0953) [M]+: 257.0950.

14. Synthesis of 6-(4-methoxyphenyl)pyrido[3,2-f][1,7]naphthyridine (4e)

According to TP10, the substituted azaphenanthrene derivative 4e was obtained from 4a (0.1 mmol) via addition of the organolithium reagent 14b (0.50 M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt₃) furnished 4e as colorless solid (25 mg, 87%).

m.p.: 156 - 157 °C.

^1H NMR (400 MHz, CDCl₃) δ/ppm: 9.21 – 9.09 (m, 2H), 8.94 (dd, J = 8.5, 1.5 Hz, 1H), 8.86 (dd, J = 8.2, 1.7 Hz, 1H), 8.42 – 8.37 (m, 2H), 7.81 (dd, J = 8.4, 4.3 Hz, 1H), 7.63 (dd, J = 8.1, 4.4 Hz, 1H), 7.12 – 7.05 (m, 2H), 3.91 (s, 3H).

^13C NMR (100 MHz, CDCl₃) δ/ppm: 163.2, 161.3, 153.2, 152.5, 150.8, 141.2, 133.6 (2C), 131.3, 130.7, 129.3, 127.9, 125.1, 122.1, 117.9, 113.5 (2C), 55.5.
MS (70 eV, EI) m/z (%): 288 (18), 287 (92), 273 (17), 272 (100), 256 (13), 244 (30), 243 (17), 122 (10).

IR ATR ν (cm⁻¹): 2956, 2927, 1605, 1574, 1552, 1449, 1436, 1354, 1299, 1213, 1175, 1030, 968, 833, 789, 712.

HRMS (EI) for C₁₈H₁₃N₃O (287.1059) [M⁺]: 287.1054.

15. Synthesis of 6-(4-(trifluoromethyl)phenyl)pyrido[3,2-f][1,7]naphthyridine (4f)

According to TP10, the substituted azaphenanthrene derivative 4f was obtained from 4a (0.1 mmol) via addition of the organolithium reagent 14c (0.65 M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt₃) furnished 4f as colorless solid (22 mg, 68%).

m.p.: 224 °C

¹H NMR (800 MHz, CDCl₃) δ/ppm: 9.20 (dd, J = 4.3, 1.8 Hz, 1H), 9.17 (dd, J = 4.2, 1.6 Hz, 1H), 9.01 (dd, J = 8.4, 1.6 Hz, 1H), 8.94 (dd, J = 8.2, 1.8 Hz, 1H), 8.43 (d, J = 8.0 Hz, 2H), 7.87 (dd, J = 8.3, 4.2 Hz, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.72 (dd, J = 8.1, 4.3 Hz, 1H).

¹³C NMR (200 MHz, CDCl₃) δ/ppm: 173.7, 162.6, 155.5, 152.9, 151.1, 141.4, 140.9, 132.1 (2C), 131.5, 131.5 (q, J = 30.5 Hz, 1C), 130.8, 129.4, 125.6, 124.9, 124.4 (q, J = 271.4 Hz, 1C), 123.0, 118.4.

MS (70 eV, EI) m/z (%): 326 (17), 325 (100), 325 (57).

IR ATR ν (cm⁻¹): 2924, 2854, 2360, 2340, 1737, 1714, 1597, 1565, 1453, 1442, 1322, 1259, 1207, 1155, 1119, 1066, 959, 784, 775, 712.

HRMS (EI) for C₁₉H₁₇N₃F₃ (325.0827): [M⁺]: 325.0821.

16. Synthesis of 6-(3-fluorophenyl)pyrido[3,2-f][1,7]naphthyridine (4g)
According to **TP10**, the substituted azaphenanthrene derivative **4g** was obtained from **4a** (0.1 mmol) *via* addition of the organolithium reagent **14d** (0.91 M, 1.5 equiv, **TP9**) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt$_3$) furnished **4g** as colorless solid (17 mg, 62%).

**m.p.:** 237 - 238 °C.

$^1$H NMR (400 MHz, CDCl$_3$) δ/ppm: 9.22 – 9.11 (m, 2H), 8.97 (dd, $J$ = 8.5, 1.7 Hz, 1H), 8.90 (dd, $J$ = 8.2, 1.8 Hz, 1H), 8.16 – 8.12 (m, 1H), 8.11 – 8.07 (m, 1H), 7.84 (dd, $J$ = 8.4, 4.3 Hz, 1H), 7.68 (dd, $J$ = 8.2, 4.4 Hz, 1H), 7.56 – 7.48 (m, 1H), 7.25 – 7.19 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ/ppm: 163.7, 162.4, 161.3, 152.8, 151.0, 140.9, 140.0, 131.4, 130.7, 129.4, 129.3, 127.6, 127.6, 124.1 (d, $J$ = 265.4 Hz, 1C), 118.9 (d, $J$ = 21.5 Hz, 1C), 118.3, 116.7 (d, $J$ = 21.5 Hz, 1C).

**MS (70 eV, EI) m/z (%):** 276 (14), 275 (100), 274 (75).

**IR ATR ν (cm$^{-1}$):** 2956, 2927, 2857, 1738, 1729, 1596, 1568, 1450, 1442, 1358, 1261, 1059, 791, 712.

**HRMS (EI) for C$_{17}$H$_{10}$FN$_3$ (275.0859):** [M]$^+$: 275.0852.

17. Synthesis of 6-(furan-2-yl)pyrido[3,2-f][1,7]naphthyridine (**4h**)

According to **TP10**, the substituted azaphenanthrene derivative **4h** was obtained from **4a** (0.1 mmol) *via* addition of the organolithium reagent **14e** (0.52 M, 1.5 equiv, **TP9**) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt$_3$) furnished **4h** as colorless solid (20 mg, 80%).

**m.p.:** 228 °C.

$^1$H NMR (600 MHz, CDCl$_3$) δ/ppm: 9.15 (dd, $J$ = 4.2, 1.6 Hz, 1H), 9.12 (dd, $J$ = 4.3, 1.8 Hz, 1H), 8.89 (dd, $J$ = 8.4, 1.6 Hz, 1H), 8.79 (dd, $J$ = 8.1, 1.8 Hz, 1H), 8.33 (dd, $J$ = 3.4, 0.7 Hz, 1H), 7.84 – 7.77 (m, 2H), 7.59 (dd, $J$ = 8.1, 4.3 Hz, 1H), 6.68 (dd, $J$ = 3.4, 1.7 Hz, 1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ/ppm: 153.2, 152.7, 152.7, 152.0, 150.8, 150.8, 145.7, 139.9, 131.1, 130.6, 128.9, 125.4, 122.1, 120.5, 117.6, 112.5.

**MS (70 eV, EI) m/z (%):** 248 (24), 247 (100), 246 (12), 220 (10), 219 (36), 218 (21), 191 (11), 44 (24), 43 (17).
IR ATR ν (cm⁻¹): 2956, 2943, 2858, 1737, 1729, 1671, 1601, 1569, 1519, 1450, 1442, 1359, 1261, 1058, 792, 712.

HRMS (EI) for C₁₅H₉N₃O (247.0746): [M]⁺: 247.0745.

18. Synthesis of 6-(thiophen-2-yl)pyrido[3,2-f][1,7]naphthyridine (4i)

According to TP10, the substituted azaphenanthrene derivative 4i was obtained from 4a (0.1 mmol) *via* addition of the organolithium reagent 14f (0.64 M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt₃) furnished 4i as white solid (12 mg, 46%).

m.p.: 221 - 223 °C.

¹H NMR (600 MHz, CDCl₃) δ/ppm: 9.21 – 9.18 (m, 1H), 9.13 (d, J = 3.9 Hz, 1H), 8.97 (d, J = 3.7 Hz, 1H), 8.93 – 8.90 (m, 1H), 8.84 – 8.80 (m, 1H), 7.84 (dd, J = 8.4, 4.2 Hz, 1H), 7.68 (d, J = 5.0 Hz, 1H), 7.60 (dd, J = 8.0, 4.3 Hz, 1H), 7.28 – 7.26 (m, 1H).

¹³C NMR (150 MHz, CDCl₃) δ/ppm: 156.5, 153.2, 152.8, 150.3, 140.7, 140.0, 133.7, 133.1, 131.3, 130.7, 128.9, 127.7, 125.5, 121.9, 117.8.

MS (70 eV, EI) m/z (%): 264 (18), 263 (100), 262 (61).

IR ATR ν (cm⁻¹): 2924, 2853, 1569, 1551, 1506, 1447, 1360, 1223, 1042, 848, 786, 714, 673.

HRMS (EI) for C₁₅H₉N₃S (263.0517): [M]⁺: 263.0512.

19. Synthesis of 6-(benzofuran-2-yl)pyrido[3,2-f][1,7]naphthyridine (4j)

According to TP10, the substituted azaphenanthrene derivative 4j was obtained from 4a (0.1 mmol) *via* addition of the organolithium reagent 14g (0.64 M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt₃) furnished 4j as colorless solid (10 mg, 34%).

m.p.: 219 - 223 °C.
\(^1\)H NMR (600 MHz, CDCl\(_3\)) δ/ppm: 9.23 (dd, J = 4.2, 1.7 Hz, 1H), 9.19 (dd, J = 4.3, 1.8 Hz, 1H), 8.96 (dd, J = 8.4, 1.6 Hz, 1H), 8.86 (dd, J = 8.1, 1.8 Hz, 1H), 8.81 (s, 1H), 7.88 (dd, J = 8.4, 4.2 Hz, 1H), 7.80 – 7.77 (m, 1H), 7.76 – 7.72 (m, 1H), 7.66 (dd, J = 8.2, 4.3 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.33 – 7.28 (m, 1H).

\(^1^3\)C NMR (150 MHz, CDCl\(_3\)) δ/ppm: 155.7, 153.1, 152.9, 152.3, 151.9, 150.9, 140.5, 131.2, 130.8, 129.2, 129.0, 126.8, 125.5, 123.2, 122.7, 122.6, 118.0, 116.7, 112.5.

MS (70 eV, EI) m/z (%): 298 (21), 297 (100), 296 (28), 269 (10), 268 (11).

IR ATR ν (cm\(^{-1}\)): 2923, 2853, 1595, 1561, 1513, 1462, 1449, 1364, 1343, 1261, 1166, 983, 789, 751, 694.

HRMS (EI) for C\(_{19}\)H\(_{11}\)N\(_3\)O (297.0902): [M]+: 297.0898.

20. Synthesis of 6-(benzo[b]thiophen-2-yl)pyrido[3,2-f][1,7]naphthyridine (4k)

According to TP10, the substituted azaphenanthrene derivative 4k was obtained from 4a (0.1 mmol) via addition of the organolithium reagent 14h (0.78 M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt\(_3\)) furnished 4k as colorless solid (16 mg, 51%).

m.p.: 215 - 216 °C.

\(^1\)H NMR (600 MHz, CDCl\(_3\)) δ/ppm: 9.32 (s, 1H), 9.20 (dd, J = 4.1, 1.4 Hz, 1H), 9.14 (dd, J = 4.1, 1.6 Hz, 1H), 8.89 (dd, J = 8.2, 1.5 Hz, 1H), 8.80 (dd, J = 8.1, 1.6 Hz, 1H), 7.98 – 7.91 (m, 2H), 7.82 (dd, J = 8.3, 4.2 Hz, 1H), 7.60 (dd, J = 8.2, 4.3 Hz, 1H), 7.44 – 7.36 (m, 2H).

\(^{13}\)C NMR (150 MHz, CDCl\(_3\)) δ/ppm: 156.4, 152.9, 152.9, 150.4, 143.6, 141.5, 140.5, 140.2, 131.3 (2C), 130.7, 128.9, 126.0, 125.5, 125.4, 124.4, 122.4, 122.3, 118.1.

\(^{13}\)C NMR (200 MHz, CDCl\(_3\)) δ/ppm: 156.5, 152.7, 152.7, 150.5, 150.4, 143.6, 141.5, 140.5, 140.2, 131.6, 131.5, 130.8, 128.9, 126.1, 125.6, 125.4, 124.4, 122.4, 122.3, 118.2.

MS (70 eV, EI) m/z (%): 314 (26), 313 (100), 312 (53), 156 (15).

IR ATR ν (cm\(^{-1}\)): 3056, 2925, 2856, 1711, 1594, 1552, 1564, 1552, 1519, 1456, 1445, 1357, 1342, 1260, 1207, 1172, 1154, 954, 784, 775, 728, 712, 687.

HRMS (EI) for C\(_{19}\)H\(_{11}\)N\(_3\)S (313.0674): [M]+: 313.0666.
21. Synthesis of 1-(pyrido[3,2-f][1,7]naphthyridin-6-yl)ethanone (4I)

According to TP10, the substituted azaphenanthrene derivative 4I was obtained from 4a (0.1 mmol) via addition of the organolithium reagent 14i (0.91 M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. After aqueous workup and extraction with EtOAc, all solvents were removed in vacuo. The crude was then re-dissolved in 2 mL of a mixture of methanol and 2 M aq. HCl (40:1, 0.05 M) and stirred at room temperature overnight. After aqueous workup, the crude was extracted with EtOAc and flash column chromatography (EtOAc + 5% NEt₃) furnished 4I as colorless solid (20 mg, 90%).

m.p.: 147 °C.

$\text{H NMR (800 MHz, CDCl}_3\text{)} \delta/\text{ppm}: 2.94 (s, 3 H), 7.75 (dd, J = 8.1, 4.3 Hz, 1 H), 7.85 (dd, J = 8.4, 4.2 Hz, 1 H), 8.91 (dd, J = 8.2, 1.7 Hz, 1 H), 8.94 (dd, J = 8.4, 1.4 Hz, 1 H), 9.16 (dd, J = 4.2, 1.5 Hz, 1 H), 9.20 (dd, J = 4.1, 1.5 Hz, 1 H).

$\text{C NMR (200 MHz, CDCl}_3\text{)} \delta/\text{ppm}: 201.7, 162.2, 153.0, 152.2, 151.9, 139.3, 131.7, 130.6, 129.3, 126.1, 123.7, 119.2, 30.0.

MS (70 eV, EI) m/z (%): 224 (15), 223 (100), 195 (30), 181 (26), 180 (80), 154 (14), 153 (18), 126 (18), 43 (16).

IR ATR υ (cm$^{-1}$): 2928, 2360, 2338, 1714, 1601, 1567, 1455, 1442, 1378, 1346, 1264, 1210, 1152(w), 904, 789, 700.

HRMS (EI) for C$_{13}$H$_9$N$_3$O (223.0746): [M]$^+$_: 223.0740.

22. Synthesis of 6-butylpyrido[3,2-f][1,7]naphthyridine (4m)

According to TP10, the substituted azaphenanthrene derivative 4m was obtained from 4a (0.1 mmol) via addition of the organolithium reagent 14j (2.43M, 1.5 equiv, TP9) and subsequent chloranil-mediated aromatization. Flash column chromatography (EtOAc + 5% NEt₃) furnished 4m as colorless solid (18 mg, 76%).
m.p.: 131 °C.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$/ppm: 9.12 (dd, $J = 4.3$, 1.6 Hz, 1H), 9.10 (dd, $J = 4.4$, 1.8 Hz, 1H), 8.88 (ddd, $J = 8.3$, 1.6, 0.3 Hz, 1H), 8.83 (ddd, $J = 8.5$, 1.7, 0.4 Hz, 1H), 7.79 (dd, $J = 8.3$, 4.3 Hz, 1H), 7.60 (dd, $J = 8.1$, 4.4 Hz, 1H), 3.70 – 3.64 (m, 2H), 2.07 – 2.00 (m, 2H), 1.56 (q, $J = 7.5$ Hz, 2H), 1.01 (t, $J = 7.4$ Hz, 3H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$/ppm: 169.7, 153.2, 152.1, 150.7, 141.4, 131.4, 130.5, 127.9, 125.4, 122.0, 117.7, 34.6, 30.9, 23.2, 14.3.

MS (70 eV, EI) m/z (%): 237 (45), 211 (15), 210 (23), 209 (20), 208 (100), 207 (42), 206 (17), 196 (53), 195 (20), 194 (25), 182 (27), 181 (26), 180 (25), 155 (12), 71 (13), 57 (21), 43 (13).

IR ATR $\nu$ (cm$^{-1}$): 2956, 2943, 2858, 1737, 1729, 1671, 1601, 1569, 1519, 1450(s), 1442, 1359, 1261, 1058, 792, 712.

HRMS (EI) for C$_{15}$H$_{15}$N$_3$ (237.1266): [M]$^+$: 237.1274.
E) NMR spectra

1. 3-Iodo-2-methylpyridine (8a)
2. 6-Chloro-3-iodo-2-methylpyridine (8b)
3. 2-Chloro-2'-methyl-3,3'-bipyridine (6a)
4. 2,5-Dichloro-2'-methyl-3,3'-bipyridine (6b)
5. 2',6-Dichloro-2-methyl-3,3'-bipyridine (6c)
6. 2-Chloro-2\textsuperscript{a}-(chloromethyl)-3,3\textsuperscript{a}\textsuperscript{-bipyridine (10a)
7. 2,5-Dichloro-2'-(chloromethyl)-3,3'-bipyridine (10b)
8. 2',6-Dichloro-2-(chloromethyl)-3,3'-bipyridine (10c)
9. 2-((2'-Chloro-[3,3'-bipyridin]-2-yl)methyl)isoindoline-1,3-dione (12a)
10. 2-((2',5'-Dichloro-[3,3'-bipyridin]-2-yl)methyl)isoindoline-1,3-dione (12b)
11. 2-((2',6-Dichloro-[3,3'-bipyridin]-2-yl)methyl)isoindoline-1,3-dione (12c)
12. Pyrido[3,2-\textit{f}][1,7]napthyridine (4a)
13. 2-Chloropyrido[3,2-\(f\)][1,7]naphthyridine (4b)
14. 8-Chloropyrido[3,2-\(f\)][1,7]naphthyridine (4c)
15. 6-Phenylpyrido[3,2-\text{f}][1,7]naphthyridine (4d)
16. 6-(4-(Trifluoromethyl)phenyl)pyrido[3,2-f][1,7]naphthyridine (4e)
17. 6-(4-(Trifluoromethyl)phenyl)pyrido[3,2-f][1,7]naphthyridine (4f)
18. 6-(3-Fluorophenyl)pyrido[3,2-f][1,7]naphthyridine (4g)
19. 6-(Furan-2-yl)pyrido[3,2-f][1,7]naphthyridine (4h)
20. 6-(Thiophen-2-yl)pyrido[3,2-f][1,7]naphthyridine (4i)
21. 6-(Benzofuran-2-yl)pyrido[3,2-f][1,7]naphthyridine (4j)
22. 6-(Benzo[b]thiophen-2-yl)pyrido[3,2-\gamma][1,7]naphthyridine (4k)
23. 1-(Pyrido[3,2-$f$][1,7]naphthyridin-6-yl)ethanone (41)
24. 6-Butylpyrido[3,2-f][1,7]naphthyridine (4m)
F) Optical characterization

All optical measurements were performed under argon using 50 µM 1,4-dioxane solutions of the respective materials. UV-Vis spectra were recorded using a Perkin-Elmer Lambda 1050 spectrometer equipped with a 150 mm InGaAs integrating sphere.

Photoluminescence (PL) measurements were performed using Photon Technology International QuantaMaster 40 spectrometer (300 nm excitation) or a home-built setup consisting of a Horiba Jobin Yvon iHR 320 monochromator equipped with a photomultiplier tube and a liquid N₂-cooled InGaAs detector (365 nm excitation, photon flux $4.9 \times 10^{17}$ s$^{-1}$ cm$^{-2}$).

Photoluminescence quantum yield (PLQY) measurements were performed using a 150 mm integrating sphere and applying the method outlined by de Mello et al.$^1$ A collimated LED (365 nm, photon flux $4.9 \times 10^{17}$ s$^{-1}$ cm$^{-2}$) equipped with a 400 nm shortpass filter was used as excitation source.

Time-correlated single photon counting (TCSPC) measurements were performed using a PicoQuant FluoTime 300 spectrometer equipped with a 403 nm picosecond diode laser (pulse power 0.3 µJ cm$^{-2}$).
G) UV-VIS spectra

Figure S1. (a)-(c) UV-VIS spectra of the substituted pyridonaphthyridines. The spectra were normalized to the low-energy double peak absorption feature for clarity. (d)-(f) The molar extinction coefficients derived from the UV-VIS spectra of the respective compounds.
H) Photoluminescence spectra

Figure S2. (a)-(c) Normalized photoluminescence spectra of the substituted pyridonaphthyridines recorded upon photoexcitation at 300 nm (4a) or 365 nm (4d, 4h-k).
I) Photoluminescence quantum yields

Photoluminescence quantum yields (PLQY) were calculated from three measurements per sample:\(^6\)

\(a\) The empty integrating sphere
\(b\) Sample inside the integrating sphere, but not directly illuminated.
\(c\) Sample inside the integrating sphere, directly illuminated.

The PLQY was then calculated as

\[
PLQY = \frac{P_c - (1 - A)P_b}{L_a A}
\]

with

\[
A = \left(1 - \frac{L_c}{L_b}\right)
\]

\(L_a, L_b, L_c, P_b, P_c\) are the integrated photon counts per energy interval in the excitation \((L)\) and PL \((P)\) range during experiments \(a, b,\) and \(c,\) respectively.

Table S1. PLQYs of the substituted pyridonaphthyridines.

| Sample | PLQY / % |
|--------|----------|
| 4d     | 23 ± 4   |
| 4h     | 11 ± 2   |
| 4j     | 10 ± 2   |
| 4i     | 8 ± 2    |
| 4k     | 1.3 ± 0.3|

The PLQY of compound 4a could not be determined due to its low absorption coefficient throughout the excitation range (~330-380 nm).

\(^6\) J. C. de Mello, H. F. Wittmann, R. H. Friend, *Adv. Mater.* **1997**, *9*, 230.
J) Time-correlated single photon counting traces

**Figure S3.** Time-correlated single photon counting (TCSPC) traces of compounds (a) 4h, (b) 4j, (c) 4i, and (d) 4k. Sample excitation was achieved by a picosecond diode laser at 403 nm. Since compounds 4a and 4d do not absorb at this wavelength, no TCSPC data could be recorded for these materials.