Supporting Information
for DOI: 10.1055/s-0030-1258081
© Georg Thieme Verlag KG Stuttgart · New York 2010
Supporting Information

Efficient Synthesis of Phenanthridines Using Hendrickson Reagent-Initiated Cascade Reaction under Mild Conditions

Jie Xi, Qing-Li Dong, Guan-Sai Liu, Shaozhong Wang, Lin Chen, Zhu-Jun Yao

a Nanjing National Laboratory of Microstructures, School of Chemistry and Chemical Engineering, Nanjing University, 22 Hankou Road, Nanjing, Jiangsu 210093, China.
b School of Chemistry and Biotechnology, Yunnan Nationalities University, Kunming, Yunnan 650031, China

Email: yaoz@nju.edu.cn

List of contents

1. Experimental details and characterizations of compounds………………………………..S-2 to S-11
2. NMRs copies of new compounds…………………………………………………………..S-11 to S-26
1. Experimental details and characterizations of compounds

1-1. General procedure for the synthesis of substrates 4a-4j via Suzuki coupling

2-Aminodiphenyl (4a): To three-necked flask under nitrogen atmosphere was added 2-iodoaniline (219 mg, 1 mmol), phenylboronic acid (134 mg, 1.1 mmol), Pd(PPh₃)₄ (58 mg, 0.15 mmol), benzene (15 mL), EtOH (0.75 mL), 2M aq. Na₂CO₃ (1.5 mL, 3 mmol). The reaction mixture was stirred at 80 °C for 12 h. After completion of the reaction, the solvent was removed under reduced pressure. The residue was diluted with H₂O (15 mL), and then the mixture was extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄ and concentrated. The residue was purified by column chromatography on silica gel afforded 4a (135 mg, 80%). ¹H NMR (CDCl₃, 300 MHz): δ 7.54-7.46 (4H, m), 7.43-7.36 (1H, m), 7.25-7.17 (2H, m), 6.89 (1H, td, J₁ = 7.5 Hz, J₂ = 0.9 Hz), 6.81 (1H, d, J = 7.8 Hz), 3.76 (2H, s). ES-IMS (m/z): 170 (M+H⁺).

Compounds 4b-4j were prepared using the above procedure by replacing phenylboronic acid with 4-methoxyphenylboronic acid, 3-methoxyphenylboronic acid, 4-methylphenylboronic acid, 3,4-dimethoxyphenylboronic acid, 2-methoxyphenylboronic acid, 4-tert-butylphenylboronic acid, 4-biphenylboronic acid, 4-bromophenylboronic acid and 3-nitrophenylboronic acid, respectively.

2-(4-Methoxyphenyl)aniline (4b): 70% yield. ¹H NMR (CDCl₃, 300 MHz): δ 7.40 (2H, d, J = 8.1 Hz), 7.18-7.11 (2H, m), 7.00 (2H, d, J = 8.4 Hz), 6.86-6.76 (2H, m), 3.86 (3H, s), 3.75 (2H, s). ESI-MS (m/z): 200 (M+H⁺).

2-(3-Methoxyphenyl)aniline (4c): 72% yield. ¹H NMR (CDCl₃, 300 MHz): δ 7.39 (1H, t, J = 8.1 Hz), 7.22-7.16 (2H, m), 7.09-7.02 (2H, m), 6.95-6.80 (1H, m), 6.80-6.77 (1H, m), 3.85 (3H, s), 3.72 (2H, s). ESI-MS (m/z): 200 (M+H⁺).

2-(3,4-Dimethoxyphenyl)aniline (4e): 88% yield. ¹H NMR (CDCl₃, 300 MHz): δ 7.19-7.12 (2H, m), 7.03-6.93 (3H, m), 6.82 (1H, td, J₁ = 7.5 Hz, J₂ = 1.2 Hz), 6.79-6.75 (1H, m), 3.93 (3H, s), 3.90 (3H, s), 3.79 (2H, s). ESI-MS (m/z): 230 (M+H⁺).

2-(2-Methoxyphenyl)aniline (4f): 72% yield. ¹H NMR (DMSO-d₆, 300 MHz): δ 7.34 (1H, td, J₁ = 7.5 Hz, J₂ = 0.9 Hz), 7.15-7.07 (2H, m), 7.04-6.98 (2H, m), 6.89 (1H, dd, J₁ = 7.5 Hz, J₂ = 1.5 Hz), 6.71 (1H, dd, J₁ = 8.1 Hz, J₂ = 0.6 Hz), 6.63-6.59 (1H, m), 4.45 (2H, s), 3.73 (3H, s). ESI-MS (m/z): 200 (M+H⁺).

2-(4-tert-Butylphenyl)aniline (4g): 91% yield. ¹H NMR (DMSO-d₆, 300 MHz): δ 7.48-7.44 (2H, m), 7.37-7.32 (2H, m), 7.02 (1H, td, J₁ = 7.2 Hz, J₂ = 1.5 Hz), 6.97 (1H, dd, J₁ = 7.8 Hz, J₂ = 1.5 Hz), 6.74 (1H, dd, J₁ = 8.1 Hz, J₂ = 0.9 Hz), 6.62 (1H, td, J₁ = 7.5 Hz, J₂ = 1.5 Hz), 4.72 (2H, s), 1.32 (9H, s). ESI-MS (m/z): 226 (M+H⁺).

2-(4-Phenylphenyl)aniline (4h):

584% yield. 1H NMR (DMSO-d$_6$, 300 MHz): $\delta$ 7.80-7.74 (4H, m), 7.59-7.50 (4H, m), 7.45-7.39 (1H, m), 7.14-7.06 (2H, m), 6.82 (1H, d, $J=7.8$ Hz), 6.70 (1H, td, $J=7.8$ Hz, $J=1.2$ Hz), 4.87 (2H, s). ESI-MS (m/z): 246 (M+H$^+$).

4'-Bromo-biphenyl-2-ylamine (4i):

88% yield. 1H NMR (DMSO-d$_6$, 300 MHz): $\delta$ 7.64-7.58 (2H, m), 7.40-7.35 (2H, m), 7.05 (1H, td, $J=7.5$ Hz, $J=1.8$ Hz), 6.96 (1H, dd, $J=7.8$ Hz, $J=0.9$ Hz), 6.75 (1H, dd, $J=8.1$ Hz, $J=0.9$ Hz), 6.82 (1H, d, $J=7.8$ Hz, $J=0.9$ Hz), 6.70 (1H, td, $J=7.8$ Hz, $J=1.2$ Hz), 4.82 (2H, s). ESI-MS (m/z): 248 (M+H$^+$).

2-(3-Nitrophenyl)aniline (4j):

71% yield. 1H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.35 (1H, t, $J=1.8$ Hz), 8.22-8.18 (1H, m), 7.83 (1H, dt, $J=7.8$ Hz, $J=1.2$ Hz), 7.62 (1H, t, $J=7.8$ Hz), 7.27-7.19 (1H, m), 7.13 (1H, dd, $J=7.8$ Hz, $J=1.5$ Hz), 6.87 (1H, td, $J=7.5$ Hz, $J=1.2$ Hz), 6.81 (1H, dd, $J=8.1$ Hz, $J=0.9$ Hz), 3.77 (2H, s). ESI-MS (m/z): 215 (M+H$^+$).

1-2. General procedure for the synthesis of amides 1a-1r.

N-(2-Phenylphenyl)acetamide (1a): To a solution of 4a (169 mg, 1 mmol) in CH$_2$Cl$_2$ (5 mL) was added pyridine (0.088 mL, 1.1 mmol) and acetyl chloride (0.078 mL, 1.1 mmol) at 0 °C under nitrogen atmosphere. The reaction mixture was warmed to rt and stirred until completion of the reaction. The solvent was removed in vacuo. The residue was diluted with H$_2$O (15 mL), and then extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated. The residue was purified by column chromatography on silica gel afforded 1a (174 mg, 83%).

8 1H NMR (CDCl$_3$, 300 MHz): $\delta$ 8.26 (1H, d, $J=8.4$ Hz), 7.53-7.34 (6H, m), 7.27-7.15 (3H, m), 2.02 (3H, s). ESI-MS (m/z): 212 (M+H$^+$).

Compounds 1b-1j were prepared using the above procedure by replacing 4a with 4b, 4c, 4d, 4e, 4f, 4g, 4h, 4i and 4j, respectively. Compounds 1l-1p were prepared using the above procedure by replacing acetyl chloride with pivaloyl chloride, 3-ethoxy-acryloyl chloride, benzoyl chloride, p-anisoyl chloride and 4-nitrobenzoyl chloride, respectively.

N-(3'-Methoxy-biphenyl-2-yl)-acetamide (1c):

991% yield. 1H NMR (DMSO-d$_6$, 300 MHz): $\delta$ 9.23 (1H, s), 7.47 (1H, d, $J=7.2$ Hz), 7.38-7.27 (4H, m), 6.96-6.92 (3H, m), 3.78 (3H, s), 1.89 (3H, s). ESI-MS (m/z): 242 (M+H$^+$).

N-(4'-Methyl-biphenyl-2-yl)-acetamide (1d):

986% yield. 1H NMR (DMSO-d$_6$, 300 MHz): $\delta$ 9.19 (1H, s), 7.45 (1H, d, $J=7.5$ Hz), 7.35-7.22 (7H, m), 2.35 (3H, s), 1.89 (3H, s). ESI-MS (m/z): 226 (M+H$^+$). (Yield = 86%).

N-(3',4'-Dimethoxy-biphenyl-2-yl)-acetamide (1e):

92% yield. mp: 168-172 °C. IR (KBr): 3373, 2955, 1688, 1517, 1241, 821, 768 cm$^{-1}$. 1H NMR (DMSO-d$_6$, 300 MHz): $\delta$ 9.18 (1H, s), 7.48 (1H, d, $J=7.8$ Hz, $J=1.2$ Hz), 7.38-7.27 (4H, m), 6.96-6.92 (3H, m), 3.78 (3H, s), 1.89 (3H, s). ESI-MS (m/z): 246 (M+H$^+$).

---

\[ d, J = 6.9 \text{ Hz}, 7.33-7.22 \ (3H, m), 7.03 \ (1H, d, J = 8.4 \text{ Hz}), 6.95 \ (1H, d, J = 2.1 \text{ Hz}), 6.91 \ (1H, dd, J_1 = 8.4 \text{ Hz}, J_2 = 2.1 \text{ Hz}), 3.79 \ (3H, s), 3.76 \ (3H, s), 1.92 \ (3H, s). \]

\[ 1^1\text{C NMR (CDCl}_3, 75 \text{ MHz): } \delta 168.2, 149.4, 148.9, 135.0, 132.0, 130.7, 130.1, 128.2, 124.3, 121.5, 121.5, 112.5, 111.7, 56.0, 56.0, 24.6. \]

ESI-MS (m/z): 272 (M+H+). Anal. calcd. for C16H17NO3: C, 70.83; H, 6.32; N, 5.16; found: C, 70.81; H, 6.21; N, 5.09.

\[ \text{N-(2'-Methoxy-biphenyl-2-yl)-acetamide (1f): } 989\% \text{ yield. } \]

\[ 1^1\text{H NMR (DMSO-d}_6, 300 \text{ MHz): } \delta 8.67 \ (1H, s), 7.58 \ (1H, d, J = 7.8 \text{ Hz}), 7.47 \ (1H, d, J = 1.5 \text{ Hz}), 7.34-7.28 \ (1H, m), 7.19-7.18 \ (2H, m), 7.13 \ (1H, dd, J_1 = 7.5 \text{ Hz}, J_2 = 1.5 \text{ Hz}), 7.09 \ (1H, d, J = 7.8 \text{ Hz}), 7.02 \ (1H, dd, J_1 = 7.5 \text{ Hz}, J_2 = 0.9 \text{ Hz}), 3.71 \ (3H, s), 1.82 \ (3H, s). \]

ESI-MS (m/z): 242 (M+H+).

\[ \text{N-(4'-tert-Butyl-biphenyl-2-yl)-acetamide (1g): } 980\% \text{ yield. } \]

\[ 1^1\text{H NMR (CDCl}_3, 300 \text{ MHz): } \delta 8.27 \ (1H, d, J = 8.1 \text{ Hz}), 7.51 \ (2H, d, J = 8.1 \text{ Hz}), 7.39-7.16 \ (6H, m), 2.05 \ (3H, s), 1.39 \ (9H, s). \]

ESI-MS (m/z): 268 (M+H+).

\[ \text{o-(4-Biphenylyl)-acetanilide (1h): } 84\% \text{ yield. } \]

\[ 1^1\text{H NMR (CDCl}_3, 300 \text{ MHz): } \delta 8.28 \ (1H, d, J = 8.1 \text{ Hz}), 7.61 \ (2H, d, J = 8.4 \text{ Hz}), 7.41-7.35 \ (1H, m), 7.26-7.18 \ (4H, m), 7.03 \ (1H, s), 2.04 \ (3H, s). \]

ESI-MS (m/z): 288 (M+H+).

\[ \text{N-(4'-Bromo-biphenyl-2-yl)-acetamide (1i): } 80\% \text{ yield. } \]

\[ 1^1\text{H NMR (CDCl}_3, 300 \text{ MHz): } \delta 8.18 \ (1H, d, J = 8.1 \text{ Hz}), 7.73 \ (2H, d, J = 8.4 \text{ Hz}), 7.69-7.65 \ (2H, m), 7.53-7.45 \ (4H, m), 7.43-7.36 \ (2H, m), 7.32-7.02 \ (3H, m), 2.06 \ (3H, s). \]

ESI-MS (m/z): 290 (M+H+).

\[ \text{N-(3'-Nitro-biphenyl-2-yl)-acetamide (1j): } 92\% \text{ yield. Mp. 122-124 °C. IR (KBr): 3262, 3038, 2361, 1658, 1527, 1344, 1293, 1098, 900, 763, 741, 685, 601 cm}^{-1}. \]

\[ 1^1\text{H NMR (CDCl}_3, 300 \text{ MHz): } \delta 8.21-8.17 \ (2H, m), 7.90 \ (1H, d, J = 8.1 \text{ Hz}), 7.71 \ (1H, dt, J_1 = 7.8 \text{ Hz}, J_2 = 1.5 \text{ Hz}), 7.65-7.58 \ (1H, m), 7.42-7.36 \ (1H, m), 7.30-7.23 \ (3H, m), 1.99 \ (3H, s). \]

\[ 1^1\text{C NMR (CDCl}_3, 75 \text{ MHz): } \delta 168.9, 148.2, 140.3, 135.2, 132.3, 132.3, 130.0, 129.6, 129.2, 125.8, 124.7, 123.8, 122.4, 23.7. \]

ESI-MS (m/z): 257 (M+H+).

\[ 2,2\text{-Dimethyl-N-(4'-methoxy-biphenyl-2-yl)-propionamide (1l): } 99\% \text{ yield. Mp. 69-71 °C. IR (KBr): 3273, 3062, 2958, 1639, 1526, 1240, 1174, 833, 758 cm}^{-1}. \]

\[ 1^1\text{H NMR (CDCl}_3, 300 \text{ MHz): } \delta 8.36 \ (1H, d, J = 8.4 \text{ Hz}), 7.51 \ (1H, s), 7.37-7.26 \ (1H, m), 7.28 \ (2H, d, J = 9.0 \text{ Hz}), 7.21 \ (1H, dd, J_1 = 7.8 \text{ Hz}, J_2 = 1.8 \text{ Hz}), 7.15-7.10 \ (1H, m), 7.07 \ (2H, d, J = 8.7 \text{ Hz}), 3.87 \ (3H, s), 1.12 \ (9H, s). \]

\[ 1^1\text{C NMR (CDCl}_3, 75 \text{ MHz): } \delta 176.3, 159.4, 135.4, 131.8, 130.6, 130.2, 128.3, 123.9, 120.8, 114.5, 55.4, 39.9, 27.5. \]

ESI-MS (m/z): 284 (M+H+). Anal. calcd. for C18H21NO2: C, 76.29; H, 7.47; N, 4.94; found: C, 76.21; H, 7.49; N, 4.79.

\[ 3\text{-Ethoxy-N-(4'-methoxy-biphenyl-2-yl)-acrylamide (1m): } 73\% \text{ Yield. Mp. 127-130 °C. IR (KBr): 3238, 2985, 1653, 1527, 1243, 1154, 825, 750 cm}^{-1}. \]

\[ 1^1\text{H NMR (DMSO-d}_6, 300 \text{ MHz): } \delta 8.87 \ (1H, s), 7.54 \ (1H, d, J = 7.8 \text{ Hz}), 7.35 \ (1H, d, J = 12.3 \text{ Hz}), 7.32-7.21 \ (5H, m), 7.00 \ (2H, dd, J_1 = 6.9 \text{ Hz}, J_2 = 2.1 \text{ Hz}), 5.48 \ (1H, d, J = 12.6 \text{ Hz}), 3.87 \ (2H, q, J = 6.9 \text{ Hz}), 3.33 \ (3H, s), 1.23 \text{ Hz}. \]


\[ \text{PCT Int. Appl., 2002064562 (2002).} \]
(3H, t, J = 6.9 Hz). $^{13}$C NMR (CDCl$_3$, 300 MHz): δ 165.2, 161.0, 159.3, 135.3, 130.5, 130.4, 130.2, 128.1, 124.0, 121.8, 114.5, 99.1, 67.4, 55.4, 14.7, 14.6. ESI-MS (m/z): 298 (M+H$^+$$)$. Anal. calcd. for C$_{18}$H$_{19}$NO$_3$: C, 72.71; H, 6.44; N, 4.71; found: C, 72.73; H, 6.29; N, 4.79.

N-(4'-Methoxy-biphenyl-2-yl)-benzamide (1n):$^{12}$ 92% yield. $^1$H NMR (CDCl$_3$, 300 MHz): δ 9.78 (1H, s), 7.80 (2H, d, J = 7.2 Hz), 7.49-7.36 (9H, m), 6.94 (2H, d, J = 8.7Hz), 3.74 (3H, s). ESI-MS (m/z): 304 (M+H$^+$).

4-Methoxy-N-(4'-methoxy-biphenyl-2-yl)-benzamide (1o):$^{12}$ 83% yield. $^1$H NMR (CDCl$_3$, 300 MHz): δ 8.51 (1H, t, J = 8.4 Hz), 7.95 (1H, s), 7.59 (2H, dt, J$_1$ = 9.6 Hz, J$_2$ = 3.0 Hz), 7.43-7.34 (3H, m), 7.28-7.25 (1H, m), 7.18 (1H, td, J$_1$ = 7.2 Hz, J$_2$ = 1.2 Hz), 7.04 (2H, dt, J$_1$ = 9.6 Hz, J$_2$ = 3.0 Hz), 6.89 (2H, dt, J$_1$ = 8.7 Hz, J$_2$ = 3.0 Hz), 3.88 (3H, s), 3.34 (3H, s). ESI-MS (m/z): 334 (M+H$^+$).

N-(4'-Methoxy-biphenyl-2-yl)-formamide (1k): To a mixture of HCO$_2$H (0.11 mL, 3 mmol) and ZnO (41 mg, 0.5 mmol) was added 4b (199 mg, 1 mmol). The reaction was then stirred 70 ºC until complete. EtOAc (15 mL) was added and ZnO was removed by filtration. The organic phase was washed with H$_2$O (10 mL x 2) and saturated aqueous NaHCO$_3$ (15 mL), and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent afforded pure product 1k (186 mg, 82%). $^1$H NMR (DMSO-d$_6$, 300 MHz): δ 9.27 (1H, s), 8.17-8.15 (1H, m), 7.88 (1H, d, J = 7.8 Hz), 7.35-7.20 (5H, m), 7.34-7.28 (1H, m), 7.37 (1H, td, J$_1$ = 7.5 Hz, J$_2$ = 1.8 Hz), 7.34-7.28 (5H, m), 7.05-7.00 (2H, m), 3.80 (3H, s). ESI-MS (m/z): 226 (M-H$^-$).

1-3. 2-Iodo-4-nitroaniline (5). To a flask containing a stirring mixture of Ph$_3$P (157 mg, 0.6 mmol) and Br$_2$ (0.03 mL, 0.6 mmol) in dry acetonitrile (5 mL) was added silver nitrate (100 mg, 0.6 mmol) and 2-iodoaniline 3 (110 mg, 0.5 mmol) at room temperature. After 5 min, the reaction mixture was filtered to remove the precipitated AgBr. The solvent was evaporated, and the residue was re-dissolved in CH$_2$Cl$_2$ (10 mL). The organic solution was washed with 5% aq. NaHCO$_3$ (5 mL x 2) and water (5 mL), dried over anhydrous Na$_2$SO$_4$. Removal of the solvent afforded pure product 5 (73 mg, 55%).$^{13}$ $^1$H NMR (DMSO-d$_6$, 300 MHz): δ 7.65 (1H, d, J = 2.4 Hz), 7.21 (1H, dd, J$_1$ = 8.7 Hz, J$_2$ = 2.4 Hz), 6.69 (1H, d, J = 8.7 Hz), 5.38 (2H, s). ESI-MS (m/z): 264 (M-H$^-$).

1-4. 4'-Methoxy-5-nitro-biphenyl-2-amine (6). To a three-necked flask under nitrogen atmosphere was added 4-methoxyphenylboronic acid (418 mg, 2.75 mmol), 5 (660 mg, 2.5 mmol), Pd(PPh$_3$)$_4$ (87 mg, 0.075 mmol), benzene (30 mL), EtOH (1.5 mL), and 2M aq. Na$_2$CO$_3$ (3.7 mL, 7.5 mmol). The reaction mixture was stirred at 80 ºC for 12 h. After completion of the reaction, the solvent was removed in vacuo. The solution was diluted with H$_2$O (30 mL), and then extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated. The crude product was purified by column chromatography on silica gel to give 6 (435 mg, 72%).$^{15}$ $^1$H NMR (DMSO-d$_6$, 300 MHz): δ 7.33 (2H, dd, J$_1$ = 6.6 Hz, J$_2$ = 2.4 Hz), 7.21 (1H, dd, J$_1$ = 8.7 Hz, J$_2$ = 2.4 Hz), 6.69 (1H, d, J = 8.7 Hz), 5.38 (2H, s). ESI-MS (m/z): 264 (M-H$^-$).

Hz, $J_2 = 2.1$ Hz), 7.15 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 2.4$ Hz), 7.05 (1H, $d$, $J = 2.4$ Hz), 7.01 (2H, dd, $J_1 = 6.6$ Hz, $J_2 = 2.1$ Hz), 6.70 (1H, $d$, $J = 8.7$ Hz), 4.90 (2H, $s$), 3.79 (3H, $s$). ESI-MS (m/z): 245 (M+H$^+$).

1-5. N-(4'-Methoxy-5-nitro-biphenyl-2-yl)-acetamide (1q). To a solution of 6 (366 mg, 1.5 mmol) in CH$_2$Cl$_2$ (8 mL) was added pyridine (0.12 mL, 1.65 mmol) and acetyl chloride (0.13 mL, 1.65 mmol) at 0 °C under nitrogen atmosphere. The mixture was warmed to rt and stirred until completion of the reaction. The solvent was removed in vacuo. The residue was diluted with H$_2$O (15 mL) and extracted with EtOAc (15 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated. The crude product was purified by column chromatography on silica gel to afford 1q (399 mg, 93%). mp: 140-143 °C. IR (KBr): 3317, 2995, 1765, 1667, 1511, 1460, 1384, 1291, 1240, 1101, 806 cm$^{-1}$. $^1$H NMR (DMSO-d$_6$, 300 MHz): $\delta$ 9.22 (1H, $s$), 7.48 (1H, $d$, $J = 1.8$ Hz), 7.45 (2H, $d$, $J = 6.9$ Hz), 7.32 (2H, dd, $J_1 = 6.6$ Hz, $J_2 = 1.8$ Hz), 7.01 (2H, dd, $J_1 = 6.6$ Hz, $J_2 = 2.1$ Hz), 3.80 (3H, $s$), 1.90 (3H, $s$). $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 168.3, 159.8, 134.1, 133.7, 132.8, 130.9, 130.3, 128.8, 123.0, 116.9, 114.7, 55.4, 24.7. ESI-MS (m/z): 287 (M+H$^+$).

1-6. 4',5-Dimethoxy-biphenyl-2-amine (10). To a flask containing fuming nitric acid (63 mg, 1 mmol) was added sulfuric acid (1 drop) and 3-iodoanisole 7 (234 mg, 1 mmol) under stirring at 0 °C. After completion of the reaction, the solution was diluted with H$_2$O (20 mL), and then extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated to give the crude product 8 (248 mg, 89%), which was used for the next step without any further purification.

To a mixture of product 8 (1.67 g, 6 mmol), Fe (3.36 g, 60 mmol) and ammonium chloride (1.28 g, 24 mmol) was added MeOH (60 mL) and H$_2$O (20 mL). The mixture was then heated in an oil bath at 50 °C. After the reaction completed, the mixture was filtered. The liquid phase was diluted with H$_2$O (100 mL), and then extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated to give crude product 9 (1.41 g, 95%). This material was used for the next step directly.

To three-necked flask containing 4-methoxyphenylboronic acid (836 mg, 5.5 mmol), 9 (5 mmol, 1.24 g), Pd(PPh$_3$)$_4$ (180 mg, 0.15 mmol) under a nitrogen atmosphere was added benzene (60 mL), EtOH (3 mL), and 2M aq. Na$_2$CO$_3$ (7.5 mL, 15 mmol). The reaction mixture was stirred at 80 °C for 12 h. After completion of the reaction, the solvent was removed in vacuo. The residue was diluted with H$_2$O (100 mL), and then extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na$_2$SO$_4$ and concentrated. The residue was purified by column chromatography on silica gel to give 10 (893 mg, 78%, and 45% for three steps). mp: 64-67 °C. IR (KBr): 3435, 3358, 2936, 1604, 1496, 1287, 1240, 1173, 873, 838 cm$^{-1}$. $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 7.40 (2H, $d$, $J = 8.7$ Hz), 7.99 (2H, $d$, $J = 8.7$ Hz), 6.79-6.70 (3H, $m$), 3.86 (3H, $s$), 3.77 (3H, $s$), 3.65 (2H, $s$). $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 158.9, 152.7, 137.3, 131.8, 130.2, 128.5, 116.8, 115.9, 114.2, 114.0, 55.8, 55.3. ESI-MS (m/z): 230 (M+H$^+$). Anal. calcd. for C$_{14}$H$_{15}$NO$_2$: C, 73.34; H, 6.59; N, 6.11; found: C, 73.37; H, 6.57; N, 6.13.

1-7. N-(4',5-Dimethoxy-biphenyl-2-yl)-acetamide (1r). To a solution of 10 (687 mg, 3 mmol) in
CH₂Cl₂ (15 mL) was added pyridine (0.24 mL, 3.3 mmol) and acetyl chloride (0.26 mL, 3.3 mmol) at 0 °C under nitrogen atmosphere. The reaction mixture was warmed to rt and stirred until completion of the reaction. The solvent was removed in vacuo. The residue was diluted with H₂O (30 mL), and then extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄ and concentrated. The crude product was purified by column chromatography on silica gel to afford 1r (723 mg, 89%). mp: 152-155 °C. IR (KBr): 3361, 2965, 1684, 1514, 1268, 1241, 1110, 824, 782 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 7.96 (1H, d, J = 8.7 Hz), 7.28 (1H, d, J = 8.7 Hz), 6.98 (3H, d, J = 8.7 Hz), 6.87 (1H, dd, J₁ = 8.7 Hz, J₂ = 3.0 Hz), 6.77 (1H, d, J = 3.0 Hz), 3.85 (3H, s), 3.79 (3H, s), 1.99 (3H, s). ¹³C NMR (CDCl₃, 75 MHz): δ 168.4, 159.4, 156.5, 134.5, 130.5, 130.3, 128.0, 124.2, 115.6, 114.4, 113.1, 55.5, 55.4, 24.3. Anal. calcd. for C₁₆H₁₇NO₃: C, 70.83; H, 6.32; N, 5.16; found: C, 70.73; H, 6.23; N, 4.99. ESI-MS (m/z): 272 (M+H⁺).

1-8. General procedure for the synthesis of phenanthridine derivatives 2a-2i, 2k-2l-2r.

6-Methyl-phenanthridine (2a): To a solution of Ph₃PO (250 mg, 0.9 mmol) in anhydrous CH₂Cl₂ (3 mL) was added Tf₂O (0.078 mL, 0.45 mmol) dropwise under nitrogen atmosphere at 0 °C. After 15 min, amide 1a (64 mg, 0.3 mmol) in anhydrous CH₂Cl₂ (2 mL) was added. The reaction was warmed to rt and stirred at this temperature until completion of the reaction. Saturated aq. NaHCO₃ solution was added to quench the reaction. The mixture was extracted with CH₂Cl₂ (15 x 3 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄ and concentrated. The crude product was purified by column chromatography on silica gel afforded 2a (55 mg, 95%).¹⁶ ¹H NMR (CDCl₃, 300 MHz): δ 8.64 (1H, d, J = 8.4 Hz), 8.55 (1H, d, J = 7.8 Hz), 8.24 (1H, d, J = 7.8 Hz), 8.11 (1H, d, J = 7.8 Hz), 7.88-7.61 (4H, m), 2.98 (3H, s). EI-MS (m/z): 193 (M⁺).

Compounds 2b-2i, 2l-2r were prepared using the above procedure by replacing 1a with 1b, 1c, 1d, 1e, 1f, 1g, 1h, 1i, 1l, 1m, 1n, 1o, 1p, 1q and 1r, respectively.

8-Methoxy-6-methyl-phenanthridine (2b):¹⁷ 95% yield. ¹H NMR (DMSO-d₆, 300 MHz): δ 8.77 (1H, d, J = 9.0 Hz), 8.67 (1H, d, J = 7.2 Hz), 7.97 (1H, d, J = 7.2 Hz), 7.67-7.61 (3H, m), 7.57 (1H, dd, J₁ = 9.0 Hz, J₂ = 2.4 Hz), 3.99 (3H, s), 2.96 (3H, s). ESI-MS (m/z): 224 (M+H⁺).

7-Methoxy-6-methyl-phenanthridine (2ca) and 9-methoxy-6-methyl-phenanthridine (2cb):¹⁸ 2ca: 26% yield. ¹H NMR (DMSO-d₆, 300 MHz): δ 8.96 (1H, dd, J₁ = 8.1 Hz, J₂ = 1.2 Hz), 8.38 (1H, d, J = 8.1 Hz), 7.94 (1H, dd, J₁ = 8.1 Hz, J₂ = 1.2 Hz), 7.83 (1H, t, J = 8.1 Hz), 7.71 (1H, td, J₁ = 6.9 Hz, J₂ = 1.5 Hz), 7.62 (1H, td, J₁ = 6.9 Hz, J₂ = 1.2 Hz), 7.30 (1H, d, J = 8.1 Hz), 4.01 (3H, s), 3.07 (3H, s). ESI-MS (m/z): 254 (M+H⁺). 2cb: 65% yield. ¹H NMR (DMSO-d₆, 300 MHz): δ 9.06 (1H, d, J = 7.2 Hz), 8.60 (1H, d, J = 9.3 Hz), 8.40 (1H, d, J = 2.4 Hz), 8.35 (1H, d, J = 7.2 Hz), 8.00 (1H, td, J₁ = 8.1 Hz, J₂ = 1.2 Hz), 7.92 (1H, td, J₁ = 8.1 Hz, J₂ = 1.2 Hz), 7.63 (1H, dd, J₁ = 9.3 Hz, J₂ = 2.1 Hz), 4.15 (3H, s), 3.29 (3H, s). ESI-MS (m/z): 254 (M+H⁺).

6,8-Dimethyl-phenanthridine (2d):¹⁸ 90% yield. ¹H NMR (DMSO-d₆, 300 MHz): δ 8.74-8.68

(2H, m), 8.11 (1H, s), 7.98 (1H, dd, J1 = 8.4 Hz, J2 = 1.5 Hz), 7.77 (1H, dd, J1 = 8.4 Hz, J2 = 1.5 Hz), 7.73-7.60 (2H, m), 2.95 (3H, s), 2.58 (3H, s). ESI-MS (m/z): 208 (M+H+).

7,8-Dimethoxy-6-methyl-phenanthridine (2e): 87% yield. mp: 245-250 °C. IR (KBr): 3451, 2930, 1645, 1513, 1270, 1151, 808, 759 cm⁻¹. ¹H NMR (DMSO-d6, 300 MHz): δ 8.85 (1H, d, J = 6.9 Hz), 8.16 (1H, s), 8.02 (1H, d, J = 6.6 Hz), 7.85-7.80 (2H, m), 7.65 (1H, s), 4.11 (3H, s), 4.02 (3H, s), 3.08 (3H, s). ¹³C NMR (DMSO-d6, 75 MHz): δ 158.0, 150.8, 130.7, 130.4, 128.5, 124.0, 123.3, 122.0, 119.0, 108.1, 103.7, 57.2, 56.5, 19.9. ESI-MS (m/z): 254 (M+H+).

10-Methoxy-6-methyl-phenanthridine (2f): 91% yield. mp: 103-106 °C. IR (KBr): 3420, 2991, 1637, 1433, 1365, 1109, 756, 713 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 9.43 (1H, dd, J1 = 8.4 Hz, J2 = 0.9 Hz), 8.10 (1H, dd, J1 = 8.1 Hz, J2 = 1.5 Hz), 7.78 (1H, dd, J1 = 8.1 Hz, J2 = 0.9 Hz), 7.72-7.66 (1H, m), 7.61-7.54 (2H, m), 7.24 (1H, d, J = 8.7 Hz), 4.07 (3H, s), 3.00 (3H, s). ¹³C NMR (CDCl₃, 75 MHz): δ 158.4, 158.3, 144.2, 129.1, 128.0, 128.0, 127.5, 126.2, 123.6, 118.7, 111.5, 55.8, 24.3. ESI-MS (m/z): 224 (M+H+).

8-tert-Butyl-6-methyl-phenanthridine (2g): 89% yield. mp: 100-103 °C. IR (KBr): 3416, 2947, 1612, 1430, 1288, 1155, 880, 857, 746, 720 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 8.52 (1H, d, J = 8.7 Hz), 8.49 (1H, dd, J1 = 8.4 Hz, J2 = 1.2 Hz), 8.15 (1H, d, J = 1.8 Hz), 8.09 (1H, dd, J1 = 8.1 Hz, J2 = 0.9 Hz), 7.90 (1H, dd, J1 = 8.7 Hz, J2 = 1.8 Hz), 7.70-7.65 (1H, m), 7.61-7.55 (1H, m), 3.06 (3H, s), 1.47 (9H, s). ¹³C NMR (CDCl₃, 75 MHz): δ 150.9, 150, 143.6, 130.4, 129.3, 128.9, 128.3, 126.3, 125.9, 123.9, 122.2, 122.0, 121.9, 35.2, 31.4, 23.5. ESI-MS (m/z): 254 (M+H+). Anal. calcd. for C₁₈H₁₉N: C, 86.70; H, 7.68; N, 5.62; found: C, 86.63; H, 7.57; N, 5.57.

8-Phenyl-6-methyl-phenanthridine (2h): 98% yield. IR (KBr): 3421, 2927, 2842, 1647, 1399, 1282, 1231, 1170, 1023, 942, 851, 759, 635 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 9.19 (2H, dd, J1 = 6.6 Hz, J2 = 1.8 Hz), 8.89 (1H, s), 8.66 (1H, d, J = 8.4 Hz), 8.25 (1H, d, J = 7.8 Hz), 8.09-8.00 (4H, m), 7.66 (2H, t, J = 7.2 Hz), 7.57 (1H, t, J = 7.2 Hz), 3.43 (3H, s). ¹³C NMR (DMSO-d6, 75 MHz): δ 162.4, 141.4, 138.0, 135.2, 133.0, 132.7, 131.5, 129.9, 129.5, 129.1, 127.8, 127.0, 124.5, 124.1, 123.9, 121.5, 19.8. ESI-MS (m/z): 270 (M+H+).

8-Bromo-6-methyl-phenanthridine (2i): 78% yield. mp: 125-128 °C. IR (KBr): 3419, 2911, 1647, 1570, 1369, 814, 752, 717, 653 cm⁻¹. ¹H NMR (DMSO-d6, 300 MHz): δ 8.78 (1H, d, J = 9.0 Hz), 8.73 (1H, dd, J1 = 8.7 Hz, J2 = 0.9 Hz), 8.47 (1H, d, J = 2.1 Hz), 8.06 (1H, dd, J1 = 8.7 Hz, J2 = 2.1 Hz), 8.00 (1H, dd, J1 = 8.1 Hz, J2 = 0.9 Hz), 7.79-7.74 (1H, m), 7.70-7.64 (1H, m), 2.95 (3H, s). ¹³C NMR (CDCl₃, 75 MHz): δ 157.7, 143.7, 133.6, 131.3, 129.6, 129.1, 129.1, 127.2, 126.8, 124.2, 123.2, 121.8, 121.3, 23.4. ESI-MS (m/z): 273 (M+H+). Anal. calcd. for C₁₄H₁₀BrN: C, 61.79; H, 3.70; N, 5.15; found: C, 61.77; H, 3.67; N, 4.90.

8-Methoxy-6-tert-Butyl-phenanthridine (2j): 93% yield. mp: 109-113 °C. IR (KBr): 3420, 2988, 1612, 1472, 1353, 1211, 1034, 820, 799, 760 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 8.59 (1H, d, J = 9.0 Hz), 8.44 (1H, d, J = 7.8 Hz), 8.12 (1H, d, J = 7.8 Hz), 8.00 (1H, s), 7.67-7.65 (2H, m), 7.43 (1H, dd, J1 = 9.0 Hz, J2 = 2.4 Hz), 4.00 (3H, s), 1.76 (9H, s). ¹³C NMR (CDCl₃, 300 MHz): δ 165.8, 157.3, 142.3, 130.3, 128.3, 127.5, 126.6, 125.6, 124.5, 123.6, 121.2, 119.2, 109.8, 55.5, 40.1, 31.1.
8-Methoxy-6-(2-ethoxy-vinyl)-phenanthridine (2m): 74% yield. IR (KBr): 3410, 2972, 2931, 2390, 2285, 1630, 1556, 1461, 1380, 1175, 1042, 802, 759 cm\(^{-1}\). \(^1\)H NMR (DMSO-\(d_6\), 300 MHz): δ 8.74 (1H, d, \(J = 9.0 \) Hz), 8.61 (1H, dd, \(J_1 = 8.4 \) Hz, \(J_2 = 1.2 \) Hz ), 7.95-7.89 (2H, m), 7.77 (1H, d, \(J = 2.4 \) Hz), 7.63 (1H, td, \(J_1 = 8.1 \) Hz, \(J_2 = 1.5 \) Hz ), 7.58-7.52 (2H, m), 6.89 (1H, d, \(J = 11.7 \) Hz), 4.17 (2H, q, \(J = 7.2 \) Hz), 3.99 (3H, s), 1.35 (3H, t, \(J = 7.2 \) Hz). \(^1\)C NMR (CDCl\(_3\), 300 MHz): δ 158.4, 155.5, 154.5, 143.0, 129.1, 127.5, 127.2, 126.1, 125.6, 123.9, 121.3, 120.4, 106.0, 101.6, 67.2, 55.4, 14.9. ESI-MS (m/z): 280 (M+H\(^+\)).

8-Methoxy-6-phenyl-phenanthridine (2n): \(^2\) 94% yield. \(^1\)H NMR (DMSO-\(d_6\), 300 MHz): δ 8.89 (1H, d, \(J = 9.0 \) Hz), 8.77 (1H, dd, \(J_1 = 9.0 \) Hz, \(J_2 = 2.4 \) Hz), 8.10-8.06 (1H, m), 7.78-7.71 (4H, m), 7.65-7.58 (4H, m), 7.42 (1H, d, \(J = 2.7 \) Hz), 3.81 (3H, s). ESI-MS (m/z): 286 (M+H\(^+\)).

8-Methoxy-6-(4-methoxyphenyl)-phenanthridine (2o): 97% yield. \(^1\)H NMR (CDCl\(_3\), 300 MHz): δ 8.62 (1H, d, \(J = 9.0 \) Hz), 8.53 (1H, d, \(J = 8.7 \) Hz), 8.20 (1H, d, \(J = 8.1 \) Hz), 7.74-7.65 (4H, m), 7.53-7.47 (2H, m), 7.10 (2H, d, \(J = 8.7 \) Hz), 3.92 (3H, s), 3.86 (3H, s). ESI-MS (m/z): 316 (M+H\(^+\)).

8-Methoxy-6-(4-nitrophenyl)-phenanthridine (2p): 75% yield. \(^1\)H NMR (CDCl\(_3\), 300 MHz): δ 8.60 (1H, d, \(J = 9.3 \) Hz), 8.51-8.48 (1H, m), 8.38 (2H, d, \(J = 9.3 \) Hz), 8.15-8.12 (1H, m), 7.89 (2H, d, \(J = 8.1 \) Hz), 7.68-7.65 (2H, m), 7.47 (1H, d, \(J = 9.6 \) Hz), 7.23 (1H, s), 3.78 (3H, s). ESI-MS (m/z): 331 (M+H\(^+\)).

8-Methoxy-6-methyl-2-nitro-phenanthridine (2q): 98% yield. Mp. 150-154 °C. IR (KBr): 3365, 2919, 1614, 1566, 1473, 1382, 1233, 1038, 828, 758 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 300 MHz): δ 8.49 (1H, d, \(J = 1.8 \) Hz), 8.36 (1H, d, \(J = 7.8 \) Hz), 7.90 (1H, d, \(J = 8.7 \) Hz), 7.68 (1H, dd, \(J_1 = 8.7 \) Hz, \(J_2 = 1.8 \) Hz), 7.42 (2H, dd, \(J_1 = 7.8 \) Hz, \(J_2 = 2.1 \) Hz), 3.97 (3H, s), 2.94 (3H, s). \(^1\)C NMR (CDCl\(_3\), 75 MHz): δ 159.1, 158.5, 141.5, 131.0, 130.8, 127.4, 125.6, 125.4, 124.3, 124.1, 121.0, 120.3, 106.9, 55.6, 23.6. ESI-MS (m/z): 269 (M+H\(^+\)).

2,8-Dimethoxy-6-methyl-phenanthridine (2r): 99% yield. mp: 150-154 °C. IR (KBr): 3365, 2919, 1614, 1566, 1473, 1382, 1233, 1038, 828, 758 cm\(^{-1}\). \(^1\)H NMR (CDCl\(_3\), 300 MHz): δ 8.49 (1H, d, \(J = 9.0 \) Hz), 7.98 (1H, d, \(J = 9.0 \) Hz), 7.78 (1H, d, \(J = 2.7 \)Hz), 7.47-7.41 (2H, m), 7.30-7.25 (1H, m), 3.99 (6H, s), 2.97 (3H, s). \(^1\)C NMR (CDCl\(_3\), 75 MHz): δ 158.5, 157.9, 155.1, 138.1, 130.6, 127.2, 126.3, 124.7, 123.9, 120.2, 117.2, 106.5, 102.4, 55.5, 55.4, 23.2. IR (KBr): 3416, 3299, 1692, 1493, 1383, 1226, 1170, 1033, 823, 804 cm\(^{-1}\). ESI-MS (m/z): 254 (M+H\(^+\)). Anal. calcd. for C\(_{16}\)H\(_{15}\)NO\(_2\): C, 75.87; H, 5.97; N, 5.53; found: C, 75.78; H, 6.08; N, 5.51.

1-9. 8-Methoxy-phenanthridine (2k). To a solution of Ph\(_3\)PO (84 mg, 0.3 mmol) in anhydrous CH\(_2\)Cl\(_2\) (3 mL) was added Tf\(_2\)O (0.026 mL, 0.15 mmol) dropwise under nitrogen atmosphere at 0 °C. After 15 min, triethylamine (0.042 mL, 0.3 mmol) was added to the mixture. Then, amide 1k (23 mg, 0.1 mmol) in anhydrous CH\(_2\)Cl\(_2\) (2 mL) was added. The mixture was warmed to rt and stirred until completion of the reaction. Saturated aq. NaHCO\(_3\) was added to quench the reaction.
The whole mixture was extracted with CH₂Cl₂ (15 x 3 mL). The combined organic phases were washed with brine, dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel to afford 2k (6 mg, 30%).¹⁰ ¹H NMR (DMSO-d₆, 300 MHz): δ 7.66 (1H, d, J = 7.8 Hz), 7.60-7.50 (1H, m), 7.51-7.43 (4H, m), 7.11-7.05 (2H, m), 3.83 (3H, s). ESI-MS (m/z): 232 (M+Na⁺).

2. NMR copies of new compounds

(1) Compound 1e
(2) Compound 1j
(3) Compound 11
(4) Compound 1m
(5) Compound 1q
(6) Compound 1r
(7) Compound 2e
(8) Compound 2f
(9) Compound 2g
(10) Compound 2h
(11) Compound 2i
(12) Compound 2′
(13) Compound 2m
(14) Compound 2q

[Chemical structure image]

[Graphical representation of chemical spectra]

S-24
(15) Compound 2r
(16) Compound 10