Mitochondria-targeted Phosphorescent Iridium(III) Complexes for Living Cell Imaging†

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S1. Synthesis

Benzoyl chloride, 2-aminothiophenol, triphenylphosphate and 6-bromocaproic acid were purchased from Sinopharm; 6(5H)-phenanthridinone, 2-benzothiophenylboronic acid and 4,4′-dimethyl-2,2′-bipyridine from Chemlin; 3-bromopropionitrile from J&K Chemical. Other chemicals and solvents were commercially available in analytical purity and used directly except otherwise specified.

2-Phenylbenzothiazole (BT)

BT was synthesized according to Chang et al.† with benzoyl chloride in place of benzaldehyde. Colorless acicular crystal. Yield 95%. GC-MS: m/z (M+) calc 211.05, found 211.1. 1H NMR (400 MHz, CDCl3) δ 8.11 (ddd, J = 8.3, 5.6, 1.2, 0.6 Hz, 3H), 7.92 (ddd, J = 8.0, 1.3, 0.7 Hz, 1H), 7.53-7.48 (m, 4H), 7.40 (ddd, J = 8.0, 7.2, 1.2 Hz, 1H).

6-Chlorophenanthridine

The mixture of 6(5H)-phenanthridone (5.11 g, 26.2 mmol) and phosphorus pentachloride (6.12 g, 29.4 mmol) was refluxed in phosphorus oxychloride (60 ml) (ATTENTION: Phosphorus oxychloride is highly toxic. The operator must be properly protected!!) at 100 °C under N2 protection for 2 h. After removing most solvent, the residue was poured into aqua ammonia generate a solid, and the solid was extracted with ethyl acetate. After drying and evaporation, the obtained solid was purified by silica gel column chromatography (eluent: Hexane/CH2Cl2 = 20 : 1) to give a light yellow powder (5.1 g, yield 91%). GC-MS: m/z ([M-H]-) calc 213.0, found 211.3. 1H NMR (400 MHz, CDCl3) δ 8.60 (d, J = 8.3 Hz, 1H), 8.55-8.45 (m, 2H), 8.09 (dd, J = 8.1, 1.0 Hz, 1H), 7.90 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.79-7.65 (m, 3H).
6-(Benzothien-2-yl)phenanthridine (BTPhen)

BTPhen was synthesized through Suzuki coupling of 6-chlorophenanthridine and 2-benzothienylboronic acid. Light yellow frazil crystal. Yield 95%. GC-MS: m/z (M⁺) calcd 311.1, found 310.1. ¹H NMR (400 MHz, CDCl₃) δ 8.70 (d, J = 8.3 Hz, 1H), 8.65 (d, J = 8.3 Hz, 1H), 8.59 (d, J = 7.8 Hz, 1H), 8.24 (dd, J = 8.2, 1.0 Hz, 1H), 7.97-7.84 (m, 4H), 7.79-7.65 (m, 3H), 7.46-7.38 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 154.26, 143.87, 142.83, 140.95, 140.23, 133.85, 130.97, 130.61, 129.20, 128.22, 127.79, 127.59, 126.24, 125.38, 125.02, 124.73, 124.50, 123.89, 122.65, 122.48, 122.15.

4-(4’-Methyl-2,2’-bipyridin-4-yl)butyric acid (MBBA)

MBBA was synthesized according to Tanaka et al² with 3-bromopropionitrile instead of 5-bromovaleronitrile. White powder. Total yield 23%. ¹H NMR (400 MHz, CDCl₃) δ 8.59 (dd, J = 10.3, 5.0 Hz, 2H), 8.16 (dd, J = 11.0, 0.9 Hz, 2H), 7.17 (td, J = 5.3, 1.3 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.48-2.39 (m, 5H), 2.12-2.02 (m, 2H).

[Ir(bt)₂](μ-Cl)₂ and [Ir(btphen)₂](μ-Cl)₂

[Ir(bt)₂](μ-Cl)₂ and [Ir(btphen)₂](μ-Cl)₂ were synthesized according to Nonoyama³, Lamansky et al⁴, and used directly without further purification and characterization. [Ir(bt)₂](μ-Cl)₂, yellow powder, yield 92%; [Ir(btphen)₂](μ-Cl)₂, dark red powder, yield 89%. [Ir(bt)₂](μ-Cl)₂ and [Ir(btphen)₂](μ-Cl)₂ were used directly without further purification.


Fig. S1 Absorption (dashed) and emission (solid) spectra of IrMitoOlivine and IrMitoNIR in DMSO/PBS (2 vol.%). Ex: IrMitoOlivine, 411 nm; IrMitoNIR, 504 nm.
Fig. S2 Confocal cell imaging of [Ir(bt)$_2$]$_2$(bpy-COOH) (1) and [Ir(btphen)$_2$]$_2$(bpy-COOH) (2) in living HeLa cells. Upper: 1, [Ir(bt)$_2$]$_2$(bpy-COOH), Ex 488 nm, Em 500-530 nm; lower: 2, [Ir(btphen)$_2$]$_2$(bpy-COOH), Ex 561 nm, Em 662-737 nm.