Glutathione Responsive Pyrrolopyrrolidone Nanotheranostic Agent for Turn-on Fluorescence Imaging Guided Photothermal/Photodynamic Cancer Therapy

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Synthesis of DPPBPh and DPPTPh

The synthetic route of DPPBPh and DPPTPh is similar and proposed in supporting information (Figure S1). Taking DPPBPh as an example, a mixture of DPP (105 mg, 0.2 mmol), 2-(diphenylmethylene)malononitrile (154 mg, 0.5 mmol), anhydrous K₂CO₃ (69 mg, 0.5 mmol), PivOH (6.2 mg, 0.06 mmol), Pd(OAc)₂ (2.3 mg, 0.006 mmol) and anhydrous DMA (2 mL) was heated to 110 °C and stirred for 4 h under N₂ atmosphere. The organic layer was extracted with CH₂Cl₂ for three times (100 mL), then washed with brine and dried with anhydrous sodium sulfate. The solvent was removed by rotary evaporation, and the crude product was purified by column chromatography (silica gel, DCM:PE = 1:2, v/v).



Figure S1 Synthetic route of DPPBPh and DPPTPh. (i) n-BuOK, 2-methyl-2-butanol, 108 °C; (ii) K₂CO₃, DMF; (iii) Pd(OAc)₂, K₂CO₃, PivOH, DMA.

For DPPBPh, ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 9.00-8.96 (2H, d), 7.93-7.86 (4H, d), 7.85-7.81 (4H, d), 7.80-7.74 (4H, d), 7.63-7.57 (4H, m), 7.55-7.48 (4H, m), 4.16-4.03 (4H, d), 1.47-1.26 (16H, m), 0.96-0.85 (12H, m). ¹³C NMR (75 MHz, CDCl₃): δ 161.89, 136.68, 132.76, 130.89, 129.75, 128.61, 125.95, 46.06, 39.31, 30.31, 29.67, 28.57, 23.55, 23.01, 14.03, 10.58. MS (ESI): calcd. m/z = 980.39; found m/z = 980.78.



Figure S2. ¹HNMR of DPPBPh in CDCl₃



Figure S3. ¹³CNMR of DPPBPh in CDCl₃

For DPPTPh, ¹H NMR (CDCl₃, 400 MHz): δ (ppm) 9.00-8.96 (2H, d), 7.93-7.86 (6H, d), 7.85-7.81 (6H, d), 7.80-7.74 (6H, d), 7.63-7.57 (6H, m), 7.55-7.48 (6H, t), 4.11-4.07 (4H, d), 1.97-1.92 (2H, s), 1.47-1.32 (16H, m), 0.94-0.85 (12H, m). ¹³C NMR (75 MHz, CDCl₃) δ 161.73, 147.98, 139.33, 136.79, 132.54, 131.03, 129.93, 128.16, 125.74, 46.23, 38.98, 30.24, 28.38, 23.75, 23.07, 14.03, 10.46. MS (ESI): calcd. m/z = 1082.46; found m/z = 1081.95.







Figure S5. ¹³CNMR of DPPBPh in CDCl₃



Figure S6. (a) Degradation of DPBF in the presence of MB in DCM with irradiation. (b) Linear fitting of the degradation of DPBF. (c) Degradation of DPBF in the presence of DPPBPh in DCM with irradiation. (d) DLS and TEM of DPPBPh NPs in water.



Figure S7. Pictures of tumors from mice in the control, DPPBPh, DPPBPh+laser, DPPTPh and DPPTPh+laser groups.