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Electronic Supplementary Information (ESI)

A triple-stimulus responsive melanin-based nanoplatform with an aggregation-induced emission-active photosensitiser for imaging-guided targeted synergistic phototherapy/hypoxia-activated chemotherapy

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Experimental

1. The measurement of fluorescence quantum yield.[1]

Fluorescence measurements were performed in a 1 cm cuvettes and excitation at 512 nm (20°C). The emission slit was 5.0 nm while the excitation slit was 10.0 nm. The fluorescence was measured at 90° to the incident excitation beam. The fluorescence intensity at a wavelength was calibrated against the detector response and the excitation light intensity. The fluorescence quantum yield was measured by using

$$\Phi_{\mathrm{f}} = \Phi_{\mathrm{f}}^{0} \times \frac{F_s}{F_0} \times \frac{A_0 \mathrm{n}_s^2}{A_{\mathrm{s}} \mathrm{n}_0^2} \tag{1}$$

in which F was the integrated fluorescence intensity, A was the absorbance at excitation wavelength, n was the refractive index of the solvent used, the subscript 0 stood for a reference compound and s represented samples. Rhodamine B in water was used as the reference (Φ_{f}^{0} =0.31).[2]

2. Calculation of the photothermal conversion efficiency.

The photothermal conversion efficiency of MTHB was determined according to previous method.[3] Detailed calculation was given as following:

Based on the total energy balance for the system:

$$\sum_i m_i C_{p,i} \frac{\mathrm{d}T}{\mathrm{dt}} = Q_{\mathrm{NPs}} + Q_{\mathrm{s}} - Q_{\mathrm{loss}} \tag{2}$$

where m and C_p are the mass and heat capacity of solvent (water), respectively. T is the solution temperature.

Q_{NPs} is the photothermal energy input by MTHB nanoparticles:

$$Q_{\mathrm{NPs}} = I(1-10^{-A_\lambda})\eta \tag{3}$$

where I is the laser power, A_λ is the absorbance of MTHB at the wavelength of 808 nm, and η is the conversion efficiency from the absorbed light energy to thermal energy.

Q_s is the heat associated with the light absorbance of the solvent, which is measured independently to be 2W/cm^2 using pure water without MTHB.

Q_{loss} is thermal energy lost to the surroundings:

$$Q_{loss} = hA\Delta T \tag{4}$$

where h is the heat transfer coefficient, A is the surface area of the container, and ΔT is the temperature change, which is defined as T-T_{surr} (T and T_{surr} are the solution temperature and ambient temperature of the surroundings, respectively).

At the maximum steady-state temperature, the heat input is equal to the heat output, that is:

$$Q_{NPs} + Q_s = Q_{loss} = hA\Delta T_{max} \tag{5}$$

where ΔT_{max} is the temperature change at the maximum steady-state temperature. According to the Eq.3 and Eq.5, the photothermal conversion efficiency (η) can be determined:

$$\eta = \frac{hA\Delta T_{max} - Q_s}{I(1-10^{-A_\lambda})} \tag{6}$$

In this equation, only hA is unknown for calculation. In order to get the hA, we herein introduce θ, which is defined as the ratio of ΔT to ΔT_{max}:

$$\theta = \frac{\Delta T}{\Delta T_{max}} \tag{7}$$

Substituting Eq.7 into Eq.2 and rearranging Eq.2:

$$\frac{\mathrm{d}\theta}{\mathrm{dt}} = \frac{hA}{\sum_i m_i C_{p,i}} \left[\frac{Q_{\mathrm{NPs}} + Q_{\mathrm{s}}}{hA\Delta T_{\max}} - \theta \right] \tag{8}$$

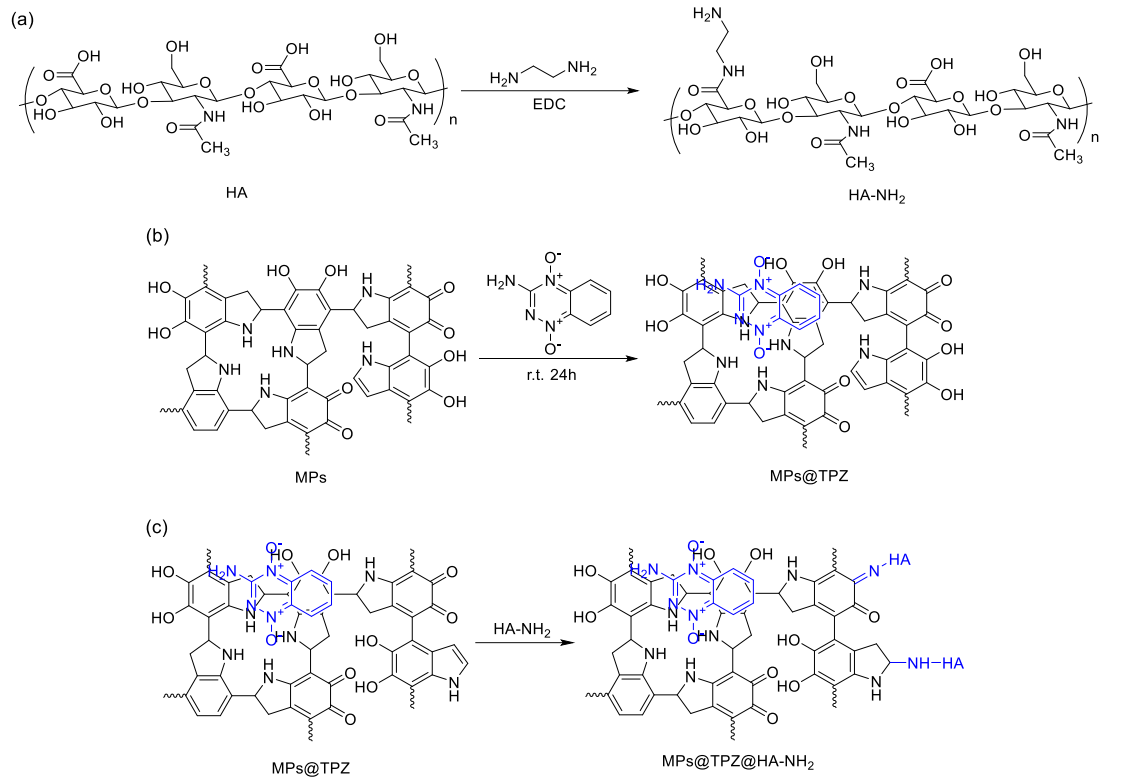
When the laser was shut off, the $Q_{\mathrm{NPs}}+Q_{\mathrm{s}} = 0$, Eq.8 changed to:

$$\mathrm{dt} = -\frac{\sum_i m_i C_{p,i}}{hA} \frac{\mathrm{d}\theta}{\theta} \tag{9}$$

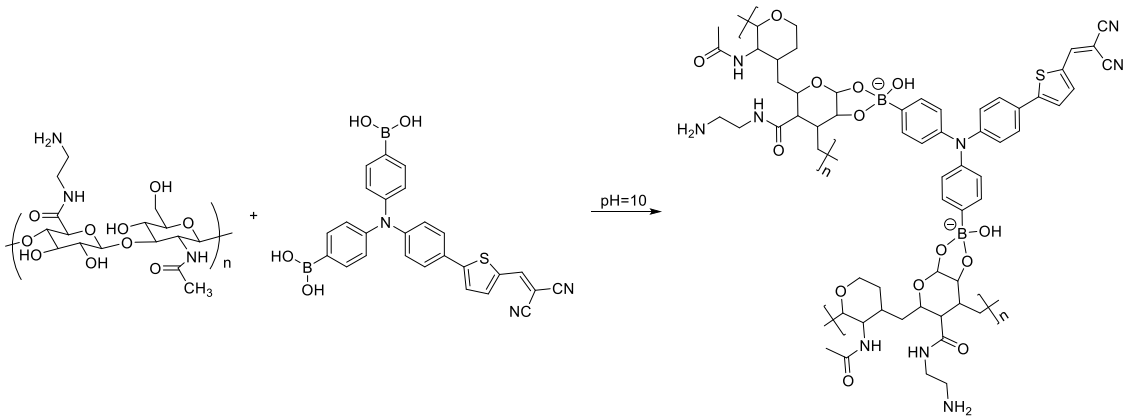
Integrating Eq.9 gives the expression:

$$\mathrm{t} = -\frac{\sum_i m_i C_{p,i}}{hA} \theta \tag{10}$$

Thus, hA can be determined by applying the linear time data from the cooling period vs $-\ln\theta$ (Fig. S20d). Substituting hA value into Eq.6, the photothermal conversion efficiency (η) of MTHB can be calculated.



Scheme S1. (a) Synthesis of ethylenediamine-functionalized hyaluronic acid. (b) (c) Schematic showing the preparation of MPs@TPZ and MPs@TPZ@HA-NH_2.



Scheme S2. Schematic showed the synthesis of MTHB.

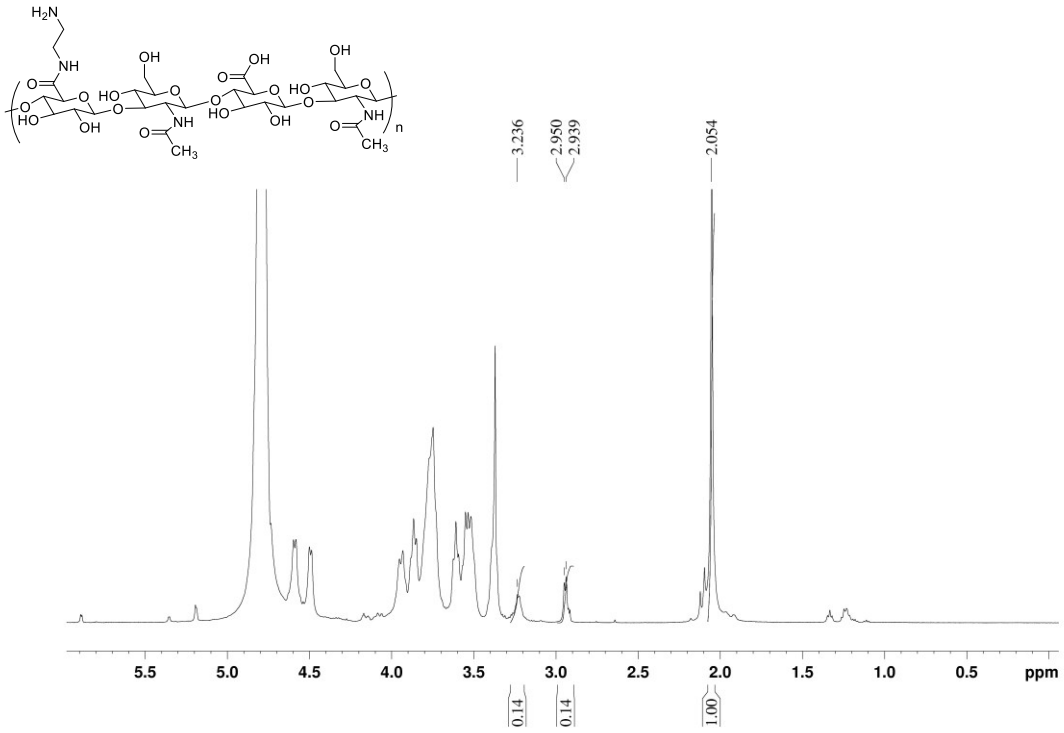


Fig. S1. [1]H-NMR of ethylenediamine-functionalized hyaluronic acid.

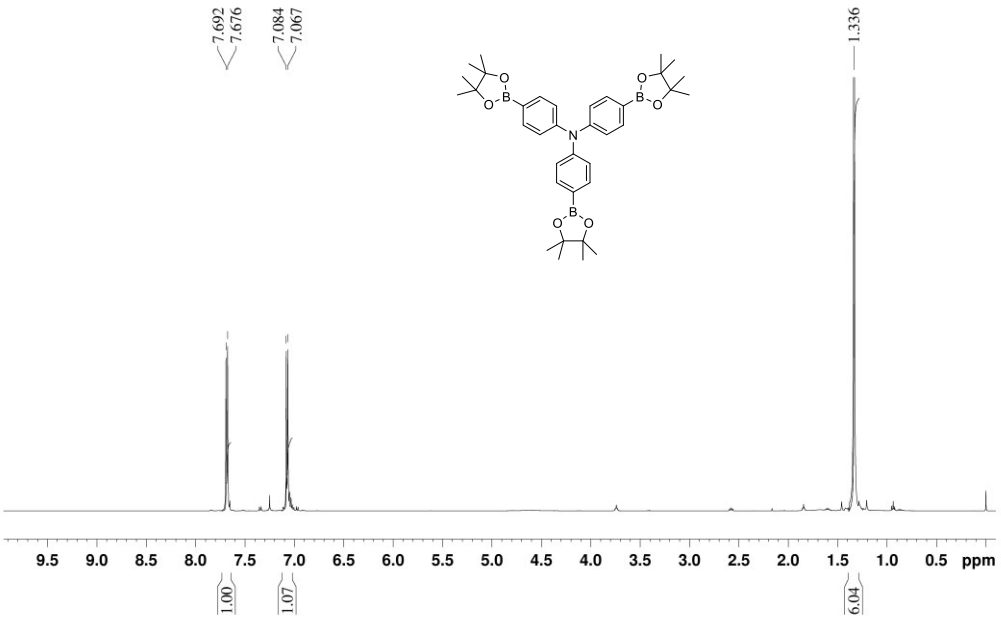


Fig. S2. [1]H-NMR of compound **1**.

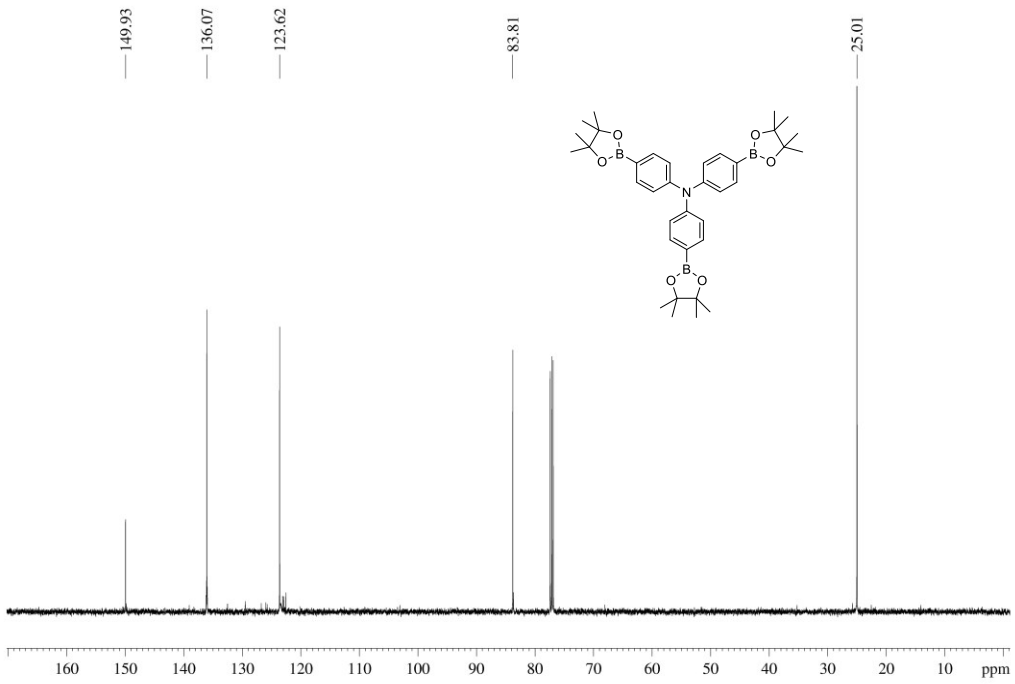


Fig. S3. ^{13}C-NMR of compound **1**.

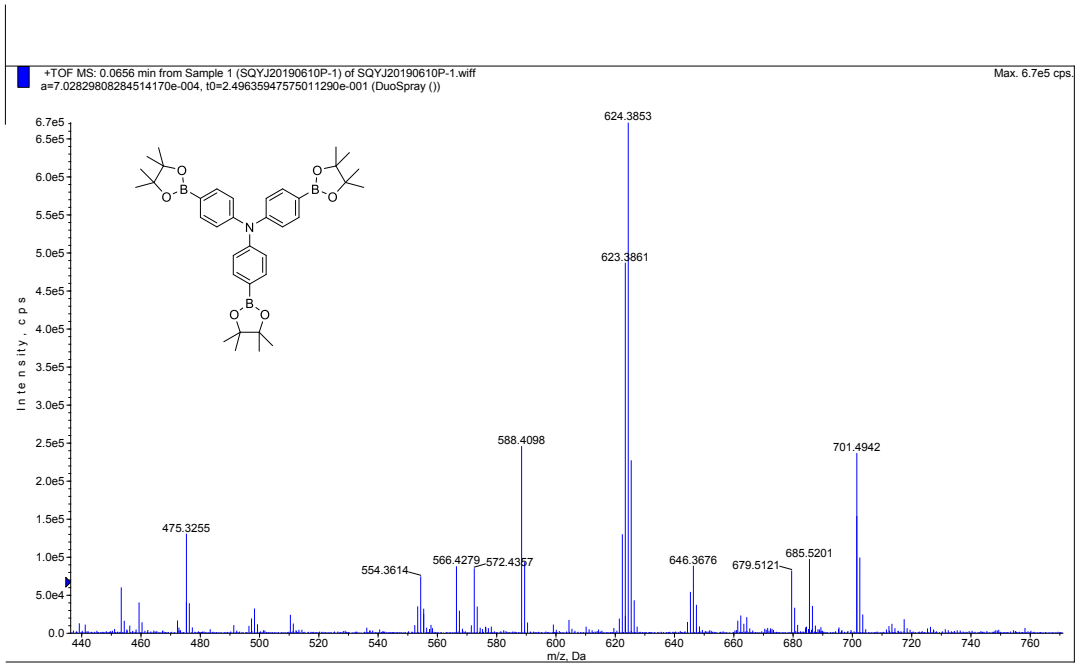


Fig. S4. HRMS spectrum of compound **1**.

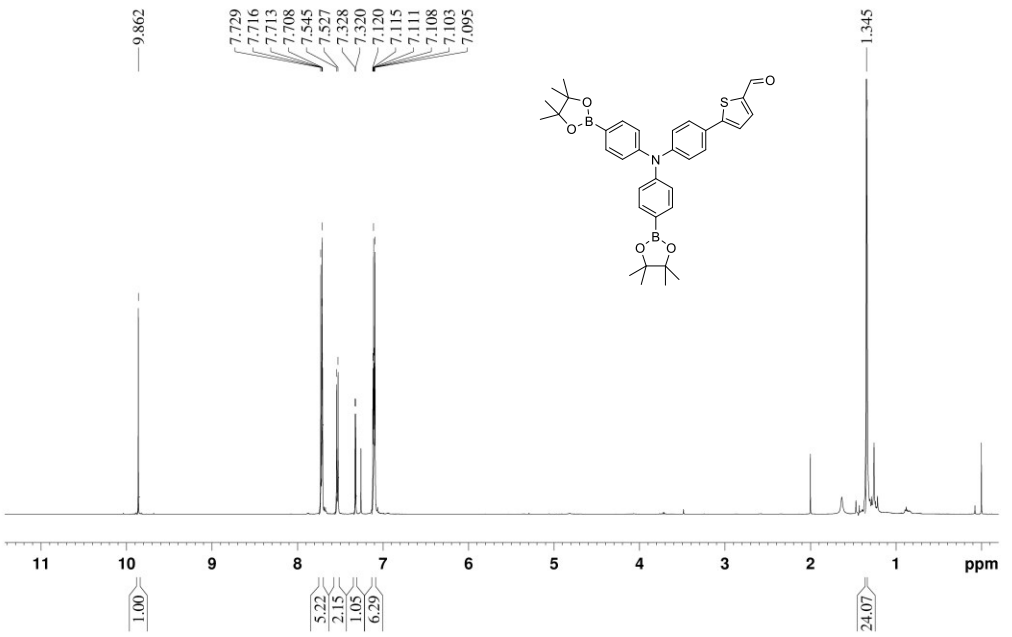


Fig. S5. ^{1}H-NMR of compound **2**.

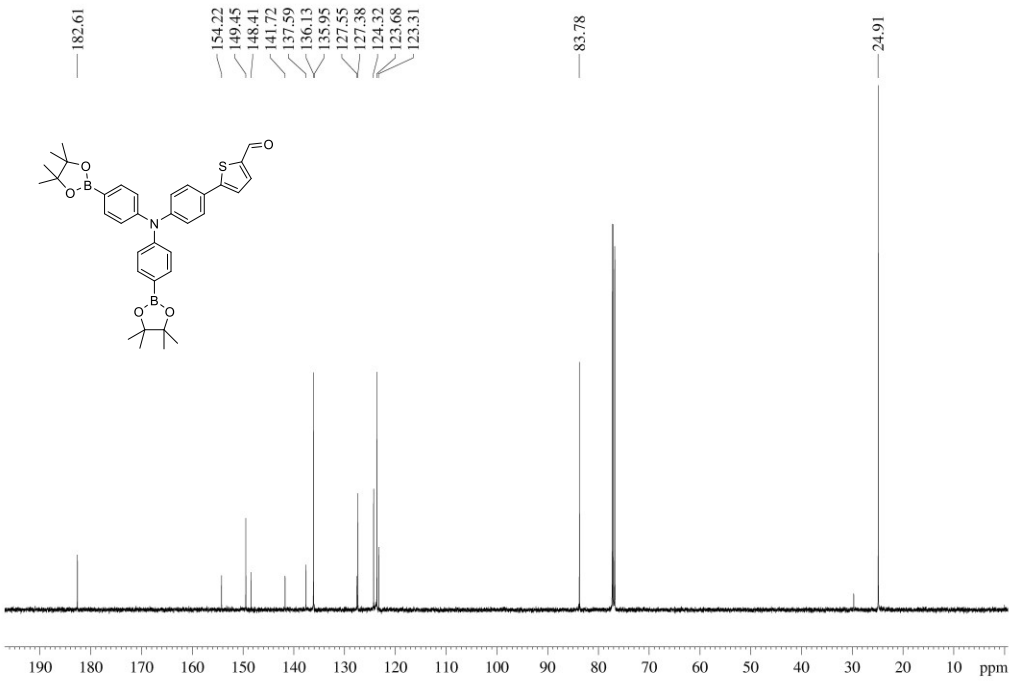


Fig. S6. ^{13}C-NMR of compound **2**.

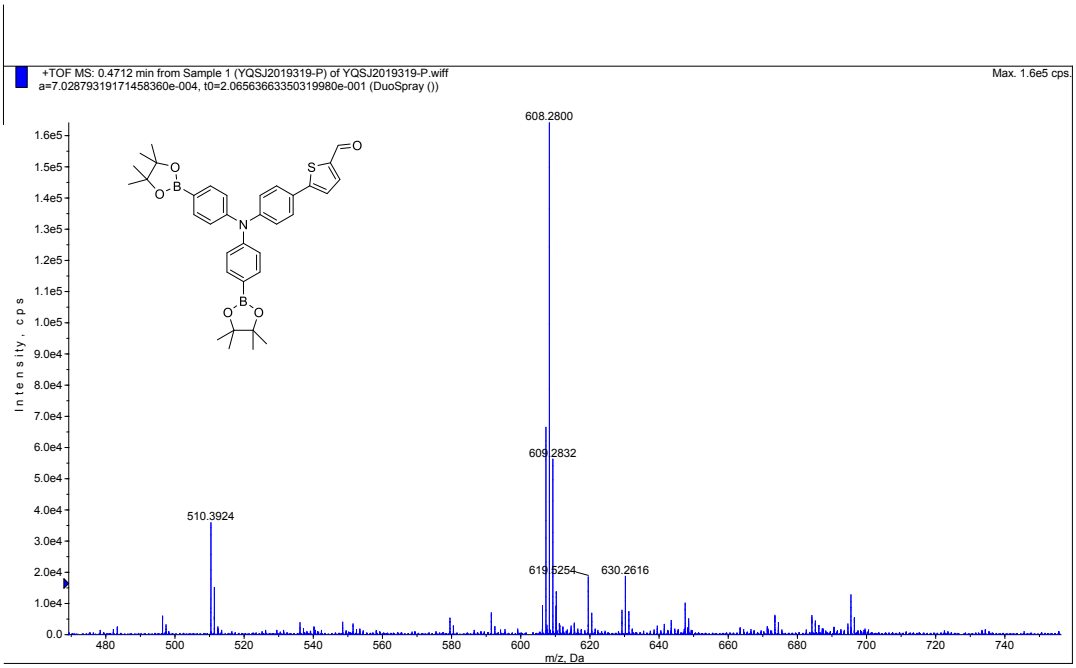


Fig. S7. HRMS spectrum of compound **2**.

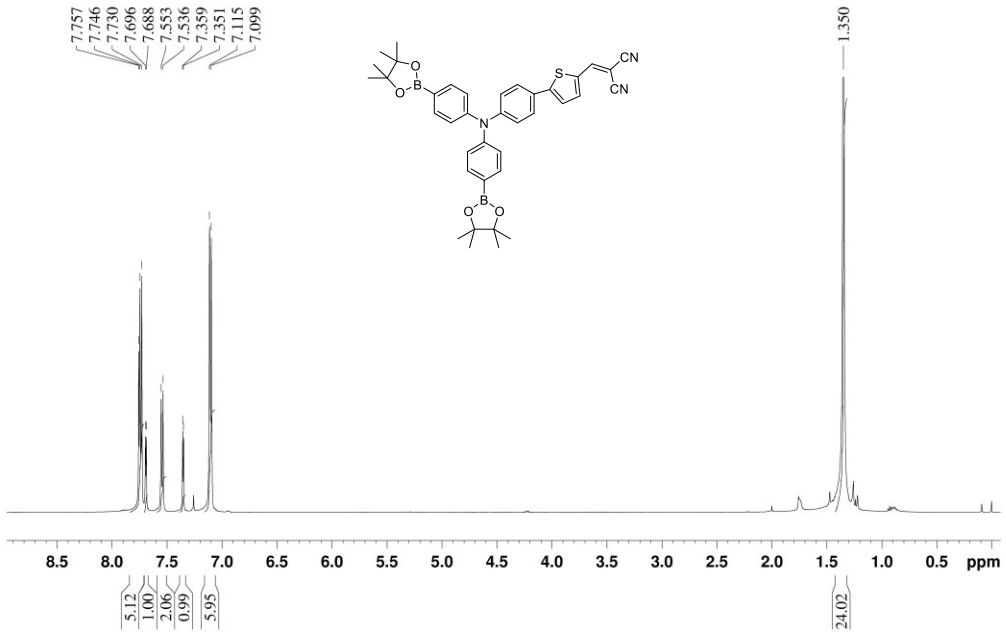


Fig. S8. [1]H-NMR of compound **3**.

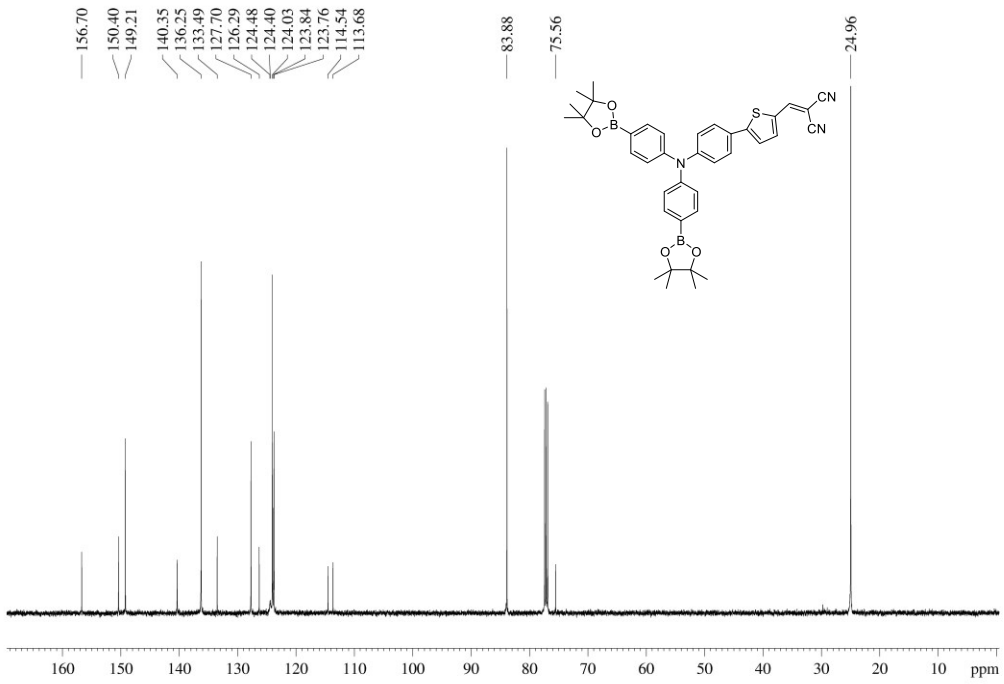


Fig. S9. ^{13}C-NMR of compound **3**.

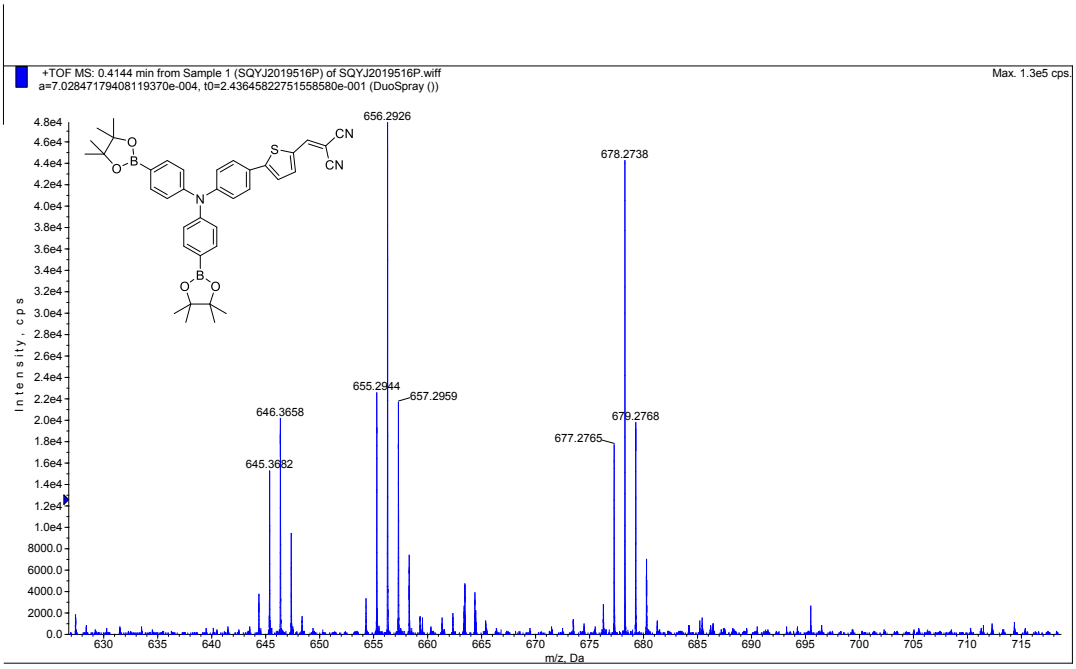


Fig. S10. HRMS spectrum of compound **3**.

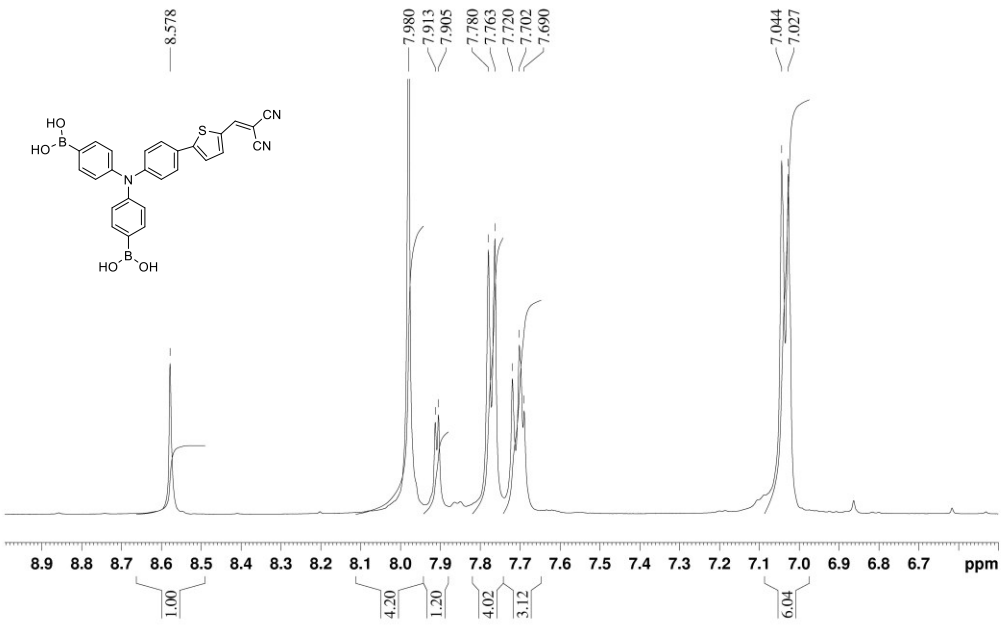


Fig. S11. ^{1}H-NMR of compound **4**.

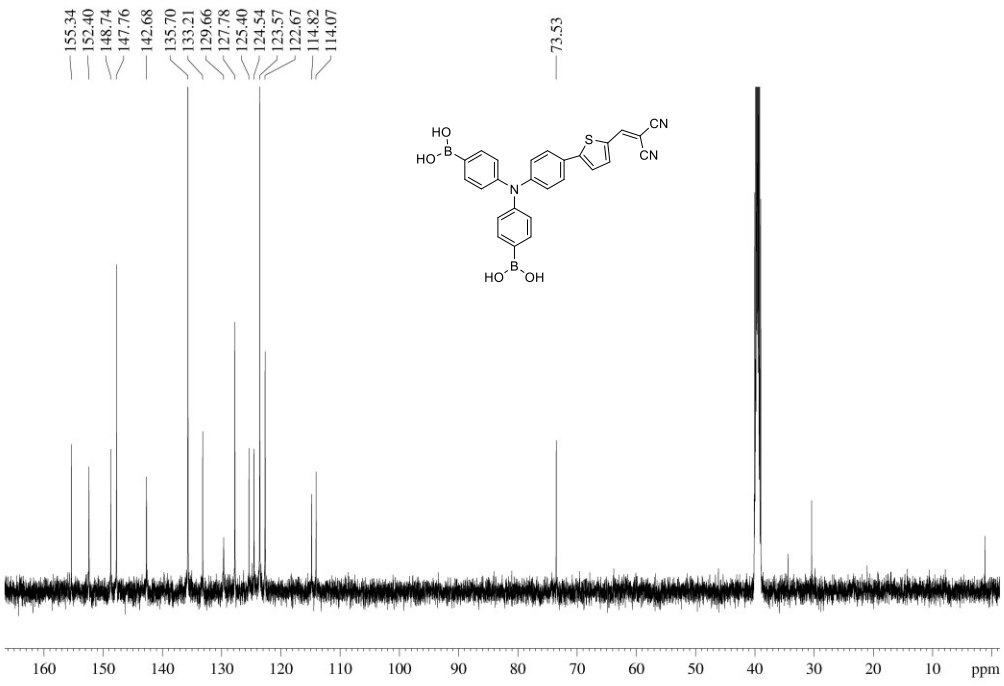


Fig. S12. ^{13}C-NMR of compound **4**.

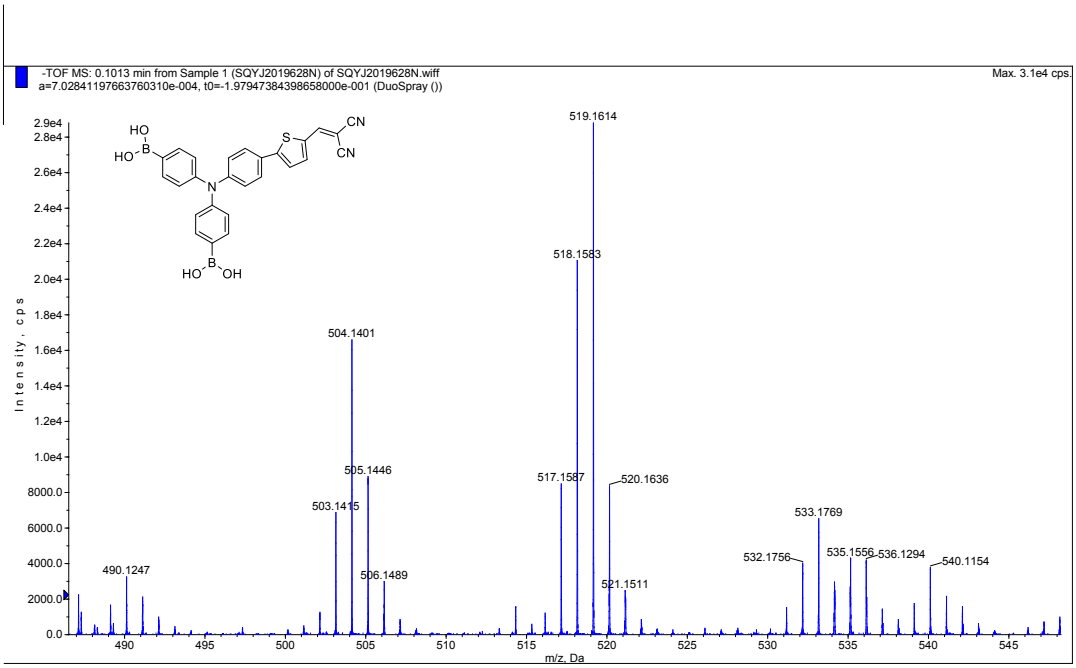


Fig. S13. HRMS spectrum of compound **4**.

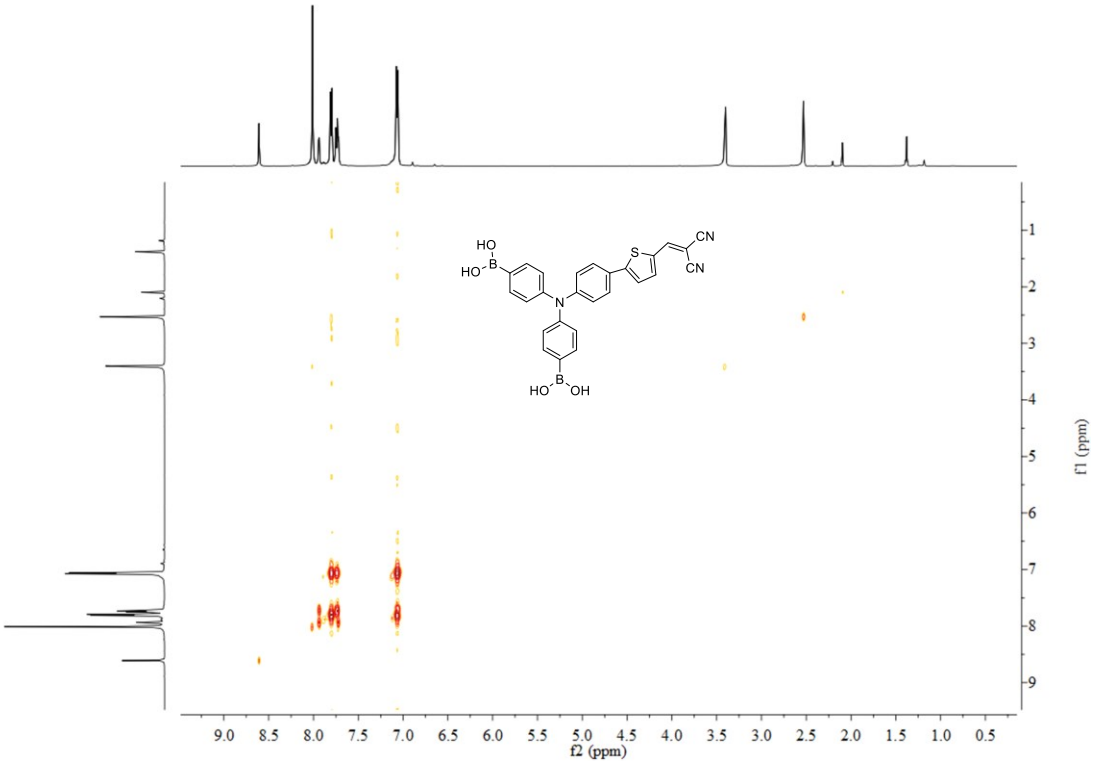


Fig. S14. COSY NMR spectrum of compound **4**.

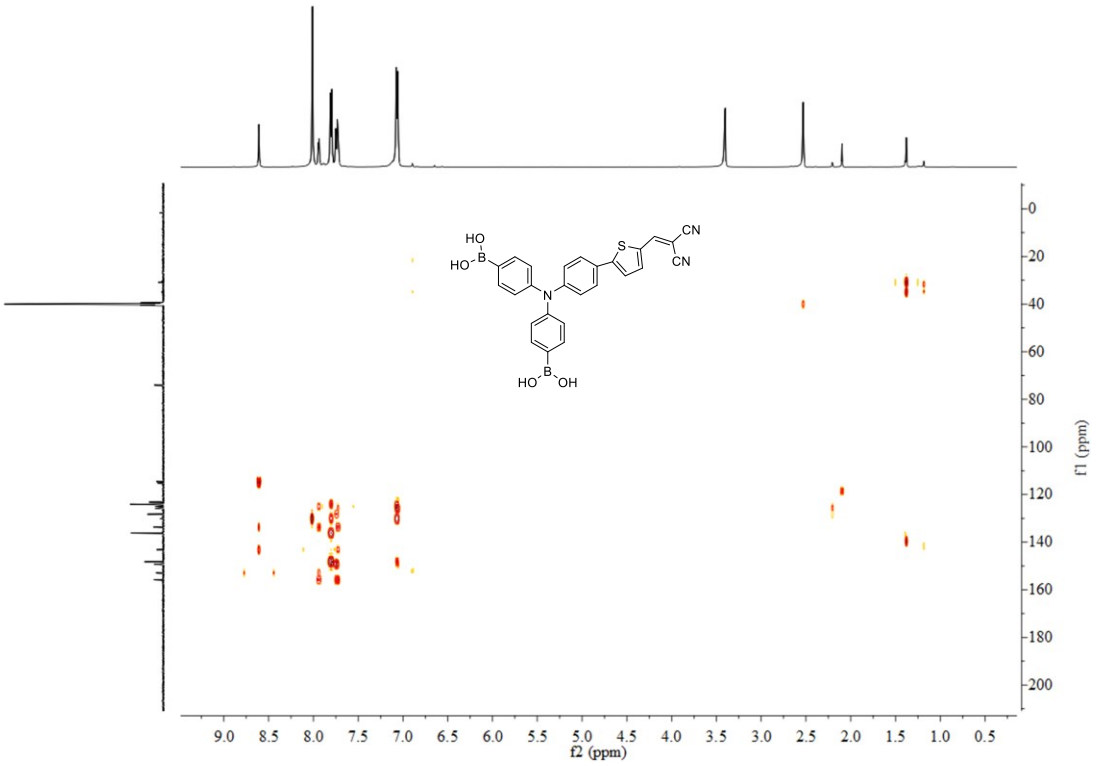


Fig. S15. HMBC NMR spectrum of compound **4**.

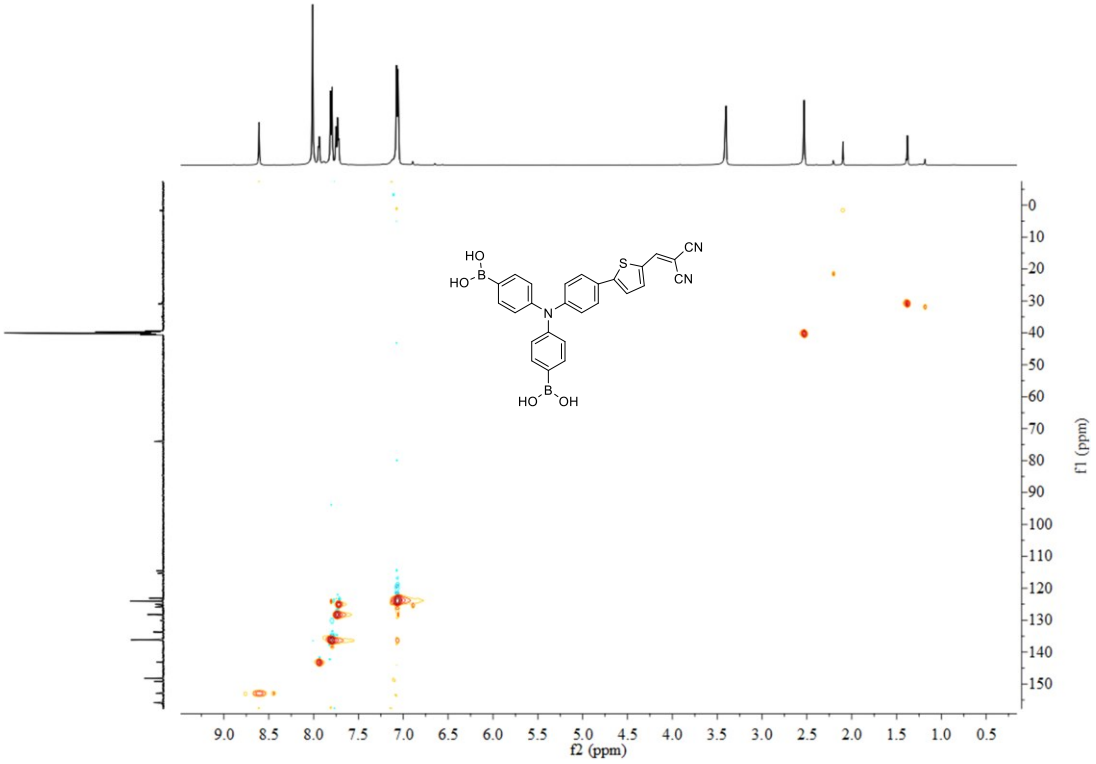


Fig. S16. HSQC NMR spectrum of compound **4**.

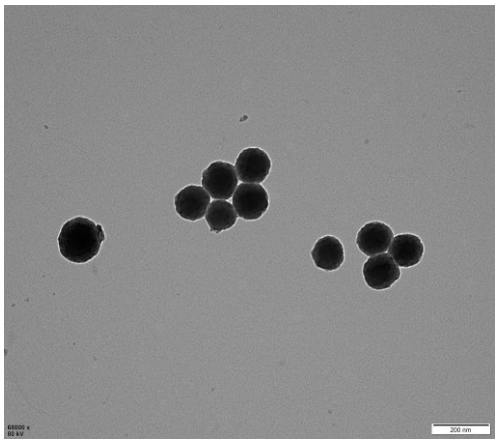


Fig. S17. TEM image of MPs.

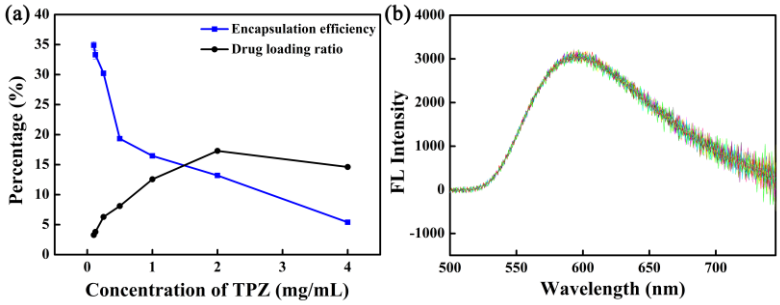


Fig. S18. (a) The drug loading ratio and encapsulation efficiency of TPZ for MPs. (b) FL spectra of BATTMN in THF after 40 scans within 15 min. Excitation wavelength: 512 nm.

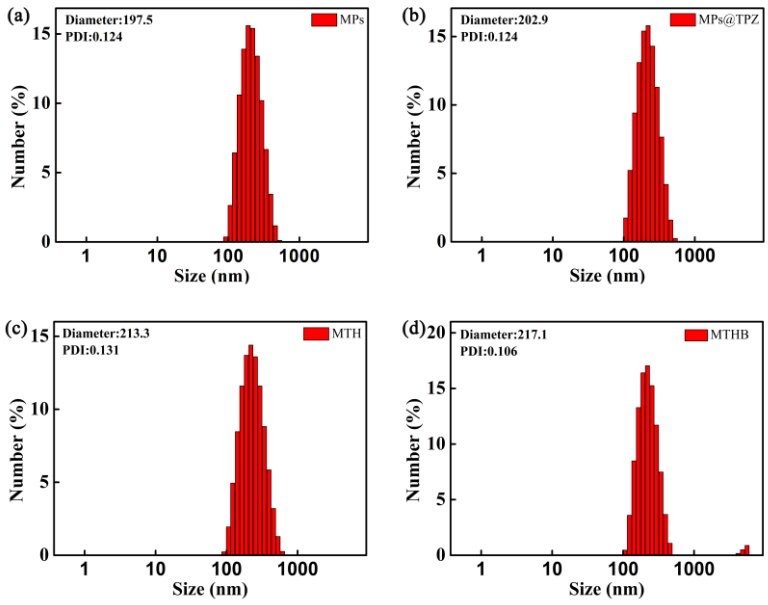


Fig. S19. Size distribution of (a) MPs, (b) MPs@TPZ, (c) MTH, and (d) MTHB determined by DLS.

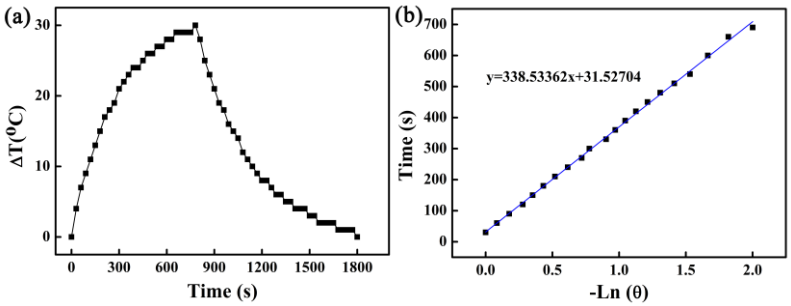


Fig. S20. (a) The photothermal response of the MTHB aqueous solution (150 μg/mL) for 780 s with an NIR laser (808 nm, 2W/cm^2) and then the laser was shut off. (b) Linear time data versus –lnθ obtained from the cooling period of Fig. S20a.

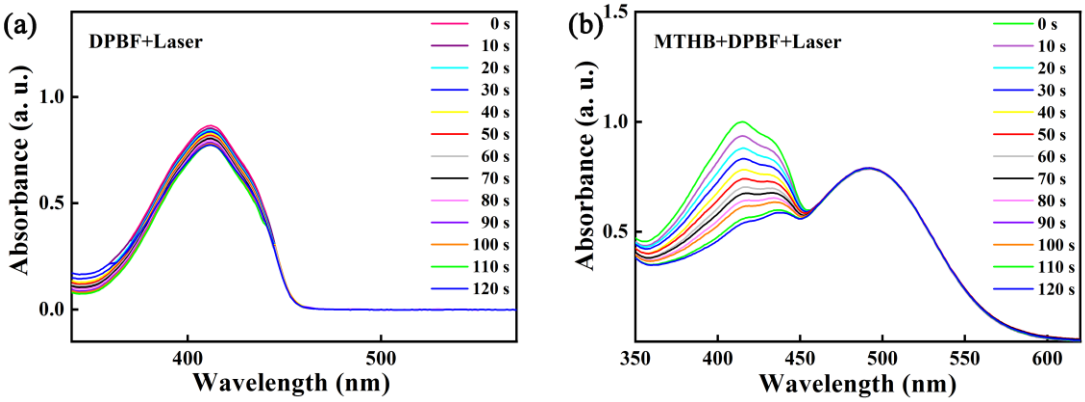


Fig. S21. UV-Vis spectra of (a) DPBF + Laser and (b) MTHB+DPBF+Laser with different irradiation time, respectively. An ethanol solution of MTHB with DPBF was exposed to white light laser illumination. The wavelength range is from 400 nm to 760 nm. The power of the white light is 1 W.

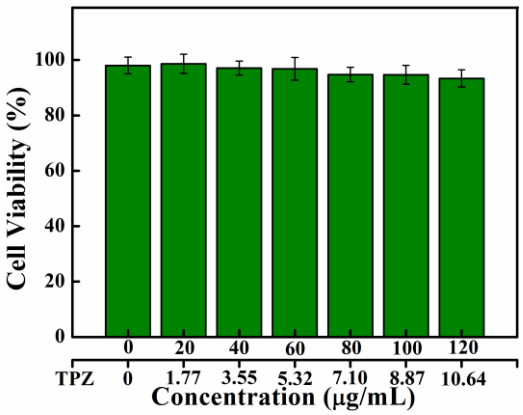


Fig. S22. Cell viability of NIH3T3 cells in response to MTHB treatments in normoxia after incubation for 24 h (n= 5).

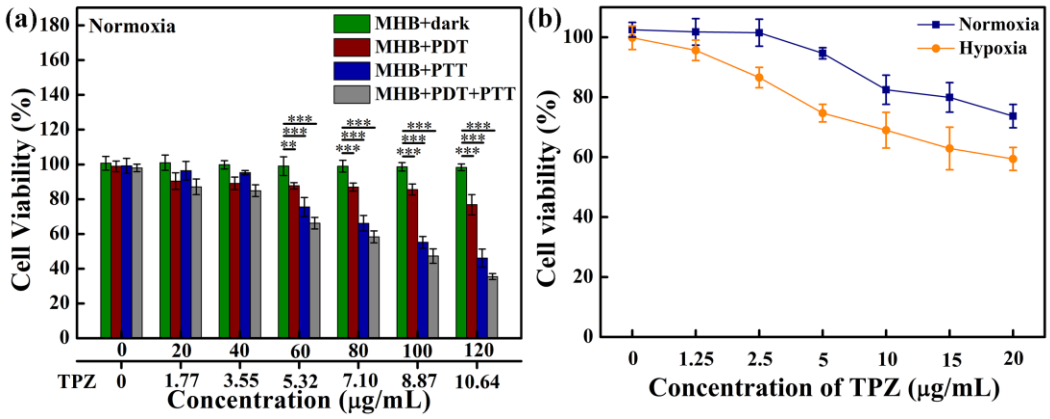


Fig. S23. (a) Cell viability of MCF-7 cells in response to MHB treatments with dark, white light irradiation, 808 nm irradiation or dual light irradiation in normoxia after 24 h incubation (*n*= 5). (b) Cell viability of MCF-7 cells in response to TPZ treatment in normoxia or hypoxia after 24 h incubation (*n*= 5).

References：

1 X. Zhang, Y. Zhang and L. Liu, *J. Lumin.*, 2014, **145**, 448-453.
2 D. Magde, G. E. Rojas and P. G. Seybold, *Photochem. Photobiol.*, 1999, **70**, 737-744.
3 D. K. Roper, W. Ahn and M. Hoepfner, *J. Phys. Chem. C.*, 2007, **111**, 3636-3641.