Electronic Supplementary Information (ESI) for

An Acceptor-Shielding Strategy of Photosensitizer for Enhancing the Generation Efficiency of Type I Reactive Oxygen Species and the Related Photodynamic Immunotherapy

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Materials

All materials were used directly without further purification. Triethyl orthoformate was purchased from TCI. Dodecylmagnesium bromide, malononitrile, pyridine, N-bromosuccinimide, and chloroform-d were purchased from Innochem. Ethyl pyruvate was purchased from Meryer. 1-Aminopyrene and N, N-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl) aniline were purchased from Bidepharm. $Pd(PPh_3)_4$ was purchased from J & K. $POCl_3$ was purchased from Xiya Reagent. Methoxy(polyethylene glycol)-2000 (DSPE-PEG_{2000}) was purchased from Tansh-Tech. Compounds ethyl 2,2-diethoxypropanoate (**1**) and 3-hydroxy-3-dodecylpentadecane-2-one (**2**) were synthesized according to the previous report.[1] 2-(3-cyano-4,5,5-trimethylfuran-2-ylidene)propanedinitrile (**FE-C1**) was synthesized according to our previous report.[2]

Dulbecco's modifies eagle medium (DMEM) and FBS were purchased from Gibco (USA). Penicillin−streptomycin was purchased from Macgene (China). LPS was purchased from Thermo Fisher Scientific. Recombinant murine IL-4 was purchased from PeproTech. Hoechst 33342 was purchased from Life Technologies. The FITC antimouse CD80 and Alexa Fluor 700 antimouse CD206 were purchased from Biolegend (USA). Calcein-AM/PI Live-Dead Cell Staining Kit were purchased from Beijing Solarbio Science and Technology Co., Lta. DCFH-DA was purchased from Beyotime.

Equipment

^1H and ^{13}C NMR spectra were recorded on a Bruker AV 400 spectrometer. High-resolution mass spectra (HRMS) and mass spectra (MS) were collected using a Finnigan Biflex III mass spectrometer. UV-vis absorption spectra were recorded on a TU-1901 UV-vis spectrophotometer. Photoluminescence spectra and PL quantum yields were measured on an Edinburgh FLS980 steady-state transient fluorescence/phosphorescence spectrometer. Dynamic light scattering was measured by using NICOMP Z3000 ZLS. TEM was detemined by JEM2100f. Single-crystal data were collected on a Bruker-AXS SMART APEX 2 CCD diffractometer. Electron spin resonance (ESR) spectra were measured on Bruker Paramagnetic Resonance

Spectrometer EMXplus. The lifetime of triplet state was determined on Edinburgh LP 980 spectrometer.

Preparation of MAP17-C1 NPs and MAP18-C12 NPs

1 mg **MAP17-C1** or **MAP18-C12** and 3 mg DSPE-PEG_{2000} were dissolved in 1 mL DMSO solution, and poured into 9 mL PBS under ultrasonic conditions. The obtained nanoparticles, named as **MAP17-C1 NPs** and **MAP18-C12 NPs**, respectively, were concentrated by centrifugation, and PBS was added to prepare a solution with a certain concentration for ROS testing and further biological applications.

Total ROS detection by indicator DCFH

75 μL 2',7'-Dichlorodihydrofluorescein (DCFH, 4×10^{-5} mol/L) as an indicator was added into 300 μL NPs (1×10^{-4} mol/L) and 2625 μL PBS. Control group were prepared by adding 75 μL DCFH into 2925 μL PBS. After that, the obtained solutions were exposed to white light (5 mW cm^{-2}) for different times, the PL intensities at 532 nm were recorded under excitation at 480 nm.

Detection of $^1O_2$ Generation by indicator ABDA

20 μL 9,10-anthracenediyl-bis(methylene)-dimalonic acid (ABDA, 1×10^{-2} mol/L) as an indicator was added into 300 μL NPs (1×10^{-4} mol/L) and 2680 μL PBS. Control group were prepared by adding 20 μL ABDA into 30 μL Rose Bengal (1×10^{-3} mol/L) and 2680 μL PBS. After that, the obtained solutions were exposed to white light (5 mW cm^{-2}) for different times, the absorption spectra of ABDA were measured.

Cell Culture

RAW 264.7 (murine macrophage cell line) and 4T1 cells (mouse breast cancer cell line) were obtained from National Infrastructure of Cell Line Resource (NICR). RAW 264.7 cells were cultured in DMEM media containing 10% FBS and 2% penicillin−streptomycin, and 4T1 cells were cultured in RPMI-1640 media containing 10% FBS and 2% penicillin−streptomycin at 37 °C in a humidified atmosphere of 5% CO_2.

In Vitro Cytotoxicity

4T1 cells (1×10^4 cells/well) were seeded in 96-well plates. After 12 h, the cells were cultured with **MAP18-C12 NPs** (10 μmol/L) for another 4 h. Followed by irradiation with increased light (660 nm) power densities (11, 22, 44, 88, 176, 350 mW cm^{-2}) for 5 min. After irradiation, the photosensitizer suspension was discarded and fresh medium was added to each well for further incubation for 24 h before testing the light cytotoxicity. Then the medium was discarded, and the cells were incubated with MTS solutions (5 mg/mL) for 2 h at 37 °C. The absorbance of each well was measured at 490 nm by a microplate reader (BioTek).

MAP18-C12 NPs Polarized M0 towards M1 Phenotype in Vitro

RAW264.7 cells were seeded in 24-well microplates at a density of 1×10^5 per well and incubated overnight at 37 °C. Then, **MAP18-C12 NPs** (10 μmol/L) was added to the wells for 4 h followed by light (660 nm, 2 W cm^{-2}, 5 min). After treatment for 24 h, the macrophages in each group were collected, washed with flow cytometry staining buffer, and stained with FITC anti-mouse CD80 at 4 °C for 30 min. Thereafter, the cells were washed with PBS and analyzed by a flow cytometer (Beckman, CytoFlex LX). Typical LPS (0.5 μg/mL) treated M1 macrophages were served as the control.

MAP18-C12 NPs Polarized M2 towards M1 Phenotype in Vitro

RAW264.7 cells were seeded into 24-well culture plates at a density of 5×10^4 per well and incubated overnight at 37 °C, followed by treatment with IL-4 for 48 h to induce the M2-polarization. Then, **MAP18-C12 NPs** (10 μmol/L) was added to the wells for 4 h followed by light (660 nm, 22 mW cm^{-2}, 5 min). After treatment for 24 h, the macrophages in each group were collected, washed with Flow Cytometry Staining Buffer, and stained with FITC anti-mouse CD80 antibodies at 4 °C for 30 min. Thereafter, the cells were washed with PBS and analyzed by a flow cytometer.

Colocalization Imaging in 4T1 Cell

4T1 cells were seeded in Φ20 mm glass bottom cell culture dishes ($1.0 \pm 0.05 \times 10^6$ cells in each dish). After overnight culture in a humidified incubator at 37 ºC with 5% CO_2, culture medium was removed and cells were stained with **MAP18-C12 NPs** (10 μmol/L) for 4 h in. After washed by PBS for 3 times, 4T1 cells were fixed with 4% fixative solution for 10 min. Before imaging, each dish was washed by PBS for 3 times. For co-localization with LysoTracker, the fixed cells were stained with LysoTracker (5 μm) for 10 min at 37 ºC.

Treatment Effects of Different Formations on 3D Multicellular Tumor Immune Spheroid Model

To form multicellular tumor-immune spheroids, the mixture of 100 μL M2 macrophages and 100 μL tumor cells (6×10^3 cells mL^{-1}) were mixed and seeded into 96-well low-attachment culture plates following the manufacturer's instructions. After incubation for 72 h in a 37 °C humidified incubator with 5% CO_2, the formed 3D tumor-immune spheres were individually treated group B (PBS), administration with PBS (100 μL) alone; group L (PBS + light), PBS administration (100 μL) followed by light irradiation (660 nm, 350 mW cm^{-2}, 5 min); group M (**MAP18-C12 NPs** + dark), administration with **MAP18-C12 NPs** (1 μmol/L, 100 μL); group M+L (**MAP18-C12 NPs** + light), administration with **MAP18-C12 NP**s (1 μmol/L, 100 μL) and followed by light irradiation (660 nm, 350 mW cm^{-2}, 5 min). Subsequently, the size of 3D spheres was monitored by CLSM at designated time intervals. Cell viability in spheres was measured using a Calcein-AM/propidium iodide (PI) double staining kit.

Animals

Animals: BALB/c (female, 4–6 weeks) mice were purchased from the River Laboratory Animal Technology Co., Ltd. (Beijing).

Statement of ethical approval: All animal studies were performed in accordance with the Regulations for Care and Use of Laboratory Animals and Guideline for

Ethical Review of Animals (China, GB/T 35892-2018) and the overall project protocols were approved by the Animal Ethics Committee of Beijing Institute of Technology. The accreditation number is BIT-EC-SCXK (Jing) 2019-0010-M-2020019 promulgated by Animal Ethics Committee of Beijing Institute of Technology.

Feeding conditions: all the animals were submitted to controlled temperature conditions (22 ~ 26 ºC), humidity (50 ~ 60%) and light (12 h light/12 h dark, 15 ~ 20 LX). They had access to water and food ad libitum in barrier system of Beijing Institute of Technology. (SYXK (Jing) 20170013)

In Vivo Biodistribution and Tumor-Targeting Capacity of the MAP18-C12 NPs

BALB/c mice (female, 4–6 weeks) bearing 4T1 tumors (≈500 mm^3) were administered intravenously with 1 mmol/L (100 μl) of **MAP18-C12 NPs**. At different time intervals (1, 2, 4, 8, 12, 24, and 48 h), the mice were imaged using an in vivo fluorescence imaging system. Besides, the mice were sacrificed at 4 h postinjection, and the tumor tissues and major organs were excised for fluorescence analysis.

In Vivo Therapeutic Studies

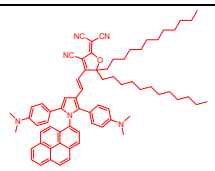
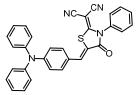
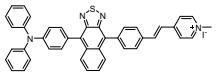
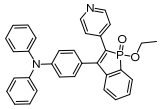
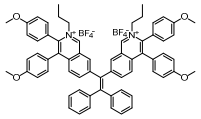
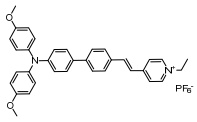
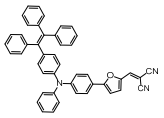
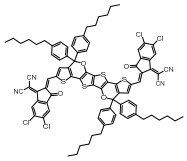
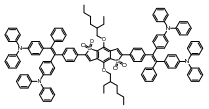
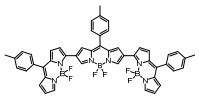
BALB/c mice (female, 4–6 weeks, 24 in total) bearing 4T1 tumors (≈100 mm^3) were randomly divided into four groups (6 in each group), group B (PBS), administration with PBS (200 μL) alone; group L (PBS + light), PBS administration (200 μL) followed by light irradiation (660 nm, 350 mW cm^{-2}, 10 min); group M (**MAP18-C12 NPs** + dark), administration with **MAP18-C12 NPs** (1 mmol/L, 200 μL); group M+L (**MAP18-C12 NPs** + light), administration with **MAP18-C12 NP**s (1 mmol/L, 200 μL) and followed by light irradiation (660 nm, 350 mW cm^{-2}, 10 min). During the treatment period, the tumor volume of all mice was measured every two days using a vernier caliper. Then, the greatest longitudinal diameter (length) and the greatest transverse diameter (width) were used to calculate the tumor volume. Tumor volume $V = \text{length} \times \text{width}^2/2$. After 15 days post-treatment, tumors in all groups were

harvested and weighed. At the end of tumor growth inhibition study, the tumor tissues of every group were digested into single-cell suspensions. The cells were collected and dispersed in 1 mL of PBS after red blood cell lysis. The tumor-associated macrophages were stained with PE antimouse CD86, Alexa Fluor 700 antimouse CD206, and Pacific Blue anti-mouse CD11b antibodies, and then the cells were analyzed by flow cytometry. For histological analysis, the hematoxylin-eosin (H&E) staining of tumor slices was carried out. Meanwhile, the fresh blood samples were collected for serum biochemistry text and blood routine. The healthy mice without any treatment were used as control.

Statistical Analysis: Results were presented as mean ± SD. Significance was calculated using Student's t-test with GraphPad Software: *P < 0.05, **P < 0.01, ***P < 0.001 and ****P < 0.0001. The P-value < 0.05 was considered statistically significant.

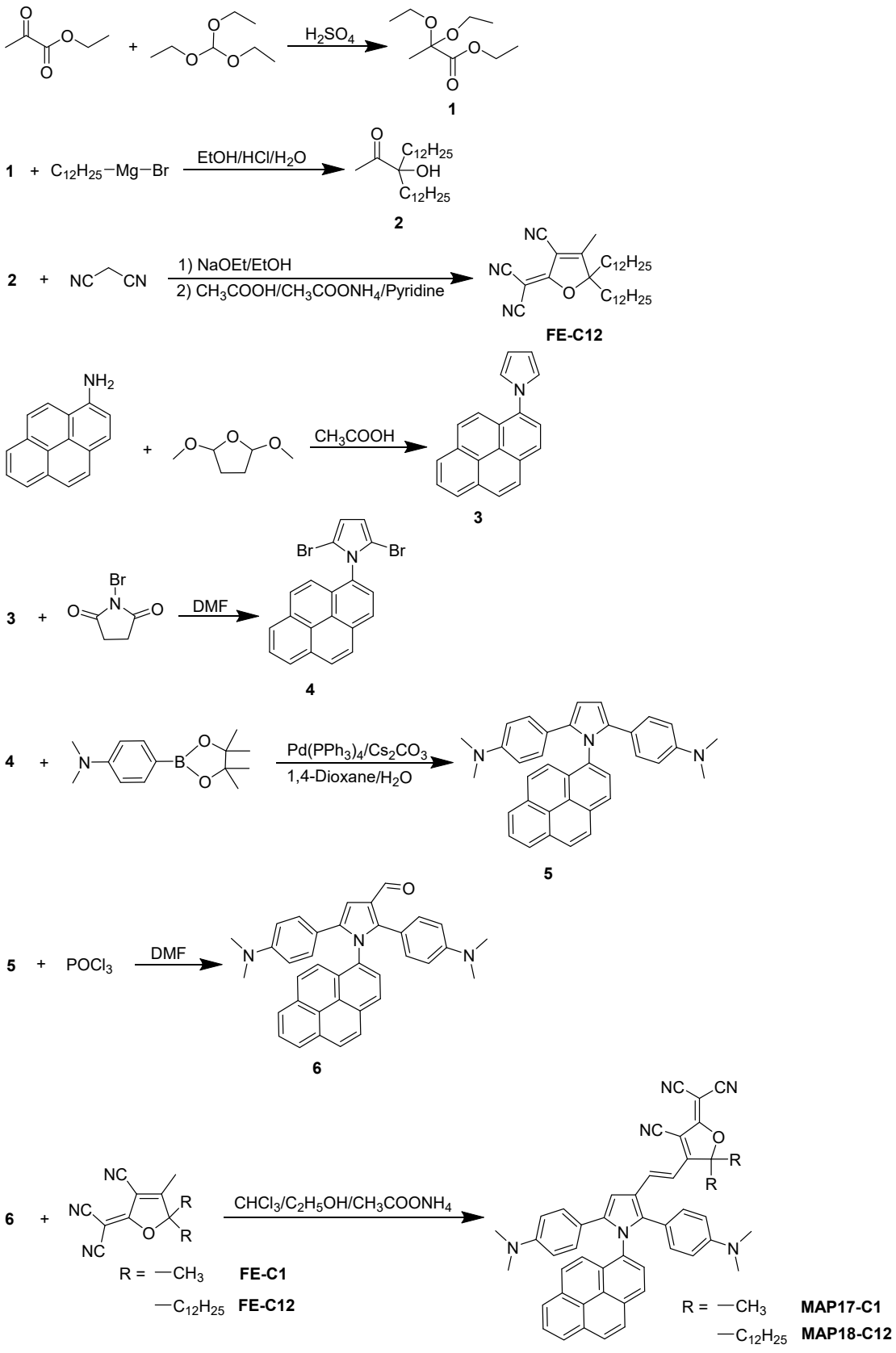
A Summary of Recent Organic Photosensitizers for Type I and/or Type II PDT.

Table S1. A summary of recent organic photosensitizers for PDT.

Name	Photosensitizer	Fluorescence $\lambda_{ex}/\lambda_{em}$ [a]	PDT		Immunotherapy	Reference
			Type	λ_{ex} [b]		
MAP18-C12		**605 nm/810 nm**	**Type I**	**660 nm**	**Yes**	**This Work**
tTDCR		~490 nm/~620 nm	Type I	white light	Yes	3
MTNZPy		528 nm/686 nm	Type I&II	543 nm	No	4
β-TPA-PIO		400 nm/563 nm	Type I	white light	No	5
TIdBO		372 nm/572 nm	Type I	405 nm	Microbe Killing	6
MeOTPPM		452 nm/667 nm	Type I&II	488 nm	No	7
TTFMN		501 nm/622 nm	Type I	white light	No	8
COi6-4Cl		856 nm/1035 nm	Type I/II	880 nm	No	9
TTB		550 nm/730 nm	Type I/II	white light	No	10
2		630 nm/700 nm	Type I	660 nm	No	11

Notes: [a] The maximum emission wavelength (λ_{em}) at a certain excitation wavelength (λ_{ex}); [b] the excited wavelength (λ_{ex}) for PDT.

Synthetic Route of Target Compounds



Scheme S1 The synthetic routes of target compounds.

Synthesis of 2-(3-cyano-4-methyl-5,5-didodecylfuran-2-ylidene) propanedinitrile (FE-C12): Malononitrile (0.6602 g, 10.0 mmol), NaOEt (0.0200 g, 0.30 mmol) and ethanol (10 mL) were added to a 50 mL round bottom flask and stirred at room temperature for 2 h, then compound **2** and pyridine was added and the solution stirred for further three days at 50 ºC to ensure complete reaction. The resulting reaction solution extracted three times with dichloromethane and water and the organic layer was evaporated under reduced pressure. Finally, the purified compound **FE-C12** was obtained by recrystallization in ethanol. Yield: 11.6%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 2.28 (s, 3H), 2.16-1.48 (m, 4H), 1.28-1.24 (m, 40H), 0.89-0.86 (t, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 181.45, 175.97, 110.99, 110.46, 108.87, 106.36, 105.05, 63.09, 57.90, 36.84, 32.82, 31.93, 29.71, 29.67, 29.62, 29.59, 29.53, 29.45, 29.37, 29.33, 29.25, 29.21, 25.75, 22.69, 22.64, 14.49, 14.12. MS (MALDI, m/z) Calcd for $C_{33}H_{53}N_3O$ $[M+Na]^+$: 530.41, found: 530.12.

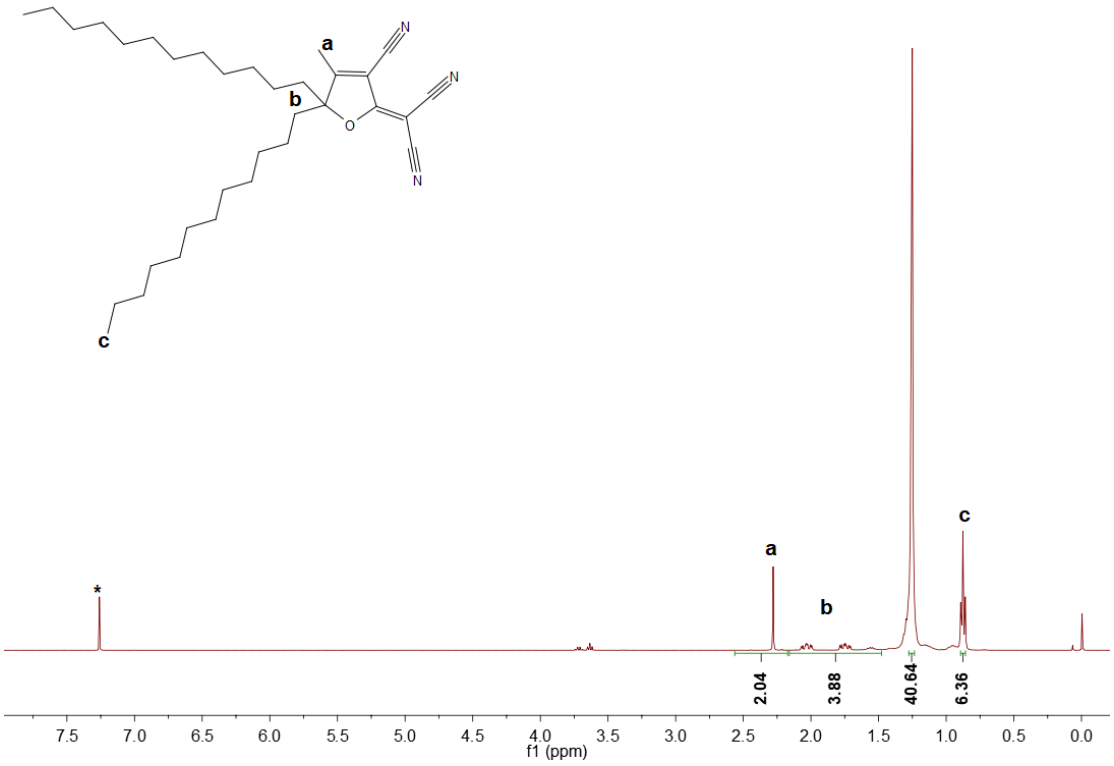


Figure S1. ^{1}H NMR spectrum of **FE-C12** in $CDCl_3$.

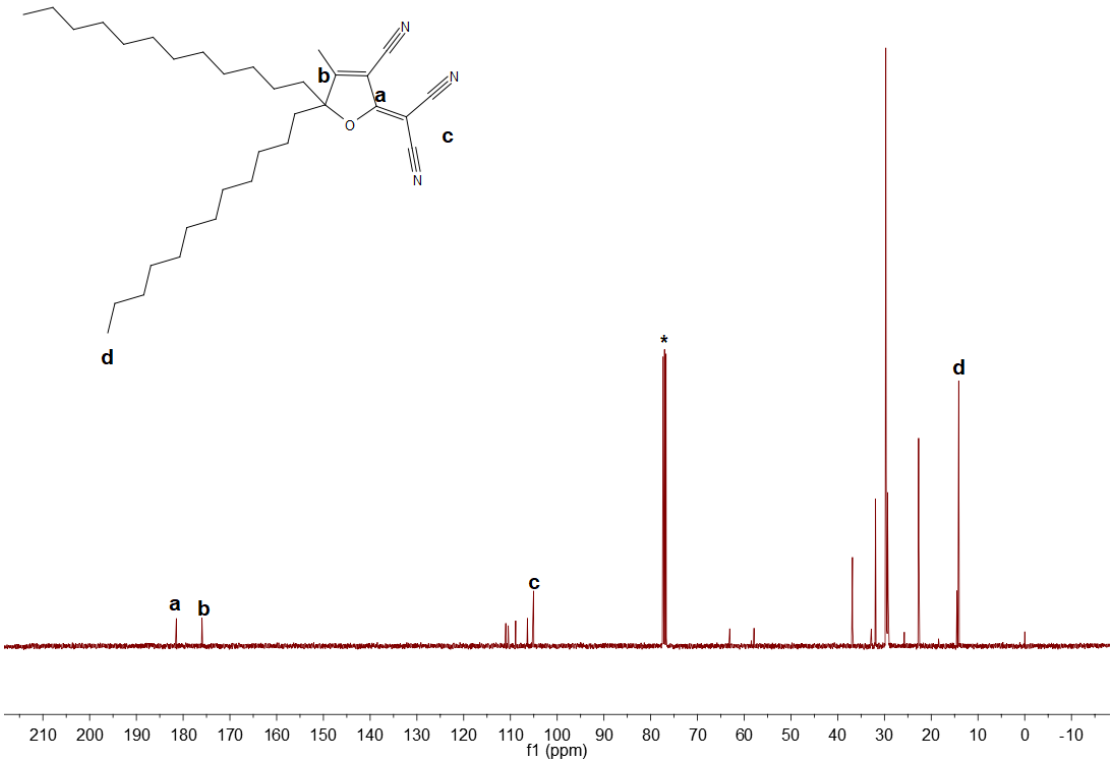


Figure S2. ^{13}C NMR spectrum of **FE-C12** in $CDCl_3$.

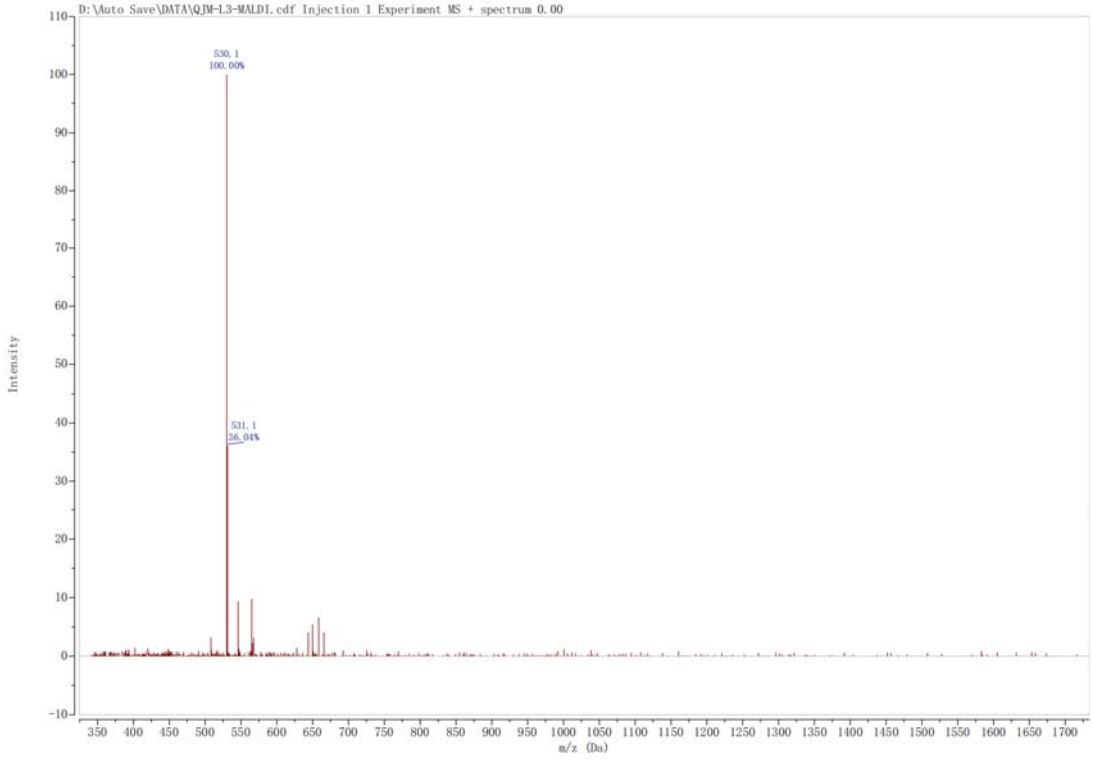


Figure S3. MS spectrum of **FE-C12**.

Synthesis of compound 3: 1-Aminopyrene (2.1910 g, 10.0 mmol) and

5-dimethoxytetrahydrofuran (1.3208 g, 10.0 mmol) were dissolved in 25 mL acetic acid, then refluxed for 12 h. After that, the solution was extracted with dichloromethane and washed with water. Later the organic layer was dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using a dichloromethane/petroleum ether mixture (1/8, V_d/V_p) as the eluent to give desired compound **3** with 76.7% yield. ^1H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.29-7.96 (m, 9H), 7.24-7.04 (m, 2H), 6.70-6.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 135.42, 131.33, 130.96, 130.56, 128.56, 127.83, 127.12, 126.66, 126.44, 125.66, 125.35, 125.22, 124.82, 124.54, 124.08, 123.75, 122.30, 109.35. MS (ESI, *m/z*) Calcd for $C_{20}H_{13}N$ $[M+H]^+$: 268.1, found: 268.1.

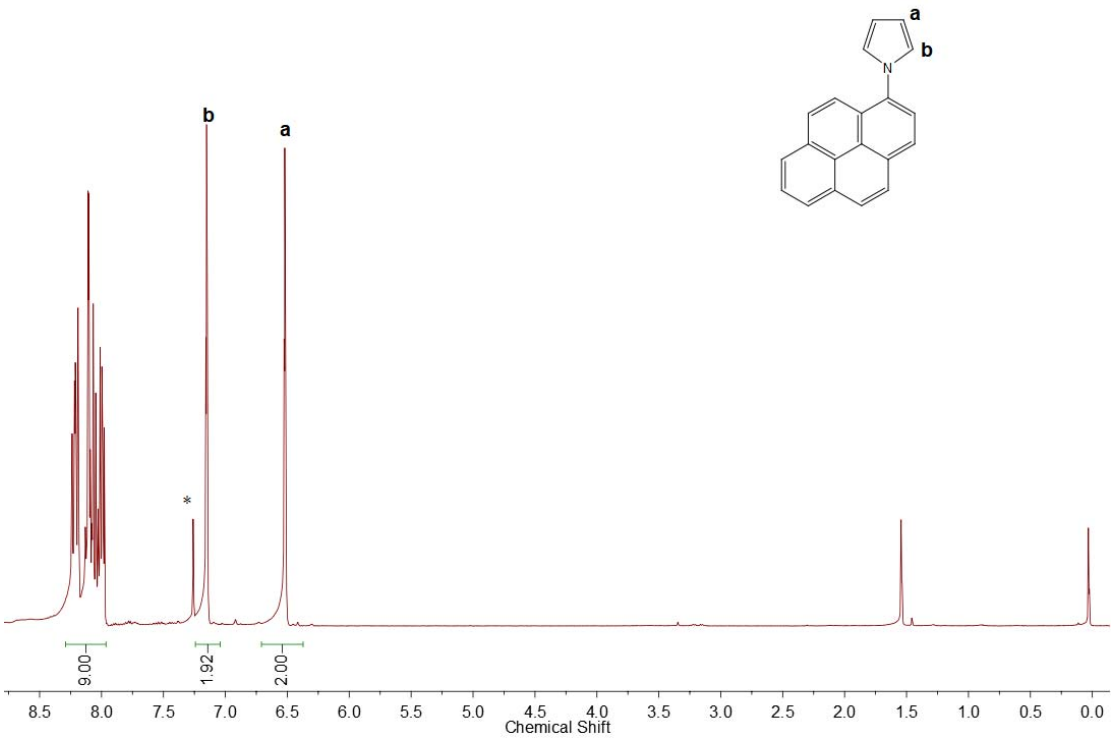


Figure S4. ^1H NMR spectrum of compound **3** in $CDCl_3$.

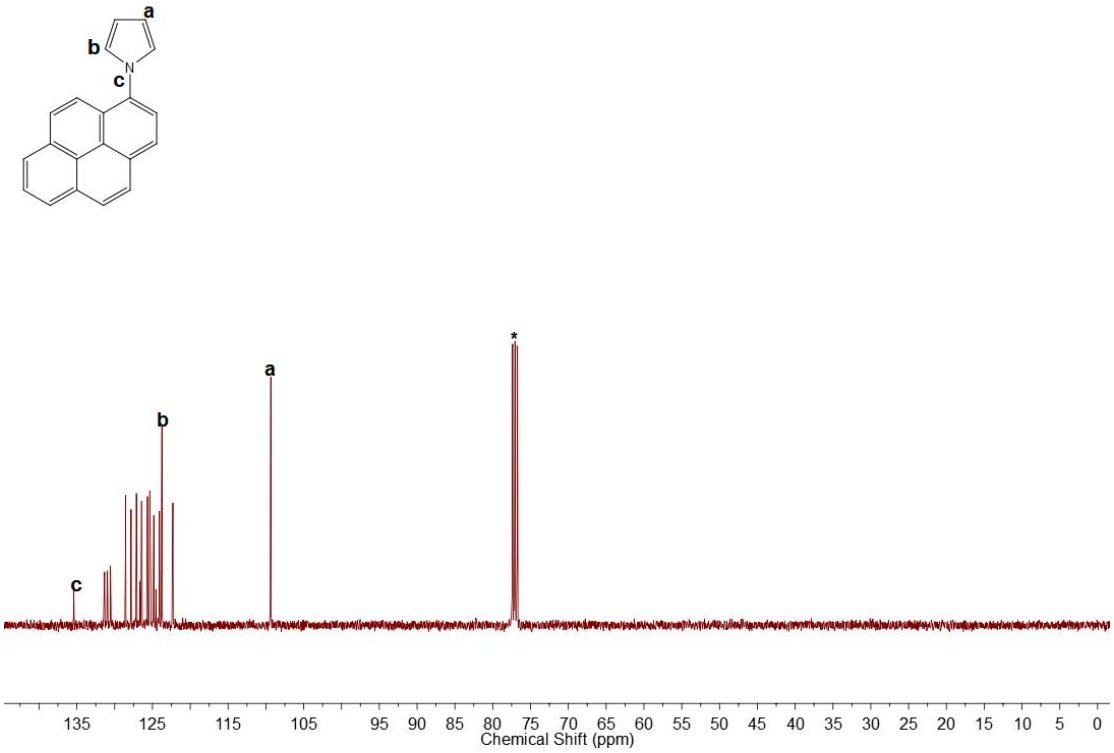


Figure S5. ^{13}C NMR spectrum of compound **3** in $CDCl_3$.

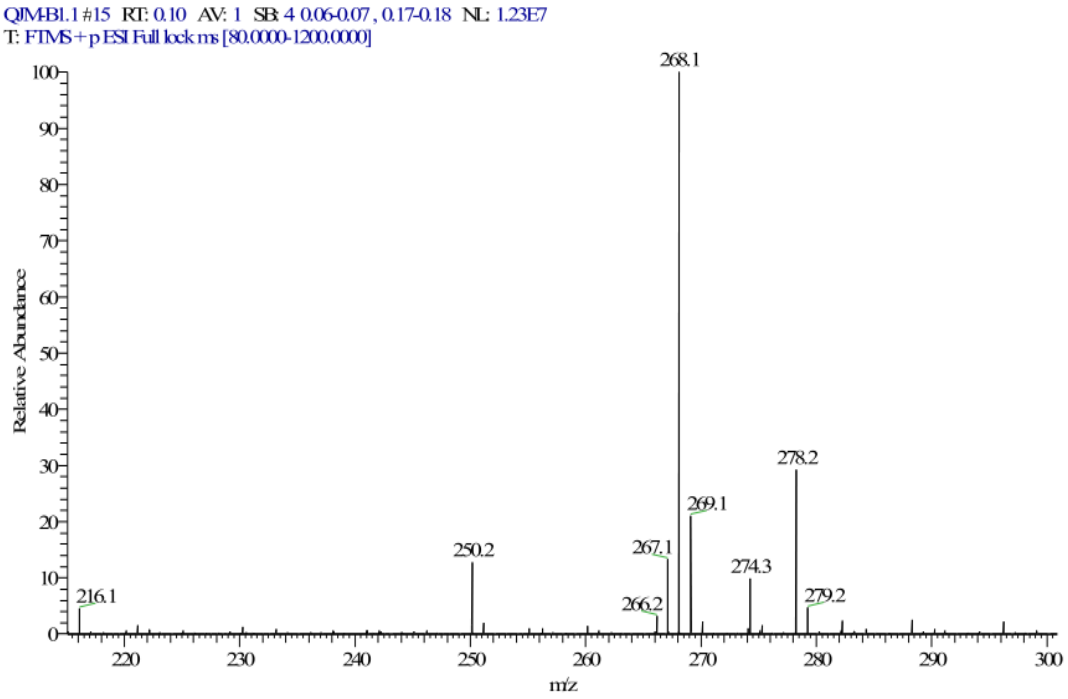


Figure S6. MS spectrum of compound **3**.

Synthesis of compound 4: N-bromosuccinimide (1.0755 g, 5.00 mmol) was dissolved in 5 mL DMF, and then added dropwise into the DMF solution of

compound **3** (1.0755 g, 5.00 mmol) with stirring. After stirring for further 1 h at room temperature, the reaction mixture was extracted with dichloromethane and washed with water. Finally, the organic layer was dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give the compound **4** with 59.7% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.31-8.05 (m, 7H), 7.91(d, J = 8.0 Hz, 1H), 7.33(d, J = 9.2 Hz, 1H), 6.52(s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 132.13, 131.40, 131.09, 130.85, 129.43, 129.39, 128.71, 127.14, 127.04, 126.59, 126.11, 126.02, 125.03, 124.59, 124.33, 121.80, 112.50, 103.93. MS (APCl, *m/z*) Calcd for $C_{20}H_{11}Br_2N$ $[M+H]^+$: 425.92, found: 425.93.

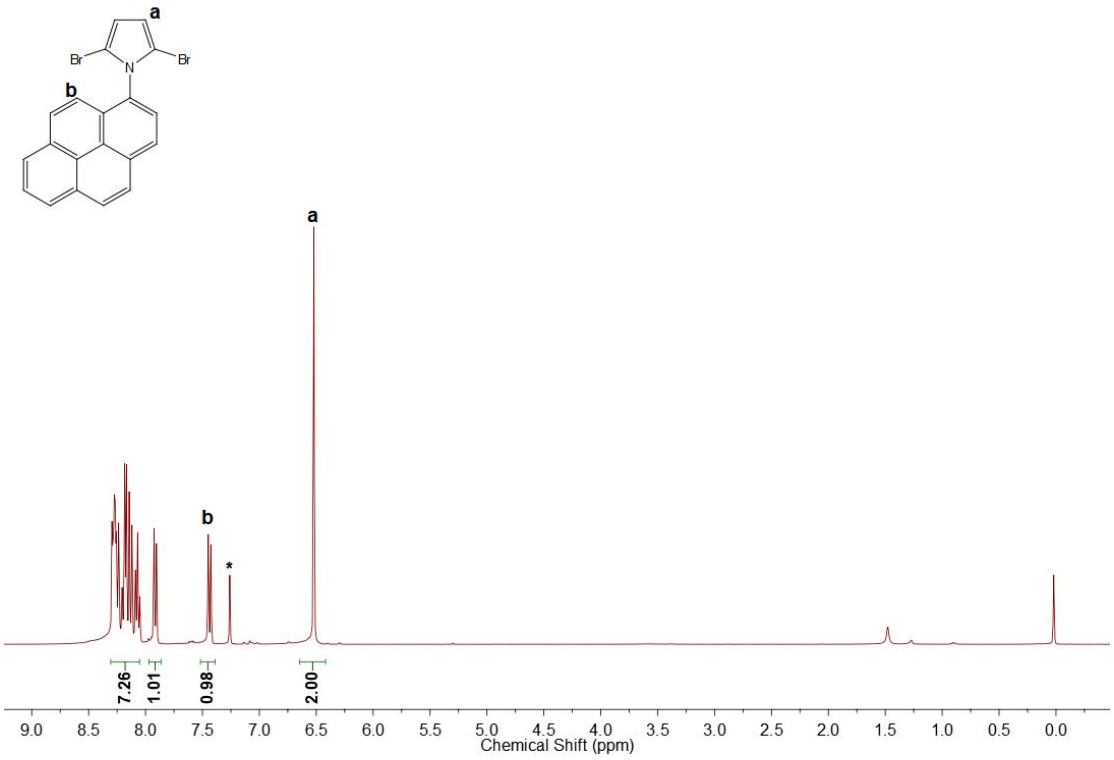


Figure S7. ^{1}H NMR spectrum of compound **4** in $CDCl_3$.

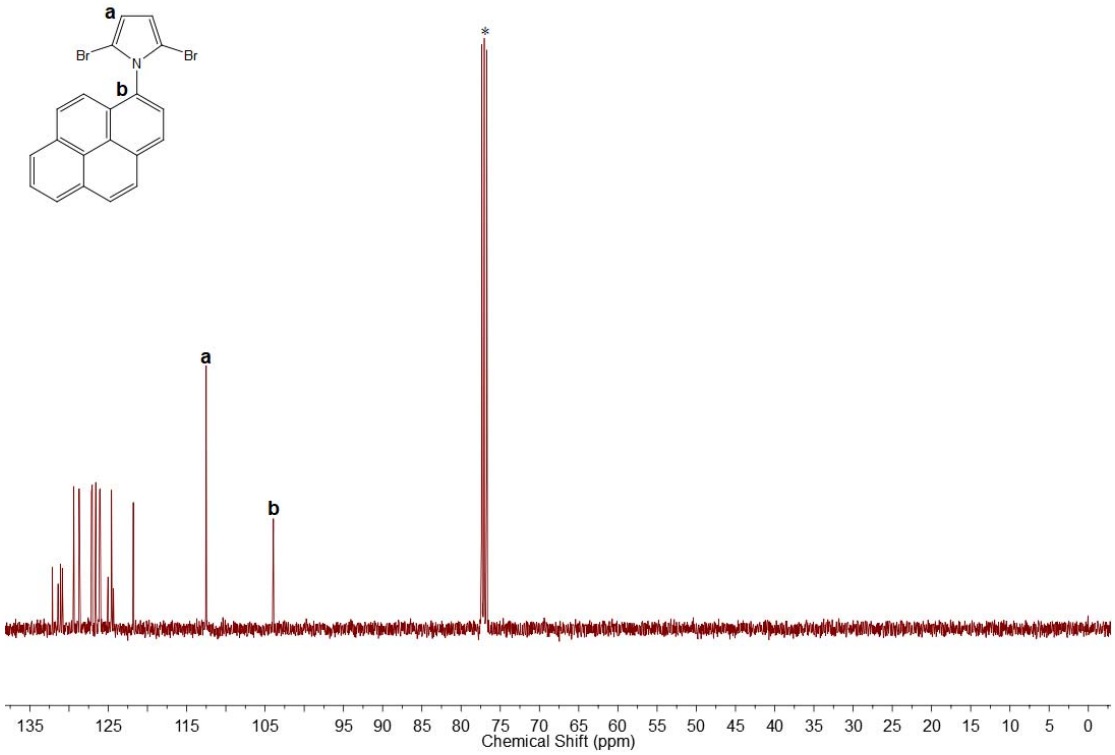


Figure S8. ^{13}C NMR spectrum of compound **4** in $CDCl_3$.

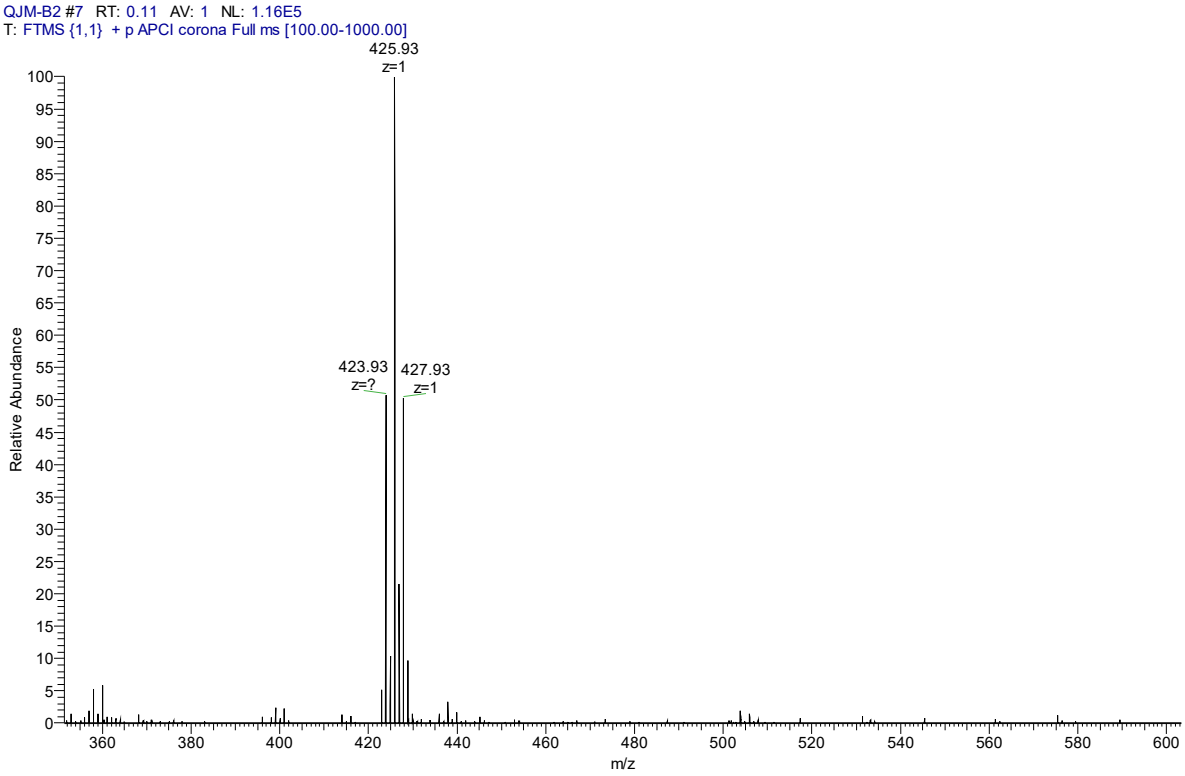


Figure S9. MS spectrum of compound **4**.

Synthesis of compound 5: N,N-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl)aniline (1.2357 g, 5.50 mmol), compound **4** (1.0623 g, 2.50 mmol), Cs_2CO_3

(1.9545 g, 6.00 mmol) and $Pd(PPh_3)_4$ (0.2315 g, 0.20 mmol) were dissolved in dioxane/H_2O (4:1, v/v, 20 mL). The mixture was stirred at 100 °C for 24 h under nitrogen atmosphere. After that, the solution was cooled to room temperature, and later extracted with dichloromethane and washed with water. Then the organic layer was dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using a dichloromethane/petroleum ether mixture (1/4, V_d/V_p) as the eluent to give desired compound **5** with 29.3% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.20 (d, J = 7.2 Hz, 1H), 8.14-7.92 (m, 7H), 7.64(d, J = 9.2 Hz, 1H), 7.09-6.76 (m, 4H), 6.75-6.40 (m, 2H), 6.41-6.12 (m, 4H), 2.74 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 131.09, 130.99, 129.01, 128.95, 128.45, 127.94, 127.72, 127.32, 126.18, 125.39, 124.91, 124.58, 124.44, 122.95, 112.46, 112.27, 112.12, 108.30, 40.52. MS (ESI, m/z) Calcd for $C_{36}H_{31}N_3$ $[M]^+$: 505.25, found: 505.06.

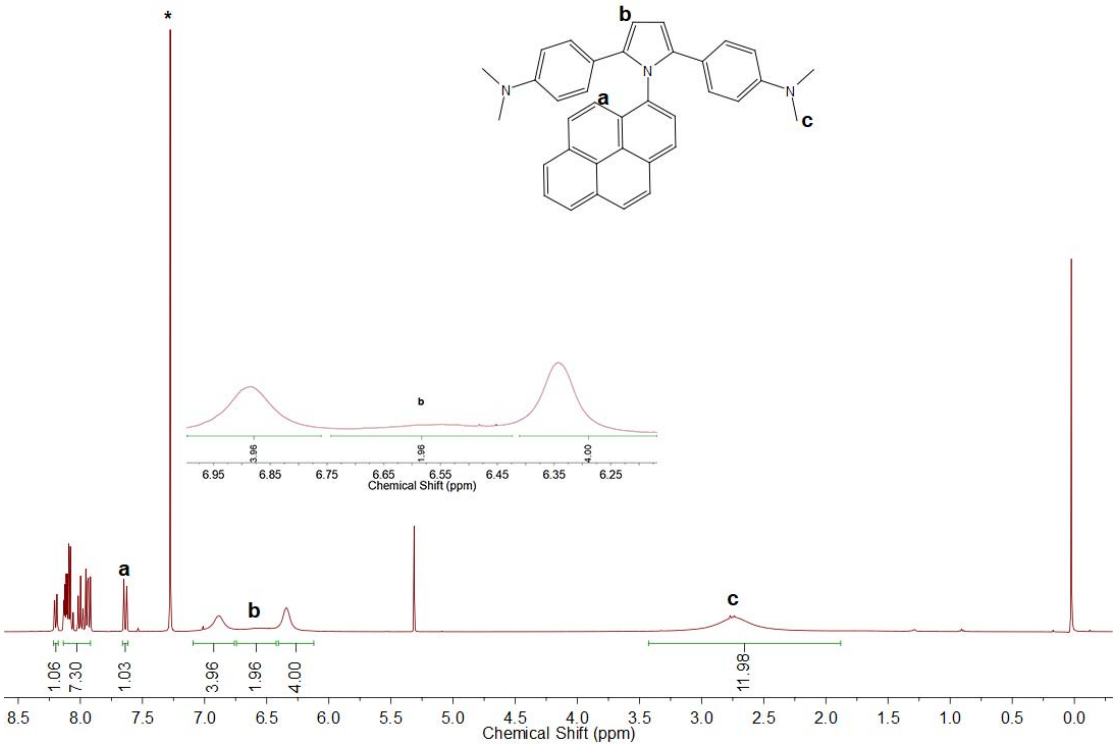


Figure S10. ^{1}H NMR spectrum of compound **5** in $CDCl_3$.

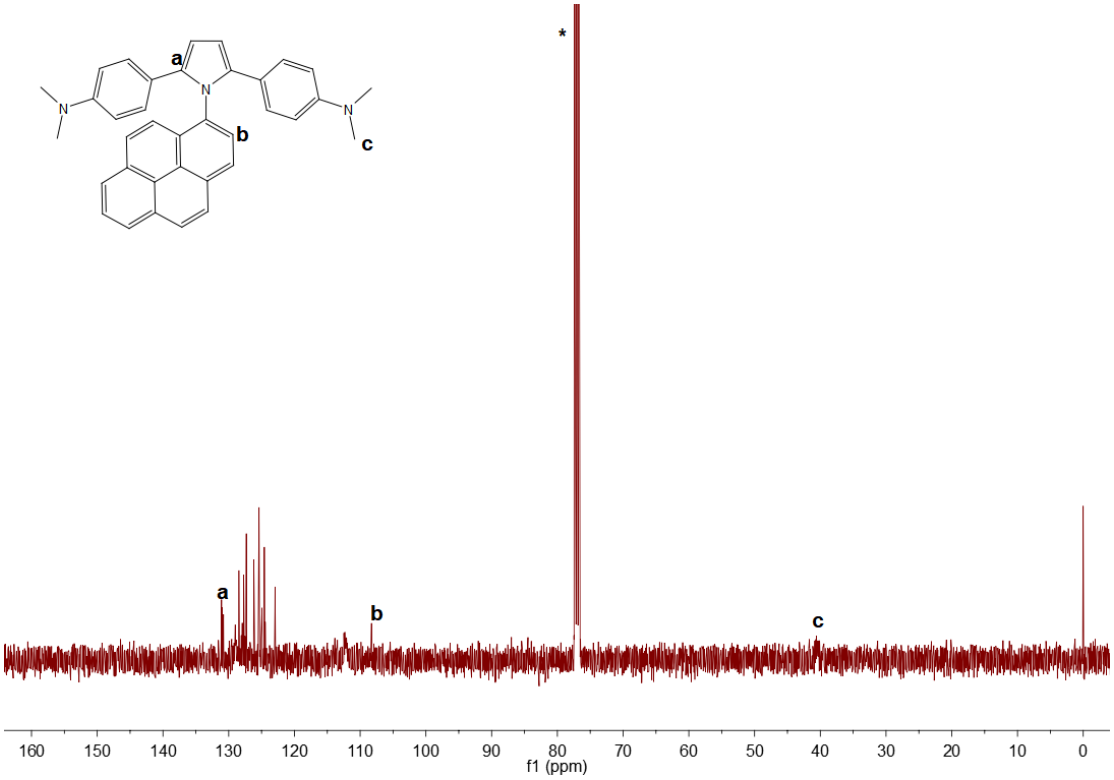


Figure S11. ^{13}C NMR spectrum of compound **5** in $CDCl_3$.

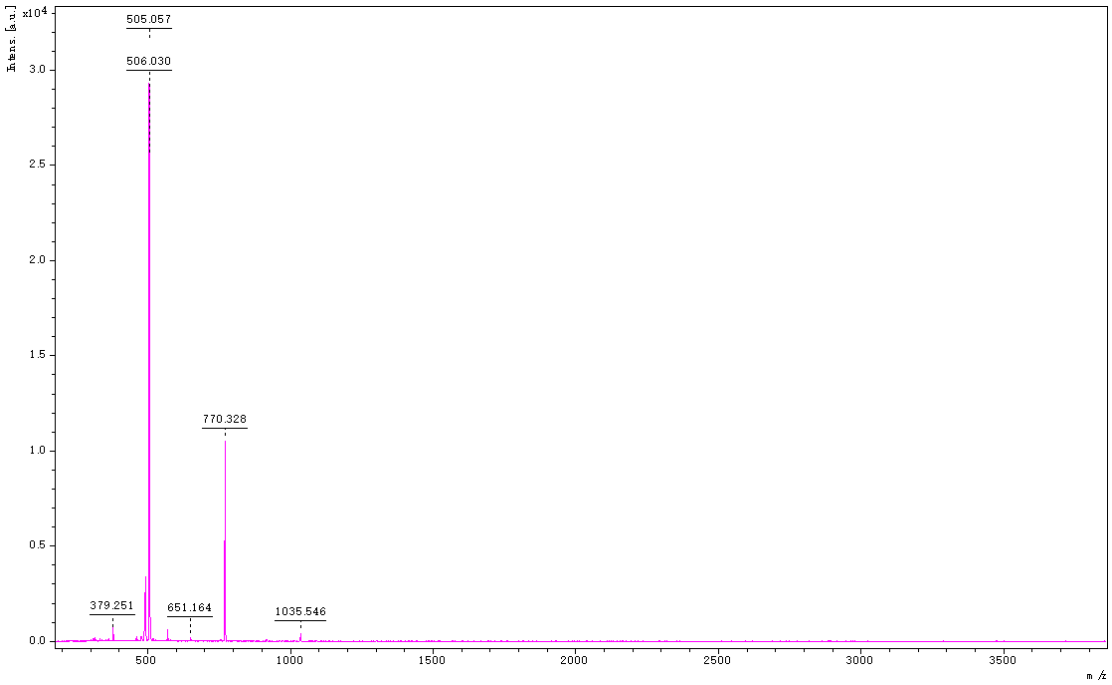


Figure S12. MS spectrum of compound **5**.

Synthesis of compound 6: $POCl_3$ (200 μL, 2.20 mmol) was added dropwise into DMF (15 mL) at 0°C and stirred for 30 min at room temperature, compound **5** (0.5053 g, 1.00 mmol) was added to the above solution. After the mixture stirred for 12 h, the residue was poured into a dilute aqueous solution of Na_2CO_3 (250 mL) and

extracted with dichloromethane. Then the organic layer was dried over anhydrous $MgSO_4$ and filtered by suction. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using a dichloromethane/petroleum ether mixture (1/2, V_d/V_p) as the eluent to give desired compound **6** with 55.6% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 9.79 (s, 1H), 8.20-7.95 (m, 7H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 9.2 Hz, 1H), 7.04 (s, 1H), 7.01-6.78 (m, 4H), 6.50-6.09 (m, 4H), 2.62 (d, *J* = 8.4 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 187.69, 149.78, 147.13, 132.01, 131.62, 131.19, 131.02, 130.83, 129.21, 129.16, 128.93, 128.10, 127.61, 127.20, 126.38, 125.75, 125.71, 124.82, 124.47, 124.28, 123.83, 122.20, 111.17, 105.58, 39.94. MS (ESI, m/z) Calcd for $C_{37}H_{31}N_3O$ $[M+H]^+$: 534.2, found: 534.3.

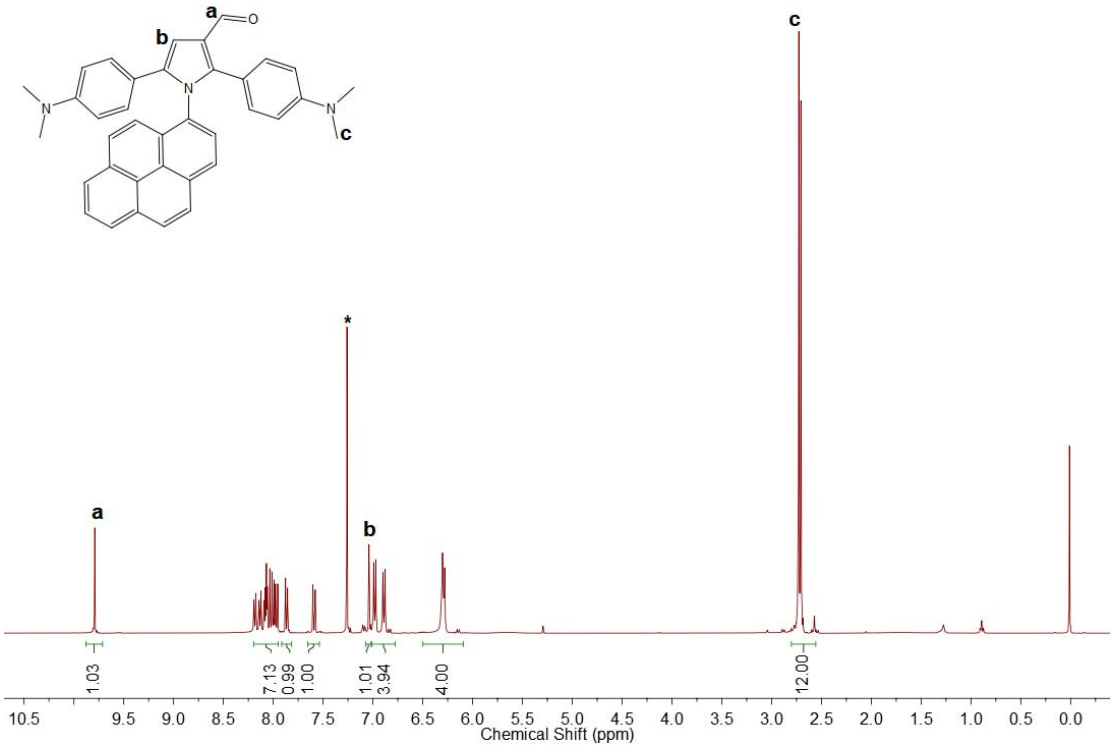


Figure S13. ^{1}H NMR spectrum of compound **6** in $CDCl_3$.

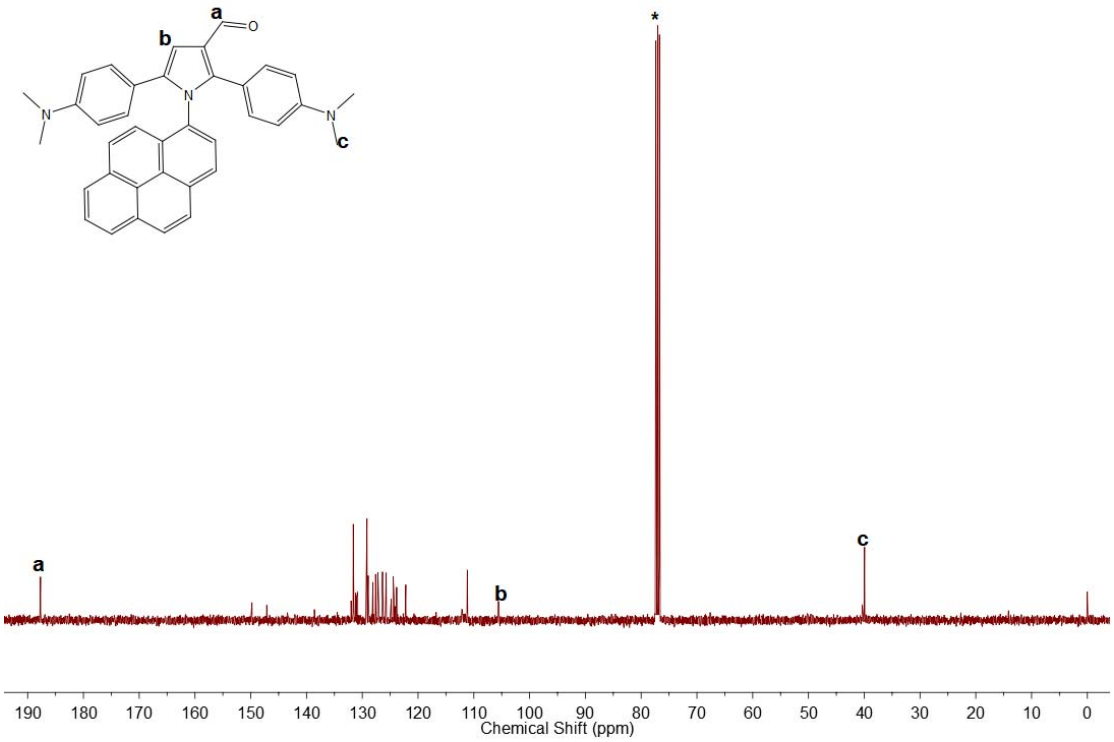


Figure S14. ^{13}C NMR spectrum of compound **6** in $CDCl_3$.

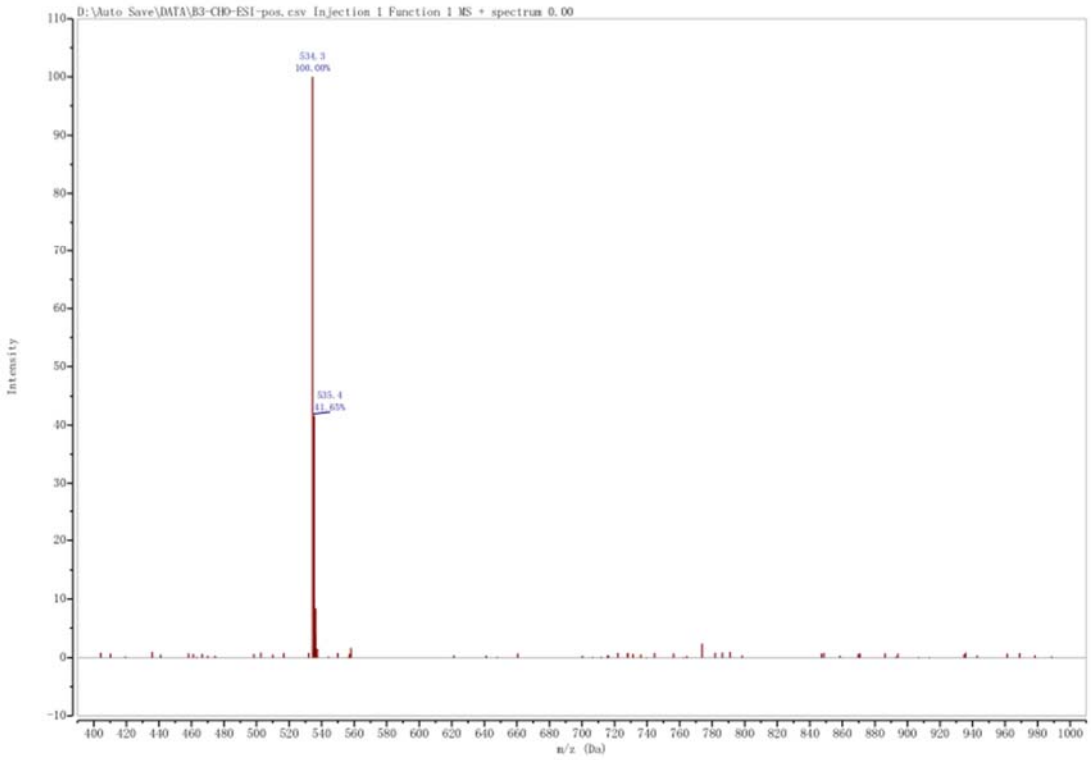


Figure S15. MS spectrum of compound **6**.

Synthesis of MAP17-C1: Compound **6** (0.1333 g, 0.25 mmol), **FE-C1** (0.0450 g,

0.30 mmol) and CH_3COONH_4 (0.0232 g, 0.30 mmol) were dissolved in 15 mL $CHCl_3/C_2H_5OH$ (4/1, v/v) mixed solvents and stirred at 45 ºC for 24 h. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using a dichloromethane/petroleum ether mixture (1/1, V_d/V_p) as the eluent to give desired **MAP17-C1** with 30.3% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.23 (d, *J* = 7.6 Hz, 1H), 8.18-7.96 (m, 6H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 15.6 Hz, 1H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.02-6.78 (m, 6H), 6.57-6.08 (m, 4H), 2.76 (d, *J* = 9.2 Hz, 12H), 1.68 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 176.61, 175.11, 150.09, 149.55, 147.26, 144.34, 141.38, 131.78, 131.38, 131.24, 131.03, 130.77, 129.18, 129.07, 128.85, 128.33, 127.28, 127.20, 126.54, 125.98, 125.86, 124.86, 124.60, 124.27, 121.84, 121.32, 118.73, 116.01, 113.04, 112.20, 111.58, 111.28, 109.83, 104.61, 96.60, 60.42, 53.89, 39.86, 31.61, 26.82, 22.64, 21.08, 14.22. HR-MS (APCI, m/z) Calcd for $C_{48}H_{38}N_6O$ $[M+H]^+$: 715.3180, found: 715.3187, error 0.95 ppm.

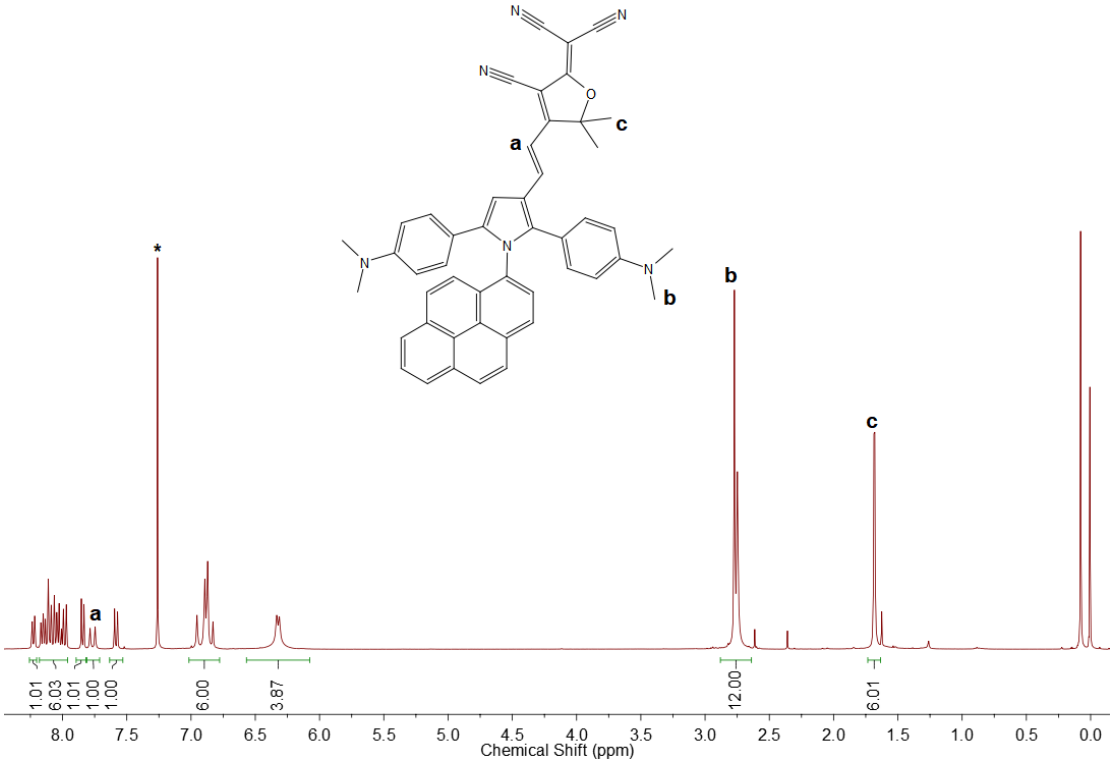


Figure S16. ^{1}H NMR spectrum of **MAP17-C1** in $CDCl_3$.

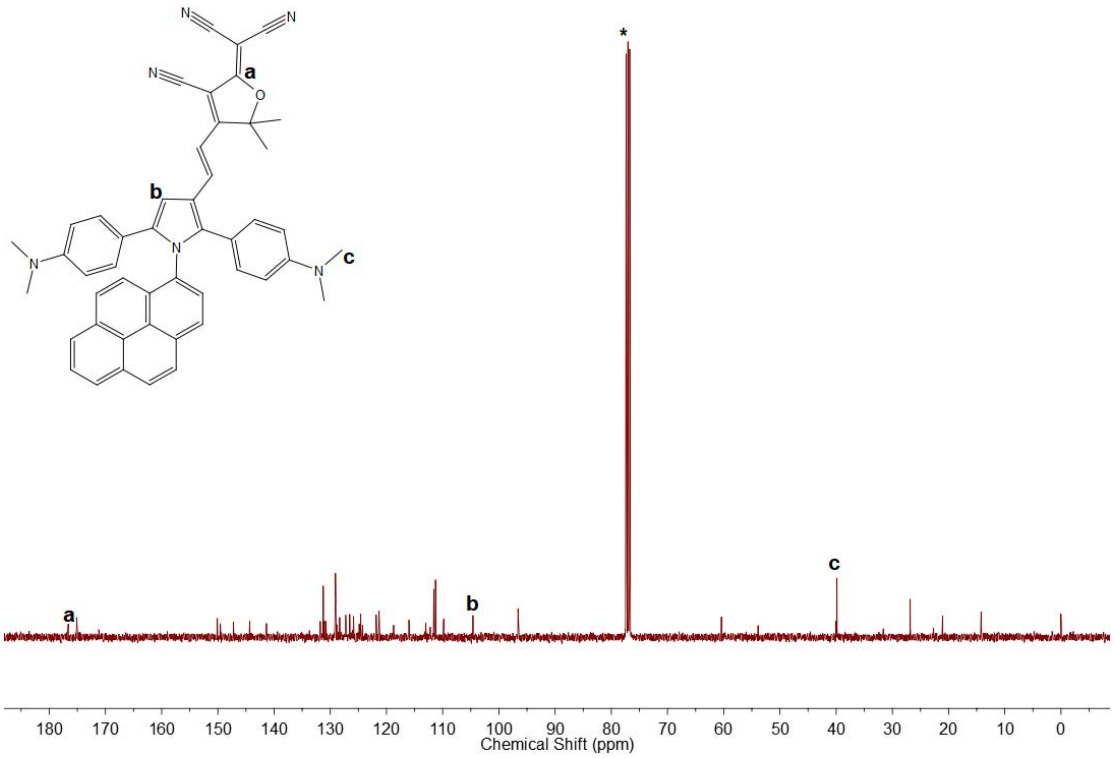


Figure S17. ^{1}H NMR spectrum of **MAP17-C1** in $CDCl_3$.

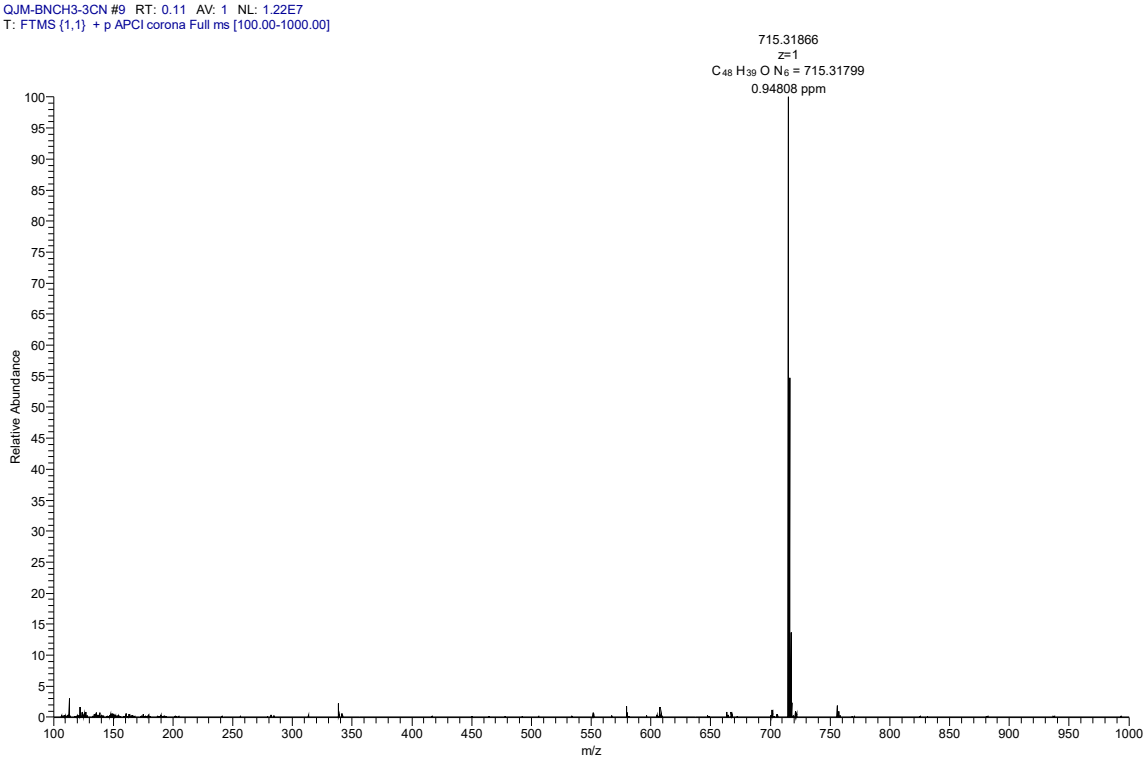


Figure S18. HR-MS spectrum of **MAP17-C1**.

Synthesis of MAP18-C12: Following a similar synthetic procedure to that described

for **MAP17-C1**, and only using compound **FE-C12** instead of **FE-C1**. **MAP18-C12** was obtained with 33.4% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm): 8.29-7.96 (m, 7H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 15.6 Hz, 1H), 7.63 (d, *J* = 9.2 Hz, 1H), 7.10-6.77 (m, 6H), 6.51-6.12 (m, 4H), 2.77 (d, *J* = 12.0 Hz, 12H), 2.15-1.73 (m, 4H), 1.36-1.09 (m, 42H), 0.97-0.79 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm): 177.59, 173.34, 131.77, 131.39, 131.26, 131.04, 130.77, 129.18, 129.09, 128.83, 128.35, 127.29, 127.20, 126.54, 126.00, 125.84, 124.87, 124.60, 124.27, 121.83, 121.22, 113.04, 112.35, 111.55, 111.29, 110.34, 102.47, 39.87, 39.41, 31.93, 29.68, 29.37, 22.71, 14.16. HR-MS (APCI, m/z) Calcd for $C_{70}H_{82}N_6O$ $[M+H]^+$: 1023.6623, found: 1023.6631, error 0.78 ppm.

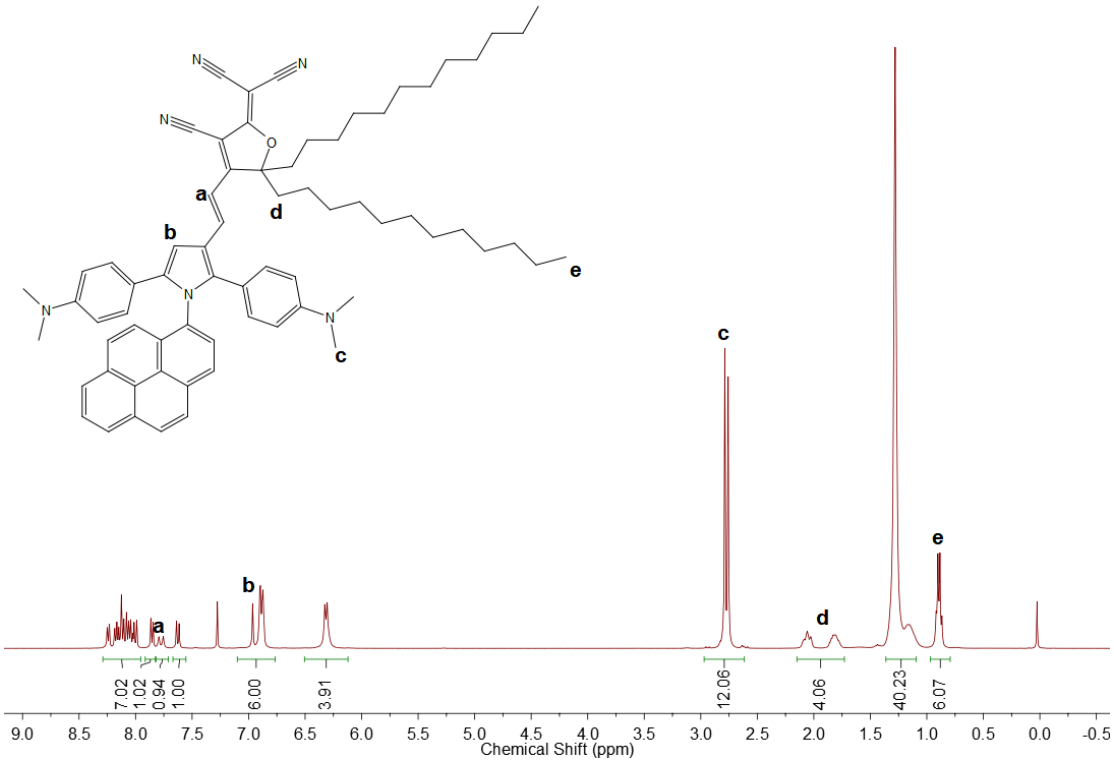


Figure S19. ^{1}H NMR spectrum of **MAP18-C12** in $CDCl_3$.

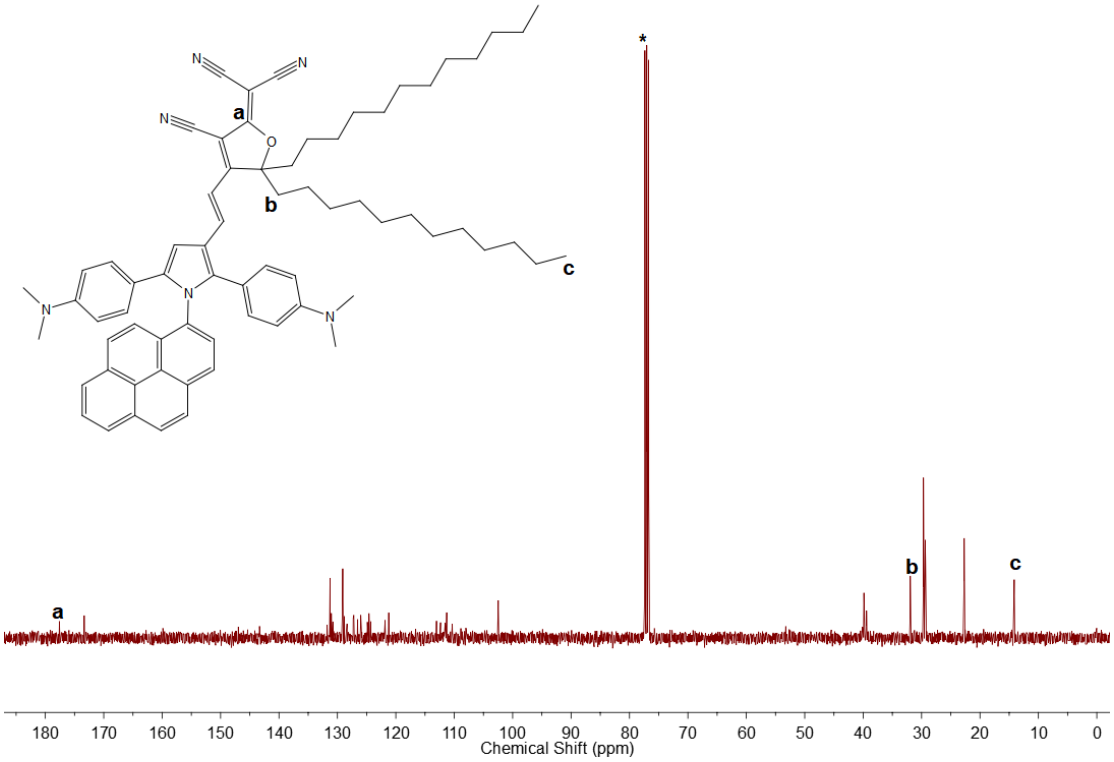


Figure S20. ^{13}C NMR spectrum of **MAP18-C12** in $CDCl_3$.

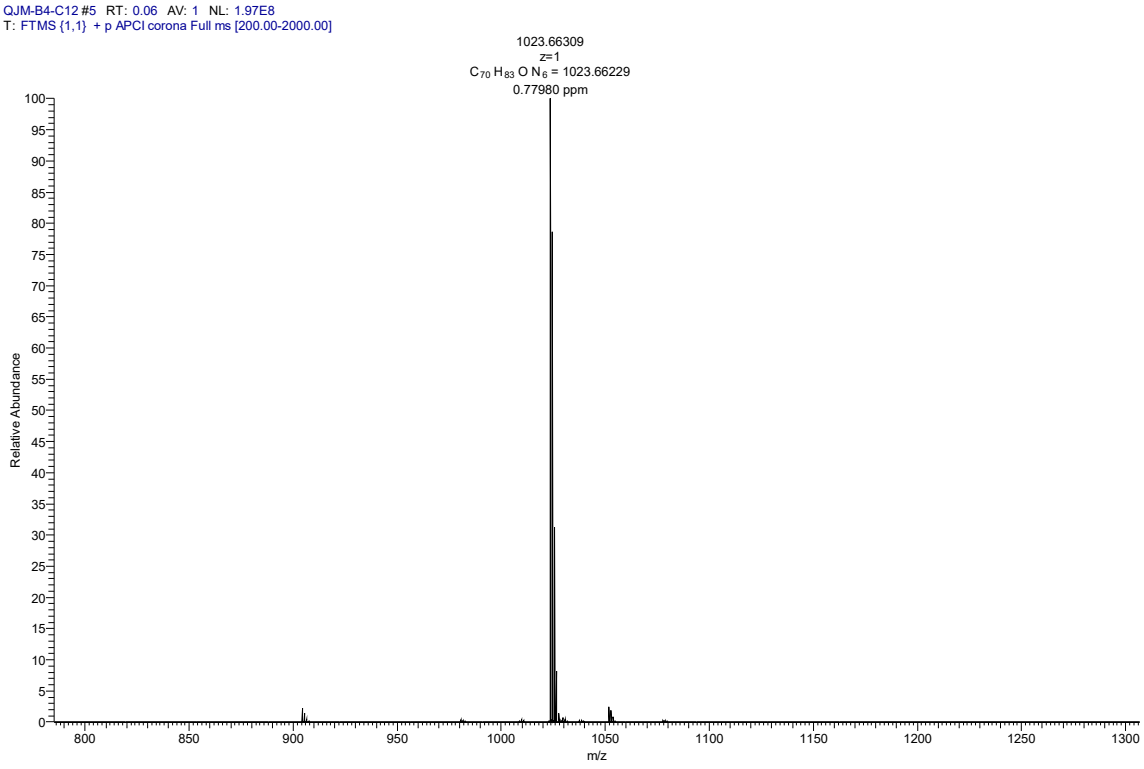


Figure S21. HR-MS spectrum of **MAP18-C12**.

Photophysical Properties, Single Crystal Structure and Theoretical Calculation

Table S2. Photophysical data of **MAP18-C12**, **MAP17-C1** and **MAP4-FE**.

Names and Structures	Solution		Nanoparticles			Solid		
	λ_{abs} [a] (nm)	ε (10^4 L·mol^{-1}·cm^{-1})	λ_{abs} (nm)	λ_{em} [b] (nm)	τ [d] (ns)	λ_{em} (nm)	Φ_f [c] (%)	τ [d] (ns)
MAP18-C12	580	3.13	605	819	0.51	893	0.51	0.33
MAP17-C1	575	2.86	599	810	0.54	899	0.28	0.35
MAP4-FE	564	2.74	590	-- [e]	-- [e]	866	-- [e]	-- [e]

Note: [a]: The longer absorption peak (λ_{abs}) and molar absorption coefficient (ε) measured in DMSO at [MAPs] = 1.0 × 10^{-5} mol L^{-1}. [b]: The maximum emission wavelength (λ_{em}) measured at the excitation wavelength λ_{ex} = 650 nm. [c]: The absolute fluorescence quantum yield (Φ_f) and the fluorescence lifetime (τ) measured at λ_{ex} = 580 nm. [d]: Calculated using one exponential. [e]: "--" means no data.

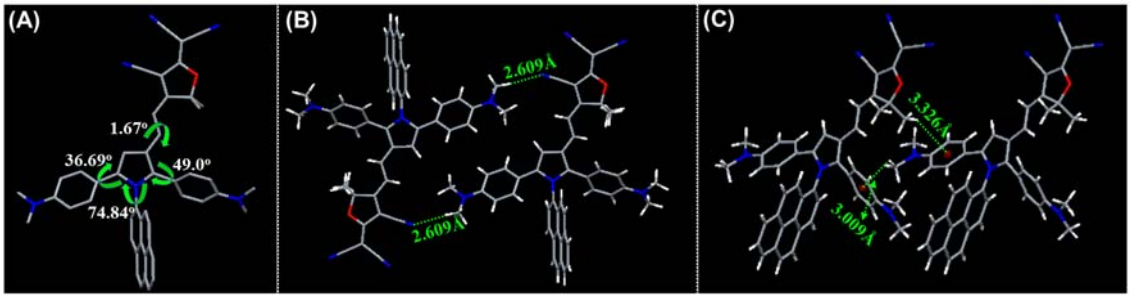


Figure S22. (A) Molecular conformation of a single crystal of **MAP17-C1** (CCDC: 2127406) without hydrogen for clarity. The intermolecular interactions of (B) C-H···N and (C) C-H···π interactions among the adjacent molecules in its single crystal of **MAP17-C1**.

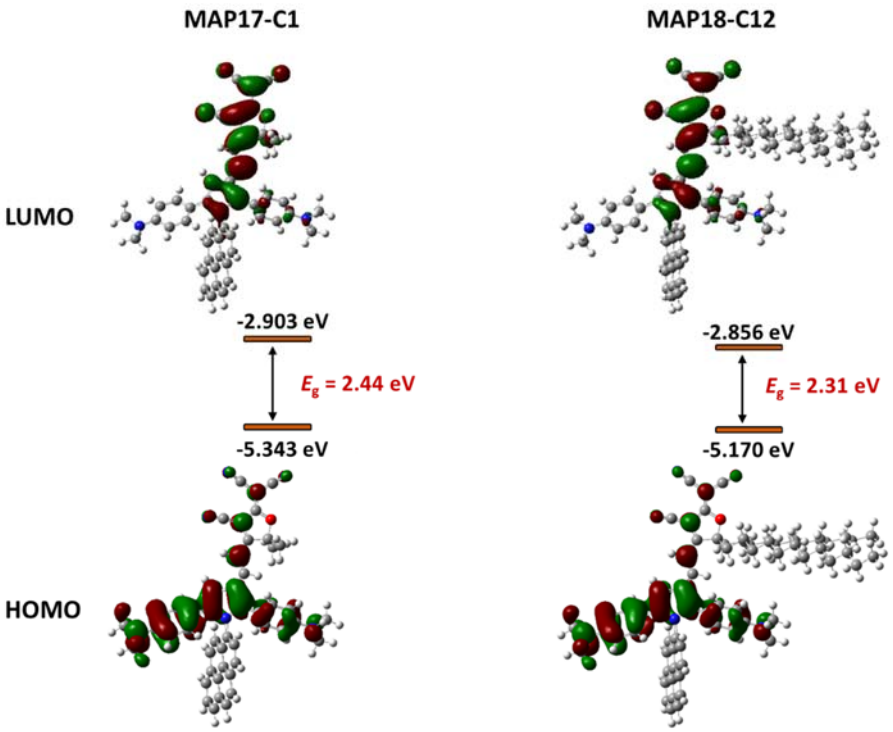


Figure S23. The HOMO and LUMO orbital energy level calculation of **MAP17-C1** and **MAP18-C12** by B3LYP/6-31G (d,p).

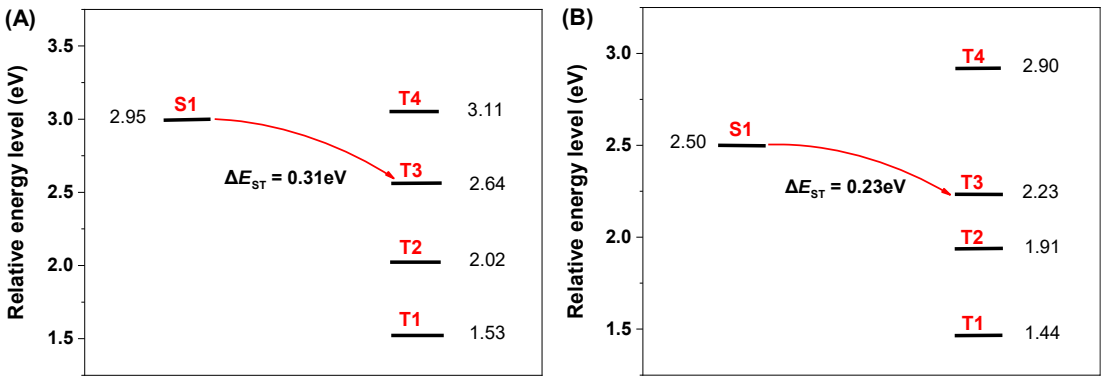


Figure S24. Relative energy levels of (A) **MAP17-C1** and (B) **MAP18-C12** calculated by TD-DFT.

Size Characterization of Nanoparticles (NPs)

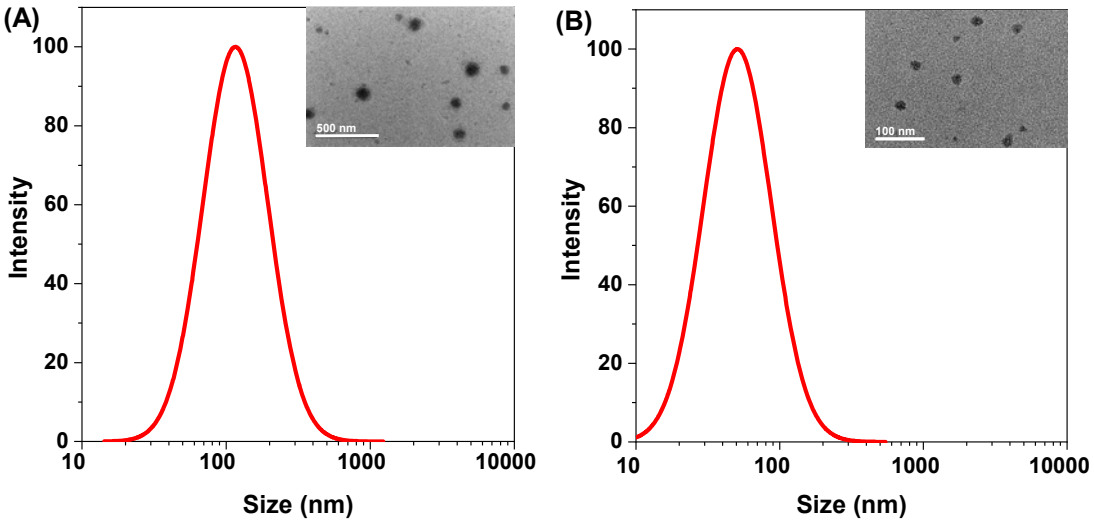


Figure S25. Dynamic laser scattering size and TEM image (insert) of (A) **MAP17-C1 NPs** and (B) **MAP18-C12 NPs**.

Photodynamic Properties

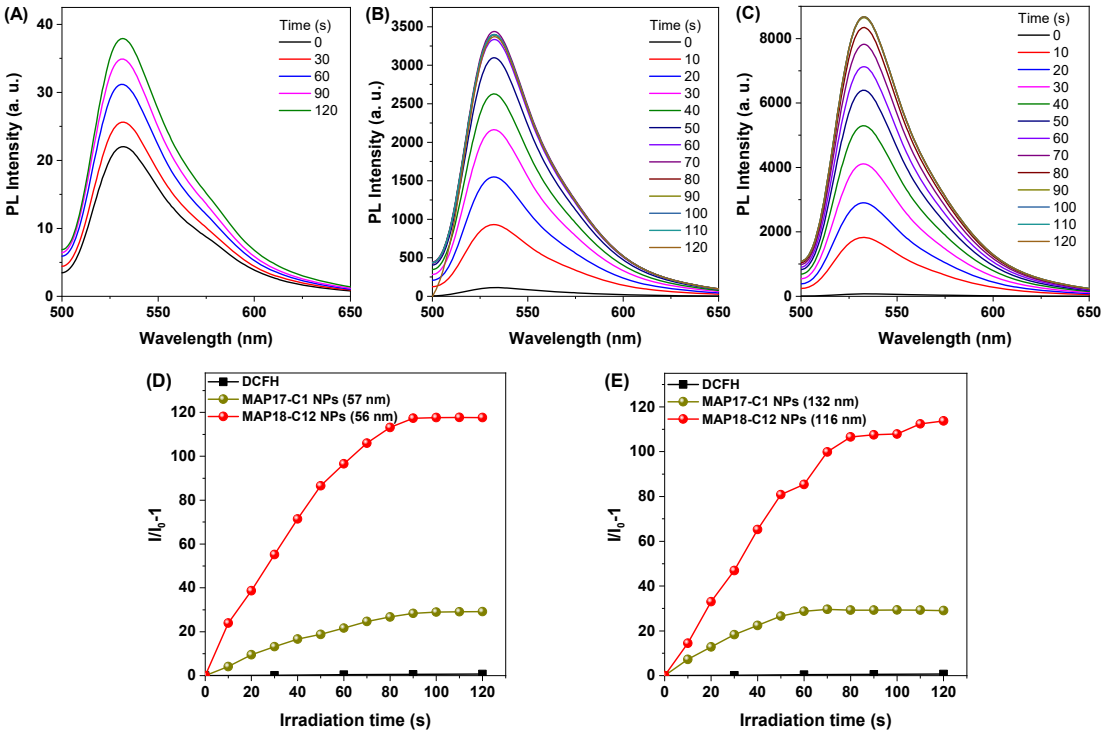


Figure S26. PL spectra of (A) DCFH, (B) **MAP17-C1 NPs** and (C) **MAP18-C12 NPs** with DCFH in PBS solution under white light irradiation (5 mW cm^{-2}). The effect of nanoparticle size on total ROS generation. (D) Fluorescence intensity net change (I/I_0-1) at 532 nm for the DCFH indicator with **MAP17-C1 NPs** (57 nm) and

MAP18-C12 NPs (56 nm). (E) Fluorescence intensity net change (I/I_0-1) at 532 nm for the DCFH indicator with **MAP17-C1 NPs** (132 nm) and **MAP18-C12 NPs** (112 nm).

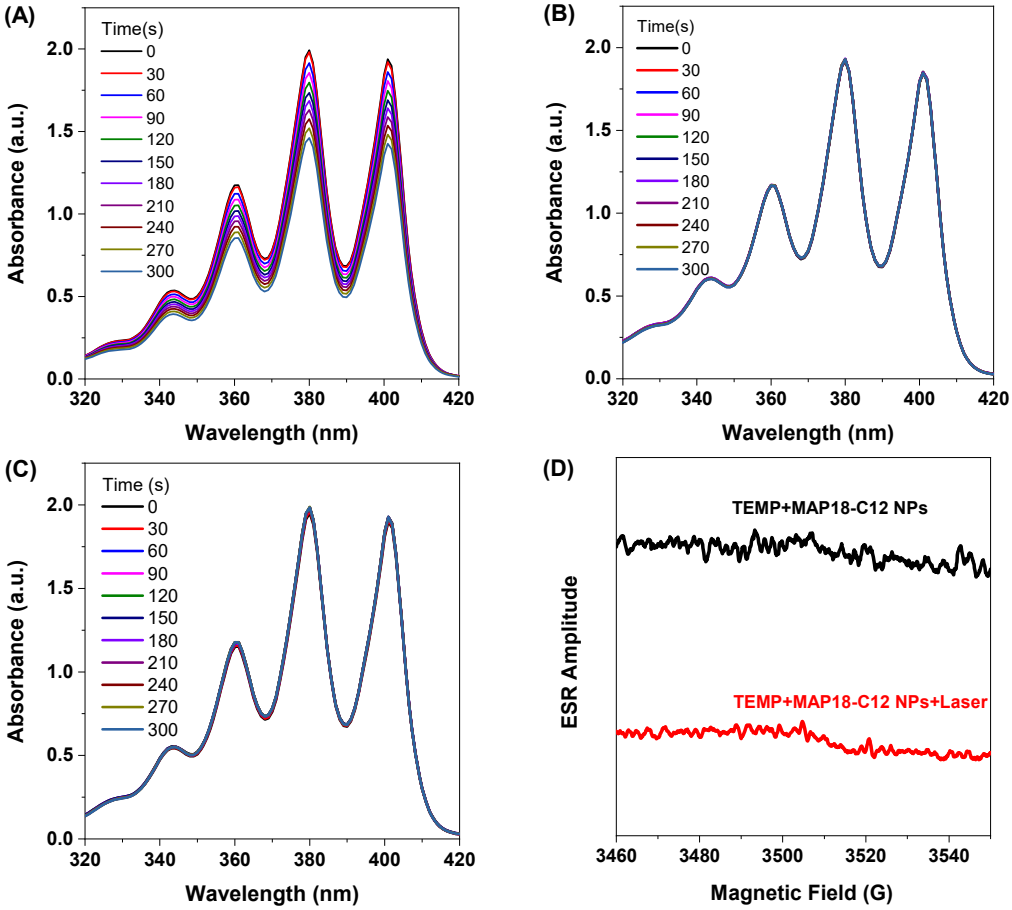


Figure S27. UV absorption spectra of (A) Rose Bengal, (B) **MAP17-C1 NPs** and (C) **MAP18-C12 NPs** with ABDA in PBS solution under white light irradiation (5 mW cm^{-2}). (D) ESR spectra of TEMP/$^1O_2$ for **MAP18-C12 NPs** under laser irradiation of 650 nm.

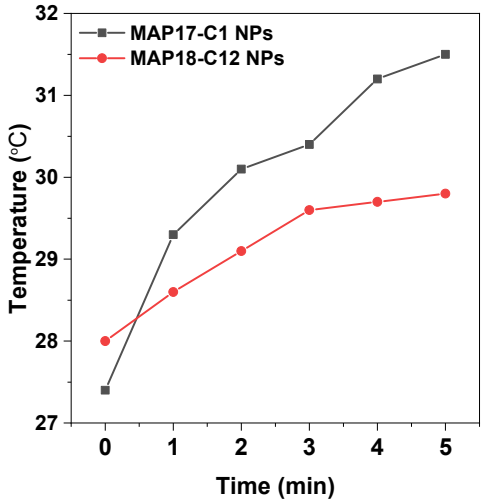


Figure S28. Photothermal properties of **MAP17-C1 NPs** and **MAP18-C12 NPs**. Photothermal heating curves of **MAP17-C1 NPs** and **MAP18-C12 NPs** aqueous

dispersions under 660 nm light irradiation (10^{-4} mol L^{-1}, 50 mW cm^{-2}).

Cell Imaging and in Vitro PDT & Immunity Therapy Performance

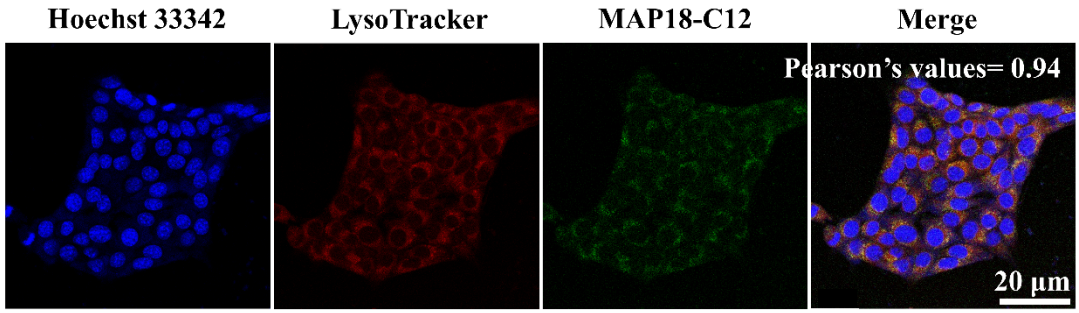


Figure S29. Confocal microscopy images of Hoechst 33342 (Nuclues maker), LysoTracker (lysosome maker), **MAP18-C12 NPs** and merge.

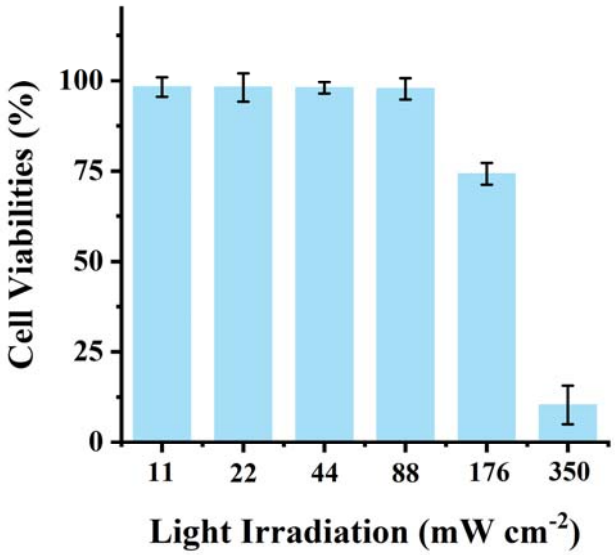


Figure S30. Cell survival rate under different irradation intensity for 5 min at [**MAP18-C12 NPs**] = 10 μmol/L.

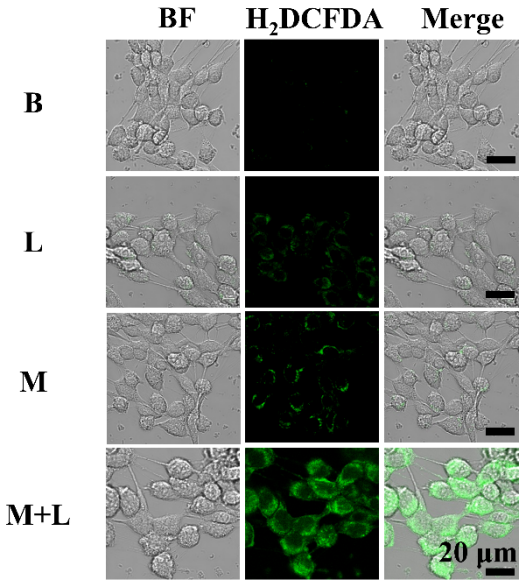


Figure S31. Fluorescence images by CLSM of 4T1 cells stained with DCFH-DA. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (22 mW cm^{-2}, 5 min).

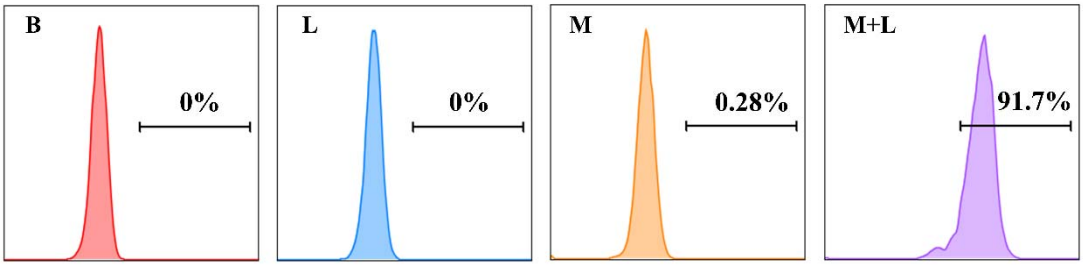


Figure S32. Flow cytometry analysis of intracellular ROS measured by a flow cytometer of 4T1 cells stained with H_2DCFDA. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (660 nm, 22 mW cm^{-2}, 5 min).

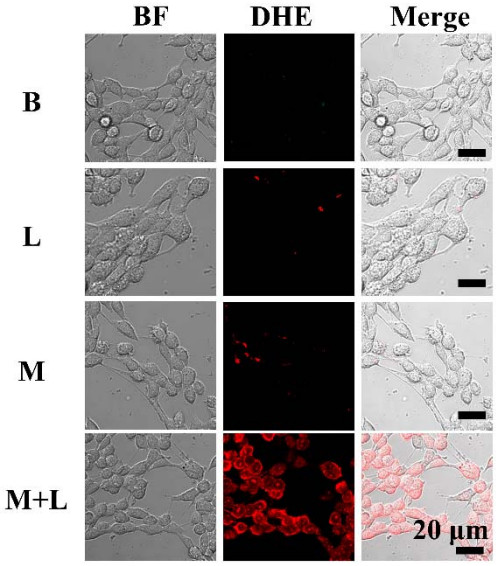


Figure S33. Fluorescence images by CLSM of 4T1 cells stained with DHE. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (660 nm, 22 mW cm^{-2}, 5 min).

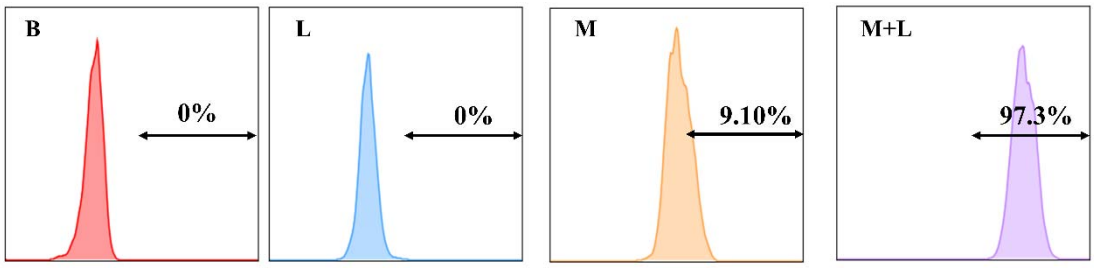


Figure S34. Flow cytometry analysis of intracellular ROS measured by a flow cytometer of 4T1 cells stained with DHE. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (660 nm, 22 mW cm^{-2}, 5 min).

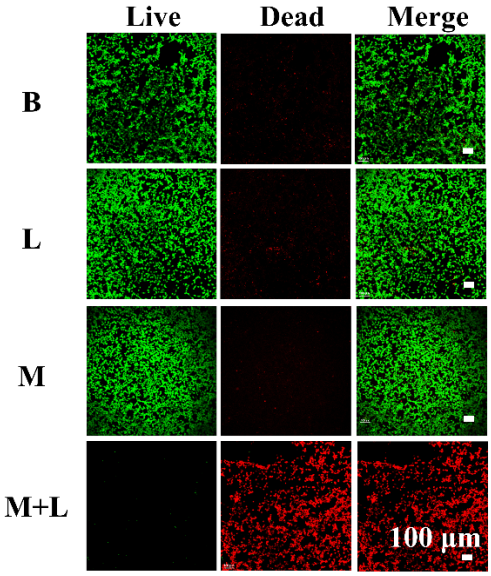


Figure S35. Fluorescence images by CLSM of 4T1 cells stained with Calcein-AM/PI. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (660 nm, 350 mW cm^{-2}, 5 min).

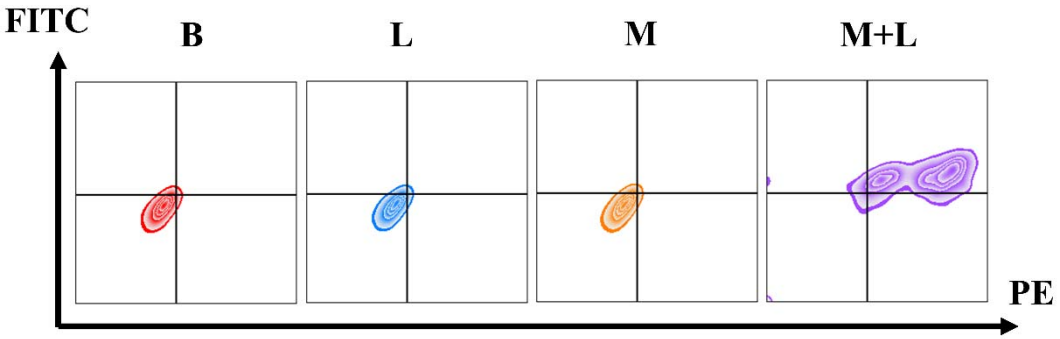


Figure S36. Flow cytometry analysis of 4T1 cells stained with Calcein-AM/PI. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (660 nm, 350 mW cm^{-2}, 5 min).

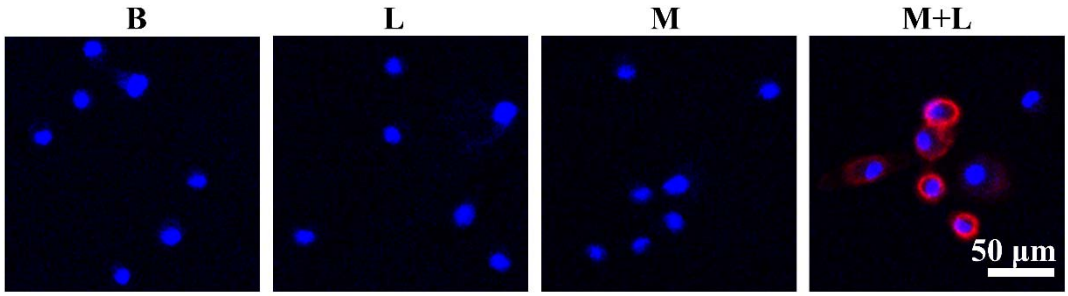


Figure S37. CLSM images of Hoechst 33342 (Nuclues maker), CD206 (M2 marker, green) and CD86 (M1 marker, red) expression on M0 before and after treatments. B:

Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**]= 10 μmol/L; laser irradiation (22 mW cm^{-2}, 5 min).

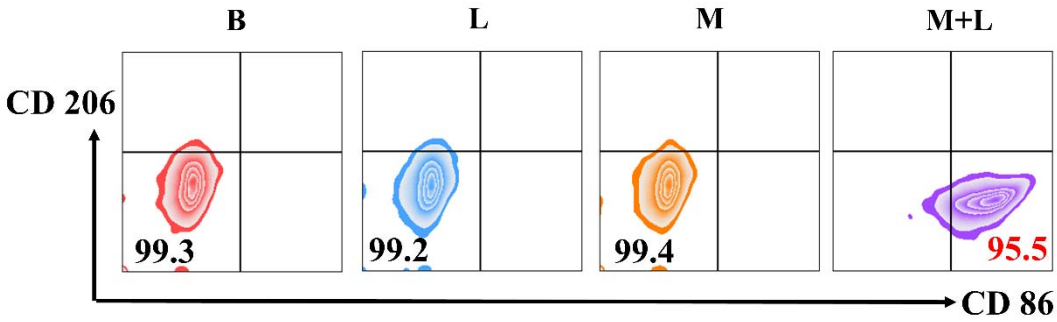


Figure S38. The flow cytometry analysis of M0 cell after different treatments. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**]= 10 μmol/L; laser irradiation (22 mW cm^{-2}, 5 min).

PDT& Immunity Therapy Performance in 3D Multicellular Tumor-Immune Spheroid Model

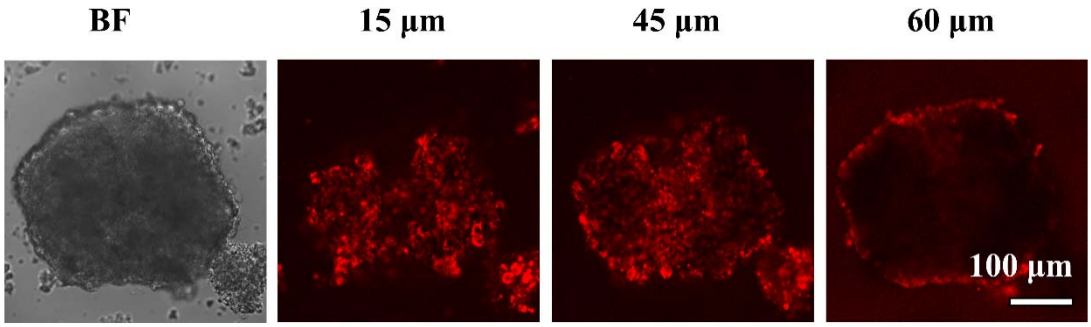


Figure S39. CLSM imaging of the **MAP18-C12 NPs** penetration in different formations in 3D multicellular spheroids model. Scale bar: 100 μm.

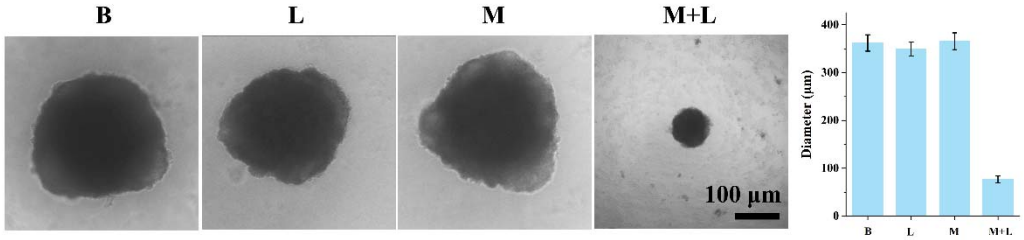


Figure S40. The image of 3D multicellular tumor-immune spheroid model and relative spheroid diameter after different treatments for 96 h. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (350 mW cm^{-2}, 5 min). Scale bar: 100 μm.

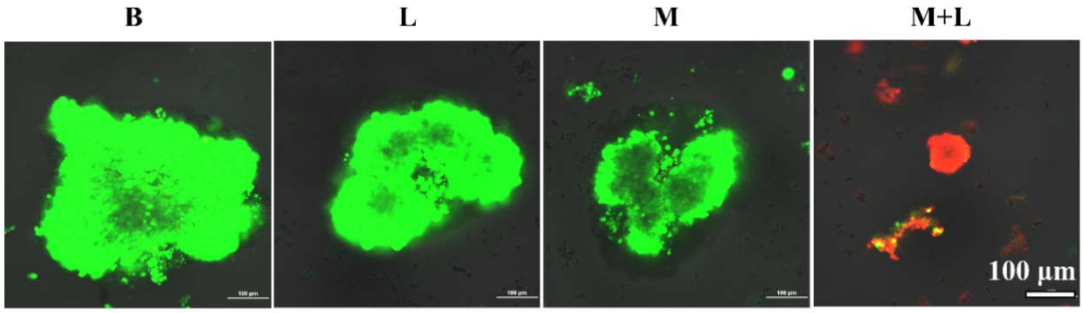


Figure S41. Representative photos of calcein-AM (green)/PI (red) assay of the 3D multicellular tumor-immune spheroids after different treatments for 96 h. B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 10 μmol/L; laser irradiation (350 mW cm^{-2}, 5 min).

H&E Staining and Serum Biochemical Parameters

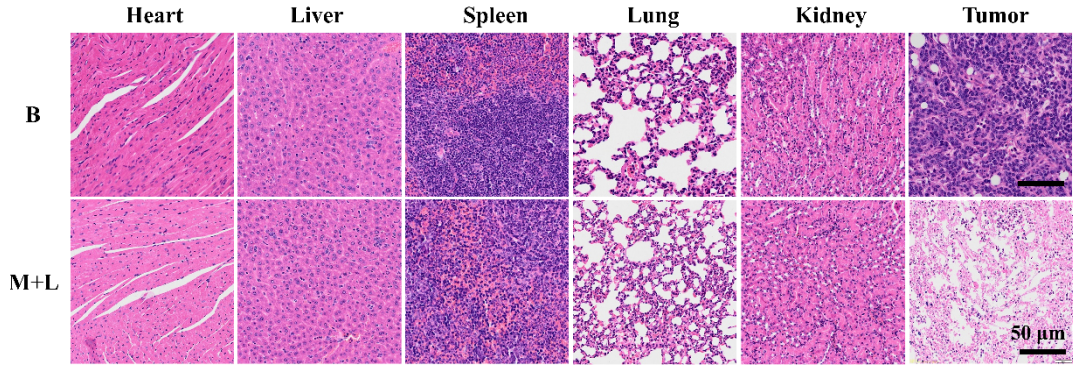


Figure S42. Histological H&E staining for different organs collected from mice in group iv on the 15th day after the treatment. B: Blank; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 1 mmol/L; laser irradiation (350 mW cm^{-2}, 10 min).

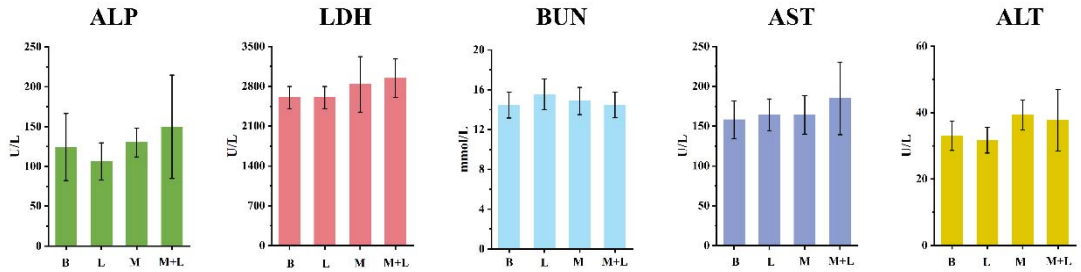


Figure S43. Serum biochemical parameters analyzed with the specimens collected from the animals received various treatments. The levels of blood urea nitrogen (BUN), aspartate alanine aminotransferase (ALT), aminotransferase (AST), lactate dehydrogenase (LDH), and alkaline phosphatase (ALP) were determined by an automated analyzer. The results represent the mean ± standard deviation (n = 6). B: Blank; L: light only; M: **MAP18-C12 NPs** only; M+L: **MAP18-C12 NPs** + light. [**MAP18-C12 NPs**] = 1 mmol/L; laser irradiation (350 mW cm^{-2}, 10 min).

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