Supporting Information

A Heterocyclic Strategy for Regulating the Proportion of Type I and Type II of Photodynamic Therapy

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Materials

All materials were used directly without further purification. iodobenzene, diphenylacetylene, 1-bromo-4-vinylbenzene, (5-formylthiophen-2-yl)boronic acid, (4-formylcyclopenta-1,3-dien-1-yl)boronic acid, (5-formylfuran-2-yl)boronic acid, Pluronic F127 and triphenylphosphane were purchased from Bidepharm. Sodium hydroxide, lithium chloride, triarylphosphines palladium(II) acetate, 2-(3-cyano-4,5,5-trimethylfuran-2-ylidene)propanedinitrile, potassium phosphate, potassium phosphate (tribasic) palladium(0) were purchased from Energy chemical. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), rose bengal (RB), tetrabutylammonium hexafluorophosphate ($(n\text{-}Bu)_4N^+PF_6^-$), methanol, petroleum ether, ethyl acetate, sodium bicarbonate, 1,4-dioxane, dimethyl sulfoxide (DMSO), dimethylformamide, dichloromethane (DCM) and piperidine were purchased from BT Reagent.

Penicillin-streptomycin was purchased from Macgene (China). RPMI-1640 and FBS were purchased from Gibco (USA). Calcein-AM/PI Live-Dead Cell Staining Kit, Reactive Oxygen Species Assay Kit and Lyso-Tracker Green were purchased from Beijing Solarbio Science and Technology Co., Lta. The 2',7'-dichlorofluorescein diacetate (DCFH-DA), dihydrorhodamine 123 (DHR123) and 9,10-anthracenediyl-bis(methylene) dimalonic acid (ABDA) required for the active oxygen test were purchased from Shanghai McLean Biochemical Technology Co., Ltd.

Equipment

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV 400 spectrometer. Mass spectra (MS) were collected using a Finnigan Biflex III mass spectrometer. The ultraviolet-visible spectra and singlet oxygen ($^{1}O_2$) were collected on the Thermo Fisher UV-2700 spectrophotometer. The PL emission spectra and reactive oxygen species (ROS) were collected on the HORIBA FluoroMax-4 spectrofluorometer. Record cell imaging using a confocal laser PL microscope (Zeiss LSM 780). Electron paramagnetic resonanc (EPR) spectra were measured on Bruker Paramagnetic Resonance Spectrometer EMXplus. *In vivo* imaging was measured on IVIS lumina series III. Transmission Electron Microscope (TEM) was measured on Talos F200S.

Preparation of TPP, TPS, and TPO NPs

1 mg PSs and 10 mg Pluronic F127 were dissolved in 1 mL DMSO solution, and poured into 9 mL ultrapure water under ultrasonic conditions. The obtained nanoparticles, named as TPP ,TPS, and TPO NPs, respectively, were concentrated by centrifugation, and ultrapure water was added to prepare a solution with a certain concentration for ROS testing and further biological applications.

Total ROS detection by indicator DCFH

First, 1 mM DCFH-DA in ethanol and 10 mM NaOH aqueous solution were prepared, then 2 mL of NaOH solution was mixed with 0.5 mL of DCFH-DA solution, and the reaction was carried out in the dark for 30 min. After the reaction, 10 mL of PBS solution was added to obtain a DCFH solution with a concentration of 40 μM. Photosensitizers dissolved in PBS (with 1% DMSO) were blended with a DCFH solution (40 μM DCFH, 10 μM PSs) and then irradiated with a white light of 2 mW cm^{-2}. The fluorescence intensity of the DCF at the maximum wavelength of 520 nm was detected. Control experiments were performed with the same procedure.

Detection of $^{1}O_2$ Generation by indicator ABDA

Photosensitizers dissolved in H_2O (with 1% DMSO) were blended with ABDA solution (0.1 mM ABDA, 10 μM PSs) and then irradiated with a white light of 2 mW cm^{-2}. Detect the intensity of the UV absorption peak of ABDA. The same experiments were done with RB as a control.

Detection of O_2^{-}• Generation by indicator DHR123

30 μL DHR123 (40 μM), 20 μL PSs (10 μM) and 1950 μL PBS were mixed, after irradiated by white light irradiation of 2 mW cm^{-2}, the fluorescence signal of indicator was monitored to indicate the O_2^{-}• generation rate with the excitation wavelength of 488 nm and the emission wavelength of 525 nm.

Cell Culture

4T1 cells (mouse breast cancer cell line) were obtained from National

Infrastructure of Cell Line Resource (NICR), and 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 were seeded in 96-well plates at a density of 5×10^3 cells/well and incubated for 24 h. Then the cells were incubated with different concentrations of TPO NPs in fresh medium. The cells were exposed to white light of 5 mW cm^{-2} for 10 min after 24 h incubation. At the same time, the TPO NPs incubated cells without laser irradiation were also conducted for the dark cytotoxicity study. After further incubation for 24 h, the medium was removed and washed with PBS for three times. Cells were then incubated with fresh serum-free medium containing 10% MTT for 4 h in the dark. Then, all the media were removed and 150 μL DMSO was added. Finally, the absorbance of the products was measured at a wavelength of 570 nm by a microplate reader. The results were expressed as the viable percentage of cells after different treatments relative to the control cells without any treatment. The following steps of MTT test were the same as the above procedures.

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 °C with 5% CO_2, culture medium was removed and cells were stained with TPO NPs (10^{-5} mol L^{-1}) 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 (50 nM) for 10 min at 37 °C.

Live/Dead Cell Staining

First, 4T1 cells were seeded and cultured in glass bottom dish for 24 h, then exposed to different following treatments: 1) Blank; 2) the cells were exposed to white light of 5 mW cm^{-2} for 10 min; 3) incubated with TPO NPs for 24 h; 4) incubated with TPO NPs for 24 h and exposed to white light of 5 Mw cm^{-2} for 10 min. After different treatments, the cells were incubated at 37 °C for another 24 h, then successively stained with PI and FDA in PBS for 10 min. Subsequently, the cells were gently washed and then imaged by CLSM. Conditions: excitation wavelength: 488 nm for FDA and 543 nm for PI; emission filter: 500-550 nm for FDA and 550-650 nm for PI.

Intracellular ROS Generation

4T1 cells were primarily seeded and cultured in glass bottom dish for 24 h. The original culture medium was then replaced with 1 mL of fresh one with or without TPO NPs, followed by incubation of 12 h. Then the cells were washed with PBS for three times, and incubated with 1 mL fresh FBS-free medium containing 10 mM DCFH-DA for another 20 min. The TPO NPs loaded cells were subsequently exposed to white light of 5 mW cm^{-2} for 10 min. After further incubation at 37 °C, the cells were imaged

by CLSM with the excitation at 488 nm and emission was collected from 500-550 nm.

Animals

Animals: BALB/c (female, 5 weeks) mice were purchased from Chengdu Dashuo Experimental Animal Co., Ltd.

Statement of ethical approval: All mice were housed in designated animal facilities, fed ad libitum and inspected regularly. All animal studies were approved by the Sichuan University Animal Charity Protection and Treatment Committee and performed in accordance with humane care and use of research animals. All animal procedures were reviewed and approved by Ethical Committees of West China School of Stomatology, Sichuan University (WCHSIRB-D-2017-042).

Fluorescence imaging of tumors and major organs

BALB/c mice (female, 5 weeks, 20 in total) bearing 4T1 tumors (≈100 mm^3) were divided into 6groups according to different circulation times: 3 h, 6 h, 9 h, 12 h, 24 h, and 48 h. TPO NPs (10 μM,100 μL) were injected into different groups of mice by tail vein injection. The enrichment of photosensitizers in tumors at different time were detected, respectively. The enrichment of TPO NPs in heart, liver, spleen, lung, kidney and tumor were also compared at 48 hours. Fluorescent images of tumors and organs were captured by IVIS Lumina Series III.

In Vivo Therapeutic Studies

BALB/c mice (female, 5 weeks, 20 in total) bearing 4T1 tumors were randomly divided into four groups (5 in each group), group PBS, administration with PBS (100 μL) alone; group Light+PBS Only, PBS administration (100 μL) followed by wight light (200 mW cm^{-2}, 10 min); group TPO NPs Only, administration with TPO NPs (10 μM, 100 μL); group TPO NPs + light, administration with TPO NPs (10 μM, 100 μL) and followed by wight light (200 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 14 days post-treatment, tumors in all groups were harvested and weighed. 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. The healthy mice without any treatment were used as control.

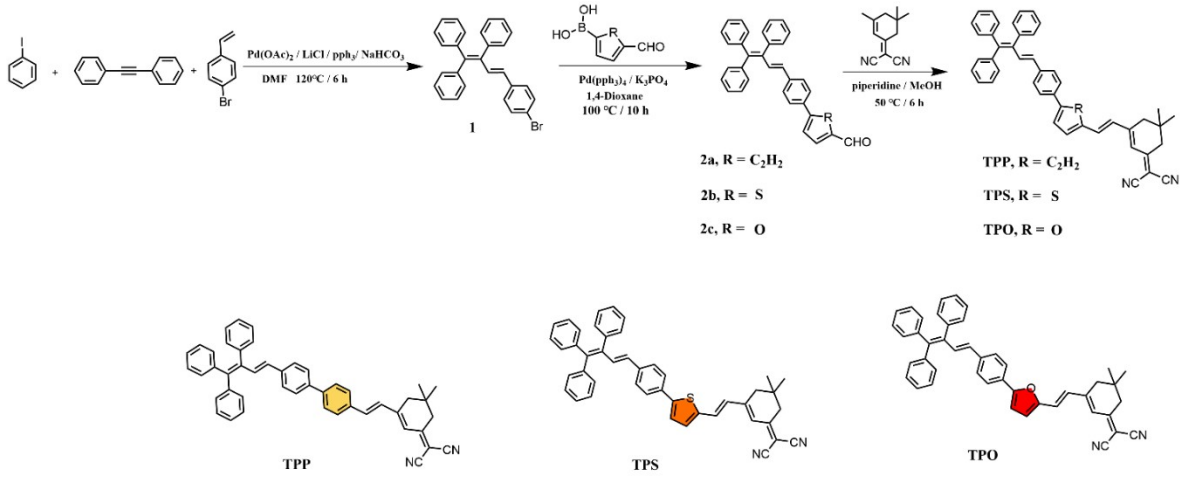

Figure S1 The synthetic routes of target compounds.

Synthesis of compound 1： iodobenzene (1.10 mL, 10 mmol), diphenylacetylene (7.12 g, 40 mmol), 1-bromo-4-vinylbenzene (1.30 mL, 10 mmol), sodium hydroxide(1.70 g, 20 mmol), lithium chloride (0.30 g, 7 mmol), triarylphosphines (0.26 g, 1 mmol) and palladium(II) acetate (0.11 g, 0.5 mmol) were dissolved in 20 mL N,N-dimethylformamide, then refluxed at 120 ℃ for 6 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 (1/20, V_d/V_p) as the eluent to give desired compound 1 with 40% yield. δ (ppm): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 7H), 7.27 – 7.10 (m, 7H), 7.09 – 6.96 (m, 5H), 6.89 (dd, J = 6.6, 3.0 Hz, 2H), 6.18 (d, J = 16.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.44, 142.75, 142.39, 140.30, 138.73, 136.75, 131.89, 131.64, 131.47, 131.26, 131.09, 128.03, 127.99, 127.94, 127.53, 127.39, 126.81, 126.39, 120.99. MS (APCl, *m/z*) Calcd for $C_{28}H_{21}Br$ $[M+H]^+$: 438.05, found: 438.05.

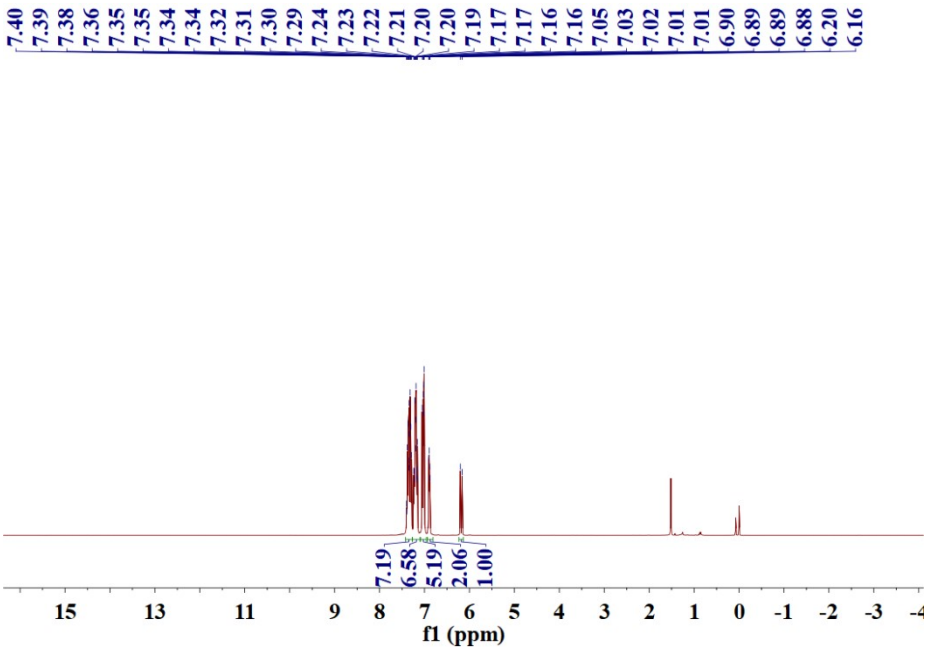

Figure S2. ^{1}H NMR spectrum of compound 1 in $CDCl_3$.

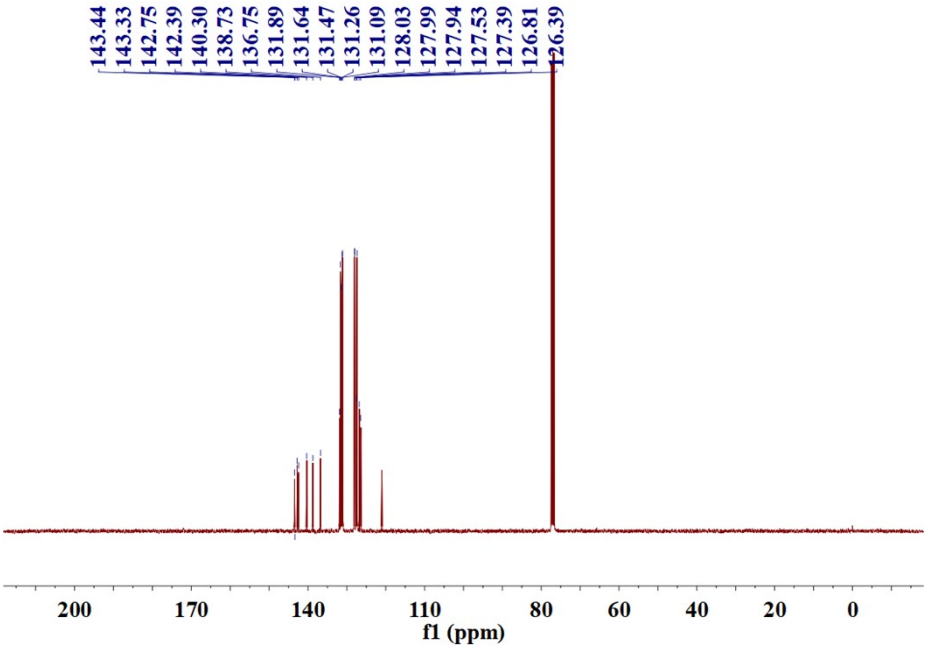

Figure S3. ^{13}C NMR spectrum of compound 1 in $CDCl_3$.

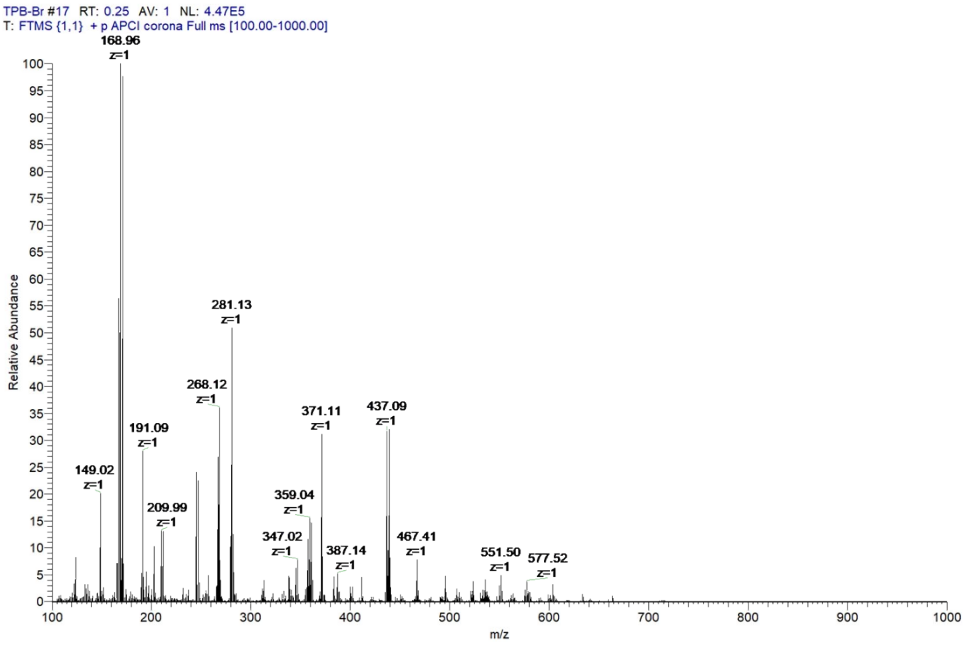

Figure S4. MS spectrum of compound 1.

Synthesis of compound 2a: Compound 1 (0.44 g, 1 mmol), (4-formylphenyl)boronic acid (0.30 g, 2 mmol) and potassium phosphate (0.42 g, 2 mmol) and tetrakis (triphenylphosphine) palladium (0.12 g, 0.1 mmol) were dissolved in 10 mL 1,4-dioxane, then refluxed at 100 ℃ for 10 h. After that, the solution was extracted with ethyl acetate 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 ethyl acetate/petroleum ether mixture (1/8, V_{ea}/V_p) as the eluent to give desired compound 2a with 82.4% yield. ^{1}H NMR (400 MHz, DMSO) δ 10.03 (s, 1H), 7.91 (dd, J = 37.5, 8.3 Hz, 4H), 7.67 (d, J = 8.3 Hz, 2H), 7.51 – 7.36 (m, 3H), 7.34 – 7.15 (m, 10H), 7.12 – 6.99 (m, 3H), 6.89 (dd, J = 7.6, 1.7 Hz, 2H), 6.21 (dd, J = 15.9, 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 184.41, 152.67, 144.08, 142.76, 142.27, 142.24, 139.98, 139.74, 138.79, 138.66, 132.23, 131.87, 131.49, 131.43, 131.10, 130.91, 128.73, 128.56, 128.23, 127.99, 127.46, 127.40, 127.05, 126.98, 125.61. MS (APCl, *m/z*) Calcd for $C_{35}H_{26}O$ $[M+H]^+$: 463.20, found: 463.20.

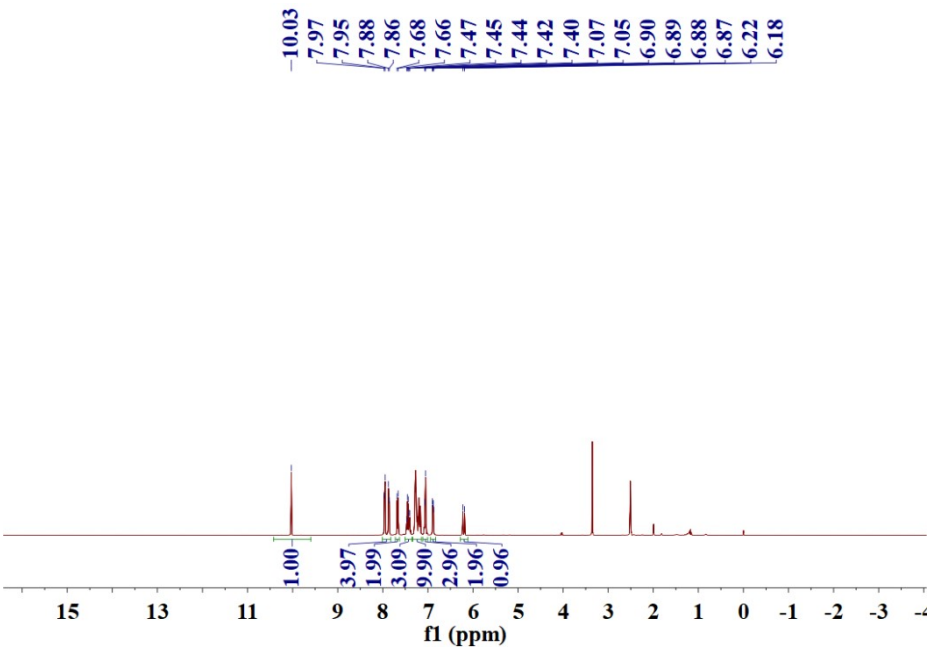

Figure S5. [1]H NMR spectrum of compound 2a in DMSO-d6.

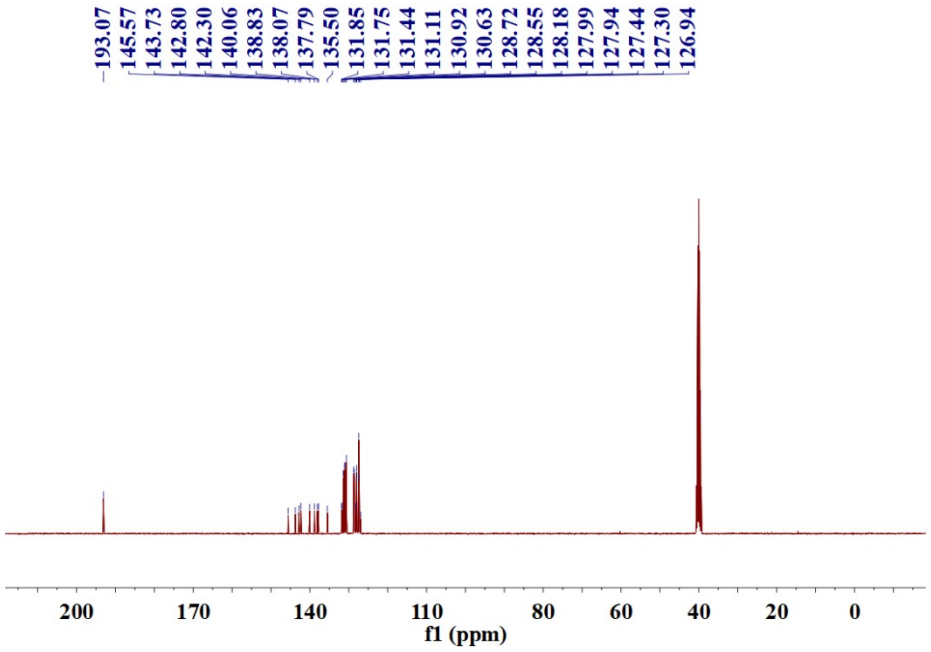

Figure S6. [13]C NMR spectrum of compound 2a in DMSO-d6.

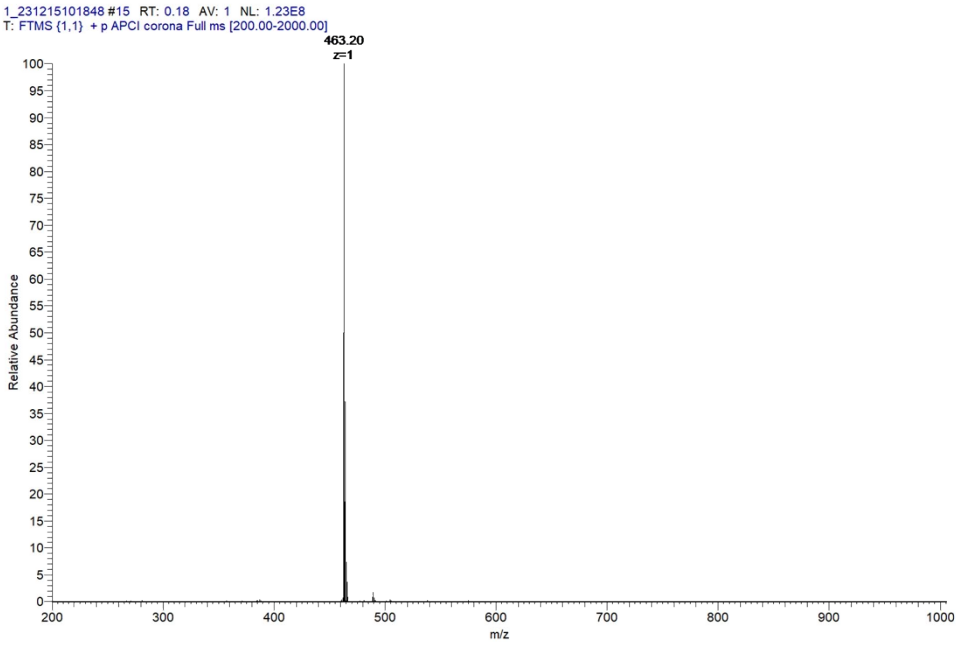

Figure S7. MS spectrum of compound 2a.

Synthesis of compound 2b: Compound 1 (0.44 g, 1 mmol), (5-formylthiophen-2-yl)boronic acid (0.31 g, 2 mmol), potassium phosphate (0.42 g, 2 mmol) and tetrakis (triphenylphosphine) palladium (0.12 g, 0.1 mmol) were dissolved in 10 mL 1,4-dioxane, then refluxed at 100 ℃ for 10 h. After that, the solution was extracted with ethyl acetate 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 ethyl acetate/petroleum ether mixture (1/10, V_{ea}/V_p) as the eluent to give desired compound 2b with 68.2% yield. ^{1}H NMR (400 MHz, DMSO) δ 9.89 (s, 1H), 8.03 (t, J = 5.8 Hz, 1H), 7.73 – 7.67 (m, 3H), 7.49 – 7.37 (m, 3H), 7.30 – 7.15 (m, 10H), 7.10 – 7.00 (m, 3H), 6.88 (dd, J = 7.7, 1.7 Hz, 2H), 6.18 (d, J = 16.0 Hz, 1H). 13C NMR (101 MHz, DMSO) δ 184.41, 152.67, 144.08, 142.76, 142.27, 142.24, 139.98, 139.74, 138.79, 138.66, 132.23, 131.87, 131.49, 131.43, 131.10, 130.91, 128.73, 128.56, 128.23, 127.99, 127.46, 127.40, 127.05, 126.98, 125.61. MS (APCl, *m/z*) Calcd for $C_{33}H_{24}OS$ $[M+H]^+$: 469.16, found: 469.16.

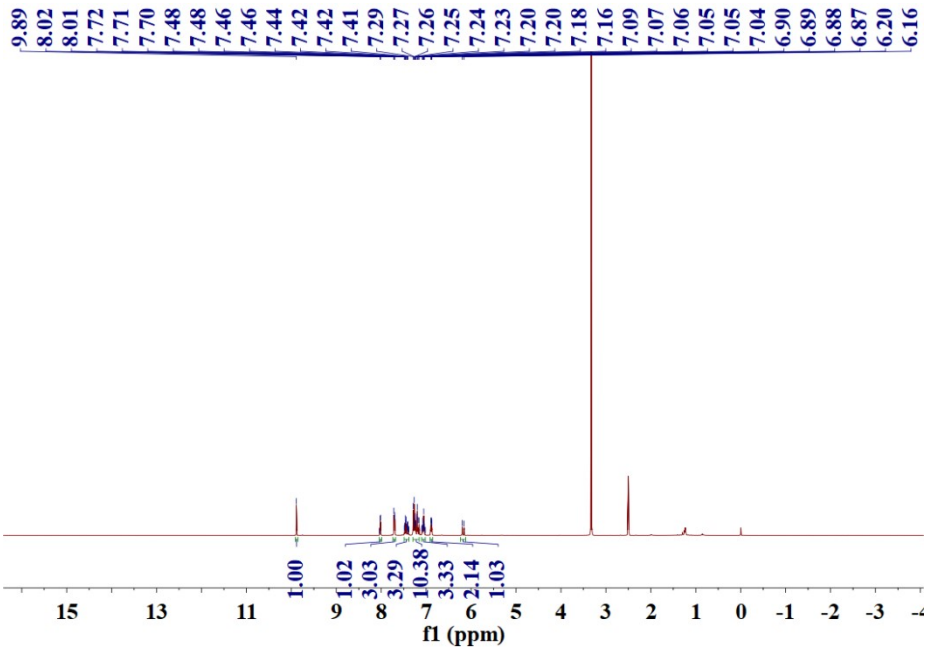

Figure S8. [1]H NMR spectrum of compound 2b in DMSO-d6.

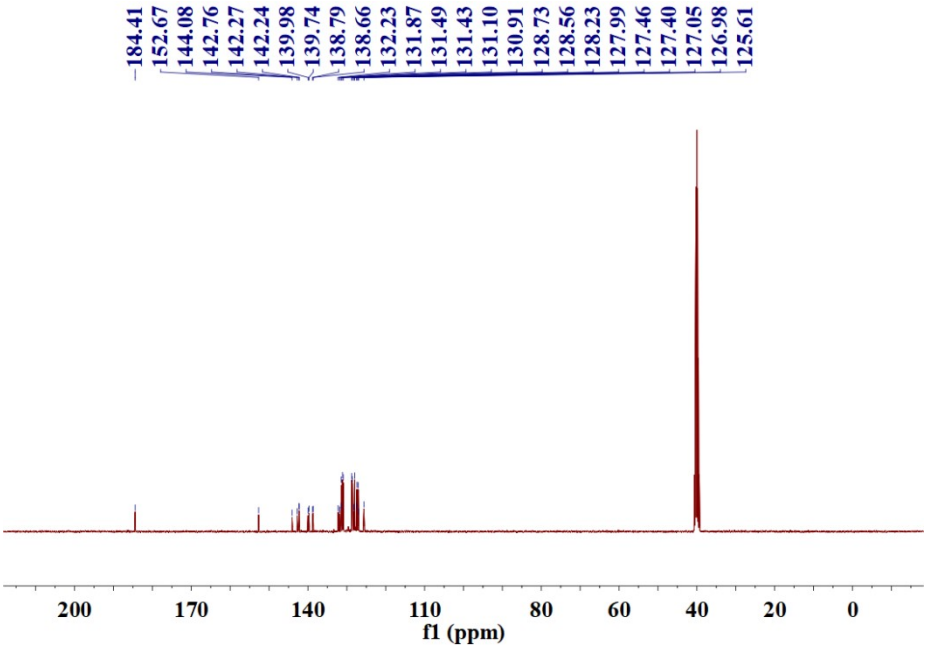

Figure S9. [13]C NMR spectrum of compound 2b in DMSO-d6.

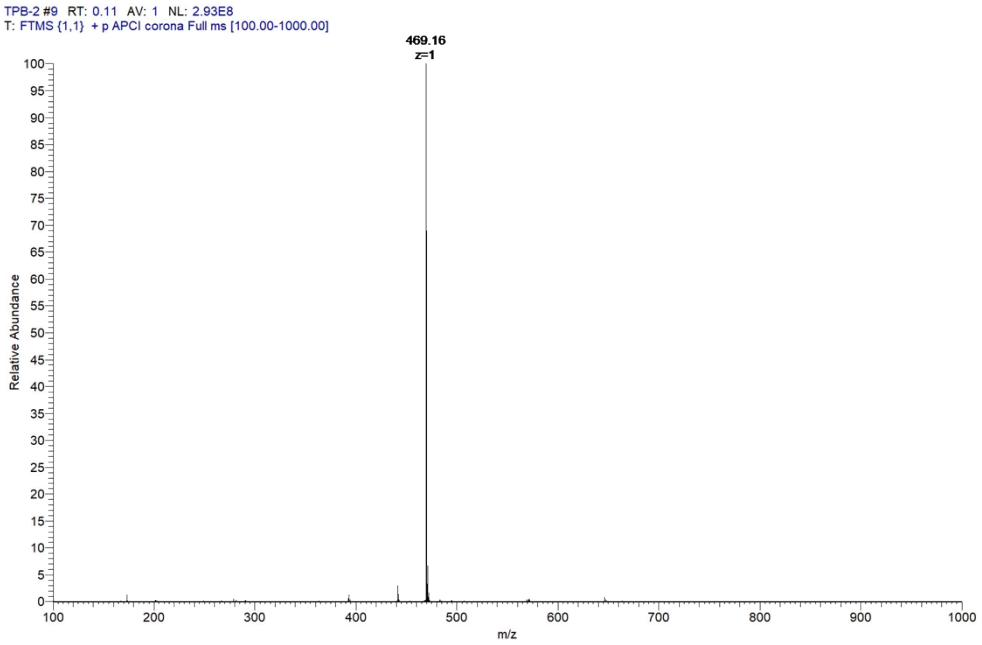

Figure S10. MS spectrum of compound 2b.

Synthesis of compound 2c： Compound 1 (0.44 g, 1 mmol), (5-formylfuran-2-yl)boronic acid (0.28 g, 2 mmol), potassium phosphate (0.42 g, 2 mmol) and tetrakis (triphenylphosphine) palladium (0.12 g, 0.1 mmol) were dissolved in 10 mL 1,4-dioxane, then refluxed at 100 ℃ for 10 h. After that, the solution was extracted with ethyl acetate 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 ethyl acetate/petroleum ether mixture (1/8, V_{ea}/V_p) as the eluent to give desired compound 2c with 45.8% yield. ^{1}H NMR (400 MHz, DMSO) δ 9.58 (s, 1H), 7.75 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 3.8 Hz, 1H), 7.49 – 7.35 (m, 3H), 7.31 – 7.16 (m, 12H), 7.10 – 7.00 (m, 3H), 6.88 (dd, J = 7.6, 1.8 Hz, 2H), 6.17 (d, J = 16.0 Hz, 1H). 13C NMR (101 MHz, DMSO) δ 178.13, 158.40, 152.11, 144.08, 142.78, 142.22, 140.01, 138.80, 138.71, 132.29, 131.67, 131.42, 131.11, 130.90, 128.73, 128.56, 128.24, 128.00, 127.94, 127.45, 127.32, 126.99, 125.91, 109.37. MS (APCl, *m/z*) Calcd for $C_{33}H_{24}O_2$ $[M+H]^+$: 453.18. found: 453.18.

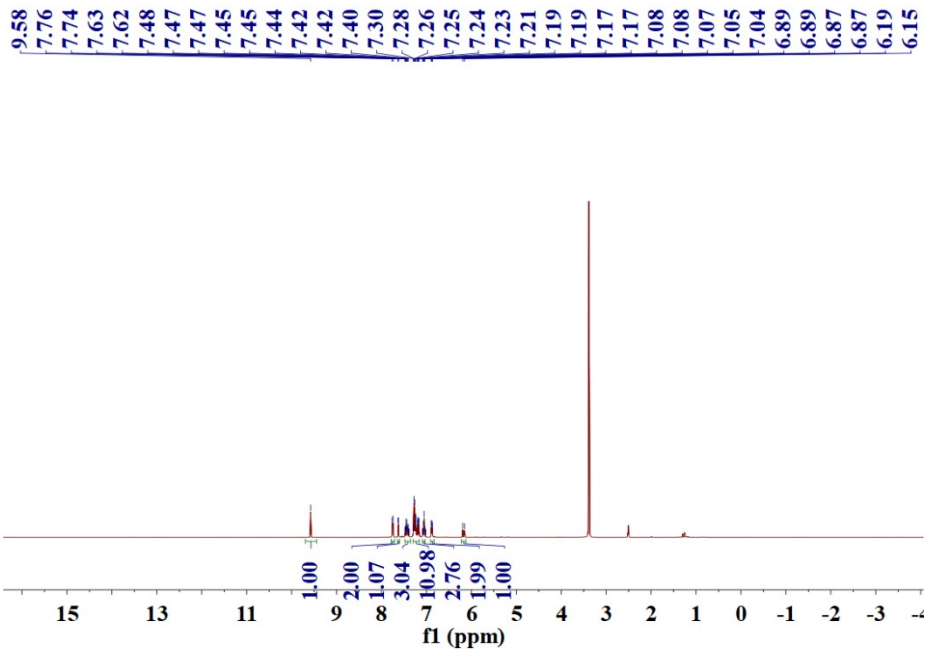

Figure S11. [1]H NMR spectrum of compound 2c in DMSO-d6.

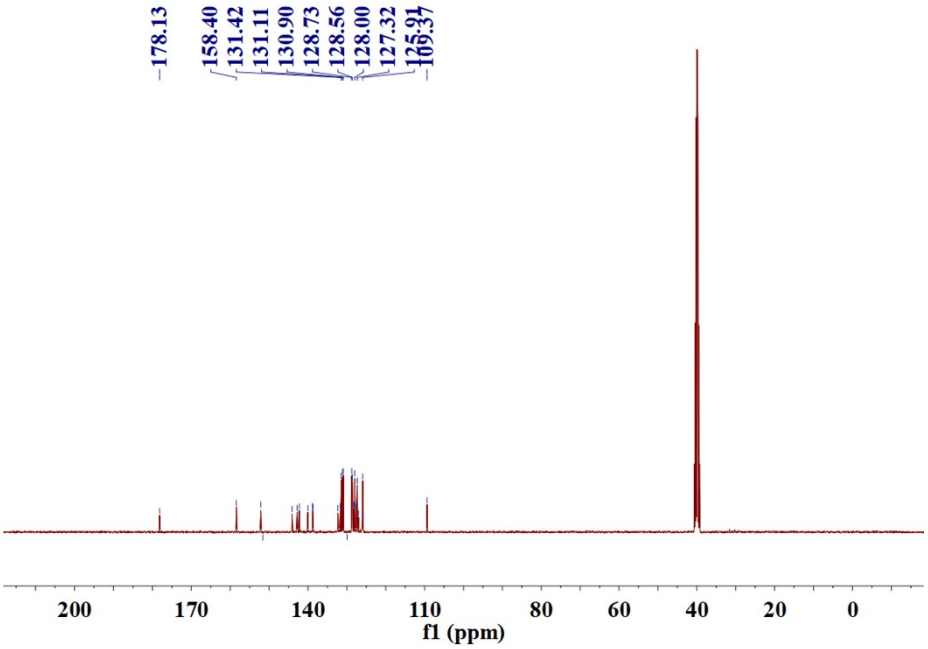

Figure S12. [13]C NMR spectrum of compound 2c in DMSO-d6.

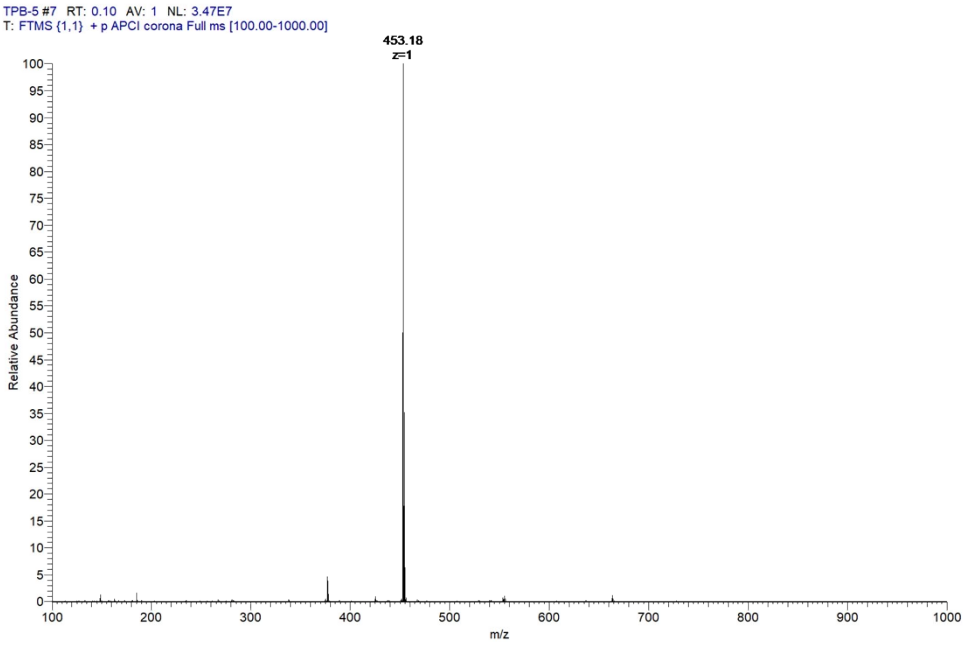

Figure S13. MS spectrum of compound 2c.

Synthesis of compound TPP: Compound 2a (0.46 g, 1 mmol), 2-(3,5,5-trimethylcyclohex-2-en-1-ylidene)malononitrile (0.37 g, 2 mmol), piperidine (0.5 mL) and methanol (10 mL) were added to a 50 mL round bottom flask and stirred at 50 ℃ for 6 h. After that, the solution was extracted with ethyl acetate 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 ethyl acetate/petroleum ether mixture (1/7, V_{ea}/V_p) as the eluent to give desired TPP with 25.4% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.47 (m, 4H), 7.39 (d, *J* = 6.4 Hz, 4H), 7.35 – 7.14 (m, 11H), 7.11 – 6.95 (m, 5H), 6.92 (d, *J* = 11.7 Hz, 2H), 6.83 (d, *J* = 16.5 Hz, 2H), 2.52 (dd, *J* = 53.0, 11.1 Hz, 4H), 1.08 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.23, 169.16, 153.92, 153.85, 138.98, 136.61, 131.92, 131.76, 131.53, 131.48, 131.35, 131.15, 129.05, 128.14, 128.03, 127.99, 127.49, 127.39, 127.27, 127.07, 127.03, 126.80, 123.64, 113.58, 112.81, 43.03, 39.25, 32.07, 28.07. MS (APCl, *m/z*) Calcd for $C_{47}H_{38}N_2$ $[M+H]^+$: 630.30. found: 630.30.

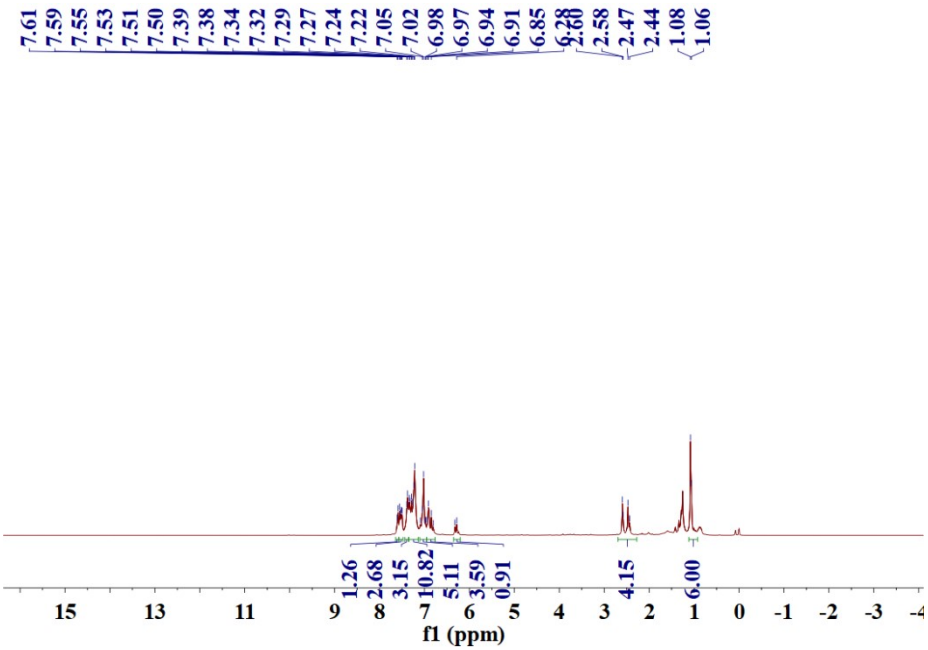

Figure S14. ^{1}H NMR spectrum of TPP in $CDCl_3$.

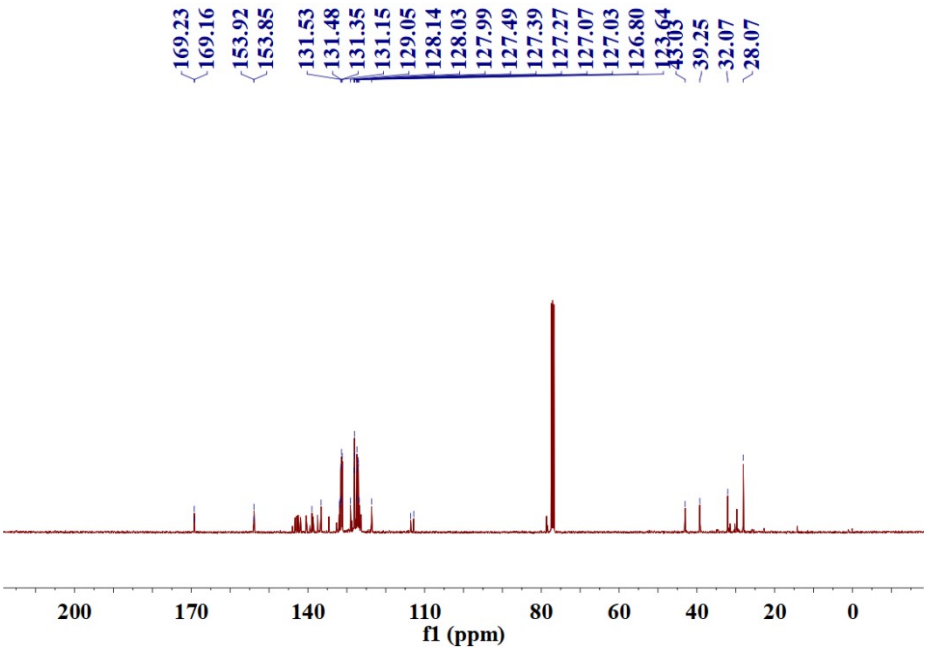

Figure S15. ^{13}C NMR spectrum of TPP in $CDCl_3$.

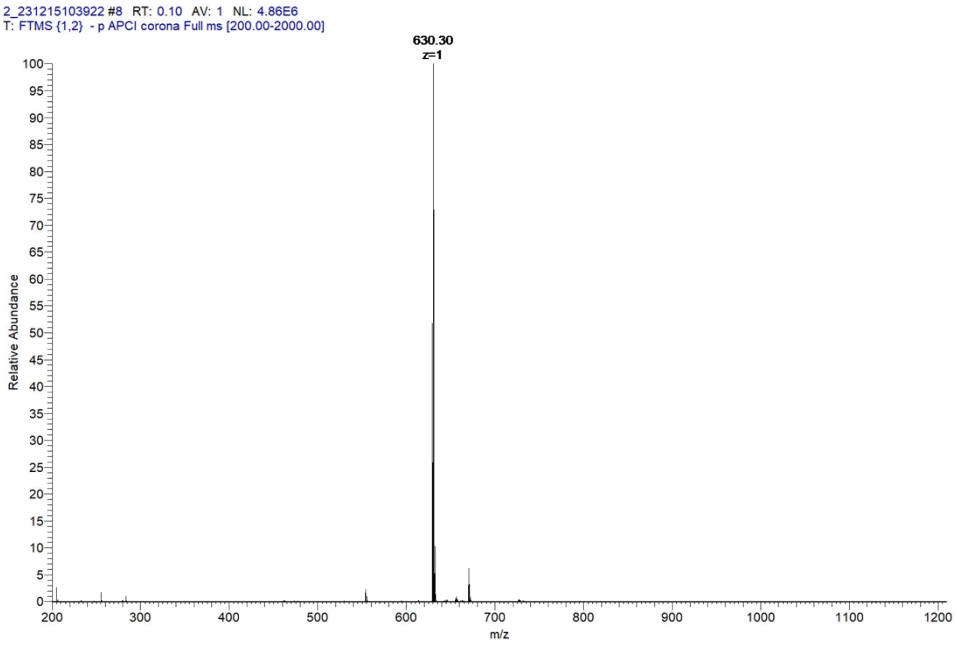

Figure S16. MS spectrum of TPP.

Synthesis of compound TPS: Compound 2b (0.47 g, 1 mmol), 2-(3,5,5-trimethylcyclohex-2-en-1-ylidene)malononitrile (0.37 g, 2 mmol), piperidine (0.5 mL) and methanol (10 mL) were added to a 50 mL round bottom flask and stirred at 50 ℃ for 6 h. After that, the solution was extracted with ethyl acetate 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 ethyl acetate/petroleum ether mixture (1/5, V_{ea}/V_p) as the eluent to give desired TPS with 25.4% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.2 Hz, 1H), 7.45 – 7.16 (m, 15H), 7.08 – 6.77 (m, 5H), 6.70 (d, *J* = 3.5 Hz, 2H), 6.61 (d, *J* = 3.4 Hz, 2H), 6.27 (d, *J* = 16.0 Hz, 1H), 2.49 (d, *J* = 73.6 Hz, 4H), 1.06 (s, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 168.82, 156.10, 155.81, 153.58, 151.72, 143.57, 142.75, 142.41, 140.30, 138.93, 138.10, 132.01, 131.68, 131.48, 131.29, 131.13, 128.02, 128.01, 127.58, 127.37, 126.97, 126.82, 126.39, 124.48, 123.32, 123.23, 116.60, 113.82, 113.10, 108.37, 42.92, 38.95, 32.01, 29.73, 28.04. MS (APCl, *m/z*) Calcd for $C_{45}H_{36}N_2S$ $[M+H]^+$: 637.27. found: 637.27.

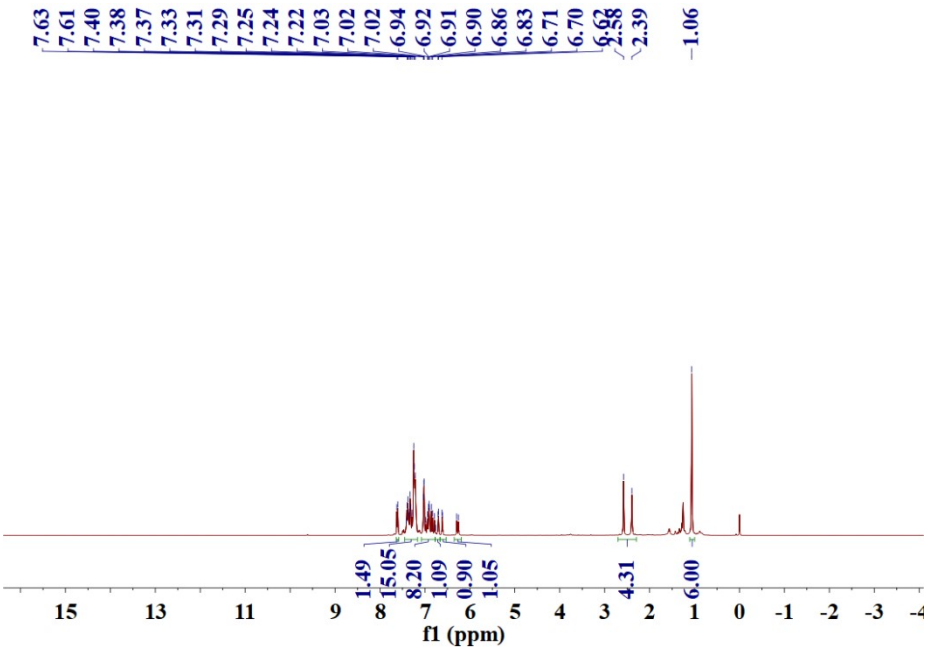

Figure S17. ^{1}H NMR spectrum of TPS in $CDCl_3$.

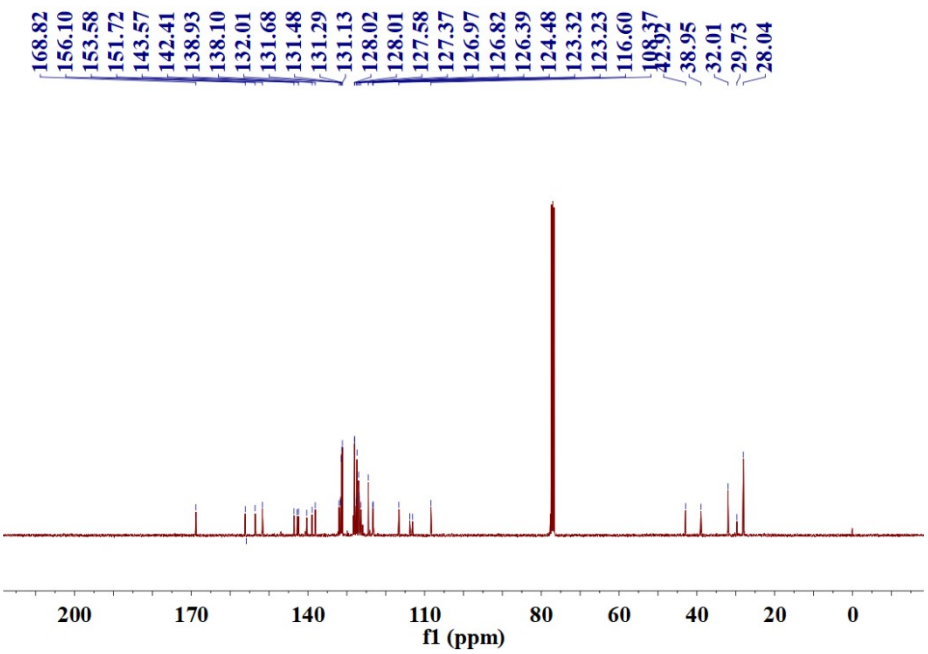

Figure S18. ^{13}C NMR spectrum of TPS in $CDCl_3$.

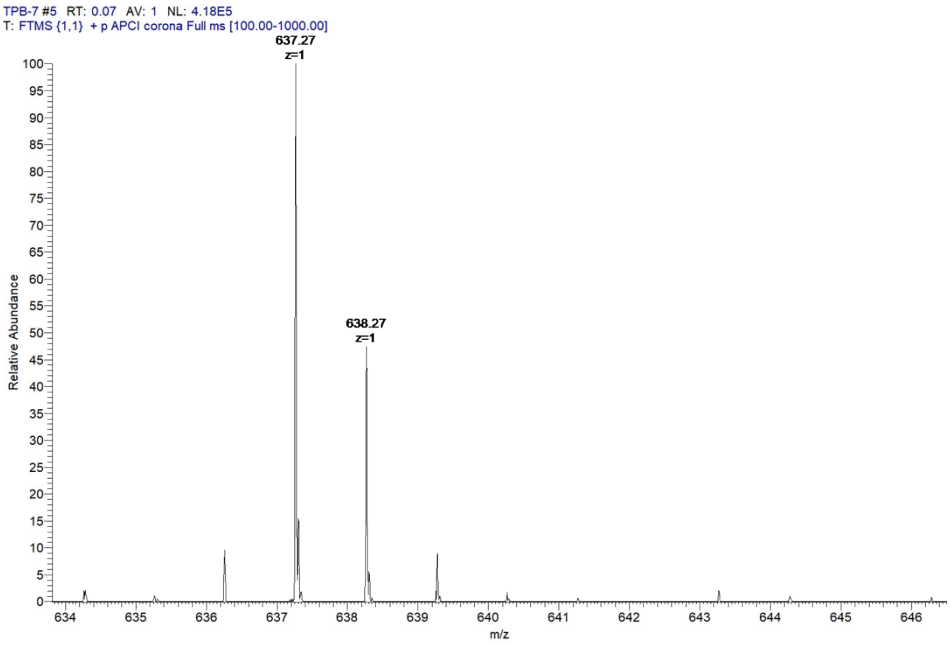

Figure S19. MS spectrum of TPS.

Synthesis of compound TPO: Compound 2c (0.45 g, 1 mmol), 2-(3,5,5-trimethylcyclohex-2-en-1-ylidene)malononitrile (0.37 g, 2 mmol), piperidine (0.5 mL) and methanol (10 mL) were added to a 50 mL round bottom flask and stirred at 50 ℃ for 6 h. After that, the solution was extracted with ethyl acetate 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 ethyl acetate/petroleum ether mixture (1/5, V_{ea}/V_p) as the eluent to give desired TPO with 40.3% yield. 1H NMR (400 MHz, CDCl3) δ 7.66 (dd, J = 26.6, 8.4 Hz, 1H), 7.48 – 7.19 (m, 14H), 7.09 – 6.79 (m, 8H), 6.76 – 6.67 (m, 1H), 6.63 (d, J = 3.6 Hz, 1H), 6.28 (d, J = 16.0, 4.6 Hz, 1H), 2.55 (s, 2H), 2.41 (s, 2H), 1.08 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.82, 156.10, 153.58, 151.72, 146.96, 143.57, 142.75, 142.41, 140.65, 140.30, 138.93, 138.11, 132.25, 132.01, 131.68, 131.48, 131.29, 131.13, 129.90, 128.34, 128.20, 128.03, 128.01, 127.58, 127.38, 127.10, 126.97, 126.86, 126.82, 126.39, 125.93, 124.49, 124.03, 123.31, 116.61, 113.83, 113.10, 108.37, 42.92, 41.02, 39.13, 38.95, 32.01, 29.73, 28.04.MS (APCl, *m/z*) Calcd for $C_{45}H_{36}N_2O$ $[M+H]^+$: 621.29. found: 621.29.

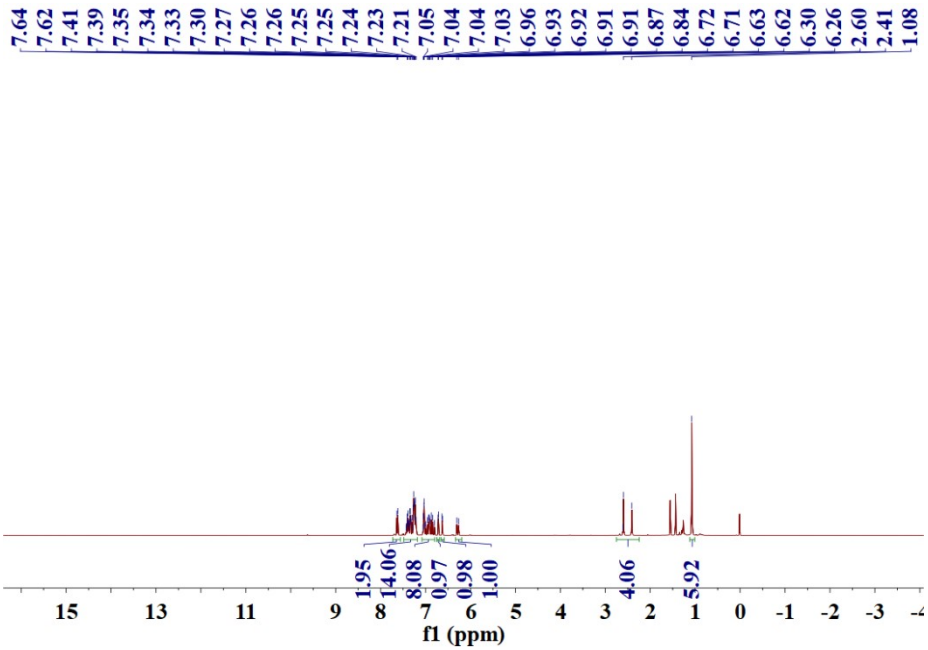

Figure S20. ^{1}H NMR spectrum of TPO in $CDCl_3$.

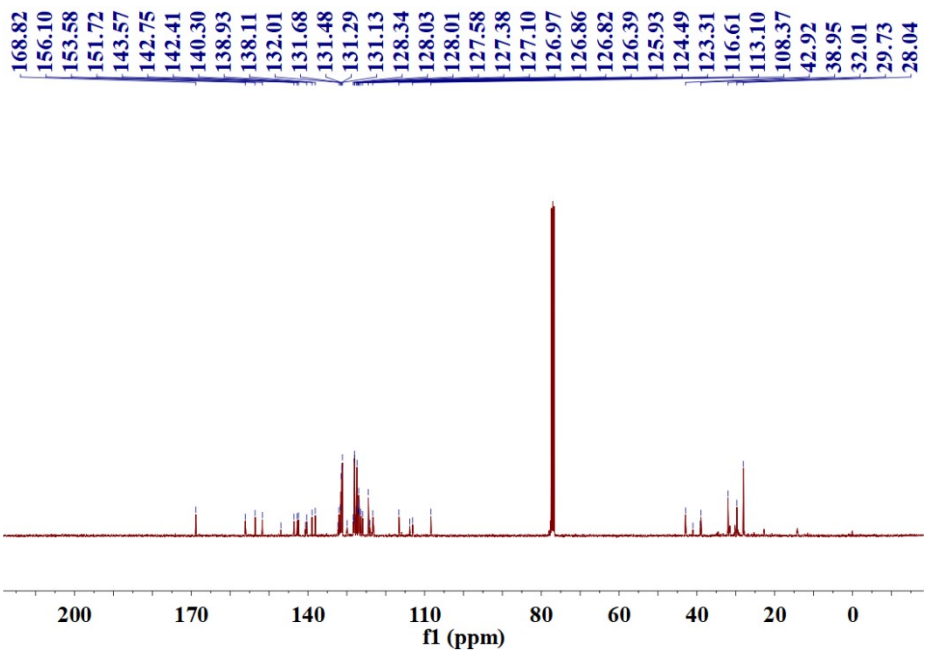

Figure S21. ^{13}C NMR spectrum of TPO in $CDCl_3$.

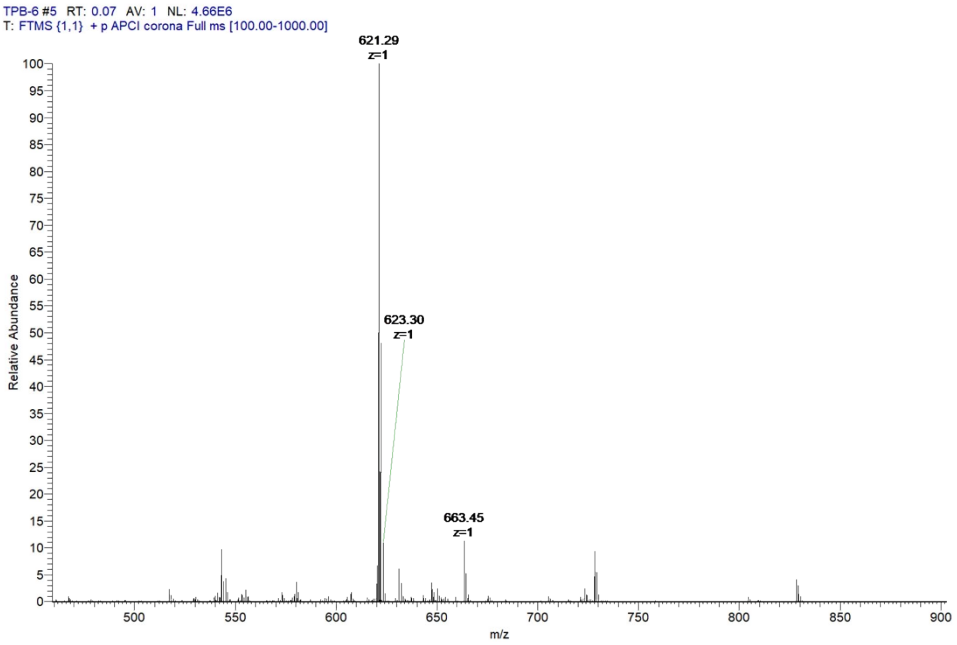

Figure S22. MS spectrum of TPO.

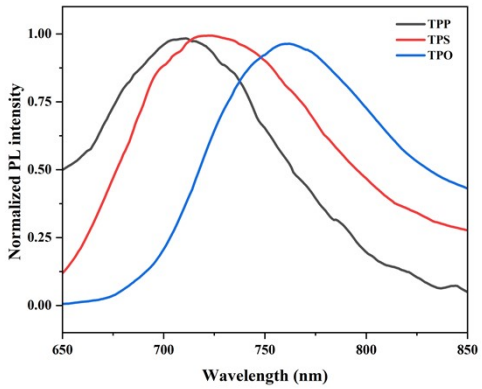

Figure S23. Normalized PL of TPP, TPS, and TPO of solid.

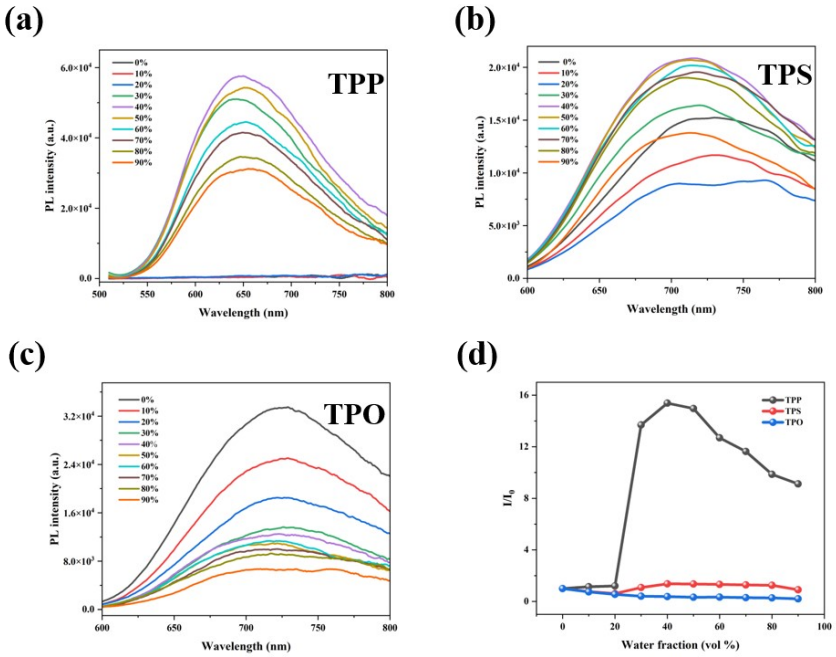

Figure S24. PL spectra of (a)TPP, (b) TPS, and (c) TPO in THF/H_2O mixture with different water fraction (f_W). (d) Plots of relative PL intensity (I/I_0) of TPP, TPS, and TPO versus water fraction.

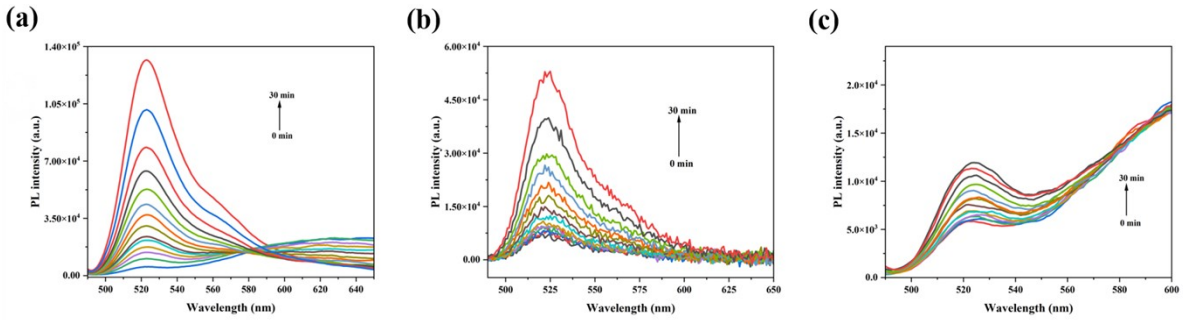

Figure S25. PL spectra of (a) TPP with DCFH and (b) only DCFH in PBS solution under white light irradiation (2 mW cm^{-2}), (c) TPP with DCFH in PBS solution in dark. [TPP] = 10 μM, [DCFH] = 40 μM.

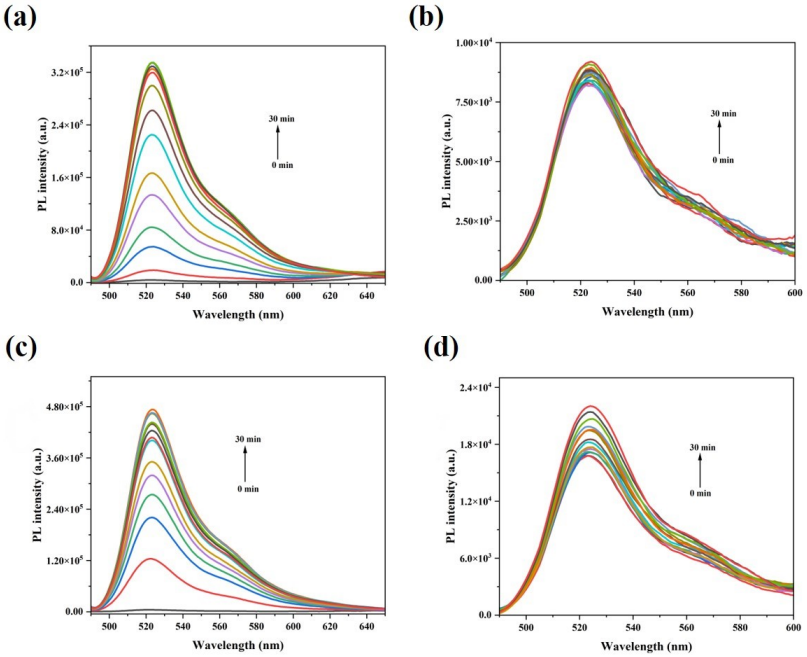

Figure S26. PL spectra of (a) TPS and (c) TPO with DCFH in PBS solution under white light irradiation (2 mW cm^{-2}), (b) TPS and (d) TPO with DCFH in PBS solution in dark. [TPS] = [TPO] = 10 μM, [DCFH] = 40 μM.

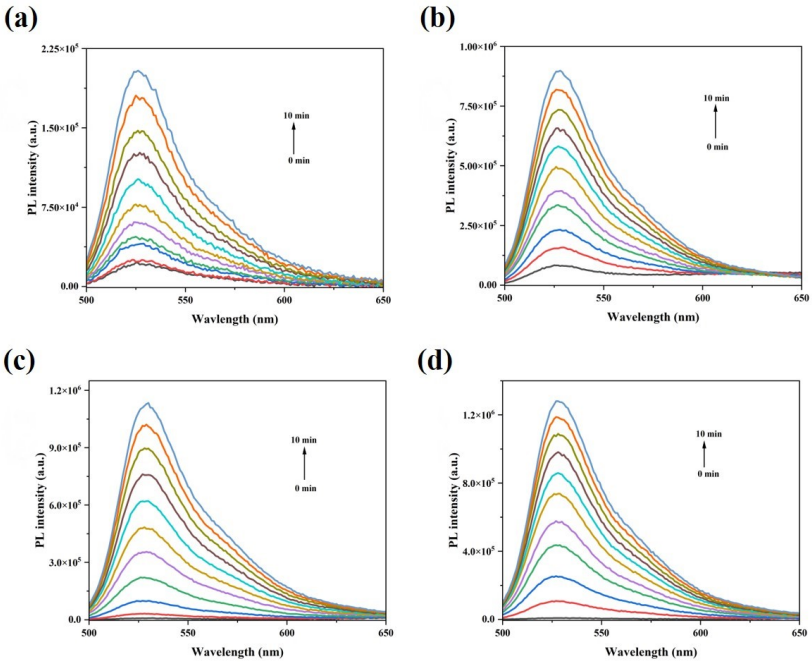

Figure S27. PL spectra of (a) DHR123 with (b) TPP, (c) TPS, and (d) TPO in PBS solution under white light irradiation (2 mW cm^{-2}). [TPP] = [TPS] = [TPO] = 10 μM, [DHR123] = 40 μM.

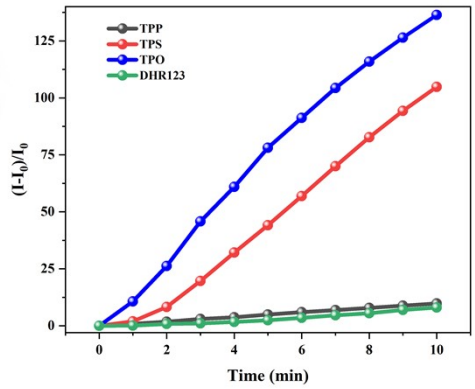

Figure S28. PL intensity change $(I-I_0)/I_0$ for the DHR123 indicator with TPP, TPS, and TPO upon white light irradiation (2 mW cm^{-2}).

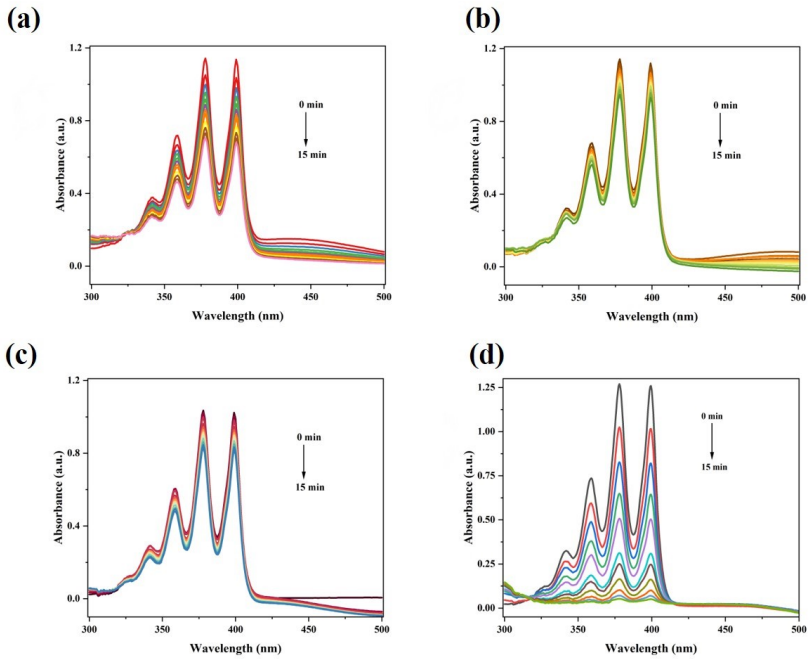

Figure S29. UV absorption spectra of (a) TPP, (b) TPS, (c) TPO, and (d) RB with ABDA in PBS solution under white light irradiation (2 mW cm^{-2}). [TPP] = [TPS] = [TPO] = 10 μM, [ABDA] = 0.1 mM.

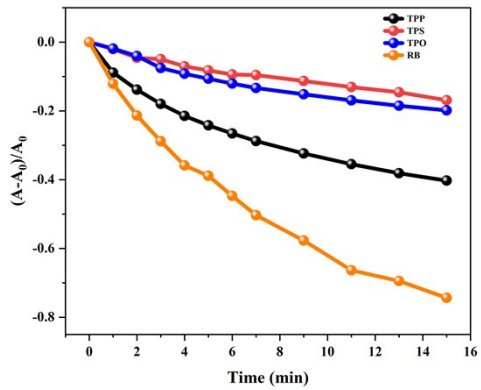

Figure S30. Absorbance intensity change $(A-A_0)/A_0$ for the ABDA indicator with TPP, TPS, TPO, and RB upon white light irradiation (2 mW cm^{-2}).

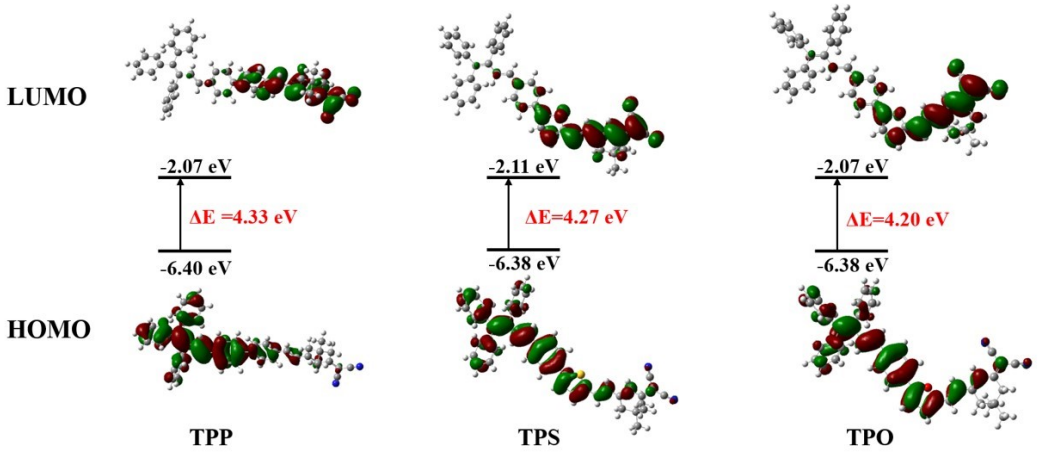

Figure S31. The HOMO and LUMO orbital energy level calculation of TPP, TPS, and TPO by B3LYP/6-31G (d,p).

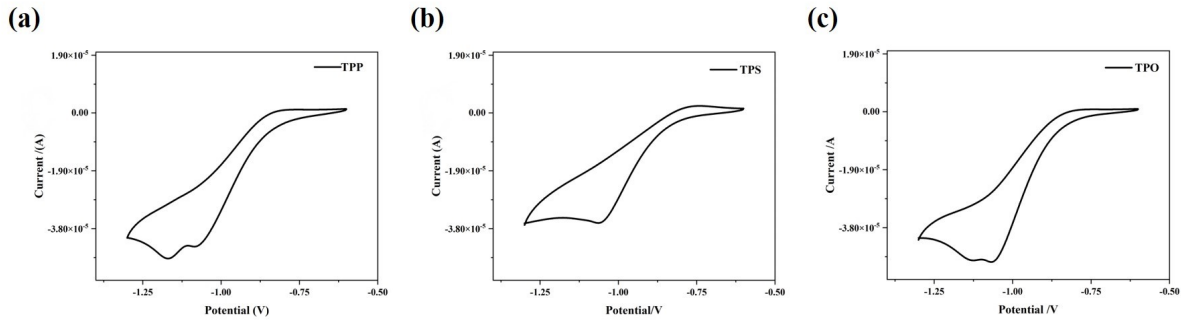

Figure S32. Cyclic voltammograms of (a) TPP, (b) TPS, and (c) TPO in DCM the 30th cycle with 0.1 M $(n\text{-}Bu)_4N^+PF_6^-$ as a supporting electrolyte, glassy carbon as a working electrode, Ag/AgCl as a reference electrode, a glassy-carbon electrode as the working electrode and a Pt wire as the counter electrode; scan rate, 50 mV s^{-1}.

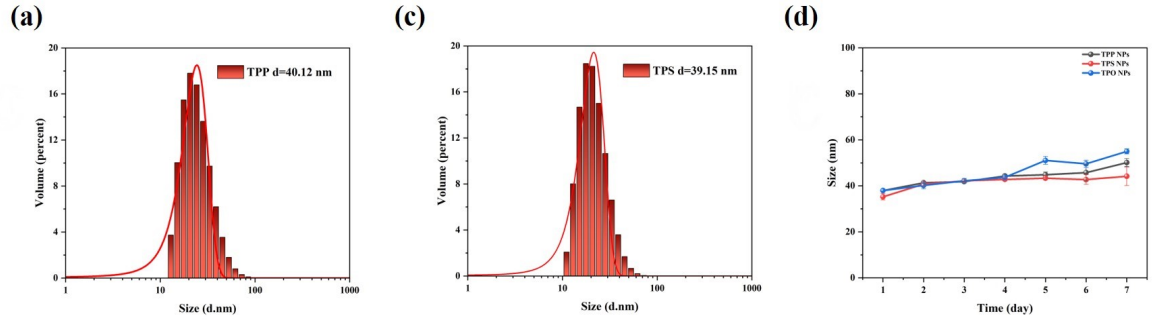

Figure S33. Dynamic laser scattering size of (a) TPP NPs and (b) TPS NPs. (c) Stability of TPP, TPS and TPO NPs.

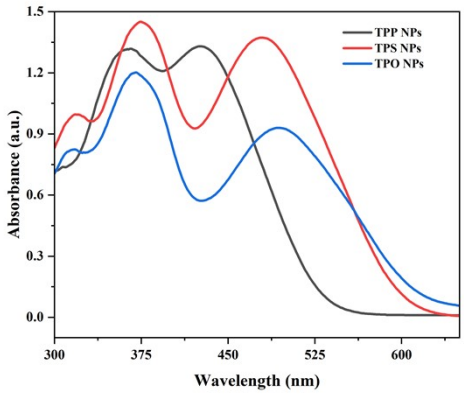

Figure S34. UV absorption spectra of TPP, TPS, and TPO NPs. [TPP NPs] = [TPS NPs] = [TPO NPs]=10 μM

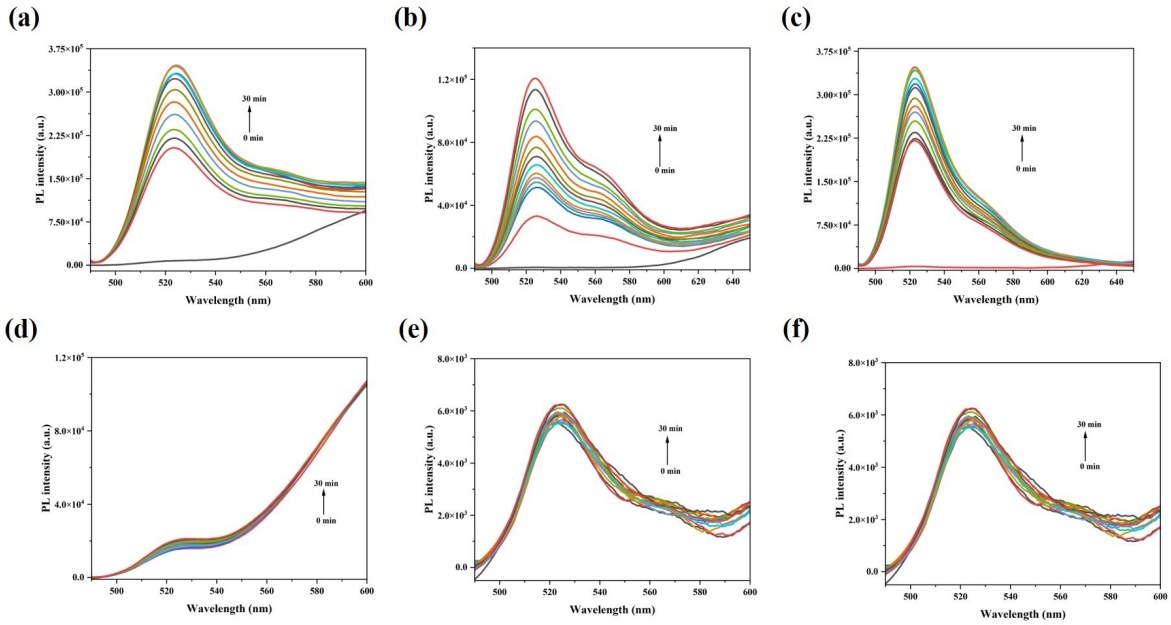

Figure S35. PL spectra of (a) TPP, (b) TPS, and (c) TPO NPs with DCFH in PBS solution under white light irradiation (2 mW cm^{-2}), (d) TPP, (e) TPS, and (f) TPO NPs with DCFH in PBS solution in dark. [TPP NPs] = [TPS NPs] = [TPO NPs] =10 μM, [DCFH]=40 μM.

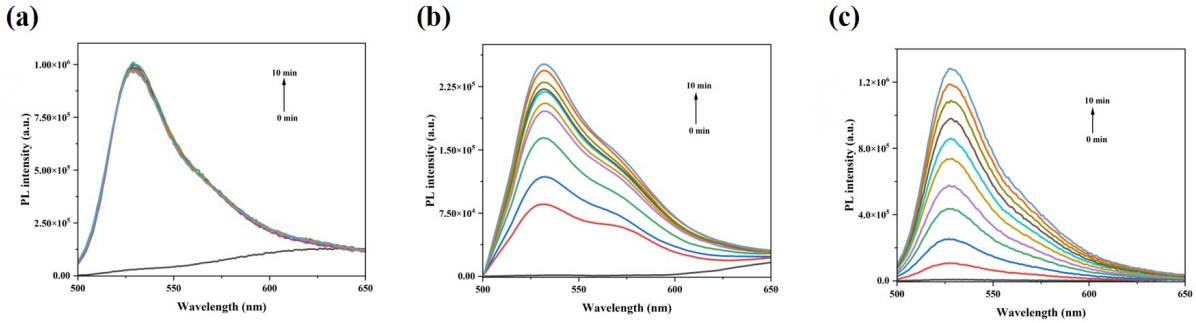

Figure S36. PL spectra of (a) TPP, (b) TPS, and (c) TPO NPs with DHR123 in PBS solution under white light irradiation (2 mW cm^{-2}) [TPP NPs] = [TPS NPs] = [TPO NPs] =10 μM, [DHR123] = 40 μM.

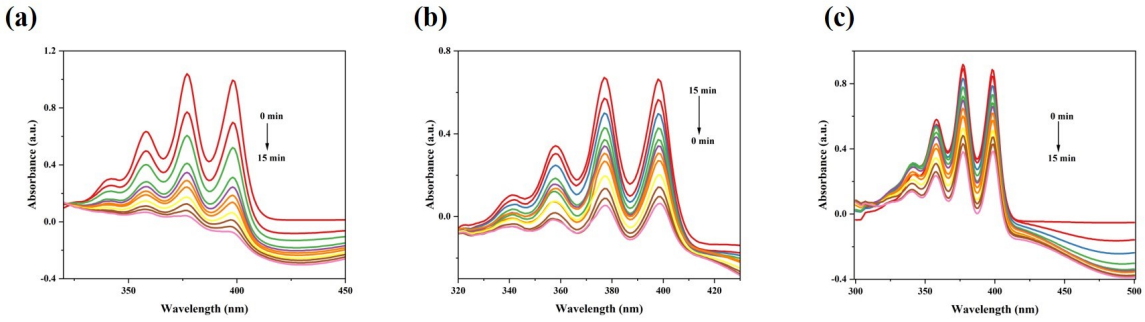

Figure S37. UV absorption spectra of (a) TPP, (b) TPS, and (c) TPO NPs with ABDA in PBS solution under white light irradiation (2 mW cm^{-2}). [TPP NPs] = [TPS NPs] = [TPO NPs] = 10 μM, [ABDA] = 0.1 mM.

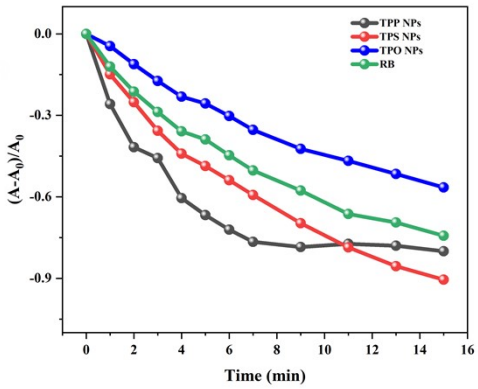

Figure S38. Absorbance intensity change $(A-A_0)/A_0$ for the ABDA indicator with TPP, TPS, and TPO NPs and RB upon white light irradiation (2 mW cm^{-2}).

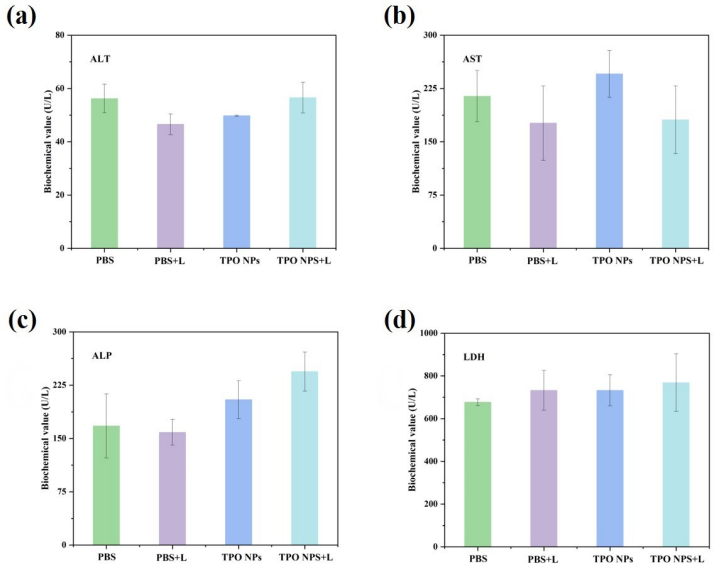

Figure S39. Serum biochemical parameters analyzed with the specimens collected from the animals received various treatments. The levels of (a) aspartate alanine aminotransferase (ALT), (b) aminotransferase (AST), (c) alkaline phosphatase (ALP), and (d) lactate dehydrogenase (LDH) determined by an automated analyzer.

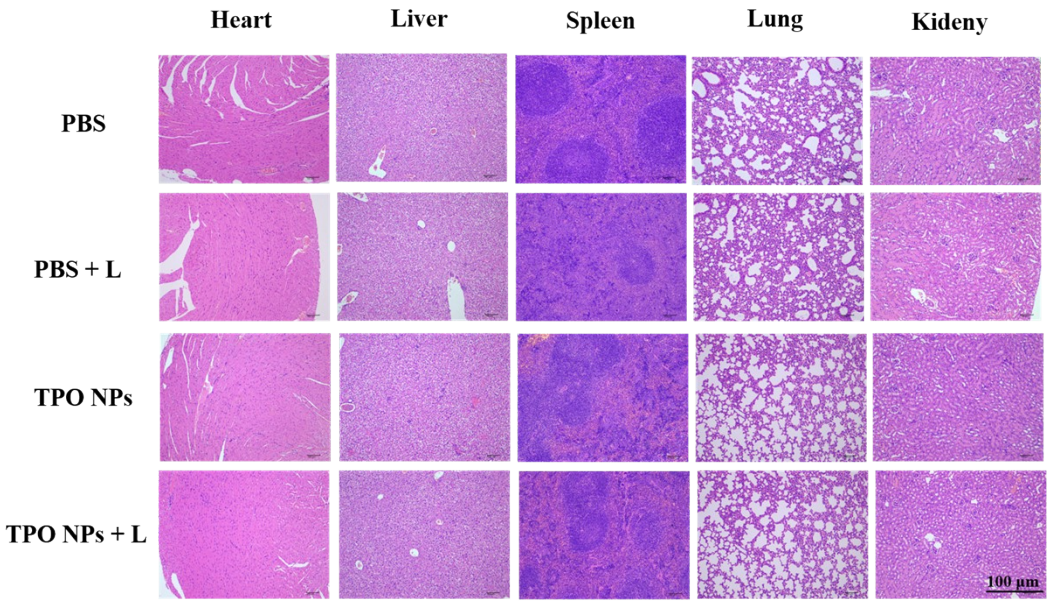

Figure S40. Histological H&E staining for different organs collected from mice in group VI on the 14th day after the treatment.