Electronic Supplementary Material (ESI) for Nanoscale Advances.

Supporting Information

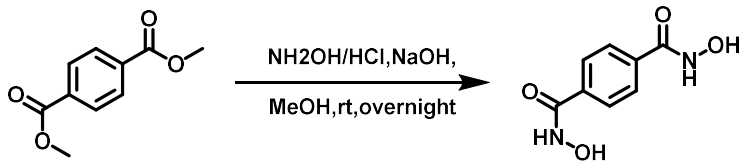
Synthesis and properties of novel type I photosensitizer Polycyclic Amide

1. Materials and Instruments

Unless otherwise noted, all reagents were obtained from commercial suppliers and were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were obtained on Bruker 400 M nuclear resonance spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. UV-vis absorption spectrum was measured on a Shimadzu UV-2550 spectrophotometer. PL spectra were recorded on a Shimadzu RF5301 spectrofluorometer. Particle size analysis was performed on a Malvern Zetasizer Nano-S90. Cyclic voltammetry experiments were conducted in dichlormethane (DCM) at room temperature using 0.1 M Bu_4NPF_6 as the electrolyte. The electron paramagnetic resonance (EPR) spectra are recorded on a Bruker EMXnano spectrometer.

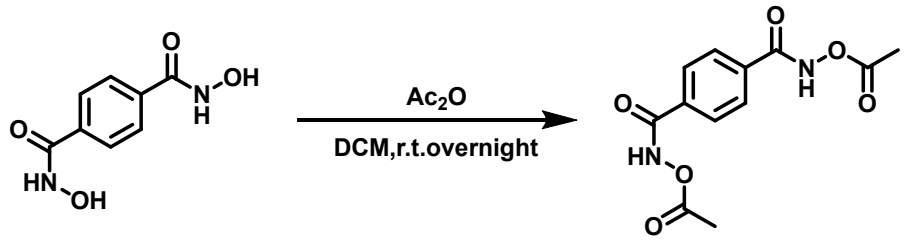
2. Synthesis

2.1 Synthesis of N^1, N^4-dihydroxyterephthalamide [1]



To a solution of MeOH (75 mL) containing NaOH (6.06 g, 151.9 mmol, 6 equiv.) was cooled to 0°C and Hydroxylamine hydrochloride (4.88 g, 75.7 mmol, 3 equiv.) was added. It was then allowed to stir at 0°C for 20 min. Then the solution of dimethyl terephthalate (4.9 g, 25.2 mmol, 1 equiv.) in MeOH (150 mL) was added to the mixture. It was then allowed to stir at 25°C overnight. The reaction was evaporated under reduced pressure and H_2O was added. It was allowed to stir for 20 min. The mixture was adjust pH to 5 with 10% HCl and then allowed to stir 2 hours. The mixture was filtered and wished with water two times and dried under reduced pressure to afford the desired product as a white solid (4.0 g, 81.0%).

2.2 Synthesis of N^1, N^4 - dihydroxyterephthalamide[1]



To a solution of aq. NaOH (2M, 29 mL, 2.8 equiv.) compound-2 (4.0 g, 20.4 mmol, 1 equiv.) was added. Then DCM (50 mL) was added and the mixture was allowed to stir

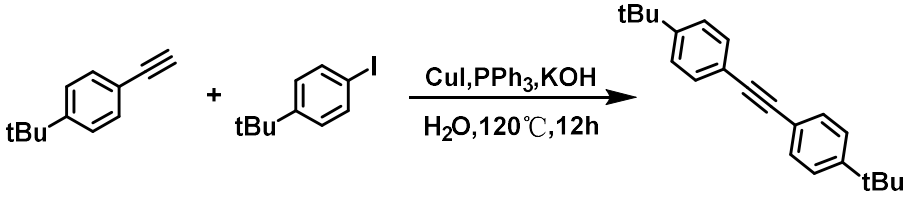
10 min. Then Ac_2O (3.64 g, 35.6 mmol, 1.7 equiv.) was added to the mixture. It was then allowed to stir at 25°C overnight. The mixture was filtered and wished with H_2O (20 mLx2), EtOH (20 mLx3) and Petroleum ether (20 mLx2) and dried under reduced pressure to afford the desired product as a white solid.

N^1, N^4-diacetoxyterephthalamide

Isolated as an amorphous white solid in 67.1% yield (3.84 g from 20.4 mmol of N^1, N^4 - dihydroxyterephthalamide).

^{1}H-NMR (400 MHz, *DMSO-d6*): δ 12.51 (s, 2H), 7.93 (s, 4H), 2.24 (s, 6H).

2.3 Synthesis of 1,2-bis(4-tert-butylphenyl)ethyne[2]



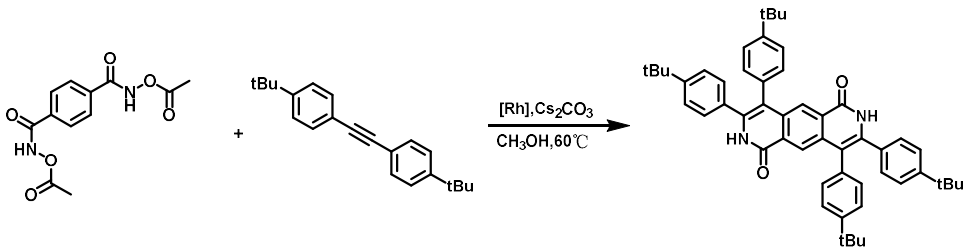
The reaction was performed in a 150 mL Schlenk tube under argon. To a Schlenk tube was added CuI (723 mg, 3.8 mmol, 0.1 equiv.), PPh_3 (2.0 g, 7.6 mmol, 0.2equiv.) and KOH (4.26 g, 76 mmol, 2.0 equiv.) and 80 mL deionized water were added. After the suspension was stirred at room temperature for 10 minutes, aryl iodine (9.88 g, 38 mmol, 1 equiv.) and arylacetylene (5.22 g, 33 mmol, 0.87 equiv.) were added. The reaction was shortly purged with argon and sealed. After 5 h at 120 °C in oil bath, the mixture was cooled to temperature, extracted with ethyl acetate (4 × 120 mL), then the combined organic layer was dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum. The residue was purified by silica gel column to afford desired product as a white solid.

1,2-bis(4-tert-butylphenyl)ethyne

Isolated as an amorphous white solid in 83.6% yield (8 g from 33 mmol of 4-tert-butylphenylacetylene).

^{1}H-NMR (400 MHz, *$CDCl_3$*) δ 7.46 (d, J = 8.4 Hz, 4H), 7.36 (d, J = 8.4 Hz, 4H), 1.33 (s, 18H).

2.4 Synthesis of PA [1]



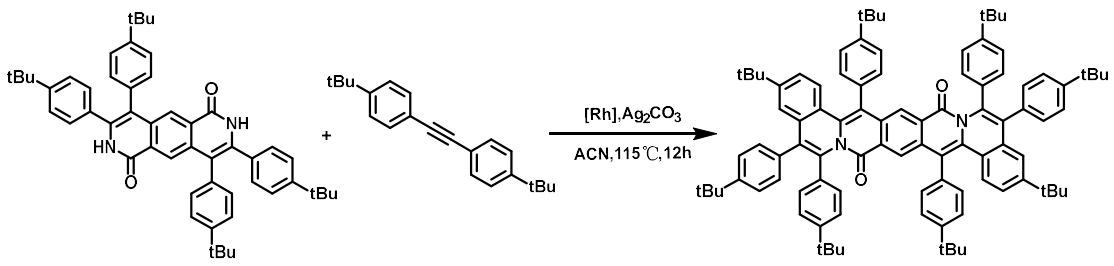
The reaction was performed in a 150 mL Schlenk tube under argon. To a Schlenk tube was added 1,2-bis(4-tert-butylphenyl)ethyne (456 mg, 1.57 mmol, 2.2 equiv.), N^1, N^4-diacetoxyterephthalamide (200 mg, 0.71 mmol, 1.0 equiv.), CsOAc (411 mg, 2.14 mmol, 3.0 equiv.), $[Cp^*RhCl_2]_2$ (22 mg, 0.036 mmol, 0.05 equiv.) and MeOH (0.055 mmol /mL). The reaction mixture was heated at 60°C for 6 hours. The mixture was filtered and wished with H_2O (20 mLx2) and MeOH (20 mLx2), then dried under reduced pressure to afford the yellow solid. To a solution of ethyl acetate(1g/10mL) the yellow solid was added. It was then allowed to stir at 25°C overnight. The mixture was filtered and wished with ethyl acetate 2 times and dried under reduced pressure to afford the desired product as a yellow solid.

3,4,8,9-tetrakis(4-(tert-butyl)phenyl)-2,7-dihydropyrido[3,4-g]isoquinoline-1,6-dione (PA)

Isolated as an amorphous yellow solid in 75.6% yield (400 mg from 0.71 mmol of N^1, N^4-diacetoxyterephthalamide).

^{1}H-NMR (400 MHz, *$CDCl_3$+CD_3OD*): δ 8.51 (s, 2H), 7.25 (d, J = 8.4 Hz, 4H), 7.14 (d, J = 8.4 Hz, 4H), 7.06 - 7.01 (m, 8H), 1.34 (s, 18H), 1.26 (s, 18H). MALDI-TOF MS, calculated for $C_{52}H_{56}N_2O_2$ $[M+H]^+$ 740.4, found 740.4.

2.5 Synthesis of compound-PhPA[4]



The reaction was performed in a 150 mL Schlenk tube under argon. To a Schlenk tube was added 1,2-bis(4-tert-butylphenyl)ethyne (837 mg, 2.88 mmol, 2.2 equiv.), PA (970 mg, 1.31 mmol, 1.0 equiv.), Ag_2CO_3 (1.08 g, 3.93 mmol, 3.0 equiv.), $[Cp^*RhCl_2]_2$ (41

mg, 0.066 mmol, 0.05 equiv.) and ACN (66 mL). The reaction mixture was heated at 115°C for 12 hours. The mixture was filtered and wished with DCM, and the filtrate was then purified by silica to afford the desired product as a red solid.

Isolated as an amorphous red solid in 57.9% yield (1.0 g from 1.31 mmol of 3,4,8,9-tetrakis(4-(tert-butyl)phenyl)-2,7-dihydropyrido[3,4-g]isoquinoline-1,6-dione(PA)).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 2H), 7.50 - 7.36 (m, 8H), 7.21 (s, 2H), 7.20 (d, J = 8.1 Hz, 4H), 7.02 - 6.96 (m, 8H), 6.87 (d, J = 8.1 Hz, 4H), 6.82 - 6.78 (m, 2H), 6.74 - 6.78 (m, 2H), 1.41 (s, 18H), 1.27 (s, 18H), 1.17 (s, 18H), 1.12 (s, 18H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.73, 151.55, 149.64, 149.06, 136.32, 135.03, 134.62, 134.55, 133.91, 133.41, 133.07, 131.91, 131.24, 128.91, 128.56, 127.70, 126.94, 125.85, 125.69, 124.51, 124.02, 123.79, 122.26, 117.35, 34.96, 34.81, 34.63, 34.52, 31.66, 31.51, 31.38, 31.08. MALDI-TOF MS, calculated for $C_{96}H_{104}N_2O_2$ [M+H]+ 1316.8, found 1316.8.

3. Measurement of fluorescence quantum yield

The fluorescence quantum yield (Φ) of the PA and PhPA in DCM were measured using a standard fluorescence comparison method. 9,10-Diphenylanthracene in DCM and Rhodamine 110 in water was used as reference (Φ = 95% and 85%, respectively). The UV-vis absorption spectra of compounds in DCM and reference in DCM or aqueous media were measured and the maximum absorption was limited to less than 0.05 to minimize the self-absorption effect. The fluorescence spectra then were recorded under maximum excitation. The fluorescence intensities were obtained through wavelength integration.

The fluorescence quantum yield (Φ) of compounds was calculated by the following equation:

$$\Phi_x = \Phi_{st}\left(\frac{k_x}{k_{st}}\right)\left(\frac{\eta_x^2}{\eta_{st}^2}\right)$$

where Φ_{st} is the standard fluorescence quantum yield. k_x and k_{st} are is the slope after linear fitting of fluorescence intensity integral vs. the absorption of compounds and inference, respectively. η_x and η_{st} are the refractive indexes of the solvent. The subscripts x and st denote the sample and the reference (9,10-Diphenylanthracene in

DCM or Rhodamine 110 in water).

4. Preparation of nanoparticles

The mixed THF solution (1 mL) containing PhPA (1 mg) and F127 (5 mg) was rapidly injected into water (10 mL) under sonication. After continuous sonication for 10 minutes, THF was evaporated by stirring at room temperature overnight. The obtained NPs were filtered through a 0.22 μm syringe filter and stored in the dark at 4 °C.

5. ROS generating ability test

5.1 Detection production of ROS in solution

The generation of ROS was detected indirectly using 3-diphenylisobenzofuran (DPBF) as a chemical probe, whose absorbance would be diminished in the presence of ROS. Thus, a solution of DPBF (45 μM) and PSs (10 μM) in 3 mL solvent (DCM:MeOH = 9:1) was irradiated white led intervals. The power density of the laser point is 5 mW/cm^2. The solutions were irradiated for 10 second and their absorbance spectra were recorded at 2 second intervals using a spectrometer.

5.2 Singlet oxygen ($^1O_2$) detection

The singlet oxygen generated by PhPA was measured using singlet oxygen capture agent, 9, 10-anthracenedipropanoic acid (ABDA). Briefly, the absorbance of ABDA at 380 nm was adjusted to about 1.0 in DCM. Then, PhPA was added to this cuvette to make sure the concentration of PhPA is 10 μM. Then, the cuvette was irradiated with white LED (5 mW/cm^2) for various time, and absorption spectra were measured immediately.

5.3 Detection of $O2^{-\bullet}$ production with electron paramagnetic resonance (EPR).

The $O2^{-\bullet}$ generation was also examined by EPR technology using 5,5-dimethyl-1-pyrroline-N-oxide (DMPO) as the spin-trap. Spectra of spin trapped $O2^{-\bullet}$ were obtained by mixing 50 mM DMPO with 10 mg/mL PhPA in DCM. Then the mixture was irradiated by the 300W xenon lamp (with a 400 - 760 nm filter) for 3 min. A mixture with no light irradiation was used as a control.

5.4 Superoxide anion radical ($O_2^{-\bullet}$) detection.

Dihydroethidium (DHE) is used as the superoxide anion radical indicator, which can

react with $O_2^{-\bullet}$ to emit strong red fluorescence centered at 590 nm. The $O_2^{-\bullet}$ production of PhPA@F127 in water was investigated using DHE as a probe.[5]

6. Photostability detection

Compound PA was dissolved in DCM (25 μM) and placed in cuvettes. The cuvette was irradiated with white light (5 mW/cm^2) for various time, and absorption spectra were measured immediately, meanwhile fluorescence signal of PA was monitored with the excitation wavelength at 360 nm.

Compound PhPA was dissolved in DCM (25 μM) and placed in cuvettes. The cuvette was irradiated with white light (5 mWcm^{-2}) for various time, and absorption spectra were measured immediately, meanwhile fluorescence signal of PhPA was monitored in a range of 320 - 800 nm and 500 - 800nm with the excitation wavelength at 312 nm and 480 nm, respectively.

7. Supplementary Figures and Tables

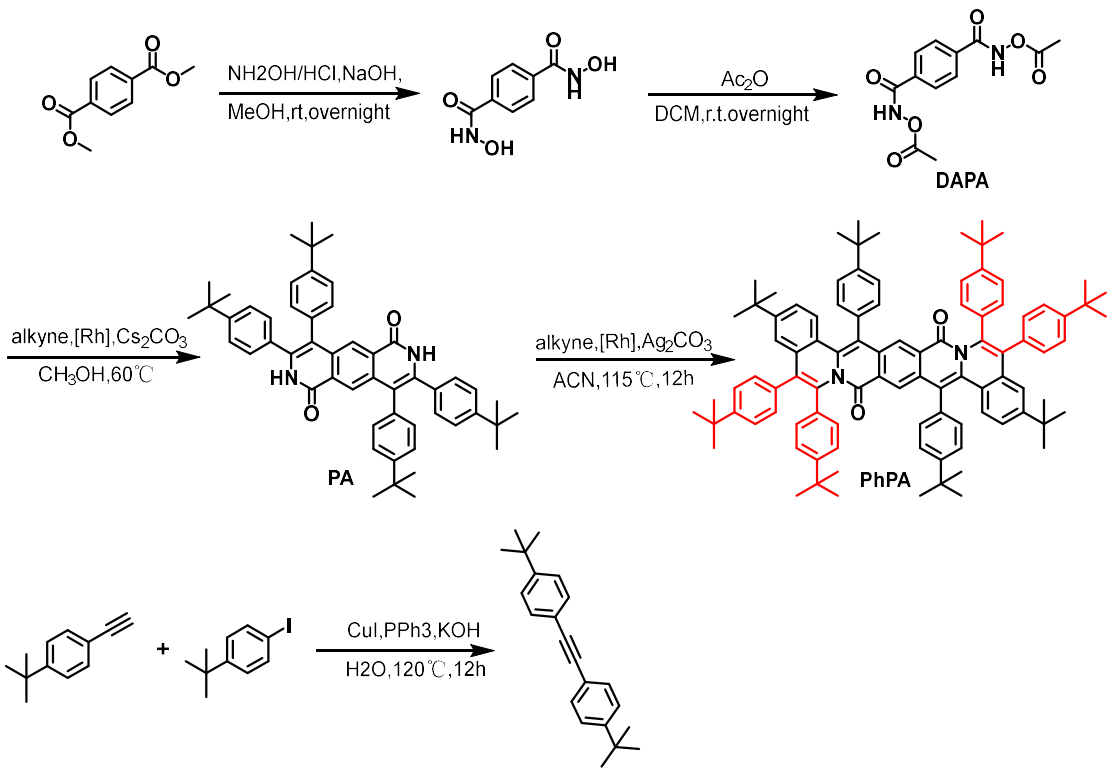


Figure S1. Synthetic route of PA and PhPA.

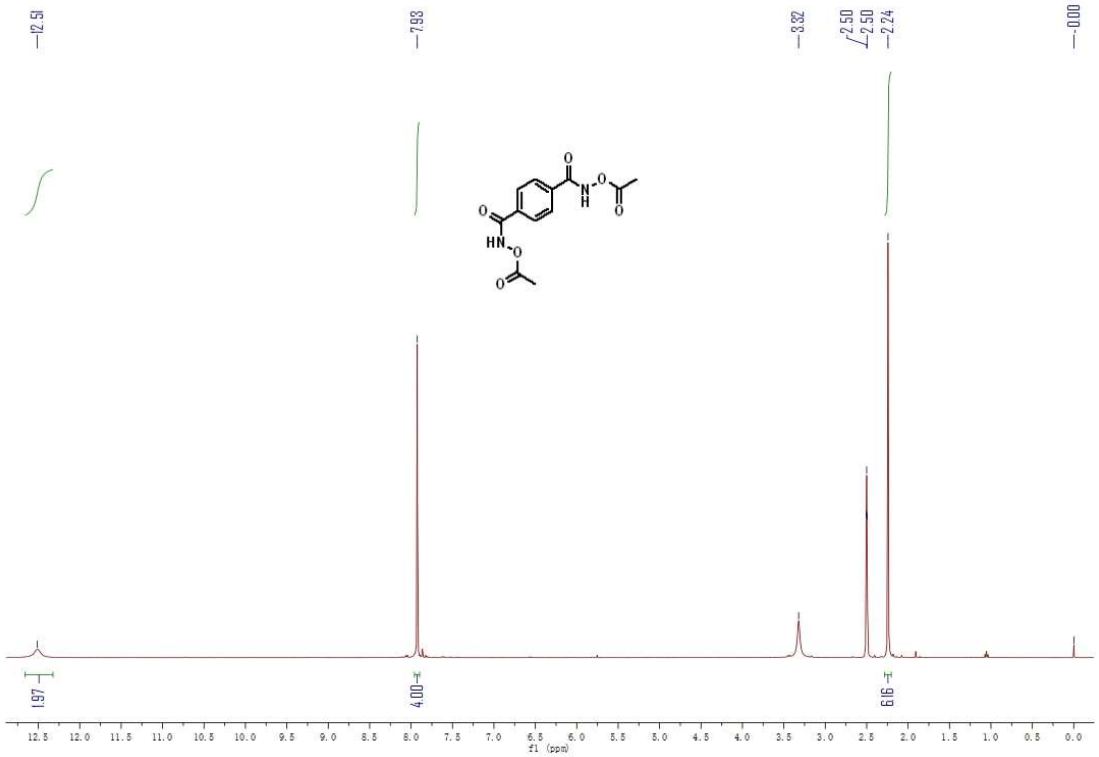


Figure S2. ^{1}H NMR spectrum of **DAPA** in DMSO-d_6.

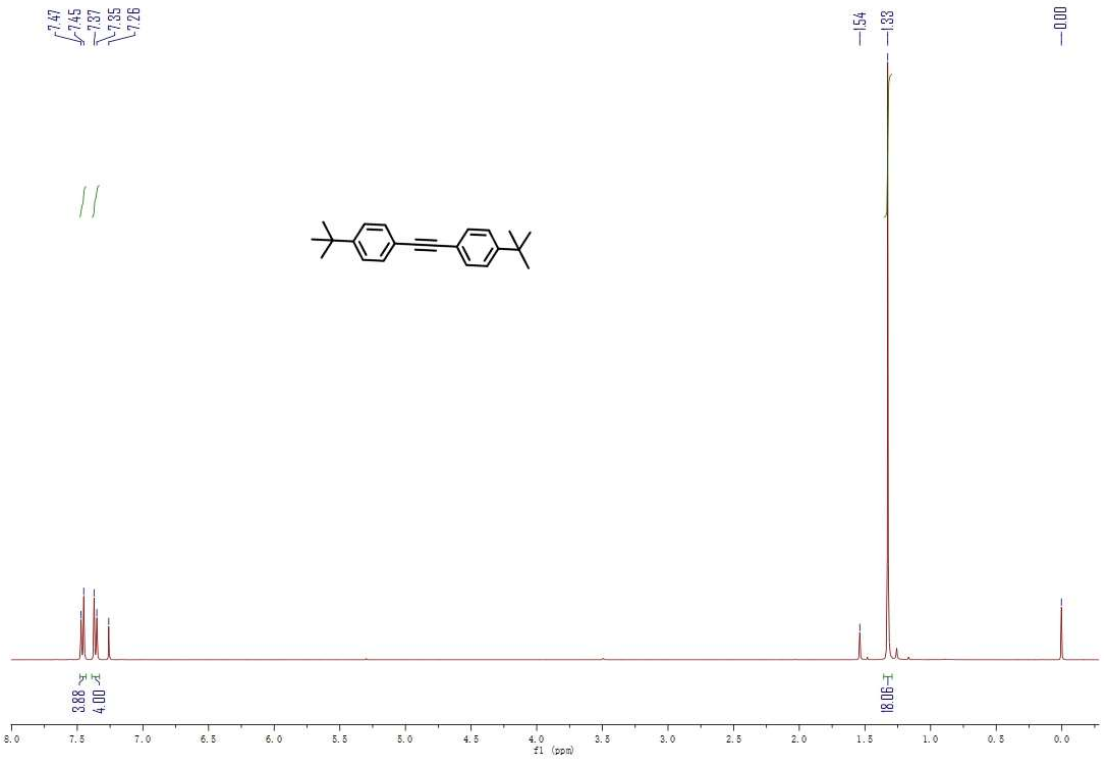


Figure S3. ^{1}H NMR spectrum of **1,2-bis(4-tert-butylphenyl)ethyne** in *$CDCl_3$*.

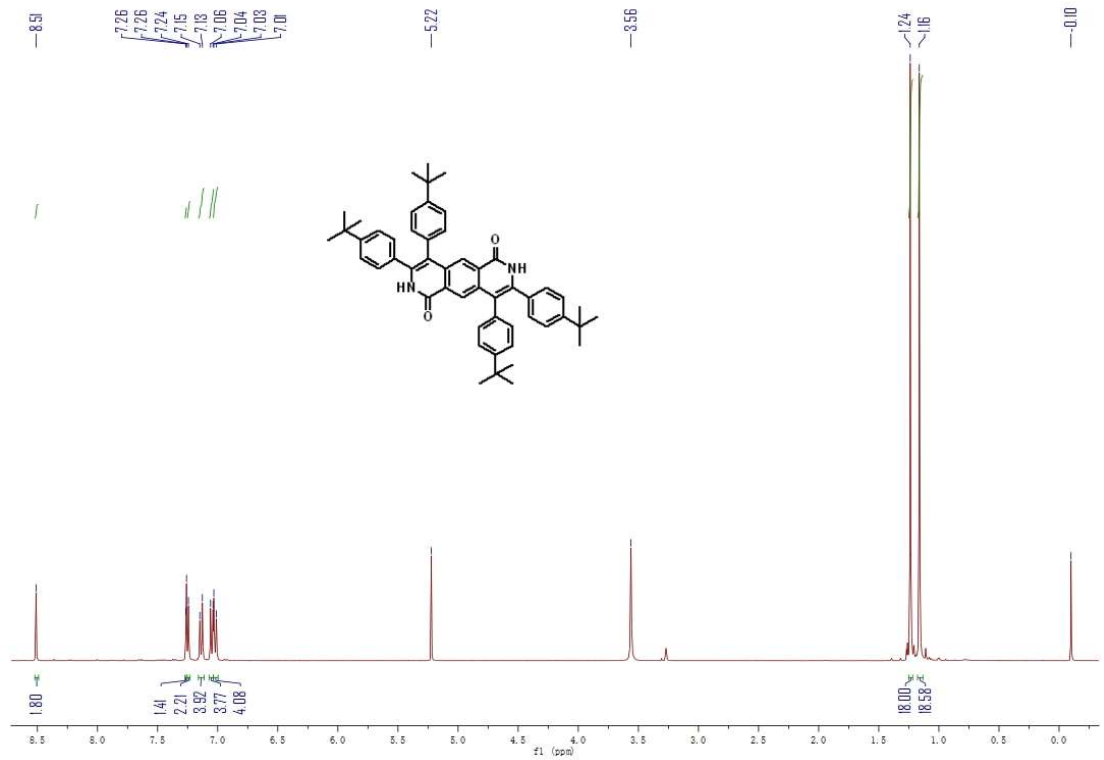


Figure S4. ^{1}H NMR spectrum of **PA** in *$CDCl_3$+CD_3OD* (0.6mL+0.1mL).

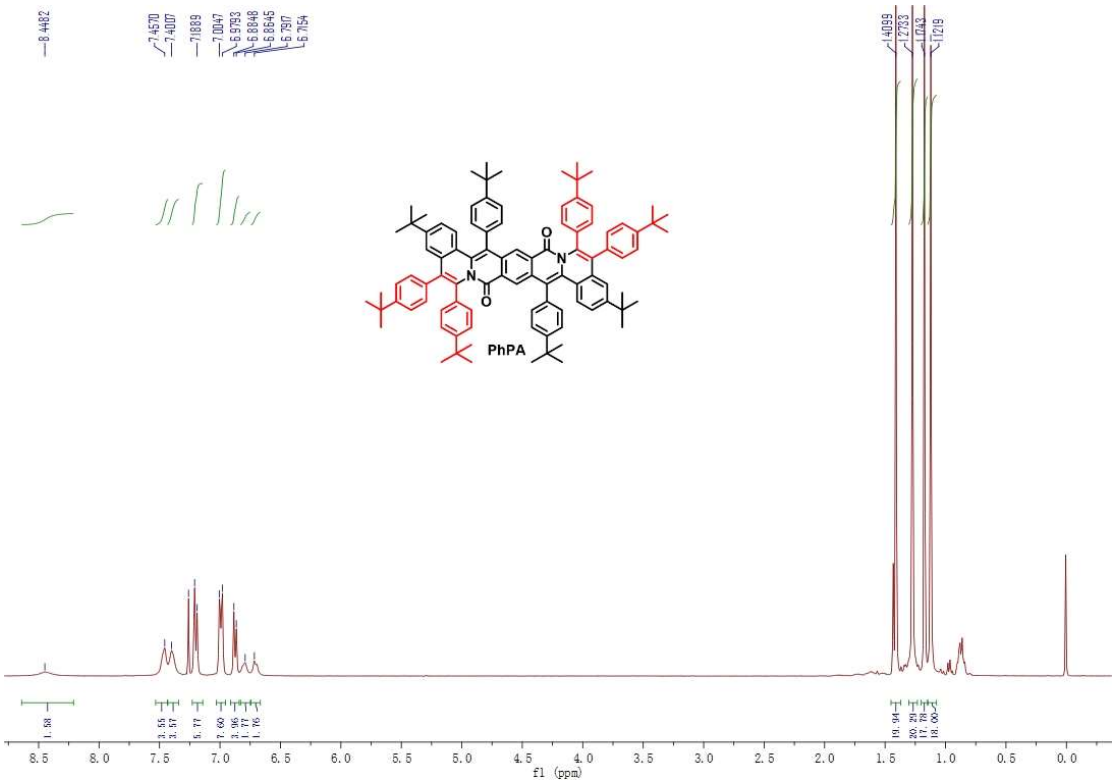


Figure S5. ^{1}H NMR spectrum of **PhPA** in *$CDCl_3$*.

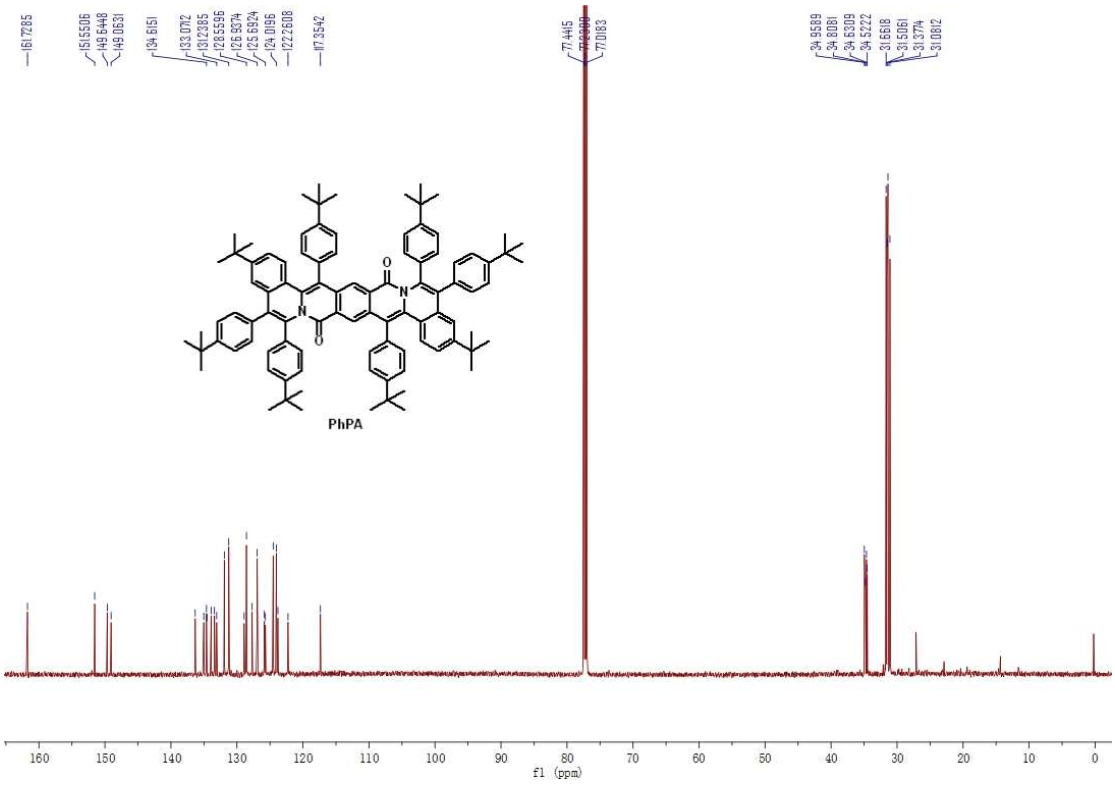


Figure S6. ^{13}C NMR spectrum of **PhPA** in *$CDCl_3$*.

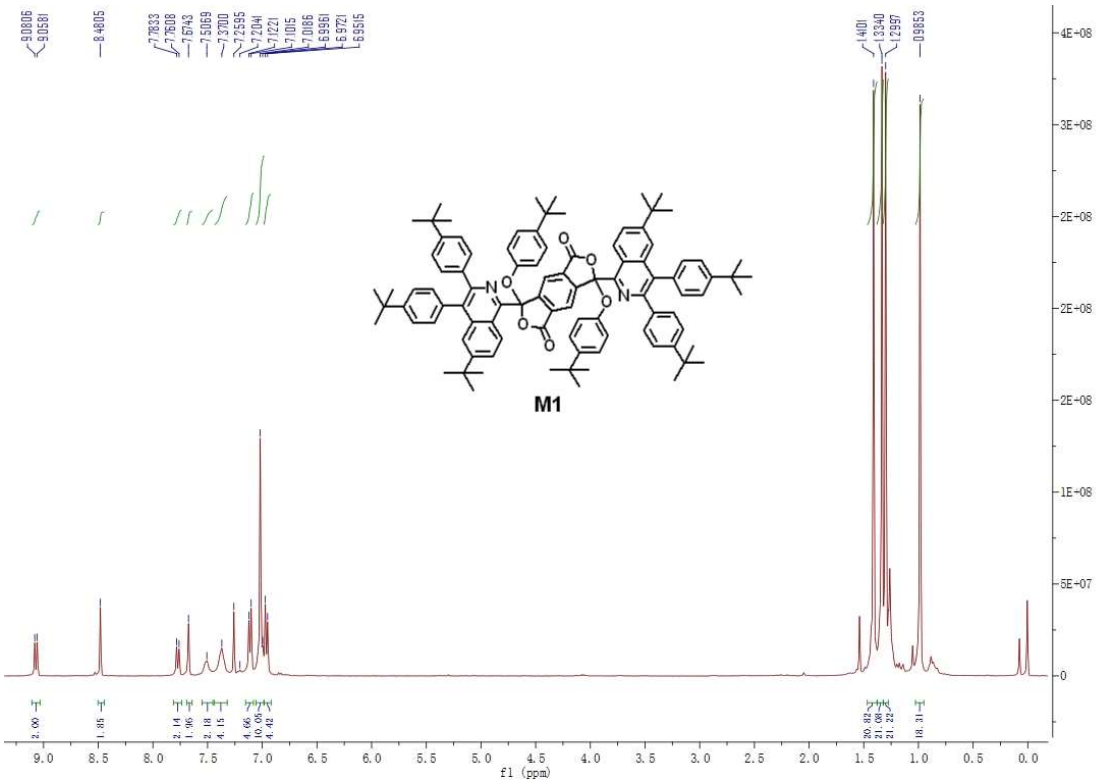


Figure S7. ^{1}H NMR spectrum of **M1** in *CDCl₃*.

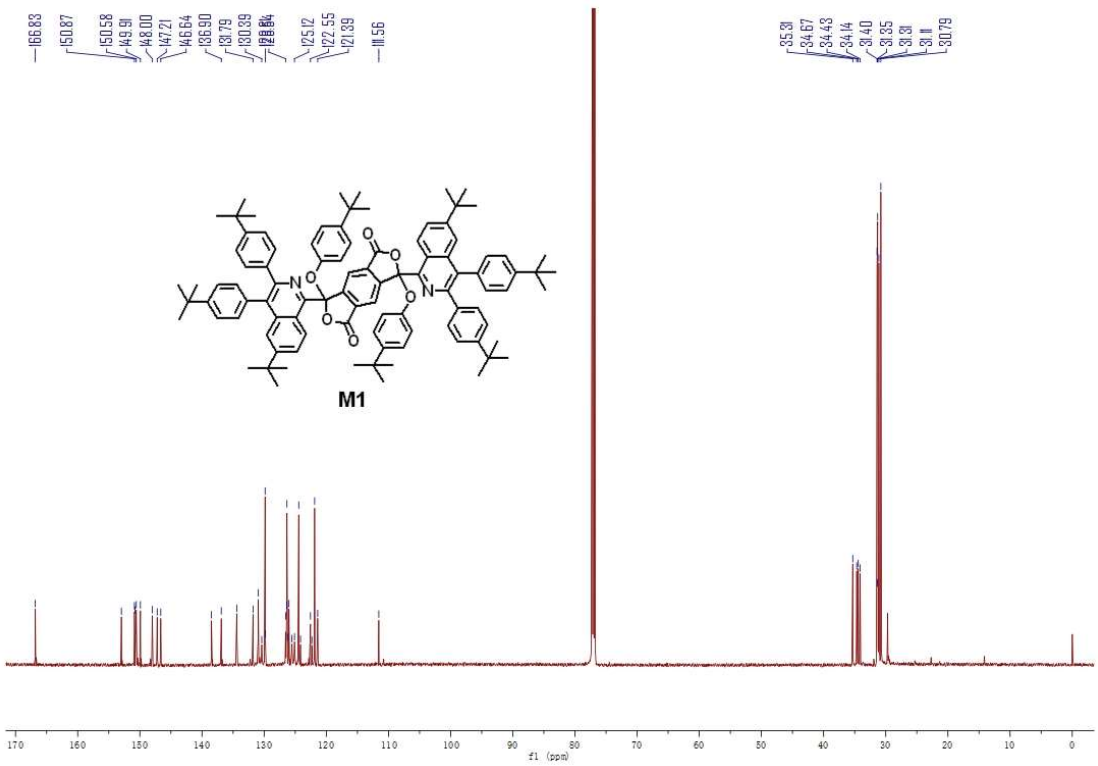


Figure S8. ^{13}C NMR spectrum of **M2** in *CDCl₃*.

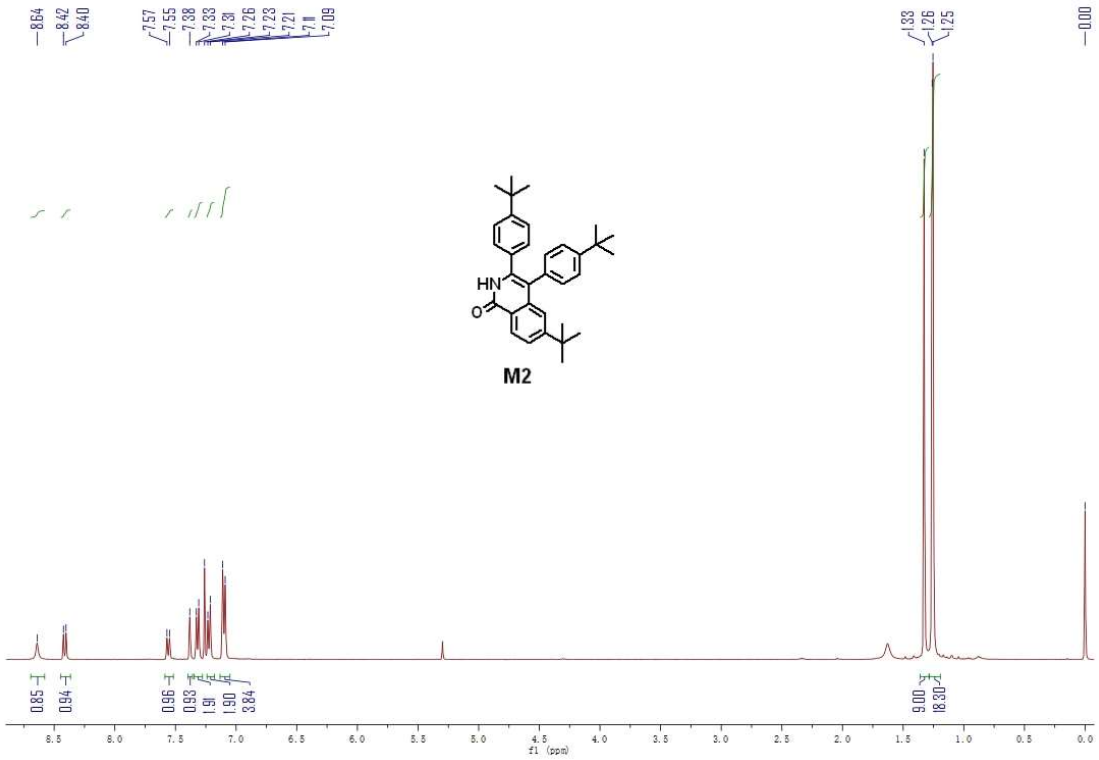


Figure S9. ^{1}H NMR spectrum of **M1** in *CDCl₃*.

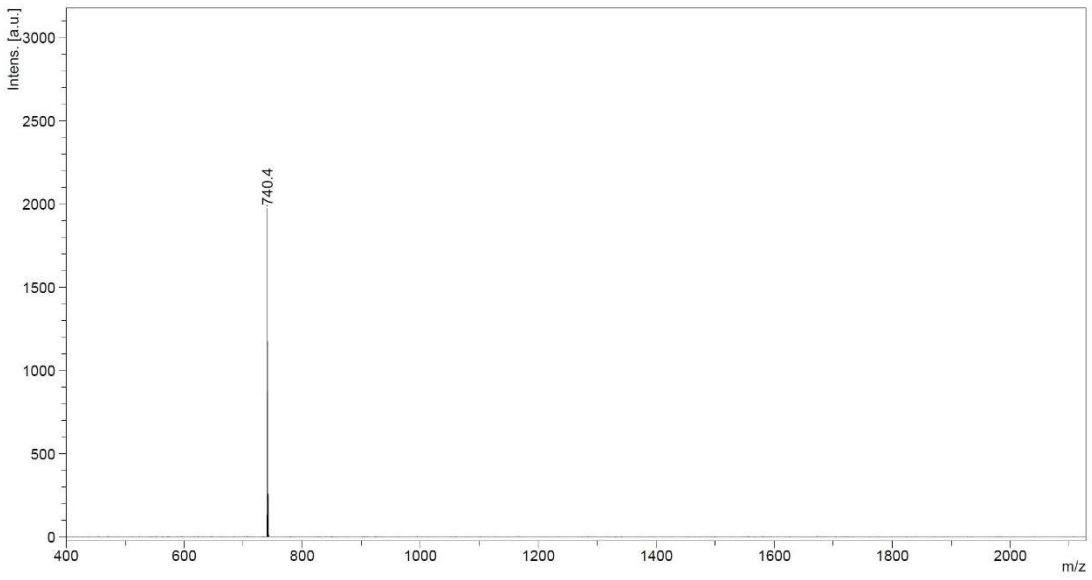


Figure S10. MALDI-TOF MS spectrum of **PA**.

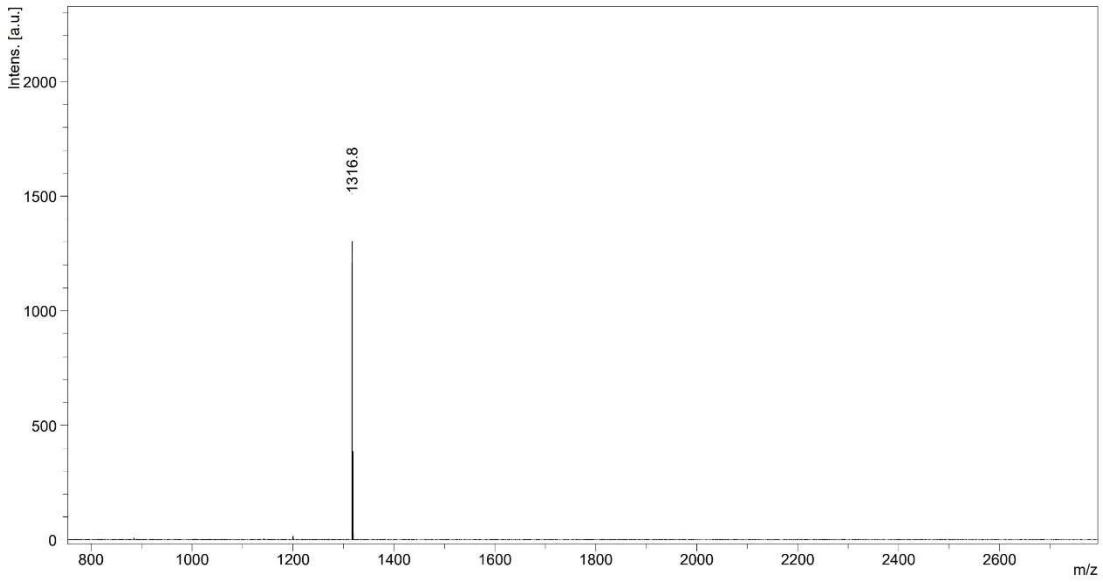


Figure S11. MALDI-TOF MS spectrum of **PhPA**.

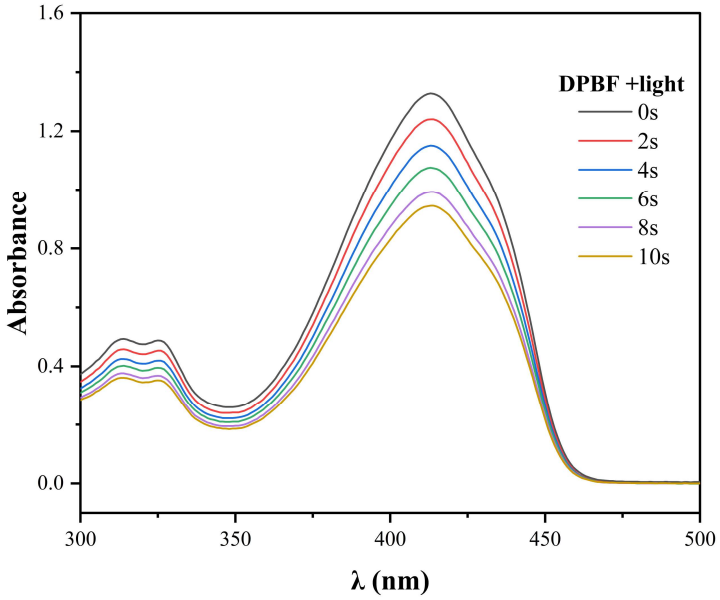


Figure S12. Time-dependent decrease of absorbance of DPBF. The samples were continuously irradiated by white light (5 mW/cm^2).

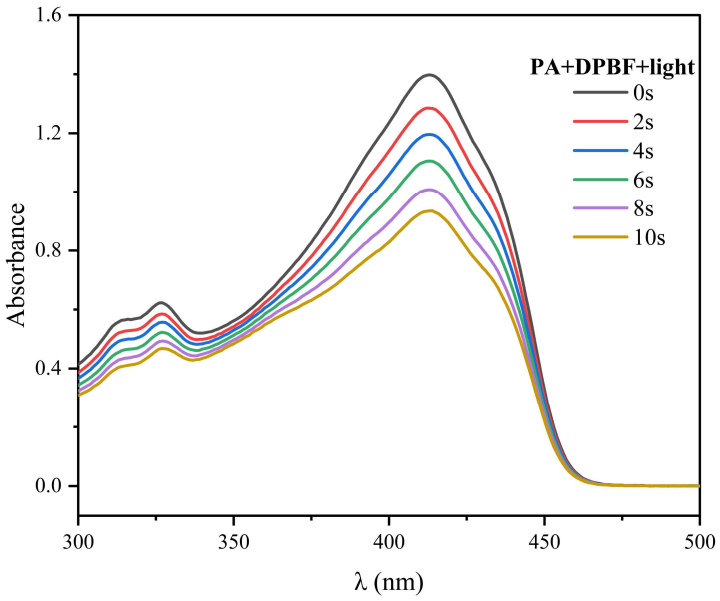


Figure S13. Time-dependent decrease of absorbance of DPBF in the presence of PA. The samples were continuously irradiated by white light (5 mW/cm^2).

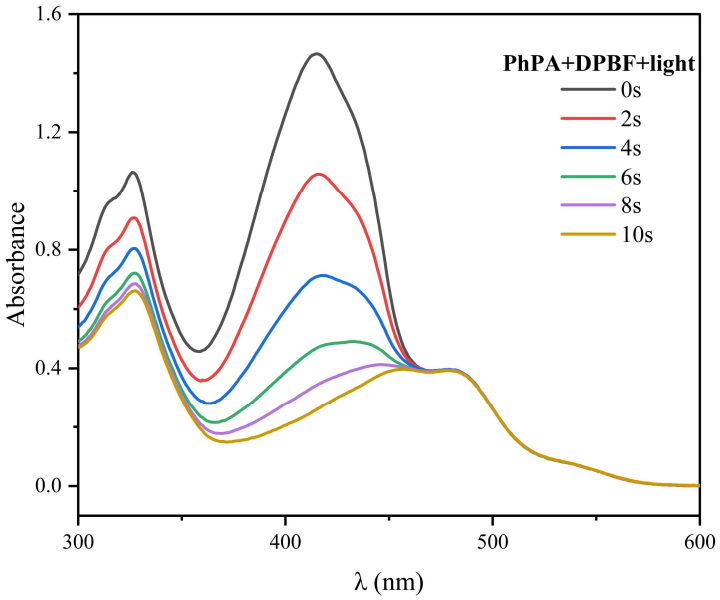


Figure S14. Time-dependent decrease of absorbance of DPBF in the presence of PhPA. The samples were continuously irradiated by white light (5 mW/cm^2).

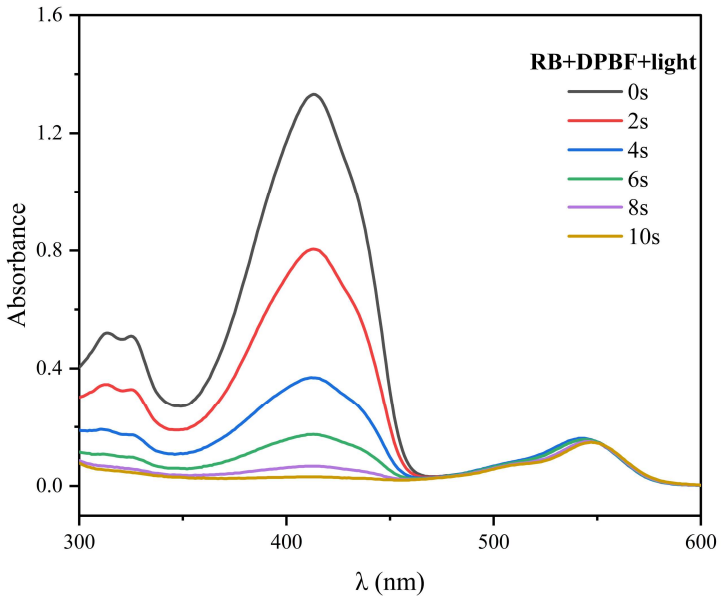


Figure S15. Time-dependent decrease of absorbance of DPBF in the presence of RB in DCM. The samples were continuously irradiated by white light (5 mW/cm^2).

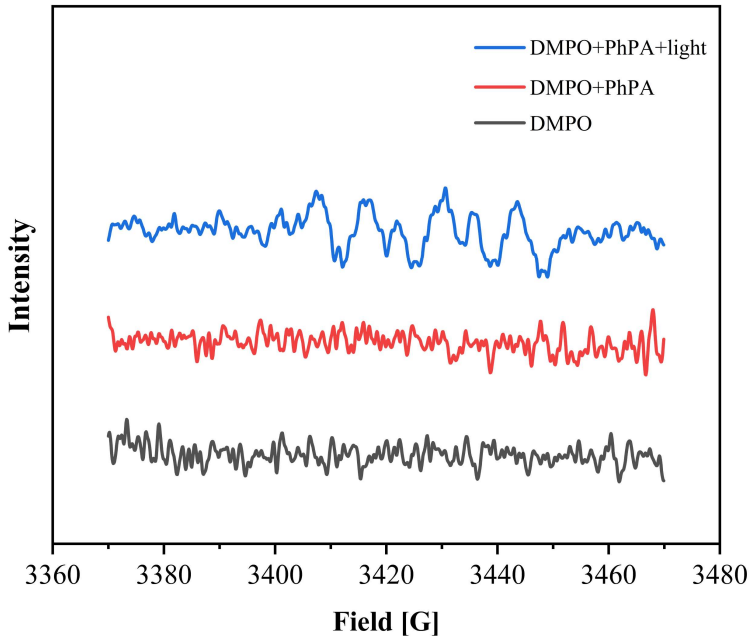


Figure S16. EPR signals of DMPO for $O2^{\bullet-}$ characterization.

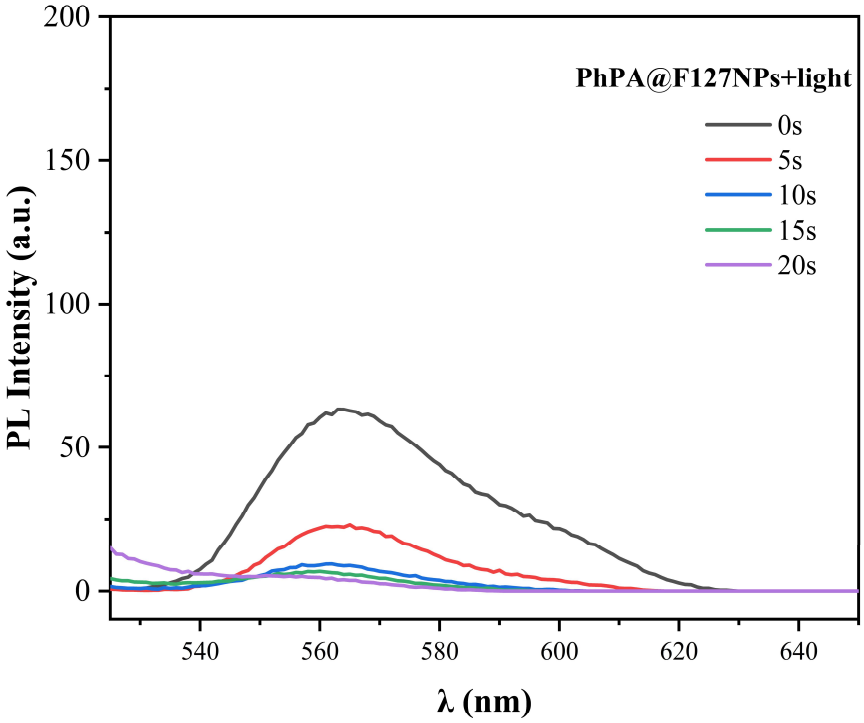


Figure S17. PL spectra of PhPA@F127NPs (at 10 μg/mL in water) with continuously irradiating by white light (5 mW/cm^2).

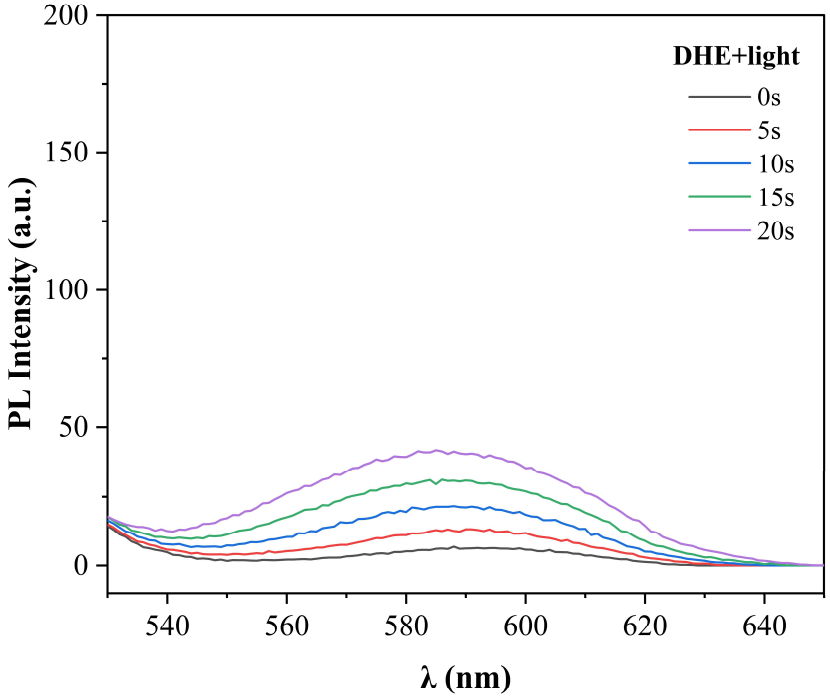


Figure S18. PL spectra of hydroethidine (at 50 μM in water) with continuously irradiating by white light (5 mW/cm^2).

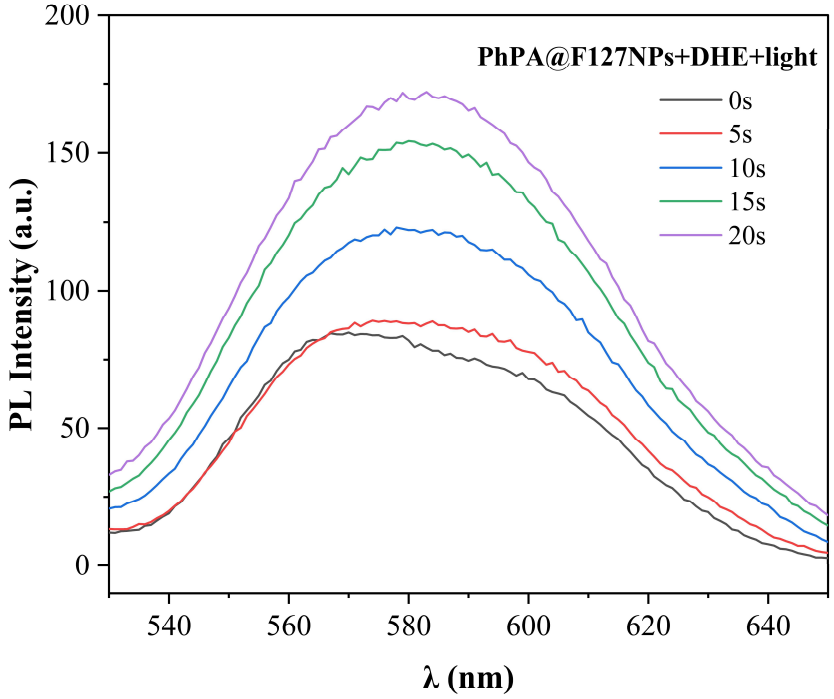


Figure S19. $O_2^{-\bullet}$ generation of PhPA@F127NPs (at 10 μg/mL in water) after irradiation for different times detected by using hydroethidine as a probe (50 μM, ex = 510 nm, em = 590 nm). Irradiation by a white light (5 mW/cm^2).

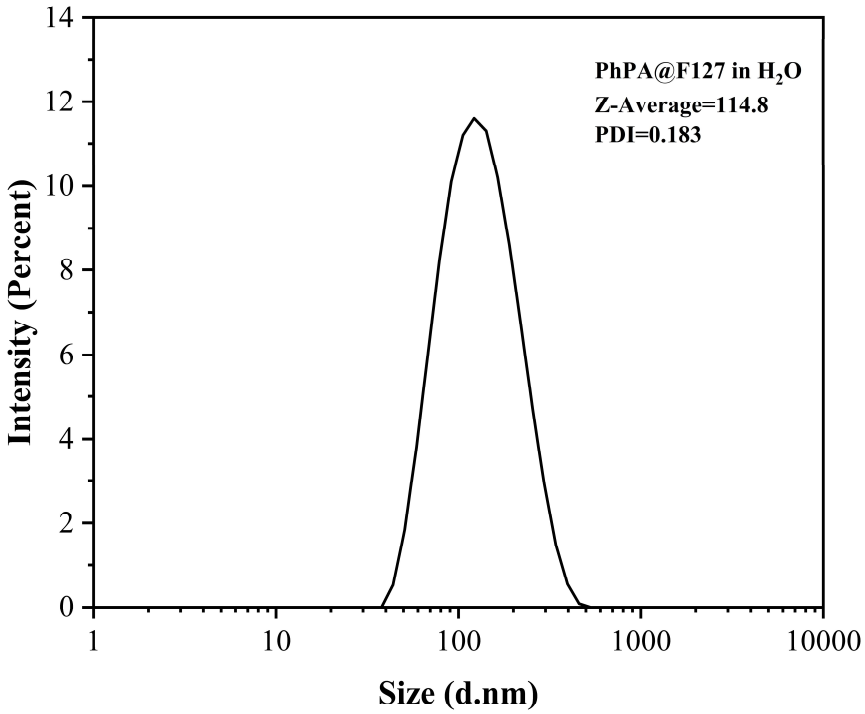


Figure S20. Size distributions of PhPA@F127 (10 μg/mL) in water detected by DLS.

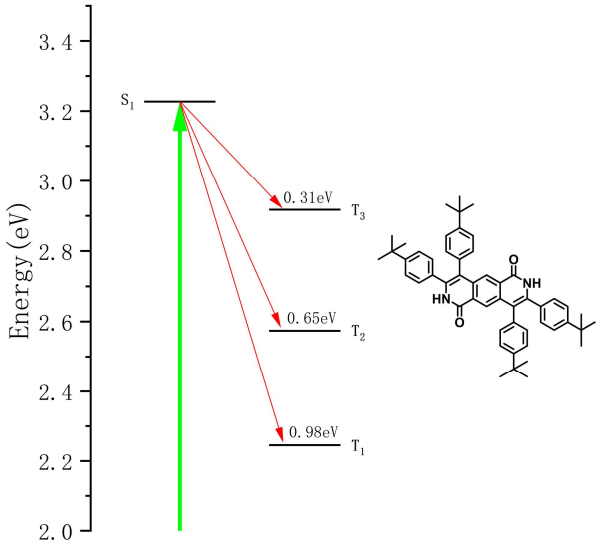


Figure S21. Possible ISC channels and $\Delta E_{S_mT_n}$ for **PA**.

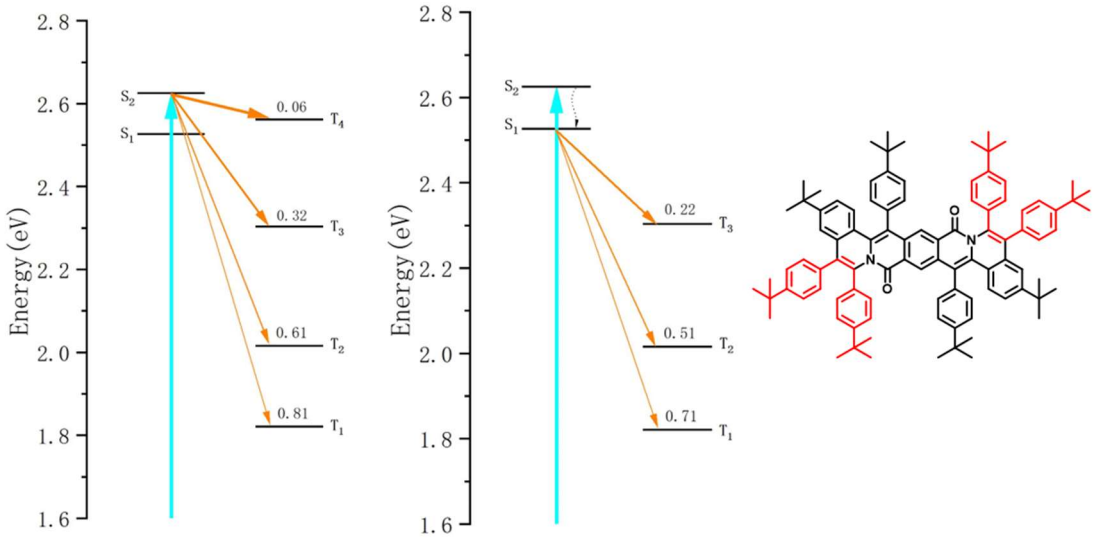


Figure S22. Possible ISC channels and $\Delta E_{S_mT_n}$ for **PhPA**. The black wavy dotted arrows indicate the internal conversions.

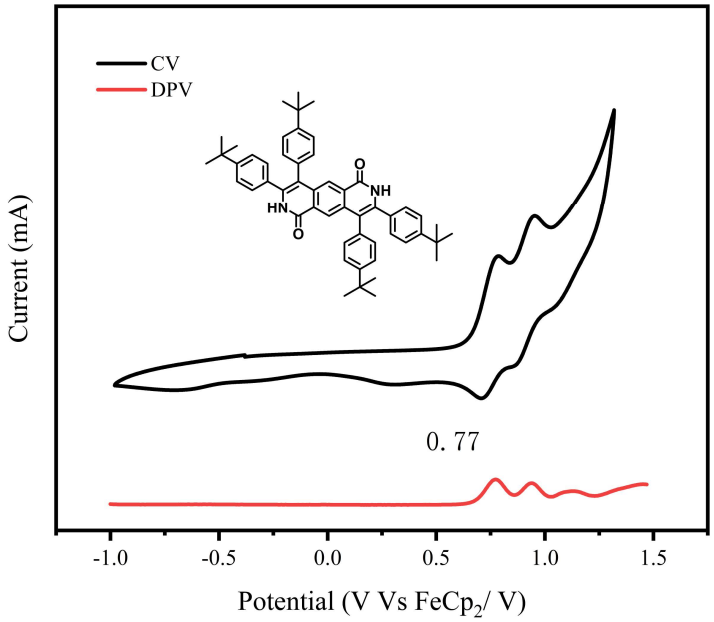


Figure S23. The DPV (red) and CV (black) of **PA** in CH_2Cl_2 and 0.1 M Bu_4NPF_6 on a Pt electrode at a scan rate of 50 mVs-1 vs Ag/AgCl wire.

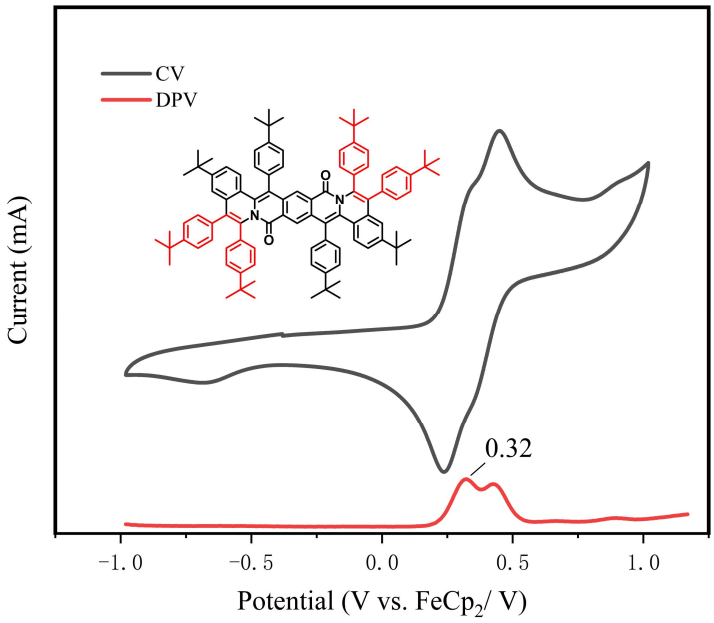


Figure S24. The DPV (red) and CV (black) of **PhPA** in CH_2Cl_2 and 0.1 M Bu_4NPF_6 on a Pt electrode at a scan rate of 50 mVs-1 vs Ag/AgCl wire.

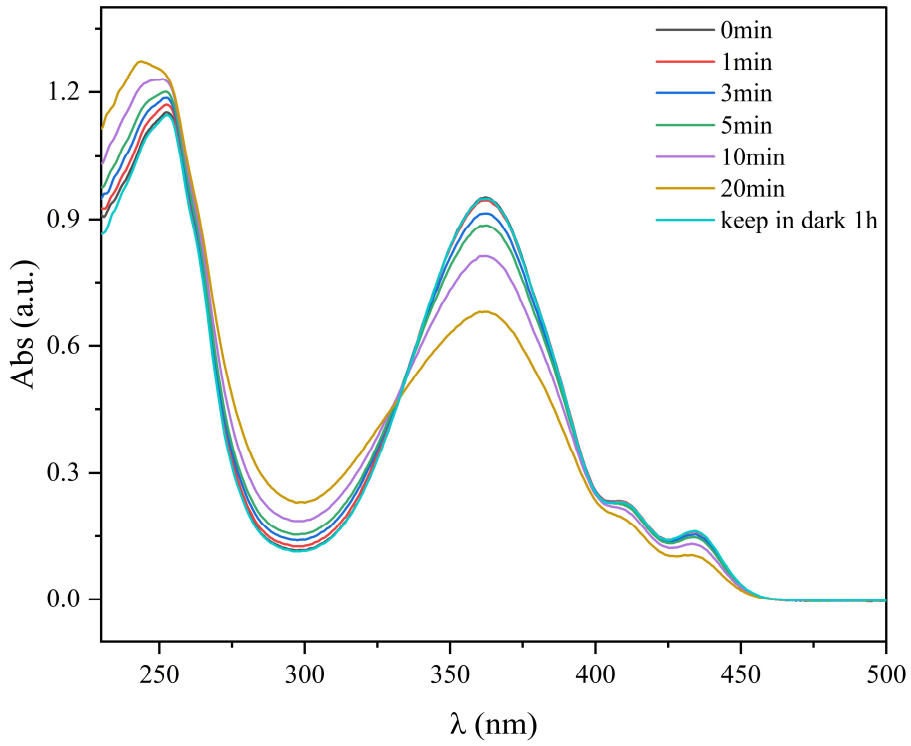


Figure S25. UV-vis absorption spectra of **PA** in DCM irradiated by white light (5 mW/cm^2) for 0, 1, 3, 5, 10, and 20 min, respectively.

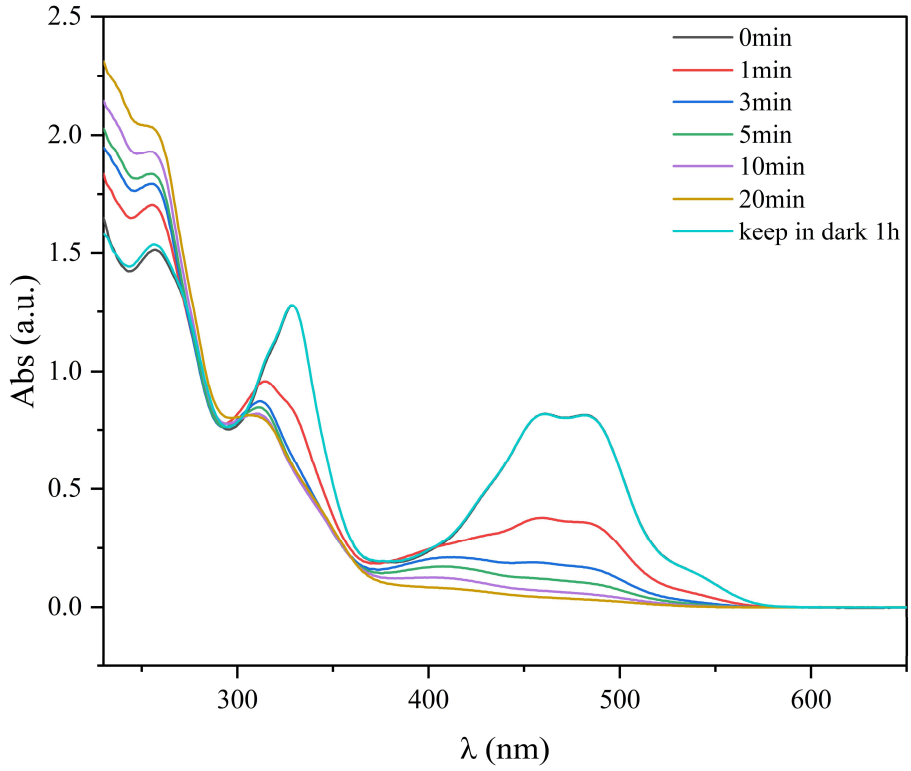


Figure S26. UV-vis absorption spectra of **PhPA** in DCM irradiated by white light (5 mW/cm^2) for 0, 1, 3, 5, 10, and 20 min, respectively.

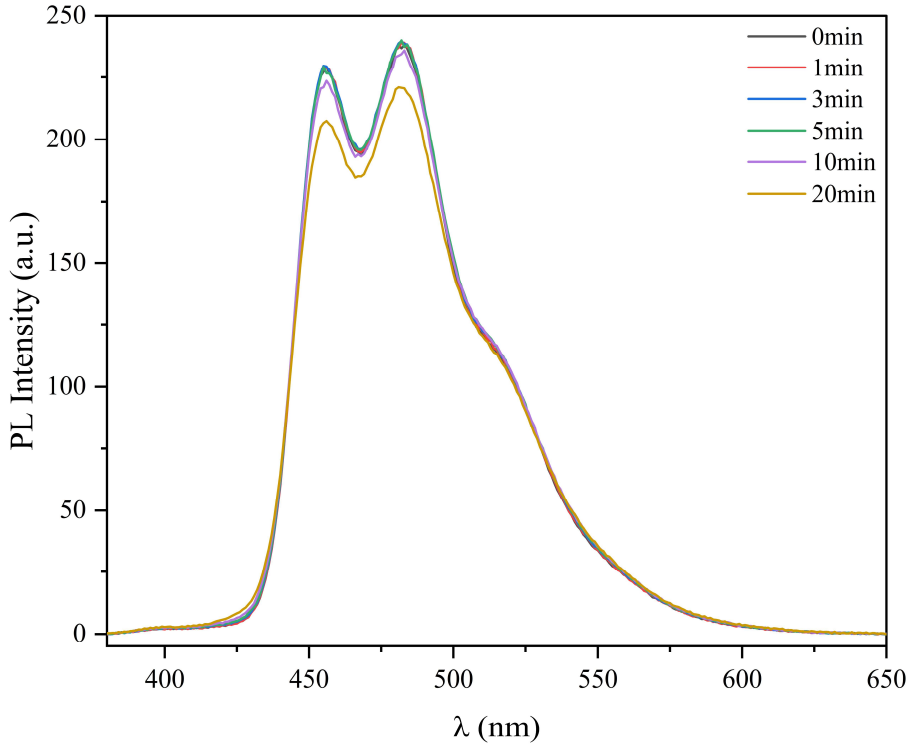


Figure S27. PL spectra of **PA** in DCM irradiated by white light (5 mW/cm^2) for 0, 1, 3, 5, 10, and 20 min, respectively.

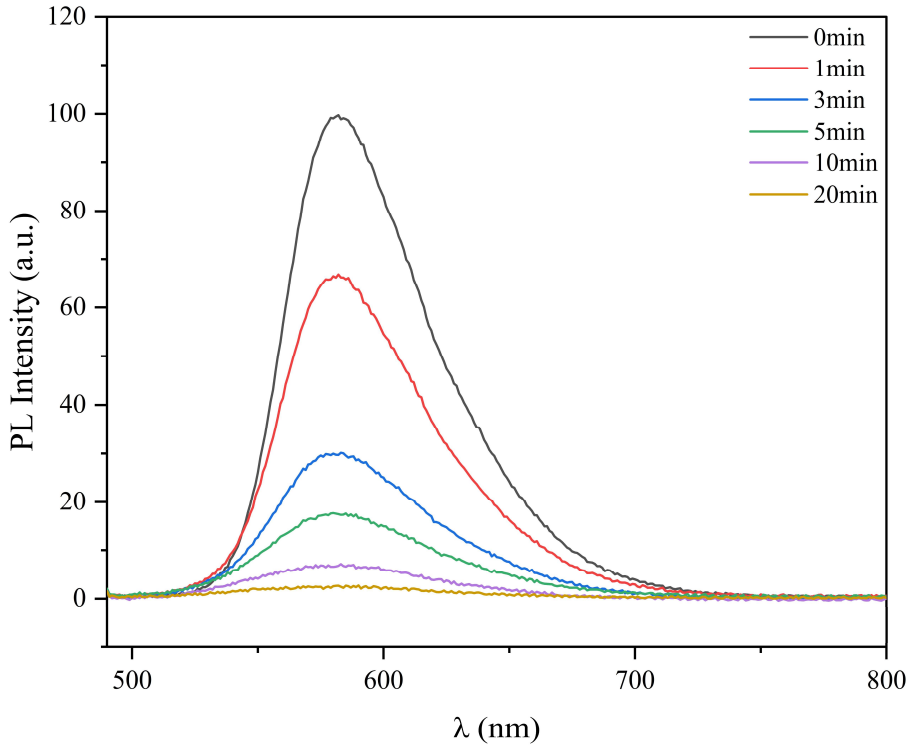


Figure S28. PL spectra of **PhPA** (ex = 486 nm) in DCM irradiated by white light (5 mW/cm^2) for 0, 1, 3, 5, 10, and 20 min, respectively.

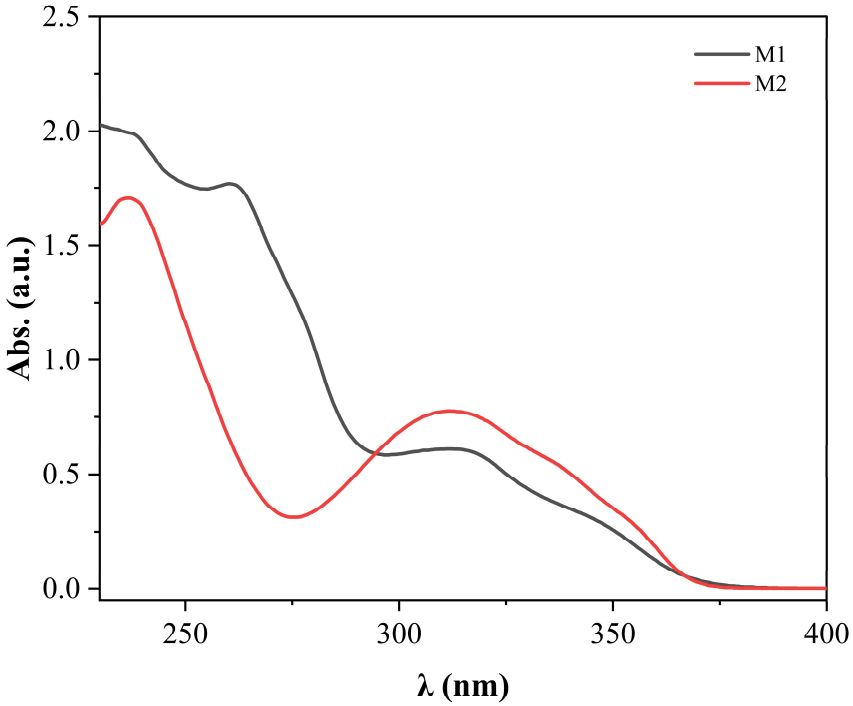


Figure S29. Absorption spectra of **M1** and **M2** in DCM.

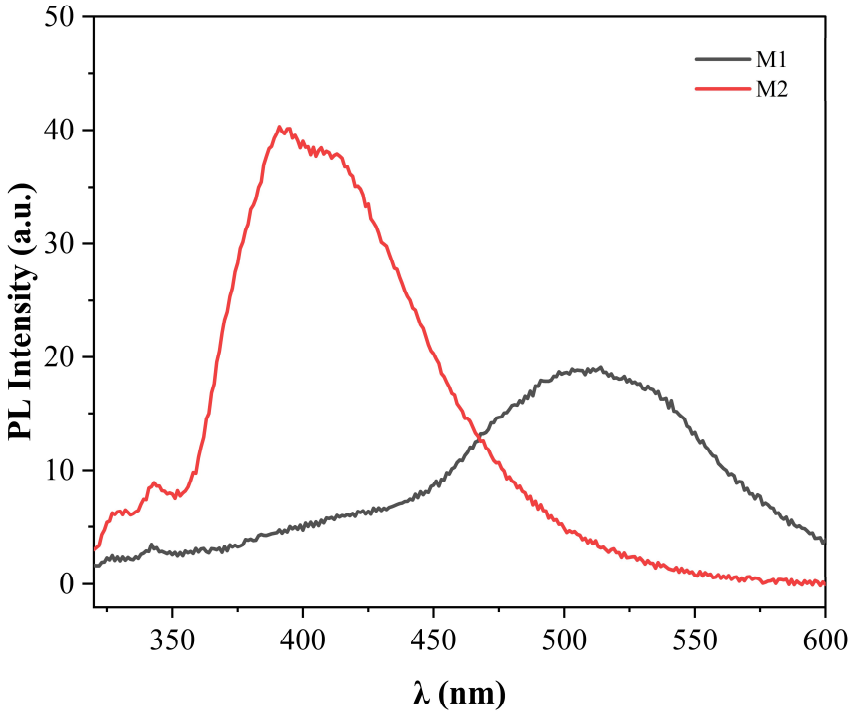


Figure S30 PL spectra of **M1** and **M2** in DCM (λ_{ex} = 312 nm).

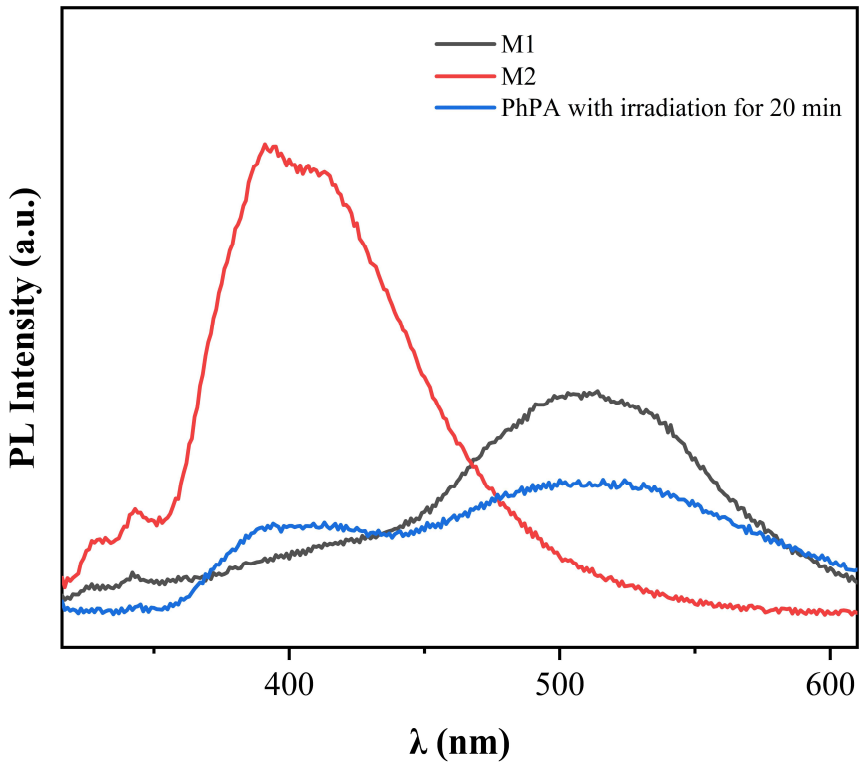


Figure S31. Absorption spectra of metabolites (PhPA with irradiation for 20 min), M1 and M2 in DCM.

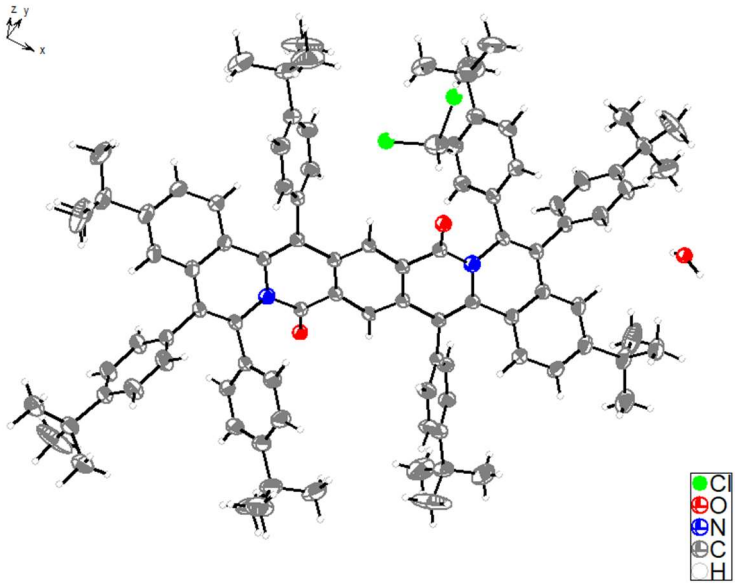


Figure S32. The Single crystal of **PhPA**.

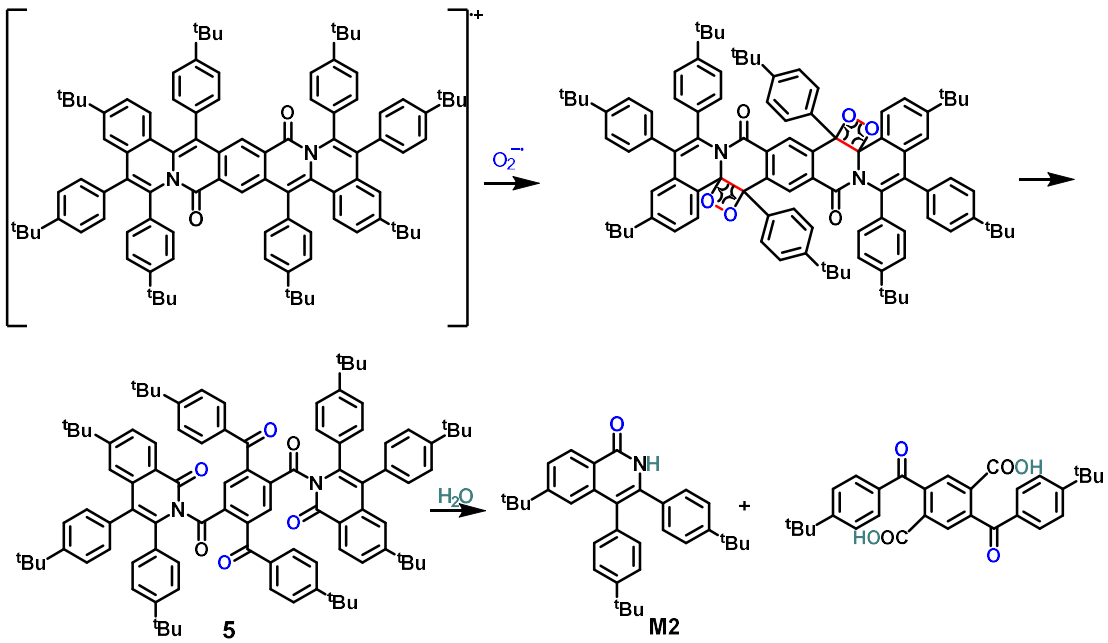


Figure S33. Another possible mechanism of PhPA photo-oxidation degradation.

Table 1. Crystal data and structure refinement for PhPA, M1 and M2.

Compounds	**PhPA**	**M1**	**M2**
CCDC Number	2219568	2214378	2214379
Empirical formula	$C_{98}H_{110}Cl_4N_2O_3$	$C_{96}H_{104}N_2O_6$	$C_{33}H_{39}NO$
Formula weight	1505.67	1381.81	465.65
Crystal system	triclinic	monoclinic	triclinic
Space group	P-1	C2/c	P-1
a/Å	10.5020(2)	30.171(7)	10.0536(8)
b/Å	14.6919(3)	17.999(4)	11.3042(8)
c/Å	14.9178(3)	16.565(4)	13.7086(11)
α/°	97.677(1)	90	87.147(7)
β/°	105.046(1)	103.772(4)	69.823(7)
γ/°	94.273(1)	90	72.826(7)
V/Å^3	2188.52(8)	8737(3)	1394.8(2)
Z	1	4	2
μ/mm^{-1}	1.056	0.064	0.497
F(000)	804.0	2968.0	504.0
Radiation	Ga Kα (λ = 1.34139)	Mo Kα	Cu Kα
2Θ range for data collection/	7.634 - 120.822	5.064 - 50.018	4.100 - 67.248
Reflection collected	26034	22099	17964
Independent reflection	9413	7697	4938
Data/restrains/parameters	9413/0/499	7697/334/610	4938 / 0 / 325
Goodness-of-fit on F2	1.043	0.963	1.001
Final R indexes [I>=2σ (I)]	R_1 = 0.0690, wR_2 = 0.1803	R_1 = 0.0797, wR_2 = 0.2118	R_1 = 0.0666, wR_2 = 0.2054
Final R indexes [all data]	R_1 = 0.0964, wR_2 = 0.1996	R_1 = 0.1655, wR_2 = 0.2685	R_1 = 0.0855, wR_2 = 0.2410
Largest diff. peak/hole / e Å-3	0.86/-0.90	0.43/-0.42	0.274/-0.259
Crystal system	triclinic	monoclinic	triclinic

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