A reactive oxygen species-responsive covalent organic framework for tumor combination therapy

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1. Experimental materials

5,10,15,20-tetrakis(4-formylphenyl)porphyrin and Bodipy-CHO were purchased from Jilin Chinese Academy of Sciences - Yanshen Technology Co., Ltd.

VC was purchased from Aladdin Reagent (Shanghai) Co., Ltd.

4-aminothiophenol and Glutathione (GSH) were purchased from Shanghai Macklin Biochemical Co., Ltd.

5,5',6,6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazolylcarbocyanine iodide (JC-1), 2',7'-dichlorodihydrofluorescein diacetate (DCFH-DA), ferrostatin-1, liproxstatin-1, N-Acetyl-L-cysteine, rotenone, antimycin, and UK5099 were purchased from MedChemExpress (Shanghai, P. R. China).

MitoTracker Deep Red FM, BODIPY581/591 undecanoic acid (C_{11}-BODIPY), and Trypan Blue were purchased from Invitrogen (Thermo Fisher Scientific Inc.).

Acridine Orange (AO), and Giemsa staining solution were purchased from Beijing Solarbio Science & Technology Co., Ltd.

The glutathione peroxidase assay kit and Bradford protein assay kit were purchased from Beyotime (Shanghai, P. R. China).

GSH assay kit was purchased from Nanjing Jiancheng Bioengineering Institute (P. R. China).

3-methyladenine (3-MA) was purchased from TCI (Shanghai) Development Co., Ltd.

Glutathione ethyl ester (GSH-OEt) was purchased from Sigma-Aldrich.

CCK-8 assay kit was purchased from Dojindo (Shanghai, P.R. China).

Paraformaldehyde (4 vol%) fix solution was purchased from Biosharp (Hefei, P. R. China).

Hematoxylin-eosin (H&E) staining kit, terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) immunofluorescence assay kit, and Ki67 immunohistochemistry staining kit were purchased from Wuhan Servicebio Technology Co., Ltd.

Trypsin (0.25 wt%) and EDTA (0.02 wt%) in Puck's saline A (trypsin/EDTA solution), Phosphate-buffered saline (PBS), and Dulbecco's phosphate-buffered saline (DPBS) were purchased from Biological Industries USA, Inc.

Certified fetal bovine serum (FBS) was purchased from VivaCell (Shanghai, P. R. China).

Hank's balanced salt solution (HBSS), GlutaMAX (100×), and soybean trypsin inhibitor powder were purchased from Gibco (Thermo Fisher Scientific Inc.).

Dulbecco's modified eagle medium (MEM) was purchased from HyClone Laboratories, Inc.

Normocin was purchased from Invivogen (San Diego, CA, USA).

Mammary epithelial cell growth medium (MEGM) BulletKit was purchased from Lonza Walkersville, Inc.

Normal saline (NS) was purchased from Shandong Qidu Pharmaceutical Co. Ltd.

Chromatographically pure solvents, including acetonitrile, isopropanol, and methanol, were purchased from Merck KGaA, Darmstadt, Germany.

2. Cell culture and experimental animals

HT-1080 (human fibrosarcoma cells) cell lines were provided by the Institute of Basic

Medicine, Shandong Academy of Medical Sciences (Jinan, P. R. China). MCF-10A (human mammary epithelia) cell line was provided by Stem Cell Bank, Chinese Academy of Sciences (Shanghai, P. R. China).
HT-1080 cells were cultured in MEM supplemented with FBS (10 vol%), human recombinant insulin (10 μg/mL) and Normocin (100 μg/mL) in a 5 vol% CO_2 atmosphere at 37 °C. MCF-10A cells were cultured using MEGM BulletKit supplemented with Normocin (100 μg/mL) in a 5 vol% CO_2 atmosphere at 37 °C. Trypsin/EDTA solution was used to dissociate cells and FBS-containing culture media when necessary.
All animal procedures were reviewed and approved by the Shandong Normal University Ethics Committee (Jinan, P. R. China), application number AEECSDNU2022050. All the animal experiments complied with relevant guidelines of the Chinese government and regulations for the care and use of experimental animals. Nude mice (BALB/cJGpt-Foxn1nu/Gpt, aged 4 weeks) were purchased from Hangzhou Ziyuan Laboratory Animal Technology Co., Ltd. The nude mice were housed in a pathogen-free facility and kept in a temperature-controlled room set to light and dark cycle of 12 h each. To establish the HT-1800 xenograft model, HT-1080 cells (5×10^6 cells) suspended in HBSS (40 μL) were subcutaneously injected into the flanks of each mouse. The length (L) and width (W) of the tumour were determined using digital calipers. The tumour volume (V) was calculated by the formula: $V = 1/2 \times L \times W^2$.

3. Experimental instrumentations

Fourier transform infrared (FT-IR) spectra were obtained in the 4000~400 cm^{-1} range using a Thermo Scientific Nicolet iS50 FT-IR Spectrometer equipped with a diamond attenuated total reflection (ATR) module. Each spectrum was the average of 16 scans.
Ultraviolet-visible (UV-vis) absorption spectra were recorded on a Shimadzu UV-2700 Double Beam UV-vis Spectrophotometer using 10 mm quartz cuvettes.
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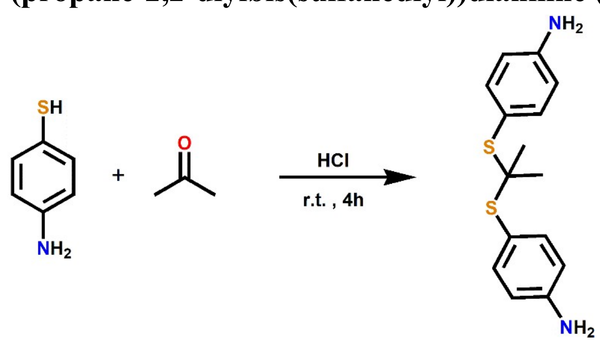
Liquid-state ^1H nuclear magnetic resonance (NMR) spectra were recorded using a Bruker AVANCE III HD 400 MHz NMR Spectrometer. Chemical shifts were reported as δ values relative to tetramethylsilane (TMS) as an internal reference. The solid-state ^{13}C cross-polarization magic angle spinning (CP-MAS) NMR spectra were recorded on a MERCURY plus 400 spectrometer operating at resonance frequencies of 400 MHz.
Electron paramagnetic resonance (EPR) spectra were recorded on a Bruker A300 EPR Spectroscopy.
Inductively coupled plasma optical emission spectrometry (ICP-OES) measurements were carried out on a Thermo Scientific iCAP 7000 ICP-OES. The standard solutions were obtained from the Reference Materials Research Center of Shandong Metallurgical Research Institute (Jinan, P. R. China). Before each analysis, the external standard method was used to establish a working curve.
Powder X-ray diffraction (PXRD) patterns were obtained on a Rigaku SmartLab SE X-Ray Powder Diffractometer with Cu Kα line focused radiation (λ = 1.5405 Å) from 2θ = 2.00° up to 30.00° with 0.01° increment.

Nitrogen-adsorption isotherms were measured at 77 K with a Micromeritics ASAP2020 HD88 Surface Area and Porosity Analyser. Before measurement, the samples were degassed in a vacuum at 120 °C for 8 h. The Brunauer-Emmett-Teller (BET) equation was used to calculate the specific surface areas. The pore size distribution was derived from the sorption curve using the non-local density functional theory (NLDFT) model.
Transmission electron microscopy (TEM) images were recorded on a Hitachi HT7700 120 kV Compact-Digital Transmission Electron Microscope. To prepare the TEM samples, the nanomaterial was dispersed in methanol by sonication for 5 min and the dispersions were placed on a carbon-coated copper TEM grid (300 mesh) and dried at room temperature.
Hydrodynamic particle size and Zeta potential were measured using Malvern Zetasizer Nano ZS90 System.
Microplate assays were carried out on a Molecular Devices SpectraMax i3x Multi-Mode Microplate Detection System.
Cell counting was performed on a Thermo Fisher Scientific Invitrogen Countess II Automated Cell Counter equipped with Countess Cell Counting Chamber Slides.
Photomicrographs of biological samples were taken with a Leica DMI3000 B Inverted Fluorescence Microscope with an objective lens (10×, 20×, and 40×).
Flow cytometry was analyzed on a BIO-RAD ZE5 Cell Analyzer.
Laser scanning confocal fluorescence images of cells were captured with a Leica TCS SP8 Confocal Laser Scanning Microscopy equipped with 405, 458, 488, 514, 561, and 633 nm lasers. Glass bottom dishes and 4/8-well chamber slides (Cellvis, Mountain View, CA, USA) were used for cell culture to provide biological replicates of each experiment. Before live-cell imaging, the original culture media or DPBS was replaced with HBSS supplemented with HEPES (15 mM) and GlutaMAX to provide better-buffering capacity under normal CO_2 concentration.
For imaging, the scan speed was 400 Hz and transmitted light was used to find the areas of interest to reduce photodamage to the biosample.

4. Statistical analysis

As indicated in figure legends, all results are depicted as means ± SD of at least three biological replicates. And data were compared with the paired or unpaired two-tailed Student's t-test with or without Welch's correction, one-way ANOVA followed by Dunnett's or Tukey's posthoc tests, or two-way ANOVA followed by Šídák's post hoc test, as appropriate. *$p < 0.05$, ***$p < 0.001$.

5. Synthesis of 4,4'-(propane-2,2-diylbis(sulfanediyl))dianiline (TK)



4-aminothiophenol (6.15 g, 49.1 mmol) and acetone (5.8 g, 98.2 mmol) were mixed with concentrated hydrochloric acid (10 mL) and stirred for 4 h at room temperature. After the reaction, the reaction solution was poured into a KOH solution (1 M, 200 mL), filtered and the resulting white solid was washed with deionized water until the filtrate was neutral. Yield, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (d, J = 8.5, 4H), 6.61 (d, J = 8.5, 4H), 3.74 (s, 4H), 1.42 (s, 6H). IR (KBr pellet cm^{-1}): 3452 (s), 3434 (s), 3349 (s), 2949 (v), 1630 (s), 1589 (s), 1492 (s), 1426 (v), 1375 (v), 1360 (v), 1306 (m), 1279 (m), 1180 (m), 1103 (s), 824 (s), 586 (v), 512 (m).

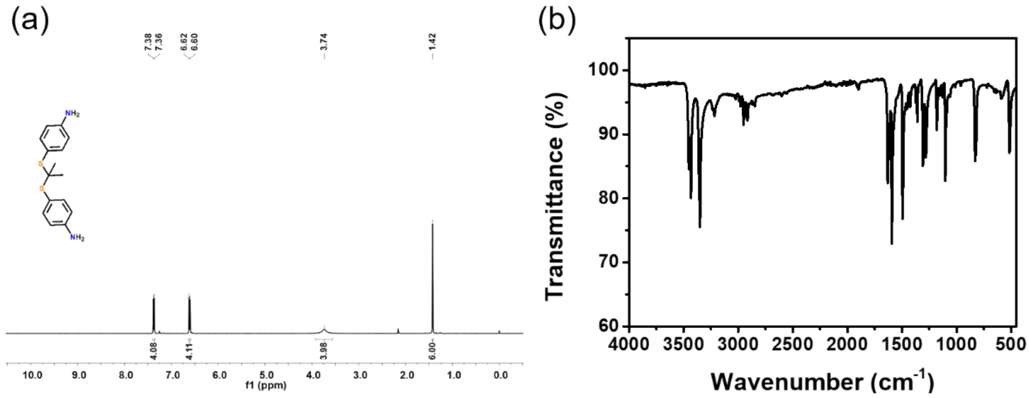


Fig. S1 (a) ^{1}H NMR of 4,4'-(propane-2,2-diylbis(sulfanediyl))dianiline. (b) FT-IR spectra of 4,4'-(propane-2,2-diylbis(sulfanediyl))dianiline.

6. Synthesis of TKPP-COF

5,10,15,20-tetrakis(4-formylphenyl)porphyrin (18.12 mg, 0.025 mmol), TK (14.50 mg, 0.05 mmol), 1.0 mL o-dichlorobenzene and 1.0 mL n-BuOH, and then the mixture was sonicated for 10 min, followed by slow addition of 0.25 mL of 6 M aqueous acetic acid. Afterward, the tube was flash-frozen at 77 K, degassed by three freeze-pump-thaw cycles, sealed under a vacuum, and heated at 120 ºC for 3 days. After cooling down to room temperature, the tube was opened and the resulting precipitate was filtered off, thoroughly washed with o-dichlorobenzene, ethanol and acetone until the filtrate was colorless, and Soxhlet extractions with trichloromethane and dichloromethane for 24 h, respectively. Finally, the resulting dark violet powder was dried under vacuum at 70 ºC overnight to give the **TKPP-COF** activated sample. Yield: 18.7 mg (61%).

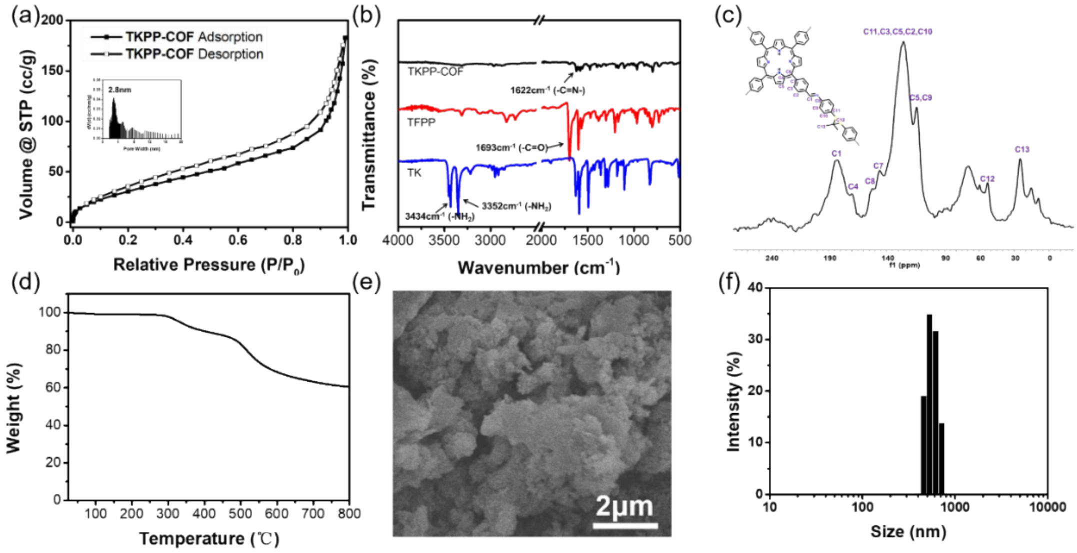


Fig. S2 (a) N_2 adsorption (solid square) and desorption (hollow square) isotherms of **TKPP-COF**. BET surface area of **TKPP-COF** = 118.8 m²/g. The pore size distribution curve based on nonlocal density functional theory (NLDFT) analysis is shown as inset. The pore width of **TKPP-COF** was centered at 2.8 nm. (b) FT-IR spectra of **TKPP-COF** and its monomers. The peaks at 3434 and 3352 cm^{-1} (for $-NH_2$) in TK and 1693 cm^{-1} (for -CHO) in TFPP basically disappeared, and the peaks at 1622 cm^{-1} (for -C=N-) appeared. (c) ^{13}C CP-MAS solid-state NMR spectrum of **TKPP-COF**. C_1 is the carbon atom for the imine bond (184 ppm), and the carbon atoms in both monomers [TFPP (C_2-C_7), TK (C_8-C_{11})] are represented in **TKPP-COF**. (d) Thermogravimetric analysis (TGA) trace of **TKPP-COF**. (e) Scanning electron microscope (SEM) image of **TKPP-COF**. (f) Dynamic light scattering (DLS) measurements of **TKPP-COF**.

Table S1. Fractional Atomic Coordinates for the Unit Cell of **TKPP-COF**

TKPP-COF AA'A'' slip-stacked mode, space group: *P*1

a = 22.3641 Å, *b* = 58.2951 Å, *c* = 13.1505 Å

α = 89.9726°, β = 89.9651°, γ = 89.9953°, *R*wp = 1.38% and *R*p = 0.84%

Atom	x	y	z
C1	0.16615	0.09696	0.00085
N2	0.92411	0.08362	0.21099
C3	0.82855	0.09426	0.22443
H4	0.07239	0.08621	0.18273
C5	0.32378	0.33279	-0.1801
C6	0.30295	0.31701	-0.26715
C7	0.36663	0.35061	-0.22714
H8	0.40045	0.342	-0.27599
H9	0.39207	0.36006	-0.16844
H10	0.34157	0.36309	-0.2747
H11	0.26552	0.30579	-0.24353
H12	0.34041	0.30607	-0.29421
H13	0.2864	0.32737	-0.33234
C14	0.31338	0.8387	-0.12855
C15	0.34893	0.82148	-0.19367

C16	0.28656	0.85666	-0.20143
H17	0.38052	0.83068	-0.24467
H18	0.31831	0.81102	-0.24135
H19	0.3763	0.80986	-0.14589
H20	0.26119	0.84806	-0.26326
H21	0.32242	0.86727	-0.23627
H22	0.25463	0.86813	-0.16184
H23	0.97032	0.08426	0.21375
H24	0.53975	0.60414	0.15413
H25	0.53328	0.56458	0.17069
N26	0.00763	0.12023	0.15515
N27	0.01444	1.04917	0.16307
H28	0.75213	0.60698	0.23844
C29	0.04663	0.15495	0.18992
C30	0.05688	0.13366	0.1466
C31	0.10965	0.12749	0.09332
C32	0.12327	0.10424	0.07034
N33	0.099	0.08581	0.11774
C34	0.48622	0.51735	0.25317
C35	0.47607	0.53819	0.20542
C36	0.15089	0.14635	0.05915
C37	0.21235	0.14574	0.08145
C38	0.24934	0.16444	0.05731
C39	0.22563	0.18419	0.01093
C40	0.16461	0.18455	-0.01383
C41	0.12794	0.1659	0.00984
C42	0.26419	0.20451	-0.00735
N43	0.24095	0.22391	-0.03673
C44	0.27156	0.24543	-0.05164
C45	0.33407	0.24712	-0.06227
C46	0.36126	0.26866	-0.07343
C47	0.3269	0.28879	-0.07502
C48	0.26475	0.28708	-0.06291
C49	0.23737	0.26559	-0.054
S50	0.36578	0.31639	-0.08137
C51	0.37256	0.59601	0.03752
C52	0.41116	0.56585	0.11638
N53	0.43719	0.58457	0.15746
C54	0.4251	0.54314	0.14548
C55	0.39106	0.52322	0.10344
C56	0.32927	0.5206	0.11915
C57	0.30043	0.50018	0.09024
C58	0.33323	0.48202	0.04705
C59	0.39445	0.48504	0.02899
C60	0.42271	0.50544	0.05535
C61	0.30424	0.4599	0.02188
N62	0.33655	0.44148	0.01093

C63	0.31539	0.41907	-0.01717
C64	0.2643	0.41598	-0.07787
C65	0.24793	0.39398	-0.11019
C66	0.28221	0.3748	-0.08315
C67	0.33195	0.37777	-0.01959
C68	0.34925	0.39982	0.01083
S69	0.25626	0.34652	-0.1229
H70	0.07728	0.16921	0.19604
H71	0.19277	0.10772	-0.04863
H72	0.45507	0.50328	0.26234
H73	0.23136	0.13111	0.12051
H74	0.29621	0.16374	0.07764
H75	0.14476	0.19941	-0.0499
H76	0.08106	0.16705	-0.00829
H77	0.31127	0.20331	0.01069
H78	0.36206	0.23201	-0.06271
H79	0.40942	0.26968	-0.0807
H80	0.23722	0.30224	-0.05919
H81	0.18924	0.26466	-0.04585
H82	0.30392	0.53397	0.15676
H83	0.25303	0.49825	0.1048
H84	0.42079	0.47147	-0.00449
H85	0.47035	0.50694	0.04256
H86	0.25598	0.45912	0.01614
H87	0.23807	0.43051	-0.10294
H88	0.20869	0.39189	-0.15746
H89	0.35758	0.36312	0.00582
H90	0.38904	0.40194	0.05674
C91	0.99981	1.01594	0.24571
C92	0.97383	1.03622	0.21342
C93	0.91281	1.04183	0.22766
C94	0.83058	1.07058	0.22556
C95	0.89027	1.06443	0.21789
C96	0.54421	0.65078	0.28739
C97	0.57087	0.63077	0.25266
C98	0.87268	1.02286	0.26125
C99	0.85325	1.02164	0.36264
C100	0.82996	1.00111	0.4016
C101	0.82673	0.98138	0.3403
C102	0.84248	0.98311	0.23707
C103	0.86465	1.00372	0.19783
C104	0.80897	0.95912	0.38571
N105	0.81741	0.93996	0.33679
C106	0.80247	0.91726	0.37219
C107	0.76064	0.9134	0.45042
C108	0.74554	0.89101	0.47899
C109	0.77234	0.87216	0.43151

C110	0.8136	0.87585	0.35296
C111	0.82822	0.89826	0.32322
S112	0.74738	0.84343	0.46554
C113	0.71278	0.57238	0.23847
C114	0.65384	0.6029	0.25034
N115	0.61794	0.58426	0.25244
C116	0.63267	0.6257	0.26009
C117	0.67481	0.64522	0.27906
C118	0.7148	0.64495	0.36141
C119	0.74836	0.66456	0.38569
C120	0.74144	0.68498	0.32993
C121	0.70259	0.68505	0.24605
C122	0.67051	0.66532	0.22003
C123	0.7738	0.70607	0.36146
N124	0.75864	0.72611	0.32582
C125	0.78514	0.74789	0.35208
C126	0.84311	0.74984	0.39308
C127	0.8668	0.77148	0.41648
C128	0.83313	0.79144	0.4004
C129	0.77628	0.78958	0.35645
C130	0.75251	0.76799	0.33305
S131	0.86692	0.81928	0.42777
H132	0.97876	1.00199	0.28647
H133	0.79263	1.05922	0.23413
H134	0.5647	0.66434	0.33144
H135	0.85932	1.03615	0.41297
H136	0.81721	1.00032	0.48101
H137	0.83952	0.96835	0.18735
H138	0.87925	1.00436	0.11947
H139	0.79184	0.95905	0.4627
H140	0.73803	0.9275	0.48739
H141	0.71226	0.88829	0.53754
H142	0.83334	0.86146	0.31336
H143	0.8595	0.90085	0.26138
H144	0.71852	0.62985	0.40903
H145	0.77821	0.66401	0.45047
H146	0.69711	0.70035	0.20032
H147	0.64028	0.66598	0.15588
H148	0.80785	0.70462	0.41957
H149	0.87064	0.73485	0.40542
H150	0.91157	0.77271	0.44726
H151	0.75059	0.80476	0.33885
H152	0.70824	0.76692	0.30044
H153	0.34336	0.56128	-0.00471
C154	0.81567	0.83125	0.52572
C155	0.85013	0.84966	0.58585
C156	0.79607	0.81252	0.60113

H157	0.7658	0.79992	0.56448
H158	0.77123	0.82022	0.66591
H159	0.8356	0.80323	0.63158
H160	0.81964	0.85898	0.63831
H161	0.87164	0.86226	0.53419
H162	0.88634	0.84166	0.6316
C163	0.0584	1.01671	0.21667
C164	0.06614	1.03711	0.16414
C165	0.11802	1.04309	0.1084
C166	0.16923	1.07326	0.00493
C167	0.12805	1.06601	0.07668
C168	0.4865	0.65075	0.25167
C169	0.47933	0.63066	0.19678
C170	0.16038	1.02416	0.07919
C171	0.22251	1.02597	0.09425
C172	0.26004	1.00699	0.07713
C173	0.23592	0.98576	0.04714
C174	0.17422	0.98412	0.03043
C175	0.13744	1.00312	0.04414
C176	0.27446	0.96527	0.035
N177	0.25036	0.94496	0.03178
C178	0.28026	0.92331	0.01905
C179	0.33769	0.92141	-0.02397
C180	0.36315	0.89975	-0.03996
C181	0.33164	0.87978	-0.01433
C182	0.27514	0.88167	0.03092
C183	0.24938	0.90327	0.046
S184	0.36631	0.85196	-0.03621
C185	0.37049	0.57236	0.04238
C186	0.41416	0.603	0.10923
C187	0.43024	0.62584	0.13267
C188	0.3979	0.64577	0.08739
C189	0.33552	0.64809	0.09499
C190	0.3075	0.66831	0.06224
C191	0.34153	0.68668	0.02419
C192	0.40353	0.68408	0.01384
C193	0.43121	0.66375	0.04388
C194	0.31249	0.7087	-0.00068
N195	0.34204	0.72782	0.00836
C196	0.31914	0.75057	-0.00863
C197	0.26829	0.75485	-0.06884
C198	0.24809	0.77734	-0.08338
C199	0.27871	0.79583	-0.03984
C200	0.32868	0.79162	0.02158
C201	0.34918	0.76916	0.03581
S202	0.25034	0.82476	-0.05917
H203	0.09125	1.00348	0.23117

H204	0.19823	1.06259	-0.04093
H205	0.45403	0.66433	0.26194
H206	0.24177	1.04179	0.12227
H207	0.3076	1.00866	0.09057
H208	0.15406	0.96813	0.00637
H209	0.09019	1.00094	0.03164
H210	0.32252	0.96738	0.03279
H211	0.36239	0.93645	-0.04746
H212	0.40711	0.89849	-0.074
H213	0.25089	0.86651	0.05404
H214	0.20513	0.90444	0.07911
H215	0.30884	0.63464	0.12924
H216	0.25956	0.67002	0.07046
H217	0.43071	0.69786	-0.01641
H218	0.4793	0.66236	0.03721
H219	0.26532	0.70869	-0.01864
H220	0.24449	0.74102	-0.10566
H221	0.20888	0.78039	-0.12972
H222	0.3518	0.80568	0.05809
H223	0.38821	0.76616	0.08269
H224	0.75172	0.56146	0.23228
H225	0.34709	0.60671	-0.01386
C226	0.70673	0.33085	0.46346
C227	0.71633	0.31404	0.55108
C228	0.66827	0.35073	0.50378
H229	0.65165	0.36173	0.44108
H230	0.62819	0.34398	0.54398
H231	0.69424	0.36143	0.55796
H232	0.74121	0.32224	0.61452
C233	0.98611	0.15424	0.2276
C234	0.9649	0.13257	0.20366
C235	0.90548	0.12514	0.22215
C236	0.88708	0.10191	0.21605
C237	0.54565	0.51689	0.27857
C238	0.57016	0.5376	0.24798
C239	0.86117	0.14301	0.25162
C240	0.84268	0.14516	0.35318
C241	0.81106	0.16466	0.3849
C242	0.79861	0.18246	0.31596
C243	0.81447	0.17968	0.21326
C244	0.84487	0.16002	0.18132
C245	0.77109	0.20405	0.35232
N246	0.77843	0.22299	0.30145
C247	0.75469	0.24522	0.32674
C248	0.70403	0.24808	0.38919
C249	0.67932	0.26992	0.40346
C250	0.70475	0.28914	0.35629

C251	0.7559	0.28642	0.29641
C252	0.78056	0.26461	0.28143
S253	0.66558	0.31648	0.35941
C254	0.71302	0.59608	0.242
C255	0.65348	0.56561	0.2449
C256	0.63213	0.54275	0.24887
C257	0.67424	0.52298	0.25859
C258	0.71183	0.52093	0.34347
C259	0.73979	0.49997	0.36528
C260	0.72932	0.48057	0.30429
C261	0.6949	0.48306	0.21564
C262	0.66862	0.50417	0.1921
C263	0.75195	0.45784	0.3371
N264	0.73439	0.43909	0.29218
C265	0.74858	0.41581	0.32077
C266	0.78944	0.4103	0.39874
C267	0.79877	0.38742	0.42691
C268	0.76742	0.3697	0.37894
C269	0.72878	0.37496	0.29839
C270	0.71926	0.39785	0.27004
S271	0.78161	0.34018	0.41745
H272	0.96287	0.16794	0.26661
H273	0.78866	0.10464	0.23164
H274	0.56889	0.50242	0.31098
H275	0.85518	0.13228	0.40862
H276	0.79884	0.16634	0.46426
H277	0.80449	0.19291	0.158
H278	0.85794	0.15851	0.1025
H279	0.74812	0.20408	0.4248
H280	0.68204	0.23351	0.42375
H281	0.63958	0.27184	0.44959
H282	0.77536	0.30104	0.25867
H283	0.81909	0.26272	0.23222
H284	0.71645	0.53505	0.39637
H285	0.76672	0.49855	0.43342
H286	0.68695	0.46859	0.1659
H287	0.6402	0.50541	0.12562
H288	0.77992	0.45719	0.40398
H289	0.81438	0.42337	0.43845
H290	0.83007	0.3835	0.48723
H291	0.70574	0.36138	0.25825
H292	0.68831	0.40166	0.20902
N293	0.52692	0.55077	0.20637
N294	0.53048	0.61833	0.19946
C295	0.04119	0.0001	0.46849
N296	0.82067	-0.00981	0.75798
C297	0.73794	0.00273	0.83594

H298	-0.08762	-0.00957	0.57274
C299	0.14165	0.2379	0.26424
C300	0.10053	0.22162	0.20415
C301	0.17067	0.25433	0.18718
H302	0.19188	0.24432	0.12538
H303	0.20652	0.26476	0.22252
H304	0.13675	0.26597	0.15323
H305	0.07088	0.21165	0.25514
H306	0.12748	0.20954	0.15779
H307	0.07087	0.23149	0.15235
C308	0.14211	0.74127	0.20186
C309	0.20839	0.7375	0.17682
C310	0.11797	0.76007	0.13045
H311	0.23313	0.75402	0.1799
H312	0.21264	0.73027	0.09938
H313	0.23045	0.72578	0.23122
H314	0.12078	0.75433	0.04999
H315	0.14423	0.77616	0.13679
H316	0.07032	0.76373	0.14749
H317	0.86337	-0.01022	0.72742
H318	0.39485	0.51024	0.63014
H319	0.39721	0.47009	0.6306
N320	-0.10858	0.02541	0.65265
N321	-0.11528	0.9542	0.64575
H322	0.55865	0.51657	0.8742
C323	-0.08178	0.0619	0.62459
C324	-0.06992	0.0391	0.60168
C325	-0.02221	0.03151	0.53854
C326	-0.00938	0.00798	0.51934
N327	-0.0441	-0.01012	0.54599
C328	0.33447	0.42267	0.67128
C329	0.33842	0.44312	0.6174
C330	0.01817	0.04956	0.49557
C331	0.07801	0.05117	0.52703
C332	0.11277	0.07024	0.5005
C333	0.08755	0.0884	0.44534
C334	0.02846	0.08645	0.41069
C335	-0.00533	0.06696	0.43342
C336	0.1221	0.1096	0.42777
N337	0.09448	0.12911	0.41865
C338	0.12252	0.1509	0.40101
C339	0.17497	0.15298	0.34268
C340	0.19833	0.1747	0.32067
C341	0.16975	0.19453	0.35618
C342	0.11848	0.19242	0.41675
C343	0.09435	0.17076	0.43706
S344	0.20332	0.22237	0.33005

C345	0.28342	0.50024	0.38776
C346	0.30281	0.47049	0.48733
N347	0.31364	0.48947	0.54306
C348	0.30739	0.44794	0.52589
C349	0.2776	0.42854	0.47192
C350	0.2158	0.42897	0.45323
C351	0.18633	0.40924	0.41891
C352	0.21798	0.38869	0.40393
C353	0.28029	0.38863	0.41732
C354	0.30977	0.40841	0.45021
C355	0.18491	0.36731	0.38113
N356	0.21079	0.34739	0.38975
C357	0.18306	0.32525	0.37756
C358	0.12623	0.32233	0.33299
C359	0.1005	0.30049	0.3269
C360	0.13122	0.28126	0.36333
C361	0.18788	0.28402	0.407
C362	0.21376	0.30584	0.41315
S363	0.09502	0.25334	0.35959
H364	-0.05788	0.07707	0.60071
H365	0.07706	0.01025	0.43681
H366	0.30469	0.40839	0.6573
H367	0.09714	0.03796	0.57453
H368	0.15838	0.07132	0.52716
H369	0.00799	0.10027	0.36819
H370	-0.05152	0.06624	0.40942
H371	0.1705	0.10894	0.42969
H372	0.19706	0.13795	0.31244
H373	0.23881	0.17611	0.27597
H374	0.09693	0.20749	0.44757
H375	0.05372	0.16941	0.48147
H376	0.18994	0.44422	0.46992
H377	0.13829	0.40974	0.40863
H378	0.30595	0.37312	0.40582
H379	0.35734	0.40766	0.46482
H380	0.13754	0.36857	0.36573
H381	0.10145	0.33667	0.30243
H382	0.05656	0.29854	0.29346
H383	0.21169	0.26933	0.43687
H384	0.25746	0.30773	0.44765
C385	0.86421	0.91782	0.68932
C386	0.8487	0.94067	0.70292
C387	0.80115	0.94828	0.76626
C388	0.73599	0.97915	0.83423
C389	0.78731	0.97171	0.78496
C390	0.35704	0.55688	0.74606
C391	0.39184	0.53723	0.73902

C392	0.76257	0.93021	0.81345
C393	0.76218	0.92691	0.91919
C394	0.7347	0.90751	0.96147
C395	0.70722	0.8911	0.8987
C396	0.70441	0.89519	0.79345
C397	0.73107	0.91474	0.75164
C398	0.68242	0.86983	0.94382
N399	0.66759	0.85252	0.88654
C400	0.64216	0.83107	0.91983
C401	0.61355	0.82853	1.0147
C402	0.5853	0.80786	1.03994
C403	0.58559	0.78939	0.97186
C404	0.61432	0.79176	0.87784
C405	0.64237	0.81246	0.85214
S406	0.54065	0.76417	1.00011
C407	0.52767	0.48161	0.84538
C408	0.46938	0.51109	0.80498
N409	0.43915	0.49181	0.77988
C410	0.44641	0.5336	0.79148
C411	0.48138	0.5545	0.82236
C412	0.50889	0.55664	0.91813
C413	0.53827	0.577	0.94528
C414	0.53682	0.59616	0.88086
C415	0.50948	0.59407	0.78553
C416	0.48464	0.57327	0.75503
C417	0.56325	0.61821	0.91347
N418	0.54932	0.63705	0.86612
C419	0.57184	0.65961	0.88745
C420	0.62773	0.66328	0.93372
C421	0.64901	0.68564	0.94815
C422	0.61461	0.7045	0.91753
C423	0.55947	0.70087	0.86997
C424	0.53825	0.67857	0.85531
S425	0.64328	0.73343	0.9333
H426	0.84534	0.90285	0.72593
H427	0.7001	0.96871	0.86433
H428	0.36202	0.5708	0.79982
H429	0.78509	0.93889	0.96853
H430	0.73671	0.90493	1.04298
H431	0.68254	0.88312	0.74317
H432	0.7298	0.91729	0.67029
H433	0.67918	0.86865	1.02575
H434	0.61078	0.8426	1.06795
H435	0.56193	0.80639	1.11178
H436	0.61341	0.77788	0.82329
H437	0.6634	0.81419	0.77832
H438	0.50703	0.54281	0.97269

H439	0.56079	0.57808	1.01766
H440	0.50764	0.60847	0.73384
H441	0.46588	0.57214	0.67927
H442	0.5922	0.61856	0.97944
H443	0.65542	0.649	0.95652
H444	0.69219	0.68832	0.98325
H445	0.53305	0.71532	0.84434
H446	0.49554	0.676	0.81827
H447	0.27125	0.46523	0.3293
C448	0.59903	0.74382	1.04448
C449	0.64245	0.75552	1.11851
C450	0.56675	0.72447	1.10255
H451	0.53032	0.71691	1.05623
H452	0.54577	0.7313	1.17295
H453	0.59855	0.71074	1.12479
H454	0.61752	0.76413	1.18087
H455	0.67042	0.76848	1.07896
H456	0.67326	0.74264	1.15219
C457	-0.08961	0.91737	0.6215
C458	-0.07747	0.93996	0.59583
C459	-0.03001	0.94673	0.53093
C460	0.03849	0.97654	0.46356
C461	-0.01325	0.96978	0.5128
C462	0.31775	0.55642	0.66561
C463	0.32904	0.53634	0.61258
C464	0.00653	0.92808	0.48508
C465	0.06126	0.92171	0.52892
C466	0.09038	0.90169	0.4972
C467	0.06445	0.88747	0.42307
C468	0.0108	0.8944	0.37653
C469	-0.01757	0.91465	0.40676
C470	0.09156	0.86488	0.40082
N471	0.05912	0.84833	0.36395
C472	0.07832	0.82502	0.3491
C473	0.13883	0.81896	0.3358
C474	0.15523	0.79583	0.32832
C475	0.11186	0.77859	0.33437
C476	0.05167	0.78457	0.34518
C477	0.03499	0.80765	0.35063
S478	0.13397	0.74863	0.33907
C479	0.28361	0.47659	0.39086
C480	0.30192	0.50768	0.48282
C481	0.30451	0.53069	0.51663
C482	0.28004	0.54967	0.45257
C483	0.22056	0.54924	0.41856
C484	0.19639	0.5681	0.36698
C485	0.23072	0.58794	0.35054

C486	0.29071	0.58818	0.38207
C487	0.31525	0.56914	0.43177
C488	0.20244	0.60831	0.30363
N489	0.22343	0.62884	0.31917
C490	0.19659	0.64964	0.28144
C491	0.16302	0.65013	0.19111
C492	0.13549	0.67046	0.15934
C493	0.14102	0.69069	0.21613
C494	0.17456	0.69019	0.30643
C495	0.20321	0.66995	0.33732
S496	0.0964	0.71531	0.17467
H497	-0.06657	0.90206	0.59648
H498	0.07202	0.96561	0.4293
H499	0.28612	0.56976	0.6461
H500	0.08006	0.93174	0.59043
H501	0.13164	0.89669	0.53424
H502	-0.01	0.8839	0.31876
H503	-0.05982	0.91935	0.37265
H504	0.13675	0.8616	0.4266
H505	0.17333	0.83193	0.33128
H506	0.20166	0.79123	0.31882
H507	0.01786	0.77134	0.35051
H508	-0.01168	0.81203	0.35935
H509	0.19233	0.53458	0.43448
H510	0.15005	0.56751	0.34321
H511	0.31843	0.60314	0.36919
H512	0.36139	0.56982	0.45668
H513	0.1605	0.60599	0.26376
H514	0.15815	0.63492	0.14476
H515	0.10905	0.67037	0.0904
H516	0.17768	0.70505	0.35477
H517	0.22875	0.66987	0.40726
H518	0.5649	0.4714	0.87211
H519	0.2706	0.51069	0.32339
C520	0.67757	0.24398	1.01066
C521	0.72179	0.2265	1.05358
C522	0.65132	0.25754	1.10007
H523	0.61436	0.26886	1.07448
H524	0.63278	0.24566	1.15824
H525	0.68631	0.2682	1.13632
H526	0.76009	0.23515	1.09123
C527	0.8713	0.06206	0.69083
C528	0.85534	0.03939	0.70712
C529	0.80728	0.03239	0.77031
C530	0.79027	0.00923	0.78733
C531	0.378	0.42331	0.74472
C532	0.40639	0.44434	0.73566

C533	0.77102	0.05108	0.81718
C534	0.77946	0.05706	0.91959
C535	0.75569	0.0776	0.95765
C536	0.72448	0.09267	0.89331
C537	0.71345	0.08604	0.7923
C538	0.73589	0.0653	0.75498
C539	0.70604	0.11556	0.9306
N540	0.70026	0.13254	0.8671
C541	0.68326	0.15569	0.89182
C542	0.64722	0.161	0.97649
C543	0.6277	0.18357	0.99252
C544	0.6445	0.20108	0.92529
C545	0.68099	0.19591	0.84194
C546	0.69986	0.17334	0.82503
S547	0.6151	0.22998	0.94112
C548	0.52426	0.50523	0.84634
C549	0.47485	0.47385	0.80307
C550	0.45856	0.45064	0.78919
C551	0.49735	0.43166	0.82684
C552	0.50736	0.42812	0.93111
C553	0.53626	0.40814	0.9649
C554	0.55491	0.39132	0.89508
C555	0.54654	0.39531	0.79063
C556	0.51842	0.4153	0.75707
C557	0.58228	0.36967	0.93146
N558	0.58799	0.3523	0.87003
C559	0.61479	0.33038	0.89177
C560	0.65372	0.32682	0.97453
C561	0.68306	0.30575	0.98602
C562	0.67334	0.28788	0.91669
C563	0.6343	0.2913	0.83508
C564	0.60526	0.31239	0.82282
S565	0.72001	0.26239	0.92097
H566	0.85234	0.07731	0.72486
H567	0.7039	0.01383	0.86756
H568	0.38862	0.40961	0.79725
H569	0.80691	0.04644	0.96846
H570	0.76433	0.08231	1.03585
H571	0.68881	0.09717	0.7414
H572	0.72929	0.06102	0.67562
H573	0.70172	0.11835	1.0117
H574	0.63237	0.1477	1.02803
H575	0.59881	0.18737	1.05641
H576	0.69382	0.20929	0.78912
H577	0.72717	0.16953	0.75914
H578	0.49108	0.44036	0.98639
H579	0.54245	0.4055	1.04575

H580	0.56098	0.38285	0.73471
H581	0.511	0.41769	0.67638
H582	0.59564	0.36835	1.01033
H583	0.66367	0.34041	1.0278
H584	0.71466	0.30349	1.04736
H585	0.62784	0.27789	0.77925
H586	0.57625	0.31495	0.75788
N587	0.38156	0.45644	0.65883
N588	0.37285	0.52442	0.65975
C589	0.31212	0.09532	-0.49771
N590	1.09567	0.08106	-0.21264
C591	0.99959	0.09056	-0.19201
H592	0.23801	0.08453	-0.29122
C593	0.47624	0.32813	-0.711
C594	0.45104	0.30988	-0.78394
C595	0.52711	0.34071	-0.76688
H596	0.55984	0.3282	-0.79804
H597	0.55214	0.3522	-0.715
H598	0.50912	0.35106	-0.83091
H599	0.41031	0.3017	-0.75232
H600	0.485	0.29642	-0.79953
H601	0.43806	0.31788	-0.85741
C602	0.36253	0.82928	-0.59052
C603	0.43028	0.82481	-0.58607
C604	0.34893	0.84631	-0.67693
H605	0.45595	0.84099	-0.59359
H606	0.44418	0.81344	-0.64956
H607	0.44338	0.81687	-0.5129
H608	0.35915	0.83843	-0.7519
H609	0.37619	0.86215	-0.67038
H610	0.30089	0.85118	-0.67584
H611	1.14195	0.08231	-0.21667
H612	0.66694	0.60252	-0.21787
H613	0.69973	0.56197	-0.26882
N614	0.16917	0.11778	-0.30846
H615	0.84847	0.60669	0.01681
C616	0.21462	0.15045	-0.26248
C617	0.21858	0.13075	-0.3207
C618	0.2652	0.12551	-0.38908
C619	0.27649	0.10246	-0.41718
N620	0.25768	0.08406	-0.36303
C621	0.65196	0.51139	-0.25389
C622	0.65006	0.53302	-0.29781
C623	0.30193	0.14488	-0.43067
C624	0.36476	0.14416	-0.42977
C625	0.39828	0.1634	-0.4592
C626	0.36972	0.18382	-0.48885

C627	0.30701	0.18442	-0.4914
C628	0.27369	0.16513	-0.46371
C629	0.40581	0.20439	-0.51398
N630	0.38051	0.22423	-0.52925
C631	0.41061	0.24556	-0.55097
C632	0.47024	0.24652	-0.58554
C633	0.49816	0.2677	-0.6014
C634	0.46718	0.28819	-0.58426
C635	0.40747	0.28738	-0.55215
C636	0.37926	0.26619	-0.53673
S637	0.50717	0.31528	-0.59246
C638	0.57229	0.59157	-0.50428
C639	0.60433	0.56169	-0.41567
N640	0.61983	0.5807	-0.36255
C641	0.61457	0.53873	-0.38391
C642	0.58538	0.51926	-0.44011
C643	0.52304	0.51841	-0.45346
C644	0.49583	0.4988	-0.49453
C645	0.52989	0.47934	-0.51883
C646	0.59227	0.48033	-0.50786
C647	0.61965	0.50024	-0.47122
C648	0.49983	0.45834	-0.55622
N649	0.52684	0.43857	-0.55362
C650	0.50144	0.41715	-0.58672
C651	0.45919	0.41597	-0.6658
C652	0.43505	0.39479	-0.69472
C653	0.45269	0.37452	-0.64593
C654	0.49507	0.37568	-0.56746
C655	0.52013	0.39678	-0.53971
S656	0.41397	0.34795	-0.67833
H657	0.24721	0.16411	-0.25651
H658	0.33365	0.10615	-0.55364
H659	0.62628	0.49638	-0.27409
H660	0.38793	0.12897	-0.40351
H661	0.44663	0.16252	-0.45627
H662	0.28361	0.19991	-0.51318
H663	0.22541	0.16626	-0.46484
H664	0.45399	0.20277	-0.51407
H665	0.49554	0.23111	-0.60069
H666	0.54412	0.26817	-0.62689
H667	0.3832	0.30312	-0.53759
H668	0.33327	0.26582	-0.511
H669	0.49534	0.5327	-0.43015
H670	0.44798	0.49863	-0.50625
H671	0.61996	0.46578	-0.52796
H672	0.66768	0.50038	-0.46153
H673	0.45353	0.45946	-0.58005

H674	0.44489	0.43129	-0.70534
H675	0.40172	0.3942	-0.75429
H676	0.50806	0.36046	-0.52627
H677	0.55296	0.39735	-0.47928
C678	0.73472	0.62856	-0.22597
C679	0.97991	0.99749	-0.07135
C680	0.98518	0.97797	-0.13319
C681	1.01841	0.9795	-0.22346
C682	0.95938	0.95583	-0.09992
N683	0.97769	0.93676	-0.14096
C684	0.95972	0.91377	-0.11523
C685	0.90946	0.90887	-0.05439
C686	0.89269	0.88611	-0.03577
C687	0.92753	0.86797	-0.07307
C688	0.97699	0.87279	-0.13462
C689	0.99274	0.89551	-0.15589
S690	0.90615	0.83825	-0.05185
C691	0.81928	0.57186	-0.02052
C692	0.77907	0.60136	-0.10141
N693	0.75329	0.58236	-0.1402
C694	0.77127	0.62372	-0.14044
C695	0.80384	0.64299	-0.09077
C696	0.78556	0.65056	0.00562
C697	0.81099	0.67018	0.04862
C698	0.85411	0.68284	-0.00469
C699	0.87535	0.6744	-0.09813
C700	0.85117	0.65435	-0.13982
C701	0.8741	0.70514	0.03661
N702	0.90234	0.71981	-0.02047
C703	0.92129	0.74252	0.00822
C704	0.9216	0.75022	0.1099
C705	0.94129	0.77236	0.13317
C706	0.96061	0.78716	0.05597
C707	0.96085	0.77957	-0.04487
C708	0.94116	0.75742	-0.0685
S709	0.9936	0.81455	0.08908
H710	0.92872	0.95571	-0.03629
H711	0.88248	0.92241	-0.02262
H712	0.85275	0.88259	0.00807
H713	1.00317	0.85892	-0.1665
H714	1.03099	0.89894	-0.20413
H715	0.75049	0.64162	0.0464
H716	0.79552	0.67597	0.12204
H717	0.90985	0.68347	-0.13966
H718	0.86764	0.64821	-0.21233
H719	0.86048	0.70962	0.11296
H720	0.90816	0.73925	0.17203

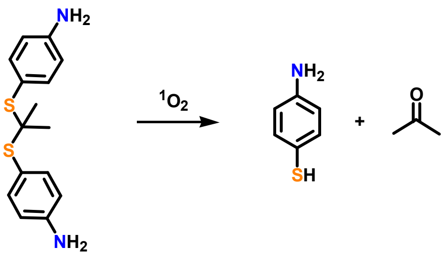
H721	0.94224	0.77791	0.21164
H722	0.97713	0.79067	-0.1048
H723	0.94175	0.75175	-0.14691
H724	0.55808	0.55692	-0.56281
C725	0.92674	0.83343	0.08414
C726	0.94366	0.85532	0.14258
C727	0.8729	0.82241	0.13777
H728	0.85572	0.8075	0.09421
H729	0.83564	0.83492	0.14468
H730	0.88573	0.81652	0.21481
H731	0.90539	0.86734	0.14788
H732	0.98249	0.86405	0.10684
H733	0.95651	0.8508	0.22171
C734	0.66129	0.62794	-0.33504
C735	0.36325	0.98595	-0.43986
C736	0.34854	0.96127	-0.45718
N737	0.38727	0.94385	-0.46347
C738	0.37234	0.91848	-0.47134
C739	0.41946	0.90263	-0.46975
C740	0.40814	0.87903	-0.47074
C741	0.34936	0.87088	-0.47594
C742	0.30193	0.88668	-0.47806
C743	0.31323	0.91038	-0.47622
S744	0.33347	0.84023	-0.46697
C745	0.57491	0.56803	-0.50379
C746	0.59863	0.59904	-0.41487
C747	0.60695	0.62231	-0.38492
C748	0.56276	0.64151	-0.41329
C749	0.50741	0.63731	-0.4625
C750	0.46969	0.65536	-0.49269
C751	0.48387	0.67818	-0.46946
C752	0.53416	0.68238	-0.40931
C753	0.57179	0.66443	-0.37998
C754	0.44605	0.6973	-0.50747
N755	0.45405	0.71825	-0.47548
C756	0.42263	0.7383	-0.51116
C757	0.39991	0.73986	-0.61069
C758	0.37111	0.75989	-0.64331
C759	0.36498	0.77878	-0.57818
C760	0.38678	0.77717	-0.47842
C761	0.4166	0.75727	-0.4461
S762	0.3193	0.80284	-0.62141
H763	0.46514	0.90868	-0.46498
H764	0.44513	0.8672	-0.46431
H765	0.2562	0.88059	-0.48005
H766	0.27611	0.92229	-0.47719
H767	0.49097	0.62023	-0.47553

H768	0.42903	0.65141	-0.53387
H769	0.54449	0.6996	-0.38399
H770	0.60673	0.66902	-0.32766
H771	0.41133	0.6935	-0.56234
H772	0.40491	0.72581	-0.6637
H773	0.35309	0.76064	-0.71965
H774	0.37969	0.79103	-0.42509
H775	0.43381	0.75639	-0.36926
H776	0.84703	0.56162	0.02922
H777	0.55622	0.60181	-0.56701
C778	0.88694	0.32665	0.09919
C779	0.89587	0.30475	0.16088
C780	0.8274	0.33765	0.13046
H781	0.81642	0.3525	0.08103
H782	0.79039	0.32516	0.12263
H783	0.82953	0.34363	0.21042
H784	0.89666	0.30836	0.24384
C785	1.13448	0.1293	-0.24193
C786	1.07288	0.12233	-0.21292
C787	1.05684	0.09889	-0.20656
C788	0.69273	0.51217	-0.17684
C789	0.71605	0.53418	-0.17564
C790	1.02941	0.1412	-0.18999
C791	0.99545	0.14124	-0.09996
C792	0.96466	0.16106	-0.06926
C793	0.96769	0.18127	-0.1273
C794	0.99819	0.18071	-0.22073
C795	1.02819	0.16088	-0.25199
C796	0.94222	0.20304	-0.08751
N797	0.95934	0.22256	-0.1258
C798	0.94161	0.24537	-0.09602
C799	0.8908	0.25002	-0.03581
C800	0.87428	0.27283	-0.01496
C801	0.90884	0.29118	-0.05197
C802	0.95899	0.28644	-0.11193
C803	0.97523	0.26381	-0.13346
S804	0.8851	0.32107	-0.04015
C805	0.81968	0.59539	-0.02631
C806	0.7776	0.56429	-0.0909
C807	0.7628	0.5411	-0.10946
C808	0.79736	0.52242	-0.05852
C809	0.79457	0.51905	0.04705
C810	0.81851	0.49912	0.0907
C811	0.84298	0.48178	0.02925
C812	0.84843	0.48572	-0.07577
C813	0.82669	0.50598	-0.11882
C814	0.85988	0.45941	0.07461

N815	0.87173	0.4419	0.01651
C816	0.88695	0.41886	0.04685
C817	0.88916	0.41166	0.1492
C818	0.90659	0.38922	0.17327
C819	0.92123	0.3736	0.09617
C820	0.91813	0.38057	-0.00547
C821	0.90085	0.40298	-0.02977
S822	0.9512	0.3456	0.12987
H823	0.95861	0.10029	-0.18534
H824	0.70387	0.49798	-0.12723
H825	0.99586	0.12649	-0.05009
H826	0.94175	0.16101	0.003
H827	1.00046	0.19583	-0.26842
H828	1.05308	0.16128	-0.32265
H829	0.91268	0.20249	-0.02231
H830	0.86282	0.23629	-0.00767
H831	0.83393	0.27619	0.02803
H832	0.98501	0.30037	-0.14367
H833	1.01394	0.26059	-0.18089
H834	0.77193	0.53139	0.095
H835	0.81565	0.49679	0.17209
H836	0.86801	0.4729	-0.12518
H837	0.82945	0.50825	-0.20046
H838	0.85985	0.45781	0.15648
H839	0.87836	0.42314	0.21095
H840	0.90935	0.38404	0.25222
H841	0.93059	0.36887	-0.06571
H842	0.89935	0.40818	-0.1088
N843	0.68923	0.54697	-0.249
N844	0.68612	0.61636	-0.25612
C845	0.17754	0.01384	-0.20395
H846	0.16046	-0.00047	-0.16086
N847	0.18329	0.04715	-0.28833
C848	1.14814	0.03404	-0.22795
C849	1.08754	0.03883	-0.20338
C850	1.00406	0.06702	-0.18882
C851	1.06373	0.06145	-0.20294
C852	1.04735	0.01874	-0.18261
C853	1.01111	0.01764	-0.09528
C854	1.04848	-0.00029	-0.24831
H855	0.96703	0.0554	-0.17795
H856	1.00947	0.0319	-0.04268
H857	1.07515	0.00014	-0.31698
C858	0.23259	0.01476	-0.24923
C859	0.23463	0.03519	-0.30291
C860	0.28079	0.04176	-0.37083
C861	0.31675	0.07166	-0.49303

C862	0.28355	0.06438	-0.41002
C863	0.32938	0.02498	-0.39758
C864	0.38943	0.03177	-0.38827
C865	0.43567	0.01628	-0.40656
C866	0.31678	0.00202	-0.42597
H867	0.26642	0.00154	-0.24443
H868	0.3424	0.06102	-0.54449
C869	0.16092	0.14967	-0.21207
C870	0.69664	0.64663	0.64079
C871	0.74143	0.64757	0.7115
H872	0.69012	0.65871	0.57938
H873	0.7752	0.66077	0.71434
C874	1.42296	0.99357	0.5685
H875	1.39112	0.95368	0.53875
H876	1.46001	0.98187	0.5574
H877	1.27079	0.99646	0.5662
H878	1.40064	1.04905	0.63515
H879	1.4817	1.0218	0.60071
H880	0.95437	0.99674	0.99839
H881	1.02264	0.96486	0.72647

7. Model reaction



4,4'-(propane-2,2-diylbis(sulfanediyl))dianiline (TK) (290 mg, 1 mmol) dissolved in 5 mL ethanol, then 5 mL of dilute hydrochloric acid with pH = 3 was added. After addition of 1 mL (10 mM) of Protoporphyrin IX (PpIX, a typical type II photosensitizer) solution, the mixture was stirred at room temperature for 24 h under the irradiation of a 660 nm laser with a power of 600 mW/cm^2. Then, the above reaction solution was poured into water, extracted three times with dichloromethane, and purified by column chromatography to afford 4-aminothiophenol in 96 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.11 (d, *J* = 8.5, 2H), 6.51 (d, *J* = 8.5, 2H), 3.63 (s, 2H), 3.32 (s, 1H). IR (KBr pellet cm^{-1}): 3439 (m), 3359 (s), 3210 (m), 3026 (v), 2779 (m), 2550 (m), 1620 (s), 1595 (s), 1489 (vs), 1423 (v), 1402 (v), 1284 (s), 1204 (v), 1177 (m), 1120 (v), 1084 (v), 1007 (v), 818 (s), 755 (v), 690 (v), 631 (v), 502 (m).

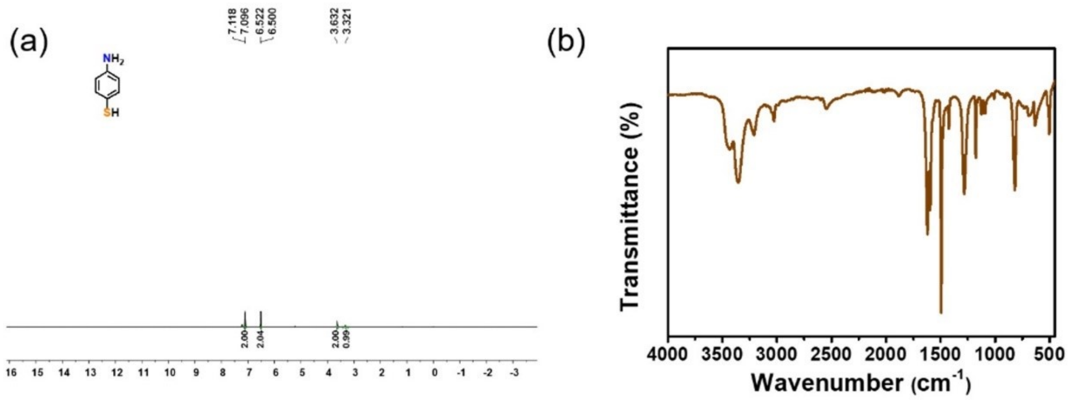


Fig. S3 (a) ^{1}H NMR of 4-aminothiophenol. (b) FT-IR spectra of 4-aminothiophenol.

8. Single-line state oxygen detection

The single-linear oxygen specificity detection probe SOSG was used to detect the production of $^1O_2$. (2 μL, 2.5 mM) was added to 1 mL of PpIX (50 μM) and **TKPP-COF** (50 μg/mL), respectively. And then irradiated with a 660 nm laser with a power of 100 mW/cm^2 for different times. The excitation wavelength was set at 488 nm and the emission spectra were collected in the range of 500-600 nm. The rate of $^1O_2$ production is determined by the enhancement of fluorescence over time. To characterize the difference in the rate of $^1O_2$ introduced by different materials, the ratios F/F_0 of fluorescence intensity F and the initial fluorescence intensity F_0 at the maximum fluorescence intensity were calculated for different irradiation times and plotted as an ordinate of the irradiation time.

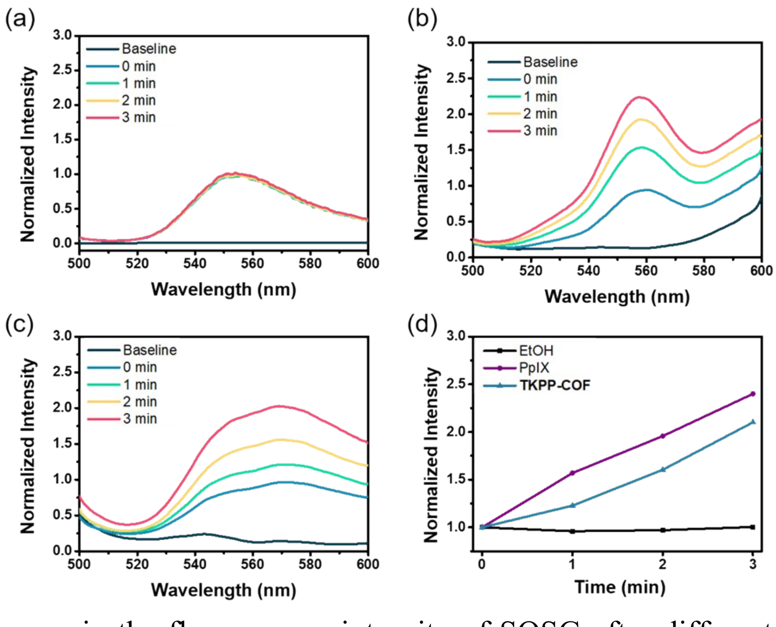


Fig. S4 Changes in the fluorescence intensity of SOSG after different times of light exposure in different substances. (a) In EtOH. (b) In the PpIX solution. (c) In **TKPP-COF** dispersion. (d) Comparison of fluorescence changes of SOSG in different media.

9. Synthesis of nano TKPP-COF

The ethanol dispersion of **TKPP-COF** at a concentration of 1 mg/mL was irradiated with a 660 nm laser at a power of 100 mW/cm^2 for 24 h at room temperature and separated by vacuum filtration to obtain **nano TKPP-COF**.

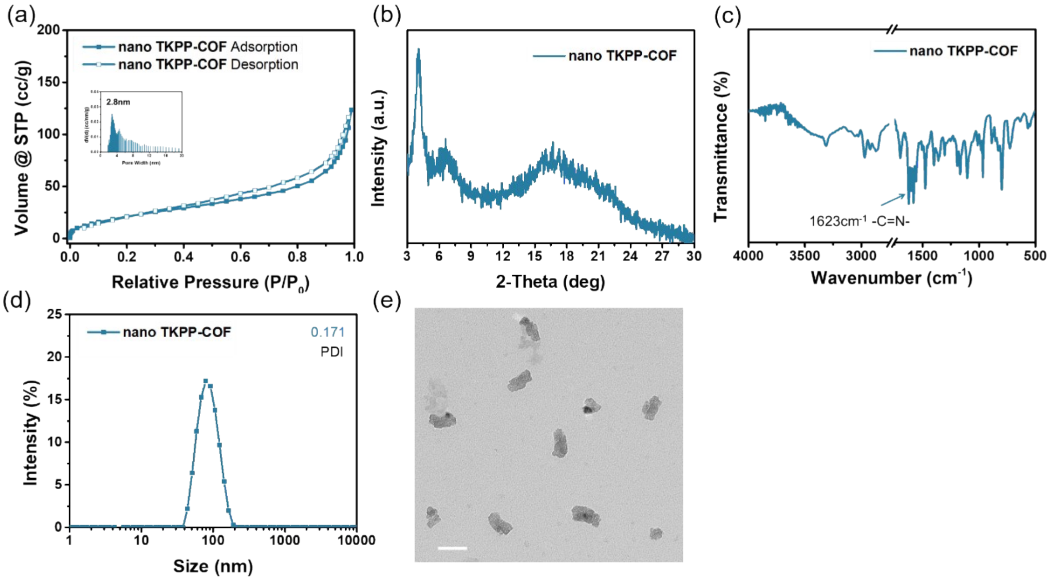


Fig. S5 (a) N_2 adsorption (solid square) and desorption (hollow square) isotherms of **nano TKPP-COF**. BET surface area of **nano TKPP-COF** = 85.8 m²/g. The pore size distribution curve of **nano TKPP-COF** based on nonlocal density functional theory (NLDFT) analysis is shown as an inset. The pore width of **nano TKPP-COF** was centered at 2.8 nm. (b) PXRD patterns **nano TKPP-COF**. (c) FT-IR spectra of **nano TKPP-COF**. The peaks at 1623 cm^{-1} for -C=N-. (d) DLS plots and PDI of **nano TKPP-COF**. (e) Transmission electron microscope (TEM) image of **nano TKPP-COF**. Scale bar, 100 nm.

10. Synthesis of DC_AC50@nano TKPP-COF

nano TKPP-COF (5 mg) was added into ethanol (5 mL, containing 0.1% DMSO) containing DC_AC50 (5 mg), and then the suspension was sonicated for 10 min. After being stirred at 25 °C and 800 rpm for 24 h, the solid particle was separated by vacuum filtration followed by washing with water 3 times. Finally, the product **DC_AC50@nano TKPP-COF** was resuspended in water and stored at 4 °C until use.

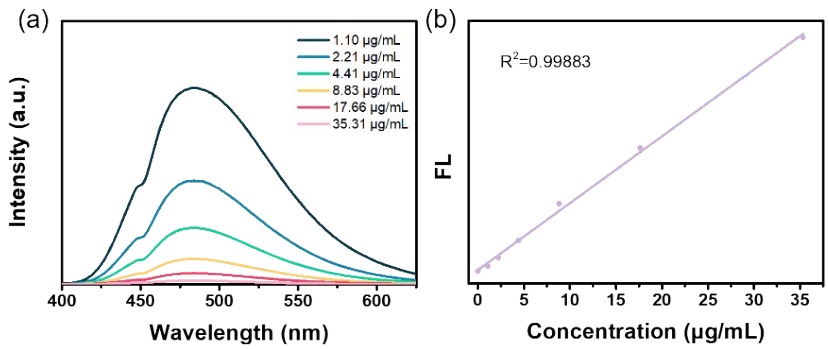


Fig. S6 (a) Fluorescence spectra of different concentrations of DC_AC50 in ethanol. (b) Standard curve of different concentrations of DC_AC50 in ethanol.

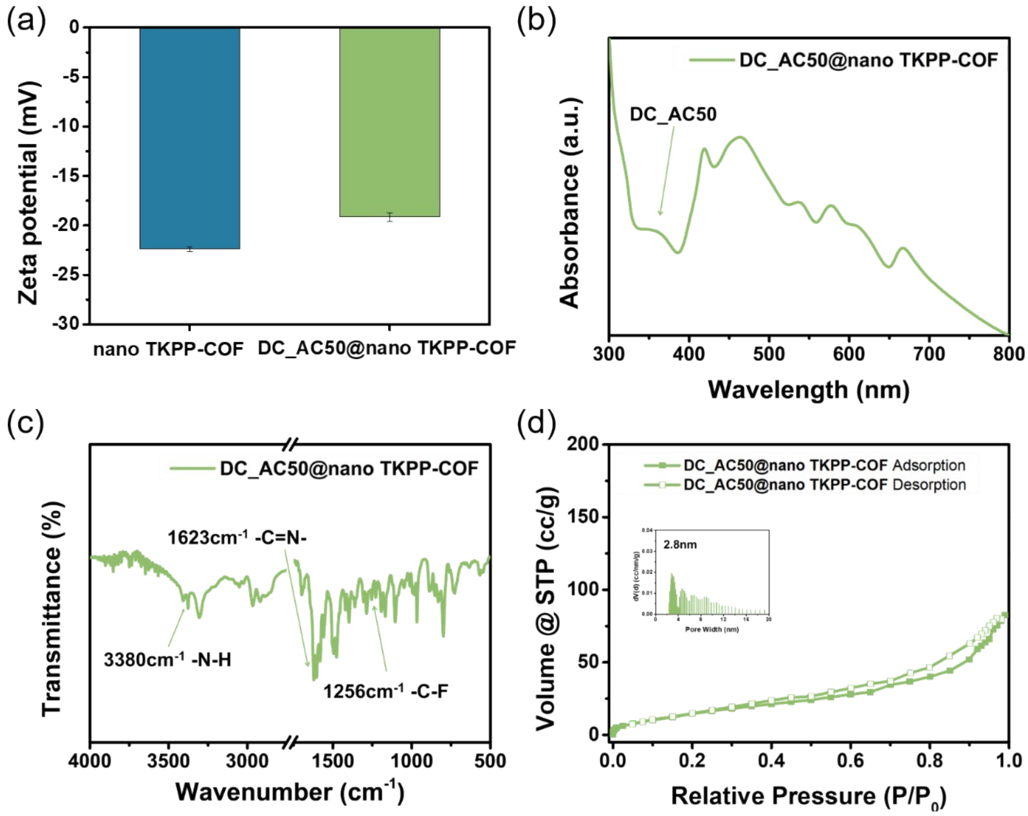


Fig. S7 (a) Zeta potential of **nano TKPP-COF** and **DC_AC50@nano TKPP-COF**. (b) Ultraviolet−visible (UV−vis) absorption spectrum of **DC_AC50@nano TKPP-COF**. The UV absorption spectrum of **DC_AC50@nano TKPP-COF** showed a DC_AC50 absorption peak at 358 nm. (c) FT-IR spectrum of **DC_AC50@nano TKPP-COF**. C=N stretching vibration was found at 1623 cm^{-1} for **DC_AC50@nano TKPP-COF**, and the N-H stretching vibration associated with the amide bond in DC_AC50 was located at 3380 cm^{-1}. (d) N_2 adsorption (solid square) and desorption (hollow square) isotherms of **DC_AC50@nano TKPP-COF**. BET surface area of **DC_AC50@nano TKPP-COF** = 56.2 m^2/g. The pore size distribution curve of **DC_AC50@nano TKPP-COF** based on nonlocal density functional theory (NLDFT) analysis is shown as an inset. The pore width of **DC_AC50@nano TKPP-COF** was centered at 2.8 nm.

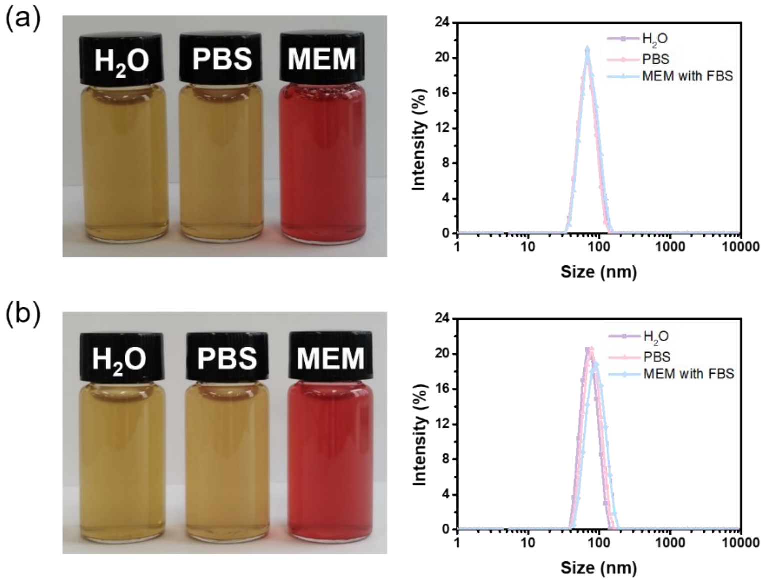


Fig. S8 The stability of **DC_AC50@nano TKPP-COF** in different physiological solutions (H_2O, PBS, and MEM with 10% fetal bovine serum). (a) 0 h. (b) 72 h.

11. EPR-trapping tests

As for the $^1O_2$ trapping-EPR tests, the acetone dispersion of **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (200 μL, 50 μg/mL) and 10 μL TEMP were added to a test tube, and irradiated with a red LED (50 mW/cm^2) for 120 s. After being illuminated, the mixture was characterized using a Bruker EMX plus model spectrometer operating at the X-band frequency (9.4 GHz) at room temperature.

12. Photodynamic property

The dispersion of **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (2 mL, 50 μg/mL) and DPBF DMF solution (200 μL, 1 mM) were added to a quartz dish and irradiated with a red LED (50 mW/cm^2) for 120 s. The absorbance of DPBF at 414 nm in the mixture was recorded at 20 s intervals. The $^1O_2$ generation rate was determined from the reduced absorbance over time. To characterize the difference in the rate of $^1O_2$ introduced by different nanodrugs, the ratios A/A_0 of absorbance A and the initial absorbance A_0 at 414 nm at different irradiation times were calculated and plotted as the ordinate for the irradiation time. The dispersion of **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (2 mL, 50 μg/mL) was used as the reference for this UV−vis measurement.

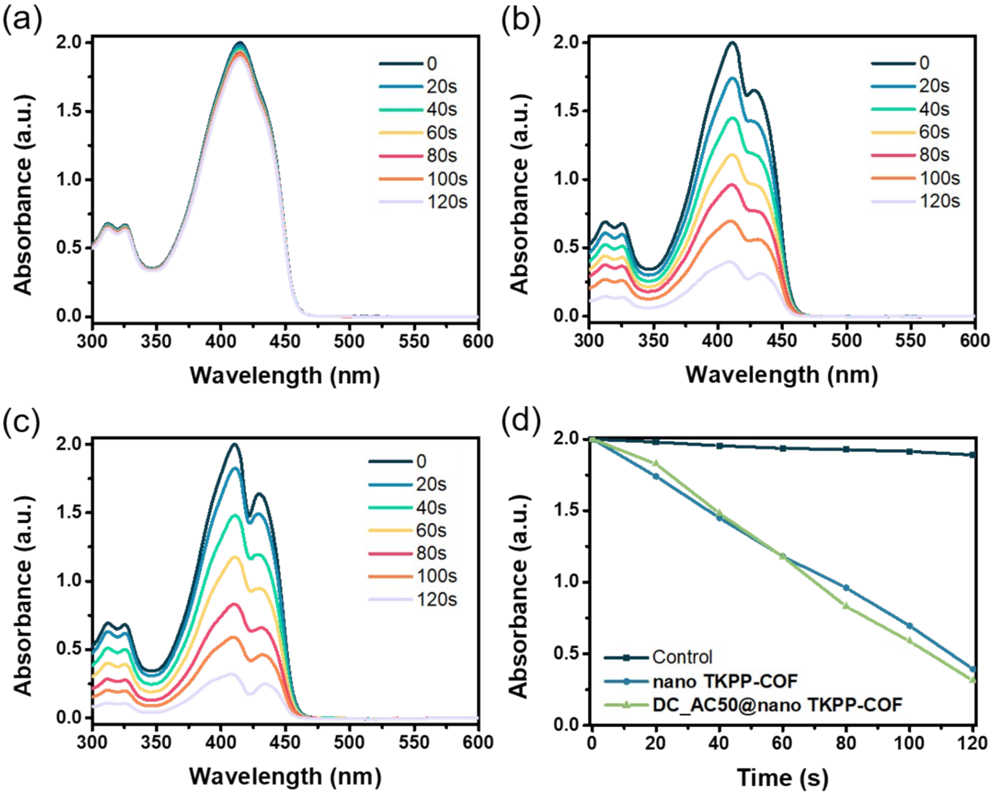


Fig. S9 (a) UV−vis spectra of DPBF induced by DMF under a 660 nm (50 mW/cm^2, 2 mL) irradiation. (b) UV−vis spectra of DPBF induced by **nano TKPP-COF** under a 660 nm (50 mW/cm^2, 50 μg/mL, 2 mL) irradiation. (c) UV−vis spectra of DPBF induced by **DC_AC50@nano TKPP-COF** under a 660 nm (50 mW/cm^2, 50 μg/mL, 2 mL) irradiation. (d) Comparison of absorbance decay rates of DPBF at 414 nm induced by **nano TKPP-COF** (50 μg/mL), **DC_AC50@nano TKPP-COF** (50 μg/mL), and DMF (2 mL) under NIR irradiation (660 nm, 50 mW/cm^2, 120 s).

13. Drug release experiments

For the drug release study, **DC_AC50@nano TKPP-COF** (8 mg) was suspended in 8 mL PBS. The system was maintained at a magnetic stirring speed of 100 rpm. For NIR smart controlled release, **DC_AC50@nano TKPP-COF** was exposed to 660 nm NIR laser (200 mW/cm^2) for 10 min followed by an interval of 10 min, and the procedure was repeated three times. For the drug release potential of **DC_AC50@nano TKPP-COF**, the dispersions of **DC_AC50@nano TKPP-COF** were exposed to lasers of different powers (0, 200 mW/cm^2, 600 mW/cm^2) of 660 nm. For the release potential of **DC_AC50@nano TKPP-COF** with short irradiation time, the dispersions of **DC_AC50@nano TKPP-COF** were exposed to laser at 660 nm with a power of 100 mW/cm^2 for 8 min. Every once in a while, 3 mL of the above dispersion liquids were taken out and centrifuged immediately and refilled with the same volume of fresh PBS, the solids obtained by centrifugation were also put back together. The amount of released DC_AC50 was quantified by fluorescence spectrum and the accumulated drug release (ADR) of DC_AC50 from **DC_AC50@nano TKPP-COF** was calculated according to the following formula:

$$\text{ADR (wt \%)} = \left\{ \left(8Cn + 3\sum_{i=n}^{n-1} Ci \right) / \text{weight of loaded DC\_AC50} \right\} \times 100\%$$

, where Cn is the concentration of DC_AC50 in the supernatant at the time point of n.

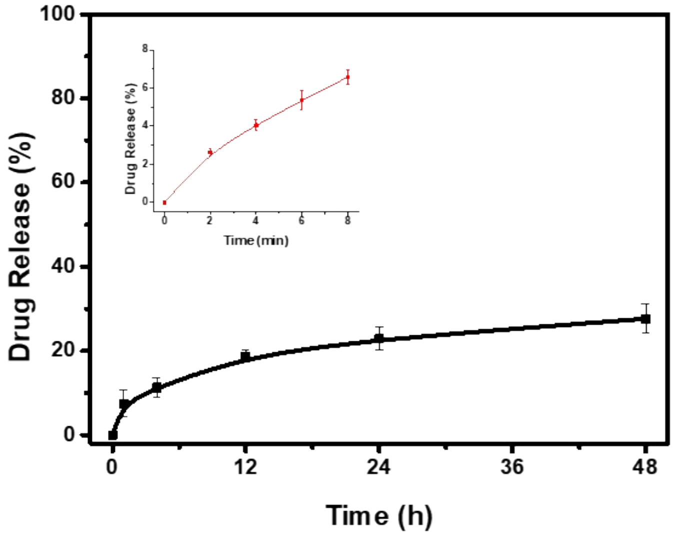


Fig. S10 Drug release at 48 h after 8 min of irradiation (660 nm, 100 mW/cm^2, 8 min). The inset shows the drug release profile during irradiation.

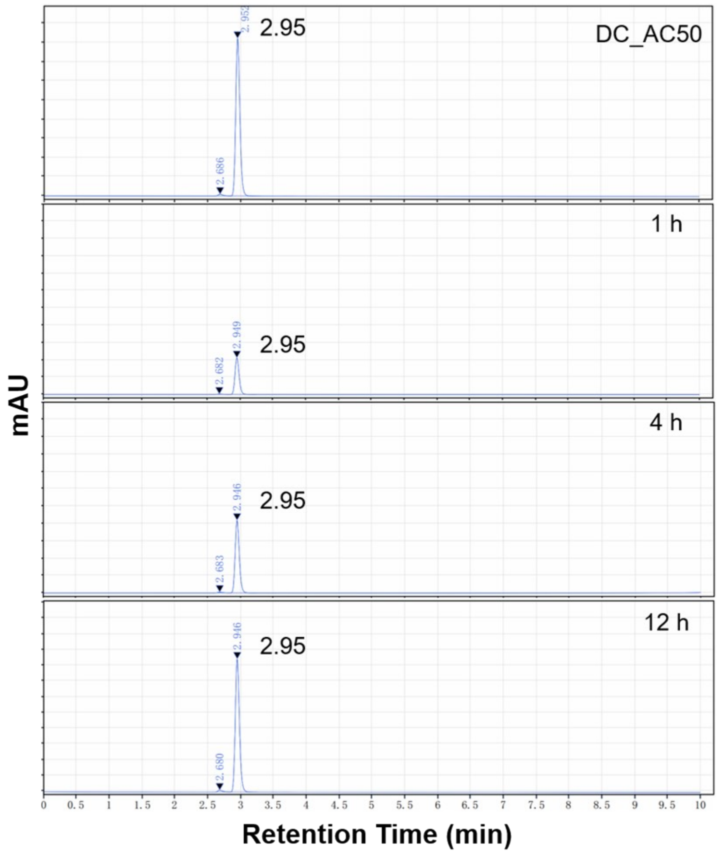


Fig. S11 High-performance liquid chromatogram (HPLC) of DC_AC50 released from **DC_AC50@nano TKPP-COF** dispersion (1 mg/mL, in PBS) at different time points by near-infrared light irradiation (660 nm, 600 mW/cm^2). Chromatographic column, Shim-pack VP-ODS; mobile phase, CH_3CN-H_2O (19:1, v/v); flow rate, 1.0 mL/min; λ, 254 nm.

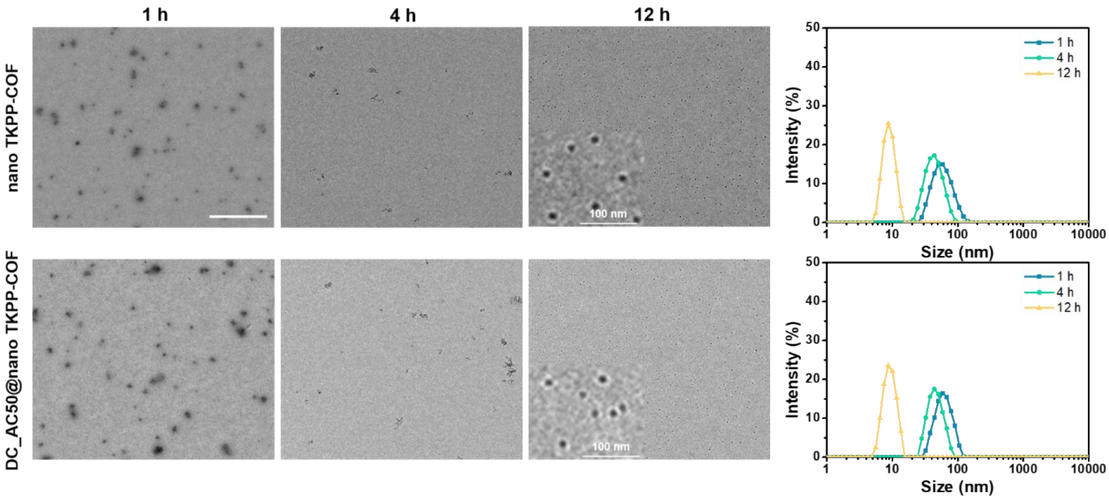


Fig. S12 Degradation of **nano TKPP-COF** and **DC_AC50@nano TKPP-COF** (1 mg/mL, in PBS) under NIR light irradiation (660 nm, 600 mW/cm^2) were examined by TEM and DLS. Scale bar, 500 nm.

14. Cell uptake and subcellular localization

To study the cell uptake, intracellular distribution, and subcellular localization, **nano TKPP-COF** was labelled with the fluorescent dye Bodipy-CHO. Briefly, **nano TKPP-COF-Bodipy** was prepared as follows: first, **nano TKPP-COF** (1.0 mg), Bodipy-CHO (1.0 mg) were added to ethanol (2.0 mL); then, acetic acid (20 μL, 6.0 M) was added into the suspension; after being stirred at 70 °C and 500 rpm for 24 h in the dark, the supernatant was discarded after centrifugation, and the solids were fully washed with ethanol; finally, the solid was re-dispersed into DPBS (1.0 mL) to obtain a stock solution of **nano TKPP-COF-Bodipy** (1.0 mg/mL).

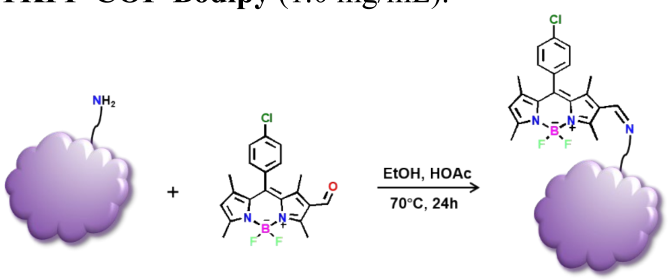


Fig. S13 Schematic diagram of the synthesis of **nano TKPP-COF-Bodipy**.

For subcellular localization, HT-1080 cells were incubated with **nano TKPP-COF-Bodipy** (200 μL, 10 μg/mL) for 4 h in a CO_2 incubator, and washed with DPBS twice carefully. After an additional 4 h incubation, LysoTracker Red DND-99 (200 μL, 50 nM, 10 min) and MitoTracker Deep Red FM (200 μL, 50 nM, 10 min) were added respectively. Finally, the cells were washed with DPBS twice and the laser scanning confocal fluorescence images were captured. The images of **nano TKPP-COF-Bodipy** were excited by 488 nm light, and the emission wavelength range was collected at 520 ± 15 nm. The images of LysoTracker Red DND-99 were excited by 561 nm light, and the emission wavelength range was collected at 597 ± 17 nm. The images of MitoTracker Deep Red FM were excited by 633 nm light, and the emission wavelength range was collected at 665 ± 15 nm. Controls were conducted as needed to make sure images were free of crosstalk. Colocalization was analyzed by ImageJ software.

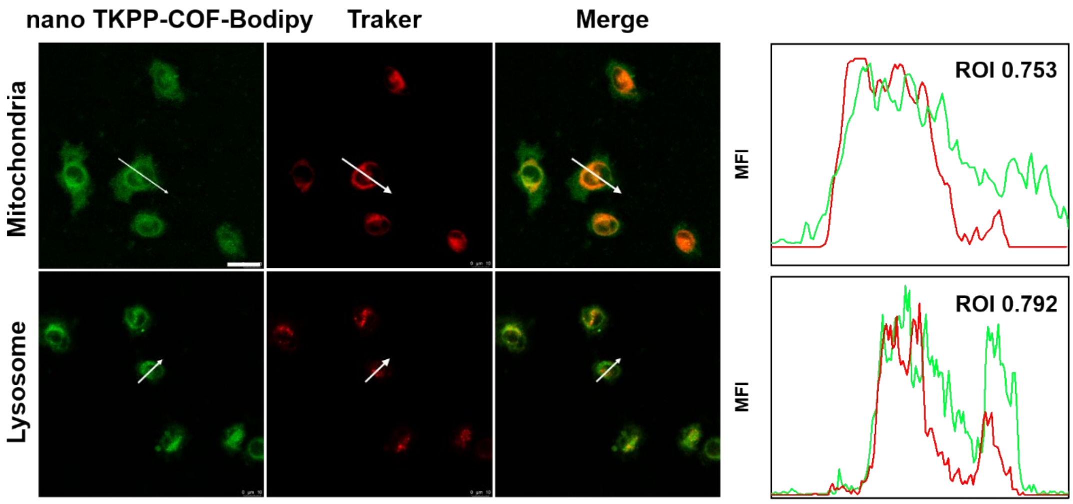


Fig. S14 Subcellular localization of **nano TKPP-COF-Bodipy** in HT-1080 cells. Scale bar, 20 μm.

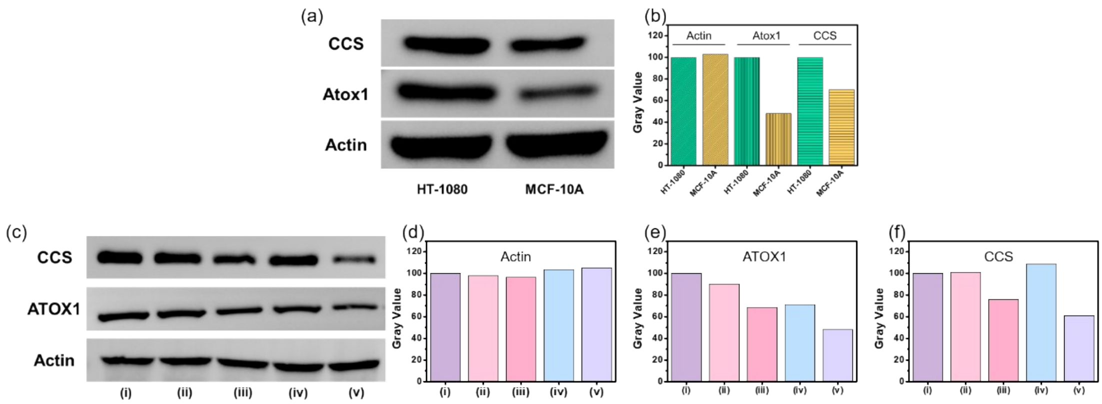


Fig. S15 (a) Expression of Atox1 and CCS in cancer cells (HT-1080) and normal cells (MCF-10A). (b) The gray values of WB bands of different proteins were quantified by using ImageJ software. (c) Expression of Atox1 and CCS in HT-1080 cells after treatment with different nanodrugs. (d)-(f) The gray values of WB bands of different proteins were quantified by using ImageJ software. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

15. Total copper content in HT-1080 cells by ICP-MS detection

Cells were seeded and cultured in 10 cm culture dishes for 24 h and treated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (5 mL, 30 μg/mL) for 4 h in a CO_2 incubator. After being rinsed with DPBS carefully, for PDT, the cells were exposed to a red LED (50 mW/cm^2, 5 min). After that, the cells were cultured for an additional 12 or 24 h. The total copper content of cells was determined using ICP-MS spectroscopy. We collected 8 x 10^6 cells in 150 μL DPBS buffer for total Cu uptake experiments and acidified them with 200 μL 70% nitric acid incubated for 12 h at 80 °C, diluted to 5 mL by H_2O, and used for analysis.

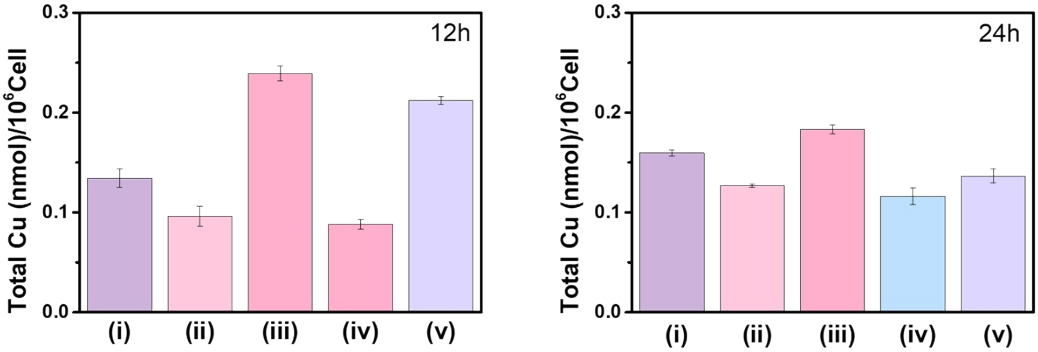


Fig. S16 The total copper content in HT-1080 cells were incubated with different nanodrugs at different times. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

16. Intracellular total ROS measurements

Levels of intracellular ROS were measured by the cell-permeable dye DCFH-DA. Experimentally, cells were treated with DC_AC50 (500 μL, 20 μM), **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (500 μL, 30 μg/mL) for 4 h in a CO_2 incubator. And then the cells were washed with DPBS carefully. Afterward, the cells were loaded with DCFH-DA (200 μL, 100 nM) for 15 min in a CO_2 incubator and washed with DPBS twice. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min). Finally, the laser scanning confocal fluorescence images were captured. The green images were excited by a 488 nm light, and the emission wavelength range was collected at 525 ± 20 nm. Cells without any nano-drug treatment were used as a control group.

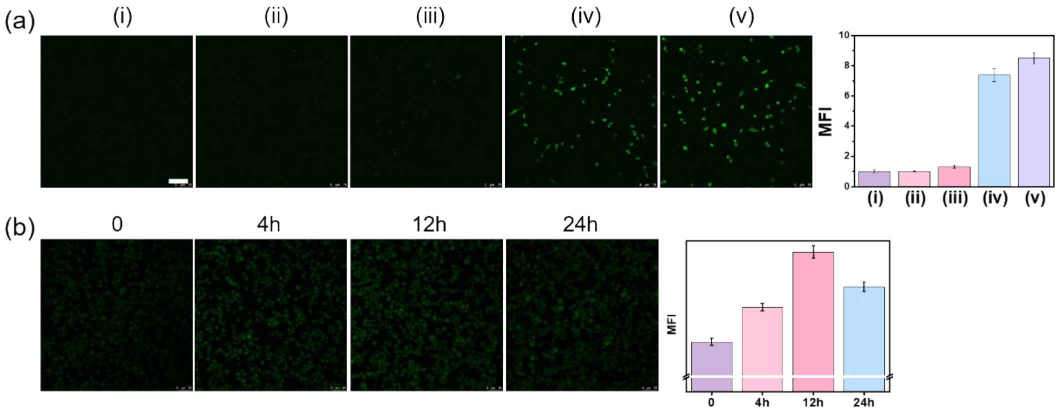


Fig. S17 (a) Detection of $^1O_2$ in HT-1080 cells treated with different nanodrugs using DCFH-DA. (b) The effect of free DC_AC50 on ROS in HT-1080 cells. DC_AC50 was able to increase the ROS level in cancer cells such as HT-1080 cells, which is beneficial to the sustained drug release of **DC_AC50@nano TKPP-COF** *in vitro*. Scale bar, 50 μm. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

17. Mitochondrial membrane potential measurements

Mitochondrial membrane potential was measured by a fluorescent lipophilic carbocyanine dye JC-1. Experimentally, cells were treated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (500 µL, 30 µg/mL) for 4 h in a CO_2 incubator. And then the cells were washed with DPBS carefully. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min). After additional 4 h incubation, the cells were incubated with JC-1 (200 µL, 15 µM) for 10 min in a CO_2 incubator and washed with DPBS twice. Finally, the laser scanning confocal fluorescence images were captured. The green images of the monomer were excited by 488 nm light, and the emission wavelength range was collected at 530 ± 15 nm. The red images of J-aggregate were excited by 561 nm light, and the emission wavelength range was collected at 590 ± 17 nm. Cells without any nano-drug treatment were used as a control group.

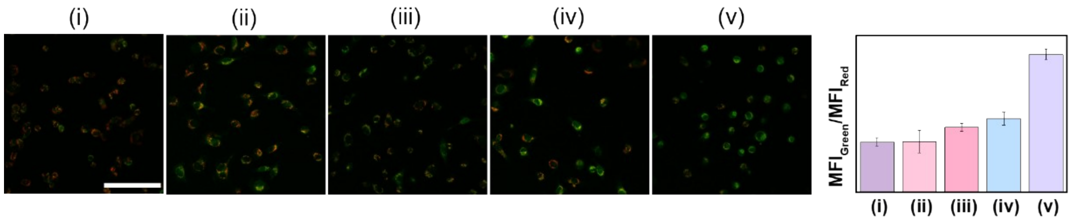


Fig. S18 Laser scanning confocal fluorescence microscopy images of JC-1 staining for determining mitochondrial membrane potential. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

18. Intracellular ATP production measurement

The level of intracellular ATP was measured using an ATP assay kit. Experimentally, cells were seeded and cultured in 10 cm culture dishes for 24 h and treated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (5 mL, 30 µg/mL) for 4 h in a CO_2 incubator. After being rinsed with DPBS carefully, for PDT, the cells were exposed to a red LED (50 mW/cm^2, 5 min). After that, the cells were cultured for an additional 24 h and taken for ATP measurements according to the manufacturer's guidelines of the assay kit. Luminescence was measured with a spectrofluorometer (SPECTRA Max Gemini; Molecular Probe) immediately after the addition of ATP enzyme mix to the cell suspension. The ATP content was normalized to the total protein amount of the cell lysates from a parallel plate and expressed as a percentage value relative to the control group value.

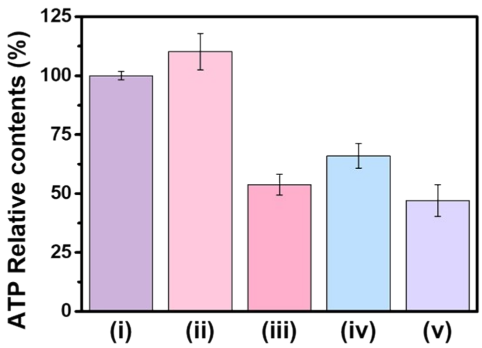


Fig. S19 The intracellular ATP content of HT-1080 cells was incubated with different nanodrugs. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

19. Intracellular and extracellular lactate measurement

Experimentally, cells were seeded and cultured in 10 cm culture dishes for 24 h and treated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (5 mL, 30 μg/mL) for 4 h in a CO_2 incubator. After being rinsed with DPBS carefully, for PDT, the cells were exposed to a red LED (50 mW/cm^2, 5 min). After that, the cells were cultured for an additional 24 h and washed with DPBS twice. The cells without treatment were used as control. Next, the cell media were collected for extracellular lactate measurements; the cells were lysed in the presence of Triton X-100 (1%) at 4 °C for intracellular lactate measurements. The lactate measurements were used with a Lactate Assay Kit according to the protocol provided by the kit supplier.

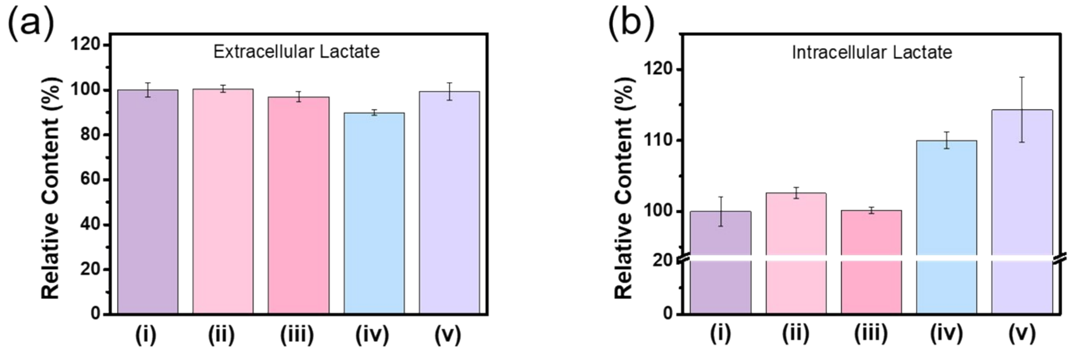


Fig. S20 (a) Extracellular lactate content of HT-1080 cells. (b) Intracellular lactate content of HT-1080 cells. Scale bar, 100 μm. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

20. Lysosomal membrane permeabilization detections

Lysosomal membrane permeabilization was measured by a lysosomotropic metachromatic fluorochrome AO. Experimentally, cells were treated with various **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (500 μL, 30 μg/mL) for 4 h in a CO_2 incubator. And then the cells were washed with DPBS carefully. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min). After additional 4 h incubation, the cells were incubated with AO (200 μL, 15 μM) for 10 min in a CO_2 incubator and washed with DPBS twice. Finally, the laser scanning confocal fluorescence images were captured. The green images of deprotonated AO were excited by 488 nm light, and the emission wavelength range was collected at 530 ± 20 nm. The red images of protonated AO were excited by 561 nm light, and the emission wavelength range was collected at 640 ± 20 nm. Cells without any nano-drug treatment were used as a control group.

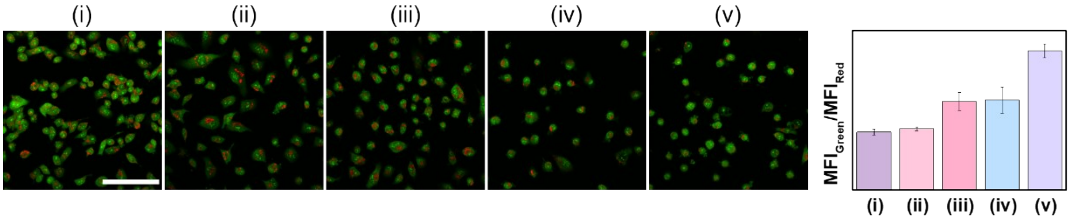


Fig. S21 Laser scanning confocal fluorescence microscopy images of AO staining for determining lysosomal membrane permeabilization. Scale bar, 100 μm. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

21. CCK-8 cell viability assays

Standard CCK-8 assay was applied to evaluate the cell cytotoxicity of the nanodrugs. Experimentally, cells were cultured in 96-well plates for 24 h and treated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (100 μL, 0~30 μg/mL) for 4 h in a CO_2 incubator. And then the cells were washed with DPBS carefully. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min), and cultured for an additional 24 h. Subsequently, the CCK-8 solution (10 μL) was added to each well and the plate was incubated in a CO_2 incubator for about 2 h. The absorbance at 450 nm was determined using a multi-mode microplate detection system. The cells without treatment were used as the control. The wells without cells were used as blanks. The cell viability was expressed as a percentage value relative to the control group value.

22. Calcein-AM/PI double staining

Cells were seeded into 60 mm culture dishes and incubated overnight in a CO_2 incubator. After removal of the culture medium, the cells were incubated with DPBS dispersion of **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (2 mL, 30 μg/mL) for 4 h in a CO_2 incubator. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min). After additional 24 h incubation, the cells were collected using Trypsin solution, washed with DPBS twice carefully, and incubated with calcein-AM (500 μL, 2 μM) and PI (500 μL, 4 μM) for 15 min. Finally, the cells were carefully washed twice with DPBS, the cancer cells were redispersed with DPBS, and the dispersed cells were placed in a glass dish and imaged with a laser scanning confocal microscope. The green images of living cells were excited by 488 nm light, and the emission wavelength range was collected at 520 ± 20 nm. The red images of dead cells were excited by 514 nm light, and the emission wavelength range was collected at 640 ± 20 nm.

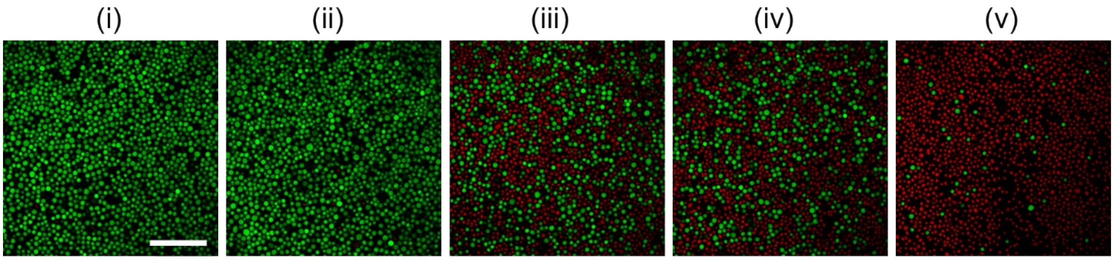


Fig. S22 Calcein-AM/PI double staining. Scale bar, 200 μm. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano**

TKPP-COF + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively. For group iv and group v, the power of the LED lamp was 50 mW/cm^2, and the illumination time was 5 min.

23. Colony formation assays

Cells were seeded into 35 mm culture dishes at a density of 5 × 10^4 cells/well and incubated overnight in a CO_2 incubator. After removal of the culture medium, the cells were incubated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (100 μL, 30 μg/mL) for 4 h in a CO_2 incubator. And then the cells were washed with DPBS carefully. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min) and cultured for an additional 24 h. Subsequently, the cells were released with trypsin/EDTA solution followed by harvesting and staining by Trypan Blue (0.4 wt%) to determine live cell number. The same number of live cells were re-seeded into 60 mm culture dishes at a density of ~1000 live cells/dish, and cultured for about a week until small colonies could be seen. For crystal violet staining, the cell colonies were washed with DPBS 3 times, fixed in cold methanol for 30 min, stained with fresh Crystal Violet solution for 30 min, and rinsed with water. Cells without any nano-drug treatment were used as a control group.

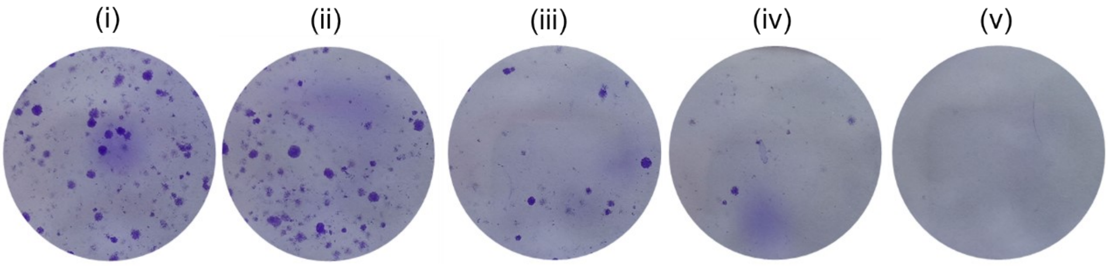


Fig. S23 *In vitro* clonogenic assay of HT-1080 cells pretreated with different nanodrugs. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively. For group iv and group v, the power of the LED lamp was 50 mW/cm^2, and the illumination time was 5 min.

24. HT-1080 cells invasion assay

Cells were seeded into 35 mm culture dishes at a density of 5 × 10^4 cells/well and incubated overnight in a CO_2 incubator. After removal of the culture medium, the cells were incubated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (100 μL, 30 μg/mL) for 4 h in a CO_2 incubator. And then the cells were washed with DPBS carefully. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min) and cultured for an additional 24 h. The medium was changed to a serum-free medium and incubated for 24 h to further remove the effect of serum. The cells were digested, terminated by centrifugation, washed with a serum-free culture medium, and resuspended in a serum-free culture medium and the cell density of live cells was adjusted to 5 × 10^5. 500 μL of complete medium containing 10% FBS was added to the 24-well plate and 200 μL of cell suspension was added to the Cell Culture Inserts small chamber. At the end of incubation, the medium was discarded and the cells outside the Cell Culture Inserts small chamber were stained with 0.1% crystalline violet for 20 min after wiping off the stromal gel and cells in the Cell Culture Inserts small chamber with a cotton swab.

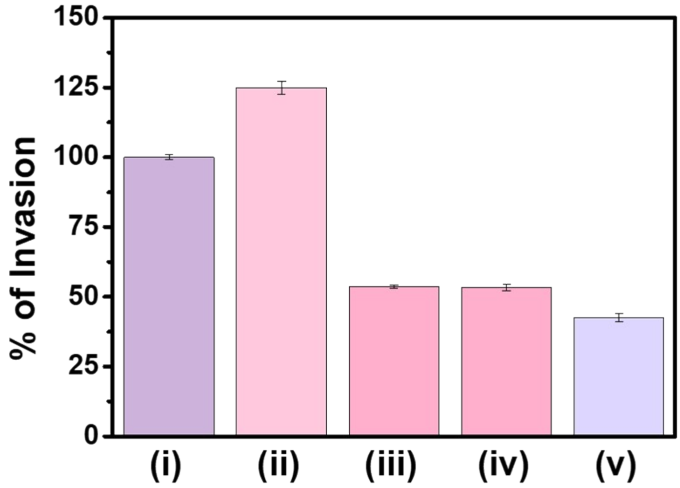


Fig. S24 The results of the matrigel invasion assay. (i-v) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, respectively.

25. Cell death rescue experiments

For cell death rescue experiments, cells were cultured in 96-well plates for 12 h. The designated modulating compound including Z-VAD-FMK (100 μL, 200 μM), ferrostatin-1 (100 μL, 20 μM), liproxstatin-1 (100 μL, 20 μM), necrostatin-1 (100 μL, 2000 nM), 3-MA (100 μL, 100 μM), N-Acetyl-L-cysteine (100 μL, 20 μM), VC (100 μL, 10 μM), rotenone (100 μL, 0.5 μM), UK5099 (100 μL, 0.5 μM), were added to each well, pretreated the cells for 2 h. And then treated with **DC_AC50@nano TKPP-COF** (100 μL, 30 μg/mL) for 4 h in a CO_2 incubator. For PDT, the cells were exposed to red LED (50 mW/cm^2, 8 min). After additional 24 h incubation, the CCK-8 solution (10 μL) was added to each well and the plate was incubated in a CO_2 incubator for 2 h. The absorbance at 450 nm was determined using a multi-mode microplate detection system. The wells without cells were used as blanks.

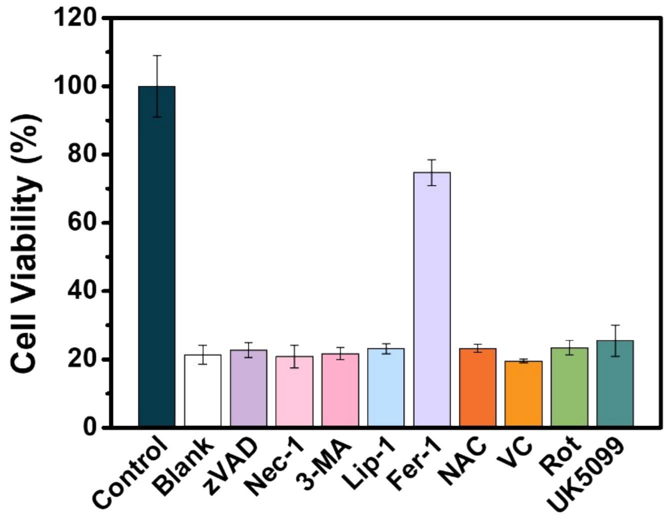


Fig. S25 Effects of different inhibitors on **DC_AC50@nano TKPP-COF** + Light induced cell death in HT-1080 cells.

26. Intracellular lipid peroxidation assays

Cells were treated with **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (500 µL, 30 µg/mL) for 4 h in a CO_2 incubator. For PDT, the cells were exposed to red LED (50 mW/cm^2, 5 min). And then the cells were washed with DPBS carefully and cultured for an additional 4 h. After that, the cells were incubated with C_{11}-BODIPY (200 µL, 2.0 µM) for 30 min in a CO_2 incubator and washed with DPBS twice. Finally, the laser scanning confocal fluorescence images were captured. The green images of the oxidized C_{11}-BODIPY dye were excited by a 488 nm light, and the emission wavelength range was collected at 510 ± 20 nm. The red images of the reduced C_{11}-BODIPY dye were excited by a 561 nm light, and the emission wavelength range was collected at 591 ± 20 nm. Cells without any nanodrug treatment were used as a control group.

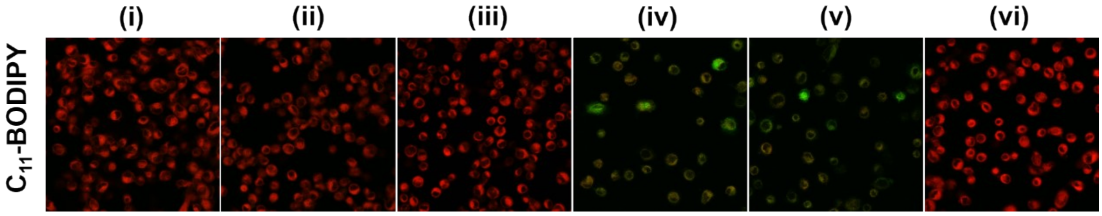


Fig. S26 LCSM images of HT-1080 cells under different treatment conditions for the detection of intracellular lipid peroxidation using C_{11}-Bodipy. (i-vi) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, (vi) **DC_AC50@nano TKPP-COF** + light + Fer-1, respectively.

27. Hemolysis analysis

First, fresh nude mouse blood samples (2 mL) were added to PBS solution (4 mL), and red blood cells (RBC) were separated by centrifugation at 3000 rpm for 10 minutes. After washing 5 times with 10 mL PBS solution, the purified red blood cells were diluted to the original solution with PBS (10 times). For the hemolysis assay, 0.2 mL diluted RBCs suspension was mixed with 1.0 mL PBS as the negative control, 1.0 mL deionized water as the positive control, and 1.0 mL **DC_AC50@nano TKPP-COF** suspension at a concentration range of 1 to 200 µg/mL. All mixtures were then allowed to stand at 37 °C for 5 h and centrifuged at 13300 rpm for 10 minutes. The absorbance of 541 nm supernatant was measured by synergy SpectraMax i3x multi-mode microplate reader. The hemolytic percentage of red blood cells was calculated by the following formula: Hemolysis Rate = [(Dt – Dnc)/(Dpc – Dnc)] ×100%.

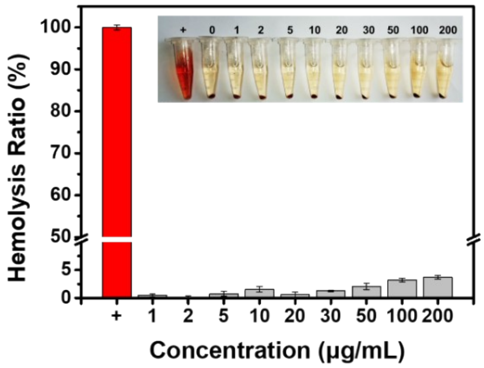


Fig. S27 Hemolytic assay using red blood cells incubated with control solvents and different concentrations of **DC_AC50@nano TKPP-COF**.

28. In vivo antitumor therapy

HT-1080 cancer cells (5×10^6 cells) suspended in HBSS (40 μL) were subcutaneously injected into the flanks of each nude mice to establish the HT-1080 xenograft model. The length (L) and width (W) of the tumor were determined by digital calipers. The tumor volume (V) was calculated by the formula $V = 1/2 \times L \times W^2$. When the tumor size reached ~100 mm^3, the nude mice bearing HT-1080 tumors (n = 20) were randomly distributed into four groups, i.e., (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv)**nano TKPP-COF +** light, (v) **DC_AC50@nano TKPP-COF +** light, and (vi) **DC_AC50@nano TKPP-COF +** light + Fer-1 groups. After intratumoral injection PBS (100 μL), **nano TKPP-COF** or **DC_AC50@nano TKPP-COF** (50 μL, 1 mg/mL, equivalent 3.3 mg/kg of COF, equivalent to 4.0 μmol/kg of DC_AC50), the nude mice were fed for 4 h, and for the treatment group, light treatment (660 nm laser, 100 mW cm^{-2}, 8 min) was performed on the tumor site. For **DC_AC50@nano TKPP-COF** + light + Fer-1 groups, after injection **DC_AC50@nano TKPP-COF**, Fer-1 (5.0 mg/kg) was injected. The mice continued to be fed for 12 days. The tumor volume and nude mouse body weight were recorded every other day during the experimental period.

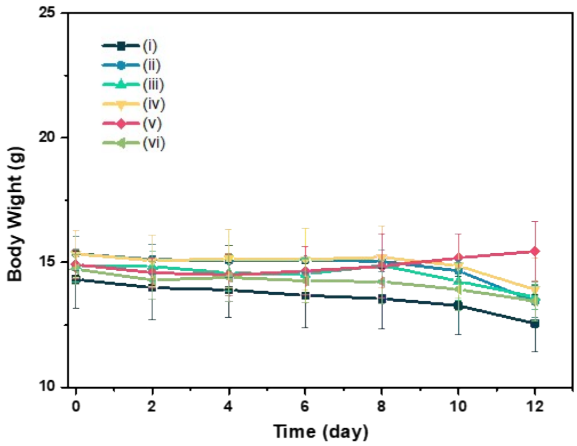


Fig. S28 Body weight of nude mice after treatment. (i-vi) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, (vi) **DC_AC50@nano**

TKPP-COF + light + Fer-1, respectively.

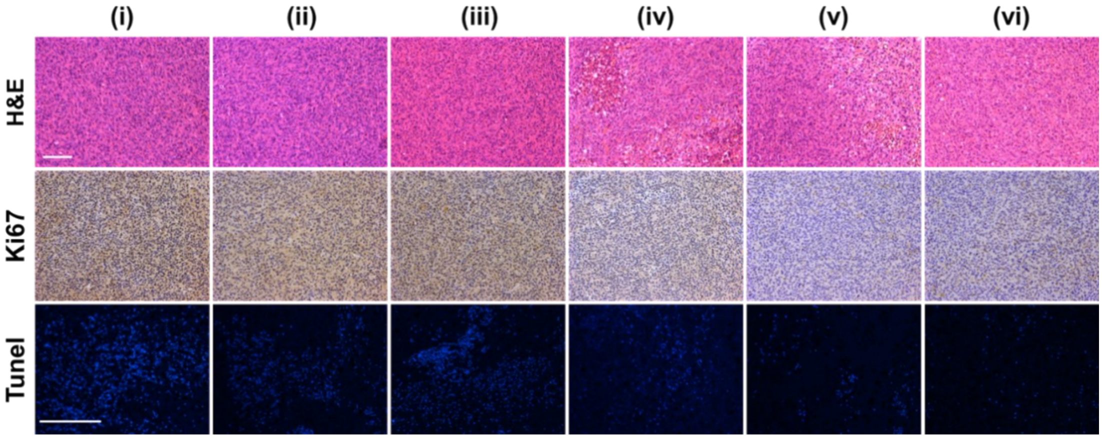


Fig. S29 Representative images of H&E, Ki67, and TUNEL staining of tumor tissues were obtained at the treatment endpoint, scale bar, 100 μm. (i-vi) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, (vi) **DC_AC50@nano TKPP-COF** + light + Fer-1, respectively.

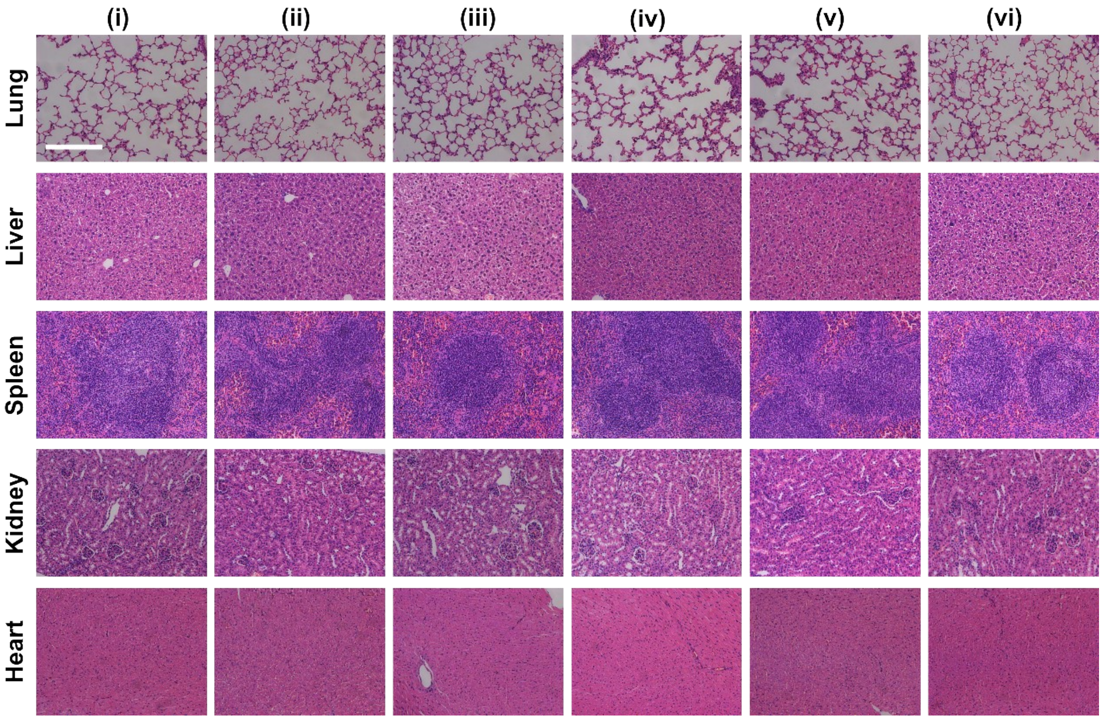


Fig. S30 H&E stained tissue sections from the lung, liver, spleen, kidney, and heart, of the nude mice at the end of the treatment. Scale bar, 200 μm. (i-vi) in the figure represent (i) control, (ii) **nano TKPP-COF**, (iii) **DC_AC50@nano TKPP-COF**, (iv) **nano TKPP-COF** + light, (v) **DC_AC50@nano TKPP-COF** + light, (vi) **DC_AC50@nano TKPP-COF** + light + Fer-1, respectively.