Supporting Information

Acid-Responsive Singlet Oxygen Nanodepot

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Experimental Section

Materials. *N,N*-diethylaminoethyl methacrylate (DEAEMA) purchased from Aldrich was removed inhibitor by distillation under vacuum and stored at -20 °C prior to use. Dulbecco's modified Eagle's medium (DMEM, GIBCO) was used as received. Methanol, dioxane, tetrahydrofuran (THF), dimethylfomamide (DMF), dimethyl sulfoxide (DMSO), and all other reagents were purchased from Adamas-beta and used as received. Water was deionized with a Milli-Q SP reagent water system (Millipore) to a specific resistivity of 18.4 MΩ cm. RAFT chain transfer agent PEG-CEP[1] was synthesized according to literature procedures.

Sample Preparation.

Synthesis of VBP. Pyridin-2(1H)-one (10 mmol), 4-chloromethylstyrene (10 mmol), K_2CO_3 (20 mmol), KI (10 mmol) and acetone (5 mL) were charged into a reaction flask, the mixture was refluxed for 12 h. After evaporating all the solvents, the residues were dissolved in CH_2Cl_2, successively washed with saturated aqueous NaCl and water, dried over anhydrous $MgSO_4$, filtered, and then concentrated on a rotary evaporator. The crude product was subjected to further purification by silica gel column chromatography using ethyl acetate/petroleum ether as the eluent, affording 1-(4-vinylbenzyl)pyridin-2(1H)-one (VBP) as a white solid (67% yield). ^{1}H NMR (Figure S1, $CDCl_3$, δ, ppm, TMS): 7.4 (6H, aromatic protons), 6.6 (1H, -C*H*=CH_2), 5.7 (1H, -CH=C*H*H), 5.2 (1H, -CH=CH*H*), 5.1 (2H, -CH_2-).

*Synthesis of **P1-P4**.* A reaction flask was charged with PEO-CEP (1 mmol), DEAEMA (0-30 mmol), VBP (45-60 mmol), AIBN (0.2 mmol) and dioxane (25 mL). The reaction system was deoxygenated and backfilled with nitrogen through three freeze-vacuum-thaw cycles. Polymerization was performed at 70 °C for 8 h. Monomers and other impurities were removed by precipitation three times in excess cold ether. The final polymer was dried in a vacuum oven overnight at room temperature to give a yellow sticky solid.

*RAFT End Group Removing of **P1-P4** Block Copolymers.* A glass ampoule was charged with ***P1-P4*** (100 mg), excess AIBN (5 mg), and DMSO (2 mL). The reaction system

was deoxygenated and backfilled with nitrogen through three freeze-vacuum-thaw cycles. After stirring at 70 °C for 2 h, the mixture was precipitated into an excess of diethyl ether for three times. The final product was dried in a vacuum oven overnight at room temperature to yield a white solid.

Characterization. Nuclear magnetic resonance (NMR) spectra were performed on a Bruker AV300 NMR 300 MHz spectrometer (samples dissolved in $CDCl_3$ or D_2O). The molecular weight and molecular weight distribution of the block polymers and their precursors were determined by size exclusion chromatography (SEC) with a Waters 1515 pump and a Waters 2414 differential refractive index detector set at 30 °C. The SEC separation column used two Styragel columns (HR2 and HR4) at 45 °C and THF as eluent (flow rate 1.0 mL/min). Calibration was performed using a series of low polydispersity polystyrene standards. A Hitachi H-800 electron microscope was used to acquire transmission electron microscopy (TEM) images. The sample for TEM observations was prepared by placing 10 μL of dispersion of nanoparticle (0.5 g/L) on copper grids coated with thin films of Formvar and carbon successively. Confocal lasers canning microscopy (CLSM) images were acquired using a Leica TCS SP5 microscope. Dynamic Laser Scattering (DLS) was measured using an ALV5000.

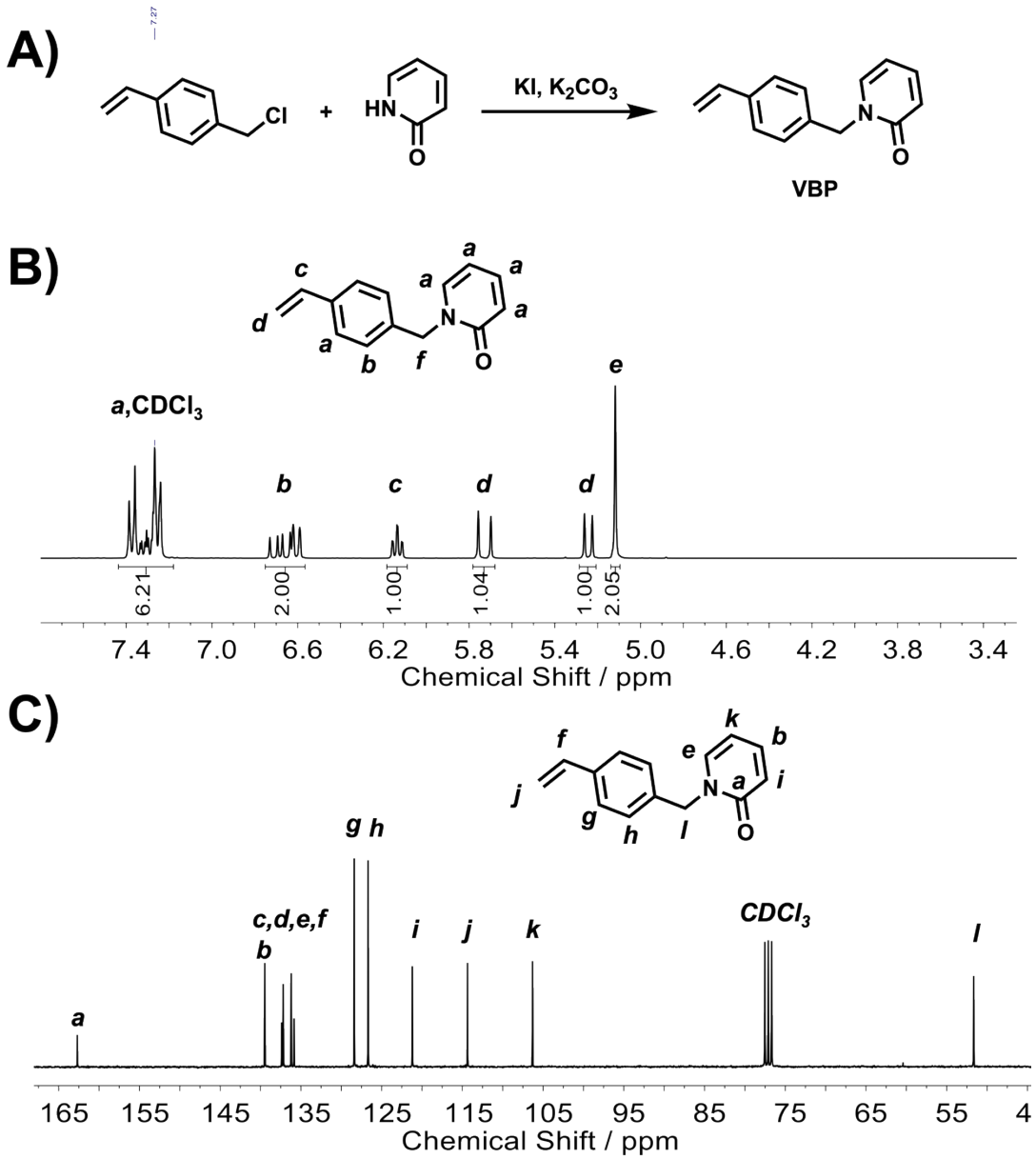

Figure S1. Synthetic schemes (A), ^{1}H NMR (B), and ^{13}C NMR (C) recorded for 1-(4-vinylbenzyl)pyridin-2(1H)-one (VBP).

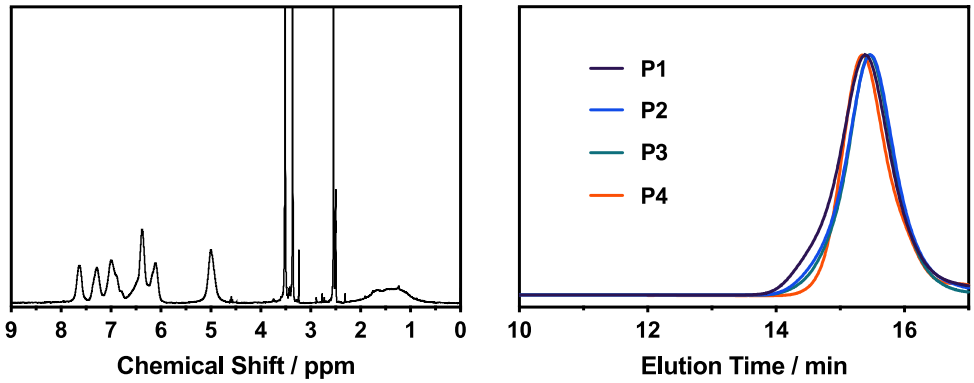

Figure S2. ^{1}H NMR spectra recorded (left) and THF GPC traces (right) for **P1-P4**.

Table S1. Molecular parameters of polymers.

Entry	$M_{n,\ NMR}$ (kDa) [a]	$M_{n,\ GPC}$ (kDa) [b]	M_w/M_n [b]
P1	15.0	16.4	1.20
P2	13.3	14.7	1.21
P3	13.5	14.9	1.23
P4	13.8	15.1	1.24

[a] Calculated from ^{1}H NMR results. [b] Determined by GPC using THF as the eluent (1.0 mL/min).

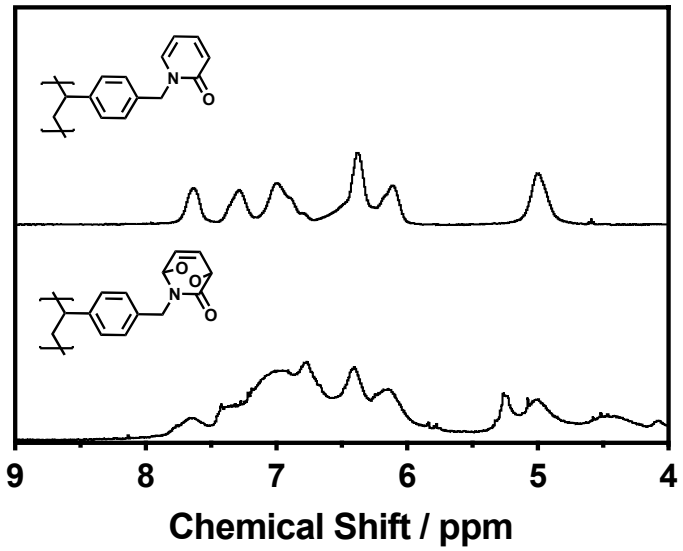

Figure S3. ^1H NMR spectra recorded in for **P1** before and after $^1O_2$ loading.

Table S2. The content of $^1O_2$ loaded on OP1-OP4.

Entry	Content of $^1O_2$ loaded [a]
OP1	51%
OP2	53%
OP3	62%
OP4	56%

[a] Calculated from ^1H NMR results.

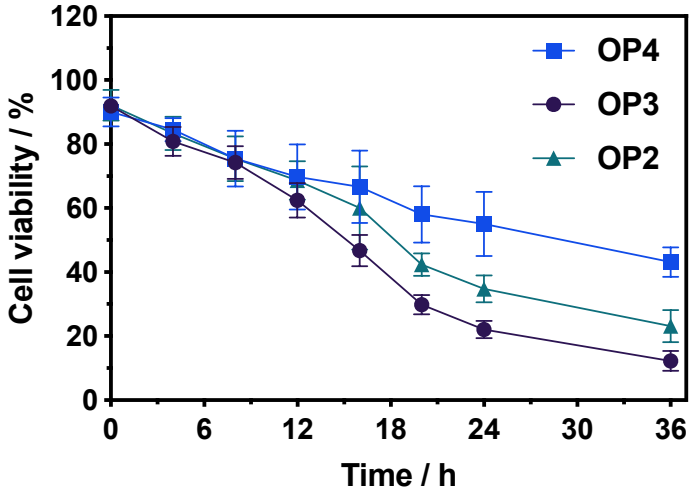

Figure S4. Time-dependent cytotoxicity of **OP2-OP4** (0.1 g/L) to HepG2 cells by MTT assay.

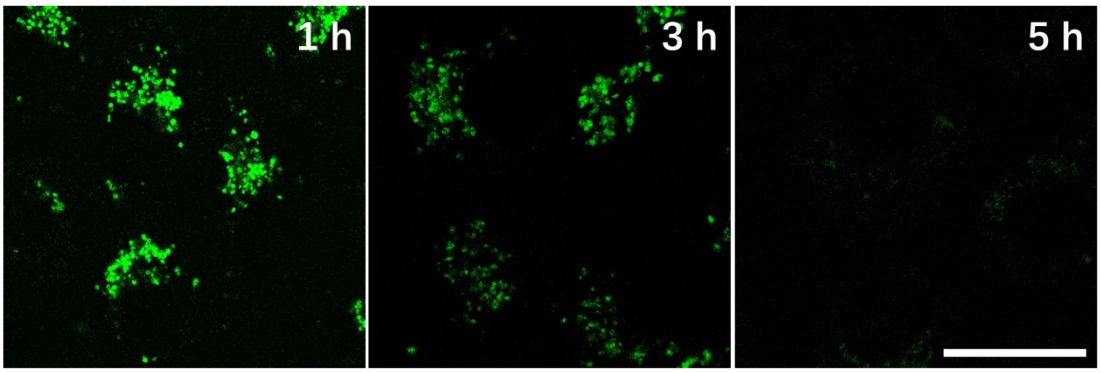

Figure S5. CLSM images of Lysotracker Green incubated with HepG2 cells after treating with **OP3** for varying times. Scale bar: 25 μm.

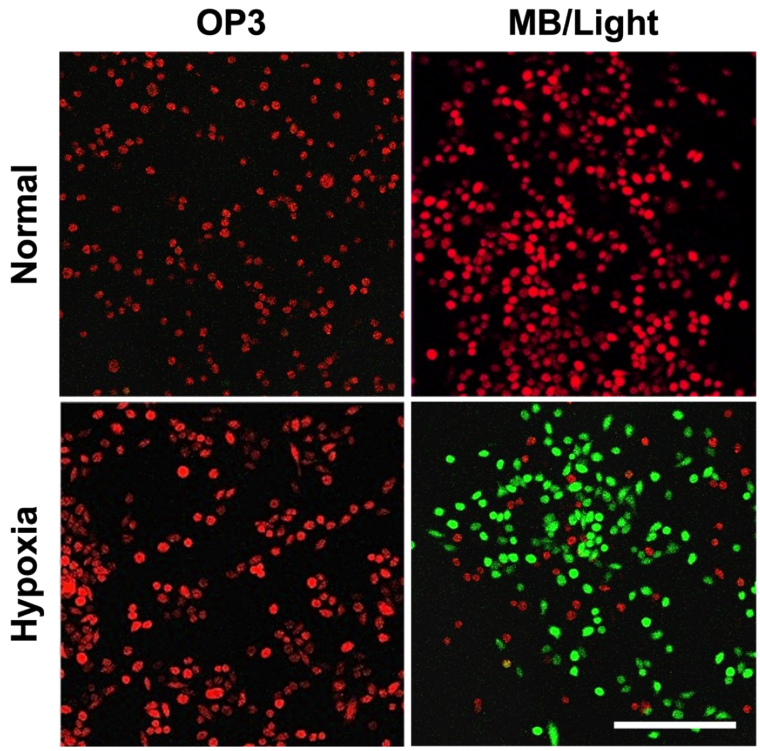

Figure S6. Live (green channel) / dead (red channel) assay with HepG2 cells incubated of **OP3** aSOND (0.1 g/L) and MB (10 μM) based PDT under normal and hypoxia condition. Green and red channel emissions were collected at 530 ± 20 nm and 610 ± 20 nm, respectively. Scale bar: 100 μm.

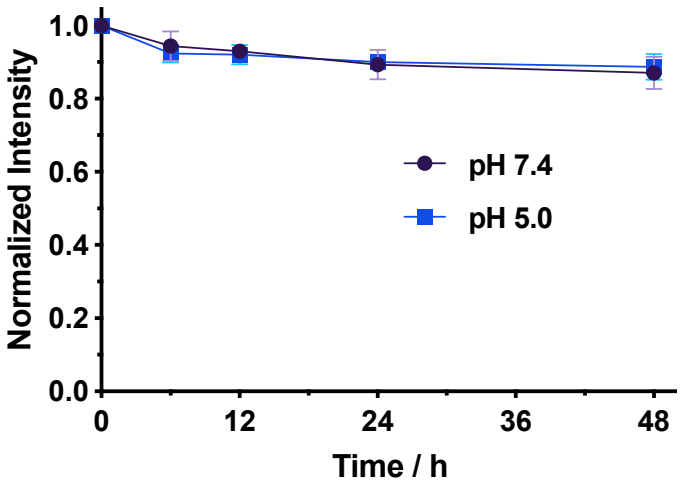

Figure S7. Fluorescence emission intensity for DOX (2 μM, λ_{ex} = 540 nm) incubating with **OP3** (0.1 g/L) at pH 7.4 and 5.0.

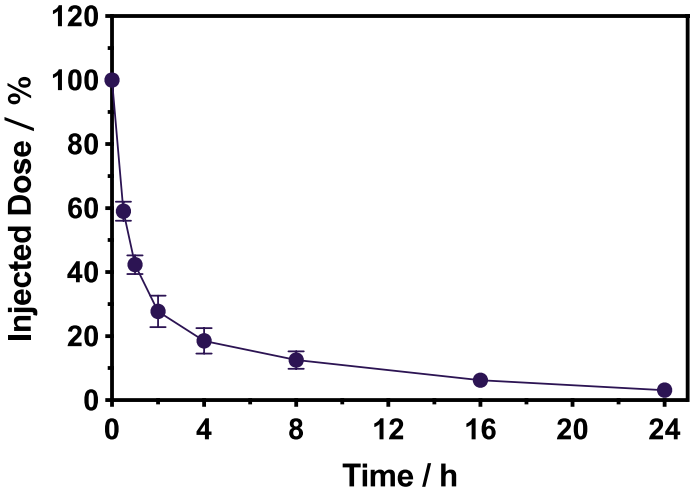

Figure S8. Time-dependent blood level upon tail vein injection of **OP5**, calculated as percentage of injected dose remaining in the blood.

1 Xu, X.; Flores, J. D.; McCormick, C. L. *Macromolecules,* 2011, **44**, 1327-1334.