Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

for

Fluorous photosensitizers enhance photodynamic therapy with perfluorocarbon nanoemulsions

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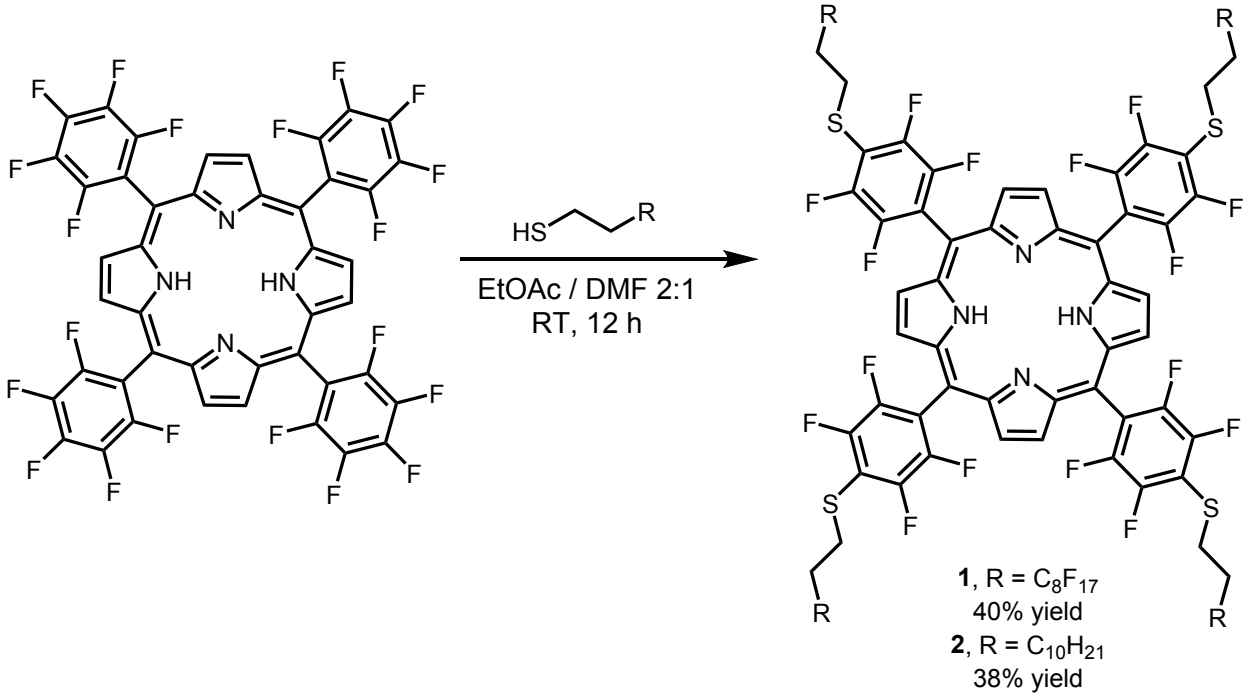
Supporting schemes

Scheme S1. Synthesis of 5,10,15,20-Tetrakis[4-(10H,10H,20H,20H-perfluorododecyl) -2,3,5,6- tetrafluorophenyl] porphyrin **1**, and 5,10,15,20-Tetrakis[4-(10H,10H,20H,20H-dodecyl) -2,3,5,6- tetrafluorophenyl] porphyrin **2**.



Supporting Figures

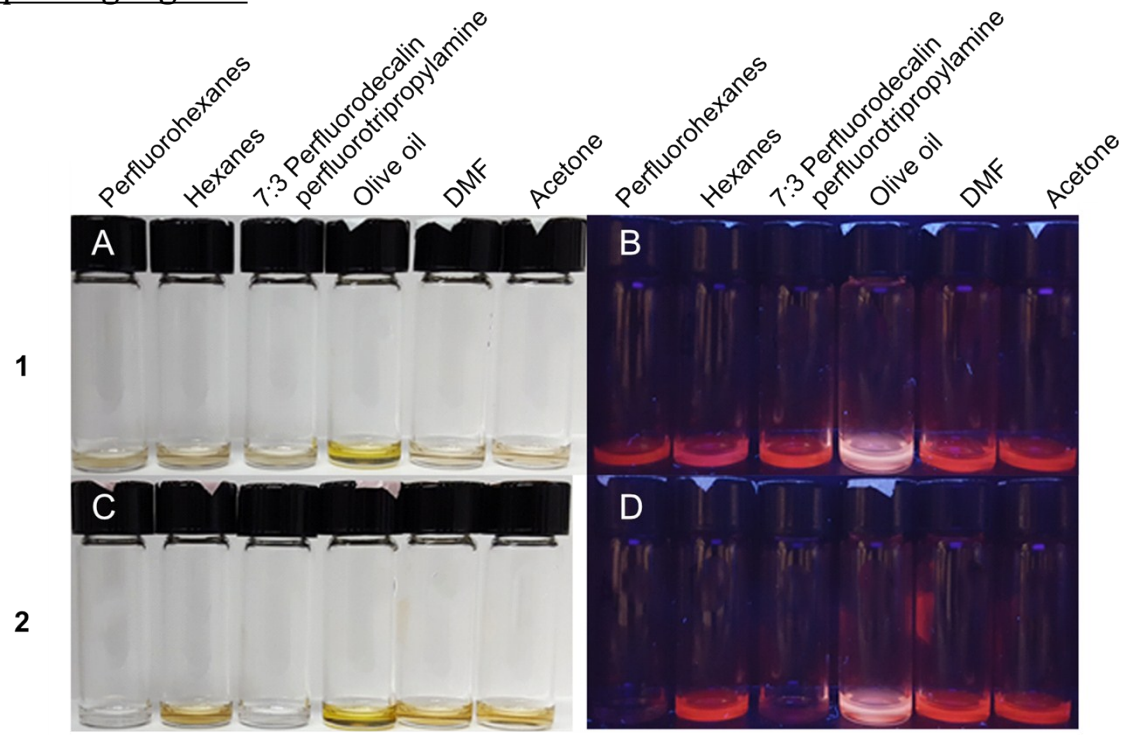


Figure S1. Solubility of photosensitizers.

Porphyrins **1** (A, B) or **2** (C, D) (18.6 nmol) were dissolved in selected solvents (200 μL). Photographs were taken in either visible (A, C) or long-wave UV light (B, D).

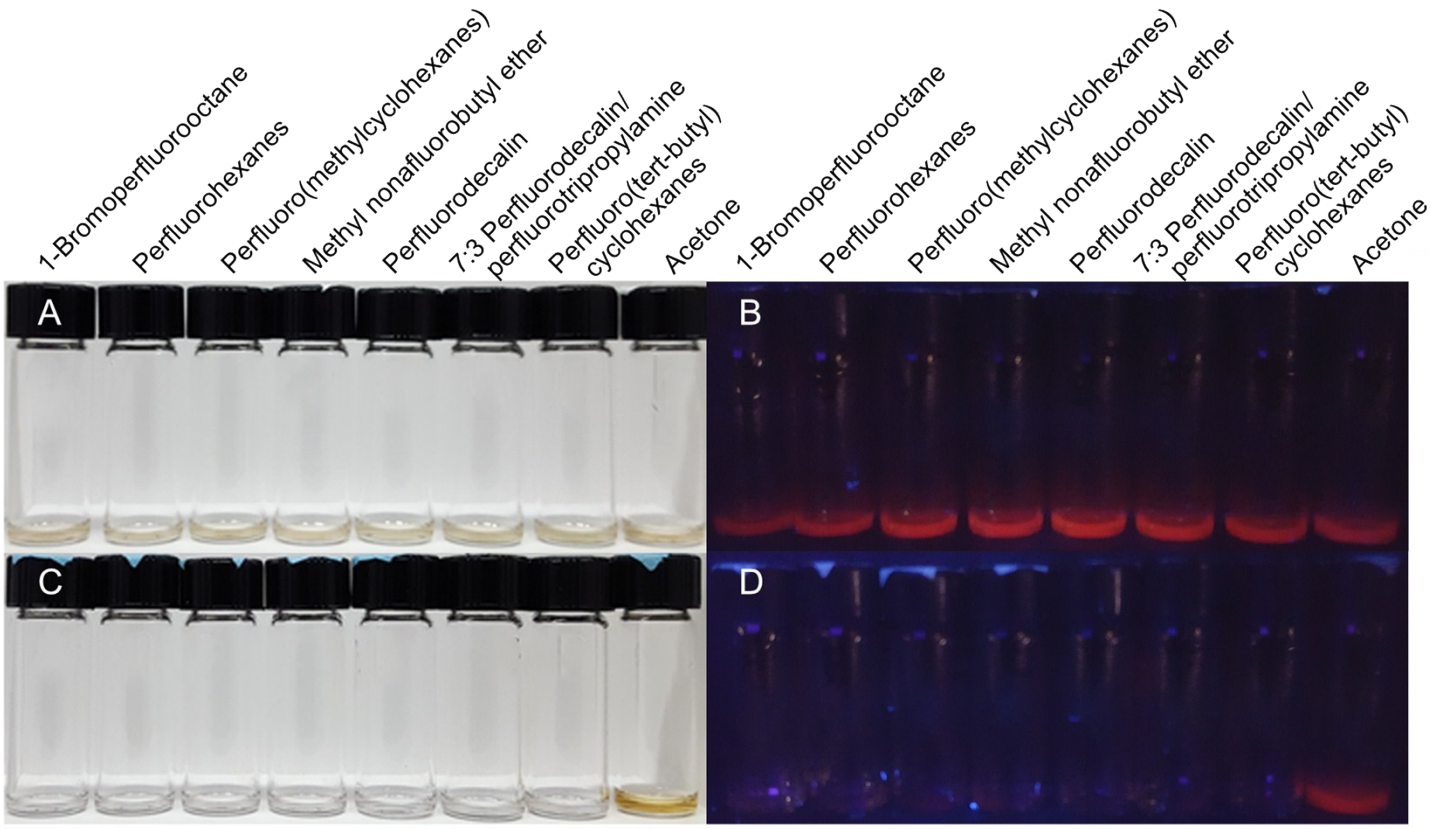


Figure S2. Solubility of photosensitizers.

Porphyrins **1** (A, B) or **2** (C, D) (18.6 nmol) were dissolved in selected fluorous solvents (200 μL). Photographs were taken in either visible (A, C) or long-wave UV light (B, D).

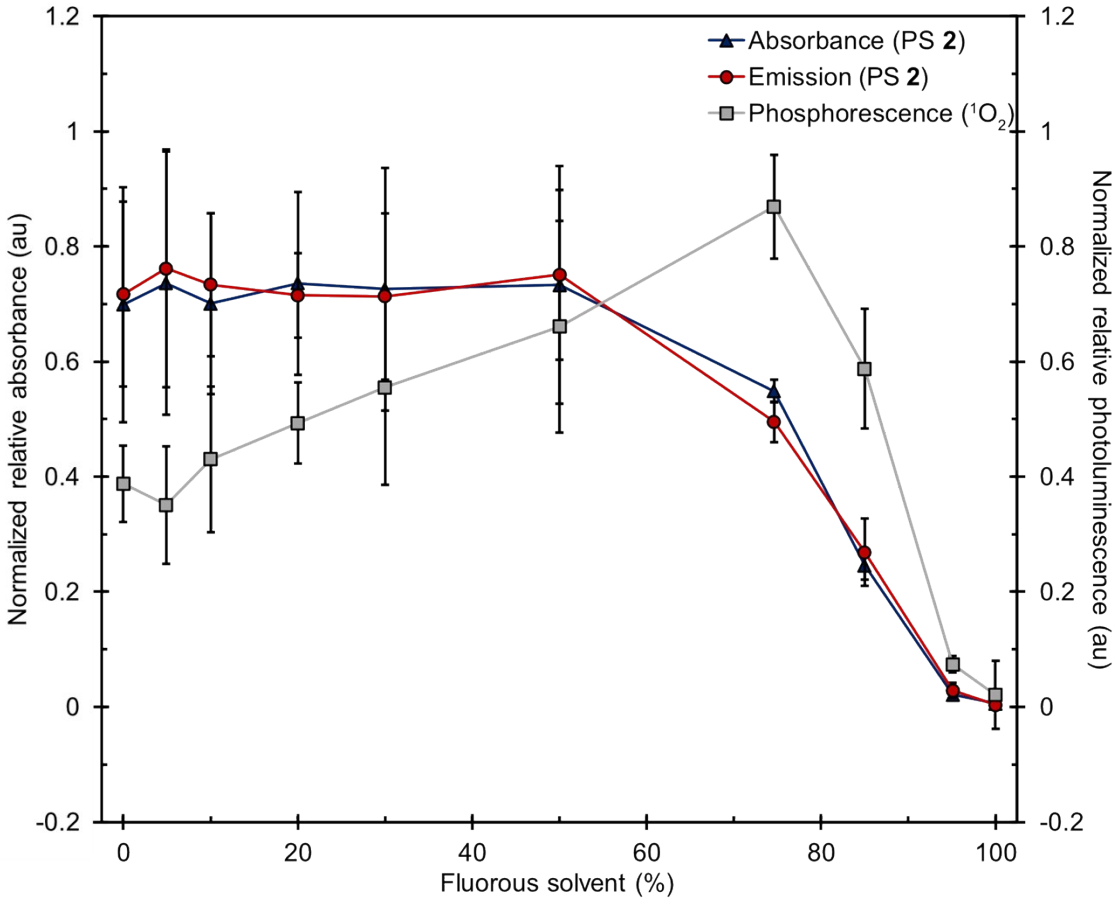


Figure S3. Aggregation of hydrophobic porphyrin **2** in fluorous solvent.
Porphyrin **2** (1.16 nmol) was dissolved in dimethylformamide with increasing amounts of methoxyperfluorobutane added (total volume = 0.75 mL). All data were normalized relative to $\lambda_{max,\ abs}$, $\lambda_{max,\ em}$, and $\lambda_{max,\ phos}$. Plotted are the averages of the normalized $\lambda_{max,abs}$ (blue, $\lambda_{max,abs}$ = 410 nm), $\lambda_{max,em}$ (red, Ex 410 nm, $\lambda_{max,em}$ = 705 nm), and $\lambda_{max,phos}$ (grey, Ex 410 nm, collected with 1000 nm longpass filter, $\lambda_{max,phos}$ = 1274 nm). Error bars represent the standard deviation of three samples.

With 50% fluorous solvent the absorbance and emission of **2** begin to decrease, indicating a loss of solubility. The $^1O_2$ phosphorescence continues to increase until 70% fluorous solvent due to the increased oxygen content in the media. After 70% fluorous solvent, decreased solubility outweighs the increased oxygen content.

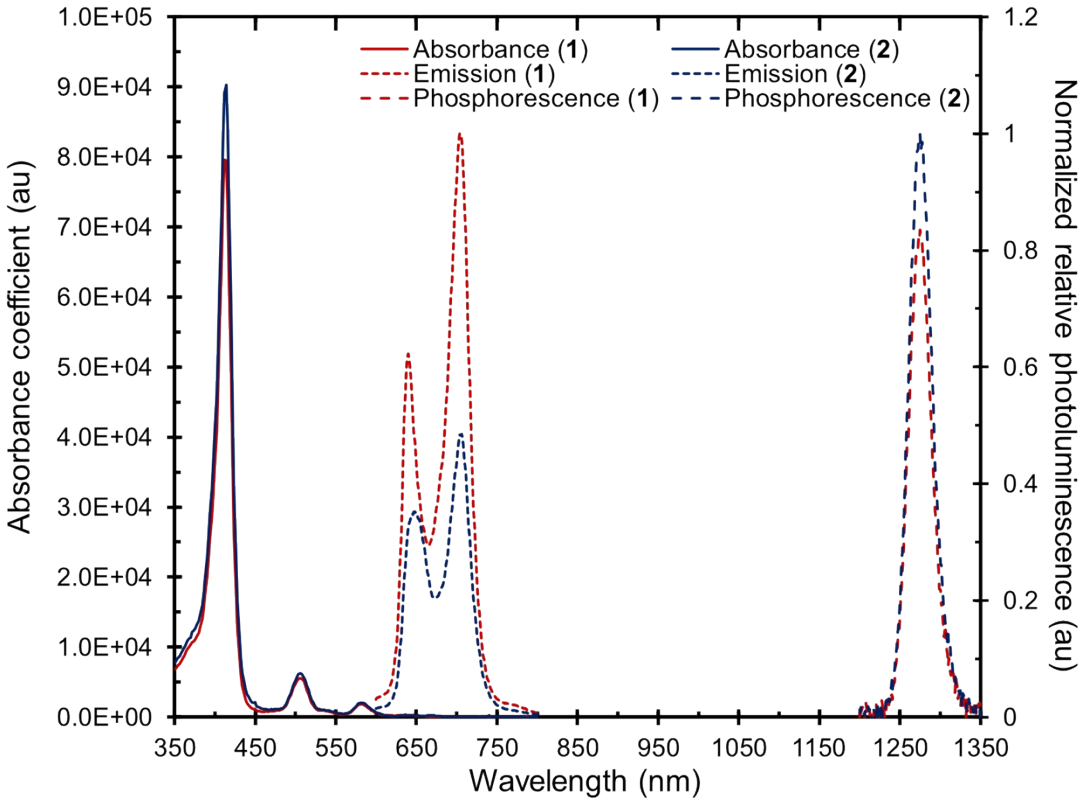
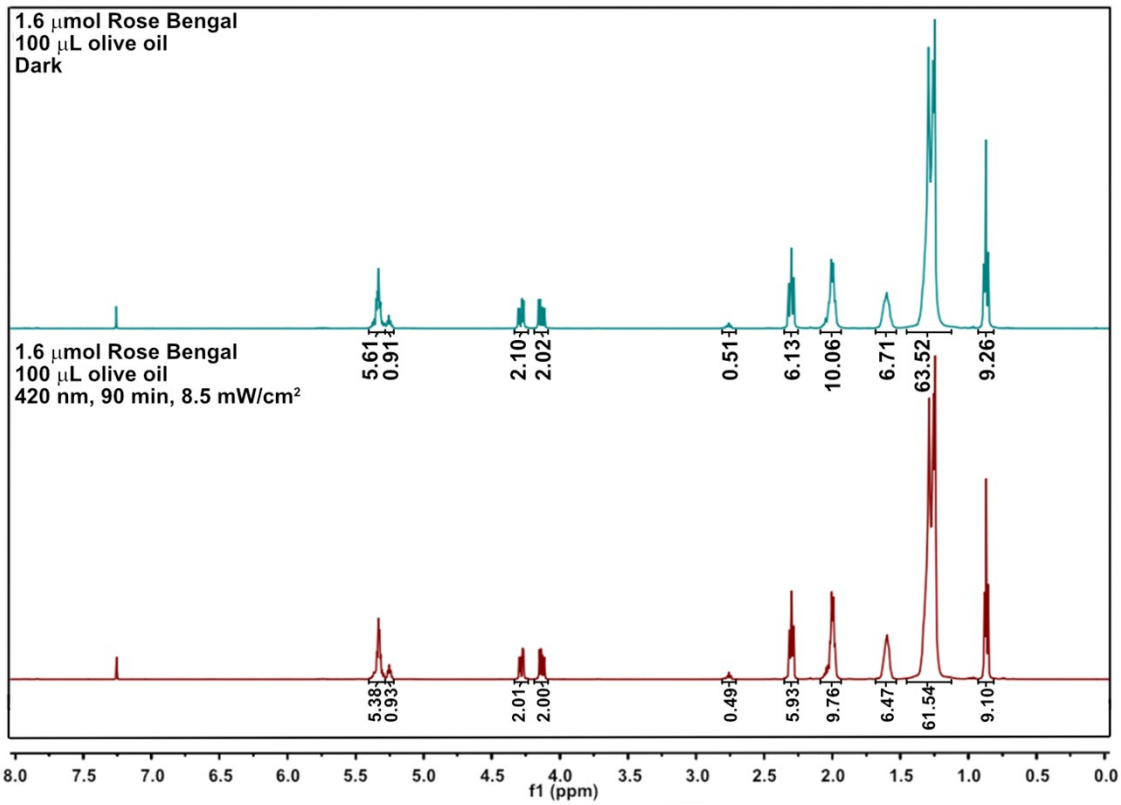


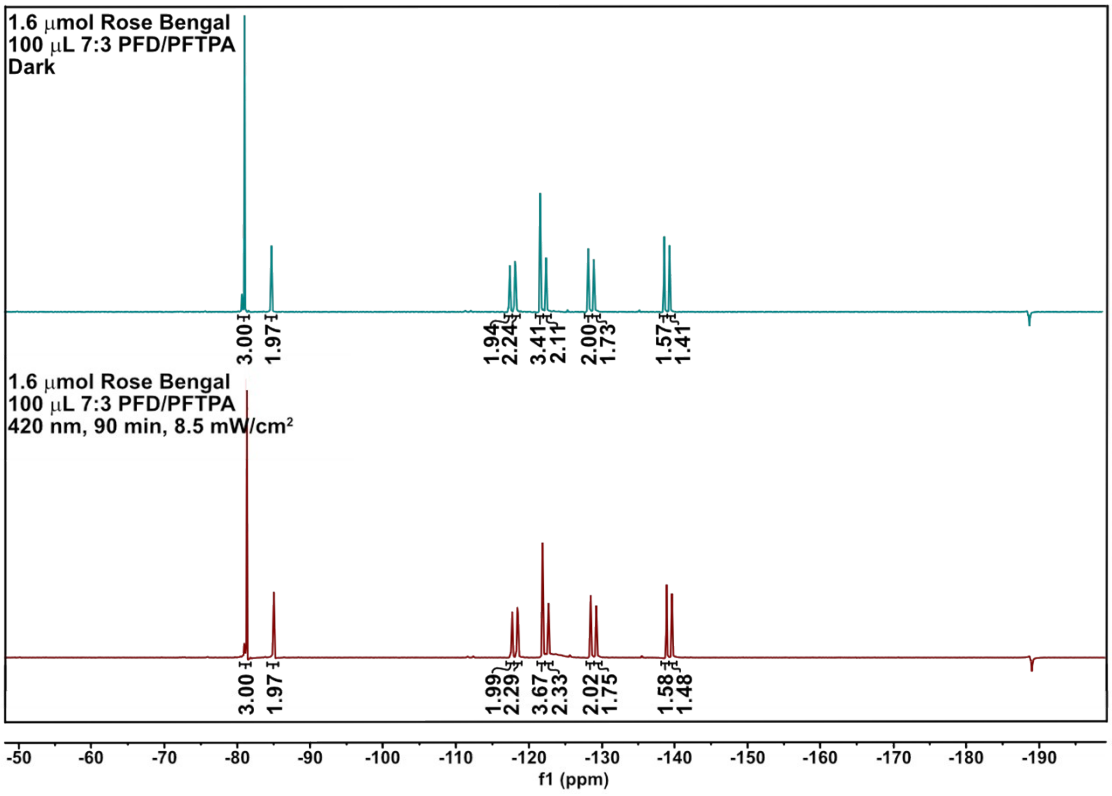
Figure S4. Characterization of porphyrins **1** and **2** in dimethylformamide (30 μM).

Absorbance coefficient (solid line), fluorescence (dotted, Ex 410 nm), and singlet oxygen phosphorescence (dashed, Ex 410 nm, collected with 1000 nm longpass filter) were measured.

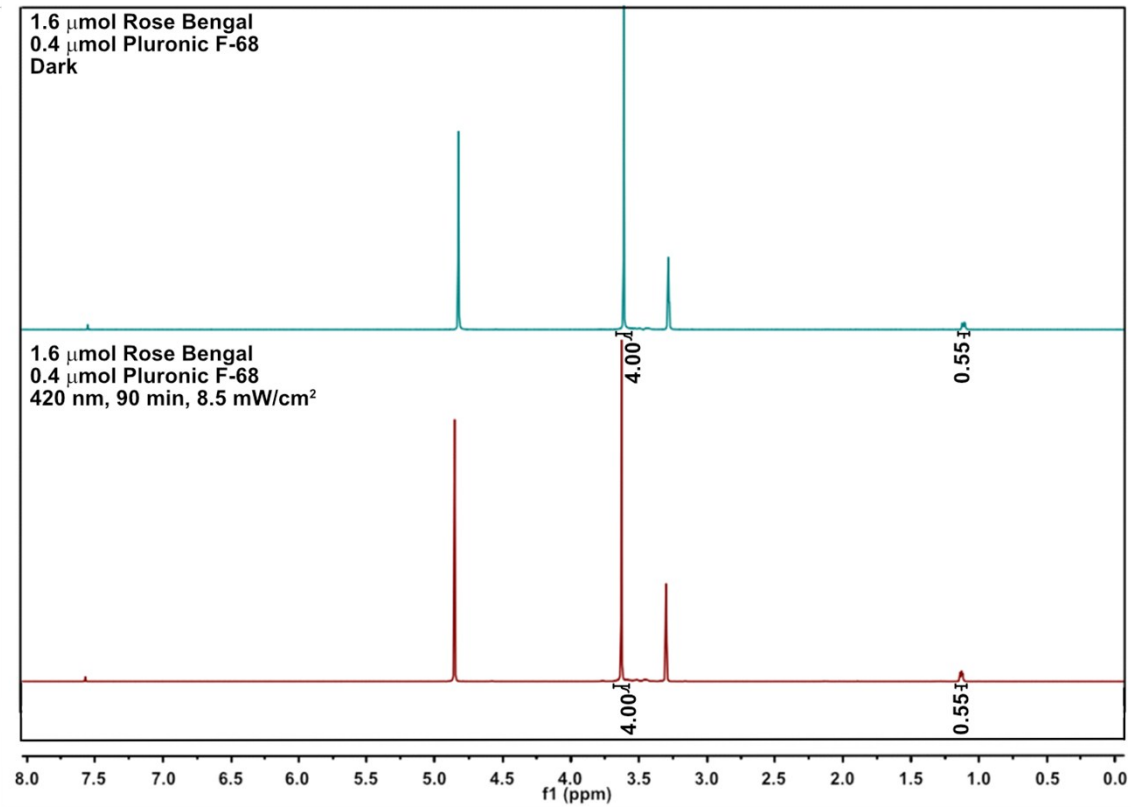
A.


1.6 μmol Rose Bengal
100 μL olive oil
Dark
5.61
0.91
2.10
2.02
0.51
6.13
10.06
6.71
63.52
9.26
1.6 μmol Rose Bengal
100 μL olive oil
420 nm, 90 min, 8.5 mW/cm²
5.38
0.93
2.01
2.00
0.49
5.93
9.76
6.47
61.54
9.10
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

B.


1.6 μmol Rose Bengal
100 μL 7:3 PFD/PFTPA
Dark
3.00
1.97
1.94
2.24
3.41
2.11
2.00
1.73
1.57
1.41
1.6 μmol Rose Bengal
100 μL 7:3 PFD/PFTPA
420 nm, 90 min, 8.5 mW/cm²
3.00
1.97
1.99
2.29
3.67
2.33
2.02
1.75
1.58
1.48
-50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

C.


1.6 μmol Rose Bengal
0.4 μmol Pluronic F-68
Dark
4.00
0.55
1.6 μmol Rose Bengal
0.4 μmol Pluronic F-68
420 nm, 90 min, 8.5 mW/cm²
4.00
0.55
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

D.

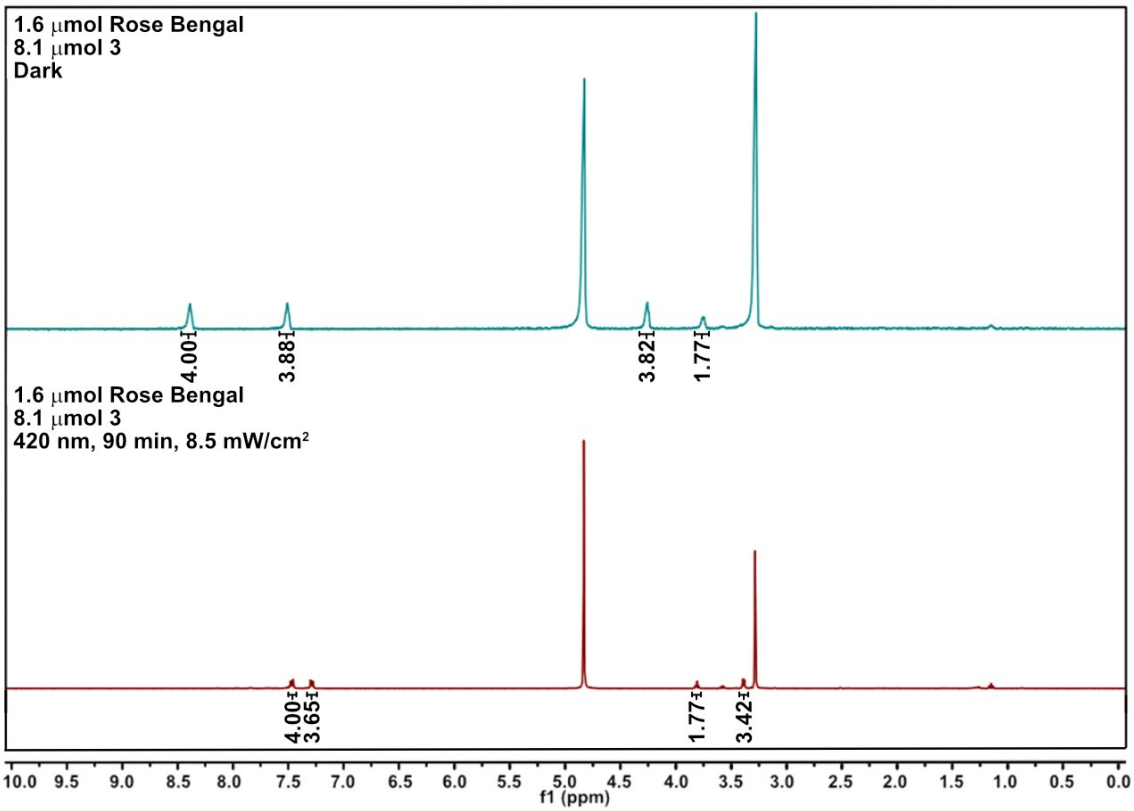

1.6 μmol Rose Bengal
8.1 μmol 3
Dark
4.00
3.88
3.82
1.77
1.6 μmol Rose Bengal
8.1 μmol 3
420 nm, 90 min, 8.5 mW/cm²
4.00
3.65
1.77
3.42
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

Figure S5. Stability of oil, perfluorocarbon solvents and Pluronic F-68 in the presence of $^1O_2$.

(A) Rose Bengal (1.6 μmol) and olive oil (100 μL) were combined in $CDCl_3$ (0.5 mL) and kept in the dark or irradiated with light. ^1H-NMR spectra were collected. (B) Rose Bengal (1.6 μmol) and 7:3 perfluorodecalin/perfluorotripropylamine (100 μL) were combined in $CDCl_3$ and kept in the dark or irradiated with light. ^{19}F-NMR spectra were collected. (C) Rose Bengal (1.6 μmol) and Pluronic F-68 (0.4 μmol) were combined in CD_3OD (0.5 mL) and kept in the dark or irradiated with light. ^1H-NMR spectra were collected. (D) Rose Bengal (1.6 μmol) and **3** (8.1 μmol) were combined in $CDCl_3$ (0.5 mL) and kept in the dark or irradiated with light. ^1H-NMR spectra were collected. (A-D) Dark samples are in the top panel (blue) and irradiated samples are in the bottom panel (red). Irradiation was performed with 420 nm, 90 min, 8.5 mW/cm^2.

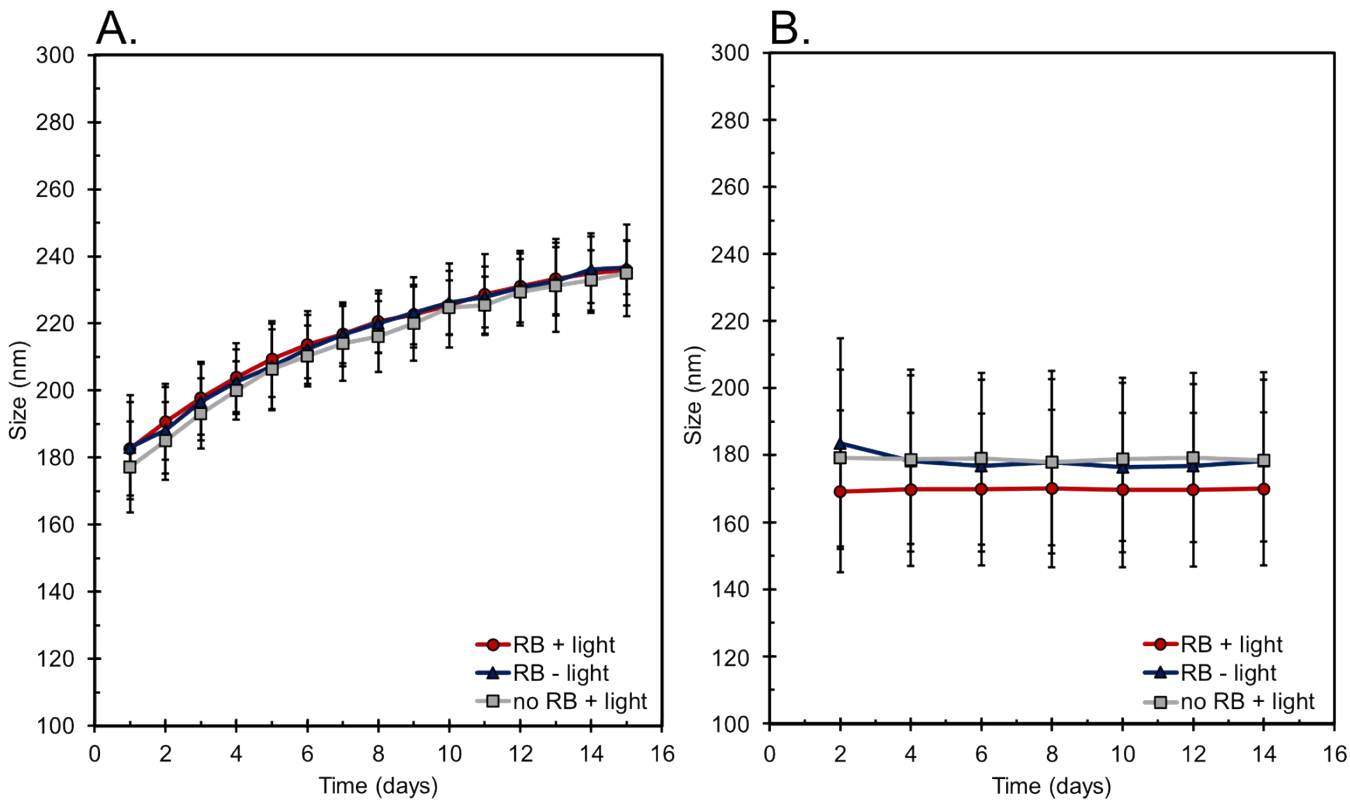


Figure S6. Stability of emulsions in the presence of $^1O_2$

(A) Perfluorocarbon nanoemulsions and (B) olive oil emulsions were prepared through ultrasonication (35% amp, 90 sec) of solutions containing fluorous or organic phase (10 vol%) and Pluronic F-68 (2.8 wt%) in phosphate buffered saline (PBS, pH 7.4). Rose Bengal (RB, 4 μM) was added to the aqueous phase (red, blue) and the size of the emulsions was monitored by dynamic light scattering (DLS) over two weeks. Emulsions were exposed to light (420 nm, 30 min, 8.5 mW/cm^2) prior to every measurement (red, grey). A no light control was also performed (blue). Error bars represent standard deviation of the product of the $Z_{average}$ and the polydispersity index of three replicate samples.

Note that all the perfluorocarbon nanoemulsions display Ostwald ripening, which has been previously characterized.[1] However, there is no difference between emulsions irradiated and not irradiated, indicating no singlet-oxygen dependent degradation.

Rose Bengal was employed as a photosensitizer rather than **1** or **2** because the absorption of **1** and **2** interfered with the 632 nm laser in the dynamic light scattering instrument.

1. A. Levin, T. O. Mason, L. Adler-Abromovich, A. K. Buell, G. Meisl, C. Galvagnion, Y. Bram, S. A. Stratford, C. M. Dobson, T. P.J. Knowles, E. Gazit. *Nature Commun.* 2014, 5, 5219-5226.

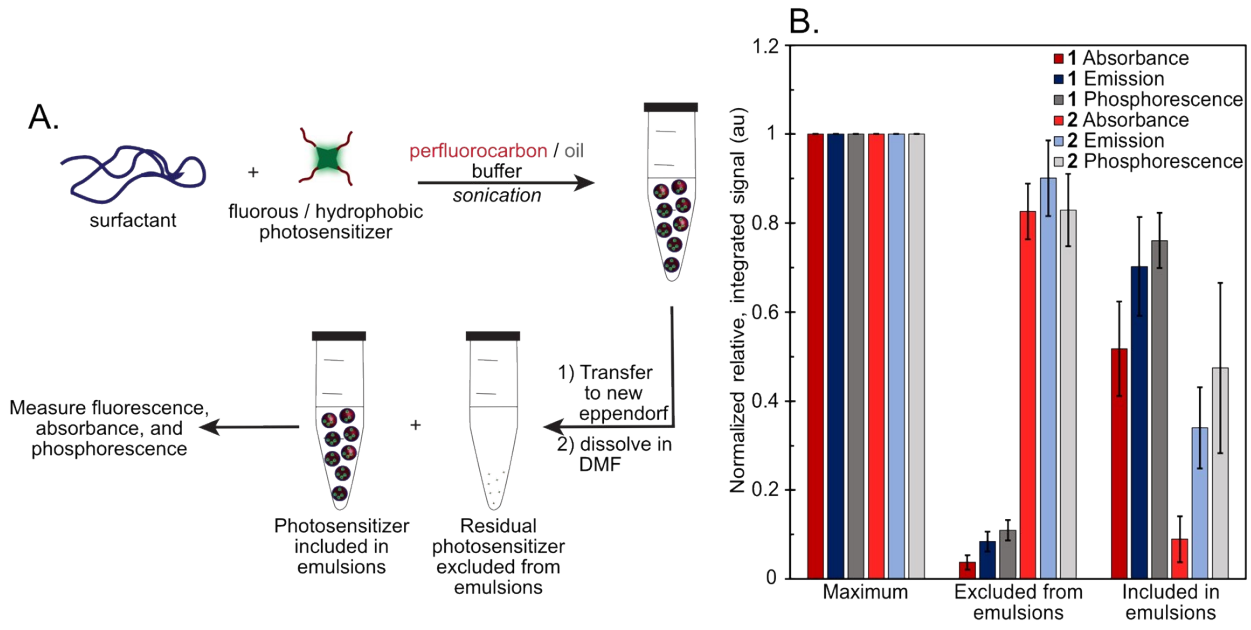


Figure S7. Analysis of the uptake of porphyrins **1** and **2** into perfluorocarbon nanoemulsions.

Porphyrin **1** or **2** (6 nmol) was dissolved in 7:3 perfluorodecalin/perfluorotripropylamine (20 μL, 10 vol%) and emulsified in the presence of Pluronic F-68 (2.8 wt%) in PBS (35% amp, 90 s, 0 ˚C). Emulsions were transferred from the Eppendorf tube in which emulsification occurred into a new Eppendorf tube. The emulsions were diluted with dichloromethane (1 mL) and then evaporated to dryness. Dimethylformamide (500 μL) was added to the original Eppendorf tube as well as the dry emulsions. Absorbance (red), fluorescence (blue, Ex 410 nm), and singlet oxygen phosphorescence (grey, Ex 410) were measured. Error bars represent the standard deviation of three samples.

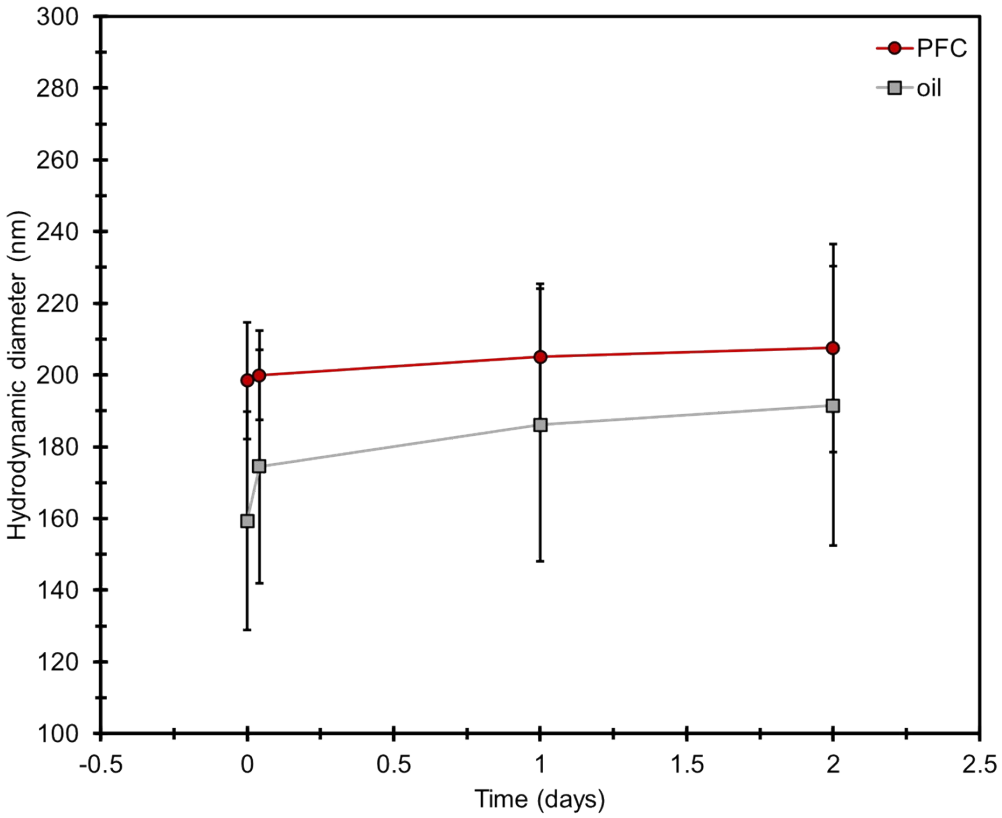


Figure S8. Stability of emulsions in presence of 1-octanol.

Perfluorocarbon (red, circle) and olive oil (grey, square) emulsions were prepared (10 vol% fluorous or organic phase, 2.8 wt% Pluronic F-68, 35% amp, 90 s) and diluted to 2 mL. Half the sample (1 mL) was taken and placed in the presence of 1-octanol (0.5 mL). The size of PFC and oil emulsions were measured before and after addition of 1-octanol, and then over three days of continuous rocking in the presence of 1-octanol. Hydrodynamic diameters were determined by dynamic light scattering. Error bars represent the standard deviation of the product of the $Z_{average}$ and the polydispersity index of three samples.

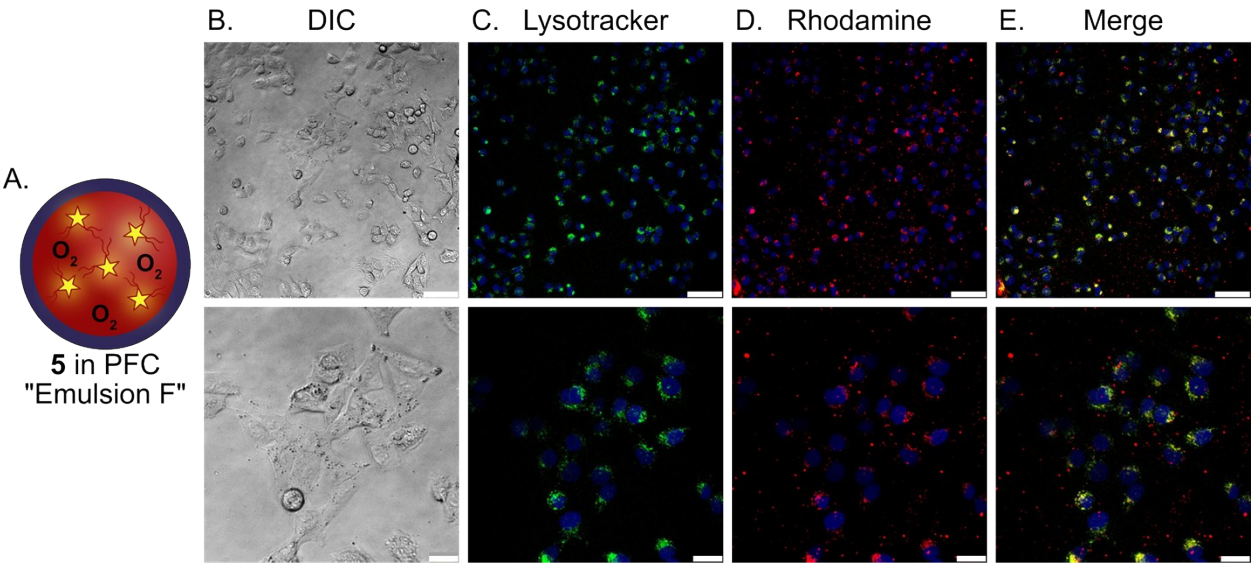


Figure S9. Colocalization of Emulsion F and Lysotracker green.

(A) Emulsion **F**. PFC emulsions containing rhodamine **5** (0.57 mM). (B/C/D/E) A375 cells were incubated with emulsion **F** for 3 h, washed, and stained with Hoechst dye and Lysotracker green. Cells were imaged via excitation at 488 nm to visualize the lysotracker green (C), 532 nm to visualize the rhodamine (D), and merged to show colocalization (E). Differential interference contrast (DIC) is shown in (B). Scale bars represent 75 μm (top panel), 25 μm (bottom panel).

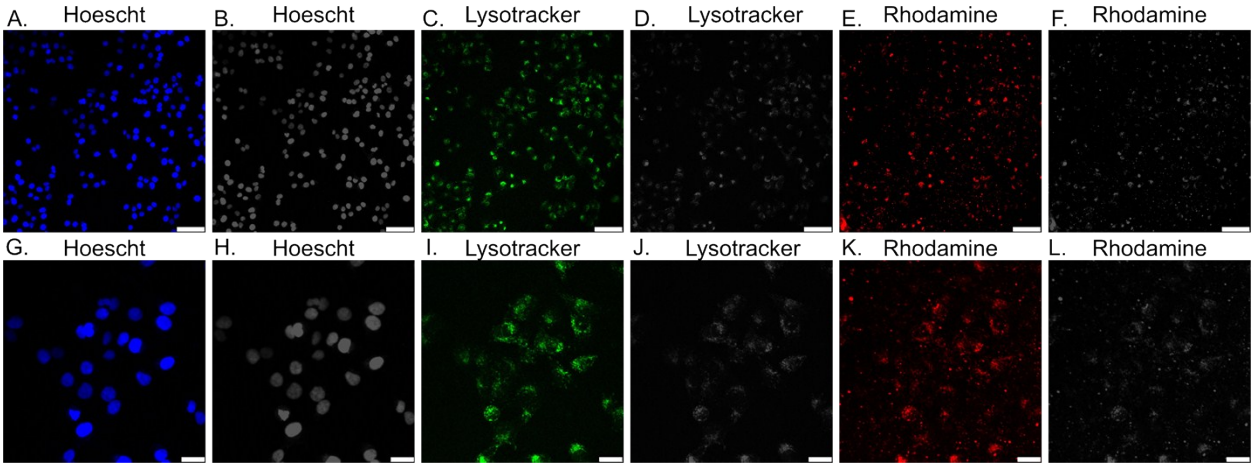


Figure S10. Single channel images for Figure S9.

Hoechst dye fluorescence (A-B, G-H), Lysotracker green (C-D, I-J), and rhodamine fluorescence (E-F, K-L) In all cases, cells were treated with Hoechst stain and Lysotracker before imaging. Scale bars represent 75 μm (top panel), 25 μm (bottom panel).

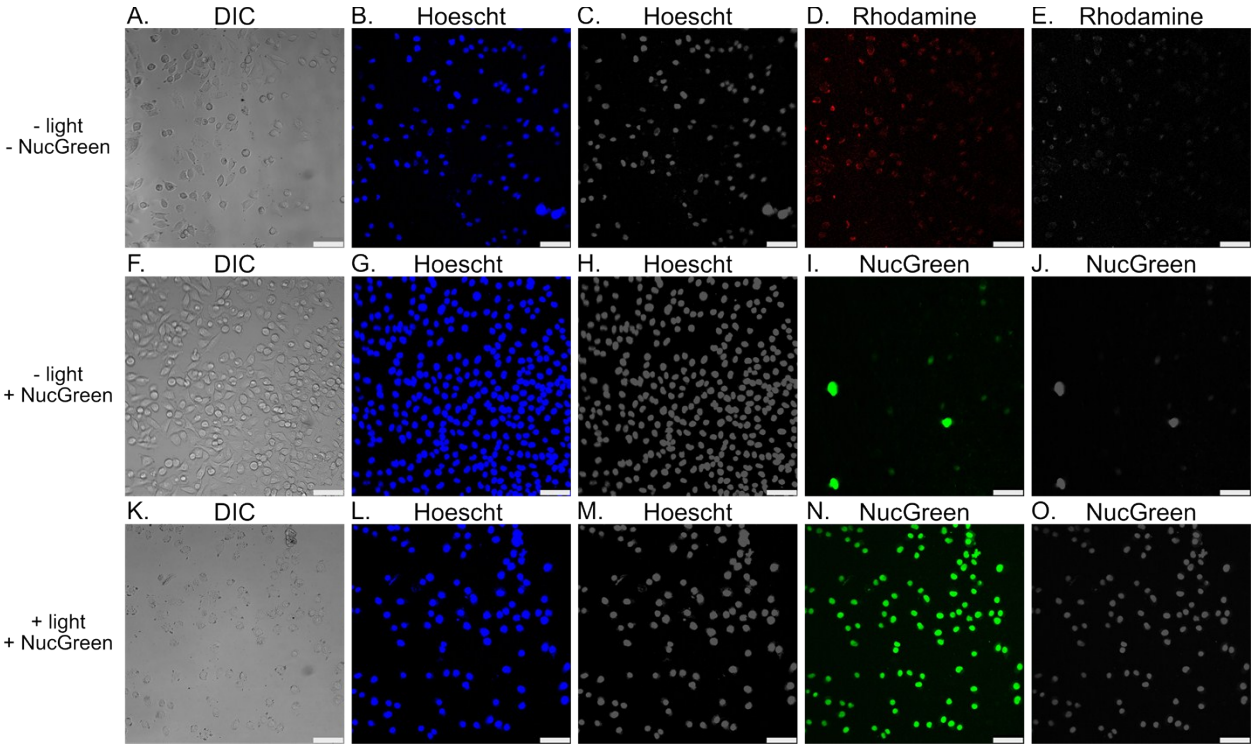


Figure S11. Single channel images for Figure 4C-E.

Differential interference contrast images (A, F, K), Hoechst dye fluorescence (B-C, G-H, L-M), rhodamine fluorescence (D-E), and NucGreen™ fluorescence (I-J, N-O). (A-E) A375 cells were treated with emulsion **E** without NucGreen™ and without light. (F-J) A375 cells treated with emulsion **E**, NucGreen™ and without light. (K-O) A375 cells treated with emulsion **E**, NucGreen™, and 420 nm light (30 min, 8.5 mW/cm^2). (A-O) In all cases, cells were treated with Hoechst stain before imaging. Scale bars represent 75 μm.

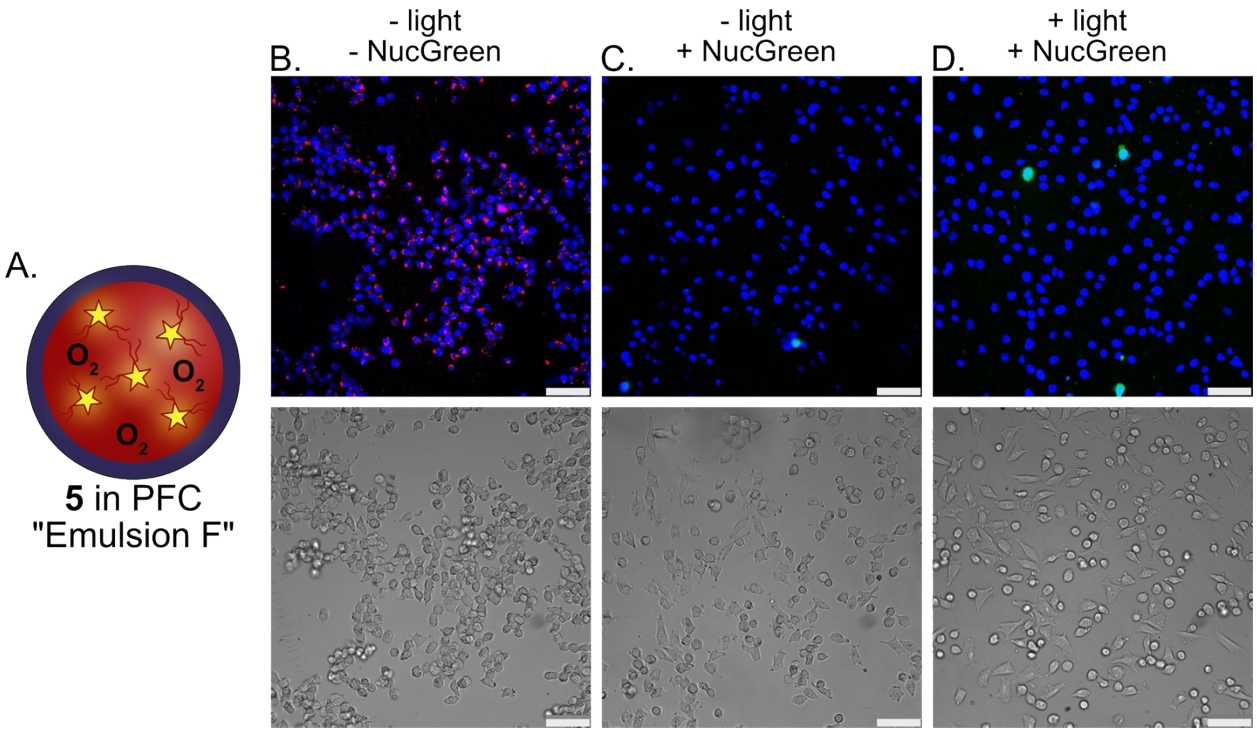


Figure S12. Control experiment for Figure 4B-E performed with emulsions containing rhodamine **5** but no photosensitizer.

(A) Emulsion **F**. PFC emulsions containing rhodamine **5** (0.57 mM). (B/C/D) A375 cells were incubated with emulsion **F** for 3 h, washed, and stained with Hoechst dye. Cells were imaged via excitation at 532 nm to visualize the rhodamine (B), then subjected to the cell death stain NucGreen™ and excited at 488 nm to visualize NucGreen™ (C), then irradiated (420 nm light, 30 min, 8.5 mW/cm^2) and again excited at 488 nm to visualize cell death via NucGreen™ (D). Scale bars represent 75 μm.

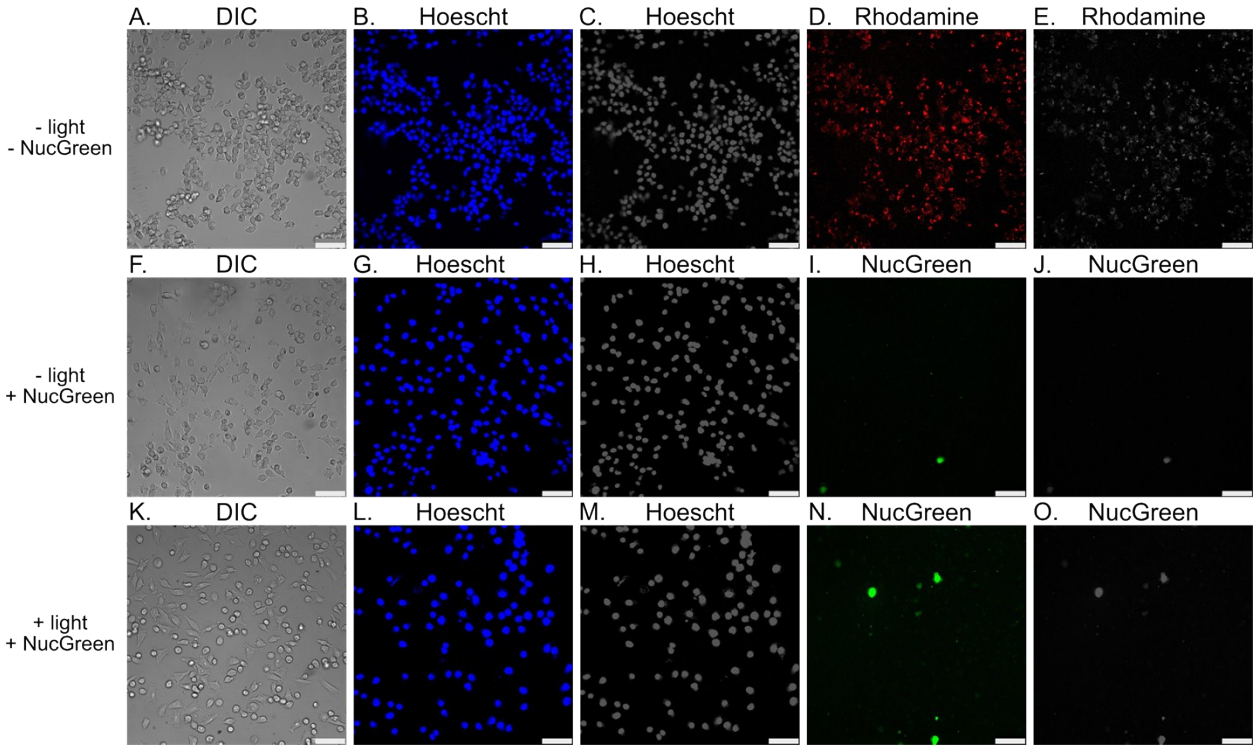


Figure S13. Single channel images for Figure S12.

Differential interference contrast images (A, F, K)**,** Hoechst dye fluorescence (B-C, G-H, L-M)**,** rhodamine fluorescence (D-E)**,** and NucGreen™ fluorescence (I-J, N-O). (A-E) A375 cells were treated with emulsion **F** without NucGreen™ and without light. (F-J) A375 cells treated with emulsion **F**, NucGreen™ and without light. (K-O) A375 cells treated with emulsion **E**, NucGreen™, and 420 nm light (30 min, 8.5 mW/cm^2). (A-O) In all cases, cells were treated with Hoechst stain before imaging. Scale bars represent 75 μm.

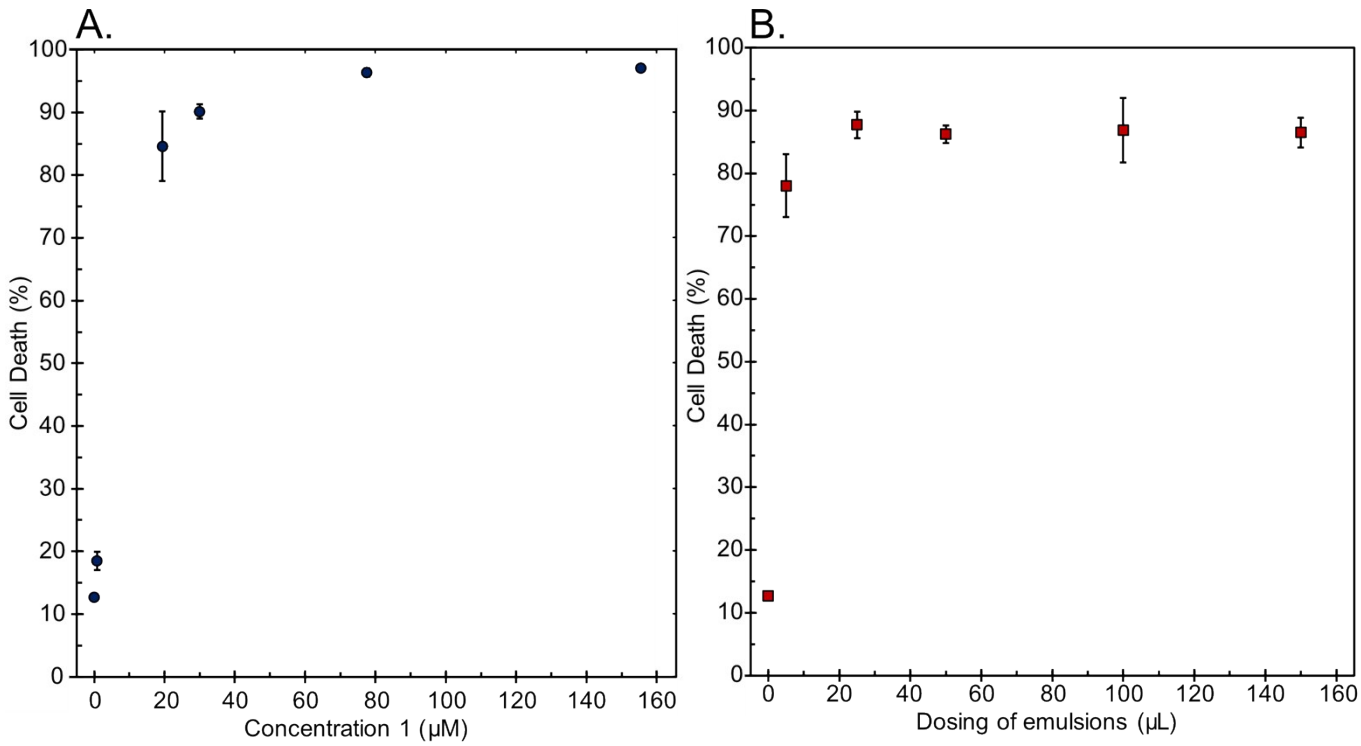


Figure S14. Dose-dependent photodynamic therapy response of emulsion **A**.

HEK293 cells were placed in a v-bottom 96-well plate (200,000 cells/150 μL/well). (A) PFC emulsions were prepared with varying concentrations of **1** (0–155 μM). The emulsions were diluted 1:5 and this dilution (50 μL) was added to HEK cells for a final volume of 200 μL per well or (B) cells were treated with varying amounts of emulsion **A** (30 μM), diluted 1:5 and varying amounts of this dilution (5-150 μL) were added to the HEK cells. The volume in each well was adjusted to 200 μL. (A/B) Cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h), washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS with 1% FBS) to a final volume of 200 μL. Cells were irradiated (30 min, 420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on FACSCalibur flow cytometer. 10,000 cells were collected per sample. Error bars represent standard deviation of three samples.

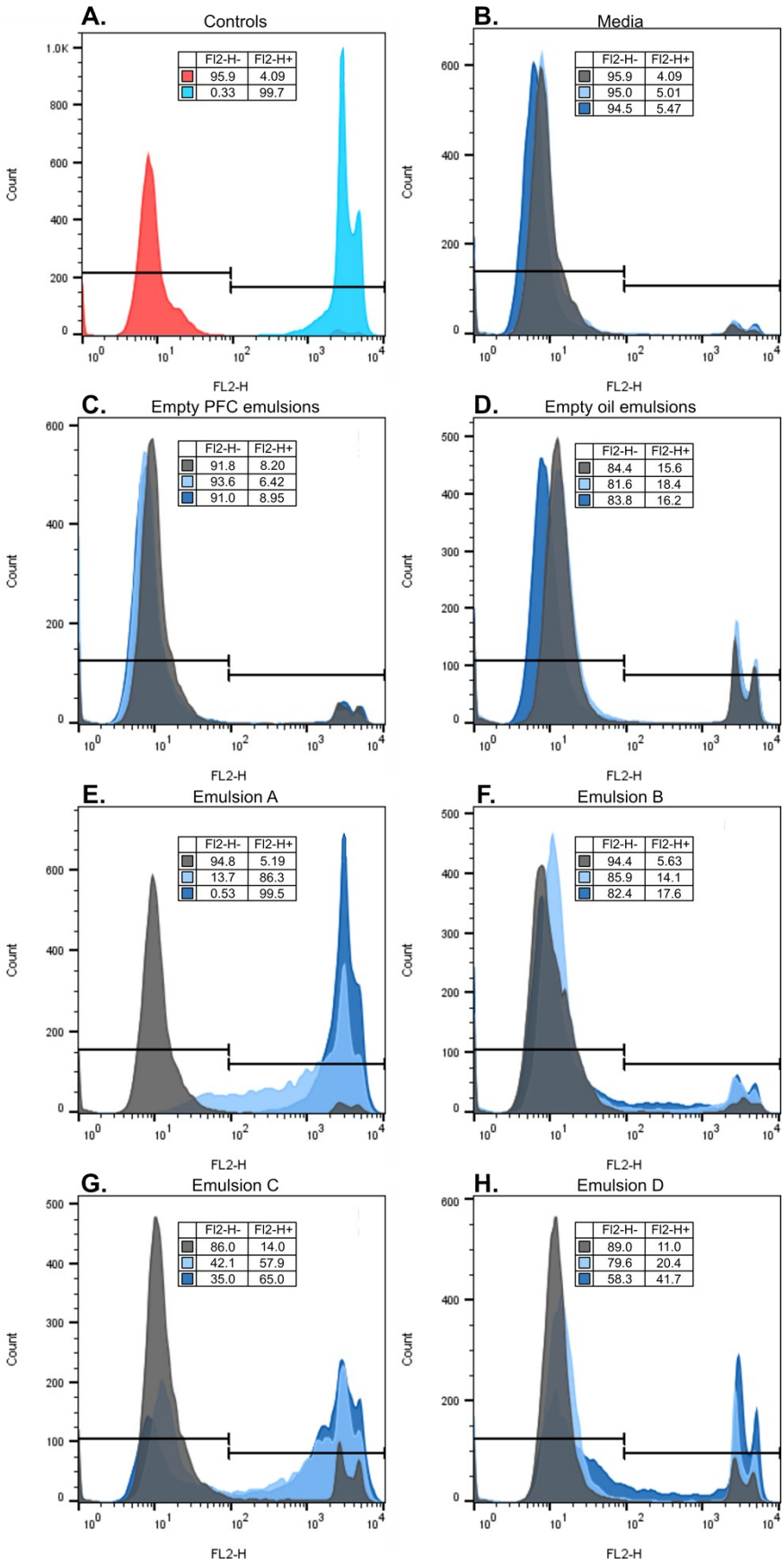

A.
Controls
Fl2-H-
Fl2-H+
95.9
4.09
0.33
99.7
B.
Media
Fl2-H-
Fl2-H+
95.9
4.09
95.0
5.01
94.5
5.47
C.
Empty PFC emulsions
Fl2-H-
Fl2-H+
91.8
8.20
93.6
6.42
91.0
8.95
D.
Empty oil emulsions
Fl2-H-
Fl2-H+
84.4
15.6
81.6
18.4
83.8
16.2
E.
Emulsion A
Fl2-H-
Fl2-H+
94.8
5.19
13.7
86.3
0.53
99.5
F.
Emulsion B
Fl2-H-
Fl2-H+
94.4
5.63
85.9
14.1
82.4
17.6
G.
Emulsion C
Fl2-H-
Fl2-H+
86.0
14.0
42.1
57.9
35.0
65.0
H.
Emulsion D
Fl2-H-
Fl2-H+
89.0
11.0
79.6
20.4
58.3
41.7
Count
FL2-H

Figure S15. Histograms for flow cytometry data in Figure 4F.

Emulsions **A**-**D** were prepared containing **1** or **2** (6 nmol). A375 cells were placed in a v-bottom 96-well plate (200,000 cells/150 μL/well). Emulsions were diluted 1:5 with PBS and this dilution (50 μL) was added to the A375 cells to give a final volume of 200 μL per well. The cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h), washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS + 1% FBS) to a final volume of 200 μL. Cells were irradiated with light for 0, 10 or 30 min (420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on a FACSCalibur flow cytometer. 15,000 cells were collected per sample. (A) Controls used to calibrate FACSCalibur. Red = heat killed cells (70 ˚C, 1 min, +PI). Blue = healthy unlabeled cells. (B) No emulsions. (C) Empty perfluorocarbon nanoemulsions. (D) Empty oil emulsions. (E-H) Emulsions **A-D**, respectively. (B-H) Grey = dark control, light blue = 10 min irradiation, and dark blue = 30 min irradiation. Irradiation = 420 nm, 8.5 mW/cm^2. (A-H) FL2-H+ shows cells with high FL2 fluorescence (dead cells). FL2-H- shows percentage cells with low FL2 fluorescence (live cells).

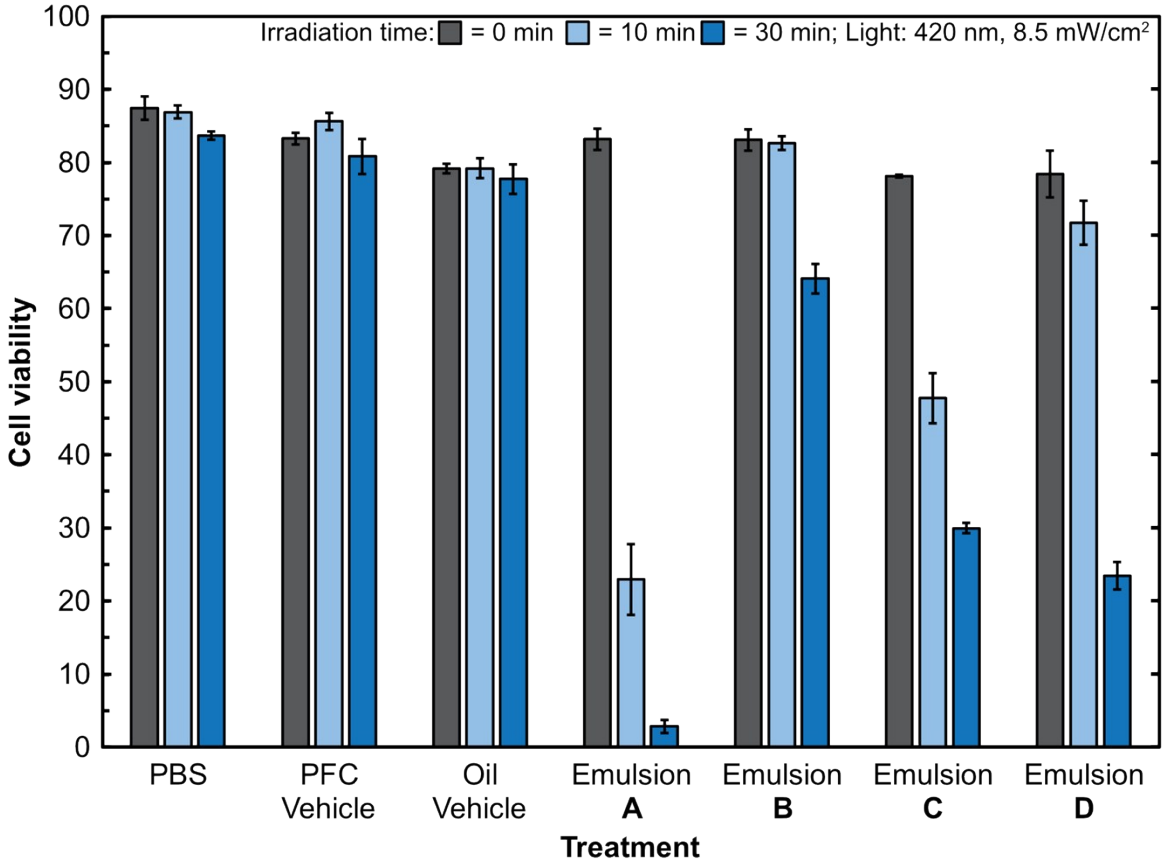


Figure S16. Photodynamic therapy response of emulsions **A**-**D** on MCF7 cells.

Emulsions **A**-**D** were prepared containing **1** or **2** (6 nmol). MCF7 cells were placed in a v-bottom 96-well plate (200,000 cells/150 μL/well). Emulsions were diluted 1:5 with PBS and this dilution (50 μL) was added to the MCF7 cells to give a final volume of 200 μL per well. The cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h), washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS + 1% FBS) to a final volume of 200 μL. Cells were irradiated with light for 0, 10 or 30 min (420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on a FACSCalibur flow cytometer. 15,000 cells were collected per sample. Error bars represent the standard deviation of 3 replicate samples.

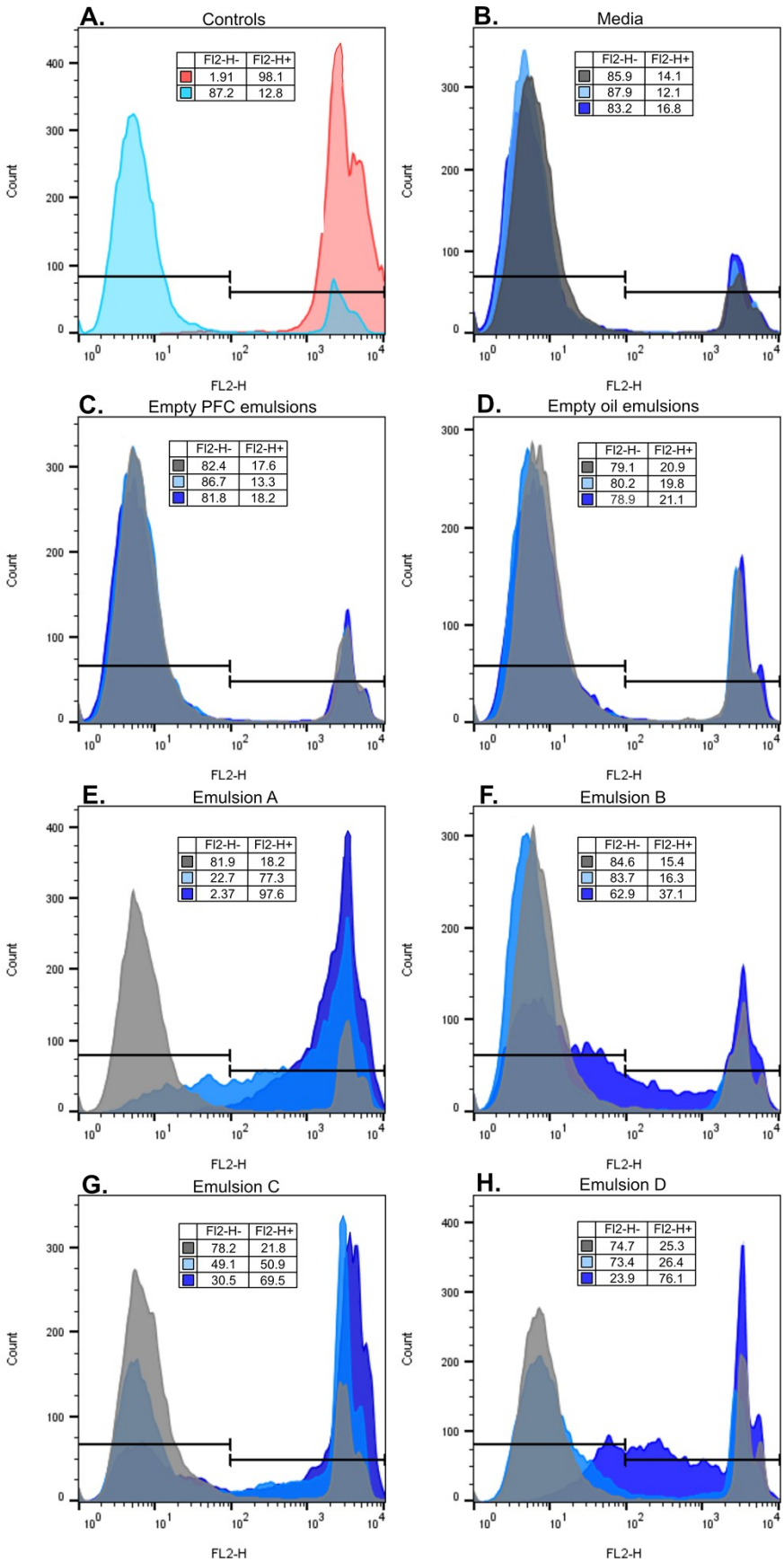

A.
Controls
Fl2-H-
Fl2-H+
1.91
98.1
87.2
12.8
B.
Media
85.9
14.1
87.9
12.1
83.2
16.8
C.
Empty PFC emulsions
82.4
17.6
86.7
13.3
81.8
18.2
D.
Empty oil emulsions
79.1
20.9
80.2
19.8
78.9
21.1
E.
Emulsion A
81.9
18.2
22.7
77.3
2.37
97.6
F.
Emulsion B
84.6
15.4
83.7
16.3
62.9
37.1
G.
Emulsion C
78.2
21.8
49.1
50.9
30.5
69.5
H.
Emulsion D
74.7
25.3
73.4
26.4
23.9
76.1
Count
FL2-H

Figure S17. Histograms for flow cytometry data in Figure 4F.

Emulsions **A**-**D** were prepared containing **1** or **2** (6 nmol). MCF7 cells were placed in a v-bottom 96-well plate (200,000 cells/150 μL/well). Emulsions were diluted 1:5 with PBS and this dilution (50 μL) was added to the MCF7 cells to give a final volume of 200 μL per well. The cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h), washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS + 1% FBS) to a final volume of 200 μL. Cells were irradiated with light for 0, 10 or 30 min (420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on a FACSCalibur flow cytometer. 15,000 cells were collected per sample. (A) Controls used to calibrate FACSCalibur. Red = heat killed cells (70 ˚C, 1 min, +PI). Blue = healthy unlabeled cells. (B) No emulsions. (C) Empty perfluorocarbon nanoemulsions. (D) Empty oil emulsions. (E-H) Emulsions **A-D**, respectively. (B-H) Grey = dark control, light blue = 10 min irradiation, and dark blue = 30 min irradiation. Irradiation = 420 nm, 8.5 mW/cm^2. (A-H) FL2-H+ shows cells with high FL2 fluorescence (dead cells). FL2-H- shows percentage cells with low FL2 fluorescence (live cells).

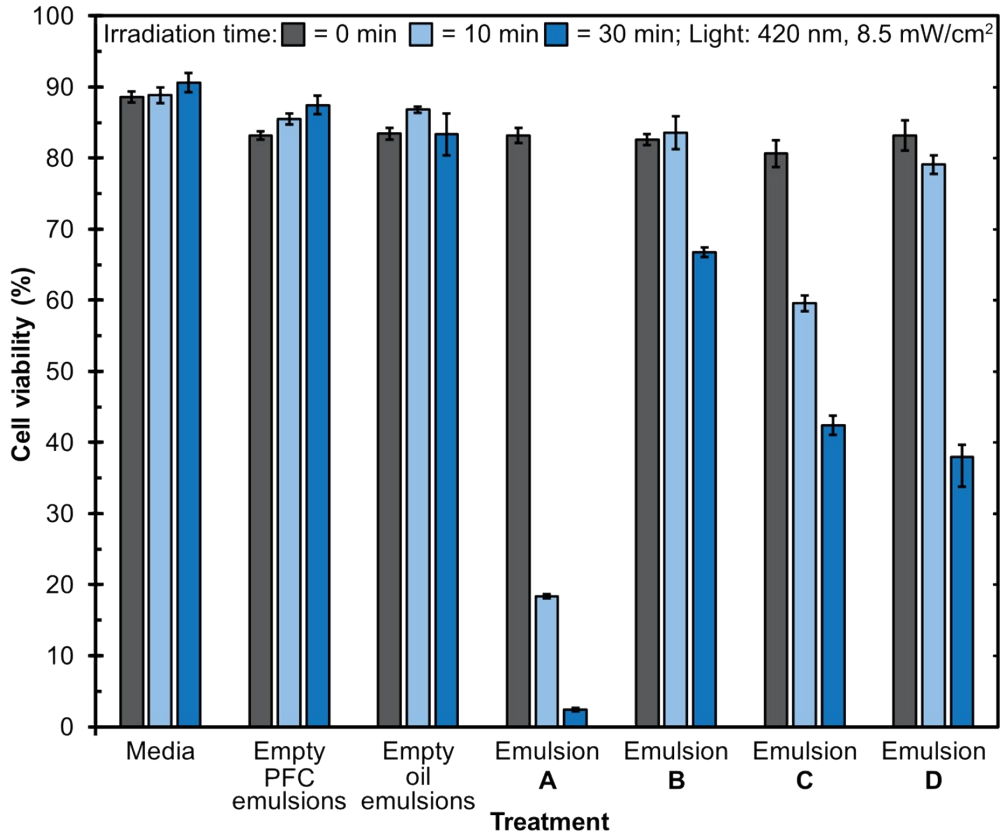


Figure S18. Photodynamic therapy response of emulsions **A**-**D** on HEK293 cells.

Emulsions **A**-**D** were prepared containing **1** or **2** (6 nmol). HEK cells were placed in a v-bottom 96-well plate (200,000 cells/150 μL/well). Emulsions were diluted 1:5 with PBS and this dilution (50 μL) was added to the HEK cells to give a final volume of 200 μL per well. The cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h), washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS + 1% FBS) to a final volume of 200 μL. Cells were irradiated with light for 0, 10 or 30 min (420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on a FACSCalibur flow cytometer. 15,000 cells were collected per sample. Error bars represent the standard deviation of 3 replicate samples.

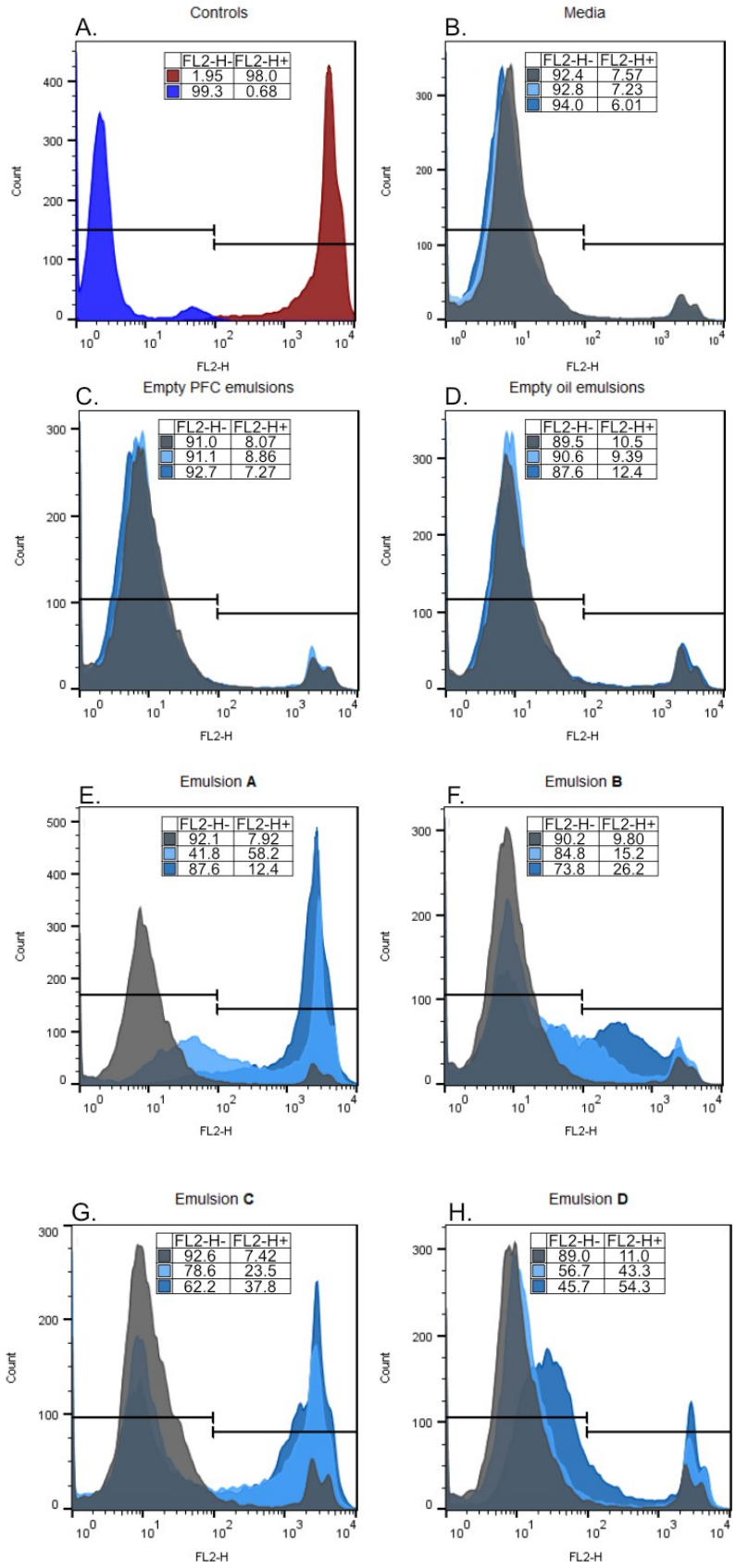

Controls
A.
FL2-H- FL2-H+
1.95 98.0
99.3 0.68
Media
B.
FL2-H- FL2-H+
92.4 7.57
92.8 7.23
94.0 6.01
Empty PFC emulsions
C.
FL2-H- FL2-H+
91.0 8.07
91.1 8.86
92.7 7.27
Empty oil emulsions
D.
FL2-H- FL2-H+
89.5 10.5
90.6 9.39
87.6 12.4
Emulsion A
E.
FL2-H- FL2-H+
92.1 7.92
41.8 58.2
87.6 12.4
Emulsion B
F.
FL2-H- FL2-H+
90.2 9.80
84.8 15.2
73.8 26.2
Emulsion C
G.
FL2-H- FL2-H+
92.6 7.42
78.6 23.5
62.2 37.8
Emulsion D
H.
FL2-H- FL2-H+
89.0 11.0
56.7 43.3
45.7 54.3
Count
FL2-H

Figure S19. Histograms for flow cytometry data in Figure S17.

Emulsions **A**-**D** were prepared containing **1** or **2** (6 nmol). HEK293 cells were placed in a v-bottom 96-well plate (200,000 cells/150 μL/well). Emulsions were diluted 1:5 with PBS and this dilution (50 μL) was added to the HEK cells to give a final volume of 200 μL per well. The cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h), washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS + 1% FBS) to a final volume of 200 μL. Cells were irradiated with light for 0, 10 or 30 min (420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on a FACSCalibur flow cytometer. 15,000 cells were collected per sample. (A) Controls used to calibrate FACSCalibur. Red = heat killed cells (70 ˚C, 1 min, +PI). Blue = healthy unlabeled cells. (B) No emulsions. (C) Empty perfluorocarbon nanoemulsions. (D) Empty oil emulsions. (E-H) Emulsions **A-D**, respectively. (B-H) Grey = dark control, light blue = 10 min irradiation, and dark blue = 30 min irradiation. Irradiation = 420 nm, 8.5 mW/cm^2. (A-H) FL2-H+ shows cells with high FL2 fluorescence (dead cells). FL2-H- shows percentage cells with low FL2 fluorescence (live cells).

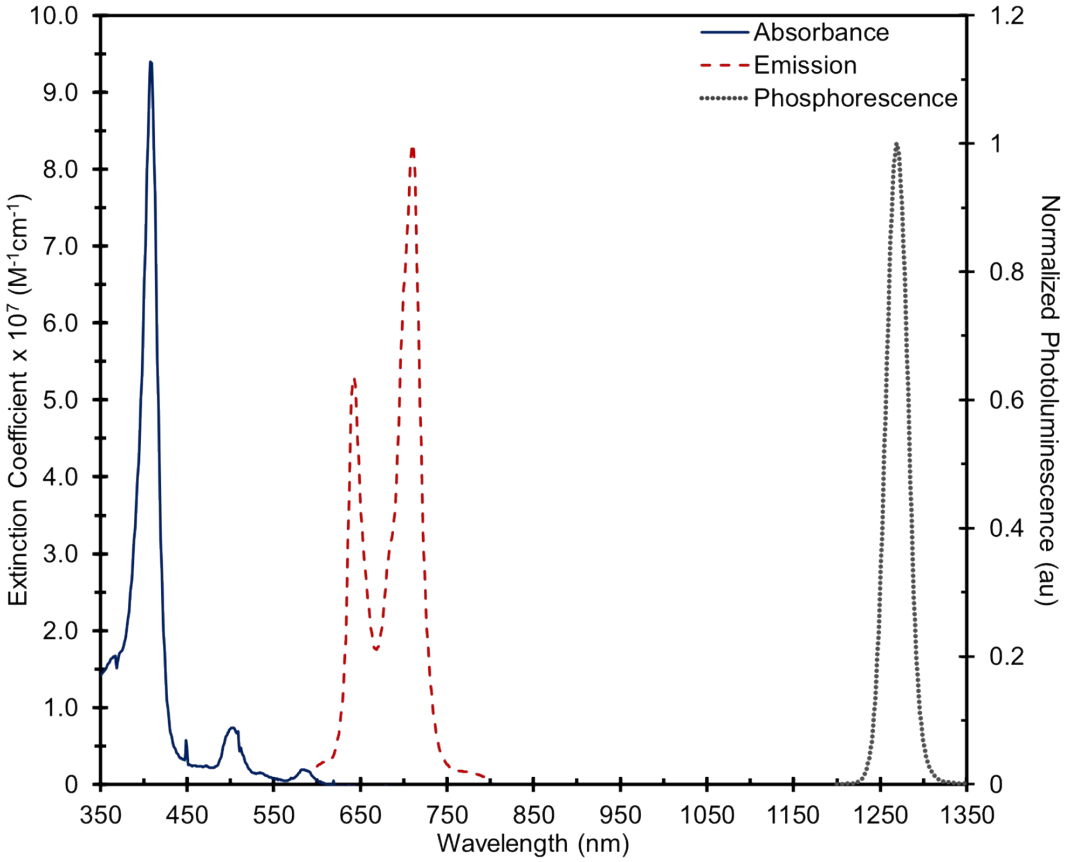


Figure S20. Characterization of fluorous porphyrin **1** in 7:3 perfluorodecalin/perfluorotripropylamine (30 μM).

Absorbance (blue), fluorescence (red-dashed, Ex 410 nm), and singlet oxygen phosphorescence (grey-dotted, Ex 410 nm, collected with 1000 nm longpass filter) were measured.

General experimental procedures

Chemical reagents were purchased from Sigma-Aldrich, TCI America or Acros Organics and used without purification unless noted otherwise. Anhydrous and deoxygenated dimethylformamide (DMF) was dispensed from a Grubb's-type Phoenix Solvent Drying System. Thin layer chromatography was performed using Silica Gel 60 F_{254} (EMD Millipore) plates. Flash chromatography was performed with technical grade silica gel with 60 Å pores and 40–63 μm mesh particle size (Sorbtech Technologies). Solvent was removed under reduced pressure with a Büchi Rotovapor with a Welch self-cleaning dry vacuum pump and further dried with a Welch DuoSeal pump. Bath sonication was performed using a Branson 3800 ultrasonic cleaner. Emulsions were prepared using a QSonica (Q125) sonicator. Nuclear magnetic resonance (^{1}H NMR and ^{19}F NMR) spectra were taken on Bruker Avance 500 (^{1}H NMR), Bruker Avance 400 (^{1}H NMR, ^{19}F NMR) or Bruker Avance 300 (^{19}F NMR) instruments and processed with TopSpin or MNova software. Size and surface charge were measured with Malvern Zetasizer Nano instrument.

General photophysics procedures

Absorbance spectra were collected on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 4000 nm/min scan rate after blanking with the appropriate solvent. Photoluminescence spectra were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer. Quartz cuvettes (1 cm) were used for absorbance and photoluminescence measurements unless otherwise noted. Extinction coefficients were calculated with serial dilutions in DMF in volumetric glassware. Error was taken as the standard deviation of the triplicate measurement. Relative singlet oxygen quantum yields were determined in DMF as described in relative quantum yield experimental procedure. Absolute quantum yields were determined in acetone with an integrating sphere as described in absolute quantum yield experimental procedure.

All irradiation was performed with THORLabs M420L3 (420 nm) LED with SM1P25-A lens. Power was supplied with a KORAD KD3005D Digital-control DC Power Supply: 0-30V, 0-5A. Samples were placed 18 cm from the lens and kept in the center of the light. Power densities were measured with a FieldMate Laser Power Meter + Iris.

General cell culture procedures

HEK293 cells were donated by the lab of Professor Jorge Torres. A375 and MCF7 cells were purchased from ATCC.

HEK293 cells and A375 cells were cultured in Dulbecco's Modified Eagle Media (Life Technologies, cat# 11995073) supplemented with 10% fetal bovine serum (Corning, lot# 35016109) and 1% penicillin-streptomycin (Life Technologies, cat# 15070063). MCF7 cells were cultured in Minimal Essential Medium supplemented with 10% fetal bovine serum (Corning, lot# 35016109) and 1% penicillin-streptomycin (Life Technologies, cat# 15070063). Cells were washed with PBS, or PBS supplemented with 1% fetal bovine serum (FACS buffer). Cells were incubated at 37 ˚C, 5% CO_2, during treatments and throughout culturing, in HERACell 150i CO_2 incubators. Cells were pelleted through use of Sorvall ST 40R centrifuge. All cell work was performed in 1300 Series A2 biosafety cabinets.

For cell viability experiments: following incubation, cells were washed three times by centrifugation (526xg, 3 min, 4 ˚C). 2 μL of propidium iodide solution (1 mg/mL in PBS) was added to each well. Cells/PI were transferred to FACS tubes with a final volume of 300 μL FACS buffer (PBS + 1% FBS). Cells were incubated on ice for 15 minutes prior to flow cytometry measurement. PI fluorescence was measured on FL2 channel. Data was analyzed by splitting the population at 10^2 as a live/dead line. Flow cytometry was performed on a BDBiosciences FACSCalibur equipped with 488 nm and 635 nm lasers. For assessment of the statistical significance of differences, a one-tailed Student's t-test assuming unequal sample variance was employed.

Confocal microscopy was performed on a TCS SPE Leica confocal microscope containing 405 nm, 488 nm, 532 nm and 635 nm lasers.

Calculating quantum yield procedures

1. Relative measures of singlet oxygen quantum yield

The singlet oxygen quantum yield of a photosensitizer is defined as follows

$$QY_{\Delta s} = \left(\frac{I_{\Delta r}}{I_{\Delta s}}\right) * QY_{\Delta r} \qquad (1)$$

Where $I_{\Delta r}$ is the integral from 1200-1350 nm of singlet oxygen phosphorescence of the reference, and $I_{\Delta s}$ is of the sample. $QY_{\Delta r}$ is the known singlet oxygen quantum yield of the reference in a specified solvent.

Rose Bengal and zinc phthalocyanine were used as references in DMF. References of Rose Bengal (47%, DMF) and zinc phthalocyanine (56%, DMF)[2] were used to check the method, then used to calculate the singlet oxygen quantum yields of **1** and **2**. The following parameters were used: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time, 0.1 s. (ex: 560 nm, 660 nm, collection 1200-1350 nm).

2. R. W. Redmond, J. N. Gamlin, Photochem. Photobiol. 1999, 70, 391-475.

Each photosensitizer was excited at their respective absorbance λ_{max}, and phosphorescence was collected at a 90˚ angle to excitation. Excitation slit widths were 5 nm, and the emission slit widths were opened to 30 nm to allow maximum detection. A 1000 nm longpass filter was placed before the entrance slit of the detector to block any emission below 1000 nm, and the trace was integrated for 0.1 seconds.

2. Absolute measures of fluorescence quantum yield

The photoluminescence quantum yield of a dye or material is defined as follows

$$QY = \frac{P_E}{P_A} \qquad (2)$$

Where P_E, P_A are the number of photons absorbed and emitted respectively. To determine absolute quantum yield, we either use a known standard (relative method), or measure the number of photons absorbed and emitted independently (absolute method).

An integrating sphere is utilized to measure the absolute quantum yields, in which a standard cuvette is illuminated on all sides by scattering a laser against white Teflon. The direct scatter is diminished by a baffle, and a side port is used with a large-area detector (Horiba Instruments PTI QuantaMaster Series fluorometer). Excitation is provided by a xenon lamp and excitation monochromator, both of which are shared with

the steady state system. The sample compartment and excitation correction fixture (RCQC) are shared. An emission correction file (in quanta/nm) for the sphere/fiber/mono/PMT combination is provided (EMCORsphere). The measurement consists of two emission scans, which are excitation and emission corrected during the acquisition. Emission corrections are necessary to correct for the wavelength dependent efficiency of the detection system and to convert to quanta. Excitation corrections are recommended since they correct for fluctuation in lamp power and for intensity drifts.

The number of fluorescence quanta is found by integrating the sample emission curve without a neutral density filter over all the fluorescence. The number of absorbed quanta is given by the integral of (blank excitation curve – sample excitation curve) over the excitation wavelength. The number of emitted quanta is given by the integral of (blank emission curve – sample emission curve) over the emission range. PTI software contains an integration function. The product of the scaling factor and the absorbed/emitted quanta accounts for potential attenuation of the scattered excitation peak.

Scaling factors for the filter were calculated by finding the integration of the reference excitation without the filter divided by the reference excitation with the filter. All calculations were done through the Trace Math function of the software. The excitation traces were integrated over several ranges, giving a range of scaling factors that all gave the same quantum yield in further calculations.

Experiments were performed on 0.45 μM, 0.9 μM, and 1.8 μM of both **1** and **2** in dimethylformamide, all giving the same values.

Figure experimental procedures

Figure 2B.

The $\lambda_{max,abs}$ values were obtained in dimethylformamide (DMF) on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 2000 nm/min scan rate. Extinction coefficient values were obtained from serial dilutions using volumetric flasks. All masses were determined on a Sartorius MSE6.6S-000-DM Cubis Micro Balance. $\lambda_{max,em}$ values were obtained in DMF on a Horiba Instruments PTI QuantaMaster Series fluorometer. For the emission of **1** and **2**, the following parameters were used: slits 5 nm, step size 1 nm, integration time, 0.1 s. Emission collection were as follows: **1** and **2** (Ex 410, collection 600 – 800 nm). For the $^1O_2$ phosphorescence of **1** and **2**, the following parameters were used: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time, 0.1 s. The $^1O_2$ phosphorescence settings were as follows: **1** and **2** (Ex 410, collection 1200 – 1350 nm, 1000 nm longpass filter). The Φ_F for **1** and **2** in DMF, the following parameters were used: slits 5 nm, step size 1 nm, integration time 1.0 s. Excitation were: **1** and **2** (Ex 410, collection 390-430 nm). Emission were: **1** and **2** (Ex 410, collection 600-750 nm). Scaling factor measurements were as follows: ex_{slits} 3 nm, em_{slits} 4.2 nm, step size 1 nm, integration time, 1.0 s. Excitation were: **1** and **2** (Ex 410, collection 390-430 nm). Excitation and emission were collected of **1** and **2,** and blanks of DMF. The Φ_Δ were calculated through integration of the $^1O_2$ phosphorescence peak at 1274 nm. The following parameters were used: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time, 0.1 s. Emission were: **1** and **2** (Ex 410, collection 1200–1350 nm). References of Rose Bengal (47%, DMF) and zinc phthalocyanine (56%, DMF)[3] with the following parameters were used: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time, 0.1 s. (Ex 560 nm, 660 nm, collection 1200-1350 nm).

3. R. W. Redmond, J. N. Gamlin, Photochem. Photobiol. 1999, 70, 391-475.

Figure 2C.

Spectra were taken in hexanes and perfluorohexanes (6 nmol, 0.02 mg **1**, 0.011 mg **2**). Absorbance values were obtained on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 2000 nm/min scan rate. Emission values were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer with the following settings: slits 5 nm, step size 1 nm, integration time 0.1 s (Ex 410 nm, collection 600-800 nm). $^1O_2$ phosphorescence were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer with the following settings: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time 0.1 s, 1000nm longpass filter (Ex 410 nm, collection 1200-1350nm).

Figure 3A.

Emulsions A-D were prepared by predissolving **1** or **2** (6 nmol, 0.02 mg **1** or 0.011 mg **2**) in 7:3 perfluorodecalin/perfluorotripropylamine or in olive oil (10 vol%, 20 μL) in an

Eppendorf tube. Pluronic F-68 was predissolved in PBS pH 7.4 (28 mg/mL) and this solution (200 μL, 2.8 wt%) was added to the fluorous solvent or olive oil. Sonication (35% amp, 90 s, 0 ˚C) resulted in emulsions of sizes shown in Figure 3B and Figure 3C without filtration.

Figure 3B/C.
Empty emulsions were prepared by sonicating 7:3 perfluorodecalin/ perfluorotripropylamine (10 vol%, 20 μL) with Pluronic F-68 predissolved in PBS pH 7.4 (28 mg/mL, 2.8 wt%, 200 μL). Emulsions were diluted in MilliQ H_2O (20 μL emulsions in 2 mL MilliQ H_2O, **Ω** = -18 mV) in a plastic cuvette. The size was monitored with Malvern Zetasizer Nano dynamic light scattering and data is representative of three replicate measurements. Error bars represent the standard deviation of three measurements.

Figure 3E.
Emulsions containing **1** and **2** were prepared as described in Figure 3A**.** Emulsions were diluted in PBS (200 μL emulsion in 3 mL PBS). To this dilution was added **3** (25 μL of 1 mg/mL stock, 61 μM final concentration). This solution (1 mL) was irradiated (420 nm, 8.5 mW/cm^2) for 30 min. Emission values were collected over 30 min on a Horiba Instruments PTI QuantaMaster Series fluorometer with the following settings: ex_{slits} 5 nm, em_{slits} 2, step size 1 nm, integration time 0.1 s (ex: 375 nm, collection 390-500 nm). A control of **3** alone was irradiated (420 nm, 8.5 mW/cm^2) to determine background photobleaching. The data was integrated from 390-500 nm, and the control photobleaching of **3** was added to each data set to account for the photobleaching of **3** alone. Emulsion A is statistically significant from emulsions B-D with $p<0.001$. Statistical significance was determined with a one tailed, unequal variance T-test.

Figure 3F/G.
Emulsions containing **1** or **2** were prepared as described in Figure 3A except the concentration of **1** and **2** was 0.04 μmol (0.13 mg **1** or 0.07 mg **2** in 20 μL 7:3 PFD/PFTPA or oil, 10 vol%) and diluted (200 μL emulsions in 5 mL). A portion of these solutions (1 mL) was taken and placed in the presence of 1-octanol (0.5 mL) in an Eppendorf tube. The biphasic samples were then rocked for 1 week. The Eppendorf tubes containing the samples were allowed to roll freely on a KJ-201BD Orbital shaker at 20 rpm. The fluorescence of the 1-octanol layer was monitored to determine the amount of **1** and **2** that diffused out of the emulsions (Figure 3F). Emission values were obtained by taking an aliquot (200 μL) of the 1-octanol in a 0.3 mL quartz cuvette and measuring the fluorescence on a Horiba Instruments PTI QuantaMaster Series fluorometer with the following settings: slits 5 nm, step size 1 nm, integration time 0.1 s (Ex 410 nm, collection 600-750nm). The 1-octanol was returned to the sample after the measurement. Emulsion B is statistically significant from emulsions A, C and D with $p<0.001$. Statistical significance was determined with a one tailed, unequal variance T-test.

Figure 4C-E/Figure S10

Emulsion E was prepared by predissolving **1** (6 nmol, 0.02 mg) and **5** (0.11 μmol, 0.25 mg) in 7:3 perfluorodecalin / perfluorotripropylamine (10 vol%, 20 μL) in an Eppendorf tube. Pluronic F-68 predissolved in PBS pH 7.4 (28 mg/mL, 2.8 wt%, 200 μL) was added to the fluorous solvent. Sonication (35% amp, 90 s, 0 ˚C) resulted in emulsion E. Emulsions were diluted in FACS buffer (200 μL in 1 mL, PBS buffer + 1% FBS).

A375 cells (30,000 cells/50 μL) were plated on a single well glass microscope slide (VWR 10118-600) that had been treated with FBS (2 mL, 30 min) and allowed to dry at RT in a biosafety cabinet to maintain sterility. Cells were allowed to adhere (O/N) and were washed with FACS buffer (PBS buffer + 1% FBS, 3x). Cells were treated with emulsion E (50 μL dilution in 100 μL media, 3 h). Cells were stained with Hoechst and NucGreen™ from ReadyProbes Cell Viability Imaging Kit (ThermoFisher, ref # R37609). Cells were stained with Hoechst (1 drop/1mL media, 15 min) before confocal images were taken. Cells were imaged before light treatment without NucGreen™. Cells were then stained with NucGreen™ (1 drop/1mL media, 15 min) and imaged before and after light treatment. Confocal settings were as follows: Rhodamine (532 laser-51%, 970 gain, offset -0.4, collection 540-700nm), Hoechst (405 laser-51%, 970 gain, offset -0.4, collection 420-500nm), NucGreen™ (488 laser-51%, 970 gain, 0ffset -0.4, collection 500-550 nm), DIC (scan-BF, 450 gain, offset -0.7). Scale bar represents 75 μm. Images were processed in ImageJ.

Figure 4F/Figure S14

Emulsions A-D were prepared as described in Figure 3A. A375 cells were placed in a 96-well plate (200,000 cells per 150 μL/well). Emulsions were diluted in FACS buffer (200 μL in 1 mL, PBS buffer + 1% FBS). Cells suspended in 150 μL media were treated with 50 μL of the diluted emulsions. Cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h). Cells were washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS with 1% FBS) to a final volume of 200 μL. Cells were irradiated (30 min, 420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/ml solution). Cell death was analyzed by FL2 channel on FACSCalibur. 15,000 cells were collected per sample. Emulsions A, B, and C were statistically significant after 10 min irradiation from the dark control with $p<0.05$. All emulsions were statistically significant after 30 min irradiation from the dark control with $p<0.0001$. Statistical significance was determined with a one tailed, unequal variance T-test.

Supporting figure procedures

Figure S1-2
Photosensitizer **1** or **2** (18.6 nmol, 0.06 mg **1**, 0.03 mg **2**) were dissolved in the indicated solvents (200 μL) through inversion or minimal sonication (<10 sec, bath sonicator). Photographs were taken in either visible or long-wave UV light (UVGL-25, 365 nm).

Figure S3.
Photosensitizer **2** (1.16 nmol, 0.002 mg) was dissolved in dimethylformamide with increasing percentages of methoxyperfluorobutane (0-100%, TCI America). The total volume was kept consistent at 0.75 mL. Absorbance was measured on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 2000 nm/min scan rate. Photoluminescence spectra were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer. Emission spectra: slits 5 nm, step size 1 nm, integration time 0.1 s (Ex 410 nm, collection 600-750nm). Phosphorescence spectra: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time 0.1 s (Ex 410 nm, collection 1200-1350nm, 1000 nm longpass filter). All data was normalized to $\lambda_{max,abs}$, $\lambda_{max,em}$, and $\lambda_{max,phos}$. The average of the normalized data is plotted. Error bars represent the standard deviation of three samples.

Figure S4.
Characterization of photosensitizer **1** and **2** in dimethylformamide (DMF) (30 μM, 6 nmol in 200 μL). Spectra were taken in a 300 μL quartz cuvette. Extinction coefficient was calculated through serial dilution of **1** and **2** in DMF, performed in a 1 mL volumetric flask. Extinction coefficient was measured on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 2000 nm/min scan rate. Photoluminescence spectra were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer. Emission spectra: slits 5 nm, step size 1 nm, integration time 0.1 s (Ex: 410 nm, collection 600-750 nm). Phosphorescence spectra (grey, dotted): ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time 0.1 s (Ex: 410 nm, collection 1200-1350 nm, 1000 nm long-pass filter).

Figure S5.
NMR samples were prepared with each of the components of PFC or oil emulsions in the presence of Rose Bengal (1.6 μmol, 1 mg), a known photosensitizer. A final volume of 0.5 mL for each of the NMRs were prepared, with 100 μL of either 7:3 perfluorodecalin (PFD)/ perfluorotripropylamine (PFTPA) or olive oil, or Pluronic F-68 (0.4 μmol, 1.1 mg). Anthracene, **3**, was used as a control (8.1 μmol, 2 mg) to ensure $^1O_2$ was being produced in high enough quantities to interact with the fluorous solvent, oil,

or Pluronic F-68. NMR samples were then kept in the dark or irradiated (420 nm, 90 min, 8.5 mW/cm^2). NMRs were taken on Bruker AV-500 or AV-300 instruments.

Figure S6.
Emulsions were prepared as described in Figure 3B/C. Emulsions were diluted (20 μL emulsions in 2 mL MilliQ H_2O, **Ω** = -18 mV), and Rose Bengal was added (0.4 μM, 2 μL of 1 mM stock). Size measurements of the emulsions were taken over a period of two weeks in the presence of Rose Bengal, with and without light (420 nm, 30 min, 8.5 mW/cm^2). Size was monitored with Malvern Zetasizer Nano dynamic light scattering and data is representative of three replicate measurements. Error bars represent the standard deviation of the product of the $Z_{average}$ and the polydispersity index of three measurements.

Figure S7.
Emulsions A-D were prepared as described in Figure 3A. The emulsions were transferred to a new Eppendorf tube and diluted with dichloromethane (1 mL) and evaporated to dryness. Dimethylformamide (0.5 mL) was added to the dried emulsions (denoted "included in emulsions"), and the original Eppendorf tube the emulsions were prepared in (denoted "excluded from emulsions"). The maximum control was **1** or **2** (6 nmol, 0.02 mg **1** or 0.011 mg **2**) dissolved in dimethylformamide (0.5 mL). Absorbance was measured on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 2000 nm/min scan rate. Photoluminescence spectra were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer. Emission spectra: slits 5 nm, step size 1 nm, integration time 0.1 s (Ex 410 nm, collection 600-750 nm). Phosphorescence spectra: ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time 0.1 s (ex: 410 nm, collection 1200-1350 nm, 1000 nm longpass filter). Data was normalized relative to the maximum control. Error bars represent the standard deviation of three samples.

Figure S8.
Emulsions were prepared as in Figure 3B/C. A portion of these solutions (1 mL) was taken and placed in the presence of 1-octanol (0.5 mL) in an Eppendorf tube. The biphasic samples were then rocked for three days. The Eppendorf tubes containing the samples were allowed to roll freely on a KJ-201BD Orbital shaker at 20 rpm. Each day, the aqueous layer was removed and placed in a 1 mL plastic cuvette and the size of the emulsions was measured by dynamic light scattering. After the measurement, the emulsions were replaced and returned to rocking. Error bars represent the standard deviation of the product of the $Z_{average}$ and the polydispersity index of three samples.

Figure S9/10.
Emulsion F was prepared by predissolving **5** (0.11 μmol, 0.25 mg) in 7:3 perfluorodecalin / perfluorotripropylamine (10 vol%, 20 μL) in an Eppendorf tube. A

solution of Pluronic F-68 in PBS pH 7.4 (28 mg/mL, 2.8 wt%, 200 μL) was added to the fluorous solvent. Sonication (35% amp, 90 s, 0 ˚C) resulted in emulsion F.

A375 cells (30,000 cells/50 μL) were plated on a single welled glass microscope slide (VWR 10118-600) that had been treated with FBS (2 mL, 30 min) and allowed to dry at RT in biosafety cabinet to maintain sterility. Cells were allowed to adhere (O/N) and were washed with FACS buffer (PBS buffer + 1% FBS, 3x). Cells were treated with emulsion F (50 μL in 100 μL media, 3 h). Cells were stained with Hoechst from ReadyProbes Cell Viability Imaging Kit (ThermoFisher, ref # R37609) (1 drop/1mL media, 15 min) before confocal images were taken. Cells were stained with LysoTracker Green DND-26 (Cell Signaling #8783, 1:20,000 in PBS buffer, 100 μL, 5 min) and washed with FACS buffer (PBS buffer + 1% FBS, 3x). Cells were imaged via excitation at 405 nm (Hoescht), 488 nm (LysoTracker Green), and 532 nm (Rhodamine). Images were processed in ImageJ. Scale bar represents 75 μm (top panel), 25 μm (bottom panel).

Figure S12/13

Emulsion F was prepared by predissolving **5** (0.11 μmol, 0.25 mg) in 7:3 perfluorodecalin/perfluorotripropylamine (10 vol%, 20 μL) in an Eppendorf tube. A solution of Pluronic F-68 in PBS pH 7.4 (28 mg/mL, 2.8 wt%, 200 μL) was added to the fluorous solvent. Sonication (35% amp, 90 s, 0 ˚C) resulted in emulsion F.

A375 cells (30,000 cells/50 μL) were plated on a single welled glass microscope slide (VWR 10118-600) that had been treated with FBS (2 mL, 30 min) and allowed to dry at RT in biosafety cabinet to maintain sterility. Cells were allowed to adhere (O/N) and were washed with FACS buffer (PBS buffer + 1% FBS, 3x). Cells were treated with emulsion F (50 μL in 100 μL media, 3 h). Cells were stained with Hoechst and NucGreen™ from ReadyProbes Cell Viability Imaging Kit ThermoFisher, (ref # R37609). Cells were stained with Hoechst (1 drop/1mL media, 15 min) before confocal images were taken. Cells were imaged before light treatment without NucGreen™. Cells were stained with NucGreen™ (1 drop/1mL media, 15 min) and imaged before and after light treatment (30 min, 420 nm, 8.5 mW/cm^2). Confocal settings were as follows: Rhodamine (532 laser-51%, 970 gain, offset -0.4, collection 540-700 nm), Hoechst (405 laser-51%, 970 gain, offset -0.4, collection 420-500 nm), NucGreen™ (488 laser-51%, 970 gain, offset -0.4, collection 500-550 nm), DIC (scan-BF, 450 gain, offset -0.7). Images were processed in ImageJ. Scale bar represents 75 μm.

Figure S14.

200,000 HEK cells/150 μL media were placed in 96-well plates.

(A) Emulsion A was prepared with varying amount of **1** (0-155 μM, 0-0.1 mg). Emulsions were diluted with FACS buffer (PBS, 1% FBS, 200 μL emulsions in 1 mL). Cells suspended in 150 μL media were treated with 50 μL diluted emulsions.

(B) Emulsions containing **1** were prepared as described in Figure 3A**.** Emulsions were diluted in PBS (200 μL emulsion in 1 mL PBS). HEK cells suspended in media were treated with varying amounts of diluted emulsions (5-150 μL, 200 μL emulsion diluted in 1 mL FACS buffer) to a final volume of 200 μL.

Cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h). Cells were washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS with 1% FBS) at a final volume of 200 μL. Cells were irradiated (30 min, 420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/mL solution). Cell death was analyzed by FL2 channel on FACSCalibur. The live/dead line was drawn at 10^2. 10,000 cells were collected per sample. Error bars represent the standard deviation of three samples.

Figure S16-17.
Emulsions A-D were prepared as described in Figure 3A. MCF7 cells were placed in a 96-well plate (200,000 cells per 150 μL/well). Emulsions were diluted in FACS buffer (200 μL in 1 mL, PBS buffer + 1% FBS). Cells suspended in 150 μL media were treated with 50 μL of the diluted emulsions. Cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h). Cells were washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS with 1% FBS) to a final volume of 200 μL. Cells were irradiated (30 min, 420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/ml solution). Cell death was analyzed by FL2 channel on FACSCalibur. 15,000 cells were collected per sample. Emulsions A, B, and C were statistically significant after 10 min irradiation from the dark control with $p<0.05$. All emulsions were statistically significant after 30 min irradiation from the dark control with $p<0.0001$. Statistical significance was determined with a one tailed, unequal variance T-test.

Figure S18-19.
Emulsions A-D were prepared as described in Figure 3A. HEK293 cells were placed in a 96-well plate (200,000 cells per 150 μL/well). Emulsions were diluted in FACS buffer (200 μL in 1 mL, PBS buffer + 1% FBS). Cells suspended in 150 μL media were treated with 50 μL of the diluted emulsions. Cells were incubated in the presence of emulsions (37 ˚C, 5% CO_2, 3 h). Cells were washed by centrifugation (3x, 526xg, 3 min) and resuspended in FACS buffer (PBS with 1% FBS) to a final volume of 200 μL. Cells were irradiated (30 min, 420 nm, 8.5 mW/cm^2). After irradiation, cells were diluted to 300 μL with FACS buffer and incubated (0 ˚C, 15 min) with propidium iodide (2 μL, 1 mg/ml solution). Cell death was analyzed by FL2 channel on FACSCalibur. 15,000 cells were collected per sample. Emulsions A, B, and C were statistically significant after 10 min irradiation from the dark control with $p<0.05$. All emulsions were statistically significant after 30 min irradiation from the dark control with $p<0.0001$. Statistical significance was determined with a one tailed, unequal variance T-test.

Figure S20.
Characterization of photosensitizer **1** in 7:3 perfluorodecalin (PFD)/ perfluorotripropylamine (PFTPA) (30 μM **1,** 6 nmol in 200 μL). Spectra were taken in a 300 μL quartz cuvette. Extinction coefficient was calculated through serial dilution of **1** in 7:3 PFD/PFTPA, performed in a 1 mL volumetric flask. Extinction coefficient was measured on a JASCO V-770 UV-Visible/NIR spectrophotometer with a 2000 nm/min scan rate. Photoluminescence spectra were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer. Emission spectra: slits 5 nm, step size 1 nm, integration time 0.1 s (Ex: 410 nm, collection 600-750 nm). Phosphorescence spectra (grey, dotted): ex_{slits} 5 nm, em_{slits} 30 nm, step size 1 nm, integration time 0.1 s (Ex: 410 nm, collection 1200-1350 nm, 1000 nm long-pass filter).

Scheme experimental procedures

Fluorous Porphyrin (1)
5,10,15,20-Tetrakis[4- (10H,10H,20H,20H-perfluorododecyl) -2,3,5,6-tetrafluorophenyl] porphyrin[3] 5,10,15,20-Tetrakis(pentafluorophenyl)porphyrin (11.5 mg, 11.8 μmol, 1 equiv., TCI America) was dissolved in DMF (1 mL, anhydrous). 1H, 1H, 2H, 2H-perflurododecane-1-thiol (38 mL, 112 μmol, 9.5 equiv.) and diethylamine (20 μL, 194 μmol, 16 equiv.) were dissolved in 2:1 ethyl acetate/DMF under nitrogen (3 mL). The 5,10,15,20-Tetrakis(pentafluorophenyl)porphyrin dissolved in DMF was added to the solution of 1H, 1H, 2H, 2H-perflurododecane-1-thiol and diethylamine. The resulting solution was stirred overnight at room temperature and evaporated onto silica gel. Photosensitizer **1** was purified via silica gel chromatography, eluting with hexane/acetone. (R_f = 0.6 in 20:1 hexane/acetone). This procedure gave pure **1** (37.9 mg, 11.8 μmol, 40%). ^{1}H NMR (300 MHz, $CDCl_3$, 5% TFA): δ 8.98 (s, 8H), 3.61 (t, *J* = 9 Hz, 8H), 2.78-2.73 (m, 8H), -0.72 (br s, 2H). ^{19}F (282 MHz, $CDCl_3$, 5% TFA): δ -81.08 (t, *J* = 10 Hz, 12F), -114.09 (m, 8F), -121.77 (m, 8F), -122.04 (m, 16F), -122.88 (m, 8F), -123.31 (m, 8F), -126.32 (m, 8F), -132.22 (m, 8F), -137.80 (m, 8F). HRMS (MALDI): Calculated for $C_{84}H_{27}F_{84}N_4S_4^+$ $[M+H]^+$: 2814.9772; found: 2814.9798. Absorbance (DMF): 408 nm ($\varepsilon = 8.4 \times 10^4\ M^{-1}cm^{-1}$). Emission (DMF, Ex 410 nm): 704 nm, $\Phi_F = 0.02 \pm 0.03$ (DMF), $\Phi_\Delta = 86 \pm 0.8$ % (DMF).

2. A. Varotto, L. Todaro, M. Vinodu, J. Koehne, G. Liu, C. M. Drain, Chem. Comm. 2008, 1, 4921-4923.

Hydrophobic Porphyrin (2)
5,10,15,20-Tetrakis[4- (10H,10H,20H,20H-dodecyl) -2,3,5,6-tetrafluorophenyl] porphyrin 5,10,15,20-Tetrakis(pentafluorophenyl)porphyrin (11.5 mg, 11.8 μmol, 1 equiv.) was dissolved in DMF (1 mL, anhydrous). Dodecane-1-thiol (150 μL, 600 μmol, 50 equiv.) and diethylamine (36 μL, 354 μmol, 30 equiv.) were dissolved in 2:1 ethyl acetate/DMF under nitrogen (3 mL). The 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin dissolved in DMF was added to the solution of dodecane-1-thiol and diethylamine. The resulting mixture was stirred overnight at room temperature and evaporated onto silica gel. Photosensitizer **2** was purified via silica gel chromatography, eluting with pentane ether solvent gradient of: pentane, 1000:1 pentane: ether, 500:1 pentane: ether, 250:1 pentane: ether. This procedure gave pure **2** (7.5 mg, 2.0 μmol, 38%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 8H), 3.29 (t, *J* = 8 Hz, 8H), 1.86 (m, 8H), 1.61 (m, 8H), 1.36-1.19 (m, 64H), 0.87 (m, 12H), -2.86 (s, 2H). ^{19}F NMR (377 MHz, $CDCl_3$): δ -134.26 (m, 8F), -137.22 (m, 8F). HRMS (MALDI): Calculated for $C_{92}H_{111}F_{16}N_4S_4^+$ $[M+H]^+$: 1703.7431; found: 1703.7426. Absorbance

(DMF): 406 nm (ε = 9x10^4 M^{-1}cm^{-1}). Emission (DMF, Ex. 410 nm): 706 nm, Φ_F = 0.02 $\pm$ 0.03 (DMF), Φ_Δ = 85 $\pm$ 3.6 % (DMF).

^{1}H NMR