Hypoxia-activated NIR photosensitizer anchoring in the

mitochondria for photodynamic therapy

Feng Xu^a, Haidong Li^a, Qichao Yao^a, Haoying Ge^a, Jiangli fan^a, Wen Sun^a, Jingyun Wang^b and Xiaojun peng^{a,c,*}

^a State Key Laboratory of Fine Chemicals, Dalian University of Technology, 2

Linggong Road, Dalian 116024, P.R. China.

^b School of Life Science and Biotechnology, Dalian University of Technology, 2

Linggong Road, Dalian 116024, P.R. China.

^c Shenzhen Research Institute, Dalian University of Technology, Nanshan District,

Shenzhen 518057, P. R. China

*Email: pengxj@dlut.edu.cn. Tel/Fax: +86 -411- 84986306.

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Scheme 1 Synthetic route of ICy-N



Figure S1 (a) Transmission electron microscope (TEM) imaging of ICy-N in water. (b) UV-Vis spectra of ICy-N in PBS (10 mM, pH = 7.4) during 6 h at a concentration of 5 μ M.



Figure S2 Photodegradation curves of DPBF and linear fit of Absorbance at 415 nm with MB under 660 nm light irradiation.



Figure S3 Photodegradation curves of DPBF and linear fit of Absorbance at 415 nm with **ICy-N** under 660 nm light irradiation.



Figure S4 Photodegradation curves of DPBF and linear fit of Absorbance at 415 nm with **ICy-OH** under 660 nm light irradiation.

PS	Slope	$\Phi_{oldsymbol{\Delta}}$
MB	-1.04×10 ⁻²	57%
ICy-N	-1.31×10-4	0.72%
ІСу-ОН	-2.93×10 ⁻⁴	1.80%

Table S1 Singlet oxygen quantum yield of MB, ICy-N and ICy-OH



Figure S5 $^{1}O_{2}$ production characterize with (a) SOSG and (c) EPR. O2- production characterize with (b) DHE and (d) EPR.



Figure S6 MCF-7 cells stained with MitoTracker Green FM and ICy-N before and after the treatment of 20 μM CCCP for 30 min.



Figure S7 (a) Reactive oxygen species production in MCF-7 cells. (b) Average Fluorescence emission intensities of (a).



Figure S8 Confocal microscopy imaging of Annexin V - FITC and PI stained 4T1 cells after different treatments. The green channel of Annexin V - FITC was excited at 488 nm and collected at 500-550 nm; The red channel of PI was excited at 488 nm and collected at 500-550 nm.



Figure S9 JC-1 assay for MCF-7 cells treated with ICy-N with or without 660 nm light irradiation. The green channel was excited at 488 nm and collected at 510-550nm, the red channel was excited at 561 nm and collected at 570-610 nm.



Figure S10 Observation of morphological change MCF-7 cells after different treatments and irradiated with 635 nm laser for 1 min Red arrows represent vesicles observed.



Figure S11 Flow cytometry assay of MCF-7 cells stained with PI. (a-b) Cells were treated with light only. (c-d) Cells were stained with 2.5 μM ICy-OH and irradiated with 660 nm light for 5 mins. The samples were excited at 561 nm and collected at 590-640 nm.



Figure S12 Relative tumor volume (a) and body weight of mice (b) after different treatments.



Figure S13 Photo of 4T1 tumor bearing mice from different groups after 14 days of treatments.



Figure S14 H&E staining of organs from PBS group and PDT group after 14 days of treatment. Scale bar: 50 µm.



Figure S16 ESI-MS of 1



Figure S18 ESI-MS of 2



Figure S19¹H NMR of 3



Figure S20 ESI-MS of 3



Figure S22 ¹H NMR of 6







Figure S24 ¹H NMR of ICy-OH







Figure S26 ¹H NMR of ICy-N



Figure S28 ESI-MS of ICy-N