Umbelliferone Decorated Water-soluble Zinc(II) Phthalocyanines – *In Vitro* Phototoxic Antimicrobial Anti-cancer Agents

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1. General methods

Suspensions of compounds in ultrapure water were sonicated at room temperature in a “SONOREX RK 100” from Bandelin electronic. For freeze-drying an “Alpha 1-4 LD plus” freeze dryer from Martin Christ Gefriertrocknungsanlagen GmbH was used. Solutions were centrifuged in an “EBA 3S” centrifuge from Hettich at 100 % (5000 rpm). It was equipped with a fixed-angle rotor (4 x 10–15 mL) and was used with Schott Duran glass centrifuge tubes (1.3 x 10 cm). (Flash) column chromatography was performed with silica gel 60 M (particle size: 0.04–0.063 mm) from MACHEREY-NAGEL. Thin layer chromatography (TLC) was performed on silica coated polyester sheets “POLYG RAM-SIL G UV254” (4 x 8 cm) with a fluorescent indicator F$_{254}$ from MACHEREY-NAGEL. Preparative size exclusion chromatography (SEC) was performed on “Sephadex LH-20” from GE Healthcare. The material was equilibrated with the solvent of choice before use.

Nuclear magnetic resonance (NMR) spectra were recorded on a “DMX300” spectrometer ($^1$H: 300 MHz, $^{13}$C: 75.5 MHz) or a “DMX600” spectrometer ($^1$H: 600 MHz, $^{13}$C: 151 MHz) from Bruker. All measurements were performed at room temperature (rt) in deuterated solvents. Chemical shifts (δ) are given in parts per million (ppm) relative to the residual proton signal of the deuterated solvent in the $^1$H NMR (CDCl$_3$: 7.26 ppm, DMSO-d$_6$: 2.50 ppm, D$_2$O: 4.79 ppm, 1 M DCl in D$_2$O: 4.94 ppm)$^{[1]}$ or relative to the residual solvent signal in the $^{13}$C NMR (CDCl$_3$: 77.16 ppm, DMSO-d$_6$: 39.52 ppm)$^{[1]}$, $^{13}$C NMR spectra in 1 M DCl in D$_2$O without a solvent residual signal were referenced according to the unified scale (equation 1)$^{[2]}$. $\nu_{\text{DSS}}$ is the MHz value at 0 ppm of the referenced $^1$H NMR relative to sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS), $\Xi_{\text{reference}}$ frequency ratio of $^1$H to $^{13}$C in % with DSS as reference compound (25.144953 %) and $\nu_{\text{reference}}$ the MHz value at 0 ppm of the $^{13}$C NMR spectrum$^{[2]}$.

$$\nu_{\text{reference}} = \frac{\nu_{\text{DSS}} \cdot \Xi_{\text{reference}}}{100 \%} \quad (1)$$

The multiplicity is noted as broad (br), singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), sextett (sext), heptet (heptet) or multiplet (m) and the coupling constants (J) are given in Hz. The assay of the mass spectrometry (MS) was performed by electrospray ionisation (ESI). For high resolution ESI-MS a “maxis 4G” from Bruker or an “Orbitrap LTQ XL” from Thermo Fisher Scientific was used. Infrared spectra (IR-spectra) were recorded on a “FT/IR-430” spectrophotometer from JASCO Analytical Instruments equipped with a “MIRacleTM” ATR unit with a diamond measuring crystal. Ultraviolet and visible (UV-vis) spectroscopy measurements were recorded with a “V-550” UV-vis dual beam spectrophotometer, which was equipped with an “ETC-505T” Peltier element from JASCO Analytical Instruments. Unless otherwise stated, for spectrophotometric measurements in aqueous solutions “disposable semi-micro PMMA cuvettes” with a capacity of 1.5 mL and a light path of 10 mm from Brand® GmbH & Co. KG were used. For solutions in organic solvents “high precision Quartz SUPRASIL® cuvettes with a light path of 10 x 4 mm (“114F-10-40”; V = 1400 µL) from Hellma Analytics were used. All solvents were of spectroscopic grade. Fluorescence measurements were performed using an “RF-6000” spectrofluorometer from Shimadzu Corporation which was equipped with a cuvette holder. For fluorescence quantum yield measurements, the instrument was equipped with an “ISR-6000” integration sphere from the Shimadzu Corporation.
2. Chemicals and Solvents

For air and moisture sensitive reactions Schlenk-techniques, argon atmosphere and dried solvents were used. Therefore, unless otherwise stated, the solvents were dried over 4 Å molecular sieves. To dry CH₂Cl₂ it was distilled over dry CaCl₂ and used directly. Technical grade ethyl acetate and cyclohexane were distilled for column chromatography. K₂CO₃ was pulverized in a mortar with a pestle and dried overnight at 80 °C. Unless otherwise stated, commercially available chemicals and per analysis solvents were used without further purification. They were purchased from Sigma-Aldrich, Acros Organics, TCI, ChemPur, Alfa Aesar, abcr, Deutero, Fisher Scientific, GE Healthcare Life Sciences, Carl Roth and Merck Millipore. Ultrapure water (MilliQ water) with an electric resistance of 0.055 µS 18 MΩ was prepared with a “PURELAB® Classic UV” from ELGA LabWater Veolia Water Technologies.
3. Synthetic procedures

Scheme S1: Synthesis sequence for the formation of the ligand **I-EO$_3$-Umb**. (i) NEt$_3$ (2.2 eq), 4-dimethylaminopyridine (0.02 eq), 2-[2-(2-chloroethoxy)ethoxy]ethanol (1.0 eq), p-toluenesulfonyl chloride (1.2 eq), dry CH$_2$Cl$_2$, 12 h, rt;[5] (ii) Cl-EO$_3$-OTs (1.4 eq), 7-hydroxycoumarin (1.0 eq), dry K$_2$CO$_3$ (5.0 eq), dry DMF, 80 °C, 24 h; (iii) Cl-EO$_3$-Umb (1.0 eq), NaI (7.0 eq), acetone, 56 °C, 5 d.[6]

Scheme S2: Synthesis sequence for the generation of **ZnOP$_4$(EO$_3$-Umb)$_4$**. (i) 4-nitrophthalonitrile (1.0 eq), 3-hydroxypyridine (2.2 eq), dry K$_2$CO$_3$ (5.6 eq), dry DMF, 3 h, 80 °C;[5] (ii) CN$_2$-OPy (2.8 eq), zinc acetate (1.0 eq), 1,8-diazabicyclo[5.4.0]undec-7-ene (1.5 eq), 1-pentanol, 140 °C, 25.5 h; I-EO$_3$-Umb (22 eq), dry DMF, 70 °C, 14 d.[6]

Scheme S3: Synthesis sequence for the generation of **ZnOP$_8$(EO$_3$-Umb)$_8$**. (i) 4,5-dichlorophthalonitrile (1.0 eq), 3-hydroxypyridine (4.5 eq), dry K$_2$CO$_3$ (6.4 eq), dry DMF, 80 °C, 3 h; (ii) CN$_2$-OP$_2$ (2.8 eq), zinc acetate (1.0 eq), 1,8-diazabicyclo[5.4.0]undec-7-ene (1.5 eq), 1-pentanol, 140 °C, 19 h; (iii) ZnOP$_8$ (1.0 eq), I-EO$_3$-Umb (38 eq), dry DMF, 70 °C, 14 d.[6]
The synthesis of **Cl-EO<sub>3</sub>-OTs** was carried out according to a modified procedure by MOTOYANAGI et al.<sup>[3]</sup> The synthesis was performed under argon atmosphere. To an icecold solution of triethylamine (7.96 mL, 57.1 mmol, 2.2 eq), 4-dimethylaminopyridine (80.0 mg, 655 µmol, 0.02 eq) and 2-[2-(2-chloroethoxy)ethoxy]ethanol (3.82 mL, 26.3 mmol, 1.0 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (40 mL) was drop wise added a solution of p-toluenesulfonyl chloride (6.02 g, 31.6 mmol, 1.2 eq) in dry CH<sub>2</sub>Cl<sub>2</sub> (3 x 100 mL). The reaction mixture was heated slowly to room temperature and was stirred additional 12 h at room temperature. Distilled water (100 mL) was added and the product was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 100 mL). The combined organic phases were dried over MgSO<sub>4</sub>, filtered and the solvent was removed *in vacuo*. The compound **Cl-EO<sub>3</sub>-OTs** was obtained after silica gel flash chromatography (Cy = 100 → EtOAc = 100).

**Yield:** 8.23 g (25.5 mmol, 97 %) as a colorless liquid; **Empirical formula** (M / (g/mol)): 322.80 (C<sub>13</sub>H<sub>15</sub>ClO<sub>3</sub>S); **R<sub>f</sub>** (Cy : EtOAc = 50 : 50): 0.33; **1H NMR** (CDCl<sub>3</sub>, 300 MHz, 300 K): δ/ppm = 7.83–7.73 (m, 2H; H-8–9, H-11–12), 7.39–7.30 (m, 2H; H-8–9, H-11–12), 4.21–4.10 (m, 2H; H-6), 3.77–3.67 (m, 4H; H-5), 3.64–3.54 (m, 6H; H-1–4), 2.44 (s, 3H; H-13) (Figure S1); **13C NMR** (CDCl<sub>3</sub>, 75 MHz, 300 K): δ/ppm = 132.36, 129.11, 127.24, 70.67, 70.03, 69.88, 68.50, 68.05, 42.01, 20.90 (Figure S2); **ESI-HRMS:** m/z = 323.0720 ([M+H]<sup>+</sup>), m/z = 323.0714 calculated for [C<sub>13</sub>H<sub>15</sub>ClO<sub>3</sub>S+H]<sup>+</sup>); 345.0560 ([M+Na]<sup>+</sup>, m/z = 345.0534 calculated for [C<sub>13</sub>H<sub>15</sub>ClO<sub>3</sub>S+Na]<sup>+</sup>); 340.0982 ([M+NH4]<sup>+</sup>, m/z = 340.0980 calculated for [C<sub>13</sub>H<sub>15</sub>ClO<sub>3</sub>S+NH4]<sup>+</sup>); **IR** (neat): ν/cm<sup>-1</sup> = 2871 (w), 1597 (w), 1452 (w), 1354 (m), 1298 (w), 1246 (w), 1188 (m), 1174 (s), 1119 (m), 1095 (m), 1043 (w), 1012 (m), 918 (s), 816 (m), 773 (m), 703 (w), 661 (s).

The synthesis of **Cl-EO<sub>3</sub>-Umb** was carried out according to a modified procedure by MOTOYANAGI et al.<sup>[4]</sup> The synthesis was performed under argon atmosphere and in the dark. To a solution of **Cl-EO<sub>3</sub>-OTs** (7.90 g, 24.5 mmol, 1.4 eq) and 7-hydroxycoumarin (2.78 g, 17.1 mmol, 1.0 eq) in dry N,N'-dimethylformamide (106 mL) was added dry K<sub>2</sub>CO<sub>3</sub> (11.80 g, 85.4 mmol, 5.0 eq). The reaction was stirred at 80 °C for 24 h. The suspension was cooled down to room temperature and the solvent was removed *in vacuo*. CH<sub>2</sub>Cl<sub>2</sub> (150 mL) was added to the remaining residue and was washed with distilled water (3 x 150 mL). The organic layer was dried over MgSO<sub>4</sub>, filtered and the solvent was removed *in vacuo*. The compound **Cl-EO<sub>3</sub>-Umb** was obtained after silica gel flash chromatography (Cy : EtOAc = 50 : 50).

**Yield:** 4.69 g (15.9 mmol, 93 %) as a colorless solid; **Empirical formula** (M / (g/mol)): 312.75 (C<sub>15</sub>H<sub>17</sub>ClO<sub>3</sub>S); **R<sub>f</sub>** (Cy : EtOAc = 50 : 50): 0.19; **1H NMR** (DMSO-d<sub>6</sub>, 600 MHz, 300 K): δ/ppm = 7.99 (d, J = 9.5 Hz, 1H; H-11), 7.62 (d, J = 8.6 Hz, 1H; H-12), 7.01 (d, J = 2.4 Hz, 1H; H-8), 6.96 (dd, J = 8.6 Hz, 2.4 Hz, 1H; H-13), 6.29 (d, J = 9.5 Hz, 1H; H-10), 4.23–4.19 (m, 2H; H-6), 3.80–3.76 (m, 2H; H-5), 3.72–3.65 (m, 4H; H-1–2), 3.62–3.58 (m, 4H; H-3–4) (Figure S3); **13C NMR** (DMSO-d<sub>6</sub>, 150 MHz, 300 K): δ/ppm = 161.66 (C-7), 160.28 (C-9), 155.37 (C-14), 144.32 (C-11), 129.48 (C-12), 112.75 (C-13), 112.50 (C-10), 112.38 (C-15), 101.22 (C-8), 70.55 (C-2), 69.89 (CH<sub>2</sub>), 69.66 (CH<sub>2</sub>), 67.69 (C-5), 67.92 (C-6), 43.55 (C-1) (Figure S4); **ESI-HRMS:** m/z = 313.0803 ([M+H]<sup>+</sup>), m/z = 313.0813 calculated for [C<sub>15</sub>H<sub>17</sub>ClO<sub>3</sub>S+H]<sup>+</sup>), 355.0624
(\textit{M+Na}^+), m/z = 355.0657 calculated for \([\text{C}_{15}\text{H}_{17}\text{ClO}_5+\text{Na}]^+\); \textbf{IR} (neat): \nu / \text{cm}^{-1} = 3076 (w), 2885 (w), 1705 (s), 1610 (s), 1508 (m), 1473 (w), 1454 (m), 1429 (w), 1400 (w), 1371 (w), 1350 (m), 1308 (w), 1282 (m), 1237 (m), 1203 (m), 1159 (w), 1111 (s), 1074 (m), 1043 (m), 995 (m), 943 (m), 930 (s), 889 (m), 839 (s), 814 (m), 754 (m), 692 (w), 660 (m), 633 (m), 615 (m).

7-(2-(2-(2-Iodoethoxy)ethoxy)ethoxy)-2H-chromen-2-one (l-EO3-Umb)[4]

The synthesis of l-EO3-Umb was carried out according to a modified procedure by \textit{MOTOFANAGI \textit{et al}.}[4]. The synthesis was performed in the dark. To a solution of Cl-EO3-Umb (2.50 g, 7.99 mmol, 1.0 eq) in acetone (66 mL) was added NaI (8.40 g, 56.0 mmol, 7.0 eq). The reaction was stirred at 56 °C for 5 d under reflux. The reaction mixture was cooled down to room temperature and the solvent was removed \textit{in vacuo}. To the residue distilled water (75 mL) was added and the product was extracted with CH$_2$Cl$_2$ (4 x 75 mL). The combined organic phases were dried over MgSO$_4$, filtered and the solvent was removed \textit{in vacuo}.

\textbf{Yield:} 3.20 g (7.92 mmol, 99 %) as a yellow liquid; \textbf{Empirical formula} (\textit{M} / (g/mol)): 404.197 (C$_{15}$H$_{17}$I$_2$O$_5$); \textit{R}$_f$ (EtOAc = 100): 0.51; $^1$H NMR (DMSO-d$_6$, 600 MHz, 300 K): \delta/ppm = 7.98 (d, \textit{J} = 9.5 Hz, 1H; H-11), 7.62 (d, \textit{J} = 8.6 Hz, 1H; H-12), 7.00 (d, \textit{J} = 2.4 Hz, 1H; H-8), 6.96 (dd, \textit{J} = 8.5, 2.4 Hz, 1H; H-13), 6.28 (d, \textit{J} = 9.5 Hz, 1H; H-10), 4.22–4.19 (m, 2H; H-6), 3.80–3.77 (m, 2H; H-5), 3.66 (t, \textit{J} = 6.5 Hz, 2H; H-2), 3.62–3.57 (m, 4H; H-3–4), 3.31 (t, \textit{J} = 6.5 Hz, 2H; H-1) (Figure S5); $^{13}$C NMR (DMSO-d$_6$, 150 MHz, 300 K): \delta/ppm = 161.65 (C-7), 160.27 (C-9), 155.35 (C-14), 144.30 (C-11), 129.46 (C-12), 112.75 (C-13), 112.49 (C-10), 112.37 (C-15), 101.22 (C-8), 70.97 (C-2), 69.90 (CH$_2$), 69.30 (CH$_2$), 68.70 (C-5), 67.92 (C-6), 5.39 (C-1) (Figure S6); \textbf{ESI-HRMS:} \textit{m/z} = 405.0156 ([M+H]$^+$), \textit{m/z} = 405.0193 calculated for [C$_{15}$H$_{17}$I$_2$O$_5$+H]$^+$, 426.9978 ([M+Na]$^+$), \textit{m/z} = 427.0013 calculated for [C$_{15}$H$_{17}$I$_2$O$_5$+Na]$^+$; \textbf{IR} (neat): \nu / \text{cm}^{-1} = 3082 (w), 2927 (w), 2870 (w), 1726 (s), 1608 (s), 1556 (m), 1508 (m), 1454 (w), 1427 (w), 1400 (m), 1350 (m), 1279 (m), 1230 (m), 1200 (m), 1117 (s), 1053 (m), 993 (m), 937 (w), 891 (m), 833 (s), 752 (m), 717 (w), 633 (m), 615 (m).

4-(Pyridin-3-loyx)phthalonitrile (CN$_2$-OPy)[5]

The synthesis of CN$_2$-OPy was carried out according to a modified procedure by \textit{SPESIA \textit{et al}.}[5]. The synthesis was performed under argon atmosphere and in the dark. 4-Nitrophthalonitrile (3.00 g, 17.3 mmol, 1.0 eq), 3-hydroxy pyridine (3.63 g, 38.2 mmol, 2.2 eq) and dry K$_2$CO$_3$ (13.50 g, 97.7 mmol, 5.6 eq) were dissolved in dry N,N-dimethylformamide (26 mL). The solution was stirred for 3 h at 80 °C in the dark. The reaction mixture was cooled to room temperature, poured on iced water (300 mL) and was stored for 3 d in the fridge. The formed precipitate was collected by filtration, washed with distilled water and dried in a stream of air. The beige solid was dissolved in chloroform (50 mL) and washed with distilled water (3 x 50 mL). The organic phase was dried over MgSO$_4$, filtered and the remaining solvent was evaporated \textit{in vacuo}. The resulting colorless solid was further dried \textit{in high vacuum} for 2 d.

\textbf{Yield:} 3.51 g (15.9 mmol, 92 %) as a colorless solid; \textbf{Empirical formula} (\textit{M} / (g/mol)): 221.22 (C$_{13}$H$_{13}$N$_2$O$_2$); \textit{R}$_f$ (CH$_2$Cl$_2$ : MeOH = 90 : 10): 0.67; \textbf{1H NMR} (CDCl$_3$, 600 MHz, 300 K): \delta/ppm = 8.59 (t, \textit{J} = 3.0 Hz, 1H; H-11), 8.48 (d, \textit{J} = 1.9 Hz, 1H; H-10), 7.77 (d, \textit{J} = 8.7 Hz, 1H; H-3), 7.71 (dd, 2.0 Hz, 1H; H-2), 7.70 (dd, 1.9 Hz, 1H; H-3), 7.66 (t, \textit{J} = 4.5 Hz, 1H; H-1).
7.47–7.42 (m, 2H; H-12–13), 7.33 (d, J = 2.5 Hz, 1H; H-6), 7.30–7.25 (m, 1H; H-2) (Figure S7);

$^{13}$C NMR (CDCl$_3$, 150 MHz, 300 K): δ/ppm = 161.02 (C-1), 150.58 (C-9), 147.61 (C-11), 142.98 (C-10), 135.78 (C-3), 128.12 (C-12–13), 125.04 (C-12–13), 121.86 (C-6), 121.60 (C-2), 118.16 (C-5, C-7), 115.19 (C-5, C-7), 114.78 (C-8), 110.10 (C-4) (Figure S8);

ESI-HRMS: $m/z$ = 222.0682 ([M+H]$^+$, $m/z$ = 220.0662 calculated for [C$_{13}$H$_7$N$_3$O+H]$^+$);

IR (neat): $\nu$/cm$^{-1}$ = 3111 (w), 3070 (w), 3039 (w), 2227 (m), 1595 (m), 1566 (m), 1487 (s), 1477 (s), 1423 (s), 1313 (s), 1279 (s), 1248 (s), 1215 (s), 1192 (m), 1157 (m), 1084 (m), 1024 (s), 957 (m), 945 (m), 891 (m), 852 (s), 820 (s), 706 (s), 615 (m).

2(3),9(10),16(17),23(24)-Tetrakis-[1-(2-(2-(2-((2-oxo-2H-chromen-7-yl)oxy)ethoxy)ethoxy)ethyl)pyridinium-3-oxyl]phthalocyaninato zinc(II) tetraiodide ($\text{ZnOPy}_4$(EO$_3$-Umb)$_4$)[6]

The synthesis of $\text{ZnOPy}_4$(EO$_3$-Umb)$_4$ (regioisomers*) was carried out according to a modified procedures by Li et al.[6]. The synthesis was performed under argon atmosphere and in the dark. To an 80 °C solution of $\text{CN}_2$-OPy (564 mg, 12.55 mmol, 2.8 eq) and zinc acetate (168 mg, 916 µmol, 1.0 eq) in 1-pentanol (30 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 200 µL, 1.37 mmol, 1.5 eq). The reaction was stirred at 140 °C for 25.5 h, cooled down to room temperature and the solvent was removed in vacuo. To the residue was added CH$_2$Cl$_2$, filtered and washed with CH$_2$Cl$_2$. The crude product was dried in high vacuum. The dark blue intermediate 2(3),9(10),16(17),23(24)-tetrakis-(pyridin-3-oxyl)phthalocyaninato zinc(II) ($\text{ZnOPy}_4$) was obtained after silica gel chromatography (CH$_2$Cl$_2$: MeOH : NH$_4$OH = 95 : 5 : 1 ) followed by size exclusion chromatography on Sephadex LH-20 (N,N’-dimethylformamide = 100). 30 mg of the intermediate $\text{ZnOPy}_4$ (31.6 µmol, 1.0 eq) were obtained. The crude intermediate was used without further purification and analytical characterization.

$\text{ZnOPy}_4$ (20 mg, 21.0 µmol, 1.0 eq) and I-EO$_3$-Umb (185 mg, 458 µmol, 22 eq) were dissolved in dry N,N’-dimethylformamide (1.8 mL) and stirred at 70 °C for 14 d. The solution was cooled down to room temperature and the solvent was removed in vacuo. To the residue was added CH$_2$Cl$_2$, filtered, washed with CH$_2$Cl$_2$ and dried in vacuo. The compound $\text{ZnOPy}_4$(EO$_3$-Umb)$_4$ was obtained after size exclusion chromatography on Sephadex LH-20 (N,N’-dimethylformamide = 100). The product was suspended by sonication for 15 min in ultrapure water and freeze dried for 5 d.

*Due to the synthetic pathway, the pyridinium-3-oxyl groups can be located at one of the two peripheral positions of the four isoindoline units of the phthalocyanine core unit. Hence, four different regioisomers are possible, which cannot be separated during the purification steps.
Yield: 52.61 mg (20.5 μmol, 4.8 %) as a dark green solid; Empirical formula (M / (g/mol)): 4556.146 (C₁₁₂H₉₆aN₄₂O₂₄Zn); Rf (EtOAc = 100): 0.00; ¹H NMR (DMSO-d₆, 600 MHz, 300 K): δ/ppm = 9.50–9.36 (m, 8H; H-8), 9.37–9.28 (m, 8H; H-10), 9.16–9.07 (m, 8H; H-5), 9.02 (dd, J = 12.6, 5.0 Hz, 8H; H-11), 8.75–8.61 (m, 8H; H-13), 8.39–8.28 (m, 8H; H-12), 8.12 (qt, J = 10.2, 5.1 Hz, 8H; H-7), 7.65–7.56 (m, 8H; H-24), 7.26–7.15 (m, 8H; H-25), 6.67–6.60 (m, 8H; H-21), 6.60–6.54 (m, 8H; H-26), 6.05–5.93 (m, 8H; H-23), 4.99–4.88 (m, 16H; H-14), 4.07–4.00 (m, 16H; H-15), 4.00–3.92 (m, 16H; H-16), 3.70–3.55 (m, 48H; H-17–19) (Figure S9); ¹³C NMR (DMSO-d₆, 150 MHz, 300 K): δ/ppm = 161.14 (C-20), 159.96 (C-22), 156.39 (Cq), 156.35 (Cq), 155.73 (Cq), 154.91 (C-27), 152.67 (Cq), 152.24 (Cq), 143.82 (C-24), 140.49 (C-11), 139.95 (Cq), 136.45 (C-10), 135.31 (C-6), 134.50 (C-13), 129.03 (C-12, C-25), 124.90 (C-8), 121.84 (C-7), 113.42 (C-5), 112.21 (C-26), 112.18 (C-23), 111.99 (C-28), 100.76 (C-21), 69.74 (CH₂), 69.72 (CH₂), 68.63 (C-15), 68.58 (CH₂), 67.70 (C-16), 60.77 (C-14) (Figure S10); ESI-HRMS: m/z = 514.14825 calculated for [C₁₁₂H₉₆aN₄₂O₂₄Zn-4I]₄⁺ (Figure S17–S18); IR (neat): ν/ cm⁻¹ = 3055 (w), 2929 (w), 2868 (w), 1720 (m), 1707 (m), 1610 (s), 1581 (m), 1556 (w), 1491 (m), 1464 (m), 1400 (m), 1335 (m), 1279 (s), 1230 (m), 1201 (m), 1119 (s), 1093 (s), 1045 (s), 993 (m), 945 (m), 835 (s), 748 (m), 679 (m), 615 (m) (Figure S21).

4,5-Bis(pyridin-3-yl)(pyridin-3-yl)phthalonitrile (CN₂OPy₂)[⁶]

The synthesis of CN₂OPy₂ was carried out according to a modified procedure by Li et al.[⁶]. The synthesis was performed under argon atmosphere and in the dark. 4,5-Dichlorophthalonitrile (3.01 g, 15.3 mmol, 1.0 eq), 3-hydroxyypyridine (6.60 g, 69.4 mmol, 4.5 eq) and dry K₂CO₃ (13.50 g, 97.7 mmol, 6.4 eq) were dissolved in dry N,N'-dimethylformamide (45 mL). The solution was stirred for 3 h at 80 °C in the dark. The reaction mixture was cooled to room temperature, poured on iced water (300 mL) and was stored for 3 d in the fridge. The formed precipitate was collected by filtration, washed with distilled water and dried in a stream of air. The solid was dissolved in acetone, dried over MgSO₄ and the solvent was removed in vacuo. The compound CN₂OPy₂ was obtained after silica gel flash chromatography (CH₂Cl₂ : MeOH = 98 : 2).

Yield: 4.38 g (13.9 mmol, 91 %) as a colorless, crystalline solid; Empirical formula (M / (g/mol)): 314.08 (C₁₈H₁₀N₄O₂); Rf (CH₂Cl₂ : MeOH = 90 : 10): 0.51; ¹H NMR (CDCl₃, 300 MHz, 300 K): δ/ppm = 8.57–8.49 (m, 2H; PyH), 8.44–8.39 (m, 2H; PyH), 7.44–7.34 (m, 4H; PyH), 7.29 (s, 2H; H-1) (Figure S11); ¹³C NMR (CDCl₃, 75 MHz, 300 K): δ/ppm = 151.12, 151.07, 147.18, 141.66, 126.75, 124.89, 123.31, 114.50, 112.04 (Figure S12); ESI-HRMS: m/z = 315.0895 ([M+H⁺]⁺, m/z = 315.0877 calculated for [C₁₈H₁₀N₄O₂⁺H⁺]), 337.0689 ([M+Na⁺]⁺, m/z = 337.0696 calculated for [C₁₈H₁₀N₄O₂Na⁺]), IR (neat): ν/ cm⁻¹ = 3111 (w), 3059 (w), 3026 (w), 2237 (w), 1601 (w), 1560 (m), 1496 (s), 1471 (s), 1421 (s), 1398 (m), 1304 (s), 1240 (m), 1211 (s), 1124 (m), 1097 (m), 1076 (m), 1038 (w), 1016 (m), 947 (w), 914 (m), 881 (m), 841 (m), 806 (s), 752 (m), 723 (w), 702 (s), 613 (m).
The synthesis of \( \text{ZnOPy}_8 \) was performed according to a modified procedure by Li et al.\(^6\). The synthesis was carried out under argon atmosphere and in the dark. To a 80 °C solution of \( \text{CN}_2\text{OPy}_2 \) (400 mg, 1.27 mmol, 2.8 eq) and zinc acetate (84 mg, 458 µmol, 1.0 eq) in 1-pentanol (15 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 100 µL, 669 µmol, 1.5 eq). The reaction was stirred at 140 °C for 19 h, cooled down to room temperature and the solvent was removed \textit{in vacuo}. To the residue was added CH\(_2\)Cl\(_2\), centrifuged (10 min, 100 %) and the supernatant was removed. The procedure was repeated three times with CH\(_2\)Cl\(_2\) as well as acetone and cold MeOH. The residue was collected and dried for 1 d in high vacuum.

**Yield:** 241 mg (182 µmol, 57 %) as a dark green solid; **Empirical formula** (\( M / (g/mol) \)): 1322.570 (\( \text{C}_{72}\text{H}_{40}\text{N}_{16}\text{O}_8\text{Zn} \)); \( ^1\text{H NMR} \) (1 M DCl in D\(_2\)O, 600 MHz, 300 K): \( \delta / ppm = 9.07 \) (s, 8H; H-3), 8.83 (d, \( J = 2.7 \) Hz, 8H; H-6), 8.49 (d, \( J = 5.8 \) Hz, 8H; H-7), 8.44 (dd, \( J = 9.0, 2.8, 1.1 \) Hz, 8H; H-9), 7.94 (dd, \( J = 8.9, 5.8 \) Hz, 8H; H-8) (Figure S13); \( ^{13}\text{C NMR} \) (1 M DCl in D\(_2\)O, 150 MHz, 300 K): \( \delta / ppm = 158.01 \) (C\(_q\)), 153.38 (C\(_q\)), 149.97 (C\(_q\)), 140.19 (C-7), 138.22 (C-9), 136.50 (C\(_q\)), 134.96 (C-6), 131.89 (C-8), 119.22 (C-3) (Figure S14); \( \text{MALDI-HRMS} \) (DCTB, 1-pentanol): \( m/z = 1321.59 \) ([M+H]+, \( m/z = 1321.26 \) calculated for \([\text{C}_{72}\text{H}_{40}\text{N}_{16}\text{O}_8\text{Zn}+\text{H}]^+\)); \( \text{IR} \) (neat): \( \nu / \text{cm}^{-1} = 3032 \) (w), 2924 (w), 2850 (w), 1614 (w), 1574 (m), 1473 (s), 1448 (s), 1421 (s), 1396 (s), 1335 (w), 1275 (s), 1209 (s), 1186 (m), 1136 (m), 1084 (s), 1043 (m), 1020 (s), 943 (w), 885 (s), 860 (m), 808 (m), 746 (m), 702 (s), 617 (m).
2.3.9.10.16.17.23.24-Octakis-[1-(2-(2-(2-oxo-2H-chromen-7-yl)oxyethoxy)ethoxy)ethyl)pyridinium-3-oxyl]phthalocyaninato zinc(II) octaiodide (ZnOPy$_8$-(EO$_3$-Umb)$_8$)

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The synthesis of ZnOPy$_8$-(EO$_3$-Umb)$_8$ was carried out according to a modified procedure by Li et al.$^{[6]}$. The synthesis was performed under argon atmosphere and in the dark. ZnOPy$_8$ (20 mg, 15.1 µmol, 1.0 eq) and I-EO$_3$-Umb (232 mg, 574 µmol, 38 eq) were dissolved in dry $N,N'$-dimethylformamide (1 mL) and stirred at 70 °C for 14 d. The solution was cooled down to room temperature and the solvent was removed in vacuo. The residue was washed with MeOH, CH$_2$Cl$_2$ and dried in vacuo. The compound ZnOPy$_8$-(EO$_3$-Umb)$_8$ was obtained after size exclusion chromatography on Sephadex LH-20 ($N,N'$-dimethylformamide = 100). The product was suspended by sonication for 15 min in ultrapure water and freeze dried for 5 d.

Yield: 56 mg (12.3 µmol, 81 %) as a dark green solid; Empirical formula ($M / (g/mol)$): 4556.146 ($C_{192}H_{176}I_8N_{16}O_{48}Zn$); $R_t$ (EtOAc = 100): 0.00; $^1$H NMR (DMSO-$d_6$, 600 MHz, 300 K): $\delta$/ppm = 9.39 (s, 8H; H-3), 9.31 (d, $J$ = 2.5 Hz, 8H; H-9), 8.97 (d, $J$ = 6.0 Hz, 8H; H-8), 8.65 (dd, $J$ = 8.6, 2.3 Hz, 8H; H-6), 8.26 (dd, $J$ = 8.9, 5.9 Hz, 8H; H-7), 7.63 (t, $J$ = 9.2 Hz, 8H; H-20), 7.27 (d, $J$ = 8.6 Hz, 8H; H-21), 6.69 (d, $J$ = 2.3 Hz, 8H; H-17), 6.64 (dd, $J$ = 8.6, 2.4 Hz, 8H; H-22), 6.02 (dd, $J$ = 9.5, 5.9 Hz, 8H; H-19), 4.88 (s, 16H; H-10), 4.07–3.93 (m, 32H; CH$_2$), 3.68–3.60 (m, 32H; CH$_2$), 3.59–3.50 (m, 16H; CH$_2$) (Figure S15); $^{13}$C NMR (DMSO-$d_6$, 150 MHz, 300 K): $\delta$/ppm = 161.17 (C-16), 160.04 (C-18), 155.89 (C-5), 154.96 (C-23), 152.43 (PC-Cq), 146.47 (PC-Cq), 143.92 (C-20), 140.94 (C-8), 136.66 (PC-Cq), 135.46 (C-9), 133.46 (C-6), 129.15 (C-21), 129.05 (C-7), 116.50 (C-3), 112.25 (C-24, C-22), 112.09 (C-19), 100.86 (C-17), 69.68 (CH$_2$), 69.69 (CH$_2$), 68.57 (CH$_2$), 67.75 (CH$_2$), 60.75 (CH$_2$) (Figure S16); ESI-HRMS: $m/z$ = 442.13803 [(M-8I)$_5$, $m/z$ = 442.13838 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-8I]$_5^{[8]}$], 510.29694 [(M-8I+Cl)$_7^{[7]}$, $m/z$ = 510.29664 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-8I+Cl]$_7^{[7]}$], 523.43030 [(M-7I)$_7^{[7]}$, $m/z$ = 523.43030 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-7I]$_7^{[7]}$], 631.81975 [(M-6I)$_5^{[6]}$, $m/z$ = 631.819575 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-6I]$_5^{[6]}$], 783.56508 [(M-5I)$_5^{[5]}$, $m/z$ = 783.56442 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-5I]$_5^{[5]}$], 1011.82891 [(M-4I)$_5^{[4]}$, $m/z$ = 1011.18178 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-4I]$_5^{[4]}$], 1390.54711 [(M-3I)$_5^{[3]}$, $m/z$ = 1390.54404 calculated for [C$_{192}$H$_{176}$I$_8$N$_{16}$O$_{48}$Zn-3I]$_5^{[3]}$] (Figure S19–S20); IR (neat): ν / cm$^{-1}$ = 3045 (w), 2931 (w), 1722 (m), 1707 (m), 1608 (s), 1581 (m), 1556 (w), 1496 (s), 1446 (m), 1402 (s), 1348 (w), 1281 (s), 1230 (m), 1201 (m), 1119 (s), 1088 (s), 1039 (m), 1022 (m), 993 (m), 893 (m), 831 (s), 748 (m), 706 (w), 677 (m), 634 (w), 615 (s) (Figure S22).
4. $^1$H- and $^{13}$C NMR-spectra

Figure S1: $^1$H NMR (CDCl$_3$ (*), 300 MHz, 300 K) spectrum of Cl-EO$_3$-OTs.

Figure S2: $^{13}$C NMR spectrum (CDCl$_3$ (*), 75 MHz, 300 K) of Cl-EO$_3$-OTs.
Figure S3: $^1$H NMR spectrum (DMSO-$d_6$ (*), 600 MHz, 300 K) of Cl-EO$_3$-Umb (** H$_2$O).

Figure S4: $^{13}$C NMR spectrum (DMSO-$d_6$ (*), 150 MHz, 300 K) of Cl-EO$_3$-Umb.
**Figure S5**: $^1$H NMR spectrum (DMSO-$d_6$ (*), 600 MHz, 300 K) of I-EO$_3$-Umb.

**Figure S6**: $^{13}$C NMR spectra (DMSO-$d_6$ (*), 150 MHz, 300 K) of I-EO$_3$-Umb.
Figure S7: $^1$H NMR spectrum (CDCl$_3$ (*), 600 MHz, 300 K) of CN$_2$-OPy.

Figure S8: $^{13}$C NMR spectrum (CDCl$_3$ (*), 150 MHz, 300 K) of CN$_2$-OPy.
Figure S9: $^1$H NMR spectrum (DMSO-$d_6$ (*), 600 MHz, 300 K) of ZnOPy$_4$-(EO$_3$-Umb)$_4$ (** DMF, *** H$_2$O).

Figure S10: $^{13}$C NMR spectrum (DMSO-$d_6$ (*), 150 MHz, 300 K) of ZnOPy$_4$-(EO$_3$-Umb)$_4$ (** DMF).
Figure S11: $^1$H NMR spectrum (CDCl$_3$ (*), 300 MHz, 300 K) of CN$_2$-OPy$_2$.

Figure S12: $^{13}$C NMR spectrum (CDCl$_3$ (*), 75 MHz, 300 K) of CN$_2$-OPy$_2$. 
Figure S13: $^1$H NMR spectrum (1 M DCl in D$_2$O (*), 600 MHz, 300 K) of ZnOPy$_8$.

Figure S14: $^{13}$C NMR spectrum (1 M DCl in D$_2$O, 150 MHz, 300 K) of ZnOPy$_8$. 
Figure S15: $^1$H NMR spectrum (DMSO-$d_6$ (*), 600 MHz, 300 K) of ZnOPy$_8$-(EO$_3$-Umb)$_8$ (** H$_2$O).

Figure S16: $^{13}$C NMR spectrum (DMSO-$d_6$ (*), 150 MHz, 300 K) of ZnOPy$_8$-(EO$_3$-Umb)$_8$. 
5. Selected mass spectra

Figure S17: Overview ESI high-resolution mass spectrum of ZnOPy₄-(EO₃-Umb)₄.

Figure S18: Cutout of the high resolution mass spectrum of ZnOPy₄-(EO₃-Umb)₄.

Figure S19: Overview ESI high resolution mass spectrum of ZnOPy₈-(EO₃-Umb)₈.
Supporting Information

measured for
$[\text{M-RI}]^{\text{+}}$

calculated for
$[\text{C}_{160}^\text{H}_{179}\text{N}_{10}\text{O}_{44}\text{Zn}]^{\text{+}}$

measured for
$[\text{M-RI+Cl}]^{\text{+}}$

calculated for
$[\text{C}_{160}^\text{H}_{179}\text{N}_{10}\text{O}_{44}\text{ZnCl}]^{\text{+}}$

measured for
$[\text{M-7I}]^{\text{+}}$

calculated for
$[\text{C}_{160}^\text{H}_{179}\text{N}_{10}\text{O}_{44}\text{ZnI}]^{\text{+}}$
Figure S20: Cutouts of the high resolution mass spectrum of ZnOPy$_8$-(EO$_3$-Umb)$_8$. 
6. Selected infrared spectra

Figure S21: IR-spectrum (ATR) of ZnOPy₄(EO₃-Umb)₄.

Figure S22: IR-spectrum (ATR) of ZnOPy₈(EO₃-Umb)₈.
7. Absorption-, emission- and excitation measurements

For the dilution series stock solutions of the representative photosensitizer of 100 µM in DMF and 50 µM in water or PBS were diluted with the appropriate solvent to 10 µM, followed by the dilution to final concentrations of 0.25, 0.50, 0.75, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 5.0, 6.0, 8.0 and 10 µM. All solvents for this studies were of spectroscopic grade and degassed in vacuo before use. All measurements were carried out in “high precision Quartz SUPRASIL® cuvettes with a light path of 10 x 4 mm ("114F-10-40"; V = 1400 µL) from Hellma Analytics. For all solutions absorbance--, emission- and excitation spectra were recorded (Figures S23, Figure S25 and S26).

Molar absorption coefficient \( \varepsilon \) was determined using the Lambert-Beer law (equation (1))\[8\] by plotting the absorbance \( A \) as function of the concentration \( c \) at a specific concentration. \( b \) is standing for the light path way of the cuvette. The slope \( m \) is then defined as \( \varepsilon \) times \( b \). By rearranging this formula and a light path way of 1 cm the molar absorption coefficient can be determined (equation (2)). Hence the molar absorption coefficient can vary by several powers of ten within an absorption spectrum it is given as \( \log(\varepsilon) \).[9]

\[
A = \varepsilon b c \tag{1}
\]
\[
m = \varepsilon b \rightleftharpoons \varepsilon = \frac{m}{b} \tag{2}
\]

Results are summarized in Table S1 and Figure S23.

Table S1: Absorption maxima of ZnOPy\(_4\)-(EO\(_3\)-Umb)\(_4\) and ZnOPy\(_8\)-(EO\(_3\)-Umb)\(_8\) in water, PBS and DMF (\( c = 1.0 \mu M, \ast \text{ Q-band})\).

| Compound          | Solvent | \( \lambda_{\text{Abs.}} / \text{nm} \) (\( \log_{10} \varepsilon \)) |
|-------------------|---------|--------------------------------------------------------------------------|
| ZnOPy\(_4\)-(EO\(_3\)-Umb)\(_4\) | H\(_2\)O | 683* (5.15), 614 (4.44), 326 (4.88), 289 (4.72) |
|                   | PBS     | 683* (4.89), 616 (4.32), 326 (4.76), 288 (4.60) |
|                   | DMF     | 679* (5.27), 671* (5.24), 608 (4.54), 327 (4.94) |
| ZnOPy\(_8\)-(EO\(_3\)-Umb)\(_8\) | H\(_2\)O | 681* (5.29), 614 (4.51), 323 (5.08), 289 (4.99) |
|                   | PBS     | 682* (5.21), 616 (4.20), 323 (5.00), 288 (4.91) |
|                   | DMF     | 678* (5.35), 611 (4.57), 325 (5.14), 293 (5.01) |
Figure S23: Absorption spectra in concentration from 0.25 µM to 10 µM of (A), (C) and (E) ZnOPy$_4$-(EO$_3$-Umb)$_4$ and (B), (D) and (F) ZnOPy$_8$-(EO$_3$-Umb)$_8$ in H$_2$O (A) and (B), PBS (C) and (D), DMF (E) and (F). Insert: Lambert-Beer law verified at $\lambda_{\text{max}}$.

The Stokes-shift was determined between the absorption maximum of the Q-band and the emission maximum in nm and cm$^{-1}$. For the latter, the wavelengths were converted in the wavenumbers in cm$^{-1}$ before subtraction. Results are shown in Table 2, the corresponding spectra are shown in Figure S24.
Table 2: Molar absorption coefficient $\varepsilon$ for the Q-band, absorption-, excitation- and emission maxima, Stokes-shift of ZnOPy$_4$-(EO$_3$-Umb)$_4$ and ZnOPy$_8$-(EO$_3$-Umb)$_8$ in water, PBS and DMF ($c = 1.0 \, \mu$M).

| Compound               | Solvent | $\lambda_{\text{Abs.}}$ / nm (log$_{10} \varepsilon$) | $\lambda_{\text{EX}}$ / nm | $\lambda_{\text{EM}}$ / nm | Stokes-shift $\lambda$ / nm | Stokes-shift $\bar{\nu}$ / cm$^{-1}$ |
|------------------------|---------|-------------------------------------------------|-----------------|-----------------|--------------------------|-----------------|
| ZnOPy$_4$-(EO$_3$-Umb)$_4$ | H$_2$O   | 683 (5.15)                                      | 684             | 691             | 8                        | 170             |
|                        | PBS     | 683 (4.89)                                      | 684             | 691             | 8                        | 170             |
|                        | DMF     | 679 (5.27)                                      | 679             | 683             | 4                        | 86              |
|                        |         | 671 (5.24)                                      | 671             | 684             | 13                       | 283             |
| ZnOPy$_8$-(EO$_3$-Umb)$_8$ | H$_2$O   | 681 (5.29)                                      | 682             | 687             | 6                        | 128             |
|                        | PBS     | 682 (5.21)                                      | 684             | 689             | 7                        | 149             |
|                        | DMF     | 678 (5.35)                                      | 677             | 683             | 5                        | 108             |

Figure S24: Absorption (---), excitation (- - -) and emission (——) spectra (A), (C) and (E) of ZnOPy$_4$-(EO$_3$-Umb)$_4$ and (B), (D) and (F) of ZnOPy$_8$-(EO$_3$-Umb)$_8$ 1.0 $\mu$M in H$_2$O (A) and (B), PBS (C) and (D), DMF (E) and (F).
Figure S25: Excitation (——) and emission (- - -) spectra in concentrations from 0.25 µM to 10 µM of ZnOPy$_4$·(EO$_3$·Umb)$_4$ in H$_2$O (A) and (B), PBS (C) and (D), DMF (E) and (F).
Figure S26: Excitation (—) and emission (- - -) spectra in concentrations from 0.25 µM to 10 µM of ZnOPy₈(EO₃-Umb)₈ in H₂O (A) and (B), PBS (C) and (D), DMF (E) and (F).
8. Fluorescence quantum yield measurements

The samples from the dilution series were used to determine the fluorescence quantum yields at different concentrations. Measurements with low absorption factors (low concentrated solutions) were excluded from the calculation. The results are plotted in Figure S27 and summarized in Table S3.

![Figure S27](image)

**Figure S27**: Fluorescence quantum yield measurements of ZnOPy$_4$-(EO$_3$-Umb)$_4$ and ZnOPy$_8$-(EO$_3$-Umb)$_8$ in H$_2$O, PBS and DMF with error bars ($c = 0.5$–$10$ µM, $\lambda_{\text{EX}} = 645$ nm).

**Table S3**: Fluorescence quantum yields of ZnOPy$_4$-(EO$_3$-Umb)$_4$ and ZnOPy$_8$-(EO$_3$-Umb)$_8$ in H$_2$O, PBS and DMF ($c = 0.5$–$10$ µM, $\lambda_{\text{EX}} = 645$ nm).

| Compound          | Solvent | $\Phi_F$  |
|-------------------|---------|-----------|
| ZnOPy$_4$-(EO$_3$-Umb)$_4$ | H$_2$O | 0.17±0.05 |
|                   | PBS     | 0.03±0.01 |
|                   | DMF     | 0.19±0.04 |
| ZnOPy$_8$-(EO$_3$-Umb)$_8$ | H$_2$O | 0.15±0.08 |
|                   | PBS     | 0.05±0.01 |
|                   | DMF     | 0.17±0.05 |
9. Singlet oxygen quantum yield measurements

The relative singlet oxygen quantum yields $\Phi$ were determined by comparison with methylene blue in PBS (1x) (Gibco) as well as in water ($\Phi_A = 0.52^{[10]}$) or unsubstituted zinc(II) phthalocyanine (ZnPc) in DMF ($\Phi_A = 0.56^{[11]}$) as a reference. The representative photosensitizer and references were dissolved in degassed PBS, water or DMF followed by 1 h of sonication to generate stock solutions of $c = 100 \mu M$ (water, PBS) or $c = 10 \mu M$ (DMF). The methylene blue (MB) stock solutions in degassed water and PBS were sonicated for 15 min and had a final concentration of 500 µM. All stock solutions were diluted with air-saturated solvents to reach an absorbance of 0.2 (Figure S28 and Figure S30). Singlet oxygen quantum yields were calculated according to equation (2)$^{[12]}$, where r is the singlet oxygen generation rate, which is measured as slope of the monitored bleaching over time. In water and PBS the decay of the ADMDMA emission integral ($\lambda_{EM} = 380–550$ nm) was monitored and plotted against the irradiation time $t$ $^{[13]}$ (Figures S29 and S31). In DMF the decay of the DPBF absorbance ($\lambda = 414$ nm) was monitored and plotted as ln ($A$/$A_0$) against the irradiation time $t$ $^{[13]}$ (Figure S32). $\lambda_1$–$\lambda_2$ is the irradiation wavelength interval, $A(\lambda)$ is the absorbance and $I_0(\lambda)$ is the incident spectral photon flow. The latter can be approximated by a constant value and therefore it can be drawn in front of the integral so that it can be eliminated by shorting the fraction.$^{[12]}$ All measurements were performed in triplicate and the standard deviation was determined.

$$\Phi_A = \Phi_B \frac{\int_{\lambda_1}^{\lambda_2} I_0(\lambda)(1 - 10^{-A_r(\lambda)}) d\lambda}{\int_{\lambda_1}^{\lambda_2} I_0(\lambda)(1 - 10^{-A_s(\lambda)}) d\lambda}$$  \hspace{1cm} (2)

The samples were irradiated in steps of 5 s (0–30 s) or in water in steps of 10 s (0–60 s) with a halogen cold light source “VisiLight CL-150” (VWR) equipped with a 150 W “64620 EFR 5” (OSRAM) and a 600 nm cut-on filter “R-60” (Shimadzu). The red light irradiation intensity was measured with a power meter “Solarmeter 9.6” (Solartech) and adjusted to 2.0 mW/cm$^2$. Samples were mixed vigorously between each irradiation step.

For singlet oxygen quantum yield measurements in water a stock solution of 0.1 mg/mL 9,10-anthacenediyl-bis(methylene)dimalonic acid (ADMDMA) ($\lambda_{EX} = 370$ nm) in slightly alkaline water was prepared. 10 µL of the stock solution were added right before the measurement to 1000 µL of adjusted photosensitizer solution and mixed vigorously. Attention was paid to a uniform starting value.

Singlet oxygen generation in PBS was determined using 9,10-anthacenediyl-bis(methylene)dimalonic acid (ADMDMA) ($\lambda_{EX} = 370$ nm). A stock solution in degassed PBS of $c = 200 \mu M$ was prepared and sonicated for 15 min. 5 µL of the stock solution were added right before the measurement to 1000 µL of adjusted photosensitizer solution and mixed vigorously.

For the measurements in DMF a stock solution of 1,3-diphenylisobenzofuran (DPBF) was prepared and sonicated for 15 min. The initial concentration of DPBF in the photosensitizer solution was adjusted to an absorbance of 1.0. The samples were irradiated in steps of 5 s (0–30 s) or 10 s (0–60 s) in case of ADMDMA in water with a halogen cold light source “VisiLight CL-150” (VWR) equipped with a 150 W “64620 EFR 5” (OSRAM) and a 600 nm cut-on filter “R-60” (Shimadzu). The red light irradiation intensity was measured with a power meter “Solarmeter 9.6” (Solartech) and adjusted to 2.0 mW/cm$^2$. Samples were mixed vigorously between each irradiation step. The measured data is summarized in Table S4.
Table S4: Singlet oxygen quantum yields of ZnOPy₄-(EO₃-Umb)₄ and ZnOPy₈-(EO₃-Umb)₈ in water, PBS and DMF. The results are the mean ± standard deviation from three individual measurements.

| Compound          | Solvent | Reference | Indicator | ΦΔ      |
|-------------------|---------|-----------|-----------|---------|
| ZnOPy₄-(EO₃-Umb)₄ | H₂O     | MB        | ADMDMA    | 0.52±0.09 |
|                   | PBS     | MB        | ADMDMA    | 0.05±0.02 |
|                   | DMF     | ZnPC      | DPBF      | 0.57±0.03 |
| ZnOPy₈-(EO₃-Umb)₈ | H₂O     | MB        | ADMDMA    | 0.64±0.09 |
|                   | PBS     | MB        | ADMDMA    | 0.12±0.04 |
|                   | DMF     | ZnPC      | DPBF      | 0.44±0.02 |

Figure S28: (A)–(C) UV-vis spectra of (A) methylene blue, (B) ZnOPy₄-(EO₃-Umb)₄ and (C) ZnOPy₈-(EO₃-Umb)₈ in water.
Figure S29: (A)–(D) Change of the ADMDMA emission signal upon irradiation with light ($\lambda > 600$ nm) (A) without any photosensitizer, with (B) methylene blue, (C) ZnOPy$_4$-(EO$_3$-Umb)$_4$ and (D) ZnOPy$_8$-(EO$_3$-Umb)$_8$ in water. (E) Plot of the emission intensity integral depending on the irradiation time for the sample without photosensitizer, with methylene blue, ZnOPy$_4$-(EO$_3$-Umb)$_4$ or ZnOPy$_8$-(EO$_3$-Umb)$_8$ in water. Error bars are the mean ± standard deviation from three individual measurements.
Figure S30: (A)–(C) UV-vis spectra of (A) methylene blue, (B) ZnOPy$_4$-(EO$_3$-Umb)$_4$ and (C) ZnOPy$_8$-(EO$_3$-Umb)$_8$ in PBS.
Figure S31: (A)–(D) Change of the ADMDMA emission signal upon irradiation with light (λ > 600 nm) (A) without any photosensitizer, with (B) methylene blue, (C) ZnOPy₄-(EO₃-Umb)₄ and (D) ZnOPy₈-(EO₃-Umb)₈ in PBS. (E) Plot of the emission intensity integral depending on the irradiation time t for the sample without photosensitizer, with methylene blue, ZnOPy₄-(EO₃-Umb)₄ or ZnOPy₈-(EO₃-Umb)₈ in PBS. Error bars are the mean ± standard deviation from three individual measurements.
Figure S32: (A)–(D) Change of the absorption spectra of DPBF in DMF with additional (B) ZnPC, (C) ZnOPy$_4$-(EO$_3$-Umb)$_4$ and (D) ZnOPy$_8$-(EO$_3$-Umb)$_8$ due to irradiation (λ > 600 nm) for 0–25 s. Insert: change of ln(A$_0$/A) at 414 nm depending on the irradiation time $t$. Error bars are the mean ± standard deviation from three individual measurements.
10. Cell experiments

10.1 Preparation of photosensitizer stock solutions

The respective photosensitizer was dissolved in degassed PBS (1x) (Gibco) by sonication for 60 min to obtain 100 µM stock solutions.

10.2 Confocal laser scanning microscopy of HepG2

The confocal laser scanning microscopy with photodynamic compounds was performed according to an adjusted literature protocol.[14] We seeded 2 x 10^4 HepG2 cells in 200 µL DMEM (Dulbecco's Modified Eagle's Medium) (Thermo Fisher Scientific) supplied with 10 % (v/v) fetal calf serum (FCS) (Life Technologies GmbH) Antibiotic-Antimycotic (Life Technologies GmbH) into a “µ-Slide 8 Well” (Ibidi). The cells were incubated at 37 °C and 5 % CO₂ overnight for adherence. The cells were stained with 200 µL 20 ng/µL “Hoechst 33342” (Thermo Fisher Scientific) in PBS for 30 min at 37 °C and 5 % CO₂. Optionally the cells were stained with 200 µL CellBrite® Green (Biotium) diluted 1:200 in PBS for 30 min at 37 °C and 5 % CO₂, to stain the outer plasma membrane and by vesicular traffic intracellular membrane compartments. The cells were washed with PBS three times. We then applied 200 µL DMEM with 50 µM of the respective compound and incubated the cells for 30 min at 37 °C and 5 % CO₂. The compound was removed and the cells washed with PBS twice. We performed confocal laser scanning microscopy with a “Leica TCS SP8X Falcon” (Leica). The cells were incubated at 37 °C and 5 % CO₂ during the live cell microscopy. Maximum projection images and 3D images were generated from image stacks using “LasX” (Leica).
Figure S33: Live cell microscopy images of HepG2 cells treated with (A) ZnOPy₄-(EO₃-Umb)₄ or (B) ZnOPy₈-(EO₃-Umb)₈ (red). The nuclei were stained with Hoechst 33342 (blue) and the cytoplasm with CellBrite® Green (green). An untreated control (C) verified that the stains do not add to the compounds fluorescence signal by crosstalk or create artefacts. Magnifications are indicated by a frame. Scale bars represent 10 µm.
**Figure S34**: Image stacks from live cell microscopy with HepG2 cells treated with ZnOPy₄(EO₃-Umb)₄ (red) and stained with Hoechst (blue) and CellBrite® Green (green) were used to generate maximum projection images (A) and a 3D model of the cells (B). Slices through the indicated axis of the model (C) show the internalization of the compound. The scale bars represent 10 µm.
**Figure S35:** Image stacks from live cell microscopy with HepG2 cells treated with $\text{ZnOPy}_8(\text{EO}_3\text{-Umb})_8$ (red) and stained with Hoechst (blue) and CellBrite® Green (green) were used to generate maximum projection images (A) and a 3D model of the cells (B). Slices through the indicated axis of the model (C) show the internalization of the compound. The scale bars represent 10 µm.
10.3 Phototoxicity assay

The phototoxicity assay was performed according to an adjusted literature protocol.[14] We seeded $1 \times 10^4$ HepG2 cells in 100 µL DMEM (Thermo Fisher Scientific) supplied with 10 % (v/v) fetal calf serum (FCS) (Life Technologies GmbH) Antibiotic-Antimycotic (Life Technologies GmbH) into a “Corning 96 Well” microplate (Sigma Aldrich). The cells were incubated at 37 °C and 5 % CO$_2$ overnight. To avoid filter effects during the assay the DMEM was exchanged for Fluorobrite DMEM (Thermo Fisher Scientific) supplied with the respective compound solved in PBS. The dilution of the medium was adjusted for the controls and the cells were incubated for 30 min at 37 °C and 5 % CO$_2$. After the incubation the compound was removed and the cells washed with PBS once before new Fluorobrite DMEM was applied. The exposure took place at room temperature under a laminar flow cabinet to provide a sterile environment. To induce phototoxicity, the cells were irradiated with 1.2 mW/cm$^2$ using a “Visilight CI-150 halogen lamp” (VWR) equipped with an “R-60” filter (Shimadzu) to block light-radiation under 600 nm. After the irradiation, the cells were incubated at 37 °C and 5% CO$_2$ overnight. To determine the viability of the cells, 20 µL “Cell Titer Aqueous One” (Promega) were added to the media. After 30 min, absorption at 490 nm was detected with a “Promega Glow Max” (Promega). The results were normalized to dark and irradiation controls and are the mean of three replicates ± standard deviation.

72 h (Dark) toxicity assay

The dark toxicity assay was performed according to an adjusted literature protocol.[14] We seeded $1 \times 10^4$ HepG2 cells in 100 µL DMEM (Thermo Fisher Scientific) supplied with 10 % (v/v) fetal calf serum (FCS) (Life Technologies GmbH) Antibiotic-Antimycotic (Life Technologies GmbH) into a “Corning 96 Well” microplate (Sigma Aldrich) and the respective compound solved in PBS. The dilution of the medium was adjusted for the controls and the cells were incubated for 72 h at 37 °C and 5% CO$_2$. To determine the viability of the cells, 20 µL “Cell Titer Aqueous One” (Promega) were added to the media. After 30 min, absorption at 490 nm was detected with a “Promega Glow Max” (Promega). The results were normalized to dark and irradiation controls and are the mean of three replicates ± standard deviation.
Figure S36: (A) and (B): Dark control for the compounds’ toxicity during photo-treatment. HepG2 cells were treated with the respective compound concentrations and not exposed to light, but kept in the dark for (A) 60 min and (B) 72 h. Data were normalized against untreated controls and are the mean ± standard deviation from three replicates. (C) Irradiation control without photosensitizers for HepG2 cells exposed to 1.2 mW/cm² light for 0 min (Control), 15 min (1.1 J/cm²), 30 min (2.2 J/cm²), 45 min (3.2 J/cm²) and 60 min (4.3 J/cm²) without the respective compounds. Data were normalized against non-irradiated controls and are the mean ± standard deviation from three replicates.
11. Photobiological studies on bacteria

11.1 Preparation of photosensitizer stock solutions
The respective photosensitizer was dissolved in degassed PBS (1x) (Gibco) by sonication for 60 min to gain 100 µM stock solutions.

11.2 Bacterial strains and culture conditions
Experiments were performed by slight modification of the previously published method\cite{15}. Bacterial strains *B. subtilis* DB104, *S. aureus* 3150/12, *E. coli* UTI89, and *E. coli* Nissle 1917 were grown on lysogeny broth (LB; Miller) agar and stored at 4 °C. One single isolated colony was taken from this plate, transferred to 3 mL LB broth, and incubated aerobically overnight at 37 °C in a shaker incubator at 180 rpm (rotations per minute). Bacteria were then suspended in 10 mL of fresh LB medium to an optical density \(OD_{600} \approx 0.1\) and grown to an attenuation of \(OD_{600} \approx 0.4\). The bacterial suspensions were then centrifuged at 4000 rpm for 5 min and PBS was added to achieve the concentration of approximately \(1 \times 10^8\) cells per mL. This suspension was used for the irradiation experiments.

11.3 Photoinactivation of bacteria
1 mL bacterial suspension containing a certain amount of photosensitizer was incubated in the dark for 15 min at 37 °C and the samples were centrifuged for 5 min at 4000 rpm. After the supernatant was discarded, the pellet was suspended in 1 mL of PBS and placed in 24-well plate. Irradiation was performed with an LED lamp (660 ± 24 nm) (“GLU-150” from RoHs). Fluence rates were routinely measured using a power meter (“Solarmeter 9.6” from Solartech). After irradiation, the living bacterial cells were determined by serial dilutions of the bacterial suspension and plated on LB agar plates. After the incubation overnight at 37 °C, the number of CFU/mL was counted using an automated colony counter “ProtoCOL2” from Synbiosis. The results are the mean of three replicates ± standard deviation.

![Figure S37](image-url): Photoinactivation with ZnOPy\(_4\)-(EO\(_3\)-Umb)\(_4\) and ZnOPy\(_8\)-(EO\(_3\)-Umb)\(_8\) of (A) Gram-negative *E. coli* strain UTI89 and (B) Gram-positive *S. aureus* strain 3150/12. The bacteria were exposed to 5 mW/cm\(^2\) light (> 600 nm) for 15 min (4.5 J/cm\(^2\)) or 30 min (9.0 J/cm\(^2\)). Control samples did not contain PC and were irradiated for 30 min (9.0 J/cm\(^2\)). Error bars are the mean ± standard deviation from three replicates.
11.4 Fluorescence imaging

Fluorescence microscopy images were recorded using a “Nikon inverted microscope TS2R” (Nikon Corporation, Tokyo, Japan) equipped with an “IS-DMK3UX174” monochrome camera and an LED filter block as described previously\[16\]. Bacterial suspensions labelled with “Hoechst 33342” were further incubated with the solutions containing corresponding photosensitizer in the dark for 15 min at 37 °C and centrifuged for 5 min at 4000 rpm. Supernatants were discarded and the pellets were fixed overnight at 4 °C with 2 % glutaraldehyde. An aliquot of the supernatant was then transferred to an object slide and fluorescence images were recorded. “Hoechst 33342” was excited with the light passing through a 338–390 nm band-pass filter and emission was recorded with a 475–490 nm band-pass filter. Zinc(II) phthalocyanine was excited with light passing through a 621–658 nm band-pass filter and emission was recorded with a 706–773 nm band-pass filter.

Figure S38: Co-localization of \( \text{ZnOPy}_4(\text{EO}_3\text{-Umb})_4 \) and \( \text{ZnOPy}_8(\text{EO}_5\text{-Umb})_8 \) with the DNA in \( E. coli \) UTI89 bacteria.
11.5 Live/Dead assay

Bacterial cells were treated in the same way as for evaluation with CFU counting. After irradiation, samples were incubated with the dyes contained in the "LIVE/DEAD®" assay ("BacLight™ Bacterial Viability Kit", Invitrogen L13152) for 15 min according to the manufacturer's instructions and fluorescence images were acquired (excitation at 480 nm and long pass filters were used).

Figure S39: Live/dead assay of Gram-negative *E. coli* strain Nissle 1917 and Gram-positive *B. subtilis* strain DB104. The scale bares are indicating a length of 50 µm.
Table S5: Overview of the properties of selected literature known photosensitizers with similar structural motifs and comparison with the molecules synthesized in this publication. (+) corresponds to cationic charge, (EO) to ethylene glycols, and (PC) to phthalocyanine with n arms (L).

| Literature | Name | Compound structure | PC  | EO | Coumarin | Bacteria | Organic solvent | Aqueous solvents | Φ<sub>α</sub> |
|------------|------|-------------------|-----|----|----------|----------|-----------------|-----------------|---------|
| 1          | This publication | ZnOPy<sub>4</sub>-(EO<sub>3</sub>-Umb)<sub>4</sub> | Zn+4L | √  | √  | √  | HepG2: 20% viable, 1 µM, 1.1 J/cm²; no dark toxicity | √  | √  | 0.57 | - | 0.05 | 0.52 |
| 2          | This publication | ZnOPy<sub>8</sub>-(EO<sub>3</sub>-Umb)<sub>8</sub> | Zn+8L | √  | √  | √  | HepG2: 30% viable, 1 µM, 1.1 J/cm²; no dark toxicity | √  | √  | 0.44 | - | 0.12 | 0.64 |
| 3          | Zhou et al<sup>[17]</sup> | 10b | Zn+1L | -  | √  | √  | HepG2: IC<sub>50</sub> = 0.018 µM, 1.5 J/cm²; TC<sub>50</sub> = >10 µM | -  | -  | 0.57 | - | - | - |
| 4          | Zhou et al<sup>[17]</sup> | 12b | Zn+1L | -  | √  | -  | HepG2: IC<sub>50</sub> = 0.063 µM, 1.5 J/cm²; TC<sub>50</sub> = >10 µM | -  | -  | 0.60 | - | - | - |
| 5          | Li et al<sup>[18]</sup> | 11 | Zn+8L | √  | √  | -  | HEP2: IC<sub>50</sub> = 2.2 µM, 1 J/cm²; measurable dark toxicity 85 µM | -  | -  | -  | 0.12 | - | - |
| 6          | Tuncel et al<sup>[19]</sup> | 1 | Zn+4L | -  | √  | -  | HT-29: no phototoxicity 1–500 µM, 3.6 J/cm² | -  | -  | -  | 0.59 | - | 0.05 (ADMDMA) 0.09 (TX-100; ADMDMA) |
| Literature | Name | Compound structure | PC | EO | Coumarin | Cells | Bacteria Gram-Positive | Gram-Negative | Organic solvent | Φs | Aqueous solvents |
|------------|------|--------------------|----|----|----------|-------|----------------------|---------------|-----------------|----|-----------------|
| Tuncel et al. [18] | 3 | Zn₈L | - | √ | - | HT-29: 500 µM, 25 % killed, 3.6 J/cm² | - | - | - | 0.34 | - |
| Boyar et al. [19] | 1d | Zn₄L | √ | - | √ | EJ: 91 % viable, 1 µM, 5 J/cm²; 4 % viable, 10 µM, 5 J/cm² | - | - | - | 0.13 | - |
| Schnurpfeil et al. [20] | 1h | Zn₄L | √ | - | - | - | - | 0.58 | - |
| Schnurpfeil et al. [20] | 1i | Zn₈L | √ | - | - | - | - | 0.30 | - |
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