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# Amphiphilic Phthalocyanines in Polymeric Micelles: A Supramolecular Approach toward Efficient Third-Generation Photosensitizers

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**Index**

**Contents:**

Materials and Methods: page 2

Synthesis and characterization of SiPc derivatives: pages 3 – 6

Singlet oxygen measurements: pages 7 – 8

Synthesis and characterization of ben/nap-PCL-PEG block copolymers: pages 9 – 13

Preparation and characterization of PS loaded micelles: page 14 – 17

References: page 18

**Figures:**

(S1) $^{1}$H NMR spectra of SiPc derivatives **1**, **2** and **3**.

(S2) Singlet oxygen measurements

(S3) GPC traces of synthesized polymers

(S4) Loading capacity of micellar formulations

(S5) Loading efficiency of micellar formulations

**Tables:**

(S1) GPC characterization of the synthesized polymers

(S2) Set of the micellar formulations studied

## General materials and methods

### For the synthesis and characterization of PS 1-3 and their precursors:

Chemical reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics or Fluka Chemie, and were used without further purification. $SiPcCl_2$, in particular, was purchased from Sigma-Aldrich with 85% content. All reactions were performed in standard glassware. The monitoring of the reactions has been carried out by thin layer chromatography (TLC), employing aluminum sheets coated with silica gel type 60 F254 (0.2 mm thick, E. Merck). Purification and separation of the synthesized products was performed by column chromatography, using silica gel (230-400 mesh, 0.040-0.063 mm, Merck). Nuclear magnetic resonance spectra ($^1$H NMR and $^{13}$C NMR) were recorded on Bruker AC-300 (300 MHz and 75 MHz) instruments, with solvent signal as reference. The deuterated solvents employed are indicated in parentheses. UV/Vis spectra were recorded with a Hewlett-Packard 8453 instrument. In brackets is expressed the logarithm of the molar absorption coefficient ($\varepsilon$). Infrared spectra (IR) were recorded on a Bruker Vector 22 spectrophotometer, using solid samples (KBr pellets) or as thin films (film). Melting points (Mp) were determined on a Büchi 504392-S. Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) and (MS) and high resolution MS (HR-MS) were recorded in the positive ion mode with a Bruker Ultrareflex III TOF spectrometer equipped with a Nd:YAG laser operating at 355 nm.

### For the synthesis and characterization of PCL-PEG copolymers:

ε-Caprolactone (ε-CL), Tin (II) 2-ethylhexanoate ($Sn(Oct)_2$), deuterated chloroform ($CDCl_3$) and p-nitrophenyl chloroformate (PNC), triethyleneamine (TEA), mPEG-OH (2000g/mol), 1-pentanol, benzyl alcohol, naphthalene alcohol, mesyl chloride, aquous ammonia (25%) and sodium hydroxide were obtained from Sigma-Aldrich (Zwijndrecht, the Netherlands). All other solvents were from Biosolve (Valkenswaard, the Netherlands). Toluene was dried over 4Å molecular sieves (Aldrich) prior to use. All chemicals were used as received. The $^1$H NMR spectra of polymers were recorded using a Gemini NMR spectrometer (Varian Associates Inc. NMR instruments, Palo Alto, CA). Polymers were dissolved in $CDCl_3$ at a concentration of 0.015 $g.ml^{-1}$. Peak multiplicity was denoted as s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), m (multiplet), and b (broad signal). The UV-Vis studies of PS-loaded micellar formulation were performed in a Shimadzu UV-2450 spectrophotometer (Shimadzu, Japan).

### Gel permeation chromatography:

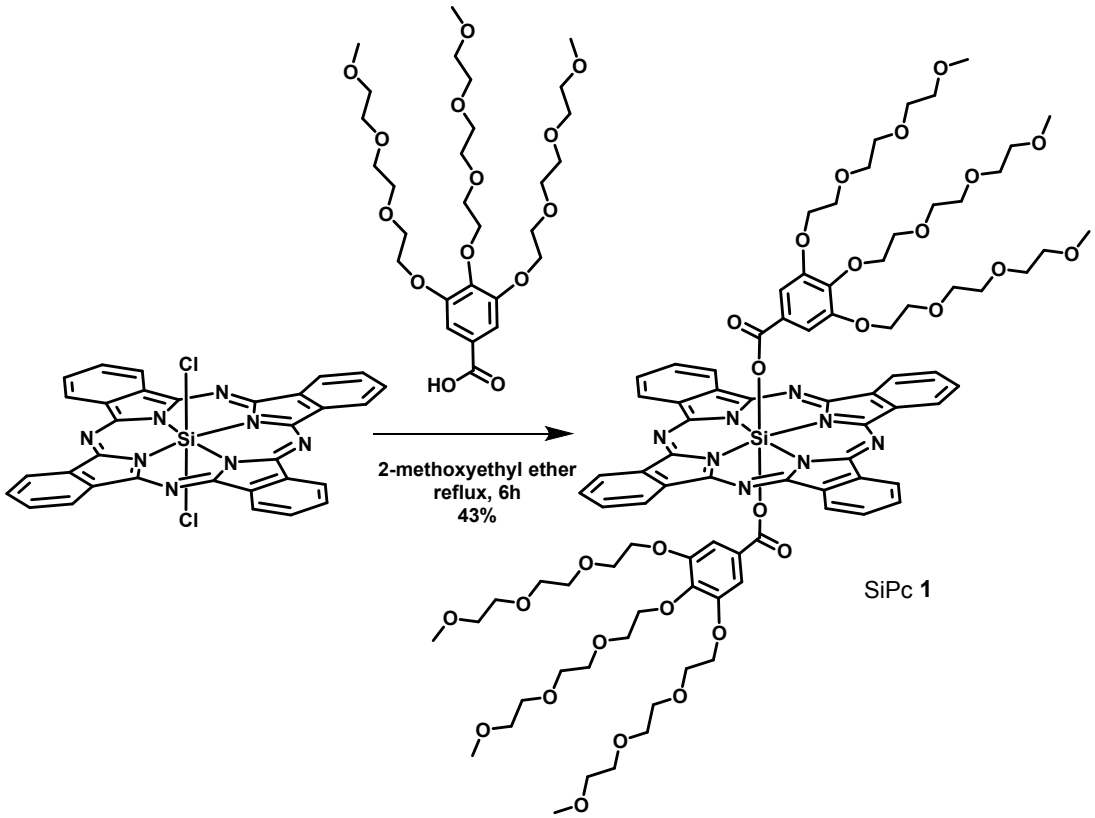
Number average and weight average molecular weights ($M_n$ and $M_w$, respectively), molecular weight distributions of purified Ben-PCL-PEG copolymers were determined by gel permeation chromatography (GPC, Viscotek, USA) equipped with a PLgel OligoPore column (300x7.5 mm, including a guard column, 50x7.5 mm) and a TDA302 triple detection array. Data were obtained from the refractometer. Narrow poly(ethylene glycol) standards ranging from 200 to 5000 g/mol were used for calibration and relative molecular weights were calculated using the OmniSEC 5.02 software. DMF with LiCl was used as an eluent at a flow rate of 1 mL/min at 30 ˚C, while sample concentrations ranged from 3-5 mg/mL.

**Synthesis of SiPc derivatives**

General procedure for the synthesis of SiPc silyl ester derivatives **1**-**3**

In a pre-dried flask, $SiPcCl_2$ was mixed with the corresponding precursor for axial derivatization, bearing a carboxylic acid as anchoring group, in 2-methoxyethyl ether (M ~ 0.7 mol/L) under argon atmosphere. The suspension was refluxed until the starting material disappeared (monitored by TLC). Purification of the desired SiPc was achieved through column chromatography on silica gel, using specific eluents in each case.

Synthesis of SiPc **1**




Methyl 3,4,5-tris(methoxytriethyleneoxy)benzoic acid (**4**)[1-2] (974 mg, 1.6 mmol) and $SiPcCl_2$ (100 mg, 0.16 mmol) were mixed in 1.5 mL of 2-methoxyethyl ether under argon atmosphere, and refluxed for 6 h. After cooling down to rt, the solvent was removed under reduced pressure. Purification of the slurry by column chromatography on silica gel (DCM/methanol, 20:1) yielded the pure compound as a blue gummy solid. Yield: 122 mg, 0.069 mmol, 43%.

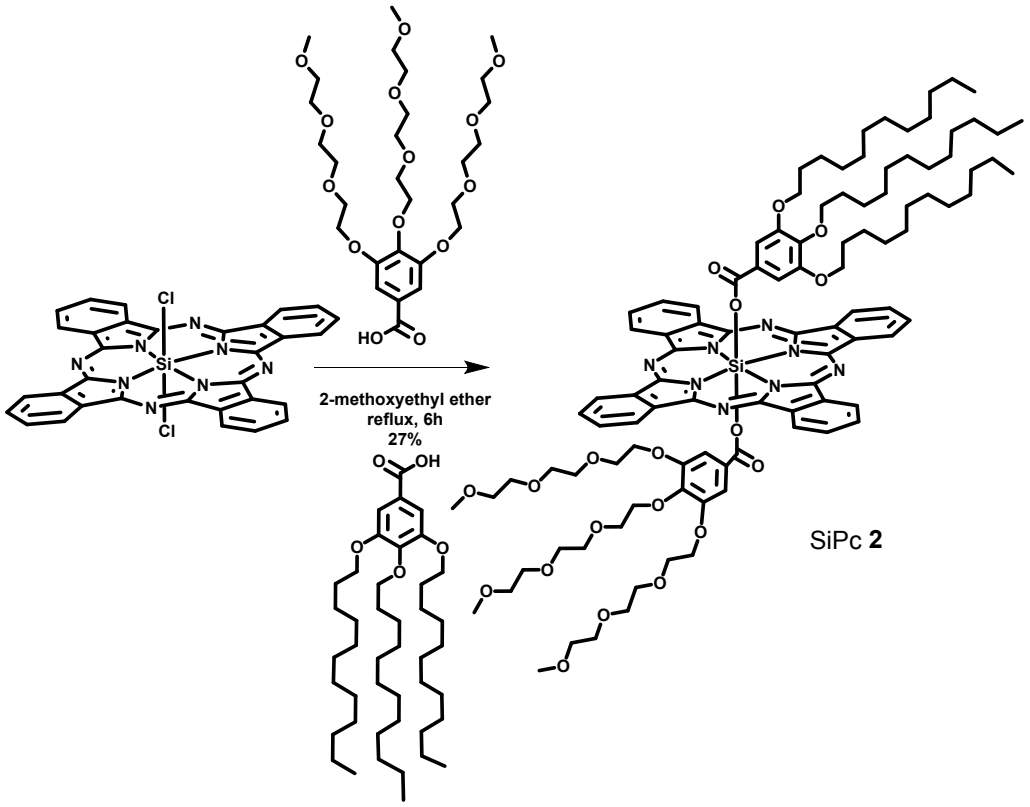
**Mp**: 120 °C.

**$^1$H NMR** (300 MHz, CDCl3): $\delta$ (ppm) = 9.71 (m, 8H, HPc), 8.41 (m, 8H, HPc), 4.19 (s, 4H, HAr), 3.73 (m, 2H, CH2), 3.68 (m, 4H, CH2), 3.61 (m, 2H, CH2), 3.56 (t, *J* = 4.8 Hz, 6H, CH2), 3.50 (m, 8H, CH2), 3.45 (m, 24H, CH2), 3.38 (m, 12H, CH2), 3.31 (m, 18H, CH3), 3.25 (m, 6H, CH2), 3.0 (t, *J* = 4.5 Hz, 8H, Ar-OCH2).

**$^{13}$C NMR** (75 MHz, CDCl3): $\delta$ (ppm) = 158.7, 150.5, 150.2, 140.1, 135.4, 131.5, 125.2, 124.1, 105.7, 71.8, 71.7, 71.7, 70.5, 70.5, 70.4, 70.3, 70.2, 70.6, 69.7, 67.4, 65.8, 58.9, 58.8, 15.2.

**FT-IR** (film), *v* (cm-1): 2920 (CH2), 2851 (CH), 1729 (C=O), 1678, 1429, 1336, 1221, 1123, 1083 (C-O-C).
**UV/Vis:** (CHCl3): $\lambda_{max}$ (nm) (log $\varepsilon$): 686 (4.99), 656 (4.08), 615 (4.12), 359 (4.44).
**MS** (HR-MALDI-TOF, PEGNa1500+PEGNa2000+NaI): Calc. for C88H110N8Na1O28Si: [M+Na] +: *m/z*: 1778.7121, found 1778.7065.

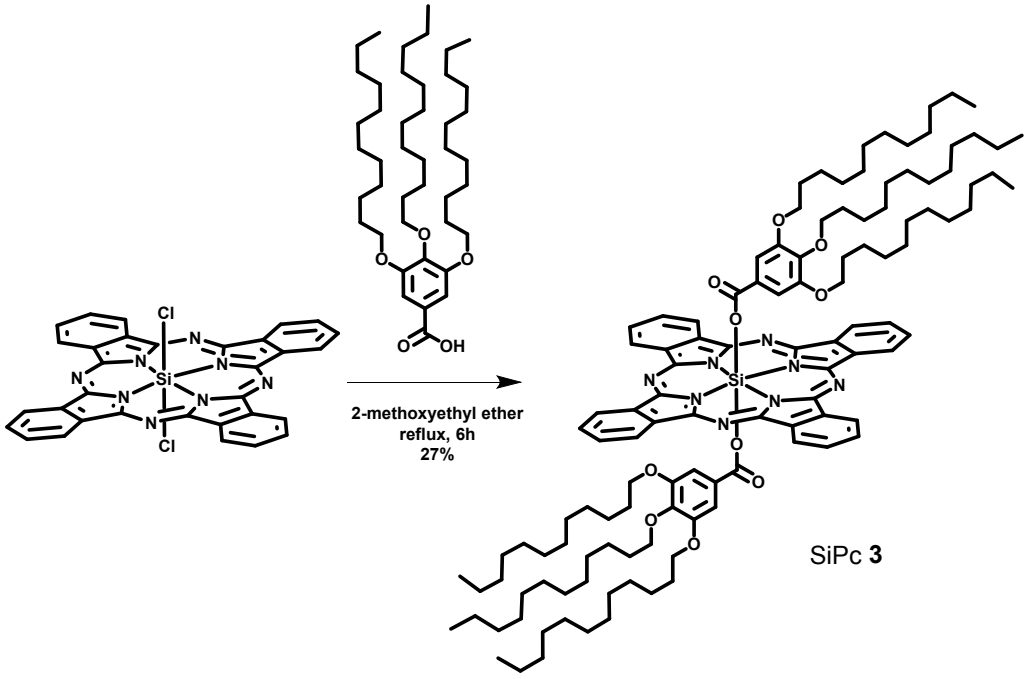
Synthesis of SiPc **2**




SiPcCl2 (150 mg, 0.245 mmol), **4** (827 mg, 1.23 mmol) and 3,4,5-tris(dodecyloxy)benzoic acid (**5**)[3,4] (746 mg, 1.23 mmol) were mixed in 4 mL of 2-methoxyethyl ether. The reaction was refluxed for 6 h under argon atmosphere. After cooling down to room temperature, the solvent was evaporated under *vacuum* and the resulting slurry was purified by gradient column chromatography (SiO2, DCM, DCM/methanol, from 60:1 to 20:1) The central fraction, corresponding to the final product, was collected and the solvent was evaporated, yielding the pure compound as a gummy blue solid. Yield: 120 mg, 0.066 mmol, 27%.
**Mp**: 115 °C.
**Transition temperature** (to liquid crystal mesophase): 56.53 °C
**$^1$H NMR** (300 MHz, CDCl3): $\delta$ (ppm) = 9.72 (m, 8H, HPc), 8.40(m, 8H, HPc), 4.21 (s, 2H, Har), 4.19 (s, 2H, Har), 3.74 (m, 2H), 3.68 (m, 4H), 3.61 (m, 2H), 3.56 (m, 4H), 3.50 (m, 4H), 3.44 (m, 10H), 3.38 (m, 4H), 3.34 (m, 2H), 3.31 (m, 9H, CH3), 3.28 (m, 4H, OCH2), 3.26 (s, 4H), 3.0 (t, *J* = 4.5 Hz, 4H, OCH2), 2.84 (t, *J* = 6.1 Hz, 4H, OCH2), 1,18 (m, 66H, CH2), 0.87 (m, 9H, CH3).

**$^{13}$C NMR** (75 MHz, CDCl3): $\delta$ (ppm): 158.9, 158.7, 151.0, 150.5, 150.2, 140.1, 140.0, 135.5, 131.5, 125.3, 124.9, 124.1, 105.7, 105.0, 72.8, 71.8, 71.8, 71.7, 70.5, 70.5, 70.3, 70.2, 70.1, 69.1, 67.7, 67.4, 31.9, 31.9, 29.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.3, 29.3, 29.2, 28.8, 25.8, 25.7, 22.7, 22.6, 14.1, 14.1.
**FT-IR** (film), *v* (cm-1): 2922 (CH2), 2852 (CH), 1729 (C=O), 1635, 1430, 1384, 1336, 1123, 1083, 1022 (C-O-C), 914, 762.
**UV/Vis:** $\lambda_{max}$ (nm) (log $\varepsilon$): 686 (5.4), 655 (4.48), 617 (4.55), 360 (4.8).
**MS** (HR-MALDI-TOF, DCTB-PEGNa 2000)**:** Calc. for C103H140N8O19Si1: [M]+: *m/z*: 1822.0029, found 1822.0035.

Synthesis of SiPc **3**




$SiPcCl_2$ (100 mg, 0.16 mmol) and **5** (1.08 g, 1.6 mmol) were mixed in 2 mL of 2-methoxyethyl ether in a pre-dried flask. The reaction was refluxed for 6 h under argon and then cooled down to room temperature. Addition of water induces precipitation of the crude, which was filtered and then purified by column chromatography (SiO2, DCM/hexane, 2:1). The residue was precipitated in methanol and filtration of the suspension gave the pure compound as a dark blue powder. Yield: 154 mg, 0.081 mmol, 51%.
**Mp:** 156-158 ºC.
**$^{1}$H NMR** (300 MHz, CDCl3): $\delta$ (ppm) =9.71 (m, 8H, HPc), 8.39 (m, 8H, HPc), 4.2 (s, 4H, Har), 3.36 (t, *J* = 6.4 Hz, 4H, OCH2), 2.85 (t, *J* = 6.1 Hz, 8H, OCH2), 1,26 (m, 60H, (CH2)9), 0,89 (m, 18H, CH3).
**$^{13}$C NMR** (75 MHz CDCl3): $\delta$ (ppm) = 159.9, 151.07, 150.2, 139.9, 135.6, 131.4, 125.1, 124.1, 105.1, 72.9, 67.7, 32.0, 29.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.6, 29.4, 29.4, 29.2, 28.8, 25.8, 22.7, 14.2.
**FT-IR** (film), *v* (cm-1): 2922 (CH2), 2851 (CH), 1762 (C=O), 1677, 1430, 1336, 1223 (CN), 1121, 1082, 914, 864, 741.

**UV/Vis:** (CHCl3): $\lambda_{max}$ (nm) (log $\varepsilon$) = 685 (5.51), 654 (4.6), 616 (4.6), 359 (4.93).
**MS** (HR-MALDI-TOF, DCTB+PEGNa2000): Calc. for C118H170N8O10Si: [M+]: *m/z*: 1887.2804, found 1887.2818.

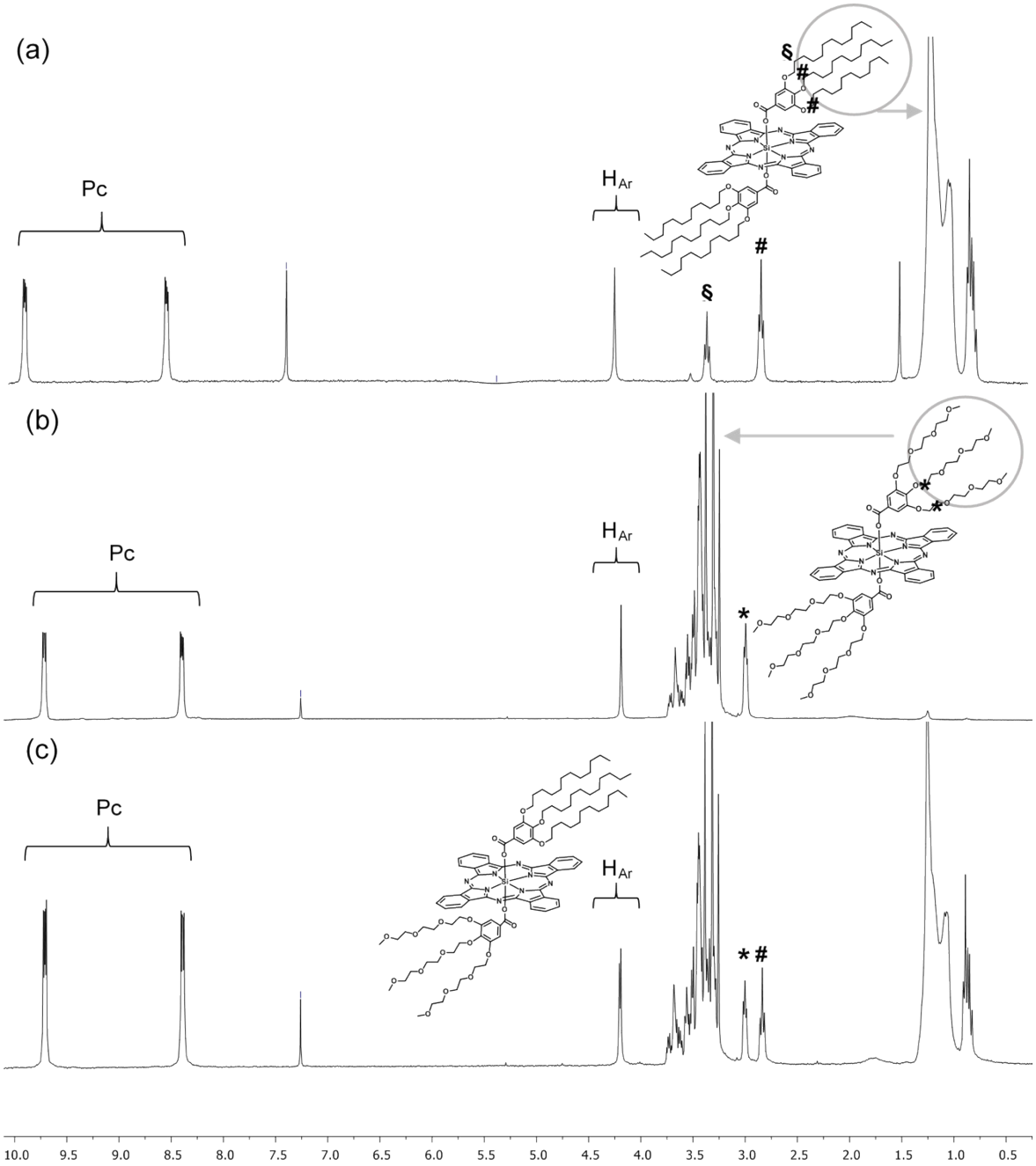



**Figure S1.** $^1$H-NMR spectra, recorded in $CDCl_3$, of the SiPc derivatives (a) **3**, (b) **2** and (c) **1**, presented in order of the complexity of their interpretation.

**Singlet oxygen measurements**

The singlet oxygen ($^1O_2$) quantum yield ($\Phi_\Delta$) of SiPcs **1**-**3** was measured in DMSO following the well-known *relative method*, based on the photoinduced decomposition of a chemical scavenger (i.e., 1,3-diphenylisobenzofuran (DPBF) that reacts readily with $^1O_2$ (Figure 3 and S2).[5] Non-substituted ZnPc was used as reference compound ($\Phi_{\Delta(DMSO)}$ = 0.67).[6] In detail, the procedure was as follows: 2.5 mL of a stock solution of DPBF (with an absorbance of ca. 1) in DMSO was transferred into a 1 x 1 cm quartz optical cell and bubbled with oxygen for 1 min. A concentrated stock solution of the SiPc in the same solvent was then added, in a defined amount to reach a final Q-band absorbance value of about 0.1. The solution was stirred and irradiated for defined time intervals, using a halogen lamp (typically, 300 W). The duration of these intervals are tuned in each experiment, in order to get a decrease in DPBF absorption of about 3-4%. Incident light was filtered through a water filter (6 cm) and an additional filter to remove light under 530 nm (Newport filter FSQ-OG530). The decrease of DPBF concentration with irradiation time was monitored at 414 nm. All experiments were performed three times and the obtained data represent mean values of those three experiments. Singlet oxygen quantum yield ($\Phi_\Delta$) values were calculated through the following equation:

$$\phi_\Delta^S = \phi_\Delta^R \frac{k^S I_{aT}^R}{k^R I_{aT}^S}$$

Where $k$ is the slope of a plot of ln ($A_0/A_t$) *versus* irradiation time $t$, with $A_0$ and $A_t$ being the absorbance of scavenger at the monitoring wavelength before and after irradiation time $t$, respectively. $I_{aT}$ is the total amount of light absorbed by the dye. Superscripts $R$ and $S$ indicate reference and sample, respectively. $I_{aT}$ is calculated as a sum of intensities of the absorbed light $I_a$ at wavelengths from the filter cutoff to 800 nm (step 0.5 nm). $I_a$ at given wavelength is calculated using Beer's law:

$$I_a = I_0(1 - e^{-2.3A})$$

Where transmittance of the filter at a given wavelength is denoted as $I_0$ and the absorbance of the dye at this wavelength is denoted as $A$.

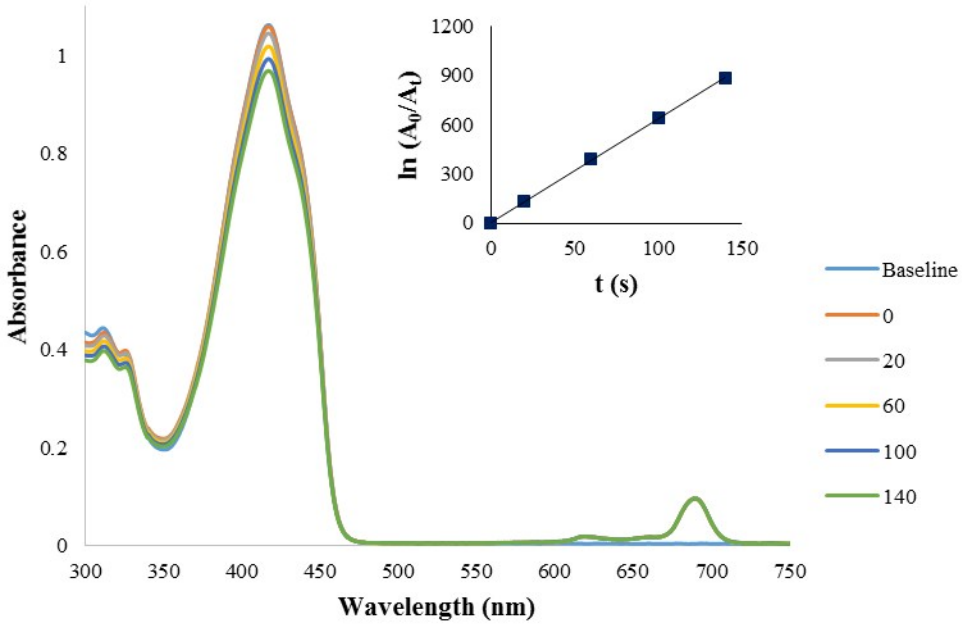



**Figure S2.** Time-dependent photobleaching of DPBF absorption in the presence of the SiPc **1** in DMSO, which is directly related to the photoinduced generation of $^1O_2$ by the PS. Similar plots were recorded for compounds **2**, **3** and **Pc 4**.

**Synthesis of ben-PCL-mPEG and nap-PCL-mPEG block copolymers**

A library of benzyl/naphthyl-poly(ε-caprolactone)-methoxypoly(ethyleneglycol) (Ben-PCL-mPEG and Nap-PCL-mPEG) block copolymers were prepared by a convergent synthetic approach. This example describes the preparation of block copolymers formed from poly(ε-caprolactone) 8-mer and a methoxy poly(ethylene glycol) with a molecular weight of ca. 2000.

a) Preparation of benzyl-$PCL_8$-OH polymer

A typical procedure for the synthesis of a benzyl-$PCL_8$-OH polymer with an average degree of polymerization of the PCL of 8.0 was as follows. A mixture of ε-caprolactone (25.00g, 0.2 mol), benzyl alcohol (2.96g, 0.027mol) and stannous octoate (1 drop) was heated and the ring opening polymerization in the melt was allowed to proceed overnight at 130°C in a nitrogen atmosphere. The product was purified by dissolution in dichloromethane followed by precipitation in a 20-fold excess of cold (-20°C) diethyl ether. The Benzyl-$PCL_8$-OH was filtered and dried overnight *in vacuo* at room temperature to give a white powder (yield: 96%).

**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 7.3 (s, aromatic protons benzyl alcohol), 5.1 (s, CC$H_2$O), 4.05 (m, CH2C$H_2$O), 3.6 (t, $CH_2CH_2$OH), 2.3 (m, OC(O)C$H_2$), 1.6 (m, $CH_2CH_2CH_2CH_2CH_2$), 1.3 (m, $CH_2CH_2CH_2CH_2CH_2$).

b) Preparation of benzoyl-$PCL_8$-PNC

Benzyl-$PCL_8$-OH (4.00g, 3.6mmol) (product of step a) was dissolved in 20mL dry toluene in a nitrogen atmosphere. The solution was cooled to 0°C and triethylamine (0.70g, 7.2mmol) and subsequently para-nitrophenylcarbonylchloride (PNC-Cl; 1.45g, 7.2mmol) were added to the solution while stirring. After 1 hour, the mixture was filtered to remove the triethyleneamine HCl salt and precipitated into cold (-20°C) diethyl ether. The product was filtered and carefully washed with a small amount of cold (-20°C) diethyl ether. The resulting product, benzyl-$PCL_8$-PNC, was dried in a vacuum oven and was obtained as a white powder (yield: 95%).

**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 8.3 (d, aromatic protons of PNC), 7.3 (m, aromatic protons of benzyl alcohol and PNC), 5.1 (s, CC$H_2$O), 4.2 (m, $CH_2CH_2$OC(O)O), 4.05 (m, CH2C$H_2$O), 2.3 (m, OC(O)C$H_2$), 1.6 (m, $CH_2CH_2CH_2CH_2CH_2$), 1.3 (m, $CH_2CH_2CH_2CH_2CH_2$).

c) Preparation of mPEG2000-$NH_2$

mPEG-$NH_2$ was synthesized according the procedure outlined by Elbert and Hubbell [Biomacromolecules (2001) 2(2), 430-441]. In a typical procedure mPEG2000-OH (50.0g, 25mmol) was dissolved in 700mL of dry toluene and dried by the removal of 350mL of solvent by azeotropic distillation. After the solution was cooled in an ice-bath, 25mL of DCM and triethylamine (14.5mL, 100mmol) were added. Subsequently, mesyl chloride (7.73mL, 100mmol) was added drop-wise under stirring and allowed to react overnight at room temperature. The solution was filtered and the product was precipitated in a large excess of cold diethyl ether. After drying, the formed mPEG2000-mesylate was reacted with 100mL of an aqueous ammonia solution (25%) for 4 days at room temperature. Subsequently the ammonia was allowed to evaporate and the pH of the solution was raised to 13, using 1M NaOH. The solution was extracted three times with 200mL DCM. The organic phases were combined and the solution was concentrated.

The mPEG2000-$NH_2$ was isolated by precipitation in cold diethyl ether, and drying in vacuo (yield: 76%).
**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 3.65 (m, PEG protons), 3,37 (s, $CH_2OCH_3$), 2.94 (t, $CH_2CH_2NH_2$).

d) Synthesis of Ben-PCL-mPEG

Benzyl-$PCL_8$-PNC (product of step b); 1.00g, 0.707mmol) was dissolved in 20mL of dry toluene. To the resulting solution, mPEG2000-$NH_2$ (product of step c); 1.41g, 0.707mmol) was added and the reaction mixture was stirred for 1 hour at room temperature under a nitrogen atmosphere. The mixture was poured into diethyl ether, filtered and carefully washed at least six times with diethyl ether to remove p-nitrophenol. The product was dried in a vacuum oven and obtained as a white powder (yield: 97%).
**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 7.3 (m, aromatic protons of benzyl alcohol), 5.1 (s, $CCH_2O$), 4.05 (m, $CH2CH_2O$), 3.64 (m, PEG protons), 3.38 (s, $OCH_3$), 2.3 (m, $OC(O)CH_2$), 1.6 (m, $CH_2CH_2CH_2CH_2CH_2$), 1.3 (m, $CH_2CH_2CH_2CH_2CH_2$).

e) Preparation of naphthyl -$PCL_8$-OH polymer

A typical procedure for the synthesis of a napthyl-$PCL_8$-OH polymer with a degree of polymerization of the PCL of 8.0 was as follows. A mixture of ε-caprolactone (25.00g, 0.2 mol), 2-Naphthalenemethanol (3.96g, 0.025mol) and stannous octoate (1 drop) was heated and the ring opening polymerization in the melt was allowed to proceed overnight at 130°C in a nitrogen atmosphere. The product was purified by dissolution in dichloromethane followed by precipitation in a 20-fold excess of cold (-20°C) diethyl ether. The napthyl-$PCL_8$-OH was filtered and dried overnight *in vacuo* at room temperature to give a white powder (yield: 96%).
**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 7.85 (m, aromatic C*H*), 7.50 (m, aromatic protons C*H*), 5.15 (s, $CCH_2O$), 4.05 (m, $CH2CH_2O$), 3.6 (t, $CH_2CH_2OH$), 2.3 (m, $OC(O)CH_2$), 1.6 (m, $CH_2CH_2CH_2CH_2CH_2$), 1.3 (m, $CH_2CH_2CH_2CH_2CH_2$).

f) Preparation of napthyl-$PCL_8$-PNC

Napthyl-$PCL_8$-OH (4.00g, 3.6mmol) (product of step a) was dissolved in 20mL dry toluene in a nitrogen atmosphere. The solution was cooled to 0°C and triethylamine (0.70g, 7.2mmol) and subsequently para-nitrophenylcarbonylchloride (PNC-Cl; 1.45g, 7.2mmol) were added to the solution while stirring. After 1 hour, the mixture was filtered to remove the triethyleneamine HCl salt and precipitated into cold (-20°C) diethyl ether. The product was filtered and carefully washed with a small amount of cold (-20°C) diethyl ether. The resulting product, napthyl-$PCL_8$-PNC, was dried in a vacuum oven and was obtained as a white powder (yield: 95%).
**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 8.3 (d, aromatic protons of PNC), 7.85 (m, aromatic C*H*), 7.50-7.3 (m, aromatic protons C*H* and PNC aromatic protons), 5.1 (s, $CCH_2O$), 4.2 (m, $CH_2CH_2OC(O)O$), 4.05 (m, $CH2CH_2O$), 2.3 (m, $OC(O)CH_2$), 1.6 (m, $CH_2CH_2CH_2CH_2CH_2$), 1.3 (m, $CH_2CH_2CH_2CH_2CH_2$).

g) Synthesis of Nap-PCL-mPEG

Napthyl-$PCL_8$-PNC (product of step b); 1.00g, 0.707mmol) was dissolved in 20mL of dry toluene. To the resulting solution, mPEG2000-$NH_2$ (product of step c); 1.41g, 0.707mmol) was added and the reaction mixture was stirred for 1 hour at room temperature under a nitrogen atmosphere. The mixture was poured into diethyl ether, filtered and carefully washed at least six times with diethyl ether to remove p-nitrophenol. The product was dried in a vacuum oven and obtained as a white powder (yield: 97%).

**$^1$H NMR (300 MHz, $CDCl_3$), δ (ppm):** 7.85 (m, aromatic C*H*), 7.50 (m, aromatic protons C*H*), 5.1 (s, C$CH_2$O), 4.05 (m, CH2$CH_2$O), 3.64 (m, PEG protons), 3.38 (s, O$CH_3$), 2.3 (m, OC(O)C$H_2$), 1.6 (m, $CH_2CH_2CH_2CH_2CH_2$), 1.3 (m, $CH_2CH_2CH_2CH_2CH_2$).

GPC characterization

**Table S1.** GPC data of the synthesized mPEG$_{45}$-$NH_2$, intermediate PCL polymers and the final Ben-PCL$_n$-mPEG$_{45}$ and Nap-PCL$_{11}$-mPEG$_{45}$ block copolymers.

| **Polymer** | **Theory (g/mol)** | **$M_n$ (g/mol) obtained by NMR** | **$M_n$ (g/mol) obtained by GPC*** | **$M_w/M_n$** |
|---|---|---|---|---|
| mPEG-$NH_2$ | 2000 | 2100 | 1500 | 1.17 |
| Benzyl-$PCL_7$-OH | 789 | 750 | 440 | 1.08 |
| Benzyl-$PCL_7$-mPEG$_{45}$ | 2789 | 3000 | 2100 | 1.18 |
| Benzyl-$PCL_{11}$-OH | 1254 | 1100 | 600 | 1.10 |
| Benzyl-$PCL_{11}$-mPEG$_{45}$ | 3254 | 3300 | 2250 | 1.15 |
| Benzyl-$PCL_{14}$-OH | 1700 | 1600 | 900 | 1.07 |
| Benzyl-$PCL_{14}$-mPEG$_{45}$ | 3700 | 3650 | 2500 | 1.18 |
| Benzyl-$PCL_{19}$-OH | 2300 | 2200 | 1250 | 1.10 |
| Benzyl-$PCL_{19}$-mPEG$_{45}$ | 4300 | 4200 | 2700 | 1.19 |
| Napthoyl- $PCL_{11}$-OH | 1254 | 1140 | 610 | 1.10 |
| Napthoyl- $PCL_{11}$-mPEG$_{45}$ | 3254 | 3340 | 2250 | 1.16 |

* Relative $M_n$ using PEG as the reference polymer.

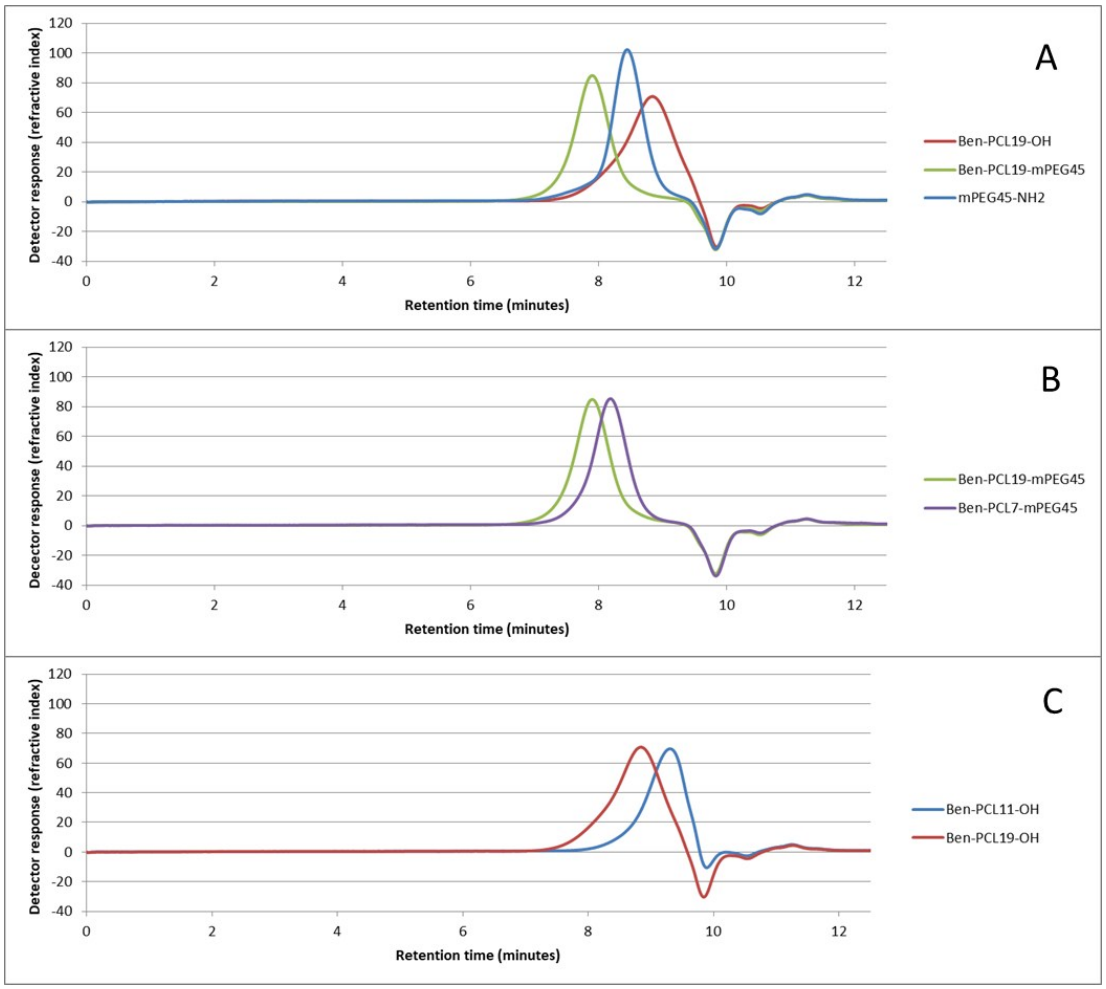
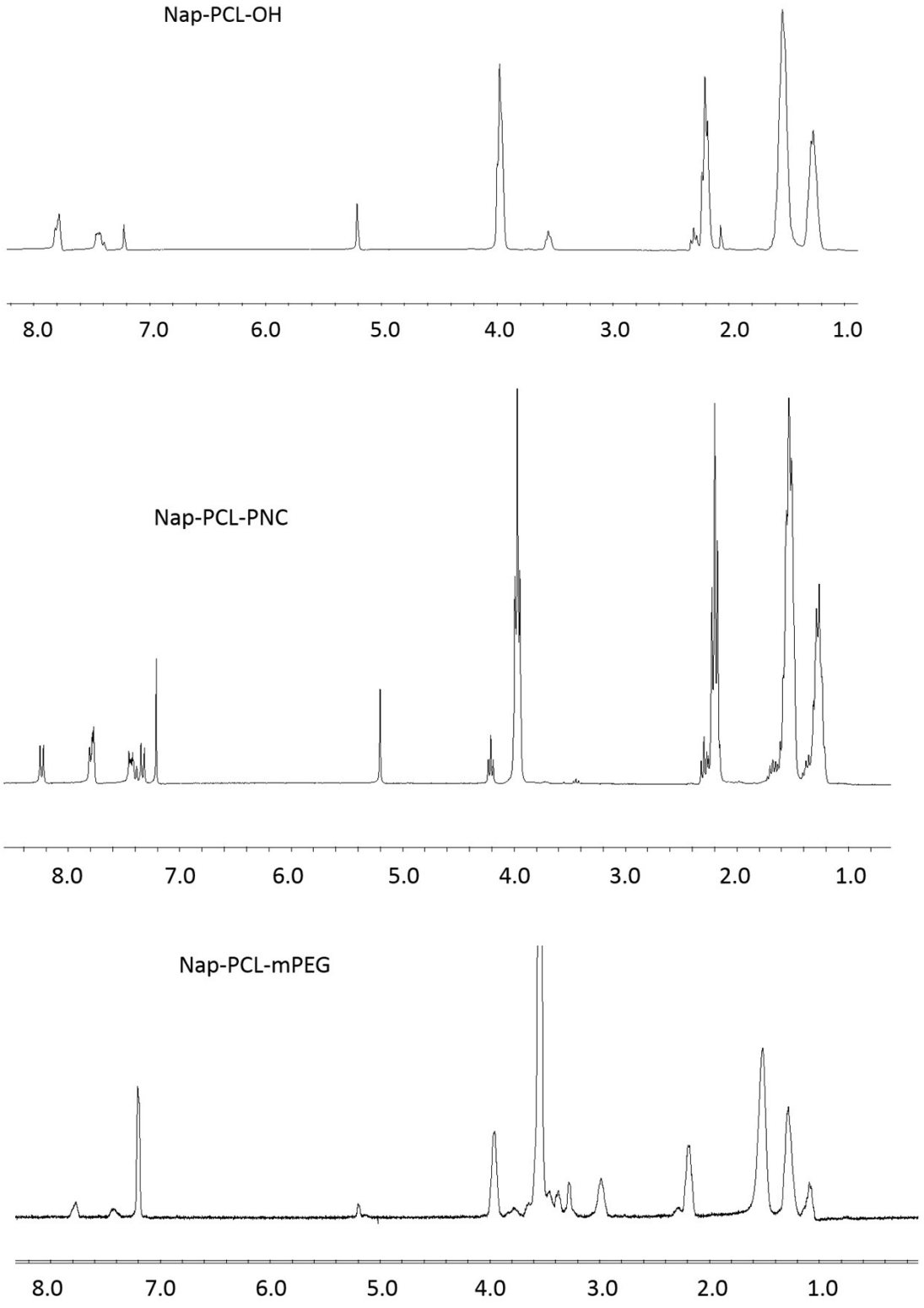



**Figure S3.** Typical GPC traces of the synthesized intermediate $mPEG_{45}$-$NH_2$, Ben-$PCL_n$-OH polymers and the final Ben-$PCL_n$-$mPEG_{45}$ Block copolymers. A) Overlay of $mPEG_{45}$-$NH_2$, Ben-$PCL_{19}$-OH, and Ben-$PCL_{19}$-$mPEG_{45}$. B) Overlay of Ben-$PCL_7$-$mPEG_{45}$ and Ben-$PCL_{19}$-$mPEG_{45}$. C) Overlay of Ben-$PCL_{11}$-OH and Ben-$PCL_{19}$-OH.

**$^1$H NMR spectra of Nap-PCL-mPEG and corresponding intermediates in $CDCl_3$.** Chemical shift ($\delta$) is given in ppm. For corresponding $^1$H NMR spectra of the Ben-PCL-mPEG polymers: see ref. 7.



## Data regarding the preparation of the PS-loaded micelles

**Table S2**. Set of formulations prepared and studied following the above protocols.

| Entry | initiator | # of caprolactone repeating units | PEG block MW (Da) | SiPc | Polymer concentration (mg/ml) | Feed ratio of SiPc (wt%) in the micelles |
|---|---|---|---|---|---|---|
| 1 | Benzyl alcohol | 11 | 2000 | **3** | 10 | 20 |
| 2 | Benzyl alcohol | 11 | 2000 | **3** | 10 | 10 |
| 3 | Benzyl alcohol | 11 | 2000 | **3** | 10 | 5 |
| 4 | Benzyl alcohol | 11 | 2000 | **3** | 10 | 2.5 |
| 5 | Benzyl alcohol | 11 | 2000 | **3** | 10 | 1 |
| 6 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 20 |
| 7 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 12.8 |
| 8 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 10 |
| 9 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 5 |
| 10 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 2.5 |
| 11 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 1 |
| 12 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 0.5 |
| 13 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 0.35 |
| 14 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 0.2 |
| 15 | Benzyl alcohol | 11 | 2000 | **1** | 10 | 0.05 |
| 16 | Benzyl alcohol | 11 | 2000 | **2** | 10 | 20 |
| 17 | Benzyl alcohol | 11 | 2000 | **2** | 10 | 10 |
| 18 | Benzyl alcohol | 11 | 2000 | **2** | 10 | 5 |
| 19 | Benzyl alcohol | 11 | 2000 | **2** | 10 | 2.5 |
| 20 | Benzyl alcohol | 11 | 2000 | **2** | 10 | 1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 21 | Napthoyl alcohol | 11 | 2000 | **3** | 10 | 20 |
| 22 | Napthoyl alcohol | 11 | 2000 | **3** | 10 | 10 |
| 23 | Napthoyl alcohol | 11 | 2000 | **3** | 10 | 5 |
| 24 | Napthoyl alcohol | 11 | 2000 | **3** | 10 | 2.5 |
| 25 | Napthoyl alcohol | 11 | 2000 | **3** | 10 | 1 |
| 26 | Napthoyl alcohol | 11 | 2000 | **1** | 10 | 20 |
| 27 | Napthoyl alcohol | 11 | 2000 | **1** | 10 | 10 |
| 28 | Napthoyl alcohol | 11 | 2000 | **1** | 10 | 5 |
| 29 | Napthoyl alcohol | 11 | 2000 | **1** | 10 | 2.5 |
| 30 | Napthoyl alcohol | 11 | 2000 | **1** | 10 | 1 |
| 31 | Napthoyl alcohol | 11 | 2000 | **2** | 10 | 20 |
| 32 | Napthoyl alcohol | 11 | 2000 | **2** | 10 | 10 |
| 33 | Napthoyl alcohol | 11 | 2000 | **2** | 10 | 5 |
| 34 | Napthoyl alcohol | 11 | 2000 | **2** | 10 | 2.5 |
| 35 | Napthoyl alcohol | 11 | 2000 | **2** | 10 | 1 |
| 36 | Benzyl alcohol | 7 | 2000 | **3** | 10 | 20 |
| 37 | Benzyl alcohol | 14 | 2000 | **3** | 10 | 20 |
| 38 | Benzyl alcohol | 19 | 2000 | **3** | 10 | 20 |
| 39 | Benzyl alcohol | 7 | 2000 | **1** | 10 | 20 |
| 40 | Benzyl alcohol | 14 | 2000 | **1** | 10 | 20 |
| 41 | Benzyl alcohol | 19 | 2000 | **1** | 10 | 20 |
| 42 | Benzyl alcohol | 7 | 2000 | **2** | 10 | 20 |
| 43 | Benzyl alcohol | 14 | 2000 | **2** | 10 | 20 |
| 44 | Benzyl alcohol | 19 | 2000 | **2** | 10 | 20 |

## Loading capacity and efficiency of the prepared formulations

All prepared formulations were tested by UV/vis spectrophotometry on loading capacity and efficiency. The obtained results are given in Figures S4 and S5.

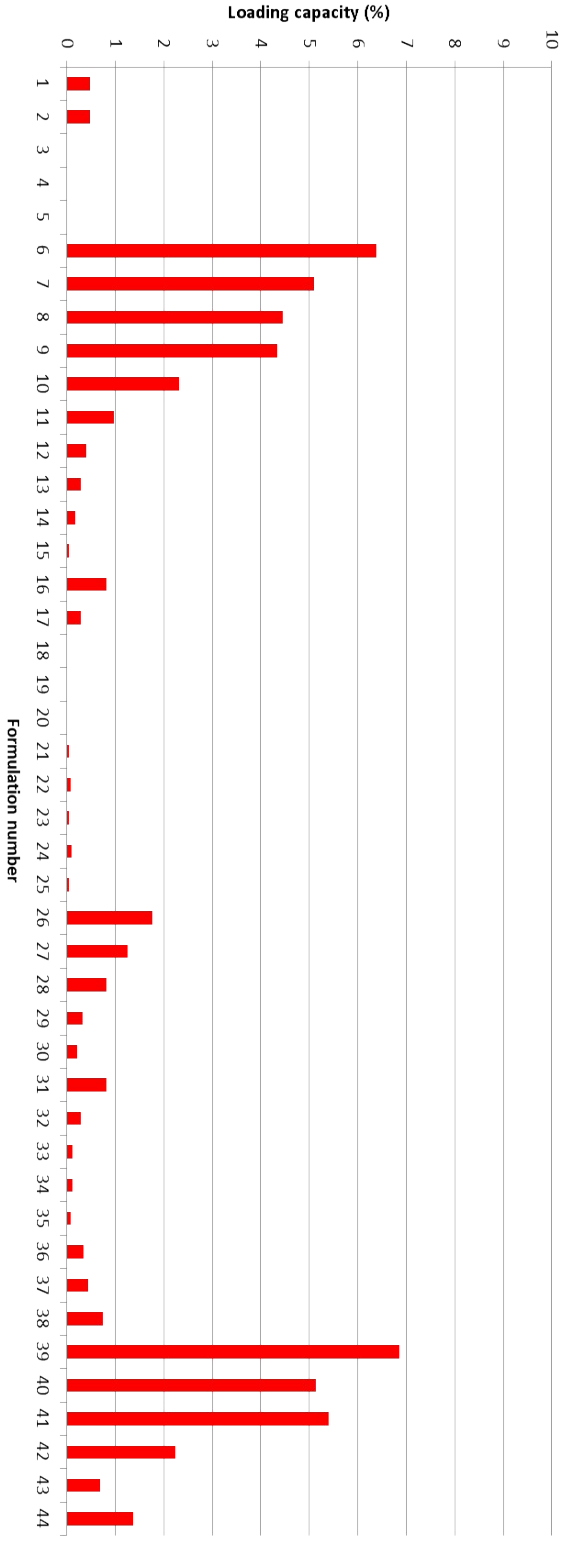



**Figure S4.** Loading capacity of the prepared formulations

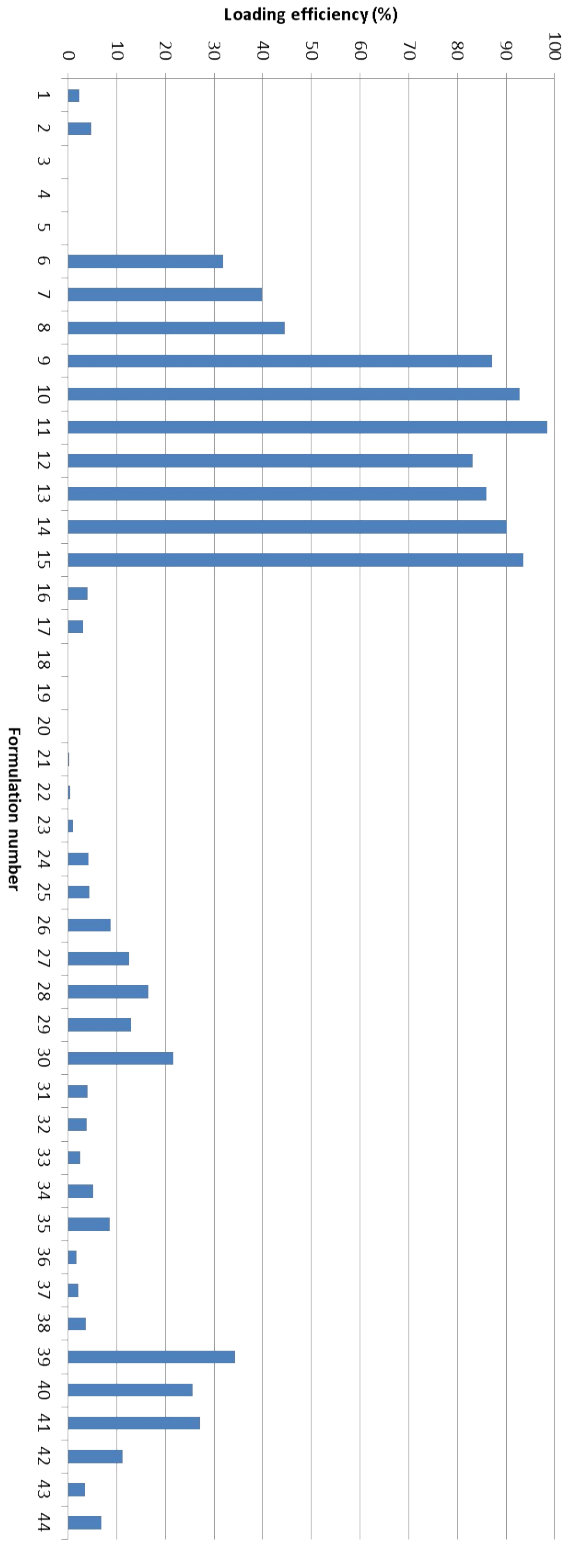



**Figure S5.** Loading efficiency of the prepared formulations

## References


[1] L. Brunsveld, H. Zhang, M. Glasbeek, J. A. J. M. Vekemans, E. W. Meijer, *J. Am. Chem. Soc*. 2000, **122***,* 6175−6182.

[2] Persec *et al.*, *Science*, **2001**, *328*, 1009−1014.

[3] V. Percec,C. H. Ahn,W. D. Cho,A. M. Jamieson, J. Kim,T. Leman, M. Schmidt, M. Gerle, S. A. Prokhorova, S. S. Sheiko, S. Z. D. Cheng, A. Zhang, G. Ungar, D. J. P. Yeardley, *J. Am. Chem. Soc.* 1998, **120***,* 8619−8631.

[4] V. Percec, C. H. Ahn, T. K. Bera, G. Ungar, D. J. P. Yeardley, *Chem. Eur. J*. 1999, **5**, 1070−1083.

[5] N. Nombona, K. Maduray, E. Antunes, A. Karsten, T. Nyokong, *J. Photochem. Photobiol. B.* 2012, **107**, 35**–**44.

[6] N. Kuznetsova, N. S. Gretsova, E. A. Kalmykova, E. A. Makarova, S. N. Dashkevic, V. M. Negrimovskii, O. L. Kaliya, E. A. Lukyanets, *Russ. J. Gen. Chem.* 2000, **70**, 133**–**140.

[7] J. W. H. Wennink, Y. Liu, P. Makinen, F. Setaro, A. de la Escosura, M Bourajjaj, J. Lappalainen, L.Holappa, J.B. van den Dikkenberg, M. al Fartousi, P. Trohopoulos, S. Yla-Herttuala, T. Torres, W.E.Hennink, C.F. van Nostrum, *Eur. J. Pharm. Sci.*, 2017, **107**, 112−125.