SUPPORTING INFORMATION

Robust molecular microcapsules for encapsulating and releasing hydrophilic contents

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Experimental

General for the characterization of compounds.

Optical absorption measurements were carried out using a Cary 5000 UV-Vis-NIR spectrophotometer in double-beam mode.

SEM images were taken with a QUANTA FEI 200 FEG-ESEM, in high vacuum mode, at acceleration voltages of 10 kV. Silicon (100) was used as substrate.

Transmission electron microscopy (TEM) was performed on the synthesized samples in order to obtain detailed views of their morphology and analyze their possible crystal structure. We performed TEM in conventional bright field mode (BF TEM) as well as Cryo-TEM at around 100 kelvin. In both cases high resolution TEM (HRTEM) was attempted. All the TEM analyses were performed on a Jeol J2011 microscope operated at 200 kV, with a point to point resolution of 0.23 nm.X-Ray spectra were obtained by using these instruments: a) Nanoviewer, from Rigaku Corporation (Japan), equipped with a point collimation and a CCD Camera as detector, operated at 40 kV and 20 mA power beam, or b) using a Hecus S3 MICRO Instrument (Graz, Austria), which is equipped with a GENIX microfocus X-ray source and a FOX 2D point-focusing element (both from Xenocs, Grenoble), operating at 50 kV and 1 mA with PSD linear detectors. The samples were placed in a sealed capillary holder 1 mm thick. X-ray irradiations were carried out for 2 hours.

Fluorescence optical microscopy was recorded with an Olympus BX51 microscope; irradiations were performed with a UV-mercury lamp Olympus U-RFL-T (105 W), and U/B filter (for UV irradiations) and GFP filter (for green irradiation) were used. The magnification was x100 for image capture and irradiations, and an Olympus U-CMAD3 camera was used.

Particle size experiments were measured with DLS taken with a Mastersizer 2000 (Malvern Instruments) with a Hydro 2000mP after 20 min. of sonication of the sample dispersed in isopropanol.

Confocal Leica TCS-SP5 AOBS microscope (Leica Microsystems Heidelberg
GmbH; Mannheim, Germany) with a Plan Apochromatic x63 objective (NA 1.4, oil) and these

systems were observed with two-channel detection. Rhodamine B or Alexa-Fluor 568® was recorded in the red channel (excitation, 561 nm; emission from 575 to 670 nm) and PTM derivatives had autofluorescence at 500 to 550 nm (excitation, 476 nm) and were recorded in the blue channel. The samples were irradiated during 5 seconds with a mercury-halide UV lamp (120W). Experiments were performed using the Live Data Mode function of the confocal, which permits monitoring time-lapse experiments. Stacks of 40 to 60 sections every 0.04 µm were captured in order to obtain three dimensional images.

Synthesis of 3,4-bis(icosyloxy)benzaldehyde 2: A mixture of 3,4-dihidroxybenzaldehyde (0.573 g, 4.150 mmol), potassium carbonate (2.289 g, 16.6 mmol) and potassium iodide (0.25 g, catalytic) in 20 mL of DMF was heated to reflux. Then, 6.0 g of 1-bromoicosane (16.6 mmol) was added dropwise, and stirred overnight. The solution was cooled down to room temperature. Then, several extractions were made with ethyl acetate and hexane (1/1), and then $CHCl_3$. The organic layer was dried with $MgSO_4$ and after filtering the solvents were removed under reduced pressure. The final product was purified by column chromatography (hexane/ethyl acetate 9.5/0.5) for obtaining a white powder (2.3 g, 80%). RfTLC (hexane/ethyl acetate 9.5/0.5) = 0.42. ^{1}H-RMN (300 MHz, $CDCl_3$) δ (ppm): 9.85 (s, 1H, CHO), 7.42 (dd, 1H, J = 8.1 Hz, J = 2.1 Hz, CAr-H), 7.41 (d, 1H, J = 2.1 Hz, CAr-H), 6.97 (d, 1H, J = 8.1 Hz, CAr-H), 4.08 (t, 2H, J = 6.7 Hz, -OCH_2-), 4.07 (t, 2H, J = 6.7 Hz, -OCH_2-), 1.87 (m, 4H, J = 6.7 Hz, -OCH_2CH_2-), 1.54-1.43 (m, 4H, -$OCH_2CH_2CH_2$-), 1.28 (m, 60H), 0.90 (t, 6H, J = 6.7 Hz, -CH_3); FT-IR (νmax, cm^{-1}): 2917, 2850 (Csp^2, Csp^3), 1686 (C=O), 1597, 1586, 1510, 1466, 1277 (CAr-OR), 1238, 1133, 720. MALDI-TOF (pos): 700.1 $[M+H]^+$.

Synthesis of 1: Under dry conditions, 96 mg (0.86 mmol) of potassium tert-butoxide was added to a solution of phosphonate **3**[9] (500 mg, 570 mmol) in 15 mL of dry THF at -78ºC. The yellow-orange ylide solution formed was stirred for 20 min, and then the temperature was increased to 0ºC with an ice bath. Then, a suspension of 0.438 mg (627 mmol) of aldehyde **2** in dry THF was added slowly. The resulting mixture was stirred for 72 h. and then finally quenched by addition of 20 mL of HCl 1 N. The crude product was extracted with CH_2Cl_2 (3 x 150 mL) and the organic layer was washed with water (100 mL), dried with $MgSO_4$, and filtered. The solvent was evaporated under reduced pressure. Chromatographic purification with silica gel (hexane /CH_2Cl_2; 8.5/1.5) yielded the compound αH-PTM **1** (0.425 mg, 61%) as a white powder. RfTLC (hexane/ethyl acetate 20/1) = 0.58; M. p. = 48ºC; ^{1}H-RMN (600 MHz, $CDCl_3$) δ (ppm): 7.08 (d, 1H, J = 2.0 Hz, Ar-H), 7.06 (dd, 1H, J = 8.4 Hz, J = 2.0 Hz, Ar-H), 7.02 (s, 1H, CAr_3-H), 7.01 (d, 1H, J = 16.4 Hz, -CH=CH-), 6.89 (d, 1H, J = 8.4 Hz, Ar-H), 6.88 (d,1H, J = 16.4 Hz, -CH=CH-), 4.07 (t, 2H, J = 6.0 Hz, -OCH_2-), 4.05 (t, 2H, J = 6.0 Hz, -OCH_2-), 1.86 (m, 4H, J = 6.0 Hz, -OCH_2CH_2-), 1.50 (m, 4H, J = 6.0 Hz, -$OCH_2CH_2CH_2$-), 1,54-1.38 (m, 4H, -CH_2-), 1.28 (m, 60H, -CH2-), 0.90 (t, 6H, -CH_3). FT-IR (νmax, cm-1): 2917,

2849 (Csp^2, Csp^3), 1509, 1467, 1267 (CAr-OR), 1137, 808 (CAr-Cl); UV-Vis (λmax, ε; in CH_2Cl_2): 335 nm (36500) MALDI-TOF (neg): 1420.7 $[M-H]^-$; 1350.6 $[M-2Cl]^-$.

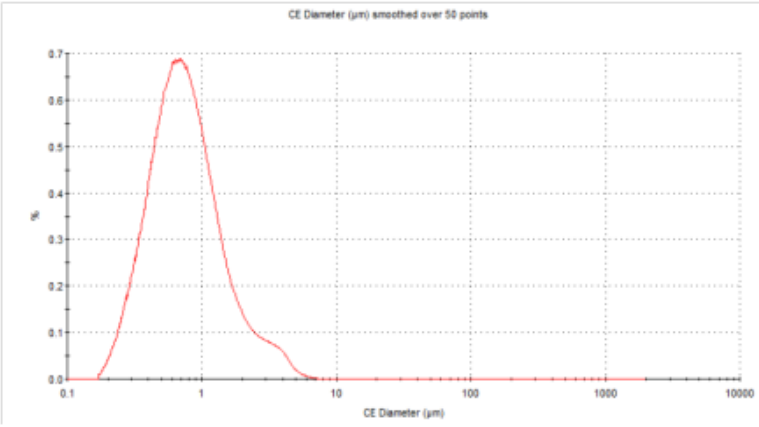


Figure S1. Light scattering measurement of the micro-capsules of **1** in isopropanol. Average diamter 0.7 µm.

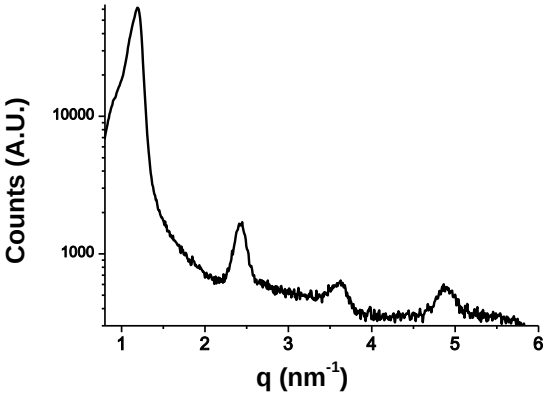


Figure S2. SAXS of capsules of **1**.

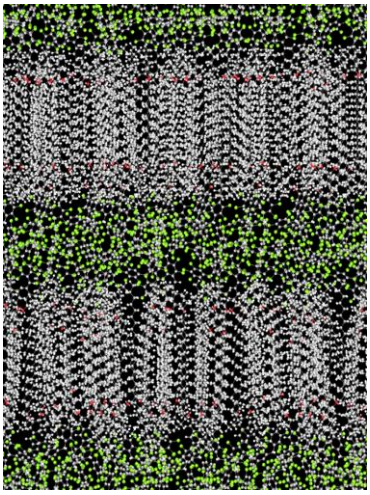


Figure S3. Schematic model of the supramolecular organization of **1** in the micro-capsules

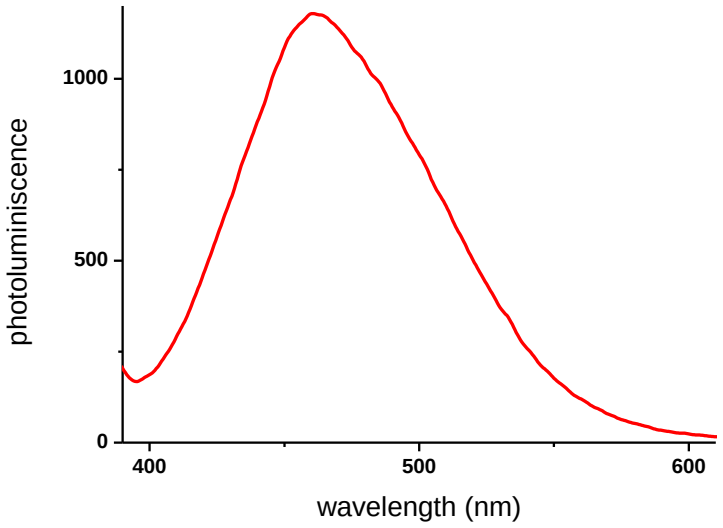
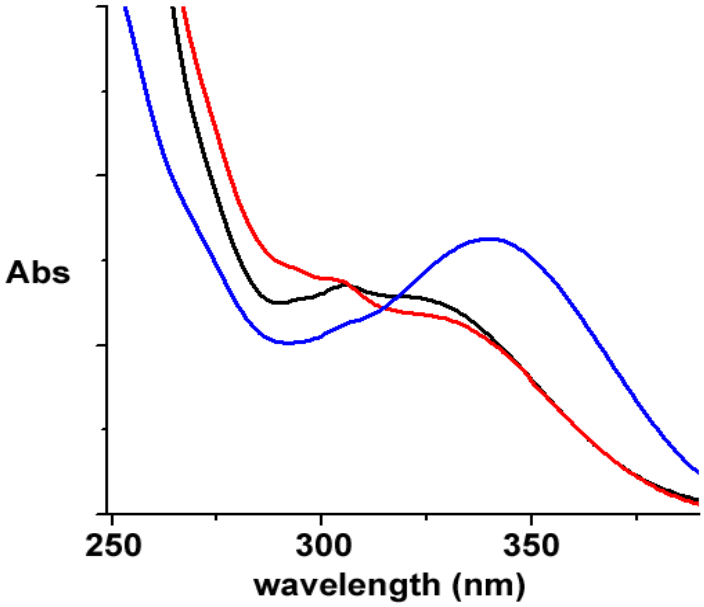


Figure S4. Emission spectrum of **1** (Excitation wavelength = 305 nm) in chloroform.

(a)



(b)

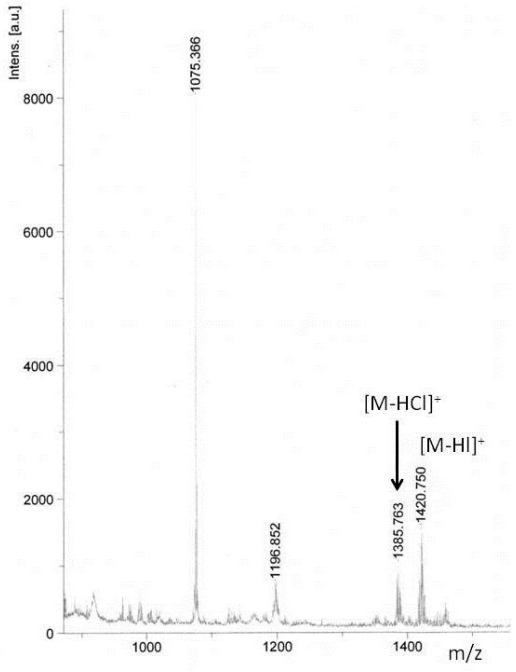


Figure S5. a) UV spectra of compound **1** in chloroform (blue), and after 5 minutes (black) and 20 minutes (red) of illuminating the solution at 254 nm. b) MALDI-TOF spectrum of **1** after irradiation for 5 min to UV light.

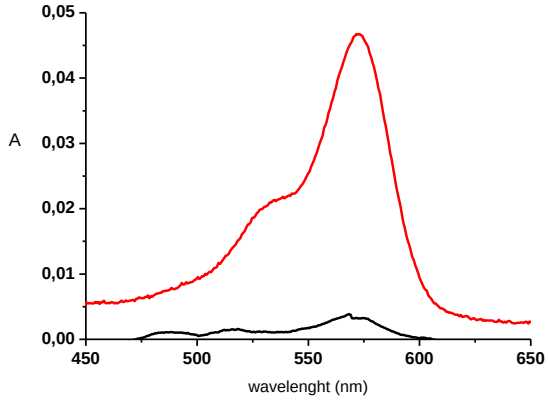


Figure S6. Absorption spectra of the solvent obtained by filtration of a suspension of capsules of **1** with AlexaFluor-568® in the lumen of the capsules. Black line corresponds to the solvent separated from the suspension of micro-capsules demonstrating that there is no free dye. Red line corresponds to the solvent separated from the suspension of micro-capsules after their UV irradiation at 305 nm for 10 seconds demonstrating that the solvent contains now the liberated dye molecules.

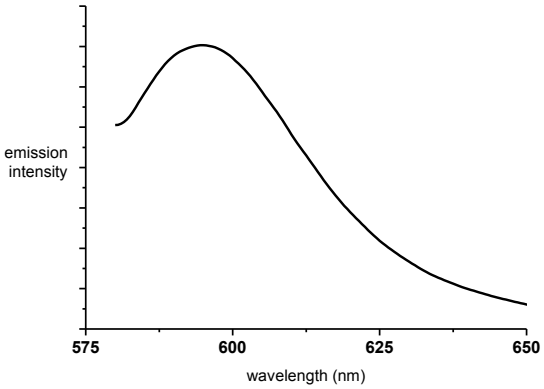


Figure S7. Emission spectra (λ_{exc} = 470 nm) of the solvent from a suspension of capsules of **1** with AlexaFluor-568® after UV irradiation at 305 nm for 10 seconds (3 times, washing waters).

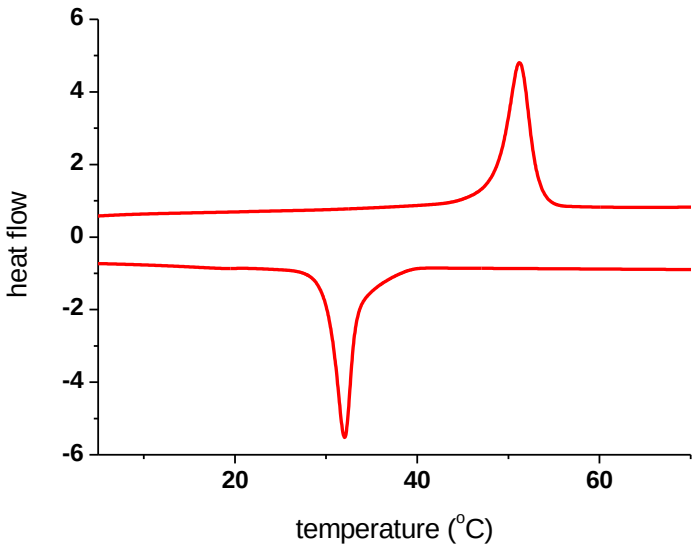


Figure S8. DSC of **1** (second cycle, exo down) of **1**. Temp. Rate: 10°C/min.