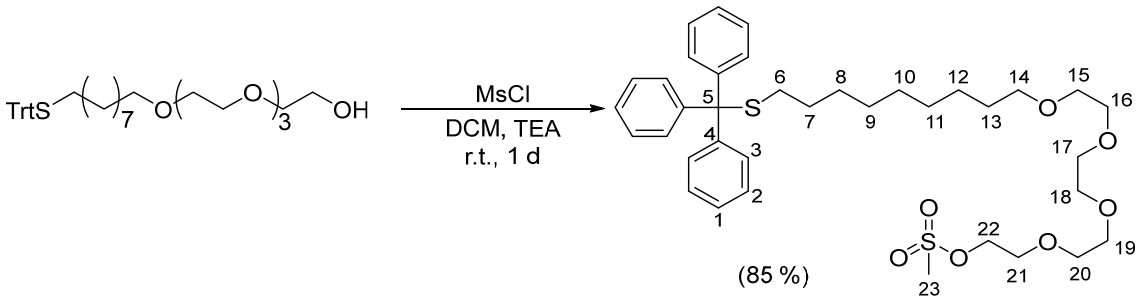
ASSOCIATED CONTENT

Supporting Information.

Organic Synthesis of Zwitterions

The synthesis of the basic structure of organic molecules was recently reported by us[36] and is based on the work of Rotello and coworkers.[S1,S2]

*1,1,1-Triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-yl methane-sulfonate **(8)***



7 **8**

The glycol precursor **7** (5.6 g, 9.41 mmol, 1.00 eq) was dissolved in dry dichloromethaneand triethylamine (TEA) (2.60 mL, 18.8 mmol, 2.00 eq) was added. After cooling the mixture in an ice bath, methanesulfonyl chloride (1.10 mL, 14.1 mmol, 1.50 eq) was added dropwise. After stirring 60 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for 1 d. Upon completion, the reaction mixture was concentrated *in vacuo*. The crude product was dissolved in dichloromethane (70 mL) and washed three times with 0.1 M HCl (100 mL), neutralized with saturated $NaHCO_3$-solution and washed with MQ-water three times. The organic layer was dried with Na_2SO_4 and the solvent removed *in vacuo*. The crude product was purified by column chromatography (silica, cyclohexane/EtOAc, 2:5, v/v). After removing the solvent, the product was obtained as a slightly yellow oil.

Yield: 4.66 g (6.94 mmol, 74 %). $\mathbf{R_f}$ (EtOAc/cyclohexane, 5:2): 0.29. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.44-7.38 (m, 6H, H-3), 7.34-7.24 (m, 6H, H-2), 7.24-7.17 (m, 3H, H-1), 4.38 (m,

2H, H-22), 3.80-3.53 (m, 14H, H-15 – H-21) 3.43 (t, $^{3}J_{14,13}$ = 6.8 Hz, 2H, H-14), 3.07 (s, 3H, H-23) 2.12 (t, $^{3}J_{6,7}$ = 7.4 Hz, 2H, H-6), 1.59-1.48 (m, 2H, H-13), 1.39-1.26 (m, 2H, H-7) 1.26-0.95 (m, 10H, H-8 – H-12) ppm. **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 145.2 (C_q, C-4), 129.7 (CH, C-2), 127.9 (CH, C-3), 126.6 (CH, C-1), 71.6, 70.8, 70.7, 70.6, 70.2, 69.4, 69.1 ($(CH_2)_9$, C-14/15/16/17/18/19 /20/21/22), 66.5 (C_q, C-5), 37.9 (CH_3, C-23), 32.2 (CH_2, C-6), 29.7, 29.5, 29.5, 29.2, 29.1, 28.7, 26.2 ($(CH_2)_7$, C-7/8/9/10/11/12/13) ppm. **HRMS** (ESI,+): found: 695.30399 $[M]^+$; calc. for $[M]^+$: 695.30467. **FT-IR (ATR):** $\tilde{\nu}$ = 3055 (w), 3024 (w), 2925 (s), 2854 (s), 1595 (w), 1486 (m), 1444 (m), 1351 (s), 1246 (m), 1174 (s), 1105 (s), 1018 (w), 970 (w), 918 (w), 798 (w), 744 (m), 700 (s), 619 (w) cm^{-1}. **UV/Vis** (acetonitrile): λ_{max}(log ε) = 256 (5.37), 290 (4.74), 320 (4.72) ($c = 2.0 \cdot 10^{-5}$ mol L^{-1}) nm.

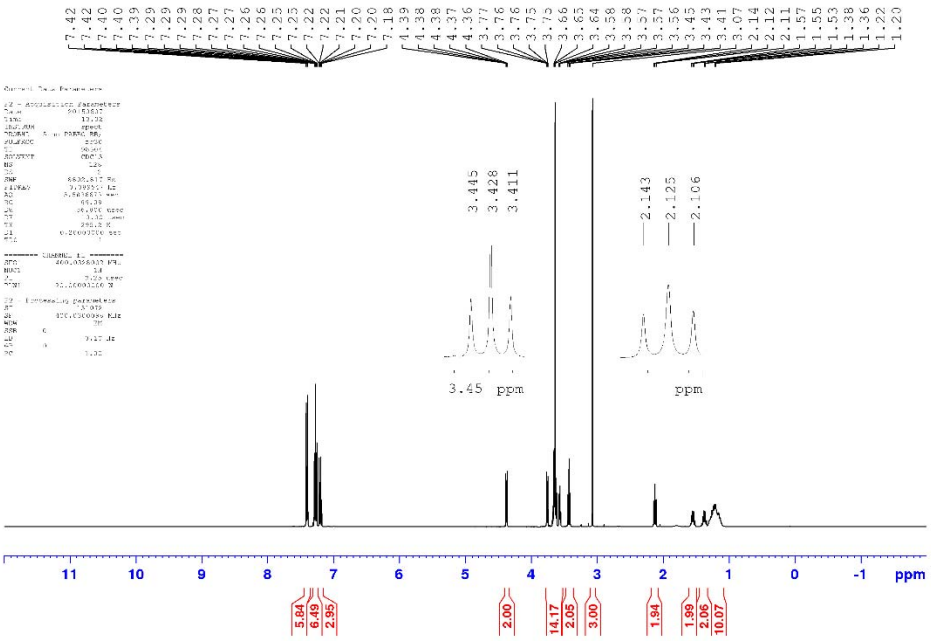


Figure S1: ^{1}H-NMR of 1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-yl methane-sulfonate (**8**).

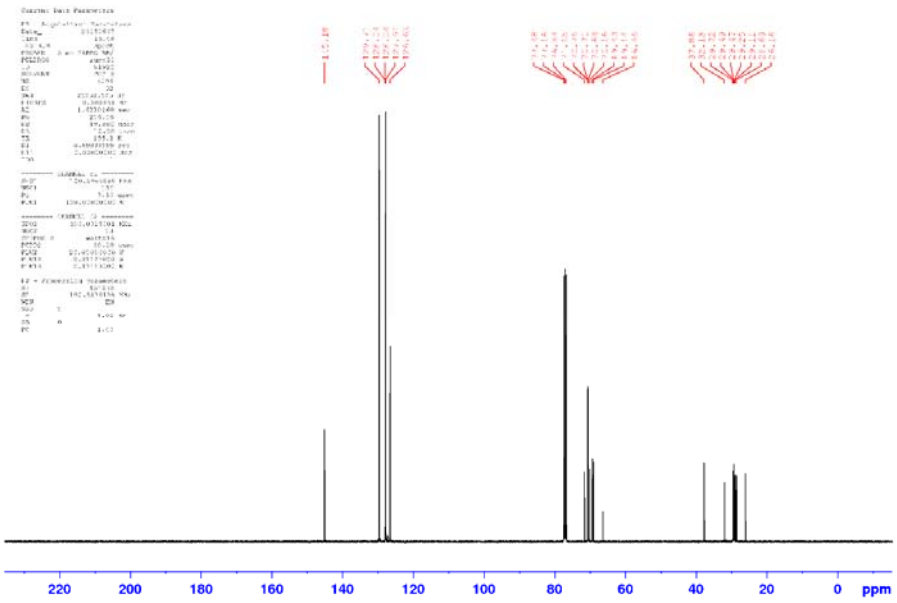


Figure S2: ^{13}C-NMR spectrum of 1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-yl methane-sulfonate (**8**).

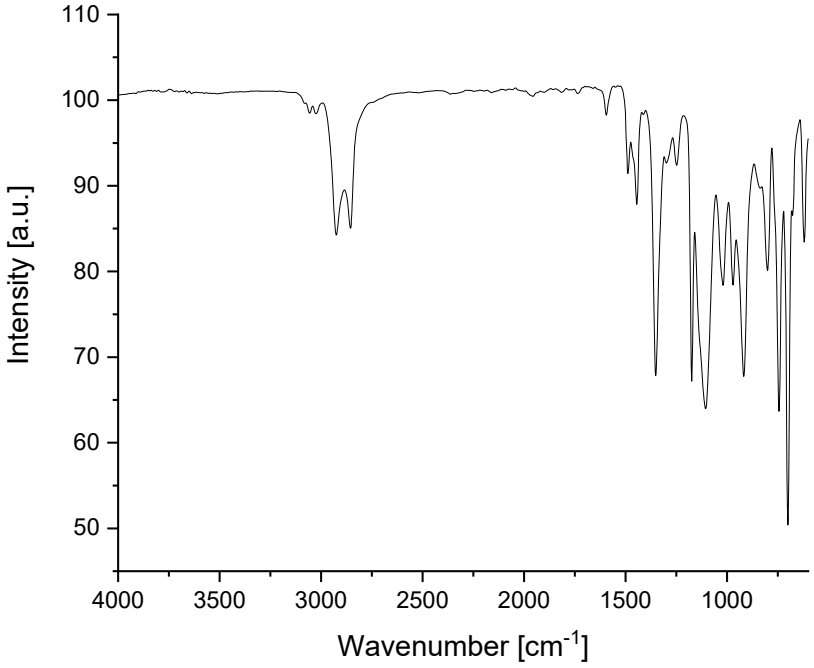
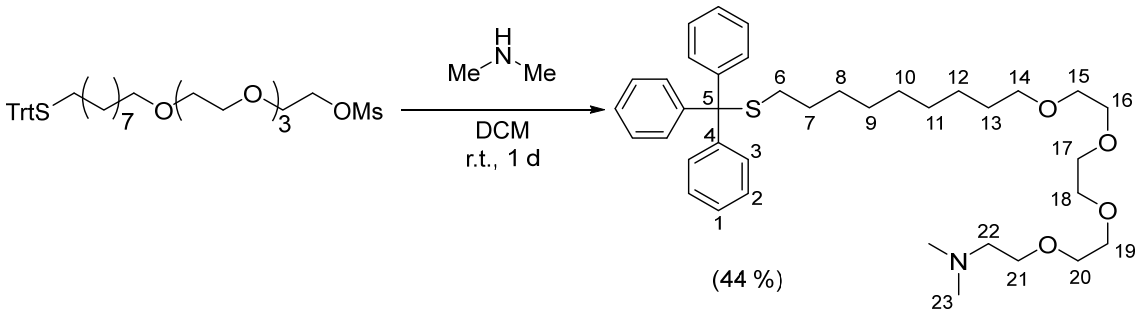


Figure S3: FT-IR ATR of 1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-yl methane-sulfonate(**8**).

*N,N-Dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-amine (**9**)*[8]



The mesylate **8** (2.38 g, 3.53 mmol, 1.00 eq) was added to an emulsion of dichloromethane (25 mL) and a 40-%-solution of dimethylamine in water (8.00 mL, 70.0 mmol, 20.0 eq). and stirred for 1 d at room temperature. After one day, the reaction mixture was extracted with deionized water and dichloromethane. The organic layer was separated and the solvent removed *in vacuo* before purifying the crude product by column chromatography (silica, cyclohexane/EtOAc, 1:4, v/v). By adding TEA (5 %) to the eluent, the product was isolated. After removing the solvent, the product was obtained as a slightly yellow oil.

Yield: 9.69 g (1.54 mmol, 44 %). $\mathbf{R_f}$ (EtOAc/cyclohexane/TEA, 76:19:5): 0.33. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.44-7.38 (m, 6H, H-3), 7.34-7.24 (m, 6H, H-2), 7.24-7.17 (m, 3H, H-1), 3.71-3,55 (m, 14H, H-15 – H-21) 3.42 (t, $^3J_{13,14}$ = 6.8 Hz, 2H, H-14), 2.50 (t, $^3J_{21,22}$ = 5.8 Hz 2H, H-22) 2.26 (s, 6H, H-23), 2.12 (t, $^3J_{6,7}$ = 7.4 Hz, 2H, H-6), 1.61-1.49 (m, 2H, H-13), 1.43-1.32 (m, 2H, H-7) 1.32-1.06 (m, 10H, H-8 – H-12) ppm. **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 144.4 (C_q, C-4), 129.5 (CH, C-2), 126.7 (CH, C-3), 126.4 (CH, C-1), 71.4, 70.5, 70.5, 70.5, 70.5, 70.3, 69.9, 68.9 ($(CH_2)_8$, C-14/15/16/17/18/19/20/21), 66.2 (C_q, C-5), 58.6 (CH_2, C-22), 45.6 (CH_3, C-23), 31.8 (CH_2, C-6), 29.5, 29.2, 29.2, 29.0, 28.8, 28.4, 25.9 ($(CH_2)_7$, C-7/8/9/10/11/12/13) ppm. **HRMS** (ESI,+): Gef.: 622,39246 ; calc.: 622,39246. **FT-IR(ATR):** $\tilde{\nu}$ = 2925 (m), 2854 (m), 1489 (w), 1444 (m), 1351 (w), 1296 (w), 1113 (m), 1036 (w), 847 (w), 744 (s), 700 (s), 619 (w) cm^{-1}. **UV/Vis** (acetonitrile): λ_{max}(log ε) = 280 (4.18), 332 (3.89), (c = $2.57 \cdot 10^{-5}$ mol L^{-1}) nm.

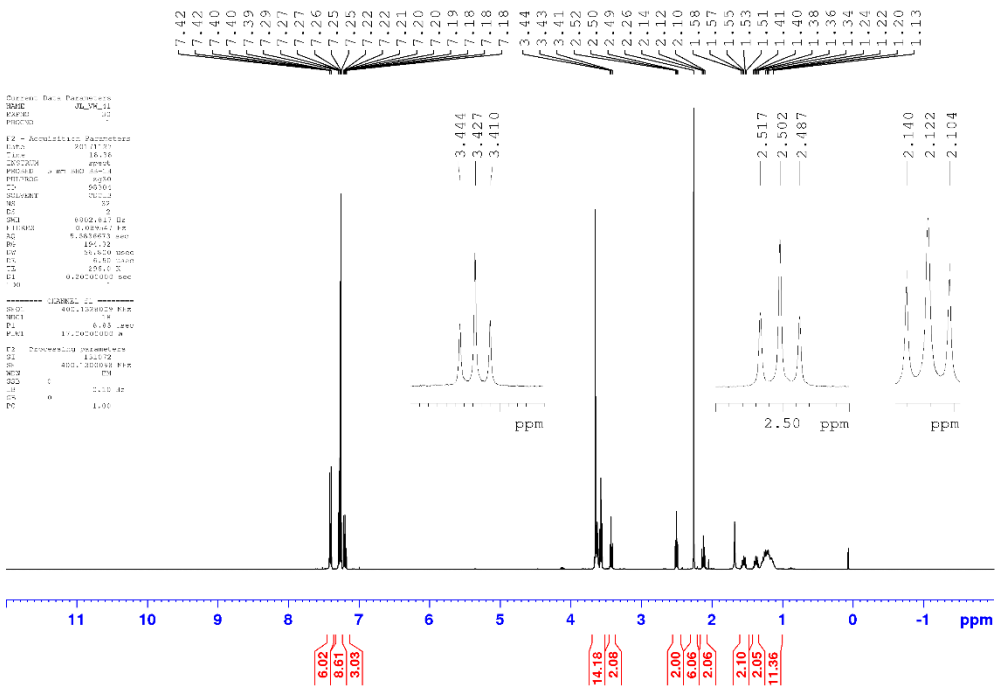


Figure S4: ^{1}H-NMR spectrum of *N*,*N*-dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-amine(**9**).

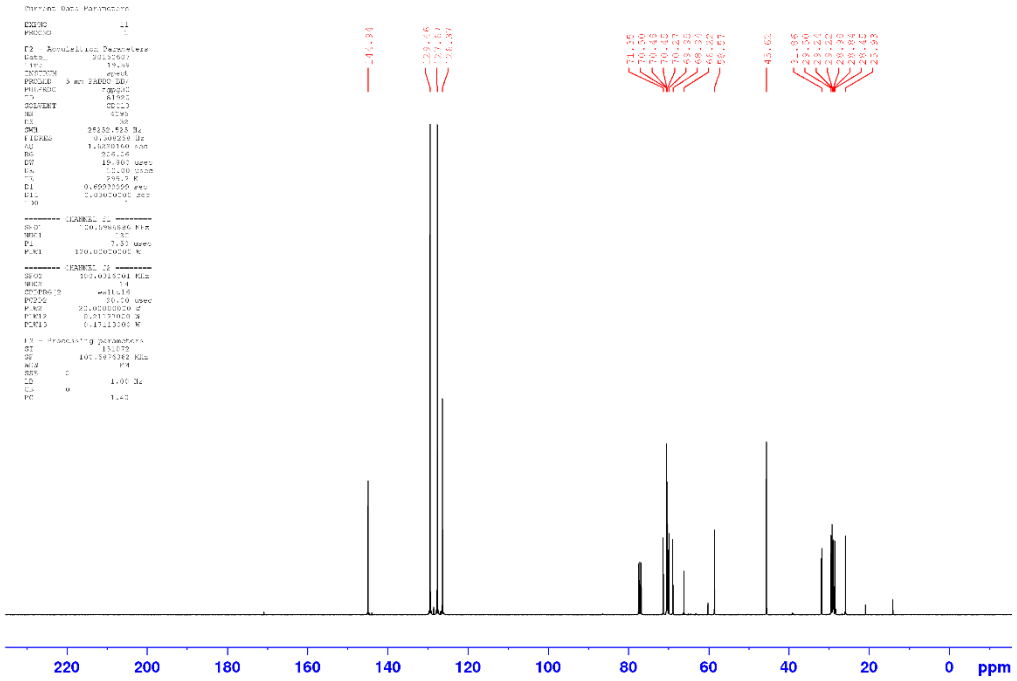


Figure S5: ^{13}C-NMR spectrum of *N*,*N*-dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-amine (**9**).

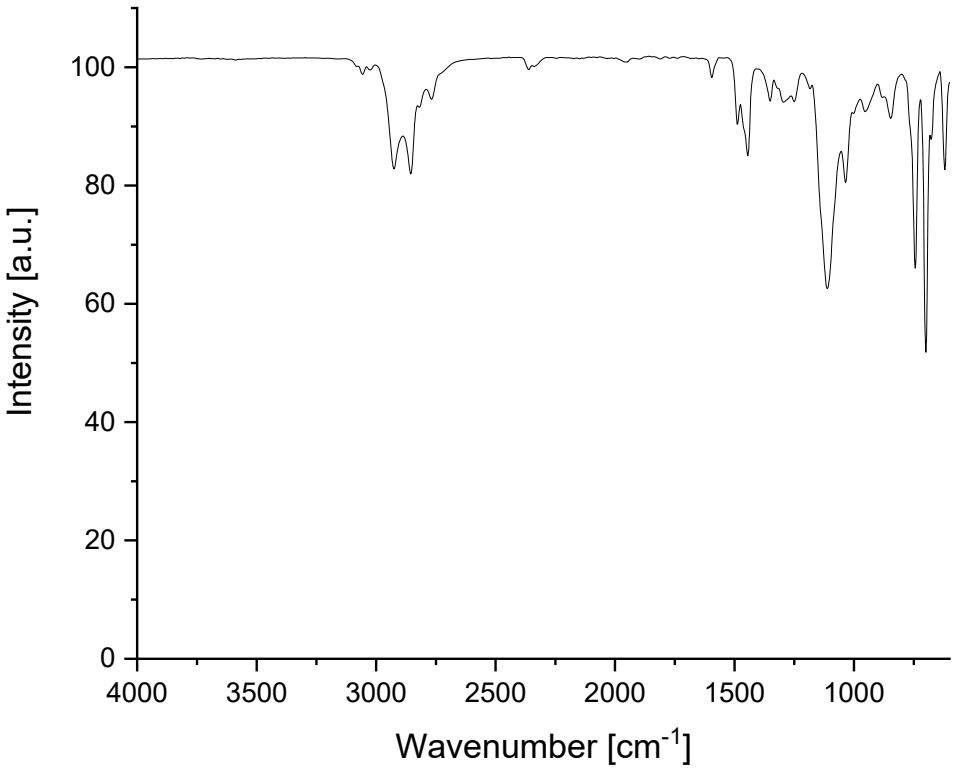
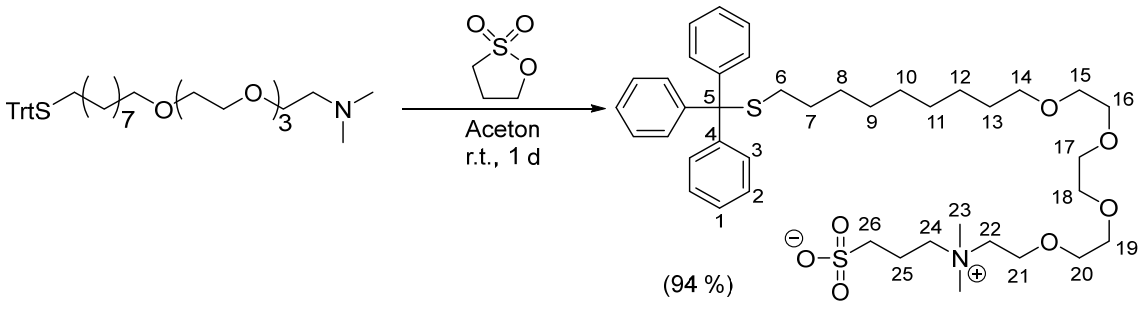


Figure S6: FT-IR ATR spectrum of *N*,*N*-dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thiatricosan-23-amine (**9**).

*24,24-Dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thia-24-azaheptacosan-24-ium-27-sulfonate **(10)***[6]



The amine **9** (960 mg, 1.54 mmol, 1.00 eq) was dissolved in dry acetone (45 mL) and 1,3-propanesultone (410 mg, 3.40 mmol, 2,20 eq) was added and the mixture was stirred for

1 d at room temperature. The resulting solid was filtered and washed with EtOAc/cyclohexane (1:4, v/v). After drying it *in vacuo*, a colorless solid was obtained.

Yield: 3,15 g (4.2 mmol, 94 %). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 7.42-7.37 (m, 6H, H-3), 7.31-7.24 (m, 6H, H-2), 7.23-7.16 (m, 3H, H-1), 4.00-3.88 (m, 2H, H-24), 3.84-3.73 (m, 2H, H-26), 3.71-3,58 (m, 12H, H-15 – H-20), 3.58-3,51 (m, 2H, H-21), 3.41 (t, $^{3}J_{13,14}$ = 6.9 Hz, 2H, H-14), 3.22 (s, 6H, H-23), 2.90 (t, $^{3}J_{21,22}$ = 6.3 Hz 2H, H-22), 2.34-2.20 (m, 2H, H-25), 2.12 (t, $^{3}J_{6,7}$ = 7.4 Hz, 2H, H-6), 1.61-1.47 (m, 2H, H-13), 1.43-1.32 (m, 2H, H-7) 1.32-1.02 (m, 10H, H-8 – H-12) ppm. **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 145.4 (C_q, C-4), 129.9 (CH, C-2), 128.1 (CH, C-3), 126.8 (CH, C-1), 71.8, 70.9, 70.8, 70.7, 70.5, 70.5, 70.3 ($(CH_2)_8$, C-14/15/16/17/18/19/20/21), 66.7 (C_q, C-5), 65.5 (CH_2, C-24), 65.2 (CH_2, C-26), 59.0 (CH_2, C-25), 52.2 (CH_3, C-23), 47.9 (CH_2, C-22) 32.4 (CH_2, C-6), 29.9, 29.7, 29.5, 29.4, 29.3, 28.9, 26.4 ($(CH_2)_7$, C-7/8/9/10/11/12/13) ppm. **HRMS** (ESI,+): found: 744.39671 $[M]^+$; calc. for $[M]^+$: 744.39622. **FT-IR (ATR):** $\tilde{\nu}$ = 3450 (br), 3055 (vw), 3022 (vw), 2925 (m), 2854 (m), 1733 (w), 1666 (w), 1597 (w), 1487 (m), 1442 (m), 1176 (s), 1105 (s), 1035 (s), 742 (s), 698 (s), 607 (m) cm^{-1}. **UV/Vis** (acetonitrile): λ_{max}(log ε) = 255 (5.34), 328 (4.91), (c = $2.15 \cdot 10^{-5}$ mol L^{-1}) nm.

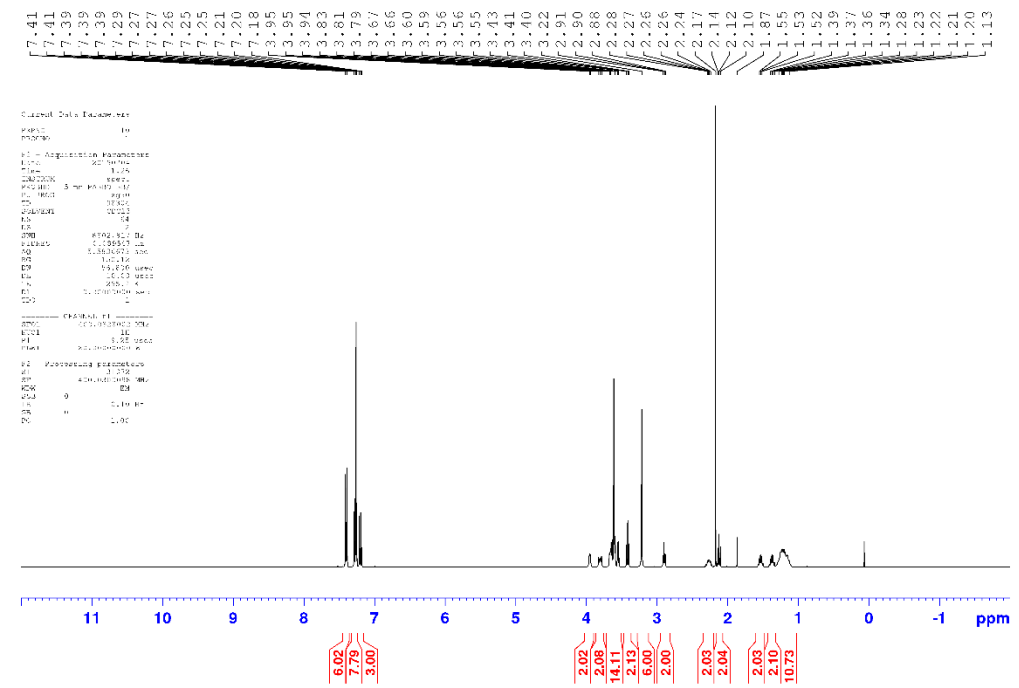


Figure S7: ^{1}H-NMR spectrum of 24,24-dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thia-24-azaheptacosan-24-ium-27-sulfonate (**10**).

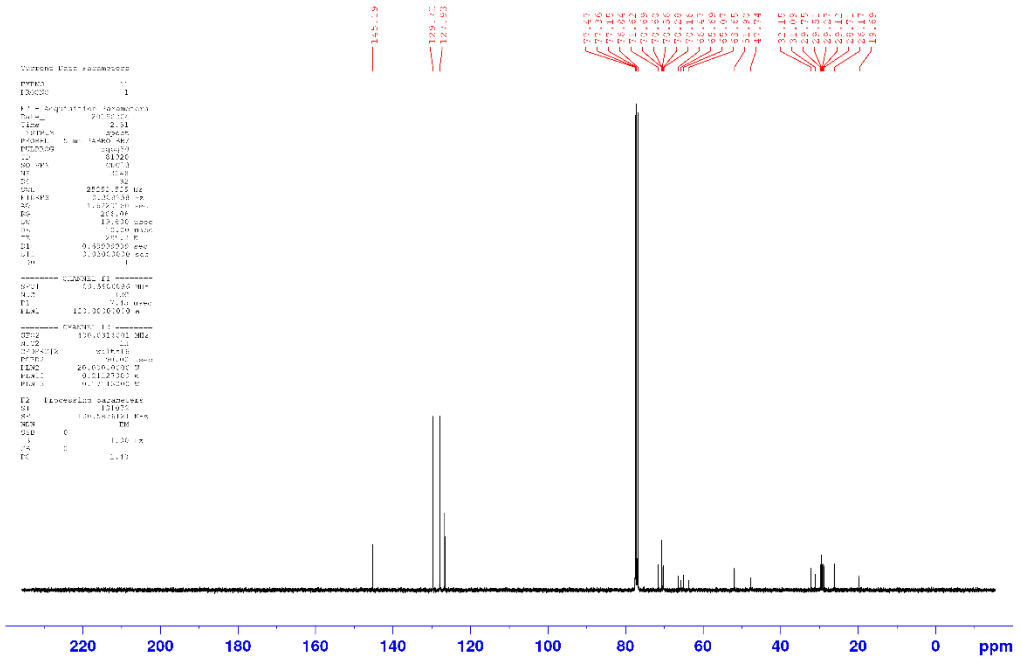


Figure S8: ^{13}C-NMR spectrum of 24,24-dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thia-24-azaheptacosan-24-ium-27-sulfonate (**10**).

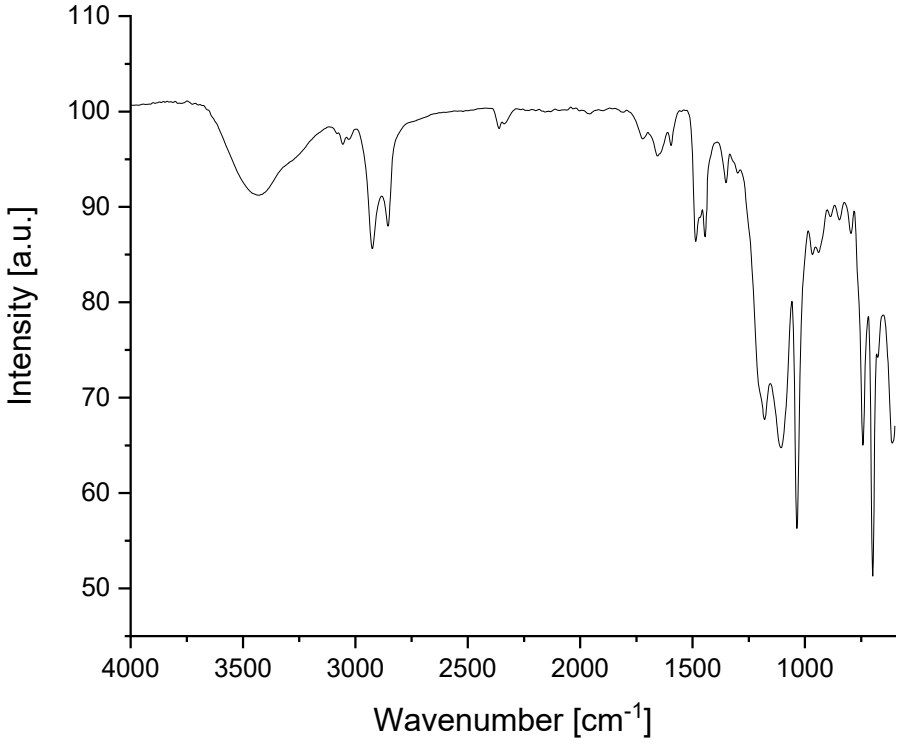
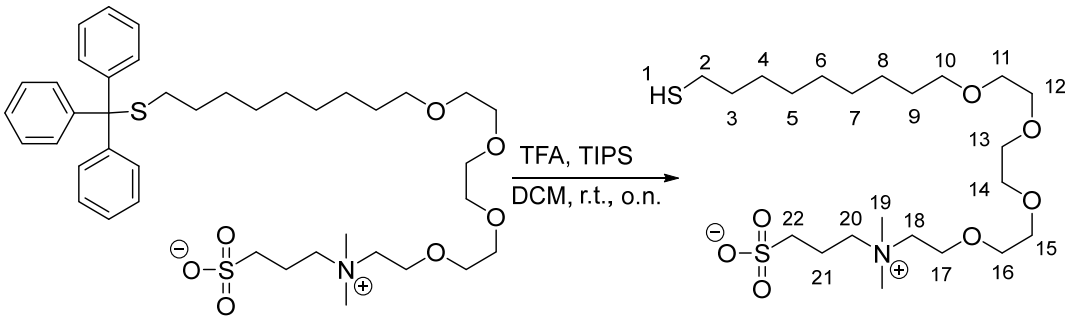


Figure S9: FT-IR ATR spectrum of 24,24-dimethyl-1,1,1-triphenyl-12,15,18,21-tetraoxa-2-thia-24-azaheptacosan-24-ium-27-sulfonate (**10**).

*25-mercapto-4,4-dimethyl-7,10,13,16-tetraoxa-4-azapentacosan-4-ium-1-sulfonate (**5**)*



The protected thiol **10** (70 mg, 94 µmol, 1.00 eq) was dissolved in dry dichloromethane (0.7 mL) and TFA (0.15 mL, 1.90 mmol, 20.00 eq), TFAH (0.04 mL, 0.30 mmol, 3.00 eq) and TIPS (0.06 mL, 0.30 mmol, 3.00 eq) were added. After adding TFA, the mixture turns yellow.

The reaction mixture was stirred overnight (16 h) at room temperature. The solvent was removed *in vacuo* and the crude product was washed with diethyl ether (3x, 1.5 mL). After drying the product *in vacuo*, a whitish solid was obtained under cooling which is melting at room temperature to form a slightly yellow oil.

Yield: 22 mg (44 µmol, 63 %). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 3.99-3.86 (m, 2H, H-20), 3.82-3.70 (m, 2H, H-22), 3.71-3.58 (m, 12H, H-11 – H-16), 3.58-3.50 (m, 2H, H-17), 3.42 (t, $^{3}J_{10,9}$ = 6.9 Hz, 2H, H-10), 3.23 (s, 6H, H-19), 2.96-2.85 (m, 3H, H-18+H-1), 2.51 (t, $^{3}J_{2,3}$ = 7.4 Hz, 2H, H-2), 2.36-2.14 (m, 2H, H-21), 1.66-1.49 (m, 4H, H-3+H-9) 1.45-1.15 (m, 10H, H-4 – H-8) ppm. **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 71.8, 70.8, 70.8, 70.7, 70.7, 70.4, 70.3, 69.1 ($(CH_2)_8$, C-10/11/12/13/14/15/16/17), 65.3 (CH_2, C-20), 65.0 (CH_2, C-22), 57.1 (CH_2, C-21), 52.1 (CH_3, C-19), 47.9 (CH_2, C-18), 34.0 (CH_2, C-2), 29.6, 29.5, 29.4, 29.0, 28.3 26.0, 24.7 ($(CH_2)_7$, C-3/4/5/6/7/8/9) ppm. **HRMS** (ESI,+): found: 524.26701 $[M]^+$; calc. for $[M]^+$: 524.26862. **FTIR (ATR):** $\tilde{\nu}$ = 3440 (br), 2934 (s), 2856 (s), 2549 (w), 1764 (m), 1458 (m), 1207 (s), 1122 (vs), 1038 (s), 964 (w), 942 (w), 802 (m), 702 (m), 595 (m). **UV/Vis** (acetonitrile): λ_{max}(log ε) = 232 (4,57), 270 (4,28), 278 (4,29), 308 (4,66), 328 (7,32), (c = $2.19 \cdot 10^{-5}$ mol L^{-1}) nm.

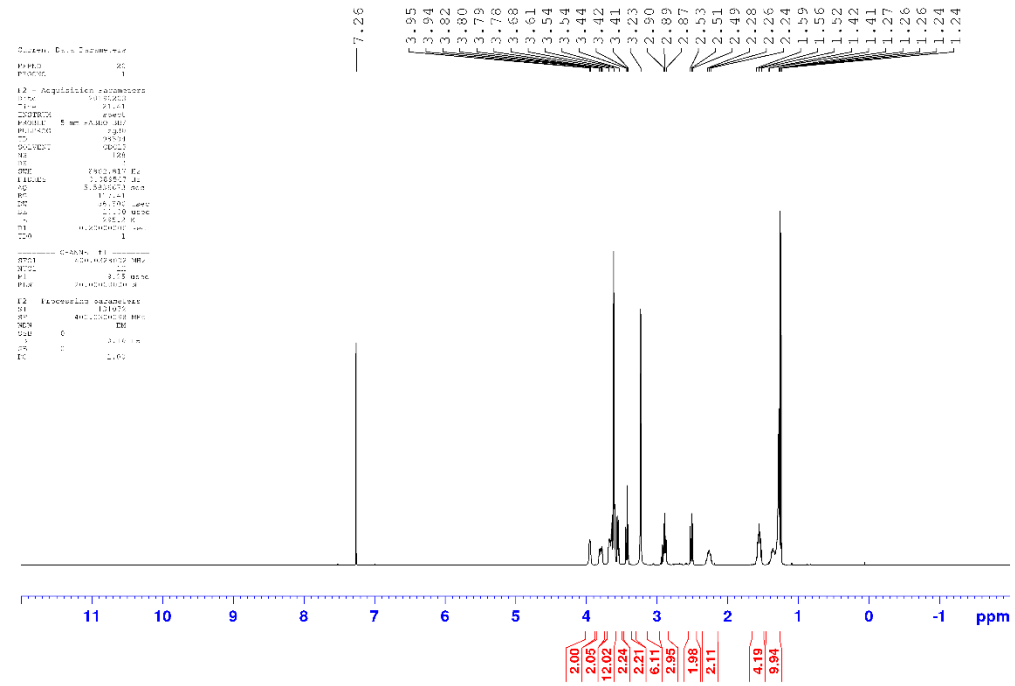


Figure S10: ^{1}H-NMR spectrum of 25-mercapto-4,4-dimethyl-7,10,13,16-tetraoxa-4-azapentacosan-4-ium-1-sulfonate (**5**).

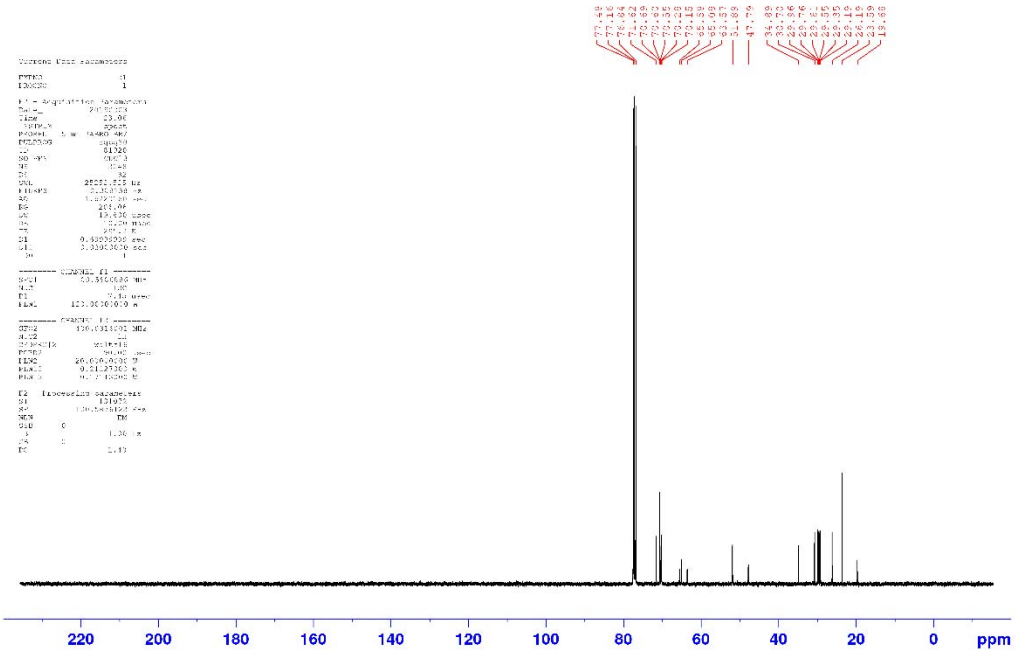


Figure S11: ^{13}C-NMR spectrum of 25-mercapto-4,4-dimethyl-7,10,13,16-tetraoxa-4-azapentacosan-4-ium-1-sulfonate (**5**).

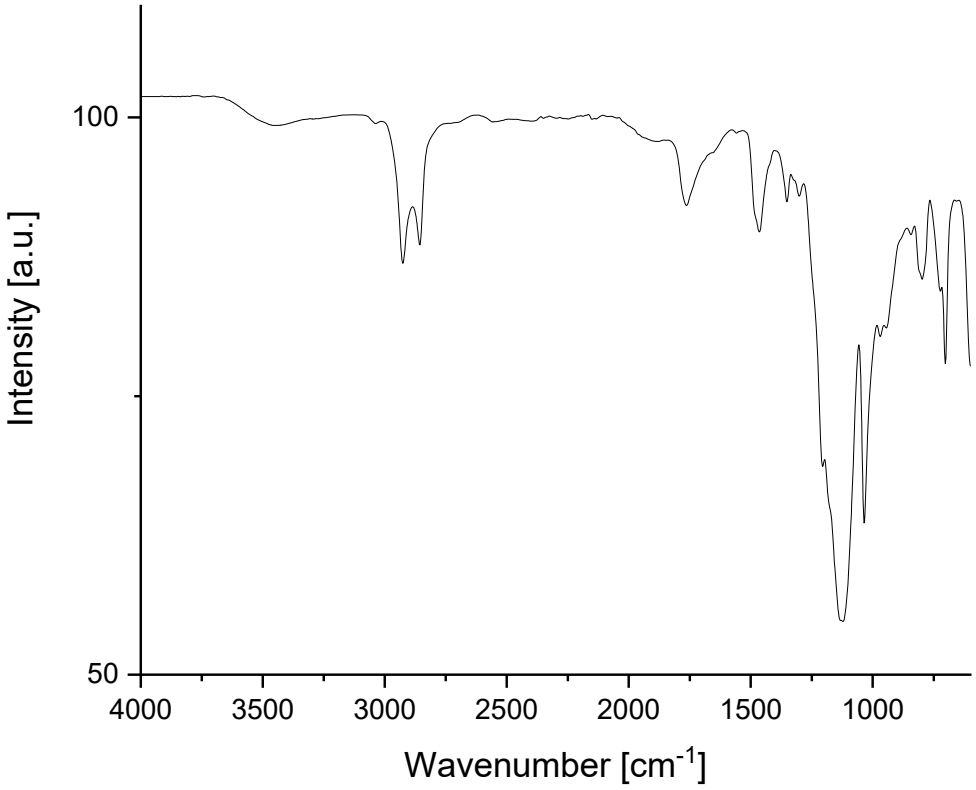


Figure S12: FT-IR ATR spectrum of 25-mercapto-4,4-dimethyl-7,10,13,16-tetraoxa-4-azapentacosan-4-ium-1-sulfonate (**5**).

Nanodiamond Functionalization

*Benzoic acid functionalized ND (**3**):*

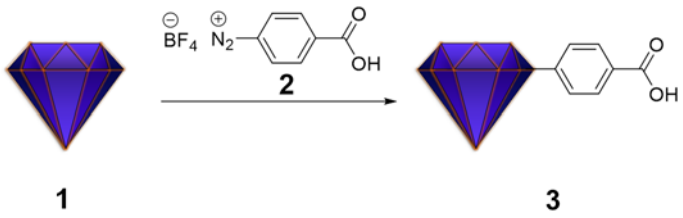


Figure S13: Functionalization of HPHT fND (**1**) with diazonium salt **2**.

As received fND (**1**) (2 mg, 1 mg/mL) was mixed with the diazonium salt **2** (10 mg in 4 mL MQ-water) in a chamber of a mini mill Pulverisette 23 for 1 h at 50 Hz vibration mode with 10x2 mm steel beads. The chamber was opened in minute 5, 20 and 45 to release the overpressure of nitrogen. After the reaction, the fNDs were washed with water, acetone, THF, dry THF in consecutive dispersion-centrifugation (16000 rpm, 10 min) steps. One part of the dispersion was then washed again in acetone and water for further analytics. The dispersion appears grey in dispersion and whitish grey when dry. As the amount of fND was too low to be able to carry out all characterizations, a larger batch of non-fluorescent but otherwise identical HTHP ND (non-fND) was functionalized using the same procedure. The thermogravimetric data have been obtained from this non-fluorescent batch of **3**.

*ND **1** (fND):* **Zeta potential**: -30.5 mV (DD-water, intrinsic pH=5.5), **Particle size** (DLS, DD-water): 10 % ≤ 71 nm, 50 % ≤ 287 nm, 90 % ≤ 887 nm.

*ND **1** (non-fND):* **Zeta potential**: -36 mV (DD-water, intrinsic pH=5.4), **Surface loading** (TGA): Δm(150-300 °C) = 0.3 %, **Particle size** (DLS, DD-water): 10 % ≤ 71 nm, 50 % ≤ 110 nm, 90 % ≤ 197 nm, **FT-IR** (DRIFTS): $\tilde{\nu}$ = 3600 (br), 1760 (m), 1604 (m), 1181 (m), 863 (s) cm^{-1}.

*ND **3** (fND):* **Zeta potential**: -28.2 mV (DD-water, intrinsic pH=5.5), **Particle size** (DLS, DD-water): 10 % ≤ 97 nm, 50 % ≤ 184 nm, 90 % ≤ 387 nm, **FT-IR** (DRIFTS): $\tilde{\nu}$ = 3400 (br), 2951 (vw), 2930 (vw), 2853 (vw), 2637 (br), 2521 (br), 1936 (w), 1704 (s), 1604 (s), 1411 (s), 1259 (m), 1179 (w), 1111 (w), 1021 (w), 963 (vw), 911 (vw), 863 (m), 788 (m), 710 (w), 634 (vw) cm^{-1}.

*ND **3** (non-fND):* **Zeta potential**: -28.8 mV (DD-water, intrinsic pH=5.6), **Surface loading** (TGA): 0.30 mmol/g = Δm(150-300 °C) = 3.8 %; **Particle size** (DLS, DD-water): 10 % ≤ 137 nm, 50 % ≤ 246 nm, 90 % ≤ 478 nm, **FT-IR** (DRIFTS): $\tilde{\nu}$ = 3400 (br), 2951 (vw), 2930 (vw), 2853 (vw), 2637 (br), 2521 (br), 1936 (w), 1704 (s), 1604 (s), 1411 (s), 1259 (m), 1179 (w), 1111 (w), 1021 (w), 963 (vw), 911 (vw), 863 (m), 788 (m), 710 (w), 634 (vw) cm^{-1}.

*Thioesterification of ND **3** to ND **6***

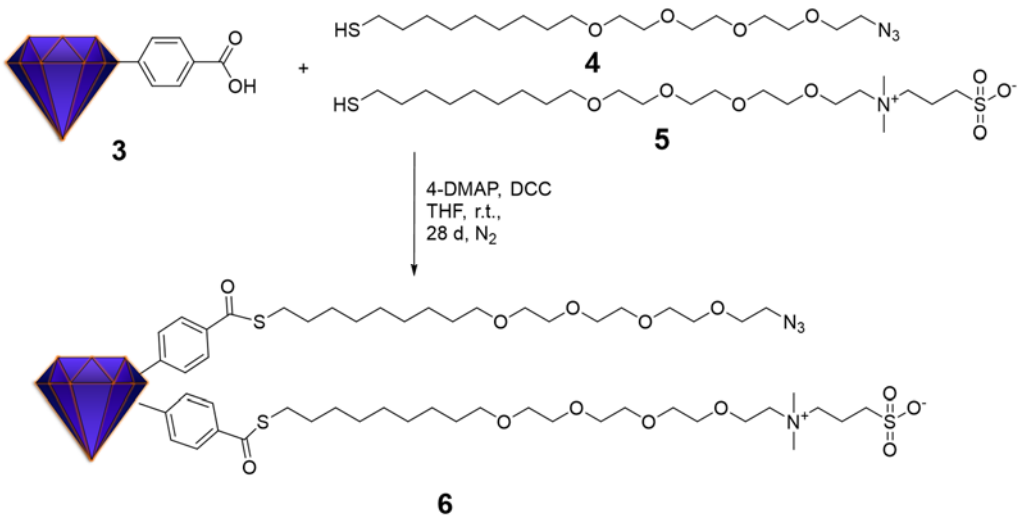


Figure S14: Thioester formation on the ND surface.

To perform this reaction, ND **3** was washed two times in THF and two times in dry THF. The dispersion was mixed with N,N'-dicyclohexylcarbodiimide (DCC) (42 mg, 202 mmol) and

4-dimethylaminopyridine (DMAP) (5 mg, 40 mmol), the respective zwitterionic compound **5** (27 mg, 53 mmol) and the azide (**4**) (20 mg, 53 mmol) linker for a thioester formation. The reaction was stirred for 28 days at room temperature and after 8 days, the same amount of starting material and linker was added to the reaction. After 28 days, water was used to quench the reaction and wash the fNDs free from organic material. Used solvents were THF, water, acetone, dichloromethane, acetone and bidestilled water.

*ND **6** (non-fND):* **Zeta potential**: -25 mV (DD-water, intrinsic pH=5.4), **Surface loading** (TGA): 0.21 mmol/g = Δm(150-300 °C) = 11.8 %, **Particle size** (DLS, DD-water): 10 % ≤ 175 nm, 50 % ≤ 216 nm, 90 % ≤ 266 nm, **FT-IR** (DRIFTS): $\tilde{\nu}$ = 3383 (br), 2930 (m), 2853 (m), 2102 (vw), 1704 (m), 1652 (m) 1604 (s), 1535 (s), 1408 (vs), 1271 (w), 1215 (vw), 1184 (w), 1021 (w), 1103 (w), 1039 (m), 1015 (m), 867 (w), 788 (m), 710 (w) cm^{-1}.

*ND **6** (fND):* **FT-IR** (DRIFTS): $\tilde{\nu}$ = 3359 (br), 3093 (m), 2938 (m), 2888 (m), 2398 (vw), 2134 (vw), 1714 (m), 1624 (s) 1607 (s), 1533 (s), 1412 (vs), 1288 (w), 1211 (w), 1188 (w), 1103 (w), 1100 (w), 1045 (w), 1021 (w), 872 (w), 869 (w), 782 (m), 720 (w) cm^{-1}.

*Click reaction to ND **8***

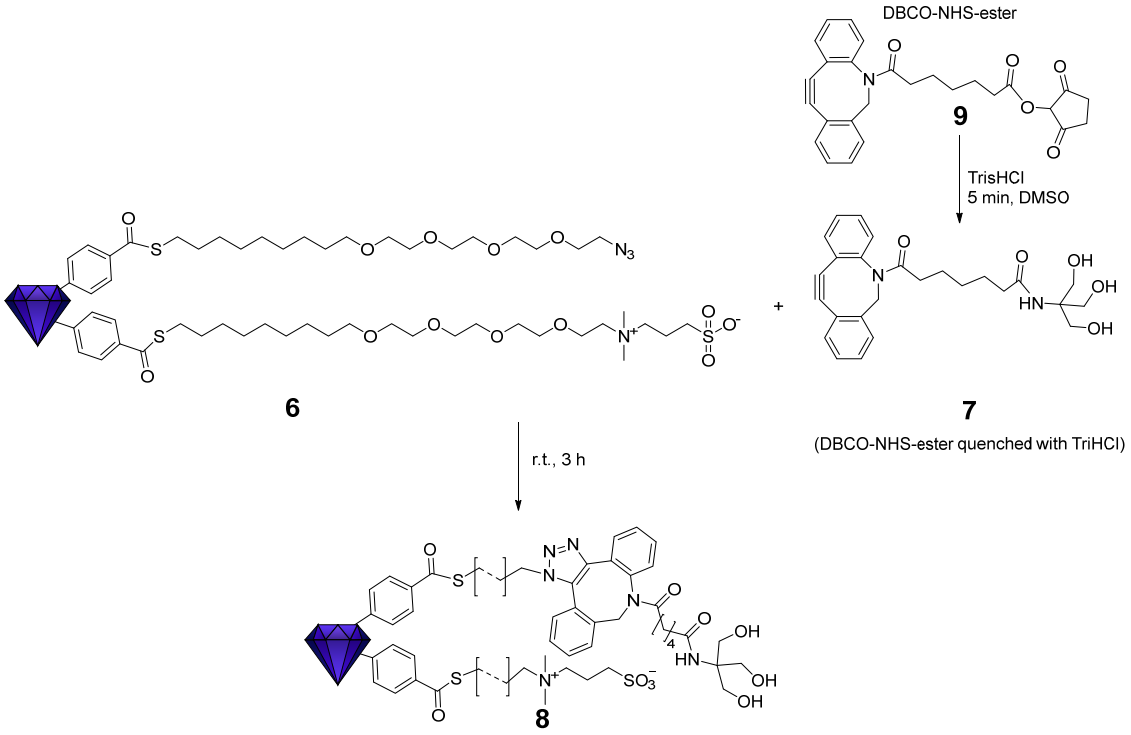


Figure SX: Click reaction between DBCO **7** and azide moieties of the functionalized fND **6**.

To inactivate the NHS-ester of the DBCO compound, the ester **9** was dissolved in DMSO (10 µL, c=1 µg/µL) and quenched immediately with 50 µL Tris-HCl buffer (pH = 8, 100 mM). The access of salts was removed with *Zeba*^{TM} *Spin Desalting Columns*, 7K MWCO from *Thermo Scientific* following the manual. To desalt DBCO, the mixture (60 µL) was applied to the dry column and centrifuged again at the (RCF = 1500, 1 min) for 2 min. After 2 min, the column is loaded with 15 µm DD water and centrifuged again for 2 min. Then, the DBCO-filtrate was mixed with 0.5 mg of fND **6** (1 mg/mL) and incubated at r.t. for 3 h. After 3 h, the reaction mixture was washed three times with DD water in consecutive dispersion centrifugation (10000xG 10 min) steps and stored at 4 °C.

Cell culture

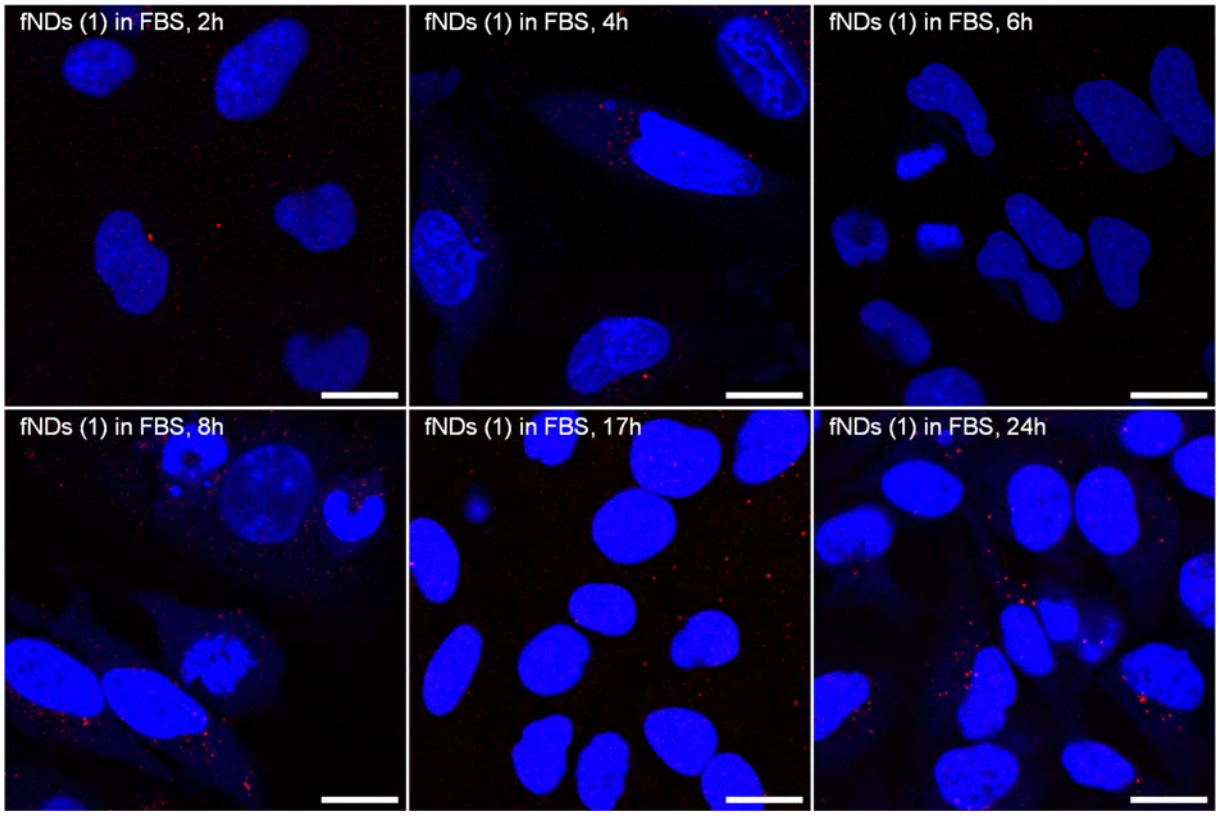


Figure S15: Representative images of HeLa cells after the incubation with fNDs **(1)**. Cell nuclei, stained with DAPI, are shown in blue. fNDs are shown in red. Scale bar – 20 μm.

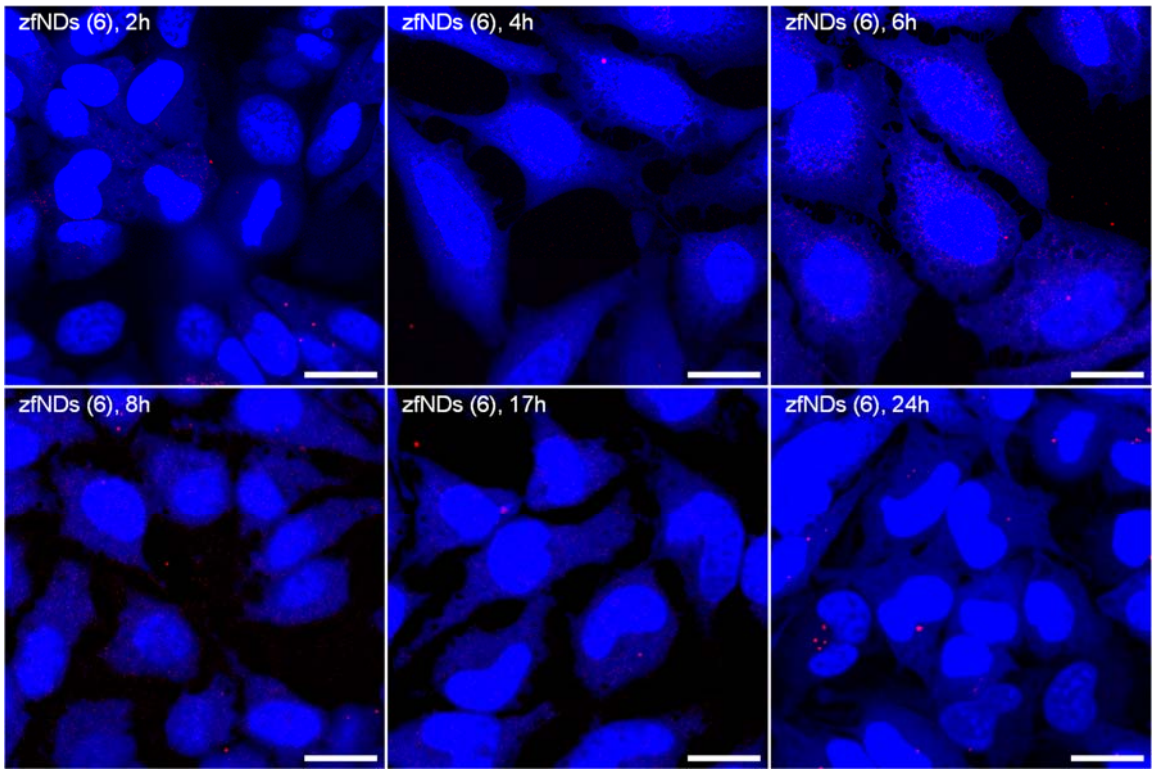


Figure S16: Representative images of HeLa cells after the incubation with zfNDs **(6)**. Cell nuclei, stained with DAPI, are shown in blue. zfNDs are shown in red. Scale bar – 20 μm.

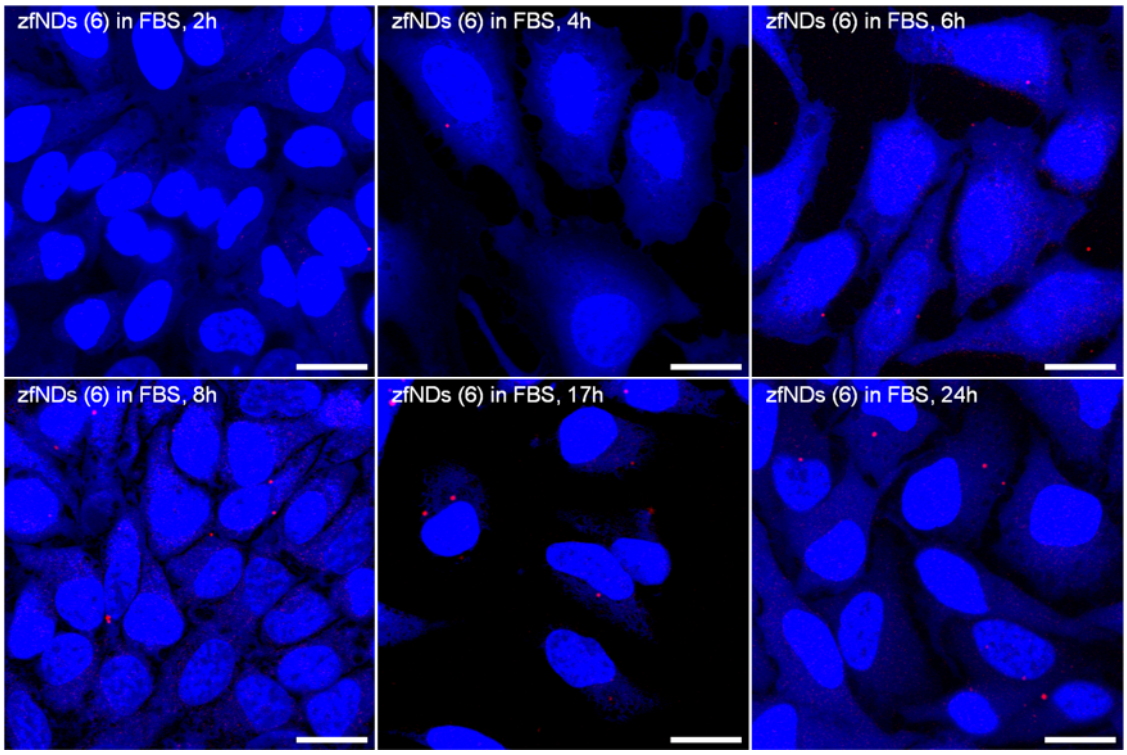


Figure S17: Representative images of HeLa cells after the incubation with zfNDs **(6)** in FBS. Cell nuclei, stained with DAPI, are shown in blue. zfNDs are shown in red. Scale bar – 20 μm.

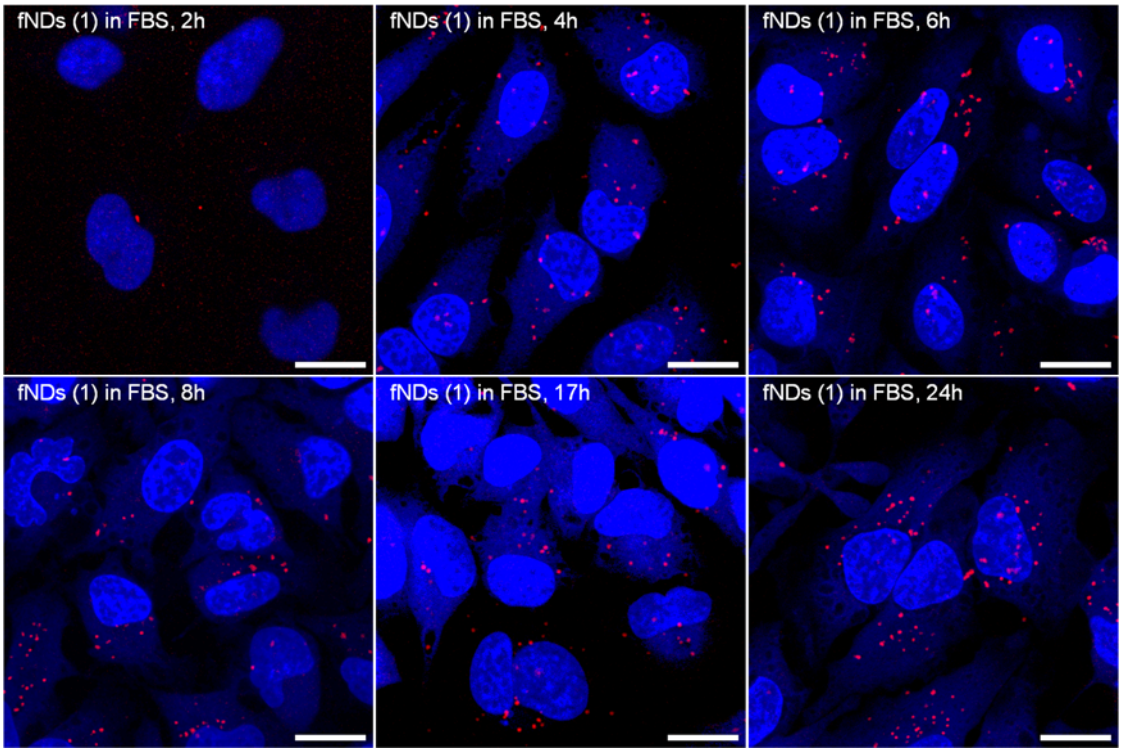


Figure S18: Representative images of HeLa cells after the transfection with fNDs **(1)** in FBS. Cell nuclei, stained with DAPI, are shown in blue. fNDs are shown in red. Scale bar – 20 µm.

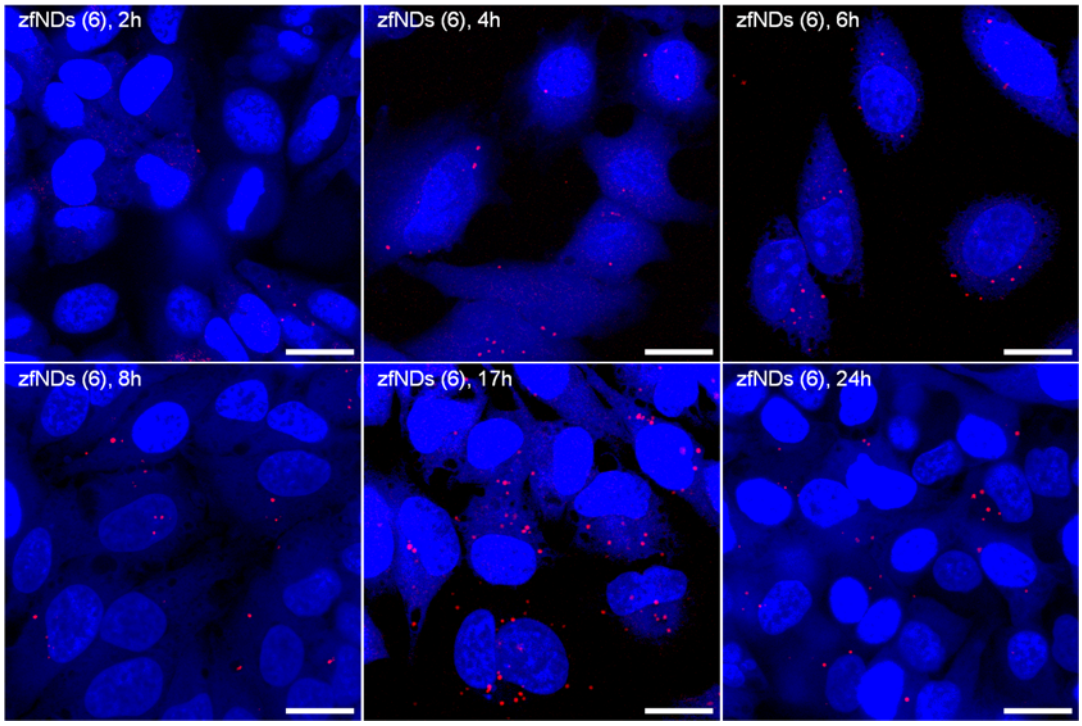


Figure S19: Representative images of HeLa cells after the transfection with zfNDs **(6)**. Cell nuclei, stained with DAPI, are shown in blue. zfNDs are shown in red. Scale bar – 20 µm.

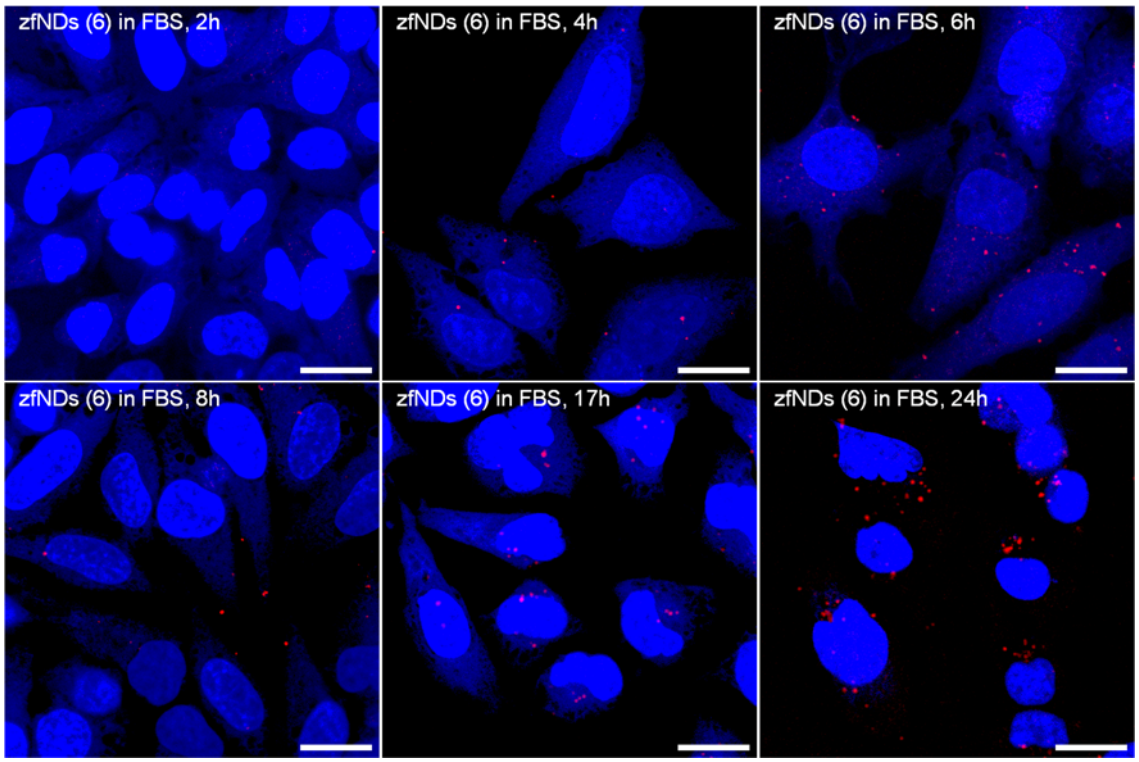


Figure S20: Representative images of HeLa cells after the transfection with zfNDs **(6)** in FBS. Cell nuclei, stained with DAPI, are shown in blue. zfNDs are shown in red. Scale bar – 20 μm.

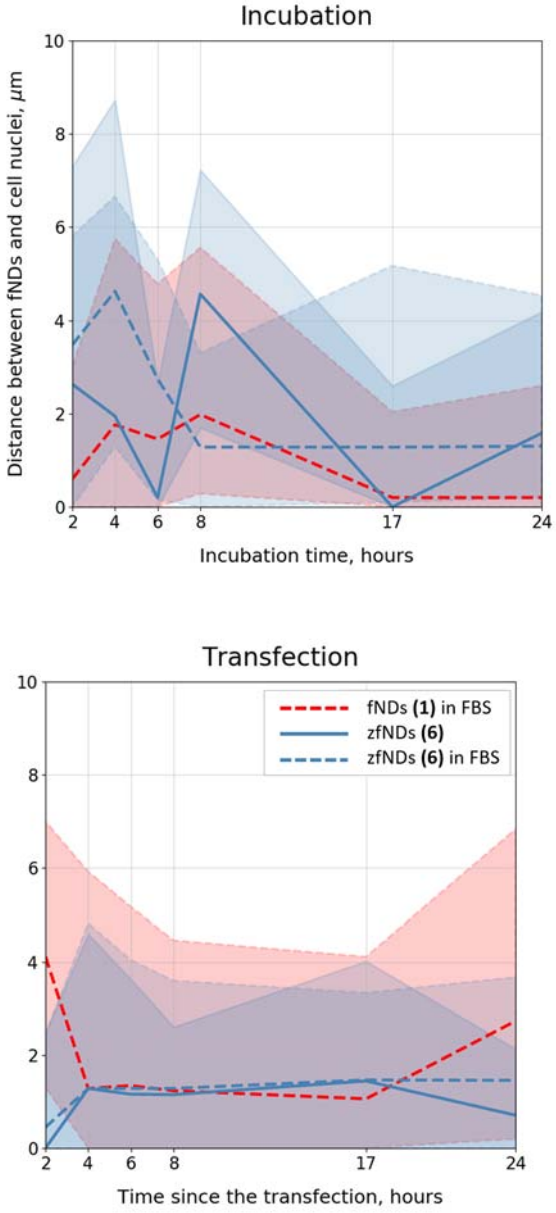


Figure S21. Distance between fNDs, internalized by HeLa cells, and cell nuclei. In case of incubation, both fNDs in FBS and zfNDs are distributed in the cytoplasm, eventually approaching the nuclei. zfNDs (**6**), on average, are located further away. After transfection, all particles tend to be in close proximity of the nucleus (within 2 μm, on average). zfNDs (**6**) reach the perinuclear region faster than non-functionalized fNDs (**1**), and stay there throughout the experiment, showing narrower distribution of distances. Lines represent the median values, shaded areas the interquartile range.

Supplementary references

[S1] C. Kim, G. Y. Tonga, B. Yan, C. S. Kim, S. T. Kim, M. H. Park, Z. Zhu, B. Duncan, B. Creran and V. M. Rotello, *Org Biomol Chem*, 2015, **13**, 2474–2479.

[S2] C. K. Kim, P. Ghosh, C. Pagliuca, Z. J. Zhu, S. Menichetti and V. M. Rotello, *J Am Chem Soc*, 2009, **131**, 1360–1361.