Supplementary Materials

Table of Contents

1. Supplementary Synthetic Data

General synthetic data and characterization of prepared quaternary ammonium compounds

Chemicals and solvents used for organic synthesis

All commercial reagents for synthesis were purchased as at least reagent grade from Sigma-Aldrich (Czech Republic) unless otherwise specified and used without further purification. Anhydrous solvents for synthesis were purchased from Sigma-Aldrich (Czech Republic) and the others were purchased from Penta chemicals Co or VWR International (Czech Republic). Acetonitrile, water and formic acid for LC-MS analyses were obtained from Sigma-Aldrich in LC-MS grade purity (Czech Republic). Thin layer chromatography was carried out on Merck silica gel 60 F254 analytical plates; detection was accomplished with Phosphomolybdic Acid Stain (10 g PMA in 100 mL EtOH), Iodine (sorption on silicagel) or ultraviolet light (254 nm lamp). Flash chromatography was carried out on silica gel 60 (70 – 230 mesh) from Sigma-Aldrich.

LC-MS analysis

High performance liquid chromatography (HPLC) coupled with mass spectrometry (MS) detector was employed to determine capacity factors of the prepared final compounds. The Dionex UltiMate 3000 RS analytical system (ThermoFisher Scientific, Bremen, Germany) was used and composed as followed: binary pump HPG-3400RS connected to vacuum degasser; heated column compartment TCC-3000; auto-sampler WTS-3000 equipped with a 25 µL loop; and Diode array detector-3400; the system was controlled by Chromeleon (version 6.80 SR13 build 3967) software (Thermo Fisher Scientific, USA). Mobile phase A was composed of ultrapure water of ASTM I type (resistance 18.2 MΩ.cm at 25 °C) prepared by Barnstead Smart2Pure 3 UV/UF apparatus (Thermo Fisher Scientific, Bremen, Germany) with 0.1% (v/v) formic acid; mobile phase B was acetonitrile (LC-MS grade, Honeywell-Sigma Aldrich, Germany) with 0.1% (v/v) of formic acid. The studied compounds were dissolved in methanol (LC-MS grade, Honeywell-Sigma Aldrich, Germany). The UV chromatograms of compounds with chromophore were recorded at a wavelength of 254 nm and the spectra were processed with Chromeleon software. Studied compounds were detected by a Q Exactive Plus hybrid quadrupole-orbitrap spectrometer (ThermoFisher Scientific, Bremen, Germany) using heated electro-spray ionization (HESI) settings: sheath gas flow rate 50 arbitrary units, aux gas flow rate 12 arbitrary units, spare gas flow rate 2.5 arbitrary units, spray voltage 3.5 kV, capillary temperature 260 °C, aux gas temperature 300 °C, S-lens RF level 50. Positive ions were monitored in the range of 100 – 1500 m/z with the resolution 140 000. The spectra were processed using Xcalibur 3.1.66.10 software (Thermo Fisher Scientific, USA).

Hydrophobicity of final compounds was established as capacity factors k and was calculated using an equation: $k = \frac{t_1 - t_0}{t_0}$; where t_1 is retention time of the analyte and t_0 is void time.

Uracil (Sigma Aldrich, Steinheim, Germany) was used as a void volume marker (t_0). Kinetex C18 (3 × 150 mm/2.6 μm) column was chosen as the stationary phase. Determination of t_1 of OEG compounds was performed by isocratic elution with ratio A : B 80 : 20 (v/v). Determination of t_1 of alkyl chain compounds was performed by isocratic elution with ratio A : B 30 : 70 (v/v). The flow-rate was set to 0.4 mL/min, column was tempered to 27 °C and injection volume of samples was 2 μL. Hydrophobicity of compounds was expressed as a dependence of log*k* to the calculated Clog*P,* which was calculated using OpenBabel 2.3.2 software. The displayed values of log*k* correspond to the average of three measurements.

High resolution mass spectra (HRMS) of products were recorded by the above-mentioned LC-MS system. Waters Atlantis dC18 (2.1 × 100 mm/3 μm) column was used as the stationary phase in this study with gradient elution as follows: At the start, the ratio was 10% of B which was kept constant for 1 min, then the concentration rose to 100% of B during 3 minutes and was kept for 1 minute and then the column stabilized in 10% B for 2.5 min. The mobile phase flow rate was set at 0.4 mL/min with column temperature of 27 °C. Injection volume was 1 μL. Ions were monitored in the range of 100 – 1500 m/z with the resolution set to 140 000.

^{1}H NMR and ^{13}CNMR spectra of the compounds were recorded at ambient temperature on a Varian S500 spectrometer (499.87 MHz for ^{1}H and 125.71 MHz for ^{13}C). The NMR spectra were proceeded with MestReNova 12.0.4-22023, 2018 Mestrelab Research S.L. The chemical shift values for ^{1}H and ^{13}C NMR spectra are reported in ppm (δ) relative to residual solvent peak $CDCl_3$ (δ_H = 7.26, δ_C = 77.16 ppm), CD_3OD (δ_H = 3.31, δ_C = 49.00 ppm) or $(CD_3)_2SO$ (δ_H = 2.50, δ_C = 39.52 ppm) or $(CD_3)_2CO$ (δ_H = 2.05, δ_C = 205.87 ppm). For ^{1}H δ are given in parts per million (ppm) relative to solvent and the coupling constants (*J*) are expressed in Hertz (Hz). Signals are quoted as s = singlet, d = doublet, dd = doublet of doublets, t = triplet, and m = multiplet.

Additional calculation of molecular electrostatic potential (ESP)

The models of prepared compounds were pre-designed in HyperChem 8.0 software (Hypercube, Gainesville, FL, USA) as free cations, energetically minimized, and exported as mol files for further calculations. In Spartan 14 (Wavefunction, Irvine, CA, USA), semi-empirical quantum chemistry RM1 method was used for determination of the compound equilibrium conformer in vacuum which automatically generated and examined up to 10 000 conformers. Electrostatic potential of the conformers with the lowest potential energy was mapped on the electron isodensity surface of 0.002 e/b^3. The atomic partial charges were determined on the same level of theory in Spartan 14 applying CHELP algorithm for a least-square fit of the partial charges to the molecular electrostatic potential (i.e. ESP atomic partial charges).

Organic synthesis

The synthesis of thiol-derivated quaternary salts of oligoethylene glycol was performed according the scheme in **Supplementary Figure S1**. The MTAB was synthesized using the protocol described previously.[1]

Preparation and characterization of compounds

All reactions were performed under a nitrogen atmosphere. Initiating OEG-compounds were evaporated three times with toluene and dry under vacuum until constant initial weight. Visualization of TLC plates was made by observation with 10% phosphomolybdic acid in ethanol, short wave UV light (254 nm lamp) or in iodine vapors.

Preparation of compounds 4-6

To an ice-cold solution of the diols **1-3** (100 mmol, 4.4 eq) in DCM (90 mL) TEA (36.37 mmol, 1.6 eq) and DMAP (2.27 mmol, 0.1 eq) were added. This reaction mixture was stirred 15 min at 0 °C. Then a solution of DMTrCl (22.73 mmol, 1 eq) in DCM (65 mL) was slowly added to the reaction mixture and stirred another 30 min at 0 °C. After this time, the reaction mixture was heated up to the r.t. and stirred for an additional 30 min. The reaction mixture was diluted with DCM (230 mL), the solution was washed with 5% $NaHCO_3$ (200 mL), water (200 mL) and brine (200 mL). The organic extract was dried over Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by flash chromatography (heptane/EtOAc). The solvents were evaporated under reduced pressure and the monoprotected oligoethylene glycols **4-6** were obtained as pale yellow oils (73 – 84%).

The HRMS analysis of intermediates were not conclusive as the compounds decomposed due to probable cleavage of dimethoxytritile group in acidic conditions during measurement. The structures of compounds were confirmed by NMR.

1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11-tetraoxatridecan-13-ol (**4**)

Pale yellow oil (73%) from **1**; mobile phase: heptane/EtOAc 1/2. ^{1}H NMR ($(CD_3)_2CO$, 500 MHz) δ 7.52 – 7.48 (m, 2H), 7.39 – 7.34 (m, 4H), 7.33 – 7.28 (m, 2H), 7.23 – 7.18 (m, 1H), 6.90 – 6.85 (m, 4H), 3.78 (s, 6H), 3.68 – 3.56 (m, 12H), 3.53 – 3.50 (m, 2H), 3.18 (t, *J* = 5.1 Hz, 2H). ^{13}C NMR ($(CD_3)_2CO$, 126 MHz) δ 159.52, 146.41, 137.19, 130.93, 129.03, 128.50, 127.41, 113.81, 86.62, 73.56, 71.51, 71.37, 71.33, 71.22, 71.19, 64.10, 62.02, 55.48.

1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11,14-pentaoxahexadecan-16-ol (**5**)

Pale yellow oil (82%) from **2**; mobile phase: heptane/EtOAc 1/3. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48 – 7.44 (m, 2H), 7.37 – 7.32 (m, 4H), 7.30 – 7.24 (m, 2H), 7.22 – 7.17 (m, 1H), 6.84 – 6.79 (m, 4H), 3.78 (s, 6H), 3.72 – 3.62 (m, 16H), 3.60 – 3.56 (m, 2H), 3.23 (t, J = 5.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 158.50, 145.20, 136.47, 130.19, 128.34, 127.85, 126.76, 113.16, 86.07, 72.67, 70.89, 70.85, 70.81,70.75, 70.74,70.72, 70.44, 63.26, 61.86, 55.32.

1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11,14,17-hexaoxanonadecan-19-ol (**6**)

Pale yellow oil (84%) from **3**; mobile phase: EtOAc. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48 – 7.43 (m, 2H), 7.37 – 7.31 (m, 4H), 7.29 – 7.24 (m, 2H), 7.22 – 7.16 (m, 1H), 6.85 – 6.78 (m, 4H), 3.78 (s, 6H), 3.73 – 3.61 (m, 20H), 3.61 – 3.57 (m, 2H), 3.25 – 3.20 (m, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 158.48, 145.20, 136.47, 130.18, 128.33, 127.85, 126.75, 113.15, 86.04, 72.68, 70.87, 70.85, 70.82, 70.78, 70.72, 70.67, 70.66, 70.43, 63.26, 61.86, 55.33.

Preparation of compounds 7-9

Monoprotected oligoethylene glycols **4-6** (10 mmol, 1 eq) were dissolved in DCM (50 mL) and cooled down to 0 °C. TEA (20 mmol, 2 eq) and DMAP (1 mmol, 0.1 eq) were added to cooled reaction mixture. After 5 min also *p*-TsCl (15 mmol, 1.5 eq) was added. The reaction was stirred 30 min at 0 °C and then was heated up to r.t. for another 2 hours. The reaction mixture was diluted with DCM (260 mL) and extracted by the solution of 5% $NaHCO_3$ (2 × 160 mL), water (160 mL) and brine (160 mL), dried over Na_2SO_4, filtered and evaporated under reduced pressure to get a pale yellow oil. The crude product was purified by flash chromatography (heptane/EtOAc). The solvents were evaporated under reduced pressure and the tosylated oligoethylene glycols (**7-9**) were obtained as pale yellow oils (92 – 97%).

The HRMS analysis of intermediates were not conclusive as the compounds decomposed due to probable cleavage of dimethoxytritile group in acidic conditions during measurement. The structure of compounds were confirmed by NMR.

1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11-tetraoxatridecan-13-yl 4-methylbenzenesulfonate (7)

Pale yellow oil (96%) from **4**; mobile phase: heptane/EtOAc 1/2. ^{1}H NMR ($(CD_3)_2CO$, 500 MHz) δ 7.82 – 7.77 (m, 2H), 7.51 – 7.47 (m, 2H), 7.45 (d, J = 7.9 Hz, 2H), 7.38 – 7.33 (m, 4H), 7.31 – 7.27 (m, 2H), 7.23 – 7.18 (m, 1H), 6.90 – 6.84 (m, 4H), 4.15 – 4.11 (m, 2H), 3.78 (s, 6H), 3.67 – 3.50 (m, 12H), 3.17 (t, J = 5.1 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR ($(CD_3)_2CO$, 126 MHz) δ 159.40, 146.35, 145.66, 137.13, 134.31 130.87, 130.75, 128.97, 128.65, 128.45, 127.37, 113.76, 86.57, 71.45, 71.29, 71.24, 71.20, 71.15, 70.60, 69.24, 64.05, 55.44, 21.44.

1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11,14-pentaoxahexadecan-16-yl 4-methylbenzenesulfonate (8)

Pale yellow oil (92%) from **5**; mobile phase: heptane/EtOAc 1/2. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.81 – 7.77 (m, 2H), 7.48 – 7.43 (m, 2H), 7.37 – 7.30 (m, 6H), 7.30 – 7.24 (m, 2H), 7.22 – 7.16 (m, 1H), 6.84 – 6.79 (m, 4H), 4.16 – 4.12 (m, 2H), 3.78 (s, 6H), 3.69 – 3.63 (m, 10H), 3.63 – 3.59 (m, 2H), 3.58 – 3.53 (m, 4H), 3.22 (t, J = 5.3 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 158.52, 145.22, 144.88, 136.48, 133.19, 130.20, 129.93, 128.35, 128.11, 127.86, 126.77, 113.16, 86.06, 70.90, 70.87, 70.85, 70.78, 70.66, 69.35, 68.80, 63.28, 55.34, 21.76.

1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11,14,17-hexaoxanonadecan-19-yl 4-methylbenzenesulfonate (9)

Pale yellow oil (97%) from **6**; mobile phase: heptane/EtOAc 1/5. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.81 – 7.78 (m, 2H), 7.48 – 7.43 (m, 2H), 7.37 – 7.30 (m, 6H), 7.29 - 7.24 (m, 2H), 7.22 – 7.16 (m, 1H), 6.84 – 6.78 (m, 4H), 4.16 – 4.13 (m, 2H), 3.78 (s, 6H), 3.74 – 3.49 (m, 20H), 3.22 (t, J = 5.3 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 158.48, 145.20, 144.88, 136.45, 133.14, 130.17, 129.92, 128.32, 128.09, 127.84, 126.75, 113.14, 86.03, 70.88, 70.84, 70.82, 70.78, 70.72, 70.68, 70.62, 69.35, 68.78, 63.26, 60.50, 55.32, 21.75.

Preparation of compounds 10-12

To solutions of the tosylated oligoethylene glycols **7-9** (10 mmol, 1 eq) in MEK (66 mL) potassium thioacetate (30 mmol, 3 eq) was added. The mixtures were heated up to reflux and stirred for 30 min. Then the reaction mixtures were cooled down, diluted with EtOAc (90 mL) and washed with H_2O (90 mL). The organic layers were dried over Na_2SO_4, filtered and evaporated under reduced pressure to get a pale yellow oil. The desired products were purified by flash chromatography (heptane/EtOAc). The solvents were evaporated under reduced pressure and the oligoethylene glycols (**10**-**12**) were obtained as pale yellow oils (88 – 96%).

The HRMS analysis of intermediates were not conclusive as the compounds decomposed due to probable cleavage of dimethoxytritile group in acidic conditions during measurement. The structures of compounds were confirmed by NMR.

(1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11-tetraoxatridecan-13-yl) ethanethioate (10)

Pale yellow oil (96%) from **7**; mobile phase: heptane/EtOAc 2/1. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48 – 7.44 (m, 2H), 7.37 – 7.31 (m, 4H), 7.30 – 7.24 (m, 2H), 7.22 – 7.17 (m, 1H), 6.85 – 6.79 (m, 4H), 3.78 (s, 6H), 3.71 – 3.64 (m, 8H), 3.63 – 3.59 (m, 4H), 3.23 (t, *J* = 5.2 Hz, 2H), 3.07 (t, *J* = 6.5 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.66, 158.50, 145.20, 136.48, 130.19, 128.34, 127.85, 126.76, 113.16, 86.06, 70.91, 70.89, 70.72, 70.50, 69.89, 63.28, 55.33, 30.67, 28.98.

(1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11,14-pentaoxahexadecan-16-yl) ethanethioate (11)

Pale yellow oil (88%) from **8**; mobile phase: heptane/EtOAc 1/1. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48 – 7.44 (m, 2H), 7.36 – 7.32 (m, 4H), 7.29 – 7.25 (m, 2H), 7.21 – 7.17 (m, 1H), 6.83 – 6.79 (m, 4H), 3.78 (s, 6H), 3.69 – 3.58 (m, 16H), 3.23 (t, *J* = 5.3 Hz, 2H), 3.07 (t, *J* = 6.5 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.63, 158.51, 145.22, 136.49, 130.20, 128.35, 127.76, 126.76, 113.23, 86.05, 71.92, 70.87, 70.82, 70.66, 70.46, 96.88, 63.29, 55.33, 30.68, 28.99.

(1,1-bis(4-methoxyphenyl)-1-phenyl-2,5,8,11,14,17-hexaoxanonadecan-19-yl) ethanethioate (12)

Pale yellow oil (93%) from **9**; mobile phase: heptane/EtOAc 1/2. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.49 – 7.44 (m, 2H), 7.38 – 7.32 (m, 4H), 7.31 – 7.25 (m, 2H), 7.23 – 7.17 (m, 1H), 6.86 – 6.80 (m, 4H), 3.79 (s, 6H), 3.74 – 3.56 (m, 20H), 3.23 (t, *J* = 5.3 Hz, 2H), 3.09 (t, *J* = 6.5 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.62, 158.48, 145.20, 136.46, 130.17, 128.32, 127.84, 126.74, 113.14, 86.03, 70.89, 70.85, 70.83, 70.79, 70.74, 70.71, 70.62, 70.43, 69.87, 63.26, 55.31, 30.68, 28.97.

Preparation of compounds 13-15

Firstly, a solution of TCA in DCE (3%, 300 mL) was prepared. Then this solution was added to initial compounds **10-12** (10 mmol, 1 eq). After 5 min at r.t. the reaction mixtures were diluted with DCM (480 mL) and extracted with a saturated solution of Na_2CO_3 (370 mL) and brine (370 mL), dried over Na_2SO_4, filtered and evaporated under reduced pressure to get a pale yellow oil. The residue was purified by flash chromatography (EtOAc/MeOH). The solvents were evaporated under reduced pressure and the thioacetate derivatives **13-15** were obtained as pale yellow oils (77 – 93%).

(2-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethyl) ethanethioate (13)

Pale yellow oil (77%) from **10**; mobile phase: EtOAc. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.74 – 3.70 (m, 2H), 3.68 – 3.57 (m, 12H), 3.08 (t, *J* = 6.5 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.68, 72.62, 70.78, 70.62, 70.48, 70.40, 69.91, 61.89, 30.68, 28.91. HRMS ($HESI^+$) *m/z*, found: 253.11029; $C_{10}H_{21}O_5S^+$ $[M+H]^+$ calculated: 253.11042.

(14-hydroxy-3,6,9,12-tetraoxatetradecyl) ethanethioate (14)

Pale yellow oil (93%) from **11**; EtOAc/MeOH 10/1.^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.73 – 3.57 (m, 18H), 3.07 (t, *J* = 6.5 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.69, 72.77, 70.70, 70.67, 70.64, 70.56, 70.39, 70.36, 69.88, 61.81, 30.66, 28.87. HRMS ($HESI^+$) *m/z*, found: 297.13678; $C_{12}H_{25}O_6S^+$ $[M+H]^+$ calculated: 297.13664.

(17-hydroxy-3,6,9,12,15-pentaoxaheptadecyl) ethanethioate (**15**)

Pale yellow oil (88%) from **12**; mobile phase: EtOAc/MeOH 10/1. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.74 – 3.56 (m, 22H), 3.08 (t, J = 6.5 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.69, 72.68, 70.75, 70.74, 70.69, 70.67, 70.63, 70.44, 70.42, 69.88, 61.86, 30.69, 28.96. HRMS (HESI$^+$) *m/z*, found: 341.16235; $C_{14}H_{29}O_7S^+$ $[M+H]^+$ calculated: 341.16285.

Preparation of compounds 16-18

Thioacetate analogs **13-15** (10 mmol, 1 eq) were dissolved in DCM (17 mL), cooled to 0 °C and then CBr_4 (13 mmol, 1.3 eq) was added. Then, pre-prepared solution of Ph_3P (13 mmol, 1.3 eq in 1 mL of DCM) was slowly added to the OEG solution. The resulting mixtures were stirred for an additional 30 min. After this time, the reactions were heated up to the r.t. and stirred over 30 min. The reactions were terminated by the addition of silica gel. Solvents were evaporated and the residues were purified by flash chromatography (heptane/EtOAc). The solvents were evaporated under reduced pressure and the bromide analogs **16-18** were obtained as pale yellow oils (80 – 81%).

(2-(2-(2-(2-bromoethoxy)ethoxy)ethoxy)ethyl) ethanethioate (**16**)

Pale yellow oil (80%) from **13**; mobile phase: heptane/EtOAc 2/1. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.81 (t, J = 6.4 Hz, 2H), 3.69 – 3.57 (m, 10H), 3.47 (t, J = 6.3 Hz, 2H), 3.08 (t, J = 6.5 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.62, 71.35, 70.78, 70.73, 70.68, 70.46, 69.90, 30.70, 30.45, 28.98. HRMS (HESI$^+$) *m/z*, found: 315.02545; $C_{10}H_{20}BrO_4S^+$ $[M+H]^+$ calculated: 315.02601.

(14-bromo-3,6,9,12-tetraoxatetradecyl) ethanethioate (**17**)

Pale yellow oil (80%) from **14**; mobile phase: heptane/EtOAc 1/1. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.82 – 3.78 (m, 2H), 3.68 – 3.61 (m, 12H), 3.59 (t, J = 6.5 Hz, 2H), 3.47 (t, J = 6.4 Hz, 2H), 3.08 (t, J = 6.5 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.62, 71.35, 70.81, 70.80, 70.75, 70.69, 70.67, 70.47, 69.90, 30.70, 30.44, 28.99. HRMS (HESI$^+$) *m/z*, found: 359.05017; $C_{12}H_{24}BrO_5S^+$ $[M+H]^+$ calculated: 359.05223.

(17-bromo-3,6,9,12,15-pentaoxaheptadecyl) ethanethioate (**18**)

Pale yellow oil (81%) from **15**; mobile phase: heptane/EtOAc 1/1. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.80 (t, J = 6.3 Hz, 2H), 3.65 – 3.58 (m, 18H), 3.46 (t, J = 6.3 Hz, 2H), 3.08 (t, J = 6.5 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.64, 71.34, 70.79, 70.78, 70.72, 70.67, 70.64, 70.45, 69.89, 30.70, 30.44, 28.97. HRMS (HESI$^+$) *m/z*, found: 403.07806; $C_{14}H_{29}BrO_6S^+$ $[M+H]^+$ calculated: 403.07844.

Preparation of compounds 19-21a

Bromides analogs **16-18** (0.25 mmol, 1 eq) were dissolved in ACN and TEA (0.3 mmol, 1.2 eq) was added. The reaction mixture was stirred at r.t. for 48 hours. Then the solution was evaporated. Diethylether (25 mL) was added to the residue and stirred for another 2 hours. Then the solvents were decanted. The residues were dried to get pure trimethylammonium salts **19-21a** in yields 87 – 99%.

***N,N,N*-trimethyl-13-oxo-3,6,9-trioxa-12-thiatetradecan-1-aminium bromide** (**19a**)

Light brown oil (87%) from **16**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.00 – 3.90 (m, 4H), 3.67 – 3.65 (m, 2H), 3.61 – 3.51 (m, 8H), 3.47 (s, 9H), 3.03 (t, J = 6.7 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.64, 70.47, 70.43, 70.37, 70.31, 69.82, 65.72, 65.29, 54.76, 30.74, 28.76. HRMS (HESI^{+}) *m/z*, found: 294.17312; $C_{13}H_{28}NO_4S^{+}$ $[M]^{+}$ calculated: 294.17336.

***N,N,N*-trimethyl-16-oxo-3,6,9,12-tetraoxa-15-thiaheptadecan-1-aminium bromide** (**20a**)

Light brown oil (99%) from **17**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.98 – 3.90 (m, 4H), 3.67 – 3.63 (m, 2H), 3.61 – 3.54 (m, 12H), 3.46 (s, 9H), 3.03 (t, J = 6.6 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.60, 70.64, 70.51, 70.49, 70.42, 70.35, 70.25, 69.75, 65.70, 65.28, 54.73, 30.69, 28.77. HRMS (HESI^{+}) *m/z*, found: 338.19983; $C_{15}H_{32}NO_5S^{+}$ $[M]^{+}$ calculated: 338.19957.

***N,N,N*-trimethyl-19-oxo-3,6,9,12,15-pentaoxa-18-thiaicosan-1-aminium bromide** (**21a**)

Light brown oil (99%) from **18**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.00 – 3.91 (m, 4H), 3.68 – 3.66 (m, 2H), 3.64 – 3.55 (m, 16H), 3.47 (s, 9H), 3.05 (t, J = 6.3 Hz, 2H), 2.32 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.64, 70.71, 70.63, 70.55, 70.44, 70.36, 70.27, 69.79, 65.77, 65.36, 54.82, 30.73, 28.82. HRMS (HESI^{+}) *m/z*, found: 382.22507; $C_{17}H_{36}NO_6S^{+}$ $[M]^{+}$ calculated: 382.22524.

Preparation of compounds 19-21b-f

Bromide derivatives **16-18** (0.25 mmol, 1 eq) were dissolved in ACN (0.6 mL) and the corresponding amine (0.3 mmol, 1.2 eq) was added. The reaction mixture was stirred under reflux for 48 hours. After that, the solutions were evaporated and diethylether (25 mL) was added to the residues and stirred for another 2 hours. Then the solvents were decanted. The residues were dried to get pure corresponding quaternary ammonium salts **19-21b-f** in yields (34 – 99%).

1-(13-oxo-3,6,9-trioxa-12-thiatetradecyl)pyridin-1-ium bromide (19b)

Light brown oil (99%) from **16**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.55 – 9.51 (m, 2H), 8.55 – 8.49 (m, 1H), 8.10 – 8.04 (m, 2H), 5.24 – 5.21 (m, 2H), 4.06 – 4.03 (m, 2H), 3.65 – 3.61 (m, 2H), 3.59 – 3.52 (m, 8H), 3.02 (t, J = 6.6 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.54, 145.98, 145.37, 127.91, 70.57, 70.41, 70.32, 70.28, 69.80, 69.54, 61.32, 30.74, 28.76. HRMS ($HESI^+$) m/z, found: 314.14172; $C_{15}H_{24}NO_4S^+$ $[M]^+$ calculated: 314.14151.

1-(13-oxo-3,6,9-trioxa-12-thiatetradecyl)-4-phenylpyridin-1-ium bromide (19c)

Brown oil (99%) from **16**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.52 – 9.48 (m, 2H), 8.18 – 8.14 (m, 2H), 7.80 – 7.76 (m, 2H), 7.58 – 7. 53 (m, 3H), 5.22 – 5.17 (m, 2H), 4.08 – 4.04 (m, 2H), 3.67 – 3.63 (m, 2H), 3.59 – 3.51 (m, 8H), 3.02 (t, J = 6.5 Hz, 2H), 2.28 (s, 3H).^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.49, 156.61, 145.85, 133.83, 132.46, 130.04, 127.91, 124.54, 70.57, 70.39, 70.30, 69.78, 69.64, 60.41, 30.69, 28.78. HRMS ($HESI^+$) m/z, found: 390.17255; $C_{21}H_{28}NO_4S^+$ $[M]^+$ calculated: 390.17281.

***N*-benzyl-*N,N*-dimethyl-13-oxo-3,6,9-trioxa-12-thiatetradecan-1-aminium bromide** (**19d**)

Brown oil (99%) from **16**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.68 – 7.39 (m, 5H), 5.02 (s, 2H), 4.04 – 3.99 (m, 2H), 3.92 – 3.89 (m, 2H), 3.69 – 3.65 (m, 2H), 3.62 – 3.59 (m, 2H), 3.57 – 3.53 (m, 4H), 3.50 (t, *J* = 6.6 Hz, 2H), 3.32 (s, 6H), 2.99 (t, *J* = 6.6 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.45, 133.41, 130.59, 129.05, 127.40, 70.31, 70.30, 70.17, 70.12, 69.62, 68.88, 65.03, 62.62, 50.55, 30.54, 28.58.

HRMS (HESI^{+}) *m/z*, found: 370.20490; $C_{19}H_{32}NO_4S^{+}$ $[M]^{+}$ calculated: 370.20465.

2-(13-oxo-3,6,9-trioxa-12-thiatetradecyl)isoquinolin-2-ium bromide (**19e**)

Light brown oil (99%) from **16**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.84 (s, 1H), 8.93 (dd, *J* = 6.8, 1.3 Hz, 1H), 8.62 (d, *J* = 8.3 Hz, 1H), 8.29 (d, *J* = 6.8 Hz, 1H), 8.16 – 8.08 (m, 2H), 7.95 – 7.91 (m, 1H), 5.34 – 5.29 (m, 2H), 4.15 – 4.10 (m, 2H), 3.66 – 3.62 (m, 2H), 3.56 – 3.50 (m, 8H), 3.00 (t, J = 6.6 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.53, 150.87, 137.59, 137.15, 135.65, 131.44, 131.28, 127.74, 127.11, 125.59, 70.60, 70.42, 70.31, 70.26, 69.80, 69.78, 60.94, 30.71, 28.76. HRMS (HESI^{+}) *m/z*, found: 364.15701; $C_{19}H_{26}NO_4S^{+}$ $[M]^{+}$ calculated: 364.15716.

1-(13-oxo-3,6,9-trioxa-12-thiatetradecyl)quinolin-1-ium bromide (**19f**)

Brown oil (38%) from **16**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.01 (dd, *J* = 5.8, 1.3 Hz, 1H), 9.11 (d, *J* = 8.3 Hz, 1H), 8.77 (d, *J* = 9.0 Hz, 1H), 8.32 – 8.29 (m, 1H), 8.20 – 8.17 (m, 1H), 8.13 – 8.09 (m, 1H), 7.95 – 7.89 (m, 1H), 5.64 – 5.60 (m, 2H), 4.18 – 4.14 (m, 2H), 3.63 – 3.59 (m, 2H), 3.54 – 3.47 (m, 8H), 3.00 (t, *J* = 6.6 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.59, 150.75, 147.36, 138.43, 136.04, 130.69, 130.18, 129.93, 121.97, 119.67, 70.69, 70.40, 70.36, 70.23, 69.74, 68.88, 57.91, 30.70, 28.76. HRMS (HESI$^+$) *m/z*, found: 364.15698; $C_{19}H_{26}NO_4S^+$ [M]$^+$ calculated: 364.15716.

1-(16-oxo-3,6,9,12-tetraoxa-15-thiaheptadecyl)pyridin-1-ium bromide (**20b**)

Light brown oil (99%) from **17**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.56 – 9.53 (m, 2H), 8.53 – 8.48 (m, 1H), 8.10 – 8.06 (m, 2H), 5.25 – 5.22 (m, 2H), 4.07 – 4.03 (m, 2H), 3.65 – 3.51 (m, 14H), 3.01 (t, *J* = 6.6 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.52, 146.02, 145.28, 127.95, 70.61, 70.53, 70.47, 70.32, 70.23, 69.76, 69.55, 61.28, 30.70, 28.73. HRMS (HESI$^+$) *m/z*, found: 358.16824; $C_{17}H_{28}NO_5S^+$ [M]$^+$ calculated: 358.16772.

1-(16-oxo-3,6,9,12-tetraoxa-15-thiaheptadecyl)-4-phenylpyridin-1-ium bromide (**20c**)

Brown oil (92%) from **17**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.53 – 9.48 (m, 2H), 8.20 – 8.15 (m, 2H), 7.79 – 7.75 (m, 2H), 7.58 – 7.52 (m, 3H), 5.20 – 5.14 (m, 2H), 4.08 – 4.03 (m, 2H), 3.65 – 3.61 (m, 2H), 3.61 – 3.51 (m, 10H), 3.48 (t, *J* = 6.6 Hz, 2H), 2.96 (t, *J* = 6.6 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.42, 156.49, 145.87, 133.86, 132.38, 129.99, 127.89, 124.55, 70.59, 70.53, 70.44, 70.43, 70.26, 70.24, 69.71, 69.61, 60.36, 30.62, 28.69. HRMS (HESI$^+$) *m/z*, found: 434.19992; $C_{23}H_{32}NO_5S^+$ [M]$^+$ calculated: 434.19902.

***N*-benzyl-*N,N*-dimethyl-16-oxo-3,6,9,12-tetraoxa-15-thiaheptadecan-1-aminium bromide** (**20d**)

Brown oil (99%) from **17**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 – 7.39 (m, 5H), 5.03 (s, 2H), 4.04 – 3.99 (m, 2H), 3.94 – 3.88 (m, 2H), 3.69 – 3.65 (m, 2H), 3.63 – 3.51 (m, 12H), 3.33 (s, 6H), 3.03 (t, *J* = 6.6 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.58, 133.57, 130.74, 129.19, 127.57, 70.65, 70.53, 70.48, 70.33, 70.27, 69.76, 68.97, 65.19, 62.73, 50.69, 30.68, 28.80. HRMS (HESI$^+$) *m/z*, found: 414.23093; $C_{21}H_{36}NO_5S^+$ [M]$^+$ calculated: 414.23032.

2-(16-oxo-3,6,9,12-tetraoxa-15-thiaheptadecyl)isoquinolin-2-ium bromide (20e)

Light brown oil (99%) from **17**. ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.85 (s, 1H), 8.95 (dd, *J* = 6.8, 1.4 Hz, 1H), 8.67 – 8.64 (m, 1H), 8.29 (d, *J* = 6.8 Hz, 1H), 8.16 – 8.09 (m, 2H), 7.96 – 7.92 (m, 1H), 5.33 – 5.29 (m, 2H), 4.15 – 4.11 (m, 2H), 3.66 – 3.50 (m, 14H), 3.00 (t, *J* = 6.6 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (CDCl$_3$, 126 MHz) δ 195.52, 150.95, 137.61, 137.12, 135.76, 131.41, 131.21, 127.80, 127.09, 125.60, 70.63, 70.61, 70.52, 70.34, 70.29, 69.86, 69.79, 61.00, 30.69, 28.80. HRMS (HESI$^+$) *m/z*, found: 408.18414; $C_{21}H_{30}NO_5S^+$ [M]$^+$ calculated: 408.18337.

1-(16-oxo-3,6,9,12-tetraoxa-15-thiaheptadecyl)quinolin-1-ium bromide (20f)

Brown oil (59%) from **17**. ^{1}H NMR (CDCl$_3$, 500 MHz) δ 9.88 (dd, *J* = 5.8, 1.3 Hz, 1H), 9.14 (d, *J* = 8.3 Hz, 1H), 8.75 (d, *J* = 9.0 Hz, 1H), 8.34 – 8.30 (m, 1H), 8.18 – 8.13 (m, 1H), 8.10 – 8.06 (m, 1H), 7.89 – 7.85 (m, 1H), 5.60 – 5.55 (m, 2H), 4.13 – 4.09 (m, 2H), 3.58 – 3.40 (m, 14H), 2.95 (t, *J* = 6.6 Hz, 2H), 2.23 (s, 3H). ^{13}C NMR (CDCl$_3$, 126 MHz) δ 195.40, 150.59, 147.46, 138.22, 136.00, 130.71, 130.07, 129.86, 121.89, 119.53, 70.60, 70.42, 70.35, 70.20, 70.19, 69.61, 68.69, 57.84, 30.56, 28.65. HRMS (HESI$^+$) *m/z*, found: 408.18414; $C_{21}H_{30}NO_5S^+$ [M]$^+$ calculated: 408.18337.

1-(19-oxo-3,6,9,12,15-pentaoxa-18-thiaicosyl)pyridin-1-ium bromide (**21b**)

Light brown oil (99%) from **18**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.56 – 9.52 (m, 2H), 8.52 – 9.46 (m,1H), 8.11 – 8.06 (m, 2H), 5.24 – 5.20 (m, 2H), 4.08 – 4.03 (m, 2H), 3.64 – 3.51 (m, 18H), 3.02 (t, J = 6.6 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.56, 146.07, 145.27, 127.97, 70.67, 70.59, 70.53, 70.50, 70.34, 70.26, 69.79, 69.59, 61.28, 50.72, 30.71, 28.77. HRMS (HESI^{+}) *m/z*, found: 402.19366; $C_{19}H_{32}NO_6S^{+}$ $[M]^{+}$ calculated: 402.19394.

1-(19-oxo-3,6,9,12,15-pentaoxa-18-thiaicosyl)-4-phenylpyridin-1-ium bromide (**21c**)

Brown oil (79%) from **18**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.54 – 9.51 (m, 2H), 8.02 – 8.16 (m, 2H), 7.81 – 7.78 (m, 2H), 7.60 – 7.55 (m, 3H), 5.21 – 5.16 (m, 2H), 4.09 – 4.05 (m, 2H), 3.66 – 3.48 (m, 18H), 3.00 (t, J = 6.6 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.55, 156.56, 145.94, 133.94, 132.44, 130.05, 127.94, 124.58, 70.66, 70.59, 70.57, 70.49, 70.48, 70.30, 70.27, 69.77, 69.70, 60.43, 30.68, 28.77. HRMS (HESI^{+}) *m/z*, found: 478.88534; $C_{25}H_{36}NO_6S^{+}$ $[M]^{+}$ calculated: 478.22578.

***N*-benzyl-*N,N*-dimethyl-19-oxo-3,6,9,12,15-pentaoxa-18-thiaicosan-1-aminium bromide** (**21d**)

Brown oil (98%) from **18**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 – 7.39 (m, 5H), 5.01 (s, 2H), 4.04 – 3.99 (m, 2H), 3.93 – 3.89 (m, 2H), 3.69 – 3.65 (m, 2H), 3.63 – 3.53 (m, 16H), 3.33 (s, 6H), 3.04 (t, J = 6.5 Hz, 2H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.62, 133.59, 130.79, 129.24, 127.57, 70.68, 70.64, 70.59, 70.53, 70.49, 70.36, 70.28, 69.80, 69.06, 65.23, 62.81, 50.75, 30.70, 28.85. HRMS (HESI^{+}) *m/z*, found: 458.25629; $C_{23}H_{40}NO_6S^{+}$ $[M]^{+}$ calculated: 458.25654.

2-(19-oxo-3,6,9,12,15-pentaoxa-18-thiaicosyl)isoquinolin-2-ium bromide (21e)

Light brown oil (87%) from **18**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.88 (s, 1H), 8.95 (dd, *J* = 6.8, 1.2 Hz, 1H), 8.65 (d, *J* = 8.3 Hz, 1H), 8.30 (d, *J* = 6.8 Hz, 1H), 8.17 – 8.08 (m, 2H), 7.97 – 7.93 (m, 1H), 5.35 – 5.29 (m, 2H), 4.17 – 4.13 (m, 2H), 3.66 – 3.63 (m, 2H), 3.63 – 3.50 (m, 16H), 3.01 (t, *J* = 6.6 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.56, 151.01, 137.63, 137.11, 135.79, 131.44, 131.21, 127.82, 127.09, 125.59, 70.69, 70.65, 70.61, 70.57, 70.54, 70.52, 70.34, 70.30, 69.90, 69.80, 61.00, 30.69, 28.80. HRMS ($HESI^+$) *m/z*, found: 452.20953 $C_{23}H_{34}NO_6S^+$ $[M]^+$ calculated: 452.20957.

1-(19-oxo-3,6,9,12,15-pentaoxa-18-thiaicosyl)quinolin-1-ium bromide (21f)

Brown oil (34%) from **18**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.04 (dd, *J* = 5.8, 1.3 Hz, 1H), 9.06 (d, *J* = 8.3 Hz, 1H), 8.80 (d, *J* = 9.0 Hz, 1H), 8.31 – 8.28 (m, 1H), 8.23 – 8.19 (m, 1H), 8.15 – 8.11 (m, 1H), 7.96 – 7.91 (m, 1H), 5.70 – 5.63 (m, 2H), 4.21 – 4.16 (m, 2H), 3.65 – 3.46 (m, 18H), 3.03 (t, *J* = 6.6 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 195.59, 151.01, 147.20, 138.50, 136.07, 130.61, 130.20, 129.95, 122.13, 119.83, 70.76, 70.69, 70.60, 70.55, 70.52, 70.37, 69.80, 68.96, 57.98, 30.70, 28.83. HRMS ($HESI^+$) *m/z*, found: 452.20972; $C_{23}H_{34}NO_6S^+$ $[M]^+$ calculated: 452.20959.

Preparation of compounds 22-24a-f

AcCl (87.50 mmol, 350 eq) was added dropwise to cooled solution (0 °C) of the quaternary ammonium salts (**19-21a-f**) (0.25 mmol, 1 eq) in MeOH/DCM (5/13 mL). The reaction mixtures were stirred 10 min at 0 °C and then additionally 48 hours at r.t. After this time, the rest of AcCl and generated HCl were removed from the reaction mixture under reduced pressure by water-pump (1 hour), then the solvents were evaporated under vacuum.

Diethyether (25 mL) was added to the residue and stirred for 2 hours. The solvent was decanted. The obtained final products (86 – 99%) were dried under vacuum.

2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)-*N,N,N*-trimethylethan-1-aminium bromide (22a)

Light brown oil (99%, isolated as disulfide) from **19a**. ^{1}H NMR (CD_3OD, 500 MHz) δ 3.98 – 3.94 (m, 2H), 3.75 – 3.55 (m, 12H), 3.22 (s, 9H), 2.92 (t, J = 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 73.59, 71.87, 70.95, 70.34, 66.95, 65.93, 62.16, 54.81, 39.45. HRMS ($HESI^+$) *m/z*, found: 252.16229; $C_{11}H_{26}NO_3S^+$ $[M]^+$ calculated: 252.16224.

1-(2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)ethyl)pyridin-1-ium bromide (22b)

Light brown oil (99%) from **19b**. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.64 – 9.56 (m, 2H), 8.51 – 8.43 (m, 1H), 8.10 – 8.00 (m, 3H), 5.31 – 5.25 (m, 2H), 4.09 – 4.03 (m, 4H), 3.66 – 3.50 (m, 10H), 2.65 (t, J = 6.3 Hz, 2H), 1.6 (t, J = 7.7 Hz, 1H). ^{13}C NMR (CD_3OD, 126 MHz) δ 146.27, 145.44, 128.13, 72.76, 70.58, 70.43, 70.30, 70.18, 69.82, 61.67, 24.39. HRMS ($HESI^+$) *m/z*, found: 272.13098; $C_{13}H_{22}NO_3S^+$ $[M]^+$ calculated:272.13094.

1-(2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)ethyl)-4-phenylpyridin-1-ium bromide (22c)

Brown oil (99%) from **19c**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.06 – 8.89 (m, 2H), 8.50 – 8.32 (m, 2H), 8.09 – 7.95 (m, 2H), 7.71 – 7.57 (m, 3H), 4.87 – 4.82 (m, 2H), 4.1 – 3.97 (m, 2H), 3.73 – 3.47 (m, 10H), 2.65 – 2.55 (m, 2H). ^{13}C NMR ($(CD_3)_2SO$, 126 MHz) δ 154.63, 145.25, 133.35, 131.99, 129.55, 128.02, 124.02, 72.13, 69.89, 69.53, 69.41, 68.65, 59.97, 59.32, 29.46, 23.35. HRMS (HESI$^+$) *m/z*, found: 348.16208; $C_{19}H_{26}NO_3S^+$ $[M]^+$ calculated: 348.16224.

_N_-benzyl-2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)-_N,N_-dimethylethan-1-aminium bromide (22d)

Brown oil (93%) from **19d**. ^{1}H NMR (CD_3OD, 500 MHz) δ 7.64 – 7.53 (m, 5H), 4.65 (s, 2H), 4.05 – 4.00 (m, 2H), 3.74 – 3.53 (m, 12H), 3.12 (s, 6H) 2.60 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 134.41, 131.90, 130.29, 129.00, 73.98, 71.46, 71.37, 71.16, 70.32, 65.78, 64.67, 51.39, 24.64. HRMS (HESI$^+$) *m/z*, found: 328.19415; $C_{17}H_{30}NO_3S^+$ $[M]^+$ calculated: 328.19409.

2-(2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)ethyl)isoquinolin-2-ium bromide (22e)

Light brown oil (99%) from **19e**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.93 (s, 1H), 8.71 (d, *J* = 6.8 Hz , 1H), 8.54 – 8.49 (m, 2H), 8.34 – 8.31 (m, 1H), 8.29 – 8.24 (m, 1H), 8.11 – 8.06 (m, 1H), 5.98 – 4.95 (m, 2H), 4.10 – 4.07 (m, 2H), 3.68 – 3.64 (m, 2H), 3.58 – 3.42 (m, 8H), 2.80 – 2.57 (m, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 151.25, 137.51, 137.09, 135.77, 131.56, 131.20, 127.85, 127.06, 125.61, 72.82, 70.59, 70.46, 70.34, 70.19, 69.95, 61.19, 24.38. HRMS (HESI$^+$) *m/z*, found: 322.14658; $C_{17}H_{24}NO_3S^+$ $[M]^+$ calculated: 322.14659.

1-(2-(2-(2-(2-mercaptoethoxy)ethoxy)ethoxy)ethyl)quinolin-1-ium bromide (22f)

Brown oil (99%) from **19f**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.46 – 9.40 (m, 1H), 9.30 – 9.25 (m, 1H), 8.62 (d, *J* = 9.0 Hz), 8.49 – 8.44 (m, 1H), 8.33 – 8.26 (m, 1H), 8.16 – 8.10 (m, 1H), 8.08 – 8.01 (m, 1H), 5.36 – 5.31 (m, 2H), 4.13 – 4.08 (m, 2H), 3.65 – 3.35 (m, 10H), 2.59 (t, *J*

= 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 151.51, 149.16, 139.46, 137.08, 132.02, 131.51, 131.18, 122.66, 119.91, 73.82, 73.46, 71.56, 71.29, 69.11, 61.97, 58.74, 24.62. HRMS (HESI$^+$) *m/z*, found: 322.14645; $C_{17}H_{24}NO_3S^+$ [M]$^+$ calculated: 322.14659.

14-mercapto-*N,N,N*-trimethyl-3,6,9,12-tetraoxatetradecan-1-aminium bromide (23a)

Light brown oil (99%) from **20a**. ^{1}H NMR (CD_3OD, 500 MHz) δ 3.98 – 3.93 (m, 2H), 3.70 – 3.54 (m, 16H), 3.22 (s, 9H), 2.79 (t, J = 6.6 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 73.65, 72.08, 71.61, 71.49, 71.43, 70.33, 70.26, 66.93, 65.95, 62.19, 54.82, 23.81. HRMS (HESI$^+$) *m/z*, found: 295.18143, z = 2; $C_{13}H_{30}NO_4S^+$ [M]$^{2+}$ calculated: 295.18063.

1-(14-mercapto-3,6,9,12-tetraoxatetradecyl)pyridin-1-ium bromide (23b)

Light brown oil (99%, isolated as disulfide) from **20b**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.06 – 9.04 (m, 4H), 8.66 – 8.59 (m, 2H), 8.18 – 8.10 (m, 4H), 4.85 – 4.81 (m, 4H), 4.04 – 3.99 (m, 4H), 3.74 – 3.51 (m, 28H), 2.64 (t, J = 6.3 Hz, 4H). ^{13}C NMR (CD_3OD, 126 MHz) δ 147.02, 146.67, 129.11, 73.65, 71.52, 71.47, 71.42, 71.37, 71.12, 70.14, 62.67, 62.17, 24.69. HRMS (HESI$^+$) *m/z*, found: 316.15802; $C_{15}H_{26}NO_4S^+$ [M]$^+$ calculated: 316.15716.

1-(14-mercapto-3,6,9,12-tetraoxatetradecyl)-4-phenylpyridin-1-ium bromide (23c)

Brown oil (99%) from **20c**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.09 – 8.91 (m, 2H), 8.50 – 8.33 (m, 2H), 8.12 – 7.94 (m, 2H), 7.72 – 7.56 (m, 3H), 4.87 – 4.80 (m, 2H), 4.1 – 3.95 (m, 2H), 3.80 – 3.44 (m, 14H), 2.63 – 2.54 (m, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 157.98, 147.07, 135.27, 133.45, 131.04, 129.39, 126.26, 73.98, 72.16, 71.73, 71.68, 71.64, 71.51, 71.15, 70.44, 62.17, 23.92. HRMS (HESI$^+$) *m/z*, found: 392.18939; $C_{21}H_{30}NO_4S^+$ [M]$^+$ calculated: 392.18885.

***N*-benzyl-14-mercapto-*N,N*-dimethyl-3,6,9,12-tetraoxatetradecan-1-aminium bromide (23d)**

Brown oil (99%) from **20d**. ^{1}H NMR (CD_3OD, 500 MHz) δ 7.65 – 7.51 (m, 5H), 4.66 (s, 2H), 4.05 – 4.00 (m, 2H), 3.71 – 3.50 (m, 16H), 3.13 (s, 6H), 2.63 (t, *J* = 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 134.46, 131.88, 130.30, 129.03, 73.62, 71.60, 71,49, 71.39, 71.33, 70.30, 65.82, 64.82, 62.15, 51.44, 23.81. HRMS (HESI$^+$) *m/z*, found: 372.22028; $C_{19}H_{34}NO_4S^+$ [M]$^+$ calculated: 372.21976.

2-(14-mercapto-3,6,9,12-tetraoxatetradecyl)isoquinolin-2-ium bromide (23e)

Light brown oil (99%) from **20e**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.94 (s, 1H), 8.71 (d, *J* = 6.8 Hz, 1H), 8.55 – 8.49 (m, 2H), 8.35 – 8.31 (m, 1H), 8.29 – 8.22 (m, 1H), 8.10 – 8.05 (m, 1H), 4.99 – 4.95 (m, 2H), 4.11 – 4.07 (m, 2H), 3.67 – 3.48 (m, 14H), 2.58 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 151.86, 139.14, 138.41, 136.32, 132.55, 131.75, 128.97, 128.51, 127.17, 73.92, 73.60, 71.61, 71.45, 71.39, 71.08, 70.14, 62.52, 62.12, 24.65. HRMS (HESI$^+$) *m/z*, found: 366.17337; $C_{19}H_{28}NO_4S^+$ [M]$^+$ calculated: 366.17281.

1-(14-mercapto-3,6,9,12-tetraoxatetradecyl)quinolin-1-ium bromide (23f)

Brown oil (98%, isolated as disulfide) from **20f**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.44 – 9.39 (m, 2H), 9.27 – 9.22 (m, 2H), 8.64 (d, *J* = 8.9 Hz, 2H), 8.48 – 8.43 (m, 2H), 8.32 – 8.27 (m, 2H), 8.16 – 8.11 (m, 2H), 8.08 – 8.03 (m, 2H), 5.35 – 5.29 (m, 4H), 4.13 – 3.07 (m, 4H), 3.67

– 3.45 (m, 28H), 2.81 (t, J = 6.3 Hz, 4H). ^{13}C NMR (CD_3OD, 126 MHz) δ 151.77, 149.20, 139.51, 137.15, 132.11, 131.61, 131.27, 122.81, 119.94, 73.60, 71.72, 71.62, 71.46, 71.39, 71.28, 70.26, 69.14, 58.84, 39.46. HRMS ($HESI^+$) *m/z*, found: 365.16595, z = 2; $(C_{19}H_{31}NO_4S)_2^+$ $[M]^{2+}$ calculated: 365.16553.

17-mercapto-N,N,N-trimethyl-3,6,9,12,15-pentaoxaheptadecan-1-aminium bromide (24a)

Light brown oil (86%) from **21a**. ^1H NMR (CD_3OD, 500 MHz) δ 3.95 (s, 2H), 3.77 – 3.54 (m, 20H), 3.22 (s, 9H), 2.94 – 2.632 (m, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 73.97, 73.64, 71.25, 71.33, 71.40, 71.46, 71.53, 71.56, 70.36, 66.93, 65.95, 62.19, 54.82, 24.67. HRMS ($HESI^+$) *m/z*, found: 340.21457; $C_{15}H_{34}NO_5S^+$ $[M]^+$ calculated: 340.21467.

1-(17-mercapto-3,6,9,12,15-pentaoxaheptadecyl)pyridin-1-ium bromide (24b)

Light brown oil (99%) from **21b**. ^1H NMR (CD_3OD, 500 MHz) δ 9.05 – 8.99 (m, 2H), 8.65 – 8.59 (m, 1H), 8.17 – 8.09 (m, 2H), 4.85 – 3.82 (m, 2H), 4.04 – 3.98 (m, 2H), 3.75 – 3.50 (m, 18H), 2.63 (t, J = 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 146.85, 146.70, 129.12, 73.92, 73.58, 71.53, 71.47, 71.40, 71.36, 71.33, 71.06, 71.06, 70.14, 62.71, 24.64. HRMS ($HESI^+$) *m/z*, found: 360.18323; $C_{17}H_{30}NO_5S^+$ $[M]^+$ calculated: 360.18337.

1-(17-mercapto-3,6,9,12,15-pentaoxaheptadecyl)-4-phenylpyridin-1-ium bromide (24c)

Brown oil (99%) from **21c**. ^1H NMR (CD_3OD, 500 MHz) δ 9.04 – 8.95 (m, 2H), 8.47 – 8.38 (m, 2H), 8.08 – 7.94 (m, 2H), 7.69 – 7.61 (m, 3H), 4.84 – 4.79 (m, 2H), 4.06 – 3.99 (m, 2H), 3.69 – 3.47 (m, 18H), 2.59 (t, *J* = 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 157.96, 146.60, 135.30, 133.38, 130.94, 129.22, 129.20, 129.17, 125.74, 125.70, 73.92, 73.57, 71.55, 71.51, 71.44, 71.41, 71.35, 71.06, 70.22, 61.82, 24.64. HRMS ($HESI^+$) *m/z*, found: 436.21448; $C_{23}H_{34}O_5S^+$ $[M]^+$ calculated: 436.21467.

***N*-benzyl-17-mercapto-*N,N*-dimethyl-3,6,9,12,15-pentaoxaheptadecan-1-aminium bromide** (**24d**)

Light brown oil (99%) from **21d**. ^{1}H NMR (CD_3OD, 500 MHz) δ 7.64 – 7.51 (m, 5H), 4.65 (s, 2H), 4.05 – 4.00 (m, 2H), 3.75 – 3.51 (m, 18H), 3.13 (s, 6H), 2.64 (t, *J* = 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 134.43, 131.87, 130.29, 129.05, 73.98, 73.63, 71.57, 71.47, 71.36, 71.34, 71.10, 70.32, 65.80, 62.17, 51.45, 24.68. HRMS ($HESI^+$) *m/z*, found: 416.24619; $C_{21}H_{38}NO_5S^+$ $[M]^+$ calculated: 416.24597.

2-(17-mercapto-3,6,9,12,15-pentaoxaheptadecyl)isoquinolin-2-ium bromide (**24e**)

Light brown oil (99%) from **21e**. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.95 (s, 1H), 8.73 – 8.69 (m, 1H), 8.55 – 8.49 (m, 2H), 8.36 – 8.31 (m, 1H), 8.29 – 8.24 (m, 1H), 8.11 – 8.06 (m, 1H), 5.00 – 4.95 (m, 2H) 4.11 – 4.08 (m, 2H), 3.67 – 3.46 (m, 18H), 2.57 (t, *J* = 6.3 Hz, 2H). ^{13}C NMR (CD_3OD, 126 MHz) δ 151.91, 139.13, 138.40 136.36, 132.54, 131.77, 128.96, 128.52, 127.14, 73.95, 73.60, 71.55, 71.48, 71.43, 71.36, 71.32, 71.08, 70.16, 62.56, 62.13, 24.65. HRMS ($HESI^+$) *m/z*, found: 410.19894; $C_{21}H_{32}NO_5S^+$ $[M]^+$ calculated: 410.19902.

1-(17-mercapto-3,6,9,12,15-pentaoxaheptadecyl)quinolin-1-ium bromide (24f)

Brown oil (99%, isolated as disulfide) from **21f**. The compound could not be characterized by ^{13}C NMR, as we failed to measure NMR spectra in any solvents. The compound was characterized by ^{1}H NMR and HRMS. Additionally, the compound was used in further analysis and fully corresponded to expectation according to the behavior of derivatives. ^{1}H NMR (CD_3OD, 500 MHz) δ 9.14 (bm, 2H), 8.85 – 7.65 (bm, 5H), 5.11 (s, 2H), 4.45 – 2.04 (m, 22H). HRMS ($HESI^+$) *m/z*, found: 409.19131, z = 2; $C_{21}H_{31}NO_5S^+$ $[M]^{2+}$ calculated: 409.19120.

Thiol-disulfide exchange evaluation

The compounds with thiol moiety tend to form the corresponding disulfide.[2,3] The conversion of thiol moiety to the expected disulfide group was confirmed by NMR spectroscopy on the compound with the aliphatic substitution of quaternary nitrogen **(24a)**. The compound **24a** was dissolved in ultrapure water (1.2 mM) and then left undisturbed at r.t. The oxidation of the thiol group was confirmed by peak shifting of the corresponding triplet of α-protons. The shifts (α-thiol → α-disulfide protons) were 2.63 → 2.87 ppm in ^{1}H NMR and 24 → 40 ppm in ^{13}C NMR spectra (**Supplementary Figure S10**). The NMR spectra confirmed that the OEG compounds contain negligible amount disulfide form after preparation and purification, which is showed in ^{1}H NMR (small peak of α-disulfide carbons were possible to found as a part of baseline in ^{13}C NMR). The increasing content of disulfide form were detected one day after compound dissolving in the water without any other structure alteration.

Additionally, the replacement of CTAB bilayer by self-assembled monolayers tethered *via* the Au-S bond can be accomplished by different organosulfur anchors including the thiol group, acyclic disulfide, cyclic disulfide, and other types of thiolated groups. The eventual disulfide formation do not affect the ligand exchange and preparation of $^{OEG+}$GNRs.[4,5]

2. Supplementary Methods

Cell viability assessment of ligands in free state

The CHO-K1 cells were seeded at a density of 8 000 cells per well and the MTT assay was performed according to the manufacturer´s protocol as was described earlier.[6] Briefly, the tested compounds were dissolved in DMSO and subsequently in the growth medium (F-12) supplemented with 10% FBS and 1% penicillin/streptomycin (the final concentration of DMSO did not exceed 0.5 % (v/v)). Cells were exposed to the serially diluted compounds for 24 hours. The medium was then replaced by a medium containing 0.5 mg/mL of MTT and the cells were allowed to produce formazan for other 3 hours under surveillance. Thereafter, the medium with MTT was removed and crystals of formazan were dissolved in DMSO (100 μL/well). The absorbance of produced formazan was measured at 570 nm with 650 nm reference wavelength on Synergy HT (BioTek, Winooski, VT, USA). IC_{50} was then calculated from the control-subtracted triplicates using non-linear regression (four parameters) of GraphPad Prism 5.03 and 7.03 software (GraphPad Software Inc., San Diego, CA, USA). Final IC_{50} and SEM values were obtained as a mean of three independent measurements.

Preparation of cetyltrimethylammonium bromide (CTAB)-stabilized gold nanorods

The synthesis of CTAB-stabilized GNRs involved the fast reduction of gold (III) salt by sodium borohydride ($NaBH_4$) in the presence of CTAB to prepare a solution of monocrystalline gold seeds (2 – 4 nm) and their subsequent addition into the growth solution of gold (I) complexed to CTAB in the presence of silver(I) in aqueous solution. The specific synthesis parameters were as follows: the seed solution (5 mL) consisted of 0.1 M CTAB and 0.25 mM $HAuCl_4$ and 0.6 mM $NaBH_4$. For the GNRs, λ_{max} ~ 633 nm, the growth solution (800 mL) consisted of 0.1 M CTAB; 0.5 mM $HAuCl_4$; 0.75 mM ascorbic acid and 0.05 mM $AgNO_3$ in water. Exactly 960 μL of the seed solution was added to the growth solution at 25 °C. For the GNRs, λ_{max} ~ 750 nm, the growth solution (80 mL) consisted of 0.1 M CTAB; 0.5 mM $HAuCl_4$; 0.70 mM ascorbic acid and 0.125 mM $AgNO_3$. Seed solution (96 μL) was added to the growth solution at 25 °C.

The length and width of more than 300 GNRs drop-casted onto a silicon wafer were characterized by field emission scanning-electron microscopy (JSM-7500f JEOL FE-SEM; JEOL, Tokyo, Japan) and analyzed by the ParticleRecognition software package.[7]

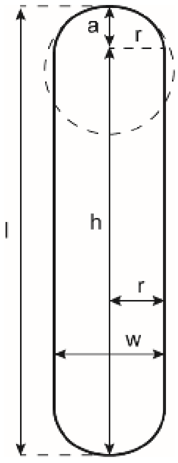
Inductively coupled plasma - optical emission spectrometry (ICP-OES) analysis

For ICP-OES measurement, the samples of GNR dispersions (1000 μL) were quantitatively transferred from 2 mL Eppendorf vial into a 15 mL PE vial and precisely weighted. The walls of the original 2 mL vial were washed with 220 μL aqua regia (prepared *in situ*) and the obtained solution was transferred to the 15 mL vial and mixed with the rest of the sample to ensure the particles dissolution. After the mixing, 10 μL of internal standard Y (1000 mg/L) was added and the weight was adjusted with deionized water to the final weight 5 g. For measurement, the inductively coupled plasma optical emission spectrometer Spectro Arcos MV (Spectro Analytical Instruments, Kleve, Germany) with axial plasma view was used. This spectrometer is equipped with a sealed fixed optic in Paschen-Runge mount, which allows simultaneous measurement of 1. order spectra in wavelength range 130 – 770 nm. Following measurement conditions were used: plasma power 1300 W, coolant gas flow 13 L/min, auxiliary gas flow 0.80 L/min, nebulizer gas flow 0.88 L/min. Sample introduction system: SeaSpray concentric nebulizer and cyclonic spray chamber. For external calibration solutions in concentration range 0 – 20 mg/L Au, 0 – 2 mg/L Ag and 0 – 0.2 mg/L S were used. The LODs vary from hundreds ng/L (S, Ag) to units µg/L (Au). All calibration solutions contained 2 mg/L Y as internal standard and 4 % aqua regia for matrix matching. All calibration solutions were prepared from Ag, Au, S and Y standard stock solutions (1000 mg/L) from Analytika, Praque, Czech Republic.

Cell viability assay of GNRs-loaded cells

The cytotoxicity of the GNRs in HeLa cells was estimated using CellTiter 96 Non-Radioactive Cell Proliferation Assay (Promega, Madison, WI, USA) according to the manufacturer's protocol. In brief, the cells were seeded into 96-well plate at the density 20,000 cells/well in the presence of GNRs (30 – 100 µM Au^0) and incubated for 24 hours. GNRs-free and ^{CTAB}GNRs-treated cells were used as negative and positive controls, respectively. Then 15 µL of MTT Dye solution was added and the cells were incubated for additional 4 hours. Next, 100 µL of solubilization/stop solution was added and incubated for 1 hour. Formazan products were measured at 595 nm by Multiscan EX microplate spectrophotometer (Thermo Fisher Scientific, Vantaa, Finland). The cell viability was expressed as a percentage of control cell absorbance. The data were calculated from three experiments.

Calculation of the surface and volume of GNRs from FE-SEM images



The surface area and the volume of the gold nanorods were calculated assuming that the nanorod is consisted of the cylindrical middle with radius (r) and height (h) and two spherical caps with radius (r) and height (a):

$$S_{GNRs} = 2\pi(r^2 + a^2) + 2\pi r h$$

$$V_{GNRs} = \frac{\pi\, a\,(3r^2 + a^2)}{3} + \pi\, r^2\, h$$

where the average length and width of GNRs calculated from more than 300 GNRs were 56.3 nm and 28.2 nm, respectively and the spherical caps were estimated about 3 nm on each side; the used dimensions were thus h = 50.3 nm, r = 14.1 nm, a = 3.0 nm. Thus, the calculated surface area of the rod was 4982.5 nm^2 and the volume was 33 236.5 nm^3.

3. Supplemental Tables and Figures

Table S1. Characterization of prepared compounds with OEG-chains (**22-24a-f**) and alkyl-chain compounds (MTAB**,** CTAB)

	Cpd	Chain length	Yield[a] [%]	k[b] ± SEM	log*k*	Clog*P*[c]	IC_{50}[d] ± SEM [mM]	logIC_{50}	N_{ESP}
Oligoethylene-chain	**22a**	$C_8H_{17}O_3S$	35	0.39 ± 0.04	-0.41	0.69	2.70 ± 0.36	-2.57	0.617
	23a	$C_{10}H_{21}O_4S$	48	0.59 ± 0.03	-0.23	0.71	> 10.00	-2.00	0.616
	24a	$C_{12}H_{25}O_5S$	46	0.83 ± 0.06	-0.08	0.73	> 10.00	-2.00	0.617
	22b	$C_8H_{17}O_3S$	40	0.49 ± 0.02	-0.31	1.39	2.44 ± 0.21	-2.61	0.401
	23b	$C_{10}H_{21}O_4S$	48	0.70 ± 0.02	-0.16	1.41	1.20 ± 0.03	-2.92	0.449
	24b	$C_{12}H_{25}O_5S$	53	0.96 ± 0.01	-0.02	1.42	1.12 ± 0.00	-2.95	0.433
	22c	$C_8H_{17}O_3S$	40	7.76 ± 0.08	0.89	2.78	2.25 ± 0.32	-2.65	0.307
	23c	$C_{10}H_{21}O_4S$	45	9.97 ± 0.21	1.00	2.80	2.88 ± 0.22	-2.54	0.393
	24c	$C_{12}H_{25}O_5S$	42	11.48 ± 0.18	1.06	2.82	1.19 ± 0.02	-2.92	0.387
	22d	$C_8H_{17}O_3S$	38	4.15 ± 0.08	0.62	2.26	3.88 ± 0.55	-2.41	0.652
	23d	$C_{10}H_{21}O_4S$	48	5.32 ± 0.07	0.73	2.28	1.08 ± 0.15	-2.97	0.655
	24d	$C_{12}H_{25}O_5S$	52	6.34 ± 0.12	0.80	2.30	1.00 ± 0.11	-3.00	0.738
	22e	$C_8H_{17}O_3S$	40	2.20 ± 0.09	0.34	2.42	1.61 ± 0.06	-2.79	0.378
	23e	$C_{10}H_{21}O_4S$	44	2.87 ± 0.07	0.46	2.43	1.34 ± 0.19	-2.87	0.353
	24e	$C_{12}H_{25}O_5S$	47	3.65 ± 0.08	0.56	2.45	0.97 ± 0.8	-3.01	0.359
	22f	$C_8H_{17}O_3S$	15	1.82 ± 0.06	0.26	2.56	2.26 ± 0.02	-2.65	0.160
	23f	$C_{10}H_{21}O_4S$	28	2.45 ± 0.04	0.39	2.58	3.11 ± 0.38	-2.51	0.172
	24f	$C_{12}H_{25}O_5S$	18	5.28 ± 0.09	0.72	2.59	1.75 ± 0.40	-2.76	0.164
Alkyl-chain	**MTAB**	$C_{16}H_{33}S$	-	0.35 ± 0.11[e]	-0.46[e]	6.10	0.03 ± 0.00	-4.52	0.637
	CTAB	$C_{16}H_{33}$	-	0.74 ± 0.10[e]	-0.13[e]	6.19	0.01 ± 0.00	-4.85	-

[a] Overall yields of final product.

[b] Capacity factors k were determined by an isocratic LC-MS method.

[c] Clog*P* was calculated in Open Babel, version 2.3.1, http://openbabel.org (accessed Oct 2011).

[d] IC_{50} was assessed by MMT assay on CHO-K1 cells.

[e] The compounds with alky chain (MTAB, CTAB) were measured under different conditions; mobile phase acetonitrile:water 70:30 (v/v) and stationary Waters Atlantis dC18 (2.1 × 100 mm/3 µm) column.

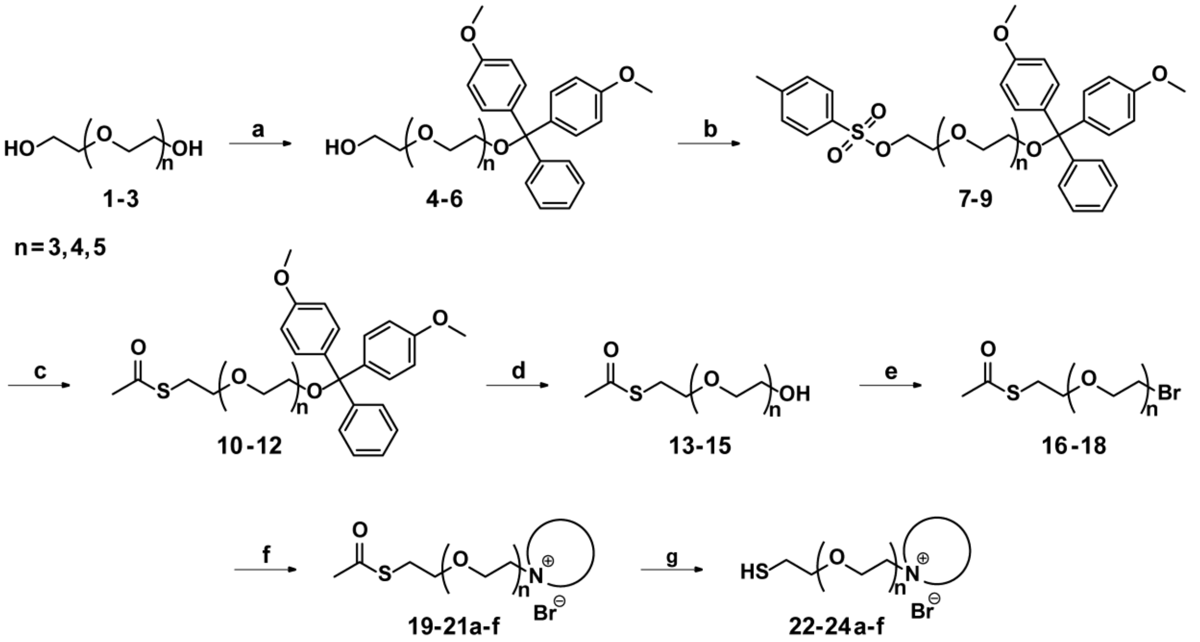


Figure S1. Synthetic pathway of compounds **22-24a-f**, n = 3, 4, 5. Reagents and conditions: a) DMTrCl, DMAP, TEA, DCM, 0 °C – r.t., 1.3 h, 73 − 84%; b) *p*-TsCl, TEA, DMAP, DCM, 0 °C – r.t, 2.6 h, 92 − 97%; c) KSAc, MEK, reflux, 0.5 h, 88 − 96%; d) TCA, DCE, r.t., 5 min, 77 − 93%; e) CBr_4, PPh_3, DCM, 0 °C – r.t., 1 h, 80 − 81%; f) corresponding amine, ACN, r.t. (**19-21a**) or reflux (**19-21b-f**), 48 h, 34 – 99% ; g) AcCl, MeOH, DCM, 0 °C – r.t, 48 h, 86 – 99%.

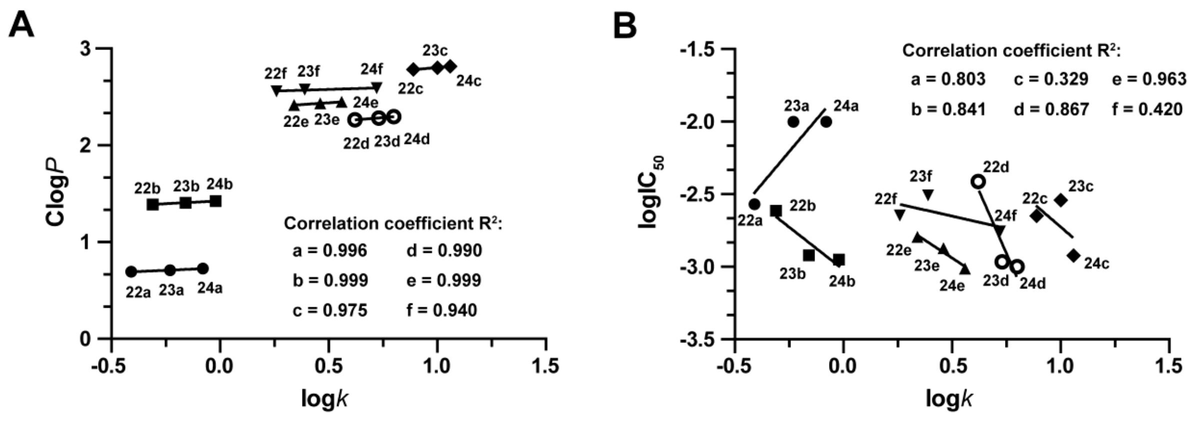
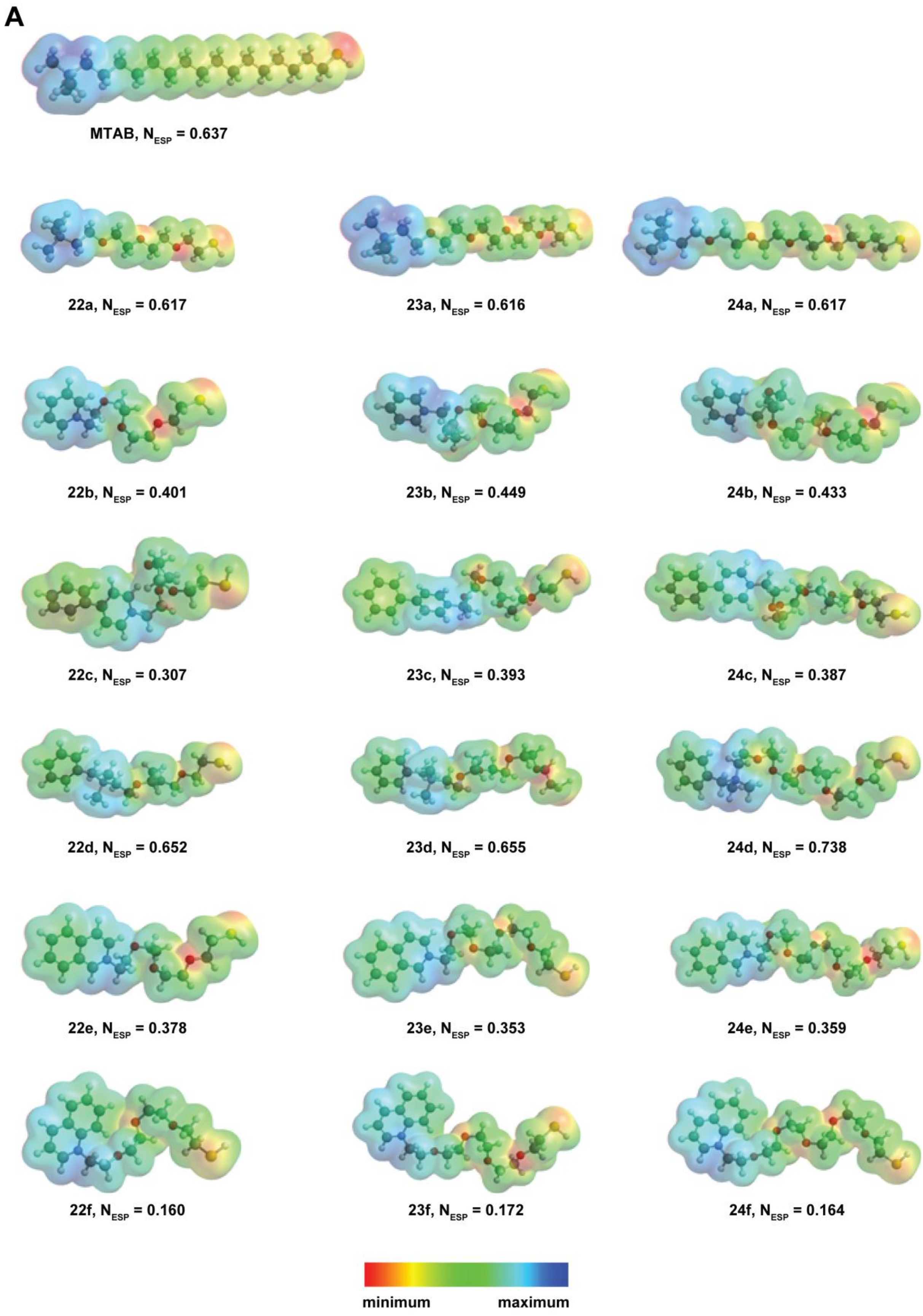


Figure S2. (**A**) Hydrophobicity of OEG compounds expressed as correlation of experimentally measured log*k* and calculated Clog*P*. The results showed slightly increasing hydrophobicity with chain length with high correlation coefficient (R^2), but the overall hydrophobicity of OEG compounds was clearly driven by hydrophobicity of quaternary ammonium head. The compounds with alky chain

(MTAB, CTAB) were measured at different set up and thus the comparison of hydrophobicity of compounds with OEG and alkyl chain was carried out using the calculated ClogP. (**B**) Correlation between experimentally evaluated hydrophobicity (log*k*) and cytotoxic potential ($logIC_{50}$) of cationic OEG compounds (22-24a-f). The OEG compounds exhibited minor increase of cytotoxic effect with their increasing hydrophobicity caused by elongation of side chain (22 → 24), except the compounds with trimethylammonium group (a), which showed the opposite trend.


A
MTAB, N_{ESP} = 0.637
22a, N_{ESP} = 0.617
23a, N_{ESP} = 0.616
24a, N_{ESP} = 0.617
22b, N_{ESP} = 0.401
23b, N_{ESP} = 0.449
24b, N_{ESP} = 0.433
22c, N_{ESP} = 0.307
23c, N_{ESP} = 0.393
24c, N_{ESP} = 0.387
22d, N_{ESP} = 0.652
23d, N_{ESP} = 0.655
24d, N_{ESP} = 0.738
22e, N_{ESP} = 0.378
23e, N_{ESP} = 0.353
24e, N_{ESP} = 0.359
22f, N_{ESP} = 0.160
23f, N_{ESP} = 0.172
24f, N_{ESP} = 0.164
minimum
maximum

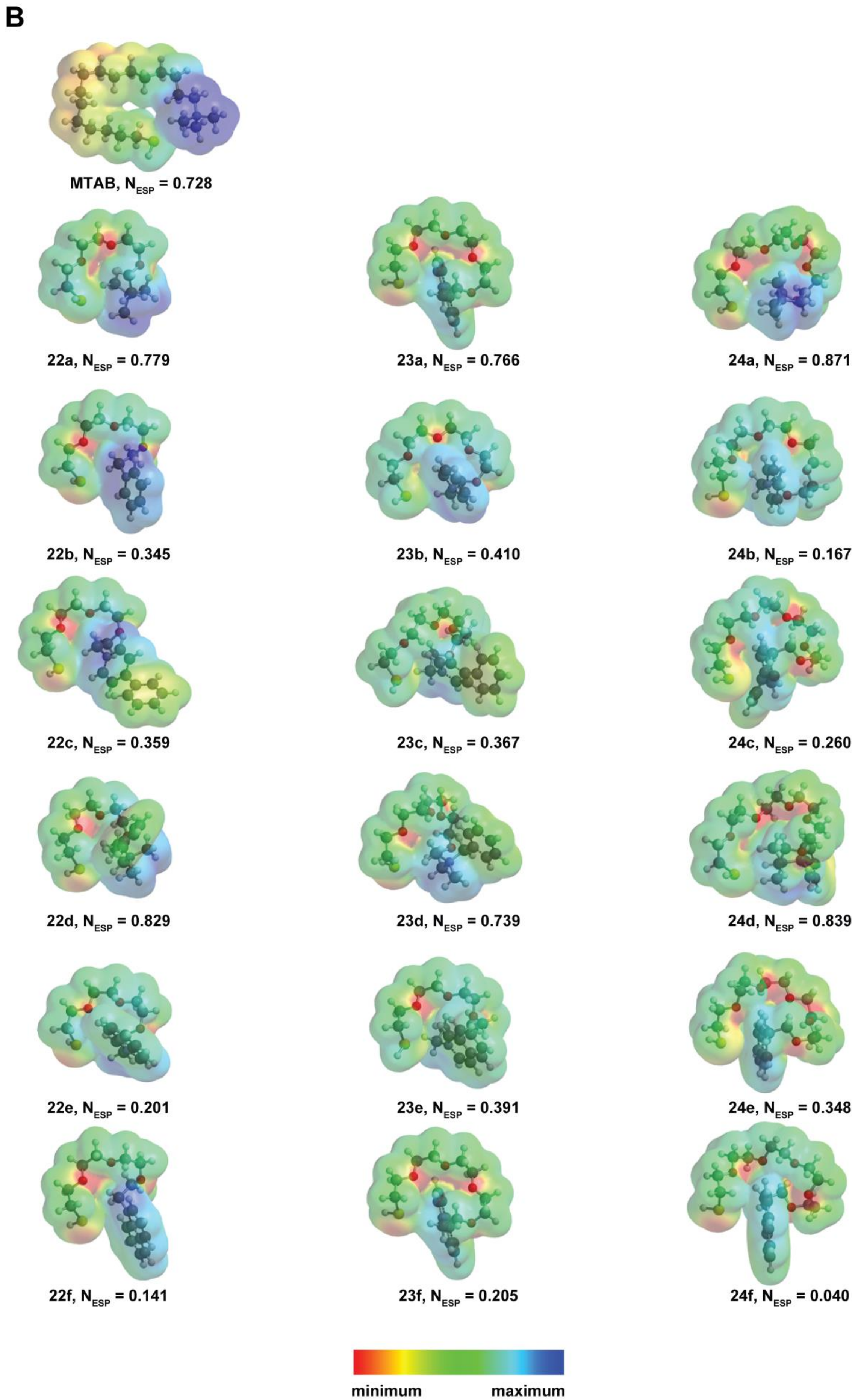

B
MTAB, N_{ESP} = 0.728
22a, N_{ESP} = 0.779
23a, N_{ESP} = 0.766
24a, N_{ESP} = 0.871
22b, N_{ESP} = 0.345
23b, N_{ESP} = 0.410
24b, N_{ESP} = 0.167
22c, N_{ESP} = 0.359
23c, N_{ESP} = 0.367
24c, N_{ESP} = 0.260
22d, N_{ESP} = 0.829
23d, N_{ESP} = 0.739
24d, N_{ESP} = 0.839
22e, N_{ESP} = 0.201
23e, N_{ESP} = 0.391
24e, N_{ESP} = 0.348
22f, N_{ESP} = 0.141
23f, N_{ESP} = 0.205
24f, N_{ESP} = 0.040
minimum
maximum

Figure S3. Electrostatic potential maps and ESP atomic partial charges on the quaternary nitrogen (N_{ESP}) of all final compounds. (**A**) Results calculated by semi-empirical method PM6 in Spartan 14 (method is in details described in manuscript). (**B**) Results calculated by molecular dynamic study in Spartan 14. These additional computational models of final products were obtained by conformational analyses on the semi-empirical RM1 theoretical level which involved investigation of up to 10 000 conformers generated by Monte Carlo based molecular dynamics, and represent therefore optimal conformers with respect to the thermodynamic distribution. The OEG compounds exhibited also higher variation of ESP along the side chain than the alkyl chain compound. Similarly, the highest positive charge showed the trimethylammonium (a) and benzalkonium (d) salts, most likely due to the electron density distribution on the nitrogen atom with tetrahedron symmetry extended towards the four attached carbon atoms. Moreover, all modeled compounds formed corona-like conformers in which the electron density on the distal sulfur atom interacted with the quaternary nitrogen atoms. The interaction may also affect the charge distribution along the molecule, especially can influence the positive charge on quaternary nitrogen through electron effect of thiol group or electron re-distribution along whole corona-like structure. Finally, this analysis suggested that the interactions of the studied compounds can be separated into intermolecular and intramolecular types, which may have significant impact on their reactivity.

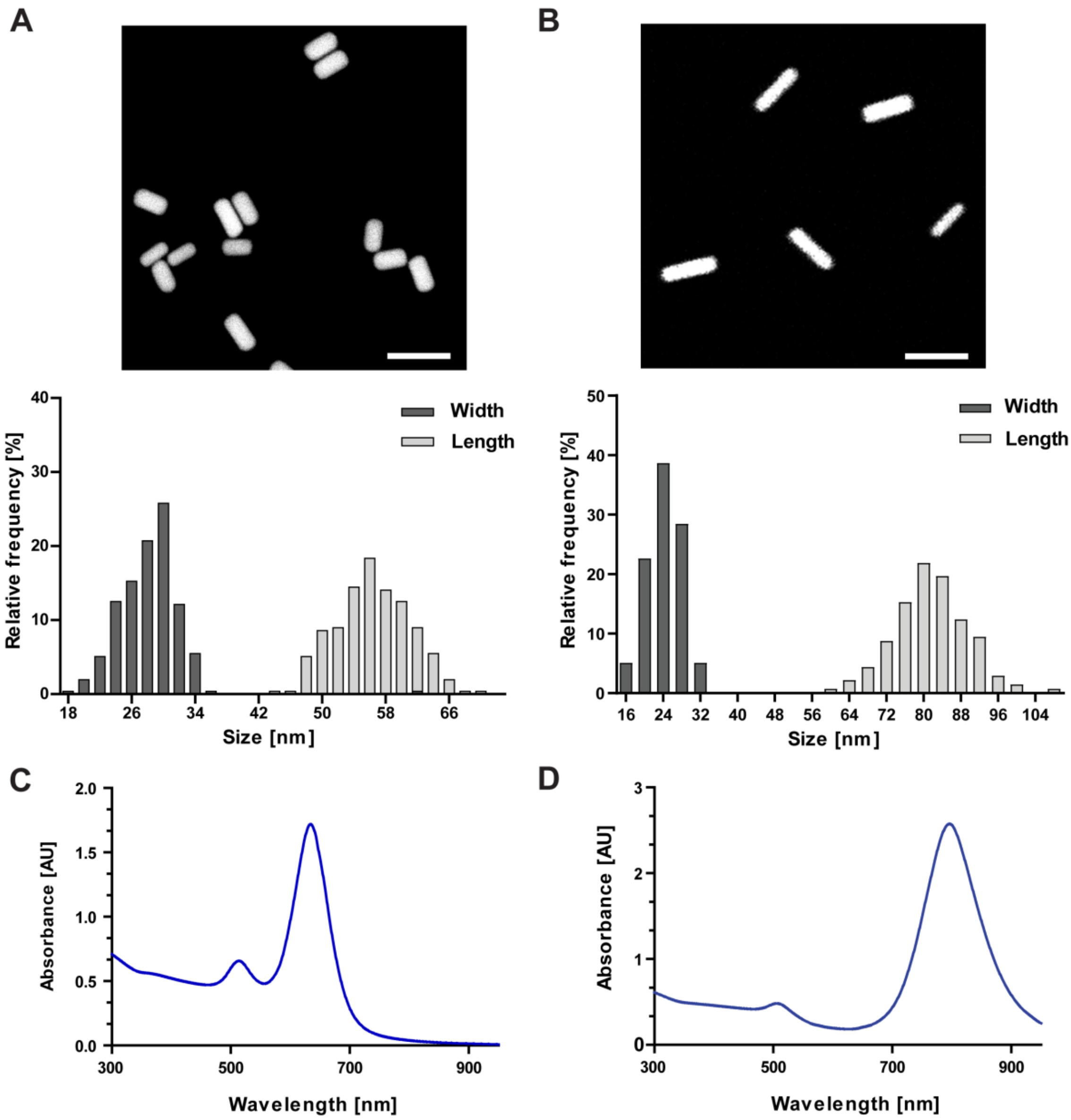


Figure S4. Representative images of FE-SEM characterization of synthesized CTAB-stabilized GNRs with longitudinal LSPR tuned to 633 nm (**A**) and to NIR region (**B**) and their size distribution histograms (scale bar, 100 nm). Representative UV-Vis-NIR spectra of CTAB-stabilized GNRs (**C**) tuned to 633 nm and (**D**) to NIR region in water.

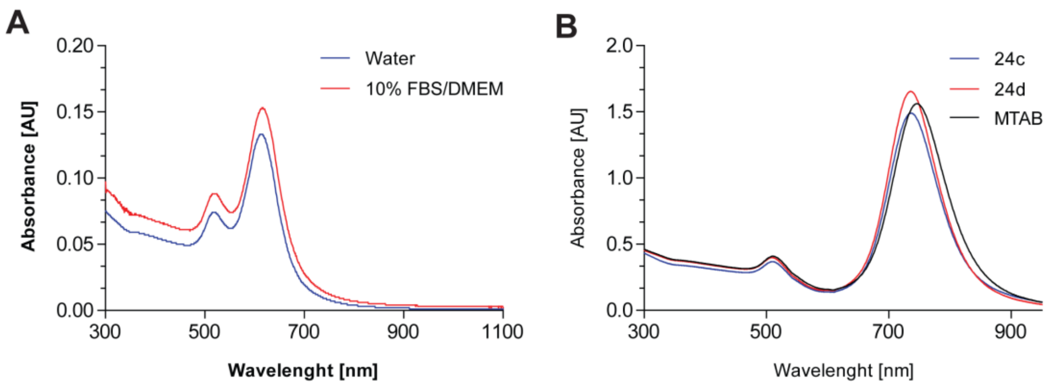


Figure S5. (**A**) UV-Vis-NIR spectra of MTAB-stabilized GNRs tuned to 633 nm in storage solution (water) normalized to 50 μM (Au^0) concentration and dispersed in 10% FBS/DMEM at 50 μM (Au^0) concentration. (**B**) UV-VIS-NIR spectra of GNRs tuned to NIR region modified by ligand 24c, 24d and MTAB after surface ligand exchange in water.

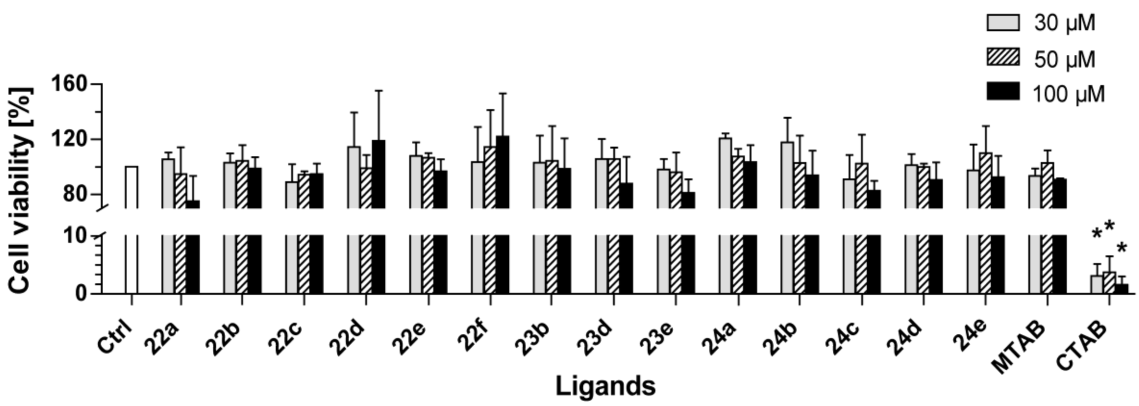
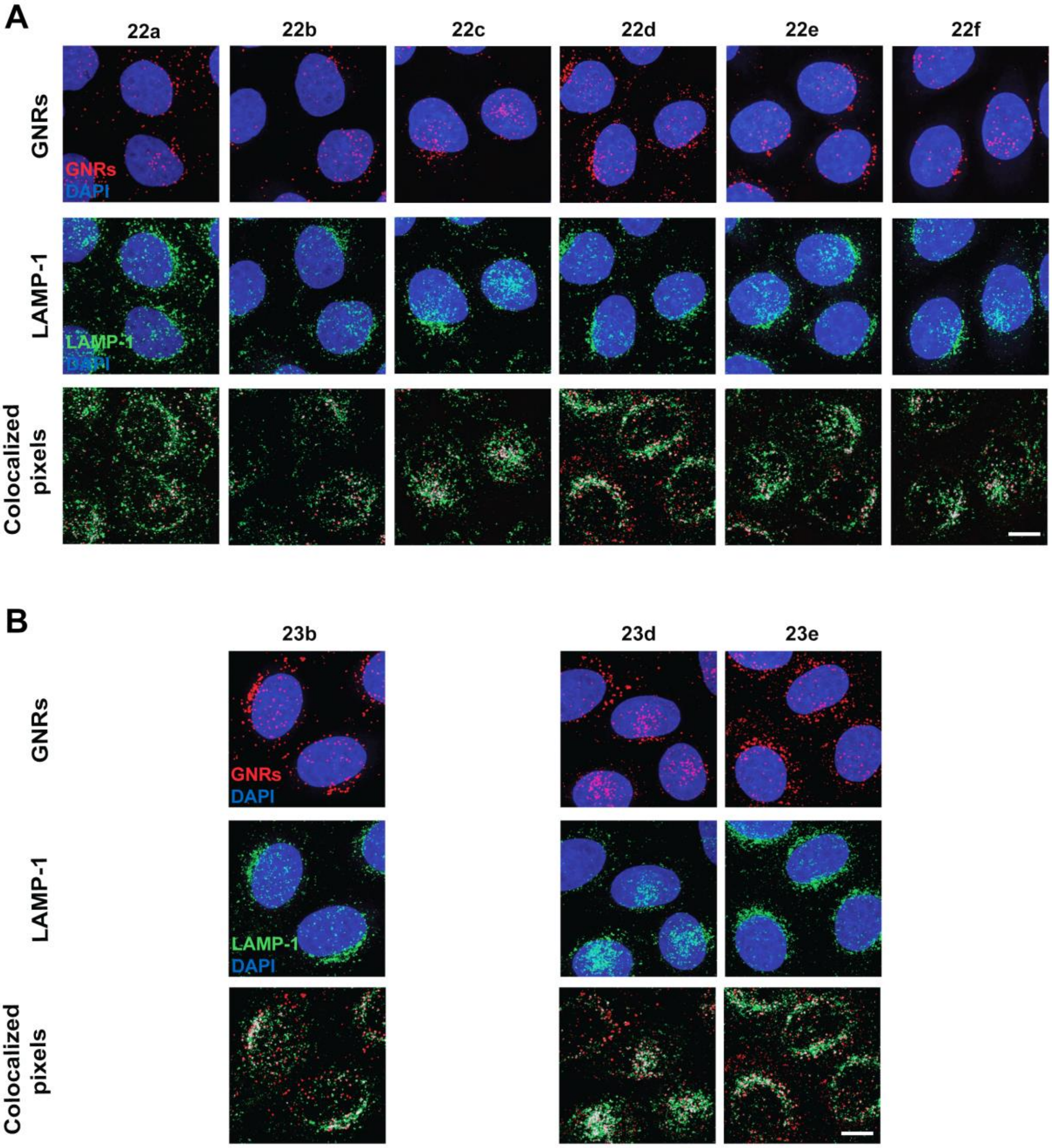


Figure S6. Evaluation of ^{Ligand}GNRs cytotoxicity based on MTT assay in HeLa cells incubated with 30, 50 and 100 μM (Au^0) GNRs for 24 hours expressed as a percentage of GNR-free control cells (Ctrl). Cytotoxic ^{CTAB}GNRs with residual non-covalently bonded CTAB molecules in solution were used as a positive control.[8]


A
22a
22b
22c
22d
22e
22f
GNRs
LAMP-1
Colocalized pixels
GNRs
DAPI
LAMP-1
DAPI
B
23b
23d
23e
GNRs
LAMP-1
Colocalized pixels
GNRs
DAPI
LAMP-1
DAPI

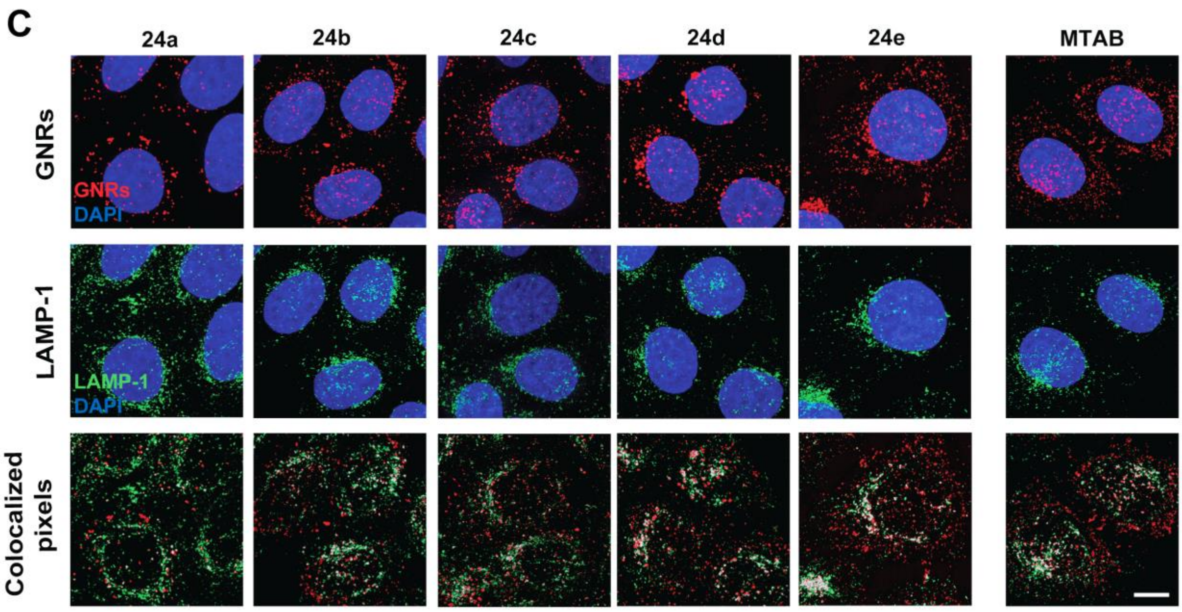


Figure S7. Colocalization of GNRs modified by (**A**) OEG_3, (**B**) OEG_4, and (**C**) OEG_5 ligand series and MTAB with lysosomes (LAMP-1) in HeLa cells after 24 h-incubation with 20 µM (Au^0) GNRs (Z-stack; bar 10 µm). Colocalized pixel maps were calculated using 'Co-localization Threshold' plug-in of Fiji (http://pacific.mpi-cbg.de/wiki/index.php/Colocalization_Threshold). Pixels with positive signals for both GNRs and lysosomes are shown in white. The nuclei were stained by DAPI.

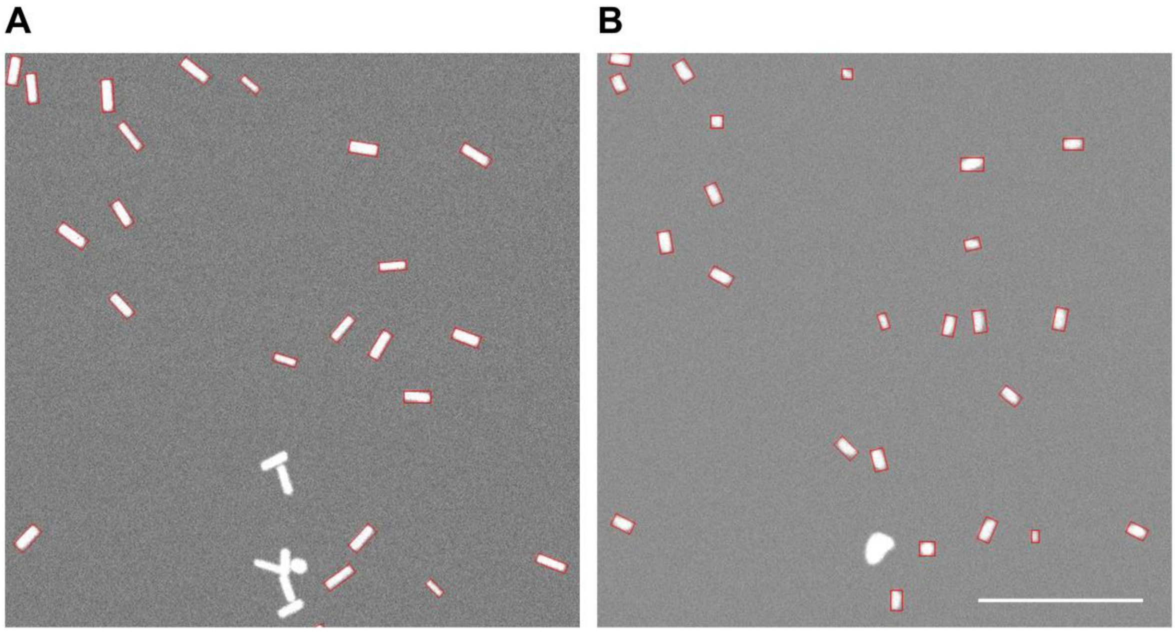
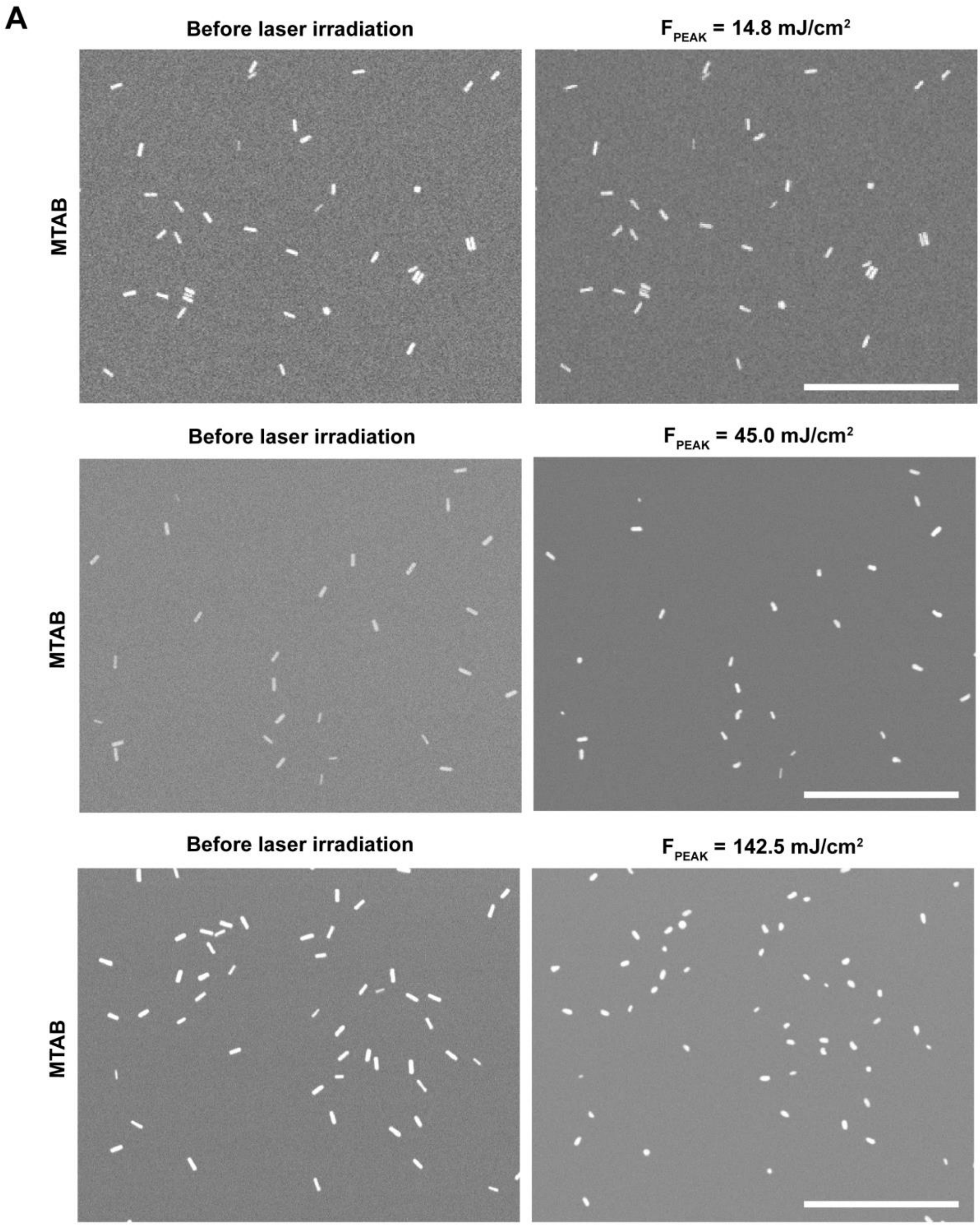
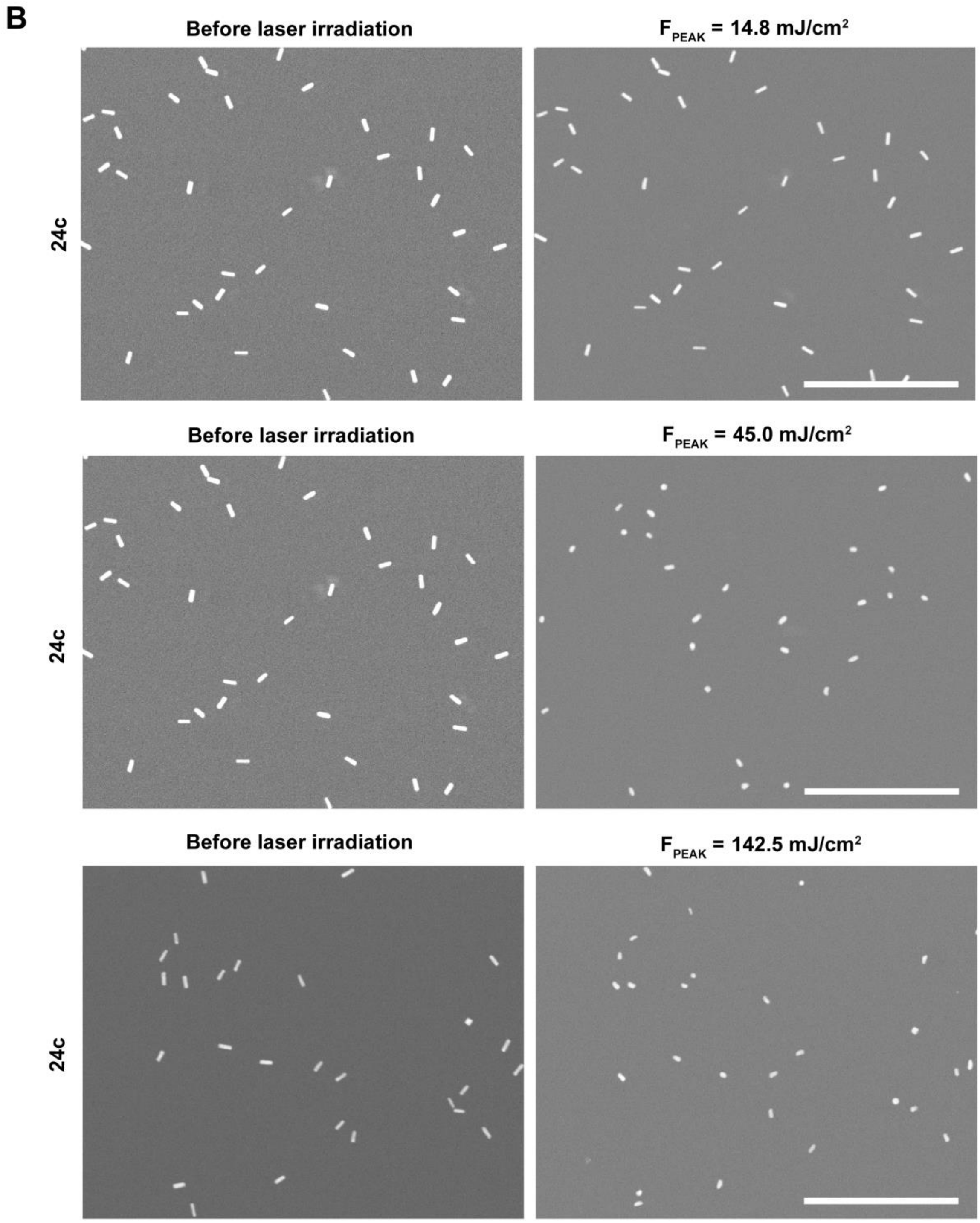


Figure S8. Illustration of FE-SEM image analysis by ParticleRecognition software package based on Wolfram Language before (**A**) and after (**B**) two-photon irradiation of MTAB-GNRs at 142.5 mJ/cm^2 laser peak fluence. The software package allowed identification and characterization of rod shaped particles without counting aggregated or other shapes (*i.e.* spherical) particles (bar, 500 nm).


A
Before laser irradiation
F_{PEAK} = 14.8 mJ/cm²
MTAB
Before laser irradiation
F_{PEAK} = 45.0 mJ/cm²
MTAB
Before laser irradiation
F_{PEAK} = 142.5 mJ/cm²
MTAB


B
Before laser irradiation
F_PEAK = 14.8 mJ/cm2
24c
Before laser irradiation
F_PEAK = 45.0 mJ/cm2
24c
Before laser irradiation
F_PEAK = 142.5 mJ/cm2
24c

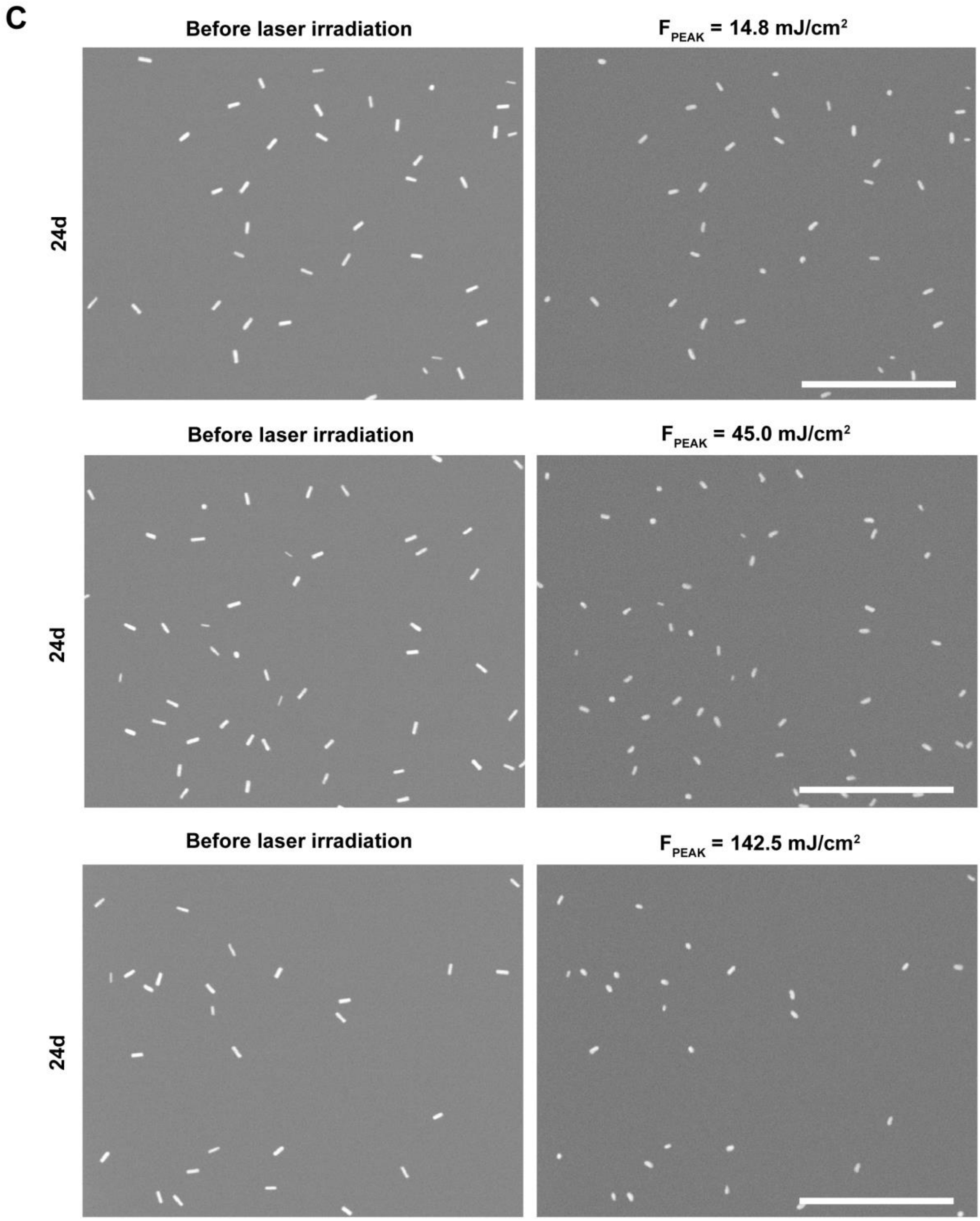


Figure S9. FE-SEM micrographs of the same location of (**A**) MTAB, (**B**) 24c- and (**C**) 24d-coated GNRs before and after two-photon irradiation at 14.8 mJ/cm^2, 45.0 mJ/cm^2 and 142.5 mJ/cm^2 laser peak fluence (F_{PEAK}; bar, 1 μm).

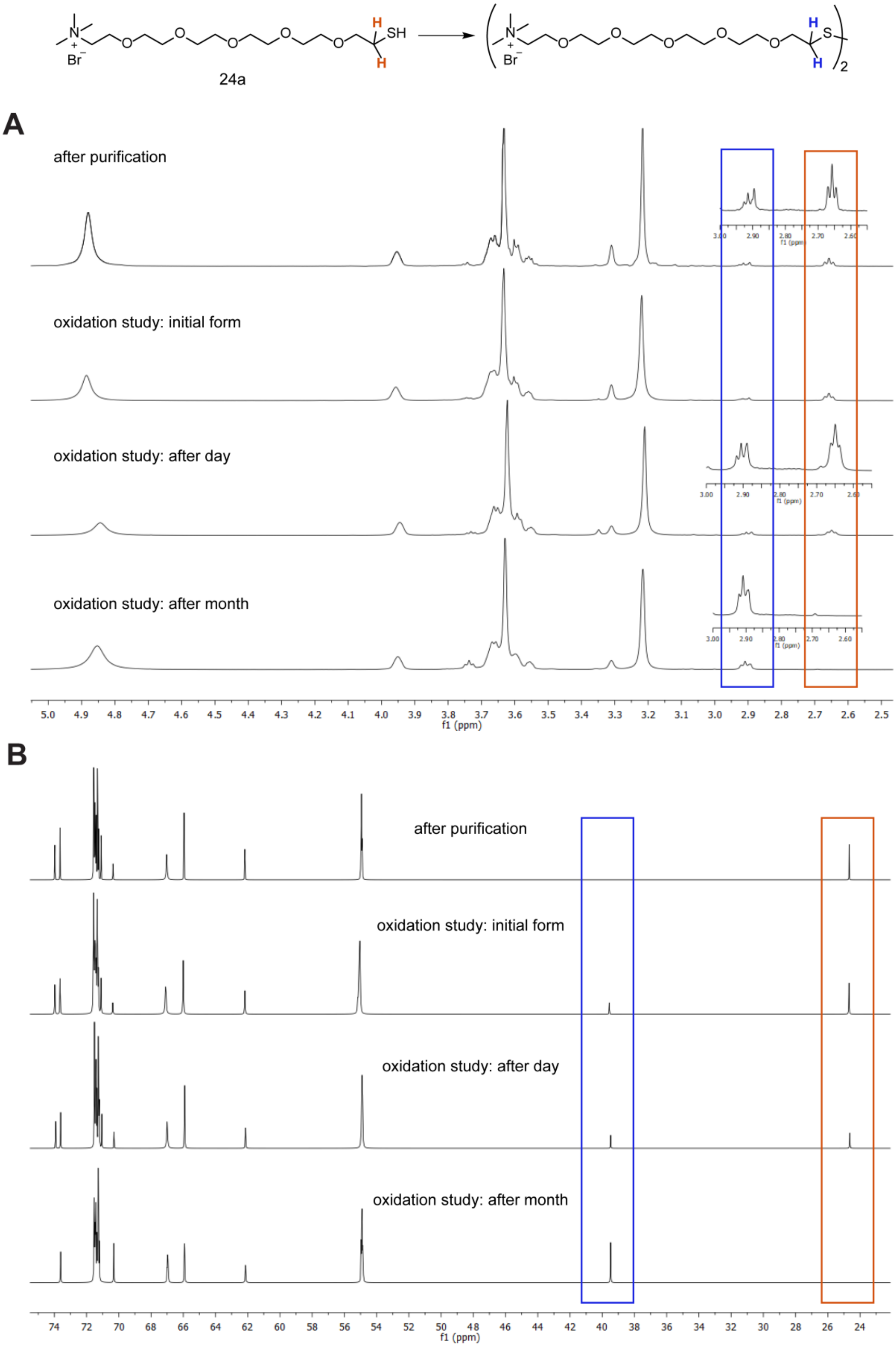

SH
Br⁻
24a
S
2
A
after purification
oxidation study: initial form
oxidation study: after day
oxidation study: after month
f1 (ppm)
B
after purification
oxidation study: initial form
oxidation study: after day
oxidation study: after month
f1 (ppm)

Figure S10. Illustration of the thiol-disulfide exchange of 24a compound confirmed by NMR spectra during one month. (**A**) ^{1}H NMR spectra with highlighted schifted peaks corresponded α-thiol (orange) → α-disulfide (blue) protons 2.63 → 2.87 ppm and (**B**) Shifts of carbons corresponded to α-thiol → α-disulfide 24 → 40 ppm in ^{13}C NMR spectra. The peak of CD_3OD were removed from ^{13}C NMR spectrum by deconvolution process.

References

1. Zarska M, Novotny F, Havel F, et al. A two-step mechanism of cellular uptake of cationic gold nanoparticles modified by (16-mercaptohexadecyl)trimethylammonium bromide (MTAB). *Bioconjugate chemistry*. 2016;27:2558-74.
2. Barrientos AG, de la Fuente JM, Rojas TC, Fernández A, Penadés S, Dai L. Gold glyconanoparticles: synthetic polyvalent ligands mimicking glycocalyx-like surfaces as tools for glycobiological studies. *Chemistry*. 2003;9:1909-21.
3. Nagy P. Kinetics and mechanisms of thiol-disulfide exchange covering direct substitution and thiol oxidation-mediated pathways. *Antioxid Redox Signal*. 2013;18:1623-41.
4. Li F, Zhang H, Dever B, Li XF, Le XC. Thermal stability of DNA functionalized gold nanoparticles. *Bioconjugate chemistry*. 2013;24:1790-7.
5. Vigderman L, Zubarev ER. Therapeutic platforms based on gold nanoparticles and their covalent conjugates with drug molecules. *Adv Drug Deliv Rev*. 2013;65:663-676.
6. Soukup O, Benkova M, Dolezal R, et al. The wide-spectrum antimicrobial effect of novel N-alkyl monoquaternary ammonium salts and their mixtures; the QSAR study against bacteria. *European Journal of Medicinal Chemistry 206*. 2020;112584.
7. Novotný F. ParticleRecognition, a Mathematica GUI interface for analysis of complex shaped nanoparticles in micrographs. *Computer Physics Communications 214*. 2017;98-104.
8. Qiu Y, Liu L, Wang L, et al. Surface chemistry and aspect ratio mediated cellular uptake of Au nanorods. *Biomaterials*. 2010;31:7606-19.