Electronic Supplementary Material (ESI) for RSC Chemical Biology.


**Supplementary Methods**
Swanson et al. 2022, *RSC Chemical Biology*

**Synthesis of (2):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 1.20 mL of 2-aminoethanol (1.21 g, 19.84 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from methanol and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 7.78 (s, 2H), 7.51 (s, 1H), 6.99 (s, 1H), 6.28 (s, 2H), 6.09 (s, 1H), 5.09 (s, 2H), 4.59 (s, 0H), 3.02 (s, 2H), 2.96 (s, 1H), 2.83 (s, 1H), 1.88 (s, 5H), 1.22 (s, 6H), 0.99 (s, 6H).

**Synthesis of (3):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 1.34 mL of 1,2-ethanediamine (1.20 g, 20.04 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. the product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 7.79 (s, 1H), 7.49 (s, 2H), 6.96 (s, 1H), 6.27 (d, $J$ = 13.4 Hz, 3H), 6.12 (s, 1H), 5.41 (s, 2H), 3.17 (s, 5H), 3.13 (s, 3H), 3.08 (s, 2H), 2.90-2.98 (s, 5H), 2.45 (s, 1H), 1.90 (s, 2H), 1.87 (s, 3H), 1.82 (s, 1H), 1.22 (d, $J$ = 14.7 Hz, 4H). A reference NMR spectrum for (3) is shown in S Fig 1.

**Synthesis of (4):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 2.34g of 6-aminohexan-1-ol (19.96 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 6.27 (s, 0H), 5.06 (s, 0H), 4.26 (s, 4H), 3.14 (s, 1H), 2.94 (s, 1H), 2.61 (s, 2H), 2.18 (s, 2H), 1.86 (s, 2H), 1.42 (s, 5H), 1.28 (s, 3H), 1.22 (s, 1H), 0.98 (s, 1H).

**Synthesis of (5):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 2.76mL of 1,6-diaminohexane (2.32 g, 19.96 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 7.77 (s, 1H), 7.50 (s, 2H), 6.99 (s, 1H), 6.26 (s, 1H), 6.05 (s, 1H), 5.07 (s, 2H), 3.14 (s, 4H), 2.61 (s, 3H), 2.57 (s, 8H), 1.87 (d, $J$ = 9.0 Hz, 3H), 1.39 (s, 17H), 1.27 (s, 8H), 1.22 (s, 4H), 1.17 (s, 2H), 1.01 – 0.96 (m, 9H).

**Synthesis of (6):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 2 mL of aminoethoxy ethanol (2.11g, 20.11mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 7.51 (s, 1H), 6.28 (s, 0H), 5.12 – 5.07 (m, 1H), 3.52 (s, 3H), 3.43 (s, 2H), 3.32 (s, 1H), 3.17 – 3.13 (m, 7H), 2.98 (s, 1H), 2.74 (s, 2H), 1.91 (s, 5H), 1.87 (s, 1H), 1.25 – 1.21 (m, 3H).

**Synthesis of (7):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 3.0mL of glucosamine (4.68g, 26.12 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 8.09 (s, 1H), 8.05 (s, 1H), 7.17 (s, 1H), 5.66 (s, 0H), 5.27 (s, 1H), 5.23 (s, 0H), 4.68 (s, 1H), 4.56 (s, 1H), 3.65 – 3.59 (m, 3H), 3.51 (s, 3H), 3.19 (s, 1H), 2.85 (s, 1H), 2.65 (s, 1H), 2.51 (s, 2H), 1.50 (s, 4H), 1.29 (s, 2H), 1.25 (s, 0H).

**Synthesis of (8):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 1.59 mL of 2-amino-2-methyl-1-propanol (1.49 g, 16.66 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ

8.25 (d, *J* = 7.4 Hz, 1H), 7.91 (d, *J* = 7.9 Hz, 3H), 7.84 (s, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 6.93 (s, 2H), 6.80 (s, 2H), 3.95 (q, *J* = 7.3 Hz, 5H), 3.28 (s, 2H), 2.59 (s, 6H), 2.12 (s, 5H), 1.26 (t, *J* = 7.4 Hz, 6H), 0.85 (s, 2H), 0.85 (d, *J* = 14.7 Hz, 1H).

**Synthesis of (9):** 2.0 g of Rhodamine 6G (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 2.06g of 2-aminobenzyl alcohol (16.70 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 8.25 (d, *J* = 7.4 Hz, 1H), 7.91 (d, *J* = 7.9 Hz, 3H), 7.84 (s, 1H), 7.68 (s, 1H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.00 (s, 1H), 6.93 (s, 2H), 6.80 (s, 2H), 6.68 (s, 1H), 6.65 (s, 1H), 4.54 (s, 1H), 3.95 (q, *J* = 7.3 Hz, 5H), 2.12 (s, 5H), 1.26 (t, *J* = 7.4 Hz, 6H), 0.85 (s, 2H), 0.85 (d, *J* = 14.7 Hz, 1H).

**Synthesis of (10)**: 2.0 g of Rhodamine B (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 1.34 mL of 1,2-ethanediamine (1.20 g, 20.04 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. The product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 7.68 (s, 0H), 7.49 (s, 1H), 7.11 (s, 1H), 6.44 (s, 1H), 6.37 (s, 3H), 6.14 (s, 1H), 3.33 (s, 6H), 3.00 (s, 2H), 2.67 (s, 2H), 2.51 (s, 1H), 2.22 (s, 1H), 1.18 (s, 1H), 1.09 (s, 6H), 0.97 (s, 6H).

**Synthesis of (11):** 2.0 g of Rhodamine B (4.1 mmol) was dissolved in 30 mL ethanol in a round bottom flask. 2.76mL of 1,6-diaminohexane (2.32 g, 19.96 mmol) and 0.570 mL triethylamine (4.1 mmol) was added, dropwise, and the mixture was heated to reflux at 80C with a water-cooled condenser for 12 hours. The mixture was cooled to room temperature and solvent was evaporated with a rotary evaporator. the product is isolated from acetonitrile and collected by suction filtration, then recrystallized. $^1$H NMR (599 MHz, DMSO-$d_6$) δ 7.76 (s, 0H), 7.51 (s, 0H), 7.03 (s, 0H), 6.32 (d, *J* = 51.2 Hz, 0H), 5.24 (s, 3H), 2.65 (s, 1H), 2.62 (s, 1H), 1.45 (s, 3H), 1.28 (s, 1H).

**Synthesis of (27):** 800 mg of (3) (1.62 mmol) and 836 uL triethylamine (6.00mmol, 3x molar excess) was dissolved in 30 mL dichloromethane and cooled in an ice bath. Separately, 250 uL acryloyl chloride (3.10 mmol) was dissolved in 3.0 mL dichloromethane. Once the solution of (3) was sufficiently cold, the acryloyl chloride solution was slowly injected via a syringe and needle over the course of 1 hour. The resulting solution was stirred rapidly and allowed to react for 24 hours as it warmed to room temperature. After 12 hours, dichloromethane was concentrated by rotary evaporation. Excess acryloyl chloride was extracted with water. Solvent was completely removed by rotary evaporation, and the compound was dried by vacuum. $^1$H NMR (599 MHz, Chloroform-*d*) δ 7.48 (s, 1H), 7.07 (s, 1H), 6.35 (d, *J* = 11.3 Hz, 1H), 6.22 (d, *J* = 17.9 Hz, 2H), 5.99 (s, 1H), 3.32 (s, 1H), 3.26 (s, 11H), 3.22 (t, *J* = 8.4 Hz, 2H), 3.10 (s, 2H), 3.05 (s, 1H), 1.94 (s, 1H), 1.90 (d, *J* = 14.0 Hz, 3H), 1.46 (s, 1H), 1.41 – 1.38 (m, 3H), 1.33 (d, *J* = 10.0 Hz, 3H), 1.26 (s, 4H).

**HSA PNP Fabrication and Cell Culture Methods:**

**Preparation of (34)-HSA NPs:** Nanoparticles (NPs) from (34) and unmodified HSA were prepared by electrohydrodynamic (EHD) jetting, by a method previously described[42-44]. Three formulations were prepared with the (34)-HSA, each containing a different mass percentage of (34)-HSA dye (5%,10% and 50%) relative to the unconjugated HSA. The lyophilized (34)-HSA was weighed and subsequently solubilized in UltraPure water (Thermo Fisher) to prepare a stock solution. The jetting formulation followed previously described protocols[42-44]. Briefly, the formulation consisted of a 7.5 % w/v protein in an 80:20 water to ethylene glycol (Sigma) solvent system. The bi-functional crosslinker (O.O'-Bis[2-N-succinimidyl-succinylamino) ethyl] polyethylene glycol ethylene glycol, 2kDa, Sigma) was added last to the protein solution at a concentration of 10% w/w relative to the protein. Control PNPs were prepared in the same manner, but with Alexa Fluor 647 (Thermo Fisher) BSA conjugate at a 0.25% w/w concentration relative to the bulk HSA protein.

Once mixed, the formulations were loaded into a 1mL syringe equipped with a 25G stainless steel blunt needle and nanoparticle formulation were produced by electrohydrodynamic (EHD) jetting. The syringe was pumped at a rate of 0.2 mL/hour and a range of 10-15 kV was applied to form a stable Taylor Cone. The PNPs were jetted upon an aluminum surface collection plate which was changed every 30 minutes. Collection plates were incubated at 37˚C for one week then collection procedures were followed. The PNPs were physically agitated in a 0.01% Tween20 (Sigma) solution in PBS. The PNP suspension was subjected to the following processing

steps: First, the PNPs were tip sonicated for 30 seconds (1 second on and 3 seconds off) at an amplitude of 5 then filtered through a 40 μm cell filter. The filtered PNPs were centrifuged for 5 minutes at 4000 rpm (3220 rcf) at room temperature to separate larger PNPs from smaller populations. The supernatant was distributed among 2 mL Eppendorf tubes and further centrifuged at 4˚C for 1 hour at 15,000 rpm (21130 rcf). The resulting supernatant was discarded, and the pellets were combined into a single tube. Finally, the pellet was washed twice with fresh PBS to remove any excess Tween20. The final pellet was resuspended in 1mL of fresh PBS and sonicated whereafter characterization was performed.

SEM images of PNPs were obtained through the Thermo Fisher Nova 200 Nanolab SEM/FIB instrument (University of Michigan Center for Materials Characterization). To prepare for PNP imaging, the following was conducted. Clean silicon wafers were placed on the collection plate during the EHD jetting where PNPs were directly jetting upon the surface. The silicon wafer was then transferred to a copper lined SEM mount and gold sputter coated for 50 seconds. SEM images were captured using a voltage of 5.0 kV and current of 0.4 nA.

**Determining Concentration of HSA NPs:** The concentration of PNPs were determined using BCA assay (Pierce) according to the manufacturer's protocol.

**Dynamic Light Scattering:** Dynamic light scattering was performed through the Malvern Zetasizer instrument to measure the hydrodynamic diameter of processed PNPs. Averages of at least three measurements was taken to obtain the resulting spectra.

**Zeta Potential:** The zeta potential of PNPs was also measured through the Malvern Zetasizer instrument using disposable folded capillary cuvettes. Averages of at least three measurements were used for the reported zeta potential.

**Antibody Functionalization of HSA NPs:** PNPs were reacted overnight at 4°C on a rotator with 20 molar excesses of azidobutyric acid NHS ester (Lumiprobe). Azide-modified PNPs were purified away from unreacted azidobutyric acid via 3 rounds of centrifugation (15,000 rpm for 1 hour at 4°C). Meanwhile, anti-mICAM antibody was functionalized via 1hr reaction at RT with a 3-fold excess of DBCO-PEG4-NHS ester (Click Chemistry Tools). The modified antibody was purified away from unreacted DBCO via centrifugal filtration using a 100kDa cutoff (Amicon). Azide-modified PNPs were then reacted overnight with DBCO-modified antibody at a 1:1500 ratio. Antibody-modified PNPs were again purified using 3 rounds of centrifugation. At the end of this process, ICAM-targeted HSA-PNPs were resuspended in aqueous buffer and characterized via dynamic light scattering.

**Pulse Chase Experiment:** REN-mICAM and REN wt cells were cultured in 8-well chamber slides (Lab Tek). Cells were incubated with a 0.2 mg/mL solution of pH sensitive (i.e., (34)) or non-pH-sensitive (i.e., AF647) ICAM-targeted HSA-PNPs for 30 minutes on ice to allow binding. Cells were washed 3 times with ice-cold buffer to remove unbound particles and then incubated at 37°C for various time periods (15-240 minutes). Cells were washed with PBS, fixed with 2% paraformaldehyde, and mounted for microscopy using ProLong™ Gold Antifade mountant with DAPI.

**Biomaterial Fabrication and Cell Culture Methods:**

**Preparation of Polymer Thin Films**: (28) was dissolved in benzene at 10% w/v at 50°C for two hours. The solution was cast on a 5-inch diameter silica wafer sandwiched between two glass plates, left at room temperature to evaporate slowly, covered by a glass dish to moderate the evaporation of solvent. After 24 hours, the film was submerged in room temperature water to exchange solvent, and dried.

**Osteoclast Cell Culture on Polymer Thin Films**: Thin films were cut to 5 mm diameter using a biopsy punch and sterilized by ethylene oxide gas (Andersen). Sterilized films were soaked in 70% ethanol to wet the surface, then washed with phosphate buffered saline (PBS, pH 7.4) and cell culture media three times. Osteoclasts were lifted using 0.02% EDTA after 72 hours of differentiation in RankL and M-CSF and plated onto polymer films at $2 \times 10^5$ cells per film for 30 minutes until cells were adherent. Then a media change was done with osteoclast differentiation media. 24 hours later osteoclasts were stained with CellTracker™ Green CMFDA Dye (5-chloromethylfluorescein diacetate) (Invitrogen) and Hoechst (Thermo Scientific) for 30 minutes, washed, and imaged live.

**Fluorescent Labelling of Osteoclasts Culture In Vitro**: Thermo Scientific Pierce Hoechst 33342 Fluorescent Stain (20 mM) (Catalog number: 62249) was used by adding directly to live cells in media at 1 uM for 15 minutes or adding to fixed cells in PBS at 1 uM for 30 minutes. ELF™ 97 Phosphatase Substrate (ELF™ 97 Phosphate), 0.2 µm Filtered (Invitrogen) (Catalog number: E6588) was applied to long bone and vertebrate sections in conjunction with the Acid Phosphatase Leukocyte (TRAP) Kit (Sigma-Aldrich) (Catalog number: 387A). SiR-actin stain (Cytoskeleton) (Catalog number: CY-SC001) was added to live osteoclast cultures at 1 uM and media was changed after 30 minutes. CellTracker™ Green CMFDA (5-chloromethylfluorescein diacetate) (Invitrogen) (Catalog number: C2925) was added to live osteoclast cultures at 1 uM for 30 minutes.

**Confocal Laser Microscopy of Polymer Thin Films:** Fluorescently active probes within (28) films were observed inverted in cell culture dishes with optical quality glass bottom (FluoroDish). A live-cell imaging chamber was used to maintain cell cultures, in a humidified environment at 37°C.

**Preparation of Nanofibrous Spongy Microspheres**: 200 mg of (28) and 200 mg of Resomer L 207S poly (L-lactic acid) (PLLA, Evonik) were dissolved in 20 mL tetrahydrofuran (THF) solvent and heated to 60°C (4% w/v). 5x volume of glycerol was heated to 50°C. Under rigorous mechanical stirring, the THF solution was gradually added to the warm glycerol. After stirring for 1 minute, the mixture was quickly poured into liquid nitrogen. After 10 minutes, water and ice were added for solvent exchange for 24 hours. The microspheres were collected by washing through molecular sieves and washed with deionized water to remove residual glycerol. Their morphology was examined by light microscopy and scanning electron microscopy. The microspheres were recovered by lyophilization and stored at -20°C.

**Bone-Targeted Probe Evaluation In Vitro and In Vivo:**

**Osteoclast Cell Culture on Bovine Bone Chips with (36):** Bovine femur bone slices (Fisher (immunodiagnostic systems)) were incubated for 30 minutes at room temperature with (36) and washed 3 times with DPBS. Osteoclasts after 72 hours of differentiation were plated on the coated bone slices at $1x10^5$ per bone slice. After 24 hours, osteoclasts were stained with CellTracker™ Green CMFDA Dye and Hoechst for 30 minutes and fixed with paraformaldehyde 4% (Fisher). Cells were imaged within 24 hours of fixing by confocal laser microscopy.

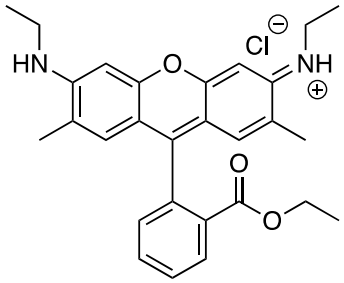
**In Vivo Administration of (36):** C57BL/6 4-month female mice were injected (intraperitoneal) with (36) at 0.5 mg/mL for two hours. Vehicle mice were injected with 1X DPBS saline solution. Mice were euthanized 2 hours post injection and long bones and vertebrate were collected.

All procedures involving animals were performed following a protocol approved by the University of Michigan Institutional Animal Care and Use Committee (IACUC, PRO00009377).

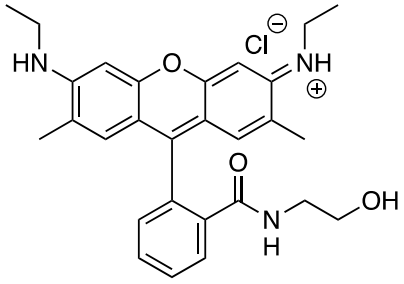
**Histologic Preparation of Bones:** Long bones and vertebrate were collected, and all soft tissue was removed. Long bones and vertebrate were placed in 4% paraformaldehyde for 72 hours. Then, long bones and vertebrate were placed into a 12% sucrose solution for 72 hours. Bones were washed in PBS once and embedded in OCT (Optimal Cutting Temperature Embedding Medium) (Fisher) in plastic cassettes. Samples were sectioned at 8 um thickness from frozen tissue blocks.

**Supplementary Information**
**List of All Compounds, Chemical Structures**

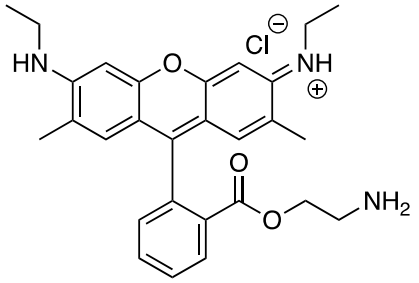
**Compound 1** (*E*)-*N*-(9-(2-(ethoxycarbonyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene) ethanaminium



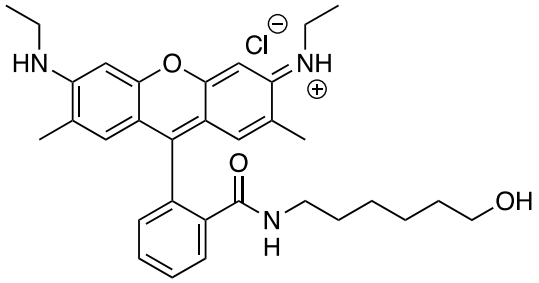

**Compound 2** (*E*)-*N*-(6-(ethylamino)-9-(2-((2-hydroxyethyl) carbamoyl) phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene) ethanaminium



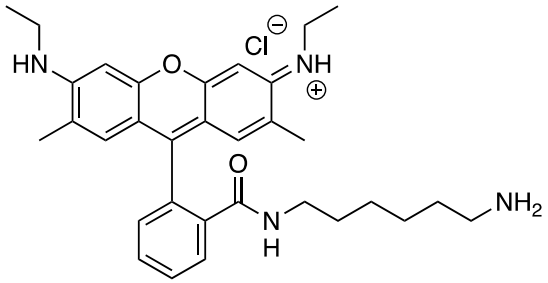

**Compound 3** (*E*)-*N*-(9-(2-((2-aminoethoxy) carbonyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene) ethanaminium



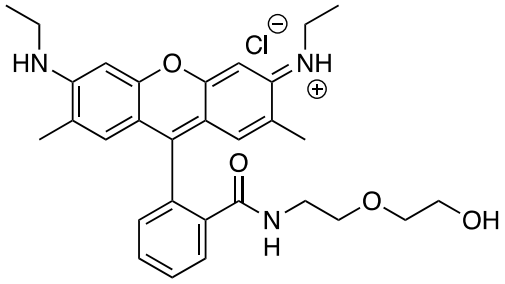

**Compound 4** (*E*)-*N*-(6-(ethylamino)-9-(2-((6-hydroxyhexyl) carbamoyl) phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene) ethanaminium



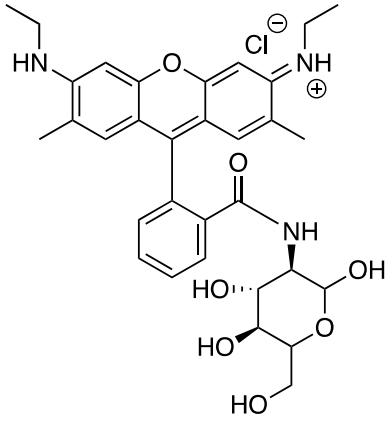

**Compound 5** (*E*)-*N*-(9-(2-((6-aminohexyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



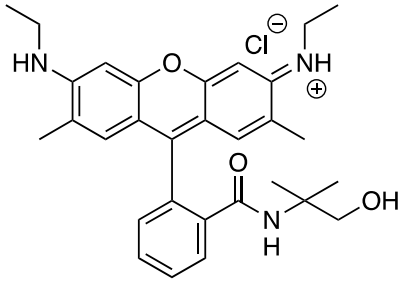
**Compound 6** (*E*)-*N*-(6-(ethylamino)-9-(2-((2-(2-hydroxyethoxy) ethyl) carbamoyl)phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



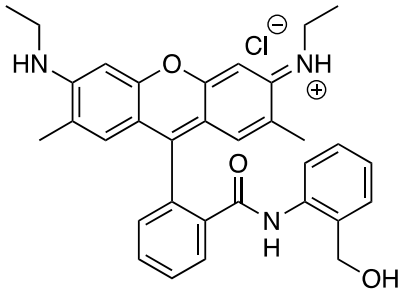
**Compound 7** *N*-((*E*)-6-(ethylamino)-2,7-dimethyl-9-(2-(((3*R*,4*R*,5*S*)-2,4,5-trihydroxy-6-(hydroxymethyl) tetrahydro-2*H*-pyran-3-yl) carbamoyl)phenyl)-3*H*-xanthen-3-ylidene)ethanaminium



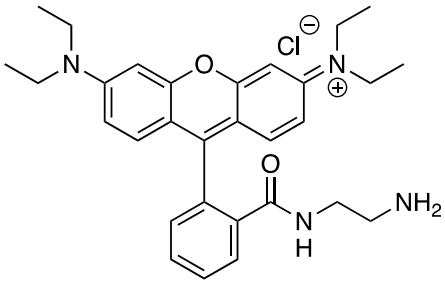
**Compound 8** (*E*)-*N*-(6-(ethylamino)-9-(2-((1-hydroxy-2-methylpropan-2-yl) carbamoyl) phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



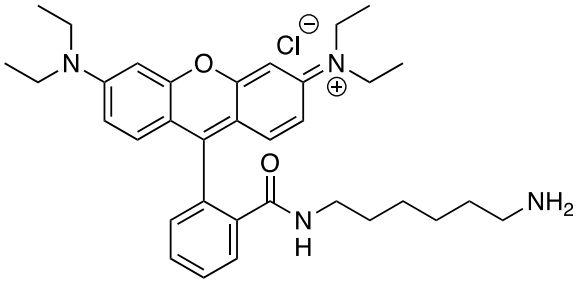
**Compound 9** (*E*)-*N*-(6-(ethylamino)-9-(2-((2-(hydroxymethyl) phenyl) carbamoyl)phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



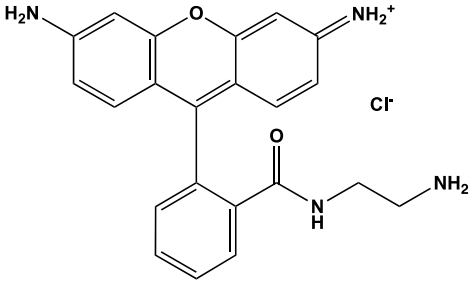
**Compound 10** *N*-(9-(2-((2-aminoethyl) carbamoyl) phenyl)-6-(diethylamino)-3*H*-xanthen-3-ylidene)-*N*-ethylethanaminium



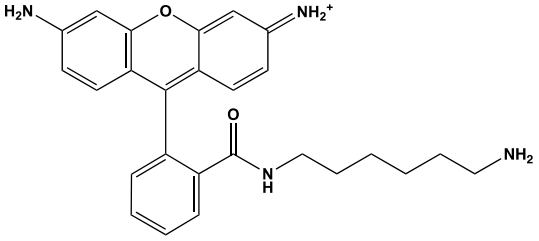
**Compound 11** N-(9-(2-((6-aminohexyl) carbamoyl) phenyl)-6-(diethylamino)-3H-xanthen-3-ylidene)-N-ethylethanaminium



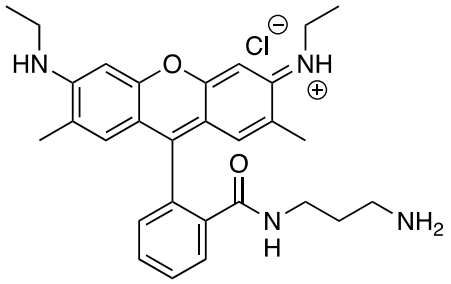
**Compound 12** 6-amino-9-(2-((2-aminoethyl)carbamoyl)phenyl)-3H-xanthen-3-iminium



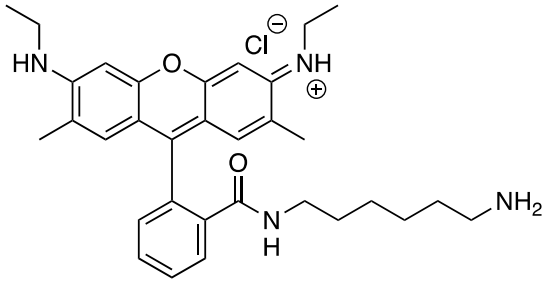
**Compound 13** 6-amino-9-(2-((6-aminohexyl)carbamoyl)phenyl)-3H-xanthen-3-iminium



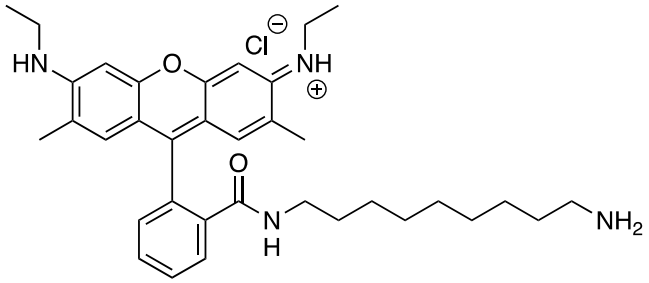
**Compound 14** (*E*)-*N*-(9-(2-((3-aminopropyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



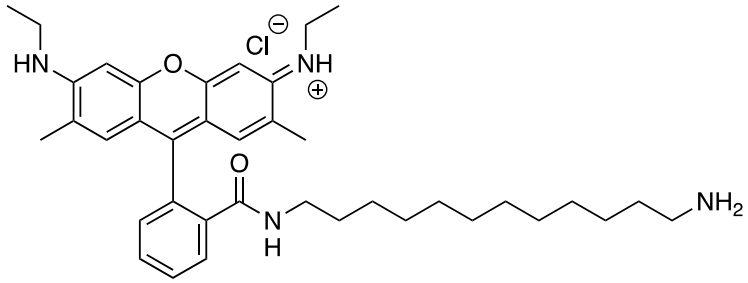
**Compound 15** (*E*)-*N*-(9-(2-((6-aminohexyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



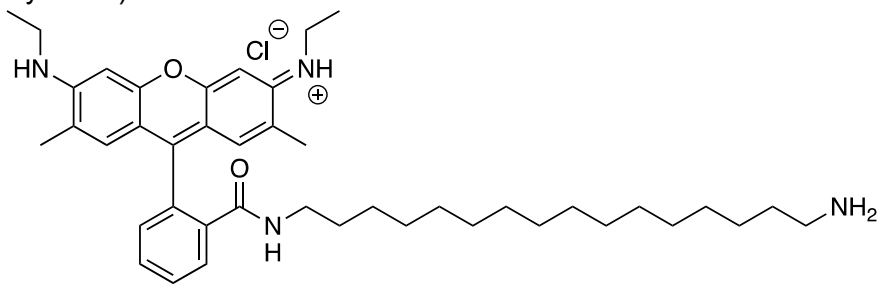
**Compound 16** (*E*)-*N*-(9-(2-((9-aminononyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



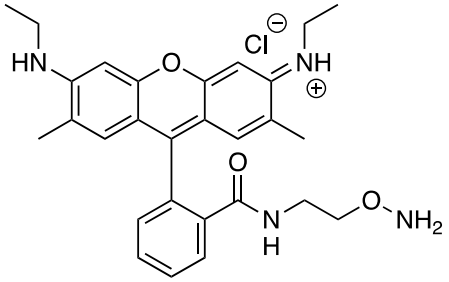
**Compound 17** (*E*)-*N*-(9-(2-((12-aminododecyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



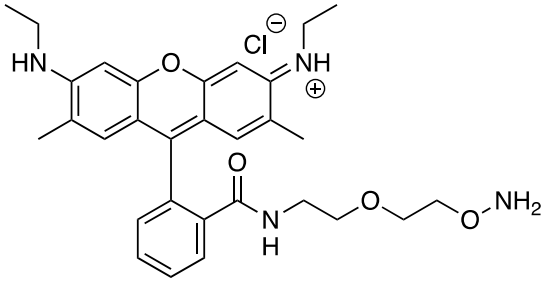
**Compound 18** (*E*)-*N*-(9-(2-((16-aminohexadecyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



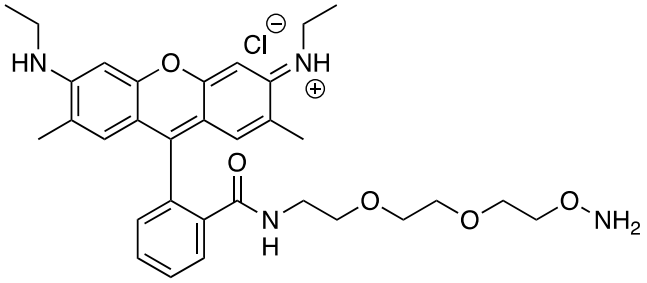
**Compound 19** (*E*)-*N*-(9-(2-((2-(aminooxy) ethyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



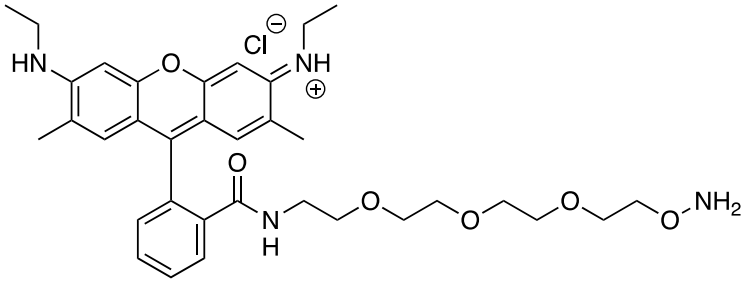
**Compound 20** (*E*)-*N*-(9-(2-((2-(2-(aminooxy) ethoxy) ethyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



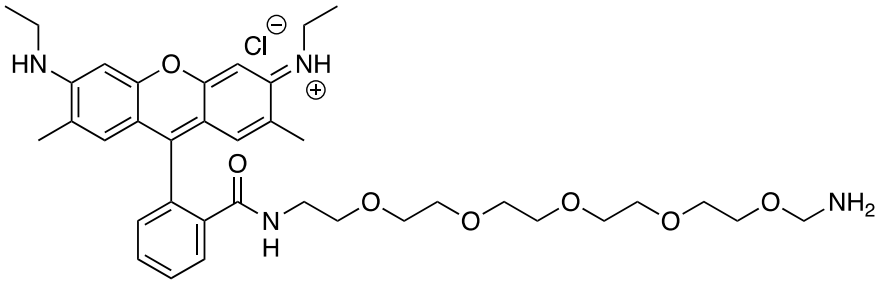
**Compound 21** (*E*)-*N*-(9-(2-((2-(2-(2-(aminooxy) ethoxy) ethoxy) ethyl) carbamoyl)phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



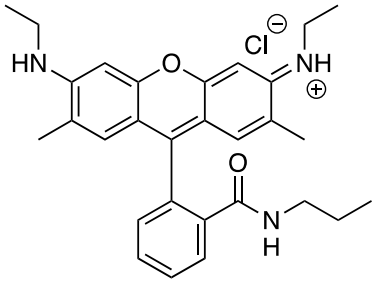
**Compound 22** (*E*)-*N*-(9-(2-((2-(2-(2-(2-(aminooxy) ethoxy) ethoxy)ethoxy)ethyl)carbamoyl)phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



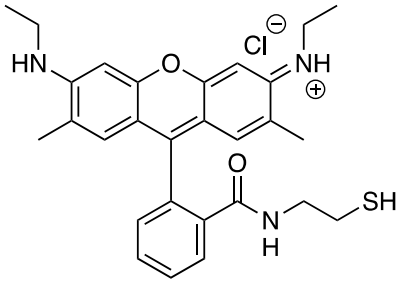
**Compound 23** (*E*)-*N*-(9-(2-((1-amino-2,5,8,11,14-pentaoxahexadecan-16-yl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



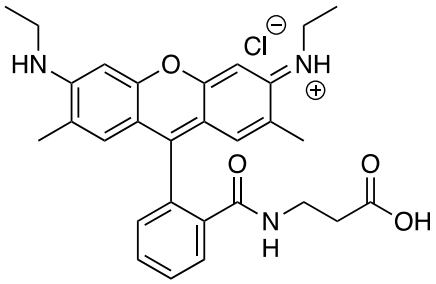
**Compound 24** (*E*)-*N*-(6-(ethylamino)-2,7-dimethyl-9-(2-(propylcarbamoyl) phenyl)-3*H*-xanthen-3-ylidene) ethanaminium



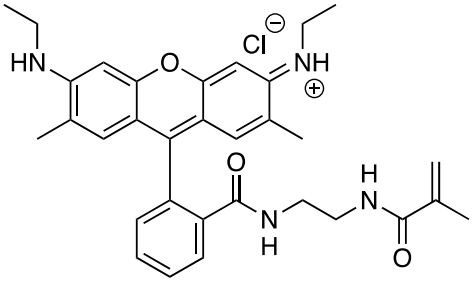
**Compound 25** (*E*)-*N*-(6-(ethylamino)-9-(2-((2-mercaptoethyl) carbamoyl) phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



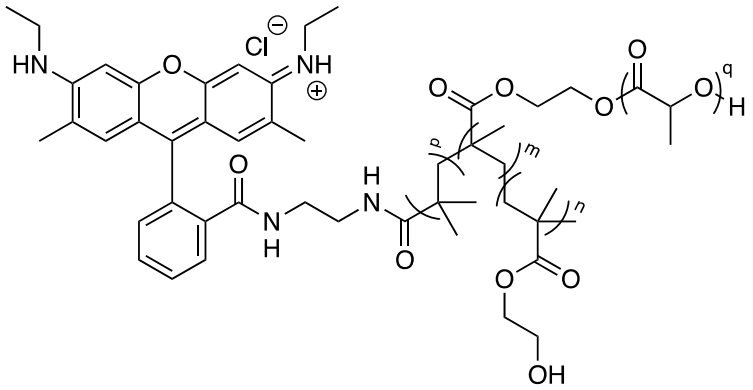
**Compound 26** (*E*)-*N*-(9-(2-((2-carboxyethyl) carbamoyl) phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



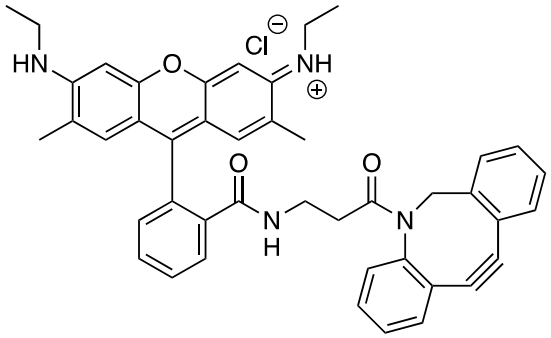
**Compound 27** (*E*)-*N*-(6-(ethylamino)-9-(2-((2-methacrylamidoethyl) carbamoyl) phenyl)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



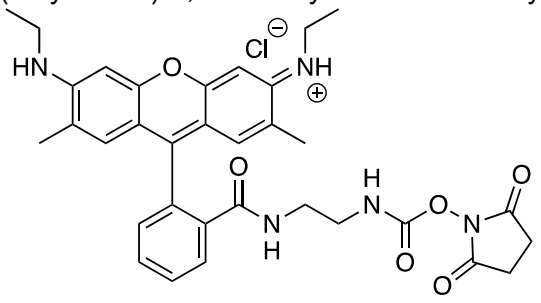
Compound 28



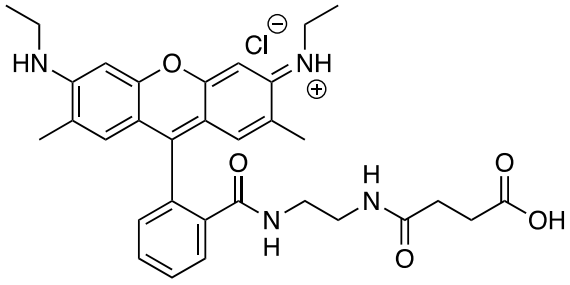
Compound 29



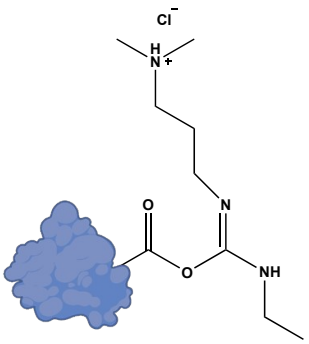
**Compound 30** (*E*)-*N*-(9-(2-((2-((((2,5-dioxopyrrolidin-1-yl) oxy) carbonyl)amino)ethyl)carbamoyl)phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



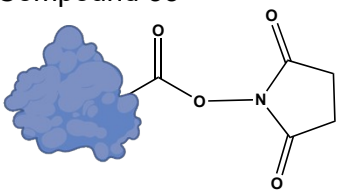
**Compound 31** (*E*)-*N*-(9-(2-((2-(3-carboxypropanamido) ethyl) carbamoyl)phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



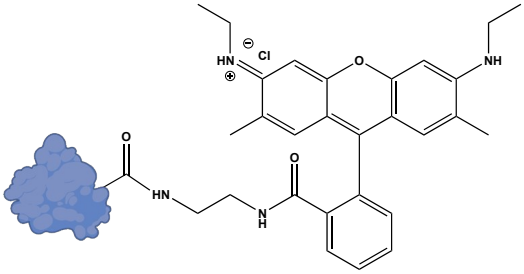
Compound 32



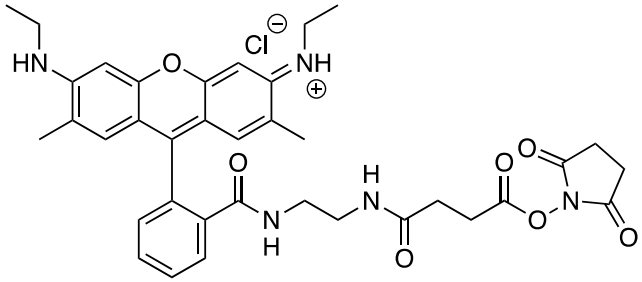
Compound 33



Compound 34



**Compound 35** (*E*)-*N*-(9-(2-((2-(4-((2,5-dioxopyrrolidin-1-yl) oxy)-4-oxobutanamido) ethyl)carbamoyl)phenyl)-6-(ethylamino)-2,7-dimethyl-3*H*-xanthen-3-ylidene)ethanaminium



**Compound 36** (*E*)-hydrogen (4-(4-((2-(2-(6-(ethylamino)-3-(ethyliminio)-2,7-dimethyl-3*H*-xanthen-9-yl) benzamido) ethyl)amino)-4-oxobutanamido)-1-hydroxy-1-phosphonobutyl)phosphonate