Supporting Information

Small Molecule-Modified Surfaces Engage Cells Through the $\alpha_v\beta_3$ Integrin

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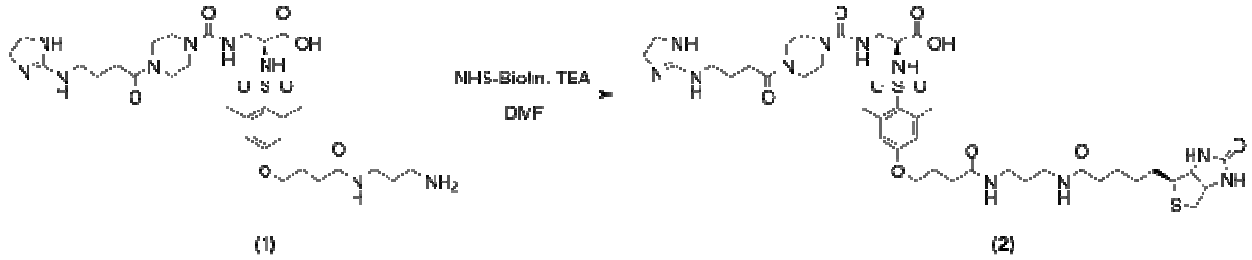
General Synthetic Procedures and Materials

Moisture-sensitive reactions were carried out in flame-dried glassware under nitrogen atmosphere. Reagents were purchased from Sigma-Aldrich Co. as reagent grade, unless otherwise noted. All compounds were used as received. Triethylamine (TEA) was distilled from calcium hydride. Dimethylformamide (DMF) was used as anhydrous grade (Sigma-Aldrich Co.). Water was purified with a MilliQ filtration system (Millipore).

High-performance liquid chromatography was performed using a Vydac C18 semi-prep column using HPLC-grade acetonitrile with 0.05% trifluoroacetic acid (TFA) (volume/volume) and MilliQ-purified water with 0.05% TFA (volume/volume).

^{1}H NMR and ^{13}C NMR were obtained at 500 MHz using a Varian INOVA 500 or Varian UNITY 500 spectrometer. Chemical shifts are reported relative to the residual solvent signal in parts per million: (D_2O) ^{1}H: δ 4.79. ^{1}H NMR data are assumed to be first order with apparent doublets (d), triplets (t), quartets (q), pentets (p) and doublets of doublets (dd). Multiplets are reported as m. Electrospray ionization liquid chromatography mass spectra (ESI-LCMS) data were obtained on a Shimadzu LCMS-2010A.

Biotin-2-{4-[3-(3-amino-propylcarbamoyl)-propoxy]-2,6-dimethyl-benzenesulfonylamino}-3-({4-[4-(4,5-dihydro-1H-imidazol-2-ylamino)-butyryl]-piperazine-1-carbonyl}-amino)-propionic acid conjugate (**2**)



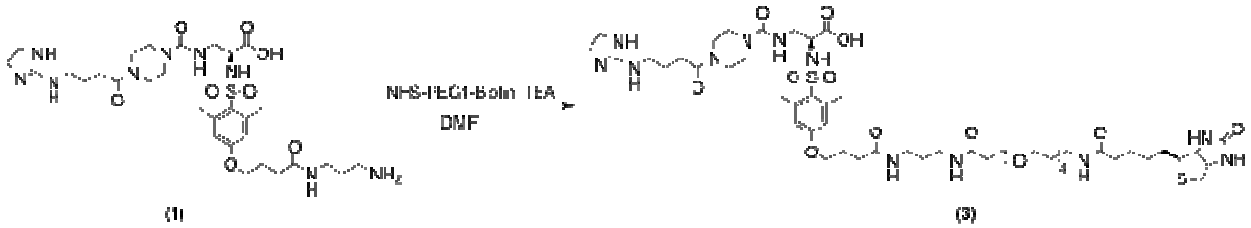
(1) (2)

To a stirred solution of **1** (5.0 mg, 7.0 μmol) and TEA (2.0 μl, 14 μmol) in DMF (200 μl) was added a solution of *N*-hydroxysuccinimidyl-biotin (Pierce) (2.4 mg, 7.0 μmol) in DMF (50 μl). This mixture was left to stir for 24 h at rt. The solution was concentrated *in vacuo* and then triturated with cold diethyl ether to remove soluble components. The crude product was purified by HPLC using a gradient solution of 5–95% (v/v) acetonitrile in water with 0.05% TFA over 60 min. to furnish **2** (3.0 mg, 3.2 μmol, 46 %).

^{1}H NMR (500 MHz, D_2O) δ (ppm): 6.75 (s, 2H); 4.52 (dd, 1H, *J* = 7.9, 4.5 Hz); 4.32 (dd, 1H, *J* = 8.1, 4.4 Hz); 4.04 (t, 2H, *J* = 5.9 Hz); 3.98 (dd, 1H, *J* = 9.9, 4.3 Hz); 3.64 (s, 4H); 3.53 (dd, 1H, *J* = 14.3, 4.3 Hz); 3.41-3.50 (m, 4H); 3.09-3.33 (m, 10H); 3.03 (t, 2H, *J* = 7.2 Hz); 2.90 (dd, 1H, *J* = 13.1, 5.0 Hz); 2.69 (d, 1H, *J* = 12.9 Hz); 2.53 (s, 6H); 2.47 (t, 2H, *J* = 7.4 Hz); 2.35 (t, 2H, *J* = 7.1 Hz); 2.16 (t, 2H, *J* = 7.3 Hz); 2.02 (p, 2 H, *J* = 6.9 Hz); 1.82 (p, 2 H, *J* = 7.2 Hz); 1.43-1.69 (m, 6 H); 1.20-1.38 (m, 2 H).

^{13}C NMR (125 MHz, D_2O) δ (ppm): 176.43, 175.66, 173.51, 165.20, 160.36, 159.76, 158.31, 141.97, 127.68, 119.68, 118.95, 117.37, 116.50, 115.05, 112.73, 67.23, 61.95, 60.14, 55.32, 55.24, 44.70, 42.68, 42.55, 41.94, 41.65, 41.12, 39.60, 36.75, 36.56, 35.33, 32.61, 29.46, 27.75, 27.70, 27.54, 25.02, 24.70, 24.00.
LCMS (SQD ESI): $C_{40}H_{63}N_{11}O_{10}S_2$ $[M+H]^+$ calc. mass 922.4, measured mass 922.6.

Biotin-OEG_4-2-{4-[3-(3-amino-propylcarbamoyl)-propoxy]-2,6-dimethyl-benzenesulfonylamino}-3-({4-[4-(4,5-dihydro-1H-imidazol-2-ylamino)-butyryl]-piperazine-1-carbonyl}-amino)-propionic acid conjugate
(**3**)

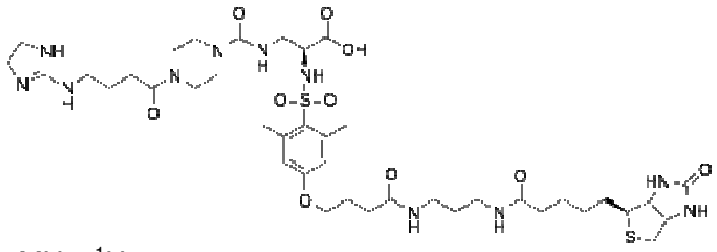


(1) (3)

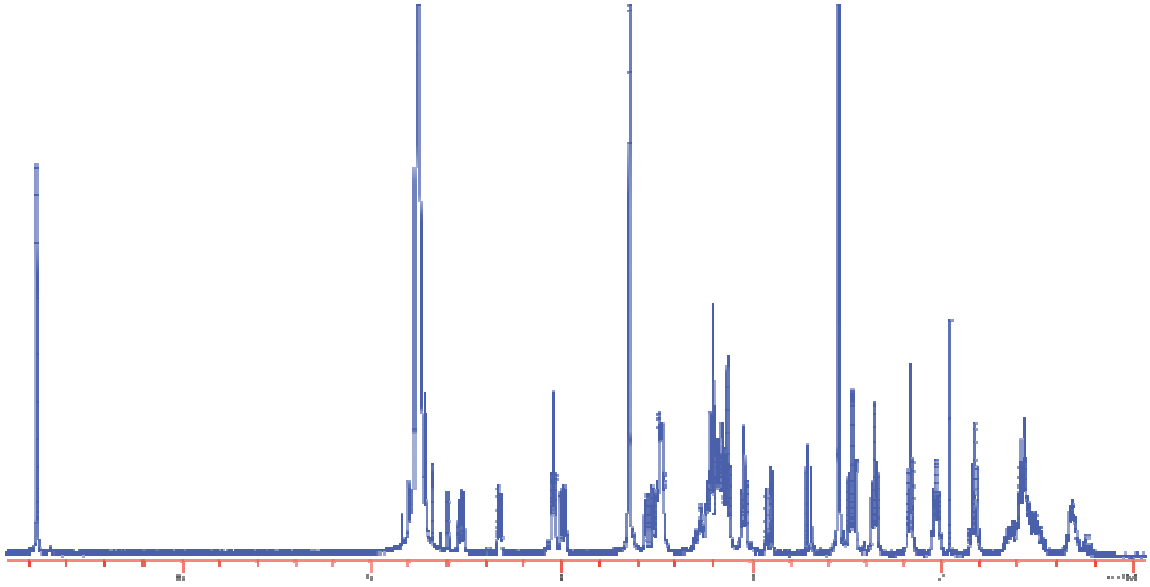
Compound **3** was synthesized using an approach similar to that used to generate **2**. To a stirred solution of **1** (5.0 mg, 7.0 μmol) and TEA (2.0 μl, 14 μmol) in DMF (200 μl), was added a solution of *N*-hydroxysuccinimide-OEG_4-biotin (Pierce) (4.0 mg, 7.0 μmol) in DMF (50 μl). This mixture was allowed to stir for 24 h at rt. The solution was concentrated *in vacuo*. The residue was triturated with cold diethyl ether to remove soluble components. The crude product was purified by HPLC using a gradient of 5–95 % (v/v) acetonitrile in water with 0.05% TFA (v/v) over 60 min. to furnish **3** (3.5 mg, 2.87 μmol, 41 %).

^{1}H NMR (500 MHz, D_2O) δ (ppm): 6.76 (s, 2H); 4.54 (dd, 1H, *J* = 7.7, 4.52 Hz); 4.34 (dd, 1H, *J* = 8.0, 4.4 Hz); 4.05 (t, 2H, *J* = 5.9 Hz); 3.98 (dd, 1H, *J* = 9.9, 4.27 Hz); 3.70 (t, 2H, *J* =6.0 Hz, 2 H) 3.64 (s, 4H); 3.58-3.62 (m, 11H); 3.53-3.57 (m, 3H); 3.45-3.53 (m, 4H); 3.33 (t, 2H, *J* =5.3 Hz); 3.10-3.30 (m, 10H); 3.08 (t, 2H, *J* = 7.0 Hz); 2.92 (dd, 1H, *J* = 13.0, 5.0 Hz); 2.71 (d, 1H *J* = 13.2 Hz); 2.54 (s, 6H); 2.42-2.49 (m, 4H); 2.33-2.38 (m, 2H); 2.20 (t, 2H, *J* = 7.3 Hz); 2.02 (p, 2H, *J*=6.5 Hz); 1.82 (p, 2H, *J* = 7.2 Hz); 1.45-1.70 (m, 7H); 1.21-1.38 (m, 3H).
^{13}C NMR (125 MHz, D_2O) δ (ppm): 176.73, 175.62, 173.75, 173.61, 173.54, 165.22, 163.39, 163.11, 162.83, 160.37, 159.79, 158.34, 141.99, 127.79, 119.72, 119.72, 117.40, 116.53, 115.08, 112.76, 69.51, 67.26, 66.90, 61.98, 60.15, 55.48, 55.28, 44.73, 42.70, 42.56, 42.51, 41.99, 41.66, 41.13, 39.62, 38.81, 36.65, 36.61, 35.98, 35.36, 33.69, 32.55, 29.46, 27.83, 27.78, 27.62, 25.07, 24.72, 24.00, 22.46.
LCMS (SQD ESI): $C_{51}H_{84}N_{12}O_{15}S_2$ $[M+2H]^{+2}$ calc. mass 585.7, measured mass 585.8.

Biotin-2-{4-[3-(3-amino-propylcarbamoyl)-propoxy]-2,6-dimethyl-benzenesulfonylamino}-3-({4-[4-(4,5-dihydro-1H-imidazol-2-ylamino)-butyryl]-piperazine-1-carbonyl}-amino)-propionic acid conjugate (**2**)

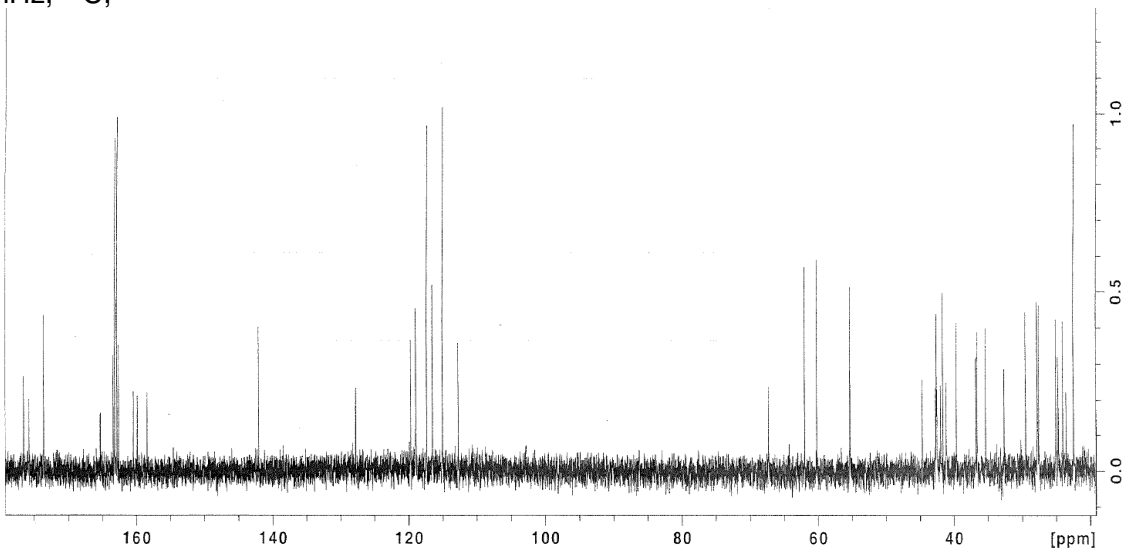


500 MHz, ^{1}H,



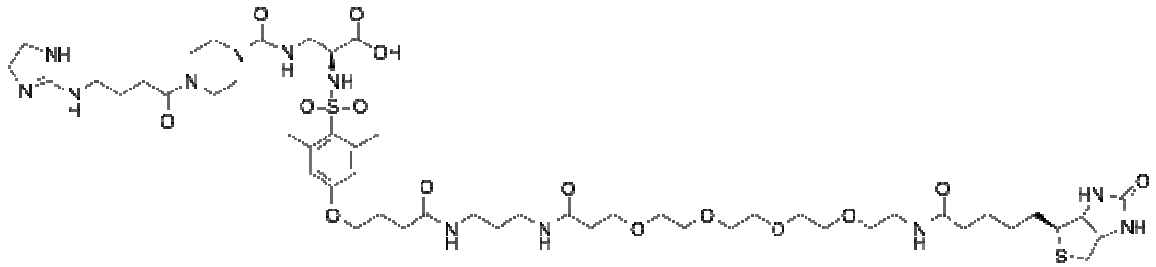
D_2O

125 MHz, ^{13}C,

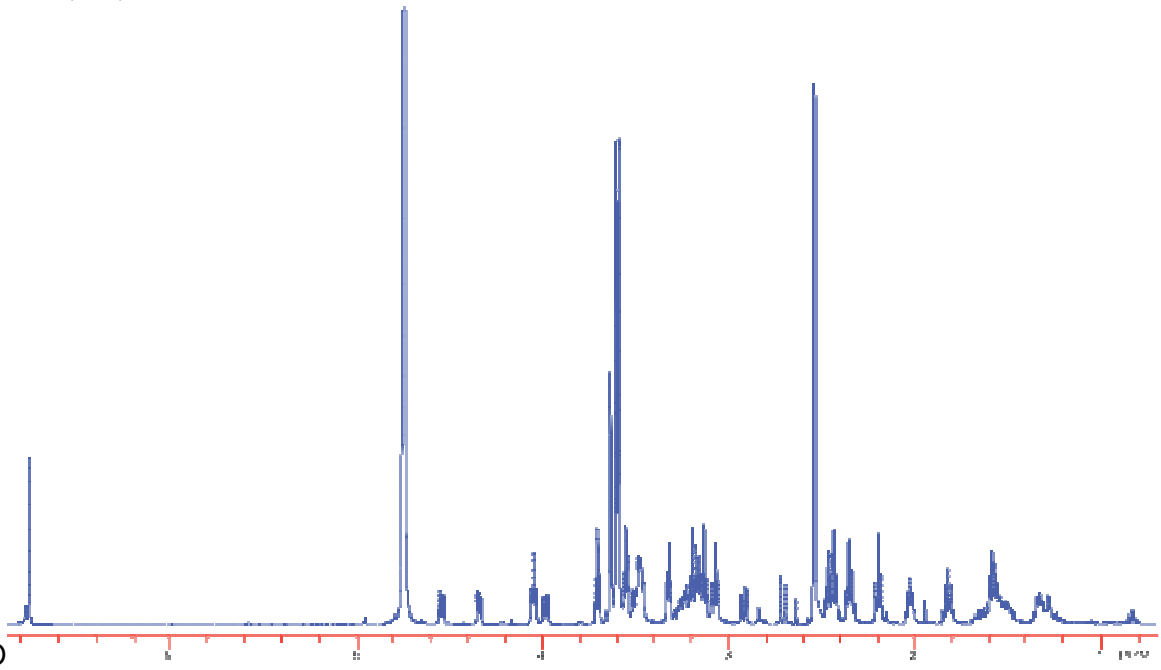


D_2O

Biotin-OEG$_4$-2-{4-[3-(3-amino-propylcarbamoyl)-propoxy]-2,6-dimethyl-benzenesulfonylamino}-3-({4-[4-(4,5-dihydro-1H-imidazol-2-ylamino)-butyryl]-piperazine-1-carbonyl}-amino)-propionic acid conjugate

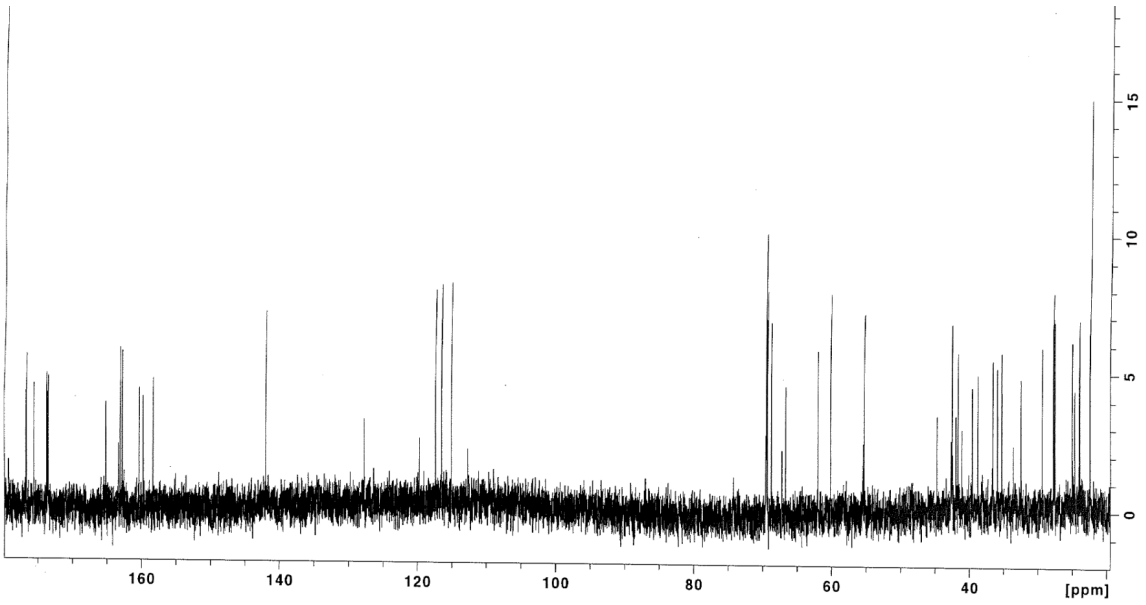


(**3**)
500 MHz, ^{1}H,



D_2O

125 MHz, ^{13}C, D_2O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140
120
100
80
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40
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15
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