Supporting Information

Bone-Targeted Acid-Sensitive Doxorubicin Conjugate Micelles as Potential Osteosarcoma Therapeutics

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SUPPORTING DATA

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Fmoc-Hydrazine

The structure and purity of synthesized Fmoc-hydrazine were verified by 1H-NMR and analytical HPLC as shown below.

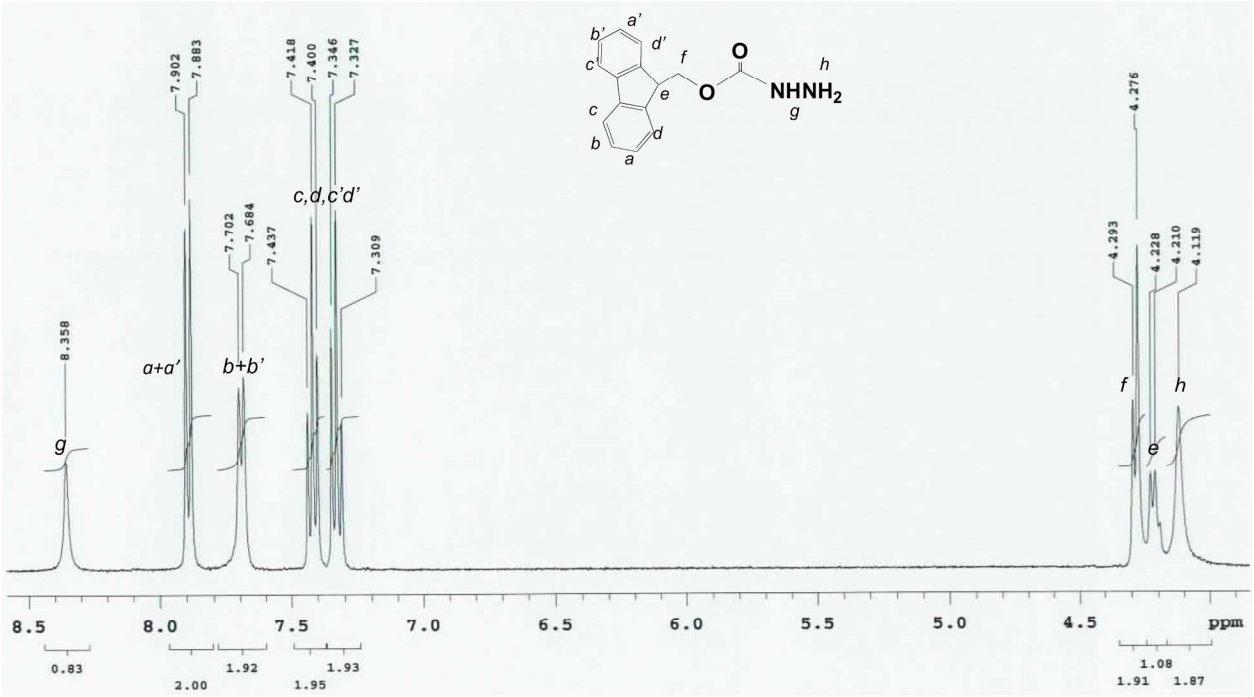

Figure S1: [1]H-NMR spectrum of Fmoc-hydrazine (using DMSO-d6 as solvent on Mercury 400 spectrometer)

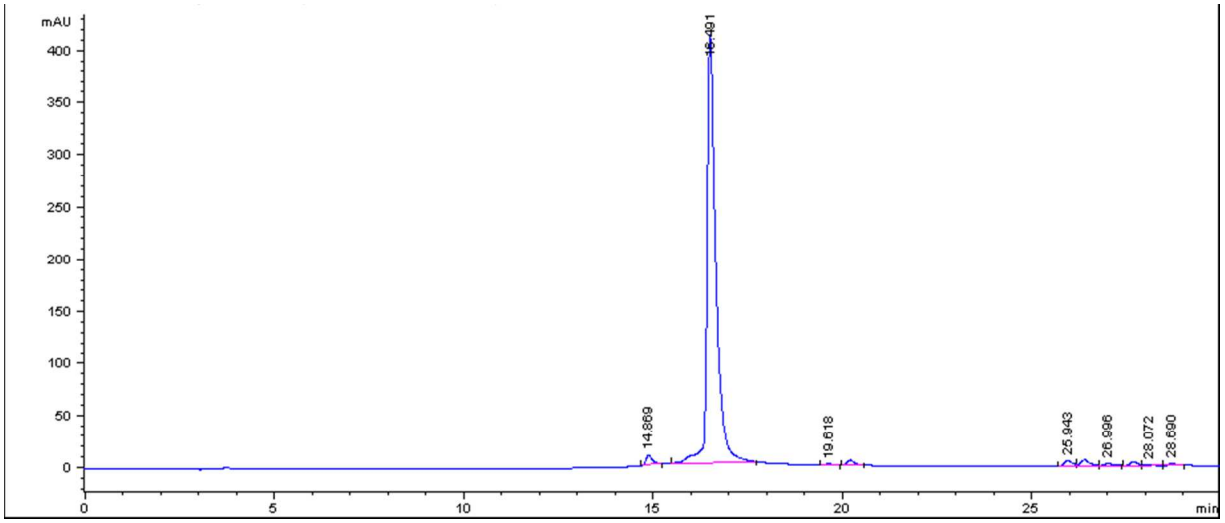

Figure S2: HPLC elution profile of Fmoc-hydrazine using Agilent Technologies 1100 series (Zorbax C18 column 4.6×250 mm) with gradient method from 2 to 90% of Buffer B within 30 min and flow rate 1.0 mL/min (Buffer A: deionized water (DI H_2O) with 0.1% TFA, Buffer B: acetonitrile containing 0.1% TFA).

Fmoc-aminoundecanoic acid

Synthesized Fmoc-aminoundecanoic acid was characterized with mass spectrum, ^{1}H-NMR and HPLC analytical profiles:

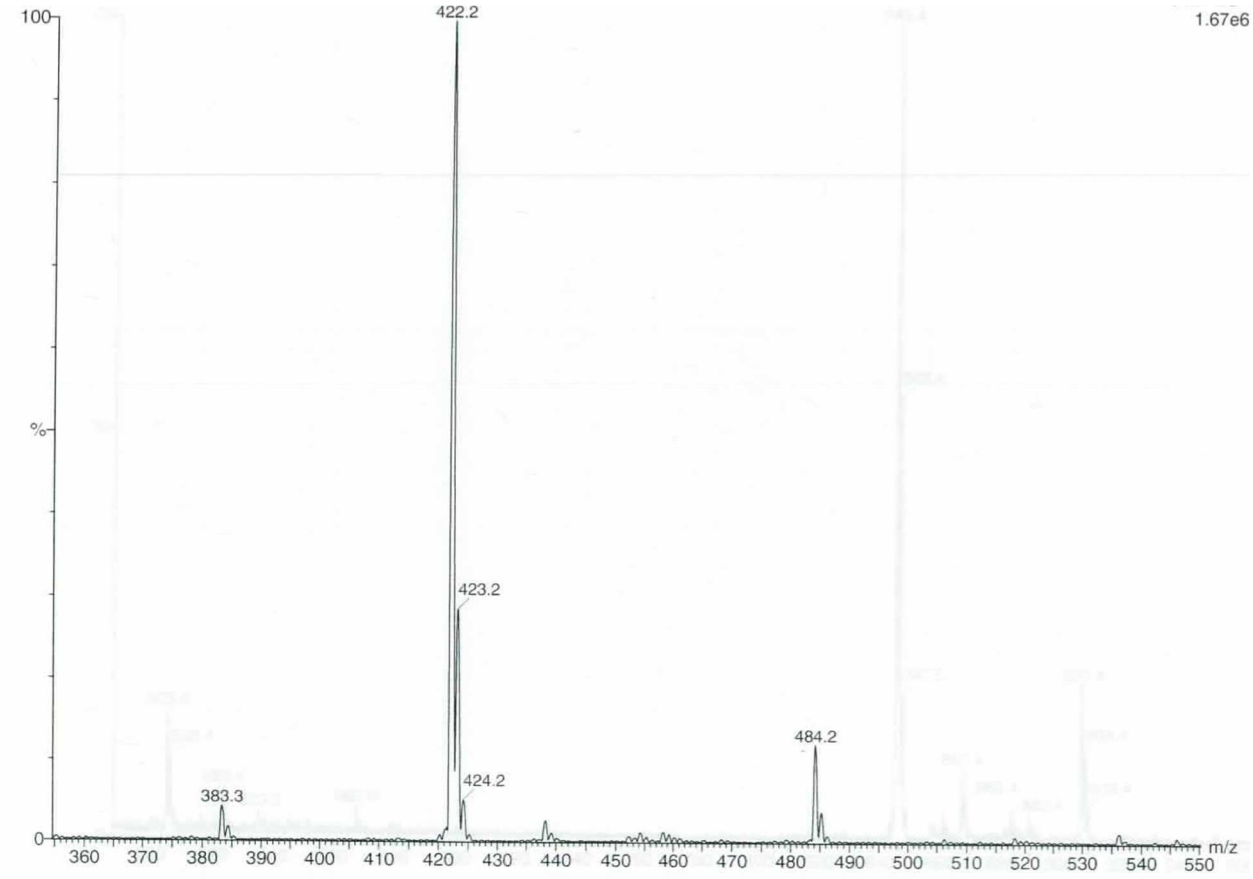

Figure S3: MALDI-ToF mass spectrum of Fmoc-aminoundecanoic acid

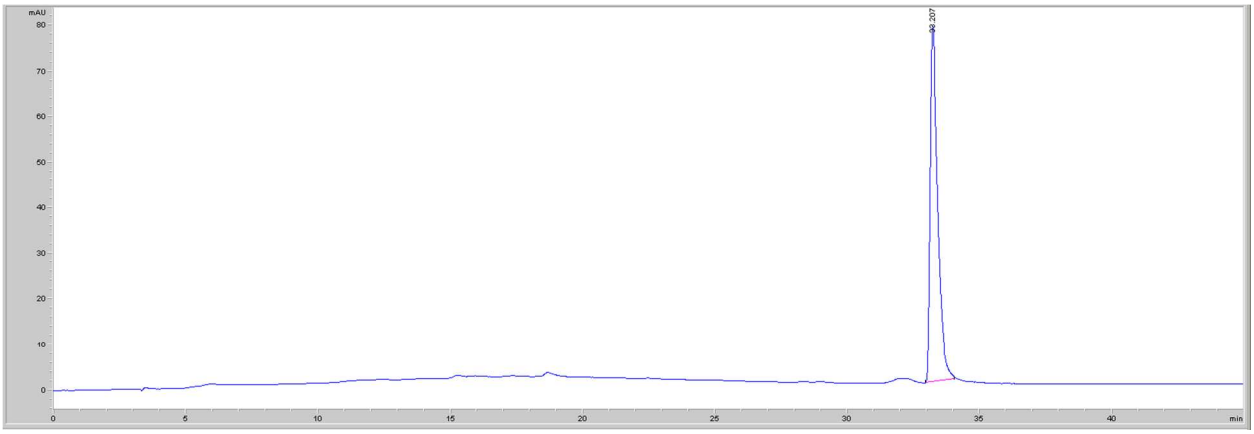

Figure S4: HPLC profile of Fmoc-aminoundecanoic acid (Fmoc-AUA) using Agilent Technologies 1100 series (Zorbax C18 column 4.6×250 mm) with gradient method from 2 to 90% of Buffer B within 30 min and flow rate 1.0 mL/min (Buffer A: deionized water (DI H_2O) with 0.1% TFA, Buffer B: acetonitrile containing 0.1% TFA).

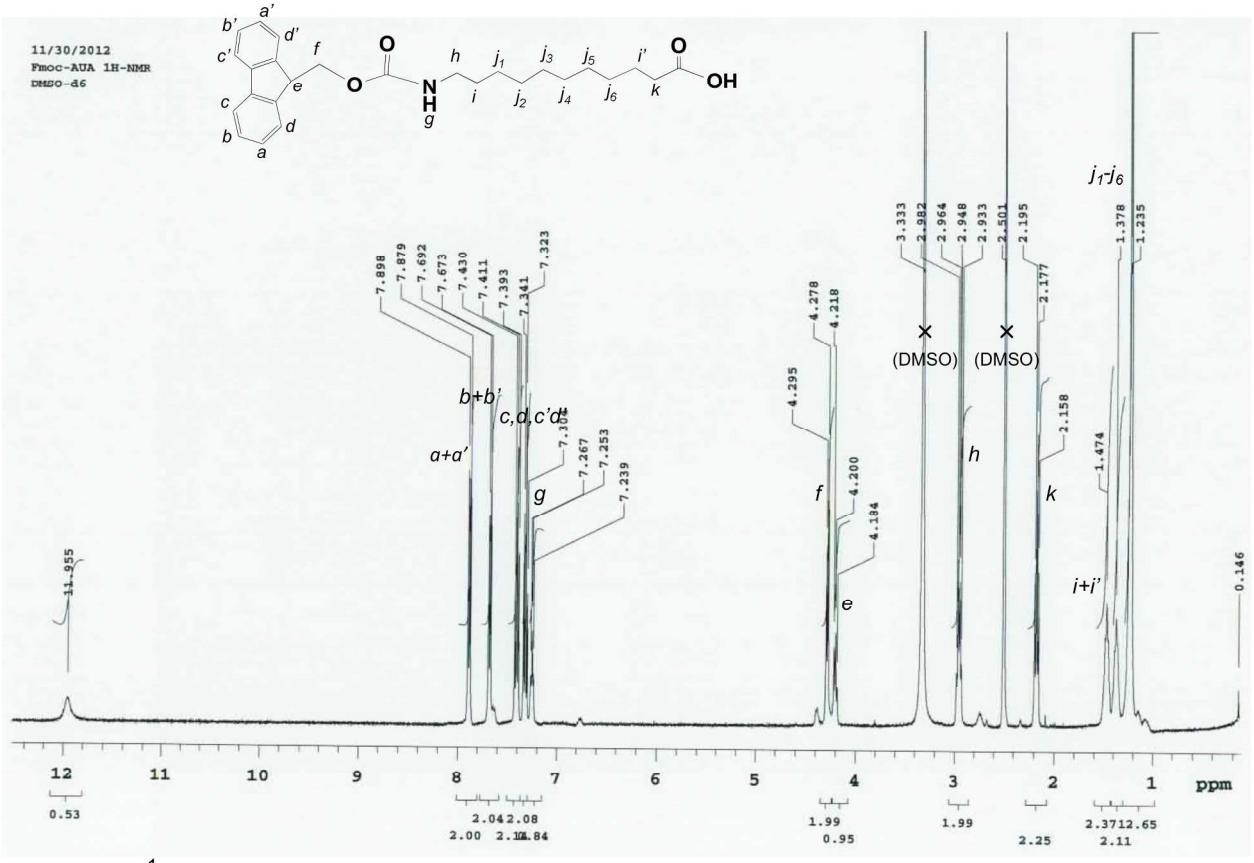

Figure S5: ^{1}H-NMR spectrum of Fmoc-aminoundecanoic acid (DMSO-d6, recorded on Mercury 400 spectrometer)

Characterization of unimers synthesized by solid phase peptide synthesis (SPPS)

Figures S6-S13 represent analytical HPLC and MALDI-ToF spectra of four unimers following solid phase peptide synthesis, cleavage, and preparative HPLC purification:

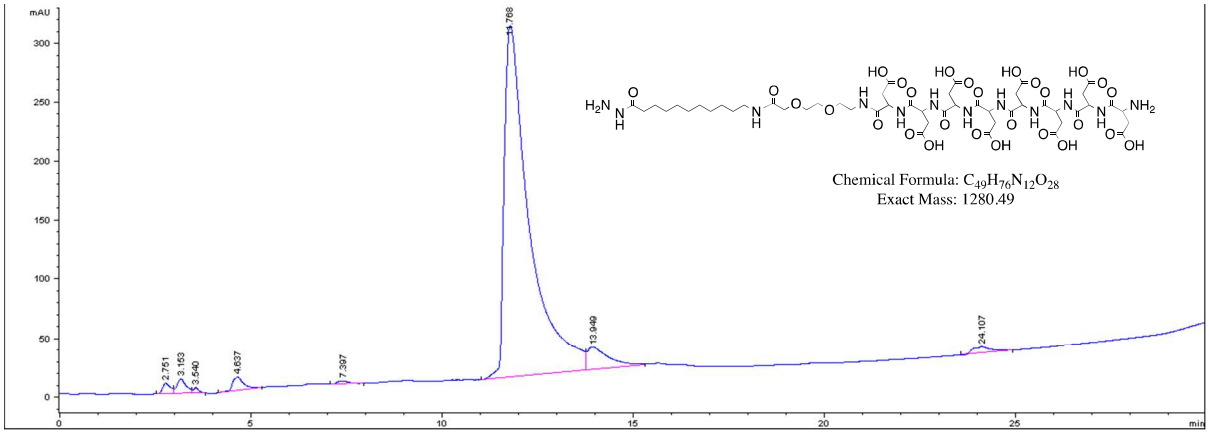

Figure S6: Structure and HPLC profile of A1-D8

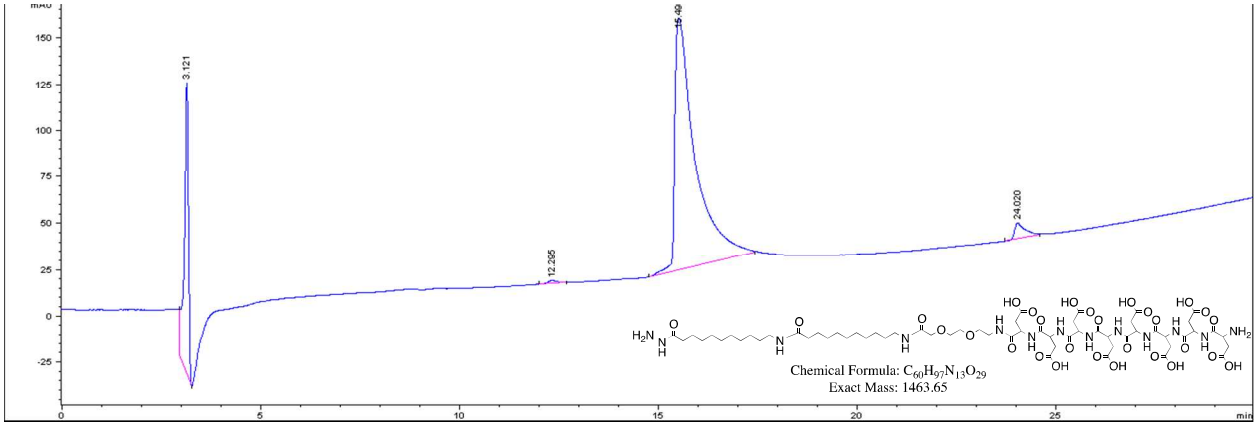

Figure S7: Structure and HPLC profile of A2-D8

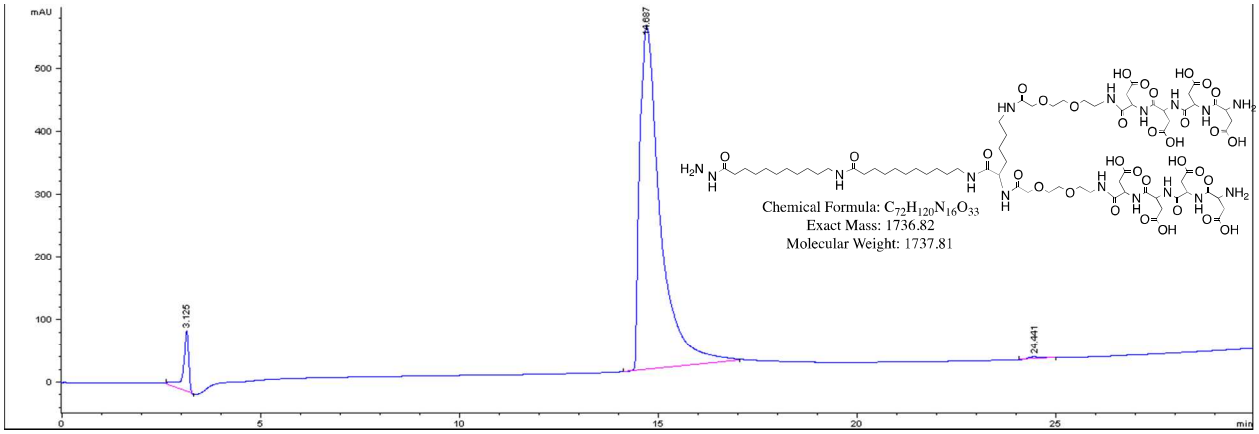

Figure S8: Structure and HPLC profile of A2-K-D4

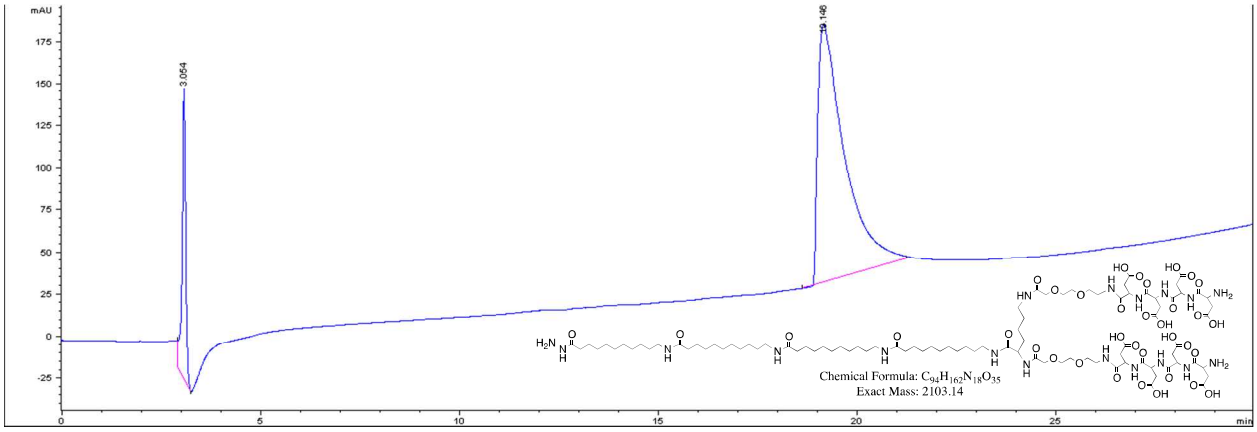

Figure S9: Structure and HPLC profile of A4-K-D4

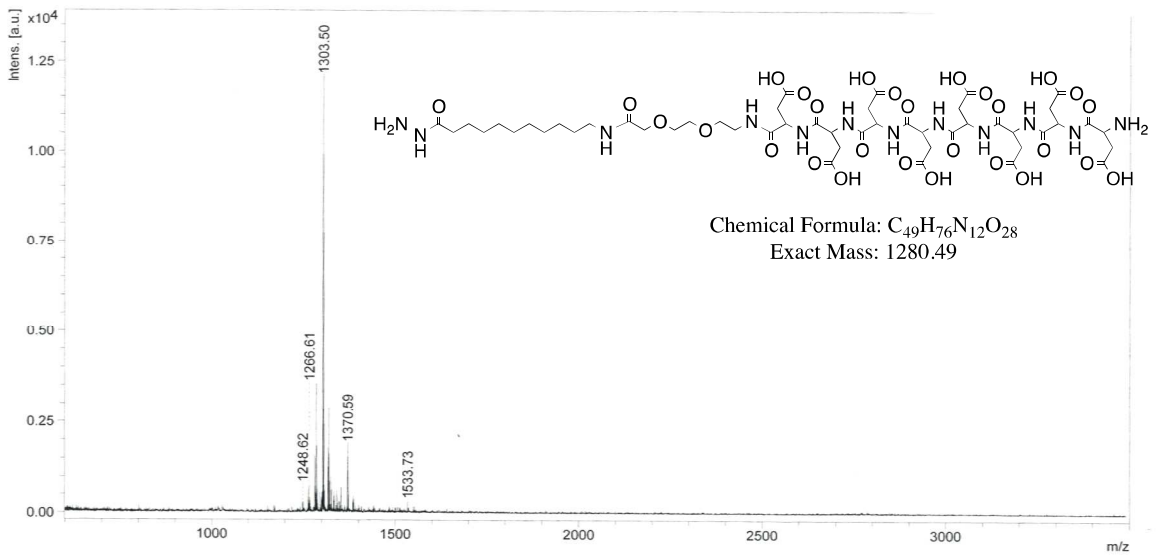

Figure S10: Structure and MALDI-ToF spectrum of A1-D8

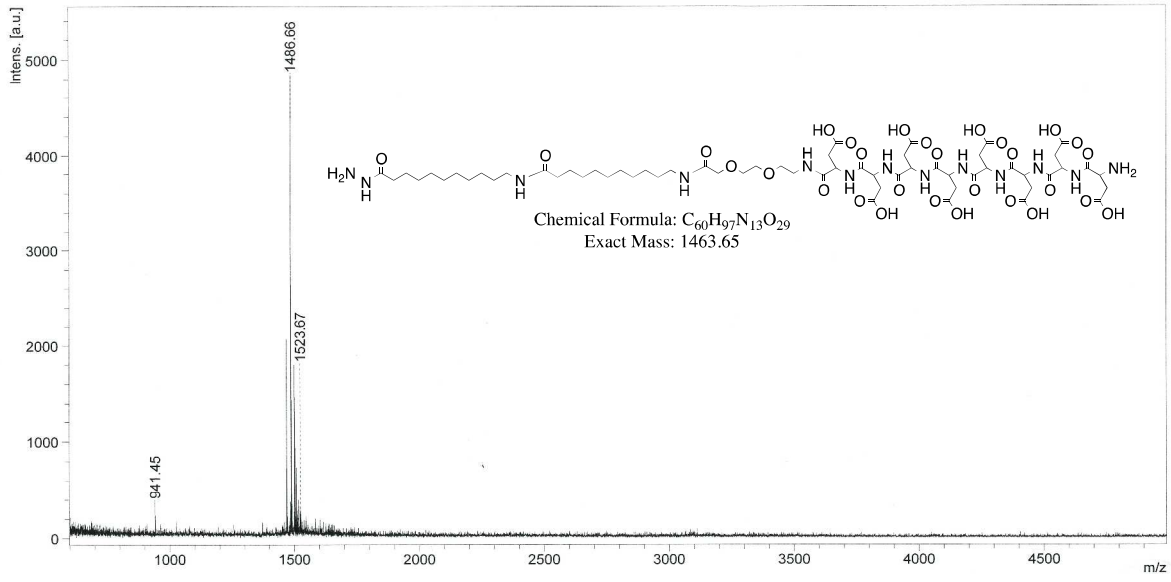

Figure S11: Structure and MALDI-ToF spectrum of A2-D8

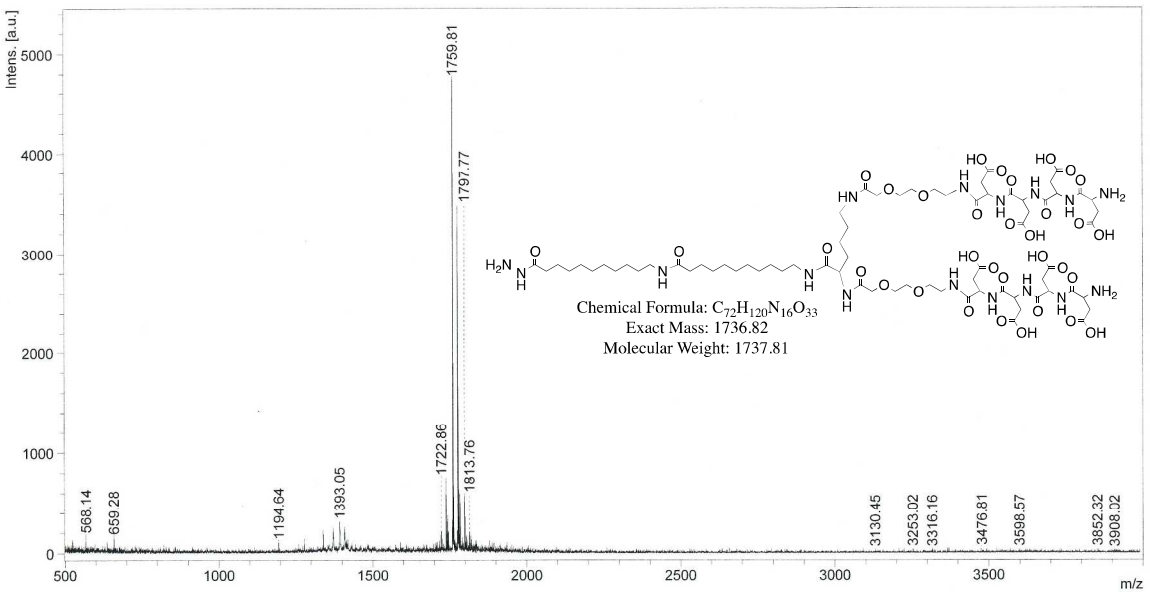

Figure S12: Structure and MALDI-ToF spectrum of A2-K-D4

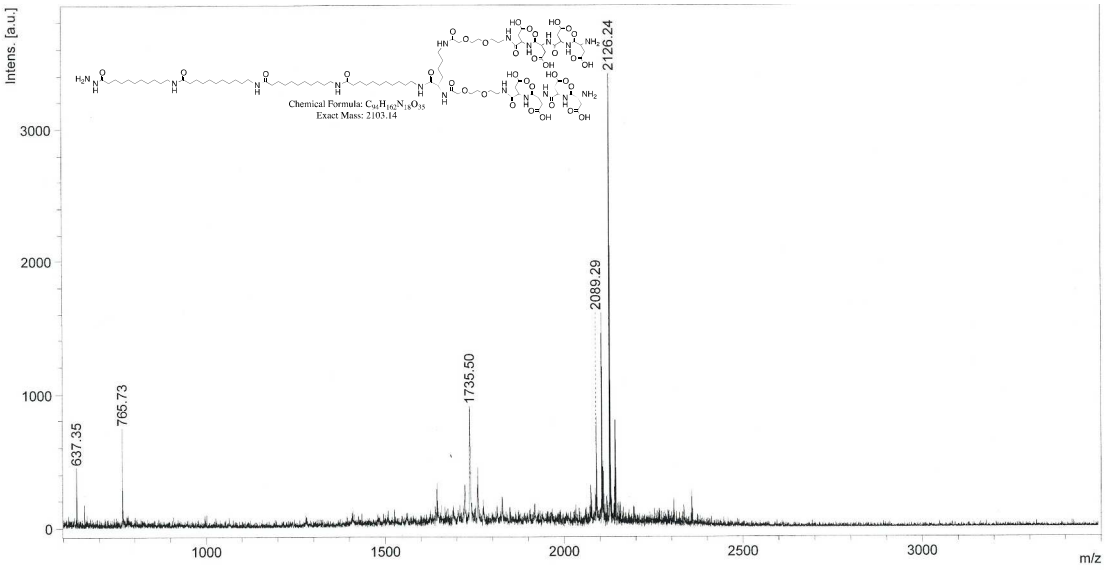

Figure S13: Structure and MALDI-ToF spectrum of A4-K-D4

Characterization of DOX – unimer conjugates

Below are HPLC profiles (S14-S17) of the four unimers (described above) following conjugation to DOX via hydrazone bond and purification on a LH20 column:

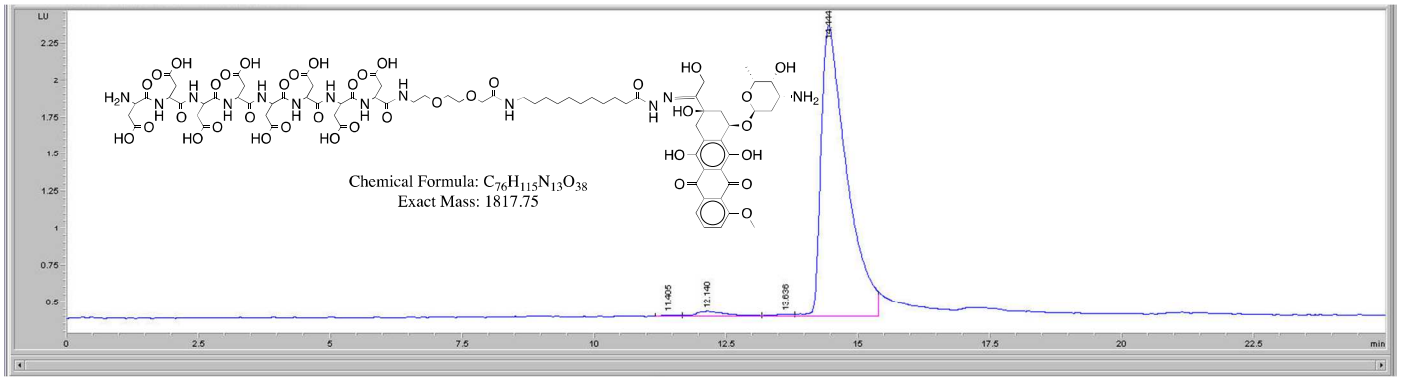

Figure S14: Chemical structure and HPLC profile of DOX-A1-D8

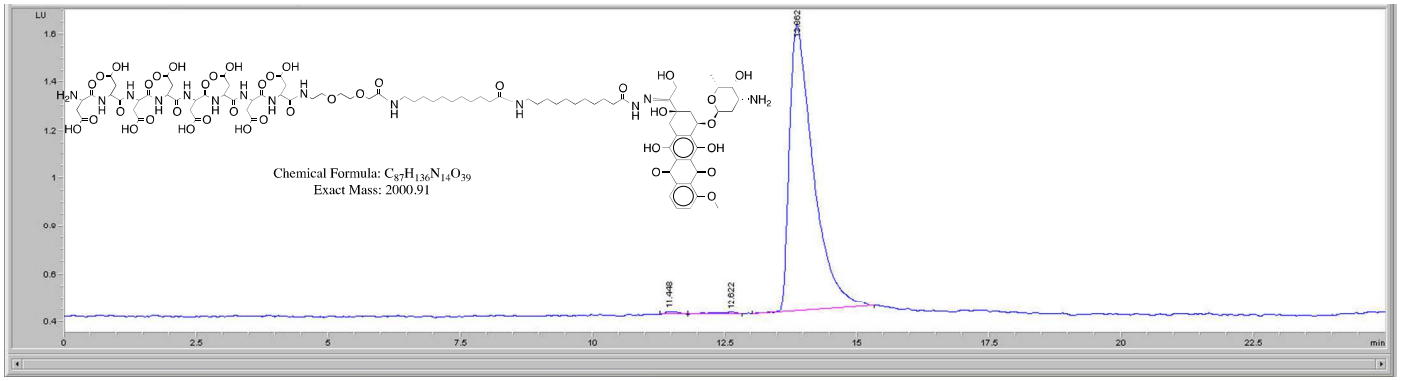

Figure S15: Chemical structure and HPLC profile of DOX-A2-D8

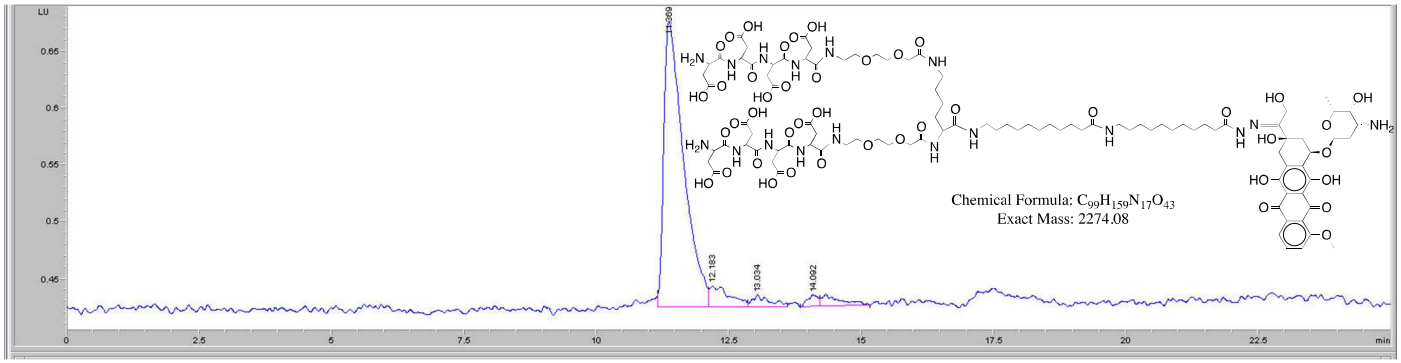

Figure S16: Chemical structure and HPLC profile of DOX-A2-K-D4

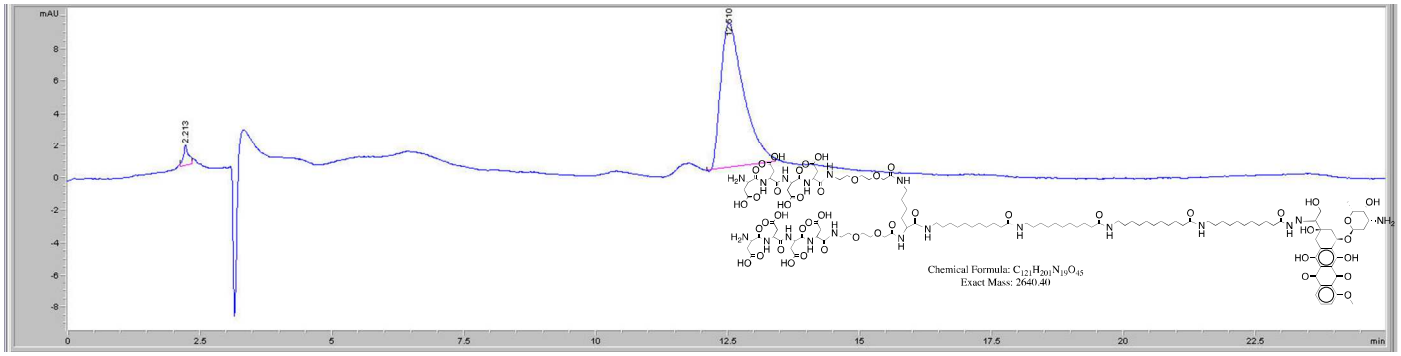

Figure S17: Chemical structure and HPLC profile of DOX-A4-K-D4