

Octreotide-Mediated Tumor-Targeted Drug Delivery via a Cleavable Doxorubicin–Peptide Conjugate

*Marco Lelle^a, Stefka Kaloyanova^a, Christoph Freidel^a, Marily Theodoropoulou^b, Michael
Musheev^c, Christof Niehrs^{c,d}, Günter Stalla^b and Kalina Peneva^{*a,e}*

^a Max Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

^b Max Planck Institute for Psychiatry, Kraepelinstraße 2, 80804 Munich, Germany

^c Institute of Molecular Biology, Ackermannweg 4, 55128 Mainz, Germany

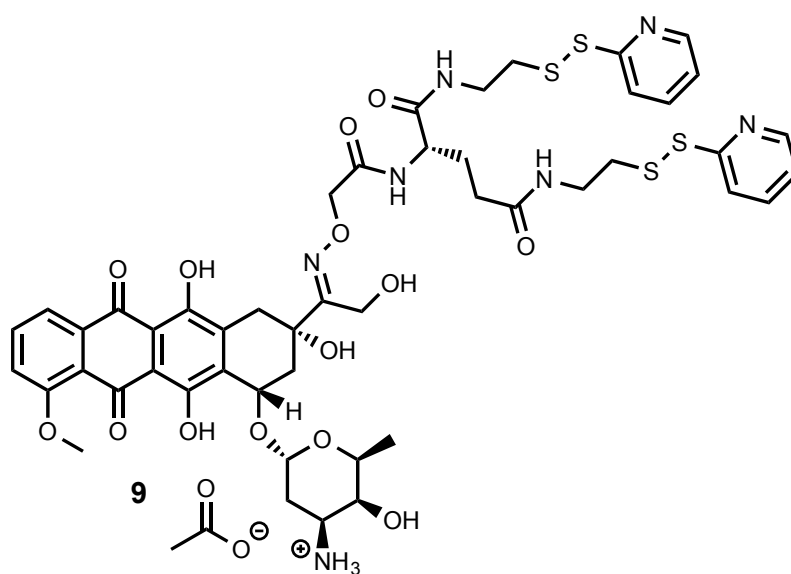
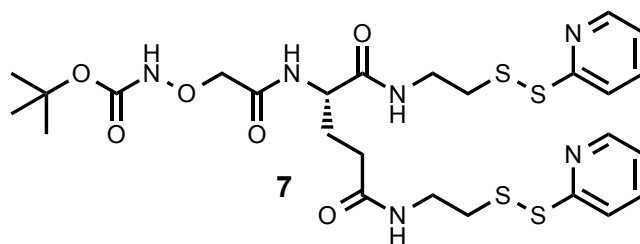
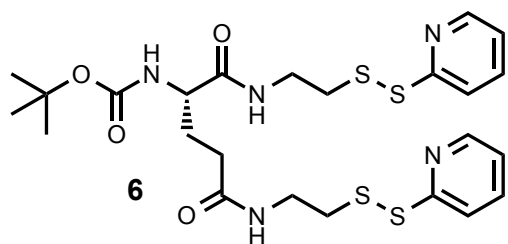
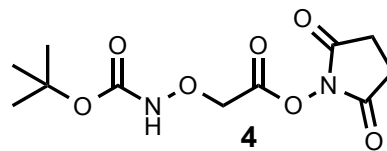
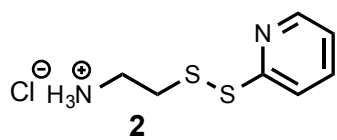
^d Division of Molecular Embryology, DKFZ-ZMBH Alliance, 69120 Heidelberg, Germany

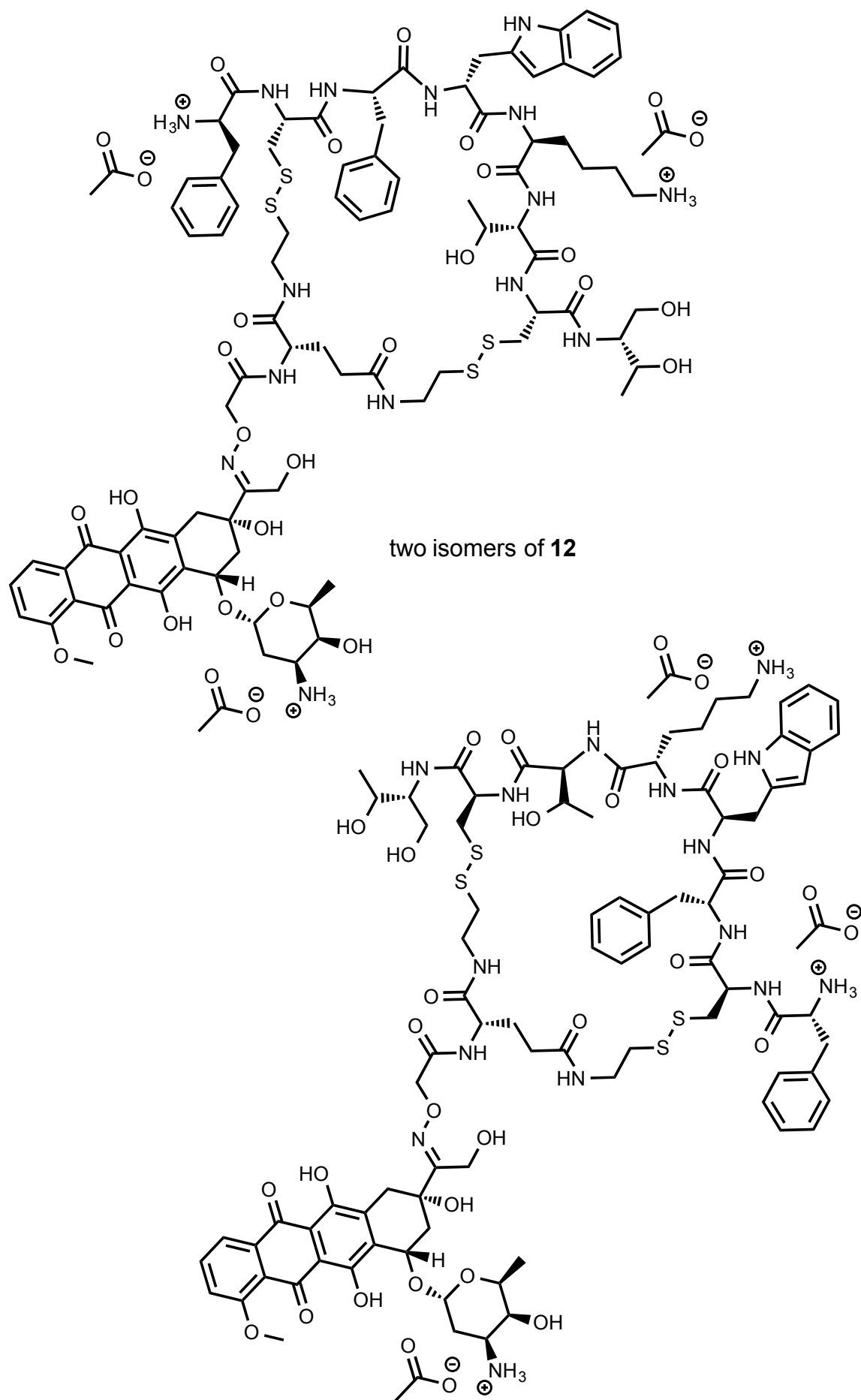
^e Institute of Organic Chemistry and Macromolecular Chemistry, Friedrich Schiller
University Jena, Lessingstrasse 8, 07743 Jena

*To whom correspondence should be addressed. Phone: +496131379136;

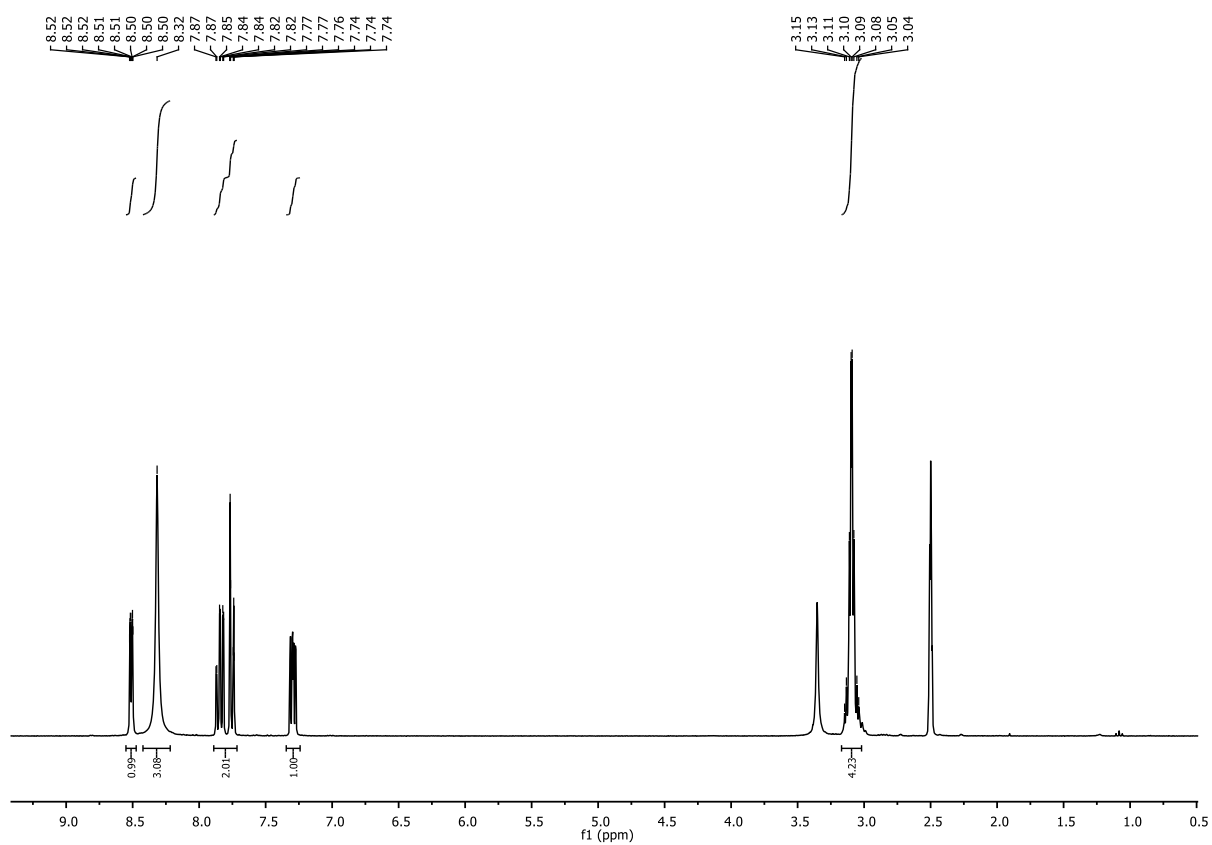
E-mail: peneva@mpip-mainz.mpg.de

Synthesized compounds:

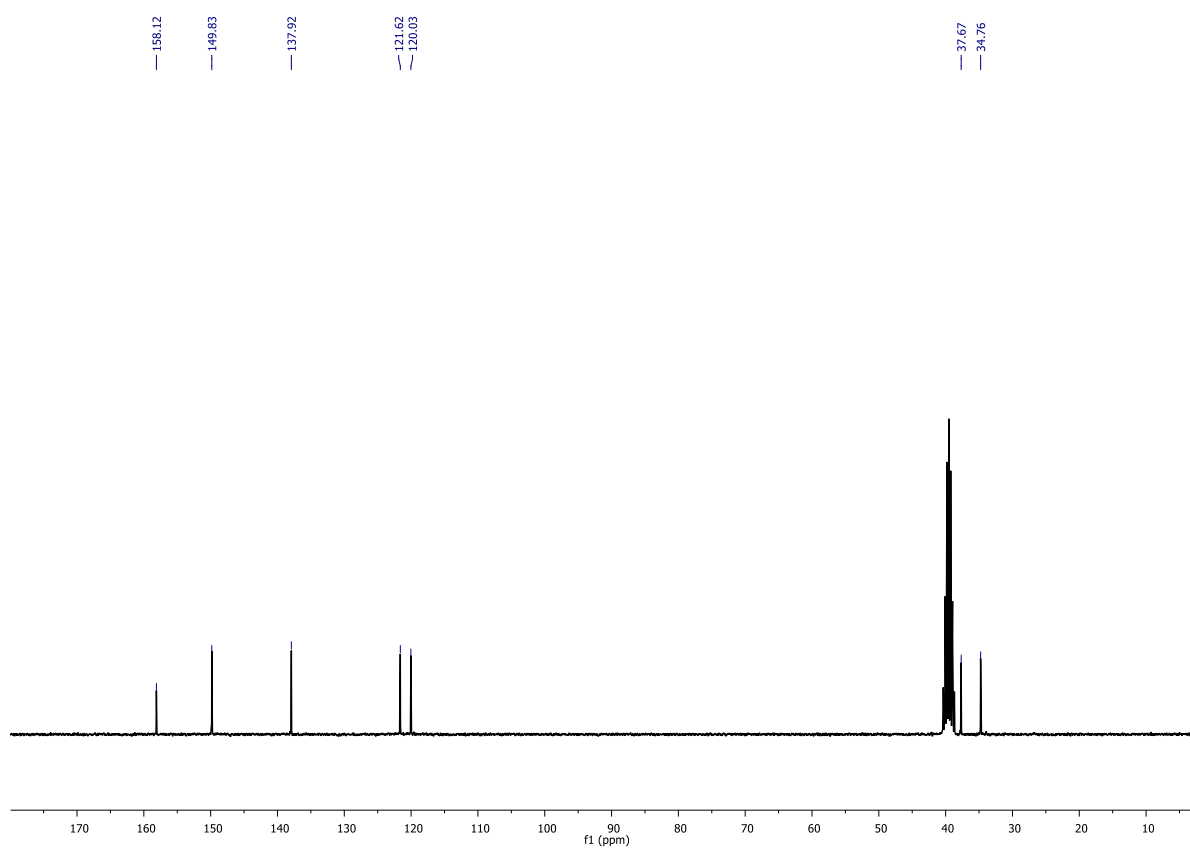




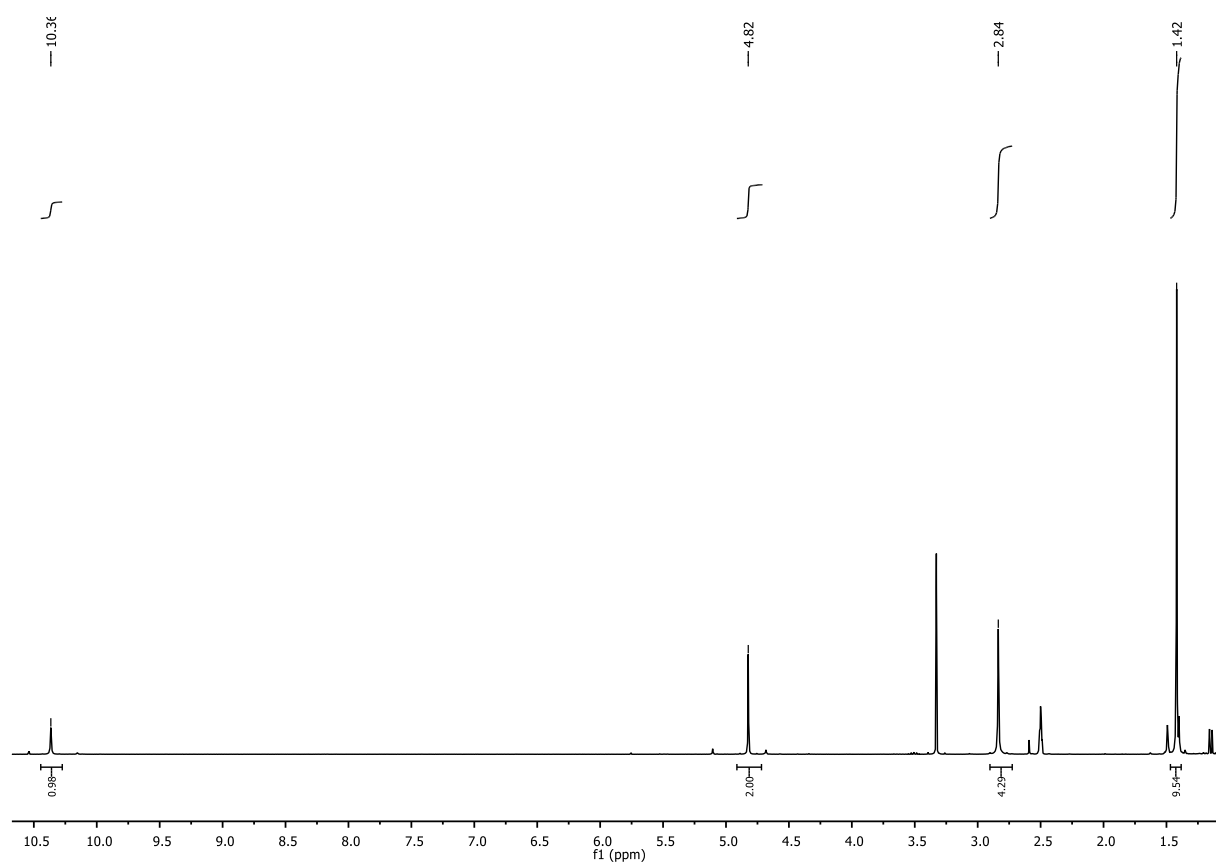
^1H NMR spectrum of compound **2** recorded in $\text{DMSO-}d^6$ at 300 MHz



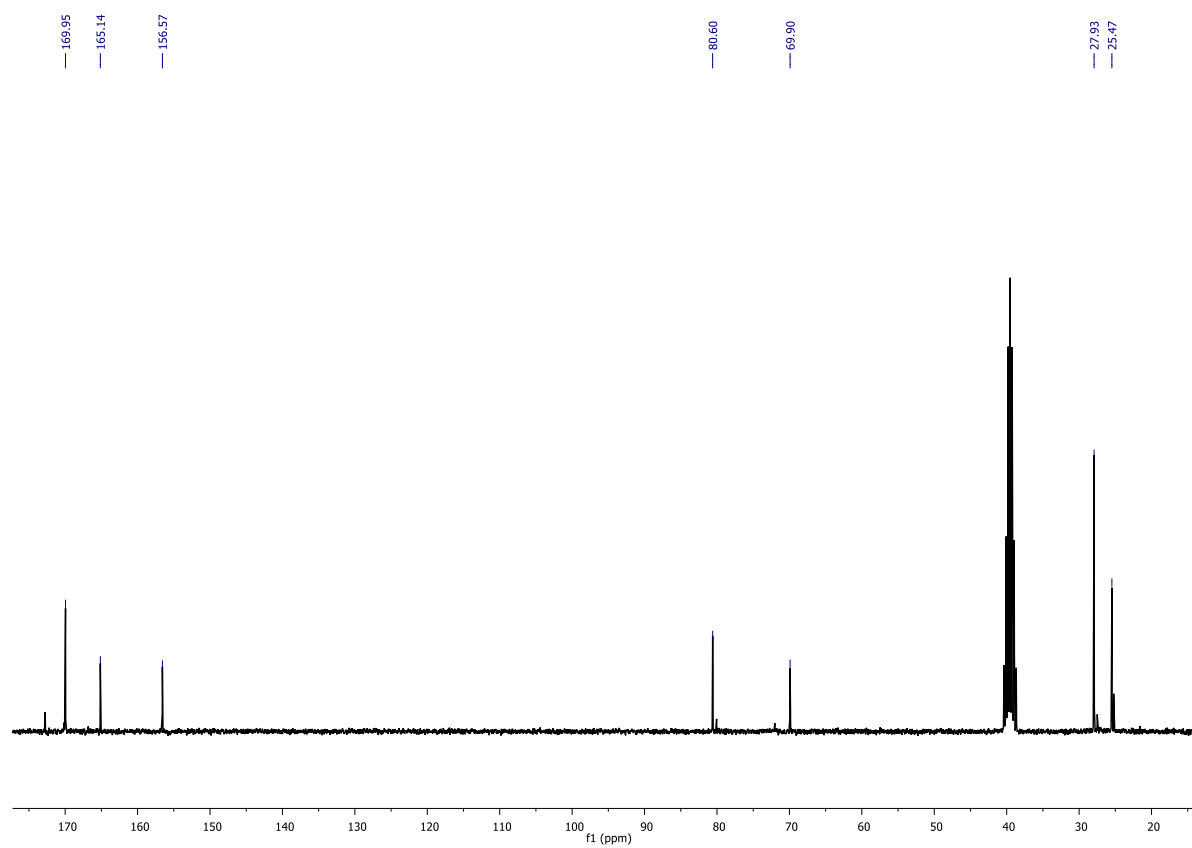
^{13}C NMR spectrum of compound **2** recorded in $\text{DMSO-}d^6$ at 75 MHz



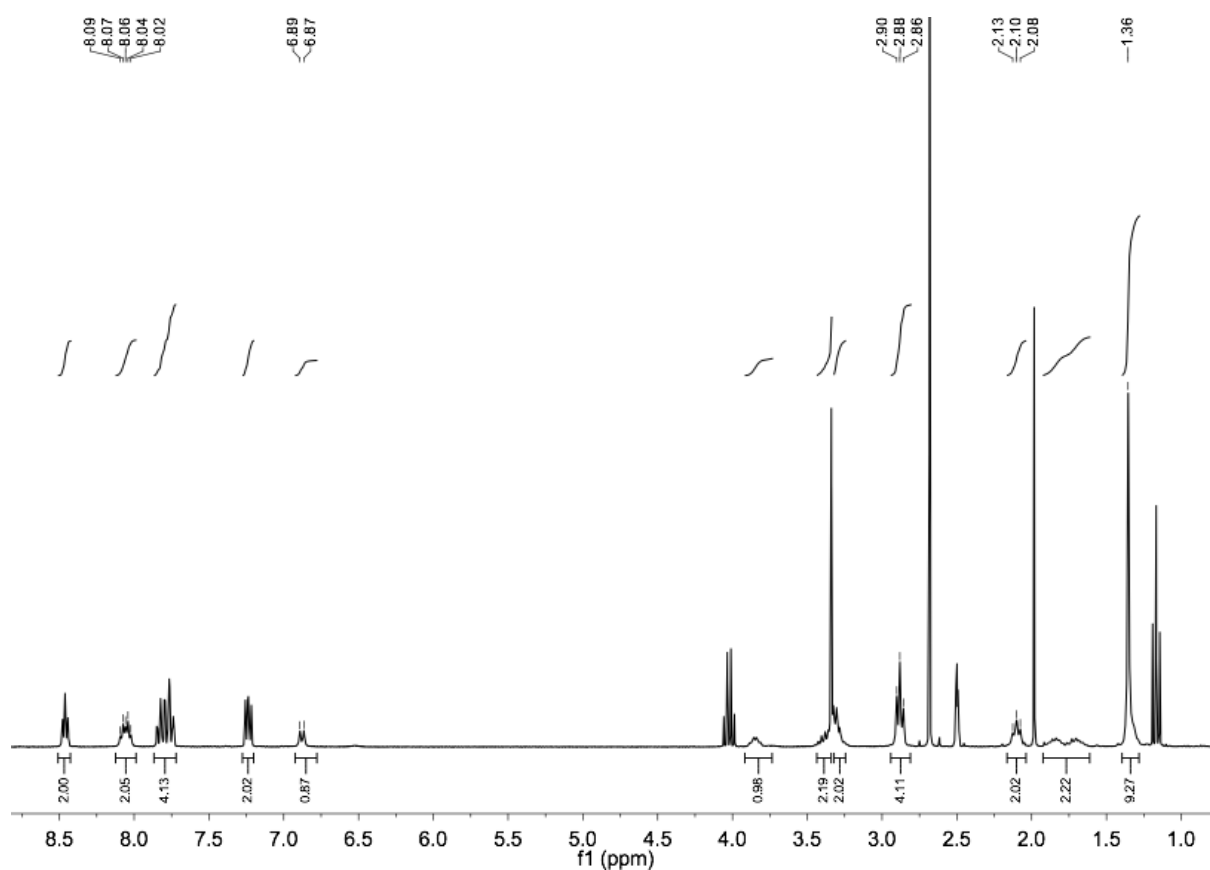
^1H NMR spectrum of compound **4** recorded in $\text{DMSO}-d^6$ at 300 MHz



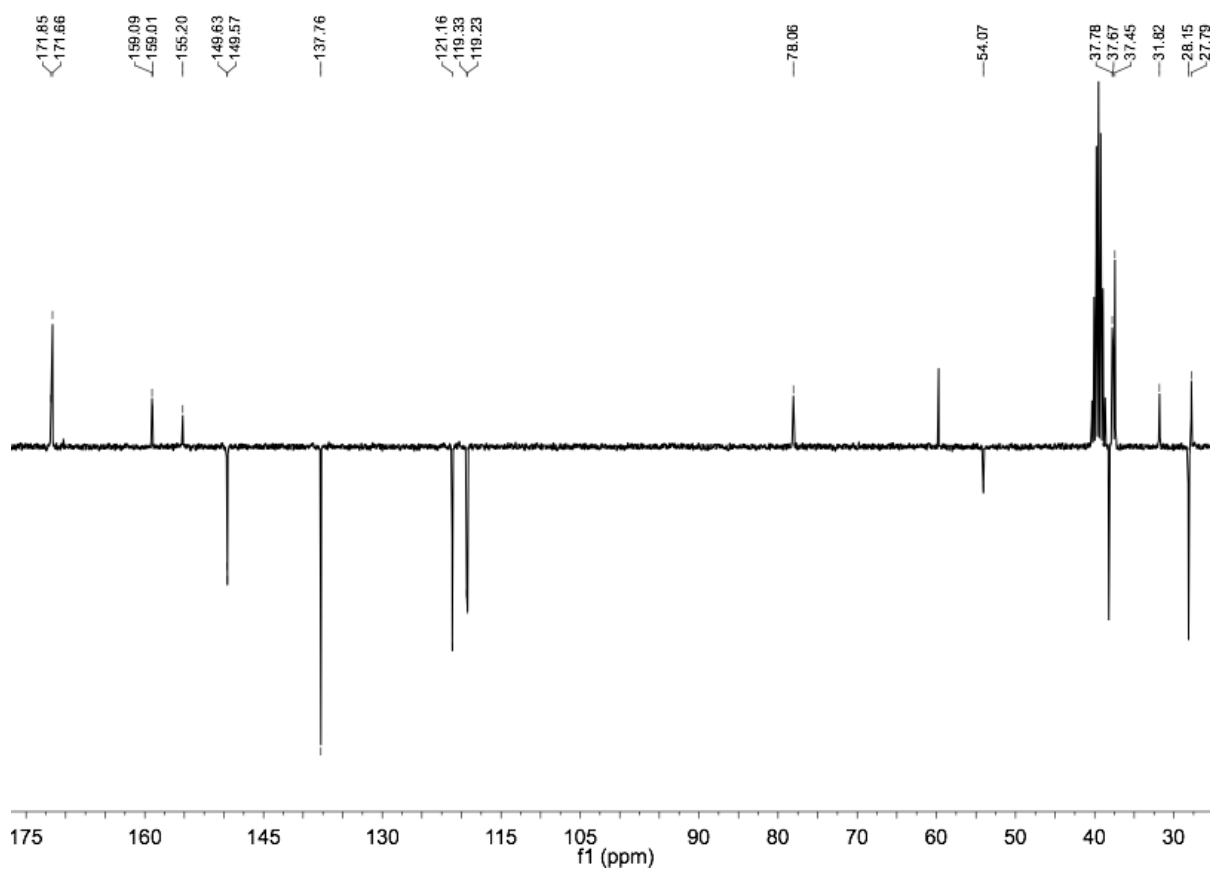
^{13}C NMR spectrum of compound **4** recorded in $\text{DMSO}-d^6$ at 75 MHz



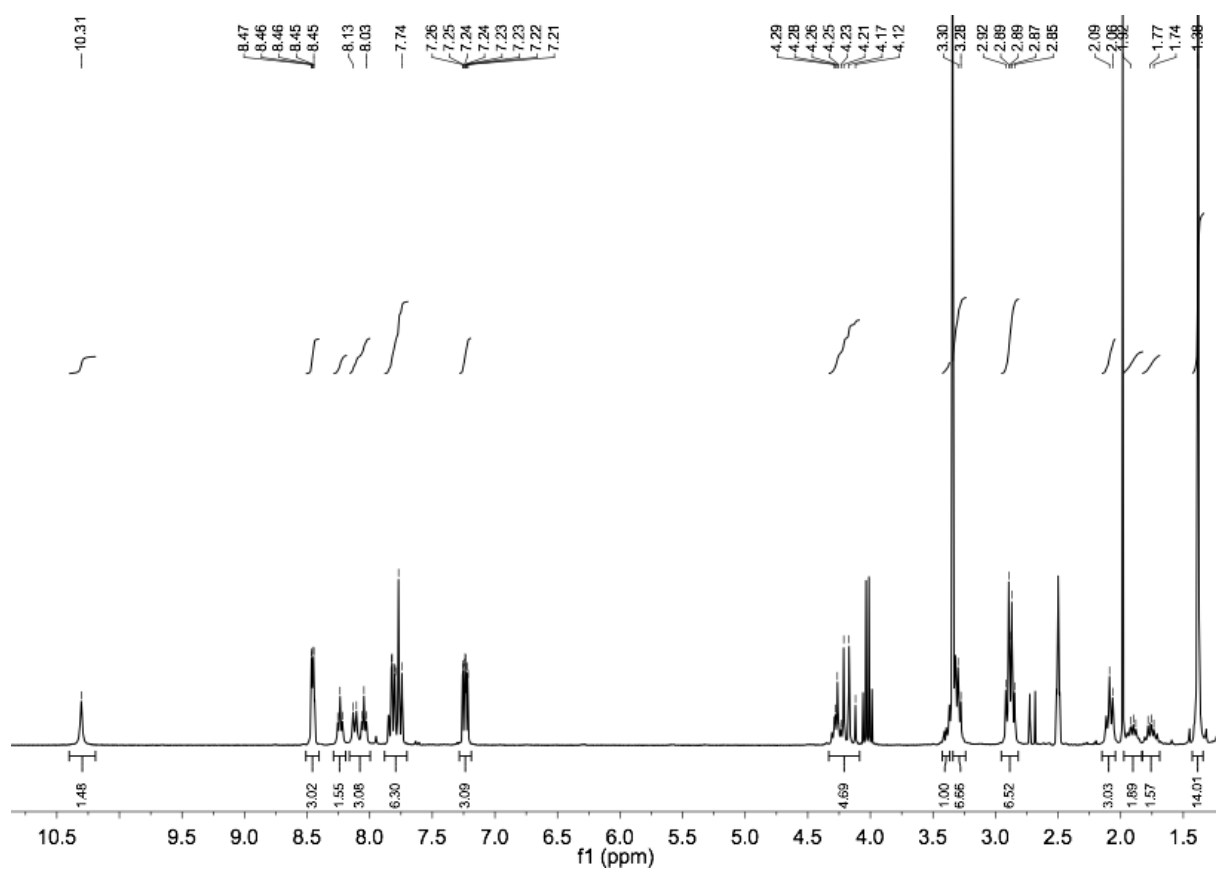
^1H NMR spectrum of compound **6** recorded in $\text{DMSO-}d^6$ at 300 MHz



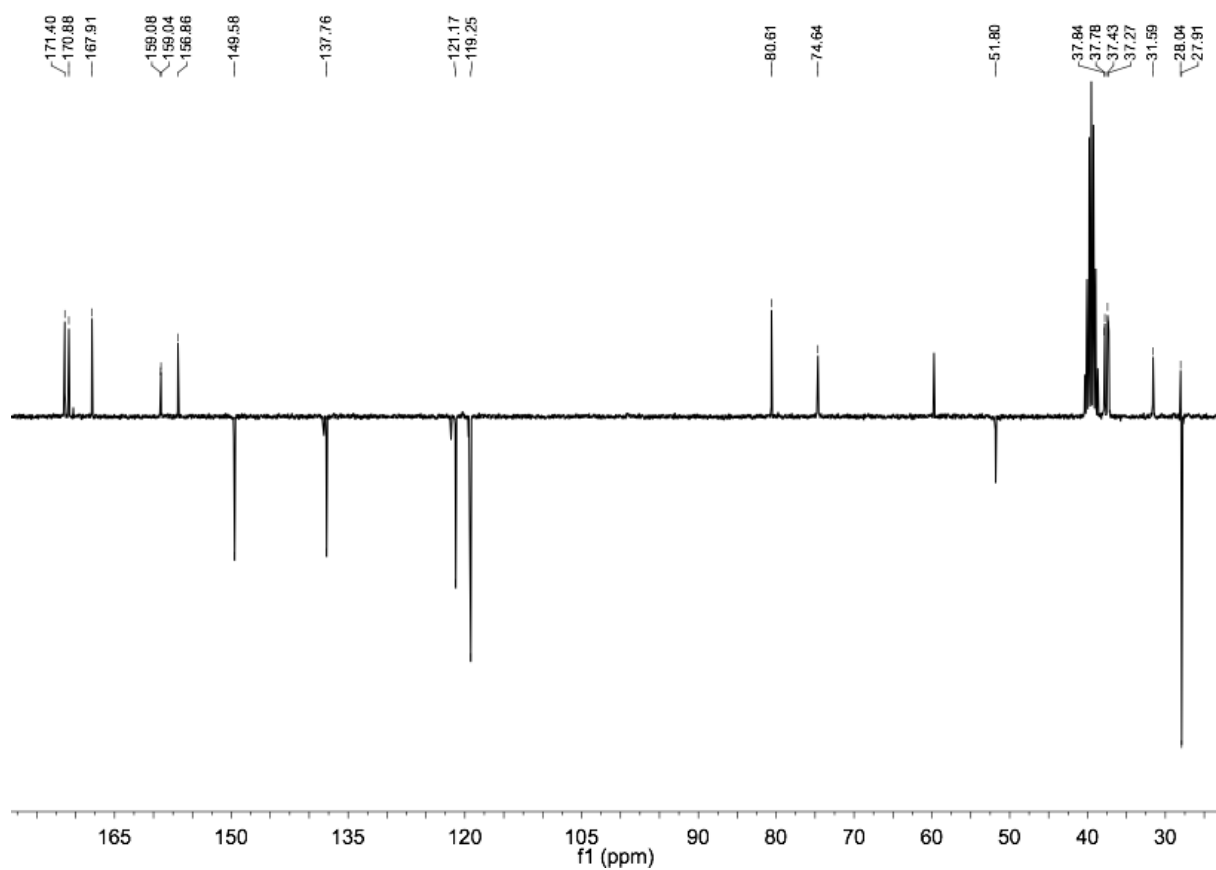
^{13}C NMR spectrum of compound **6** recorded in $\text{DMSO-}d^6$ at 75 MHz



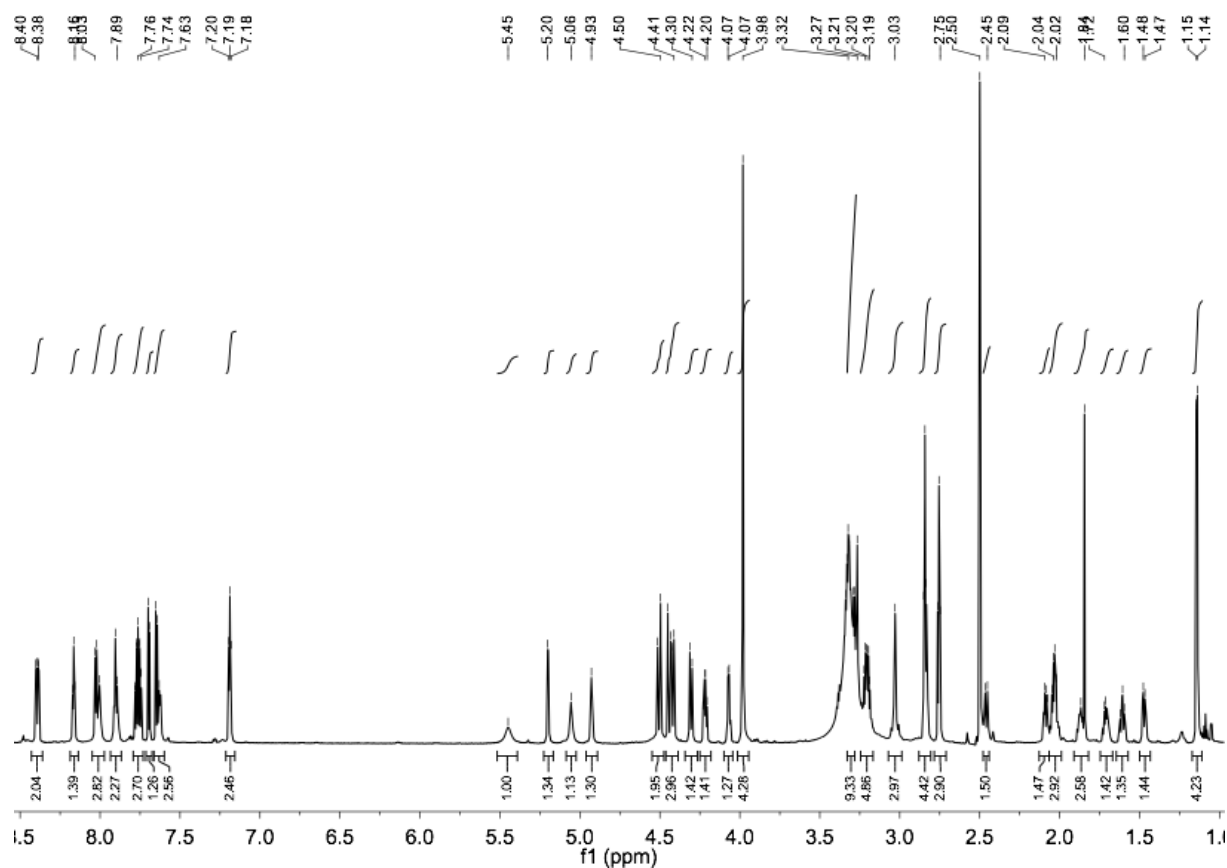
^1H NMR spectrum of compound **7** recorded in $\text{DMSO}-d_6$ at 300 MHz



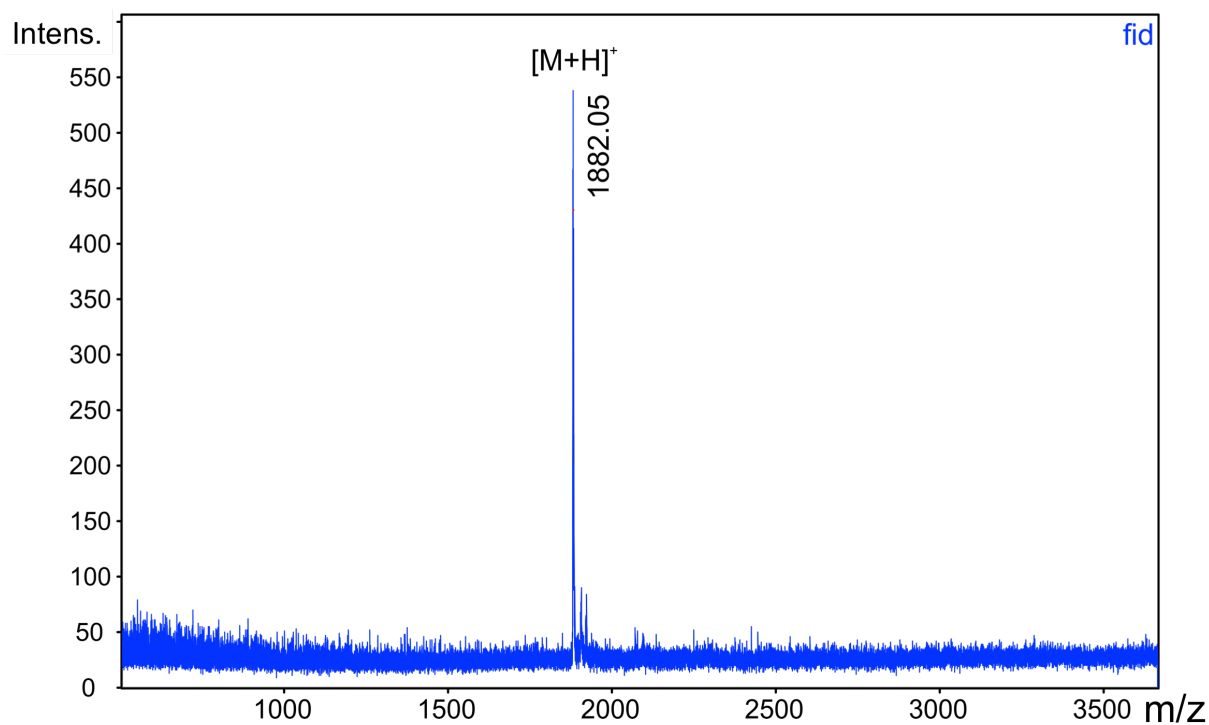
^{13}C NMR spectrum of compound **7** recorded in $\text{DMSO}-d_6$ at 75 MHz



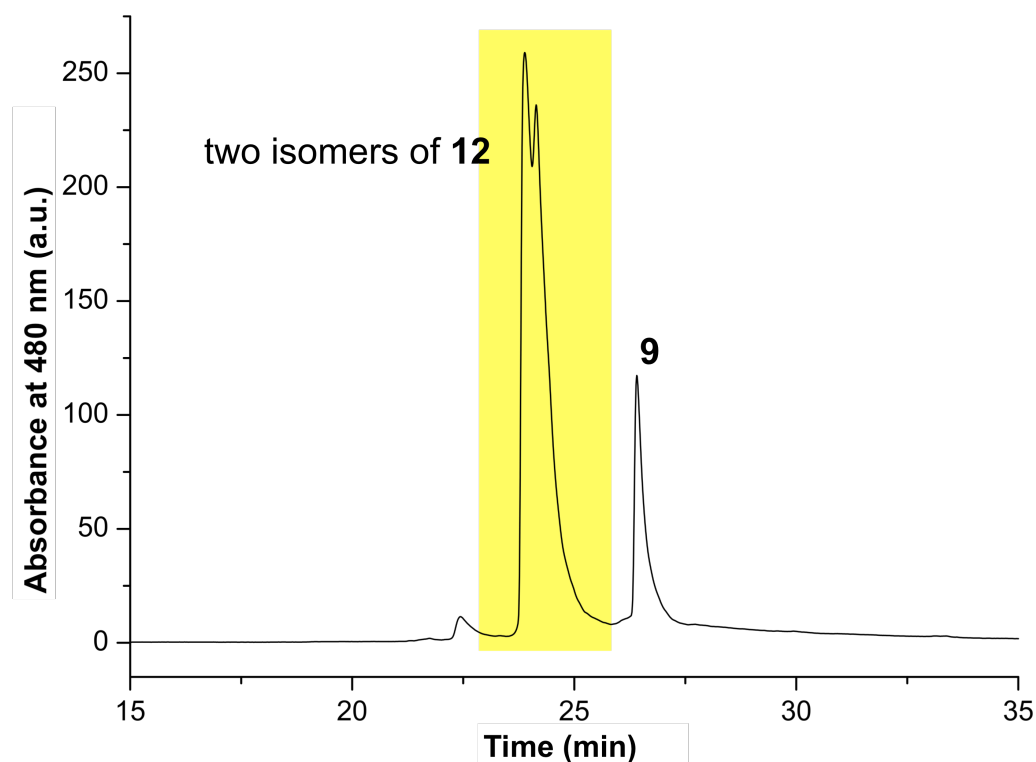
^1H NMR spectrum of compound **9** recorded in $\text{DMSO}-d_6$ at 850 MHz



MALDI-TOF mass spectrum of compound **12** (matrix: α -cyano-4-hydroxycinnamic acid)



HPLC chromatogram of a sample from the reaction mixture (after 5 minutes) of the doxorubicin-octreotide conjugate formation, which is showing the two narrow peaks for both isomers of the hybrid **12** as well as the peak for the unreacted doxorubicin derivative **9**.



Cytotoxic effect of Dox-Oct conjugate (**12**) on A549 adenocarcinomic human alveolar basal epithelial cells (72 h after incubation with the compound) as determined by the CellTiter-Glo[®] luminescent cell viability assay.

