

Design, Synthesis, and Biological Evaluation of Estrogen Receptor Antagonist–Drug Bioconjugate for Targeting Breast Cancer Cell

Kinh-Luan Dao,[‡]Rupa Sawant,[‡]James A. Hendricks, Victoria Ronga, *Robert N. Hanson,
[‡]Vladimir Torchilin

Department of Chemistry and Chemical Biology, 360 Huntington Blvd, Northeastern University,
Boston Massachusetts 02115-50000

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*Author to whom correspondence should be addressed: (Prof. Robert Hanson) Email:

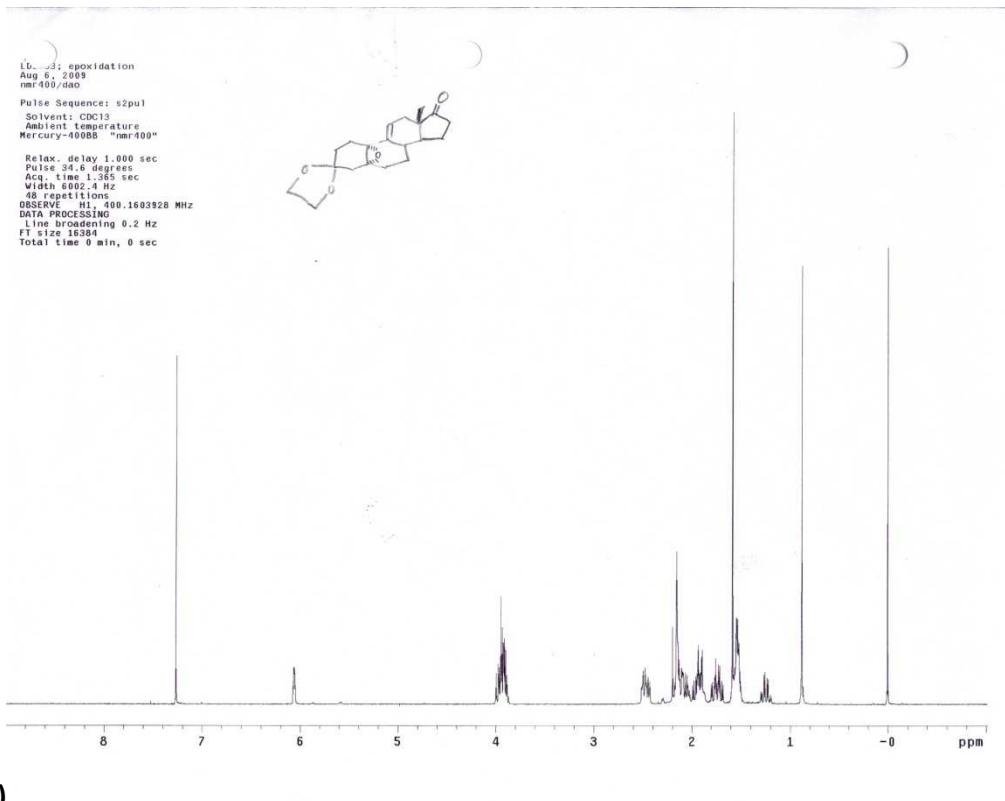
r.hanson@neu.edu. Tel: 617-373-3313; Fax: 617-373-3879.

*Bioorganic and Organic Chemistry Laboratory, Chemistry and Chemical Biology Department

‡Center for Pharmaceutical Biotechnology and Nanomedicine, Pharmaceutical Science Department

¥ Abbreviations: estrogen receptor (AE), tetraethylene glycol (TEG), tamoxifen (TAM), doxorubicin (DOX), estradiol (E₂), antiestrogen-doxorubicin hybrid (AE-DOX), antiestrogen-tamoxifen hybrid (AE-TAM), azido-tamoxifen (N₃-TAM), alkynated-doxorubicin (Ak-DOX), azido-antiestrogen (N₃-AE).

Figure S1: ¹H NMR of 3,3-ethylenedioxy-5(10)-α-epoxy-estr-9(11)-ene



(2α)

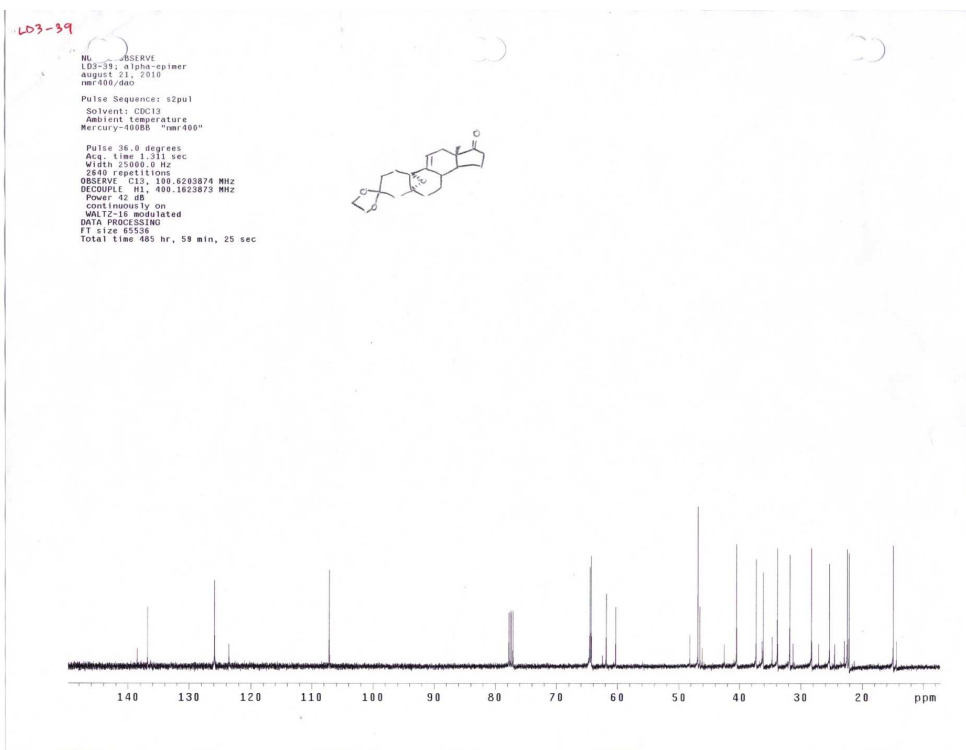


Figure S2: ¹³C NMR of 3,3-ethylenedioxy-5(10)-α-epoxy-estr-9(11)-ene (2α)

Figure S3: ^1H NMR of 11 β -(4-Hydroxy-phenyl)-estra-4,9-diene-3,17-dione (3)

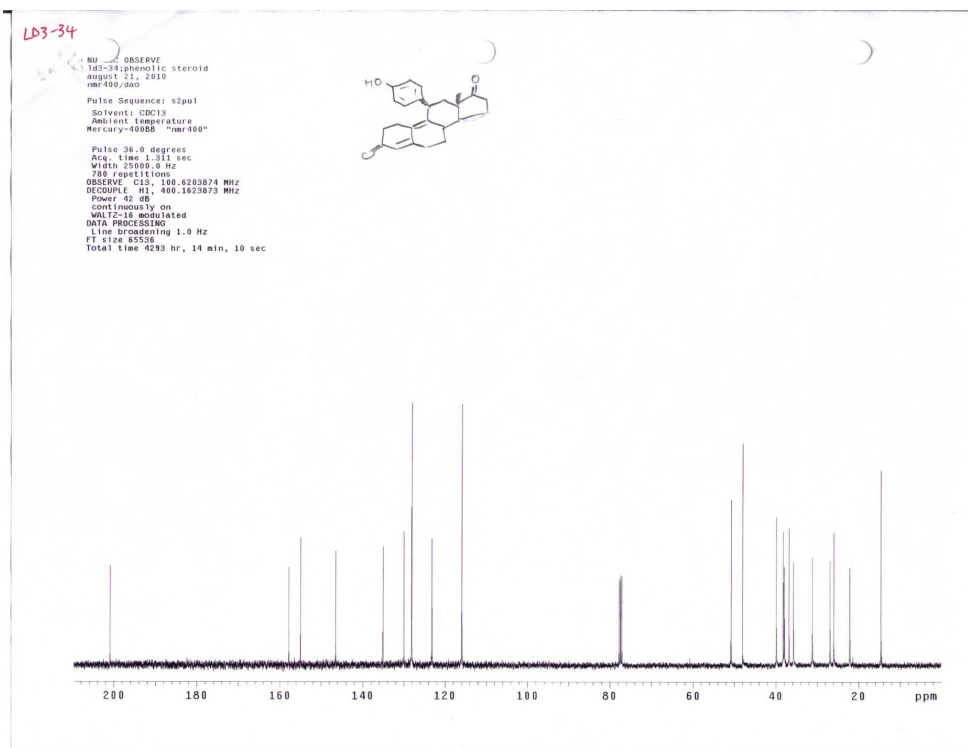
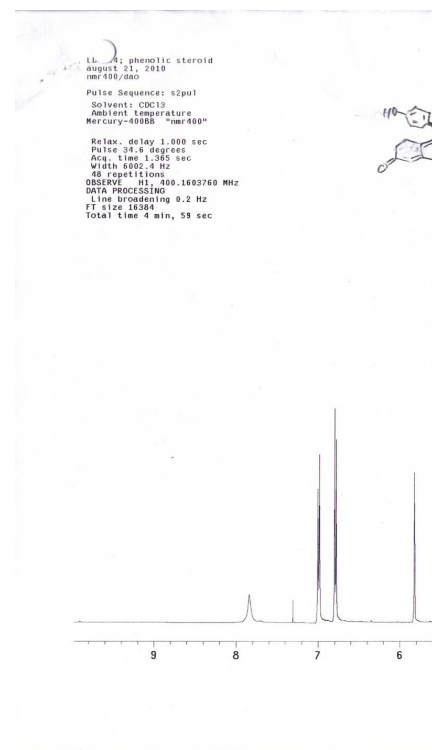


Figure S4: ^{13}C NMR of 11 β -(4-Hydroxy-phenyl)-estra-4,9-diene-3,17-dione (3)

Figure S5: ^1H NMR of 11β -[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-4,9-diene-3,17-dione (4)

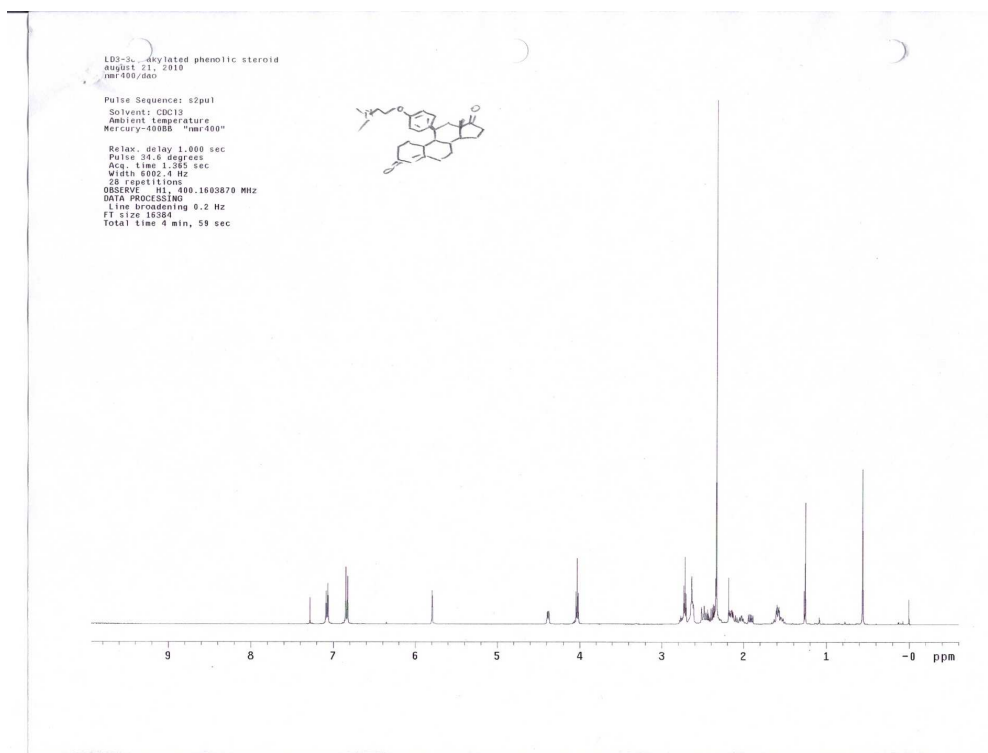
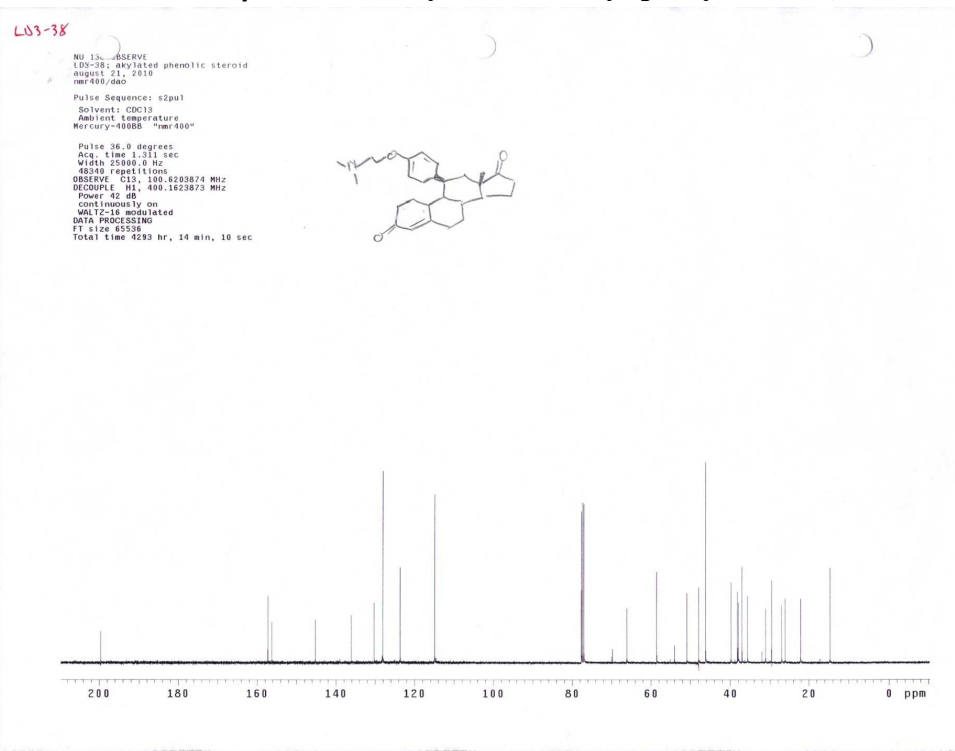


Figure S6: ^{13}C NMR of 11 β -[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-4,9-diene-3,17-dione



(4)

Figure S7: ^1H NMR of 3-Acetoxy-11 β -[4-(2-dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-17-one(5)

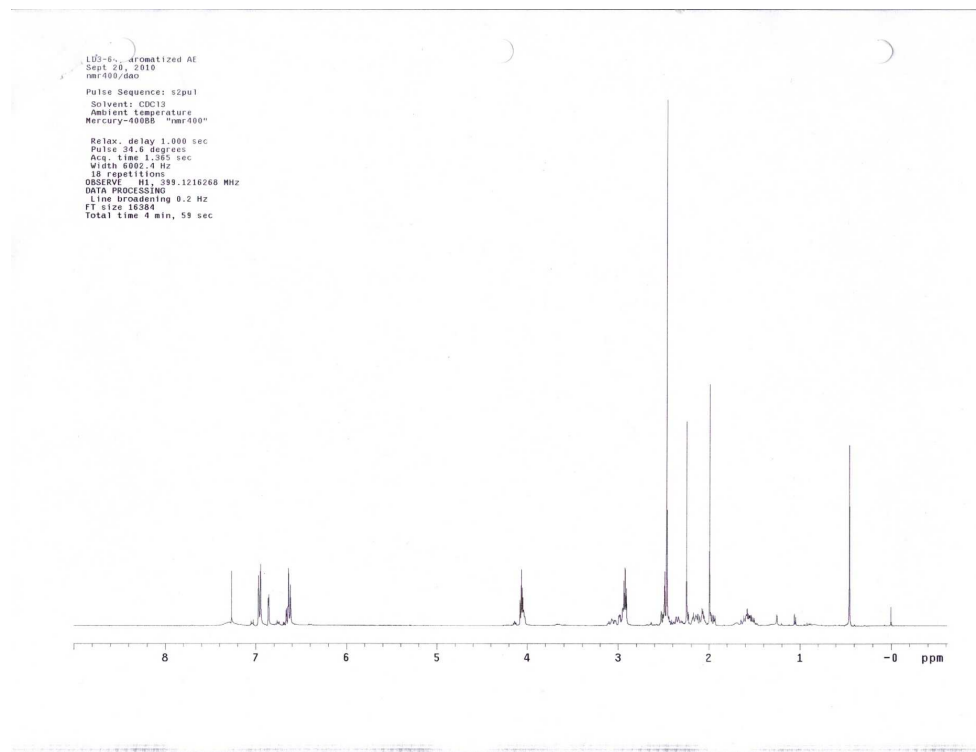
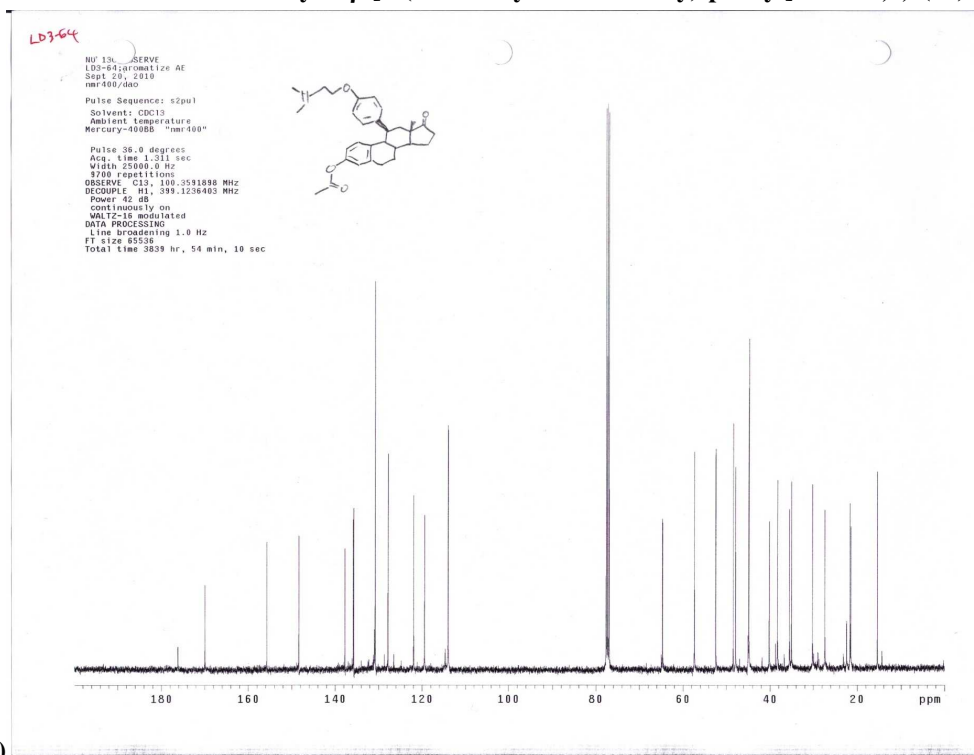


Figure S8: ^{13}C NMR of 3-Acetoxy-11 β -[4-(2-dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-17-



one(5)

Figure S9: ^1H NMR of 11 β -[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17 β -diol (6)

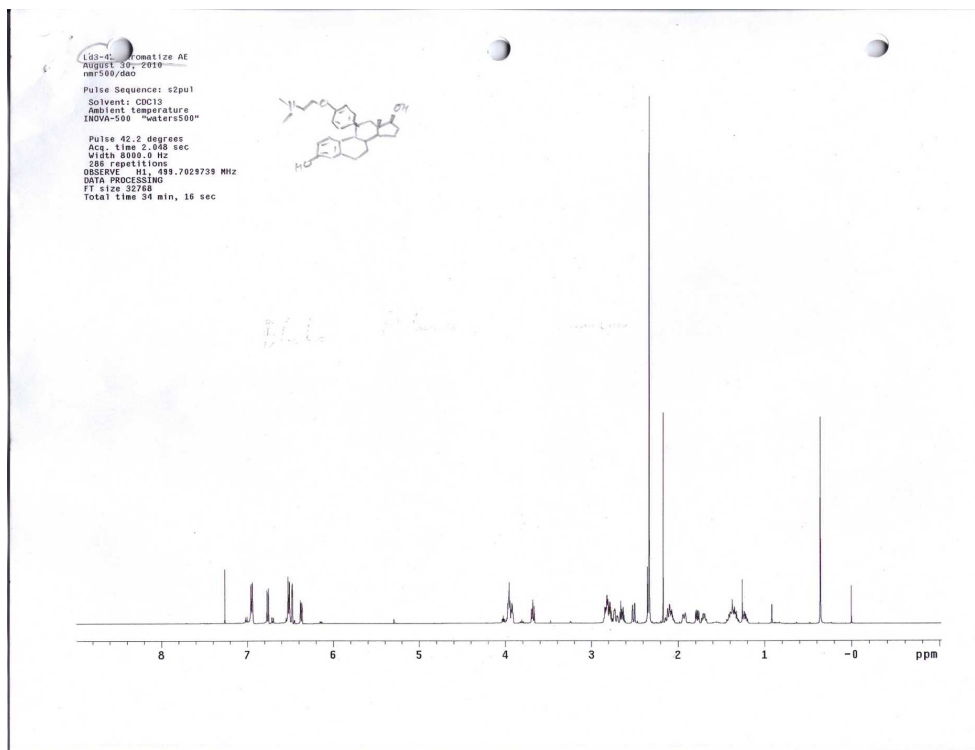


Figure S10: ^{13}C NMR of 11 β -[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17 β -diol

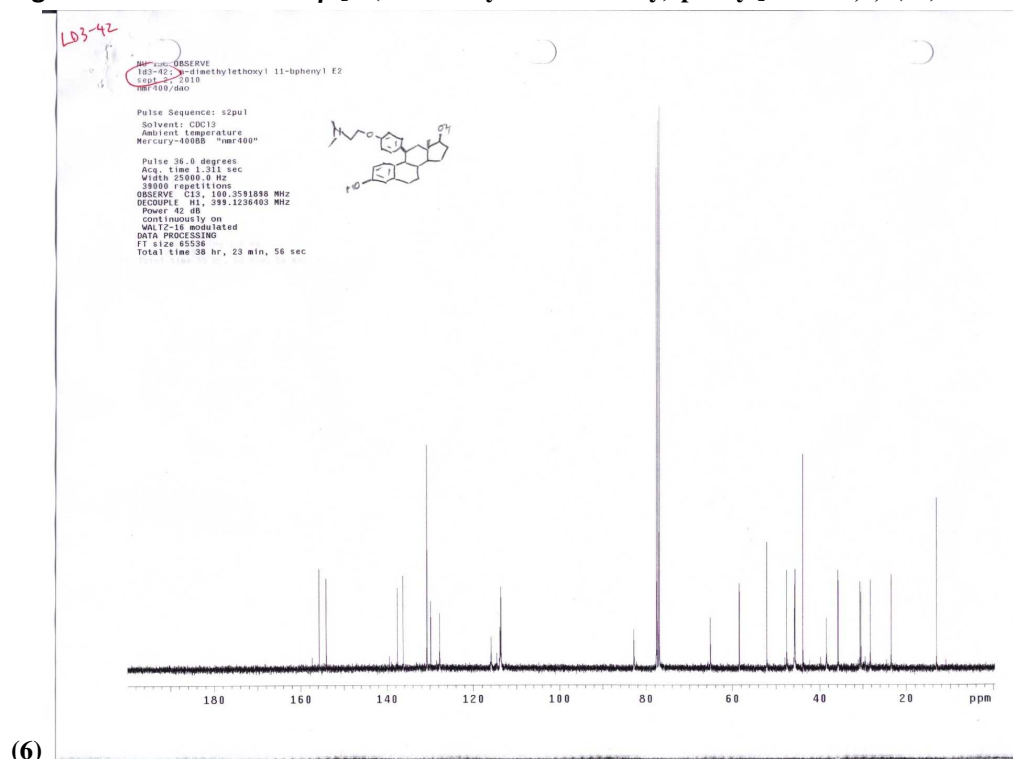


Figure S11: ^1H NMR of 11 β -[4-(2-methylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17 β -diol (7)

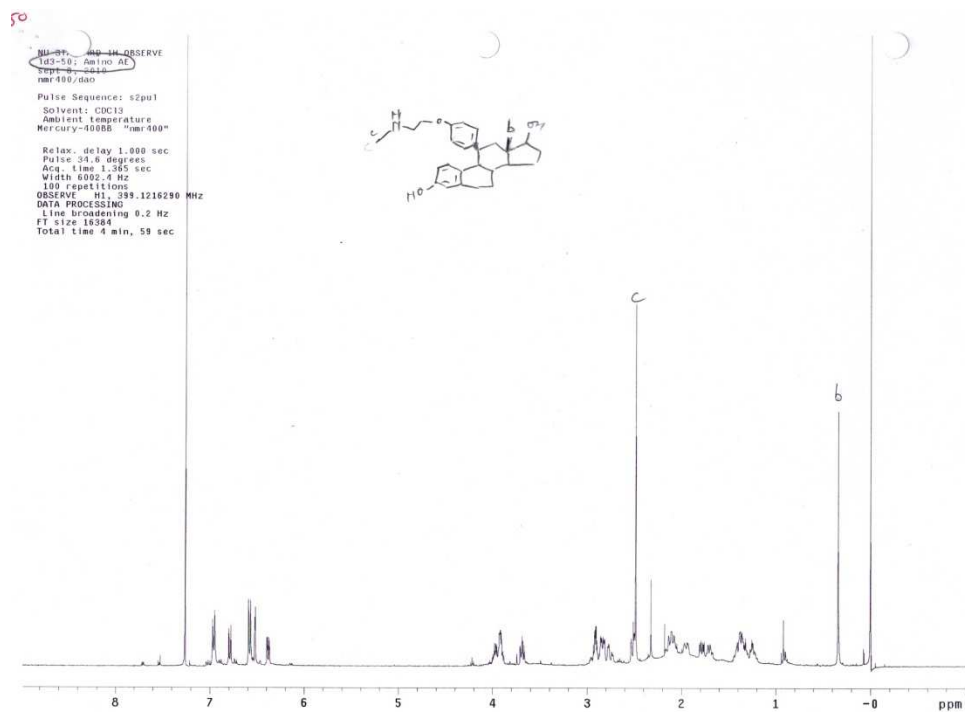


Figure S12: ^{13}C NMR of 11 β -[4-(2-methylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17 β -diol (7)

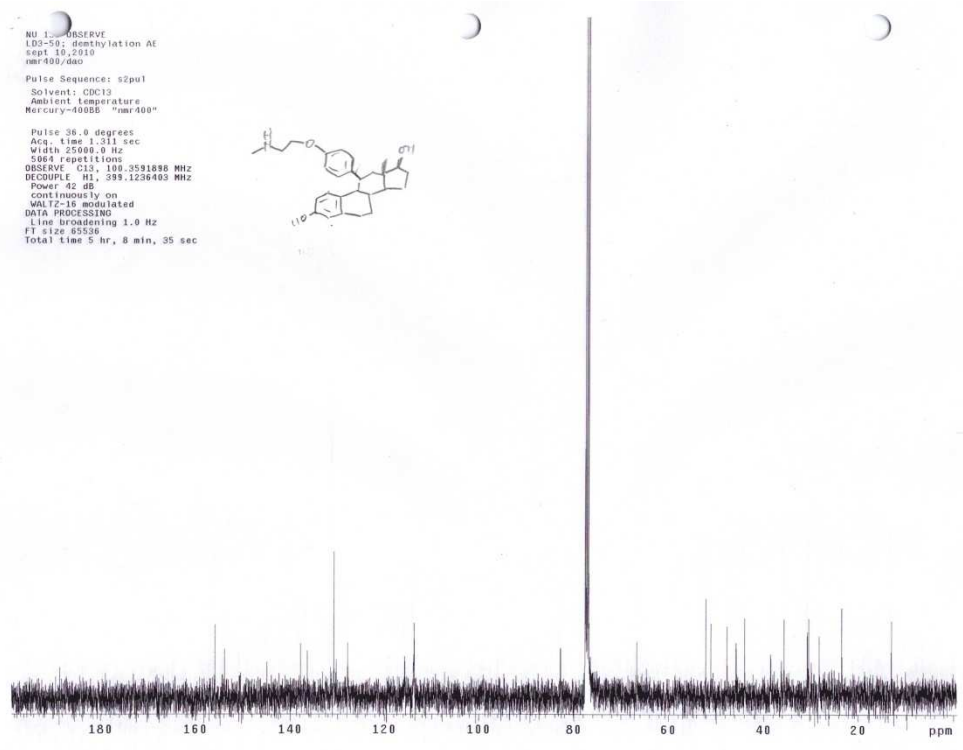


Figure S13: ^1H NMR of 2-[2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy]-ethyl tosylate (8)

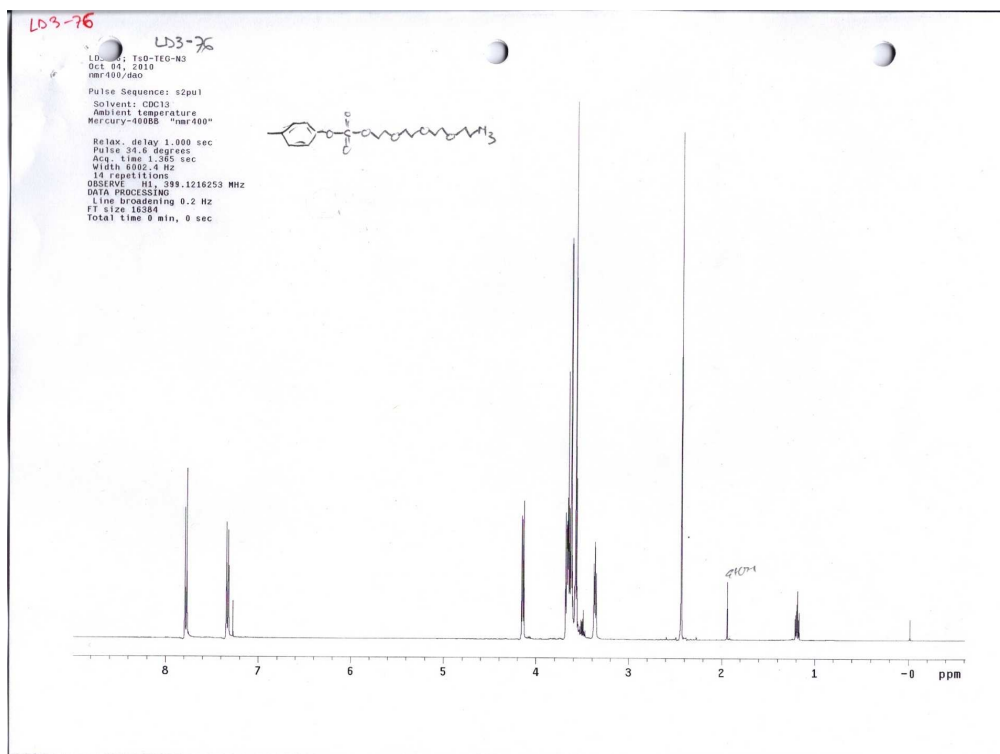


Figure S14: ^{13}C NMR of 2-{2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy}-ethyl tosylate (8)

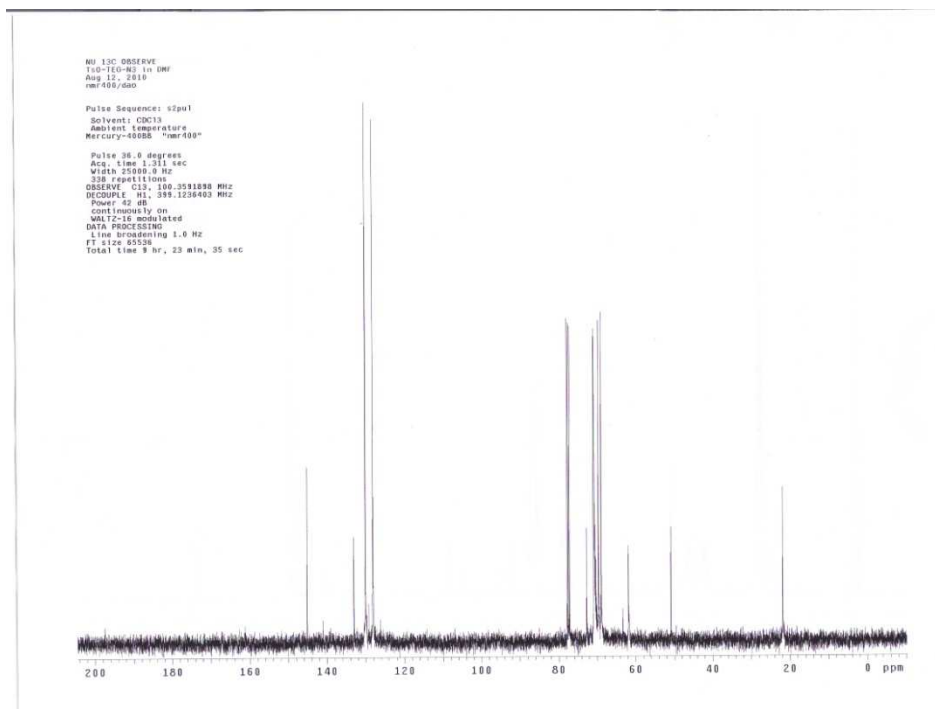


Figure S15: ^1H NMR of 11 β -(4-{2-[2-(2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy)-ethyl)-methyl-amino]-ethoxy}-phenyl)-estra-1,3,5(10)-triene-3,17 β -diol (9)

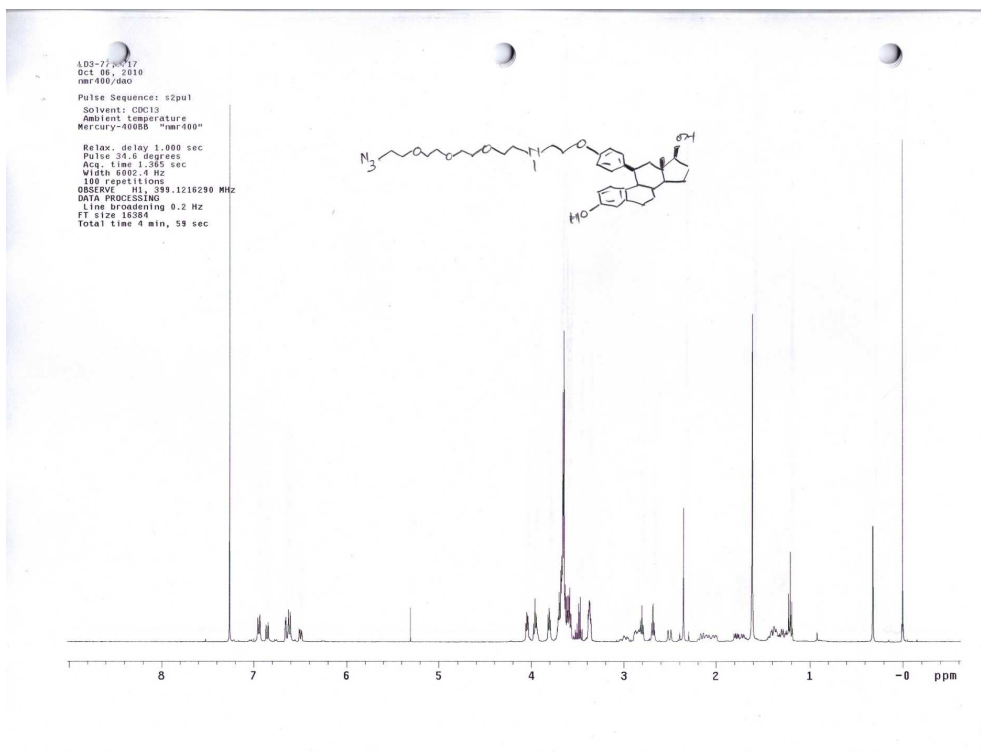


Figure S16: ^{13}C NMR of 11β -(4-{2-[(2-{2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy}-ethyl)-methyl-amino]-ethoxy}-phenyl)-estra-1,3,5(10)-triene-3,17 β -diol (9)

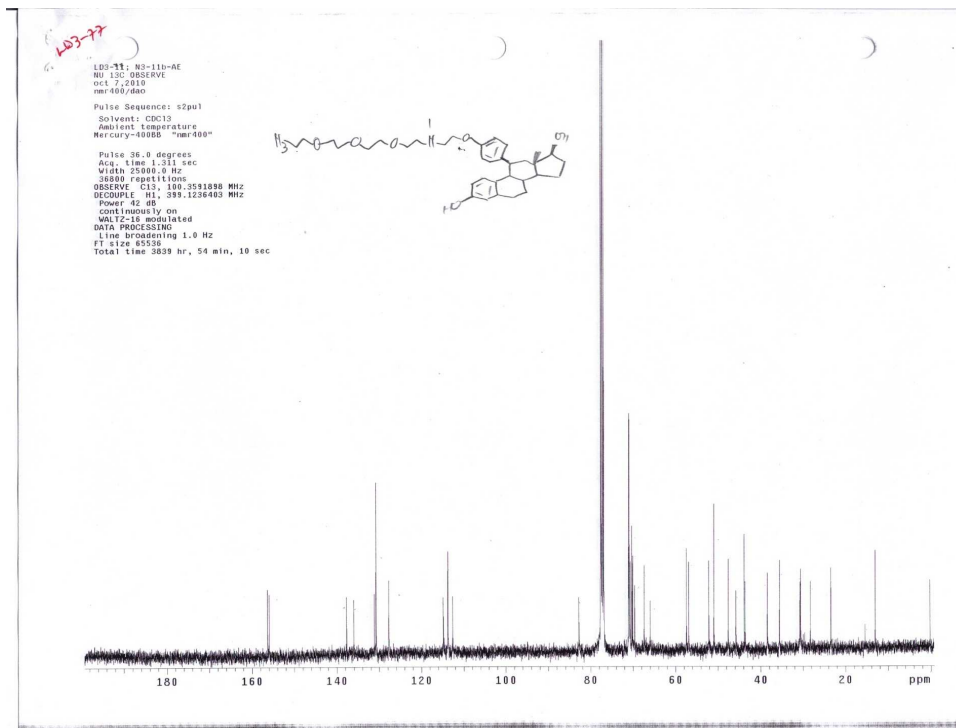


Figure S17: ^1H NMR of 2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethanol (10)

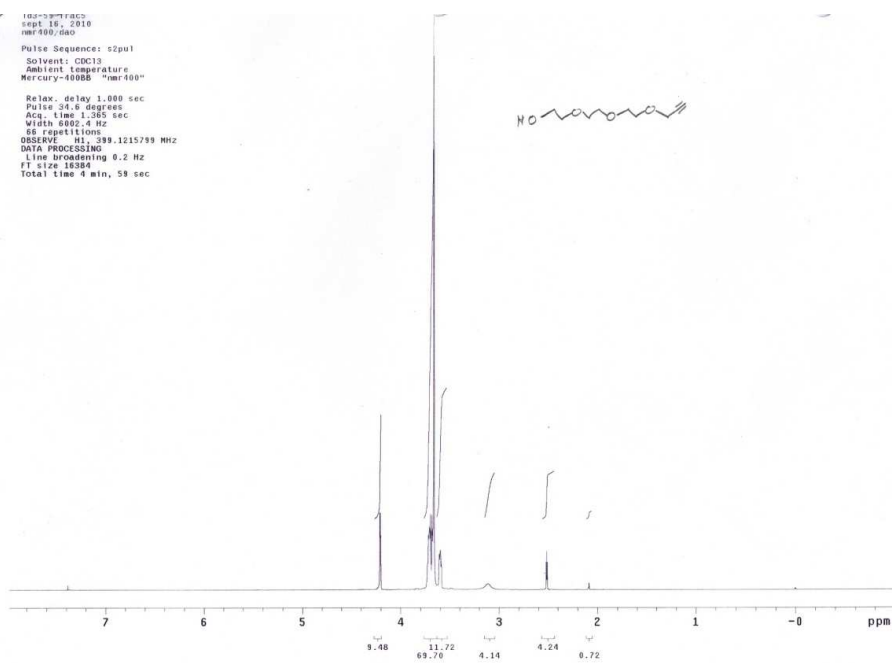


Figure S18: ^{13}C NMR of 2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethanol (10)

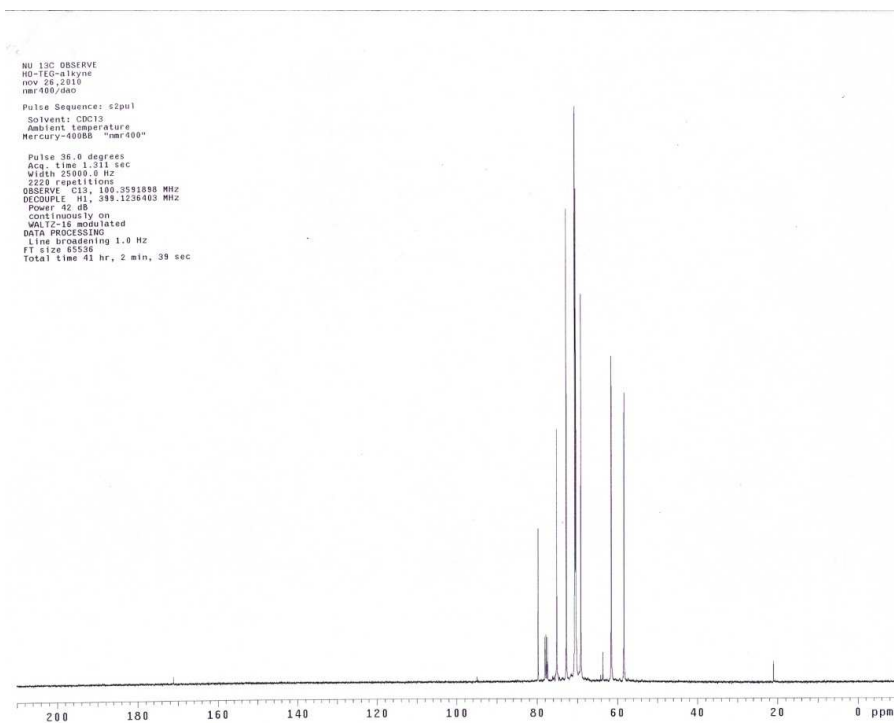


Figure S19: ^1H NMR of 2-(2-(2-(2-(Prop-2-ynyloxy)-ethoxy)-ethoxy)-ethoxy)-ethanol tosylate (11)

ynyloxy)-ethoxy)-ethoxy)-ethoxy)-ethanol tosylate (11)

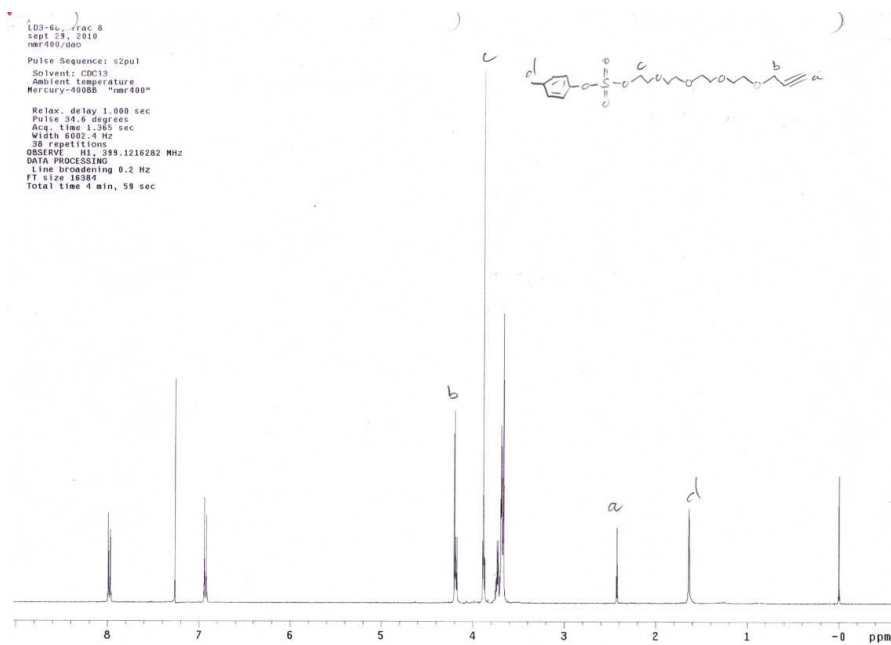


Figure S20: ^{13}C NMR of 2-(2-(2-(2-(Prop-2-ynnyloxy)-ethoxy)-ethoxy)-ethoxy)-ethanol tosylate (11)

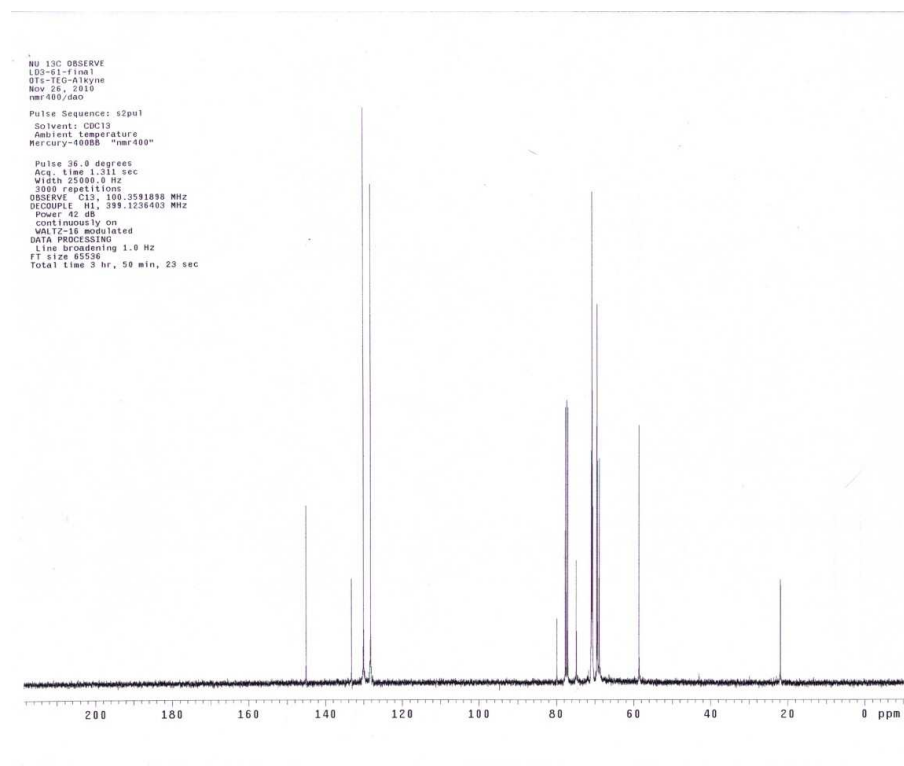
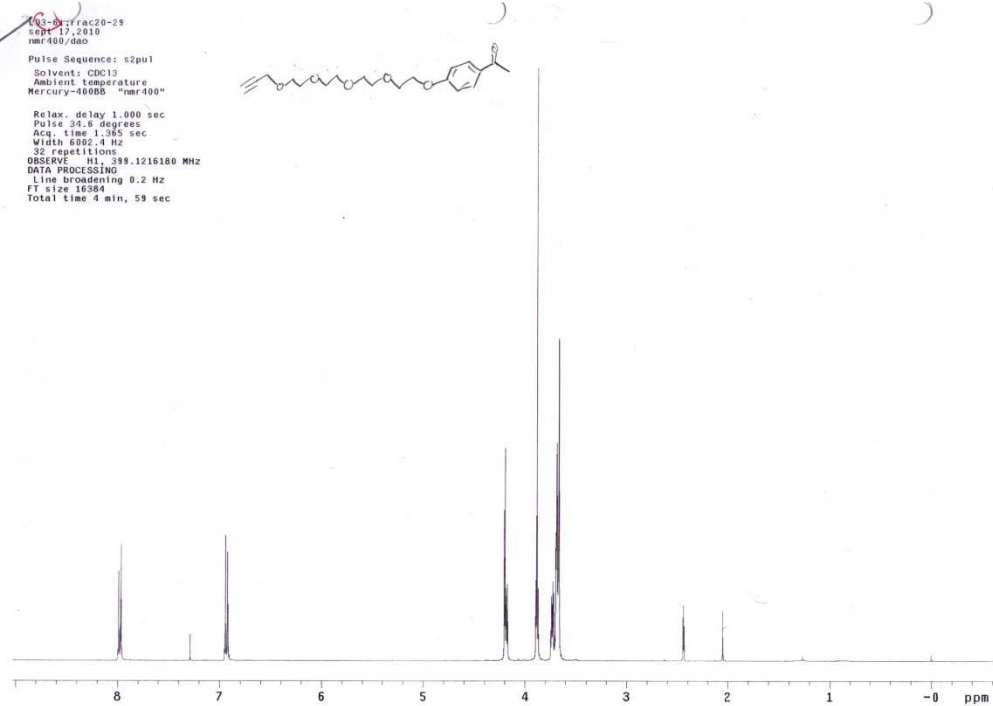


Figure S21: ^1H NMR of Methyl 4-(2-(2-(2-(2-(prop-2-ynnyloxy) ethoxy)ethoxy)ethoxy)ethoxy)benzoate



(12)

Figure S22: ^{13}C NMR of Methyl 4-(2-(2-(2-(2-(prop-2-ynyloxy) ethoxy)ethoxy)ethoxy)ethoxy)benzoate (12)

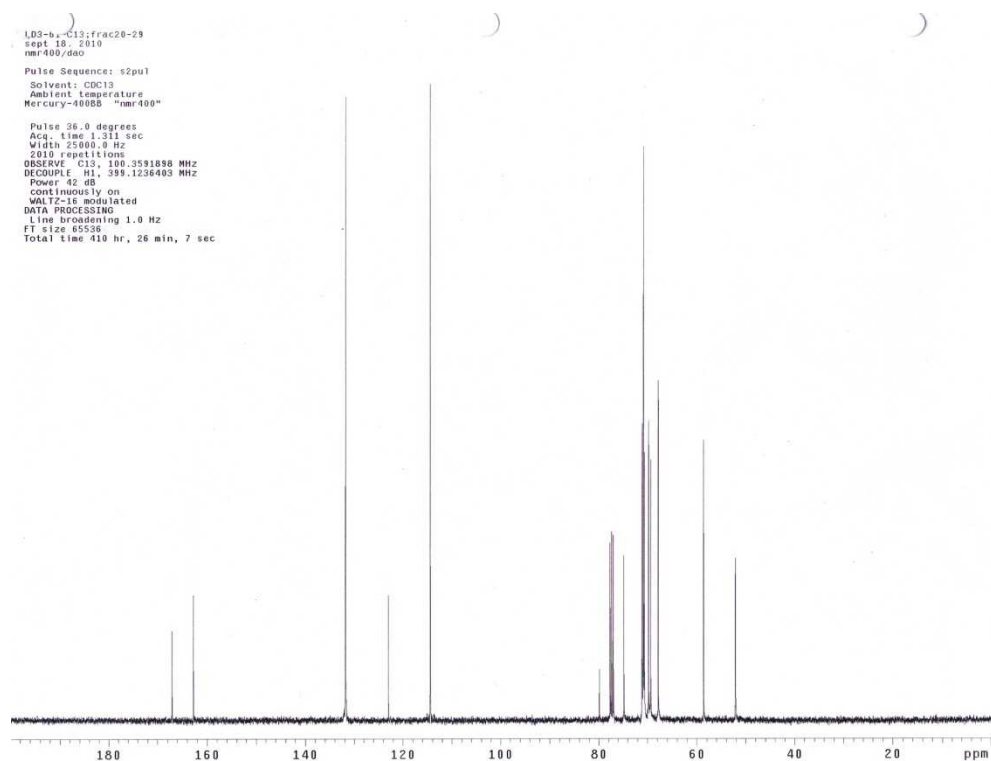


Figure S23: ^1H NMR of 4-(2-[2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy]-ethoxy)-benzoic acid hydrazide (13)

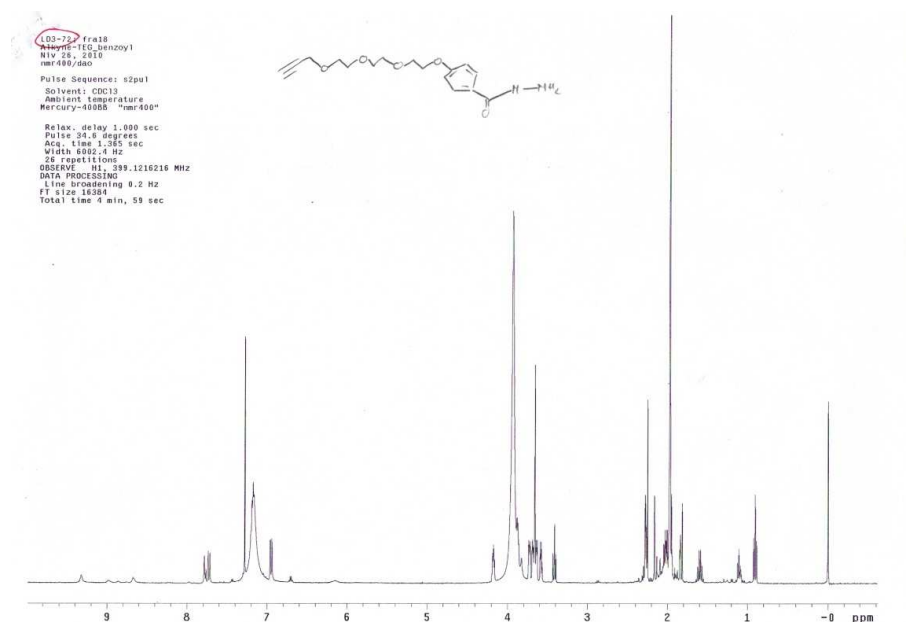
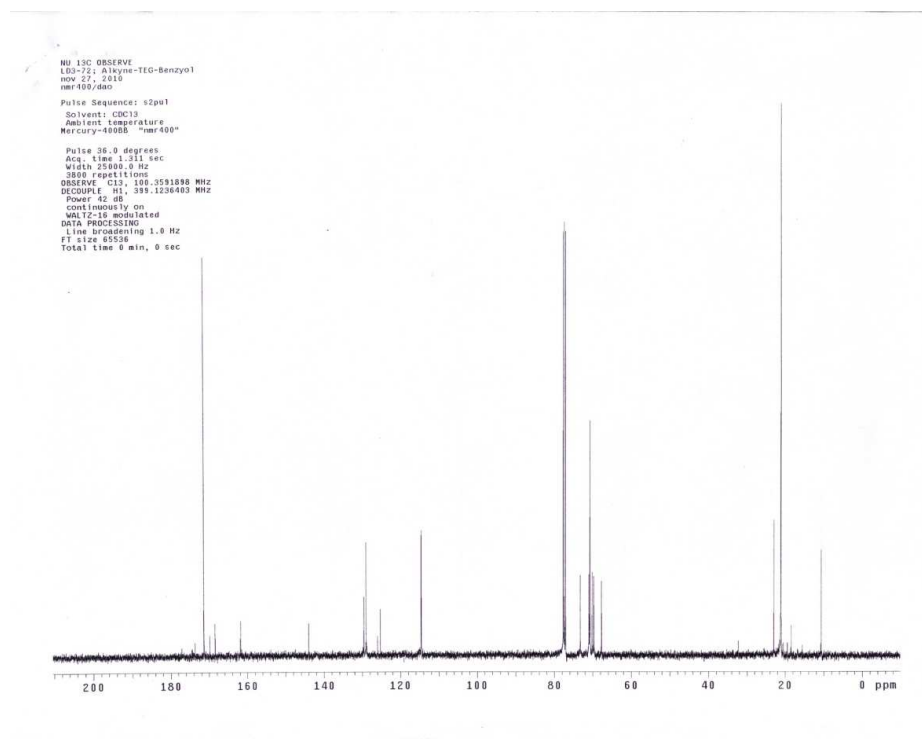


Figure S24: ^{13}C NMR of 134-(2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethoxy)-benzoic acid hydrazide (13)



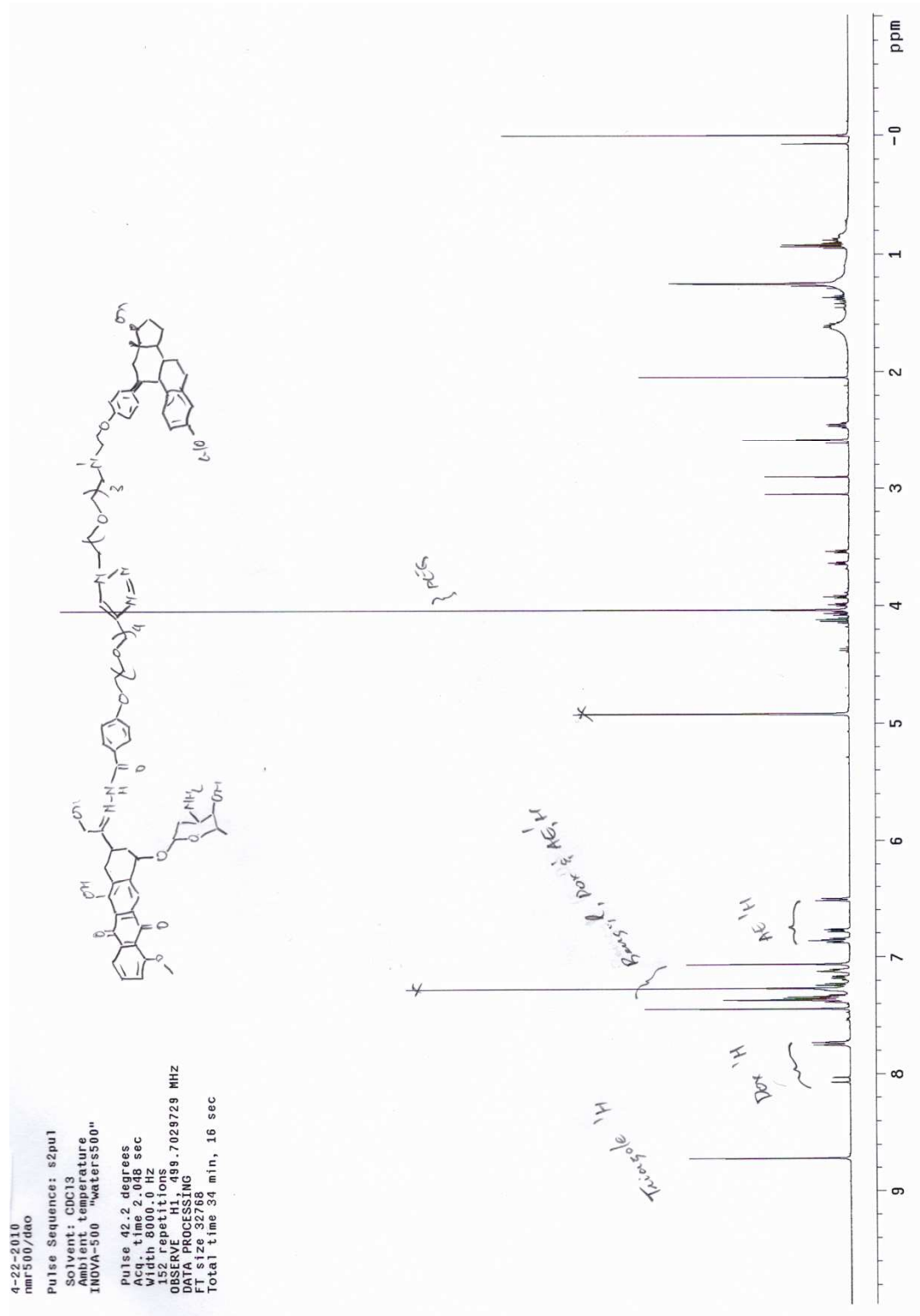
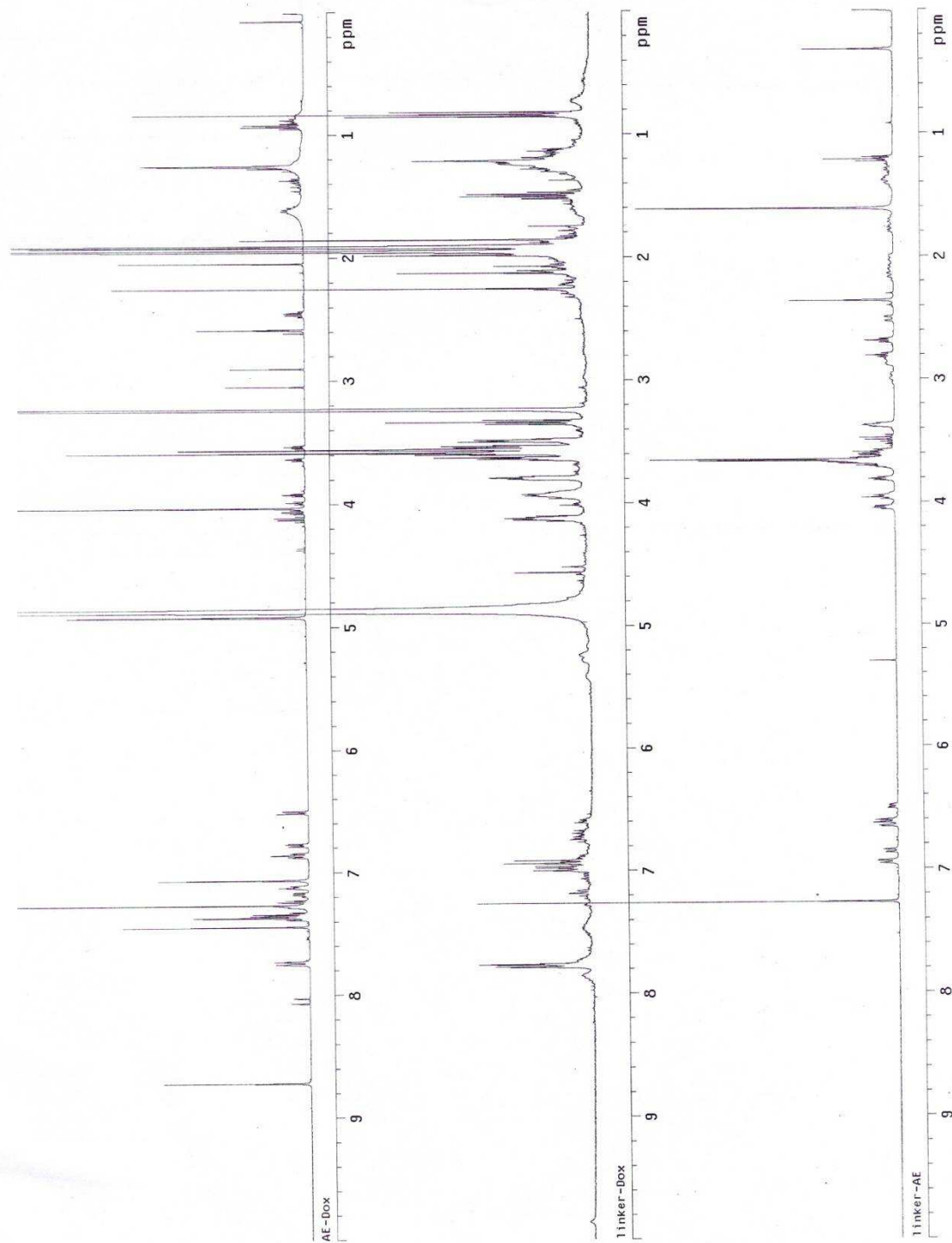


Figure S25: ¹H NMR of AE-Dox conjugate (15)

Figure S26: Stack 1H NMR of Alkynate Dox derivative 14



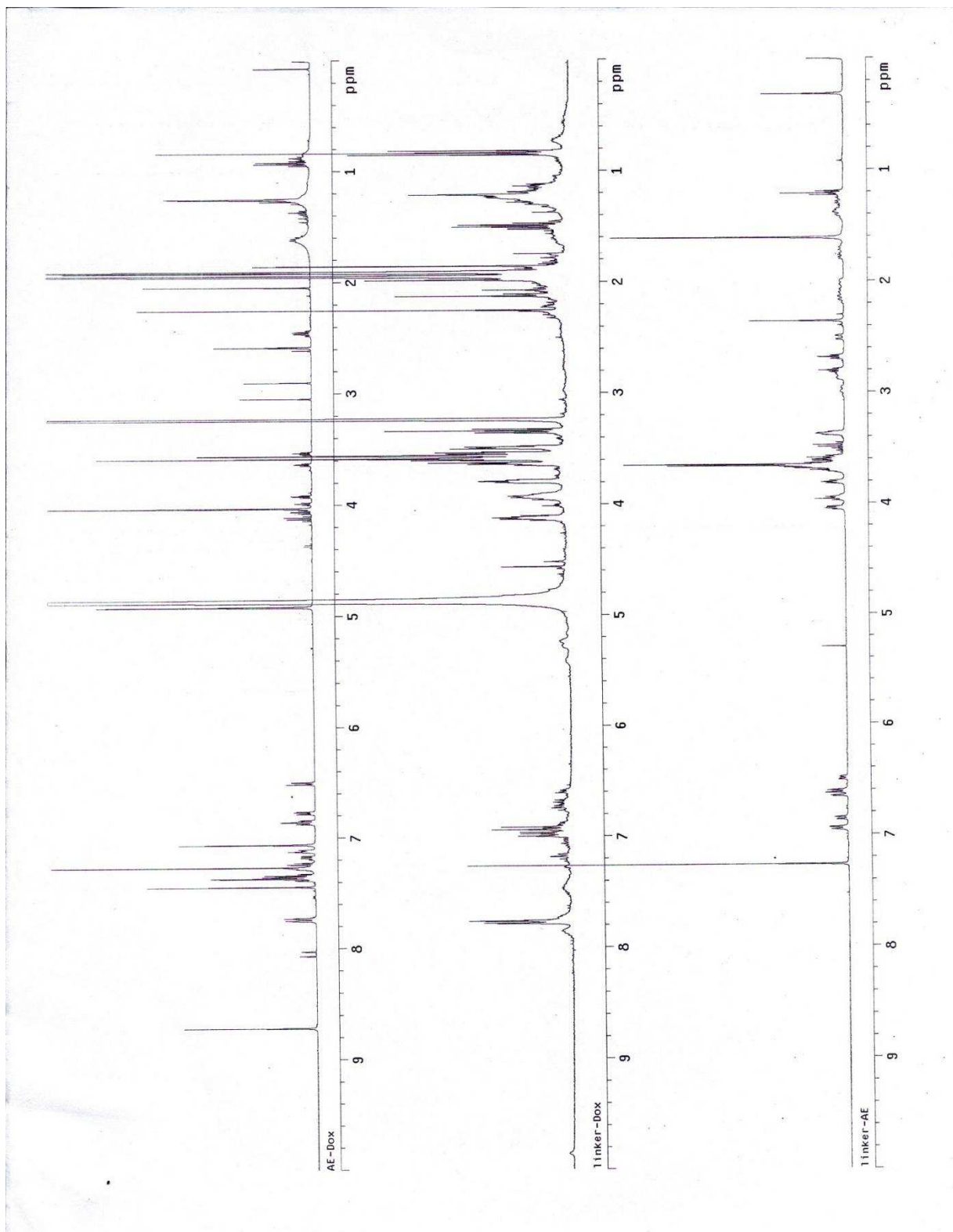


Figure S27: Stack 1H NMR of AE- Dox conjugate (15)

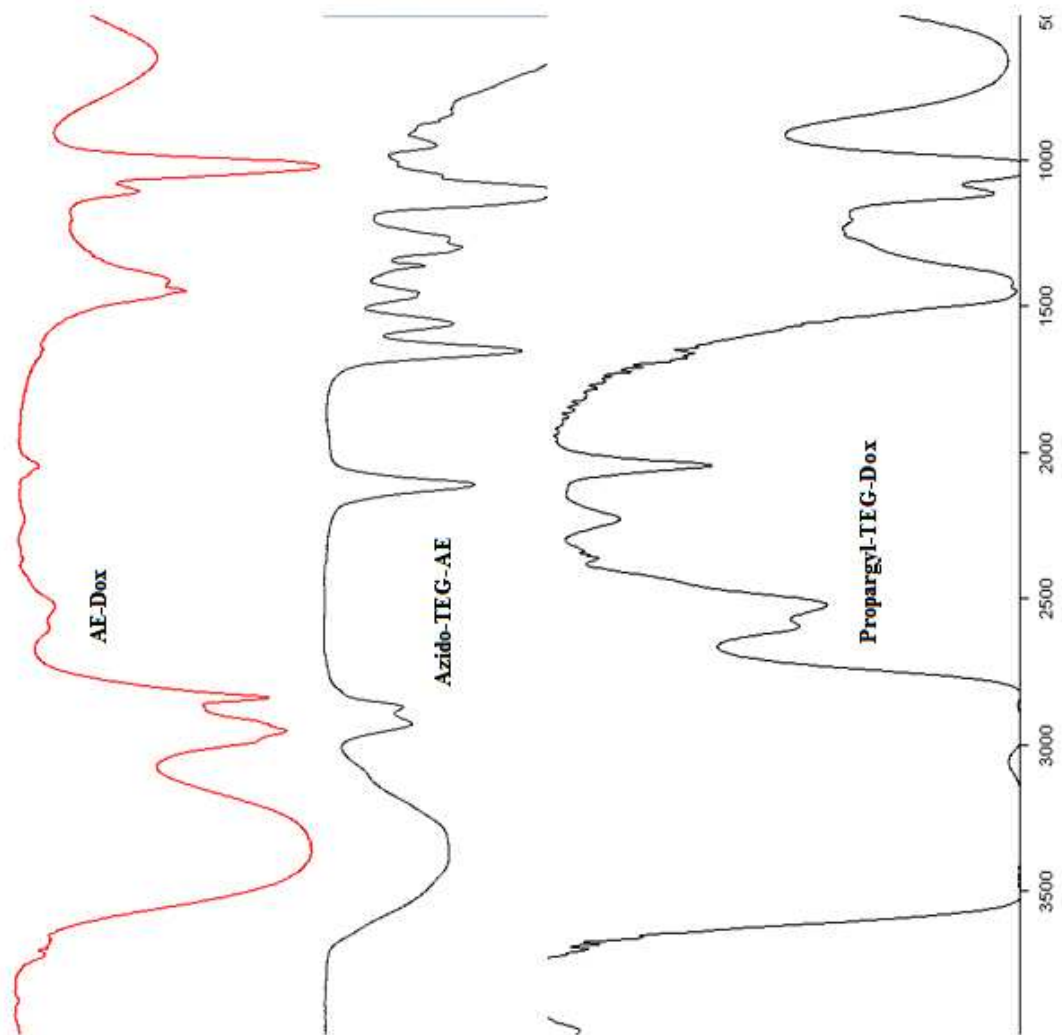


Figure S28: Stack IR of AE- Dox conjugate (15)

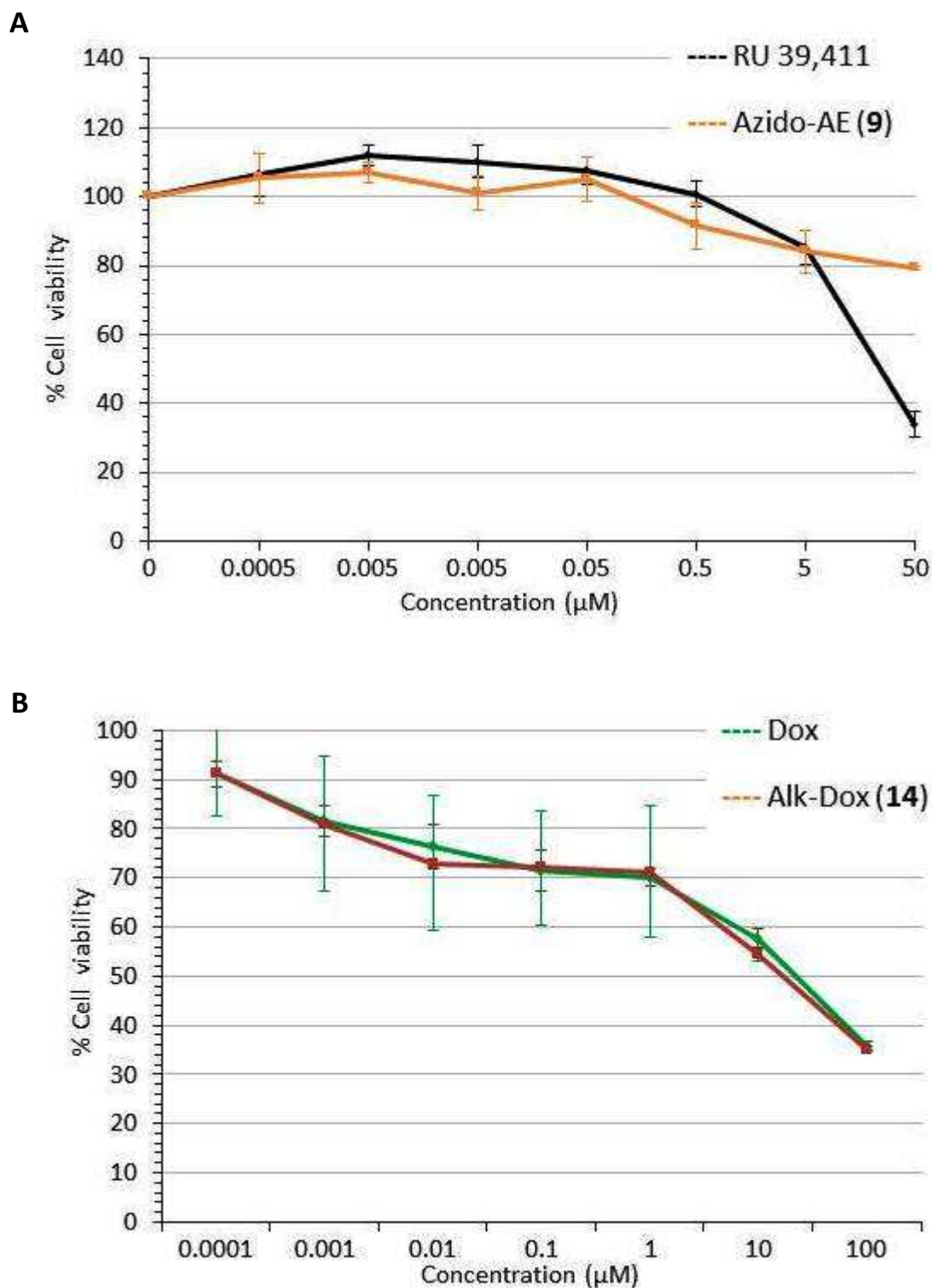


Figure S29: Comparing cytotoxicity of modified A) Azido-AE (9), and B) Alk-Dox (14) with their parent compounds treated in MCF-7 (24h)

