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

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Supporting Information

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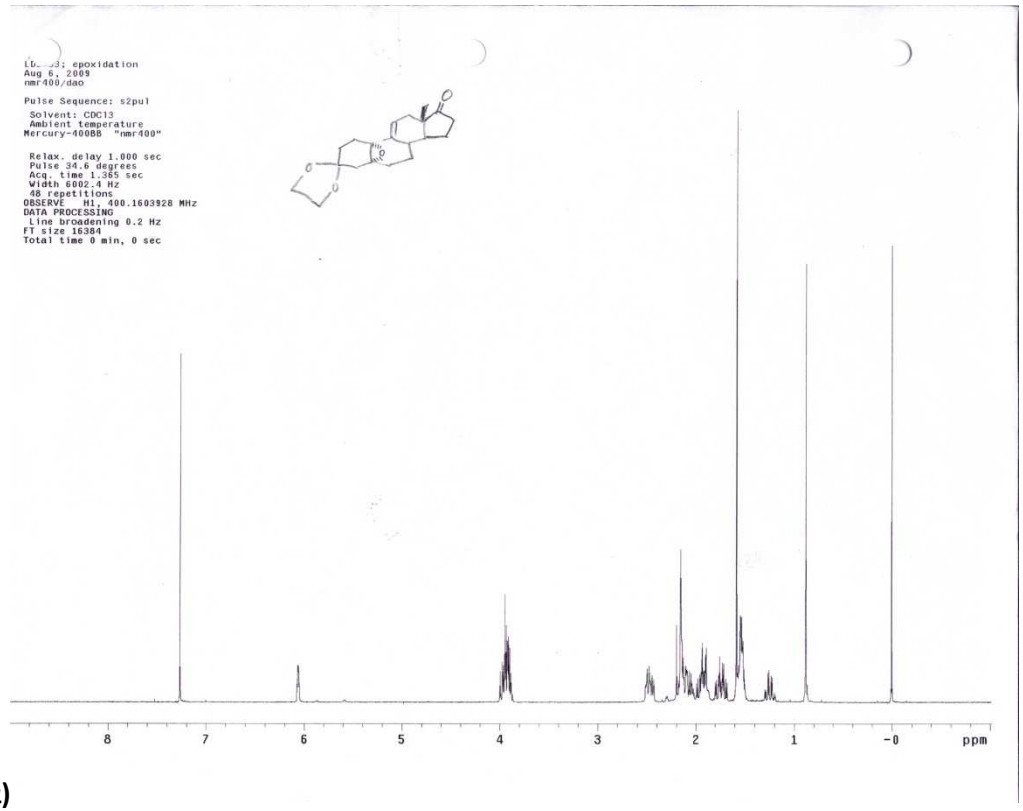
¥ Abbreviations: estrogen receptor (AE), tetraethylene glycol (TEG), tamoxifen (TAM), doxorubicin (DOX), estradiol (E_2), antiestrogen-doxorubicin hybrid (AE-DOX), antiestrogen-tamoxifen hybrid (AE-TAM), azido-tamoxifen (N_3-TAM), alkynated-doxorubicin (Ak-DOX), azido-antiestrogen (N_3-AE).

Figure S1: ^{1}H NMR of **3,3-ethylenedioxy-5(10)-α-epoxy-estr-9(11)-ene (2α)**



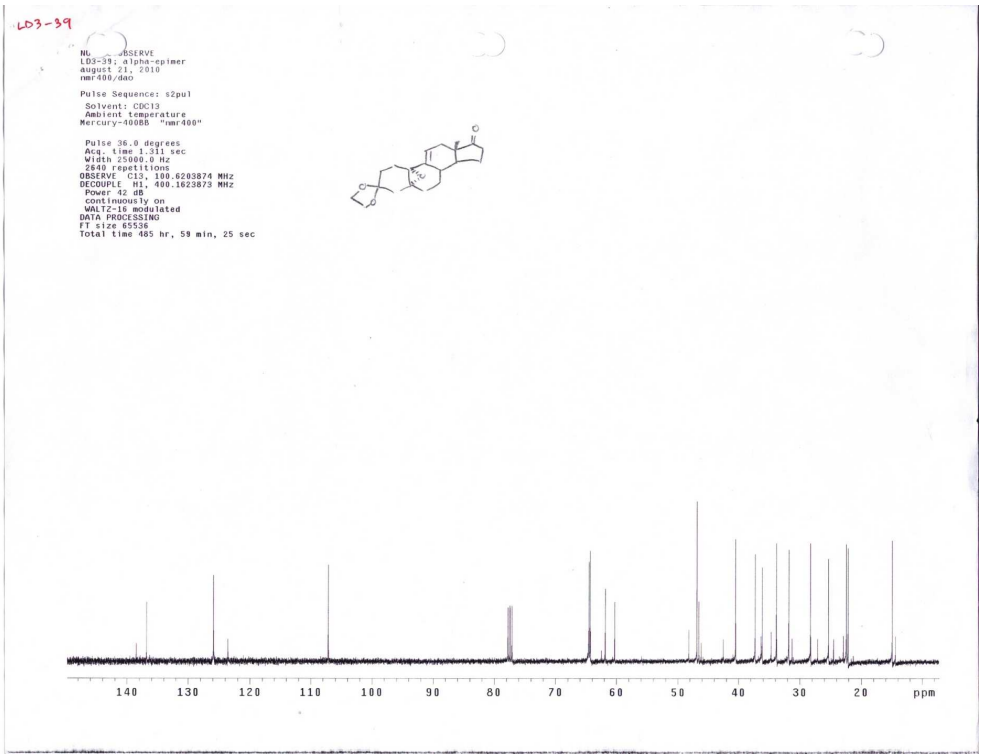
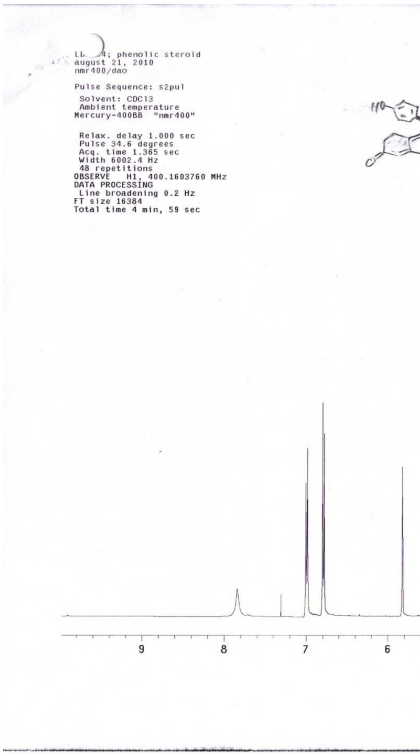


Figure S2: ^{13}C NMR of **3,3-ethylenedioxy-5(10)-α-epoxy-estr-9(11)-ene (2α)**

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



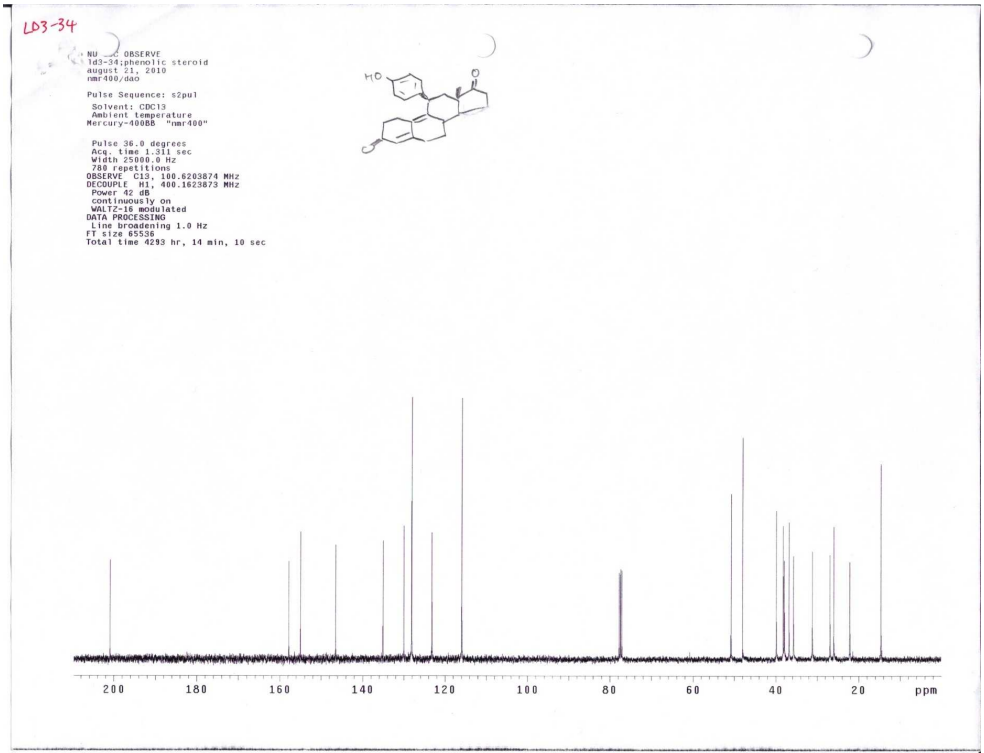


Figure S4: ^{13}C NMR of **11β-(4-Hydroxy-phenyl)-estra-4,9-diene-3,17-dione (3)**

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

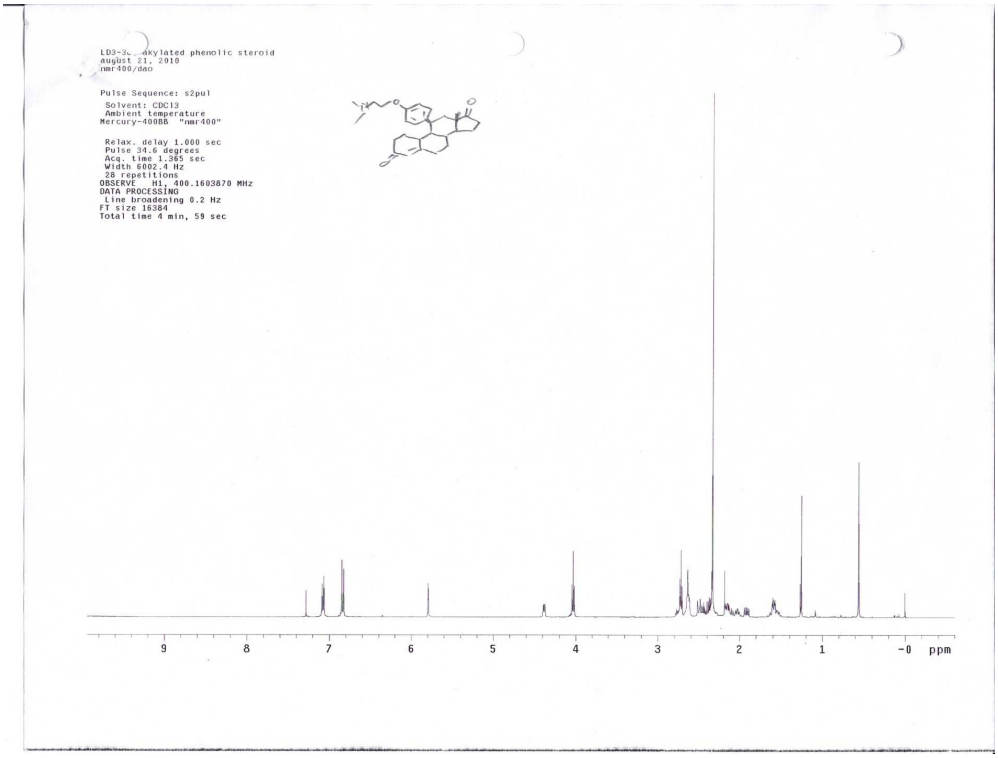
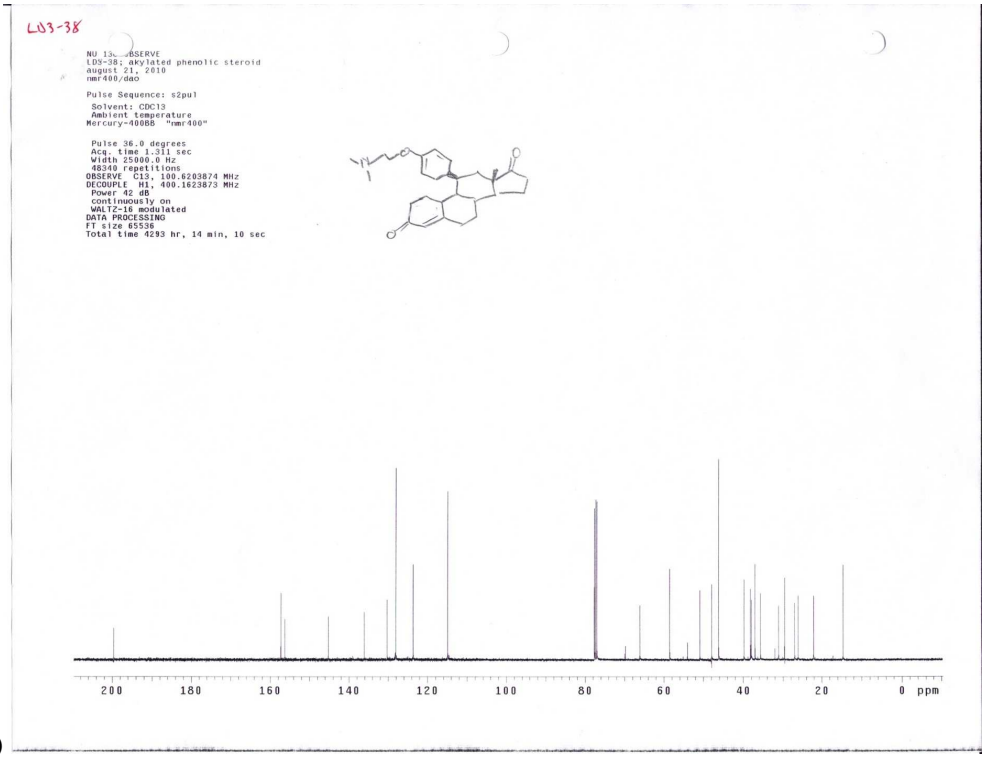


Figure S6: ^{13}C NMR of**11β-[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-4,9-diene-3,17-dione**



(4)

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

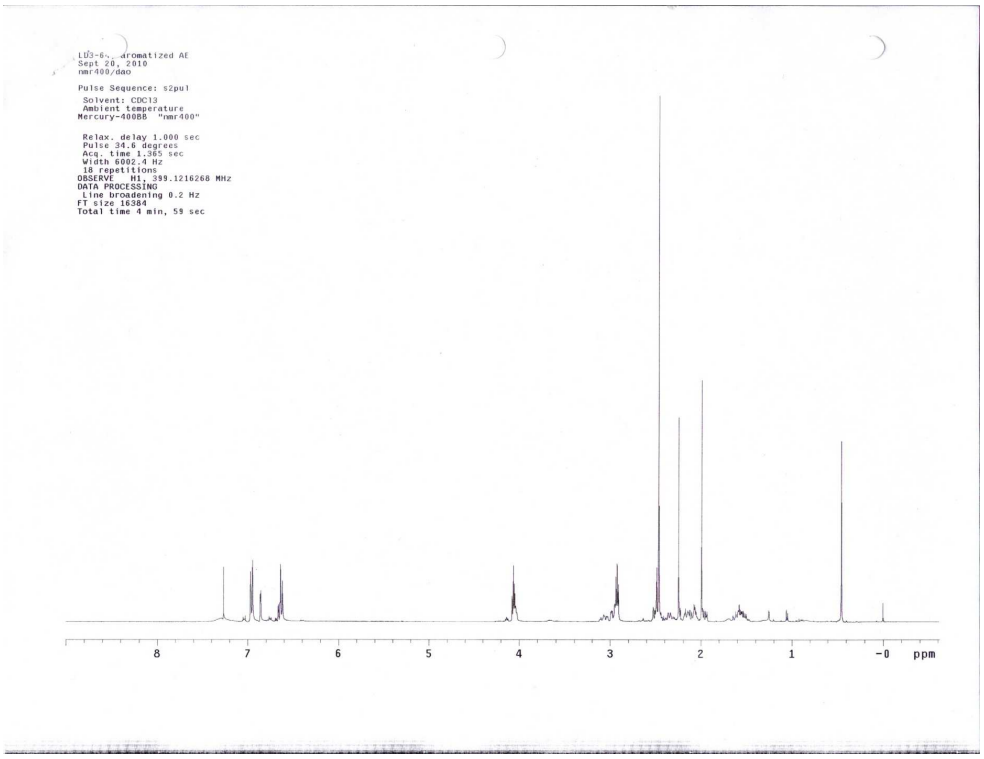


Figure S8: ^{13}C NMR of **3-Acetoxy-11β-[4-(2-dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-17-one(5)**

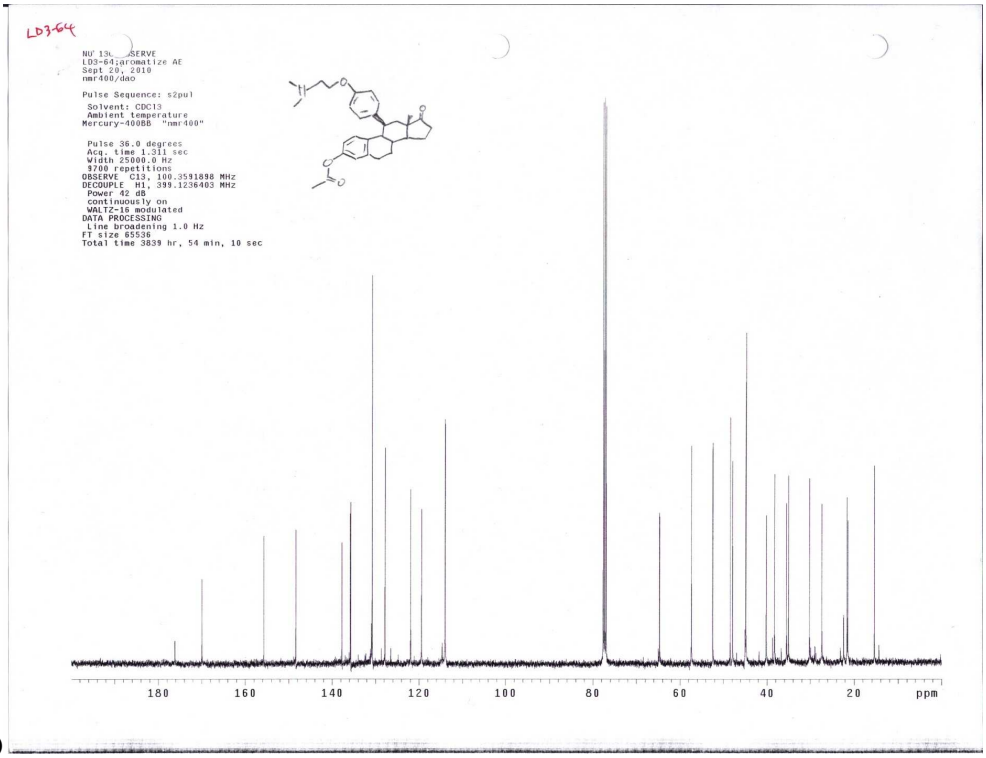


Figure S9: ^{1}H NMR of **11β-[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17ß-diol (6)**

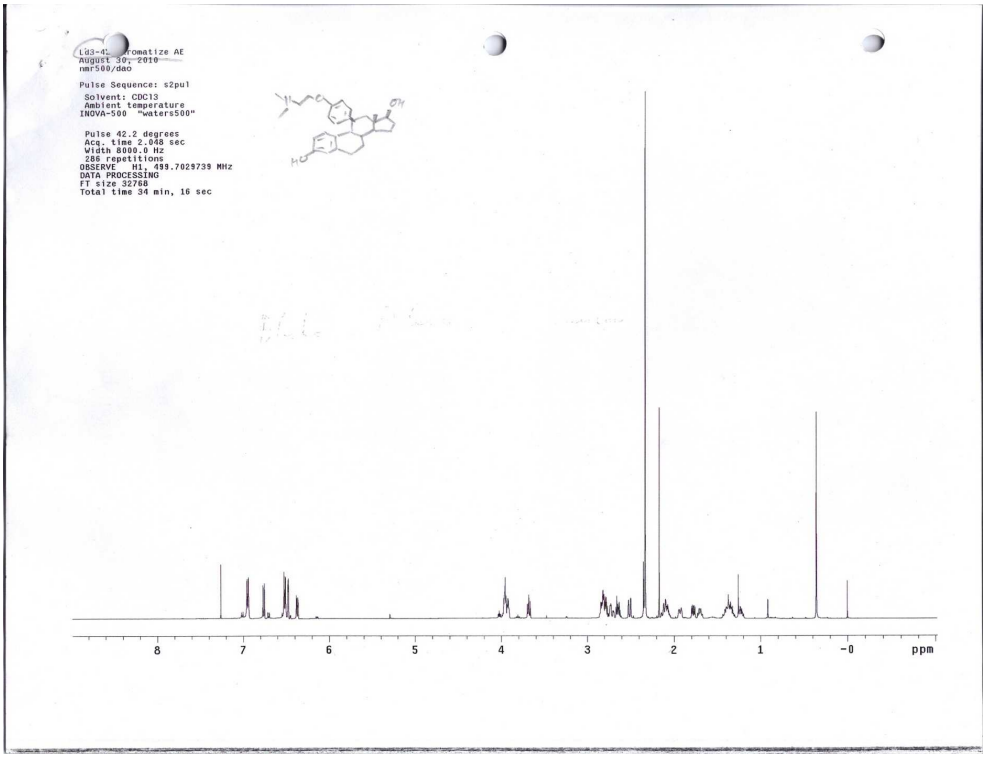
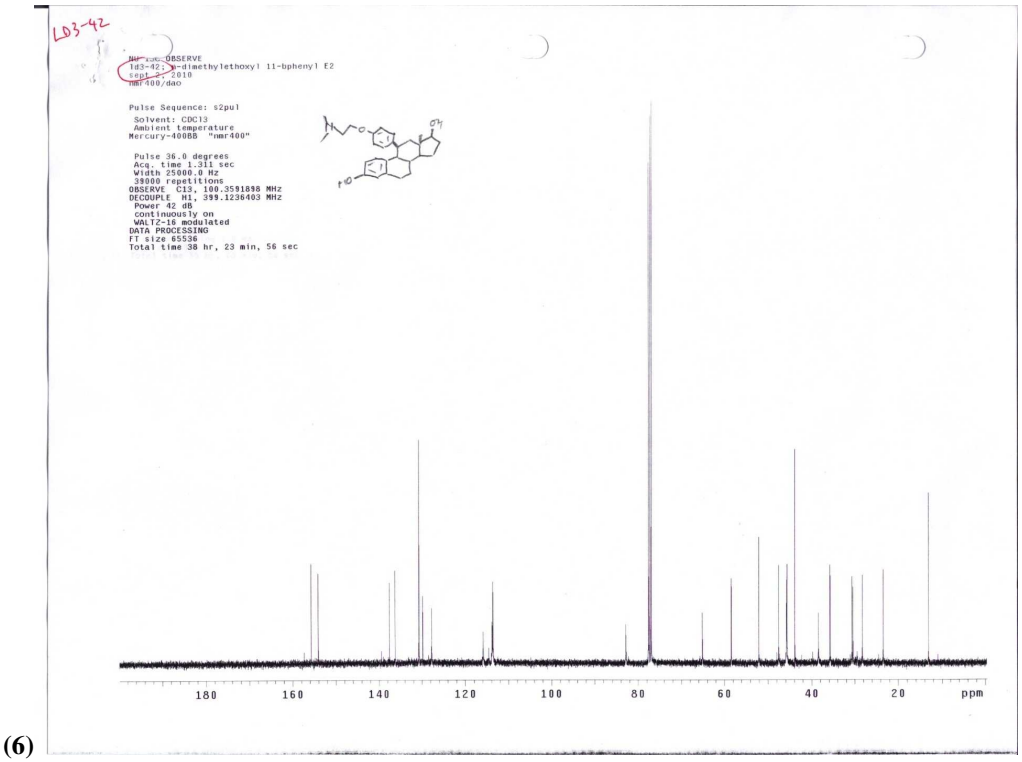


Figure S10: ^{13}C NMR of **11β-[4-(2-Dimethylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17ß-diol**



(6)

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

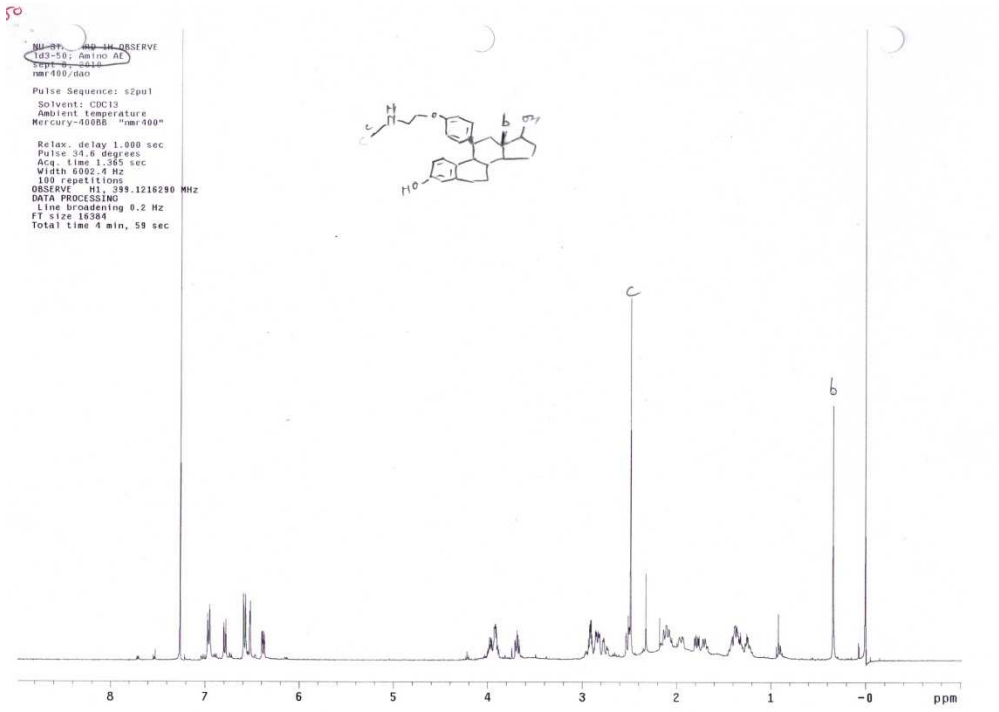


Figure S12: ^{13}C NMR of **11β-[4-(2-methylamino-ethoxy)-phenyl]-estra-1,3,5(10)-triene-3,17ß-diol (7)**

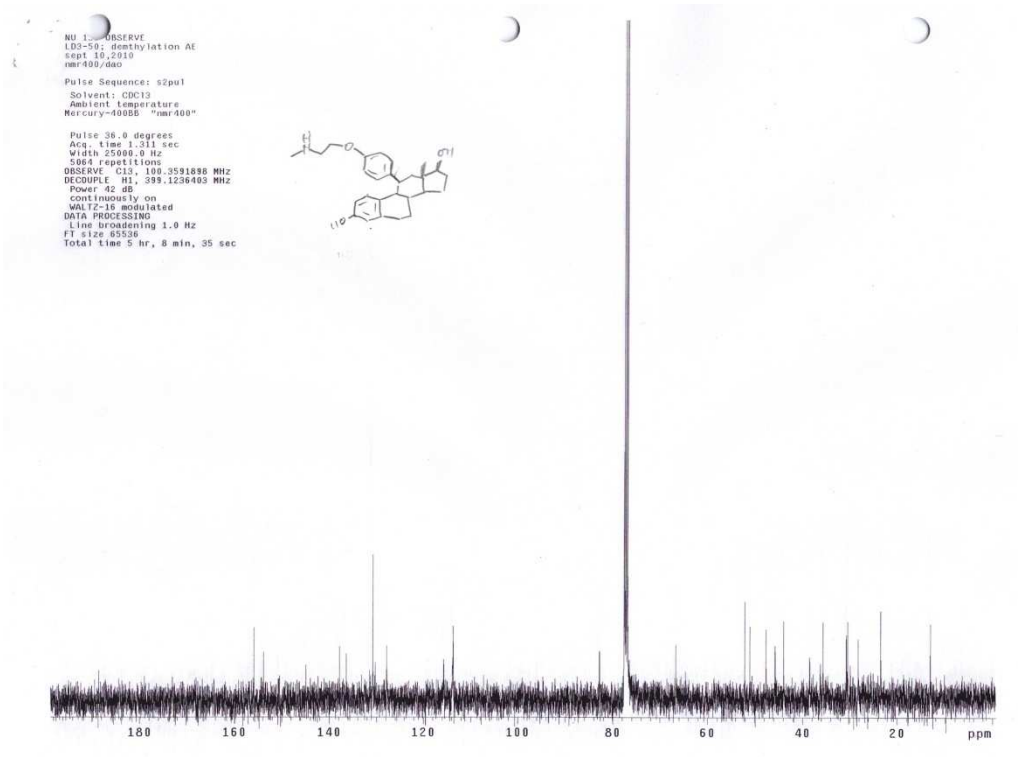


Figure S13: ^{1}H NMR of **2-{2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy}-ethyl tosylate (8)**

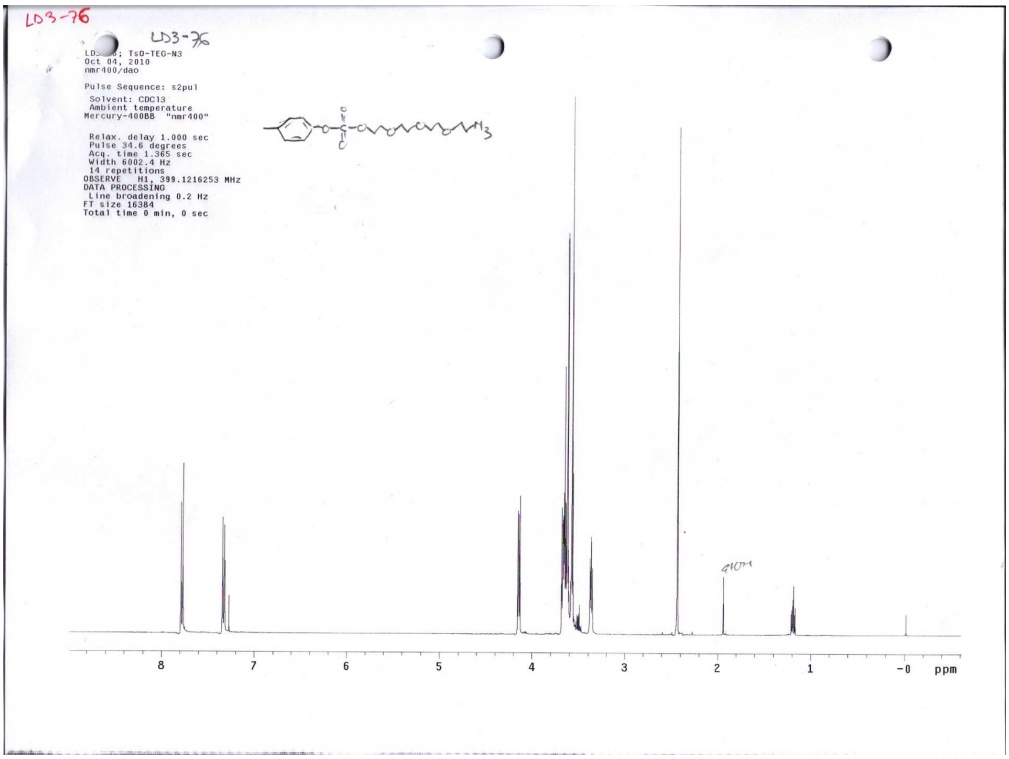


Figure S14: ^{13}C NMR of **2-{2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy}-ethyl tosylate (8)**

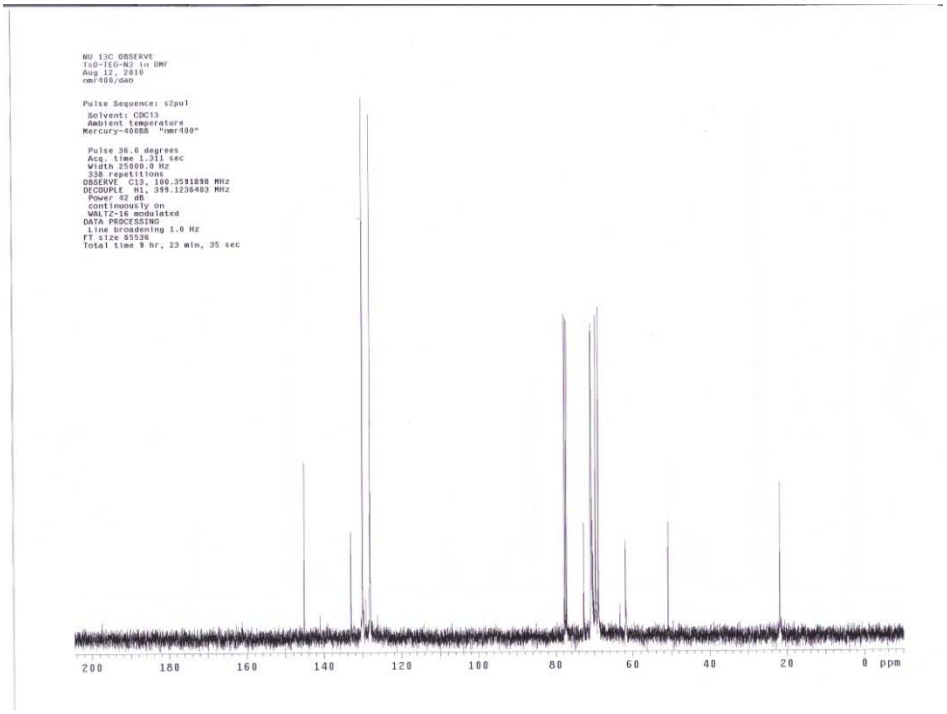


Figure S15: ^{1}H NMR of **11β-(4-{2-[(2-{2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy}-ethyl)-methyl-amino]-ethoxy}-phenyl)-estra-1,3,5(10)-triene-3,17ß-diol (9)**

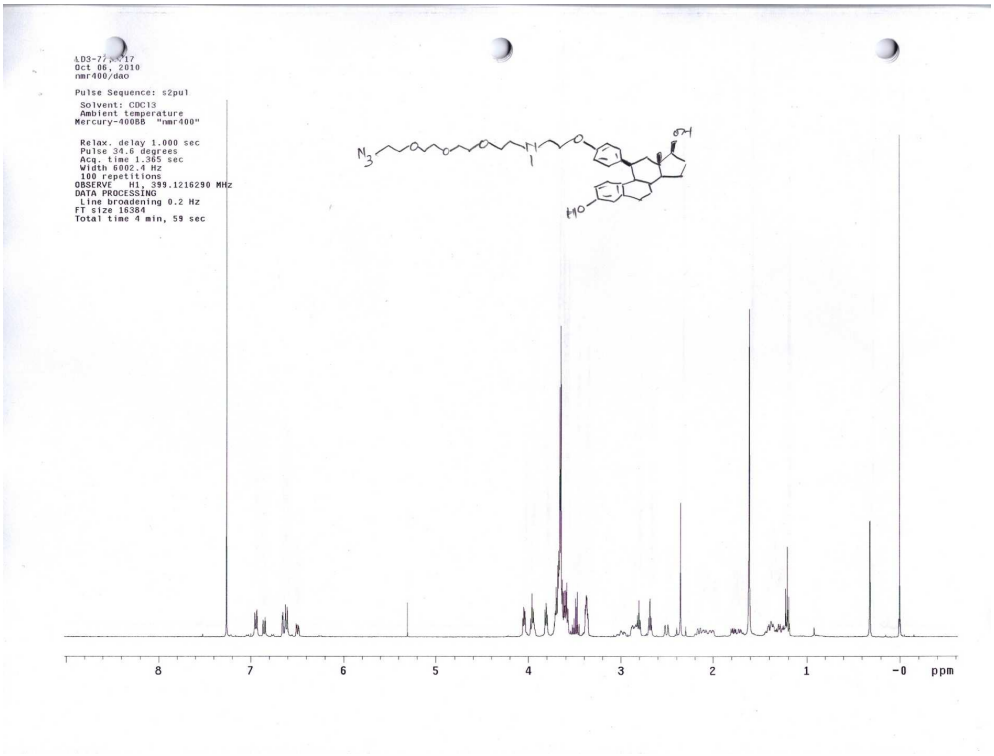


Figure S16: ^{13}C NMR of **11β-(4-{2-[(2-{2-[2-(2-Azido-ethoxy)-ethoxy]-ethoxy}-ethyl)-methyl-amino]-ethoxy}-phenyl)-estra-1,3,5(10)-triene-3,17ß-diol (9)**

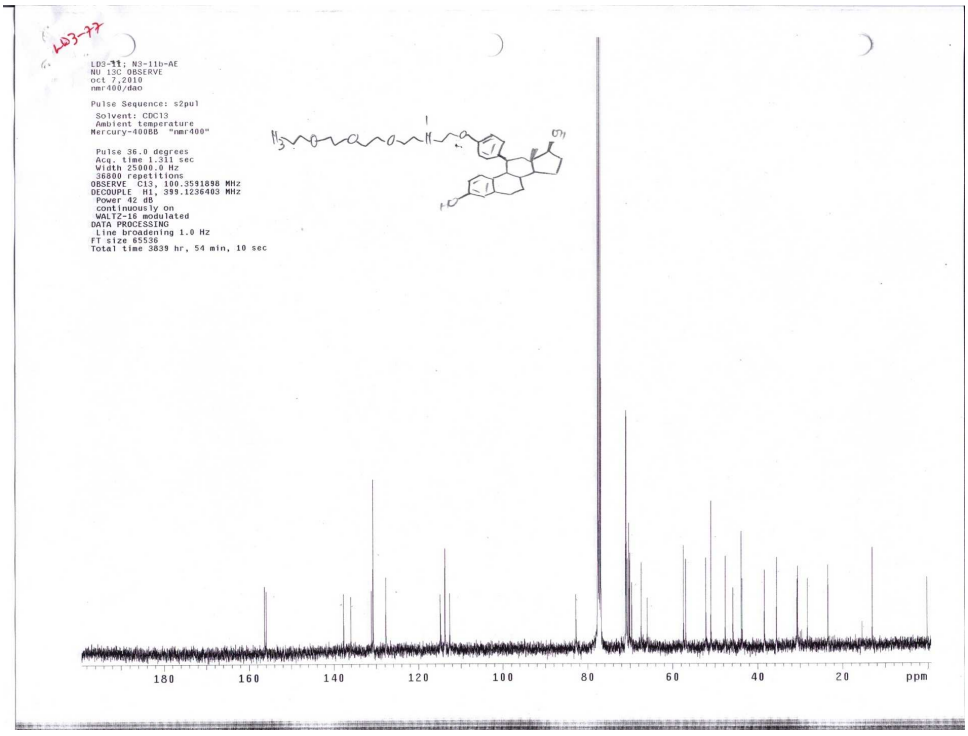


Figure S17: ^{1}H NMR of **2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethanol (10)**

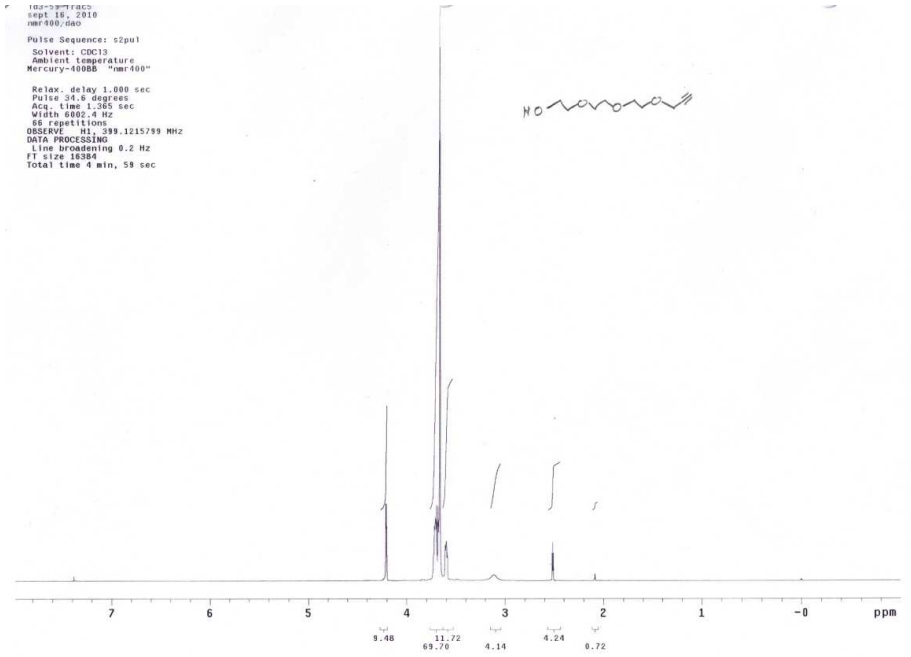


Figure S18: ^{13}C NMR of **2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethanol (10)**

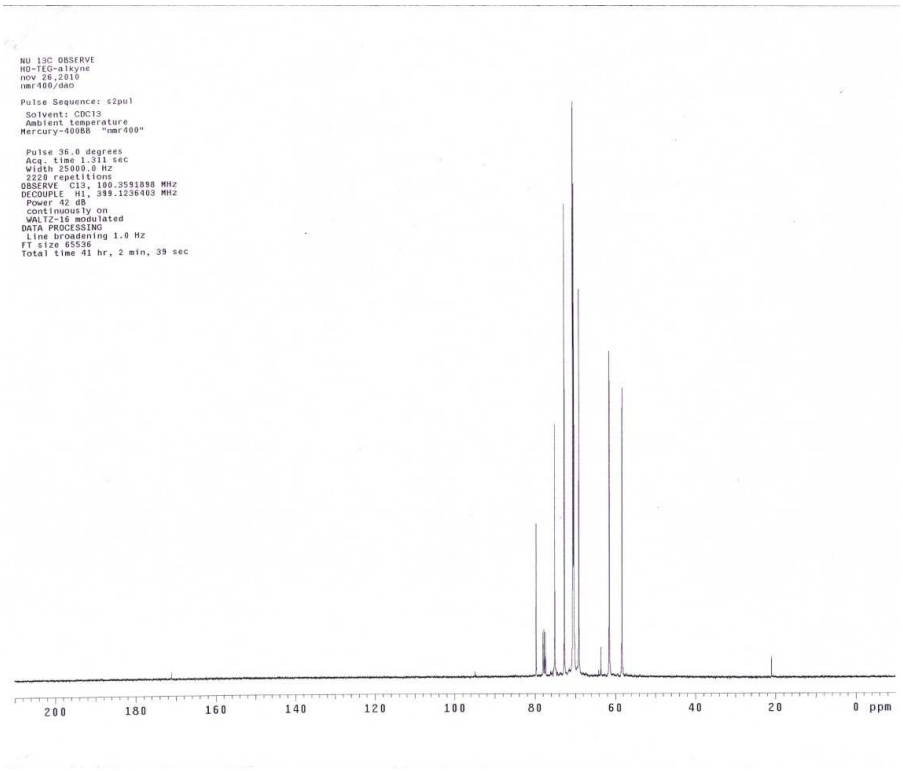


Figure S19: ^{1}H NMR of **2-(2-(2-(2-(Prop-2-ynnyloxy)-ethoxy)-ethoxy)-ethoxy)-ethanol tosylate (11)**

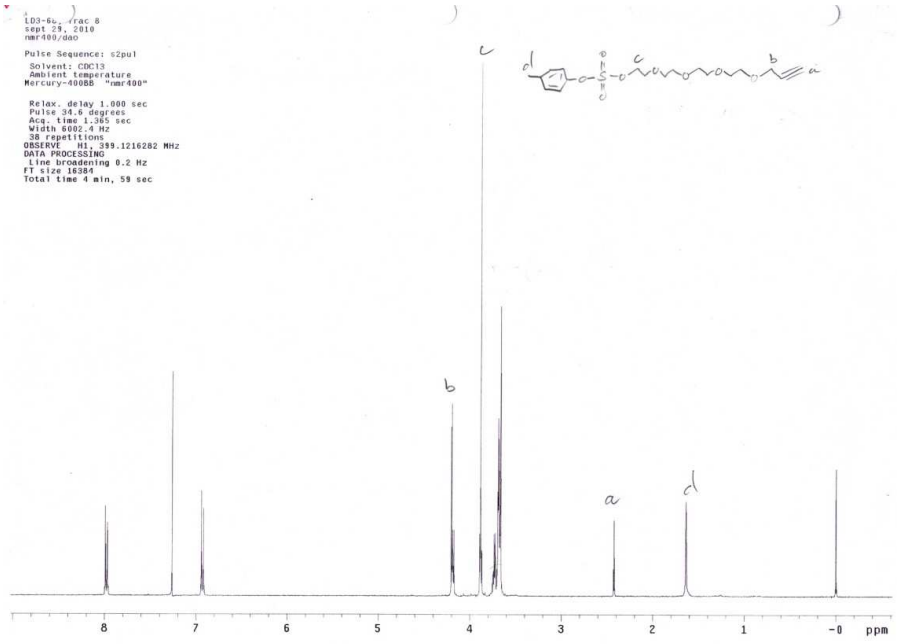


Figure S20: ^{13}C NMR of **2-(2-(2-(2-(Prop-2-ynnyloxy)-ethoxy)-ethoxy)-ethoxy)-ethanol tosylate (11)**

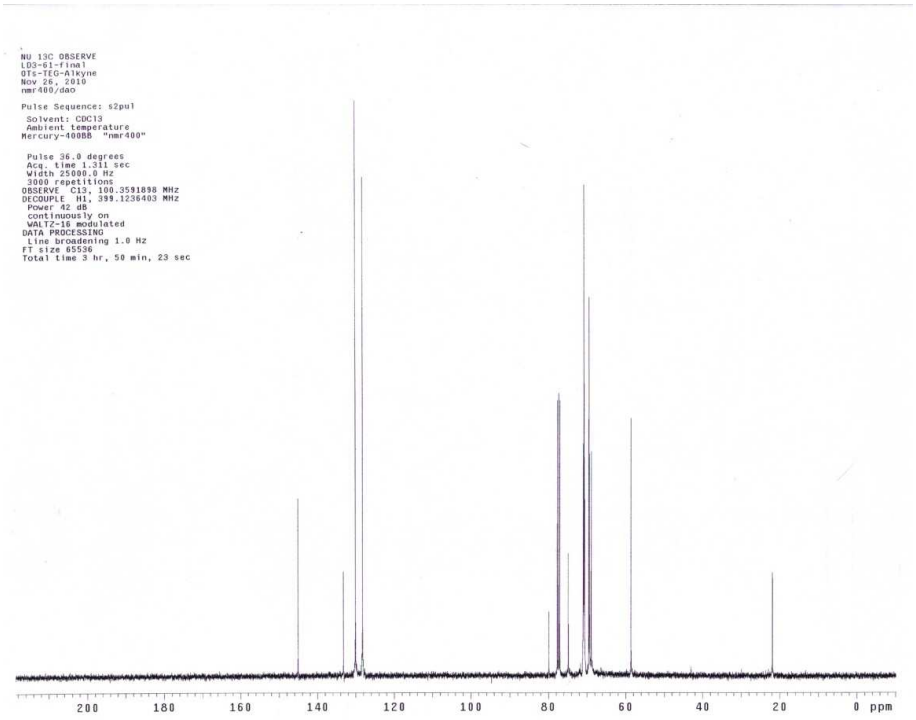
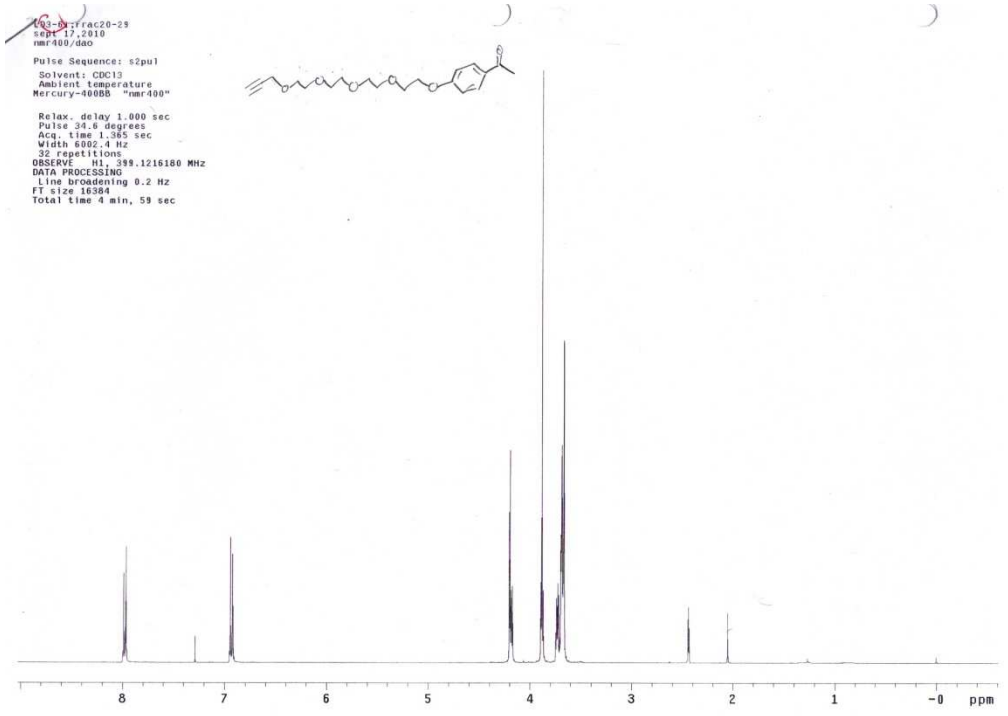


Figure S21: ^{1}H NMR of **Methyl 4-(2-(2-(2-(2-(prop-2-ynyloxy) ethoxy)ethoxy)ethoxy)ethoxybenzoate**



(12)

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

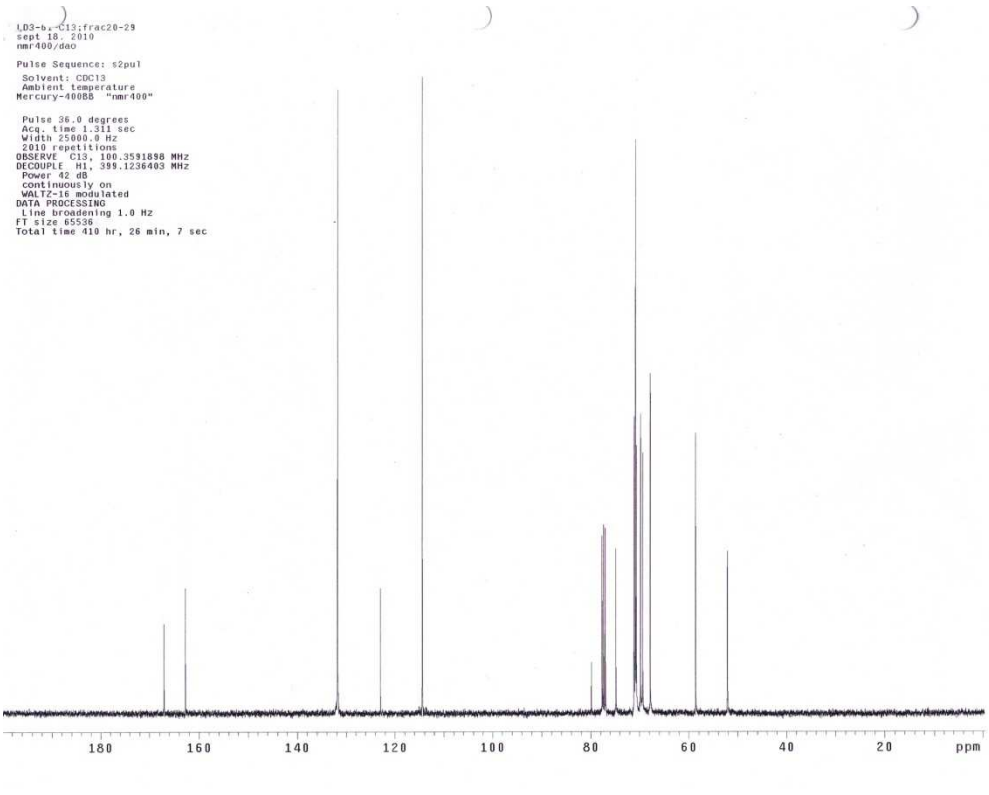


Figure S23: ^{1}H NMR of **4-(2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethoxy)-benzoic acid hydrazide (13)**

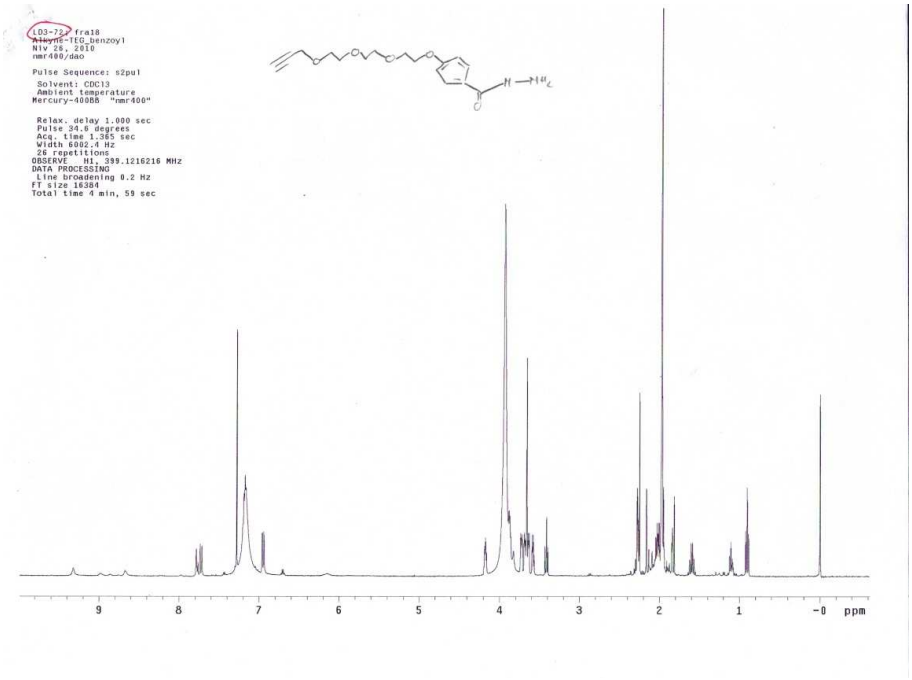
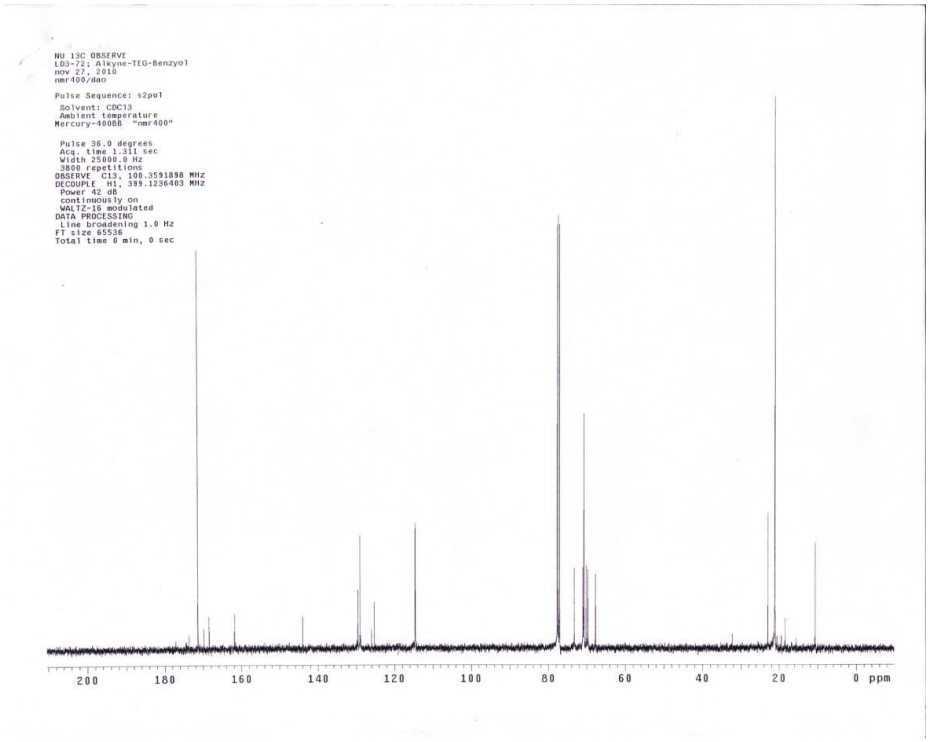


Figure S24: ^{13}C NMR of **134-(2-{2-[2-(2-Prop-2-ynyloxy-ethoxy)-ethoxy]-ethoxy}-ethoxy)-benzoic acid hydrazide (13)**



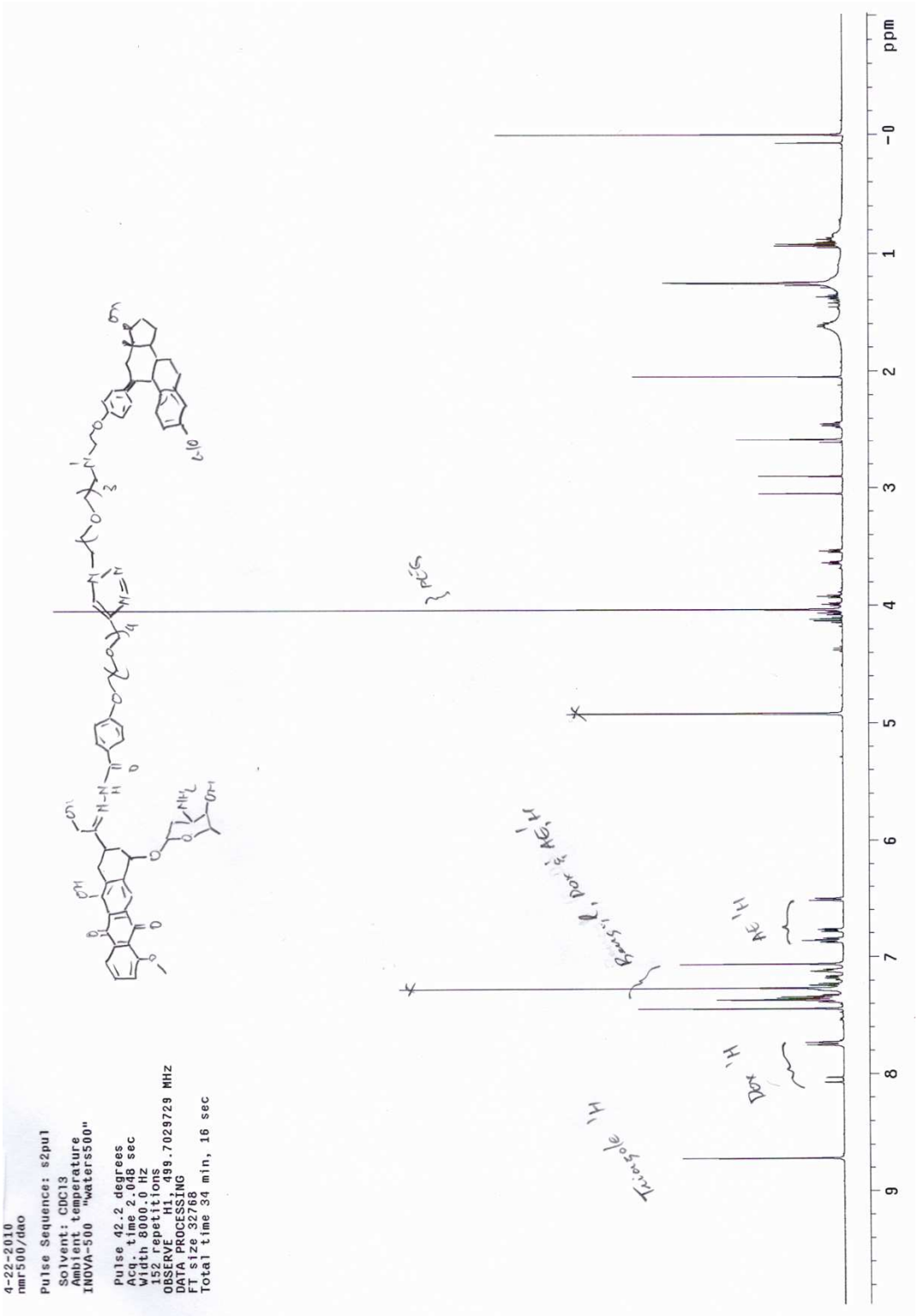
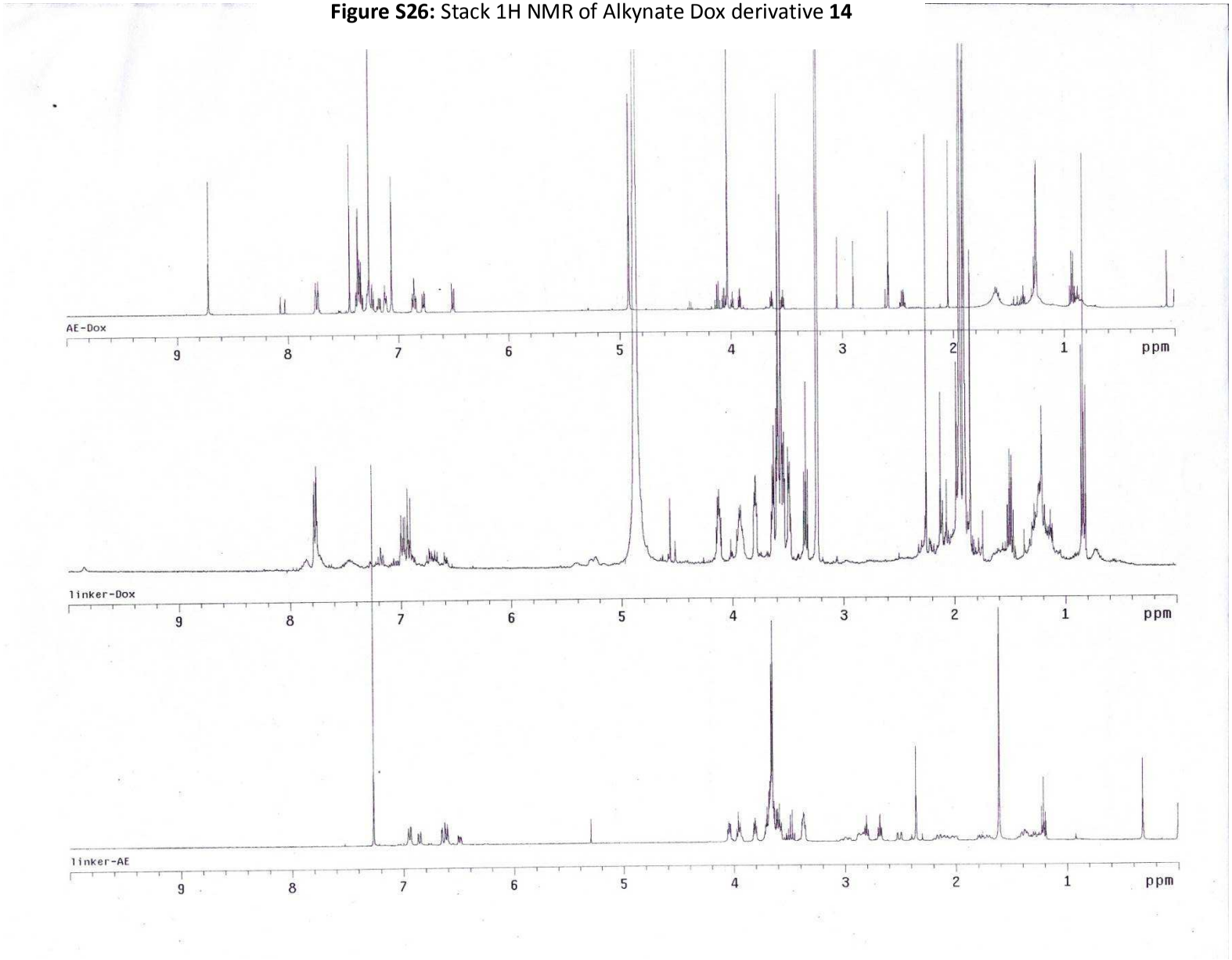


Figure S25: ^{1}H NMR of AE-Dox conjugate (15)

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



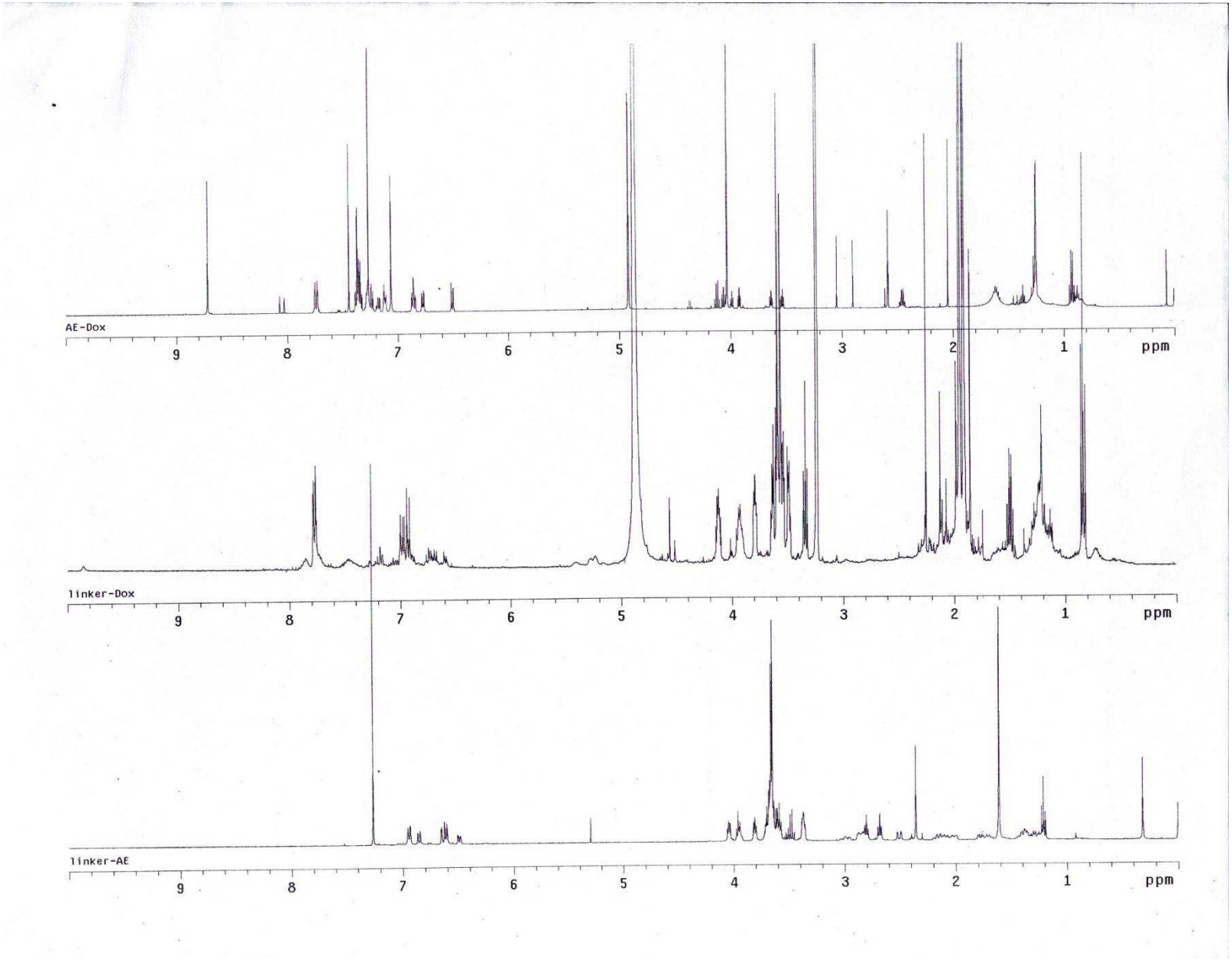


Figure S27: Stack 1H NMR of AE- Dox conjugate (**15)**

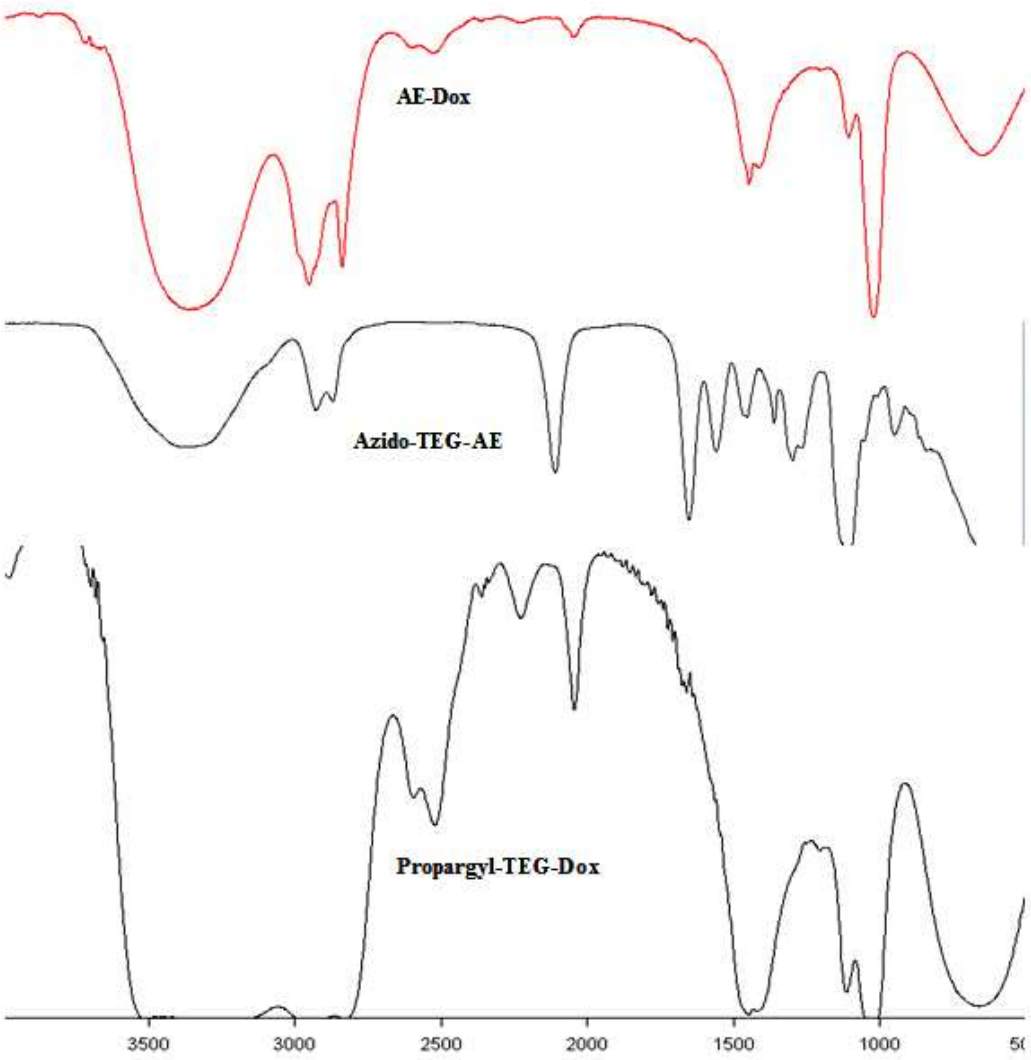


Figure S28: Stack IR of AE- Dox conjugate (**15)**

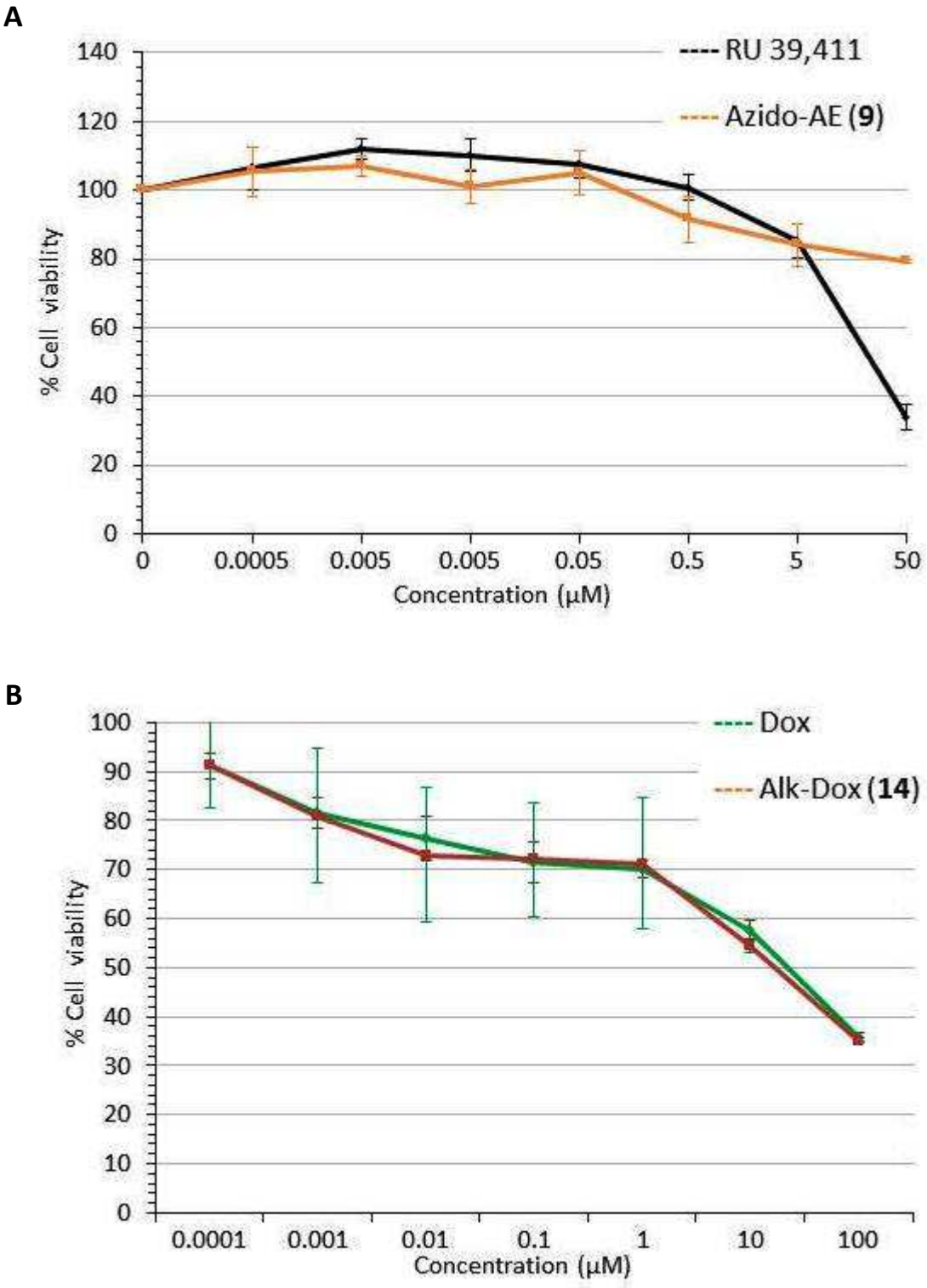


Figure S29: Comparing cytotoxicity of modified A) Azido-AE (**9**), and B)Alk-Dox (**14**) with their parent compounds treated in MCF-7 (24h)