Synthesis of cytotoxic urs-12-ene- and 28-nor-urs-12-ene- type conjugates with amino- and mercapto-1,3,4-oxadiazoles and mercapto-1,2,4-triazoles

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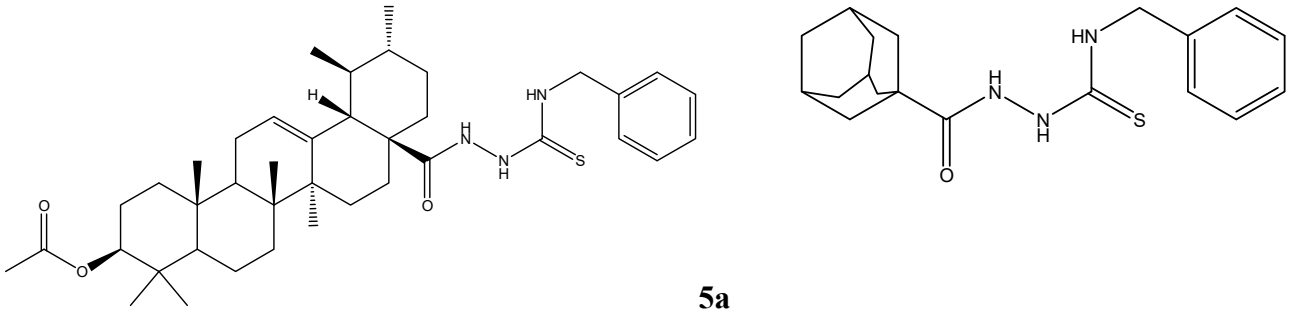


5a

Fig. S1 Structures of acylthiosemicarbazide **5a** and N-benzyl-2-(adamantanecarbonyl)hydrazine carbothioamide

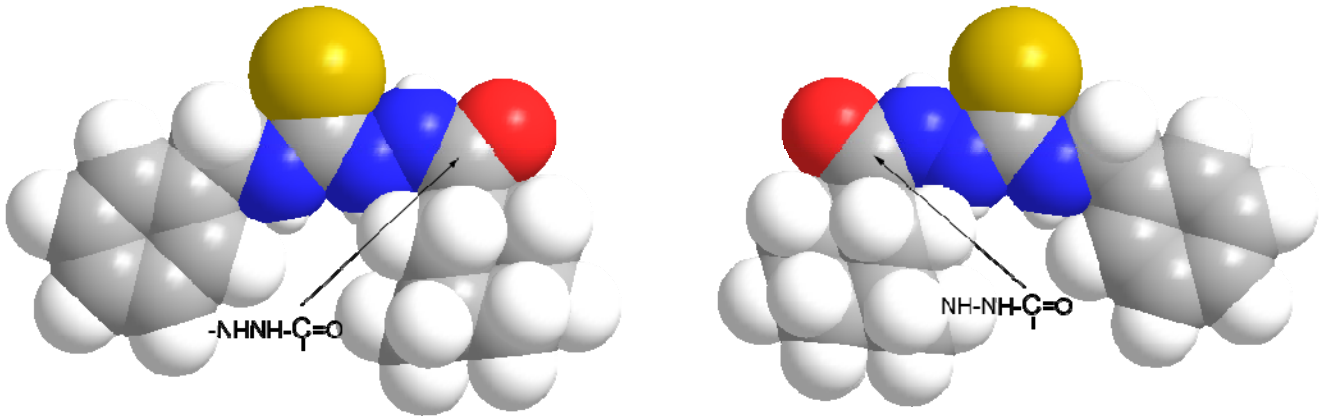


Fig. S2 Front and rear projections of molecules of adamantane type acylthiosemicarbazide on the plane O=C-NH-. Geometry of the molecules was optimized by molecular mechanics method. Atoms are shown as van der Waals spheres.

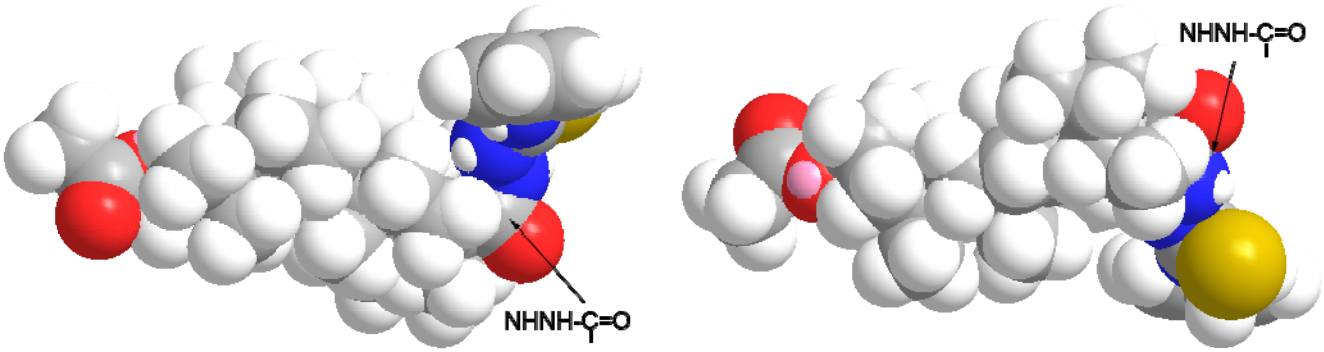


Fig. S3 Front and rear projections of molecules of ursane type acylthiosemicarbazide **5a** on the plane O=C^{28}-NH-. Geometry of the molecules was optimized by molecular mechanics method. Atoms are shown as van der Waals spheres.

A

B

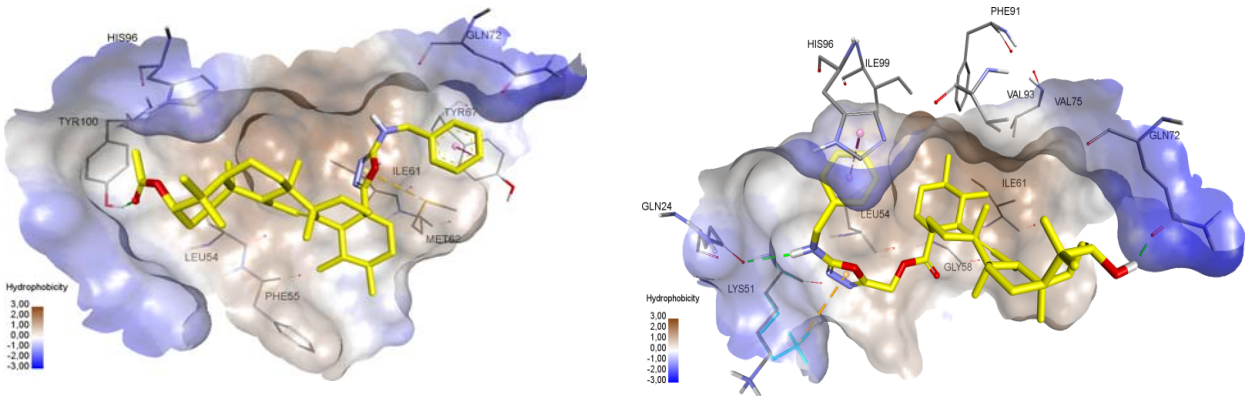


Fig. S4 Docking in MDM2 protein. Noncovalent interactions of compounds (A – **7a**, B – **12**) are shown by dotted lines: green - hydrogen bonds, purple –stacking interactions, orange – electrostatic interactions, hydrophobic interactions are omitted.

C

D

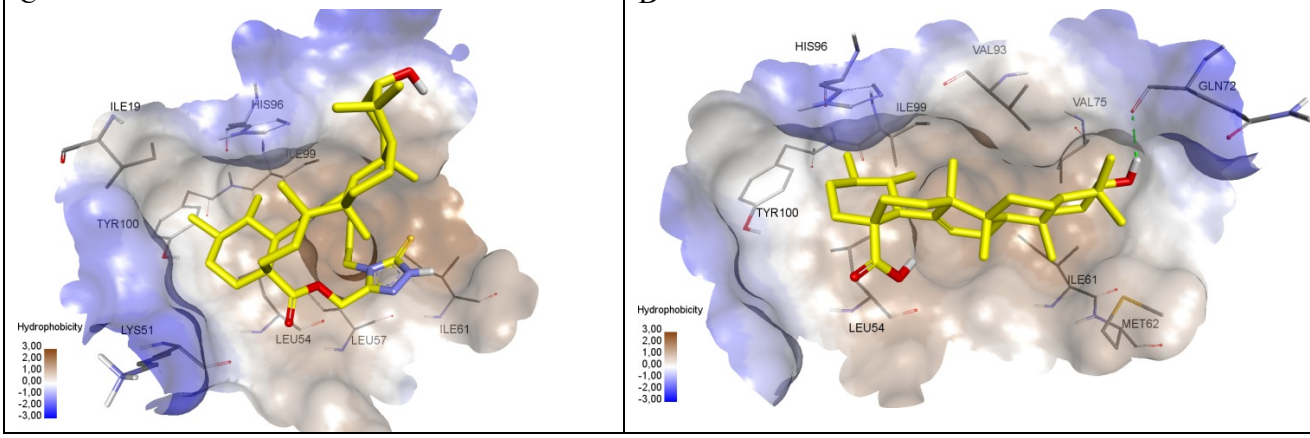
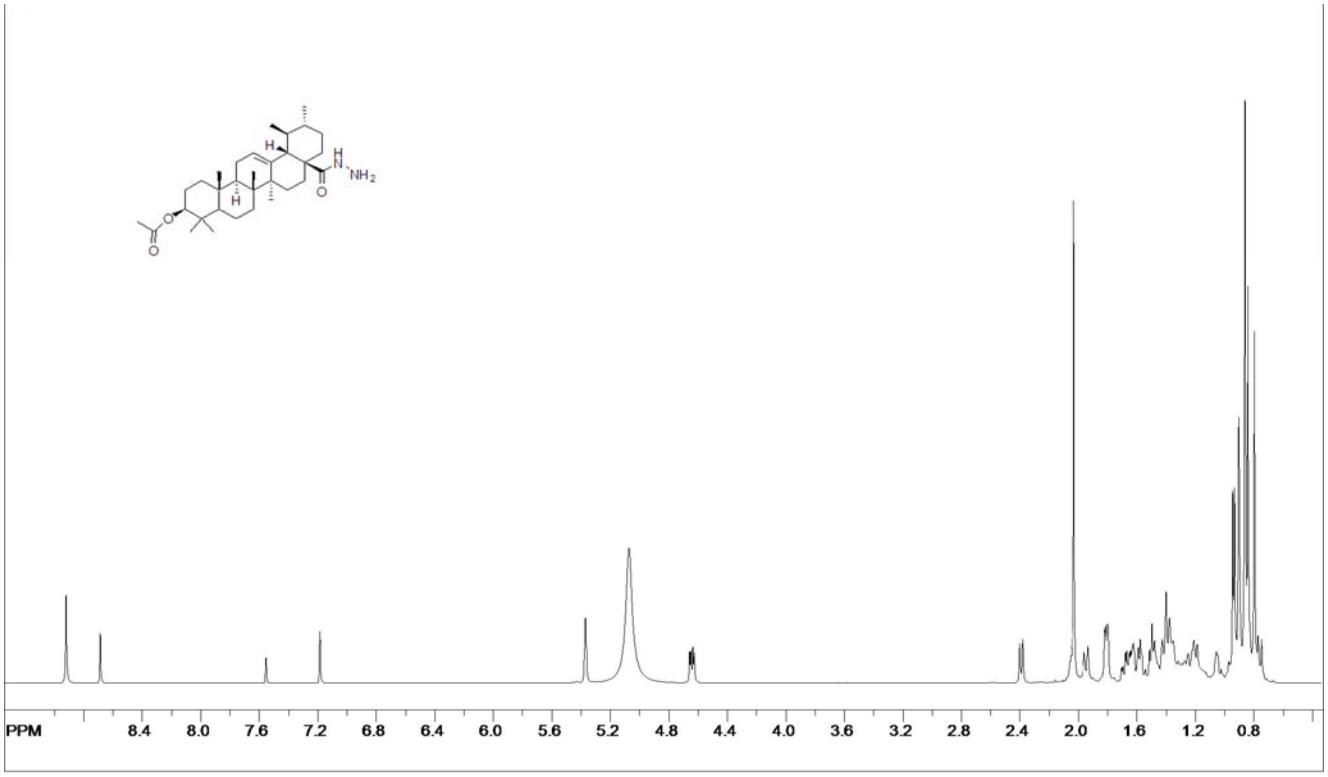


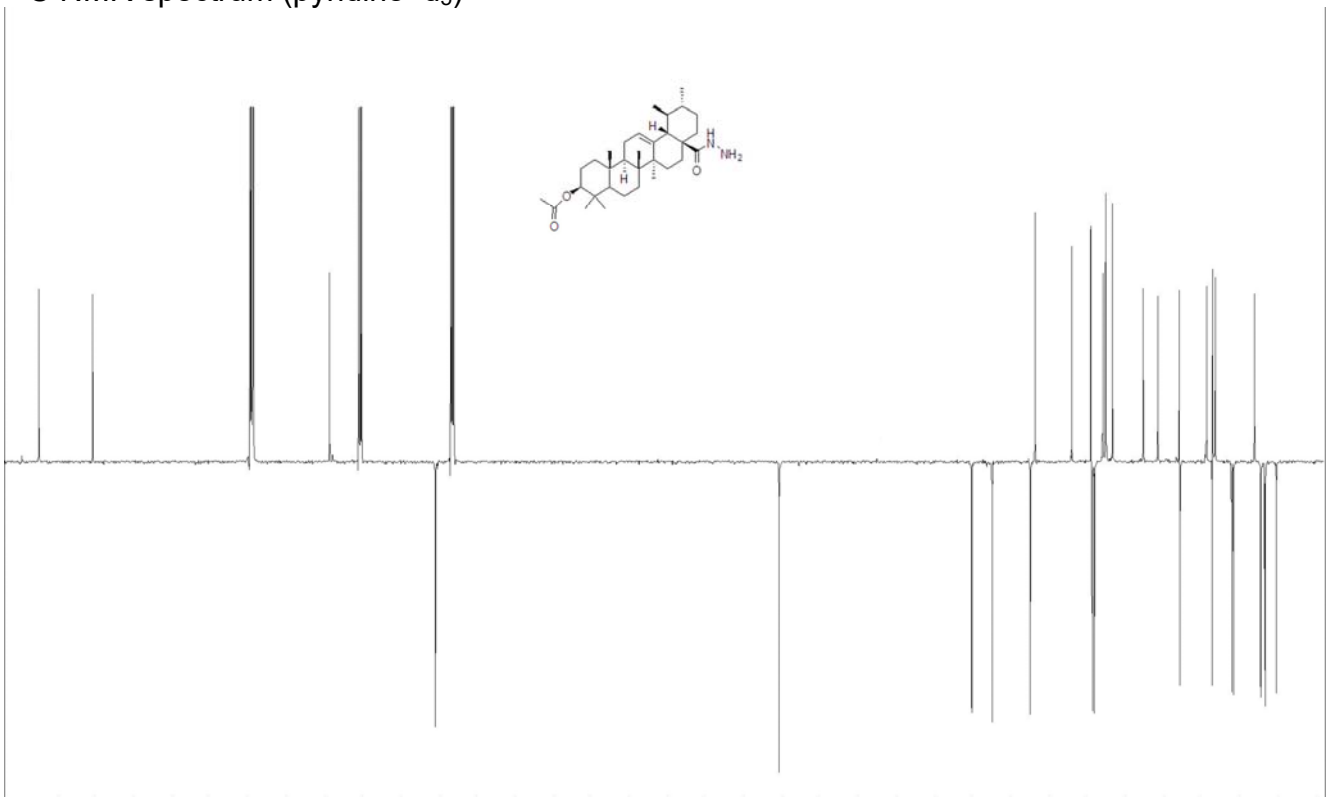
Figure S5. Docking in MDM2 protein. Noncovalent interactions of compounds (C - **12**, D – ursolic acid **1**) are shown by dotted lines: green - hydrogen bonds, purple –stacking interactions, orange – electrostatic interactions, hydrophobic interactions are omitted.

FigS6. NMR ^{1}H and NMR ^{13}C spectral data of hybrid compounds

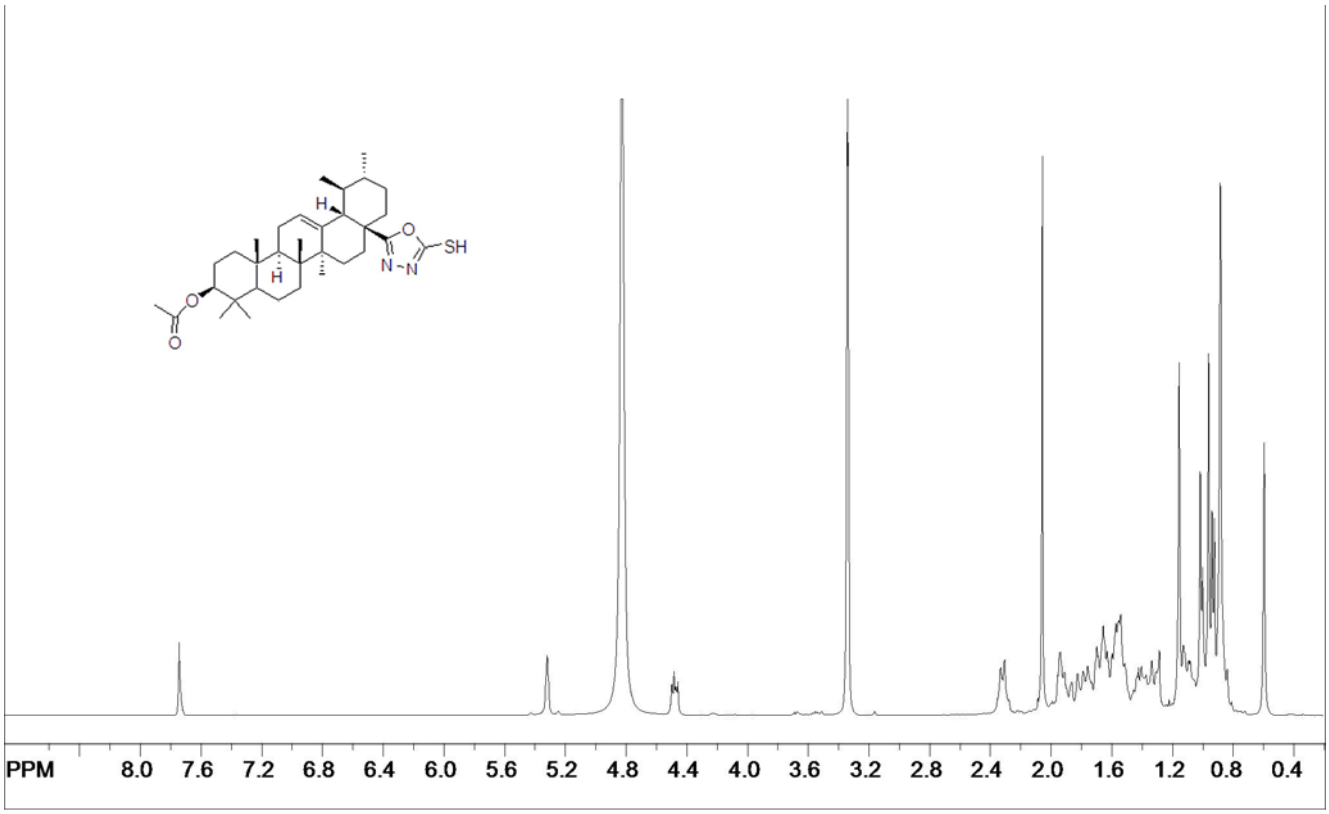
3 ^{1}H NMR spectrum (pyridine D_5)



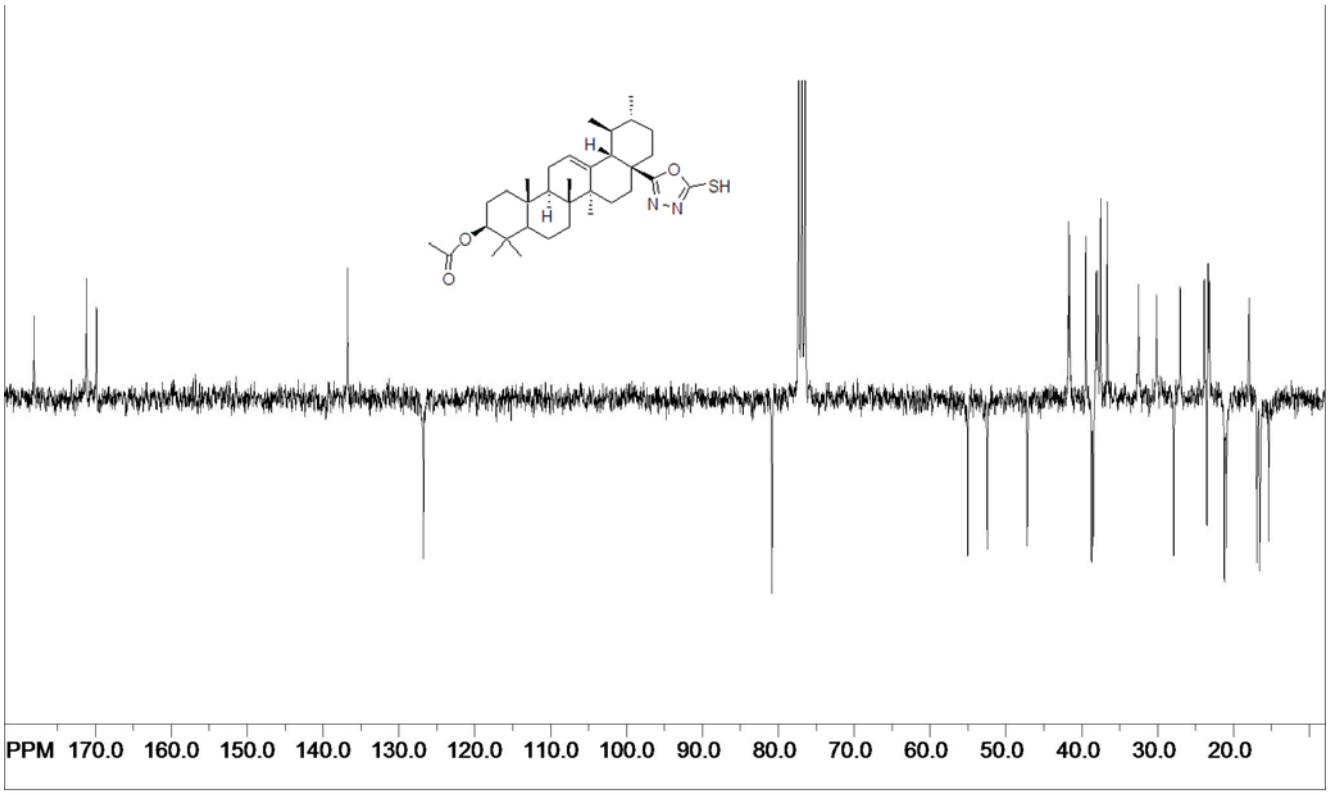
^{13}C NMR spectrum (pyridine d_5)



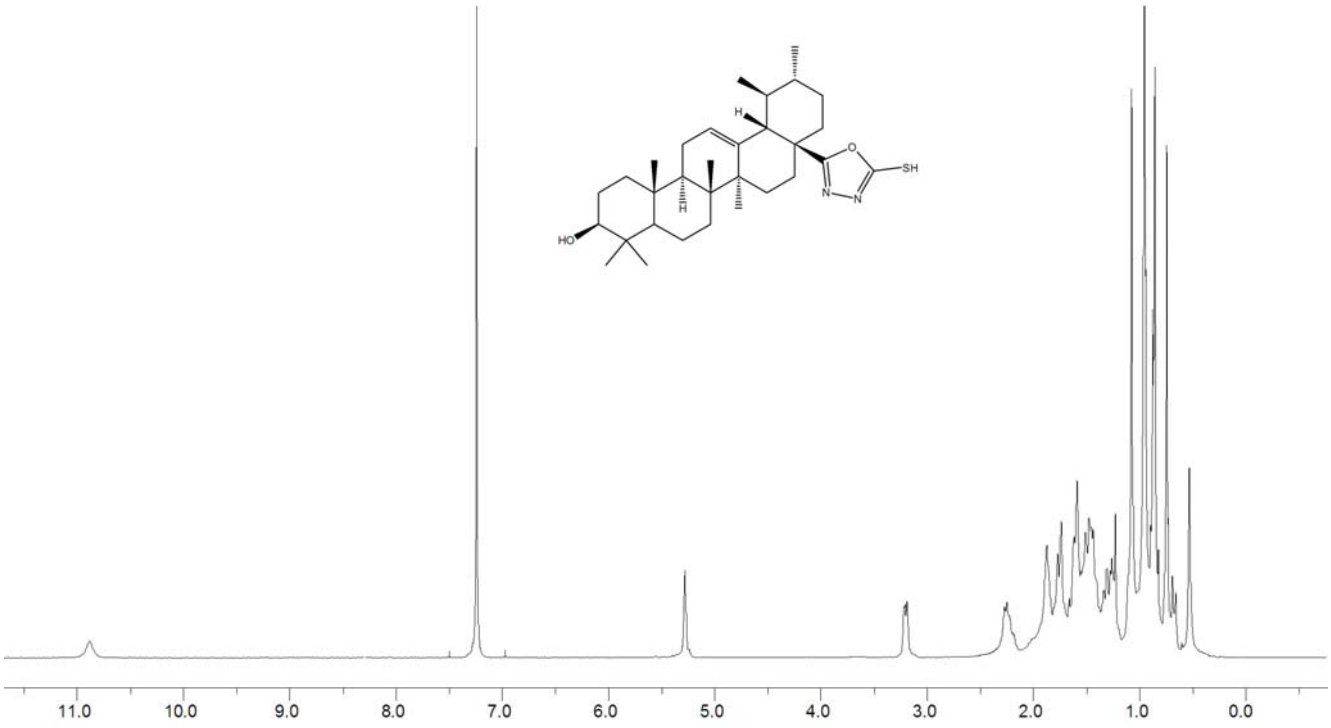
4a ^{1}H NMR spectrum ($CDCl_3$, CD_3OD)



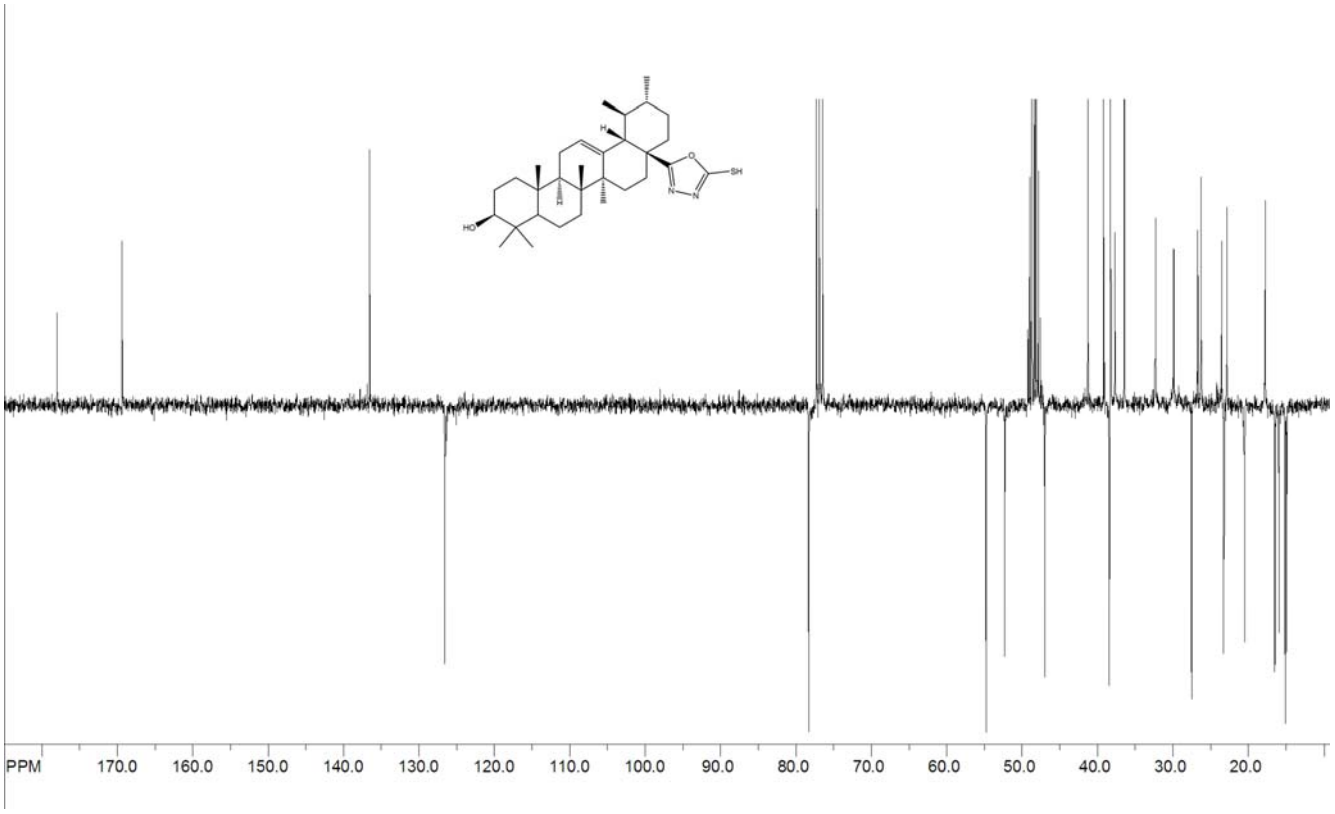
^{13}C NMR spectrum ($CDCl_3$, CD_3OD)



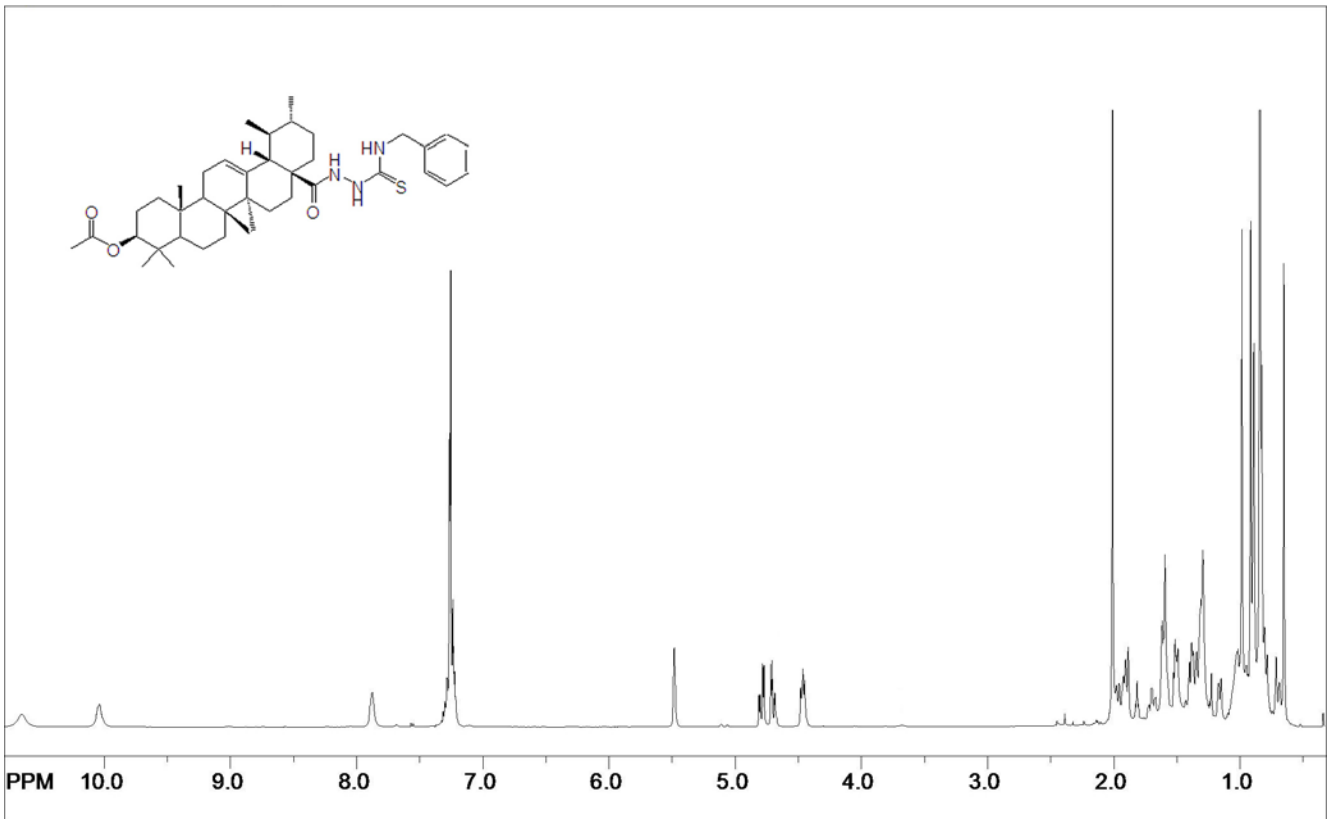
4b ^{1}H NMR spectrum ($CDCl_3$, CD_3OD)



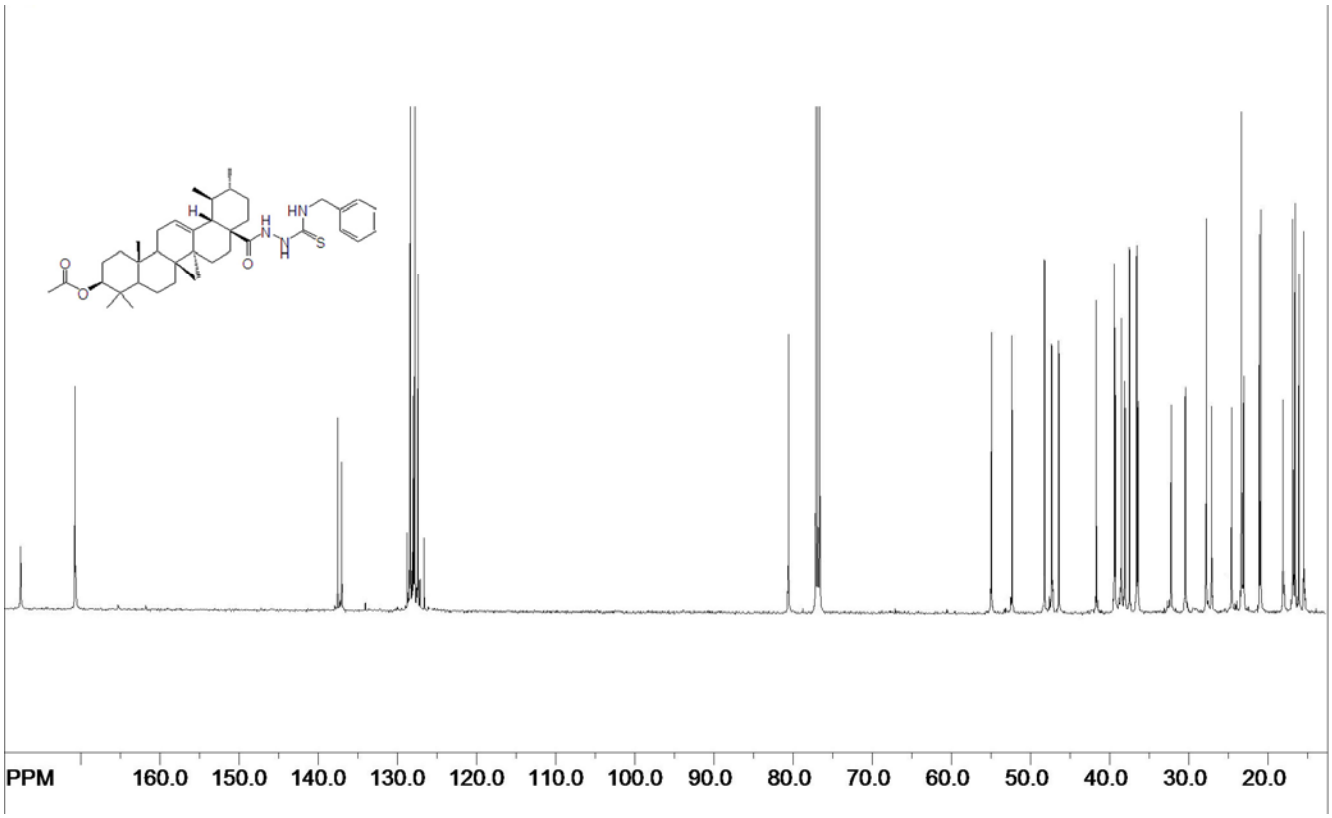
^{13}C NMR spectrum ($CDCl_3$, CD_3OD)



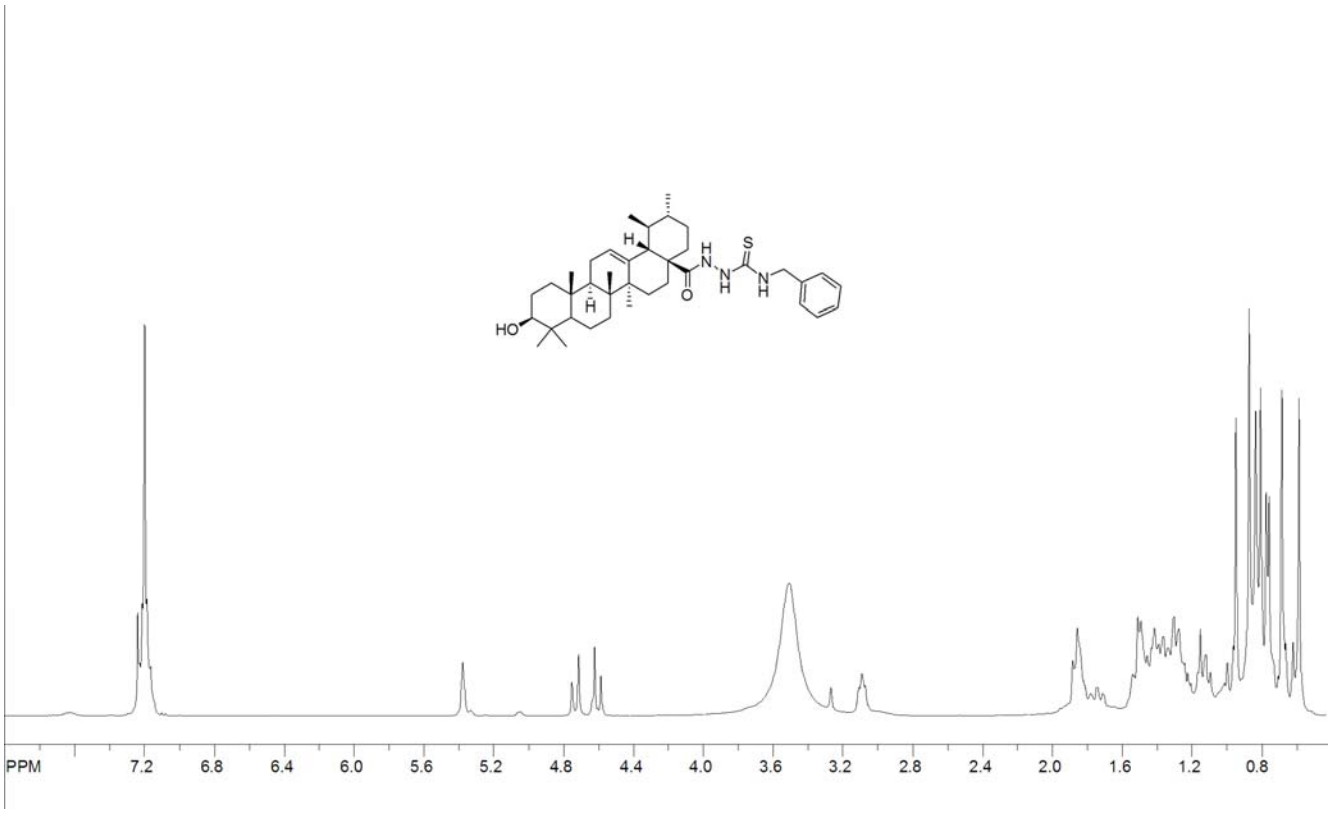
5a ^{1}H NMR spectrum ($CDCl_3$)



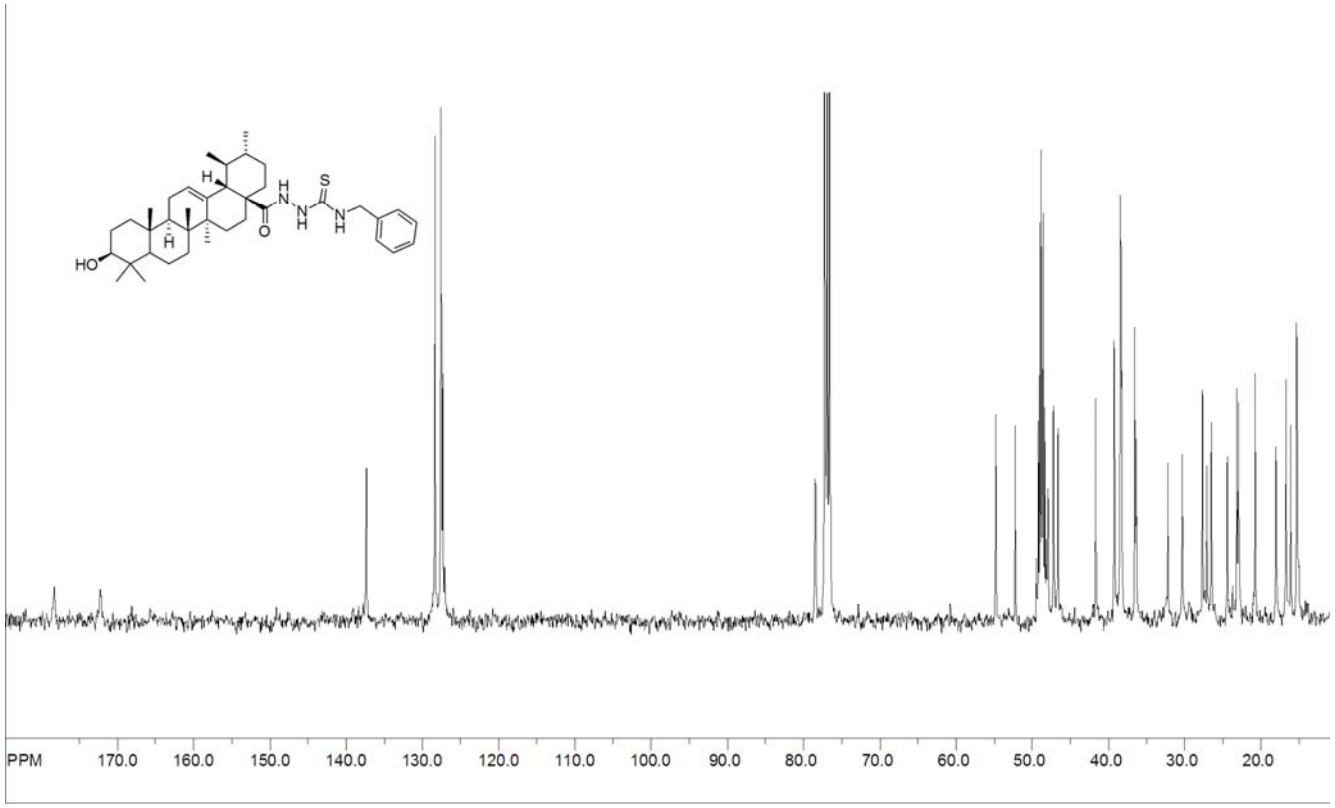
^{13}C NMR spectrum ($CDCl_3$)



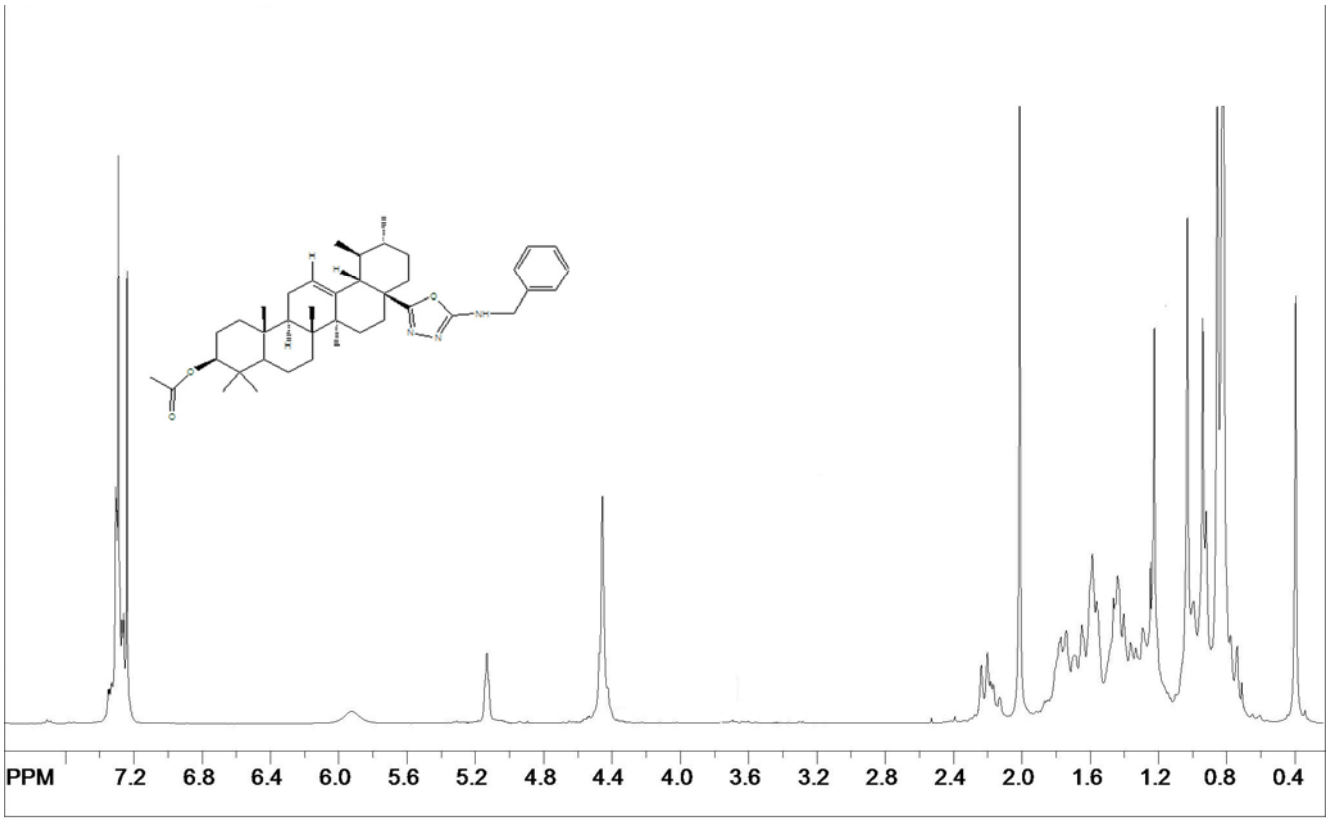
5b ^{1}H NMR spectrum ($CDCl_3$, CD_3OD)



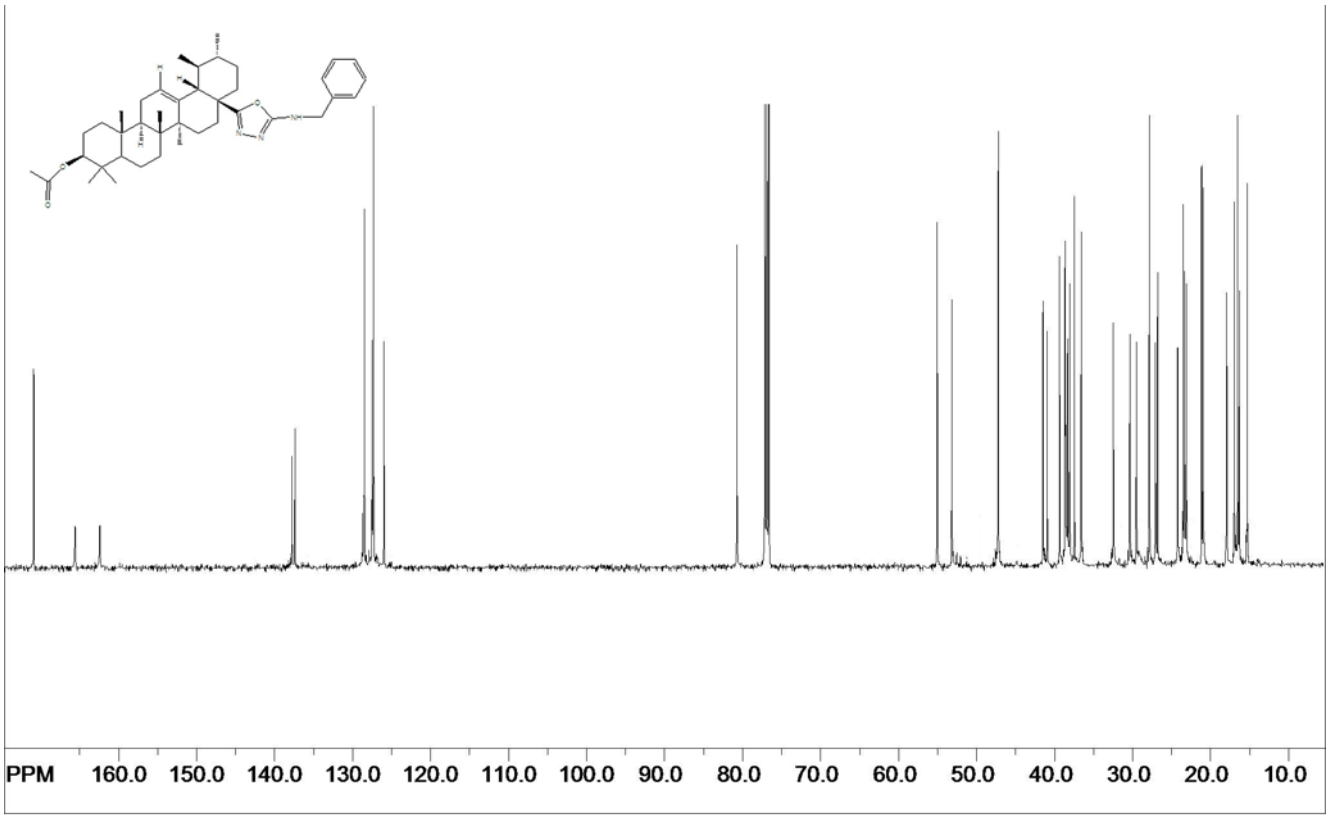
^{13}C NMR spectrum ($CDCl_3$, CD_3OD)



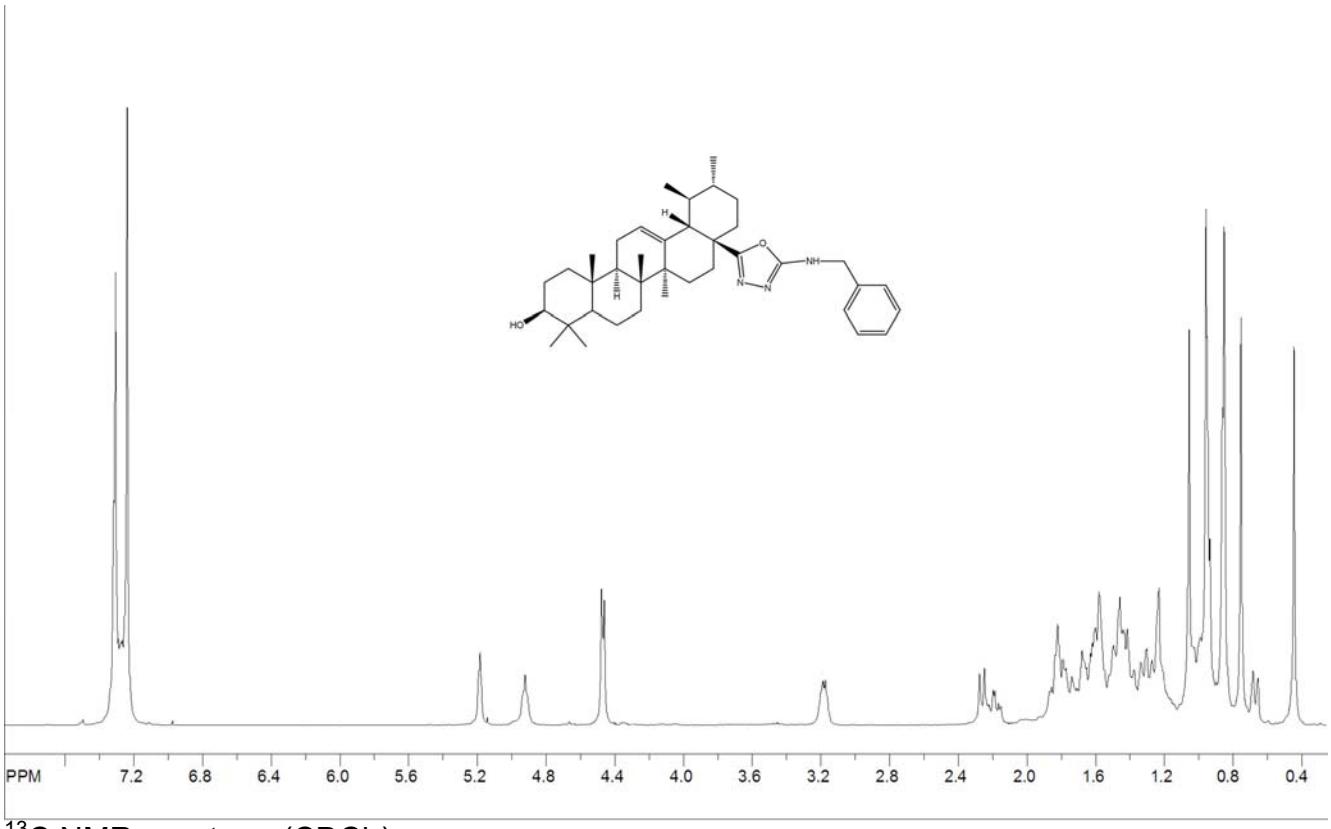
7a ^{1}H NMR spectrum ($CDCl_3$)



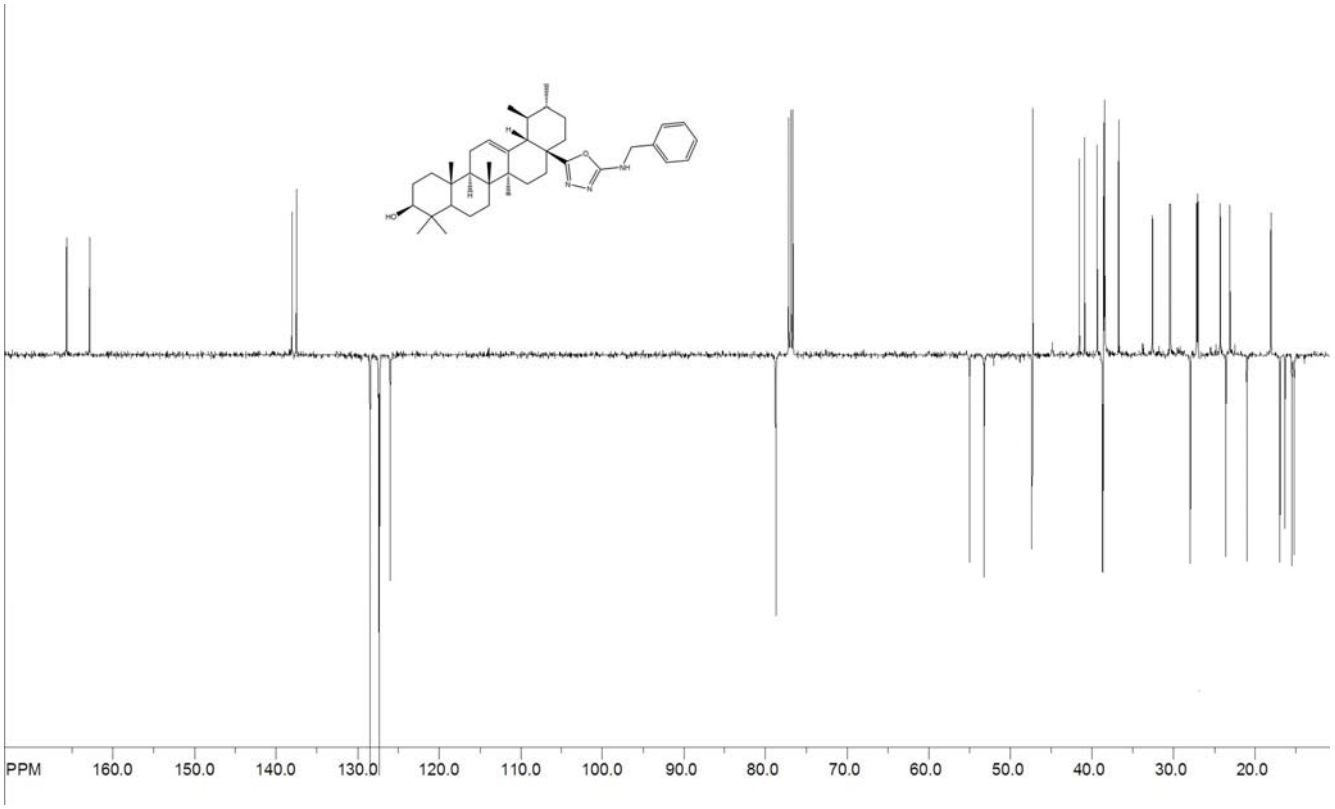
^{13}C NMR spectrum ($CDCl_3$)



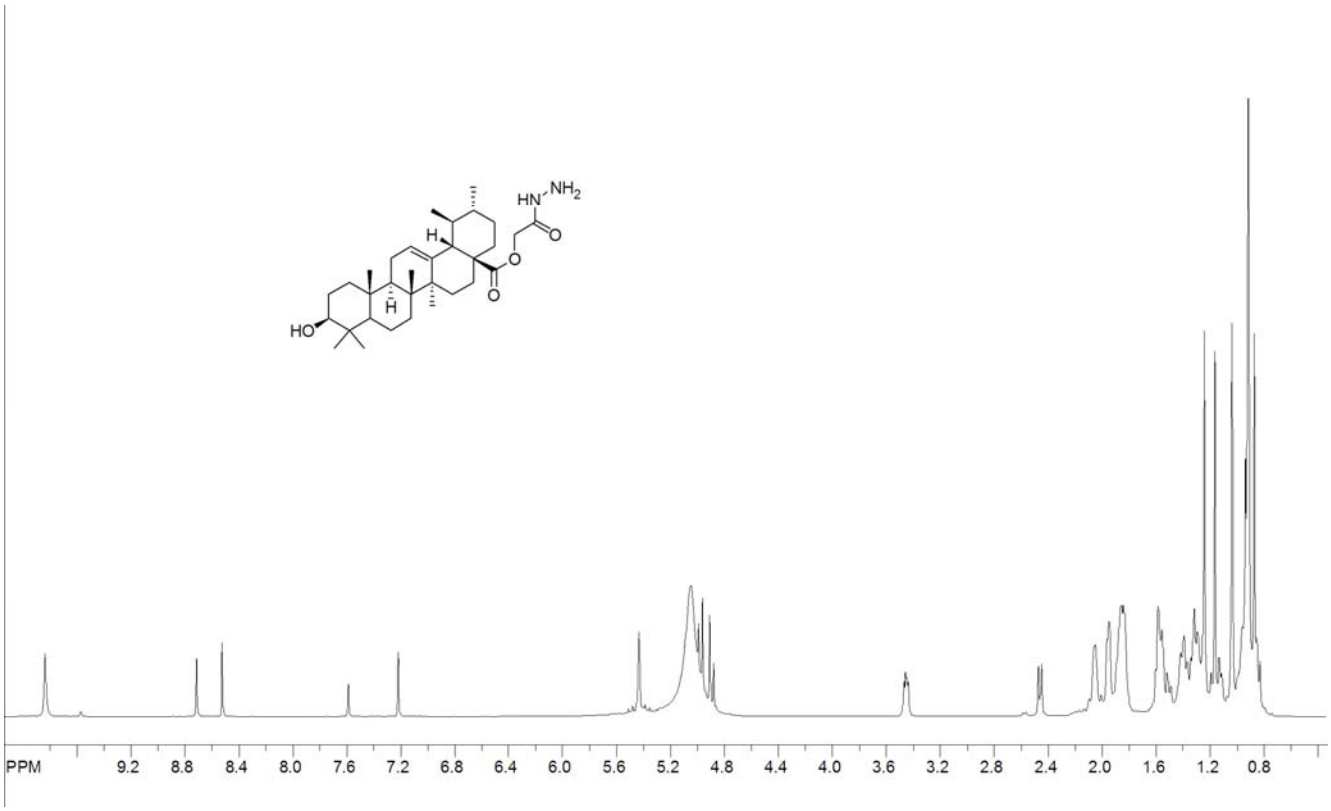
7b ^{1}H NMR spectrum ($CDCl_3$)



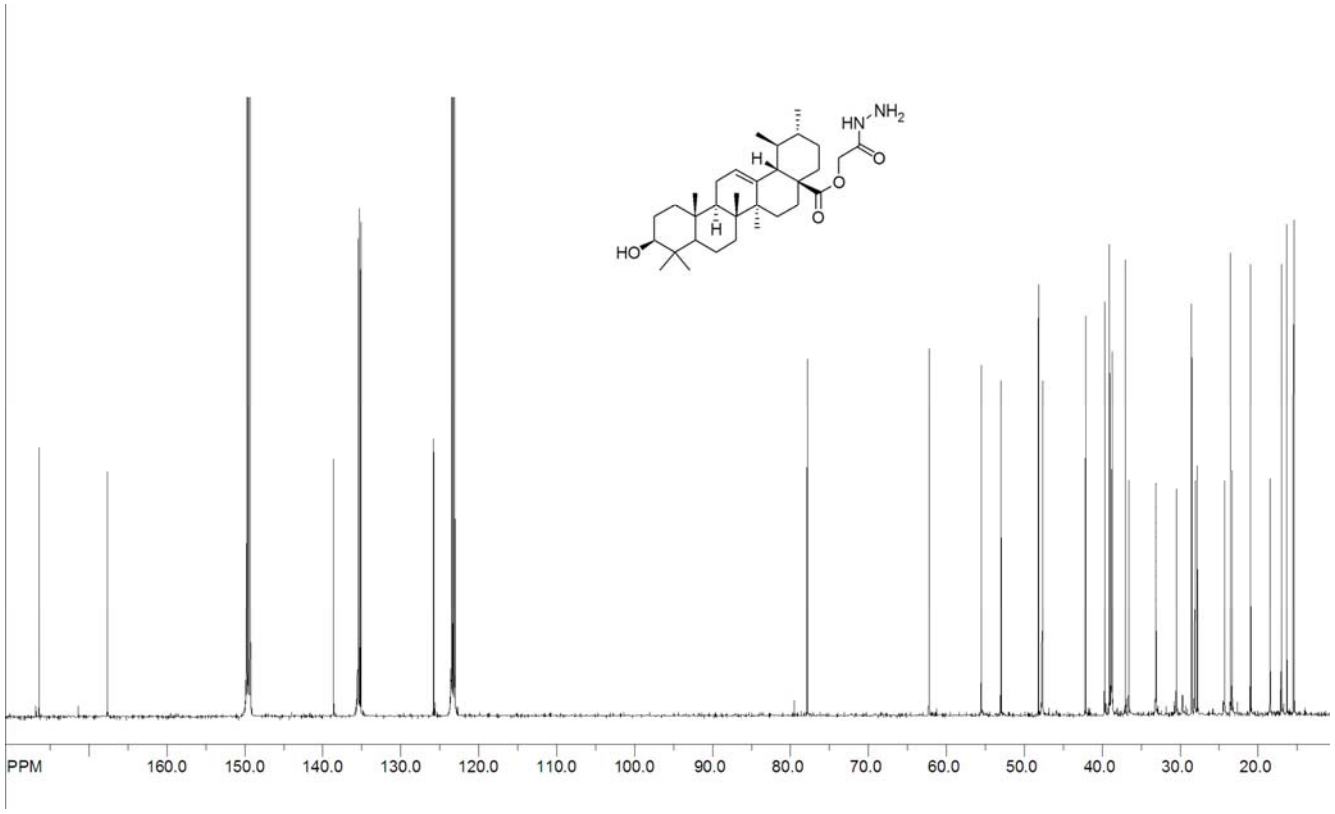
^{13}C NMR spectrum ($CDCl_3$)



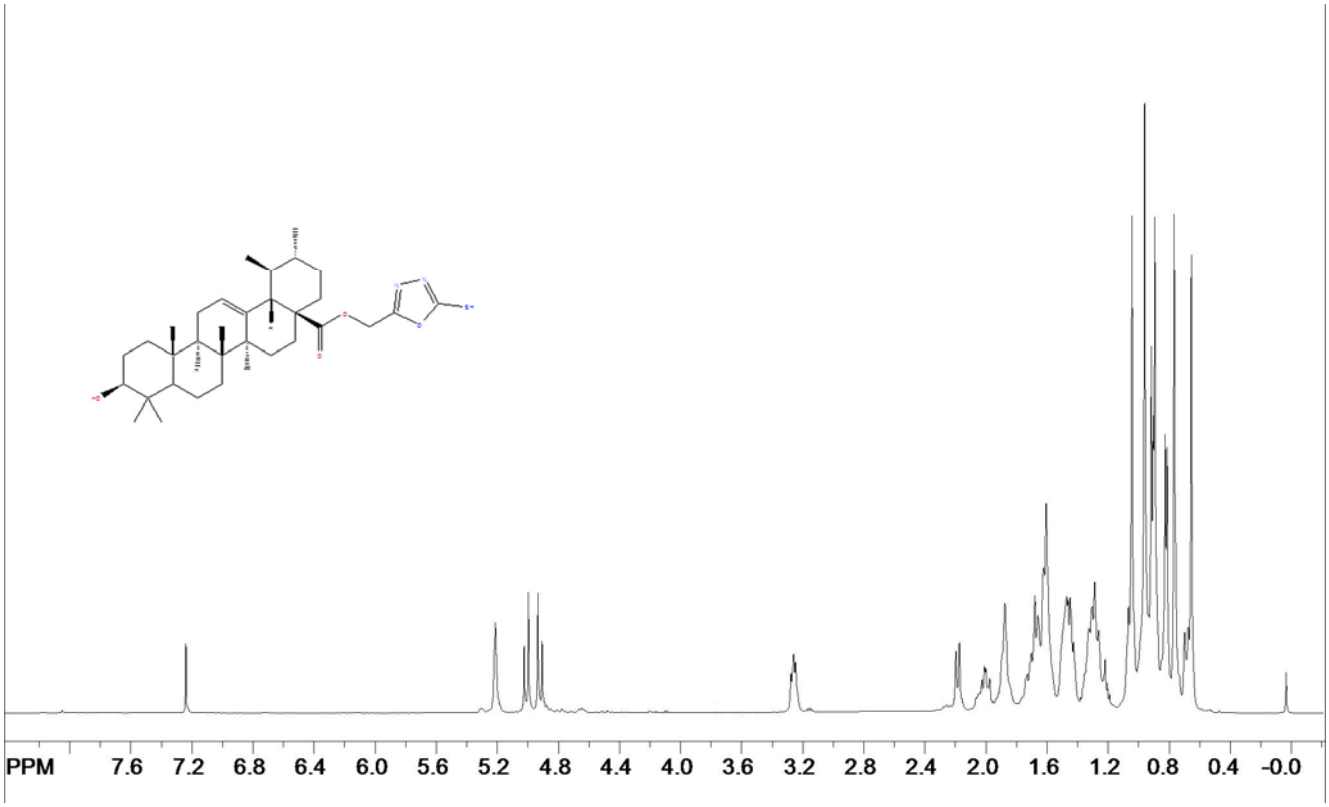
9 ^{1}H NMR spectrum (pyridine D_5)



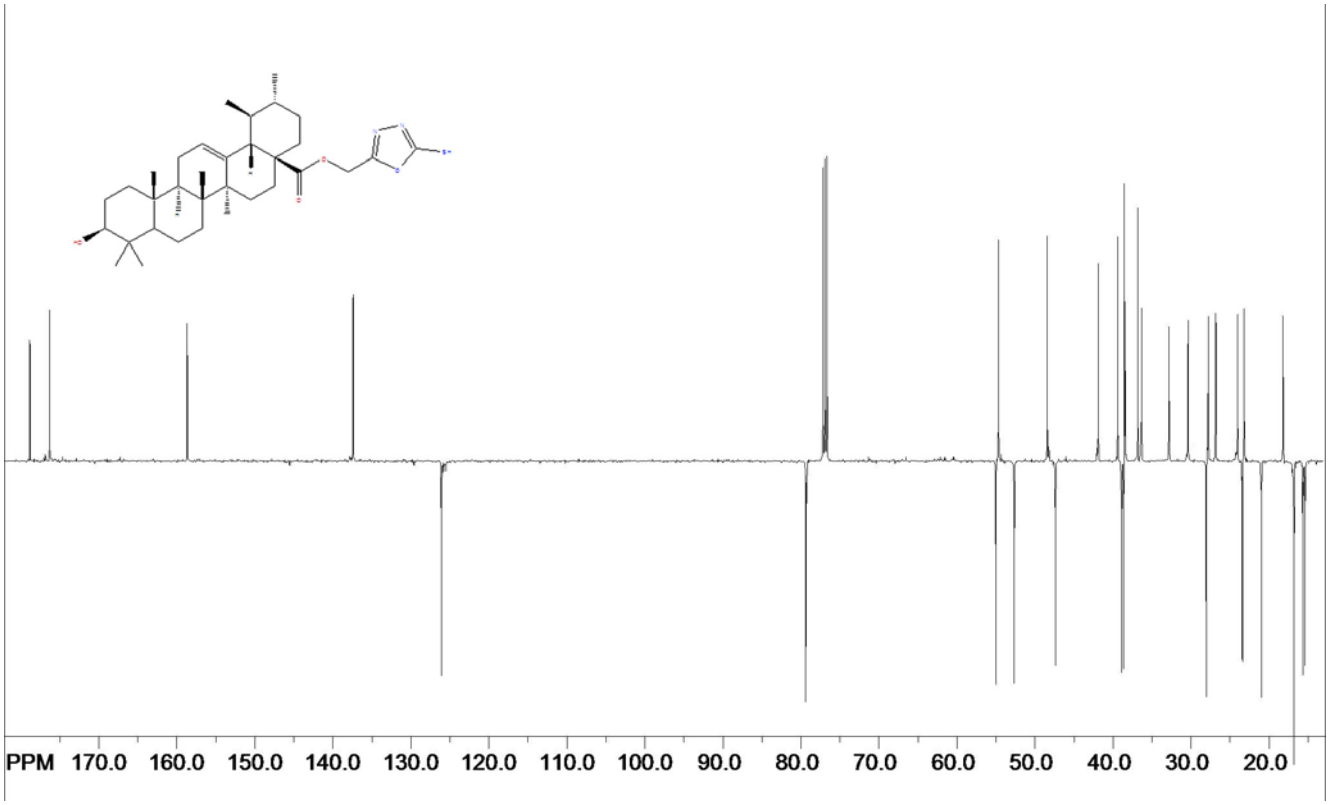
^{13}C NMR spectrum (pyridine D_5)



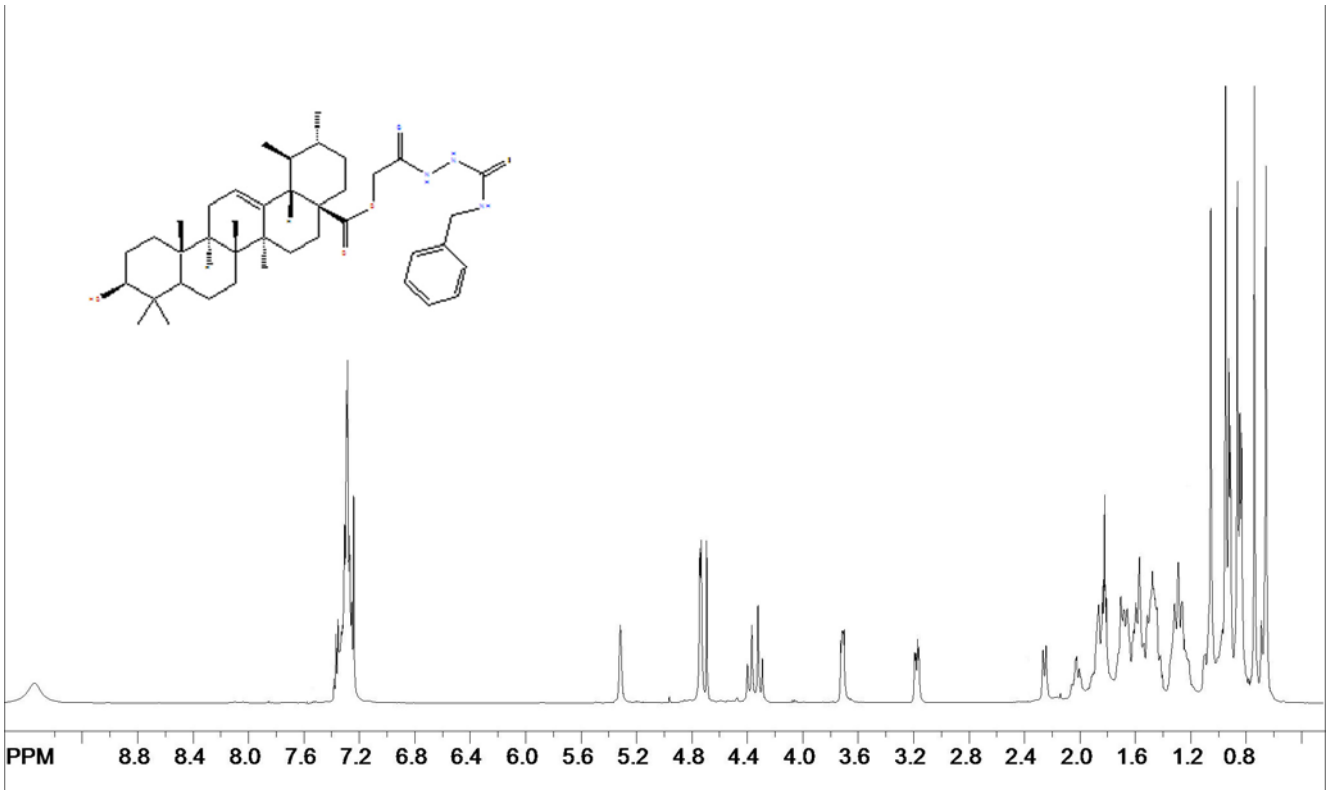
10 ^{1}H NMR spectrum ($CDCl_3$)



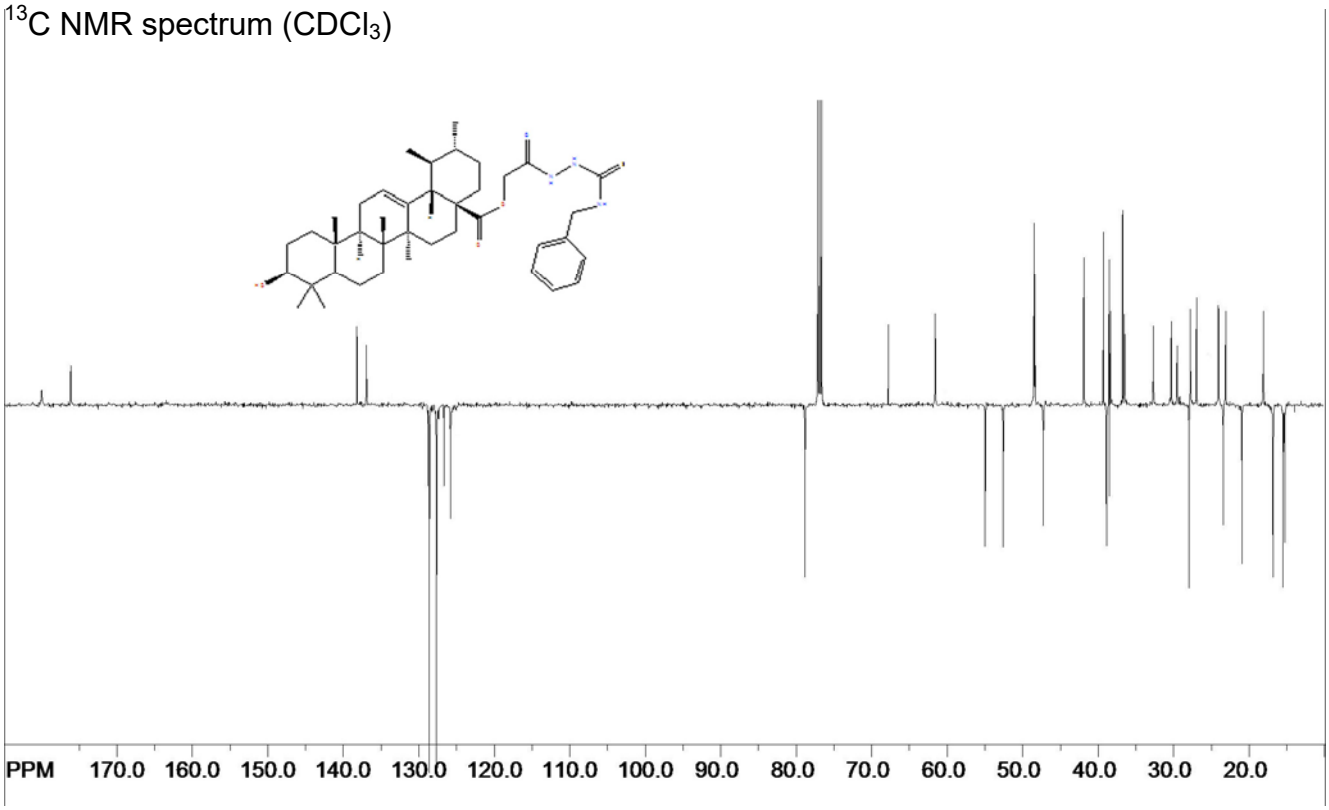
^{13}C NMR spectrum ($CDCl_3$)



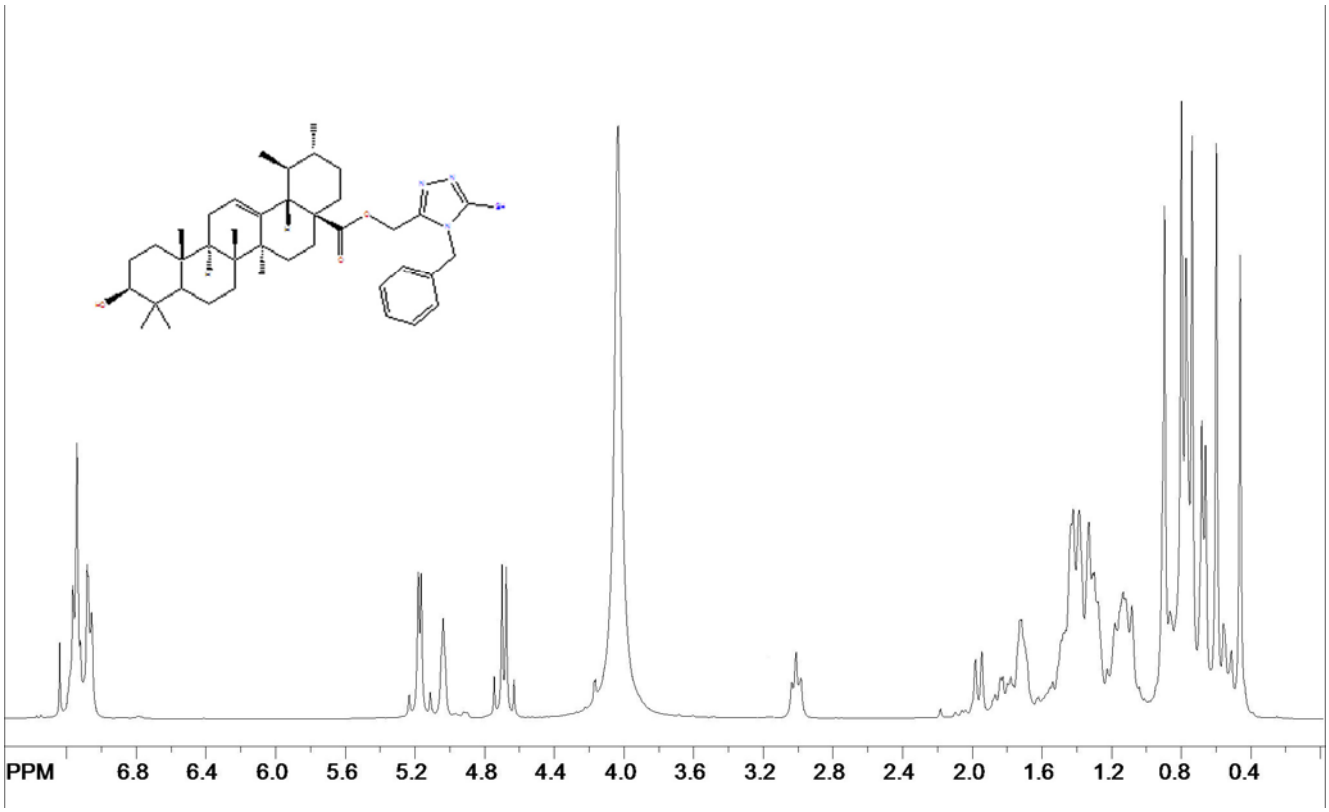
11 ^{1}H NMR spectrum ($CDCl_3$)



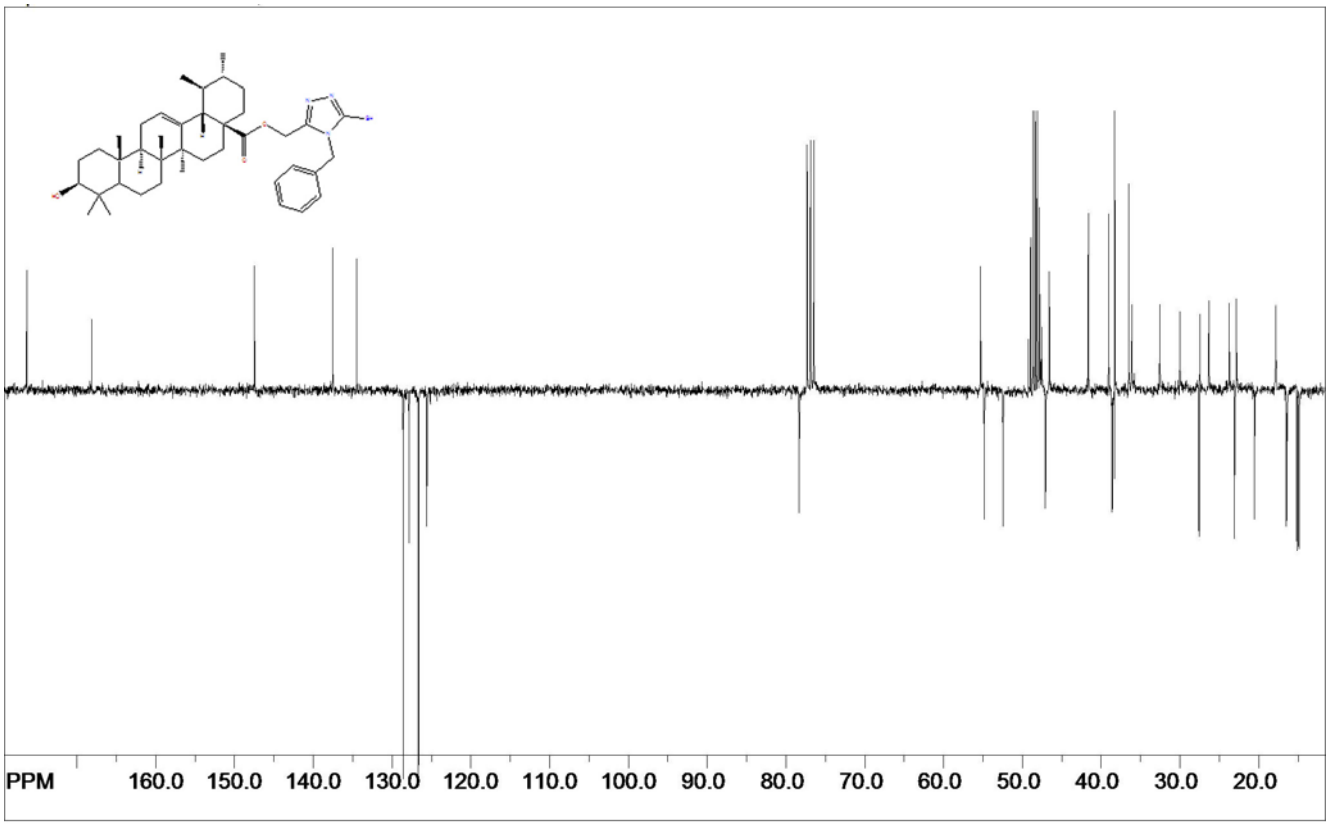
^{13}C NMR spectrum ($CDCl_3$)



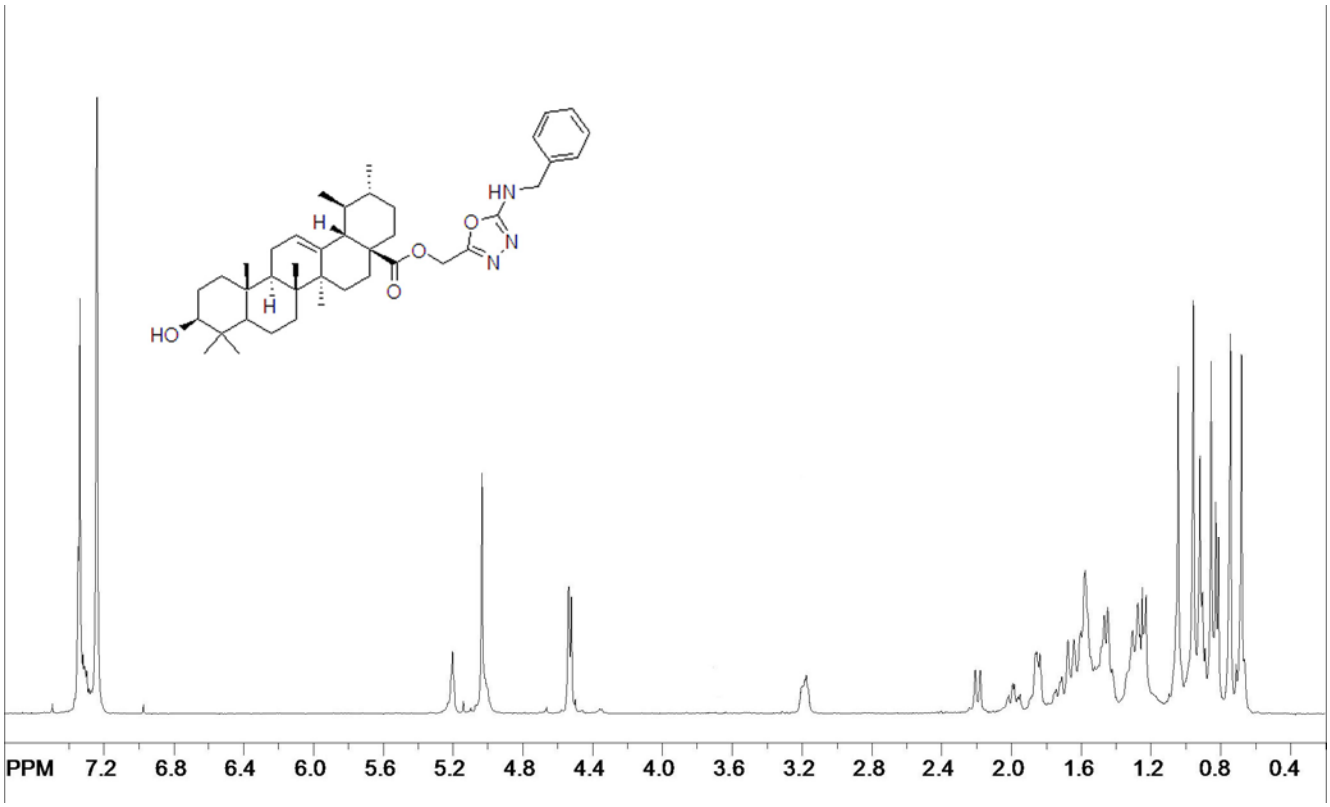
12 ^{1}H NMR spectrum ($CDCl_3$, CD_3OD)



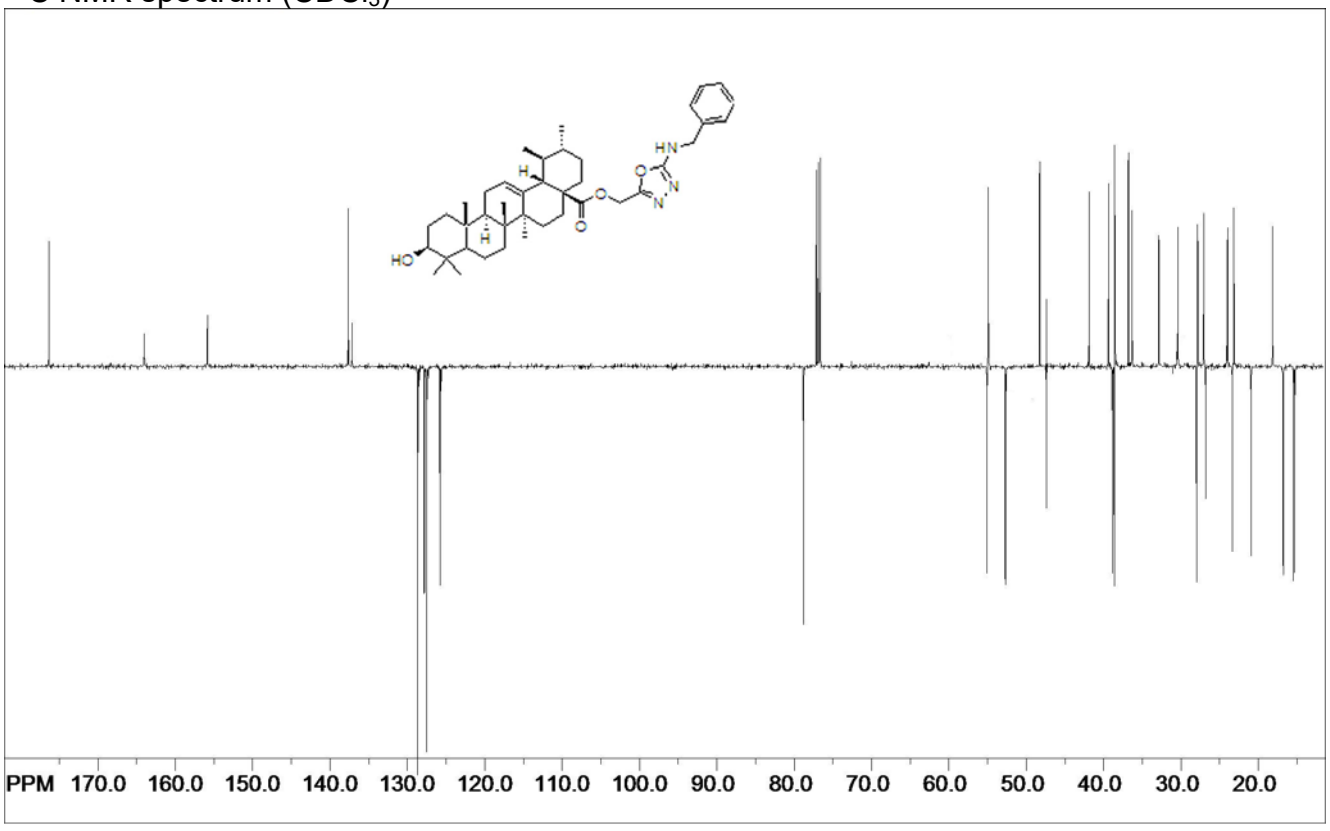
^{13}C NMR spectrum ($CDCl_3$, CD_3OD)



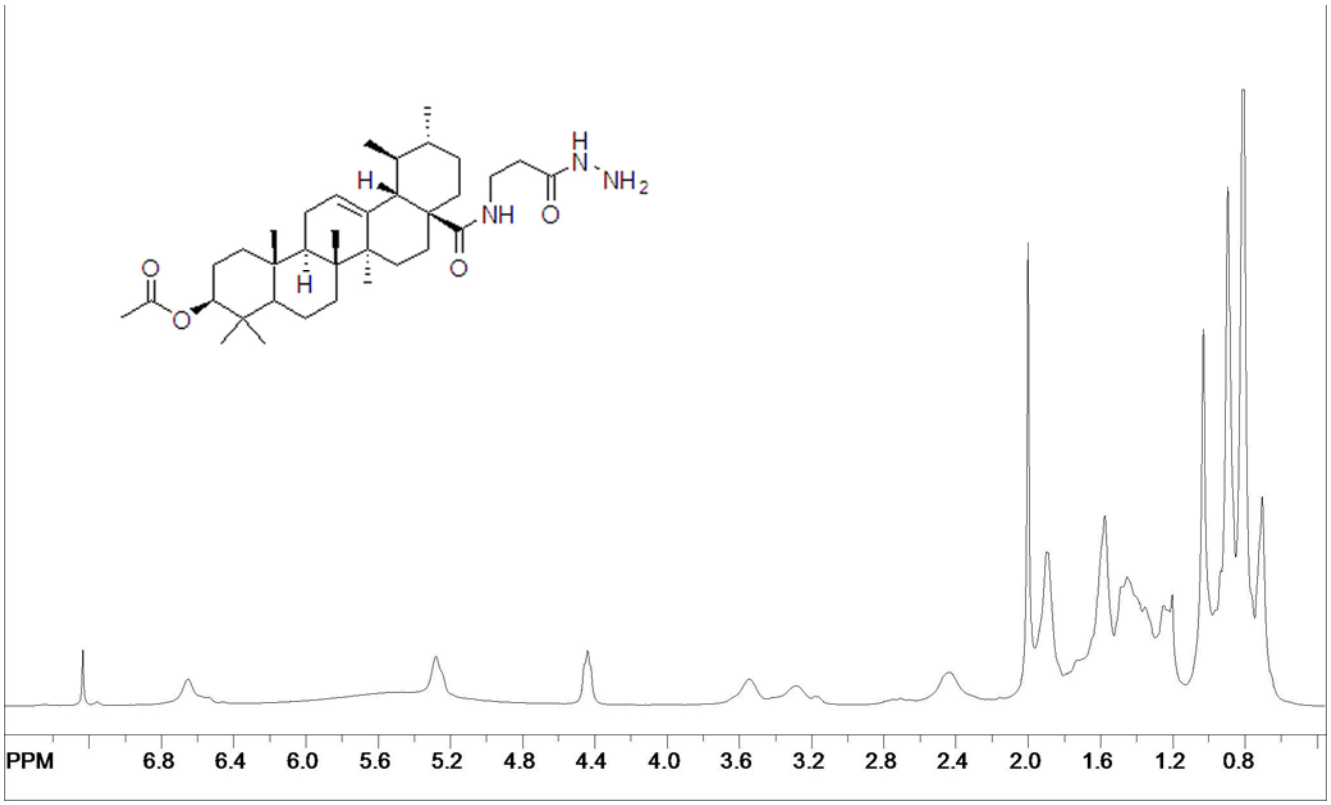
13 ^{1}H NMR spectrum ($CDCl_3$)



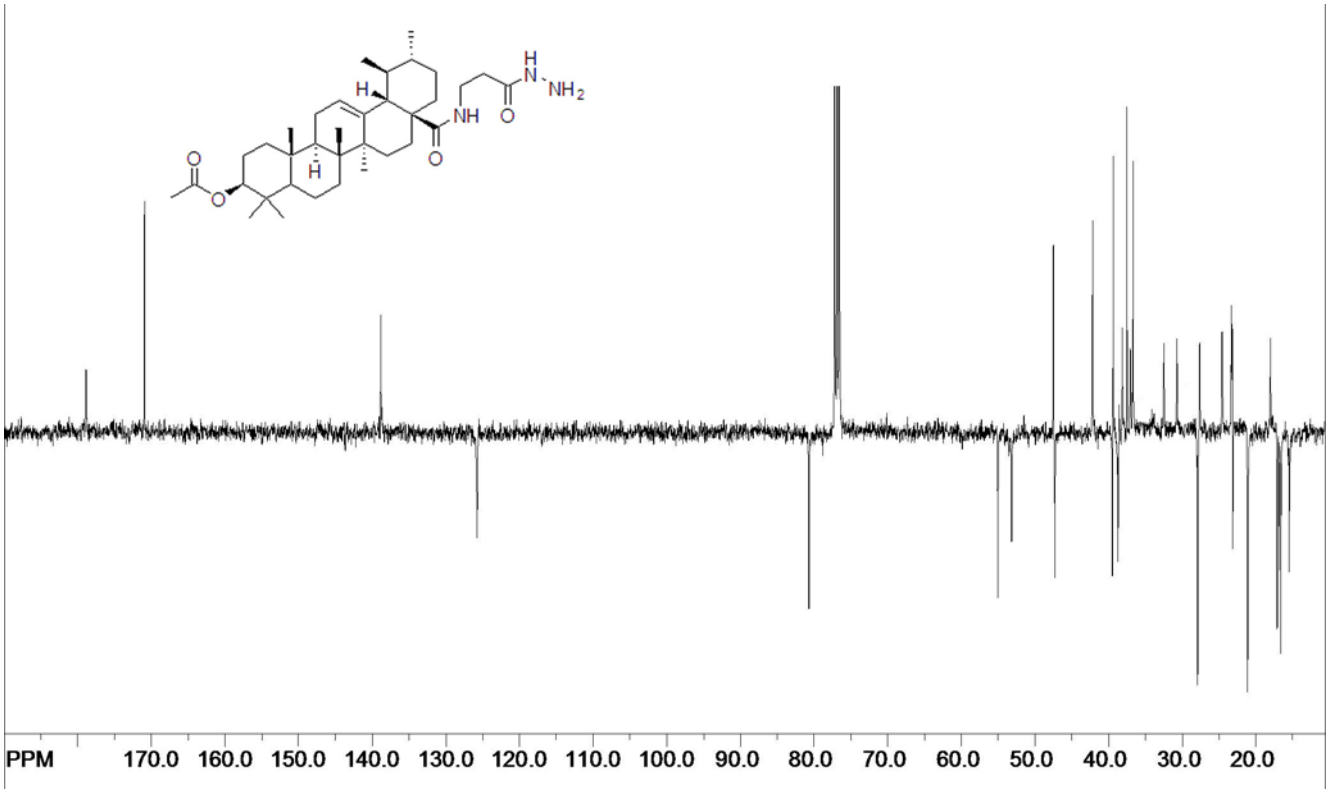
^{13}C NMR spectrum ($CDCl_3$)



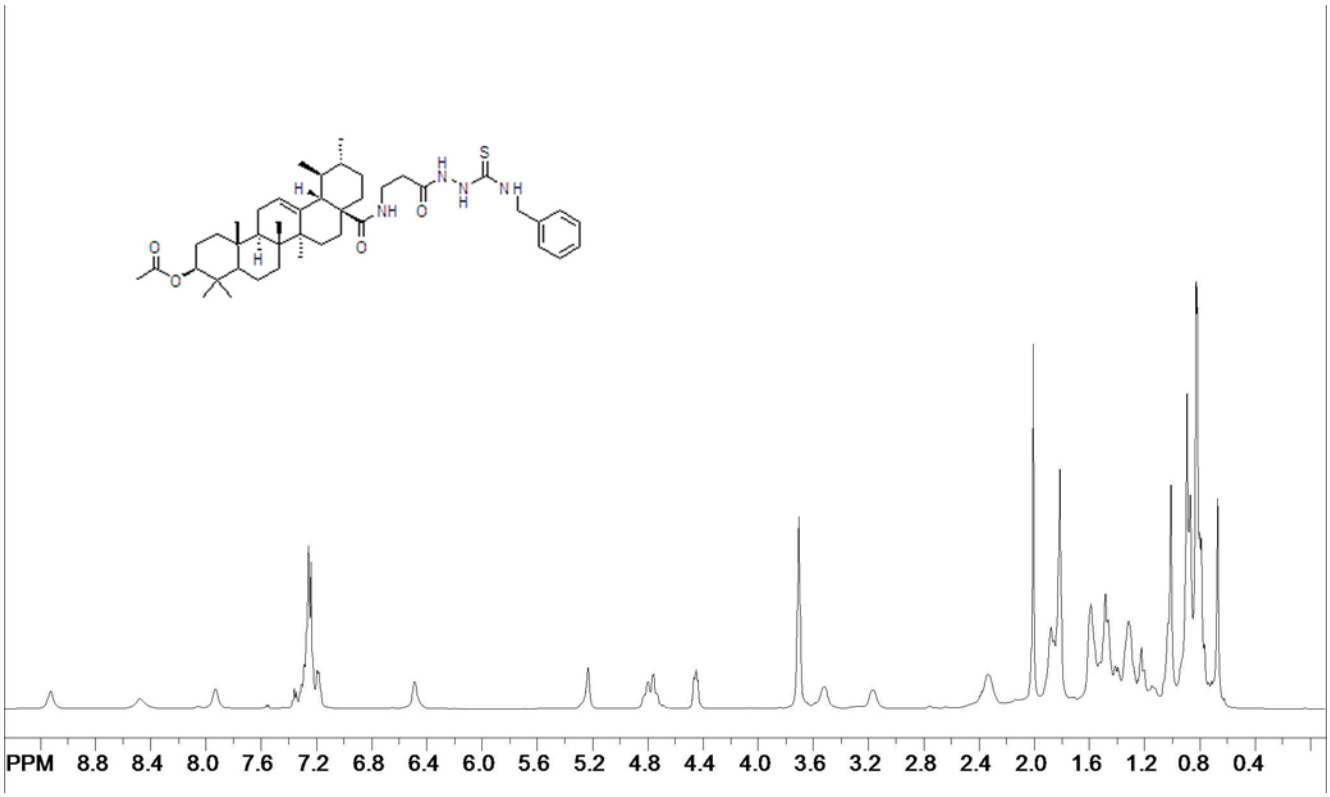
15 ^{1}H NMR spectrum ($CDCl_3$)



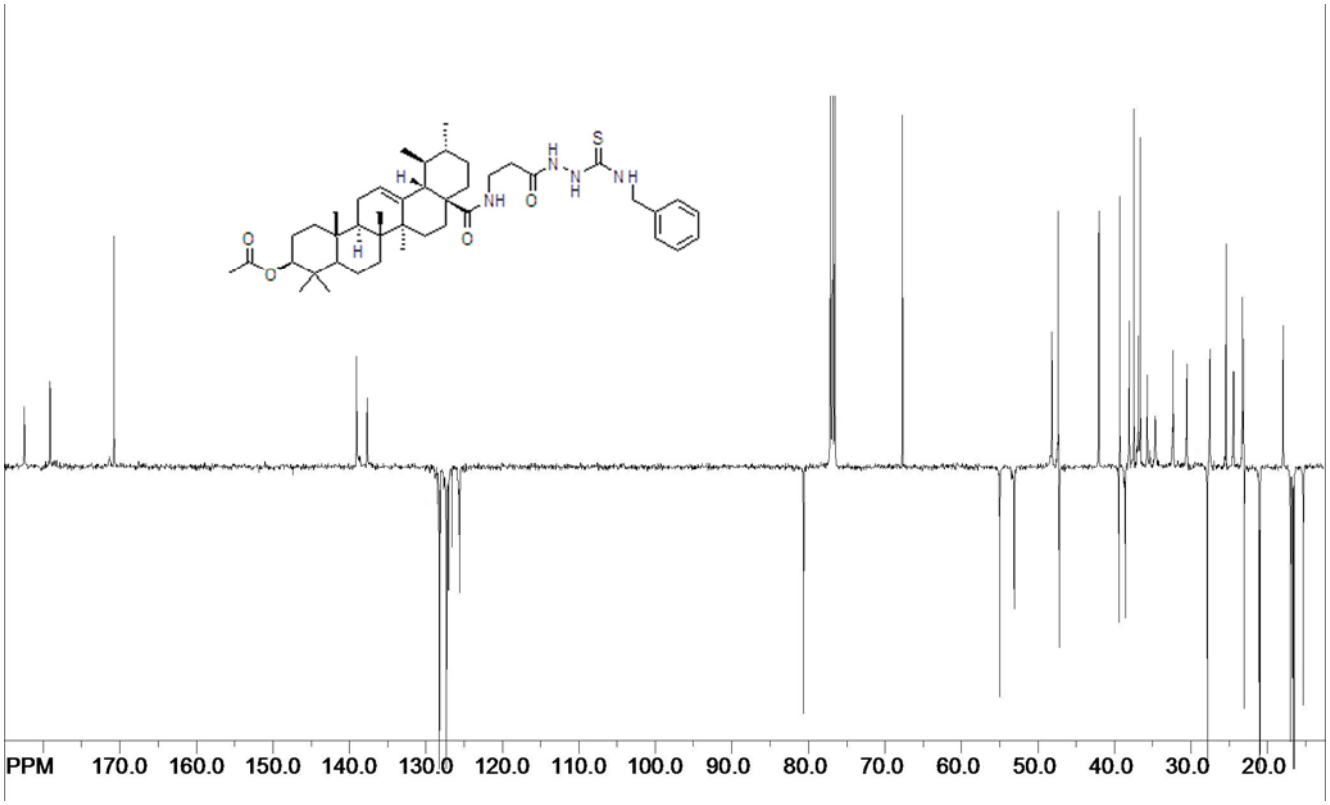
^{13}C NMR spectrum ($CDCl_3$)



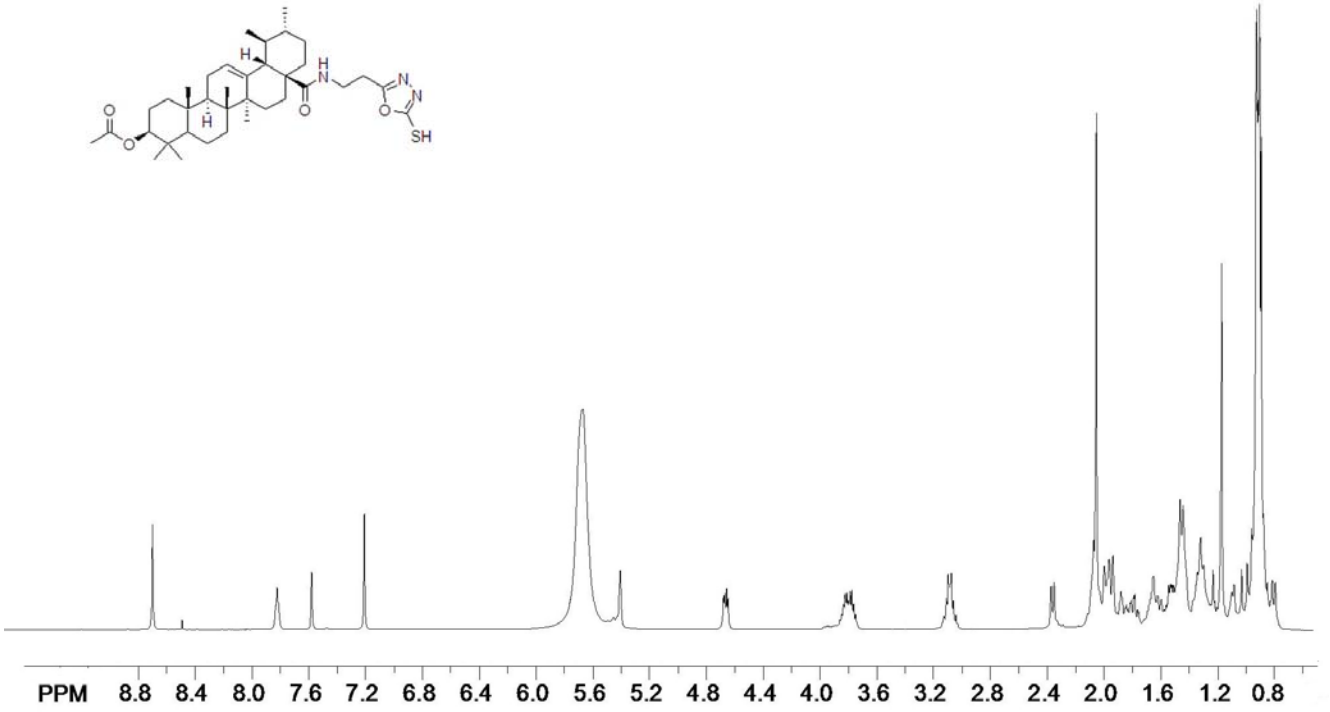
16 ^{1}H NMR spectrum ($CDCl_3$)



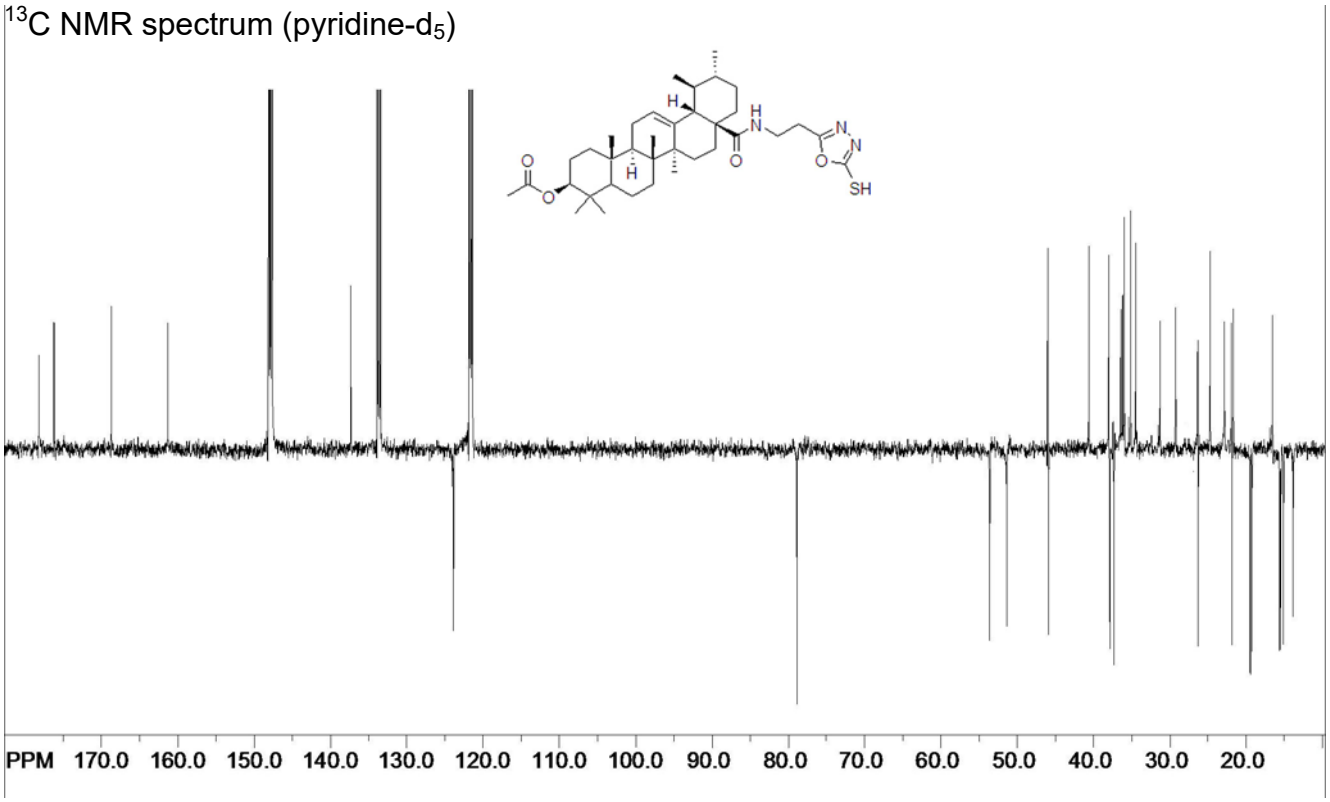
^{13}C NMR spectrum ($CDCl_3$)



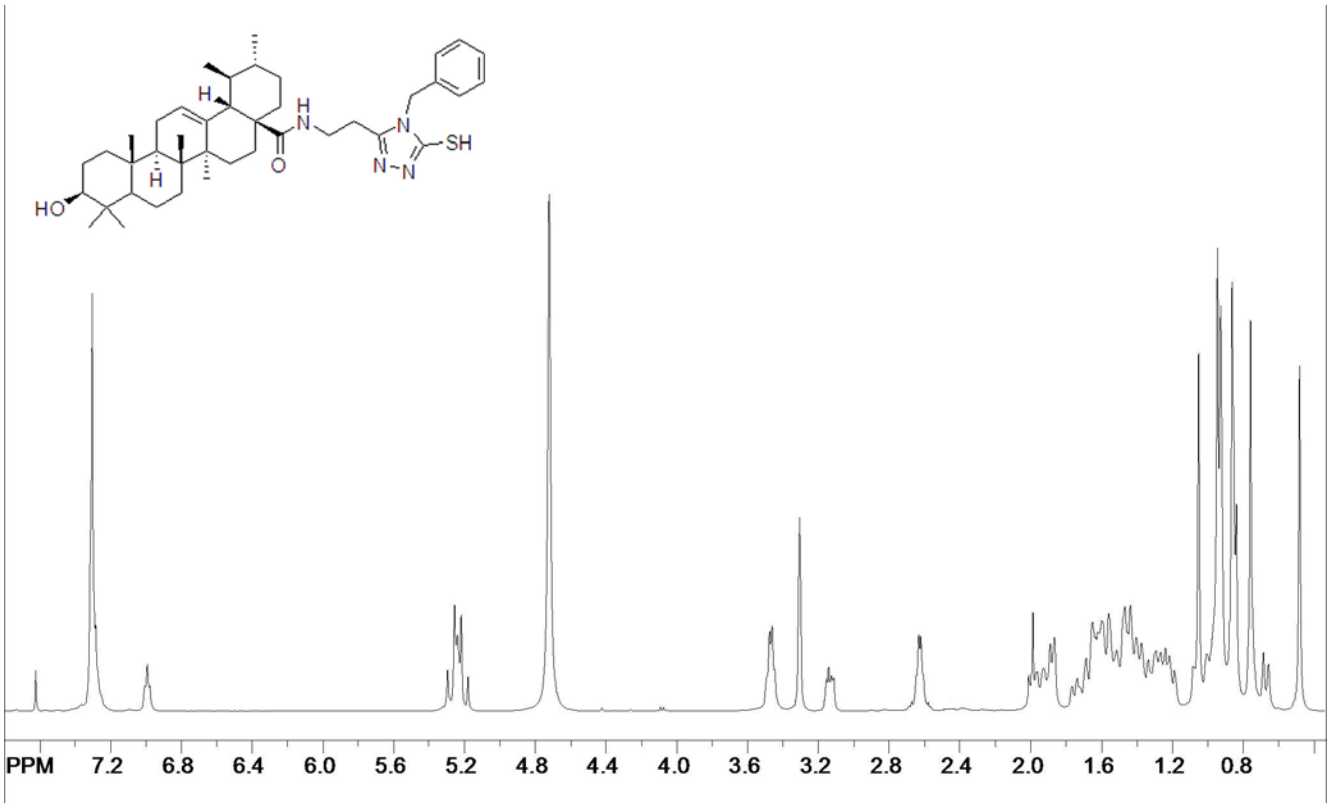
17 ^{1}H NMR spectrum (pyridine-d_5)



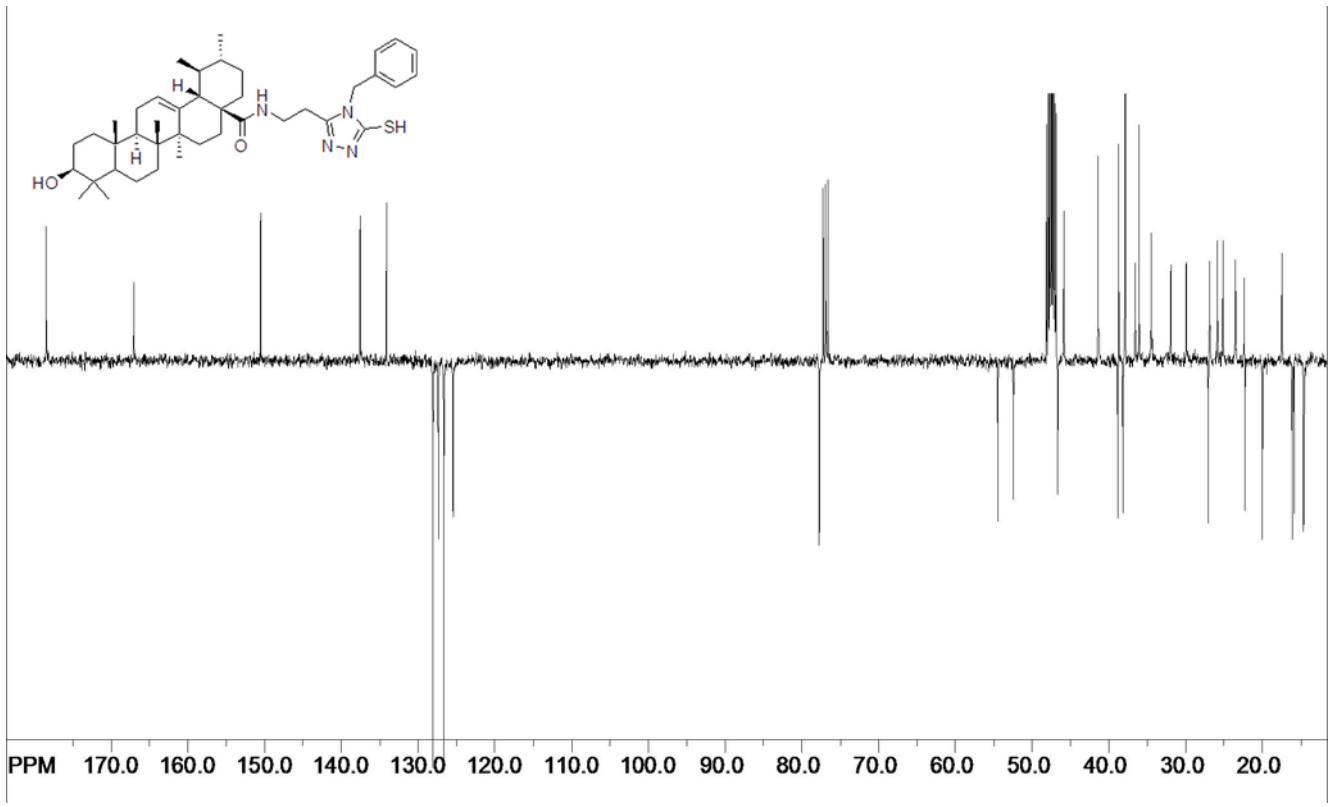
^{13}C NMR spectrum (pyridine-d_5)



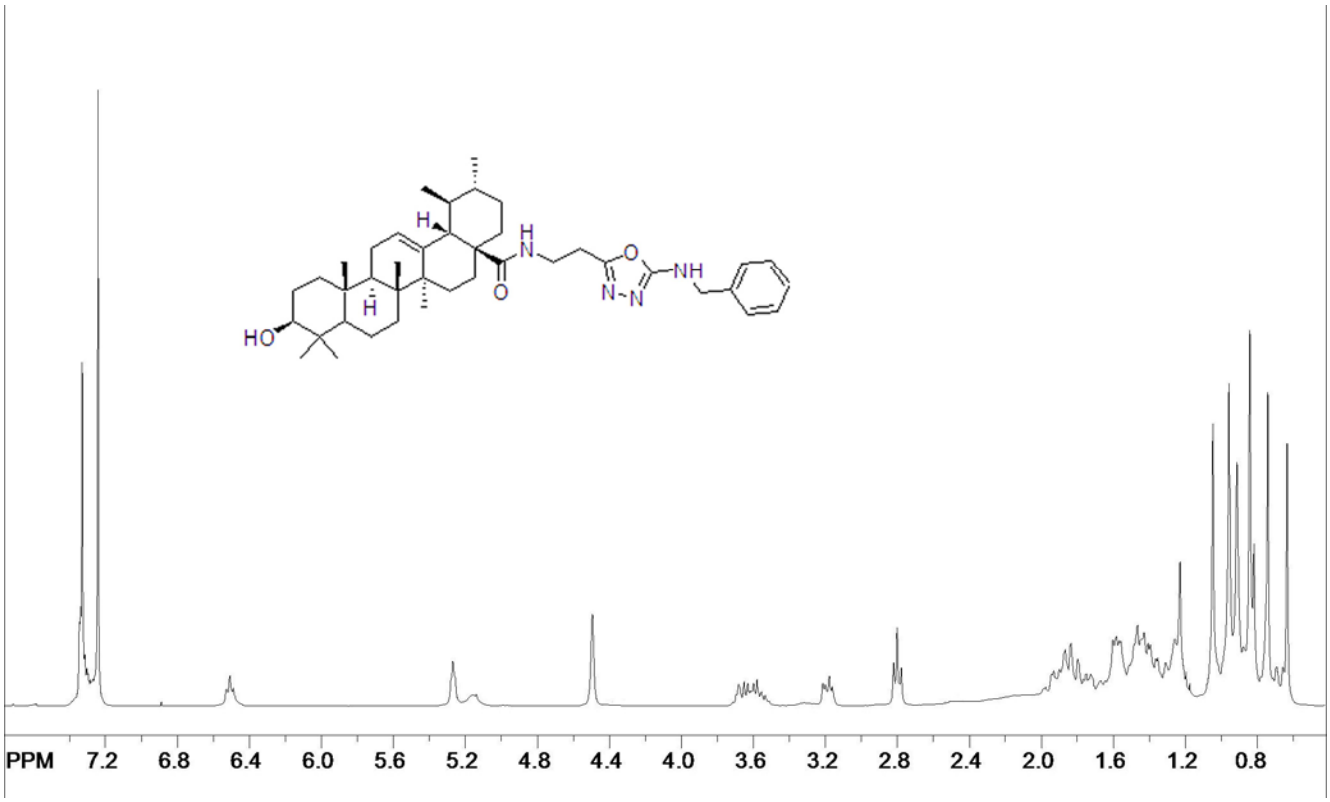
18 ^{1}H NMR spectrum ($CDCl_3$, CD_3OD)



^{13}C NMR spectrum ($CDCl_3$, CD_3OD)



19 ^{1}H NMR spectrum ($CDCl_3$-CD_3OD)



^{13}C NMR spectrum ($CDCl_3$-CD_3OD)