Electronic Supporting Information (ESI)

3-(2,6-Dichloro-benzyloxy)-11-oxo-olean-12-ene-29-oic acid, a semisynthetic analog of glycyrrhetic acid: Synthesis, antiproliferative, apoptotic and anti-angiogenesis activity¤

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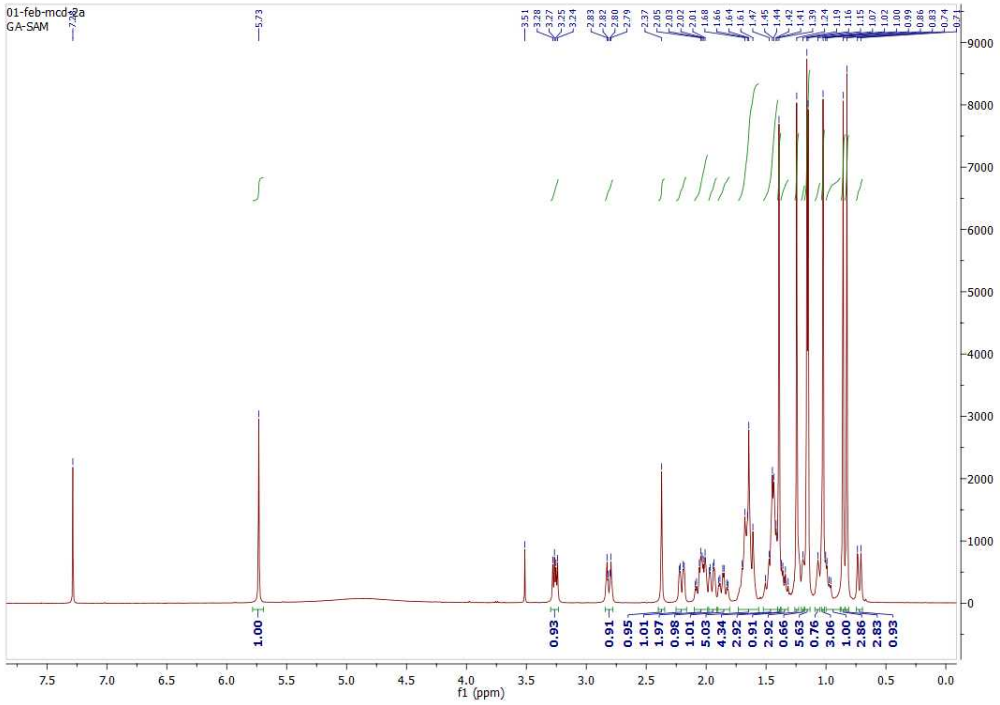
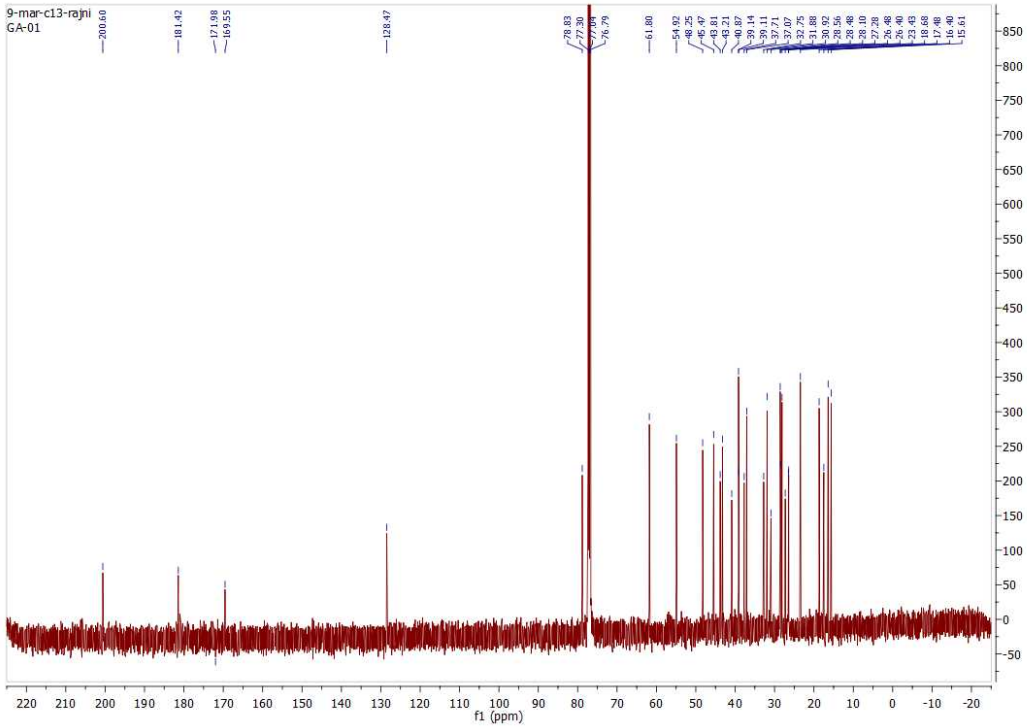
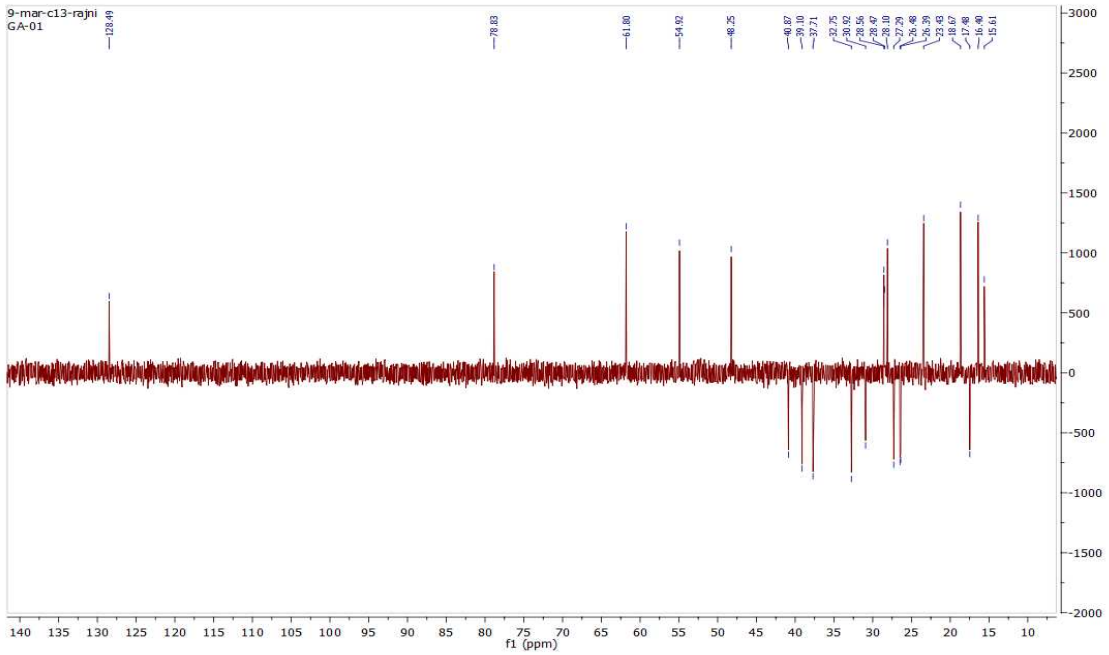
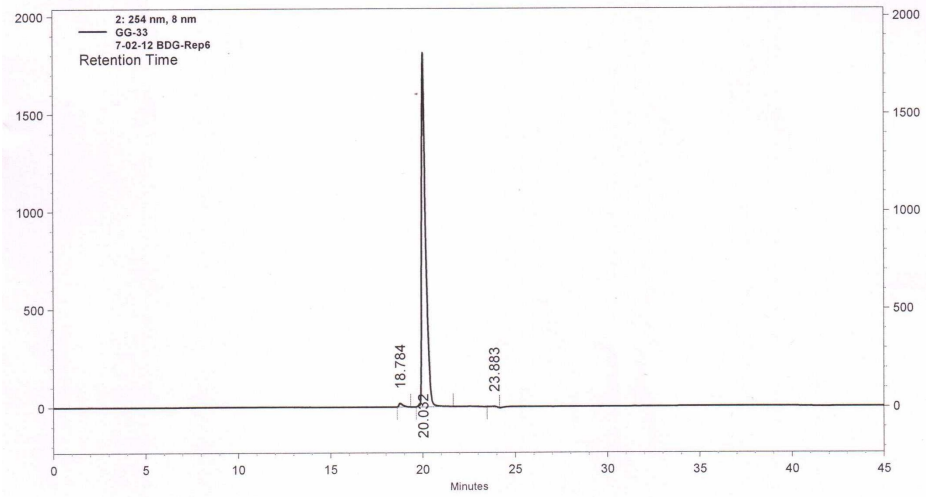




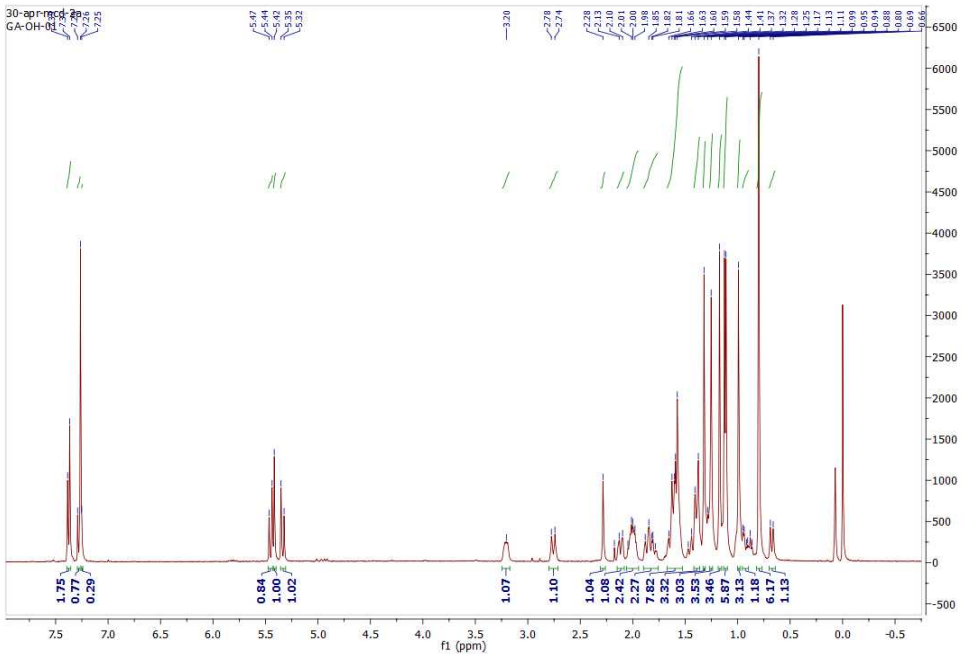


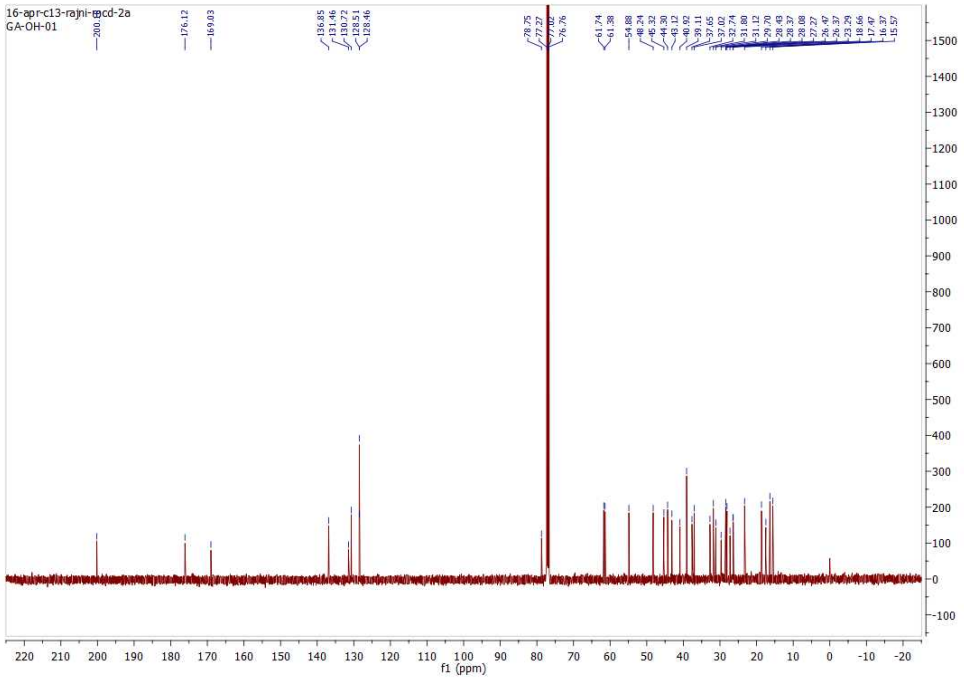


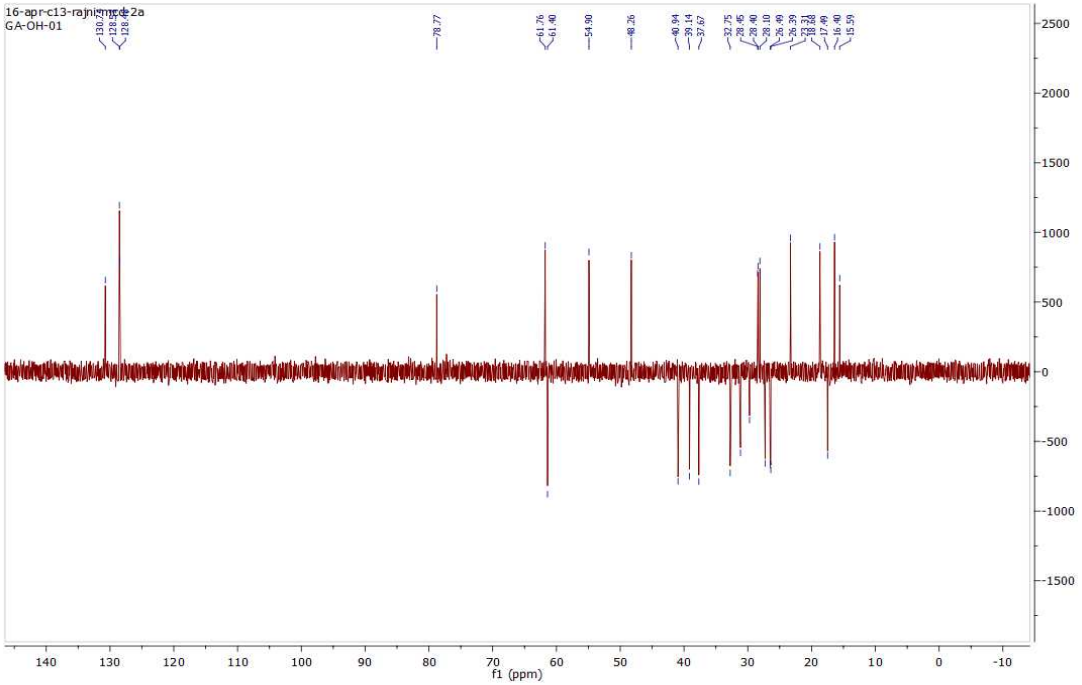
2: 254 nm, 8 nm

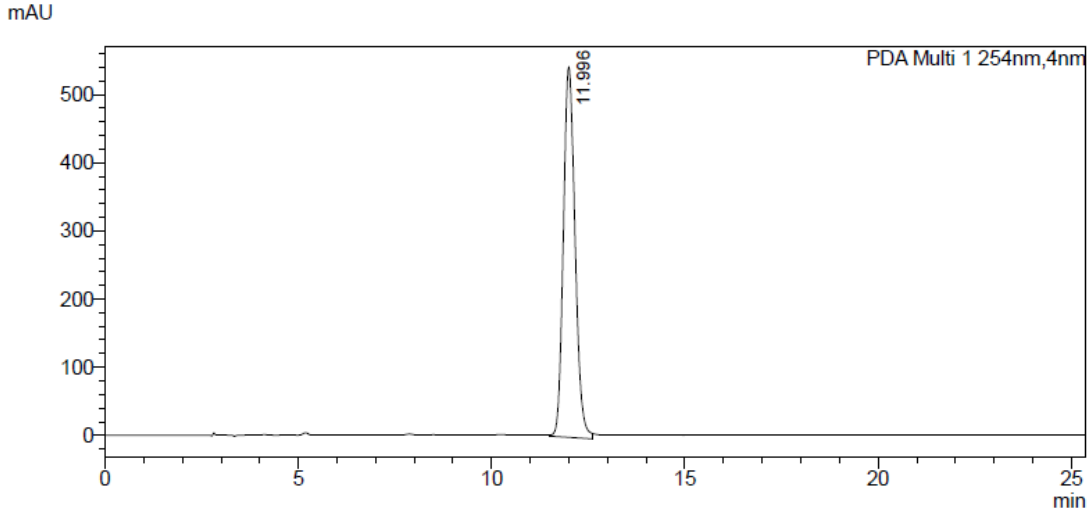
Pk #	Retention Time	Area	Area %	Height	Height %
1	18.784	279044	1.011	18312	0.999
2	20.032	27225239	98.639	1810484	98.755
3	23.883	96515	0.350	4511	0.246
Totals		27600798	100.000	1833307	100.000

S.1.2. ^{1}H, ^{13}C NMR and HPLC of 3-(2-Chloro-6-fluoro-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5a**) in $CDCl_3$









<Peak Table>

PDA Ch1 254nm

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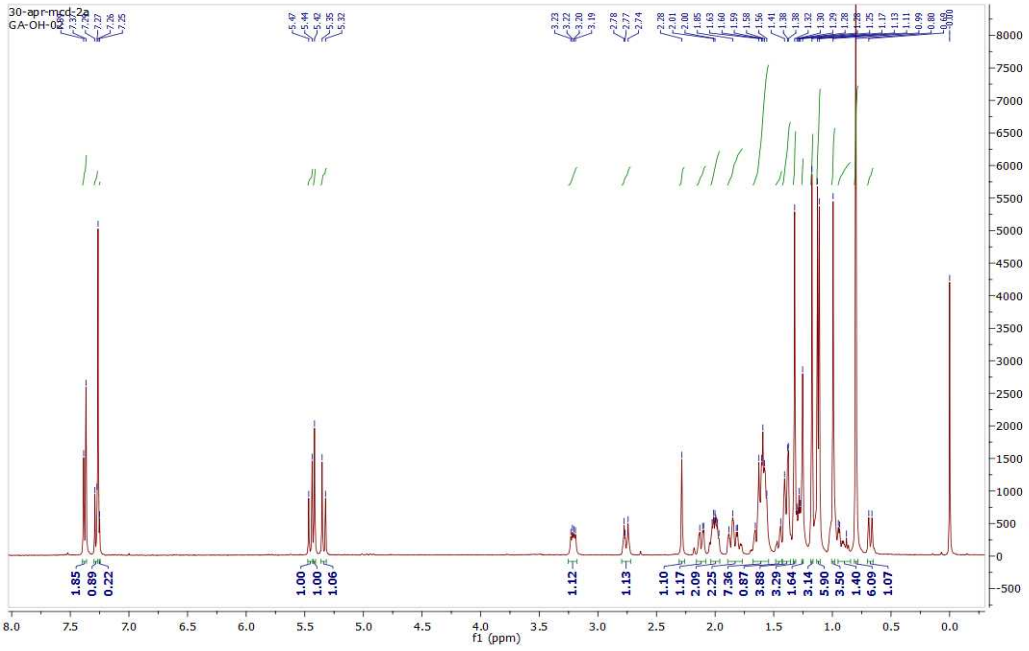
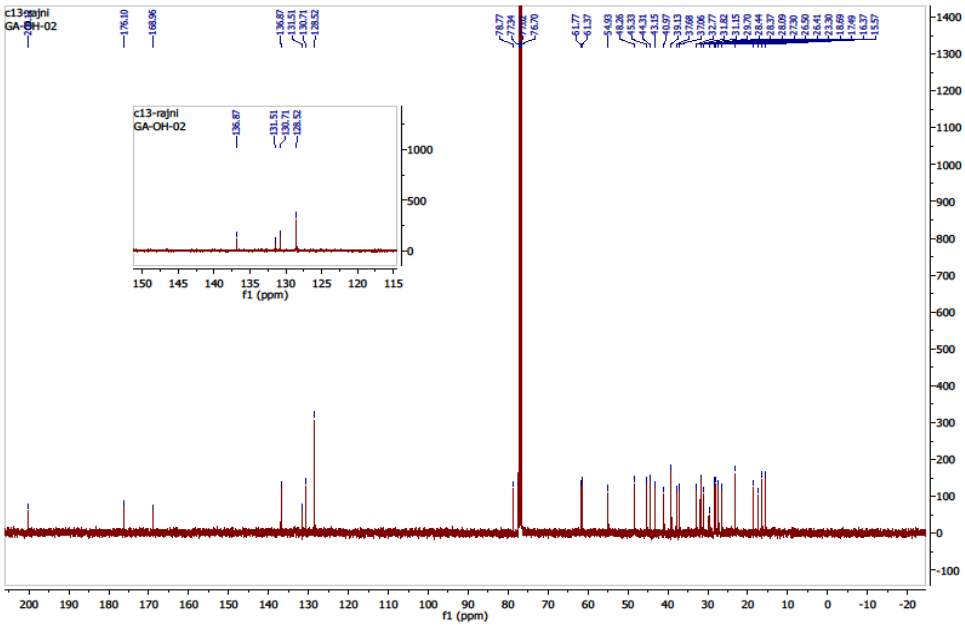
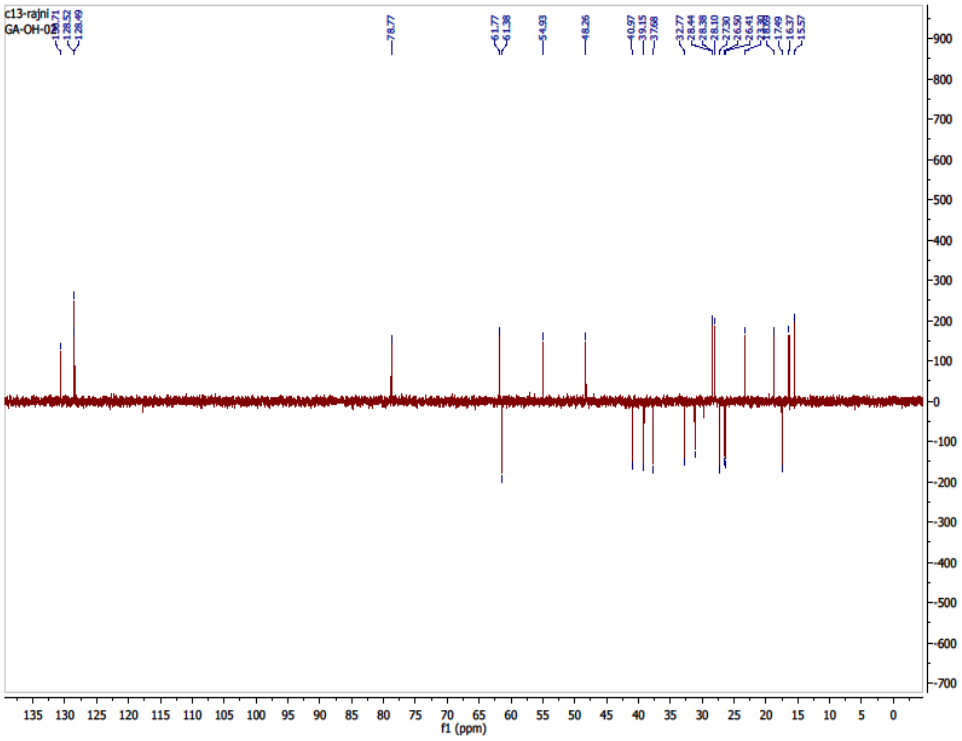
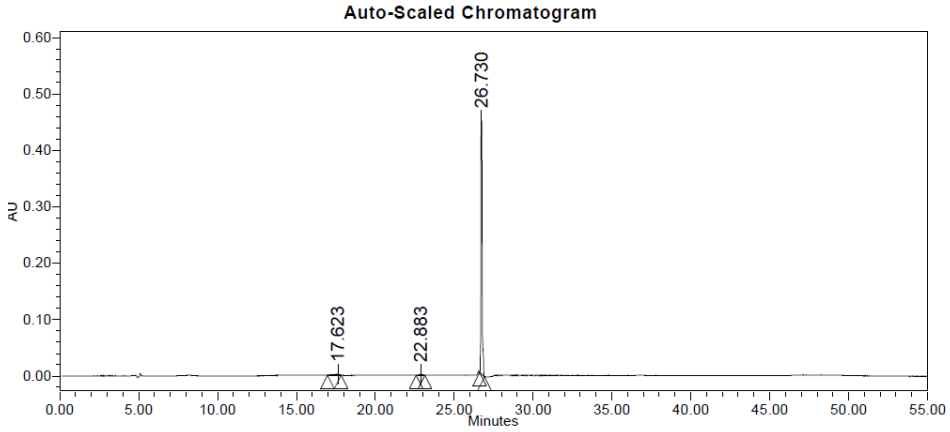
1	11.996	11430343	543234	11.499	12.597	100.000
Total		11430343	543234			100.000

S.1.3. ^{1}H, ^{13}C NMR and HPLC of 3-(2,6-dichloro-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5b**) in $CDCl_3$



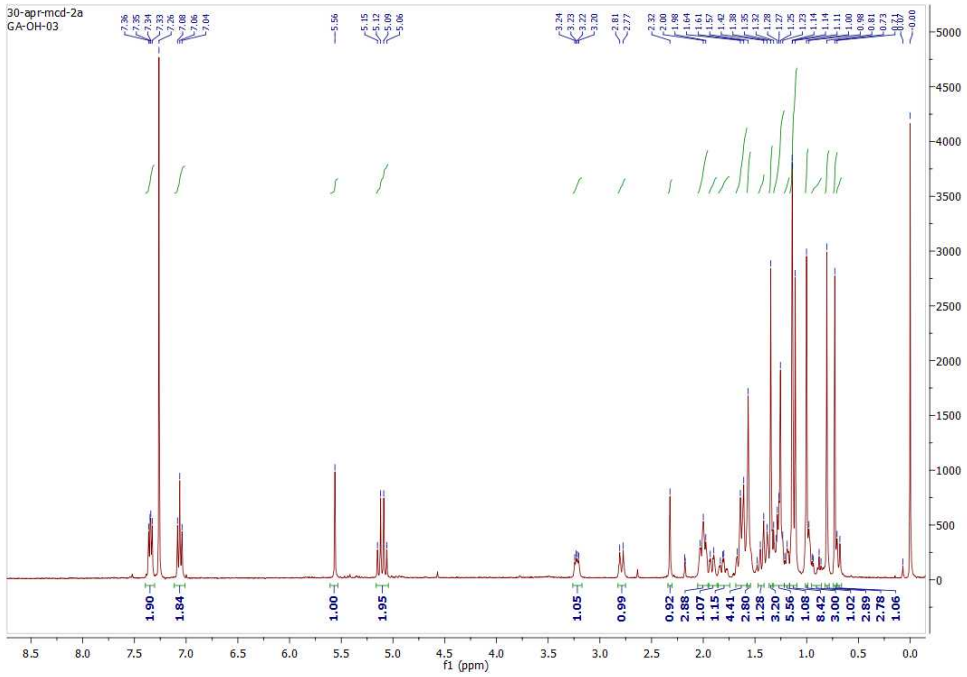


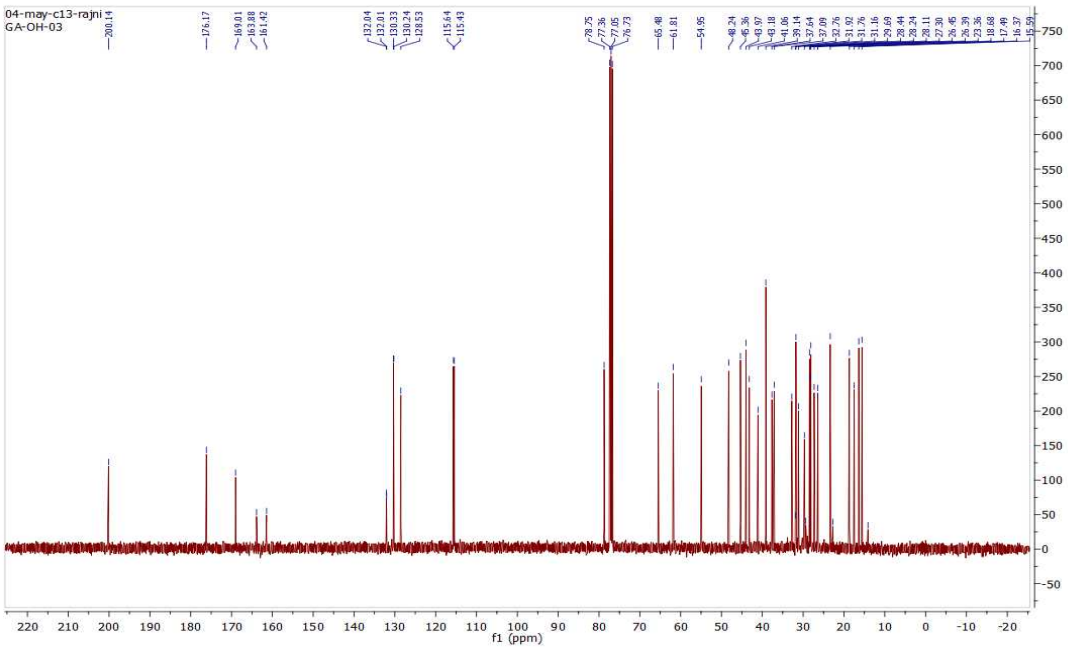


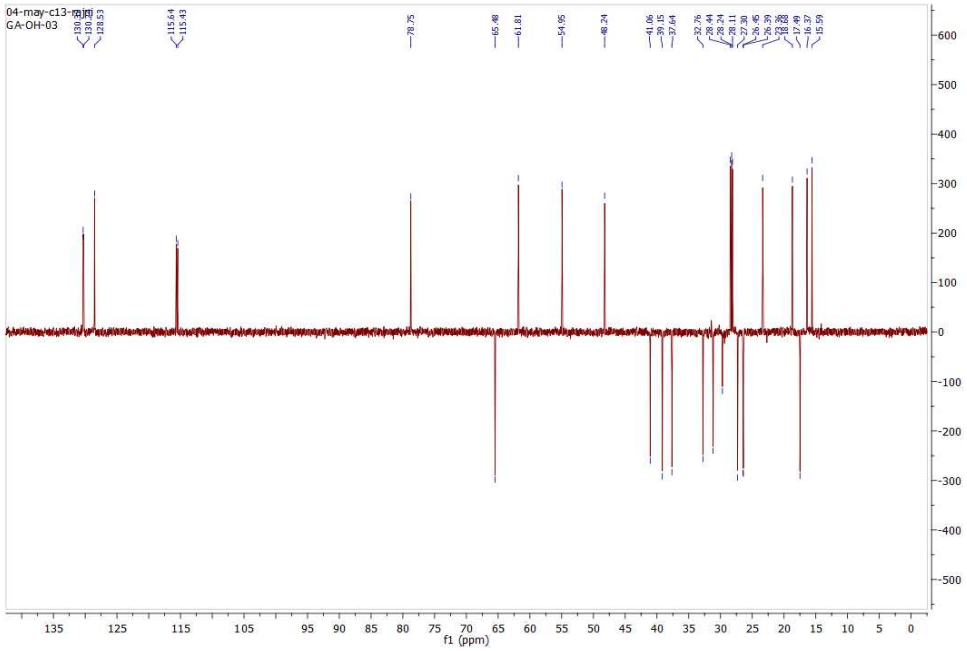


	RT	Area (μV*sec)	% Area	Height (μV)
1	17.623	37061	1.46	1375
2	22.883	18423	0.73	1258
3	26.730	2476277	97.81	481274

S.1.4. ^{1}H, ^{13}CNMR and HPLC of 3-(4-fluoro-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5c**) in $CDCl_3$







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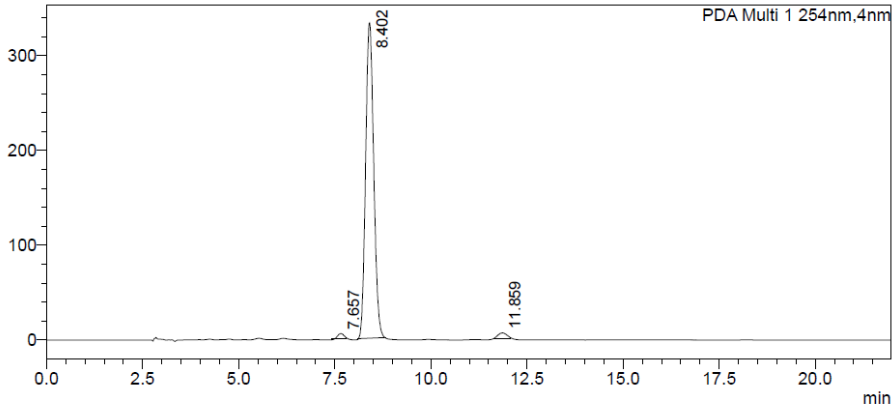
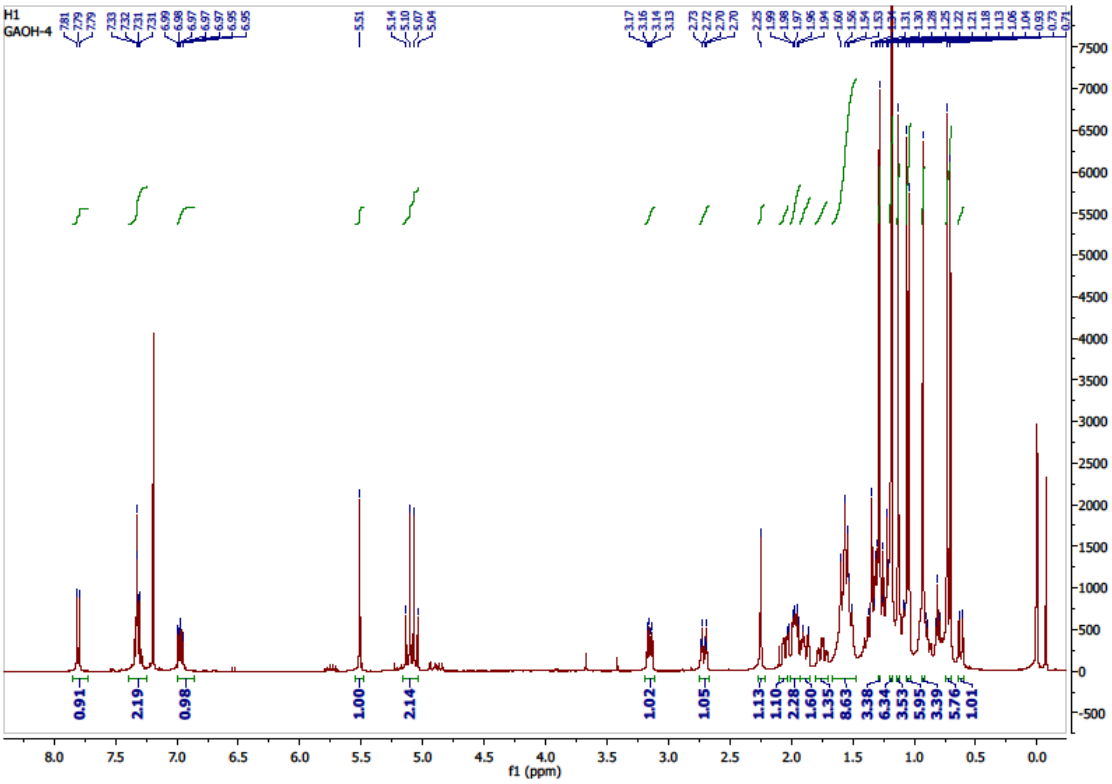


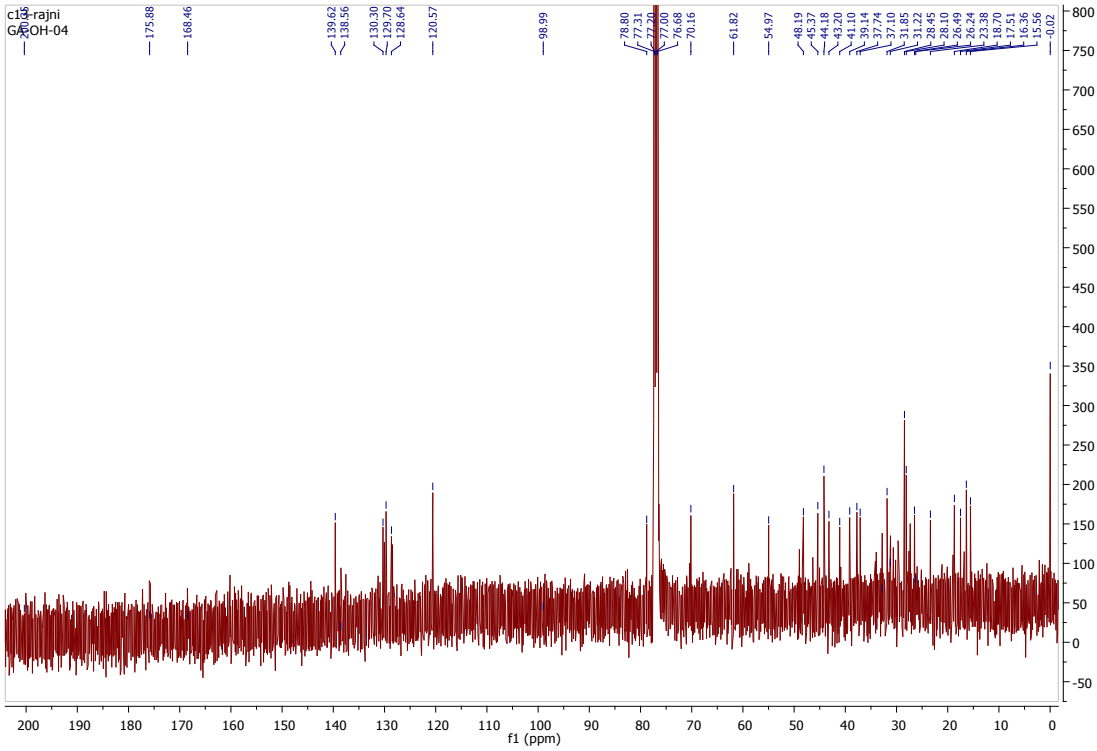
<Peak Table>

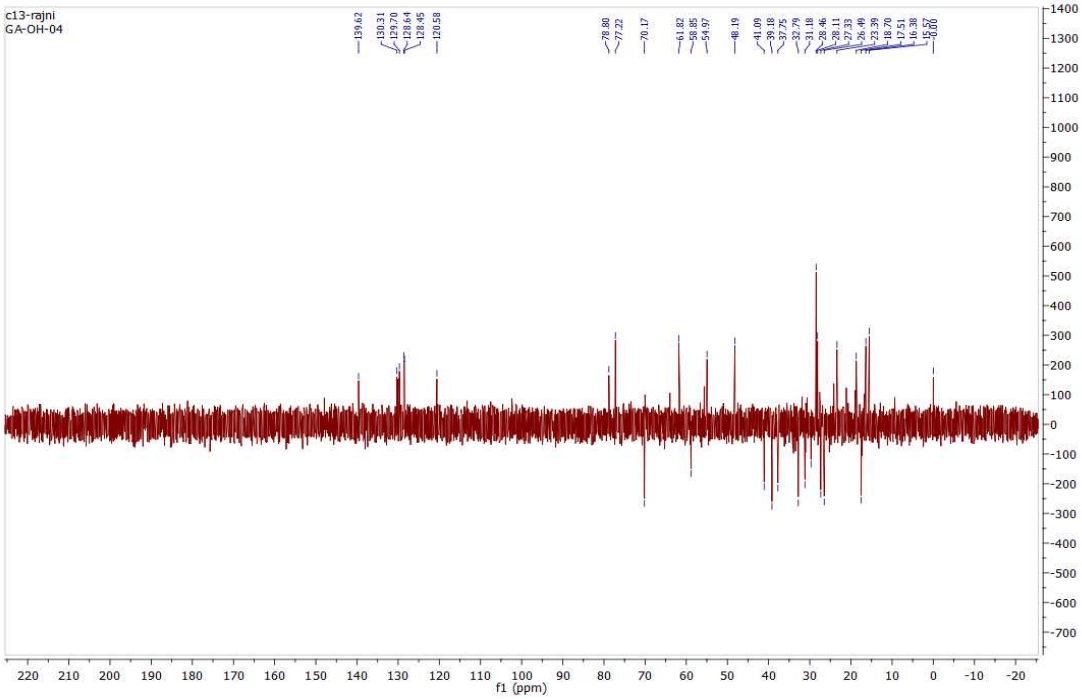
PDA Ch1 254nm

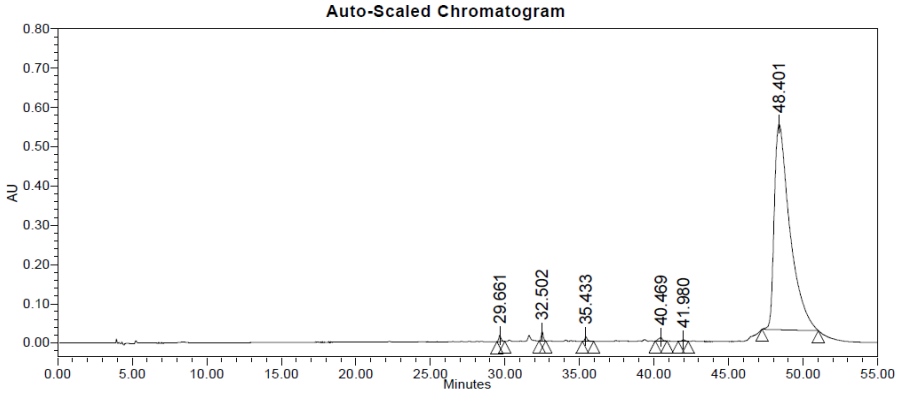
Peak#	Ret. Time	Area	Height	Conc.	Peak Start	Peak End	Area%
1	7.657	59538	5628	0.000	7.413	7.787	1.189
2	8.402	4856064	332469	0.000	8.096	8.811	96.969
3	11.859	92272	5816	0.000	11.627	12.075	1.843
Total		5007874	343914				100.000

S.1.5. ^{1}H, ^{13}C NMR and HPLC of 3-(2-iodo-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5d**) in $CDCl_3$



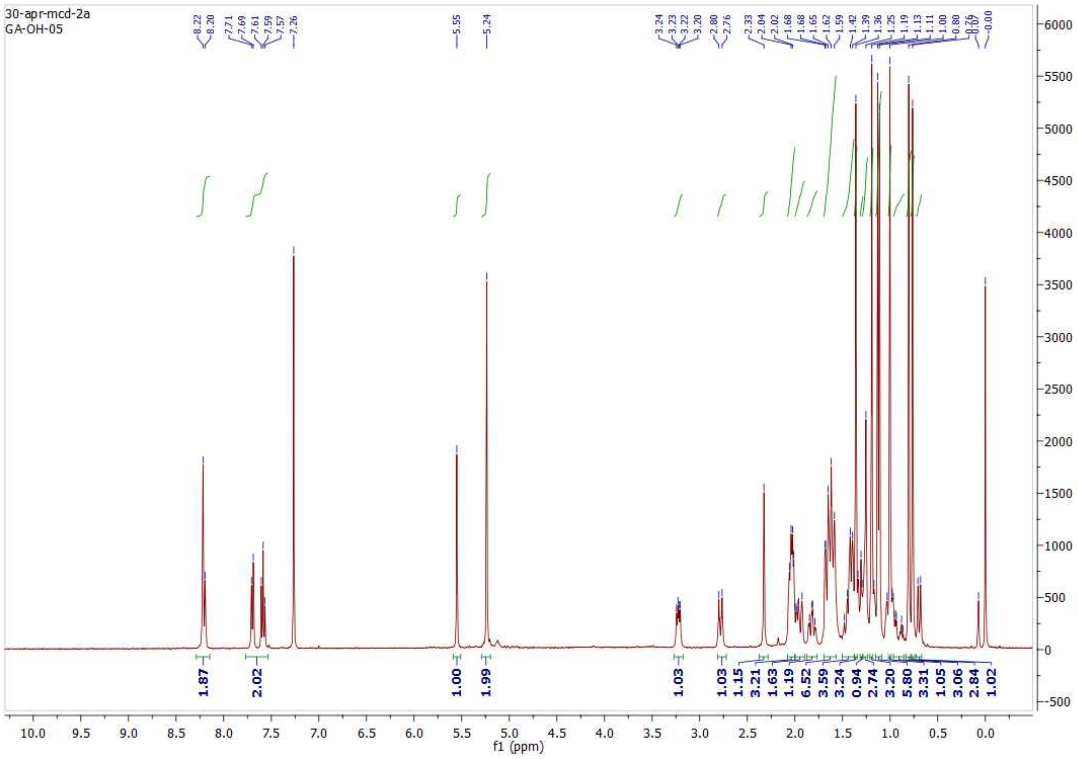


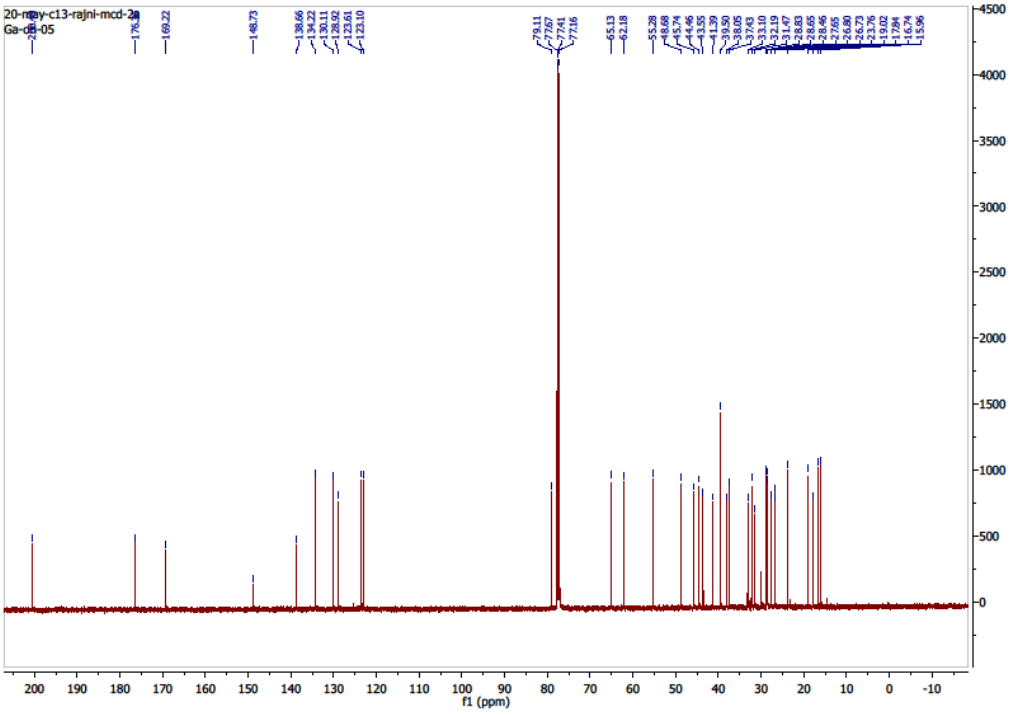


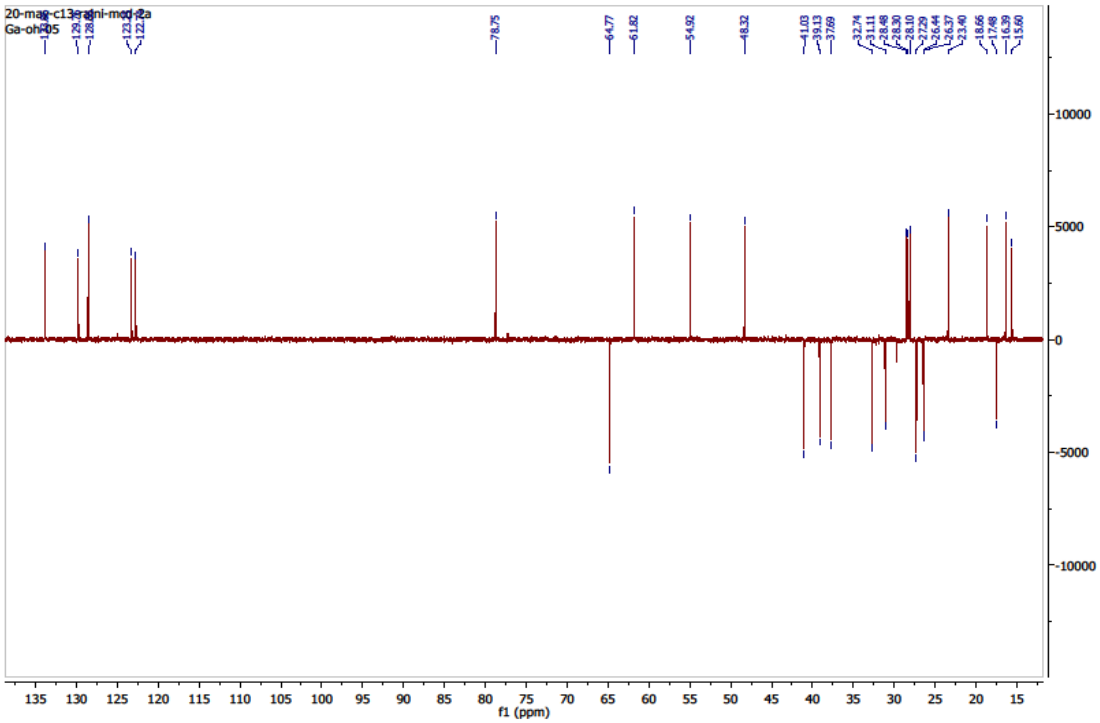


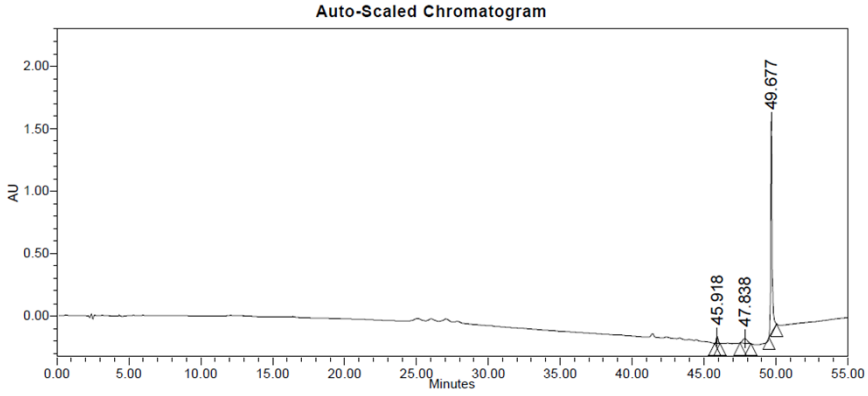
	RT	Area (μV*sec)	% Area	Height (μV)
1	29.661	164159	0.42	15526
2	32.502	223430	0.57	23296
3	35.433	135392	0.35	12288
4	40.469	148063	0.38	8761
5	41.980	56166	0.14	3996
6	48.401	38163881	98.13	523432

S.1.6 ^{1}H, ^{13}C NMR and HPLC of 3-(3-nitro-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5e**) in $CDCl_3$


30-apr-mcd-2a
GA-OH-05
f1 (ppm)

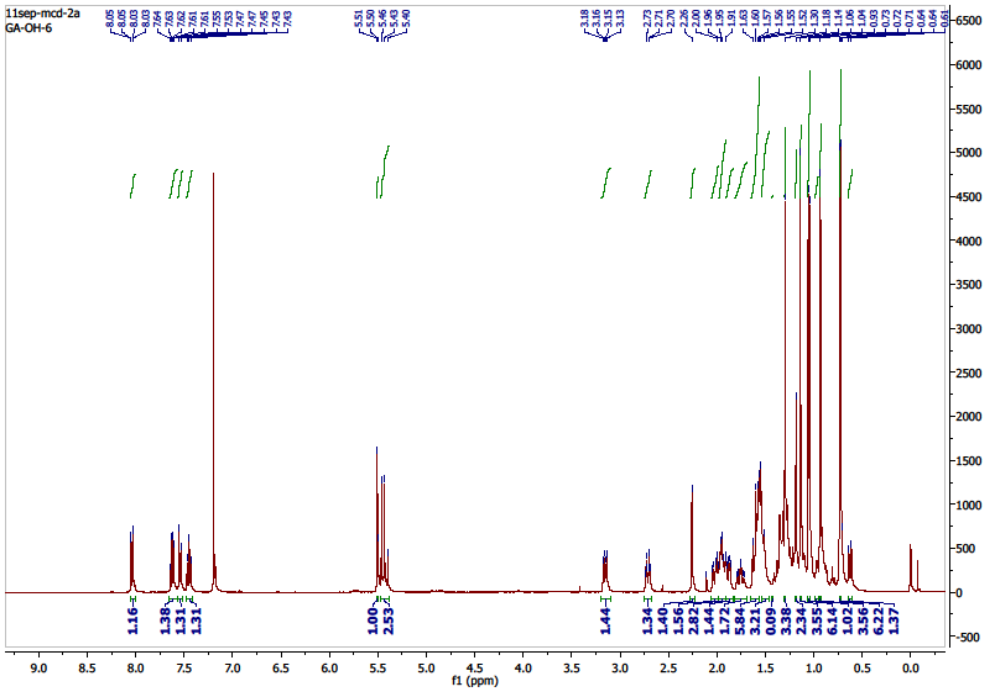

20-may-c13-rajni-mcd-2a
Ga-dB-05
f1 (ppm)

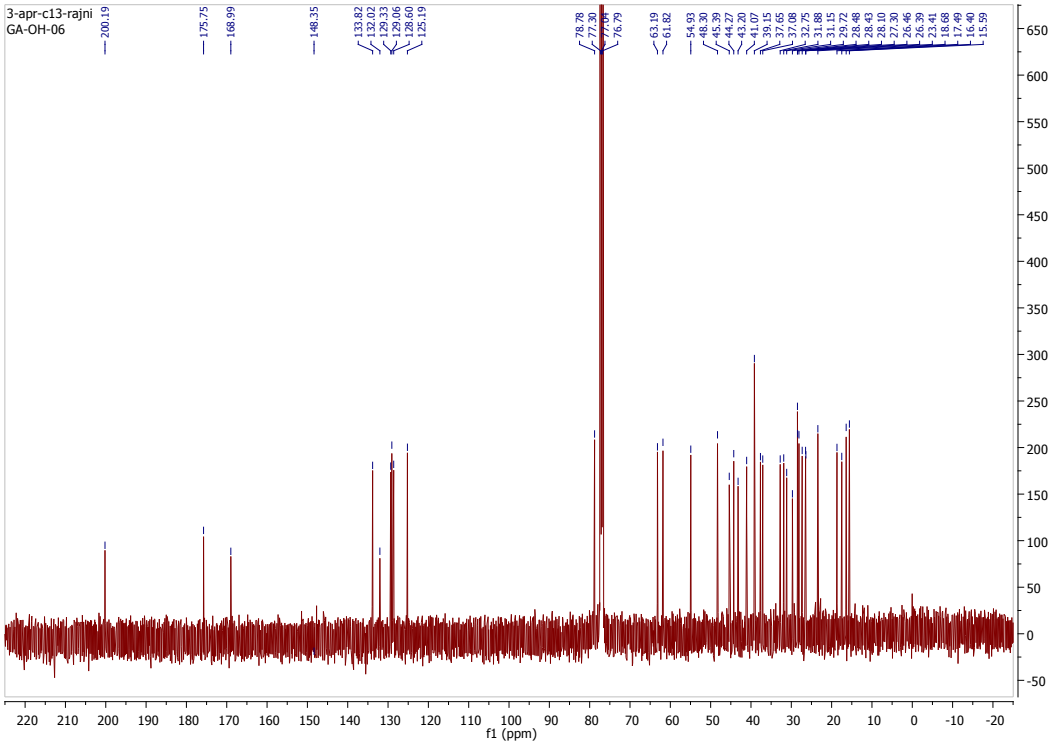


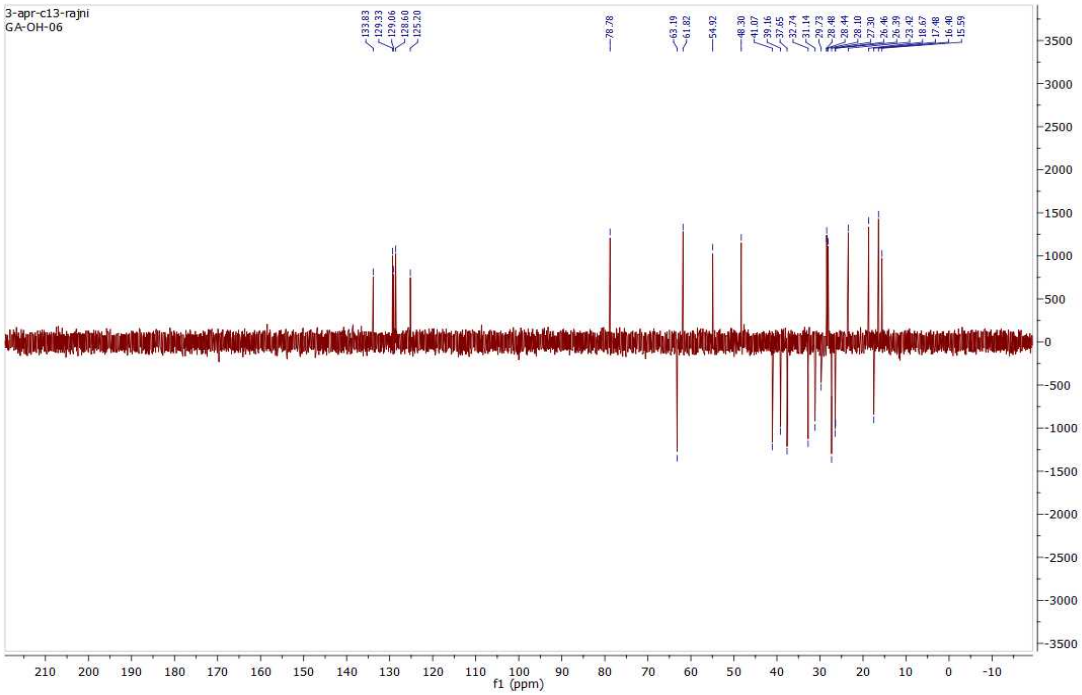


	RT	Area (μV*sec)	% Area	Height (μV)
1	45.918	453203	3.49	53459
2	47.838	843303	6.50	35996
3	49.677	11678034	90.01	1718776

S.1.7. ^{1}H, ^{13}C NMR and HPLC of 3-(2-nitro-benzyloxy)-11-oxo-olean-12-ene-29-oic acid (**5f**) in $CDCl_3$







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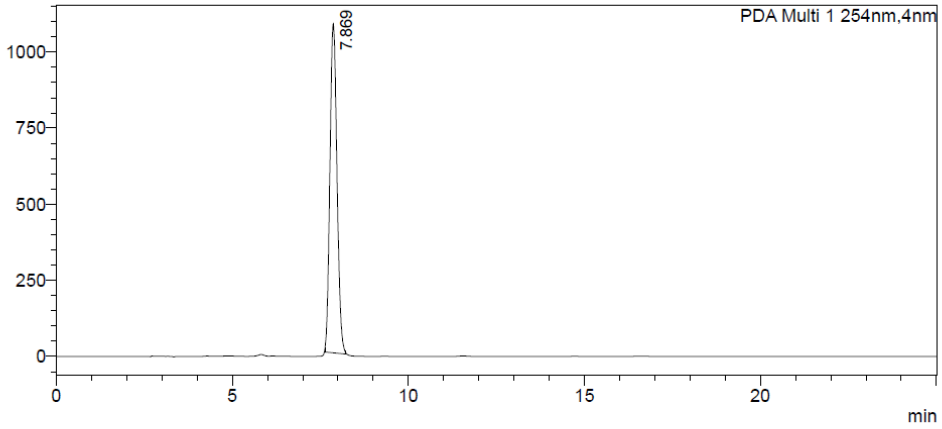
mAU

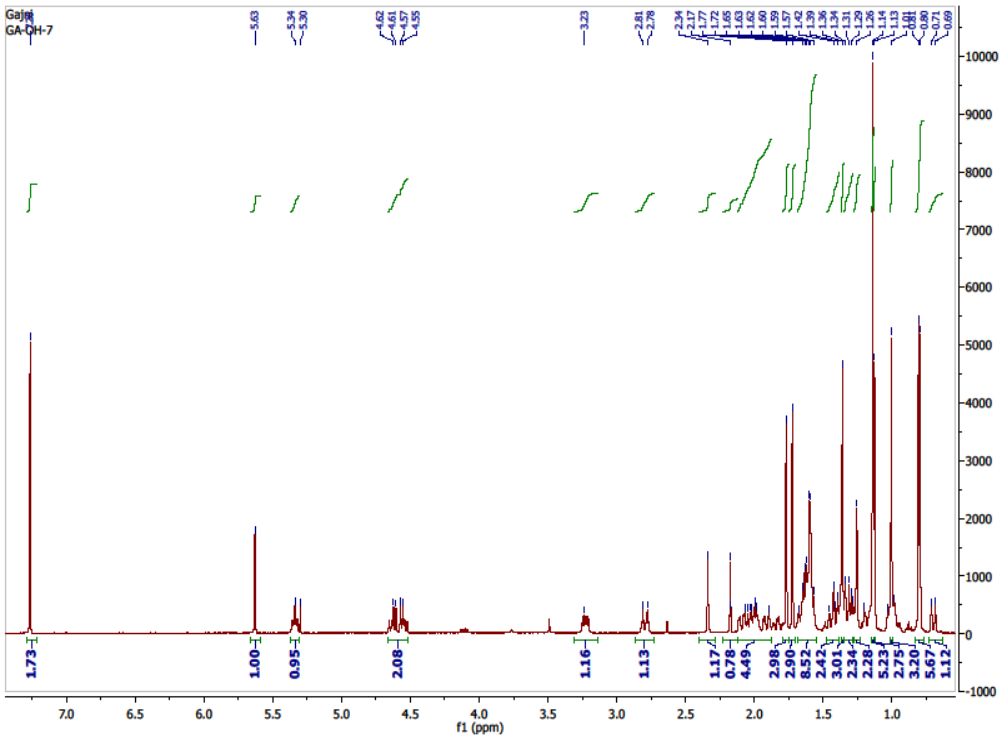


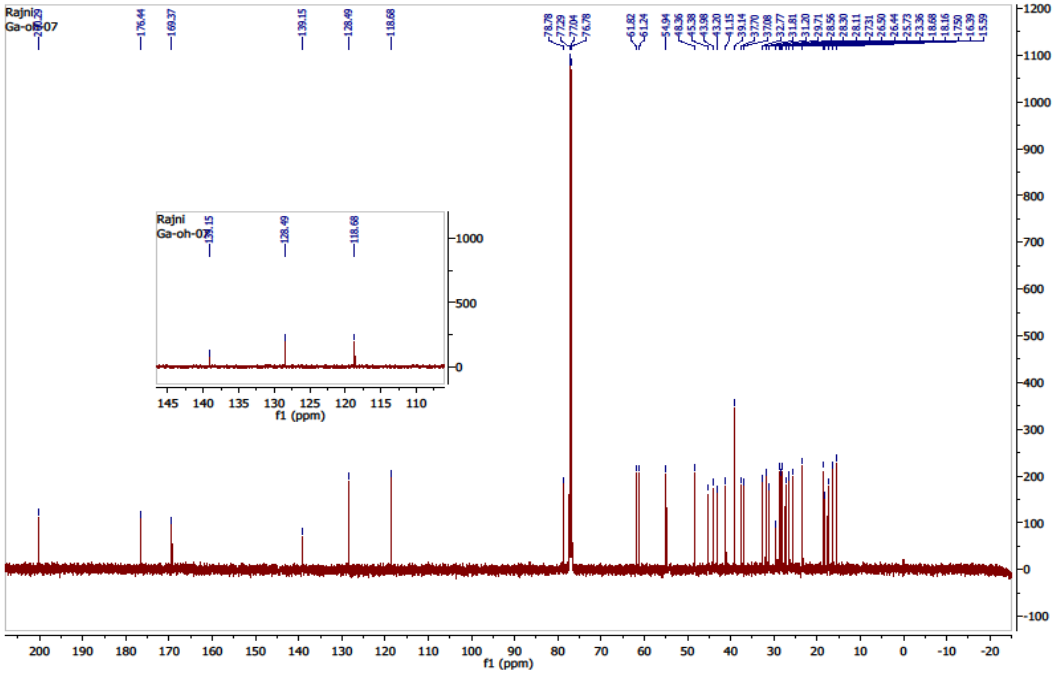
<Peak Table>

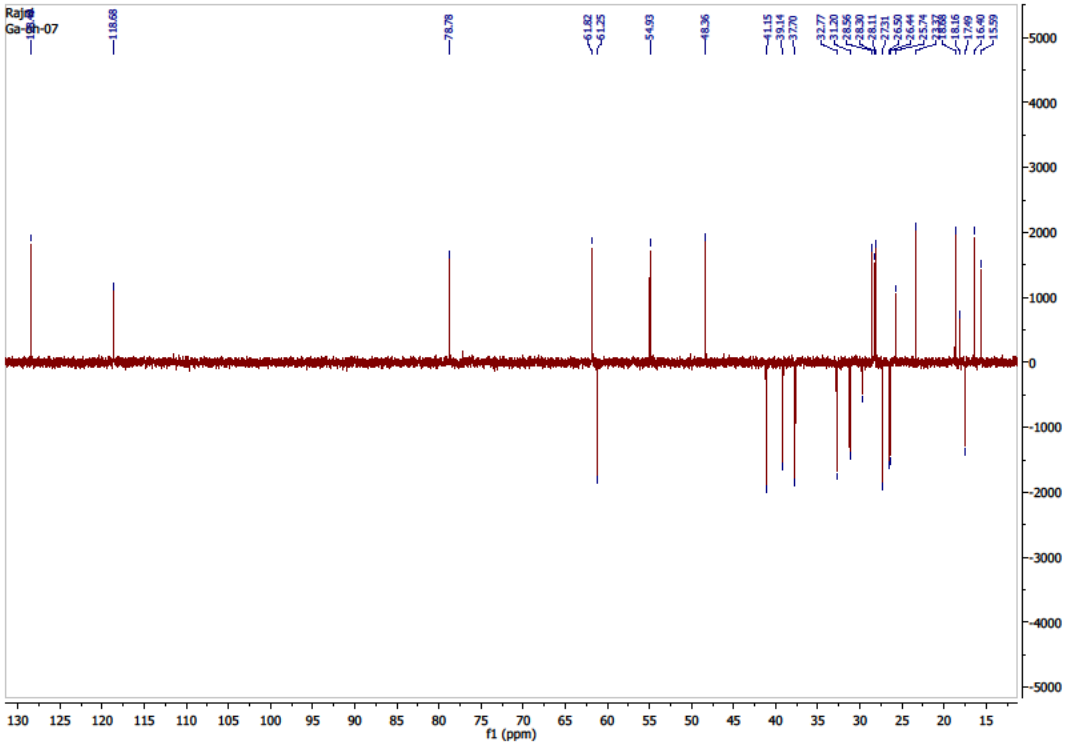
PDA Ch1 254nm

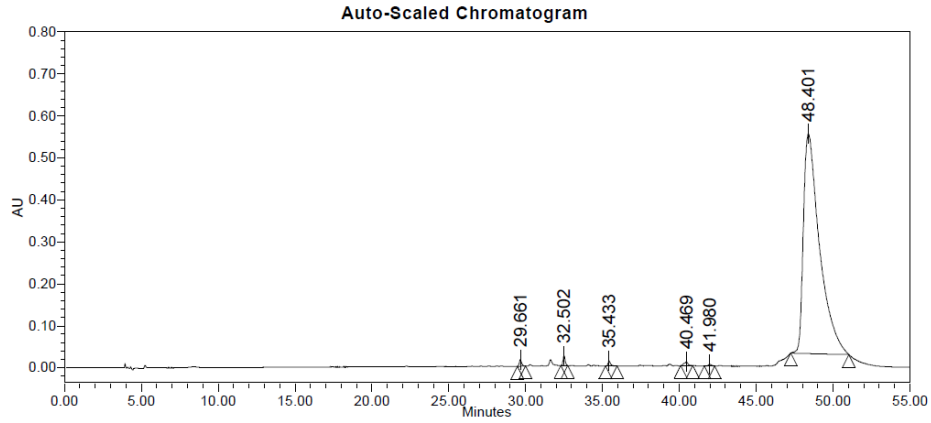
Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	7.869	15074075	1080601	7.637	8.203	100.000
Total		15074075	1080601			100.000

S.1.8. ^{1}H, ^{13}C NMR and HPLC of 3-(3-methyl-but-2-enyloxy)-11-oxo-olean-12-ene-29-oic acid (**5g**) in $CDCl_3$



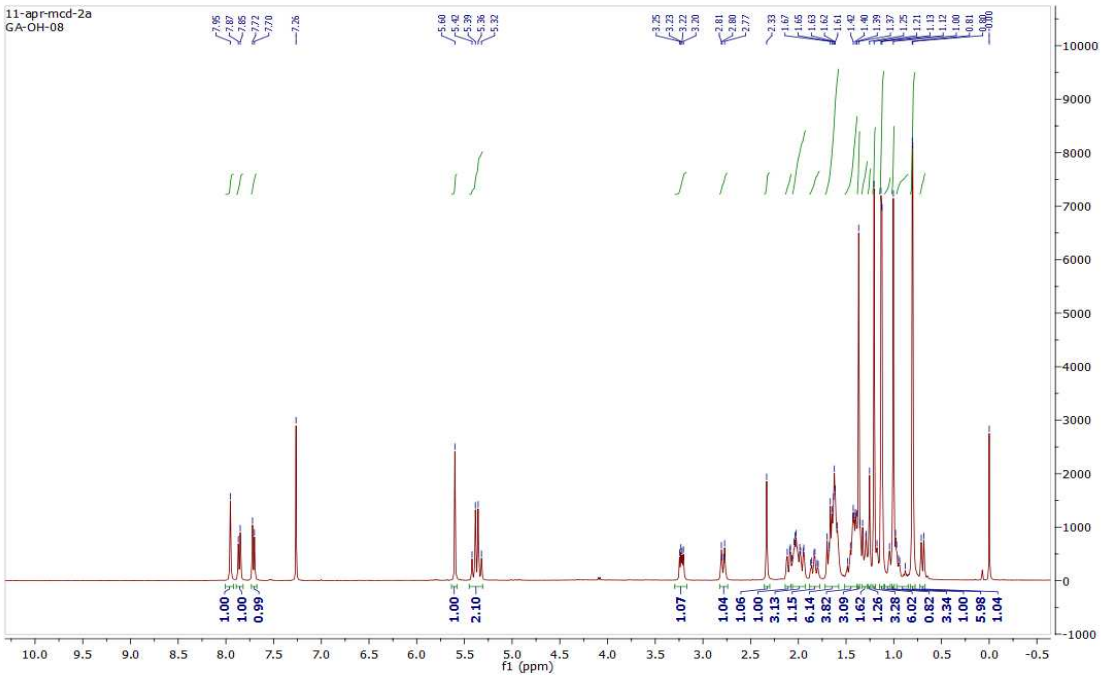


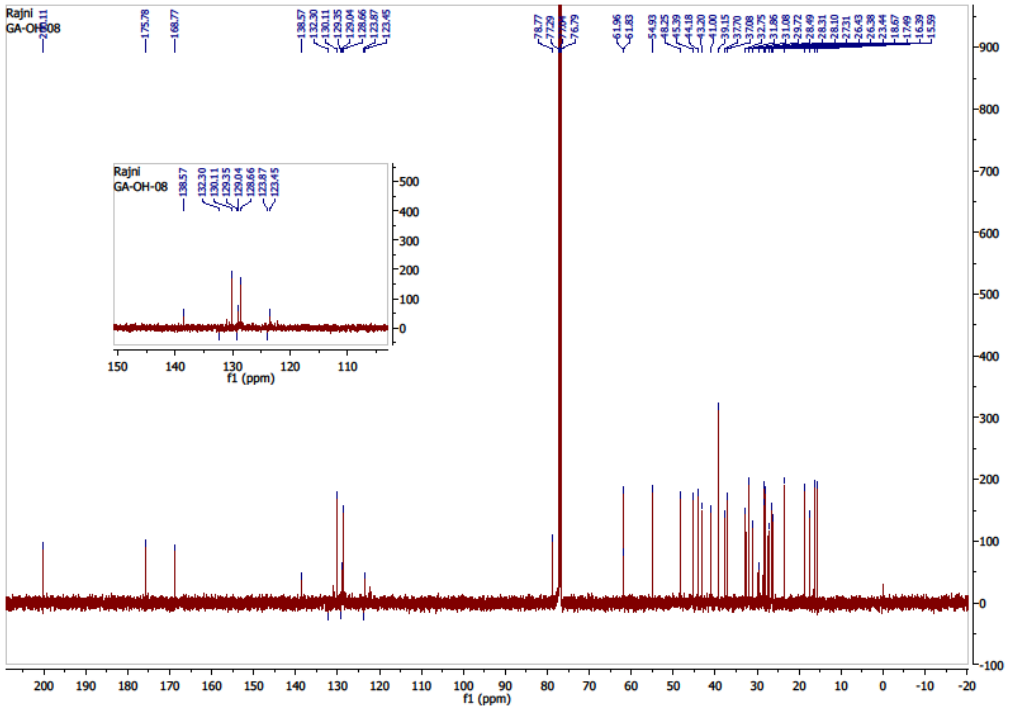


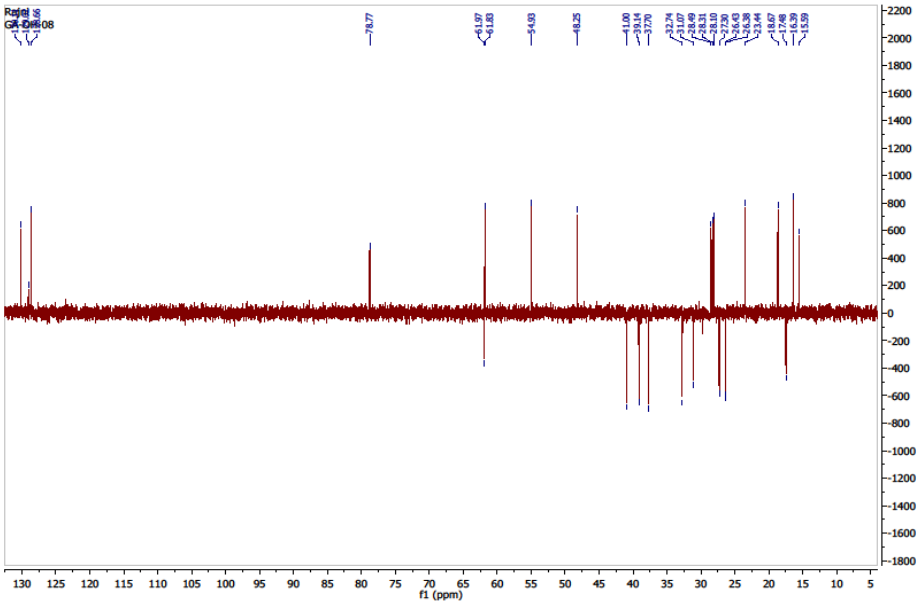


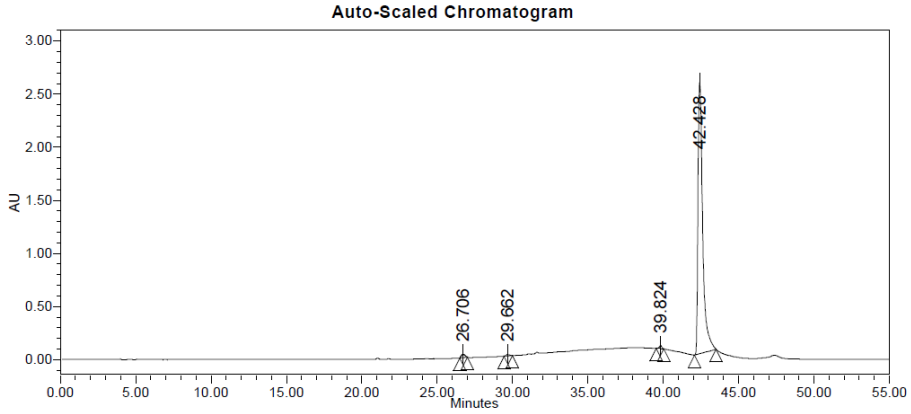
	RT	Area (µV*sec)	% Area	Height (µV)
1	29.661	164159	0.42	15526
2	32.502	223430	0.57	23296
3	35.433	135392	0.35	12288
4	40.469	148063	0.38	8761
5	41.980	56166	0.14	3996
6	48.401	38163881	98.13	523432

S.1.9. ^{1}H, ^{13}C NMR and HPLC of *3-(*2,4-Bis-trifluoromethyl-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5h**) in $CDCl_3$



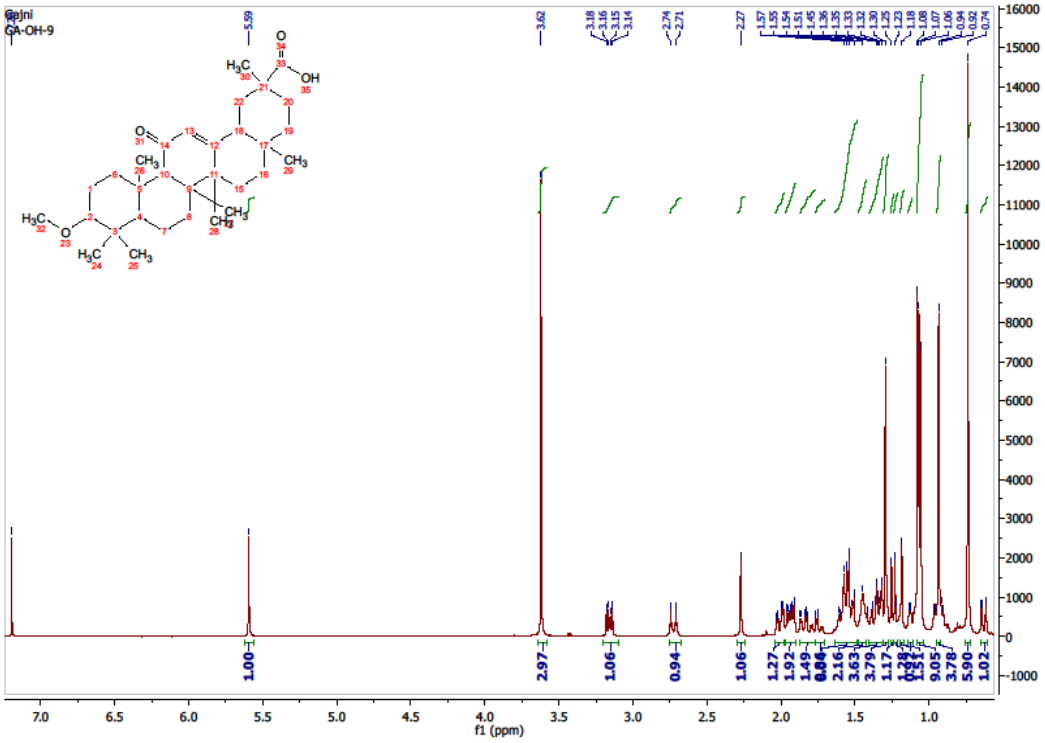


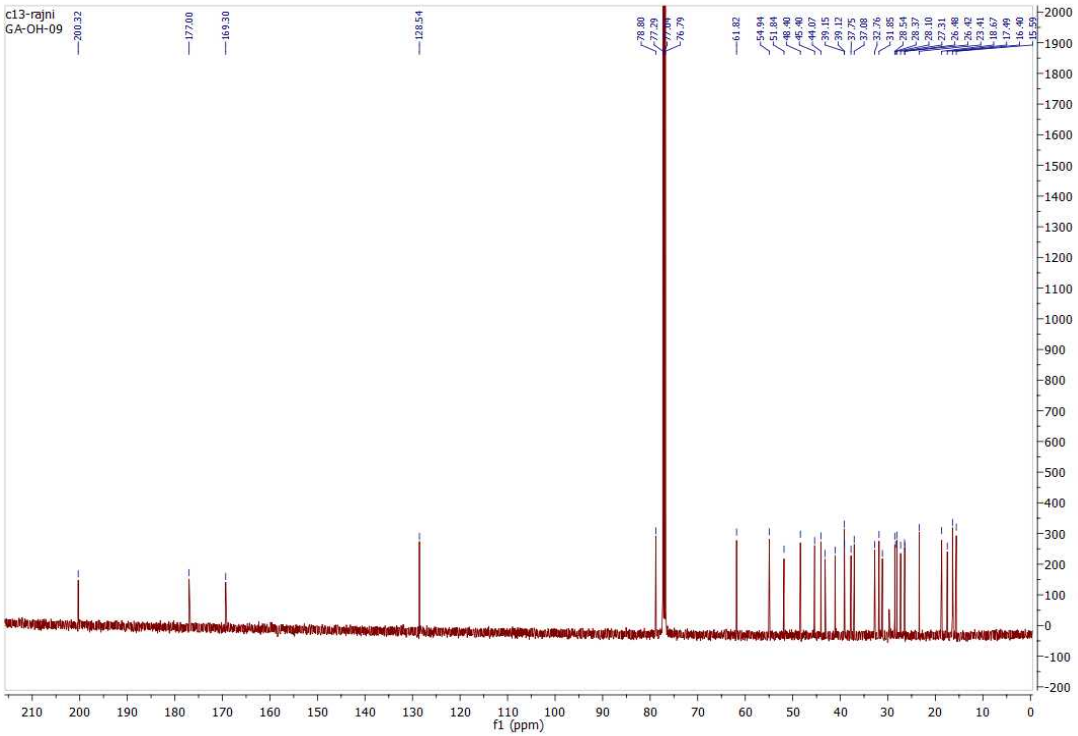


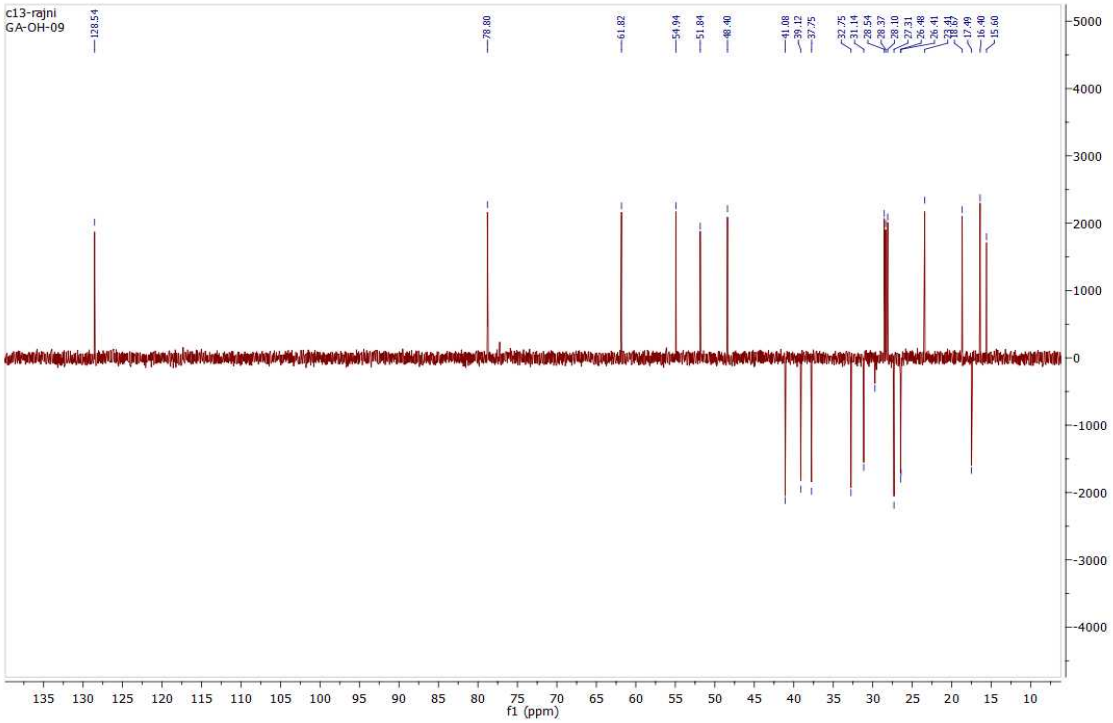


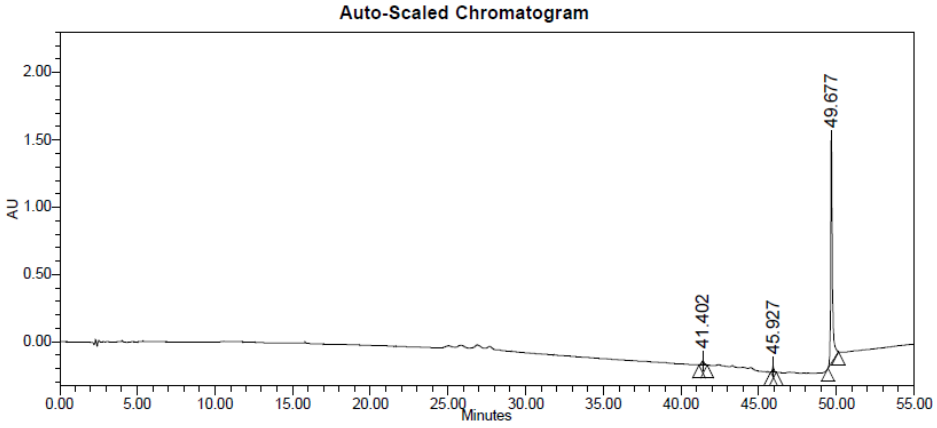
	RT	Area (μV*sec)	% Area	Height (μV)
1	26.706	551209	0.98	32803
2	29.662	224599	0.40	16282
3	39.824	324792	0.58	28128
4	42.428	55281277	98.05	2555420

S.1.10 ^{1}H, ^{13}C NMR and HPLC of 3-Methoxy-11-oxo-olean-12-ene-29-oic acid (**5i**) in $CDCl_3$



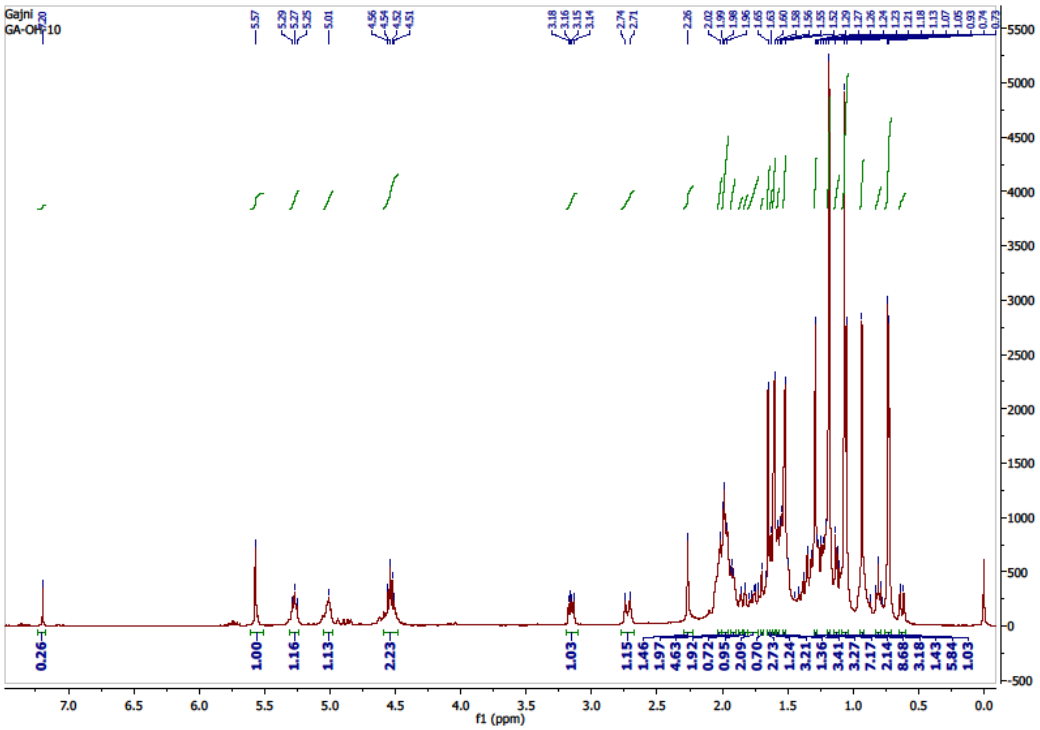


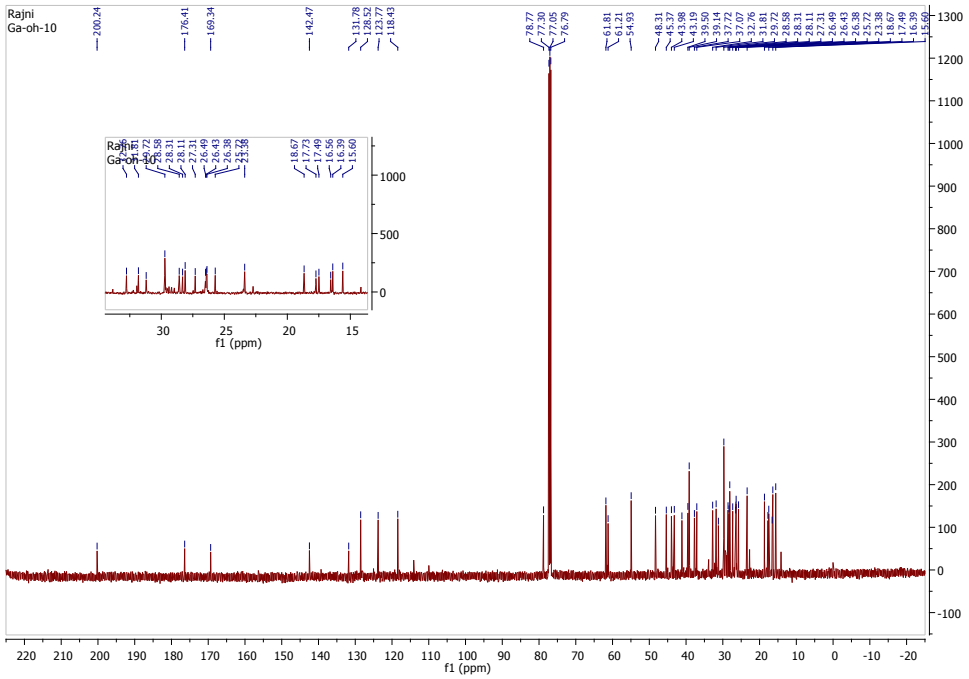


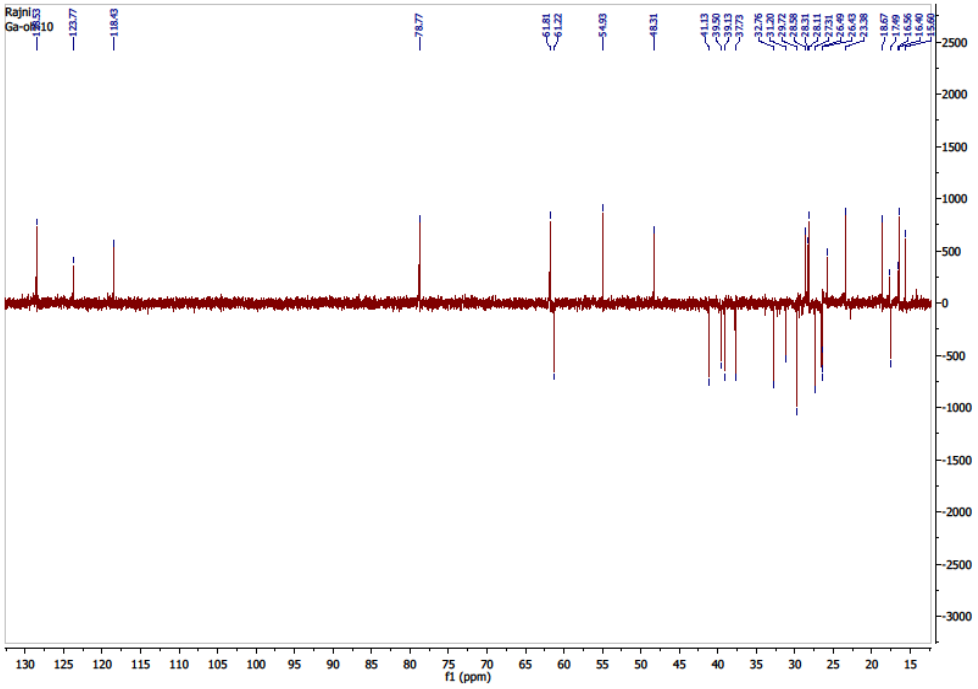


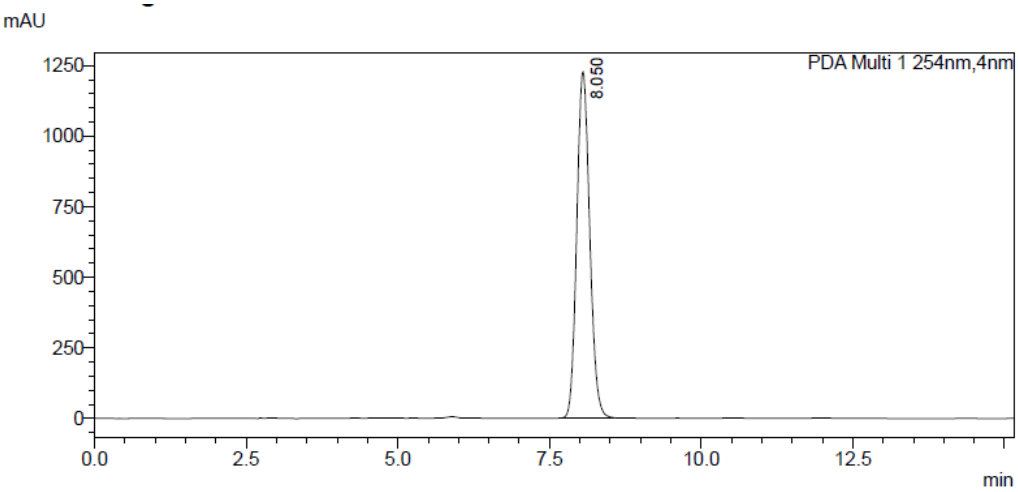
	RT	Area (µV*sec)	% Area	Height (µV)
1	41.402	325362	2.42	29012
2	45.927	280854	2.09	39147
3	49.677	12856272	95.50	1678182

S.1.11. ^{1}H, ^{13}C NMR and HPLC of 3-(3,7-dimethyl-octa-2,6-dienyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5j**) in $CDCl_3$









<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
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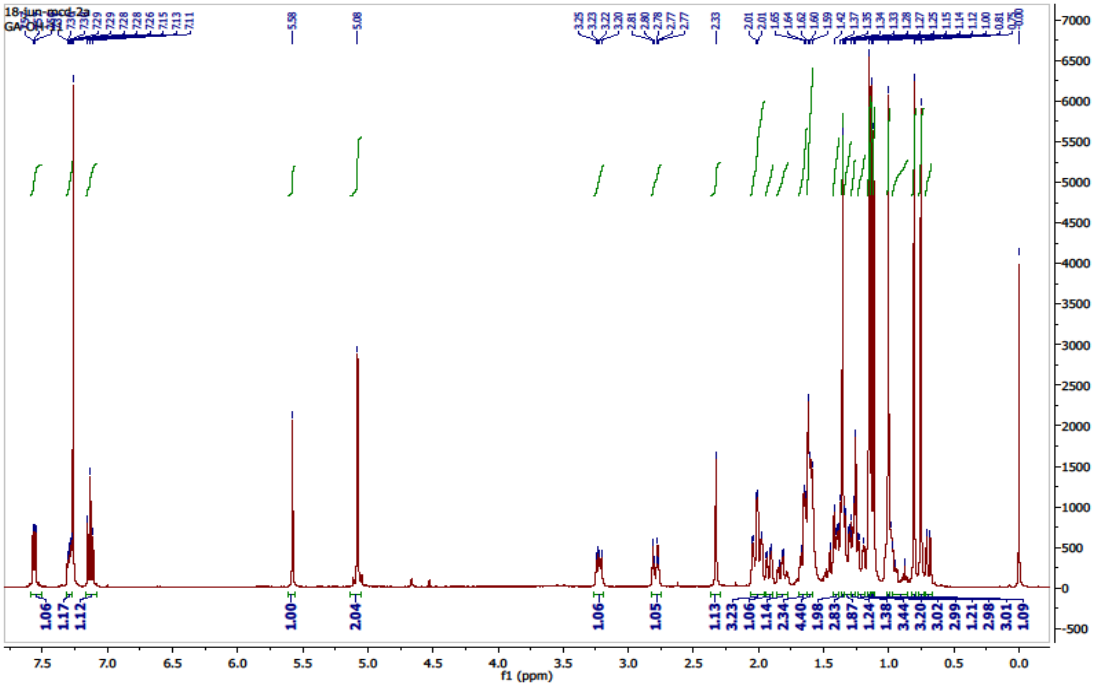
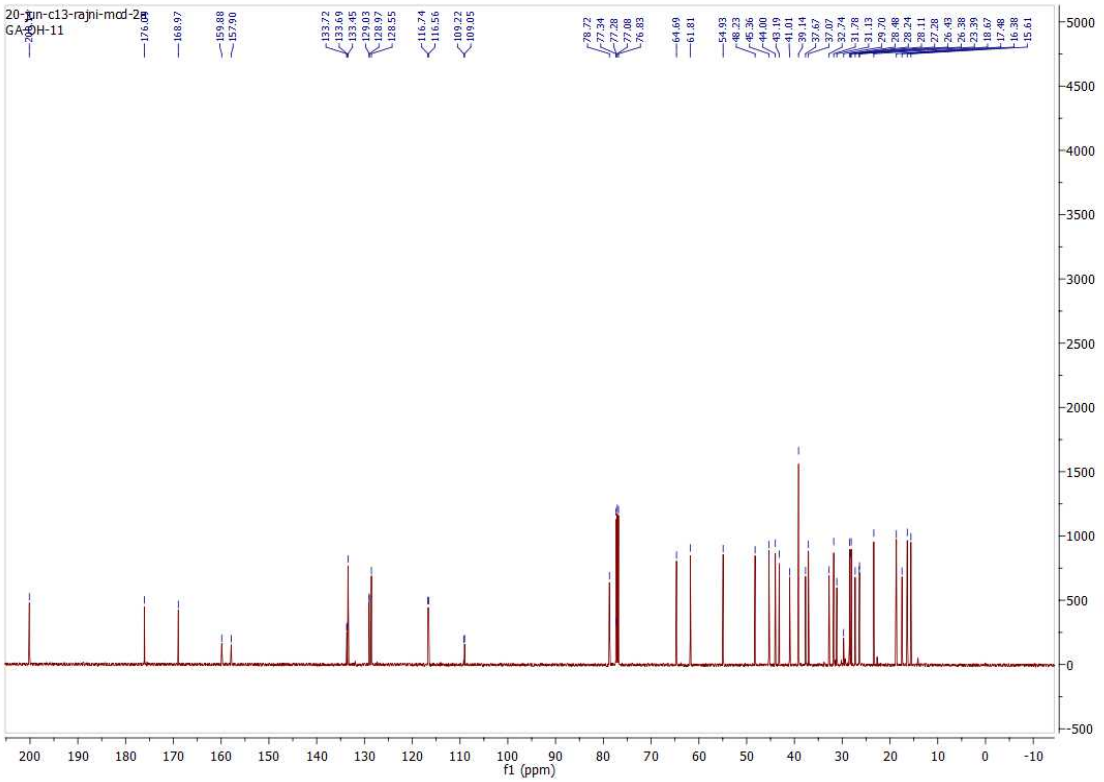
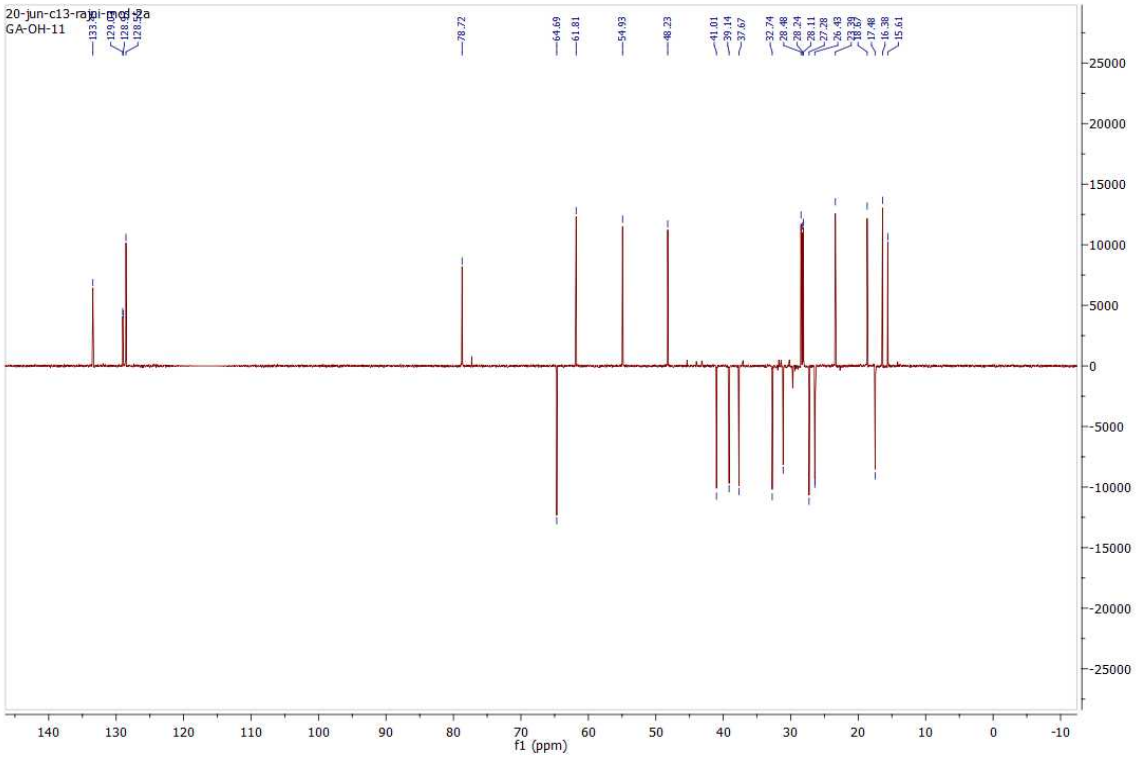
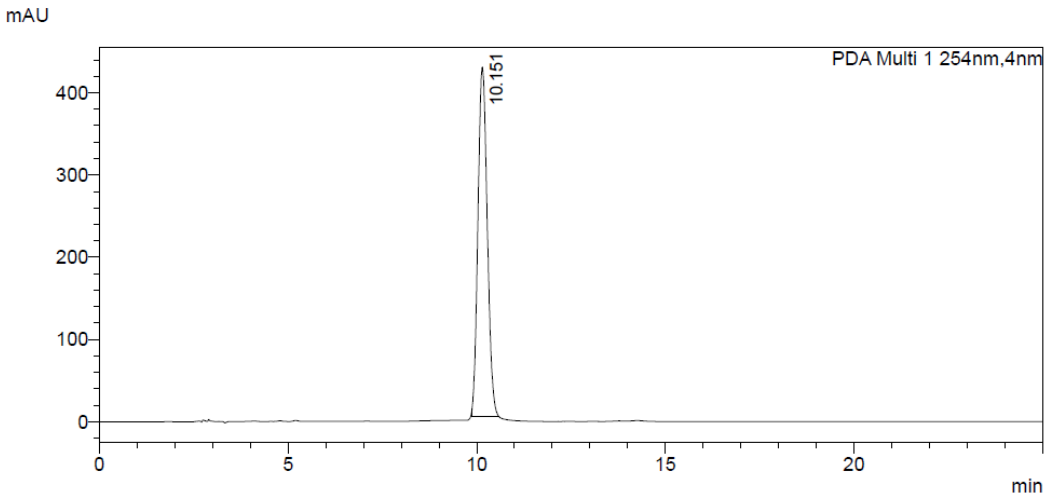
Total		18271715	1227696			100.000

S.1.12. ^{1}H, ^{13}C NMR and HPLC of 3-(3-Bromo-4-fluoro-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5k**) in $CDCl_3$







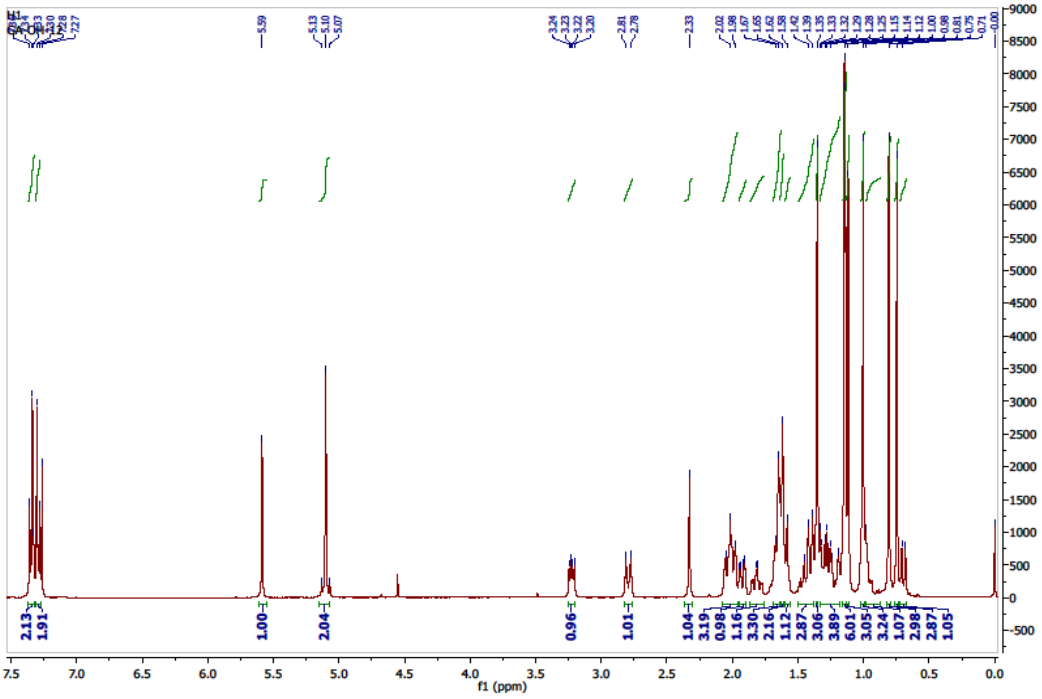


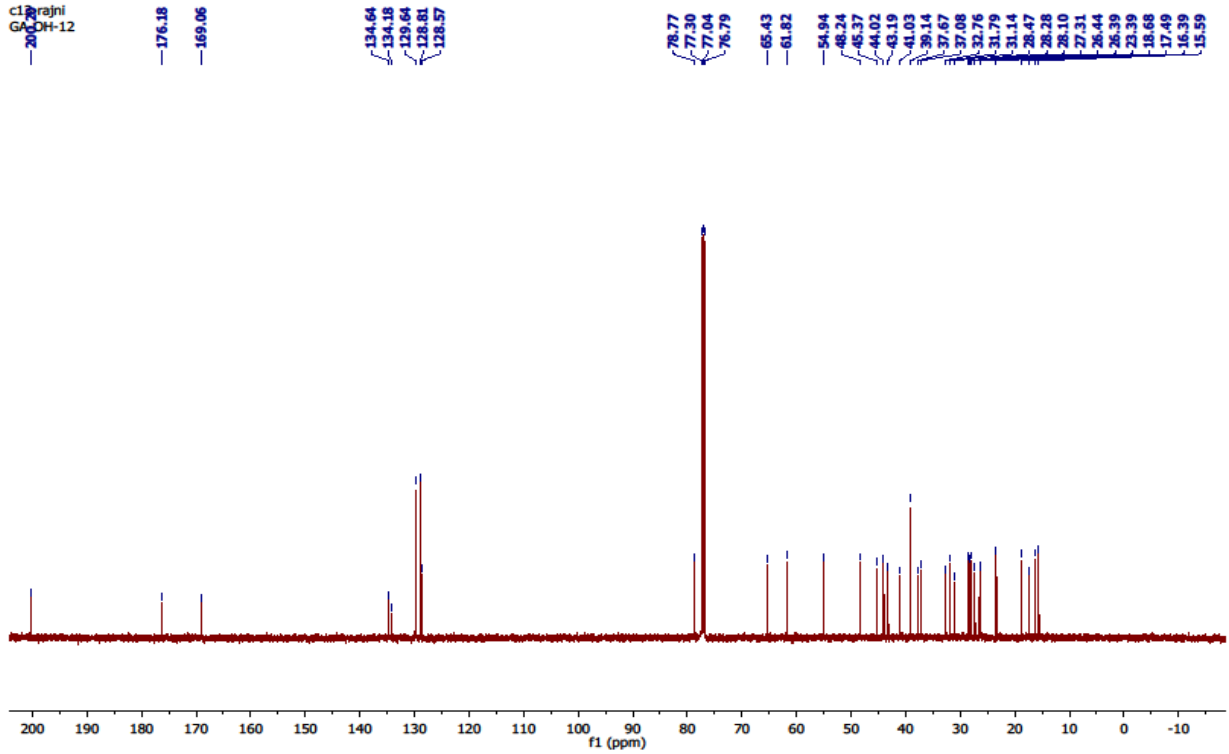
<Peak Table>

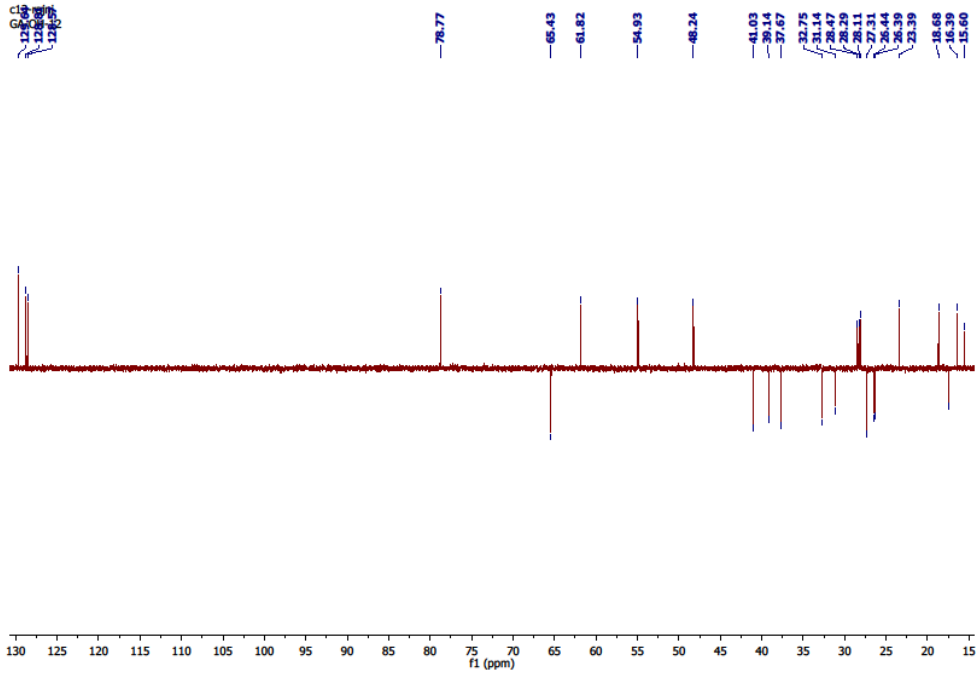
PDA Ch1 254nm

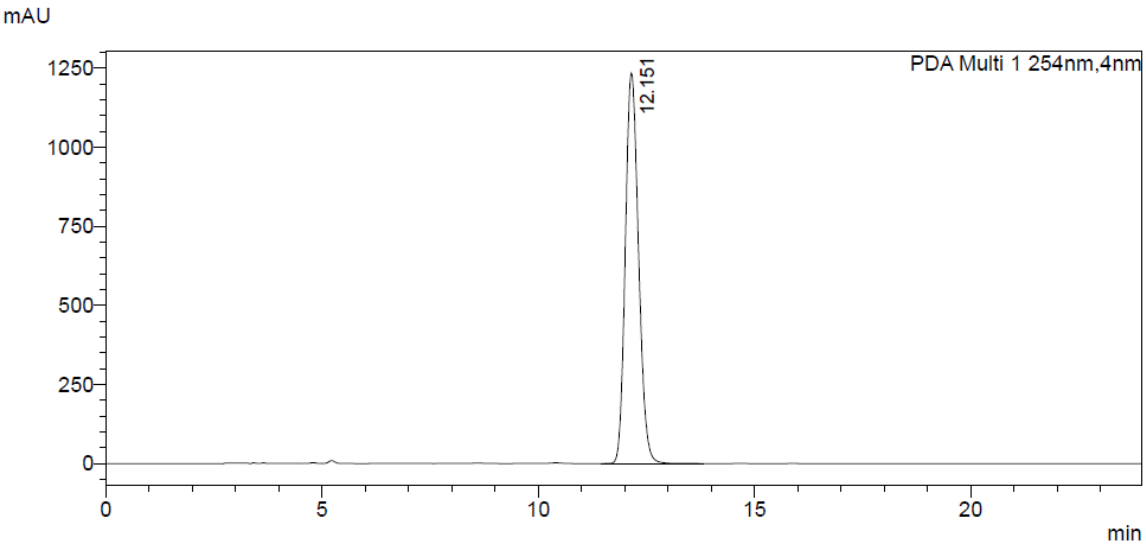
Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	10.151	7302902	424927	9.877	10.592	100.000
Total		7302902	424927			100.000

S.1.12. ^{1}H, ^{13}C NMR and HPLC of 3-(4-Chloro-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5l**) in $CDCl_3$







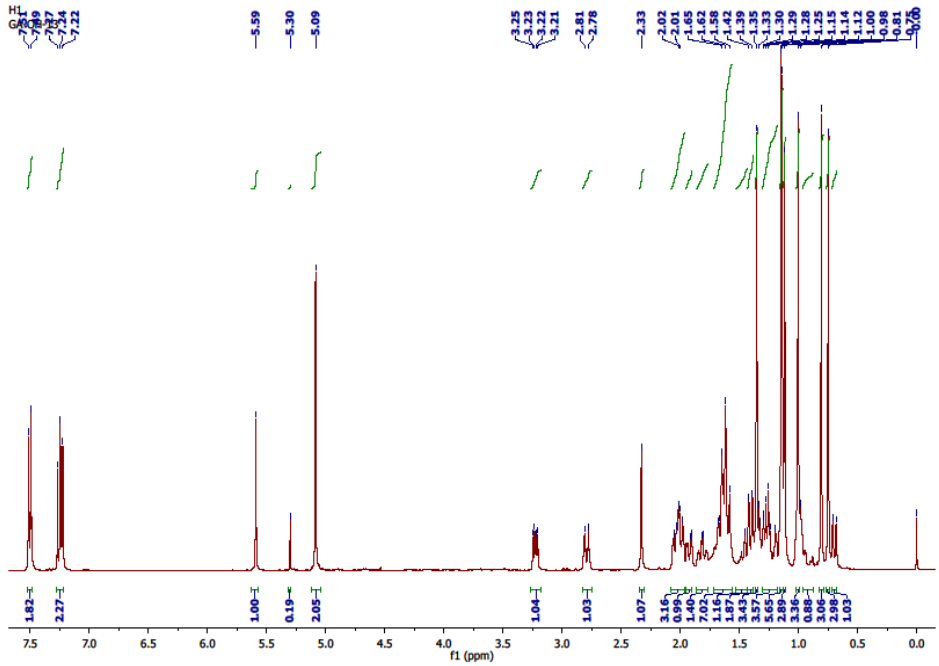


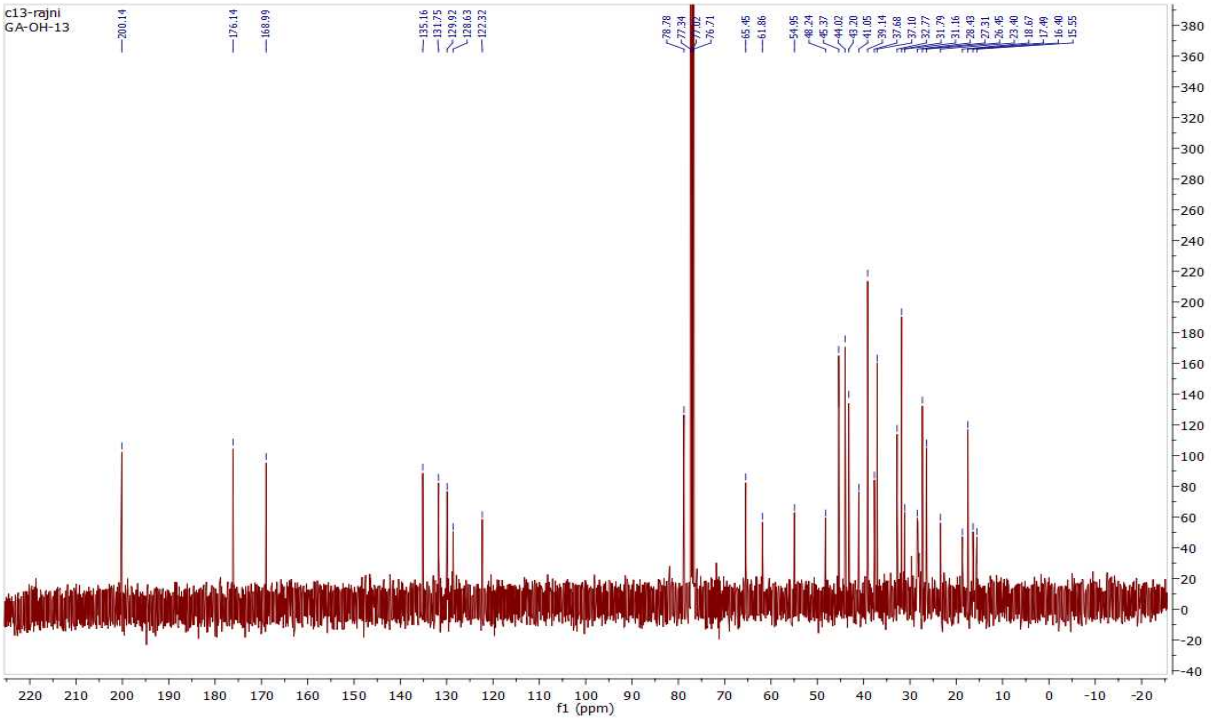
<Peak Table>

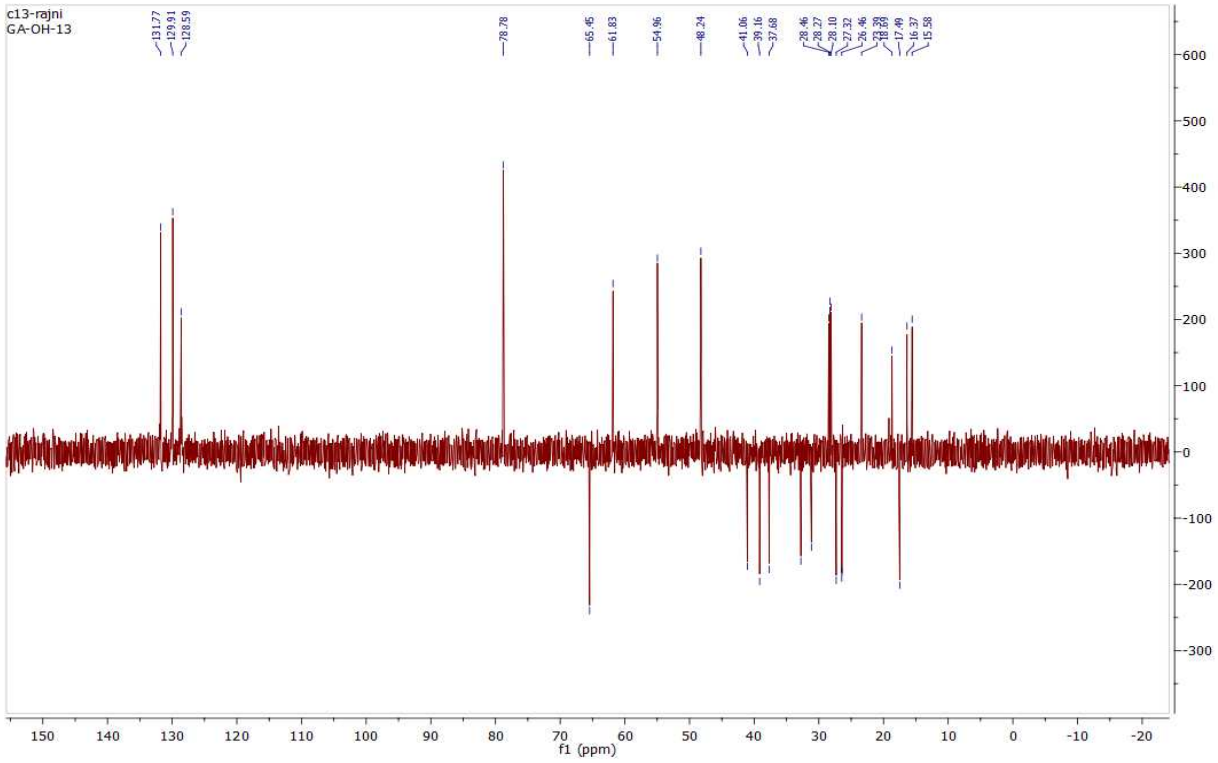
PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	12.151	26244496	1234044	11.467	13.813	100.000
Total		26244496	1234044			100.000

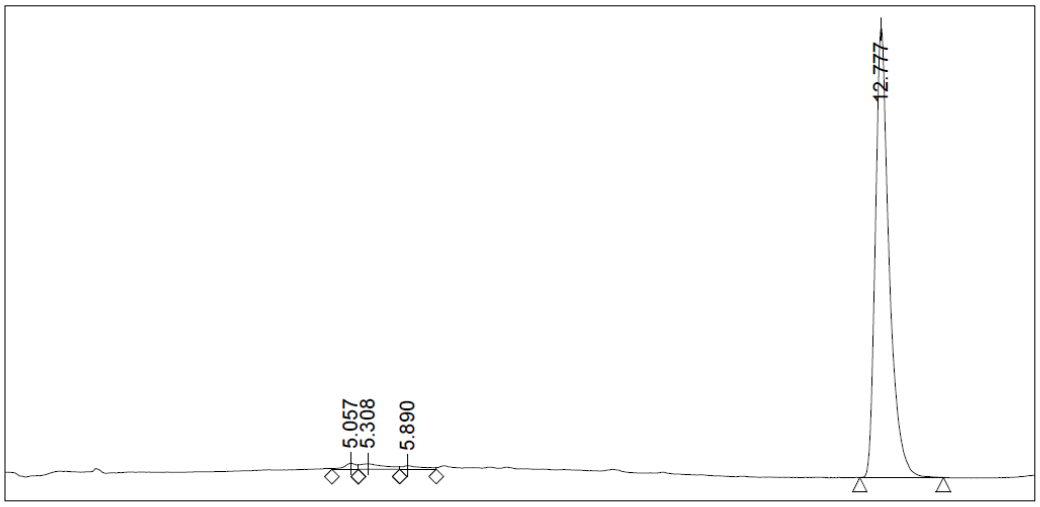
1.13. ^{1}H, ^{13}C NMR and HPLC of 3-(4-Bromo-benzyloxy)- 11-oxo-olean-12-ene-29-oic acid (**5m**) in $CDCl_3$







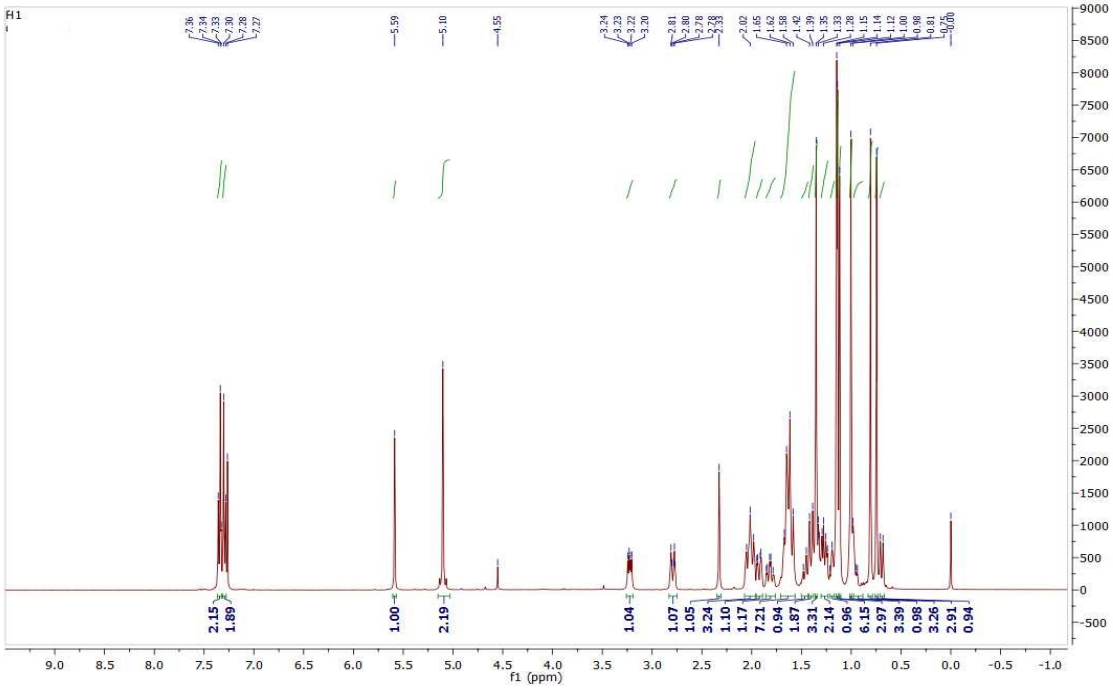
Auto-Scaled Chromatogram

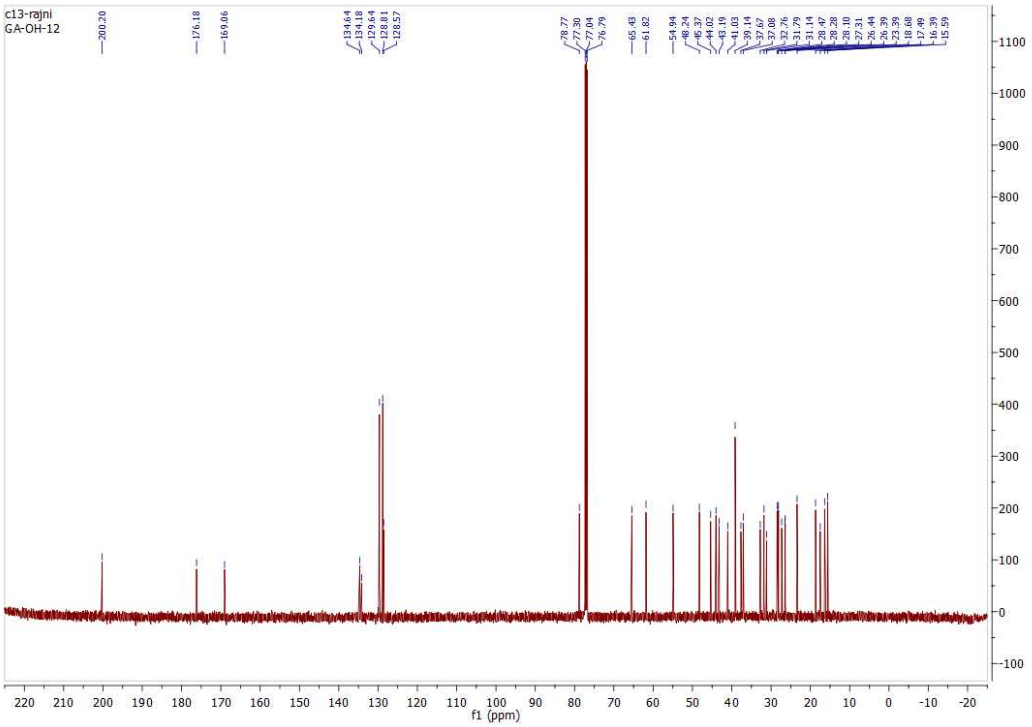


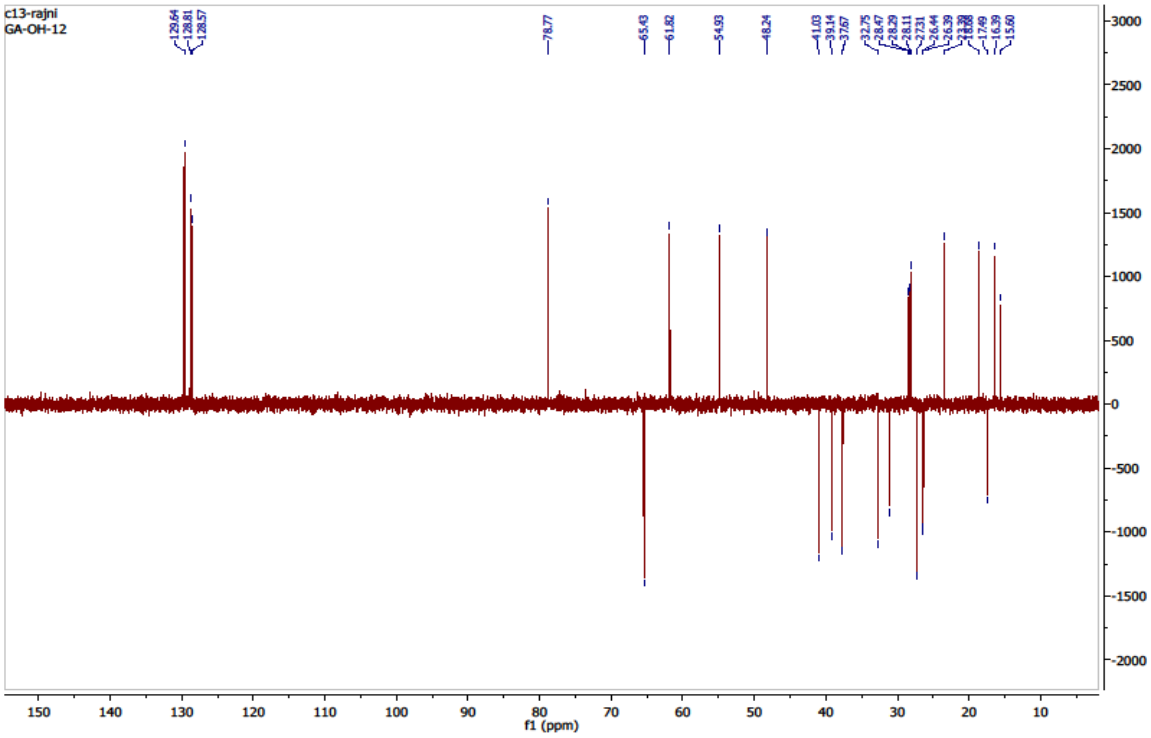
Peak Results

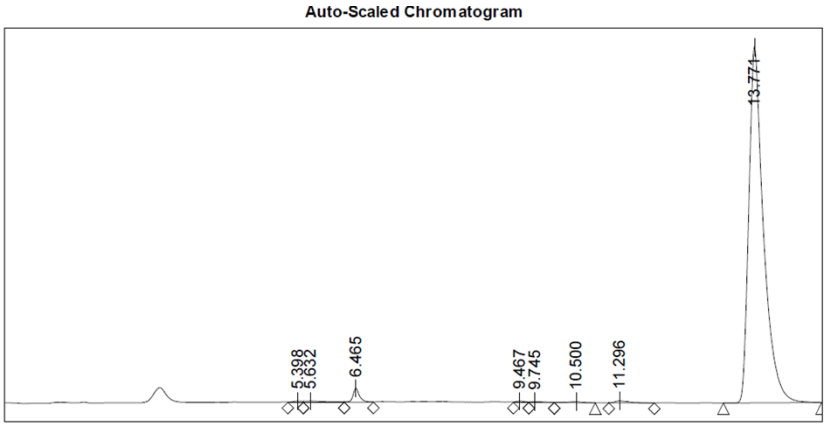
	Name	RT	Area	Height	% Area	% Height
1		5.057	68206	5446	1.16	1.31
2		5.308	125471	4926	2.14	1.18
3		5.890	64357	3228	1.10	0.78
4		12.777	5609697	402158	95.60	96.73

S.1.15. ^{1}H, ^{13}C NMR and HPLC of 3-(3-chloro-benzyloxy)-11-oxo-olean-12-ene-29-oic acid (**5n**) in $CDCl_3$





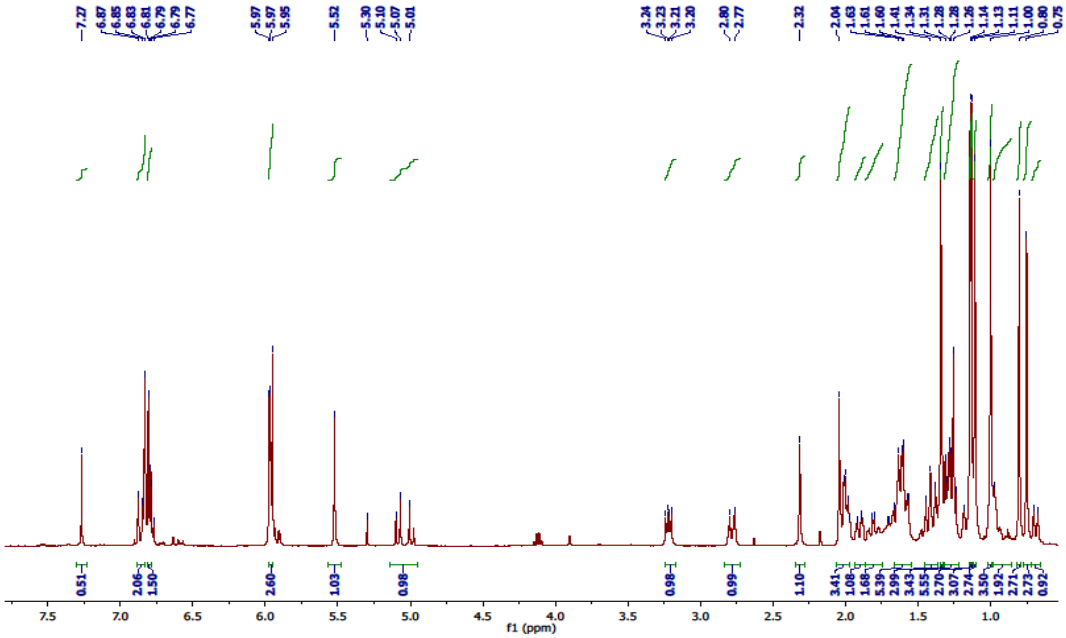


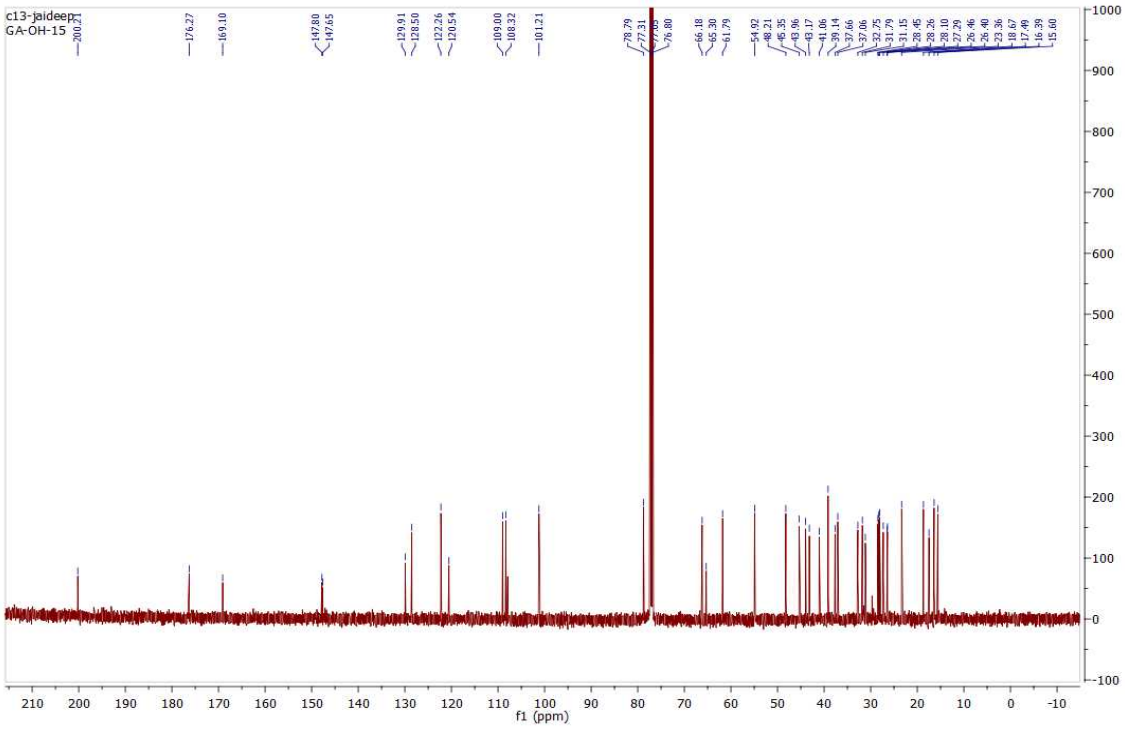


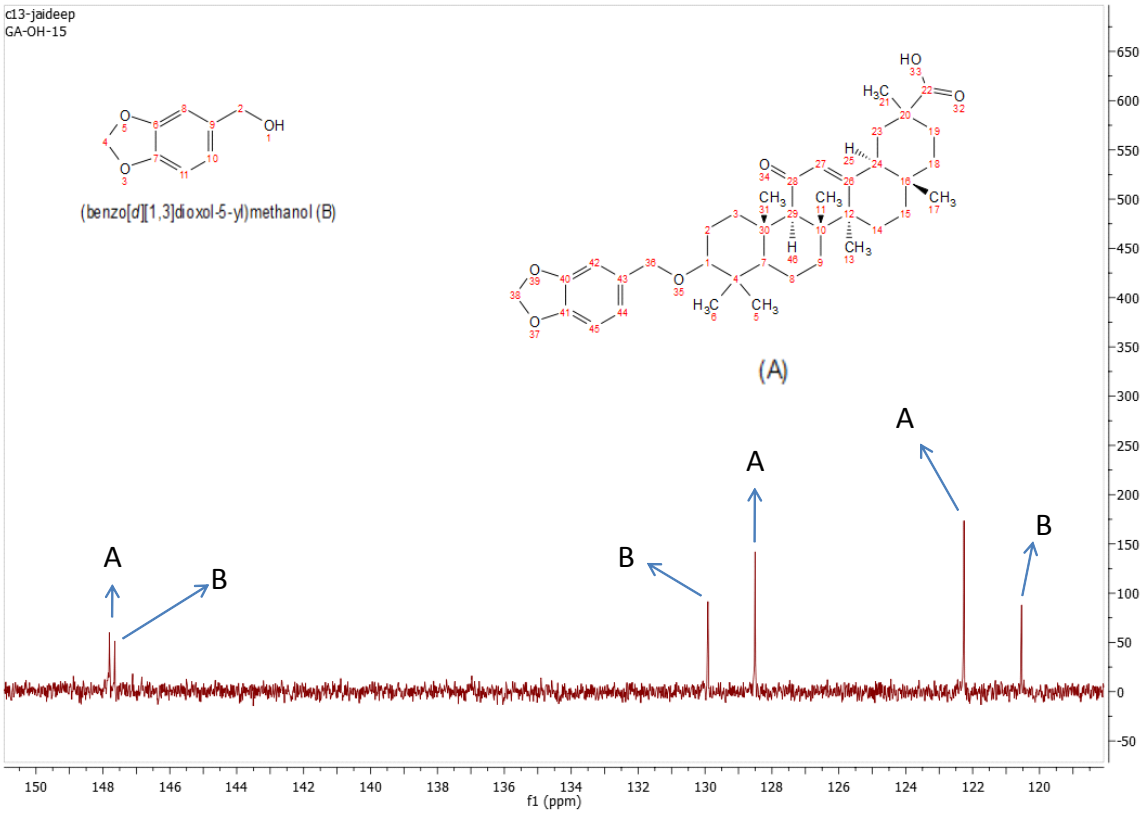
Peak Results

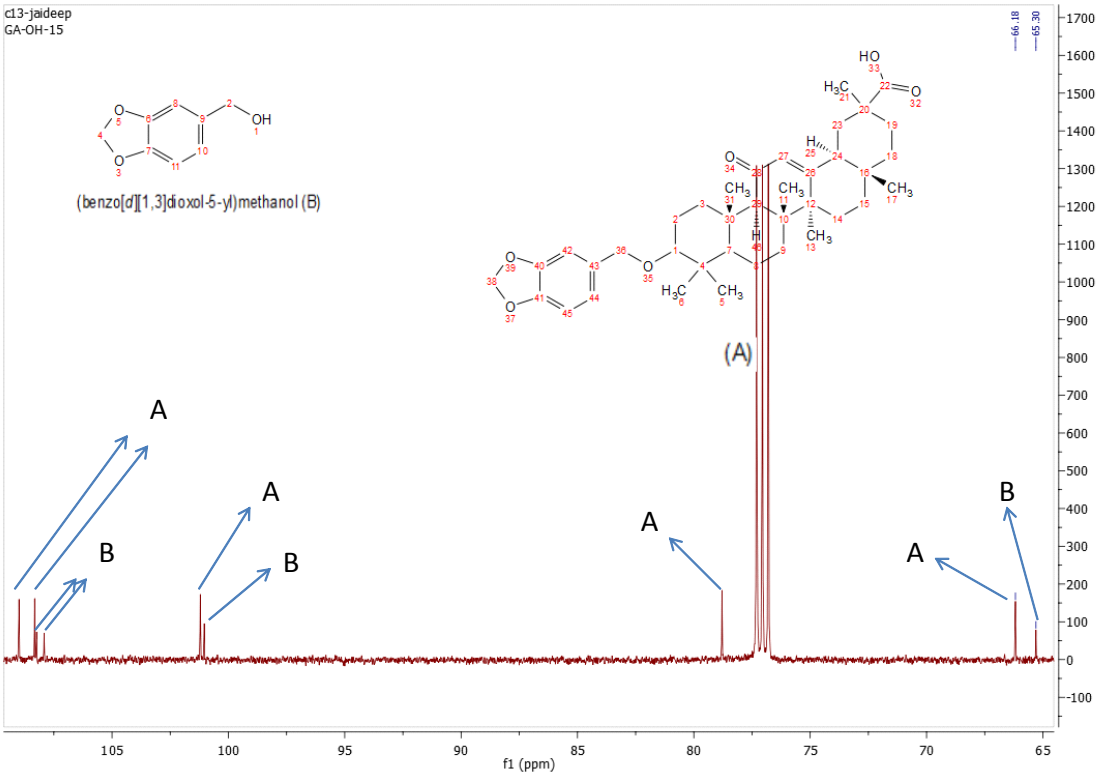
	Name	RT	Area	Height	% Area	% Height
1		5.398	59867	5424	0.18	0.30
2		5.632	140992	5463	0.43	0.31
3		6.465	540268	65540	1.66	3.68
4		9.467	64560	6100	0.20	0.34
5		9.745	63004	3231	0.19	0.18
6		10.500	79994	4471	0.25	0.25
7		11.296	157258	9284	0.48	0.52
8		13.771	31394313	1680202	96.60	94.41

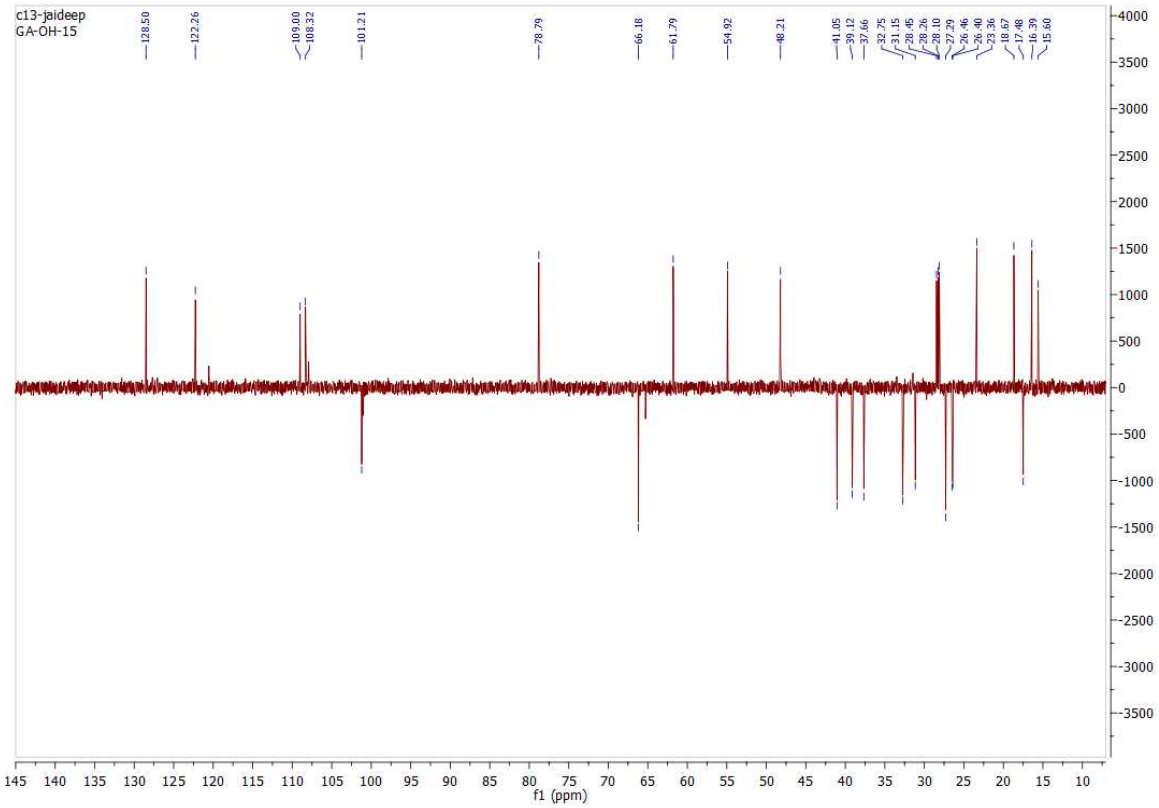
S.1.16. ^{1}H, ^{13}C NMR and HPLC of 3-(benzo[1,3]dioxol-5-ylmethoxy)-11-oxo-olean-12-ene-29-oic acid (**5o**) in $CDCl_3$ **S.1.16.** ^{1}H, ^{13}C NMR and HPLC of 3-(benzo[1,3]dioxol-5-ylmethoxy)-11-oxo-olean-12-ene-29-oic acid (**5o**) in $CDCl_3$ (This compound contains piperinol as a minor impurity, which could not be seperated due to same Rf value. Therefore the ^{13}C NMR shows few additional signals. We have clearly shown these additional signals in this file).



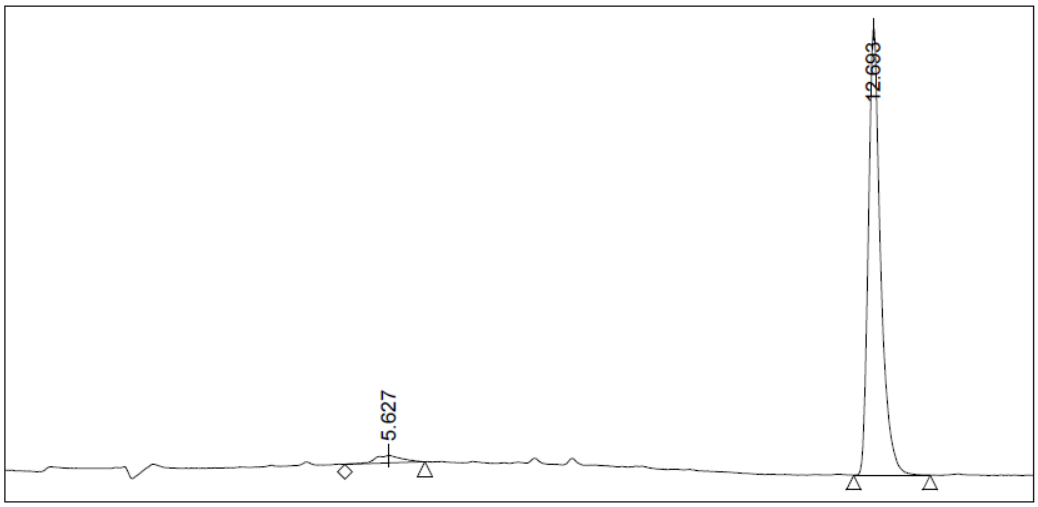



c13-jaideep
GA-OH-15
(benzo[d][1,3]dioxol-5-yl)methanol (B)
(A)
A
B
f1 (ppm)


c13-jaideep
GA-OH-15
(benzo[d][1,3]dioxol-5-yl)methanol (B)
(A)
A
B
f1 (ppm)



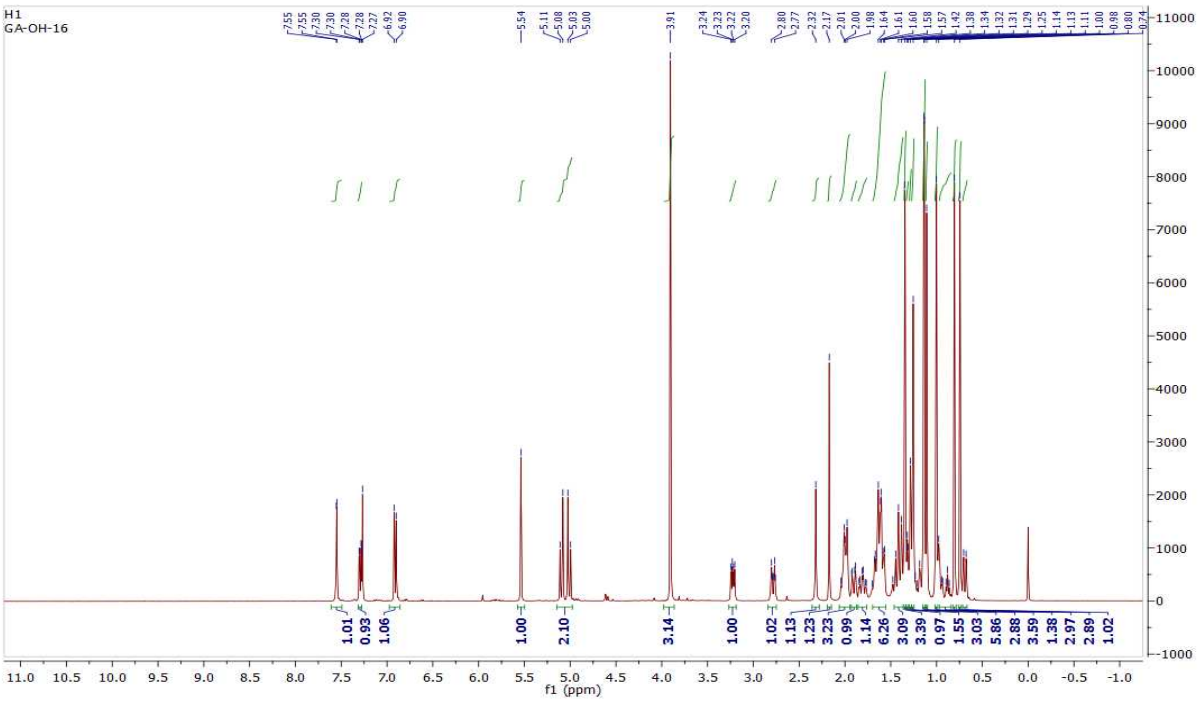
Auto-Scaled Chromatogram

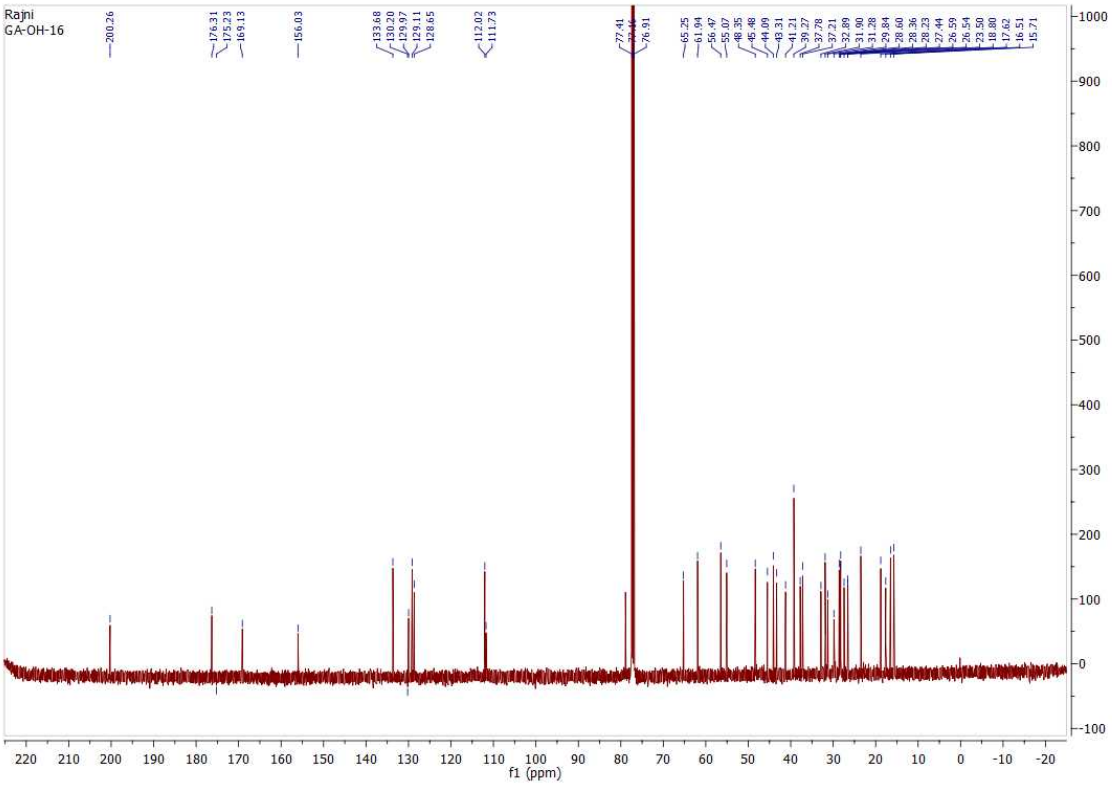


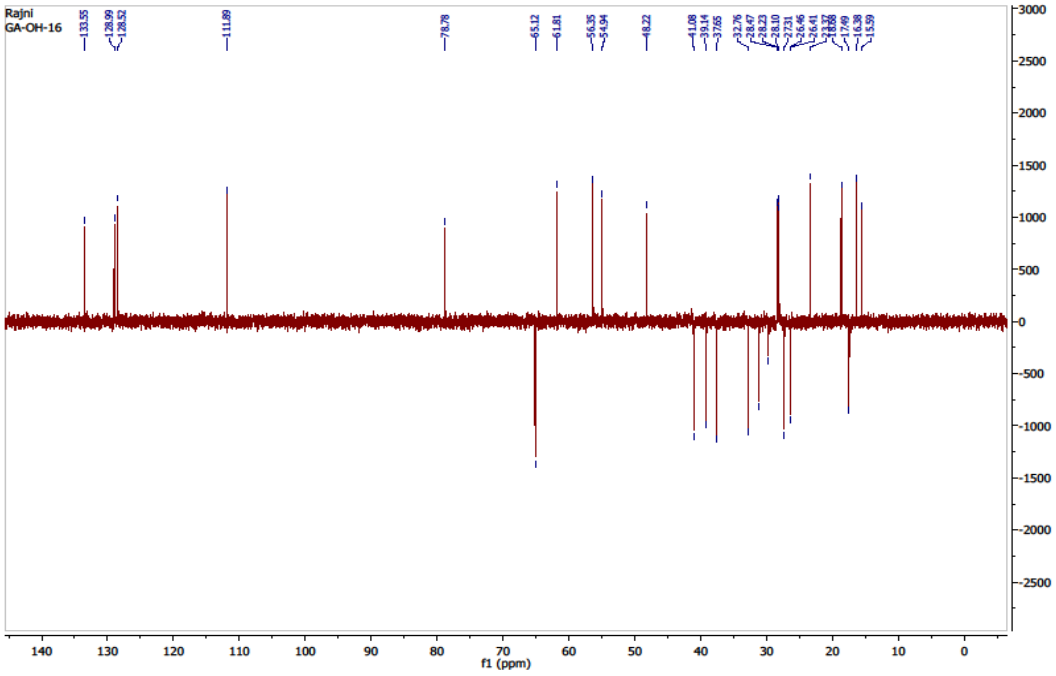
Peak Results

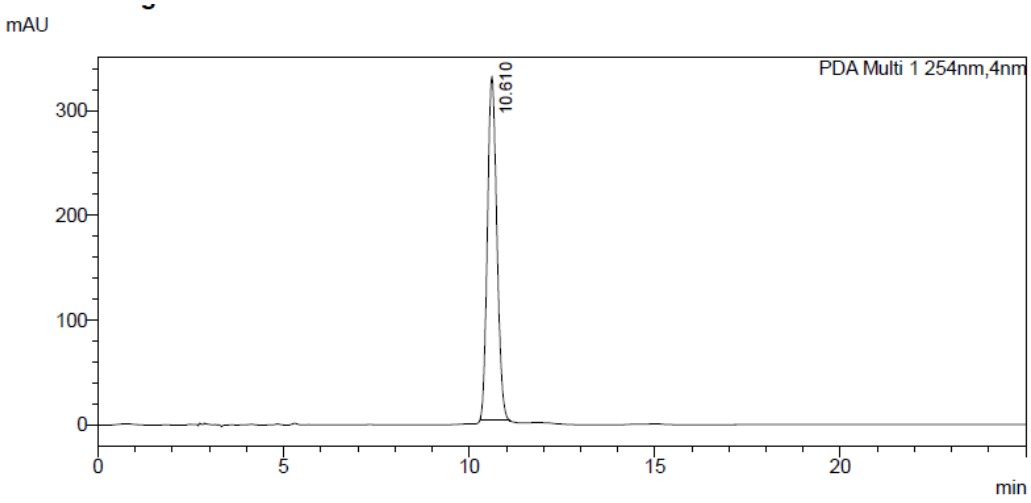
	Name	RT	Area	Height	% Area	% Height
1		5.627	140112	5153	3.50	1.63
2		12.693	3866513	310494	96.50	98.37

S.1.17. ^{1}H, ^{13}C NMR and HPLC of 3-(3-bromo-4-methoxy-benzyloxy)-11-oxo-olean-12-ene-29-oic acid (**5p**) in $CDCl_3$







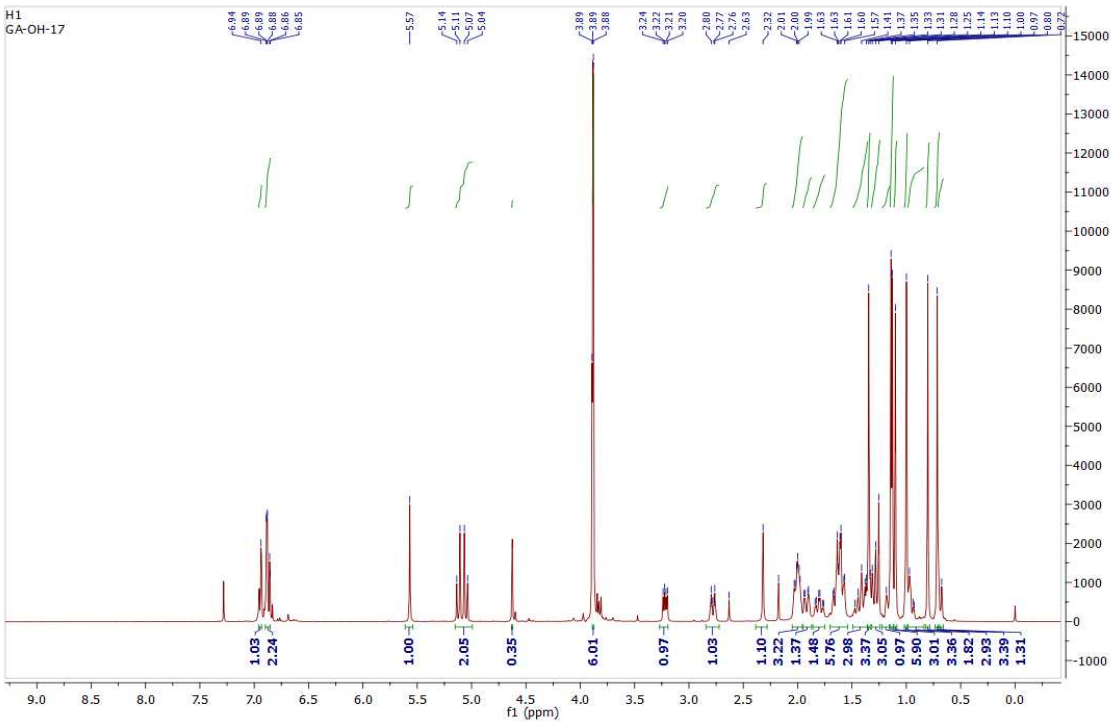


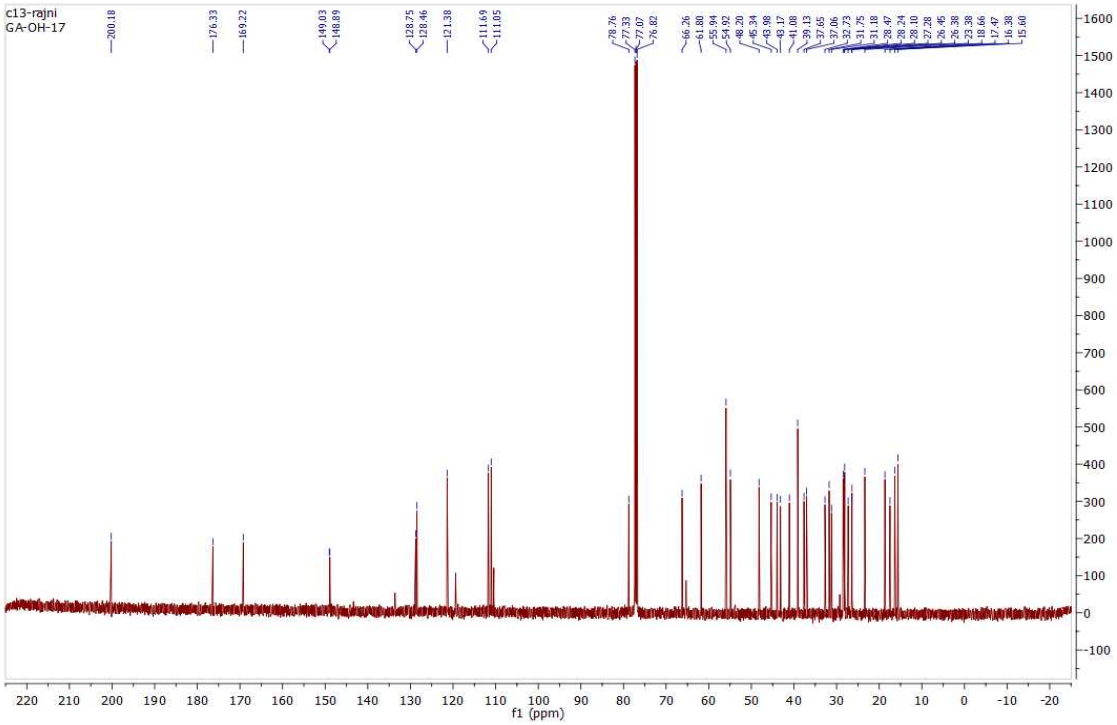
<Peak Table>

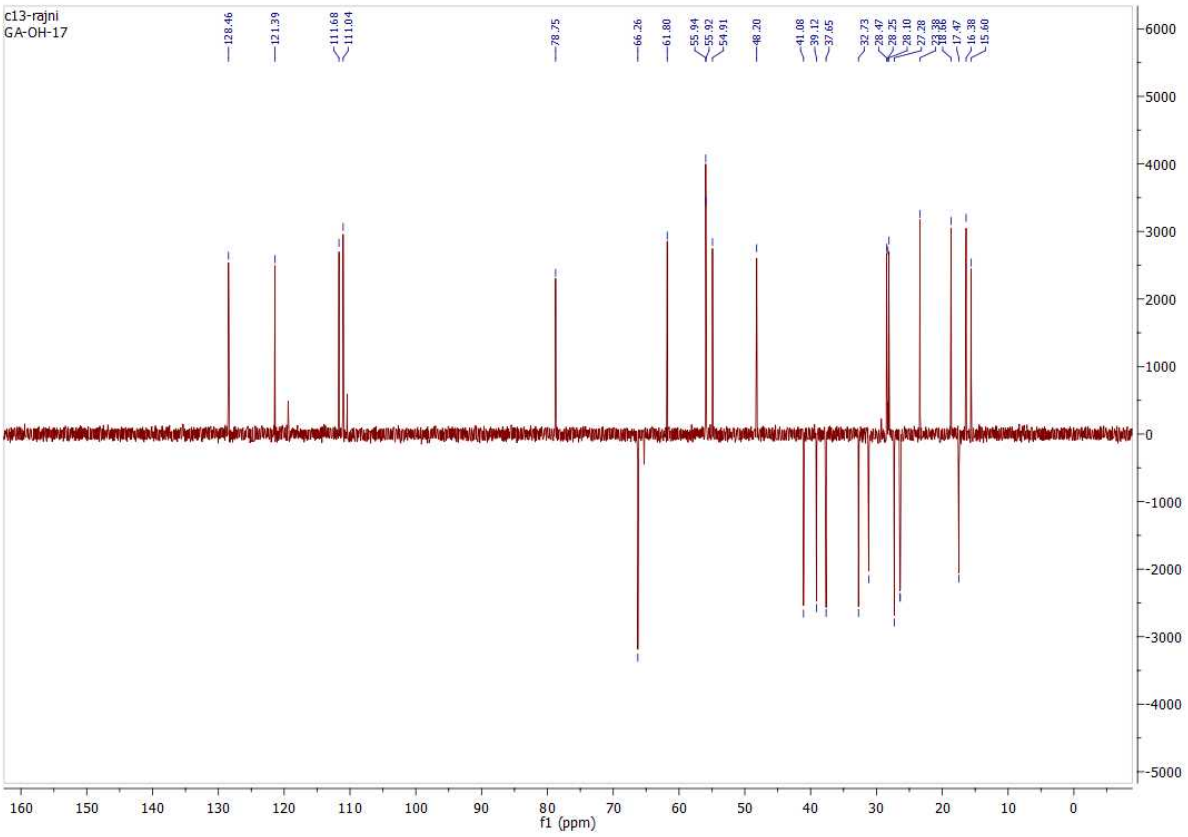
PDA Ch1 254nm

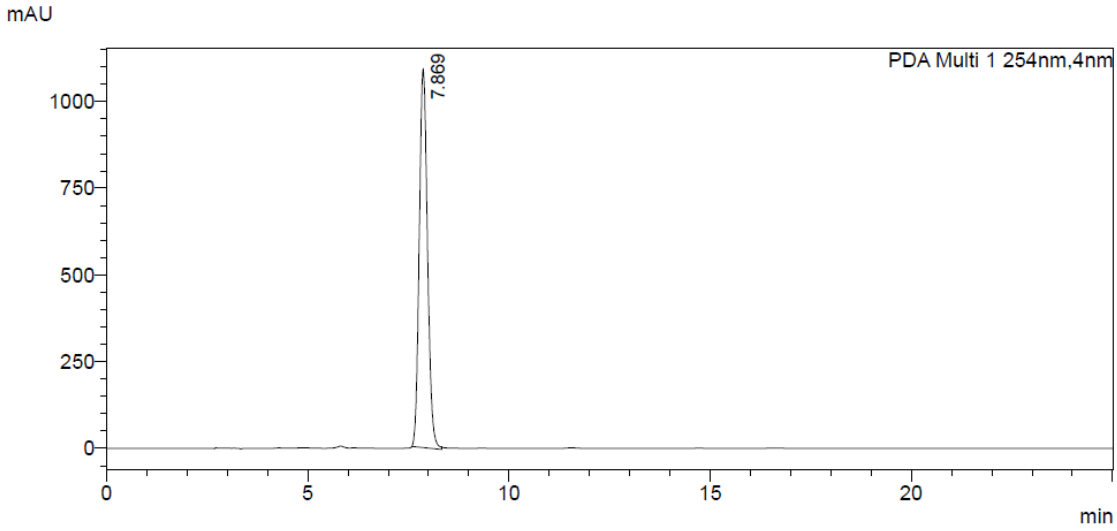
Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	10.610	5755251	326648	10.304	11.093	100.000
Total		5755251	326648			100.000

S.1.18. ^{1}H, ^{13}C NMR and HPLC of 3-(3,4-dimethoxy-benzyloxy)-11-oxo-olean-12-ene-29-oic acid (**5q**) in $CDCl_3$







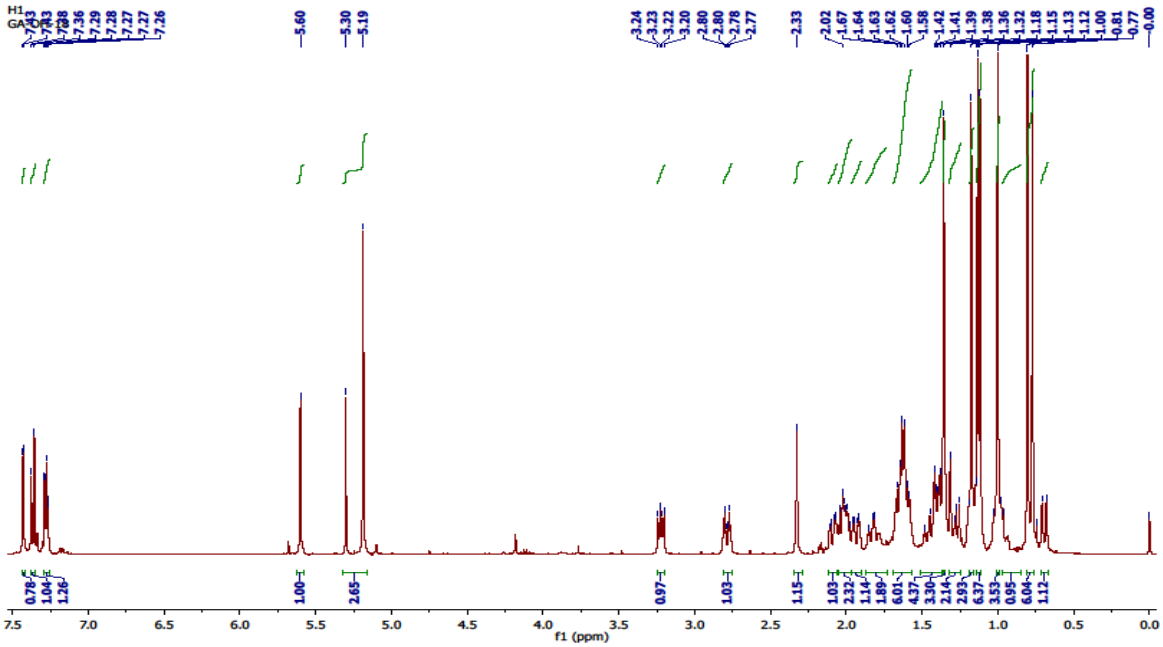


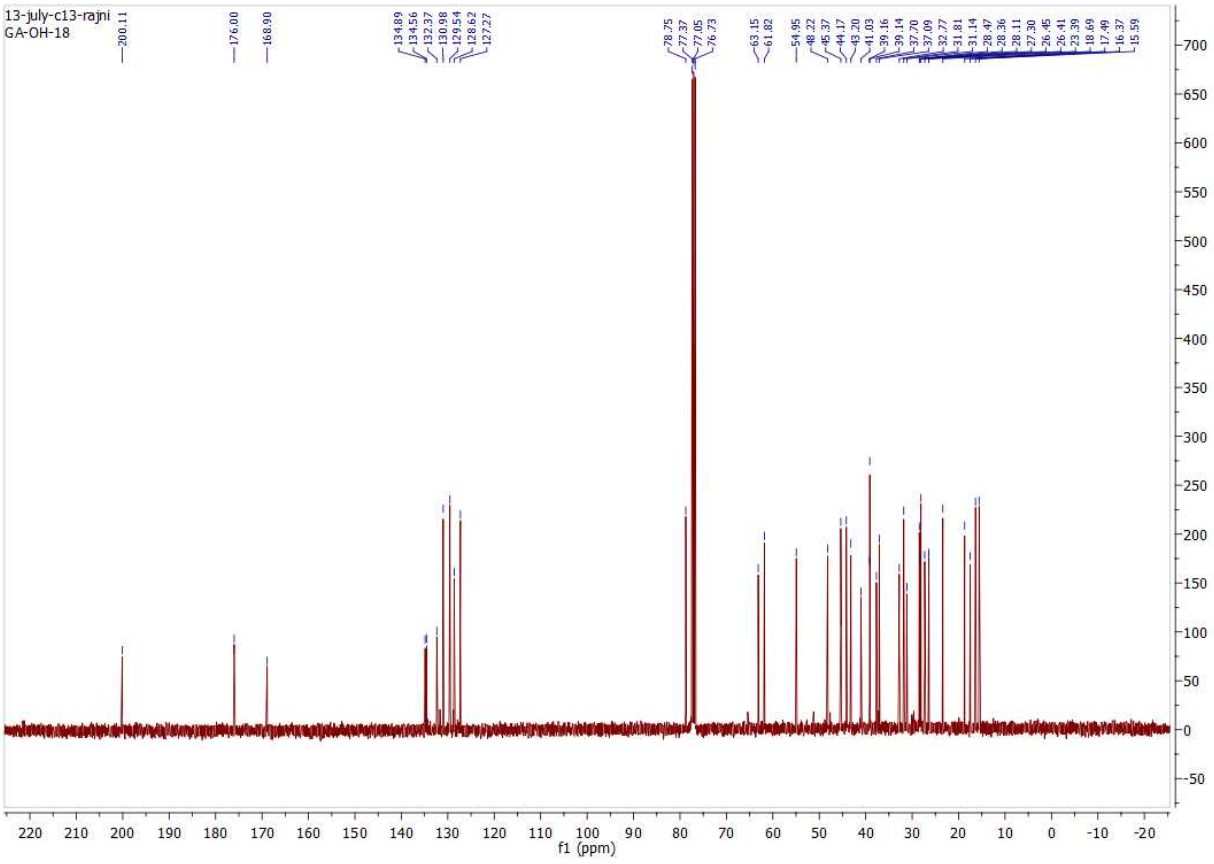
<Peak Table>

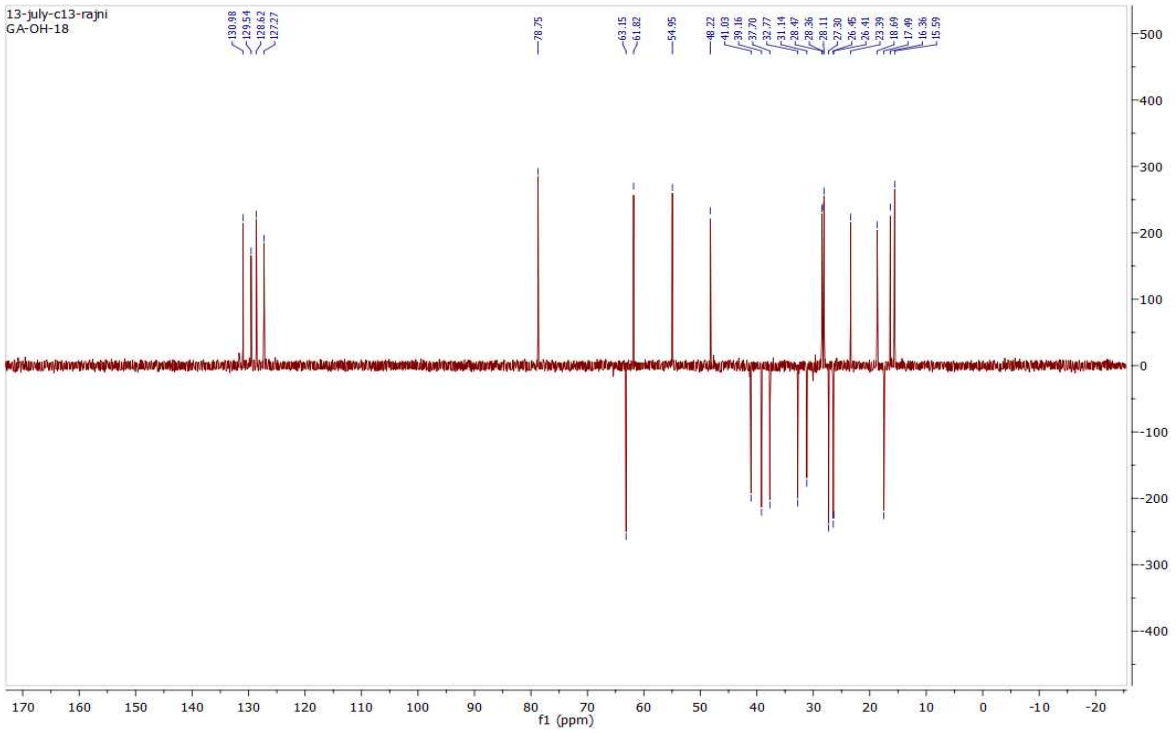
PDA Ch1 254nm

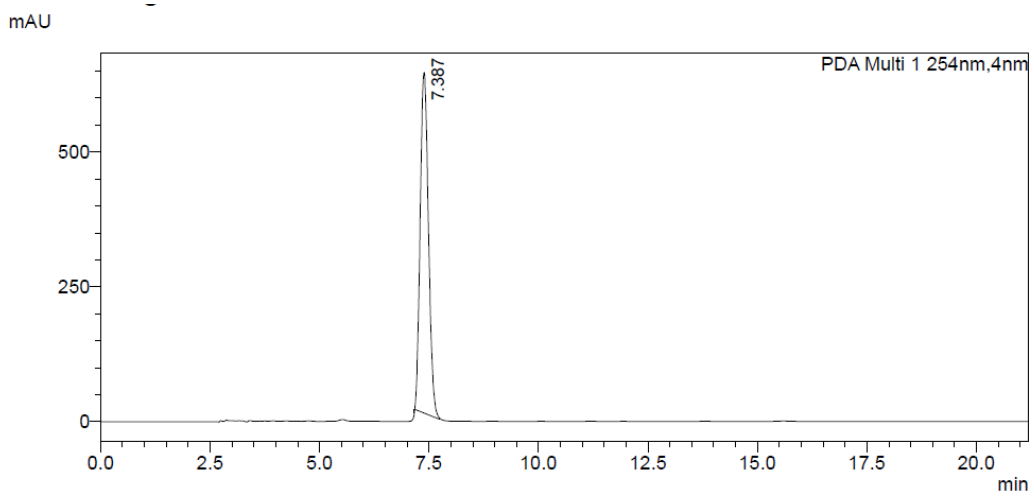
Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	7.869	15504011	1090066	7.584	8.331	100.000
Total		15504011	1090066			100.000

S.1.19. ^{1}H, ^{13}C NMR and HPLC of 3-(2,4-dichloro-benzyloxy)-11-oxo-olean-12-ene-29-oic acid (**5r**) in $CDCl_3$









<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Peak Start	Peak End	Area%
1	7.387	8295569	630748	7.168	7.733	100.000
Total		8295569	630748			100.000

S2. Cytotoxicity of Compounds obtained using Different Cancer Cell Lines

Table S1. Cytotoxicity of Compounds obtained using Different Cancer Cell Lines

Entry	IC_{50} (μM)		
	PC-3	MIAPaCa-2	HepG-2
2	>100	>100	>100
5a	10	11	40
5b	6	7	19
5c	9	12	>100
5d	90	>100	>100
5e	24	>100	>100
5f	>100	>100	>100
5g	>100	>100	>100
5h	30	>100	>100
5i	>100	>100	>100
5j	>100	>100	>100
5k	30	70	75
5l	28	85	76
5m	48	69	72
5n	31	72	70
5o	30	66	55
5p	55	58	48
5q	52	55	60
5r	18	40	45
paclitaxel	0.012	0.1	>100
camptothecin	1.2	0.19	0.2

S3. HPLC Methods

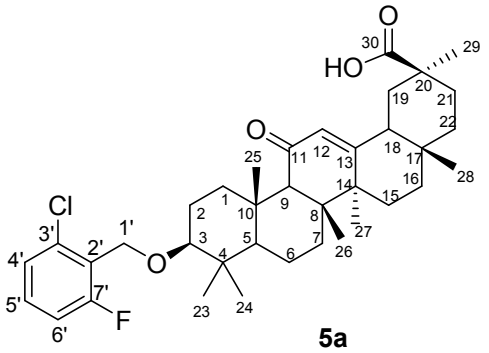
Method 1: Sample solution of compounds of concentration 0.5 mg/ml prepared in methanol and filtered through 0.45 µ membrane filter were injected (20 µl) in the HPLC system (Shimadzu) using Inertsil® C-8 column (GL Sciences Inc., 5 µ, 4.6 × 250 mm). The binary mobile phase consisting of A (water) and B (methanol) was used. A isocratic elution (A: B – 10: 90) was used at a flow rate of 1 ml/min. Results were analyzed using PDA detector. This method was used for compounds **5a**, **5c**, **5f**, **5j**, **5k**, **5l**, **5p**, **5q** and **5r**.

Method 2: Sample solution of compounds of concentration 0.5 mg/ml prepared in methanol and filtered through 0.45 µ membrane filter injected (10 µl) in the HPLC system (Waters) using Chromolith RP-18e column (Merck, 50 × 4.6 mm). The binary mobile phase consisting of A (aqueous 0.1% formic acid, v/v) and B (acetonitrile) was used. A gradient program was used as follows:

Time (min)	aqueous 0.1% formic acid, v/v (A)	Acetonitrile (B)	Flow rate
0	95	5	0.6 mL/min
5	95	5	0.6 mL/min
35	0	100	0.6 mL/min
45	0	100	0.6 mL/min
55	95	5	0.6 mL/min
5	95	5	0.6 mL/min

Results were analyzed using UV-PDA detector. This method was used for compounds **5b**, **5d**, **5e**, **5g**, **5h**, **5i**, **5m**, **5n** and **5o**.

S4. Example of compound numbering used during assignments of NMR values



5a