

Supplementary Information

Synthesis and biological evaluation of novel asiatic acid derivatives with anticancer activity

Bruno M. F. Gonçalves,^a Jorge A. R. Salvador,^{a,b,} Silvia Marín,^{c,d} and Marta Cascante,^{c,d,*}*

^a *Laboratory of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Coimbra, 3000-548, Coimbra, Portugal. Fax: +351 239 488 503; Tel: +351 239 488 400; E-mail: salvador@ci.uc.pt*

^b *Center for Neuroscience and Cell Biology, Coimbra, Portugal.*

^c *Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Barcelona, Diagonal 643, 08028 Barcelona, Spain, Tel.: +34-934021593*

^d *Institute of Biomedicine of University of Barcelona (IBUB) and Associated Unit to CSIC, Barcelona, Spain.*

Table of Contents

1 NMR data for compound 4:.....	6
1.1 ¹ H-NMR spectrum for compound 4 recorded in CDCl ₃	6
1.2 ¹³ C-NMR spectrum for compound 4 recorded in CDCl ₃	7
1.3 DEPT135 spectrum for compound 4 recorded in CDCl ₃	8
2. NMR data for compound 5.....	9
2.1 ¹ H-NMR spectrum for compound 5 recorded in CDCl ₃	9
2.2 ¹³ C-NMR spectrum for compound 5 recorded in CDCl ₃	10
2.3 DEPT135 spectrum for compound 5 recorded in CDCl ₃	11
3. NMR data for compound 6.....	12
3.1 ¹ H-NMR spectrum for compound 6 recorded in CDCl ₃	12
3.2 ¹³ C-NMR spectrum for compound 6 recorded in CDCl ₃	13
3.3 DEPT135 spectrum for compound 6 recorded in CDCl ₃	14
4. NMR data for compound 7.....	15
4.1 ¹ H-NMR spectrum for compound 7 recorded in CDCl ₃	15
4.2 ¹³ C-NMR spectrum for compound 7 recorded in CDCl ₃	16
4.3 DEPT135 spectrum for compound 7 recorded in CDCl ₃	17
5. NMR data for compound 8.....	18
5.1 ¹ H-NMR spectrum for compound 8 recorded in CDCl ₃	18
5.2 ¹³ C-NMR spectrum for compound 8 recorded in CDCl ₃	19
5.3 DEPT135 spectrum for compound 8 recorded in CDCl ₃	20
6. NMR data for compound 9.....	21
6.1 ¹ H-NMR spectrum for compound 9 recorded in CDCl ₃	21
6.2 ¹³ C-NMR spectrum for compound 9 recorded in CDCl ₃	22
6.3 DEPT135 spectrum for compound 9 recorded in CDCl ₃	23
7. NMR data for compound 13.....	24
7.1 ¹ H-NMR spectrum for compound 13 recorded in CDCl ₃	24
7.2 ¹³ C-NMR spectrum for compound 13 recorded in CDCl ₃	25
7.3 DEPT135 spectrum for compound 13 recorded in CDCl ₃	26
8. NMR data for compound 14.....	27
8.1 ¹ H-NMR spectrum for compound 14 recorded in CDCl ₃	27
8.2 ¹³ C-NMR spectrum for compound 14 recorded in CDCl ₃	28

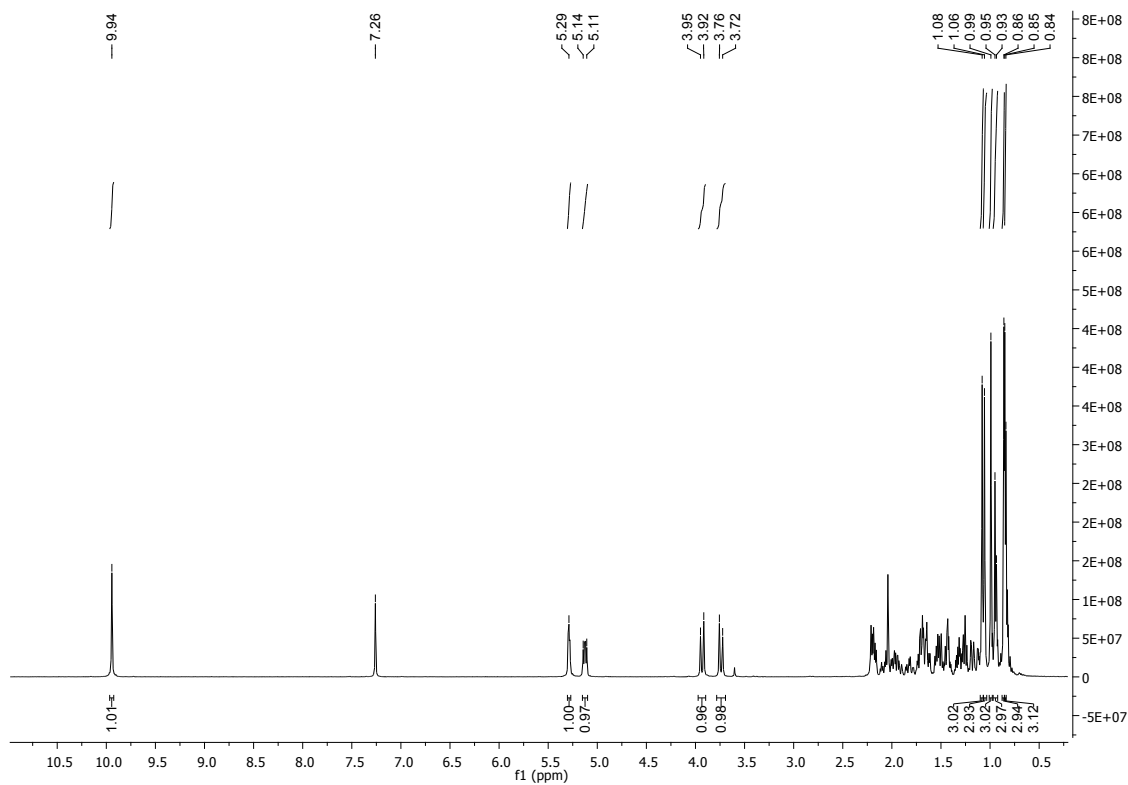
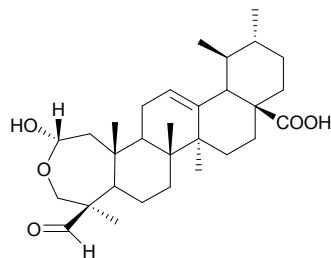
8.3 DEPT135 spectrum for compound 14 recorded in CDCl ₃	29
9. NMR data for compound 15.....	30
9.1 ¹ H-NMR spectrum for compound 15 recorded in CDCl ₃	30
9.2 ¹³ C-NMR spectrum for compound 15 recorded in CDCl ₃	31
9.3 DEPT135 spectrum for compound 15 recorded in CDCl ₃	32
10. NMR data for compound 16.....	33
10.1 ¹ H-NMR spectrum for compound 16 recorded in CDCl ₃	33
10.2 ¹³ C-NMR spectrum for compound 16 recorded in CDCl ₃	34
10.3 DEPT135 spectrum for compound 16 recorded in CDCl ₃	35
11. NMR data for compound 17.....	36
11.1 ¹ H-NMR spectrum for compound 17 recorded in CDCl ₃	36
11.2 ¹³ C-NMR spectrum for compound 17 recorded in CDCl ₃	37
11.3 DEPT135 spectrum for compound 17 recorded in CDCl ₃	38
12. NMR data for compound 18.....	39
12.1 ¹ H-NMR spectrum for compound 18 recorded in CDCl ₃	39
12.2 ¹³ C-NMR spectrum for compound 18 recorded in CDCl ₃	40
12.3 DEPT135 spectrum for compound 18 recorded in CDCl ₃	41
13. NMR data for compound 19.....	42
13.1 ¹ H-NMR spectrum for compound 19 recorded in CDCl ₃	42
13.2 ¹³ C-NMR spectrum for compound 19 recorded in CDCl ₃	43
13.3 DEPT spectrum for compound 19 recorded in CDCl ₃	44
14. NMR data for compound 20.....	45
14.1 ¹ H-NMR spectrum for compound 20 recorded in CDCl ₃	45
14.2 ¹³ C-NMR spectrum for compound 20 recorded in CDCl ₃	46
14.3 DEPT spectrum for compound 20 recorded in CDCl ₃	47
15. NMR data for compound 21.....	48
15.1 ¹ H-NMR spectrum for compound 21 recorded in CDCl ₃	48
15.2 ¹³ C-NMR spectrum for compound 21 recorded in CDCl ₃	49
15.3 DEPT135 spectrum for compound 21 recorded in CDCl ₃	50
16. NMR data for compound 22.....	51
16.1 ¹ H-NMR spectrum for compound 22 recorded in CDCl ₃	51
16.2 ¹³ C-NMR spectrum for compound 22 recorded in CDCl ₃	52
16.3 DEPT135 spectrum for compound 22 recorded in CDCl ₃	53
17. NMR data for compound 23.....	54
17.1 ¹ H-NMR spectrum for compound 23 recorded in CDCl ₃	54

17.2	¹³ C-NMR spectrum for compound 23 recorded in CDCl ₃	55
17.3	DEPT135 spectrum for compound 23 recorded in CDCl ₃	56
18.	NMR data for compound 24.....	57
18.1	¹ H-NMR spectrum for compound 24 recorded in CDCl ₃	57
18.2	¹³ C-NMR spectrum for compound 24 recorded in CDCl ₃	58
18.3	DEPT135 spectrum for compound 24 recorded in CDCl ₃	59
19.	NMR data for compound 25.....	60
19.1	¹ H-NMR spectrum for compound 25 recorded in CDCl ₃	60
19.2	¹³ C-NMR spectrum for compound 25 recorded in CDCl ₃	61
19.3	DEPT135 spectrum for compound 25 recorded in CDCl ₃	62
20.	NMR data for compound 26.....	63
20.1	¹ H-NMR spectrum for compound 26 recorded in CDCl ₃	63
20.2	¹³ C-NMR spectrum for compound 26 recorded in CDCl ₃	64
20.3	DEPT135 spectrum for compound 26 recorded in CDCl ₃	65
21.	NMR data for compound 27.....	66
21.1	¹ H-NMR spectrum for compound 27 recorded in CDCl ₃	66
21.2	¹³ C-NMR spectrum for compound 27 recorded in CDCl ₃	67
21.3	DEPT135 spectrum for compound 27 recorded in CDCl ₃	68
22.	NMR data for compound 28.....	69
22.1	¹ H-NMR spectrum for compound 28 recorded in CDCl ₃	69
22.2	¹³ C-NMR spectrum for compound 28 recorded in CDCl ₃	70
22.3	DEPT135 spectrum for compound 28 recorded in CDCl ₃	71
23.	NMR data for compound 29.....	72
23.1	¹ H-NMR spectrum for compound 29 recorded in CDCl ₃	72
23.2	¹³ C-NMR spectrum for compound 29 recorded in CDCl ₃	73
23.3	DEPT135 spectrum for compound 29 recorded in CDCl ₃	74
24.	NMR data for compound 30.....	75
24.1	¹ H-NMR spectrum for compound 30 recorded in CDCl ₃	75
24.2	¹³ C-NMR spectrum for compound 30 recorded in CDCl ₃	76
24.3	DEPT135 spectrum for compound 30 recorded in CDCl ₃	77
25.1	¹ H-NMR spectrum for compound 31 recorded in CDCl ₃	78
25.2	¹³ C-NMR spectrum for compound 31 recorded in CDCl ₃	79
25.3	DEPT135 spectrum for compound 31 recorded in CDCl ₃	80
26.	Dose-response curves of the antiproliferative effect of selected compounds (AA 1, 9, 14, 15, 24 and cisplatin) on HeLa cell line, after 72 hours of incubation	81

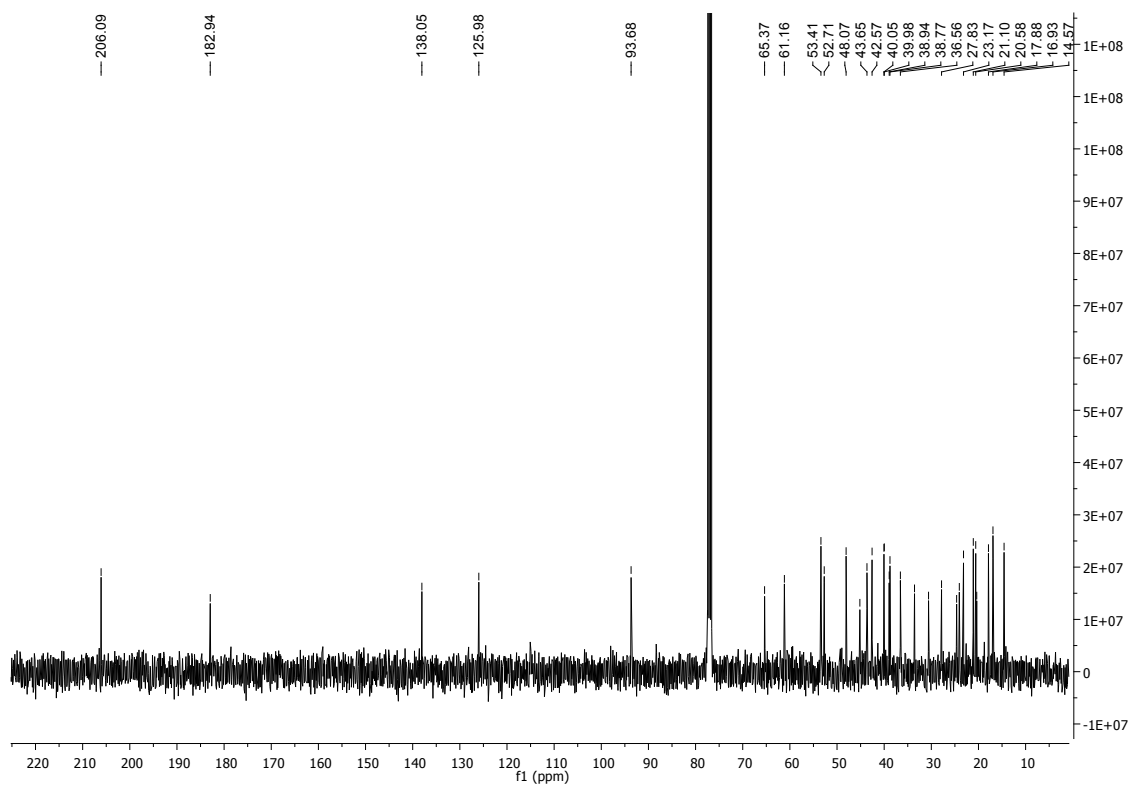
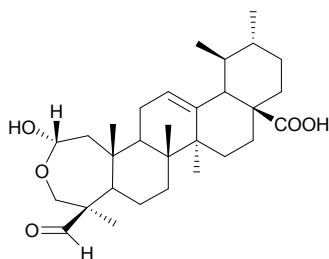
26.1 Dose-response curve of AA (1).....	81
26.2 Dose-response curve of compound 9	81
26.3 Dose-response curve of compound 14	82
26.4 Dose-response curve of compound 15	82
26.5 Dose-response curve of compound 24	83
26.6 Dose-response curve of Cisplatin	83

1 NMR data for compound 4:

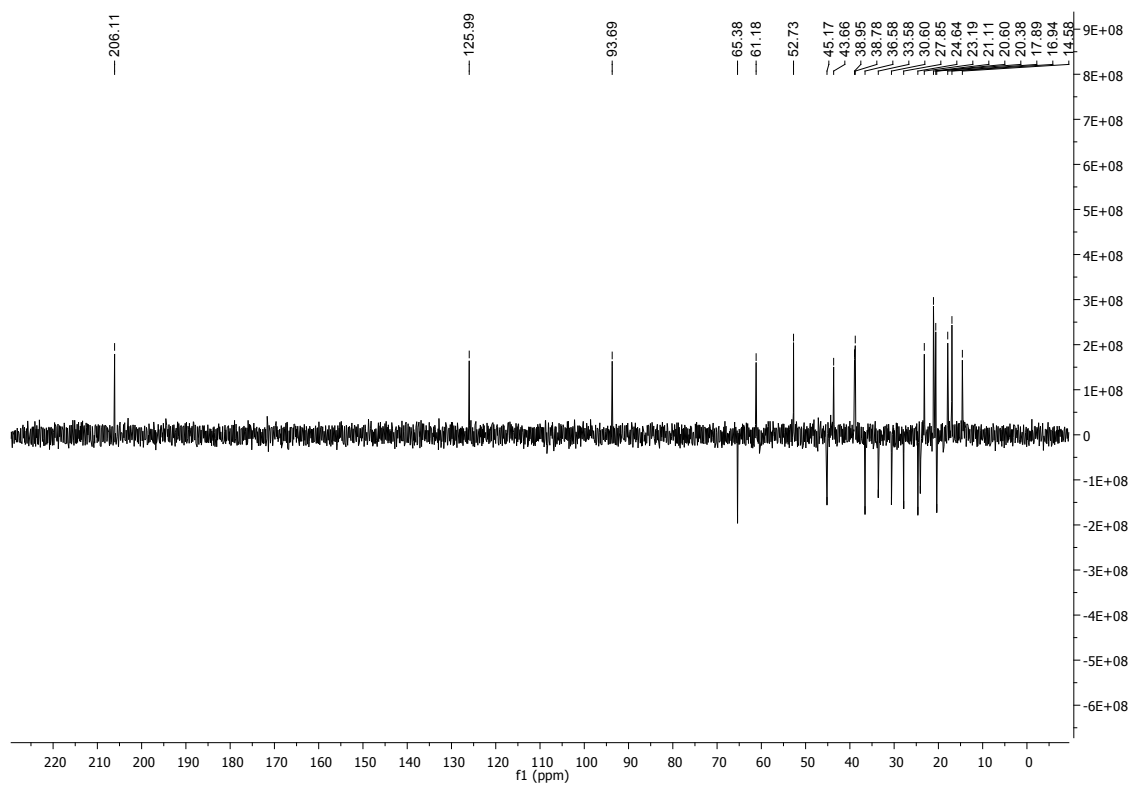
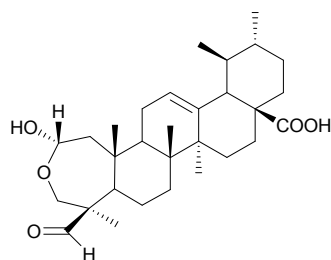
1.1 ¹H-NMR spectrum for compound 4 recorded in CDCl₃



1.2 ^{13}C -NMR spectrum for compound 4 recorded in CDCl_3

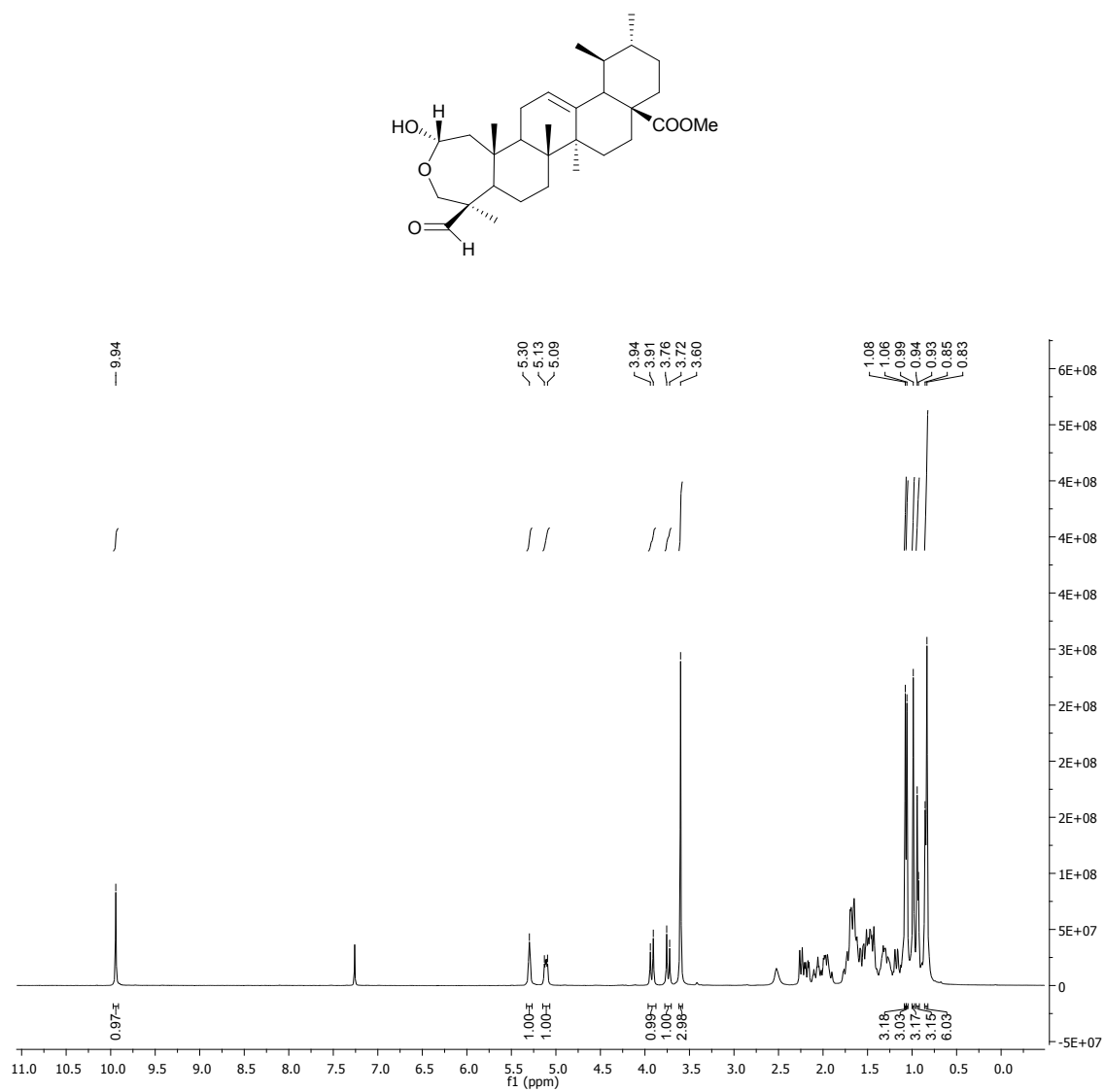


1.3 DEPT135 spectrum for compound 4 recorded in CDCl₃

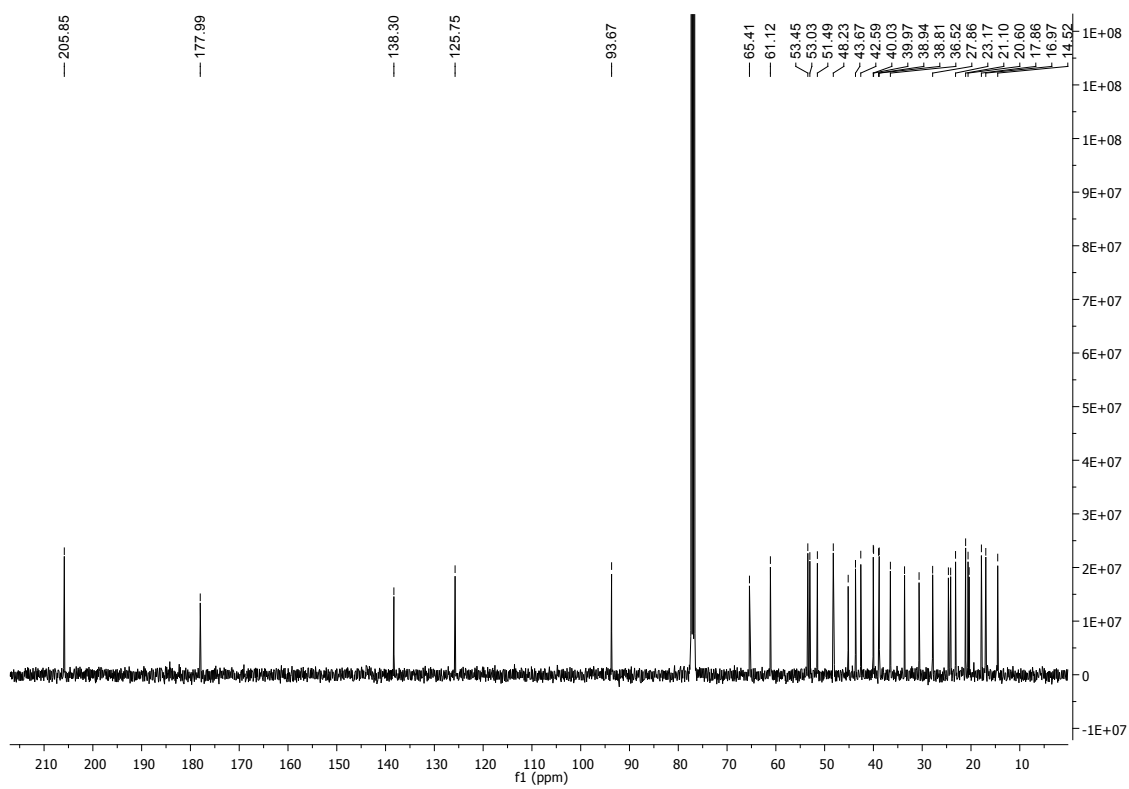
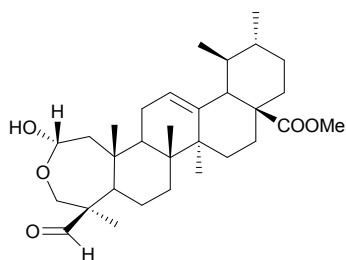


2. NMR data for compound 5

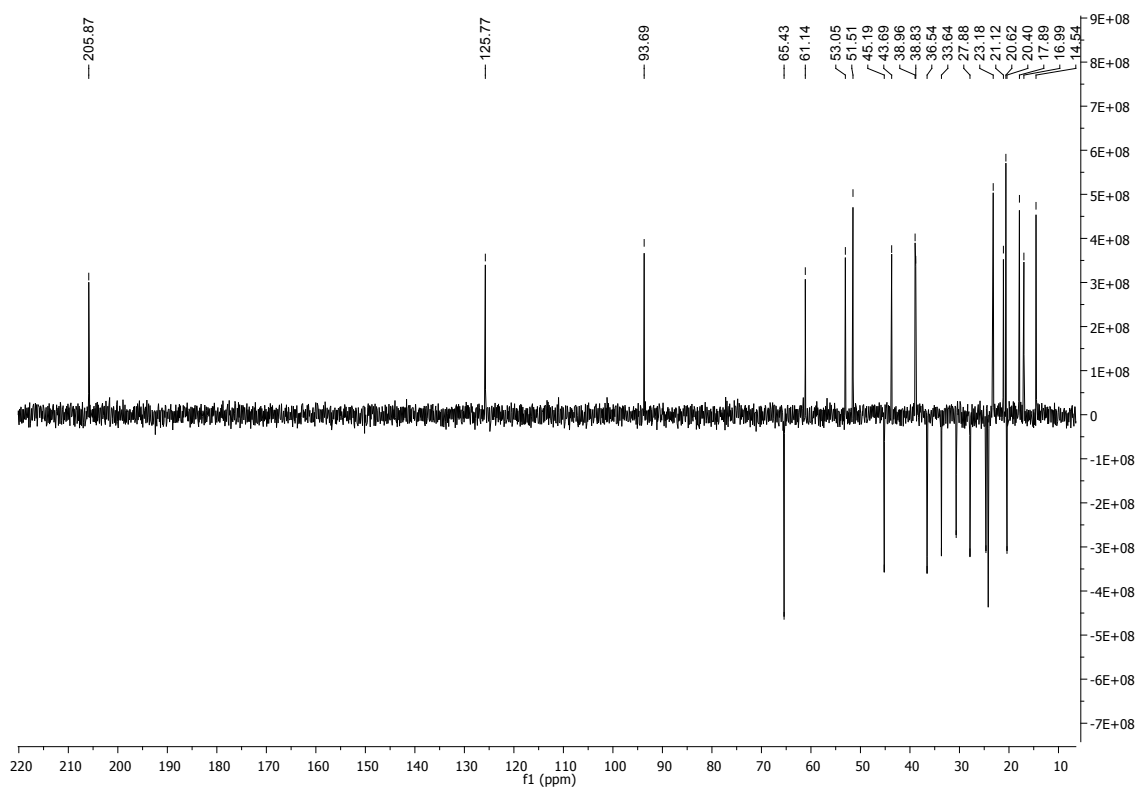
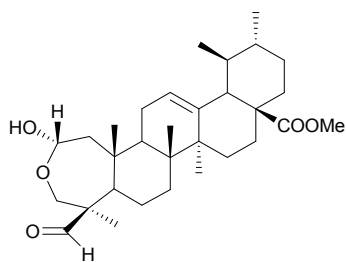
2.1 ¹H-NMR spectrum for compound 5 recorded in CDCl₃



2.2 ^{13}C -NMR spectrum for compound 5 recorded in CDCl_3

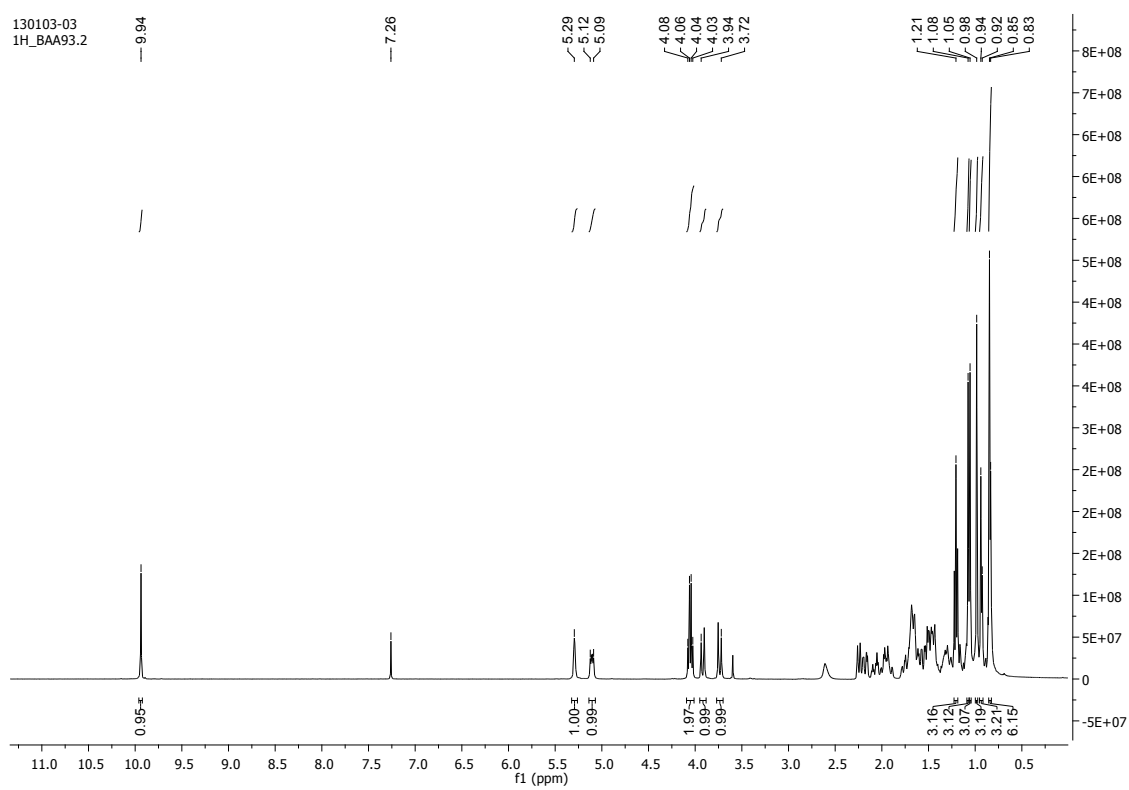
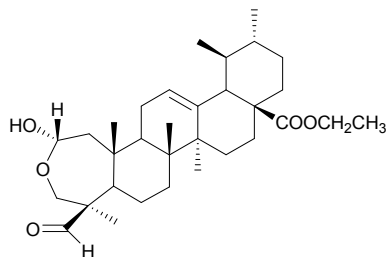


2.3 DEPT135 spectrum for compound 5 recorded in CDCl₃

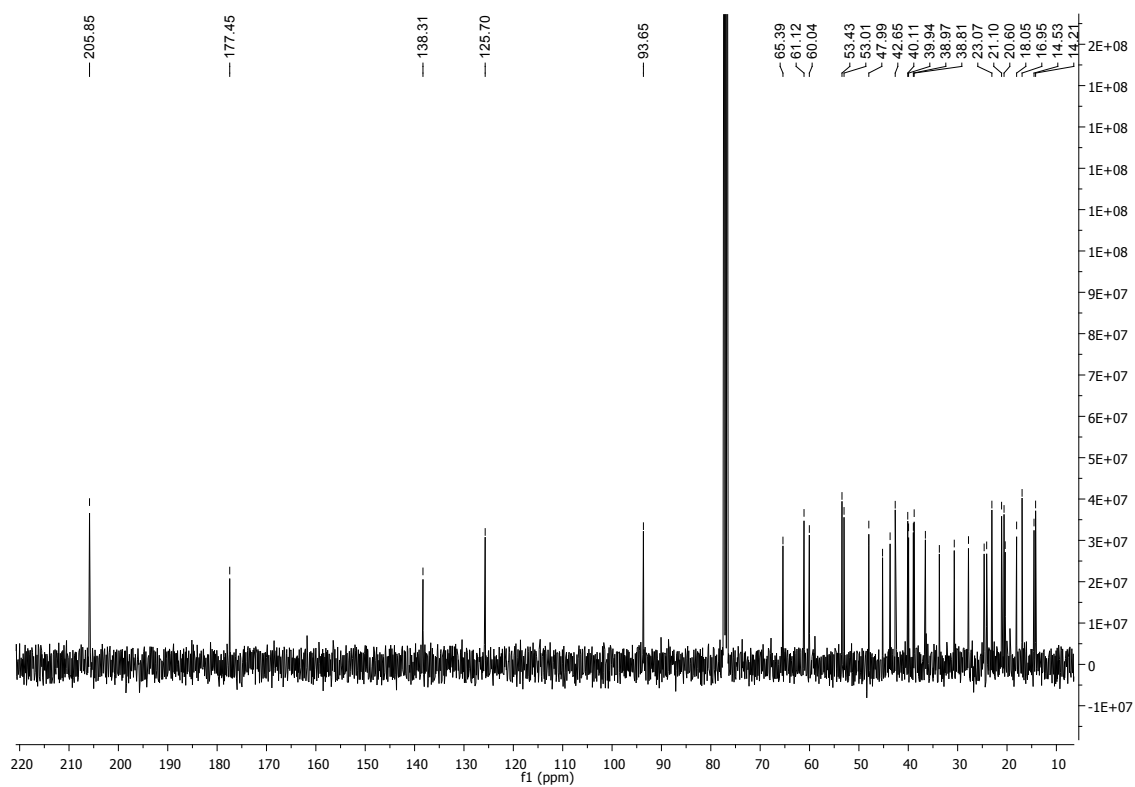
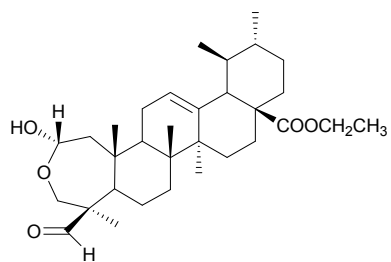


3. NMR data for compound 6

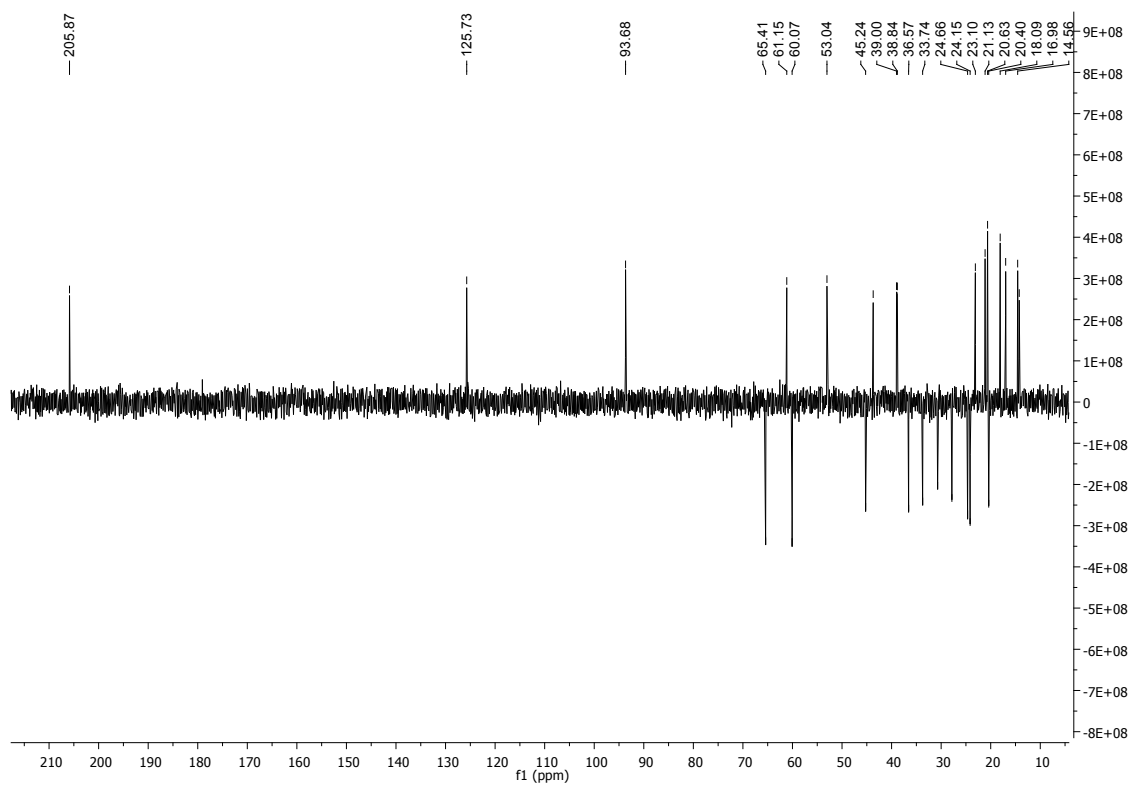
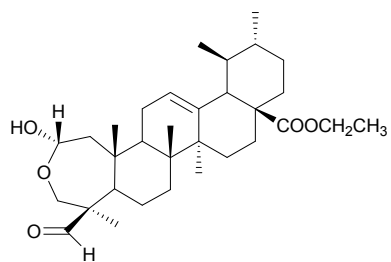
3.1 ¹H-NMR spectrum for compound 6 recorded in CDCl₃



3.2 ^{13}C -NMR spectrum for compound 6 recorded in CDCl_3

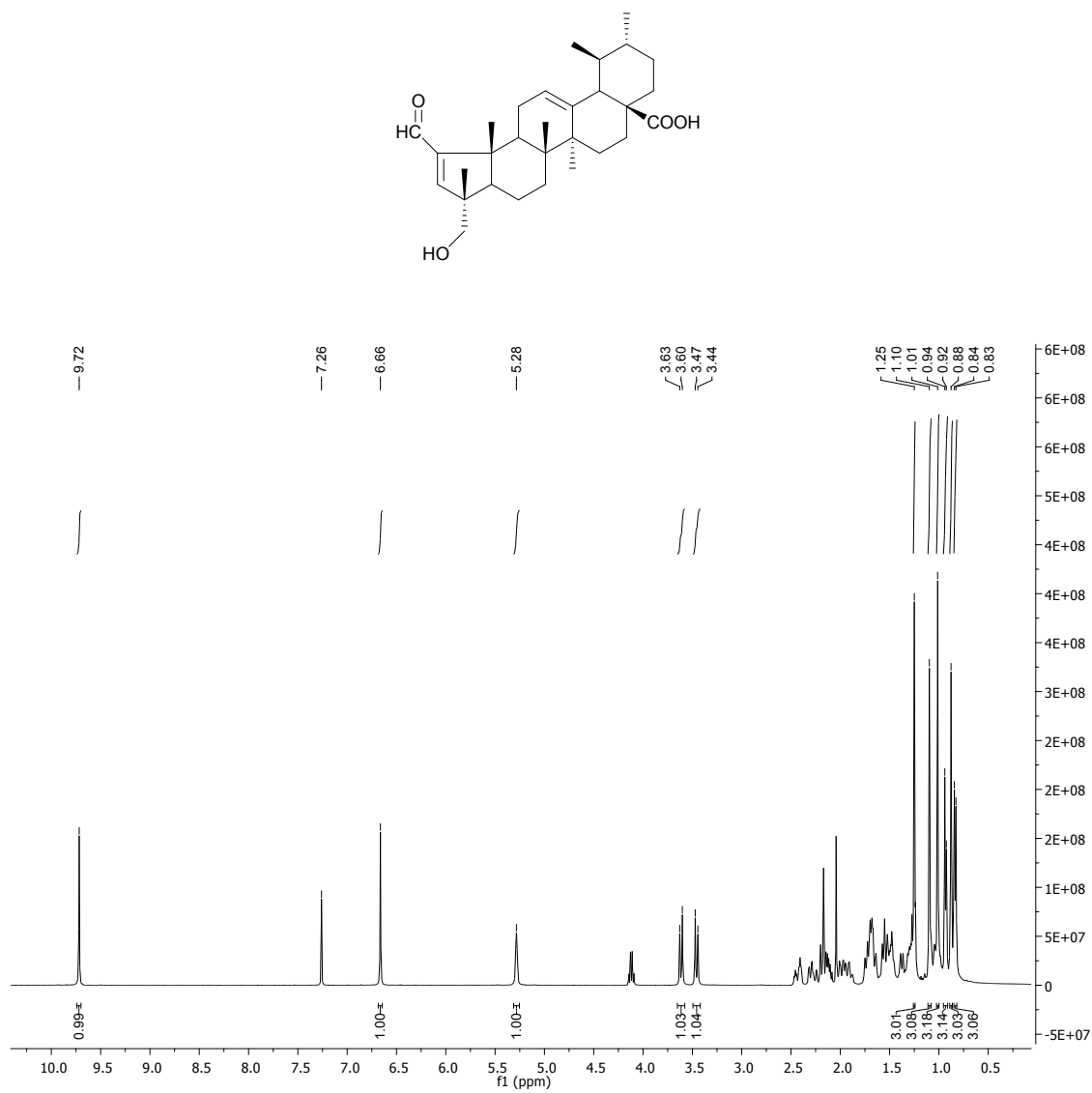


3.3 DEPT135 spectrum for compound 6 recorded in CDCl₃

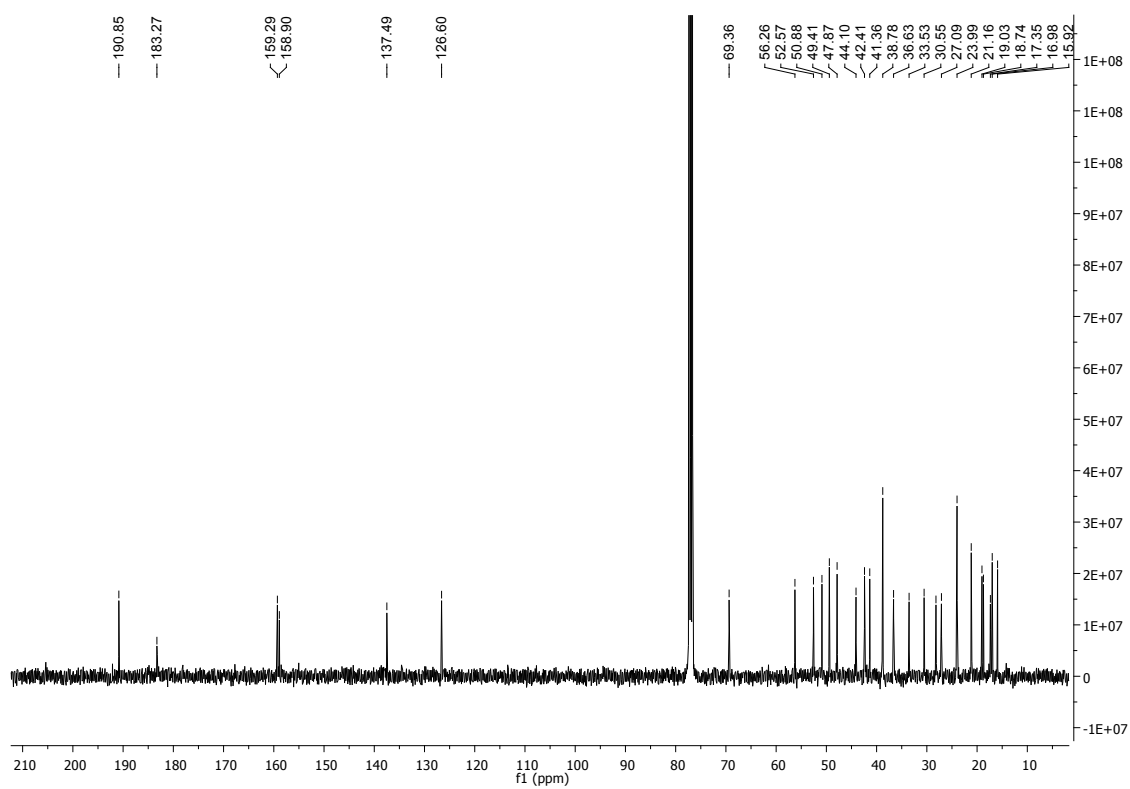
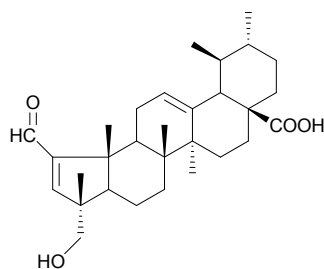


4. NMR data for compound 7

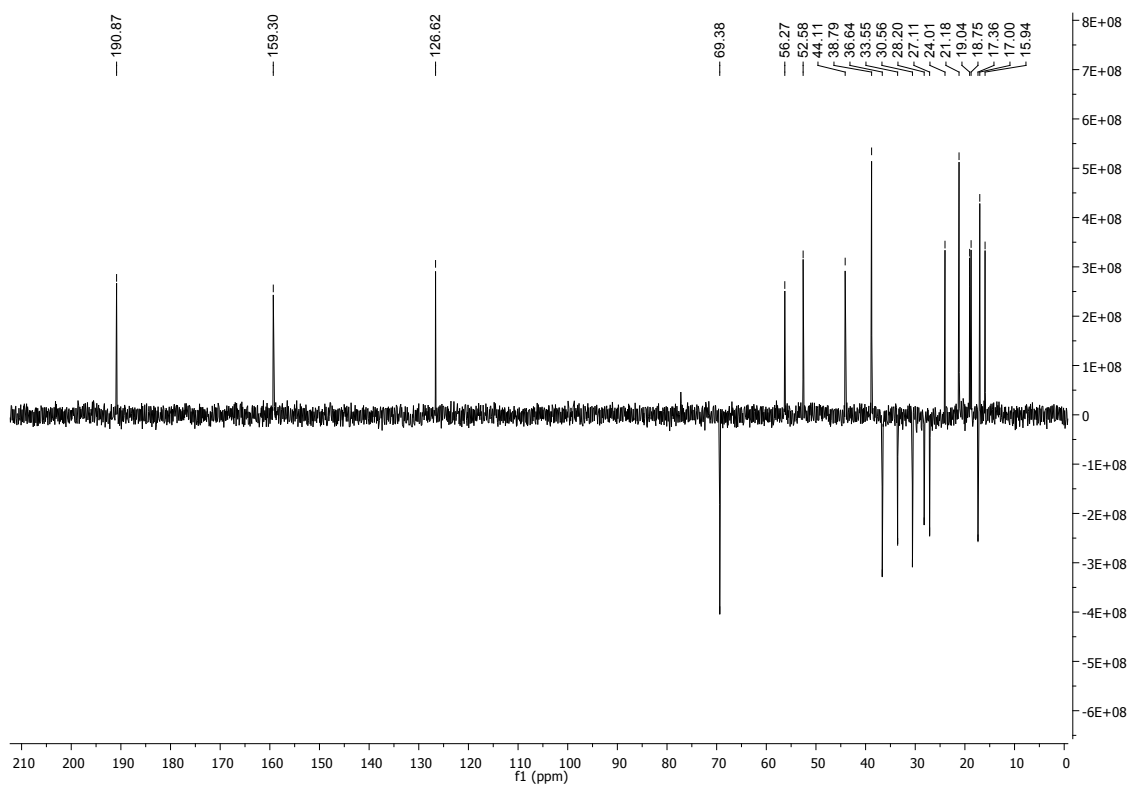
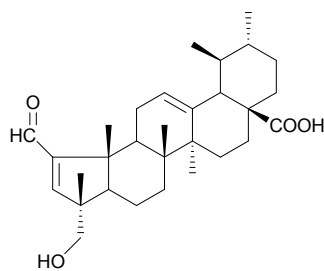
4.1 ¹H-NMR spectrum for compound 7 recorded in CDCl₃



4.2 ^{13}C -NMR spectrum for compound 7 recorded in CDCl_3

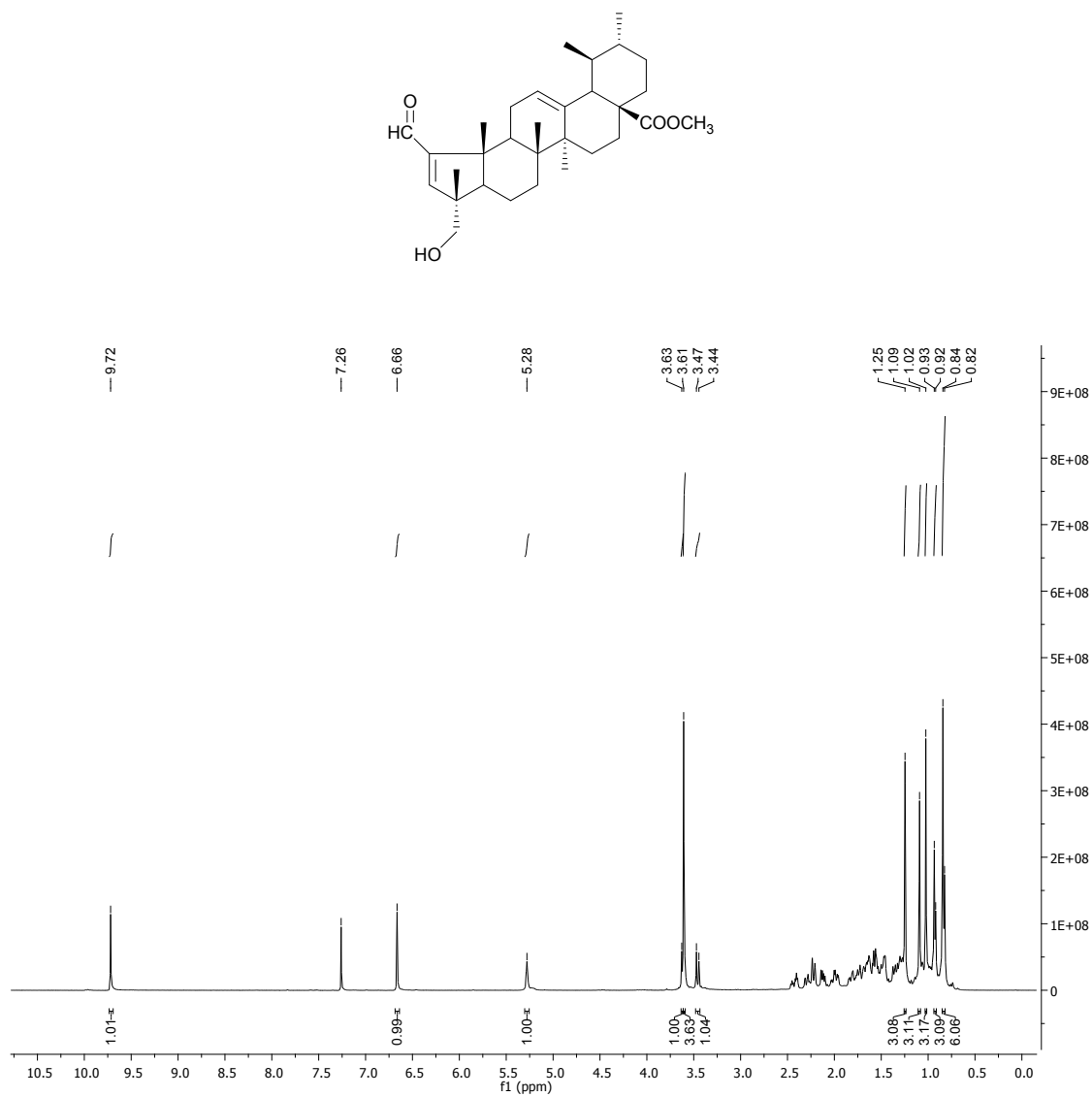


4.3 DEPT135 spectrum for compound 7 recorded in CDCl₃

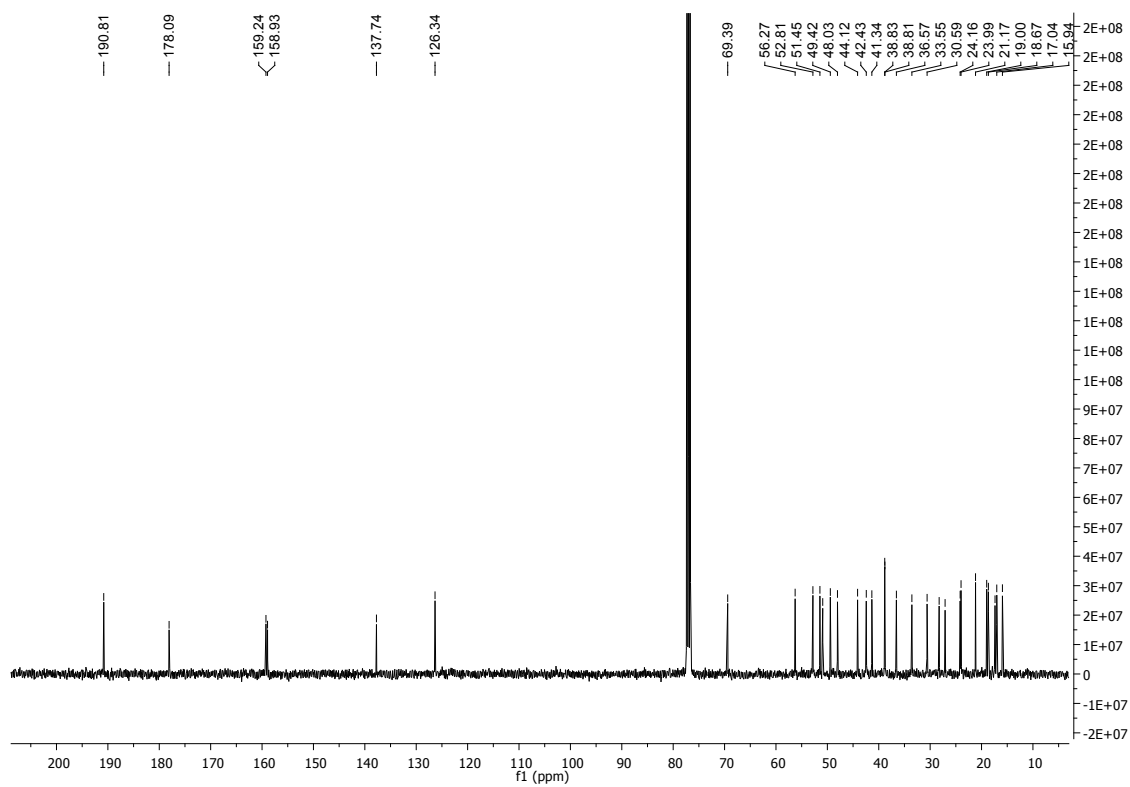
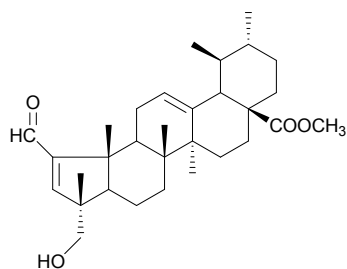


5. NMR data for compound 8

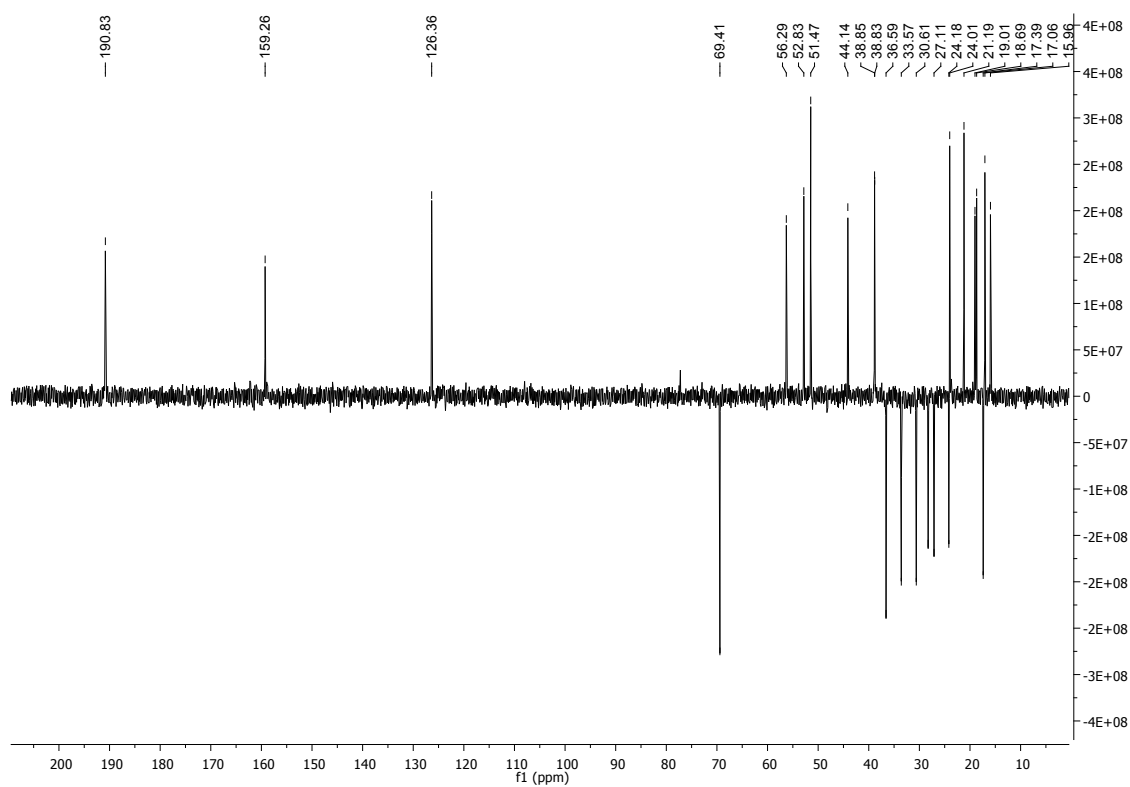
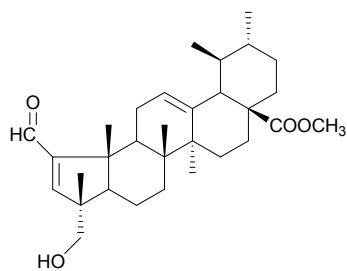
5.1 ¹H-NMR spectrum for compound 8 recorded in CDCl₃



5.2 ^{13}C -NMR spectrum for compound 8 recorded in CDCl_3

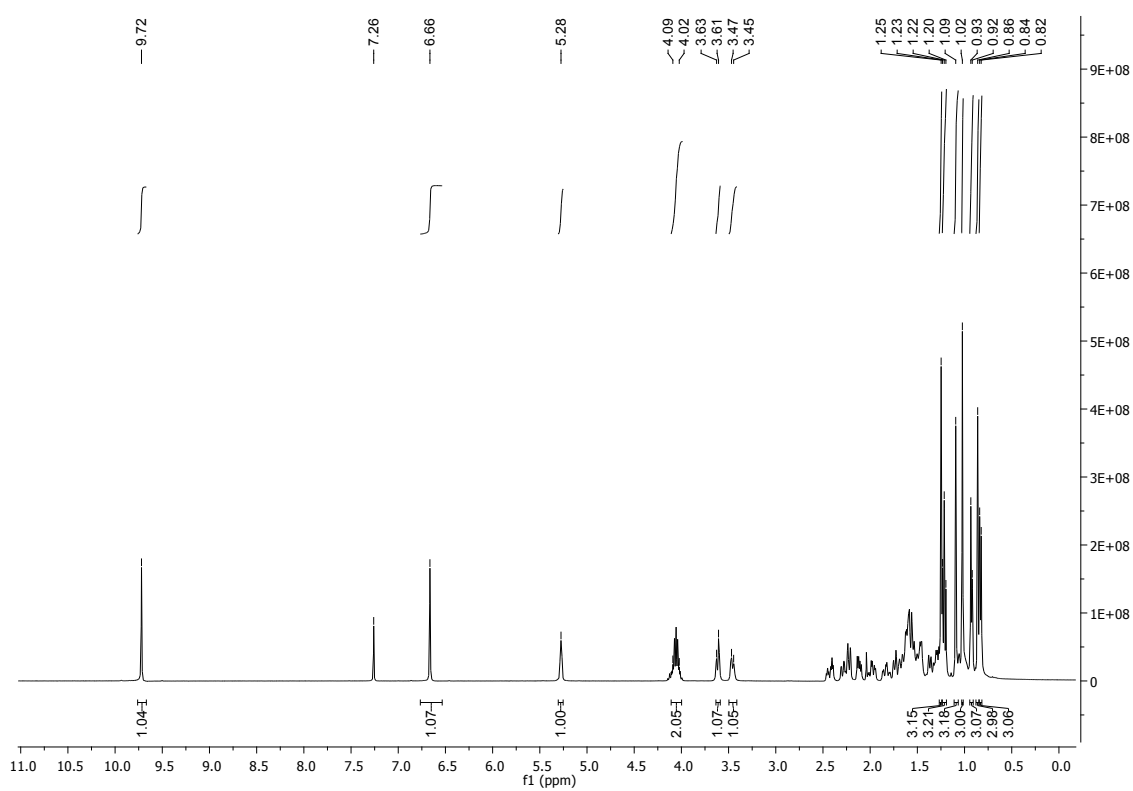
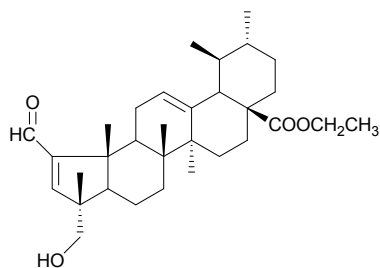


5.3 DEPT135 spectrum for compound 8 recorded in CDCl₃

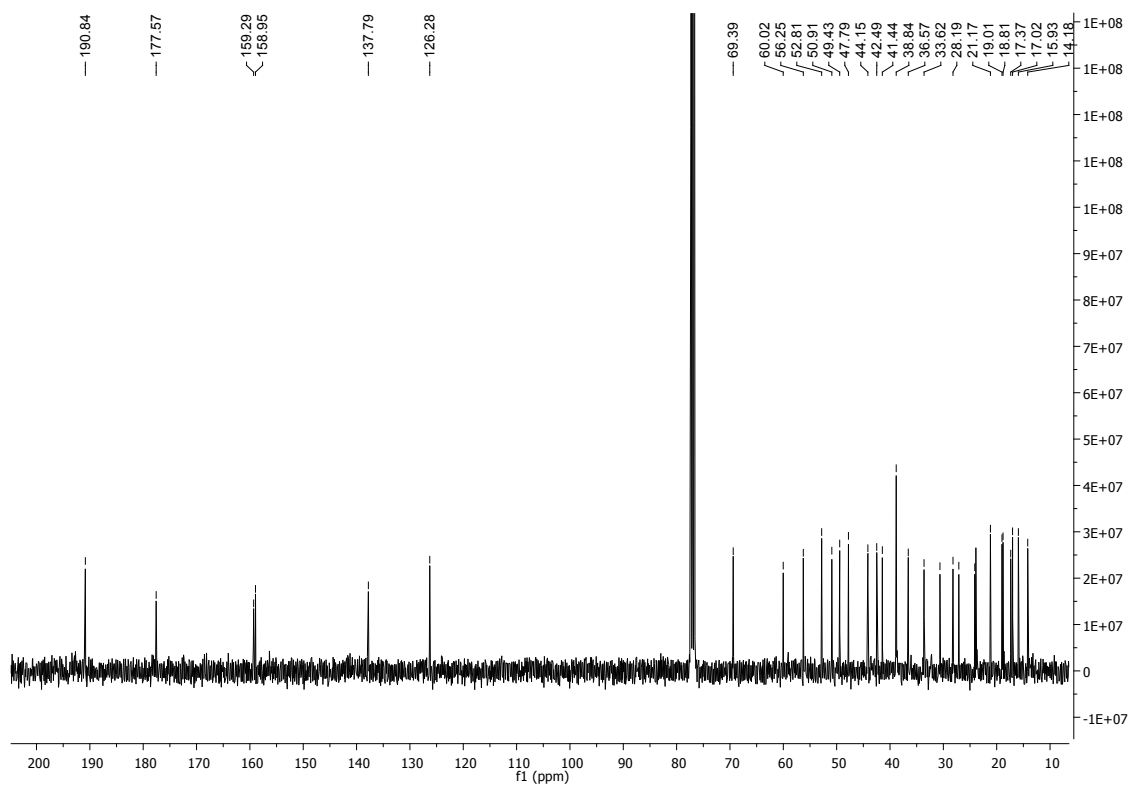
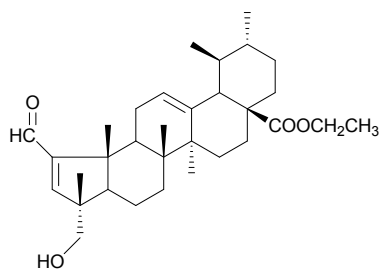


6. NMR data for compound 9

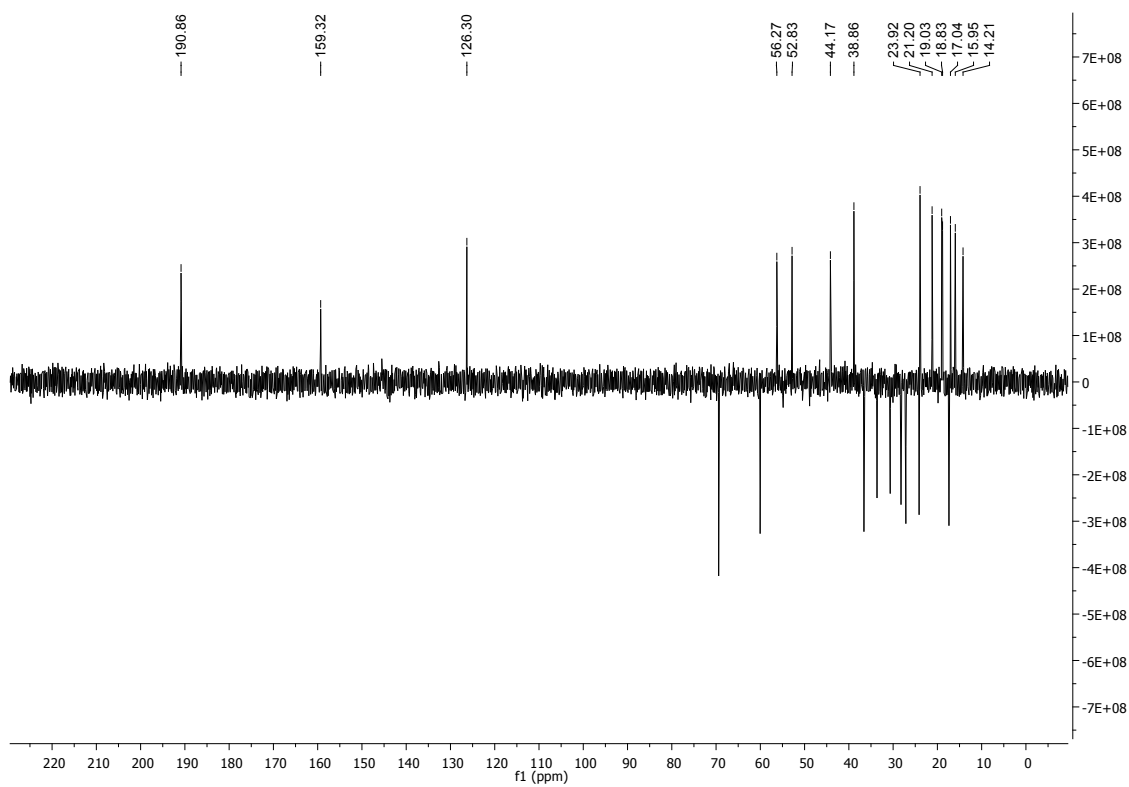
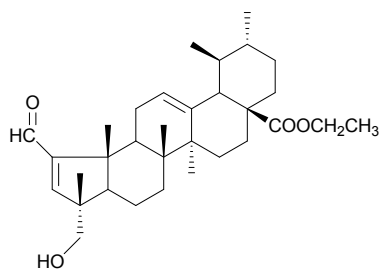
6.1 ¹H-NMR spectrum for compound 9 recorded in CDCl₃



6.2 ^{13}C -NMR spectrum for compound 9 recorded in CDCl_3

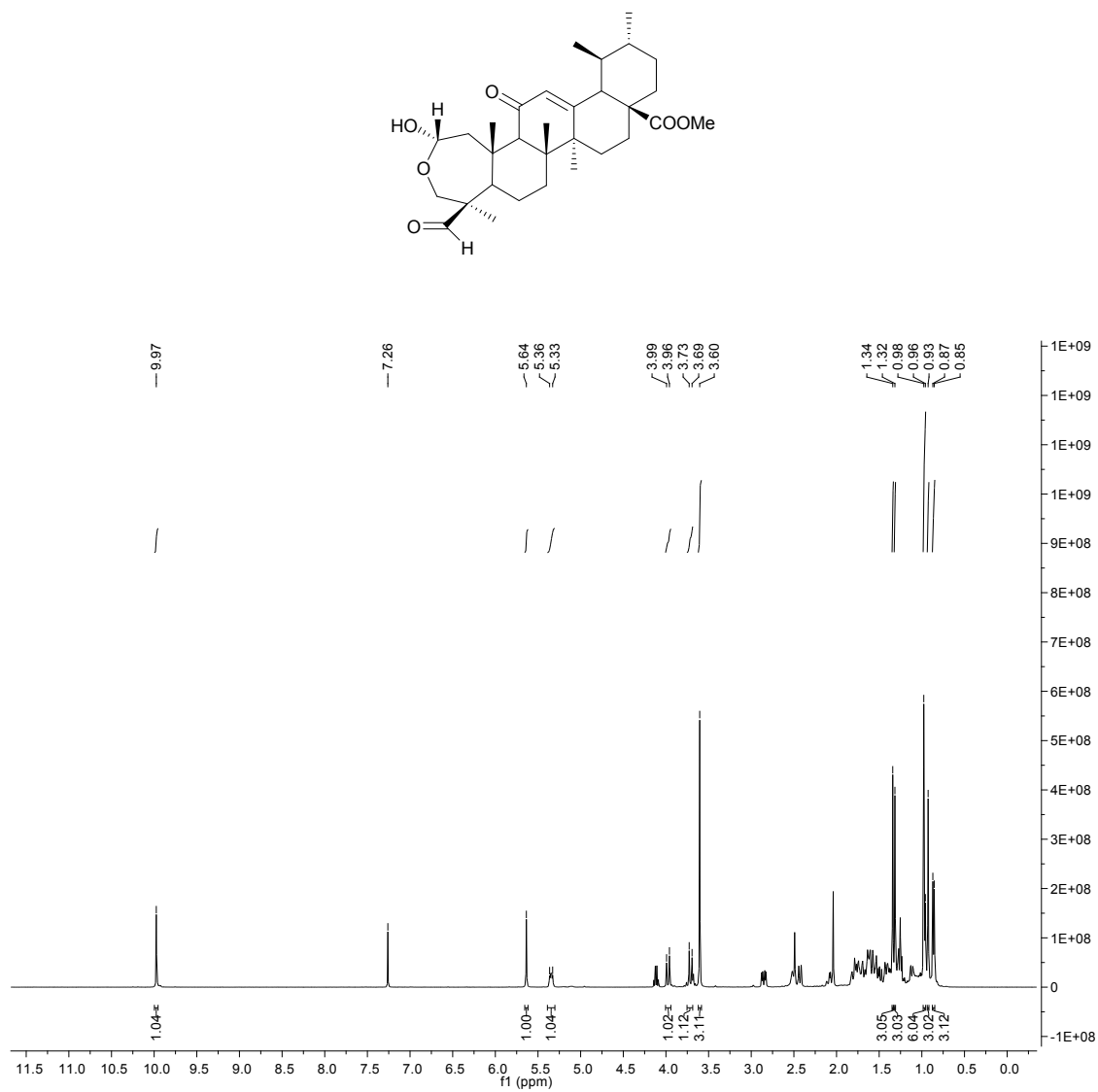


6.3 DEPT135 spectrum for compound 9 recorded in $CDCl_3$

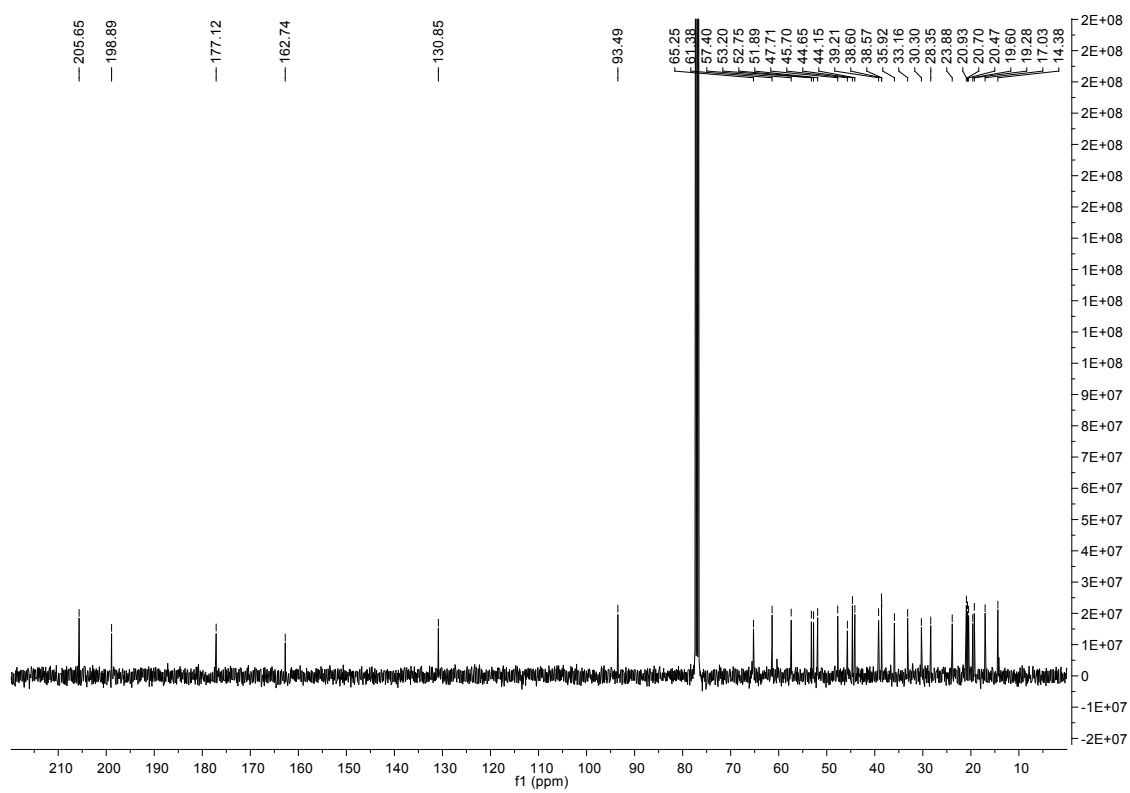
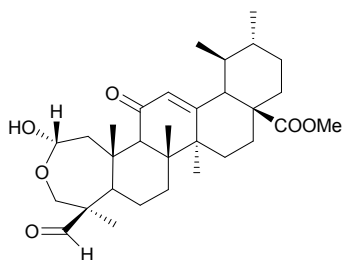


7. NMR data for compound 13

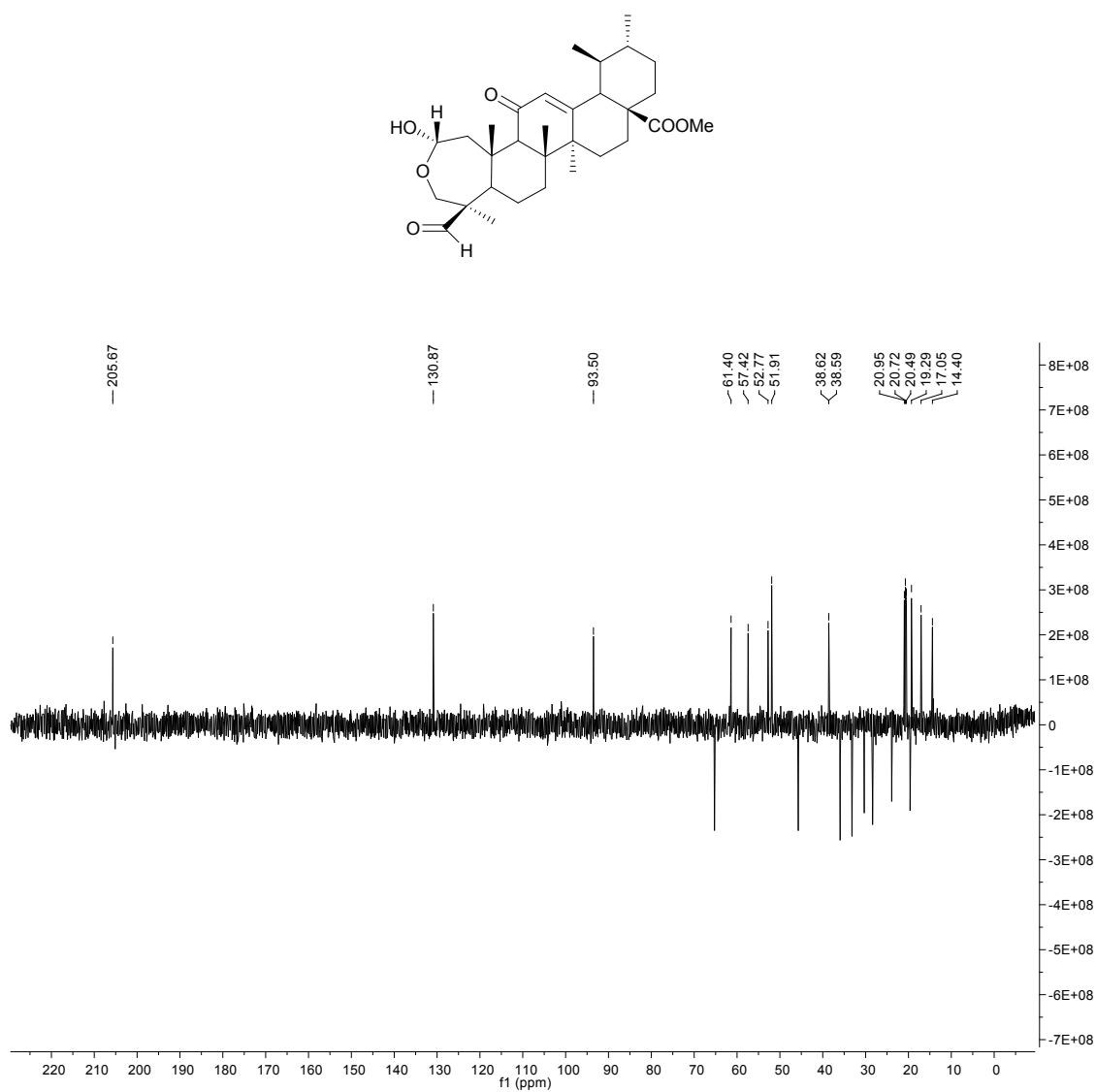
7.1 $^1\text{H-NMR}$ spectrum for compound 13 recorded in CDCl_3



7.2 ^{13}C -NMR spectrum for compound 13 recorded in CDCl_3

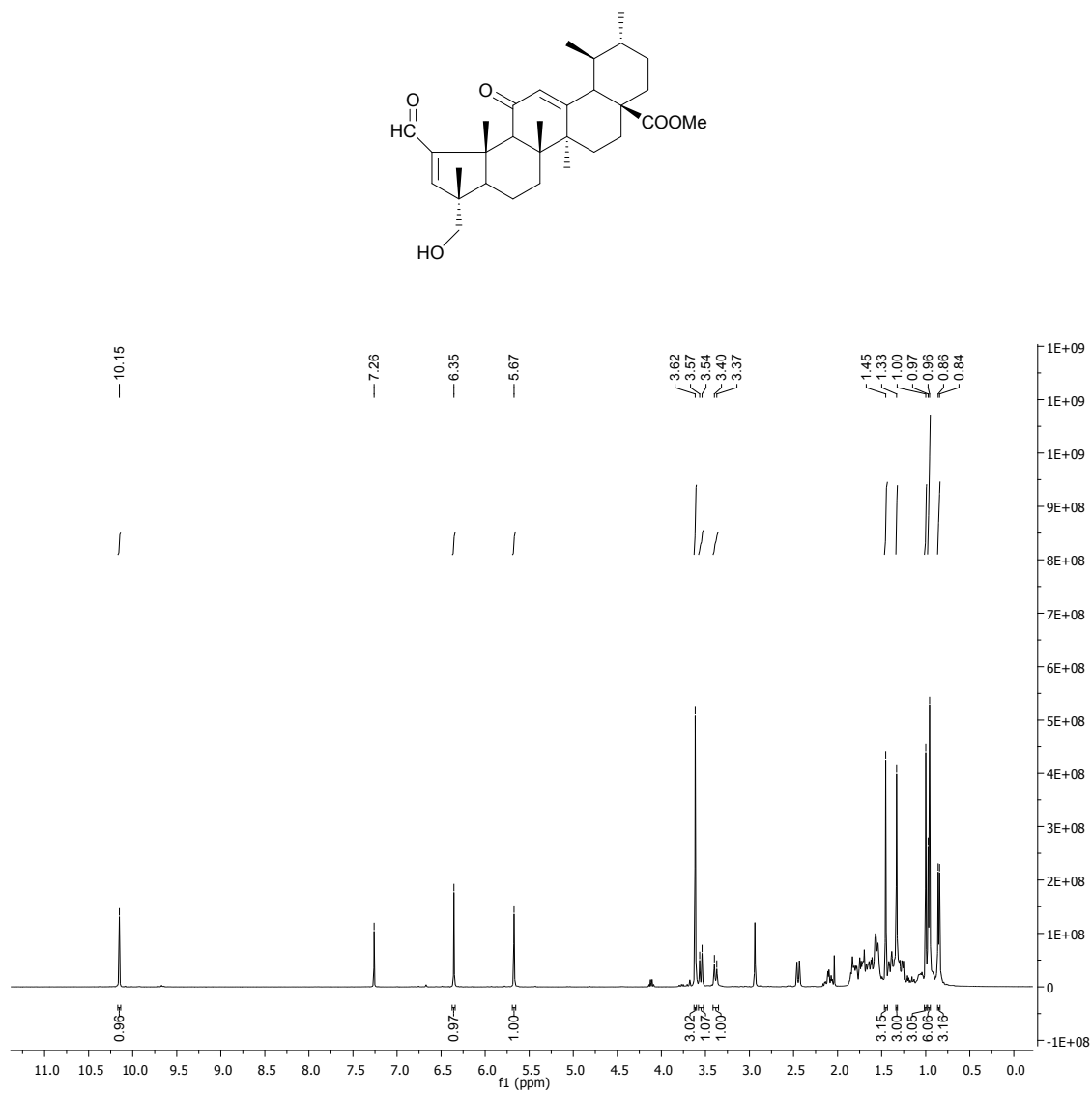


7.3 DEPT135 spectrum for compound 13 recorded in CDCl₃

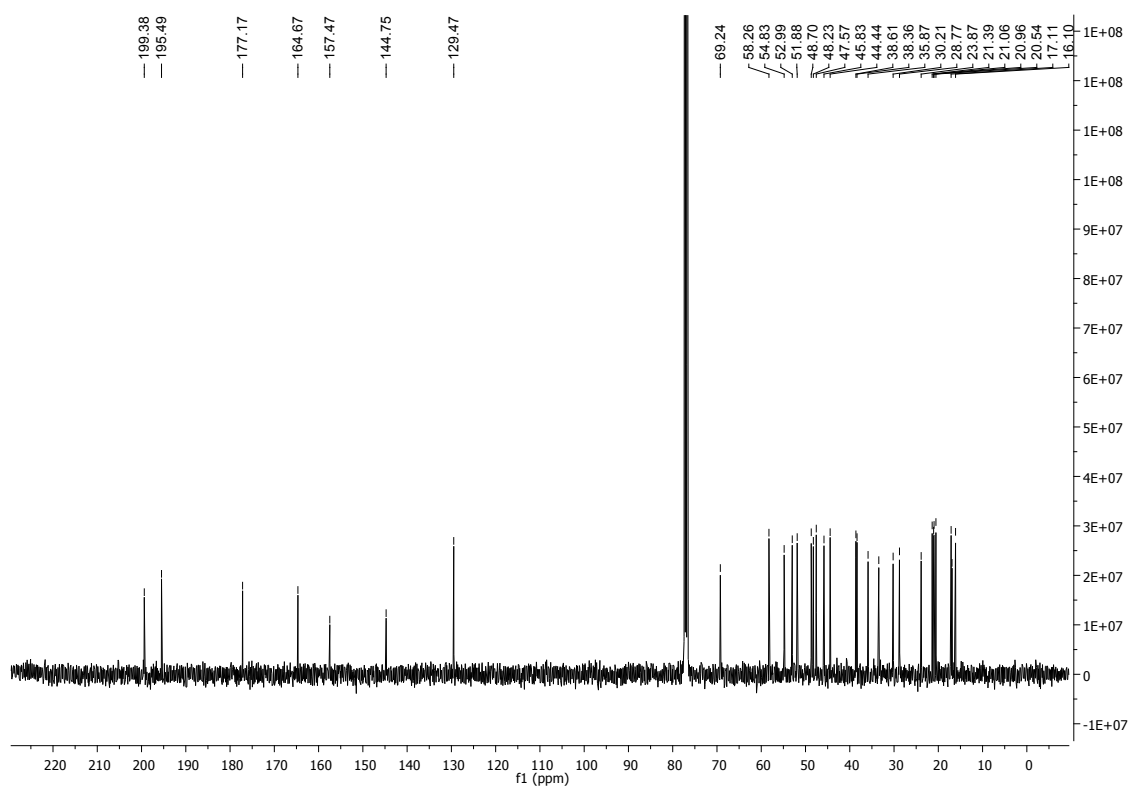
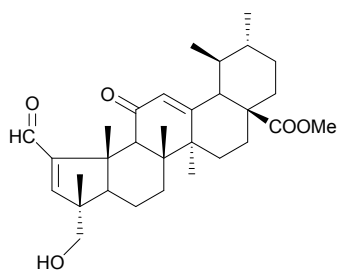


8. NMR data for compound 14

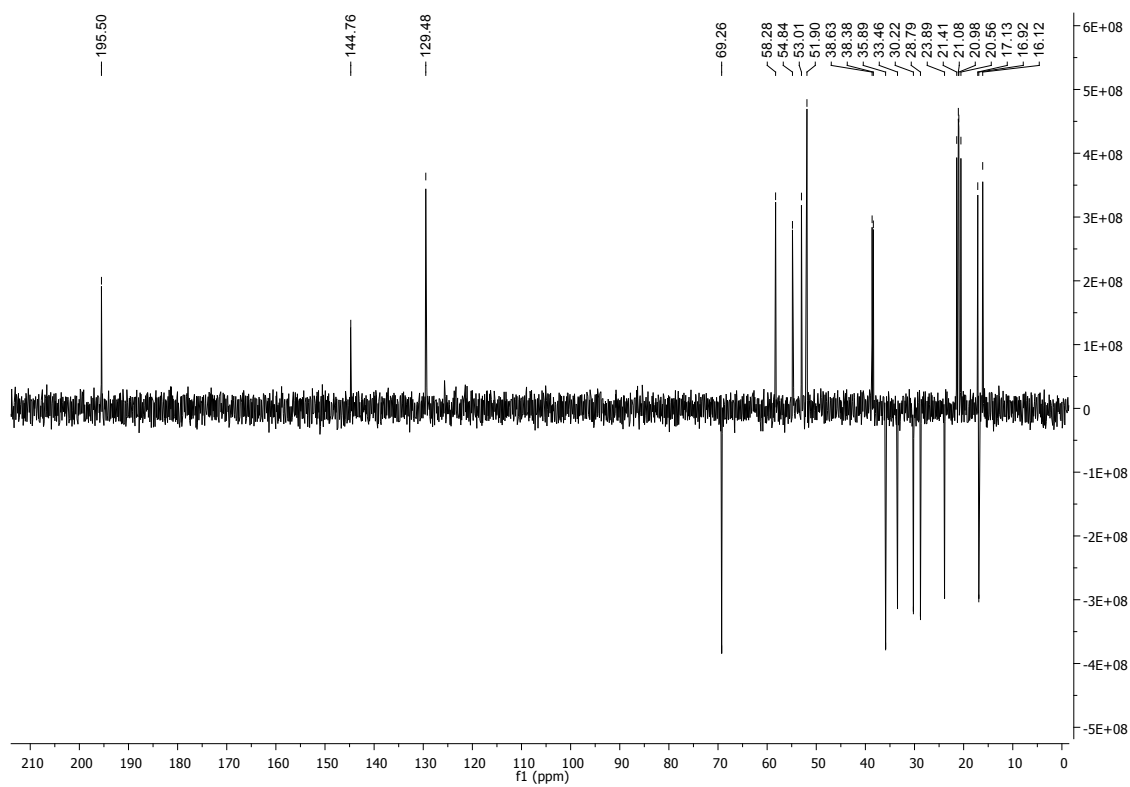
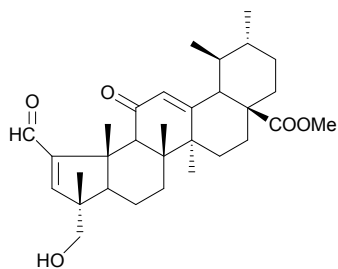
8.1 $^1\text{H-NMR}$ spectrum for compound 14 recorded in CDCl_3



8.2 ^{13}C -NMR spectrum for compound 14 recorded in CDCl_3

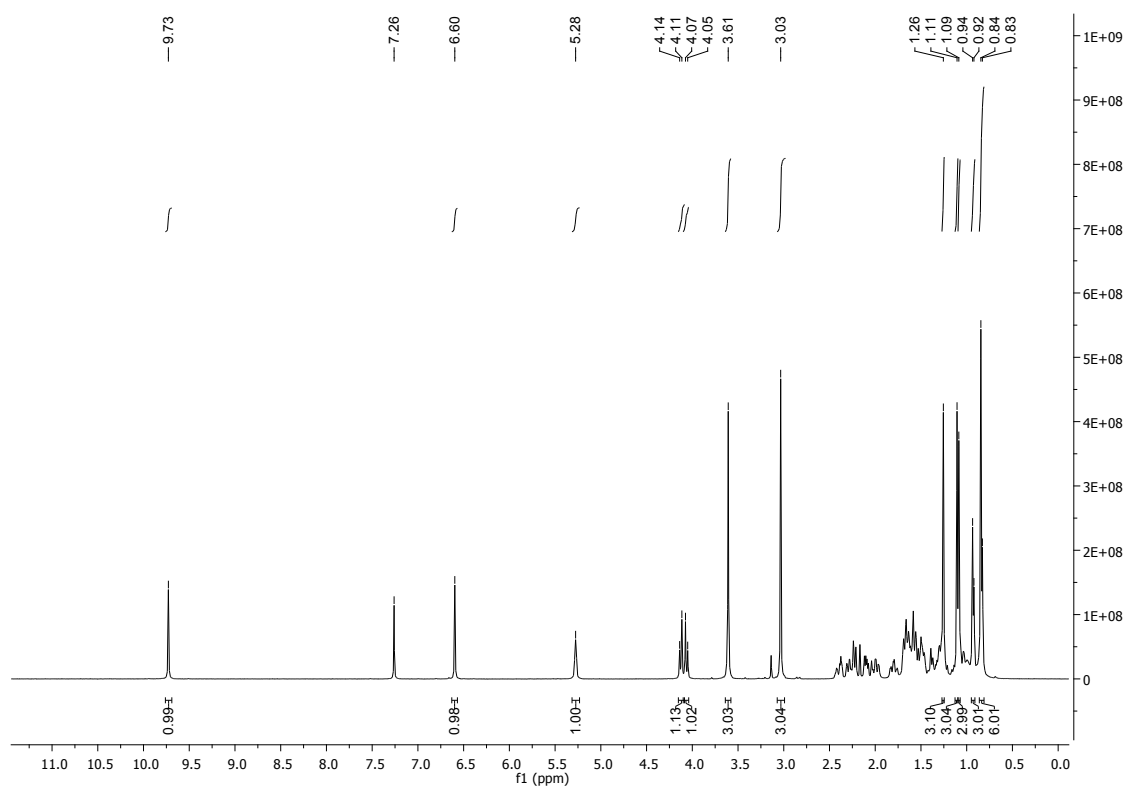
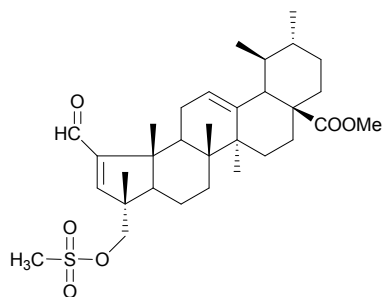


8.3 DEPT135 spectrum for compound 14 recorded in CDCl₃

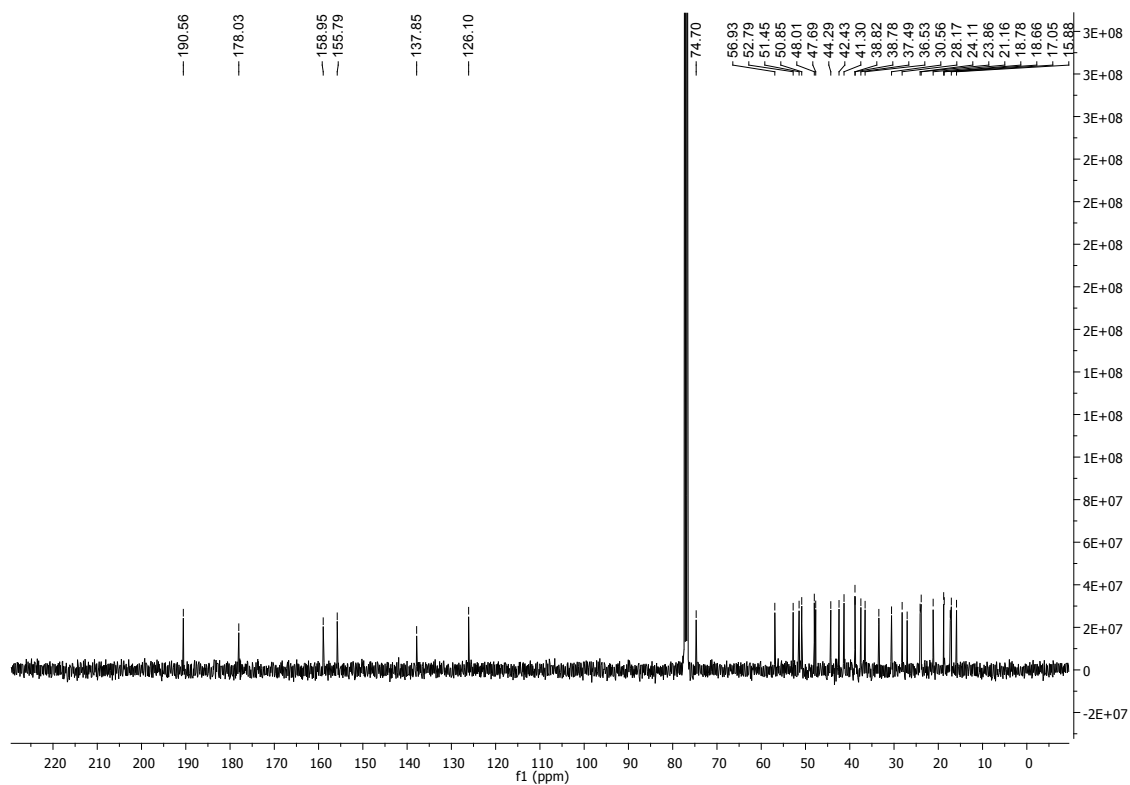
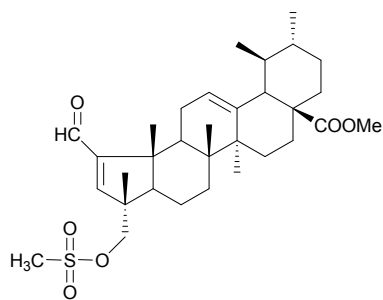


9. NMR data for compound 15

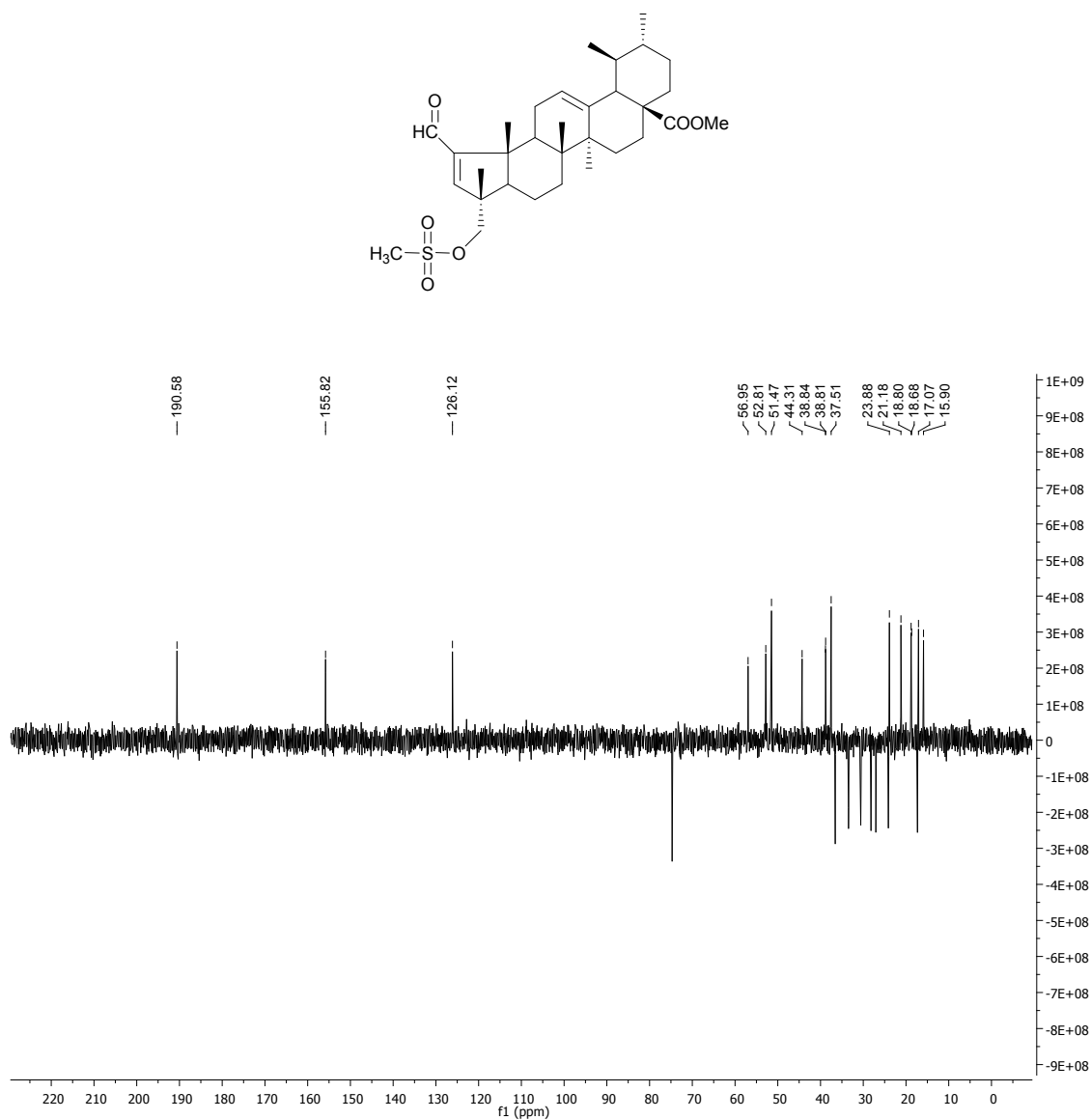
9.1 $^1\text{H-NMR}$ spectrum for compound 15 recorded in CDCl_3



9.2 ^{13}C -NMR spectrum for compound 15 recorded in CDCl_3

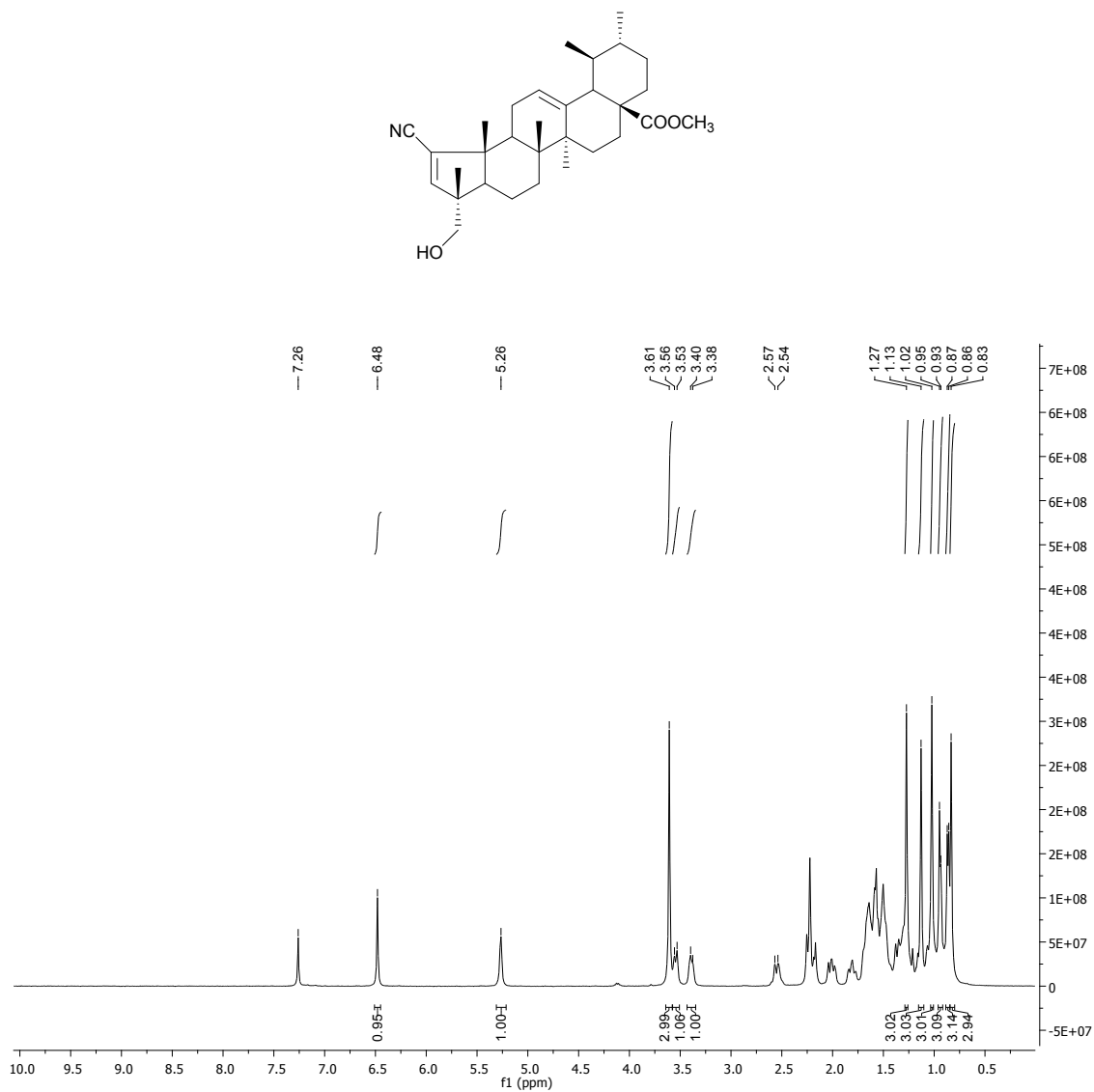


9.3 DEPT135 spectrum for compound 15 recorded in CDCl₃

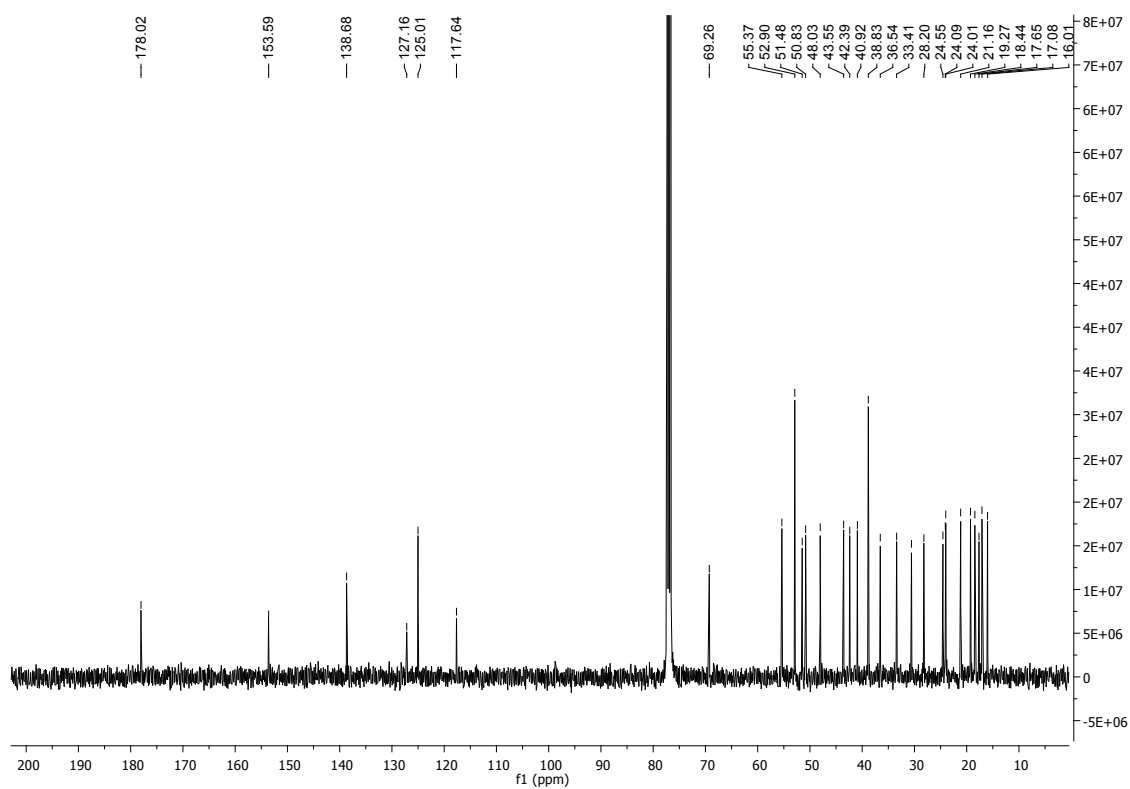
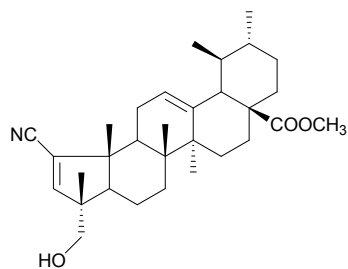


10. NMR data for compound 16

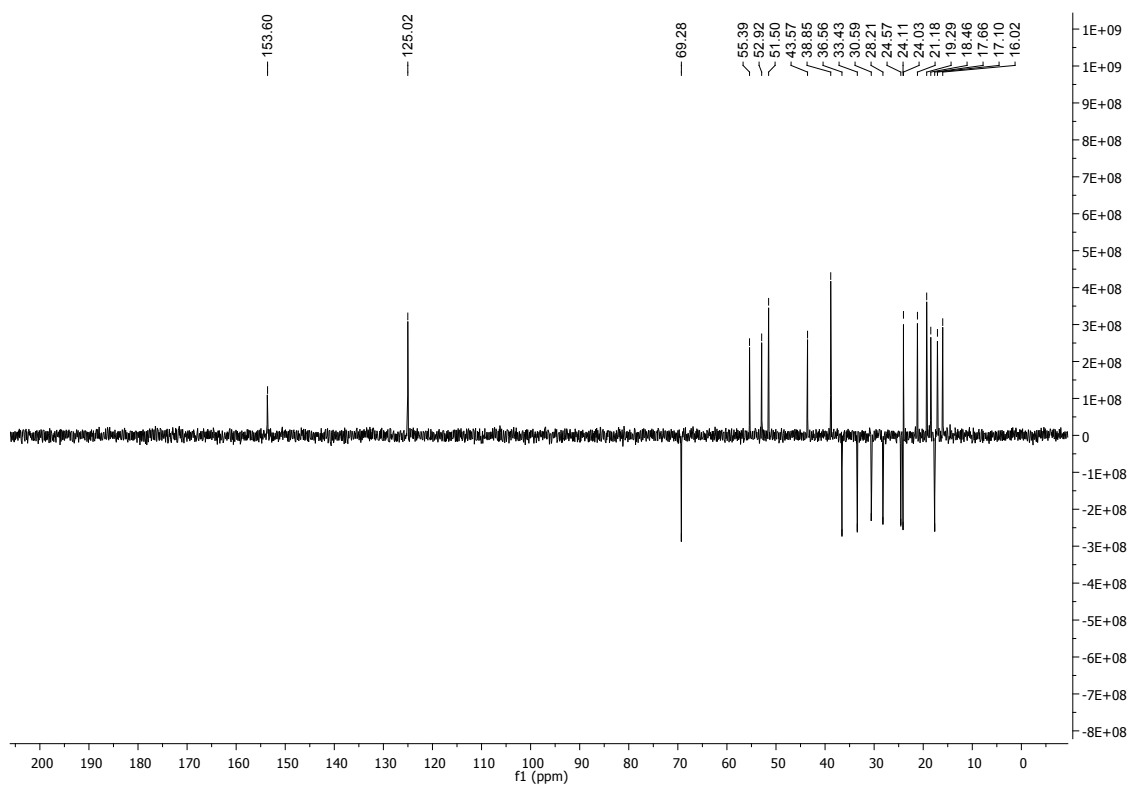
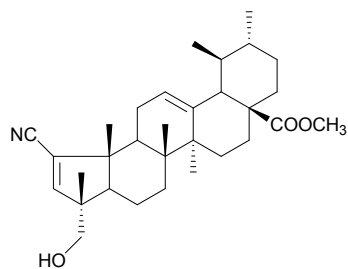
10.1 ¹H-NMR spectrum for compound 16 recorded in CDCl₃



10.2 ^{13}C -NMR spectrum for compound 16 recorded in CDCl_3

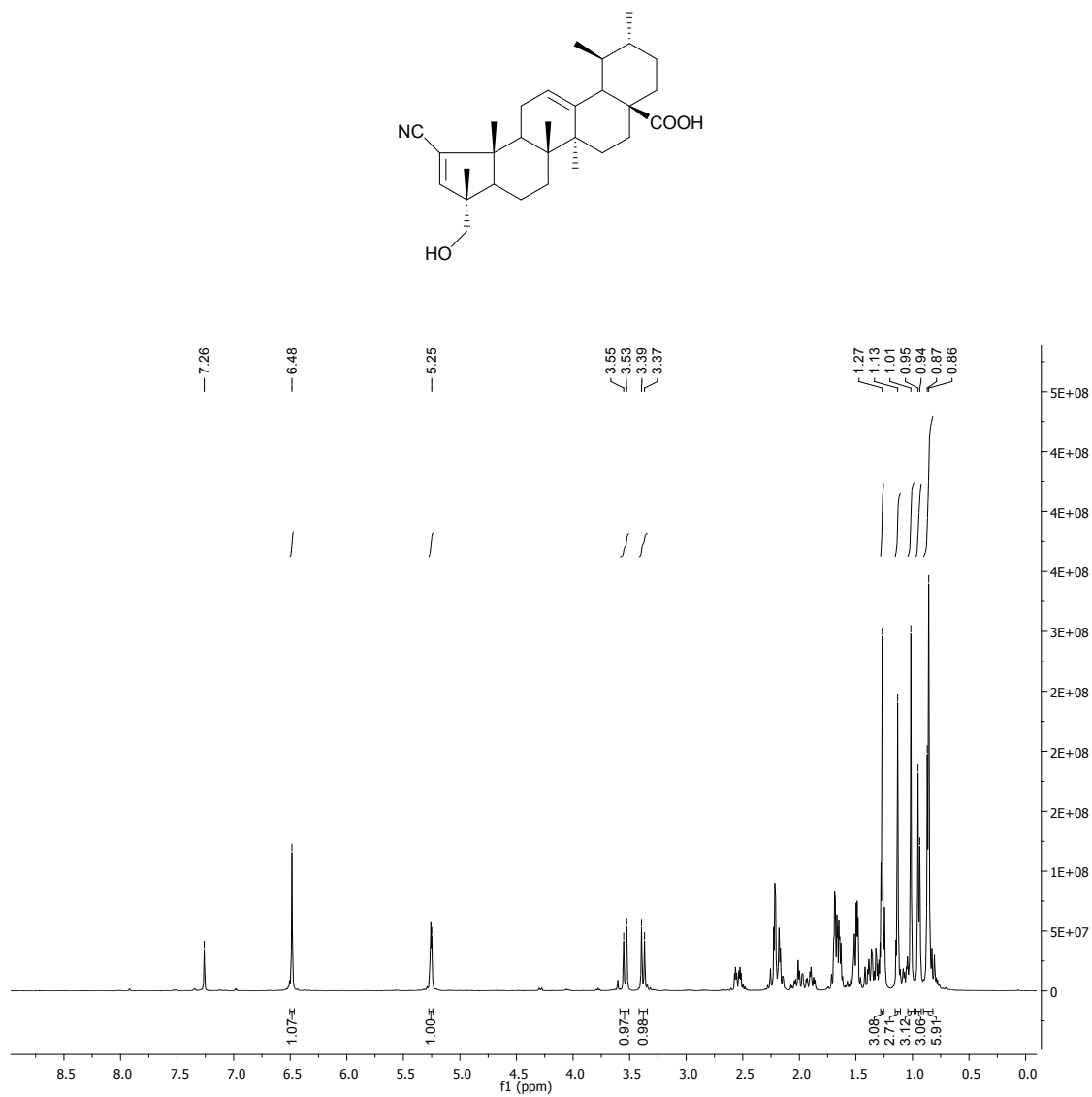


10.3 DEPT135 spectrum for compound 16 recorded in CDCl₃

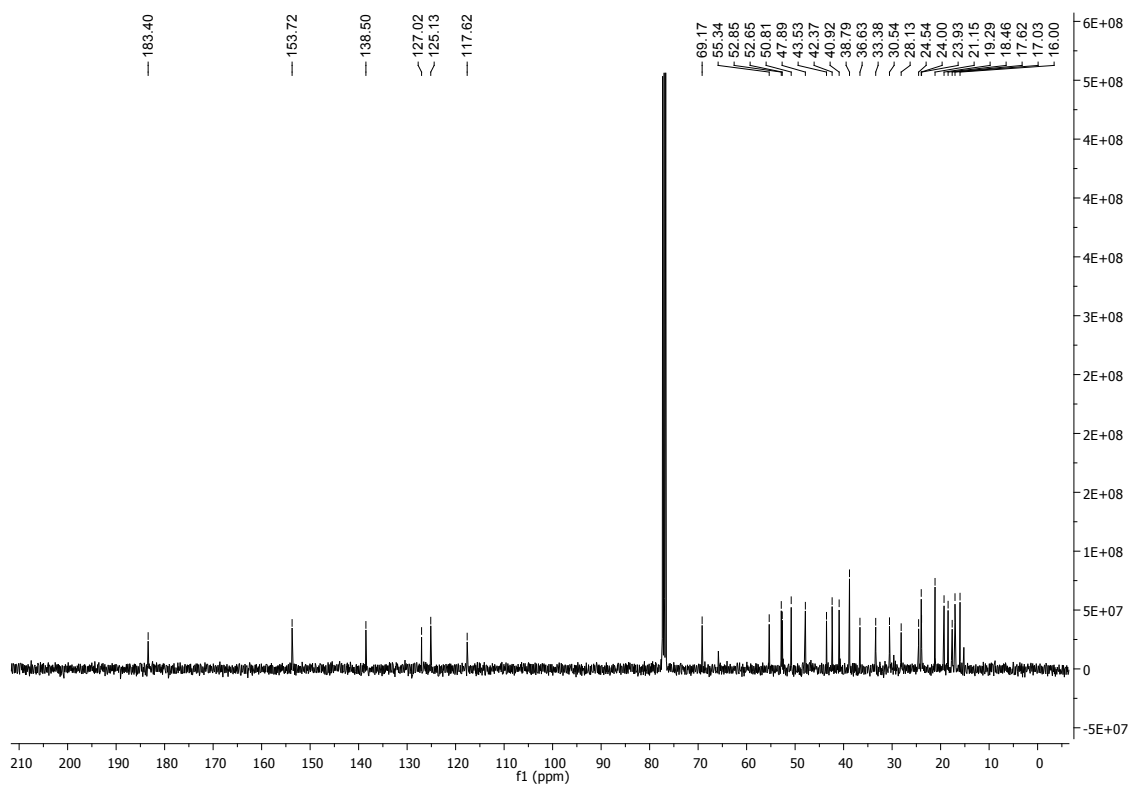
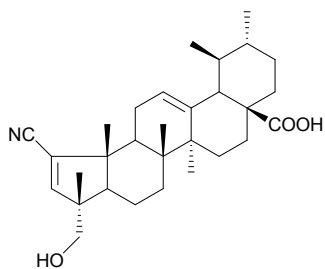


11. NMR data for compound 17

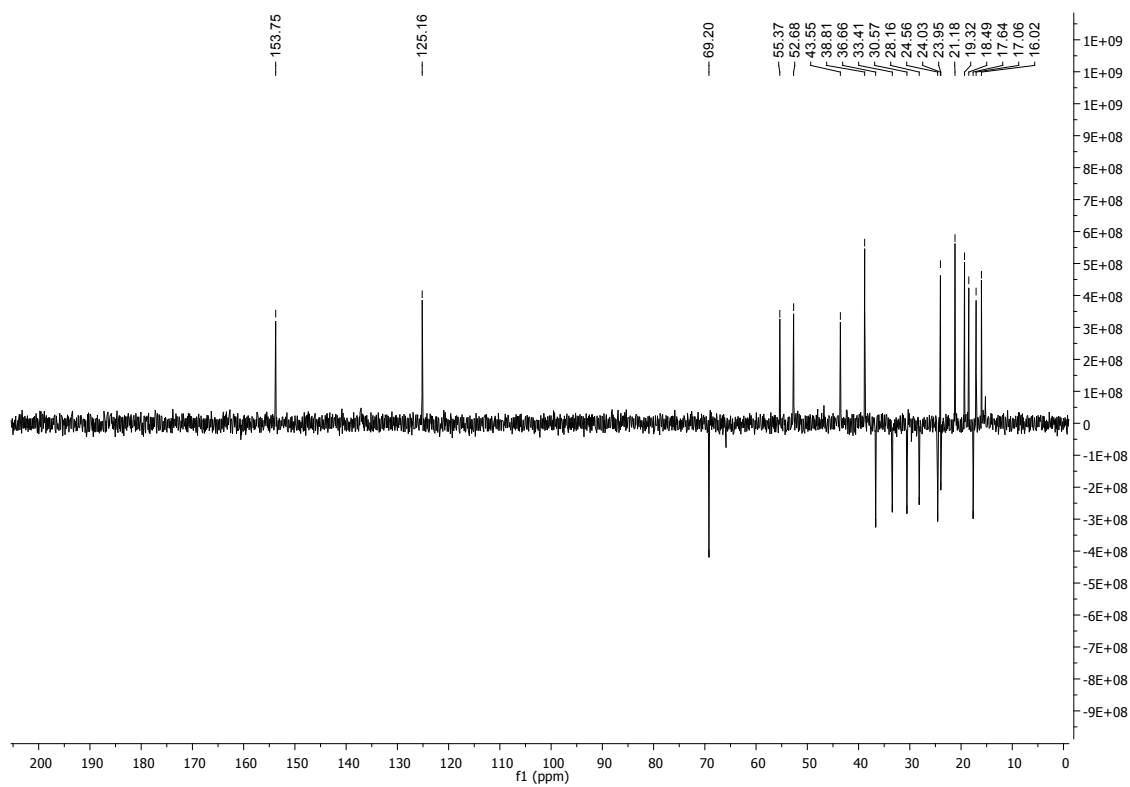
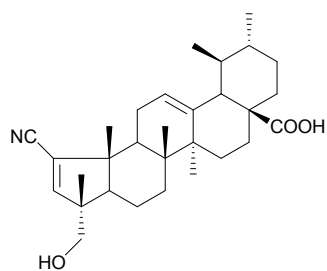
11.1 $^1\text{H-NMR}$ spectrum for compound 17 recorded in CDCl_3



11.2 ^{13}C -NMR spectrum for compound 17 recorded in CDCl_3

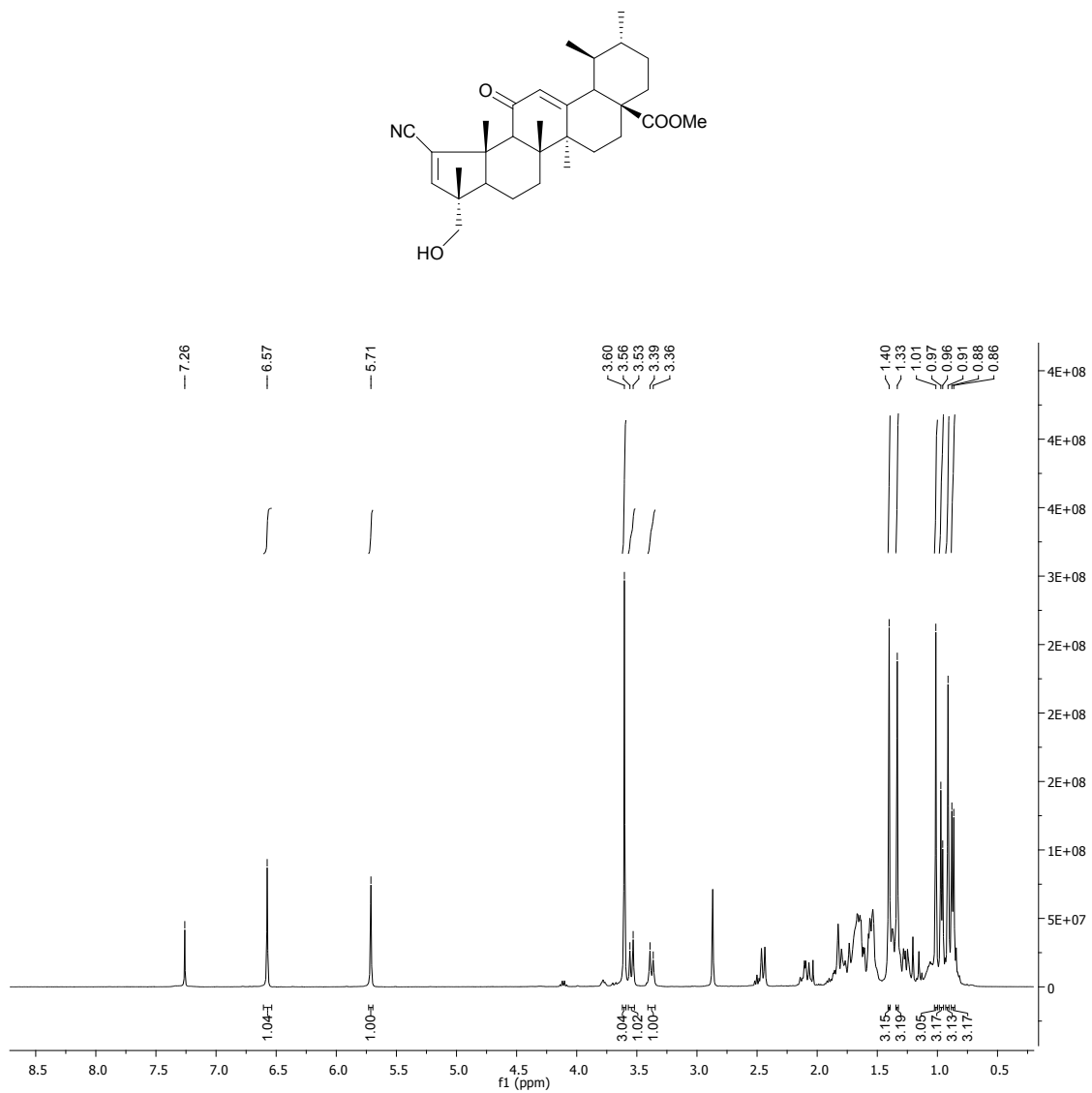


11.3 DEPT135 spectrum for compound 17 recorded in CDCl₃

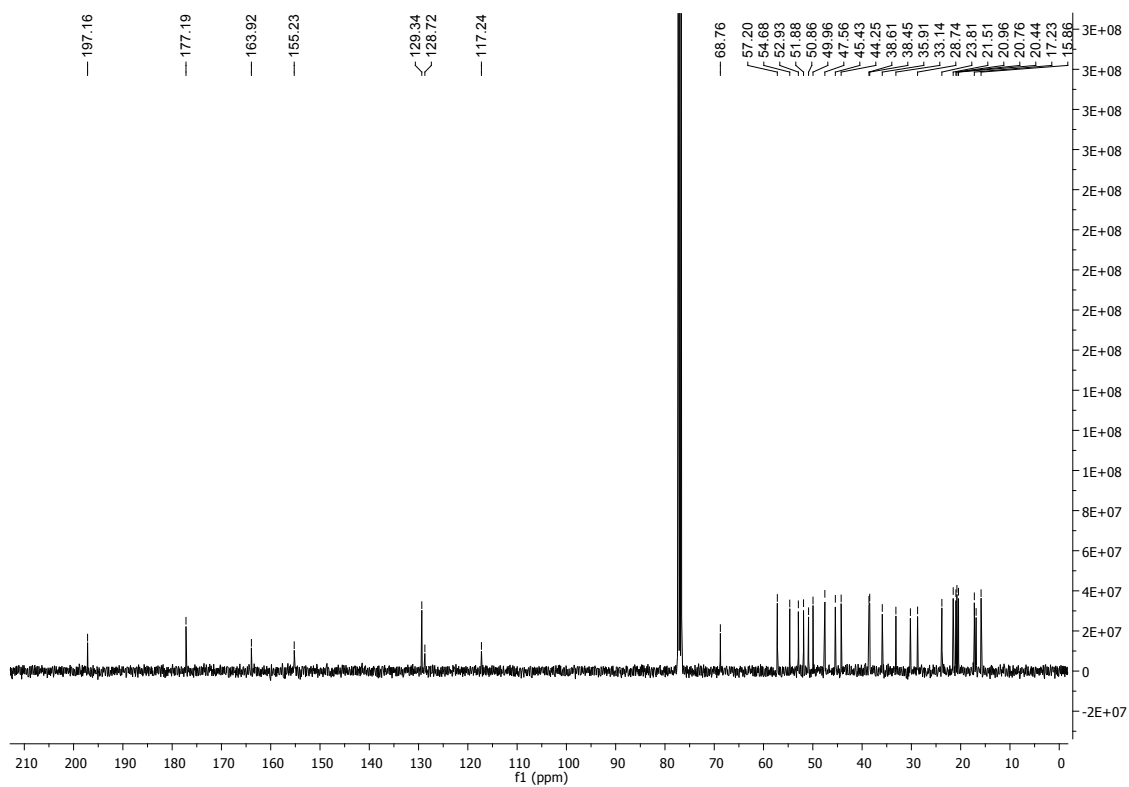
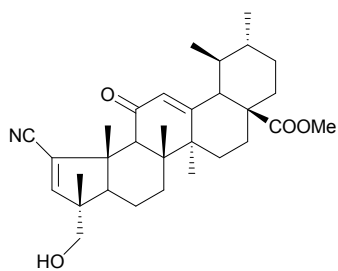


12. NMR data for compound 18

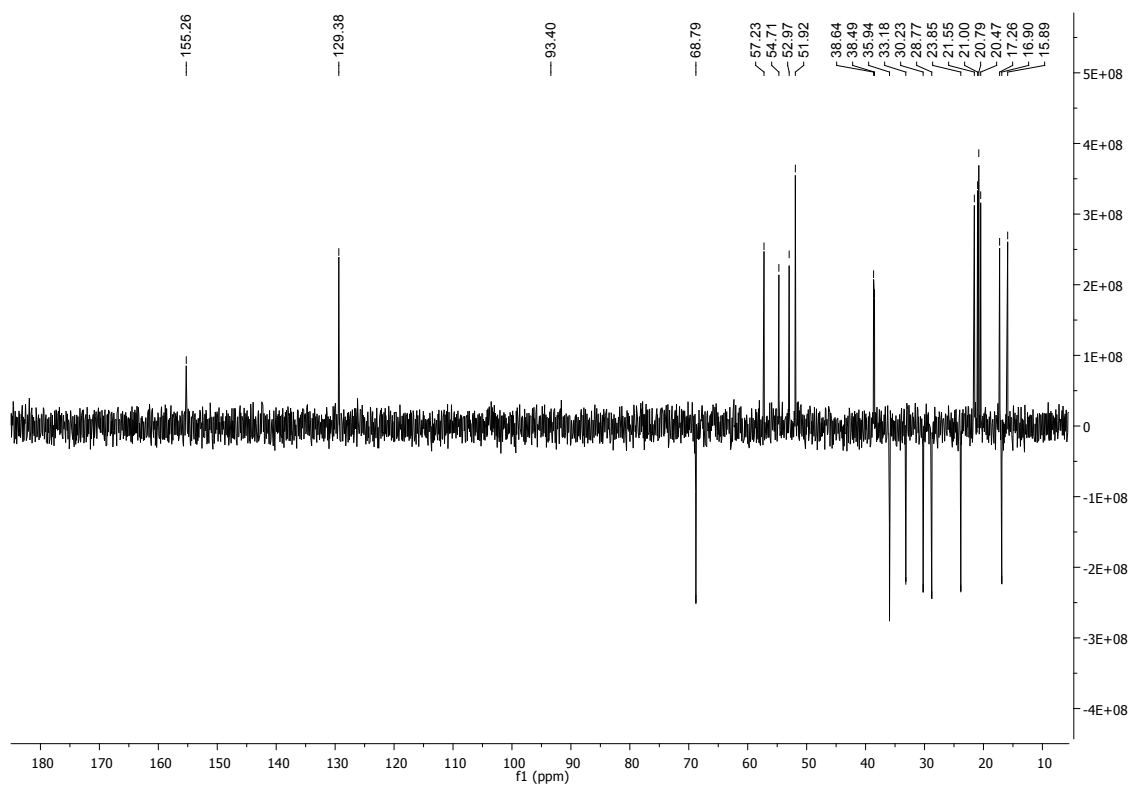
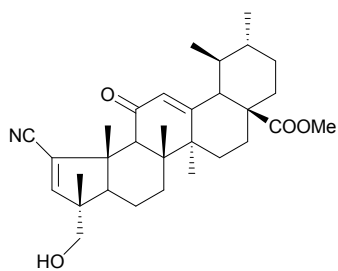
12.1 $^1\text{H-NMR}$ spectrum for compound 18 recorded in CDCl_3



12.2 ¹³C-NMR spectrum for compound 18 recorded in CDCl₃

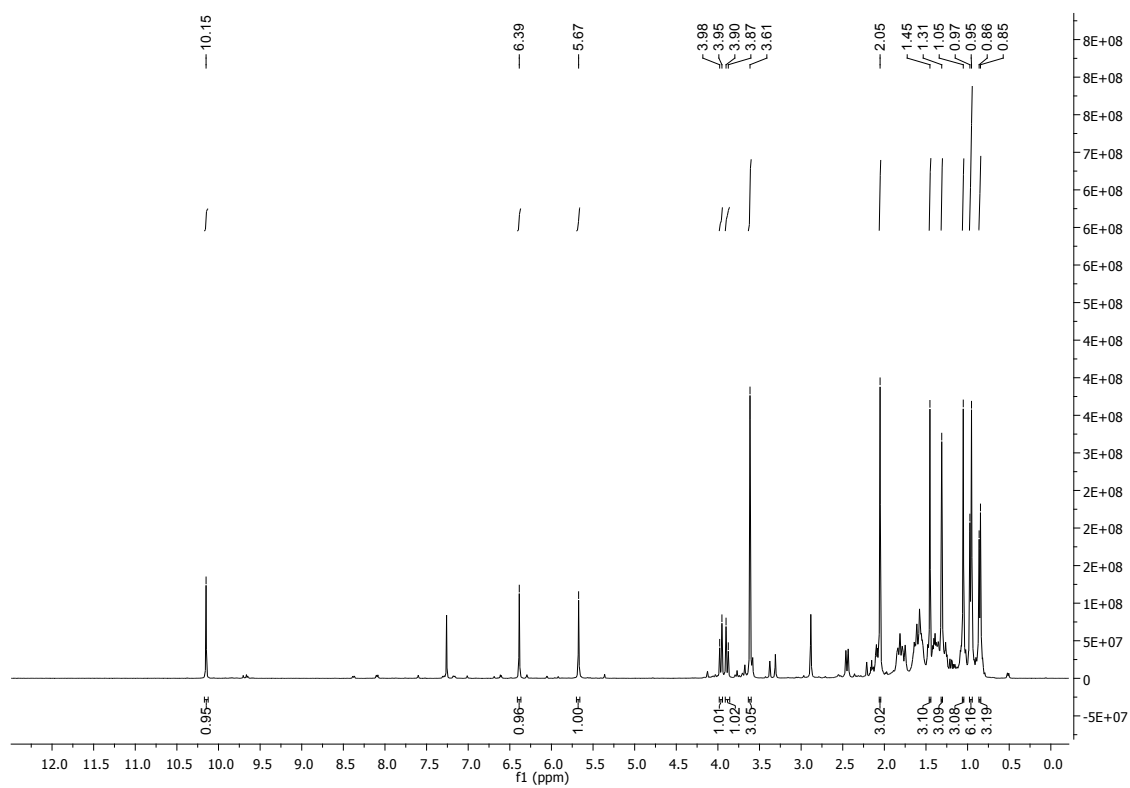
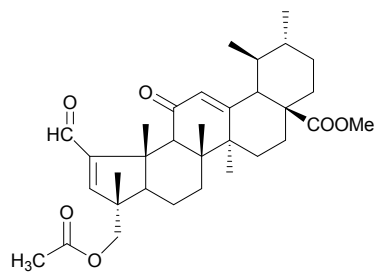


12.3 DEPT135 spectrum for compound 18 recorded in CDCl₃

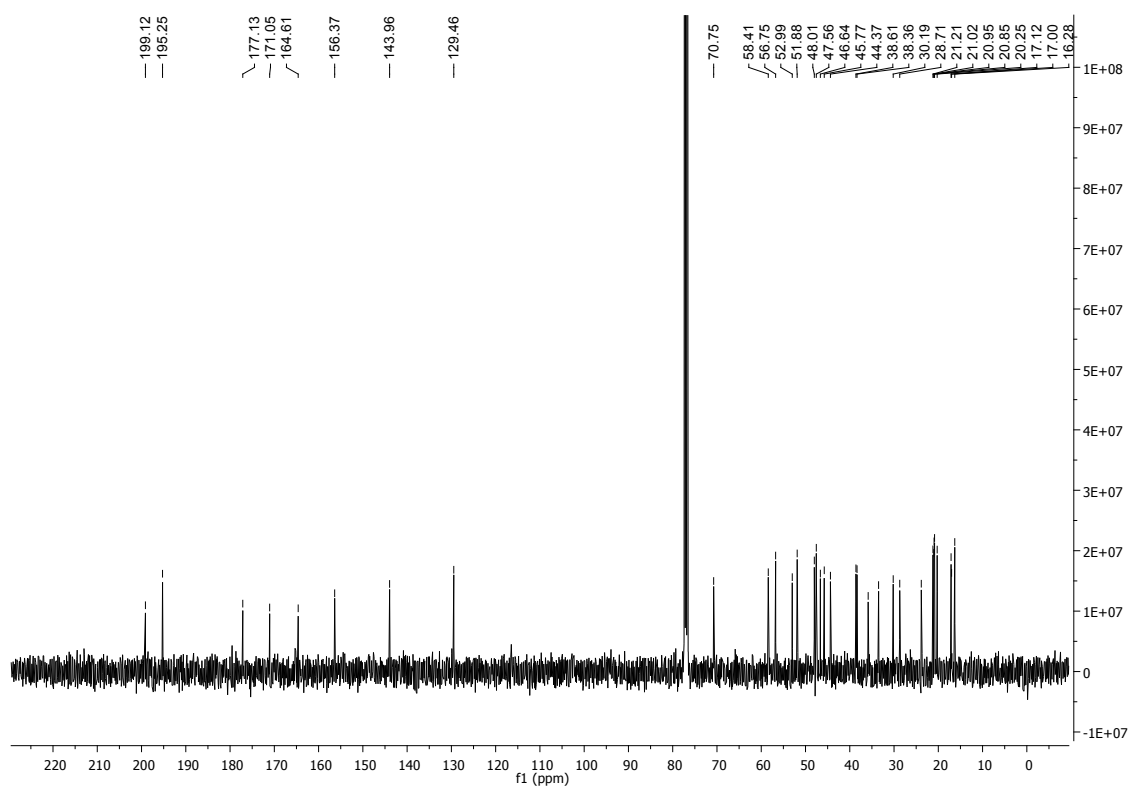
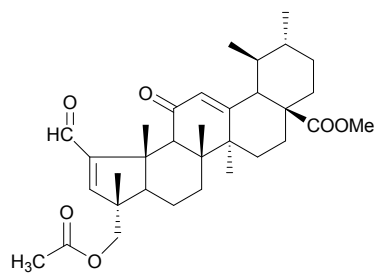


13. NMR data for compound 19

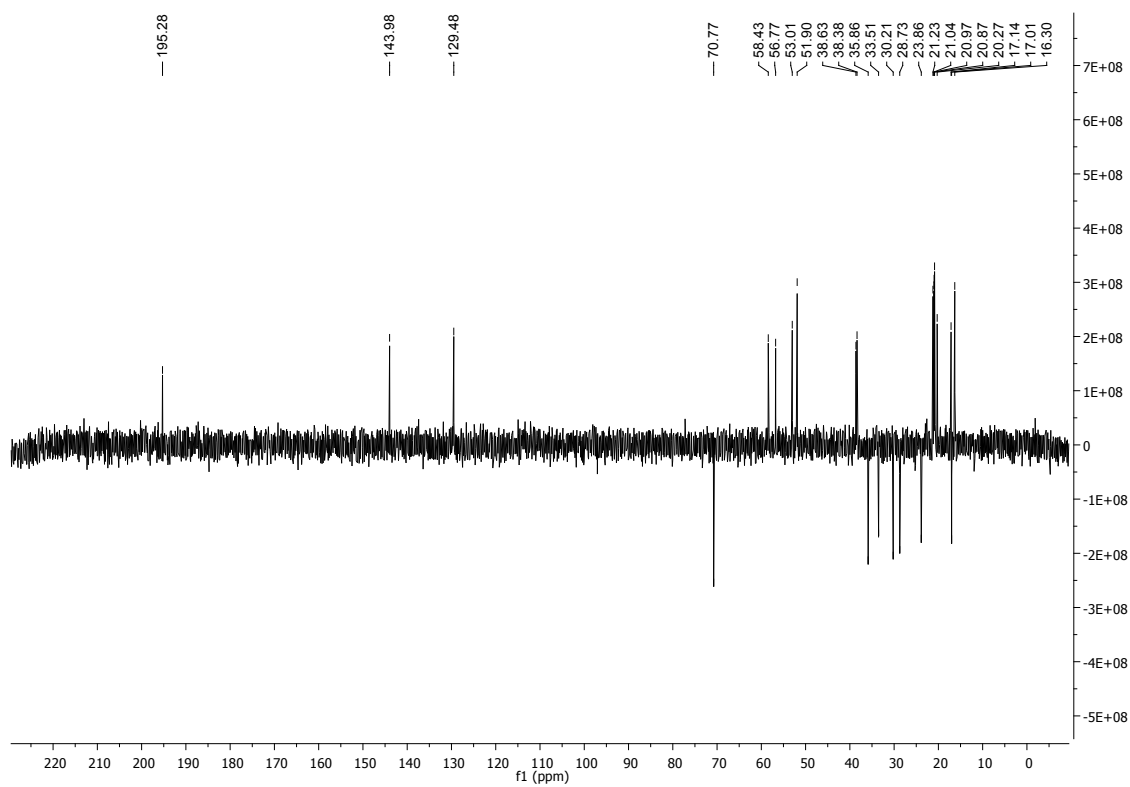
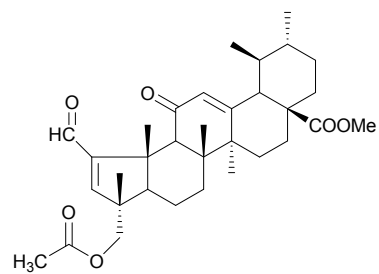
13.1 ¹H-NMR spectrum for compound 19 recorded in CDCl₃



13.2 ^{13}C -NMR spectrum for compound 19 recorded in CDCl_3

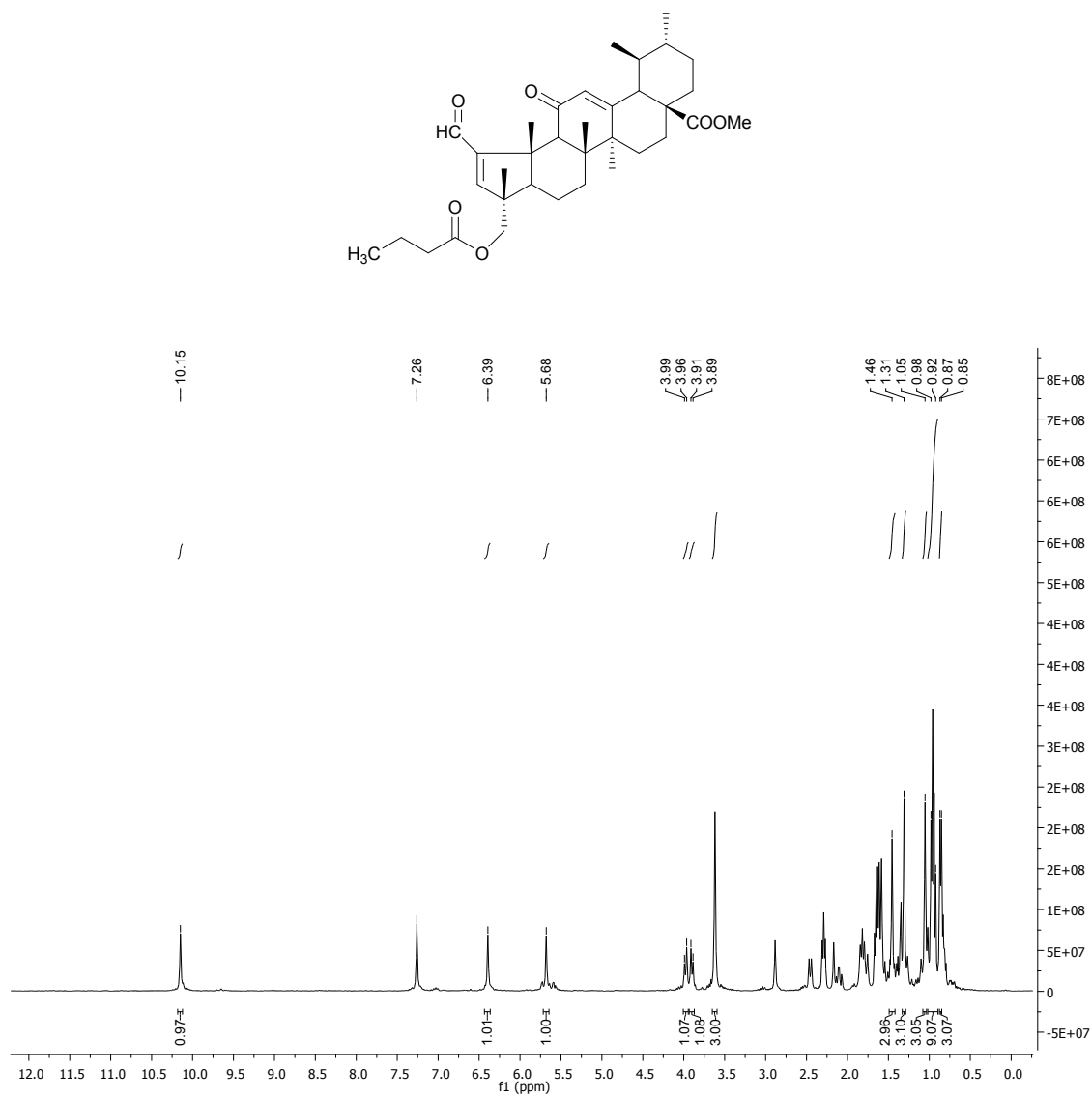


13.3 DEPT spectrum for compound 19 recorded in CDCl₃

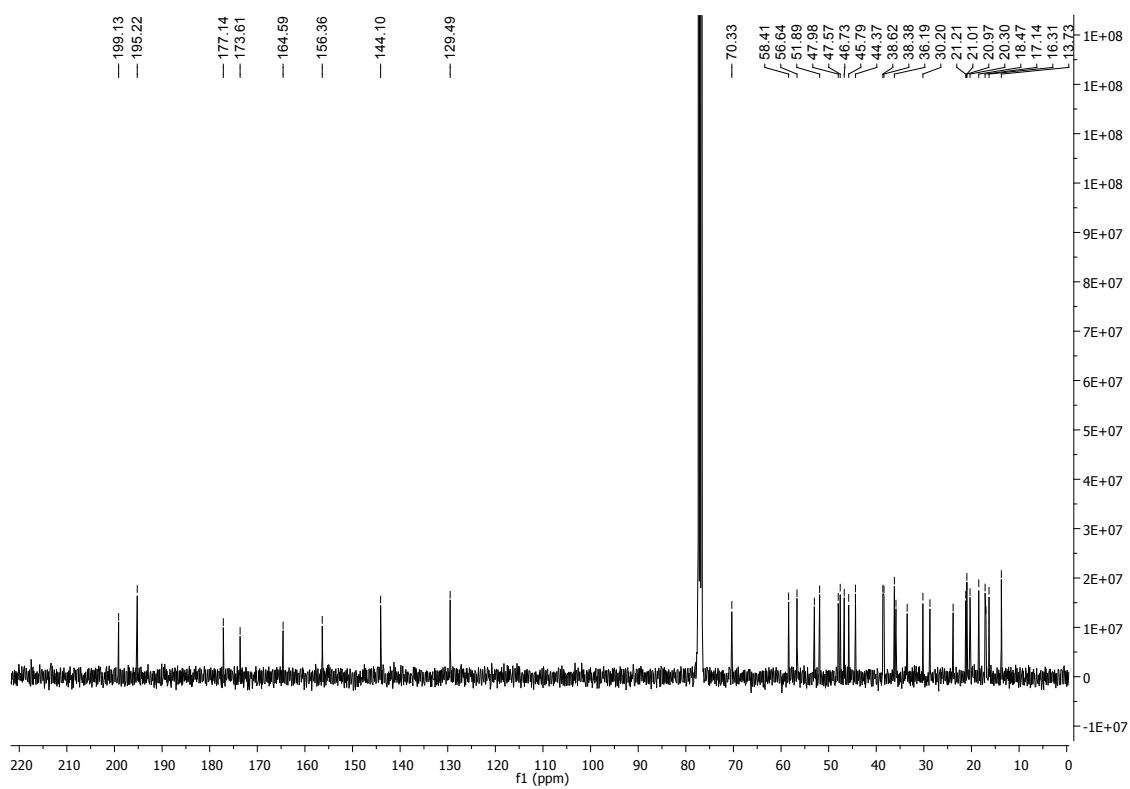
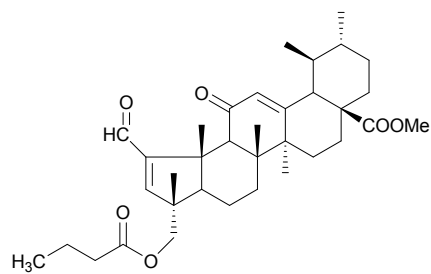


14. NMR data for compound 20

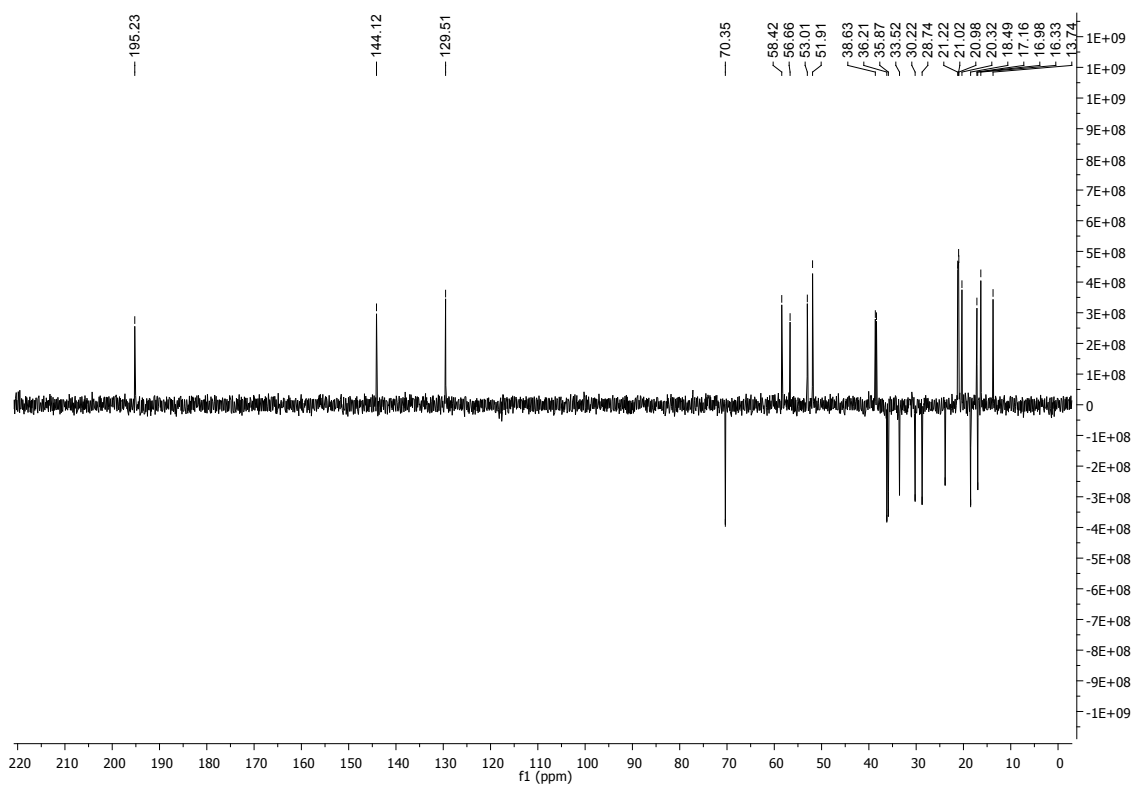
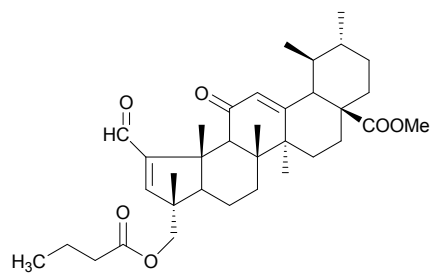
14.1 ¹H-NMR spectrum for compound 20 recorded in CDCl₃



14.2 ^{13}C -NMR spectrum for compound 20 recorded in CDCl_3

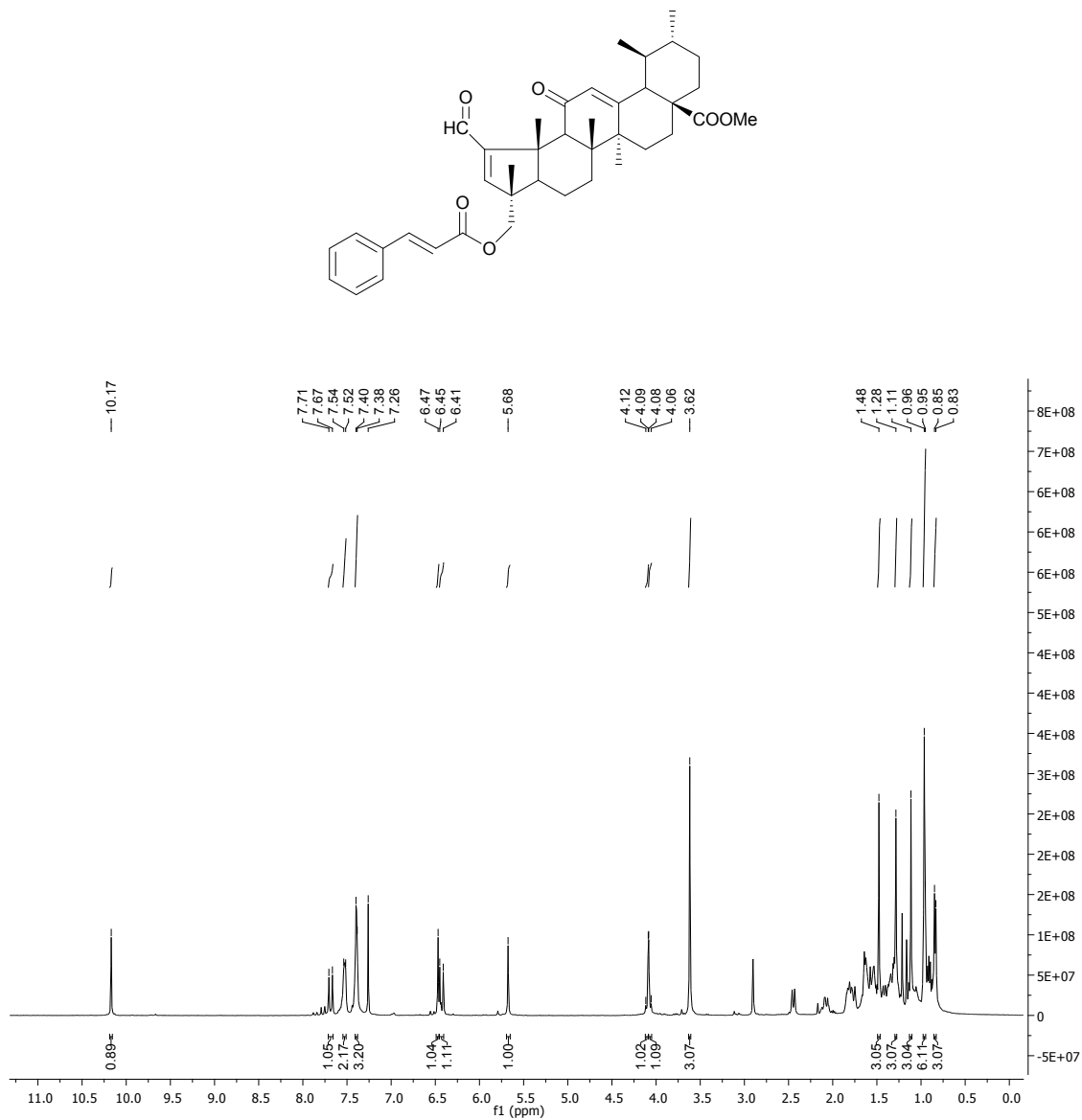


14.3 DEPT spectrum for compound 20 recorded in CDCl₃

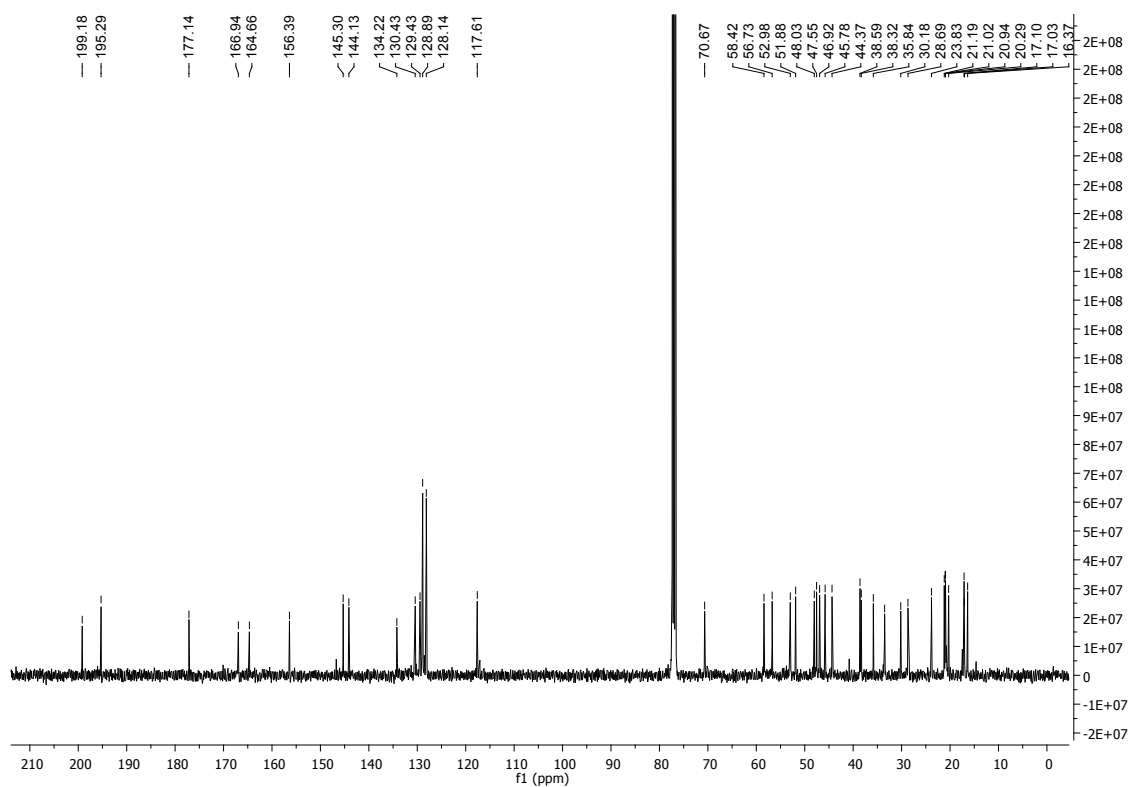
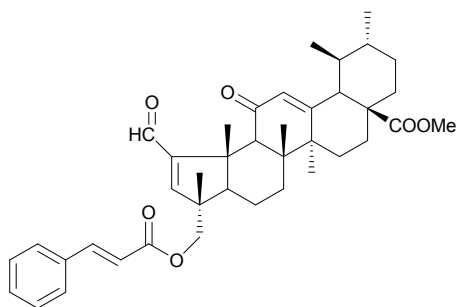


15. NMR data for compound 21

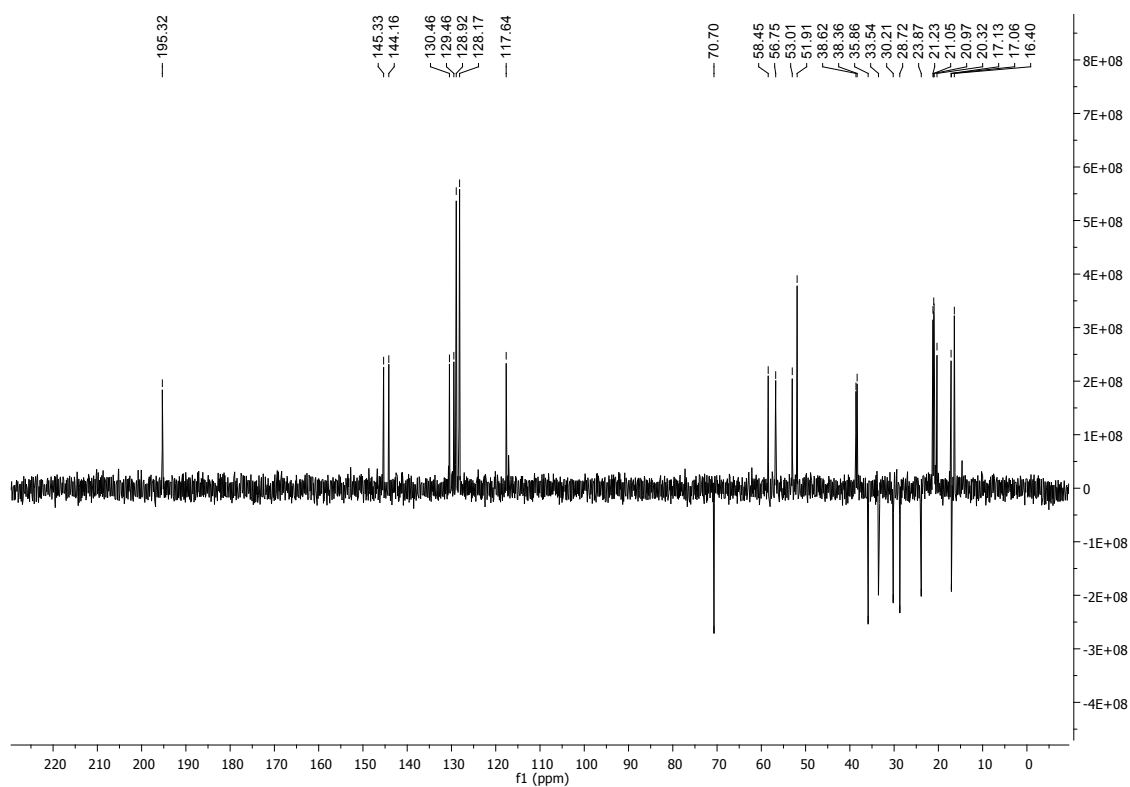
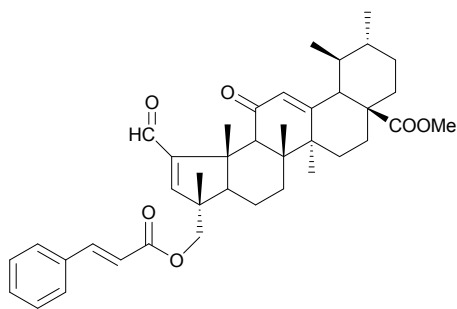
15.1 ¹H-NMR spectrum for compound 21 recorded in CDCl₃



15.2 ^{13}C -NMR spectrum for compound 21 recorded in CDCl_3

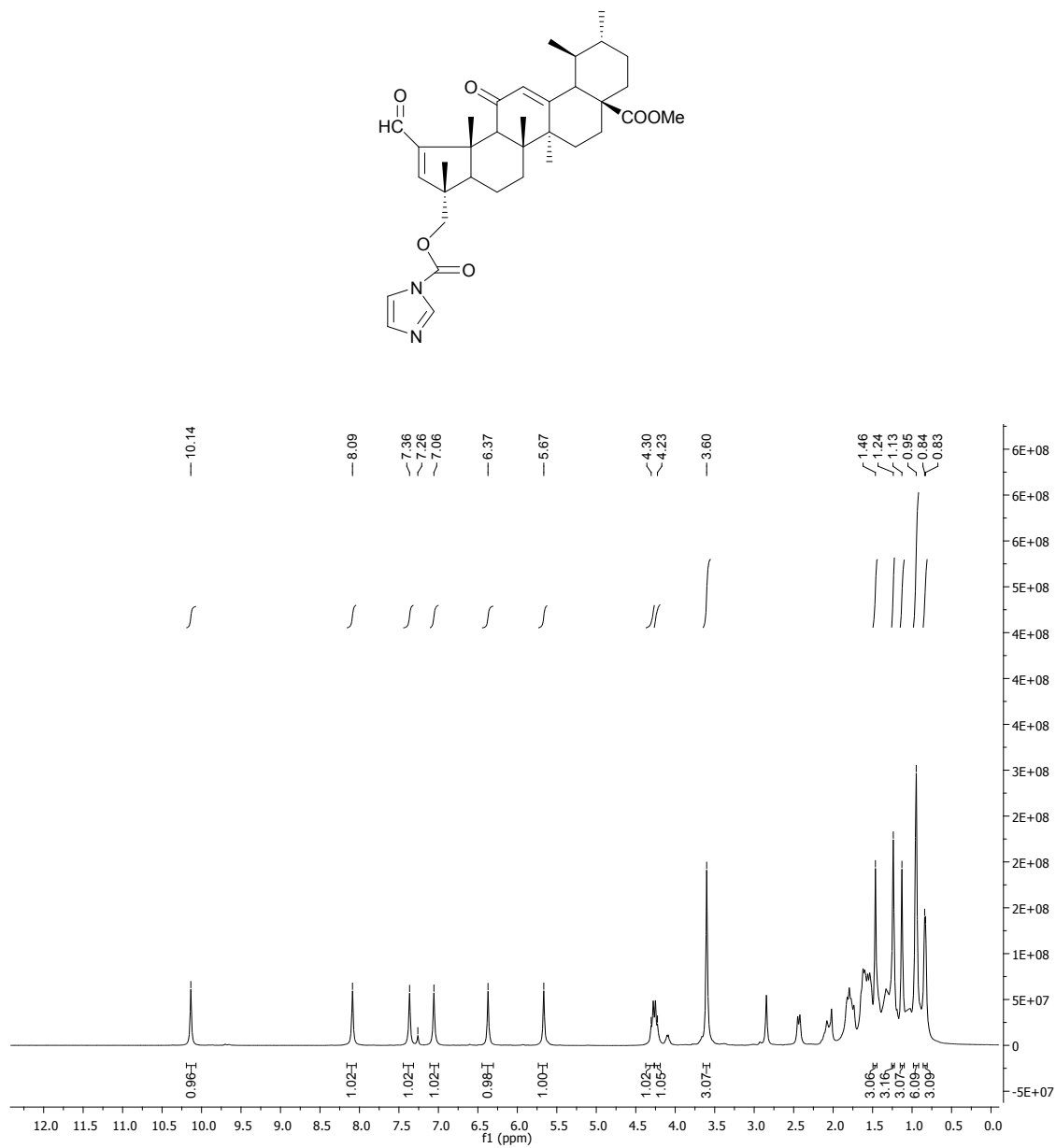


15.3 DEPT135 spectrum for compound 21 recorded in CDCl₃

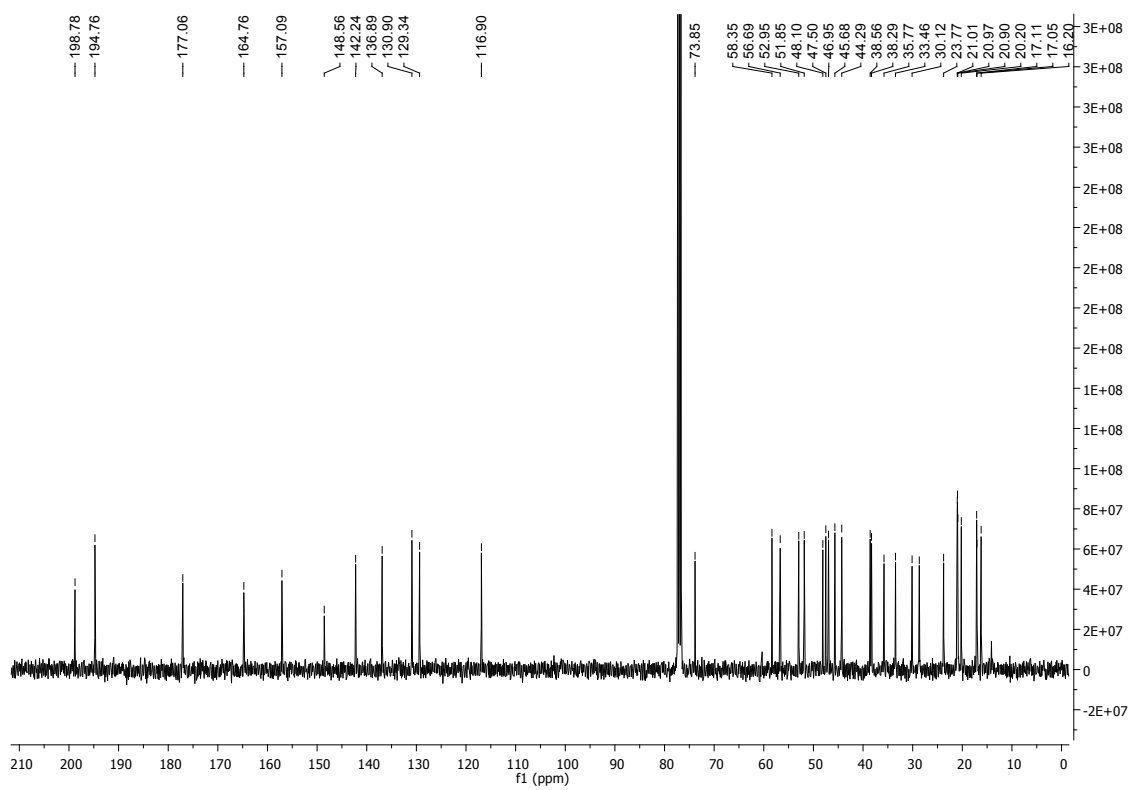
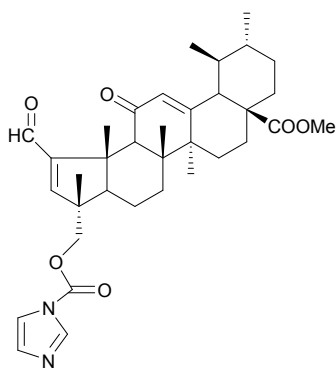


16. NMR data for compound 22

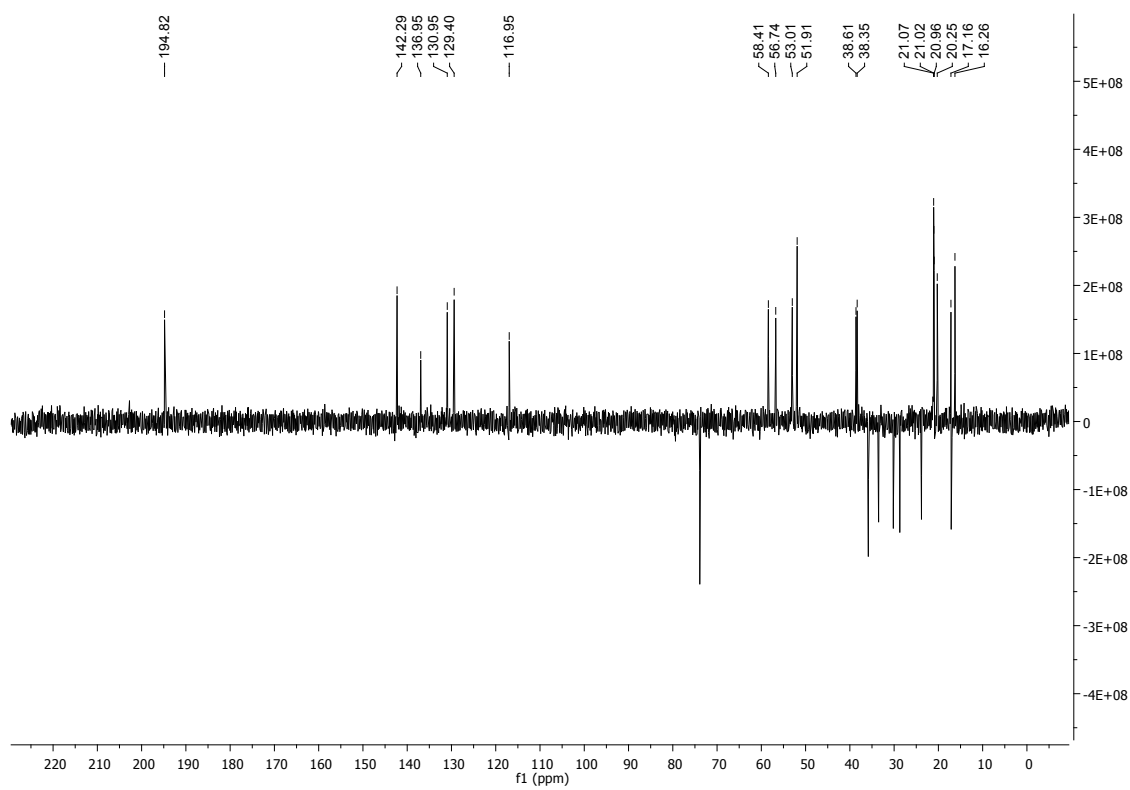
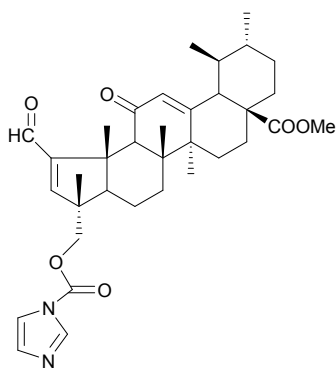
16.1 ¹H-NMR spectrum for compound 22 recorded in CDCl₃



16.2 ¹³C-NMR spectrum for compound 22 recorded in CDCl₃

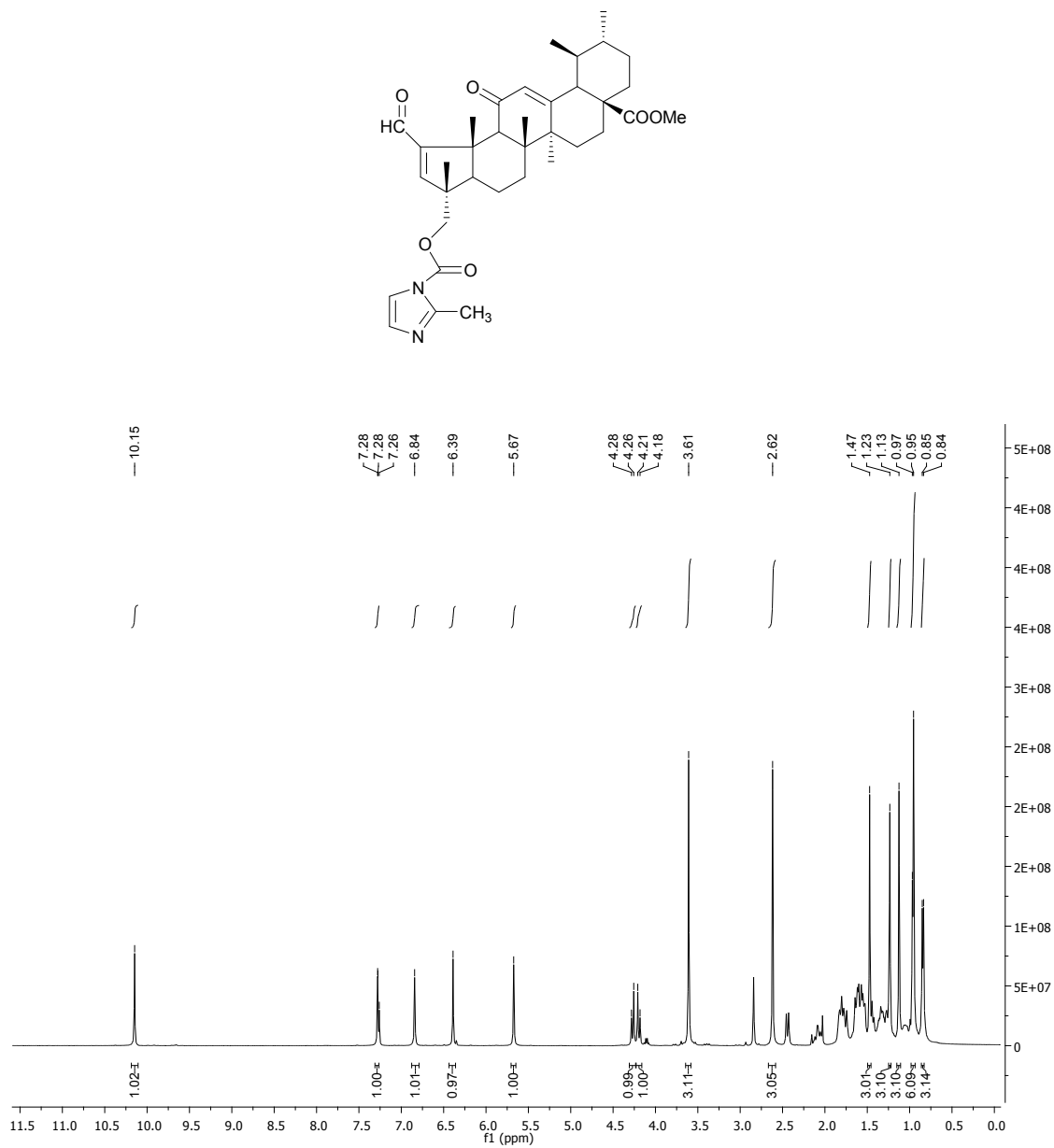


16.3 DEPT135 spectrum for compound 22 recorded in CDCl₃

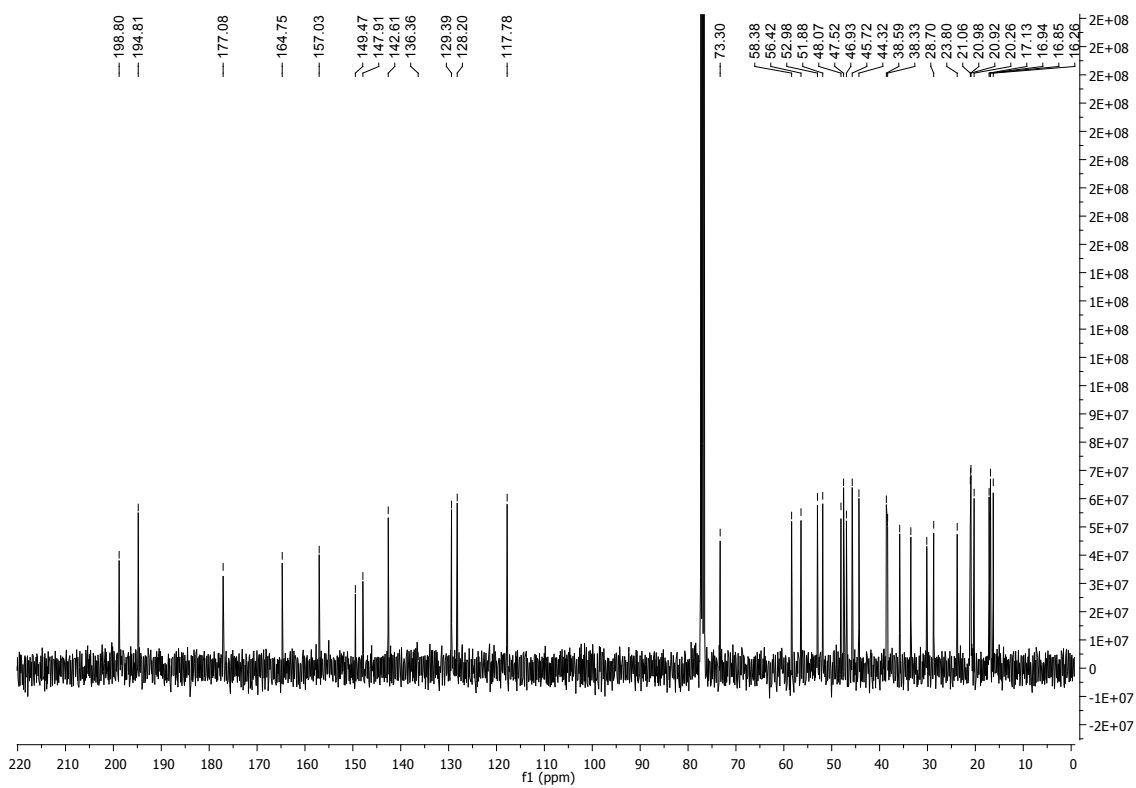
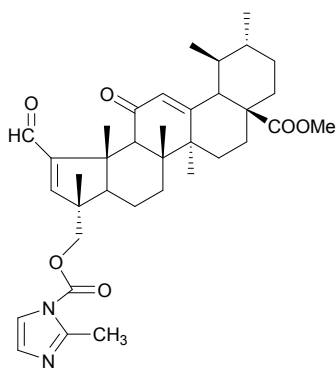


17. NMR data for compound 23

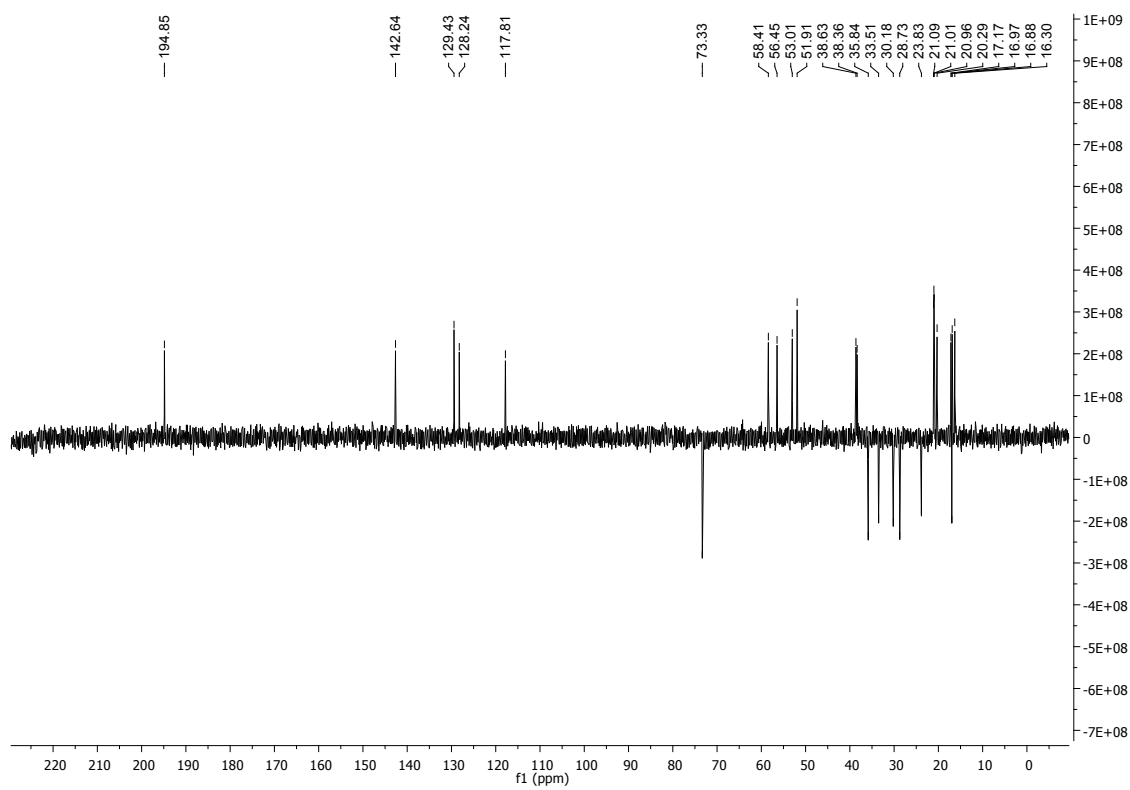
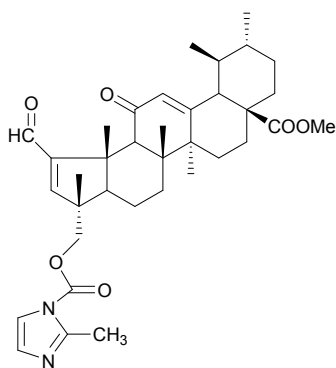
17.1 ¹H-NMR spectrum for compound 23 recorded in CDCl₃



17.2 ^{13}C -NMR spectrum for compound 23 recorded in CDCl_3

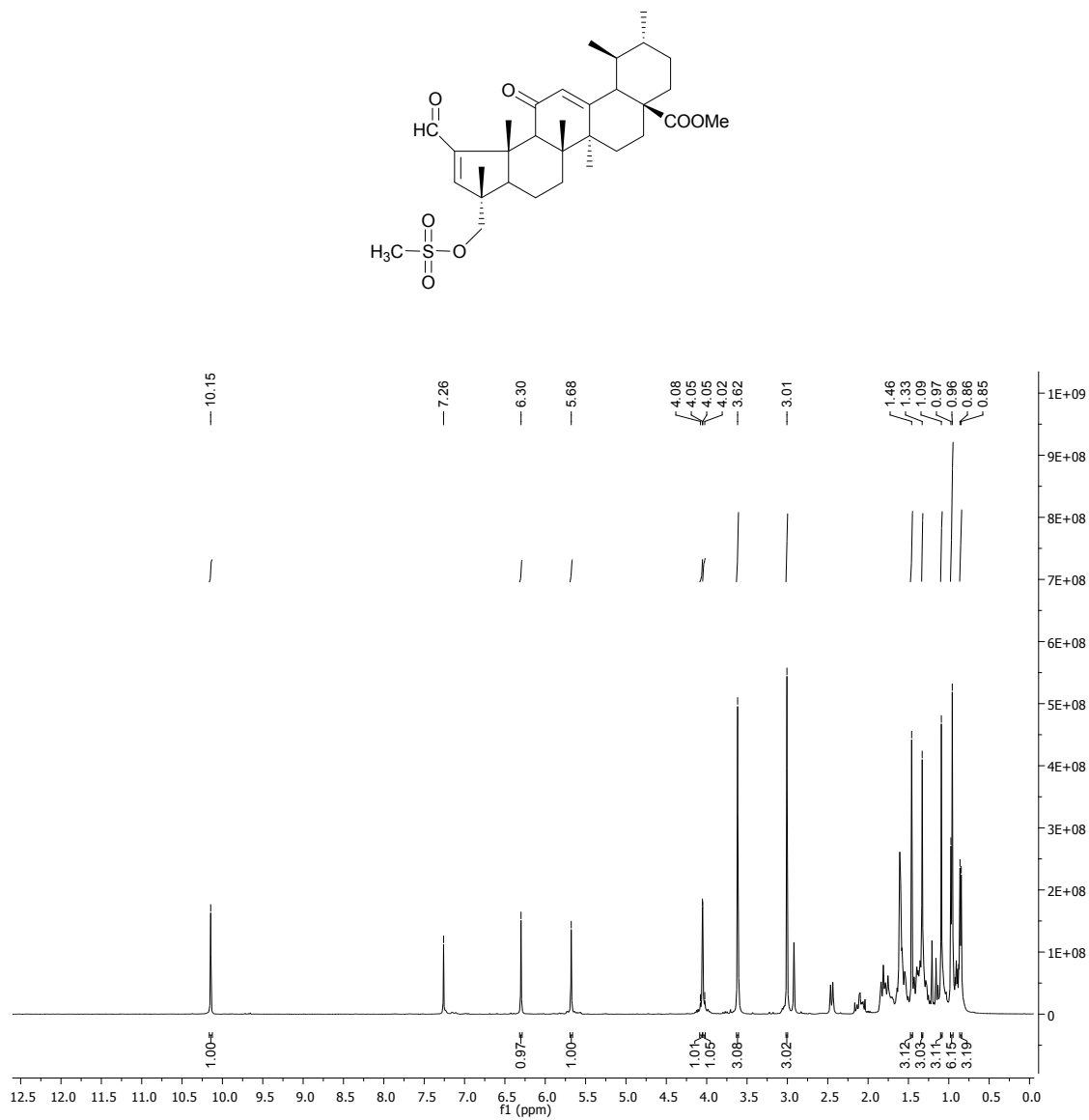


17.3 DEPT135 spectrum for compound 23 recorded in CDCl₃

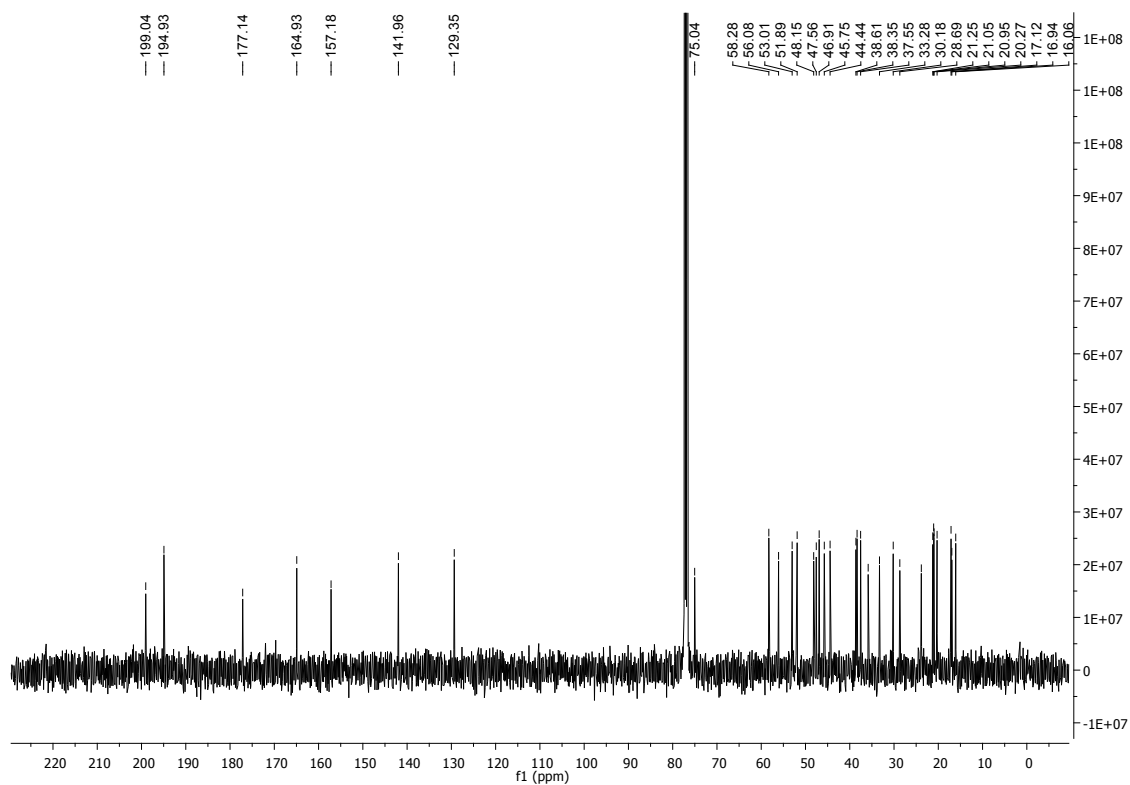
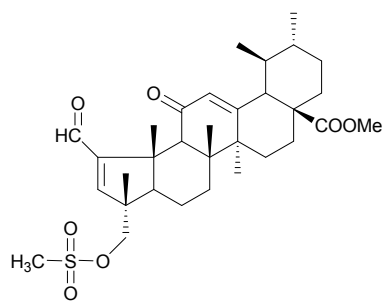


18. NMR data for compound 24

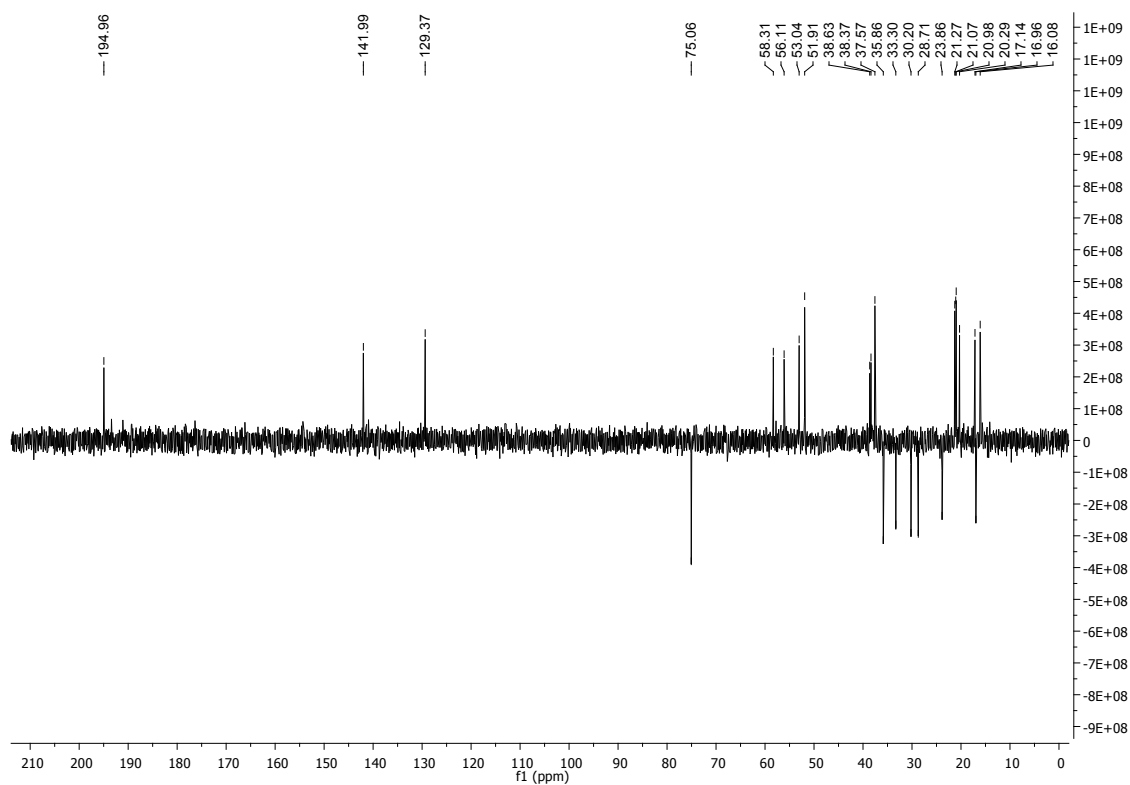
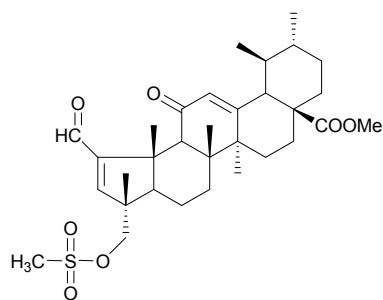
18.1 ¹H-NMR spectrum for compound 24 recorded in CDCl₃



18.2 ^{13}C -NMR spectrum for compound 24 recorded in CDCl_3

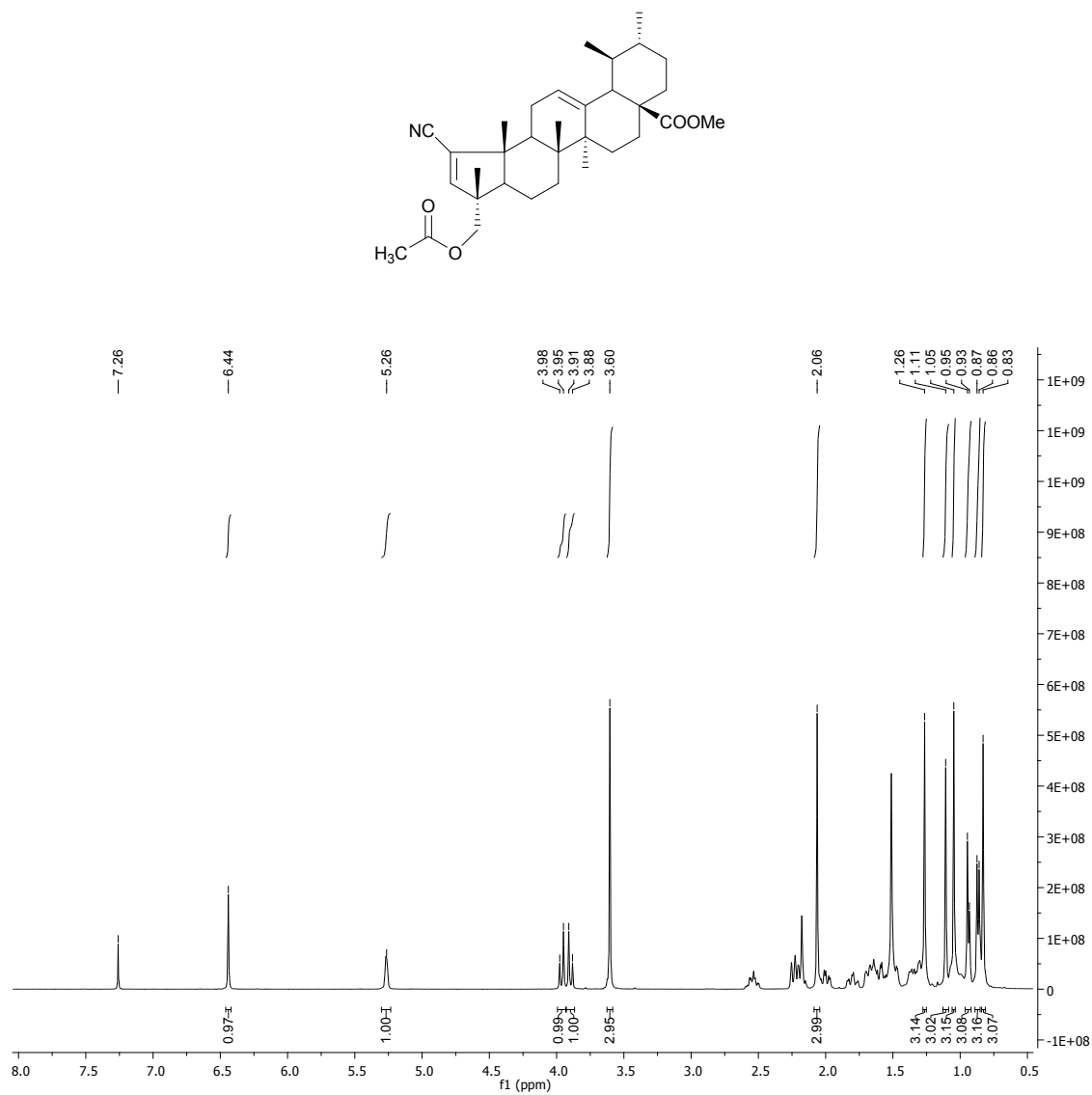


18.3 DEPT135 spectrum for compound 24 recorded in CDCl₃

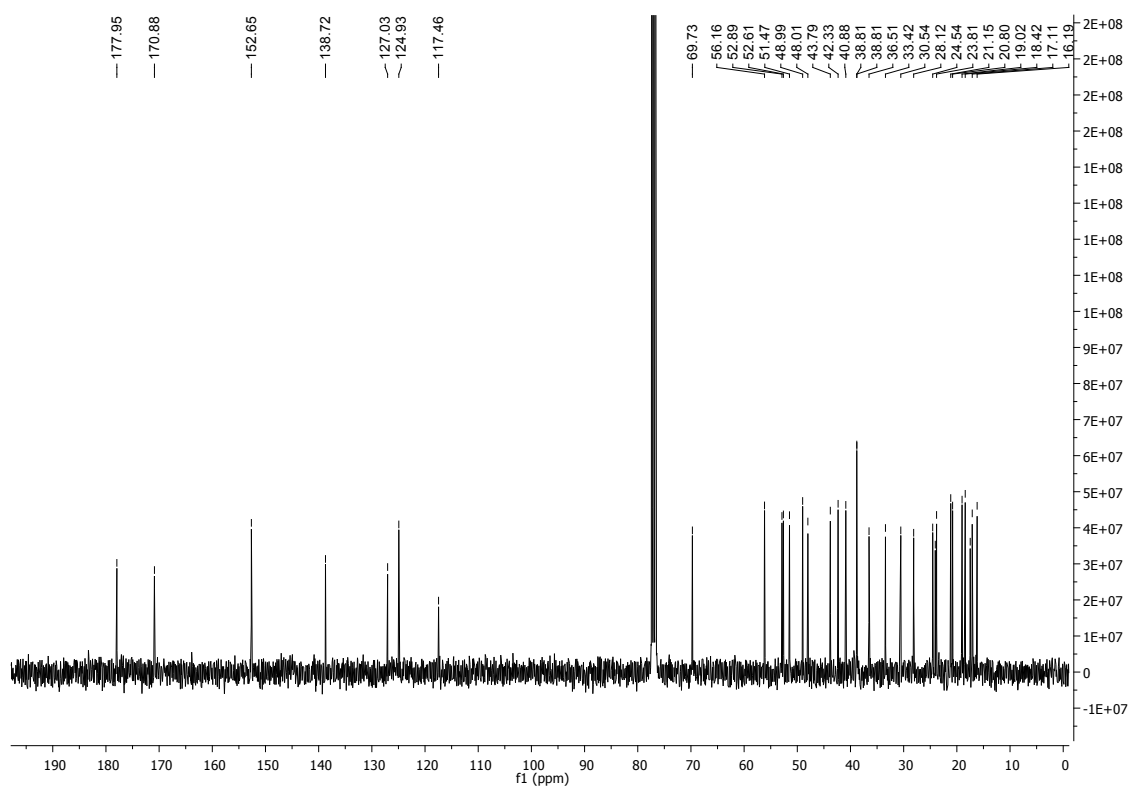
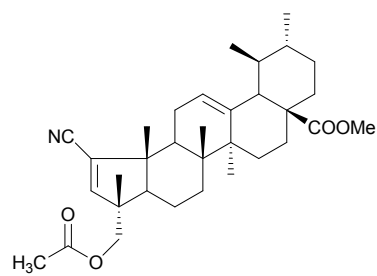


19. NMR data for compound 25

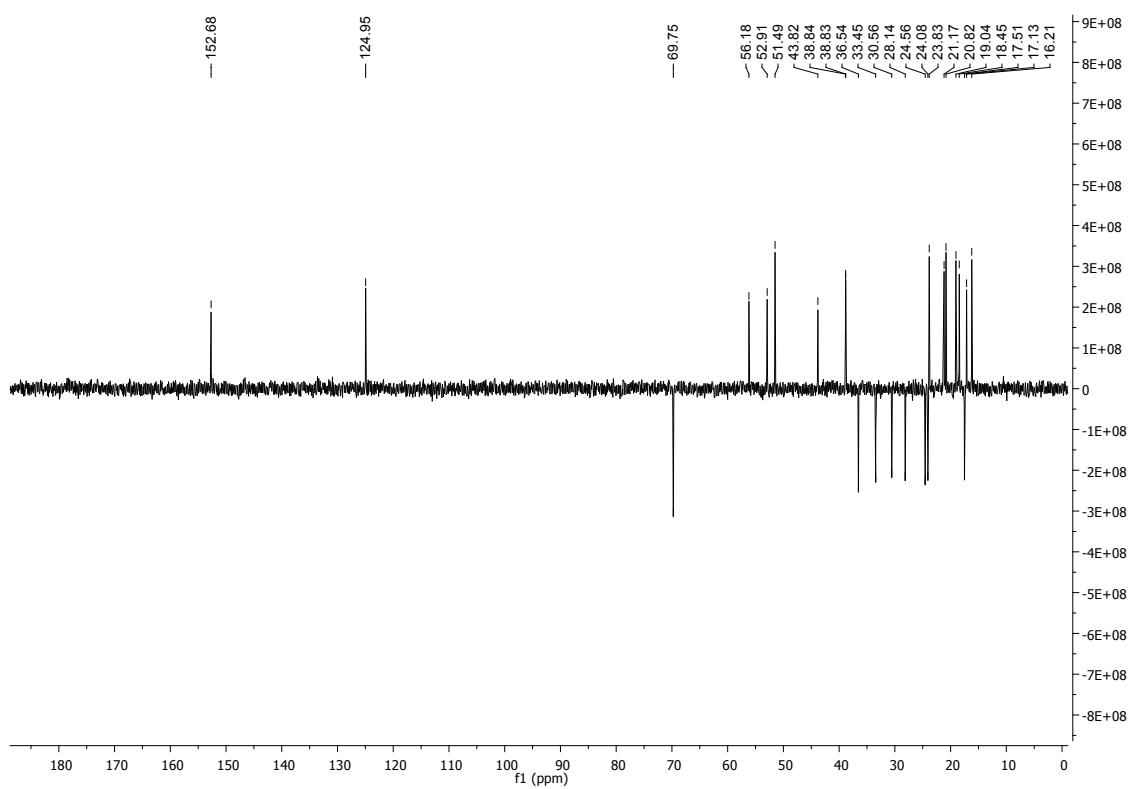
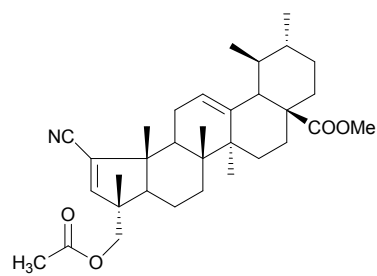
19.1 ¹H-NMR spectrum for compound 25 recorded in CDCl₃



19.2 ^{13}C -NMR spectrum for compound 25 recorded in CDCl_3

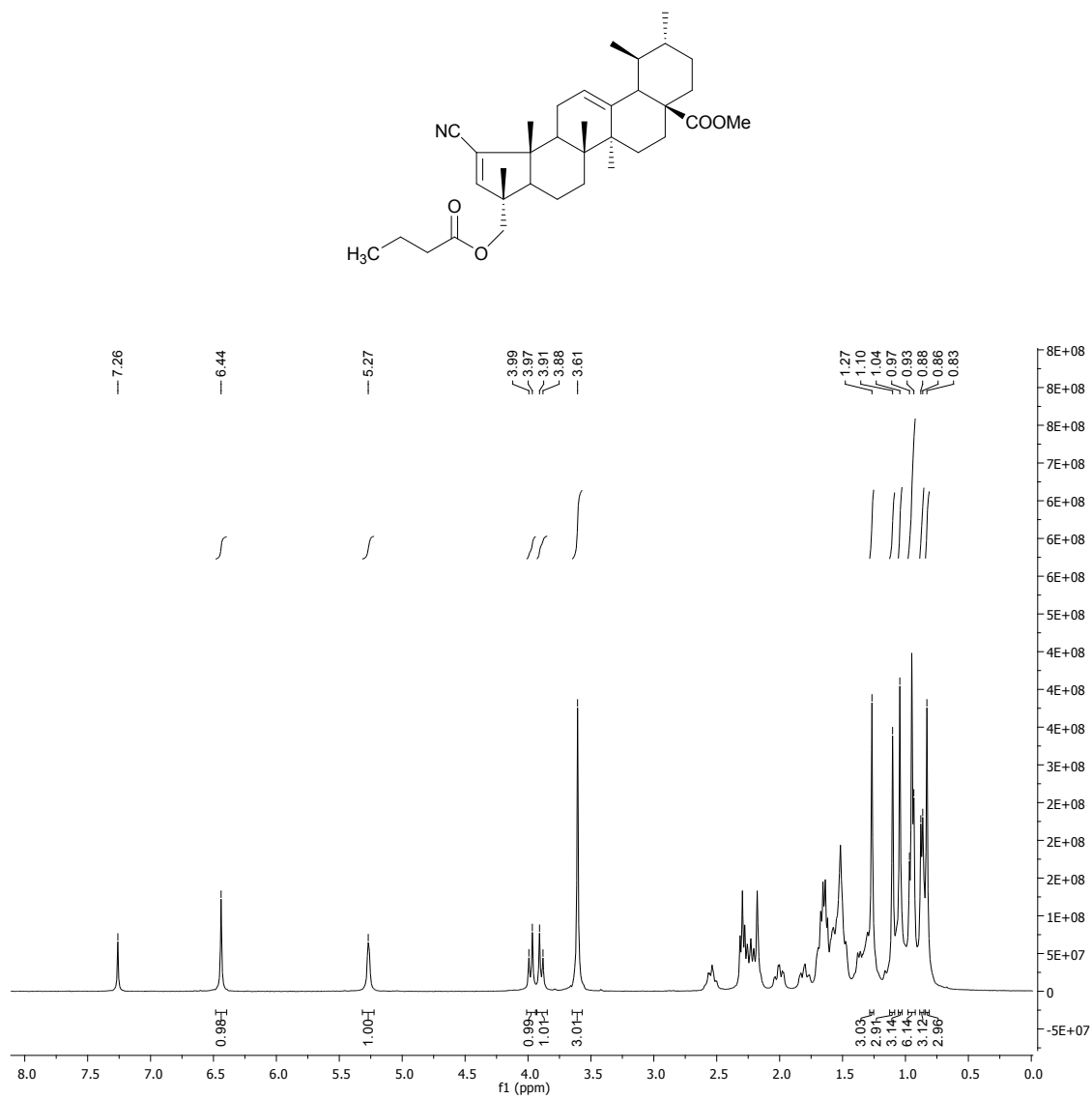


19.3 DEPT135 spectrum for compound 25 recorded in CDCl₃

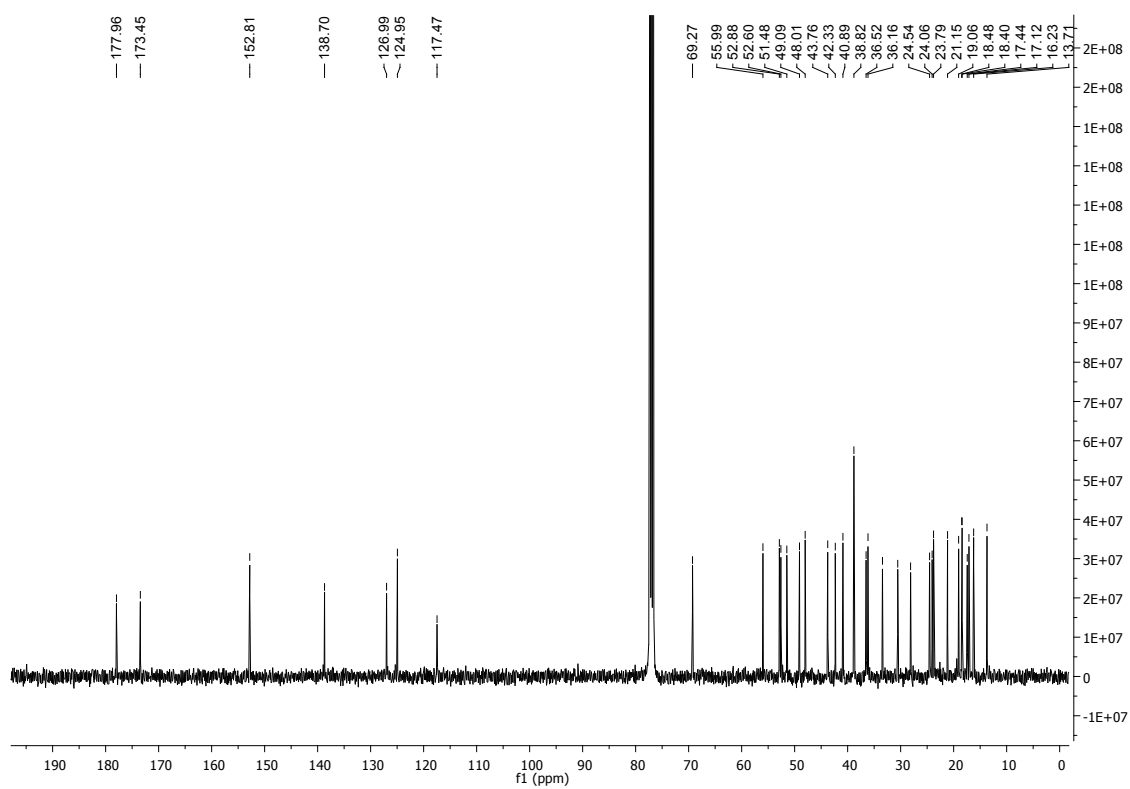
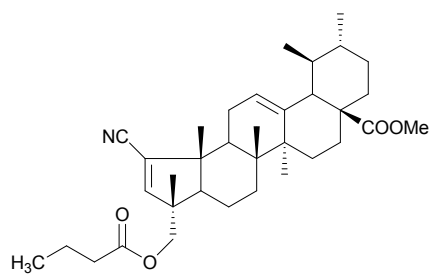


20. NMR data for compound 26

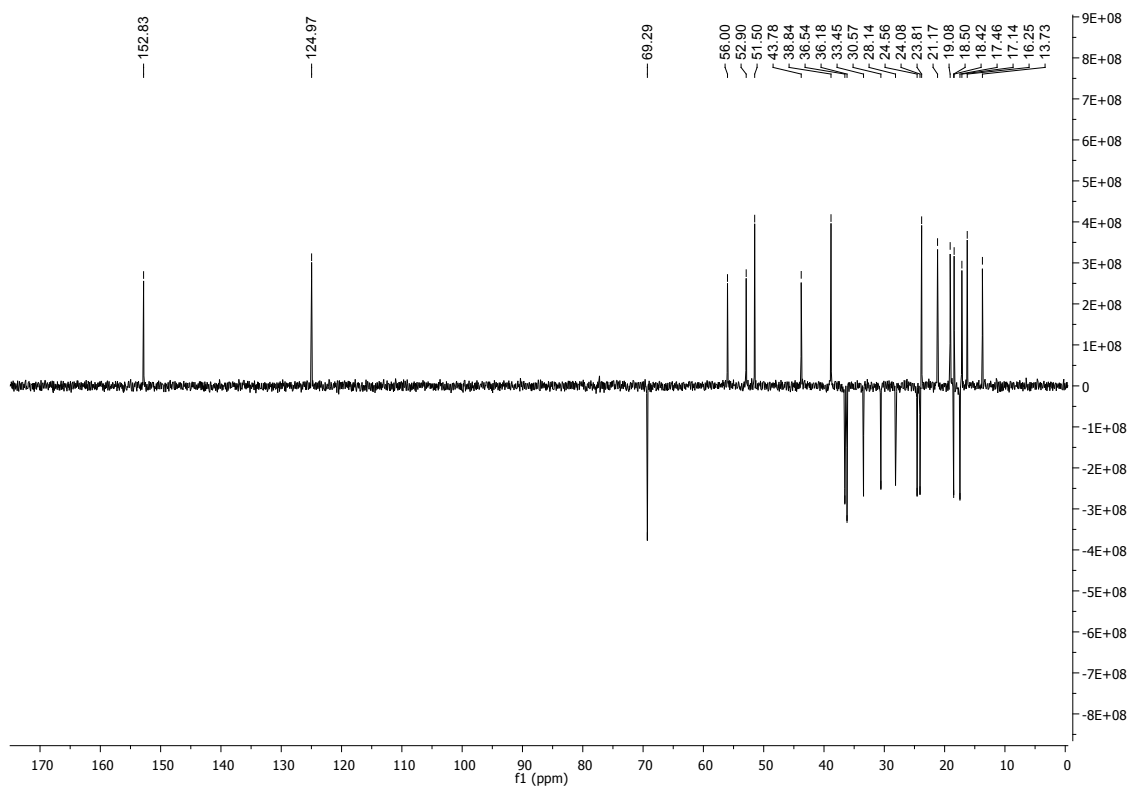
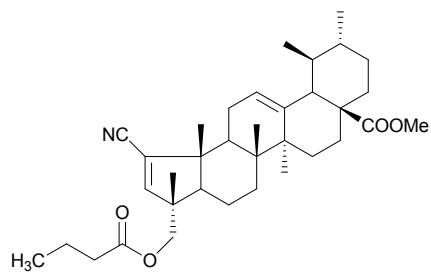
20.1 ^1H -NMR spectrum for compound 26 recorded in CDCl_3



20.2 ^{13}C -NMR spectrum for compound 26 recorded in CDCl_3

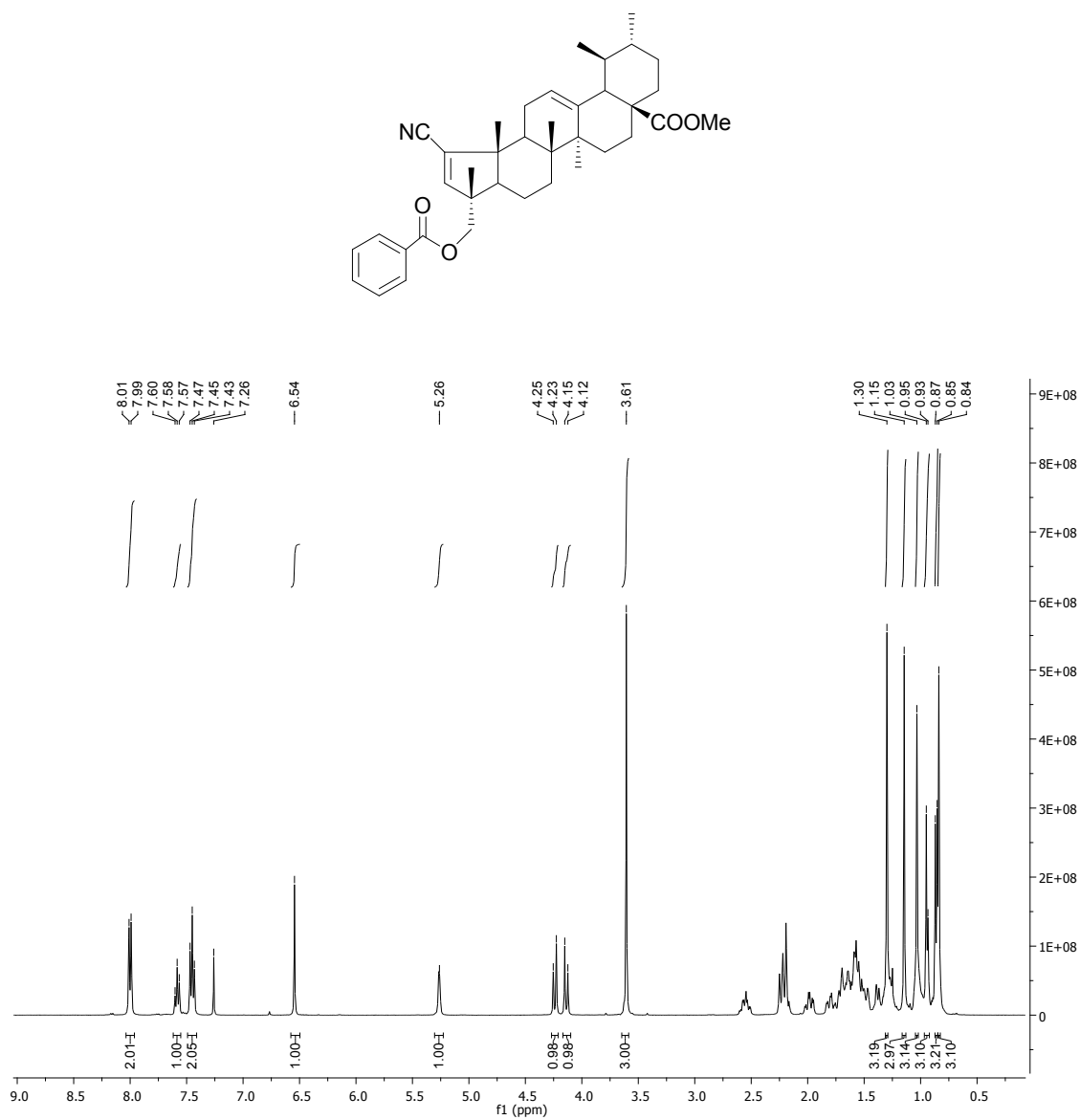


20.3 DEPT135 spectrum for compound 26 recorded in CDCl₃

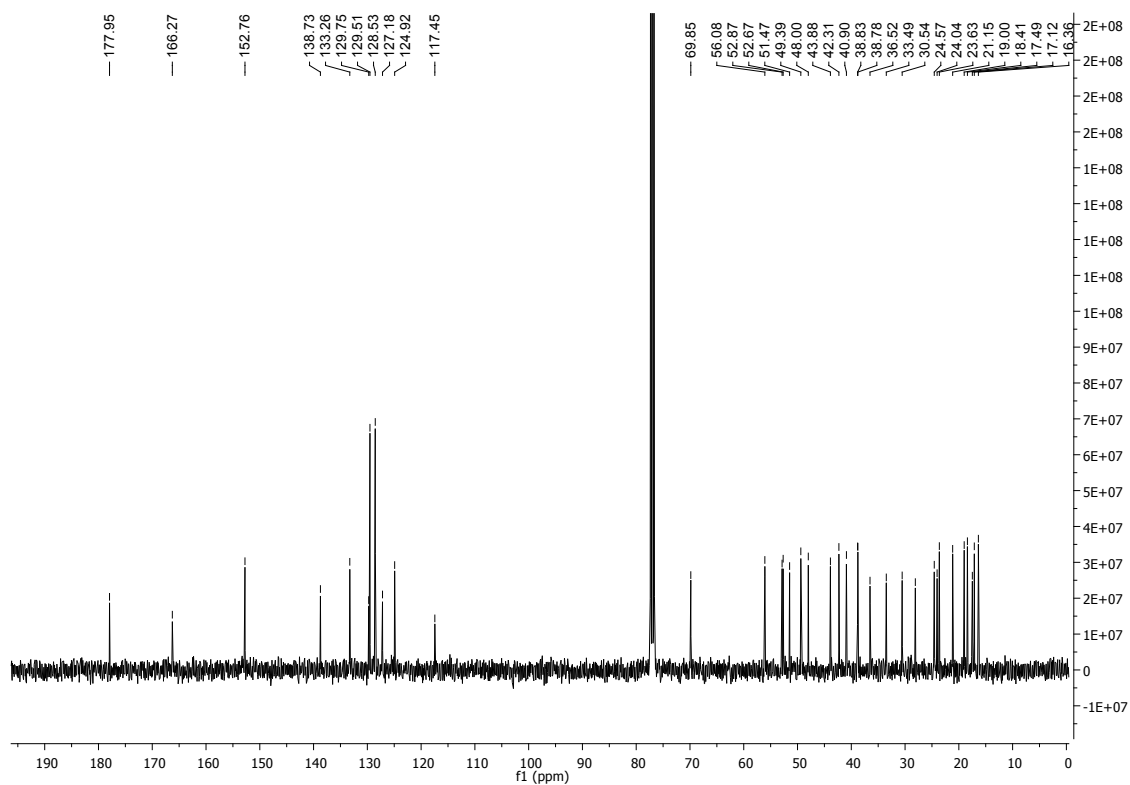
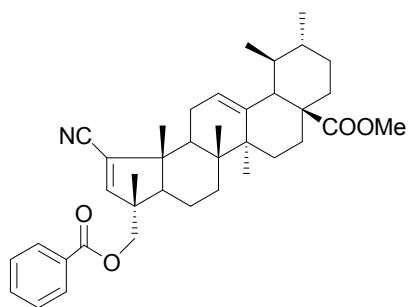


21. NMR data for compound 27

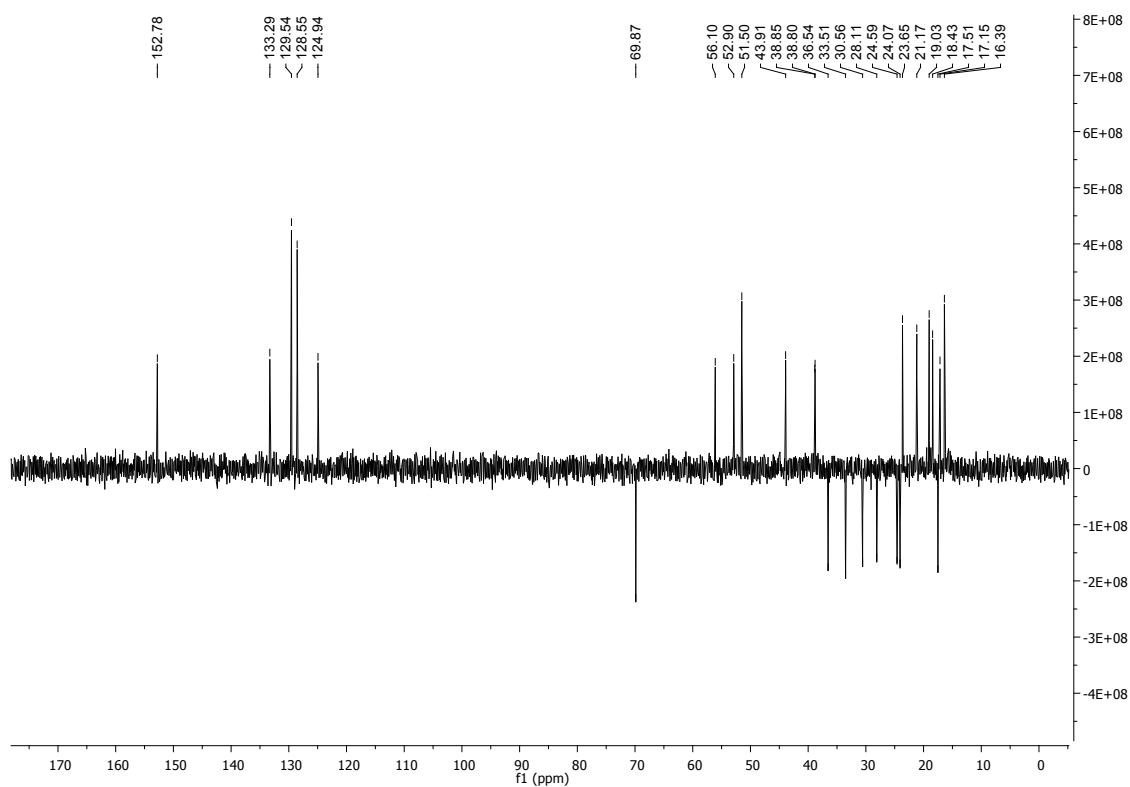
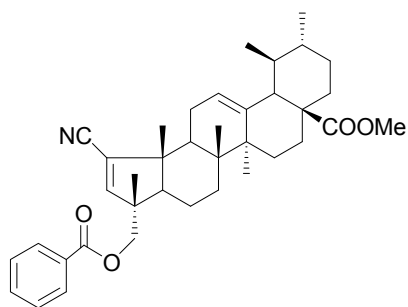
21.1 ¹H-NMR spectrum for compound 27 recorded in CDCl₃



21.2 ^{13}C -NMR spectrum for compound 27 recorded in CDCl_3

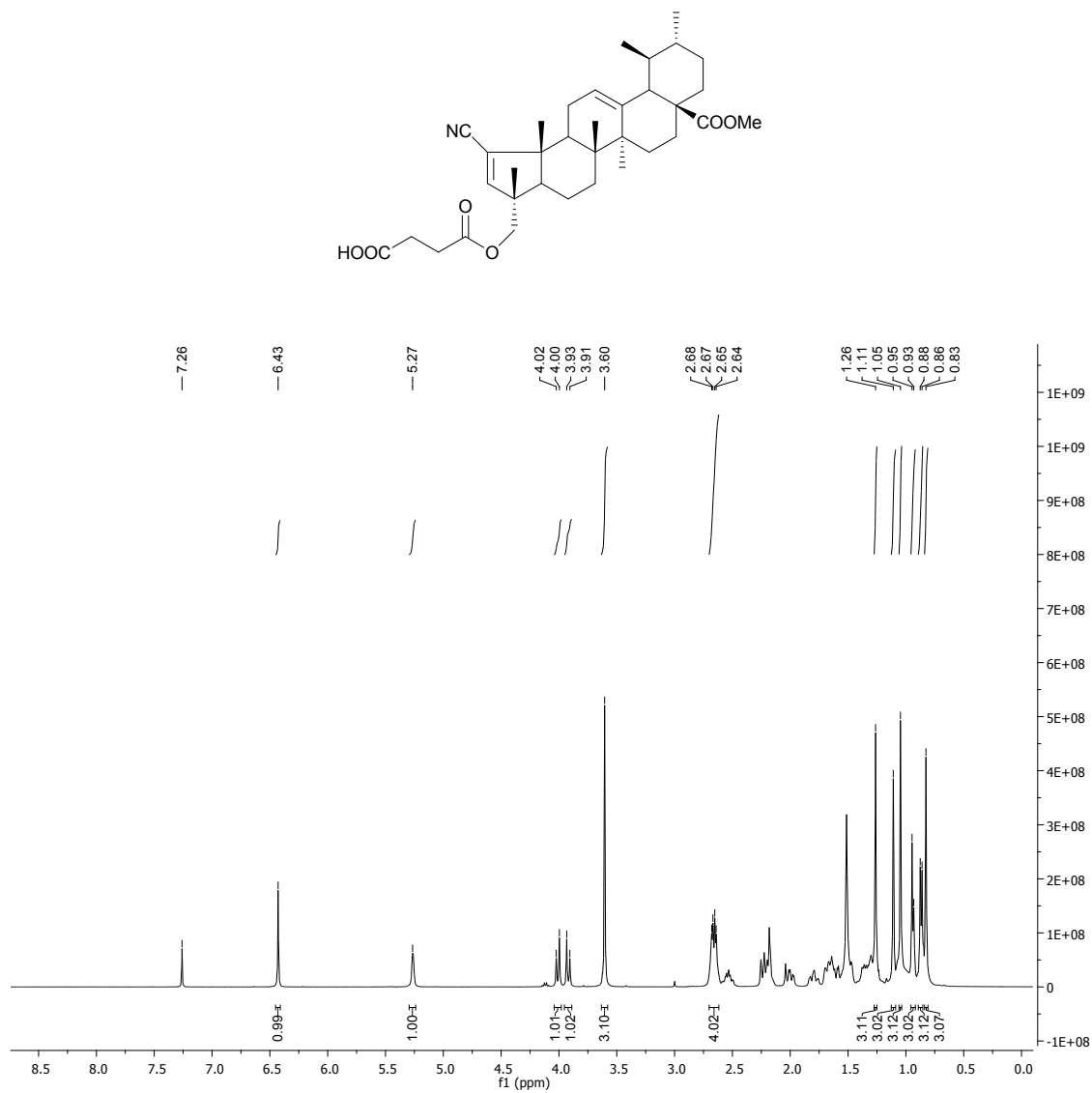


21.3 DEPT135 spectrum for compound 27 recorded in CDCl₃

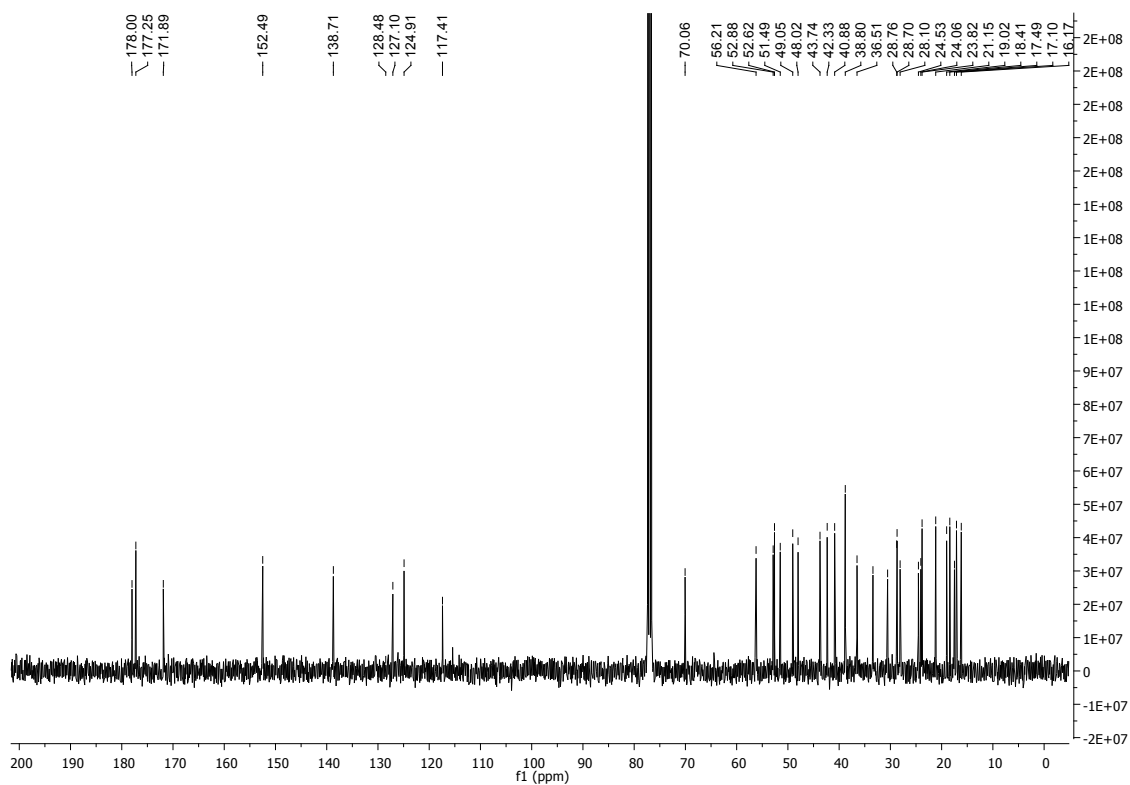
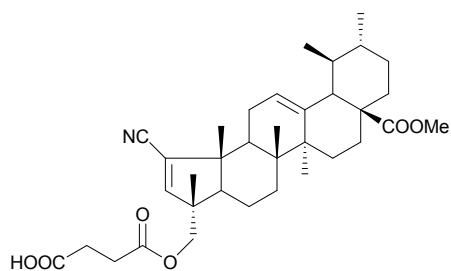


22. NMR data for compound 28

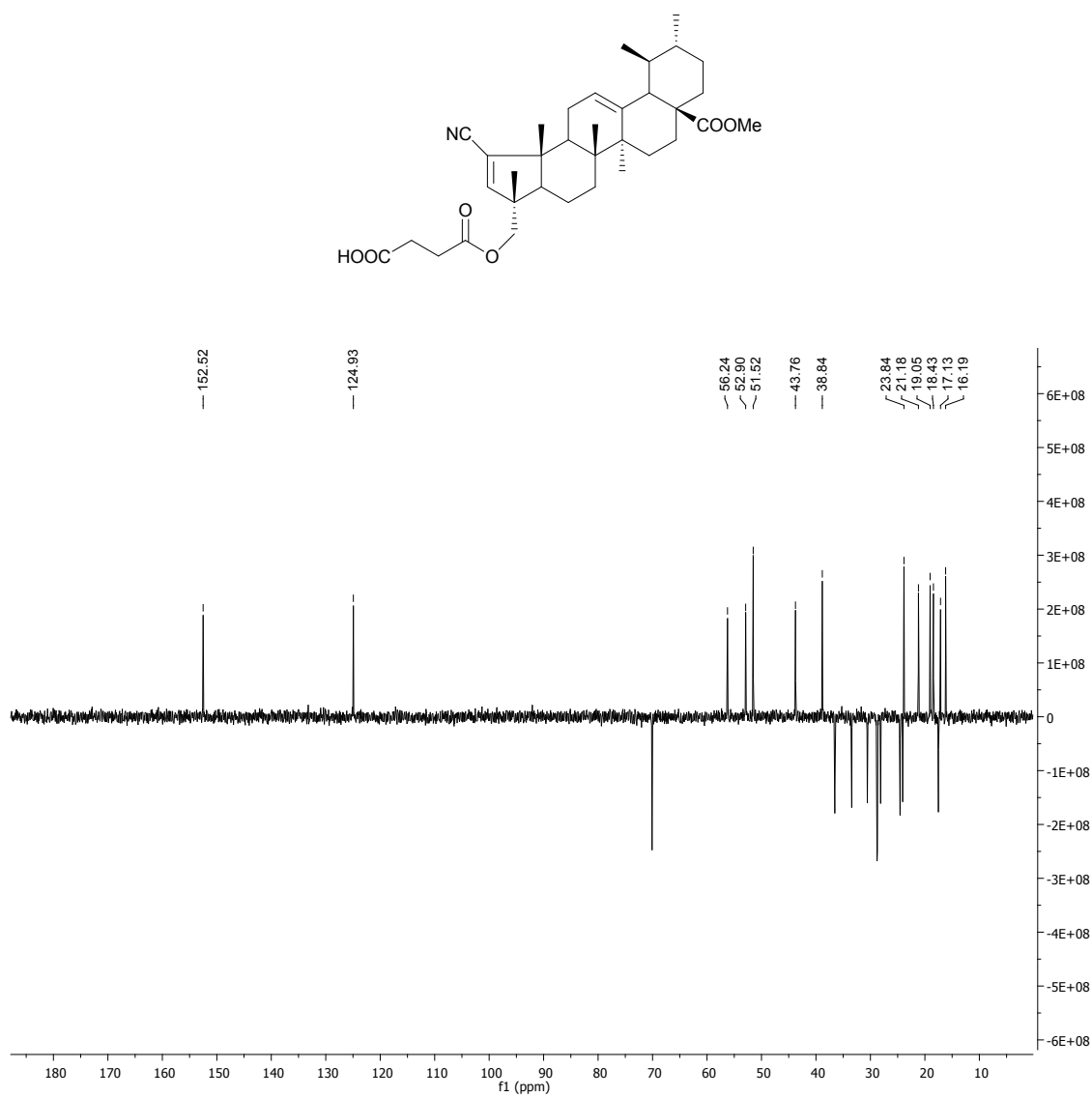
22.1 ¹H-NMR spectrum for compound 28 recorded in CDCl₃



22.2 ^{13}C -NMR spectrum for compound 28 recorded in CDCl_3

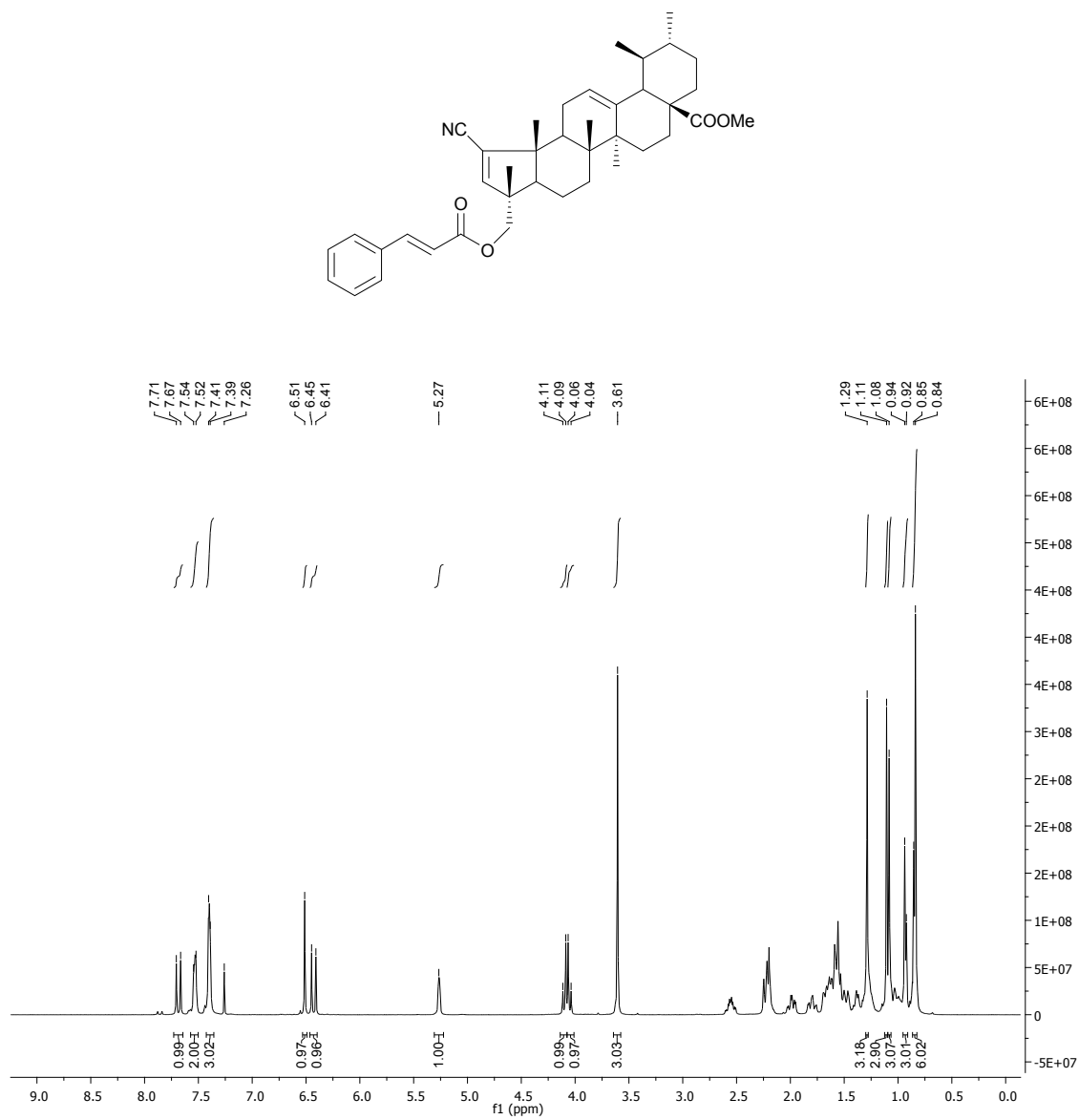


22.3 DEPT135 spectrum for compound 28 recorded in CDCl₃

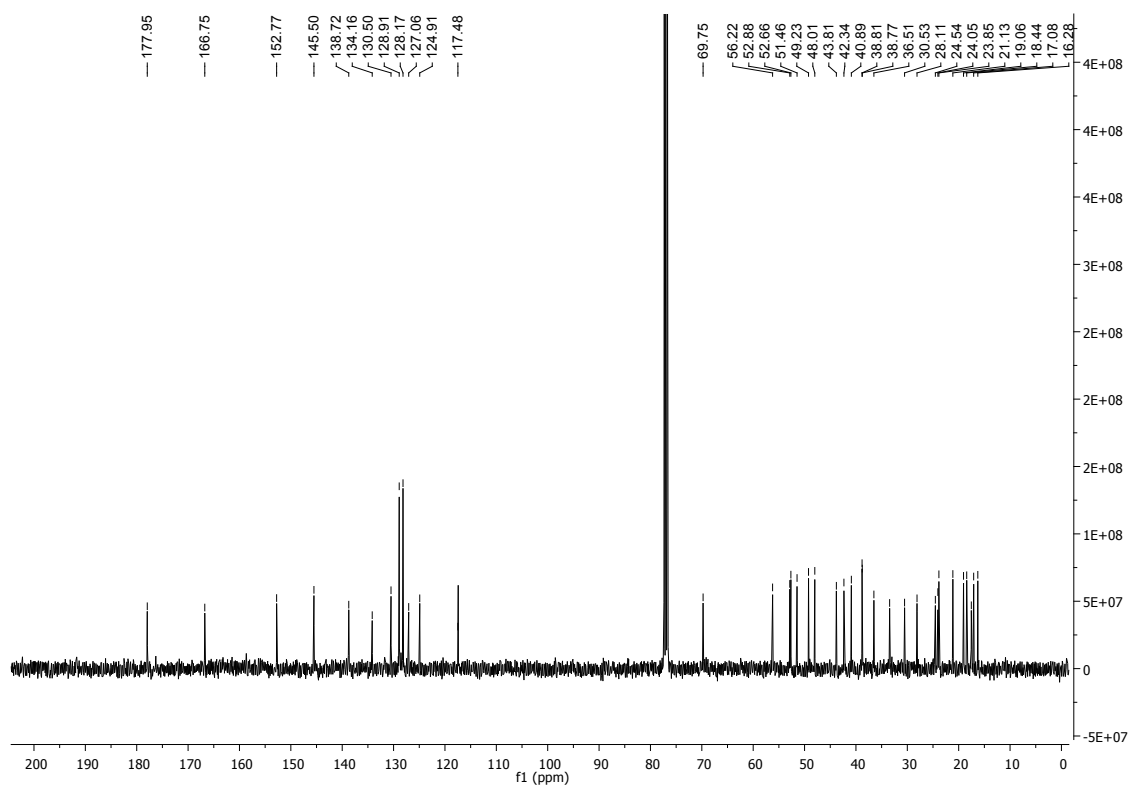
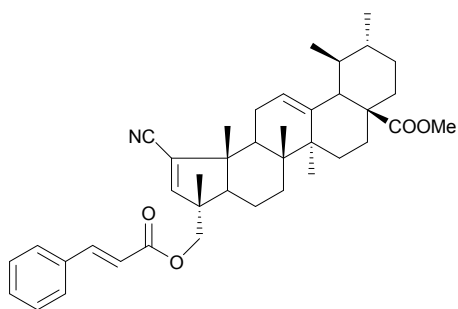


23. NMR data for compound 29

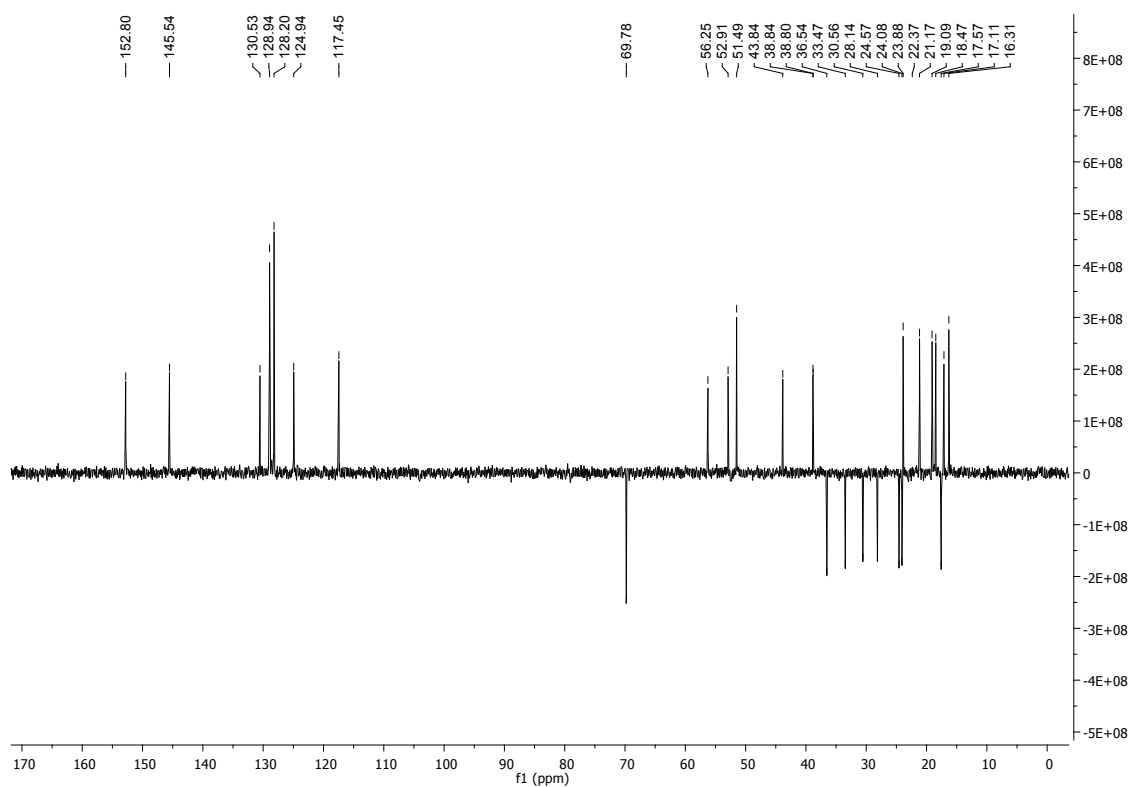
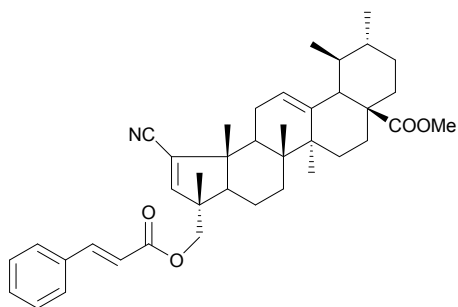
23.1 ¹H-NMR spectrum for compound 29 recorded in CDCl₃



23.2 ^{13}C -NMR spectrum for compound 29 recorded in CDCl_3

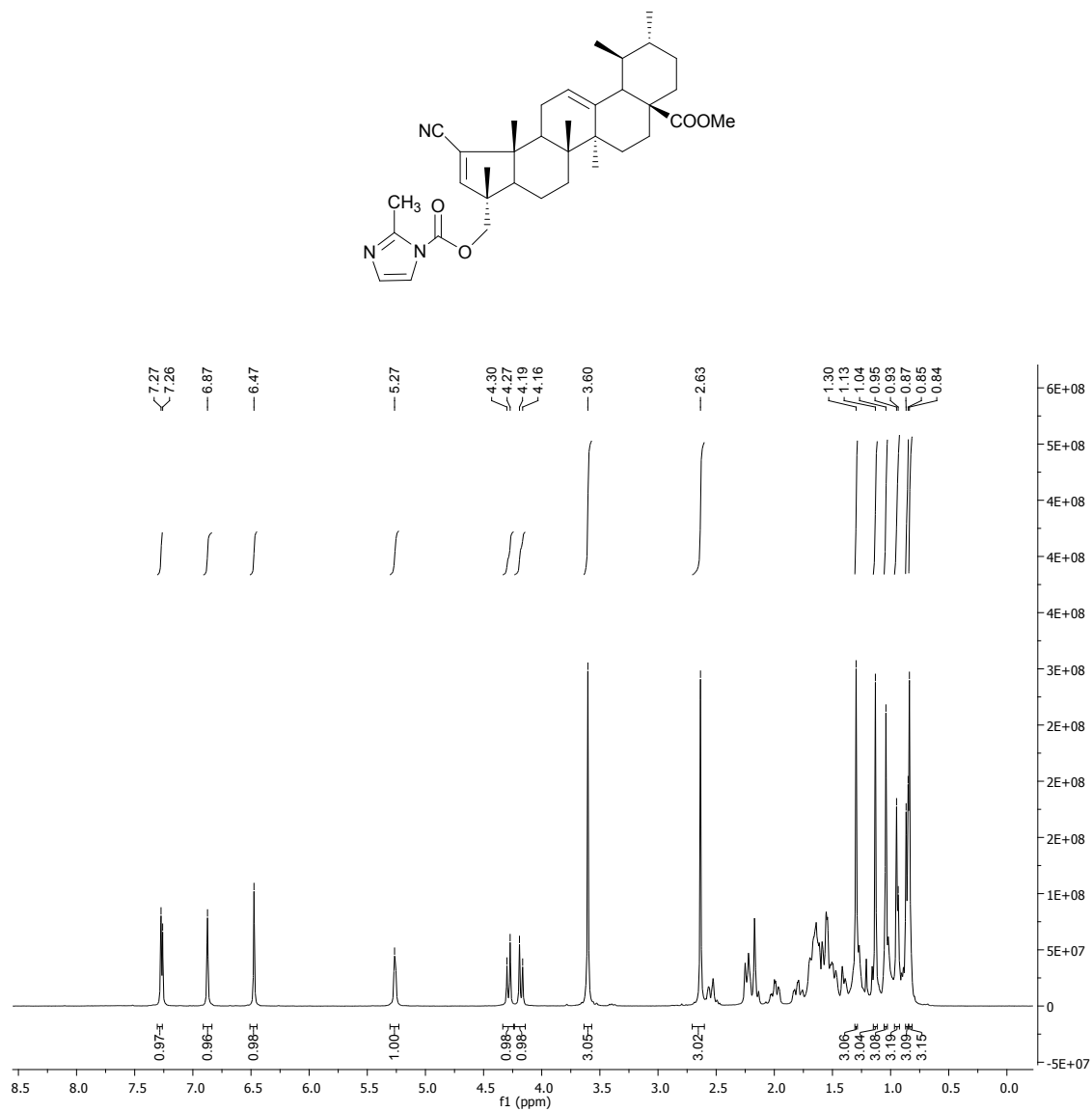


23.3 DEPT135 spectrum for compound 29 recorded in CDCl₃

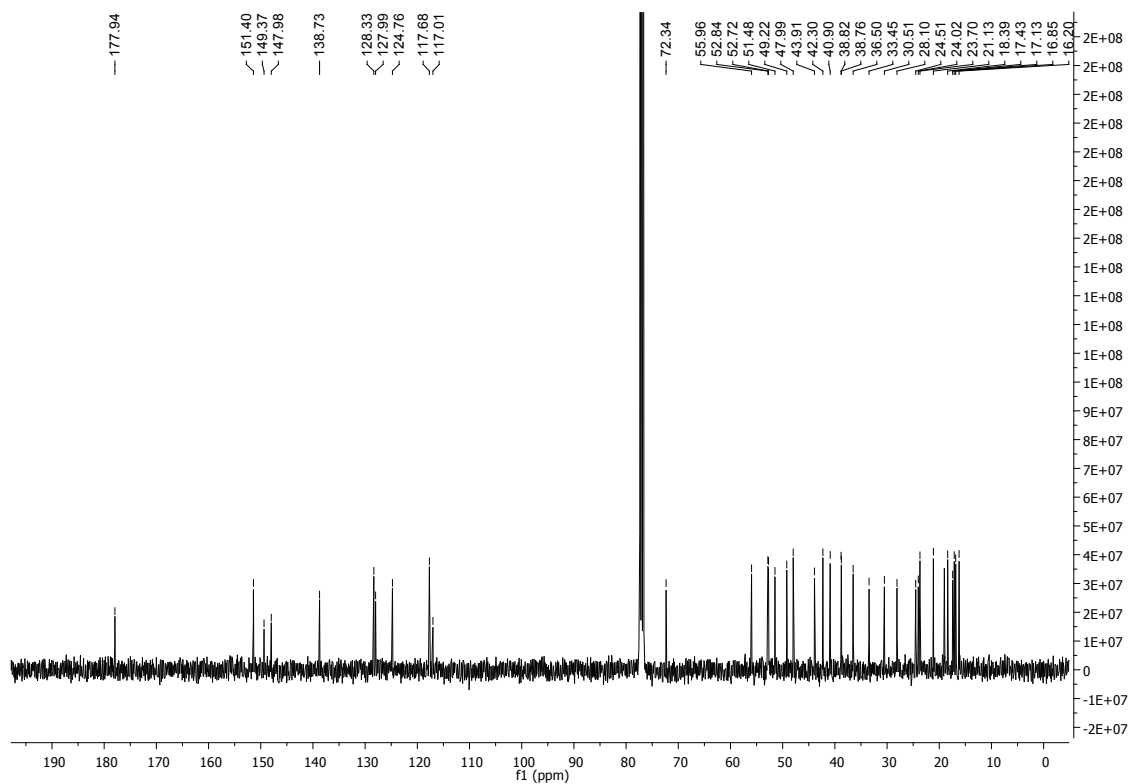
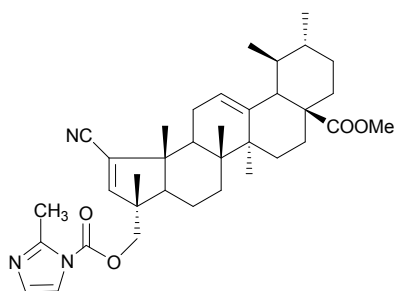


24. NMR data for compound 30

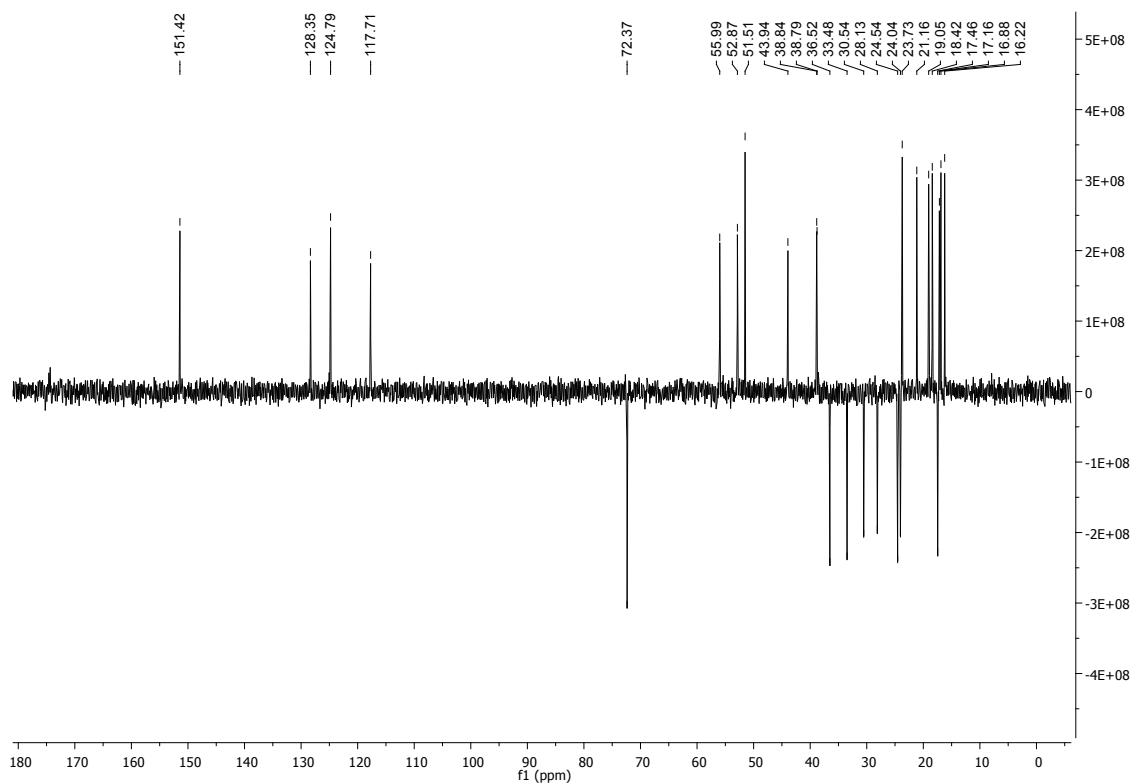
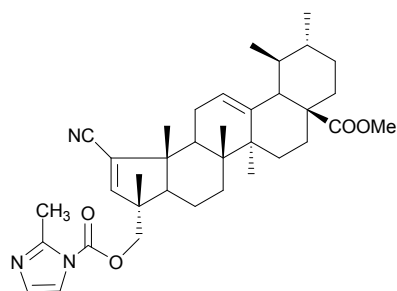
24.1 ¹H-NMR spectrum for compound 30 recorded in CDCl₃



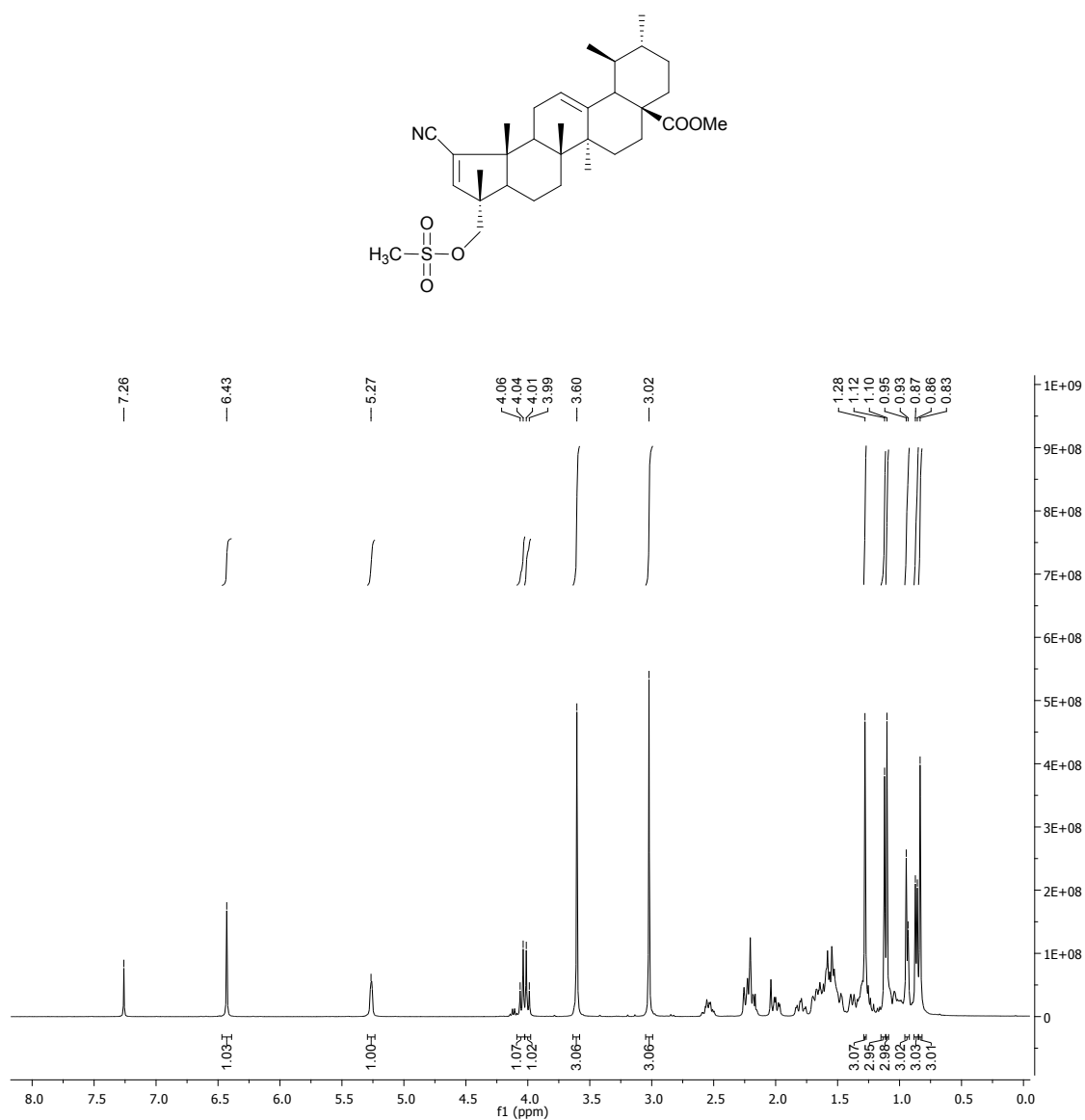
24.2 ^{13}C -NMR spectrum for compound 30 recorded in CDCl_3



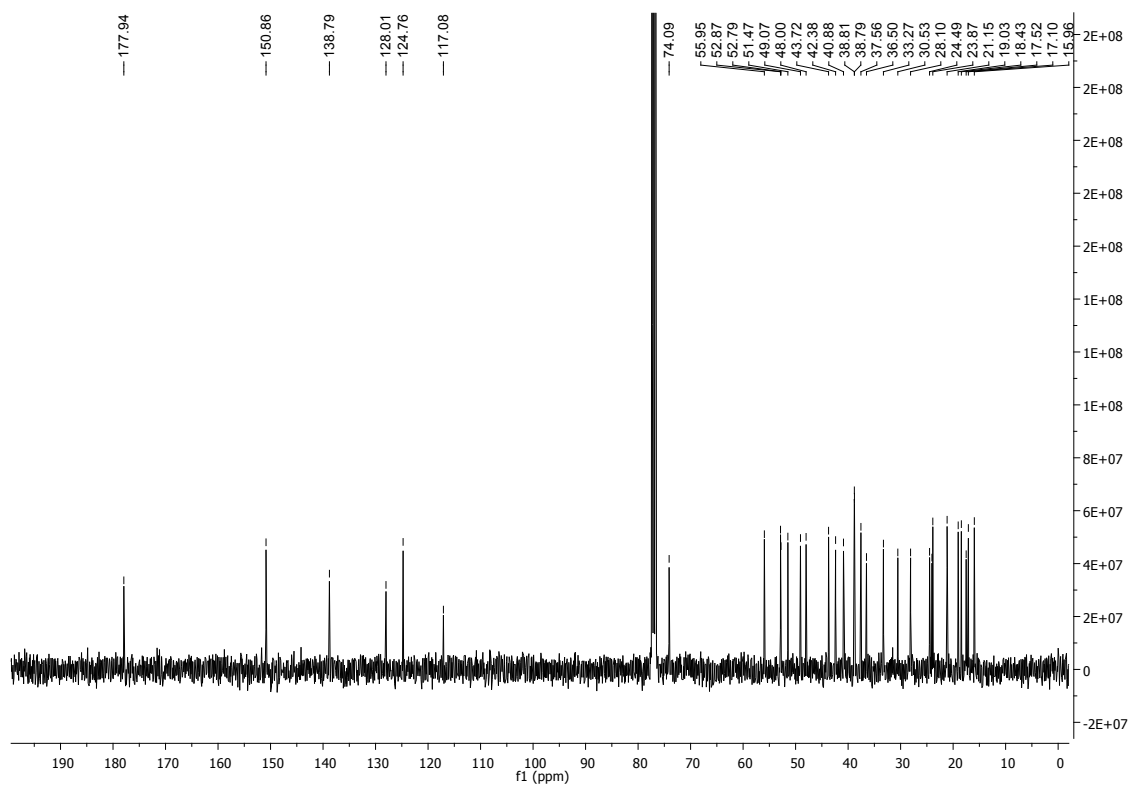
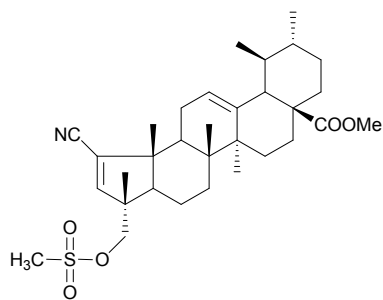
24.3 DEPT135 spectrum for compound 30 recorded in CDCl₃



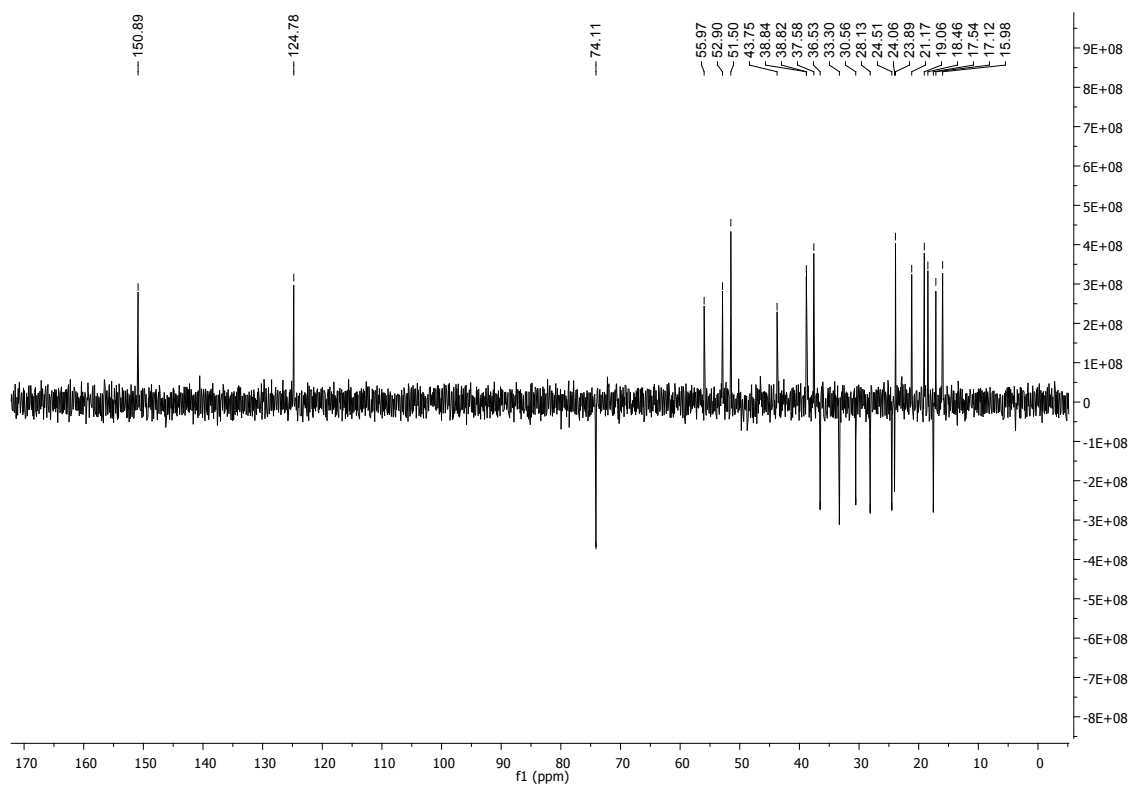
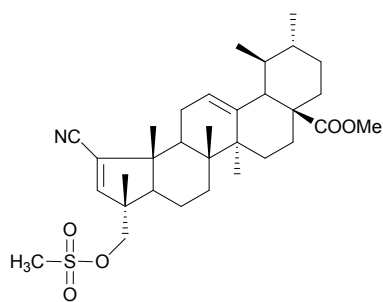
25.1 ¹H-NMR spectrum for compound 31 recorded in CDCl₃



25.2 ^{13}C -NMR spectrum for compound 31 recorded in CDCl_3

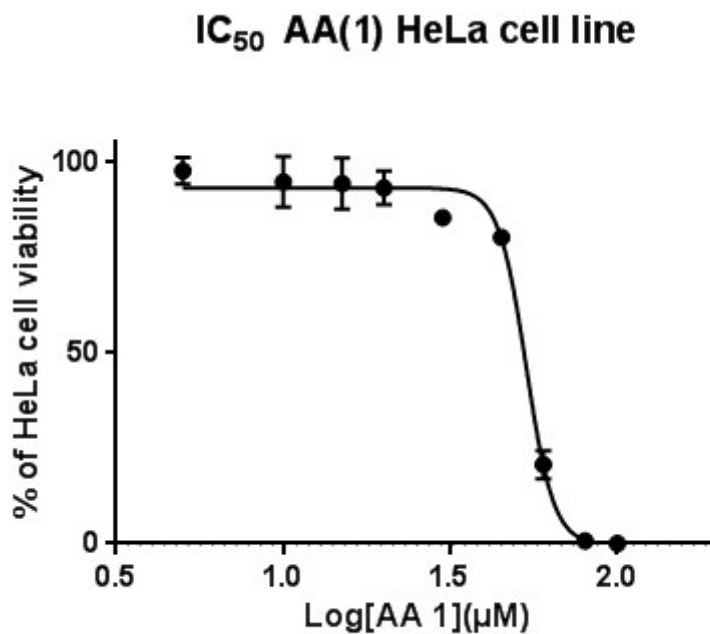


25.3 DEPT135 spectrum for compound 31 recorded in CDCl₃

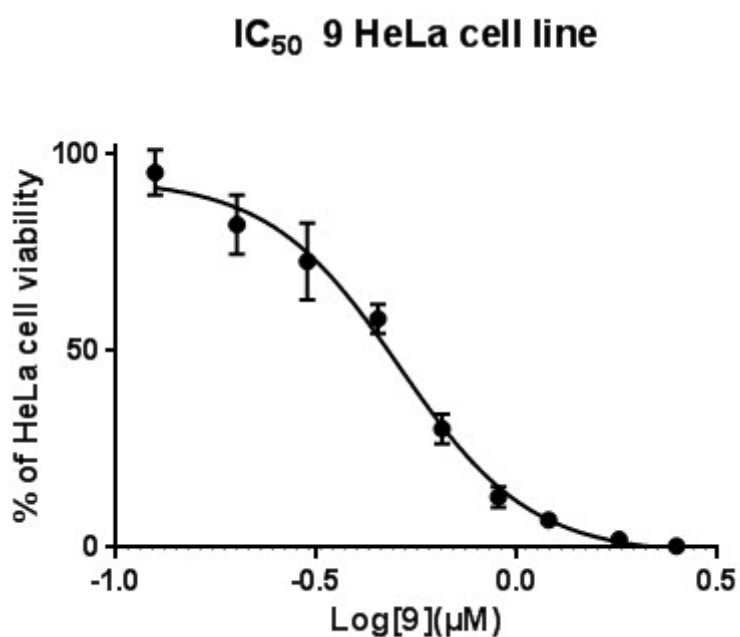


26. Dose-response curves of the antiproliferative effect of selected compounds (AA 1, 9, 14, 15, 24 and cisplatin) on HeLa cell line, after 72 hours of incubation

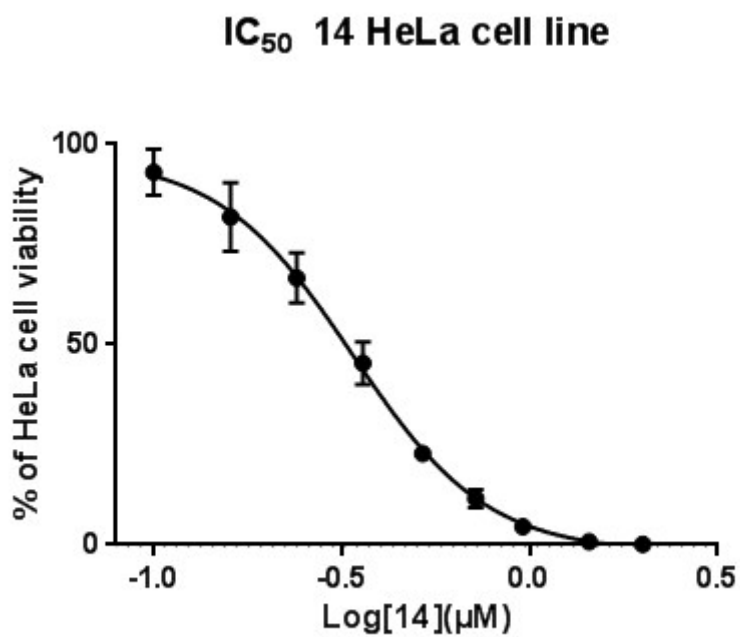
26.1 Dose-response curve of AA (1)



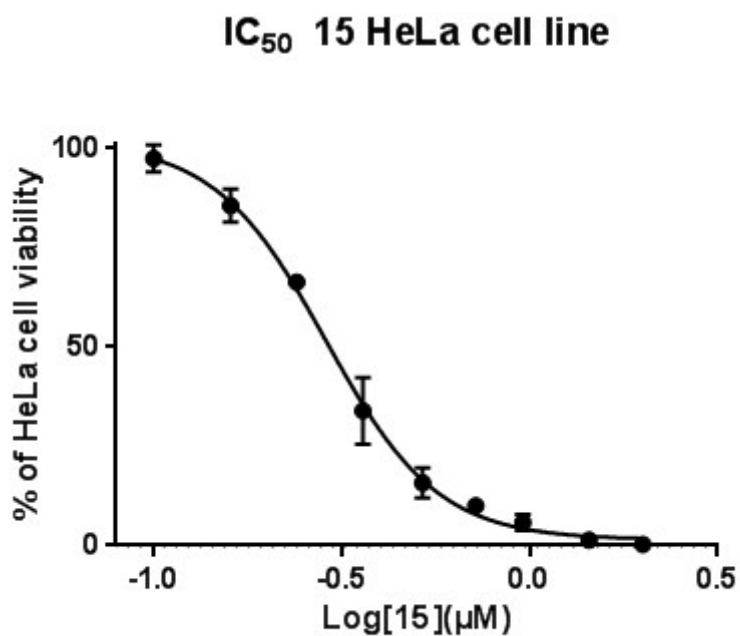
26.2 Dose-response curve of compound 9



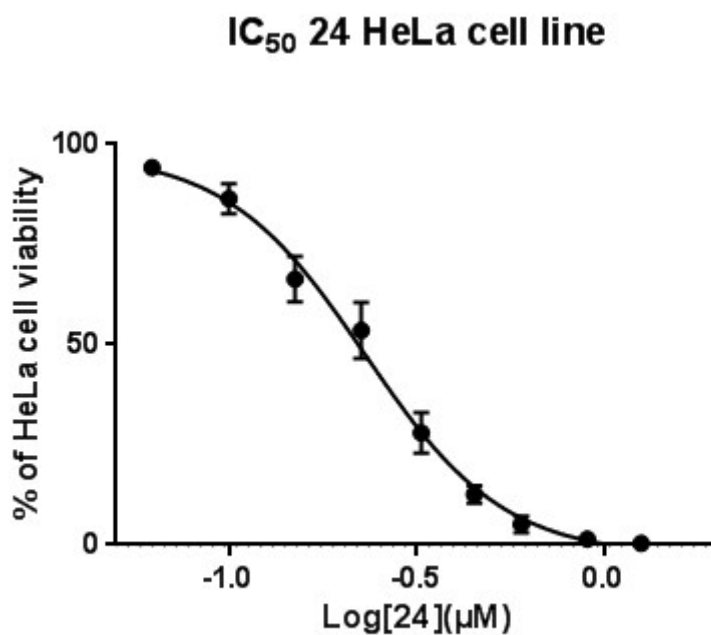
26.3 Dose-response curve of compound 14



26.4 Dose-response curve of compound 15



26.5 Dose-response curve of compound 24



26.6 Dose-response curve of Cisplatin

