Supplementary Information

Biocatalysis: Fungi mediated Selective 12β or 17β-Hydroxylation on the Basic Limonoid Skeleton

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Section A. Synthetic procedures:

2.1. Synthesis of 1,2-Dihydroazadiradione (4) and 1,2-Dihydroepoxyazadiradione (12):[1]

500 mg Azadiradione (**1**) (1.1 mmol) in 60 ml HPLC grade methanol was stirred with 45 mg 10% Pd on activated carbon under 2 atmosphere pressure of hydrogen. After 10 hours, the reaction mixture was filtered through celite bed and chromatographed on silica gel (230-400 mesh) column using a gradient mixture of methanol/dichloromethane as eluent to get 392 mg of desired 1,2-dihydroazadiradione (**4**) (0.87 mmol, yield ~ 78 %) (eluted at 0.6 % methanol in dichloromethane). Similarly, 1,2-Dihydroepoxyazadiradione (**12**) (436 mg, 0.93 mmol) was prepared from the hydrogenation of epoxyazadiradione (**10**) (500 mg, 1.07 mmol) with a yield of ~ 87 %.

2.2. Synthesis of Nimbocinol (14) and 7-Deacetylepoxyazadiradione (17):[2]

500 mg Azadiradione (**1**) (1.1. mmol), dissolved in minimum amount of methanol was added by 200 ml saturated solution of K_2CO_3 and stirred for 18 hours at room temperature. Since it was showing a complete consumption of azadiradione and formation of a more polar spot on TLC, the reaction mixture was neutralised to pH ~7.0 using 1(N) HCl and then methanol was concentrated in aspirator at 40ºC. Further, the mass was partitioned between brine solution and EtOAc. The EtOAc layer was concentrated, dried over Na_2SO_4 and 290 mg of pure nimbocinol (**14**) (0.71 mmol, yield ~ 64 %) was obtained after purification over silica gel (230-400 mesh) column at 0.8% methanol in dichloromethane. Similarly 7-deacetylepoxyazadiradione **(17)** (280 mg, 0.66 mmol) was synthesised from epoxyazadiradione **(10)** (500 mg, 1.07 mmol) with a yield of 62 %.

2.3. Synthesis of 1,2-Epoxyazadiradione (7):[3]

500 mg Azadiradione (1.1. mmol) in 65 ml methanol was stirred for 5 hours after addition of 20 drops of 5 % aqueous NaOH followed by 20 ml of 30 % H_2O_2. The reaction mixture was concentrated in vaccum at 50ºC and then extracted with dichloromethane (3 x 50 mL). The dichloromethane layer was dried over Na_2SO_4 and concentrated to get 498 mg 1,2-epoxyazadiradione (1.06 mmol, yield ~ 96 %) .

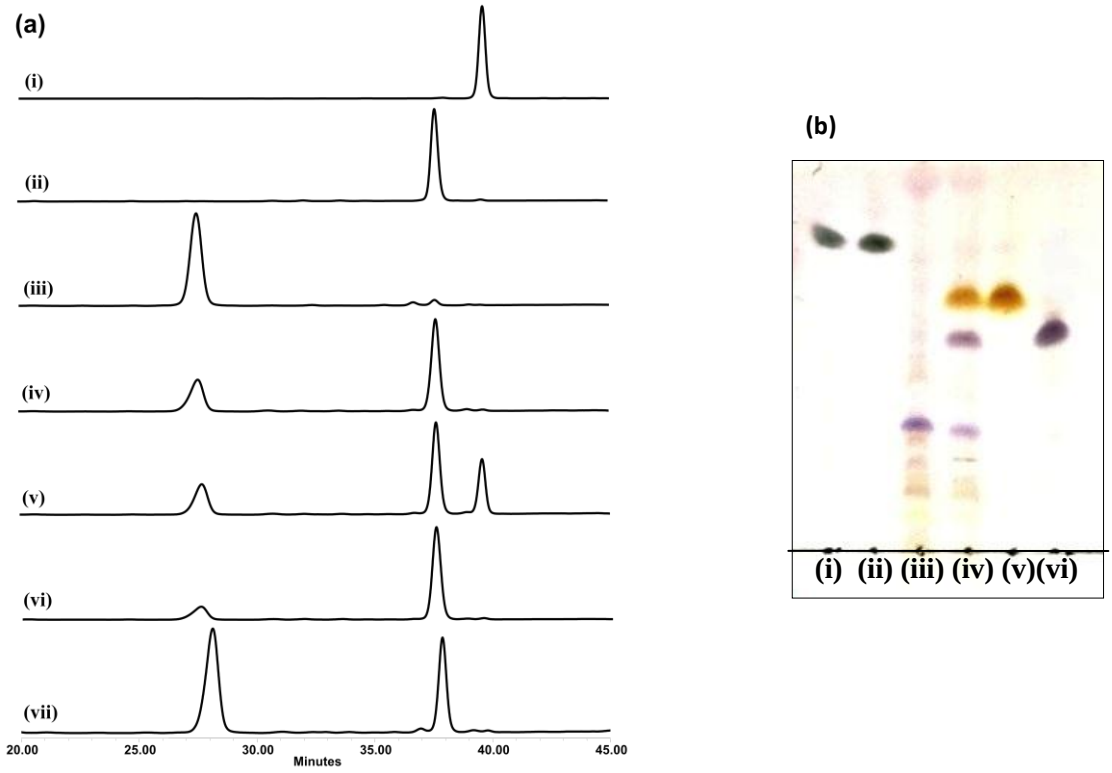
2.4. Synthesis of Gedunin (19):[1]

500 mg Epoxyazadiradione **(10)** (1.07 mmol) was taken in 10 ml HPLC grade dichloromethane and to that 615 mg (2.14 mmol) 60 % m-chloroperbenzoic acid and 180 mg (2.14 mmol) sodium bicarbonate was added sequentially. The reaction mixture was stirred at room temperature for 1 hour to observe the complete conversion of epoxyazadiradione to gedunin on TLC and then the organic reaction mixture was washed with saturated aqueous solution of sodium bicarbonate for thrice (1:3 v/v). Dichloromethane layer was further dried over Na_2SO_4, concentrated and 395 mg gedunin **(19)** (0.82 mmol, yield ~76 %) was purified from silica gel flash column chromatography using 0.4 % methanol/dichloromethane as an eluent.

References:

(1) Lavie, D.; Levy, E. C.; Jain, M. K. *Tetrahedron* **1971**, *27*, 3927-&.
(2) Siddiqui, B. S.; Rasheed, M.; Faizi, S.; Firdous; Ali, S. T.; Tariq, R. M.; Naqvi, S. *Helv. Chim. Acta* **2003**, *86*, 3342-3353.
(3) Hallur, G.; Sivramakrishnan, A.; Bhat, S. V. *J. Nat. Prod.* **2002**, *65*, 1177-1179.

Section B. HPLC and TLC profiles



ESI-Fig.1 (a) HPLC separation of the biotransformation products obtained by incubating azadiradione (**1**) with *M881* for 8 days and coinjection studies: **(i)** Standard azadiradione, **(ii)** Purified **2**, **(iii)** Purified **3**, **(iv)** Fermented azadiradione (**1**) with *M881*, **(v)** Co-injection of **1** with (iv), **(vi)** Co-injection of **2** with (iv), **(vii)** Co-injection of **3** with (iv); **(b)** Thin-layer chromatography: lane **(i)** Standard azadiradione, lane **(ii)** Substrate control, lane **(iii)** Organism control, lane **(iv)** Fermented azadiradione with *M881*, lane **(v)** Purified **2**, lane **(vi)** Purified **3**.

Analytical data of substrates and metabolites

ESI-Table 1. ^{1}H and ^{13}C NMR chemical shift values for C-12 and C-17 for substrates and metabolites

Compound	C-12		C-17	
	^{1}H δ_H(ppm)(H-12)	**^{13}C δ_C(ppm)**	**^{1}H δ_H(ppm) (H-17)**	**^{13}C δ_C(ppm)**
Azadiradione (**1**)	-[a]	30.36	3.43 (s)	60.76
17β-hydroxyazadiradione (**2**)	-[a]	22.20	×[b]	80.56
12β-hydroxyazadiradione (**3**)	4.05 (br. d, *J*= 7.3 Hz)	68.37	4.31 (s)	52.38
1,2-dihydroazadiradione (**4**)	-[a]	30.22	3.39 (s)	60.57
17β-hydroxy-1,2-dihydroazadiradione (**5**)	-[a]	22.03	×[b]	80.59
12β-hydroxy-1,2-dihydroazadiradione (**6**)	4.03 (br. d, *J*= 6.7 Hz)	68.21	4.28 (s)	52.25
1,2α-epoxyazadiradione (**7**)	-[a]	30.03	3.41 (s)	60.55
17β-hydroxy-1,2α-epoxyazadiradione (**8**)	-[a]	21.88	×[b]	80.63
12β-hydroxy-1,2α-epoxyazadiradione (**9**)	4.10 (dd, *J*= 7.3, 2.4 Hz)	68.14	4.30 (s)	52.32
Epoxyazadiradione (**10**)	-[a]	29.09	3.90 (s)	50.94
12β-hydroxyepoxyazadiradione (**11**)	3.95 (dd, *J*= 8.4, 4.9 Hz)	70.66	4.48 (s)	44.89
1,2-dihydroepoxyazadiradione (**12**)	-[a]	28.66	3.88 (s)	50.80
12β-hydroxy-1,2-dihydroepoxyazadiradione (**13**)	3.93 (m)	70.67	4.49 (s)	44.79
Nimbocinol (**14**)	-[a]	30.29	3.43 (s)	60.68
17β-hydroxynimbocinol (**15**)	-[a]	22.14	×[b]	80.76
7-Deacetylepoxyazadiradione (**17**)	-[a]	29.69	3.90 (s)	51.23
12β-hydroxy-7-deacetylepoxyazadiradione (**18**)	3.93 (m)	71.14	4.50 (s)	45.08
Gedunin (**19**)	-[a]	26.02	5.62 (s)	78.26
12β-hydroxygedunin (**20**)	3.94 (br. d, *J*= 7.6 Hz)	69.22	6.18 (s)	75.57

[a] Chemical shift is less than 2.8 ppm and appears in the overlapping region. [b] Quaternary carbon.

Azadiradione (**1**):

White solid; **$[\alpha]^{28}_{D}$** = + 29.6 (*c* 2.00, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 211 nm.

LC-ESI-MS (m/z)**:** 473.2 ($[M+Na]^+$), 451.2 ($[M+H]^+$), 391.2 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 473.2273 ($[M+Na]^+$) (Calculated: 473.2303).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 1738(Acetate carbonyl), 1702 (D ring ketone), 1668 (A ring ketone), 1598 (D ring tri-substituted double bond), 1383 (A ring geminal methyls), 1240 (Acetate C-O), 1148, 1027, 874 (Furan ring)**.**

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.48 (1H, m, H-21), 7.44 (1H, m, H-23), 7.14 (1H, d, J=10.18Hz, H-1), 6.28 (1H, m, H-22), 5.90 (1H, d, J=10.18 Hz, H-2), 5.89 (1H, s, H-15), 5.33 (1H, m, H-7), 3.43 (1H, s, H-17), 2.50 (1H, m, H-9), 2.21 (1H, m, H-5), 1.96 (3H, s,-CO$\underline{C}H_3$), 1.35 (3H, s, H-30), 1.26 (3H, s, H-19), 1.11 (3H, s, H-29), 1.10 (3H, s, H-28), 1.04 (3H, s, H-18).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 204.96 (C-16), 203.96 (C-3), 192.24 (C-14), 169.58 (C-$\underline{C}OCH_3$), 156.67 (C-1), 142.80 (C-23), 141.67 (C-21), 125.96 (C-2), 123.33 (C-15), 118.44 (C-20), 111.13 (C-22), 73.92 (C-7), 60.76 (C-17), 47.97 (C-13), 46.15 (C-5), 44.56 (C-8), 44.09 (C-4), 40.01 (C-10), 38.23 (C-9), 30.36 (C-12), 27.00 (C-28), 26.45 (C-18), 26.30 (C-30), 23.46 (C-6), 21.28 (C-29), 20.95 (C-CO$\underline{C}H_3$), 19.02 (C-19), 15.83 (C-11).

17β-Hydroxyazadiradione (**2**):

White solid; **$[\alpha]^{28}_{D}$** = + 64.7 (*c* 3.25, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 210 nm.

LC-ESI-MS (m/z)**:** 489.3 ($[M+Na]^+$), 467.3 ($[M+H]^+$), 449.2 ($[M-OH]^+$), 407.2 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 489.2254 ($[M+Na]^+$) (Calculated: 489.2252).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3448 (-OH), 1736 (Acetate carbonyl), 1706 (D ring ketone), 1665 (A ring ketone), 1598 (D ring tri-substituted double bond), 1383 (A ring geminal methyls), 1243 (Acetate C-O), 1216, 1160, 1029, 874 (Furan ring).

Position	δ_H(ppm),J(in Hz)	δ_C(ppm)	HMBC (H⟶C)	NOESY (H⟶H)
1	7.14 (d,10.04)	157.21	3,5,9,10,19	19,2,9
2	5.86 (d,10.04)	125.71	4,10	1
3	-	204.19		
4	-	43.97		
5	2.17 (m)	45.89	4,7,10,19,28,29	28,9
6	1.79-2.06 (m)	23.39		
7	5.29 (m)	74.04	5,9,8,30, -$\underline{C}OCH_3$	30,15
8	-	44.75		
9	2.3 (m)	38.62	1,8,10,11,14,19,30	18,5,1
10	-	39.85		
11	1.79-2.06 (m)	15.77		
12	β2.56 (m), α1.57(m)	22.20	β 11,13,17,18	(β) 30,12α
13	-	50.24		
14	-	193.66		
15	5.74 (s)	122.40	8,13,14,16,17	30,7
16	-	206.02		
17	-	80.56		
18	0.94 (s)	30.76	12,13,14,17	12α,9,22,21
19	1.22 (s)	19.03	1,5,9,10	29,1,30
20	-	120.17		
21	7.52 (m)	141.31	20,22,23	18
22	6.37 (m)	109.52	17,20,21,23	18,12α,23
23	7.38 (m)	142.62	20,21	22
28	1.05 (s)	26.92	29	5
29	1.07 (s)	21.15	3,4,5,28	19
30	1.34 (s)	25.11	7,8,9,14	19,12β,7,15
-CO$\underline{C}H_3$	1.91 (s)	20.9	-$\underline{C}OCH_3$	
-$\underline{C}OCH_3$	-	169.67		

12β-Hydroxyazadiradione (**3**):

White solid; $[\alpha]^{28}_D$ = - 3.3 (*c* 2.35, $CHCl_3$); **UV** (Me_2CO) λ_{max}= 210 nm.

LC-ESI-MS (m/z)**:** 489.3 ($[M+Na]^+$), 467.2 ($[M+H]^+$), 449.2($[M-OH]^+$), 407.3 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 489.2286 ($[M+Na]^+$) (Calculated: 489.2252).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3448 (-OH), 1735 (Acetate carbonyl), 1719 (A ring double bond), 1691(D ring ketone), 1670 (A ring ketone), 1600 (D ring tri-substituted double bond), 1384 (A ring geminal methyls), 1243 (Acetate C-O), 1216, 1152, 1027, 874 (Furan ring).

Position	δ_H(ppm),J(in Hz)	δ_C(ppm)	HMBC (H⟶C)	NOESY (H⟶H)
1	7.11 (d,10.38)	156.48	19,9,10,5,3	19,9,2
2	5.87 (d,10.07)	126.05	10,4	1
3	-	204.06		
4	-	44.13		
5	2.18 (m)	46.31	19,29,28,10,4,7	28,9
6	1.90 (m),2.03 (m)	23.43		
7	5.31 (m)	74.55	5,8,9,30,$\underline{C}OCH_3$	30,15
8	-	44.43		
9	2.49 (m)	37.92	19,11,10,14,30,8	18,5,1
10	-	39.76		
11	α 2.53 (m),β 1.90 (m)	28.31	(α) 9	(α) 12,11β
12	4.05 (br. d, 7.32)	68.37	18,9,11,13,14	18,11α,17,22
13	-	52.73		
14	-	189.97		
15	5.90 (m)	125.02	17,14,16,8,13	30,7
16	-	205.76		
17	4.31 (s)	52.38	18,13,12,22,20,21,16	12,22,21
18	0.99 (s)	25.22	13,12,14	12,22,9,21
19	1.24 (s)	19.26	1,9,10,5	1,29,30
20	-	118.50		
21	7.46 (m)	141.98	20,22,23	18,17
22	6.27 (m)	111.28	20,21,17	18,12,17,23
23	7.40 (m)	142.87	20,21	22
28	1.07 (s)	26.94	29	5
29	1.08 (s)	21.21	28,4,5,3	19
30	1.48 (s)	25.49	9,8,7,14	7,15,19
-$CO\underline{C}H_3$	1.94 (s)	21.02	$\underline{C}OCH_3$	
-$\underline{C}OCH_3$	-	169.58		

1,2-Dihydroazadiradione (**4**) :

White solid; **$[\alpha]^{28}_{D}$** = - 24.0 (*c* 3.10, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 209 nm.

LC-ESI-MS (m/z)**:** 475.2 ($[M+Na]^+$), 453.2 ($[M+H]^+$), 393.2 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 475.2476 ($[M+Na]^+$) (Calculated:475.2460).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 1735 (Acetate carbonyl), 1701 (D ring ketone and A ring ketone), 1598 (D ring tri-substituted double bond), 1381 (A ring geminal methyl), 1241 (Acetate C-O), 1165, 1149, 1029, 874 (Furan ring)**.**

^{1}H NMR (200 MHz, $CDCl_3$); δ(ppm): 7.45 (1H, m, H-21), 7.41 (1H, m, H-23), 6.25 (1H, m, H-22), 5.86 (1H, s, H-15), 5.29 (1H, m, H-7), 3.39 (1H, s, H-17), 2.58 (1H, m, H-2β), 2.45 (1H, m, H-2α), 2.28 (1H, m, H-9), 1.94 (3H, s, $CO\underline{C}H_3$), 1.30 (3H, s, H-30), 1.11 (3H, s, H-19), 1.05 (3H, s, H-29), 1.01 (6H, s, H-28,18).

^{13}C NMR (50 MHz, $CDCl_3$); δ(ppm): 215.90 (C-3), 205.24 (C-16), 192.87 (C-14), 169.62 (C-$\underline{C}OCH_3$), 142.66 (C-23), 141.54 (C-21), 123.23 (C-15), 118.46 (C-20), 111.10 (C-22), 74.32 (C-7), 60.57 (C-17), 48.07 (C-5), 48.03 (C-13), 46.79 (C-4), 43.85 (C-8), 42.42 (C-9), 38.35 (C-1), 37.09 (C-10), 33.72 (C-2), 30.22 (C-12), 26.17 (C-18), 25.87, 25.73 (C-28,30), 23.84 (C-6), 20.99, 20.97 (C- 29, $CO\underline{C}H_3$), 15.69 (C-11), 14.93 (C-19).

17β-Hydroxy-1,2-dihydroazadiadione (**5**) :

White solid; **$[\alpha]^{28}_{D}$** = + 44.2 (*c* 2.50, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 208 nm.

LC-ESI-MS (m/z)**:** 491.2 ($[M+Na]^+$), 469.2 ($[M+H]^+$), 451.4 ($[M-OH)^+$], 409.2 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 491.2388 ($[M+Na]^+$) (Calculated: 491.2409).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3446 (-OH), 1733 (Acetate carbonyl), 1705 (D ring ketone and A ring ketone), 1598 (D ring tri-substituted double bond), 1381 (A ring geminal methyls), 1242 (Acetate C-O), 1158, 1030, 873 (Furan ring)**.**

^{1}H NMR (500 MHz, $CDCl_3$); δ(ppm): 7.58 (1H, m, H-21),7.42 (1H, m, H-23), 6.40 (1H, m, H-22), 5.78 (1H, s, H-15), 5.31 (1H, m, H-7), 2.61 (1H, m, H-2β), 2.44 (1H, m, H-2α), 2.15

(1H, m, H-9), 1.95 (3H, s, CO<u>C</u>H$_3$), 1.33 (3H, s, H-30), 1.12 (3H, s, H-19), 1.06 (3H, s, H-29), 1.03 (3H, s, H-28), 0.97 (3H, s, H-18).

^{13}C NMR (125 MHz, CDCl$_3$); δ(ppm): 216.08 (C-3), 205.98 (C-16), 194.18 (C-14), 169.73 (C-<u>C</u>OCH$_3$), 142.78 (C-23), 141.43 (C-21), 122.53 (C-20), 120.19 (C-15), 109.53 (C-22), 80.59 (C-17), 74.49 (C-7), 50.32 (C-13), 48.03 (C-5), 46.85 (C-4), 44.22 (C-8), 42.96 (C-9), 38.47 (C-1), 37.20 (C-10), 33.78 (C-2), 30.40 (C-18), 25.80 (C-28), 24.89 (C-30), 23.96 (C-6), 22.03 (C-12), 21.03, 21.02 (C-29, CO<u>C</u>H$_3$), 15.67 (C-11), 15.14 (C-19).

<u>12β-Hydroxy-1,2-dihydroazadiadione (**6**)</u> :

White solid; **[α]$^{28}_{D}$** = - 42.6 (*c* 3.50, CHCl$_3$)**; UV** (Me$_2$CO) **λ** = 220, 201 nm.

LC-ESI-MS (m/z)**:** 491.3 ([M+Na]$^+$), 469.3 ([M+H]$^+$), 409.3 ([M-OAc]$^+$).

MALDI-TOF (m/z)**:** 491.2388 ([M+Na]$^+$) (Calculated: 491.2409).

IR (CHCl$_3$) ν_{max} (cm^{-1})**:** 3462 (-OH), 1736 (Acetate carbonyl), 1700 (D ring ketone and A ring ketone), 1600 (D ring tri-substituted double bond), 1381 (A ring geminal methyls), 1242 (Acetate C-O), 1154, 1028, 874 (Furan ring)**.**

^{1}H NMR (500 MHz, CDCl$_3$); δ(ppm): 7.46 (1H, m, H-21), 7.42 (1H, m, H-23), 6.27 (1H, m, H-22), 5.91 (1H, s, H-15), 5.30 (1H, m, H-7), 4.28 (1H, s, H-17), 4.03 (1H, br. d, J= 6.7 Hz, H-12), 2.61 (1H, m, H-2β), 2.44 (1H, m, H-2α), 2.29 (2H, m, H-9,11α), 1.95 (3H, s, CO<u>C</u>H$_3$),1.46 (3H, s, H-30), 1.11 (3H, s, H-19), 1.06 (3H, s, H-29), 1.02 (3H, s, H-28), 1.01 (3H, s, H-18).

^{13}C NMR (125 MHz, CDCl$_3$); δ(ppm): 216.09 (C-3), 206.16 (C-16), 190.70 (C-14), 169.69 (C-<u>C</u>OCH$_3$), 142.73 (C-23), 141.86 (C-21), 125.02 (C-15), 118.60 (C-20), 111.26 (C-22), 75.06 (C-7), 68.21 (C-12), 52.86 (C-13), 52.25 (C-17), 48.27 (C-5), 46.87 (C-4), 43.78 (C-8), 42.21 (C-9), 38.48 (C-1), 36.91 (C-10), 33.70 (C-2), 28.29 (C-11), 25.80 (C-28), 24.98 (C-30), 24.87 (C-18), 23.88 (C-6), 21.02(C- CO<u>C</u>H$_3$), 20.93 (C- 29), 15.23 (C-19).

1,2α-Epoxyazadiradione (**7**) :

White solid; **$[\alpha]^{28}_{D}$** = + 46.8 (*c* 2.20, $CHCl_3$)**; UV** (Me_2CO) **λ** = 218, 207 nm.

LC-ESI-MS (m/z)**:** 489.3 ($[M+Na]^+$), 467.1 ($[M+H]^+$), 407.2 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 489.2254 ($[M+Na]^+$) (Calculated: 489.2252).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 1735 (Acetate carbonyl), 1701 (D ring ketone and A ring ketone), 1599 (D ring tri-substituted double bond), 1381 (A ring geminal methyls), 1240 (Acetate C-O), 1165, 1036, 874 (Furan ring)**.**

^{1}H NMR (200 MHz, $CDCl_3$); δ(ppm): 7.45 (1H, m, H-21), 7.42 (1H, m, H-23), 6.26 (1H, m, H-22), 5.87 (1H, s, H-15), 5.27 (1H, m, H-7), 3.58 (1H, d, J=4.55 Hz, H-1), 3.41 (1H, s, H-17), 3.41 (1H, d, J=4.55 Hz, H-2), 2.75 (1H, m, H-9), 2.43 (1H, dd, J=11.87, 4.8 Hz, H-5), 1.98 (3H, s, $CO\underline{C}H_3$), 1.29 (3H, s, H-30), 1.05, 1.04 (9H, s, H-18,19,28), 0.99 (3H, s, H-29).

^{13}C NMR (50 MHz, $CDCl_3$); δ(ppm): 211.22 (C-3), 205.28 (C-16), 192.31 (C-14), 169.82 (C-$\underline{C}OCH_3$), 142.72 (C-23), 141.54 (C-21), 123.14 (C-15), 118.31 (C-20), 111.06 (C-22), 73.64 (C-7), 62.72 (C-1), 60.55 (C-17), 56.41 (C-2), 47.99 (C-13), 44.07,44.02 (C-8,4), 38.77 (C-10), 38.66 (C-5), 36.80 (C-9), 30.03 (C-12), 27.36 (C-28), 26.17,25.99 (C-30,18), 23.10 (C-6), 20.95 (C- $CO\underline{C}H_3$), 20.65 (C-29), 16.03 (C-11), 14.91 (C-19).

17β-Hydroxy-1,2α-Epoxyazadiradione (**8**) :

White solid; **$[\alpha]^{28}_{D}$** = + 132.4 (*c* 1.50, $CHCl_3$)**; UV** (Me_2CO) **λ** = 220, 204 nm.

LC-ESI-MS (m/z)**:** 505.2 ($[M+Na]^+$), 483.2 ($[M+H]^+$), 465.4 ($[M-OH]^+$), 423.2 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 505.2164 ($[M+Na]^+$) (Calculated: 505.2202).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3448 (-OH), 1738 (Acetate carbonyl), 1701 (D ring ketone and A ring ketone), 1598 (D ring tri-substituted double bond), 1381 (A ring geminal methyls), 1242 (Acetate C-O), 1159, 1033, 874 (Furan ring)**.**

^{1}H NMR (500 MHz, $CDCl_3$); δ(ppm): 7.60 (1H, m, H-21), 7.43 (1H, m, H-23), 6.41 (1H, m, H-22), 5.78 (1H, s, H-15), 5.29 (1H, m, H-7), 3.61 (1H, d, J=4.58 Hz, H-1), 3.43 (1H, d, J=4.58 Hz, H-2), 2.62 (1H, m, H-9), 2.55 (1H, m, H-12β), 2.46 (1H, m, H-5), 1.65 (1H, m, H-

12α), 1.99 (3H, s, CO<u>C</u>H$_3$), 1.34 (3H, s, H-30), 1.07 (3H, s, H-19), 1.06 (3H, s, H-18), 1.03 (3H, s, H-28), 1.01 (3H, s, H-29).

^{13}C NMR (125 MHz, CDCl$_3$); δ(ppm): 211.24 (C-3), 205.80 (C-16), 193.31 (C-14), 169.84 (C-<u>C</u>OCH$_3$), 142.88 (C-23), 141.50 (C-21), 122.44 (C-20), 120.09 (C-15), 109.50 (C-22), 80.63 (C-17), 73.83 (C-7), 62.90 (C-1), 56.55 (C-2), 50.28 (C-13), 44.38,44.17 (C-4,8), 38.88 (C-10), 38.63 (C-5), 37.29 (C-9), 30.39 (C-18), 27.45 (C-28), 25.06 (C-30), 23.24 (C-6), 21.88 (C-12), 21.03 (C- CO<u>C</u>H$_3$), 20.73 (C-29), 16.04 (C-11), 15.07 (C-19).

<u>12β-Hydroxy-1,2α-Epoxyazadiradione (**9**)</u> :

White solid; **[α]$^{28}_{D}$** = + 21.7 (*c* 2.50, CHCl$_3$)**; UV** (Me$_2$CO) **λ** = 217, 206 nm.

LC-ESI-MS (m/z)**:** 505.4 ([M+Na]$^+$), 483.2 ([M+H]$^+$), 423.2 ([M-OAc]$^+$).

MALDI-TOF (m/z)**:** 505.2164 ([M+Na]$^+$) (Calculated: 505.2202).

IR (CHCl$_3$) ν_{max} (cm^{-1})**:** 3482 (-OH), 1735 (Acetate carbonyl), 1701 (D ring ketone and A ring ketone), 1600 (D ring tri-substituted double bond), 1381 (A ring geminal methyls), 1243 (Acetate C-O), 1154, 1035, 874 (Furan ring)**.**

^{1}H NMR (500 MHz, CDCl$_3$); δ(ppm): 7.48 (1H, m, H-21), 7.44 (1H, m, H-23), 6.28 (1H, m, H-22), 5.93 (1H, s, H-15), 5.28 (1H, m, H-7), 4.30 (1H, s, H-17), 4.10 (1H, dd, J= 7.3, 2.4 Hz, H-12), 3.55 (1H, d, J=4.58 Hz, H-1), 3.42 (1H, d, J=4.58 Hz, H-2), 2.78 (1H, m, H-9), 2.59 (1H, m, H-11α), 2.45 (1H, m, H-5), 1.99 (3H, s, CO<u>C</u>H$_3$), 1.47 (3H, s, H-30), 1.09 (3H, s, H-19), 1.07 (3H, s, H-18), 1.05 (3H, s, H-28), 1.01 (3H, s, H-29).

^{13}C NMR (125 MHz, CDCl$_3$); δ(ppm): 211.15 (C-3), 205.88 (C-16), 189.87 (C-14), 169.79 (C-<u>C</u>OCH$_3$), 142.86 (C-23), 141.89 (C-21), 124.99 (C-15), 118.50 (C-20), 111.23 (C-22), 74.41 (C-7), 68.14 (C-12), 62.66 (C-1), 56.46 (C-2), 52.82 (C-13), 52.32 (C-17), 44.19, 44.01 (C-4, 8), 38.86 (C-5), 38.64 (C-10), 36.75 (C-9), 28.61 (C-11), 27.38 (C-28), 25.24 (C-30), 24.92 (C-18), 23.19 (C-6), 21.03 (C- CO<u>C</u>H$_3$), 20.69 (C-29), 15.17 (C-19).

Epoxyazadiradione (**10**):

White solid; **$[\alpha]^{28}_{D}$** = + 31.1 (*c* 2.40, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 209 nm.

LC-ESI-MS (m/z)**:** 489.2 ($[M+Na]^+$), 467.3 ($[M+H]^+$), 407.3 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 489.2249 ($[M+Na]^+$) (Calculated: 489.2252).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 1751 (Acetate carbonyl), 1734 (D ring ketone), 1670 (A ring ketone), 1375 (A ring geminal methyls), 1239 (Acetate C-O), 1129, 1029, 875 (Furan ring).

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.56 (1H, m, H-21), 7.40 (1H, m, H-23), 7.17 (1H, d, J=10.04 Hz, H-1), 6.24 (1H, m, H-22), 5.88 (1H, d, J=10.04 Hz, H-2), 4.73 (1H, m, H-7), 3.90 (1H, s, H-17), 3.41 (1H, s, H-15), 2.63 (1H, m, H-9), 2.20-2.15 (2H, m, H-5,12), 2.03 (3H, s, -CO$\underline{C}H_3$), 1.22 (3H, s, H-19), 1.21 (3H, s, H-30), 1.08 (3H, s, H-29), 1.07 (3H, s, H-28), 1.04 (3H, s, H-18).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 208.40 (C-16), 204.21 (C-3), 169.74 (C-$\underline{C}OCH_3$), 157.47 (C-1), 142.43 (C-23), 141.53 (C-21), 125.76 (C-2), 116.51 (C-20), 110.87 (C-22), 73.63 (C-7), 72.54 (C-14), 57.18 (C-15), 50.94 (C-17), 46.67 (C-5), 44.22 (C-4), 43.12 (C-8), 42.53 (C-13), 39.69 (C-9), 39.65 (C-10), 29.09 (C-12), 27.02 (C-28), 24.82 (C-18), 24.20 (C-6), 21.26 (C-CO$\underline{C}H_3$), 20.99 (C-29), 19.82 (C-19), 19.39 (C-30), 16.06 (C-11).

12β-Hydroxyepoxyazadiradione (**11**):

White solid; **$[\alpha]^{28}_{D}$** = + 16.4 (*c* 2.60, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 209 nm.

LC-ESI-MS (m/z)**:** 505.4 ($[M+Na]^+$), 483.3 ($[M+H]^+$), 423.4 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 505.2195 ($[M+Na]^+$) (Calculated: 505.2202).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3481 (-OH), 1749 (Acetate carbonyl and D ring ketone), 1669 (A ring ketone), 1376 (A ring geminal methyls), 1239 (Acetate C-O), 1133, 1026, 875 (Furan ring).

Position	δ_H(ppm),J(in Hz)	δ_C(ppm)	HMBC (H⟶C)	NOESY (H⟶H)
1	7.13 (d,10.3)	157.08	3,5,10	19,11α,2
2	5.88 (d,10.0)	125.87	4,10	1
3	-	204.22		
4	-	44.18		
5	2.14 (m)	46.59	4,9,28	9
6	1.96-1.85 (m)	24.18		
7	4.72 (m)	73.49	5,9, -$\underline{C}OCH_3$	15,6,30
8	-	43.00		
9	2.52 (m)	39.27	1,8,10,12,30	18,5
10	-	39.35		
11	α2.59 (m),β1.82 (m)	29.04		α 1,12
12	3.95 (dd,8.4,4.9)	70.66	13,14,18	18,11α,17,22
13	-	47.32		
14	-	71.24		
15	3.31 (s)	54.79	16,17	18,30,17,7, -CO$\underline{C}H_3$
16	-	208.09		
17	4.48 (s)	44.89	12,13,16,18,20,21,23	21,22,12,15,18
18	1.02 (s)	23.26	13,14,17	21,22,17,12,15,9, -CO$\underline{C}H_3$
19	1.21 (s)	19.85	1,5,10	1
20	-	116.40		
21	7.61 (m)	141.98	20,22,23	17,18
22	6.35 (m)	111.18	20,21	23,17,12,18
23	7.38 (m)	142.37	20,21	22
28	1.07 (s)	26.96	29	
29	1.08 (s)	20.88	28,3,4,5	
30	1.26 (s)	19.28	9,7,8,14	7,15
-CO$\underline{C}H_3$	2.02 (s)	21.23	-$\underline{C}OCH_3$	18,15
-$\underline{C}OCH_3$	-	169.69		

1,2-Dihydroepoxyazadiradione (**12**) :

White solid; **$[\alpha]^{28}_D$** = + 0.94 (*c* 2.40, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 218, 205 nm.

LC-ESI-MS (m/z)**:** 491.3 ($[M+Na]^+$), 469.2 ($[M+H]^+$), 409.4 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 491.2310 ($[M+Na]^+$) (Calculated: 491.2409).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 1751 (Acetate carbonyl), 1734 (D ring ketone), 1701 (A ring ketone), 1375 (A ring geminal methyls), 1240 (Acetate C-O), 1031, 875 (Furan ring).

^{1}H NMR (500 MHz, $CDCl_3$); δ(ppm): 7.56 (1H, m, H-21), 7.40 (1H, m, H-23), 6.24 (1H, m, H-22), 4.71 (1H, m, H-7), 3.88 (1H, s, H-17), 3.40 (1H, s, H-15), 2.60 (1H, m, H-2β), 2.45-2.50 (2H, m, H-2α and 9), 2.05 (3H, s, -CO$\underline{C}H_3$), 1.18 (3H, s, H-30), 1.09 (3H, s, H-19), 1.05 (3H, s, H-29), 1.04 (3H, s, H-28), 1.02 (3H, s, H-18).

^{13}C NMR (125 MHz, $CDCl_3$); δ(ppm): 216.14 (C-3), 208.74 (C-16), 169.85 (C-$\underline{C}OCH_3$), 142.39 (C-23), 141.55 (C-21), 116.64 (C-20), 110.96 (C-22), 74.08 (C-7), 72.68 (C-14), 57.40 (C-15), 50.80 (C-17), 48.30 (C-5), 46.83 (C-4), 43.99 (C-9), 42.69,42.24 (C-8,13), 39.34 (C-1), 37.10 (C-10), 33.75 (C-2), 28.66 (C-12), 25.99 (C-28), 24.58 (C-6), 24.34 (C-18), 21.34 (C- CO$\underline{C}H_3$), 20.69 (C-29), 19.07 (C-30), 16.19 (C-19), 15.98 (C-11).

12β-Hydroxy-1,2-Dihydroepoxyazadiradione (**13**) :

White solid; **$[\alpha]^{28}_{D}$** = - 14.1 (*c* 1.00, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 220, 204 nm.

LC-ESI-MS (m/z)**:** 507.3 ($[M+Na]^+$), 485.3 ($[M+H]^+$), 425.4 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 507.2367 ($[M+Na]^+$) (Calculated: 507.2358).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3502 (-OH), 1748 (Acetate carbonyl), 1736 (D ring ketone), 1714 (A ring ketone), 1377 (A ring geminal methyls), 1240 (Acetate C-O), 1026, 875 (Furan ring).

^{1}H NMR (500 MHz, $CDCl_3$); δ(ppm): 7.63 (1H, m, H-21), 7.41 (1H, m, H-23), 6.35 (1H, m, H-22), 4.72 (1H, m, H-7), 4.49 (1H, s, H-17), 3.93 (1H, m, H-12), 3.32 (1H, s, H-15), 2.61 (1H, m, H-2β), 2.48 (1H, m, H-2α), 2.37-2.43 (2H, m, H-11α and 9), 2.05 (3H, s, -CO$\underline{C}H_3$), 1.26 (3H, s, H-30), 1.10 (3H, s, H-19), 1.05 (3H, s, H-29), 1.04 (3H, s, H-28), 1.02 (3H, s,H-18).

^{13}C NMR (125 MHz, $CDCl_3$); δ(ppm): 215.83 (C-3), 208.10 (C-16), 169.74 (C- $\underline{C}OCH_3$), 142.46 (C-23), 142.02 (C-21), 116.42 (C-20), 111.18 (C-22), 73.92 (C-7), 71.23 (C-14), 70.67 (C-12), 54.91 (C-15), 48.21 (C-5), 47.24 (C-13), 46.79 (C-4), 44.79 (C-17), 43.78 (C-9), 42.14 (C-8), 39.26 (C-1), 36.89 (C-10), 33.63 (C-2), 29.25 (C-11), 25.97 (C-28), 24.59 (C-6), 22.79 (C-18), 21.34 (C- CO$\underline{C}H_3$), 20.62 (C-29), 18.97 (C-30), 16.32 (C-19).

Nimbocinol (**14**):

White solid; **$[\alpha]^{28}_D$** = + 0.63 (*c* 2.15, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 215, 206 nm.

LC-ESI-MS (m/z)**:** 431.2 ($[M+Na]^+$), 409.1 ($[M+H]^+$), 391.4 ($[M-OH]^+$).

MALDI-TOF (m/z)**:** 431.2209 ($[M+Na]^+$) (Calculated: 431.2198).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3481 (-OH)**,** 1697 (D ring ketone), 1668 (A ring ketone), 1597 (D ring tri-substituted double bond), 1382 (A ring geminal methyls), 1149, 1027, 874 (Furan ring)**.**

^{1}H NMR (200 MHz, $CDCl_3$); δ(ppm): 7.45 (1H, m, H-21), 7.41 (1H, m, H-23), 7.12 (1H, d, J=10.23 Hz, H-1), 6.25 (1H, m, H-22), 6.00 (1H, s, H-15), 5.85 (1H, d, J=10.23 Hz, H-2), 4.18 (1H, m, H-7), 3.43 (1H, s, H-17), 2.56 (1H, m, H-9), 2.45 (1H, m, H-5), 1.27 (3H, s, H-30), 1.21 (3H, s, H-19), 1.15 (3H, s, H-29), 1.10 (3H, s, H-28), 1.02 (3H, s, H-18).

^{13}C NMR (50 MHz, $CDCl_3$); δ(ppm): 205.56 (C-16), 204.74 (C-3), 194.32 (C-14), 157.35 (C-1), 142.71 (C-23), 141.51 (C-21), 125.67 (C-2), 123.34 (C-15), 118.35 (C-20), 111.10 (C-22), 71.51 (C-7), 60.68 (C-17), 48.20 (C-13), 46.47 (C-8), 44.42 (C-5), 44.12 (C-4), 40.10 (C-10), 36.37 (C-9), 30.29 (C-12), 26.99 (C-28), 26.59 (C-30), 25.91 (C-18), 25.39 (C-6), 21.39 (C-29), 19.03 (C-19), 15.61 (C-11).

17β-Hydroxynimbocinol (**15**):

White solid; **$[\alpha]^{28}_D$** = + 54.1 (*c* 3.50, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 220, 201 nm.

LC-ESI-MS (m/z)**:** 447.4 ($[M+Na]^+$), 425.3 ($[M+H]^+$), 407.3 ($[M-OH]^+$).

MALDI-TOF (m/z)**:** 447.2223 ($[M+Na]^+$) (Calculated: 447.2147).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3436 (-OH)**,** 1698 (D ring ketone), 1664 (A ring ketone), 1595 (D ring tri-substituted double bond), 1383 (A ring geminal methyls), 1159, 1035, 873 (Furan ring)**.**

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.59 (1H, m, H-21), 7.43 (1H, m, H-23), 7.15 (1H, d, J=10.23 Hz, H-1), 6.41 (1H, m, H-22), 5.91 (1H, s, H-15), 5.87 (1H, d, J=10.23 Hz, H-2),

4.19 (1H, m, H-7), 1.31 (3H, s, H-30), 1.23 (3H, s, H-19), 1.17 (3H, s, H-29), 1.12 (3H, s, H-28), 0.98 (3H, s, H-18).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 206.10 (C-16), 204.73 (C-3), 195.36 (C-14), 157.53 (C-1), 142.86 (C-23), 141.42 (C-21), 125.78 (C-2), 122.40 (C-20), 120.19 (C-15), 109.52 (C-22), 80.76 (C-17), 71.76 (C-7), 50.42 (C-13), 46.82 (C-8), 44.44 (C-5), 44.19 (C-4), 40.18 (C-10), 36.89 (C-9), 30.15 (C-18), 27.11 (C-28), 25.57 (C-30), 25.44 (C-6), 22.14 (C-12), 21.42 (C-29), 19.19 (C-19), 15.63 (C-11).

17β-Hydroxy-7-oxonimbocinol (**16**):

White solid; **$[\alpha]^{28}_{D}$** = + 7.61 (*c* 3.25, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 219, 204 nm.

LC-ESI-MS (m/z)**:** 445.3 ($[M+Na]^+$), 423.3 ($[M+H]^+$), 405.3 ($[M-OH]^+$).

MALDI-TOF (m/z)**:** 445.1926 ($[M+Na]^+$) (Calculated: 445.1990).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3421 (-OH)**,** 1708 (D ring ketone), 1673 (A ring ketone), 1595 (D ring tri-substituted double bond), 1379 (A ring geminal methyls), 1160, 1030, 874 (Furan ring)**.**

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.58 (1H, m, H-21), 7.42 (1H, m, H-23), 7.15 (1H, d, J=10.04 Hz, H-1), 6.38 (2H, m, H-22,15), 5.94 (1H, d, J=10.29 Hz, H-2), 2.98 (1H, t, J=14.56 Hz, H-6β), 2.68 (2H, m, H-9,6α), 2.48 (1H, dd, J=14.05,2.51 Hz, H-5), 1.59 (3H, s, H-30), 1.42 (3H, s, H-19), 1.18 (3H, s, H-29), 1.15 (3H, s, H-28), 0.94 (3H, s, H-18).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 206.80 (C-7), 206.07 (C-16), 203.07 (C-3), 185.34 (C-14), 155.57 (C-1), 142.84 (C-23), 141.53 (C-21), 126.76 (C-2), 126.32 (C-15), 122.40 (C-20), 109.40 (C-22), 80.27 (C-17), 54.23 (C-8), 52.79 (C-5), 50.62 (C-13), 45.33 (C-9), 44.80 (C-4), 39.72 (C-10), 36.01 (C-6), 32.03 (C-18), 26.73 (C-28), 25.86 (C-30), 23.47 (C-12), 20.94 (C-29), 18.80 (C-19), 16.99 (C-11).

7-Deacetylepoxyazadiradione (**17**):

White solid; **$[\alpha]^{28}_{D}$** = + 39.6 (*c* 1.90, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 210 nm.

LC-ESI-MS (m/z)**:** 447.1 ($[M+Na]^+$), 425.2 ($[M+H]^+$), 407.1 ($[M-OH]^+$).

MALDI-TOF (m/z)**:** 447.2151 ($[M+Na]^+$) (Calculated: 447.2148).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3501 (-OH)**,** 1749 (D ring ketone), 1652 (A ring ketone), 1390 (A ring geminal methyls), 1216, 1030, 875 (Furan ring).

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.53 (1H, m, H-21), 7.39 (1H, m, H-23), 7.18 (1H, d, J=10.38 Hz, H-1), 6.24 (1H, m, H-22), 5.86 (1H, d, J=10.38 Hz, H-2), 3.90 (1H, s, H-17), 3.64 (1H, m, H-7), 3.55 (1H, s, H-15), 2.66 (1H, m, H-9), 2.43 (1H, m, H-5), 1.19 (3H, s, H-19), 1.14 (3H, s, H-30), 1.12 (3H, s, H-29), 1.10 (3H, s, H-28), 1.05 (3H, s, H-18).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 209.32 (C-16), 204.86 (C-3), 158.25 (C-1), 142.33 (C-23), 141.50 (C-21), 125.55 (C-2), 116.85 (C-20), 111.05 (C-22), 73.24 (C-14), 71.17 (C-7), 57.64 (C-15), 51.23 (C-17), 45.28 (C-5), 44.44,44.38 (C-4,8), 42.59 (C-13), 39.83 (C-10), 38.29 (C-9), 29.69 (C-12), 27.79 (C-6), 27.15 (C-28), 25.07 (C-18), 21.24 (C-29), 19.94 (C-19), 19.61 (C-30), 16.16 (C-11).

12β-Hydroxy-7-deacetylepoxyazadiradione (**18**):

White solid; **$[\alpha]^{28}_{D}$** = + 27.6 (*c* 1.50, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 208 nm.

LC-ESI-MS (m/z)**:** 463.0 ($[M+Na]^+$), 441.1 ($[M+H]^+$), 423.1 ($[M-OH]^+$).

MALDI-TOF (m/z)**:** 463.2124 ($[M+Na]^+$) (Calculated: 463.2097).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3525 (-OH)**,** 1748 (D ring ketone), 1651 (A ring ketone), 1387 (A ring geminal methyls), 1215, 1024, 875 (Furan ring).

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.60 (1H, m, H-21), 7.40 (1H, m, H-23), 7.14 (1H, d, J=10.04 Hz, H-1), 6.36 (1H, m, H-22), 5.87 (1H, d, J=10.29 Hz, H-2), 4.50 (1H, s, H-17), 3.93 (1H, m, H-12), 3.67 (1H, m, H-7), 3.47 (1H, s, H-15), 2.57-2.60 (2H, m, H-9,11α), 2.41

(1H, m, H-5), 1.20 (3H, s, H-19), 1.18 (3H, s, H-30), 1.14 (3H, s, H-29), 1.10 (3H, s, H-28), 1.06 (3H, s, H-18).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 208.82 (C-16), 204.66 (C-3), 157.59 (C-1), 142.38,142.05 (C-23,21), 125.82 (C-2), 116.75 (C-20), 111.38 (C-22), 72.00 (C-14), 71.57 (C-7), 71.14 (C-12), 55.19 (C-15), 47.53 (C-13), 45.29,45.08 (C-17,5), 44.38,44.33 (C-4,8), 39.54 (C-10), 37.84 (C-9), 29.39 (C-11), 27.99 (C-6), 27.13 (C-28), 23.60 (C-18), 21.19 (C-29), 20.02 (C-19), 19.51 (C-20).

Gedunin (**19**):

White solid; **$[\alpha]^{28}_D$** = + 22.8 (*c* 1.50, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 214 nm.

LC-ESI-MS (m/z)**:** 505.4 ($[M+Na]^+$), 483.2 ($[M+H]^+$), 423.5 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 505.2216 ($[M+Na]^+$) (Calculated: 505.2203).

IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 1739 (Acetate carbonyl and D ring ketone), 1670 (A ring ketone), 1387 (A ring geminal methyls), 1216 (Acetate C-O), 1030, 875 (Furan ring).

^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.42 (2H, m, H-21,23), 7.10 (1H, d, J=10.07 Hz, H-1), 6.34 (1H, m, H-22), 5.87 (1H, d, J=10.38 Hz, H-2), 5.62 (1H, s, H-17), 4.56 (1H, m, H-7), 3.53 (1H, s, H-15), 2.50 (1H, m, H-9), 2.17 (1H, m, H-5), 2.11 (3H, s, -CO$\underline{C}H_3$), 1.25 (3H, s, H-18), 1.23 (3H, s, H-19), 1.16 (3H, s, H-30), 1.08 (3H, s, H-29), 1.07 (3H, s, H-28).

^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 203.93 (C-3), 169.87 (C-$\underline{C}OCH_3$), 167.42 (C-16), 156.90 (C-1), 143.08 (C-23), 141.20 (C-21), 126.01 (C-2), 120.44 (C-20), 109.86 (C-22), 78.26 (C-17), 73.24 (C-7), 69.76 (C-14), 56.89 (C-15), 46.05 (C-5), 44.05 (C-4), 42.64 (C-8), 40.04 (C-10), 39.54 (C-9), 38.74 (C-13), 27.16 (C-28), 26.02 (C-12), 23.26 (C-6), 21.18 (C-29), 21.05 (C-CO$\underline{C}H_3$), 19.72 (C-19), 18.30 (C-30), 17.74 (C-18), 14.99 (C-11).

12β-Hydroxygedunin (**20**):

White solid; **$[\alpha]^{28}_D$** = + 11.6 (*c* 1.00, $CHCl_3$)**; UV** (Me_2CO) **λ_{max}**= 214 nm.

LC-ESI-MS (m/z)**:** 521.2 ($[M+Na]^+$), 499.2 ($[M+H]^+$), 439.1 ($[M-OAc]^+$).

MALDI-TOF (m/z)**:** 521.2167 ($[M+Na]^+$) (Calculated: 521.2152).

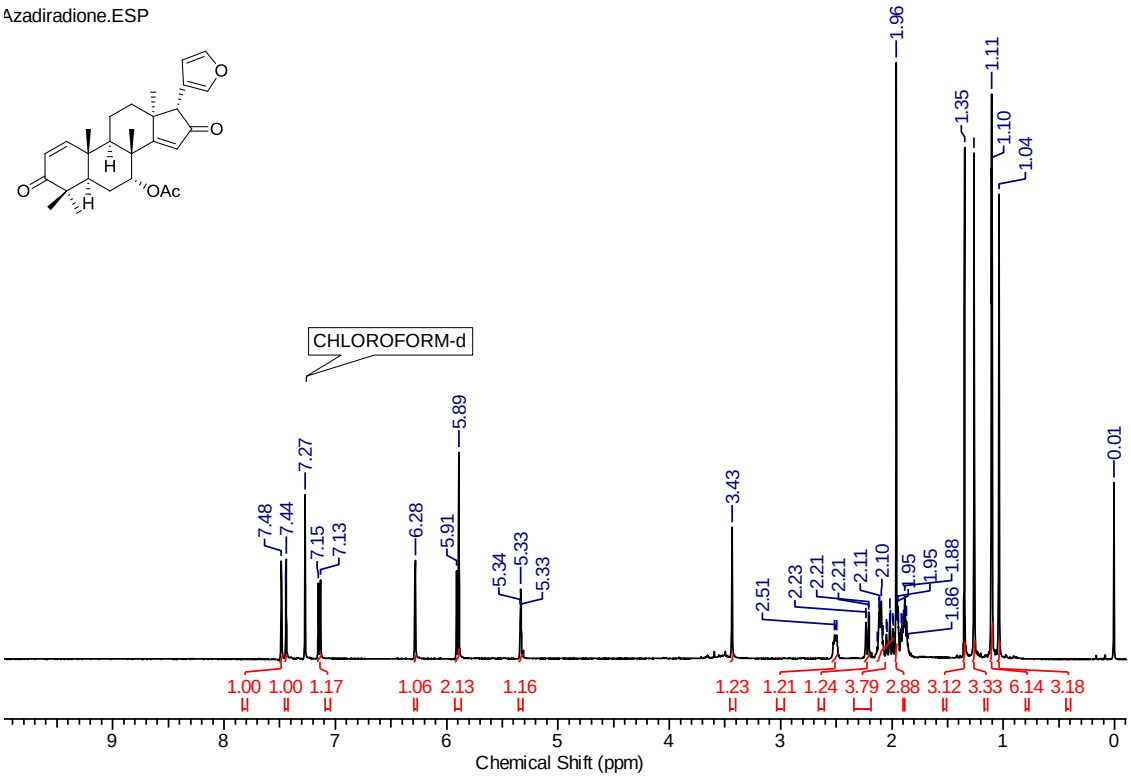
IR ($CHCl_3$) ν_{max} (cm^{-1})**:** 3393 (-OH)**,** 1734 (Acetate carbonyl and D ring ketone), 1657 (A ring ketone), 1370 (A ring geminal methyls), 1216 (Acetate C-O), 1026, 874 (Furan ring).

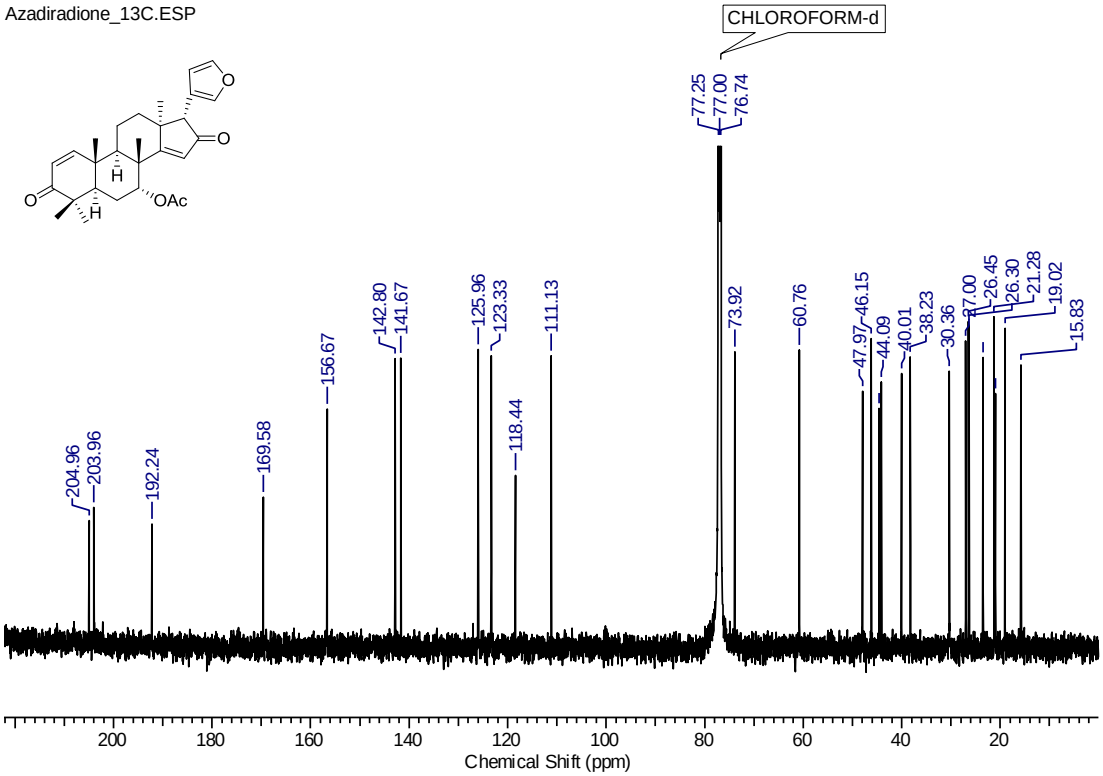
^{1}H NMR (400 MHz, $CDCl_3$); δ(ppm): 7.51 (1H, m, H-21), 7.43 (1H, m, H-23), 7.04 (1H, d, J=10.29 Hz, H-1), 6.47 (1H, m, H-22), 6.18 (1H, s, H-17), 5.87 (1H, d, J=10.04 Hz, H-2), 4.57 (1H, m, H-7), 3.94 (1H, br. d, J= 7.6 Hz, H-12), 3.45 (1H, s, H-15), 2.46-2.56 (2H, m, H-9,11α), 2.17 (1H, m, H-5), 2.12 (3H, s, -CO<u>C</u>H_3), 1.34 (3H, s, H-18), 1.25 (3H, s, H-19), 1.17 (3H, s, H-30), 1.08 (3H, s, H-29), 1.07 (3H, s, H-28).

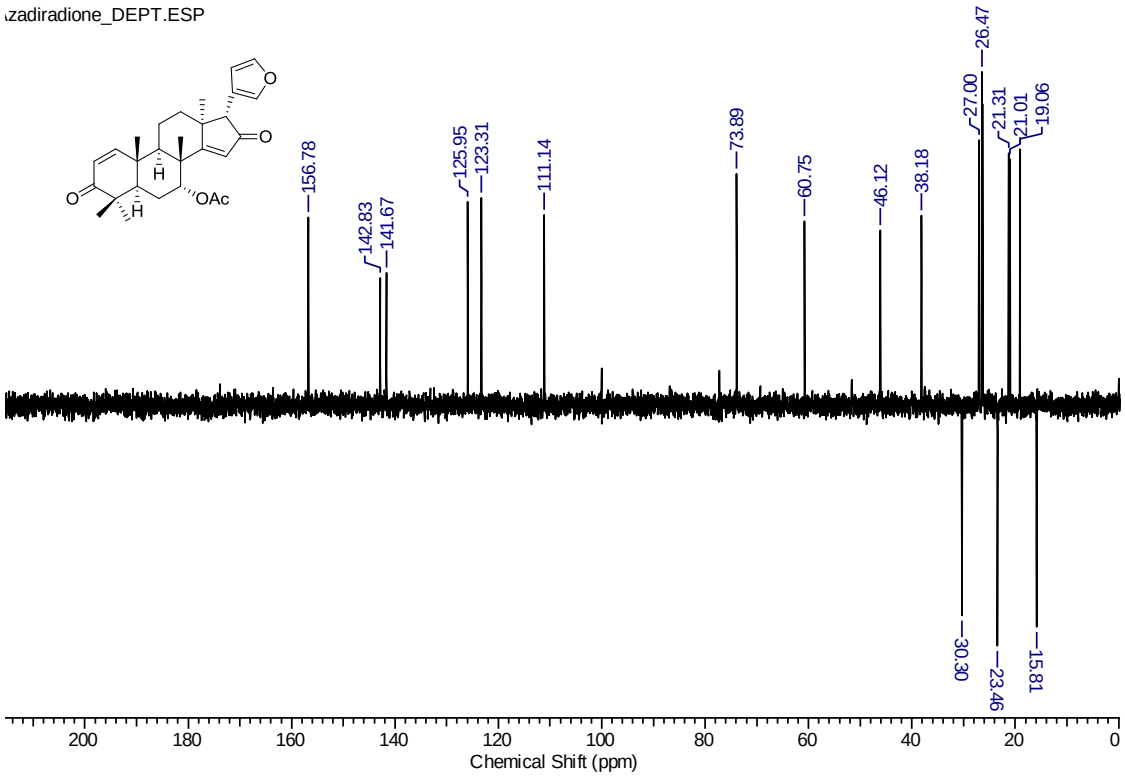
^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 203.90 (C-3), 169.89 (C-<u>C</u>OCH_3), 167.41 (C-16), 156.42 (C-1), 143.21 (C-23), 141.45 (C-21), 126.19 (C-2), 120.02 (C-20), 109.86 (C-22), 75.57 (C-17), 73.38 (C-7), 69.22 (C-12), 68.28 (C-14), 55.02 (C-15), 46.09 (C-5), 44.06 (C-4), 42.82,42.32 (C-8,13), 39.90 (C-10), 39.22 (C-9), 28.39 (C-11), 27.13 (C-28), 23.14 (C-6), 21.17 (C-29), 21.06 (C-CO<u>C</u>H_3), 19.87 (C-19), 18.16 (C-30), 15.75 (C-18).

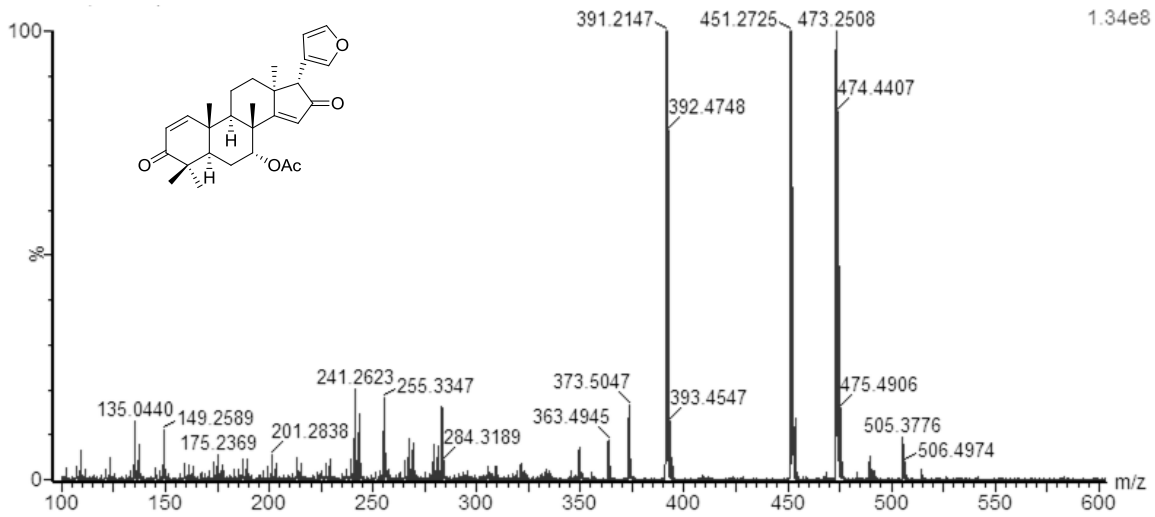
Section C. Copies of NMR and LC-MS spectra

Azadiradione (**1**)

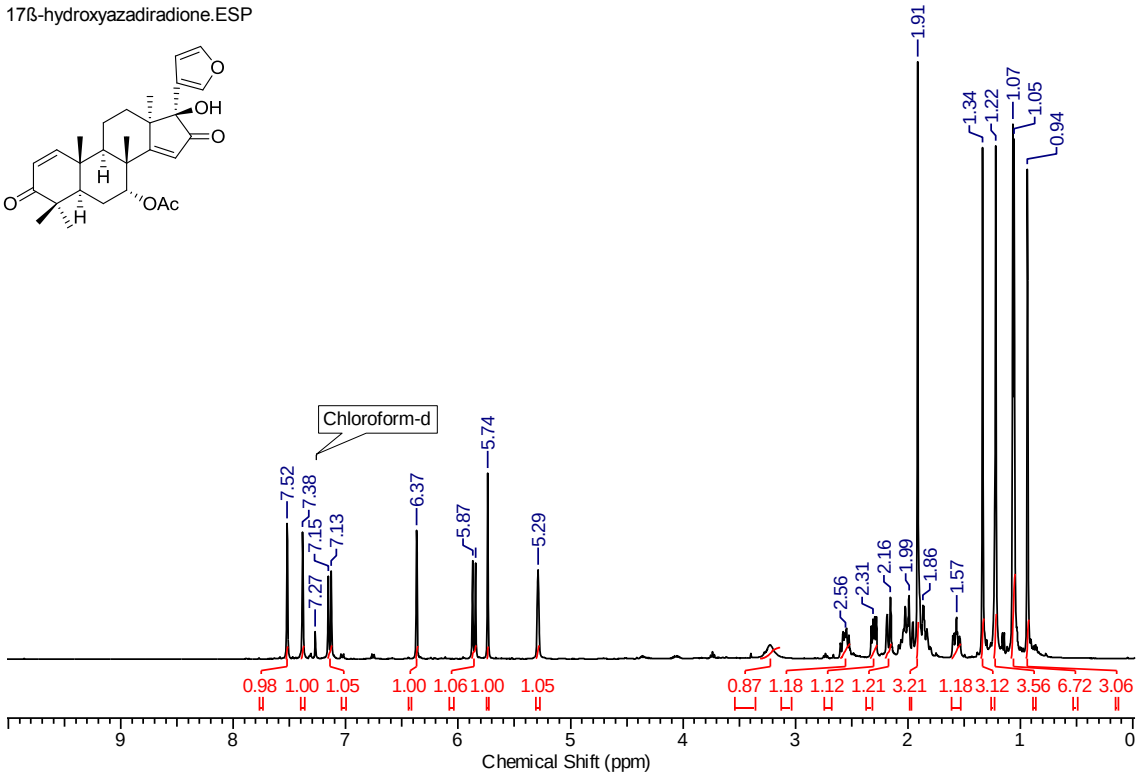


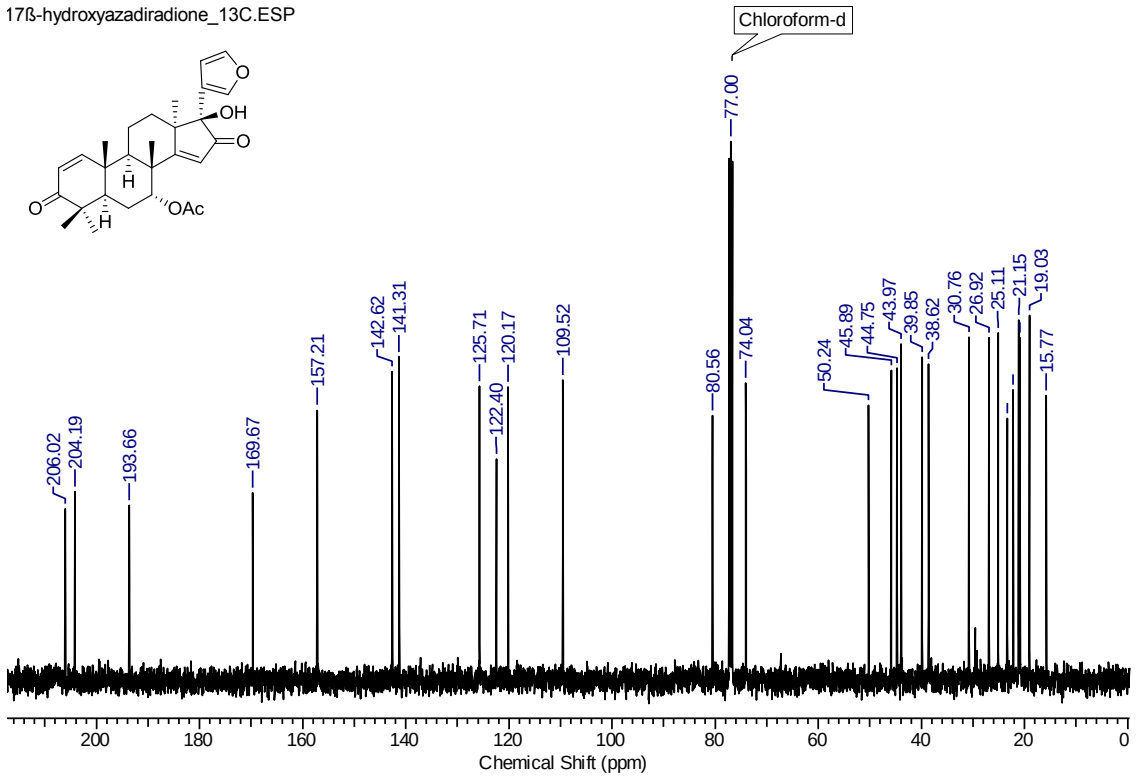


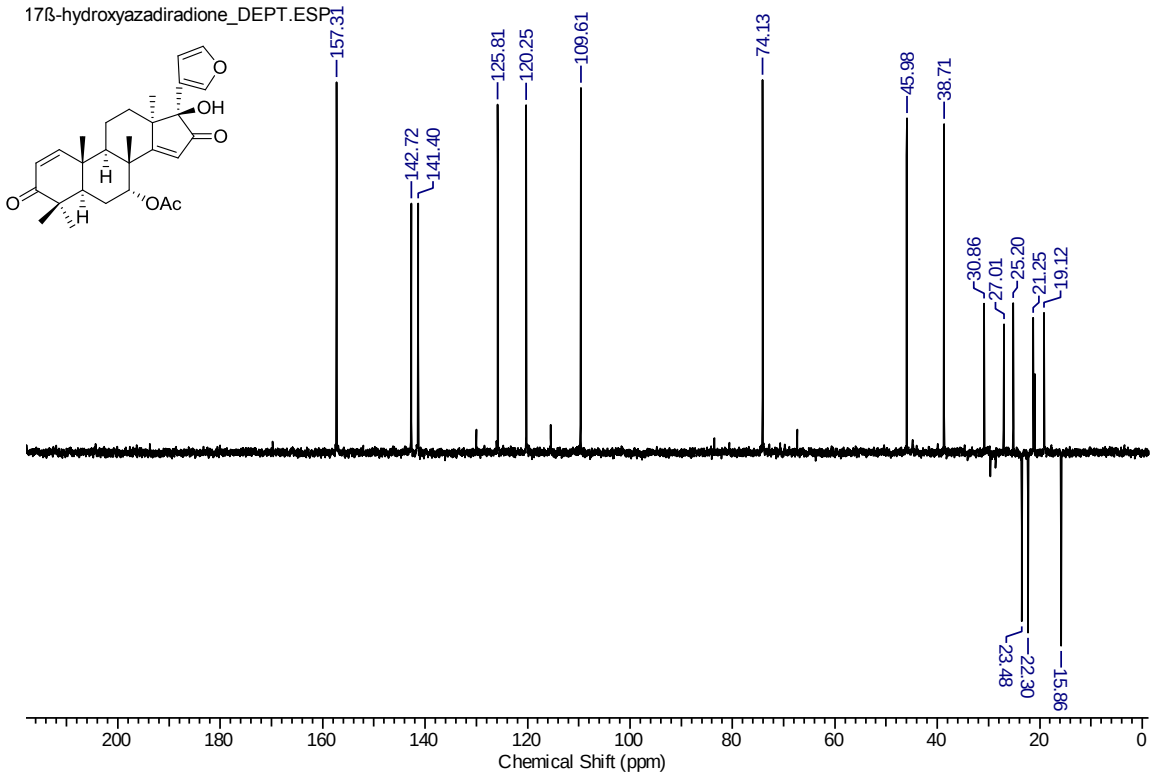

zadiradione_DEPT.ESP
156.78
142.83
141.67
125.95
123.31
111.14
73.89
60.75
46.12
38.18
27.00
26.47
21.31
21.01
19.06
30.30
23.46
15.81
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

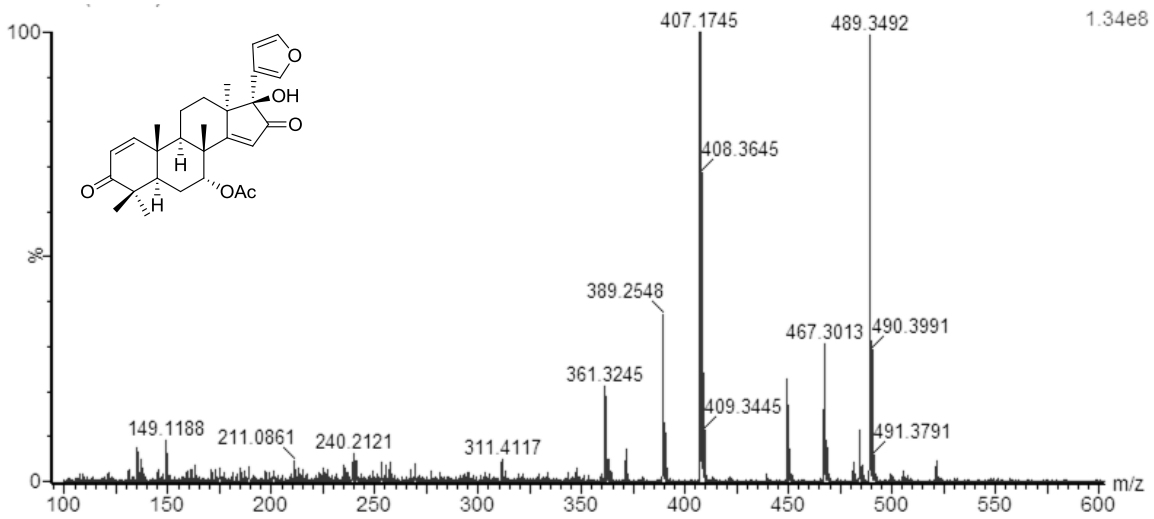

100
%
0
391.2147
451.2725
473.2508
1.34e8
474.4407
392.4748
241.2623
255.3347
373.5047
135.0440
149.2589
175.2369
201.2838
284.3189
363.4945
393.4547
475.4906
505.3776
506.4974
100
150
200
250
300
350
400
450
500
550
600
m/z

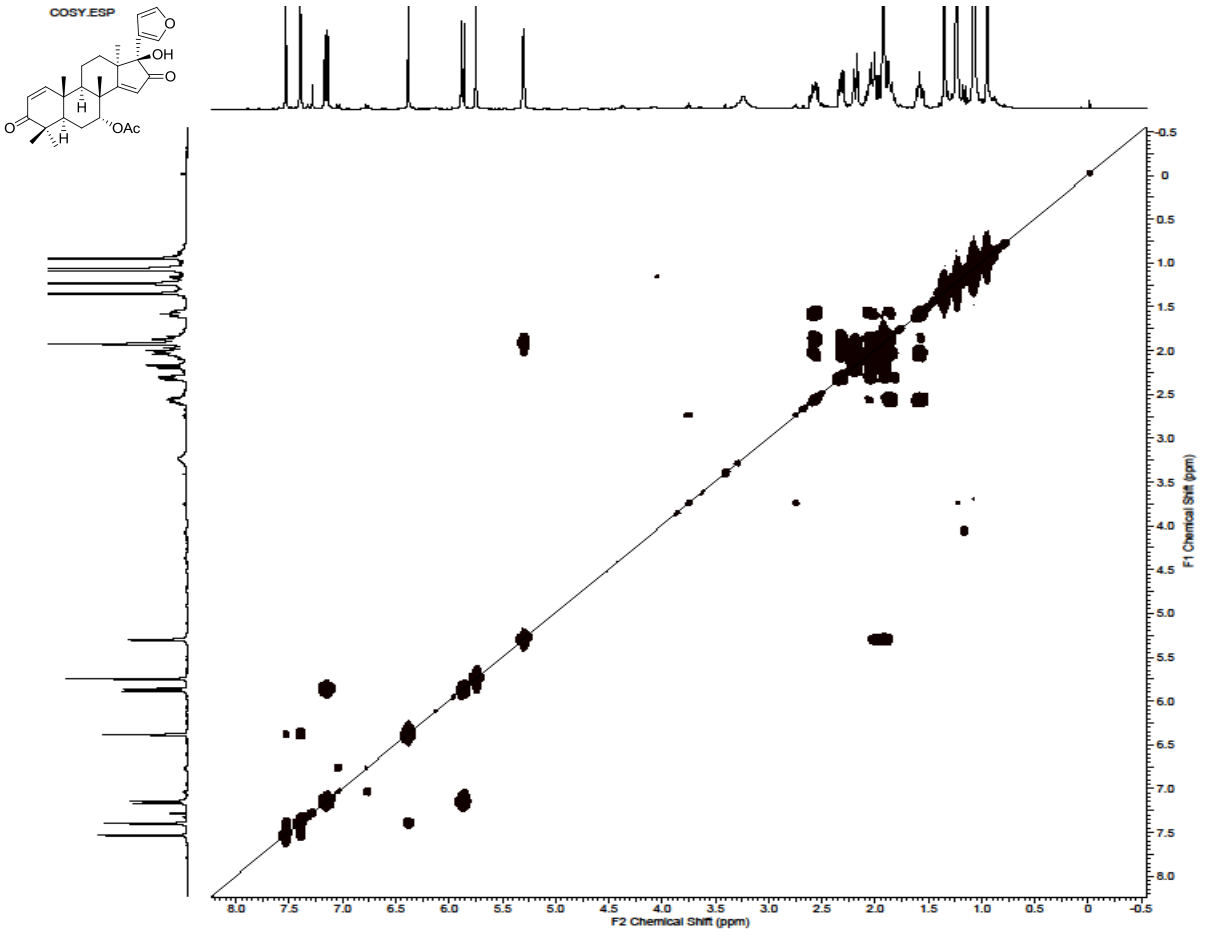
17β-Hydroxyazadiradione (**2**)

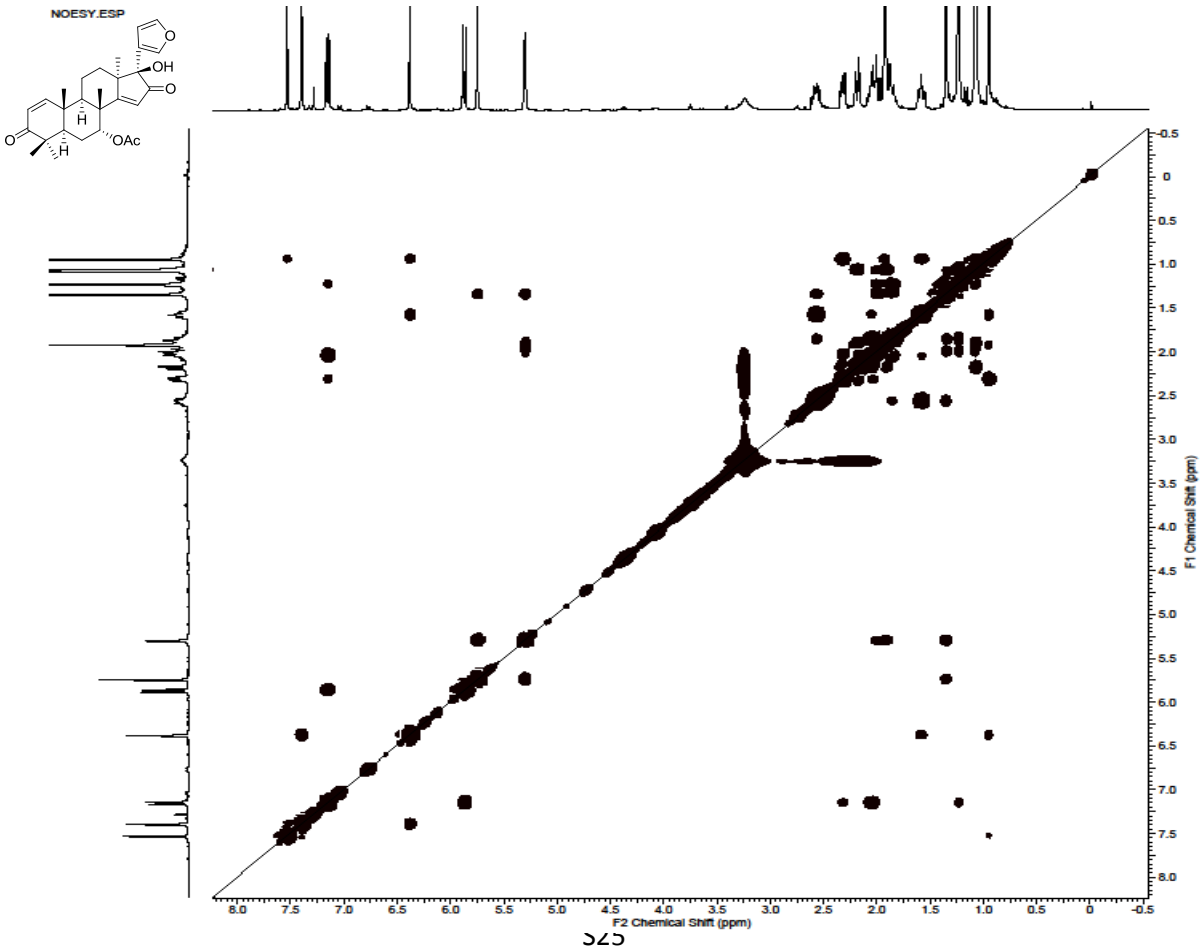


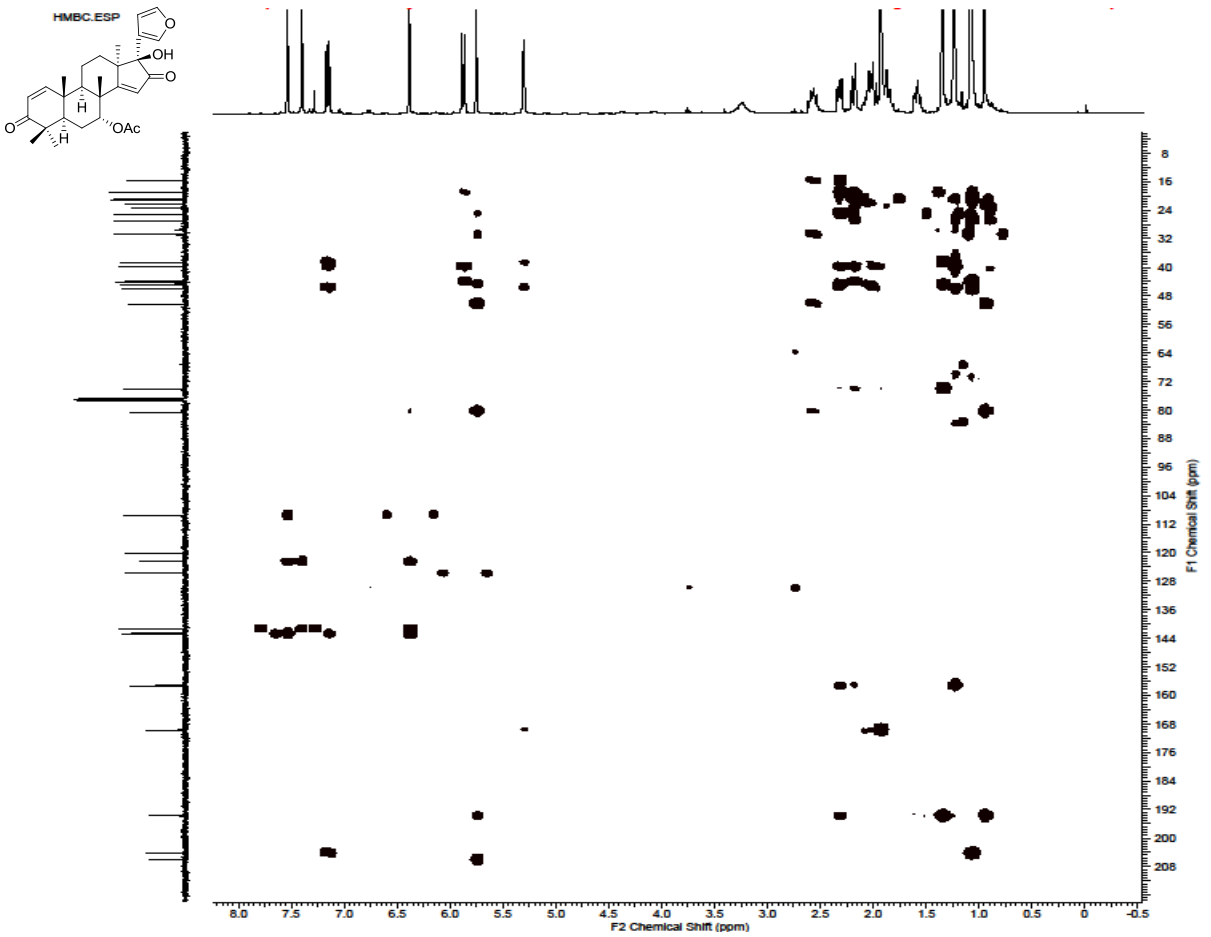


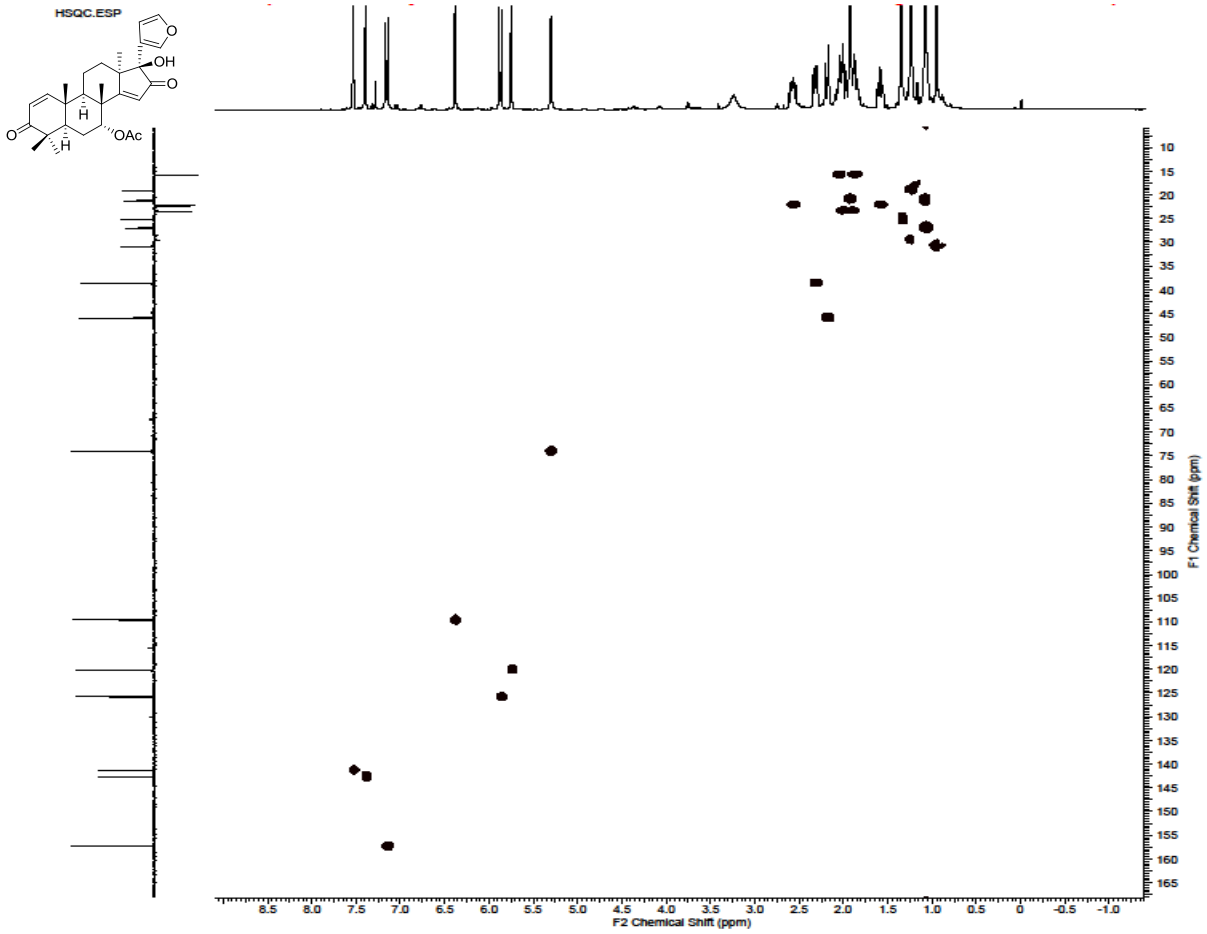

17ß-hydroxyazadiradione_DEPT.ESP
157.31
142.72
141.40
125.81
120.25
109.61
74.13
45.98
38.71
30.86
27.01
25.20
21.25
19.12
23.48
22.30
15.86
OH
O
O
H
O
H
OAc
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


100
%
0
1.34e8
407.1745
489.3492
408.3645
389.2548
467.3013
490.3991
361.3245
409.3445
491.3791
149.1188
211.0861
240.2121
311.4117
OH
O
O
H
O
H
OAc
100
150
200
250
300
350
400
450
500
550
600
m/z

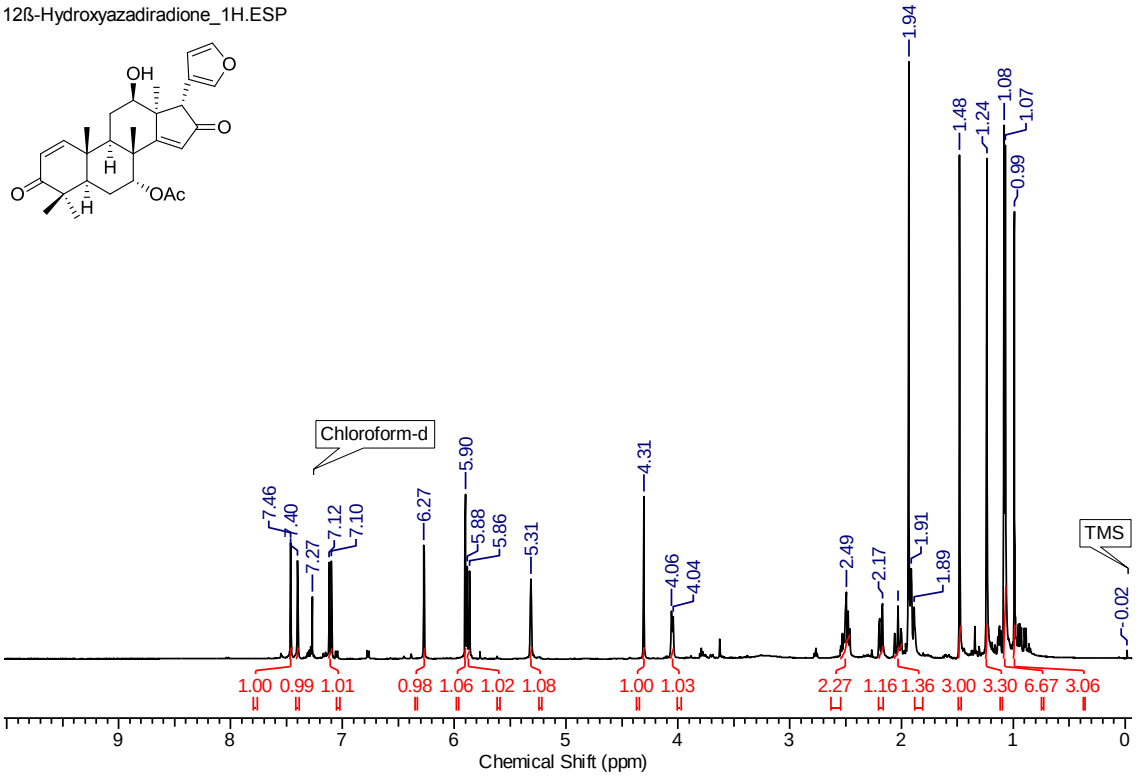


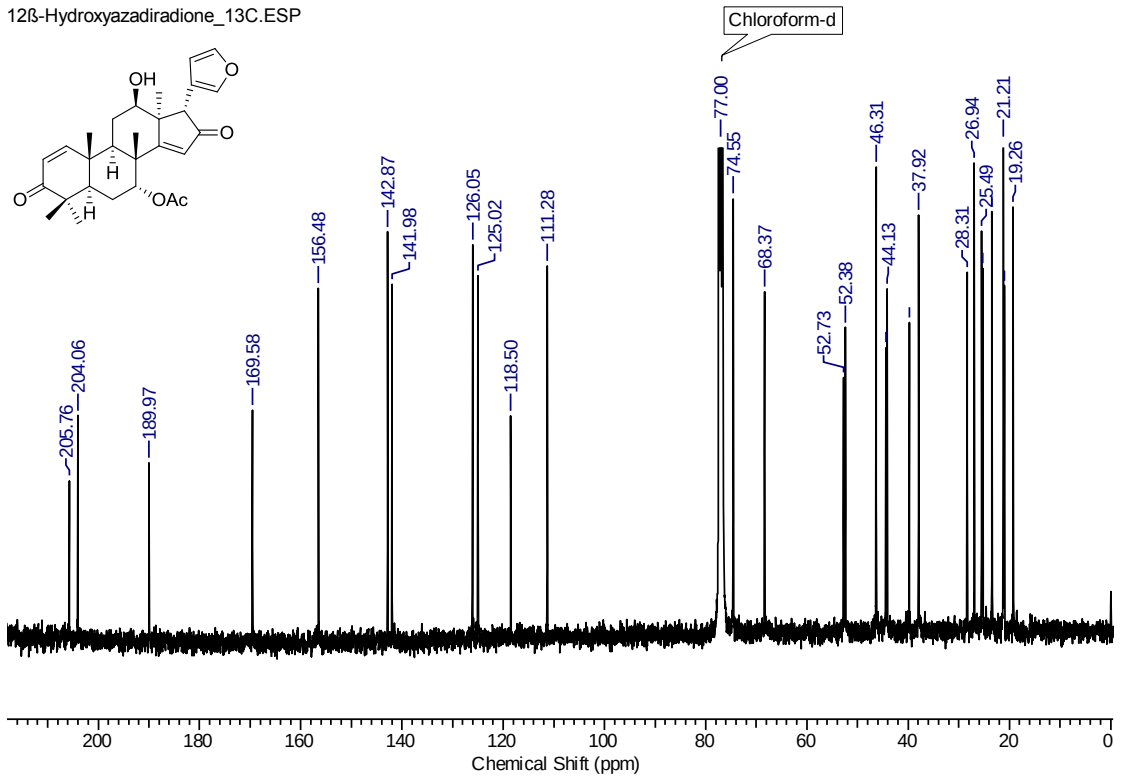


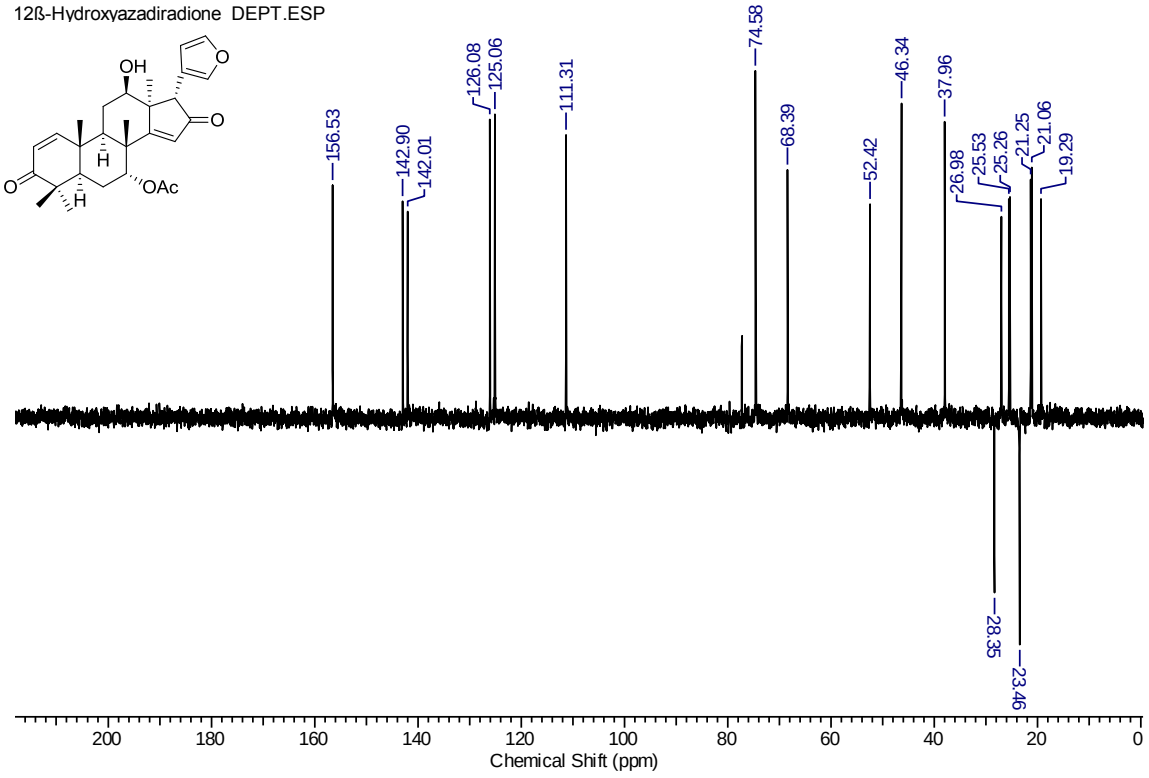


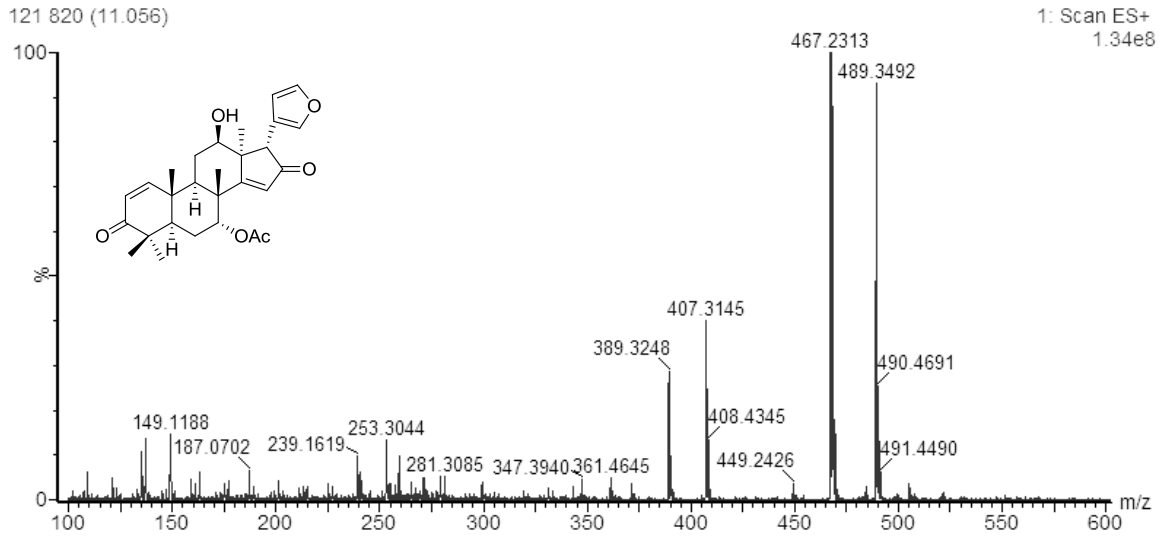


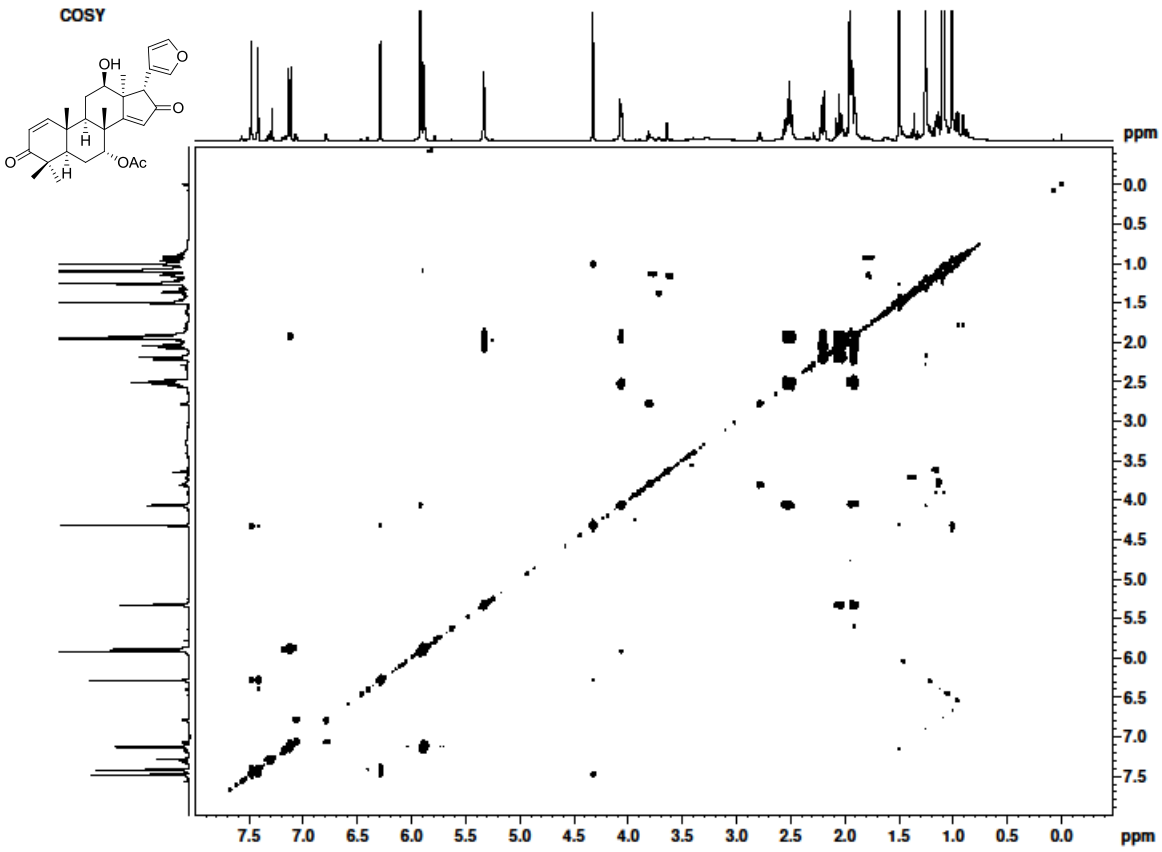
12β-Hydroxyazadiradione (**3**)

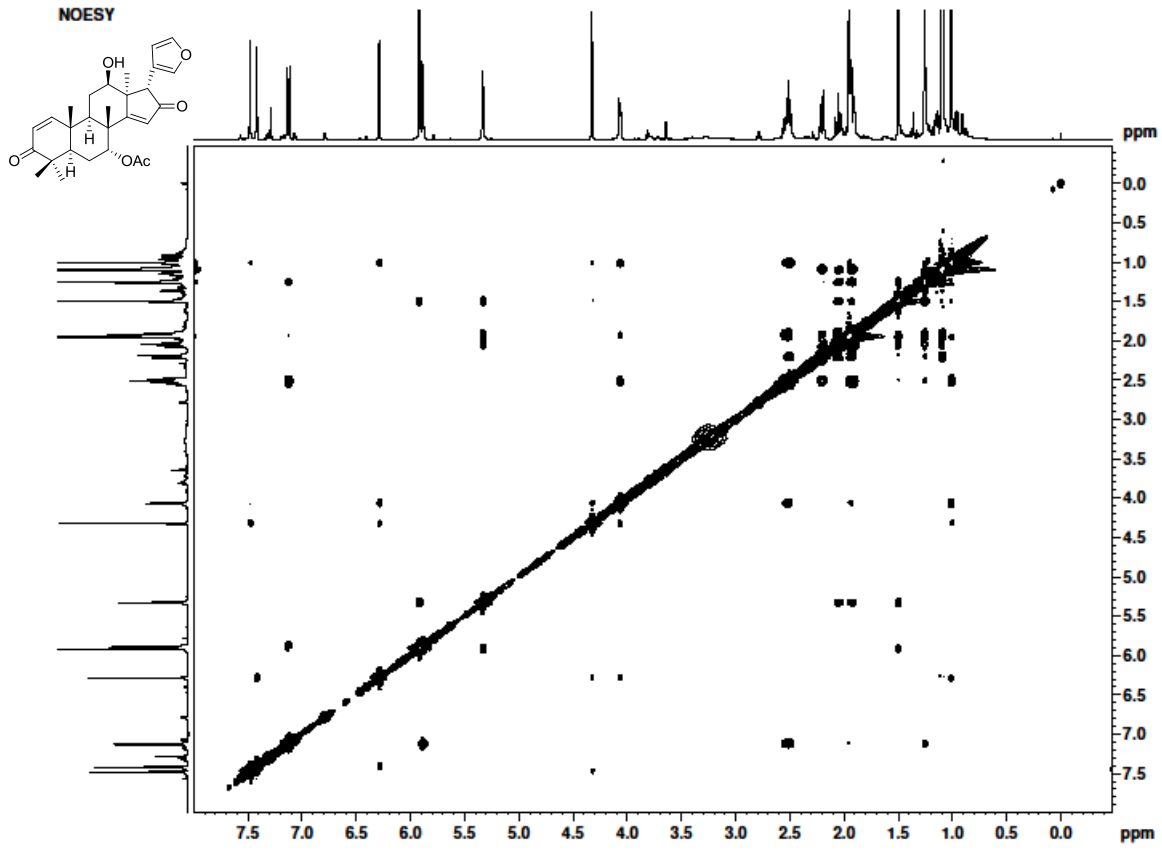


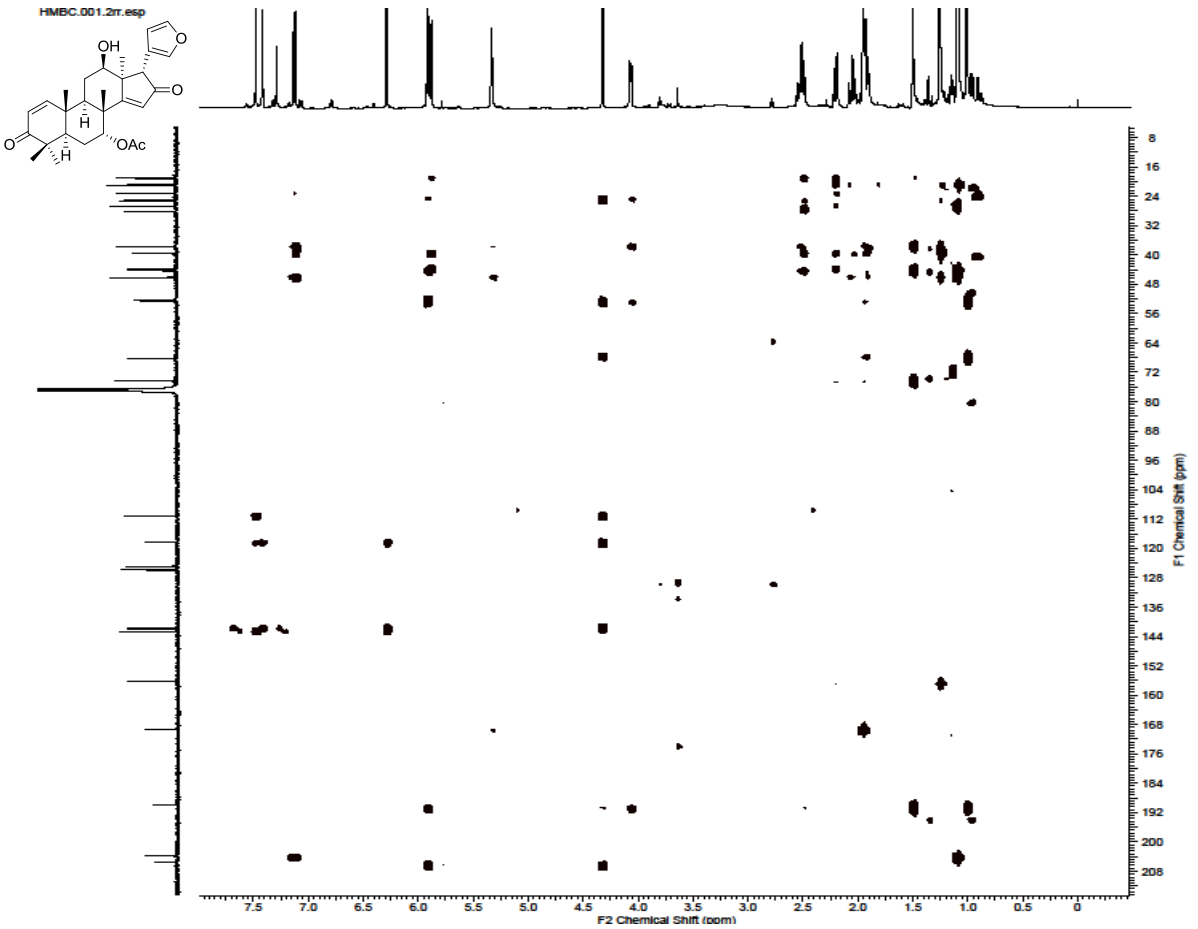


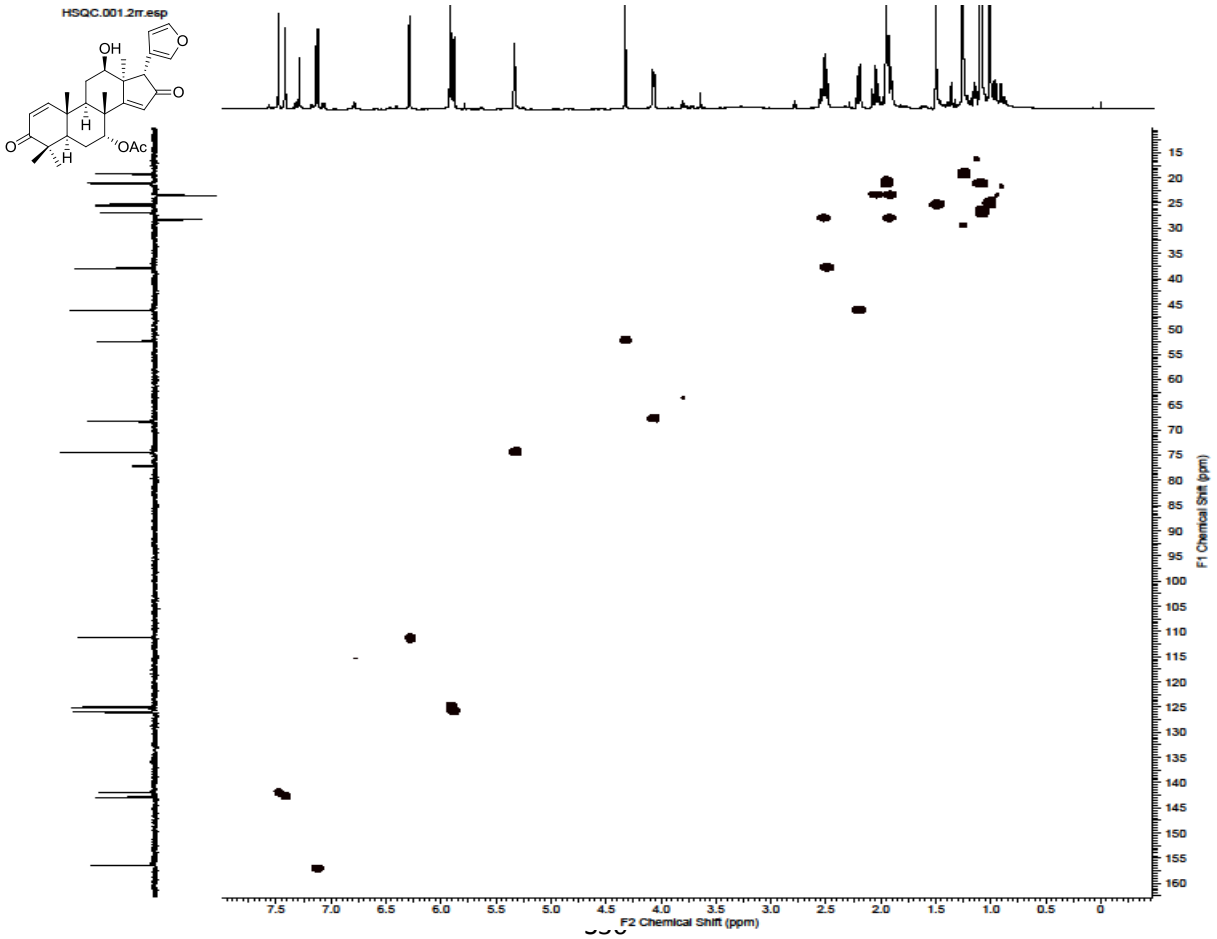






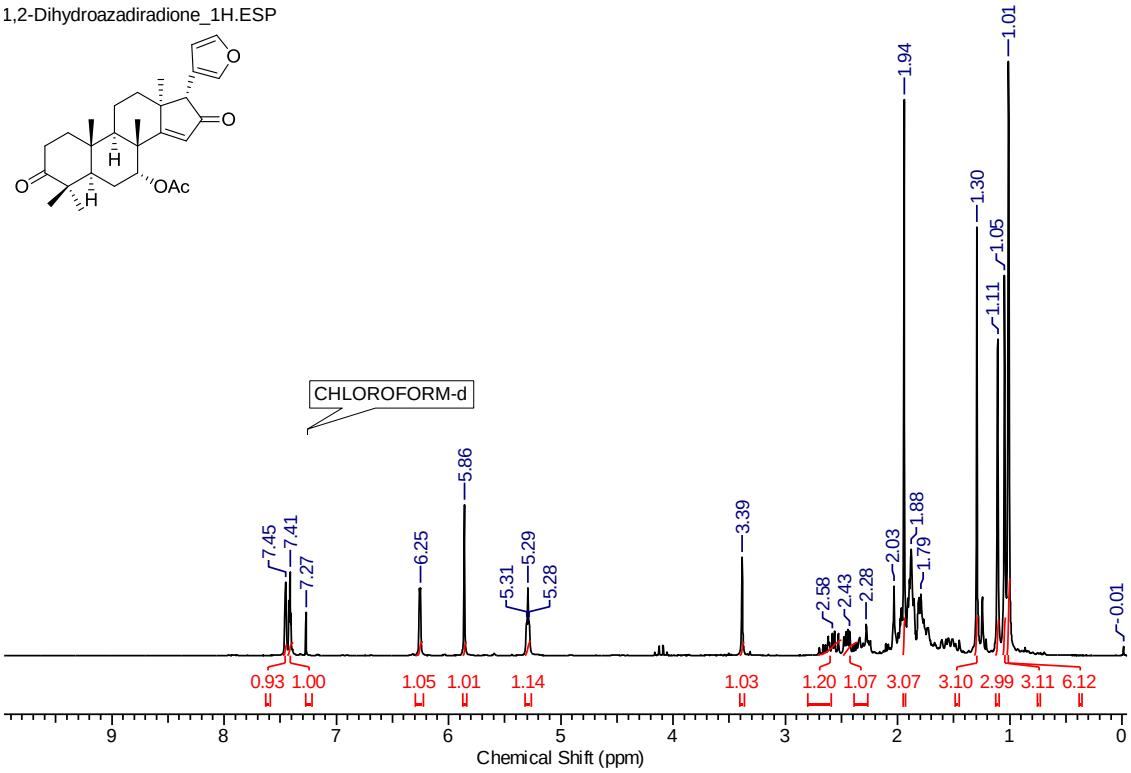




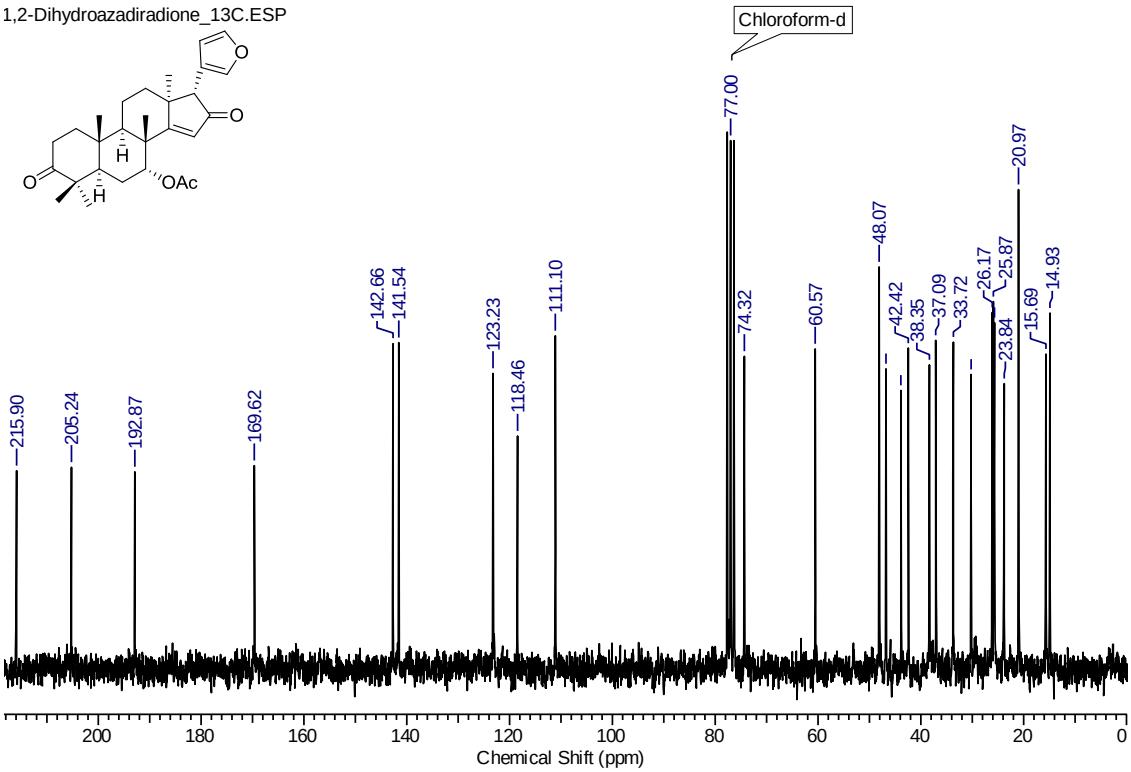


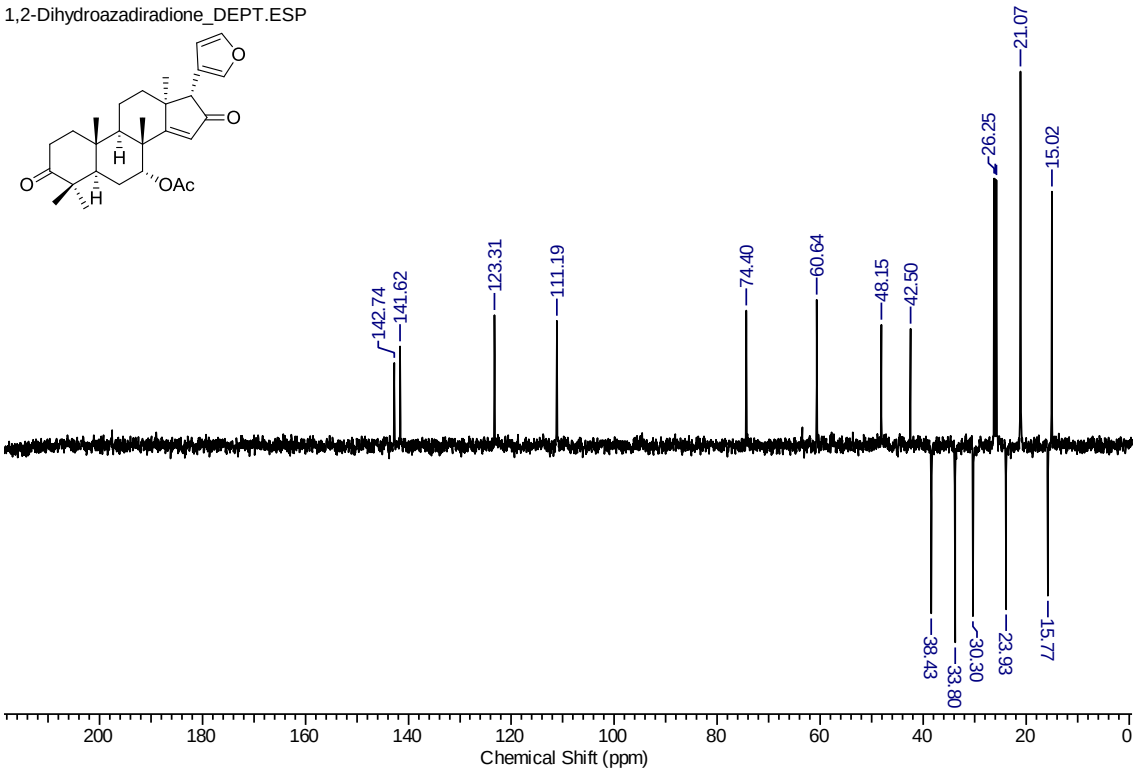
1,2-Dihydroazadiradione (**4**)

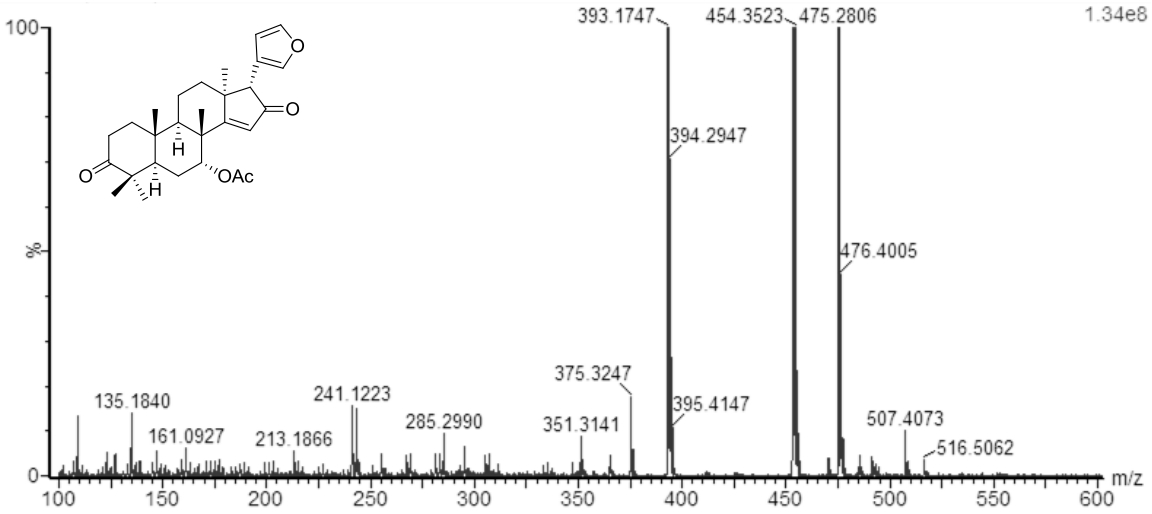
1,2-Dihydroazadiradione_1H.ESP



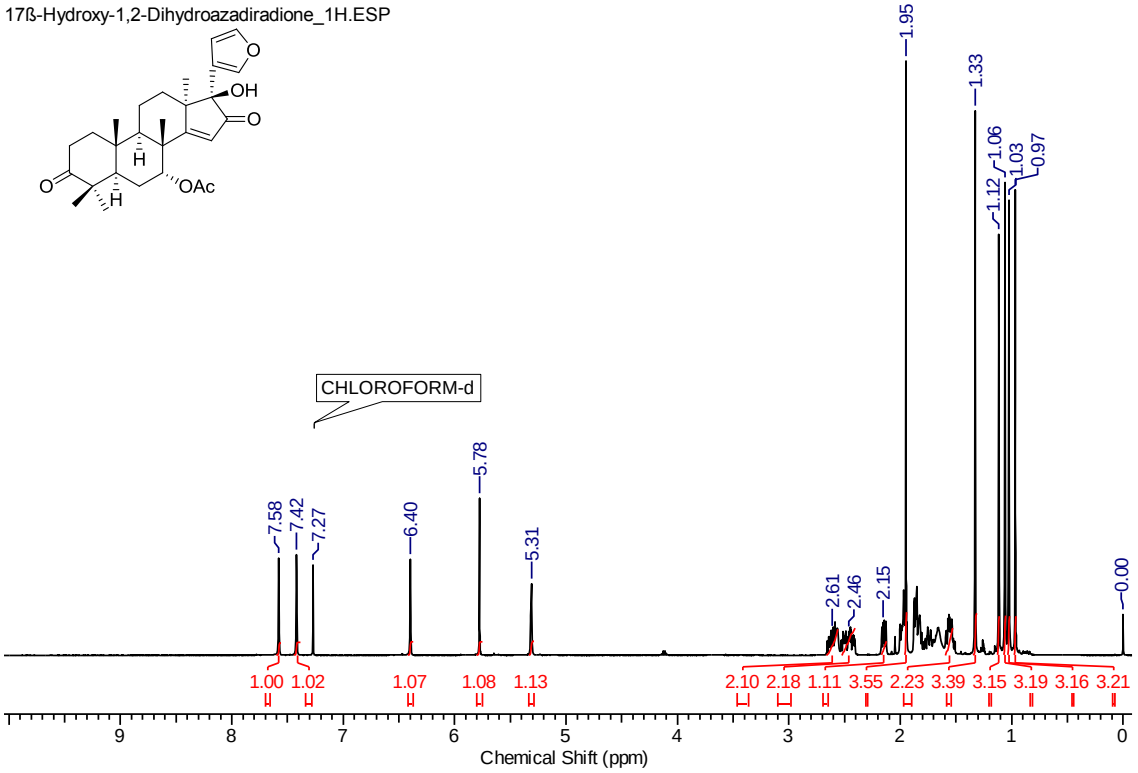
1,2-Dihydroazadiradione_13C.ESP

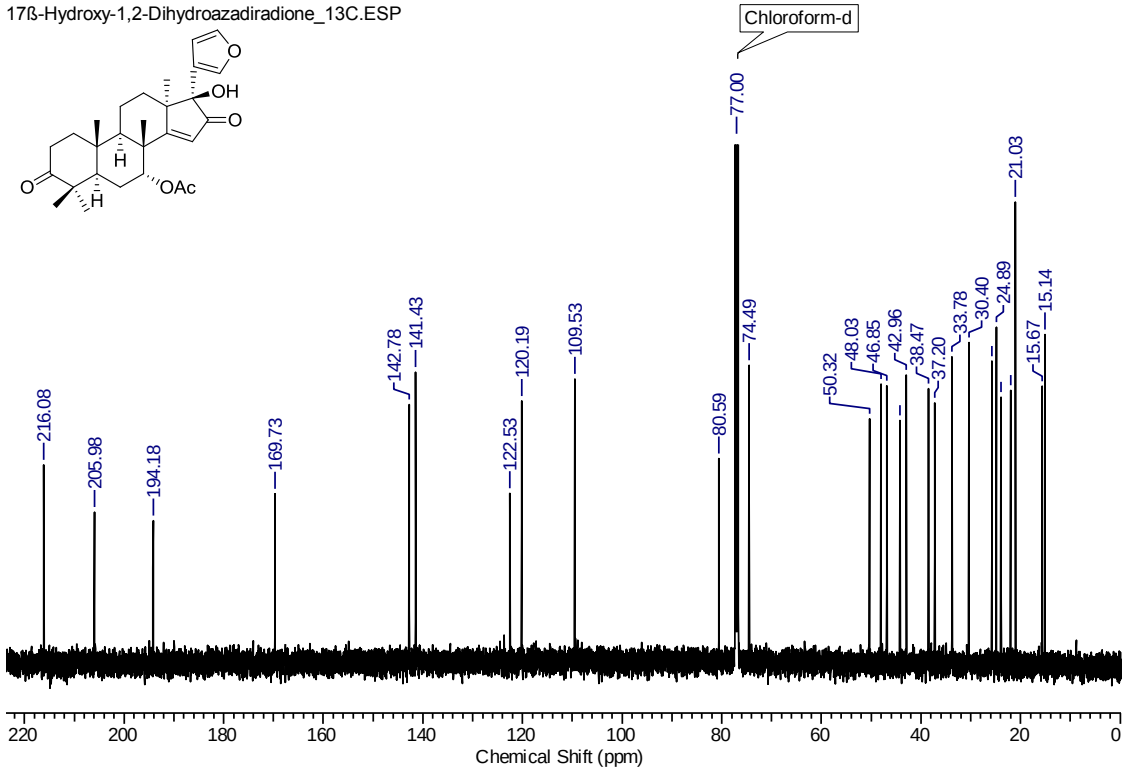


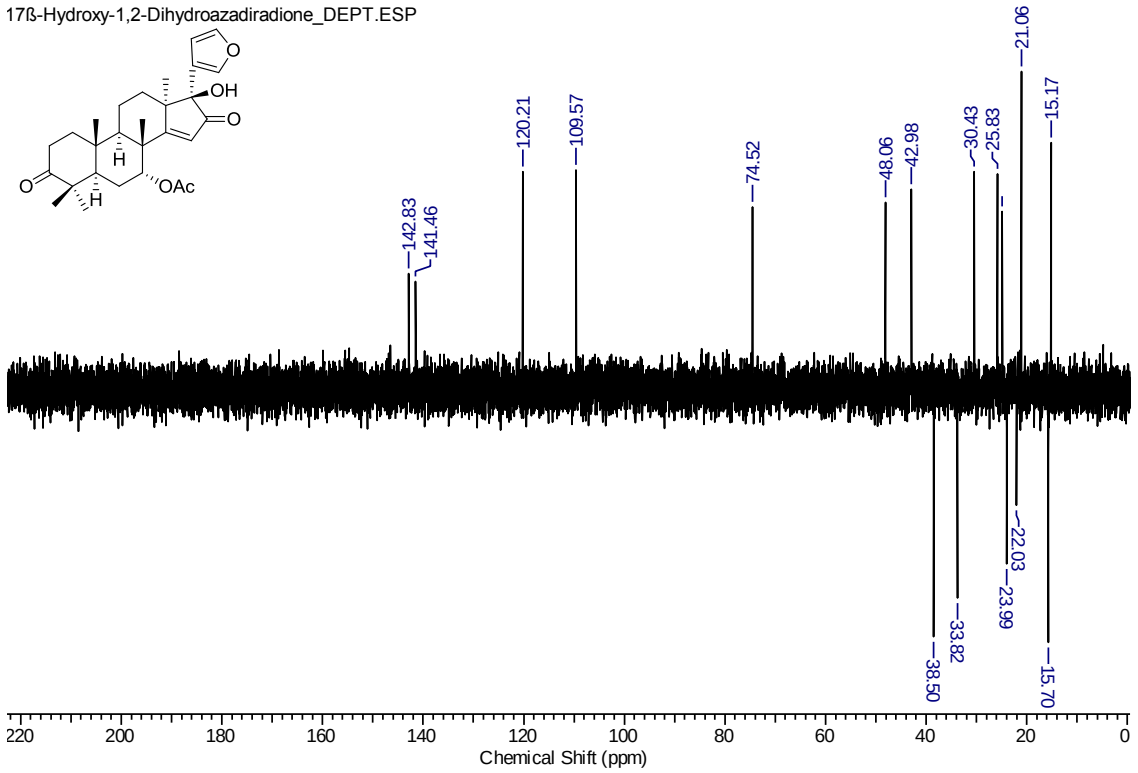


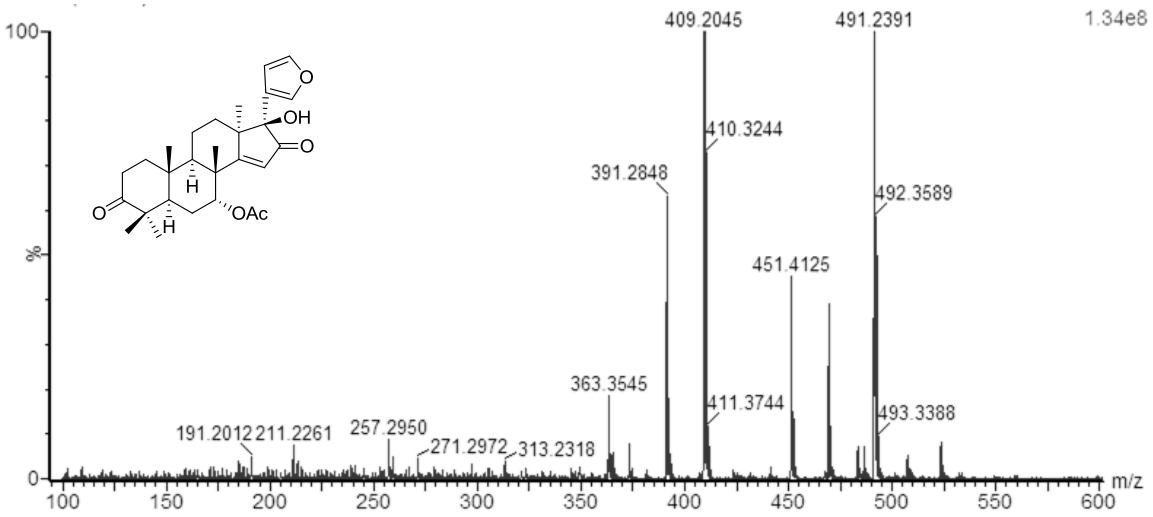


17β-Hydroxy-1,2-Dihydroazadiradione (**5**)

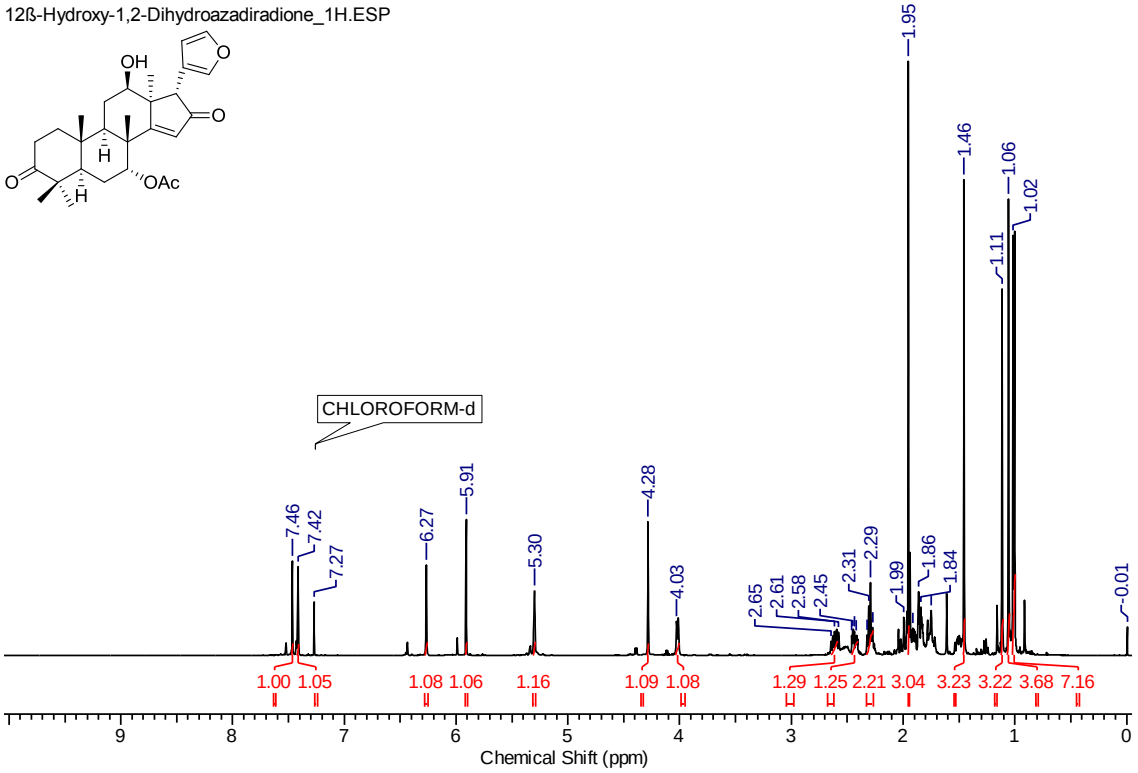

17ß-Hydroxy-1,2-Dihydroazadiradione_1H.ESP
CHLOROFORM-d
7.58
7.42
7.27
6.40
5.78
5.31
2.61
2.46
2.15
1.95
1.33
1.12
1.06
1.03
0.97
0.00
1.00 1.02 1.07 1.08 1.13 2.10 2.18 1.11 3.55 2.23 3.39 3.15 3.19 3.16 3.21
Chemical Shift (ppm)

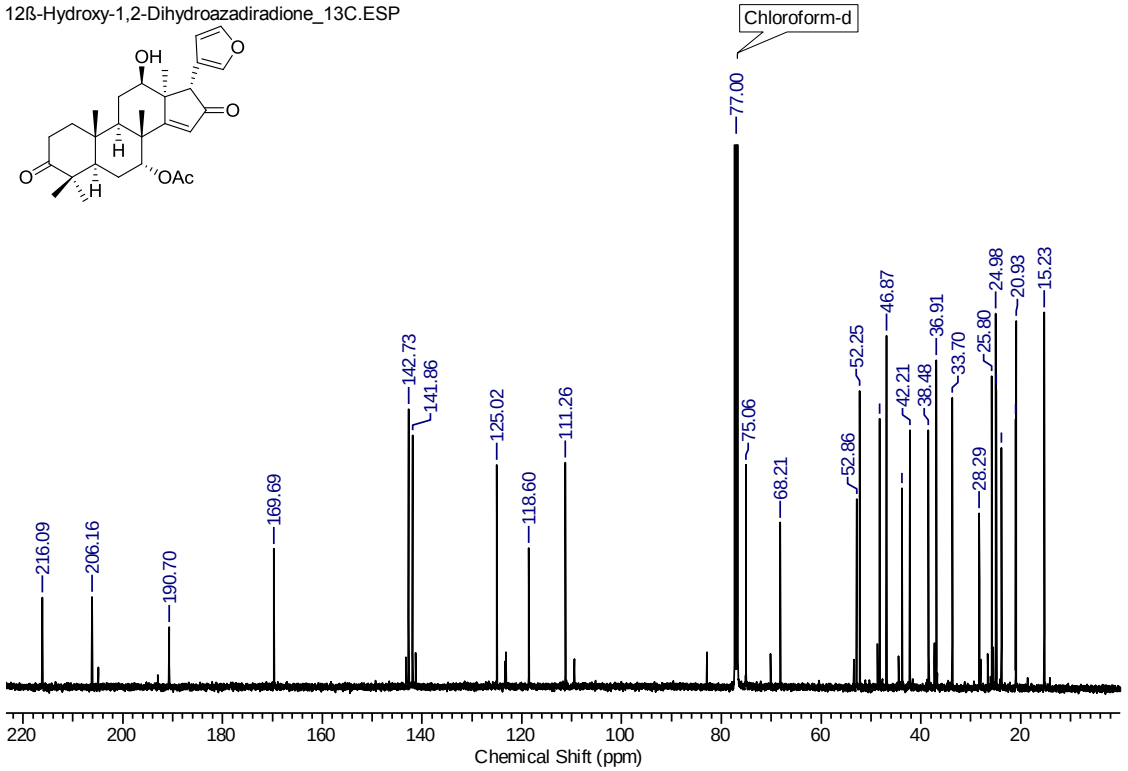

17ß-Hydroxy-1,2-Dihydroazadiradione_13C.ESP
Chloroform-d
216.08
205.98
194.18
169.73
142.78
141.43
122.53
120.19
109.53
80.59
77.00
74.49
50.32
48.03
46.85
42.96
38.47
37.20
33.78
30.40
24.89
21.03
15.67
15.14
Chemical Shift (ppm)

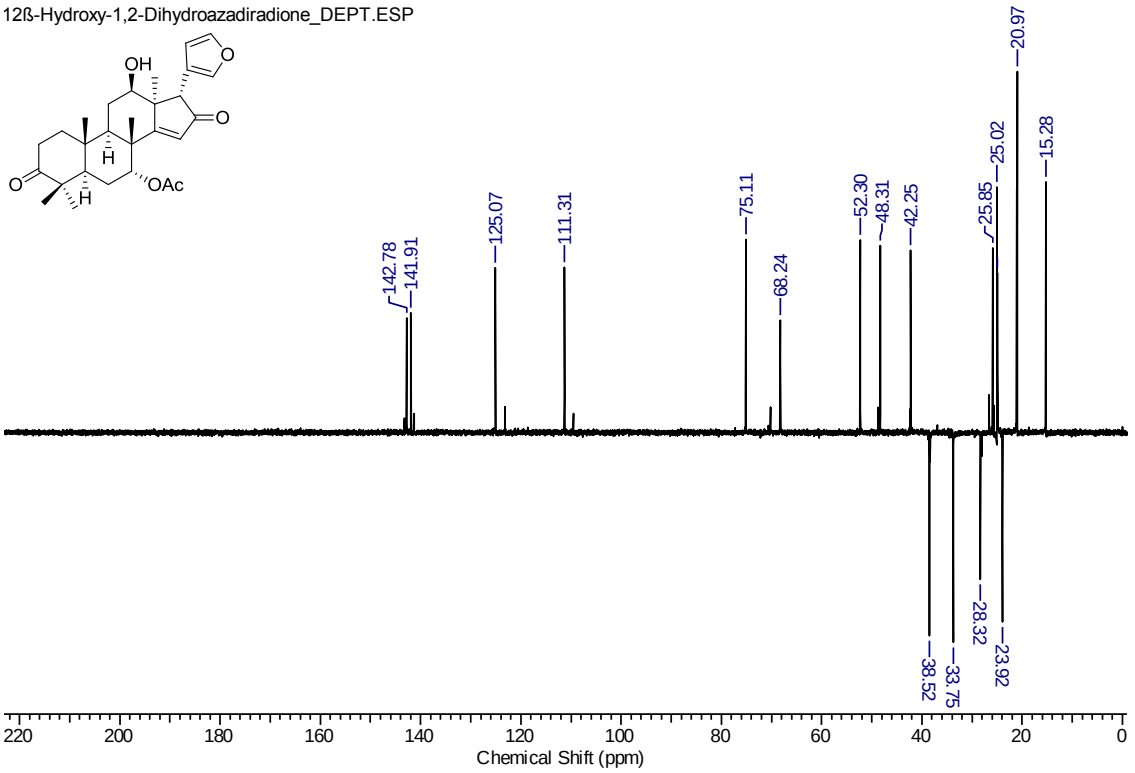


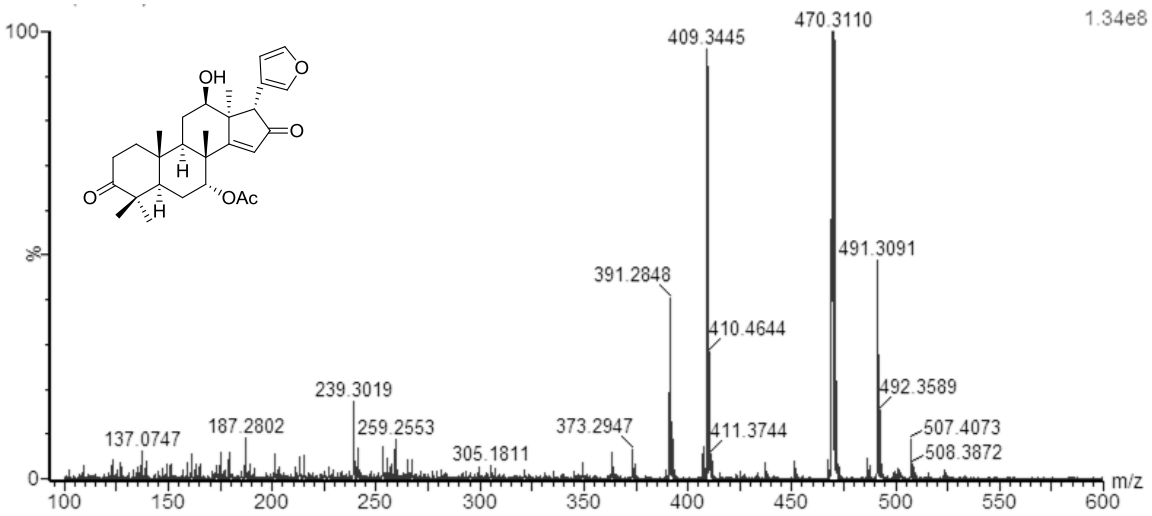


12β-Hydroxy-1,2-Dihydroazadiradione (**6**)


12ß-Hydroxy-1,2-Dihydroazadiradione_1H.ESP
OH
O
O
O
H
H
OAc
CHLOROFORM-d
1.95
1.46
1.06
1.02
1.11
7.46
7.42
7.27
6.27
5.91
5.30
4.28
4.03
2.65
2.61
2.58
2.45
2.31
2.29
1.99
1.86
1.84
0.01
1.00 1.05
1.08 1.06
1.16
1.09 1.08
1.29 1.25 2.21 3.04 3.23 3.22 3.68 7.16
9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

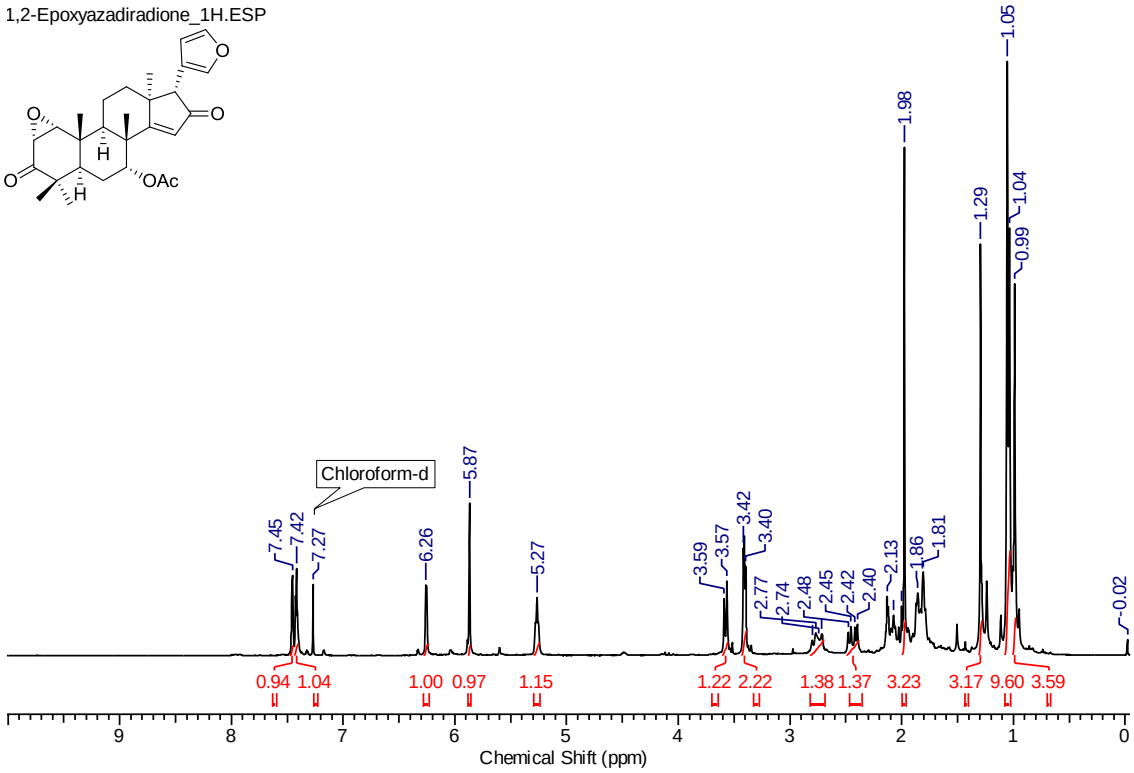

12ß-Hydroxy-1,2-Dihydroazadiradione_13C.ESP
OH
O
O
O
H
H
OAc
Chloroform-d
77.00
216.09
206.16
190.70
169.69
142.73
141.86
125.02
118.60
111.26
75.06
68.21
52.86
52.25
46.87
42.21
38.48
36.91
33.70
28.29
25.80
24.98
20.93
15.23
220 200 180 160 140 120 100 80 60 40 20
Chemical Shift (ppm)



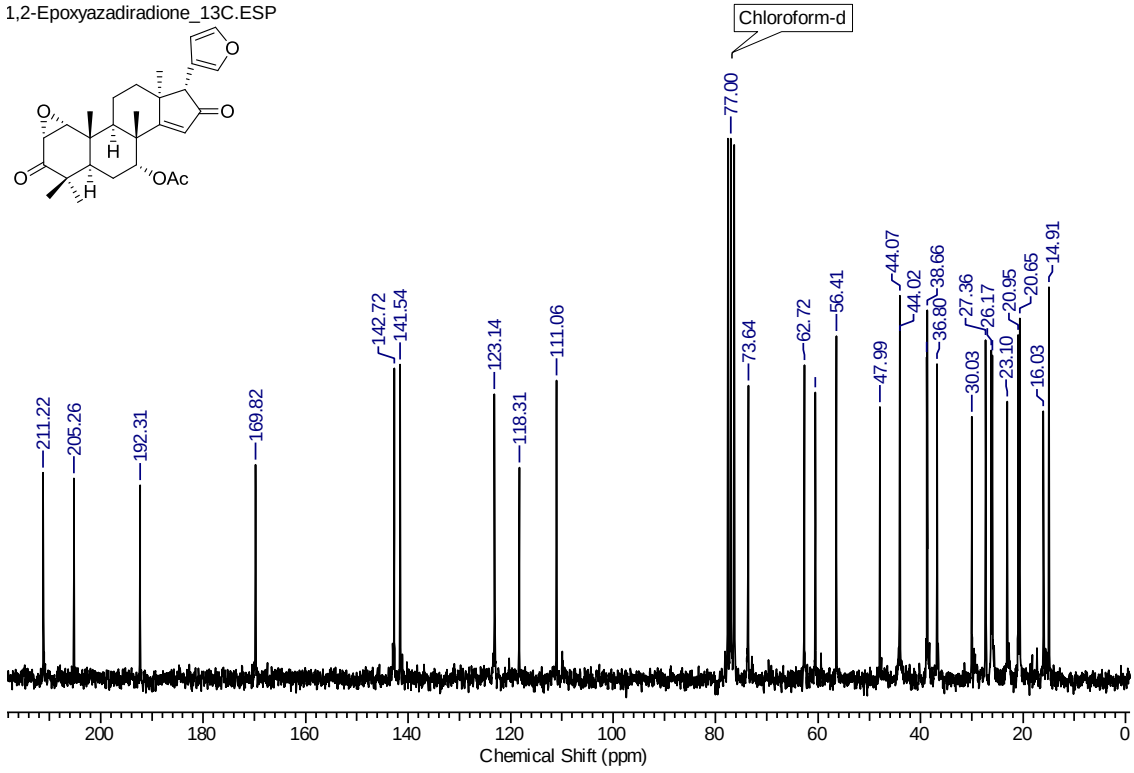


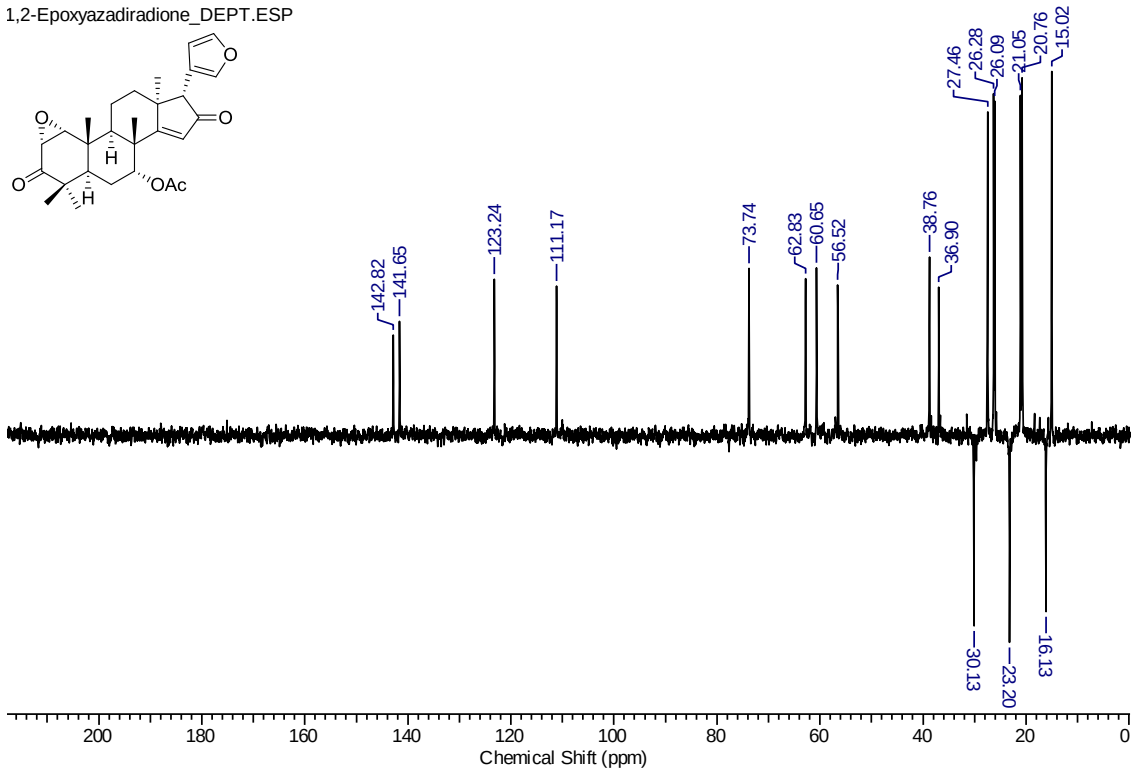
1,2α-Epoxyazadiradione (7)

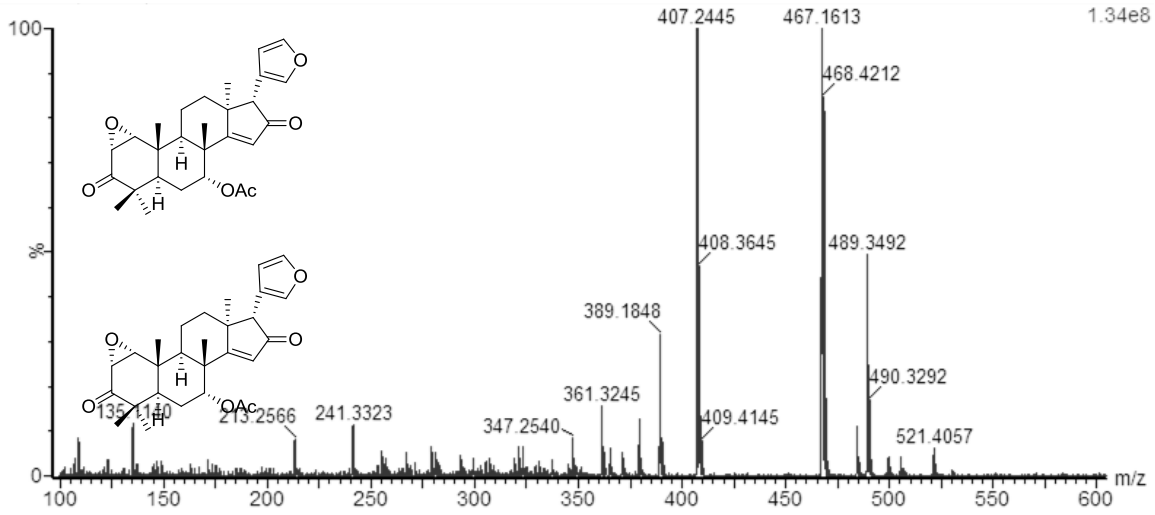
1,2-Epoxyazadiradione_1H.ESP



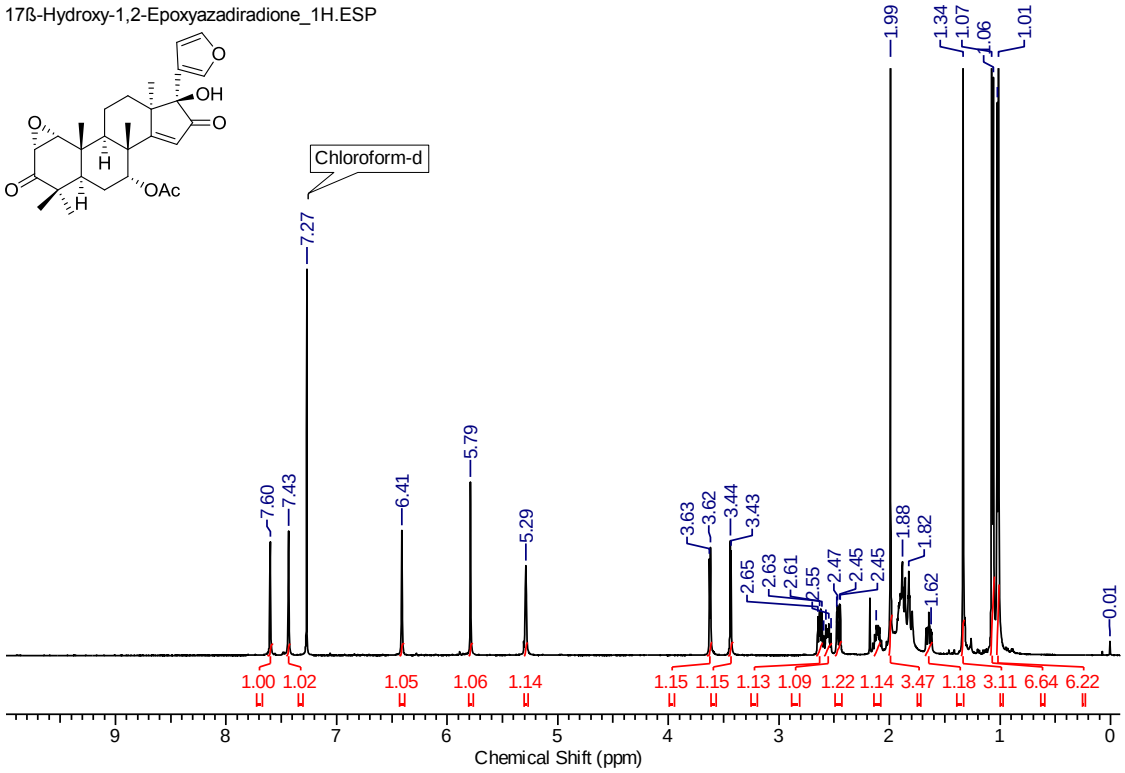
1,2-Epoxyazadiradione_13C.ESP

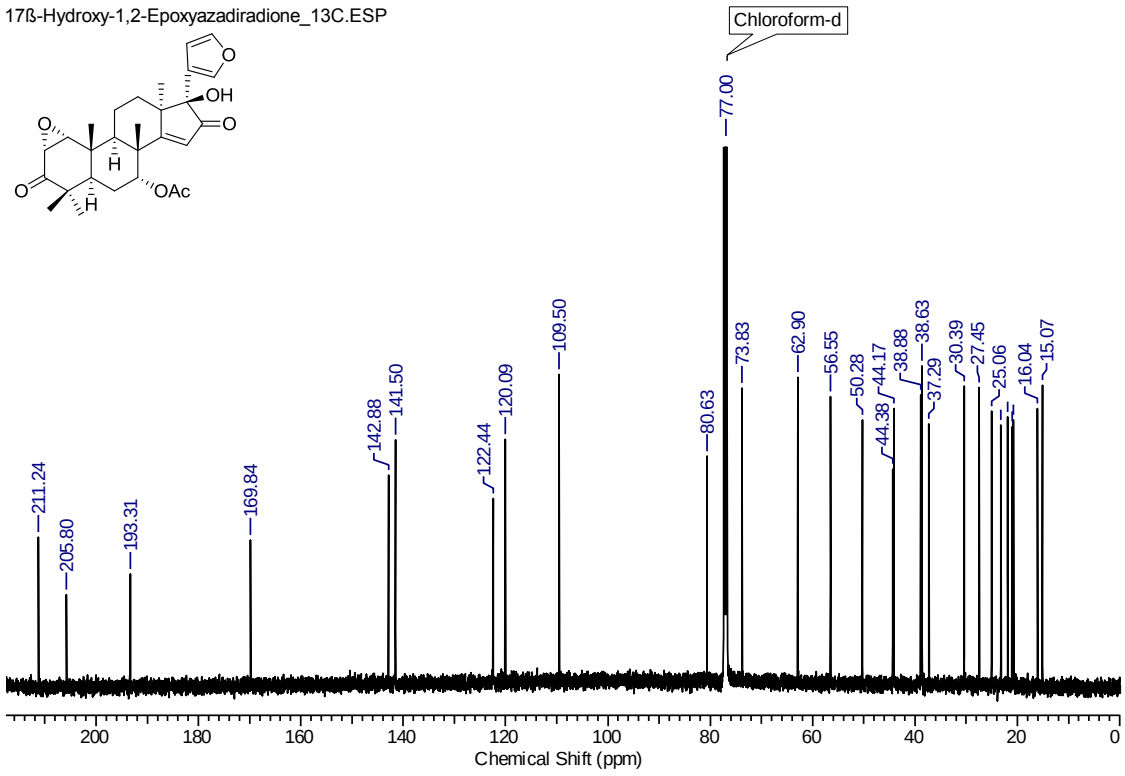


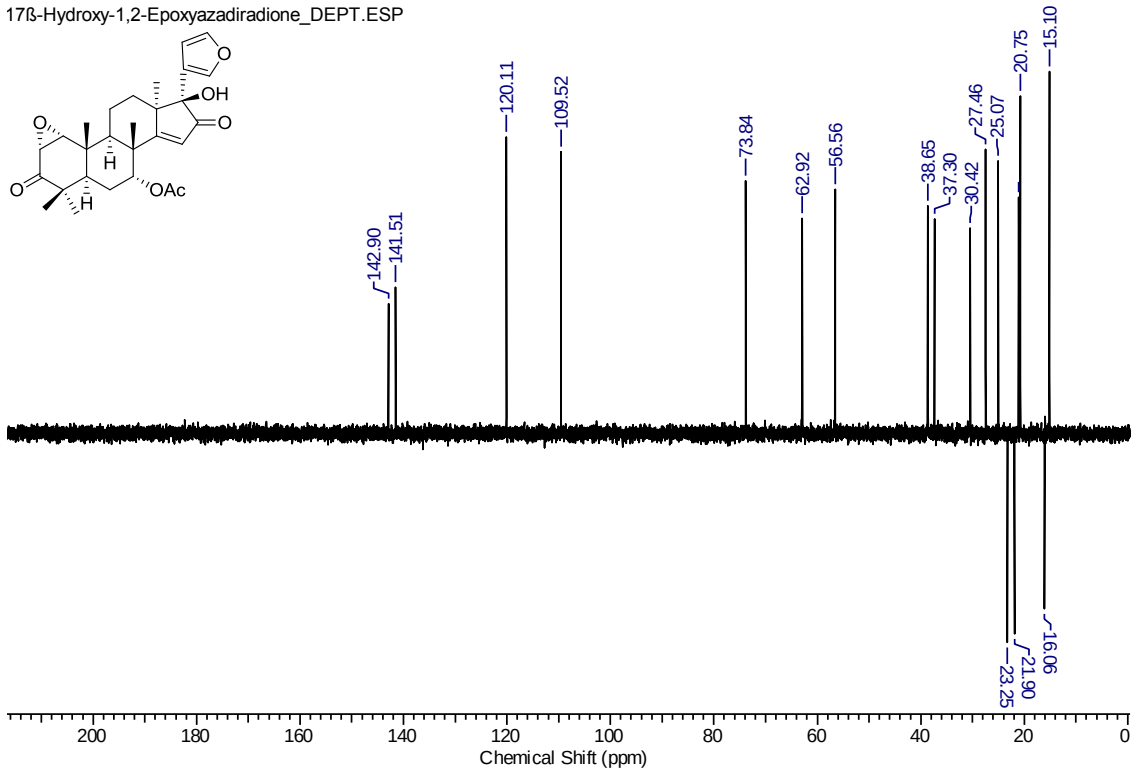

1,2-Epoxyazadiradione_DEPT.ESP
O
O
O
H
O
H
OAc
142.82
141.65
123.24
111.17
73.74
62.83
60.65
56.52
38.76
36.90
27.46
26.28
26.09
21.05
20.76
15.02
30.13
23.20
16.13
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

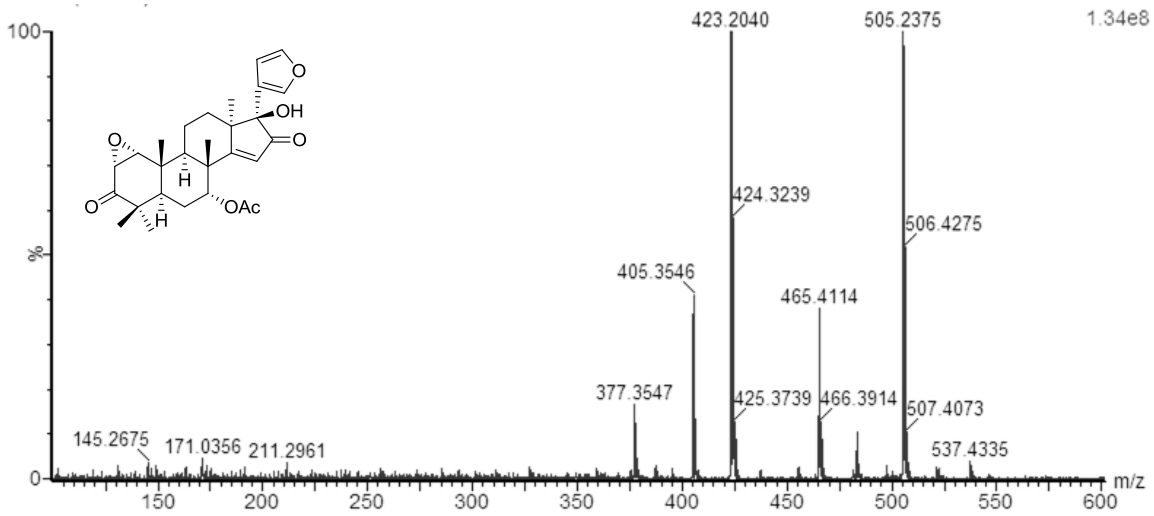

100
%
0
O
O
O
H
O
H
OAc
O
O
O
H
O
H
OAc
135.1140
213.2566
241.3323
347.2540
361.3245
389.1848
407.2445
408.3645
409.4145
467.1613
468.4212
489.3492
490.3292
521.4057
1.34e8
100
150
200
250
300
350
400
450
500
550
600
m/z

17β-Hydroxy-1,2α-Epoxyazadiradione (**8**)

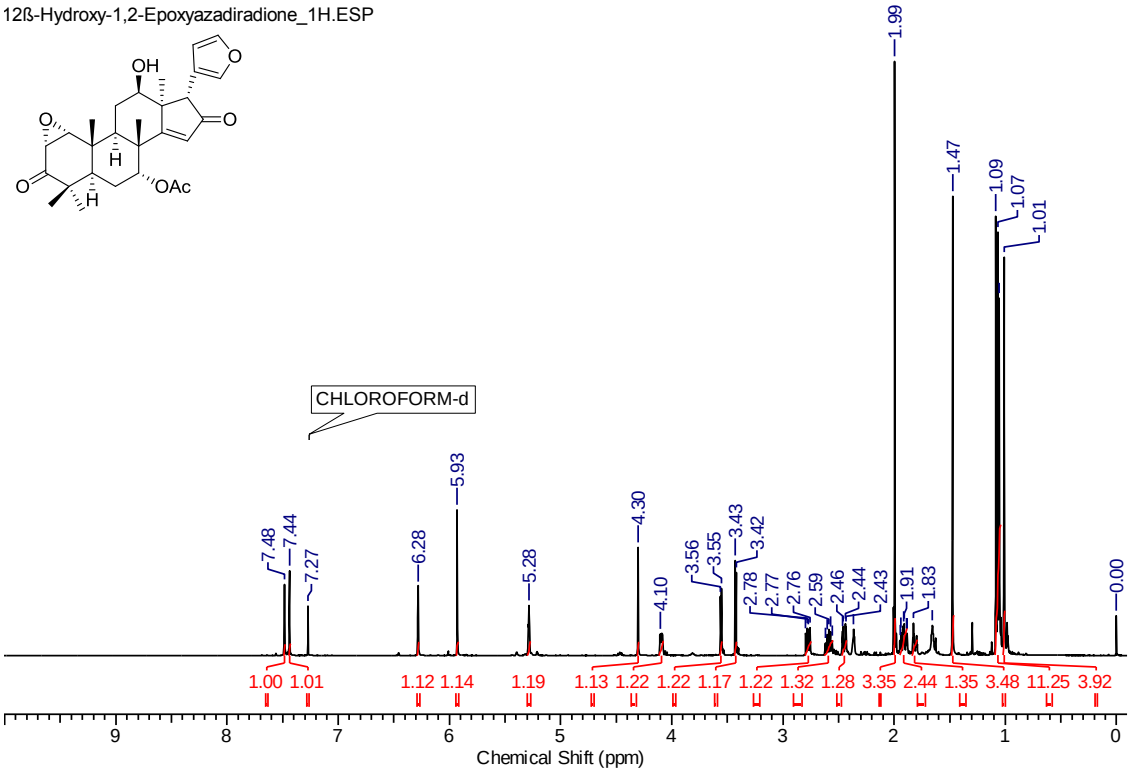


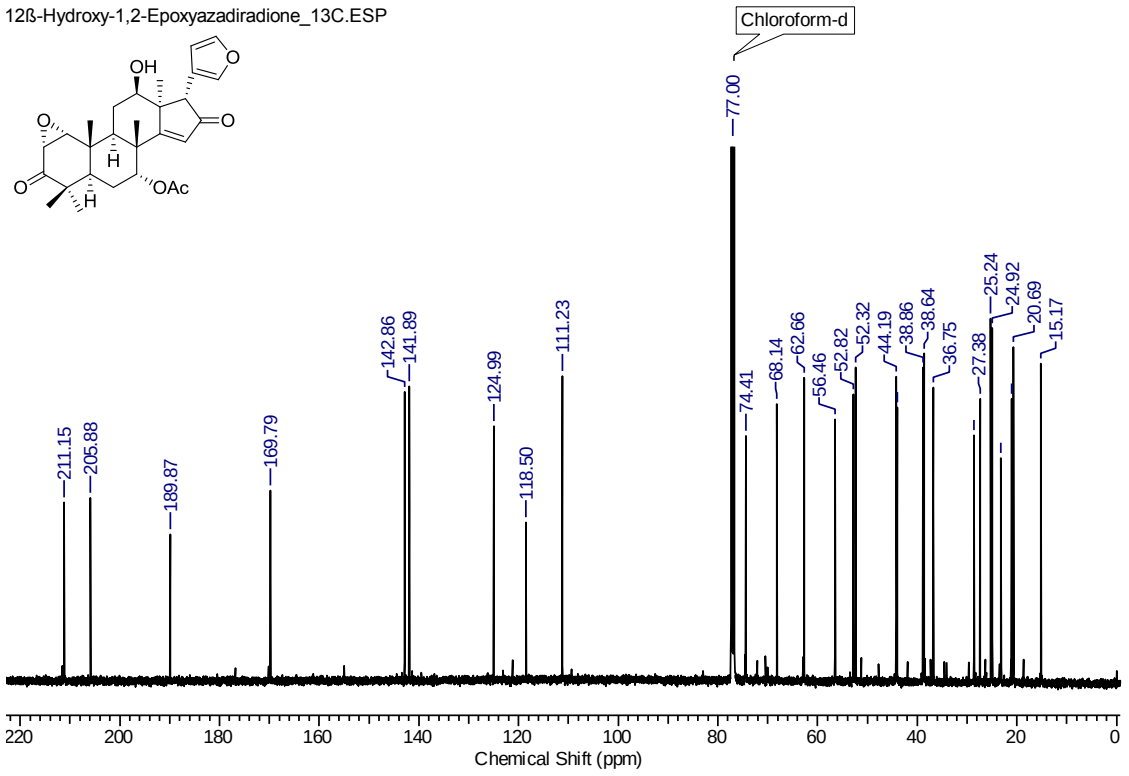


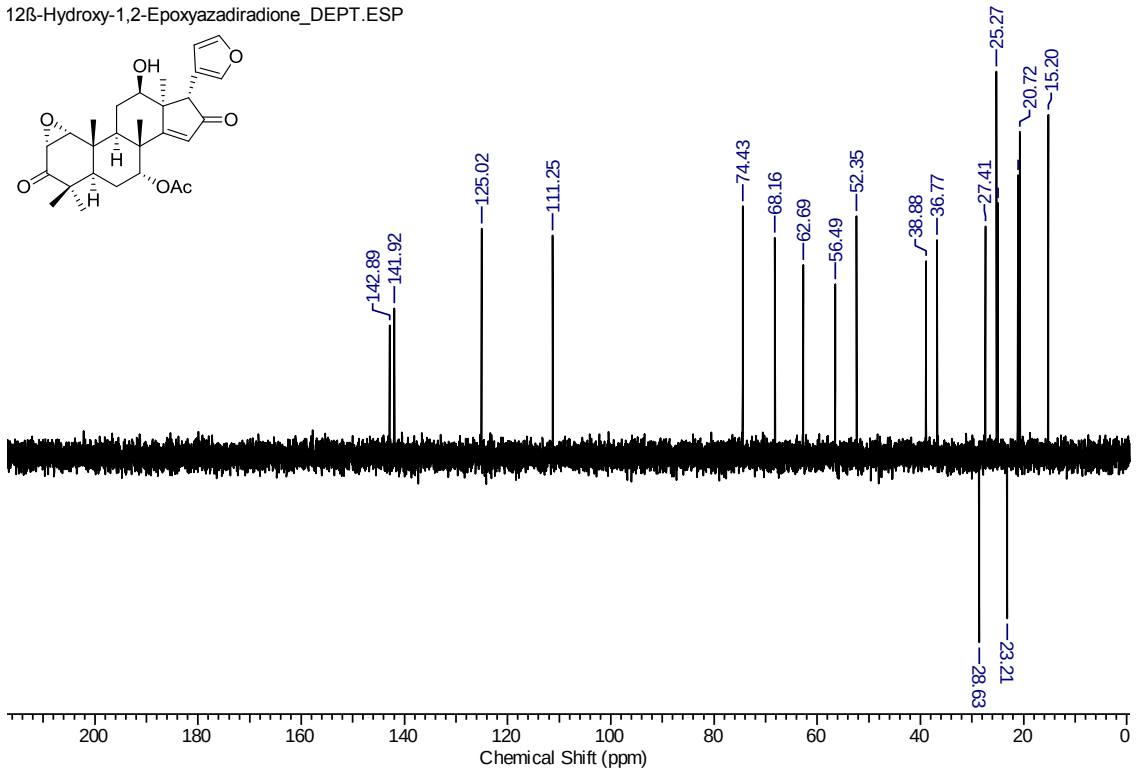

17ß-Hydroxy-1,2-Epoxyazadiradione_DEPT.ESP
OH
O
O
O
H
OAc
H
142.90
141.51
120.11
109.52
73.84
62.92
56.56
38.65
37.30
30.42
27.46
25.07
20.75
15.10
16.96
21.90
23.25
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

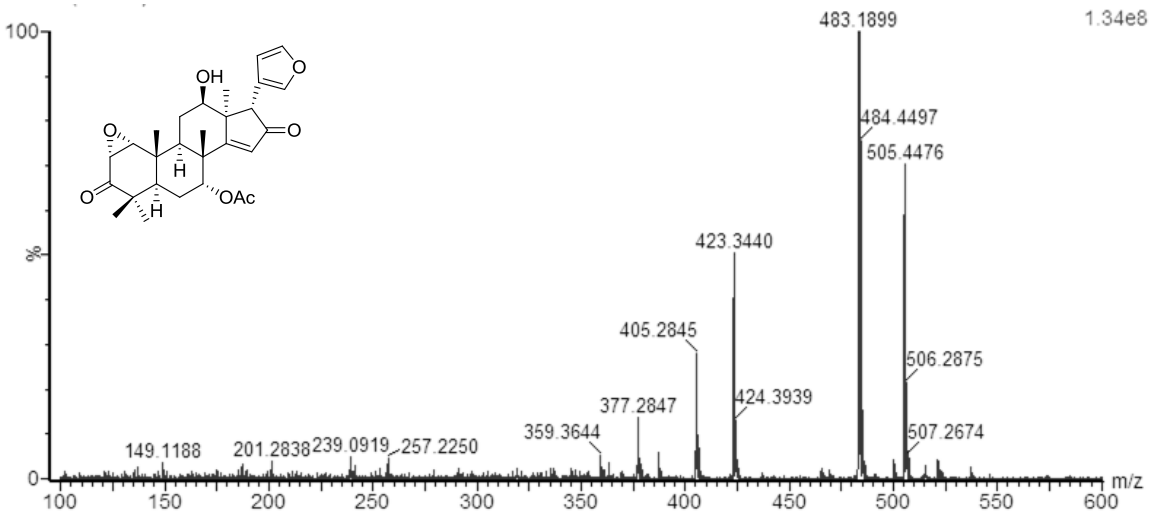

100
%
0
1.34e8
423.2040
505.2375
424.3239
506.4275
405.3546
465.4114
377.3547
425.3739
466.3914
507.4073
537.4335
145.2675
171.0356
211.2961
150
200
250
300
350
400
450
500
550
600
m/z

12β-Hydroxy-1,2α-Epoxyazadiradione (**9**)

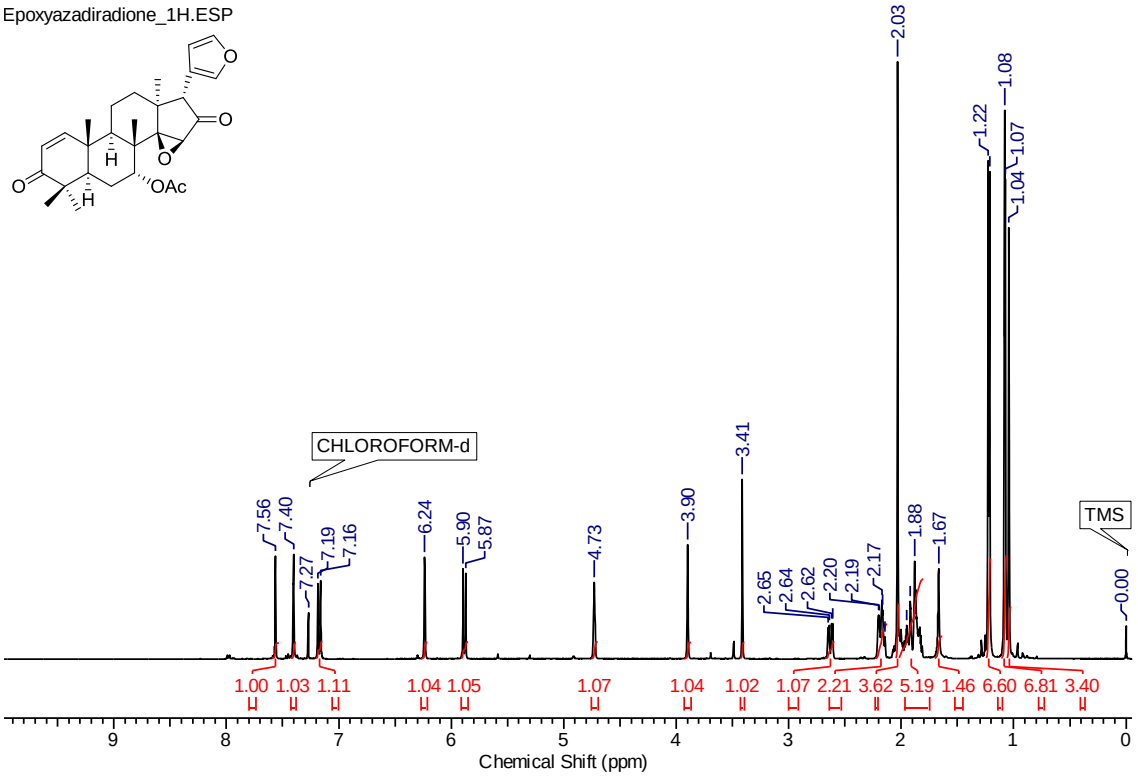


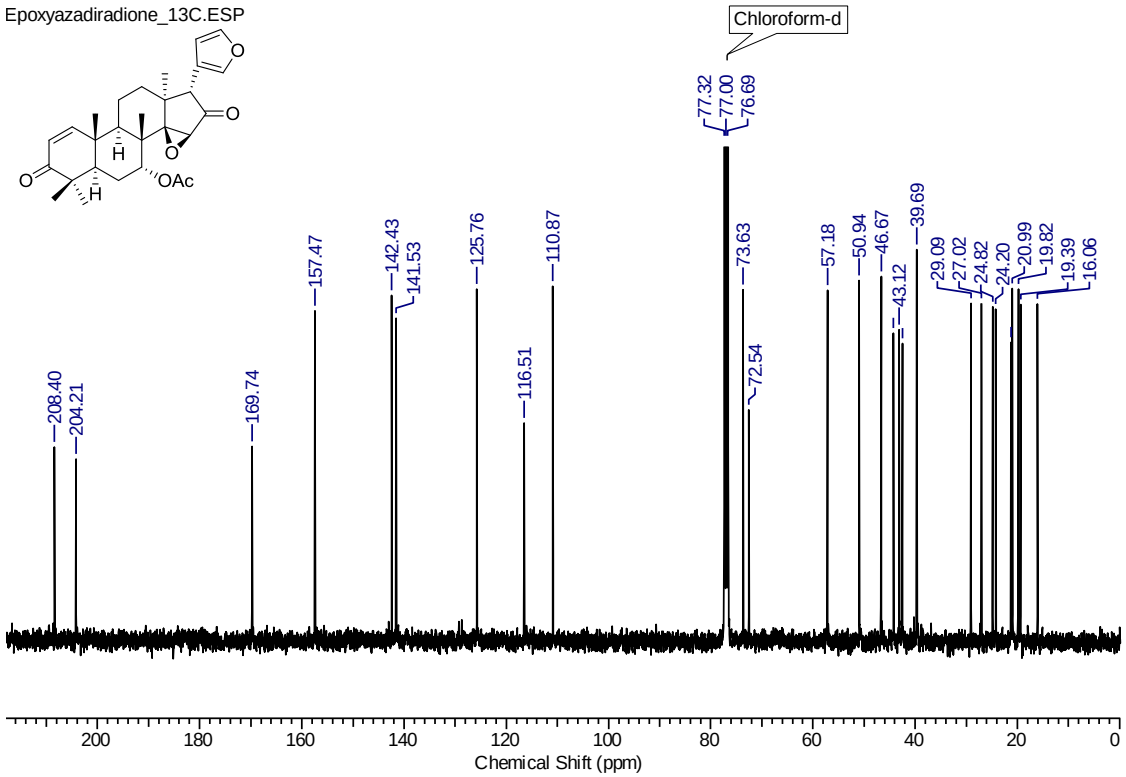


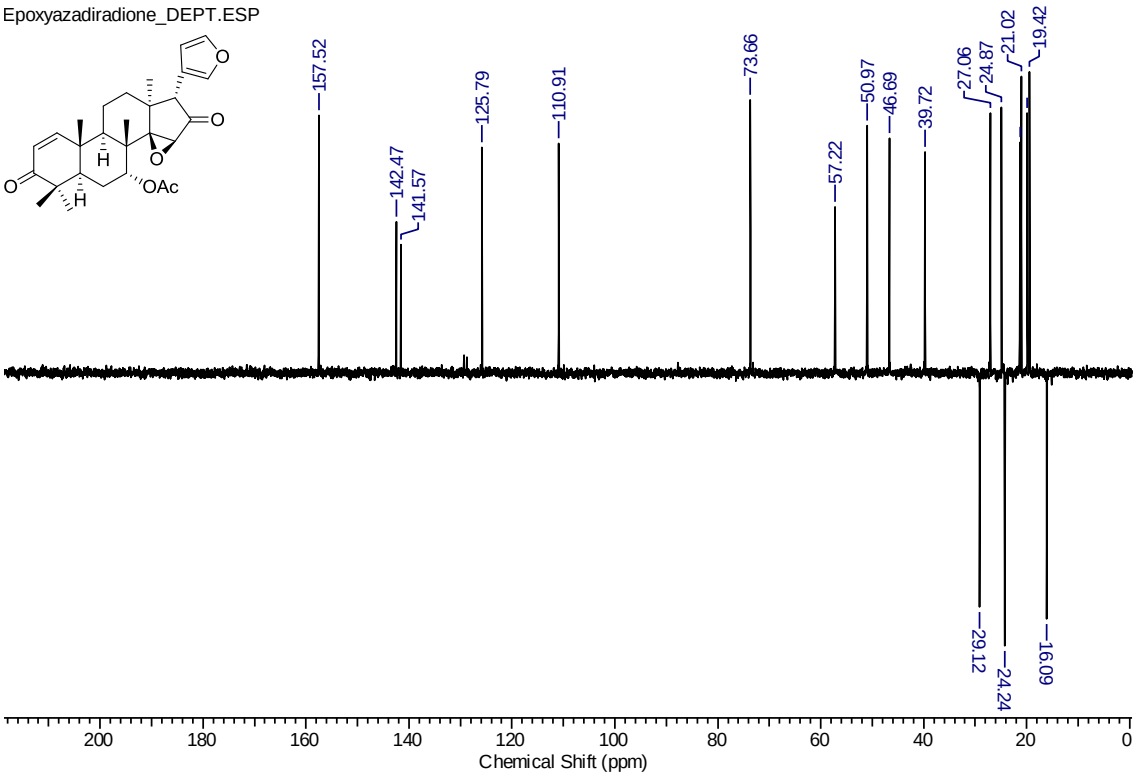

12ß-Hydroxy-1,2-Epoxyazadiradione_DEPT.ESP
OH
O
O
O
H
O
H
OAc
142.89
141.92
125.02
111.25
74.43
68.16
62.69
56.49
52.35
38.88
36.77
27.41
25.27
20.72
15.20
28.63
23.21
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

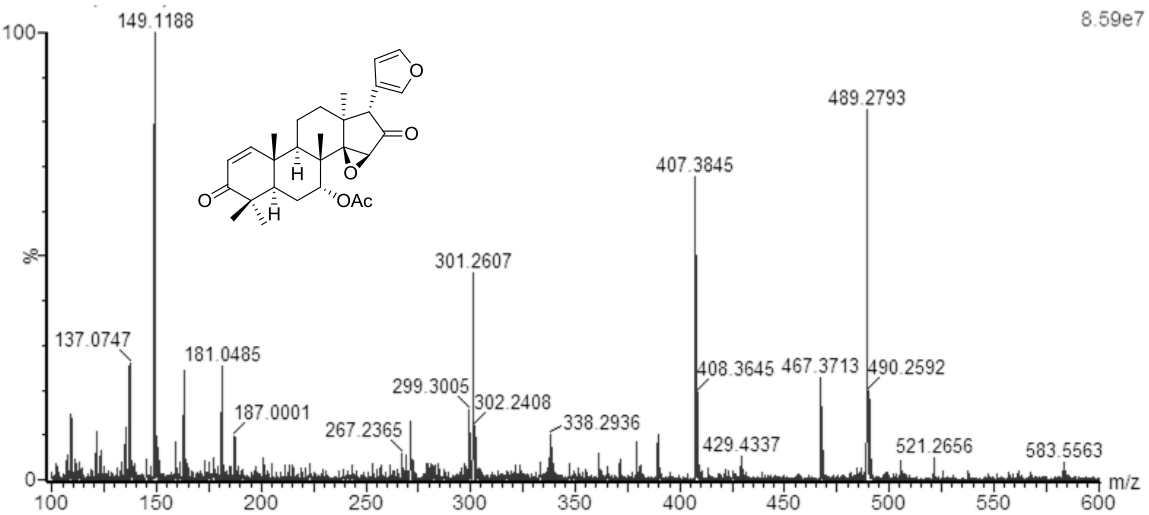

100
%
0
OH
O
O
O
H
O
H
OAc
483.1899
1.34e8
484.4497
505.4476
423.3440
405.2845
506.2875
424.3939
377.2847
359.3644
507.2674
149.1188
201.2838
239.0919
257.2250
100
150
200
250
300
350
400
450
500
550
600
m/z

Epoxyazadiradione (**10**)

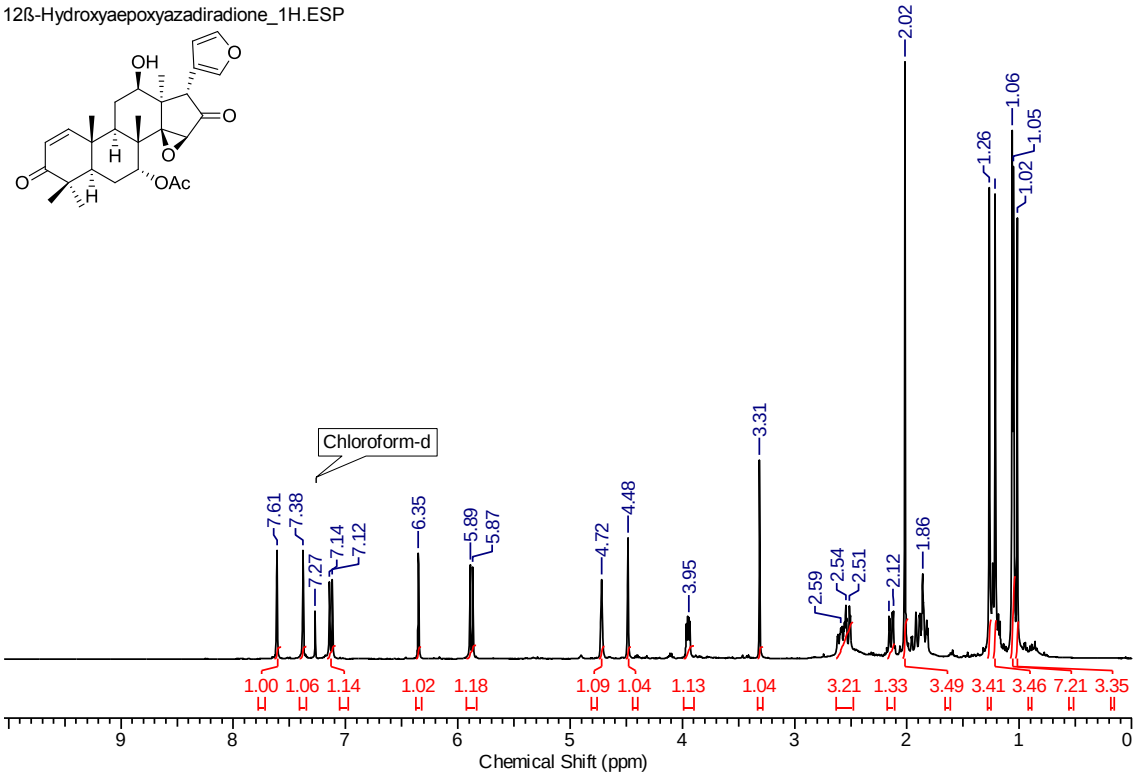


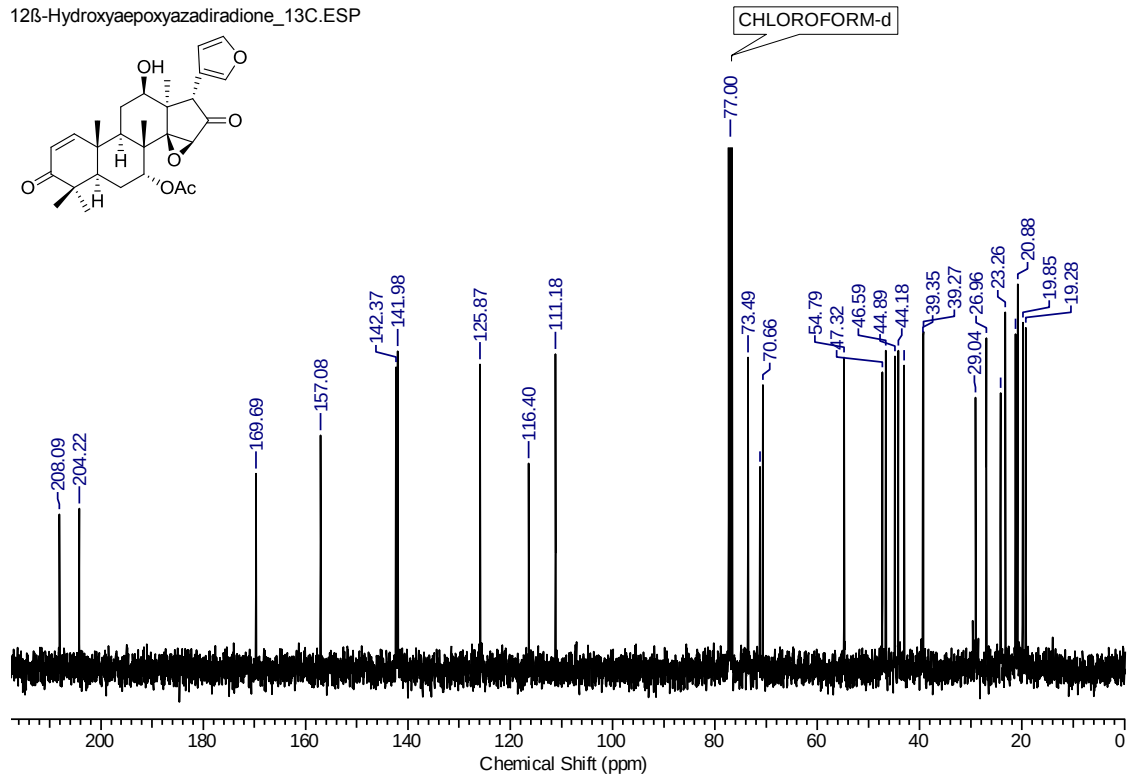


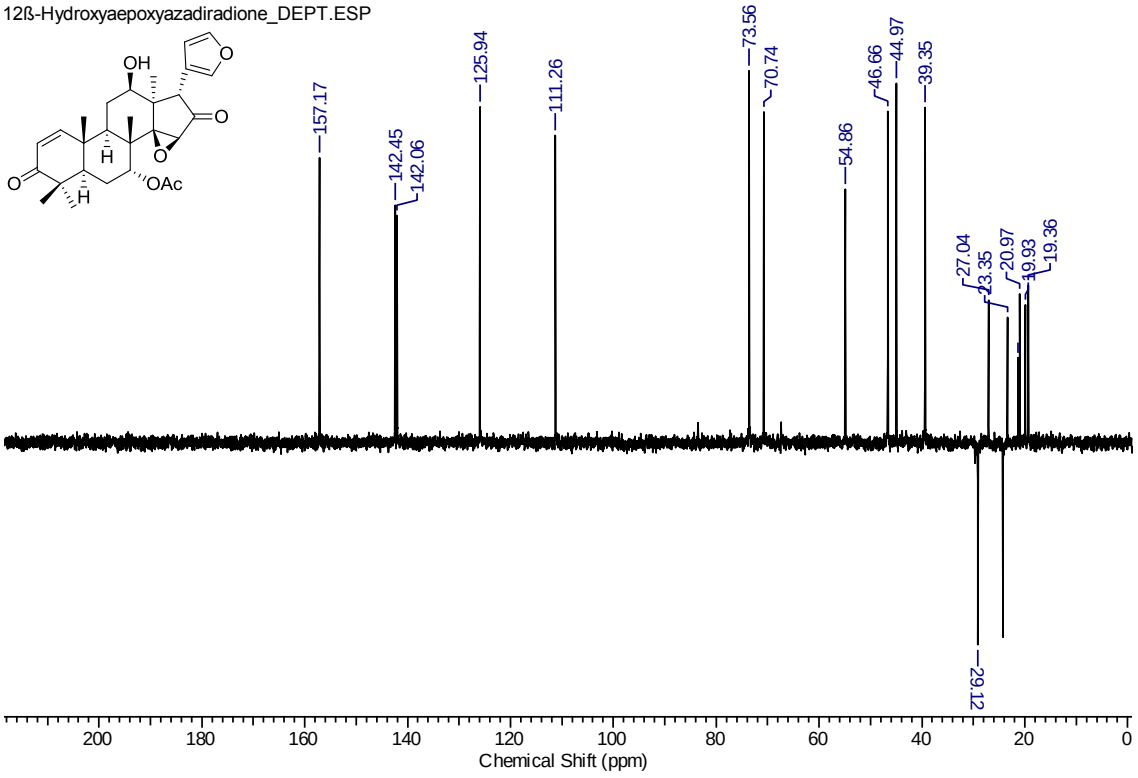

Epoxyazadiradione_DEPT.ESP
157.52
142.47
141.57
125.79
110.91
73.66
57.22
50.97
46.69
39.72
27.06
24.87
21.02
19.42
29.12
24.24
16.09
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

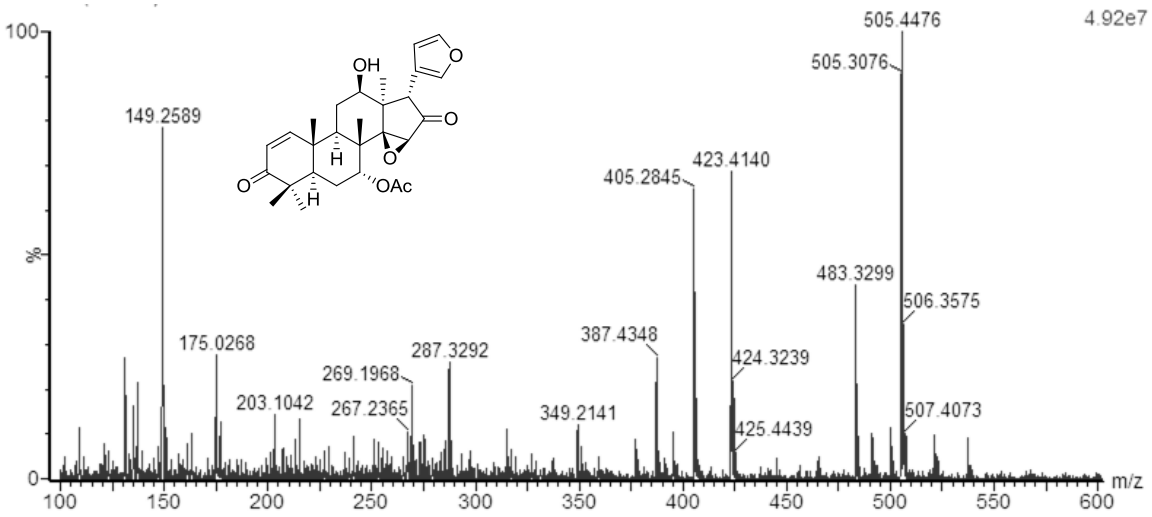

8.59e7
100
%
0
149.1188
489.2793
407.3845
301.2607
137.0747
181.0485
187.0001
299.3005
302.2408
267.2365
338.2936
408.3645
467.3713
490.2592
429.4337
521.2656
583.5563
100
150
200
250
300
350
400
450
500
550
600
m/z

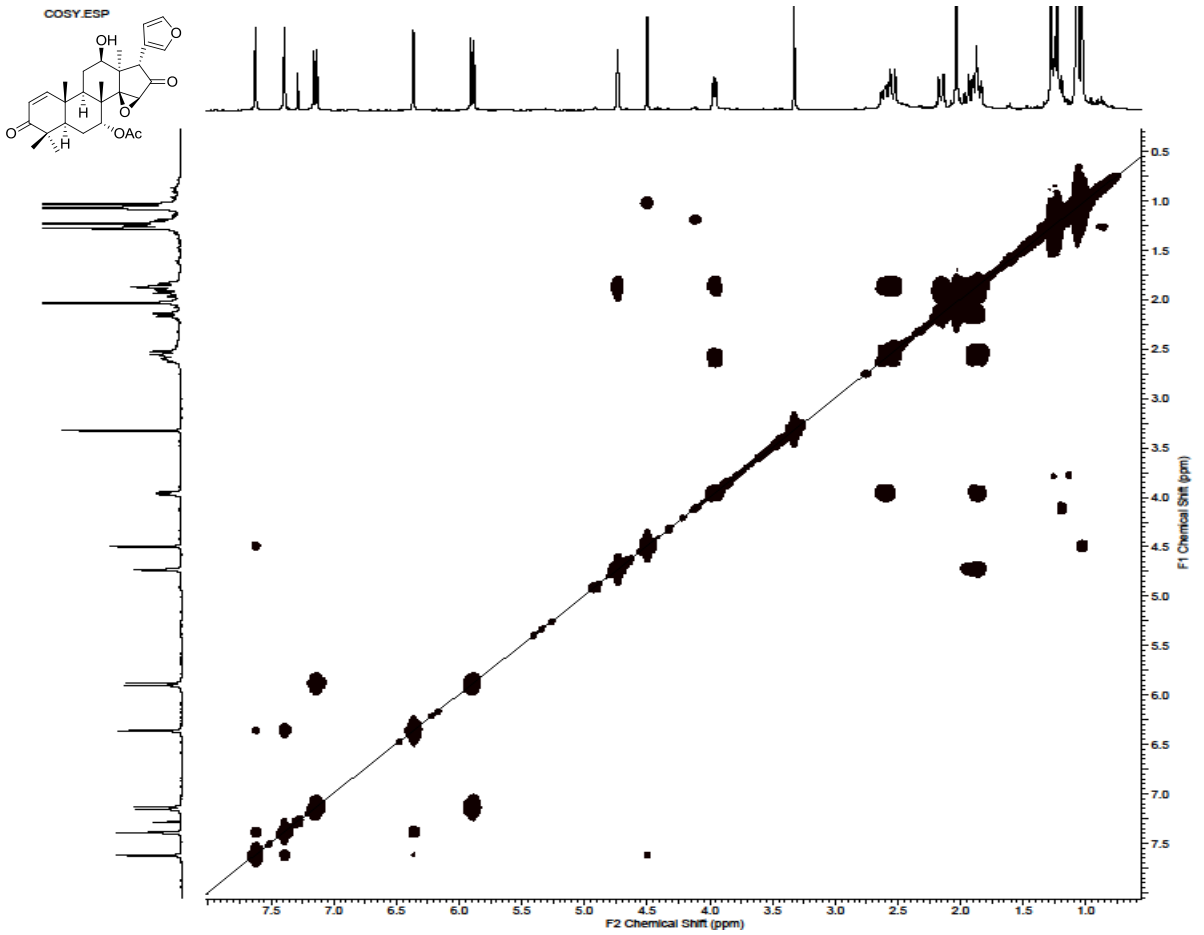
12β-Hydroxyepoxyazadiradione (**11**)

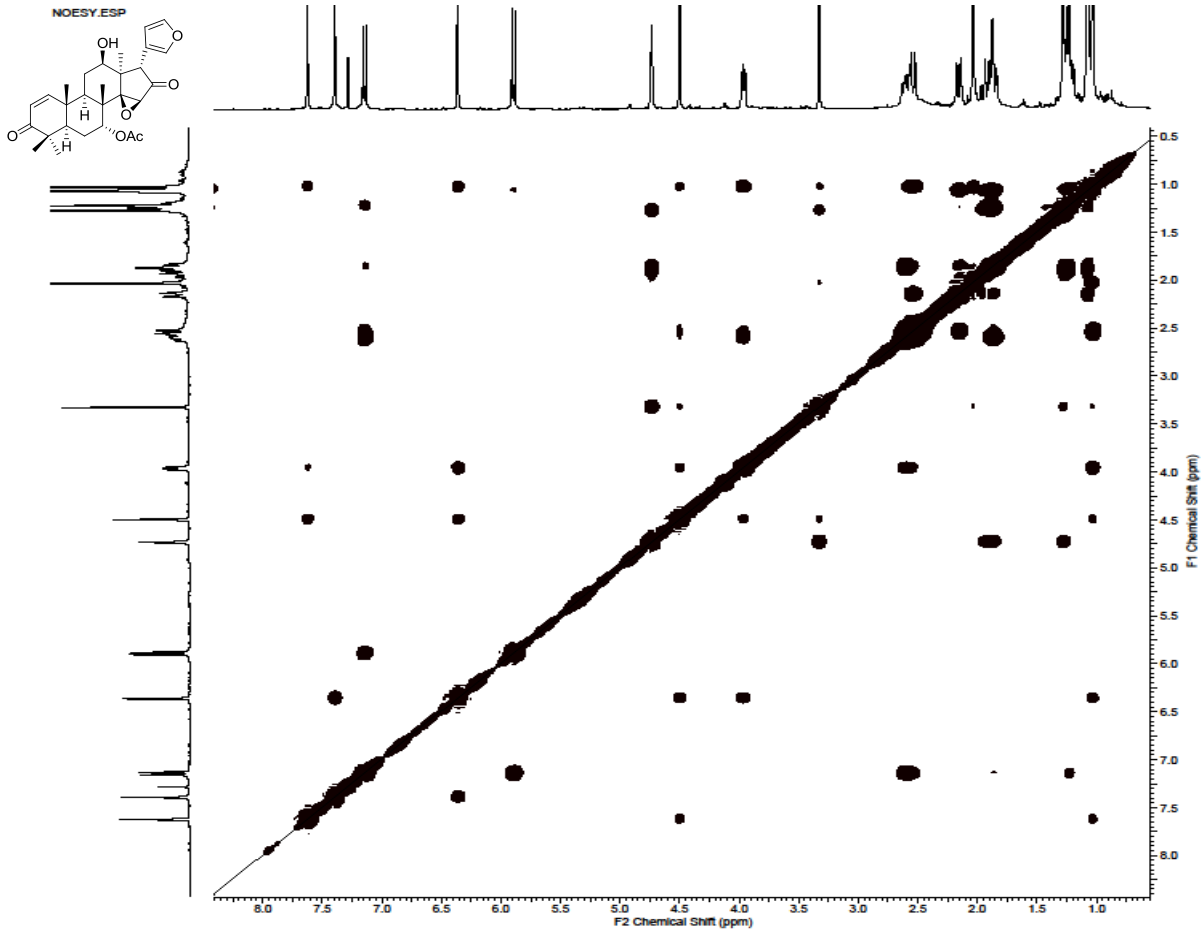


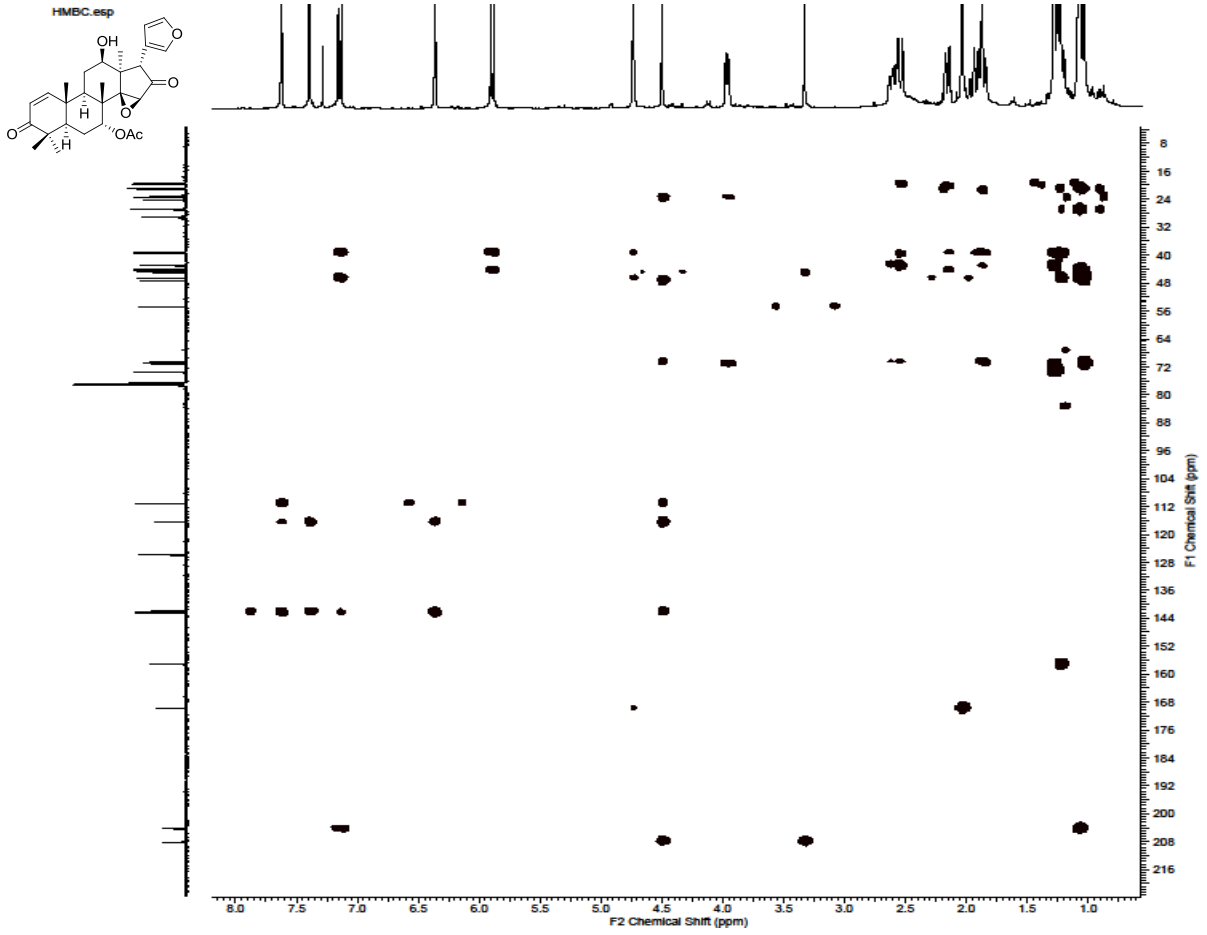


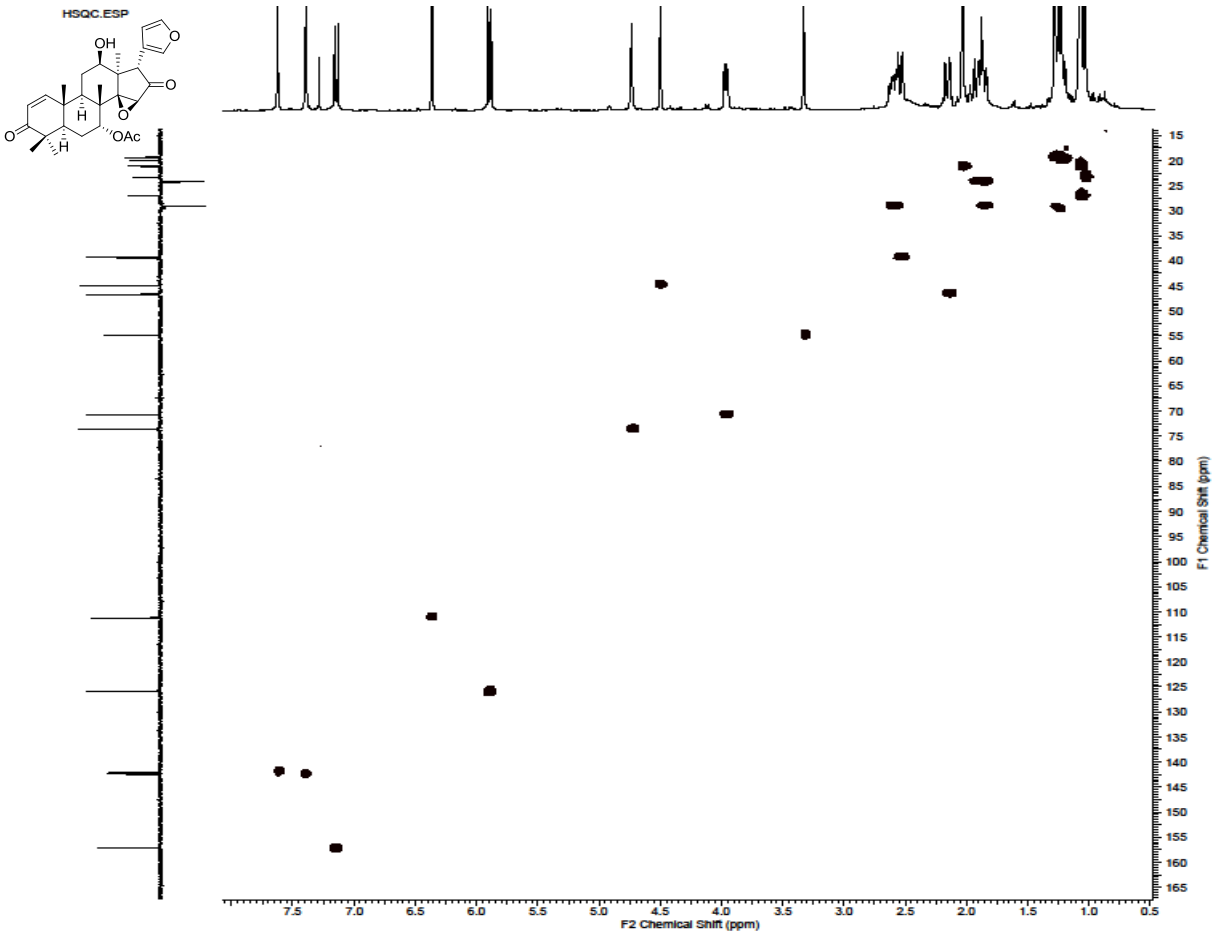

12ß-Hydroxyaepoxyazadiradione_DEPT.ESP
OH
O
O
O
H
O
H
OAc
157.17
142.45
142.06
125.94
111.26
73.56
70.74
54.86
46.66
44.97
39.35
27.04
23.35
20.97
19.93
19.36
29.12
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


100
%
0
OH
O
O
O
H
O
H
OAc
505.4476
4.92e7
505.3076
149.2589
423.4140
405.2845
483.3299
506.3575
175.0268
387.4348
287.3292
424.3239
269.1968
203.1042
267.2365
349.2141
425.4439
507.4073
100
150
200
250
300
350
400
450
500
550
600
m/z

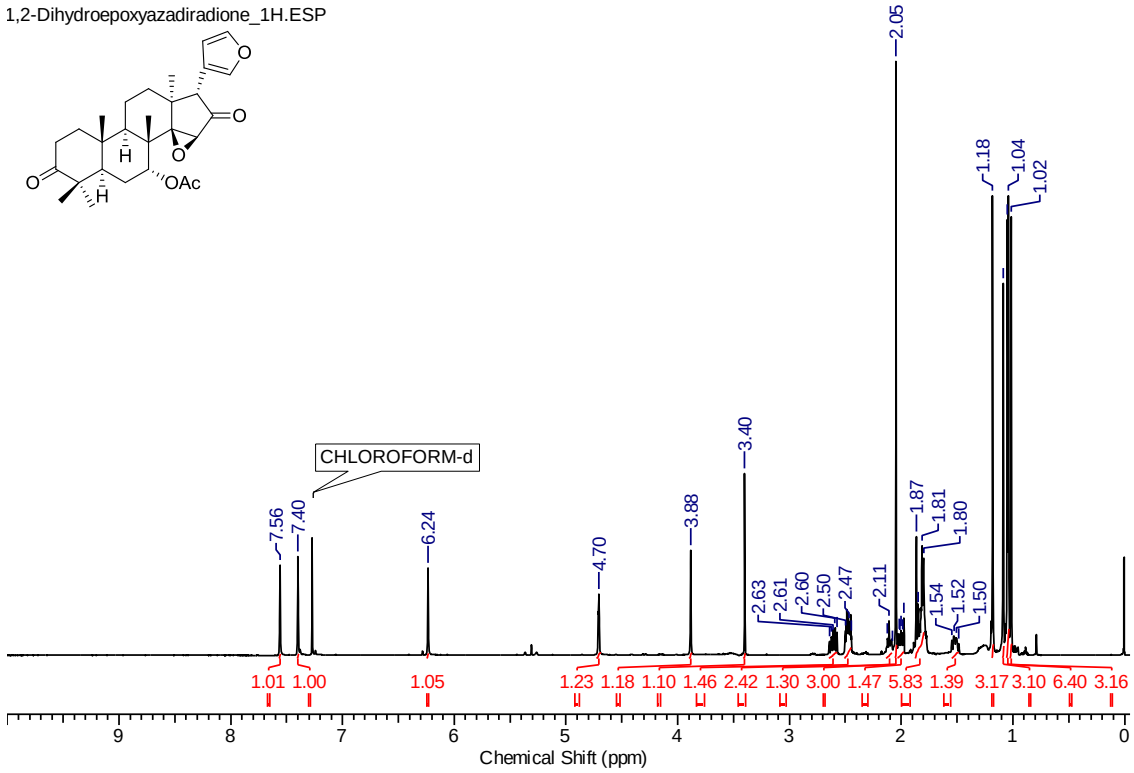


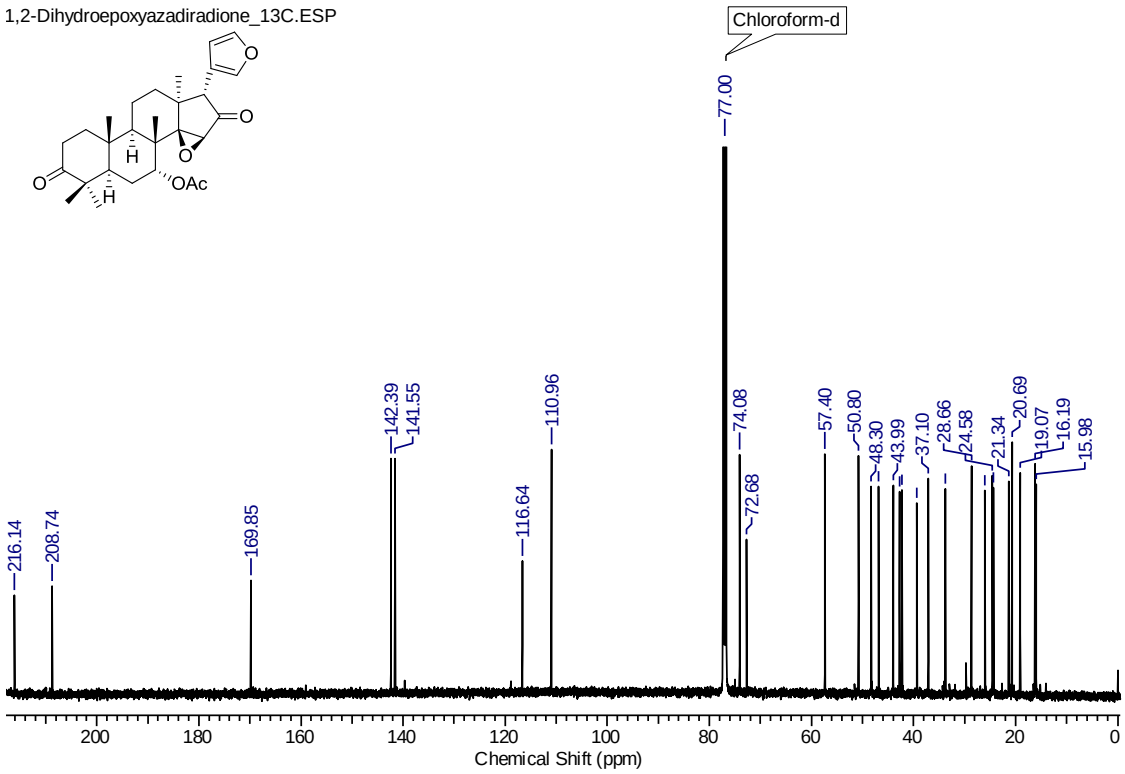


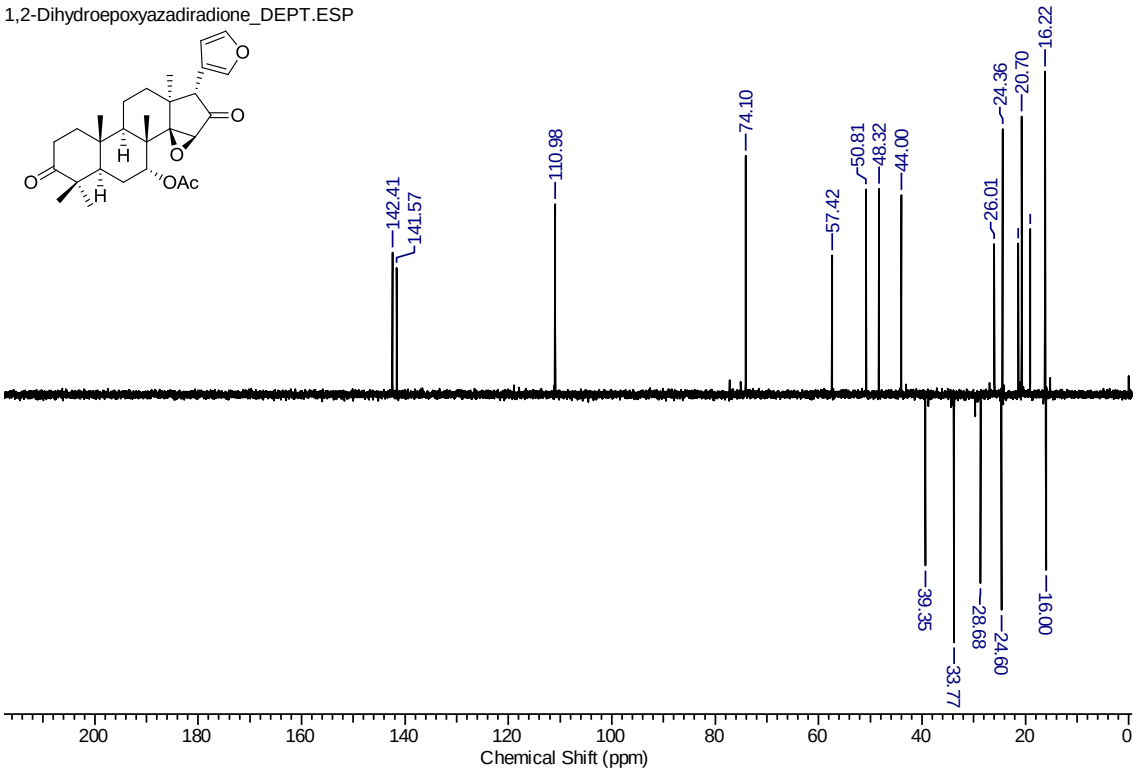


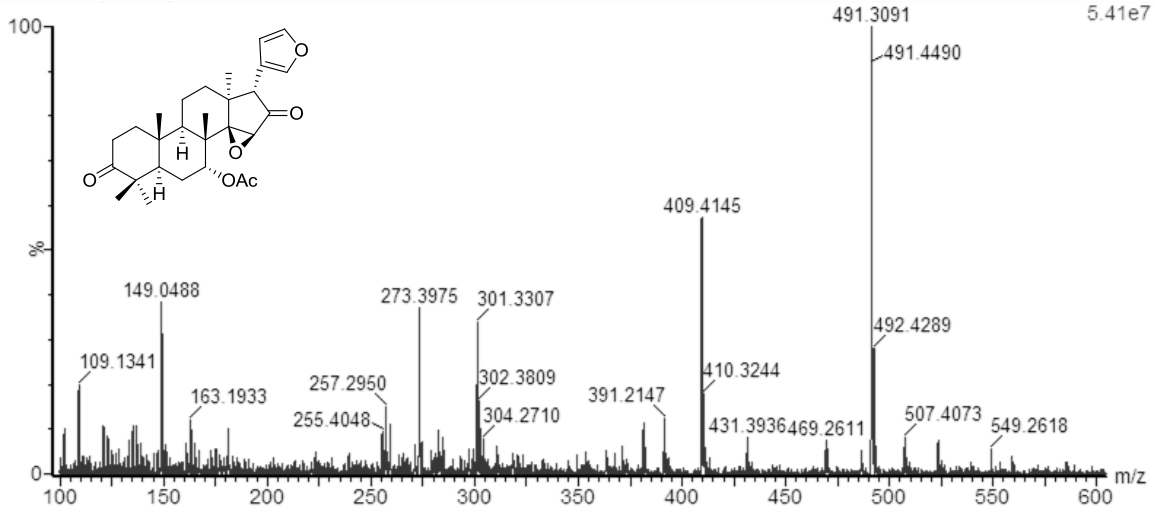


1,2-Dihydroepoxyazadiradione (**12**)

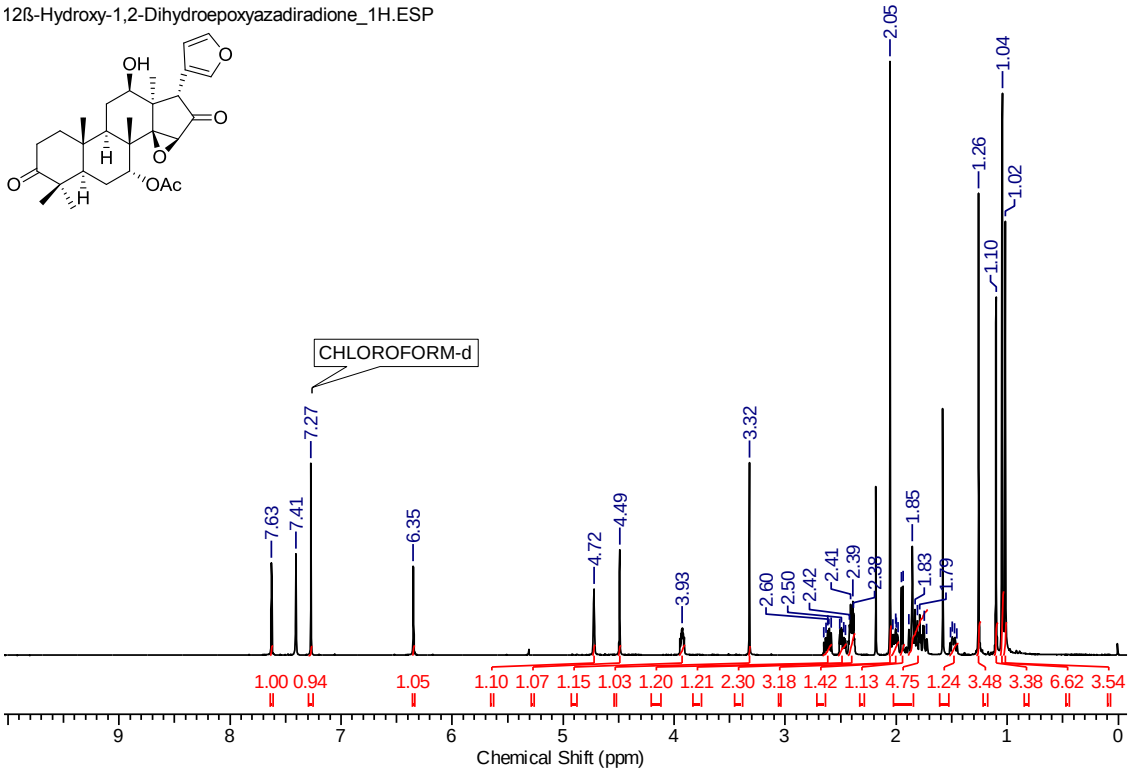


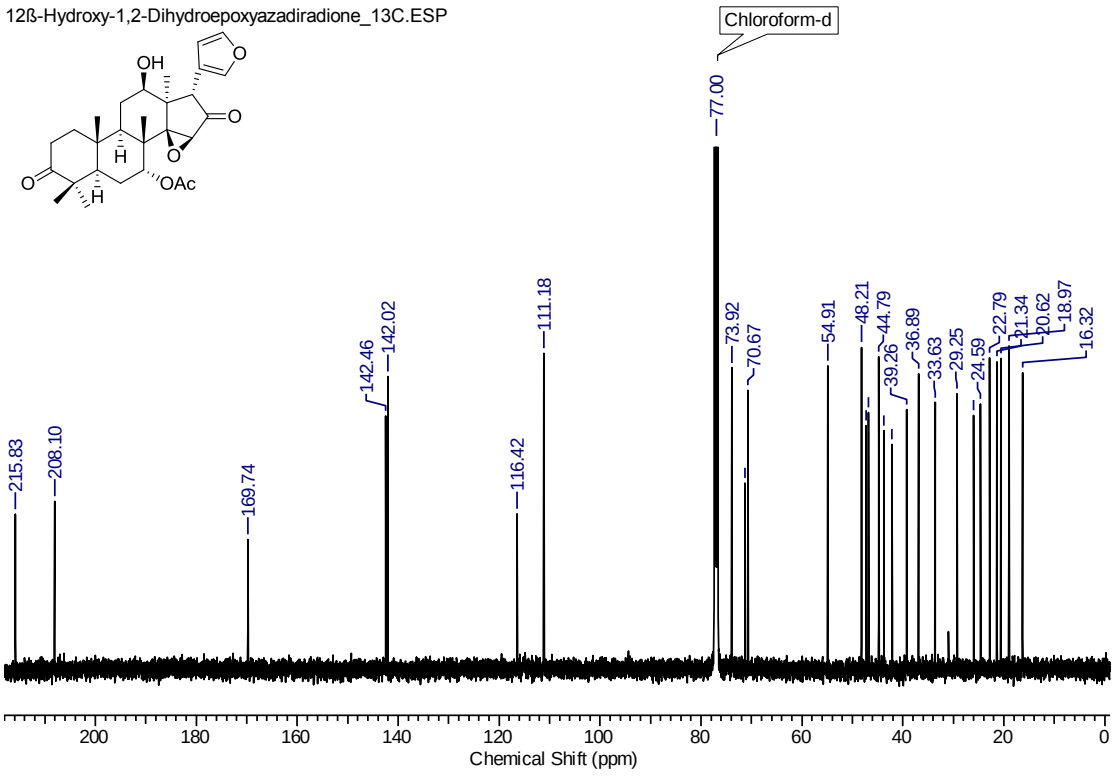


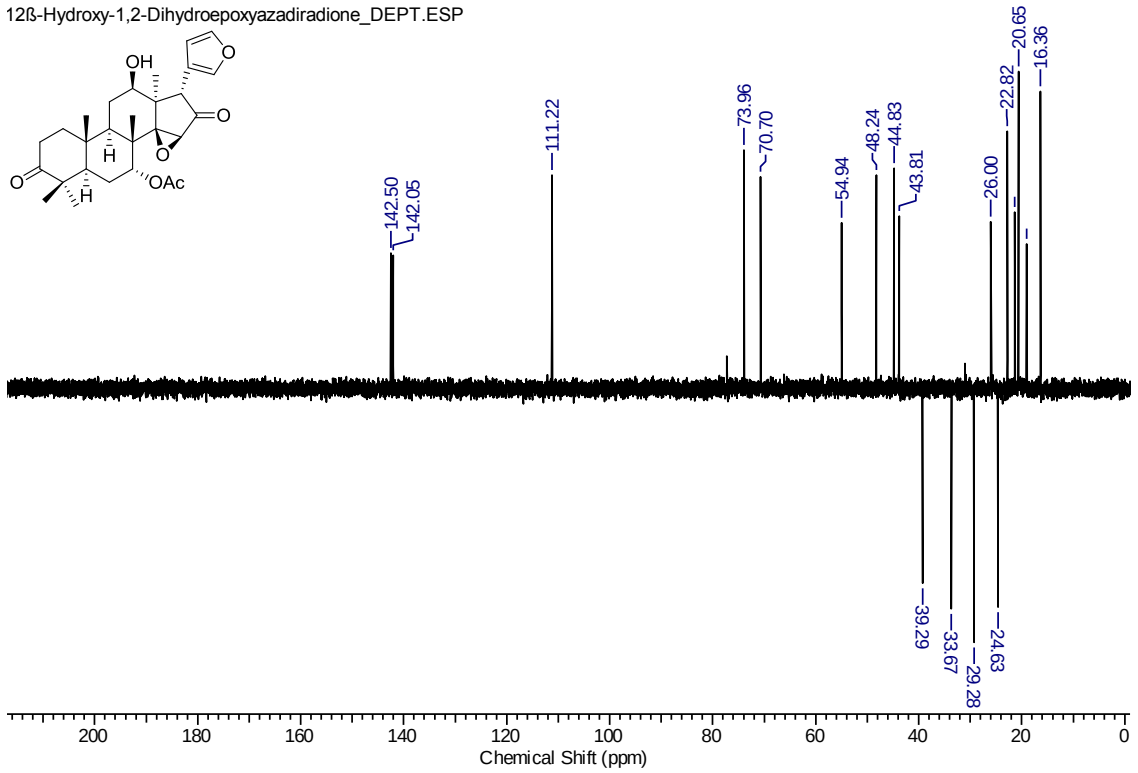


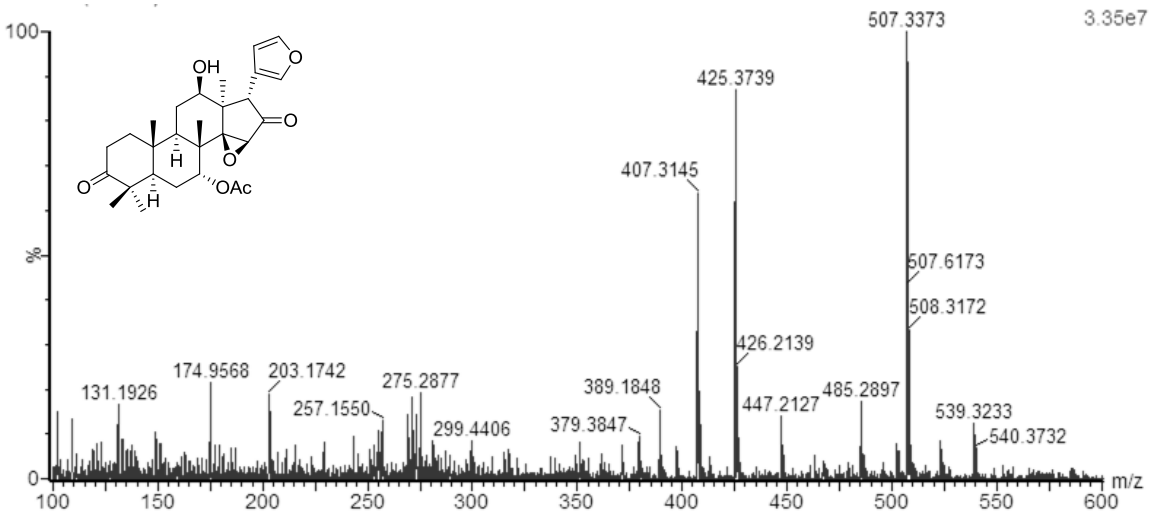


12β-Hydroxy-1,2-Dihydroepoxyazadiradione (**13**)

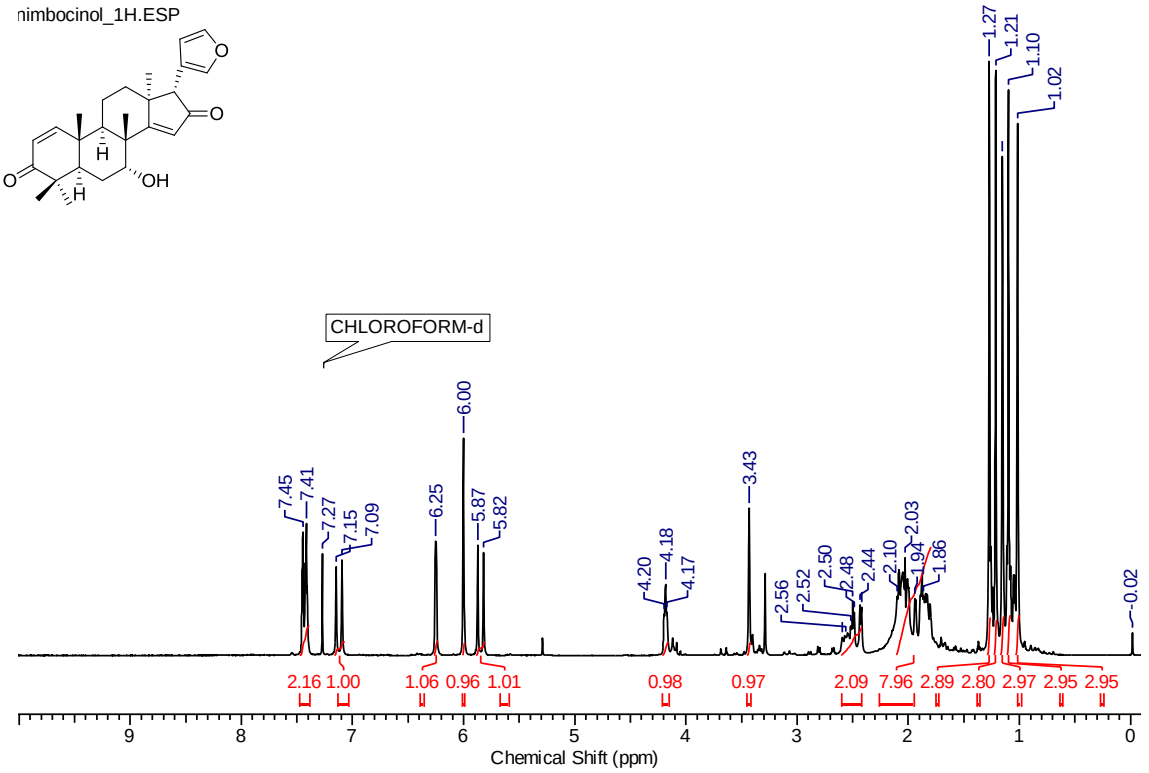


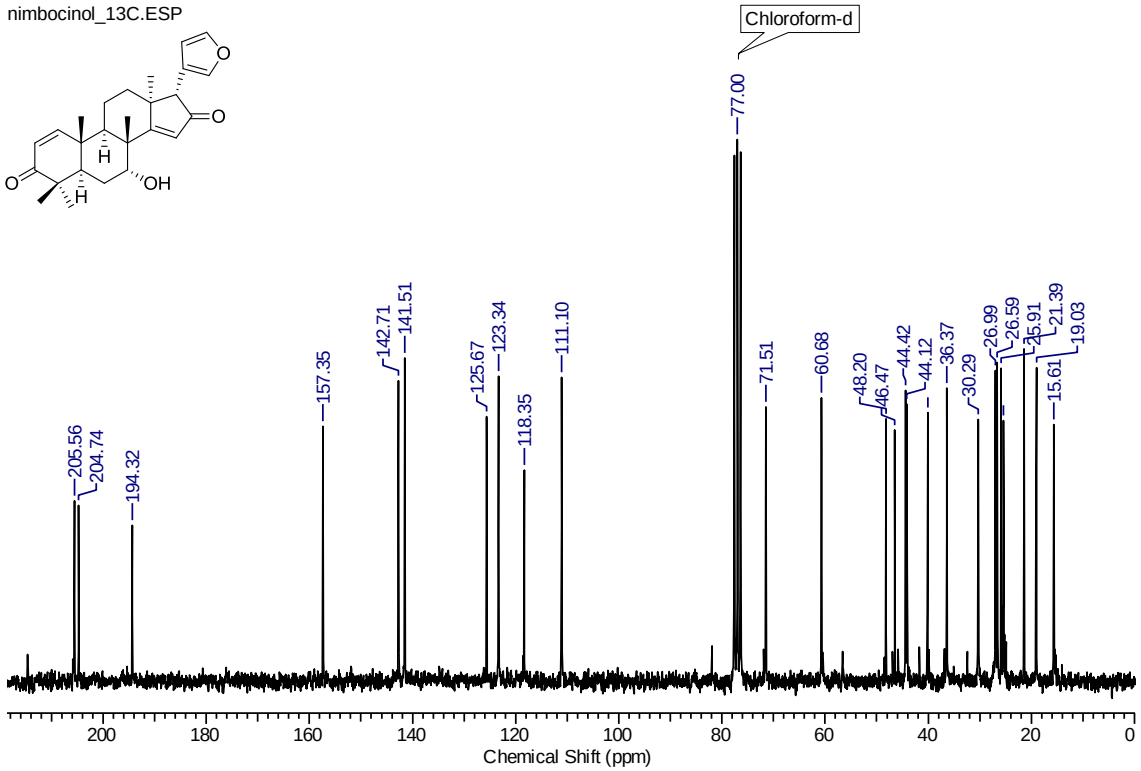


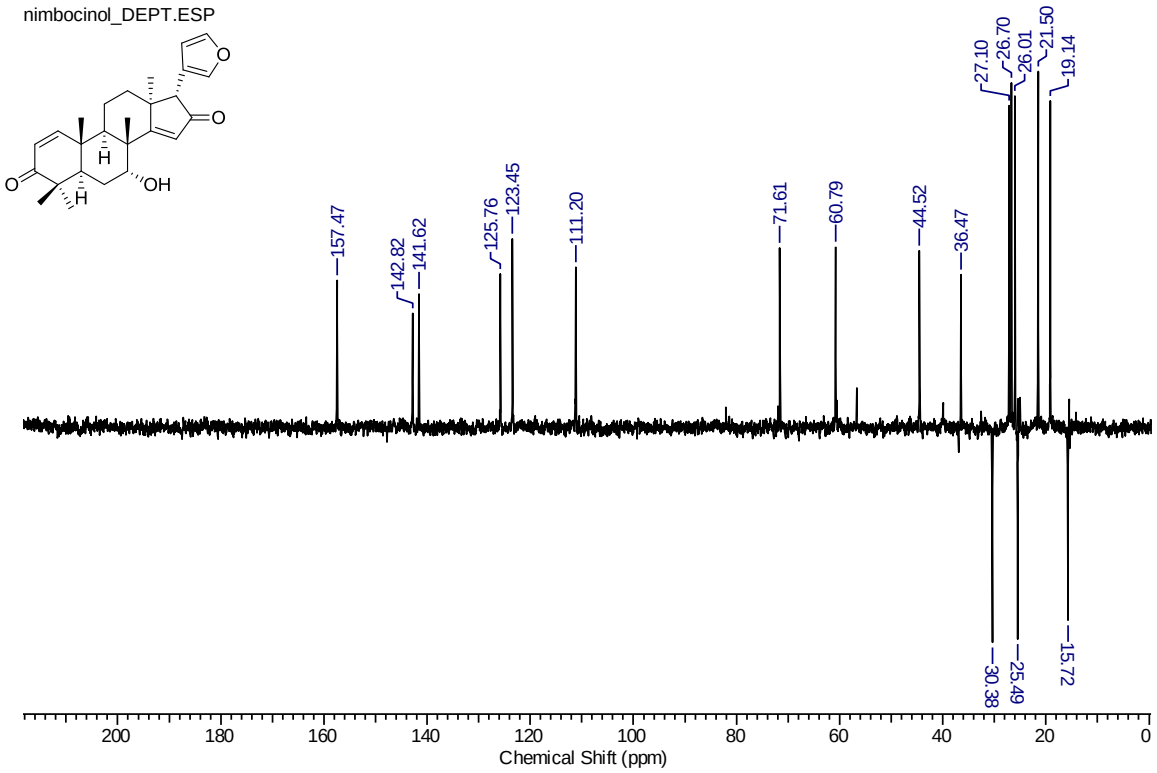

12ß-Hydroxy-1,2-Dihydroepoxyazadiradione_DEPT.ESP
OH
O
O
O
H
O
OAc
H
142.50
142.05
111.22
73.96
70.70
54.94
48.24
44.83
43.81
26.00
22.82
20.65
16.36
39.29
33.67
29.28
24.63
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

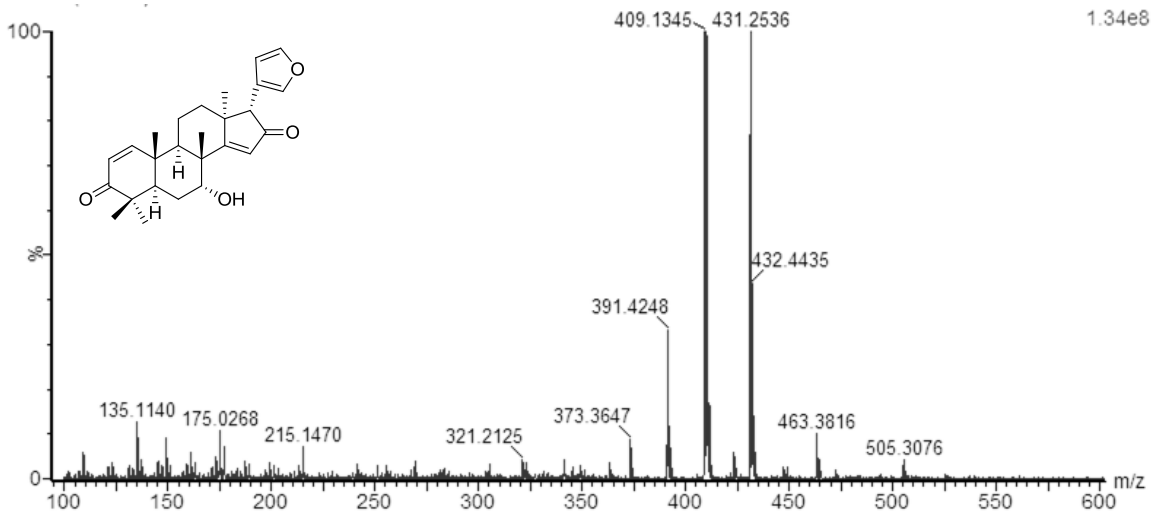

100
%
0
OH
O
O
O
H
O
OAc
H
507.3373
3.35e7
425.3739
407.3145
507.6173
508.3172
426.2139
131.1926
174.9568
203.1742
275.2877
257.1550
389.1848
447.2127
485.2897
299.4406
379.3847
539.3233
540.3732
100
150
200
250
300
350
400
450
500
550
600
m/z

Nimbocinol (**14**)

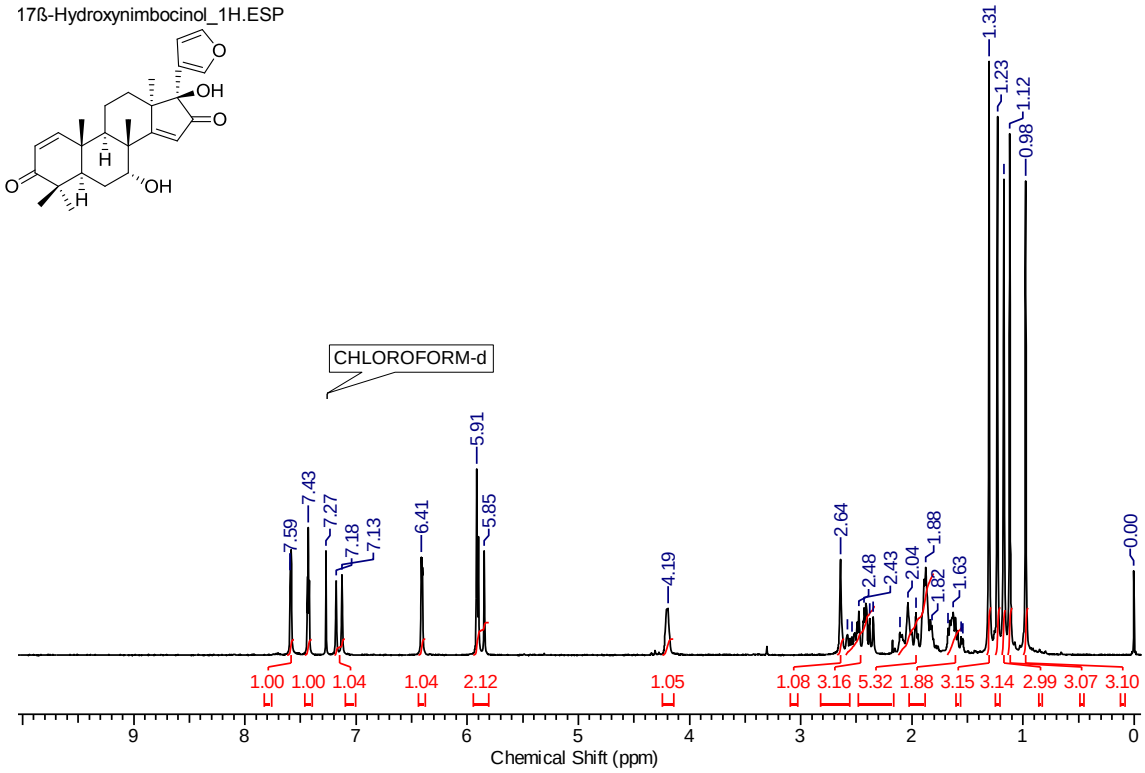


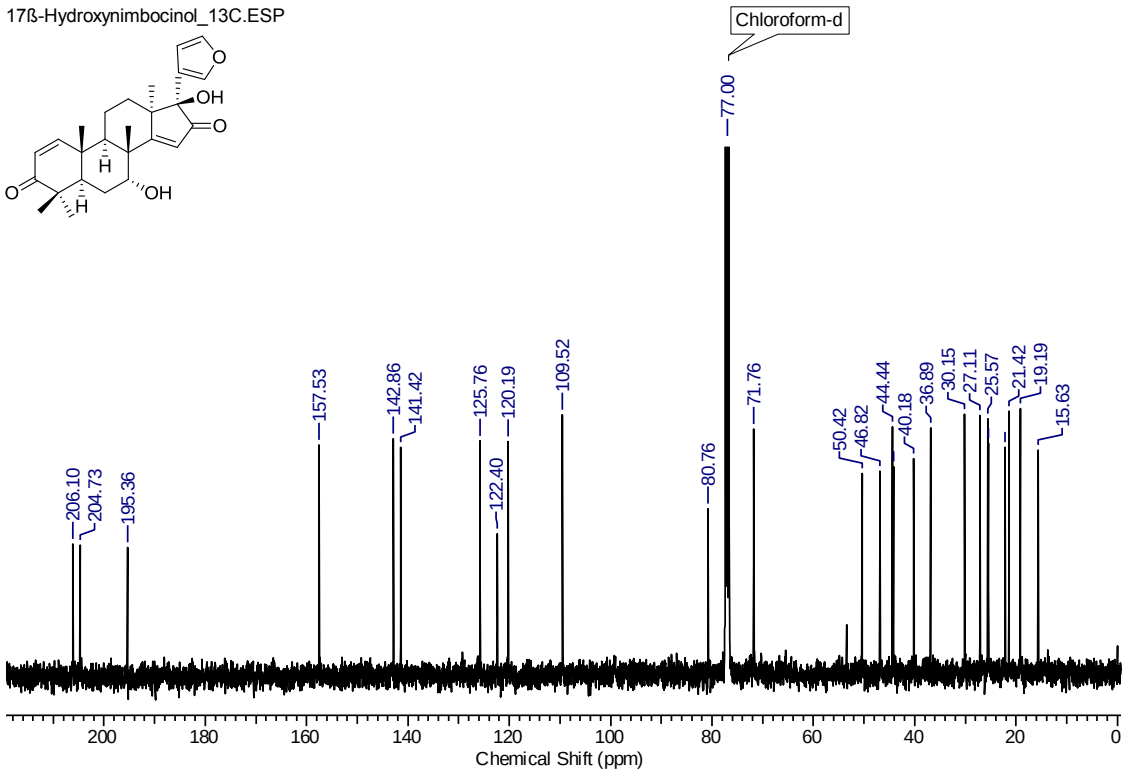


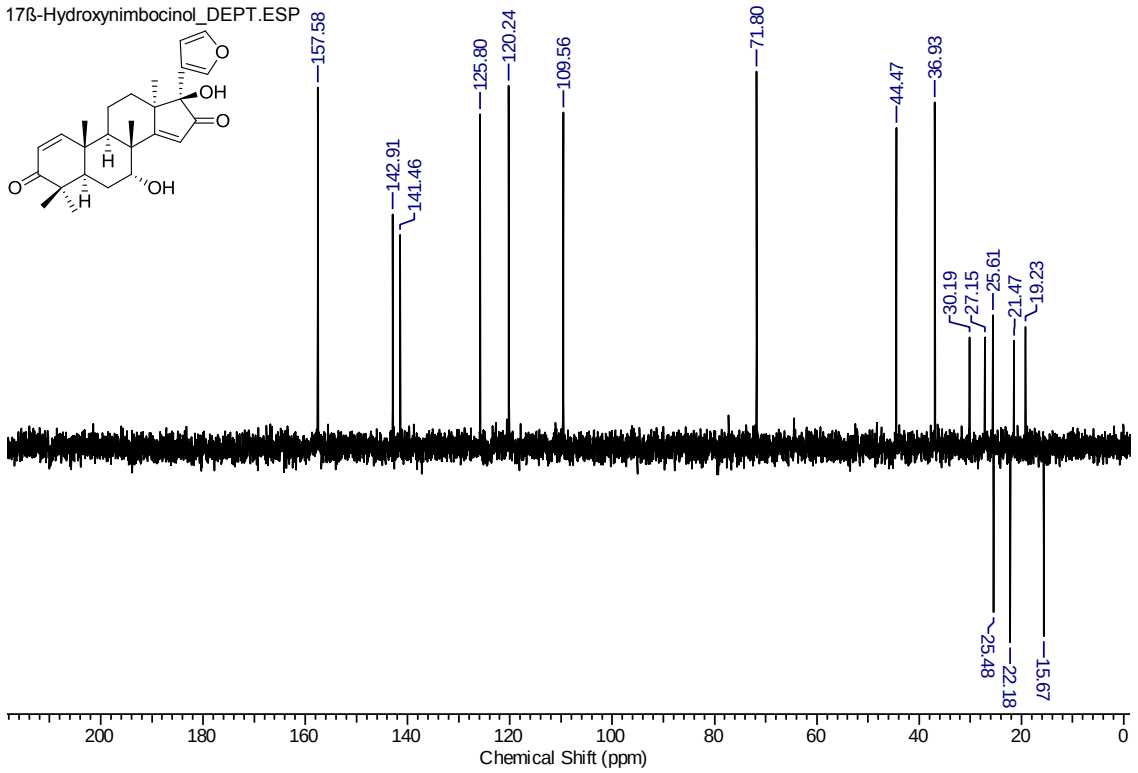


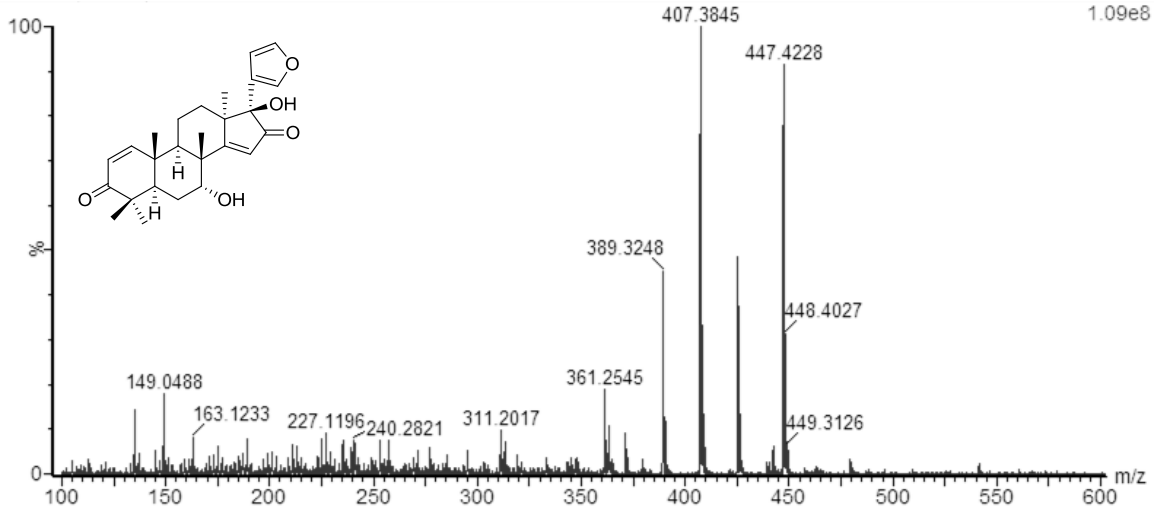


17β-Hydroxynimbocinol (**15**)

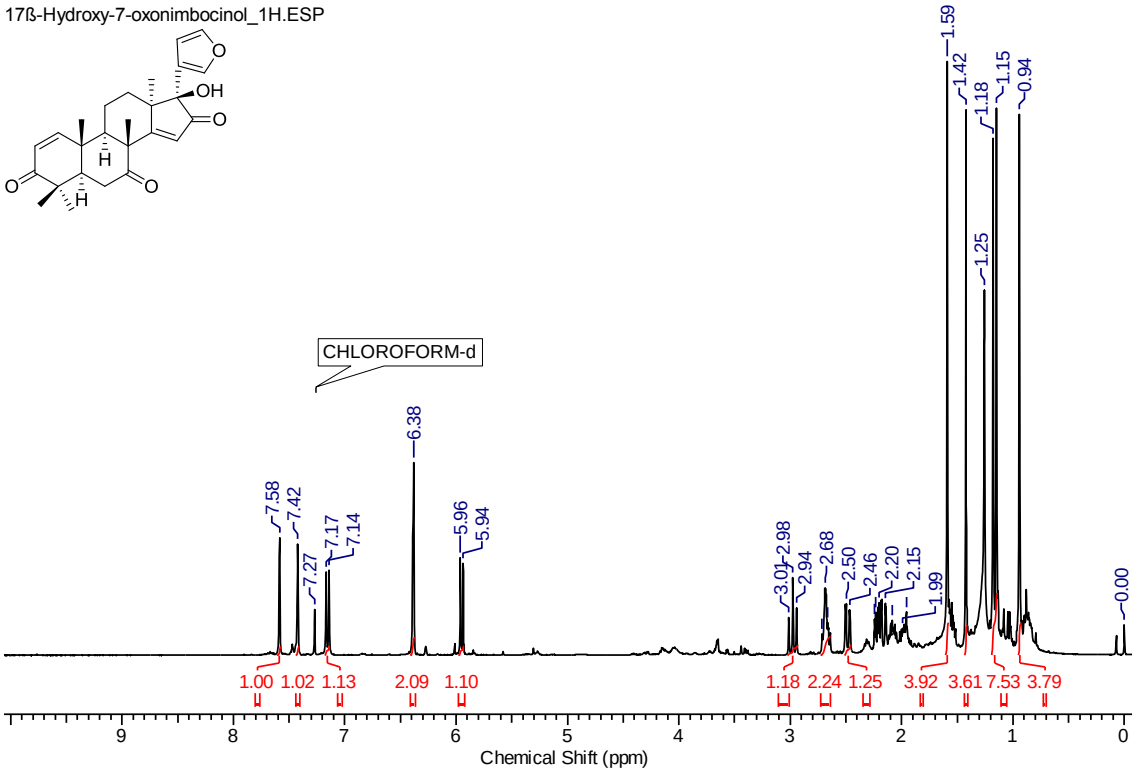


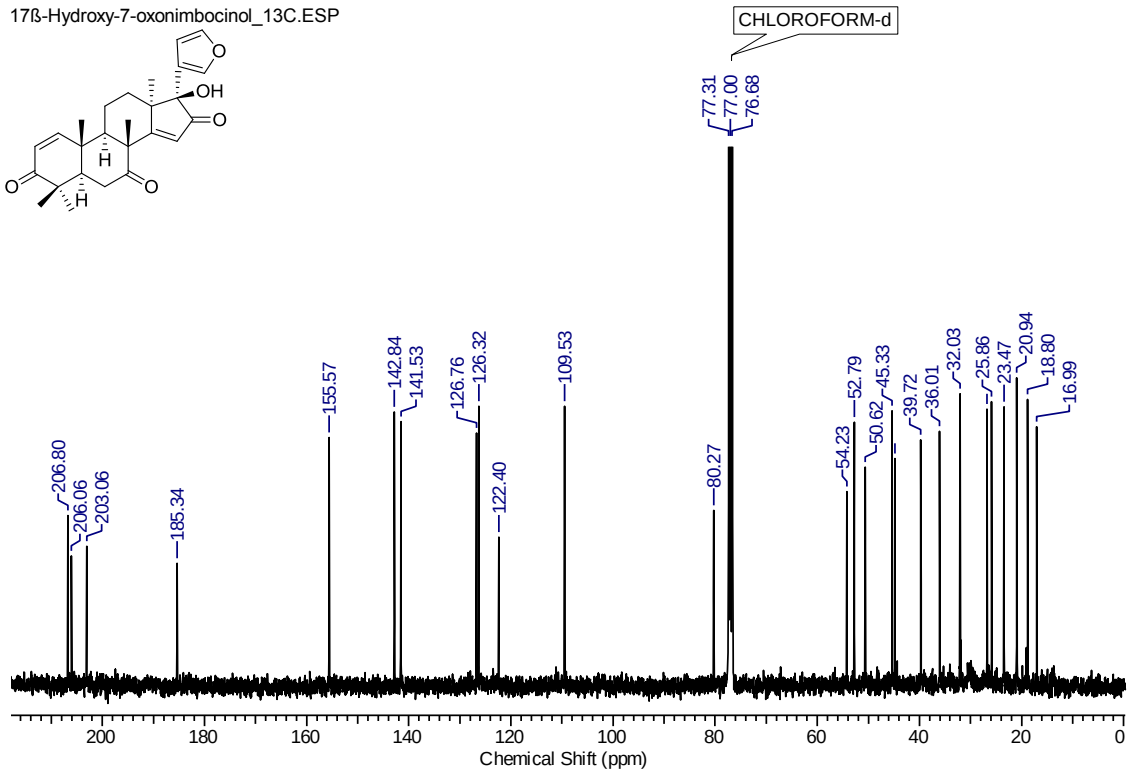


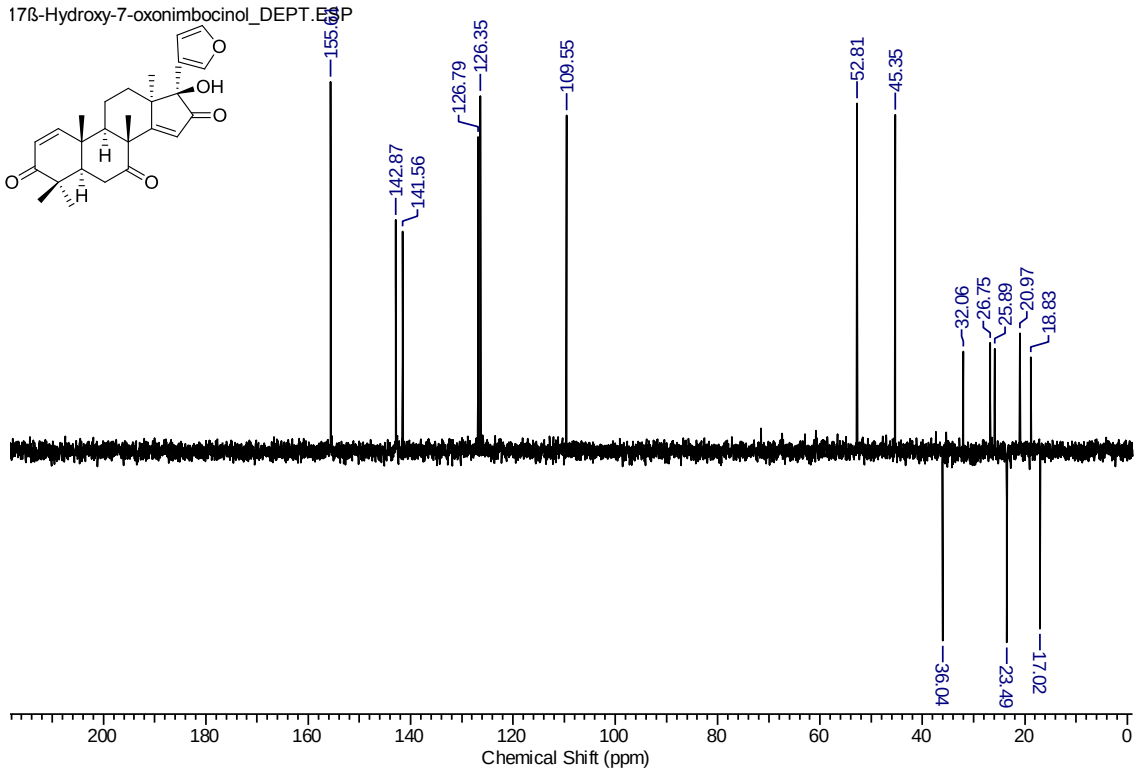

17ß-Hydroxynimbocinol_DEPT.ESP
157.58
142.91
141.46
125.80
120.24
109.56
71.80
44.47
36.93
30.19
27.15
25.61
21.47
19.23
25.48
22.18
15.67
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

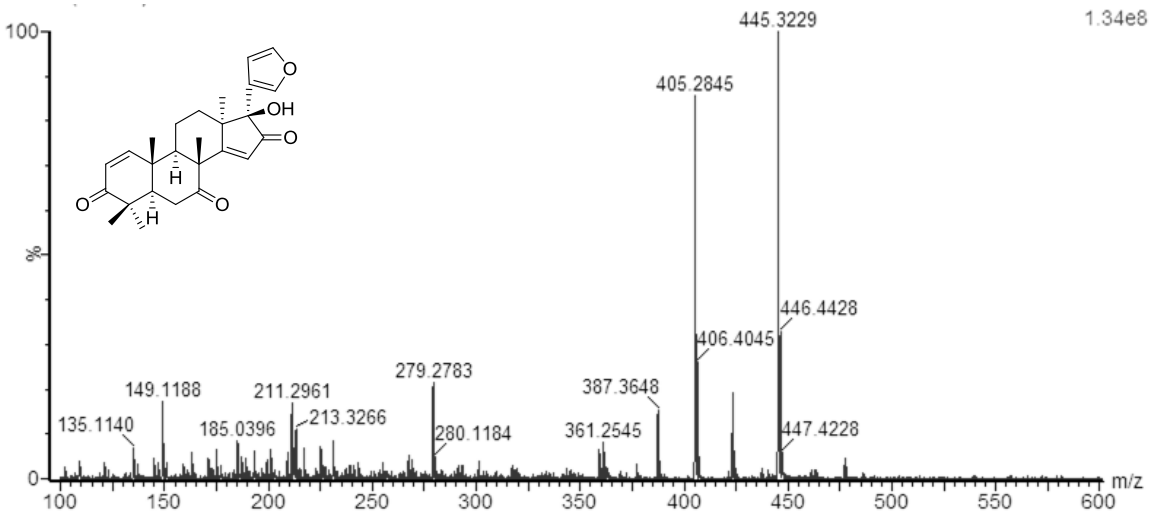

100
%
0
407.3845
1.09e8
447.4228
389.3248
448.4027
361.2545
149.0488
163.1233
227.1196
240.2821
311.2017
449.3126
m/z
100
150
200
250
300
350
400
450
500
550
600

17β-Hydroxy-7-oxonimbocinol (**16**)

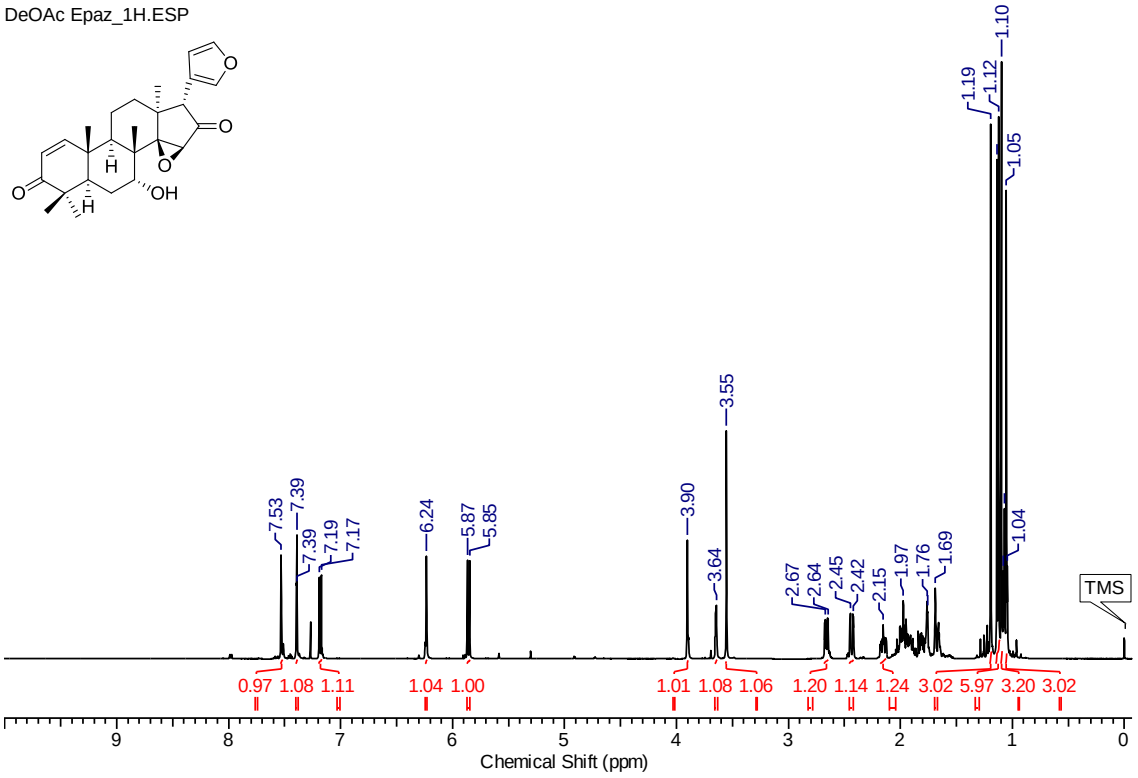


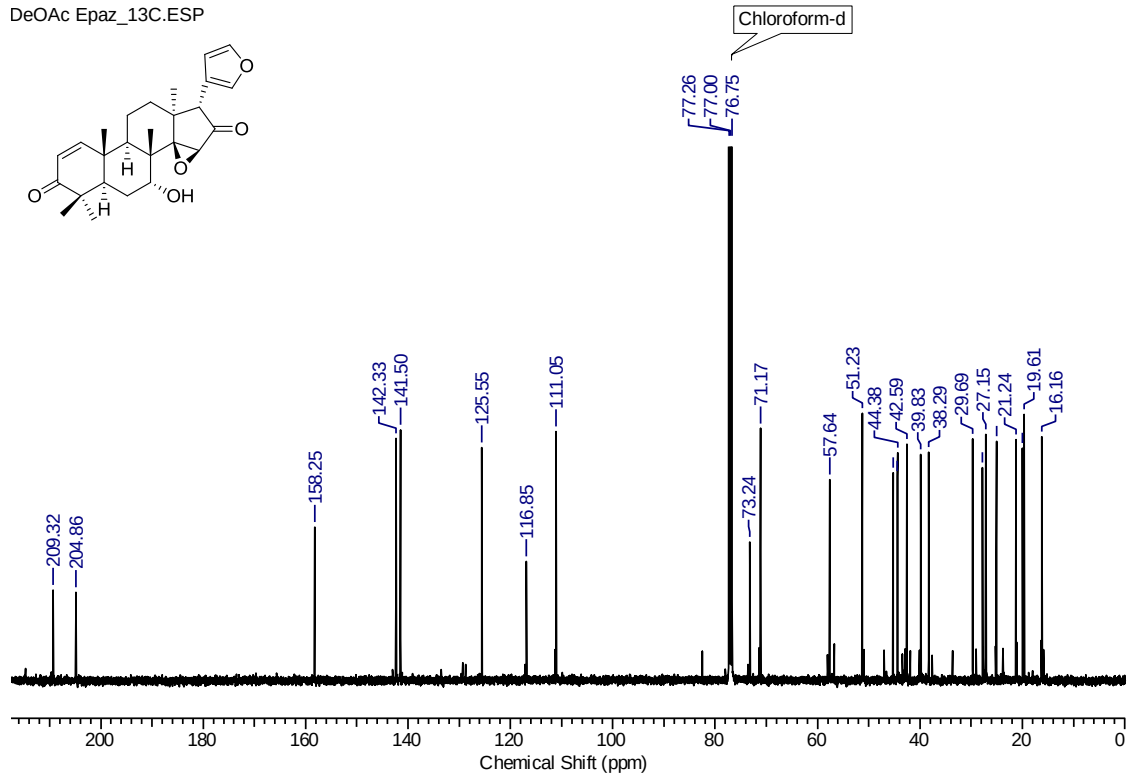


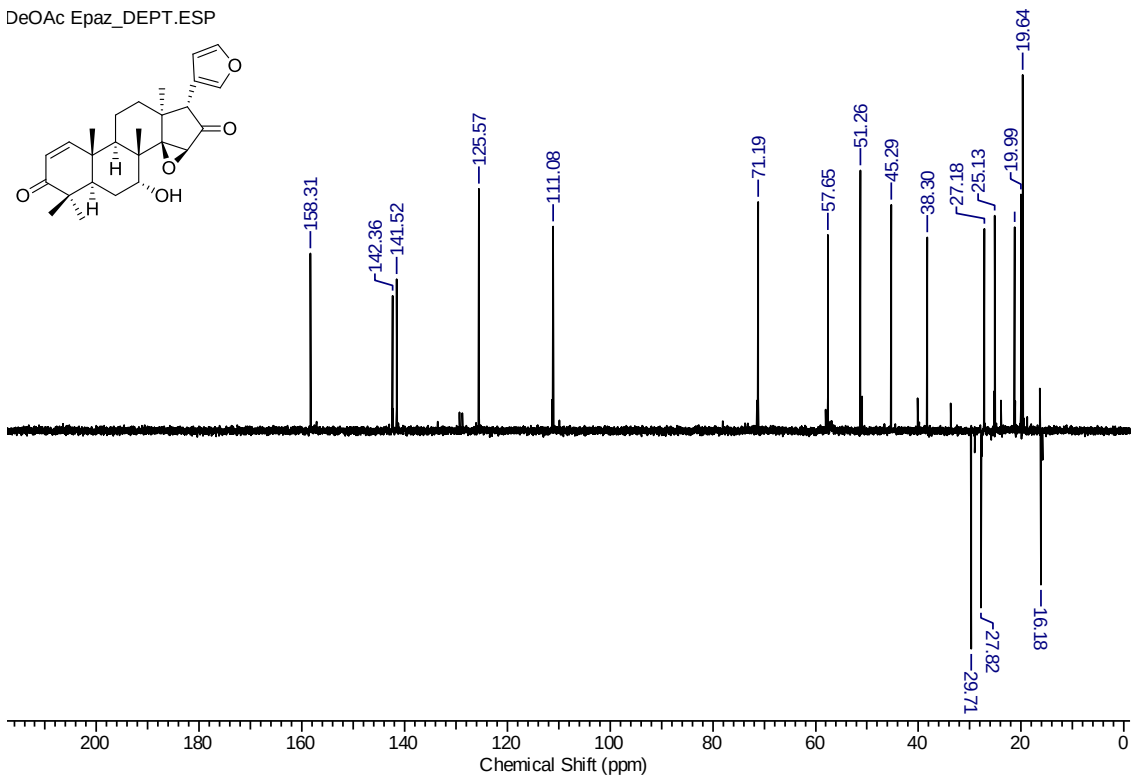

17ß-Hydroxy-7-oxonimbocinol_DEPT.ESP
155.66
142.87
141.56
126.79
126.35
109.55
52.81
45.35
32.06
26.75
25.89
20.97
18.83
36.04
23.49
17.02
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)
OH
O
H

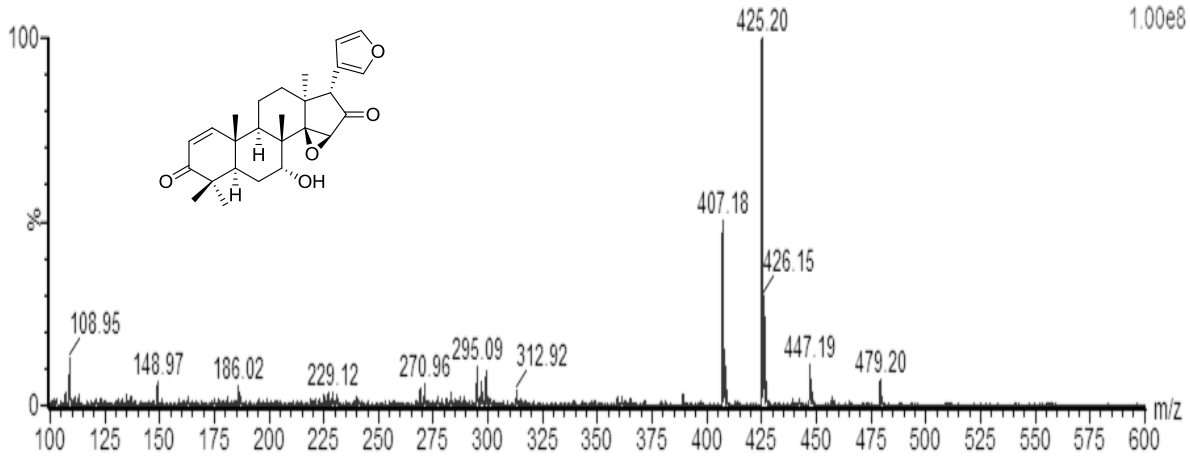

100
%
0
445.3229
1.34e8
405.2845
446.4428
406.4045
279.2783
149.1188
211.2961
387.3648
135.1140
185.0396
213.3266
280.1184
361.2545
447.4228
100
150
200
250
300
350
400
450
500
550
600
m/z
OH
O
H

7-Deacetylepoxyazadiradione (**17**)

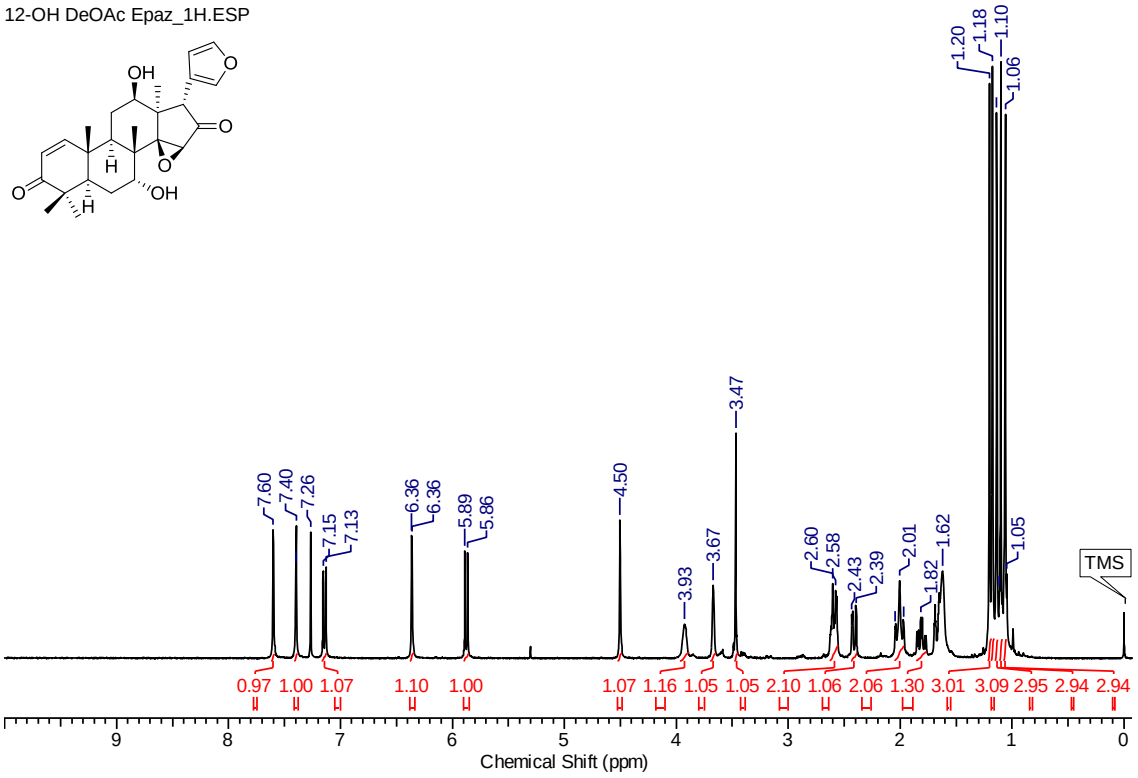


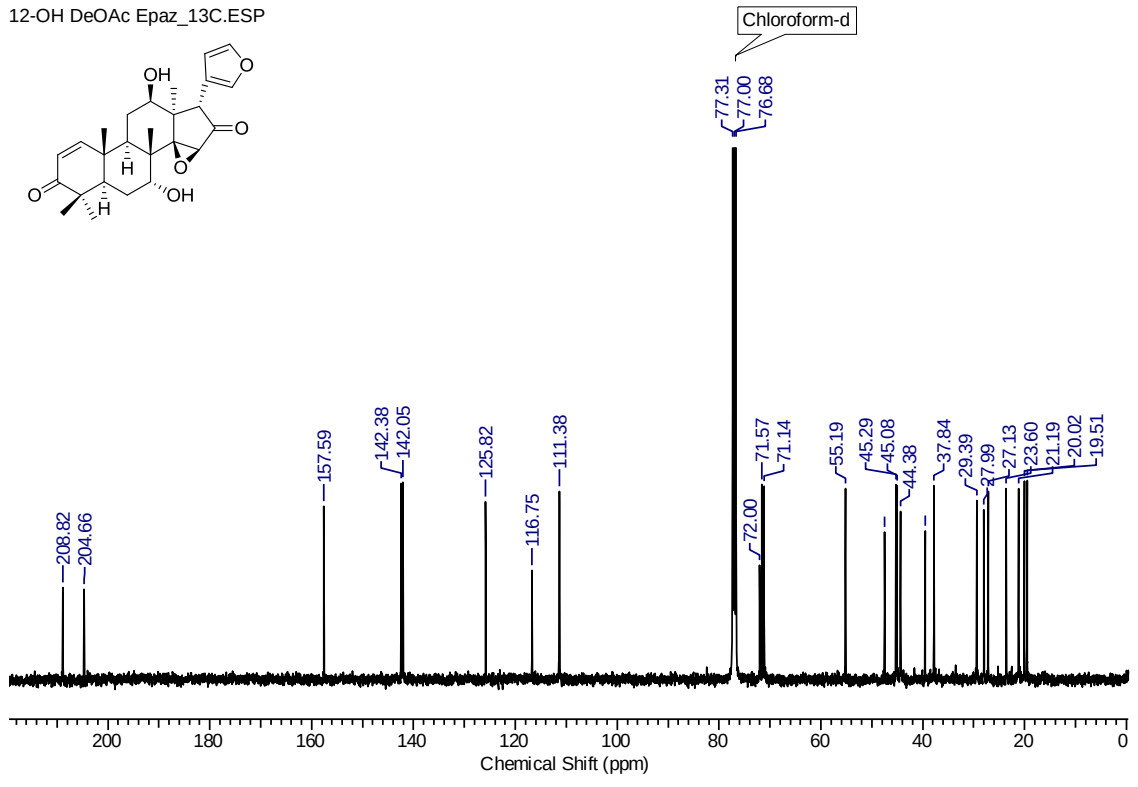


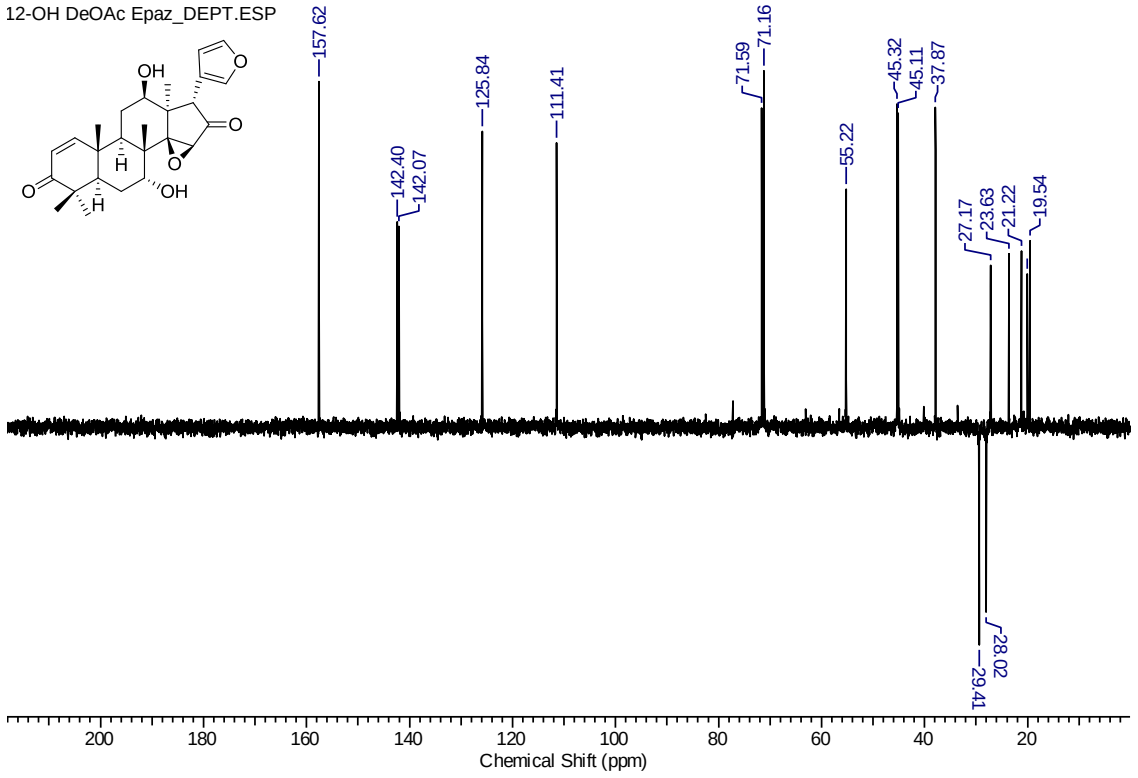

DeOAc Epaz_DEPT.ESP
158.31
142.36
141.52
125.57
111.08
71.19
57.65
51.26
45.29
38.30
27.18
25.13
19.99
19.64
28.71
27.82
16.18
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

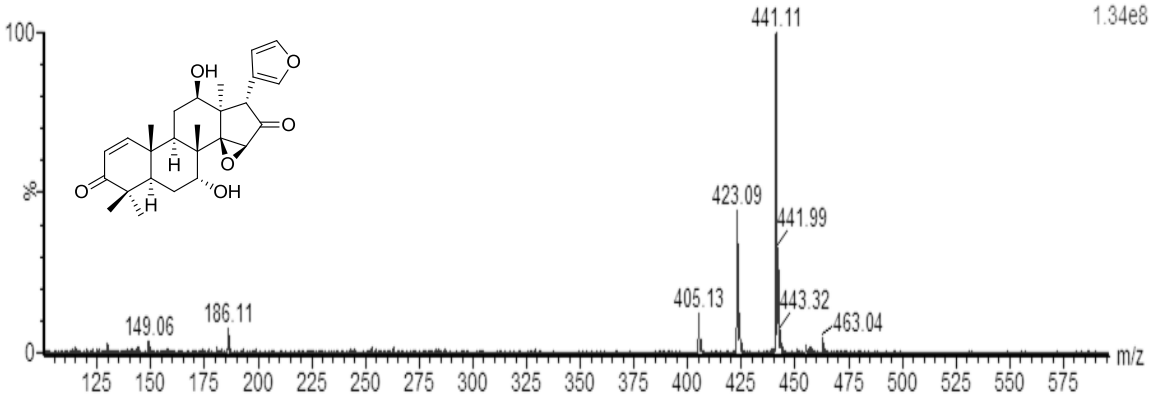

100
%
0
425.20
1.00e8
407.18
426.15
108.95
148.97
186.02
229.12
270.96
295.09
312.92
447.19
479.20
m/z
100
125
150
175
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
600

12β-Hydroxy-7-deacetylepoxyazadiradione **(18)**

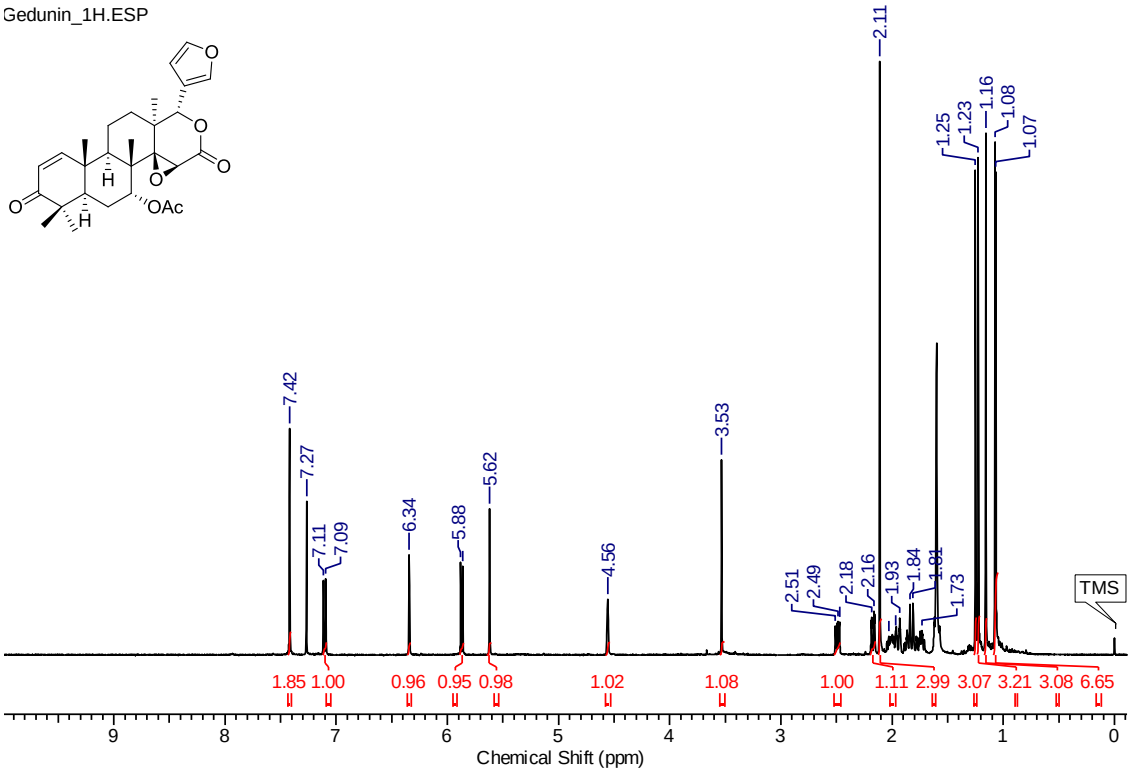


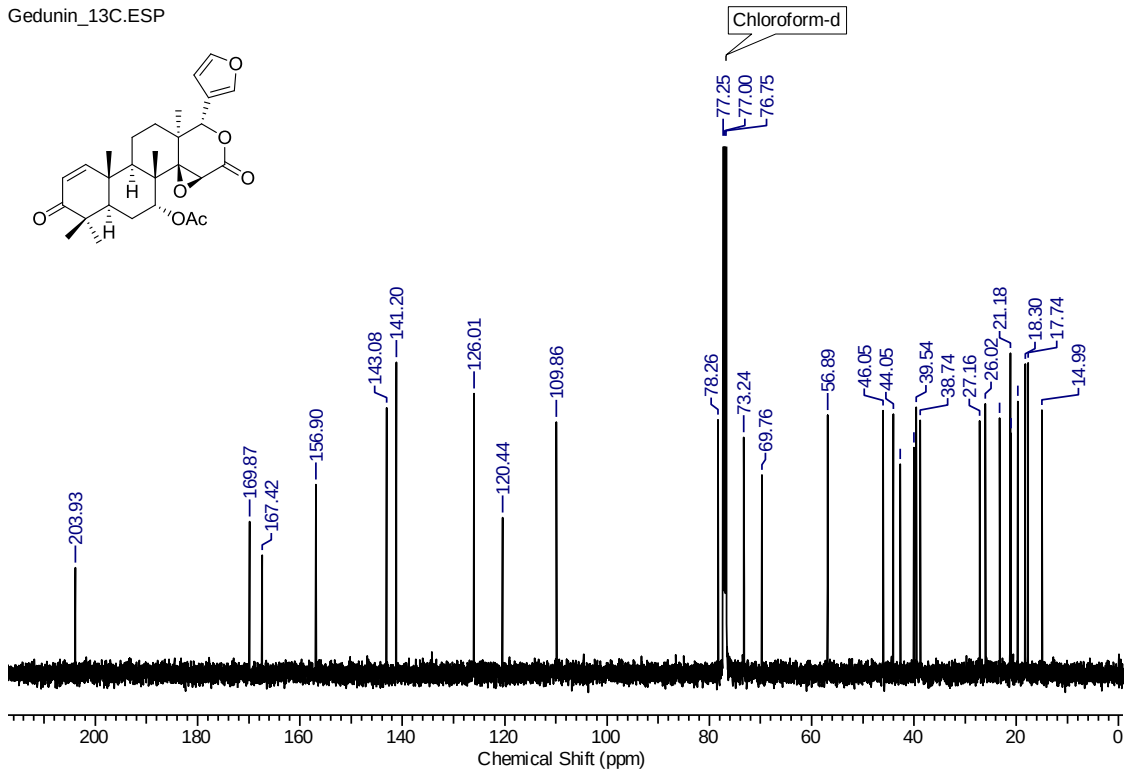


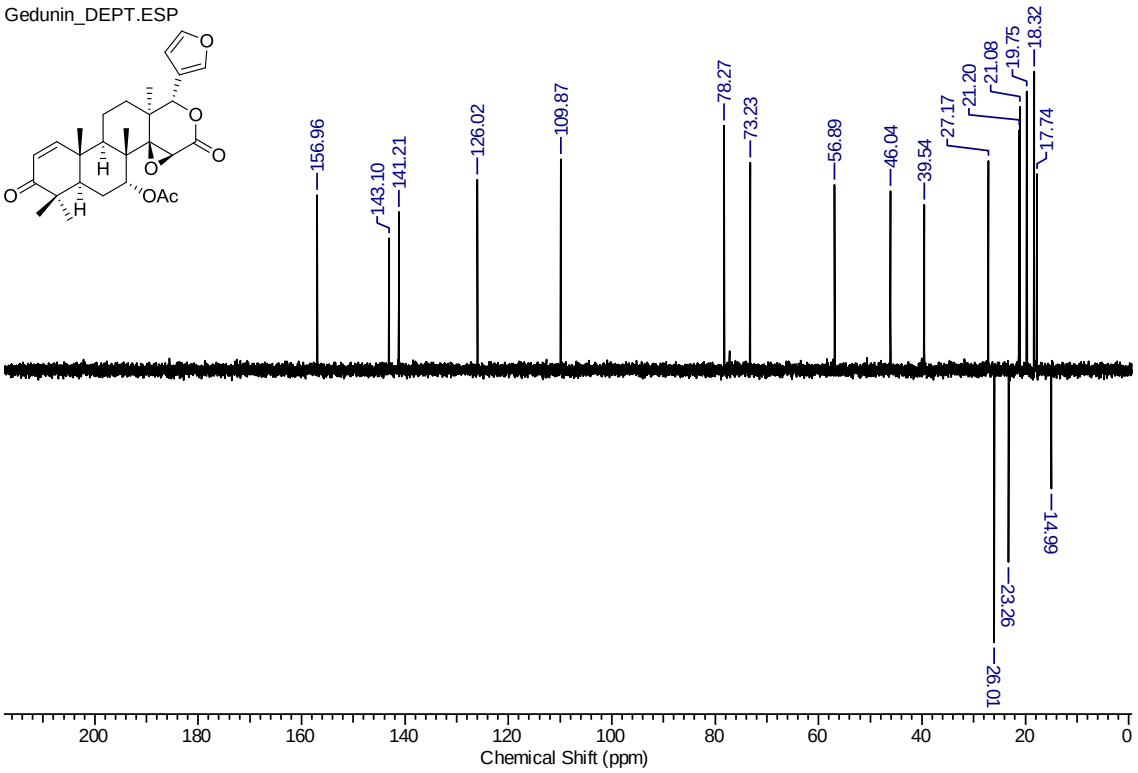


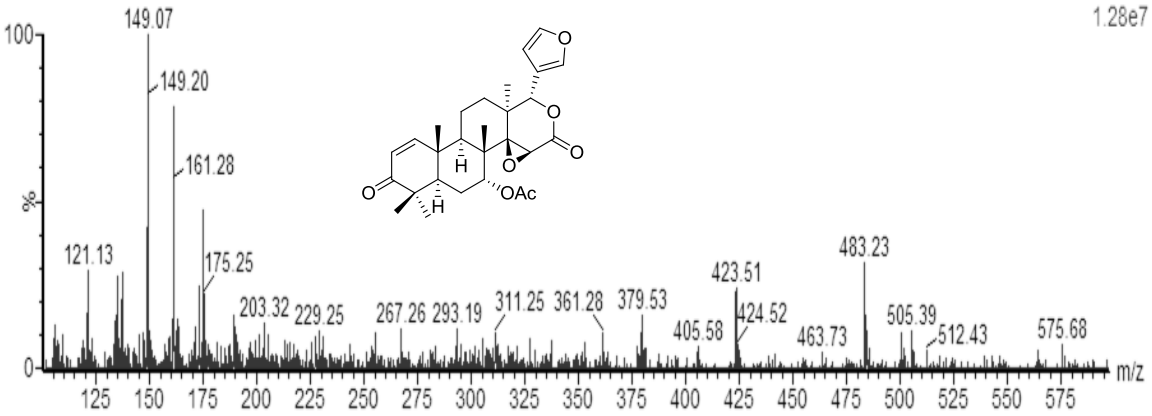


Gedunin **(19)**


Gedunin_1H.ESP
2.11
1.25
1.23
1.16
1.08
1.07
7.42
7.27
7.11
7.09
6.34
5.88
5.62
4.56
3.53
2.51
2.49
2.18
2.16
1.93
1.84
1.81
1.73
TMS
1.85 1.00 0.96 0.95 0.98 1.02 1.08 1.00 1.11 2.99 3.07 3.21 3.08 6.65
9 8 7 6 5 4 3 2 1 0
Chemical Shift (ppm)

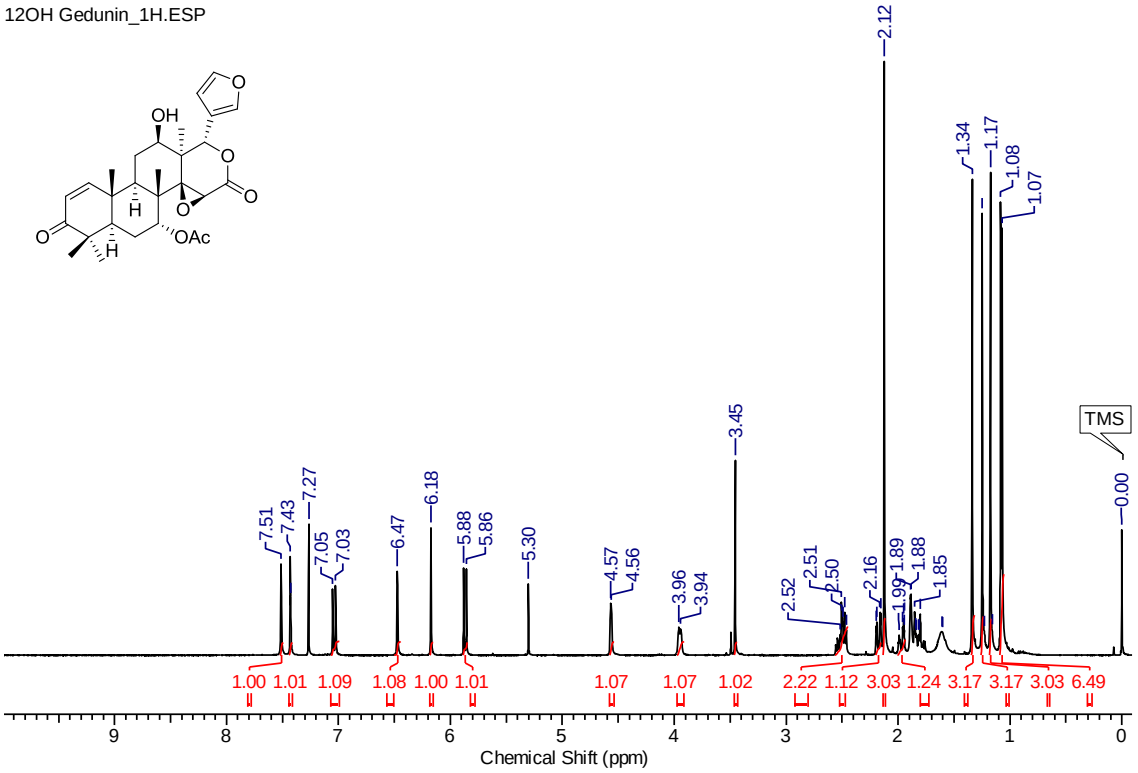

Gedunin_13C.ESP
Chloroform-d
77.25
77.00
76.75
203.93
169.87
167.42
156.90
143.08
141.20
126.01
120.44
109.86
78.26
73.24
69.76
56.89
46.05
44.05
39.54
38.74
27.16
26.02
21.18
18.30
17.74
14.99
200 180 160 140 120 100 80 60 40 20 0
Chemical Shift (ppm)


Gedunin_DEPT.ESP
156.96
143.10
141.21
126.02
109.87
78.27
73.23
56.89
46.04
39.54
27.17
21.20
21.08
19.75
18.32
17.74
14.99
23.26
26.01
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

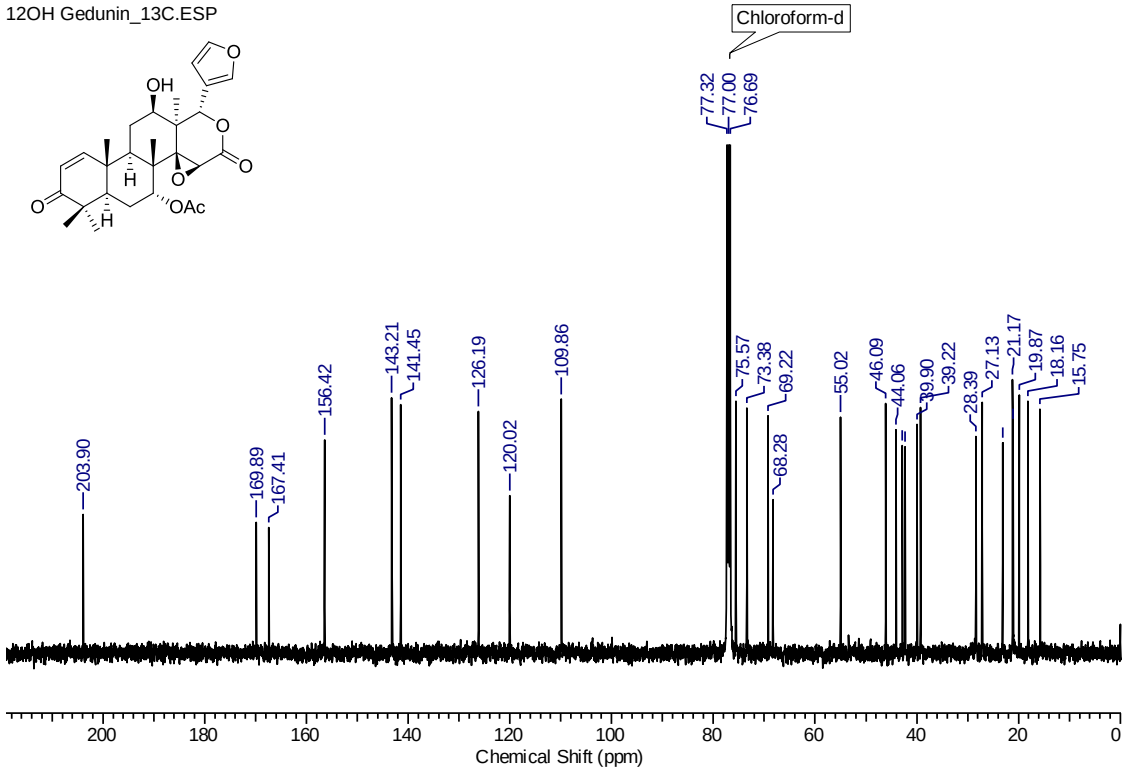

1.28e7
100
%
0
149.07
149.20
161.28
121.13
175.25
203.32
229.25
267.26
293.19
311.25
361.28
379.53
405.58
423.51
424.52
463.73
483.23
505.39
512.43
575.68
125
150
175
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
m/z

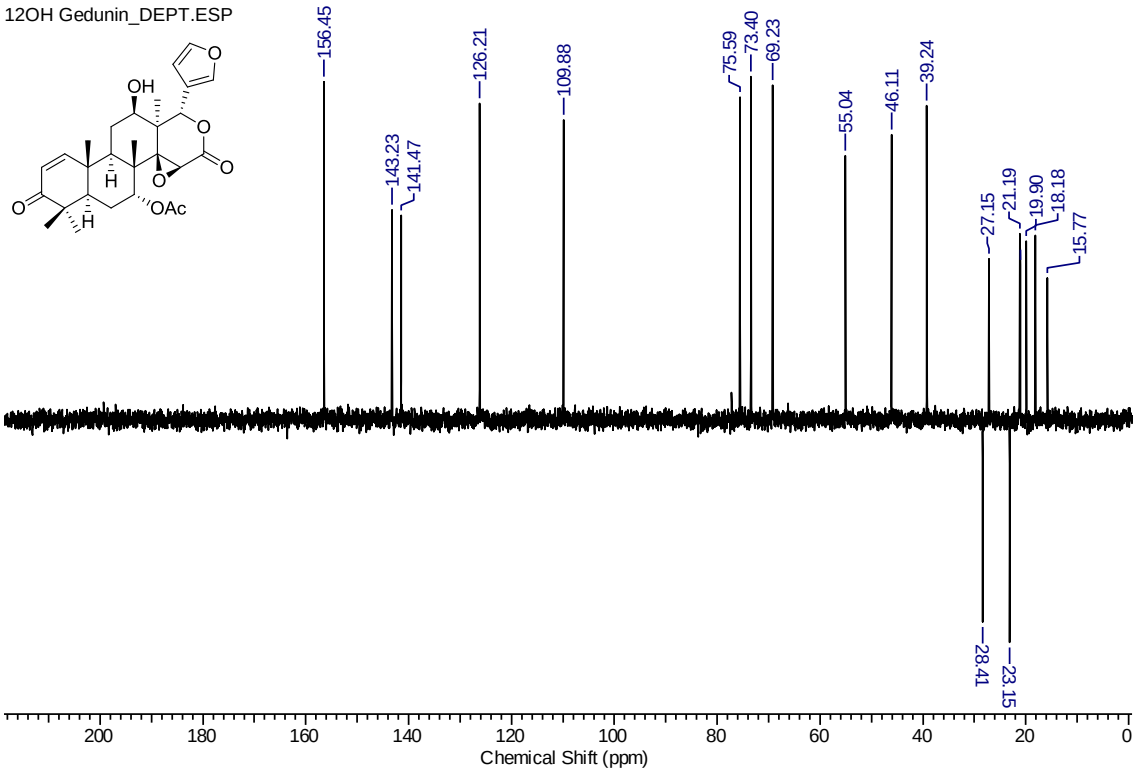
12β-Hydroxygedunin **(20)**

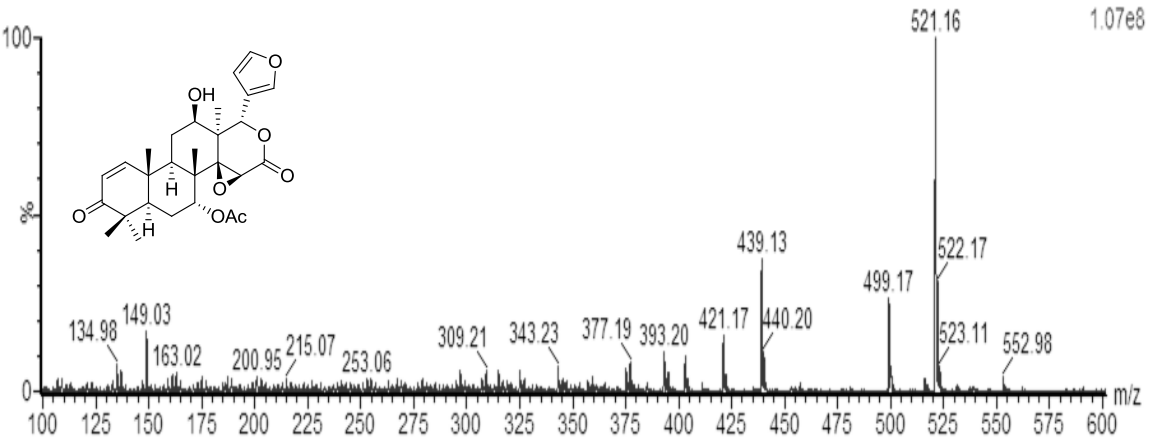
12OH Gedunin_1H.ESP



12OH Gedunin_13C.ESP




12OH Gedunin_DEPT.ESP
156.45
143.23
141.47
126.21
109.88
75.59
73.40
69.23
55.04
46.11
39.24
27.15
21.19
19.90
18.18
15.77
28.41
23.15
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)


100
%
0
521.16
1.07e8
439.13
522.17
499.17
134.98
149.03
163.02
200.95
215.07
253.06
309.21
343.23
377.19
393.20
421.17
440.20
523.11
552.98
100
125
150
175
200
225
250
275
300
325
350
375
400
425
450
475
500
525
550
575
600
m/z