

*Supporting Information For*

**Synthesis and evaluation of anticancer activities of novel C-28 guanidine-functionalized triterpene acid derivatives.**

Anna Spivak \*, Rezeda Khalitova, Darya Nedopekina, Lilya Dzhemileva \*, Milyausha Yunusbaeva, Victor Odionkov, Vladimir D'yakonov and Usein Dzhemilev.

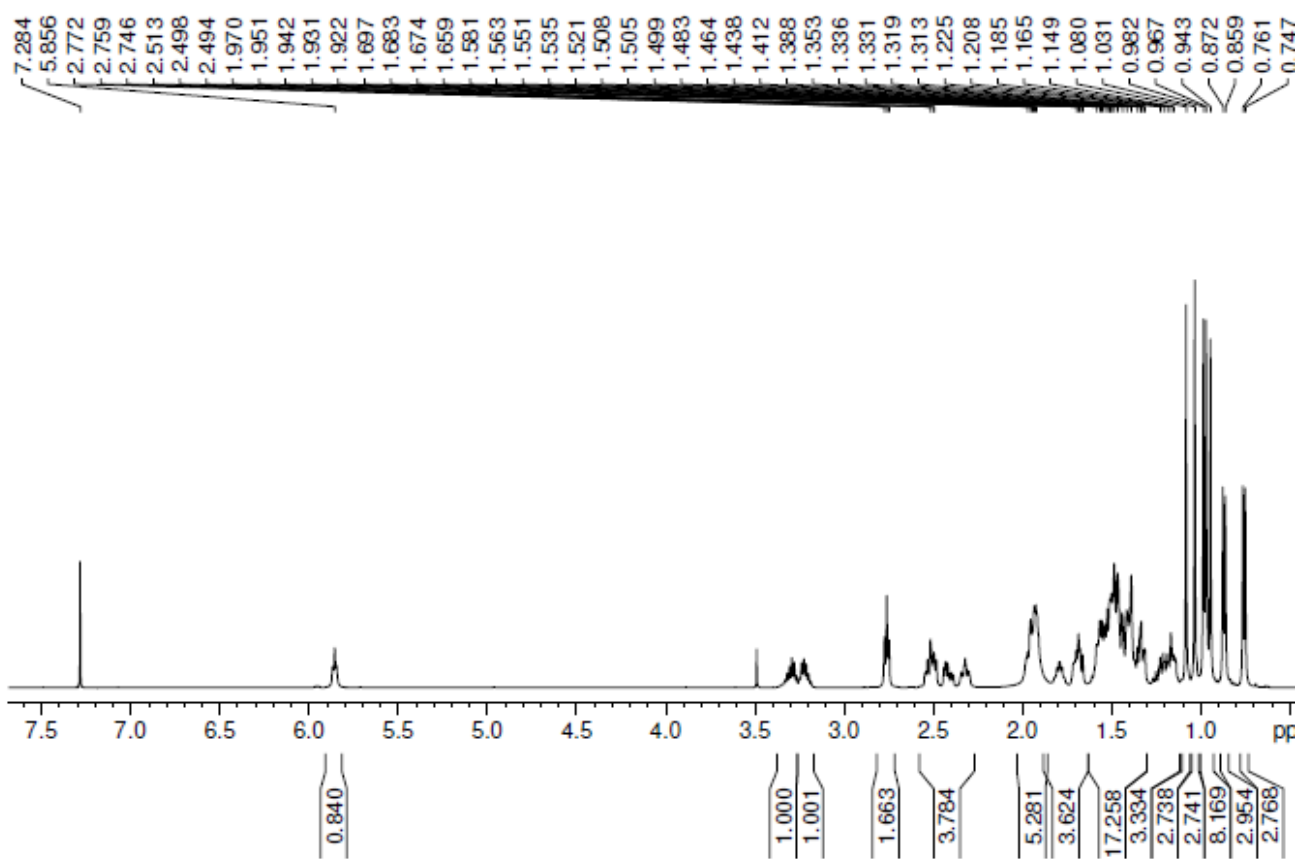
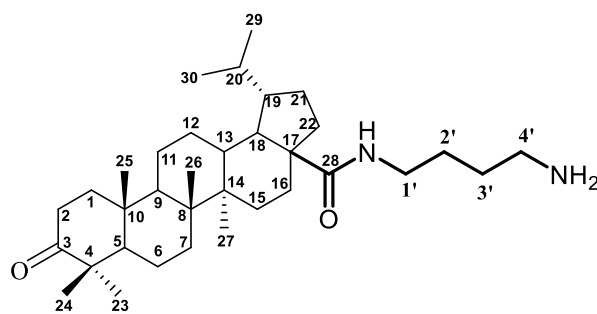
*Institute of Petrochemistry and Catalysis, Russian Academy of Sciences, 141 prosp. Oktyabrya, 450075  
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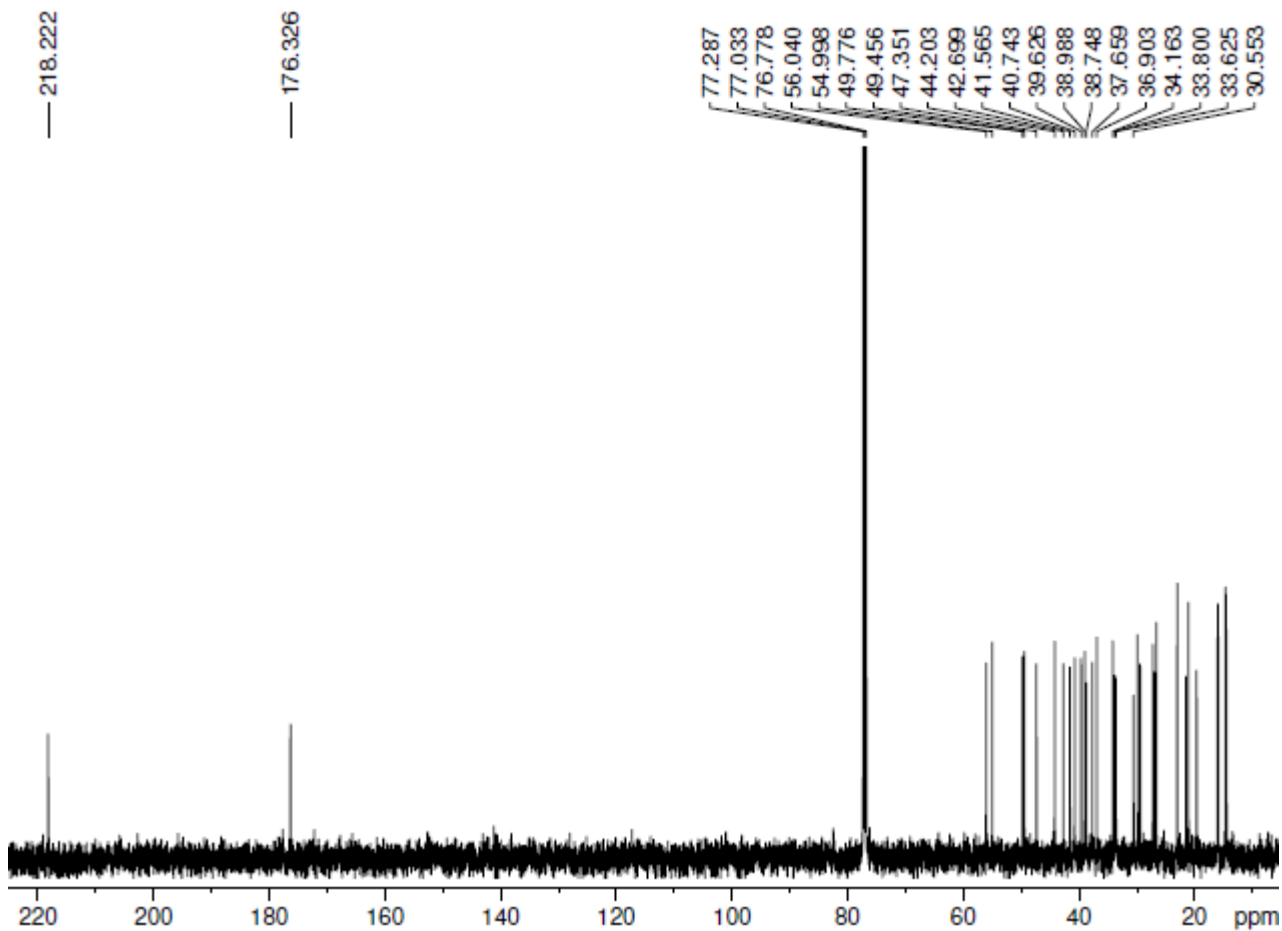
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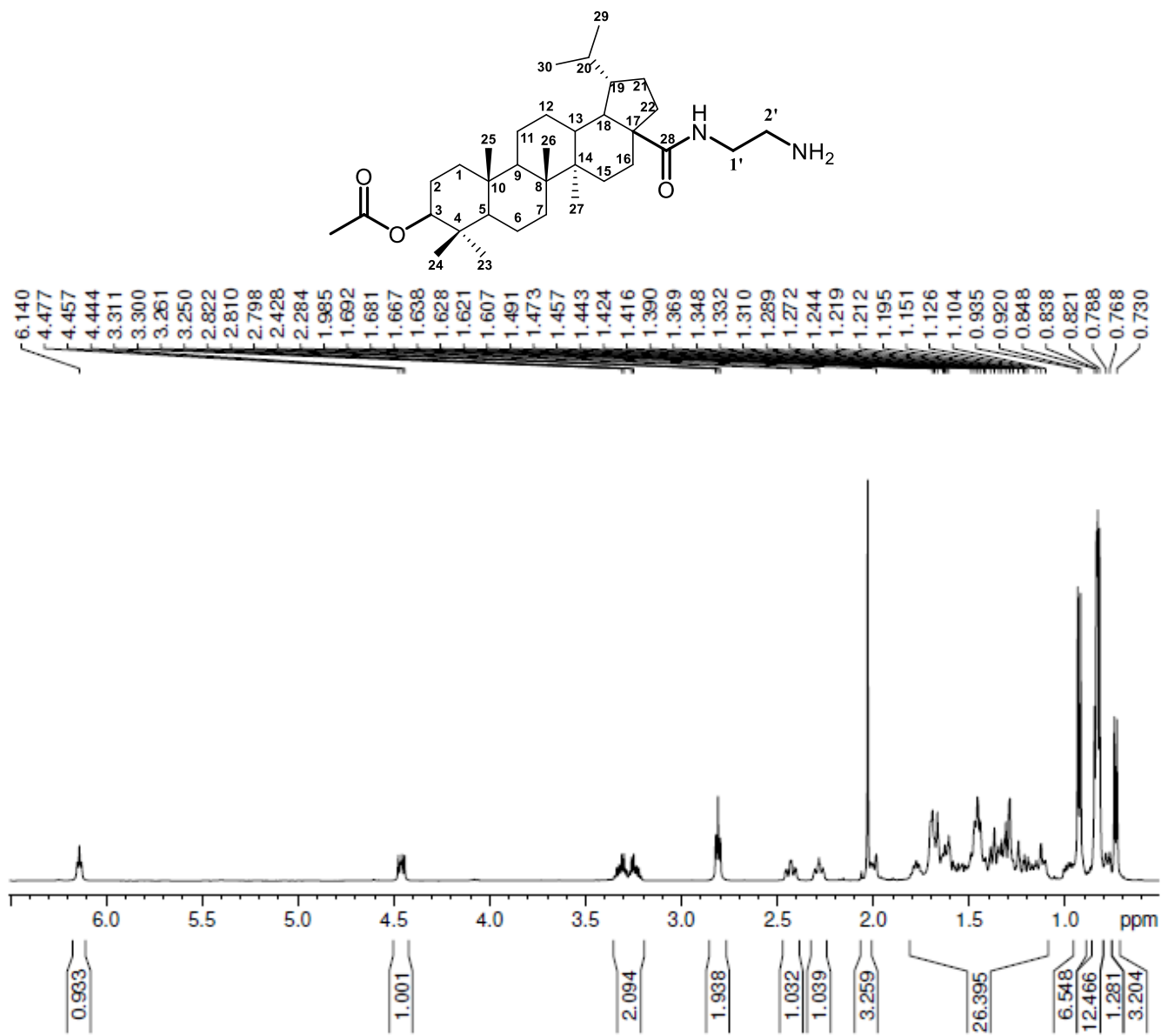
N-(4-aminobutyl)-3-oxolupane-28-amide (4). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)



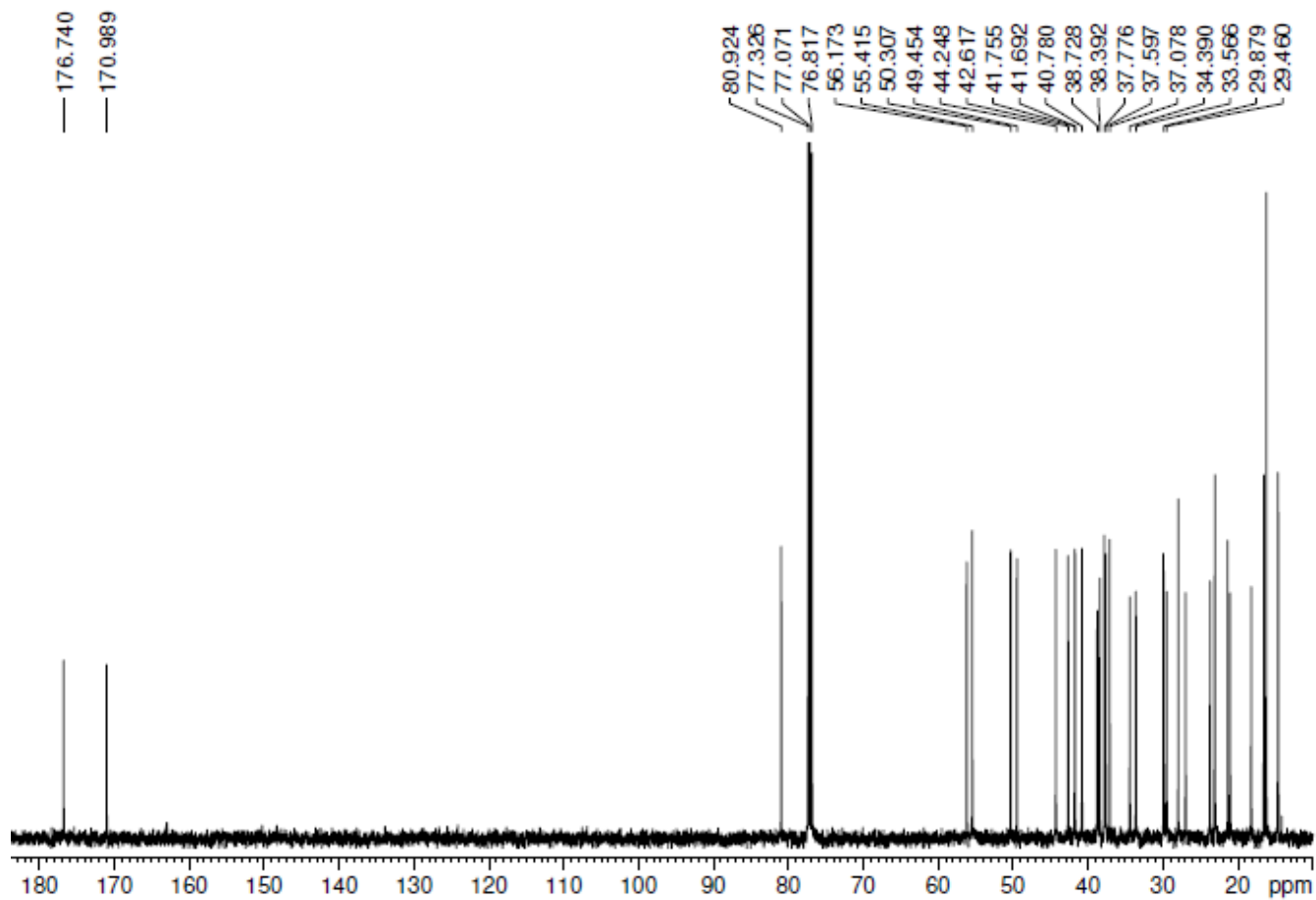
**N-(4-aminobutyl)-3-oxolupane-28-amide (4).**  $^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )



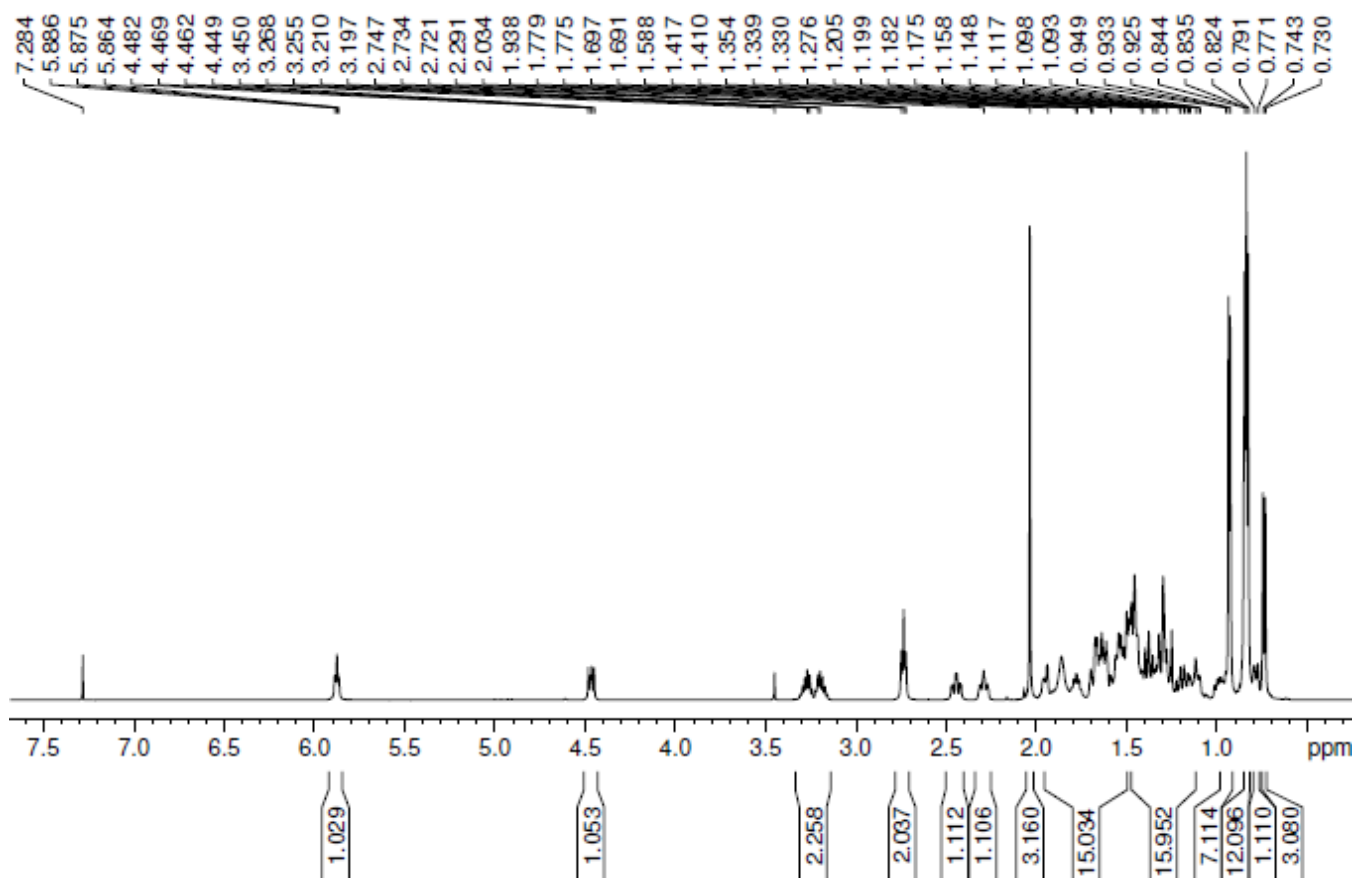
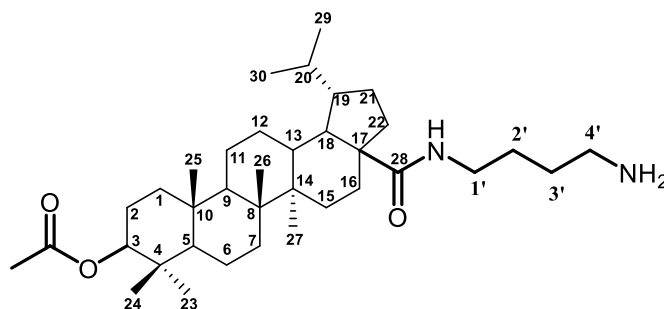
**3 $\beta$ -N-(2-aminoethyl)-3-O-acetyl-lupane-28-amide (5).**  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )



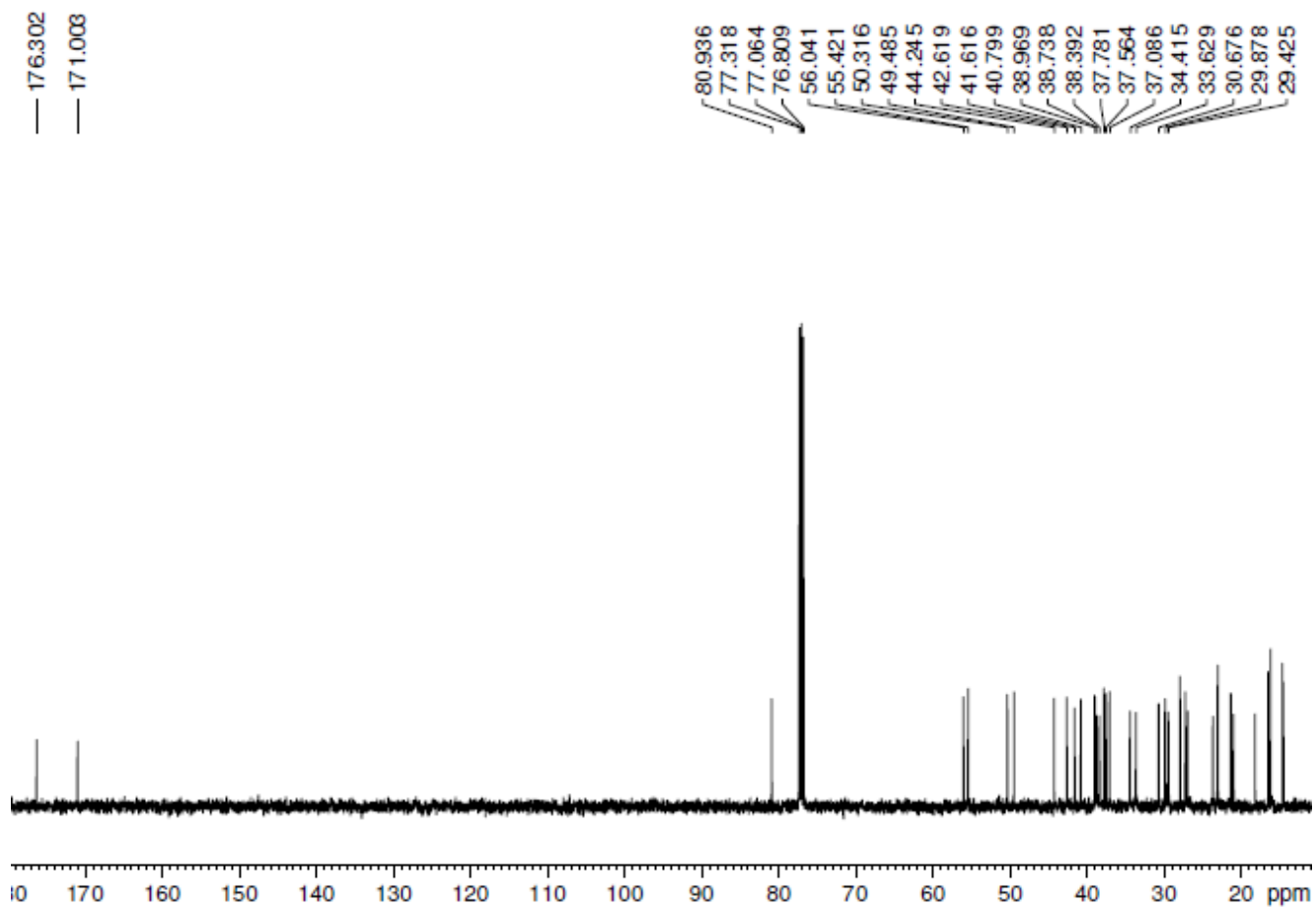
**3 $\beta$ -N-(2-aminoethyl)-3-O-acetyl-lupane-28-amide (5).**  $^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )



**3 $\beta$ -N-(4-aminobutyl)-3-O-acetyl-lupane-28-amide (6)**  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )



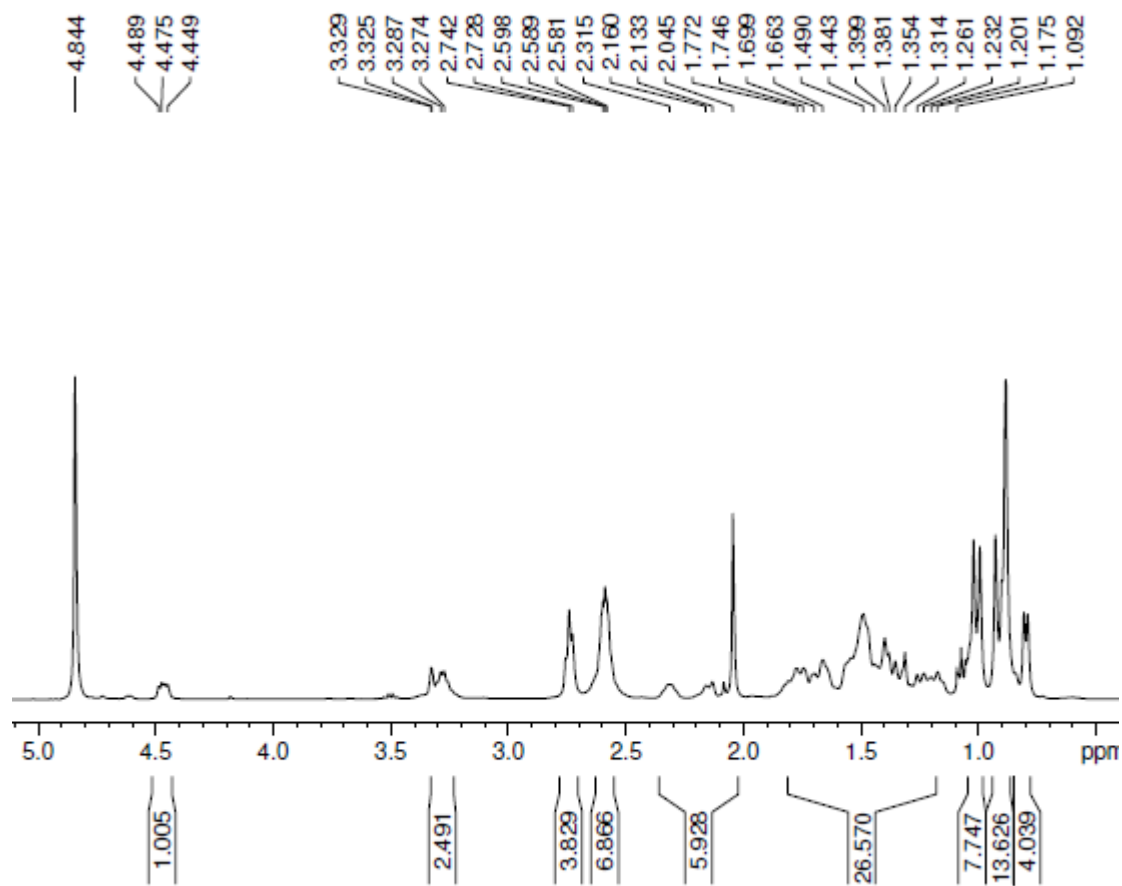
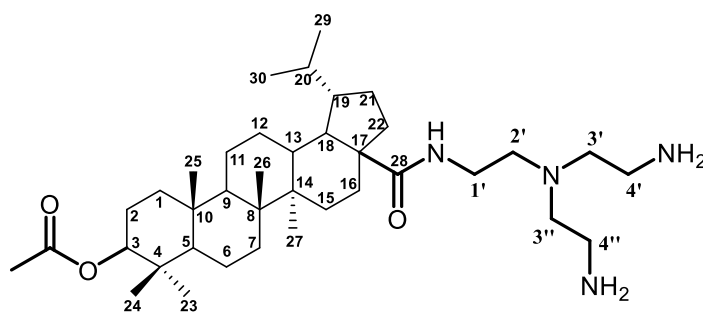
**3 $\beta$ -N-(4-aminobutyl)-3-O-acetyl-lupane-28-amide (6)** <sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)





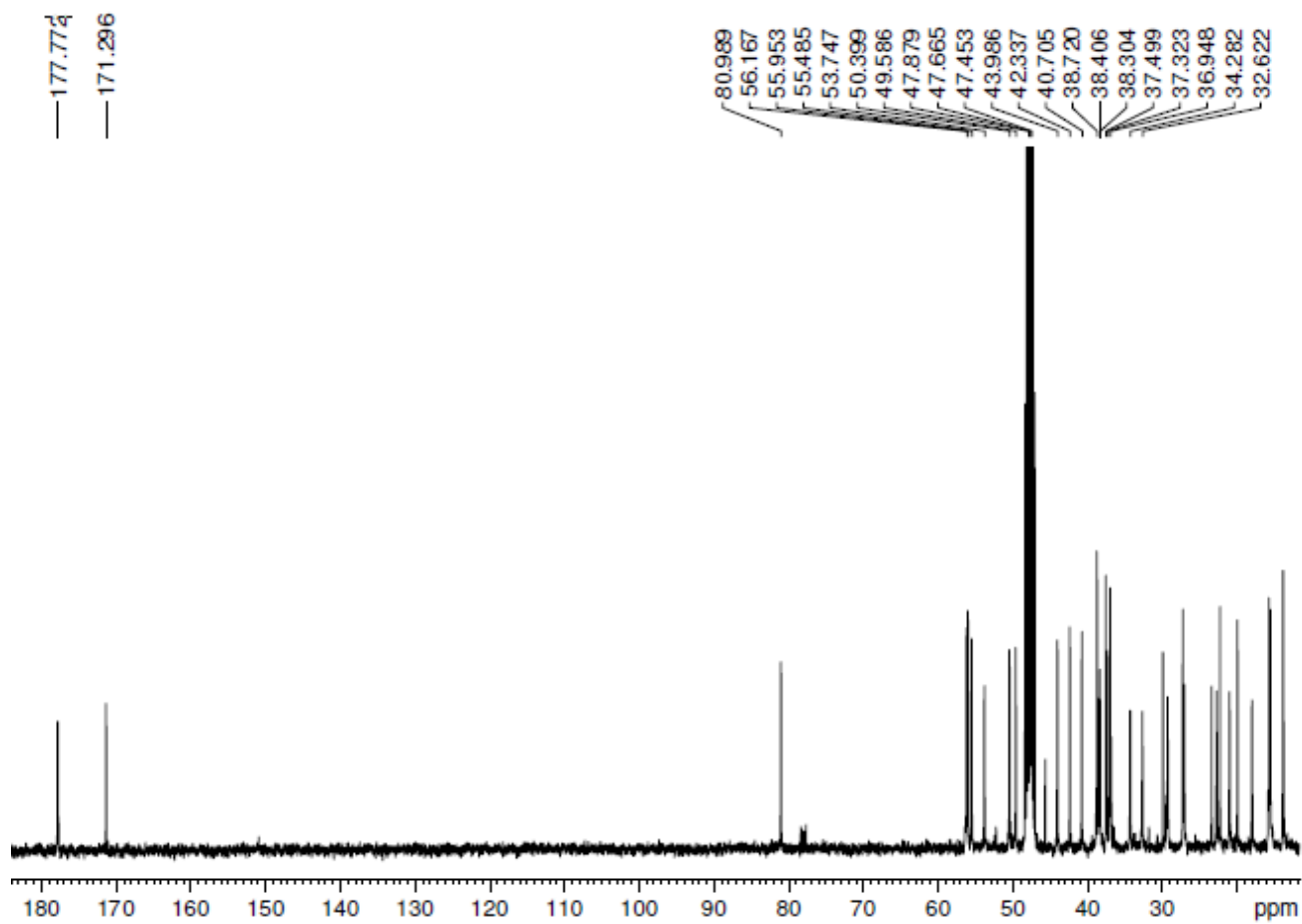
3 $\beta$ -N-[2-(N,N'-bis-aminoethyl)-aminoethyl]-3-O-acetyl-lupane-28-amide (7).

<sup>1</sup>H NMR spectra (MeOD)



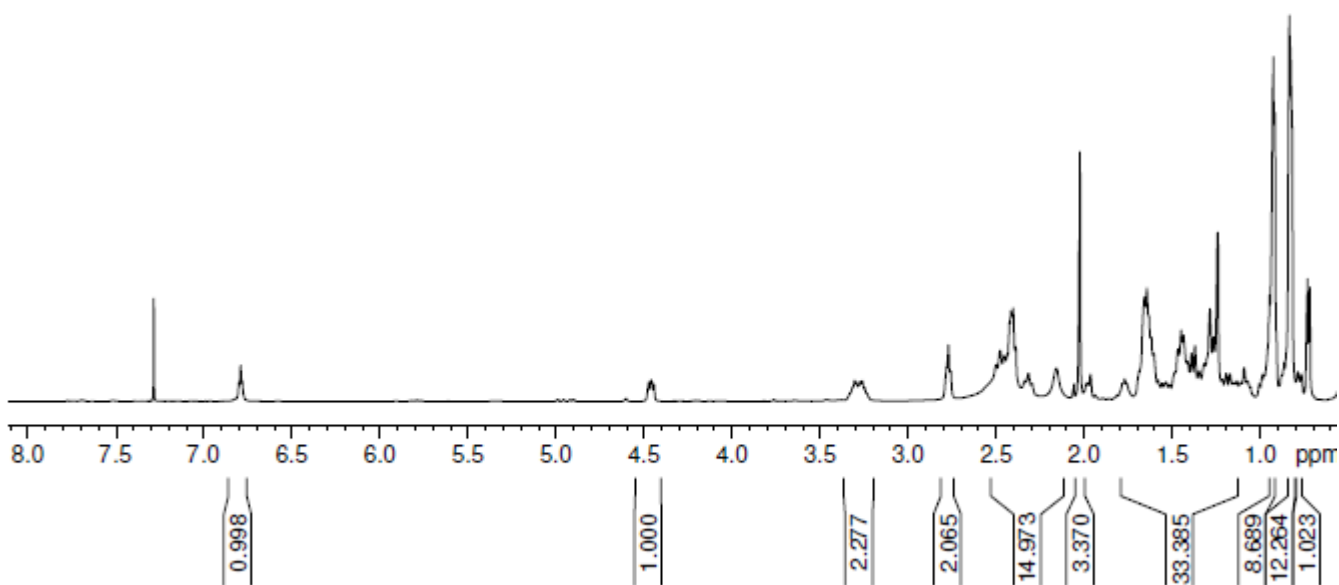
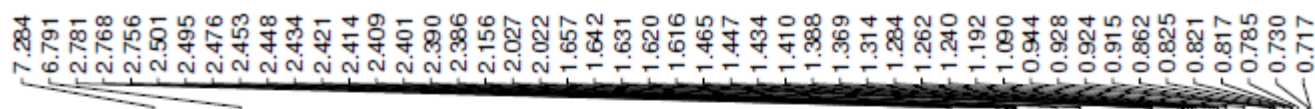
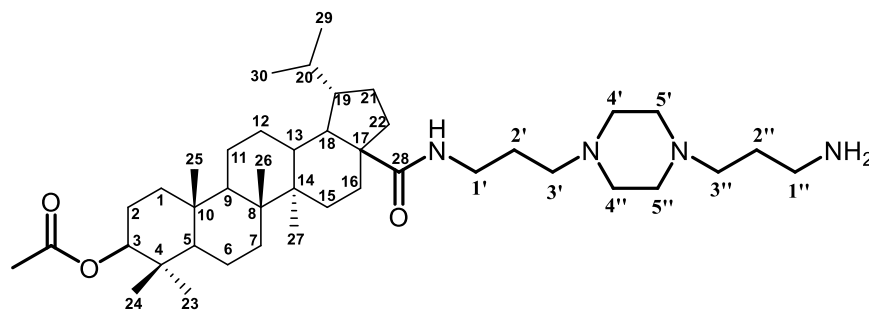
**3 $\beta$ -N-[2-(N,N'-bis-aminoethyl)-aminoethyl]-3-O-acetyl-lupane-28-amide (7).**

<sup>13</sup>C NMR spectra (MeOD)



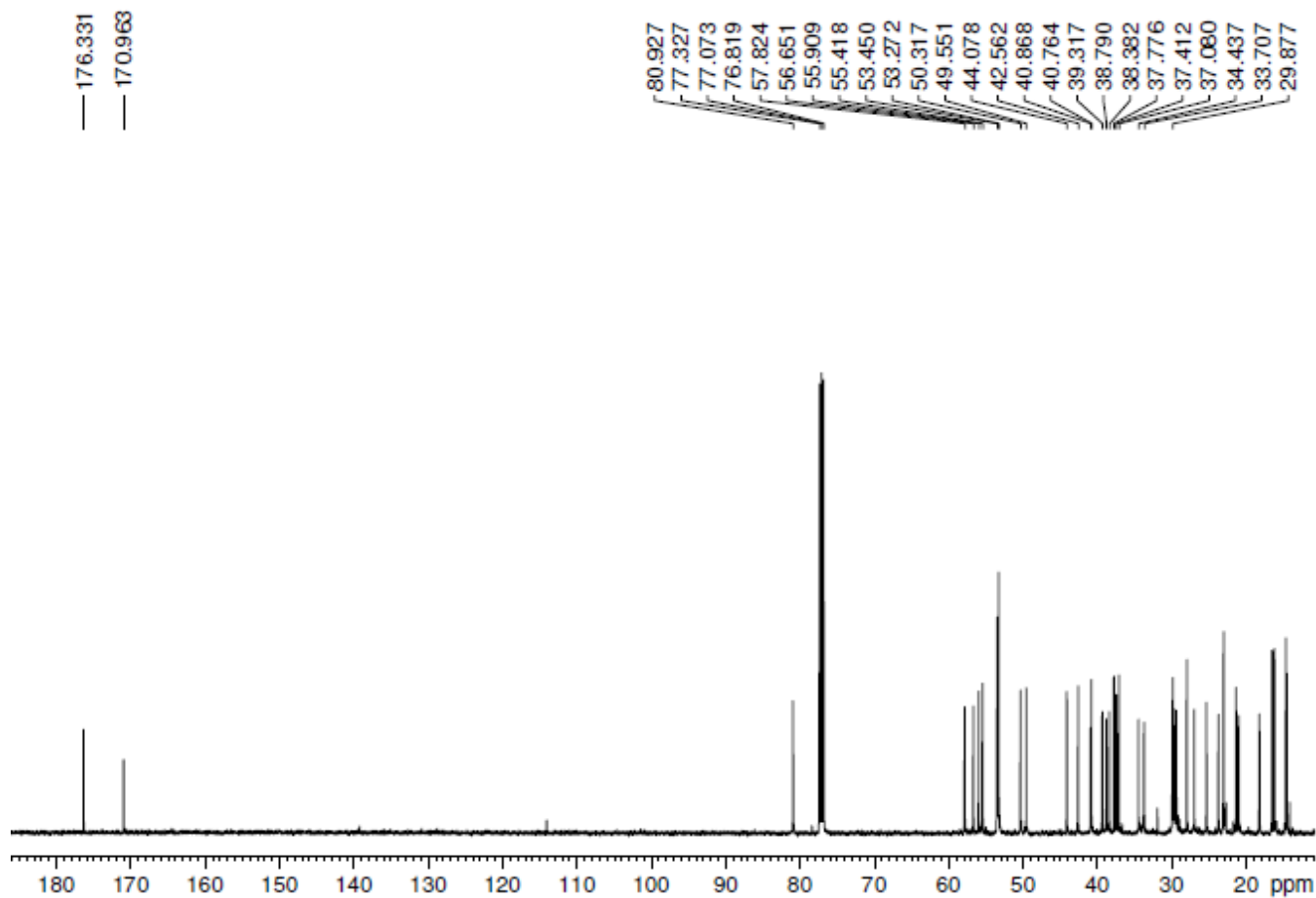
**3 $\beta$ -N-[[3-(3-aminopropyl)piperazinyl]propyl]-3-O-acetyl-lupane-28-amide (8a).**

<sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)



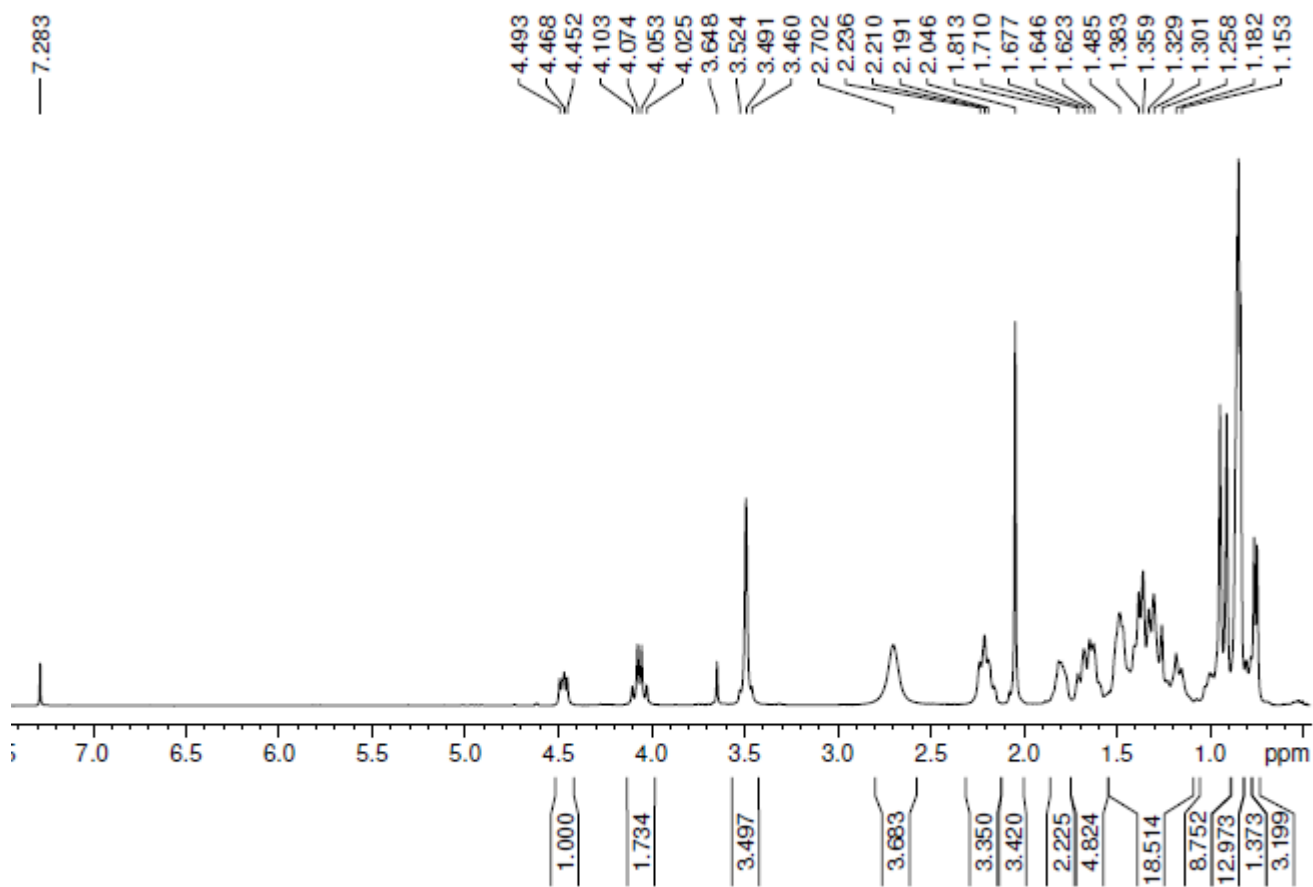
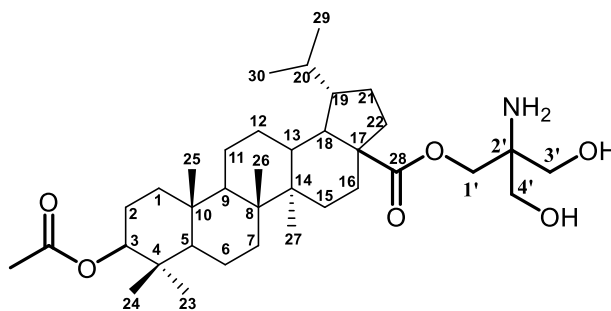
**3 $\beta$ -N-[[3-(3-aminopropyl)piperazinyl]propyl]-3-O-acetyl-lupane-28-amide (8a).**

$^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )



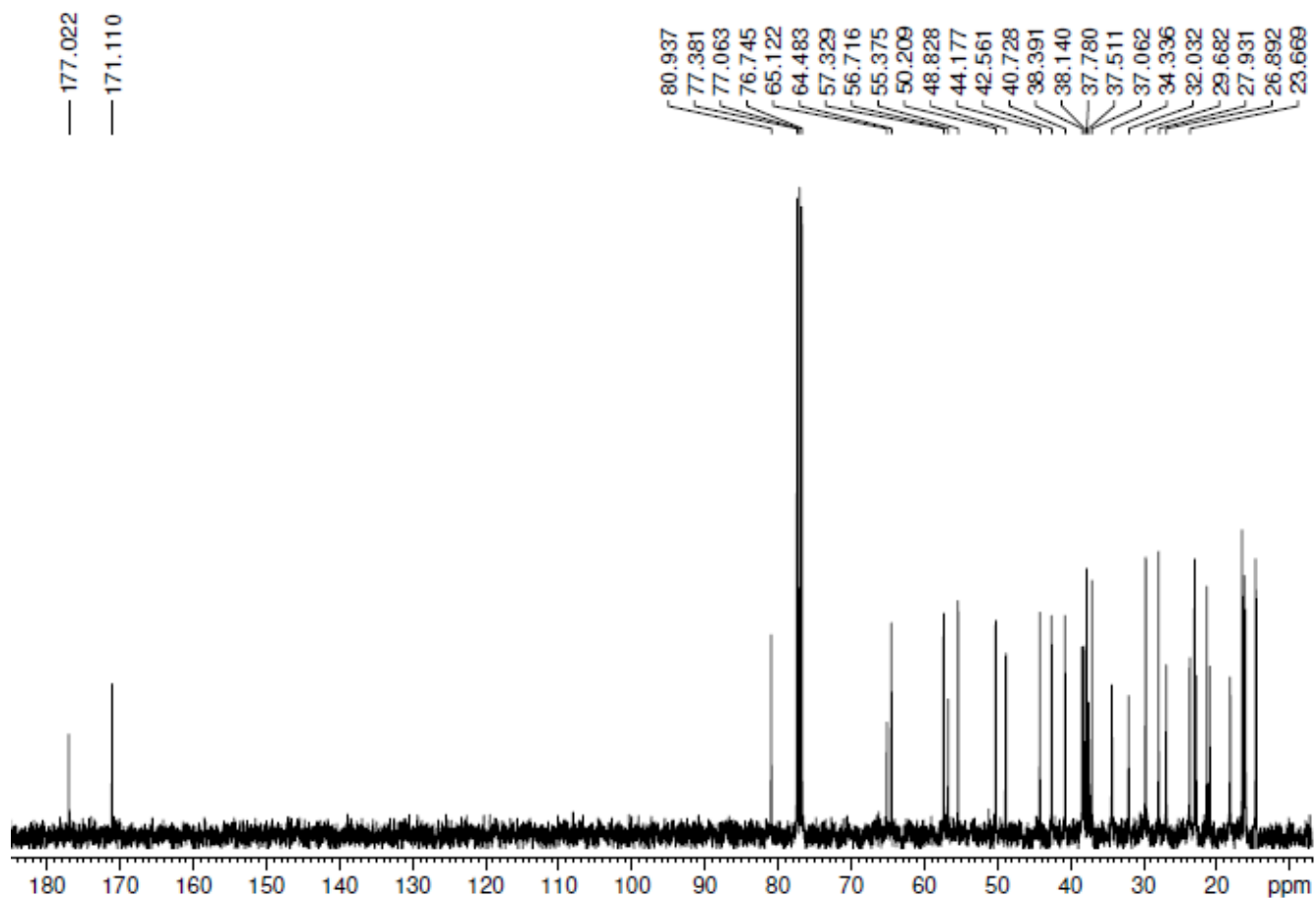
**3 $\beta$ -[2-amino-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl -lupane-28-oate (15).**

<sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)



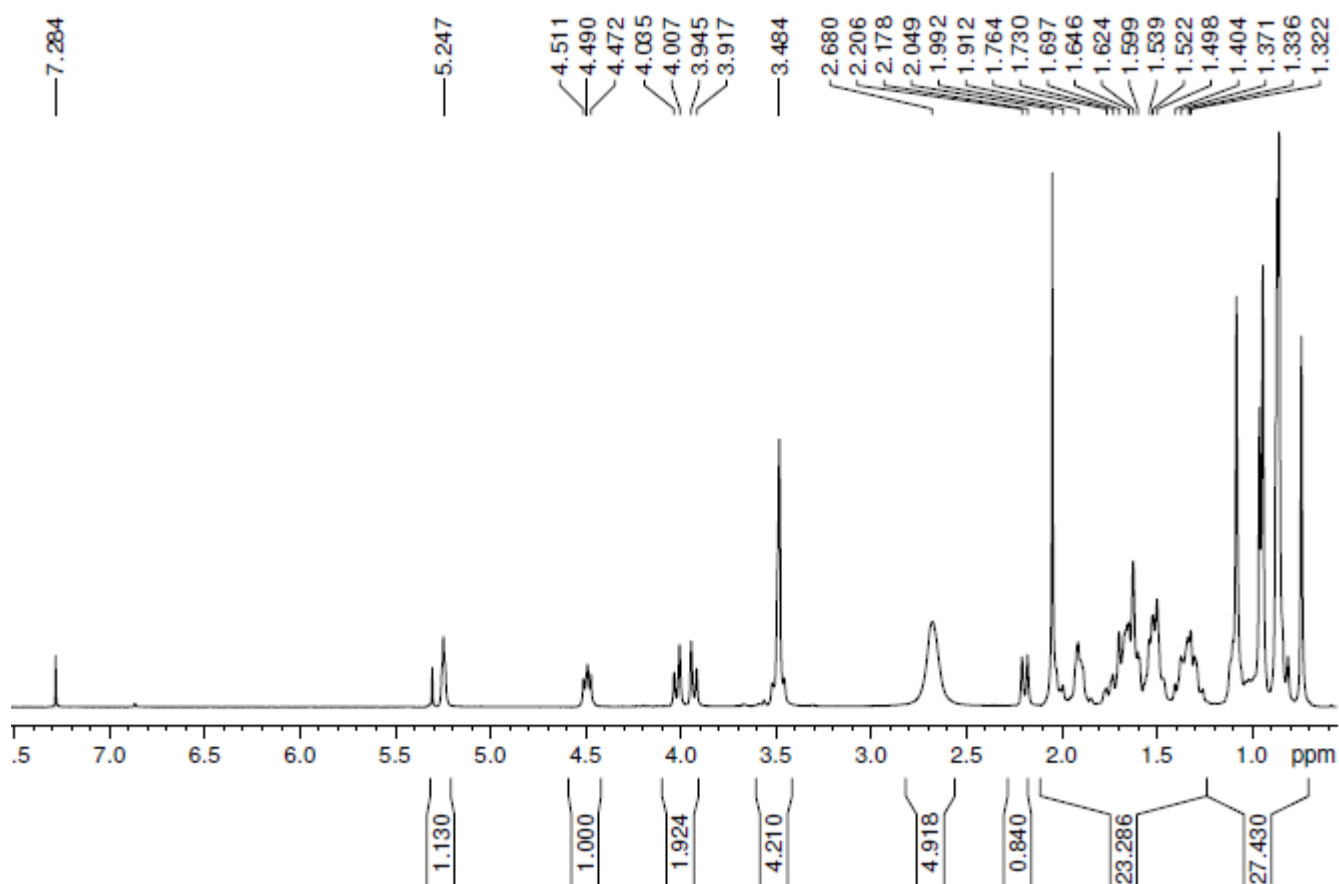
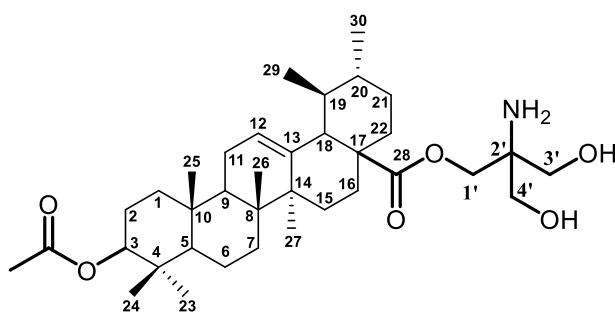
**3 $\beta$ -[2-amino-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl -lupane-28-oate (15).**

<sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)



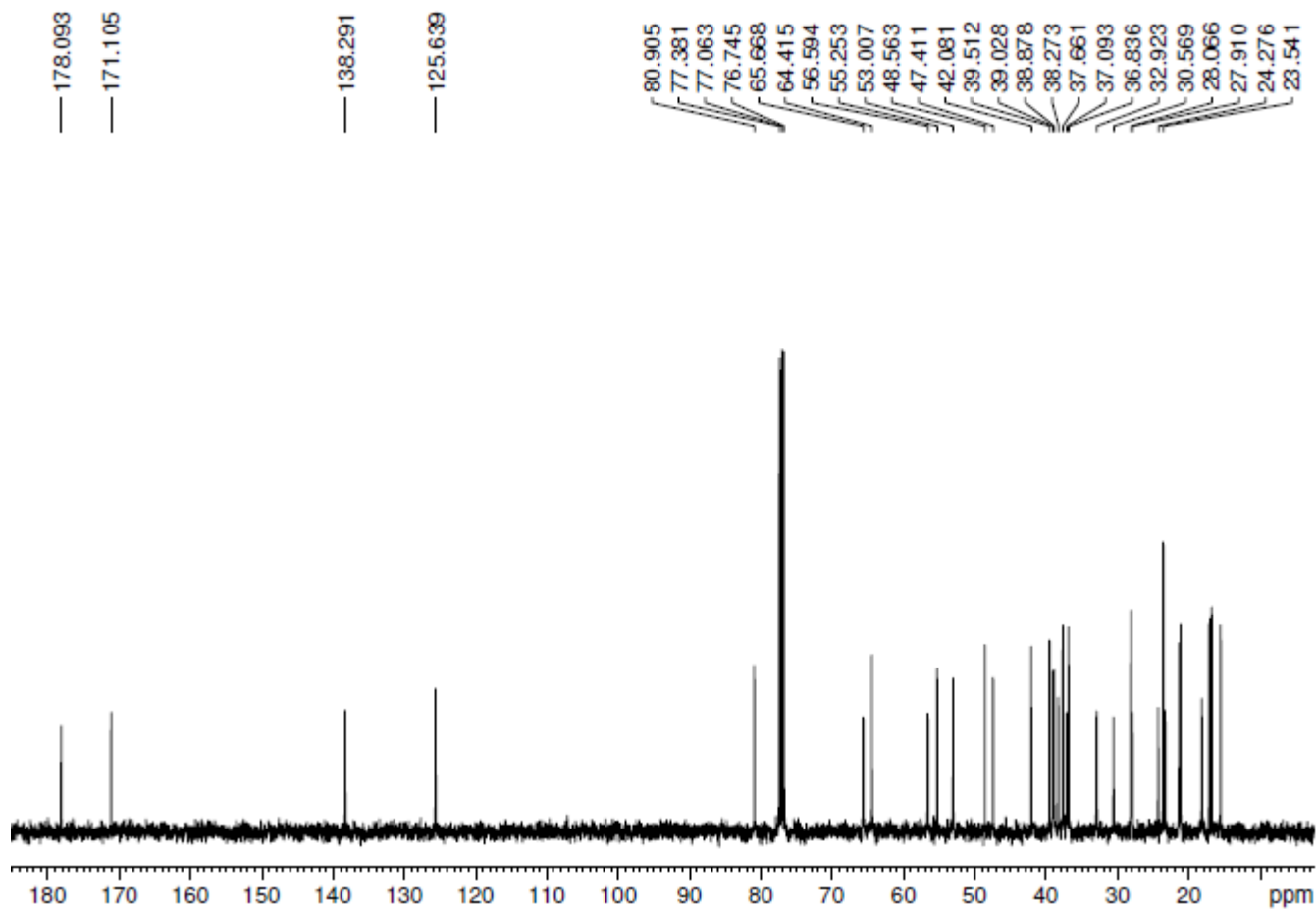
**3 $\beta$ -[2-amino-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetylurs-12-en-28-oate (18).**

$^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )



**3 $\beta$ -[2-amino-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetylurs-12-en-28-oate (18).**

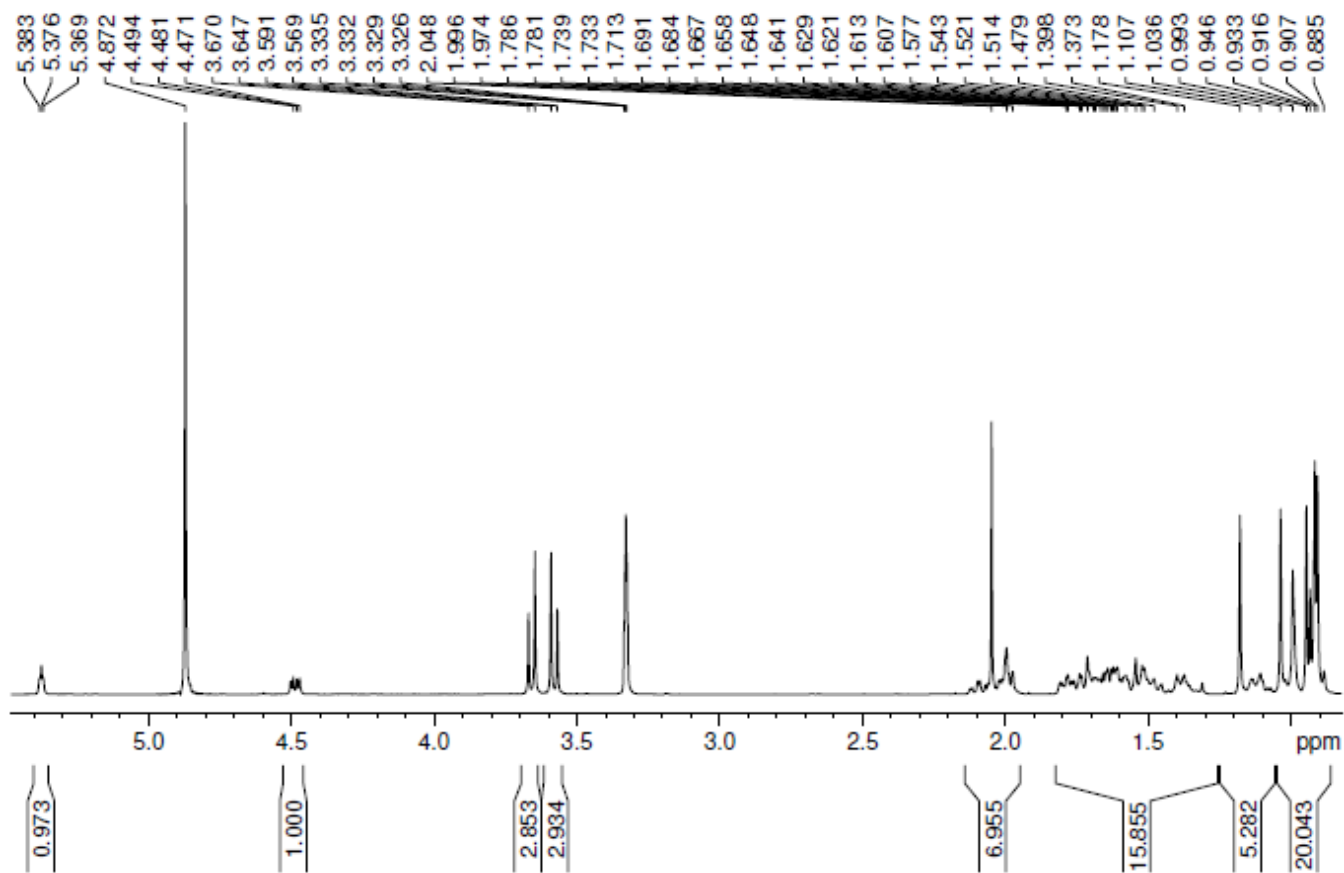
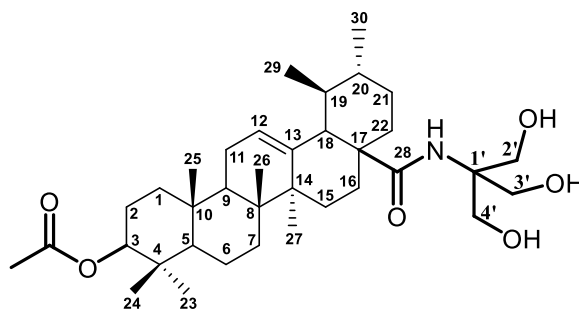
<sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)





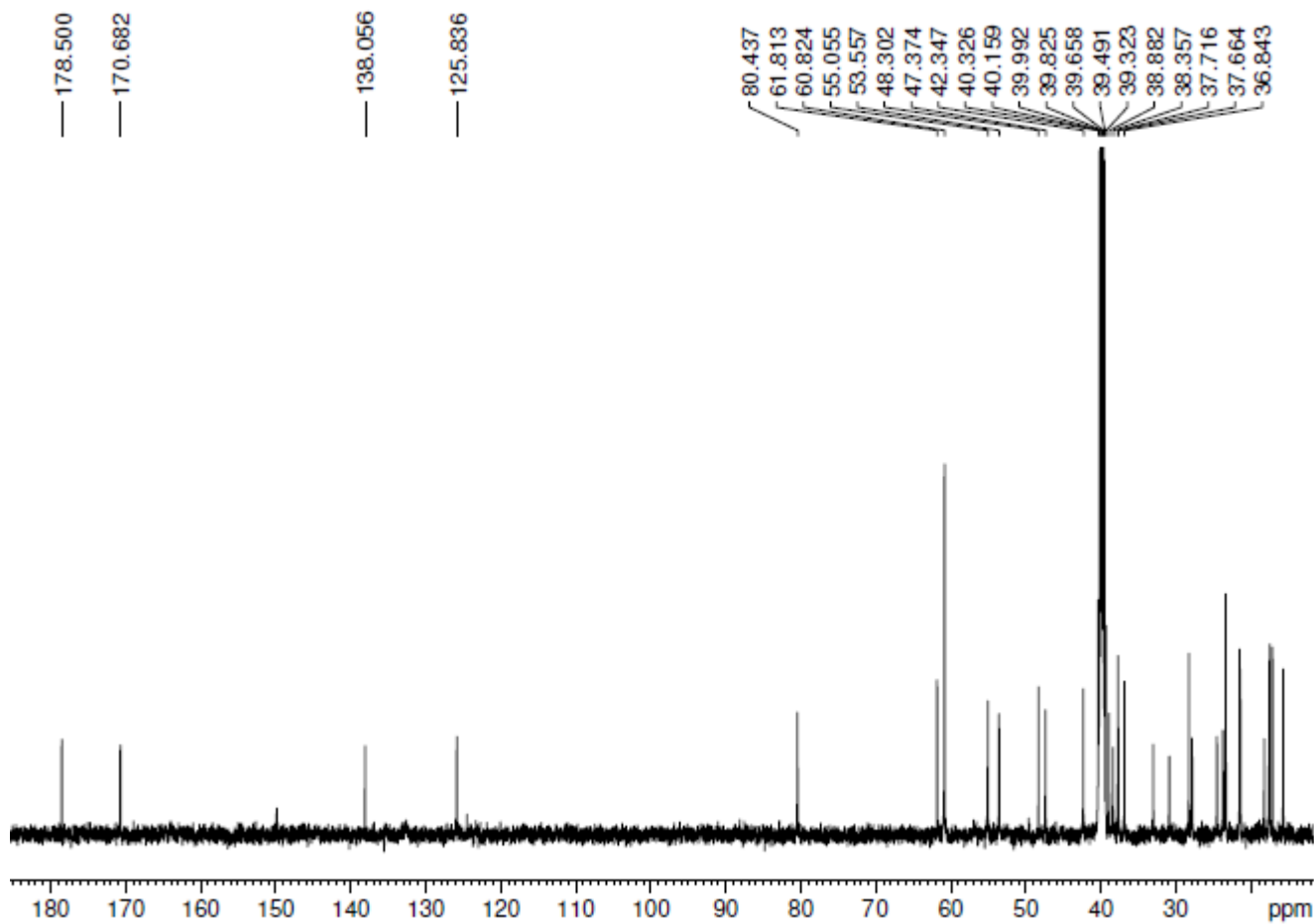
3 $\beta$ -N-[(1',1',1'-tris-hidroxymethyl)methyl]-3-O-acetyl-ursolamide (19)

$^1\text{H}$  NMR spectra (MeOD)



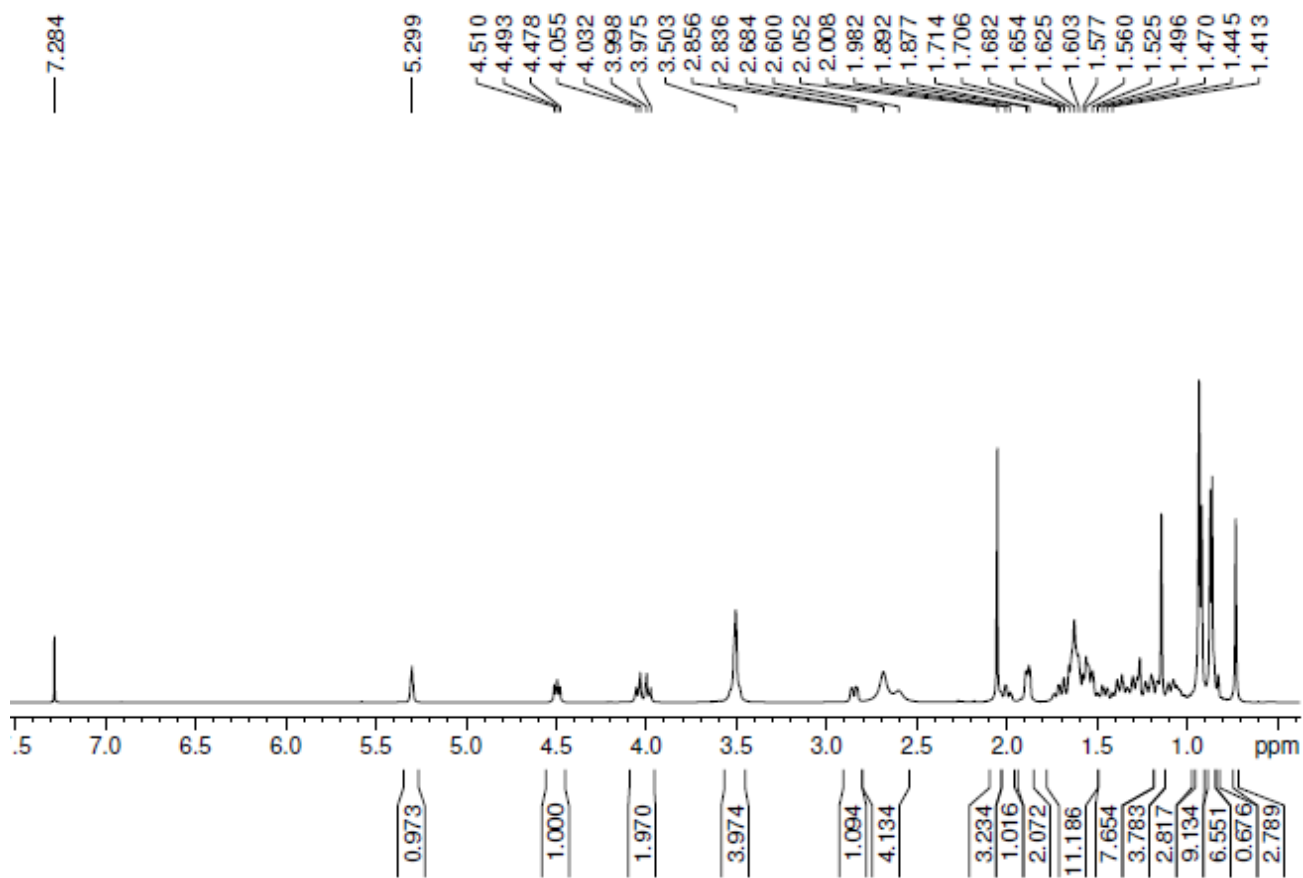
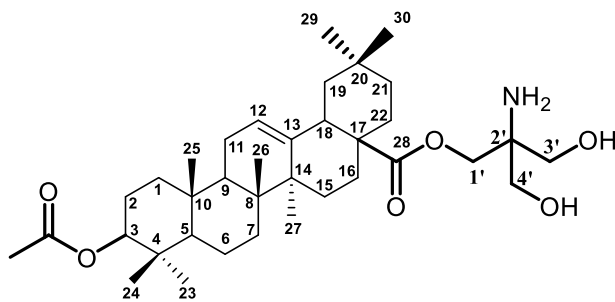
**3 $\beta$ -N-[(1',1',1'-tris-hidroxymethyl)methyl]-3-O-acetyl-ursolamide (19)**

<sup>13</sup>C NMR spectra (d5-DMSO)



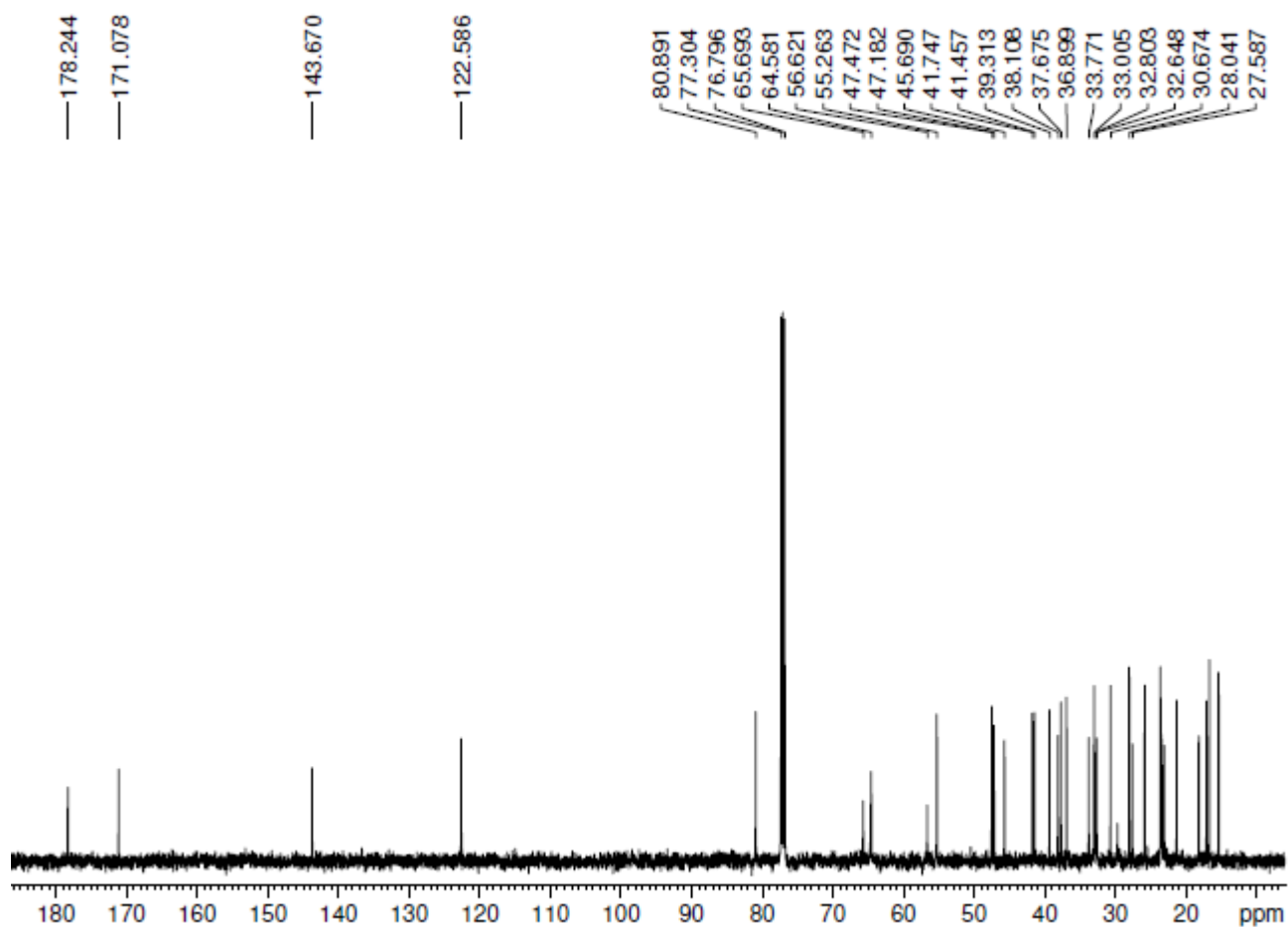
**3 $\beta$ -[2-amino-3-hydroxy-2(hydroxymethyl)propyl]-3-O-acetylolean-12-en-28-oate (20).**

$^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )



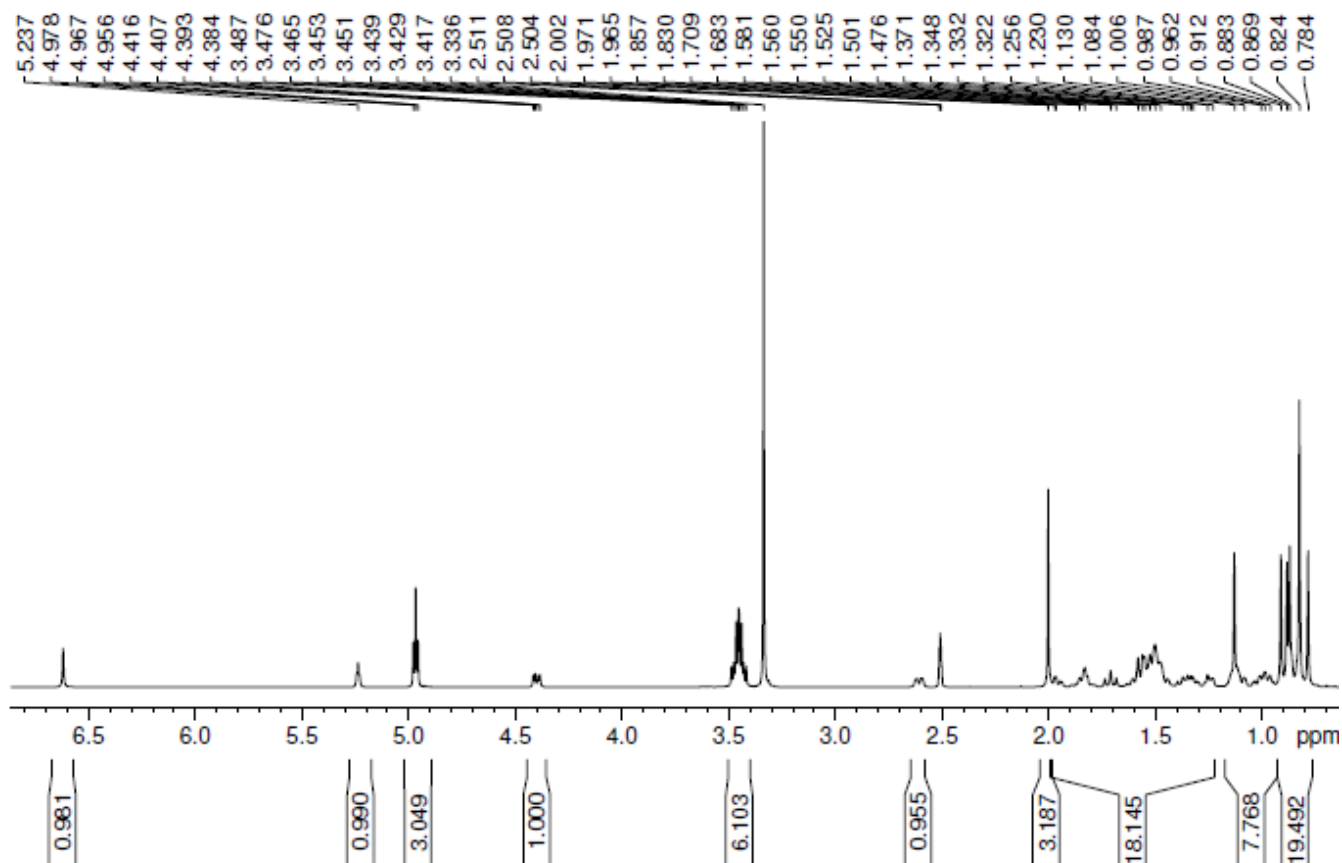
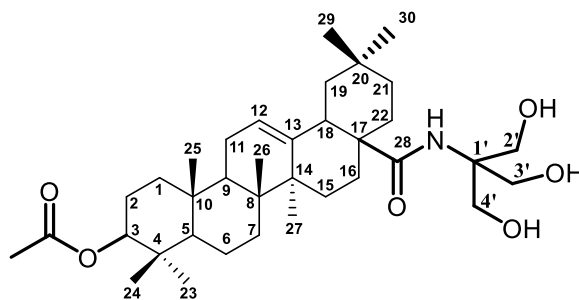
**3 $\beta$ -[2-amino-3-hydroxy-2(hydroxymethyl)propyl]-3-O-acetylolean-12-en-28-oate (20).**

<sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)



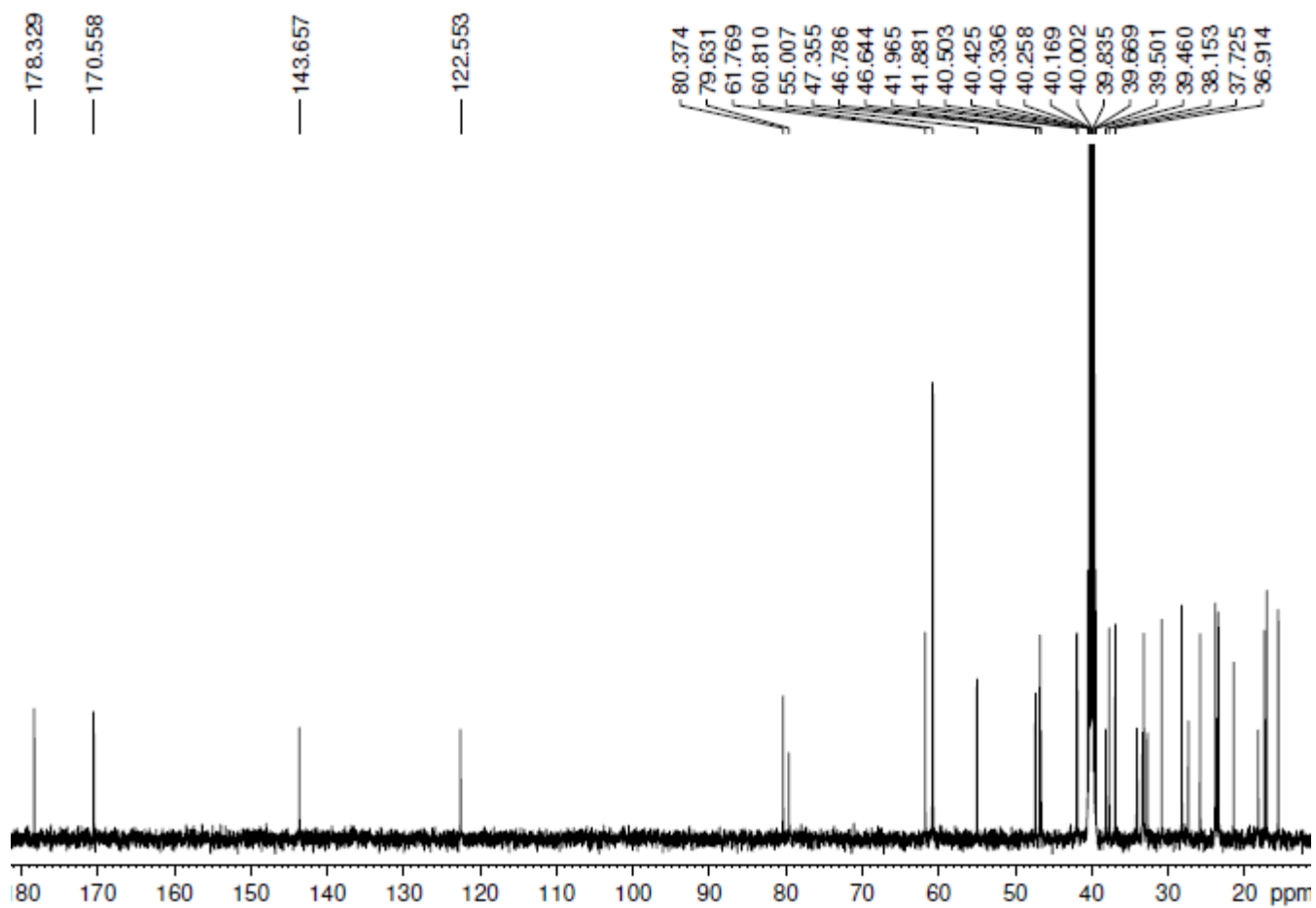
3 $\beta$ -N-[(1',1',1'-tris-hidroxymethyl)methyl]-3-O-acetyl-oleanamide (21)

<sup>1</sup>H NMR spectra (d<sub>6</sub>-DMSO)



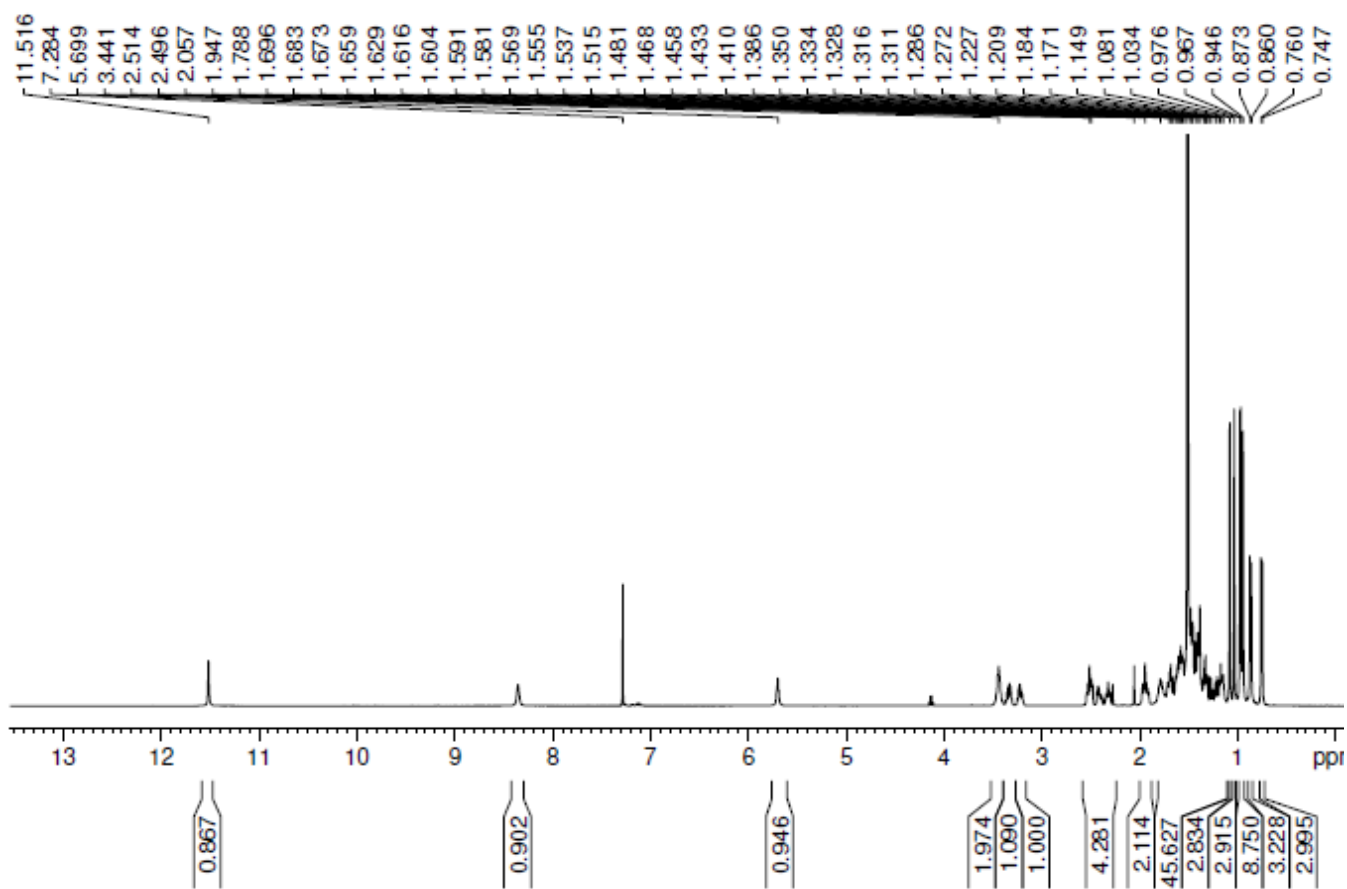
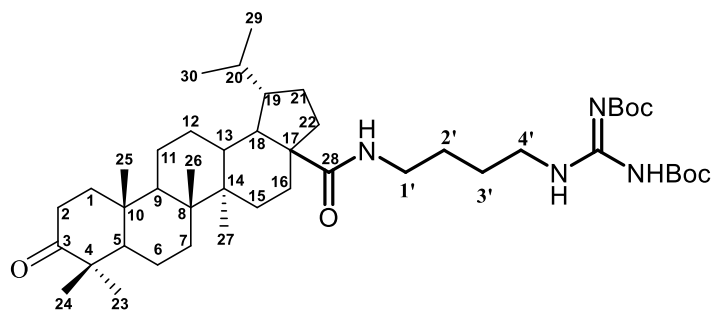
**3 $\beta$ -N-[(1',1',1'-tris-hidroxymethyl)methyl]-3-O-acetyl-oleanamide (21)**

<sup>13</sup>C NMR spectra (d<sub>6</sub>-DMSO)



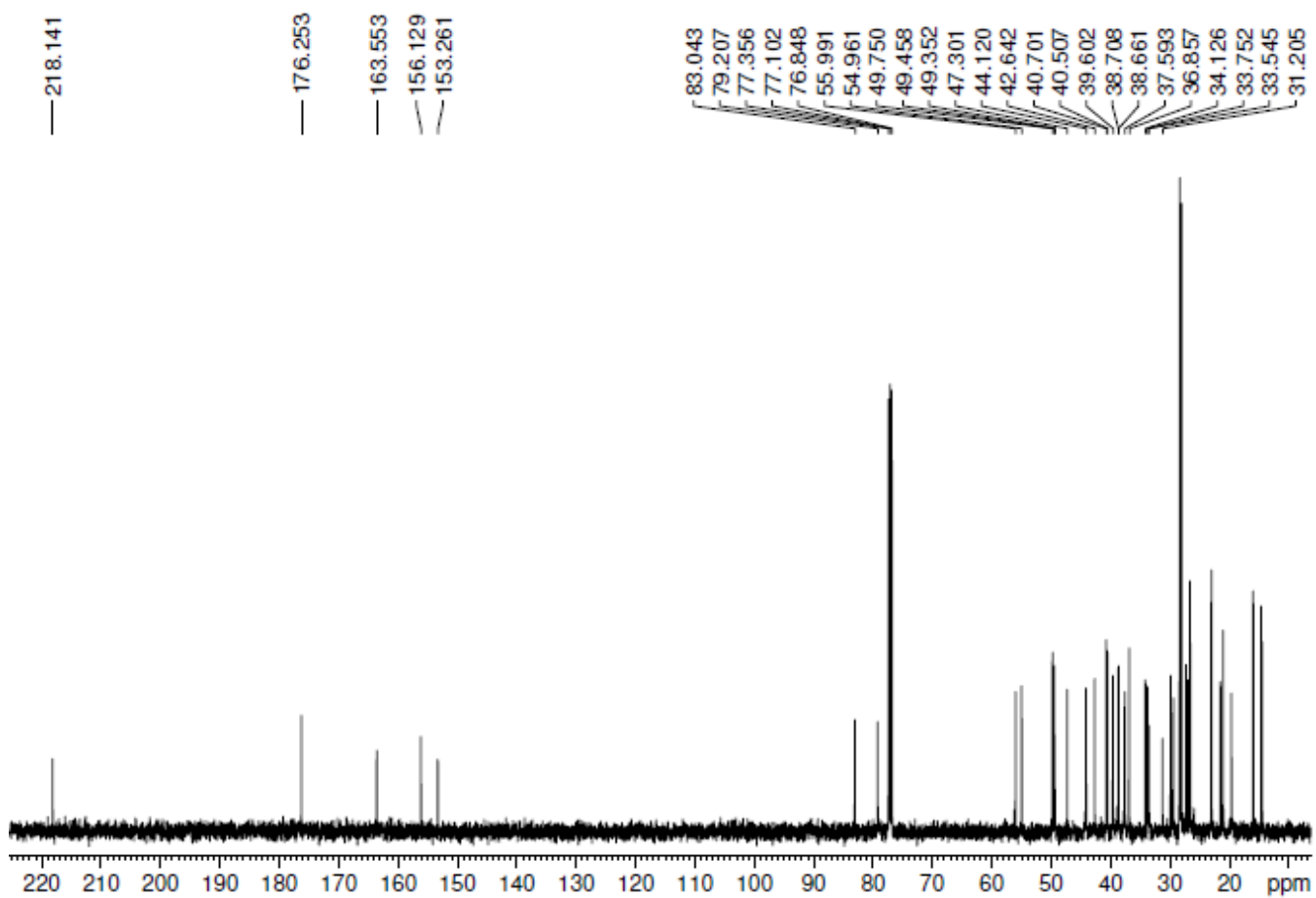
N-[4-tert-butyloxycarbonyl buthylguanidine]-3-oxo-lupane-28-amide (9)

<sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)



N-[4-tert-butyloxycarbonyl buthylguanidine]-3-oxo-lupane-28-amide (9)

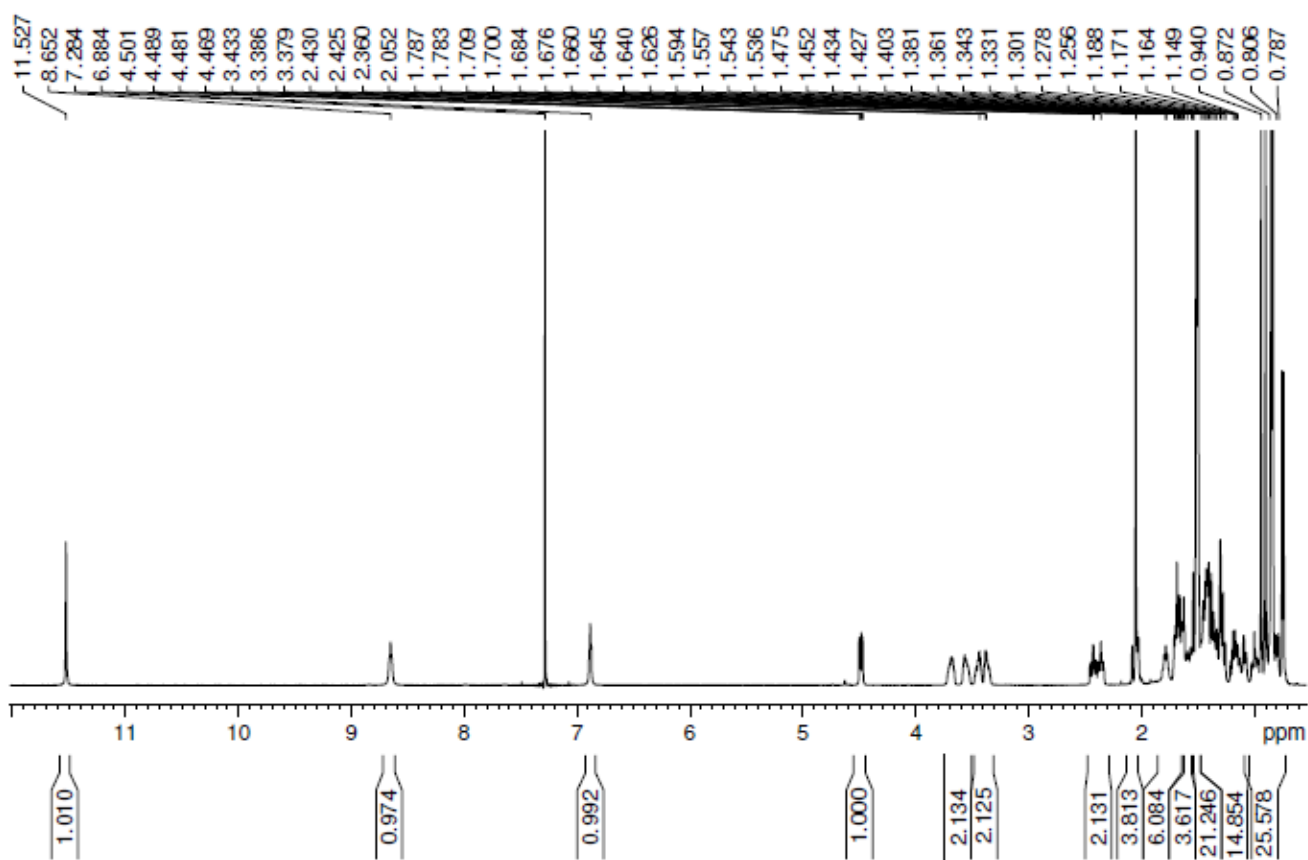
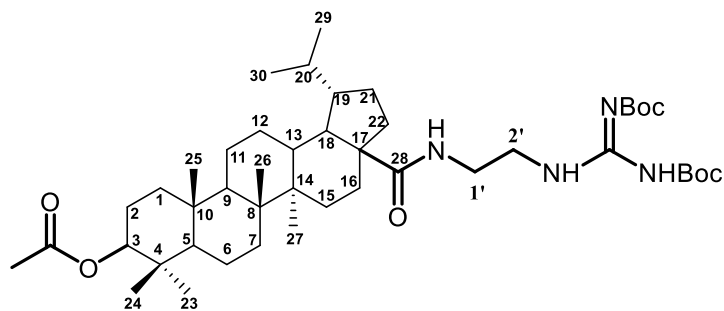
$^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )





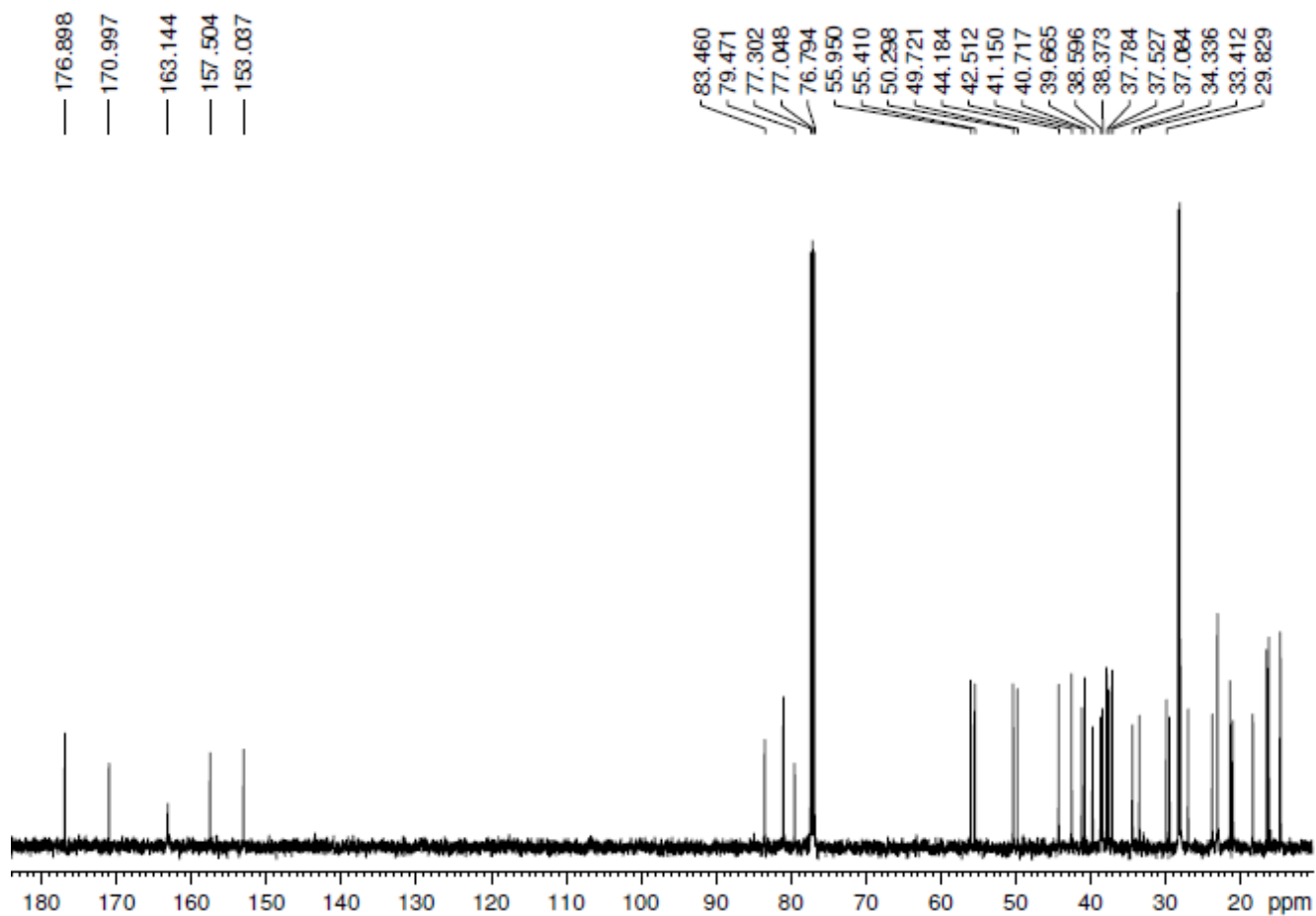
3 $\beta$ -N-(2-tert-butyloxycarbonyl ethylguanidine)-3-O-acetyl-lupane-28-amide (10).

$^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )



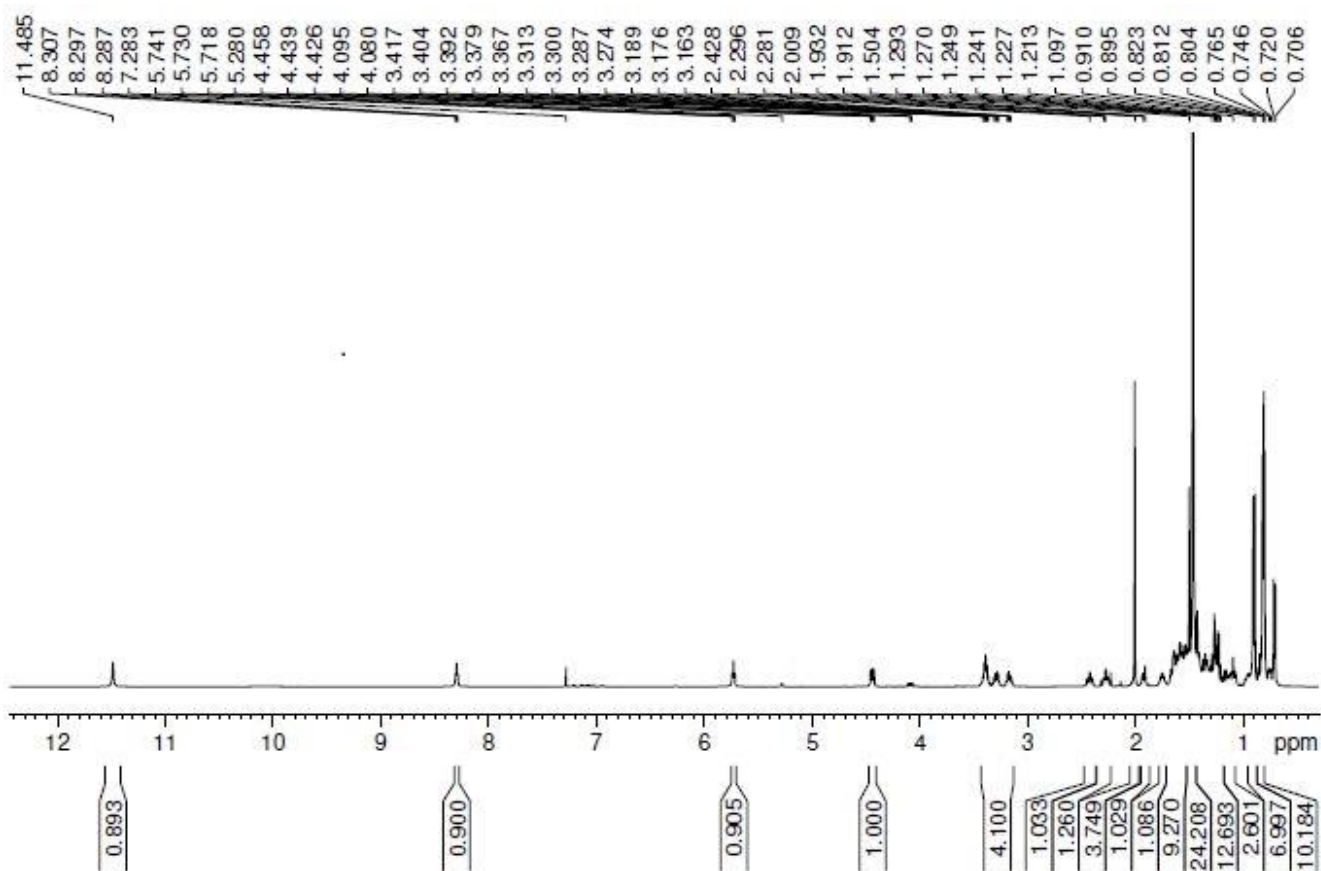
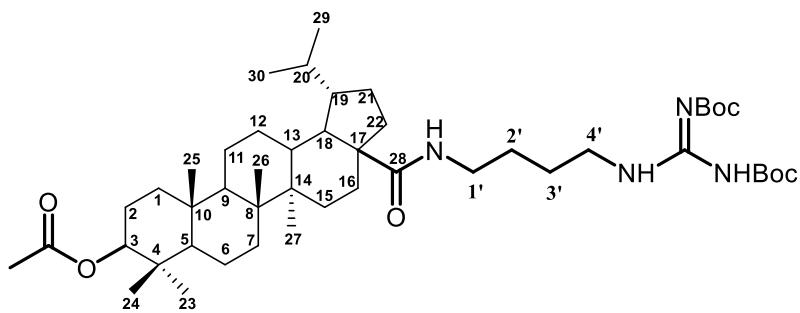
**3 $\beta$ -N-(2-tert-butyloxycarbonyl ethylguanidine)-3-O-acetyl-lupane-28-amide (10).**

$^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )



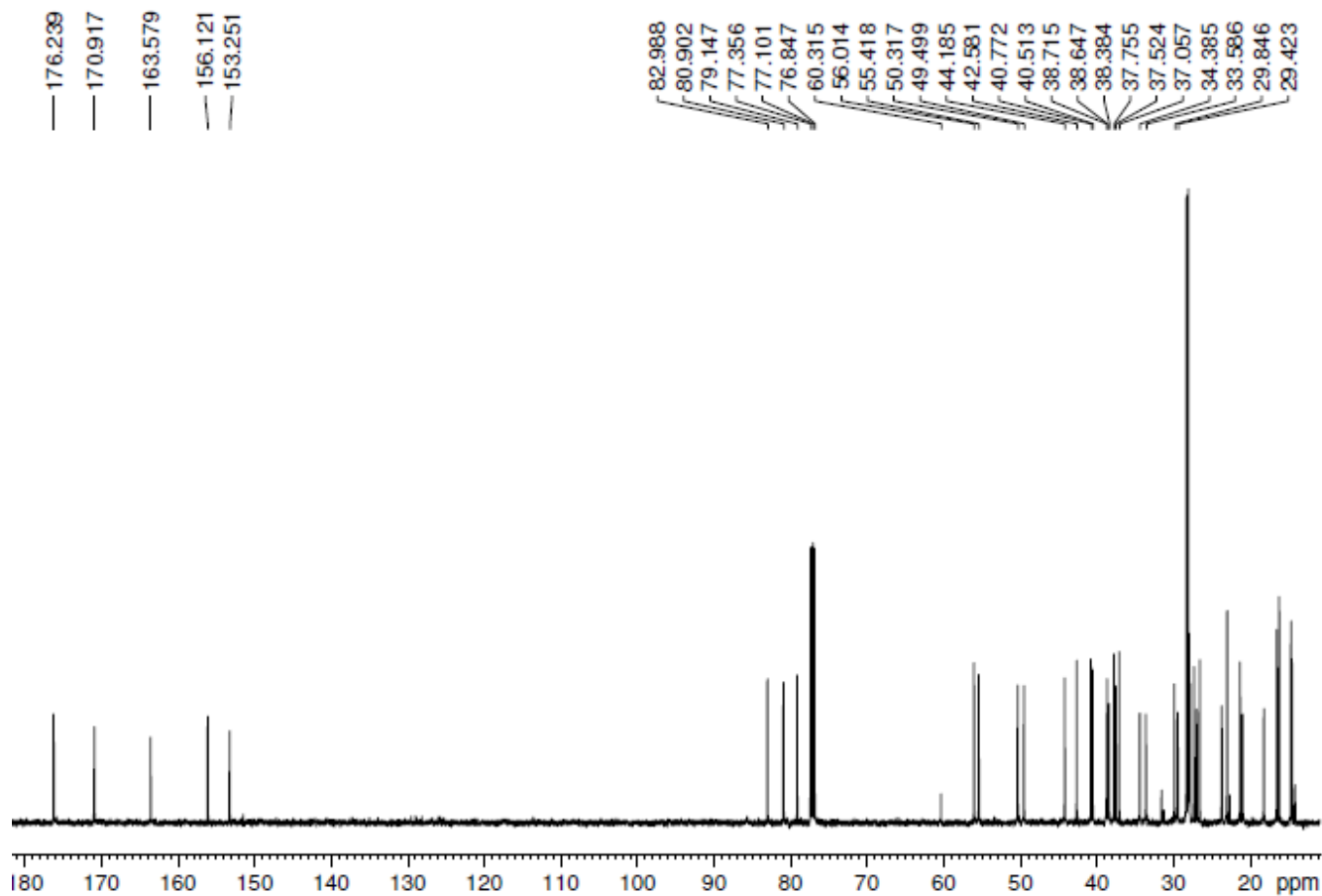
**3 $\beta$ -N-[4-tert-butyloxycarbonyl buthylguanidine]-3-O-acetyl -lupane-28-amide (11).**

$^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )

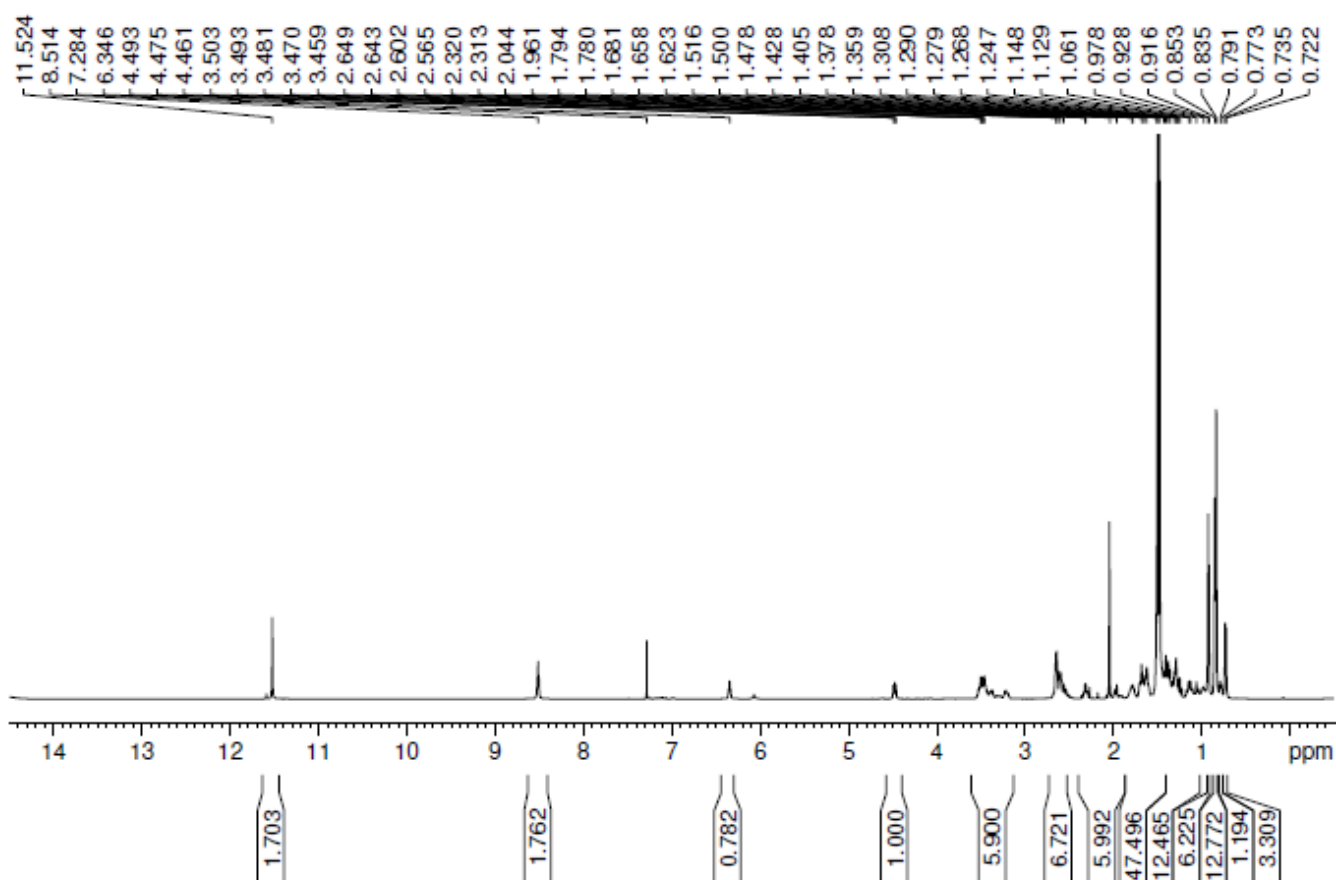
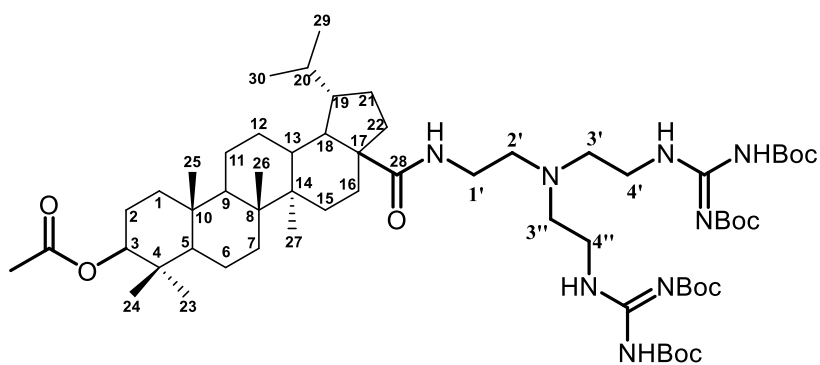


**3 $\beta$ -N-[4-tert-butyloxycarbonyl buthylguanidine]-3-O-acetyl -lupane-28-amide (11).**

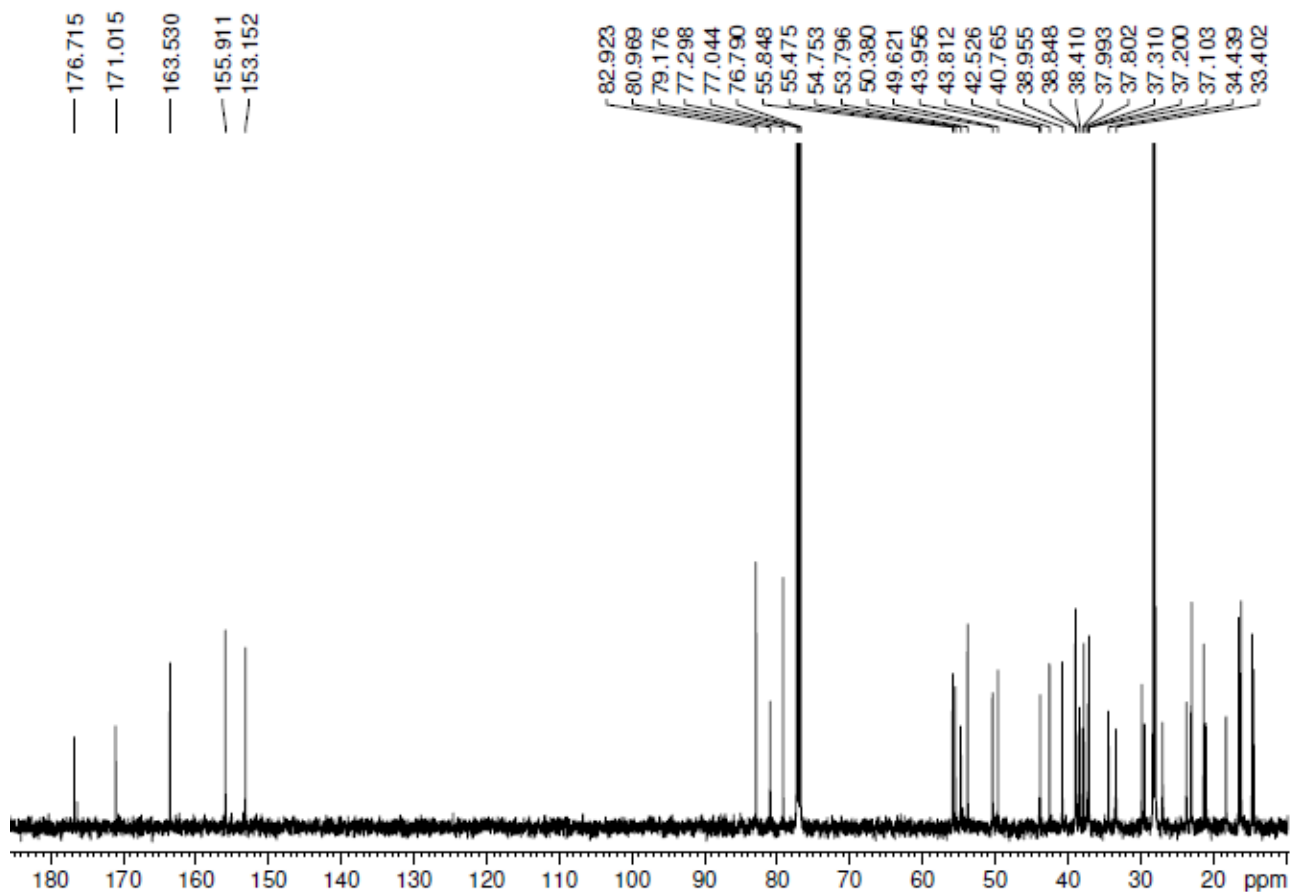
<sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)



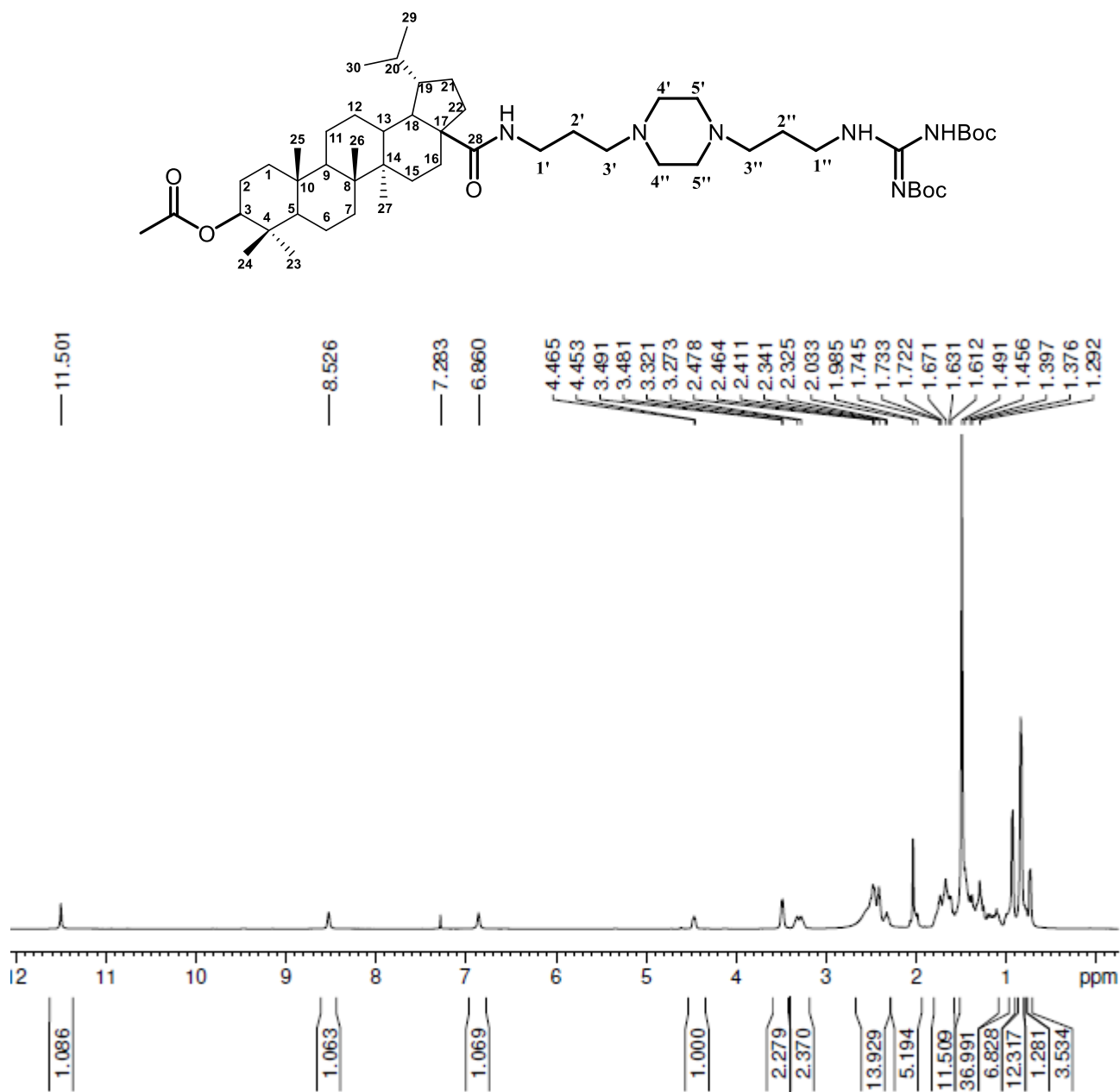
**3 $\beta$ -N-[2-(N,N'-bis-tert-butyloxycarbonyl ethylglyanidine)-aminoethyl]-3-O-acetyl-lupane-28-amide (12). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)**



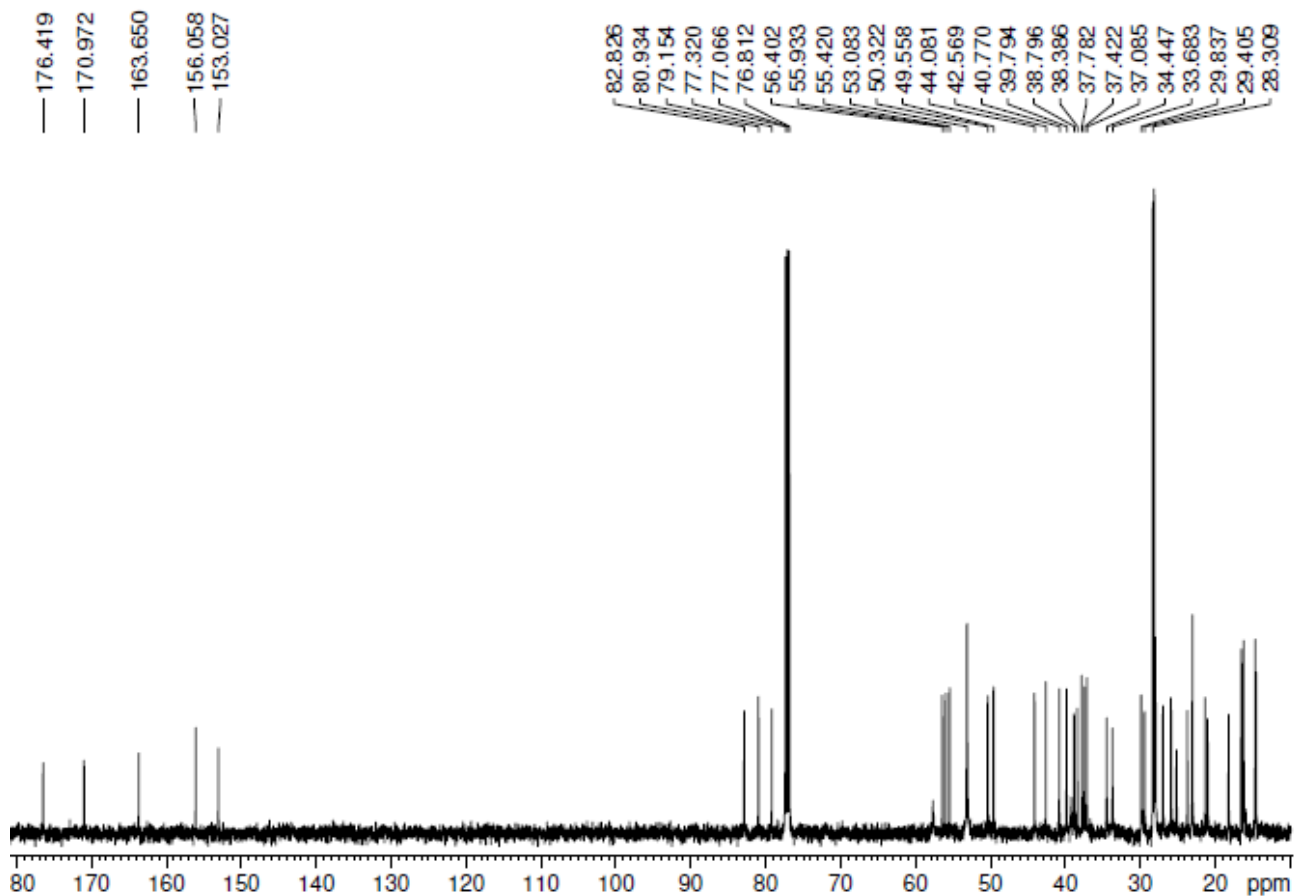
**3 $\beta$ -N-[2-(N,N'-bis-tert-butyloxycarbonyl ethyl)guanidine]-3-O-acetyl-lupane-28-amide (12).**  $^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )



**3 $\beta$ -N-[[3-(3-tert-butyloxycarbonyl propyl)guanidine]piperazinyl]propyl]-3-O-acetyl-lupane-28-  
amide (13). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)**

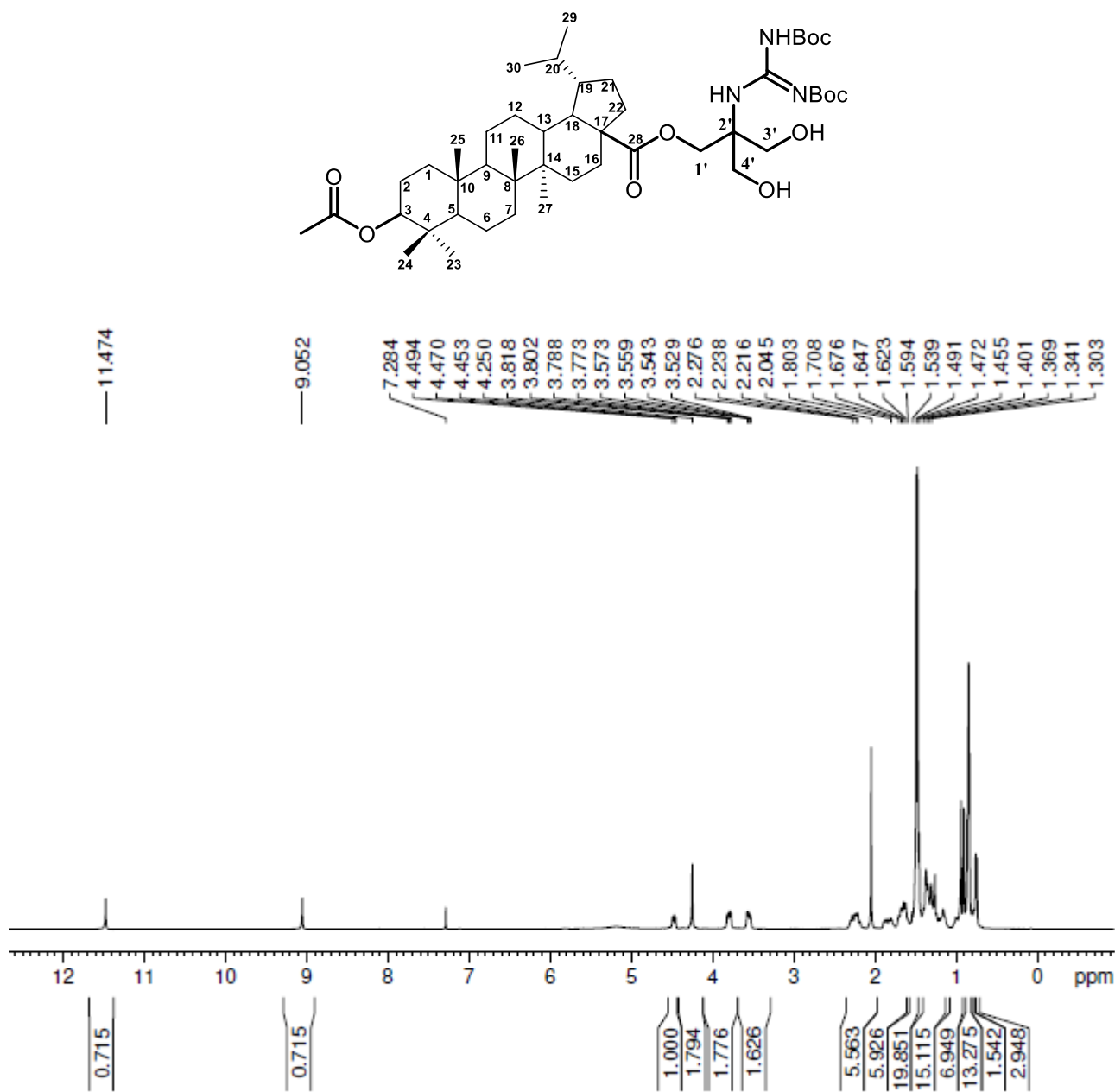


**3 $\beta$ -N-[[3-(3- tert-butyloxycarbonyl propyl)guanidine]piperazinyl]propyl]-3-O-acetyl-lupane-28-amide (13). <sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)**

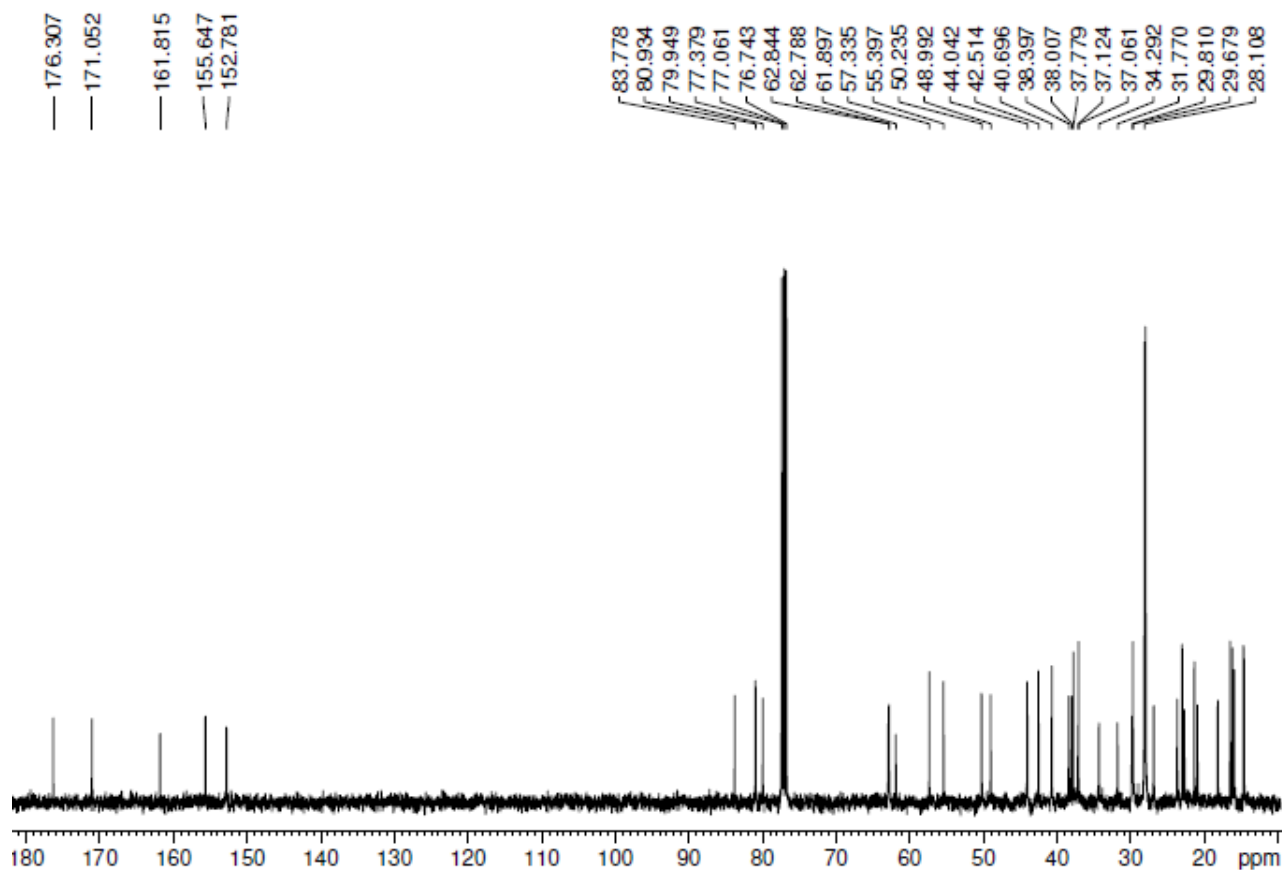




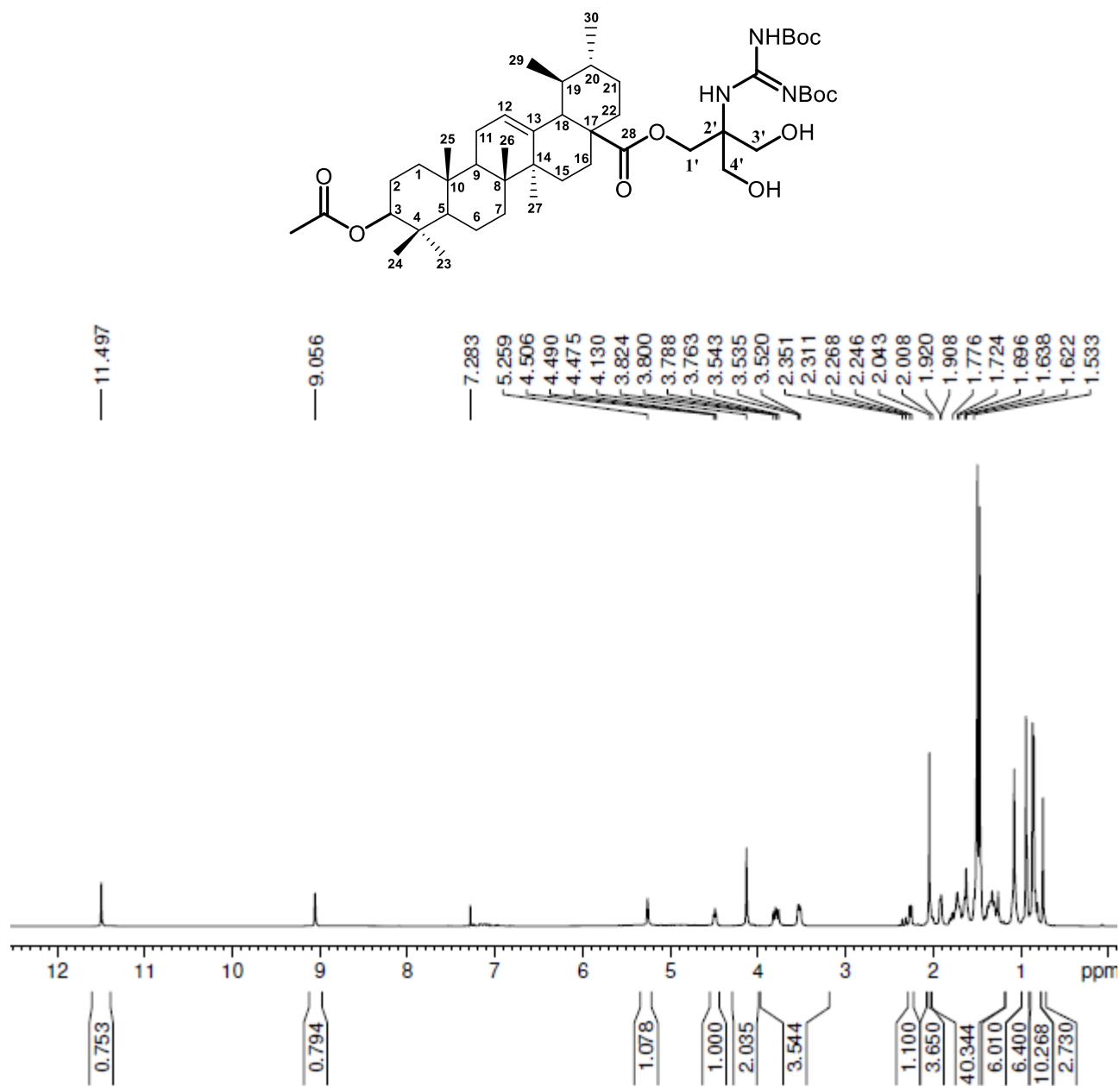
**3 $\beta$ -[2-tert-butyloxycarbonylguanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-lupane-28-oate (15a). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)**



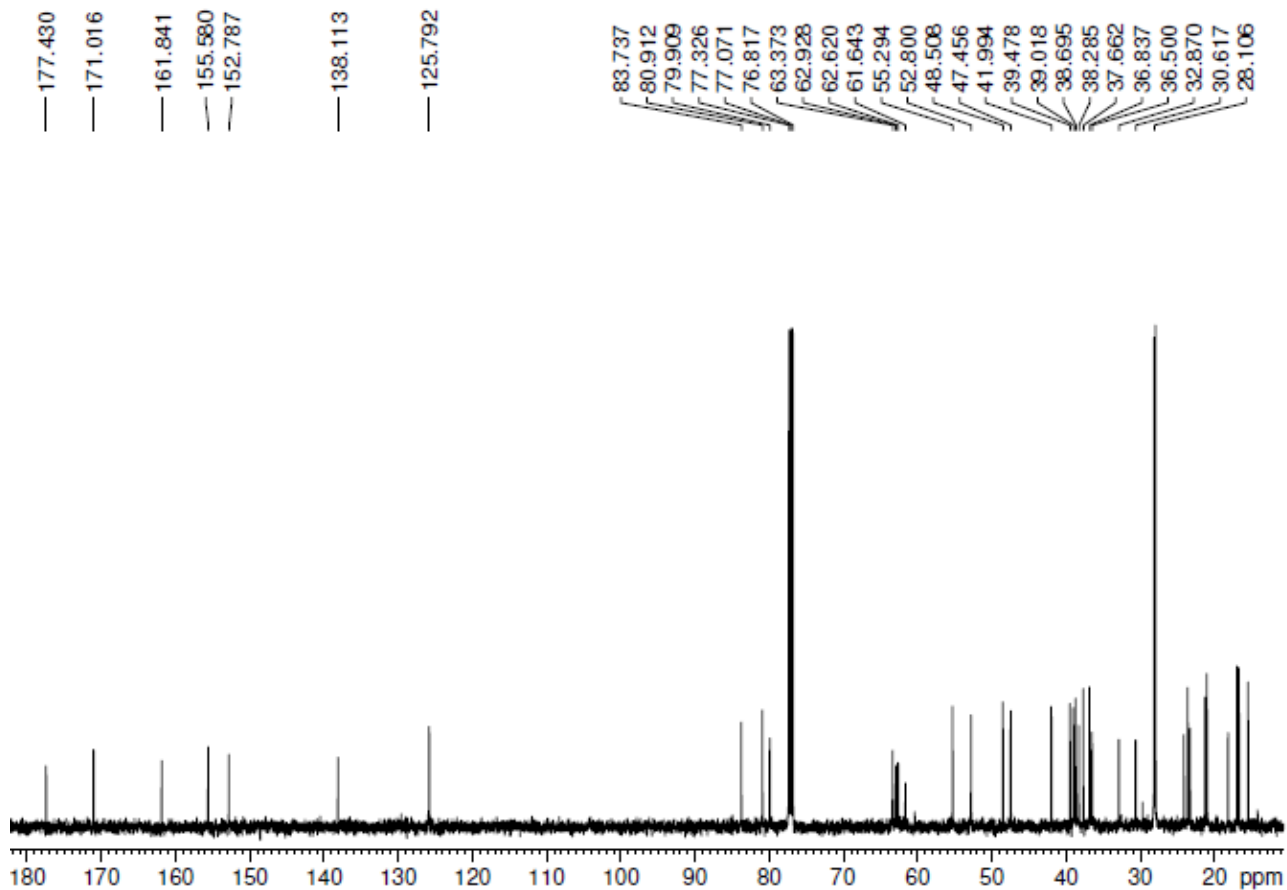
**3 $\beta$ -[2-tert-butyloxycarbonylguanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl -lupane-28-oate (15a).  $^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )**



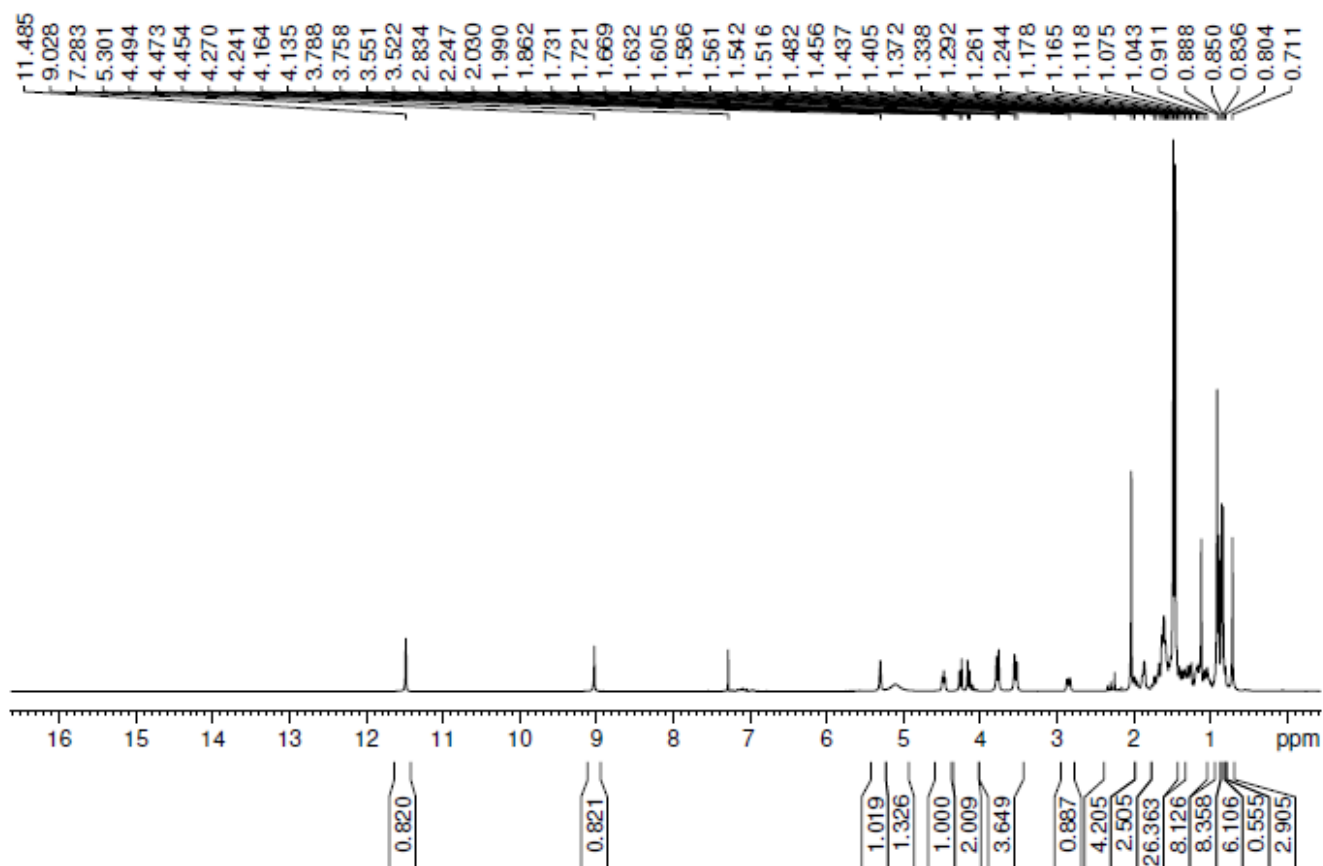
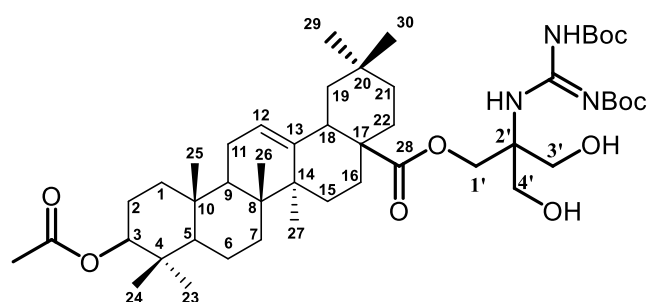
**3 $\beta$ -[2-tert-butyloxycarbonylguanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate (18a). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)**



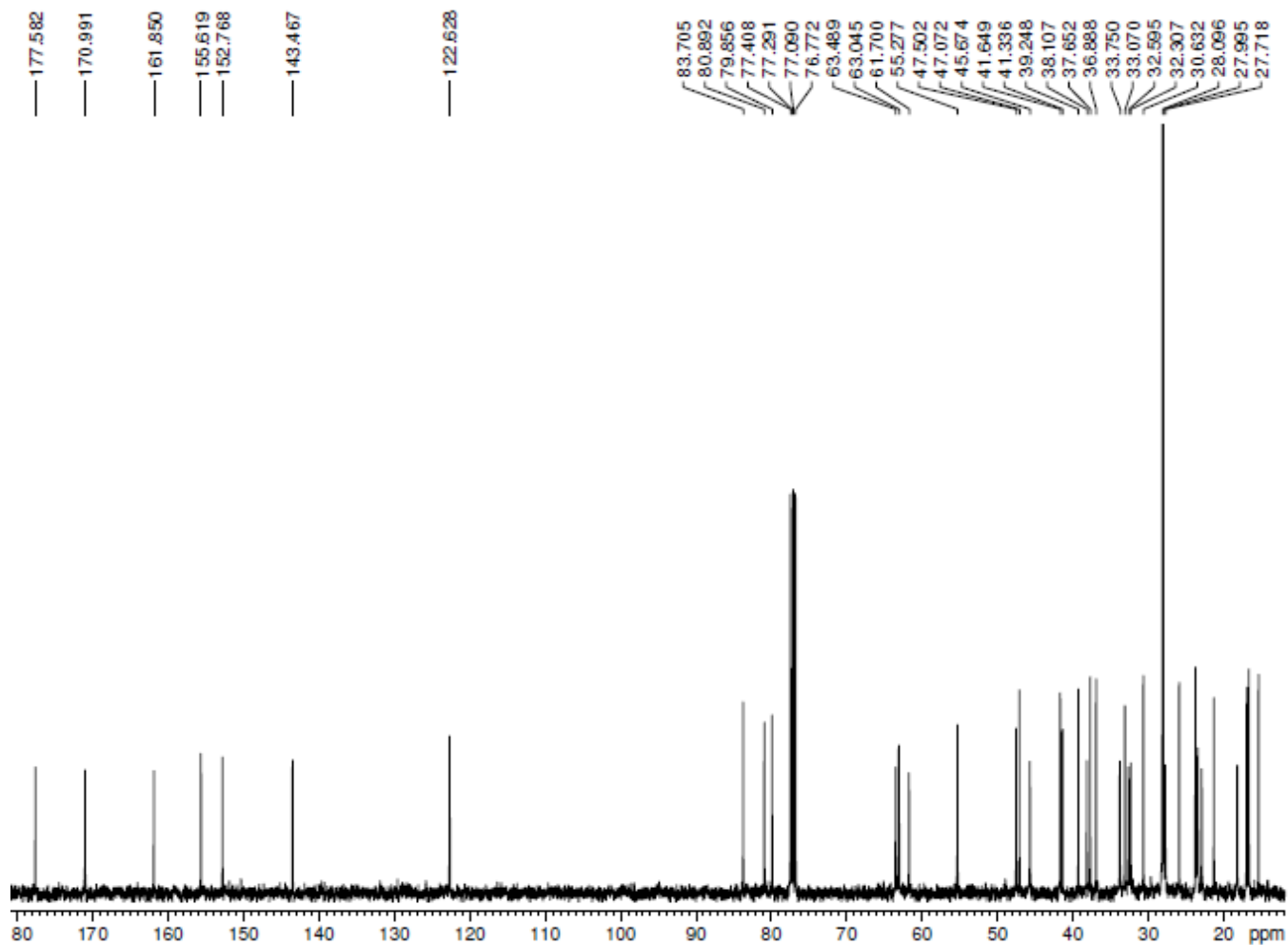
**3 $\beta$ -[2-tert-butyloxycarbonylguanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate (18a). <sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)**



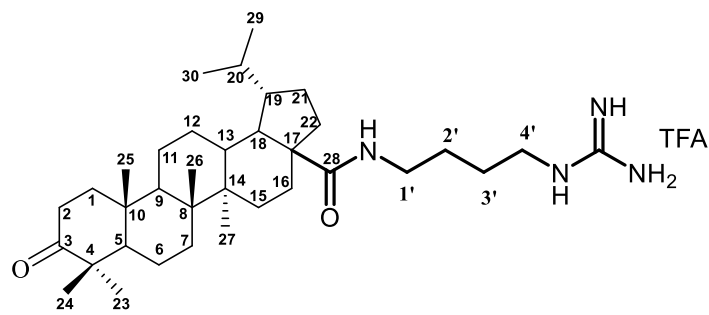
**3 $\beta$ -[2-tert-butyloxycarbonylguanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-olean-12-en-28-oate (20a). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)**



**3 $\beta$ -[2-tert-butyloxycarbonylguanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl - olean-12-en-28-oate (20a).**  $^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )



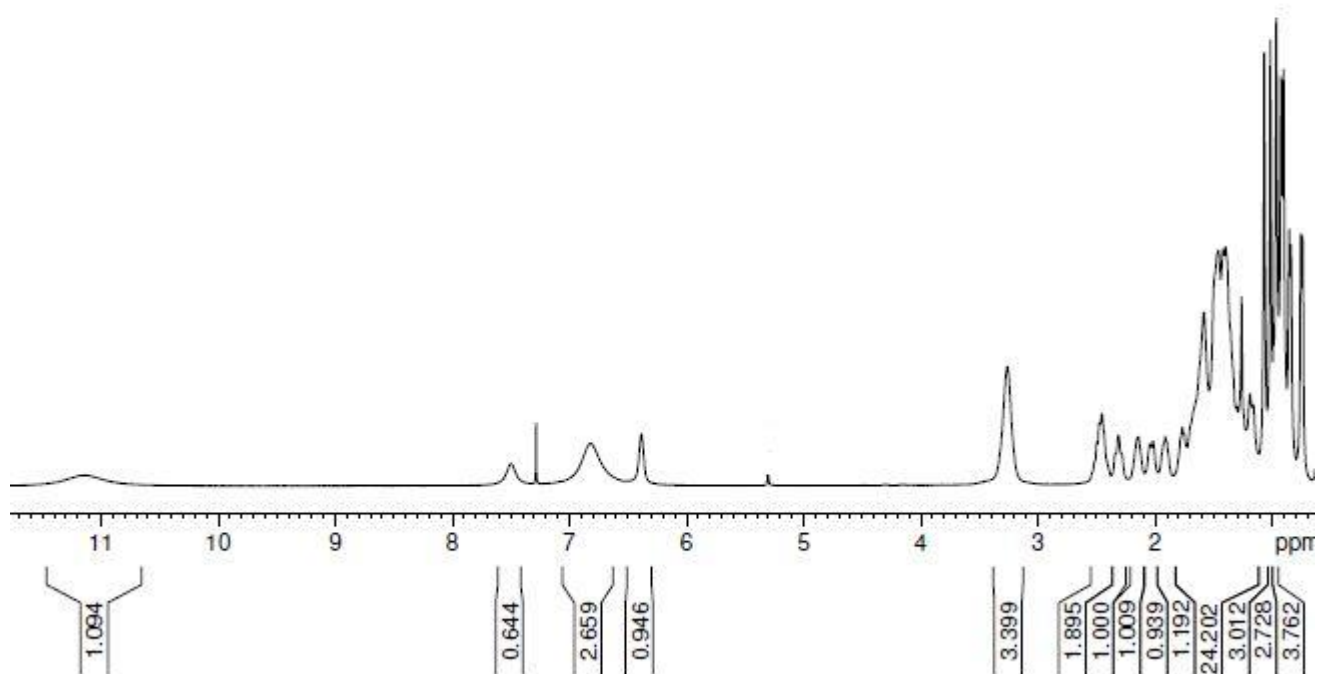
**N-(4-buthylguanidine)-3-oxolupane-28-amide trifluoroacetate (9a).**  $^1\text{H}$  NMR spectra ( $\text{CDCl}_3$ )



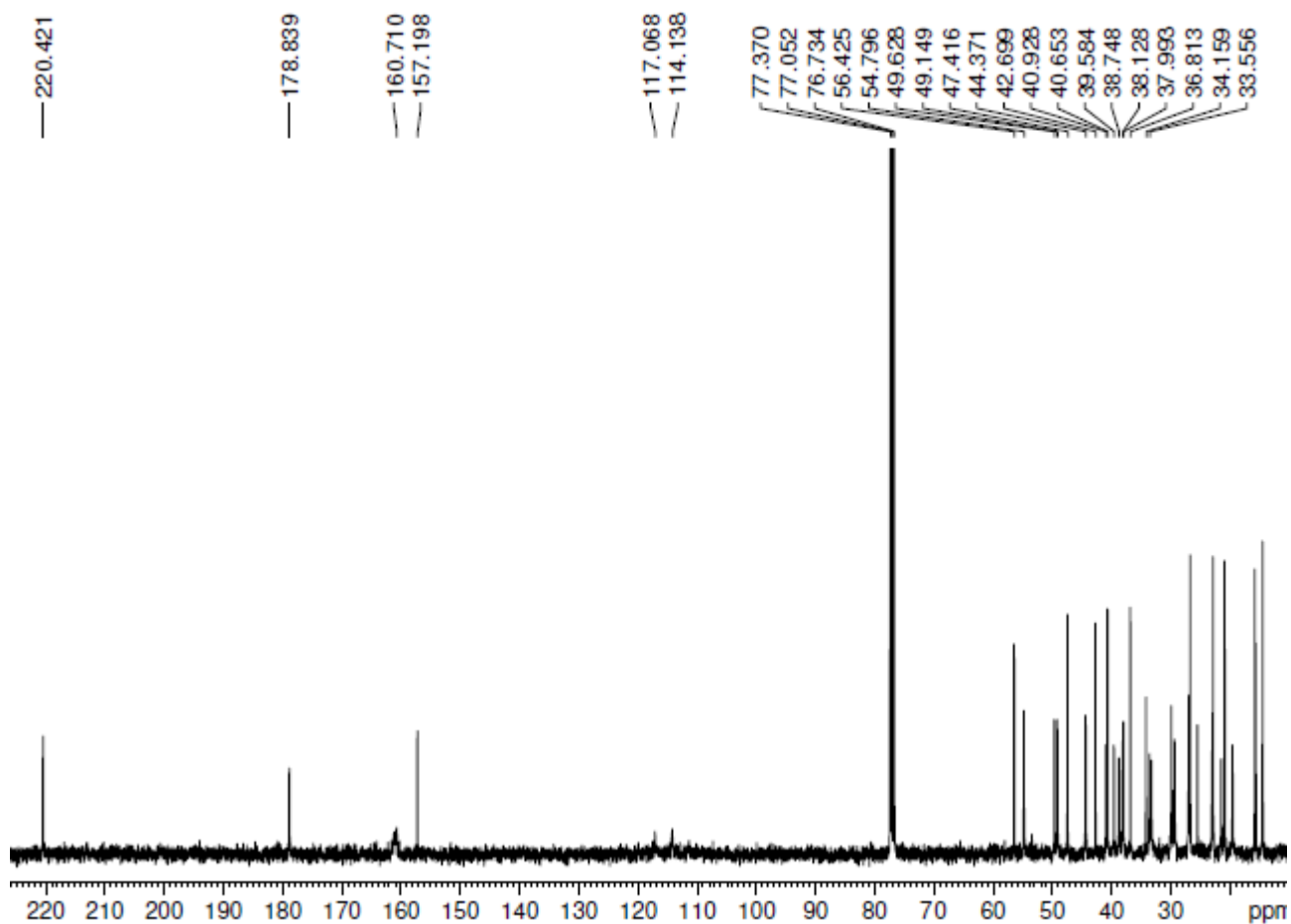
— 11.133

— 7.497  
— 7.284  
— 6.817  
— 6.385

3.260  
2.453  
2.311  
2.141  
2.043  
2.017  
1.911  
1.765  
1.582  
1.456  
1.418  
1.396  
1.260

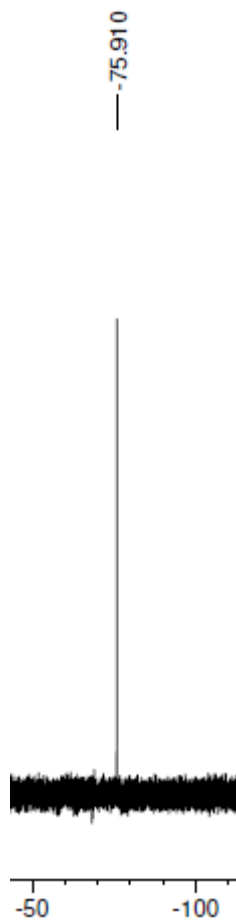


**N-(4-buthylguanidine)-3-oxolupane-28-amide trifluoroacetate (9a).**  $^{13}\text{C}$  NMR spectra ( $\text{CDCl}_3$ )

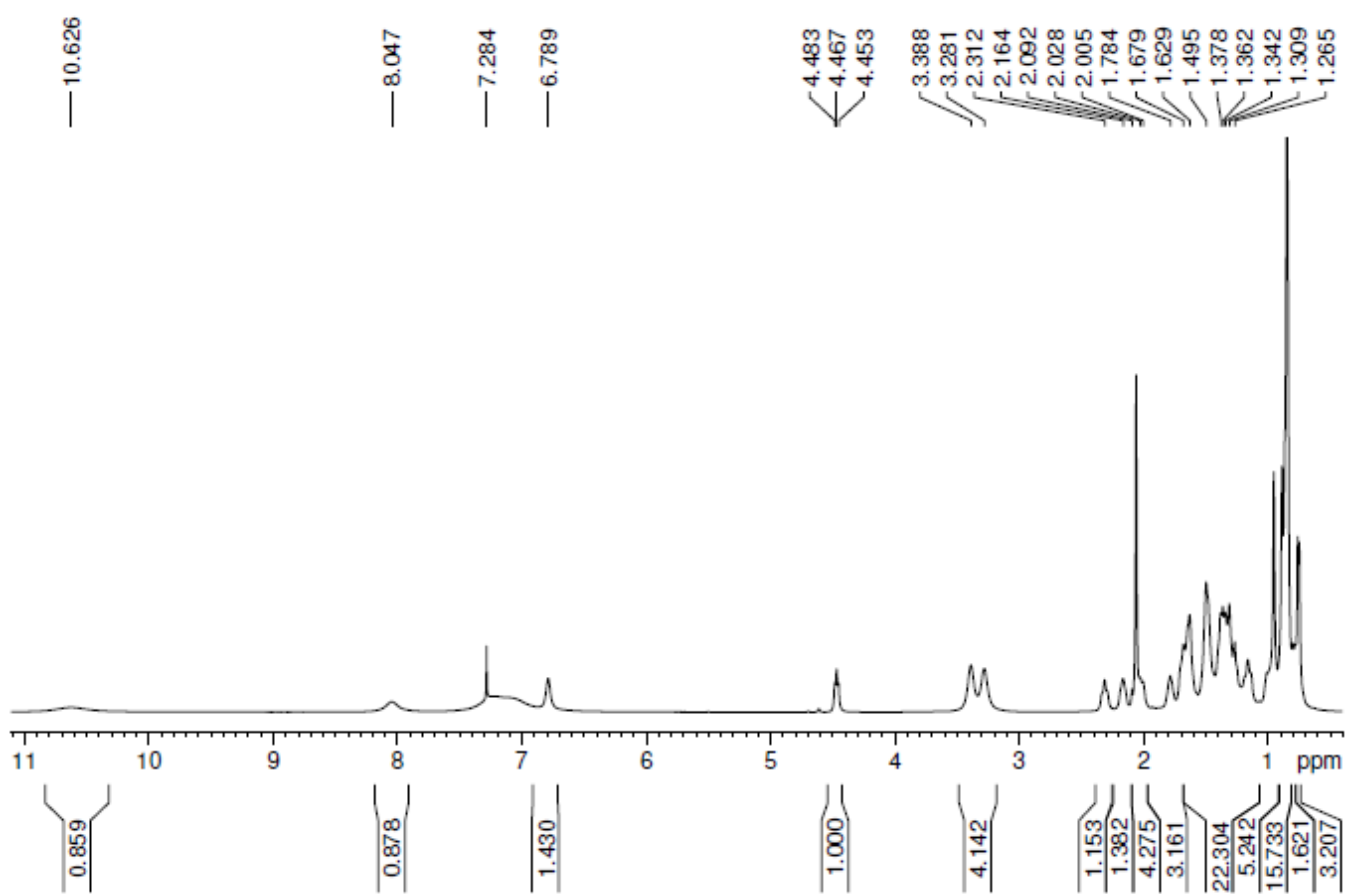
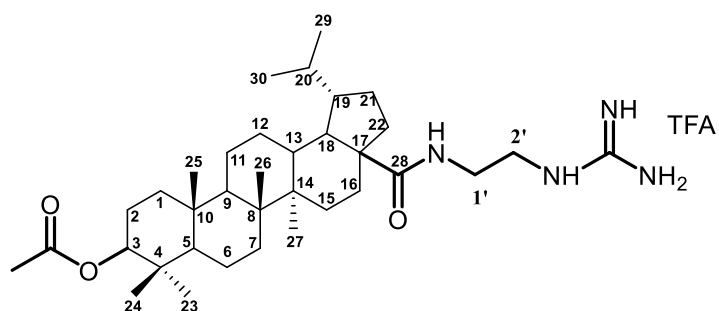




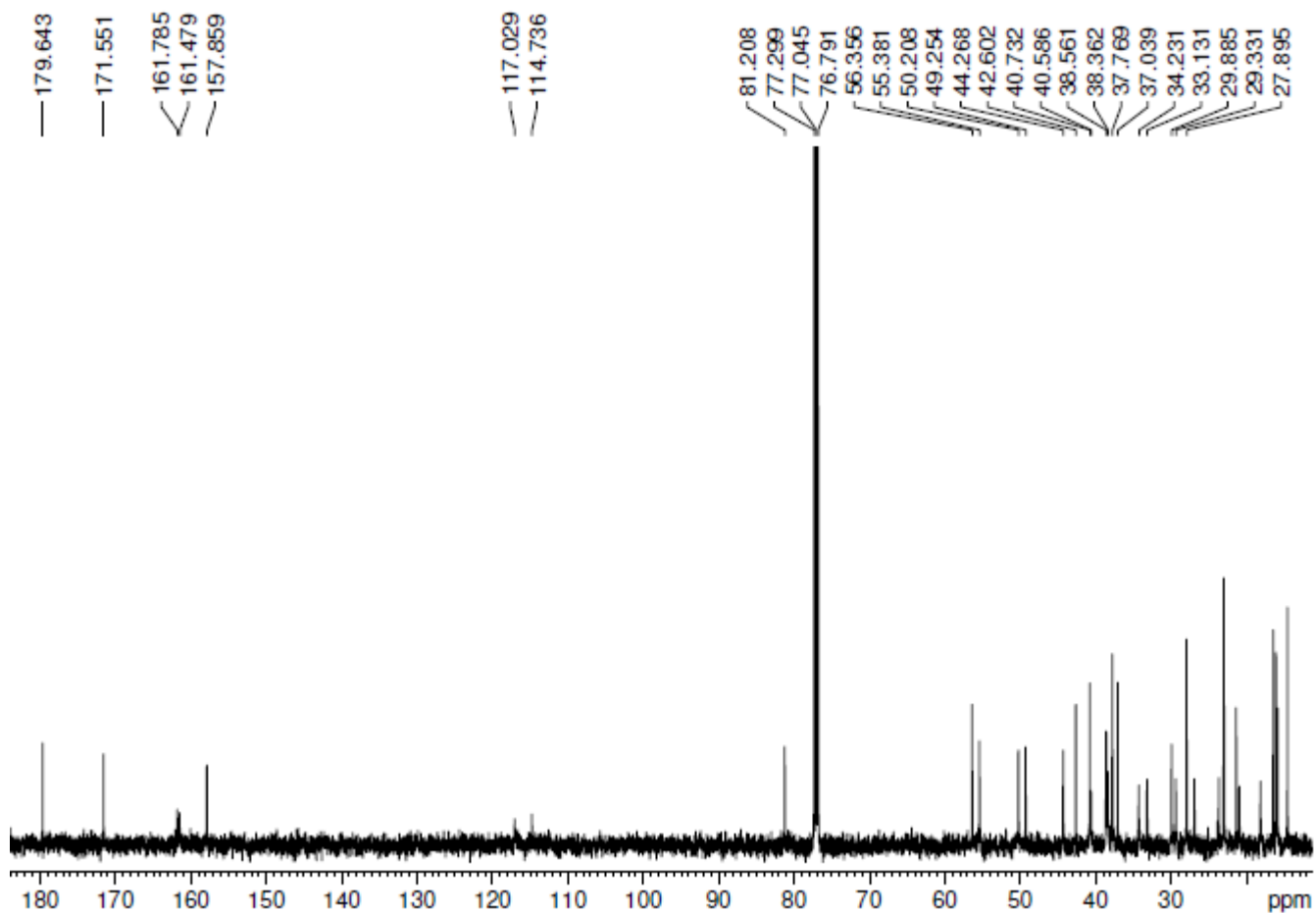
**N-(4-buthylguanidine)-3-oxolupane-28-amide trifluoroacetate (9a).**  $^{19}\text{F}$  NMR spectra ( $\text{CDCl}_3$ )



**3 $\beta$ -N-(2-ethylguanidine)-3-O-acetyl-lupane-28-amide trifluoroacetate (10a).**  $^1\text{H}$  NMR spectra  
( $\text{CDCl}_3$ )



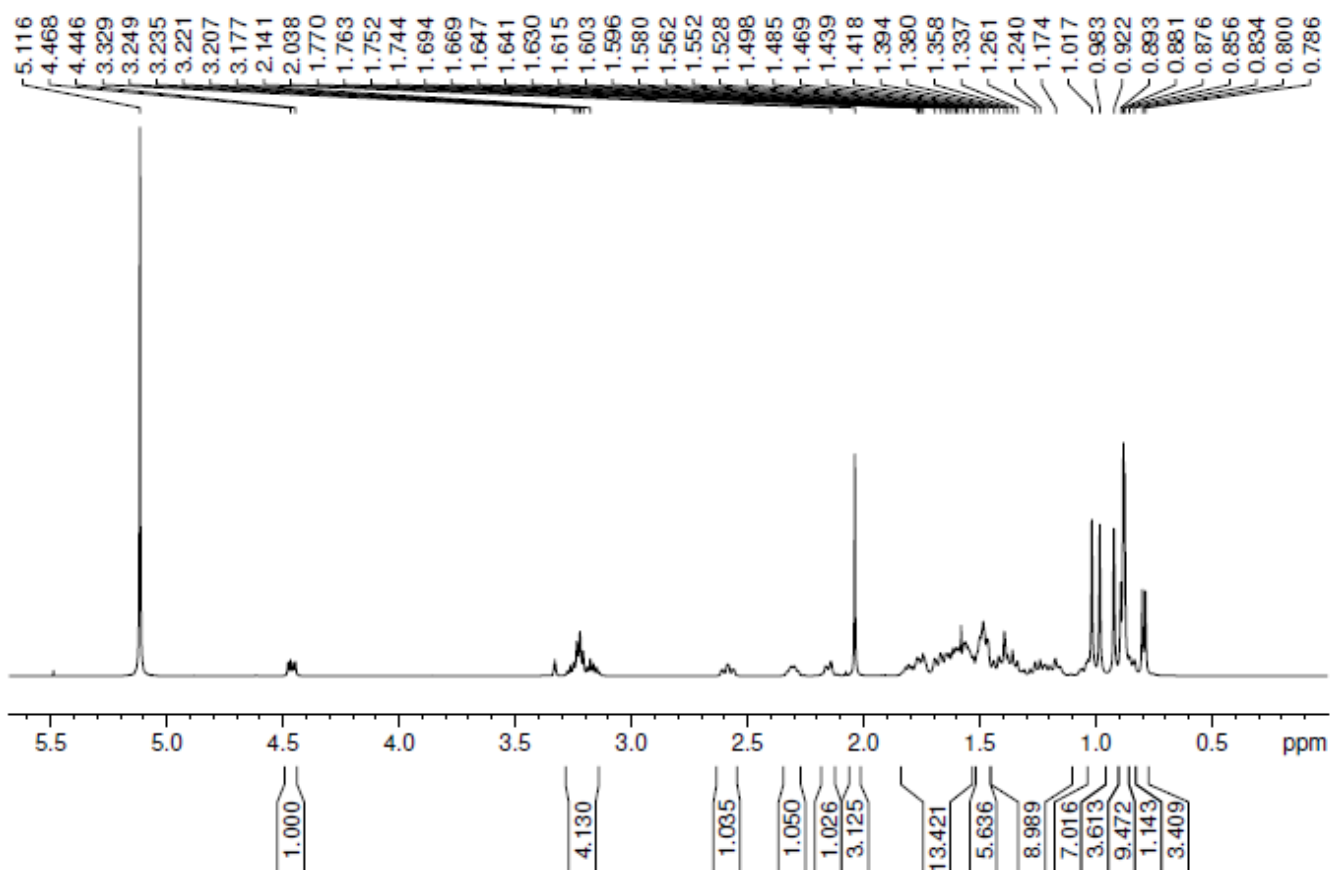
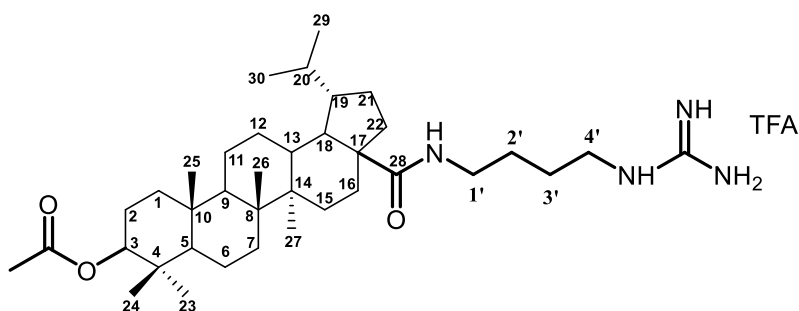
**3 $\beta$ -N-(2-ethylguanidine)-3- O-acetyl-lupane-28-amide trifluoroacetate (10a).**  $^{13}\text{C}$  NMR spectra  
( $\text{CDCl}_3$ )



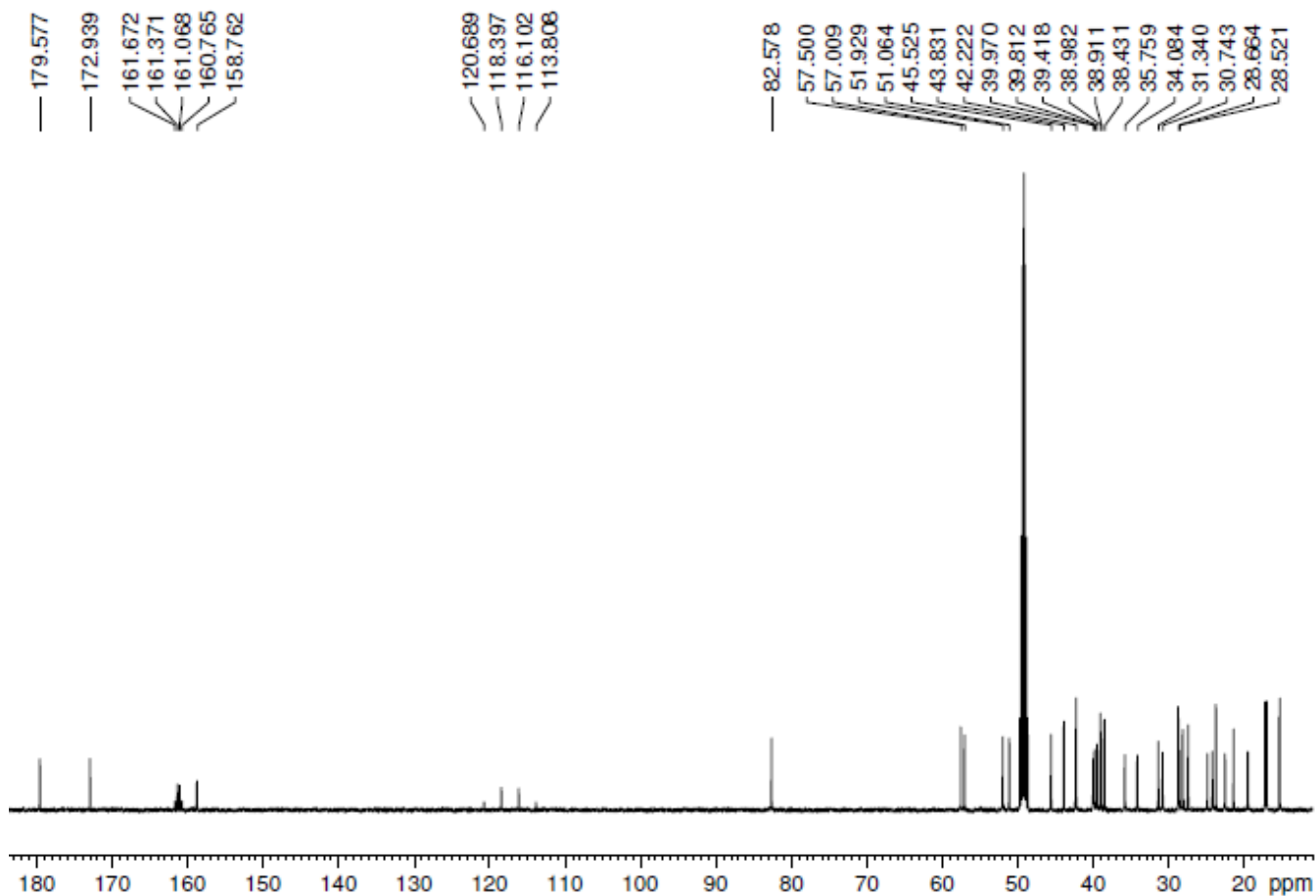
**3 $\beta$ -N-(2-ethylguanidine)-3- O-acetyl-lupane-28-amide trifluoroacetate (10a).**  $^{13}\text{F}$  NMR spectra  
( $\text{CDCl}_3$ )



**3 $\beta$ -N-(4-buthylguanidine)-3-O-acetyl-lupane-28-amide trifluoroacetate (11a).** <sup>1</sup>H NMR spectra (MeOD)



**3 $\beta$ -N-(4-buthylguanidine)-3- O-acetyl-lupane-28-amide trifluoroacetate (11a).** <sup>13</sup>C NMR spectra  
(MeOD)

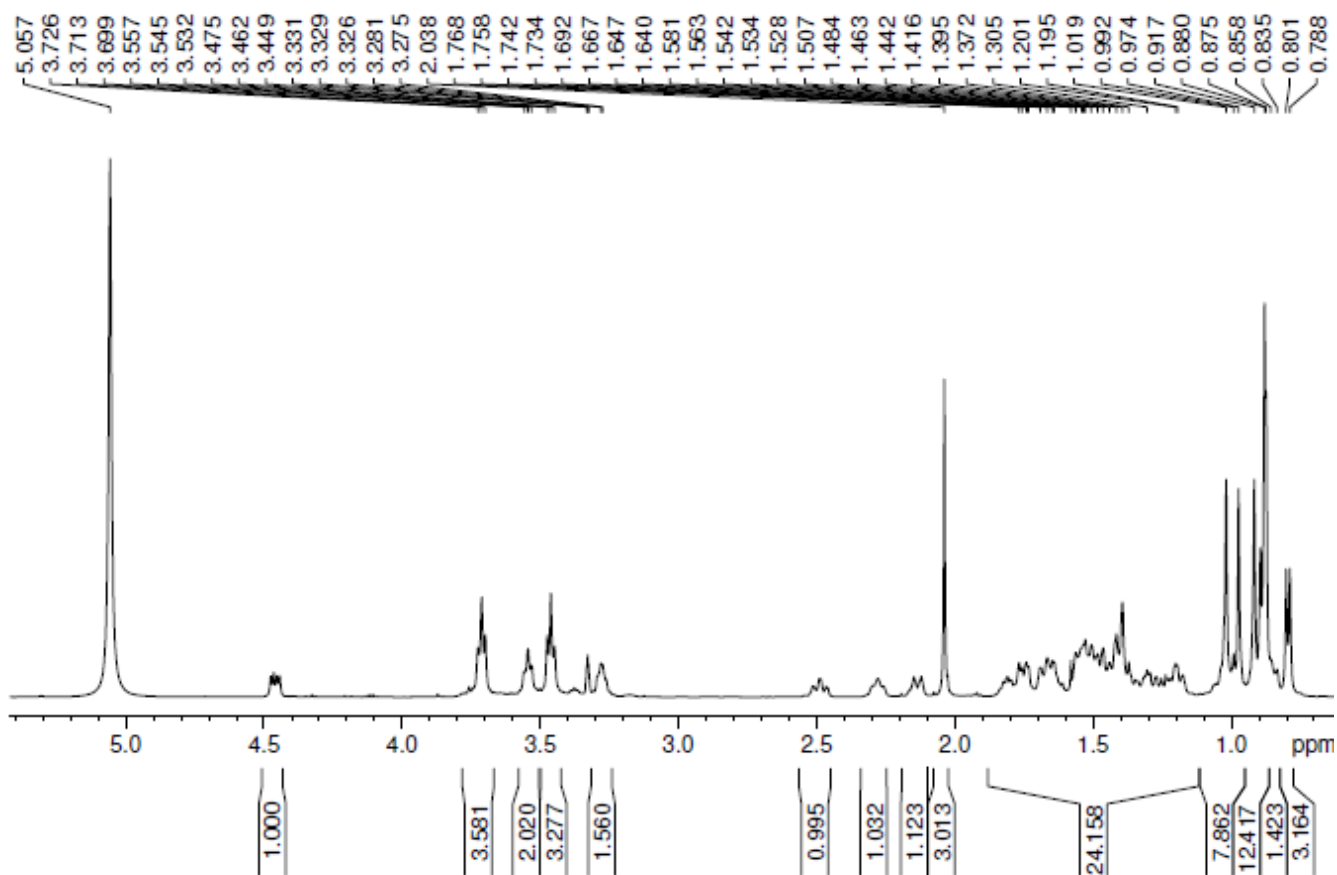
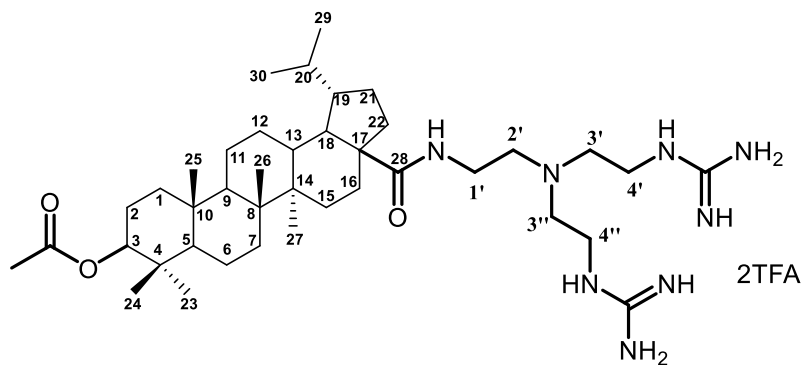


**3 $\beta$ -N-(4-buthylgyanidine)-3- O-acetyl-lupane-28-amide trifluoroacetate (11a). <sup>19</sup>F NMR spectra (MeOD)**



**3β-N-[2-(N,N'-bis-ethylguanidine)-ethyl]-3-O-acetyl-lupane-28-amide trifluoroacetate (12a)**

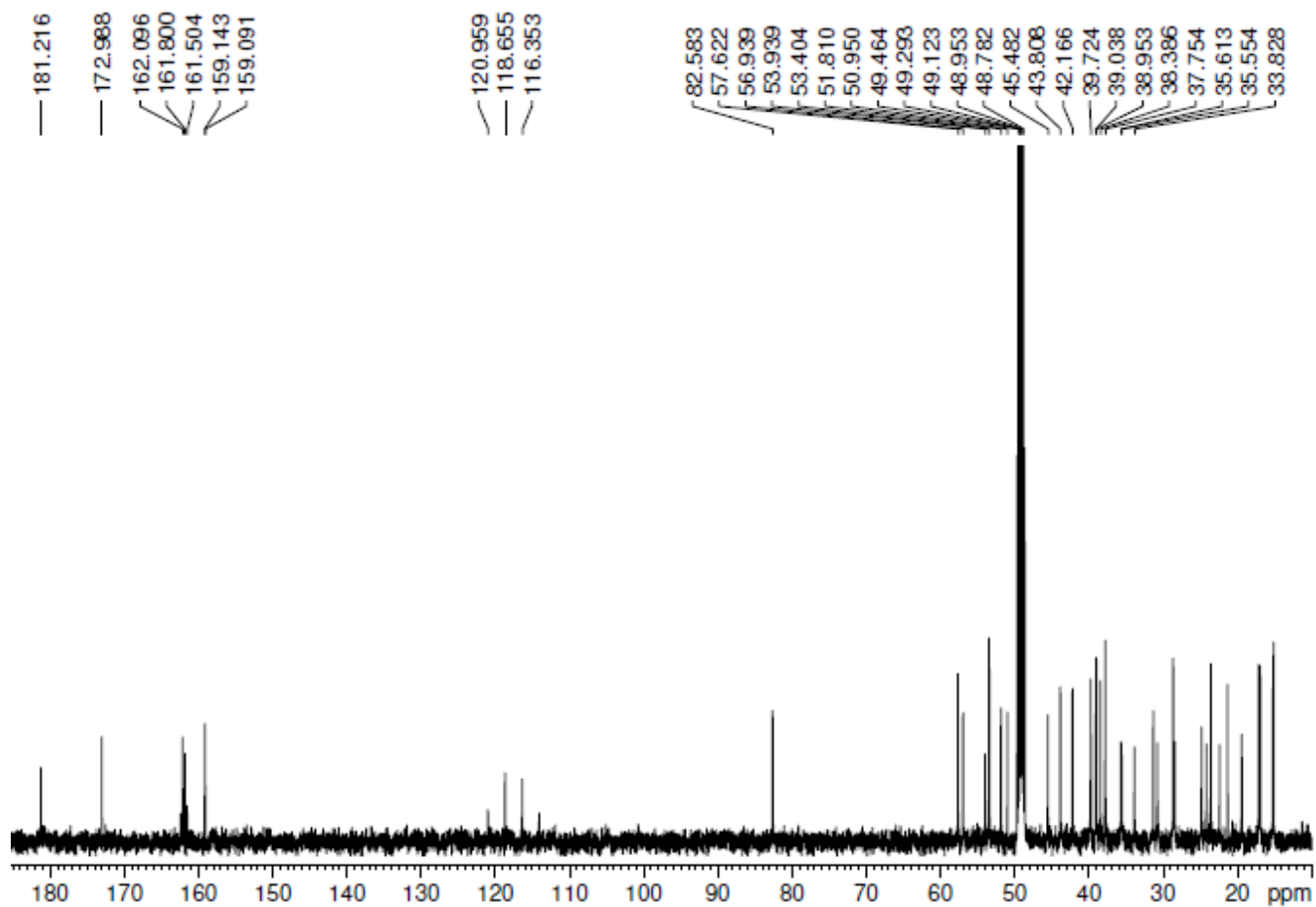
<sup>1</sup>H NMR spectra (MeOD)





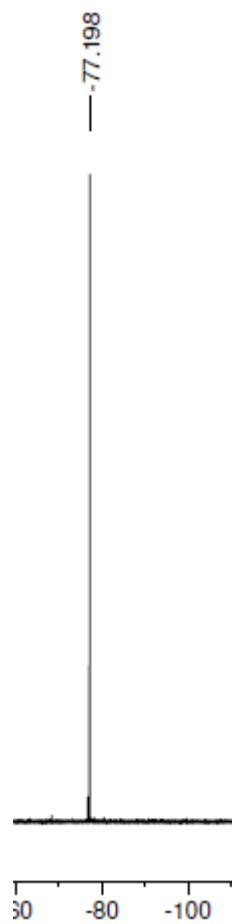
**3 $\beta$ -N-[2-(N,N'-bis-ethylguanidine)-ethyl]-3- O-acetyl -lupane-28-amide trifluoroacetate (12a).**

<sup>13</sup>C NMR spectra (MeOD)



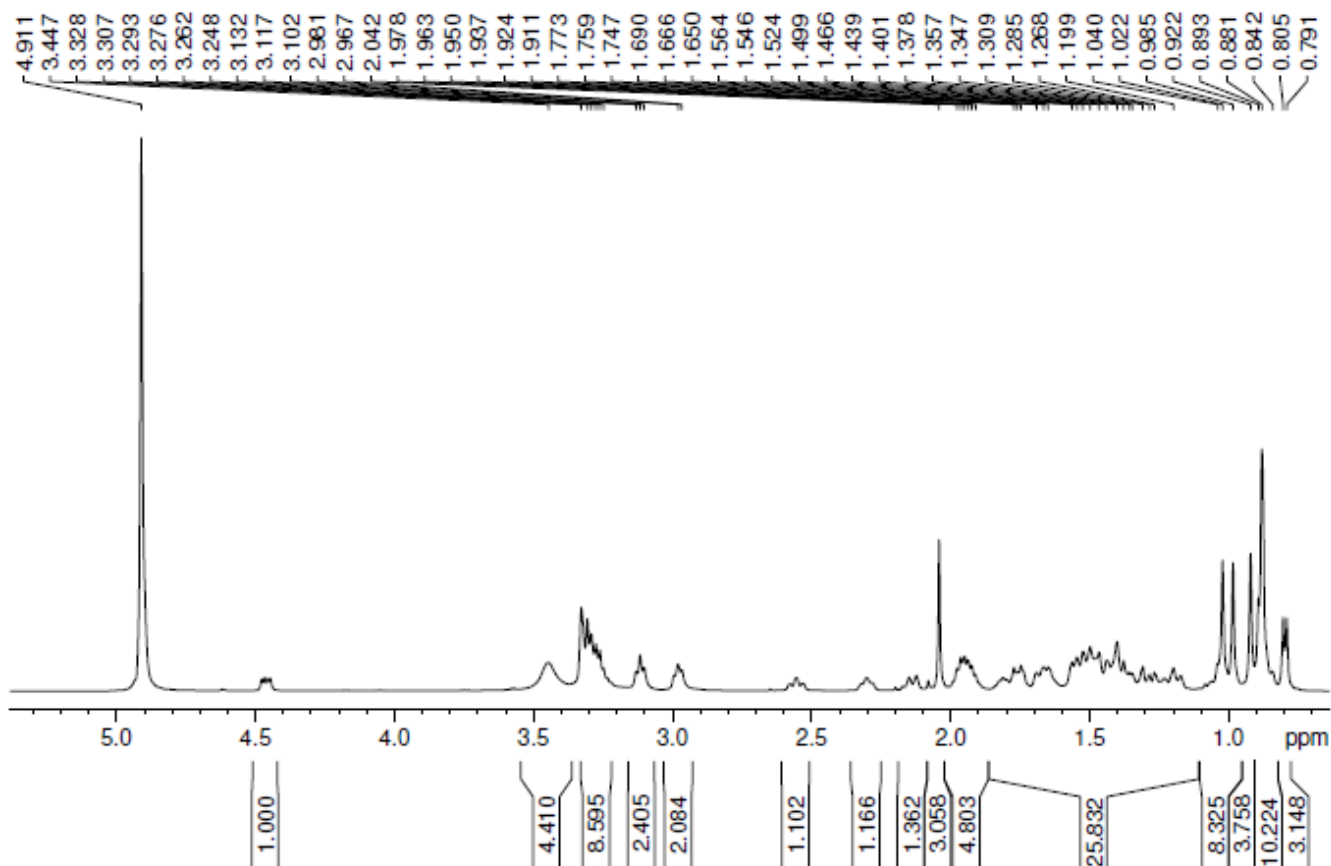
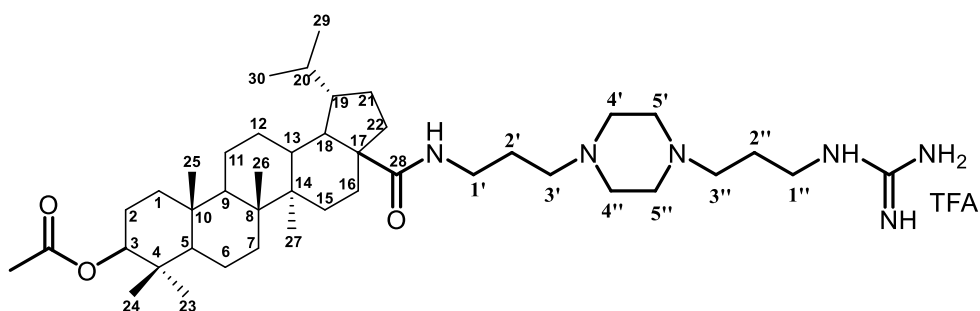
**3 $\beta$ -N-[2-(N,N'-bis-ethylguanidine)-ethyl]-3- O-acetyl -lupane-28-amide trifluoroacetate (12a).**

<sup>19</sup>F NMR spectra (MeOD)



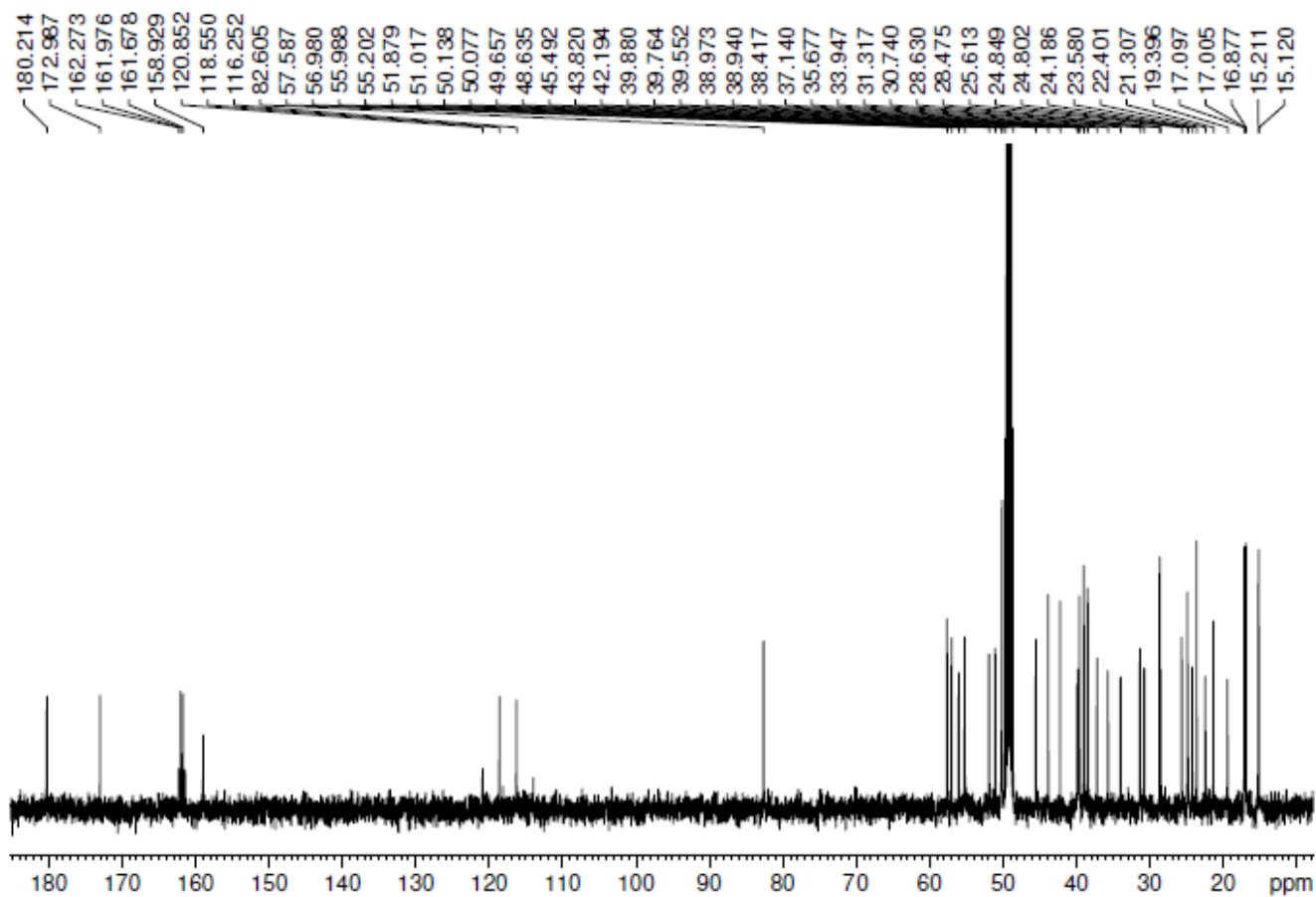
**3 $\beta$ -N-[[3-(3-propylguanidine)piperazinyl]propyl]-3-O-acetyl-lupane-28-amide trifluoroacetate (13a).**

<sup>1</sup>H NMR spectra (MeOD)



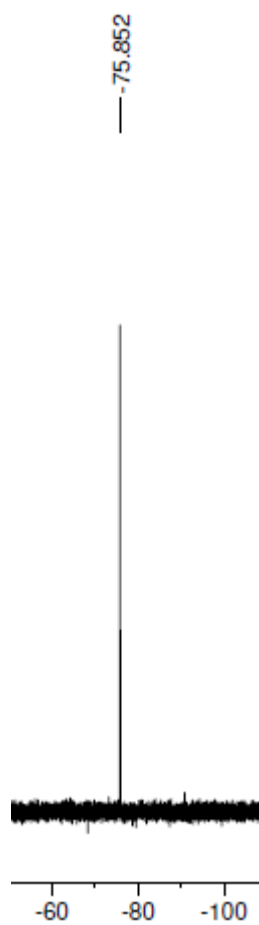
**3 $\beta$ -N-[[3-(3-propylguanidine)piperazinyl]propyl]-3-O-acetyl-lupane-28-amide trifluoroacetate (13a).**

<sup>13</sup>C NMR spectra (MeOD)

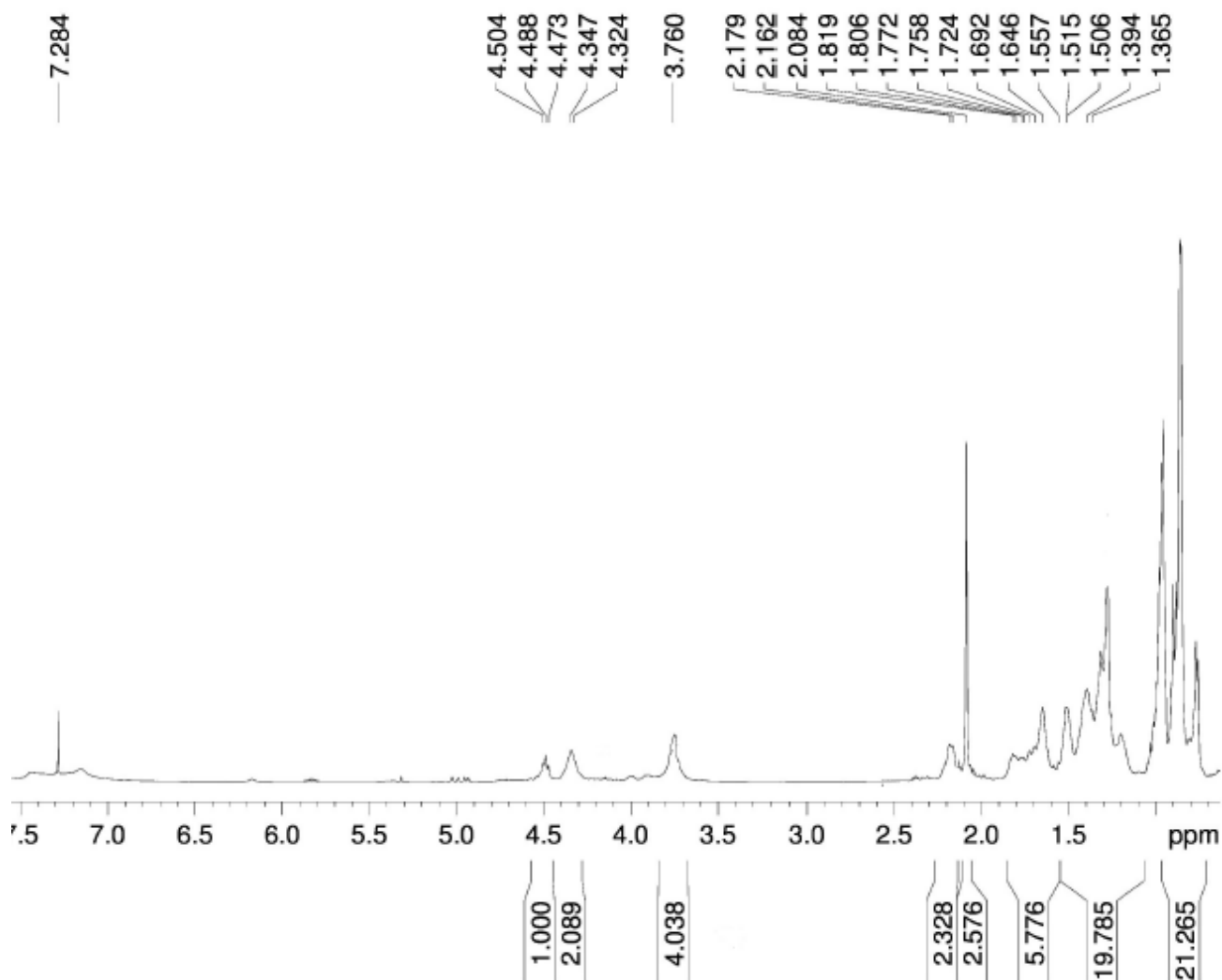
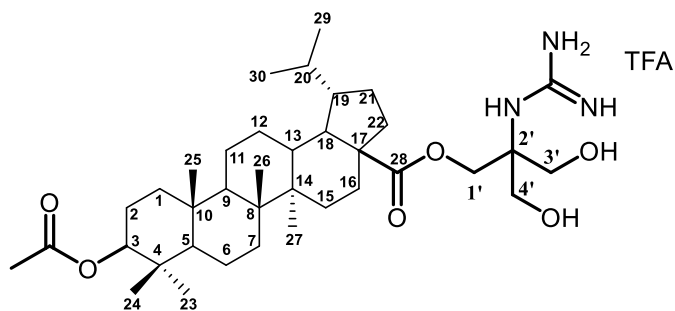


**3 $\beta$ -N-[[3-(3-propylguanidine)piperazinyl]propyl]-3-O-acetyl-lupane-28-amide trifluoroacetate (13a).**

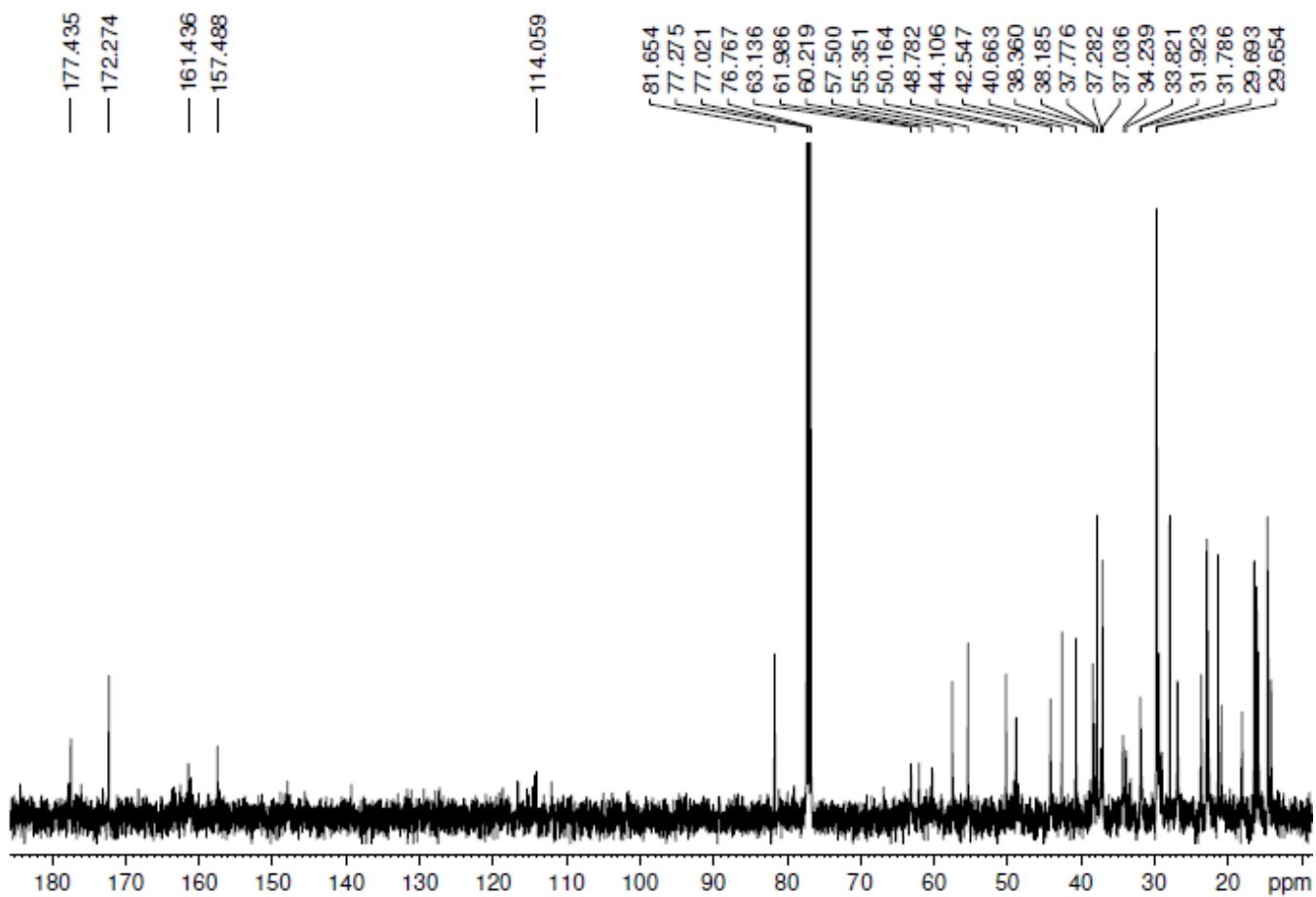
<sup>19</sup>F NMR spectra (MeOD)



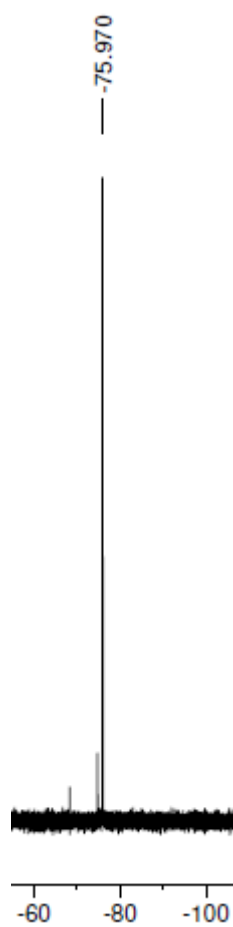
**3 $\beta$ -[2-guanidino-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-lupane-28-oate trifluoroacetate (15b). <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>)**



**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-lupane-28-oate trifluoroacetate (15b). <sup>13</sup>C NMR spectra (CDCl<sub>3</sub>)**

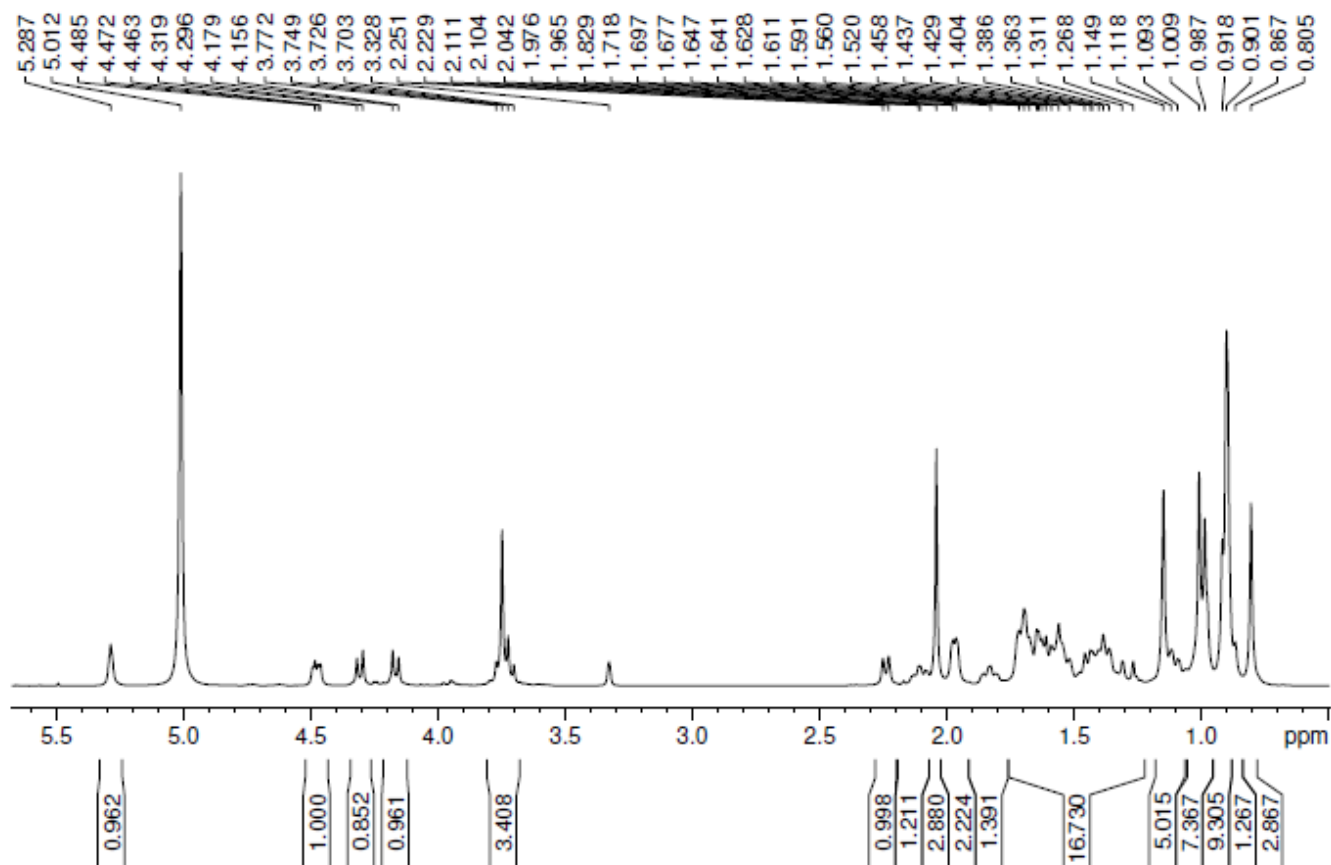
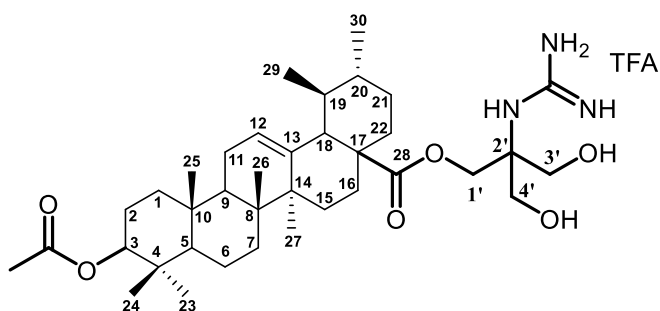


**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-lupane-28-oate trifluoroacetate (15b). <sup>19</sup>F NMR spectra (CDCl<sub>3</sub>)**

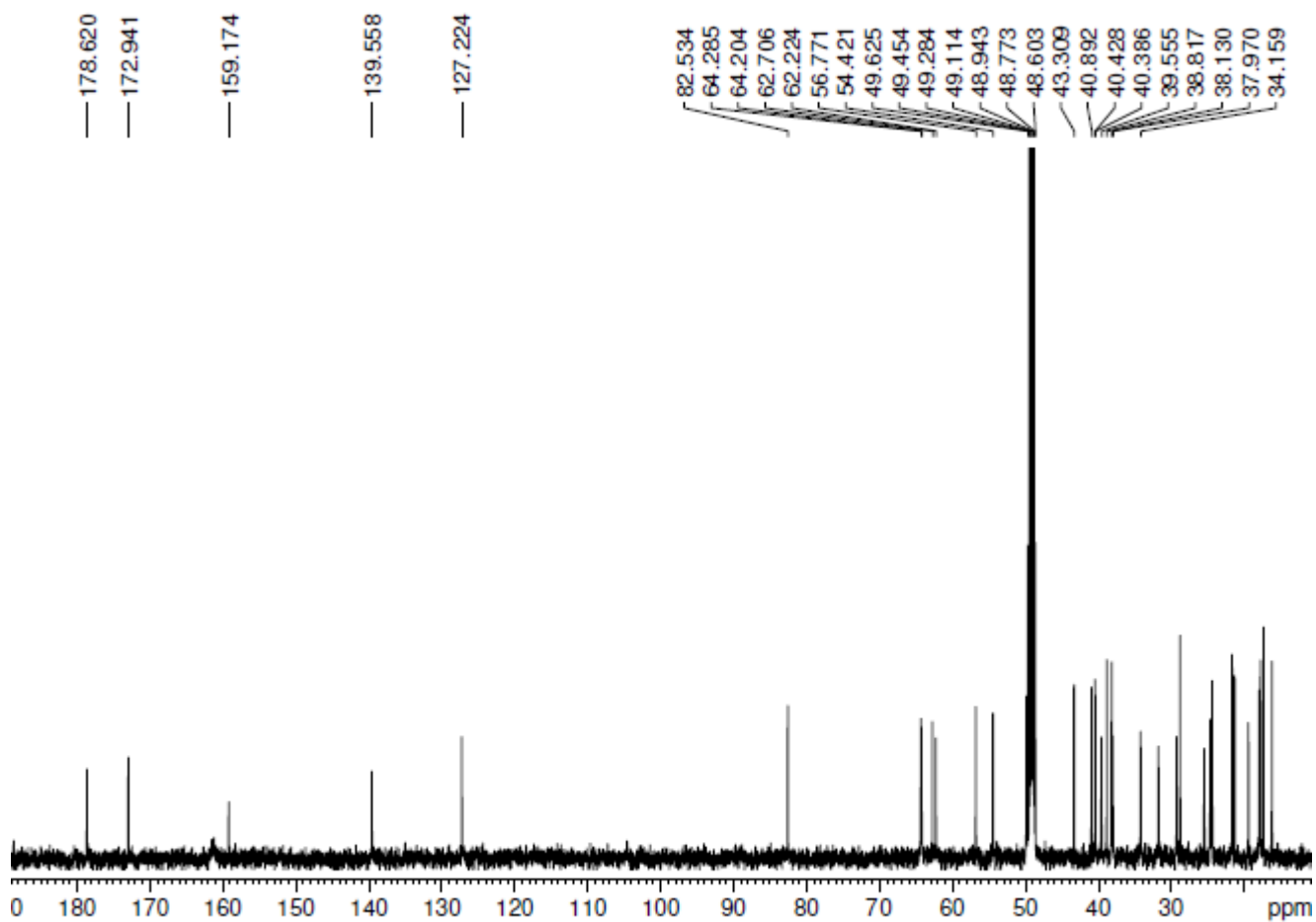




**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate trifluoroacetate (18b). <sup>1</sup>H NMR spectra (MeOD)**



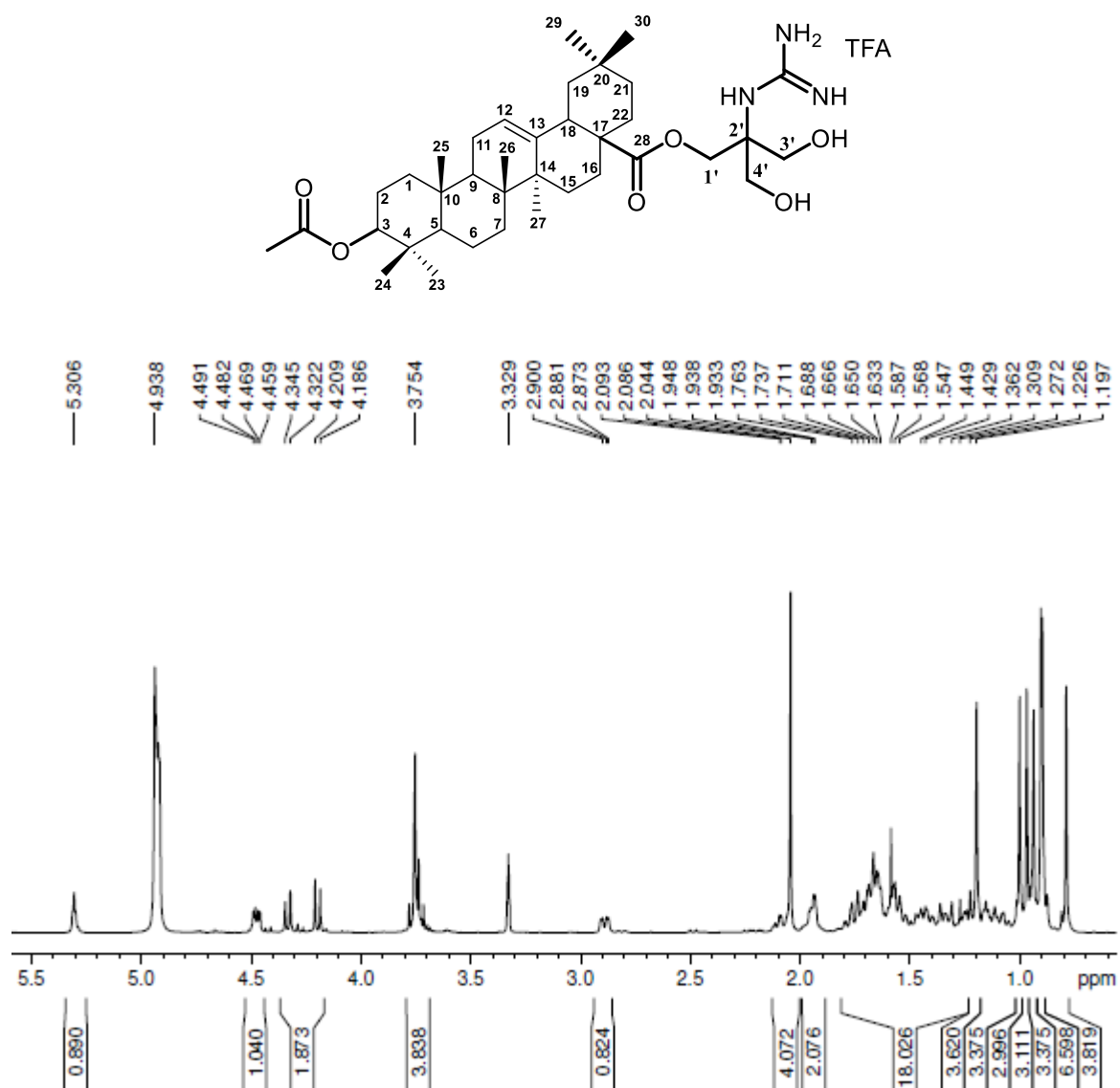
**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate trifluoroacetate (18b). <sup>13</sup>C NMR spectra (MeOD)**



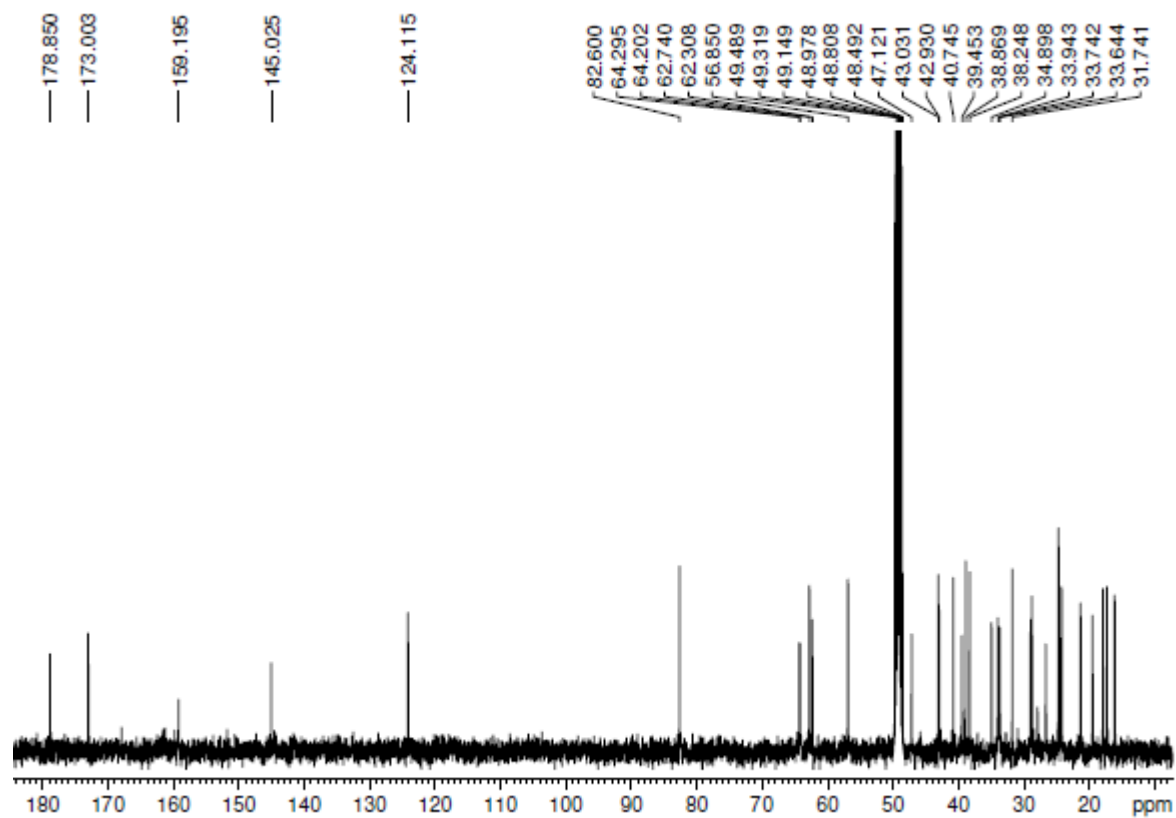
**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate trifluoroacetate (18b). <sup>19</sup>F NMR spectra (MeOD)**



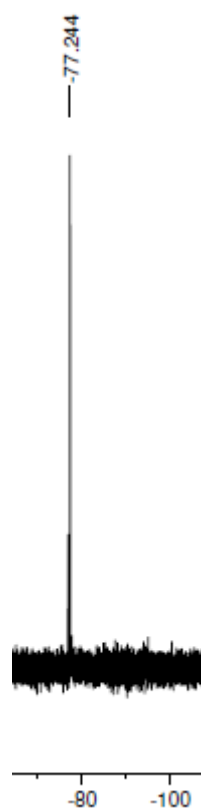
**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-olean-12-en-28-oate trifluoroacetate (20b).  $^1\text{H}$  NMR spectra (MeOD)**



**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-olean-12-en-28-oate trifluoroacetate (20b). <sup>13</sup>C NMR spectra (MeOD)**

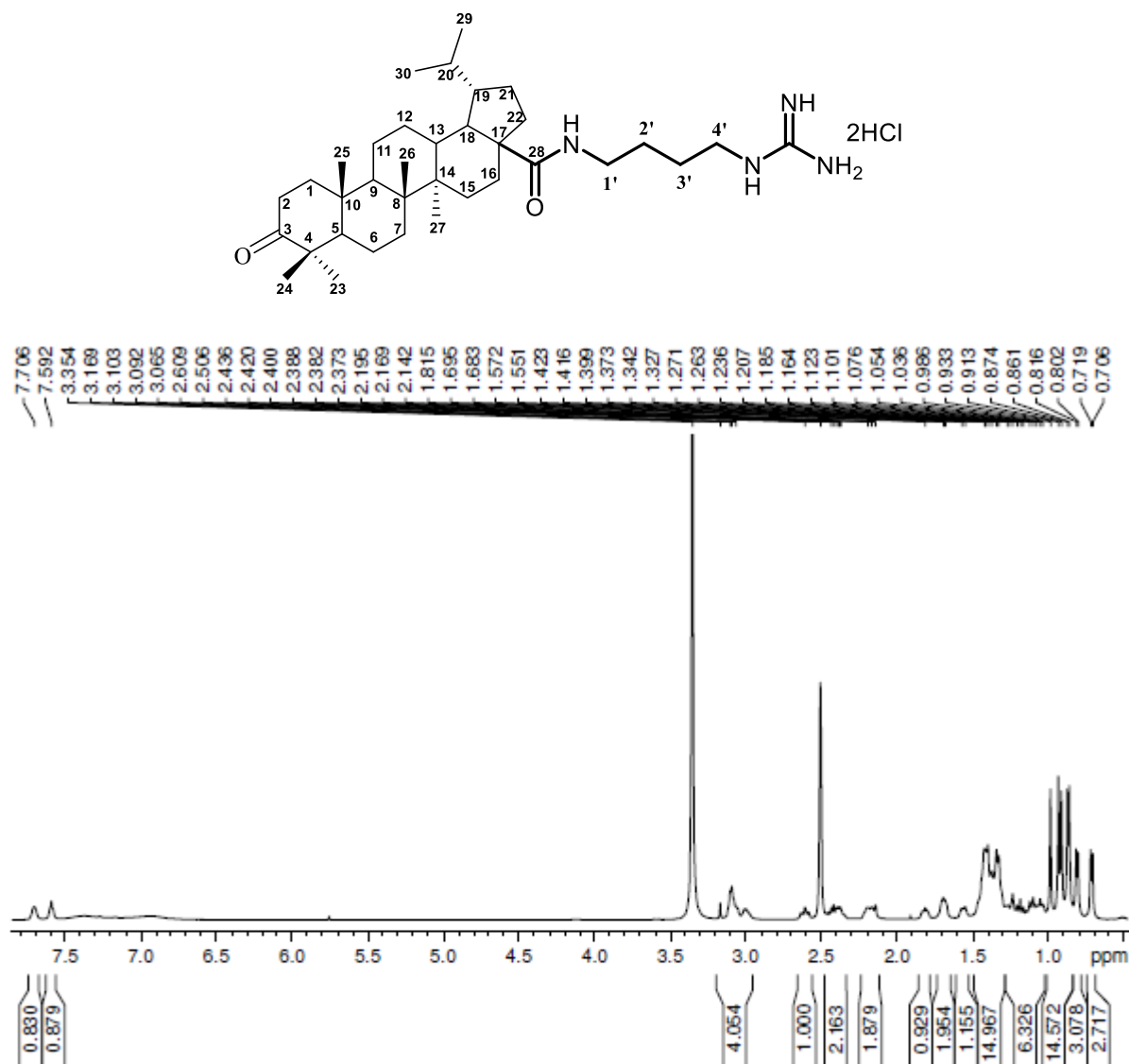


**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-olean-12-en-28-oate trifluoroacetate (20b). <sup>19</sup>F NMR spectra (MeOD)**



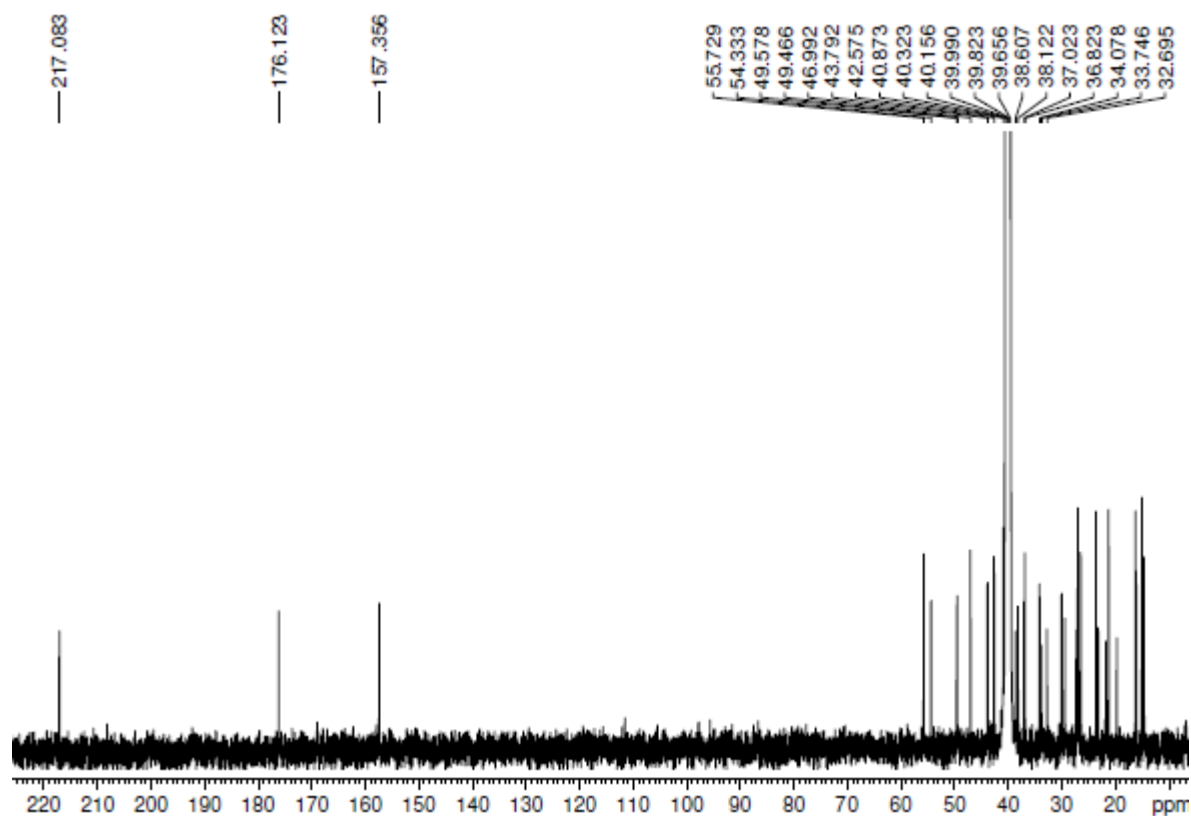
# N-(4-buthylguanidine)-3-oxolupane-28-amide dihydrochloride (9b).

<sup>1</sup>H NMR spectra (d<sub>6</sub>-DMSO)



**N-(4-buthylguanidine)-3-oxolupane-28-amide dihydrochloride (9b).**

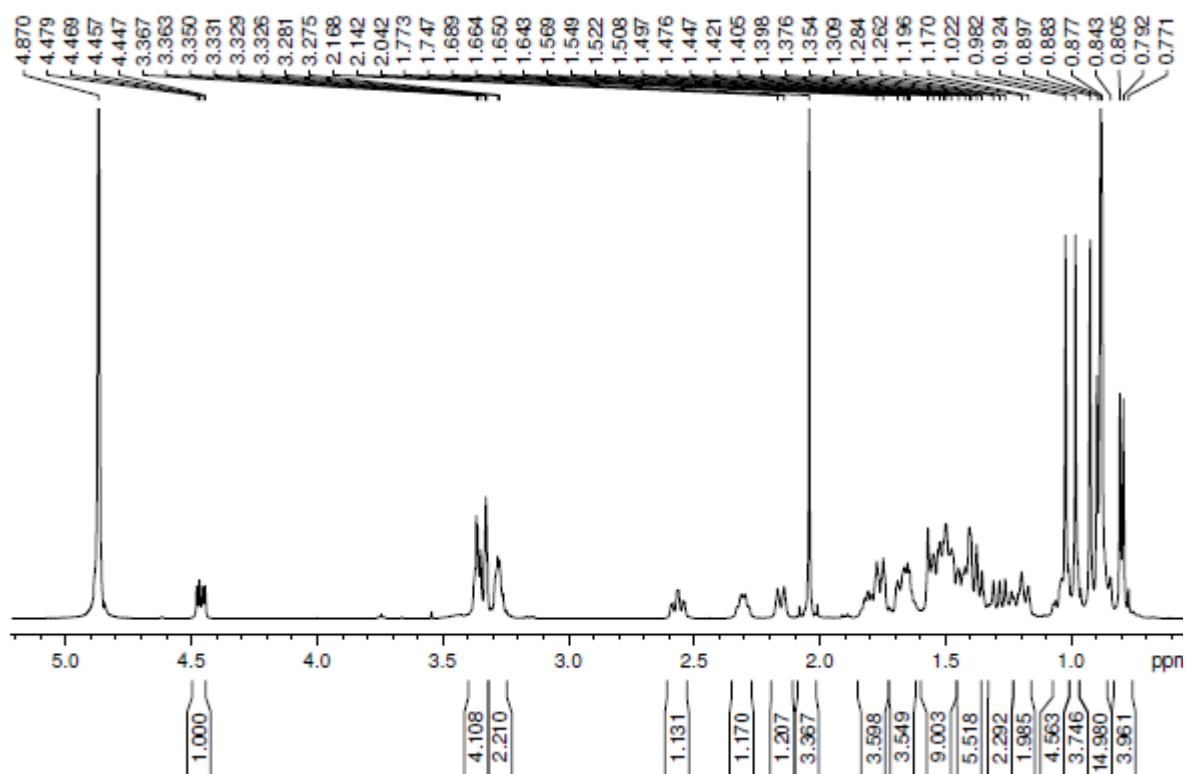
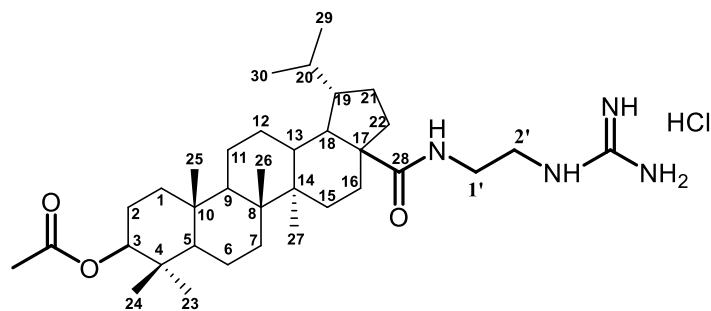
$^{13}\text{C}$  NMR spectra ( $\text{d}_6\text{-DMSO}$ )





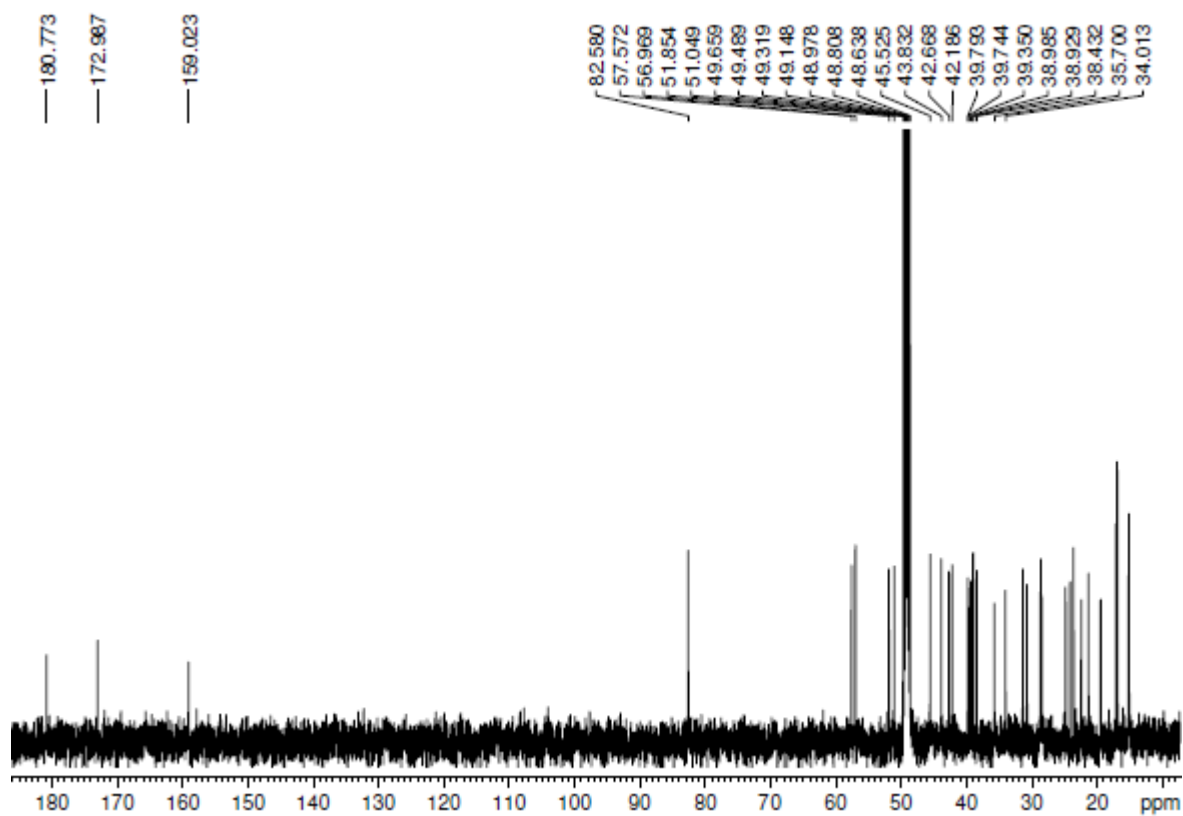
**3 $\beta$ -N-(2-ethylguanidine)-3-O-acetyl-lupane-28-amide hydrochloride (10b).**

<sup>1</sup>H NMR spectra (MeOD)



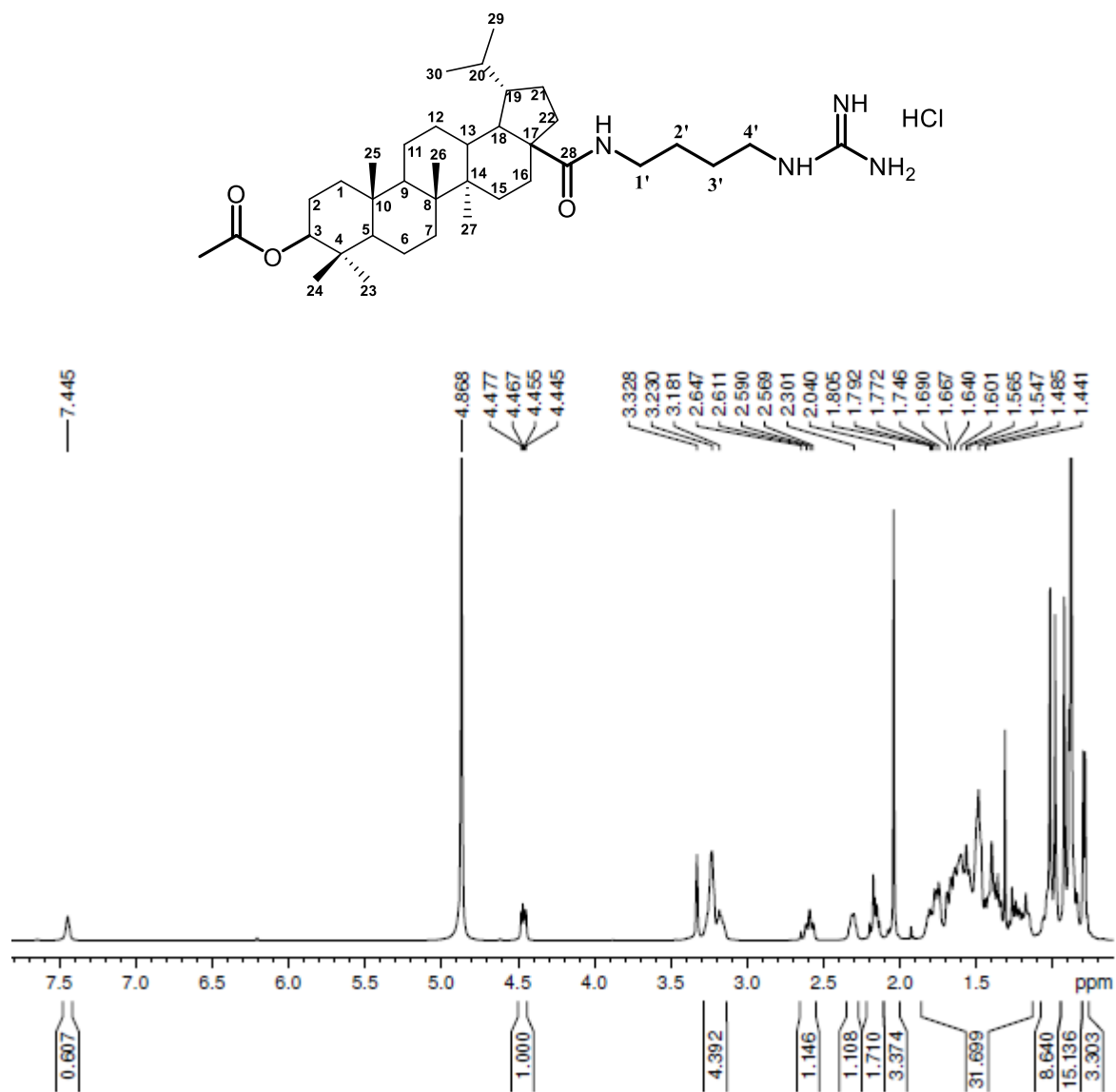
**3 $\beta$ -N-(2-ethylguanidine)-3-O-acetyl-lupane-28-amide hydrochloride (10b).**

<sup>1</sup>H NMR spectra (MeOD)



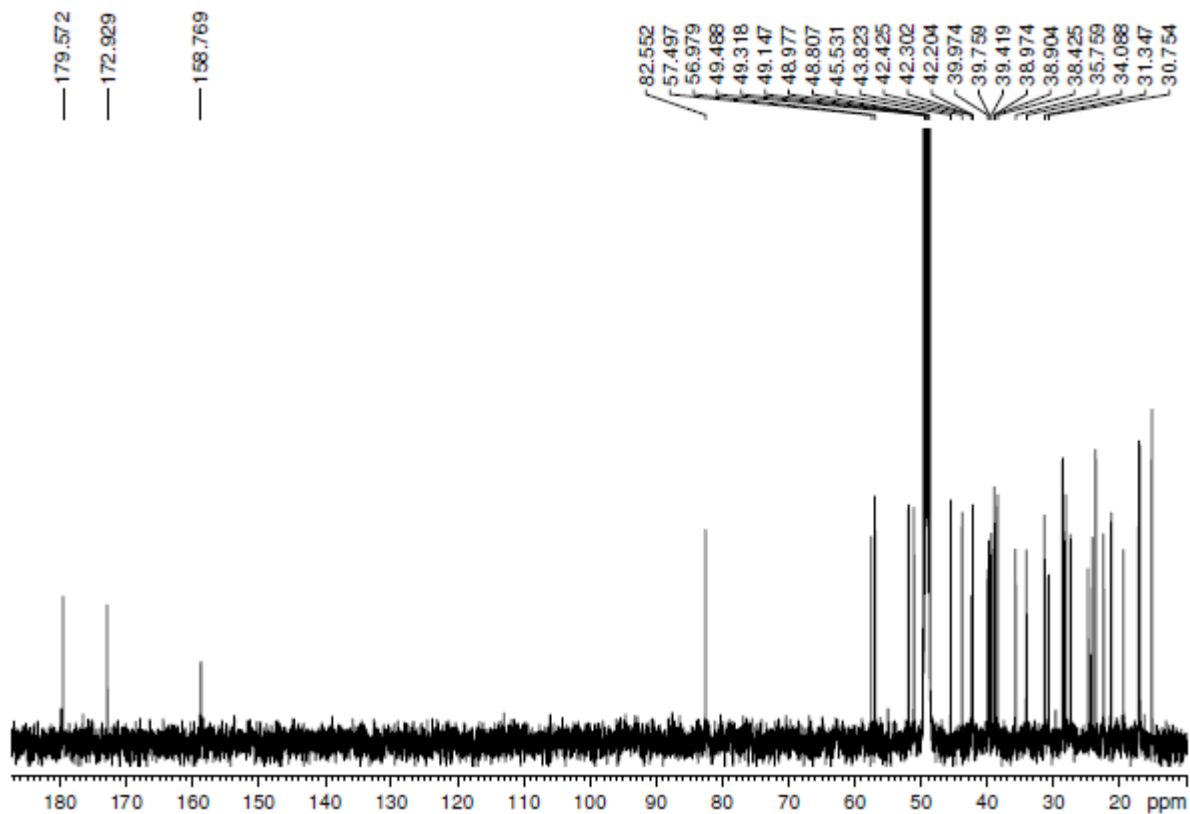
### 3 $\beta$ -N-(4-buthylguanidine)-3-O-acetyl-lupane-28-amide hydrochloride (11b).

<sup>1</sup>H NMR spectra (MeOD)



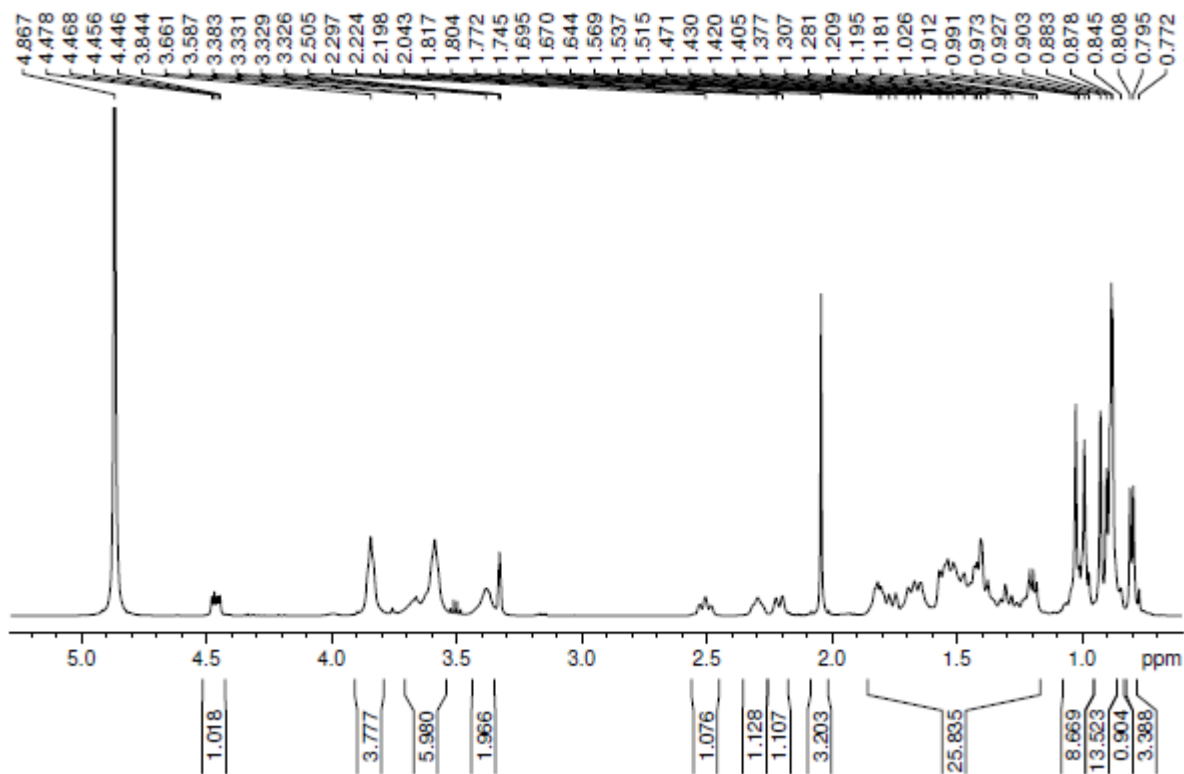
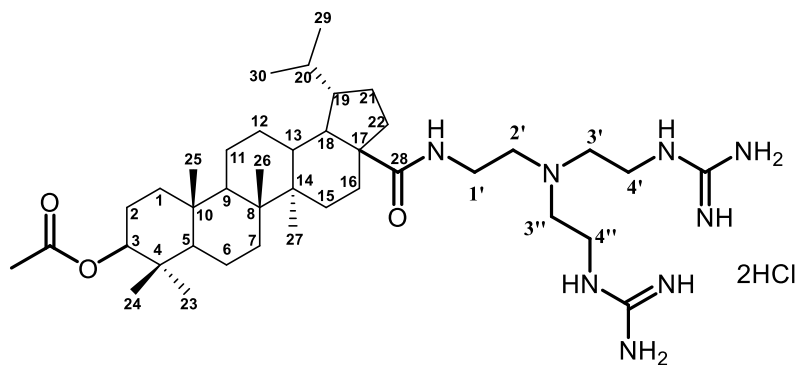
**3 $\beta$ -N-(4-buthylguanidine)-3-O-acetyl-lupane-28-amide hydrochloride (11b).**

<sup>13</sup>C NMR spectra (MeOD)



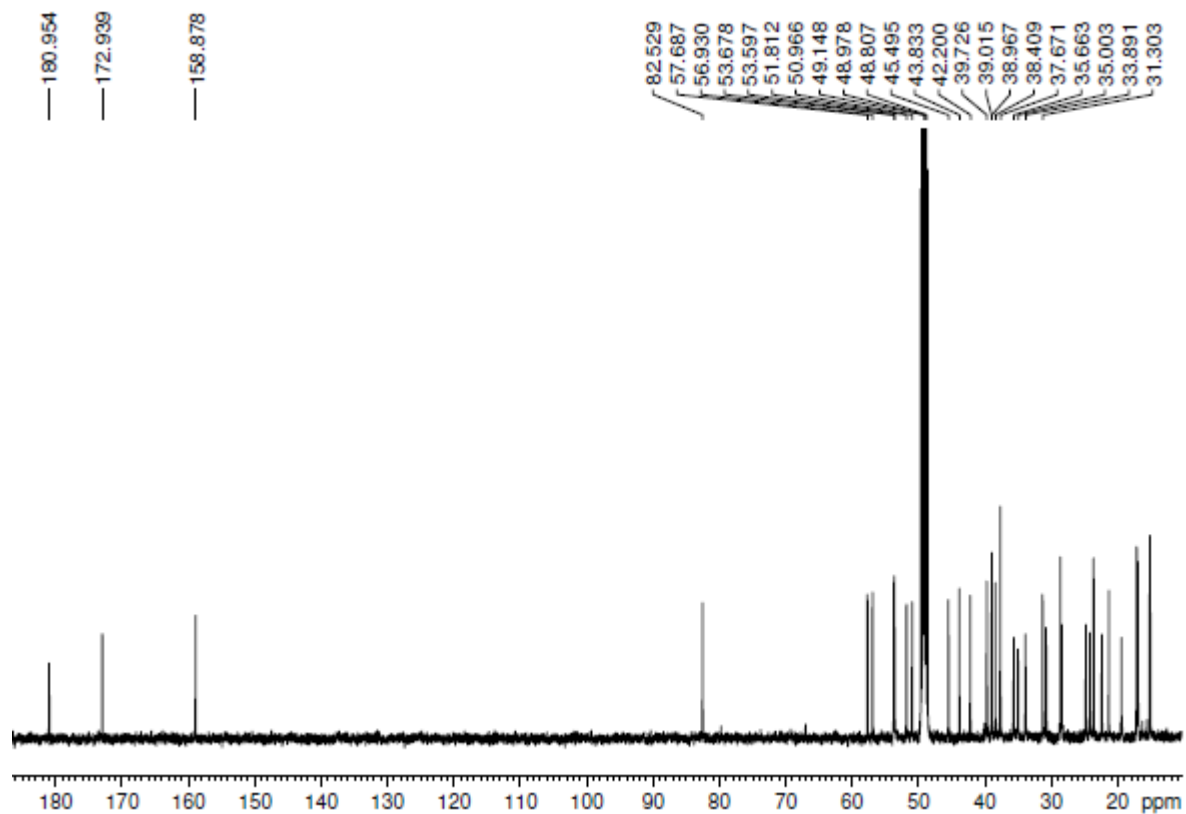
**3 $\beta$ -N-[2-(N,N'-bis-ethylguanidine)-ethyl]-3-O-acetyl-lupane-28-amide dihydrochloride (12b).**

<sup>1</sup>H NMR spectra (MeOD)

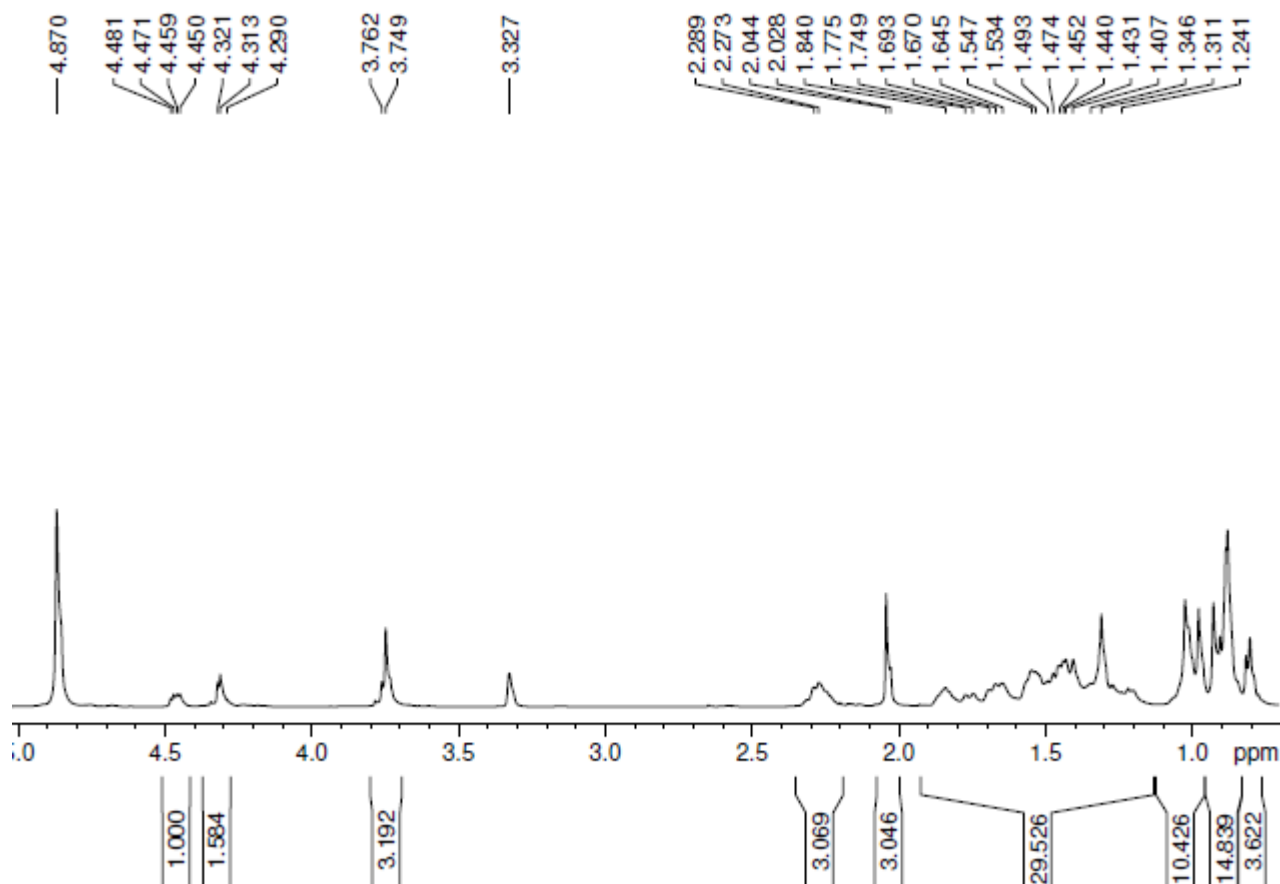
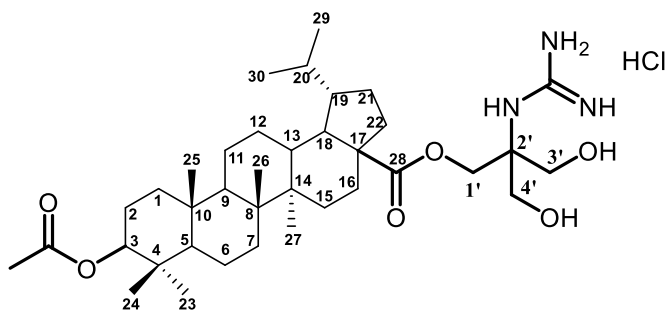


**3 $\beta$ -N-[2-(N,N'-bis-ethylguanidine)-ethyl]-3-O-acetyl-lupane-28-amide dihydrochloride (12b).**

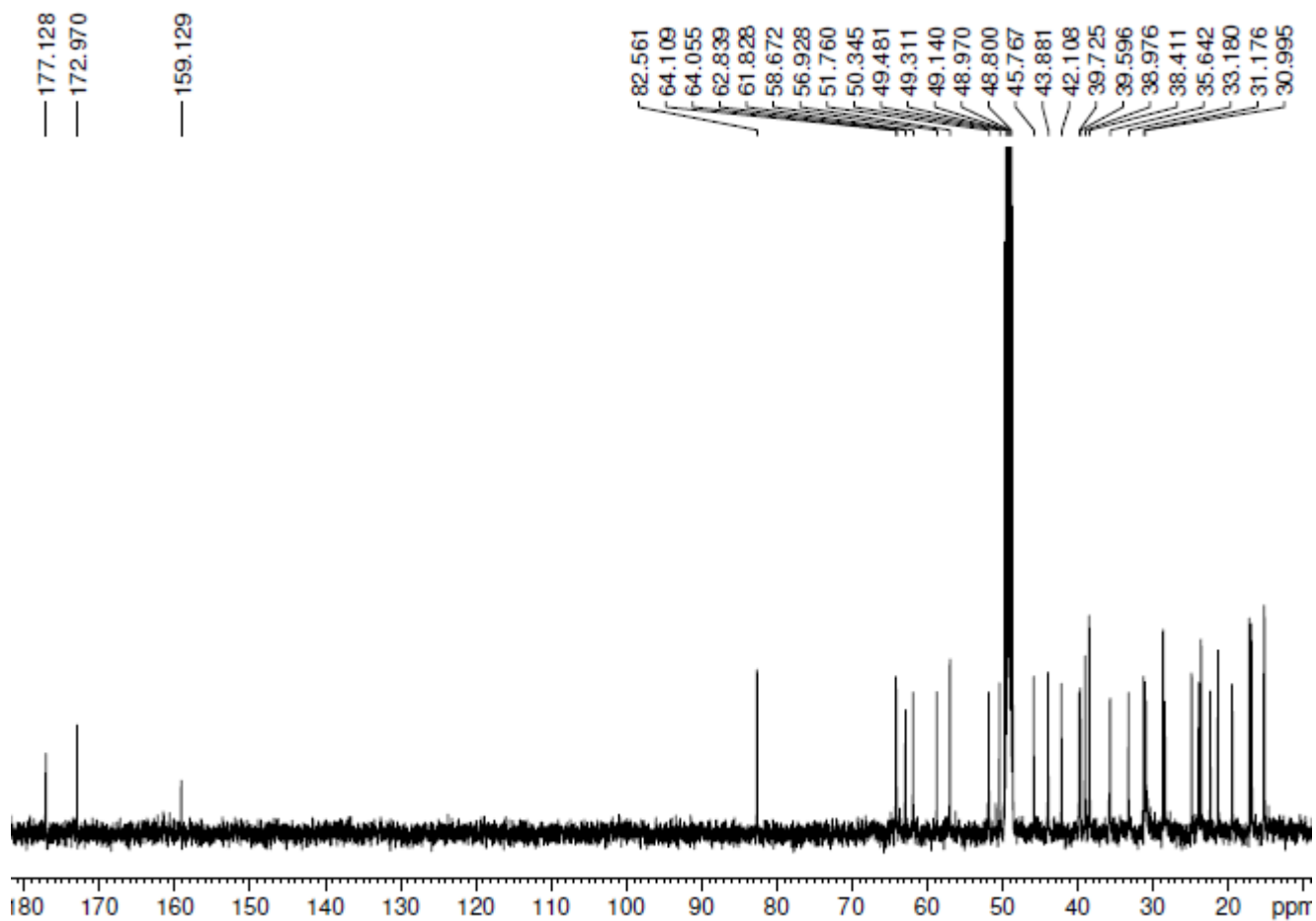
<sup>13</sup>C NMR spectra (MeOD)



**3 $\beta$ -[2-guanidino-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-lupane-28-oate hydrochloride (15c). <sup>1</sup>H NMR spectra (MeOD)**

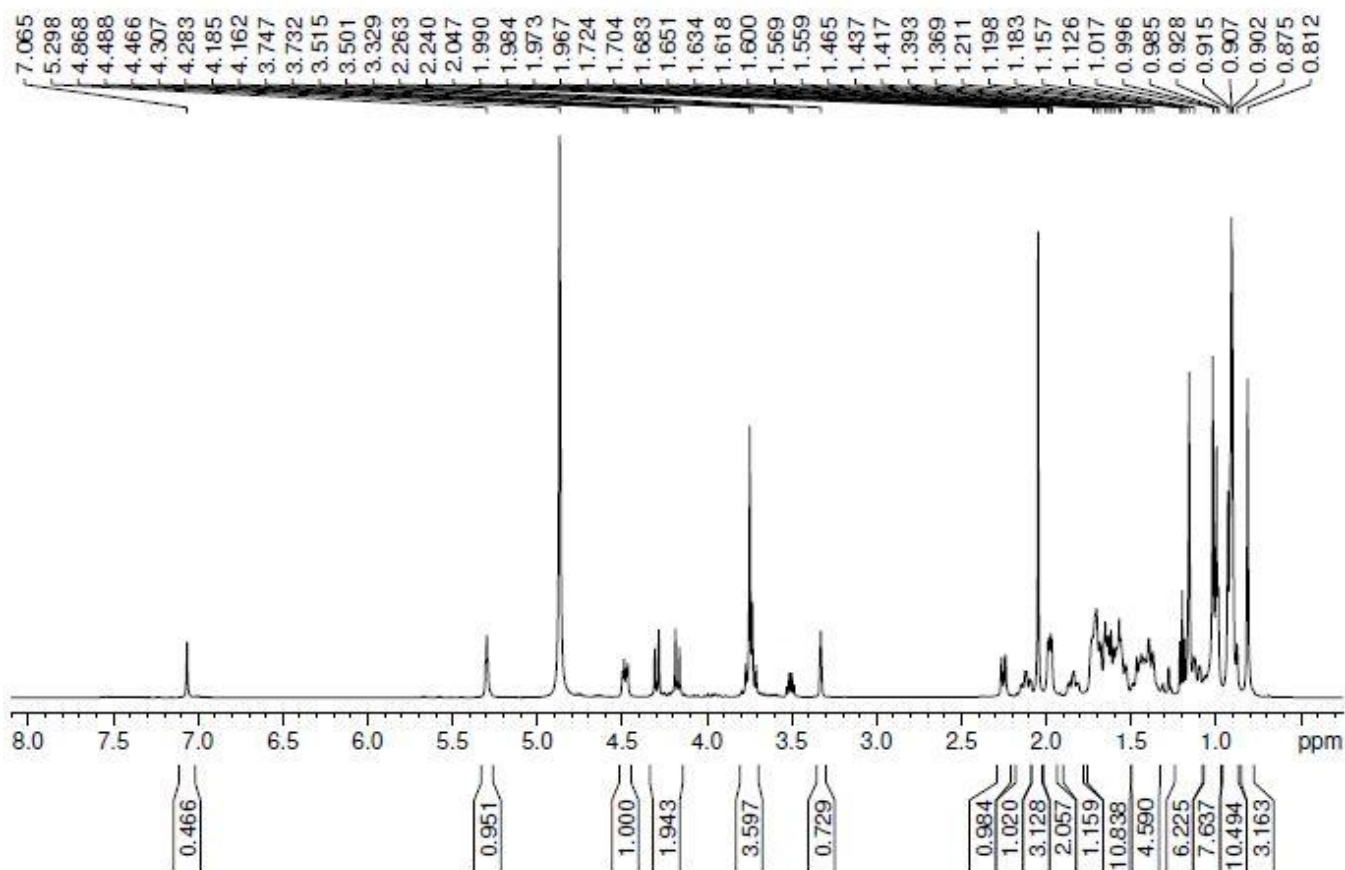
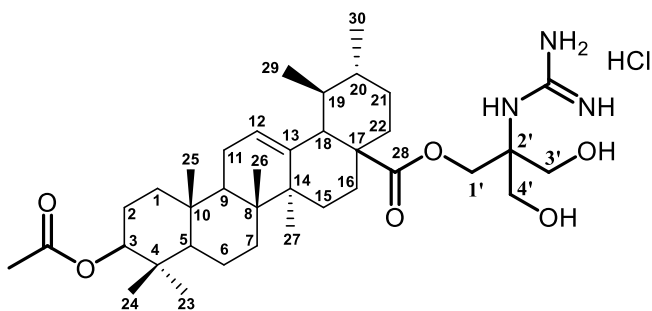


**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-lupane-28-oate hydrochloride (15c). <sup>13</sup>C NMR spectra (MeOD)**

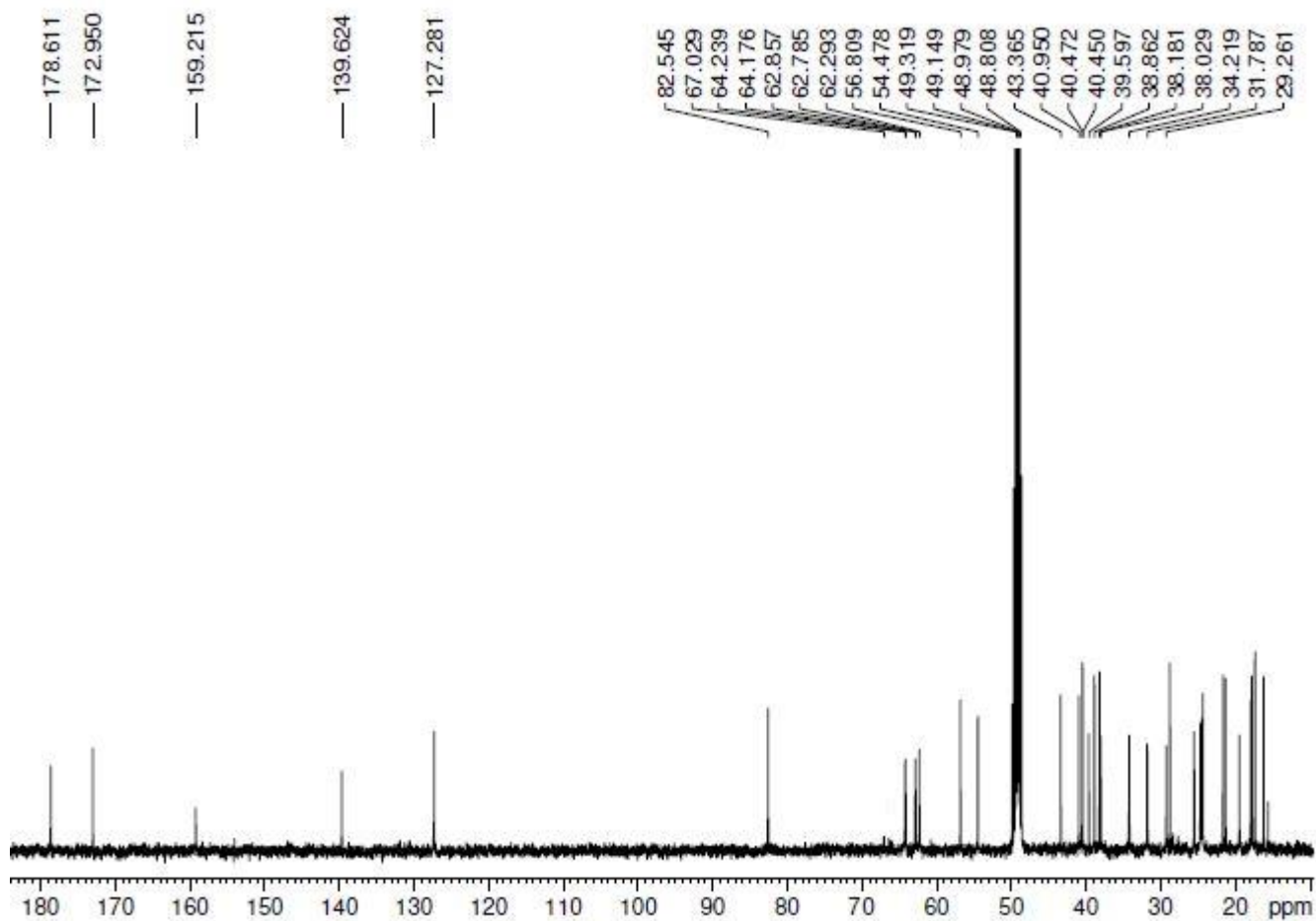




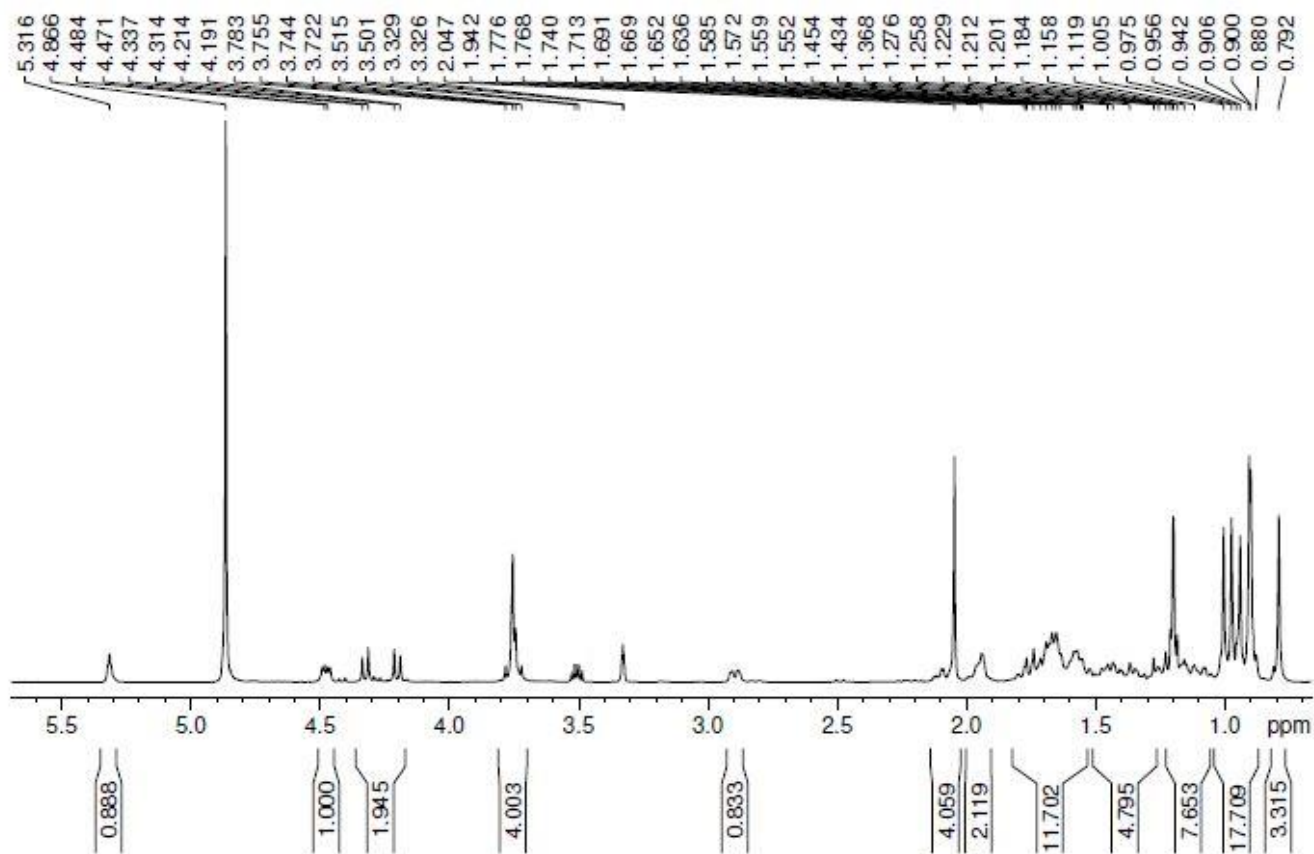
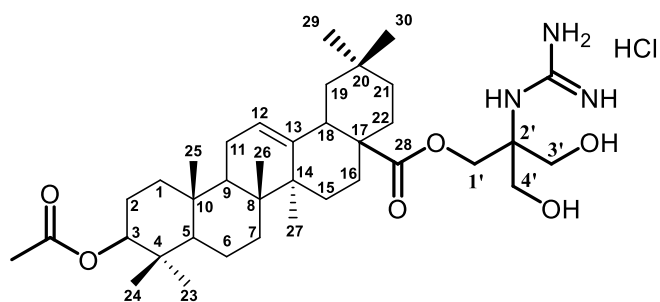
**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate hydrochloride (18c). <sup>1</sup>H NMR spectra (MeOD)**



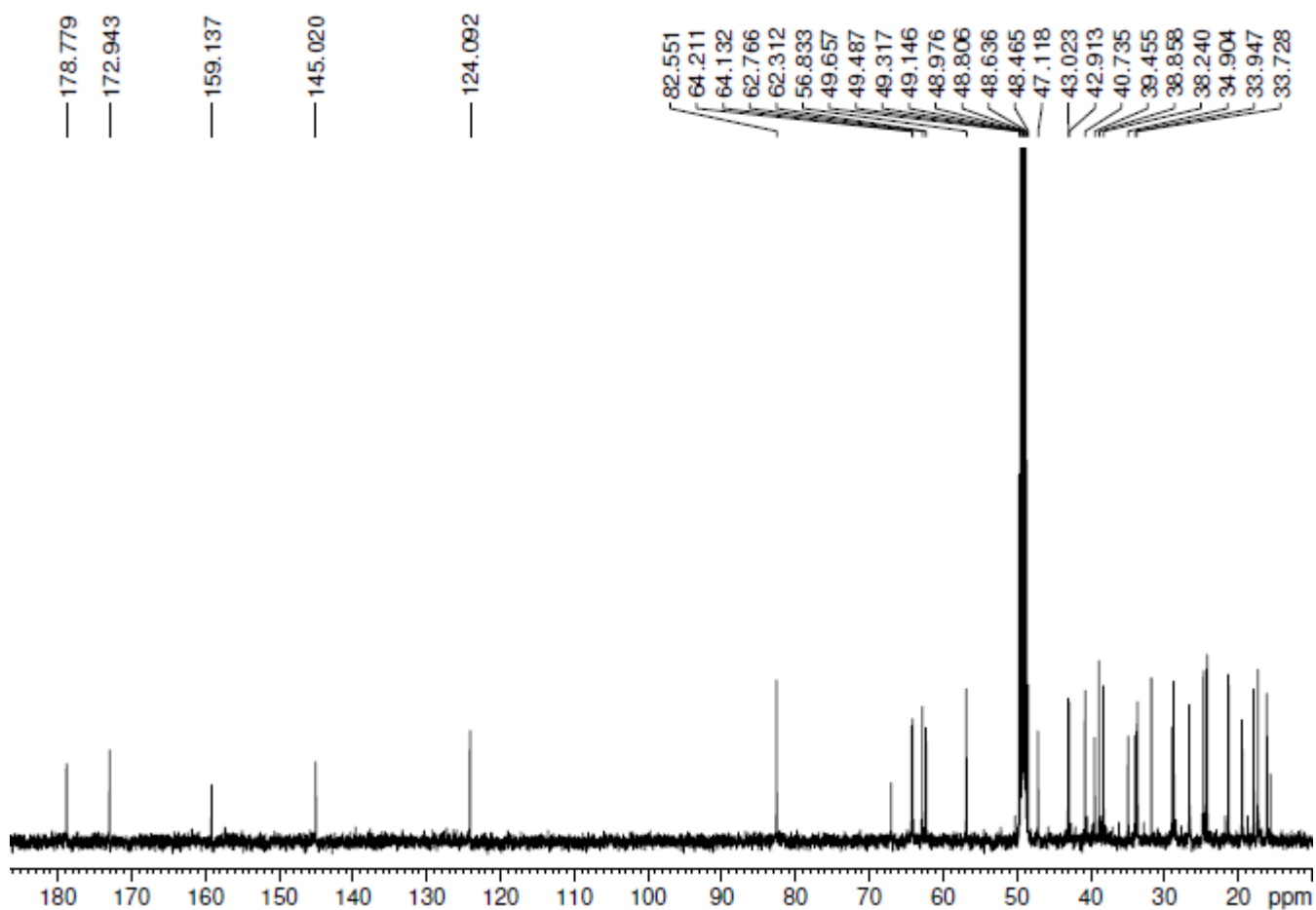
**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-urs-12-en-28-oate hydrochloride (18c). <sup>13</sup>C NMR spectra (MeOD)**



**3β-[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-olean-12-en-28-oate hydrochloride (20c). <sup>1</sup>H NMR spectra (MeOD)**

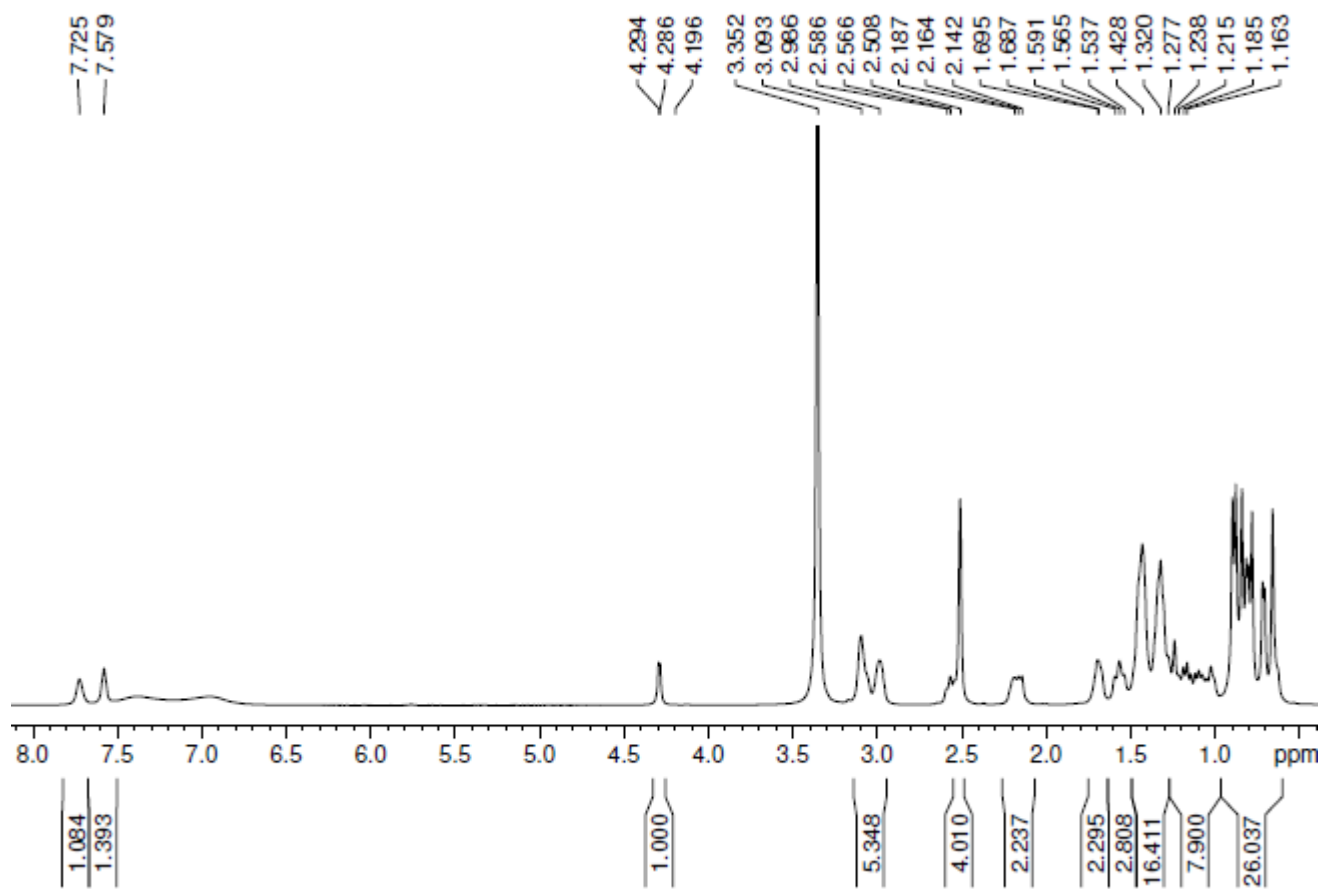
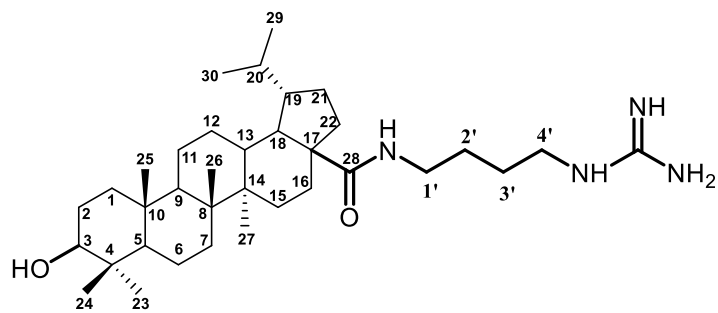


**3 $\beta$ -[2-guanidine-3-hydroxy-2-(hydroxymethyl)propyl]-3-O-acetyl-olean-12-en-28-oate hydrochloride (20c). <sup>13</sup>C NMR spectra (MeOD)**



**3 $\beta$ -N-(4-buthylguanidine)-3-hydroxy-lupane-28-amide (14).**

<sup>1</sup>H NMR spectra (d<sub>6</sub>-DMSO)



**3 $\beta$ -N-(4-buthylgyanidine)-3-hydroxy-lupane-28-amide (14).**

<sup>13</sup>C NMR spectra (d<sub>6</sub>-DMSO)

