Supporting information

Philanthotoxin analogues that selectively inhibit ganglionic nicotinic acetylcholine receptors with exceptional potency

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Present Address: School of Life Science, Biology Department, University of Zakho, Duhok, Kurdistan Region, Iraq.
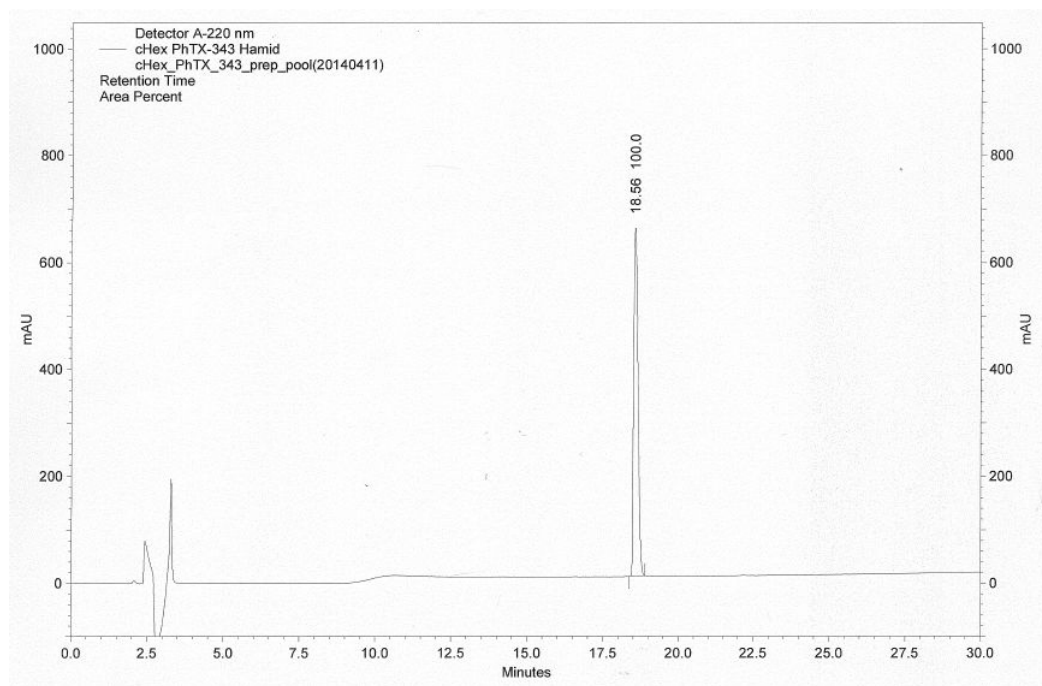
Contents

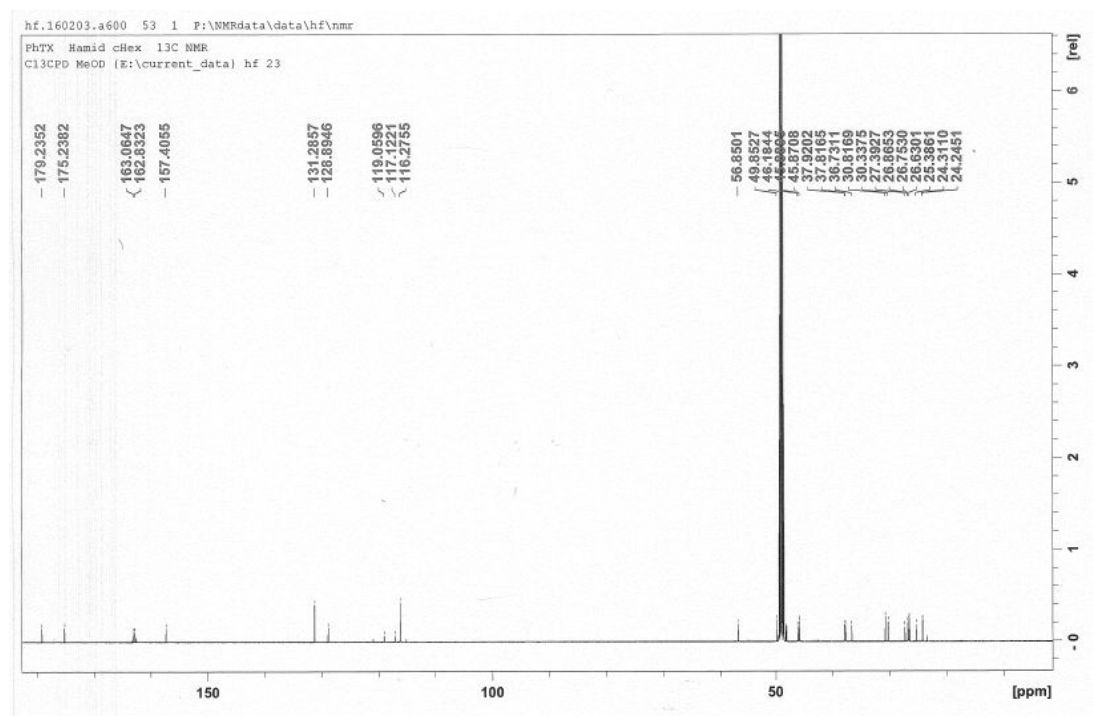# Characterization of PhTX analogues

Compound **5**: t_R = 18.56 min (purity: >99.9%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: $C_{26}H_{45}N_5O_3$ [M + H]$^+$ 476.36007, found 476.36000; ΔM = 0.1 ppm
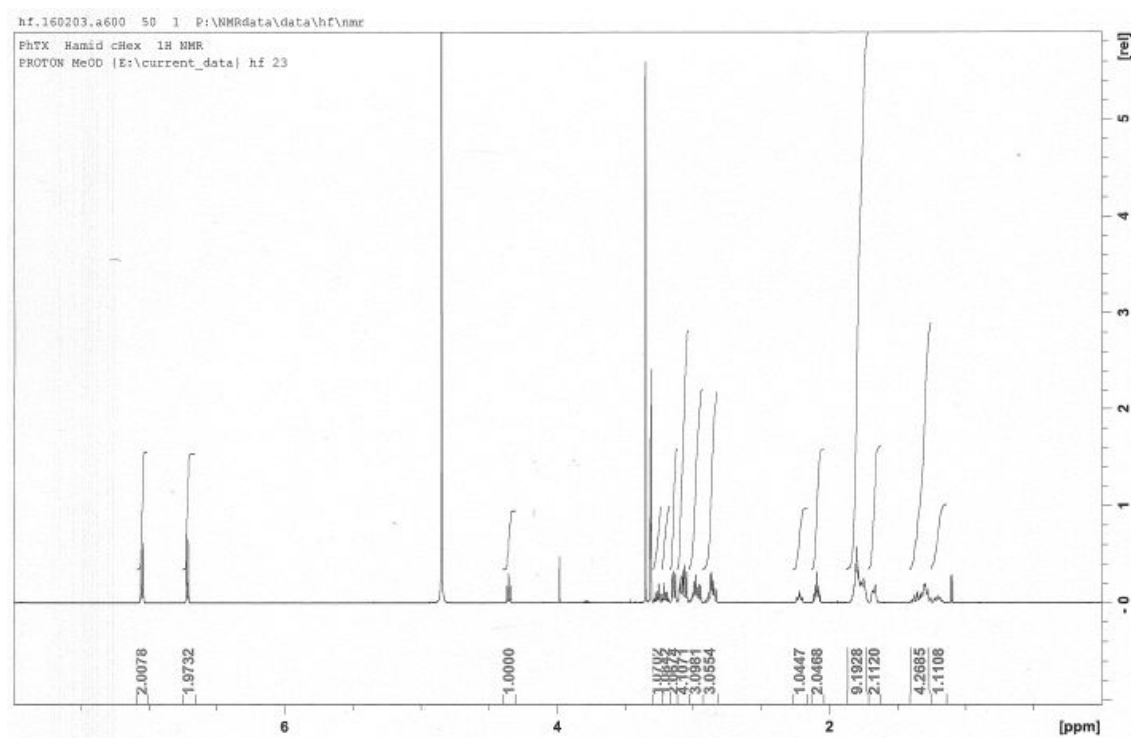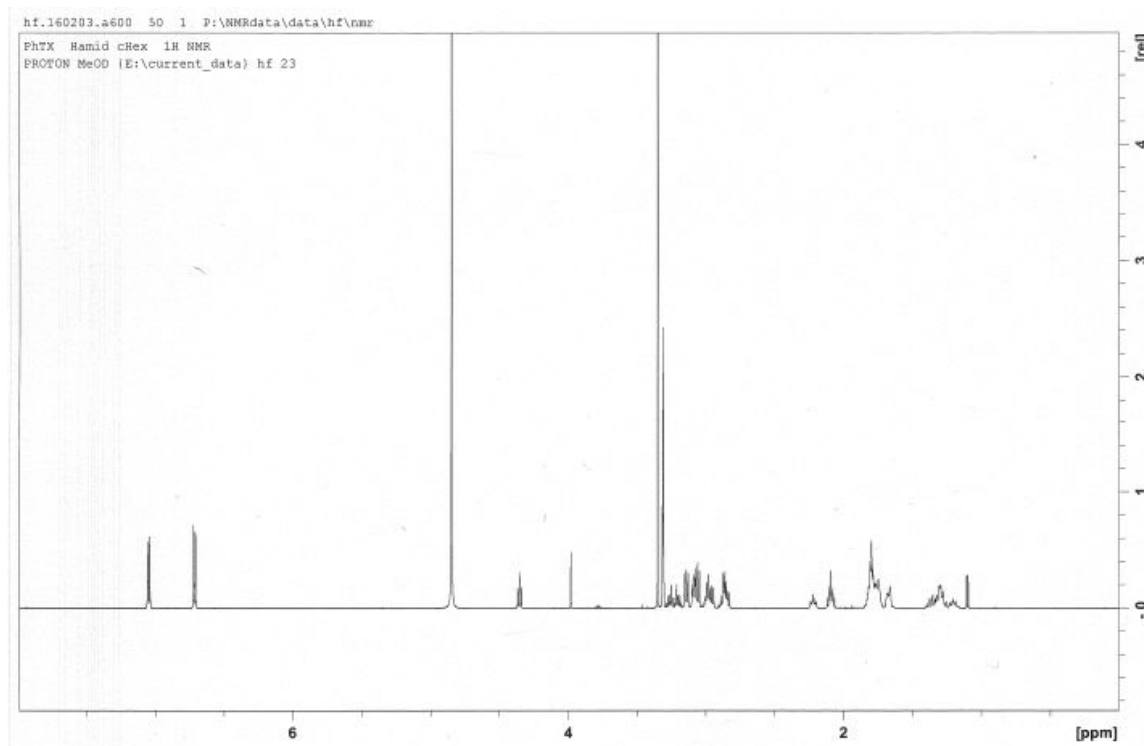
Analyt. HPLC chromatogram:

^{13}C NMR spectrum (150 MHz, methanol-d_4):

Compound **5**:

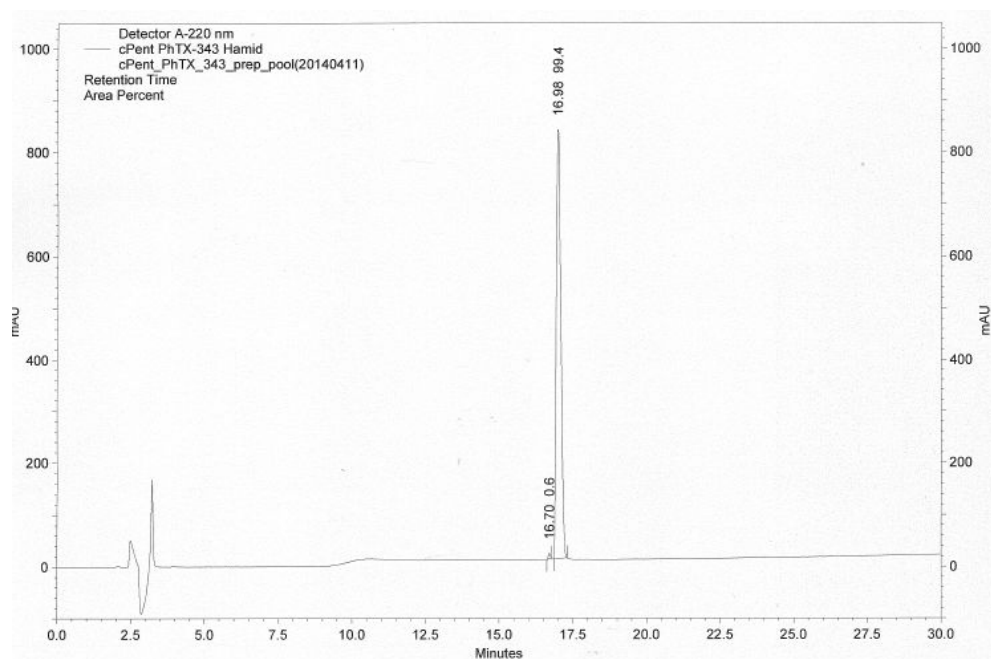^{1}H NMR spectrum (600 MHz, methanol-d$_4$):
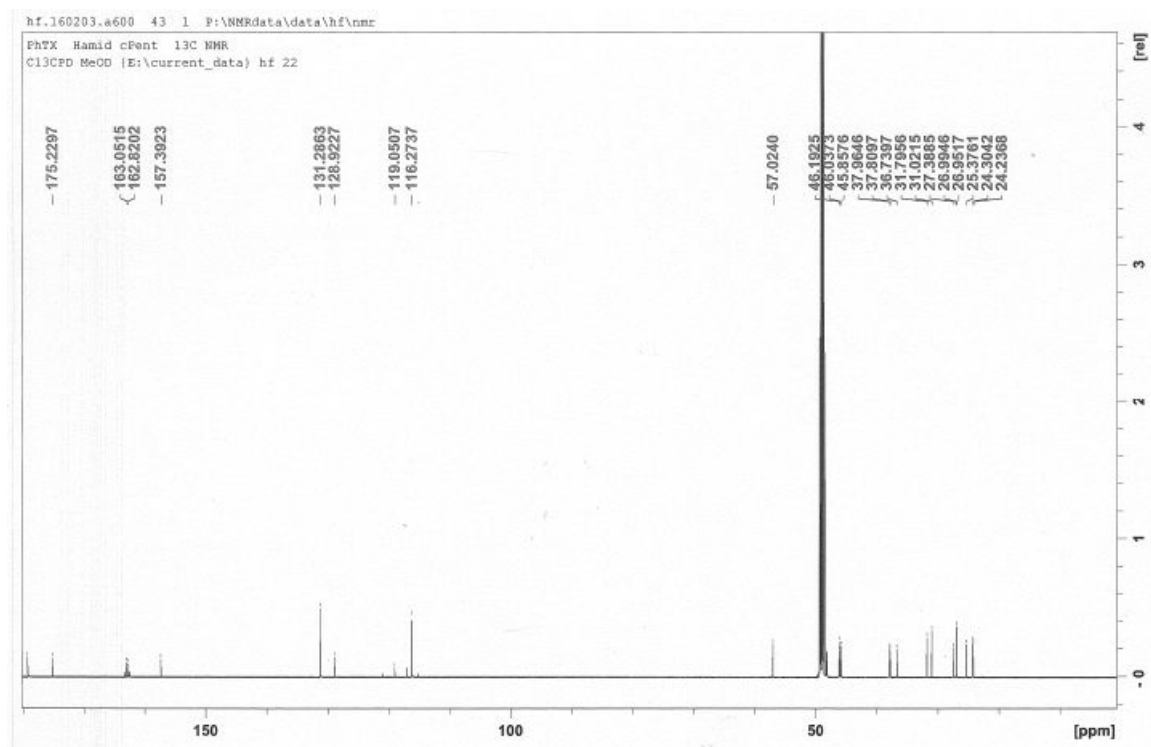
Compound **6**: t_R = 16.98 min (purity: 99.4%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{25}H_{43}N_5O_3$ $[M + H]^+$ 462.34442, found 462.34432; ΔM = 0.2 ppm.
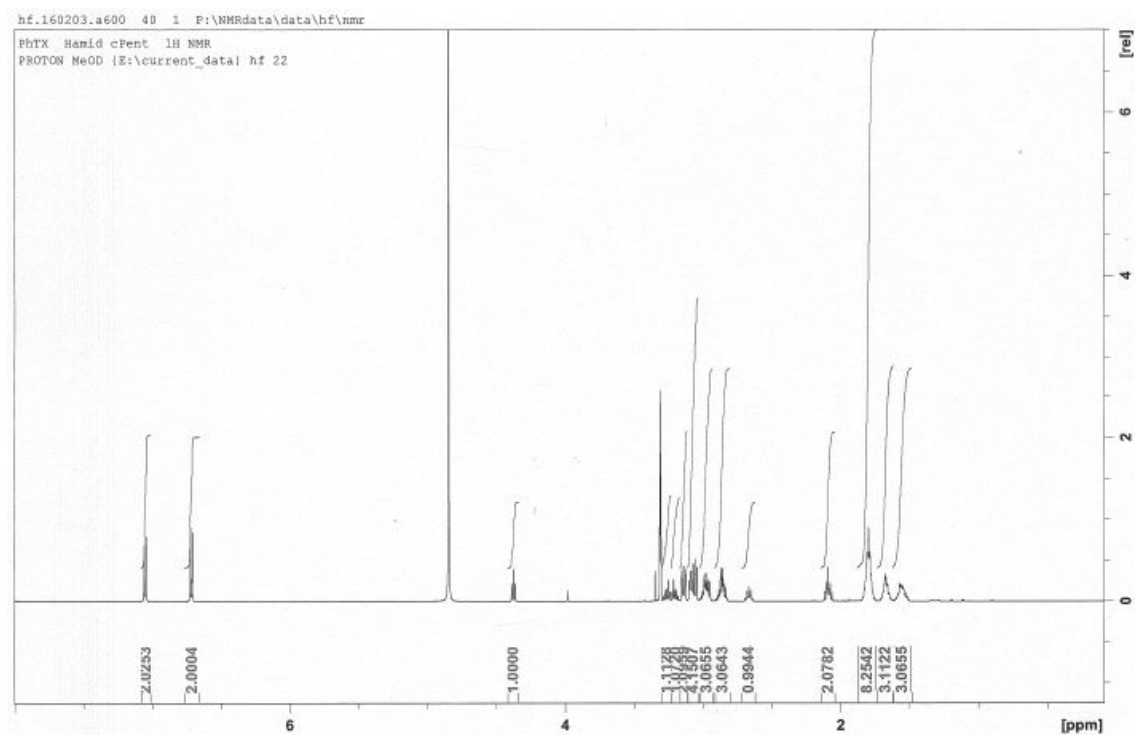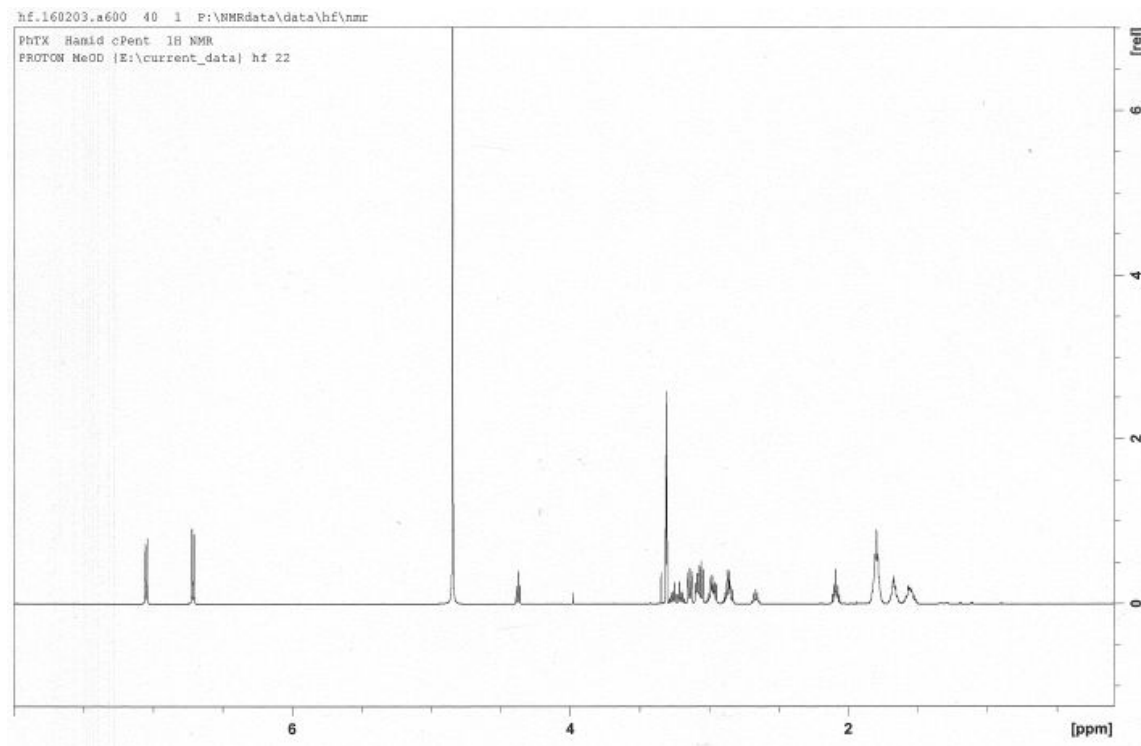
Analyt. HPLC chromatogram:

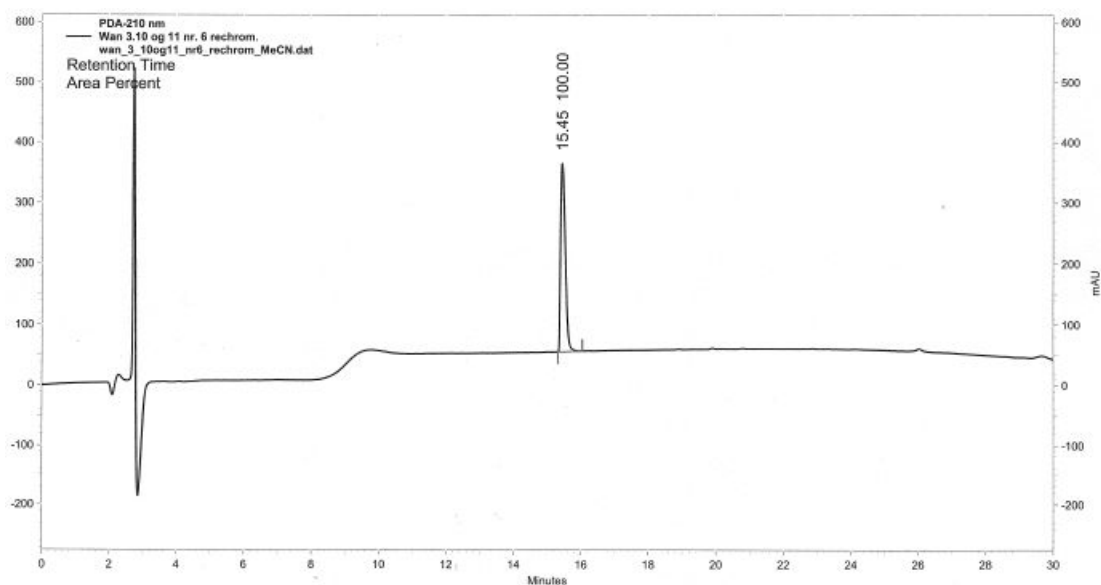^{13}C NMR spectrum (150 MHz, methanol-d_4):

Compound **6**:

^{1}H NMR spectrum (600 MHz, methanol-d$_4$):

Compound **10**: t_R = 15.45 min (purity: >99.9%). Gradient: $0 \rightarrow 100\%$ B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{24}H_{47}N_5O$ $[M + H]^+$ 438.38025, found 438.38004; ΔM = 0.4 ppm.

Analyt. HPLC chromatogram:

^{13}C NMR spectrum (150 MHz, methanol-d_4):

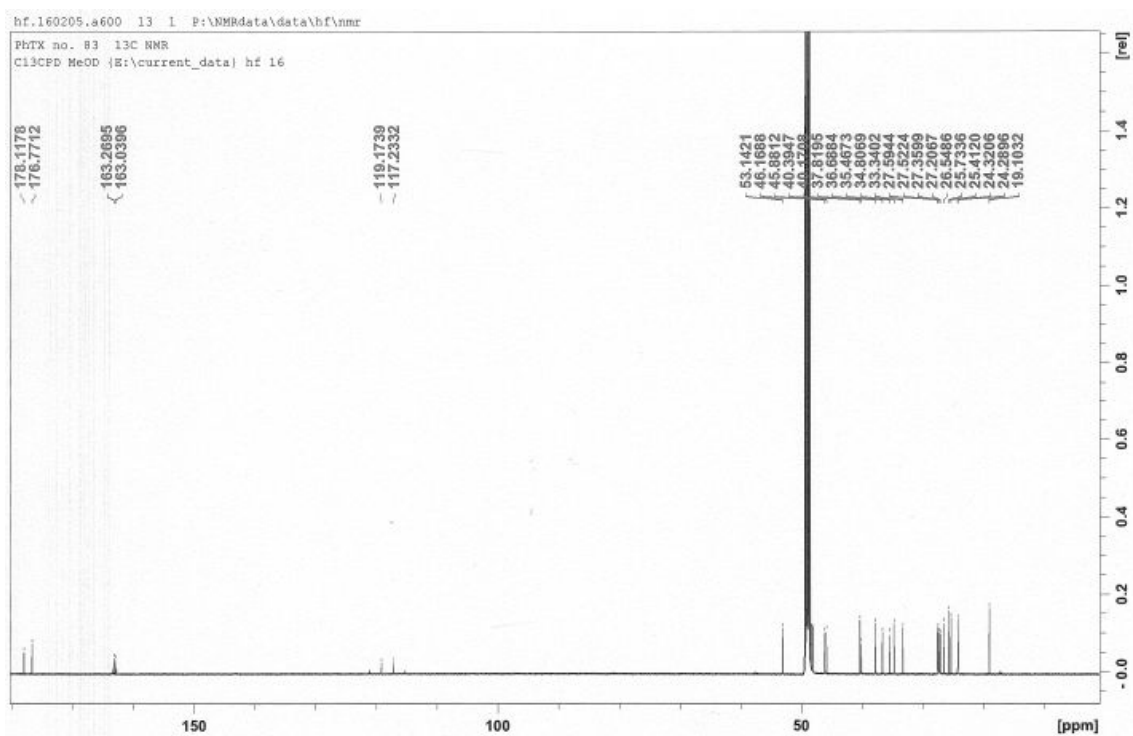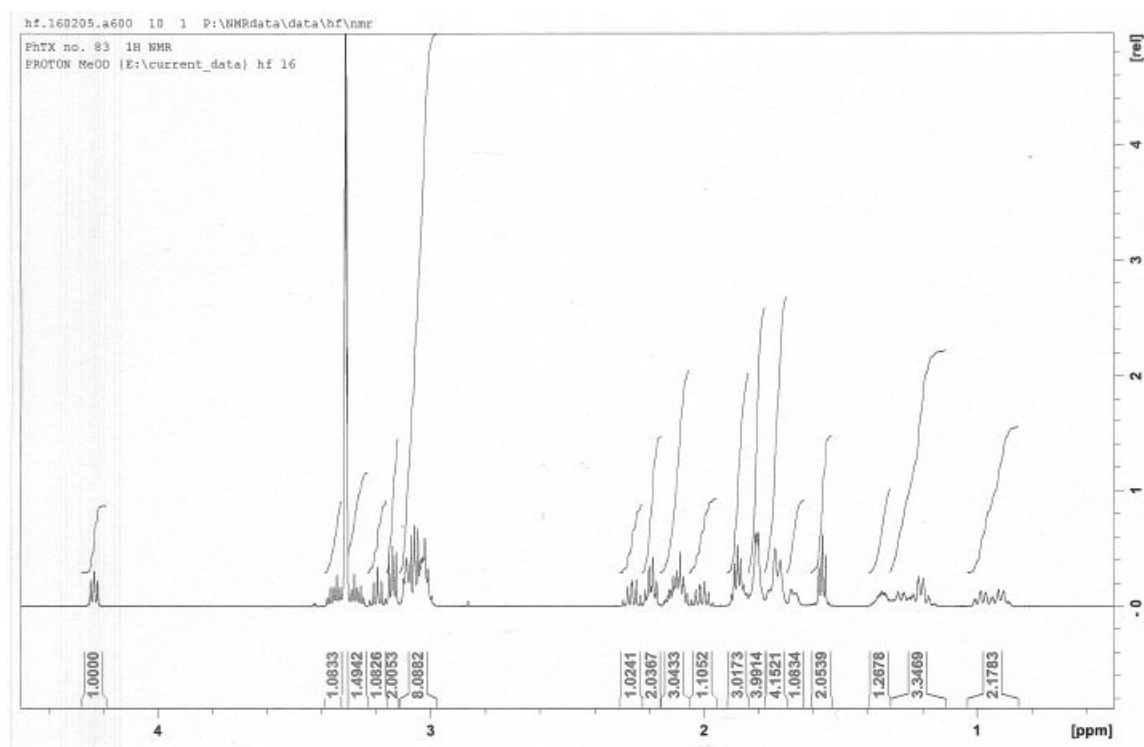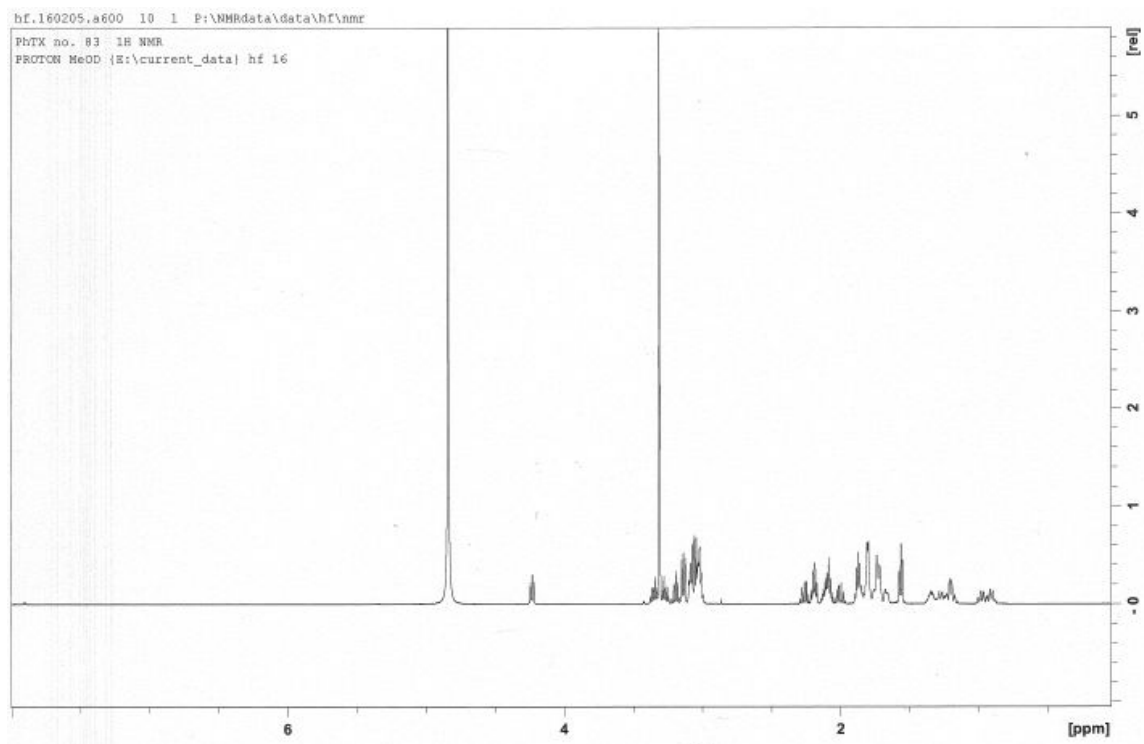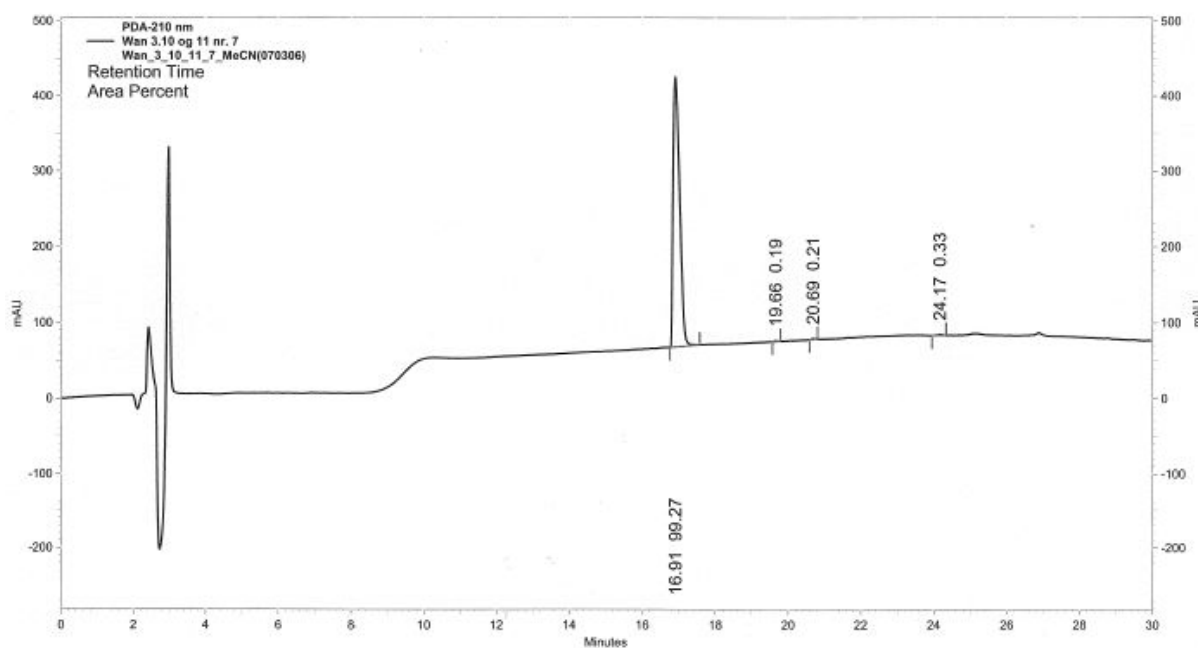Compound **10**:

^{1}H NMR spectrum (600 MHz, methanol-d$_4$):

Compound **11**: t_R = 16.91 min (purity: 99.3%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{25}H_{49}ON_5O_2$ $[M + H]^+$ 452.39590, found 452.39581; ΔM = 0.1 ppm.

Analyt. HPLC chromatogram:

^{13}C NMR spectrum (150 MHz, methanol-d_4):

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Compound **11**:

^{1}H NMR spectrum (600 MHz, methanol-d$_4$):

Compound **13**: t_R = 18.67 min (purity: 97.2%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{27}H_{54}N_5O_2$ [M + H]$^+$ 480.42720, found 480.42715; ΔM = 0.3 ppm.

Analyt. HPLC chromatogram:

^{13}C NMR spectrum (150 MHz, methanol-d_4):

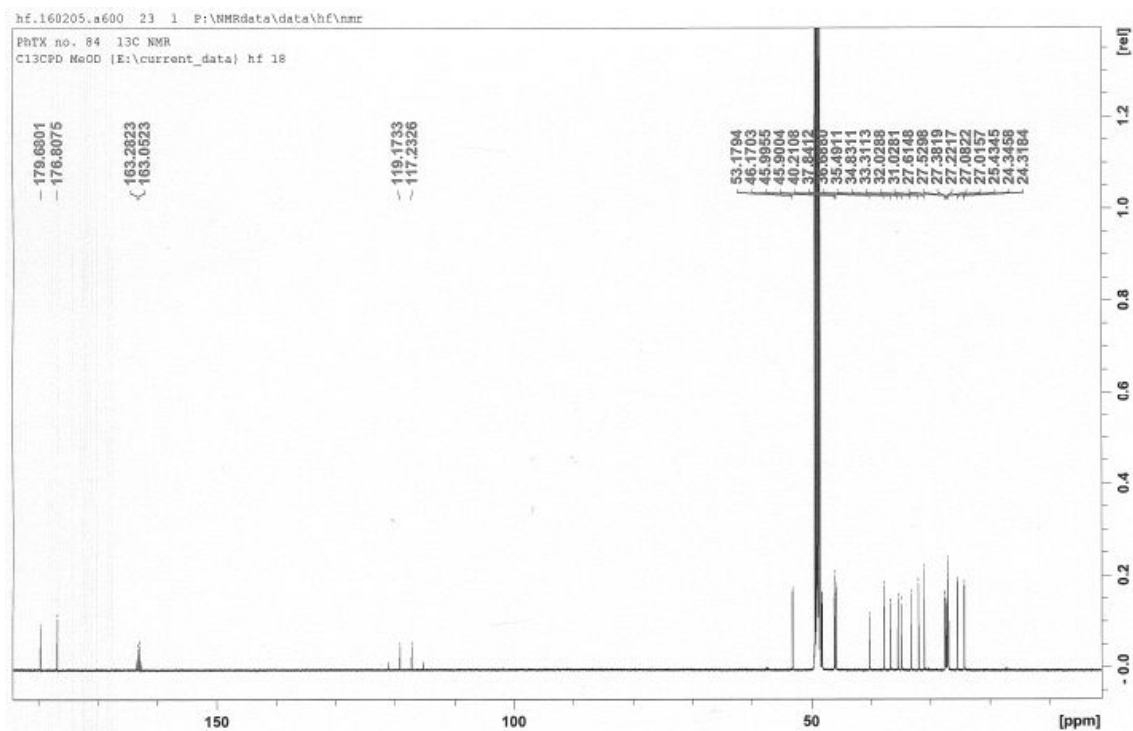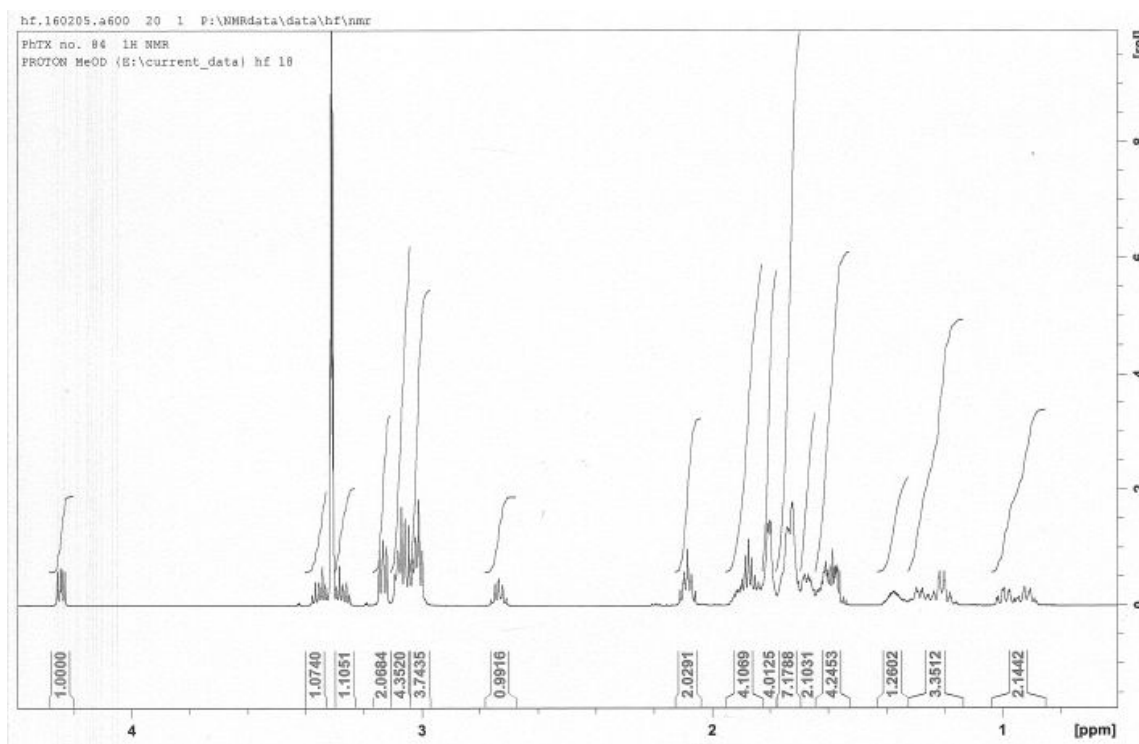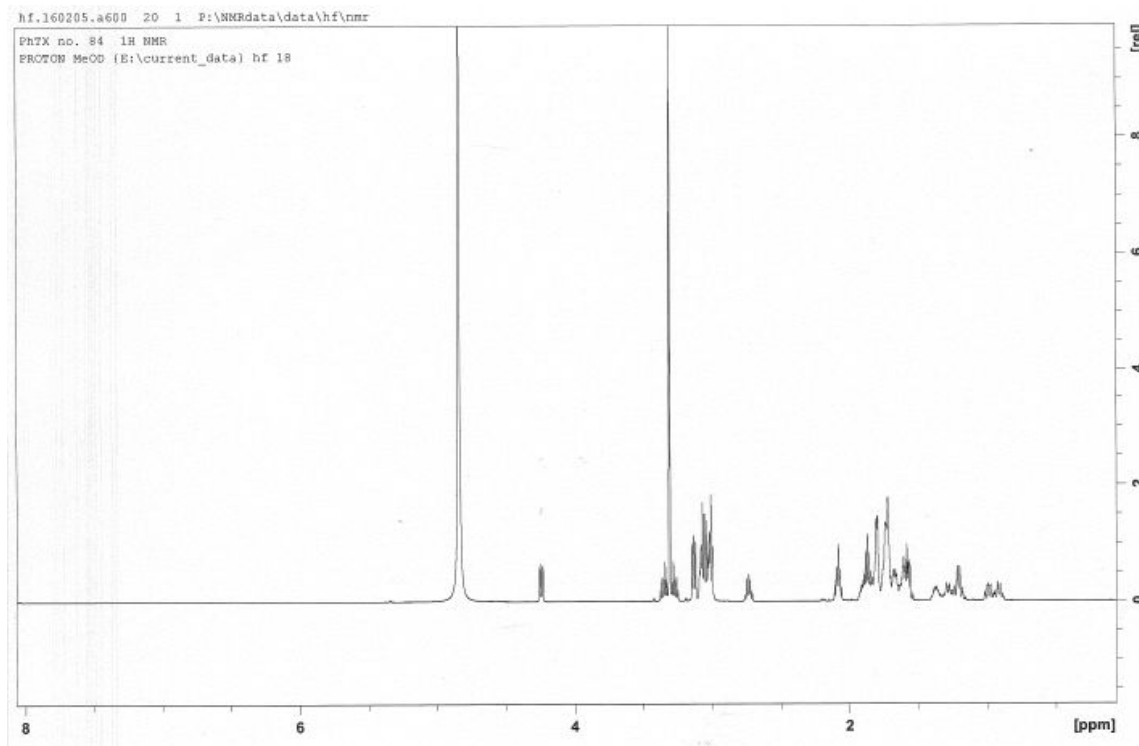Compound **13**:

^{1}H NMR spectrum (600 MHz, methanol-d$_4$):
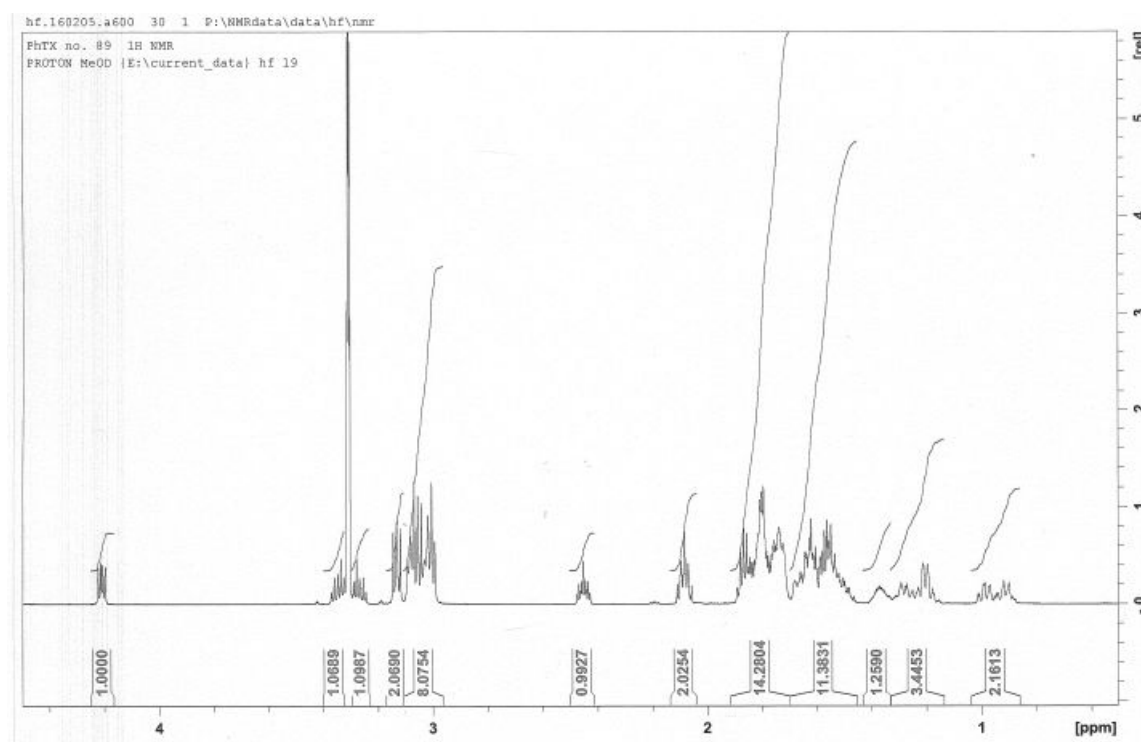
Compound **14**: t_R = 19.17 min (purity: 99.2%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{28}H_{54}N_5O_2$ $[M + H]^+$ 492.42729, found 492.42708; ΔM = 0.4 ppm.
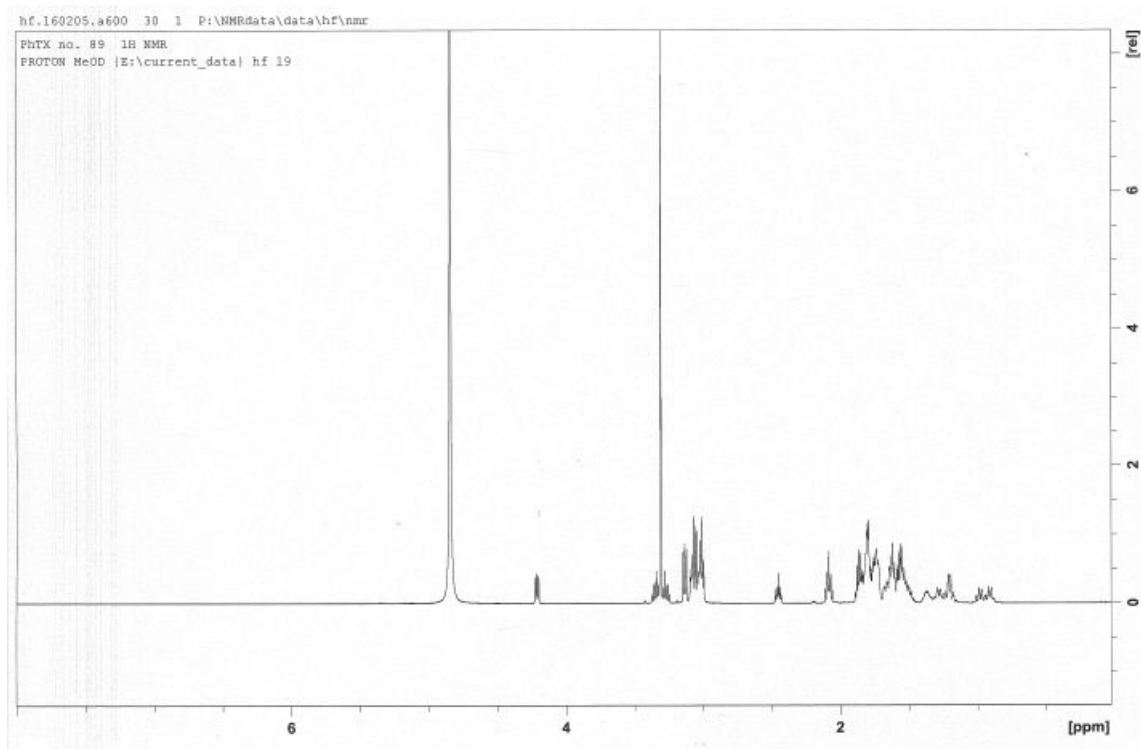
Analyt. HPLC chromatogram:
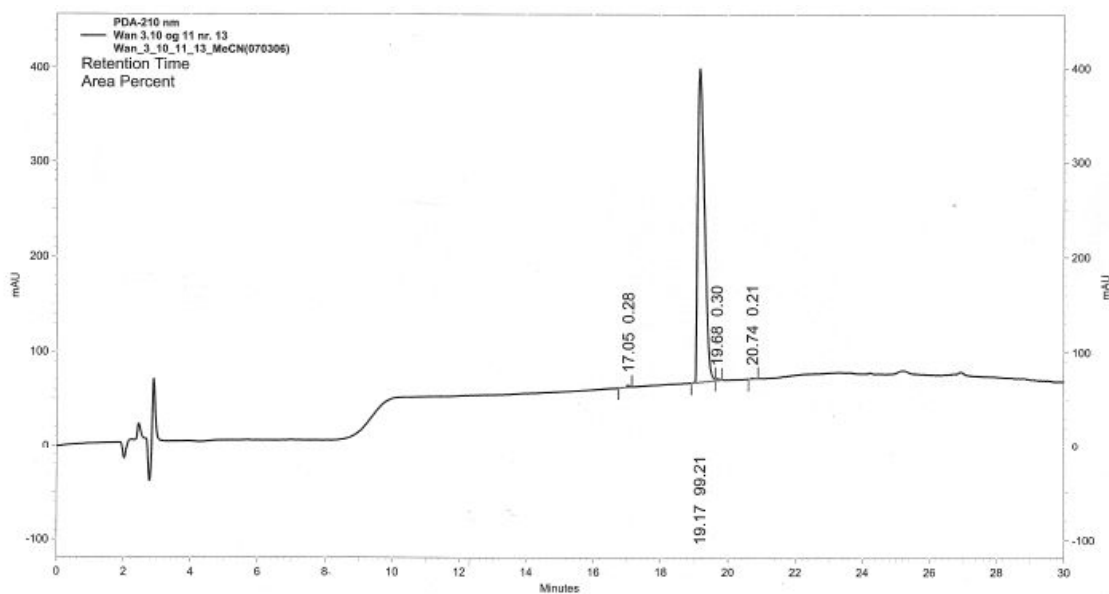

^{13}C NMR spectrum (150 MHz, methanol-d_4):

PhTX no. 90 13C NMR
C13CPD MeOD {E:\current_data} hf 20

176.6250
175.9426
175.9025
163.2829
163.0526
119.1726
117.2319
53.0040
52.9733
48.3022
46.1944
45.8997
43.7194
43.6594
42.2985
42.1884
40.6638
40.4892
38.5920
38.0449
38.0011
37.8409
36.7252
35.9229
35.4180
34.9147
33.1194
33.0931
30.9260
30.7882
29.6393
29.6036
27.5976
27.5300
27.4392
27.4264
27.2195
25.4344
24.3369
24.3188

150 100 50 [ppm]

Compound **14**:

¹H NMR spectrum (600 MHz, methanol-d₄):

hf.160205.a600 40 1 P:\NMRdata\data\hf\nmr
PhTX no. 90 1H NMR
PROTON MeOD {E:\current_data} hf 20

6 4 2 [ppm]

Compound **15**: t_R = 17.11 min (purity: 99.8%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{26}H_{46}N_5O_2$ $[M + H]^+$ 460.36460, found 460.36446; ΔM = 0.3 ppm.

Analyt. HPLC chromatogram:

^{13}C NMR spectrum (150 MHz, methanol-d$_4$):

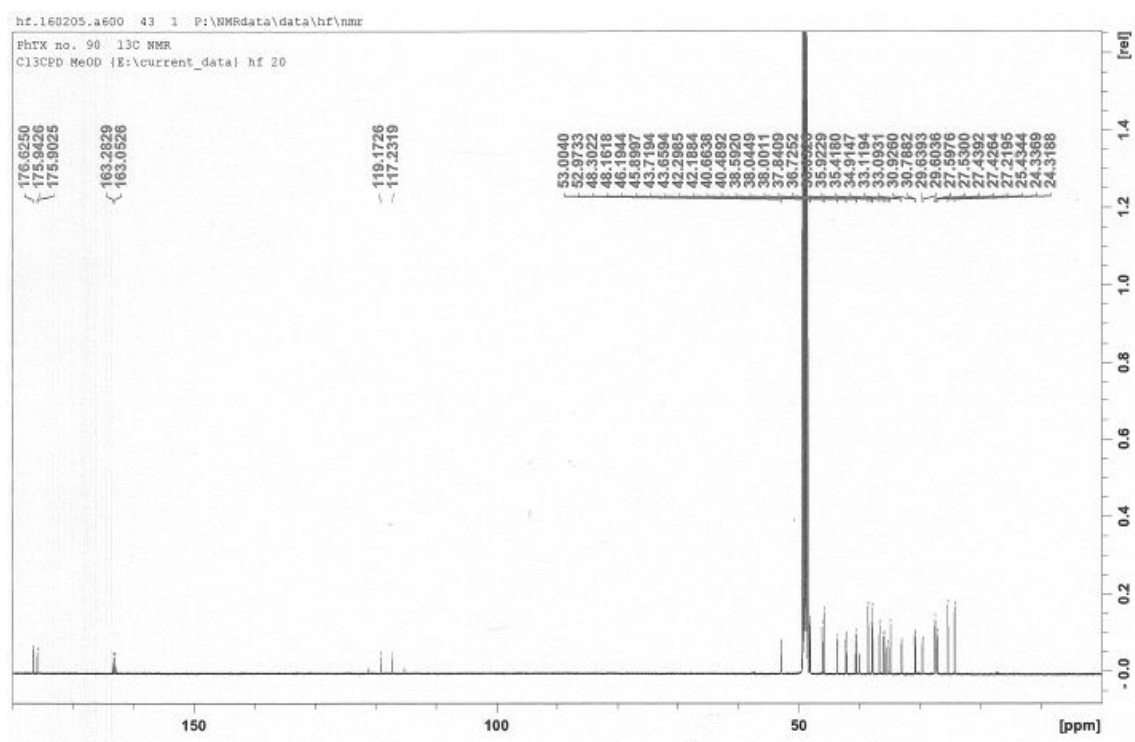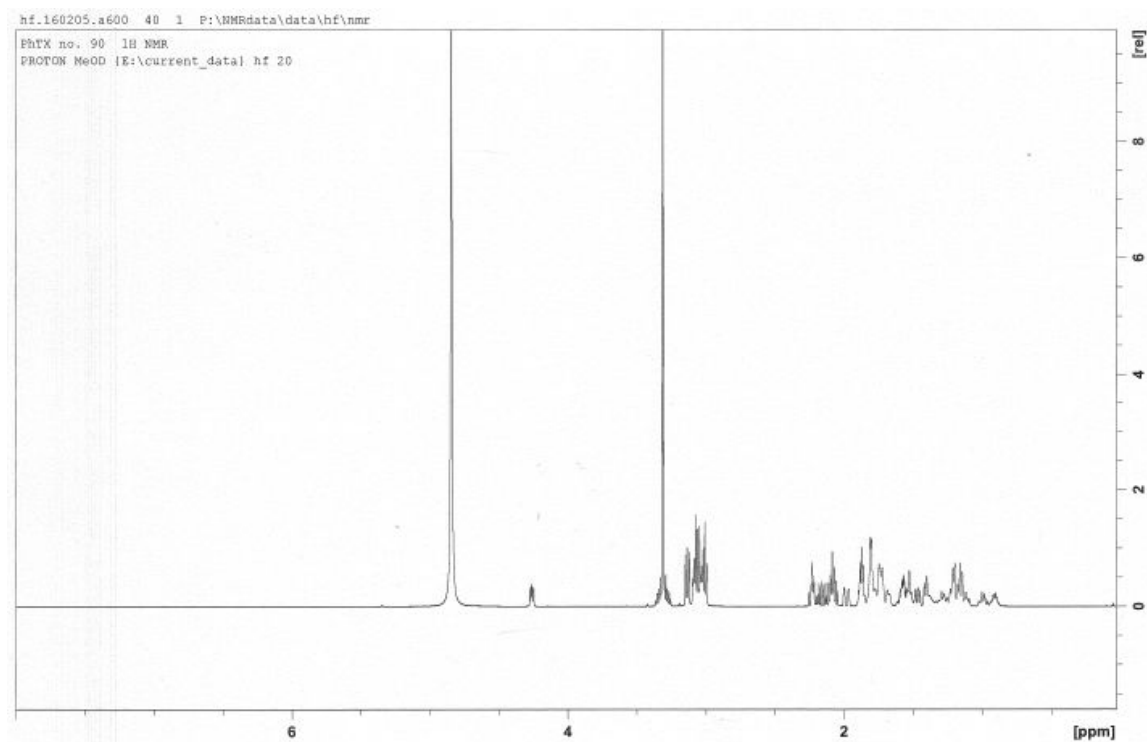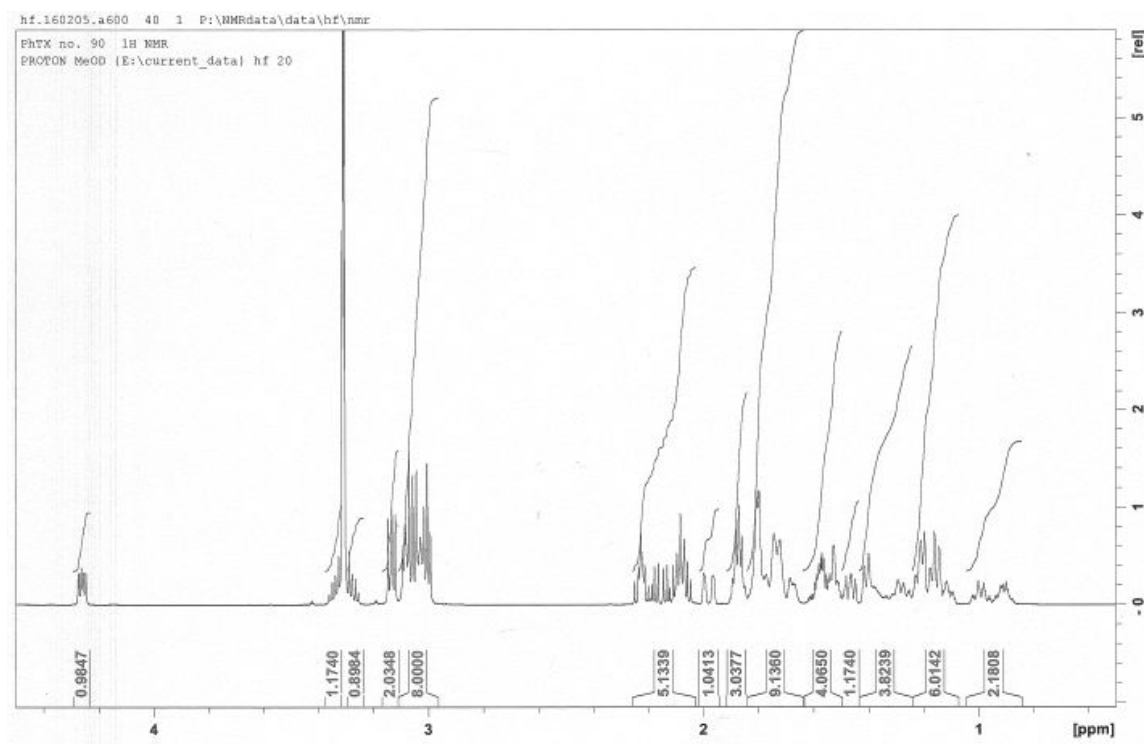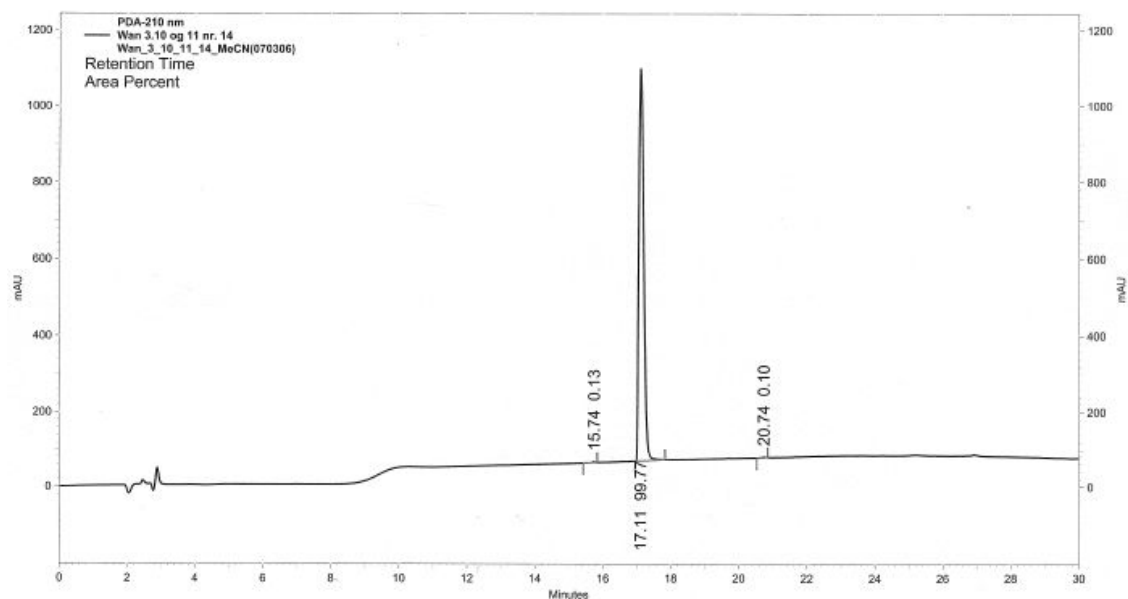Compound **15**:

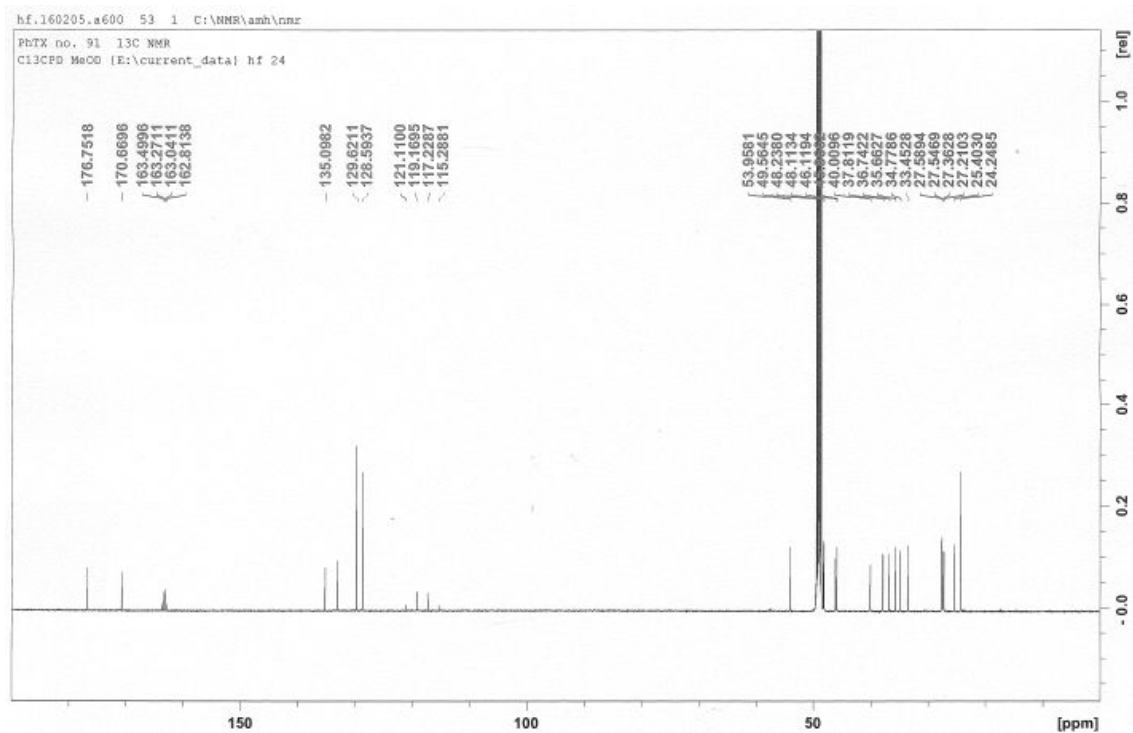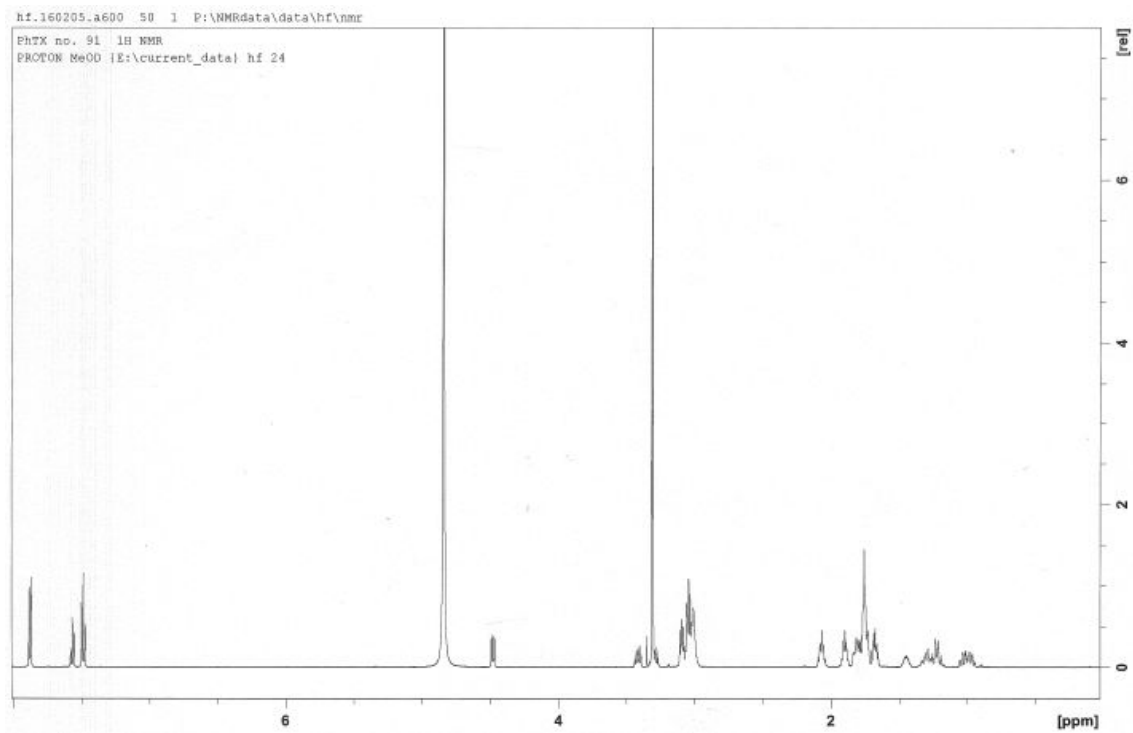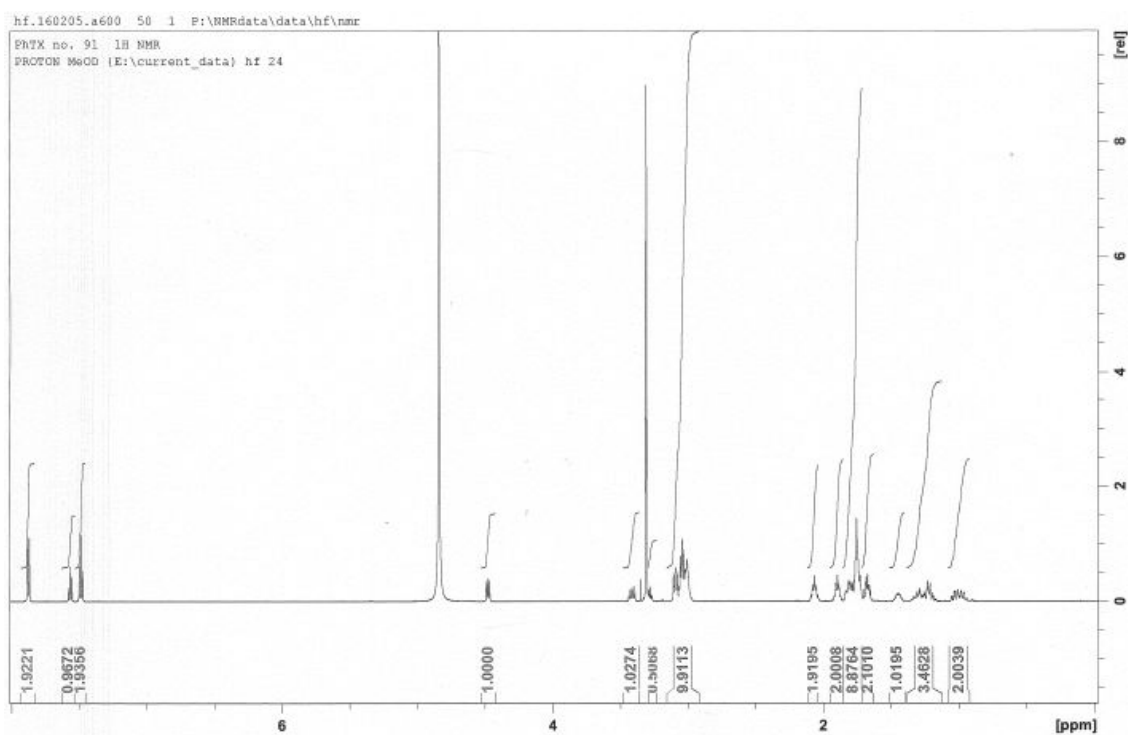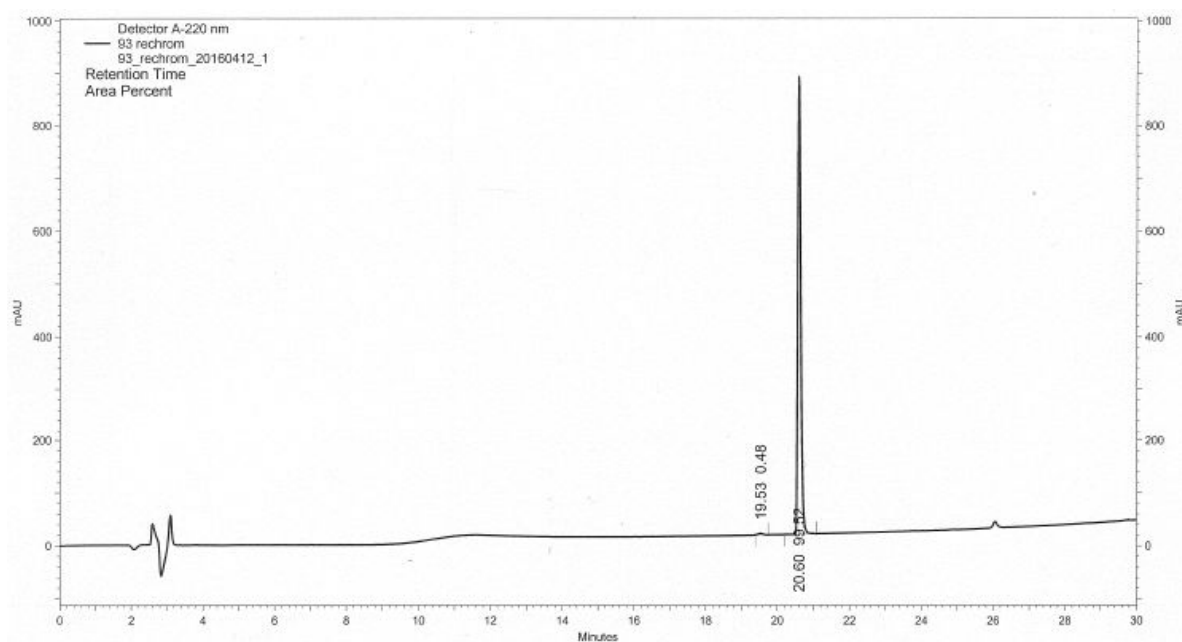^{1}H NMR spectrum (600 MHz, methanol-d$_4$):

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```
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PhTX no. 91  1H NMR
PROTON MeOD {E:\current_data} hf 24
```
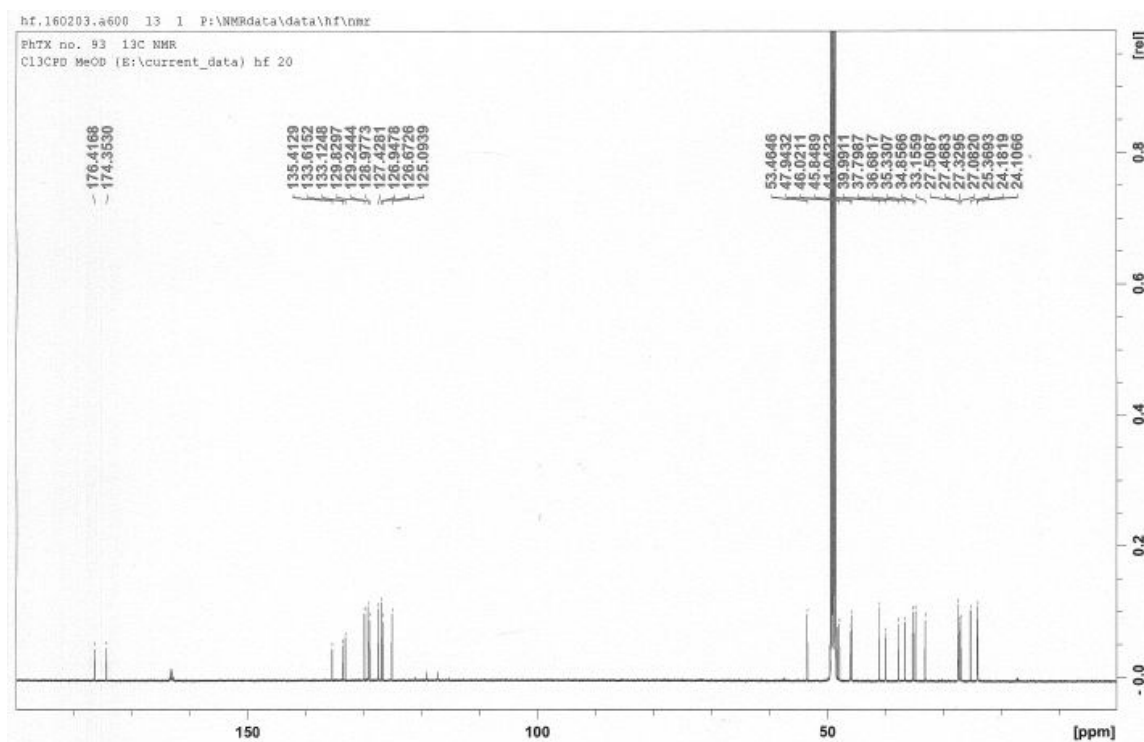
Compound **16**: t_R = 20.6 min (purity: 99.5%). Gradient: $0 \rightarrow 100\%$ B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{31}H_{50}N_5O_2$ $[M + H]^+$ 524.39645, found 524.39573; ΔM = 1.3 ppm.
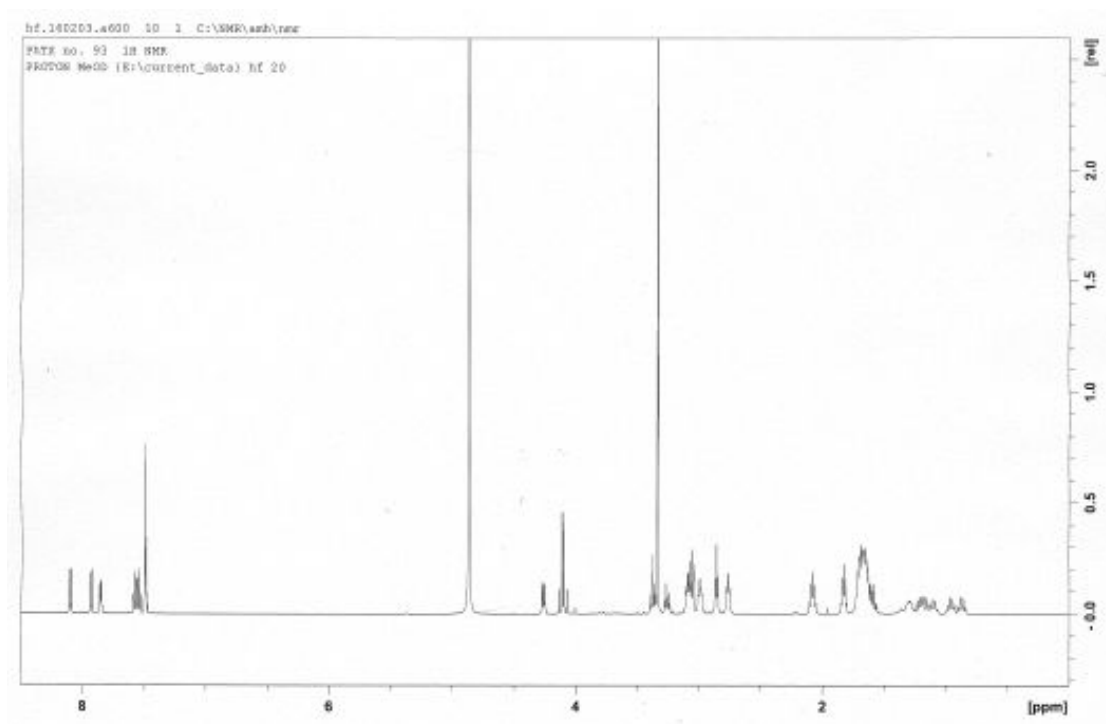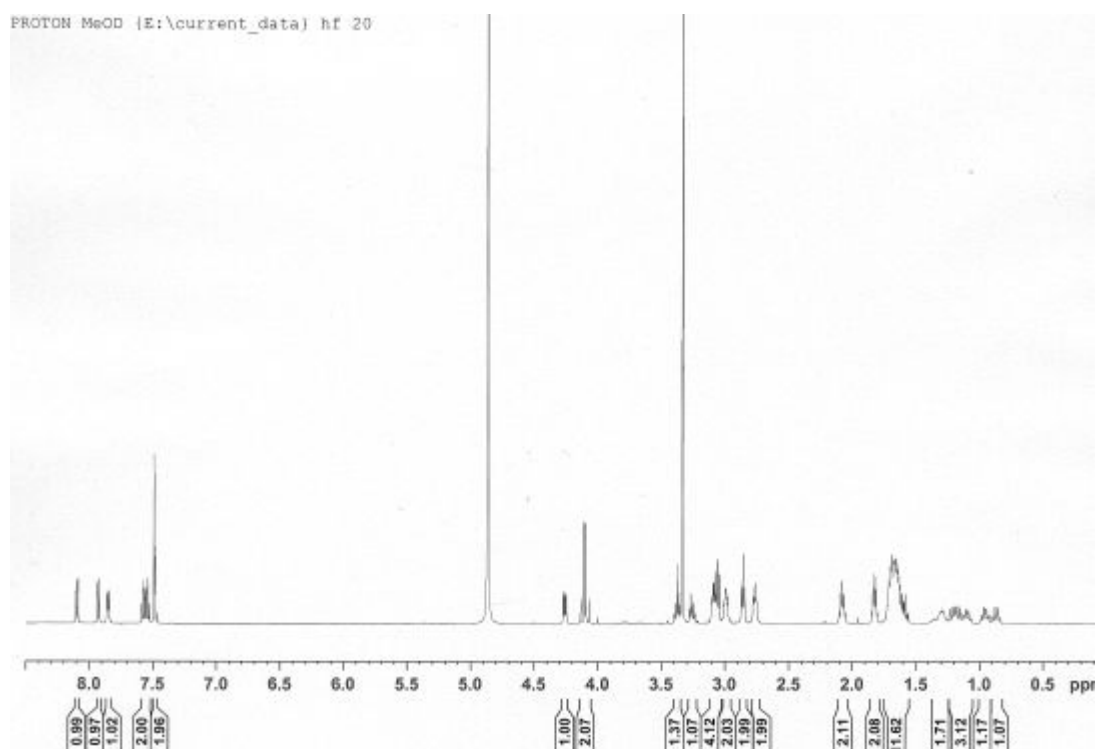
Analyt. HPLC chromatogram:

¹³C NMR spectrum (150 MHz, methanol-d₄):

The 13C NMR spectrum (150 MHz, methanol-d4) follows.

Compound **16**:
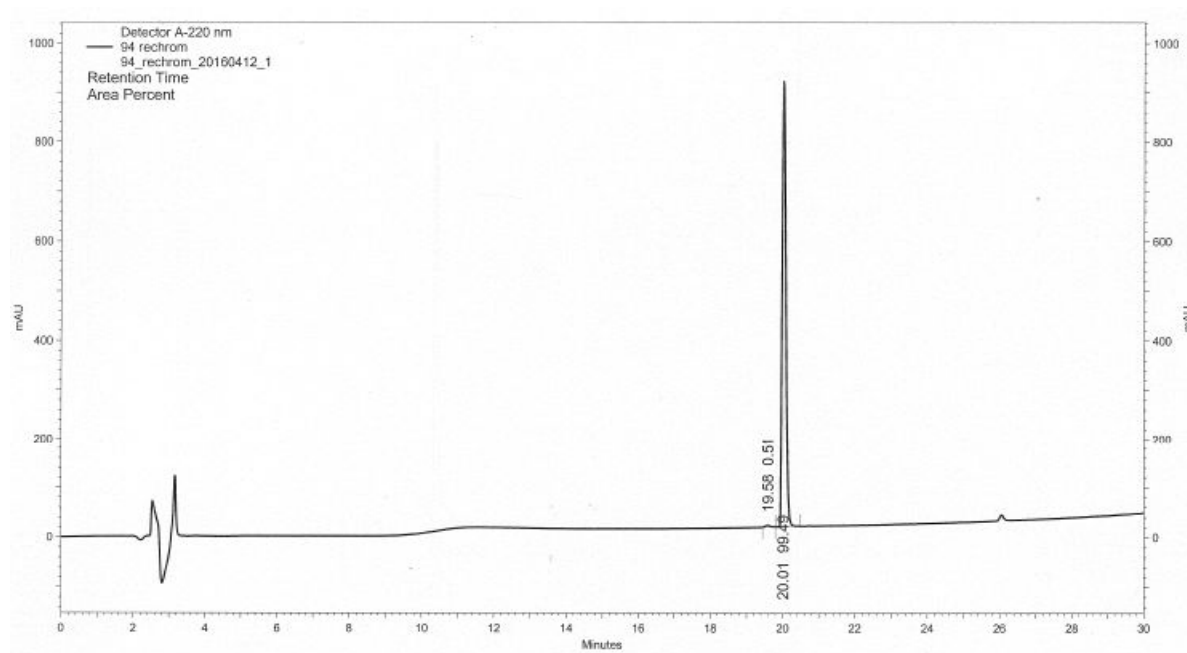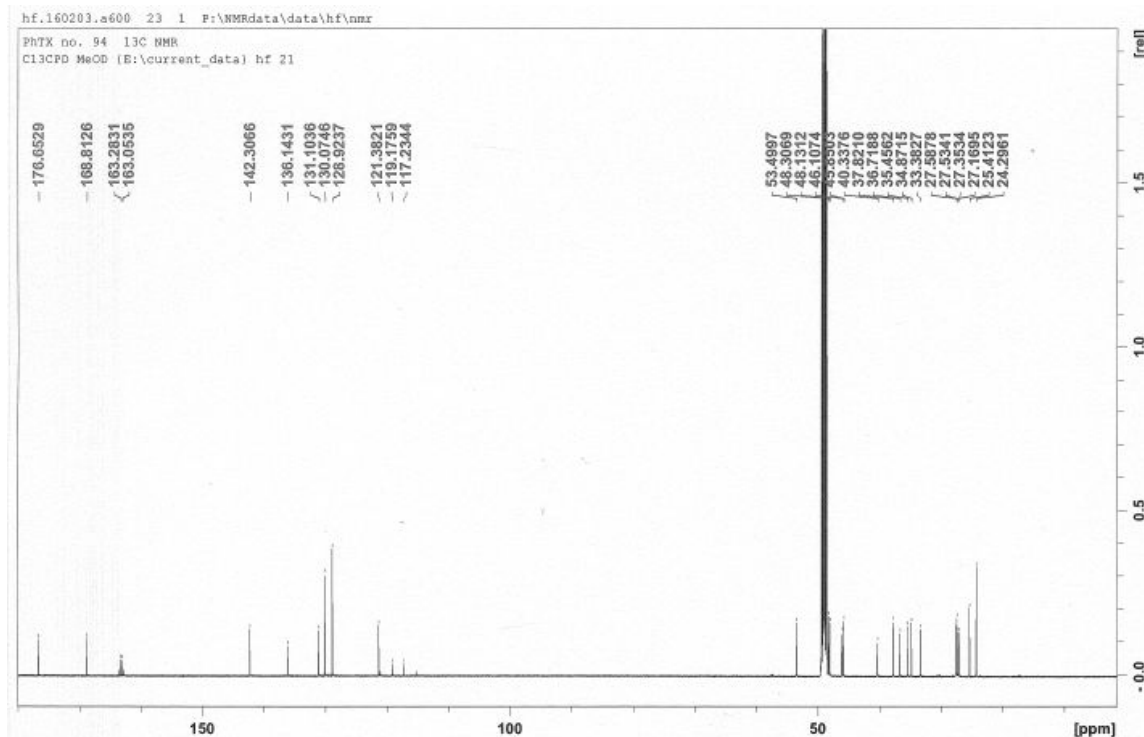
¹H NMR spectrum (600 MHz, methanol-d₄):

Compound **17**: t_R = 20.01 min (purity: 99.5%). Gradient: 0 → 100% B over 30 min; B = 95% MeCN + 0.1% TFA. HRMS: calcd for $C_{28}H_{48}N_5O_2$ [M + H]$^+$ 486.38025, found 486.38021; ΔM = 0.1 ppm.

Analyt. HPLC chromatogram:

^{13}C NMR spectrum (150 MHz, methanol-d_4):

Compound **17**:

^{1}H NMR spectrum (600 MHz, methanol-d_4):

hf.160203.a600   20   1   P:\NMRdata\data\hf\nmr

PhTX no. 94   1H NMR
PROTON MeOD (E:\current_data) hf 21

3.0088 2.9740   0.9843   1.0002   1.0747 0.8623 10.3189   2.1554 2.1020 8.2629 3.3918 1.0875 1.8642 2.0555 2.2432

6   4   2   [ppm]