

# Synthesis and biological evaluation of 3-amino-4,4-dimethyl lithocholic acid derivatives as novel, selective, and cellularly active allosteric SHP1 activators

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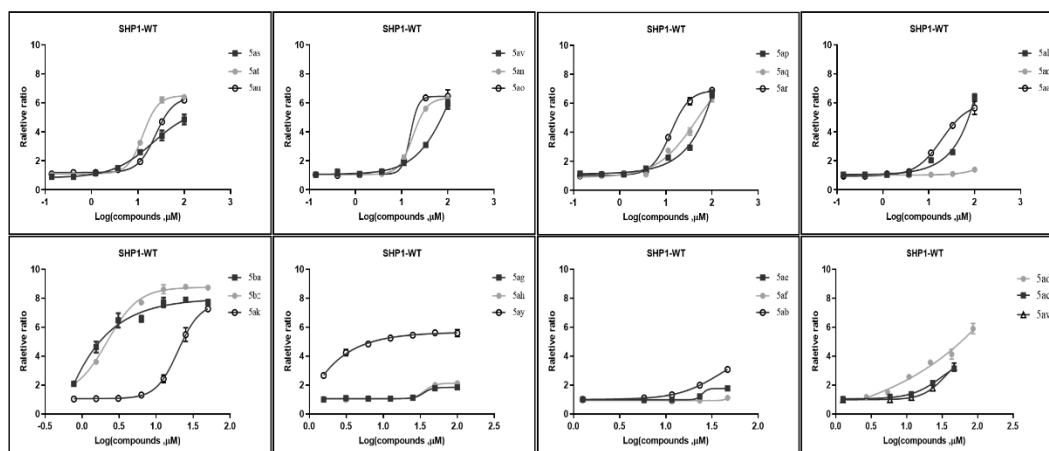
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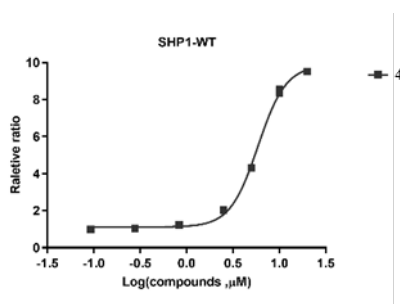
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## Dose response curves for SHP1 enzyme assay

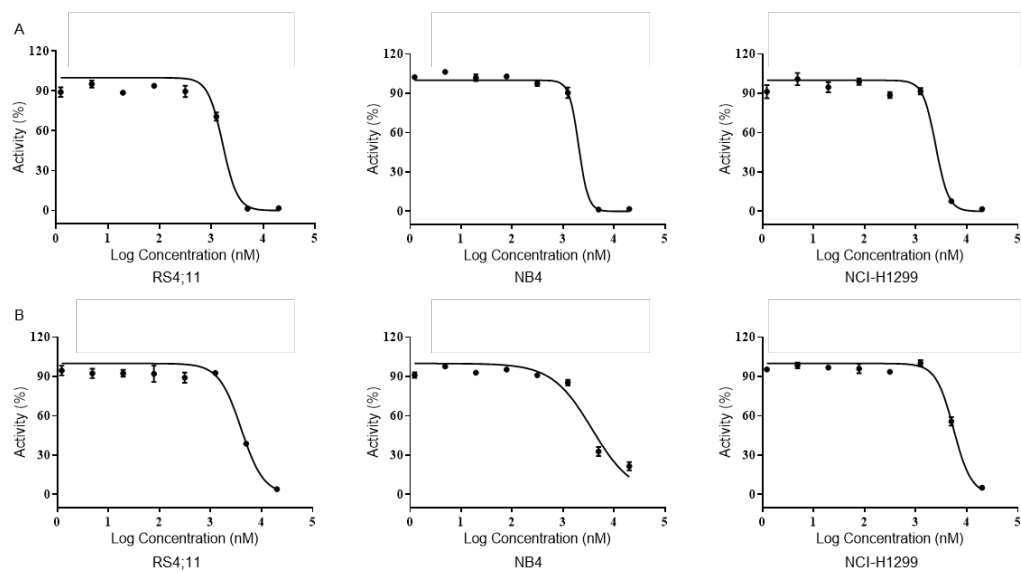


**Figure S1.** Dose responses of compound **5aa-ba** for SHP1 activation. Data are mean  $\pm$  S.E.M. (n=3).



**Figure S2.** Dose responses of positive control compound **4** for SHP1 activation. Data are mean  $\pm$  S.E.M. (n=3).

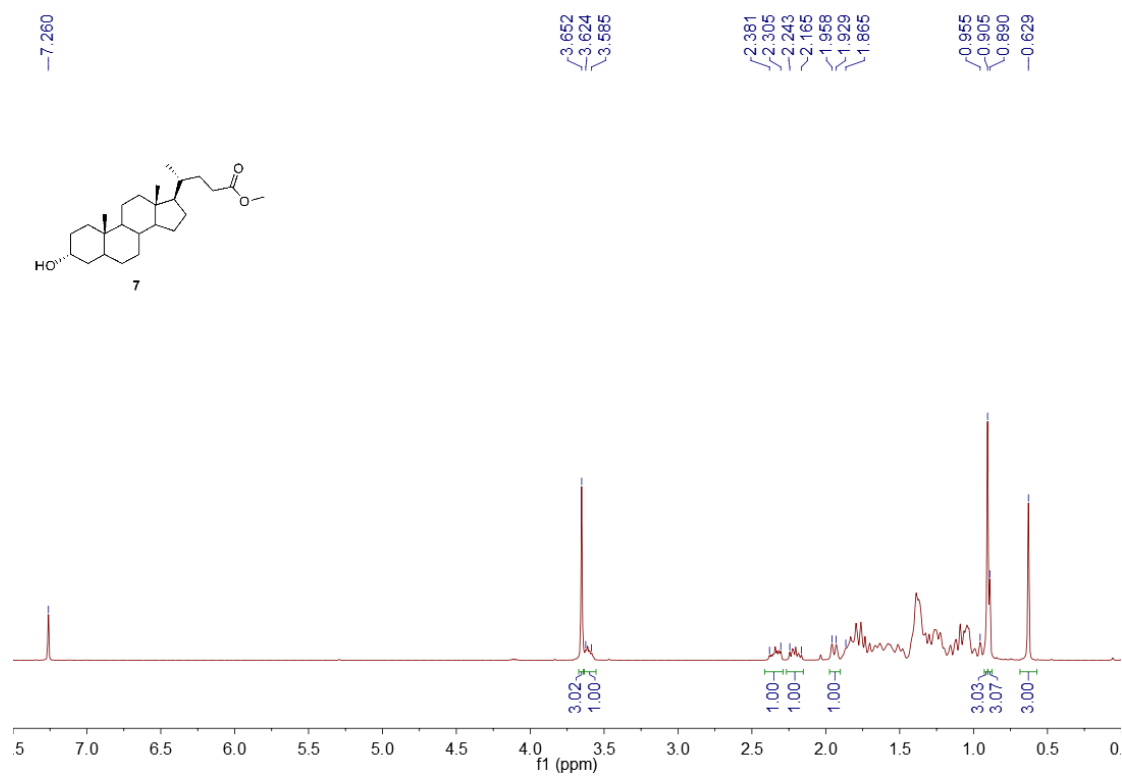
### Cell viability curves



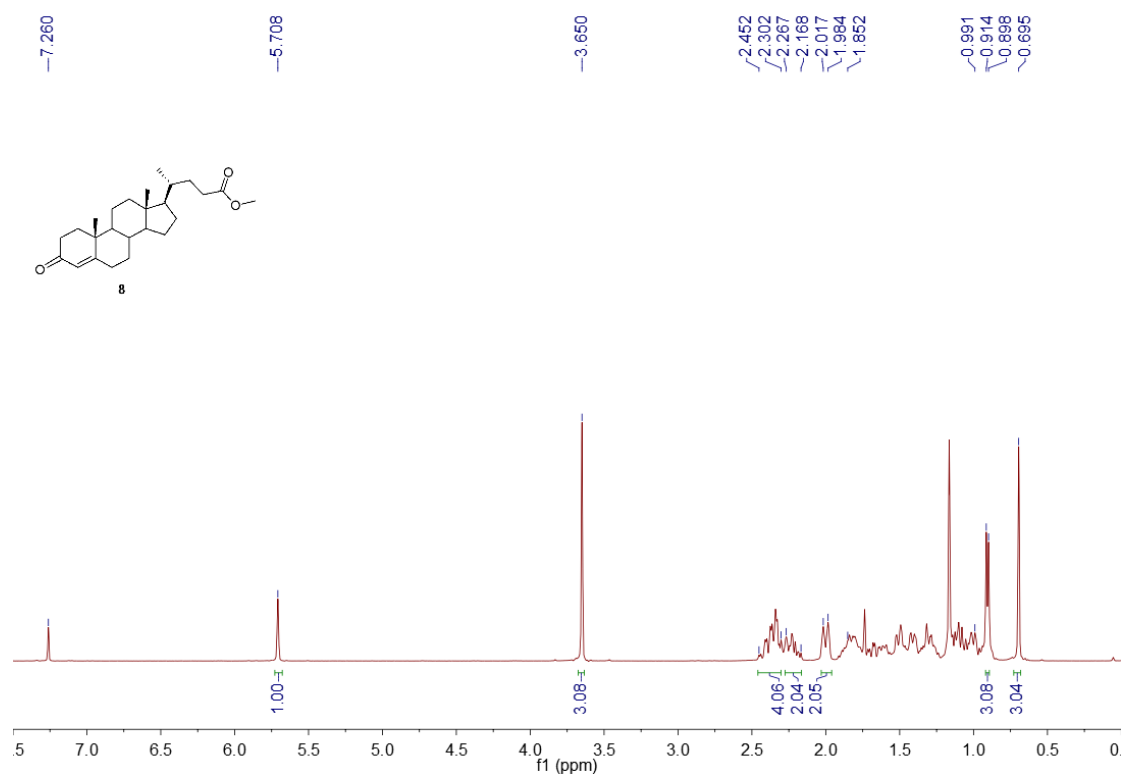
**Figure S3.** Cytotoxic activity of compound **5az** (A) and **5ba** (B) against RS4;11, NB4, NCI-H1299 cell lines. Data are mean  $\pm$  S.E.M. (n=3).

## NMR Spectra

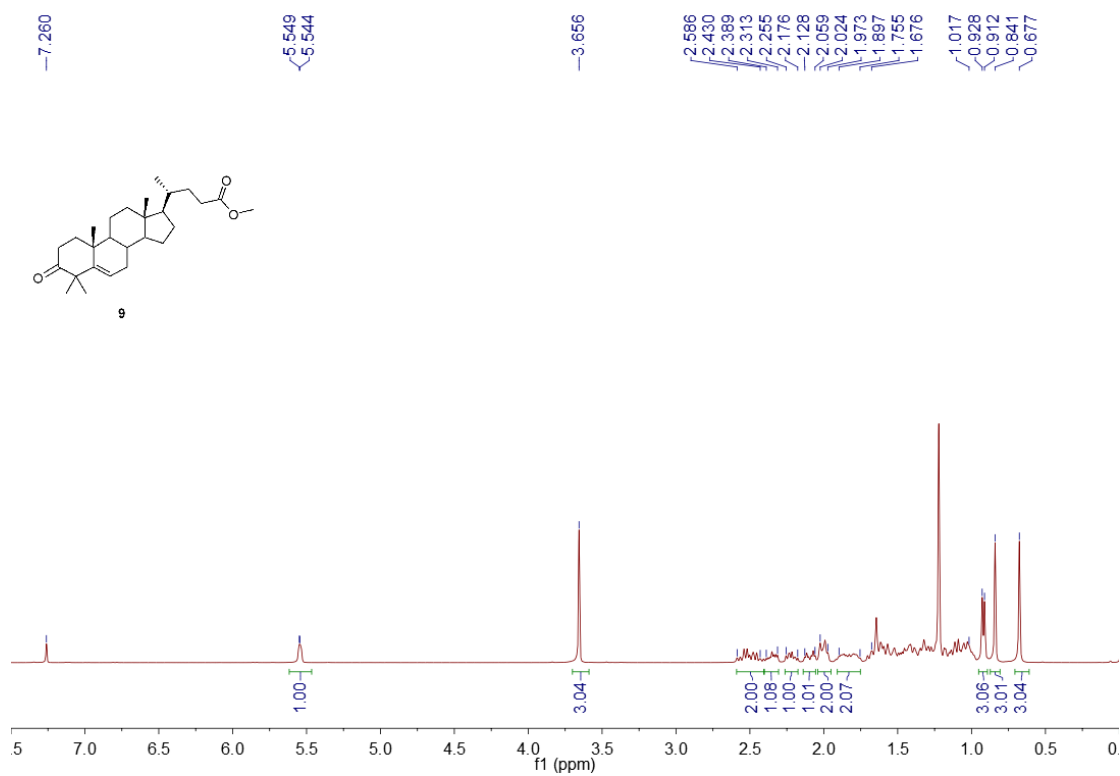
Compound **7** ( $^1\text{H}$  NMR)



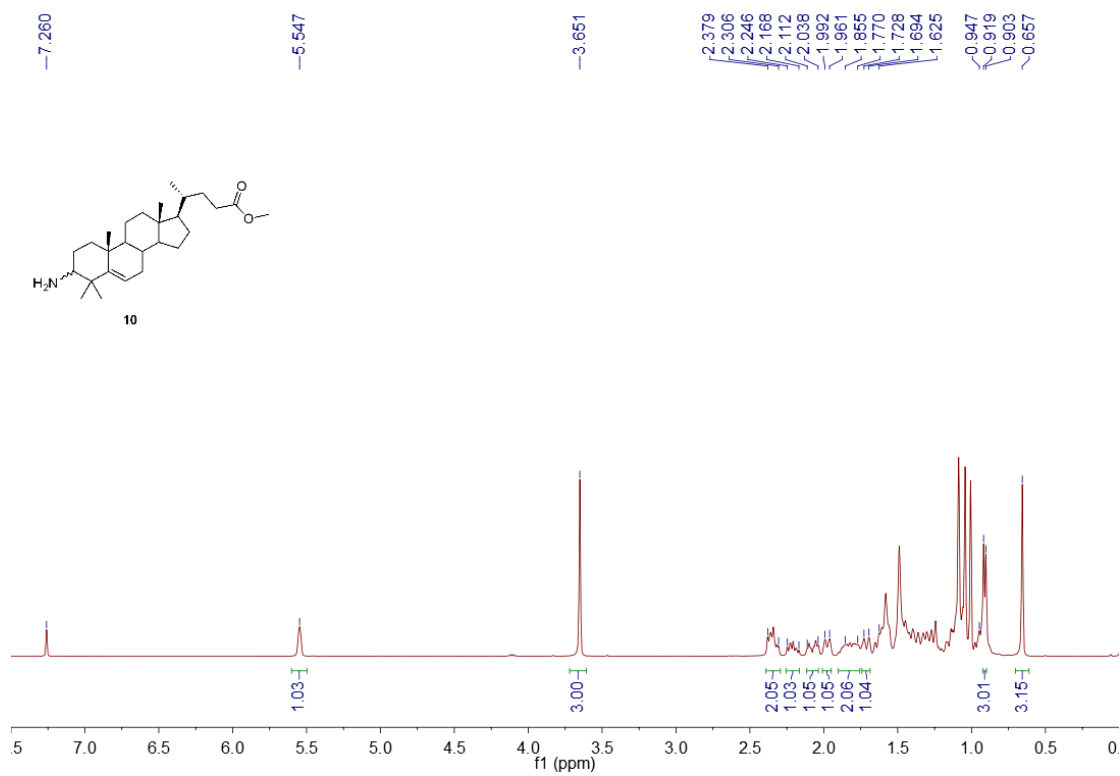
Compound **8** ( $^1\text{H}$  NMR)



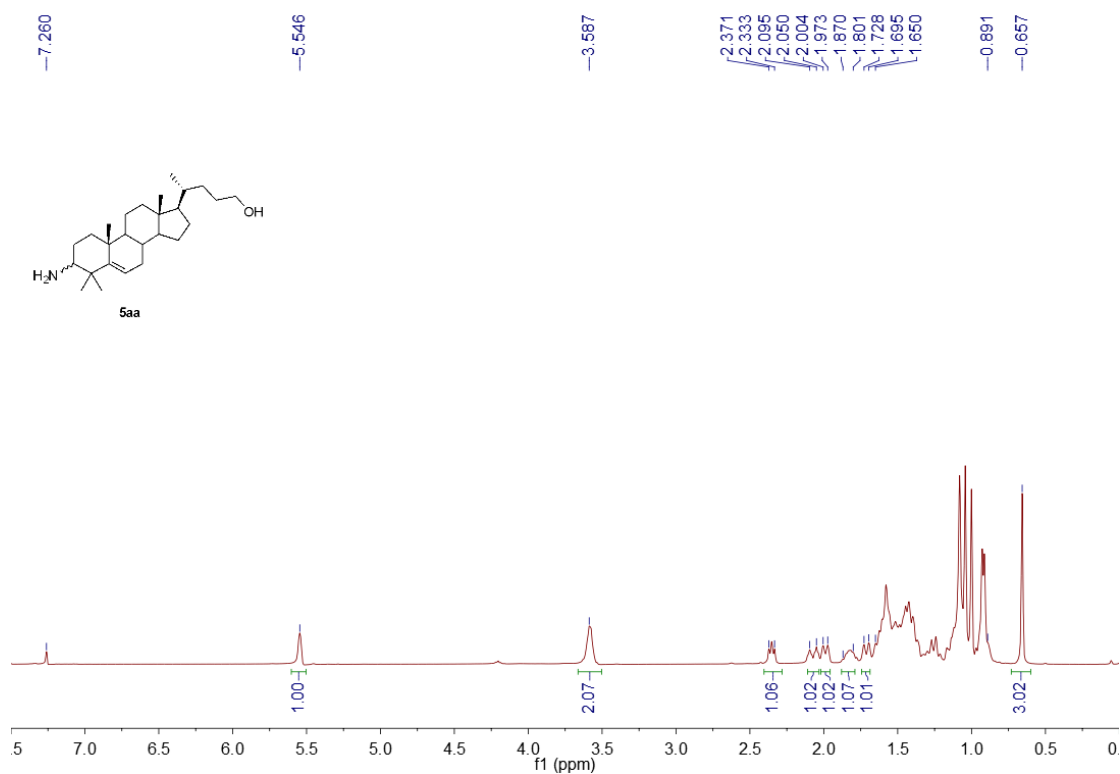
Compound **9** ( $^1\text{H}$  NMR)



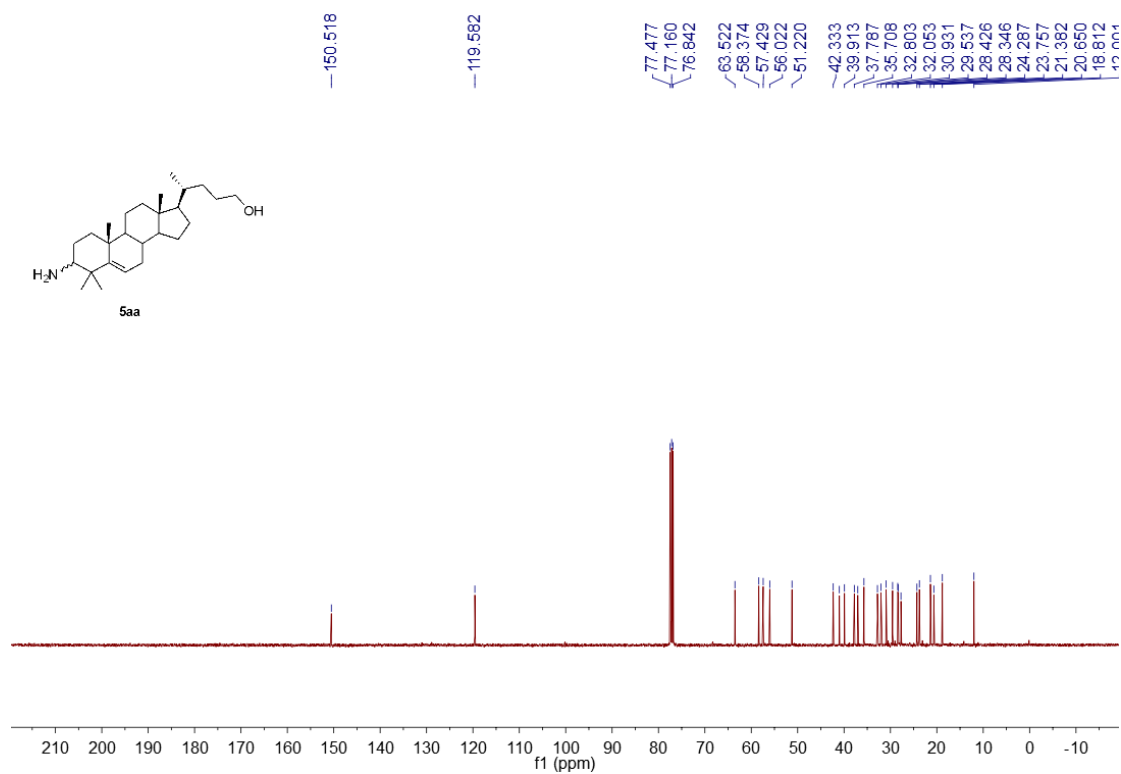
Compound **10** ( $^1\text{H}$  NMR)



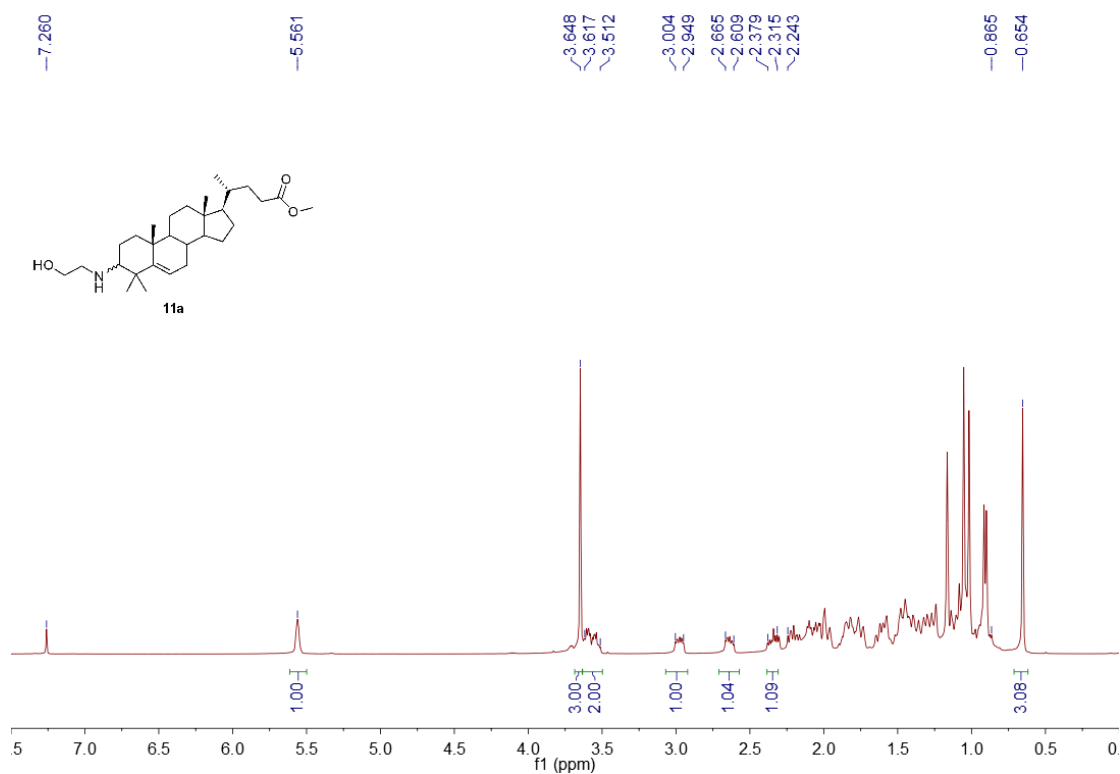
Compound **5aa** ( $^1\text{H}$  NMR)



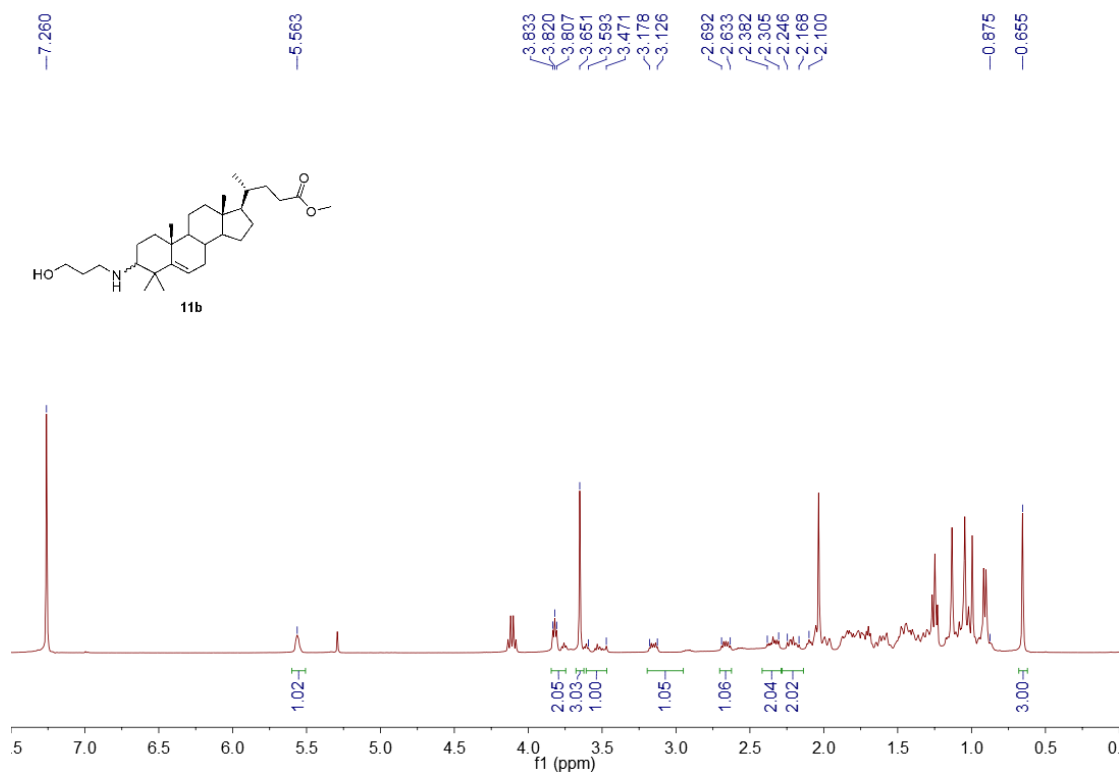
Compound **5aa** ( $^{13}\text{C}$  NMR)



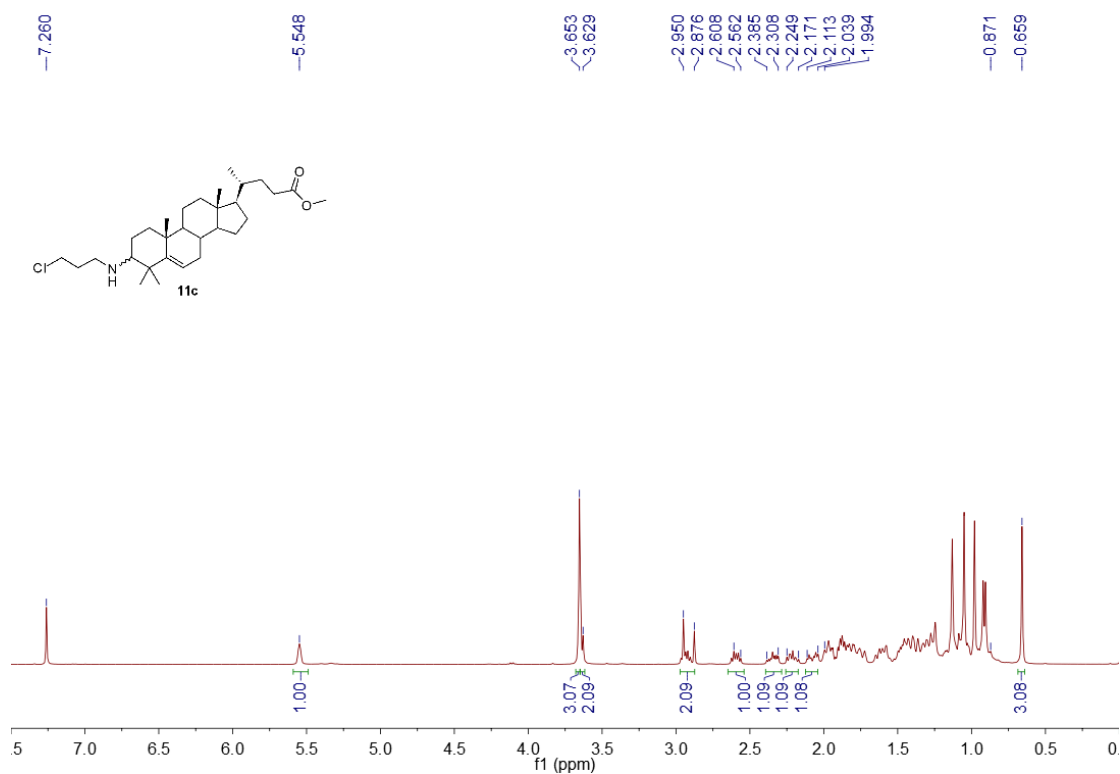
Compound **11a** ( $^1\text{H}$  NMR)



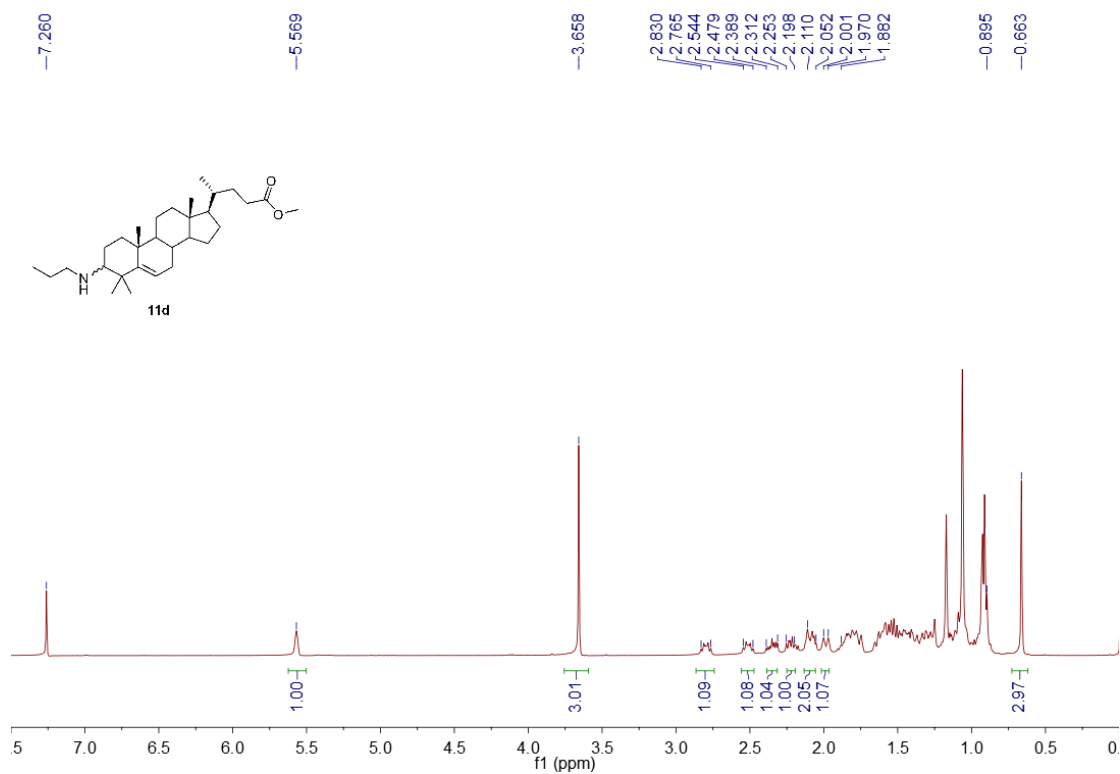
Compound **11b** ( $^1\text{H}$  NMR)



Compound **11c** ( $^1\text{H}$  NMR)

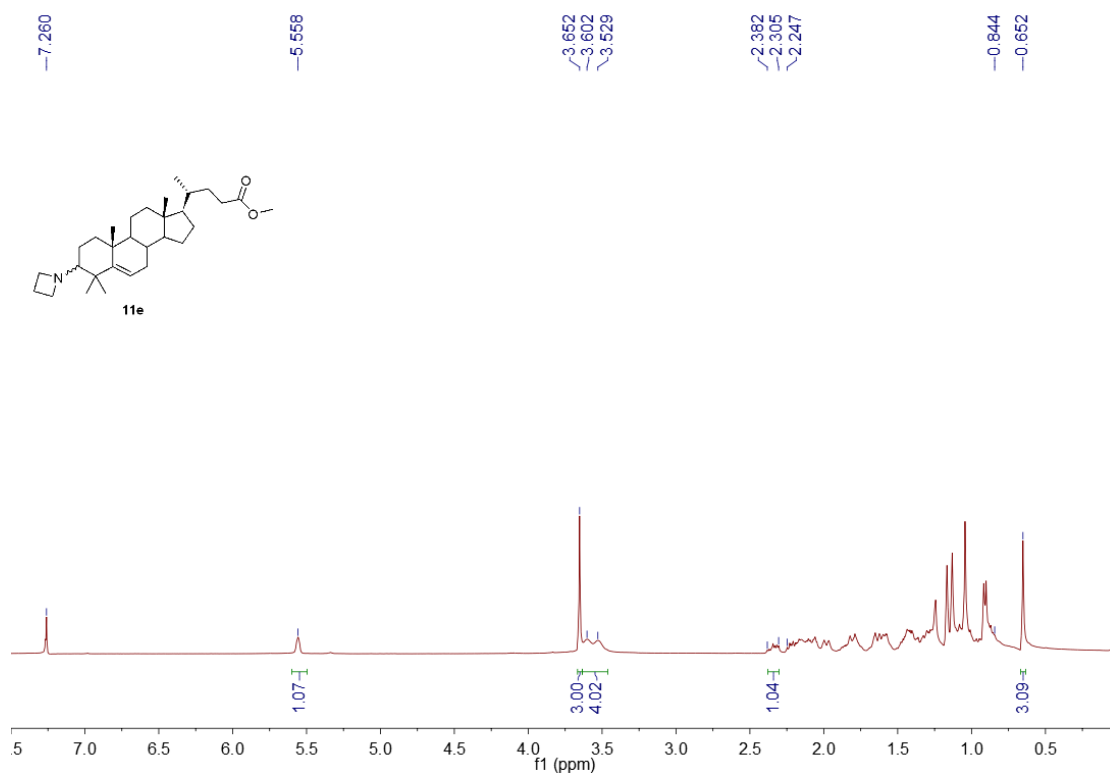


Compound **11d** ( $^1\text{H}$  NMR)

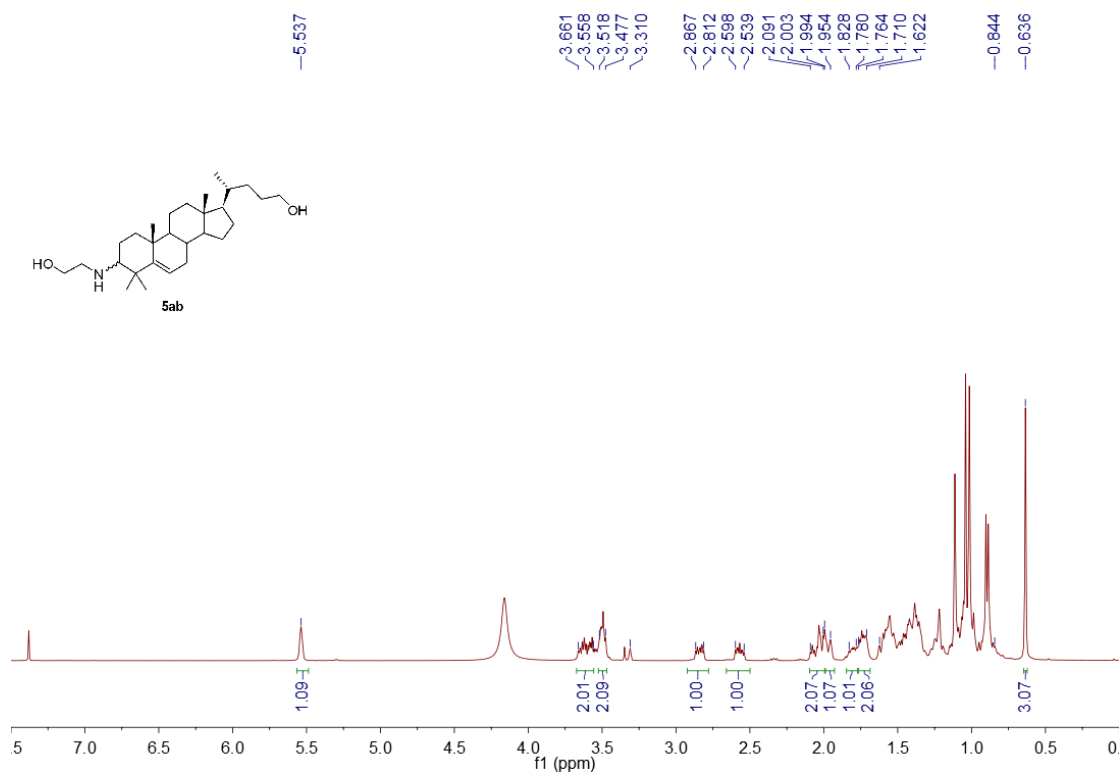




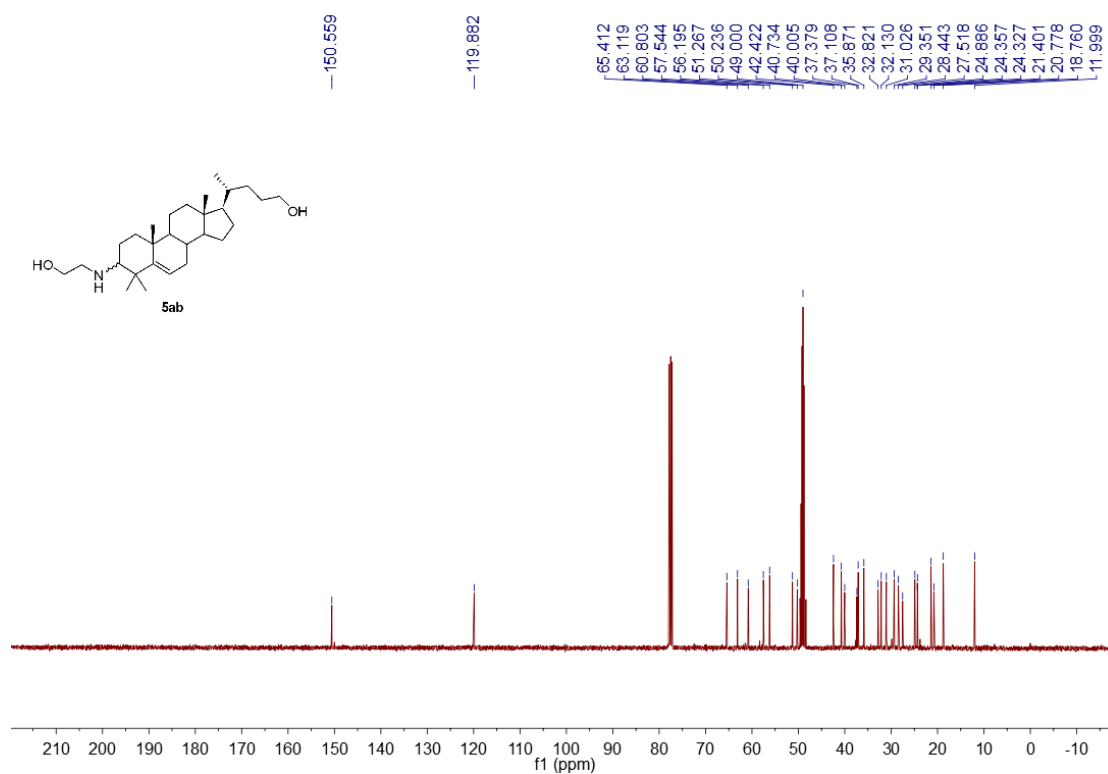
Compound **11e** ( $^1\text{H}$  NMR)



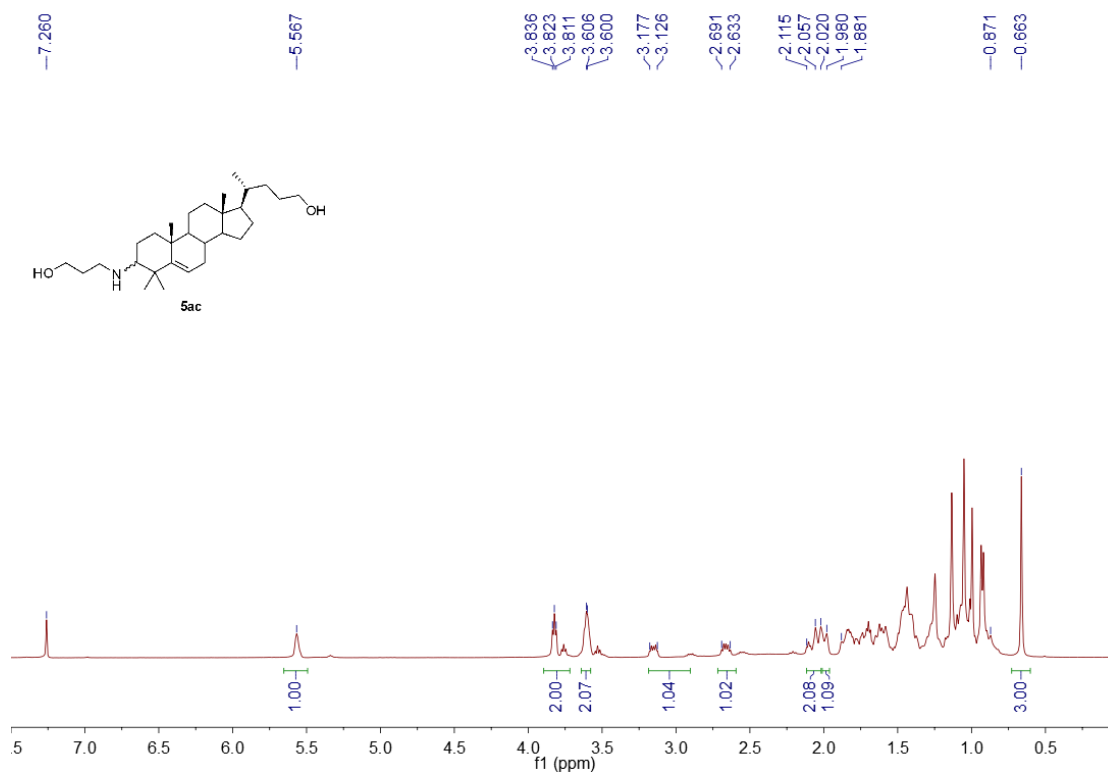
Compound **5ab** ( $^1\text{H}$  NMR)



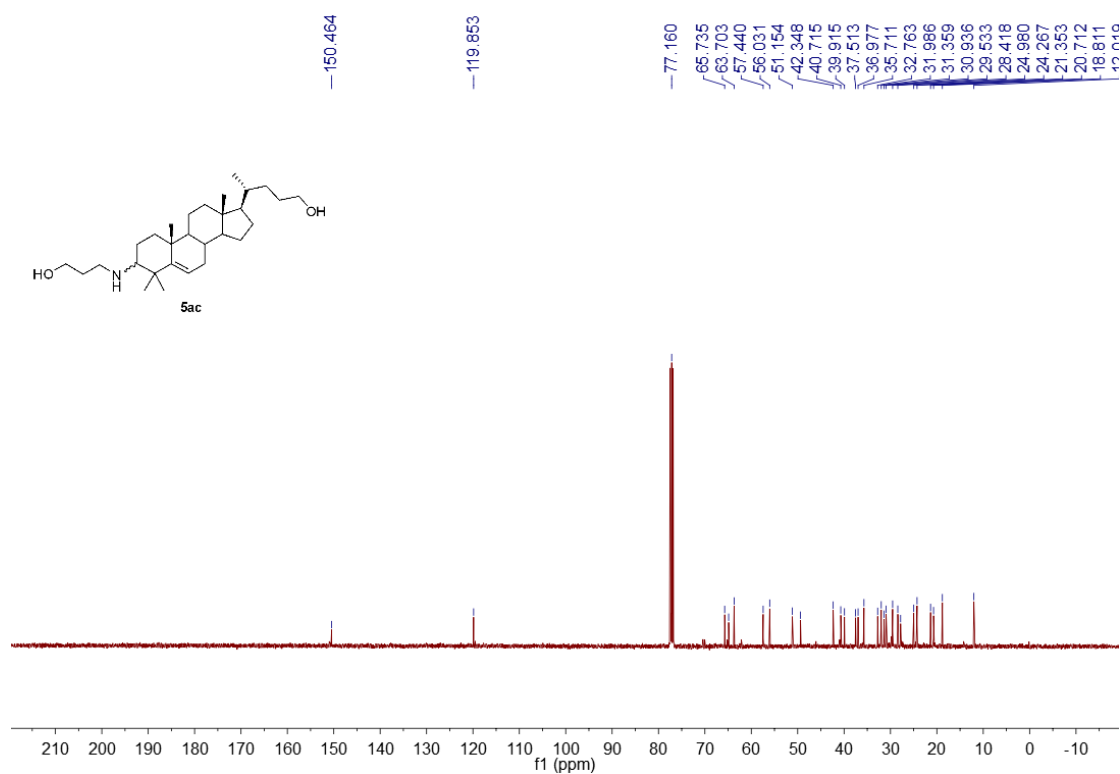
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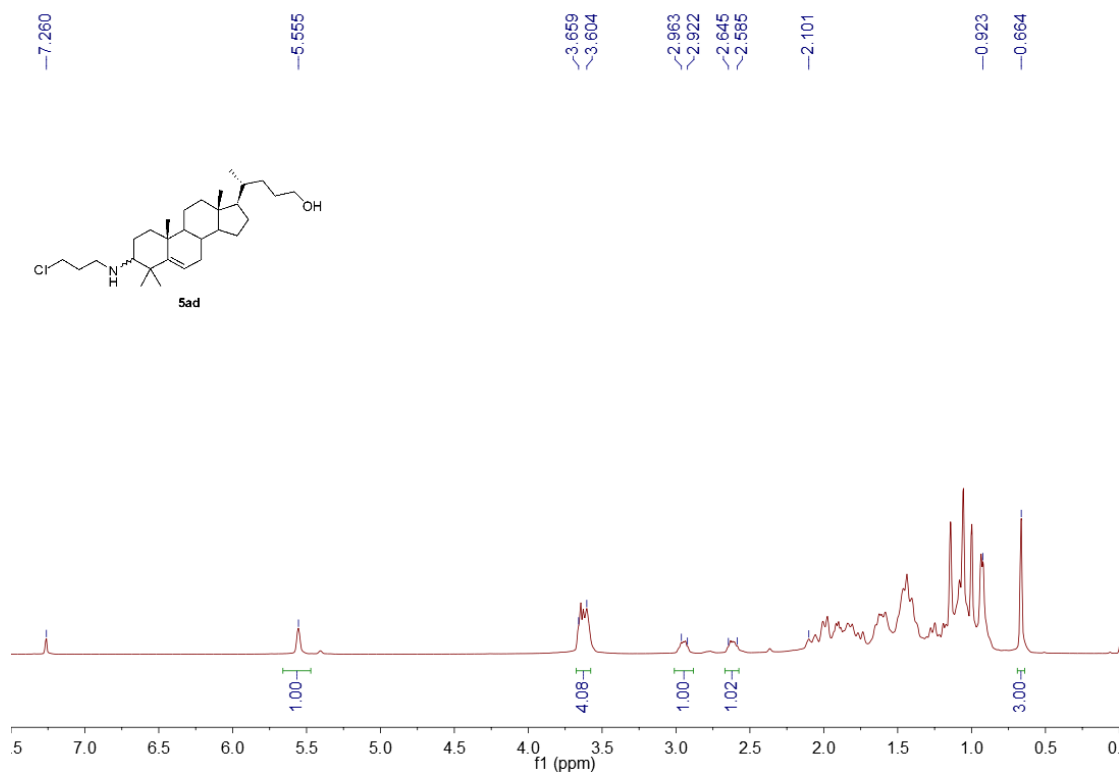
Compound **5ac** ( $^1\text{H}$  NMR)



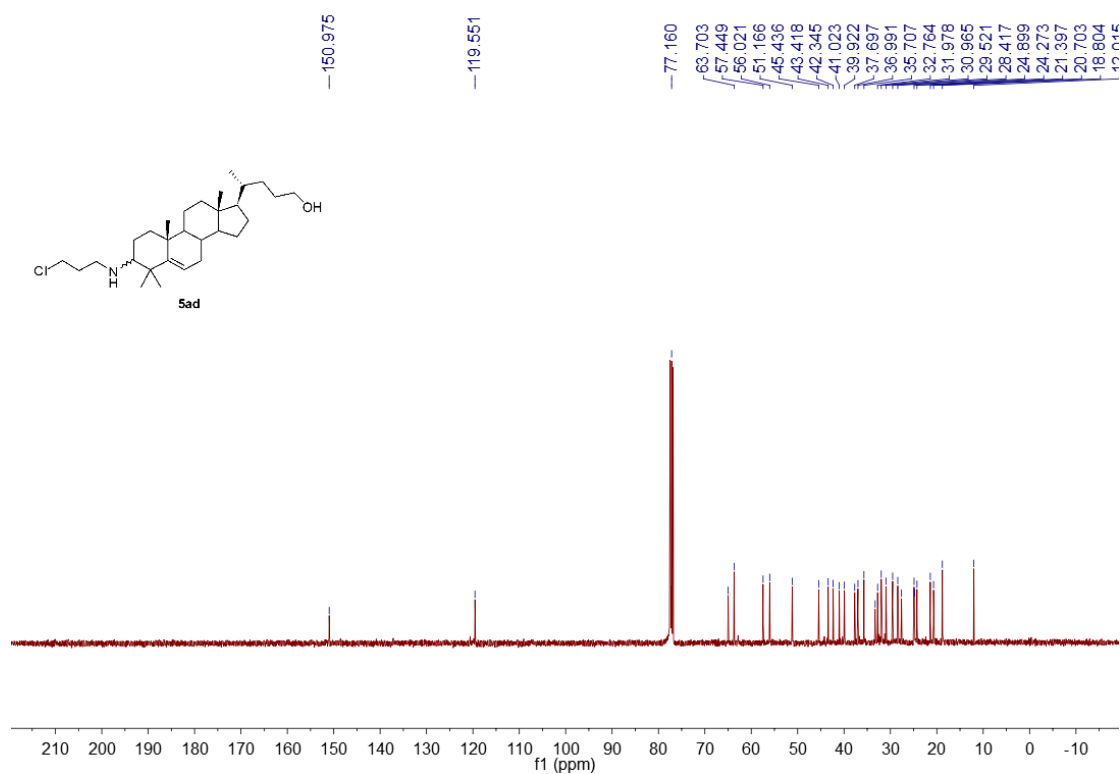
Compound **5ac** ( $^{13}\text{C}$  NMR)



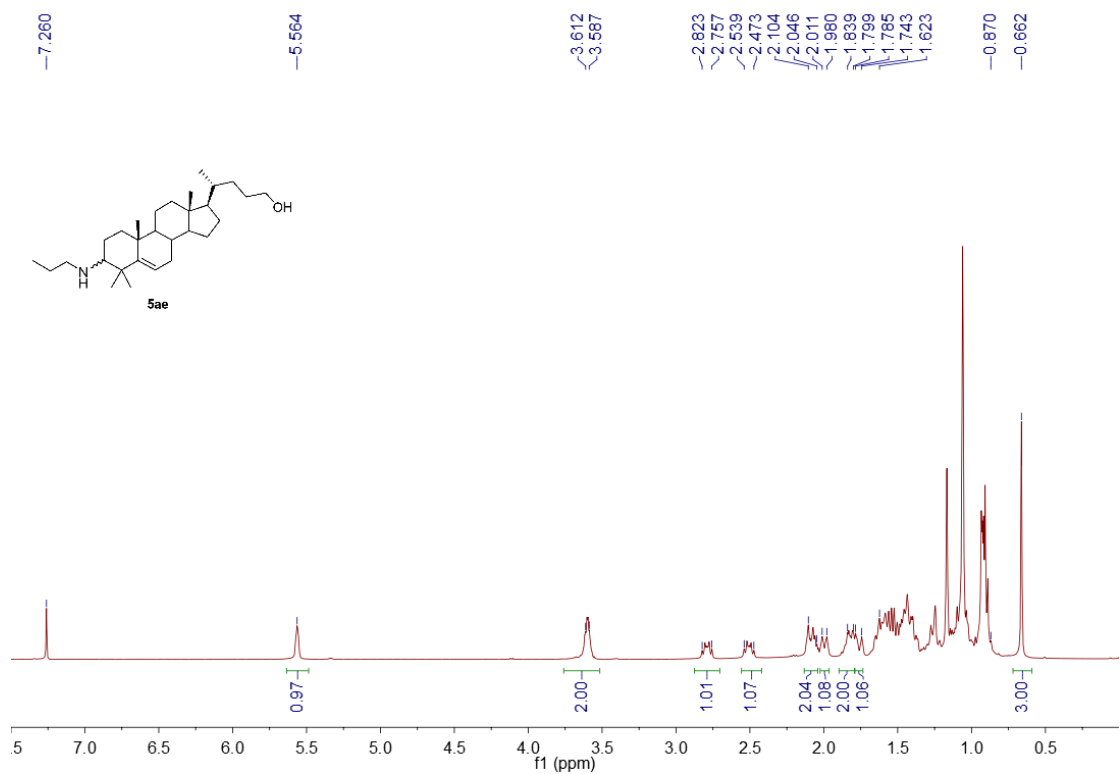
Compound **5ad** ( $^1\text{H}$  NMR)



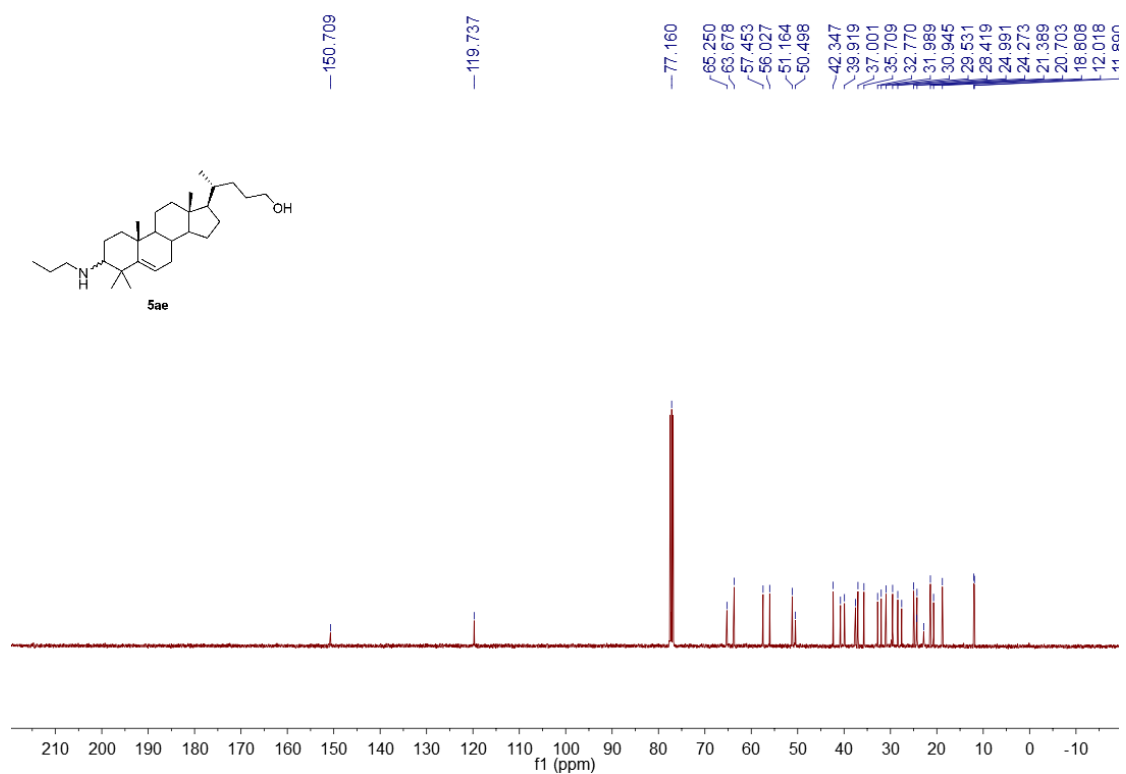
Compound **5ad** ( $^{13}\text{C}$  NMR)



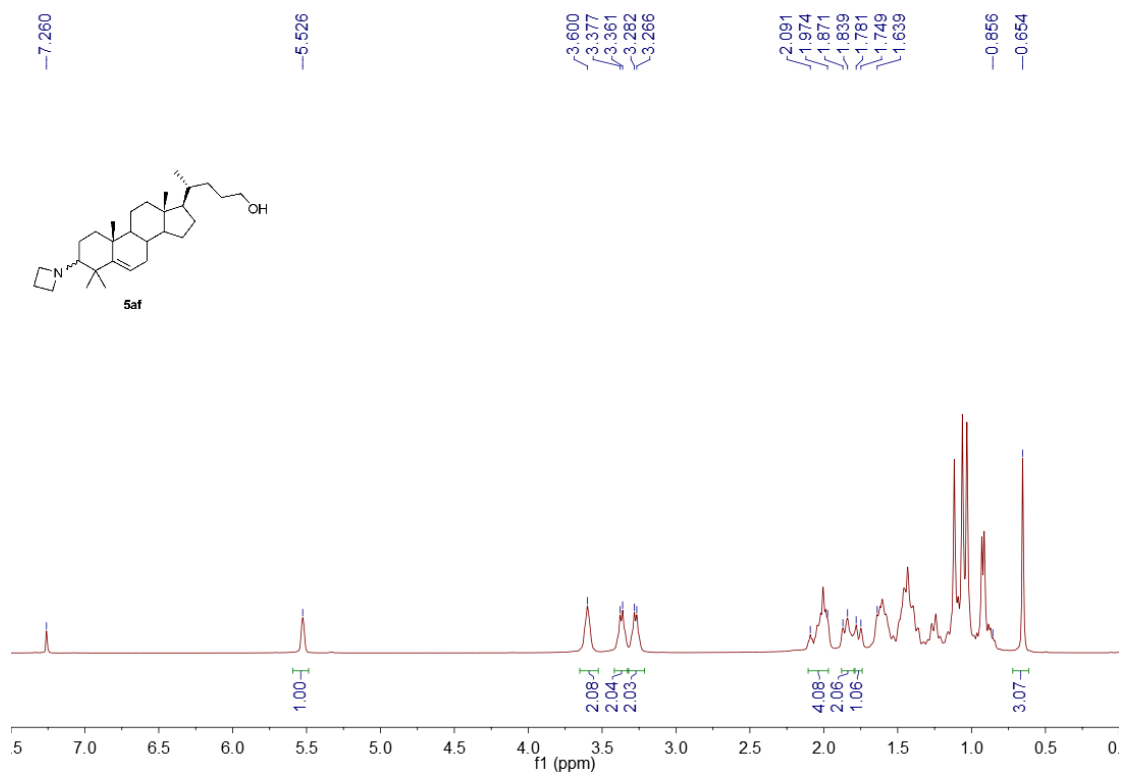
Compound **5ae** ( $^1\text{H}$  NMR)



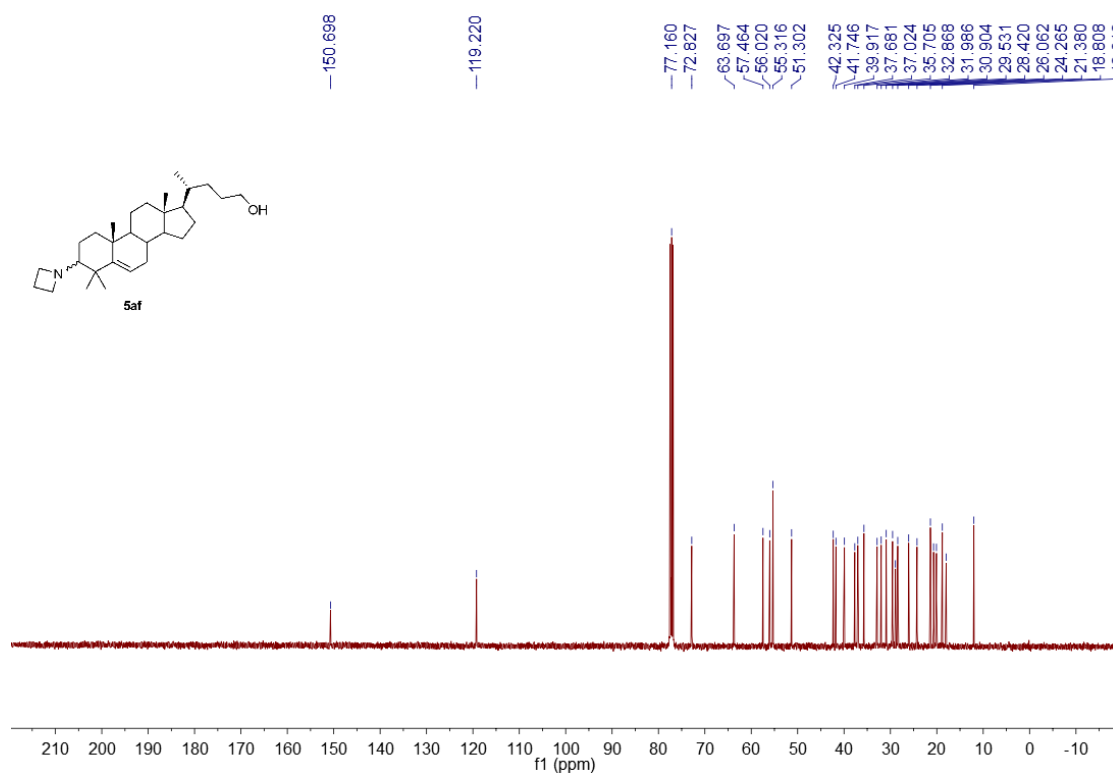
Compound **5ae** ( $^{13}\text{C}$  NMR)



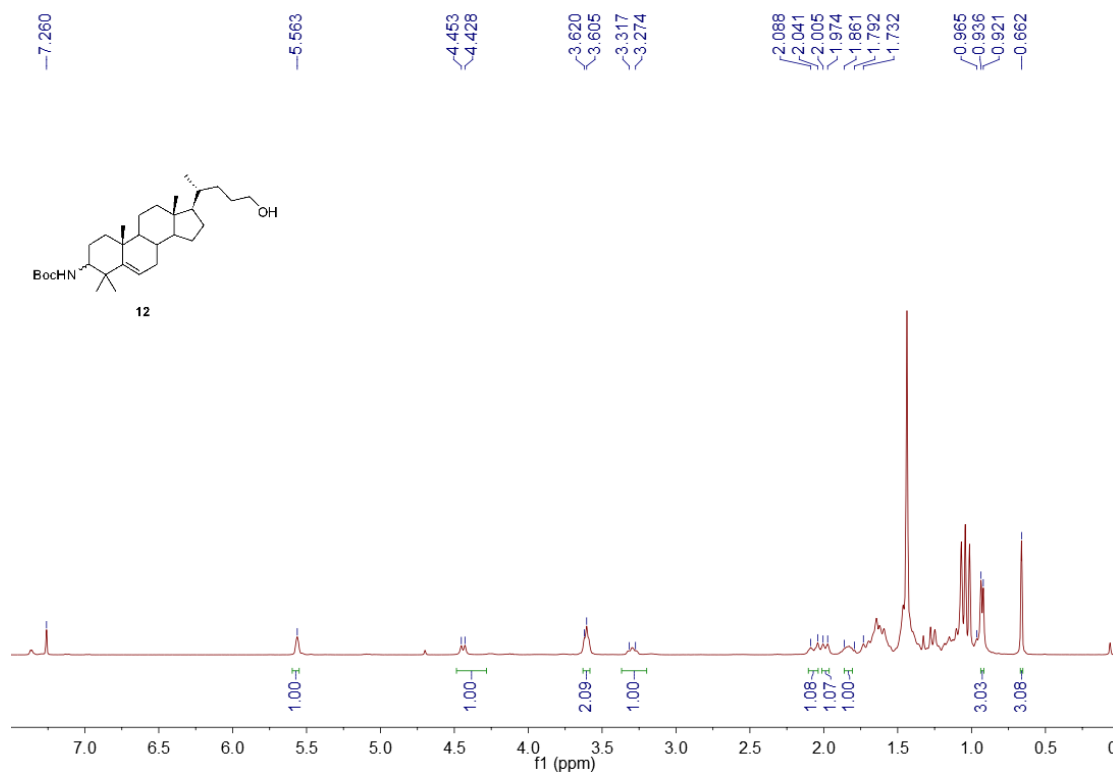
Compound **5af** ( $^1\text{H}$  NMR)



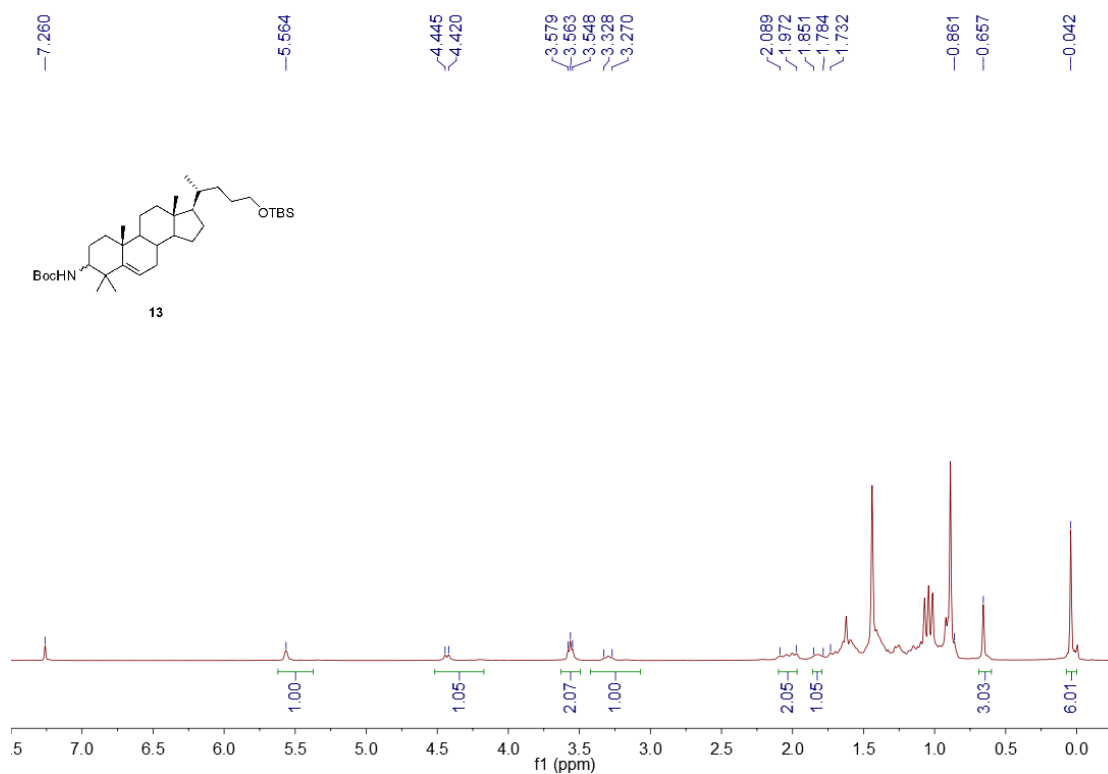
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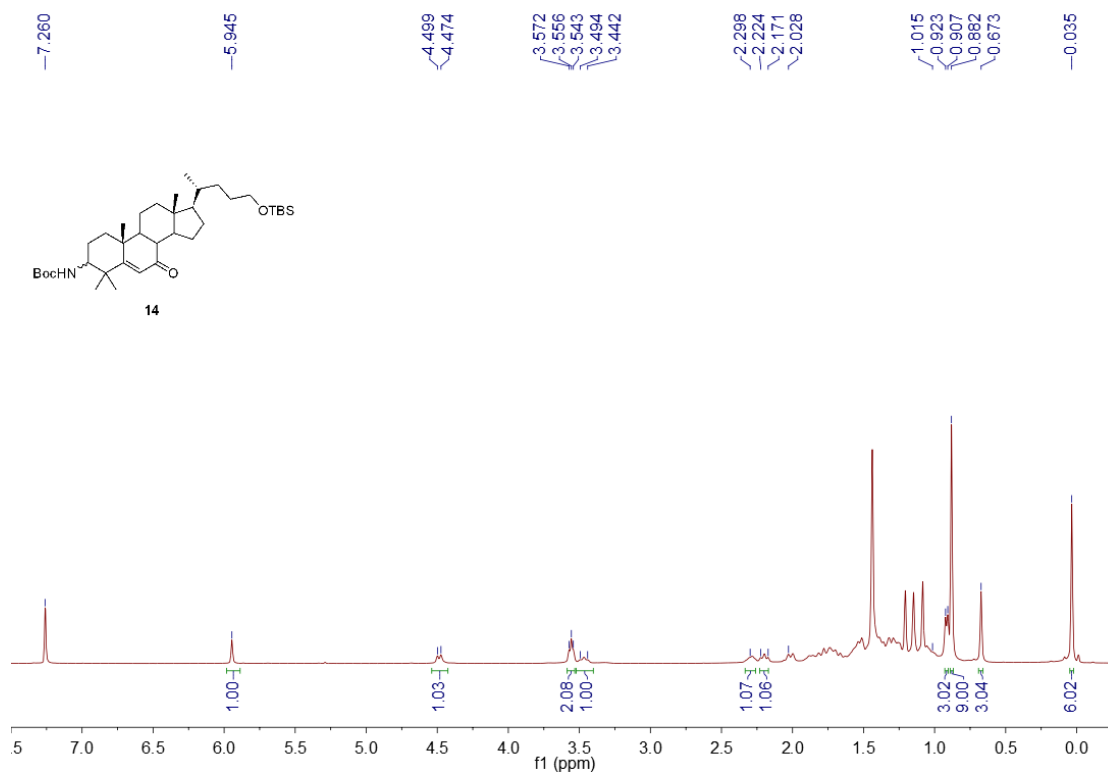
Compound **12** ( $^1\text{H}$  NMR)



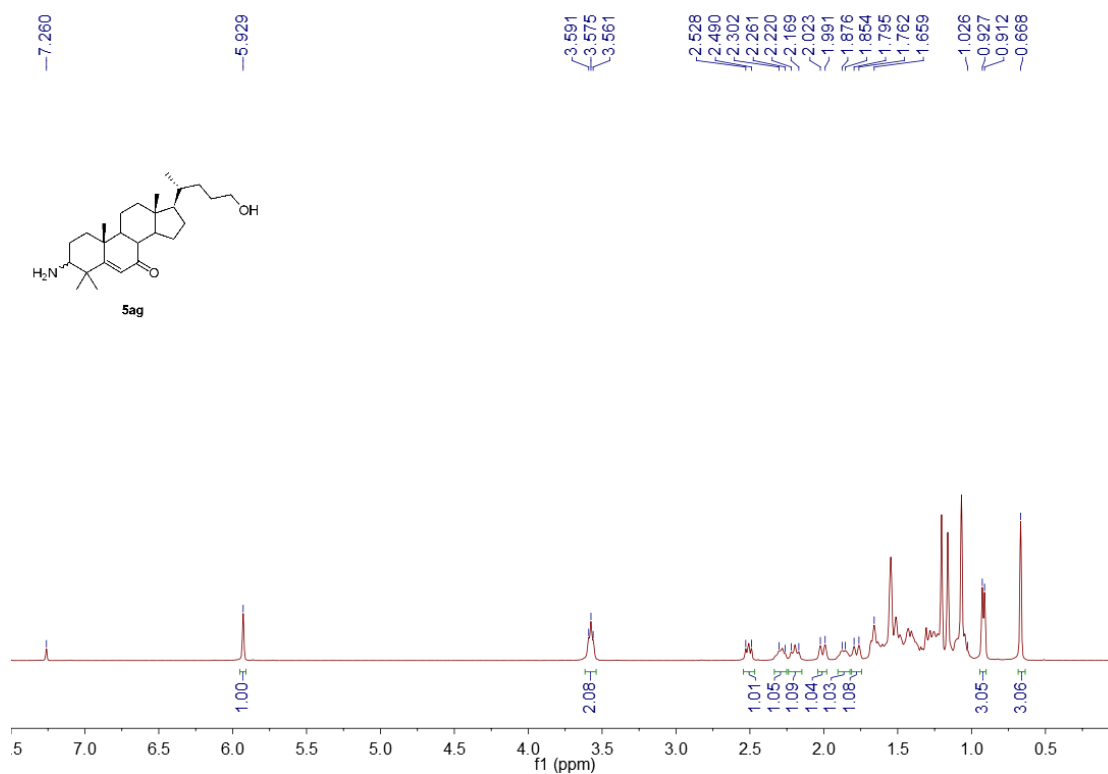
Compound **13** ( $^1\text{H}$  NMR)



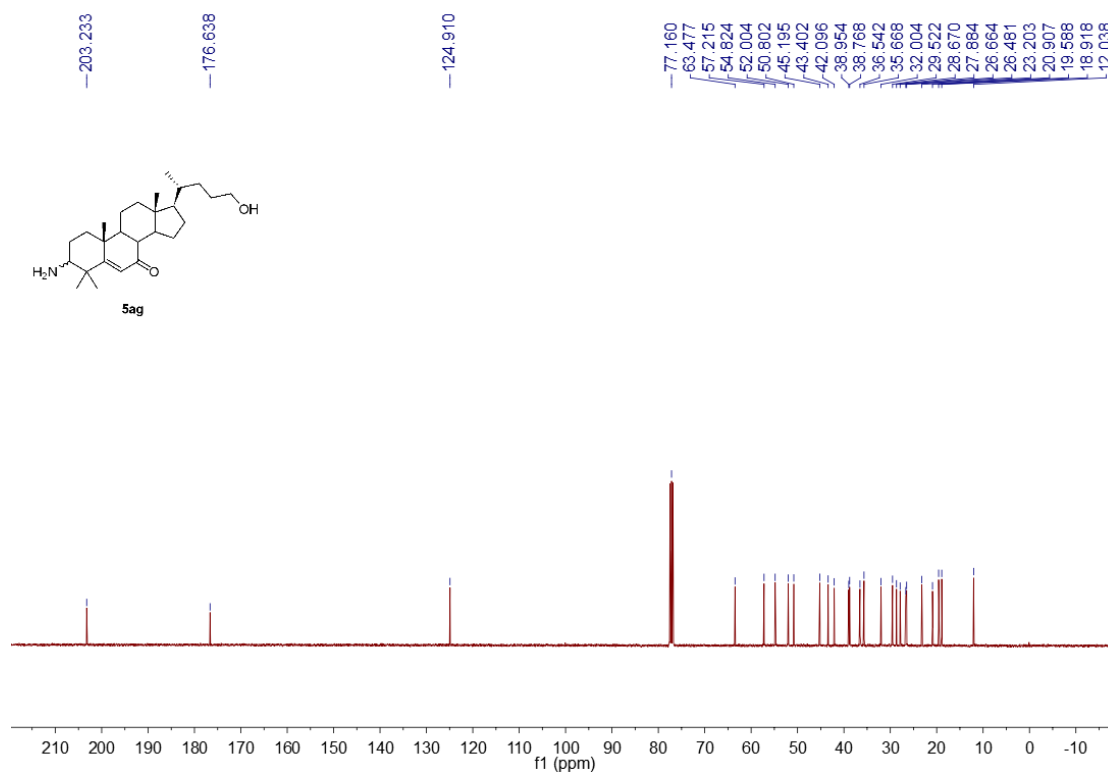
Compound **14** ( $^1\text{H}$  NMR)



Compound **5ag** ( $^1\text{H}$  NMR)

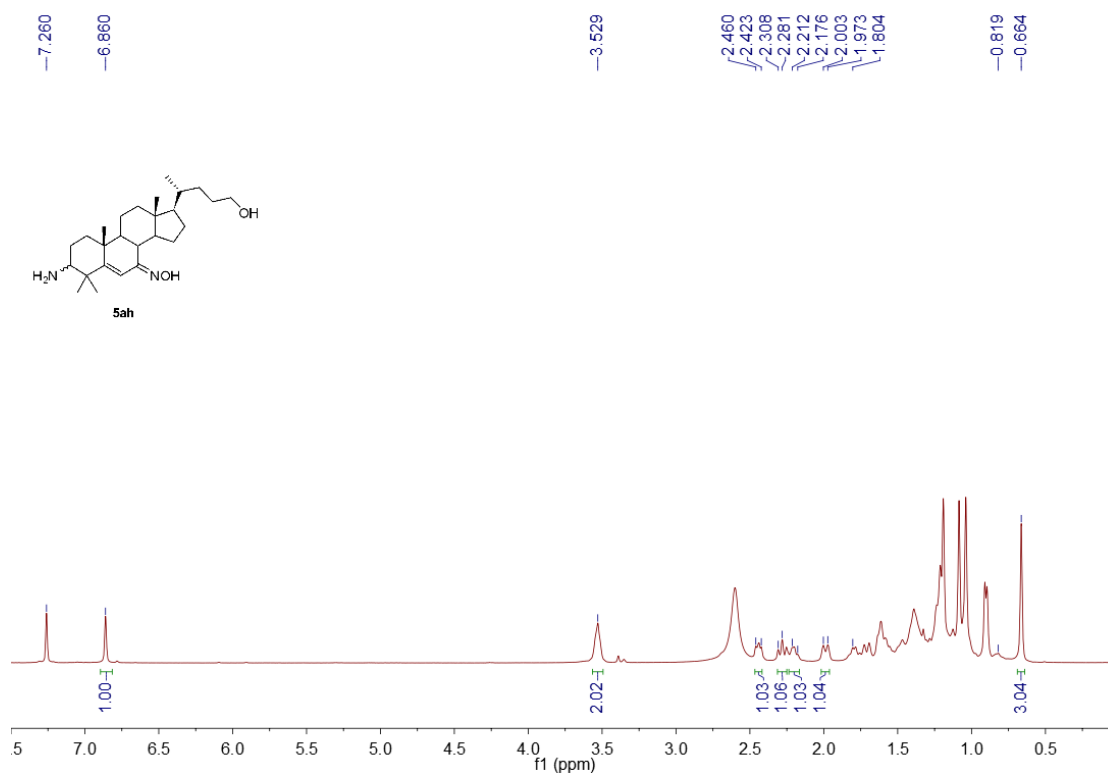


Compound **5ag** ( $^{13}\text{C}$  NMR)

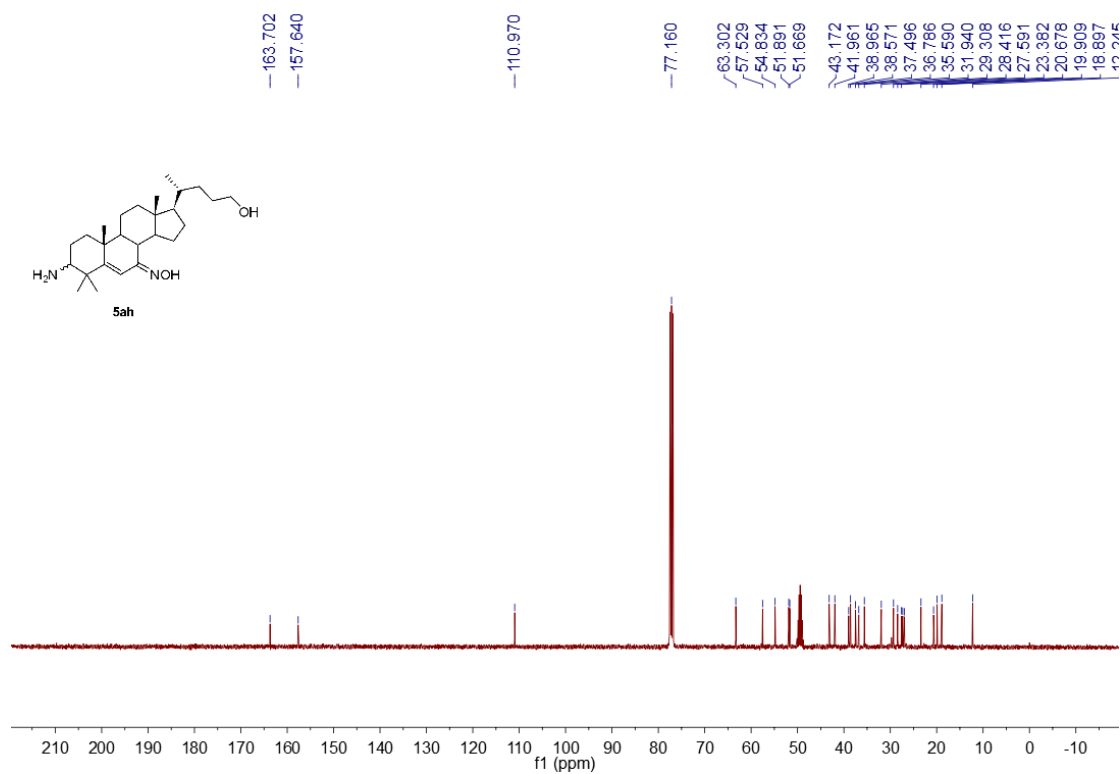




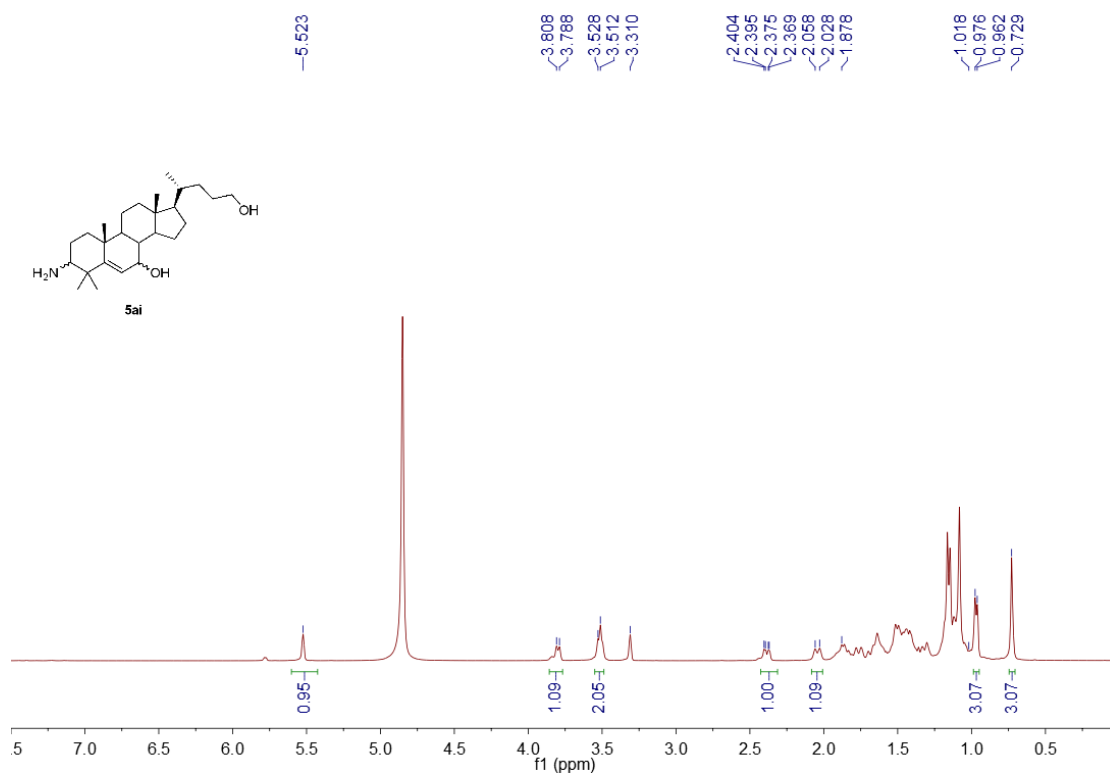
Compound **5ah** ( $^1\text{H}$  NMR)



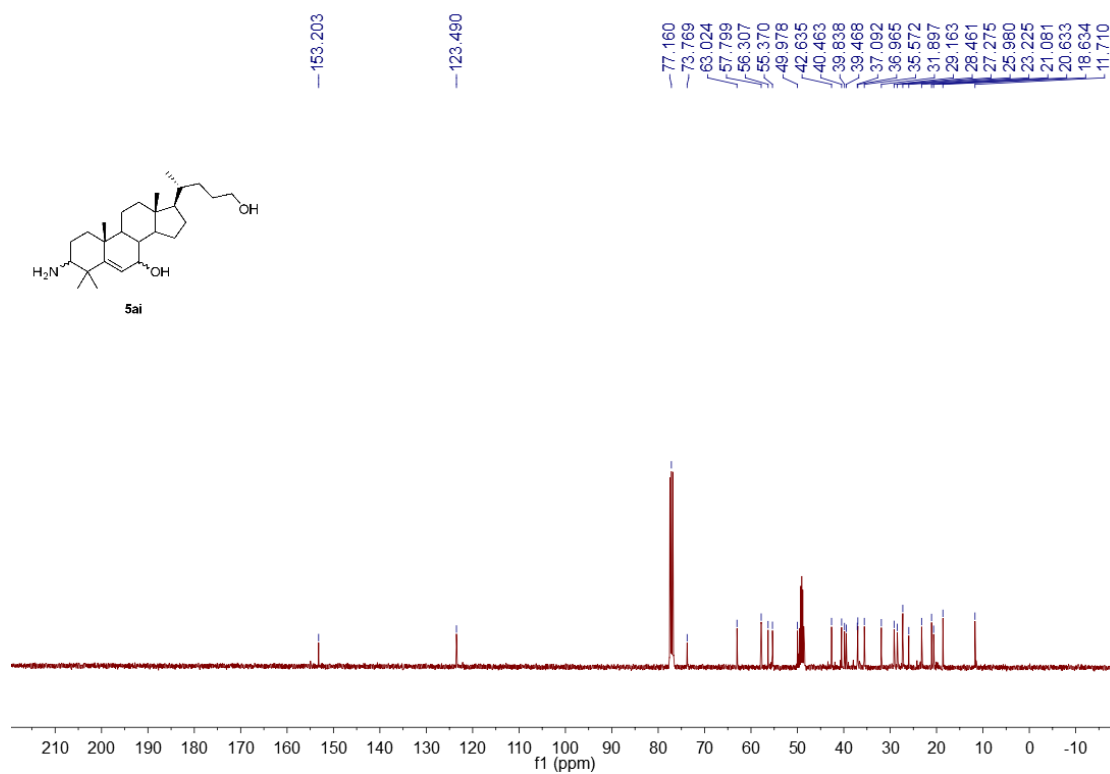
Compound **5ah** ( $^{13}\text{C}$  NMR)



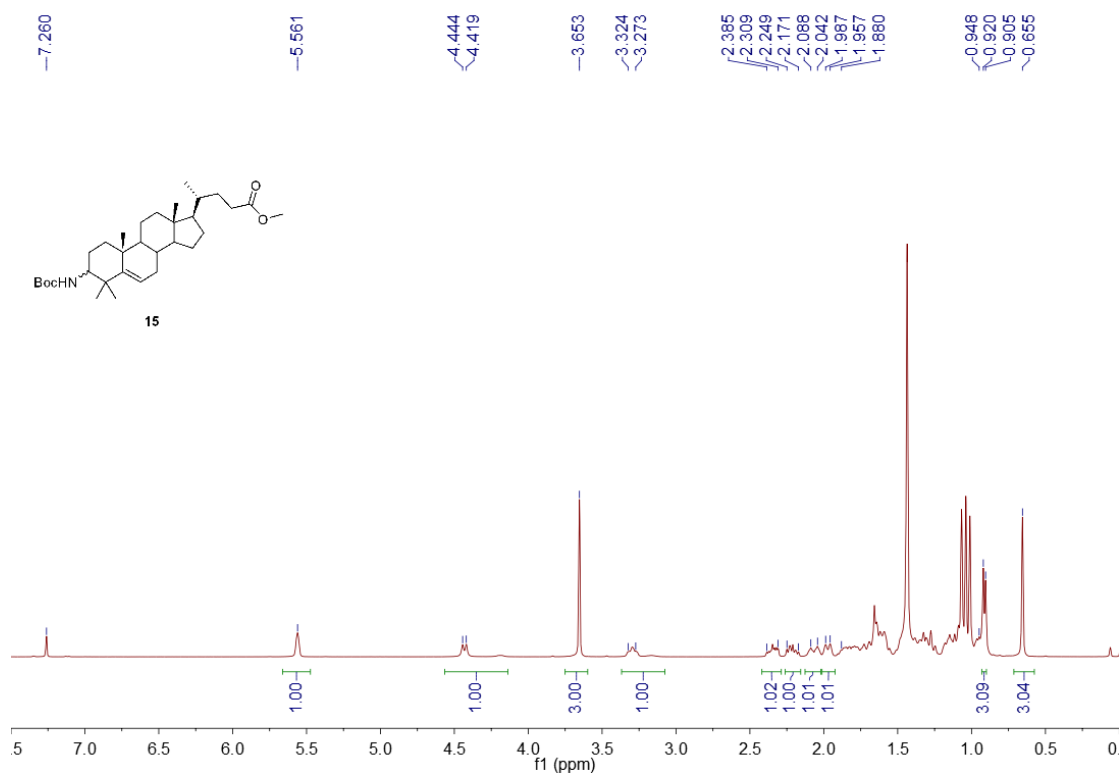
Compound **5ai** ( $^1\text{H}$  NMR)



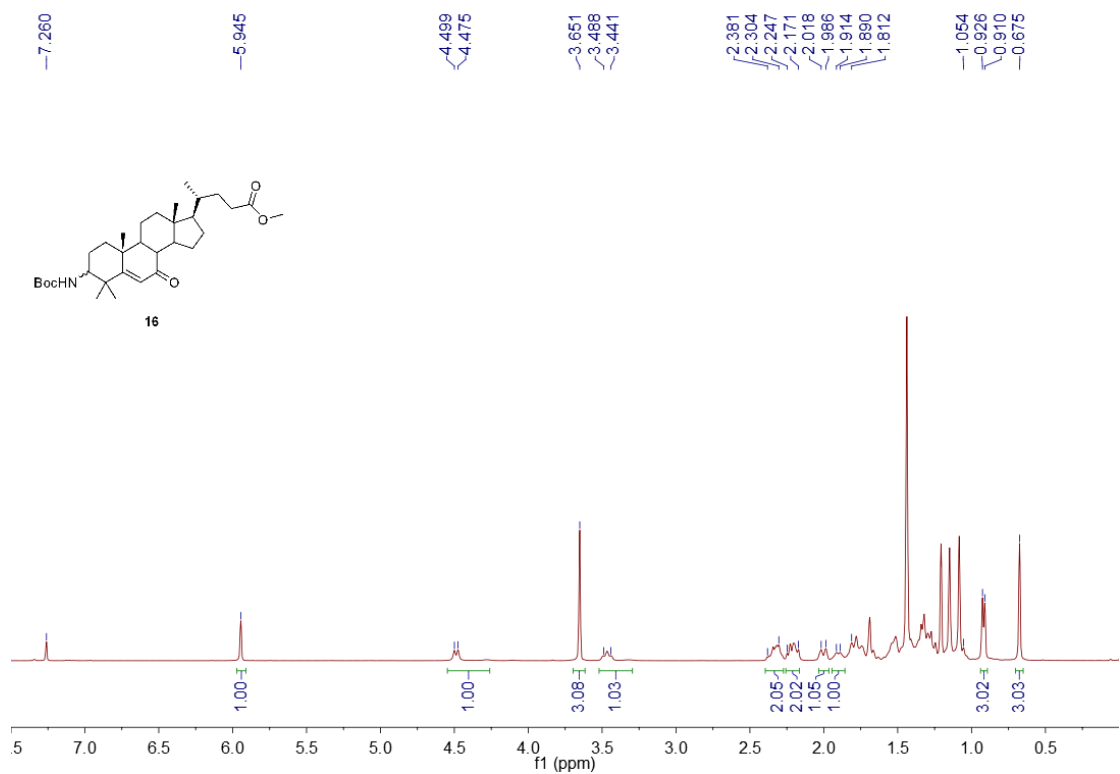
Compound **5ai** ( $^{13}\text{C}$  NMR)



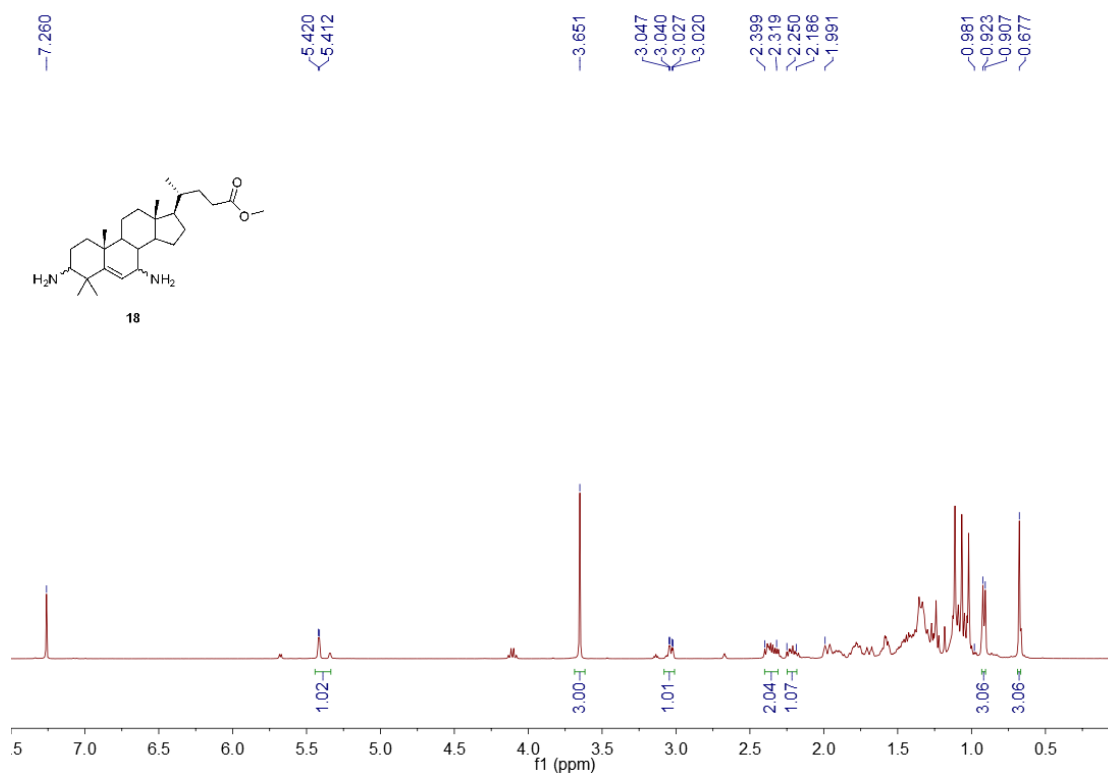
Compound **15** ( $^1\text{H}$  NMR)



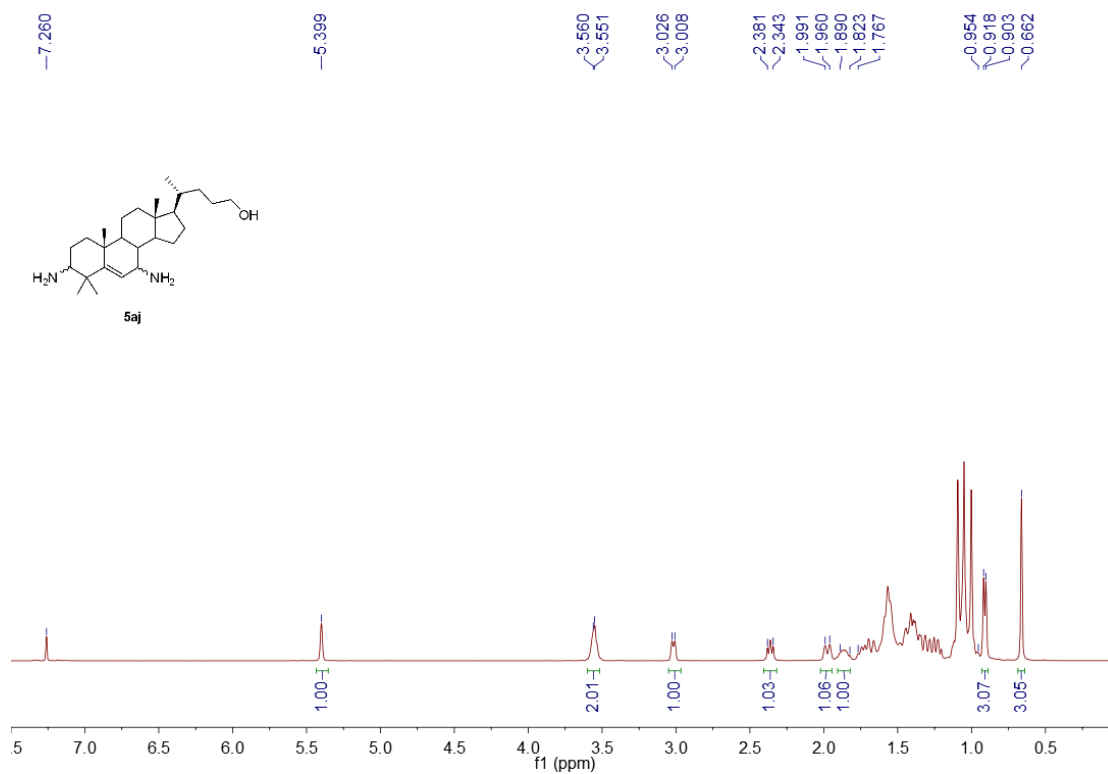
Compound **16** ( $^1\text{H}$  NMR)



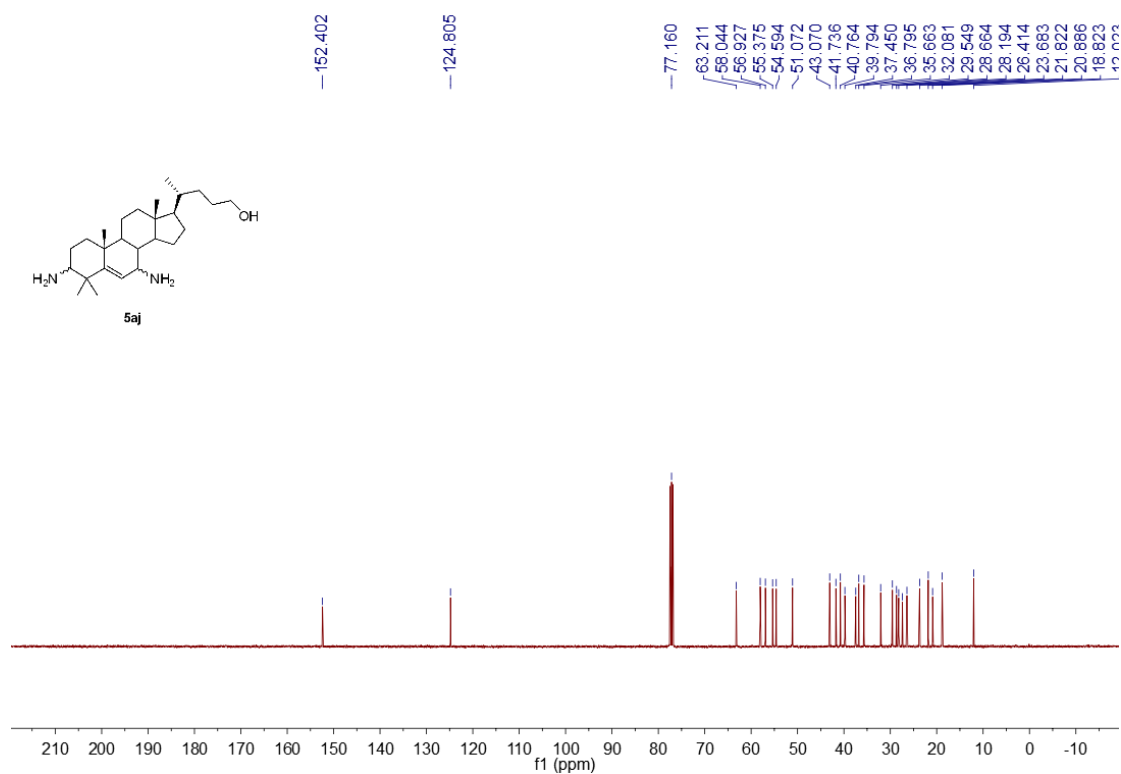
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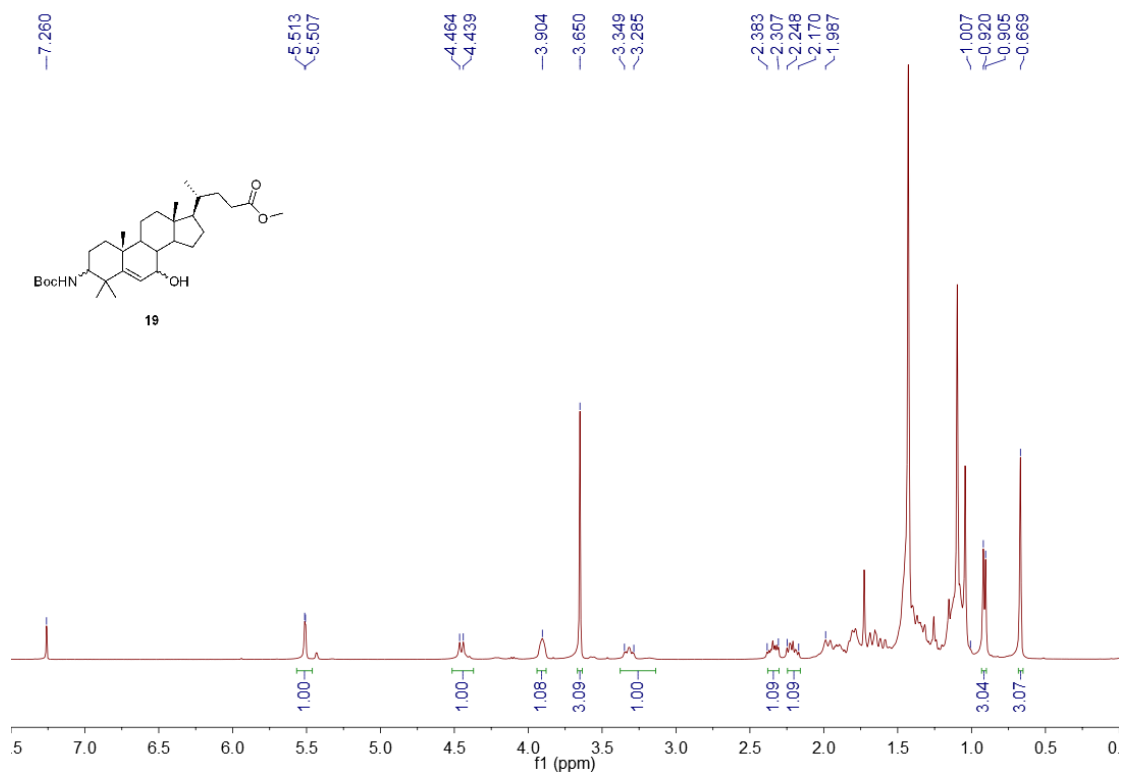
Compound **5aj** ( $^1\text{H}$  NMR)



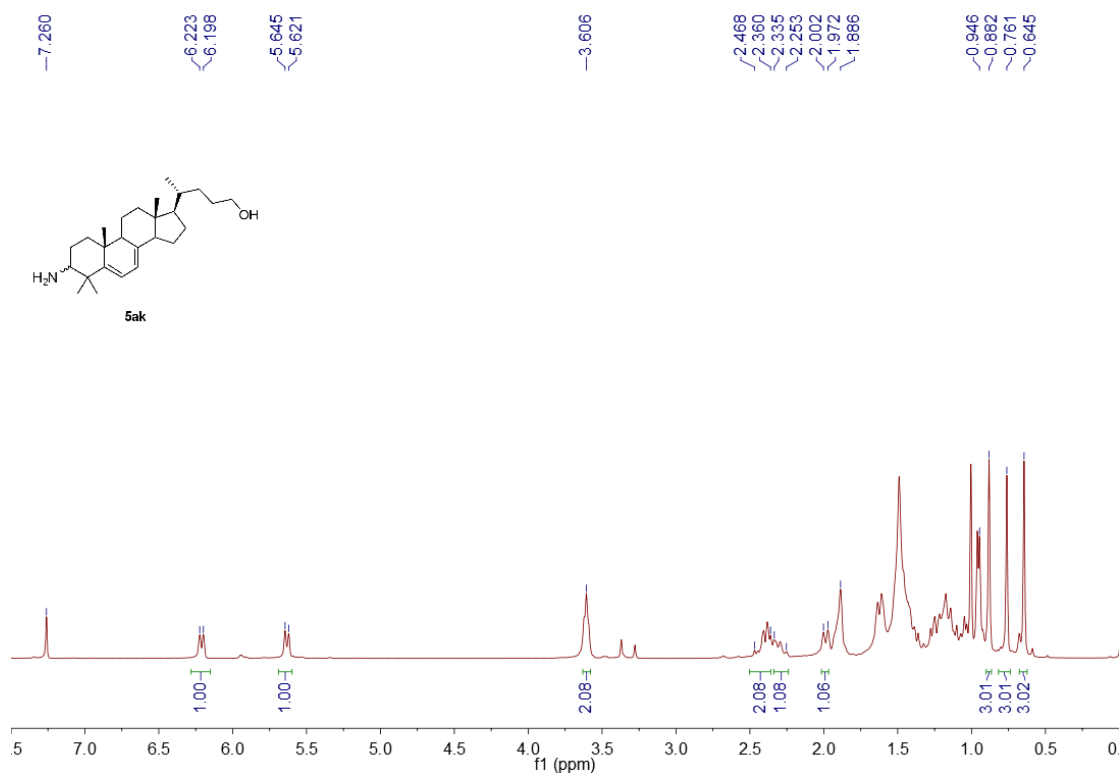
Compound **5aj** ( $^{13}\text{C}$  NMR)



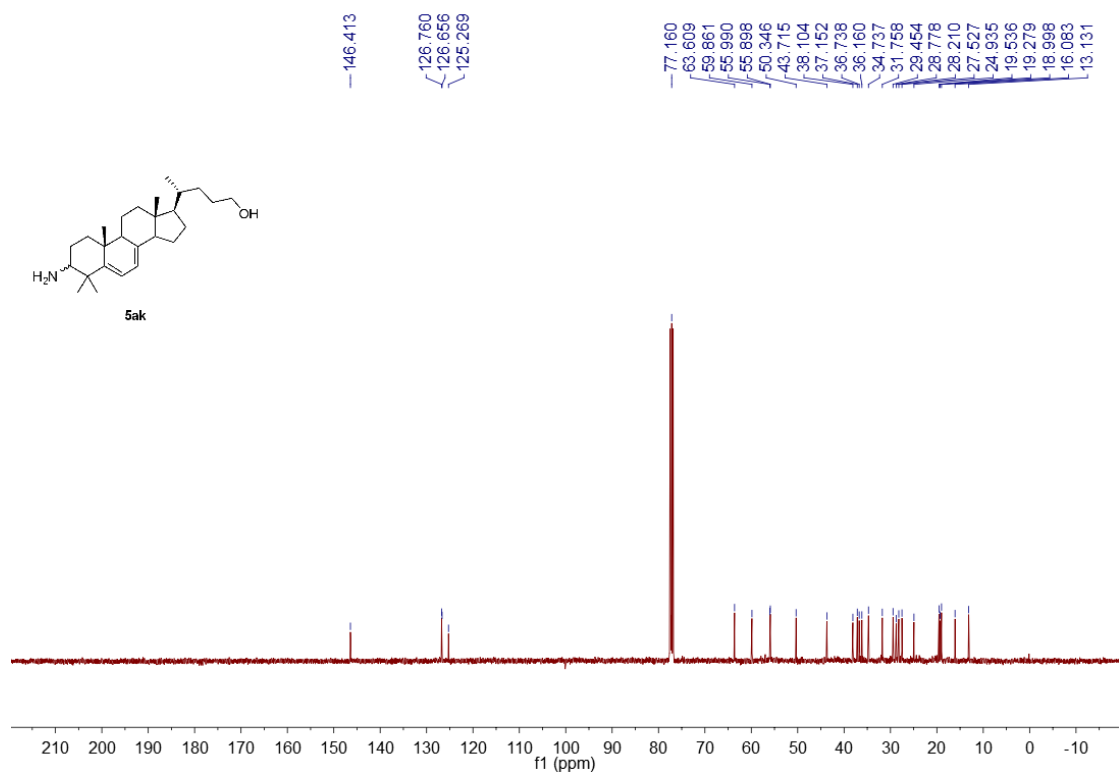
Compound **19** ( $^1\text{H}$  NMR)



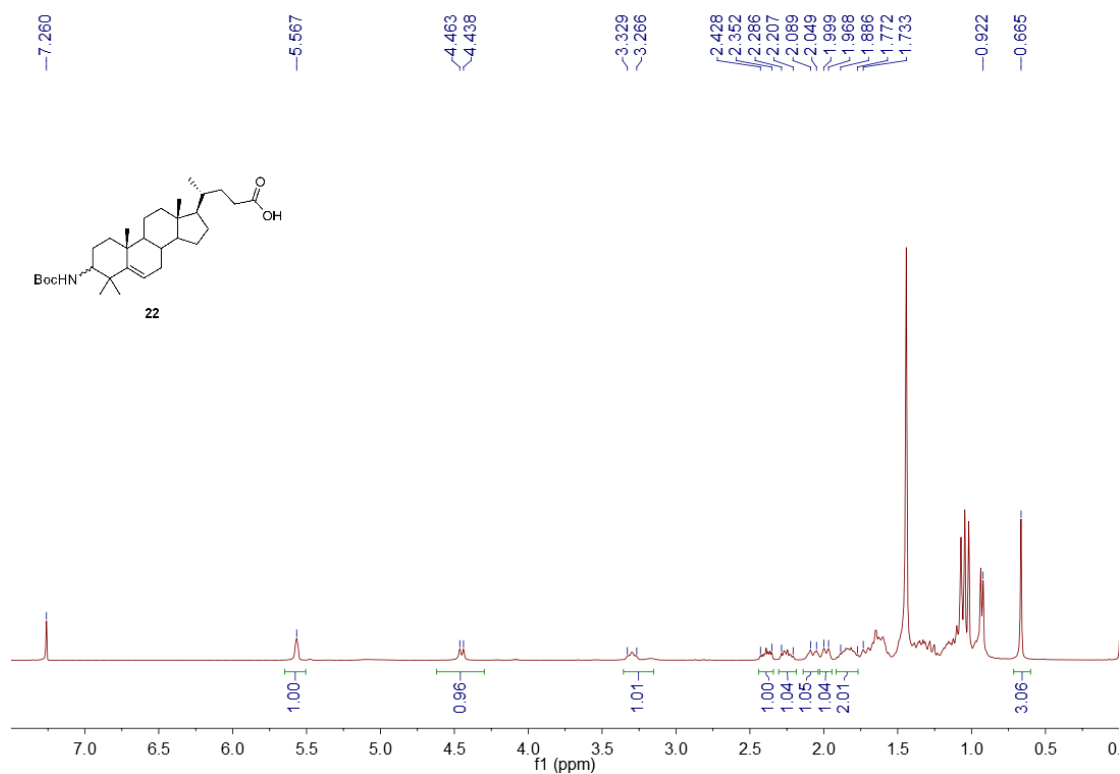
Compound **5ak** ( $^1\text{H}$  NMR)



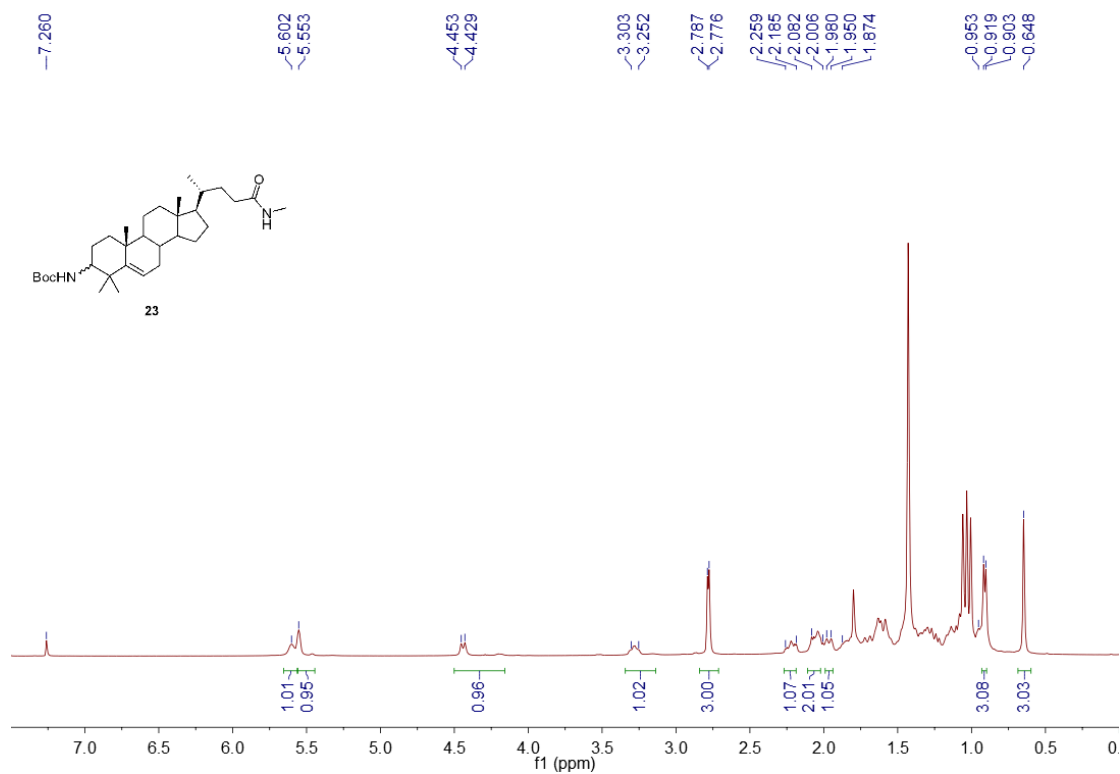
Compound **5ak** ( $^{13}\text{C}$  NMR)



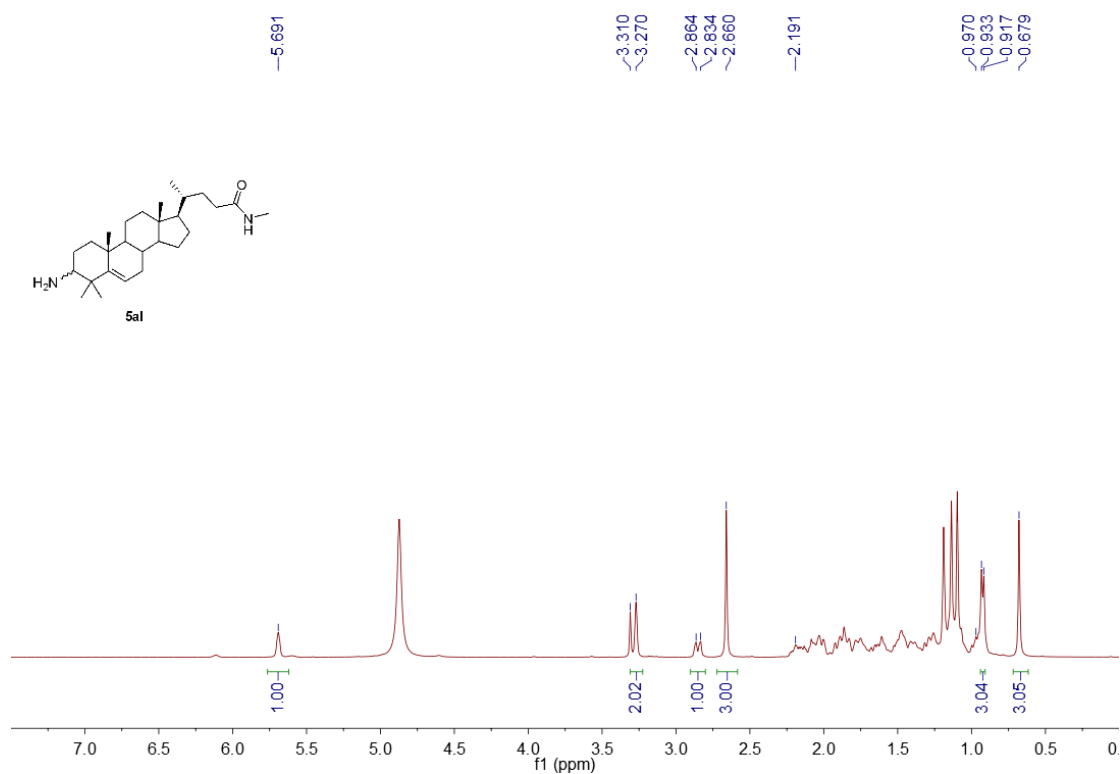
Compound **22** ( $^1\text{H}$  NMR)



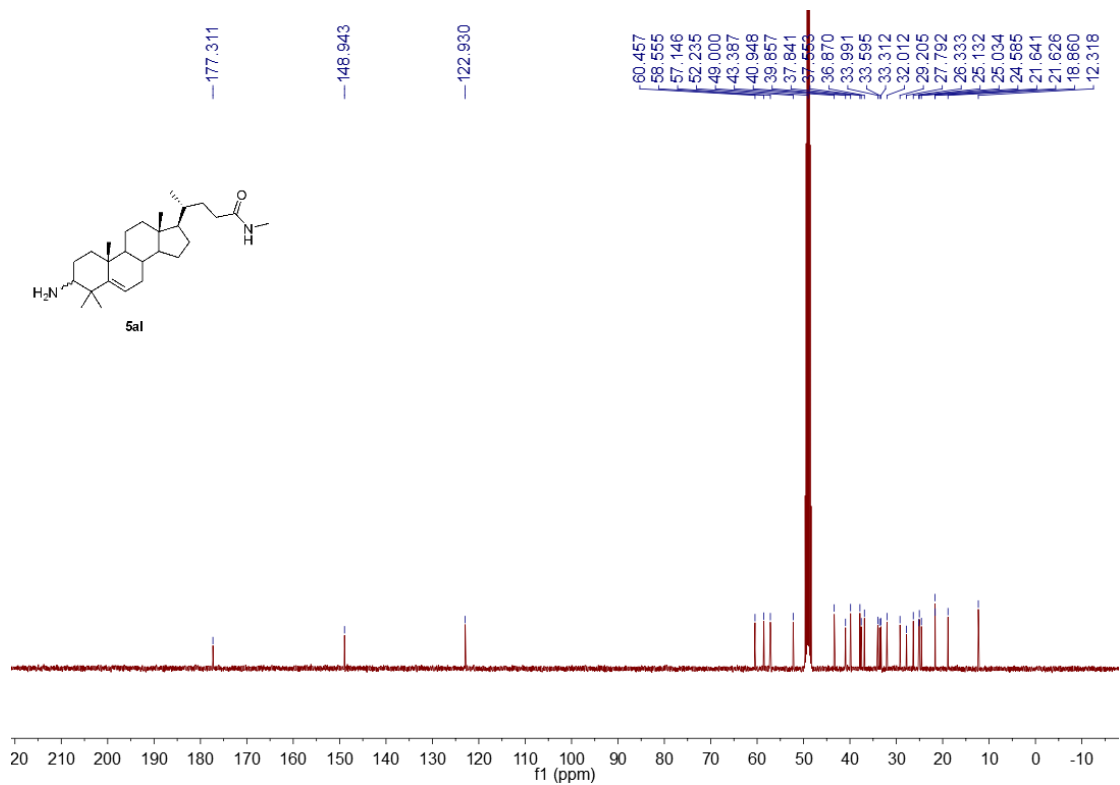
Compound **23** ( $^1\text{H}$  NMR)



Compound **5al** ( $^1\text{H}$  NMR)

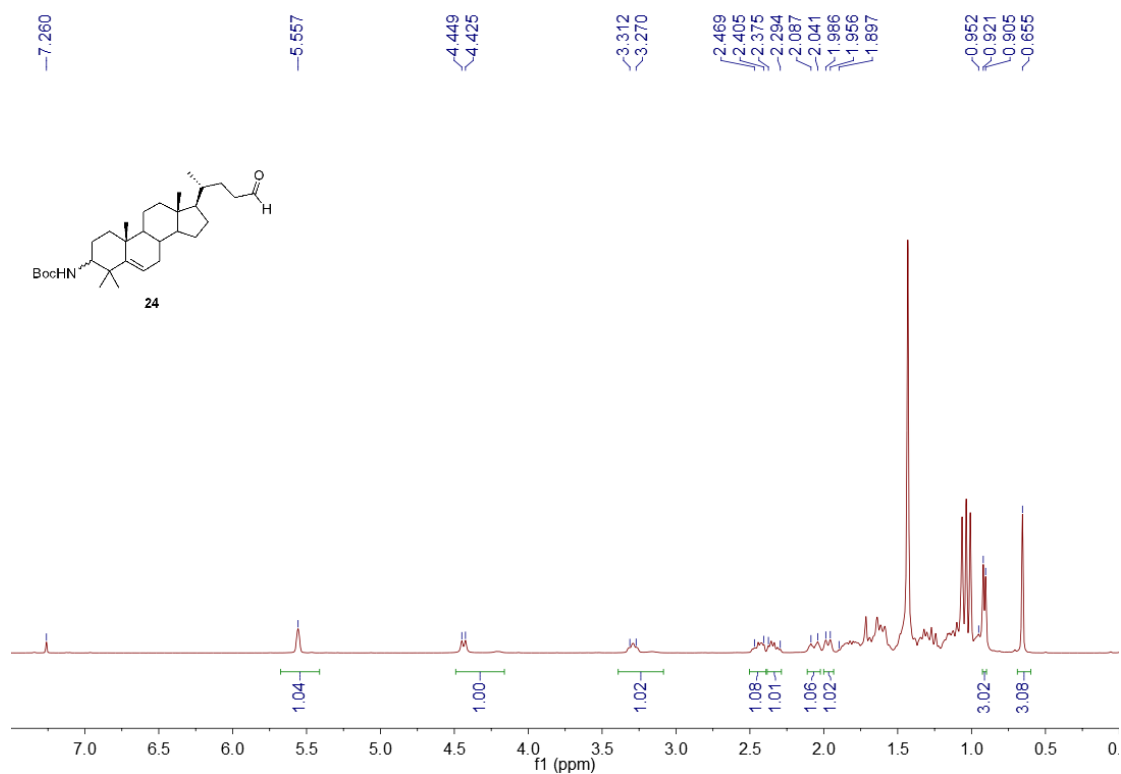


Compound **5al** ( $^{13}\text{C}$  NMR)

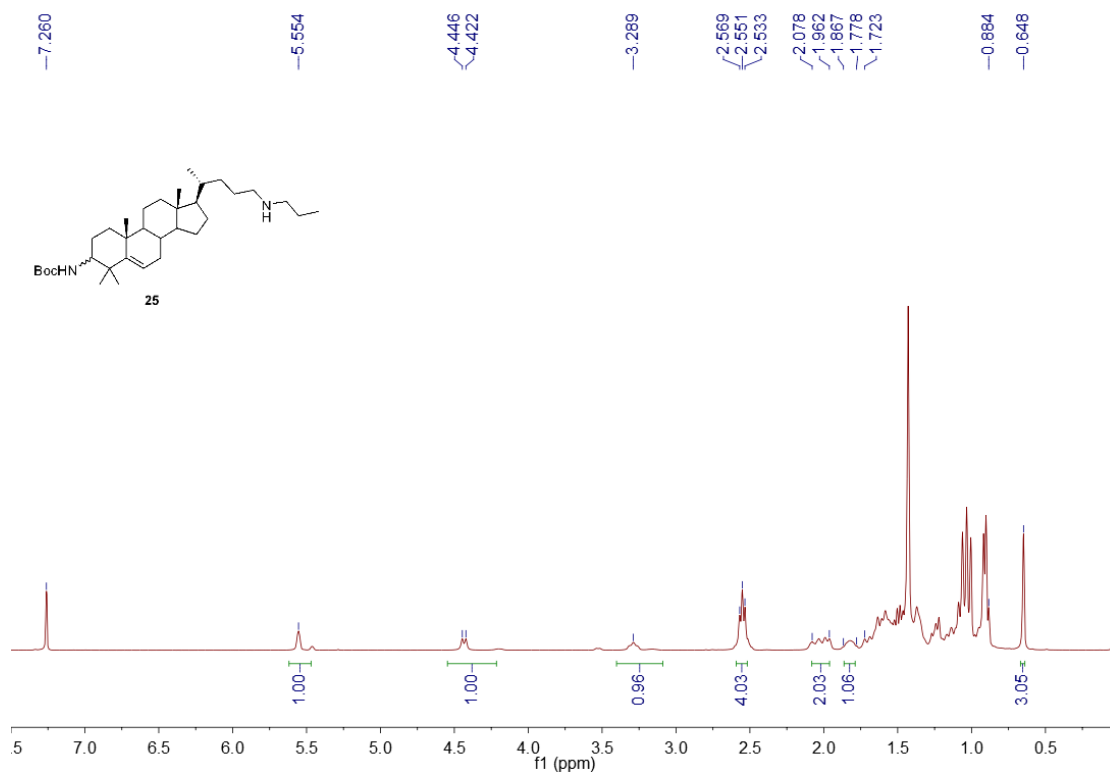




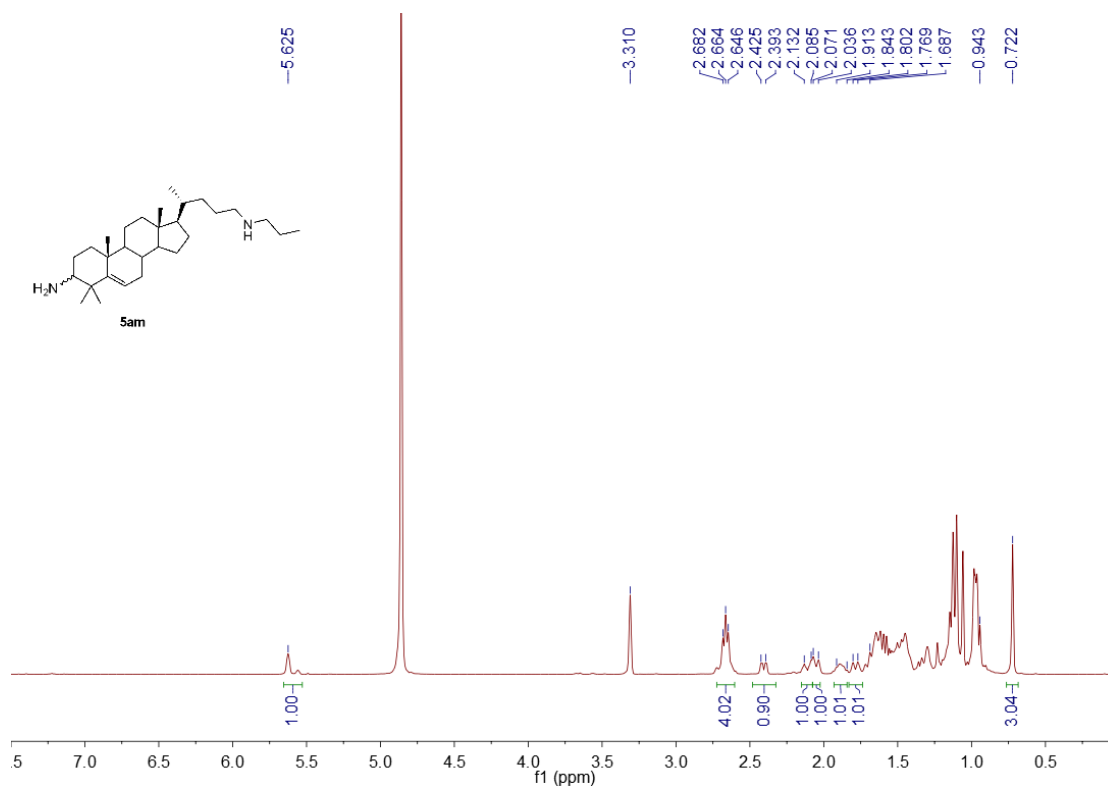
Compound **24** ( $^1\text{H}$  NMR)



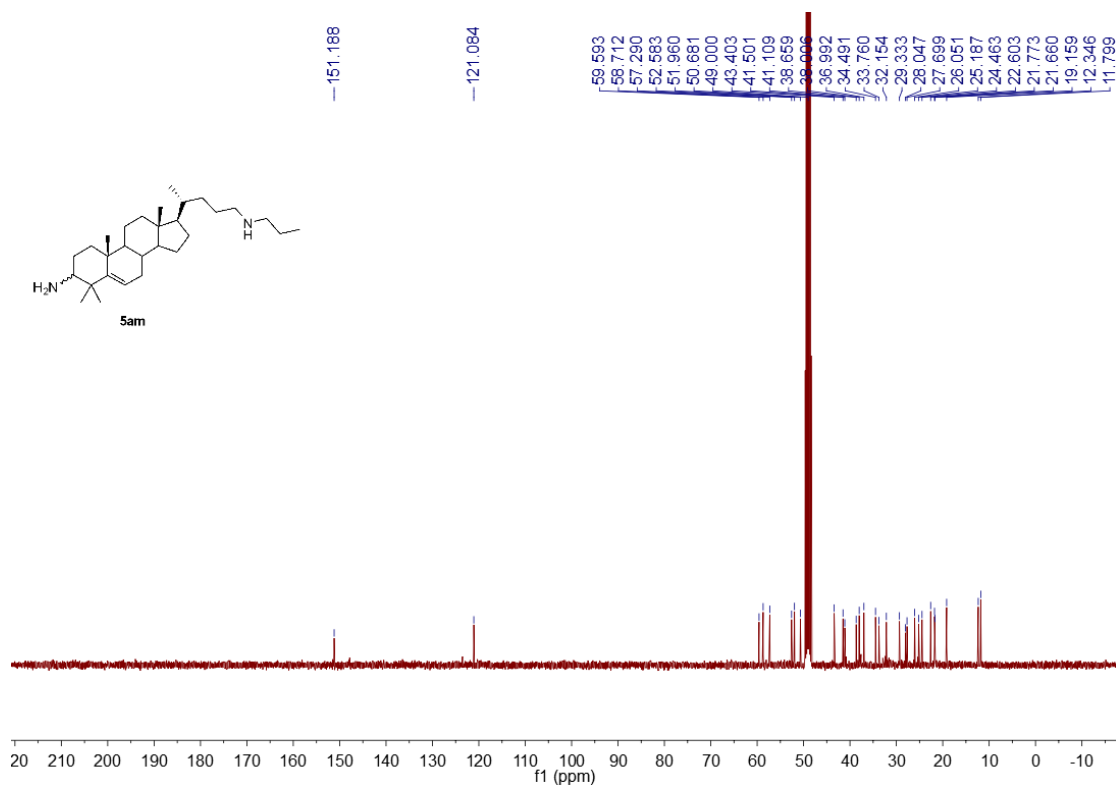
Compound **25** ( $^1\text{H}$  NMR)



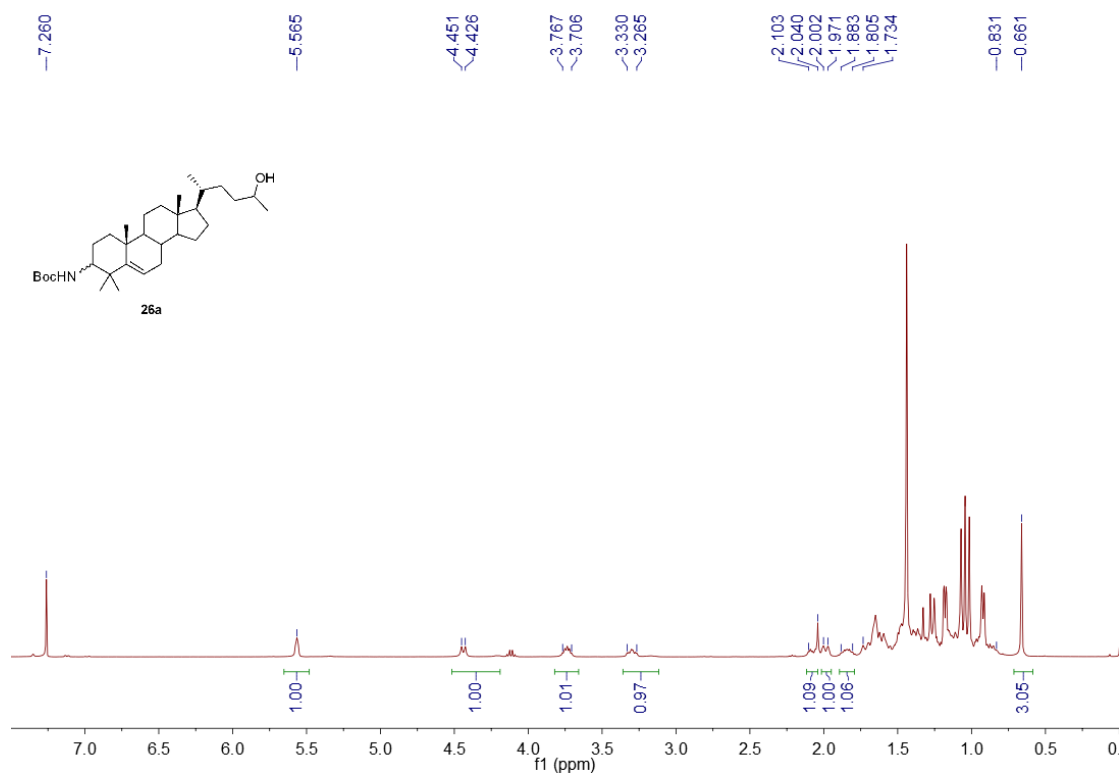
Compound **5am** ( $^1\text{H}$  NMR)



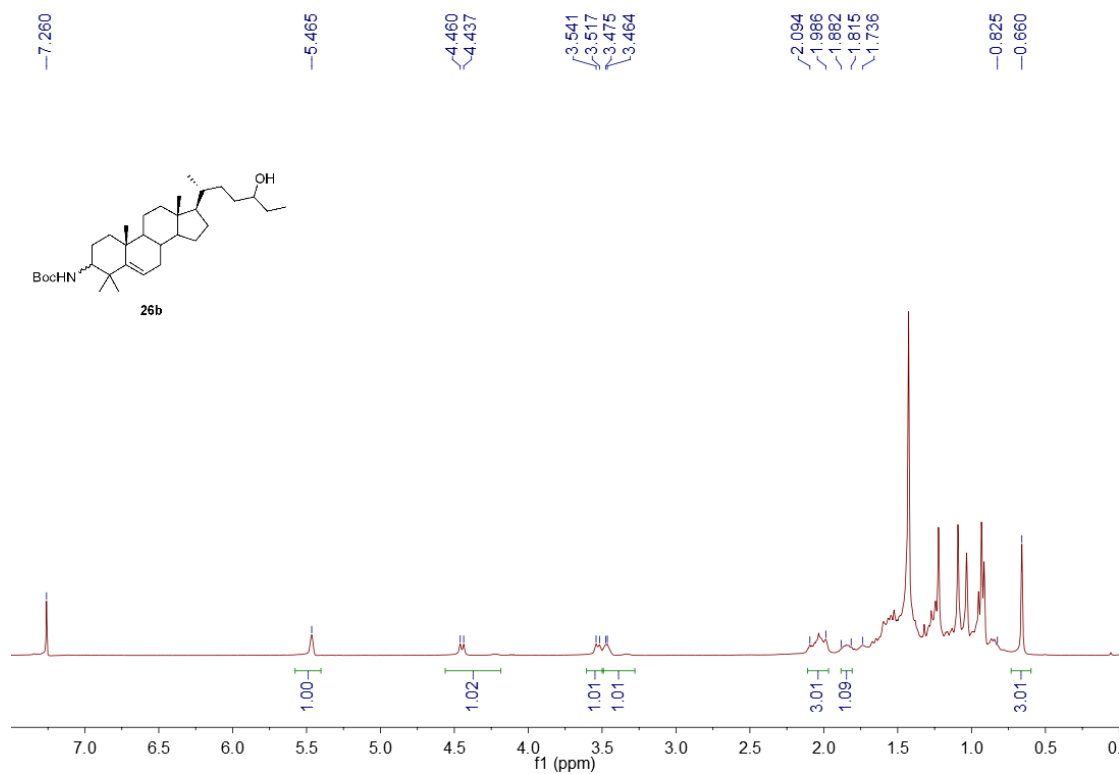
Compound **5am** ( $^{13}\text{C}$  NMR)



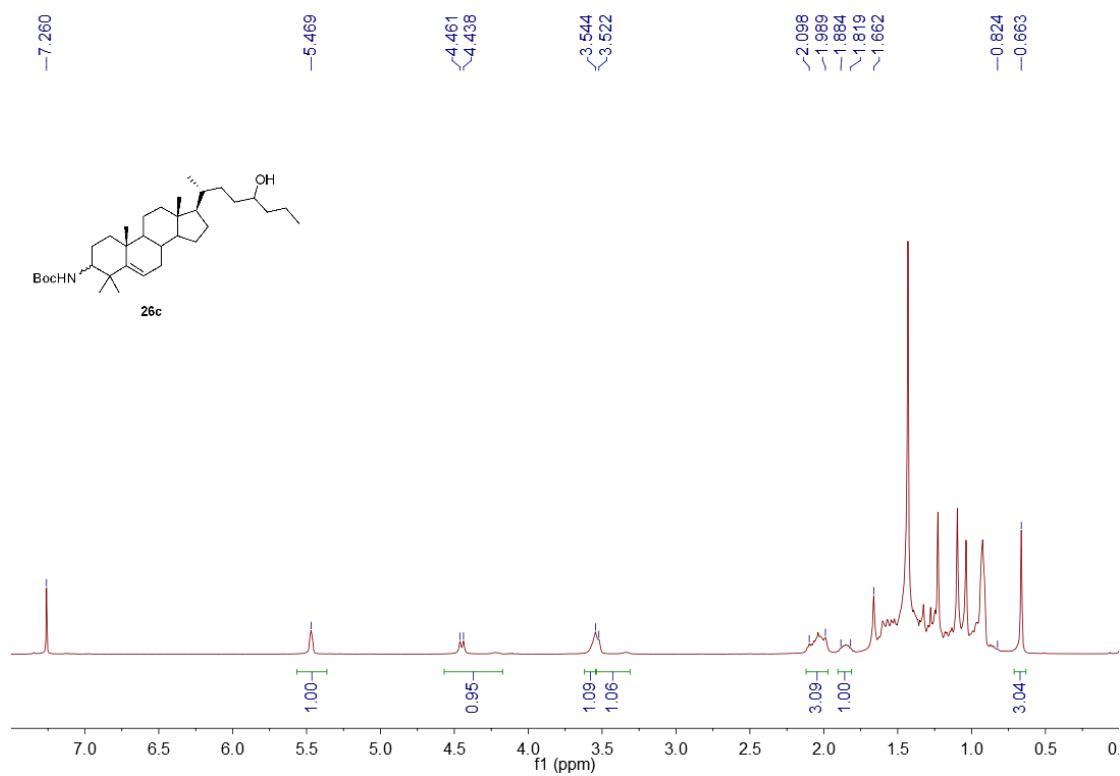
Compound **25a** ( $^1\text{H}$  NMR)



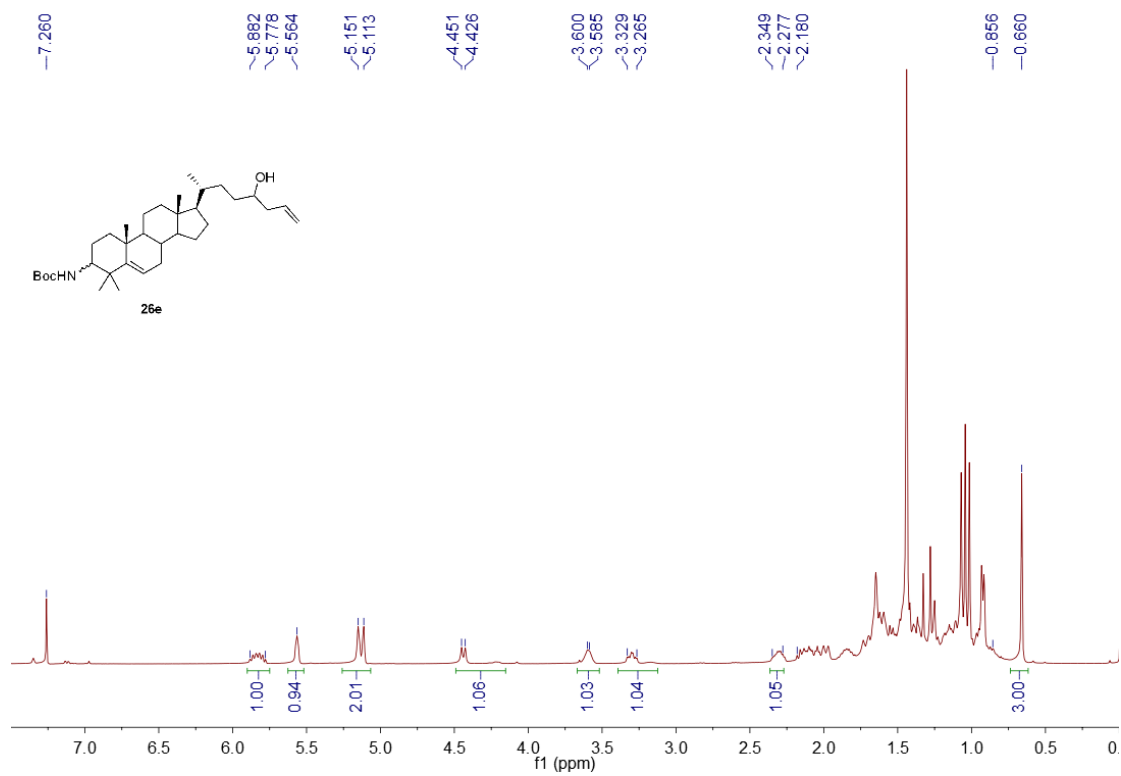
Compound **25b** ( $^1\text{H}$  NMR)



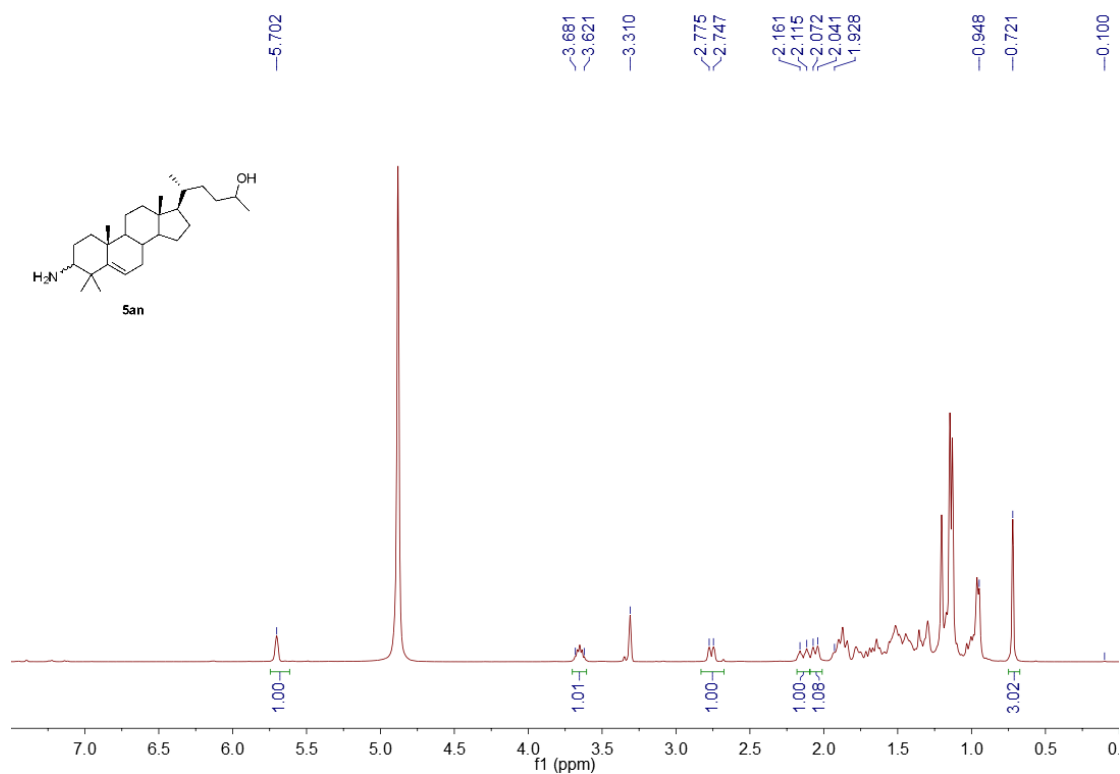
Compound **25c** ( $^1\text{H}$  NMR)



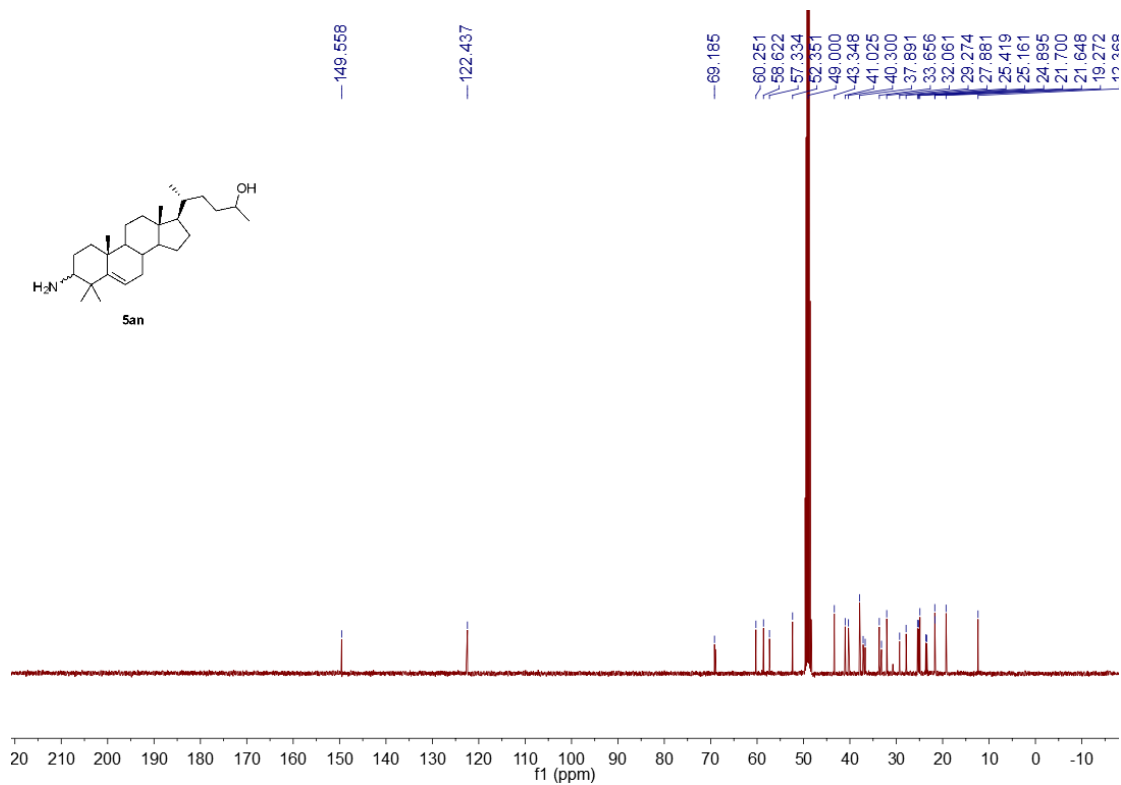
Compound **25e** ( $^1\text{H}$  NMR)



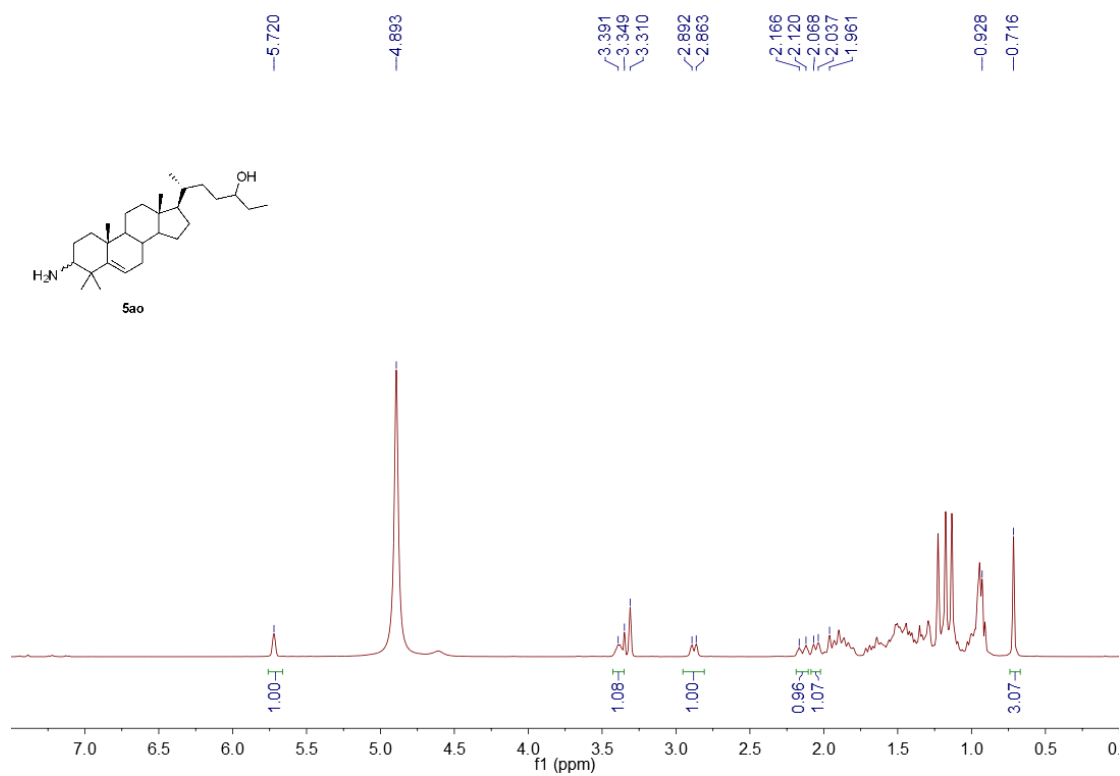
Compound **5an** ( $^1\text{H}$  NMR)



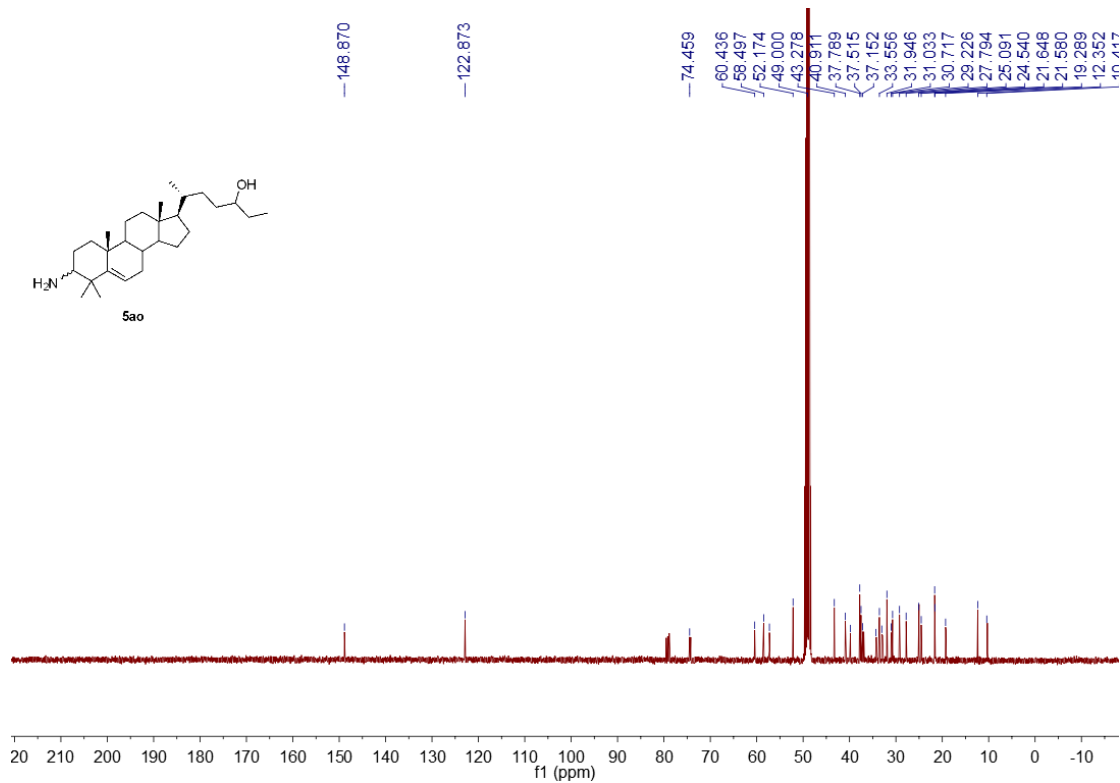
Compound **5an** ( $^{13}\text{C}$  NMR)



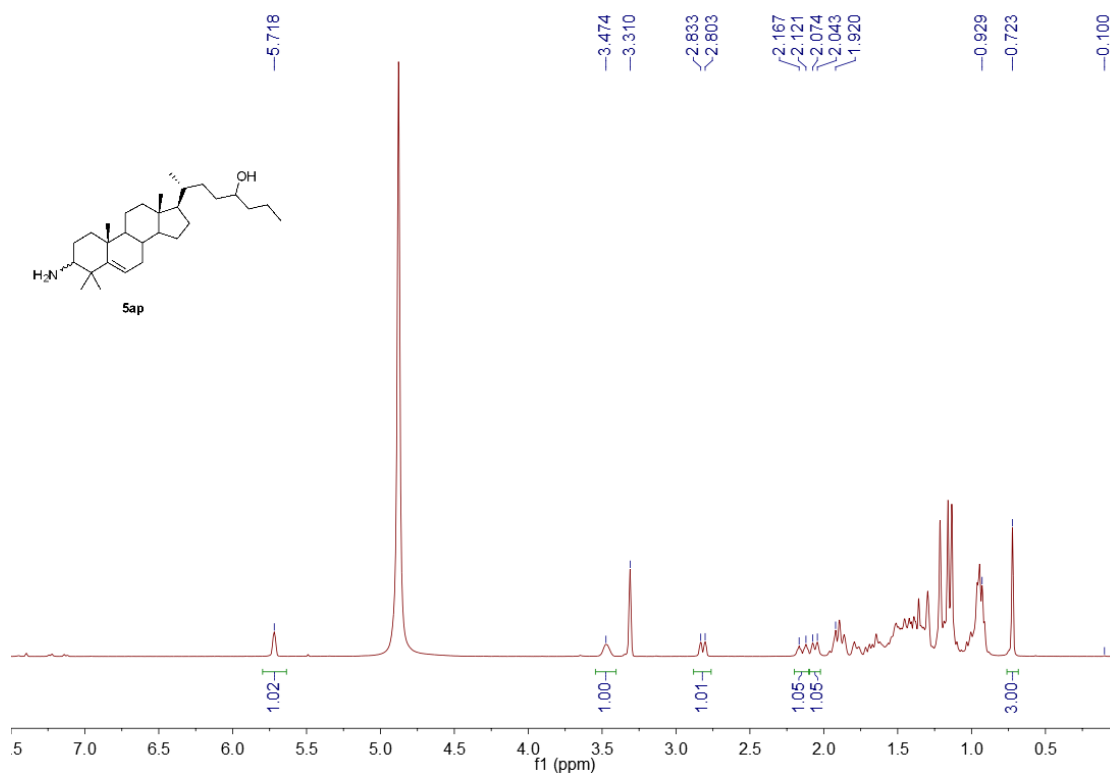
Compound **5ao** ( $^1\text{H}$  NMR)



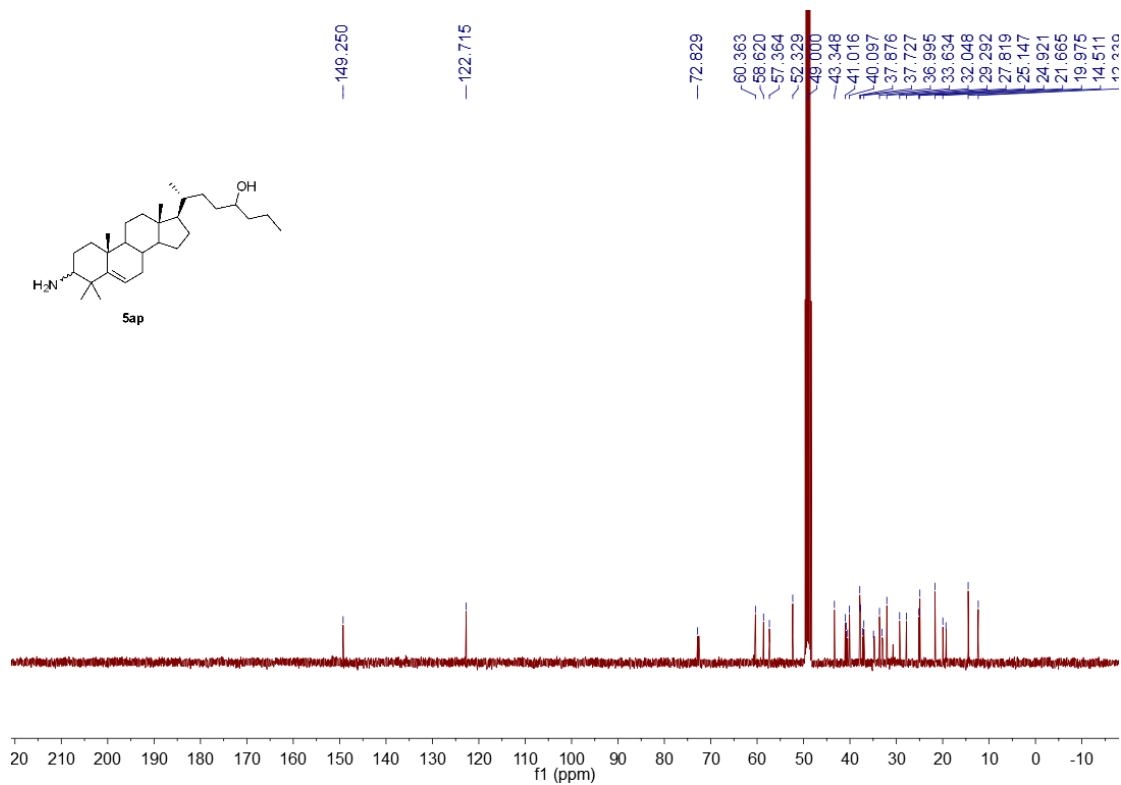
Compound **5ao** ( $^{13}\text{C}$  NMR)



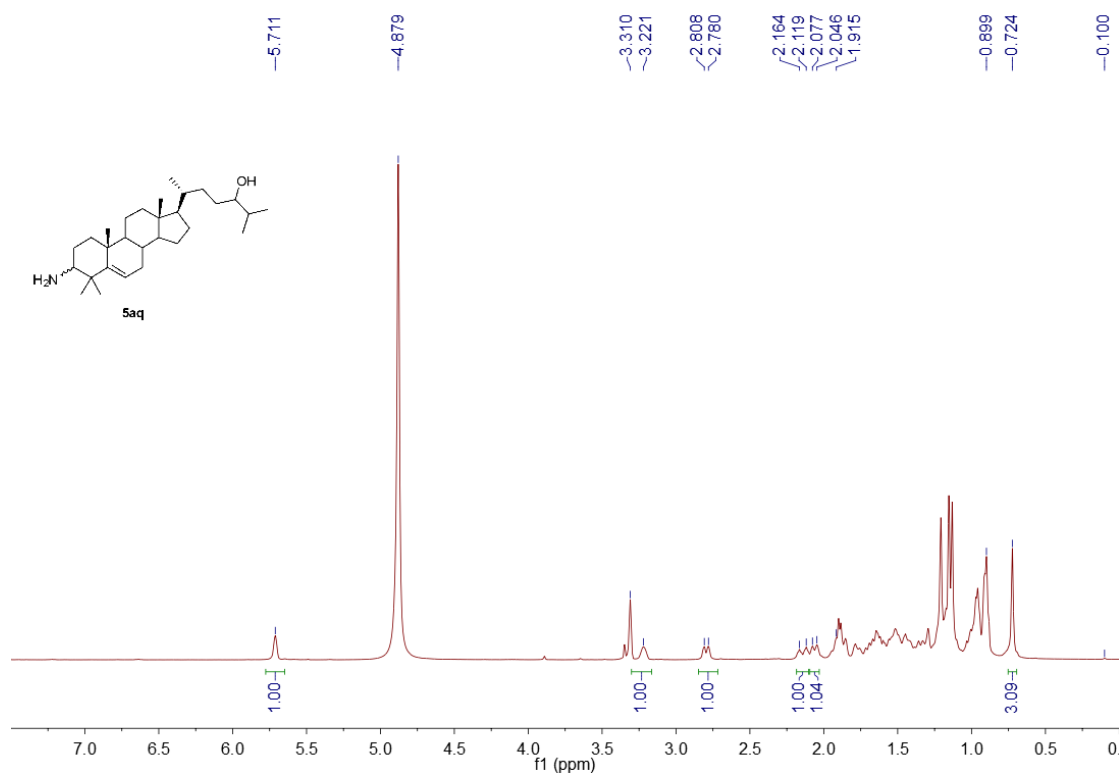
Compound **5ap** ( $^1\text{H}$  NMR)



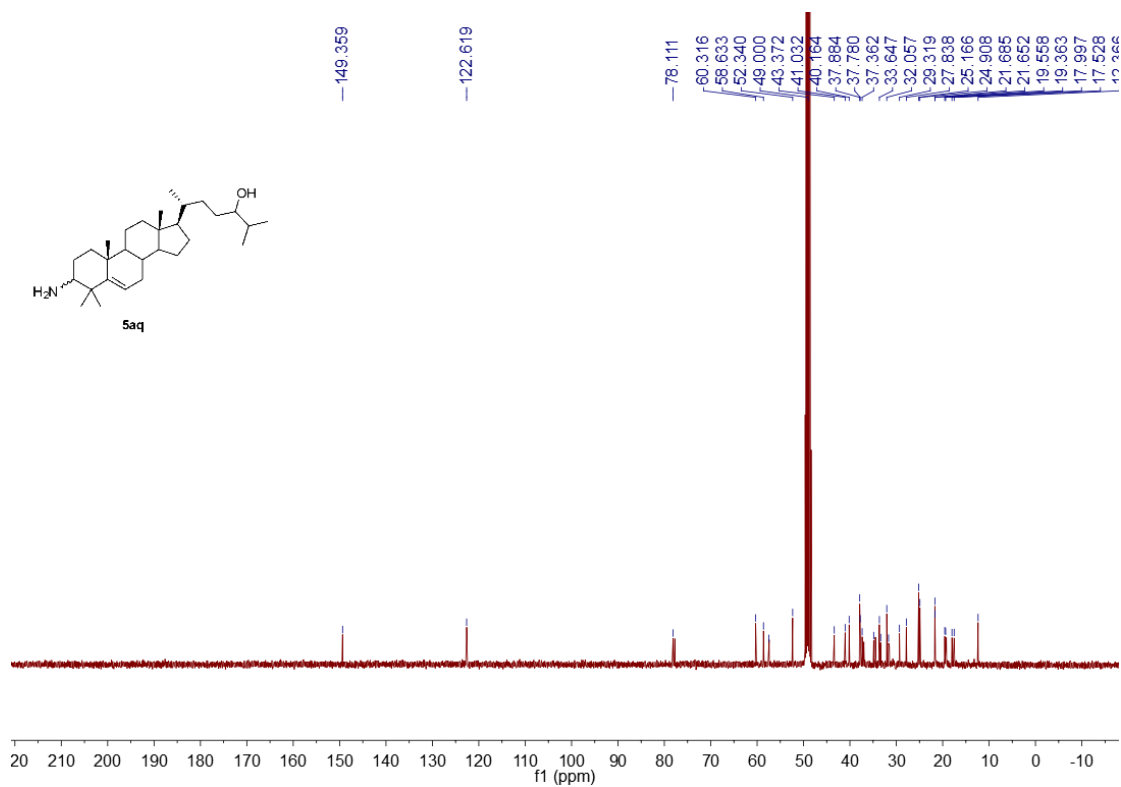
Compound **5ap** ( $^{13}\text{C}$  NMR)



Compound **5aq** ( $^1\text{H}$  NMR)

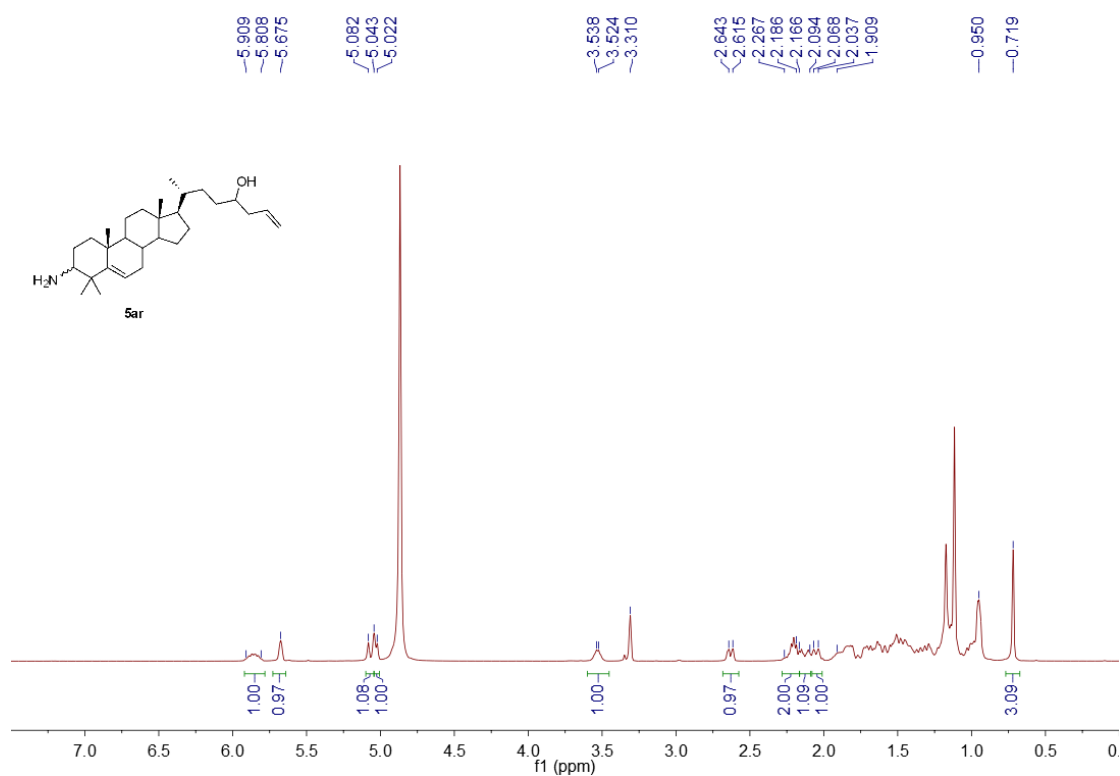


Compound **5aq** ( $^{13}\text{C}$  NMR)

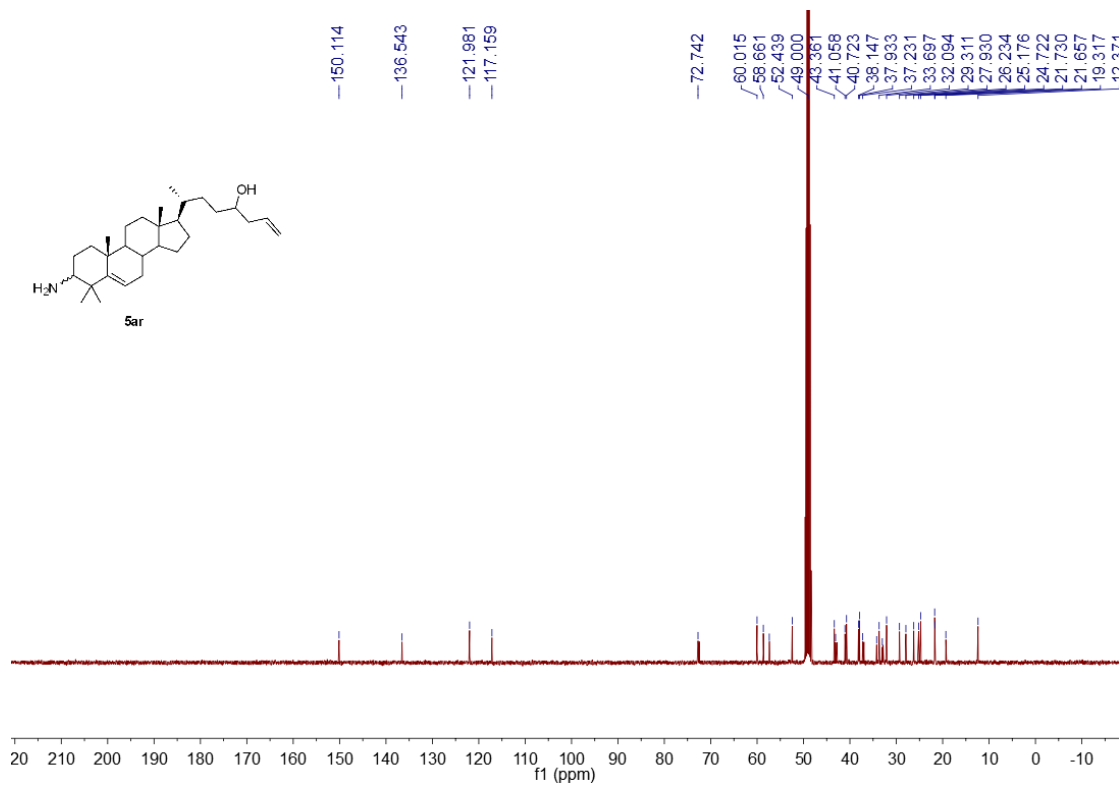




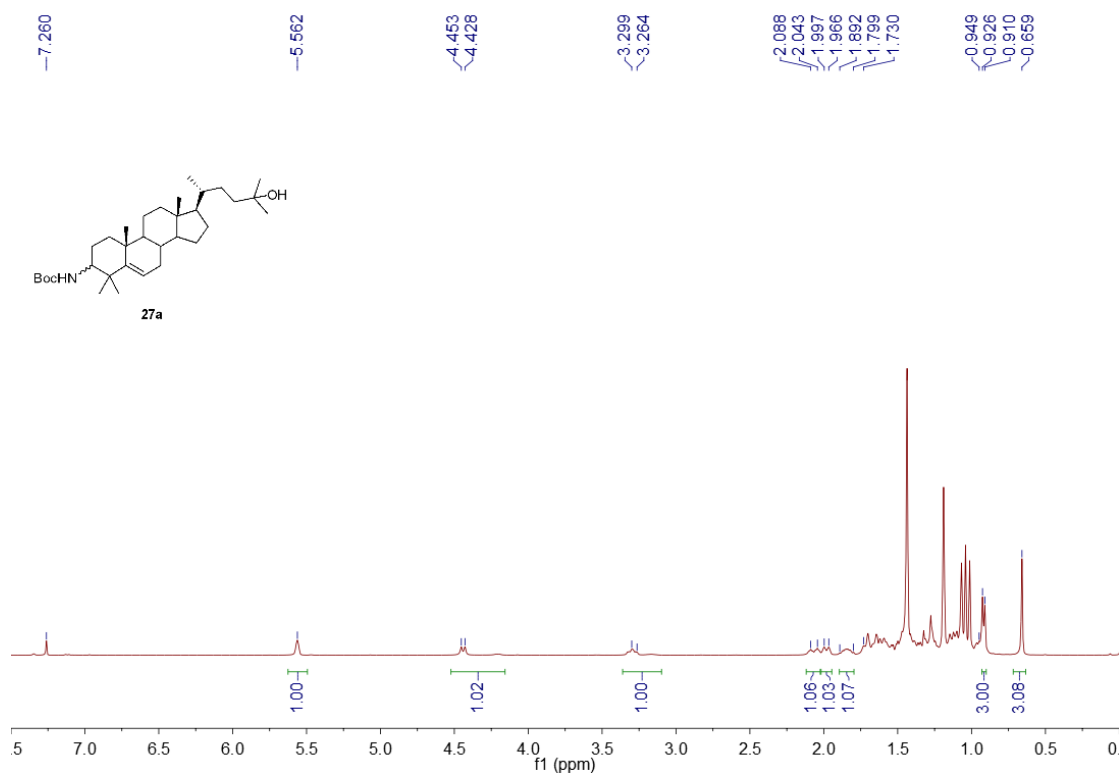
Compound **5ar** ( $^1\text{H}$  NMR)



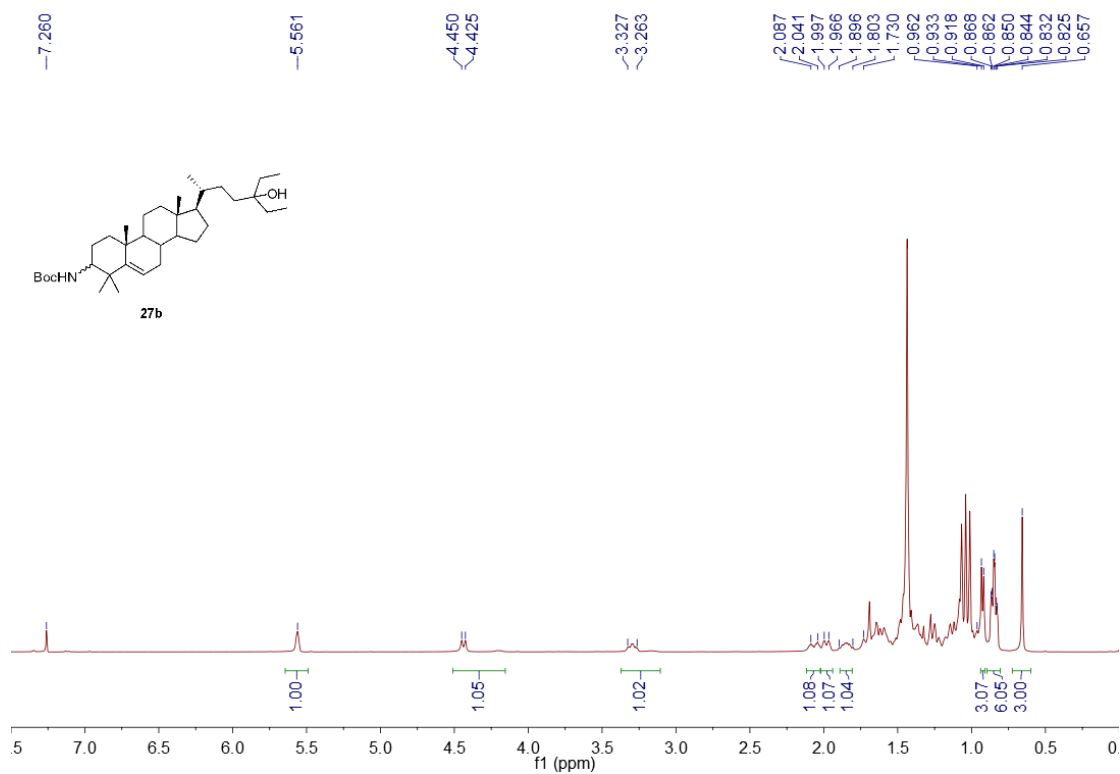
Compound **5ar** ( $^{13}\text{C}$  NMR)



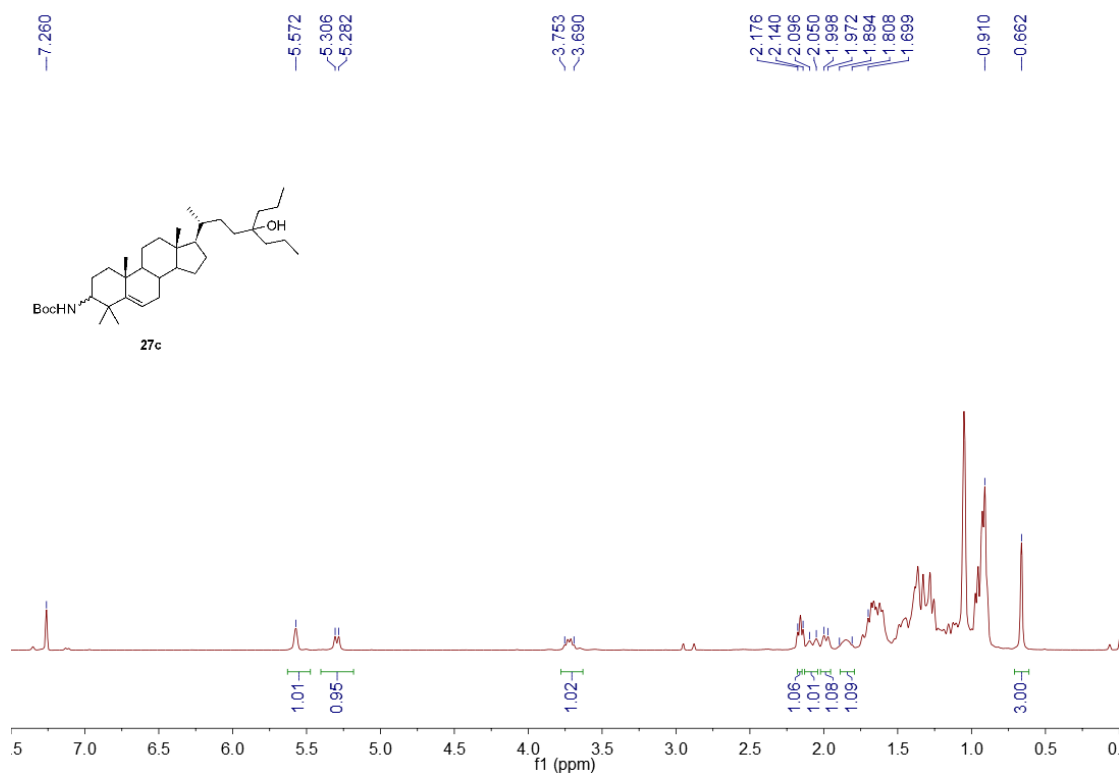
Compound **27a** ( $^1\text{H}$  NMR)



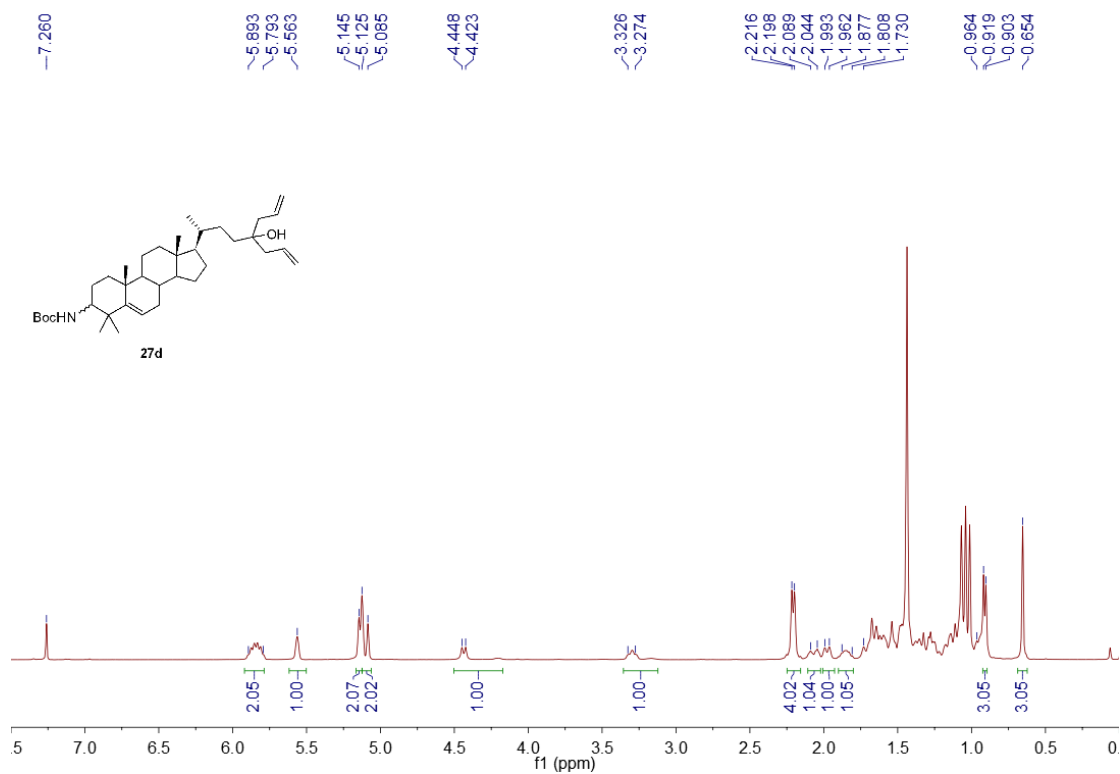
Compound **27b** ( $^1\text{H}$  NMR)



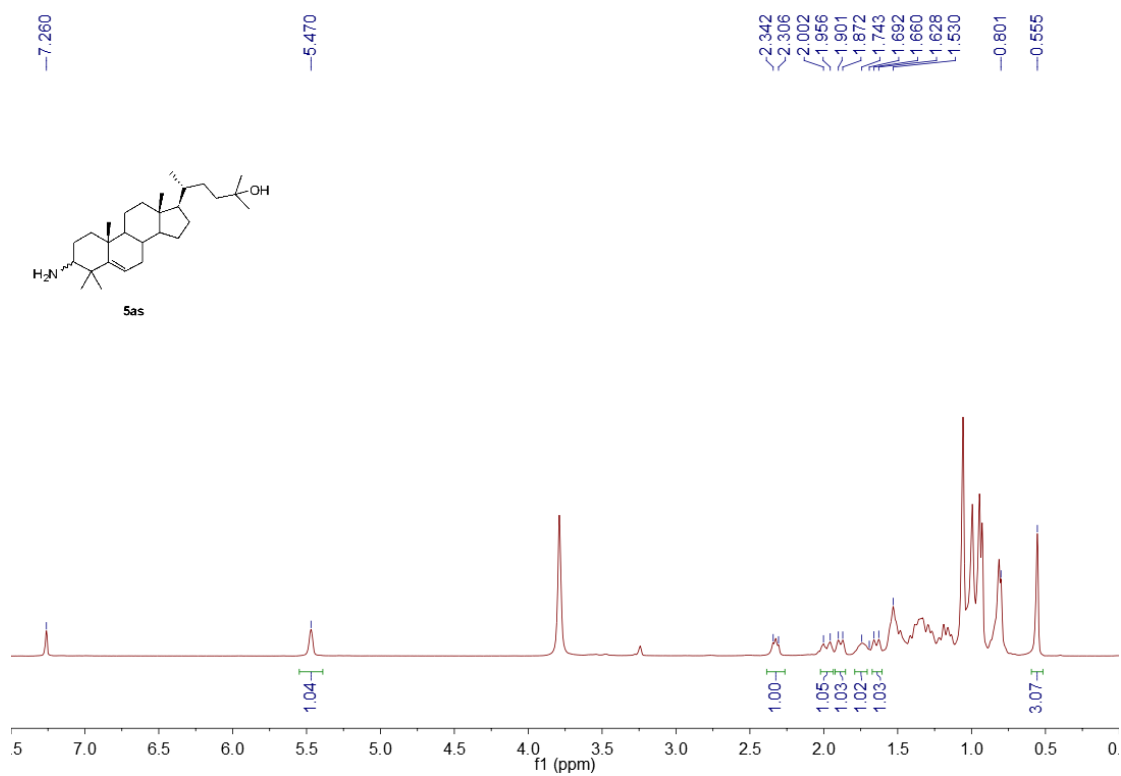
Compound **27c** ( $^1\text{H}$  NMR)



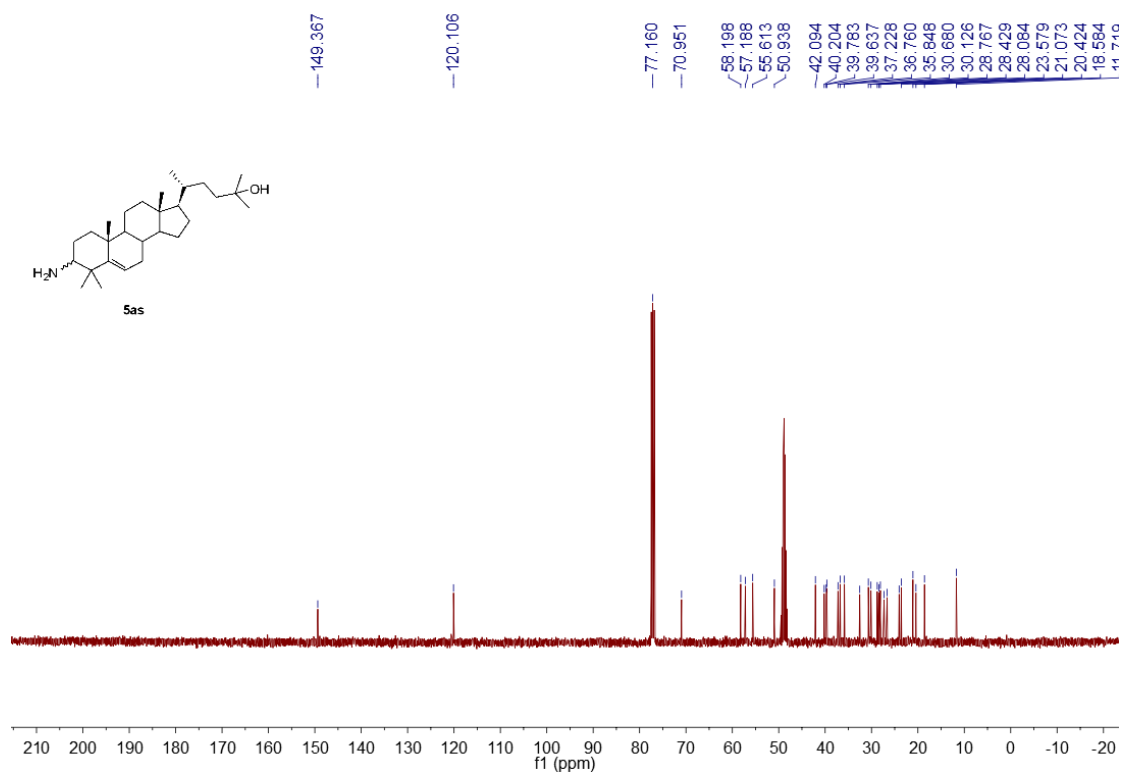
Compound **27d** ( $^1\text{H}$  NMR)



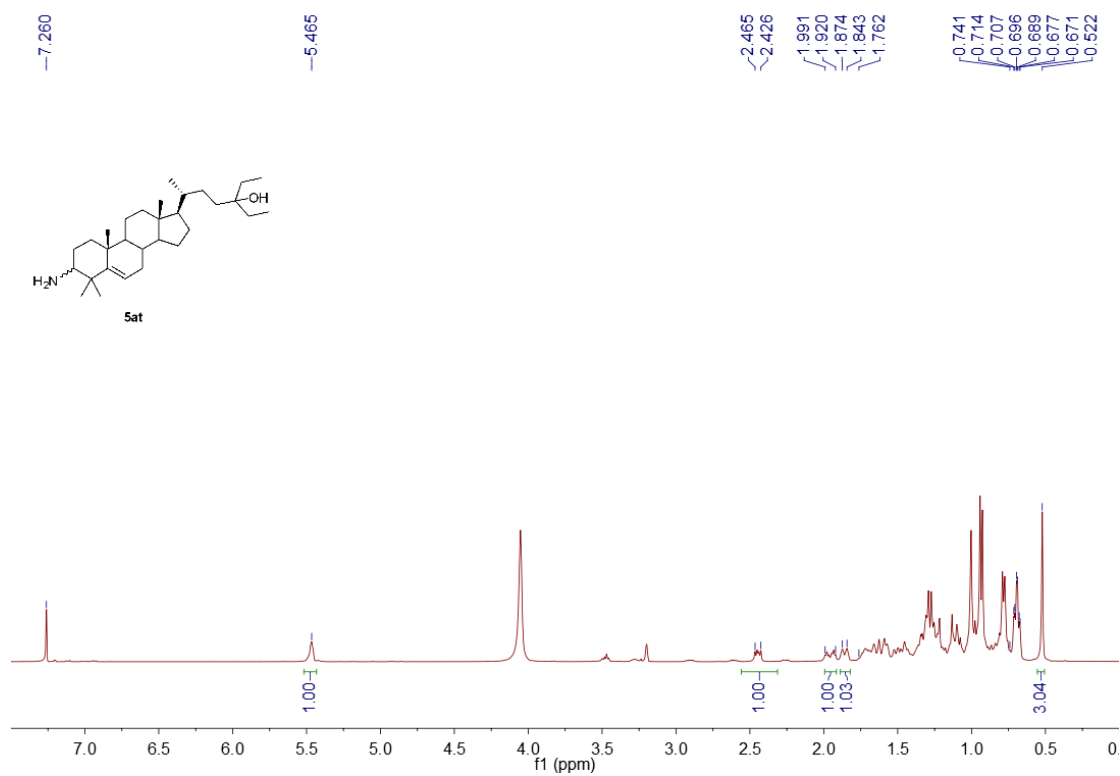
Compound **5as** ( $^1\text{H}$  NMR)



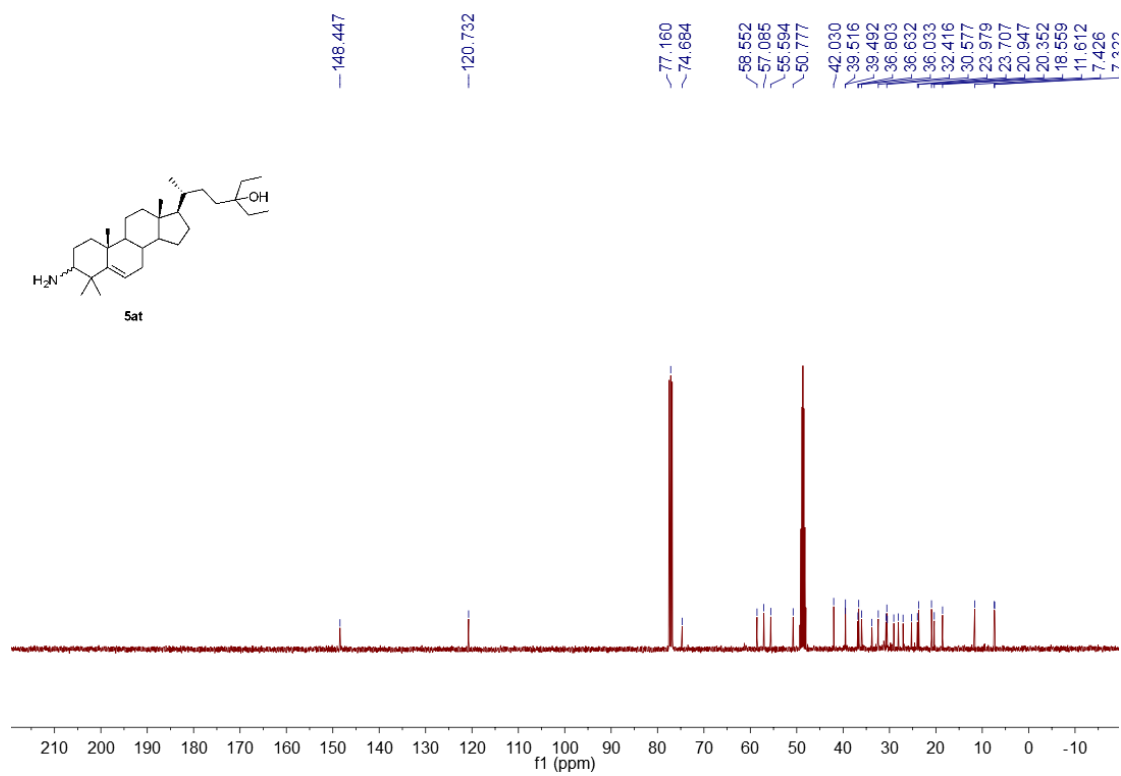
Compound **5as** ( $^{13}\text{C}$  NMR)



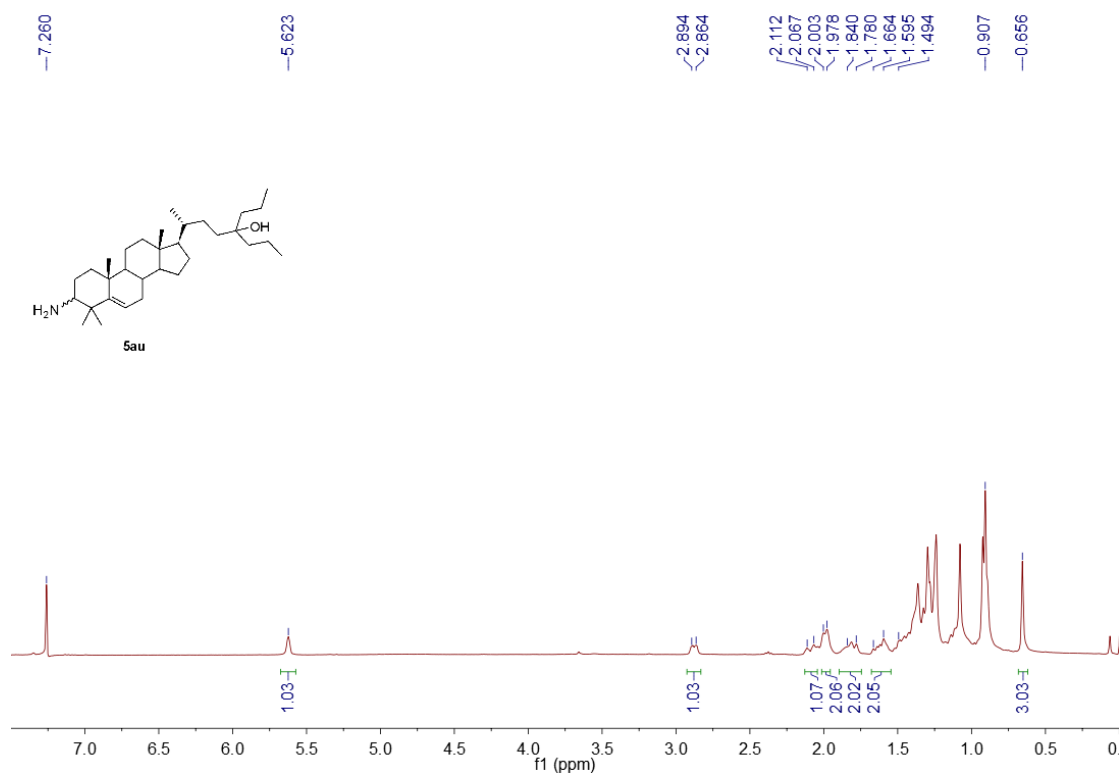
Compound **5at** ( $^1\text{H}$  NMR)



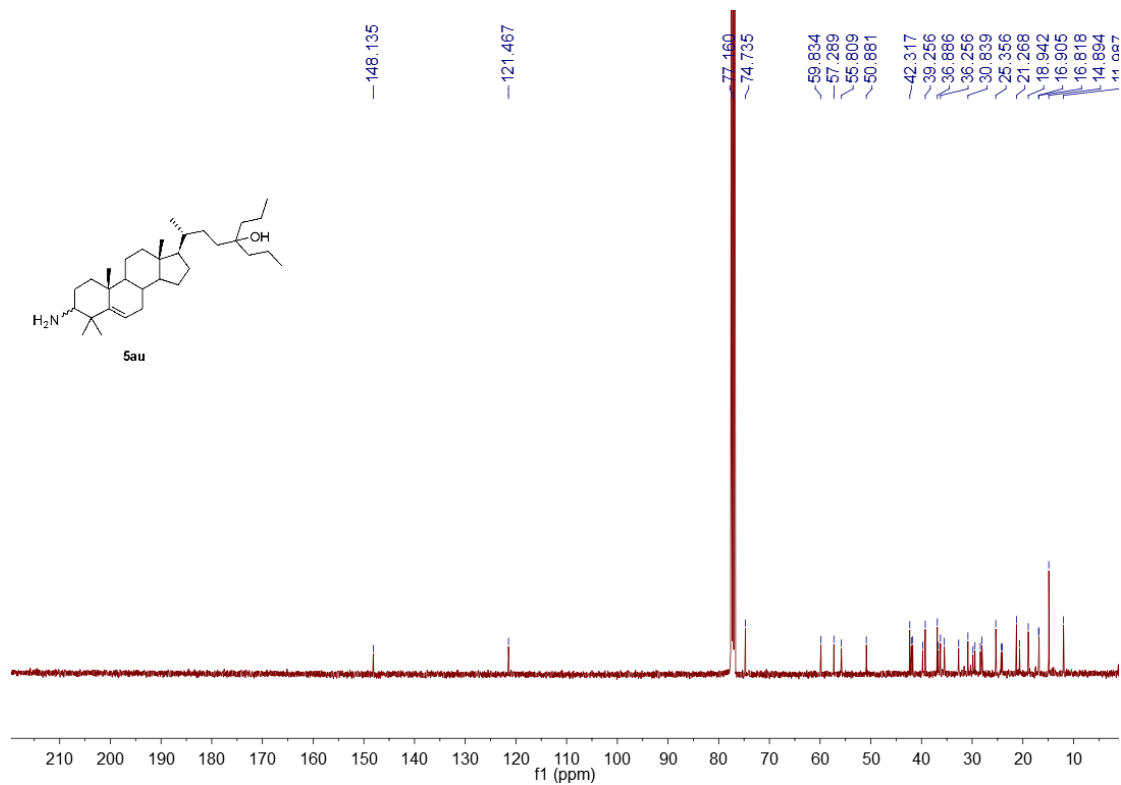
Compound **5at** ( $^{13}\text{C}$  NMR)



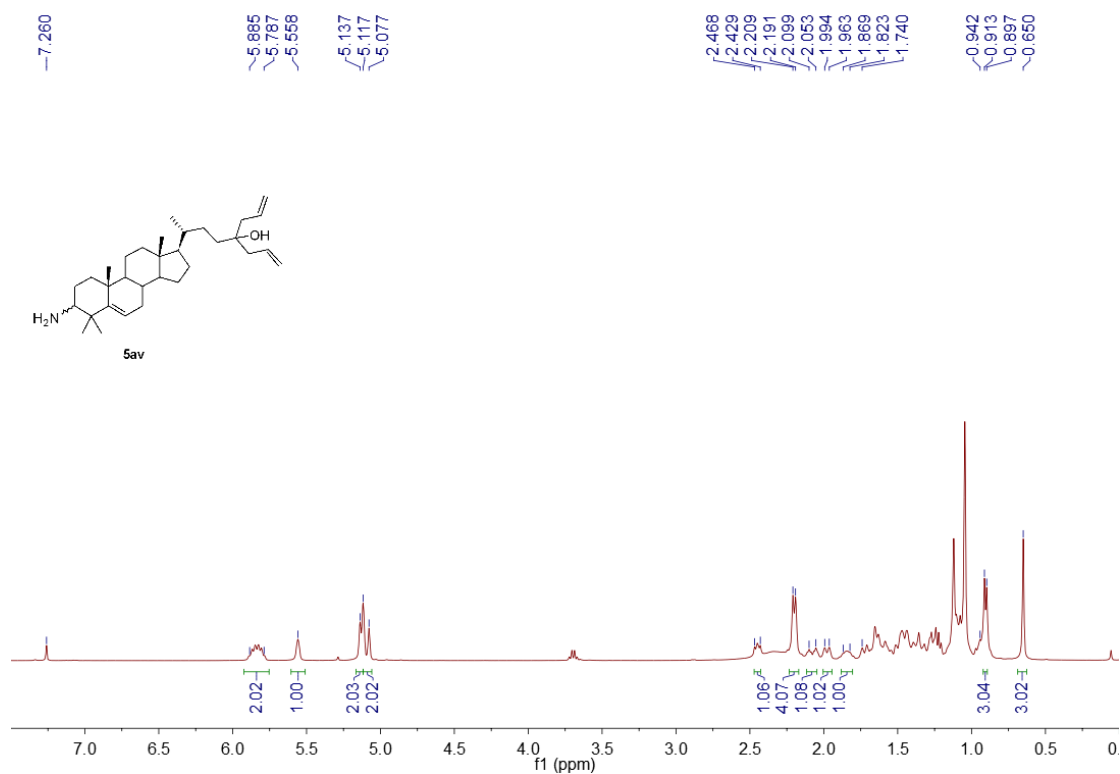
Compound **5au** ( $^1\text{H}$  NMR)



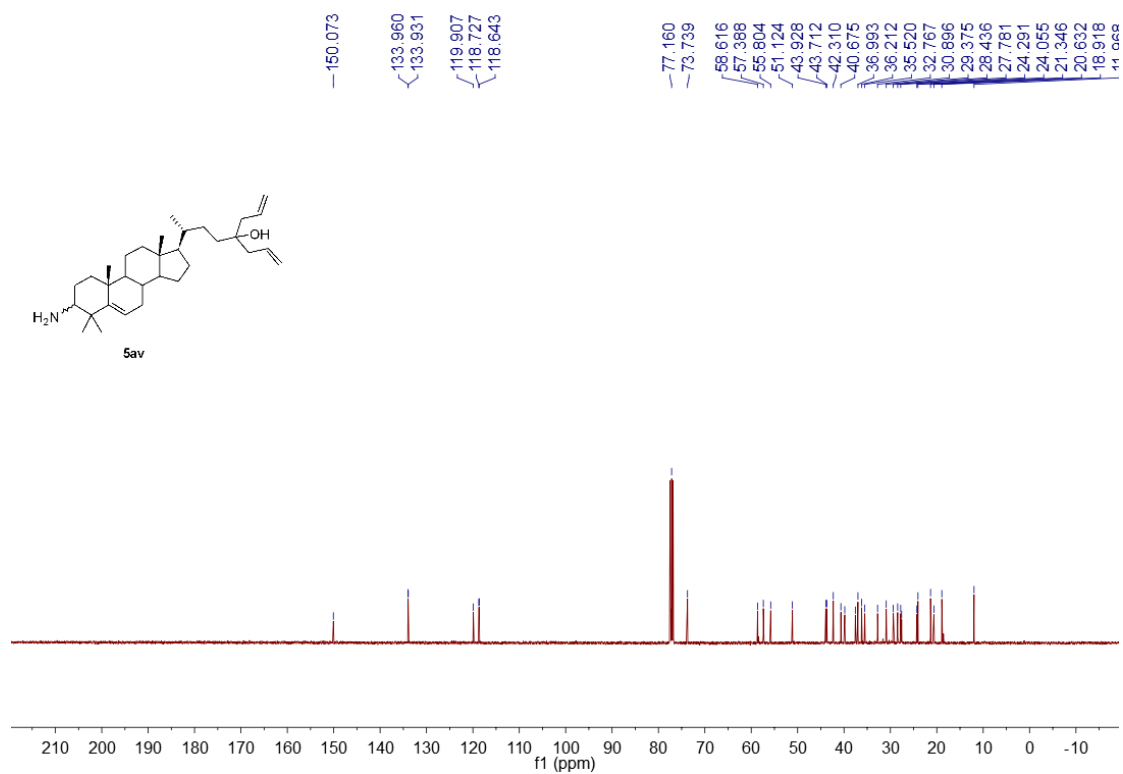
Compound **5au** ( $^{13}\text{C}$  NMR)



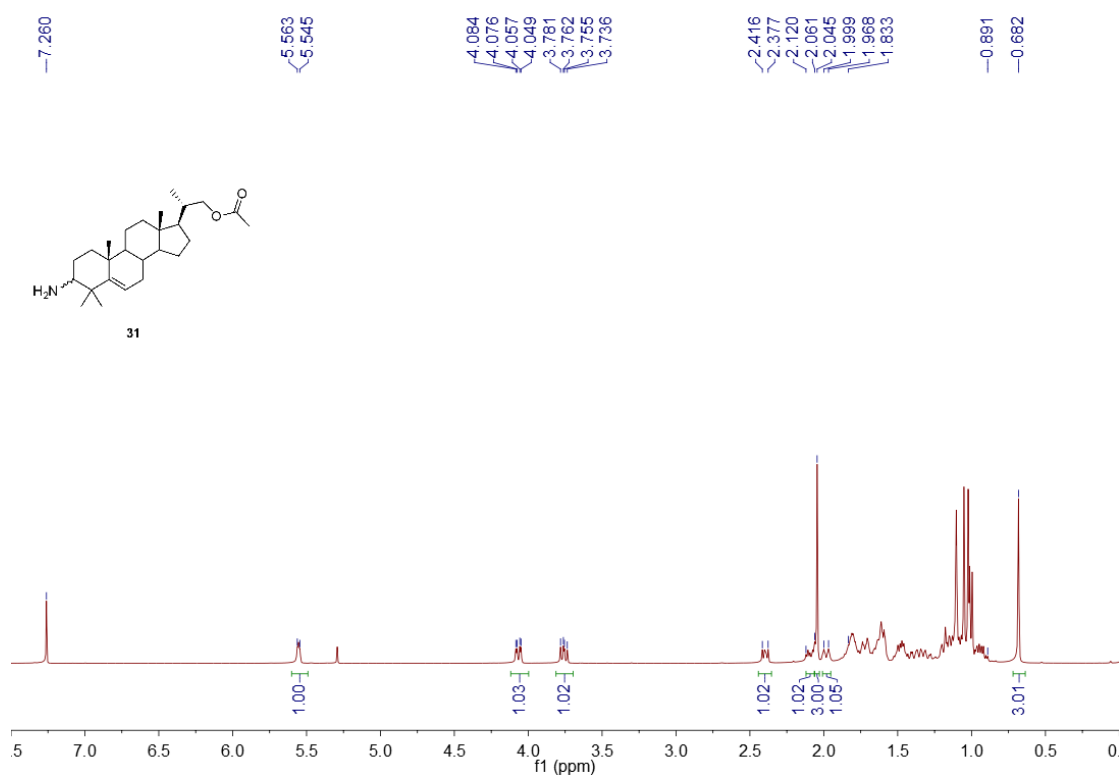
Compound **5av** ( $^1\text{H}$  NMR)



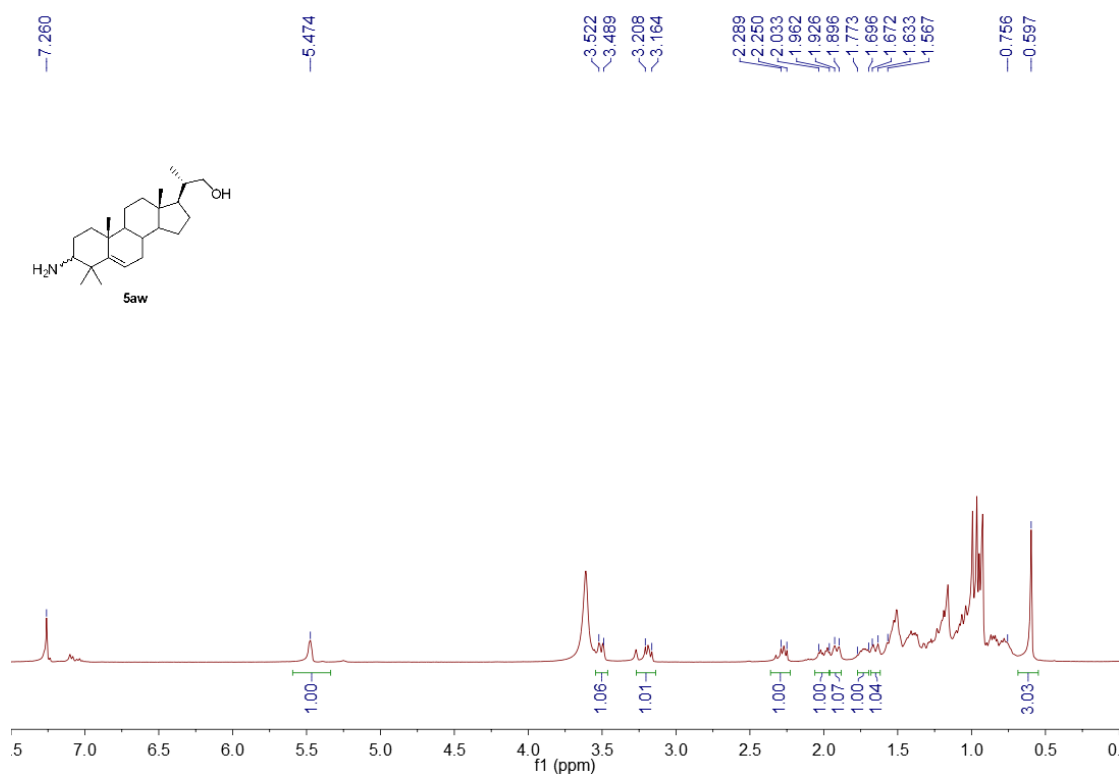
Compound **5av** ( $^{13}\text{C}$  NMR)



Compound **31** ( $^1\text{H}$  NMR)

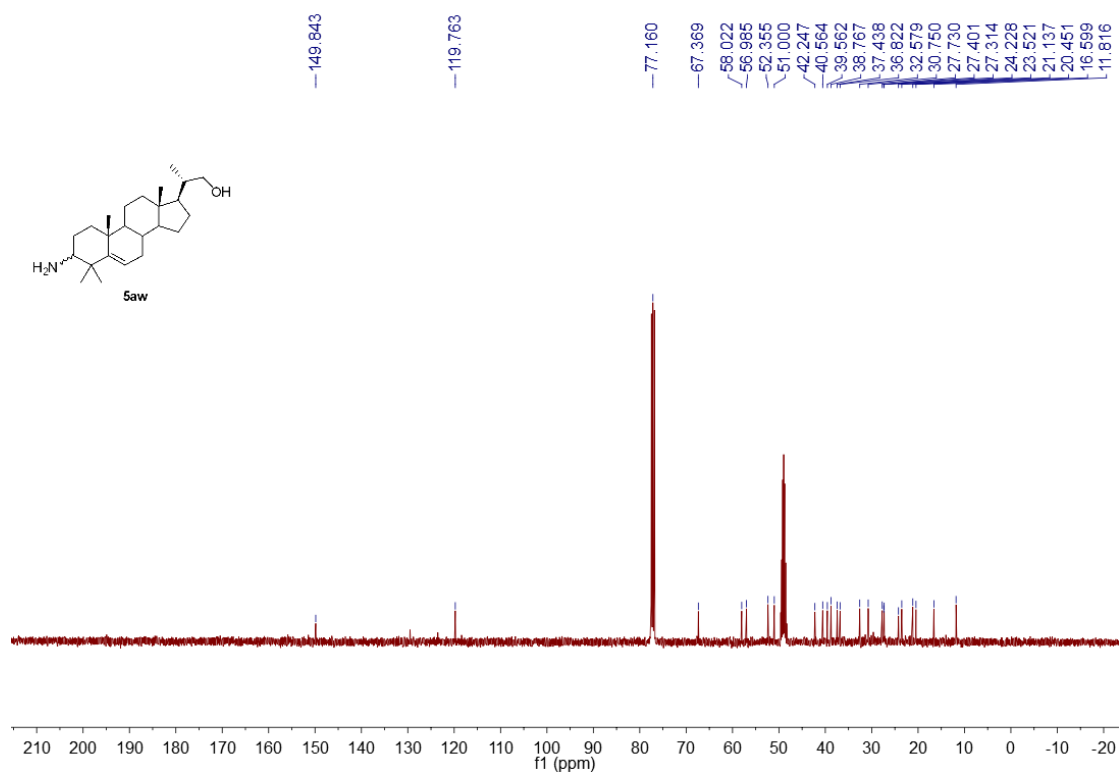


Compound **5aw** ( $^1\text{H}$  NMR)

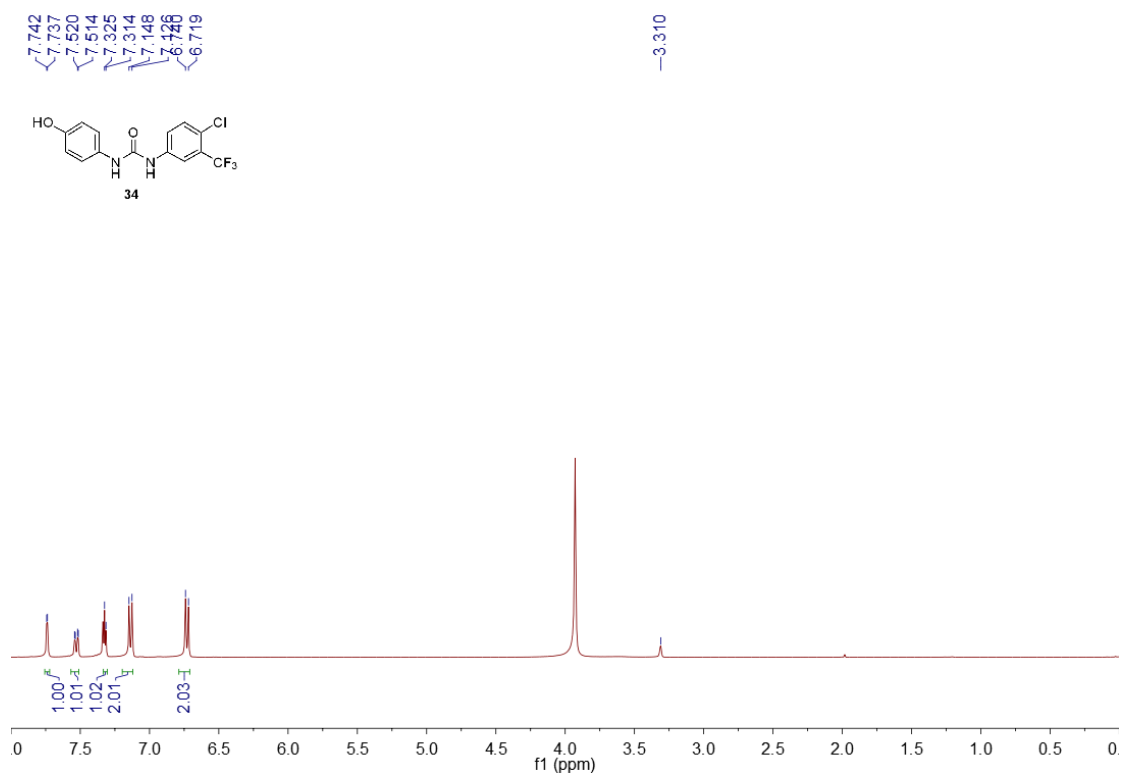




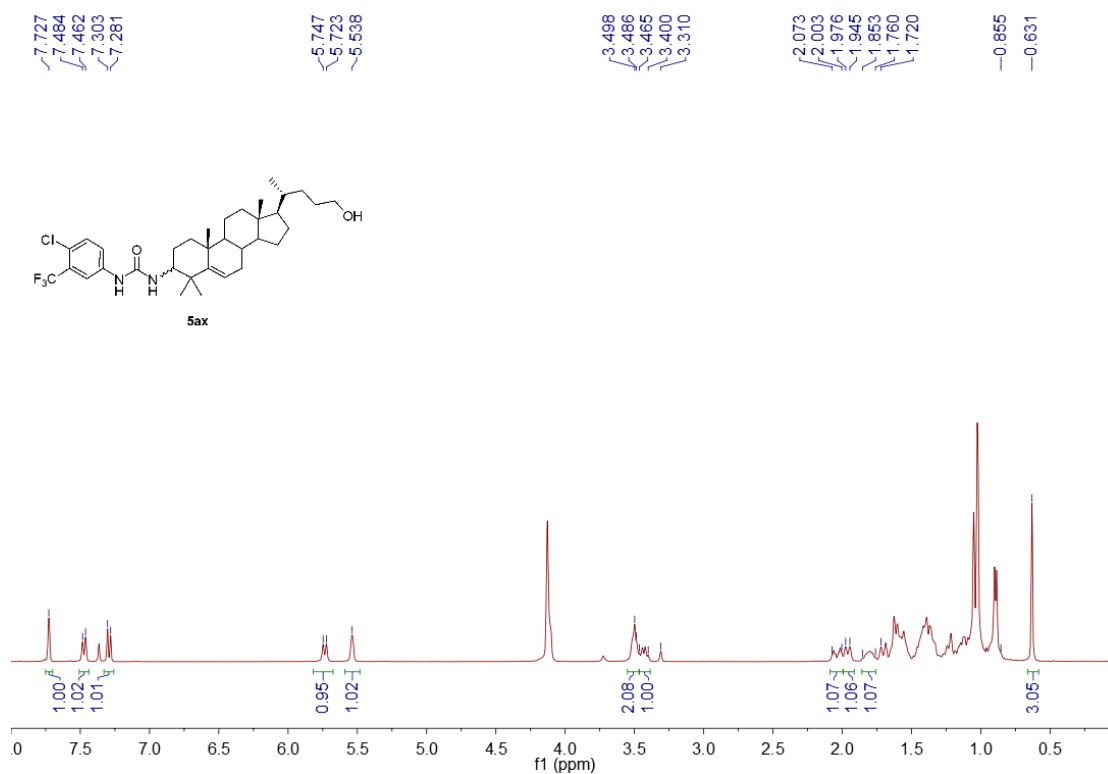
Compound **5aw** ( $^{13}\text{C}$  NMR)



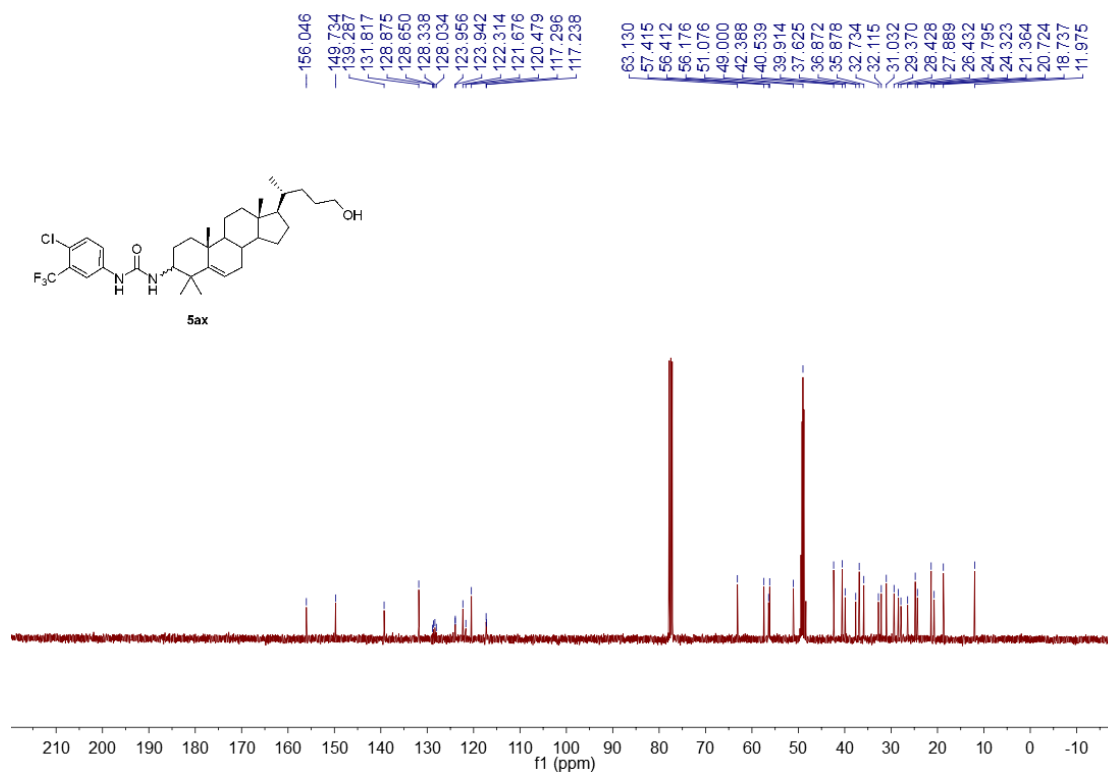
Compound **34** ( $^1\text{H}$  NMR)



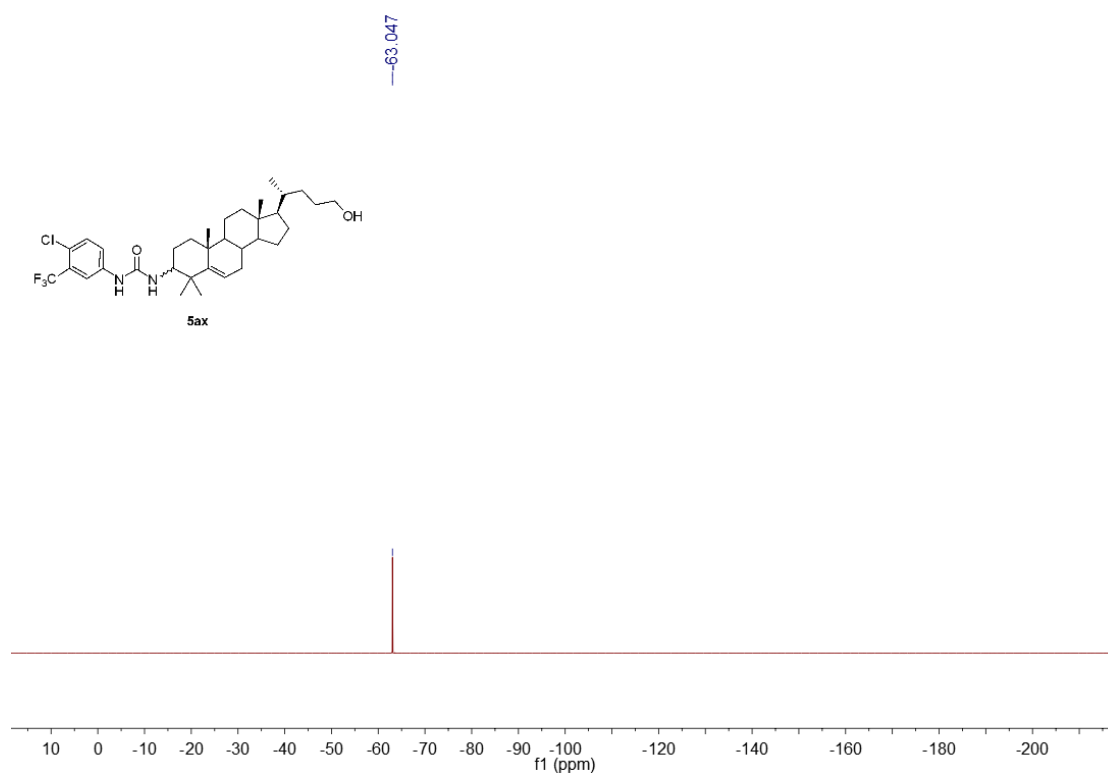
Compound **5ax** ( $^1\text{H}$  NMR)



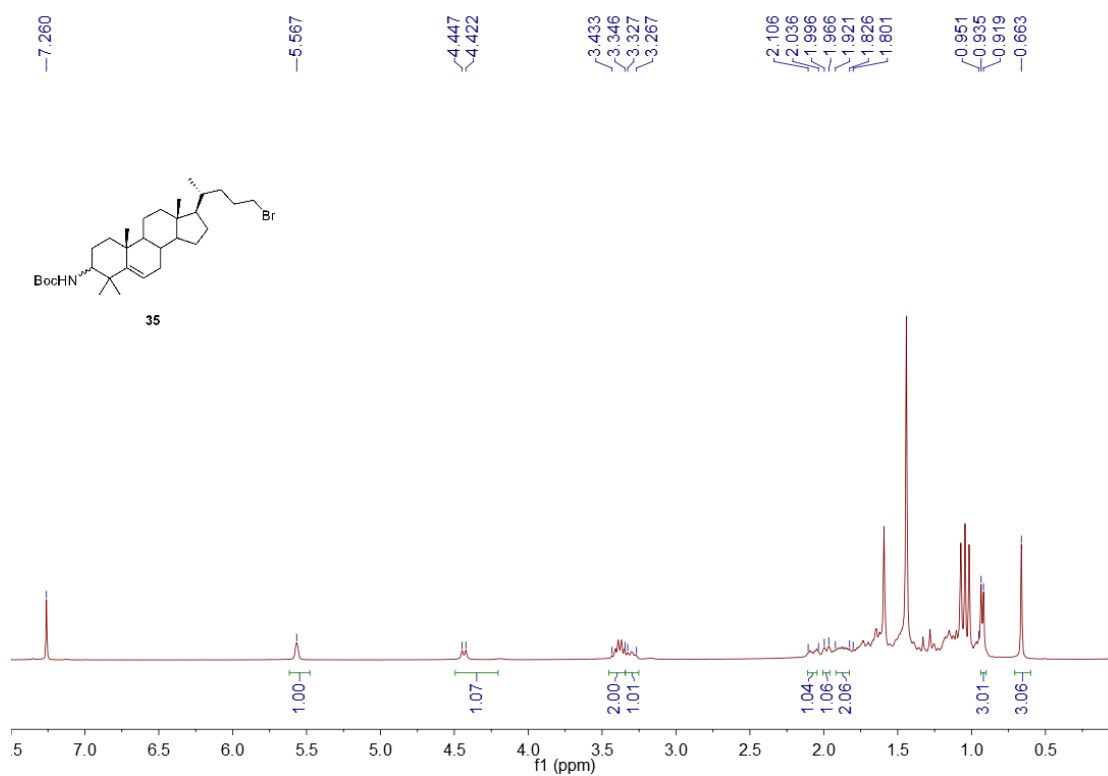
Compound **5ax** ( $^{13}\text{C}$  NMR)



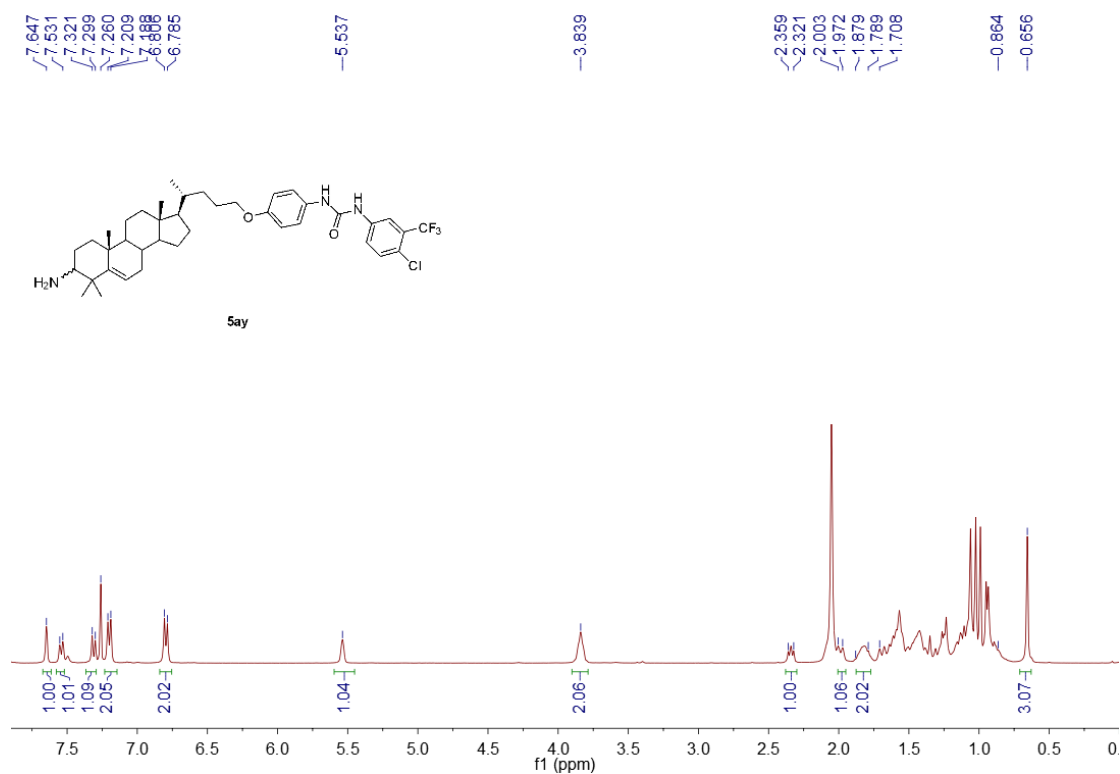
Compound **5ax** ( $^{19}\text{F}$  NMR)



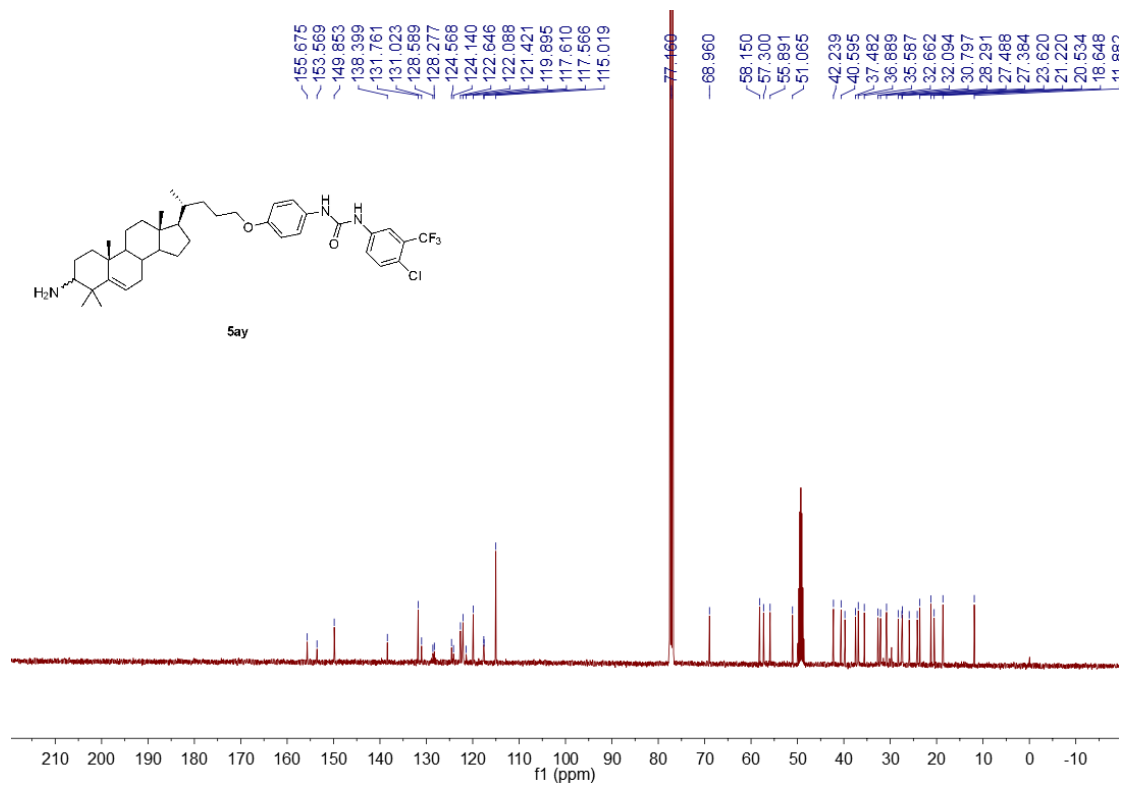
Compound **35** ( $^1\text{H}$  NMR)



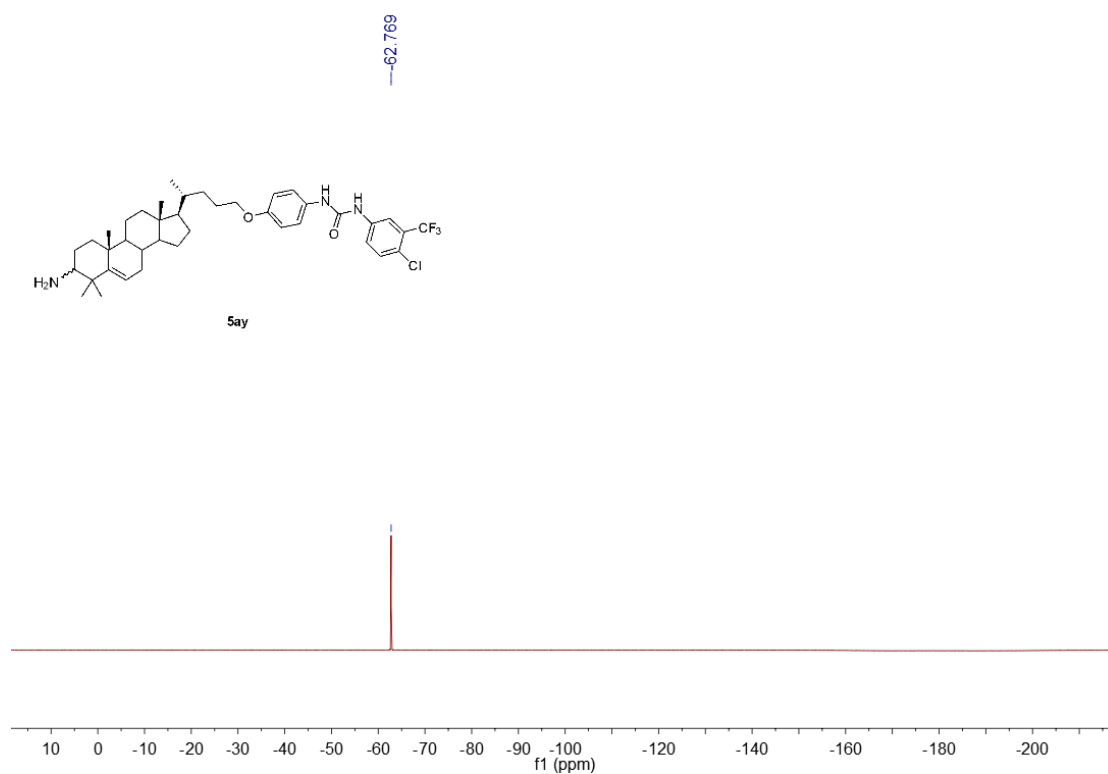
Compound **5ay** ( $^1\text{H}$  NMR)



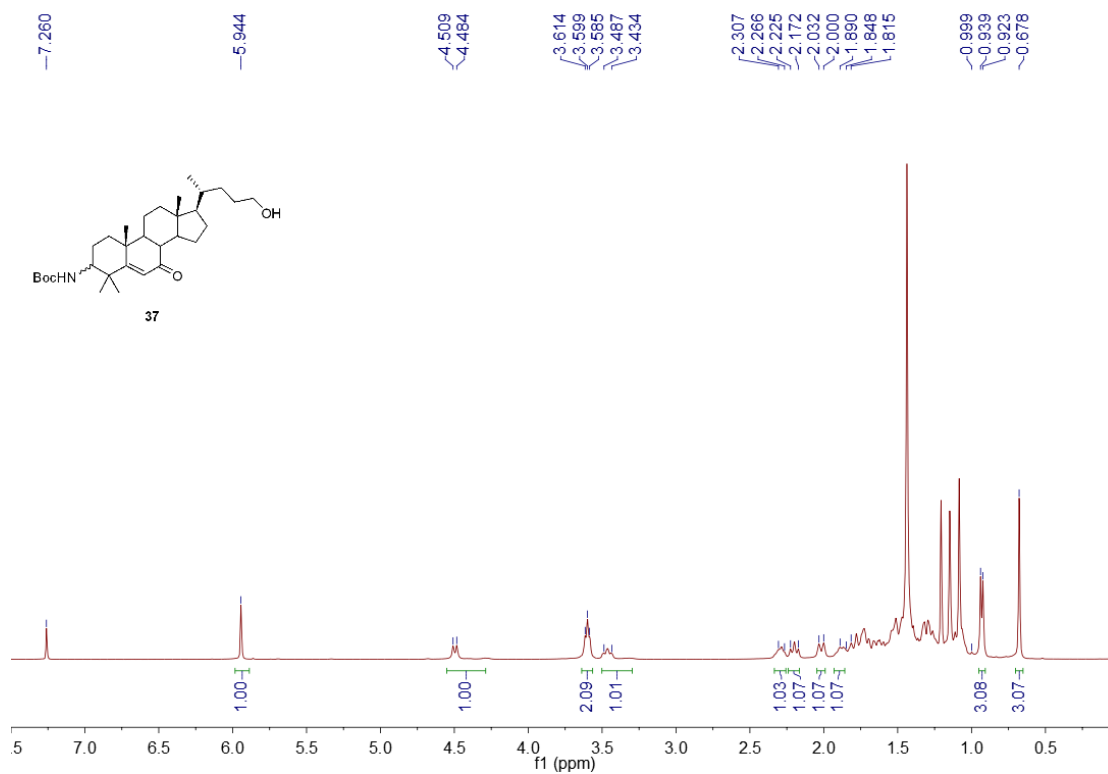
Compound **5ay** ( $^{13}\text{C}$  NMR)



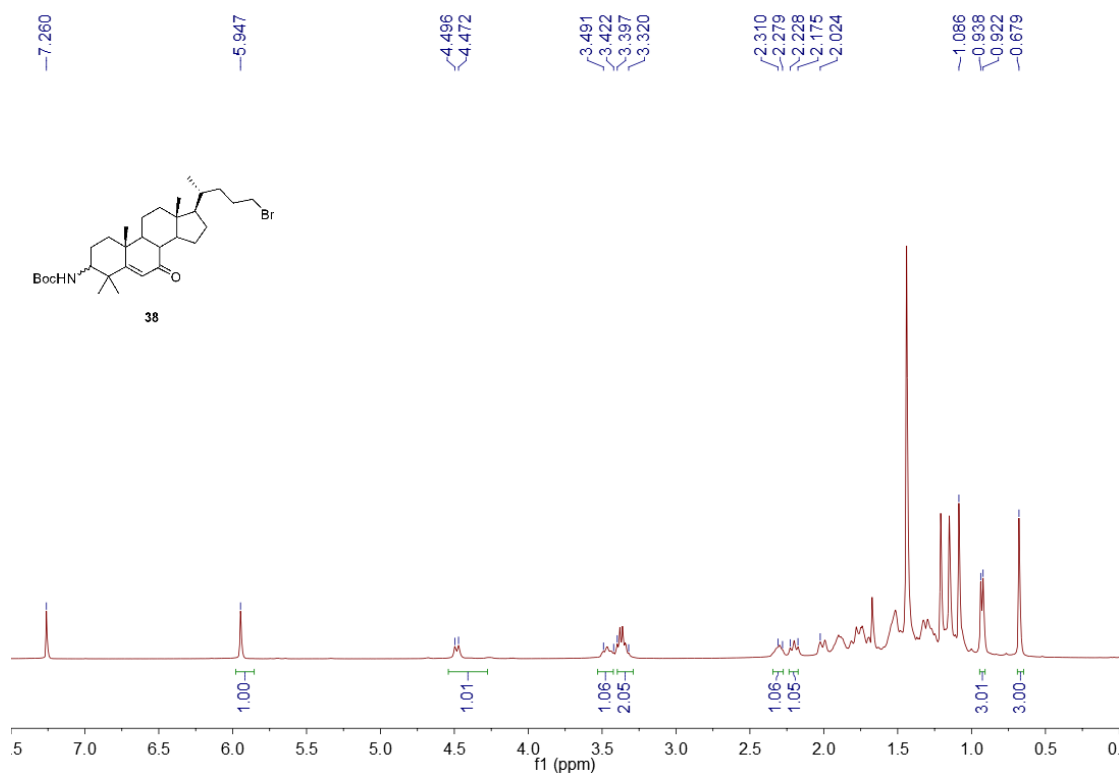
Compound **5ay** ( $^{19}\text{F}$  NMR)



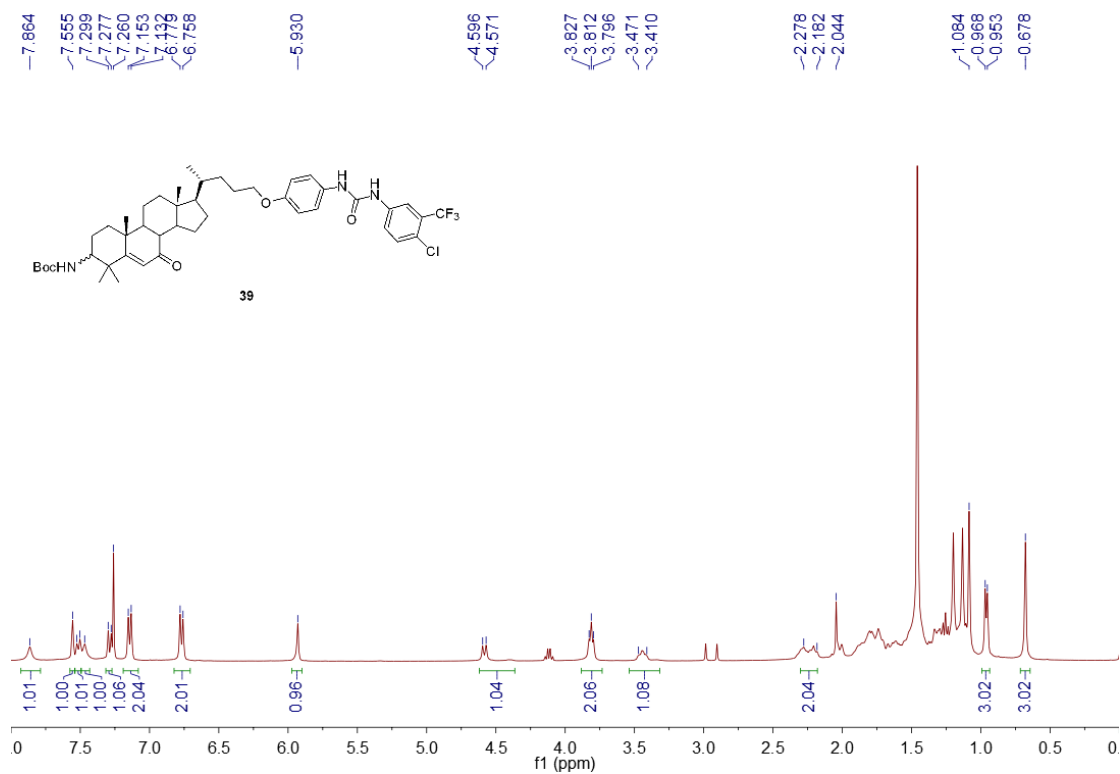
Compound **37** ( $^1\text{H}$  NMR)



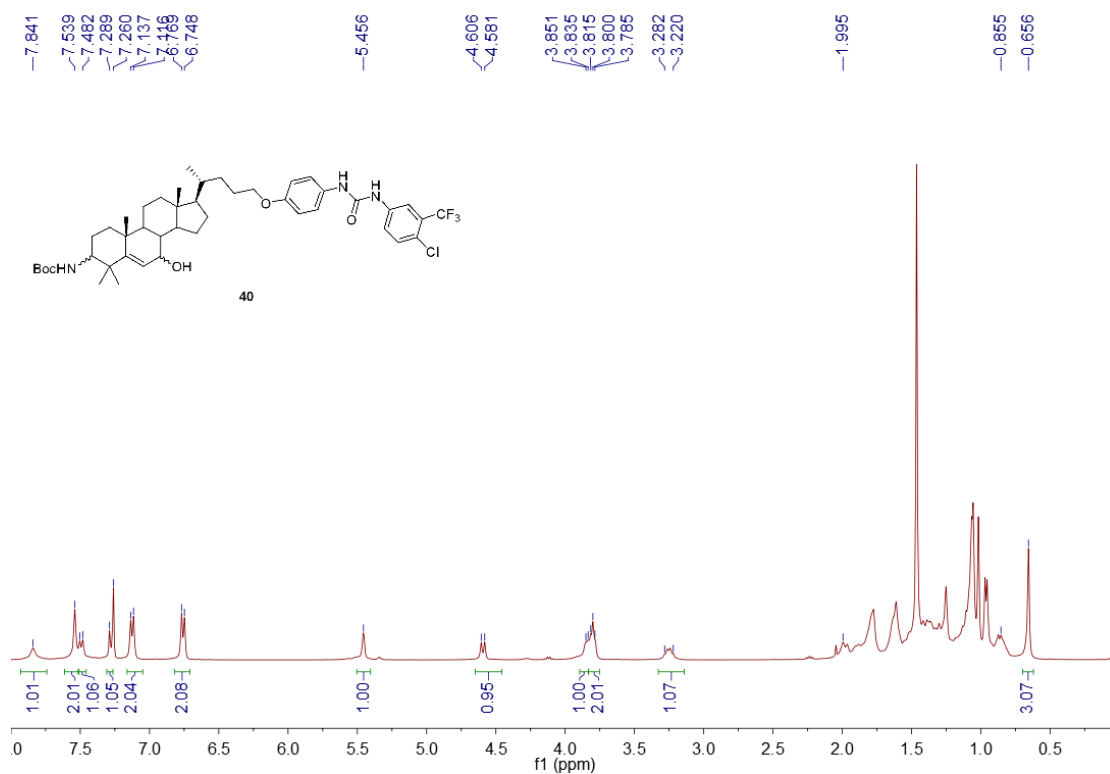
Compound **38** ( $^1\text{H}$  NMR)



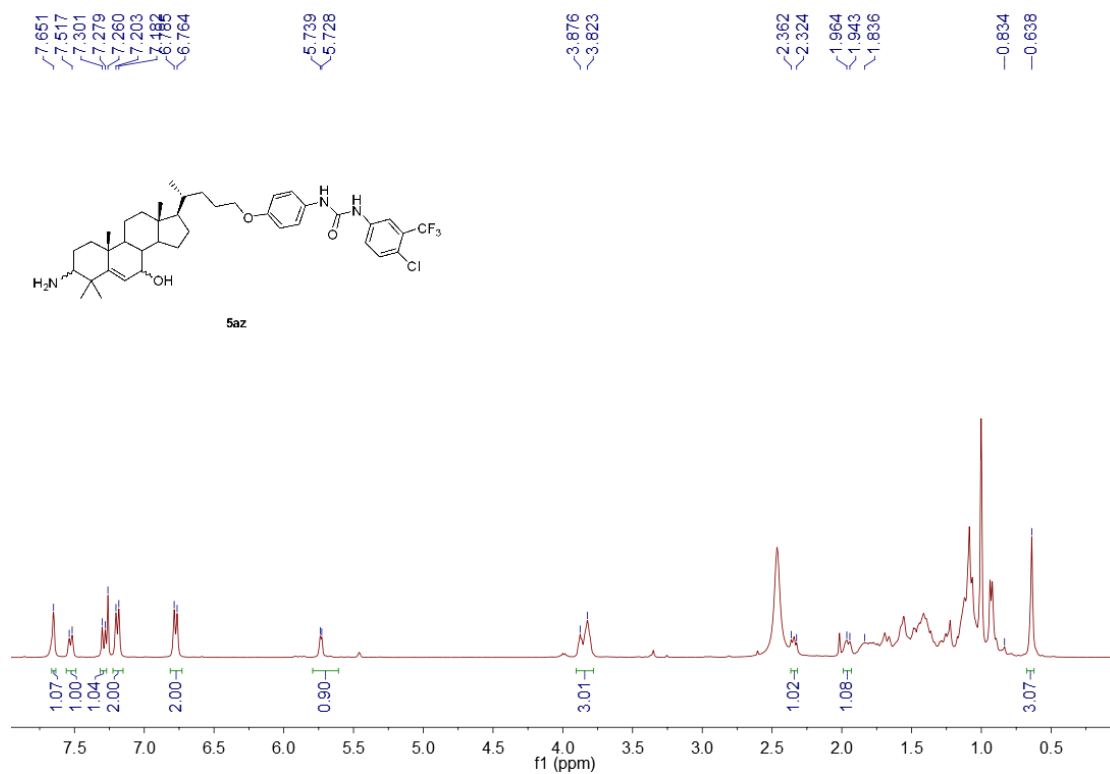
Compound **39** ( $^1\text{H}$  NMR)



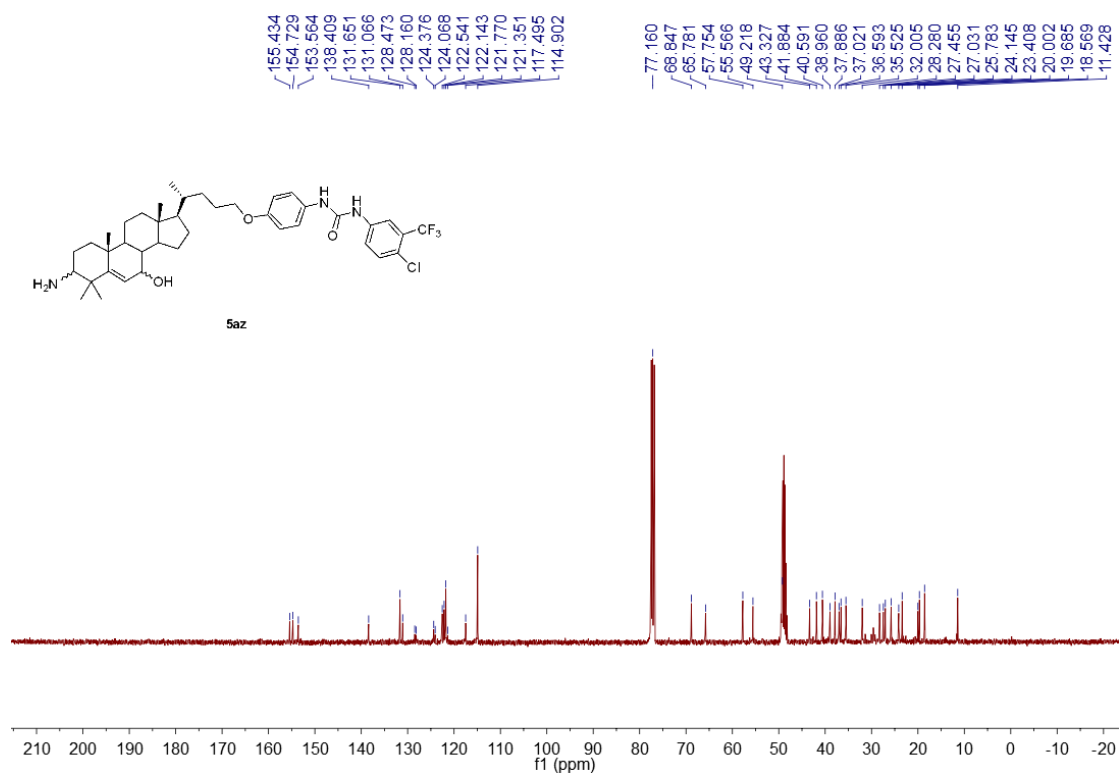
Compound **40** ( $^1\text{H}$  NMR)



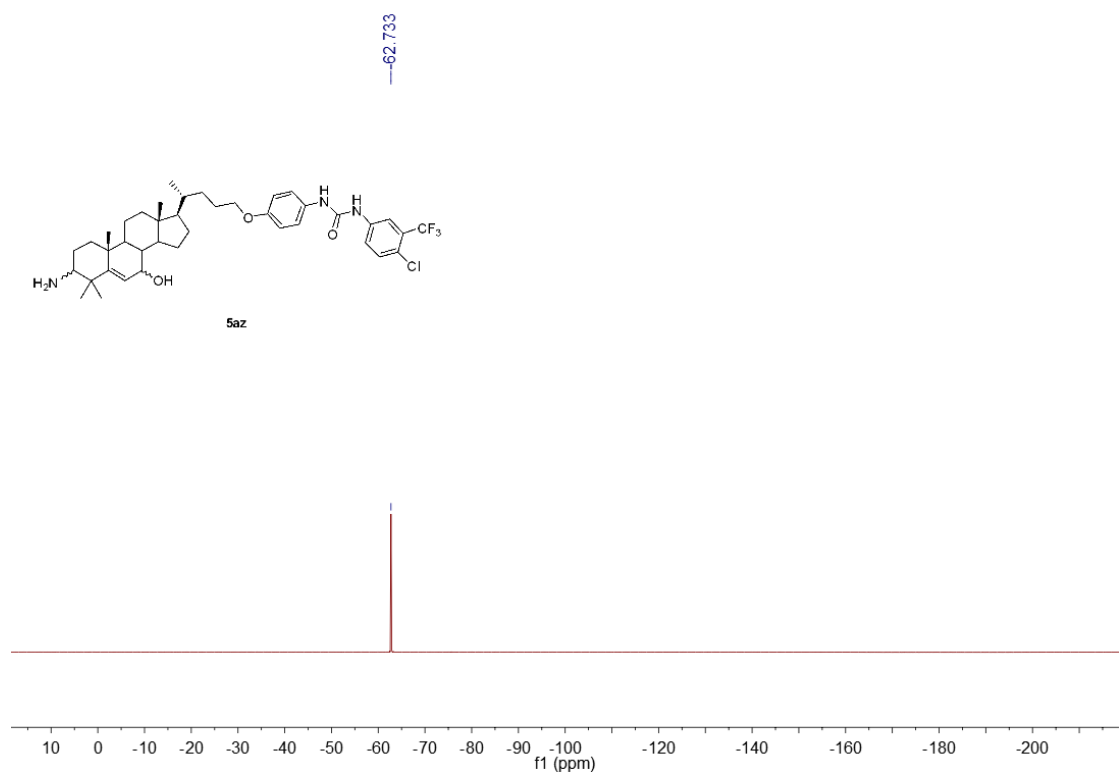
Compound **5az** ( $^1\text{H}$  NMR)



Compound **5az** ( $^{13}\text{C}$  NMR)

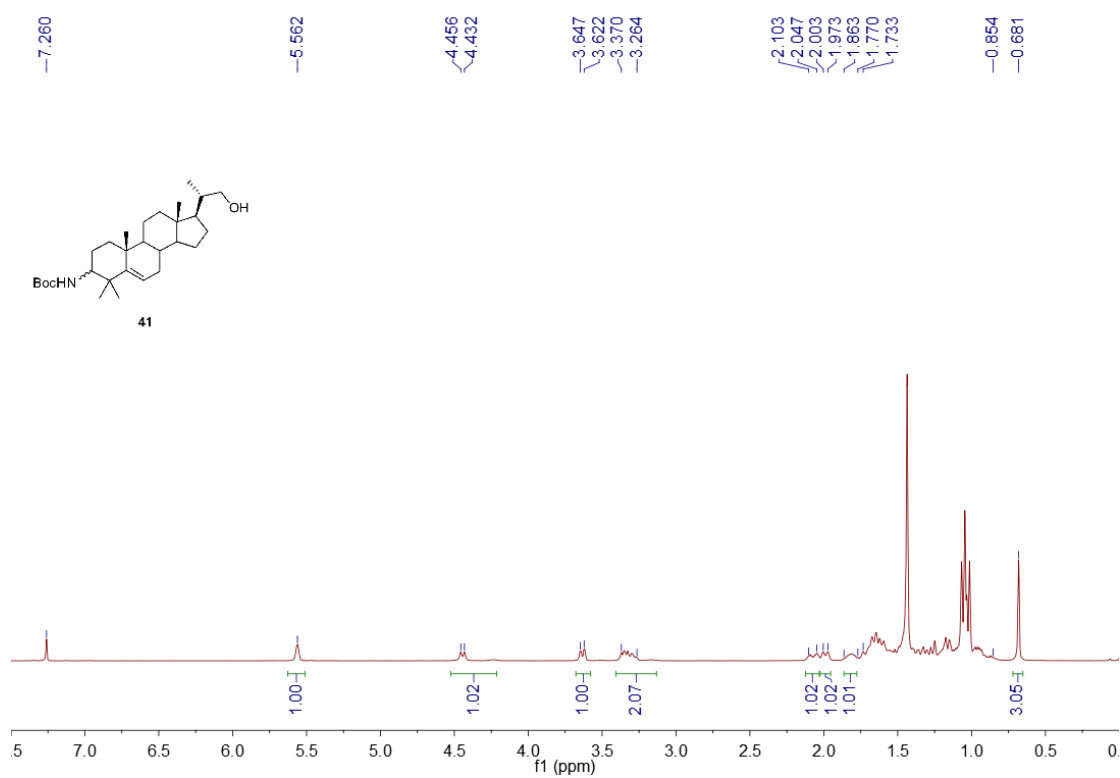


Compound **5az** ( $^{19}\text{F}$  NMR)

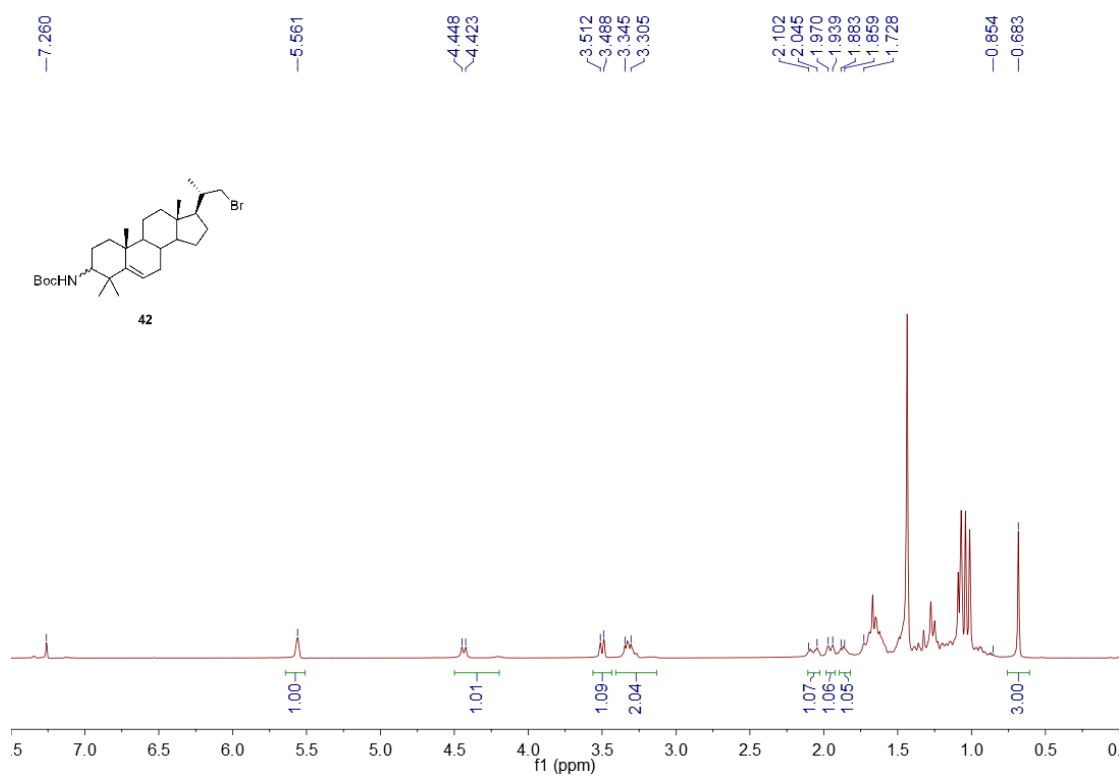




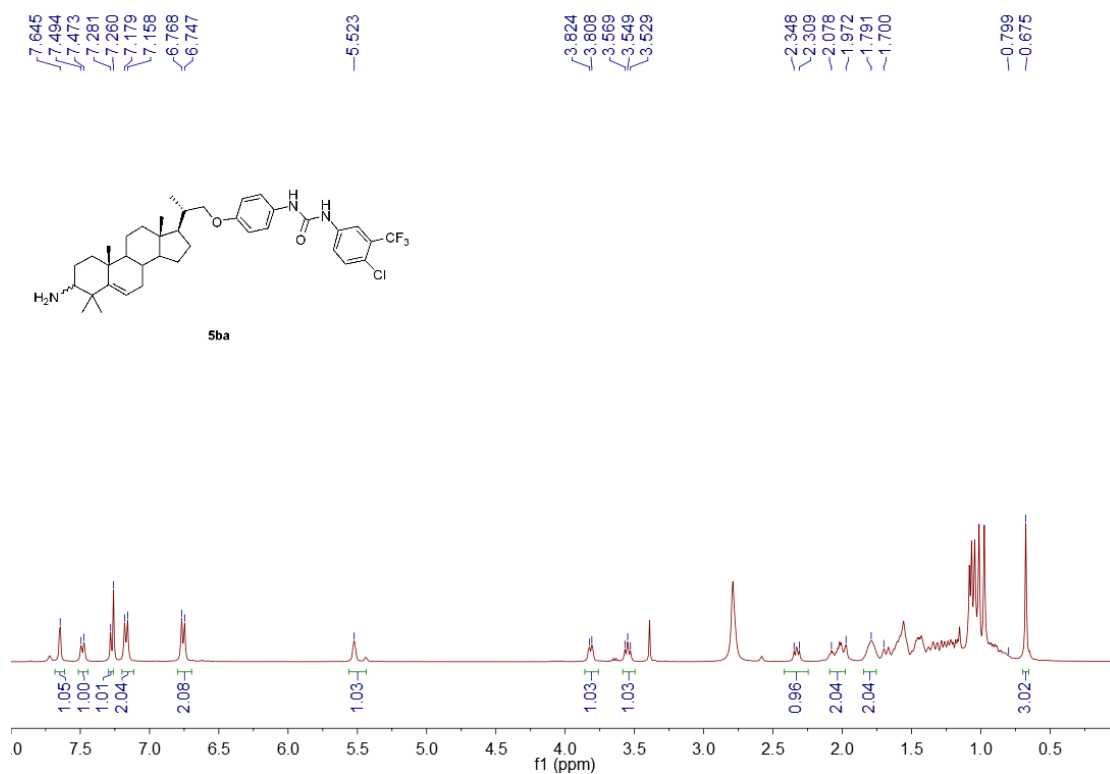
Compound **41** ( $^1\text{H}$  NMR)



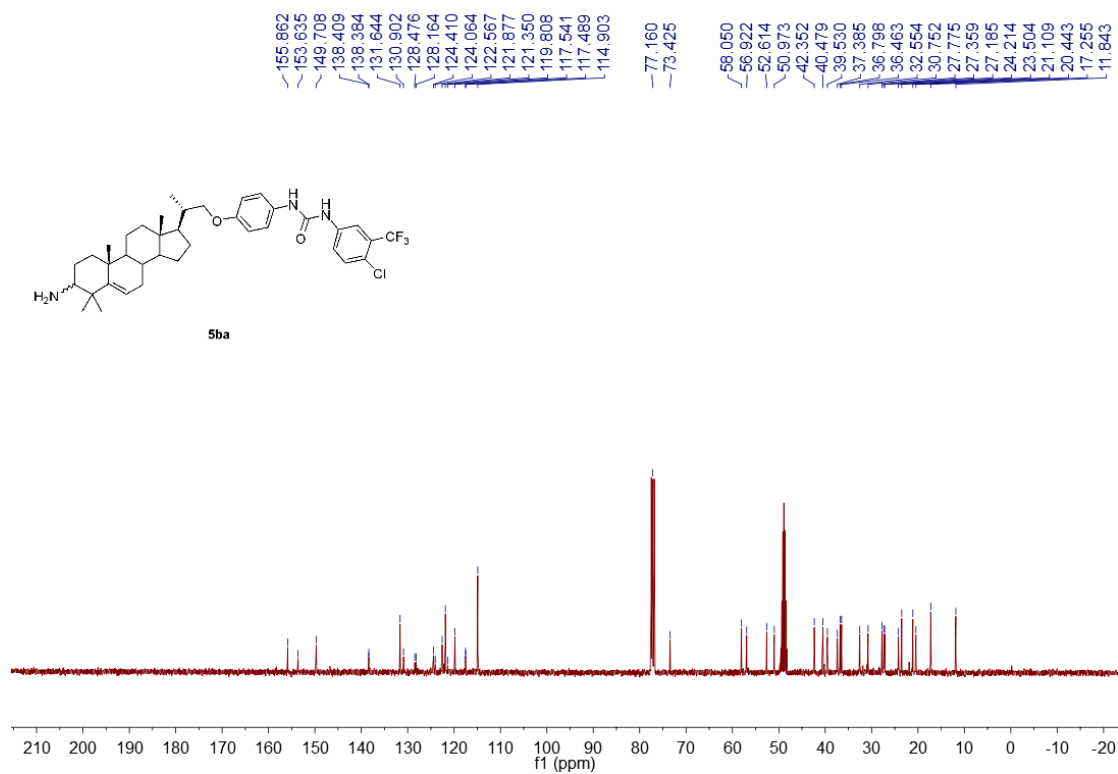
Compound **42** ( $^1\text{H}$  NMR)



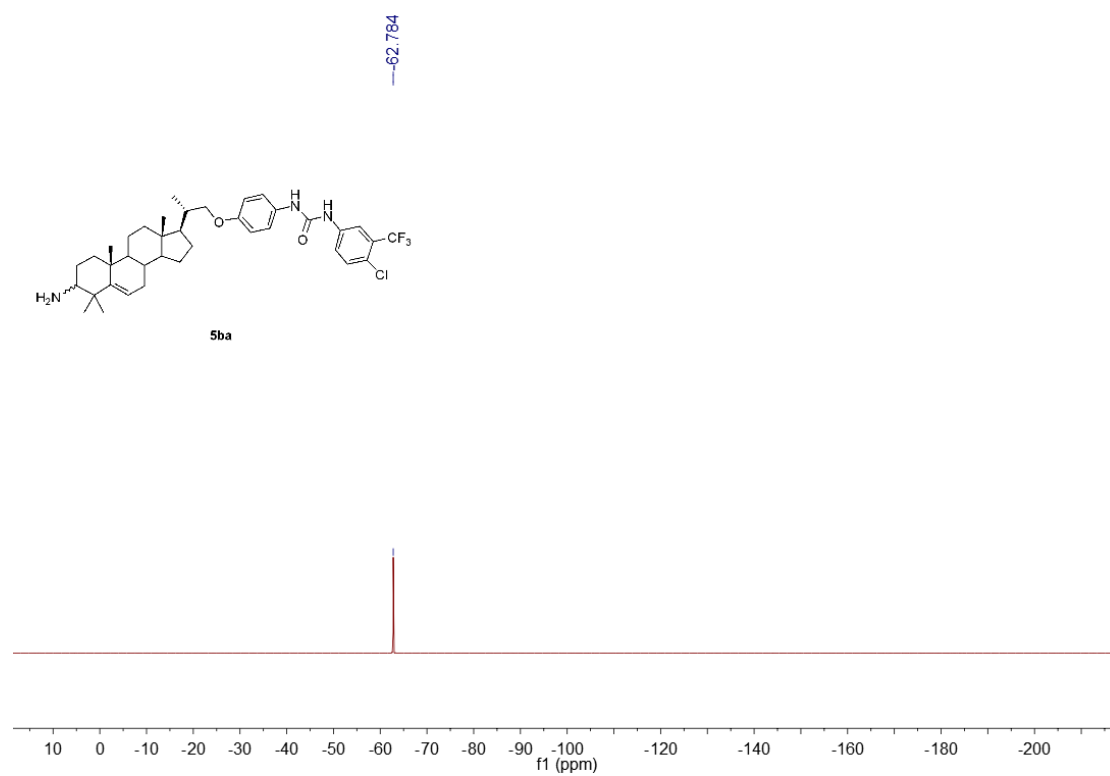
Compound **5ba** ( $^1\text{H}$  NMR)



Compound **5ba** ( $^{13}\text{C}$  NMR)

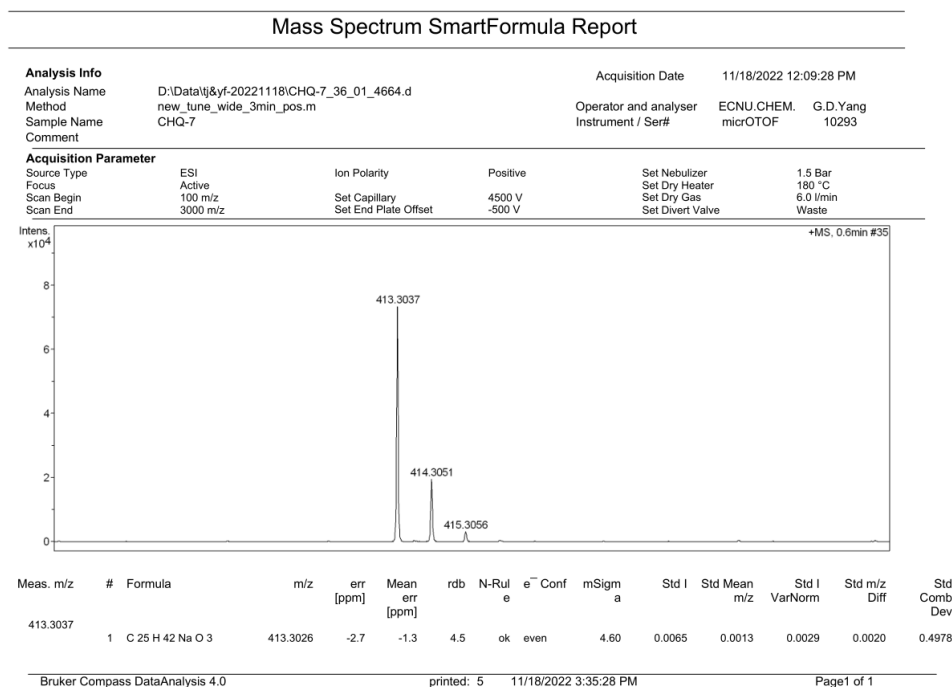


Compound **5ba** ( $^{19}\text{F}$  NMR)

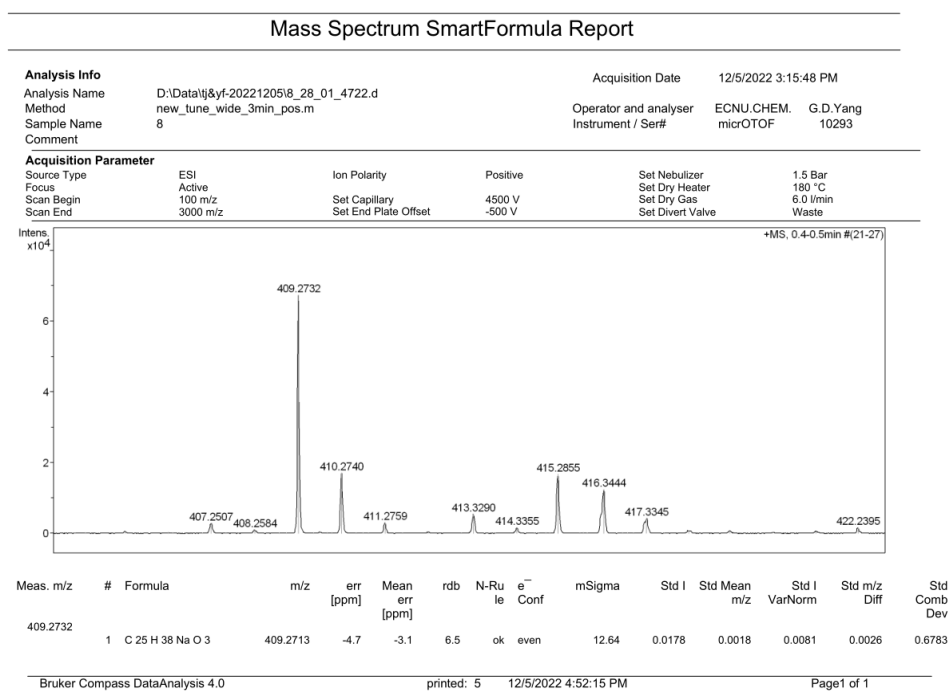


## High-resolution mass spectroscopy

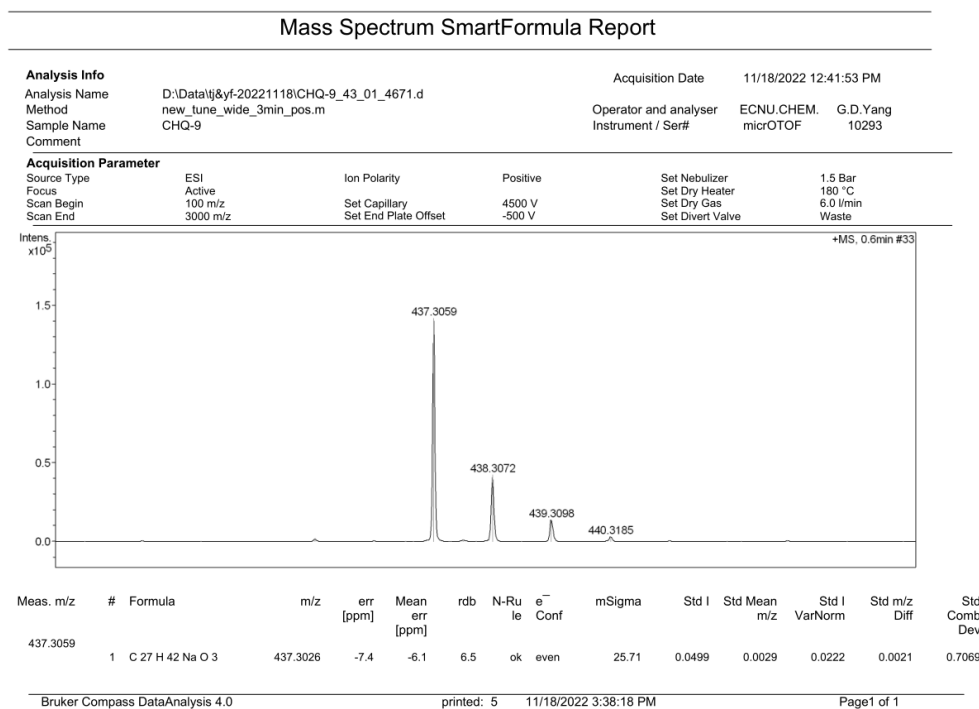
### Compound 7 (HRMS)



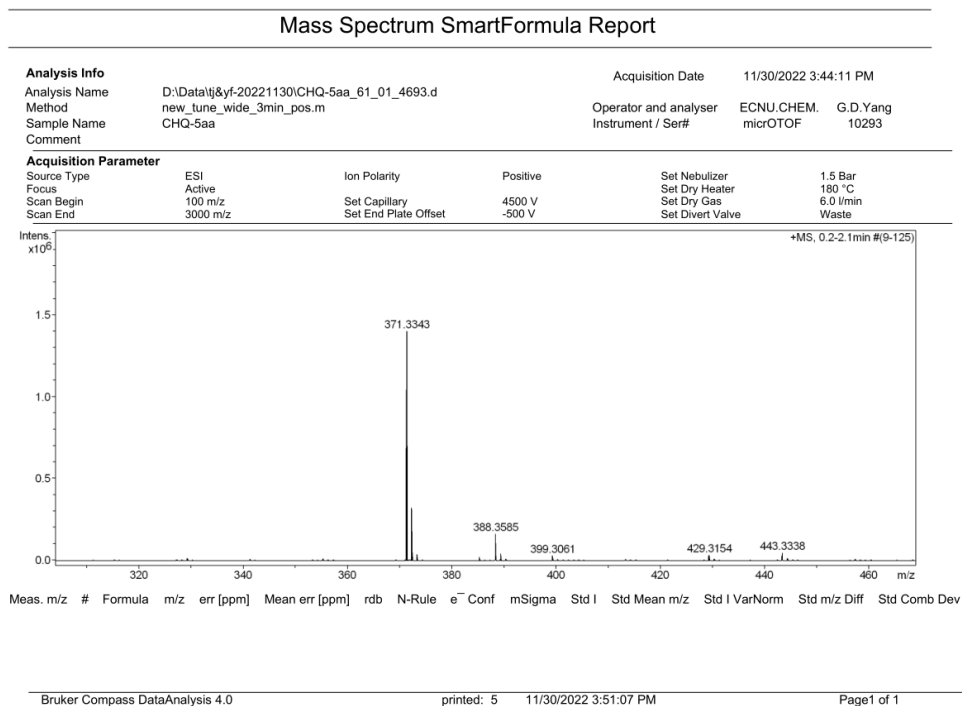
### Compound 8 (HRMS)



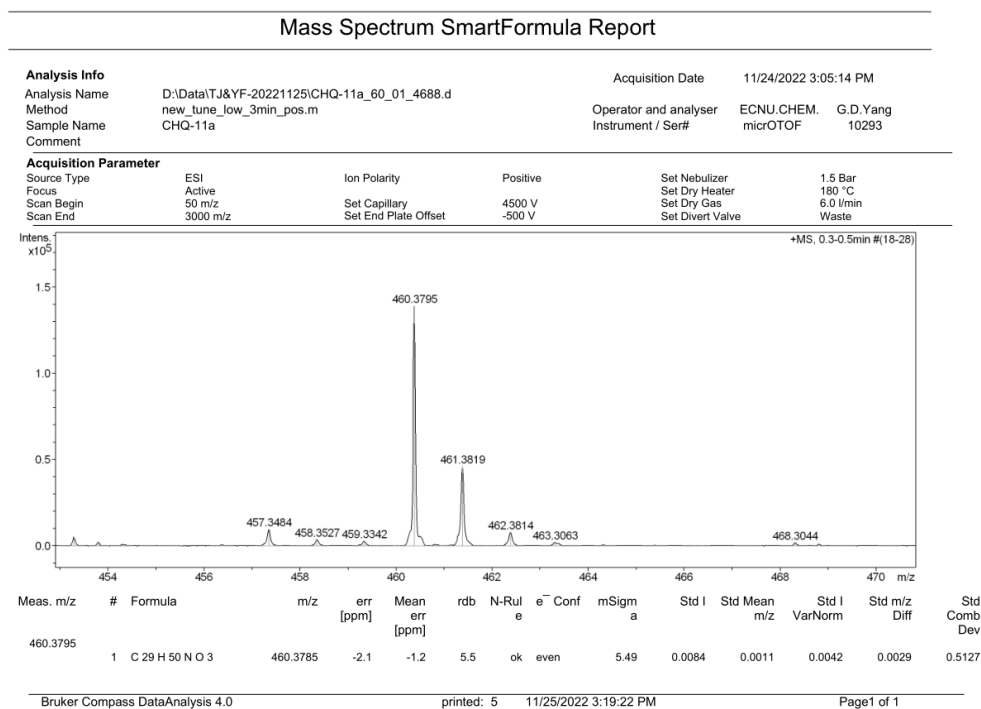
## Compound 9 (HRMS)



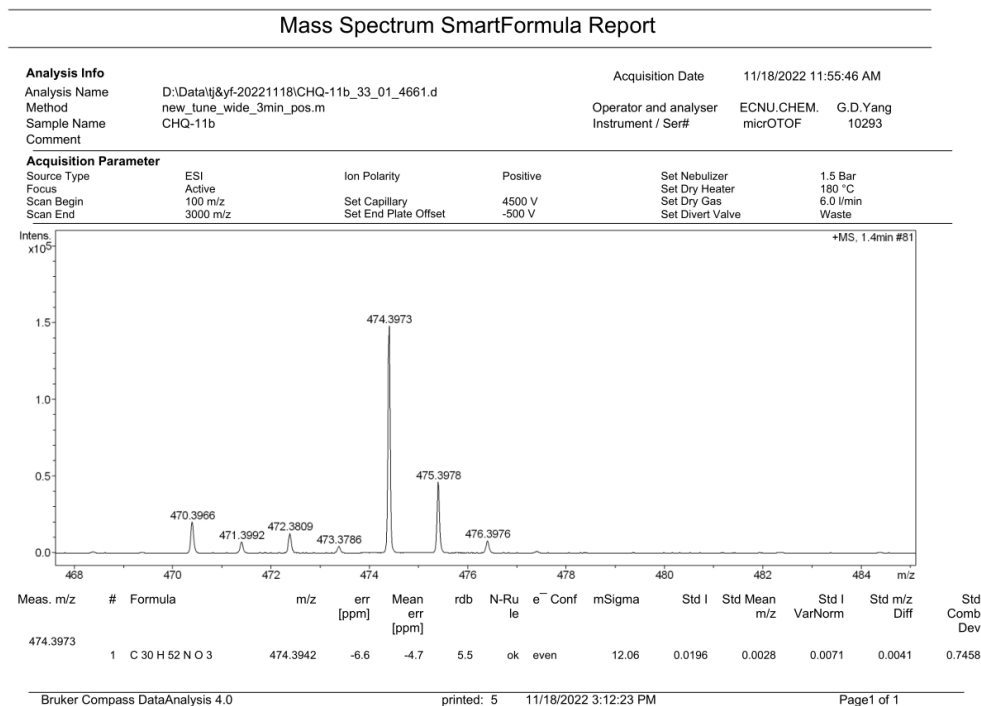
## Compound 5aa (HRMS)



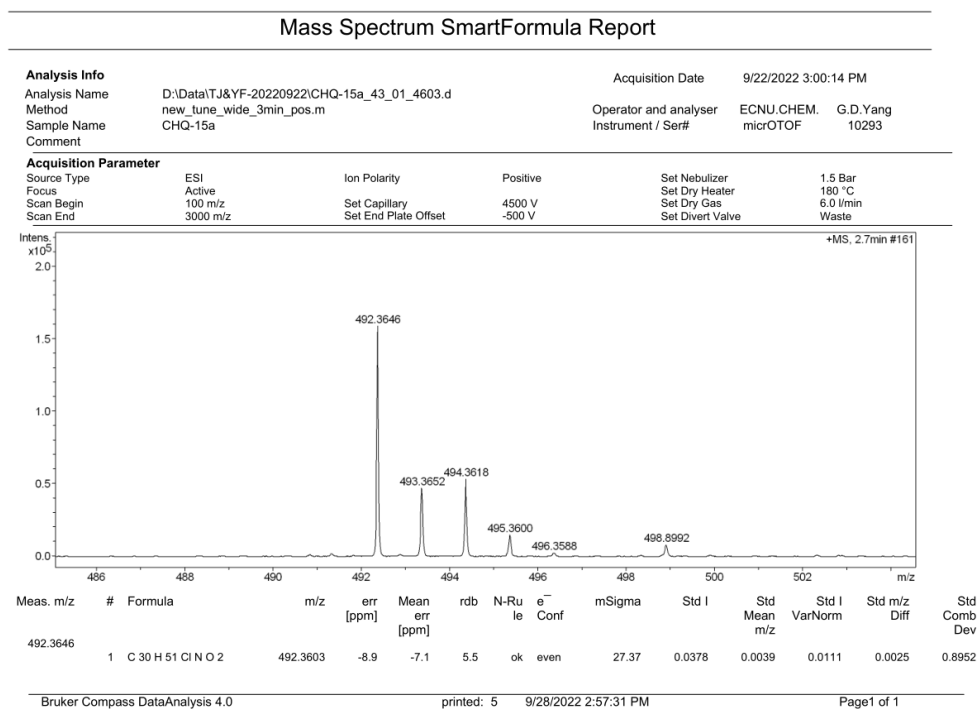
## Compound 11a (HRMS)



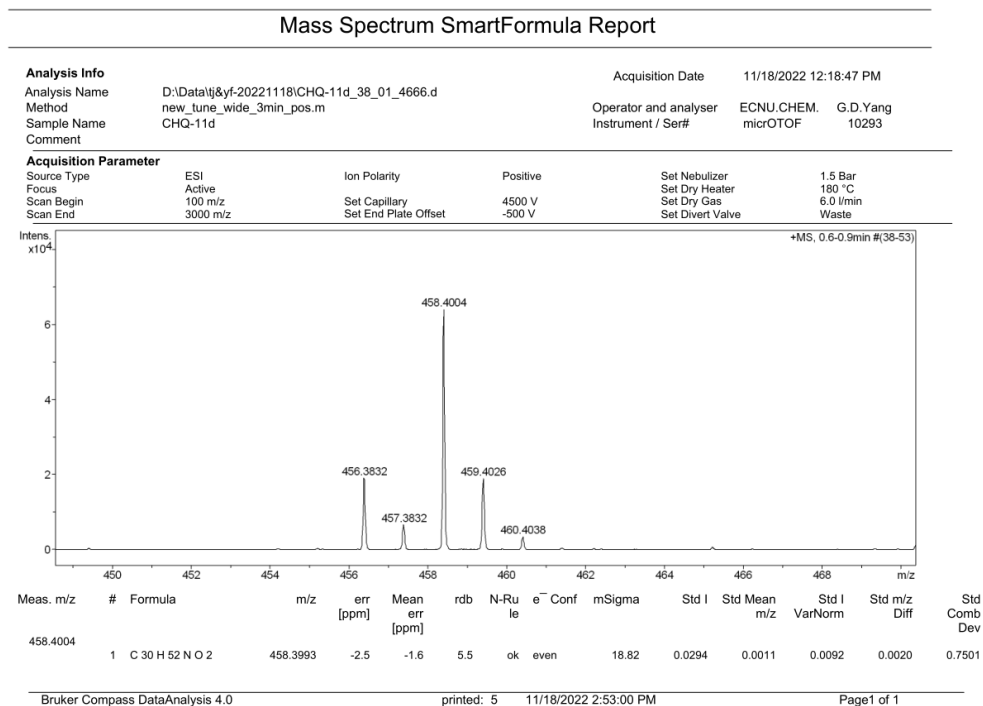
## Compound 11b (HRMS)



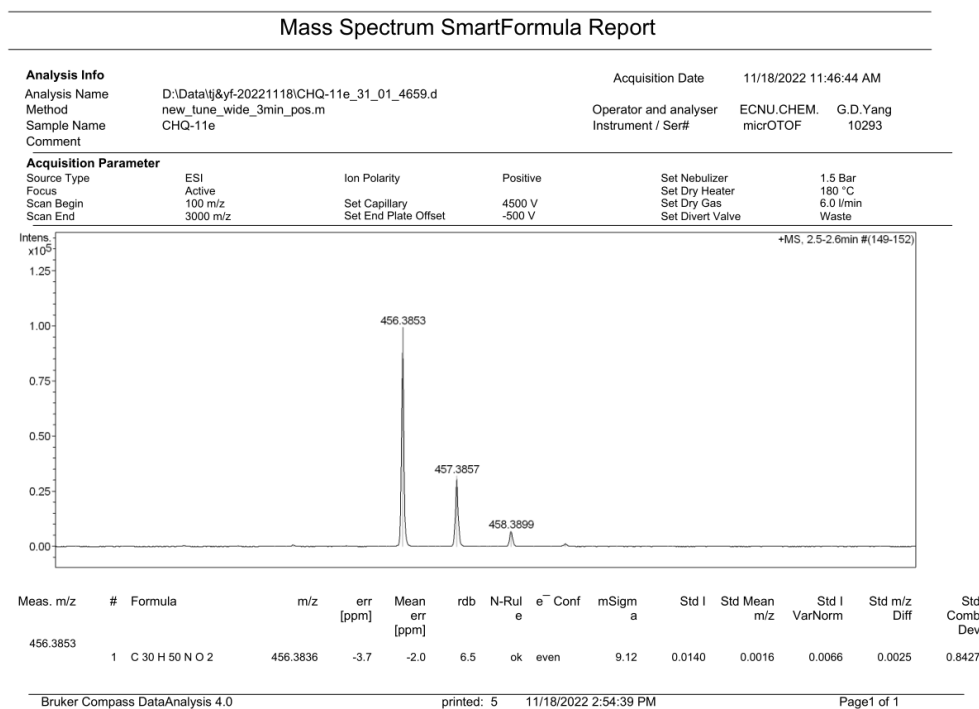
# Compound 11c (HRMS)



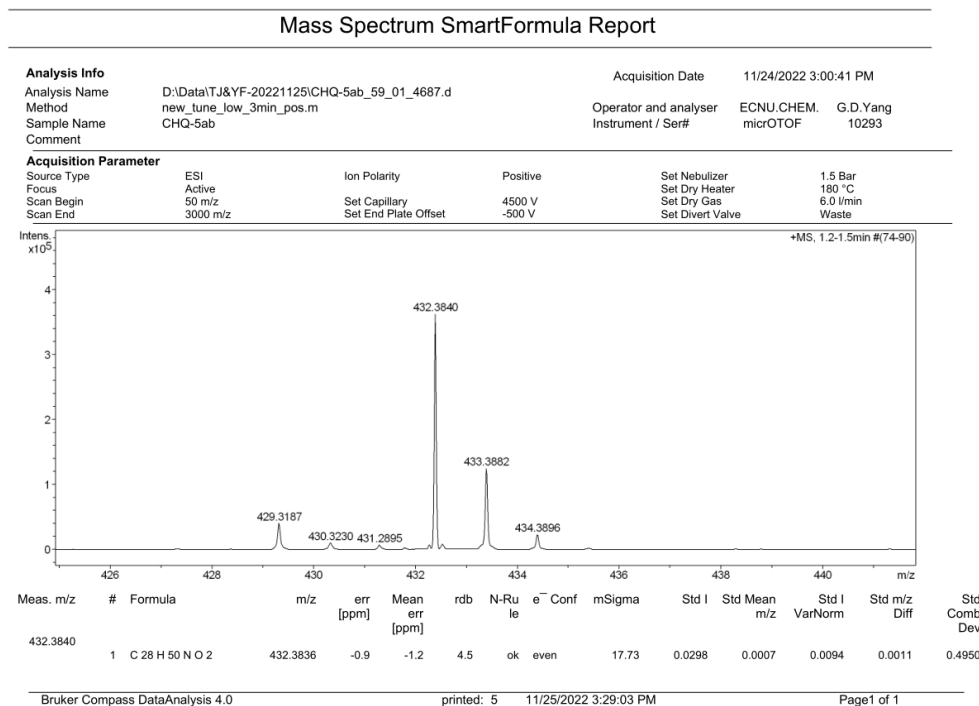
# Compound 11d (HRMS)



## Compound 11e (HRMS)

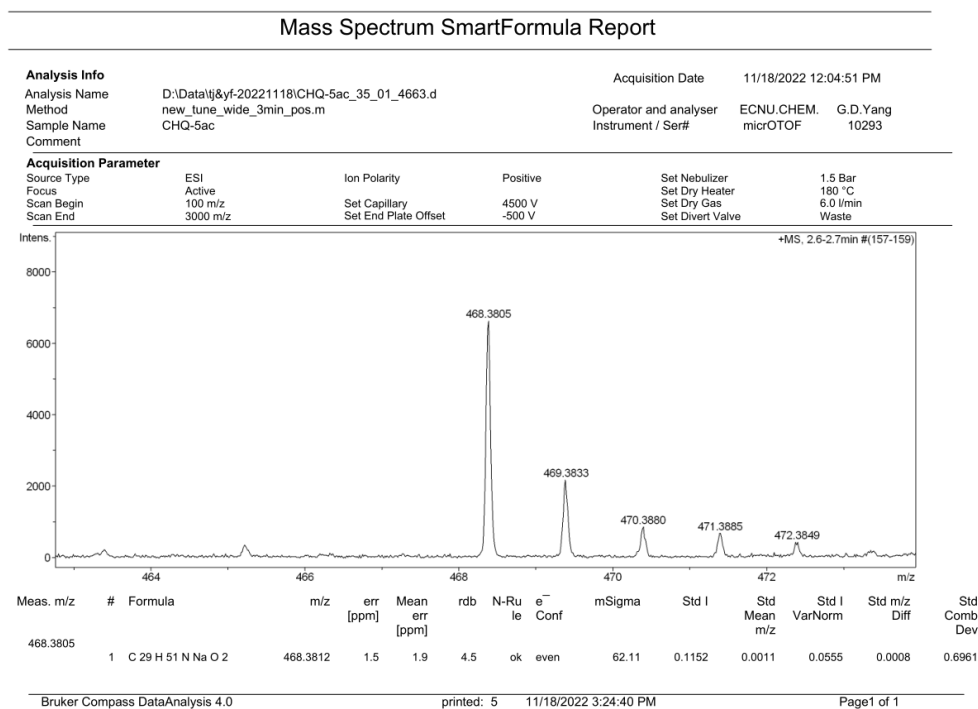


## Compound 5ab (HRMS)

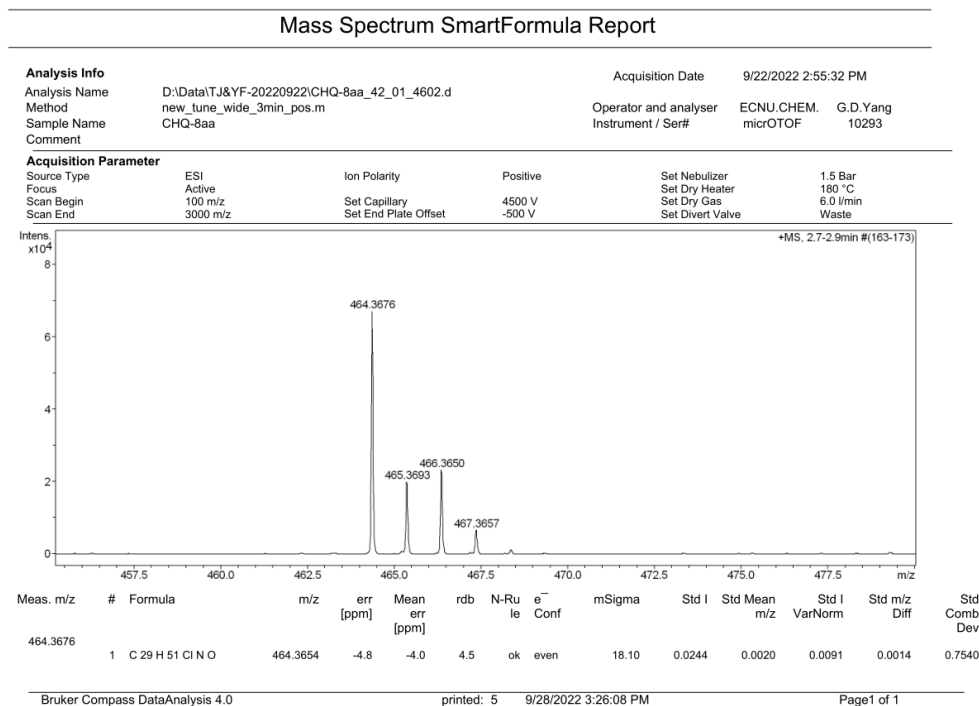




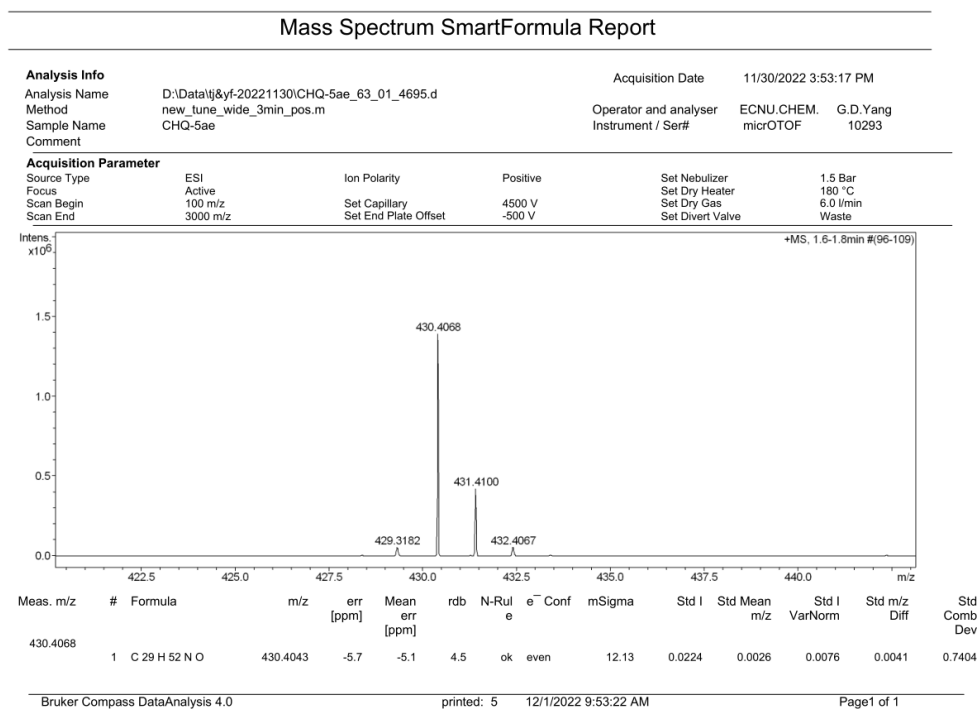
## Compound **5ac** (HRMS)



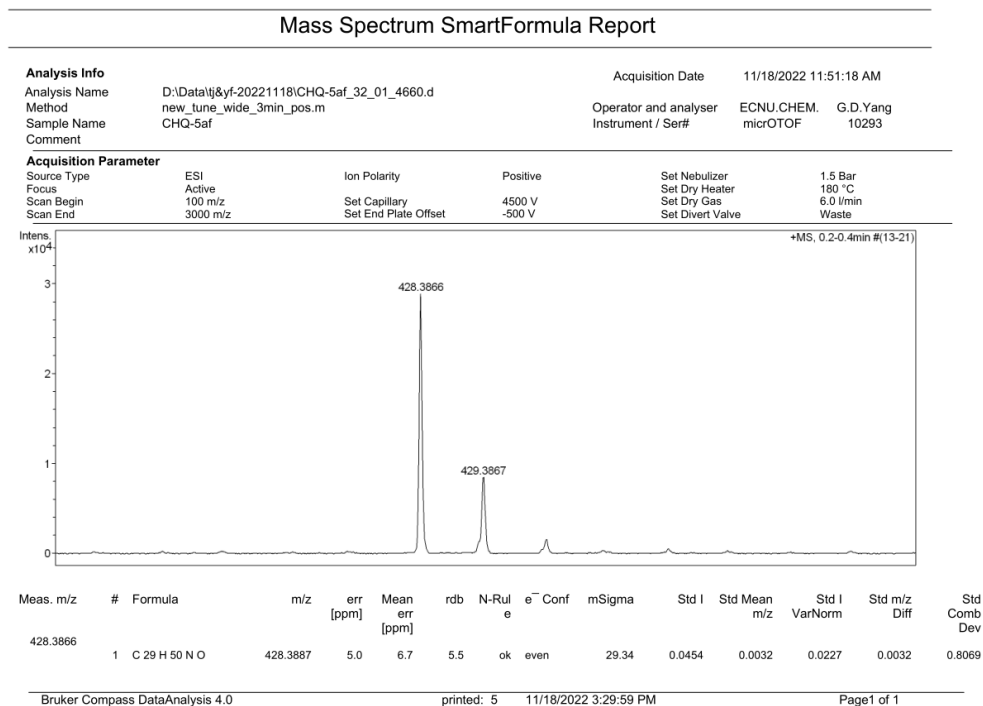
## Compound **5ad** (HRMS)



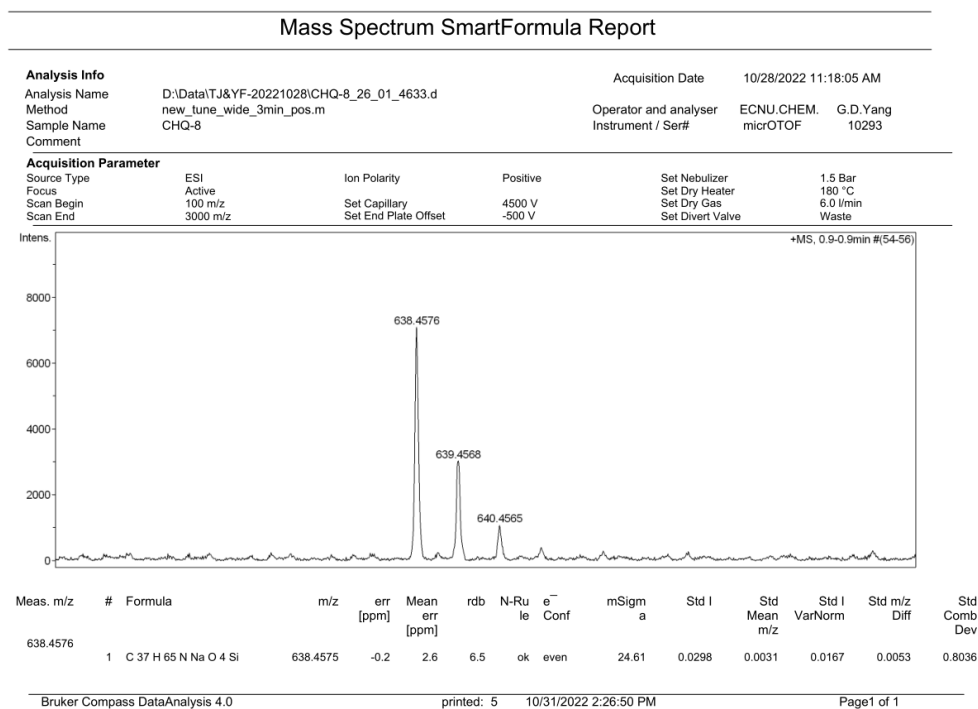
## Compound 5ae (HRMS)



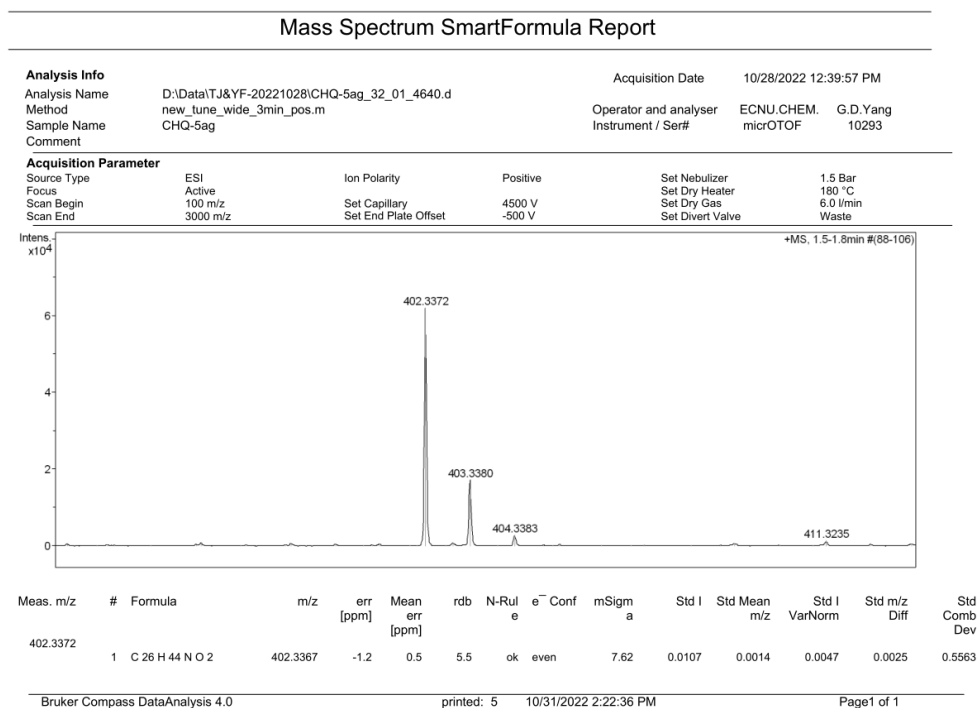
## Compound 5af (HRMS)



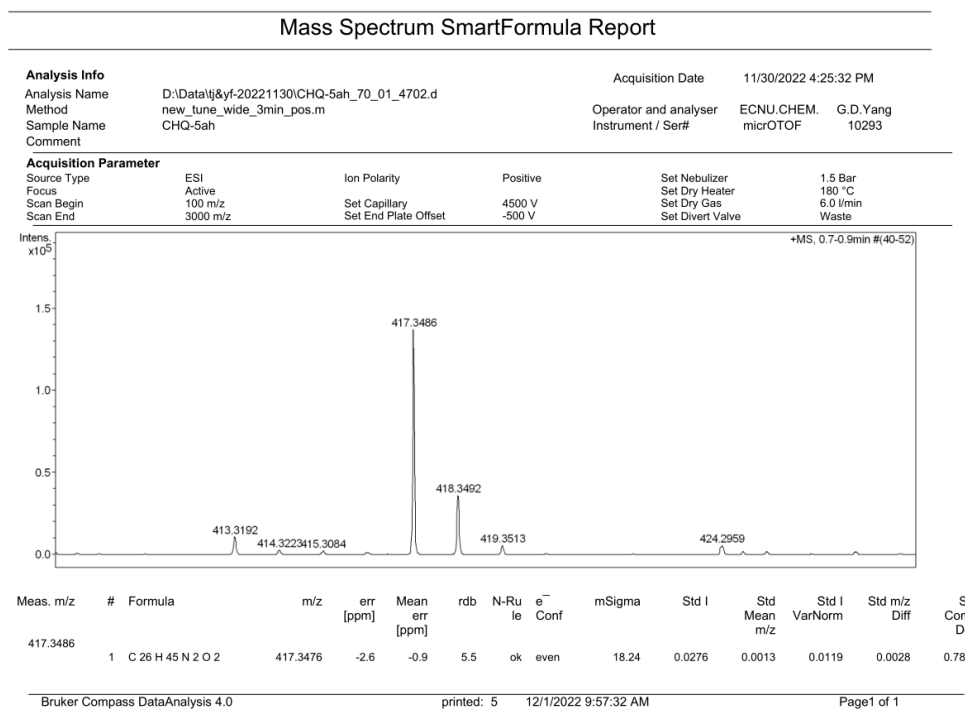
## Compound 14 (HRMS)



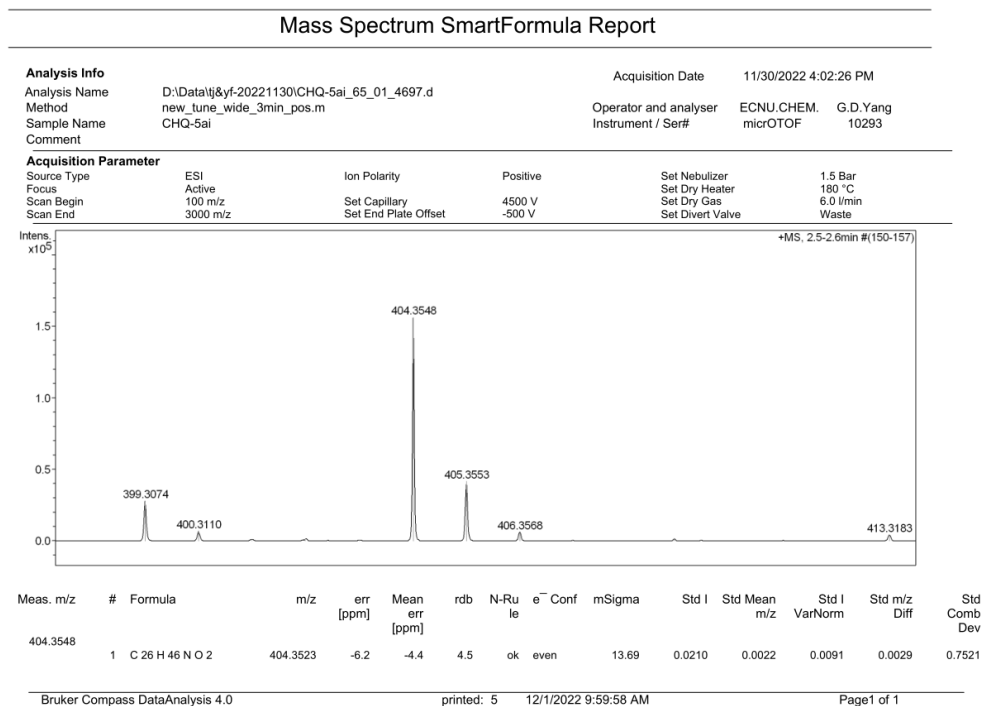
## Compound 5ag (HRMS)



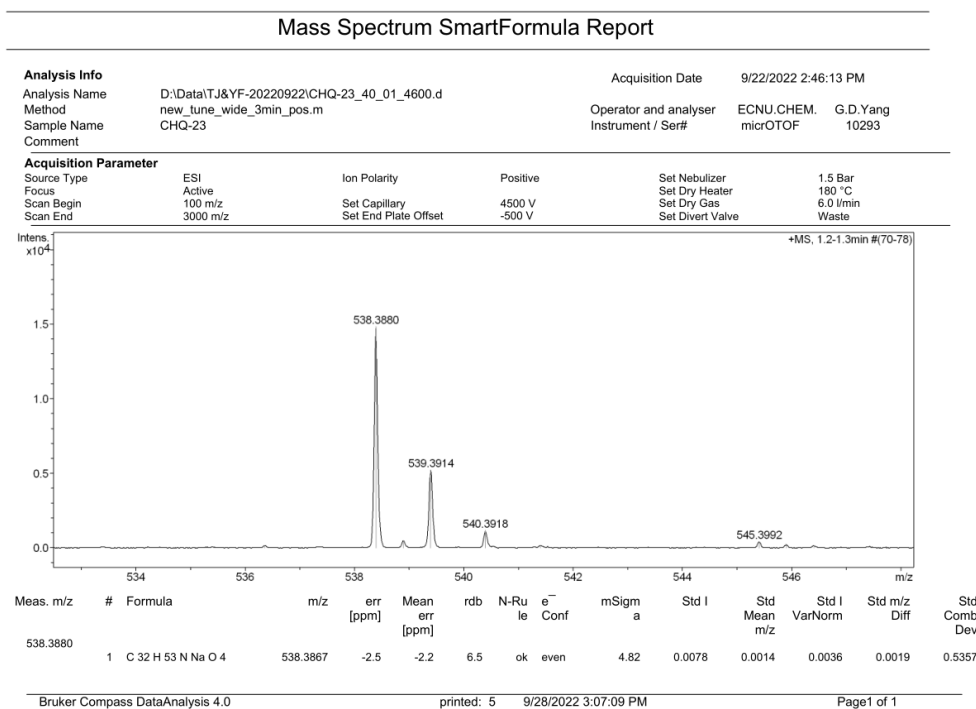
## Compound 5ah (HRMS)



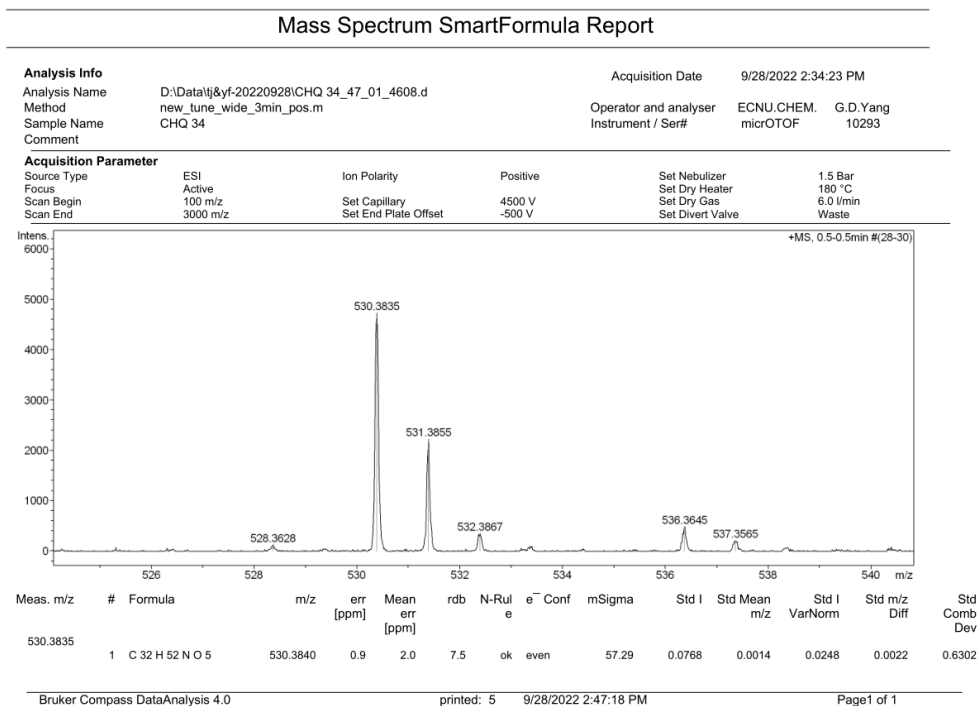
## Compound 5ai (HRMS)



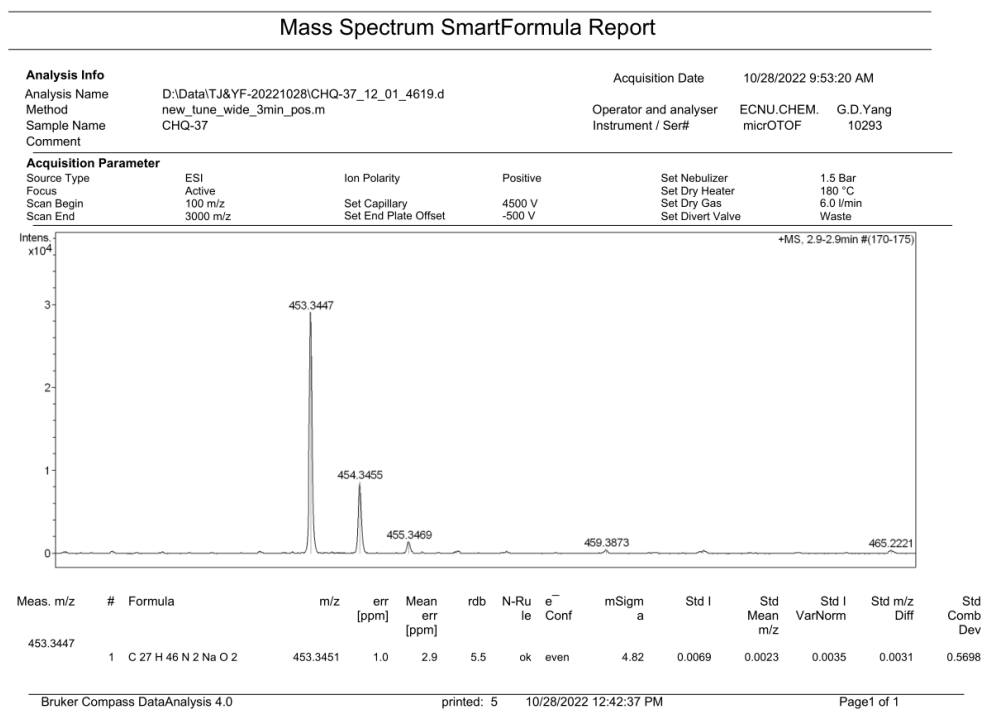
## Compound 15 (HRMS)



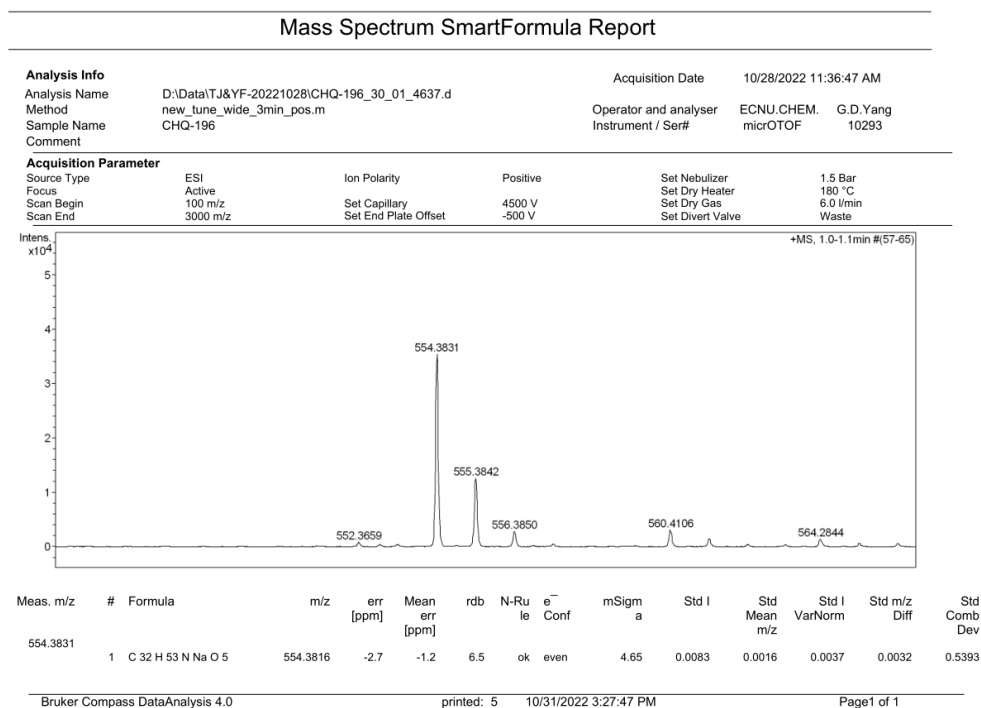
## Compound 16 (HRMS)



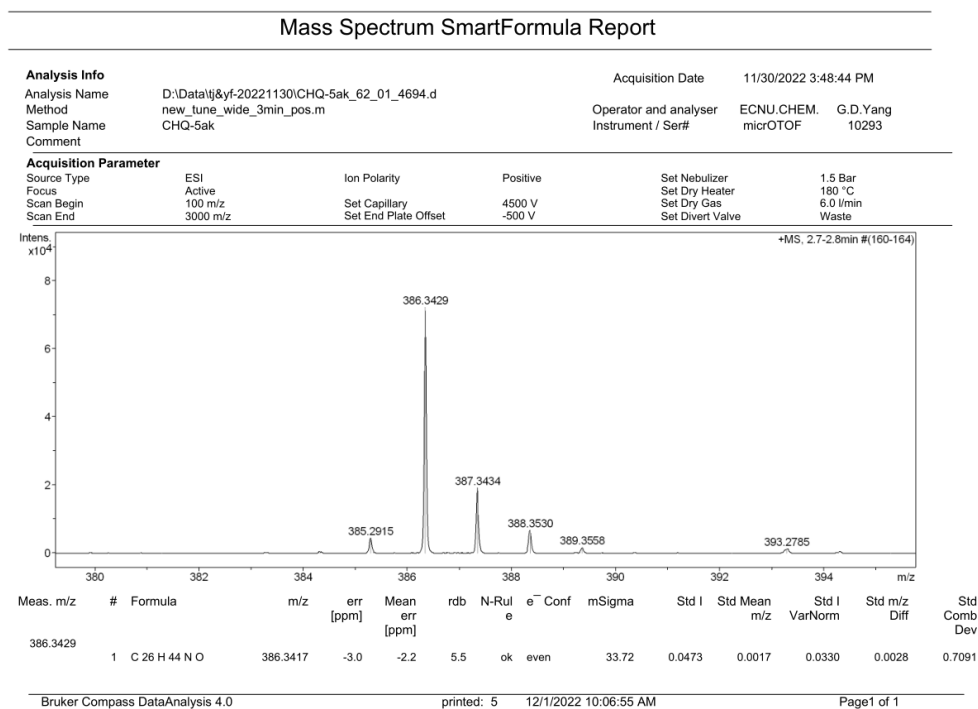
## Compound 18 (HRMS)



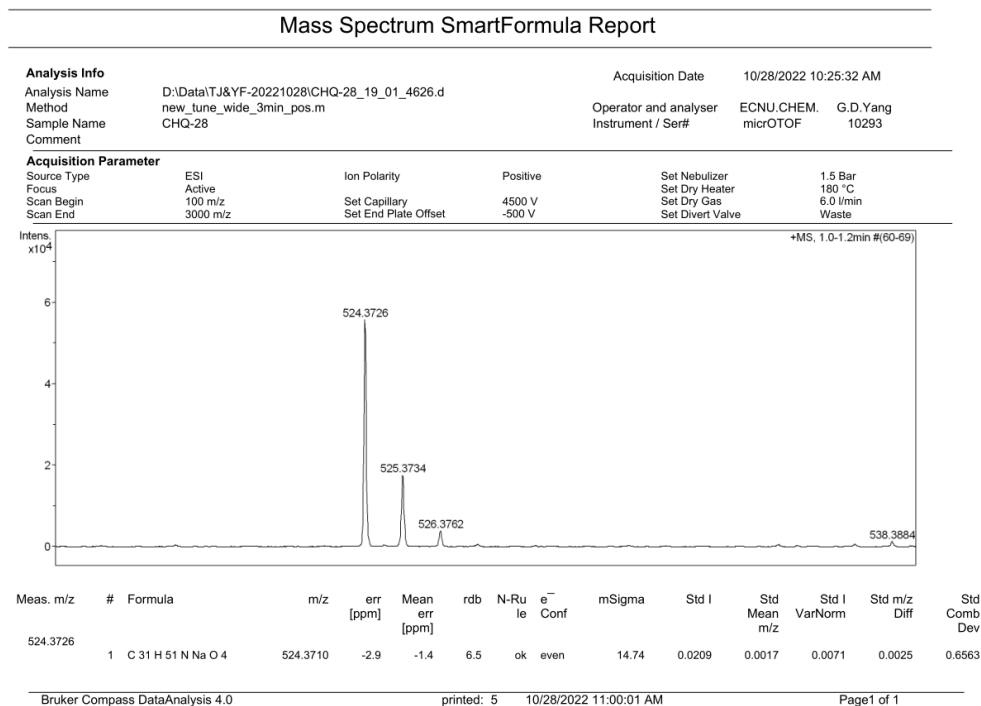
## Compound 19 (HRMS)



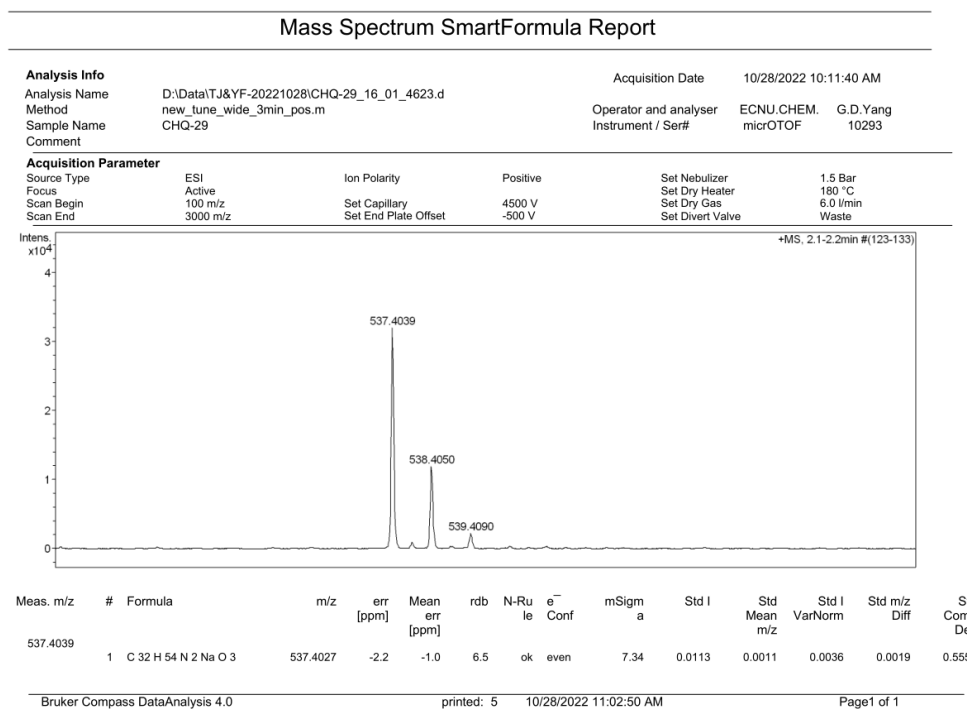
## Compound 5ak (HRMS)



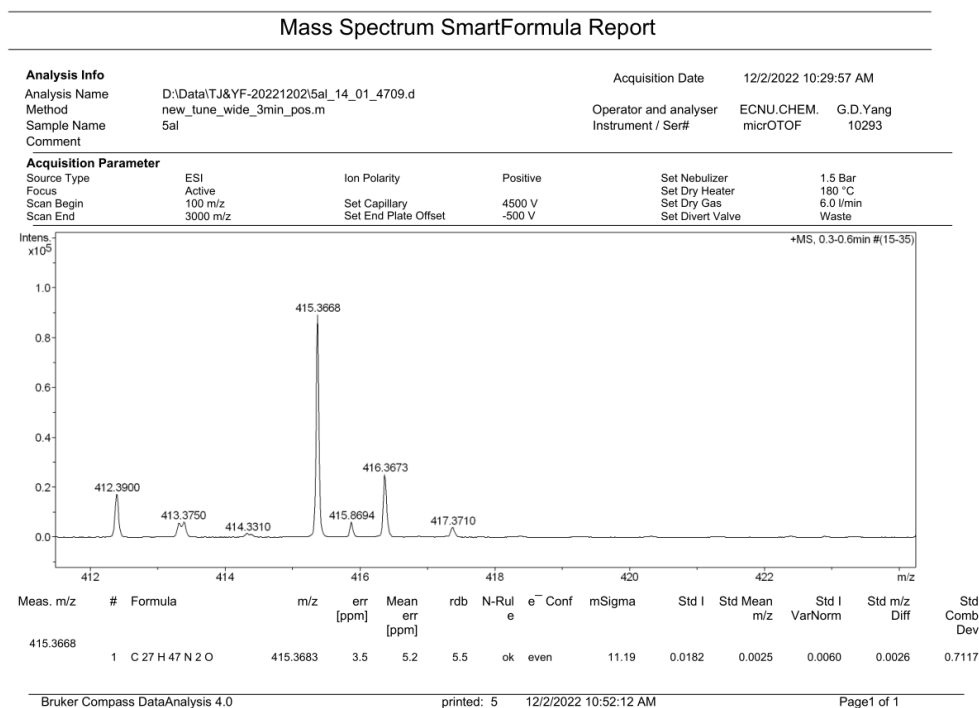
## Compound 22 (HRMS)



## Compound 23 (HRMS)

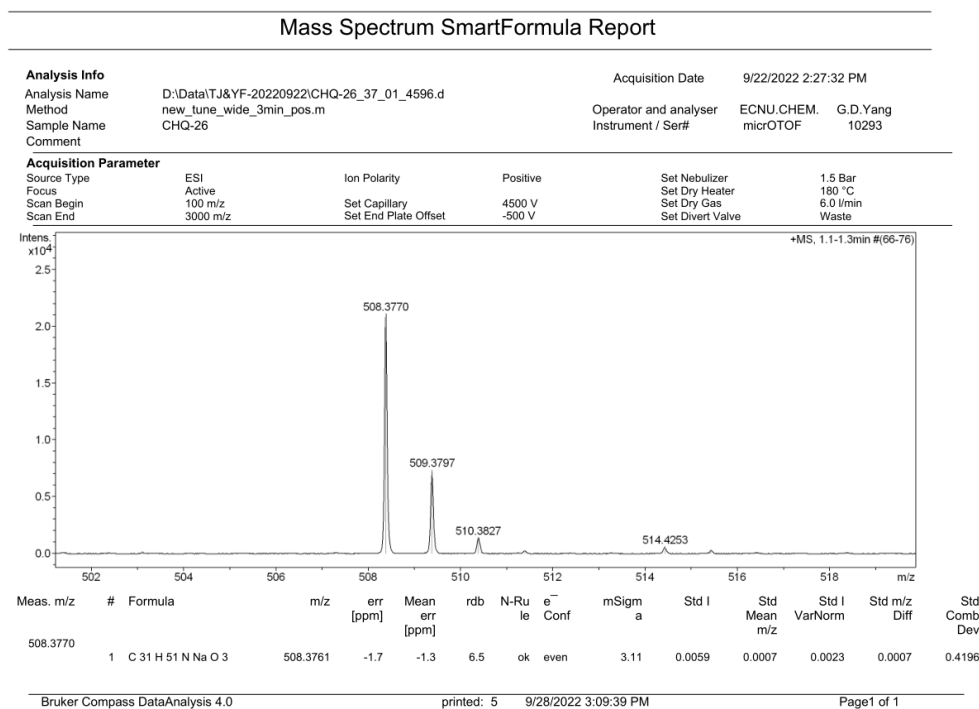


## Compound 5al (HRMS)

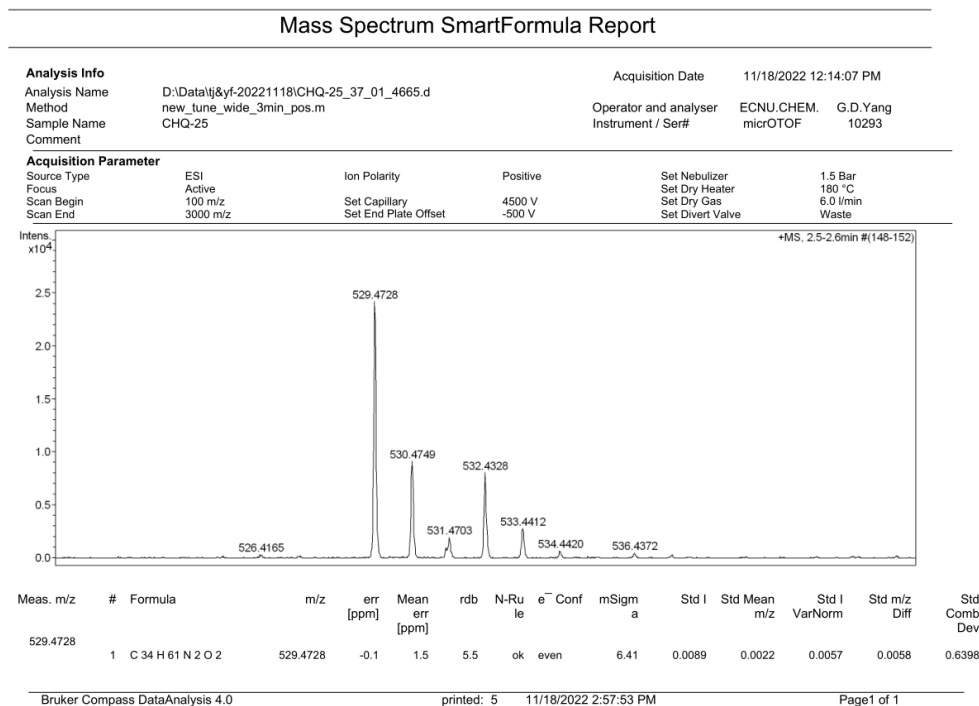




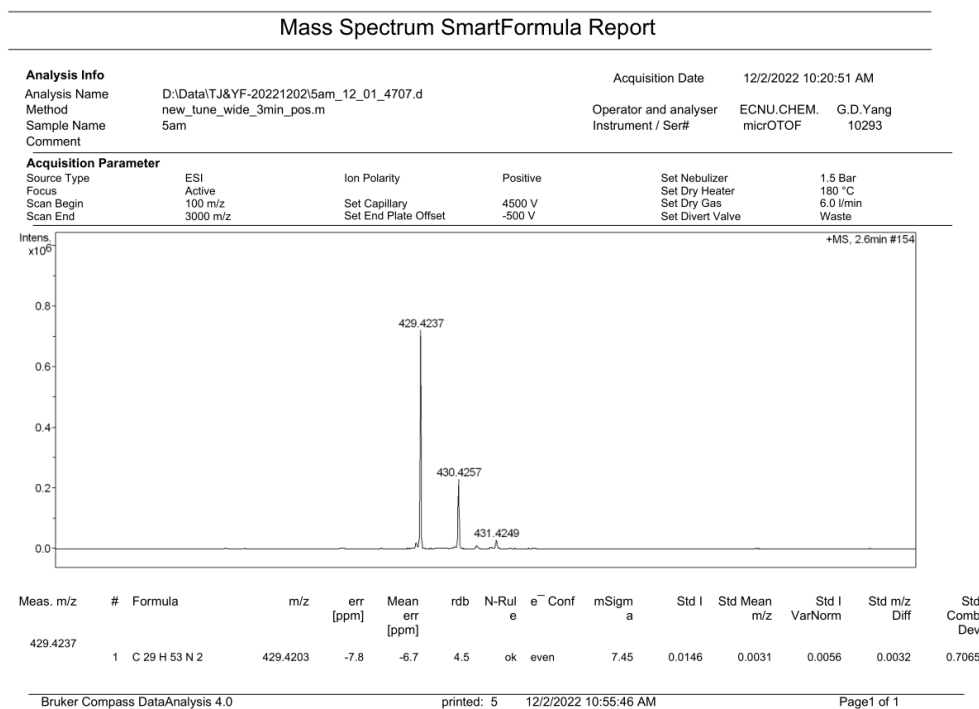
## Compound 24 (HRMS)



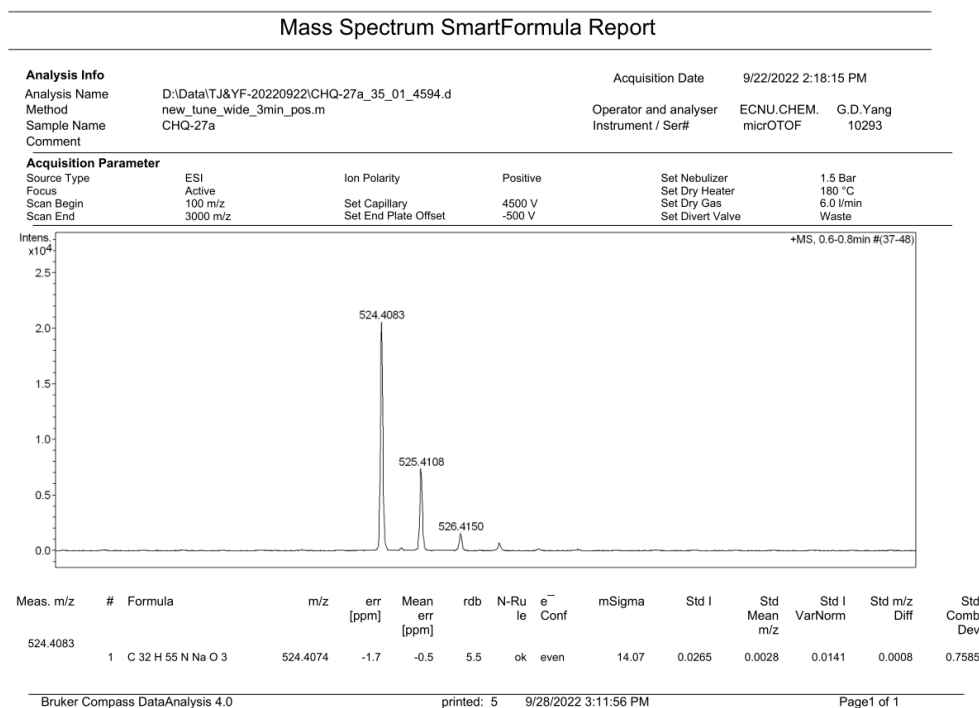
## Compound 25 (HRMS)



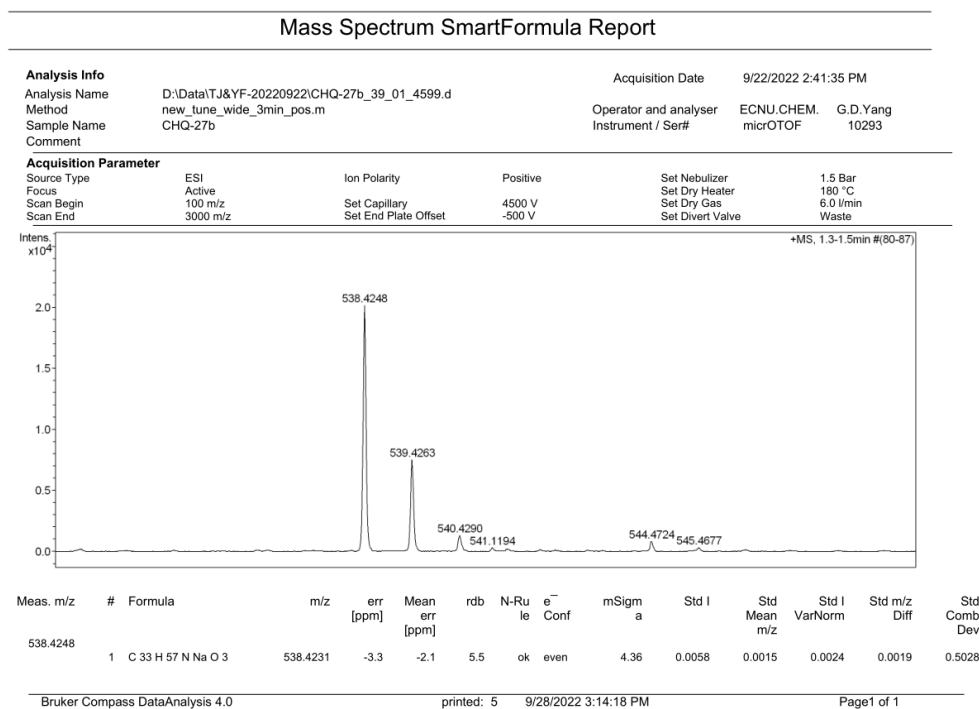
# Compound 5am (HRMS)



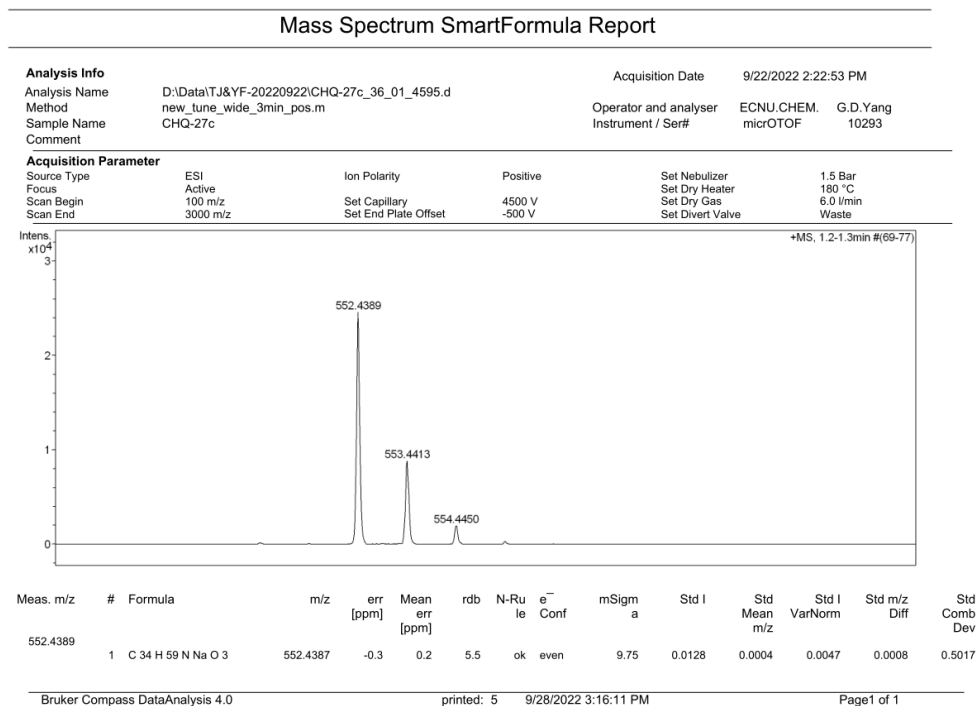
# Compound 26a (HRMS)



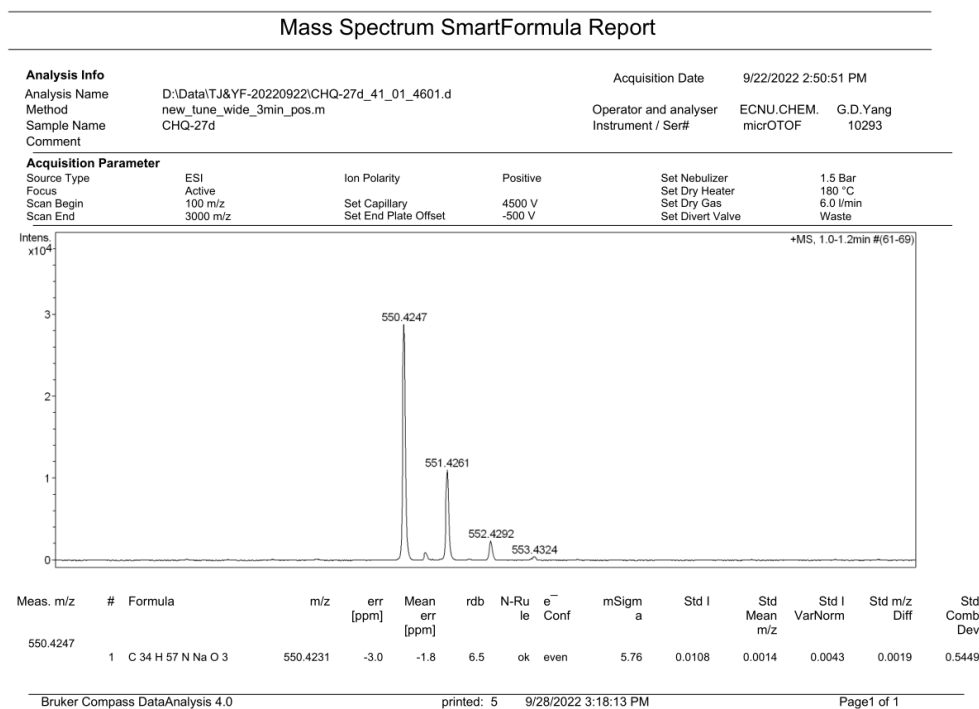
## Compound 26b (HRMS)



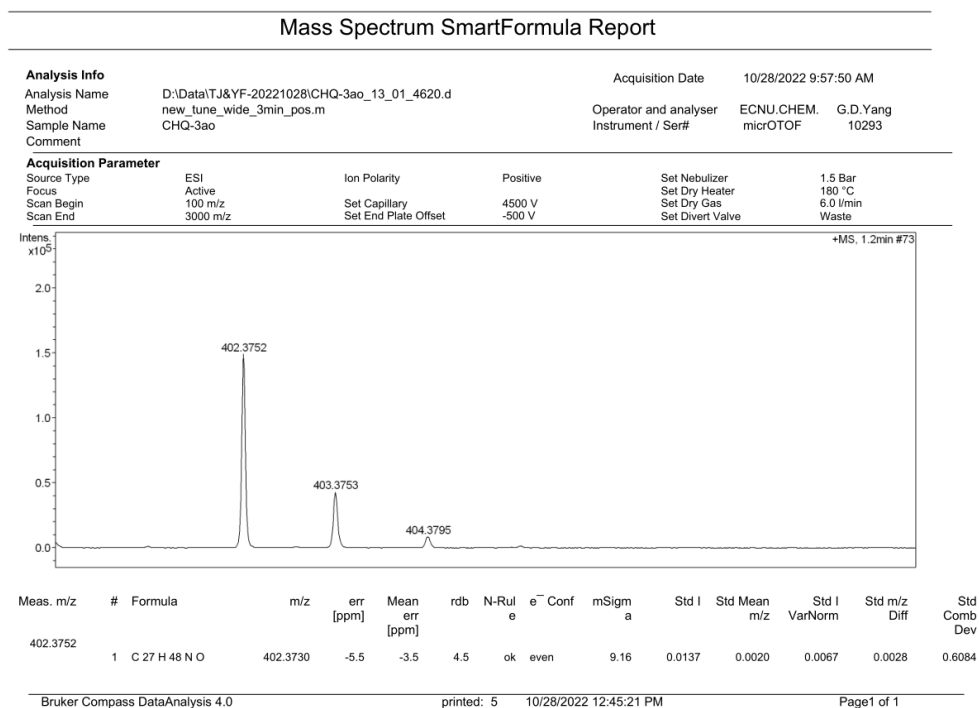
## Compound 26c (HRMS)



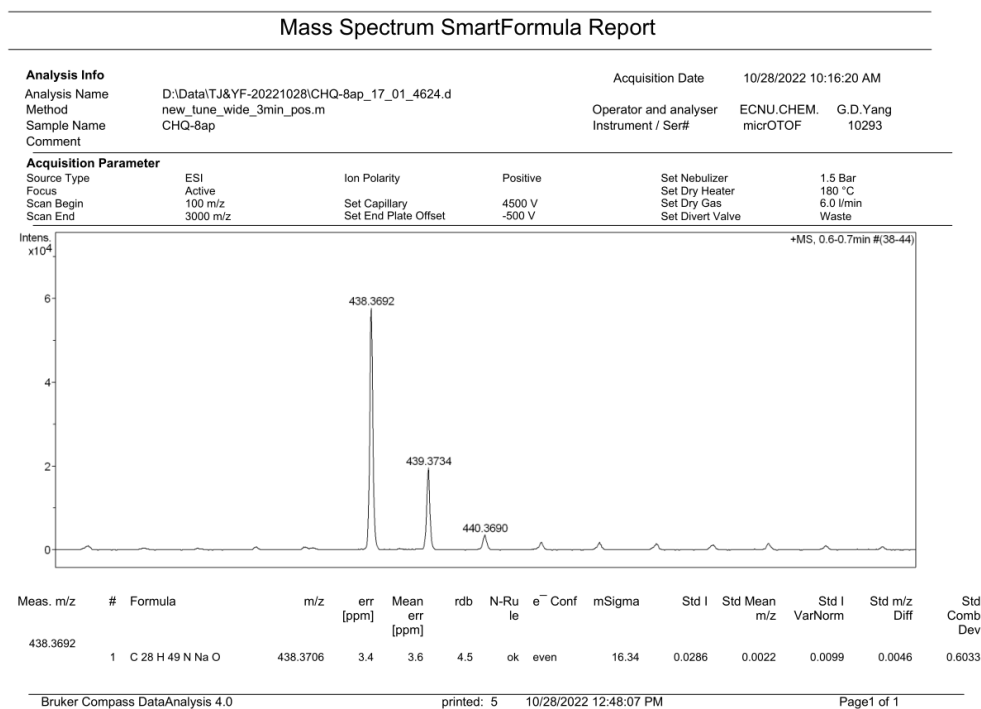
## Compound **26e** (HRMS)



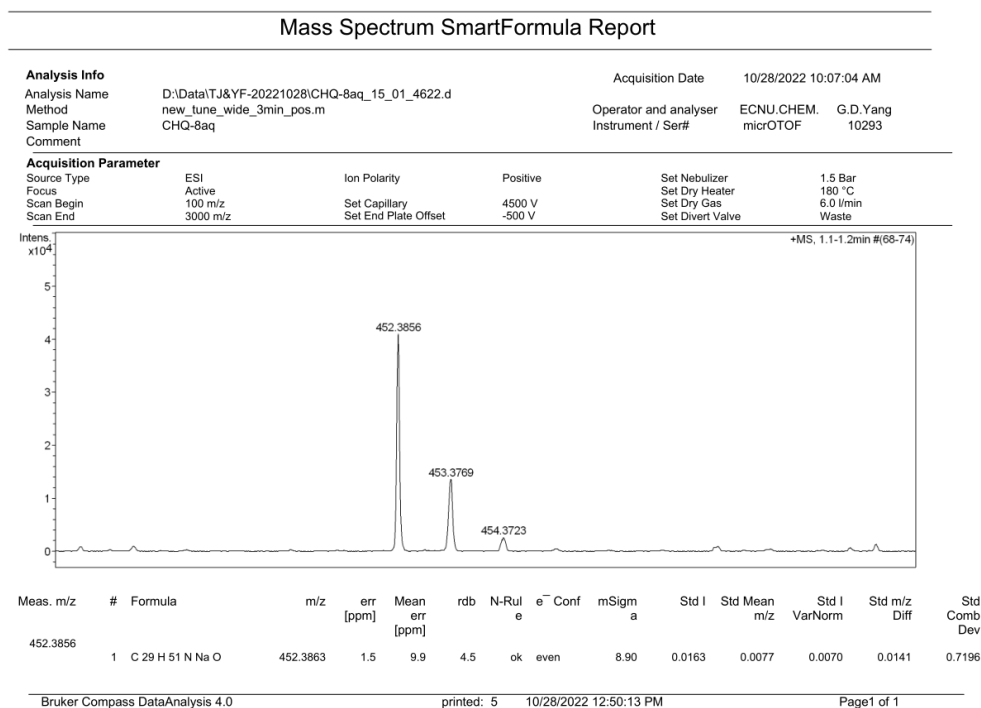
## Compound **5an** (HRMS)



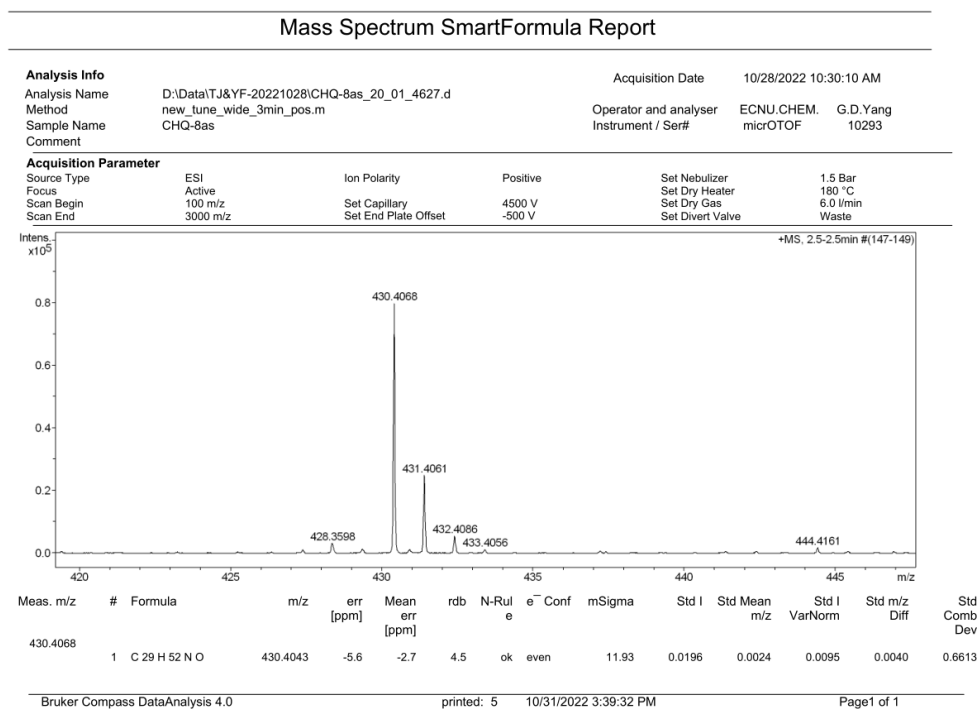
## Compound **5ao** (HRMS)



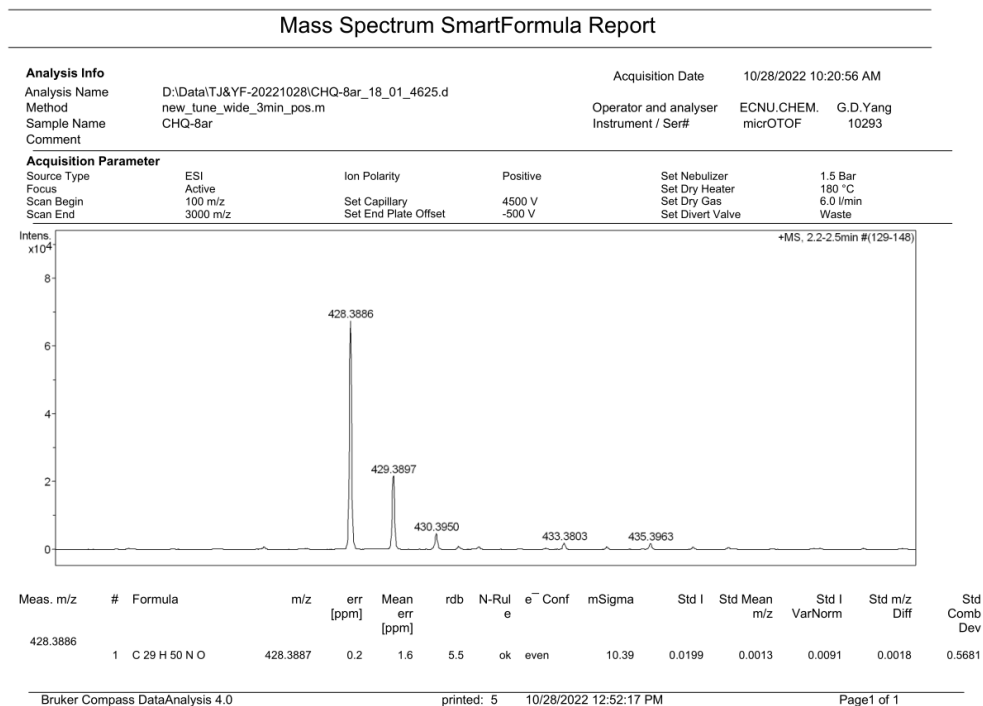
## Compound **5ap** (HRMS)



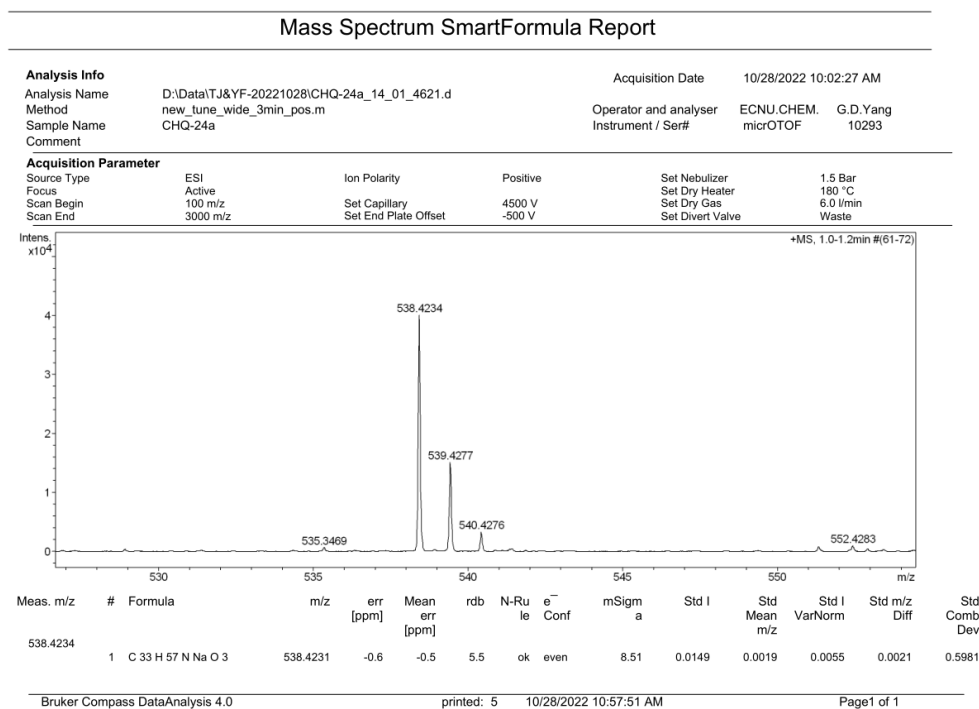
## Compound **5aq** (HRMS)



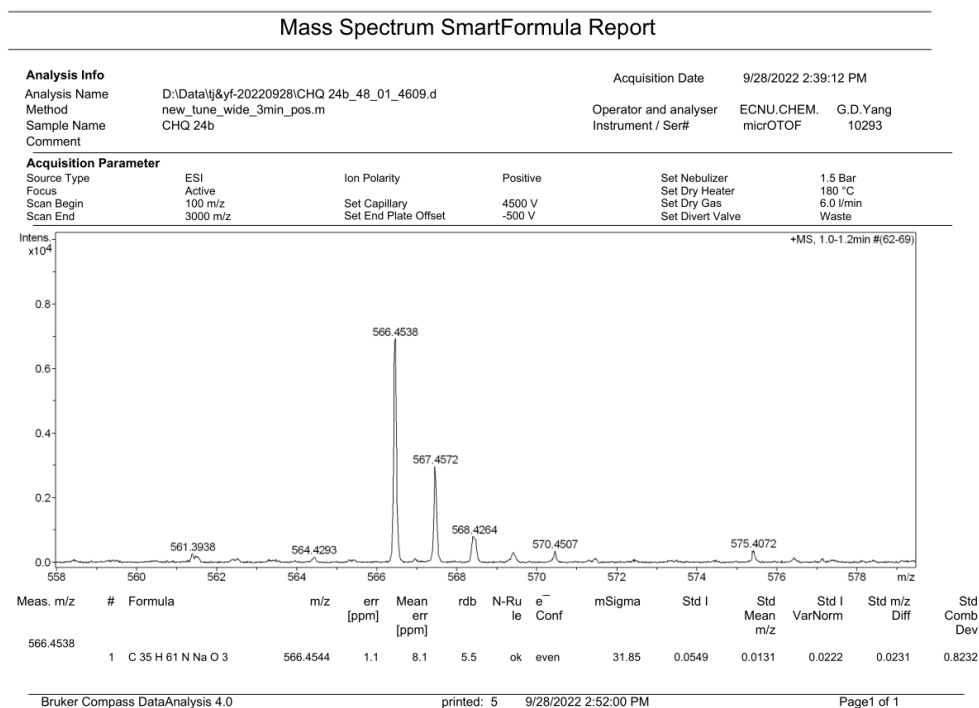
## Compound **5ar** (HRMS)



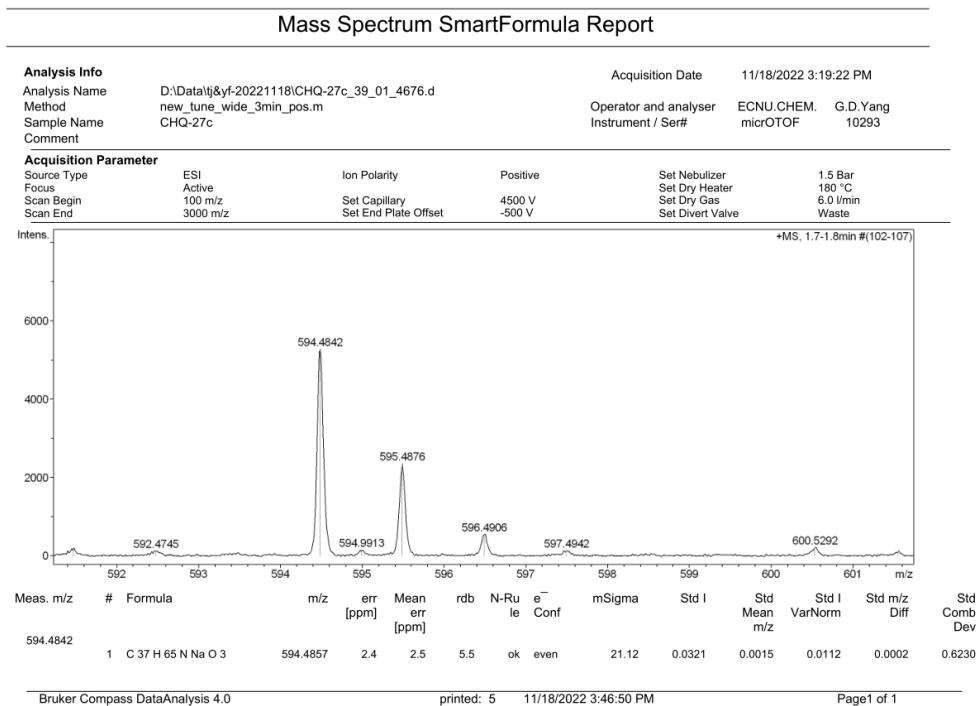
## Compound 27a (HRMS)



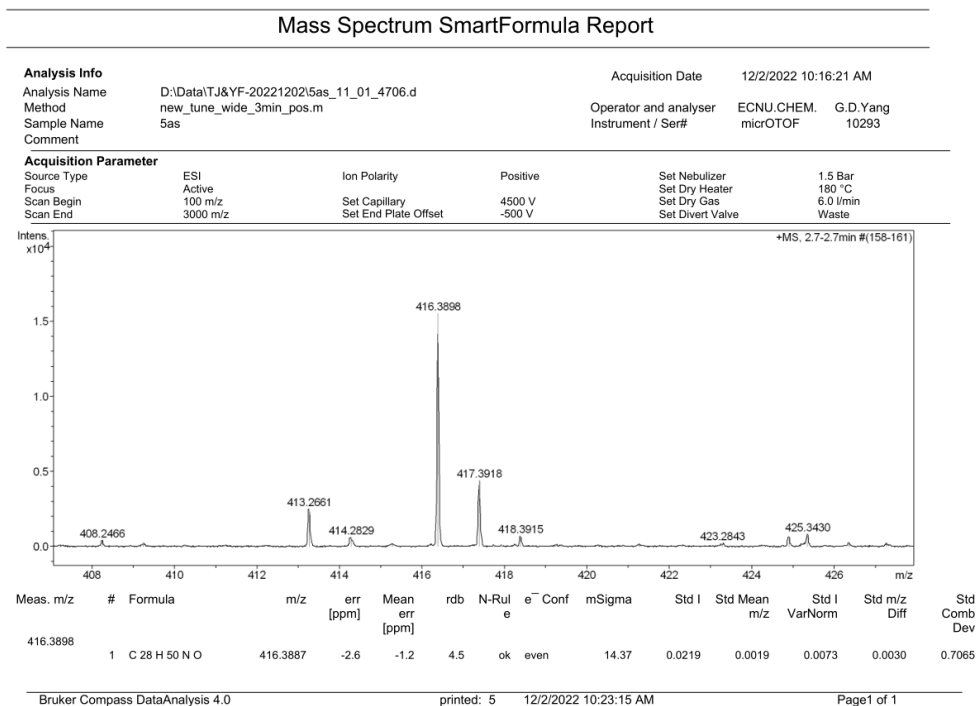
## Compound 27b (HRMS)



## Compound 27c (HRMS)

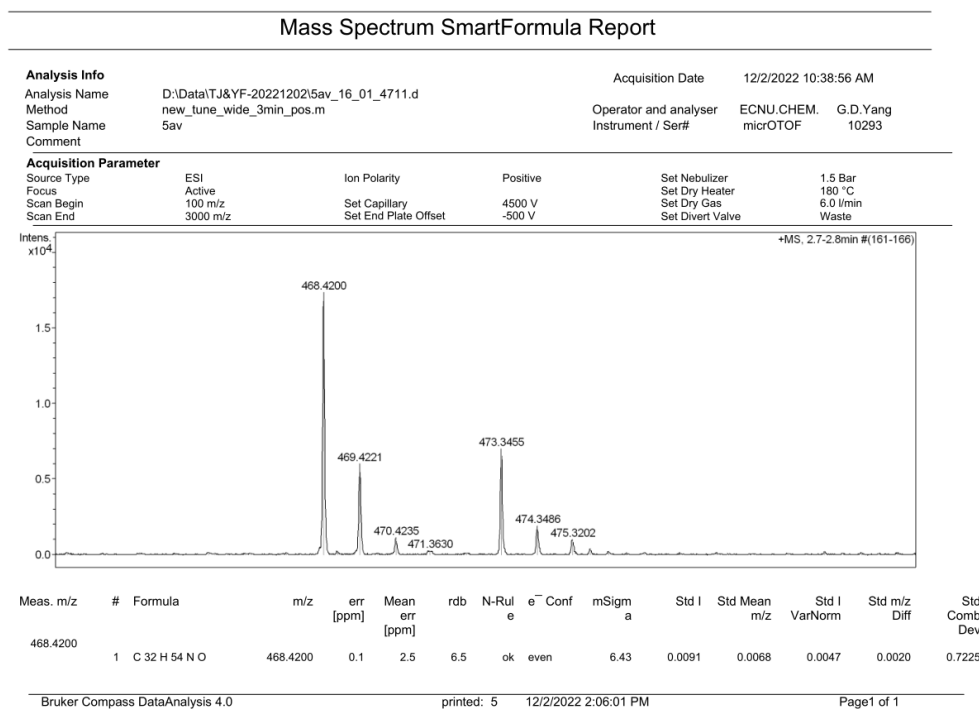


## Compound 5as (HRMS)

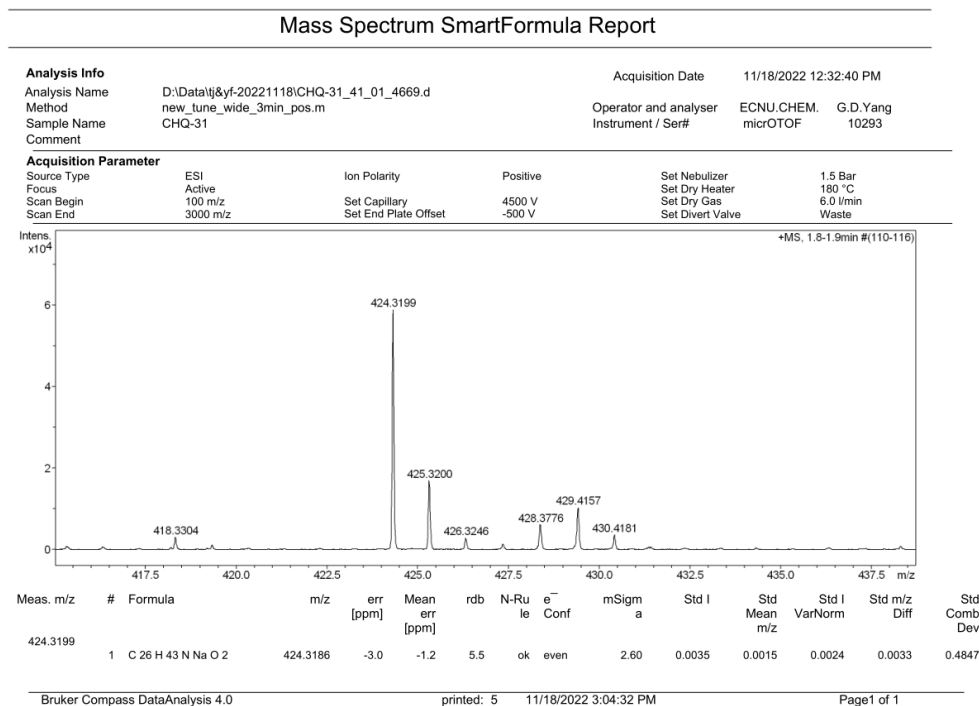




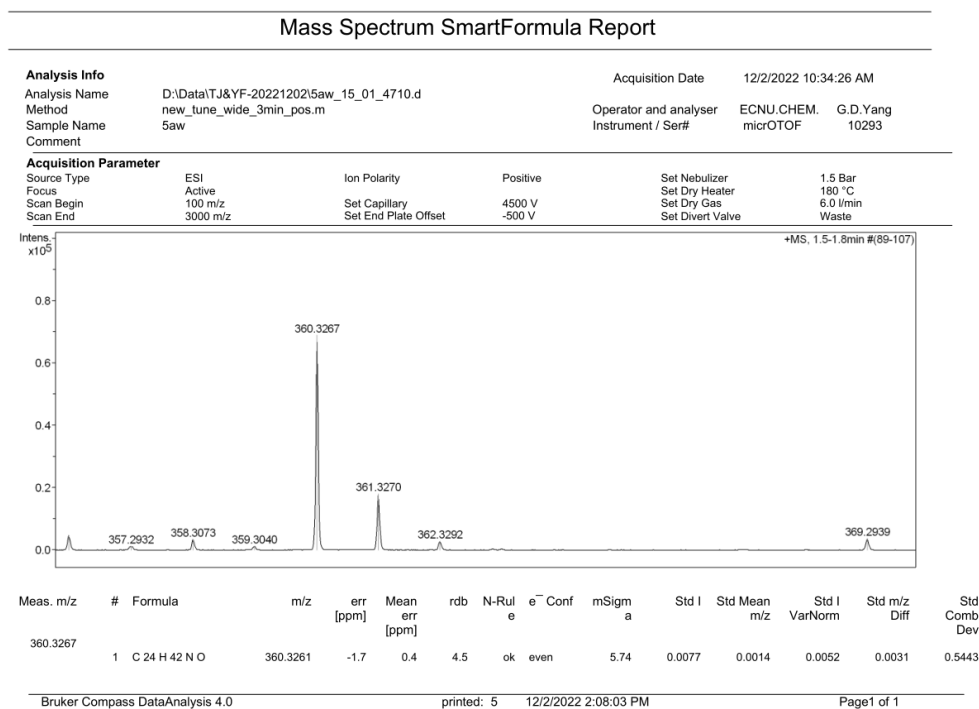
## Compound 5av (HRMS)



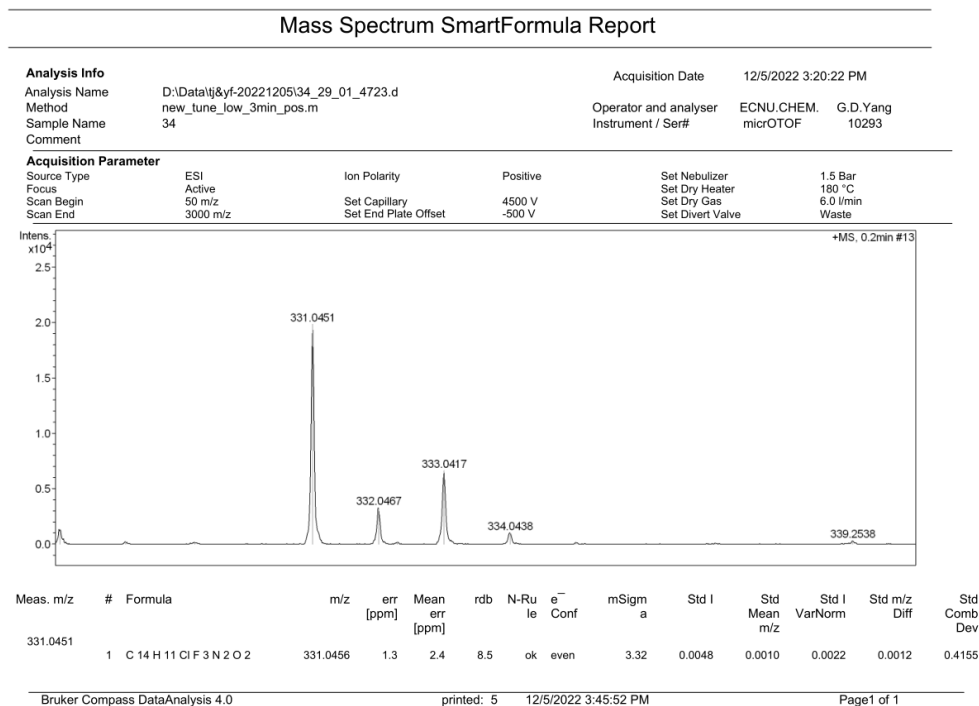
## Compound 31 (HRMS)



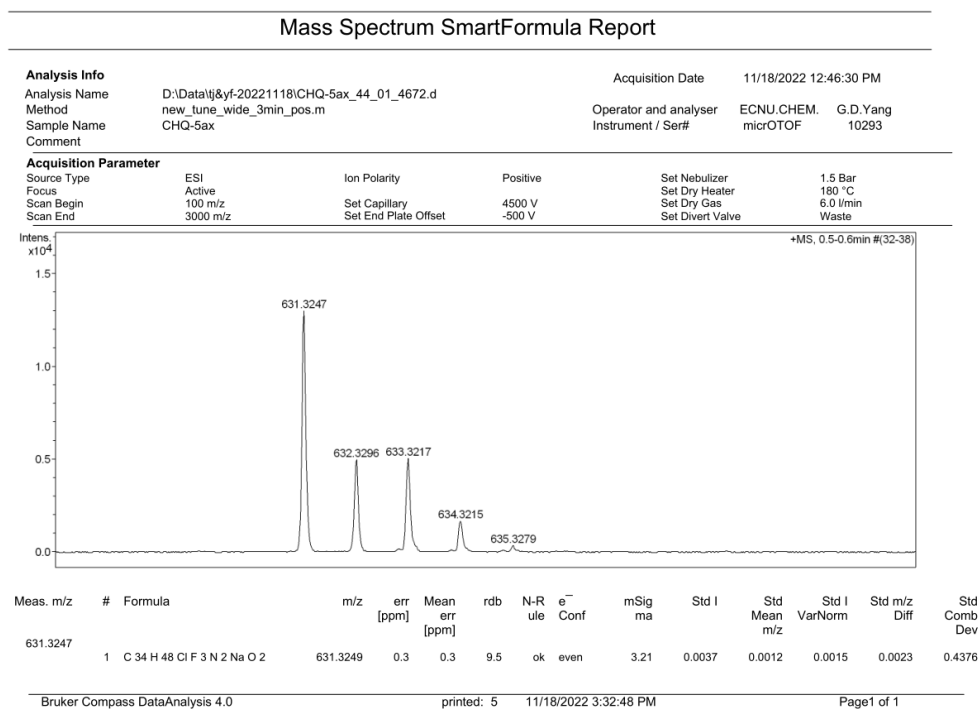
# Compound 5aw (HRMS)



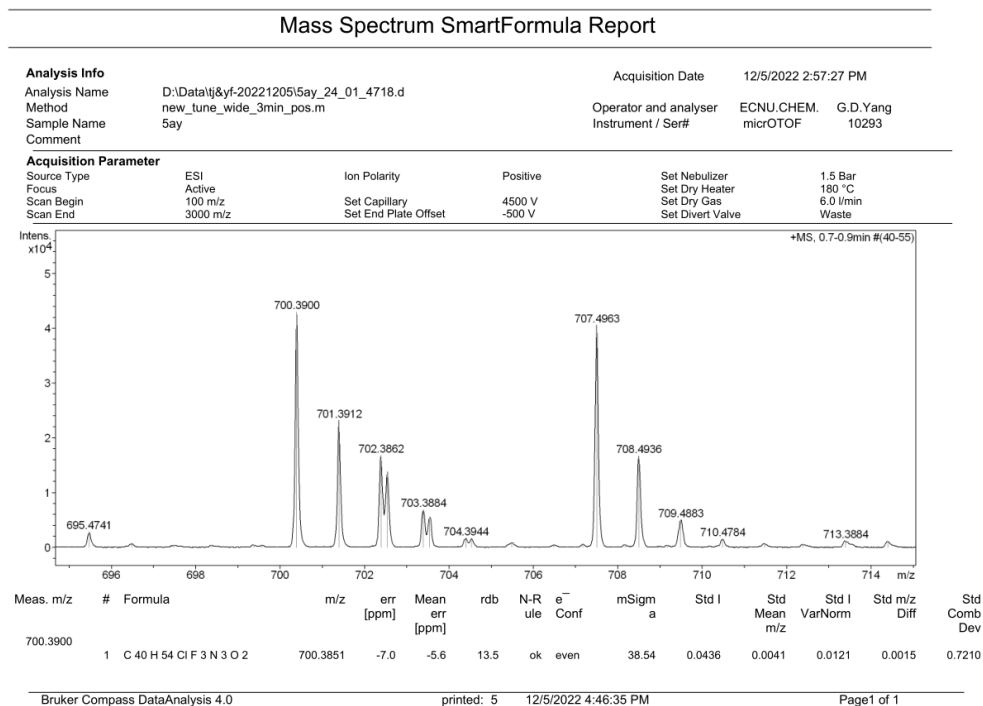
# Compound 34 (HRMS)



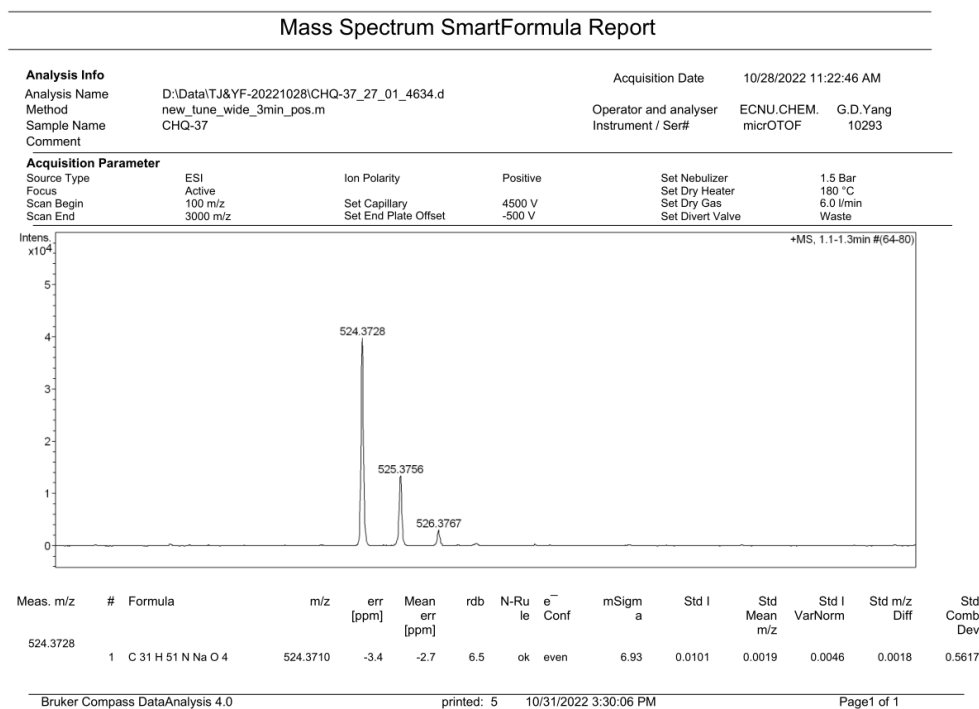
## Compound **5ax** (HRMS)



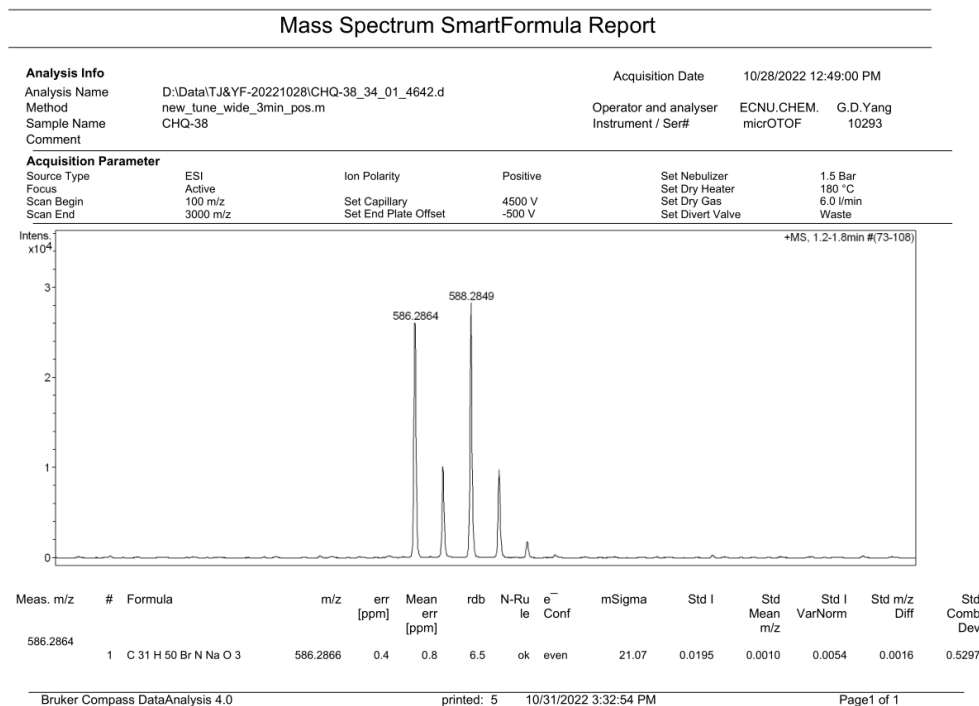
## Compound **5ay** (HRMS)



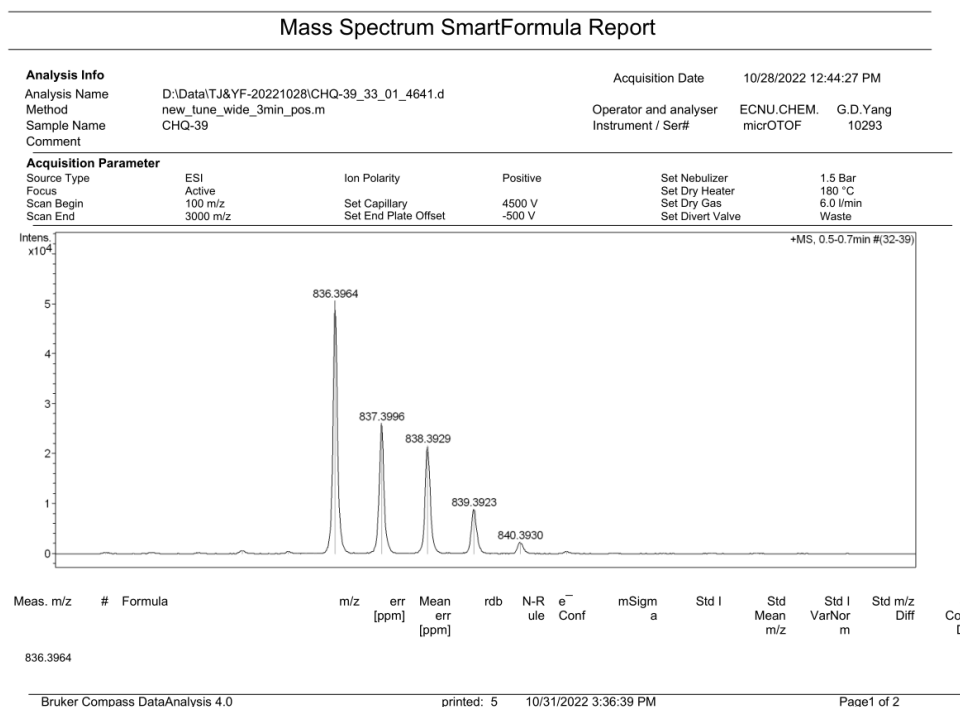
## Compound 37 (HRMS)



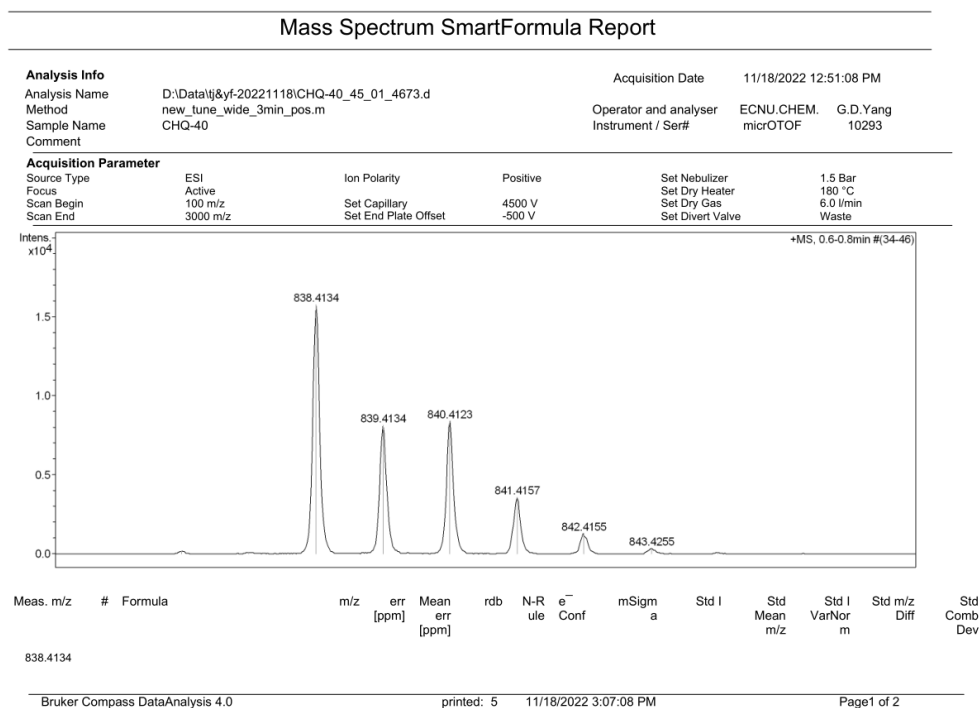
## Compound 38 (HRMS)



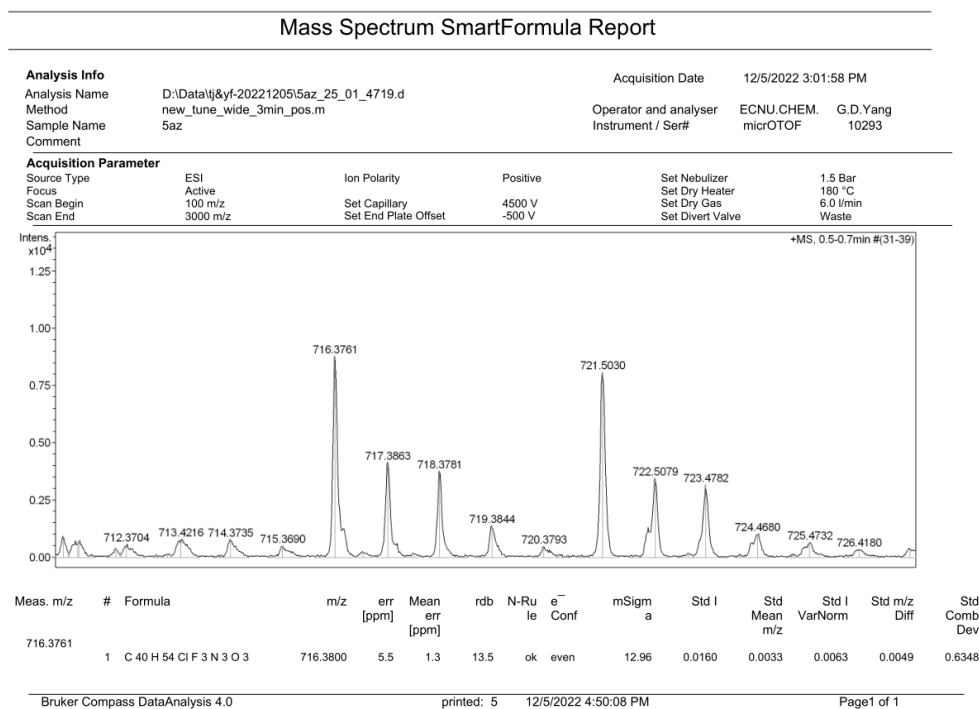
# Compound 39 (HRMS)



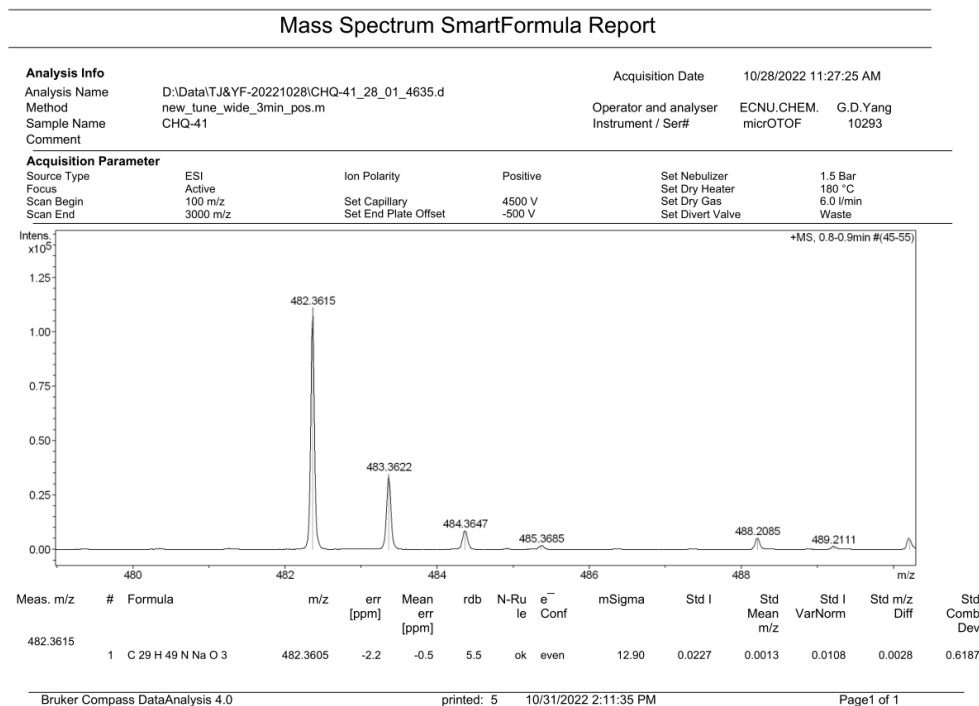
# Compound 40 (HRMS)



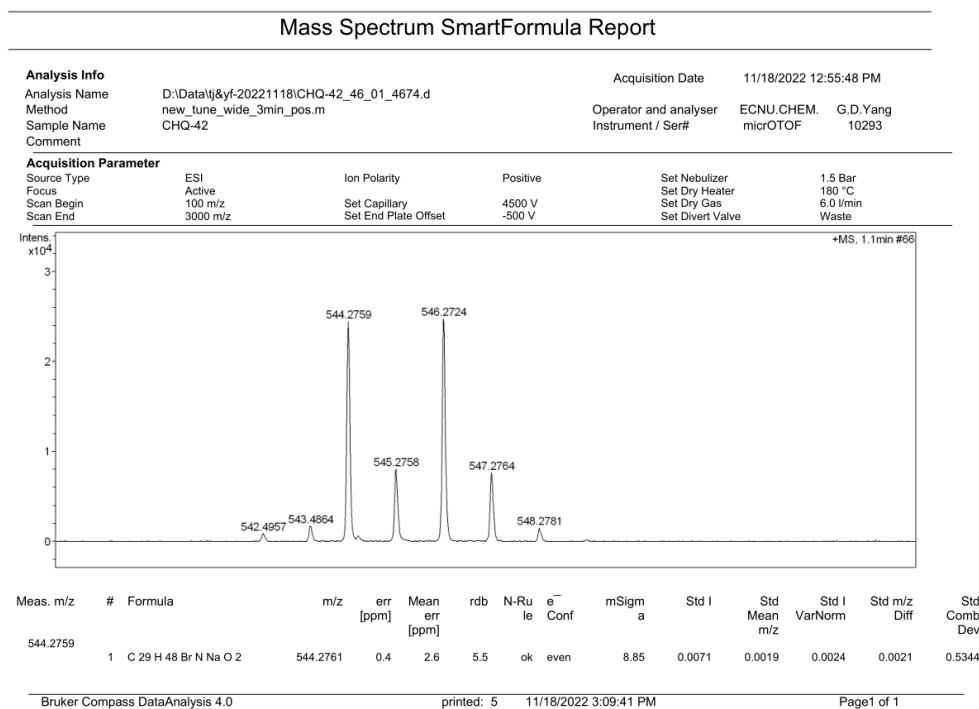
## Compound **5az** (HRMS)



## Compound **41** (HRMS)



## Compound 42 (HRMS)



## Compound 5ba (HRMS)

