Total Synthesis of Trapoxin A, a fungal HDAC-inhibitor from *Helicoma ambiens*

Phil Servatius and Uli Kazmaier*

Saarland University, Organic Chemistry I, Campus, Bldg. C4.2

D-66123 Saarbrücken, Germany.

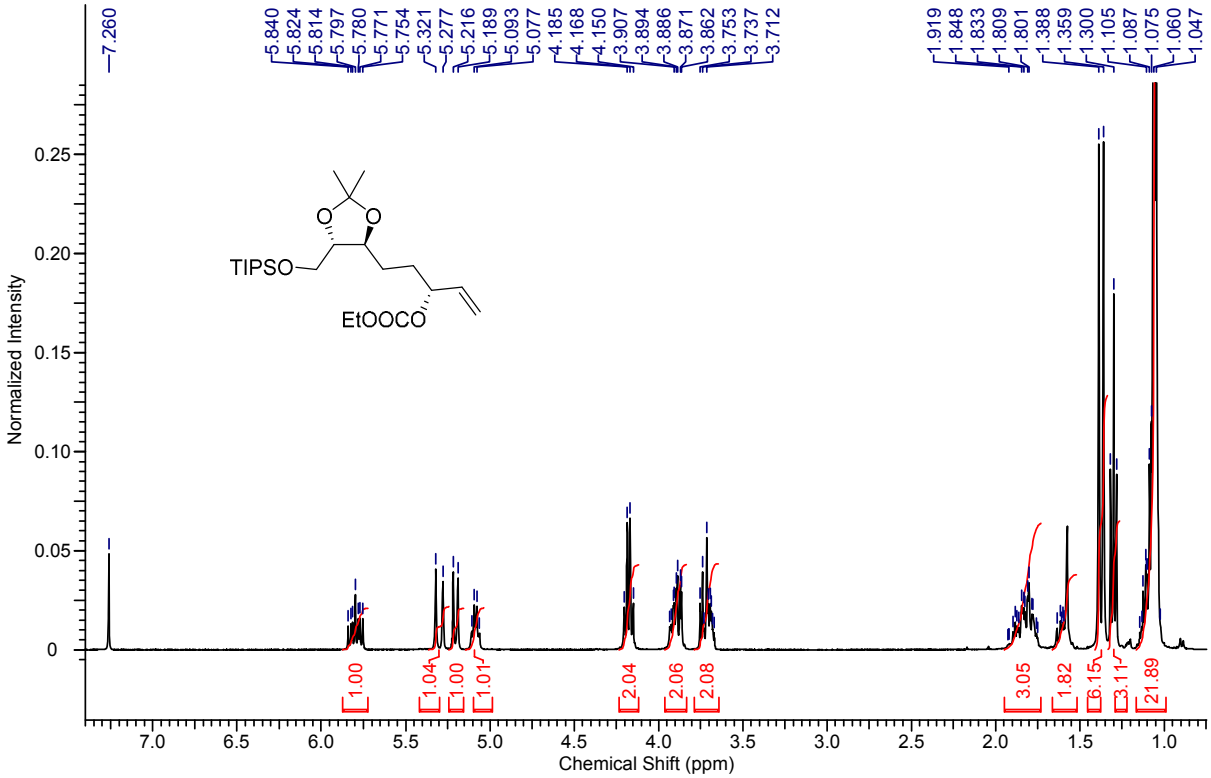
Supporting Information

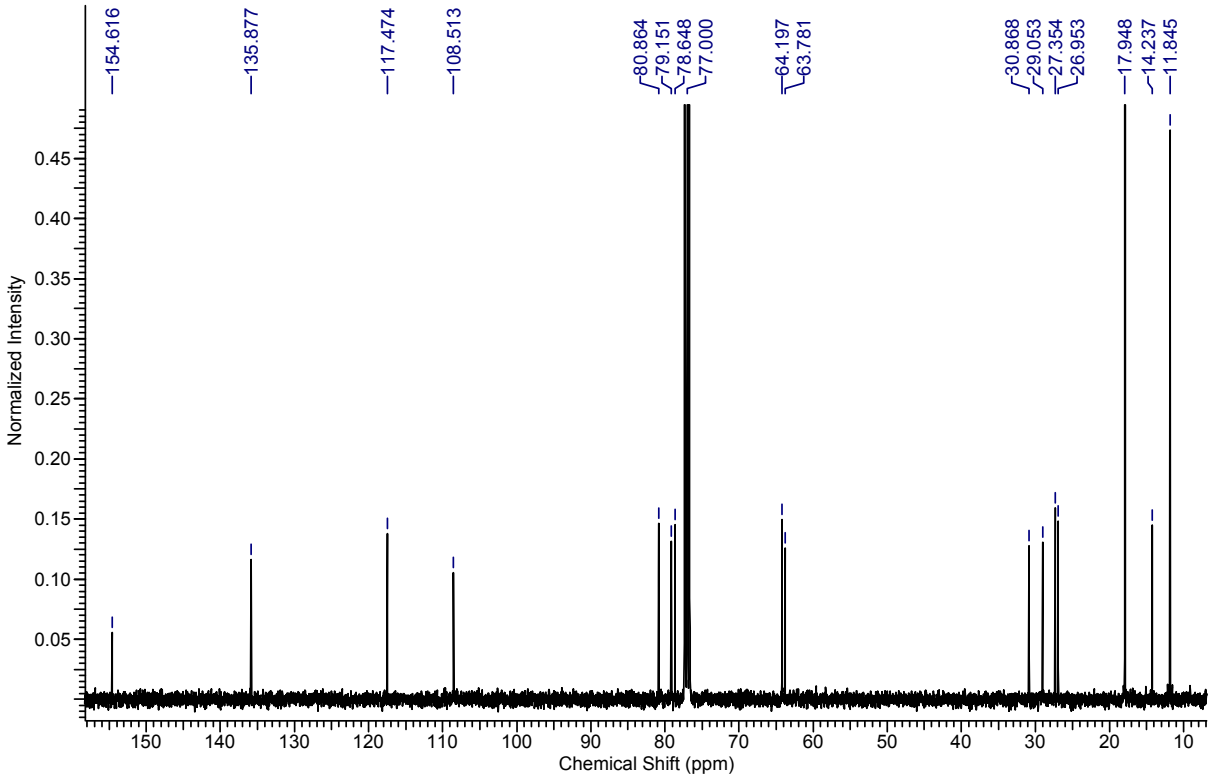
Table of Contents

Copies of NMR spectra S2

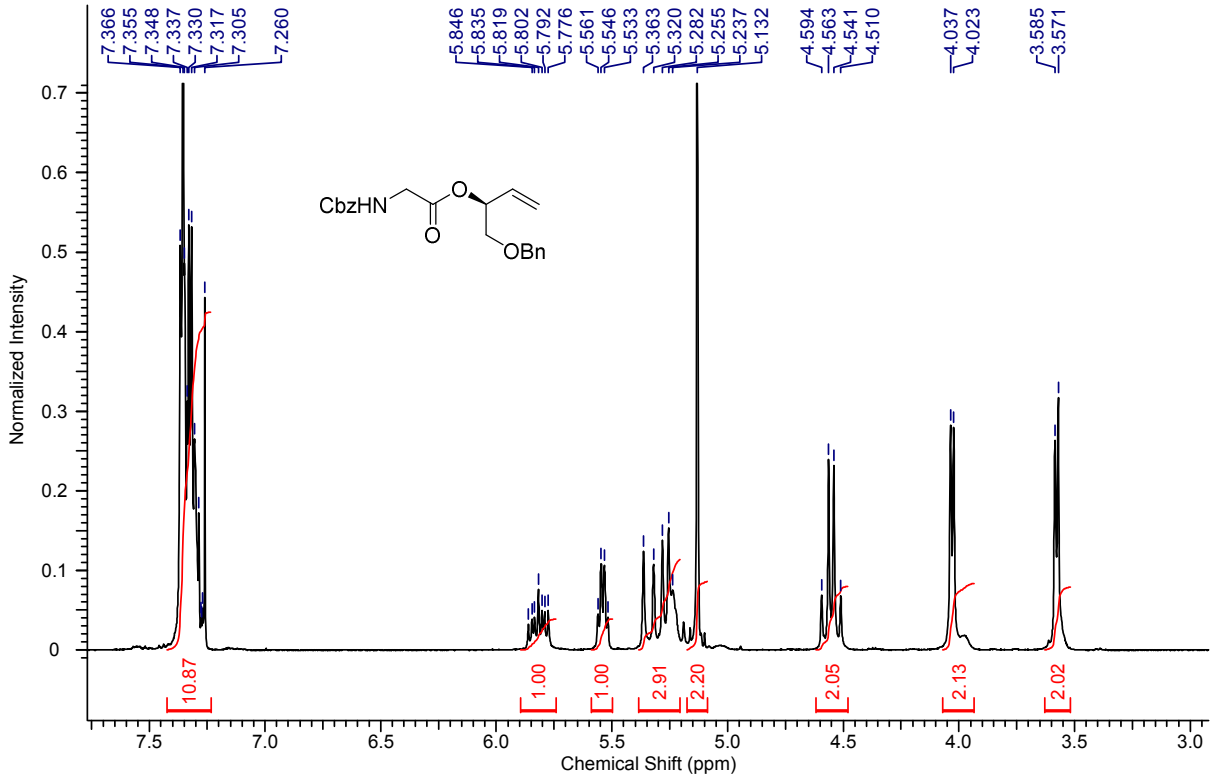
Copies of NMR spectra

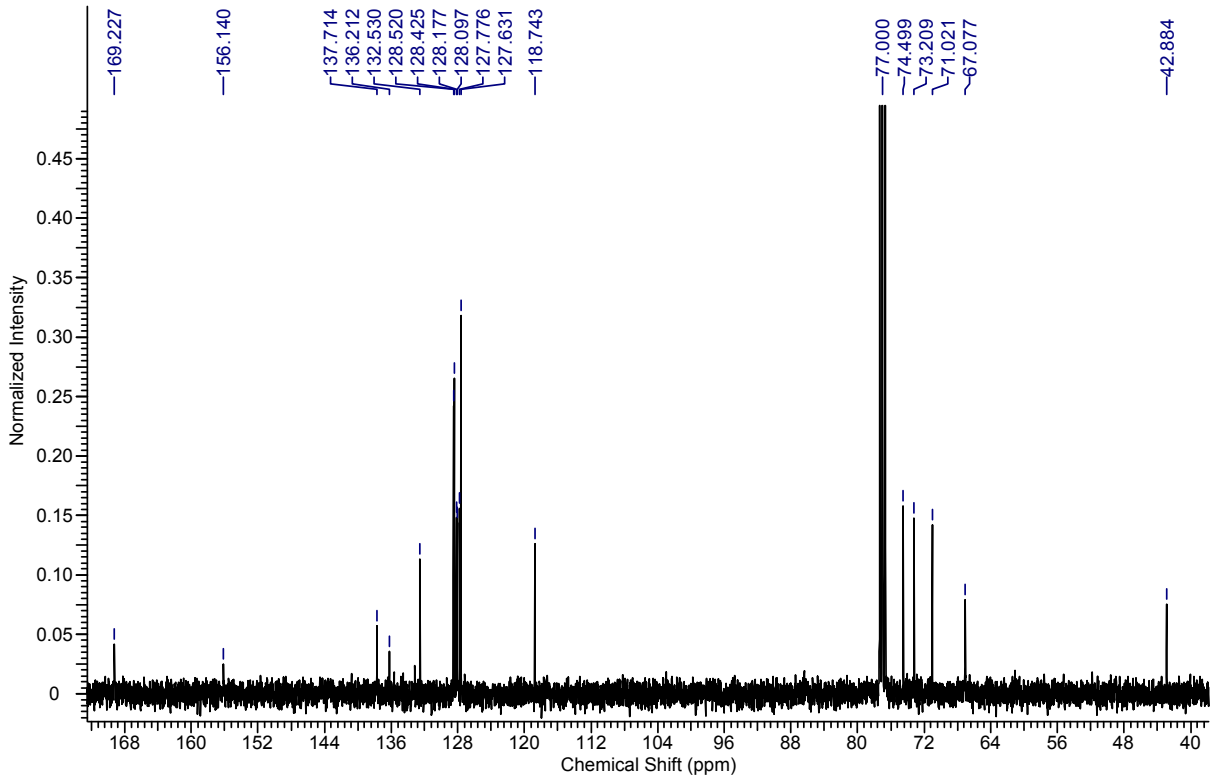
(*R*)-5-((4*S*,5*S*)-2,2-dimethyl-5-(((tri-*iso*-propylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)pent-1-en-3-yl ethyl carbonate (3)



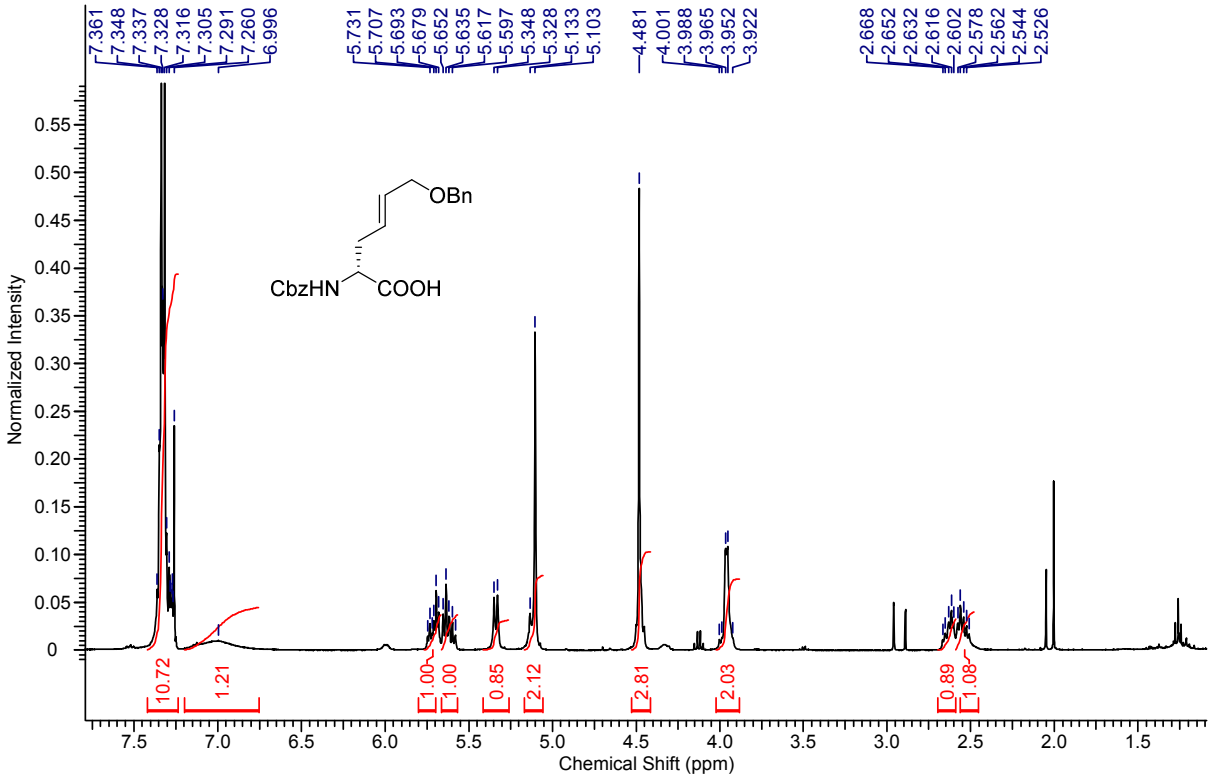


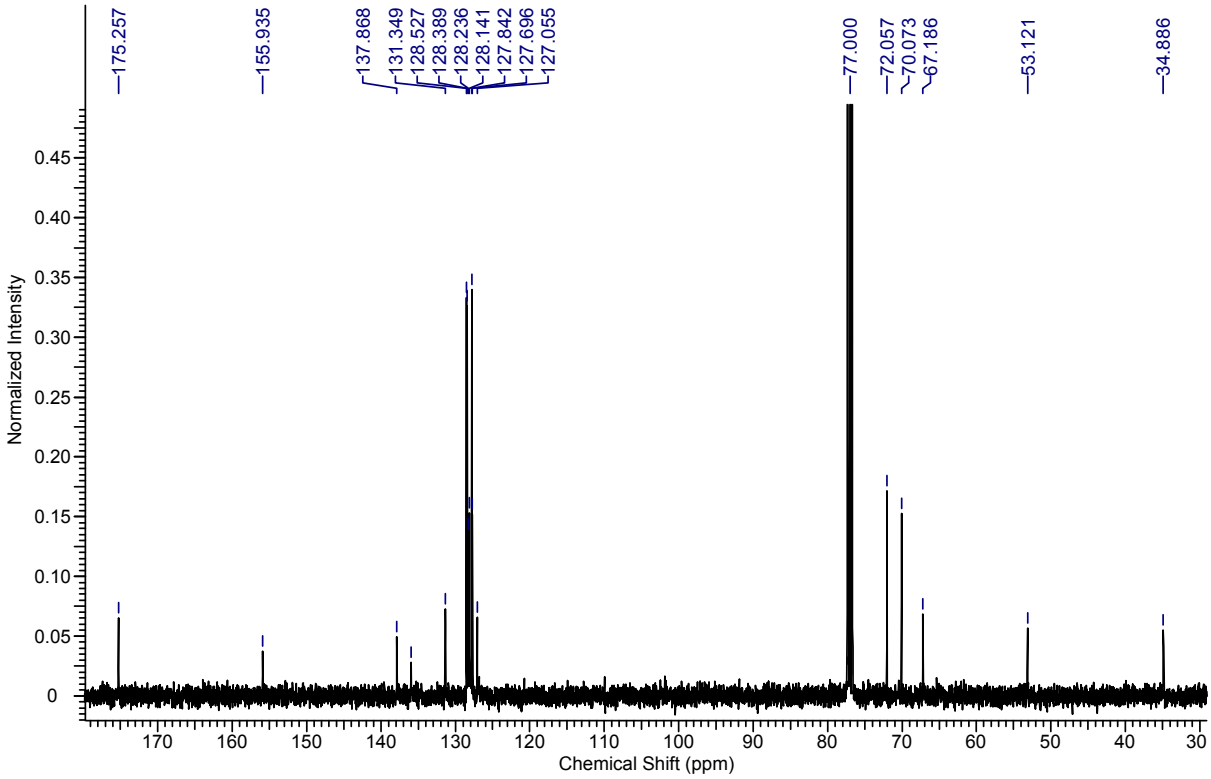
(*S*)-1-(Benzyloxy)but-3-en-2-yl ((benzyloxy)carbonyl)glycinate (4)



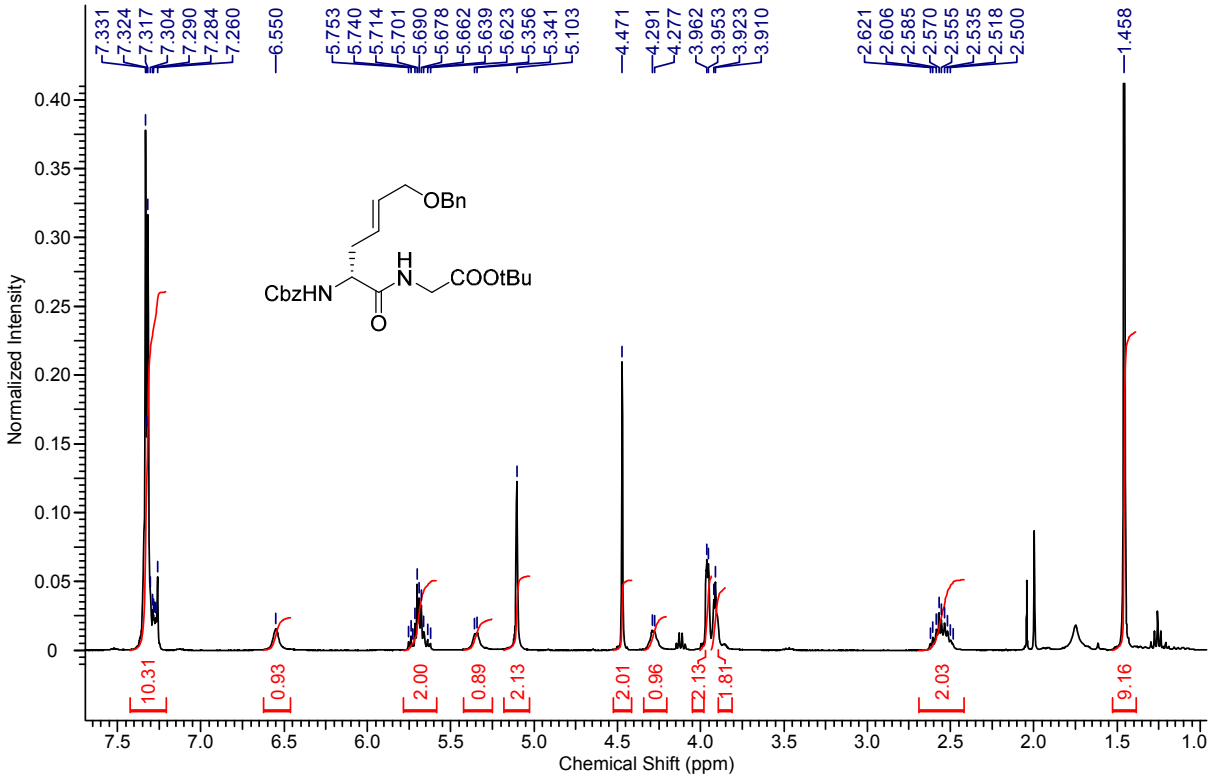


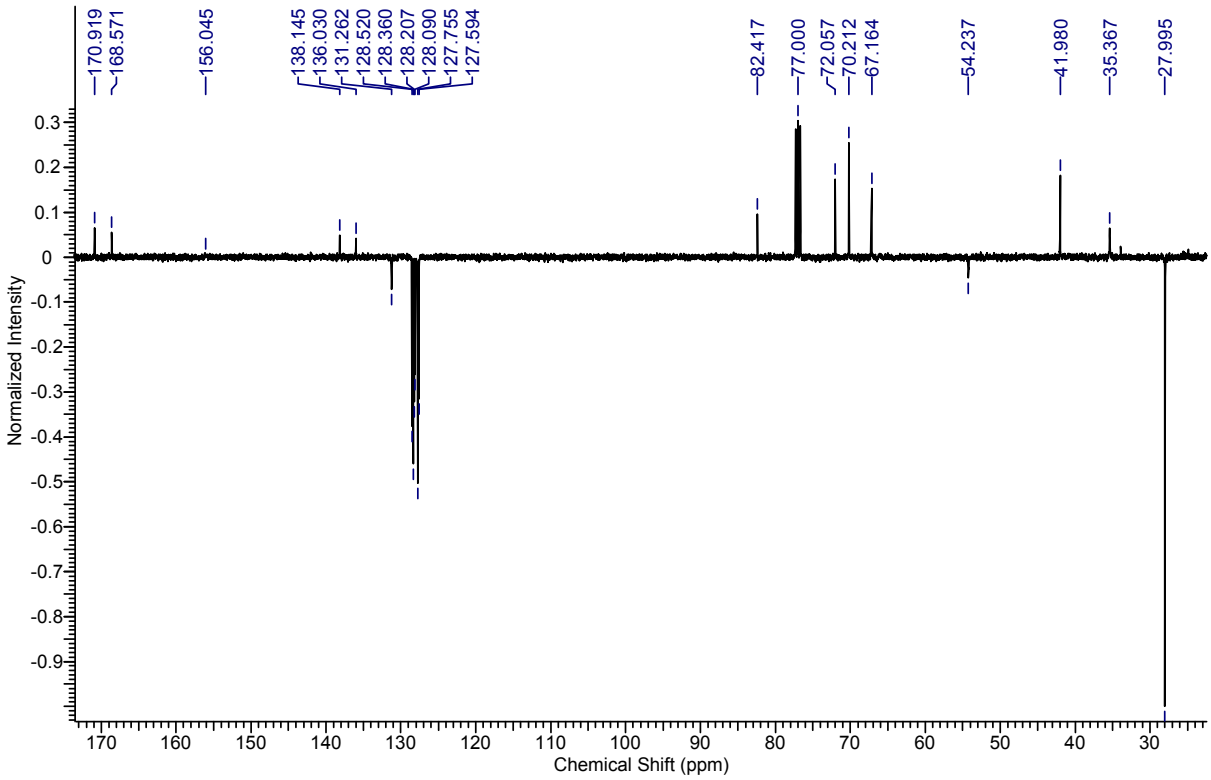
(*R*,*E*)-6-(Benzyloxy)-2-(((benzyloxy)carbonyl)amino)hex-4-enoic acid (5)



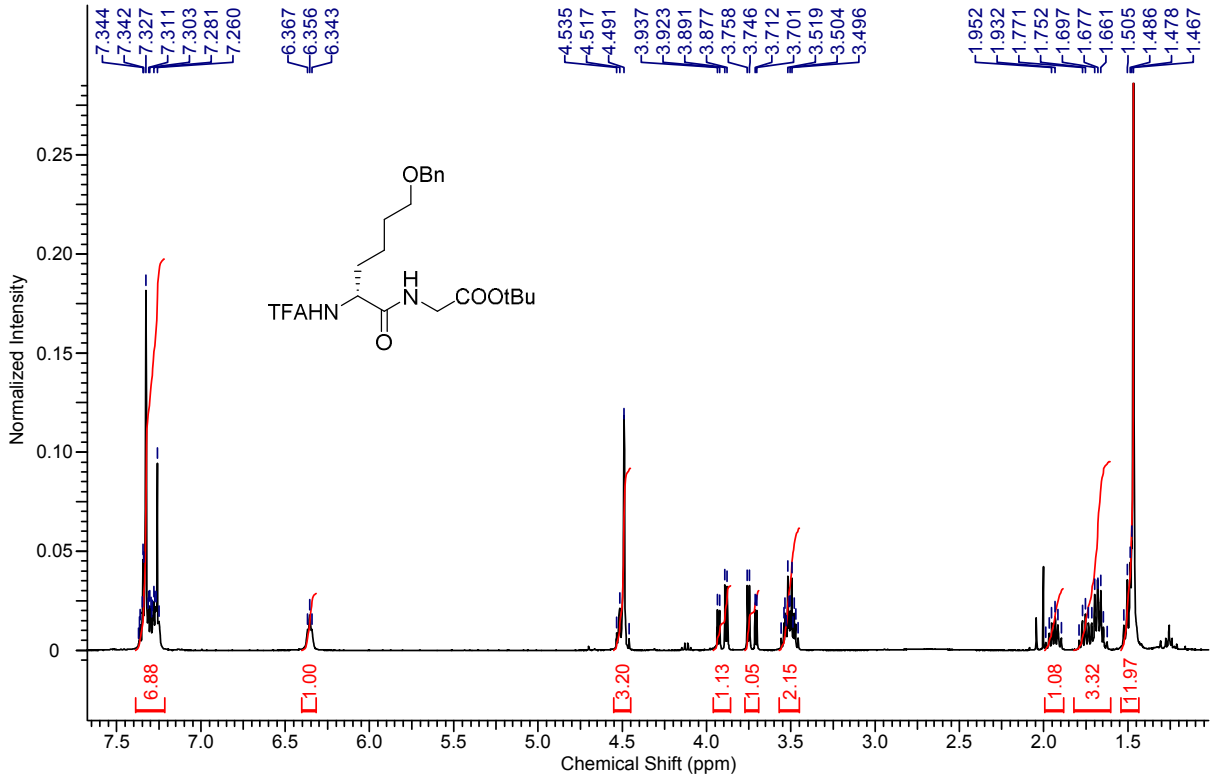


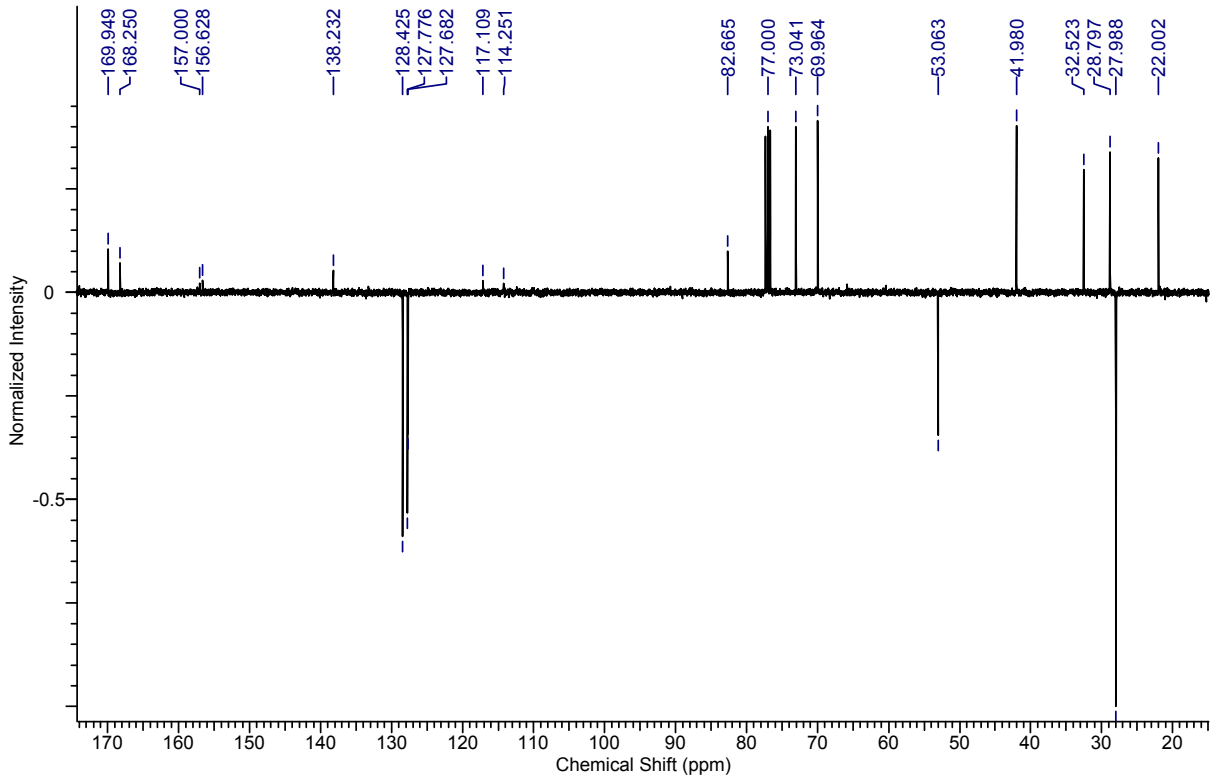
***tert*-Butyl (*R*,*E*)-(6-(benzyloxy)-2-(((benzyloxy)carbonyl)amino)hex-4-enoyl)glycinate (6)**



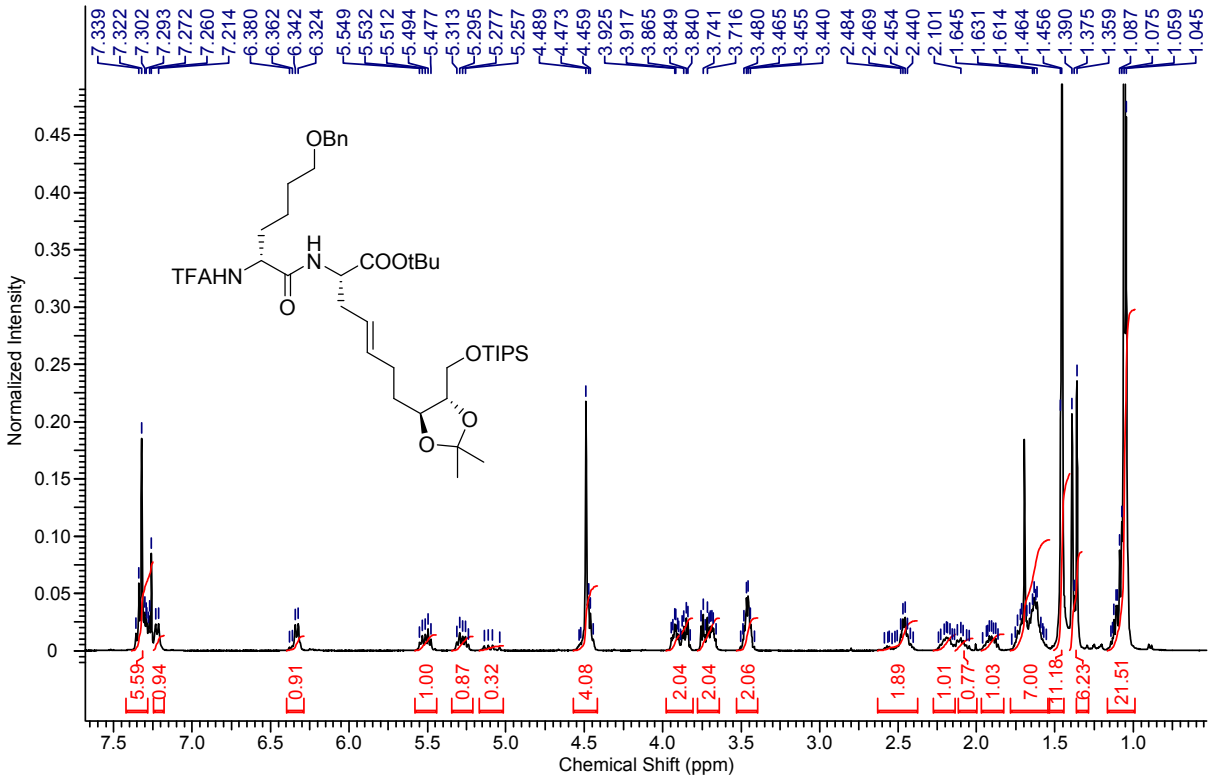


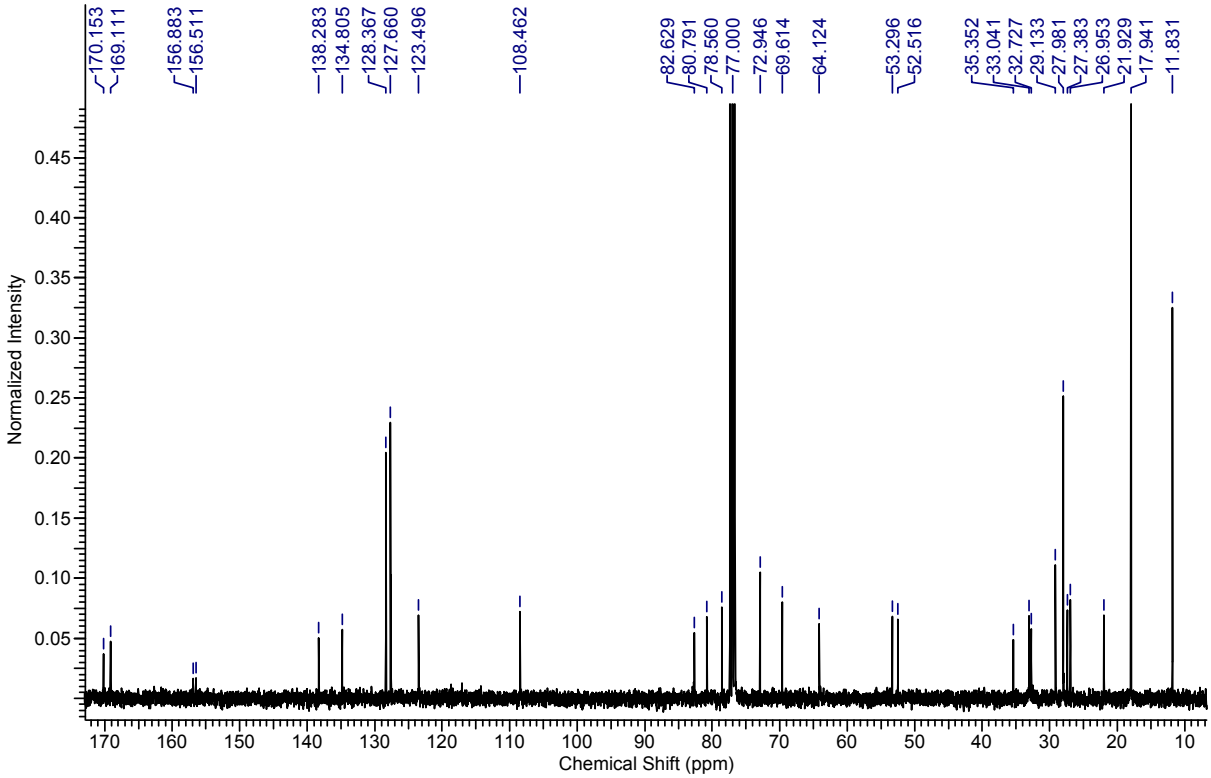
***tert*-Butyl (*R*)-(6-(benzyloxy)-2-(2,2,2-trifluoroacetamido)hexanoyl)glycinate (7)**



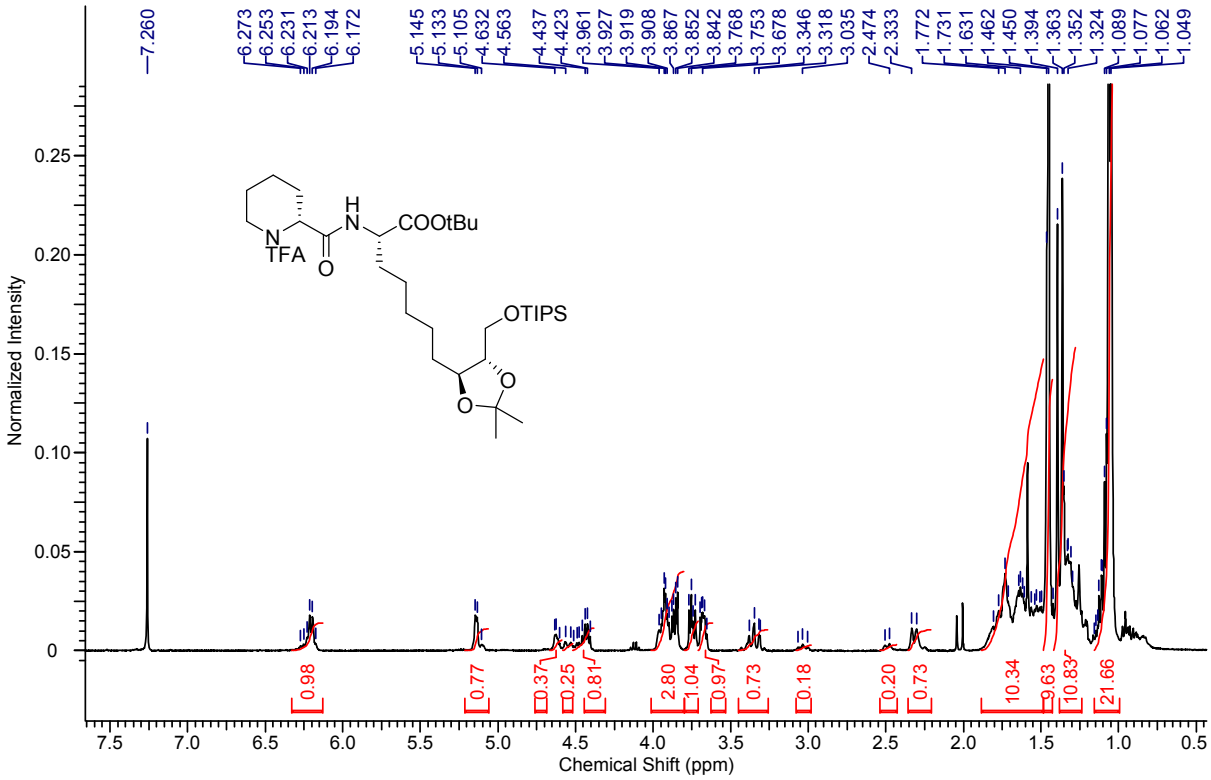


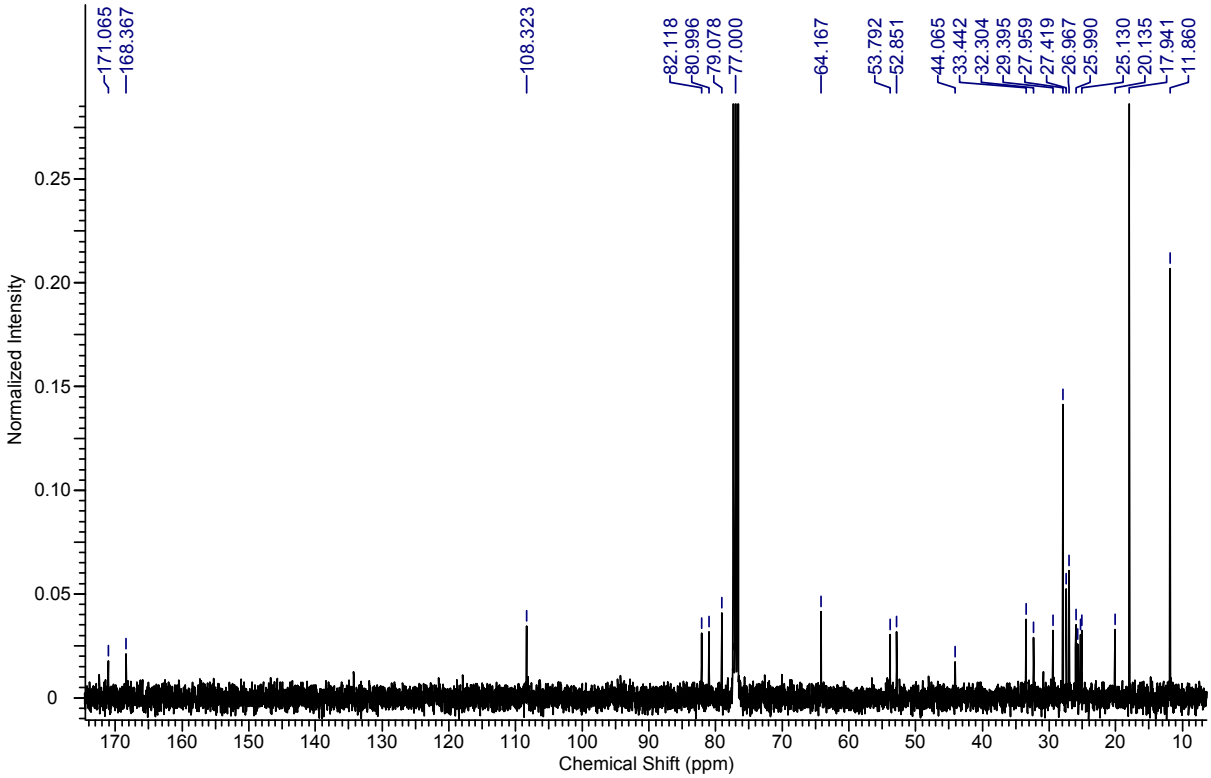
***tert*-Butyl (*S*,*E*)-2-((*R*)-6-(benzyloxy)-2-(2,2,2-trifluoroacetamido)hexanamido)-7-((4*S*,5*S*) -2,2-dimethyl-5-(((tri-*iso*-propylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)hept-4-enoate (8)**



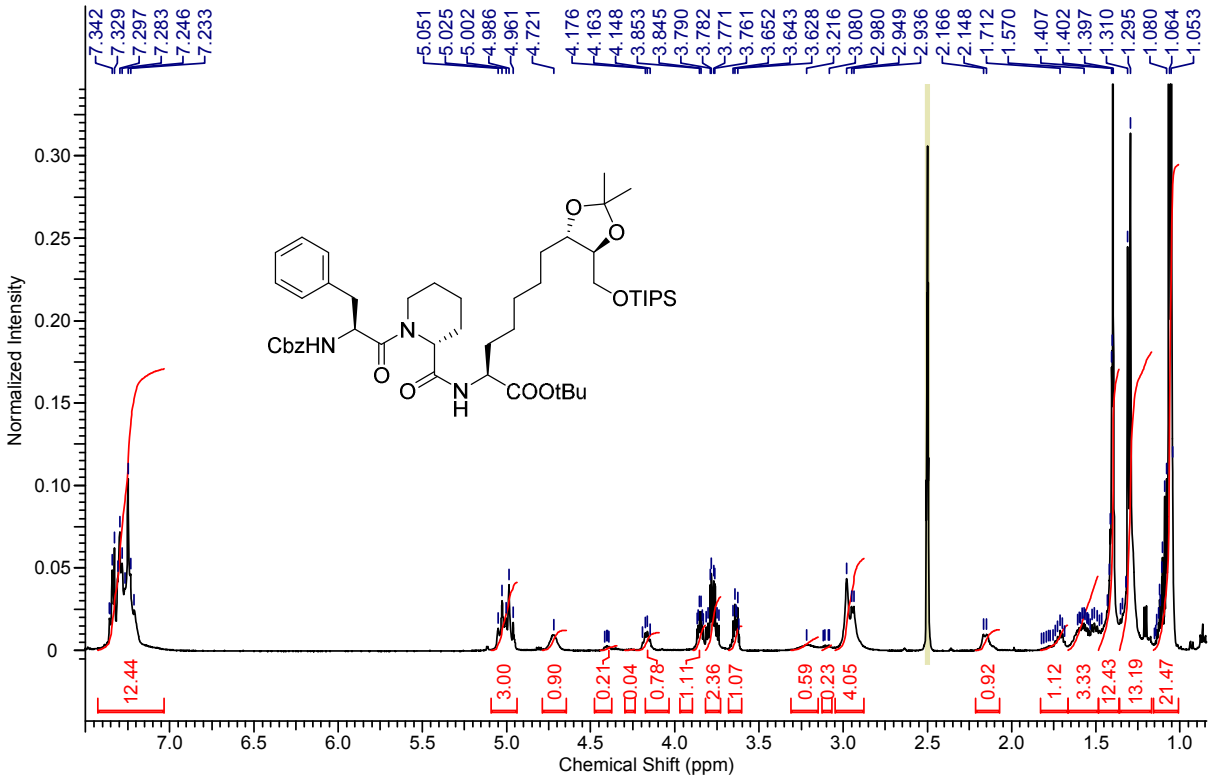


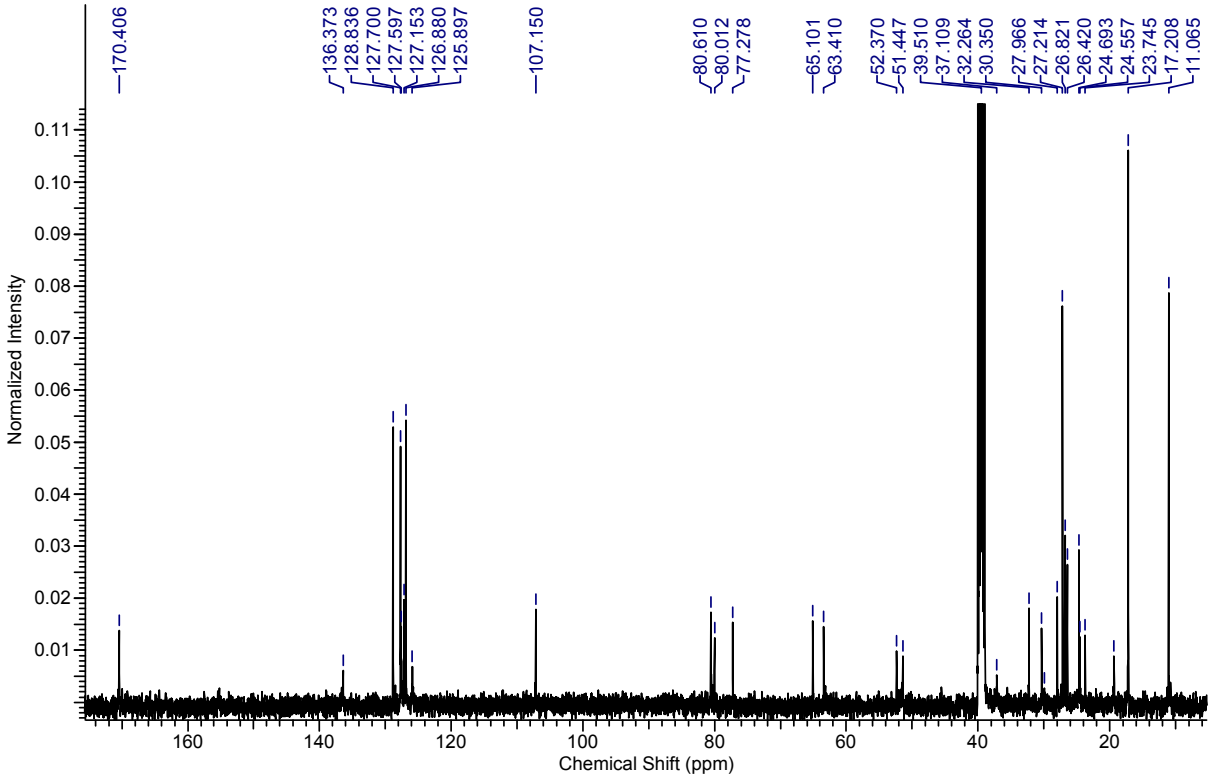
***tert*-Butyl (*S*)-7-((4*S*,5*S*)-2,2-dimethyl-5-(((tri-*iso*-propylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)-2-((*R*)-1-(2,2,2-trifluoroacetyl)piperidine-2-carboxamido)heptanoate (9)**



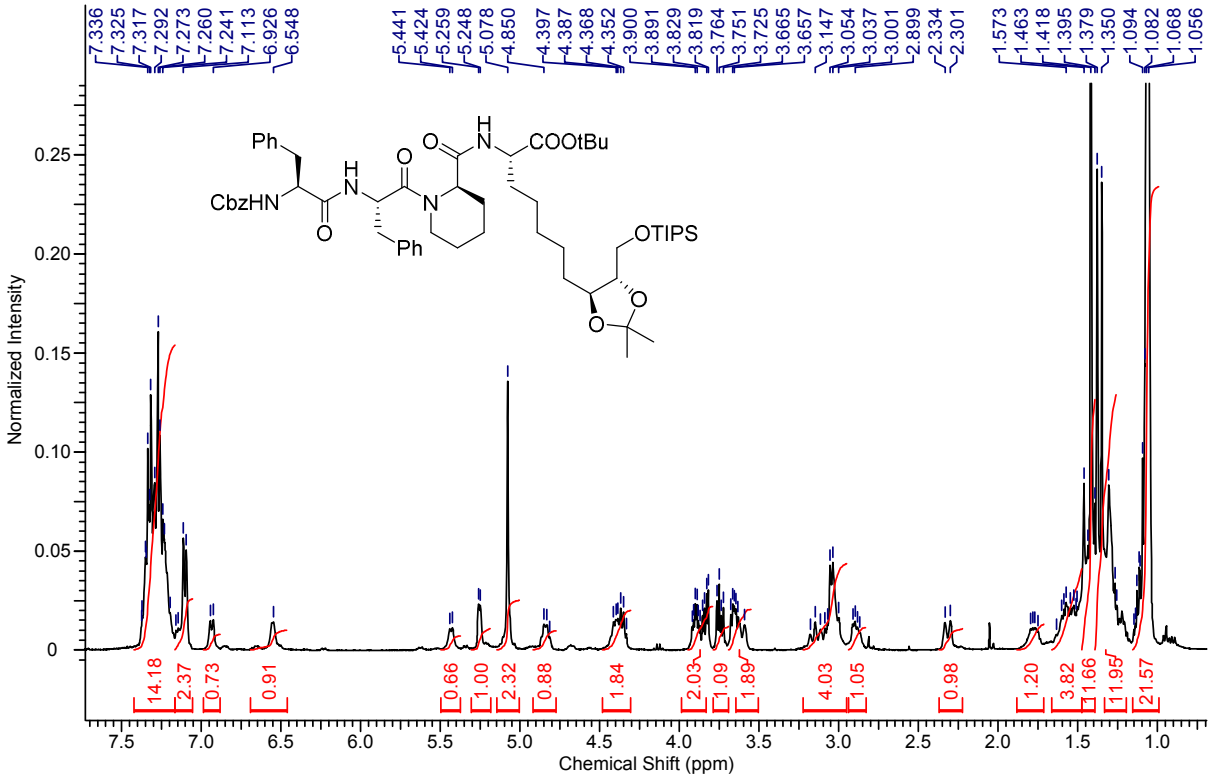


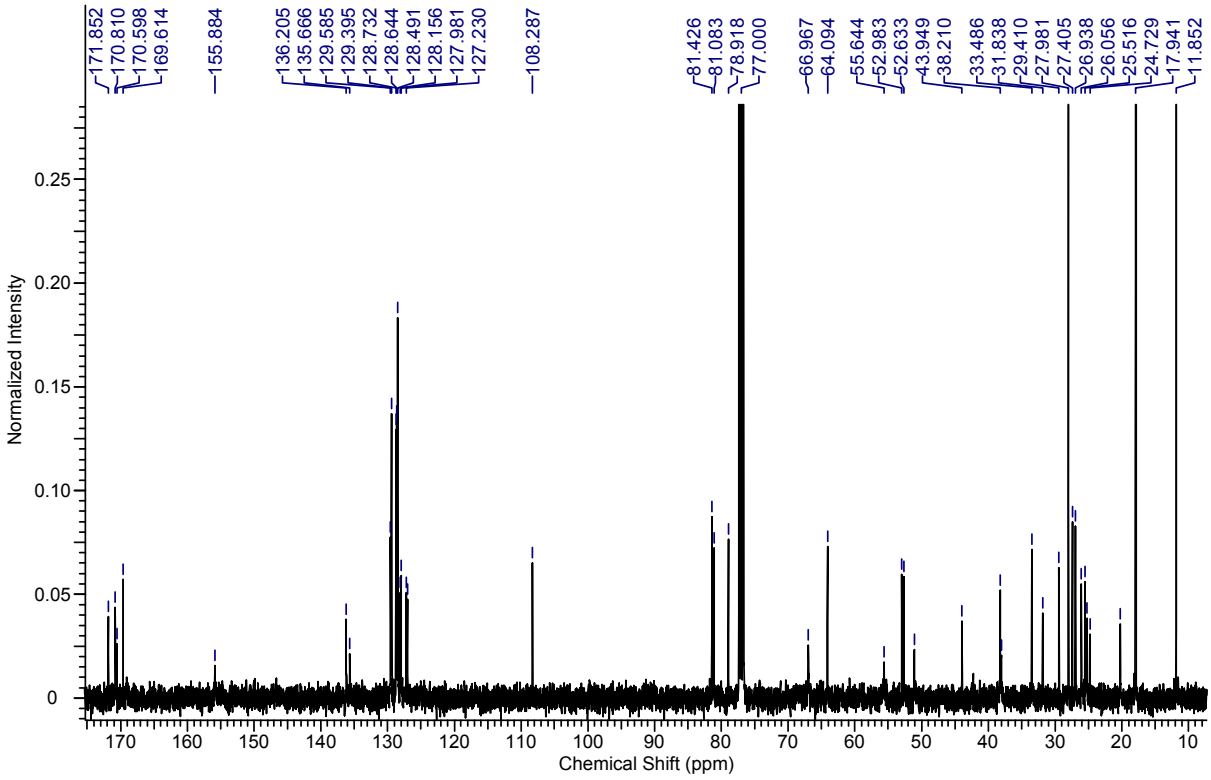
***tert*-Butyl (*S*)-2-((*R*)-1-(((benzyloxy)carbonyl)-L-phenylalanyl)piperidine-2-carboxamido) -7-((4*S*,5*S*)-2,2-dimethyl-5-(((tri-*iso*-propylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)heptano-ate (10)**



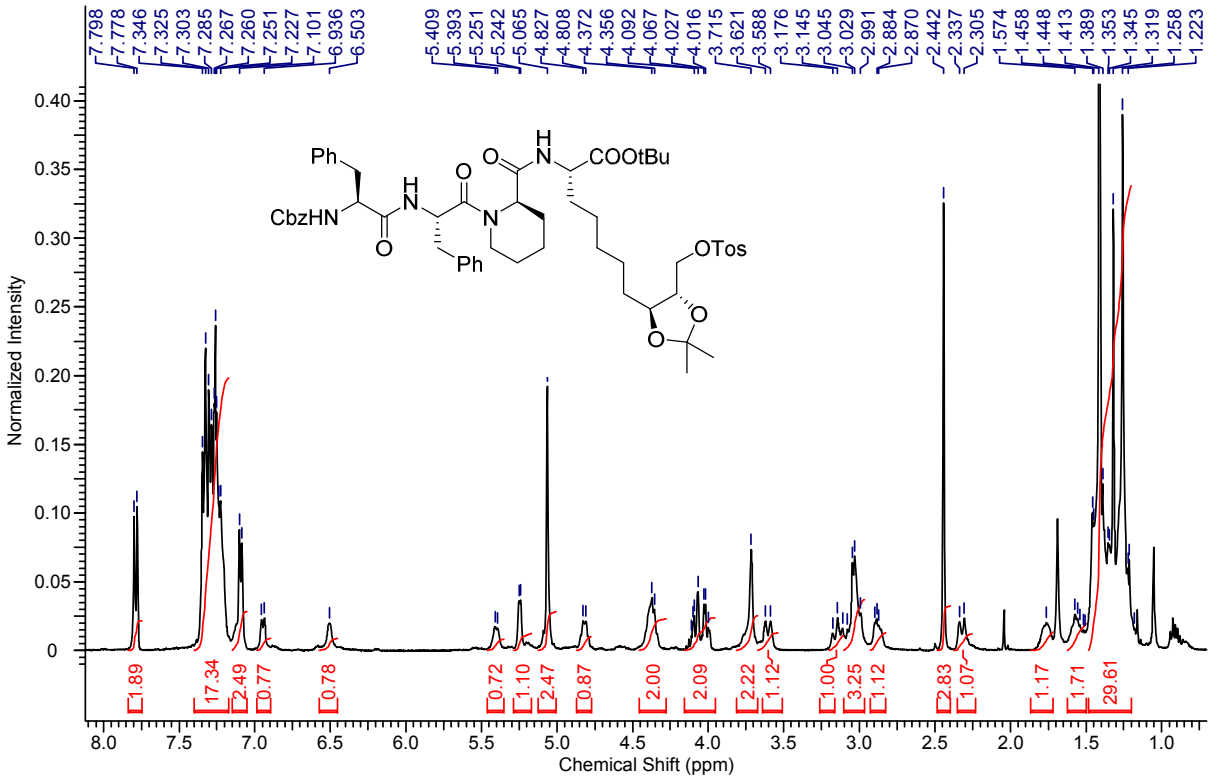


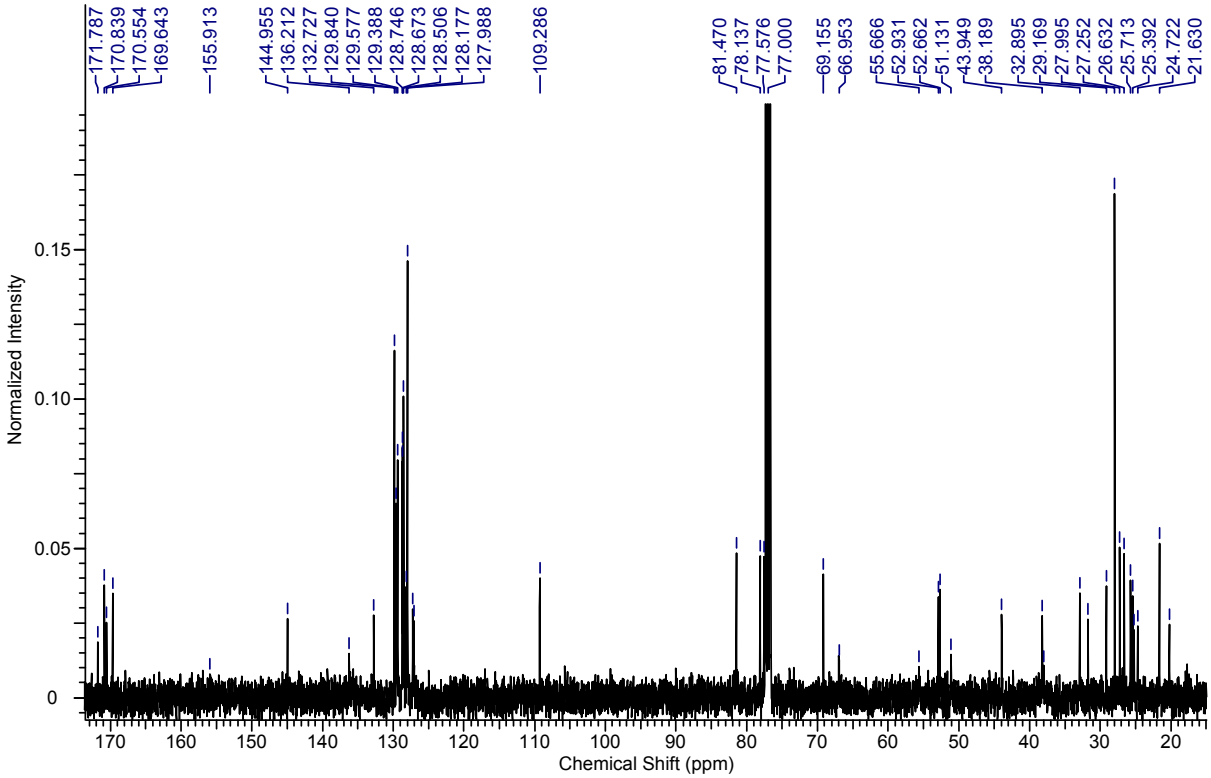
***tert*-Butyl (*S*)-2-((*R*)-1-(((benzyloxy)carbonyl)-L-phenylalanyl-L-phenylalanyl)piperidine-2-carboxamido)-7-((4*S*,5*S*)-2,2-dimethyl-5-(((tri-*iso*-propylsilyl)oxy)methyl)-1,3-dioxolan-4-yl)heptanoate (11)**



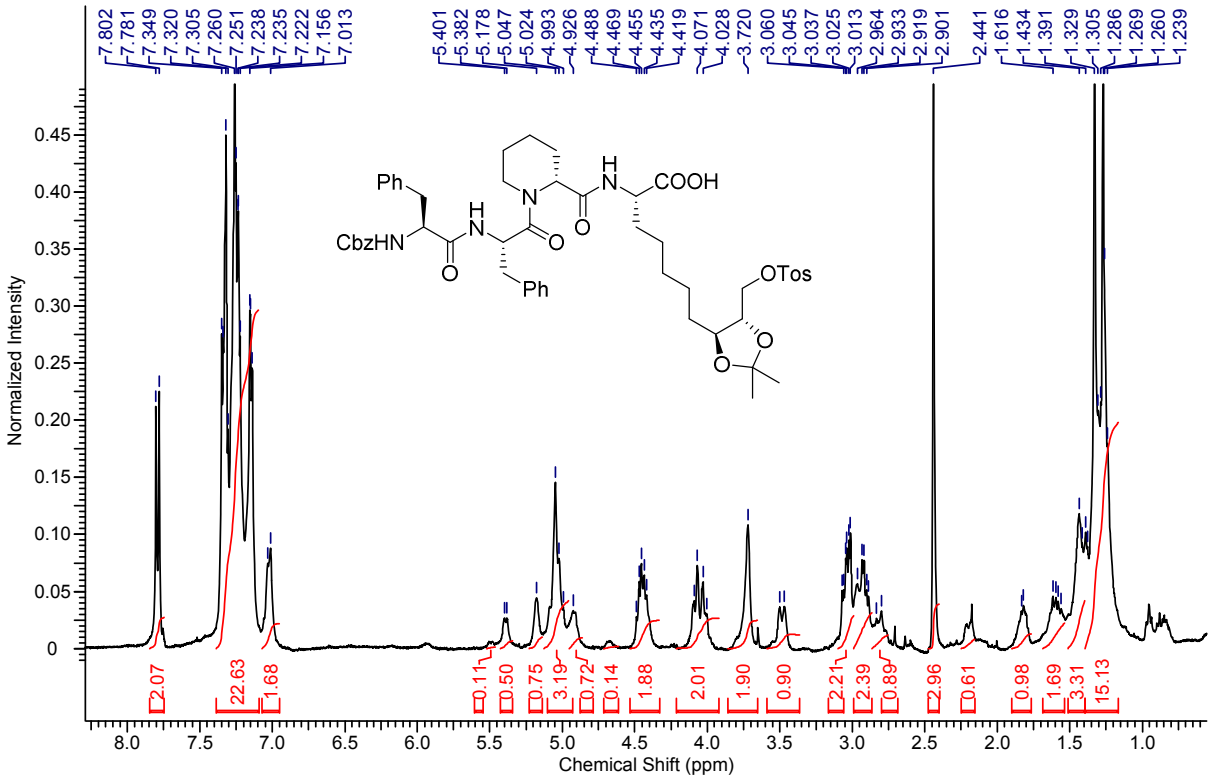


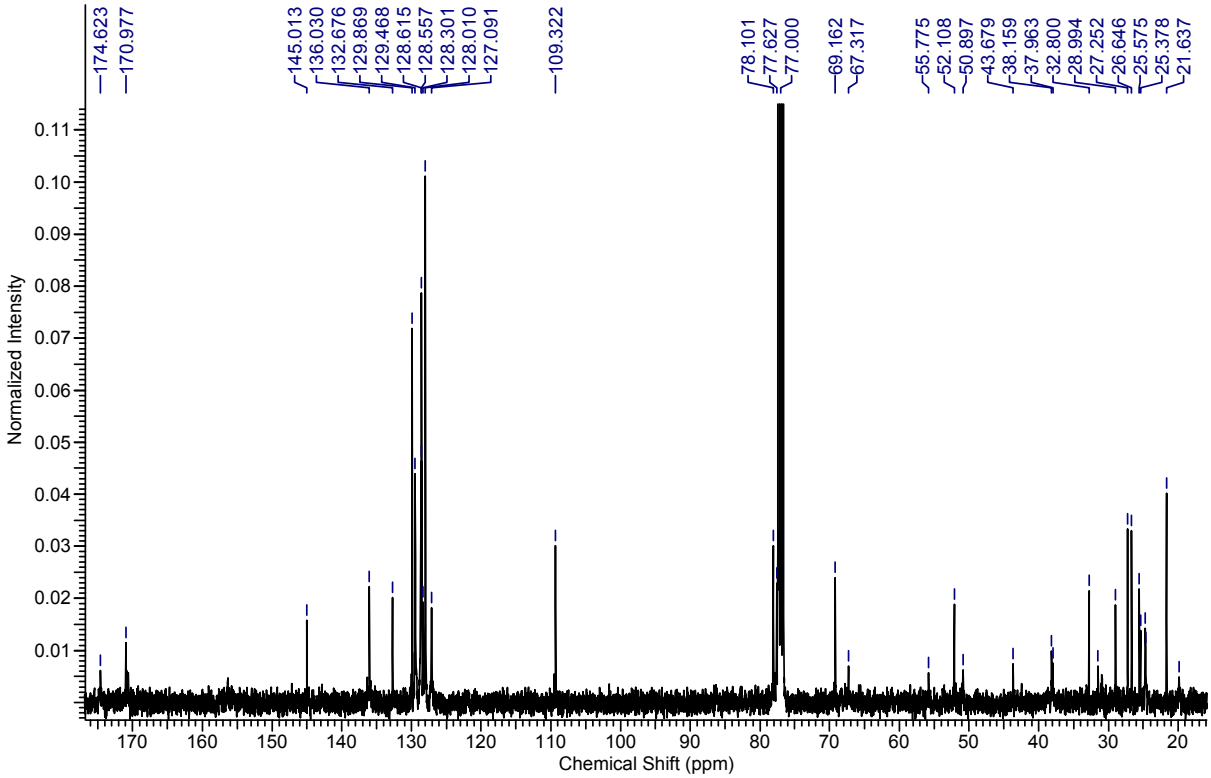
***tert*-Butyl (*S*)-2-((*R*)-1-(((benzyloxy)carbonyl)-L-phenylalanyl-L-phenylalanyl)piperidine-2-carboxamido)-7-((4*S*,5*S*)-2,2-dimethyl-5-((tosyloxy)methyl)-1,3-dioxolan-4-yl)heptanoate (12)**



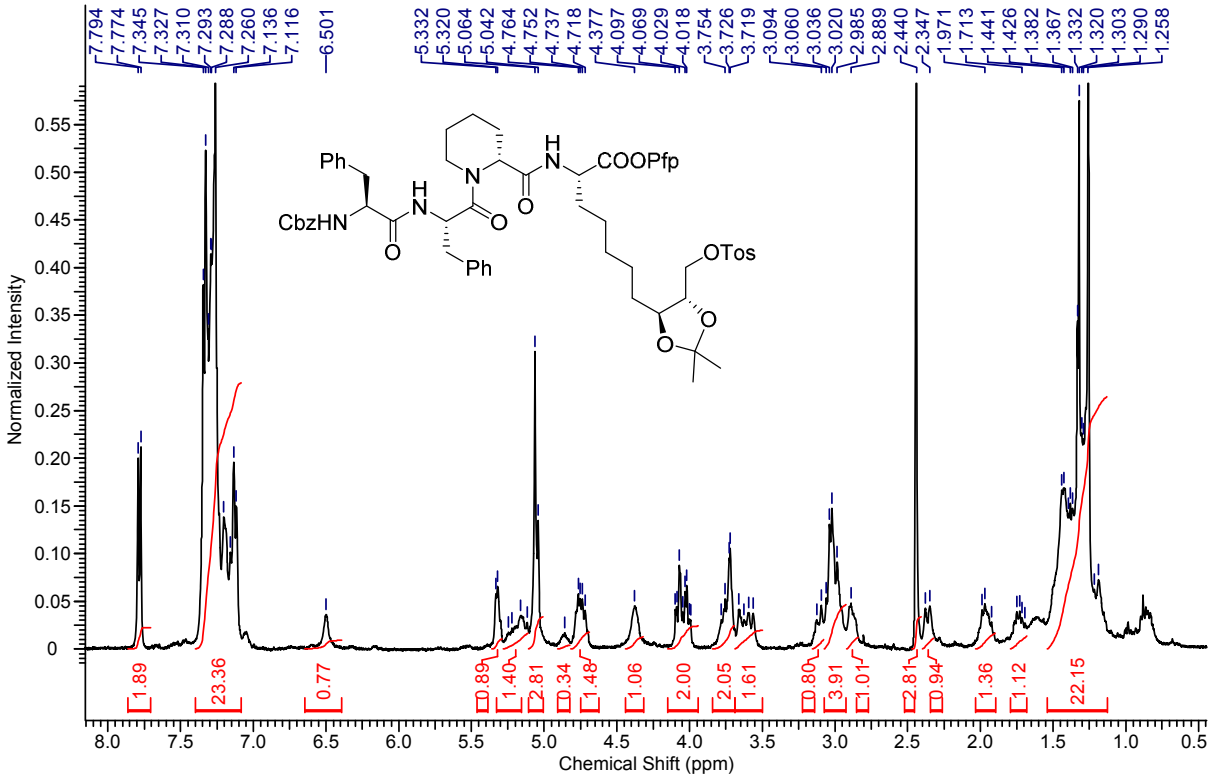


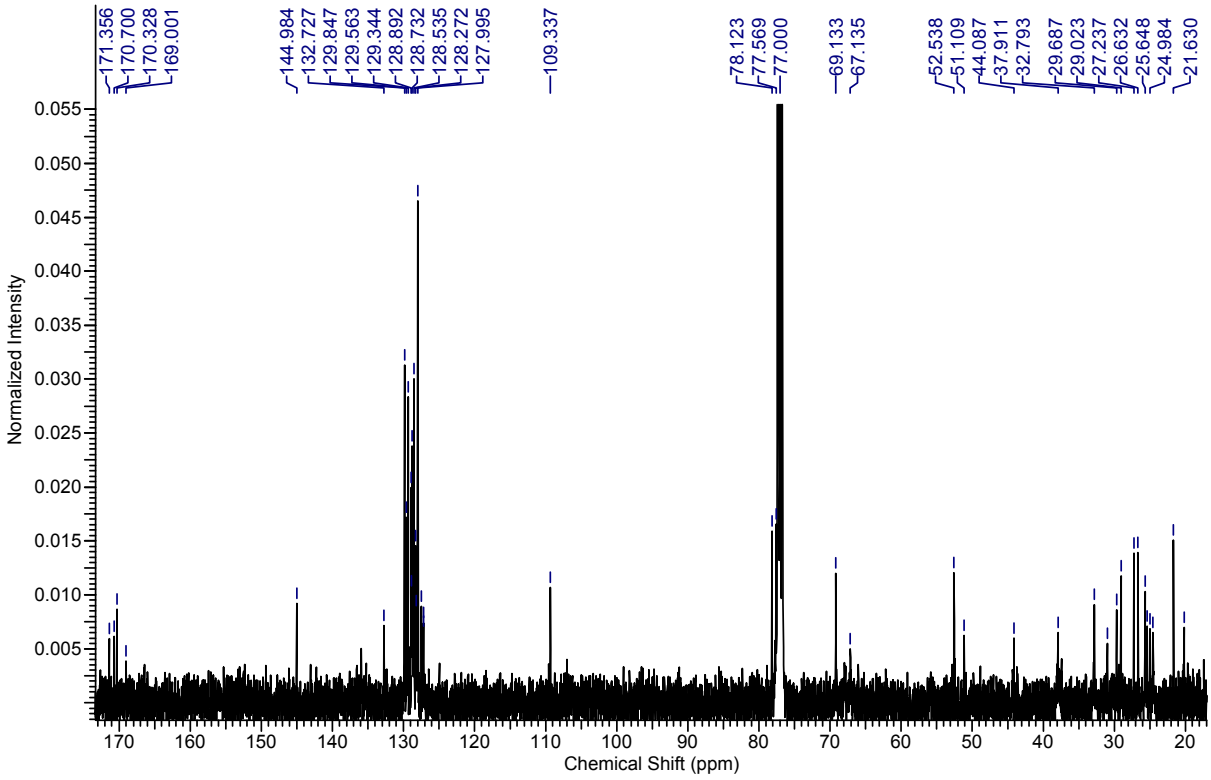
(*S*)-2-((*R*)-1-(((Benzyloxy)carbonyl)-L-phenylalanyl-L-phenylalanyl)piperidine-2-carbox-amido)-7-((4*S*,5*S*)-2,2-dimethyl-5-((tosyloxy)methyl)-1,3-dioxolan-4-yl)heptanoic acid (13)



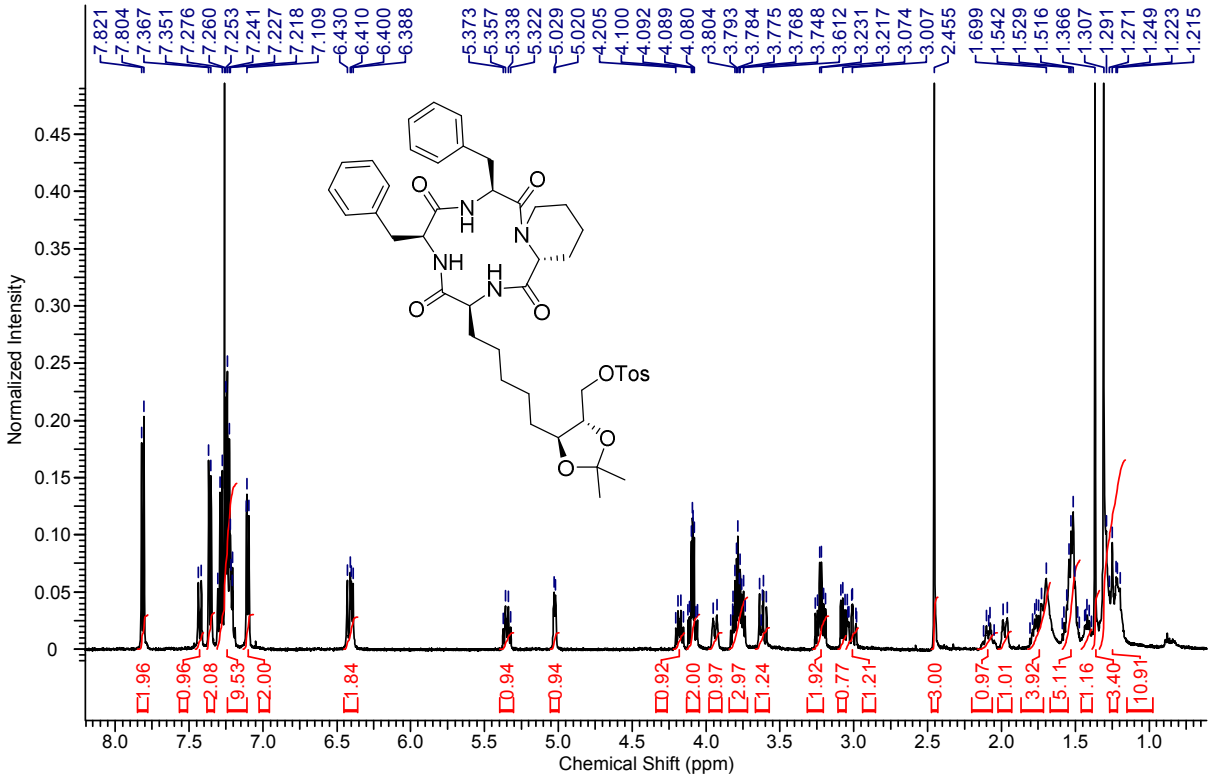


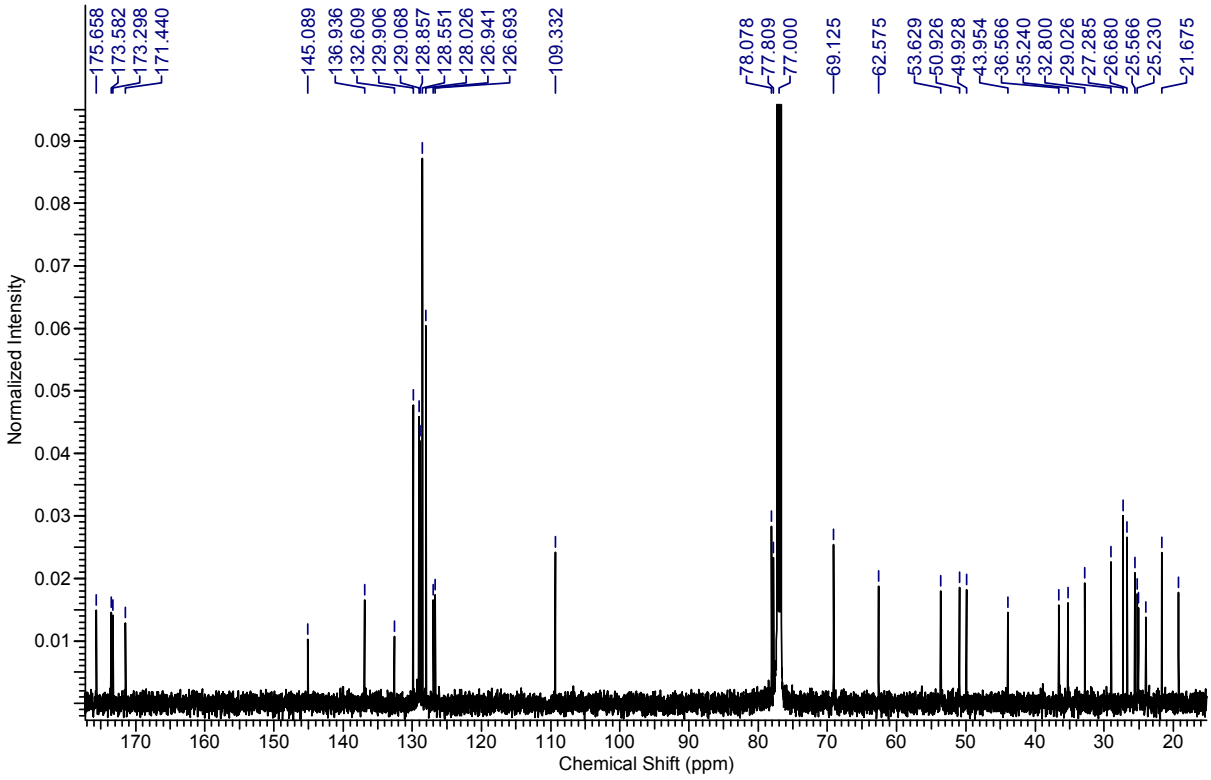
Perfluorophenyl (*S*)-2-((*R*)-1-(((benzyloxy)carbonyl)-L-phenylalanyl-L-phenylalanyl)piperidine-2-carboxamido)-7-((4*S*,5*S*)-2,2-dimethyl-5-((tosyloxy)methyl)-1,3-dioxolan-4-yl)heptanoate (14)



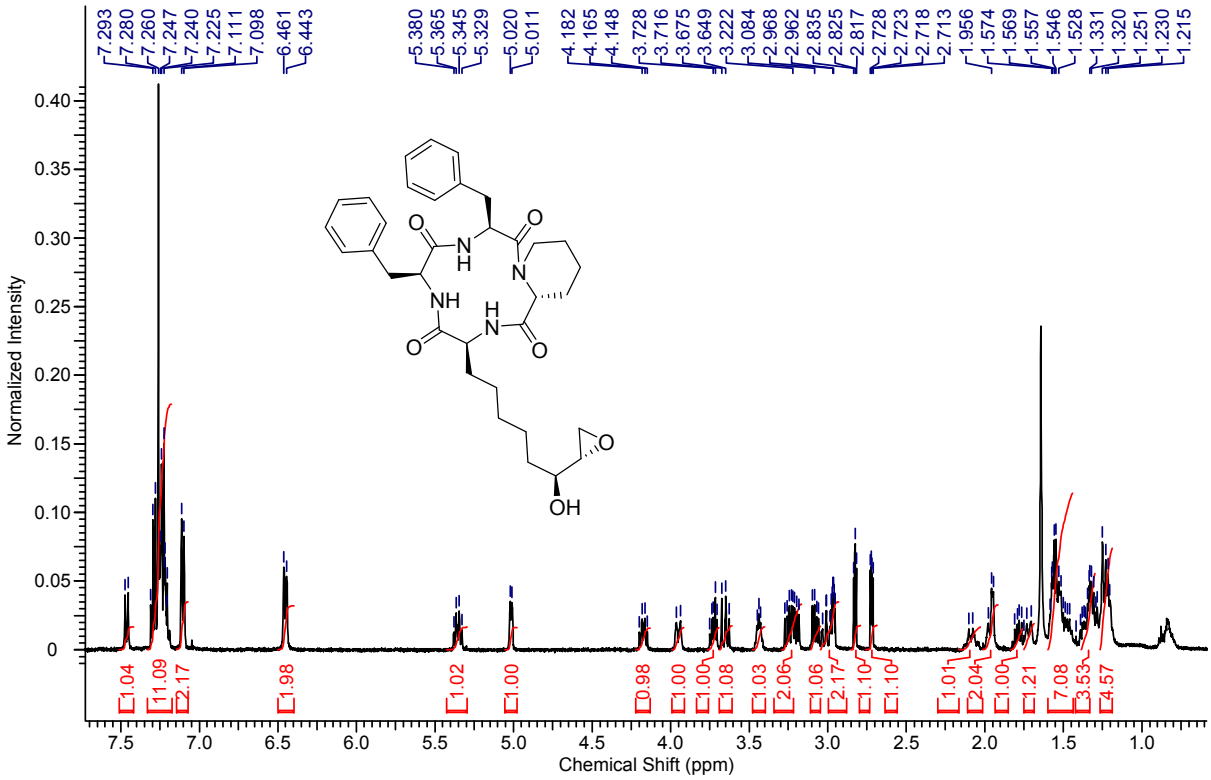


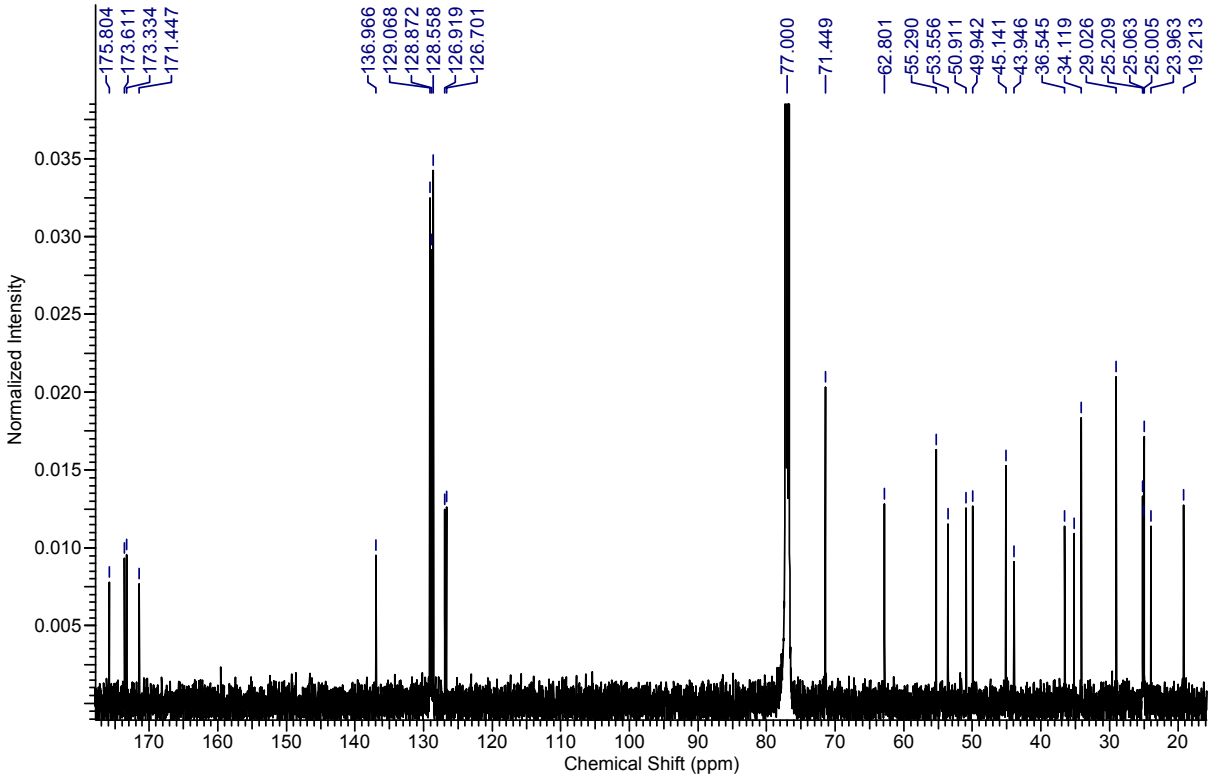
((4*S*,5*S*)-5-(5-((3*S*,6*S*,9*S*,15a*R*)-6,9-Dibenzyl-1,4,7,10-tetraoxotetradecahydro-2H-pyrido-(1,2-a)(1,4,7,10)tetraazacyclododecin-3-yl)pentyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl 4-methylbenzenesulfonate (15)



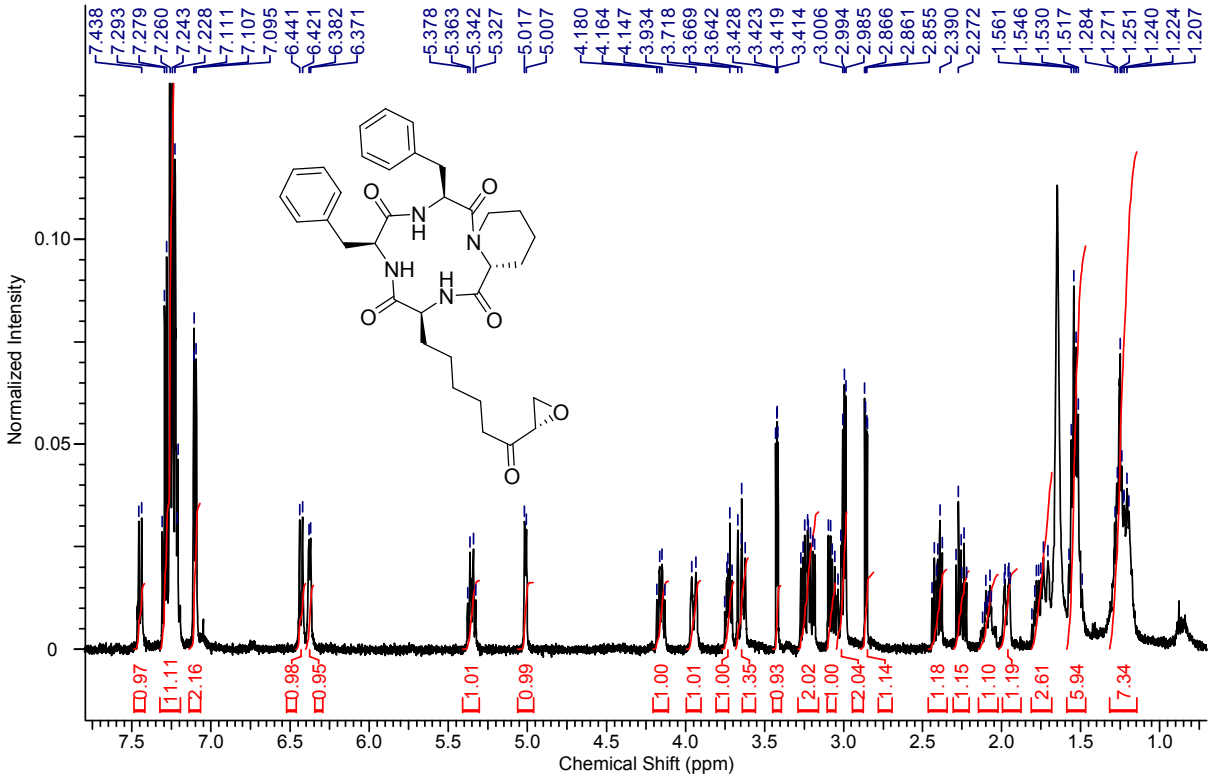


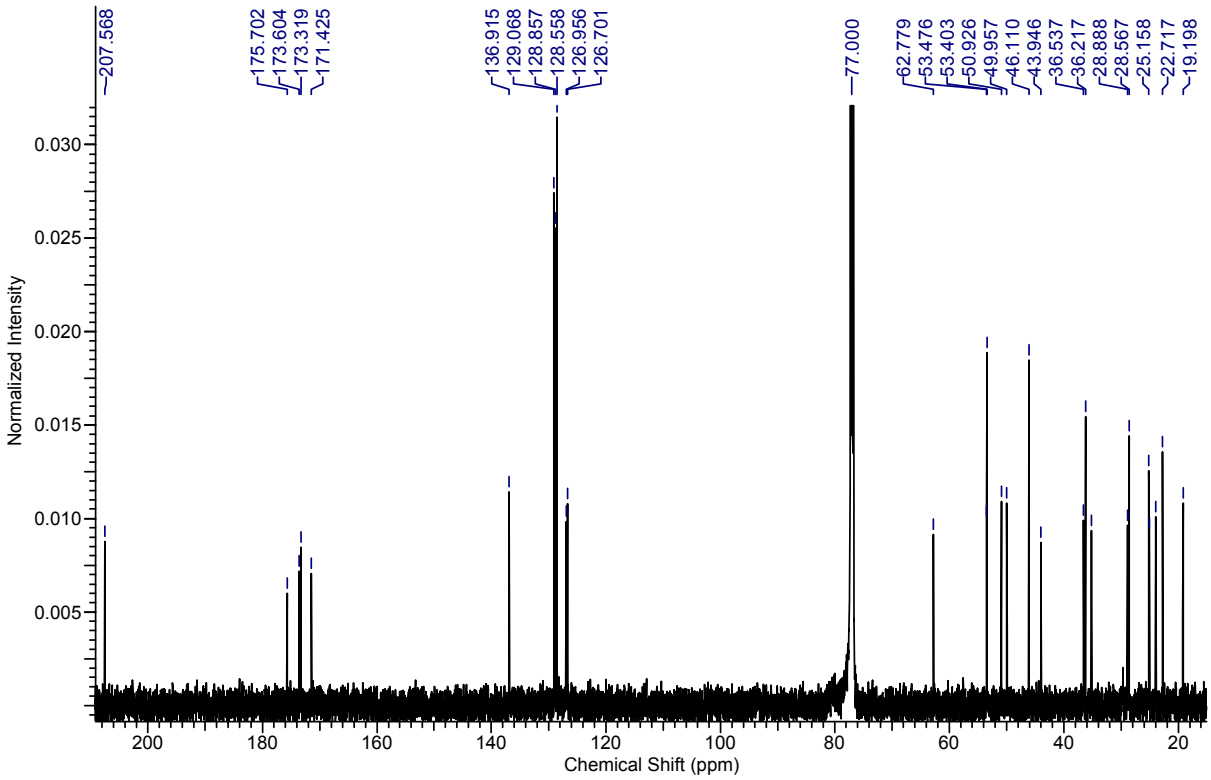
(3*S*,6*S*,9*S*,15a*R*)-6,9-Dibenzyl-3-((*S*)-6-Hydroxy-6-((*S*)-oxiran-2-yl)hexyl)octahydro-2H-pyrido(1,2-a)(1,4,7,10)tetraazacyclododecine-1,4,7,10(3H,12H)-tetraone (16)

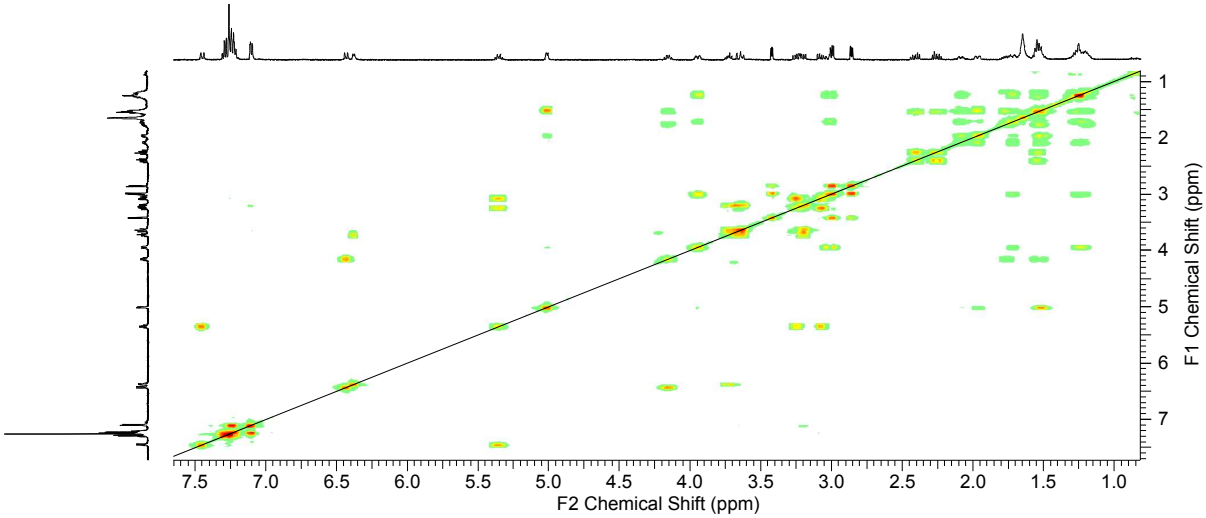




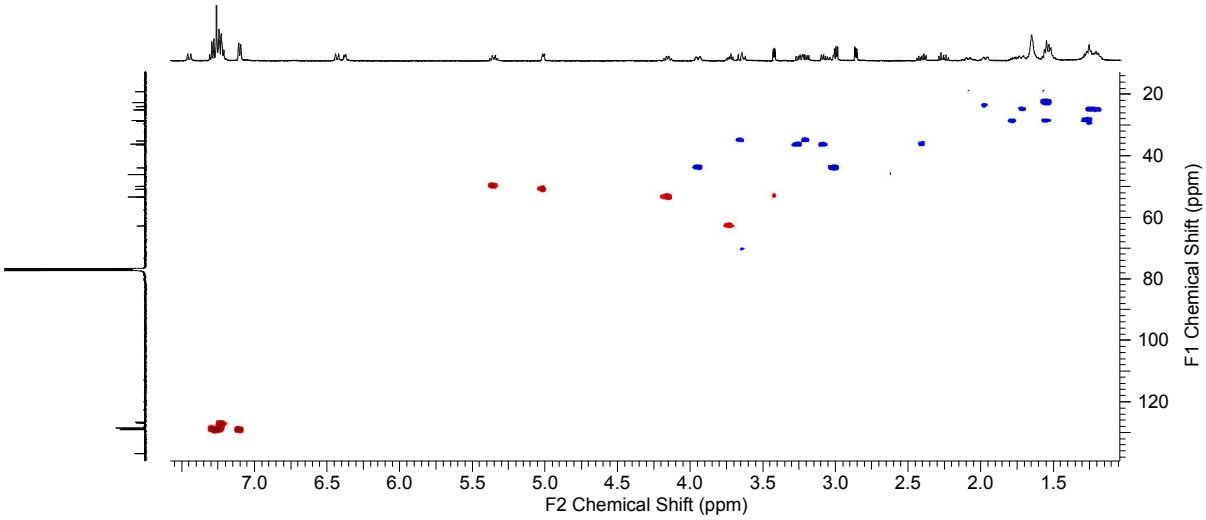
Trapoxin A


7.438
7.293
7.279
7.260
7.243
7.228
7.111
7.107
7.095
6.441
6.421
6.382
6.371
5.378
5.363
5.342
5.327
5.017
5.007
4.180
4.164
4.147
3.934
3.718
3.669
3.642
3.428
3.423
3.419
3.414
3.006
2.994
2.985
2.866
2.861
2.855
2.390
2.272
1.561
1.546
1.530
1.517
1.284
1.271
1.251
1.240
1.224
1.207
Normalized Intensity
Chemical Shift (ppm)
0.97
1.11
2.16
0.98
0.95
1.01
0.99
1.00
1.01
1.00
1.35
0.93
2.02
1.00
2.04
1.14
1.18
1.15
1.10
1.19
2.61
5.94
7.34

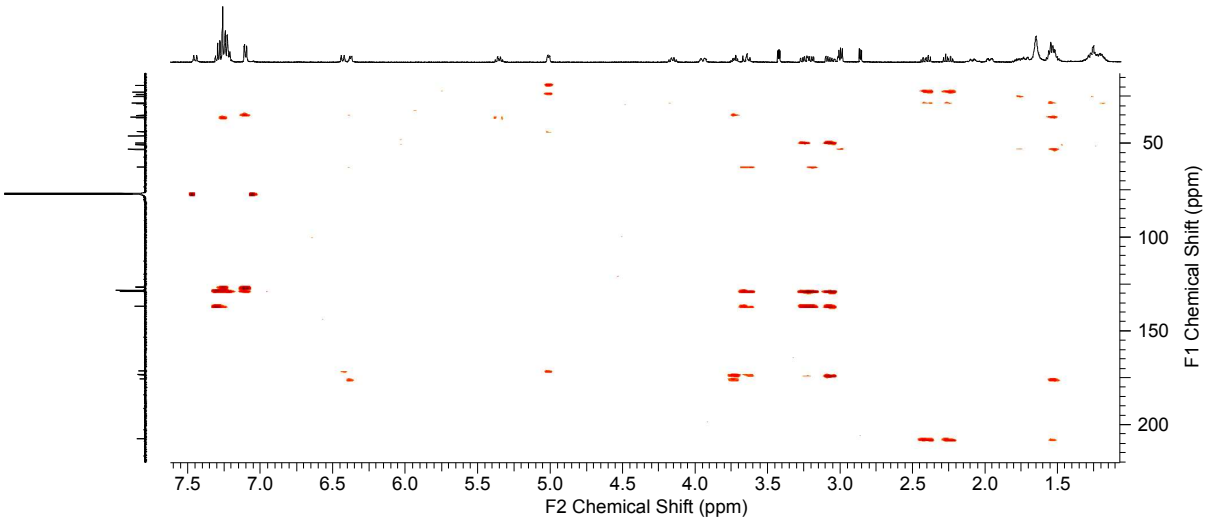

207.568
175.702
173.604
173.319
171.425
136.915
129.068
128.857
128.558
126.956
126.701
77.000
62.779
53.476
53.403
50.926
49.957
46.110
43.946
36.537
36.217
28.888
28.567
25.158
22.717
19.198
Normalized Intensity
Chemical Shift (ppm)



HH-COSY spectra of Trapoxin A.



HSQCed spectra of Trapoxin A.



HMBC spectra of Trapoxin A.