Synthesis and stereochemical analysis of β-nitromethane substituted γ-amino acids and peptides.

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Crystal structures of 2c, 2b acid & P3:

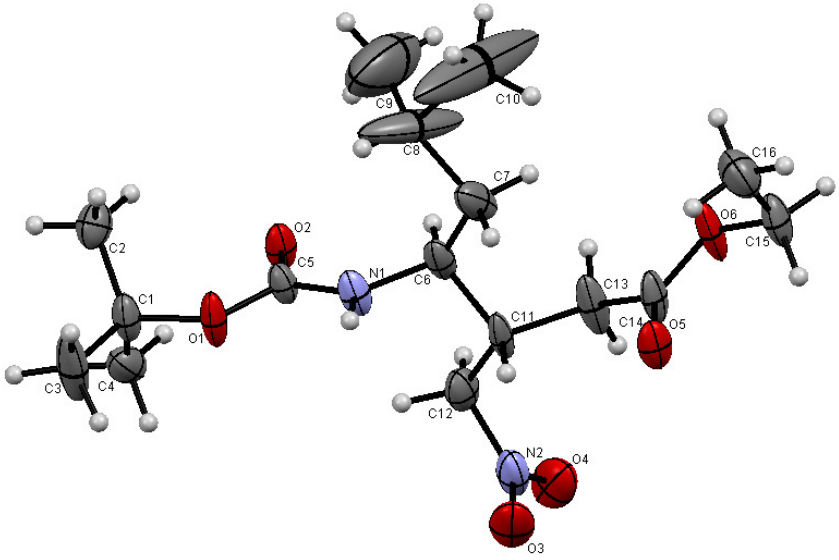


Figure2: ORTEP structure of **2c**.

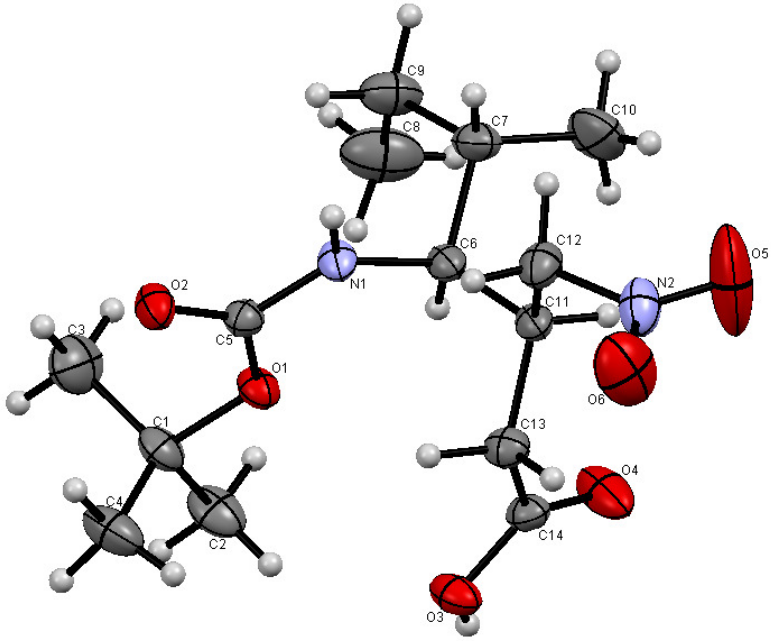


Figure3: ORTEP structure of **2b acid**.

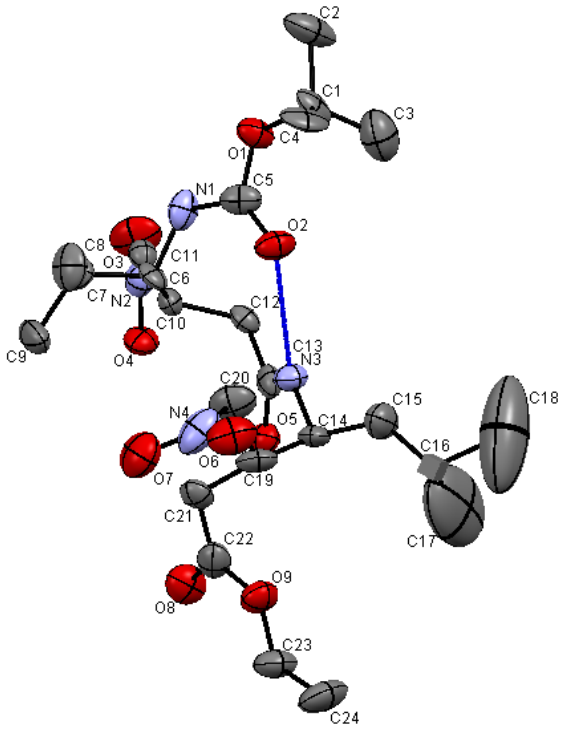


Figure 4: ORTEP structure of Dipeptide **P3** (Boc-γV(β-CH_2NO_2)-γL(β-CH_2NO_2)-COOEt.

Crystal structure analysis of Boc-γL(β-CH_2NO_2)-COOEt (2 c): Crystals were grown by slow evaporation from a solution of EtOAc. A single crystal (0.19× 0.15 × 0.12 mm) was mounted on loop with a small amount of the paraffin oil. The X-ray data were collected at 100 K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.56), for a total of 4625 independent reflections. Space group P2(1), 2(1), 2(1), a = 11.306(6), b = 31.857(16), c = 5.353(3), V = 1928.2(17) $Å^3$, Orthorhombic P, Z=4 for chemical formula $C_{16}H_{30}N_2O_6$, with one molecule in asymmetric unit; ρ calcd = 1.193 gcm^{-3}, μ = 0.091 mm^{-1}, F(000) = 752, R_{int}= 0.0616. The structure was obtained by direct methods using SHELXS-97.The final R value was 0.0927 (wR2 = 0.2645) 2600 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 224 variables, S = 1.161. The largest difference peak and hole were 0.920 and -0.470 $eÅ^3$, respectively.

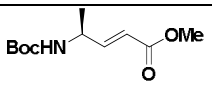
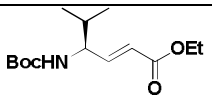
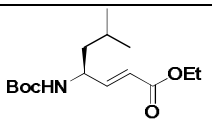
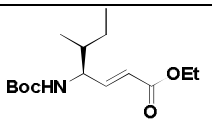
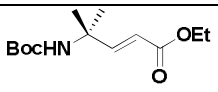
Crystal structure analysis of Boc-γI(β-CH_2NO_2)-COOH (2b acid): Crystals were grown by slow evaporation from a solution of EtOAc and Hexane. A single crystal (0.35× 0.24 × 0.20 mm) was mounted on loop with a small amount of the paraffin oil. The X-ray data were collected at 100 K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.56), for a total of 4252 independent reflections. Space group P2(1), a = 11.226(8), b = 7.133(5), c = 12.018(9), β = 110.948(15) V= 898.7(11) $Å^3$, Monoclinic P, Z=2 for chemical formula $C_{14}H_{26}N_2O_6$, with one molecule in asymmetric unit; ρ calcd = 1.176 gcm^{-3}, μ = 0.092 mm^{-1}, F(000) = 344, R_{int}= 0.0345. The structure was obtained by direct methods using SHELXS-97.The final R value was 0.0441 (wR2 = 0.1012) 3359 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 205 variables, S = 1.036. The largest difference peak and hole were 0.173 and -0.239 $eÅ^3$, respectively.

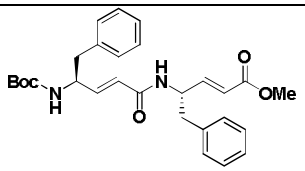
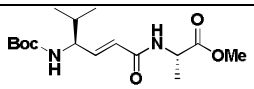
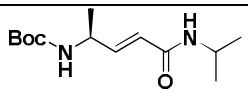
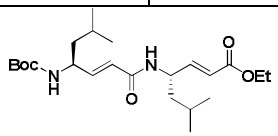
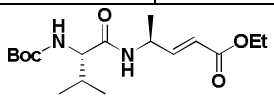
Crystal structure analysis of Boc-γV(β-CH_2NO_2)-γL(β-CH_2NO_2)-COOEt (P3): Crystals of peptide were grown by slow evaporation from a solution of EtOAc. A single crystal (0.34× 0.20 × 0.18 mm) was mounted on glass fiber with a small amount of the paraffin oil. The X-ray data were collected at 100K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 58.56), for a total of 5572 independent reflections. Space group P3(2) , a = 13.503(9), b = 13.503 (9), c = 14.005(10), α = 90.00, β = 90.00, γ = 120.00, V = 2211.44 $Å^3$, Trigonal, Z = 3, Z' = 0 for chemical formula $C_{24}H_{44}N_4O_9$, with one molecule in asymmetric unit; ρcalcd = 1.186 gcm^{-3}, μ = 0.091 mm^{-1}, F(000) = 864, R_{int} = 0.1857. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0865 (wR2 = 0.2072)1917 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 343 variables, S = 0.878. The largest difference peak and hole were 0.879 and -0.438$eÅ^3$, respectively. During the crystal analysis, it was observed that leucine side chain methyl carbons C_{17} and C_{18} are showing disorder

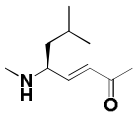
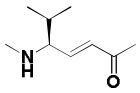
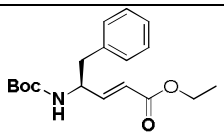
due to a large difference in the vibrating behavior and therefore H-atoms attached with them are showing short intramolecular contacts due to lack of sufficient van der waals space.

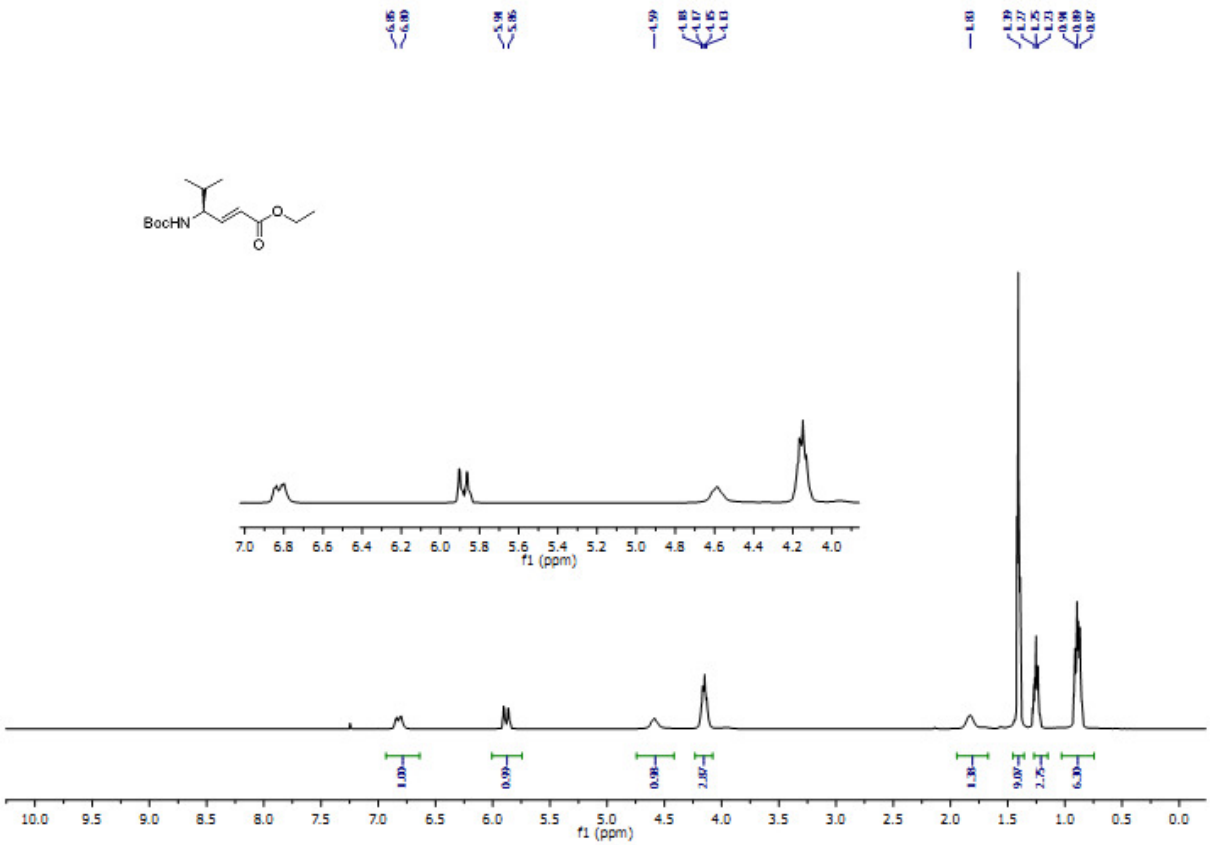
Conformational analysis of vinylogous amino acid residues in monomer and peptide single crystals

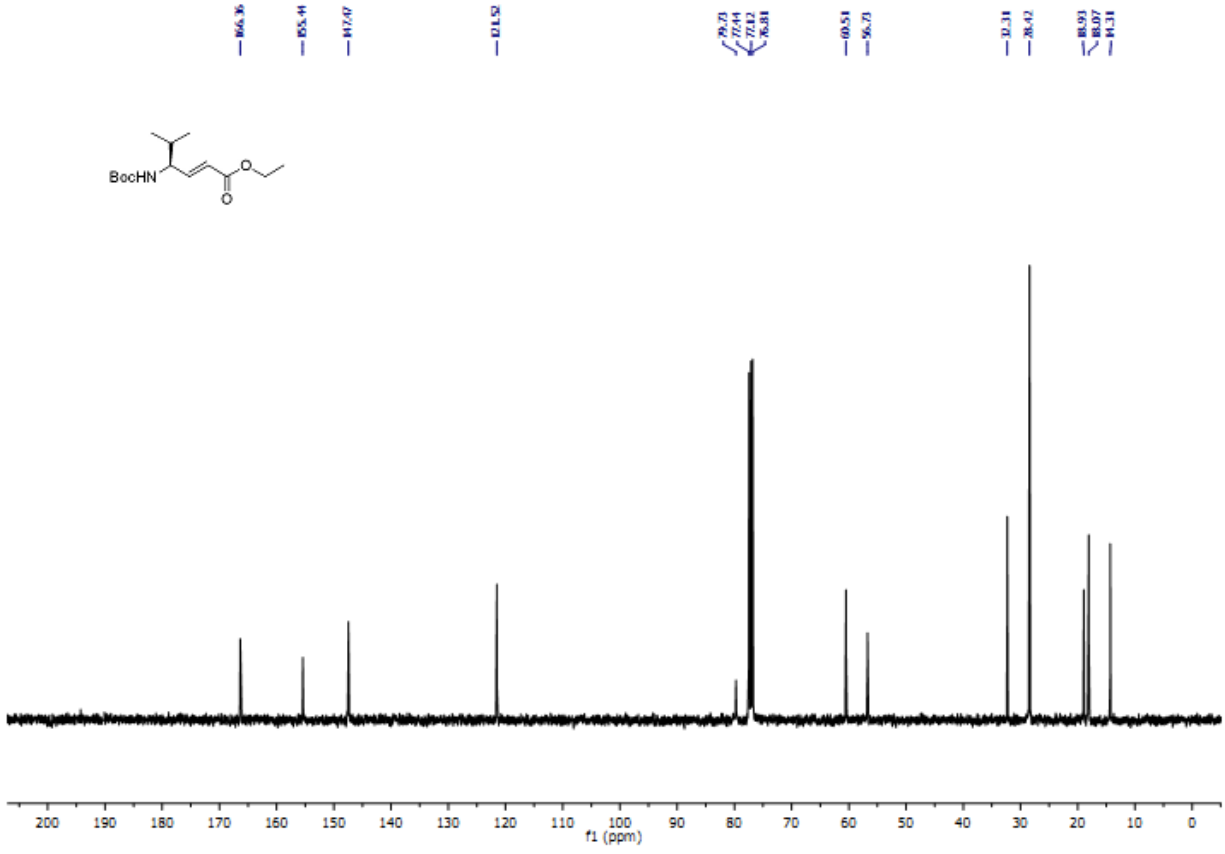
Table 2: Torsion angle of θ_1 and the eclipsed conformations of α, β-unsaturated γ-amino acid residues

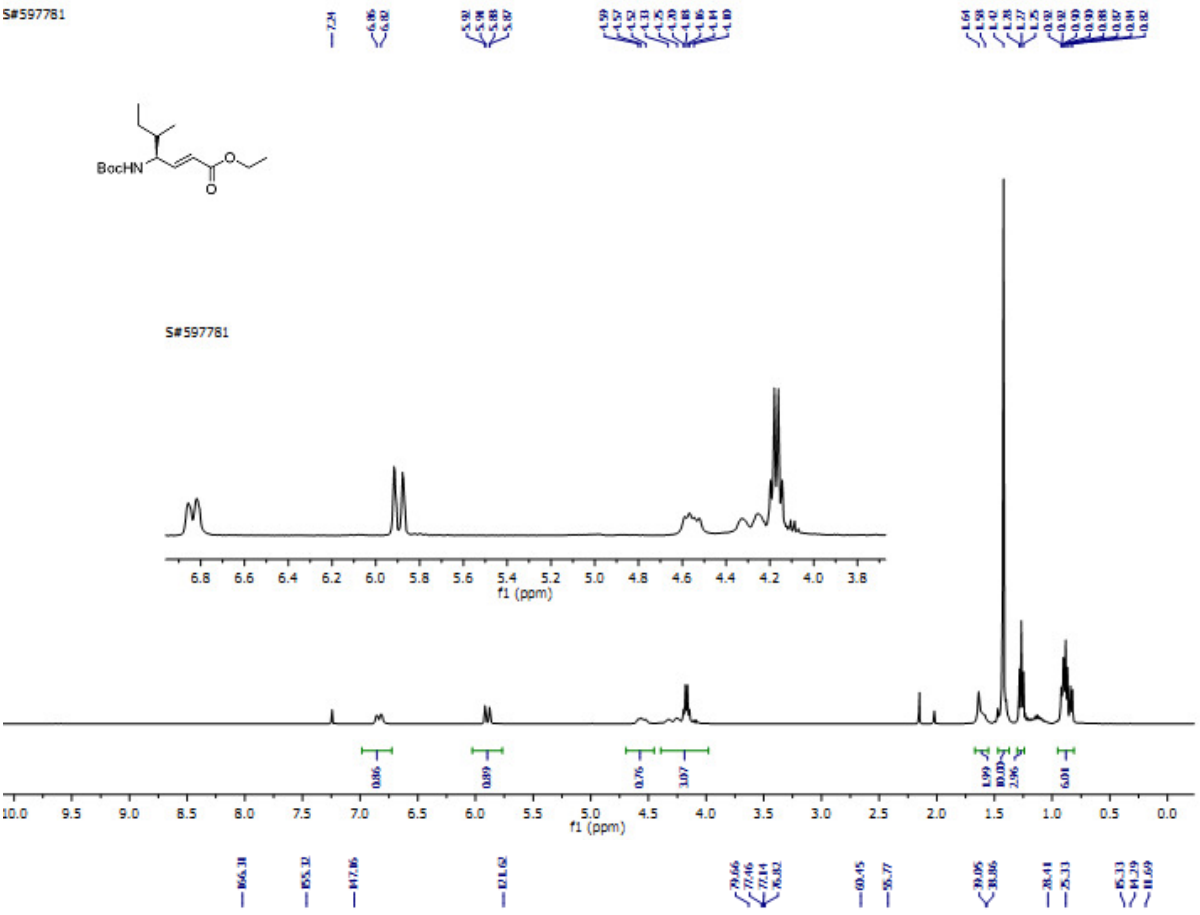
Sl. No.	Monomer/Peptide	Torsion Angle (θ_1)	Conformation (eclipsed)	Ref.
1	 Boc-dgA-OMe	-10	N-C_γ-C_β=C_α	**2**
2	 Boc-dgV-OEt	0	N-C_γ-C_β=C_α	**3**
3	 Boc-dgL-OEt	-1	N-C_γ-C_β=C_α	**3**
4	 Boc-dgI-OEt	0	N-C_γ-C_β=C_α	**3**
5	 Boc-dgU-OEt	-10	N-C_γ-C_β=C_α	**3**

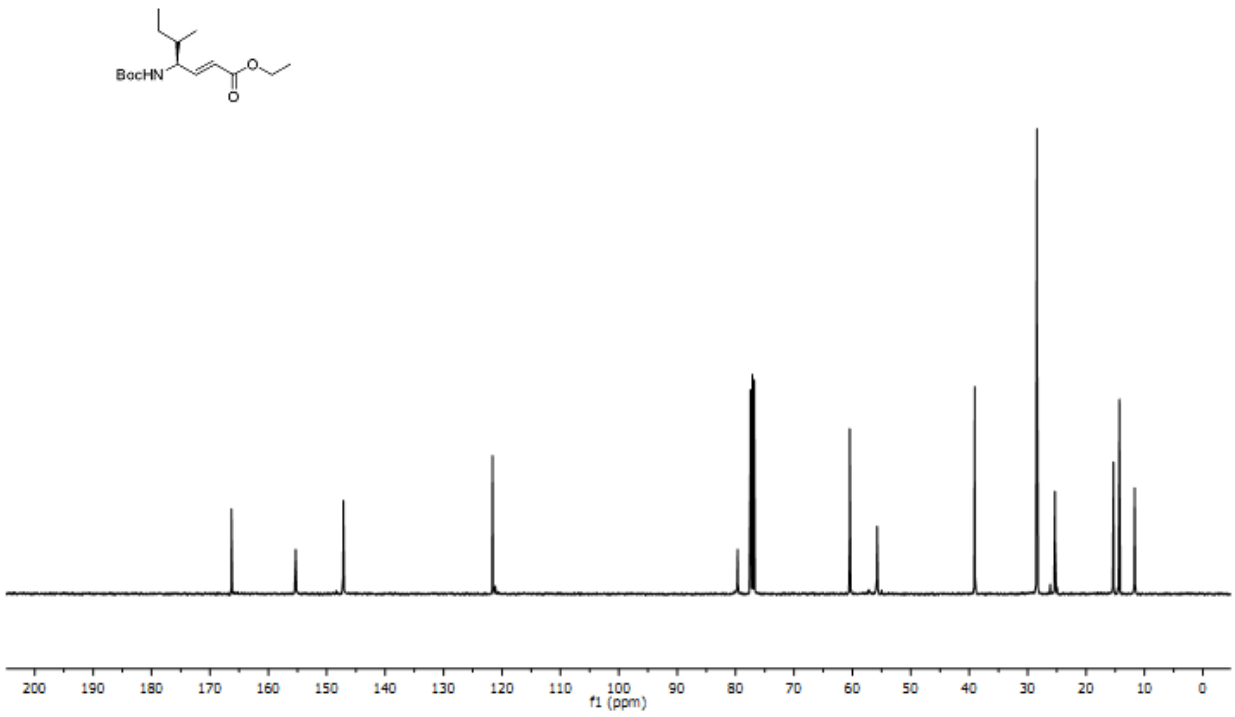
	 Boc-dgF1-dgF2-OMe			**2**
6 7	dgF1 dgF2	116 32	H-C_γ-C_β=C_α N-C_γ-C_β=C_α	**2**
8	 Boc-dgV-A-OMe dgV	112	H-C_γ-C_β=C_α	**2**
9	 Boc-dgA-NHPr^i dgA	116	H-C_γ-C_β=C_α	**2**
	 Boc-dgL1-dgL2-OEt			**3**
10 11	dgL1 dgL2	116 0	H-C_γ-C_β=C_α N-C_γ-C_β=C_α	**3**
	 Boc-V-dgA-OEt (Six molecules in asymmetric centre.)			**3**
12 13 14	a b c	9 127 -9	N-C_γ-C_β=C_α H-C_γ-C_β=C_α N-C_γ-C_β=C_α	**3**

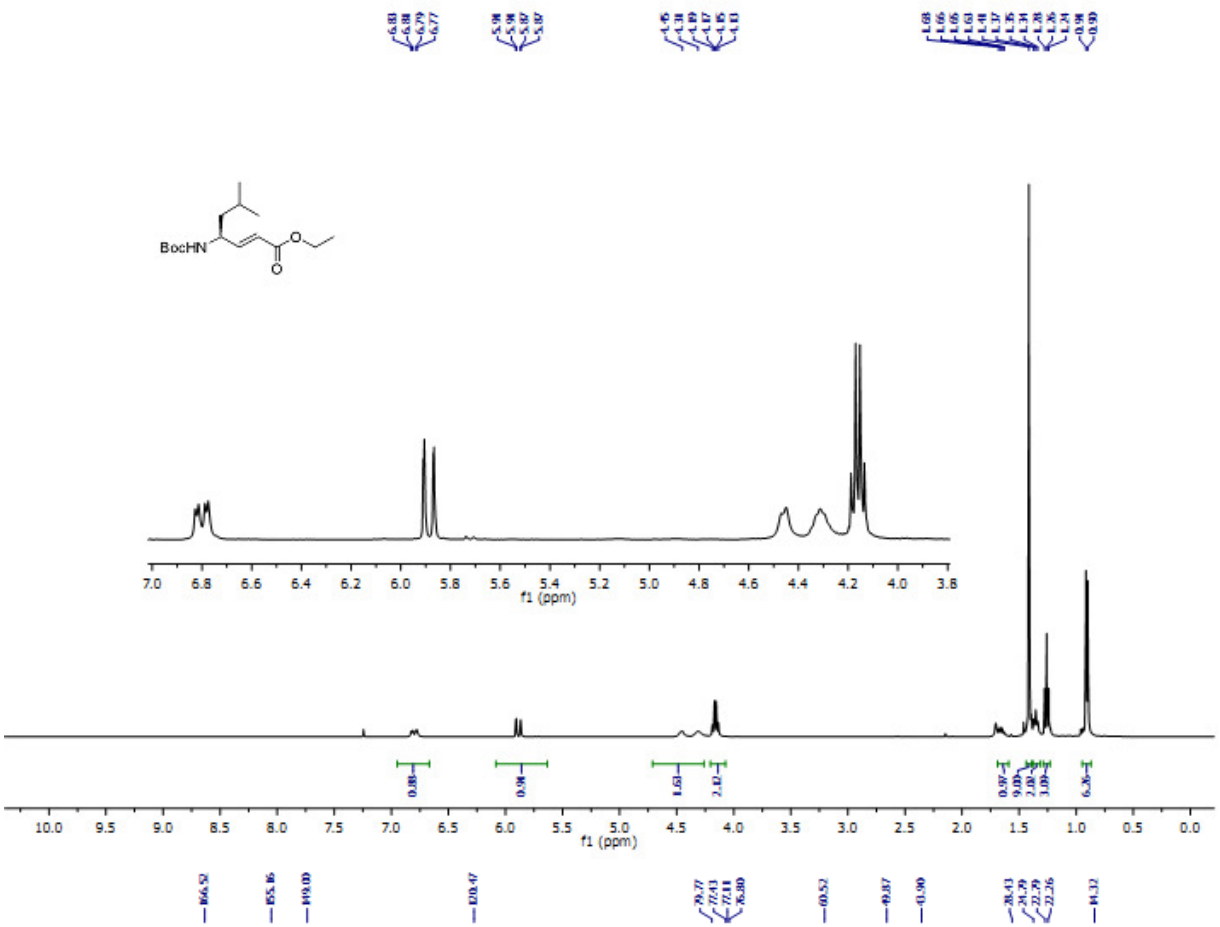
15	d	129	H-C_γ-C_β=C_α	
16	e	7	N-C_γ-C_β=C_α	
17	f	-3	N-C_γ-C_β=C_α	
	Ac-V-dgL-V-^{D}P-G-L-dgV-V-NH_2 dgL =  dgV = 			**4**
18	dgL	132	H-C_γ-C_β=C_α	**4**
19	dgV	123	H-C_γ-C_β=C_α	
20	 dgF	125	H-C_γ-C_β=C_α	**Present work**

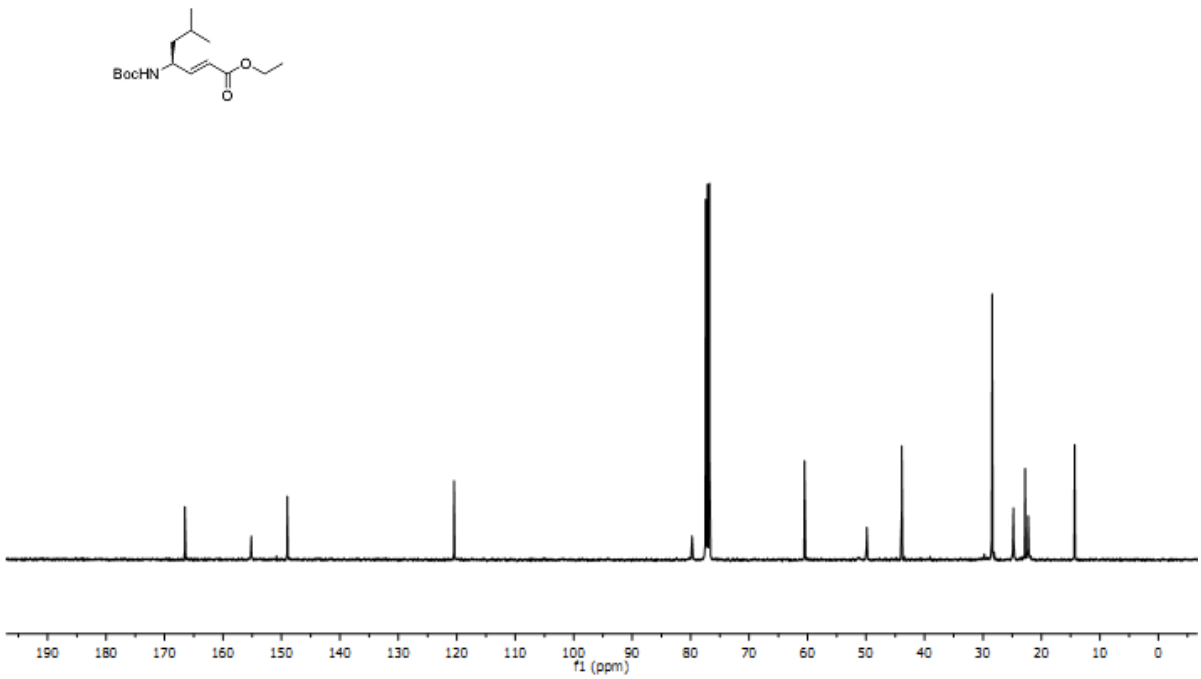


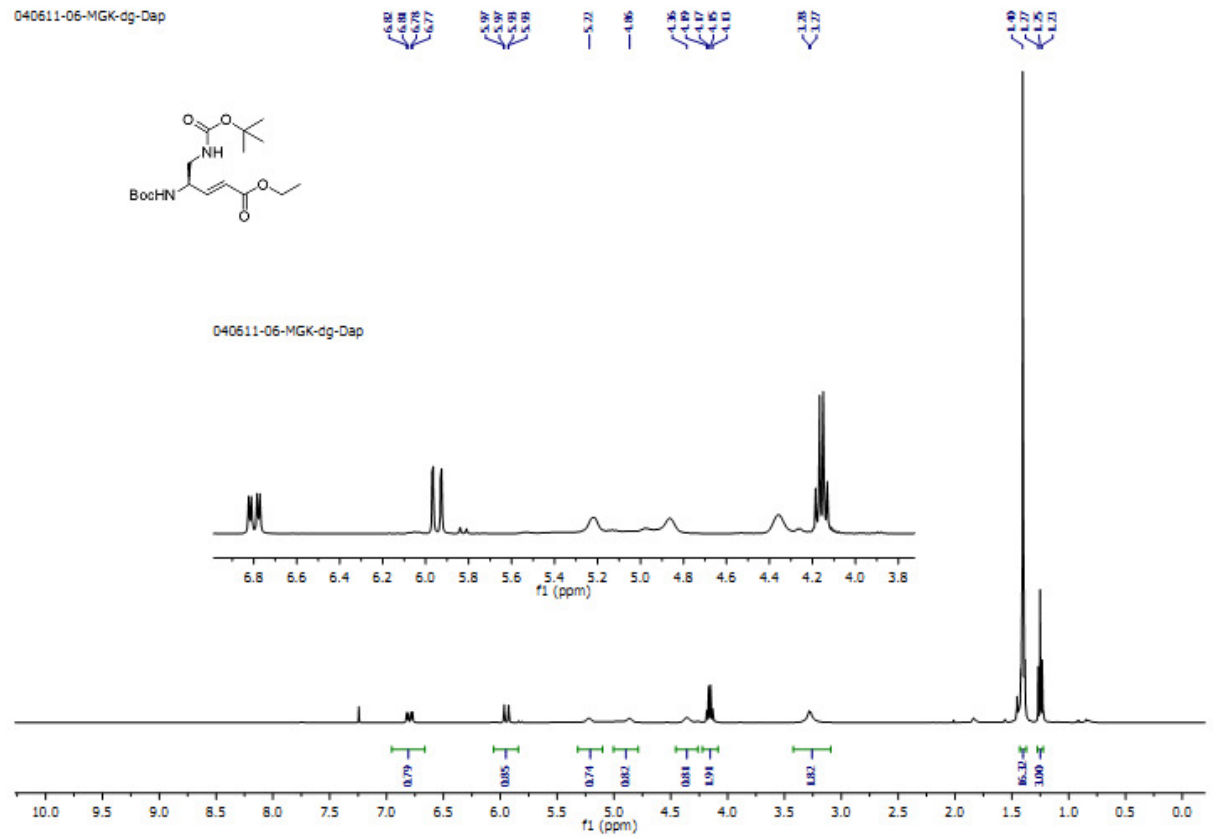


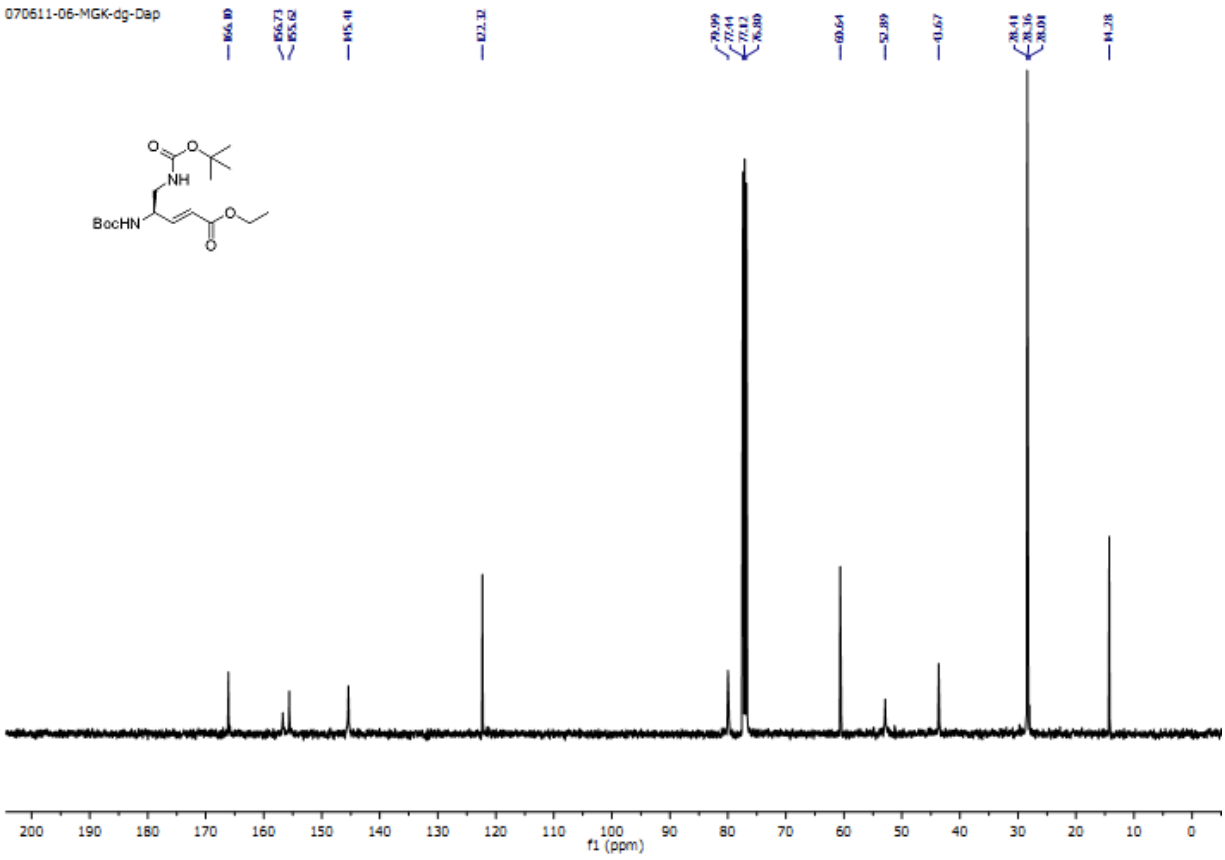


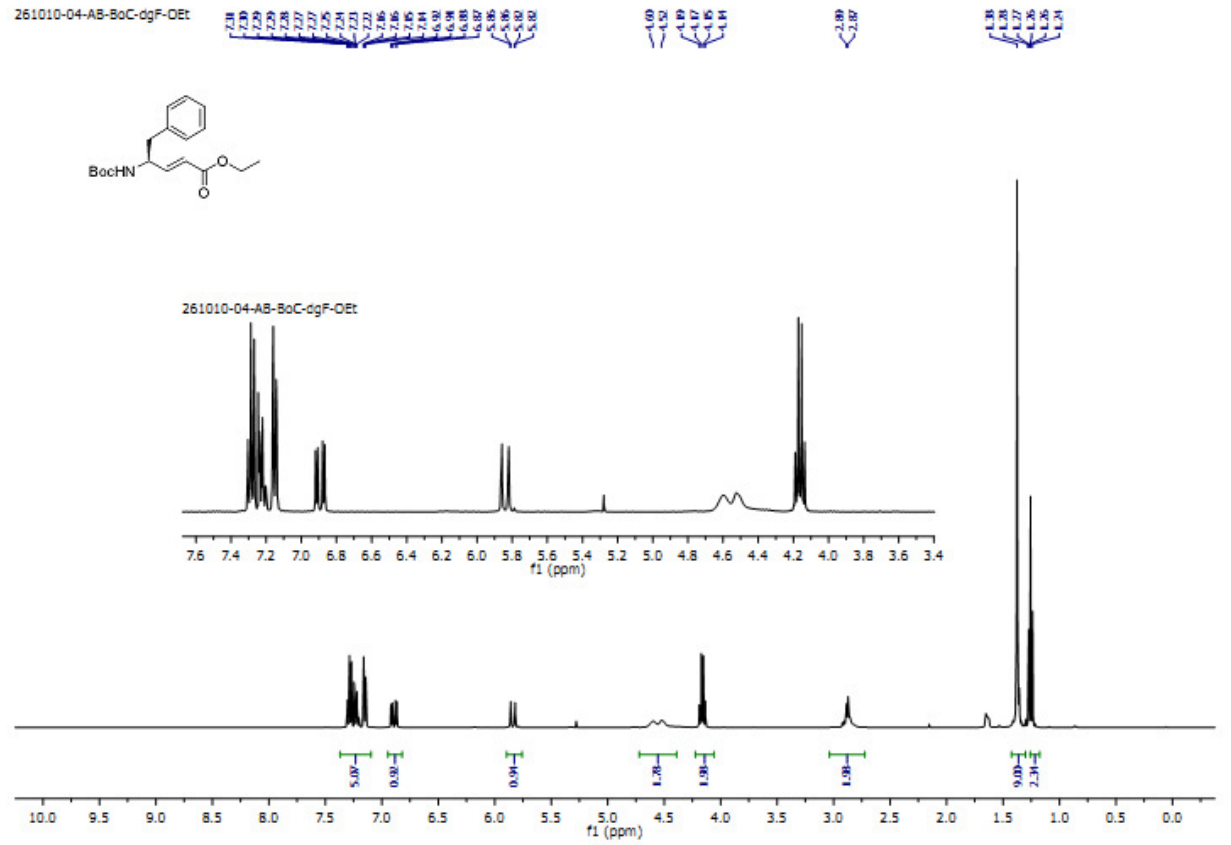


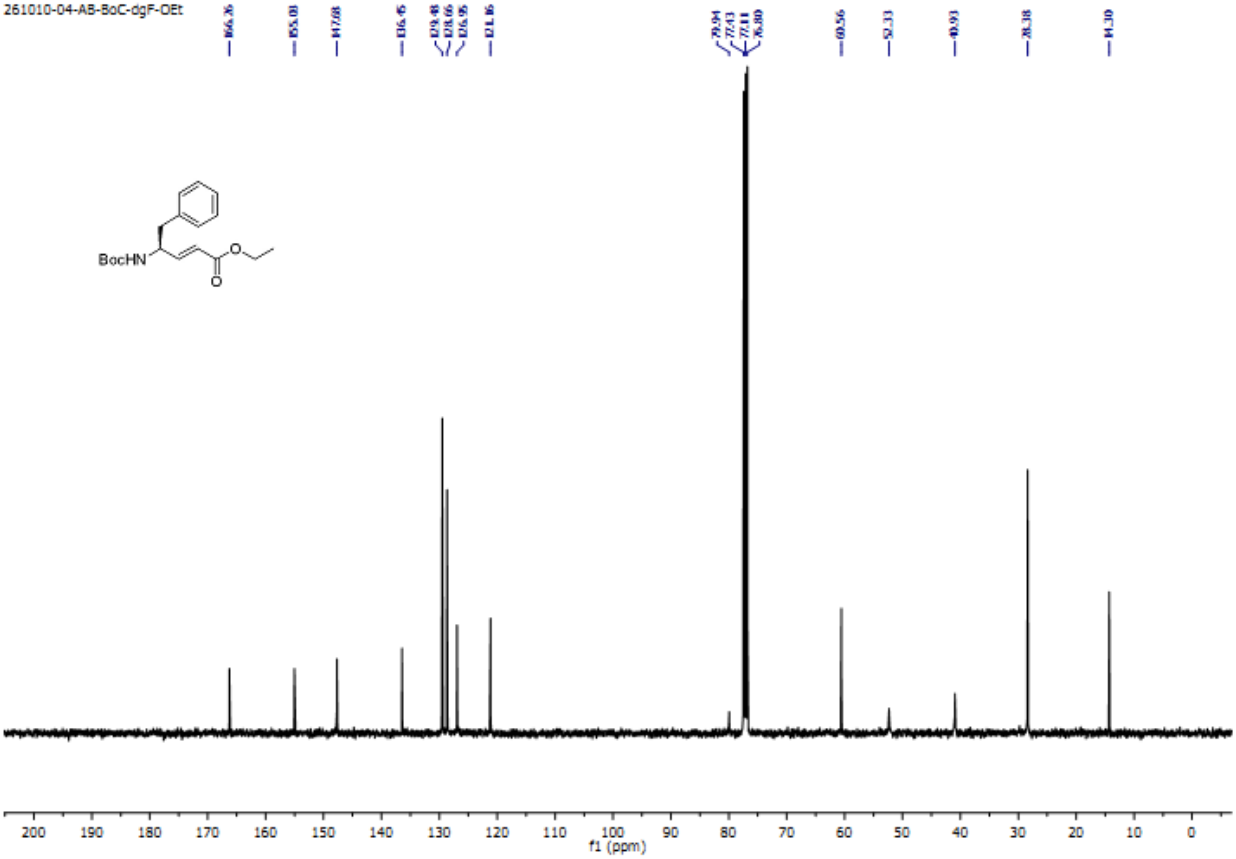


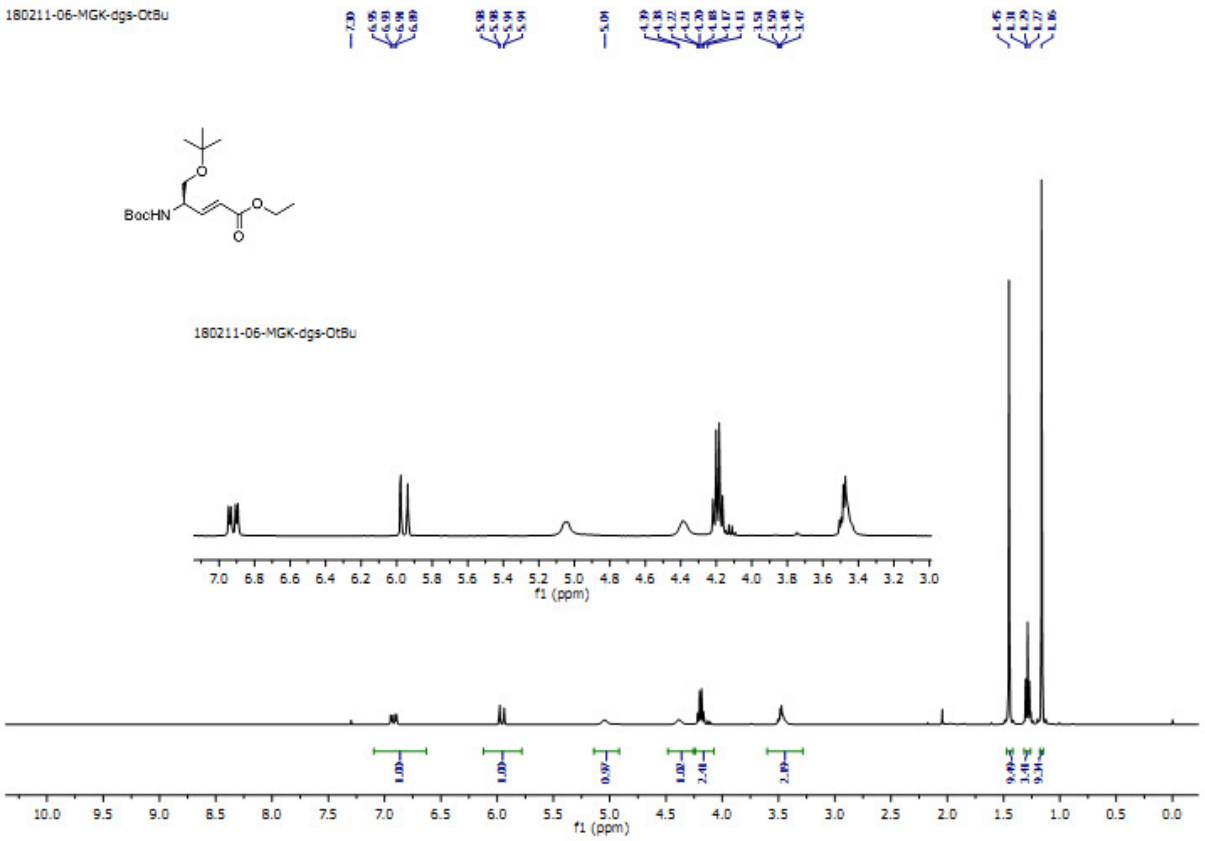


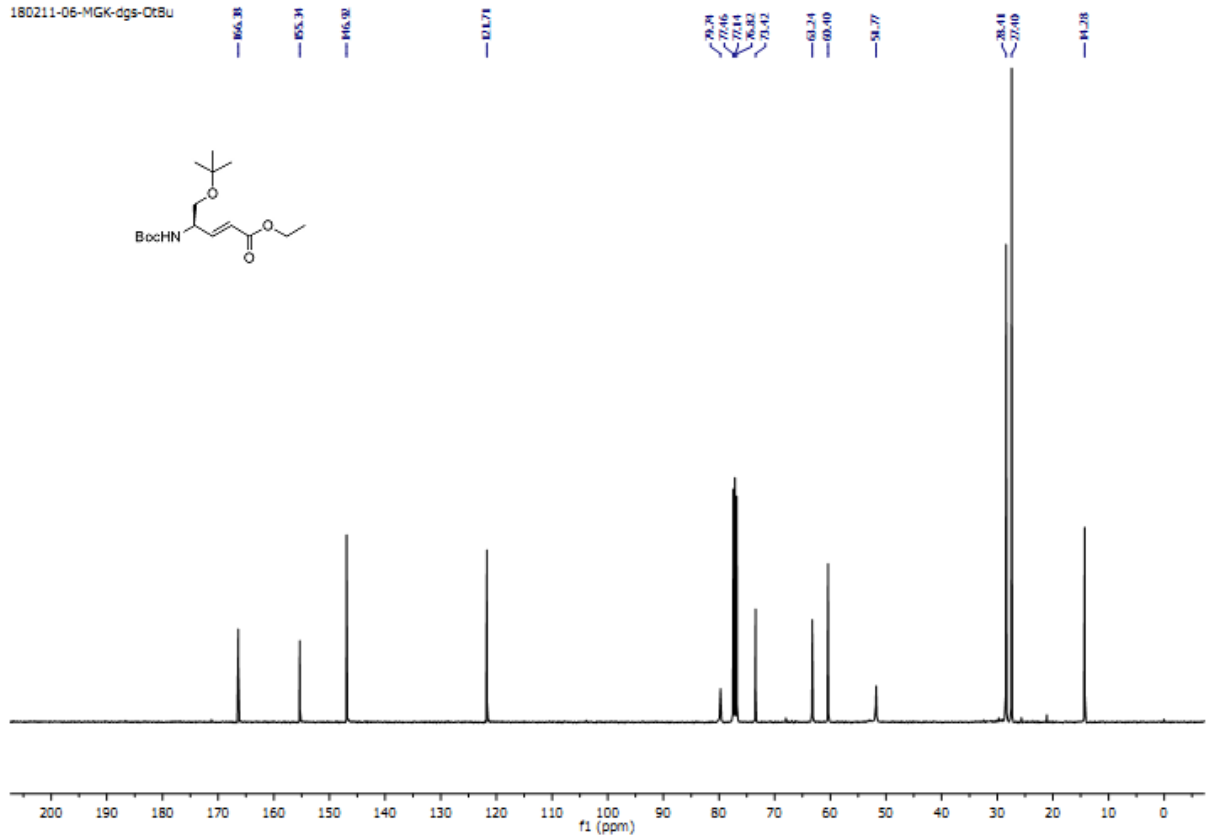


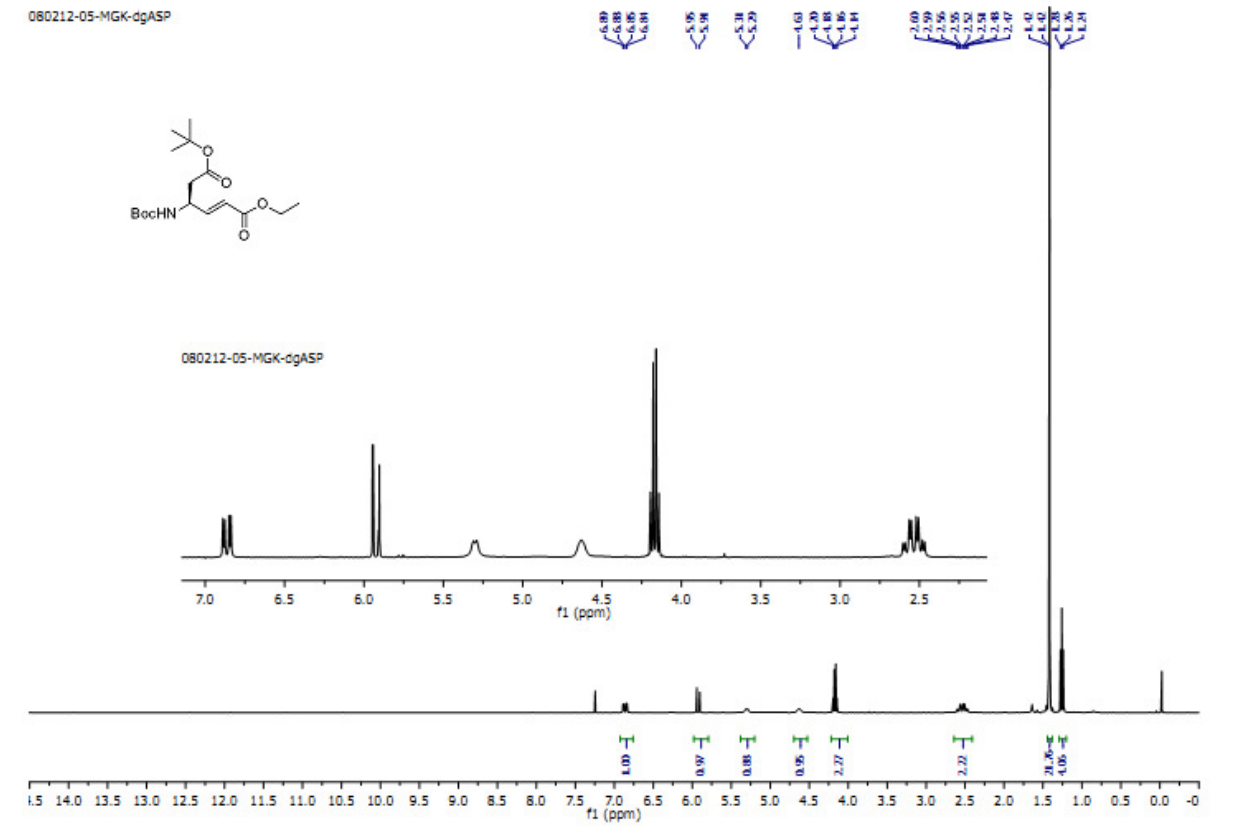


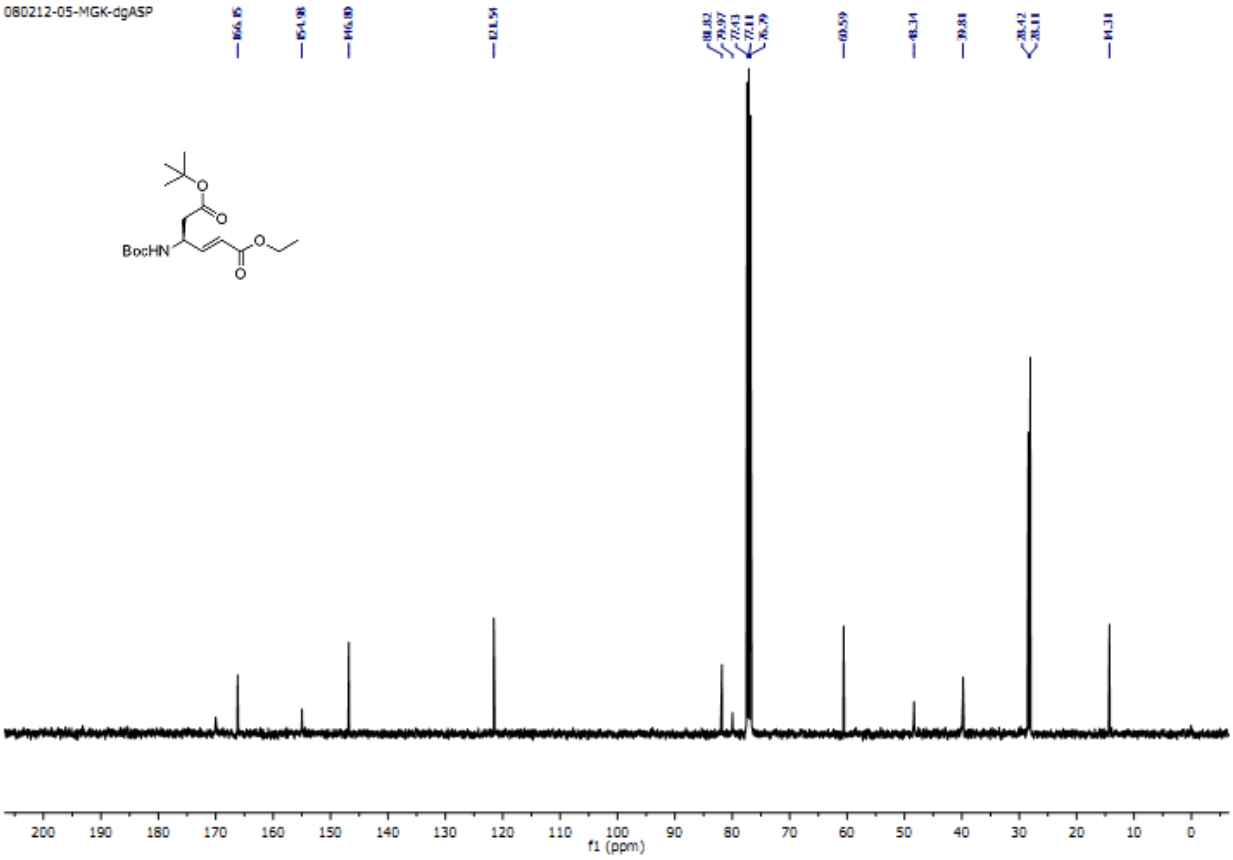


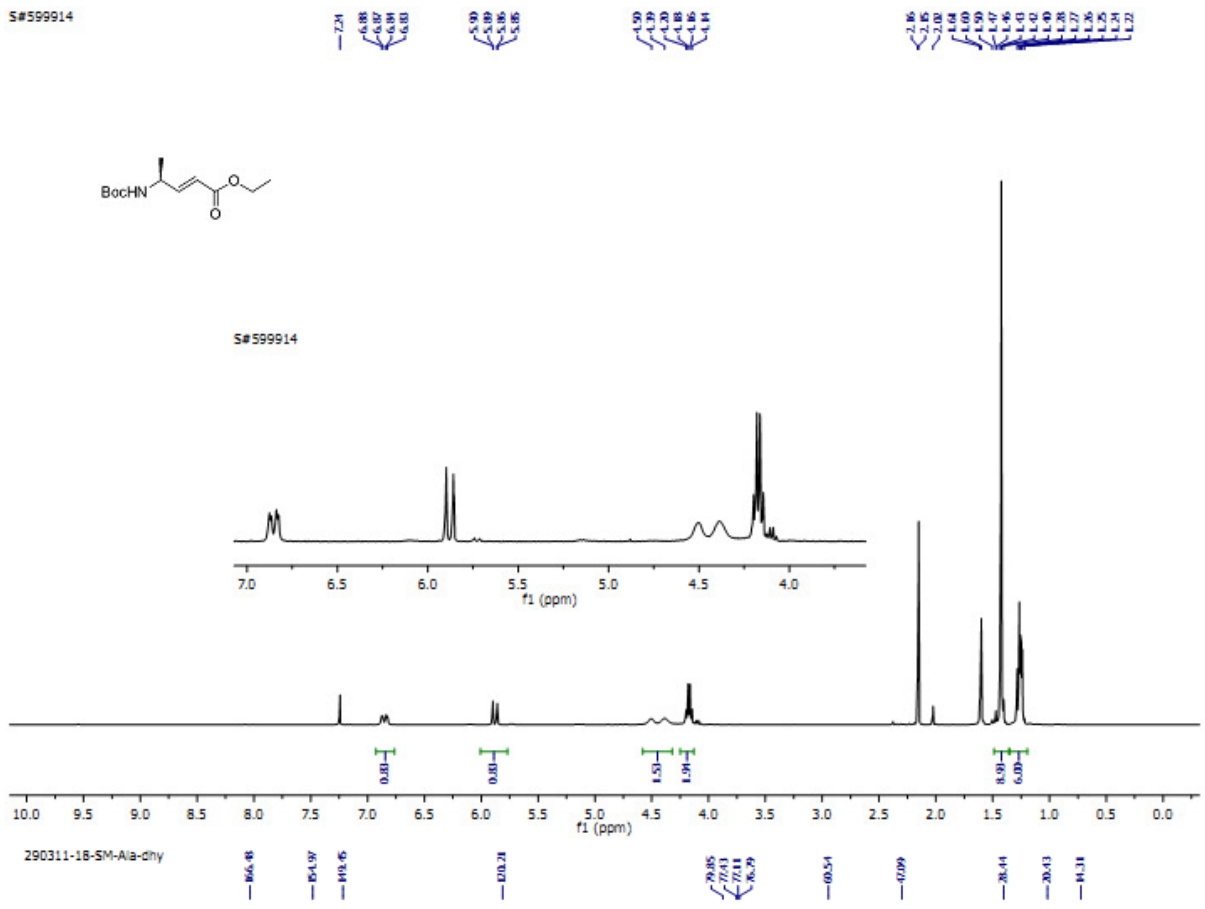








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BocHN
S#599914
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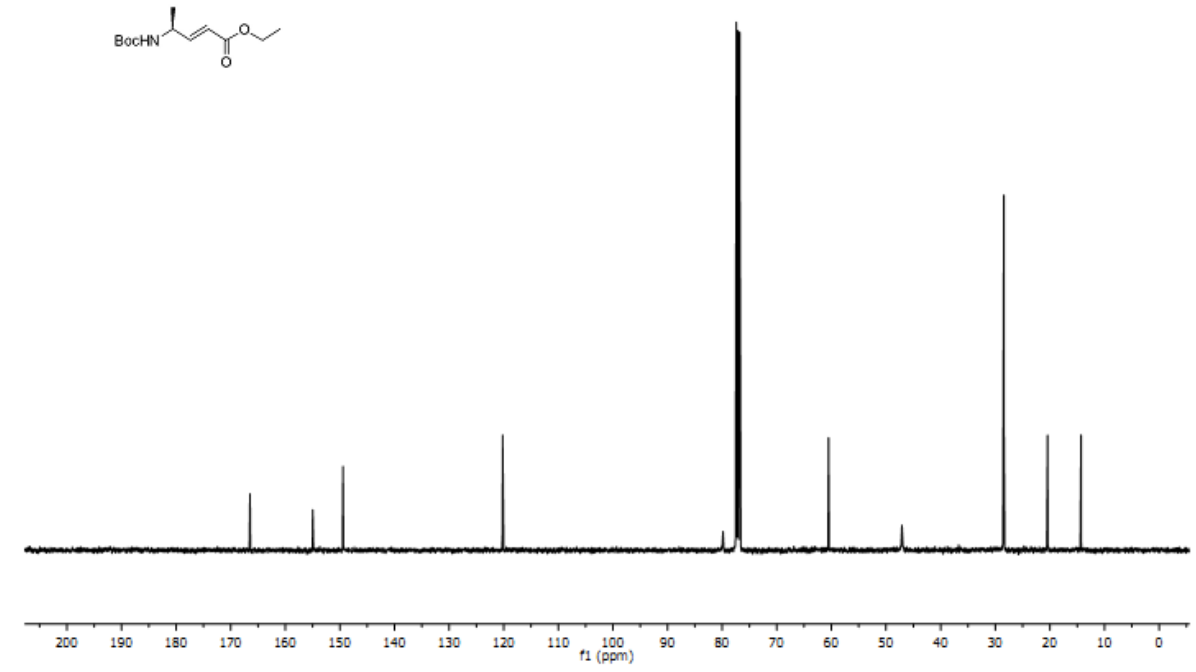
f1 (ppm)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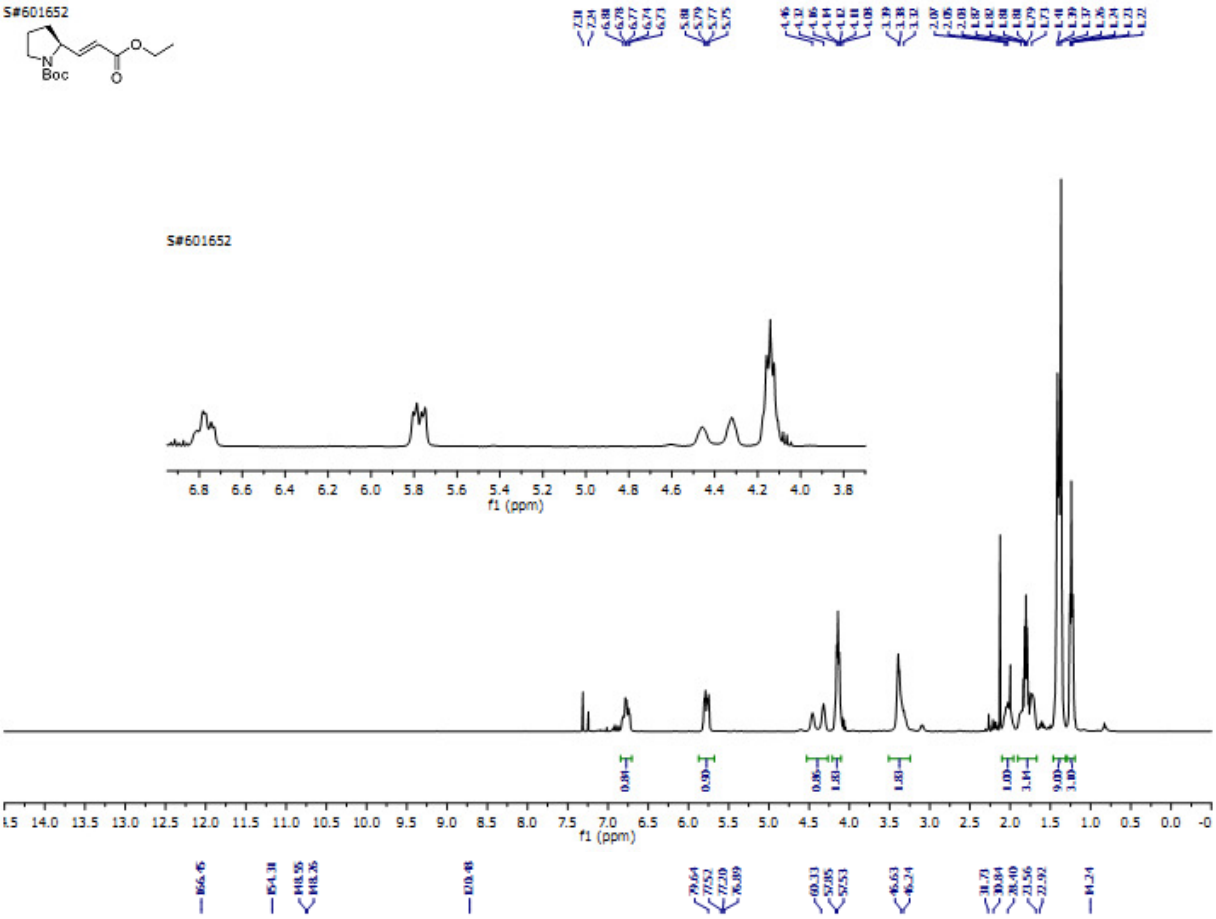

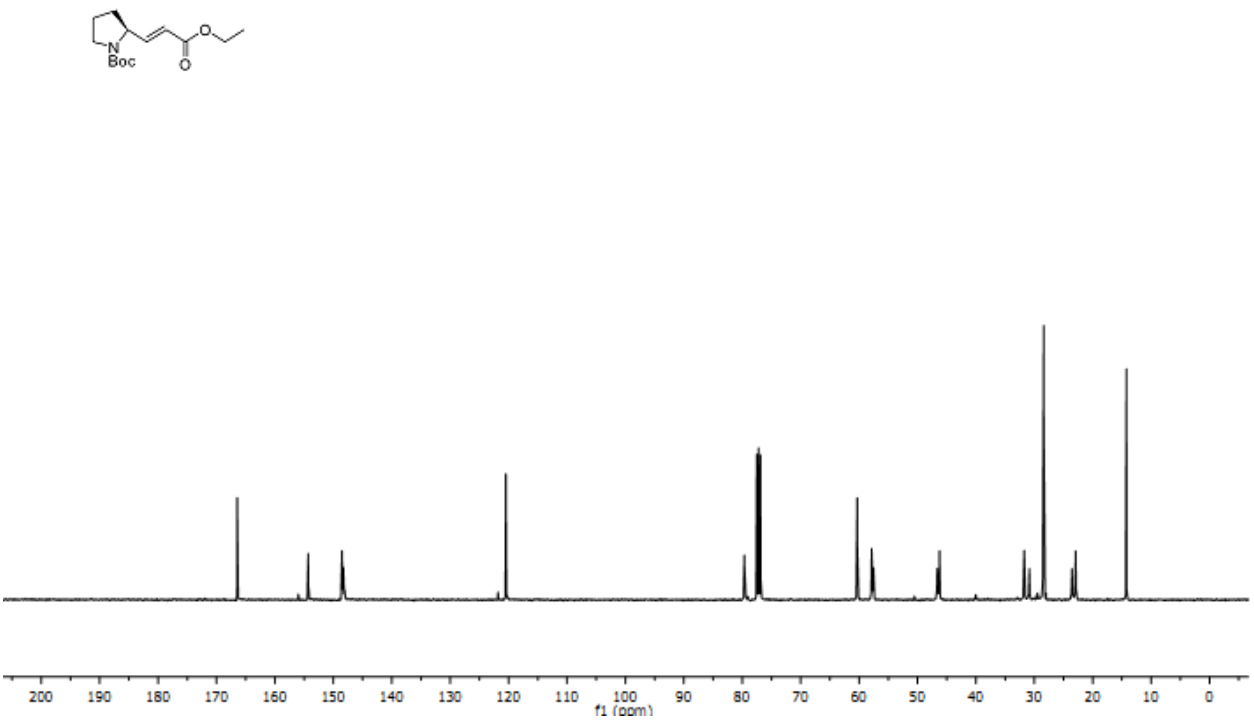

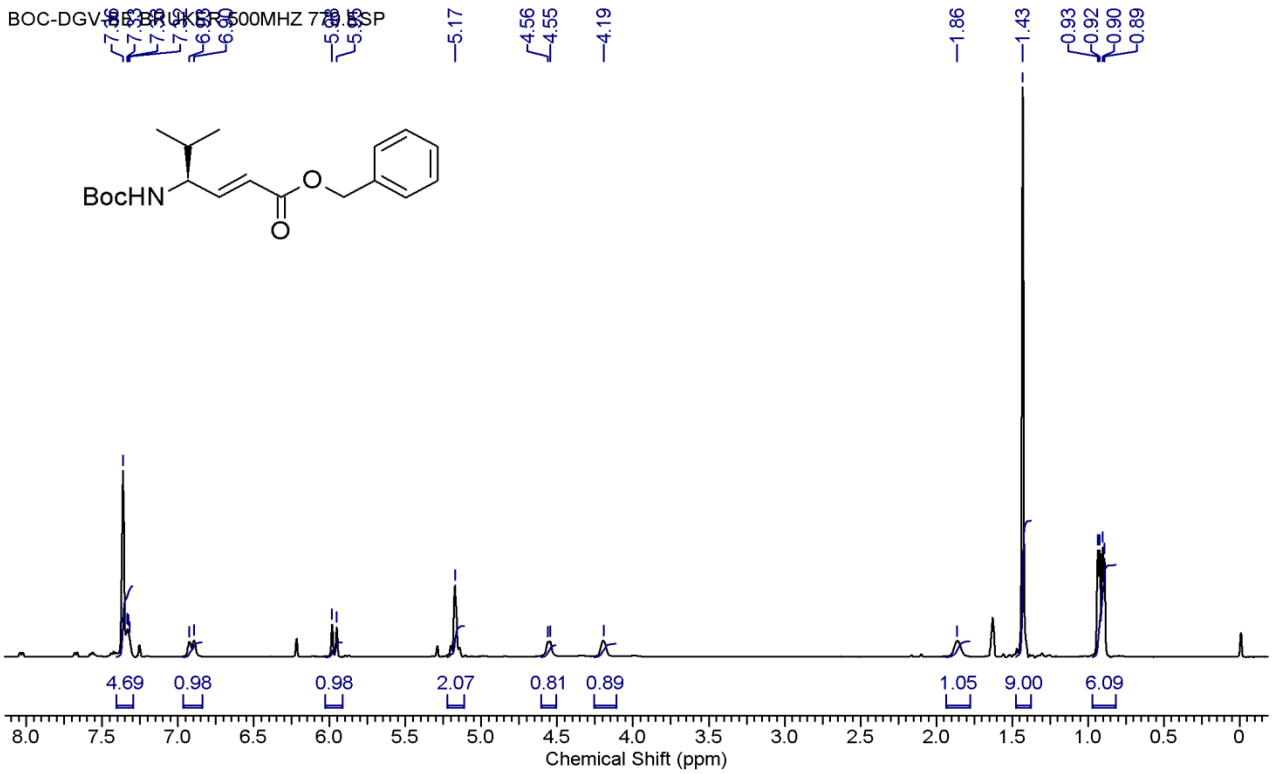

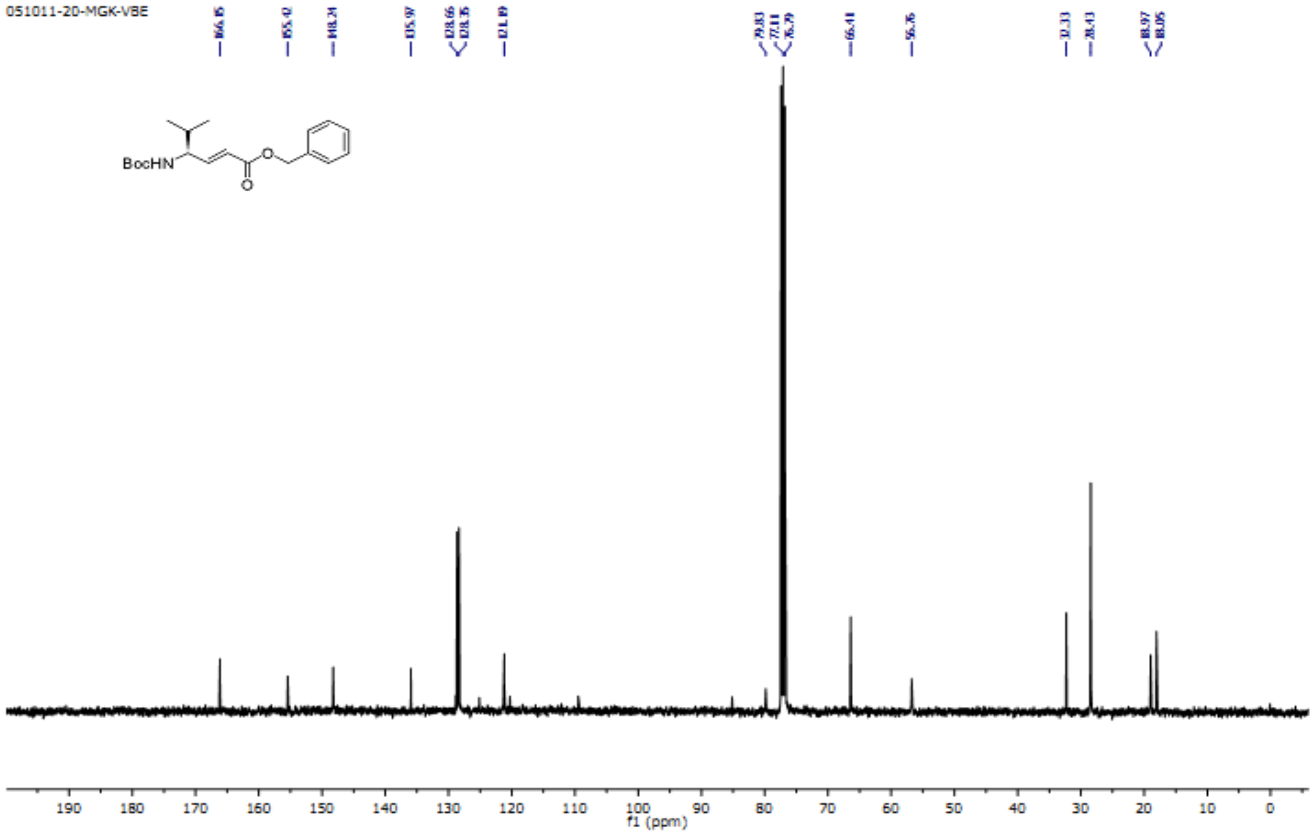

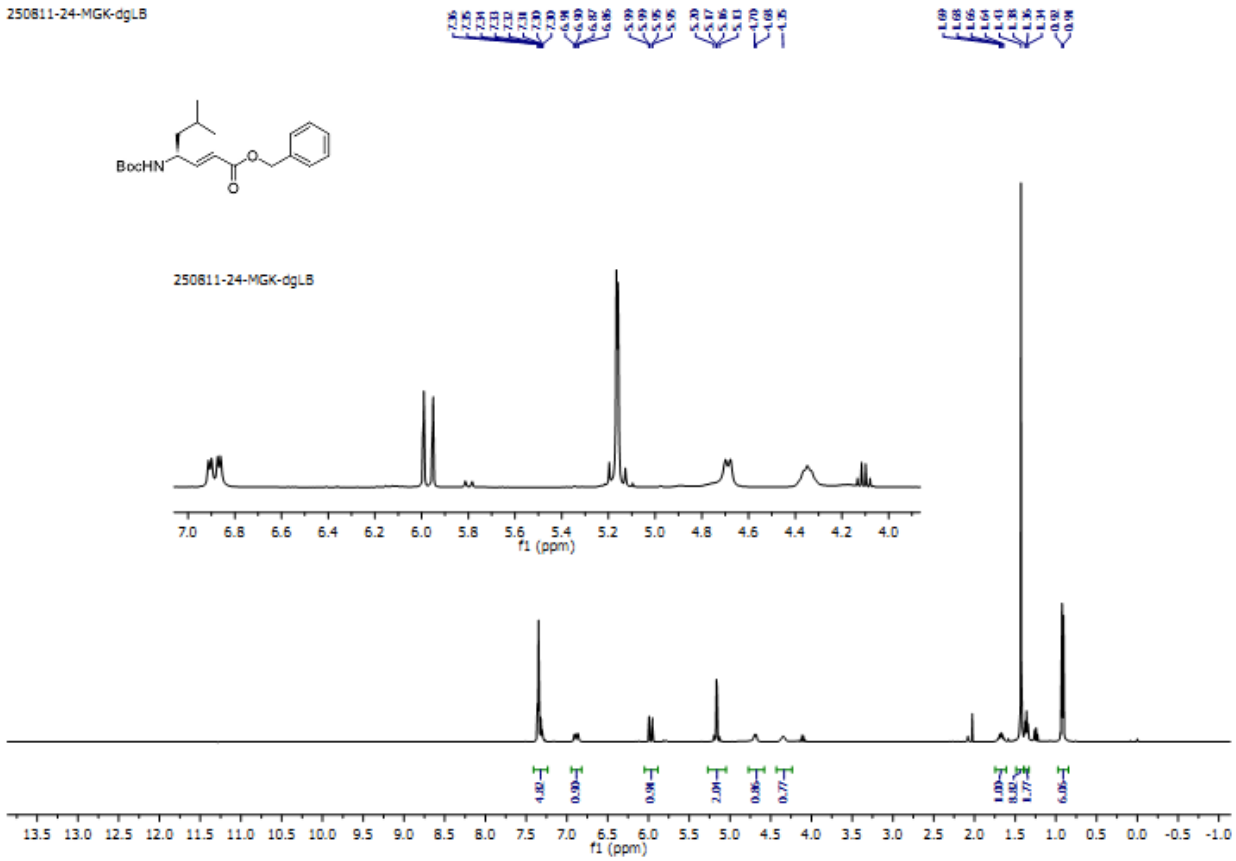
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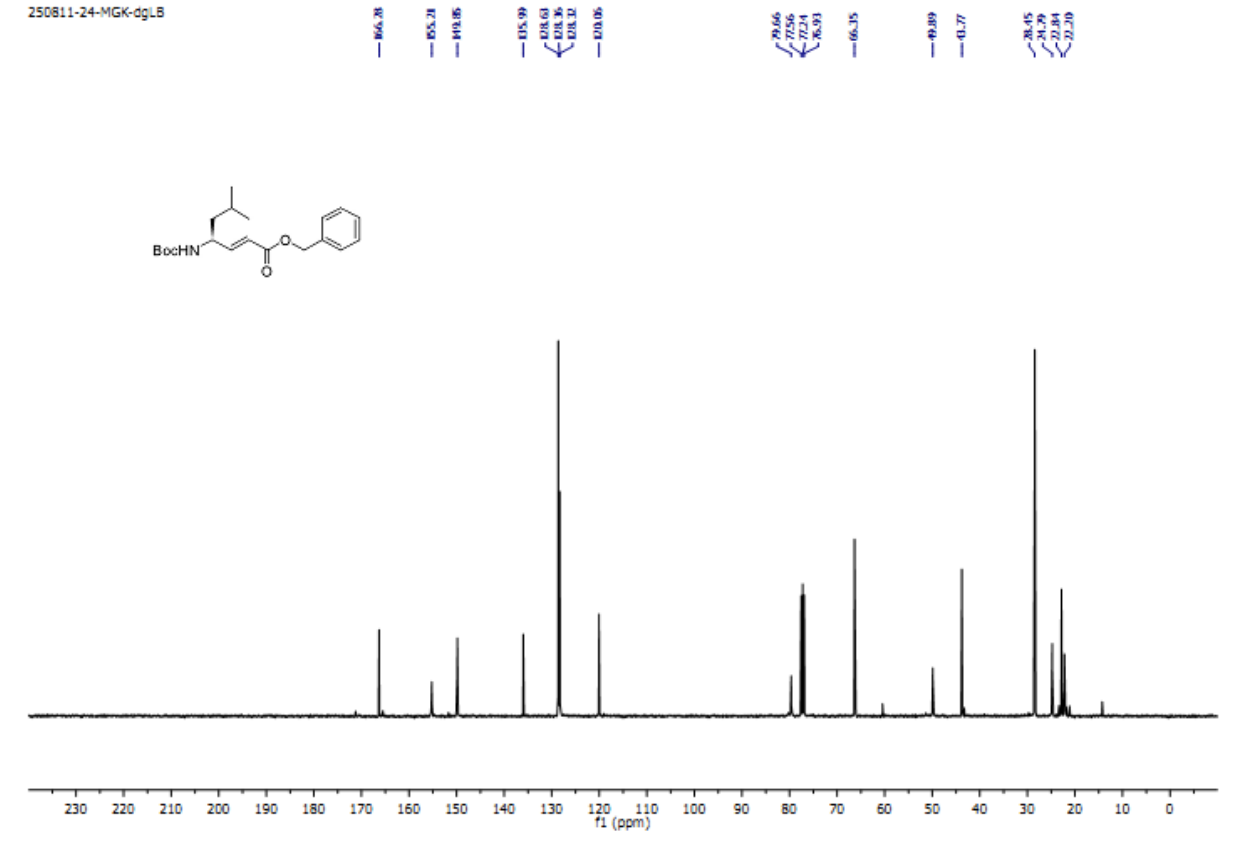
O
250811-24-MGK-dgLB
f1 (ppm)
f1 (ppm)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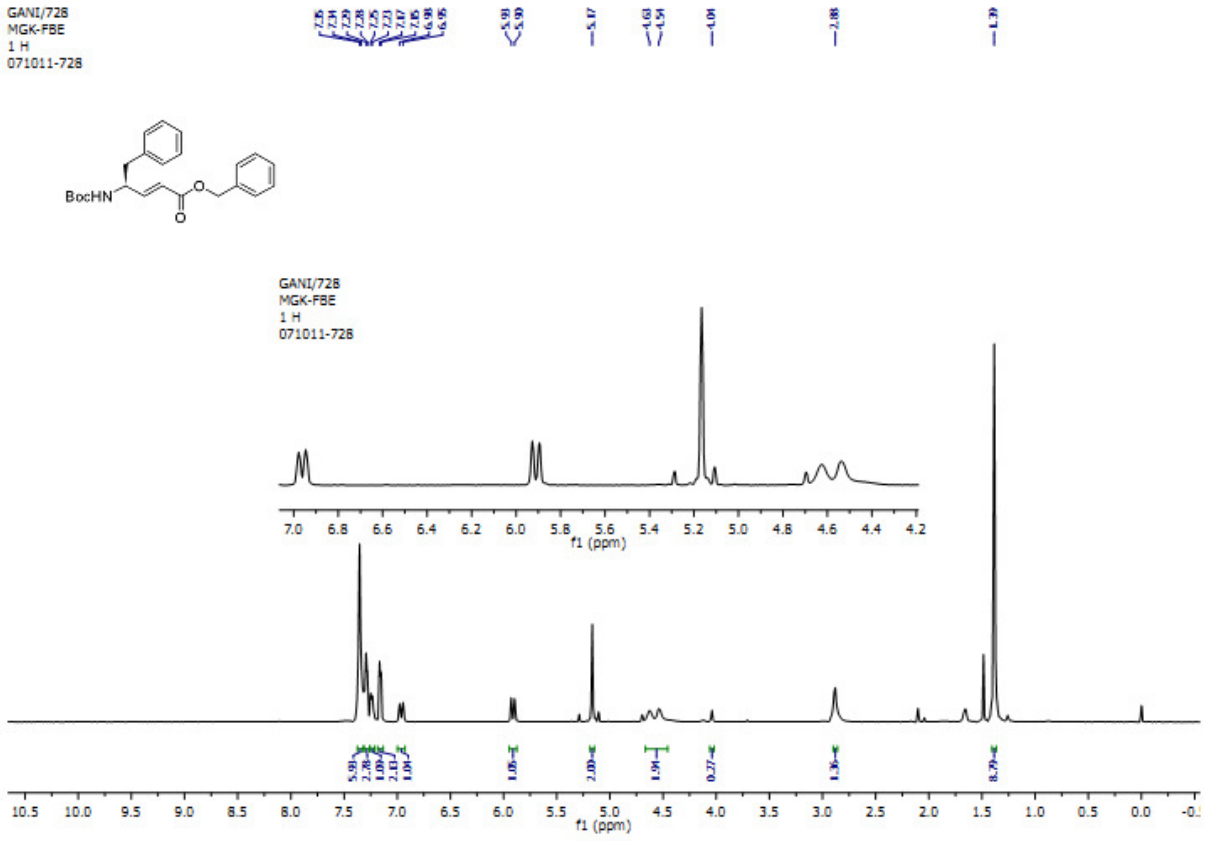
BocHN
O
O
f1 (ppm)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MGK-FBE
1 H
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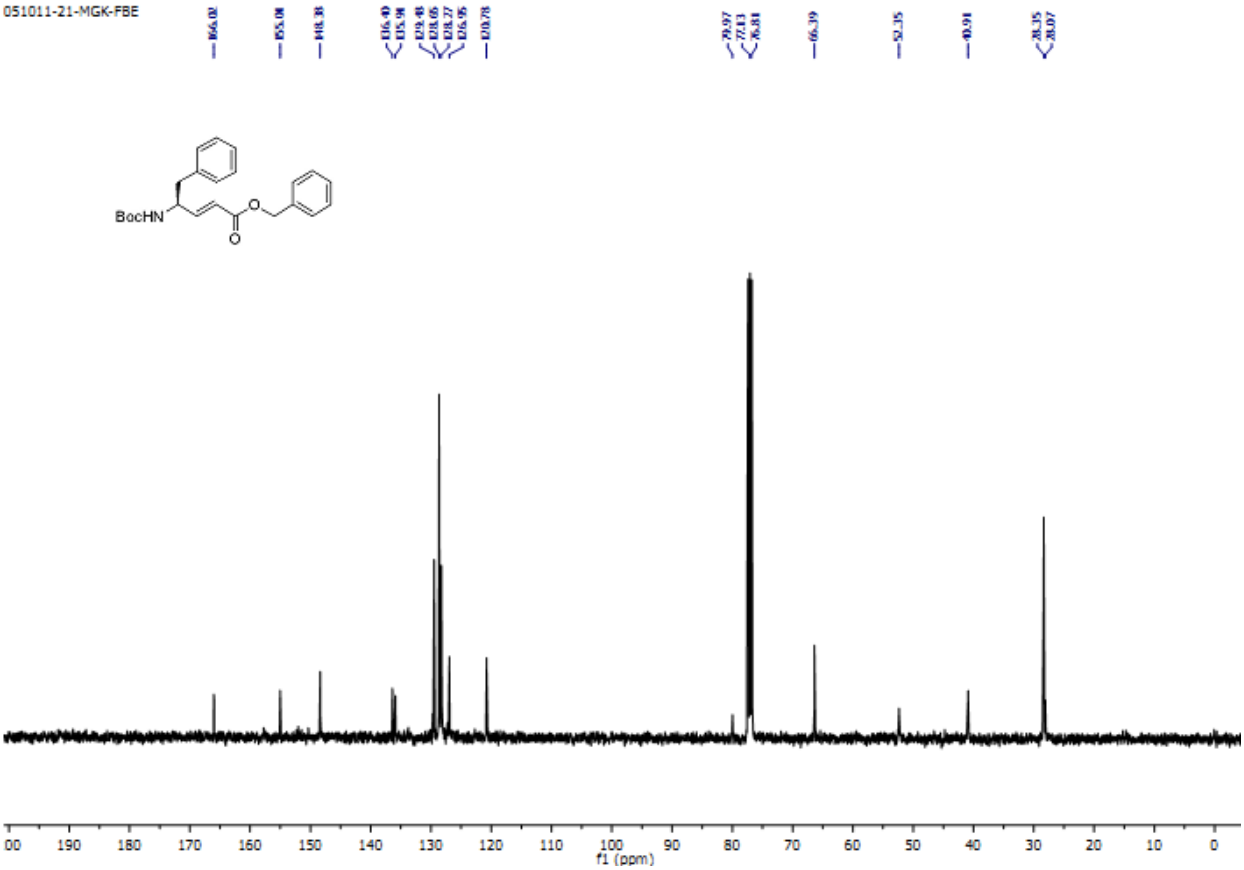
f1 (ppm)
f1 (ppm)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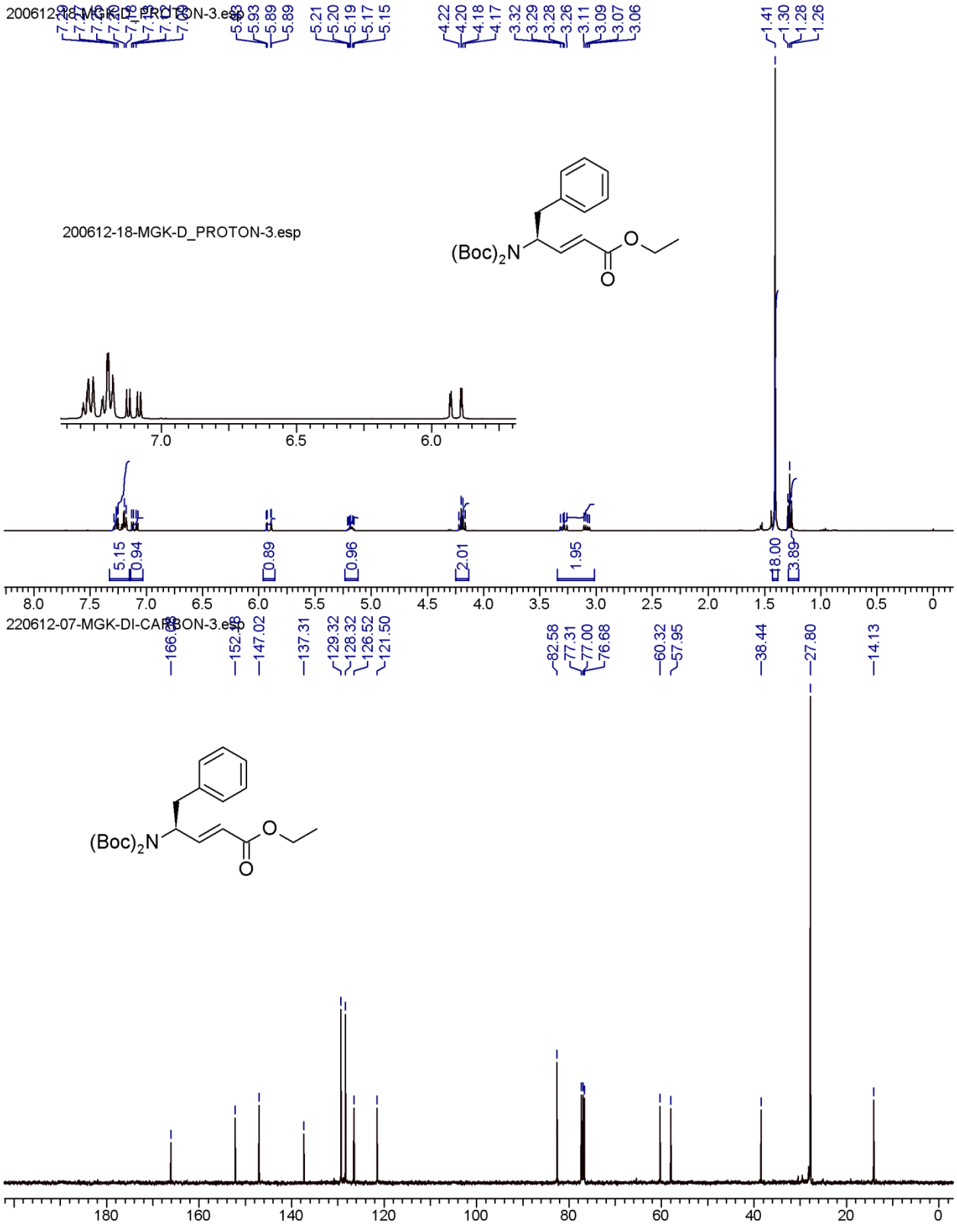
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0.89
0.96
2.01
1.95
18.00
3.89
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166.88
152.48
147.02
137.31
129.32
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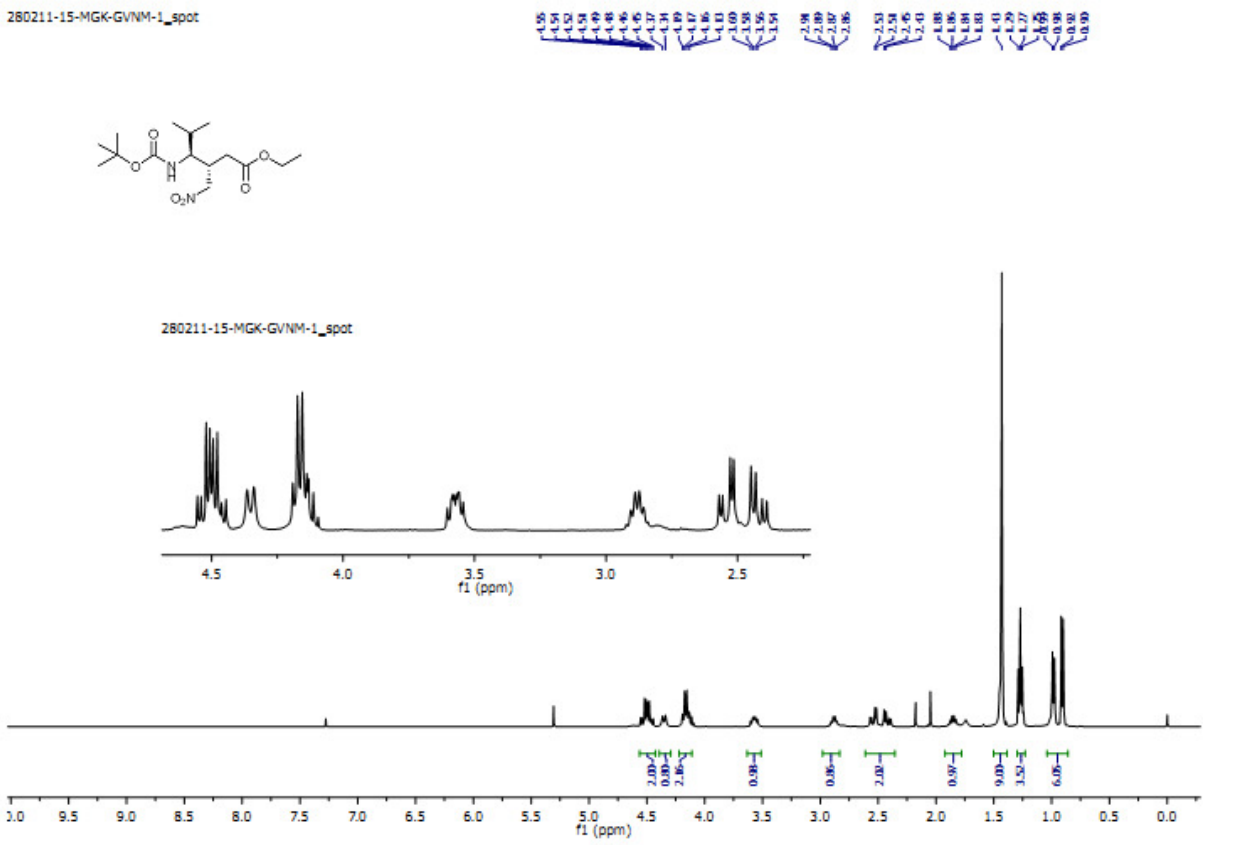
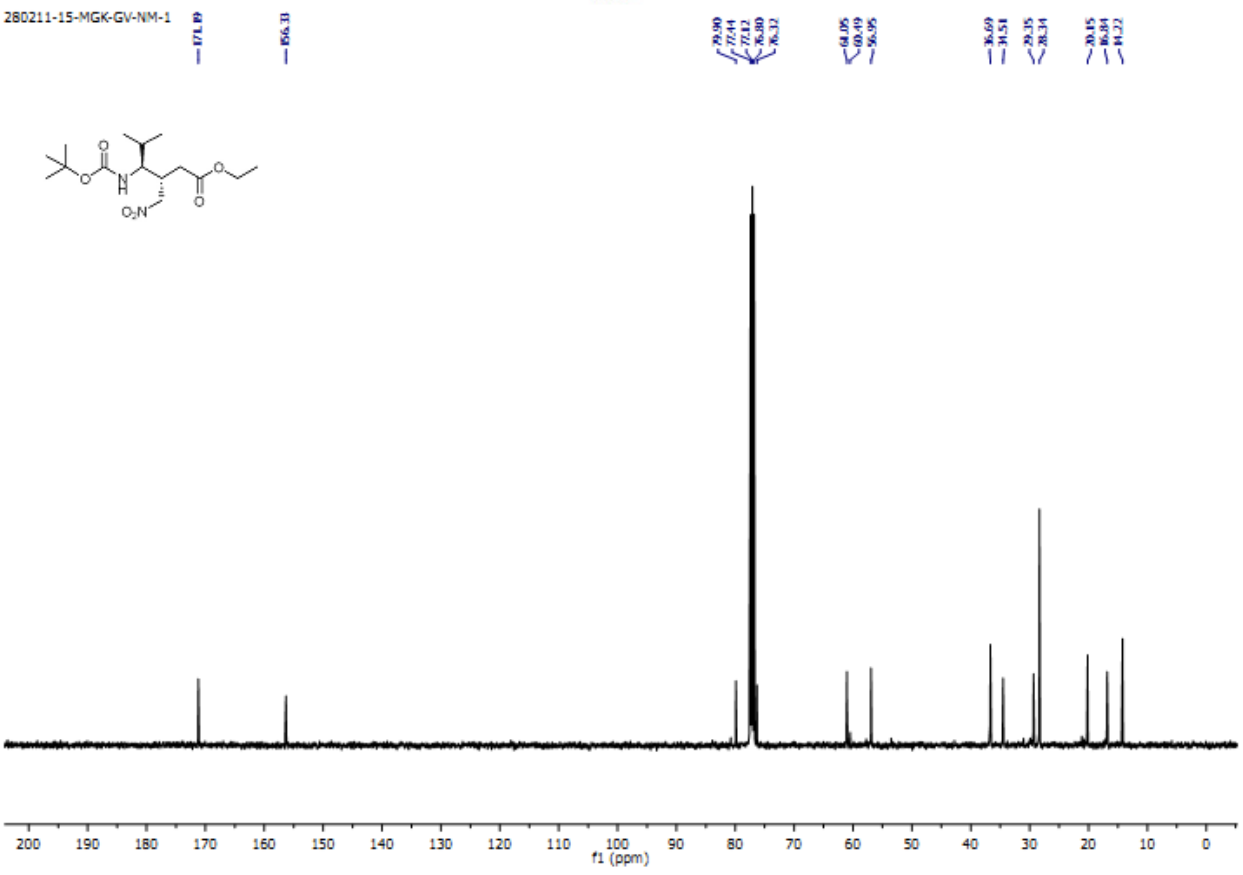
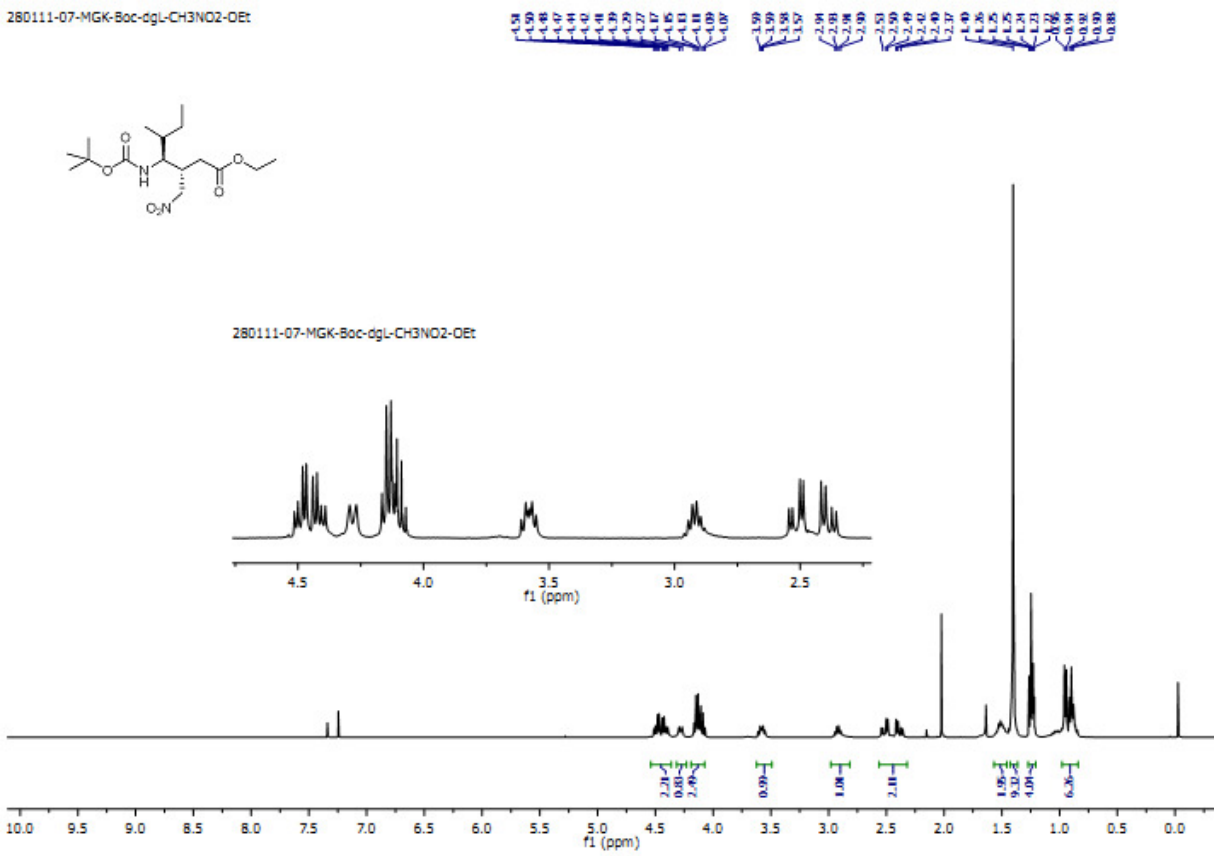
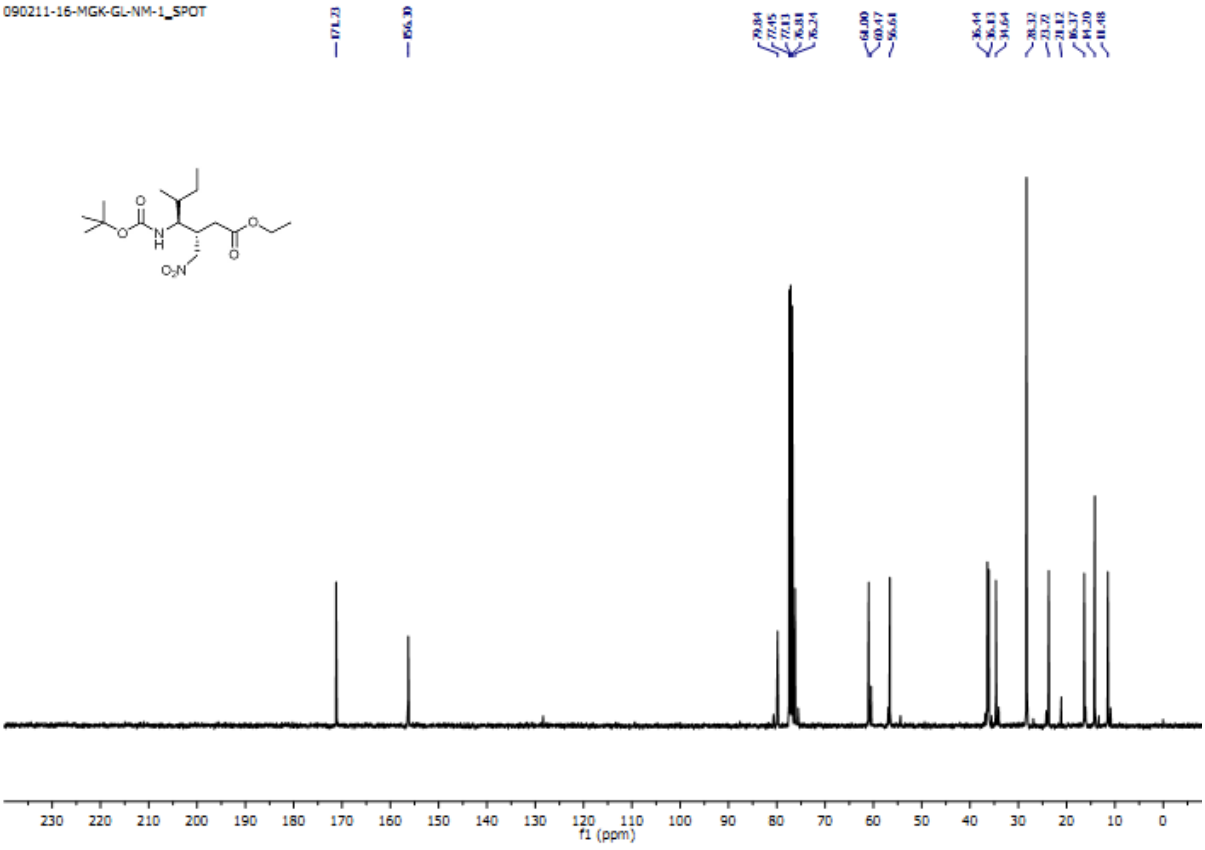
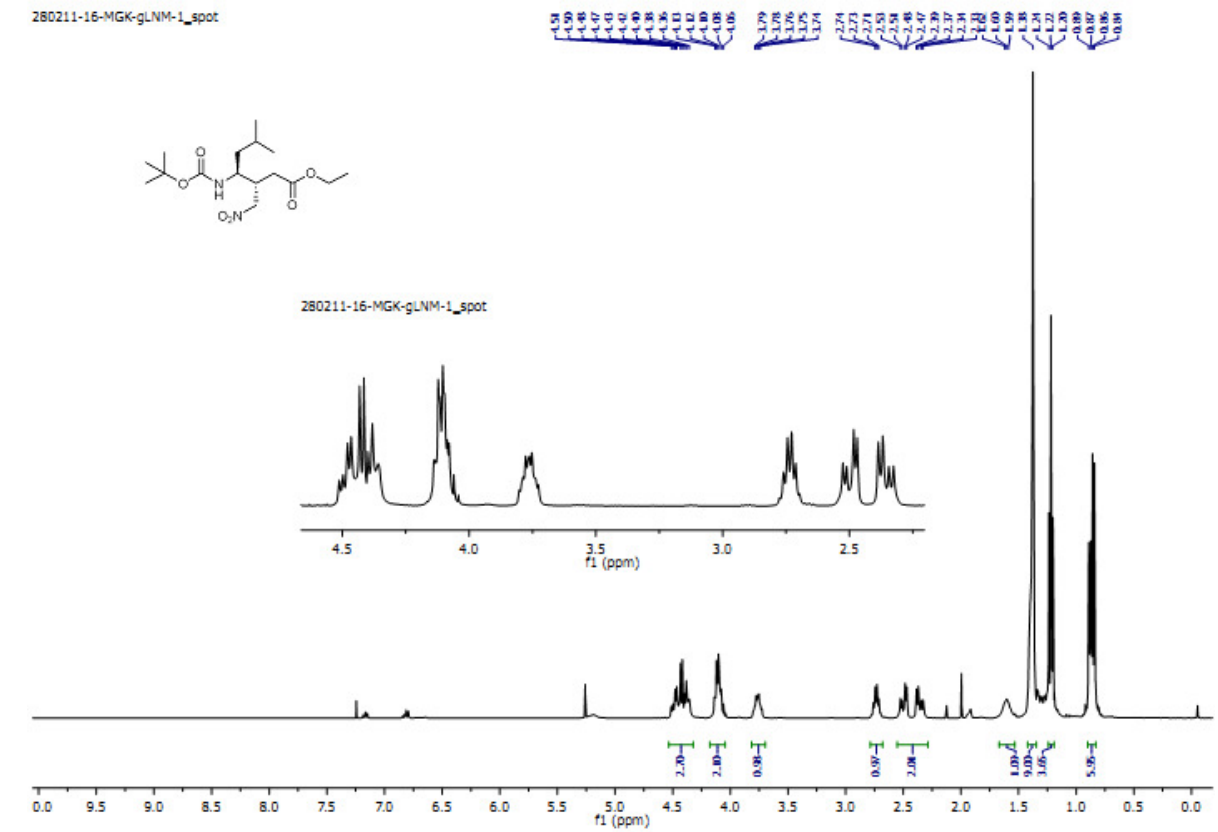
76.68
60.32
57.95
38.44
27.80
14.13



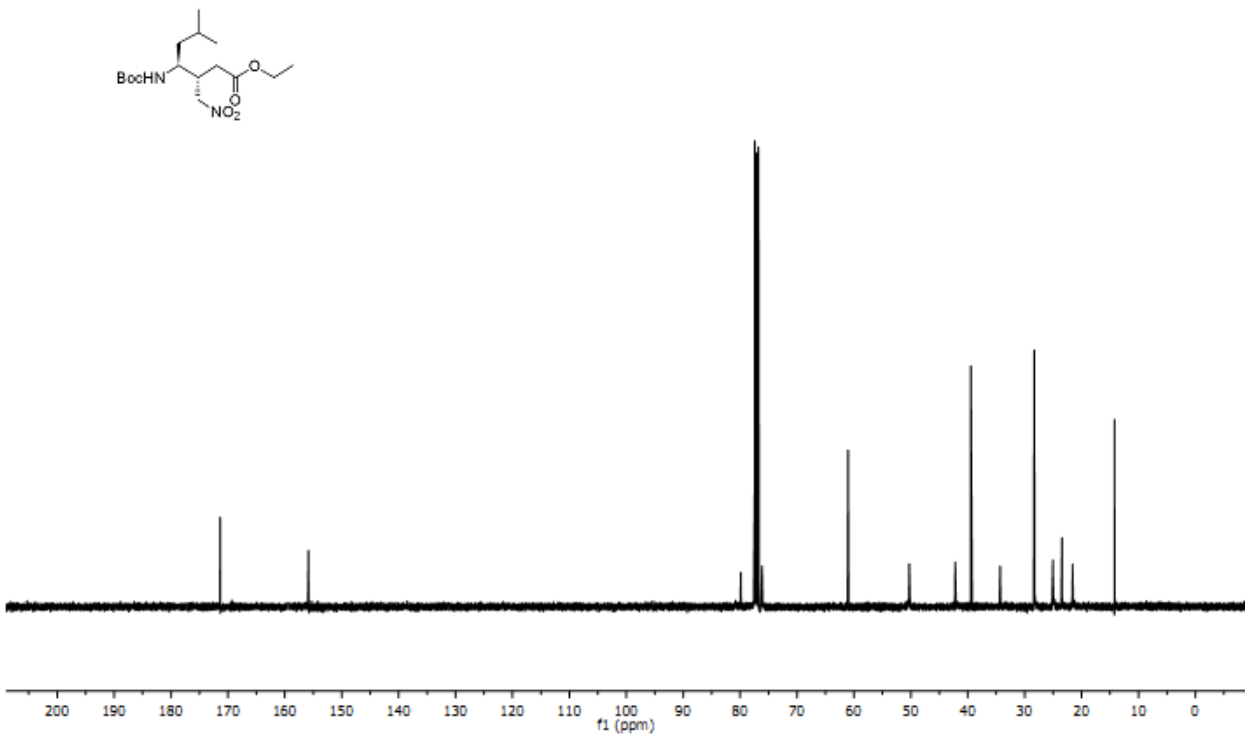


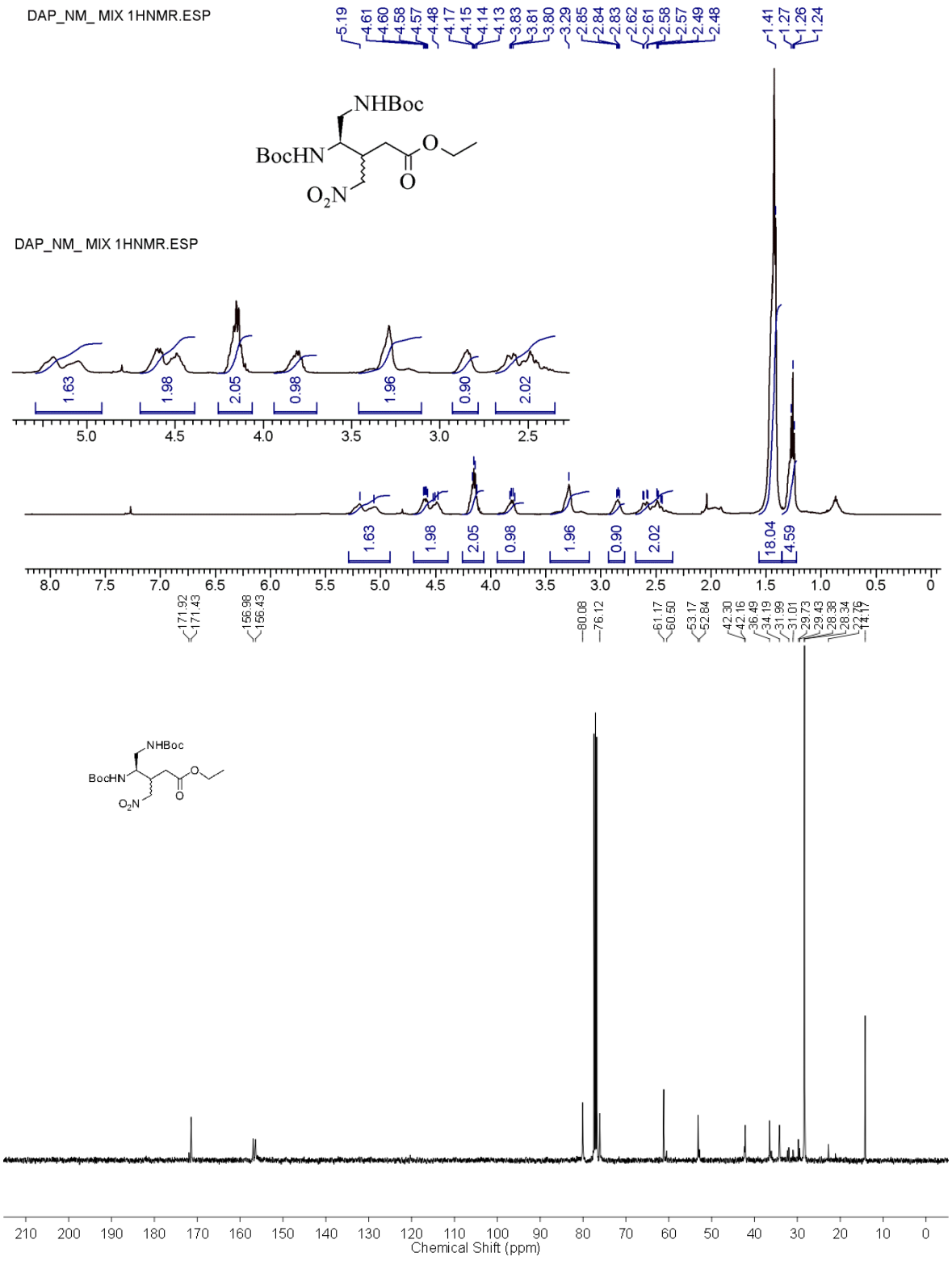


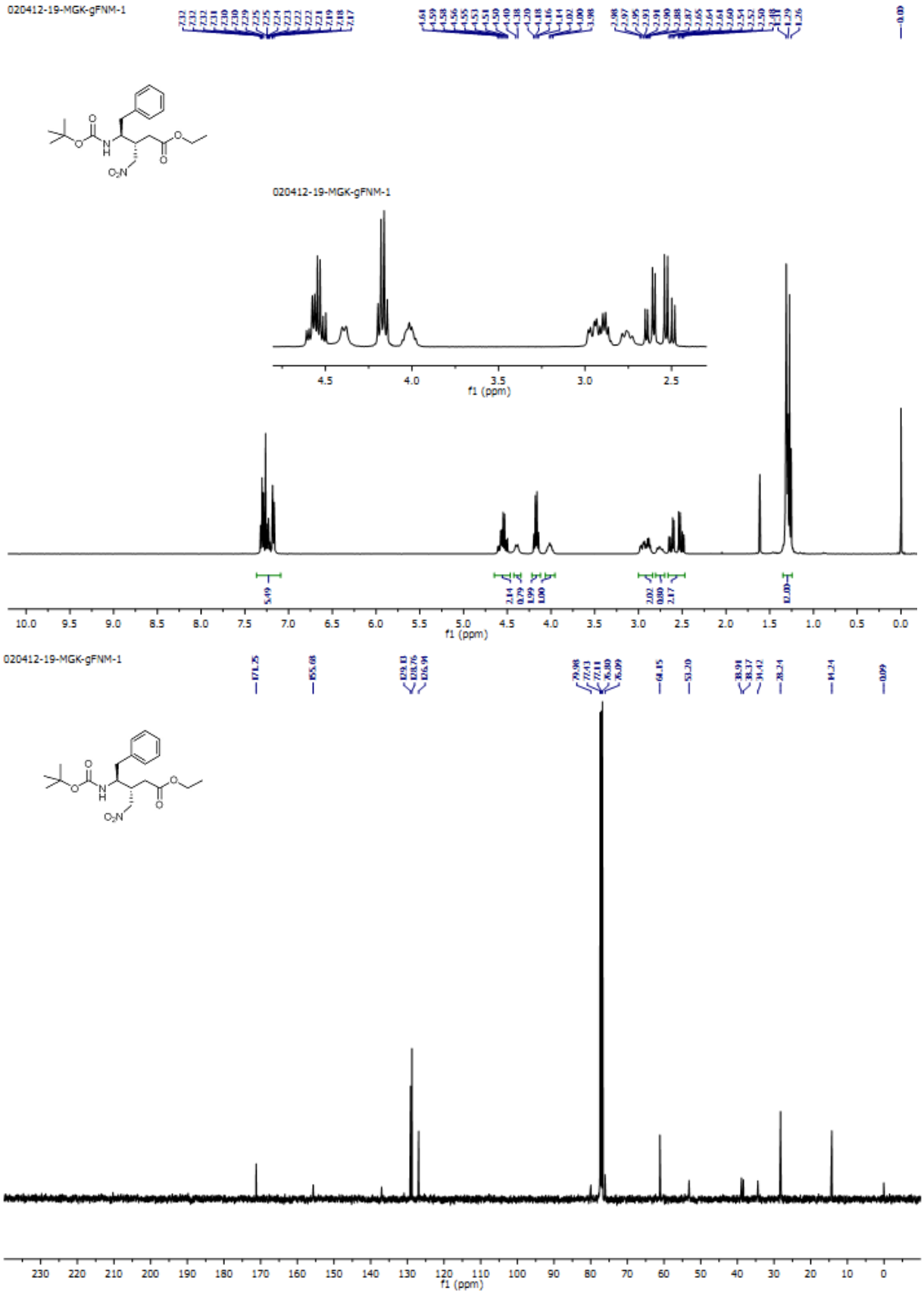


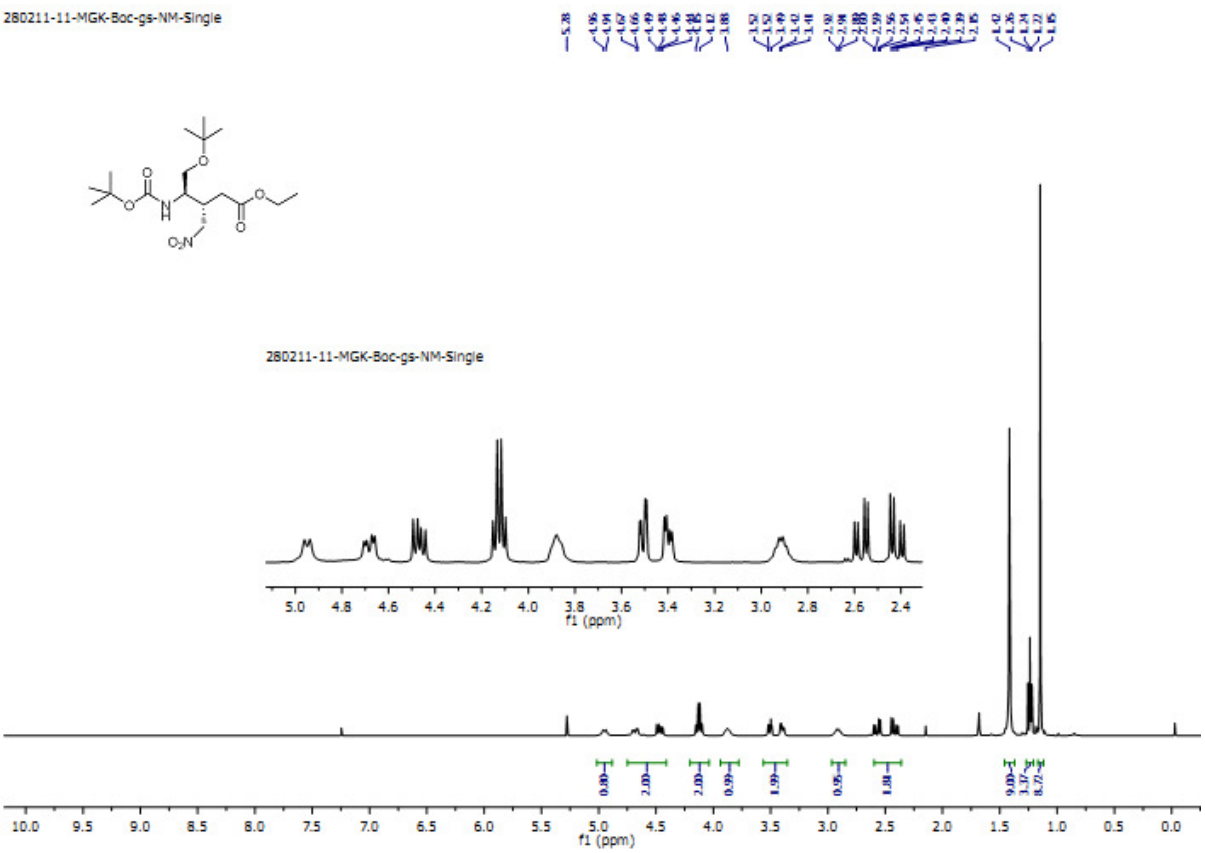

280211-16-MGK-gLNM-1_spot
280211-16-MGK-gLNM-1_spot
f1 (ppm)

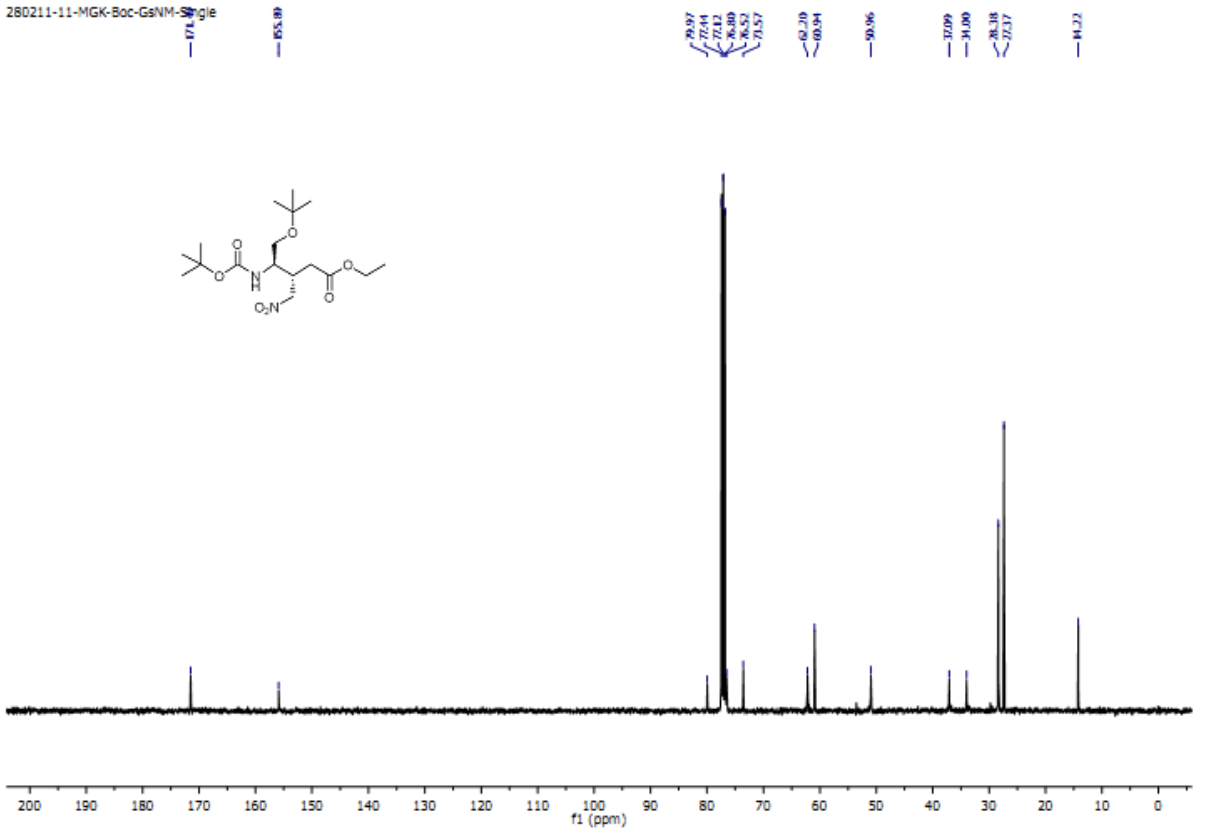
S#533876

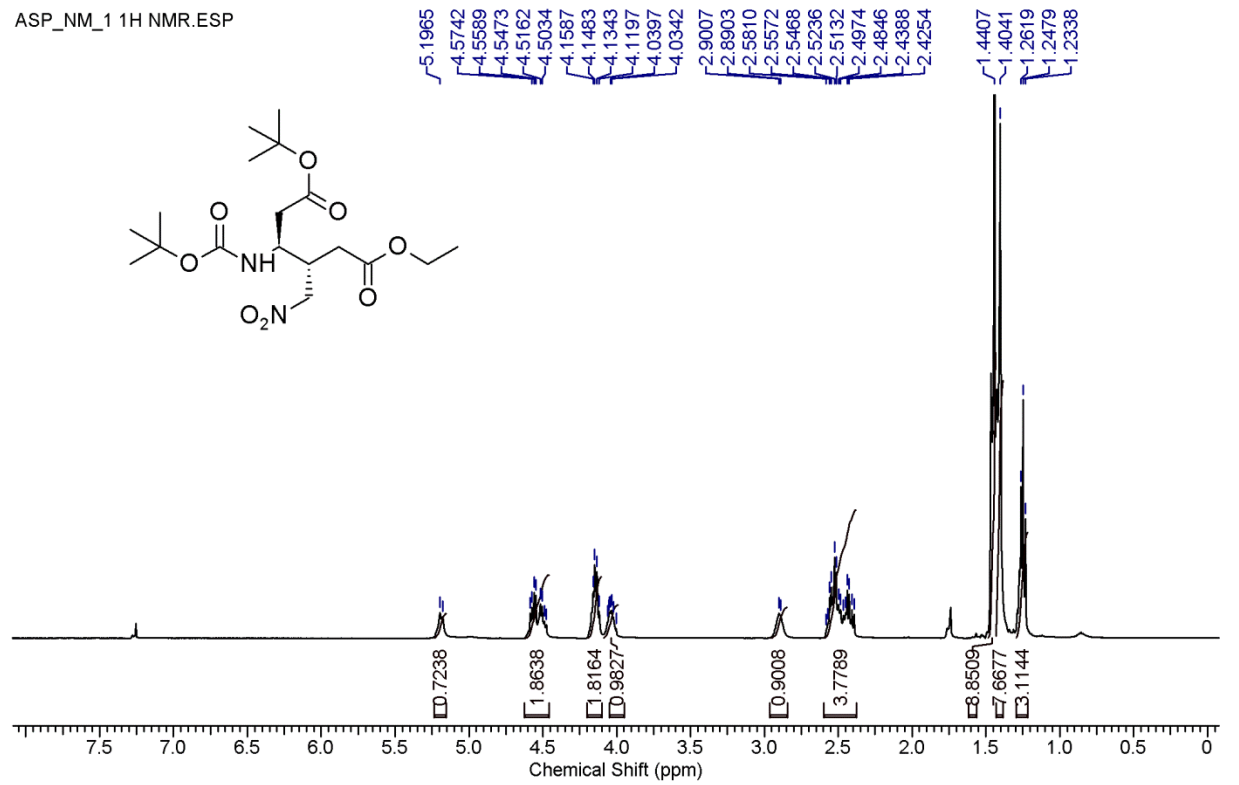

BocHN
f1 (ppm)

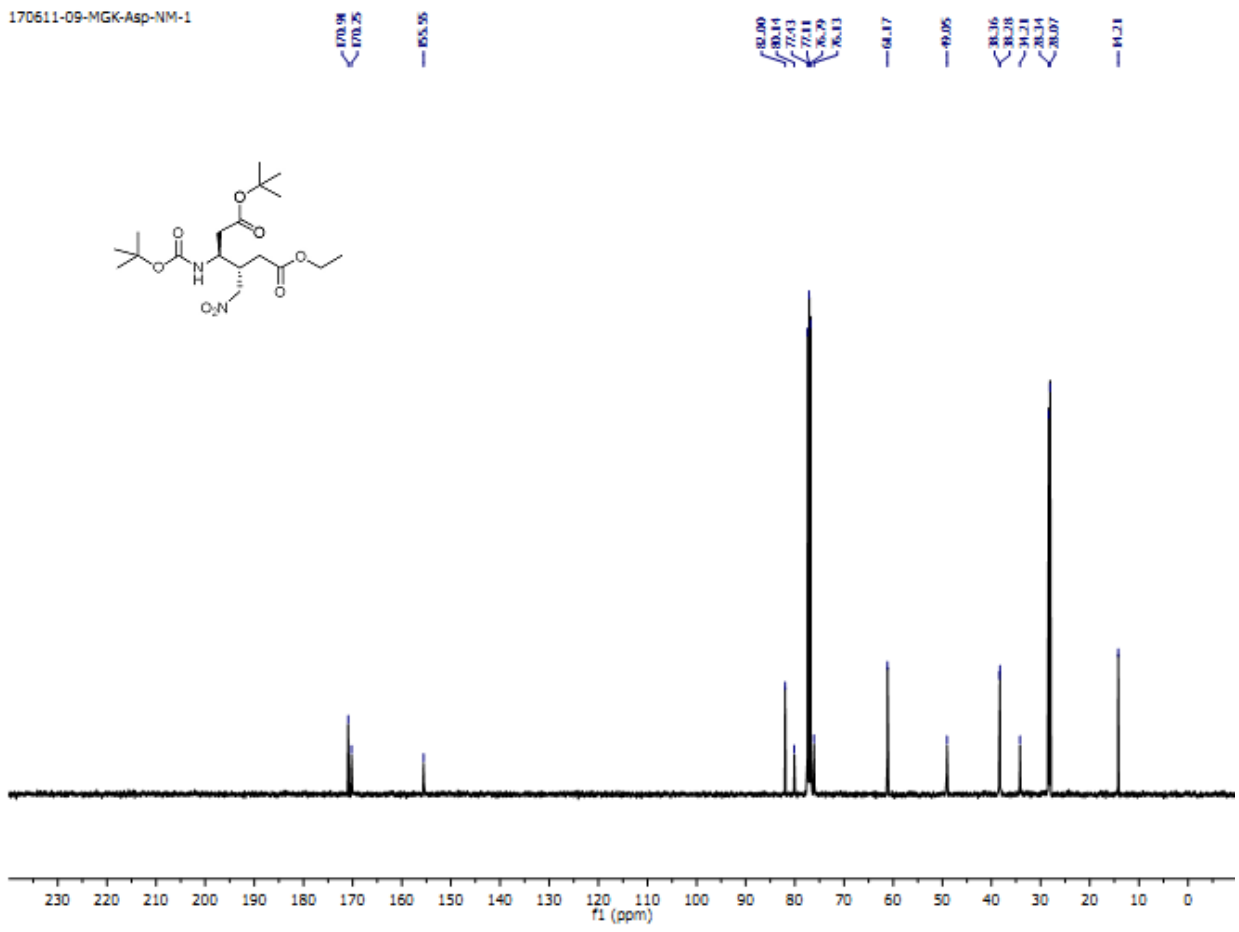


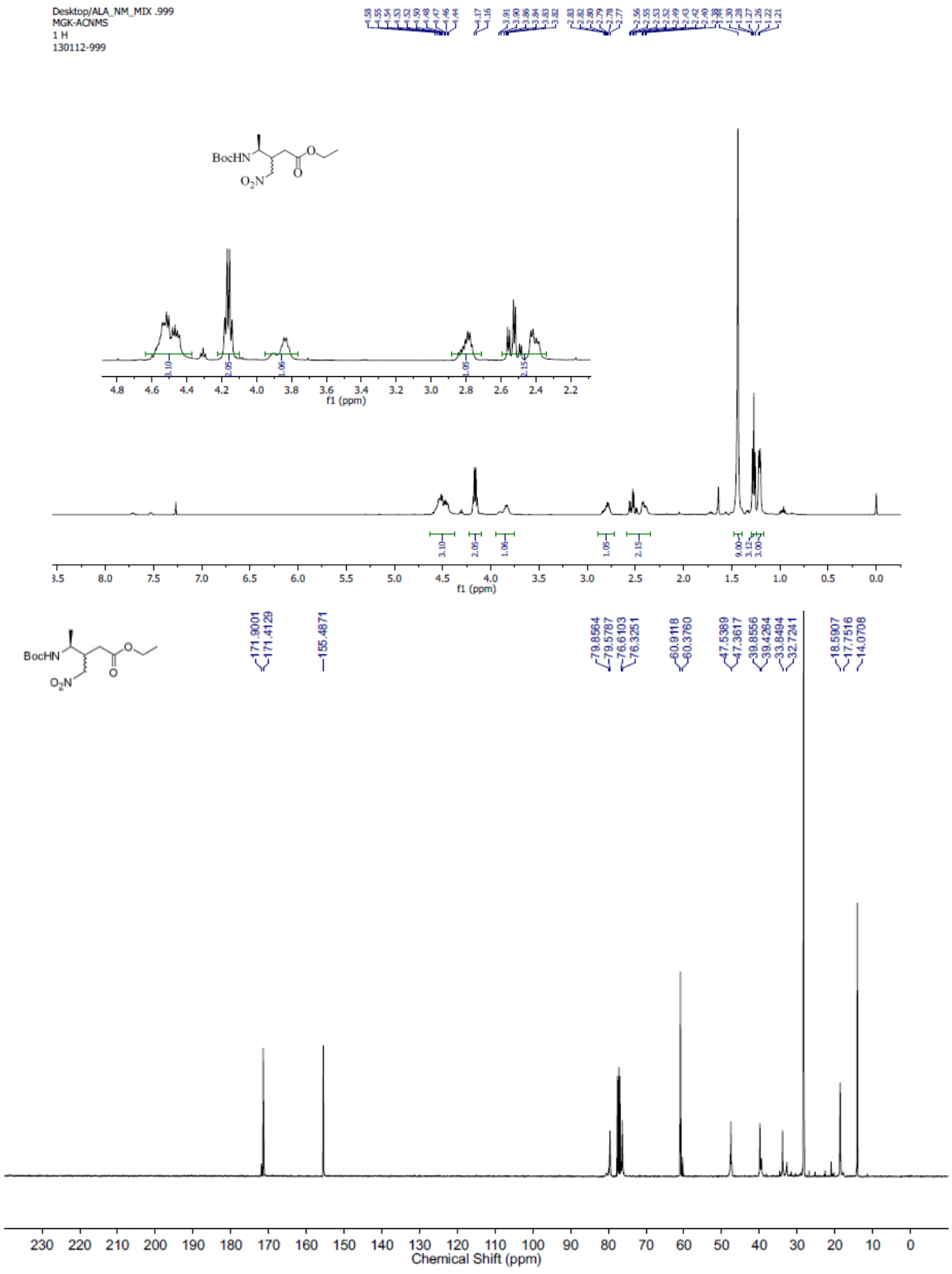

020412-19-MGK-gFNM-1
020412-19-MGK-gFNM-1
f1 (ppm)
020412-19-MGK-gFNM-1
f1 (ppm)

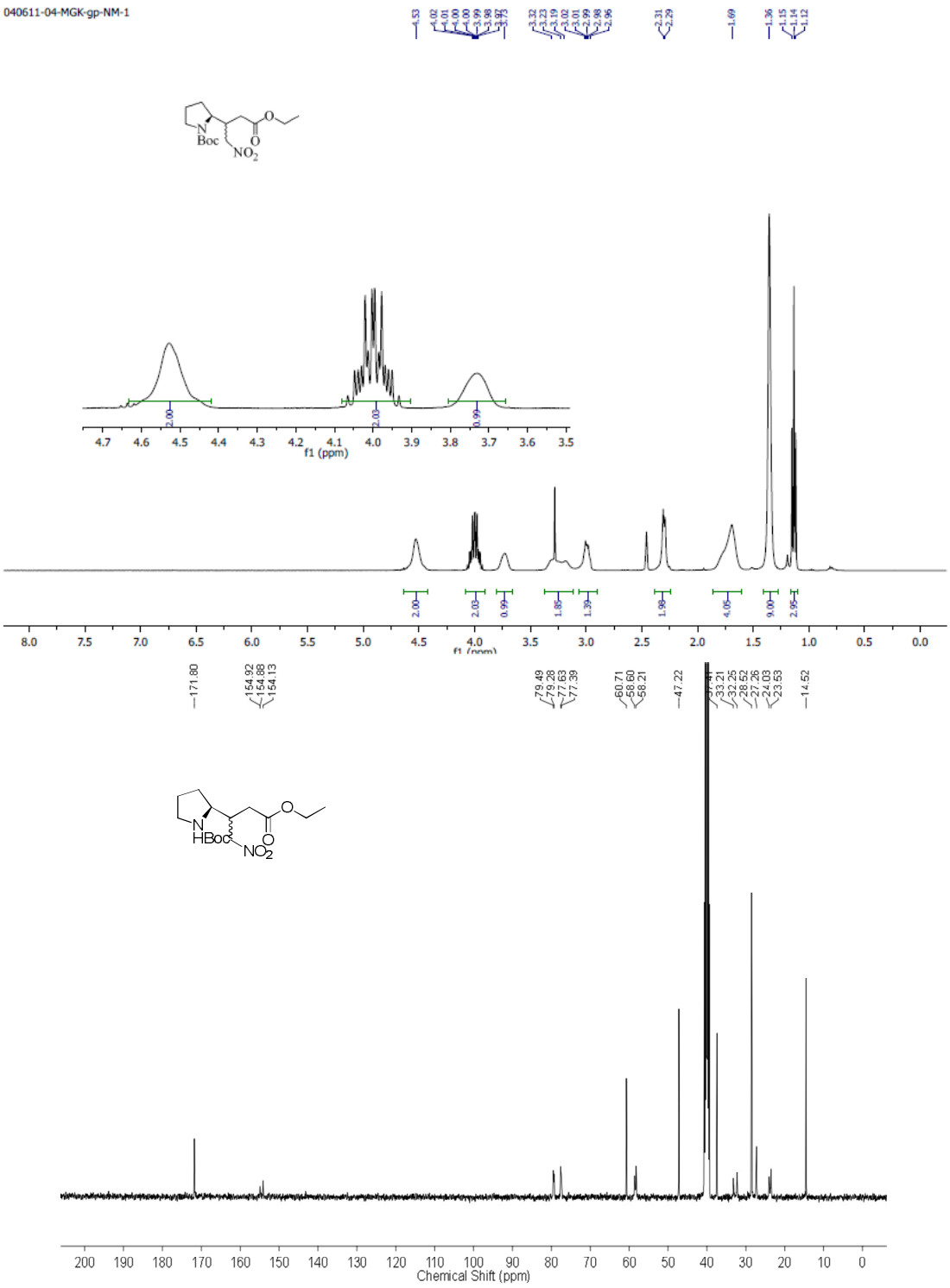

280211-11-MGK-Boc-gs-NM-Single
280211-11-MGK-Boc-gs-NM-Single
f1 (ppm)

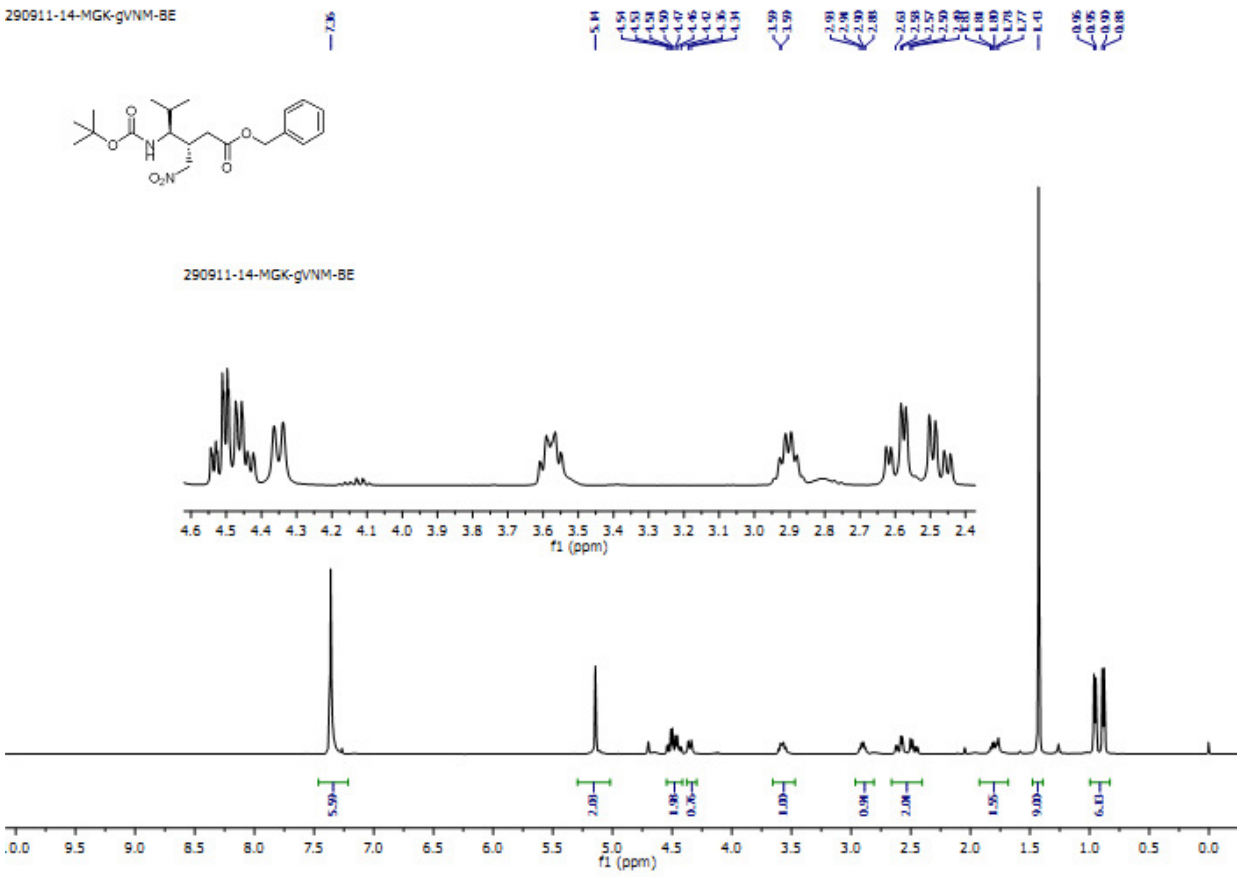

280211-11-MGK-Boc-GsNM-Single
f1 (ppm)

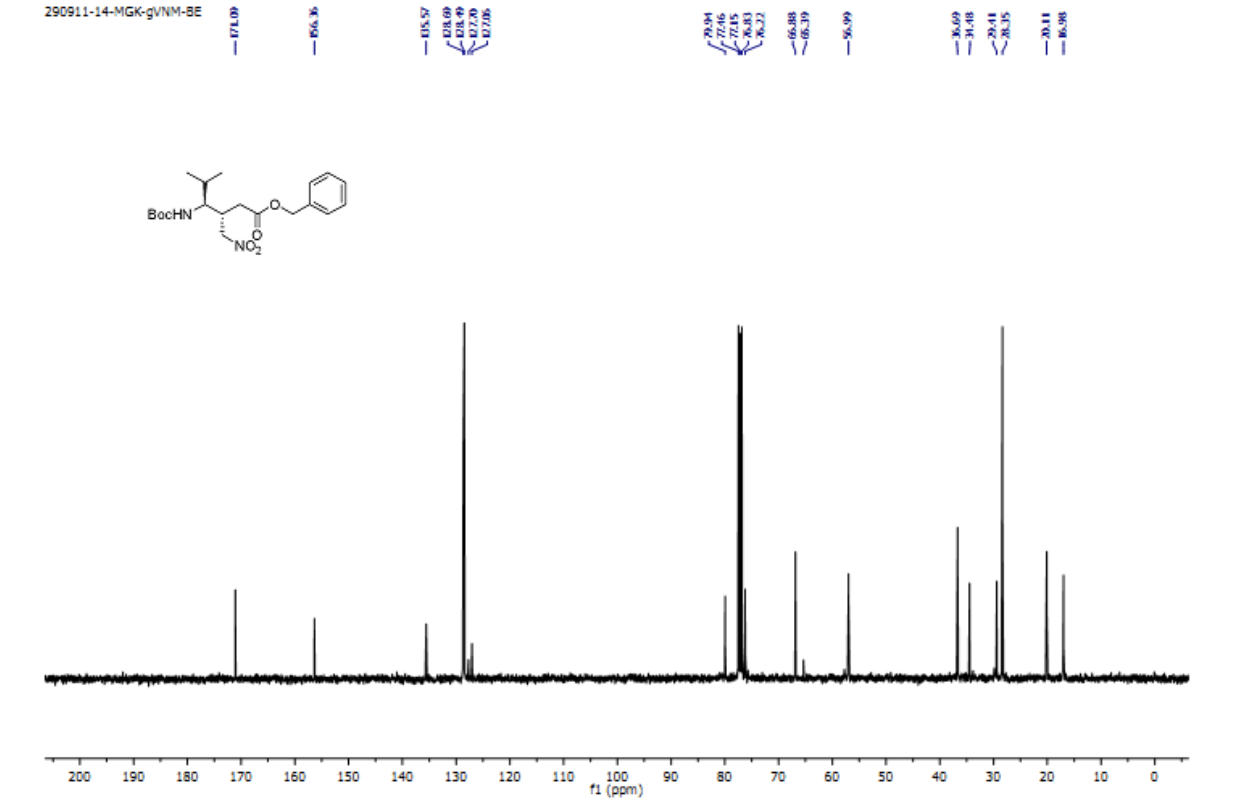

ASP_NM_1 1H NMR.ESP
5.1965
4.5742
4.5589
4.5473
4.5162
4.5034
4.1587
4.1483
4.1343
4.1197
4.0397
4.0342
2.9007
2.8903
2.5810
2.5572
2.5468
2.5236
2.5132
2.4974
2.4846
2.4388
2.4254
1.4407
1.4041
1.2619
1.2479
1.2338
NH
O2N
1.7238
1.8638
1.8164
1.9827
0.9008
3.7789
8.8509
7.6677
3.1144
Chemical Shift (ppm)

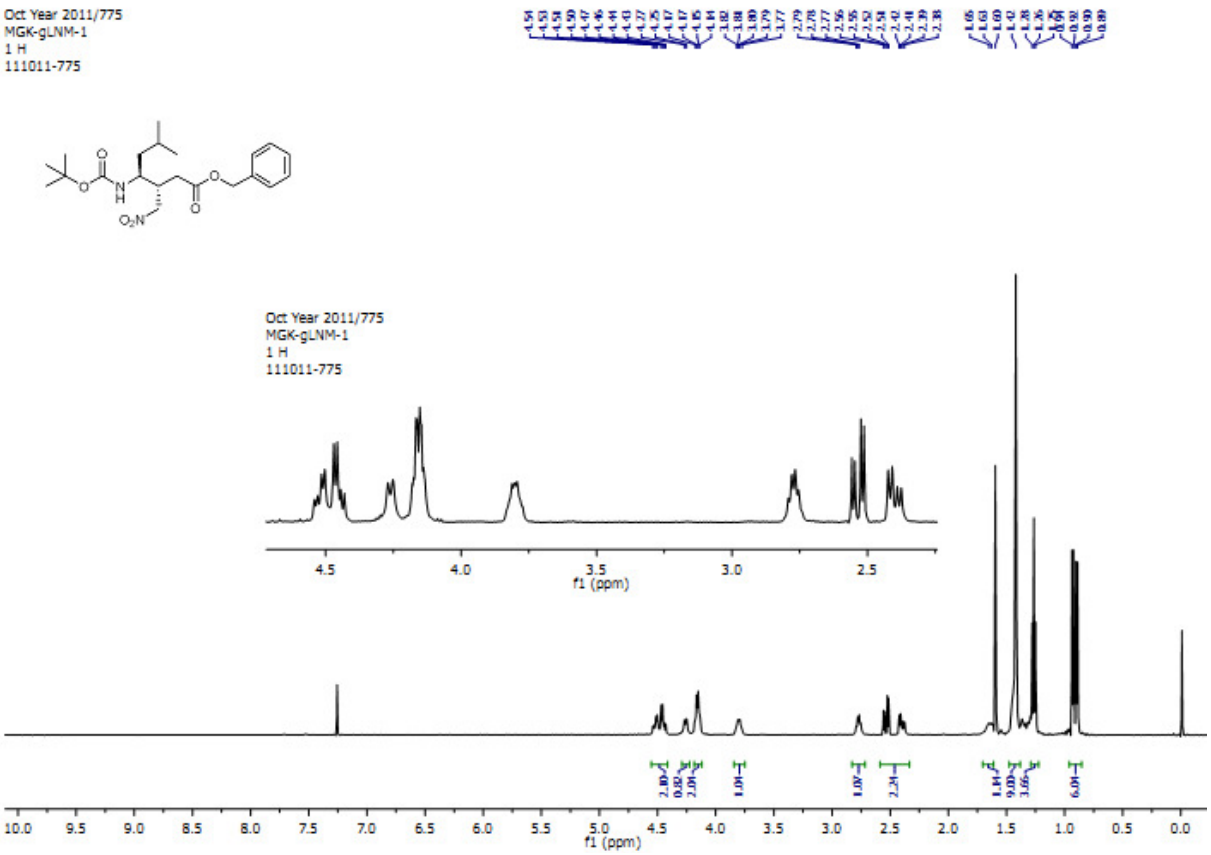

170611-09-MGK-Asp-NM-1
f1 (ppm)

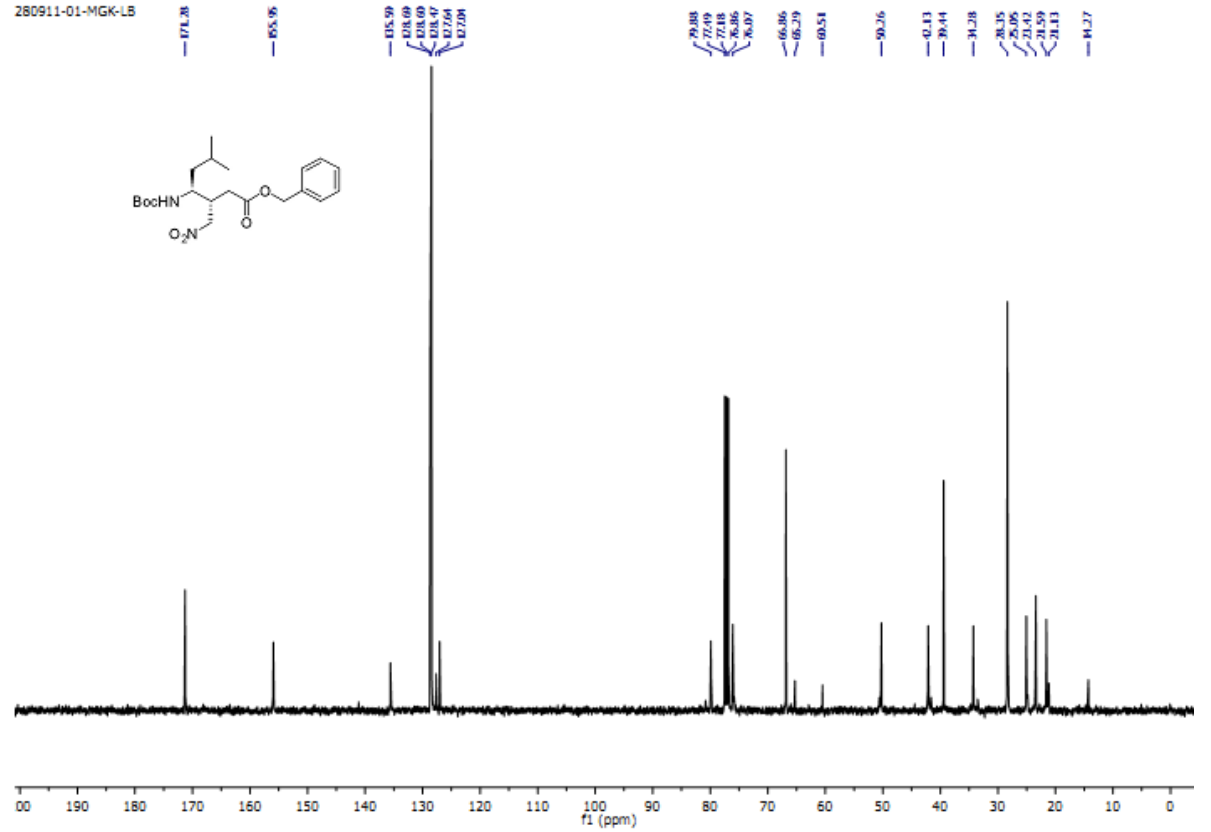

Desktop/ALA_NM_MIX .999
MGK-ACNMS
1 H
130112-999
BocHN
O2N
f1 (ppm)
171.9001
171.4129
155.4871
79.8564
79.5787
76.6103
76.3251
60.9118
60.3760
47.5389
47.3617
39.8556
39.4264
33.8494
32.7241
18.5907
17.7516
14.0708
Chemical Shift (ppm)

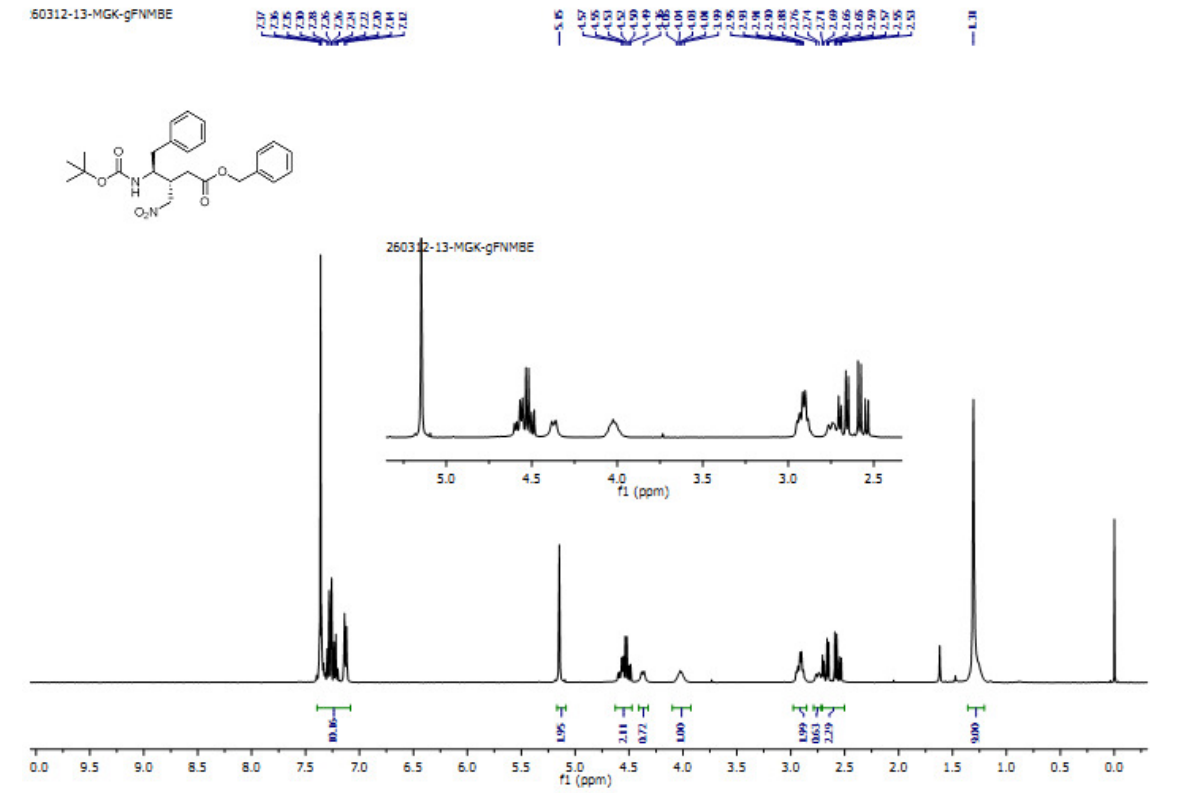

040611-04-MGK-gp-NM-1
Boc
NO2
f1 (ppm)
HBoc
NO2
Chemical Shift (ppm)

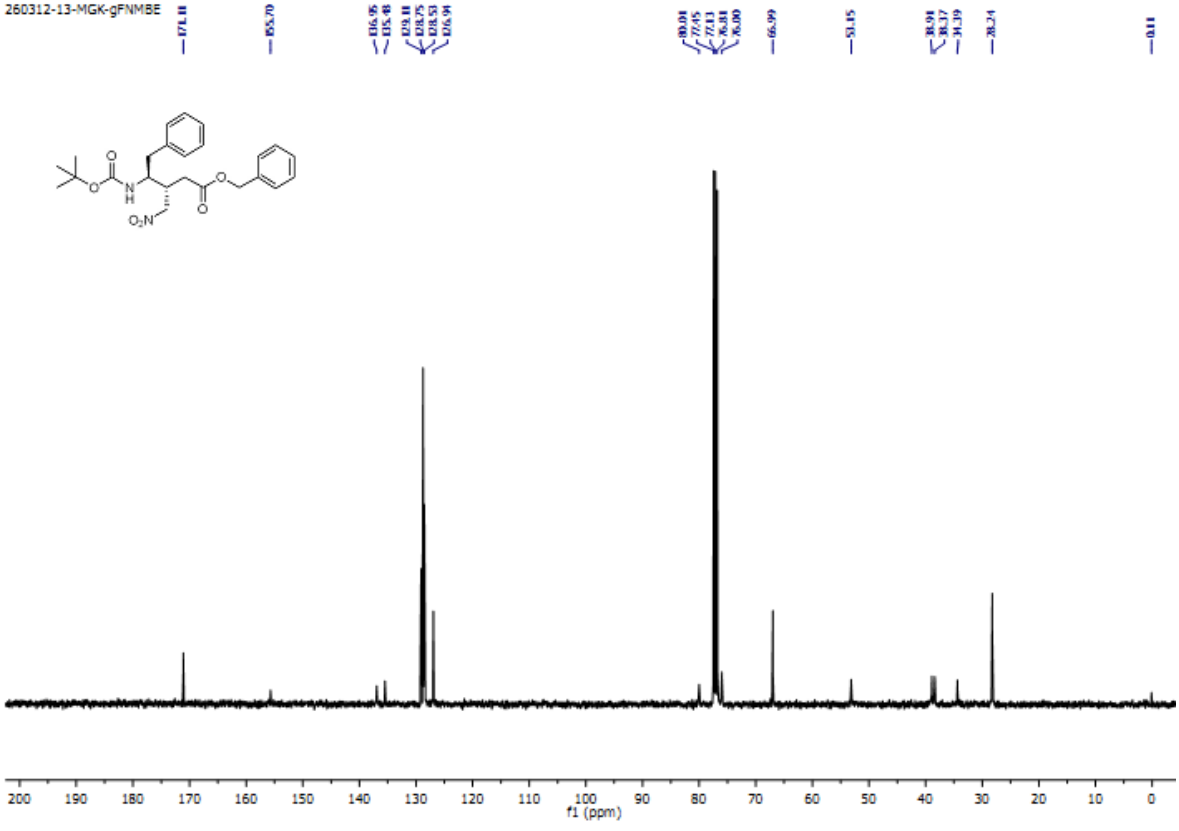

290911-14-MGK-gVNM-BE
290911-14-MGK-gVNM-BE
f1 (ppm)
f1 (ppm)

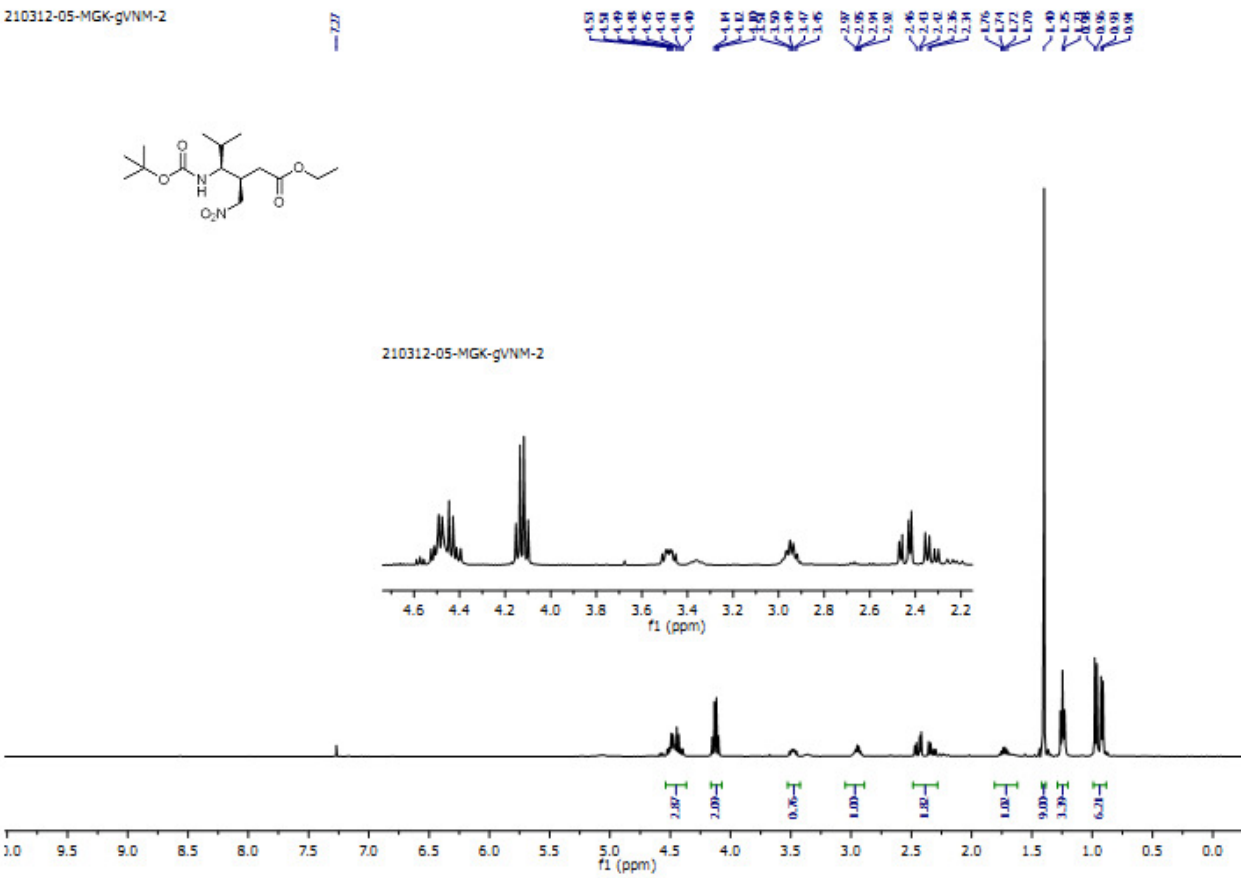

290911-14-MGK-gVNM-BE
BocHN
f1 (ppm)

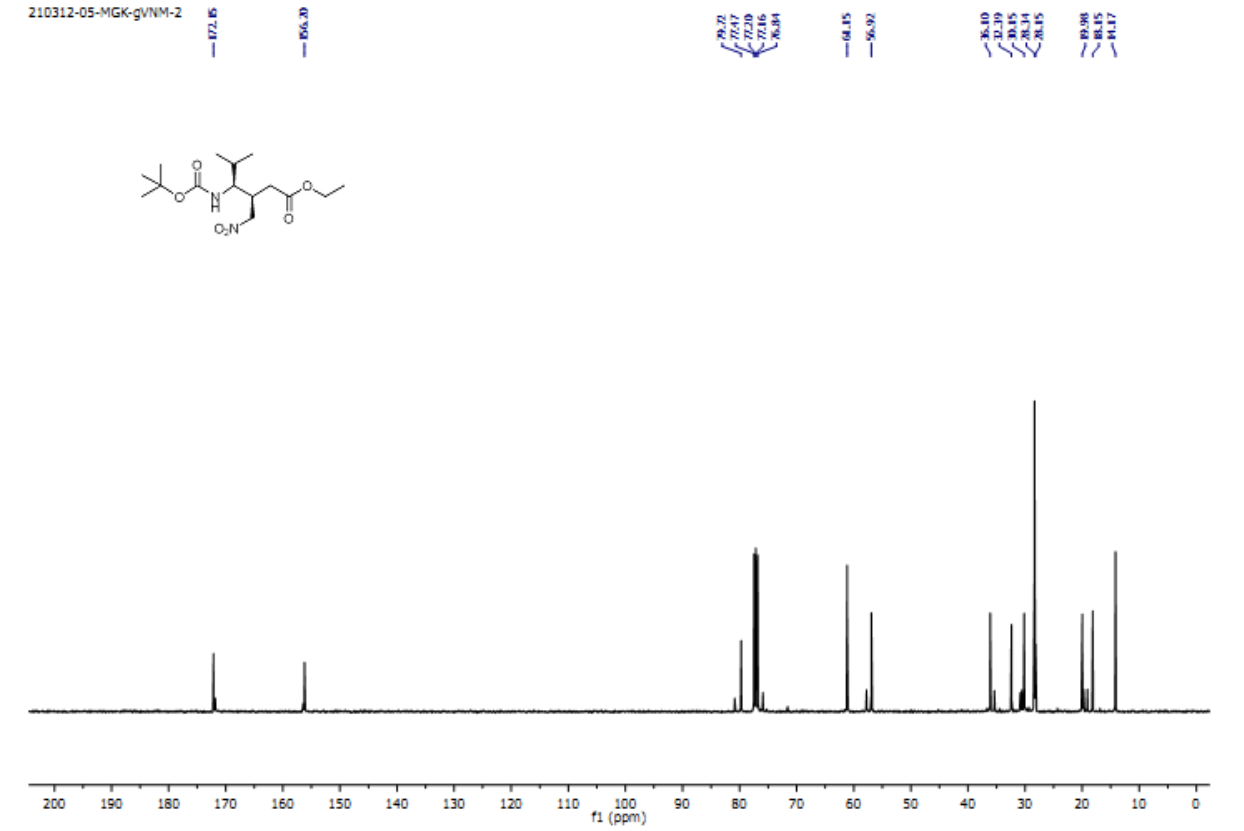

Oct Year 2011/775
MGK-gLNM-1
1 H
111011-775
Oct Year 2011/775
MGK-gLNM-1
1 H
111011-775
f1 (ppm)
f1 (ppm)

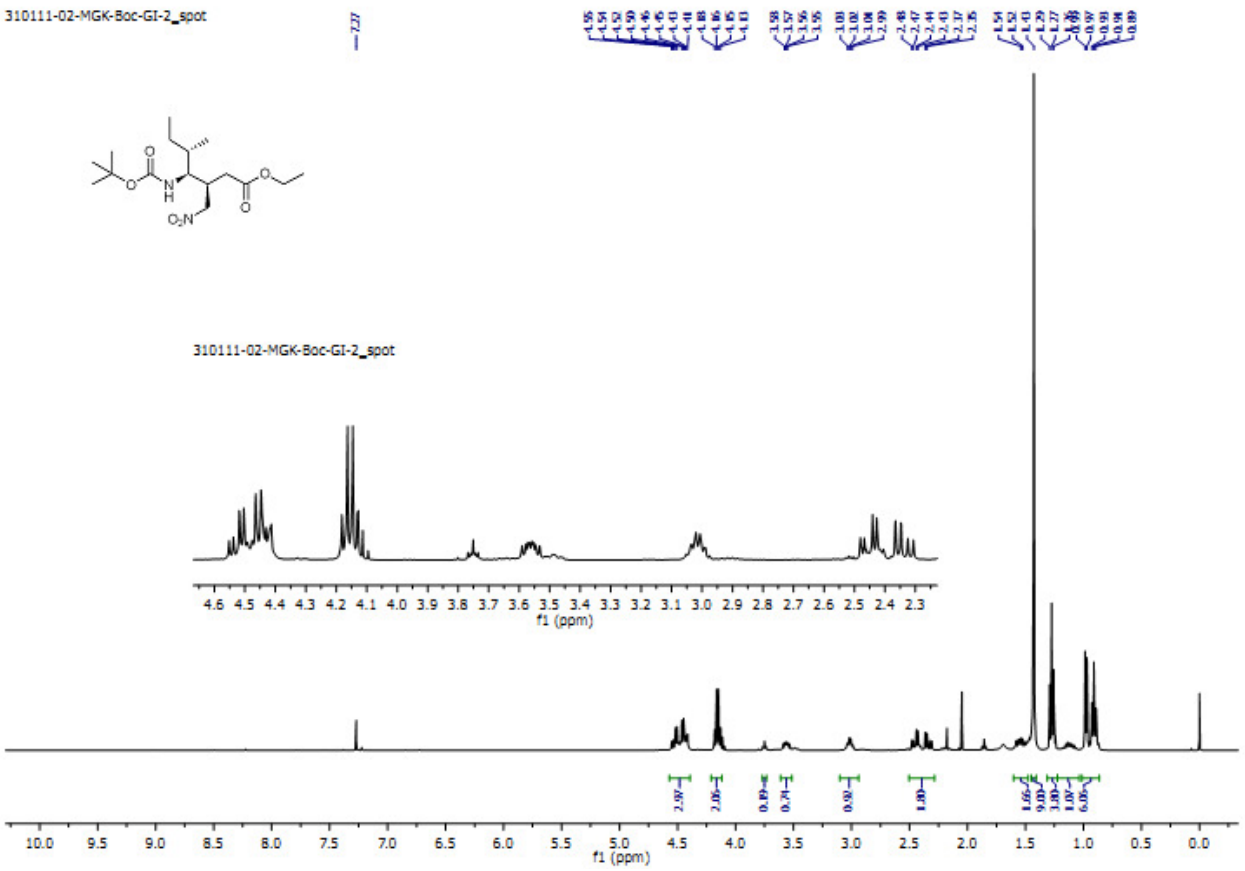

280911-01-MGK-LB
BocHN
f1 (ppm)

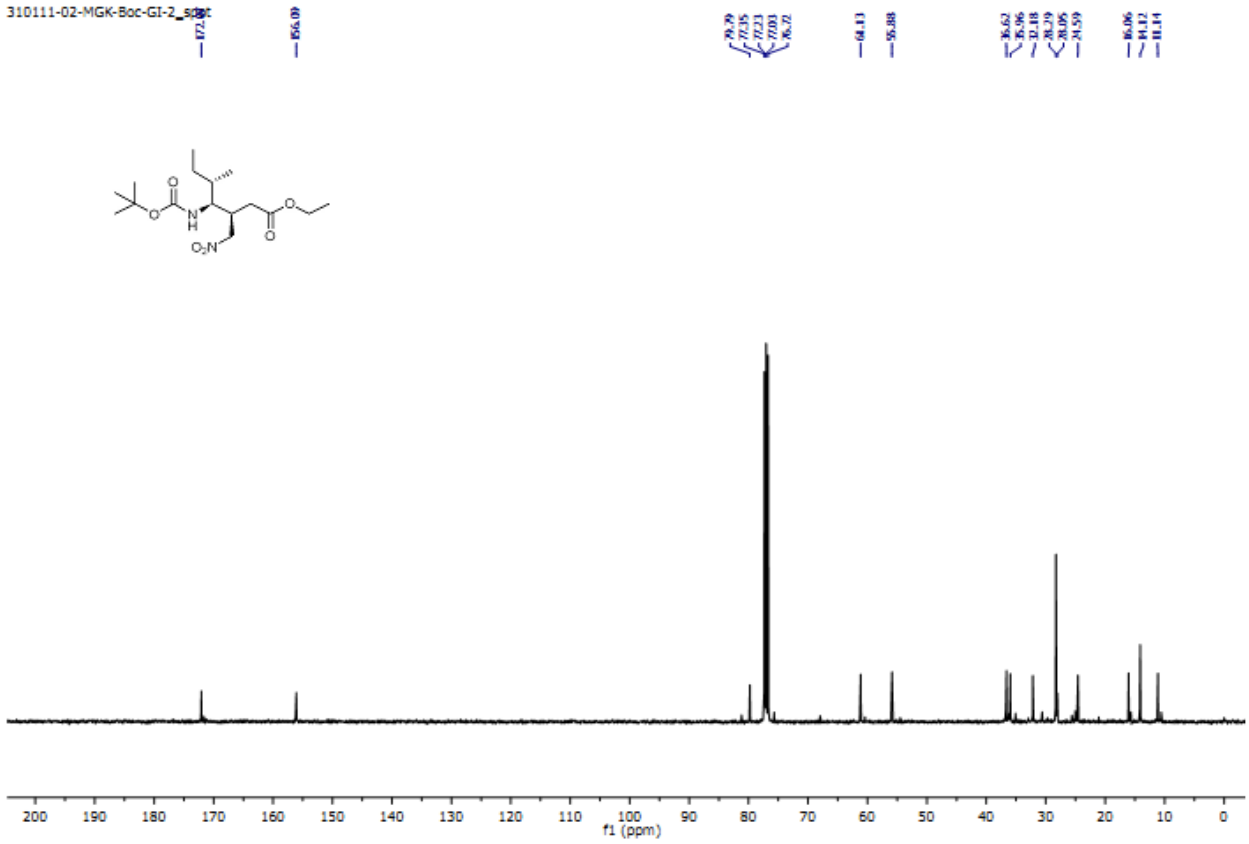


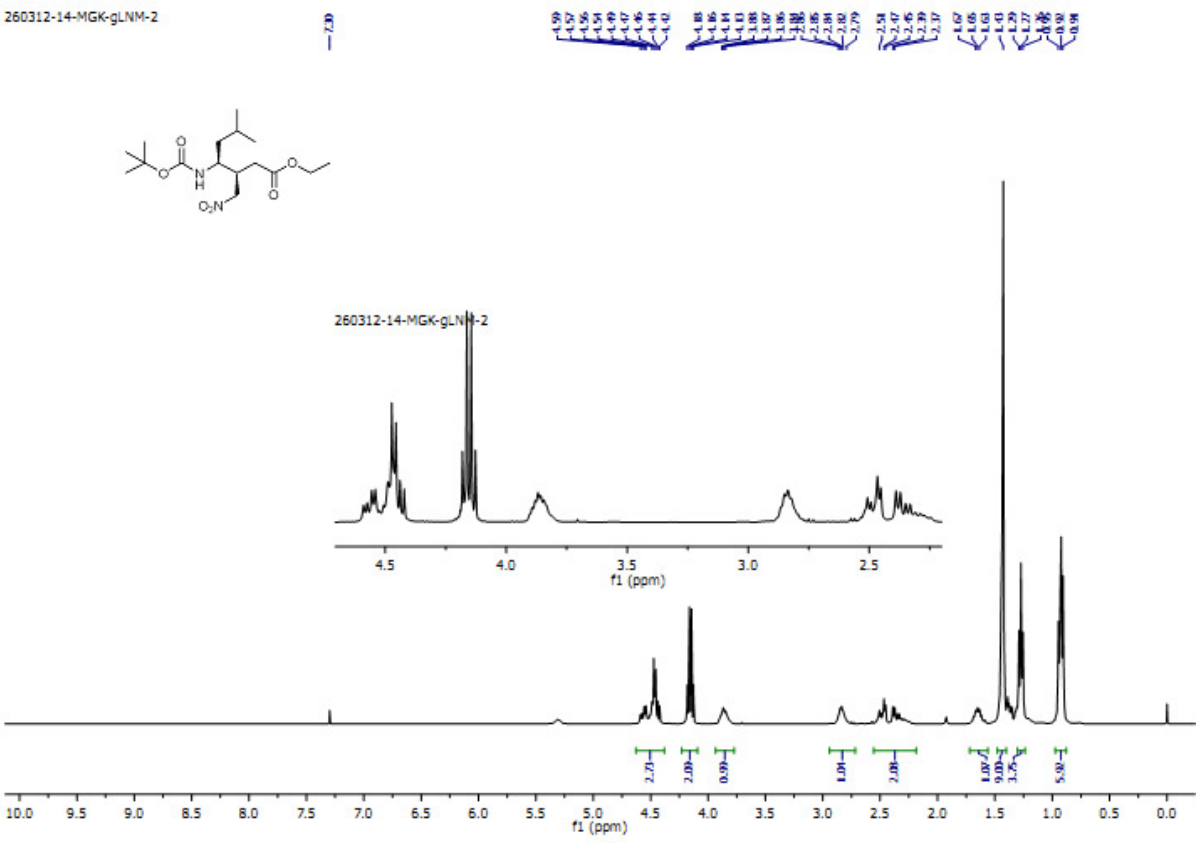


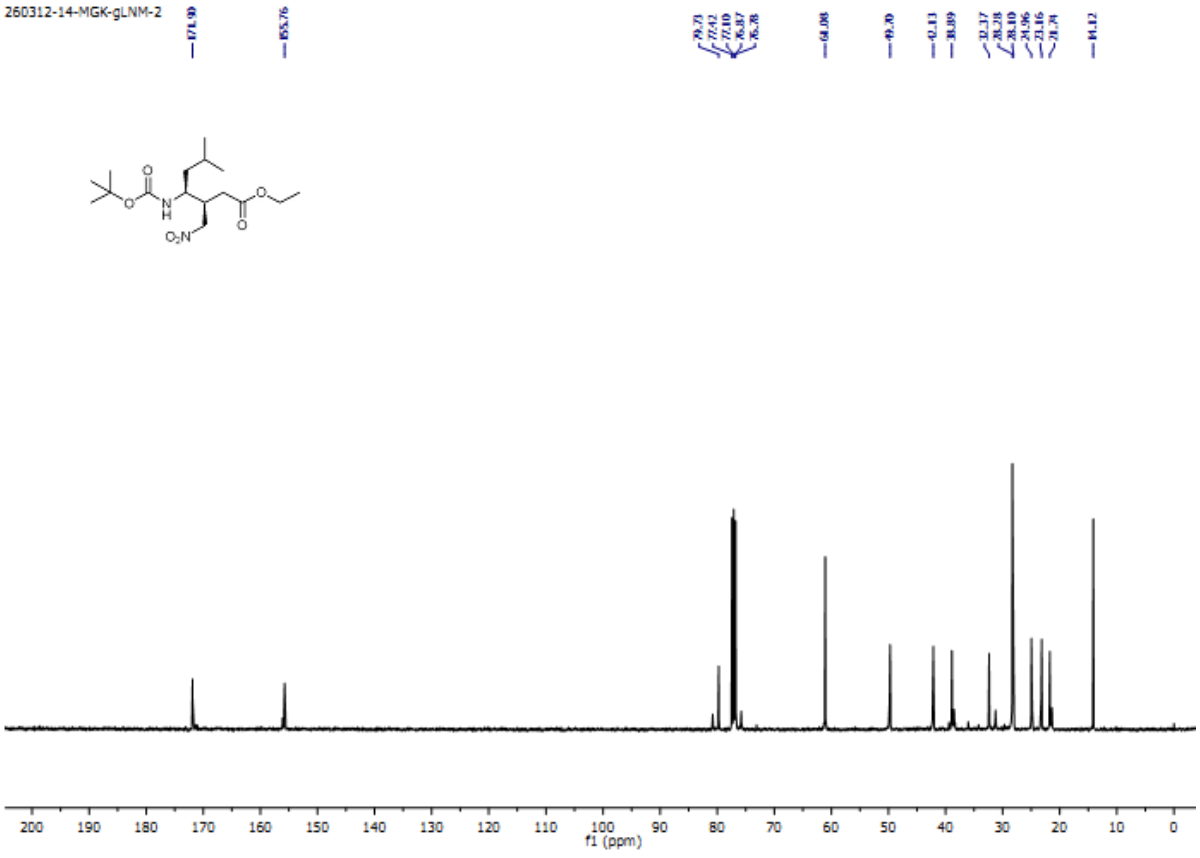

210312-05-MGK-gVNM-2
7.27
210312-05-MGK-gVNM-2
f1 (ppm)
f1 (ppm)

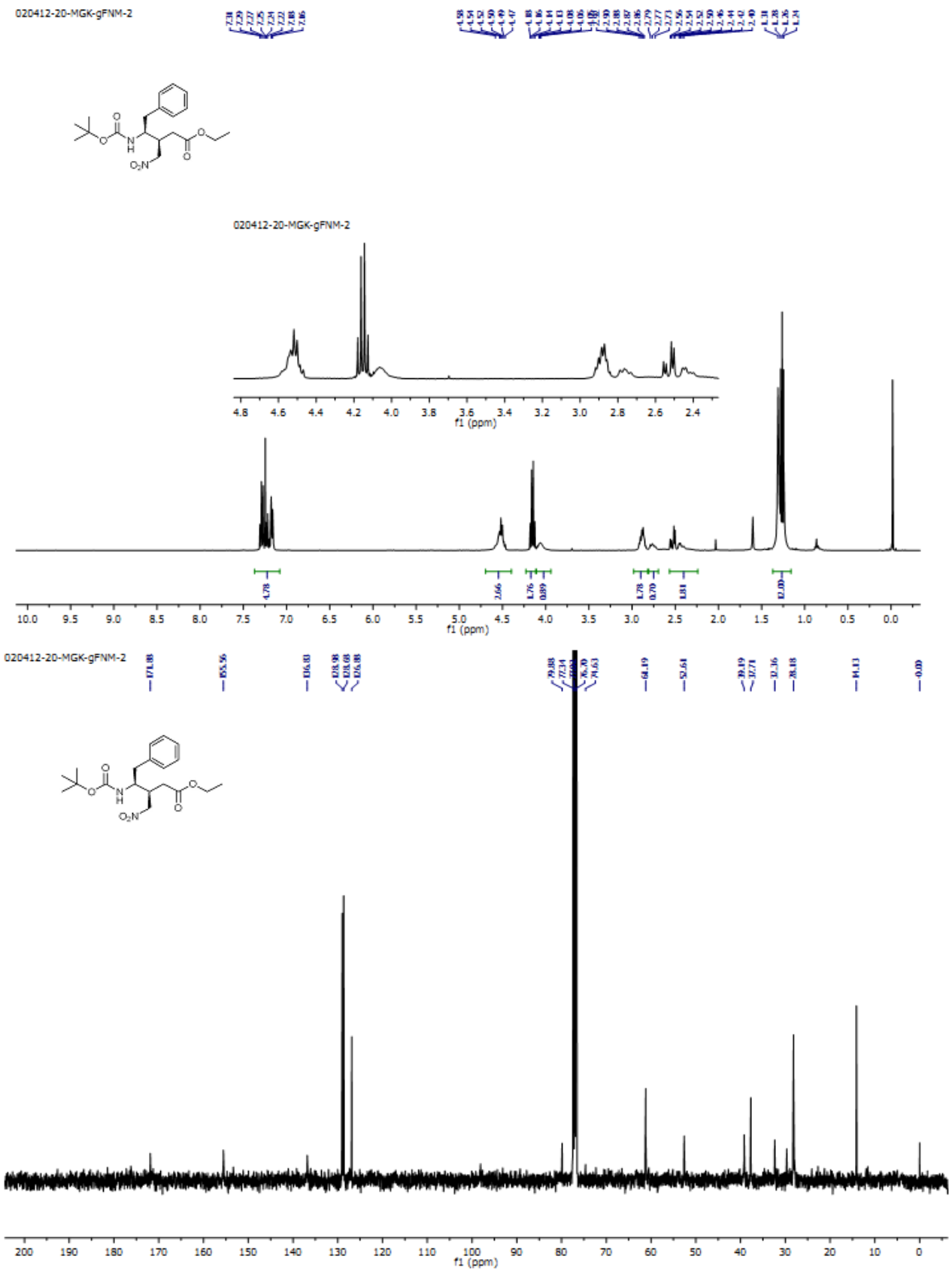

210312-05-MGK-gVNM-2
f1 (ppm)

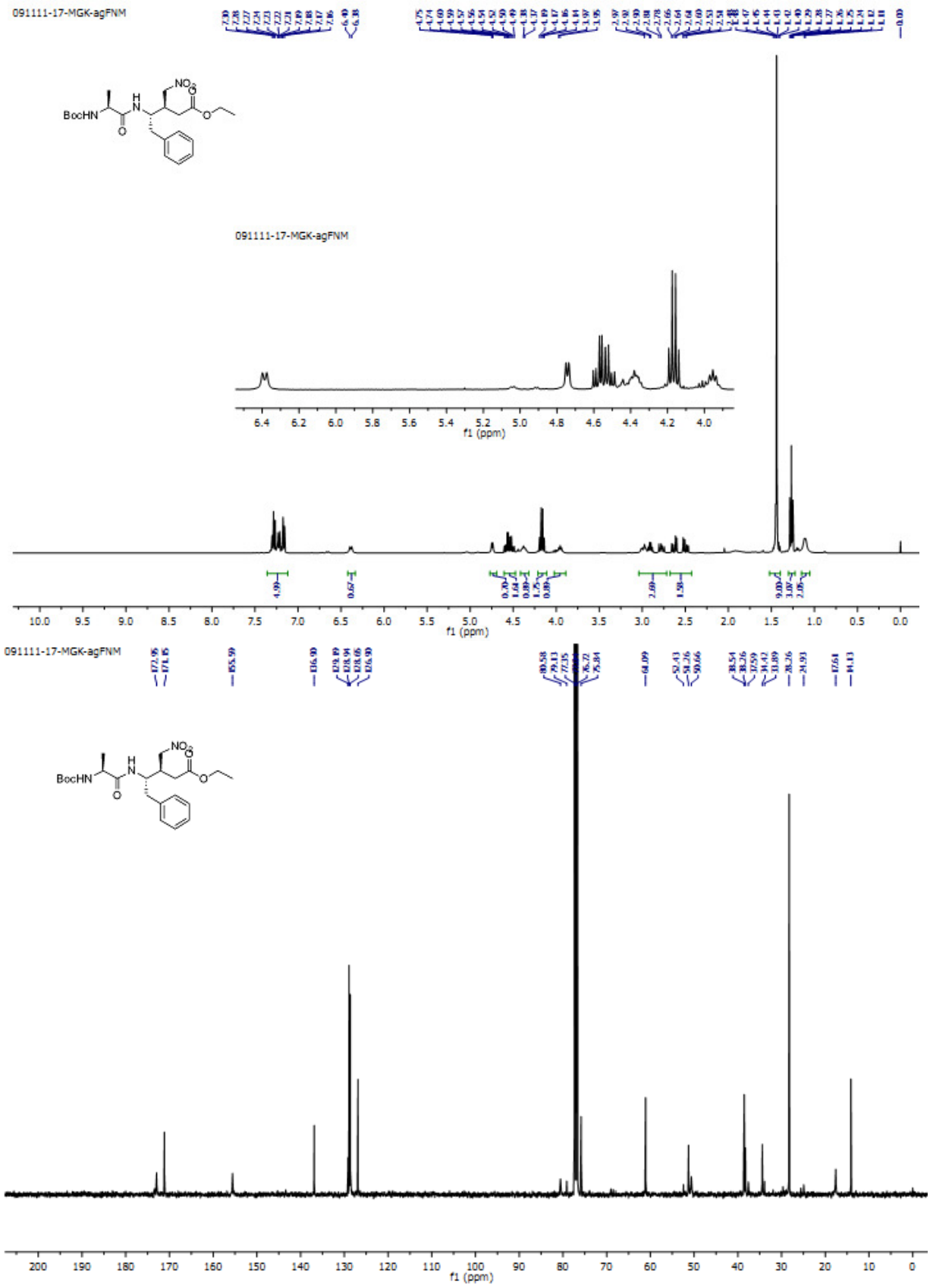

310111-02-MGK-Boc-GI-2_spot
7.27
310111-02-MGK-Boc-GI-2_spot
f1 (ppm)
f1 (ppm)

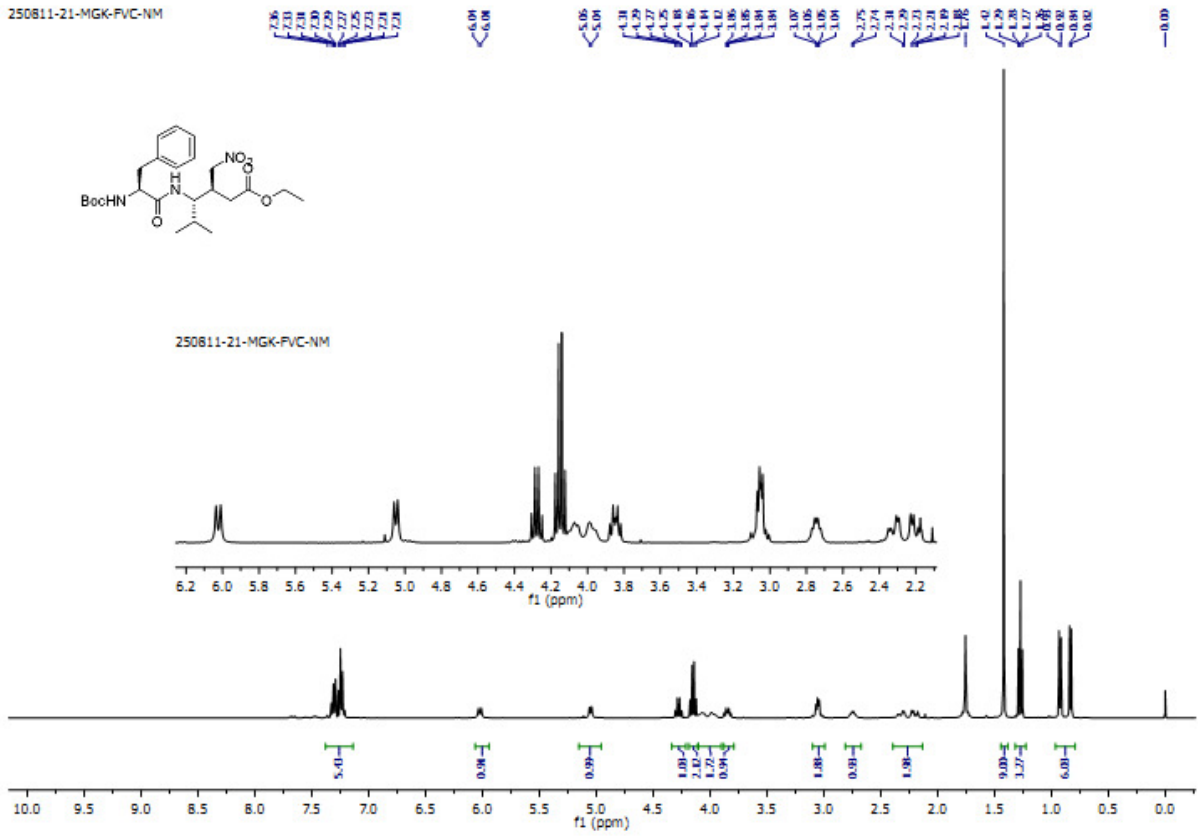

310111-02-MGK-Boc-GI-2_spot
f1 (ppm)

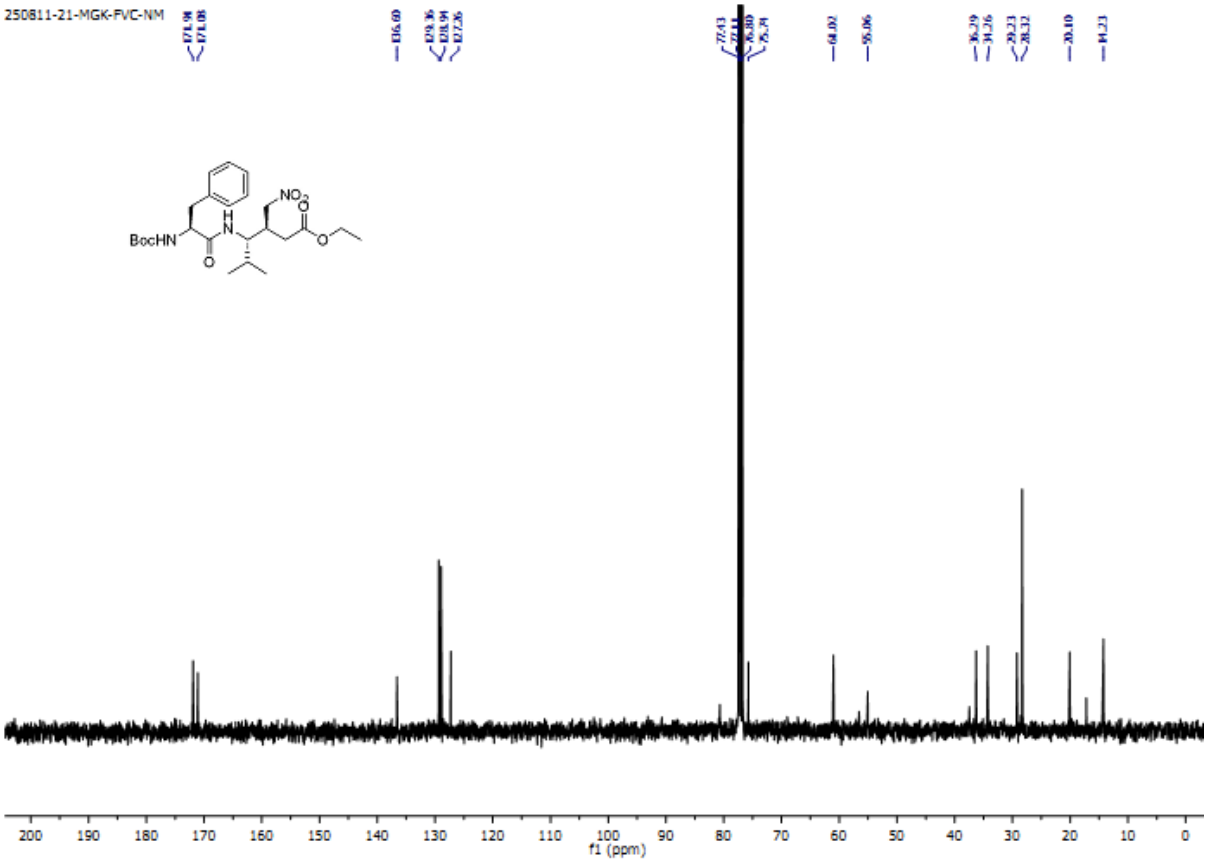

260312-14-MGK-gLNM-2
260312-14-MGK-gLNM-2
f1 (ppm)
f1 (ppm)

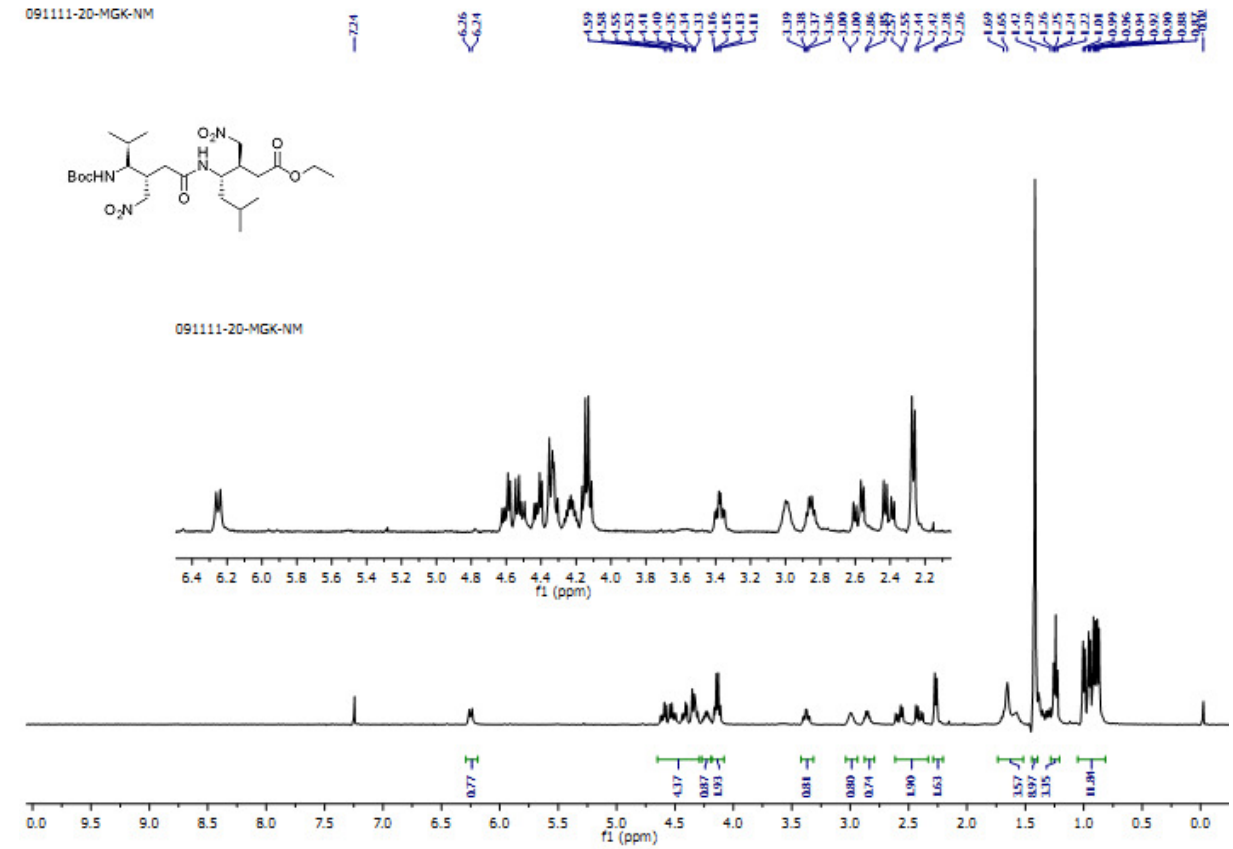

260312-14-MGK-gLNM-2
f1 (ppm)

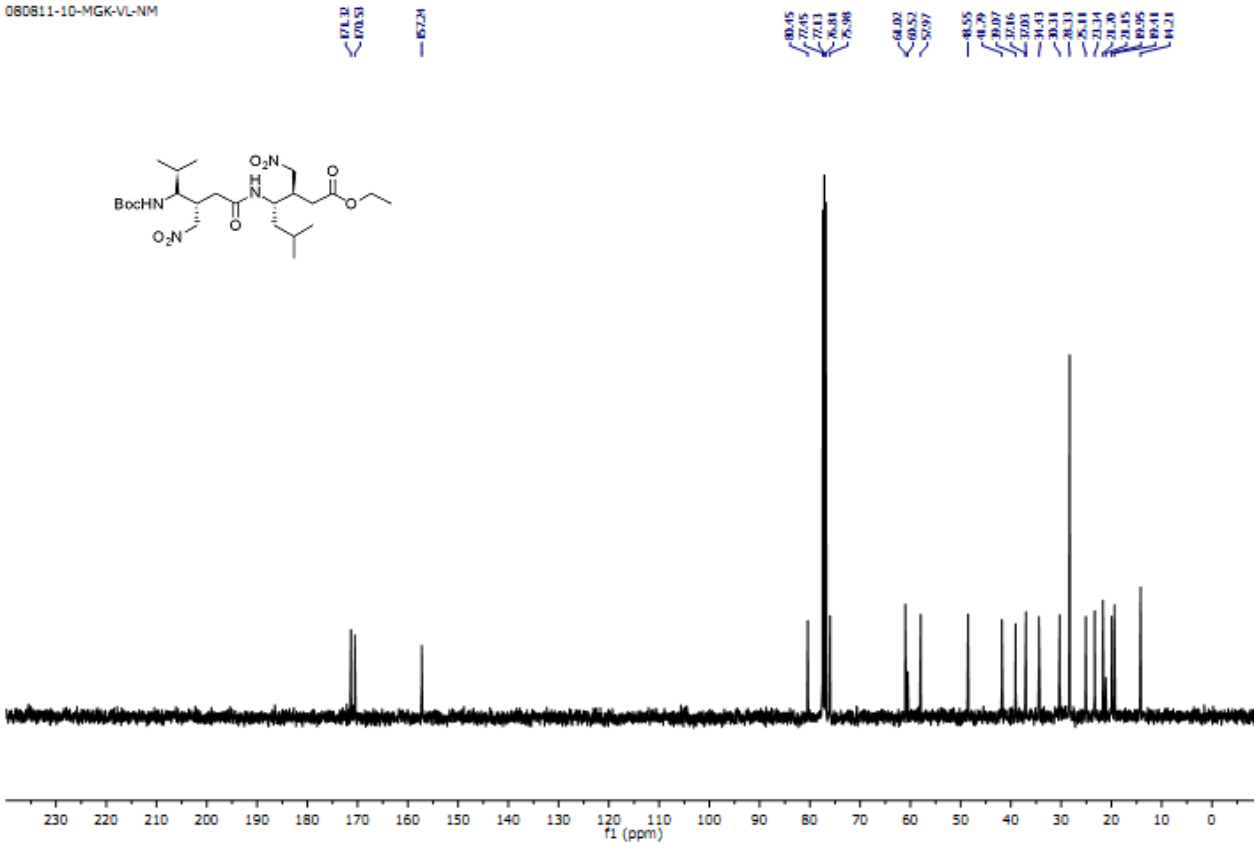

020412-20-MGK-gFNM-2
020412-20-MGK-gFNM-2
f1 (ppm)
020412-20-MGK-gFNM-2
f1 (ppm)

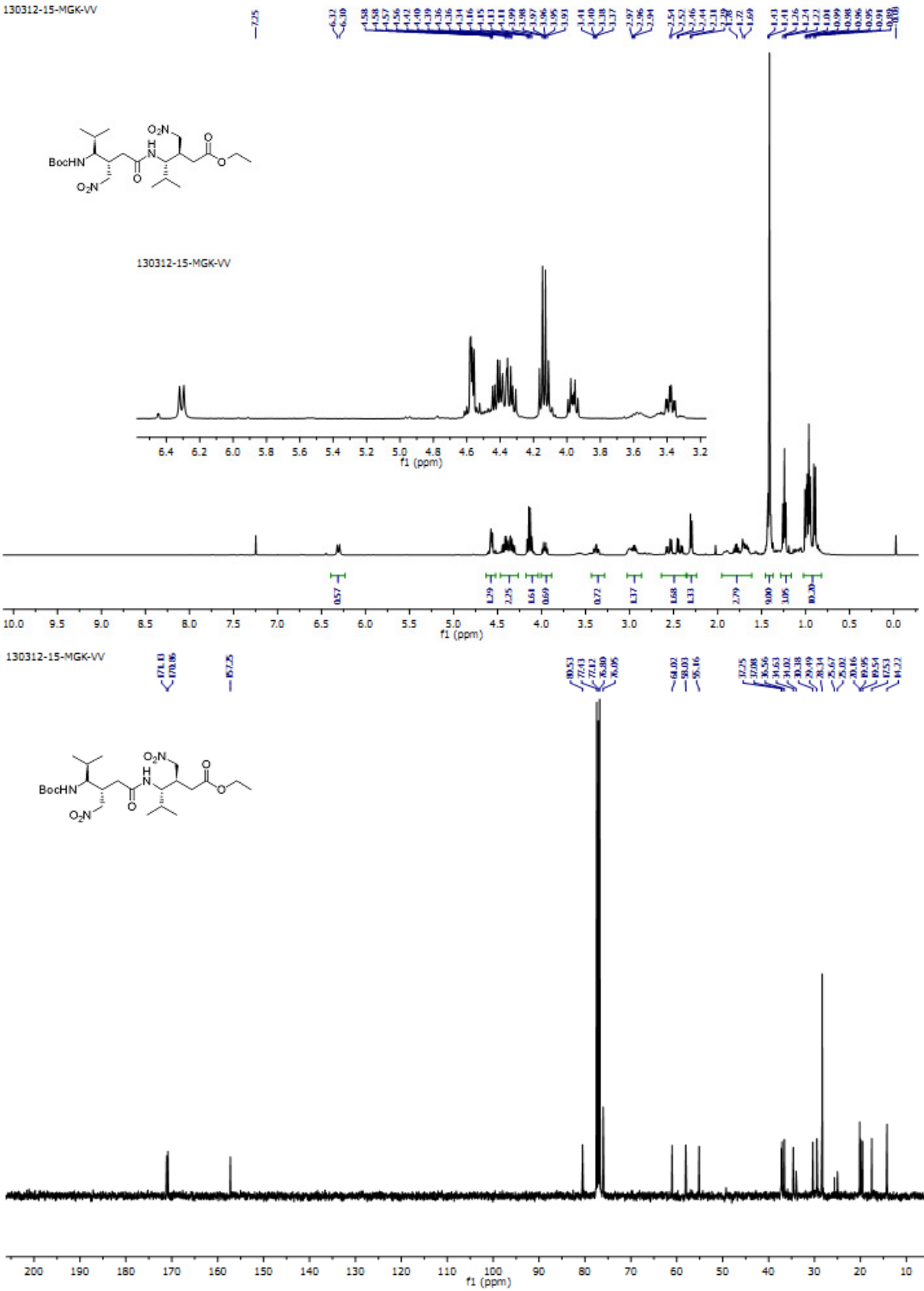

091111-17-MGK-agFNM
BocHN
NO2
O
091111-17-MGK-agFNM
f1 (ppm)
091111-17-MGK-agFNM
BocHN
NO2
O
f1 (ppm)

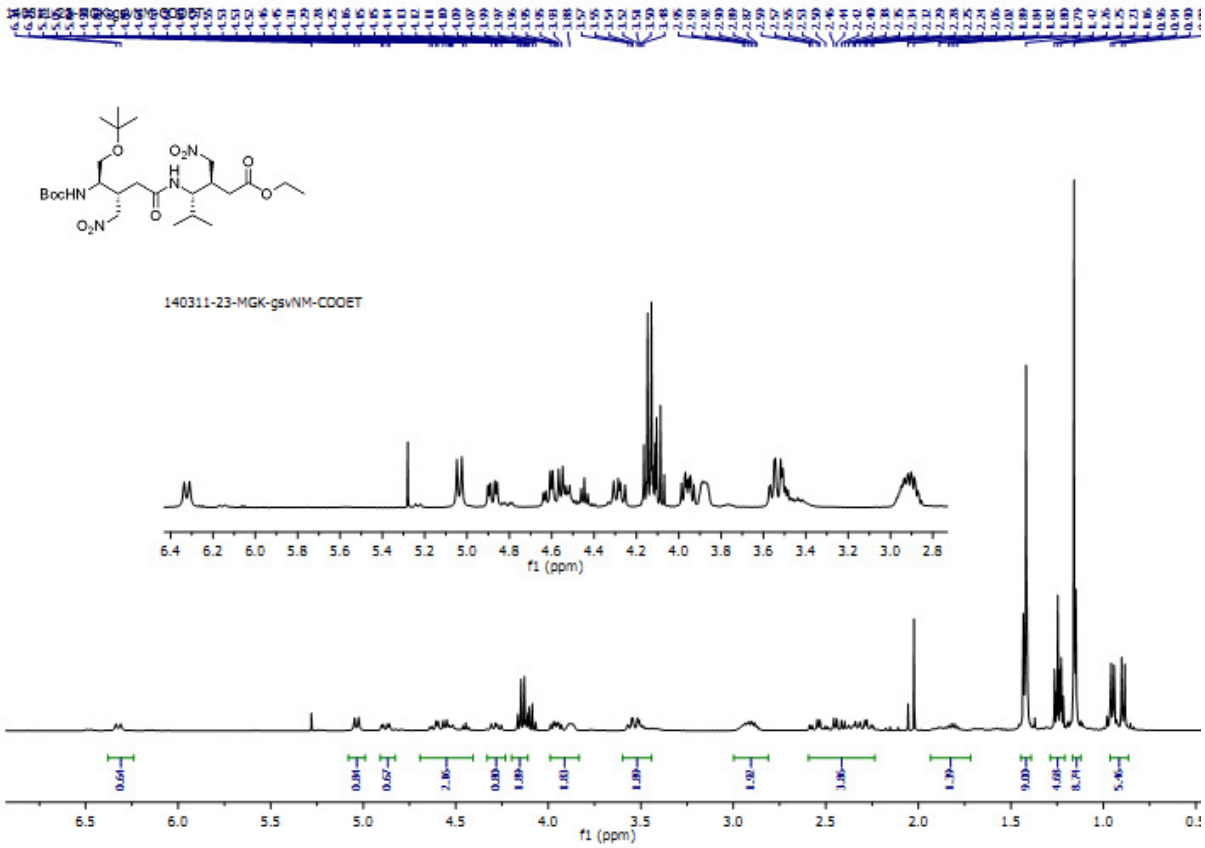

250811-21-MGK-FVC-NM
BocHN
NO2
250811-21-MGK-FVC-NM
f1 (ppm)
f1 (ppm)

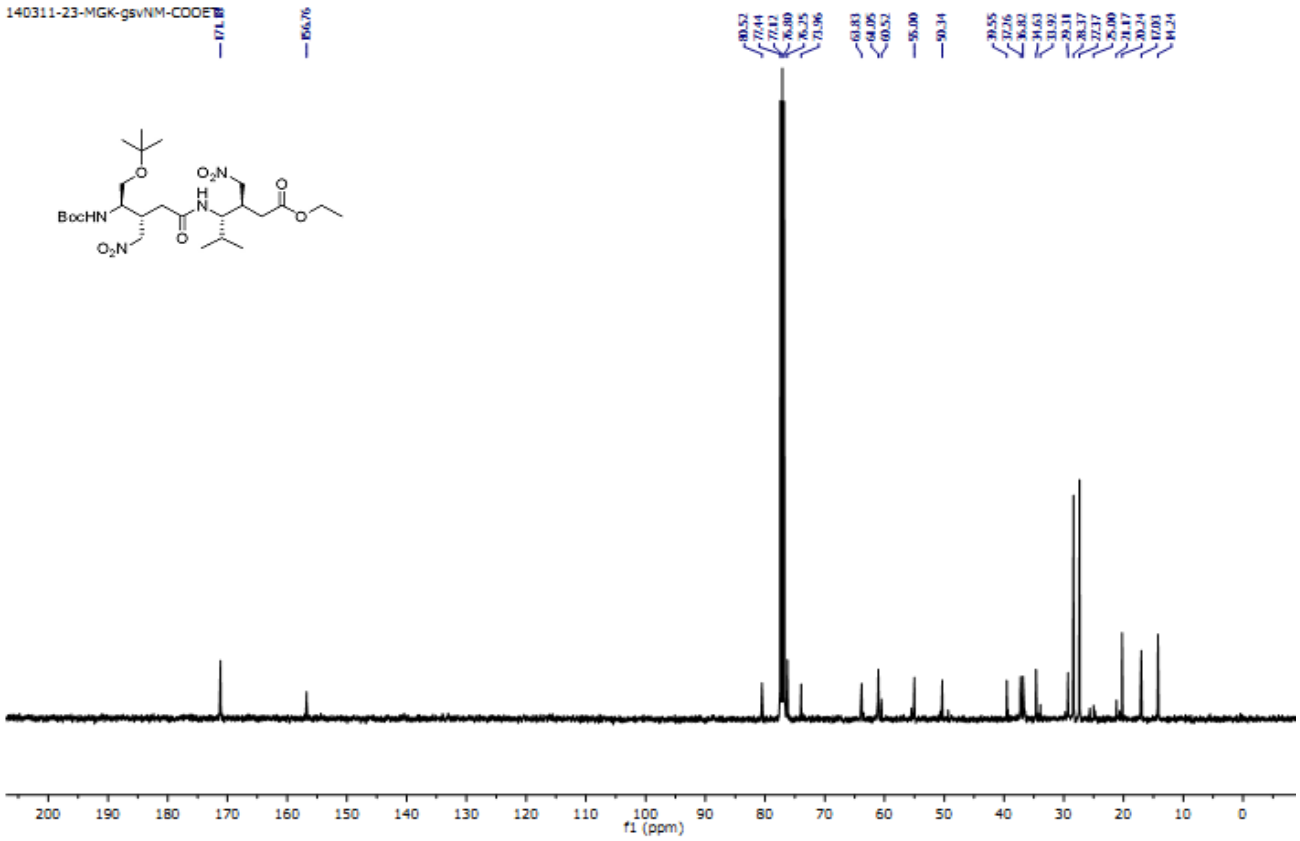

250811-21-MGK-FVC-NM
BocHN
NO2
f1 (ppm)

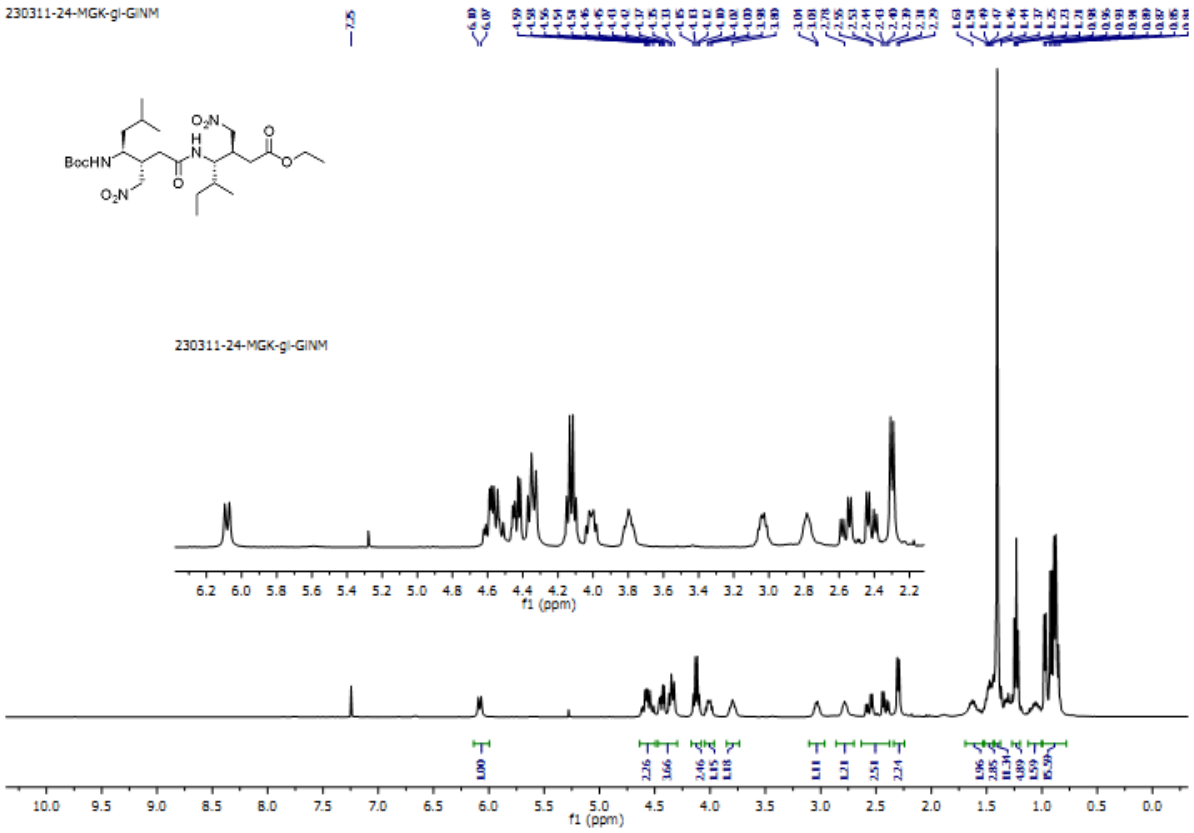


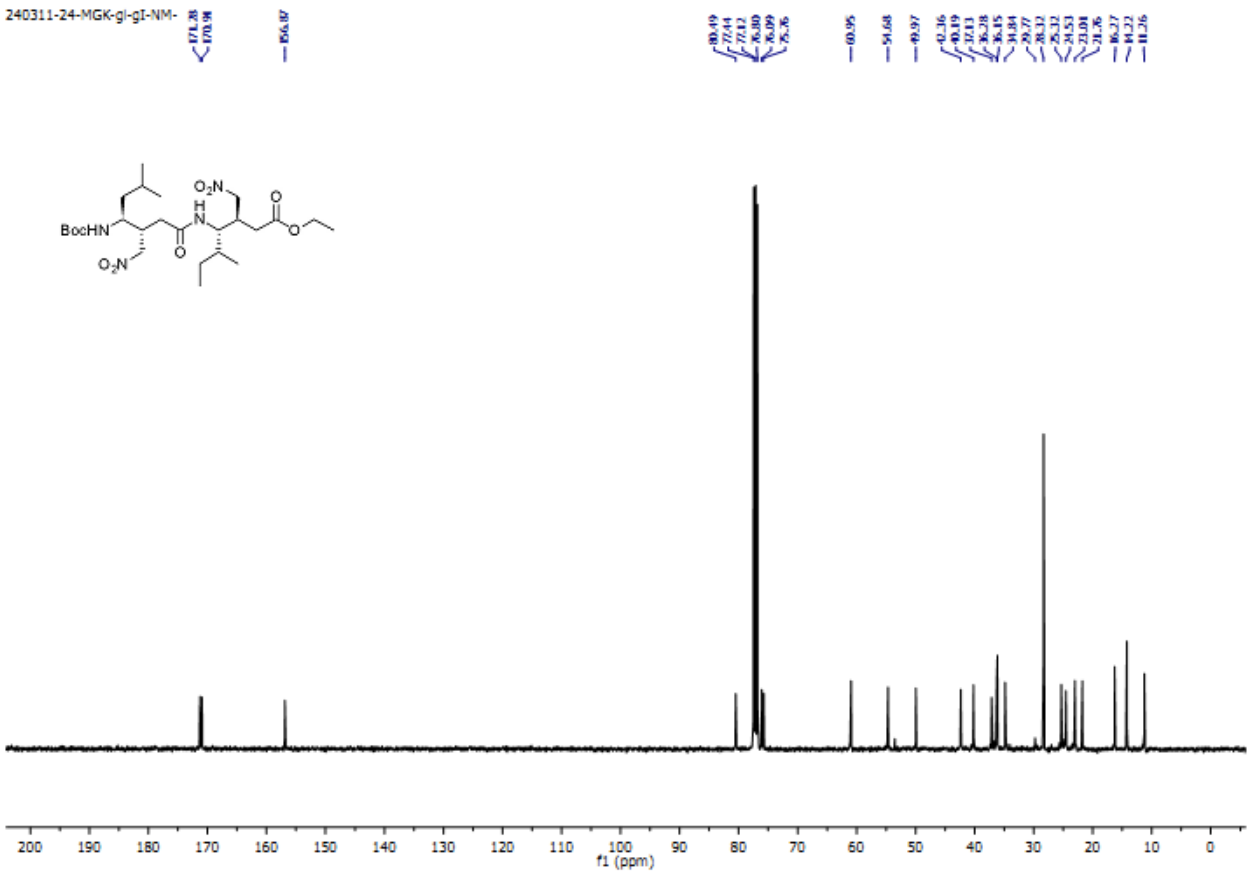


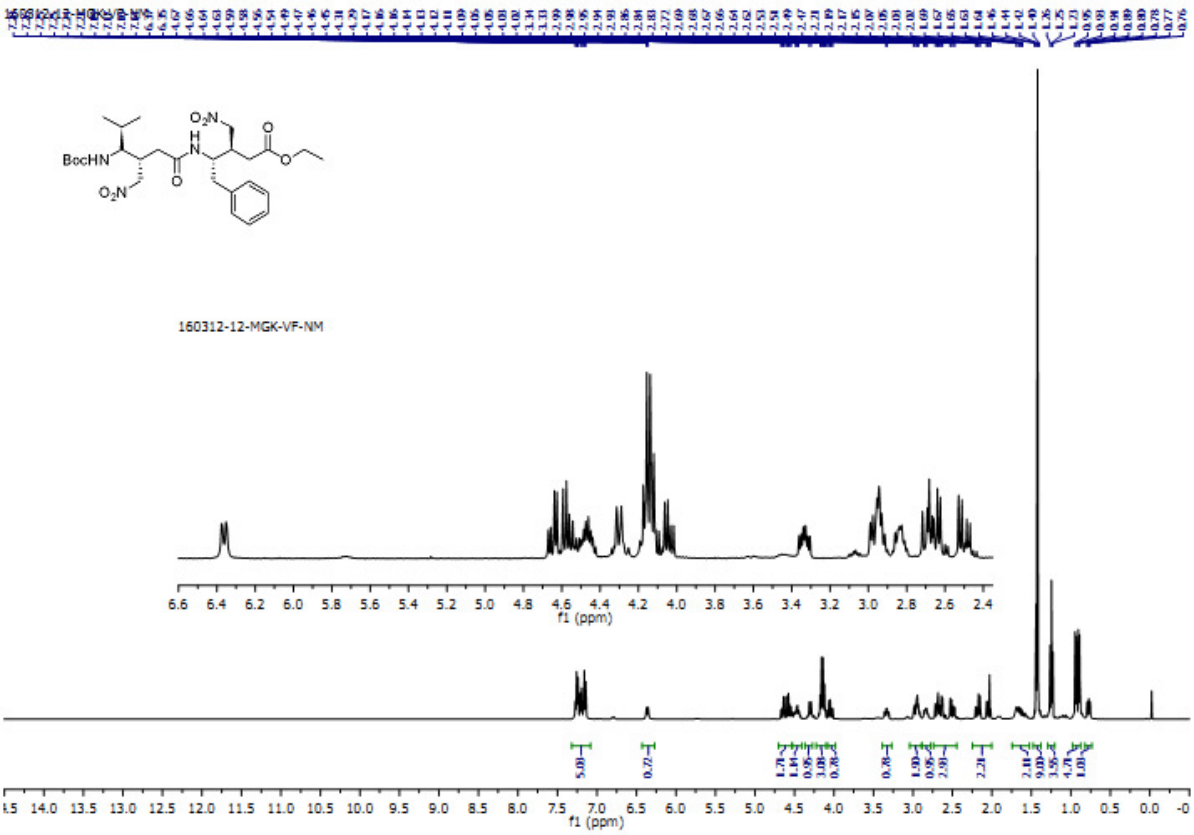

130312-15-MGK-VV
BocHN
O_2N
O_2N
H
N
O
O
O
130312-15-MGK-VV
f1 (ppm)
f1 (ppm)
130312-15-MGK-VV
BocHN
O_2N
O_2N
H
N
O
O
O
f1 (ppm)

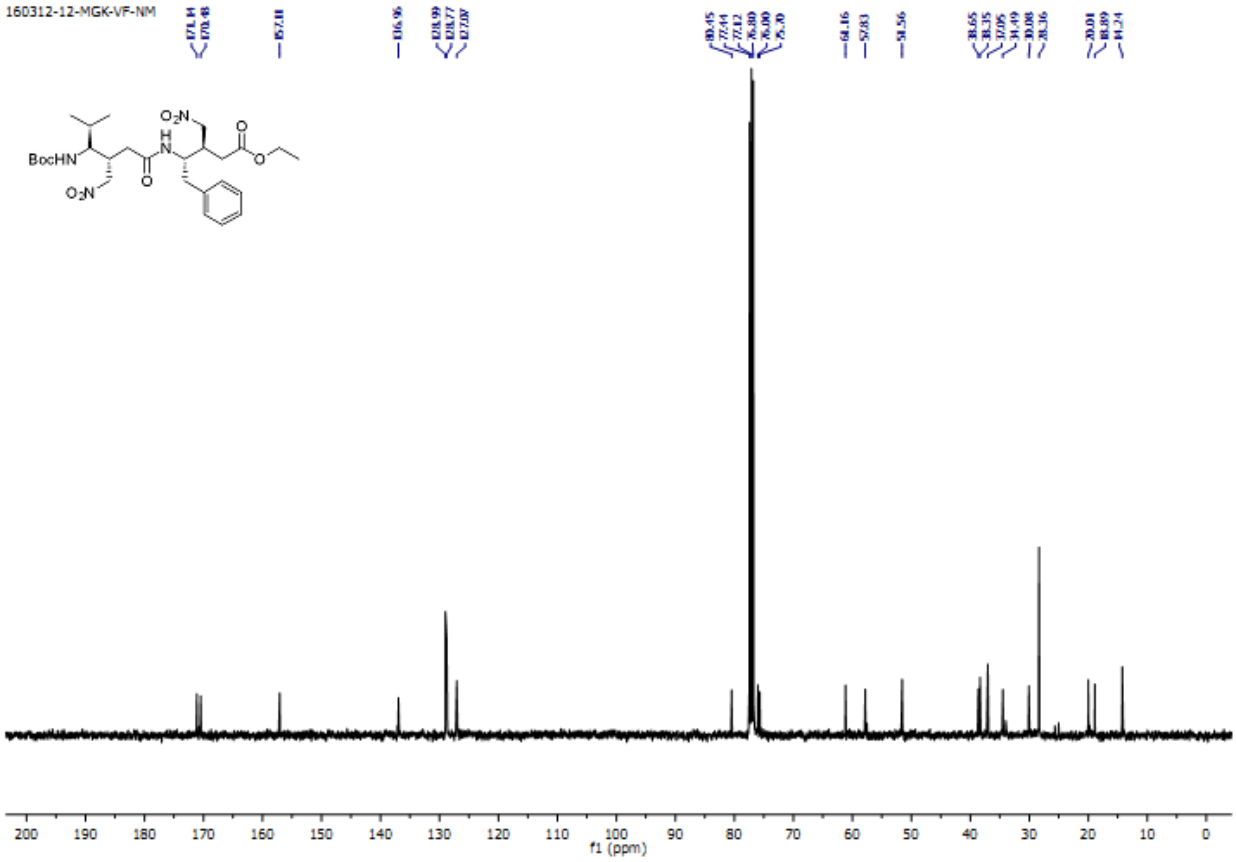




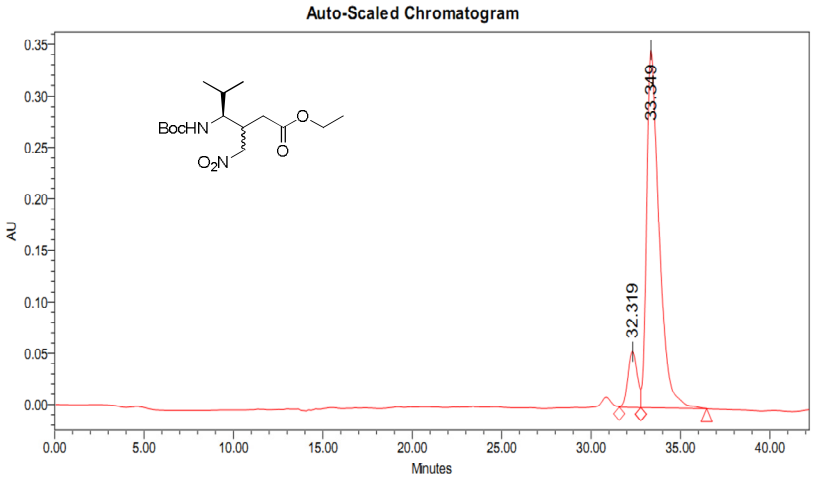

230311-24-MGK-gl-GINM
BocHN
O_2N
H
N
O
O_2N
230311-24-MGK-gl-GINM
f1 (ppm)


240311-24-MGK-gl-gI-NM-
BocHN
O_2N
H
N
O
O_2N
f1 (ppm)


BocHN
O_2N
O_2N
160312-12-MGK-VF-NM
f1 (ppm)


160312-12-MGK-VF-NM
BocHN
O_2N
O_2N
f1 (ppm)

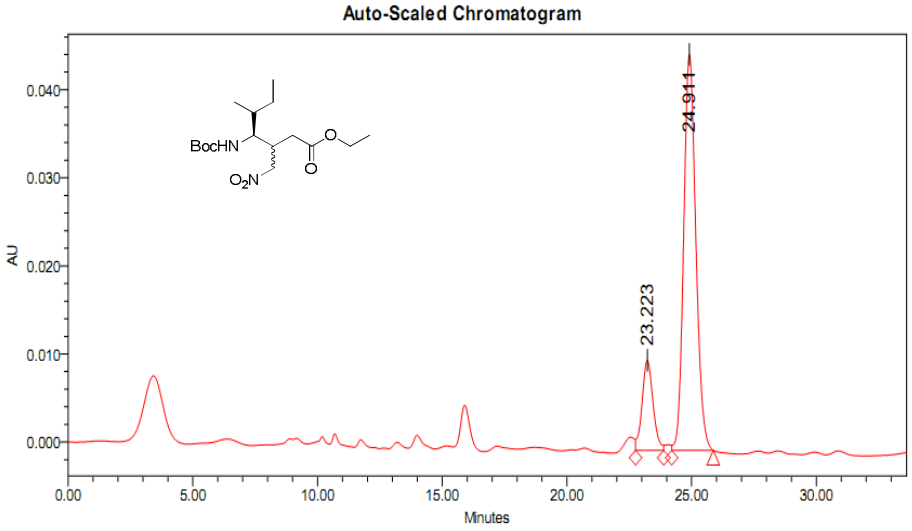
Diastereomeric ratio analysis for the compound (2a+3a):



Peak Results

	Name	RT	Area	Height	Amount	Units
1		32.319	1984098	54644		
2		33.349	16830356	347590		

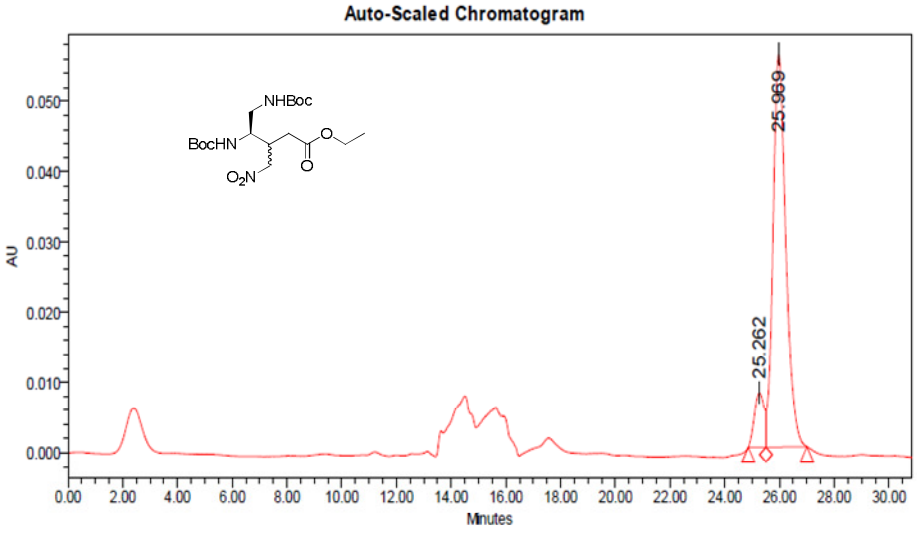
Diastereomeric ratio analysis for the compound (2b+3b):



Peak Results

	Name	RT	Area	Height	Amount	Units
1		23.223	310797	10232		
2		24.911	1517952	44961		

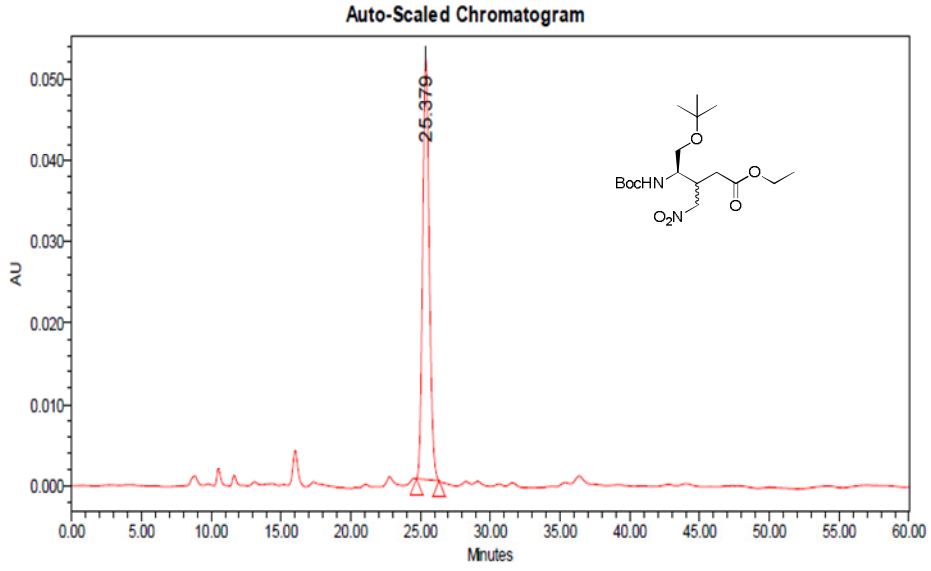
Diastereomeric ratio analysis for the compound (2d+3d):



Peak Results

	Name	RT	Area	Height	Amount	Units
1		25.262	188554	7694		
2		25.969	1815497	55843		

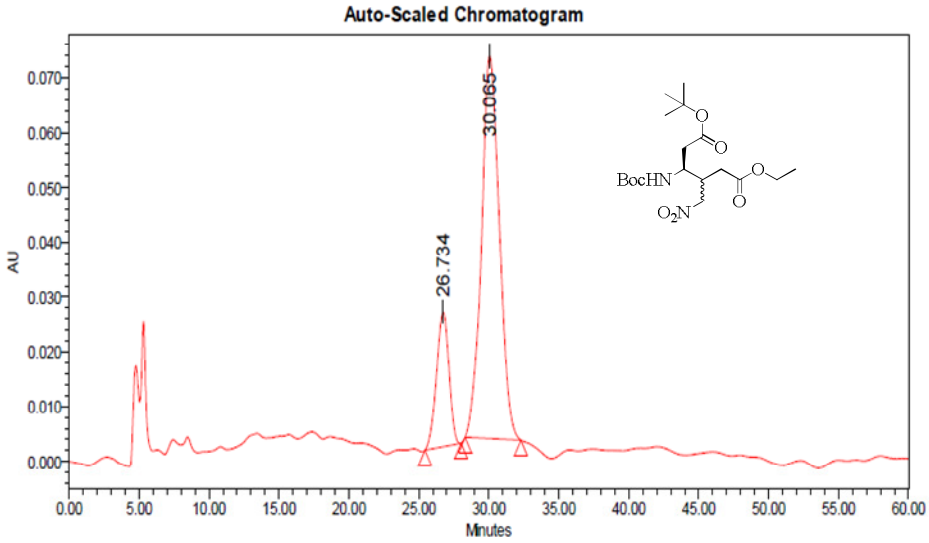
Diastereomeric ratio analysis for the compound (2f+3f):



Peak Results

	Name	RT	Area	Height	Amount	Units
1		25.379	1705314	51787		

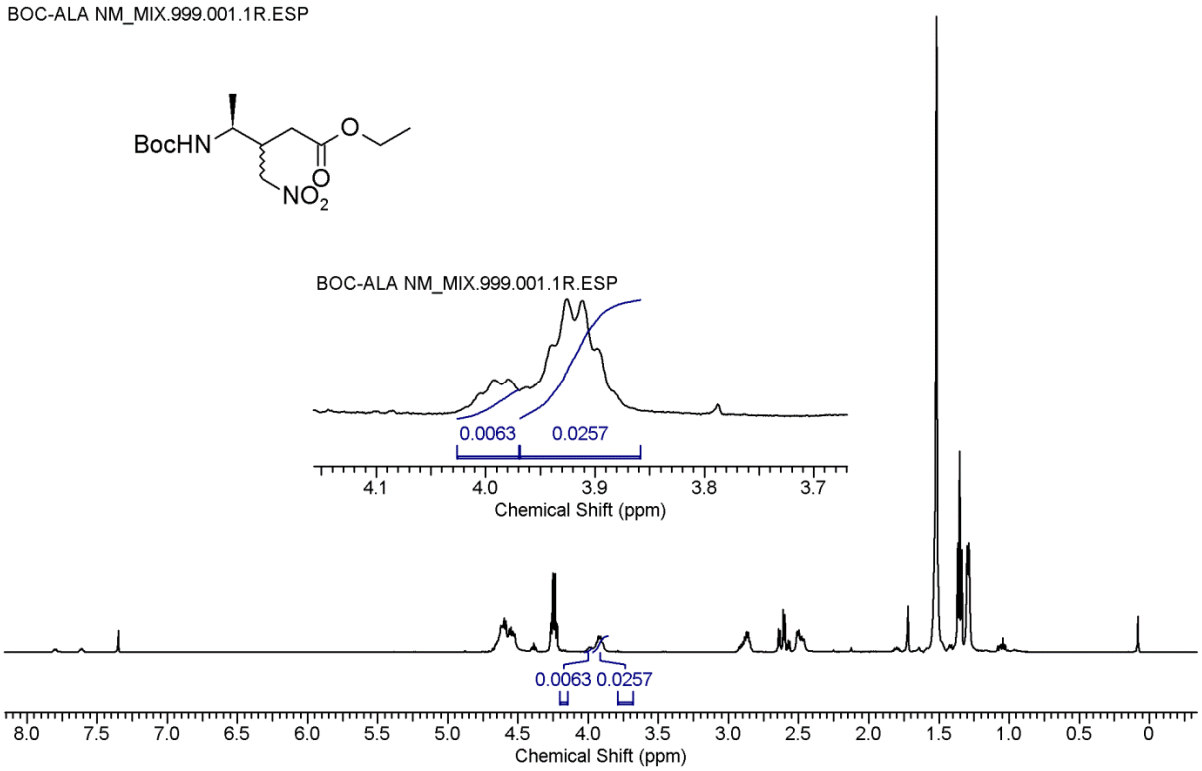
Diastereomeric ratio analysis for the compound (2g+3g):



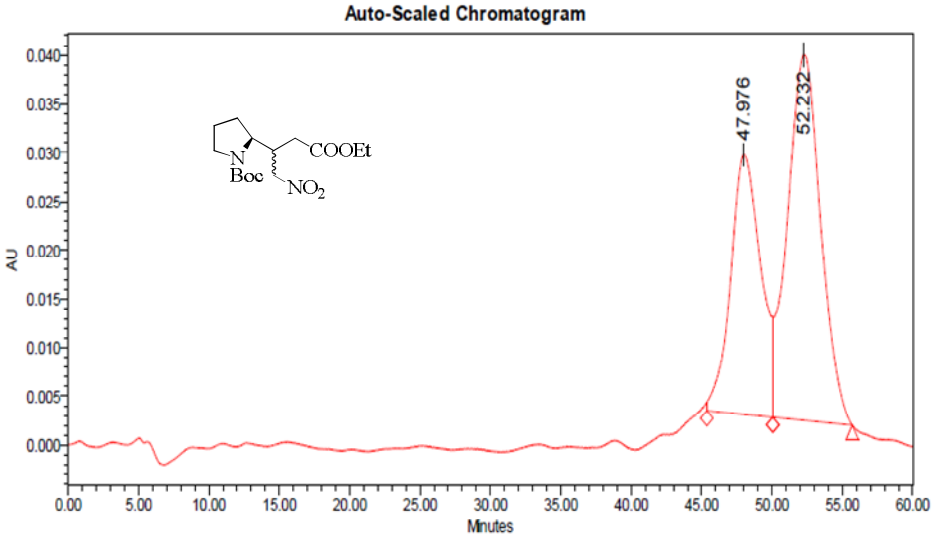
Peak Results

	Name	RT	Area	Height	Amount	Units
1		26.734	1511638	24532		
2		30.065	6206696	69712		

Diastereomeric ratio analysis for the compound (2h+3h):



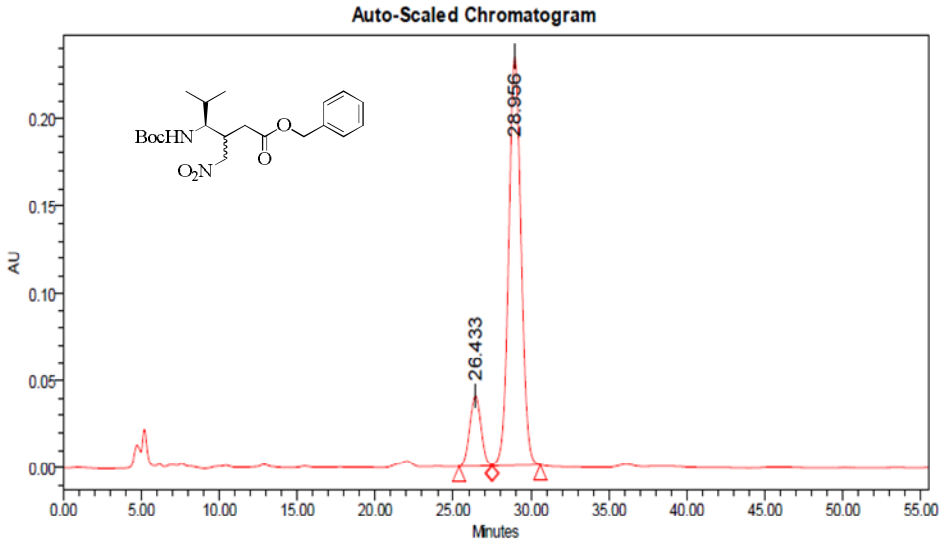
Diastereomeric ratio analysis for the compound (2i+3i):



Peak Results

	Name	RT	Area	Height	Amount	Units
1		47.976	3964415	26652		
2		52.232	6187444	37512		

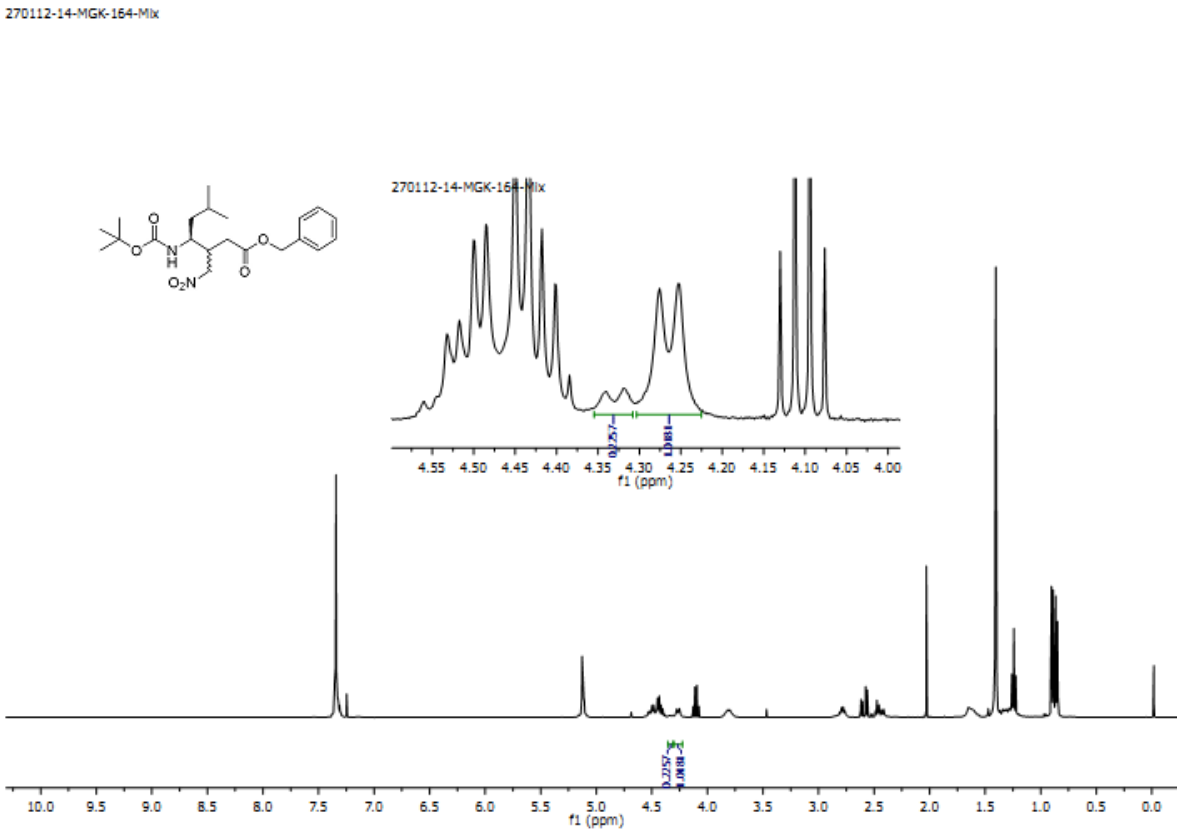
Diastereomeric ratio analysis for the compound (2j+3j):



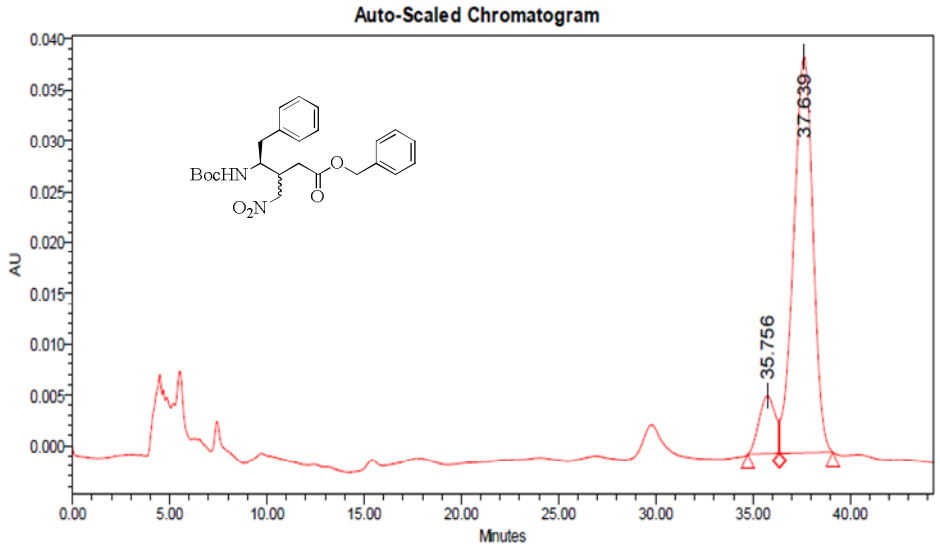
Peak Results

	Name	RT	Area	Height	Amount	Units
1		26.433	2038853	40781		
2		28.956	12890729	234460		

Diastereomeric ratio analysis for the compound (2k+3k):



Diastereomeric ratio analysis for the compound (2l+3l):



Peak Results

	Name	RT	Area	Height	Amount	Units
1		35.756	328876	5747		
2		37.639	2688665	38908