

# **A Multigram-Scale Lower E-Factor Procedure for MIBA-Catalyzed Direct Amidation and Its Application to the Coupling of alpha and beta Aminoacids**

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## **SUPPORTING INFORMATION**

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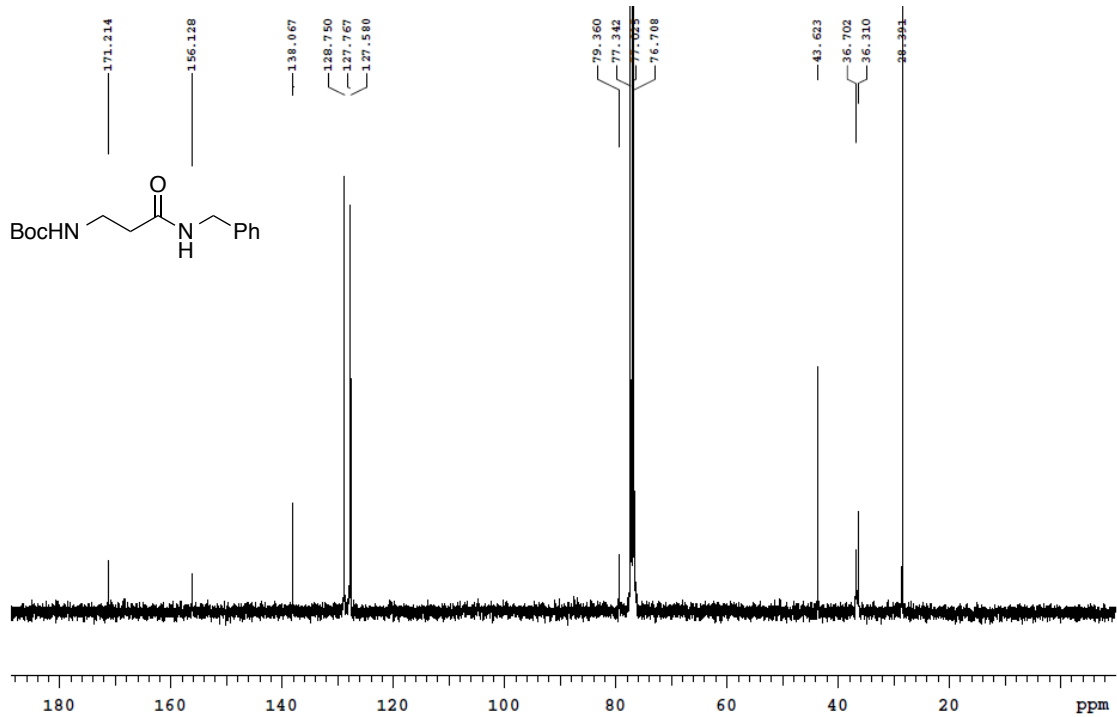
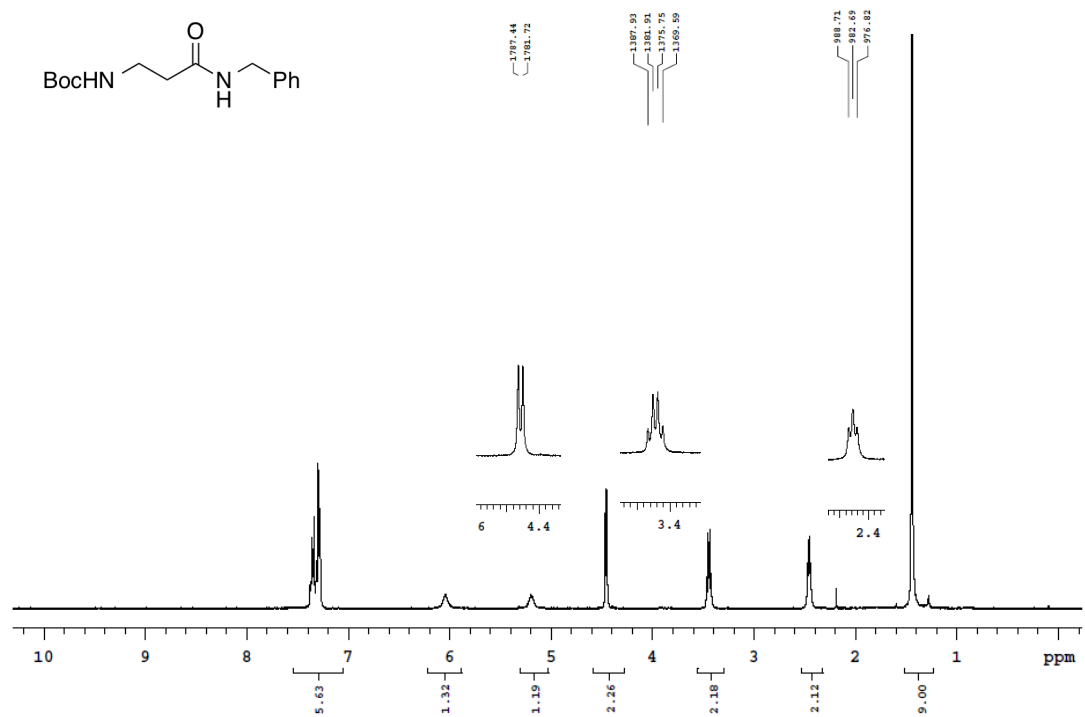
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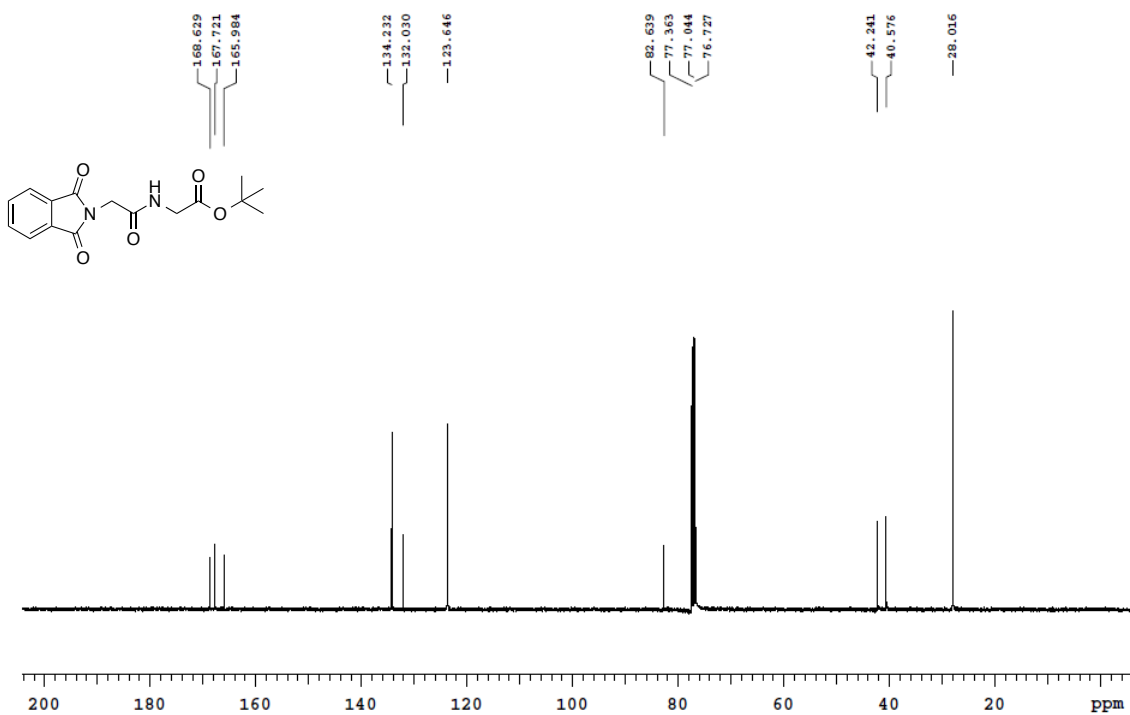
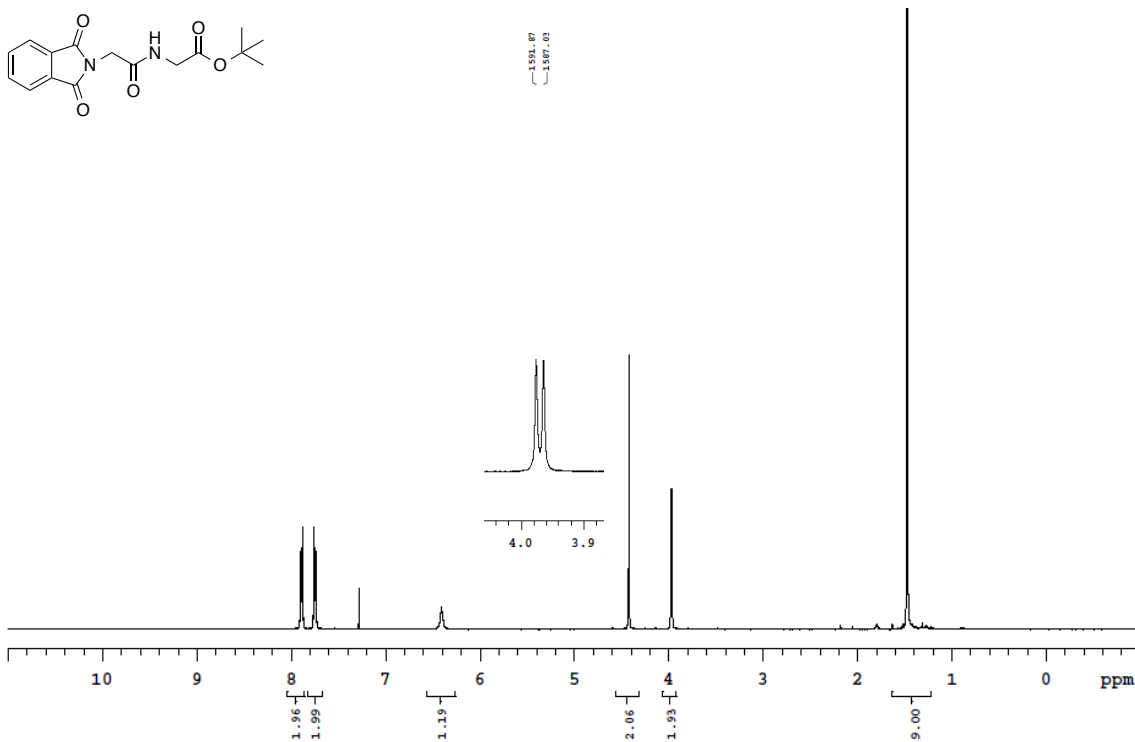
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<b>1- Stereochemical integrity in the coupling of <math>\alpha</math>-aminoacids (13 and 14).....</b>	<b>S22-S23</b>
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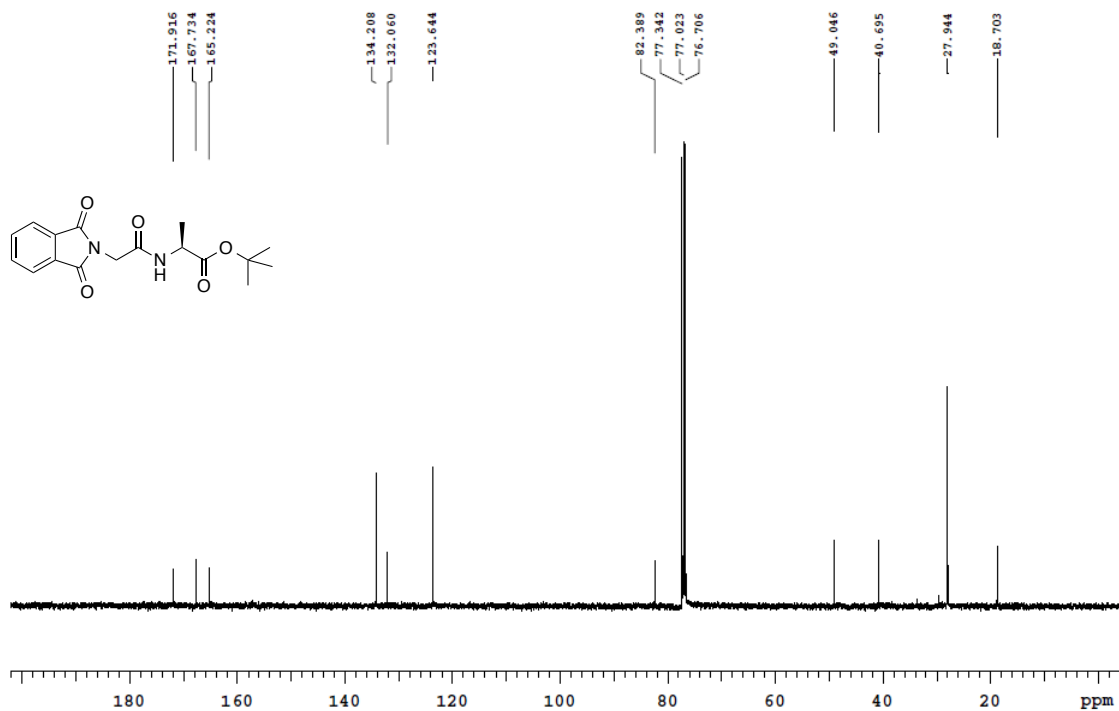
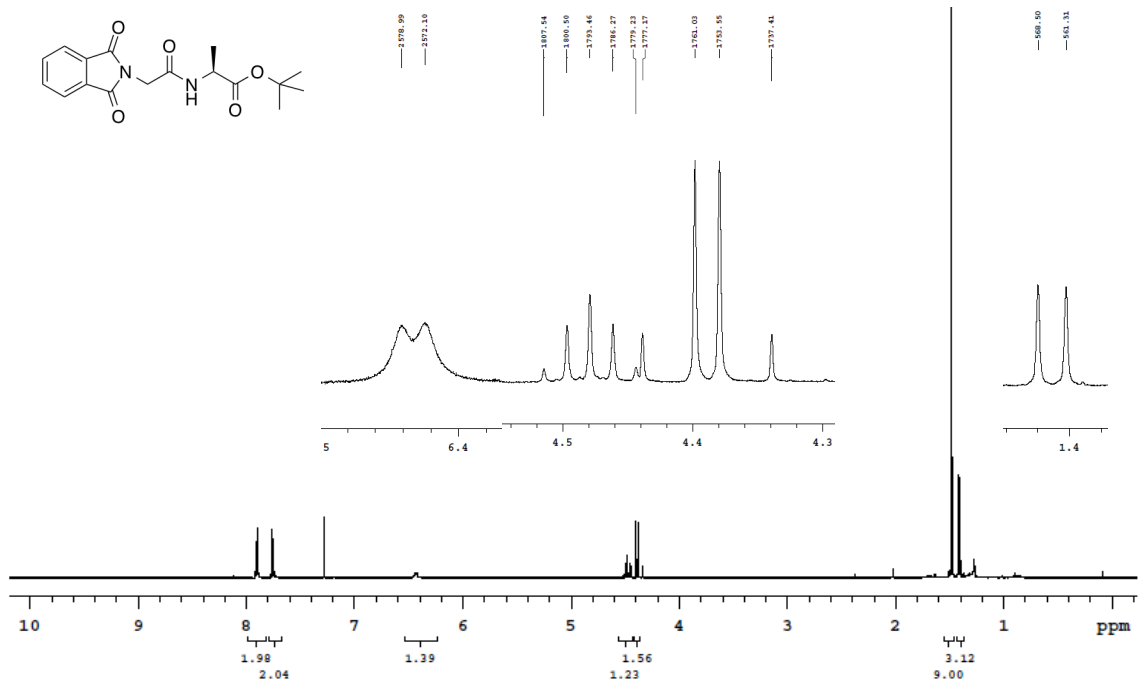
$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 25 in  $\text{CDCl}_3$  at  $27^\circ\text{C}$



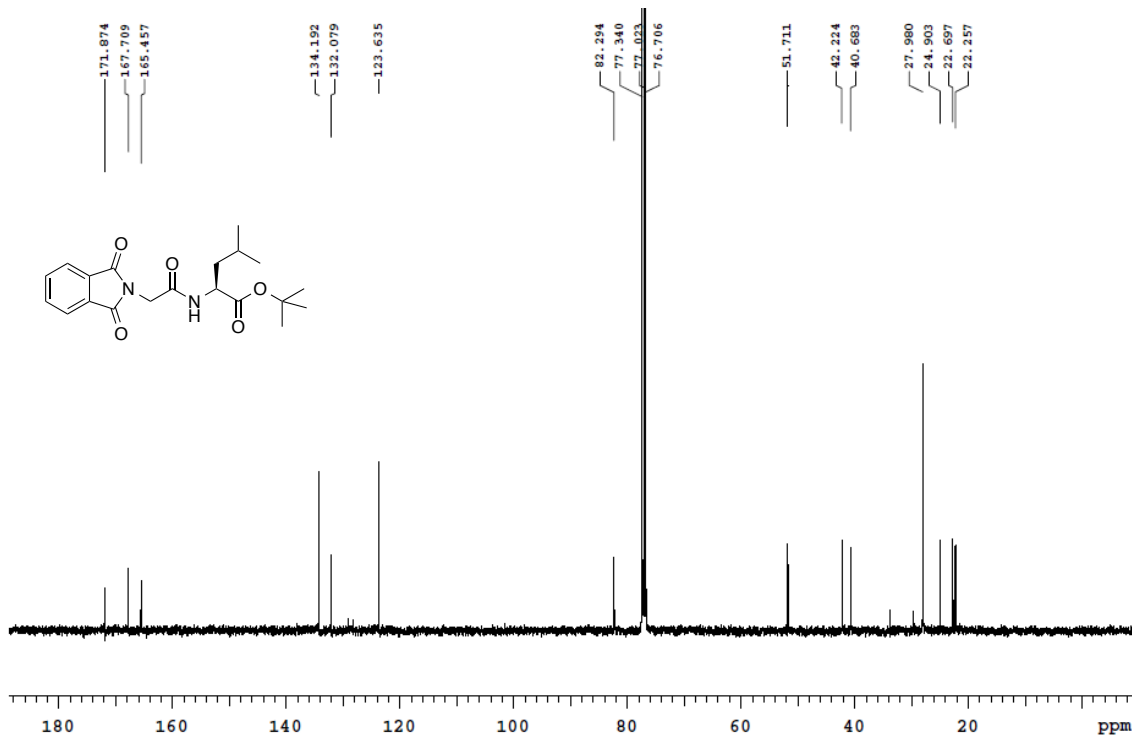
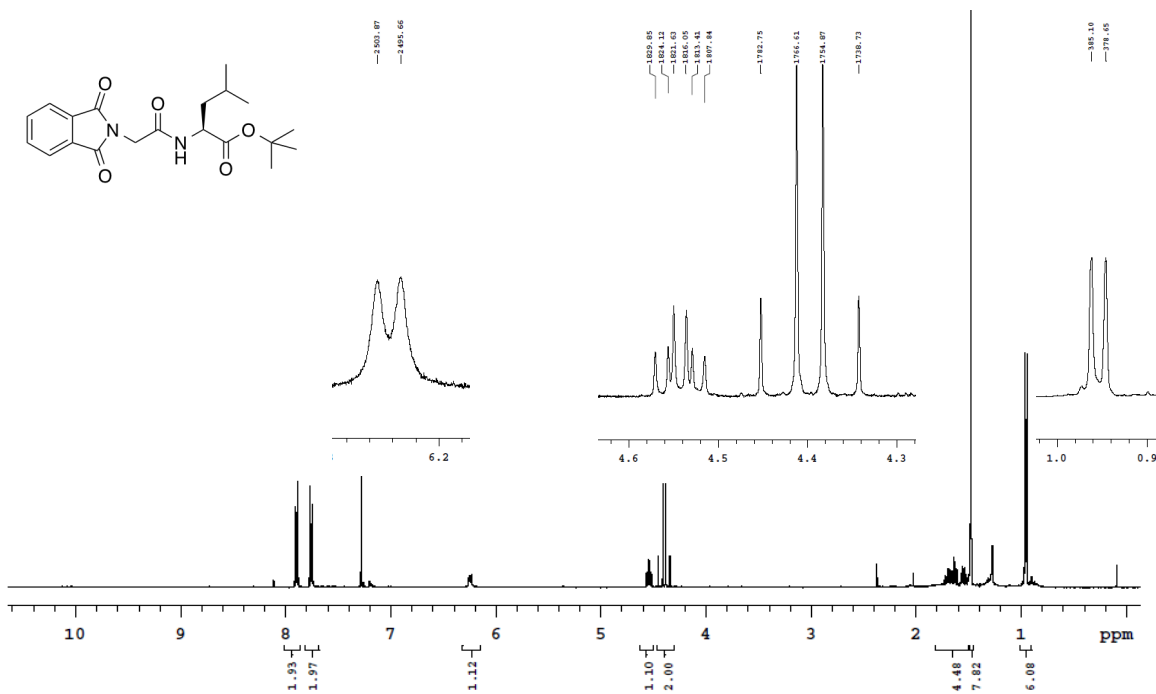
$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 32 in  $\text{CDCl}_3$  at  $27^\circ\text{C}$



**<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 33 in CDCl<sub>3</sub> at 27 °C**

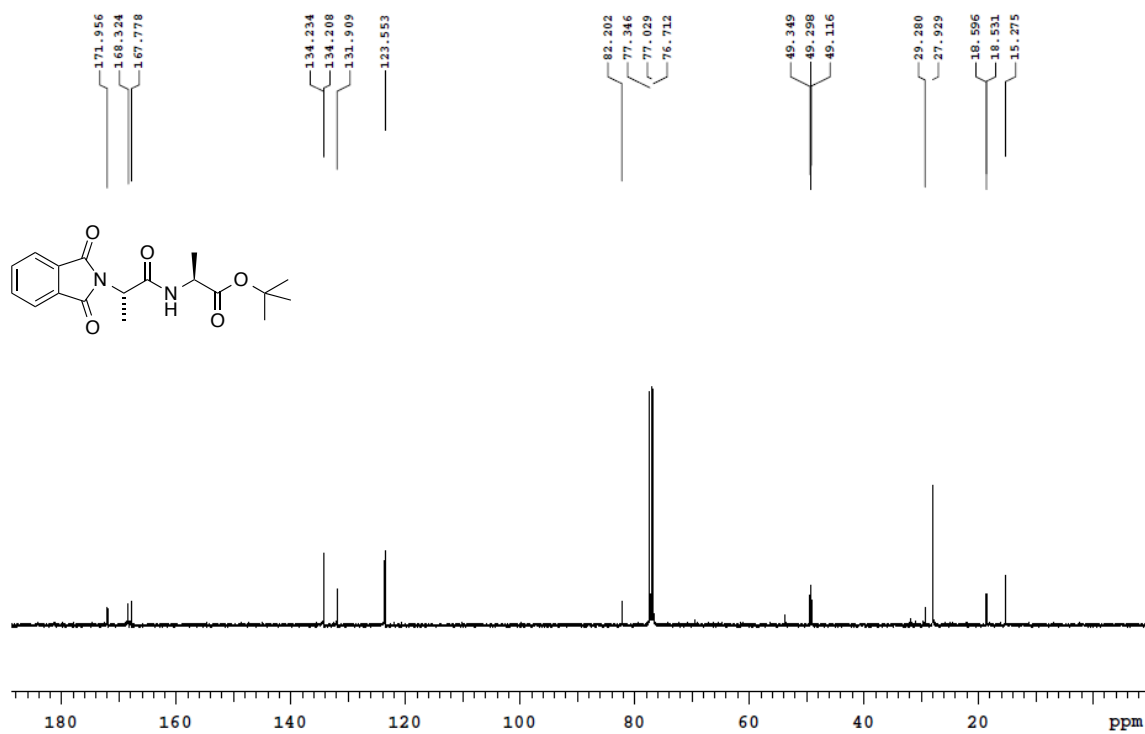
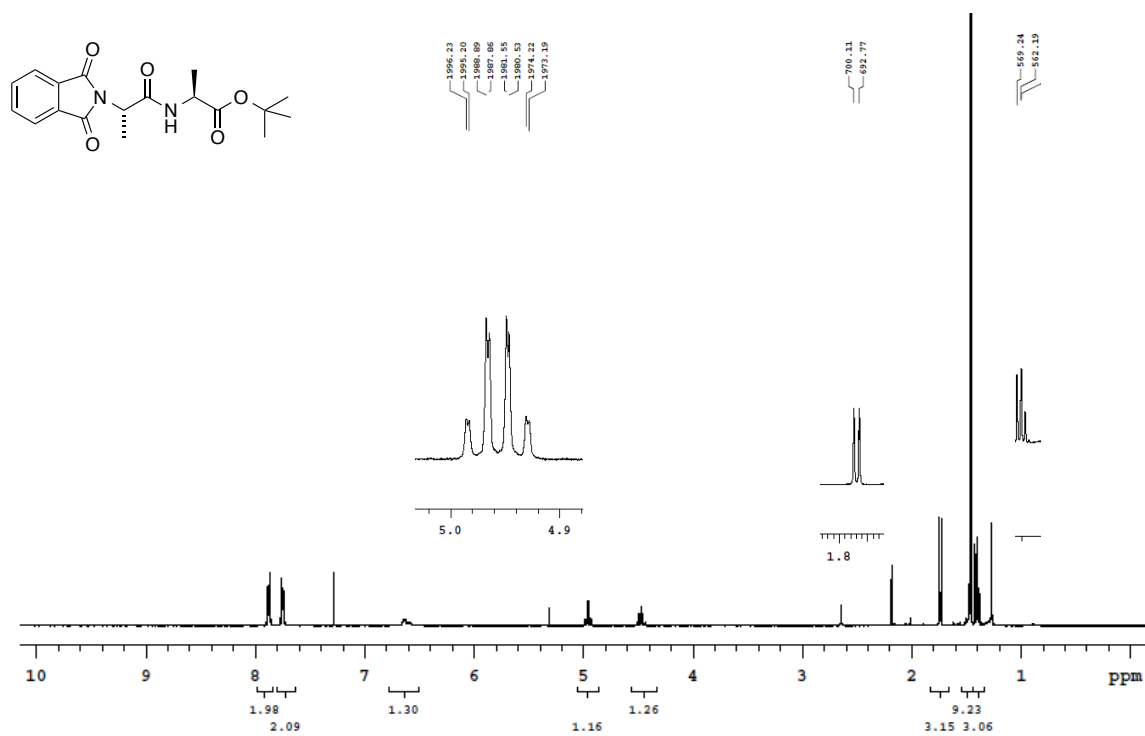


**<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 34 in CDCl<sub>3</sub> at 27 °C**

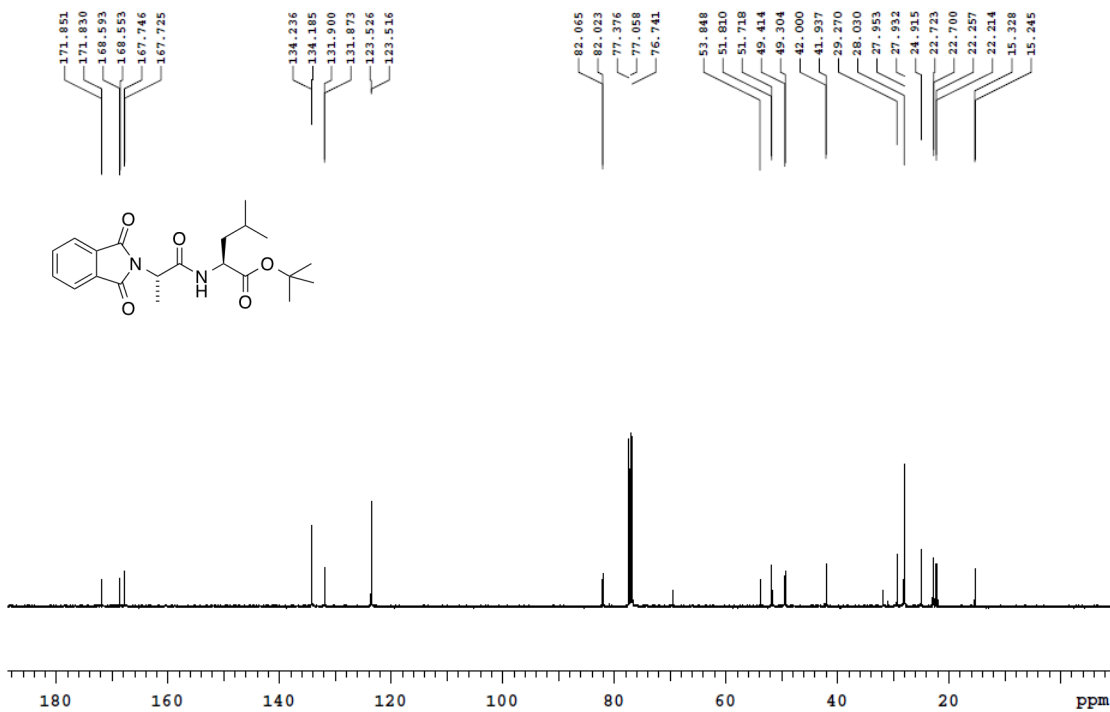
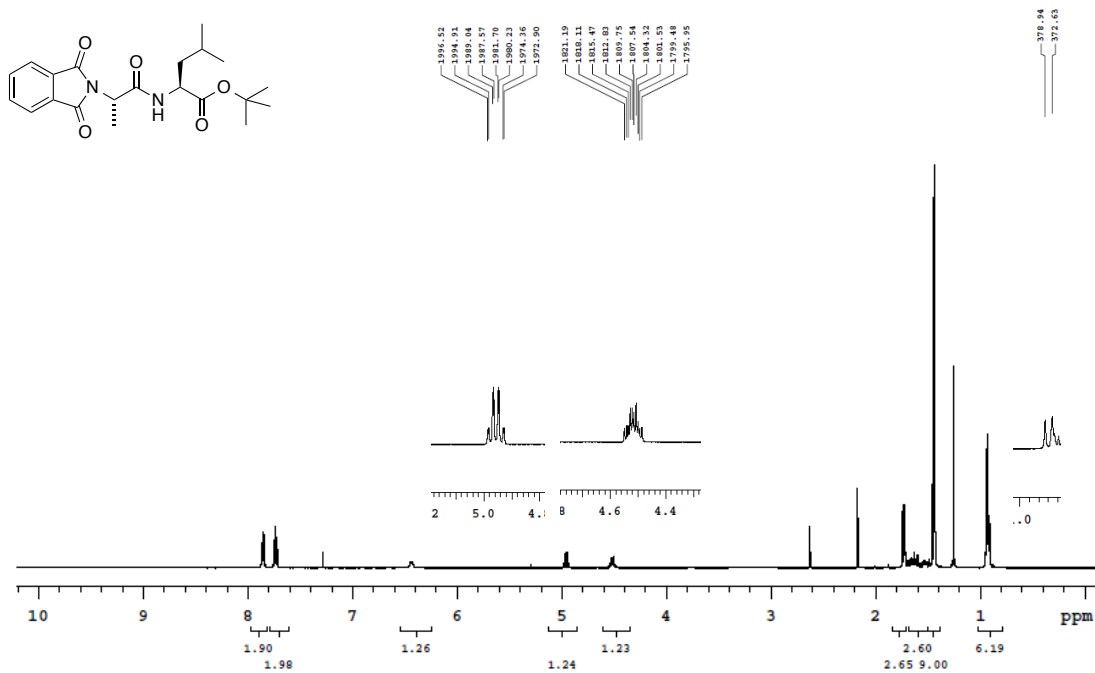




$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 36 in  $\text{CDCl}_3$  at 27 °C

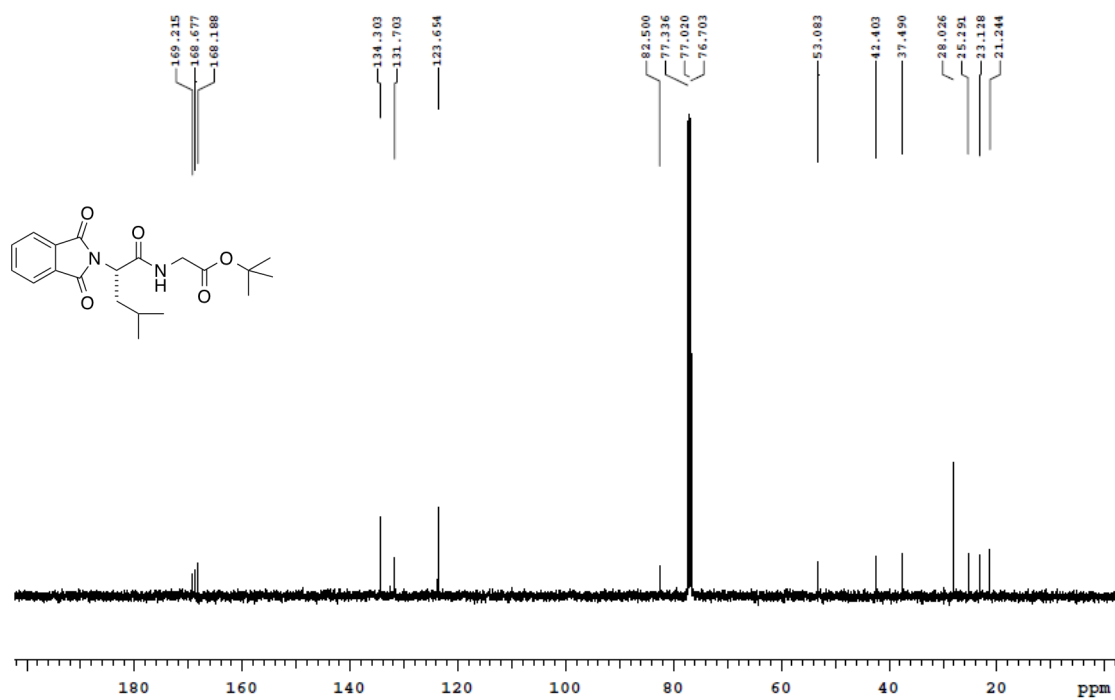
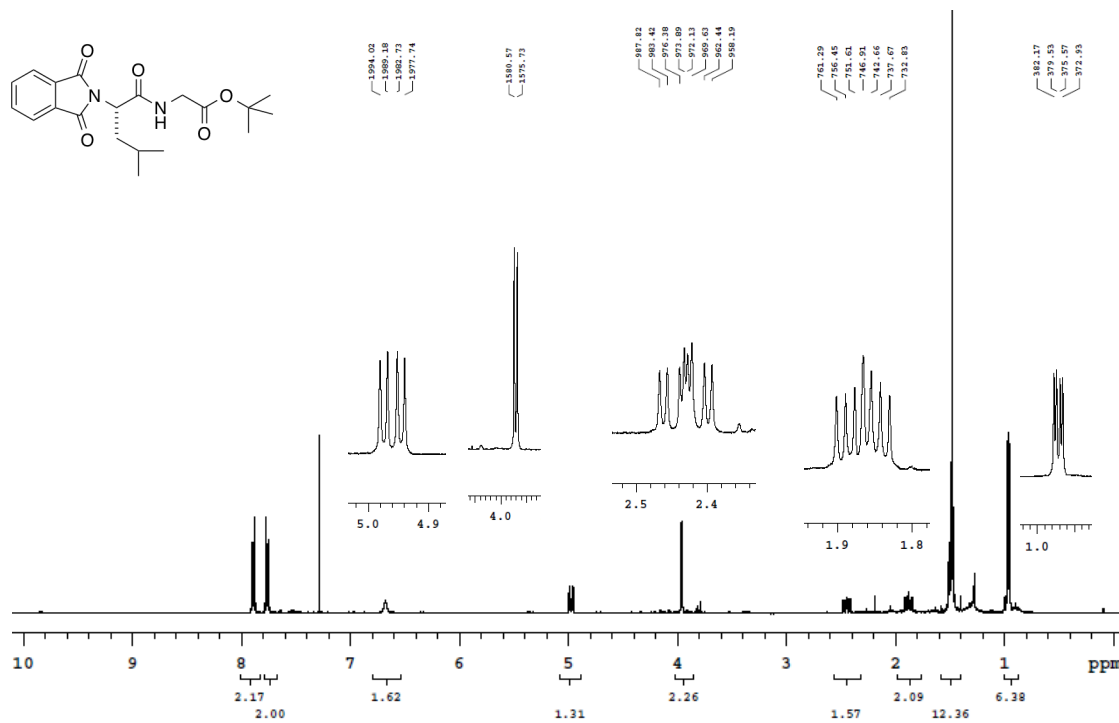


**$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 37 in  $\text{CDCl}_3$  at 27 °C**

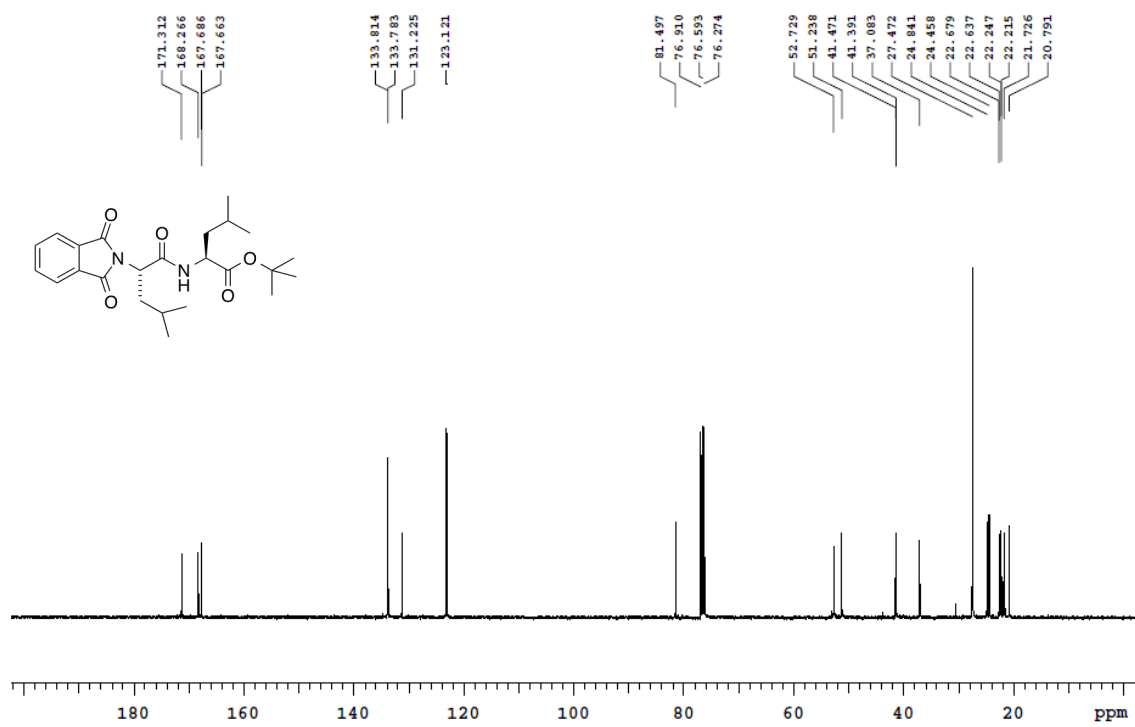
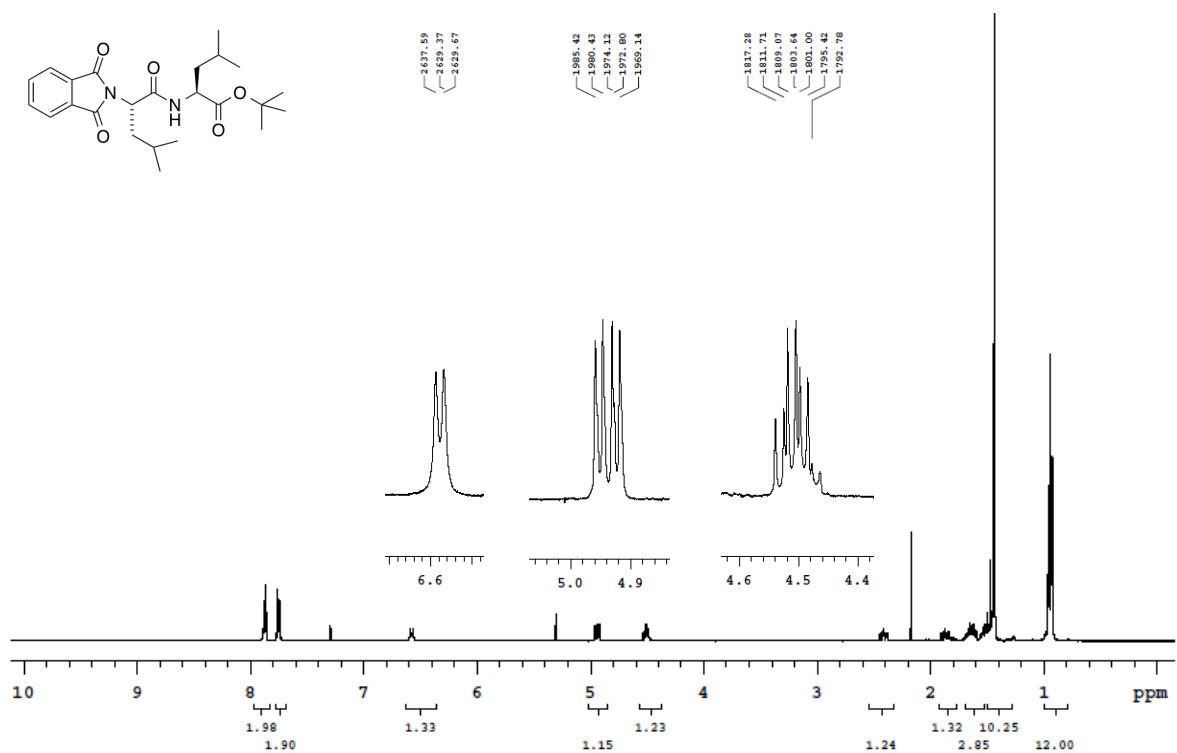




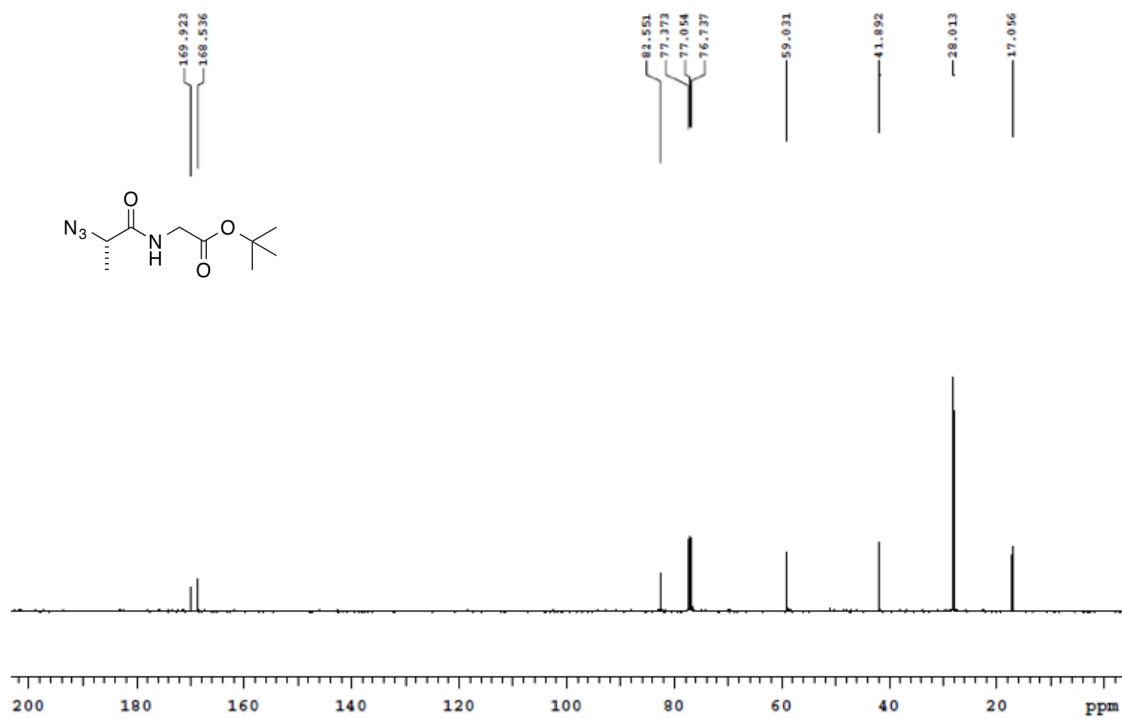
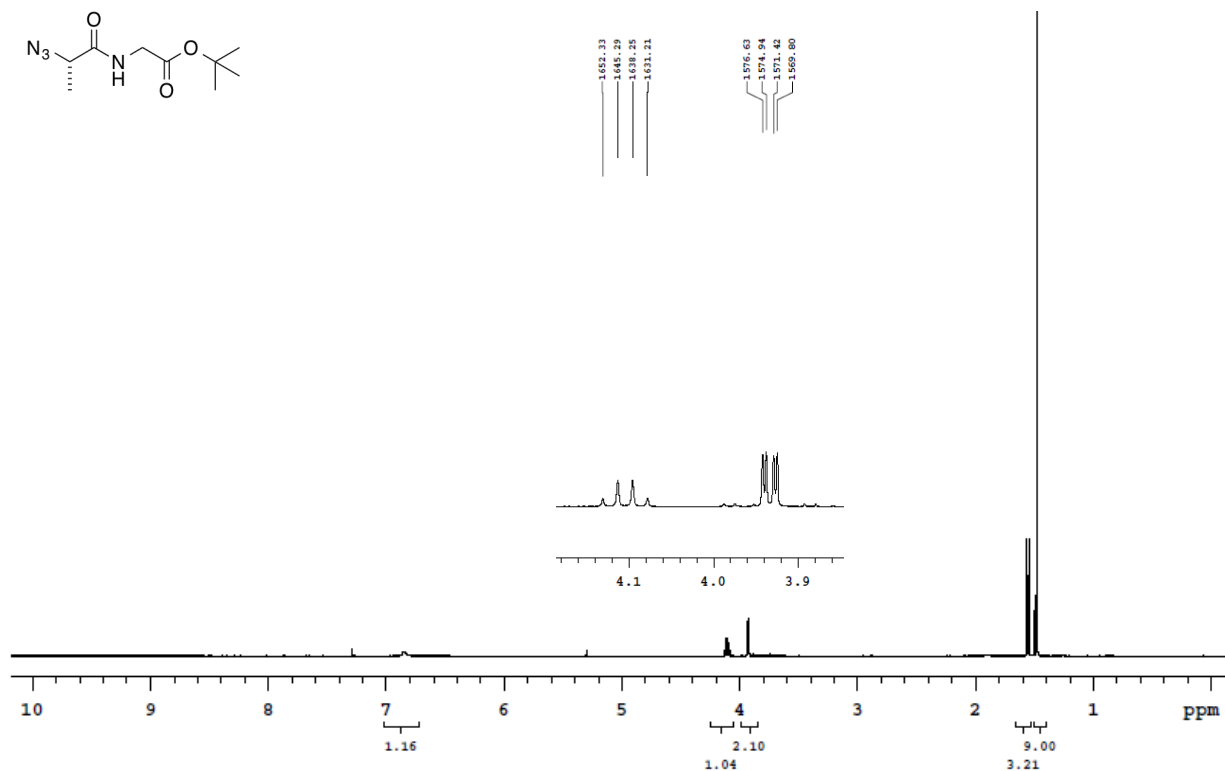
**<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 38 in CDCl<sub>3</sub> at 27 °C**



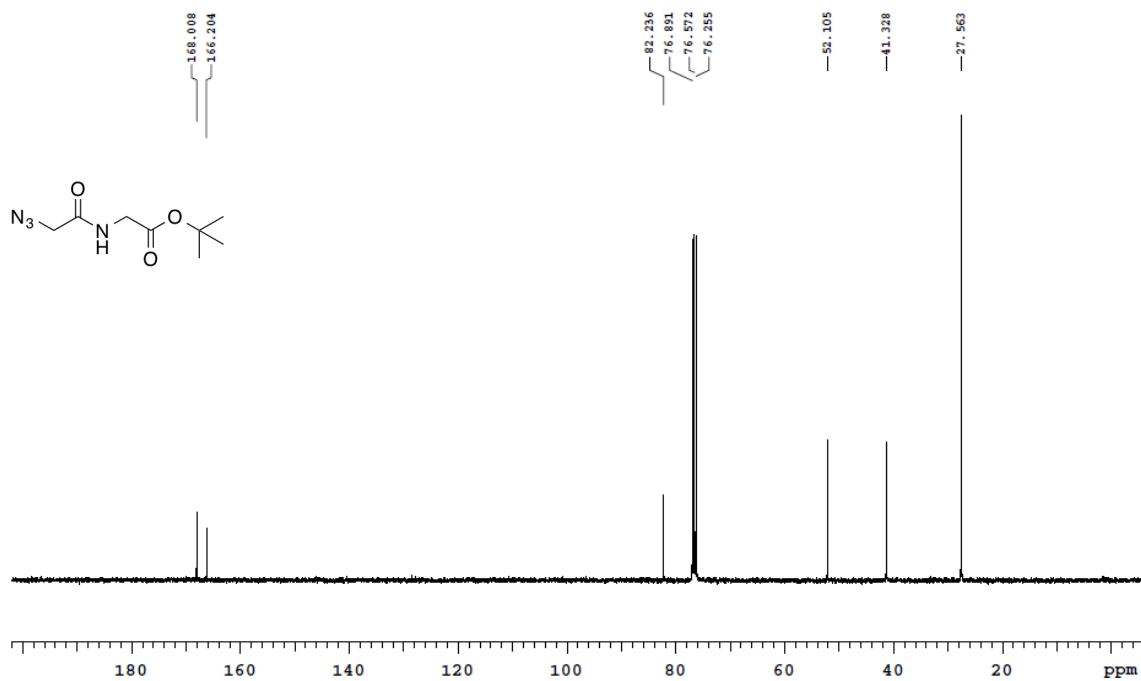
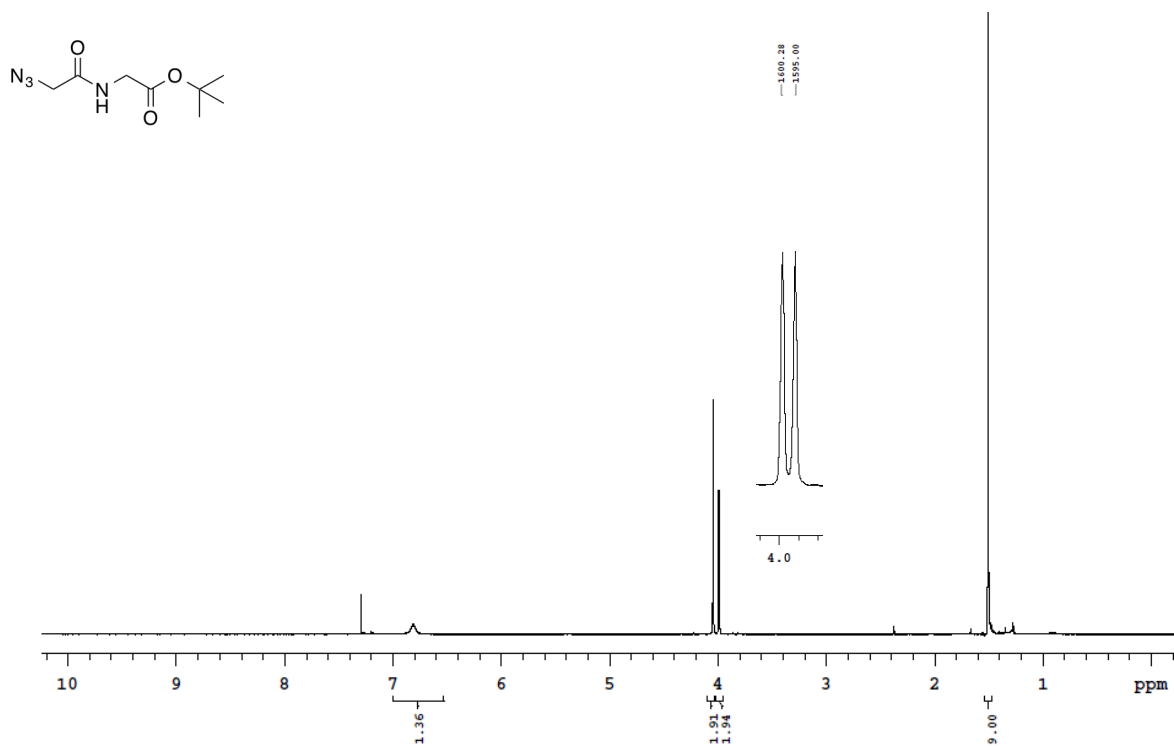
$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 39 in  $\text{CDCl}_3$  at 27 °C



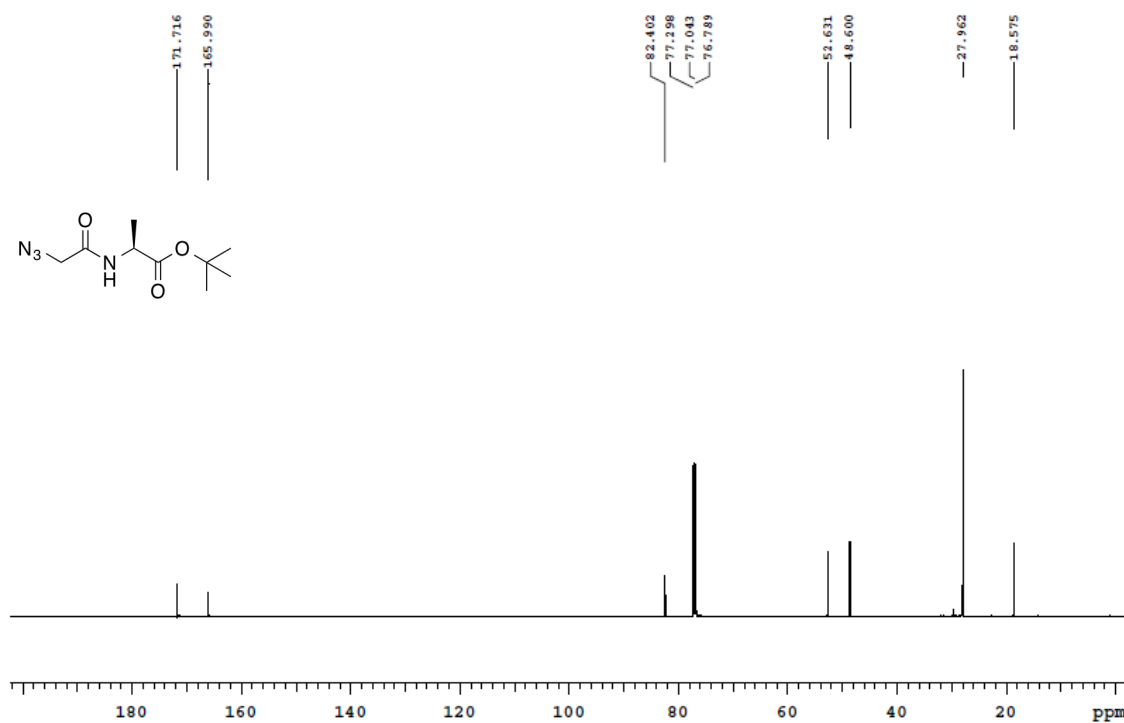
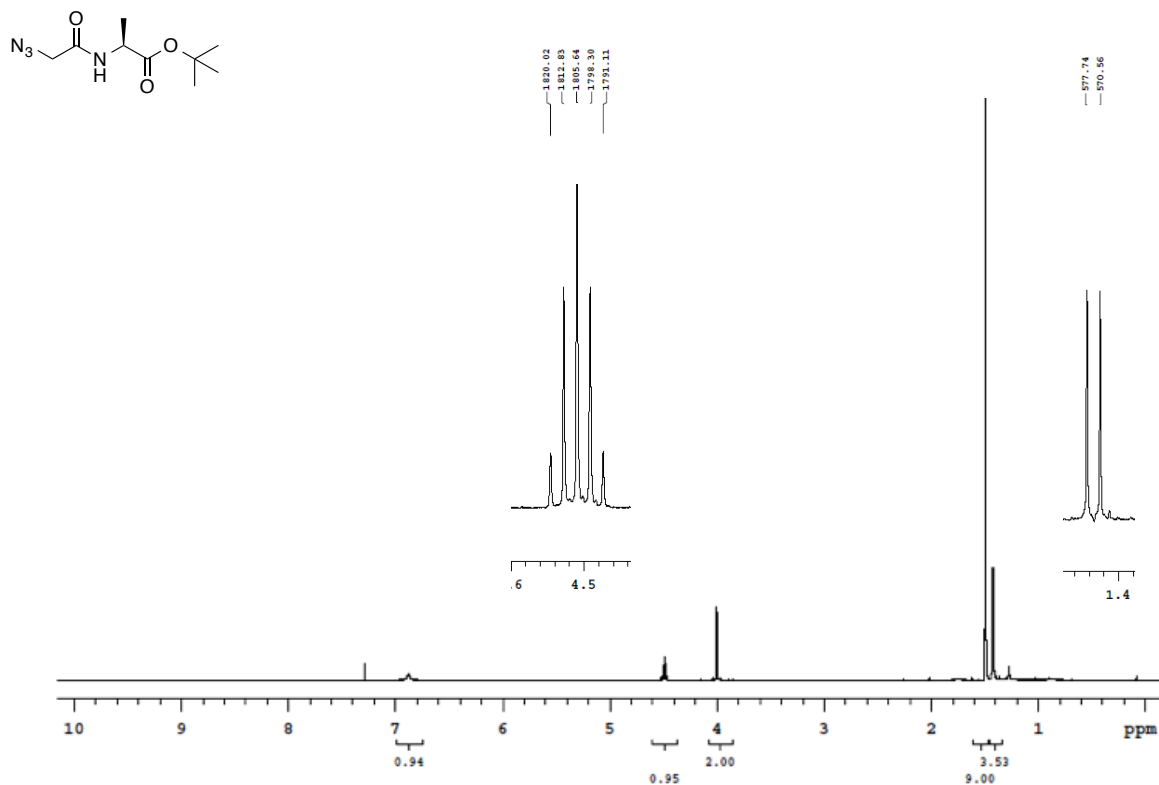
**$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 42 in  $\text{CDCl}_3$  at 27 °C**



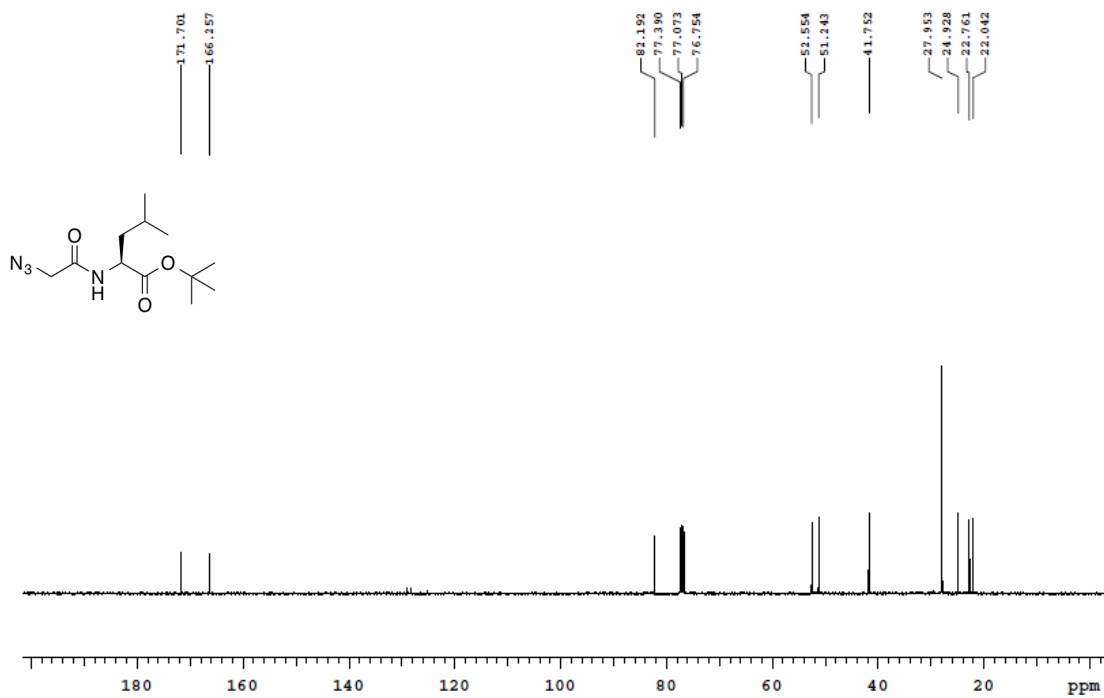
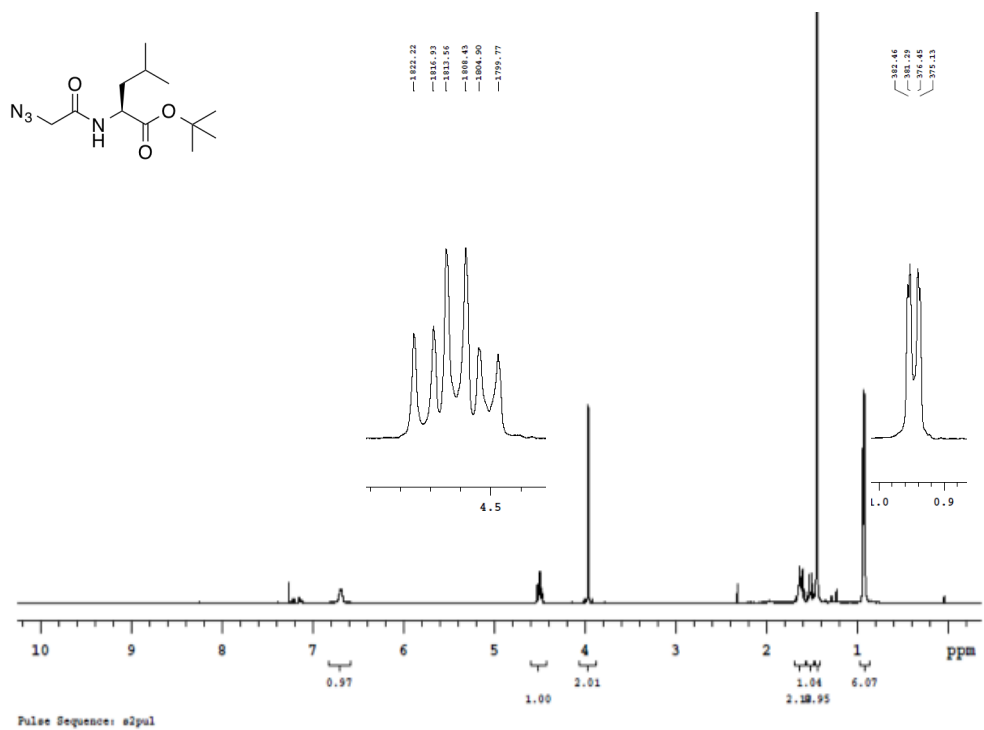
<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 43 in CDCl<sub>3</sub> at 27 °C



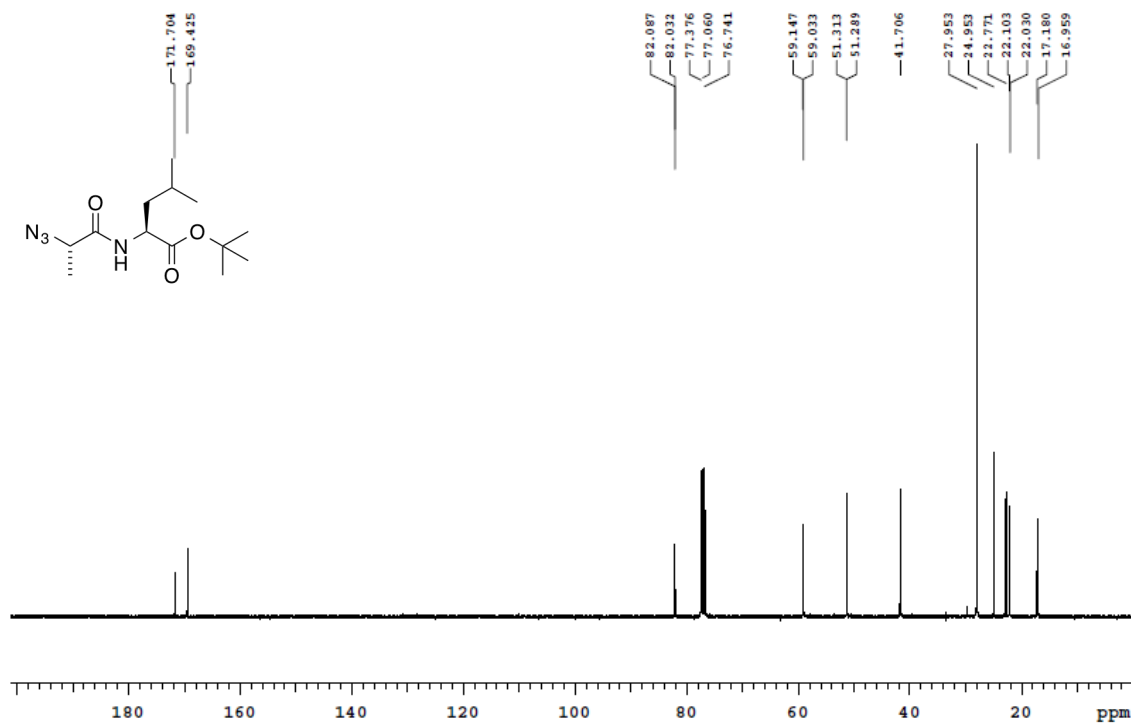
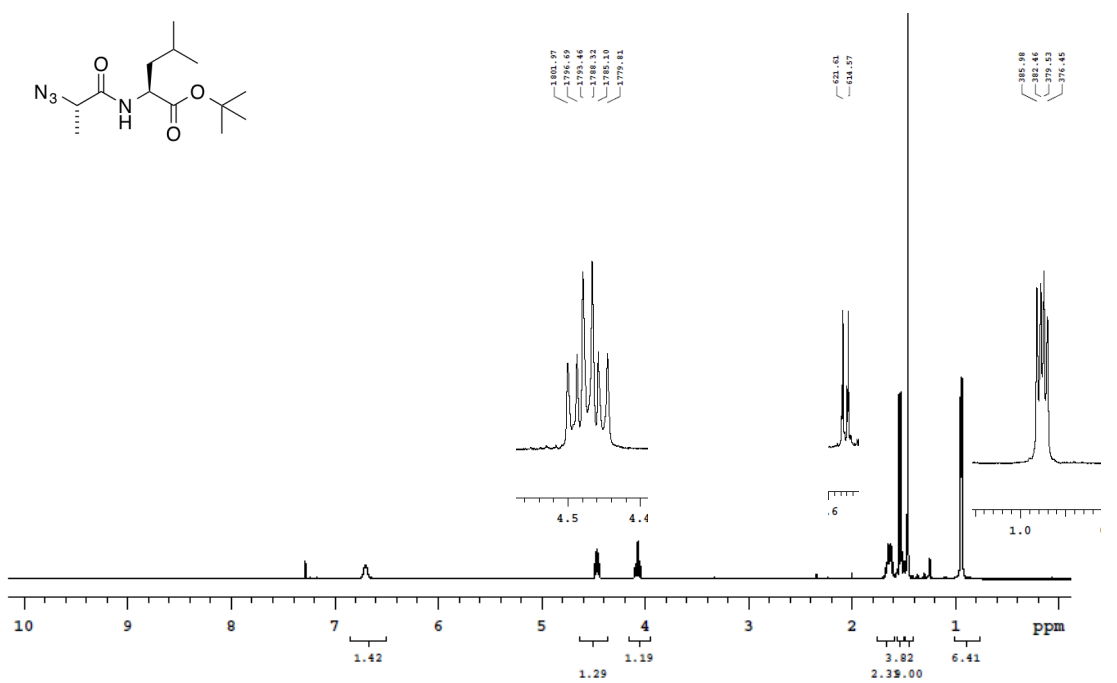
**$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 44 in  $\text{CDCl}_3$  at 27 °C**



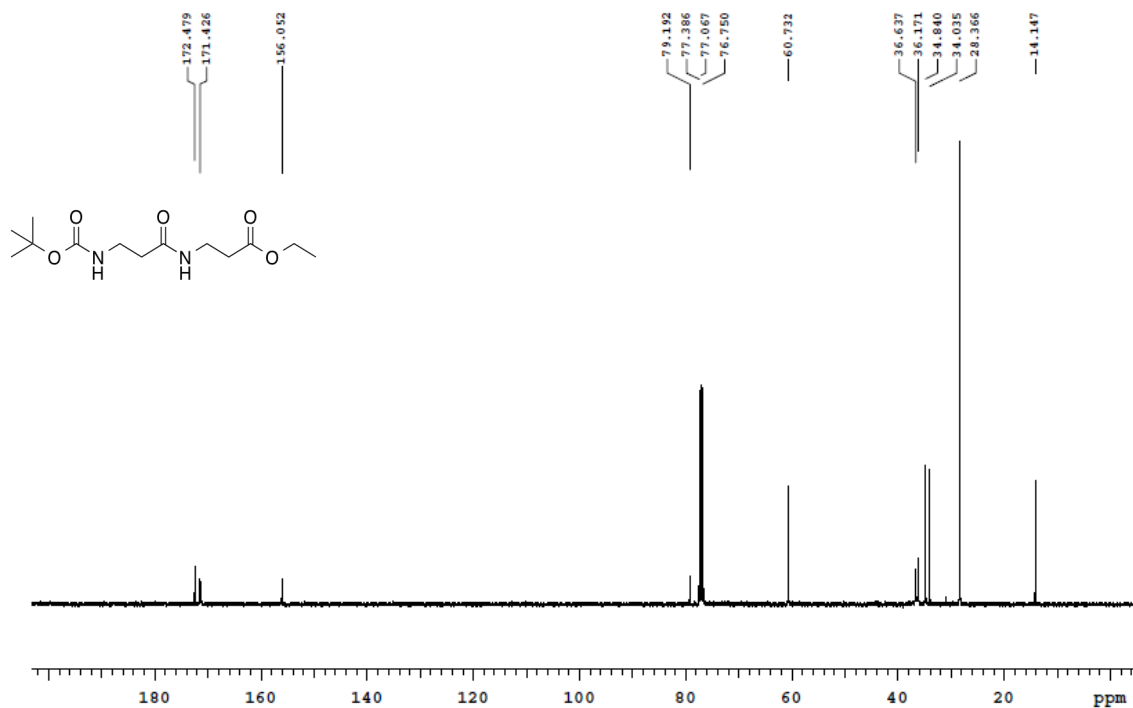
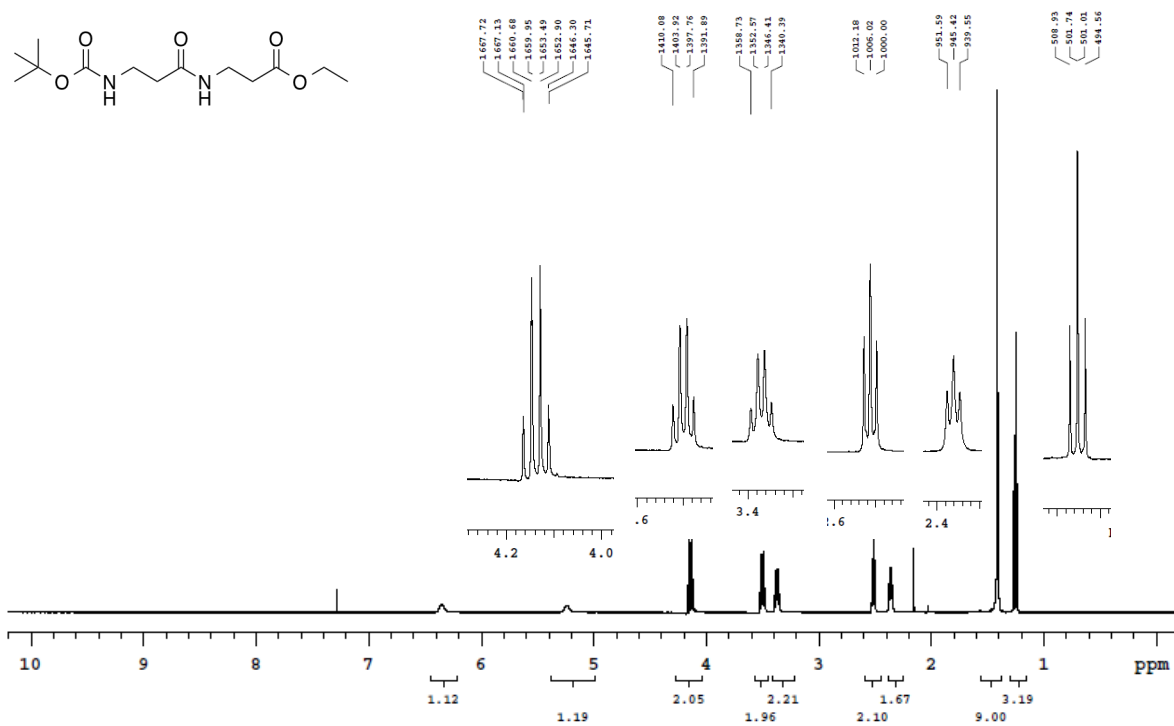
<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 45 in CDCl<sub>3</sub> at 27 °C



$^1\text{H-NMR}$  (400 MHz),  $^{13}\text{C-NMR}$  (100.6 MHz) of 46 in  $\text{CDCl}_3$  at 27 °C

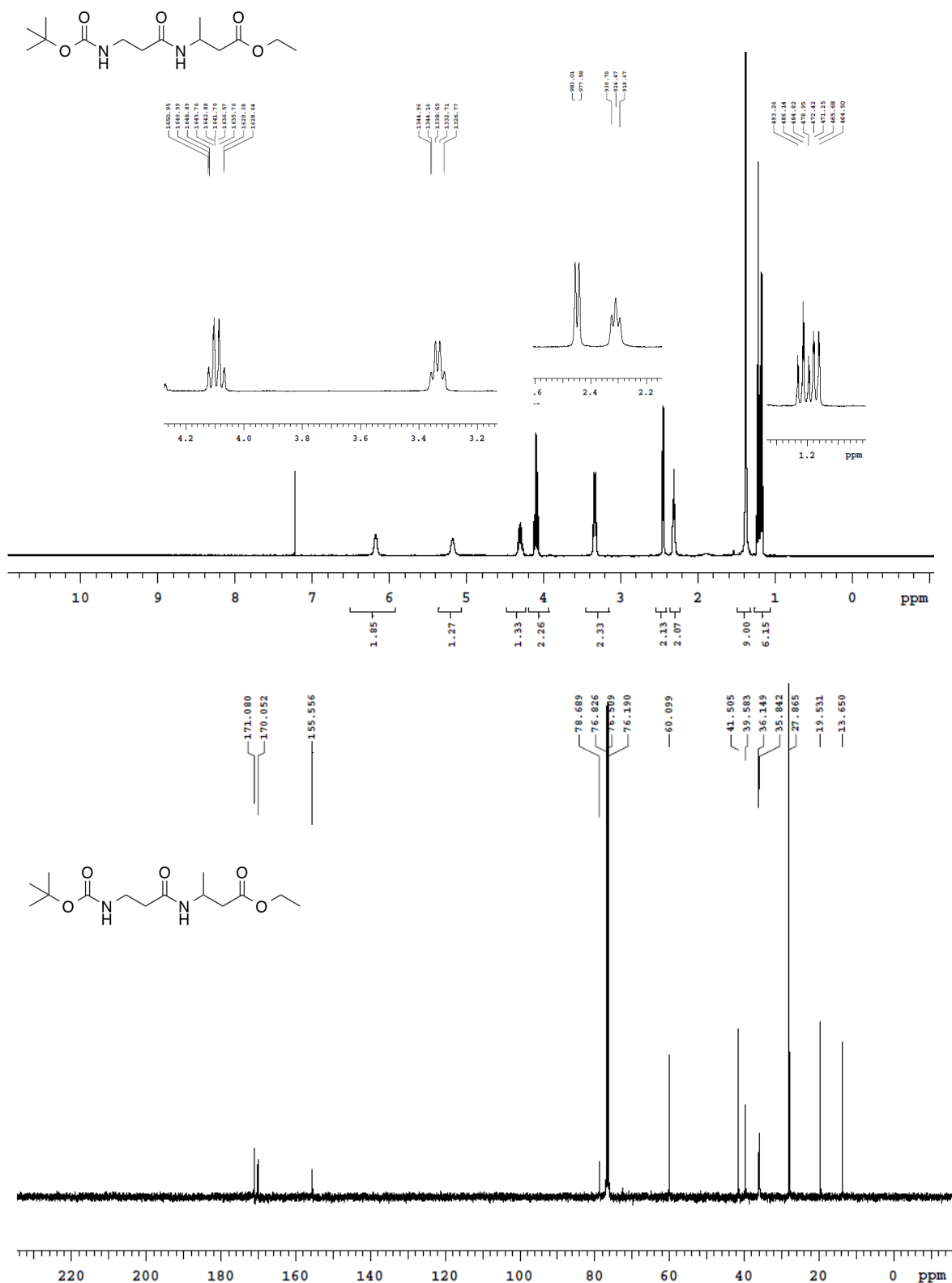


<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 48 in CDCl<sub>3</sub> at 27 °C

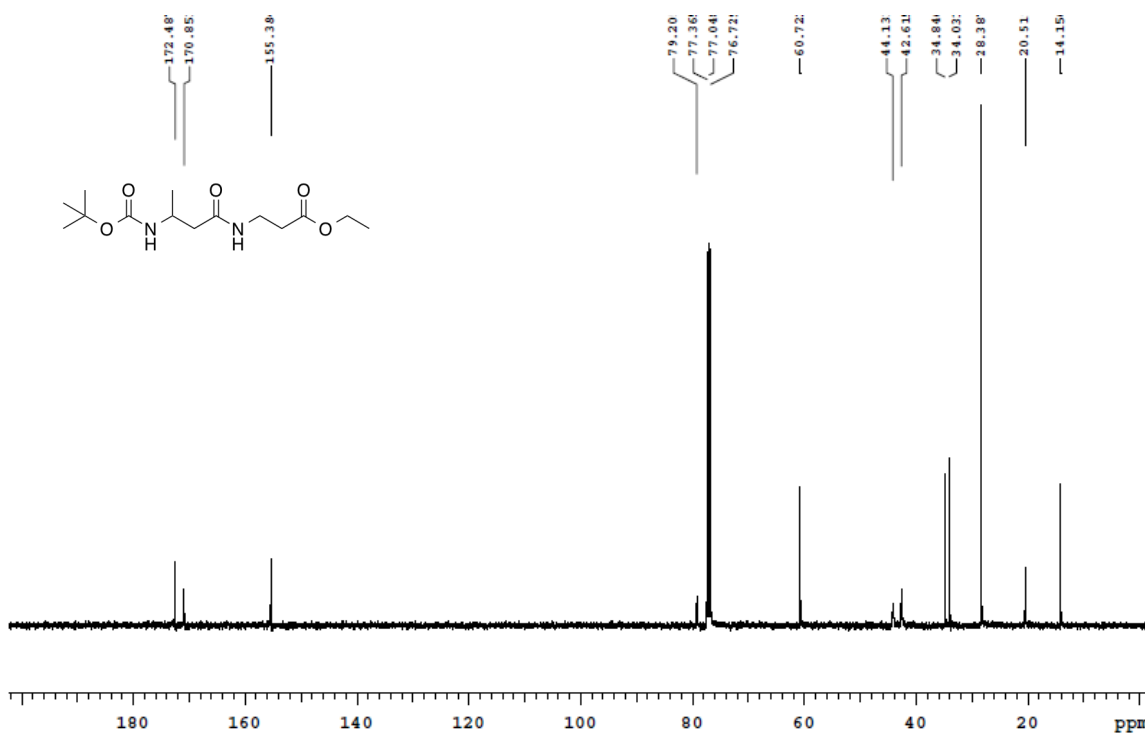
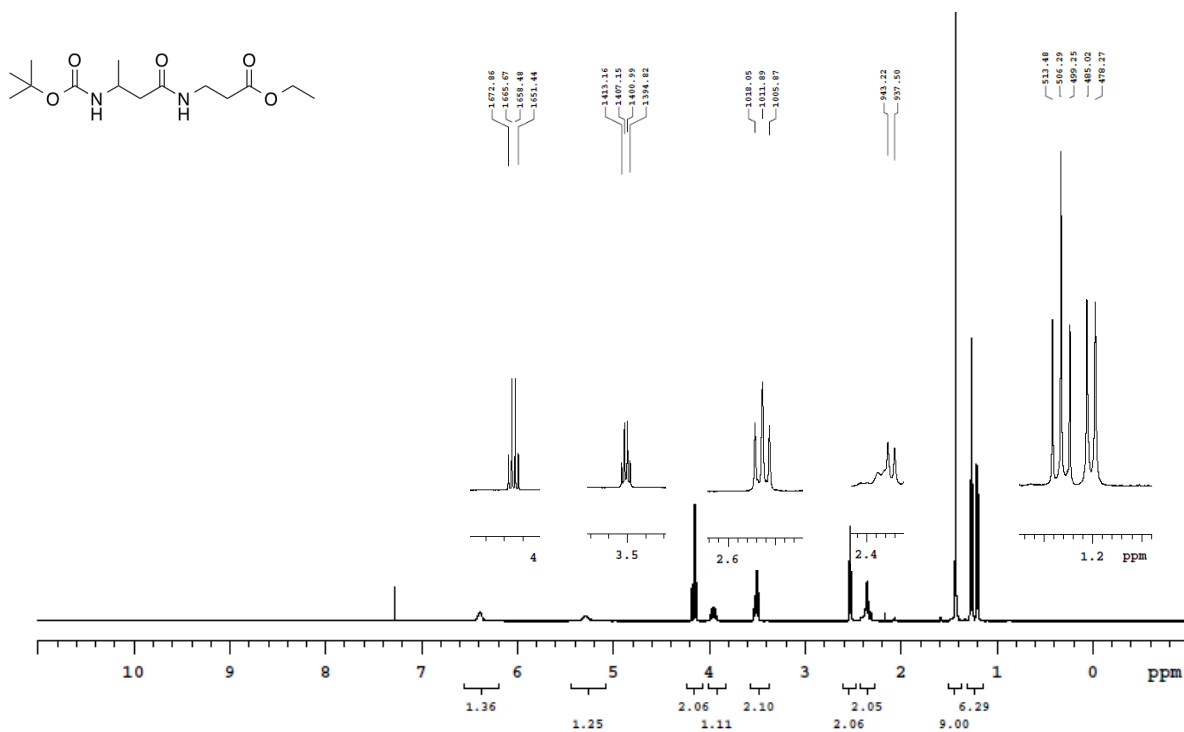




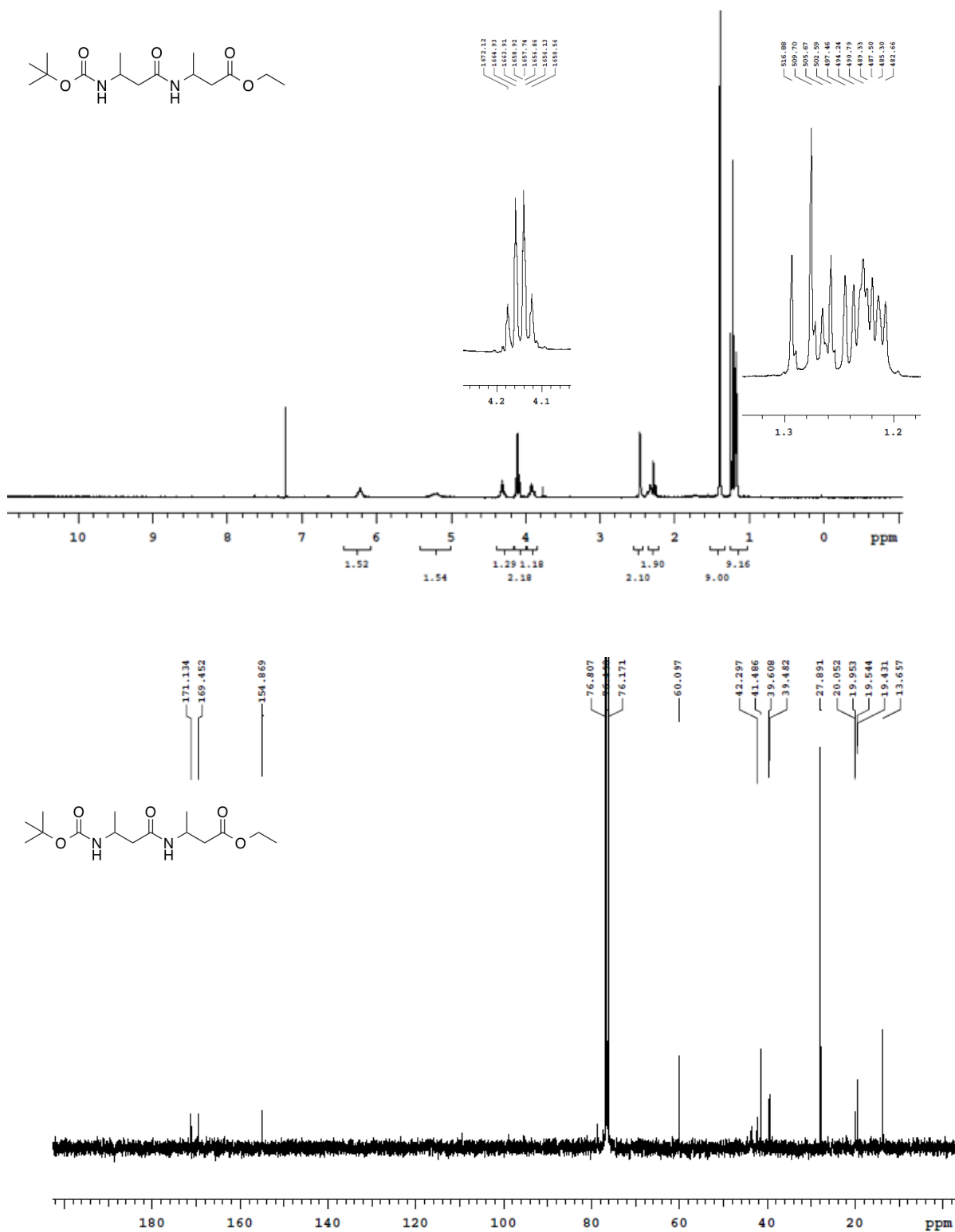
<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 51 in CDCl<sub>3</sub> at 27 °C



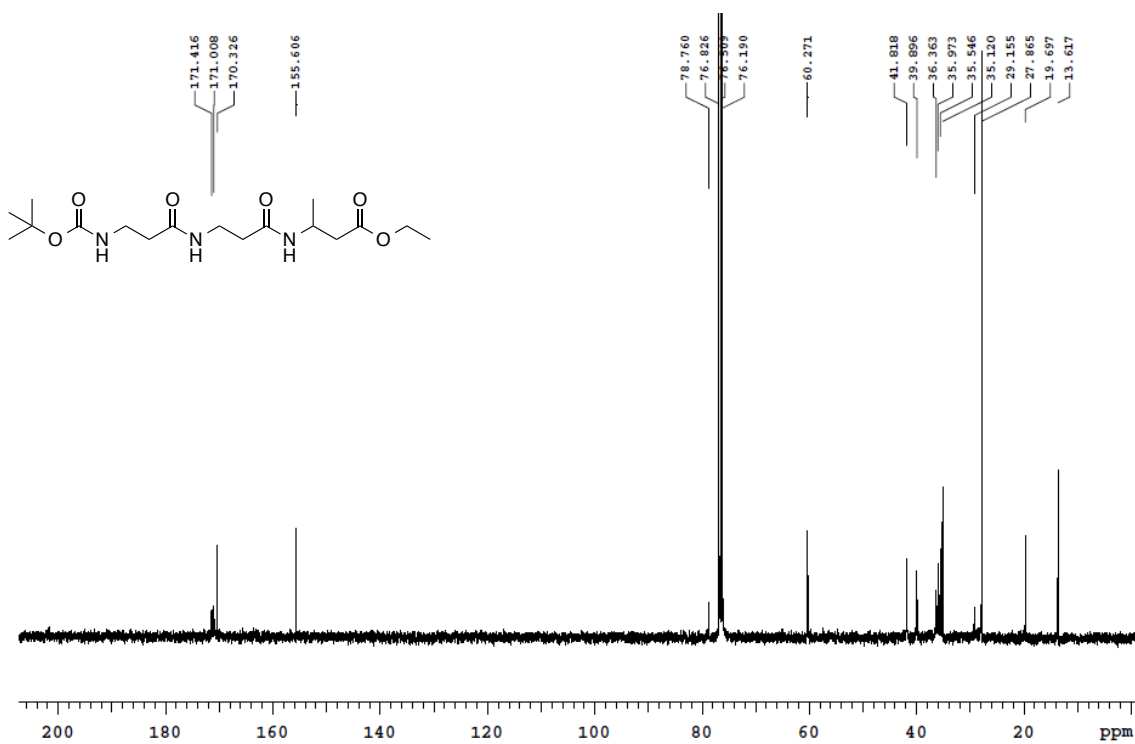
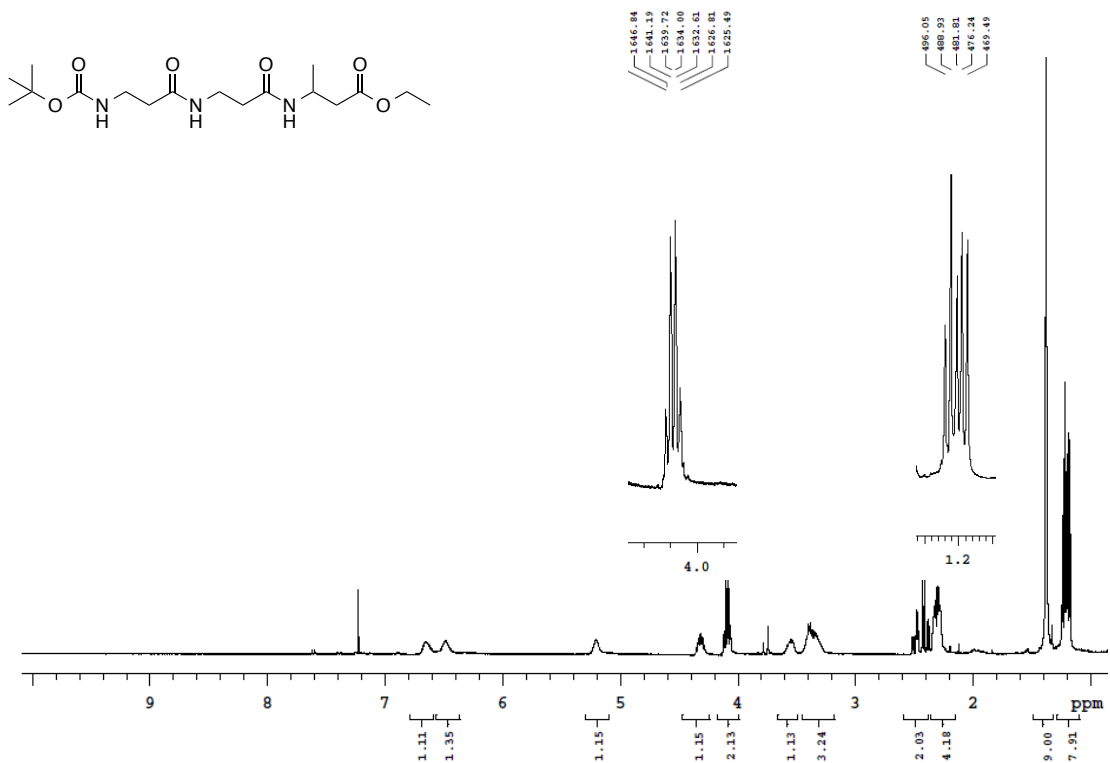
<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 52 in CDCl<sub>3</sub> at 27 °C



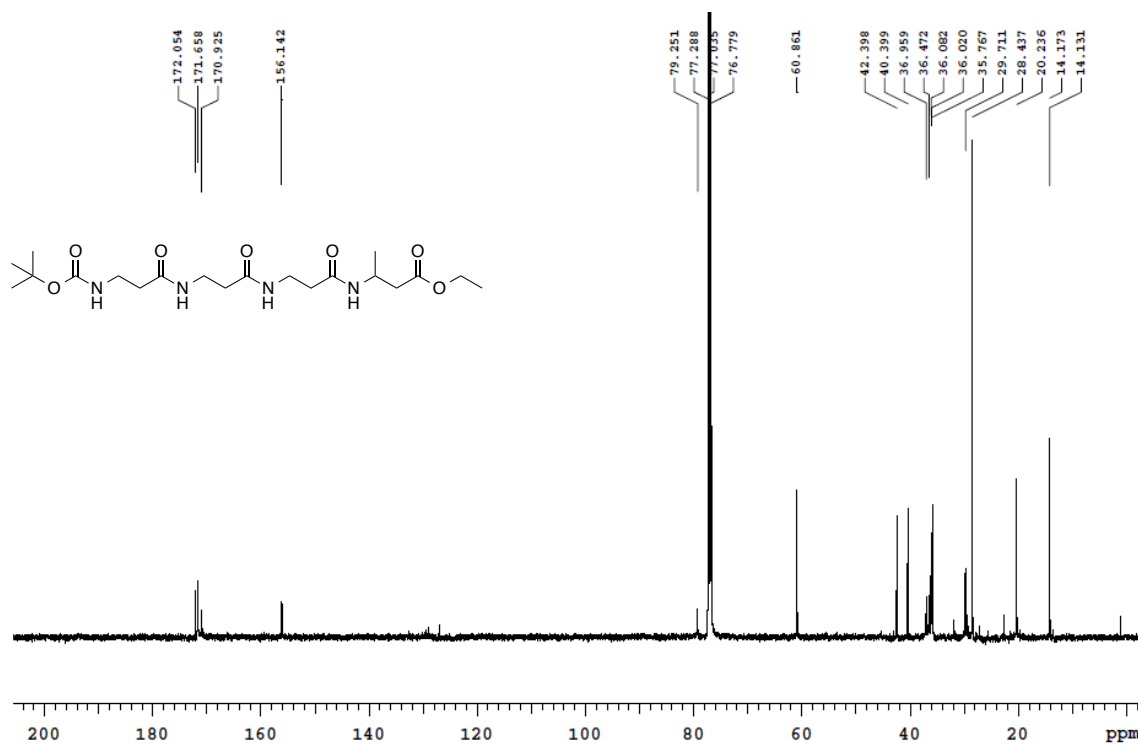
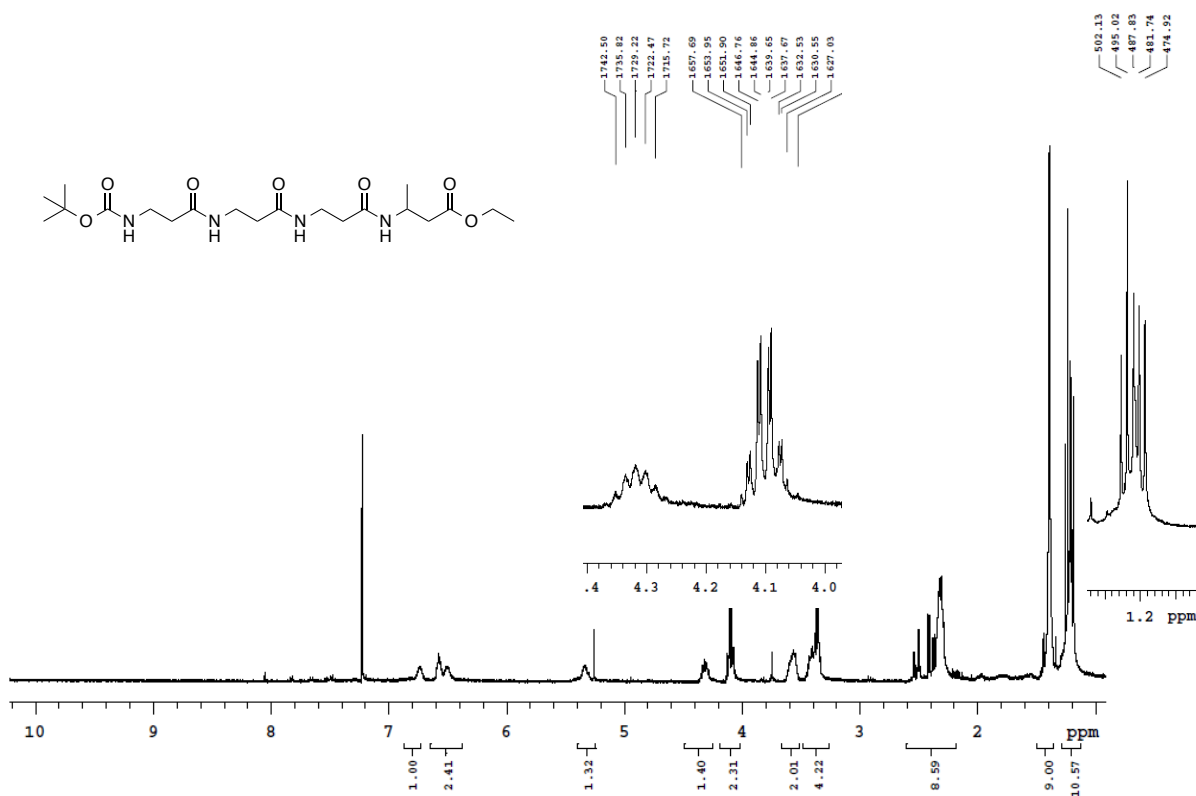
<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 53 in CDCl<sub>3</sub> at 27 °C



<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 54 in CDCl<sub>3</sub> at 27 °C

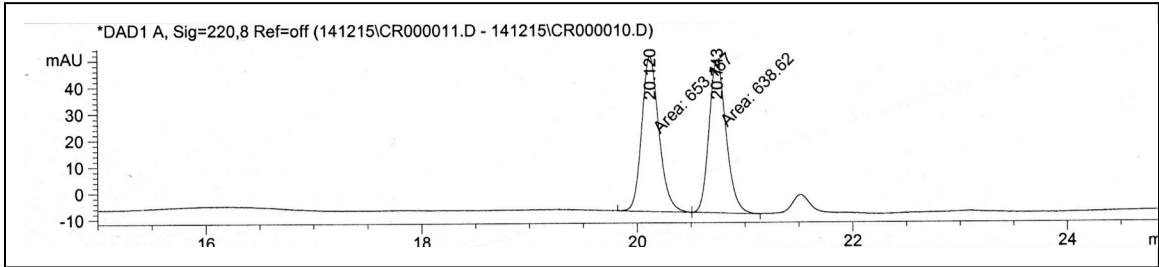
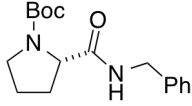


<sup>1</sup>H-NMR (400 MHz), <sup>13</sup>C-NMR (100.6 MHz) of 55 in CDCl<sub>3</sub> at 27 °C

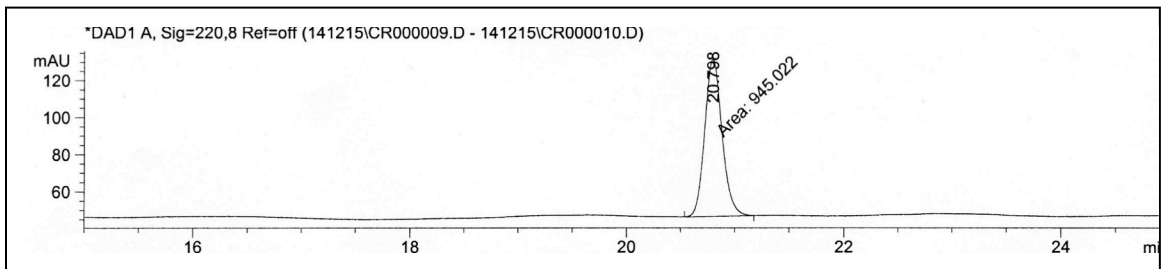


**Appendix B: Chromatograms for enantiomeric excess measurements**

**Racemic (top) and optically enriched (bottom) 13**

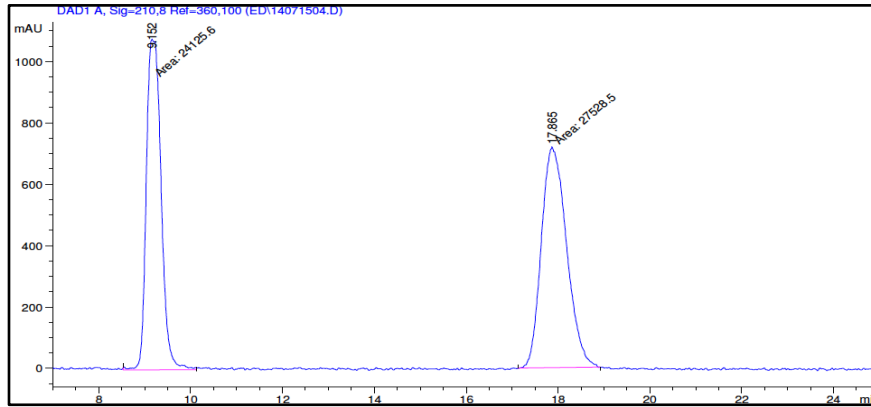
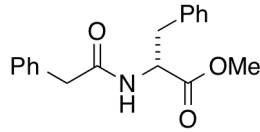


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.120	MF	0.1853	653.16650	58.76403	50.5630
2	20.743	FM	0.1832	638.61981	58.08435	49.4370
Totals :				1291.78632	116.84838	



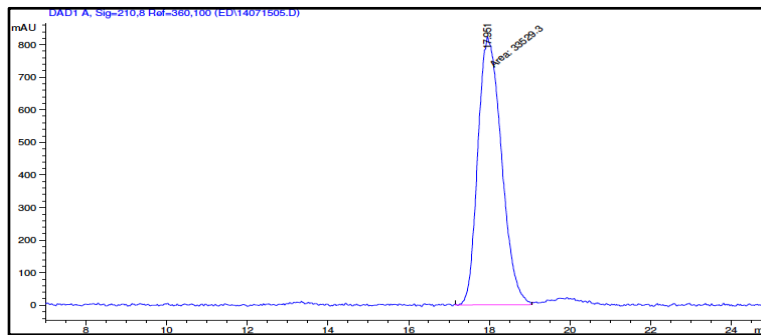
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.798	MM	0.1851	945.02228	85.07357	100.0000
Totals :				945.02228	85.07357	

**Racemic (top) and optically enriched (bottom) 14**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.859	VV	0.0757	119.50421	21.87491	0.2211
2	4.094	VV	0.1696	525.76245	38.92090	0.9726
3	4.224	VV	0.1160	324.19495	35.02998	0.5997
4	4.722	VV	0.1381	1095.04370	113.95348	2.0257
5	4.921	VV	0.1111	339.92239	41.72220	0.6288
6	9.152	MM	0.3727	2.41256e4	1078.86792	44.6287
7	17.865	MM	0.6366	2.75285e4	720.66309	50.9235

Totals : 5.40586e4 2051.03248



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.951	MM	0.6778	3.35293e4	824.52075	100.0000

Totals : 3.35293e4 824.52075