

Peptidomimetic small-molecule inhibitors of 3CLPro activity and Spike-ACE2 interaction: towards dual-action molecules against Coronavirus infections

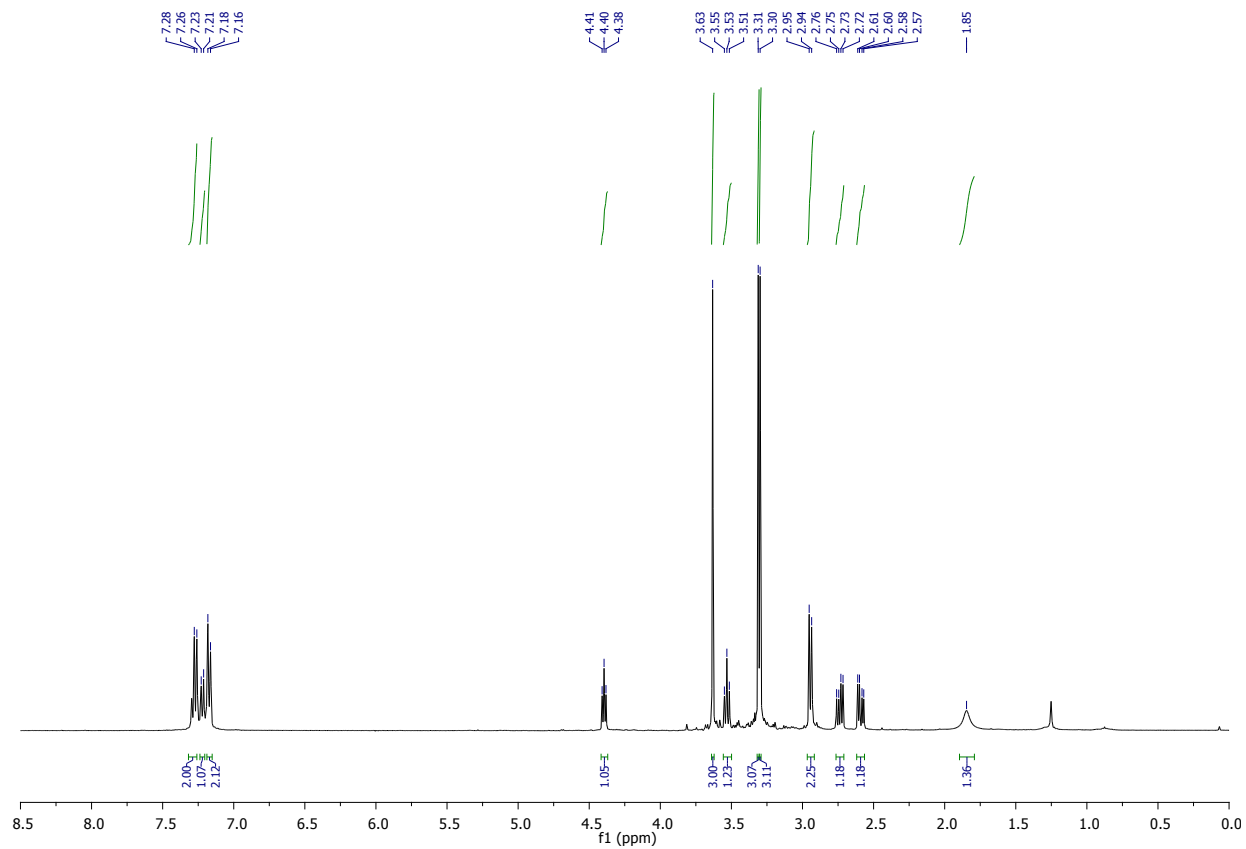
Filomena Tedesco, Lorenzo Calugi, Elena Lenci, Andrea Trabocchi*

Department of Chemistry "Ugo Schiff", University of Florence, via della Lastruccia 13, 50019 Sesto Fiorentino, Florence, Italy

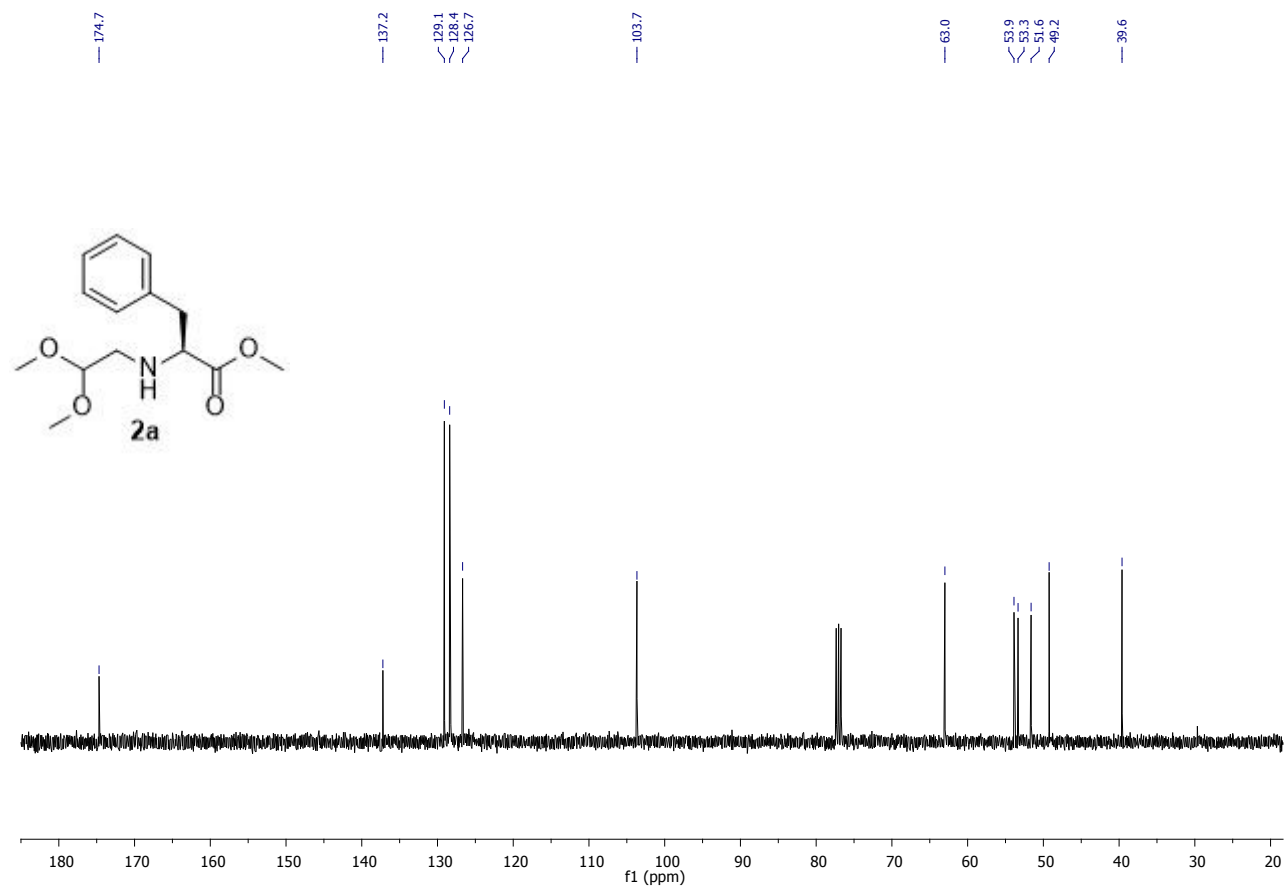
Supporting Information

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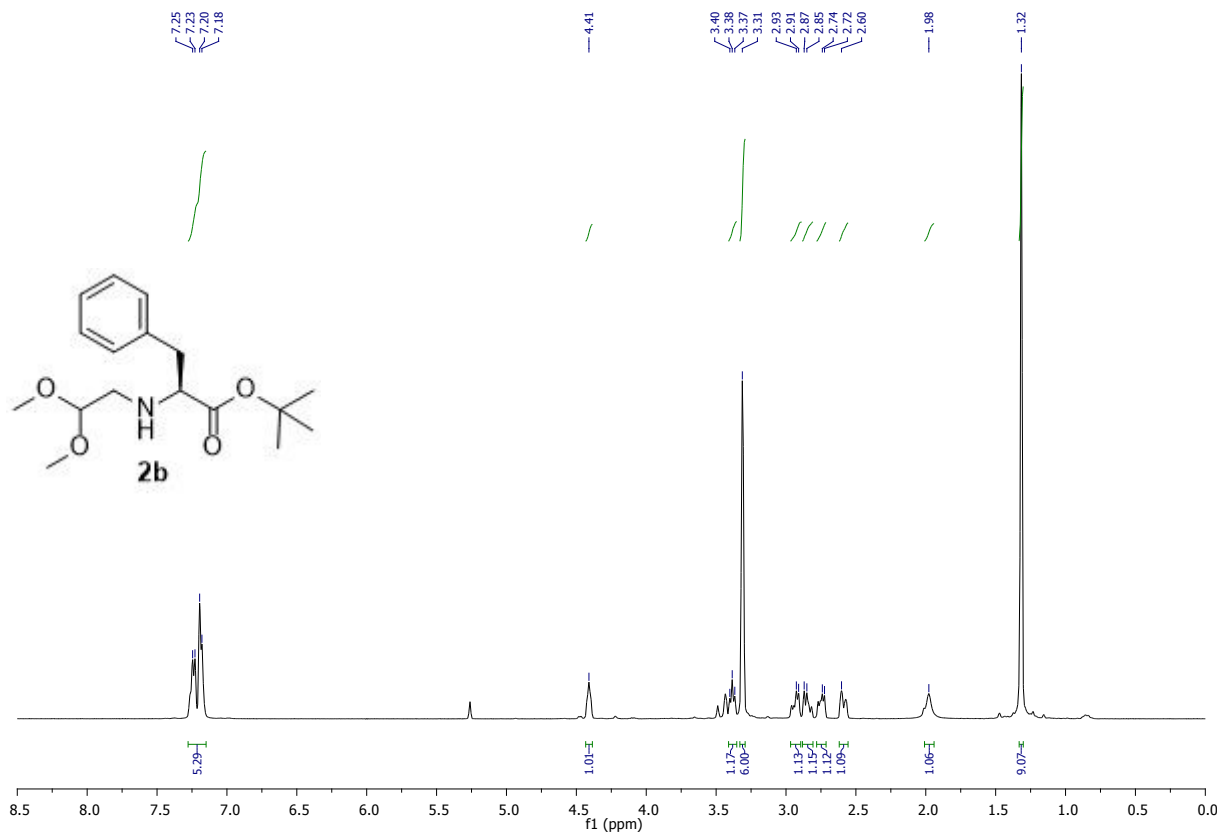
^1H NMR (400 MHz, CDCl_3)



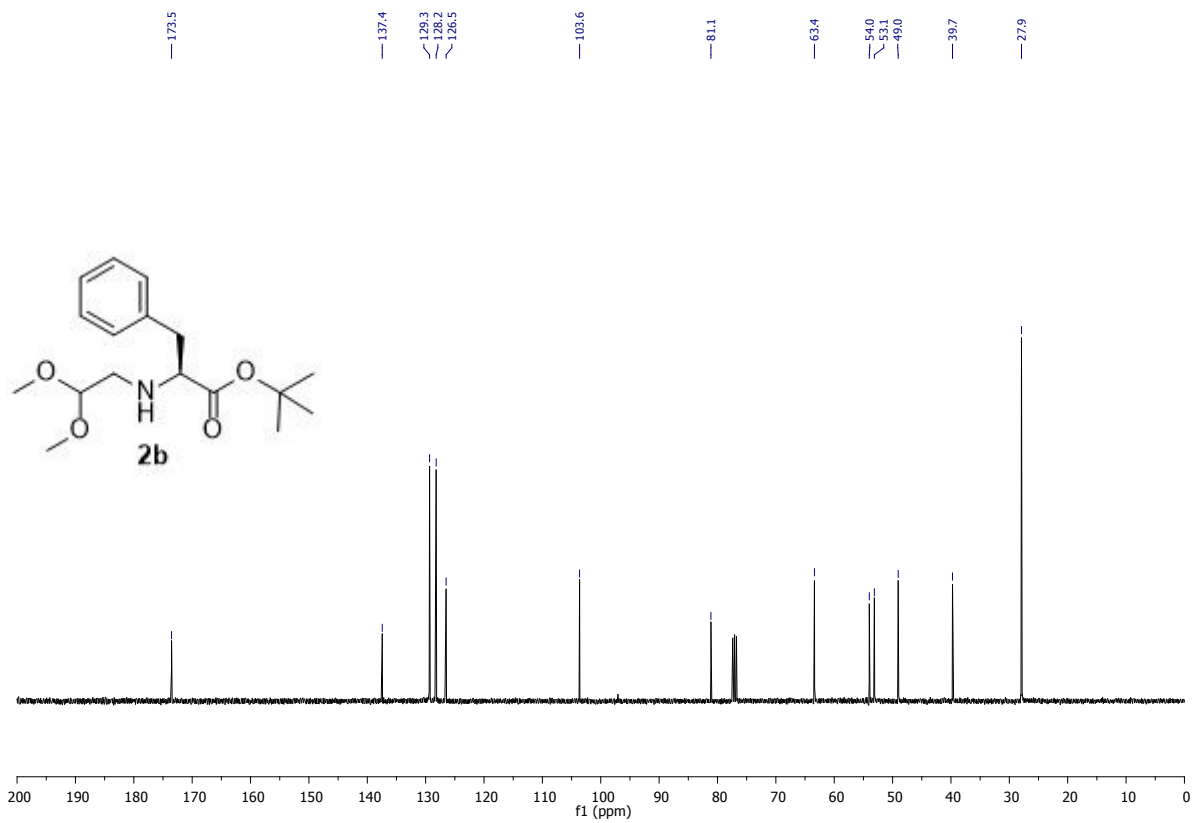
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)



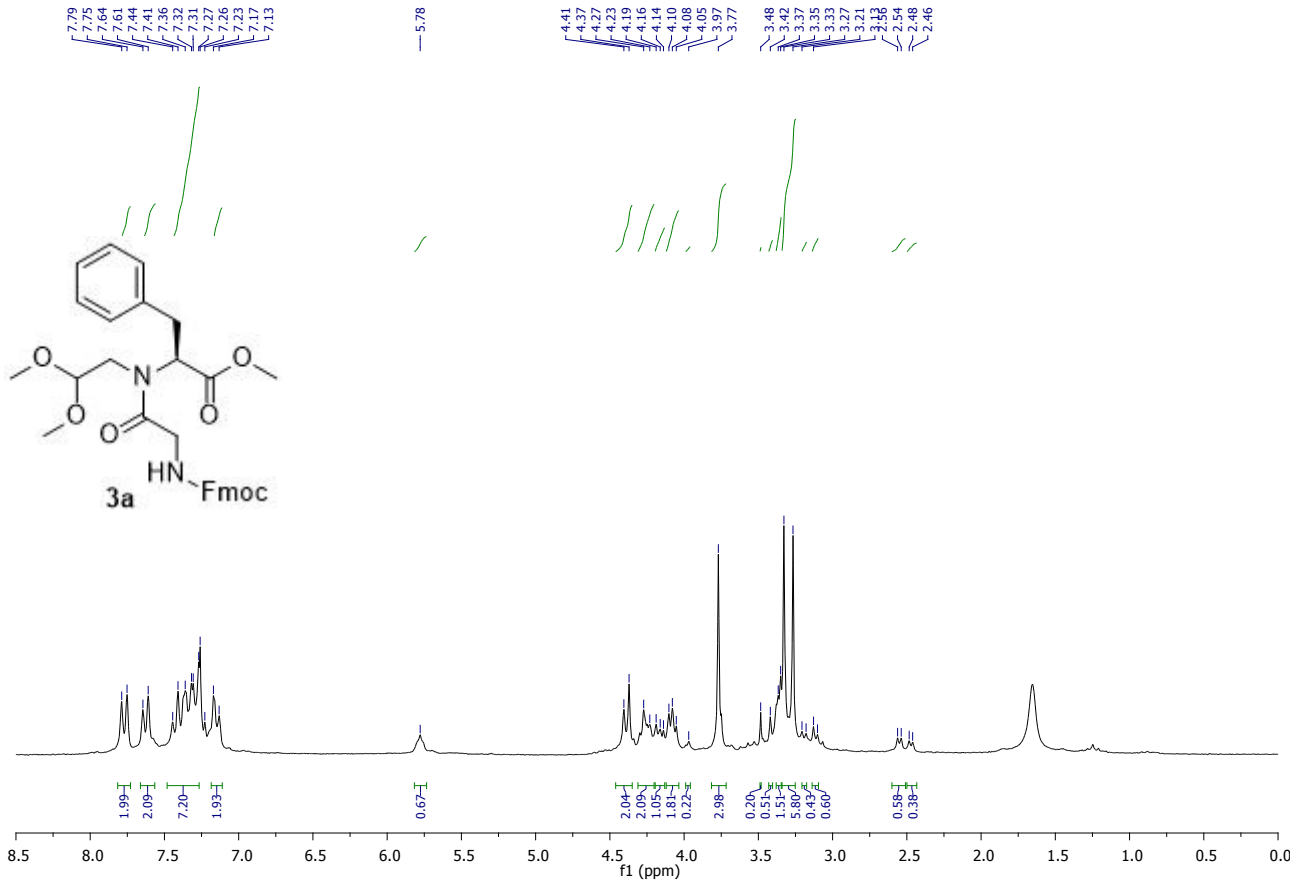
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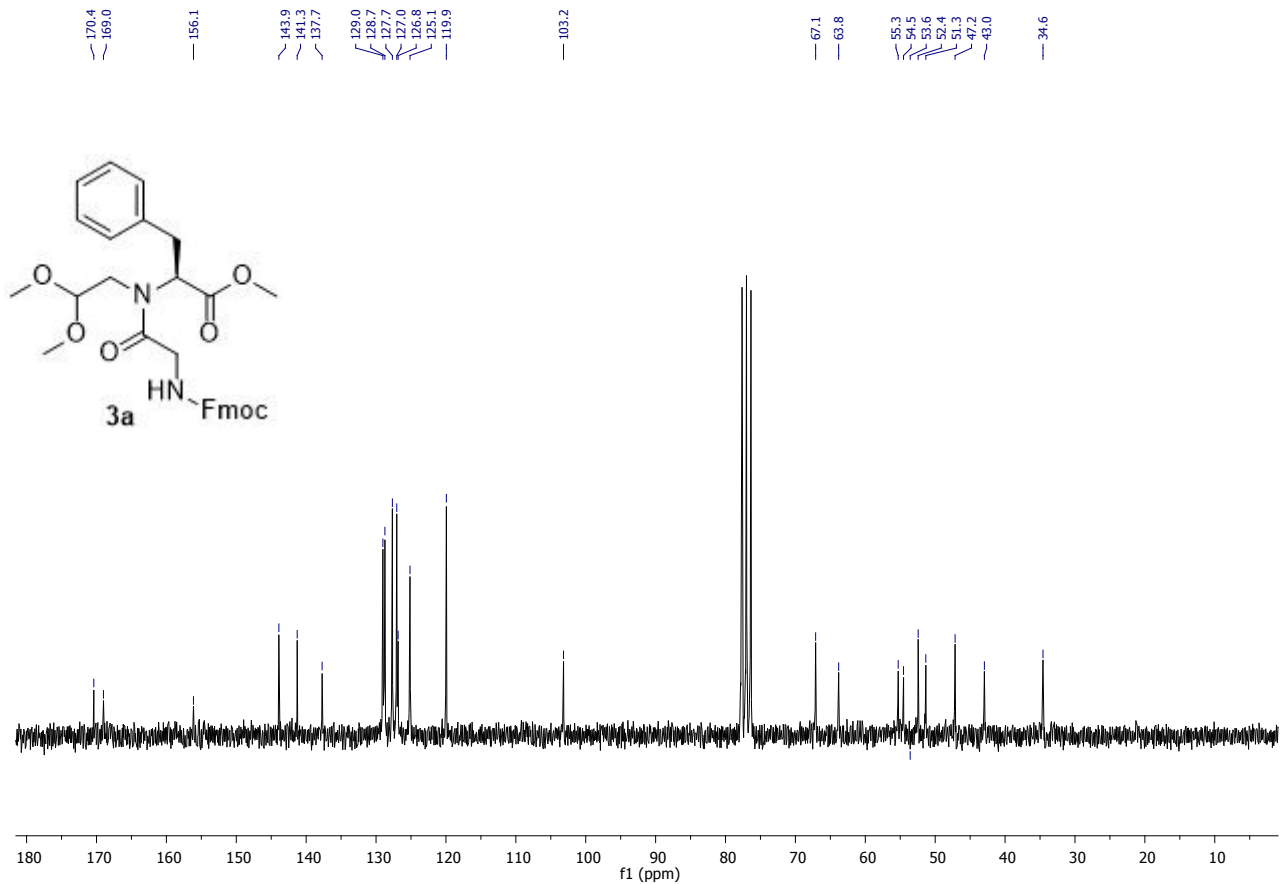
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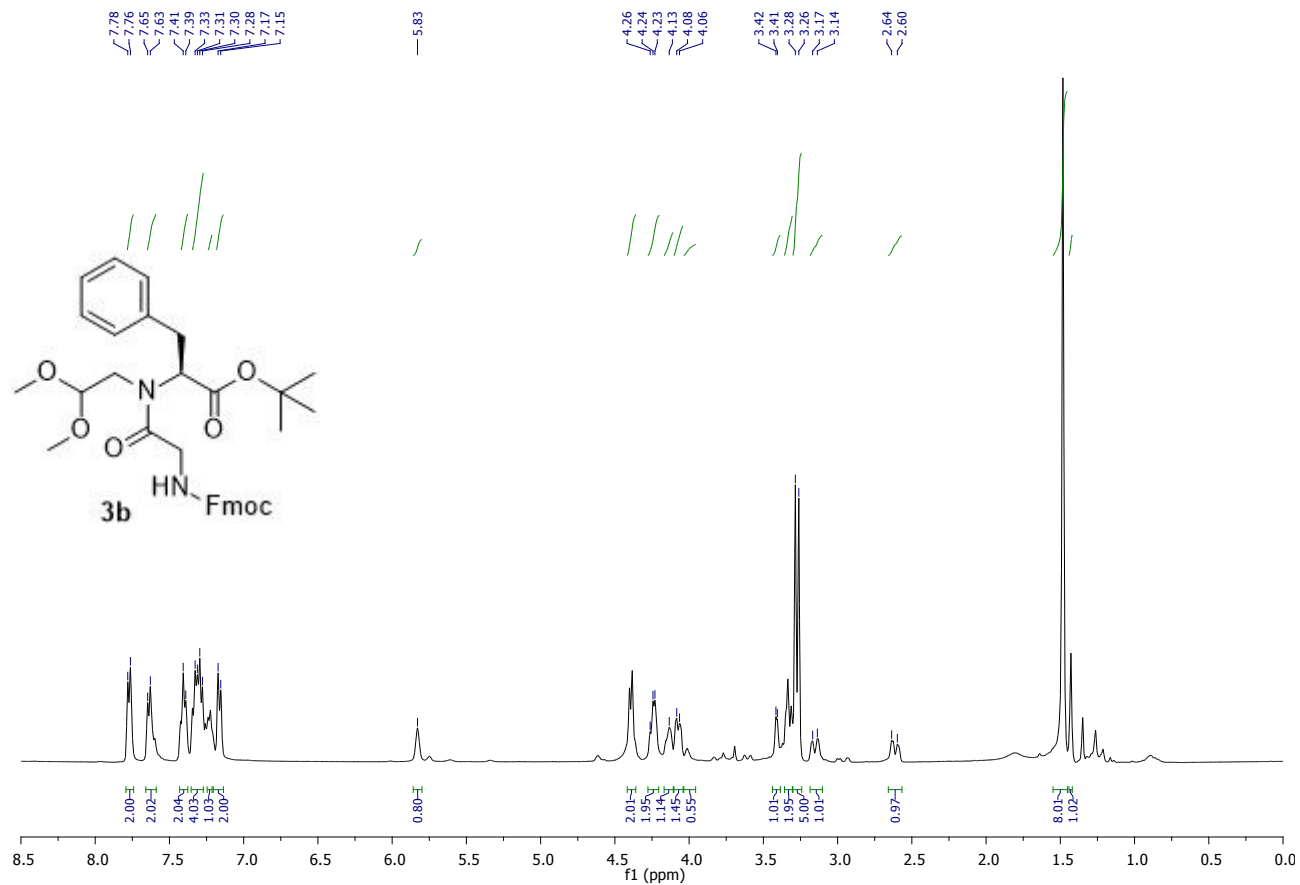
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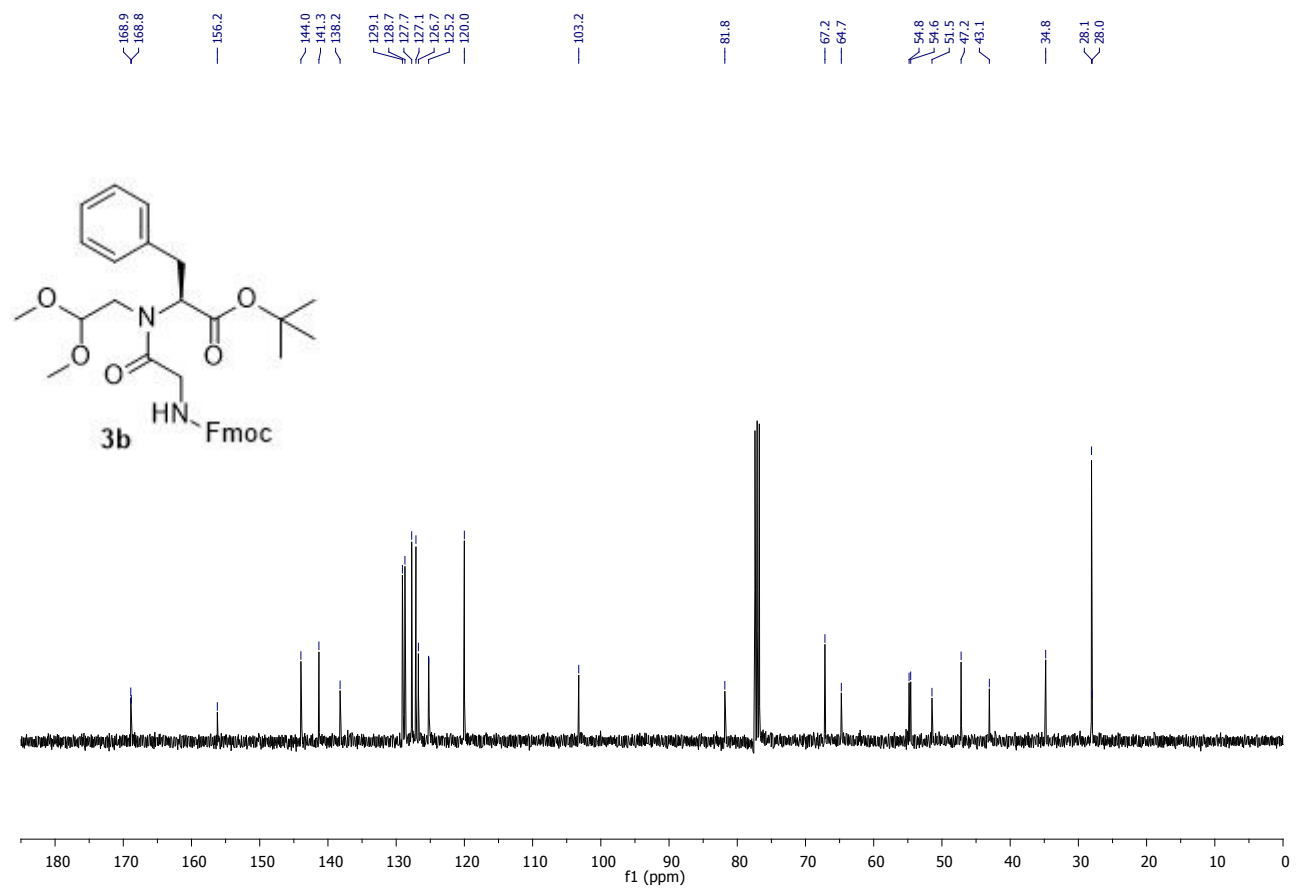
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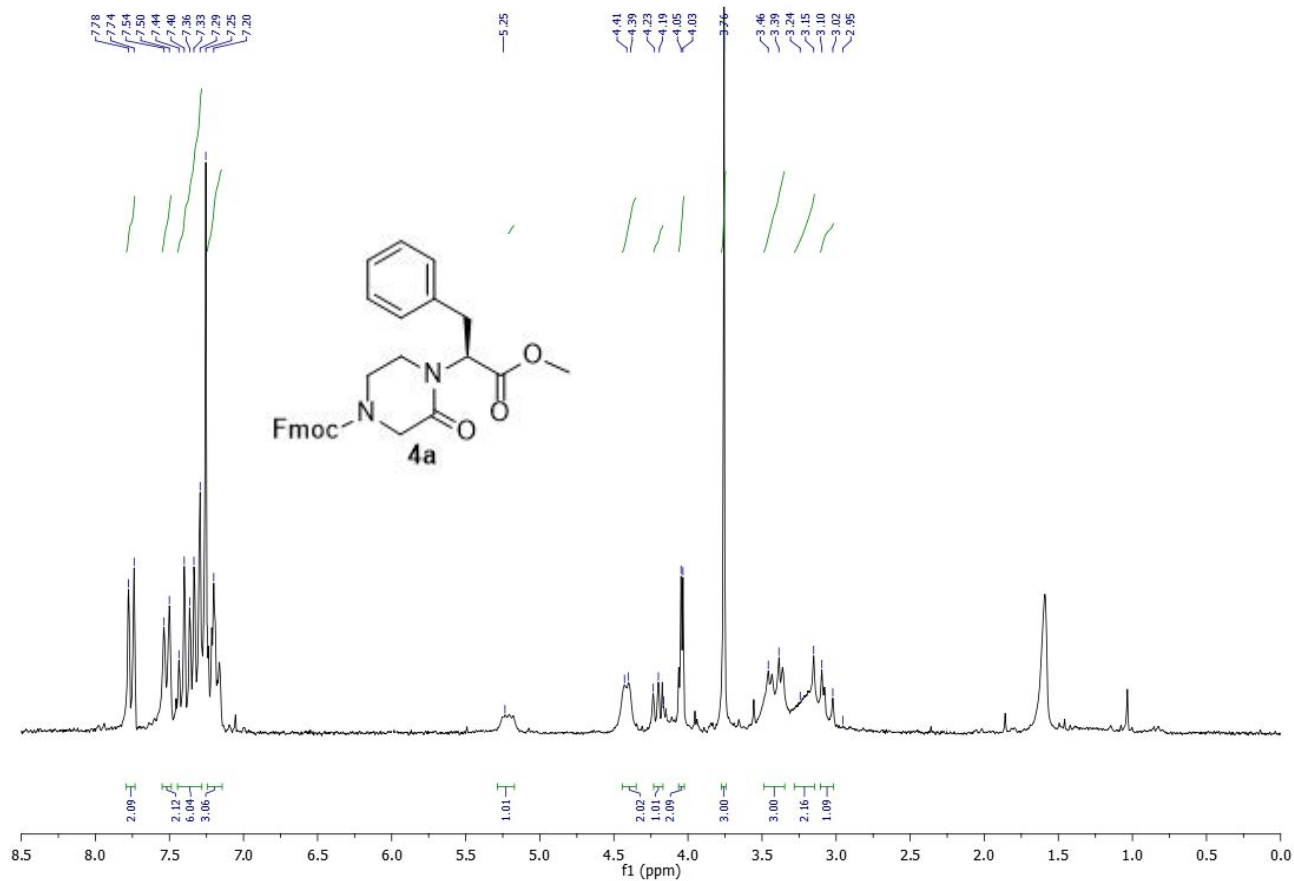
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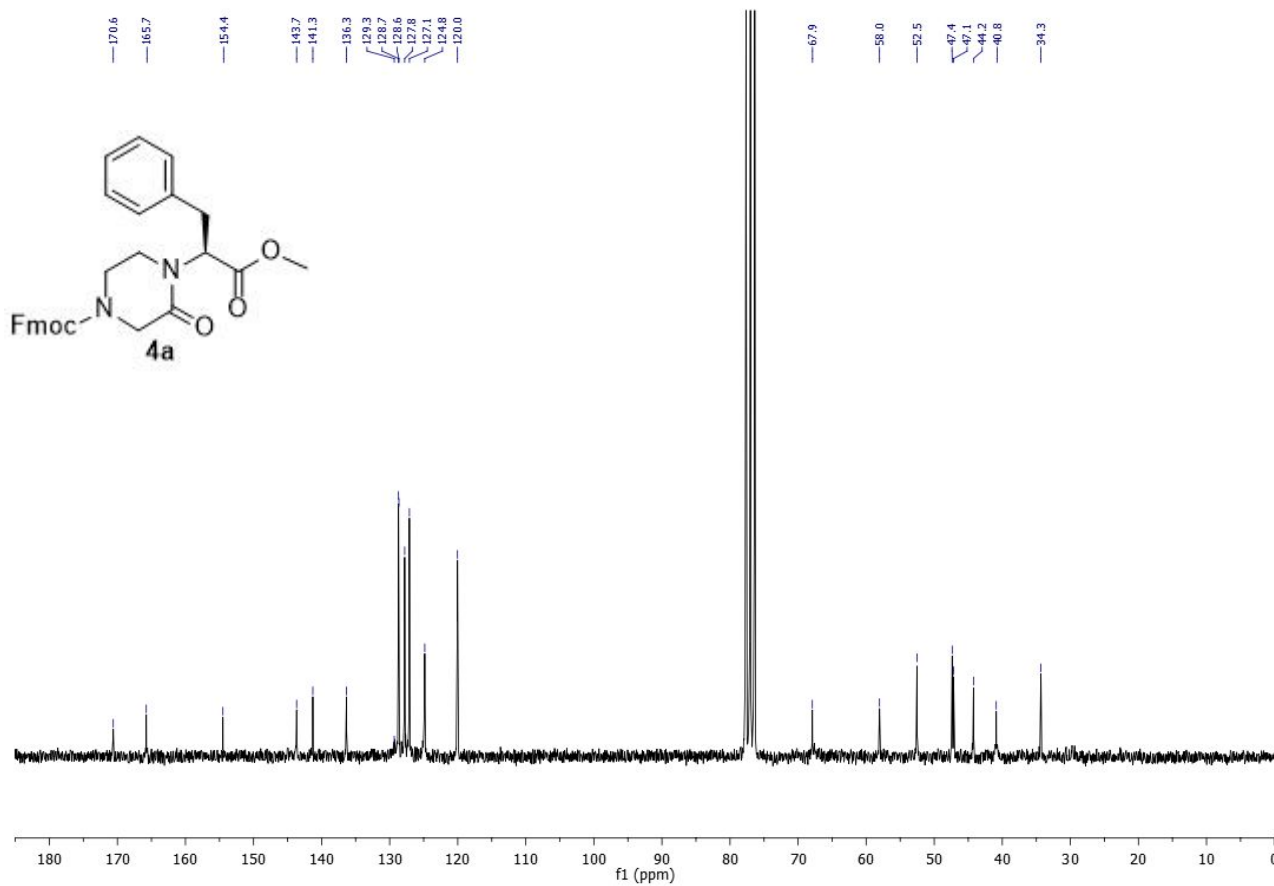
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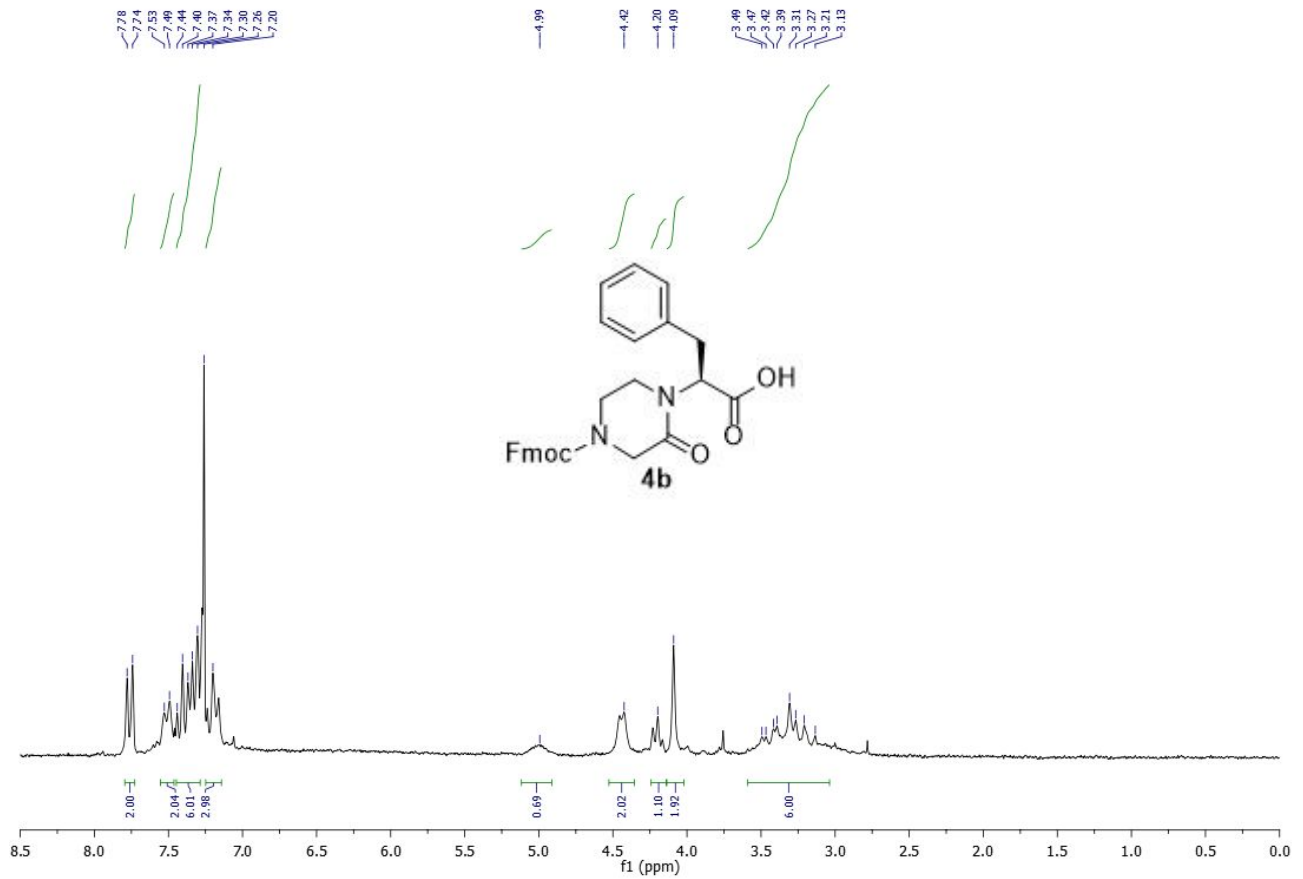
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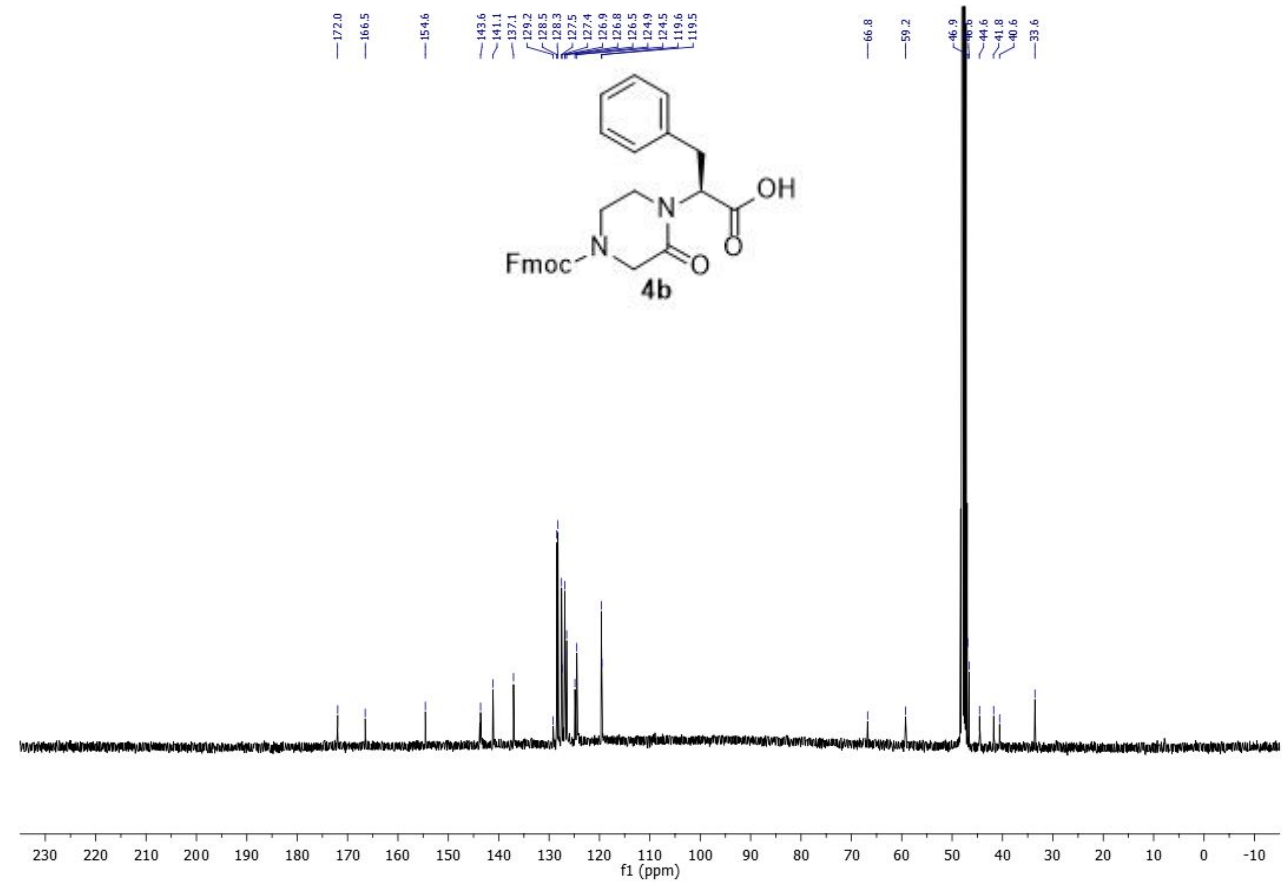
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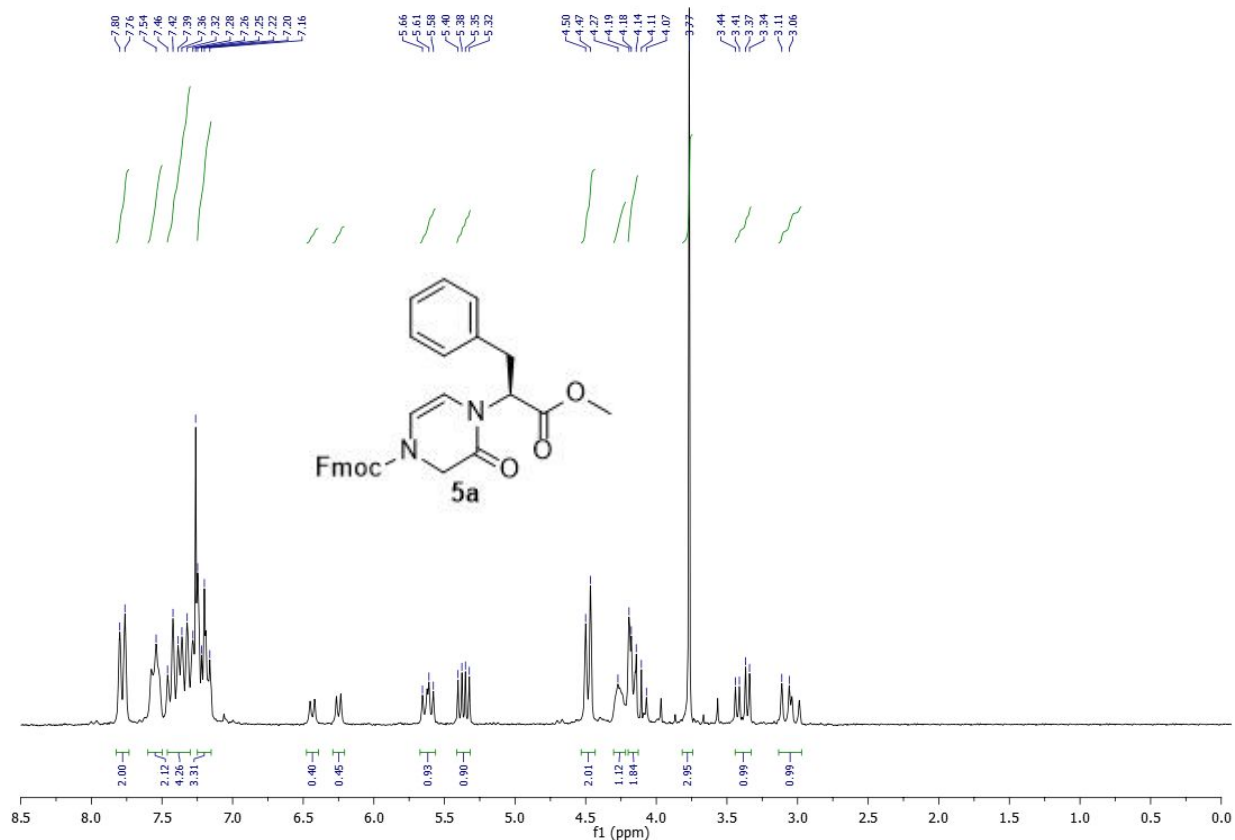
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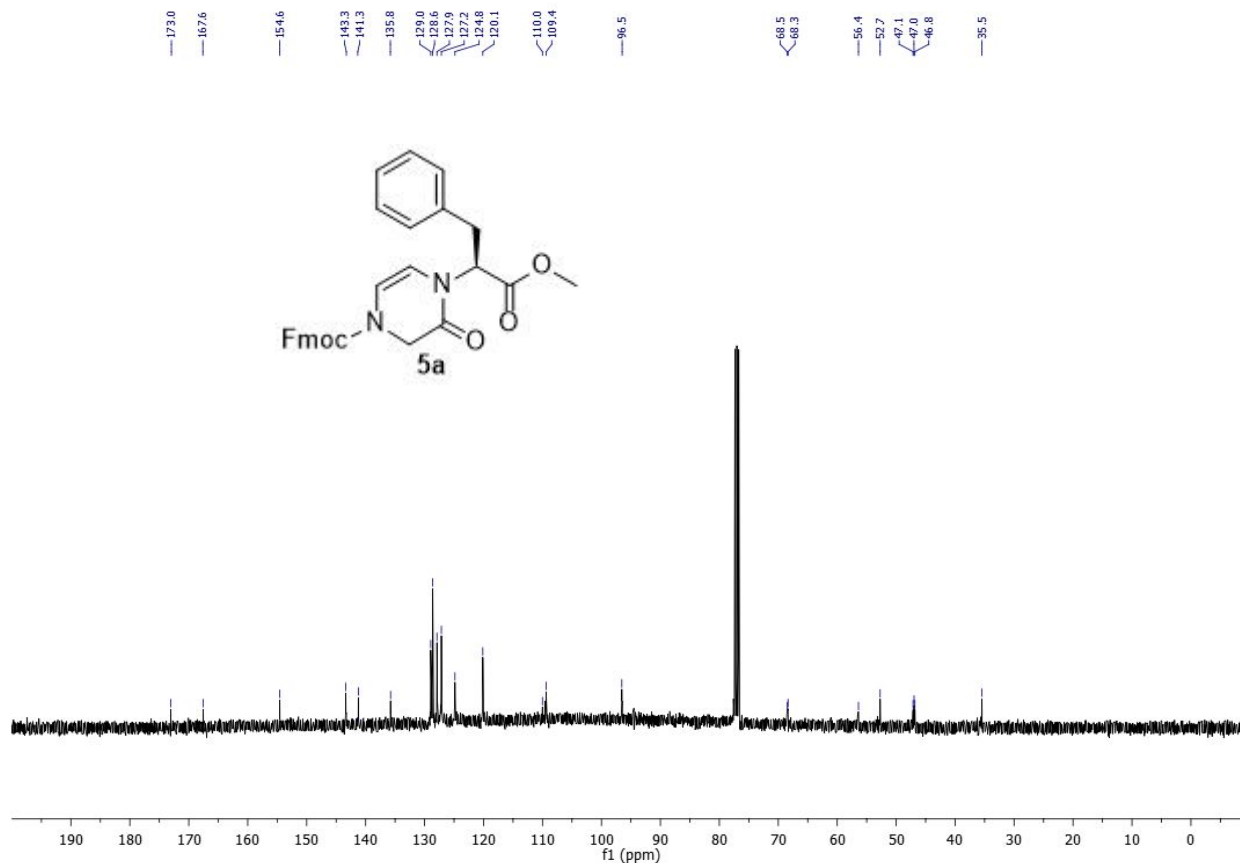
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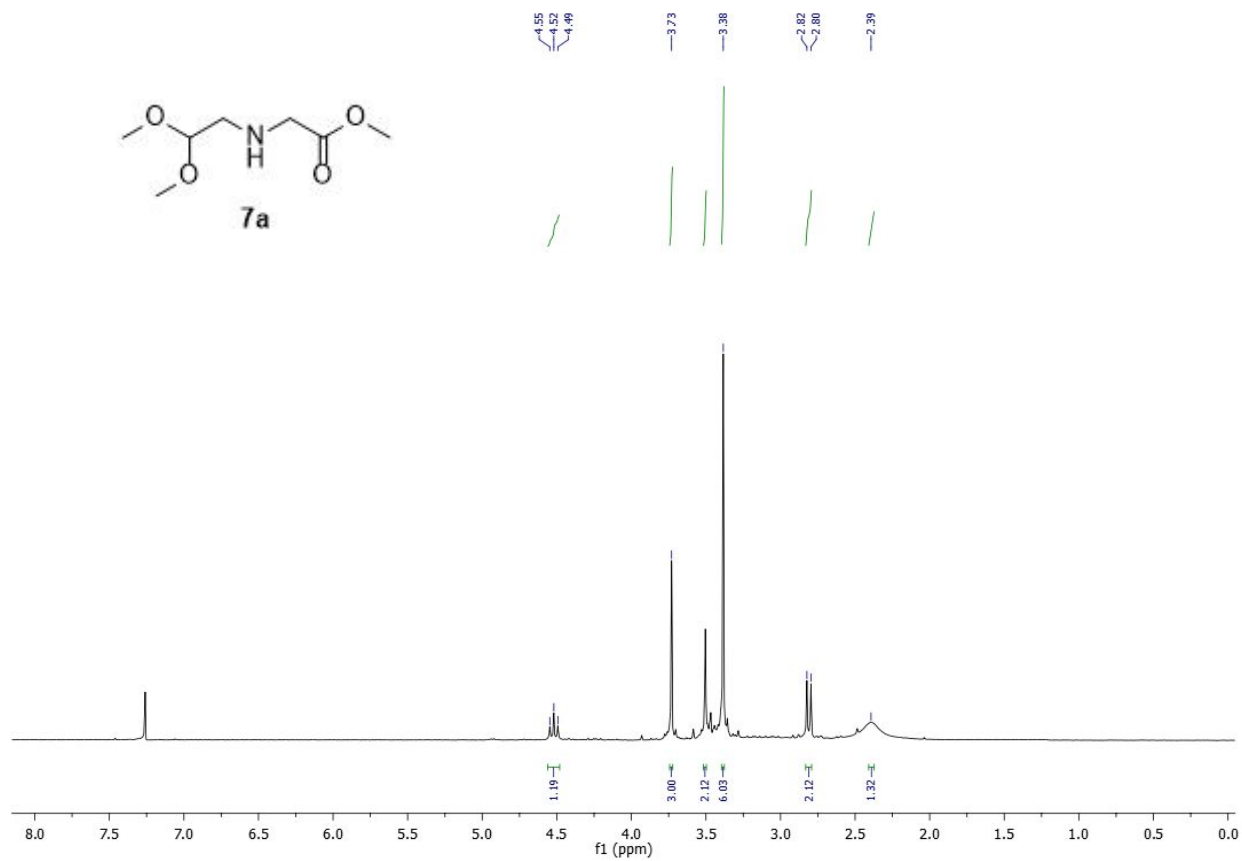
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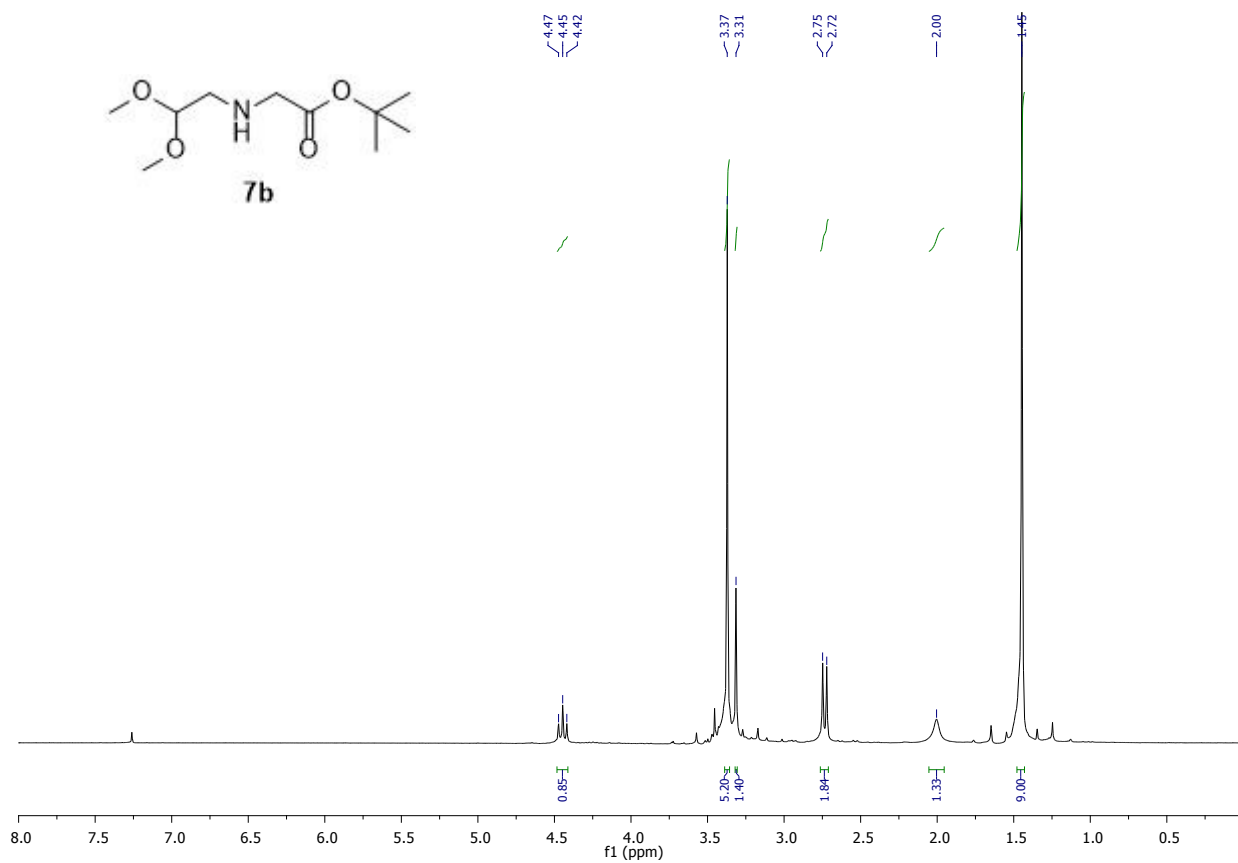
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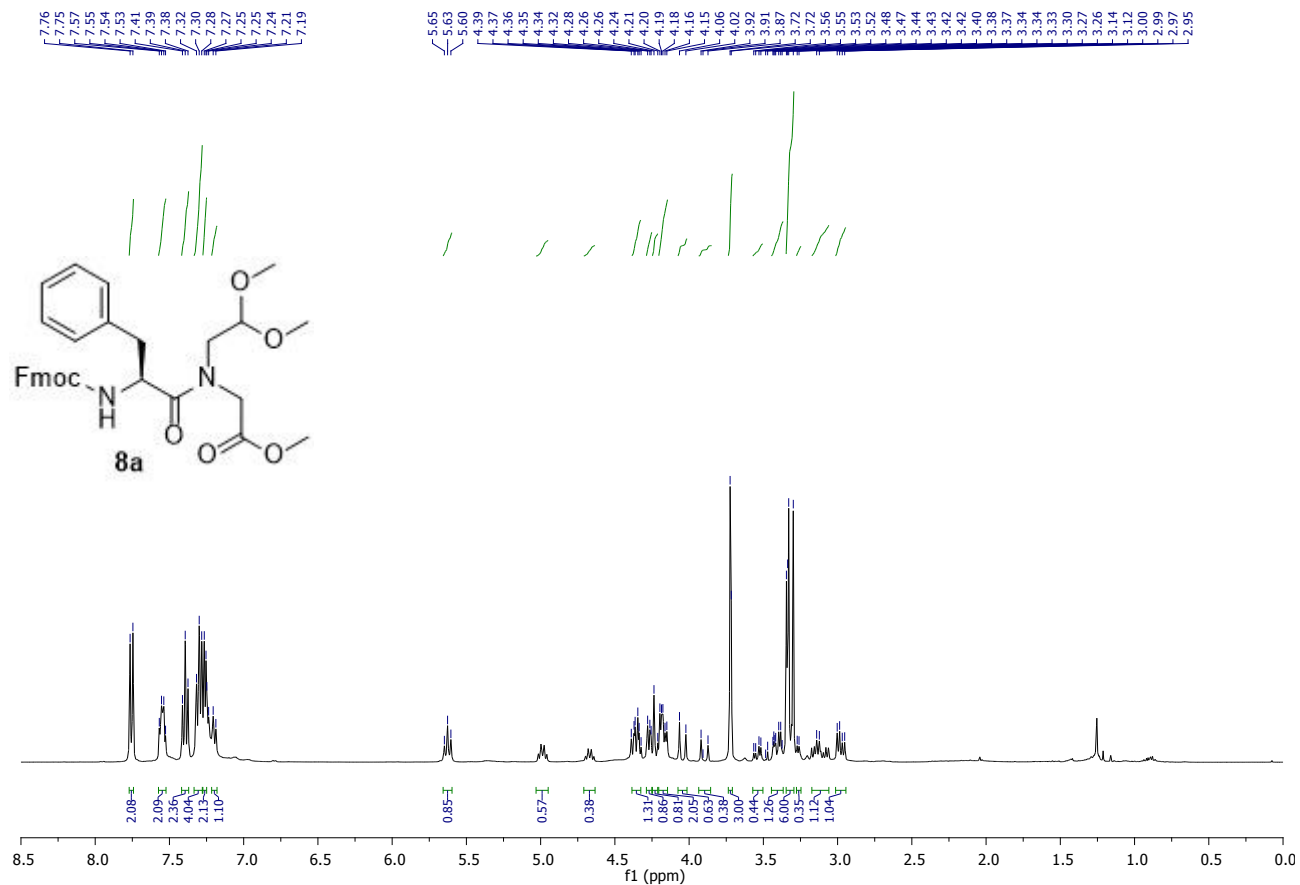
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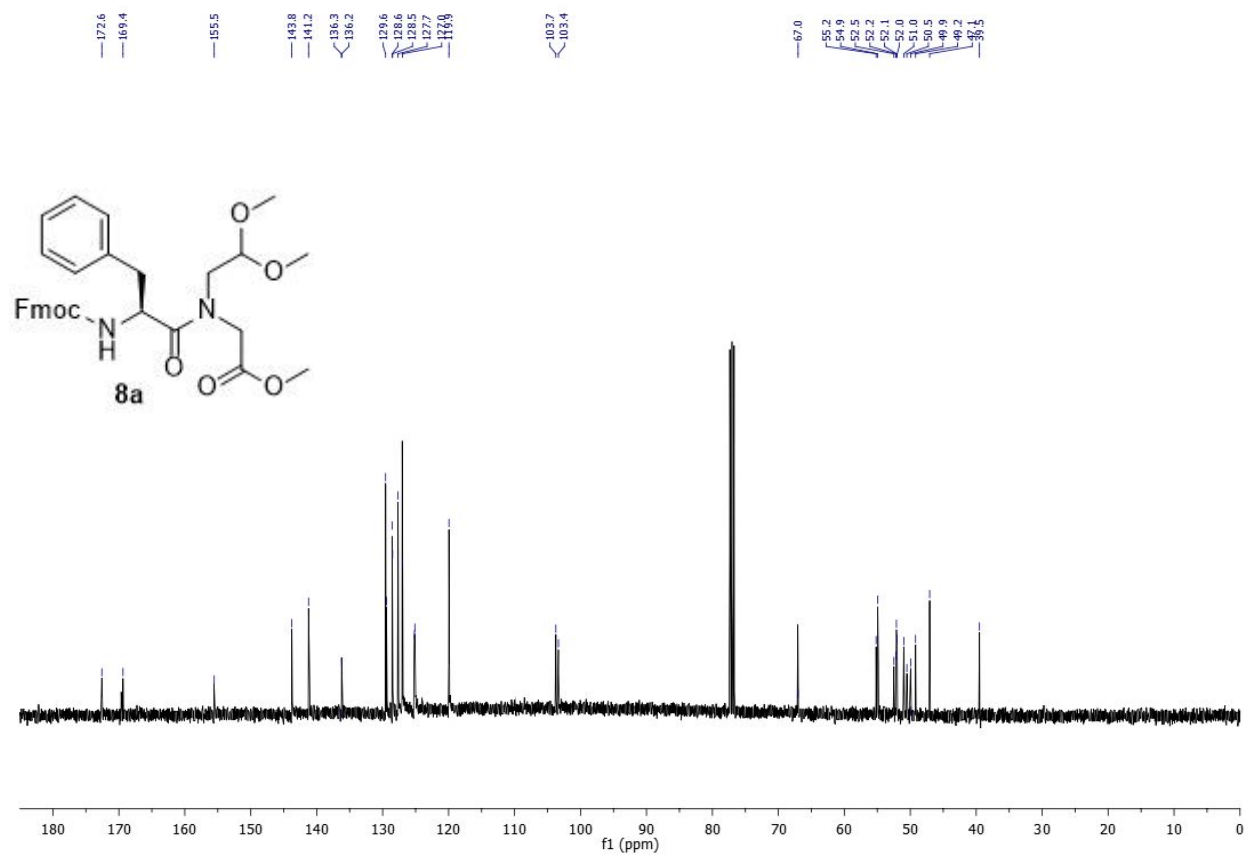
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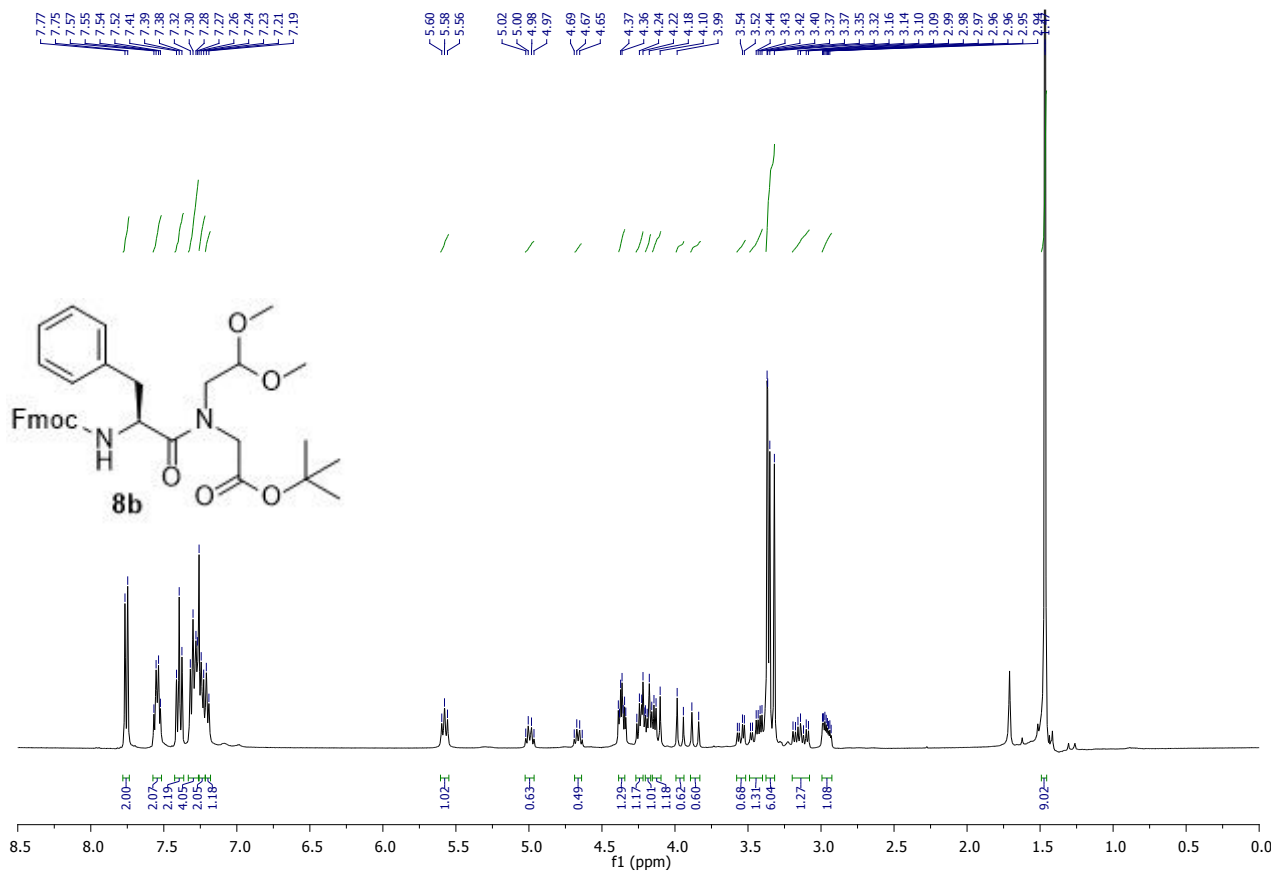
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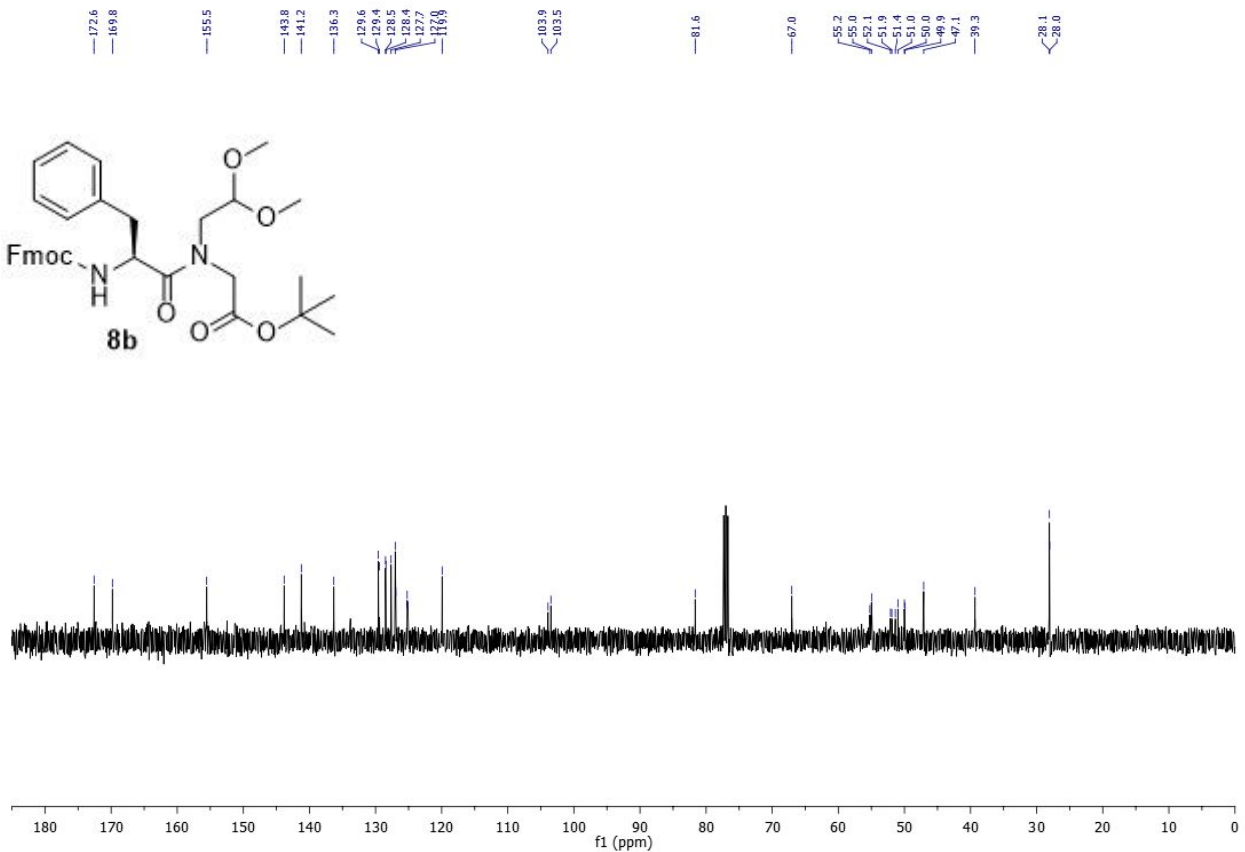
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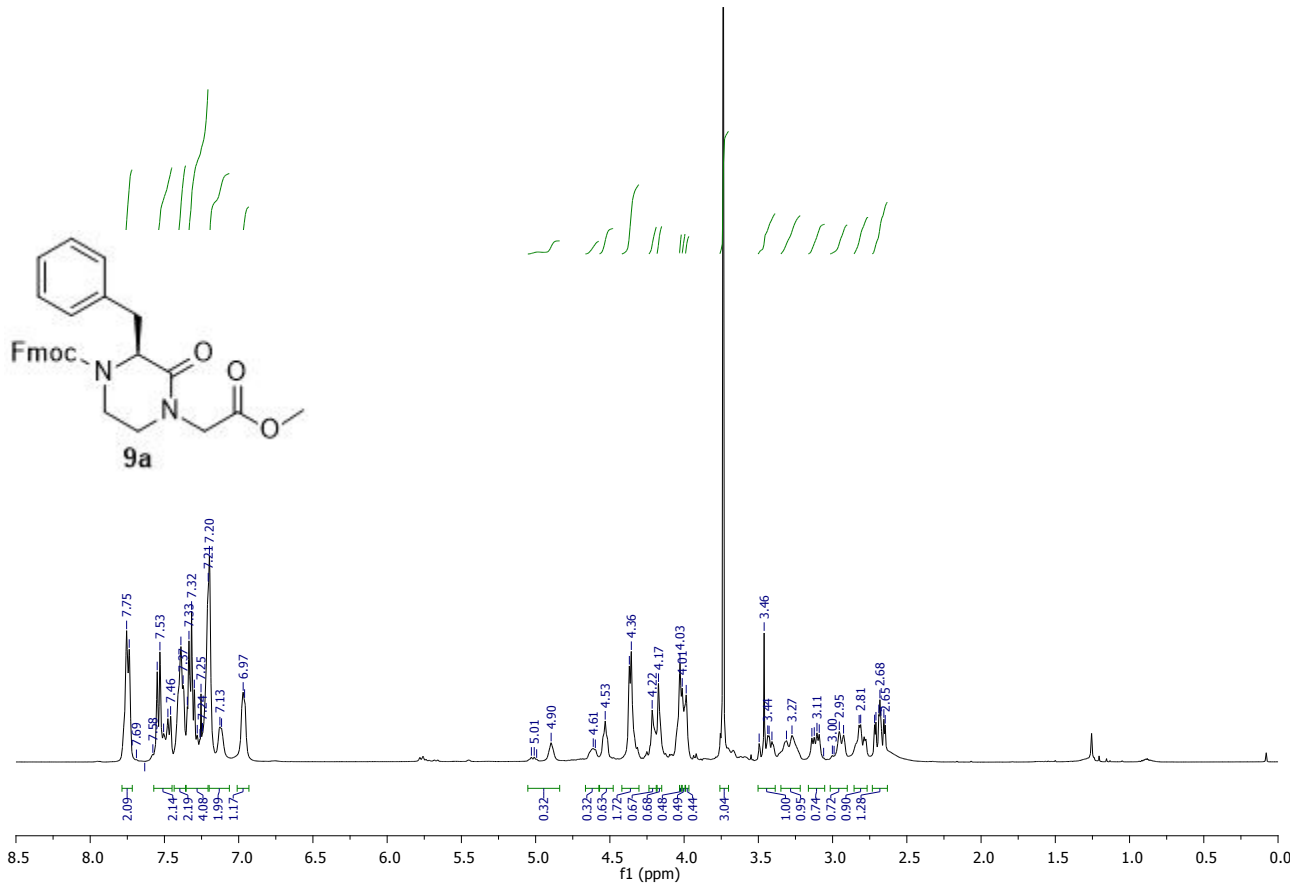
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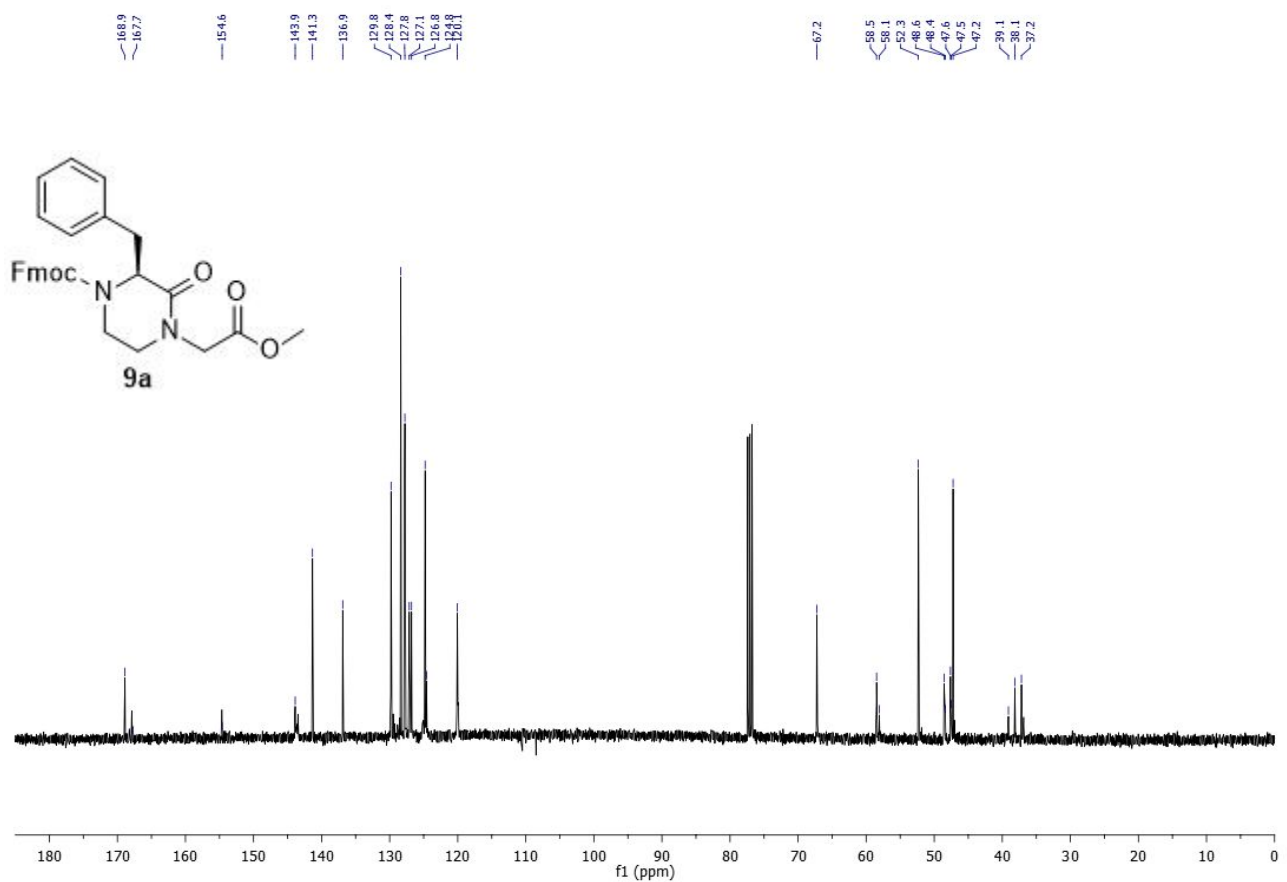
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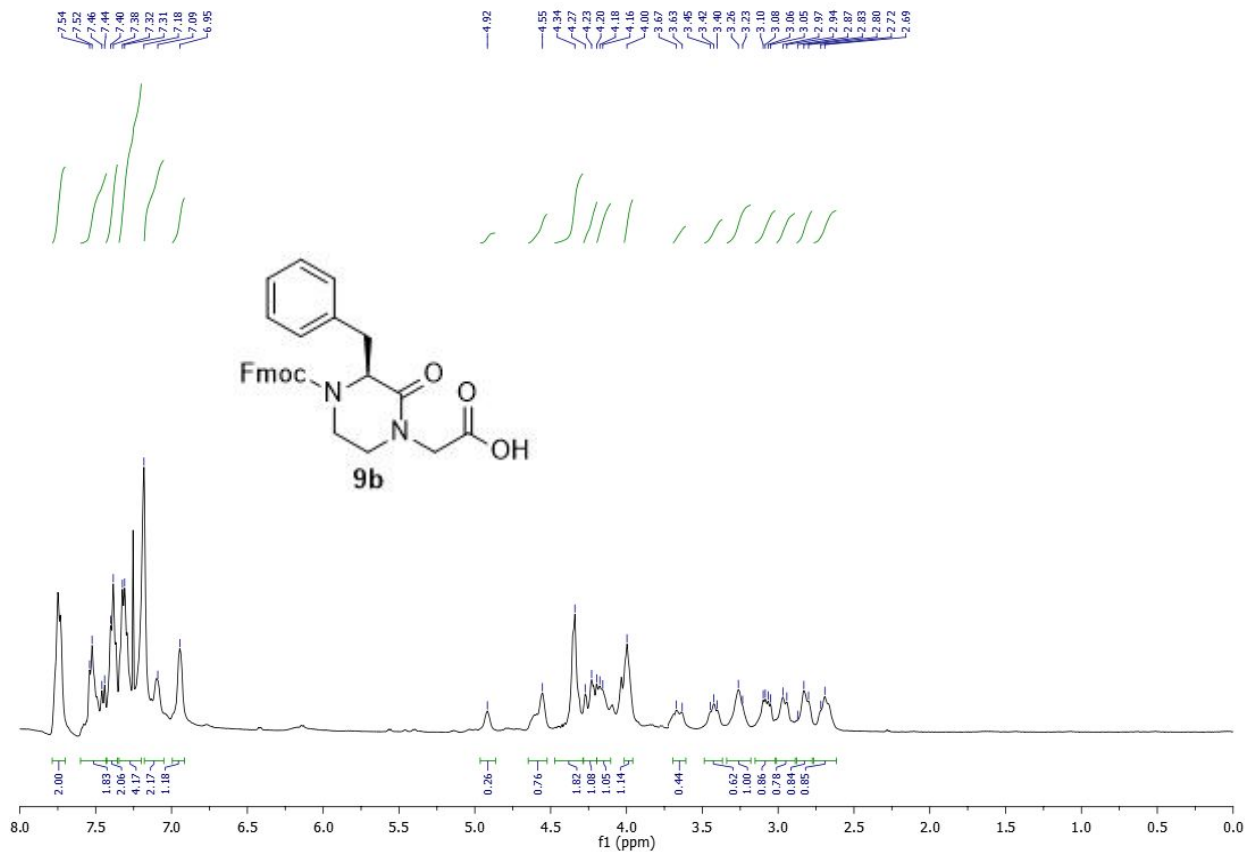
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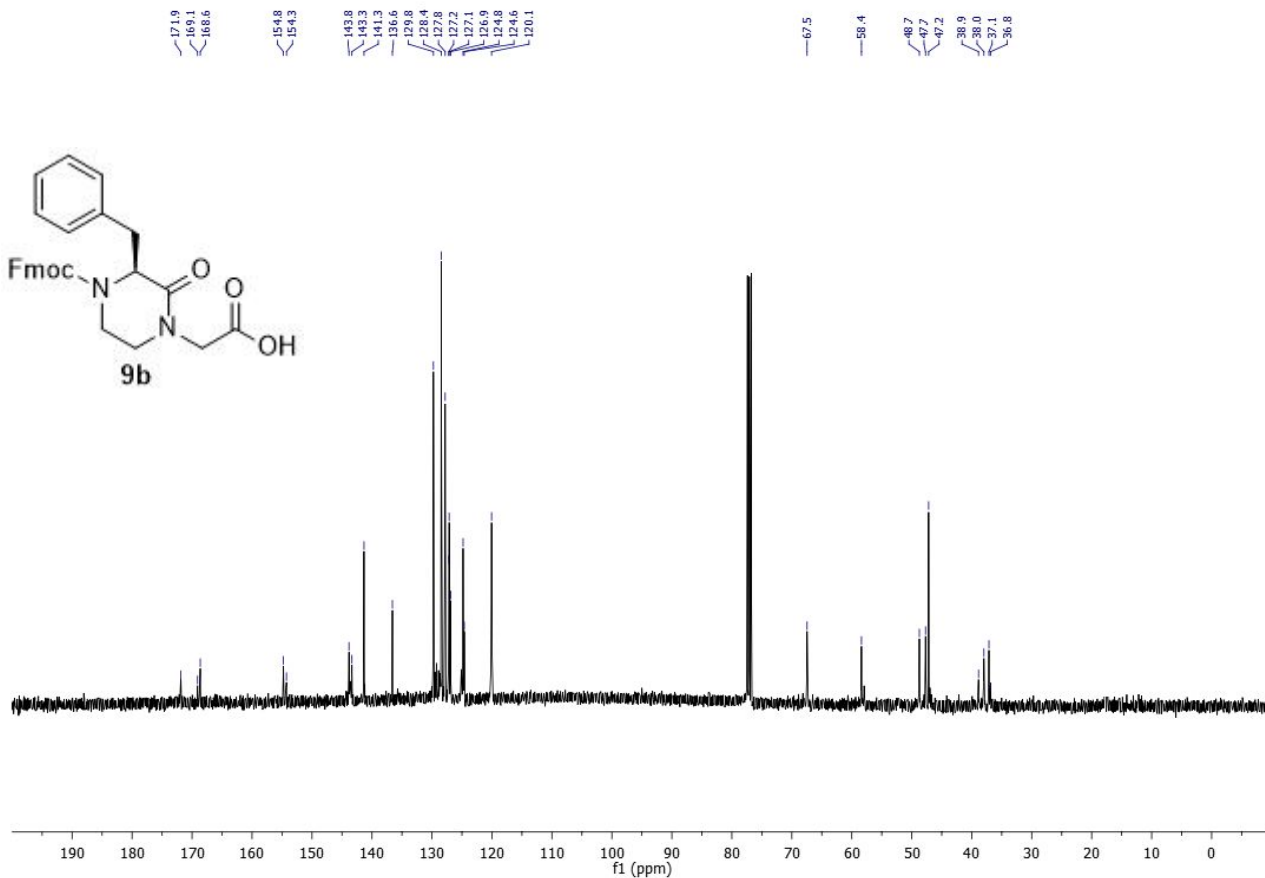
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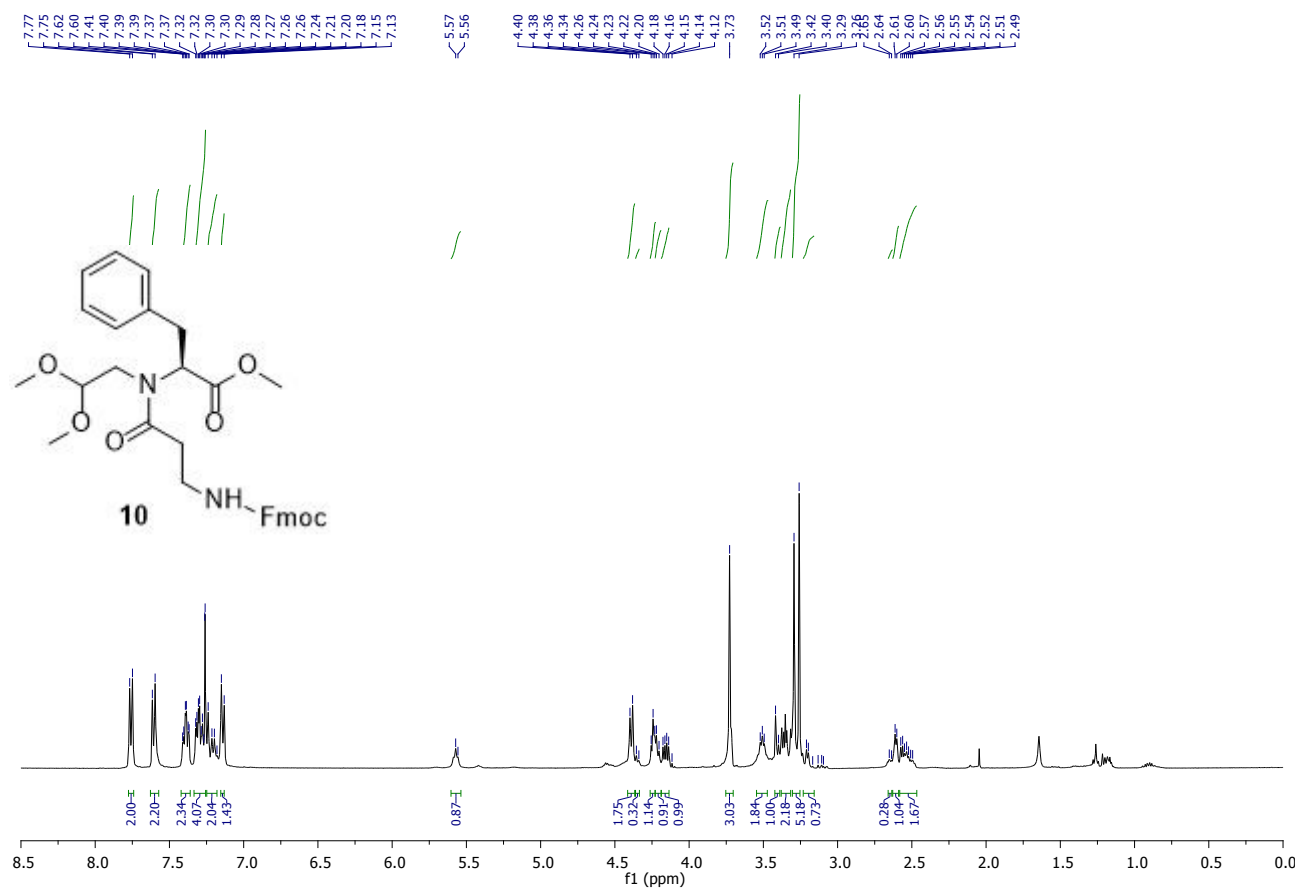
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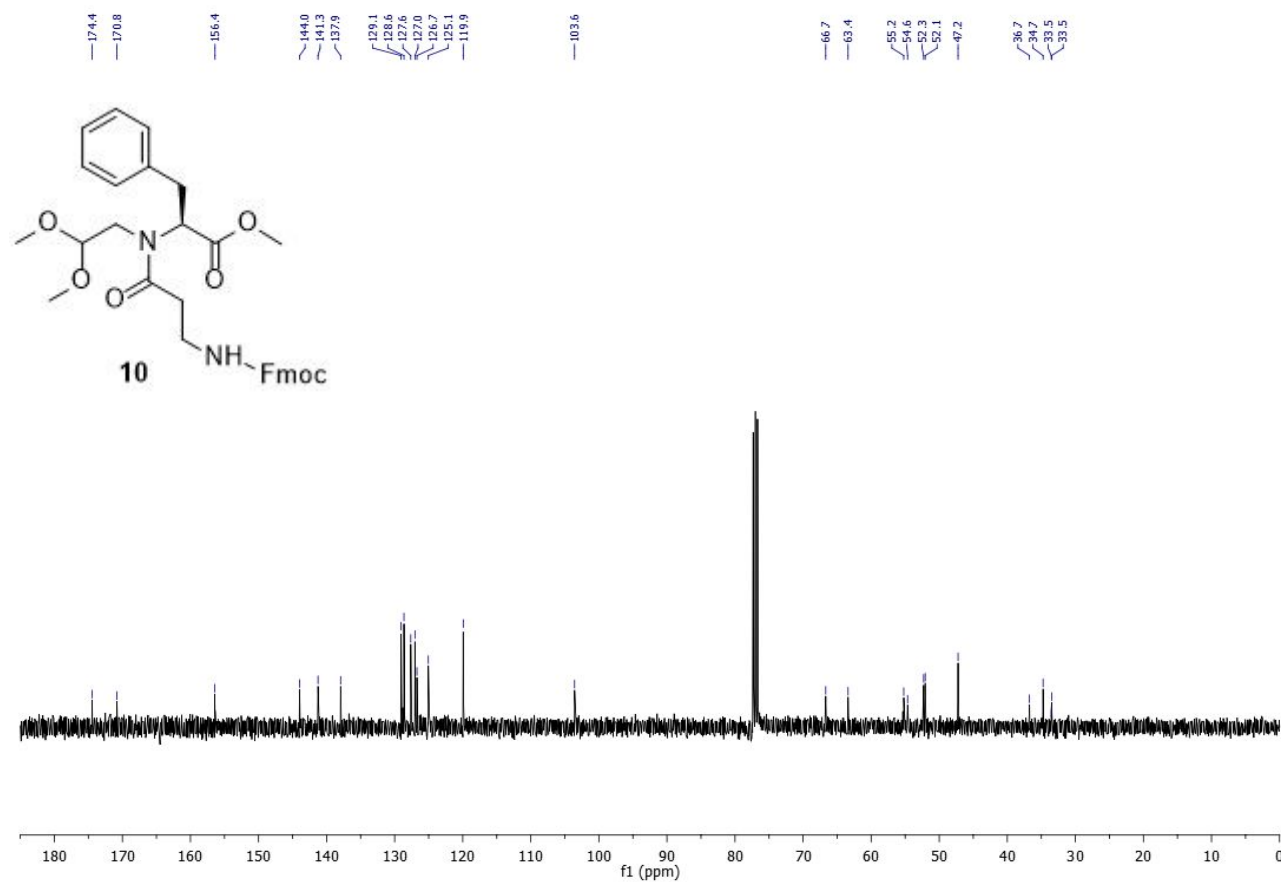
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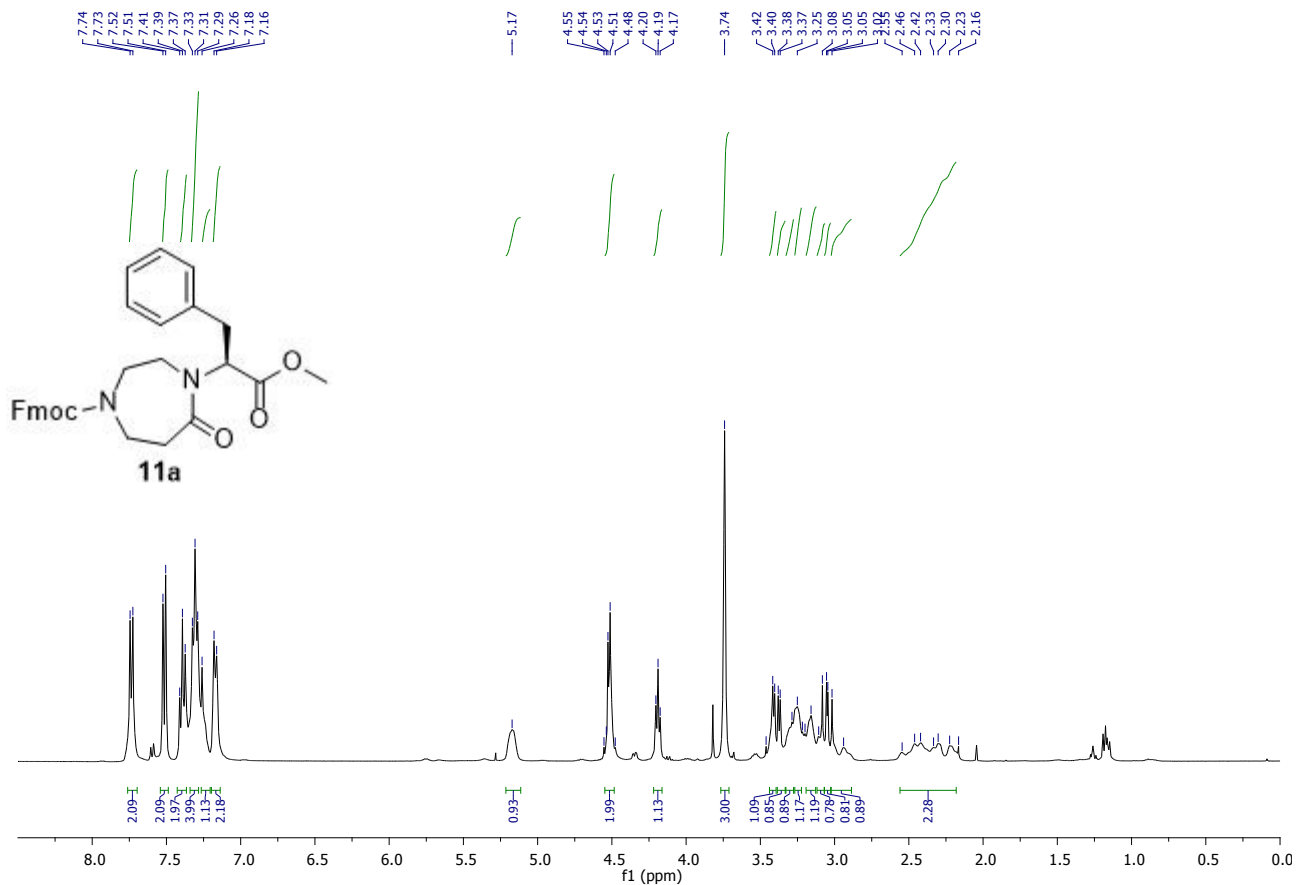
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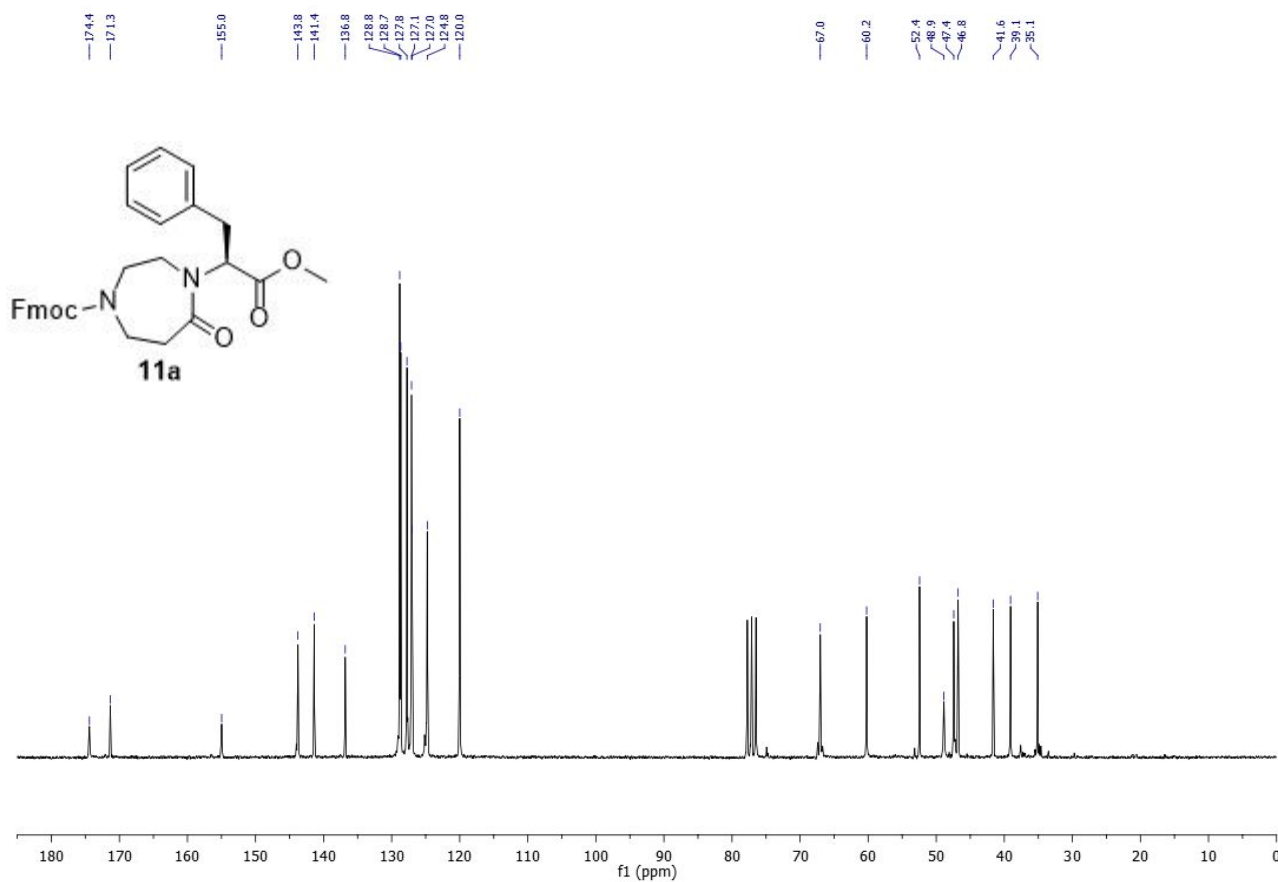
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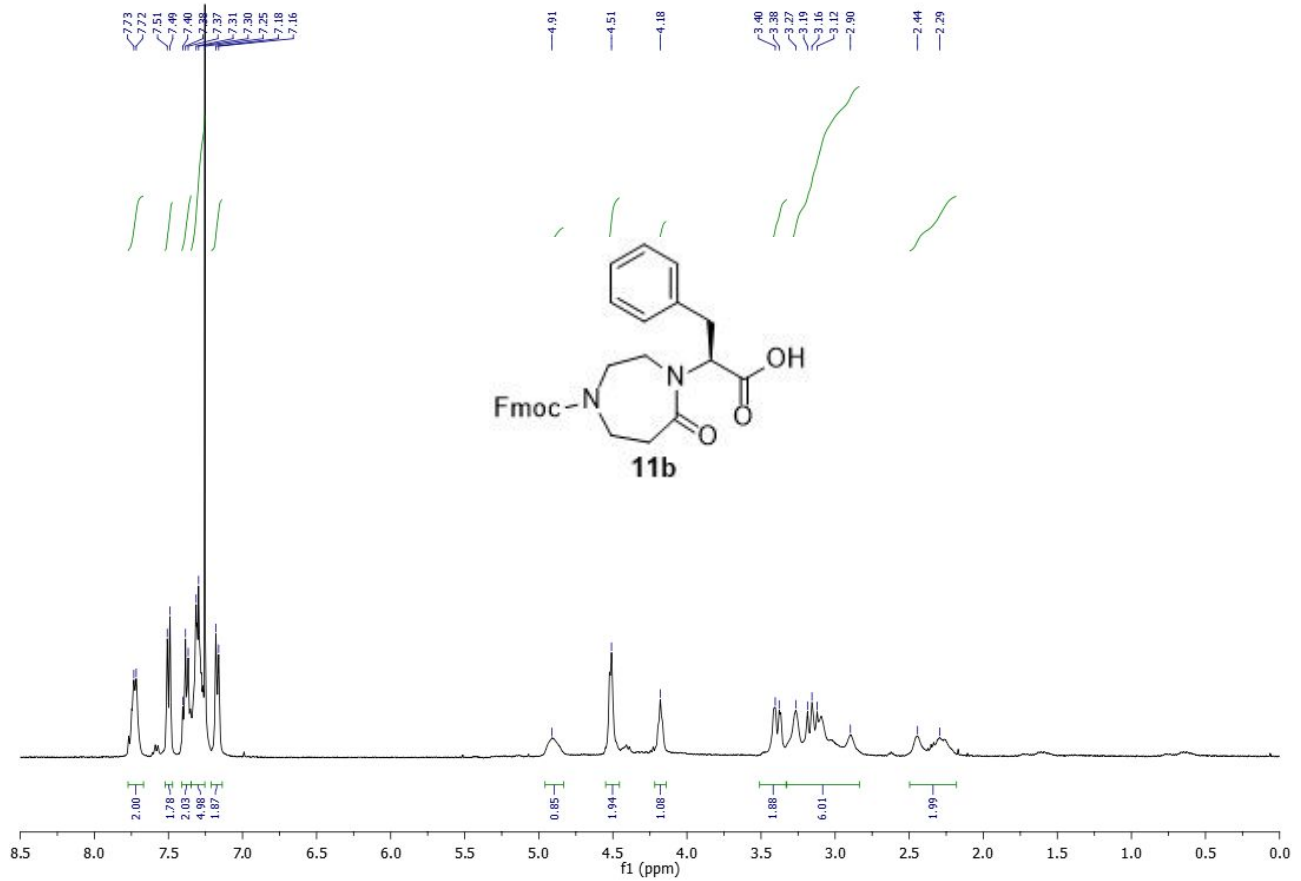
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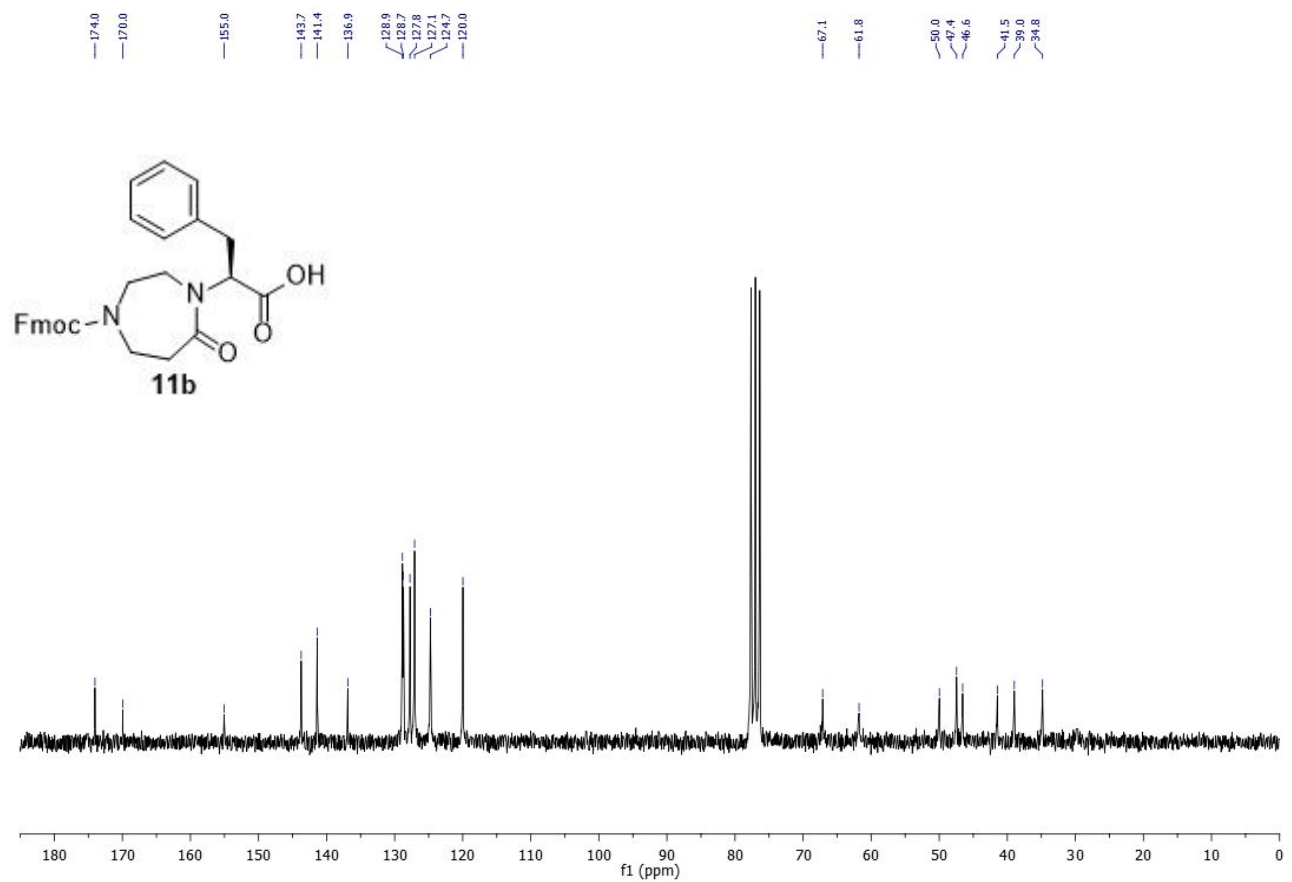
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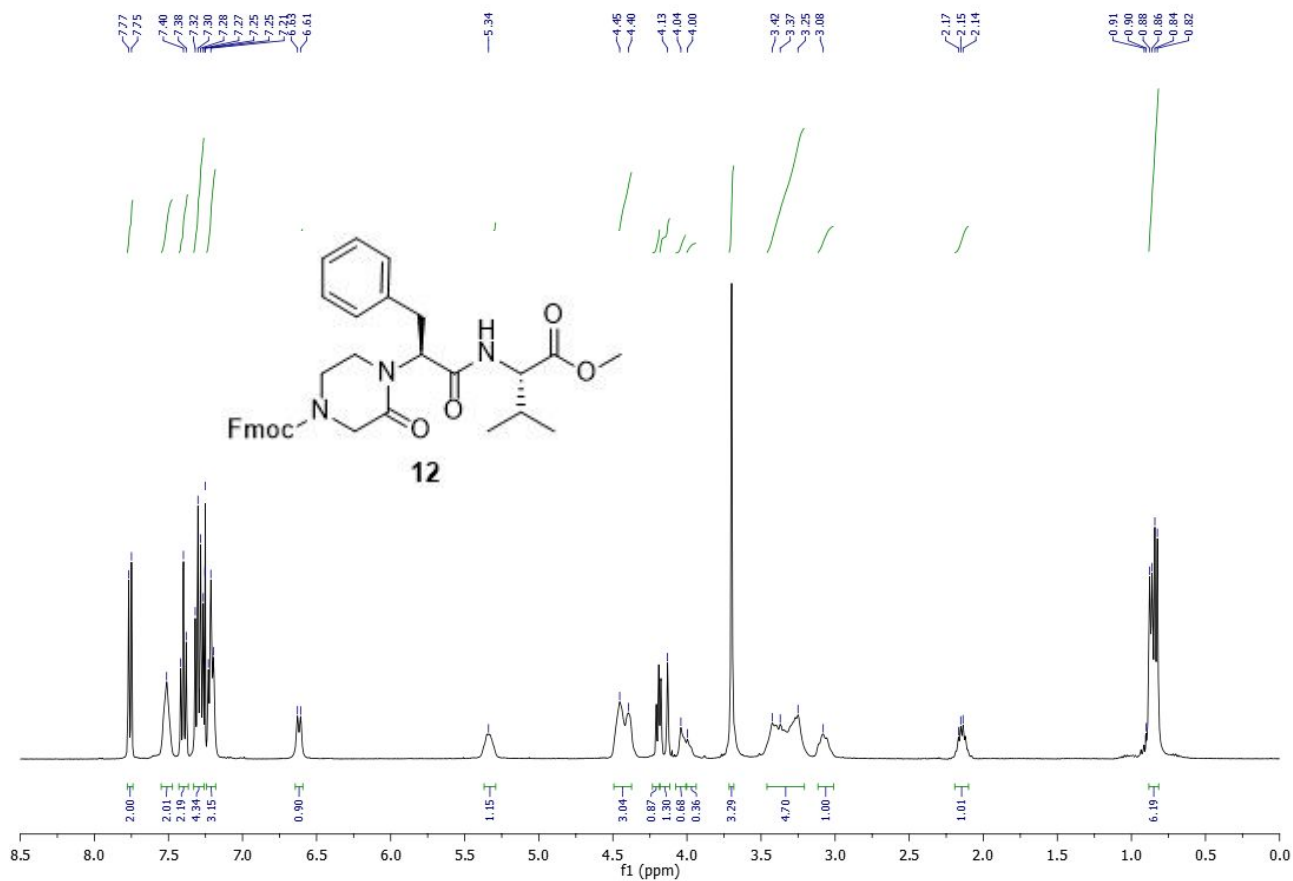
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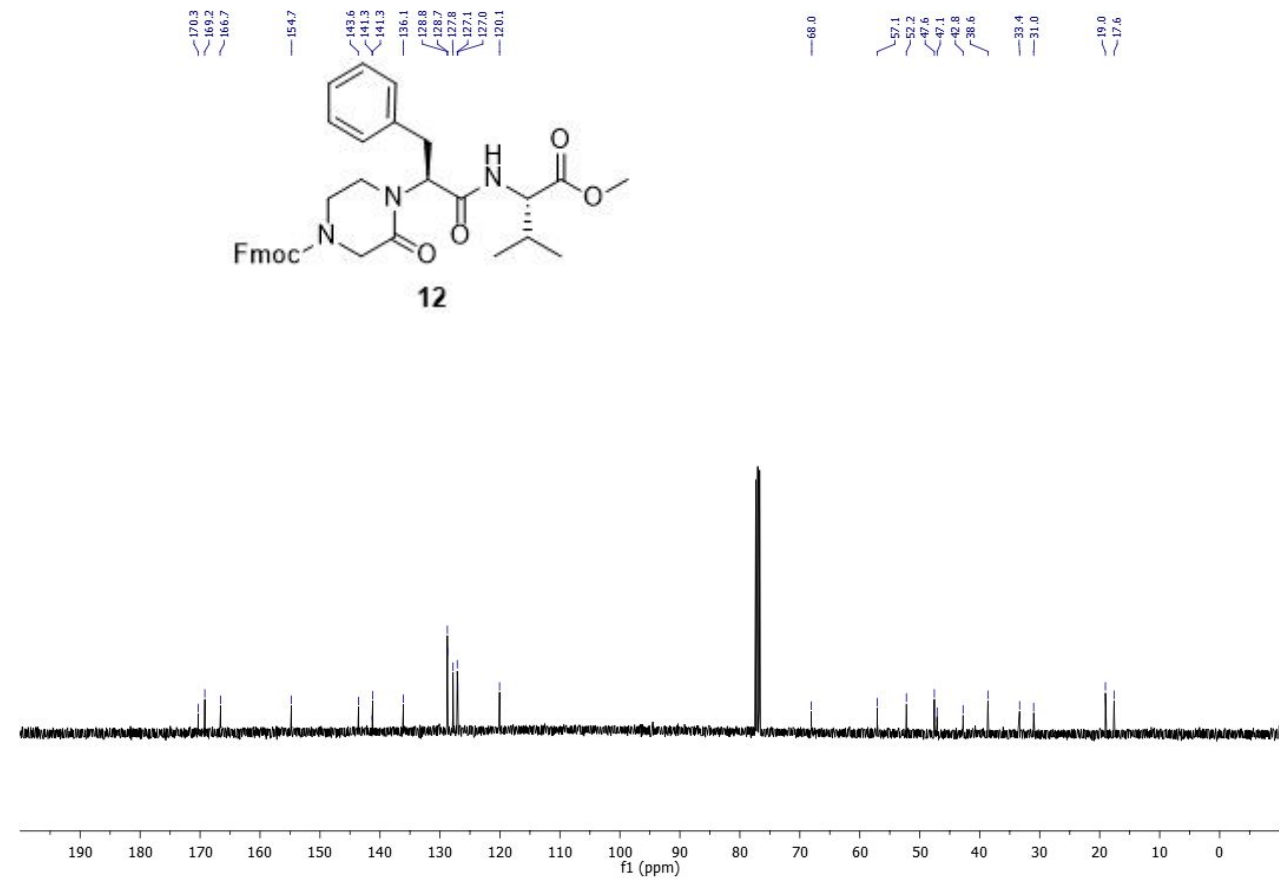
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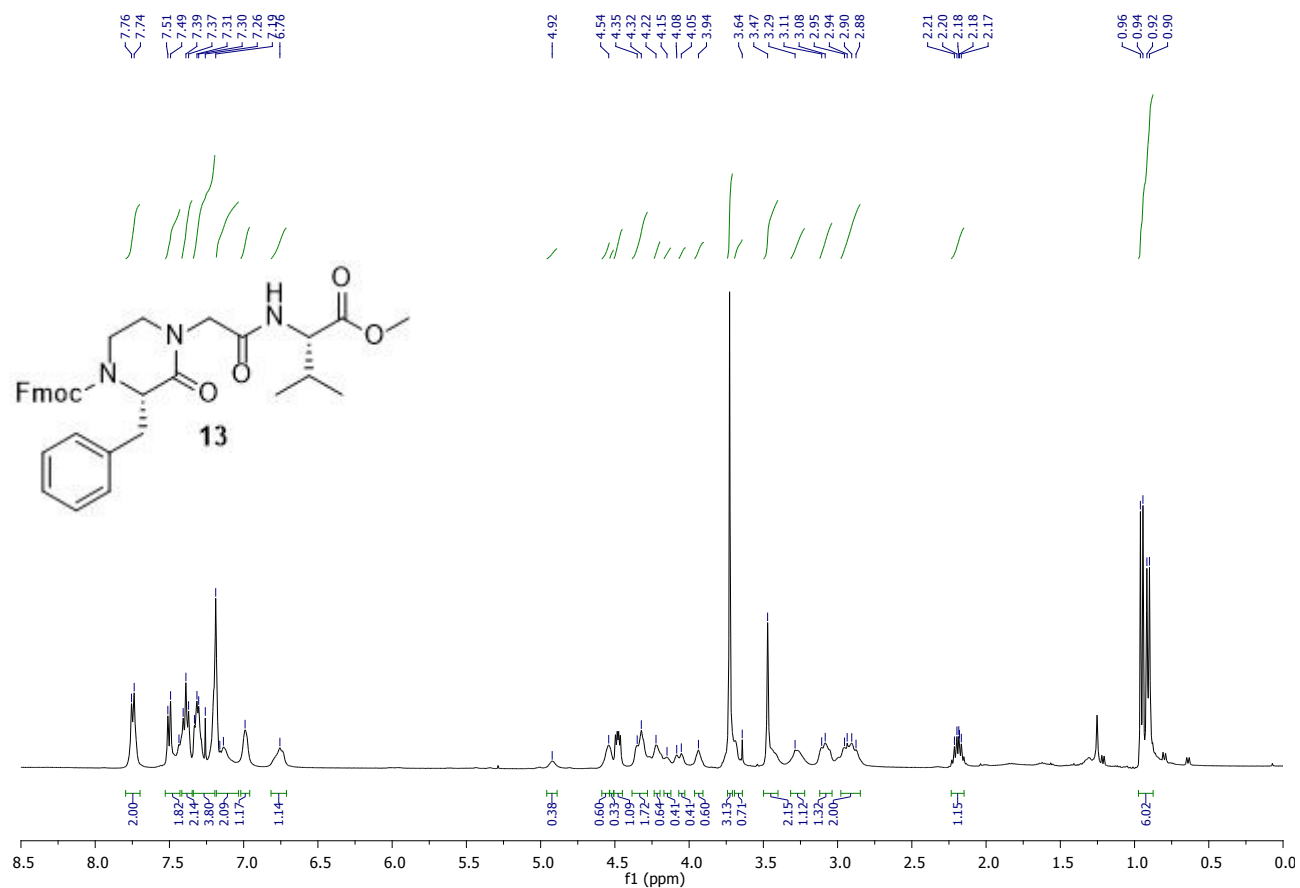
^1H NMR (400 MHz, CDCl_3)



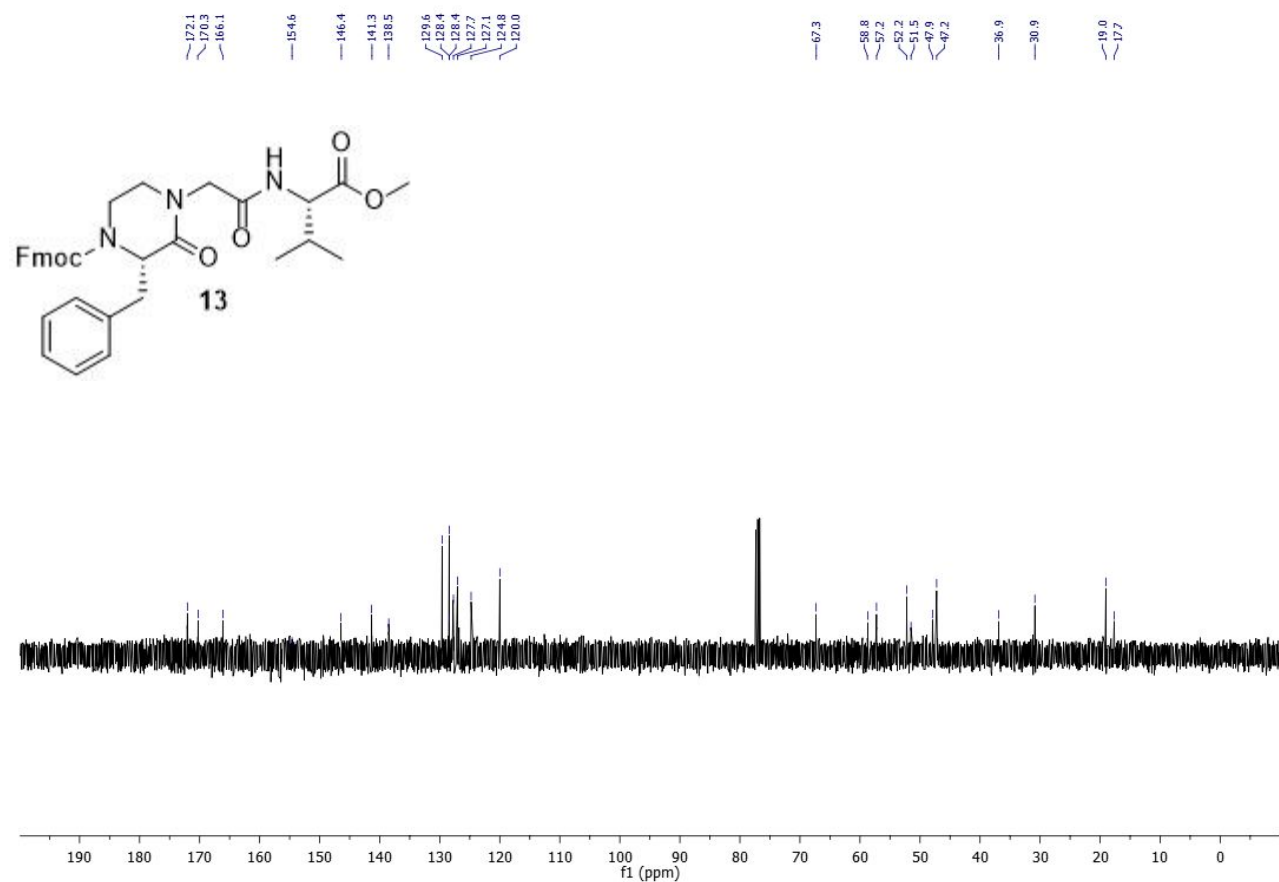
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)



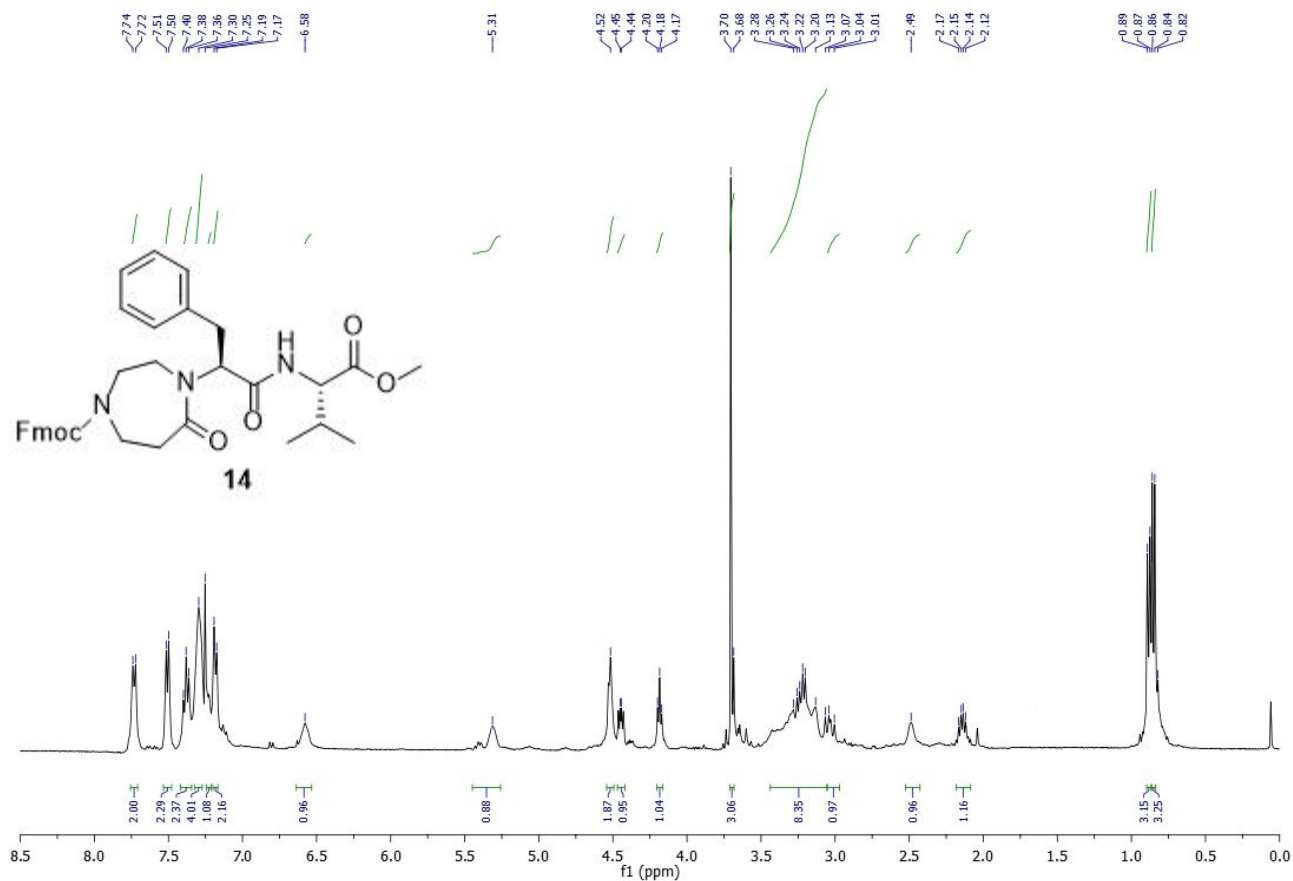
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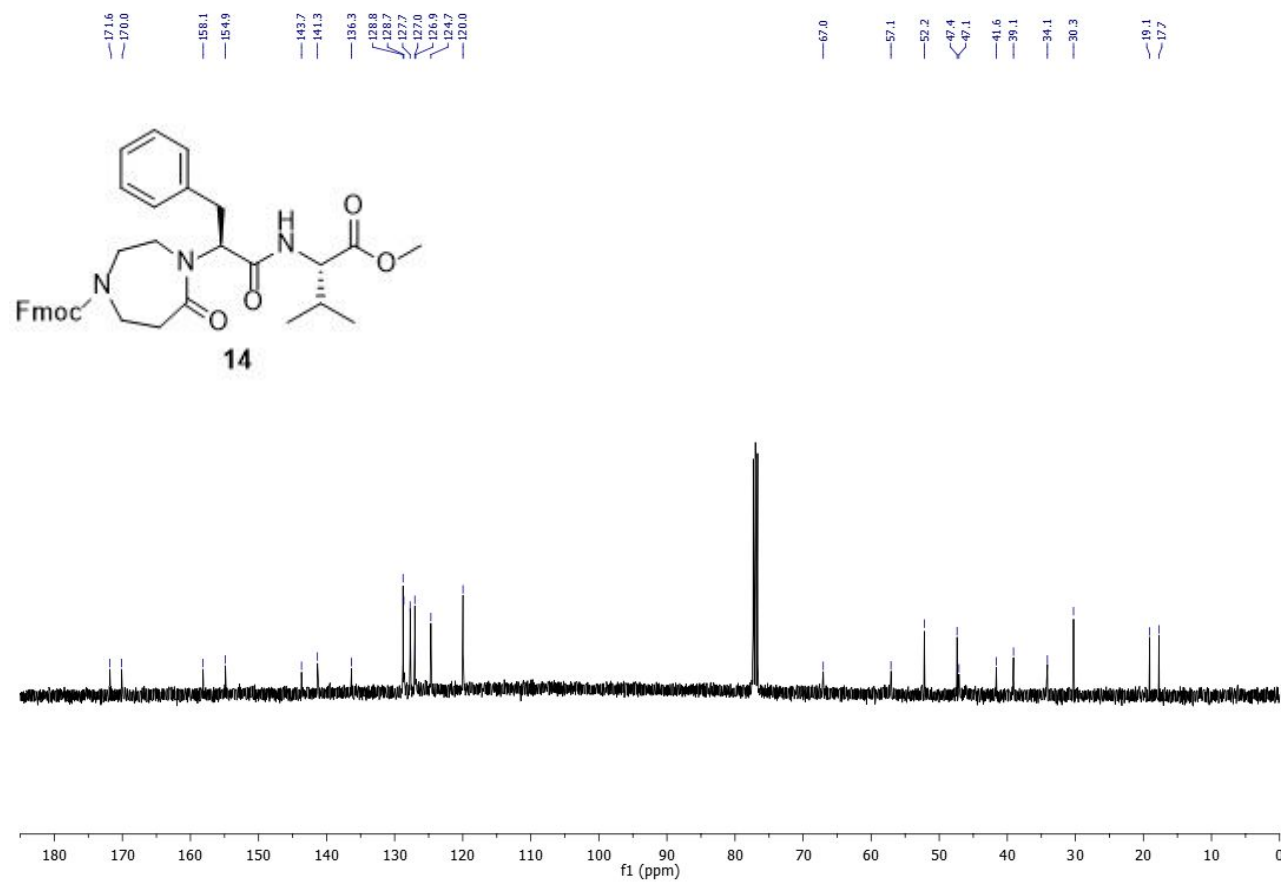
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)

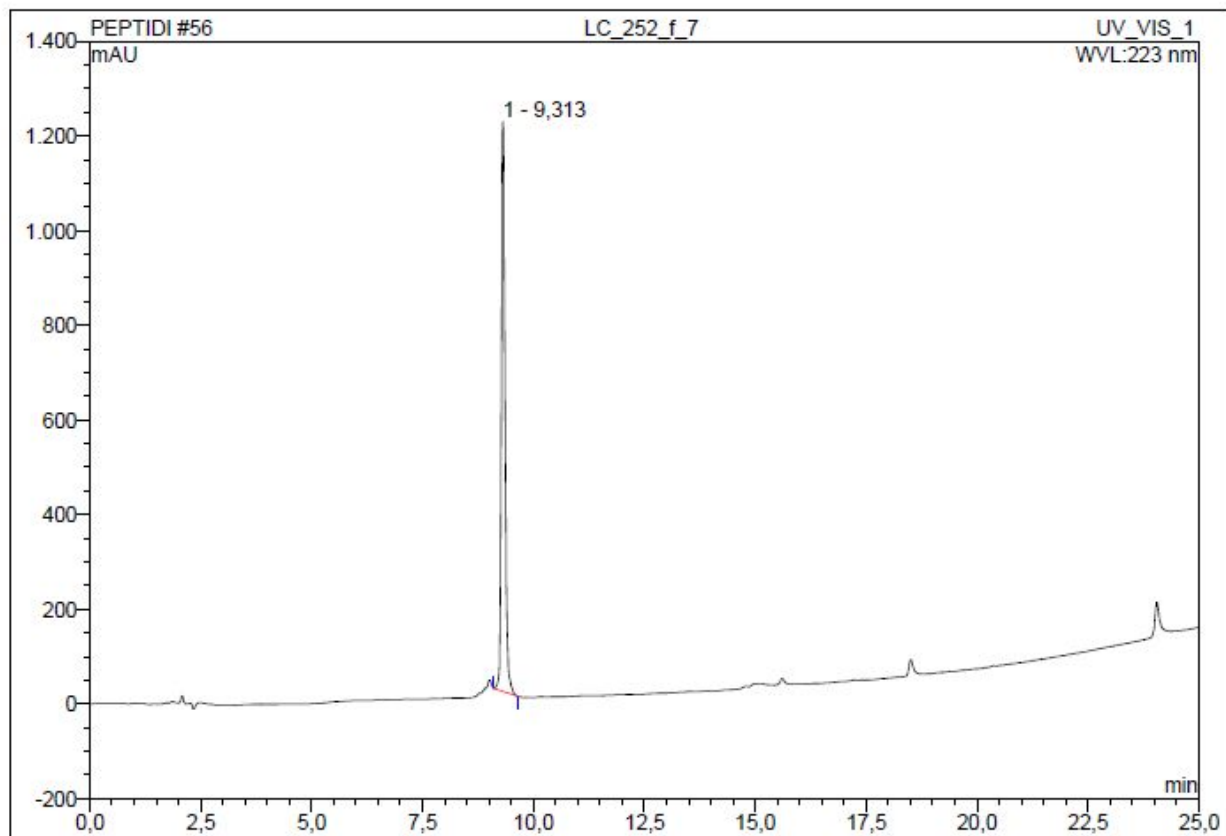


^1H NMR (400 MHz, CDCl_3)



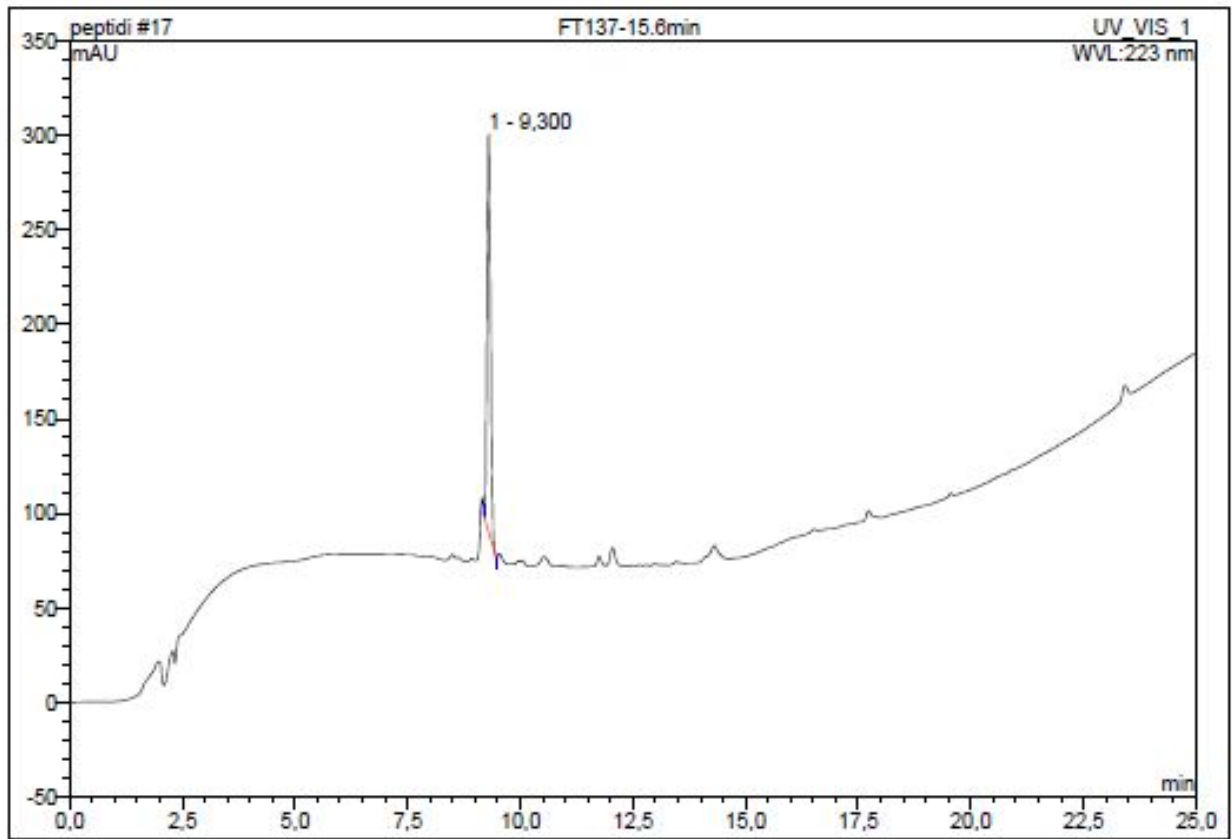
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)





| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---------------|-----------------|-----------|---------------|-----------------|---------------|--------|------|
| 1 | 9,31 | n.a. | 1203,637 | 116,137 | 100,00 | n.a. | BMB |
| Total: | | | 1203,637 | 116,137 | 100,00 | 0,000 | |

Figure S1: HPLC chromatogram of peptide 15.



| No. | Ret.Time min | Peak Name | Height mAU | Area mAU*min | Rel.Area % | Amount | Type |
|---------------|-----------------|-----------|---------------|-----------------|---------------|--------|------|
| 1 | 9,30 | n.a. | 210,440 | 18,988 | 100,00 | n.a. | BMB |
| Total: | | | 210,440 | 18,988 | 100,00 | 0,000 | |

Figure S2: HPLC chromatogram of peptide 16

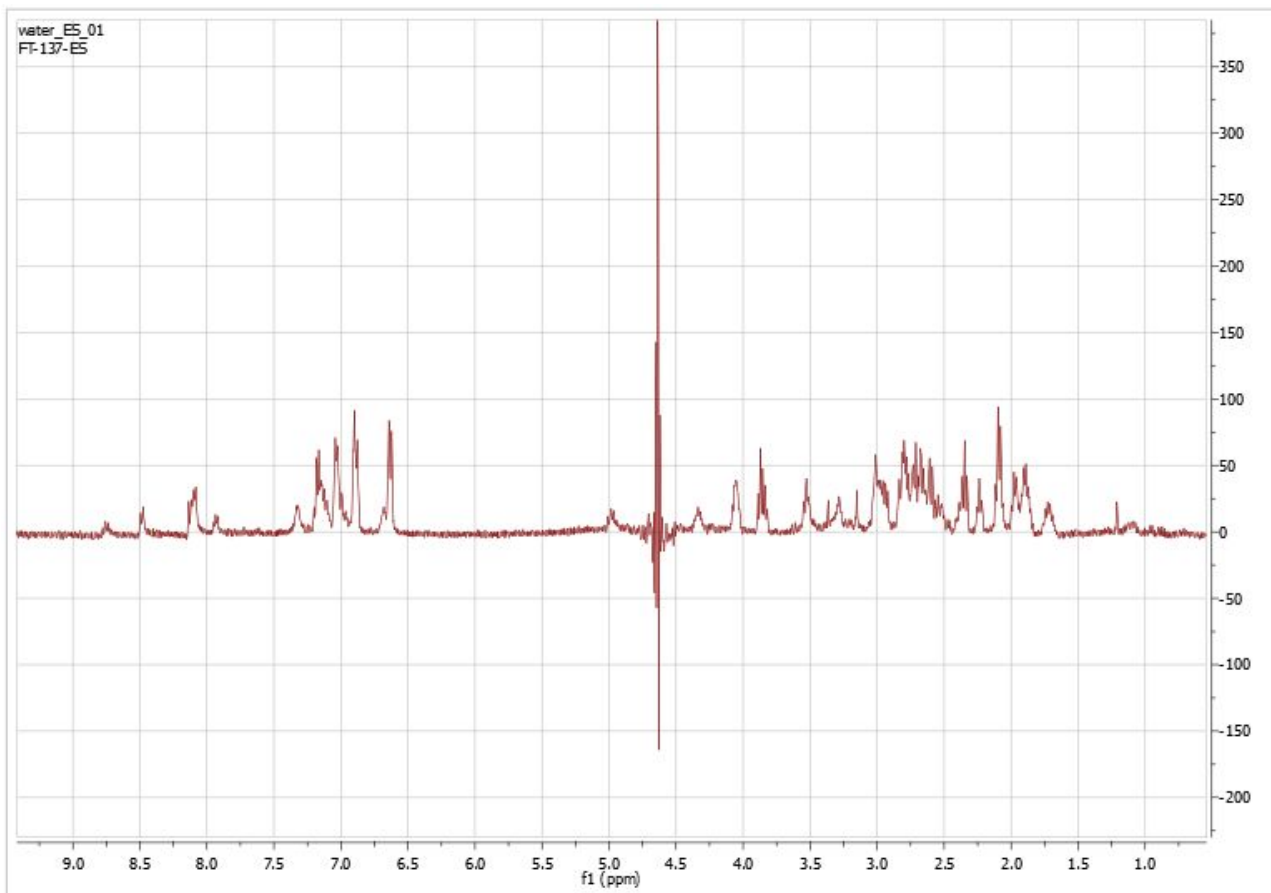


Figure S3: 1H-ES of peptide 16

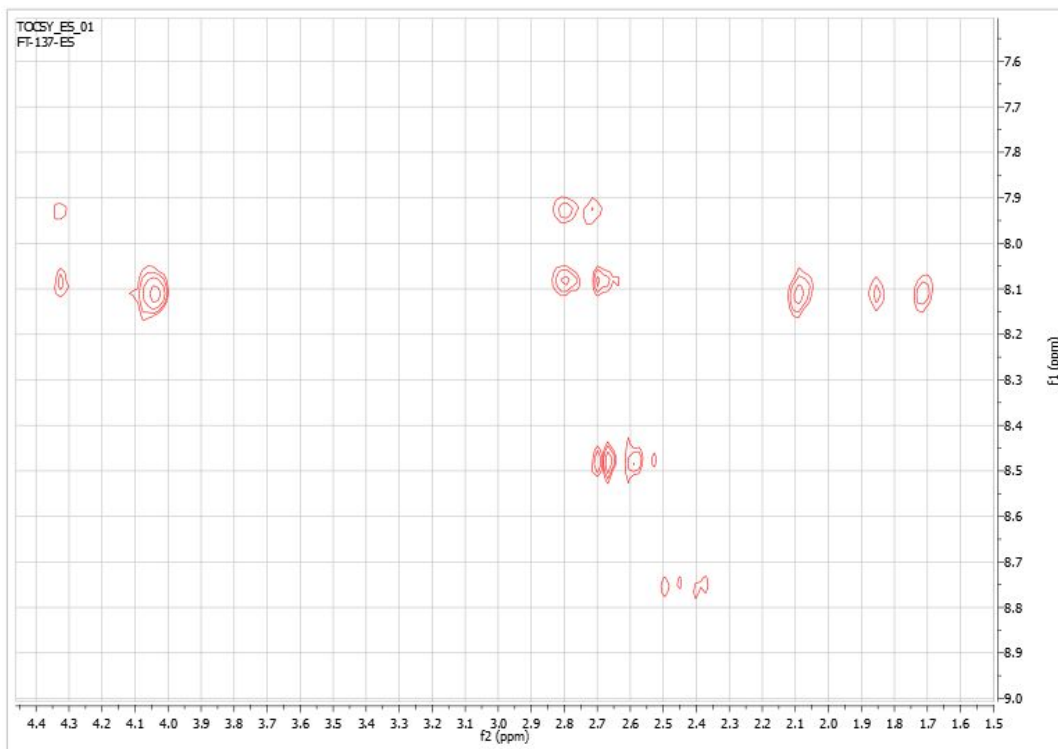
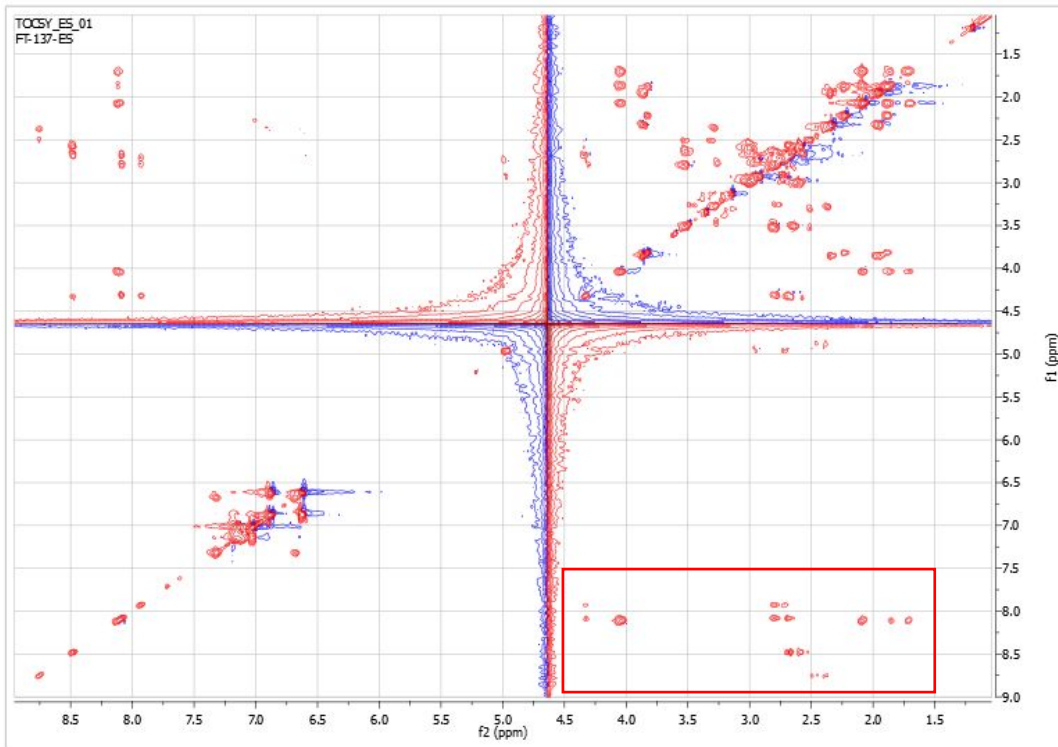


Figure S4: TOCSY-ES of peptide 16

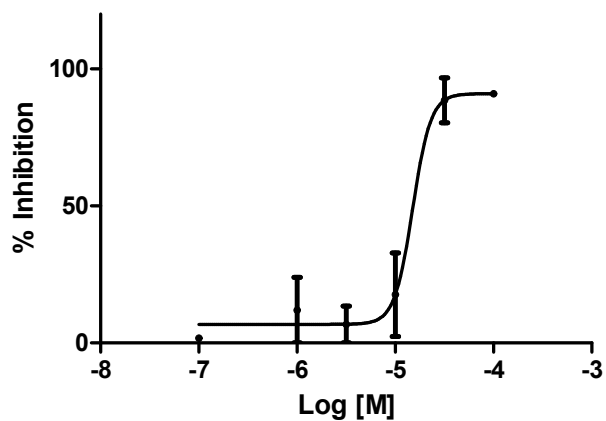


Figure S5: Inhibition curve of peptide **15** on 3CLPro enzyme. $IC_{50} = 15 \pm 6 \mu\text{M}$. Experiments were conducted in triplicate.

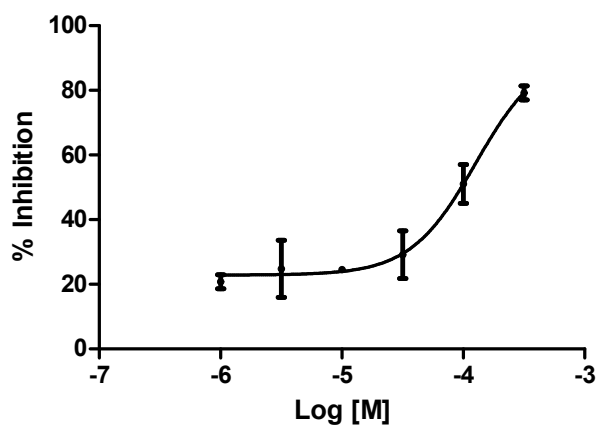


Figure S6: Inhibition curve of peptide **16** on 3CLPro enzyme. $IC_{50} = 127 \pm 76 \mu\text{M}$. Experiments were conducted in triplicate.

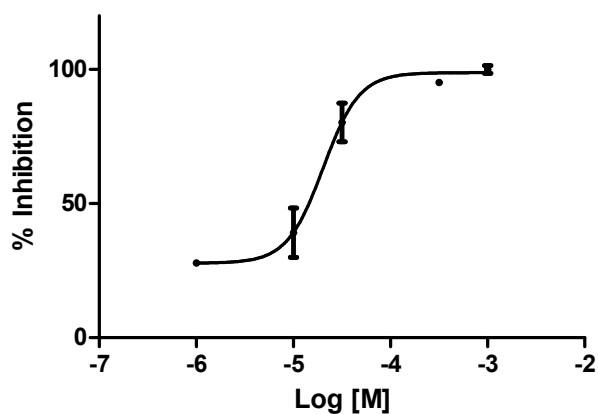


Figure S7: Inhibition curve of peptide **16** of Spike/ACE2 interaction. $IC_{50} = 20 \pm 5 \mu\text{M}$. Experiments were conducted in triplicate.