

Supplementary Material

An improved, gram-scale synthesis of protected 3-haloazetidines: Rapid diversified synthesis of azetidine-3-carboxylic acids

Youngran Ji,^a Lukasz Wojtas,^c and Justin M. Lopchuk*^{a,b,c}

^a Drug Discovery Department, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, Florida 33612, United States

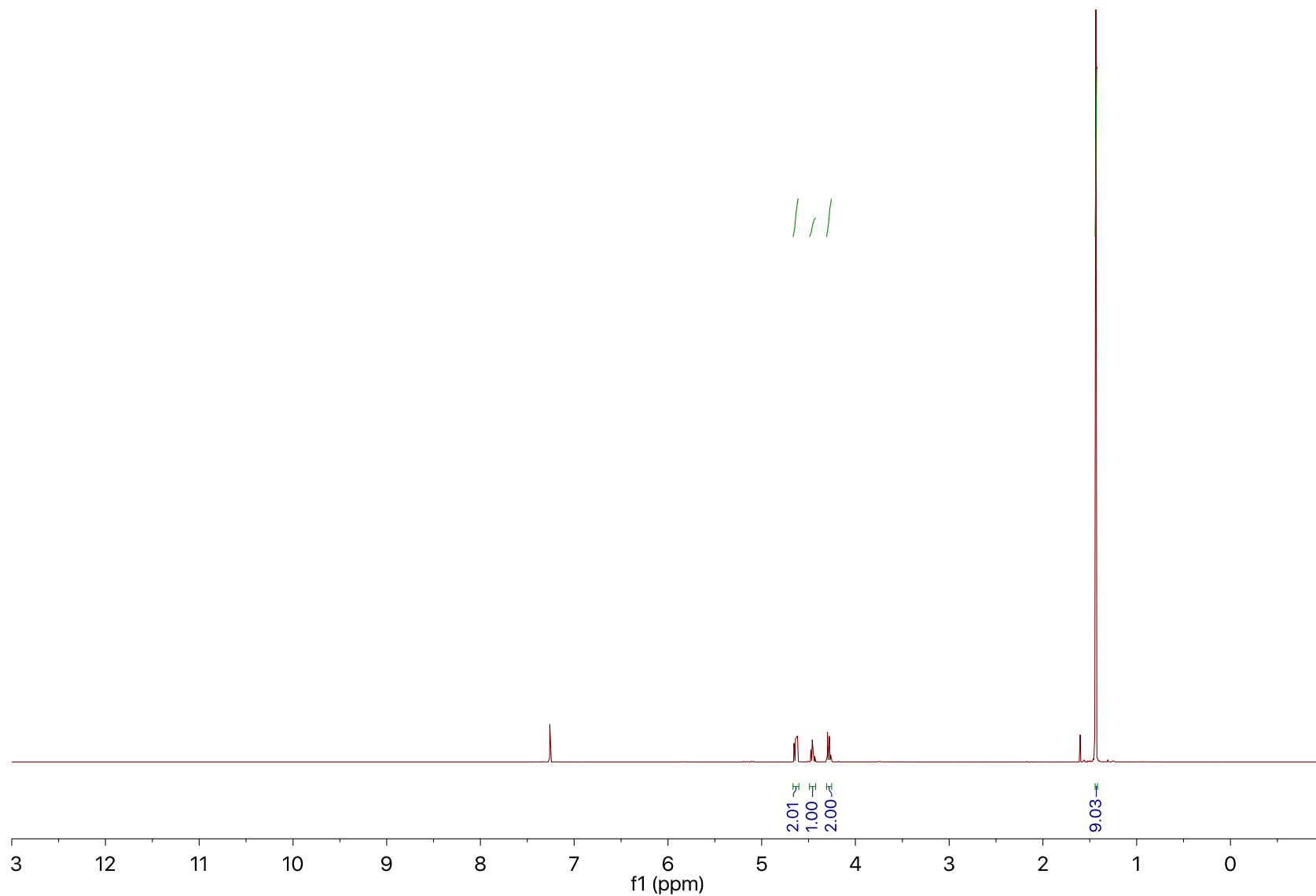
^b Department of Oncologic Sciences, College of Medicine, University of South Florida, Tampa, Florida 33612, United States

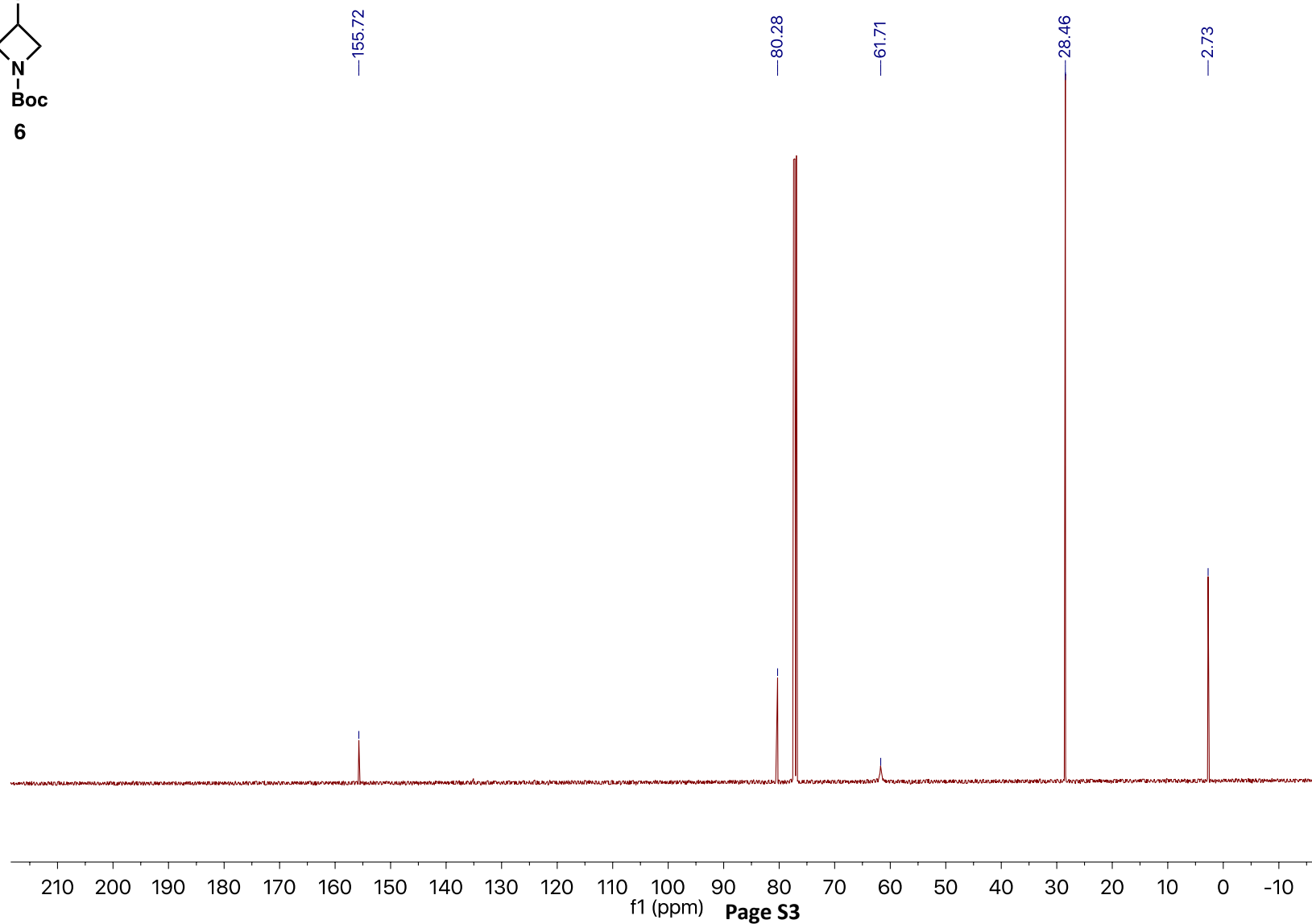
^c Department of Chemistry, University of South Florida, Tampa, Florida 33620, United States

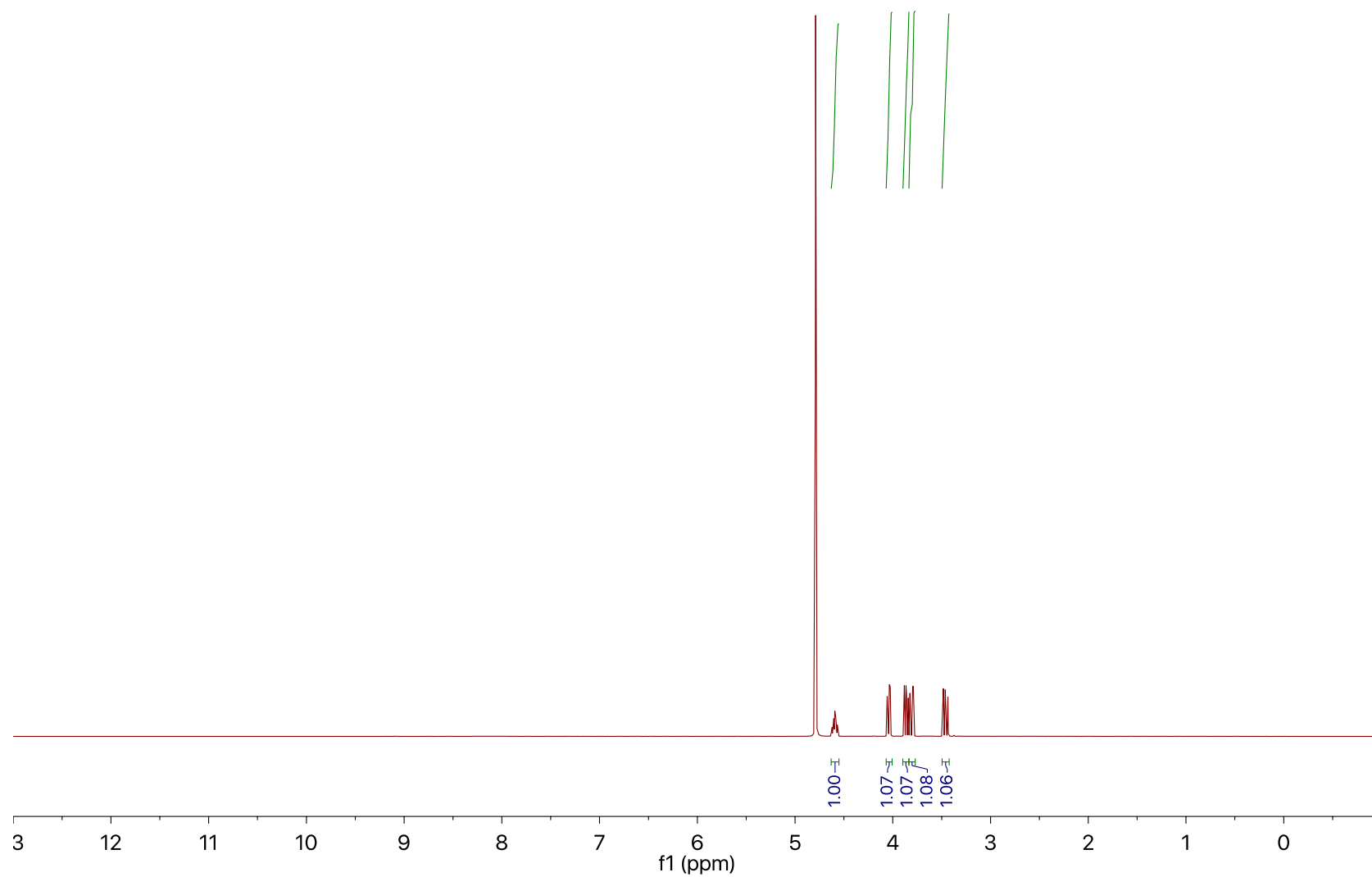
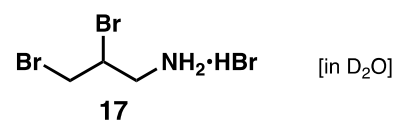
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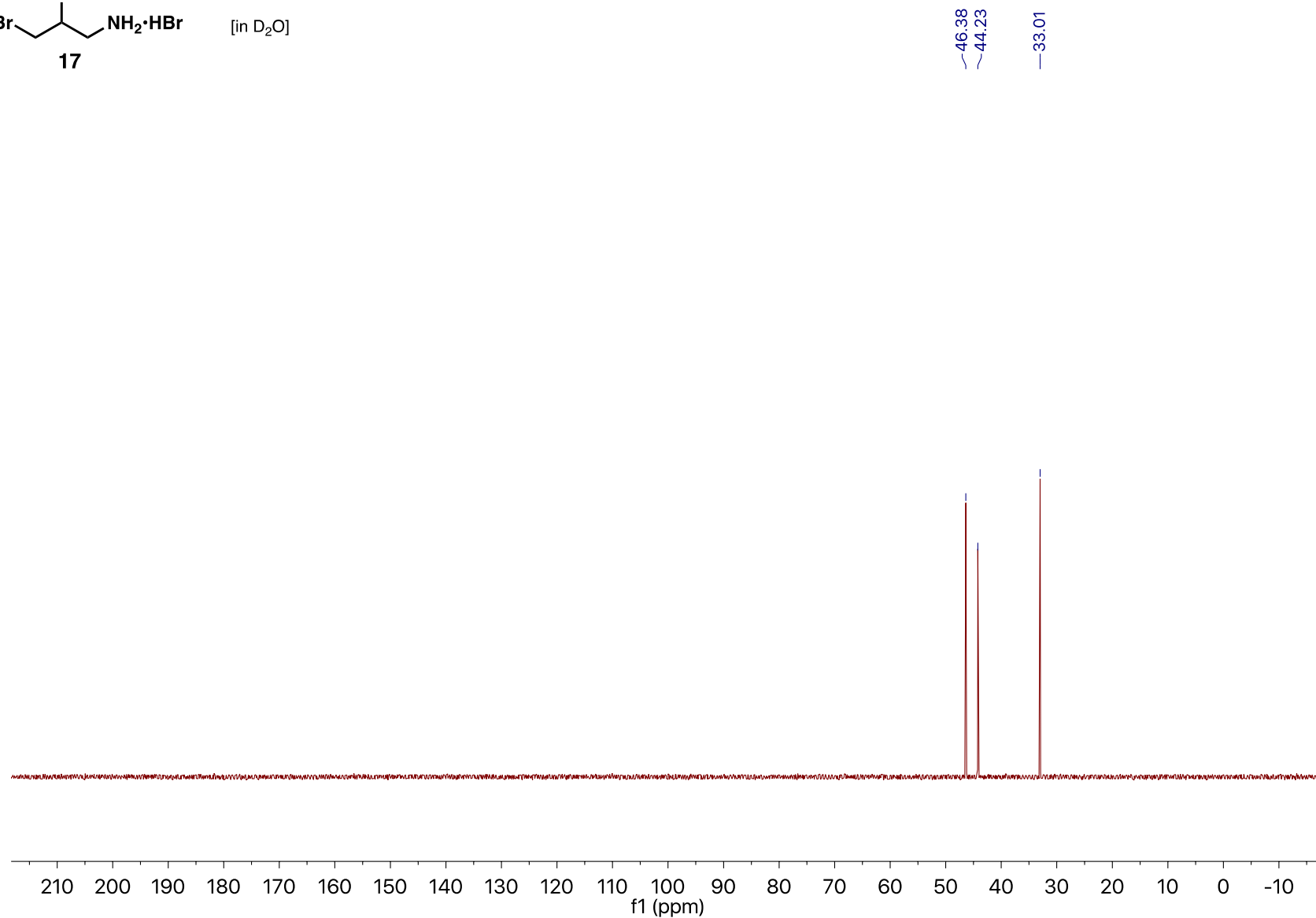
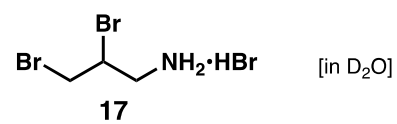
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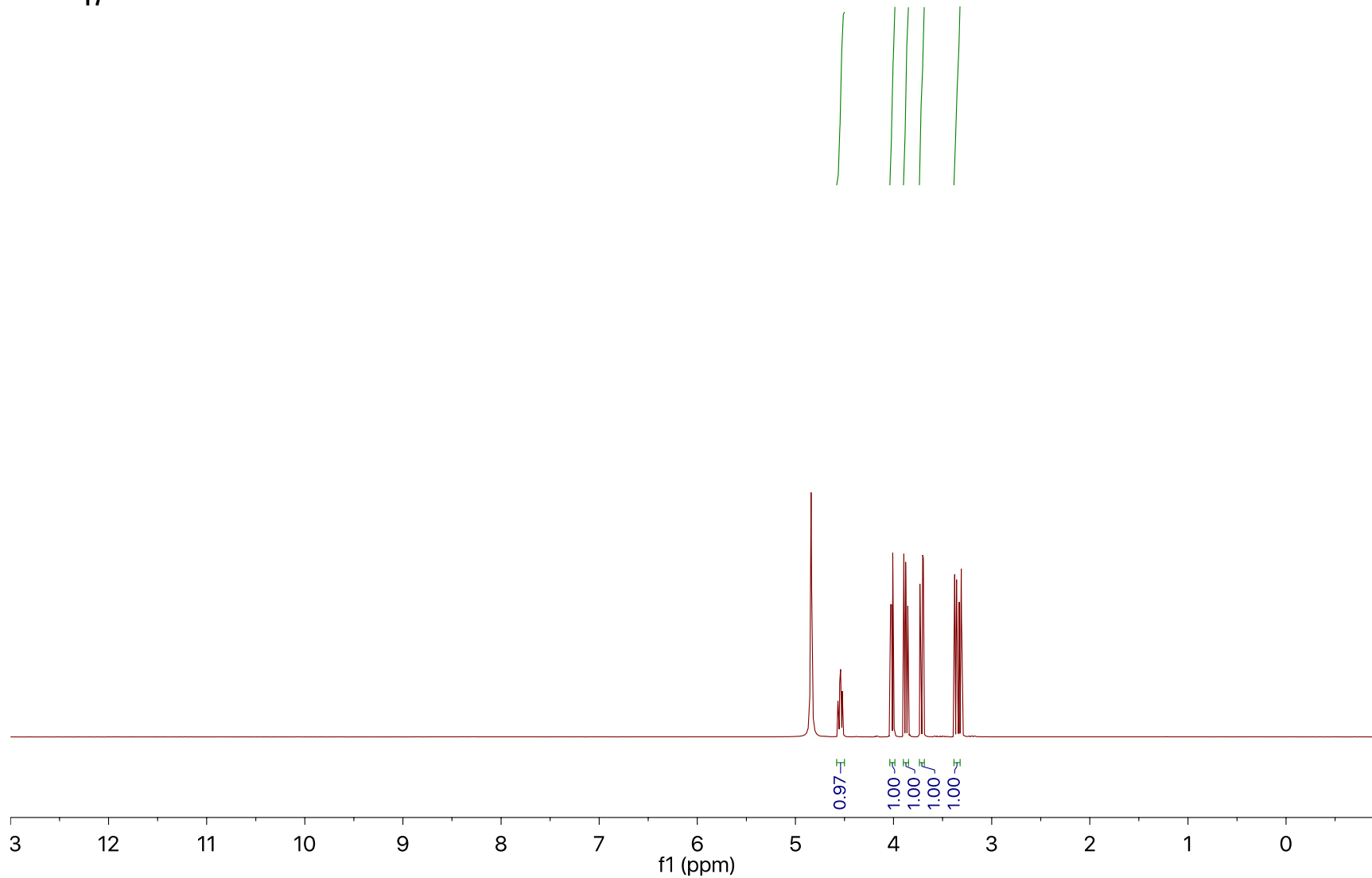
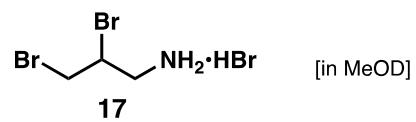
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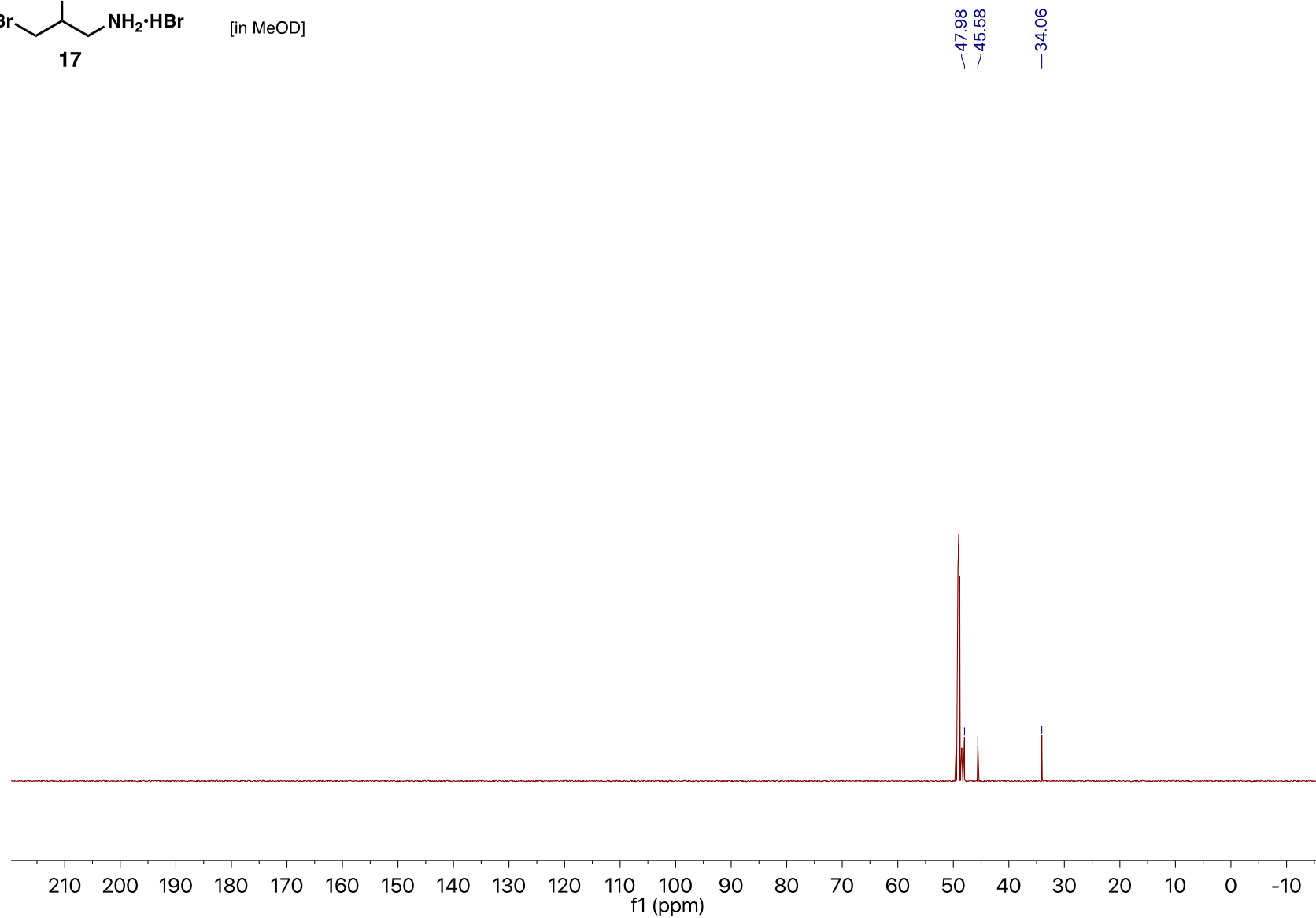
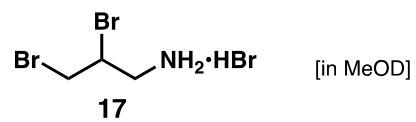


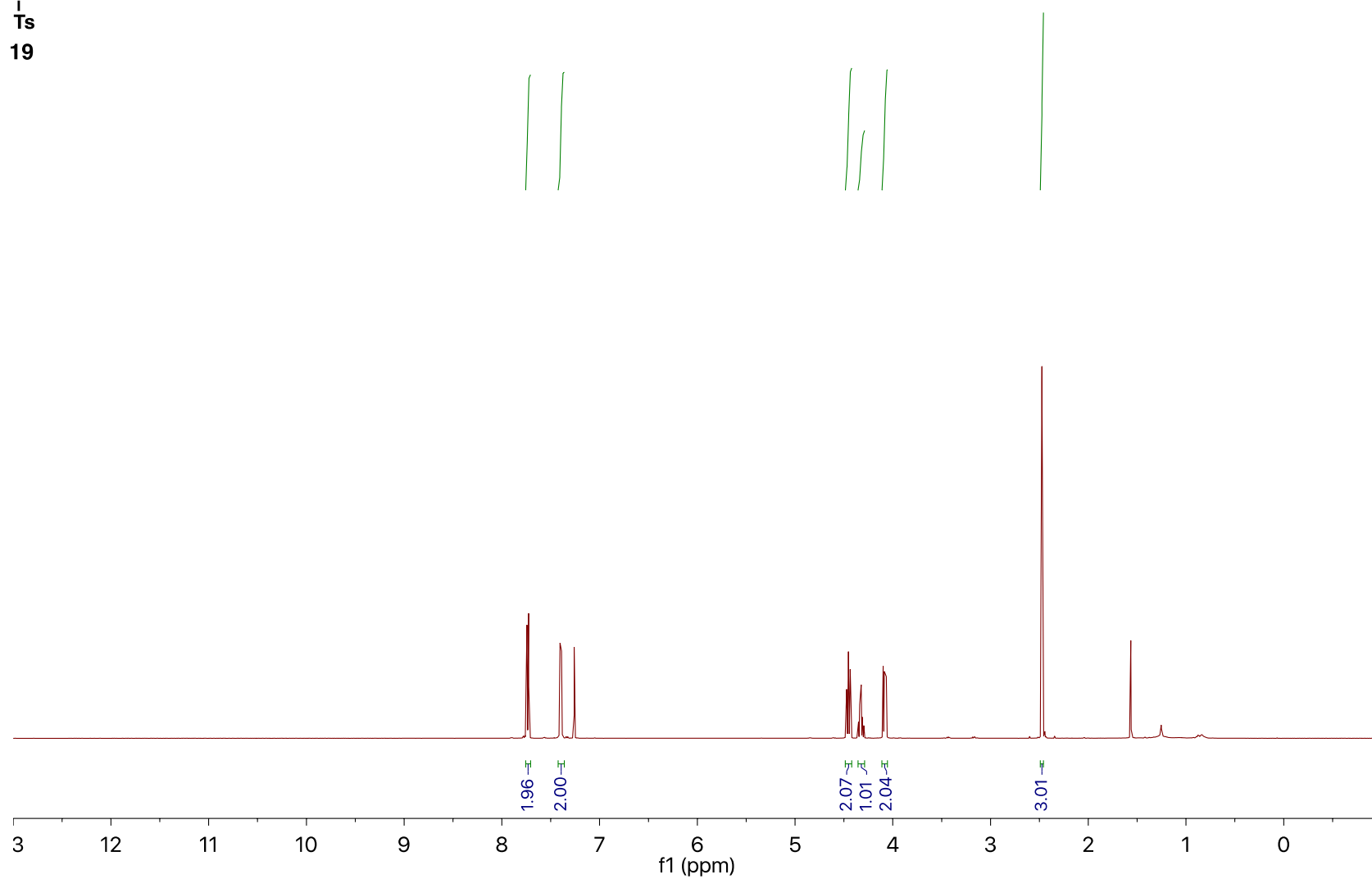
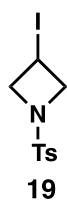


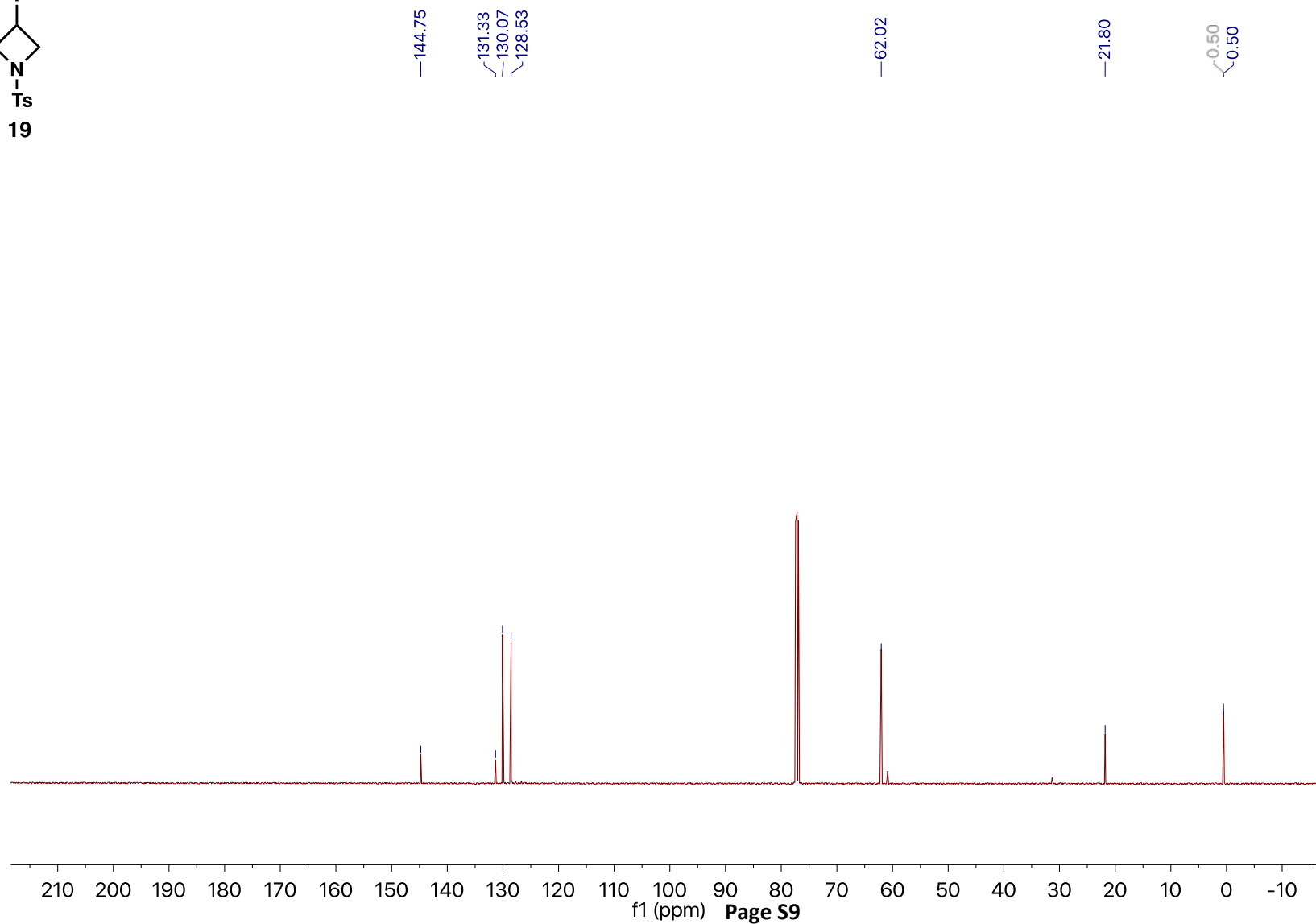
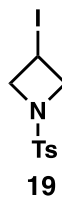


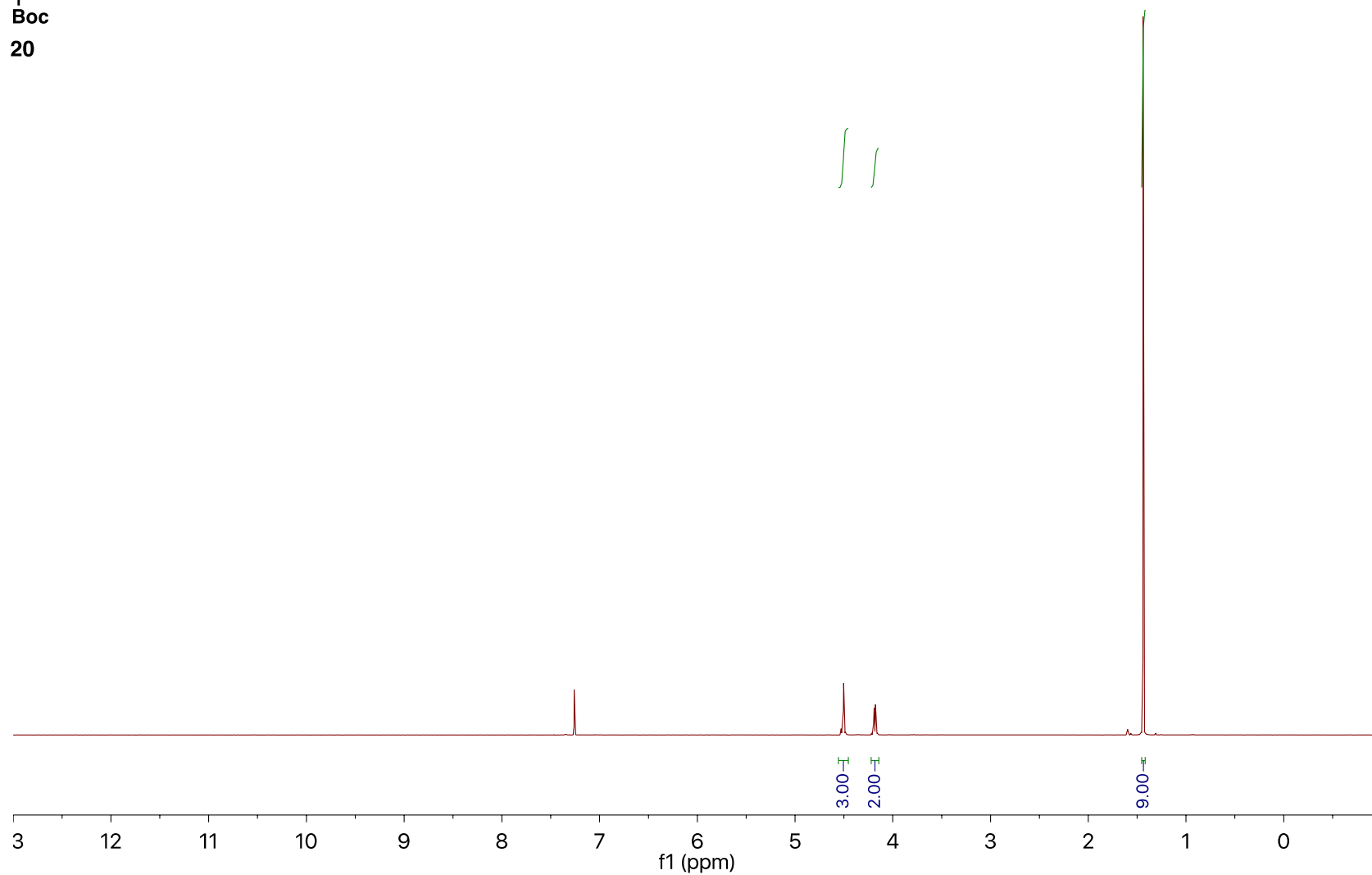














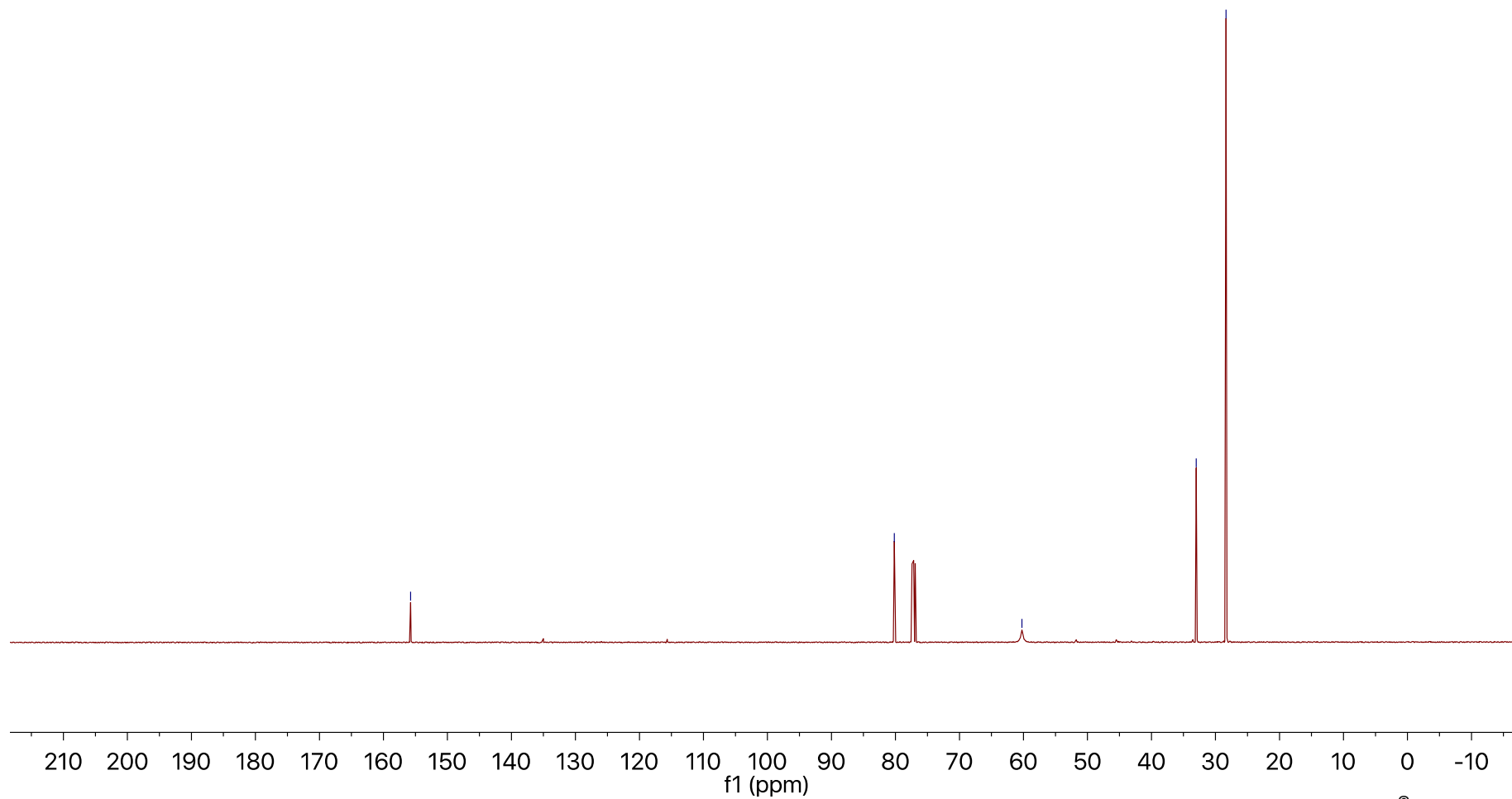
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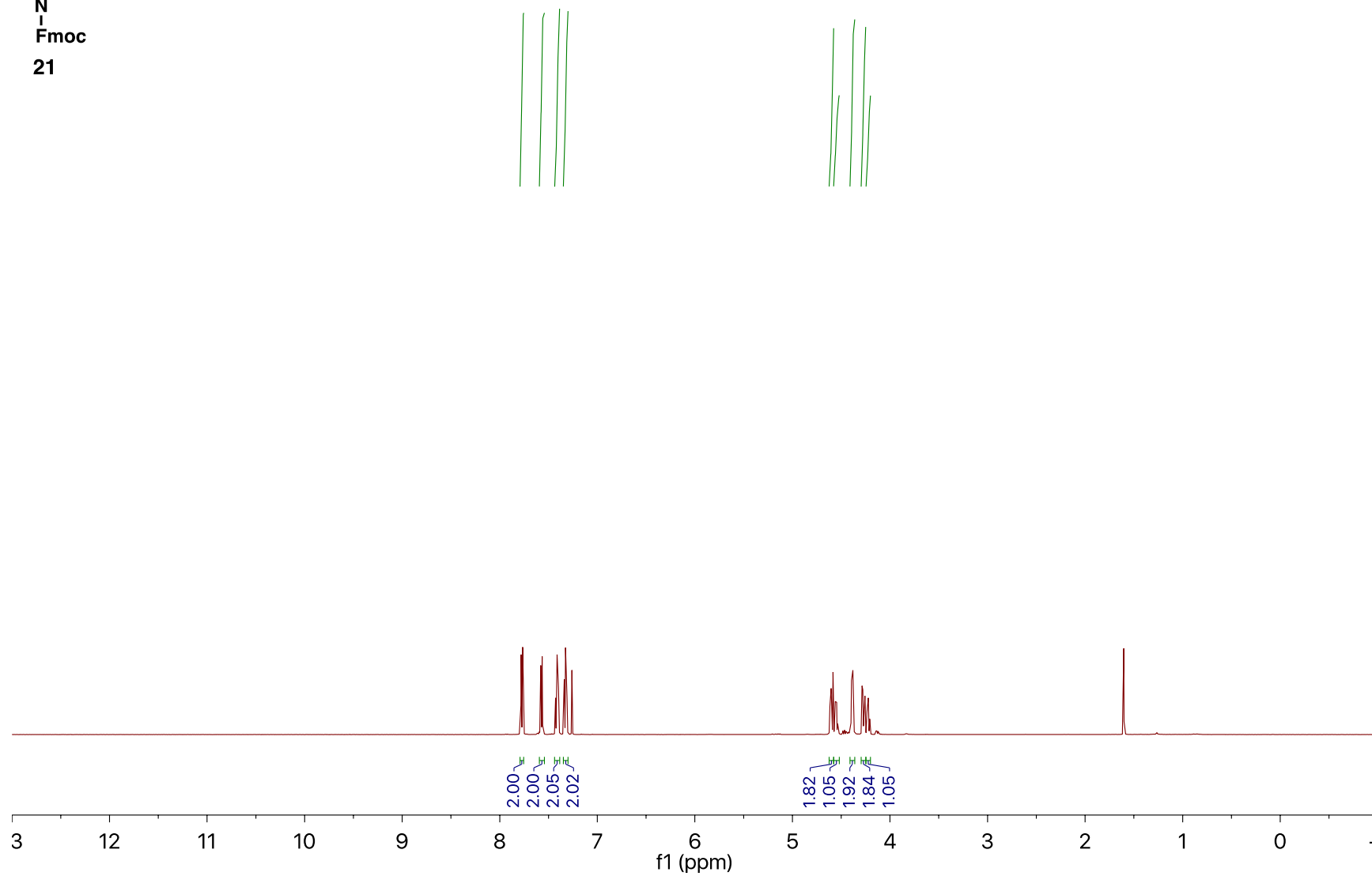
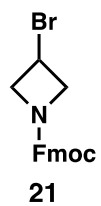
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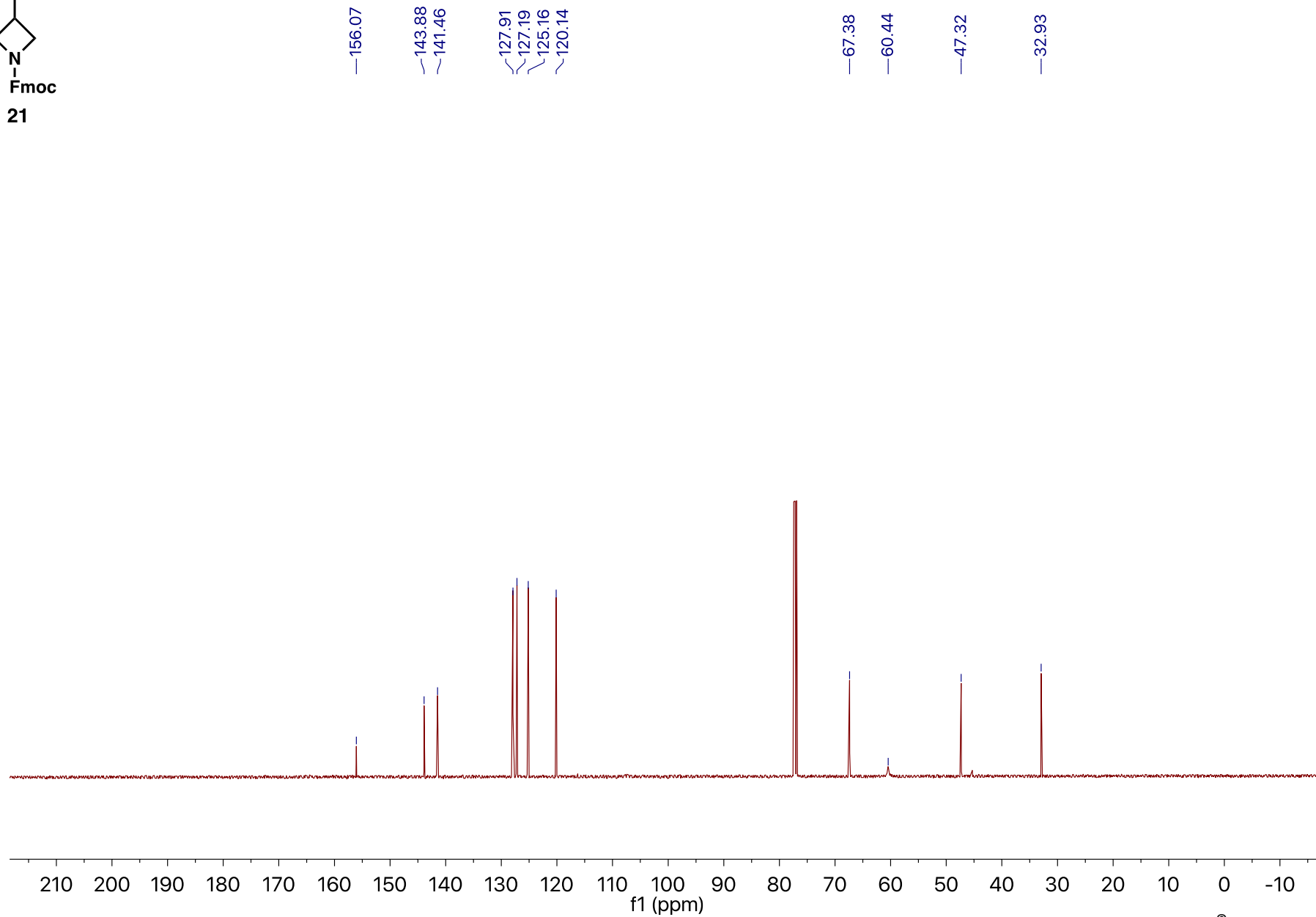
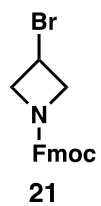
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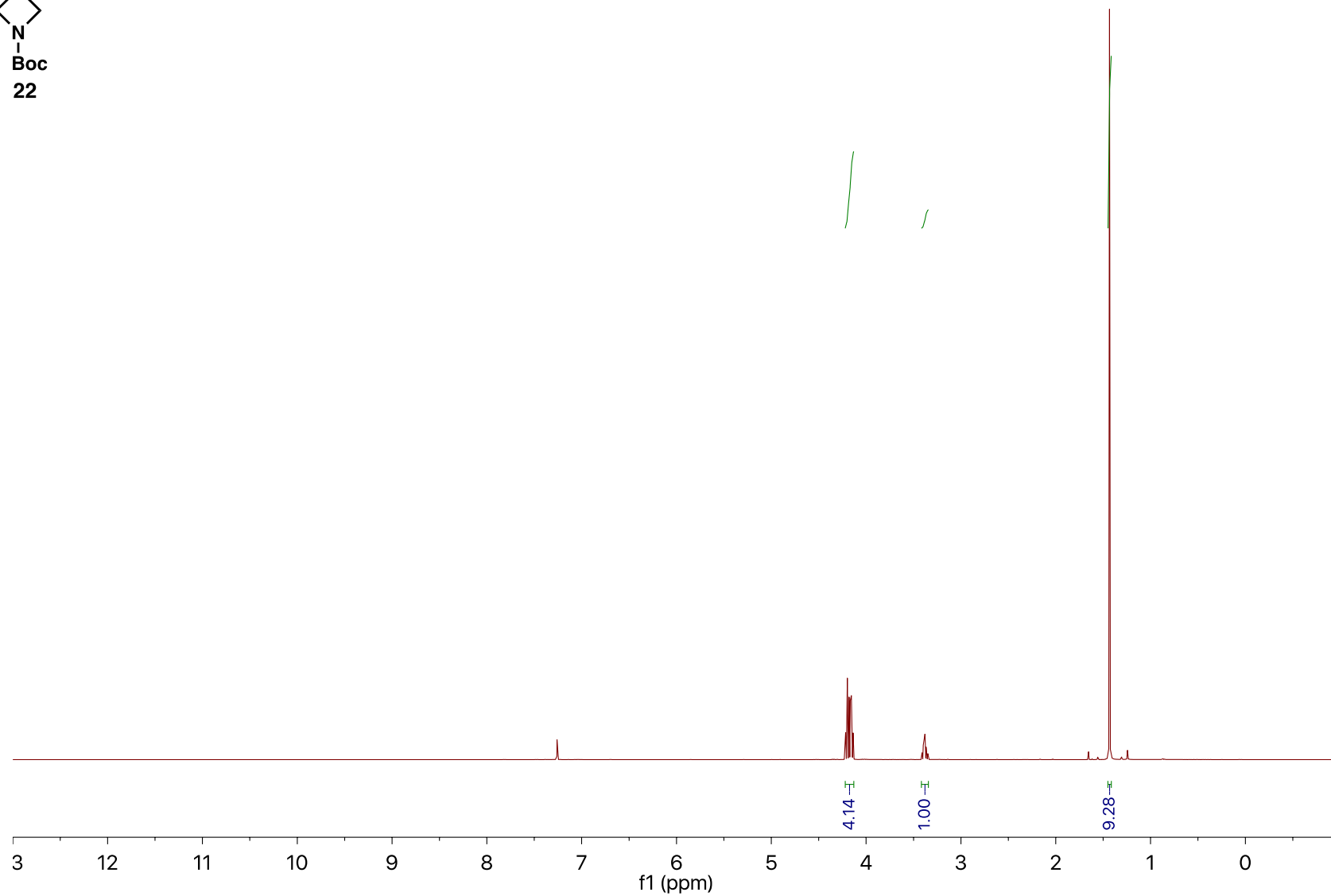
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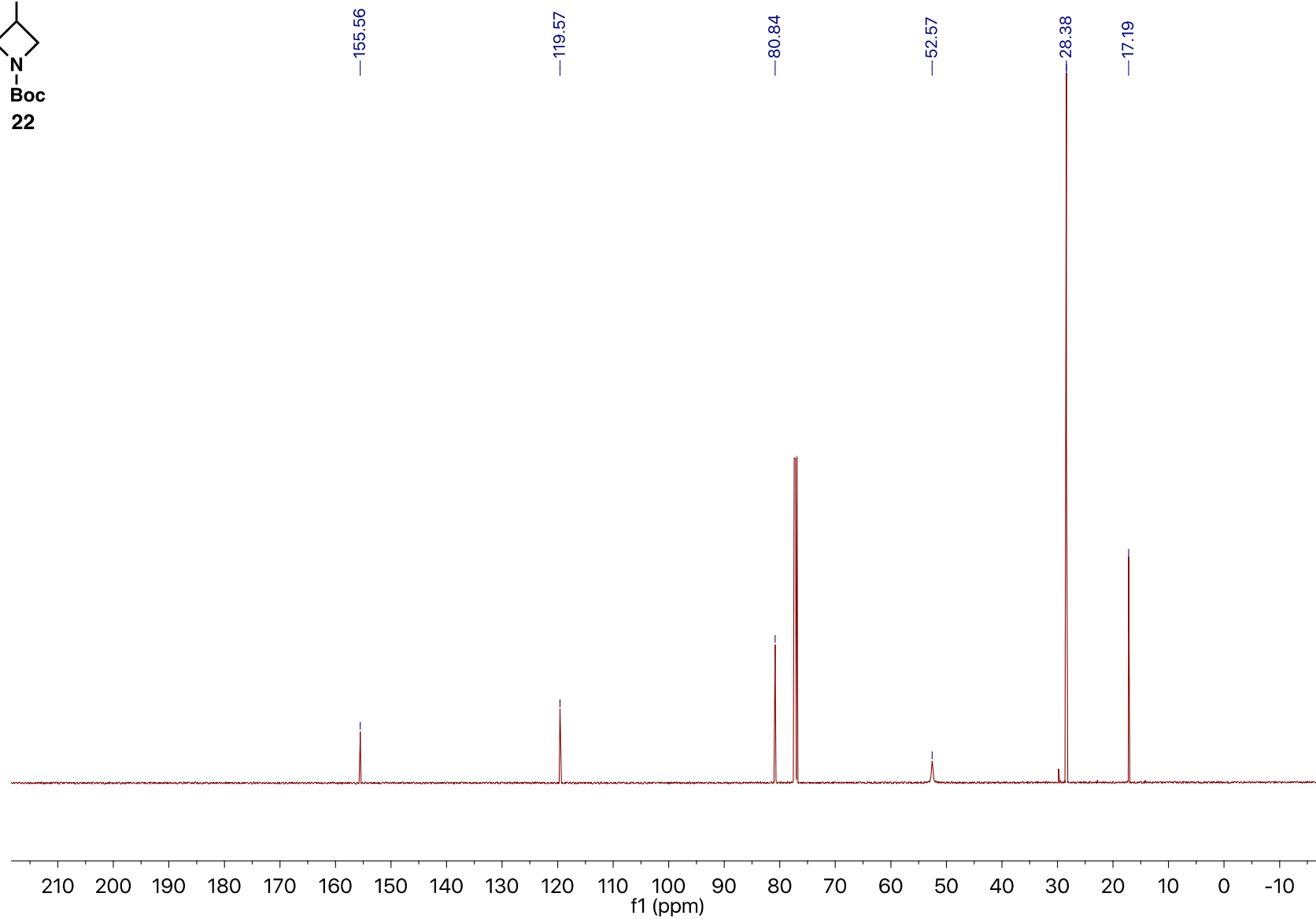
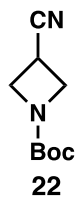
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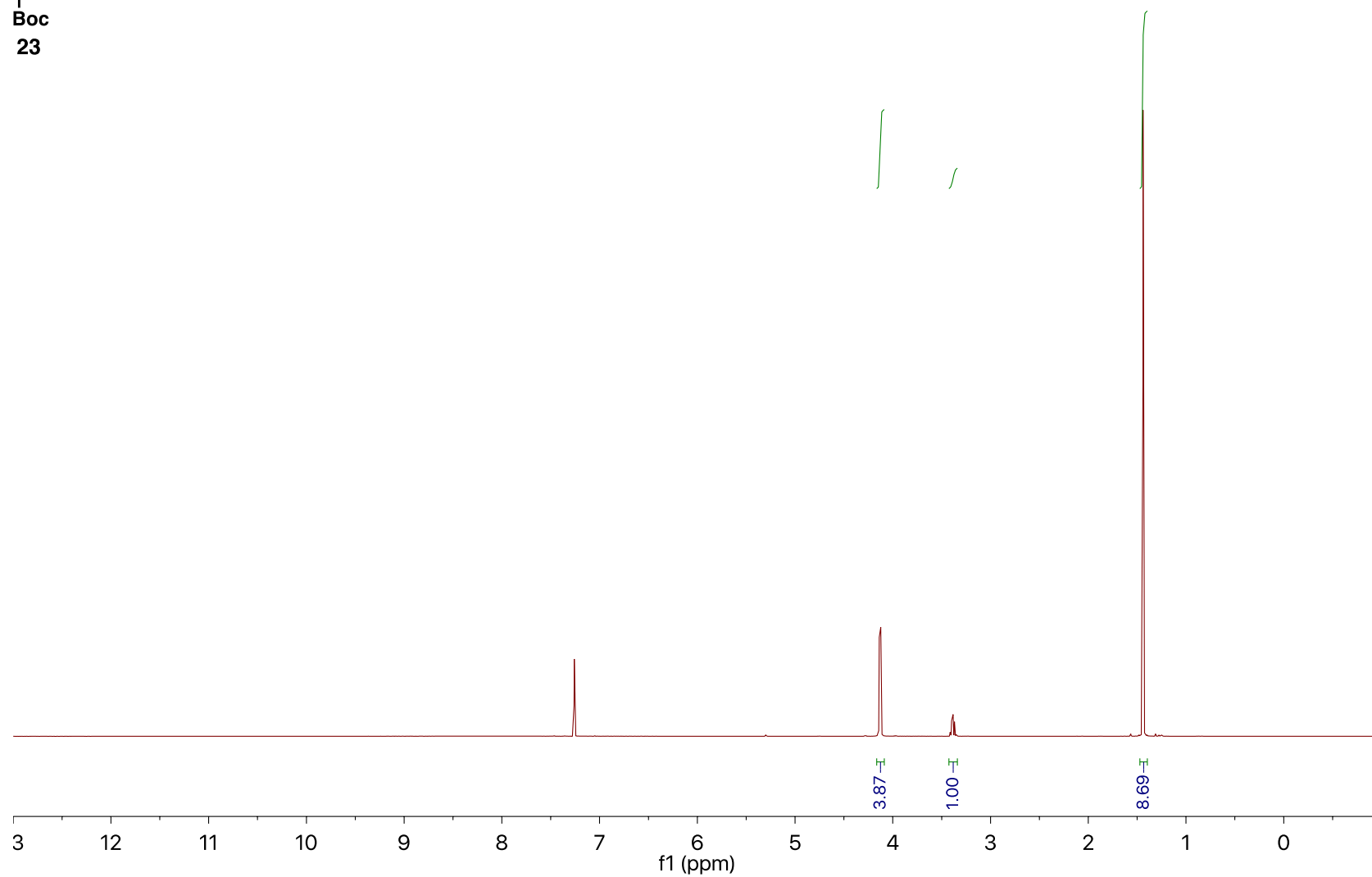
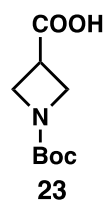


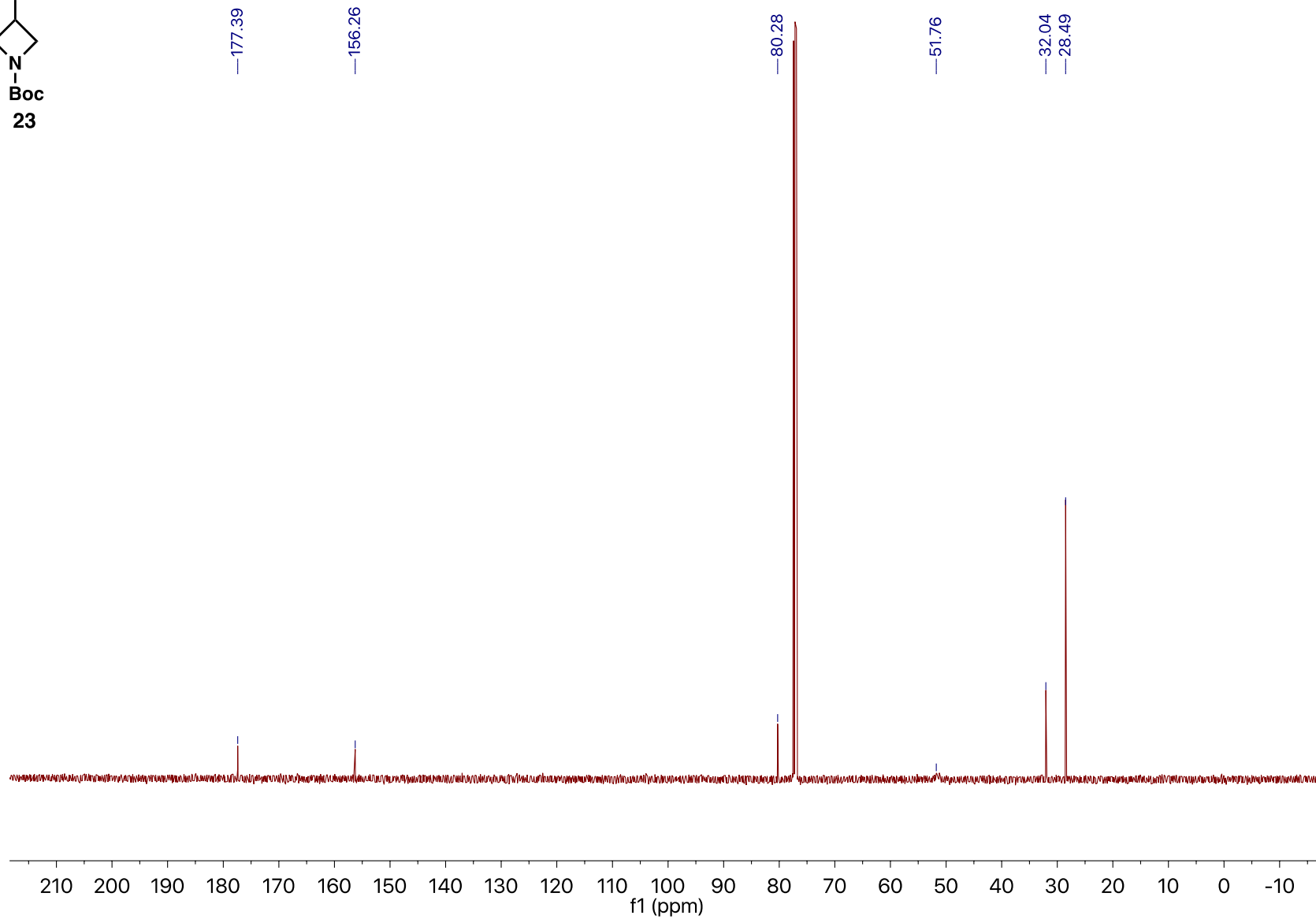
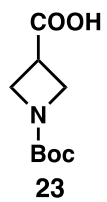


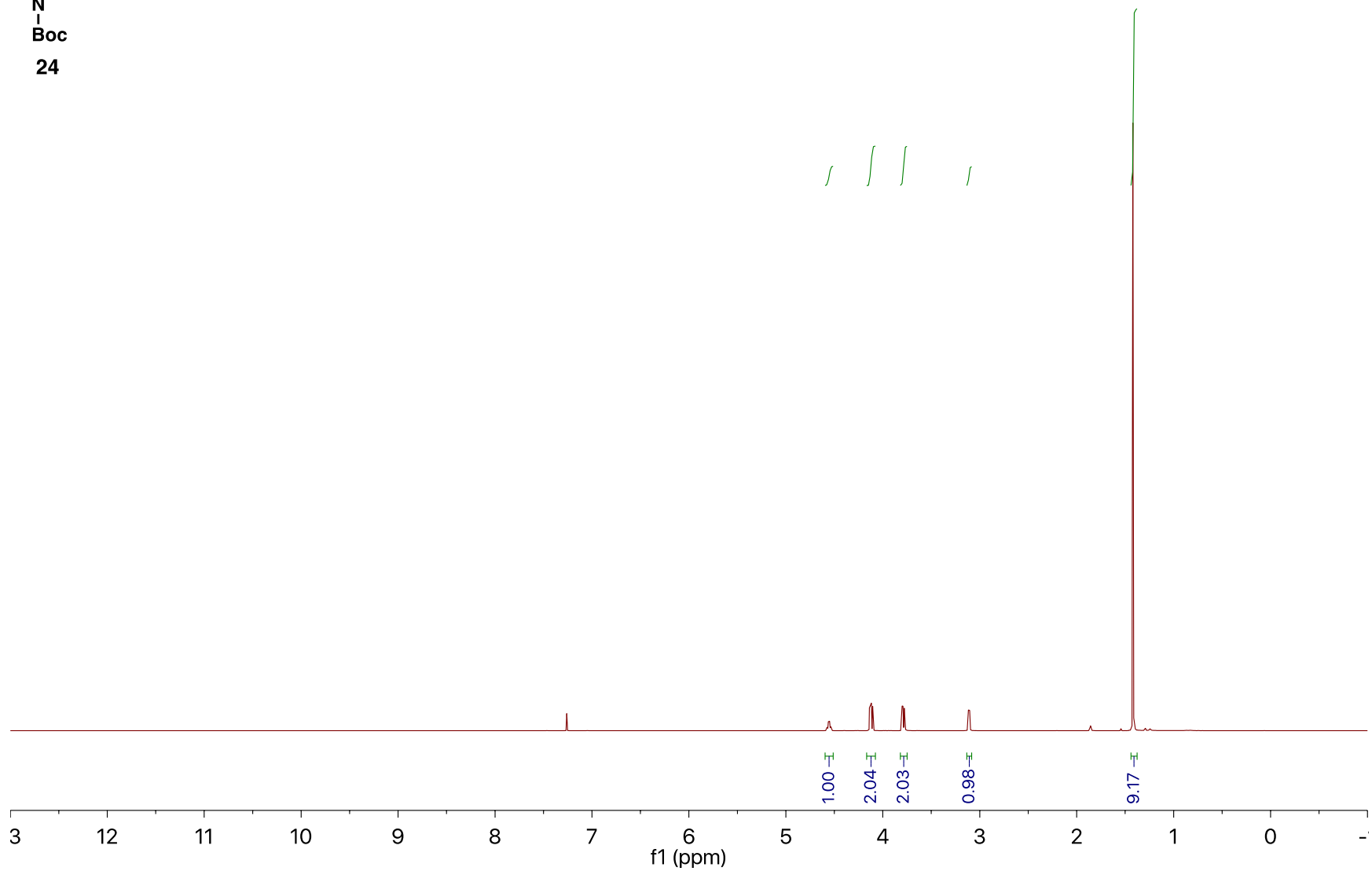


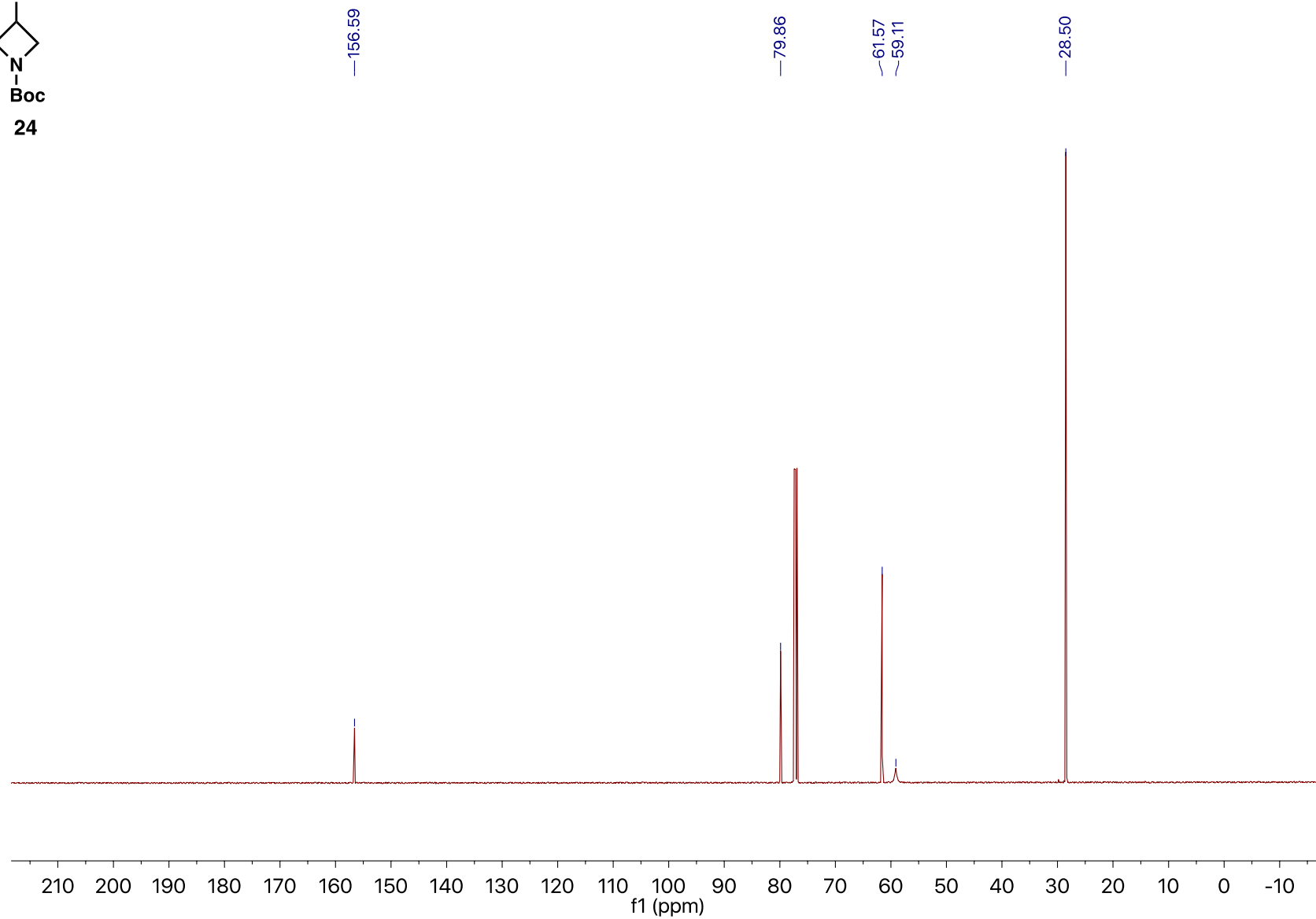


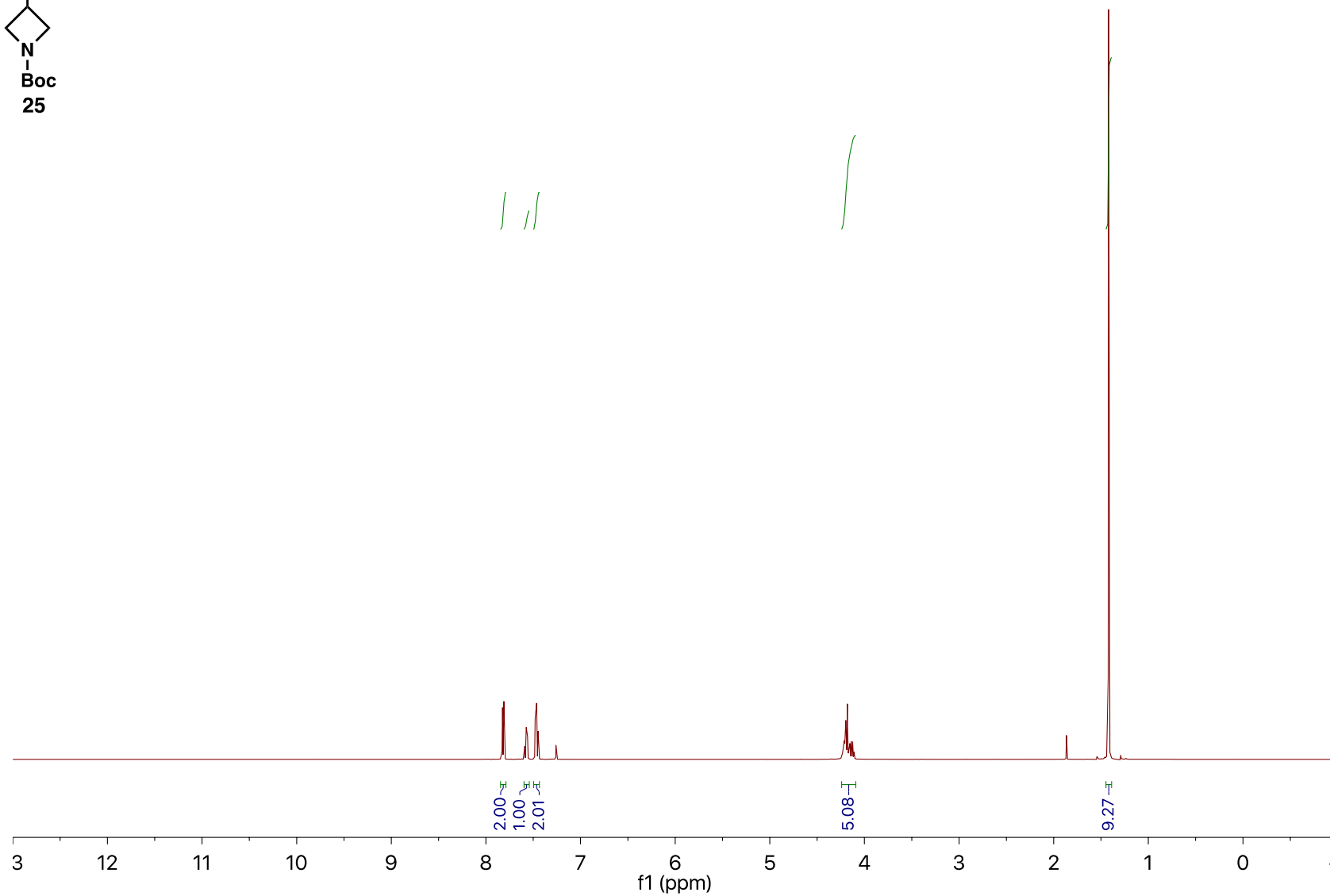
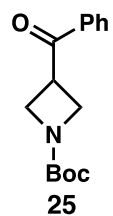


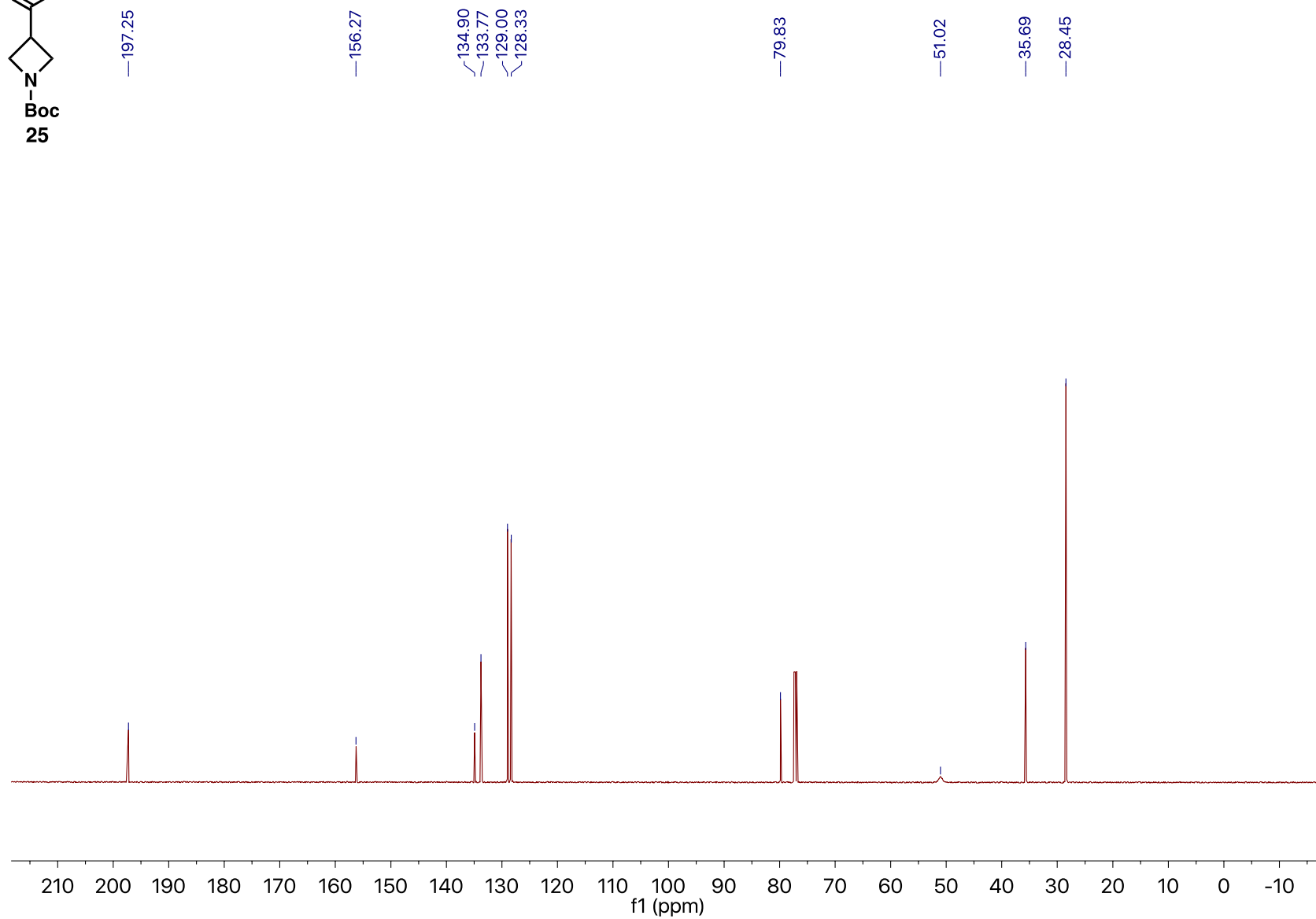
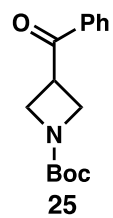


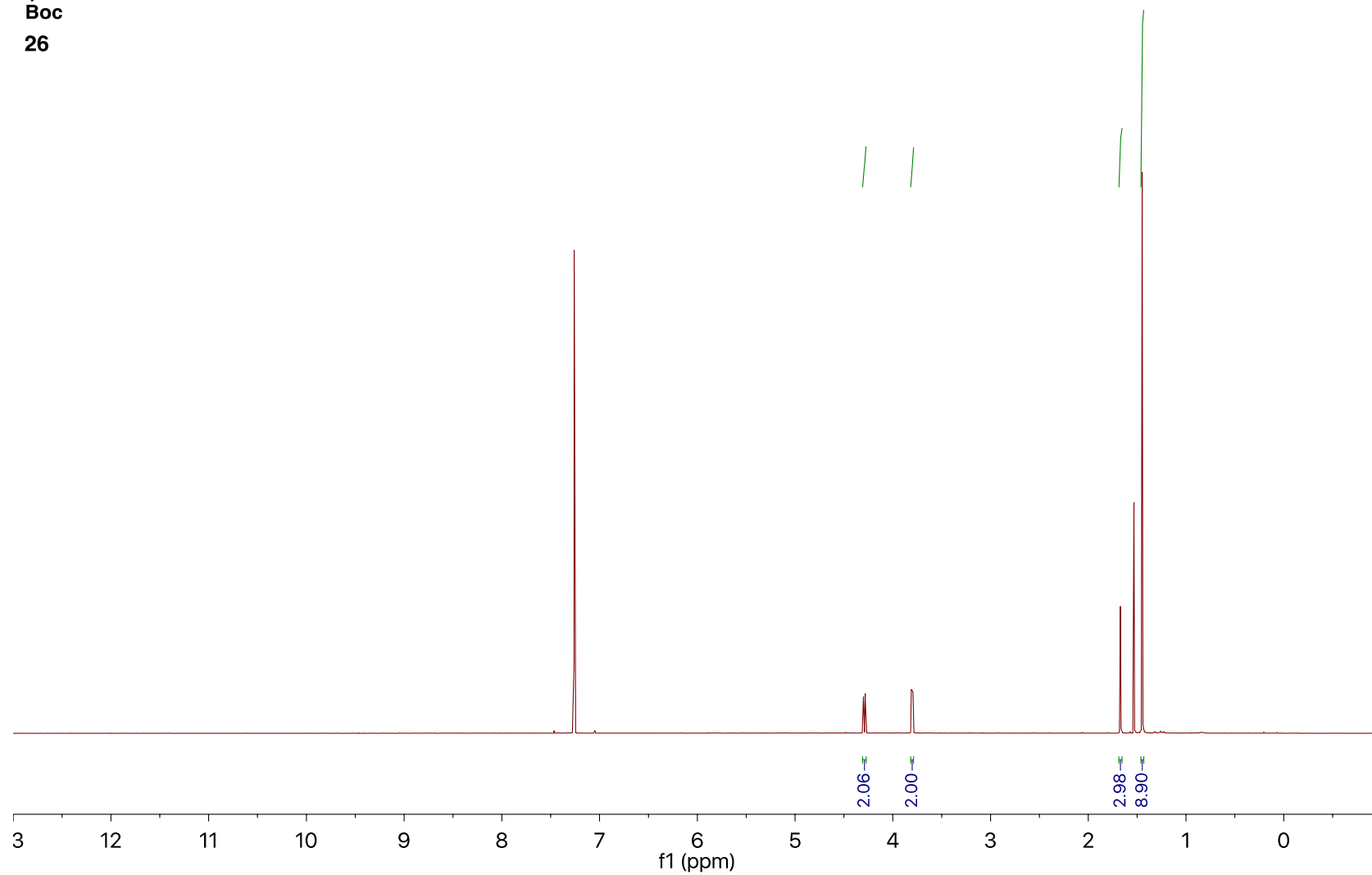
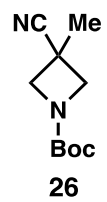


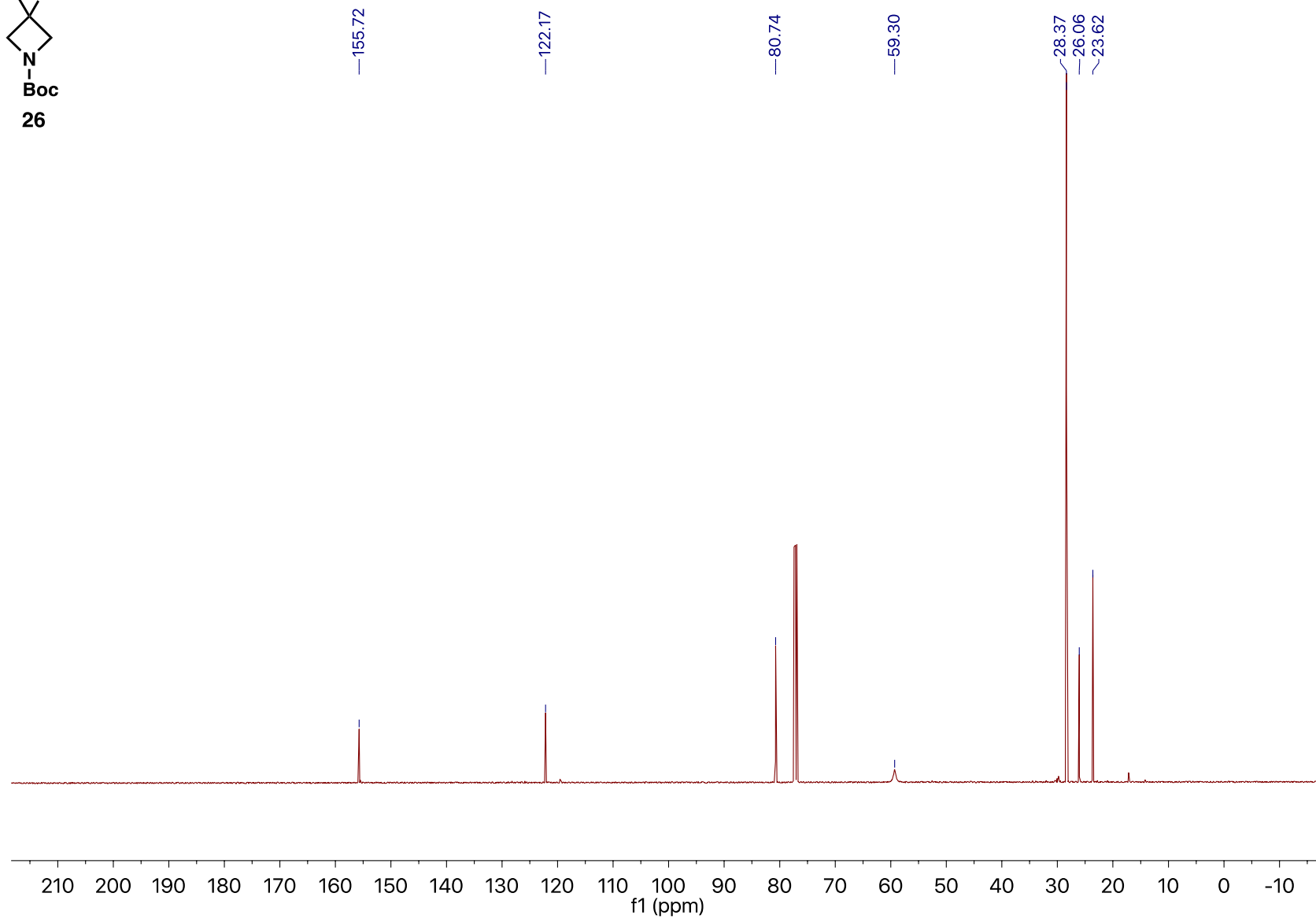
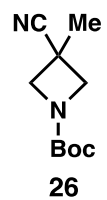


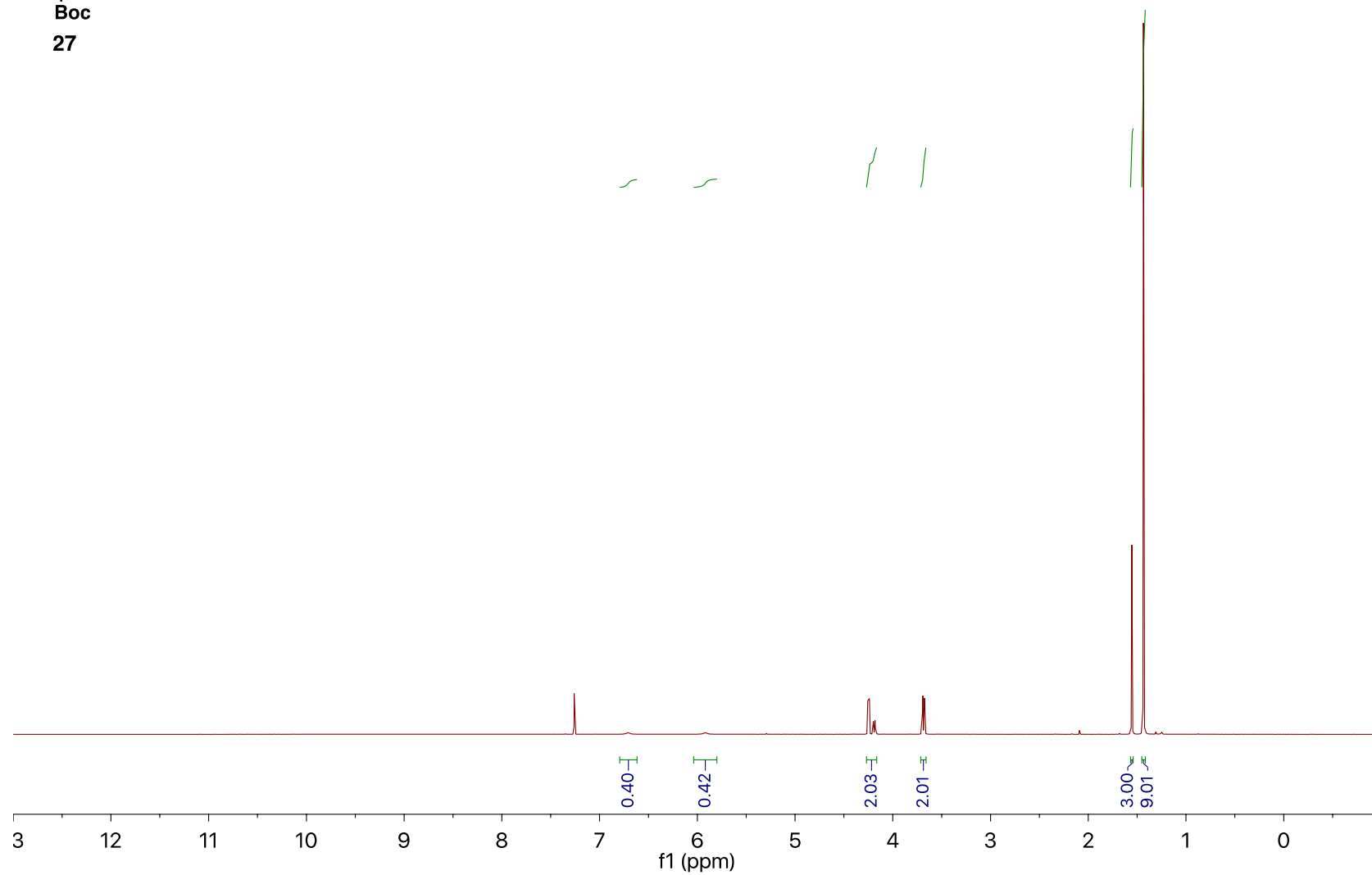
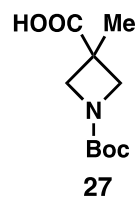


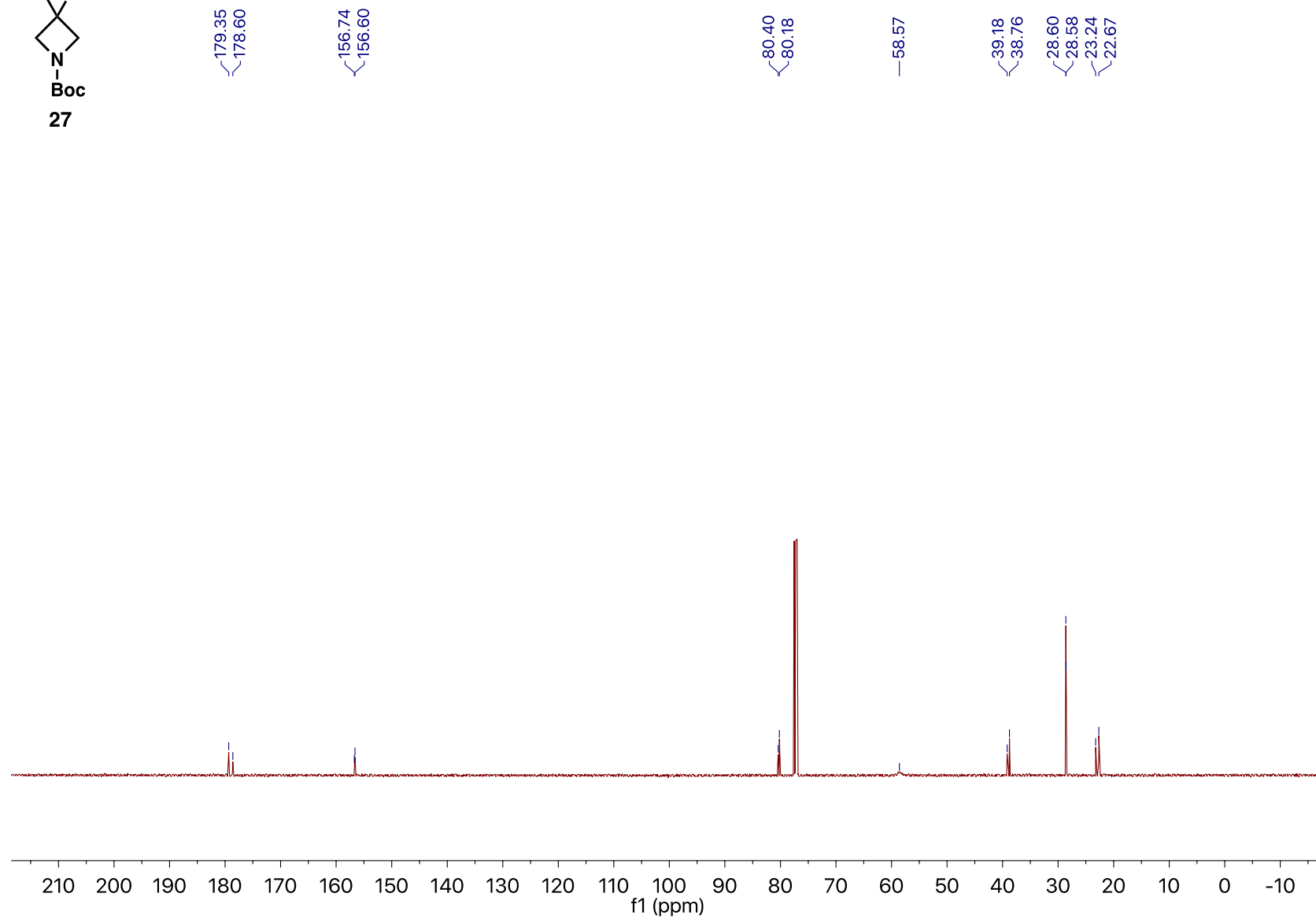
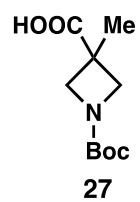


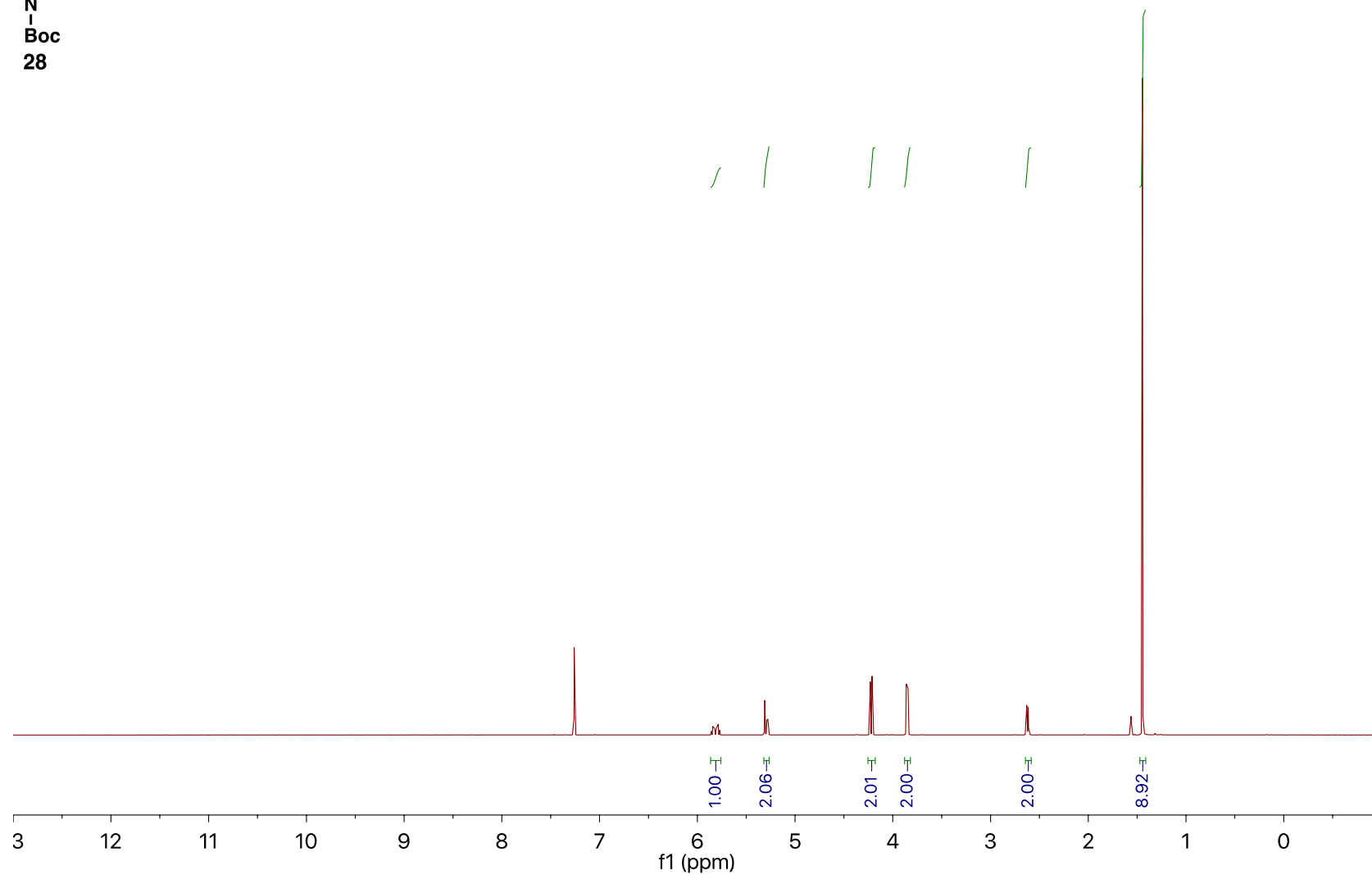
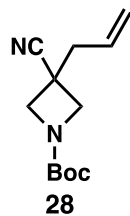


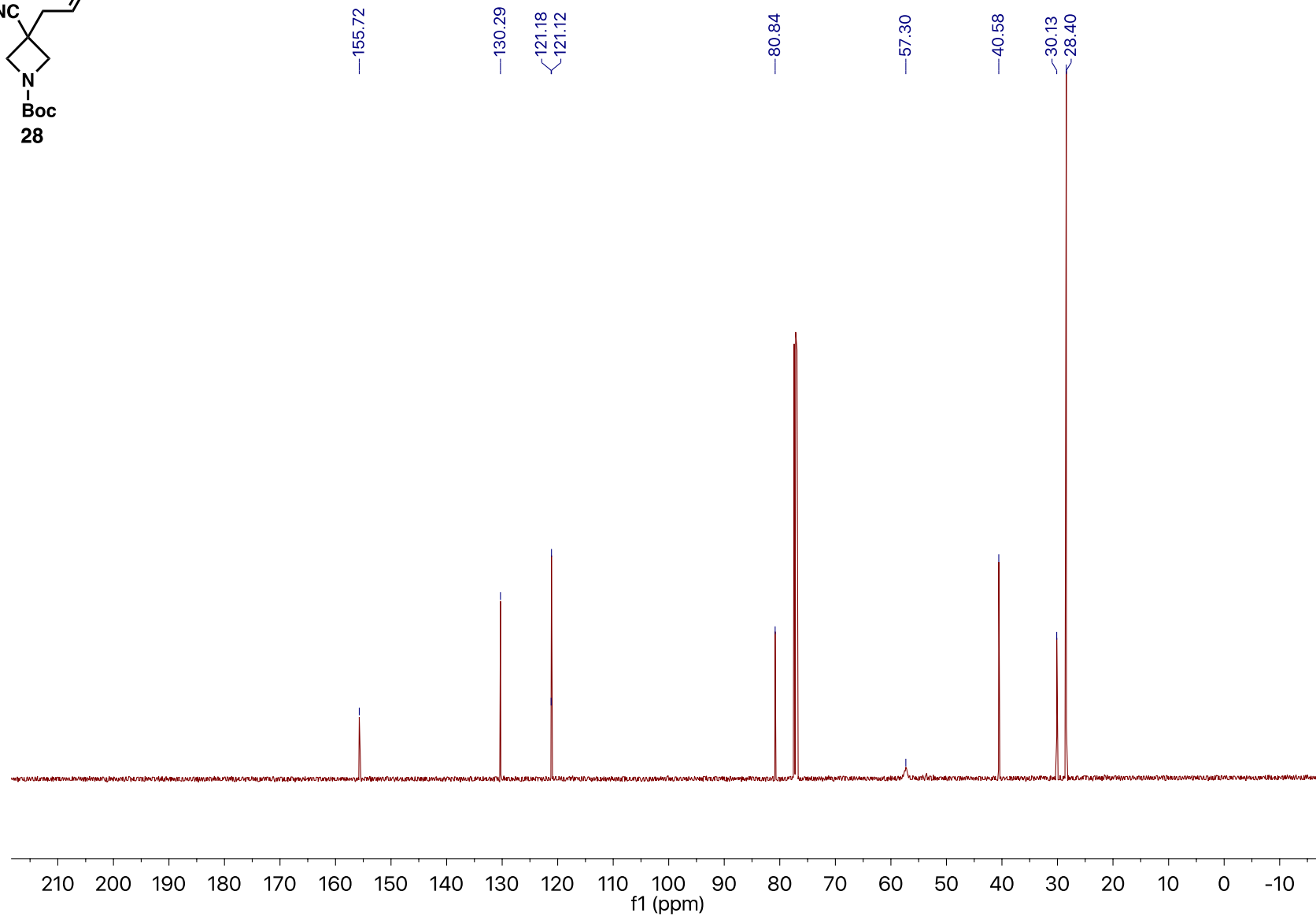
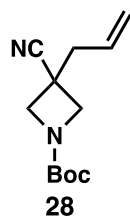


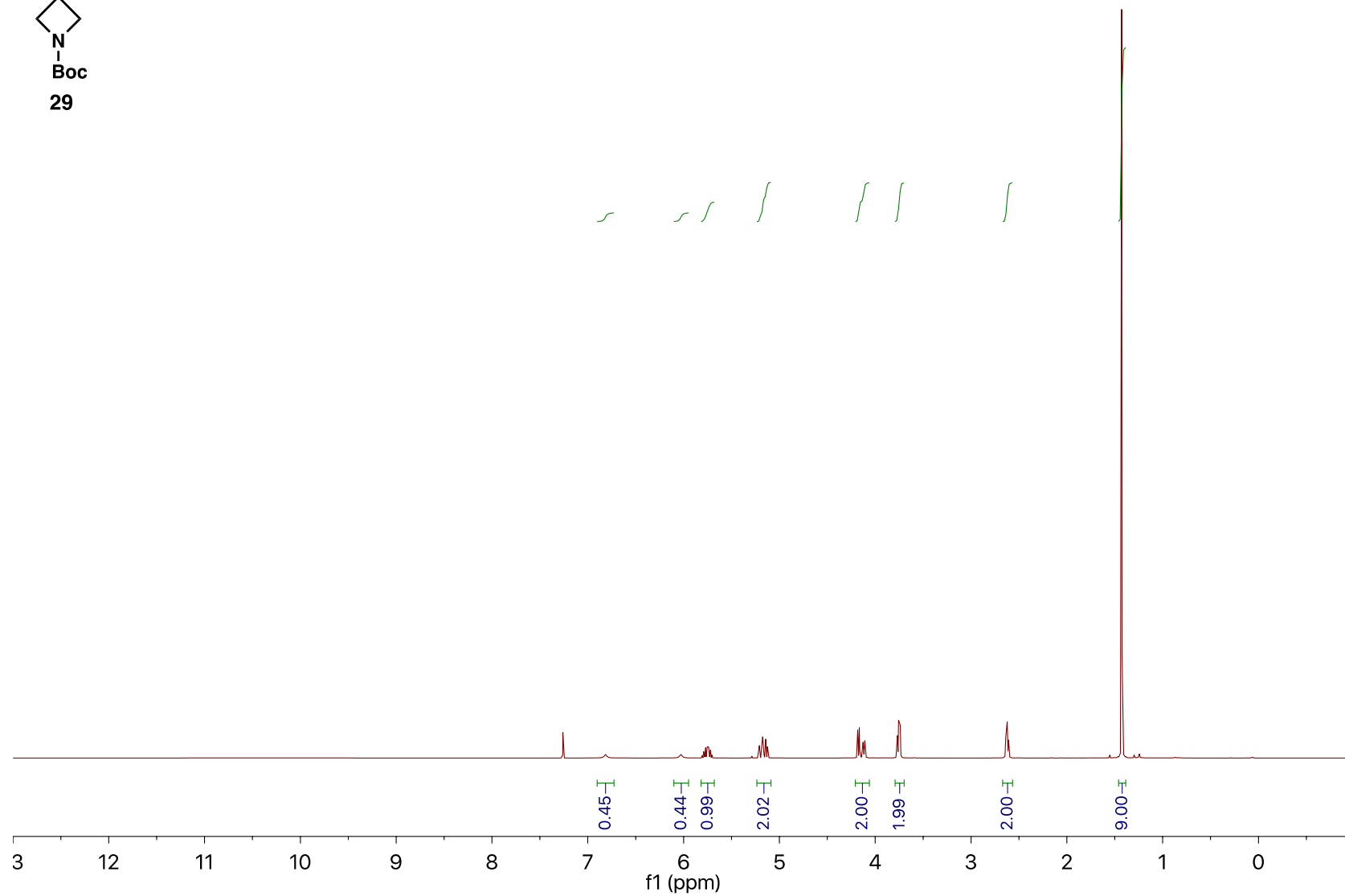
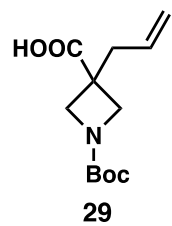


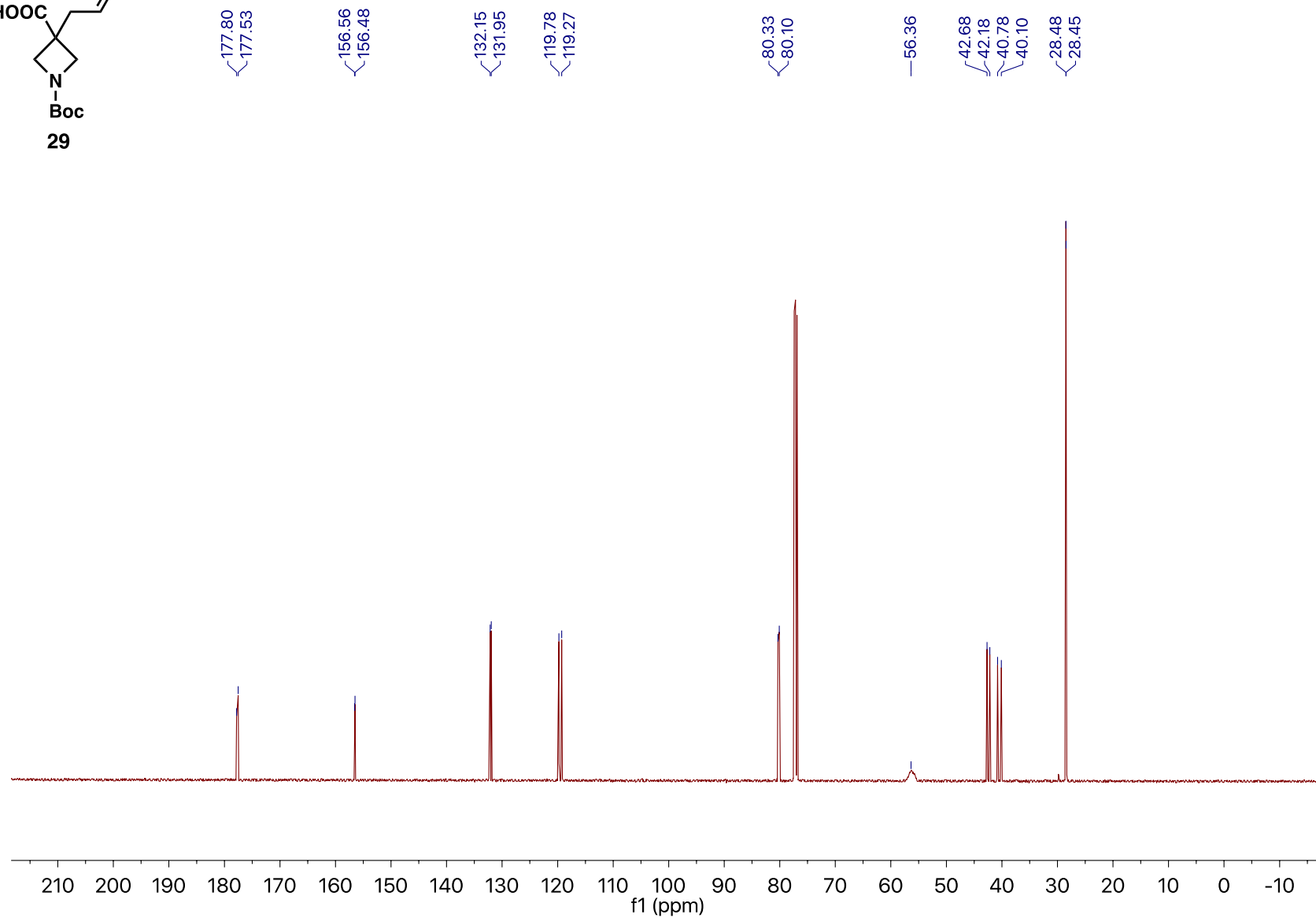
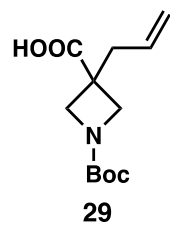


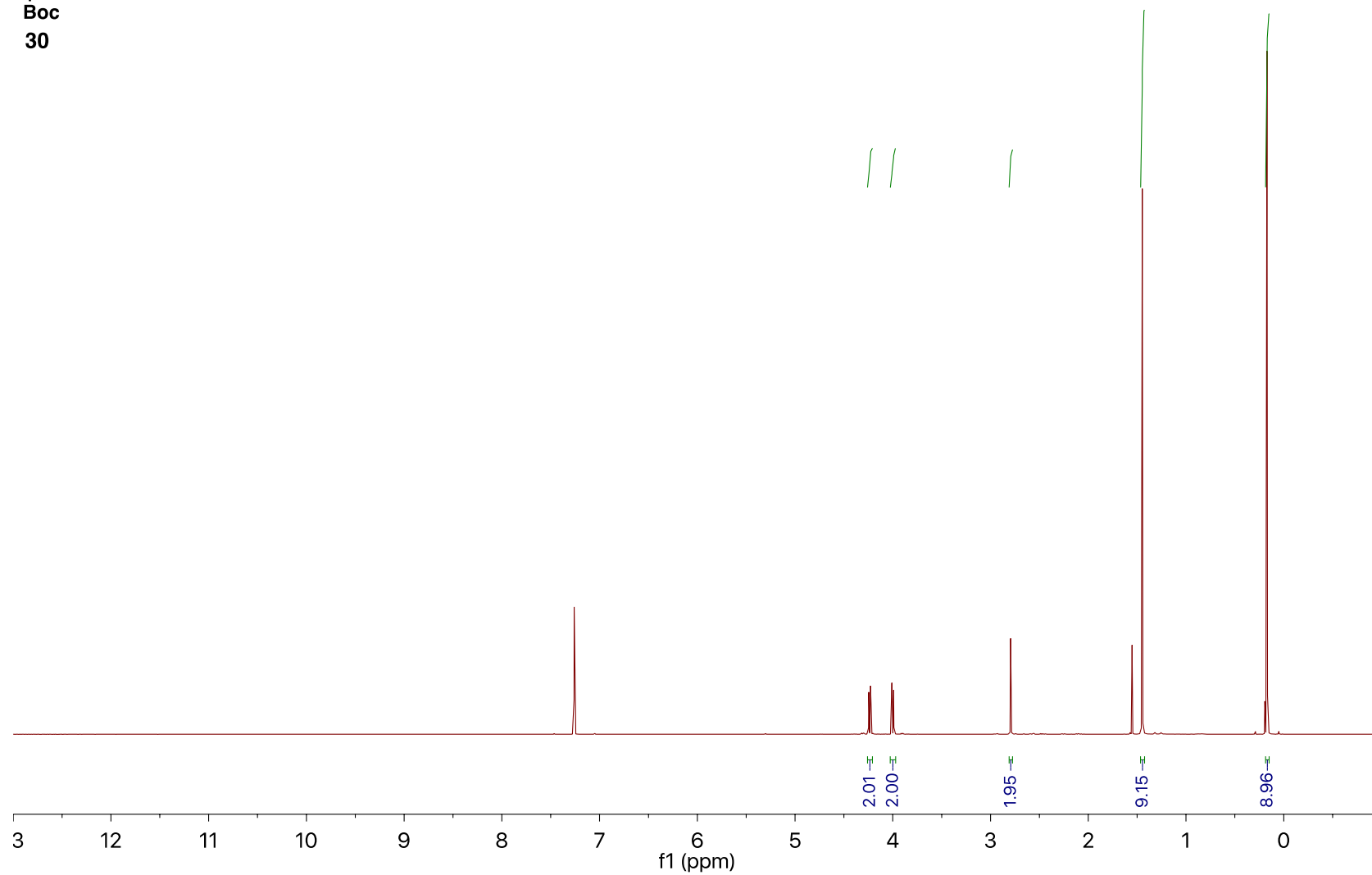
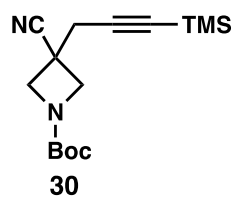


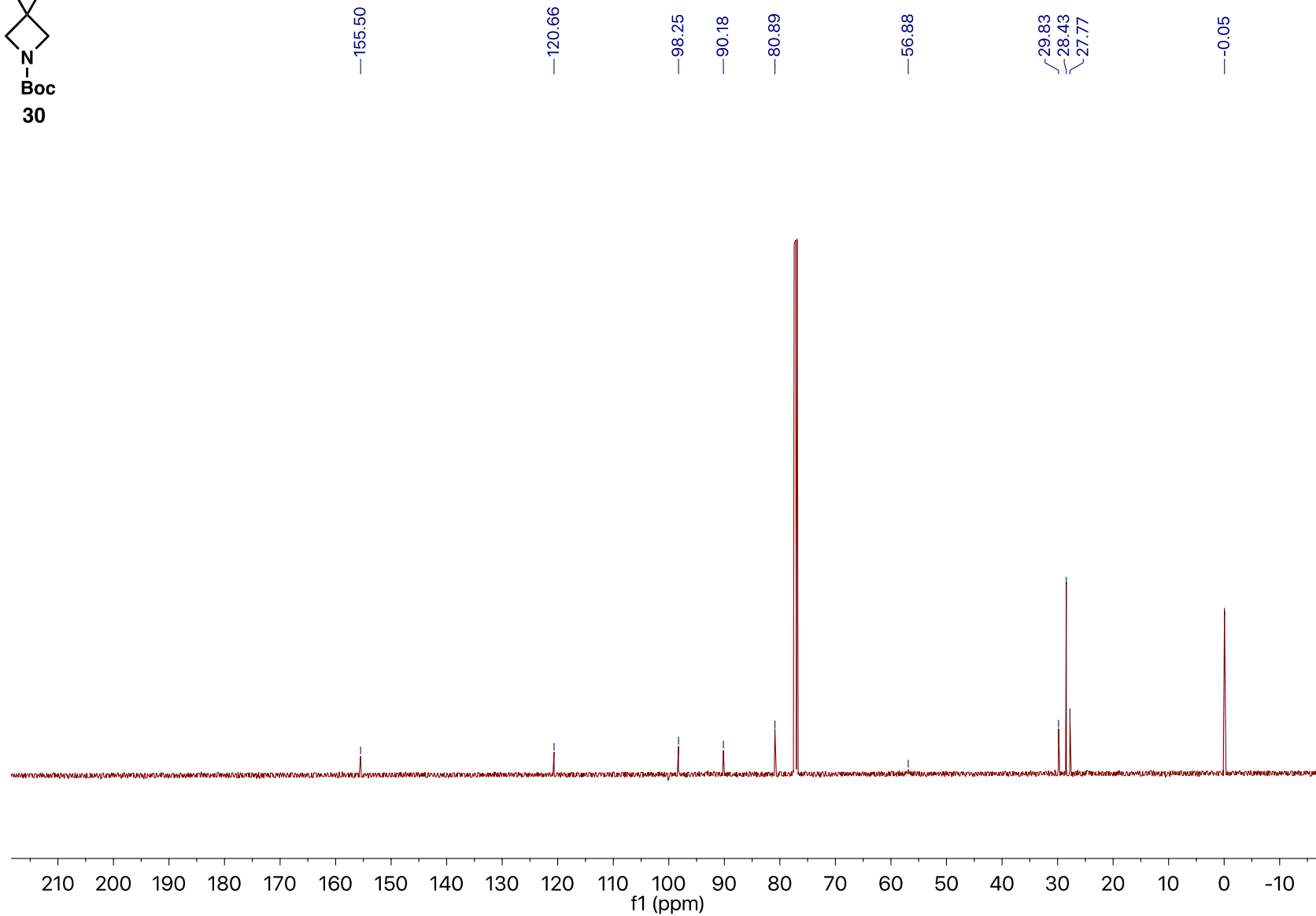
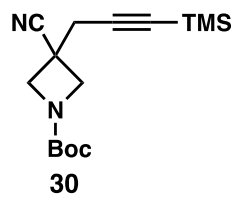


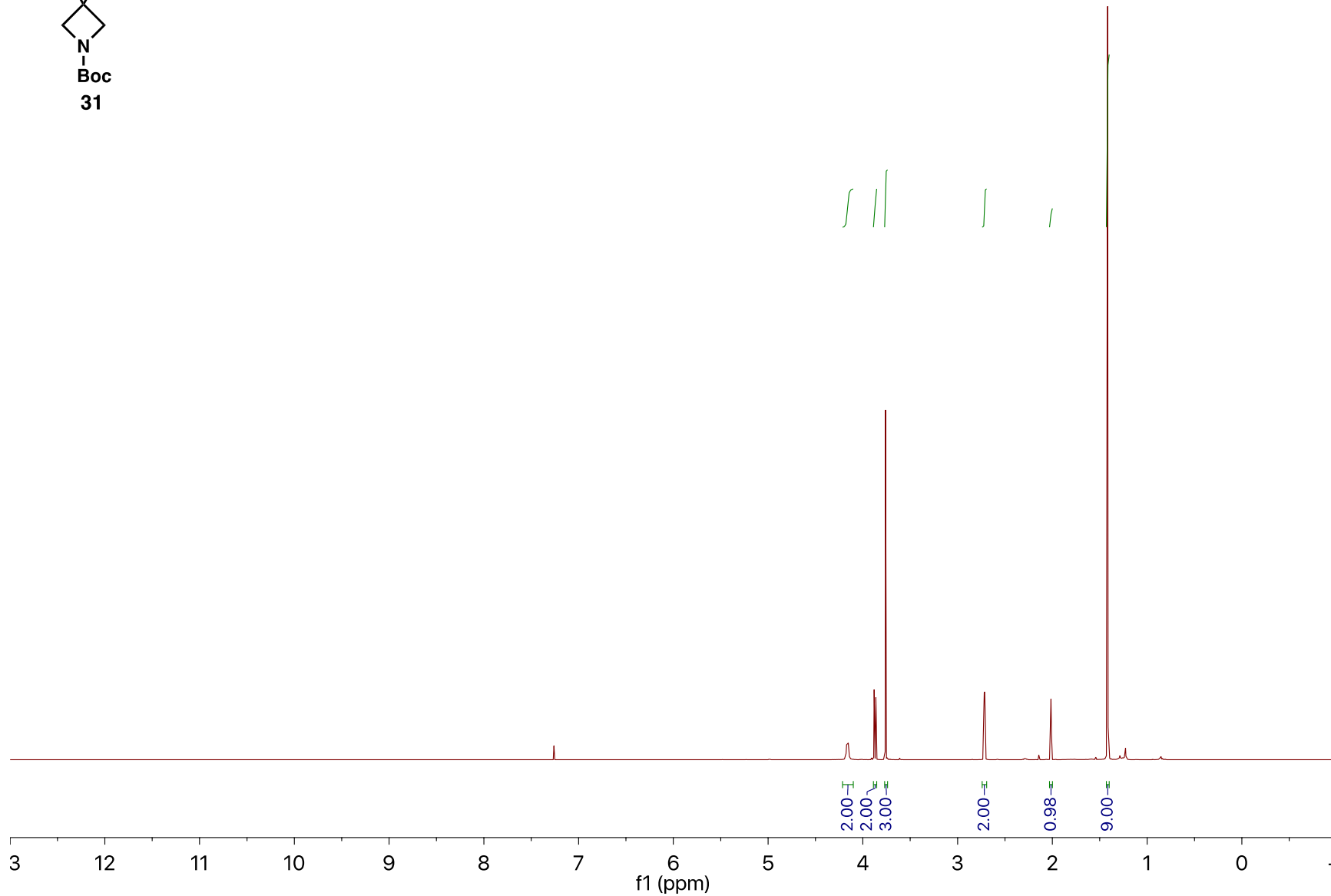
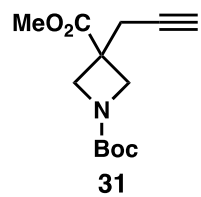


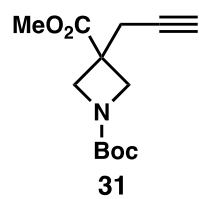












—173.12

—156.22

—79.98

—78.81

—71.04

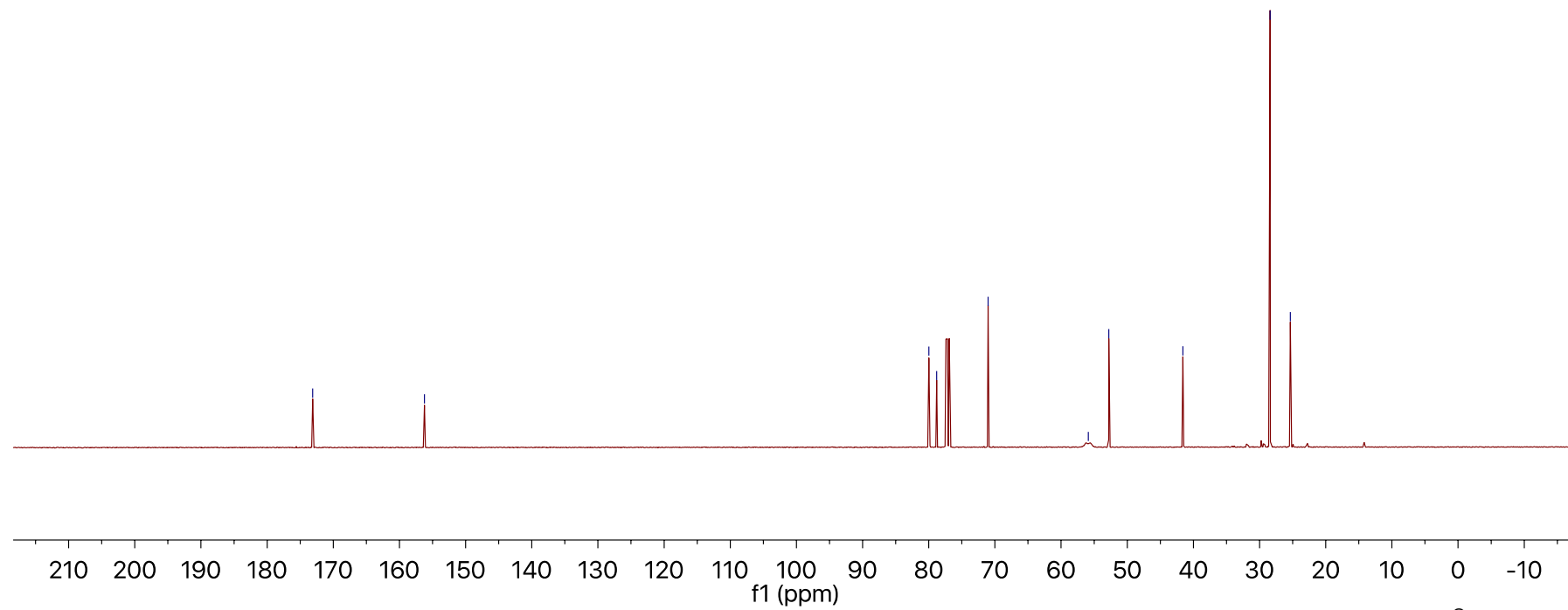
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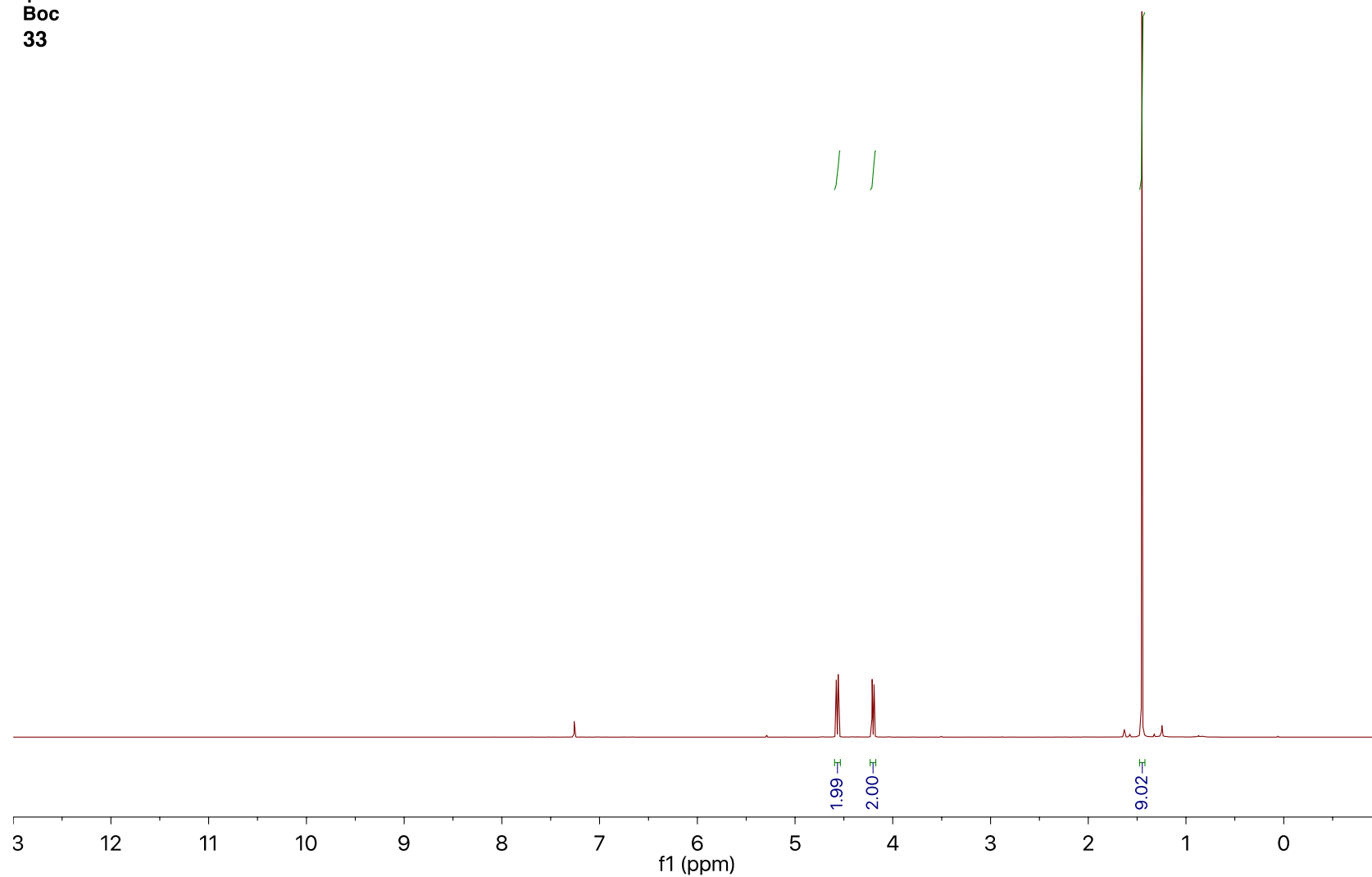
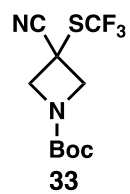
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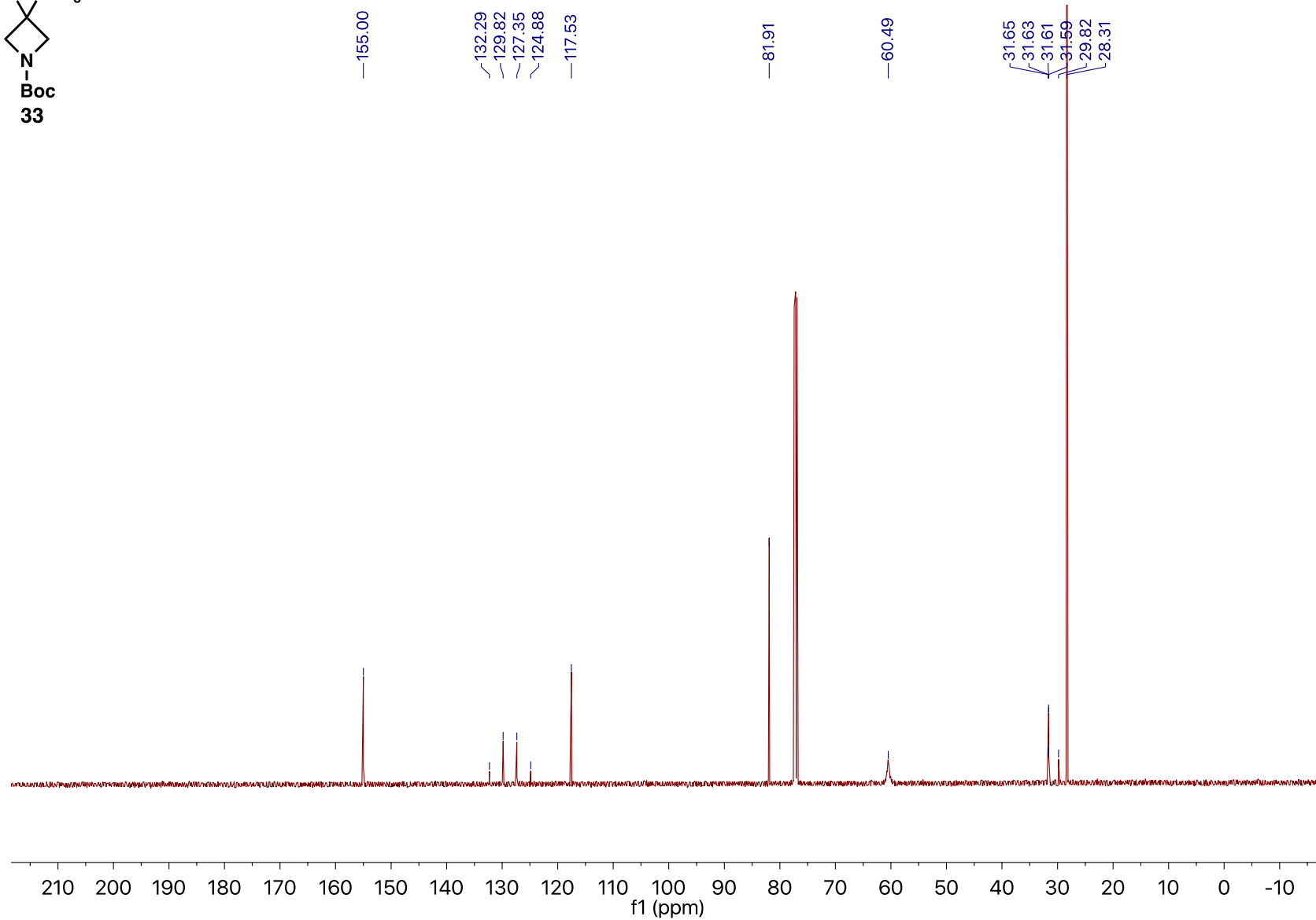
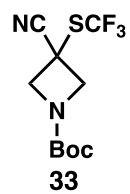
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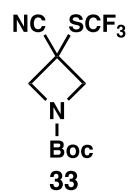
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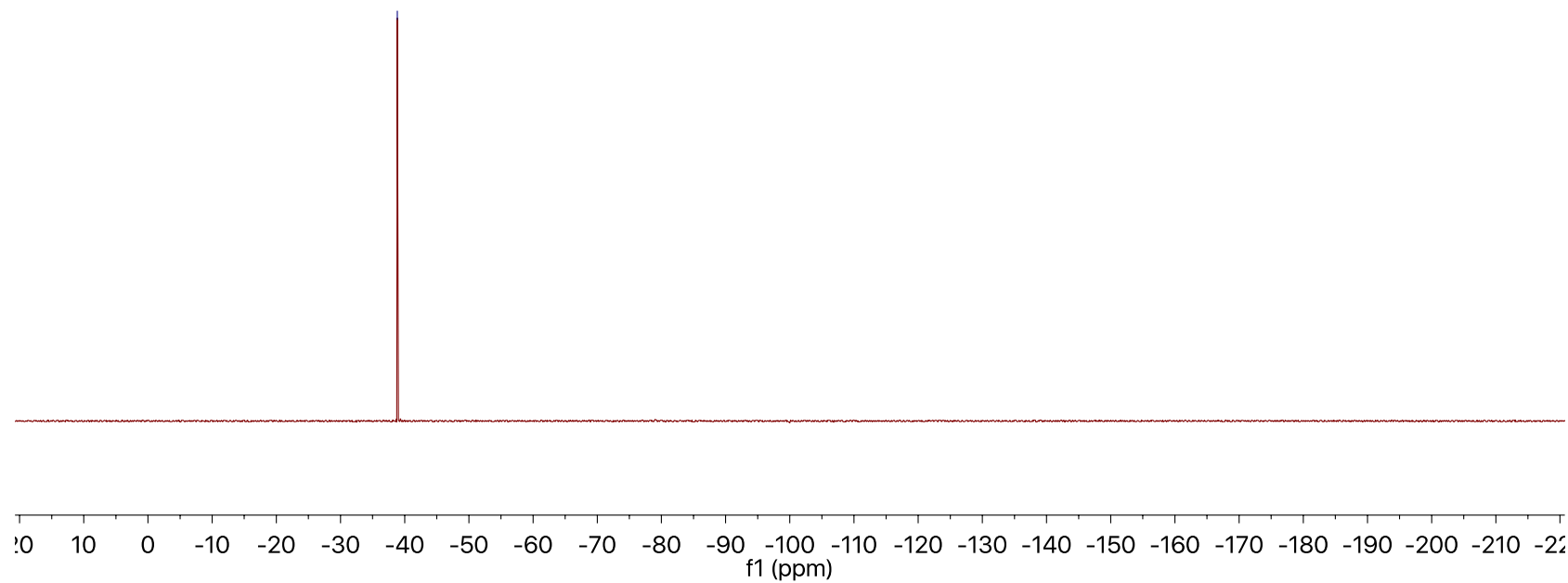


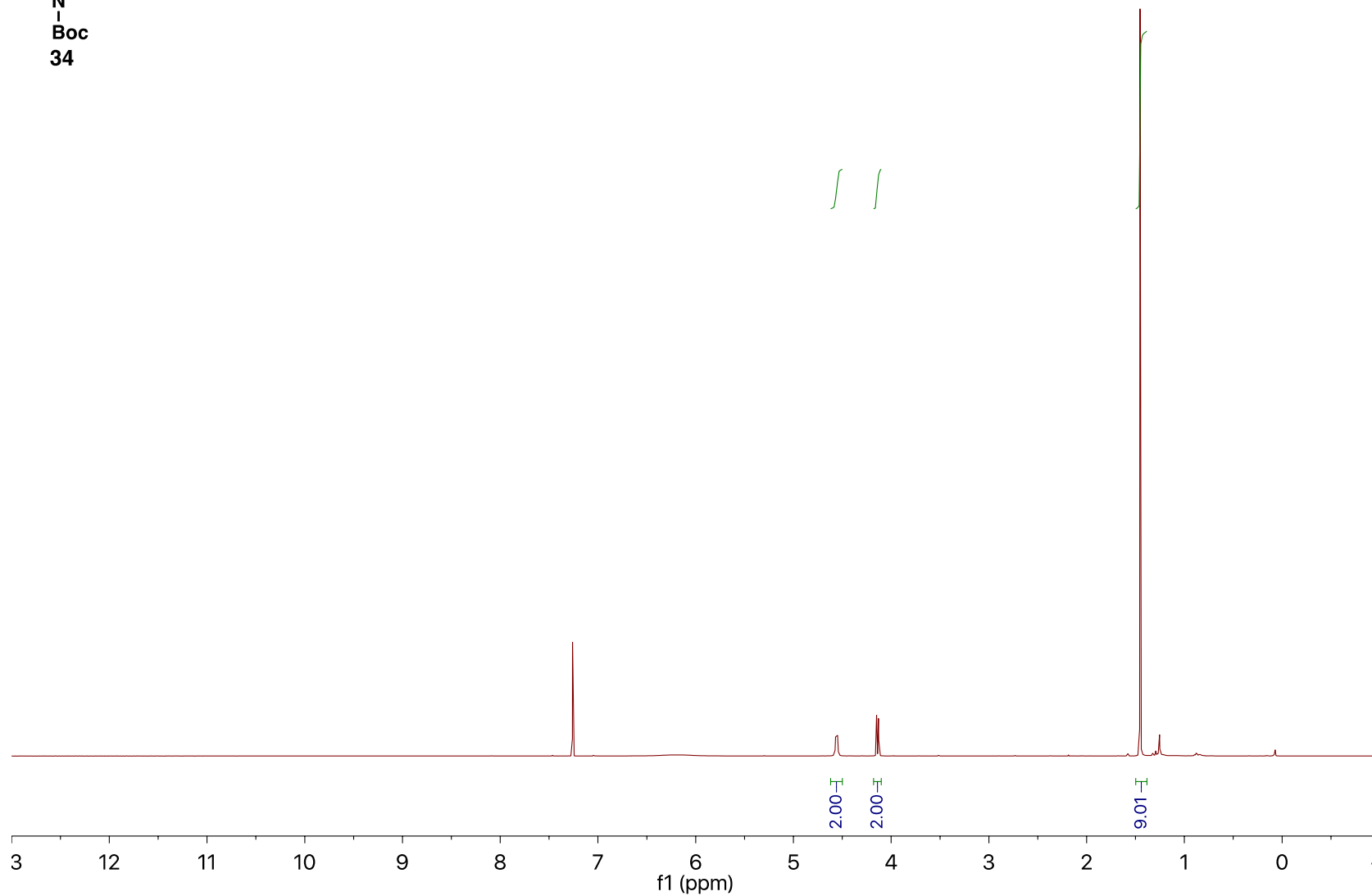
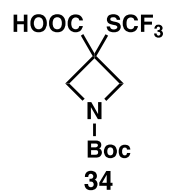


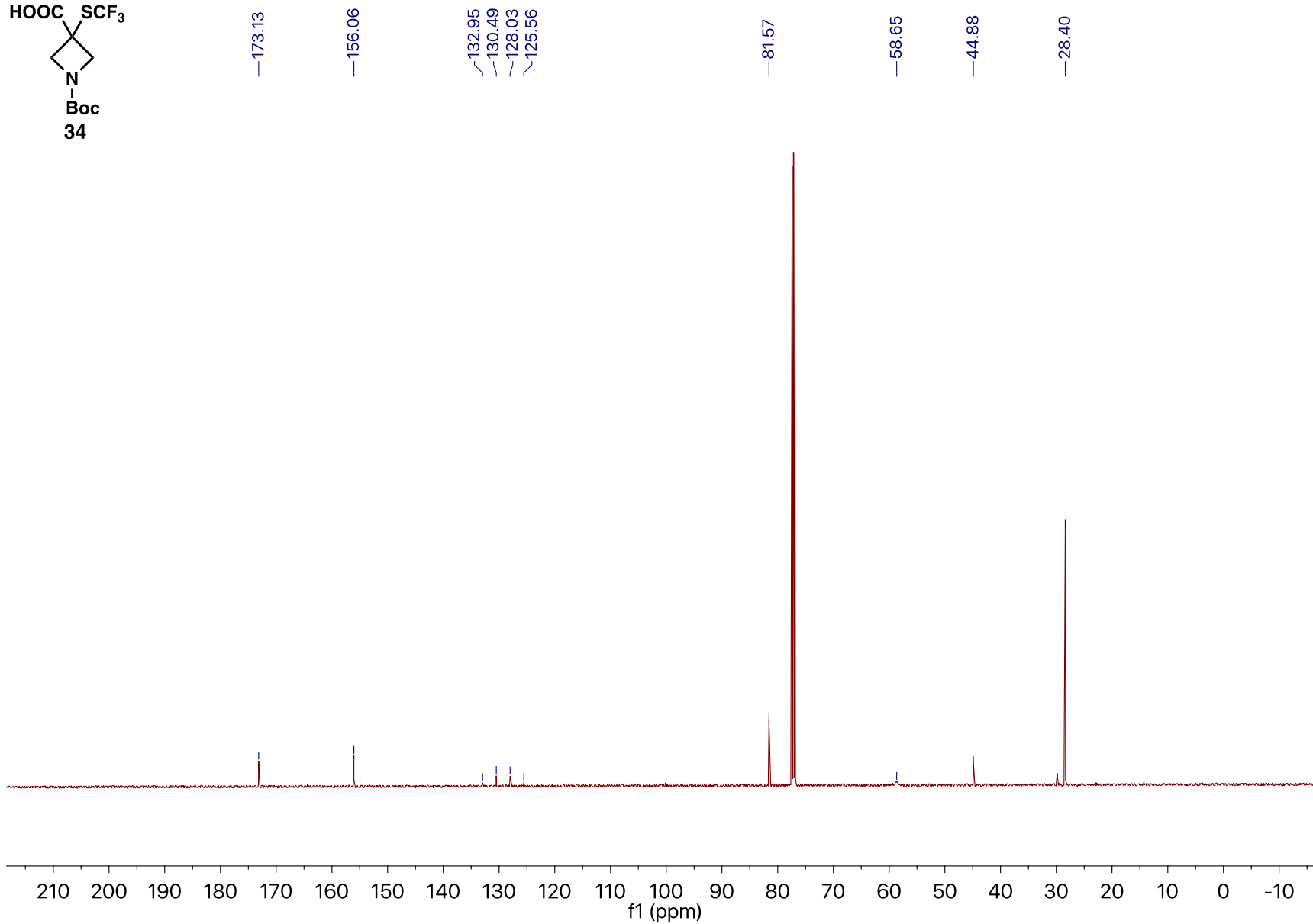
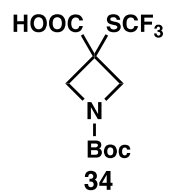


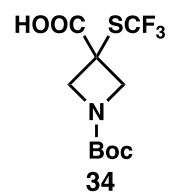


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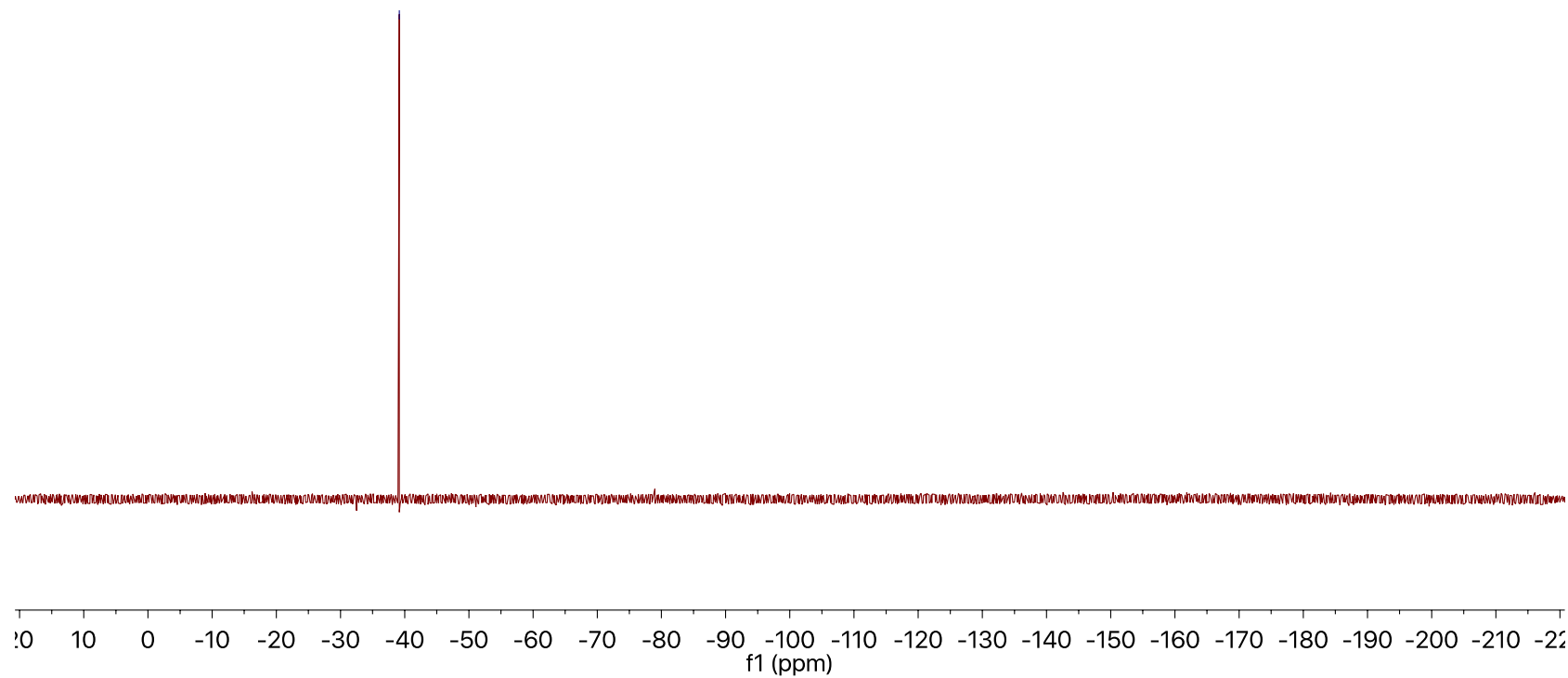


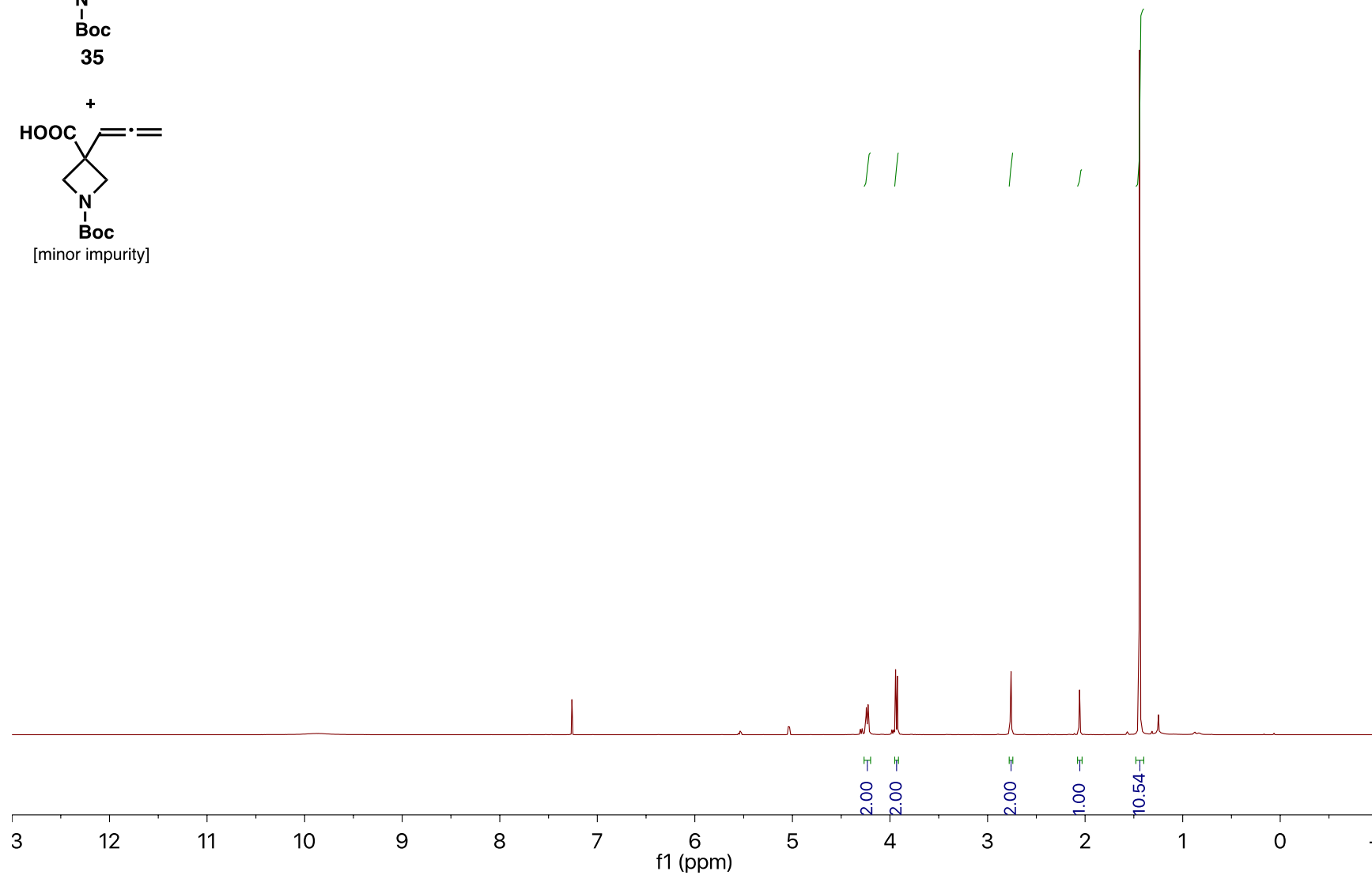
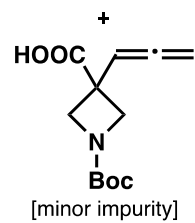
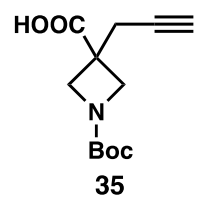


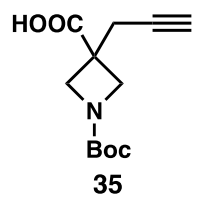




---39.15







—177.56

—156.48

~80.51

~78.69

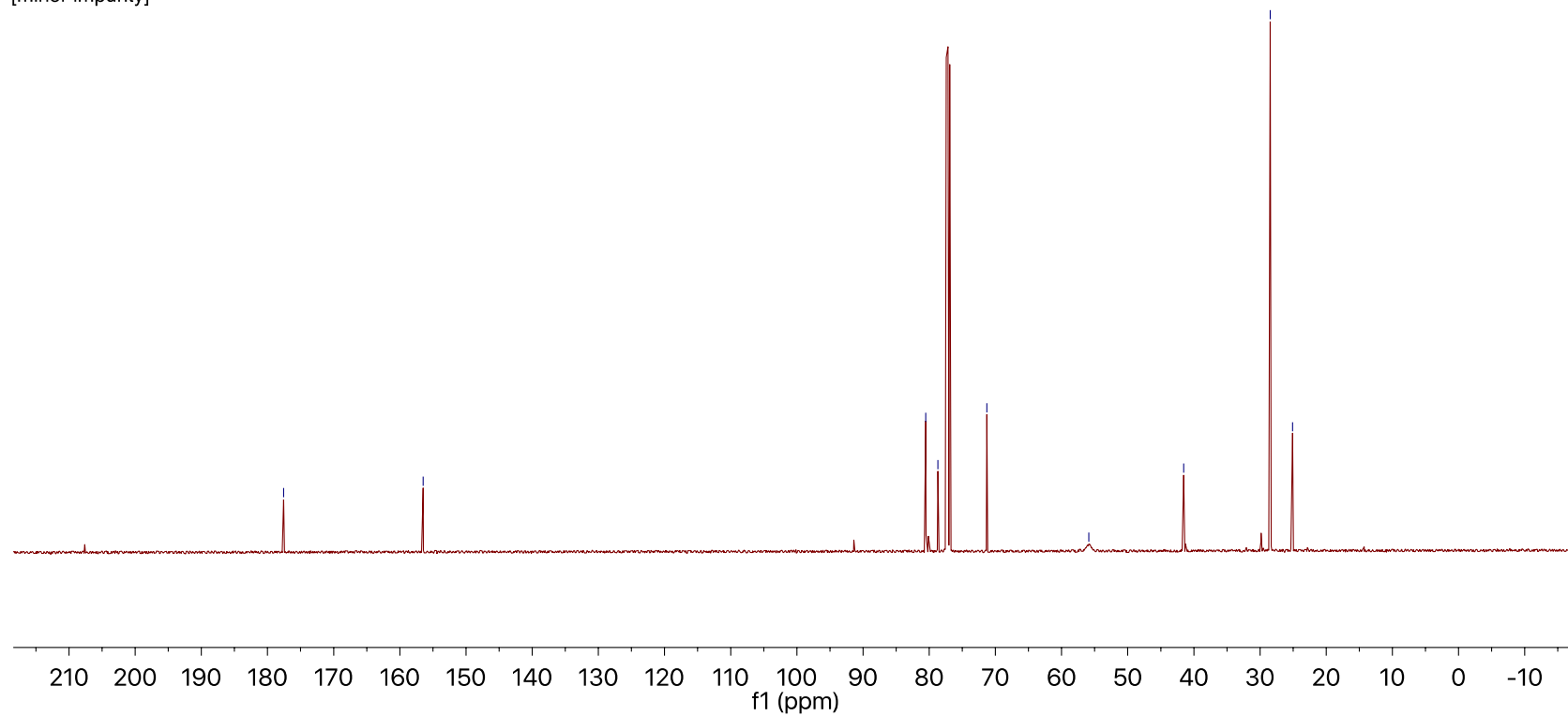
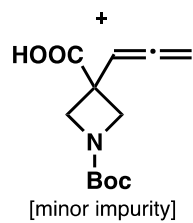
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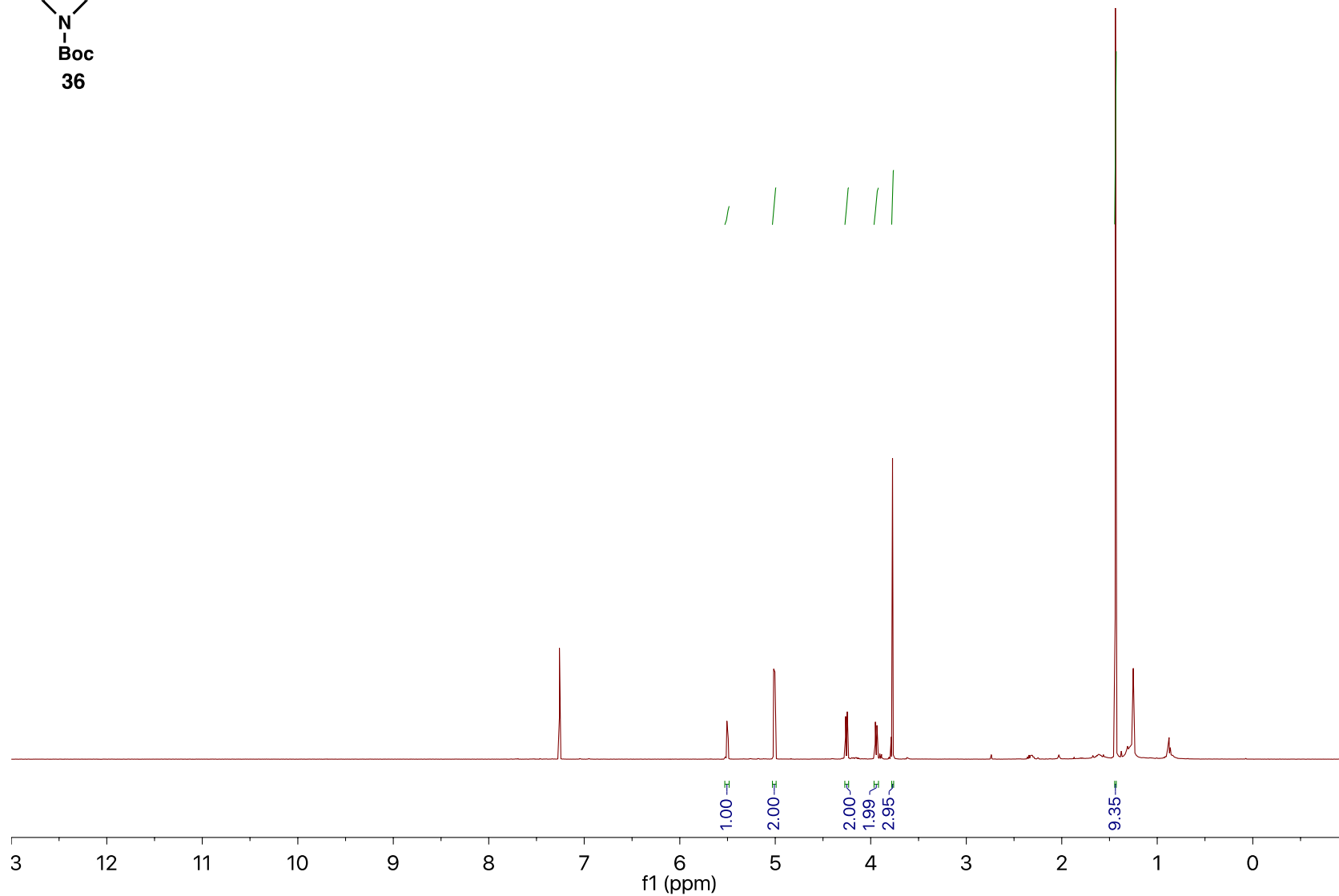
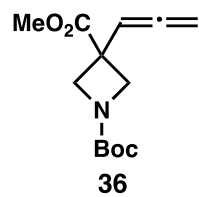
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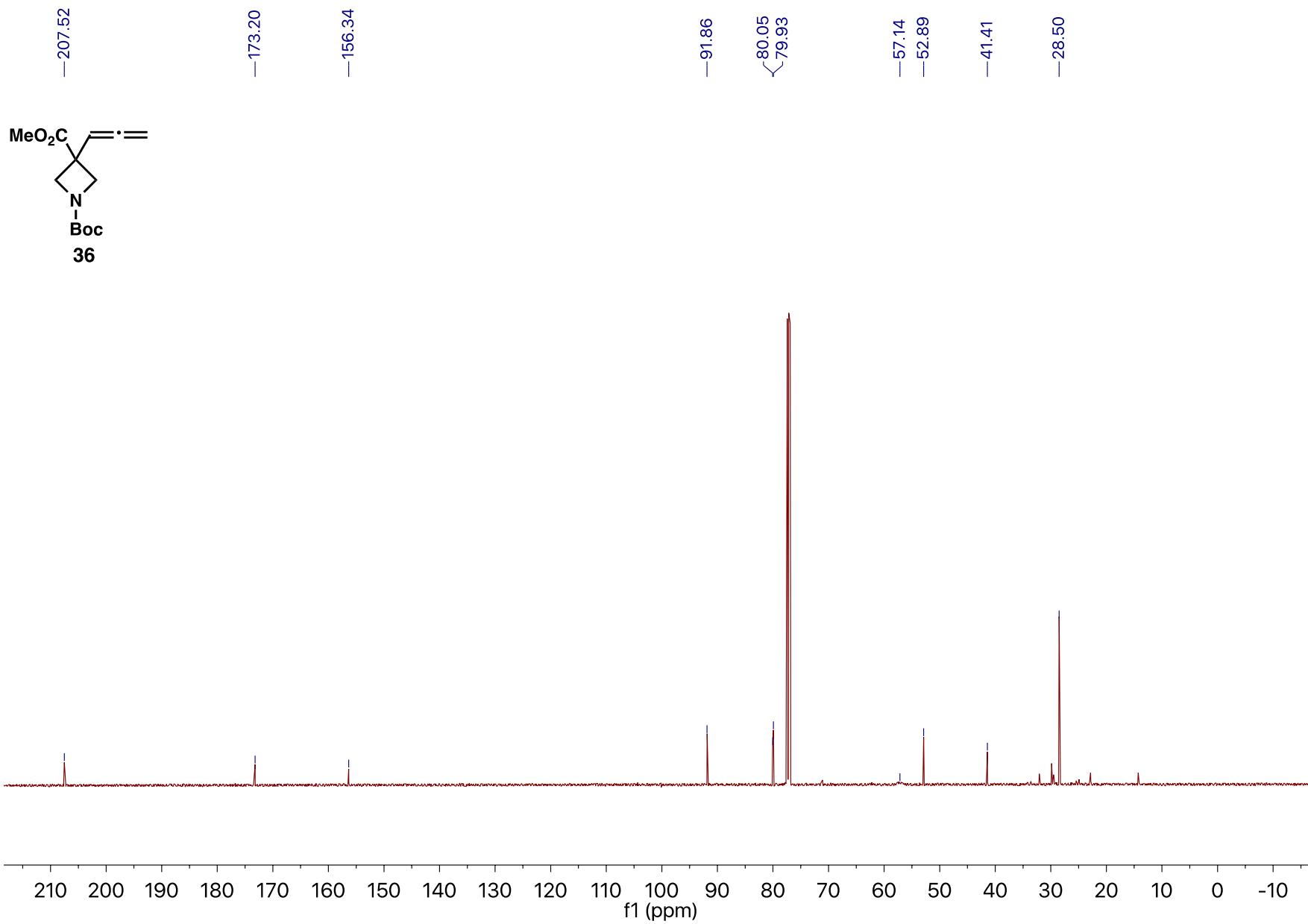
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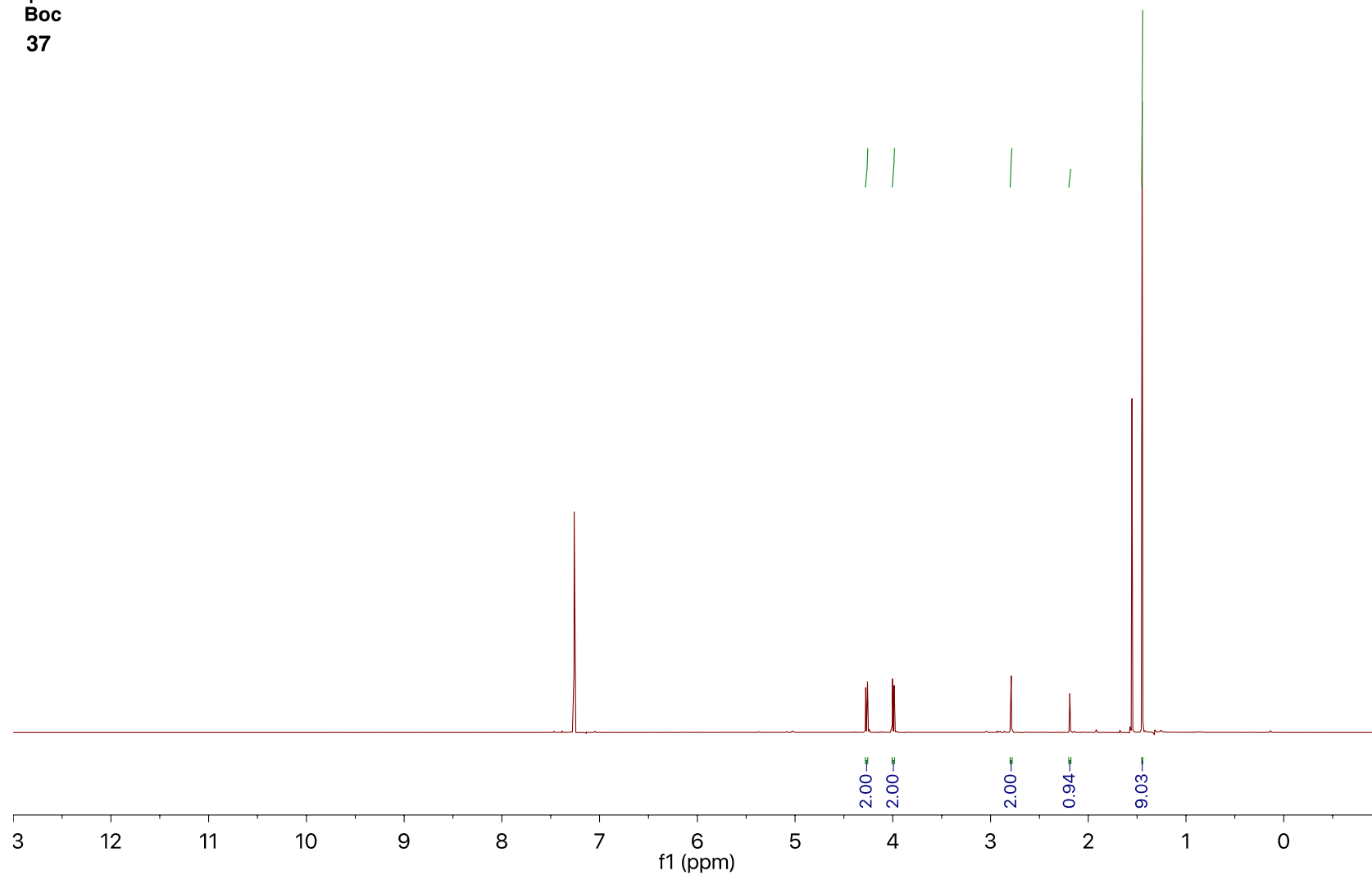
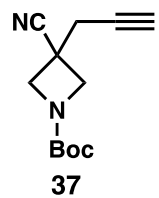
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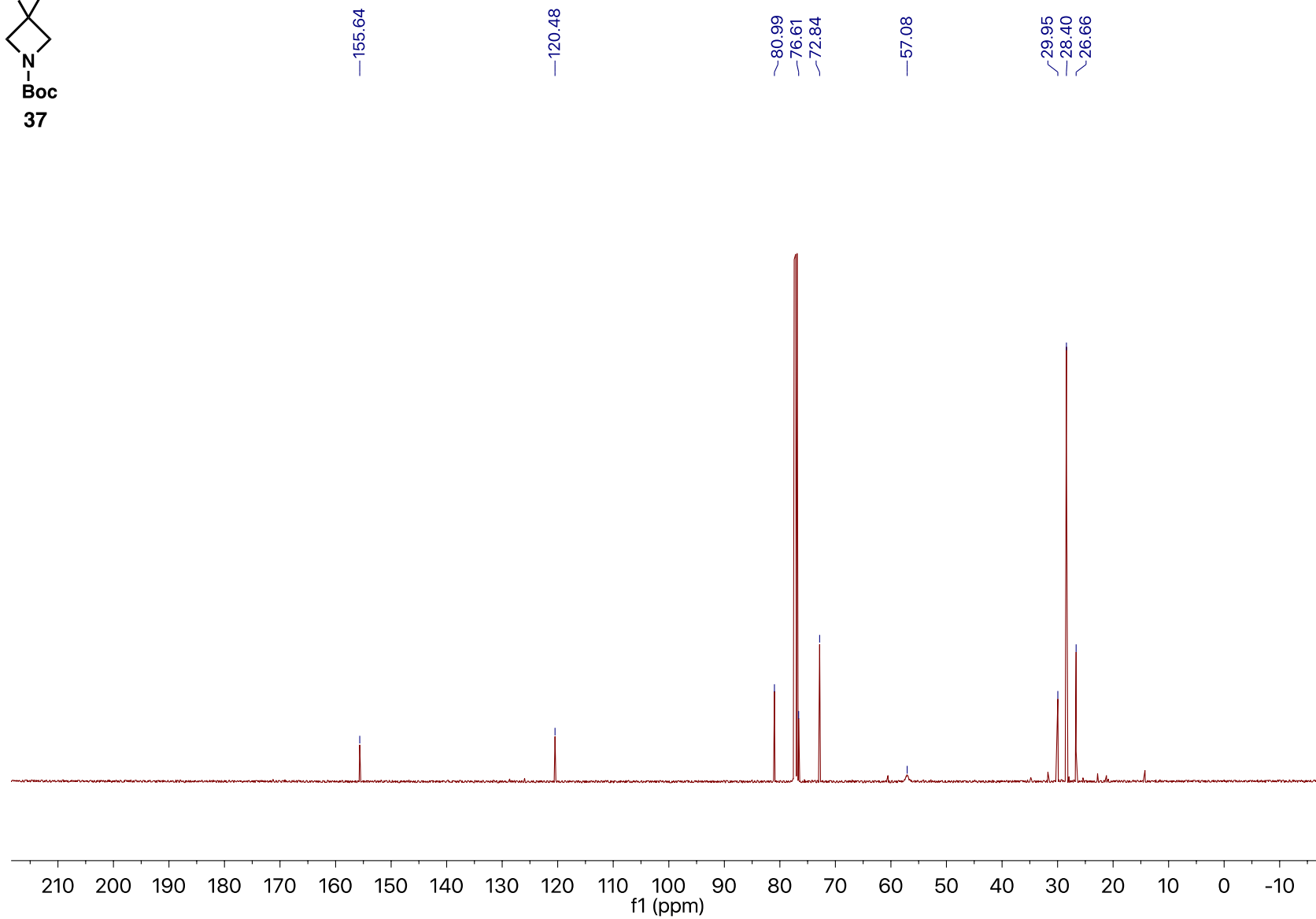
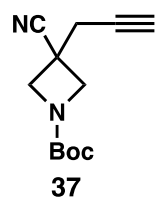
—25.08











X-ray Crystallography for Compound 33

The X-ray diffraction data were measured on Bruker D8 Venture PHOTON 100 CMOS system equipped with a Cu K α INCOATEC ImuS micro-focus source ($\lambda = 1.54178 \text{ \AA}$). Indexing was performed using Apex3 [1]. Data integration and reduction were performed using SaintPlus 6.01 [2]. Absorption correction was performed by multi-scan method implemented in SADABS [3]. Space group was determined using XPREP implemented in APEX3 [1]. Structure was solved using SHELXT [4] and refined using SHELXL-2017 [5-7] (full-matrix least-squares on F^2) through OLEX2 interface program [8]. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in geometrically calculated positions and were included in the refinement process using riding model with isotropic thermal parameters. $-\text{CF}_3$ group was modeled as disordered over two positions and was refined using restraints. Crystal data and refinement conditions are shown in Table 1.

[1] Bruker (2017). *APEX3* (Version 2015.9). Bruker AXS Inc., Madison, Wisconsin, USA.

[2] Bruker (2017) *SAINT V8.35A*. Data Reduction Software.

[3] Sheldrick, G. M. (1996). *SADABS. Program for Empirical Absorption Correction*. University of Gottingen, Germany.

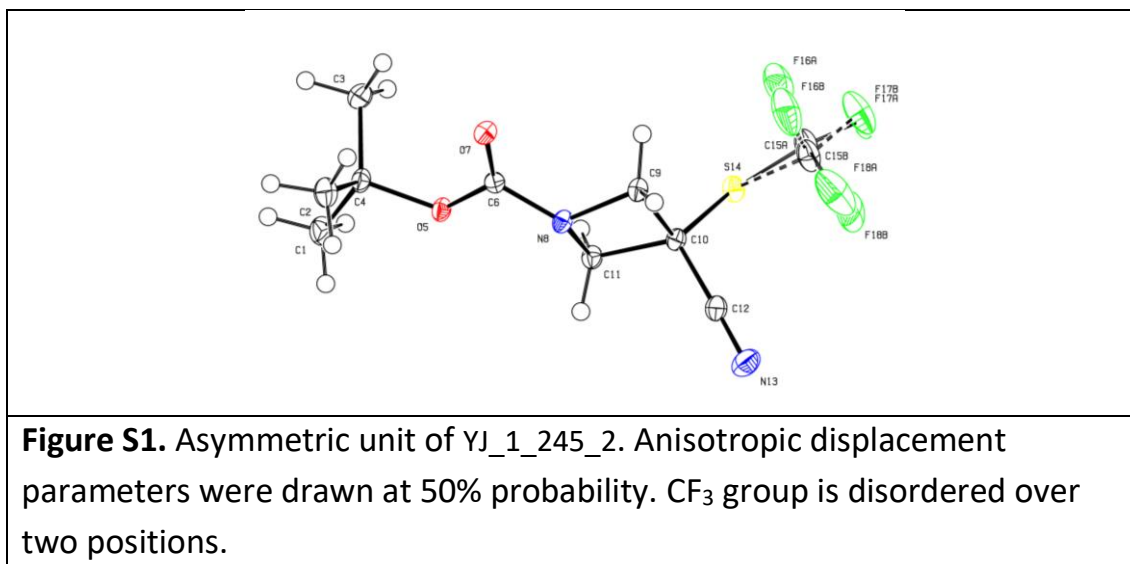
[4] Sheldrick, G. M. (2015) "SHELXT - Integrated space-group and crystal structure determination" *Acta Cryst.* A71, 3-8

[5] Sheldrick, G.M. (1990) *Acta Cryst.* A46, 467-473

[6] Sheldrick, G. M. (2008) *Acta Cryst.* A64, 112-122.

[7] G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", *Acta Cryst.*, C71, 3-8

[8] Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H., *OLEX2: A complete structure solution, refinement and analysis program* (2009). *J. Appl. Cryst.*, 42, 339-341.

**Table S1.** Crystal data and structure refinement for YJ_1_245_2.

Identification code	YJ_1_245_2
CCDC#	1826005
Empirical formula	C ₁₀ H ₁₃ F ₃ N ₂ O ₂ S
Formula weight	282.28
Temperature/K	99.99
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	12.4840(2)
b/Å	10.2765(2)
c/Å	10.8302(2)
α/°	90
β/°	110.1610(10)

$\gamma/^\circ$	90
Volume/ \AA^3	1304.29(4)
Z	4
$\rho_{\text{calc}}/\text{g}/\text{cm}^3$	1.438
μ/mm^{-1}	2.553
F(000)	584.0
Crystal size/ mm^3	$0.116 \times 0.058 \times 0.045$
Radiation	CuK α ($\lambda = 1.54178$)
2θ range for data collection/ $^\circ$	7.544 to 148.818
Index ranges	$-15 \leq h \leq 15, -12 \leq k \leq 12, -13 \leq l \leq 13$
Reflections collected	19918
Independent reflections	2659 [$R_{\text{int}} = 0.0450, R_{\text{sigma}} = 0.0211$]
Data/restraints/parameters	2659/118/246
Goodness-of-fit on F^2	1.069
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0287, wR_2 = 0.0644$
Final R indexes [all data]	$R_1 = 0.0369, wR_2 = 0.0682$
Largest diff. peak/hole / $e \text{\AA}^{-3}$	0.22/-0.27