Electronic Supplementary Information

A novel one-pot reaction: organocopper-mediated reduction/asymmetric alkylation via transmetalation leading to the diastereoselective synthesis of (*Z*)-fluoroalkene dipeptide isosteres

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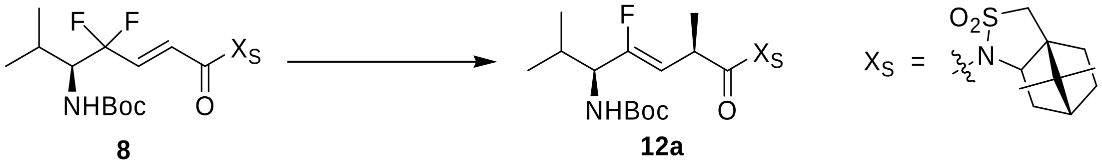
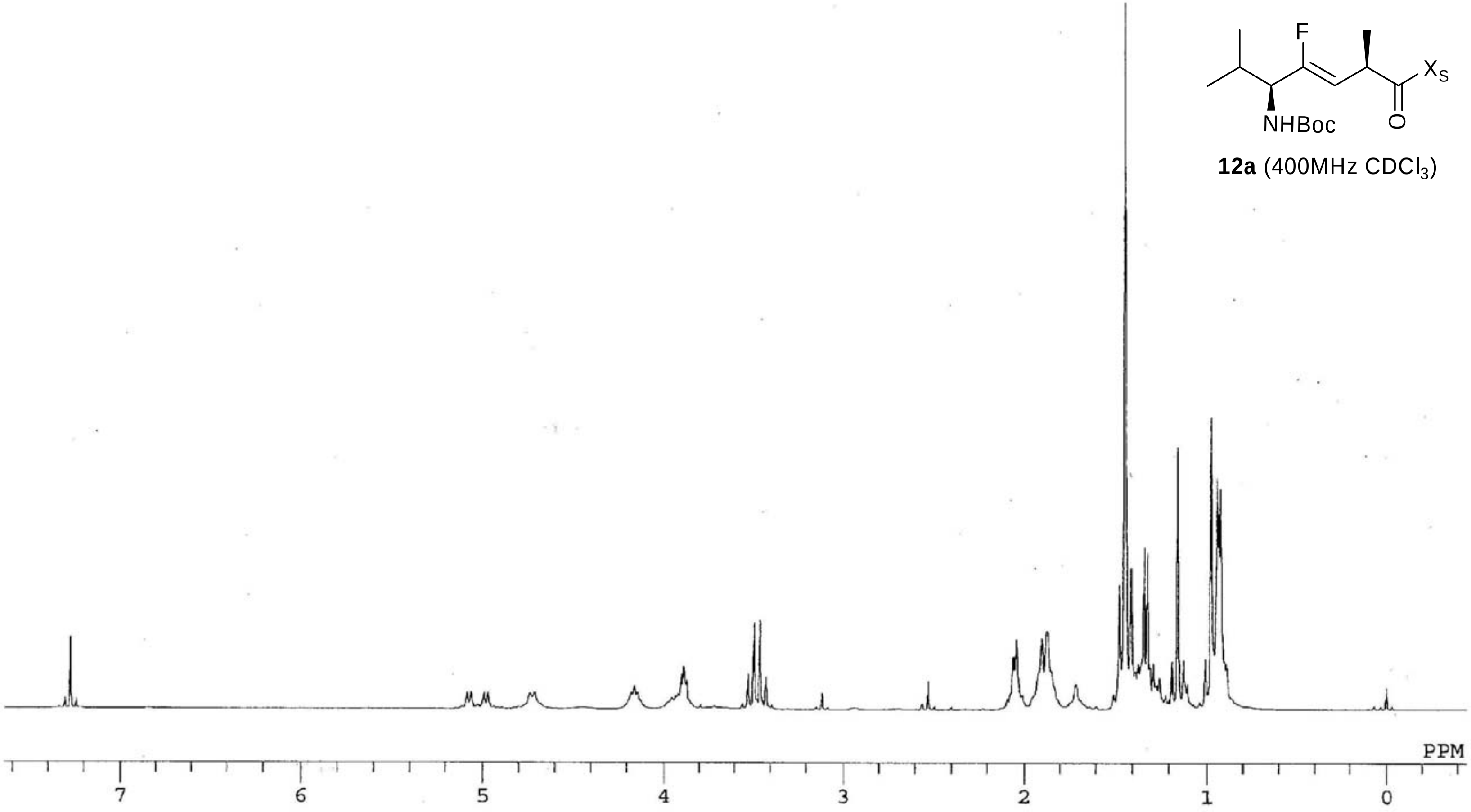
General Methods. ^{1}H NMR spectra were recorded using a JEOL AL-400 spectrometer. Chemical shifts are reported in δ (ppm) relative to TMS (in $CDCl_3$) or solvent peak (in D_2O, CD_3OD) as internal standard. ^{13}C NMR spectra were recorded using a JEOL AL-400 and referenced to the residual $CHCl_3$ signal. Exact mass (HRMS) spectra were recorded on a JMS-HX/HX 110A mass spectrometer. Optical rotations were measured with a Horiba high-sensitive polarimeter SEPA-200 (Kyoto, Japan). For flash chromatographies, Wakosil C-300 was employed. For HPLC separations, a Cosmosil 5C$_{18}$-ARII analytical (4.6 x 250 mm, flow rate 1 mL/min) column and eluting products were detected by UV at 220 nm. A solvent system consisting of 0.1% aqueous TFA solution (v/v) and 0.1% TFA in CH_3CN (v/v) were used for HPLC elution.

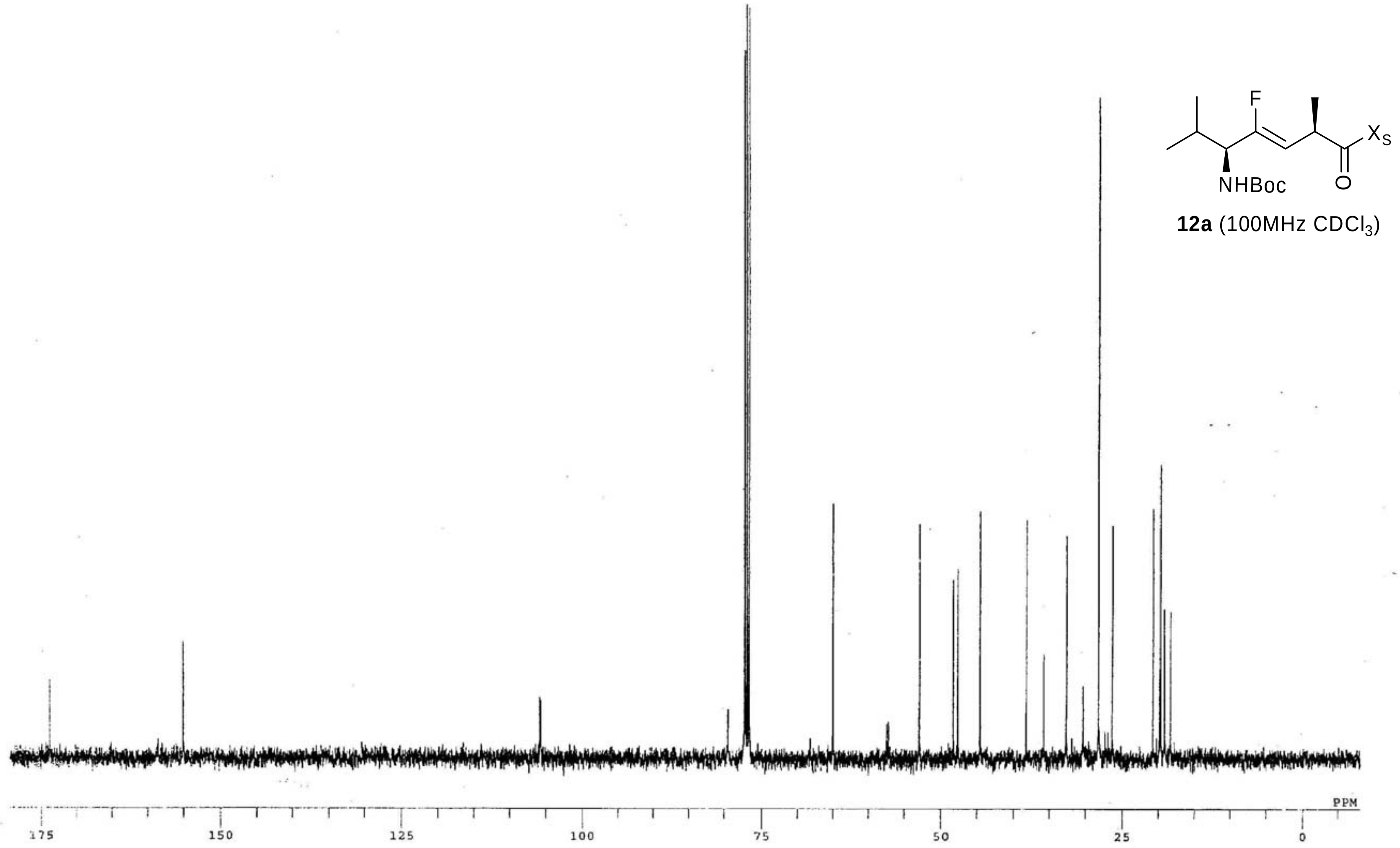


General Procedure for one-pot rduction/asymmetric alkylation via transmetalation. (2*R*,5*S*,3*Z*)-5-[*N*-(*tert*-Butoxycarbonyl)amino]-4-fluoro-2,6-dimethylhept-3-enoyl (*S*)-sultam (12a). To a suspension of CuI (64.0 mg, 0.335 mmol) in THF (1 mL) was added dropwise a solution of MeLi·LiBr complex in Et_2O (1.5 M, 0.45 mL, 0.670 mmol) at –78 °C under argon, and the mixture was stirred for 10 min at 0 °C. To the solution of the above organocopper reagent was added dropwise a solution of the *N*-enoyl sultam (*E*)-**8** (40.0 mg, 0.0815 mmol) in THF (1.5 mL) at –78 °C. The mixture was stirred for 30 min at –78 °C and HMPA (233 μl, 1.34 mmol) was added dropwise to the mixture. After stirring for 30 min at –78 °C, a solution of triphenyltin chloride (64.6 mg, 0.168 mmol) in THF (1.5

ml) was added dropwise, and the mixture was then stirred for 30 min at –40 °C and methyl iodide (0.095 ml, 0.670 mmol) was added dropwise. The mixture was stirred for 20 h at –40 °C. The reaction was quenched at –40 °C by addition of a 1:1 saturated NH_4Cl-28% NH_4OH solution (4 mL) with additional stirring at room temperature for 30 min. The mixture was extracted with Et_2O and the extract was washed with brine and dried over $MgSO_4$. Concentration under reduced pressure followed by flash chromatography over silica gel with *n*-hexane-EtOAc (5:1) gave the title compound **12a** (36.9 mg, 93% yield) as a colorless oil; $[\alpha]^{24.3}_{D}$ = –95.5 (c 0.945, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 0.92–0.94 (m, 6H), 0.97 (s, 3H), 1.16 (s, 3H), 1.19–1.41 (m, 2H), 1.33 (d, J = 7.1 Hz, 3H), 1.44 (s, 9H), 1.81–1.96 (m, 4H), 2.02–2.06 (m, 2H), 3.42–3.52 (m, 2H), 3.86–3.97 (m, 1H), 3.89 (t, J = 6.1 Hz, 1H), 4.12–4.19 (m, 1H), 4.70 (d, J = 9.8 Hz, 1H), 5.02 (dd, J = 37.8, 9.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 19.3, 19.8, 20.8 (2C), 26.4, 28.3 (3C), 30.4, 32.8, 35.9, 38.3, 44.6, 47.7, 48.4, 53.0, 57.4, 65.0, 79.6, 105.9, 155.7, 157.4, 173.8; HRMS (FAB), *m/z* calcd for $C_{24}H_{40}FN_2O_5S$ (MH^+) 487.2642, found 487.2636.



12a (400MHz $CDCl_3$)



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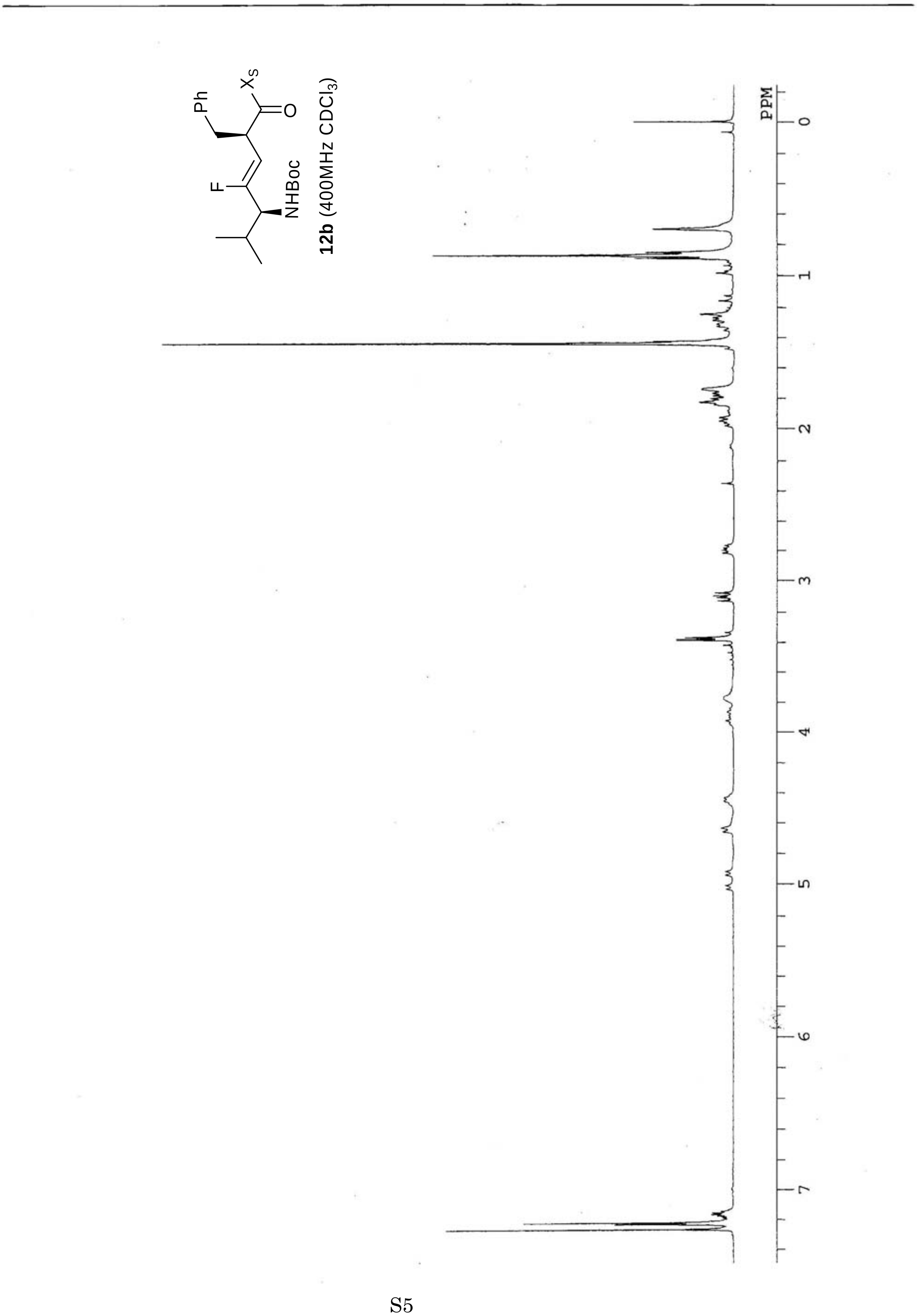

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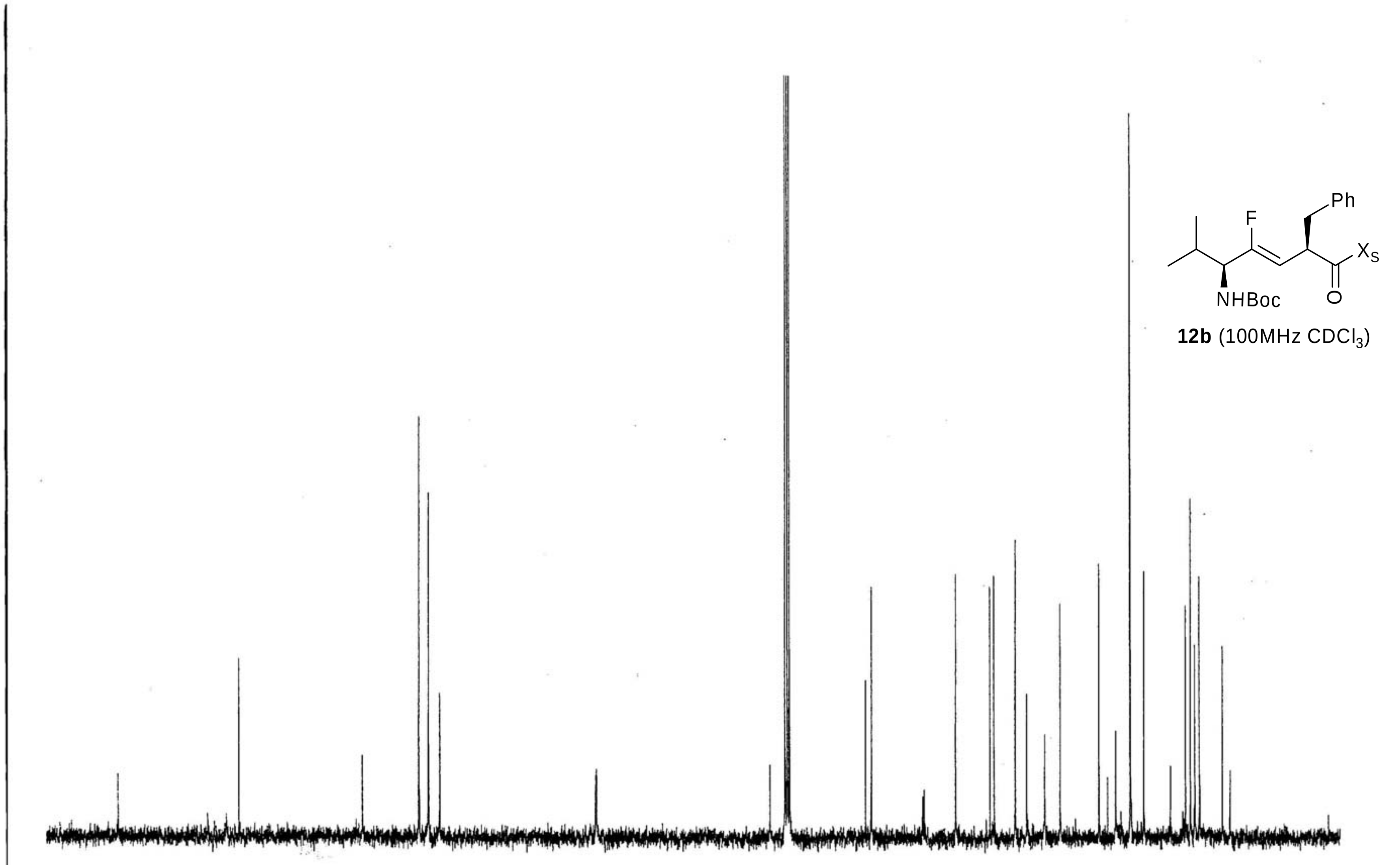

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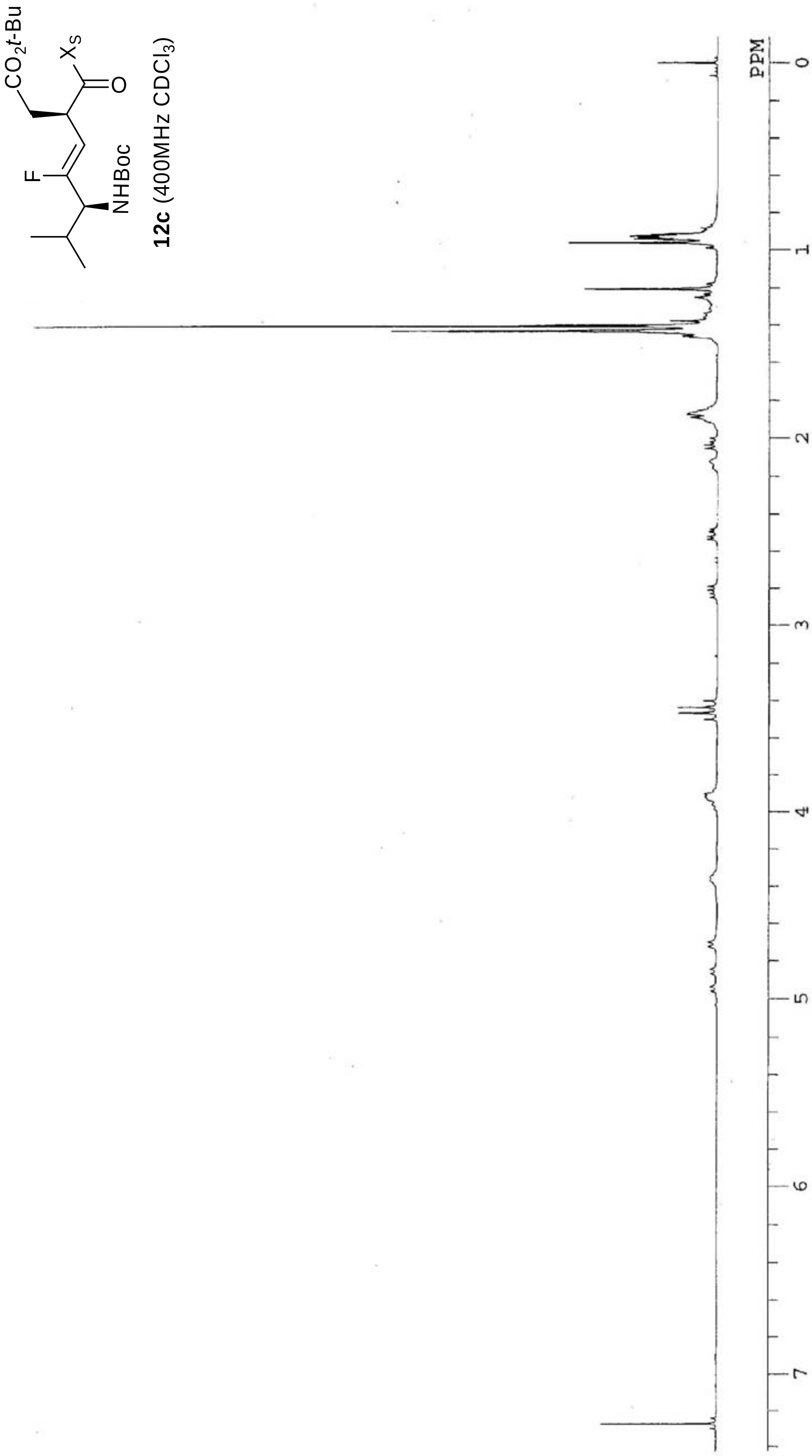

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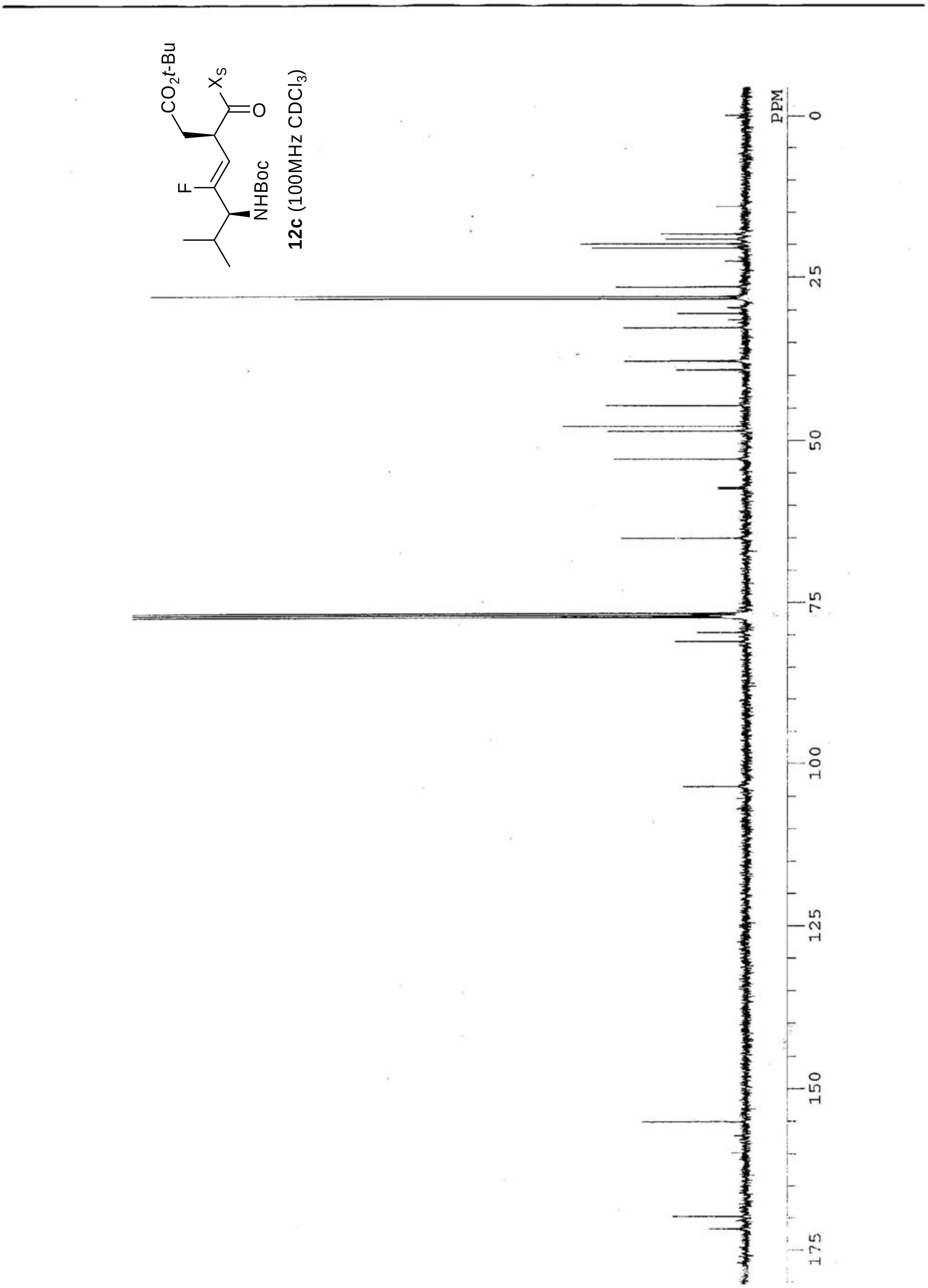

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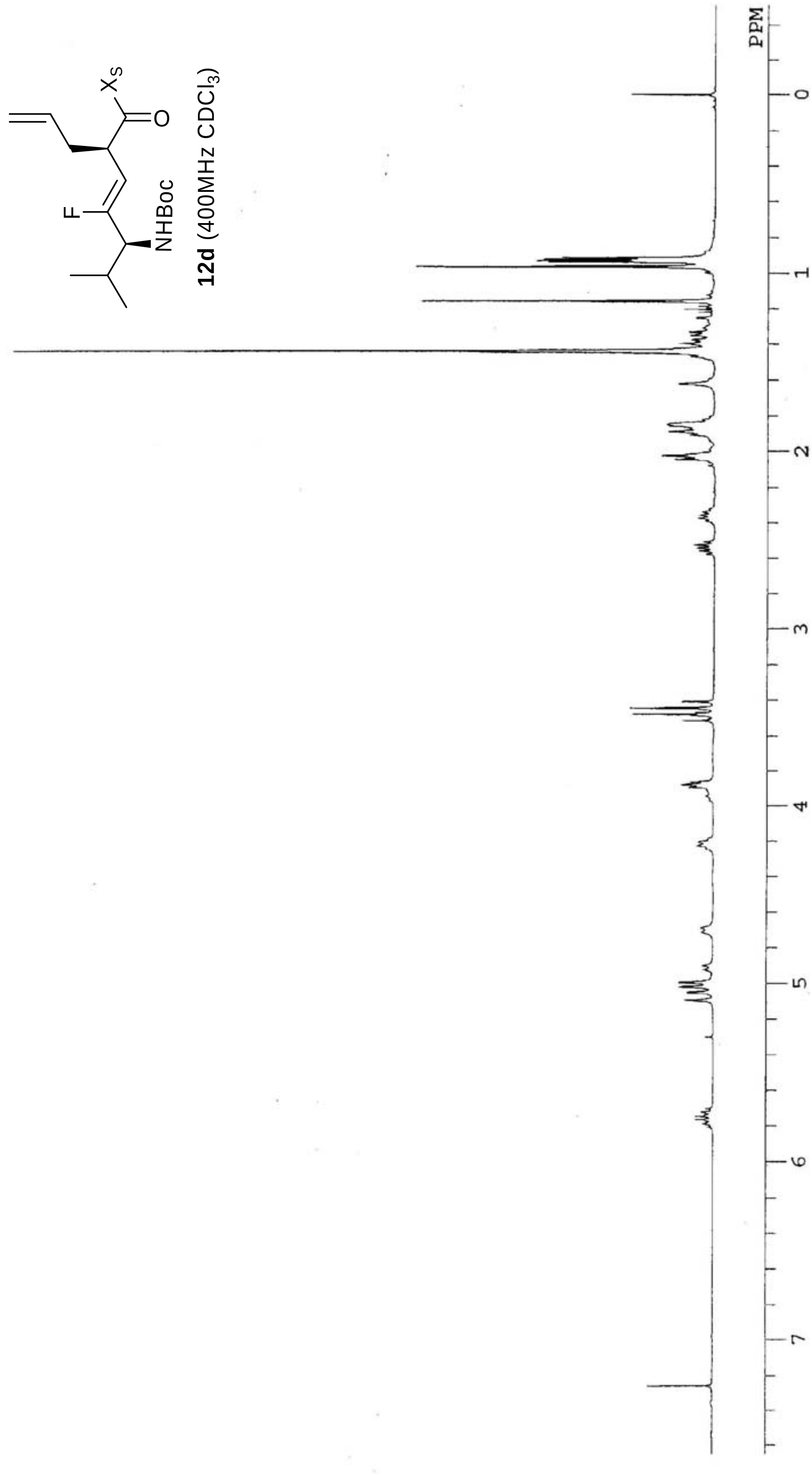

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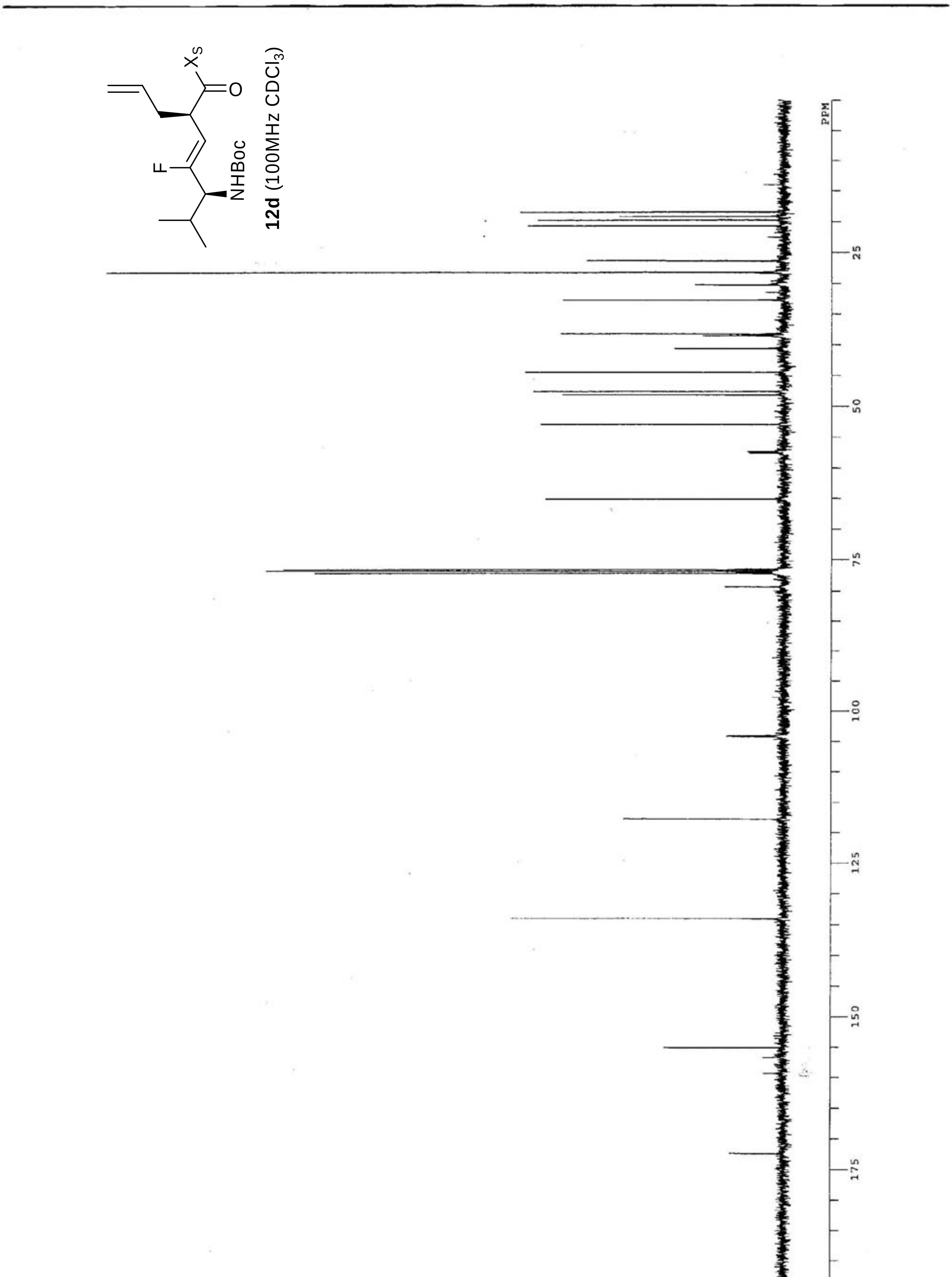

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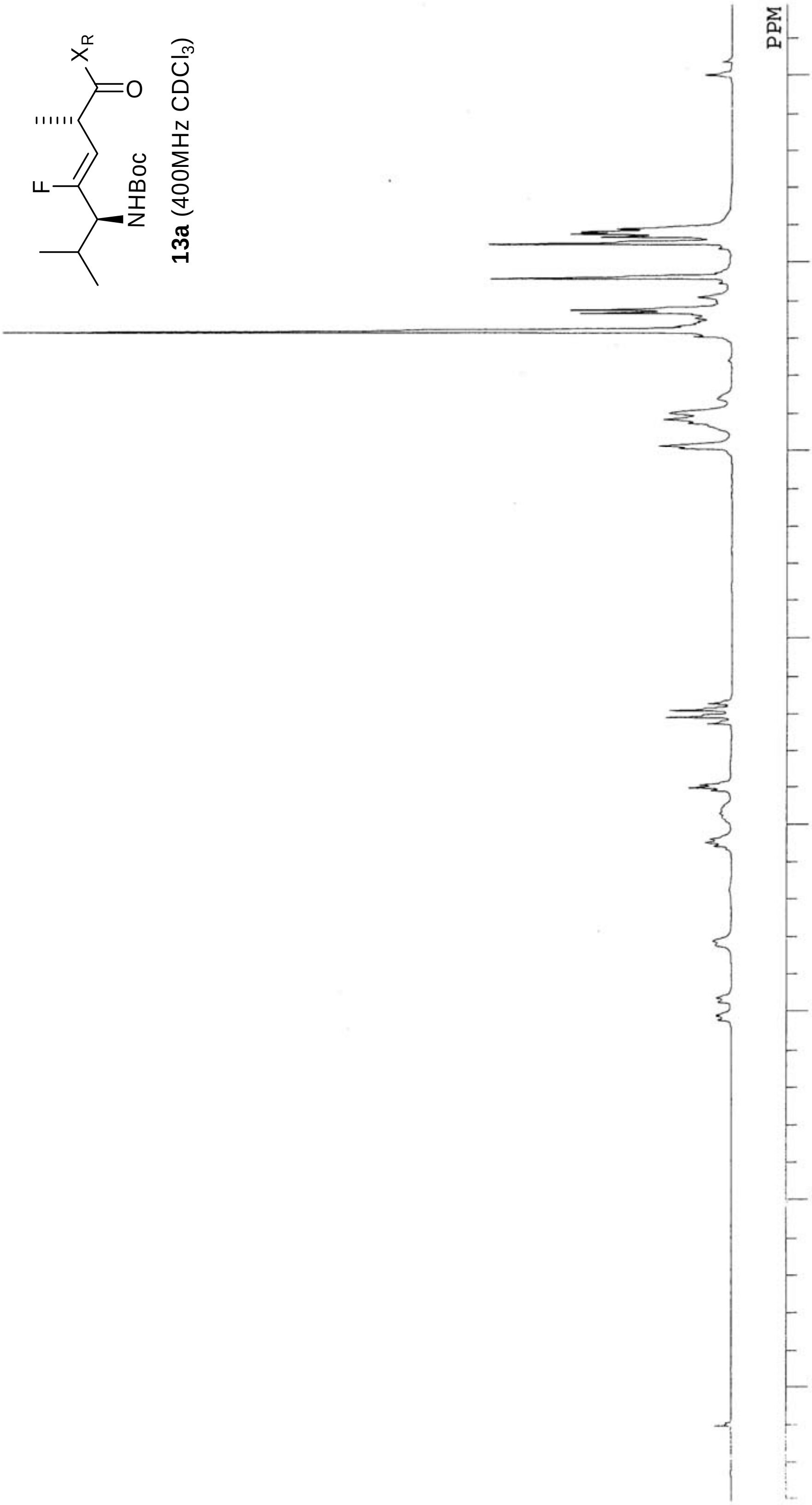

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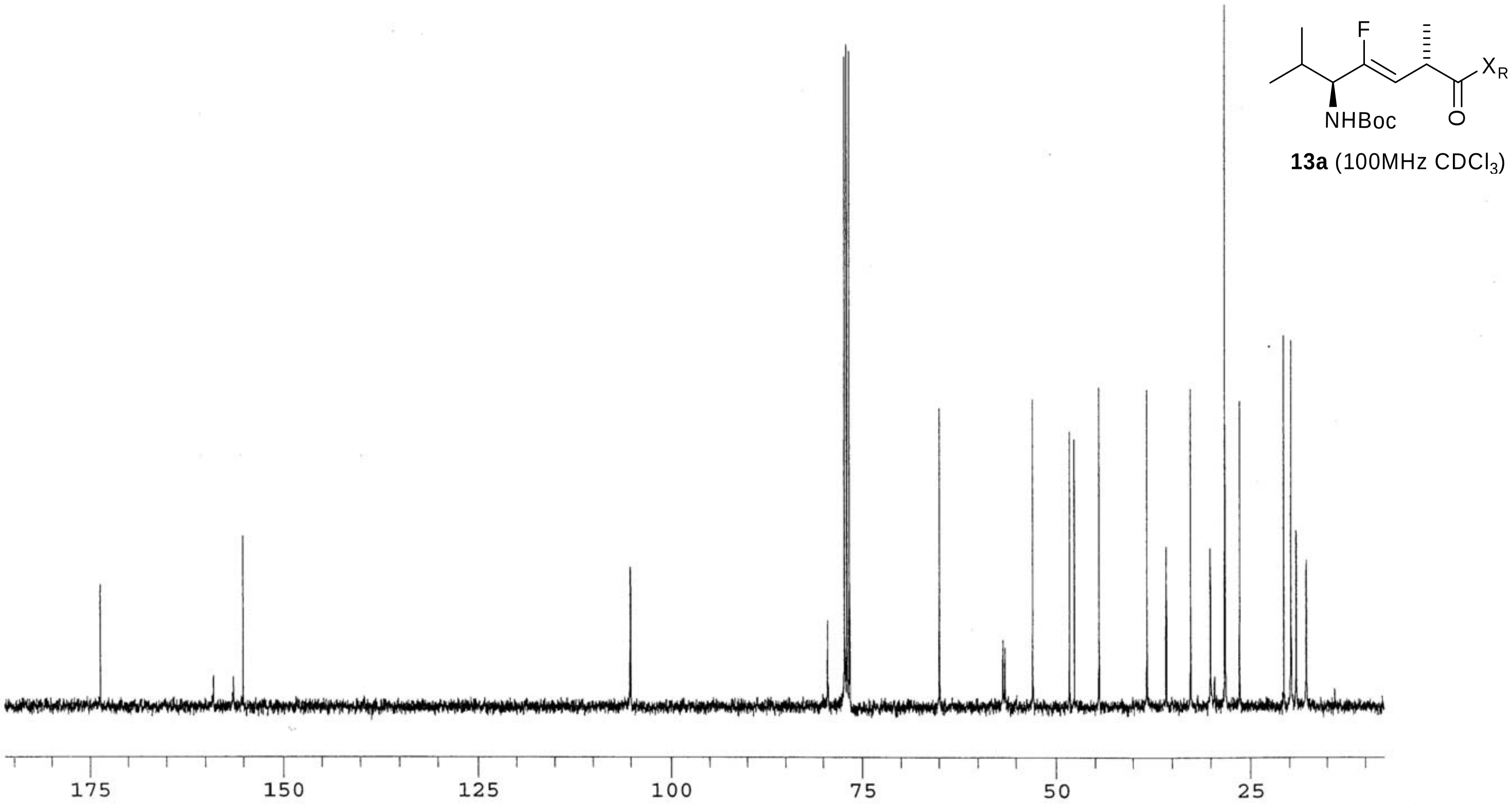

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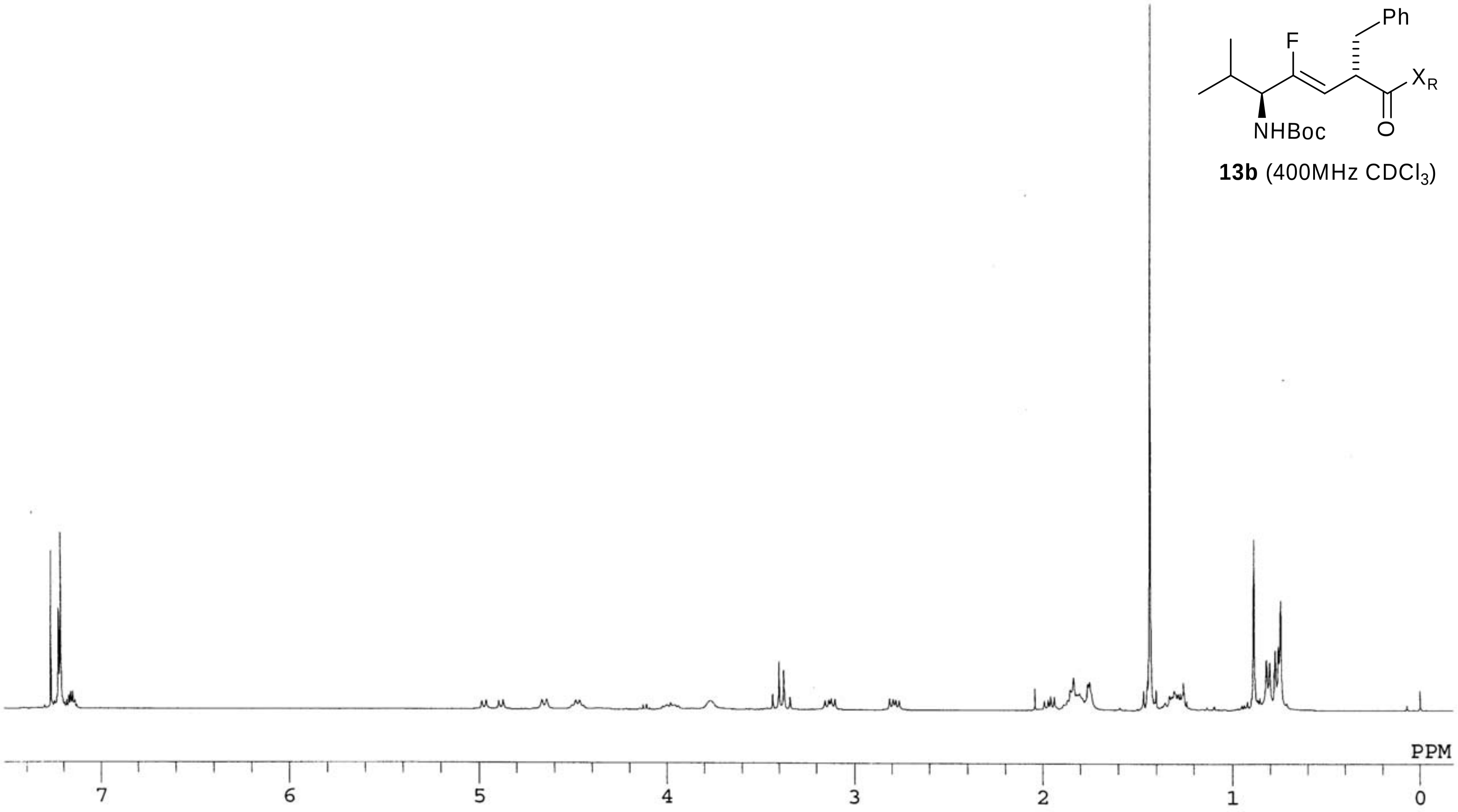
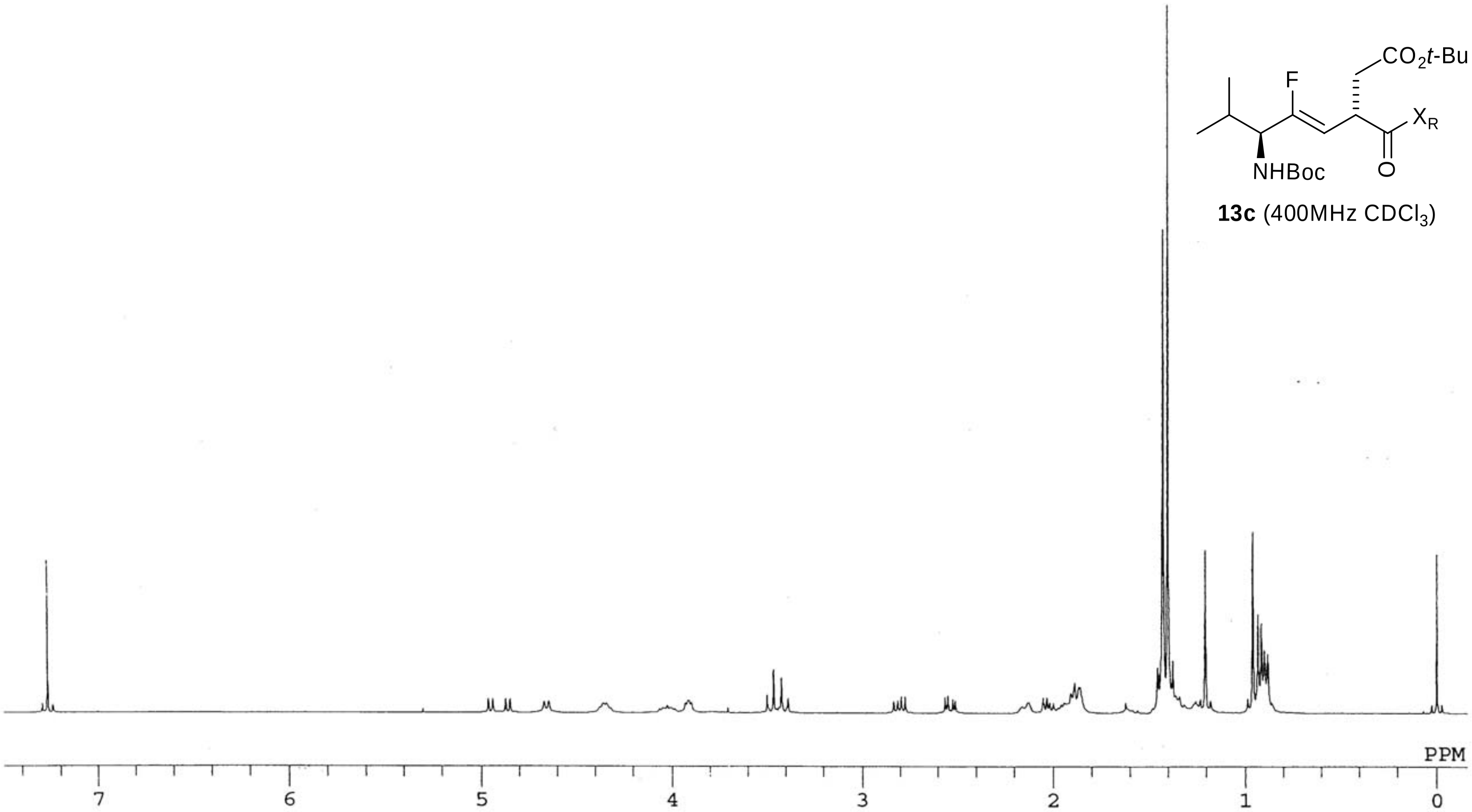


13b (400MHz $CDCl_3$)

13b (100MHz $CDCl_3$)



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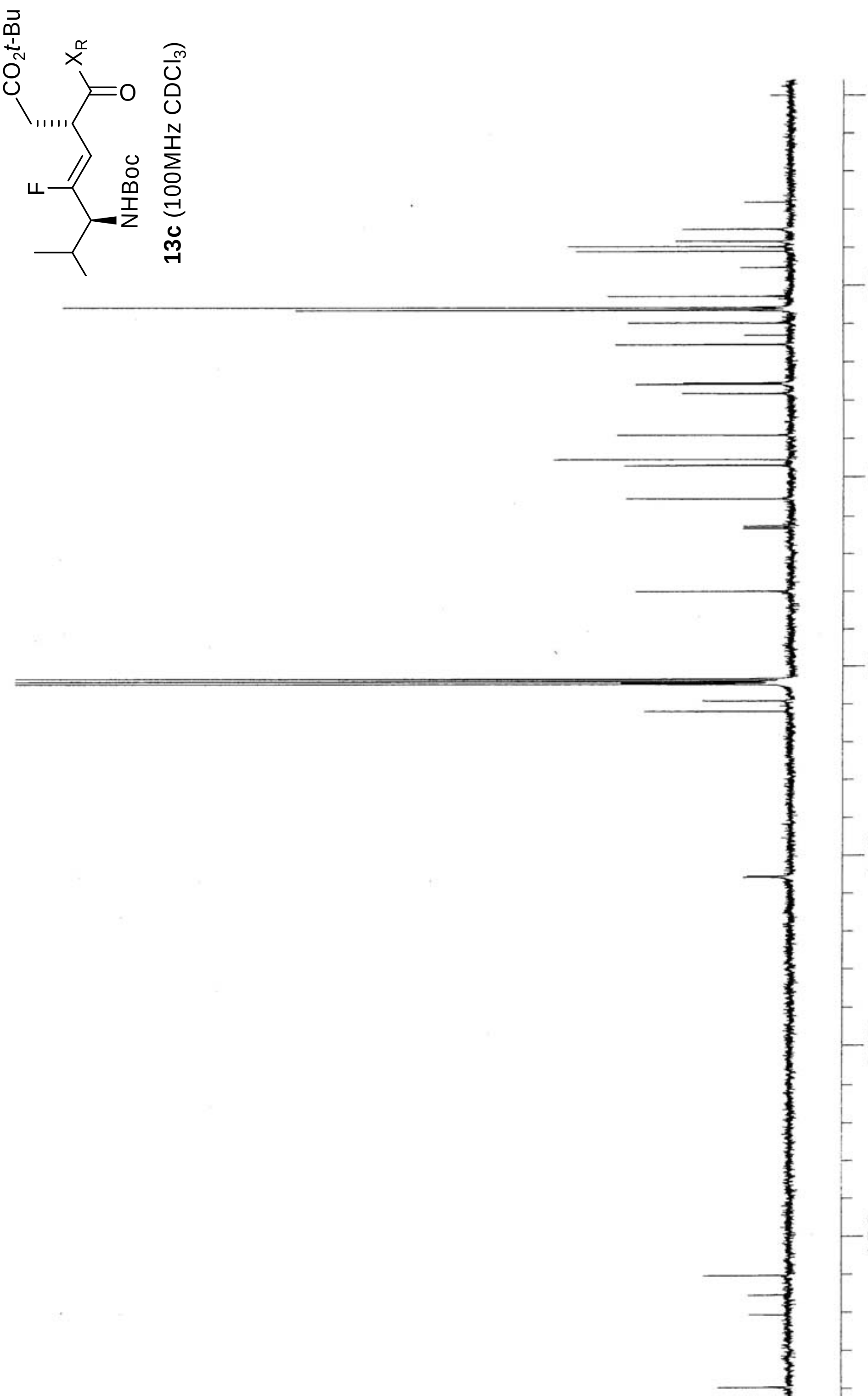

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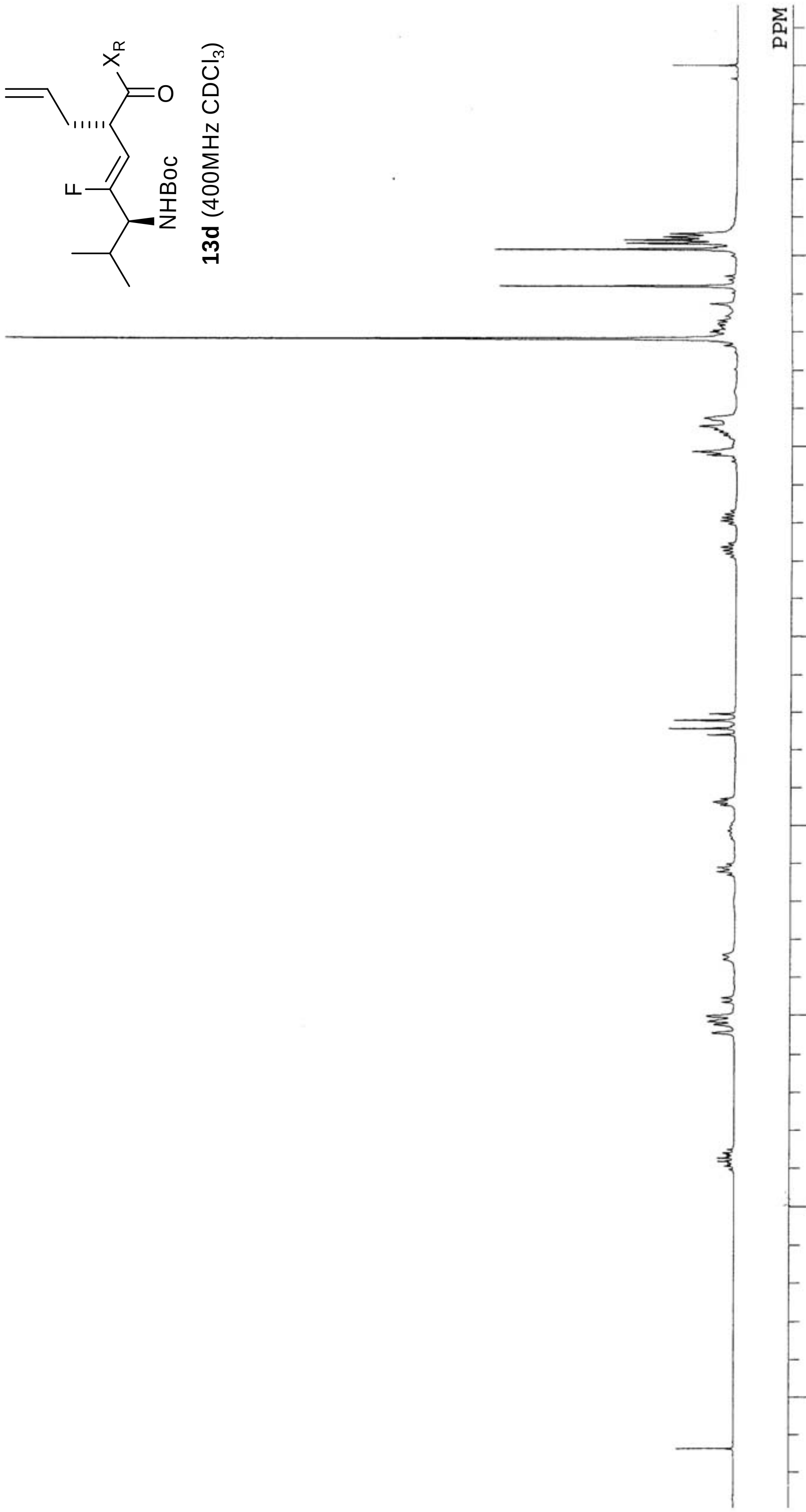
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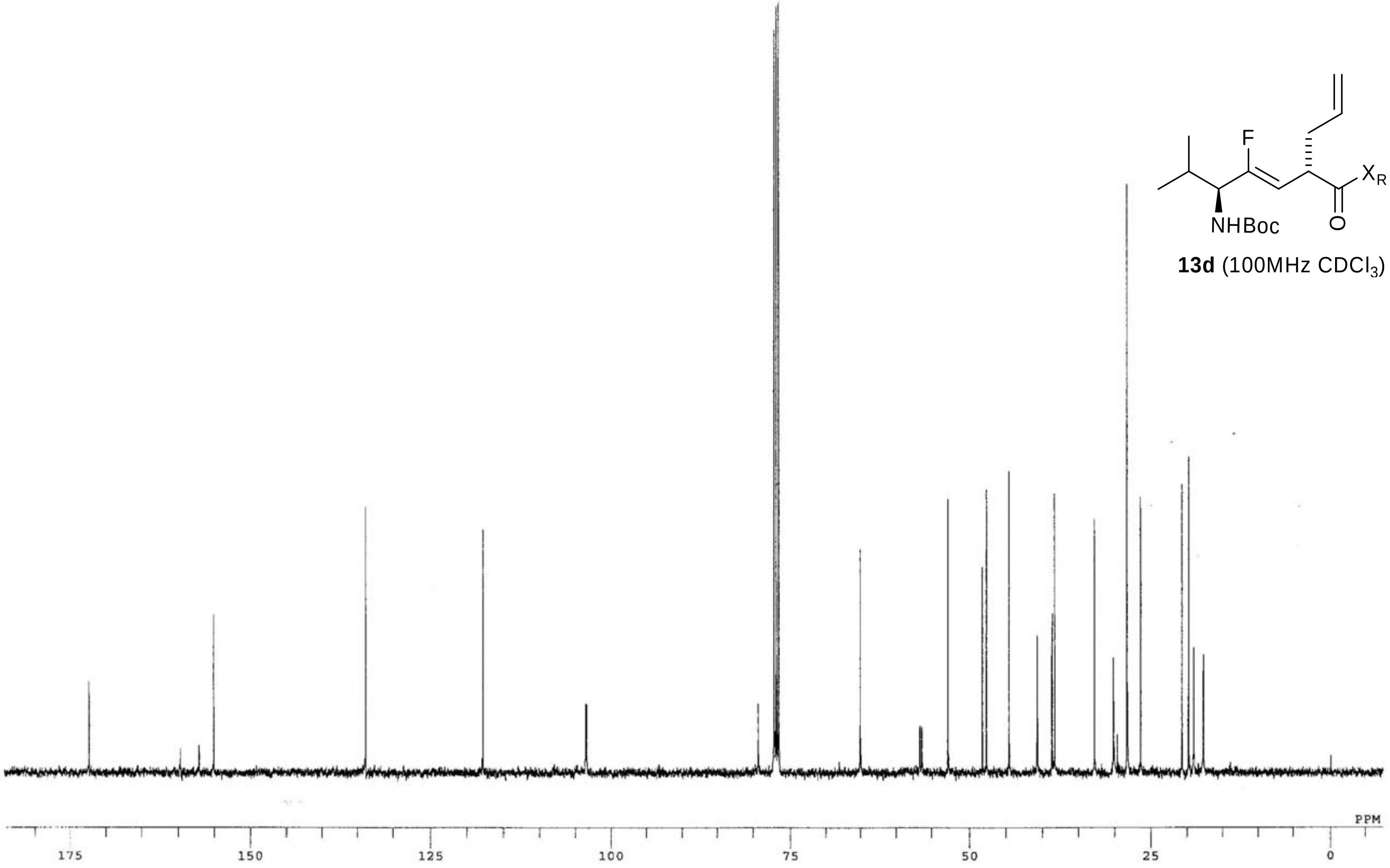

13d (100MHz $CDCl_3$)

CD Spectra of L-Val-L/D-Ala-OMe (100 μM)