

SUPPLEMENTARY MATERIAL

Semi-synthesis of A Novel Hybrid Isoxazolidino Withaferin via Chemoselective and Diastereoselective 1,3-Dipolar Nitronc Cycloaddition Reaction

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Abstract: A facile, atom-economic synthesis of isoxazolidino withaferin, a novel hybrid of withaferin A, has been accomplished via two-step reaction of nitronc synthesis followed by nitronc 1,3-dipolar cycloaddition. The reaction is highly chemoselective (preferential reaction only on one of the two double bonds present on withaferin A) and diastereoselective affording exclusively the cis-fused products. The structure was determined by detailed analysis of 1D, 2D NMR and mass spectral data.

Keywords: Withaferin A; Nitronc-cycloaddition; Semi-synthesis; Isoxazolidine; 2D NMR (HSQC, HMBC, COSY, NOESY);

Figure S1: ^1H NMR of Withaferin A

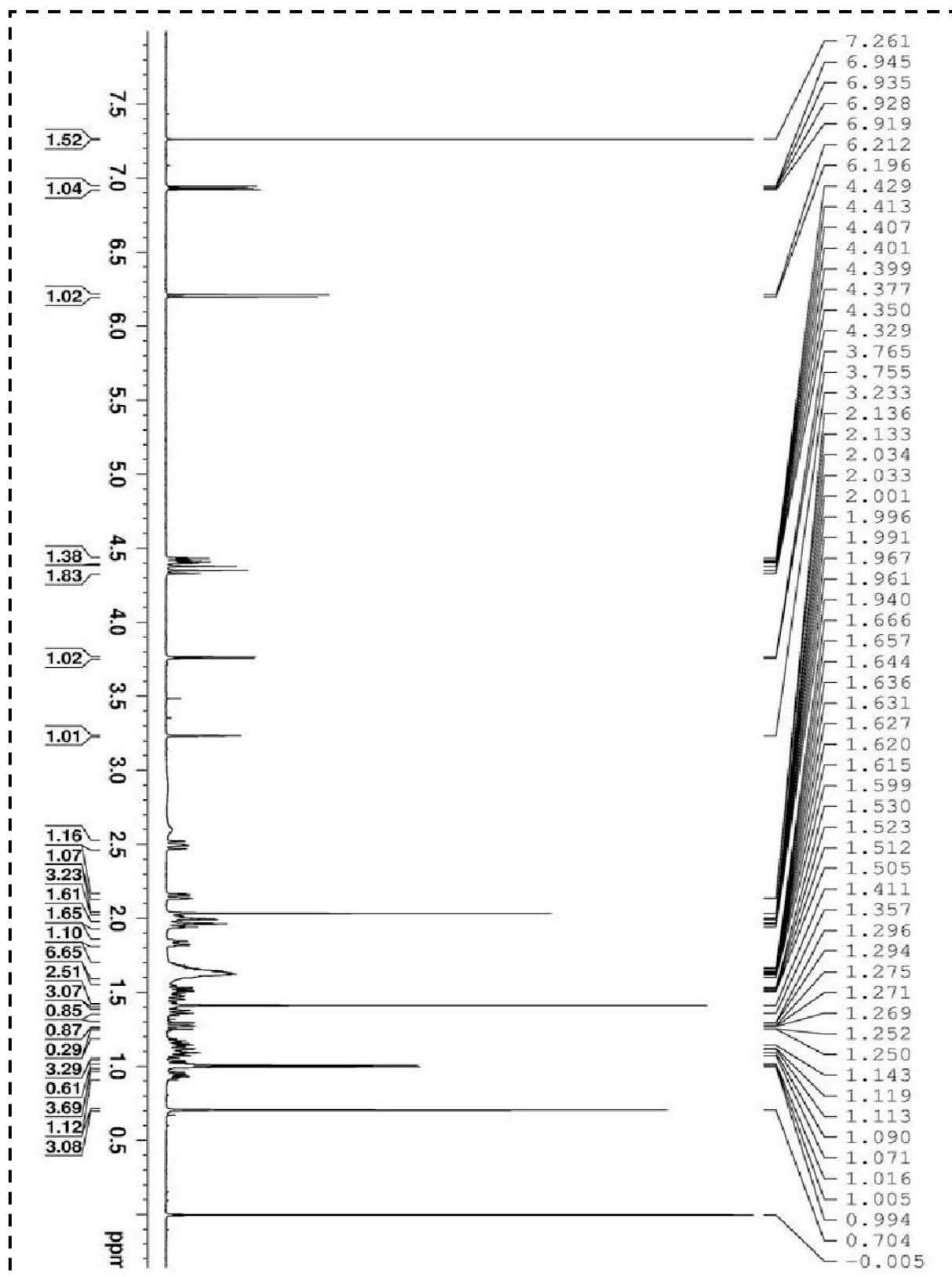


Figure S2: ^1H NMR of Withaferin A

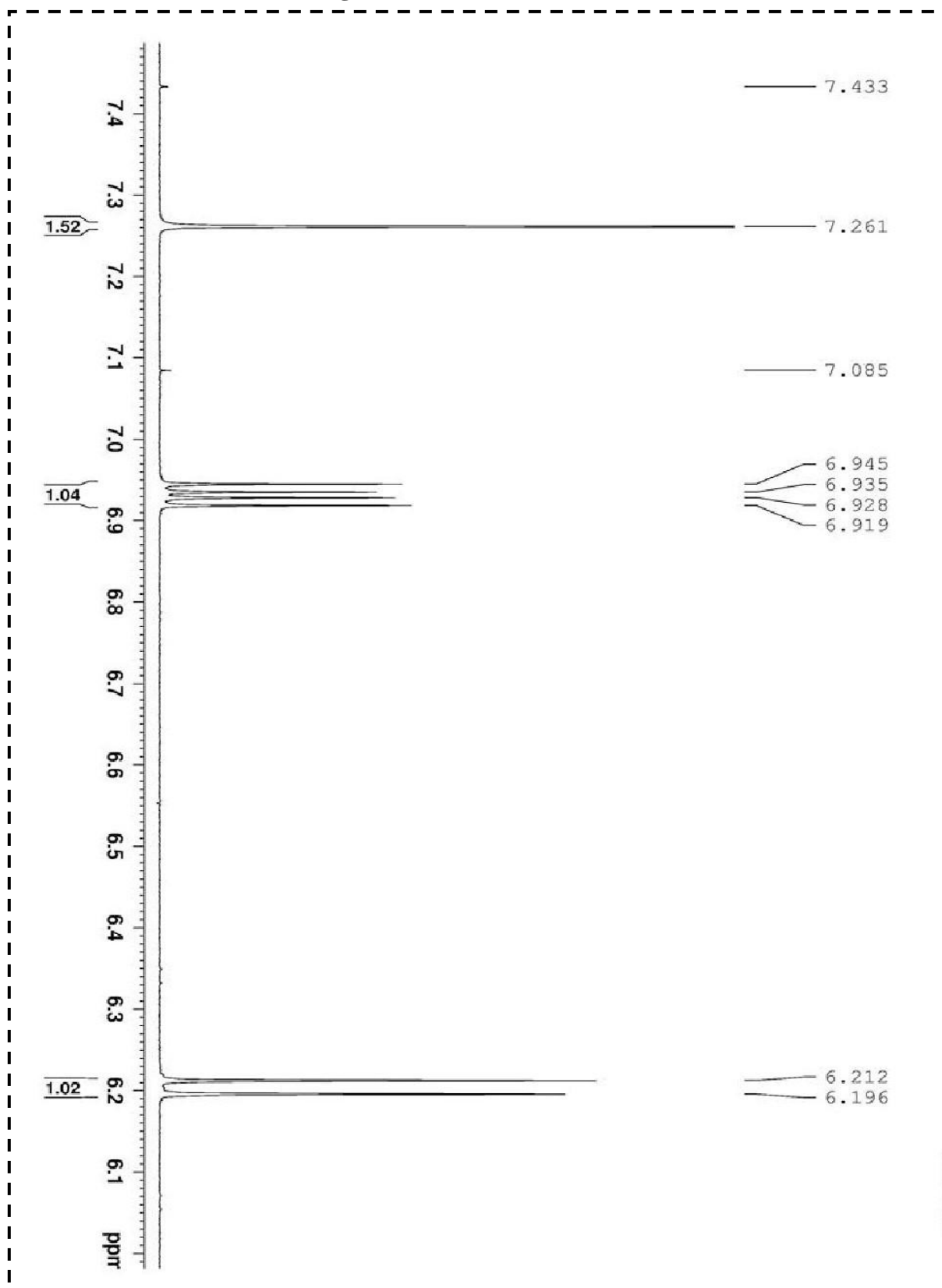


Figure S3: ^1H NMR of Withaferin A

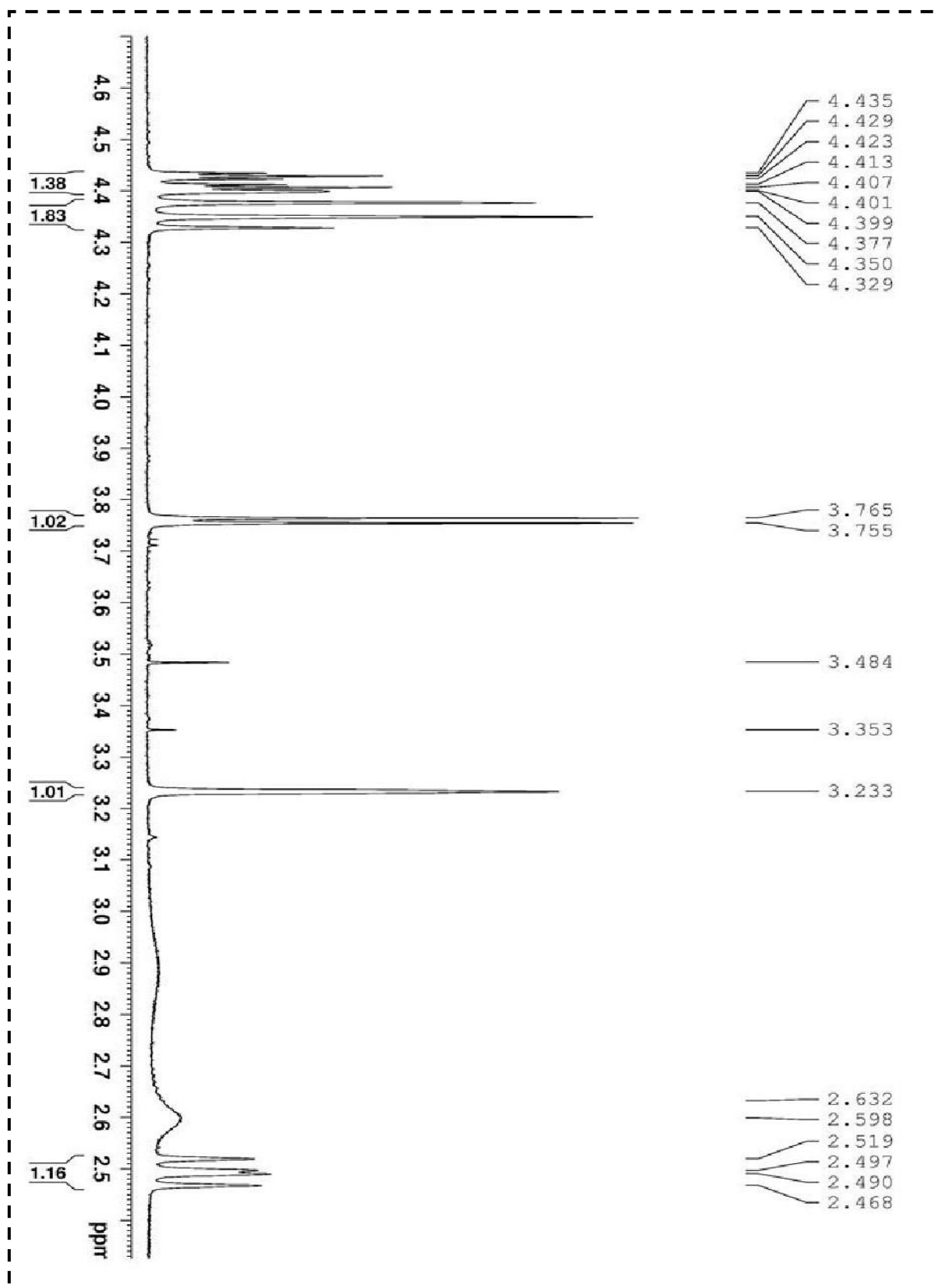


Figure S4: ^1H NMR of Withaferin A

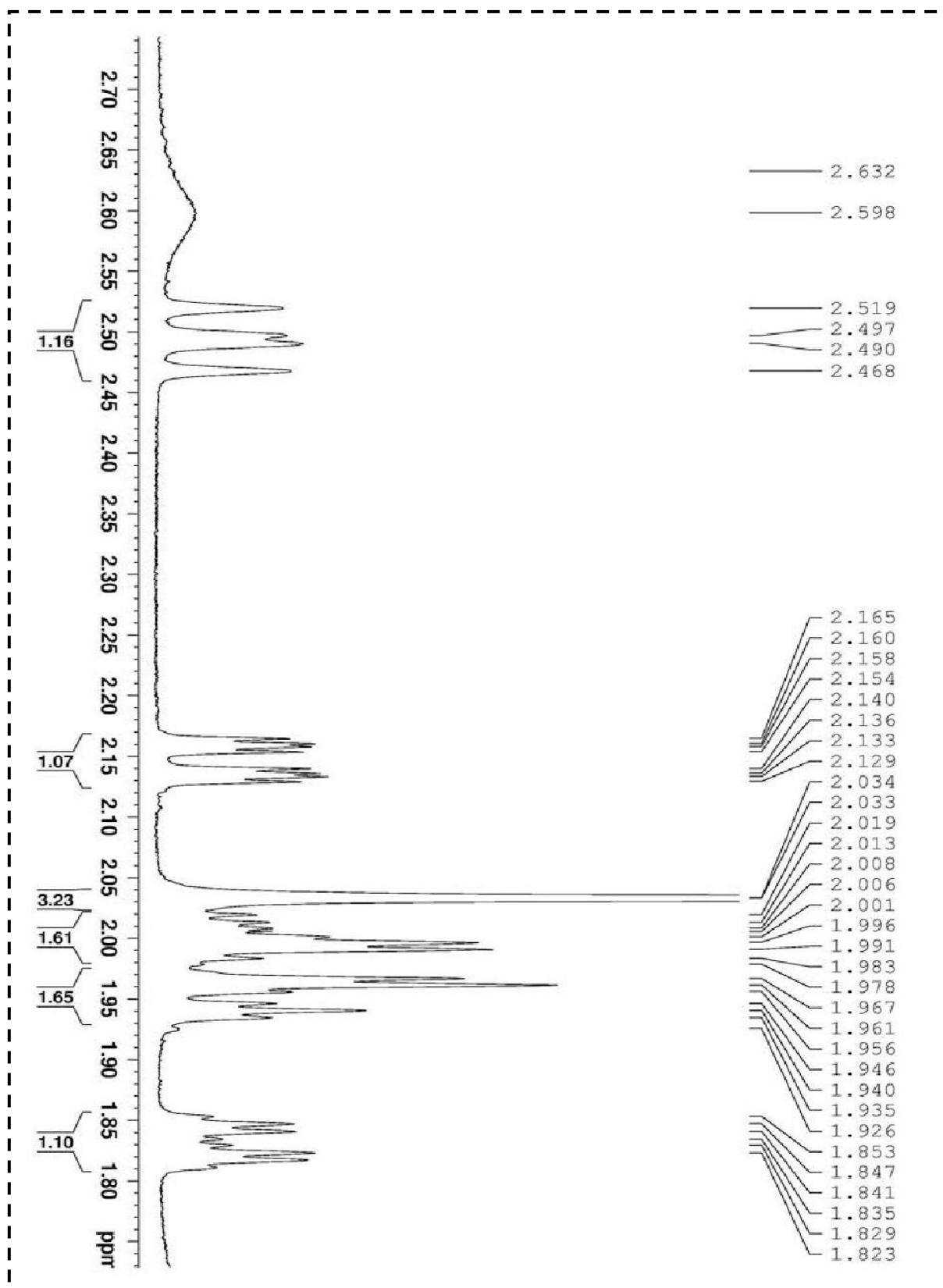


Figure S5: ^1H NMR of Withaferin A

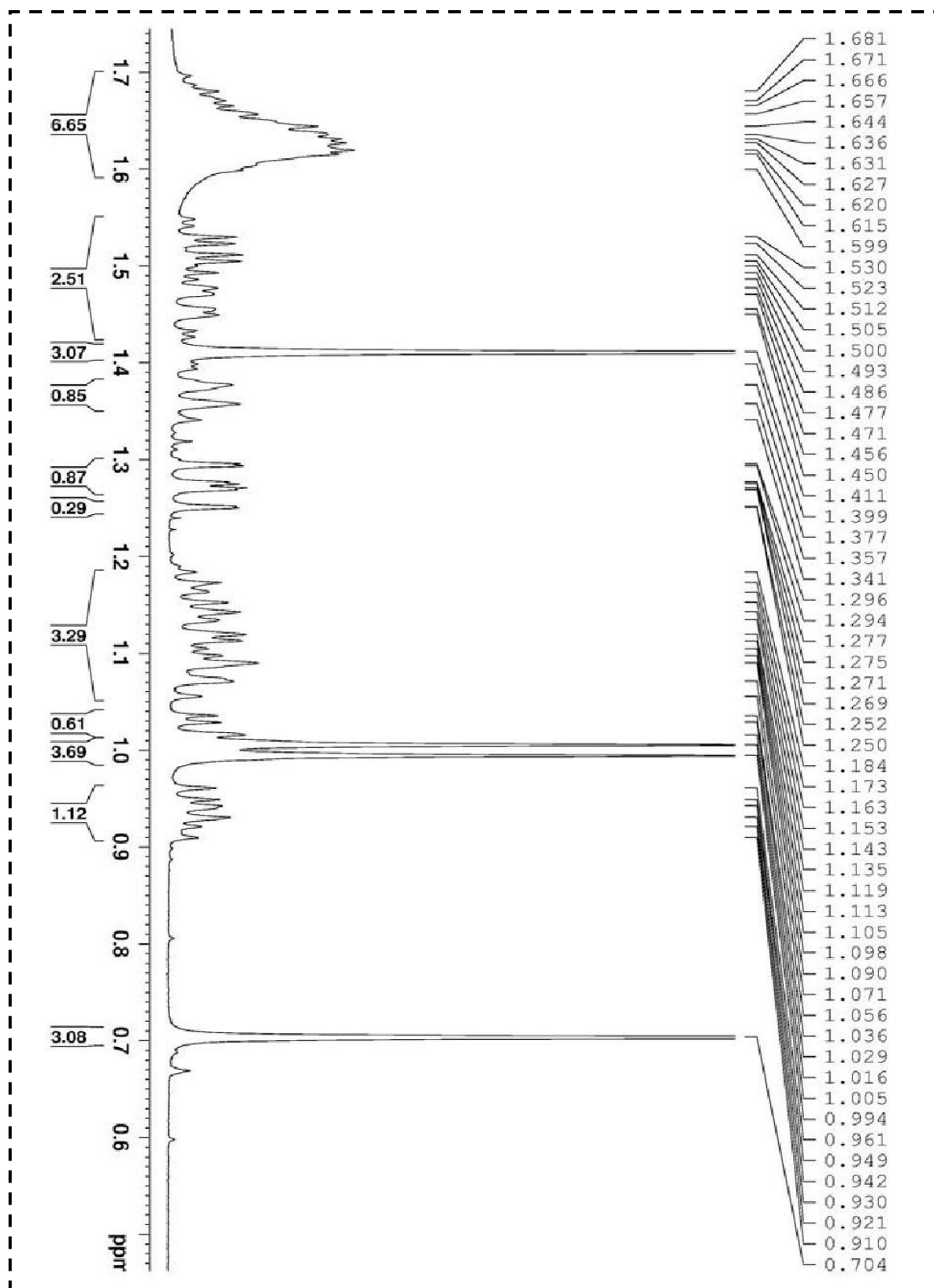


Figure S6: ^{13}C NMR of Withaferin A

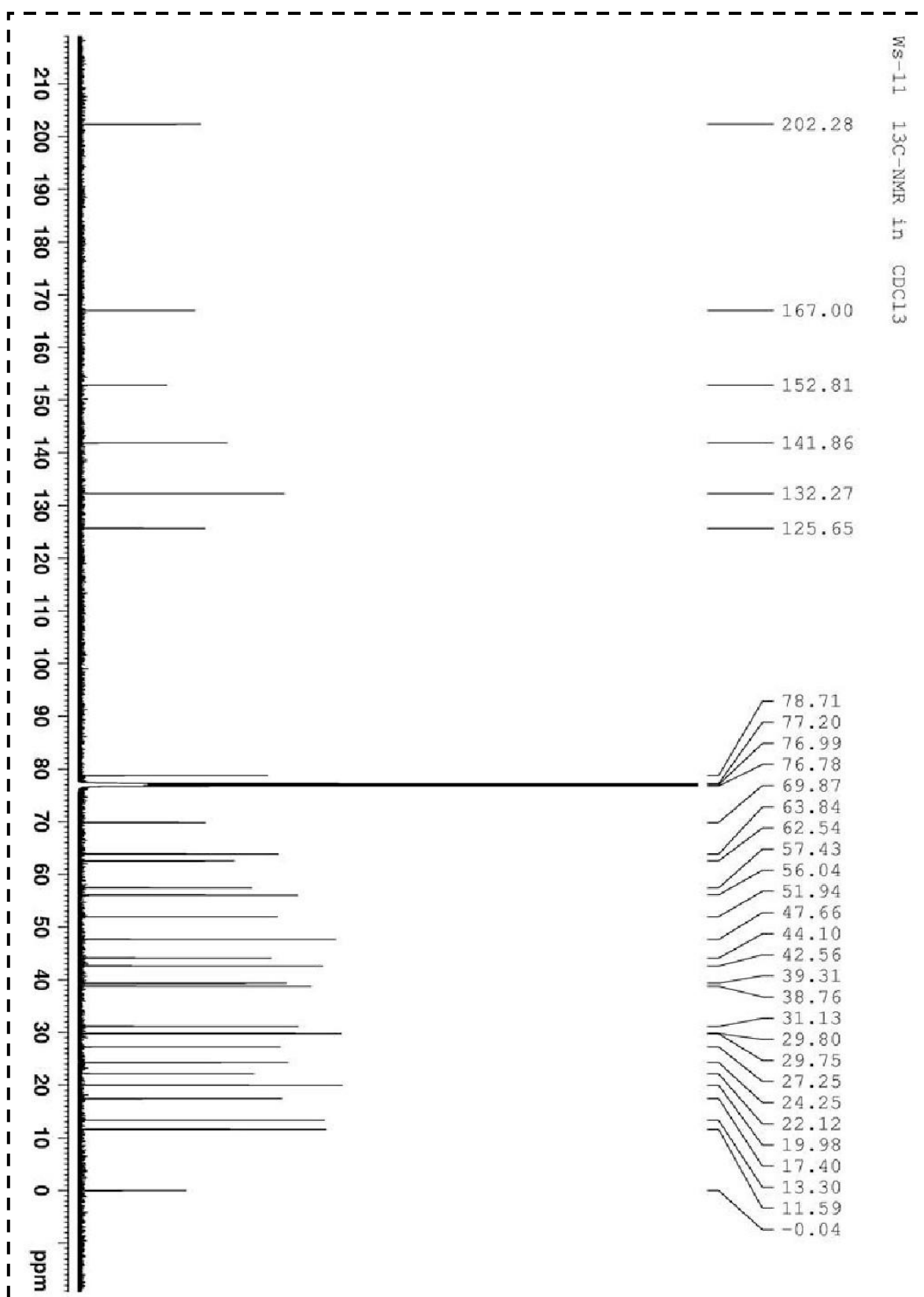


Figure S7: ^{13}C NMR, DEPT 90, 135 of Withaferin A

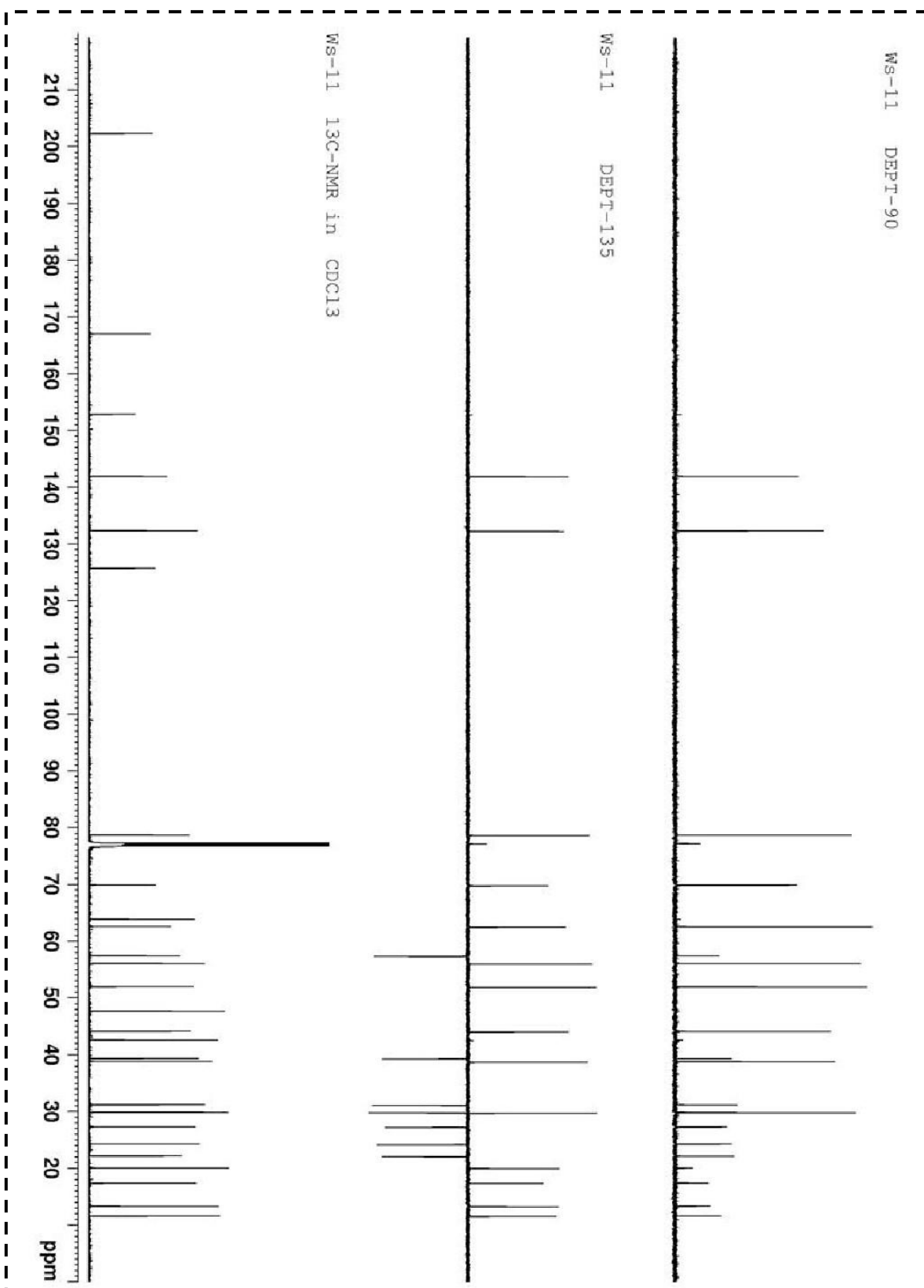


Figure S8: HPLC Profile of Compound 3A

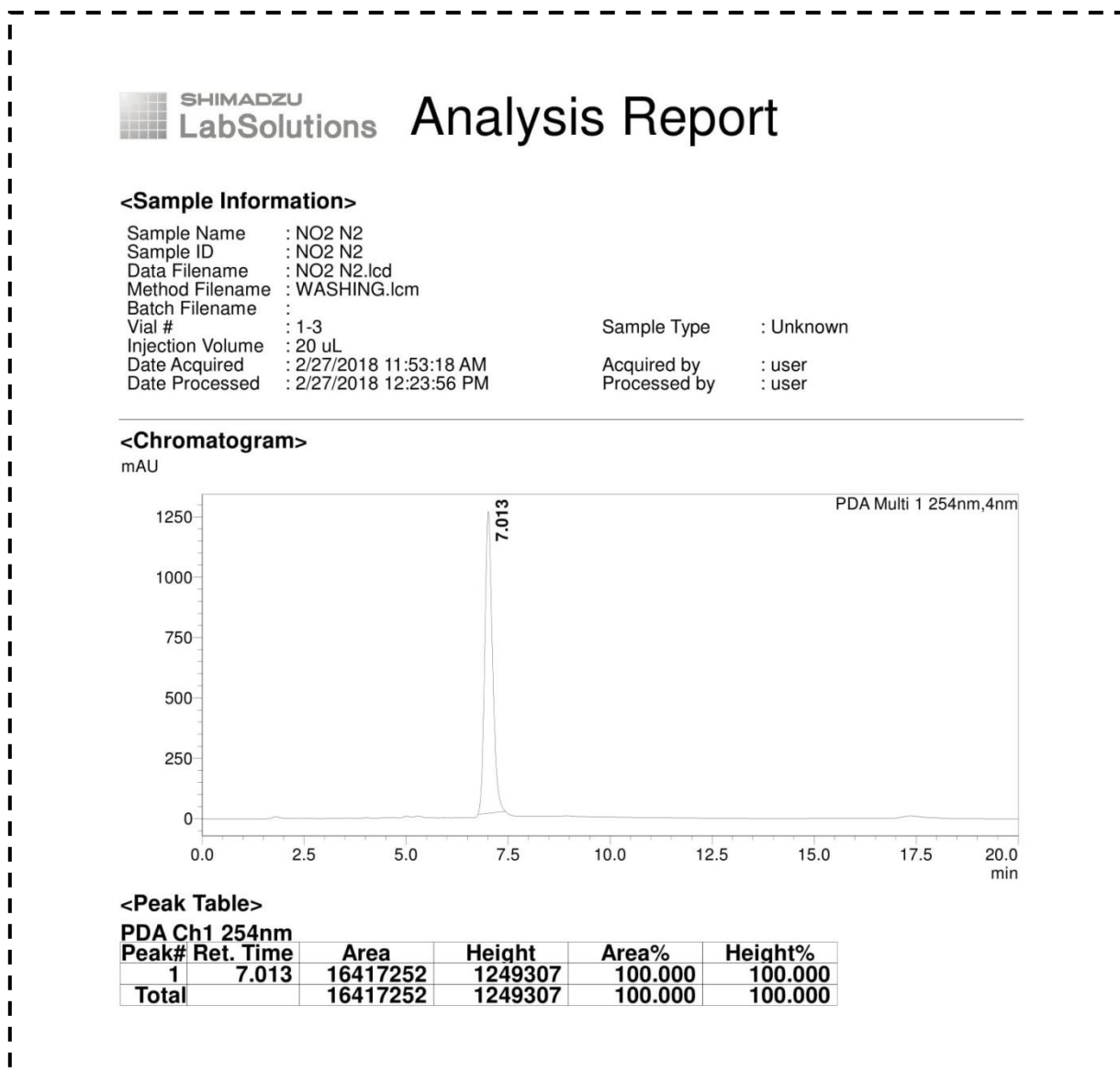


Figure S9: Mass Spectra of Compound 3A

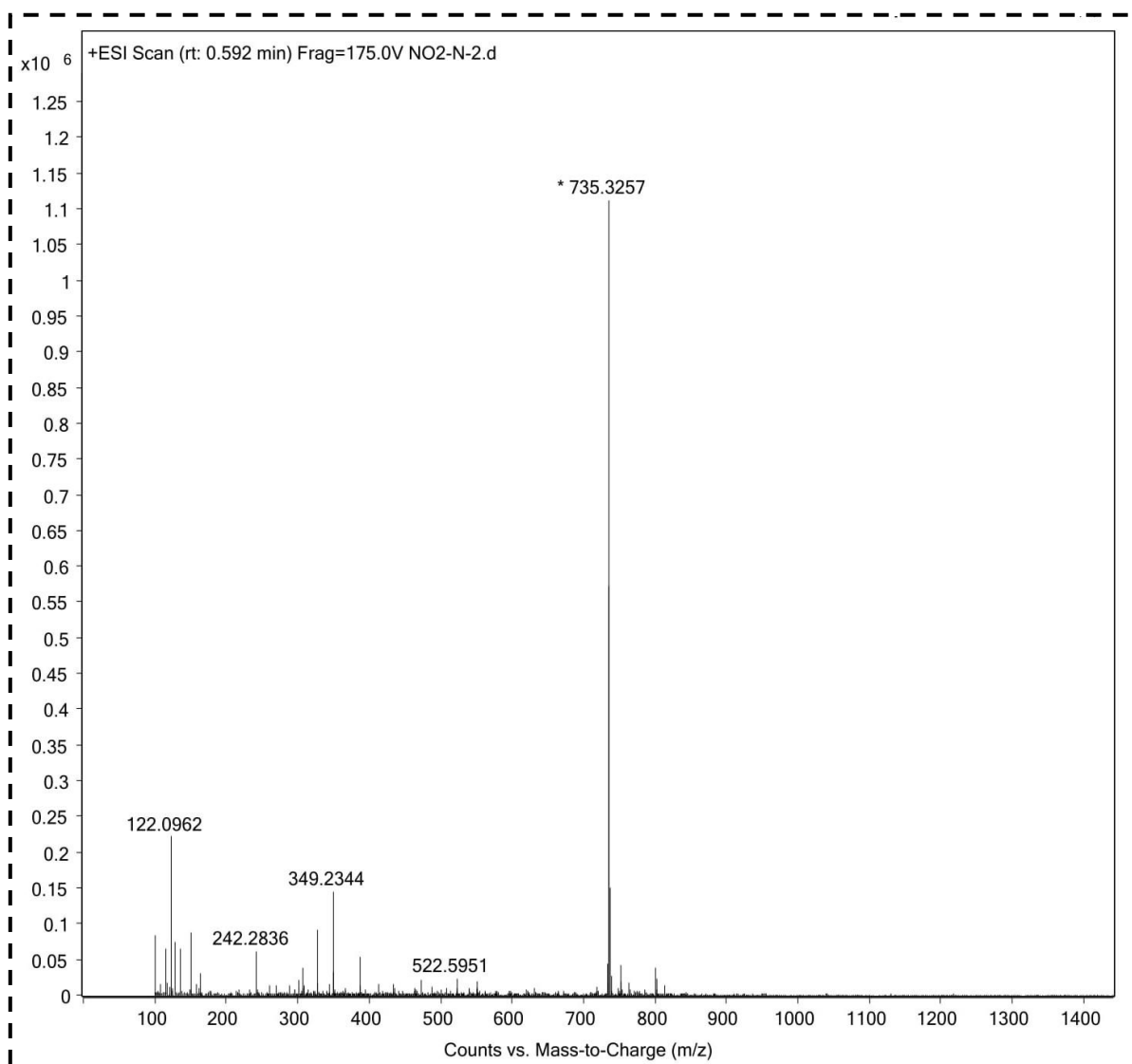


Figure S10: ^1H NMR of Compound 3A

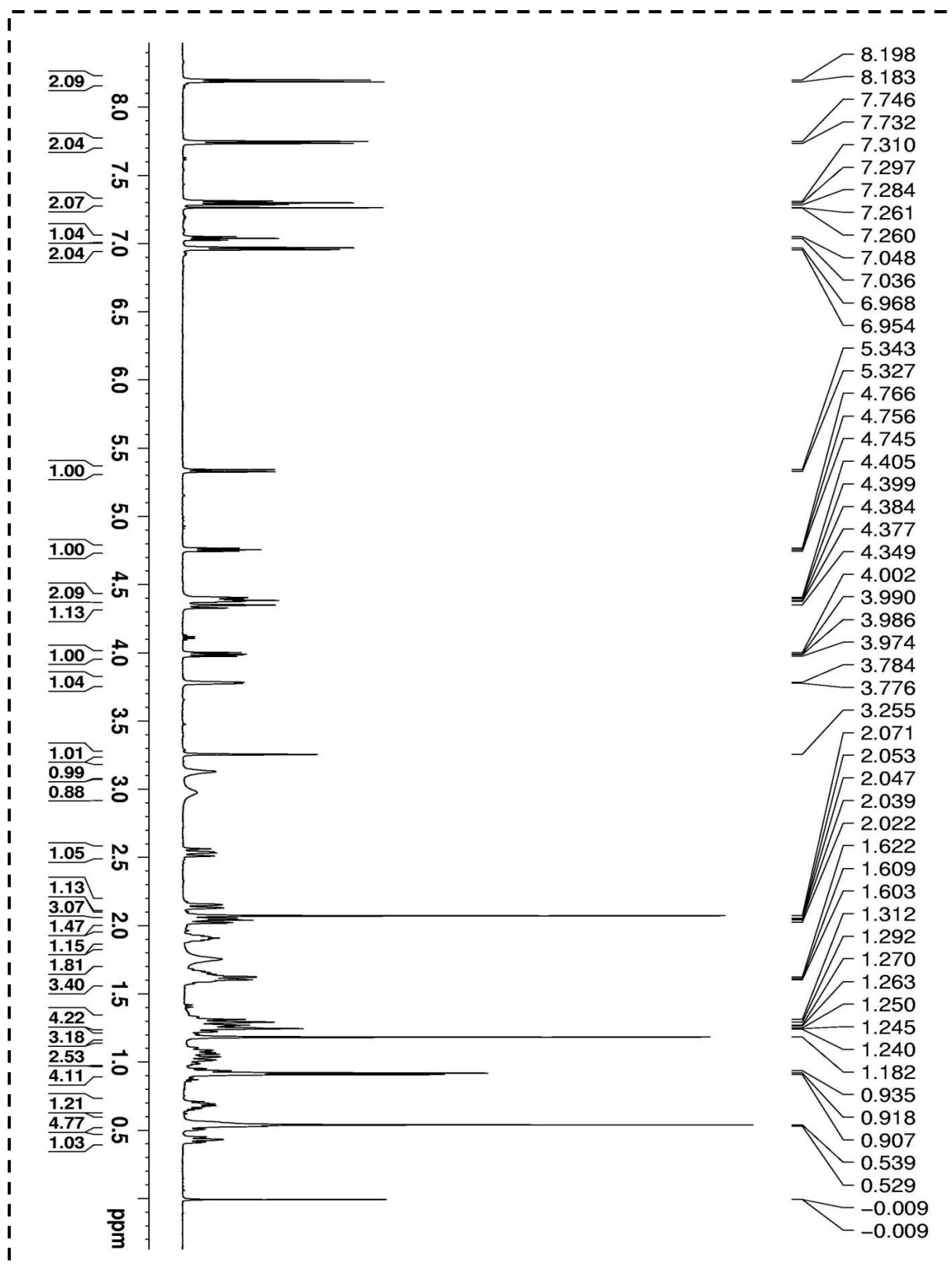


Figure S11: ^1H NMR of Compound 3A

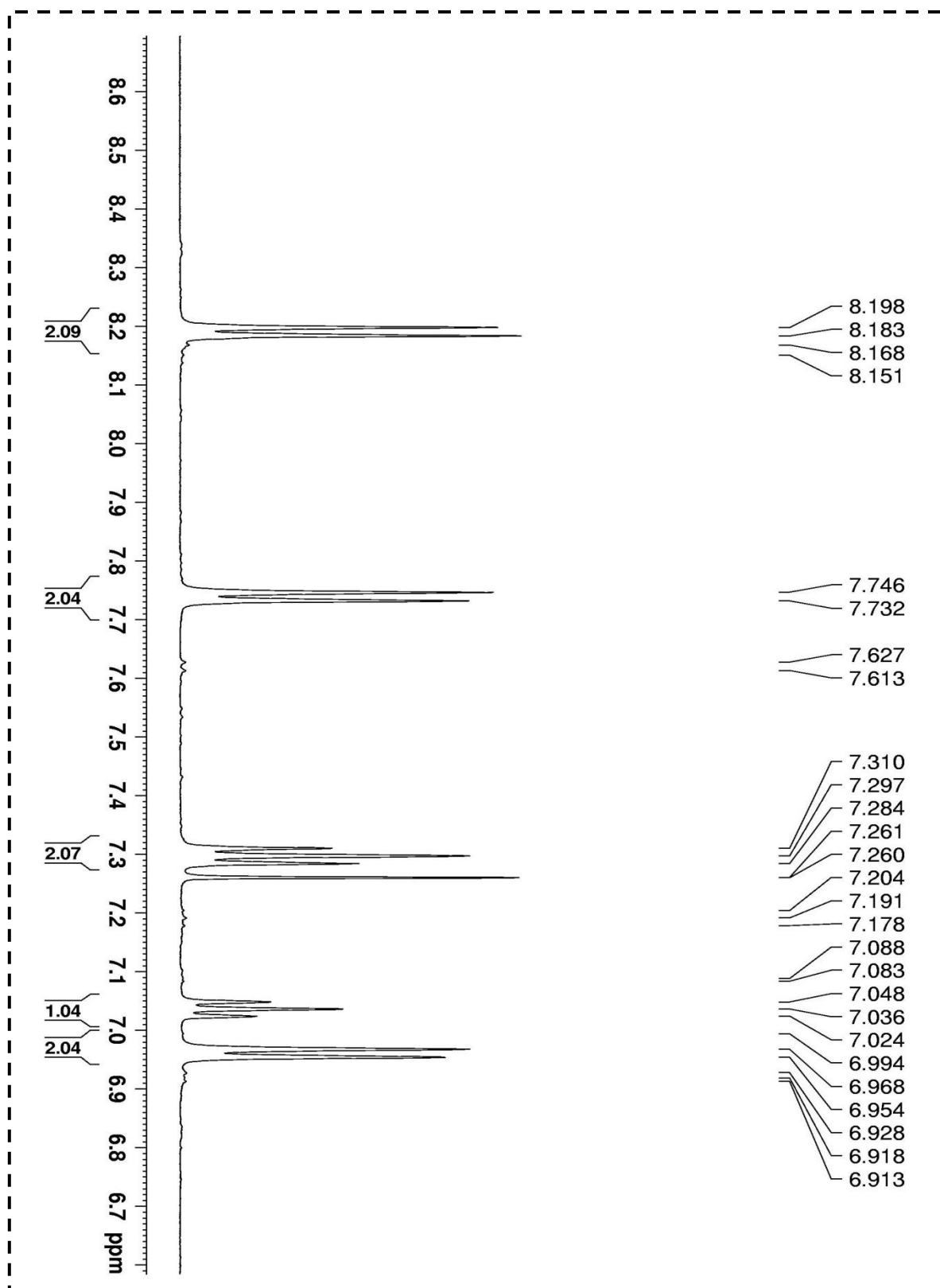


Figure S12: ^1H NMR of Compound 3A

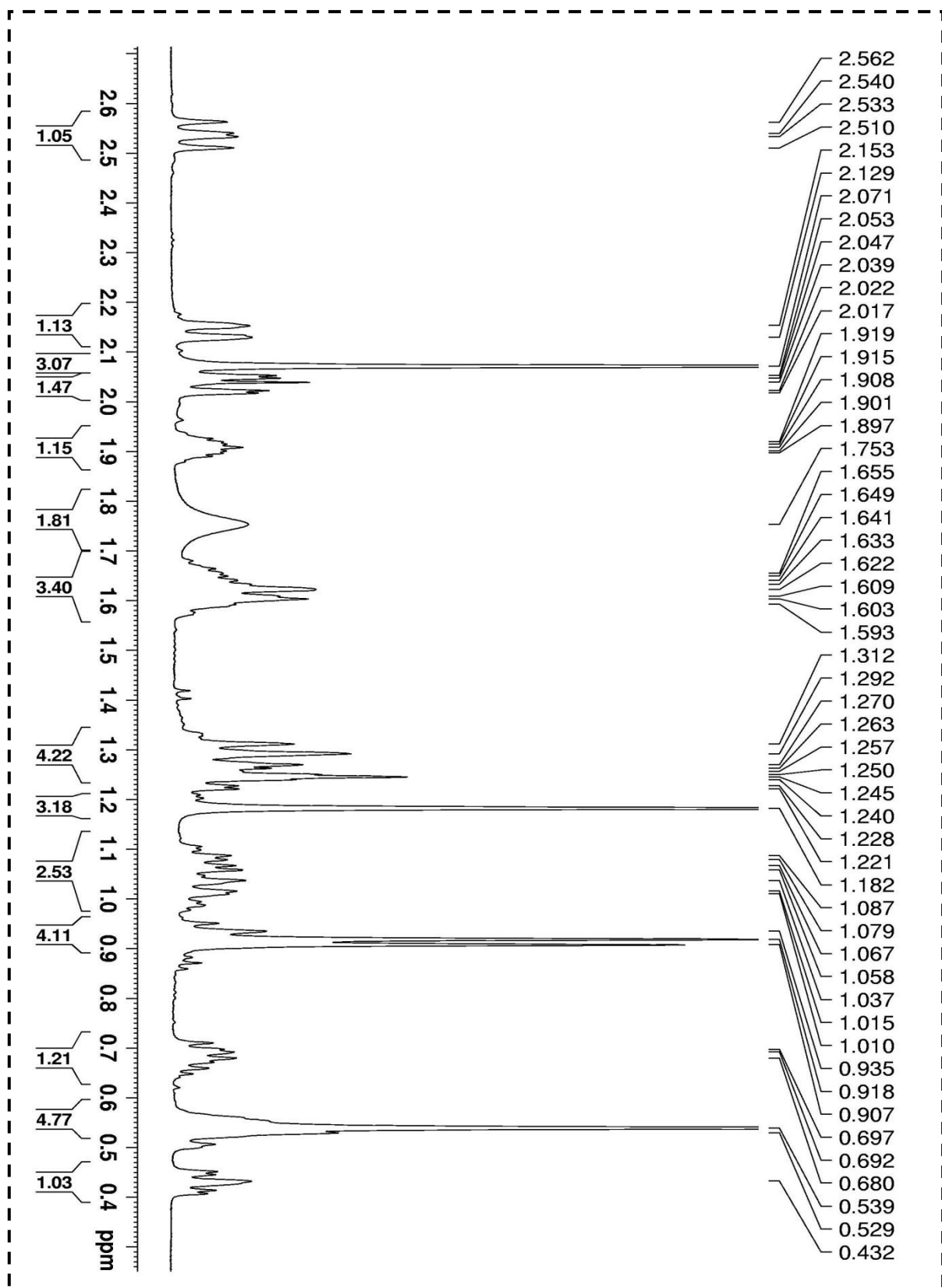


Figure S13: ^{13}C NMR of Compound 3A

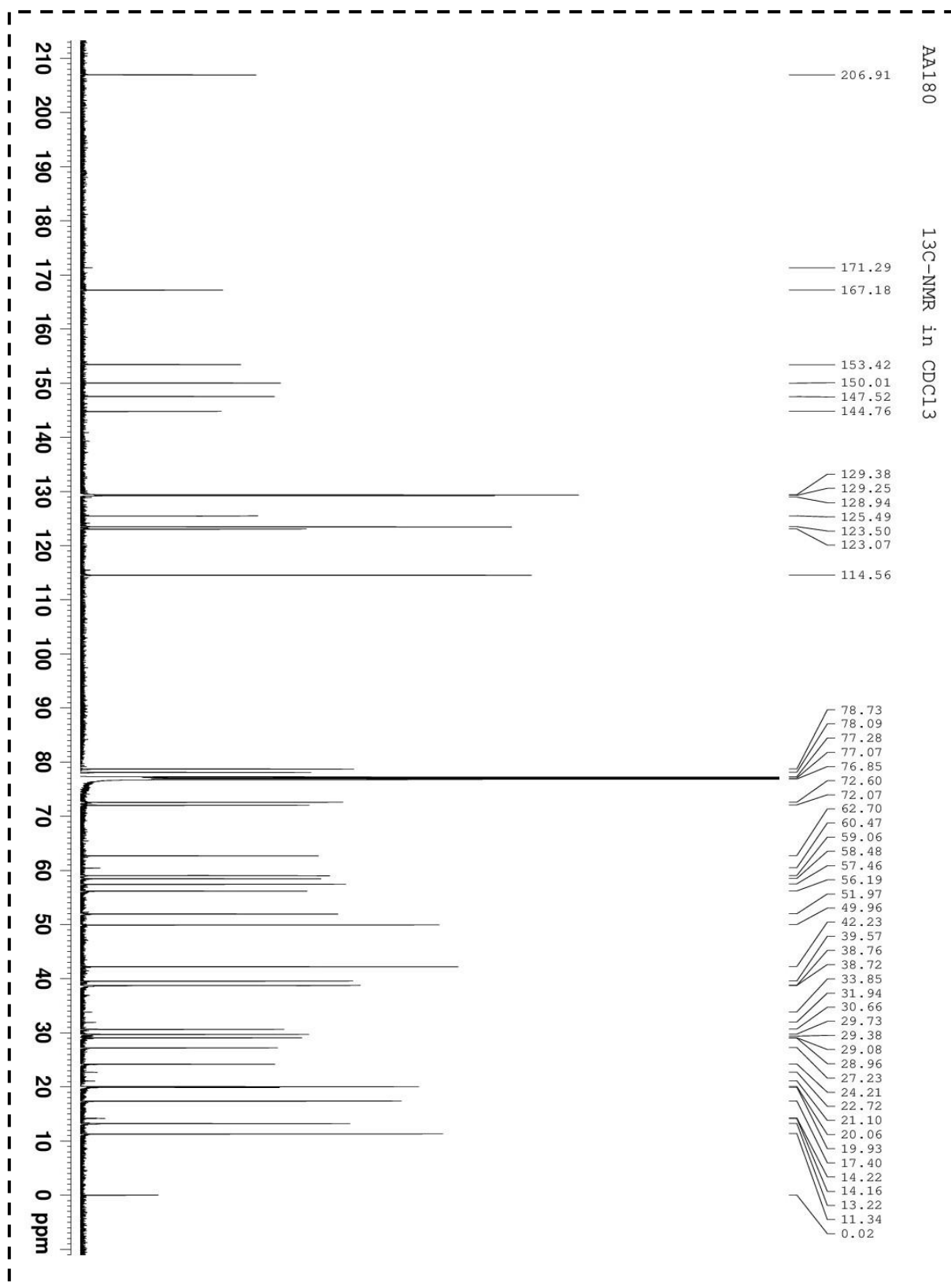


Figure S14: ^{13}C NMR of Compound 3A

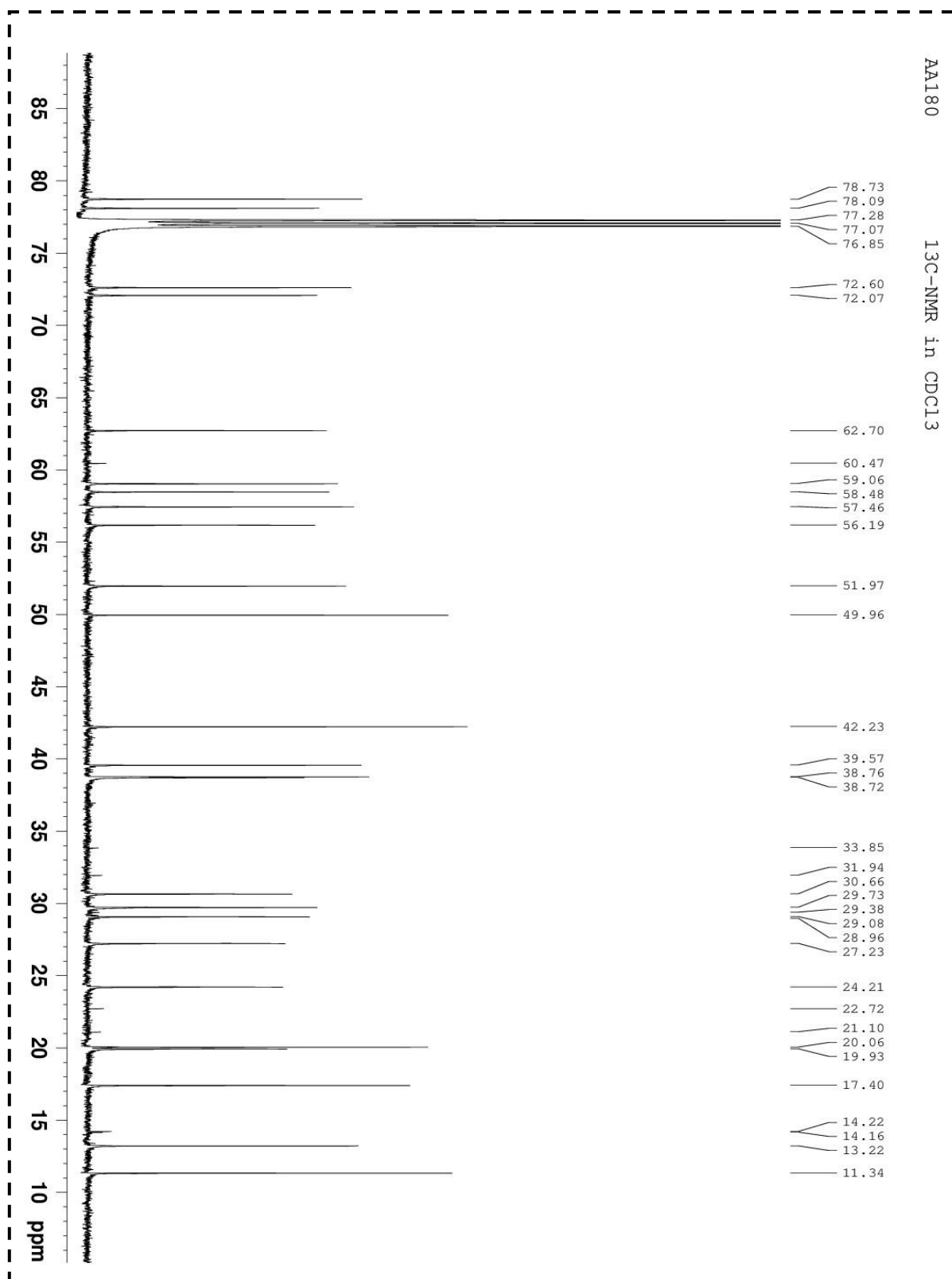


Figure S15: DEPT 135 of Compound 3A

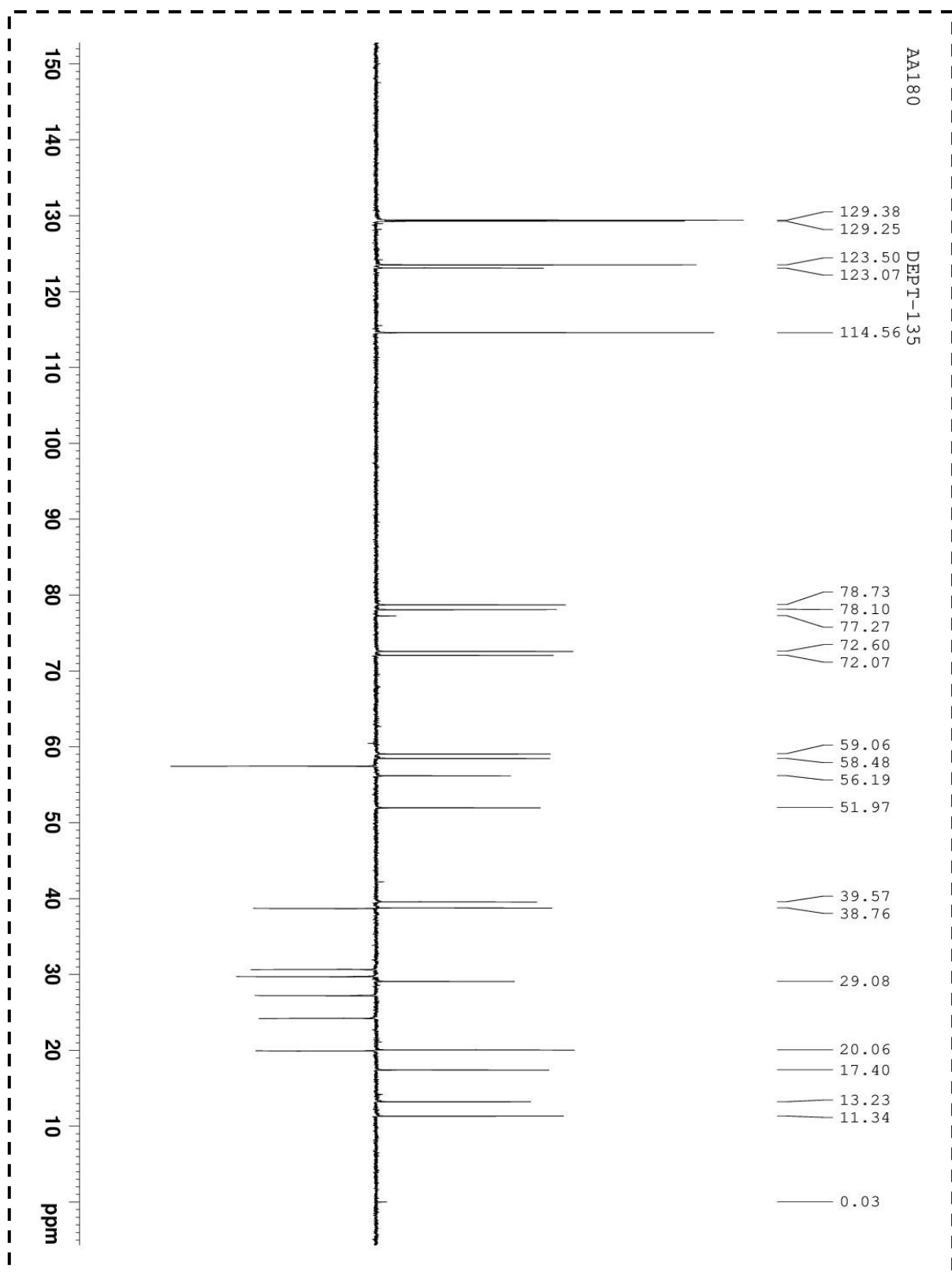


Figure S16: COSY of Compound 3A

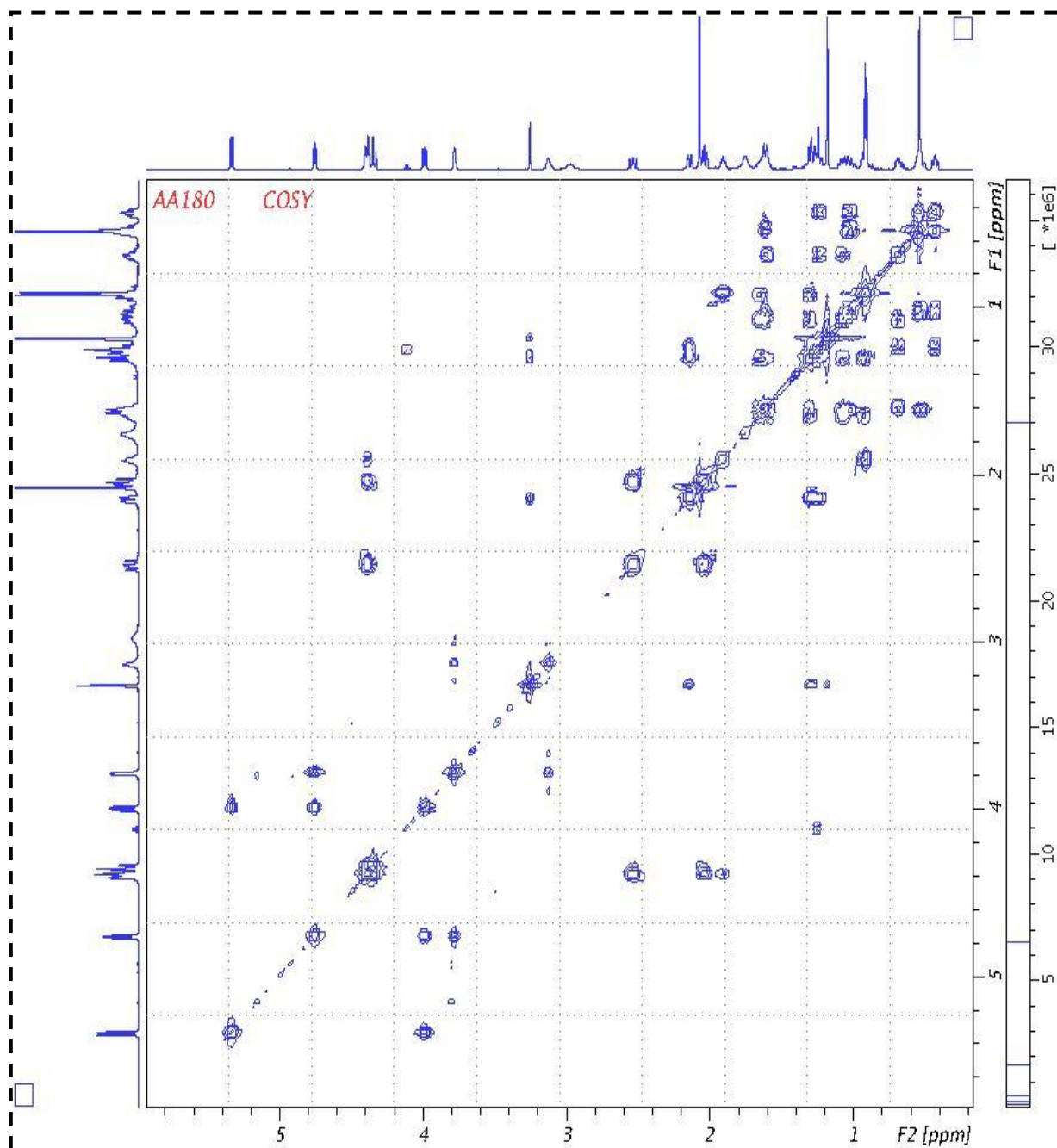


Figure S17: NOESY of Compound 3A

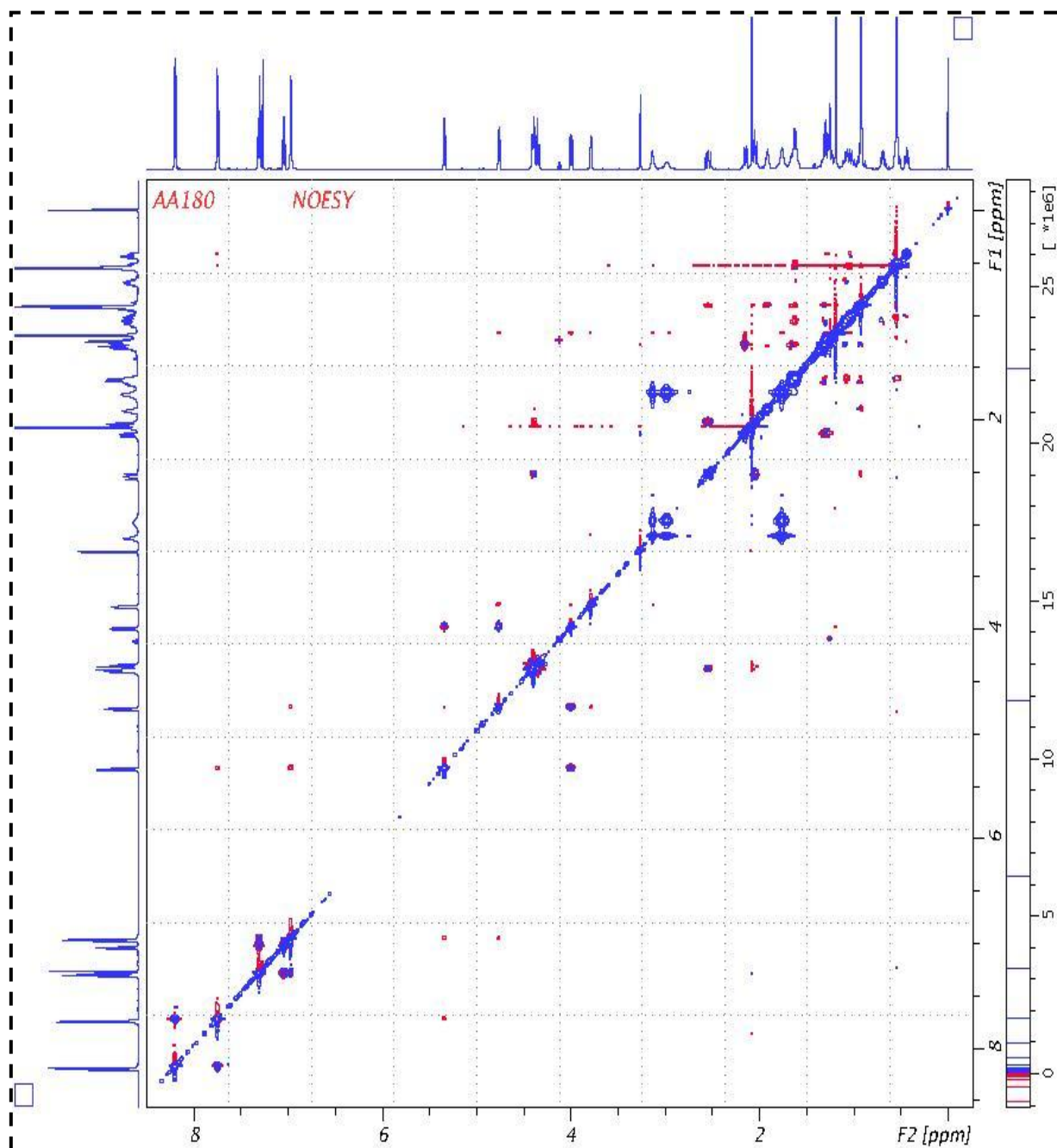


Figure S18: HMBC of Compound 3A

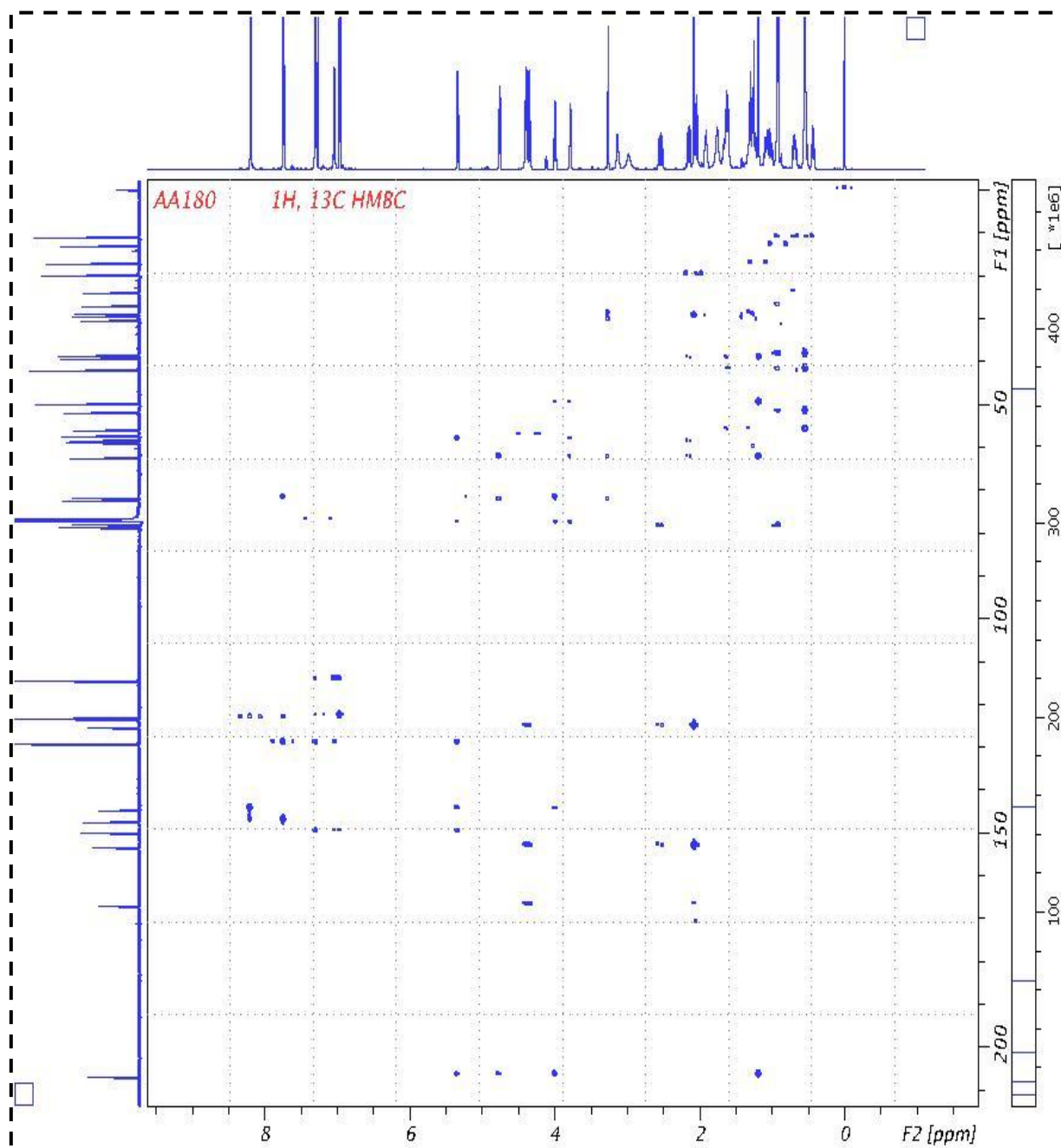


Figure S19: HMBC of Compound 3A

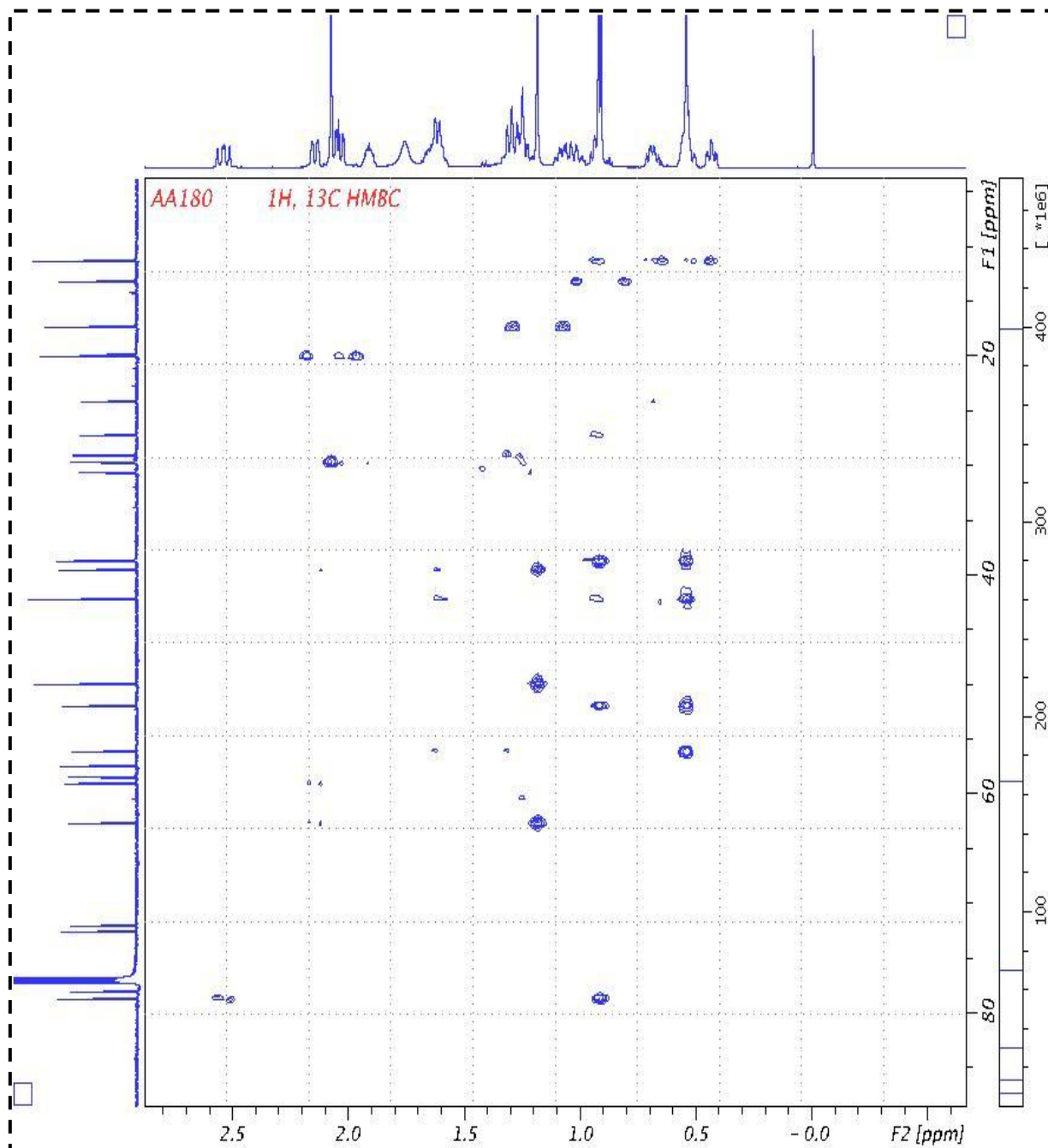


Figure S20: HSQC of Compound 3A

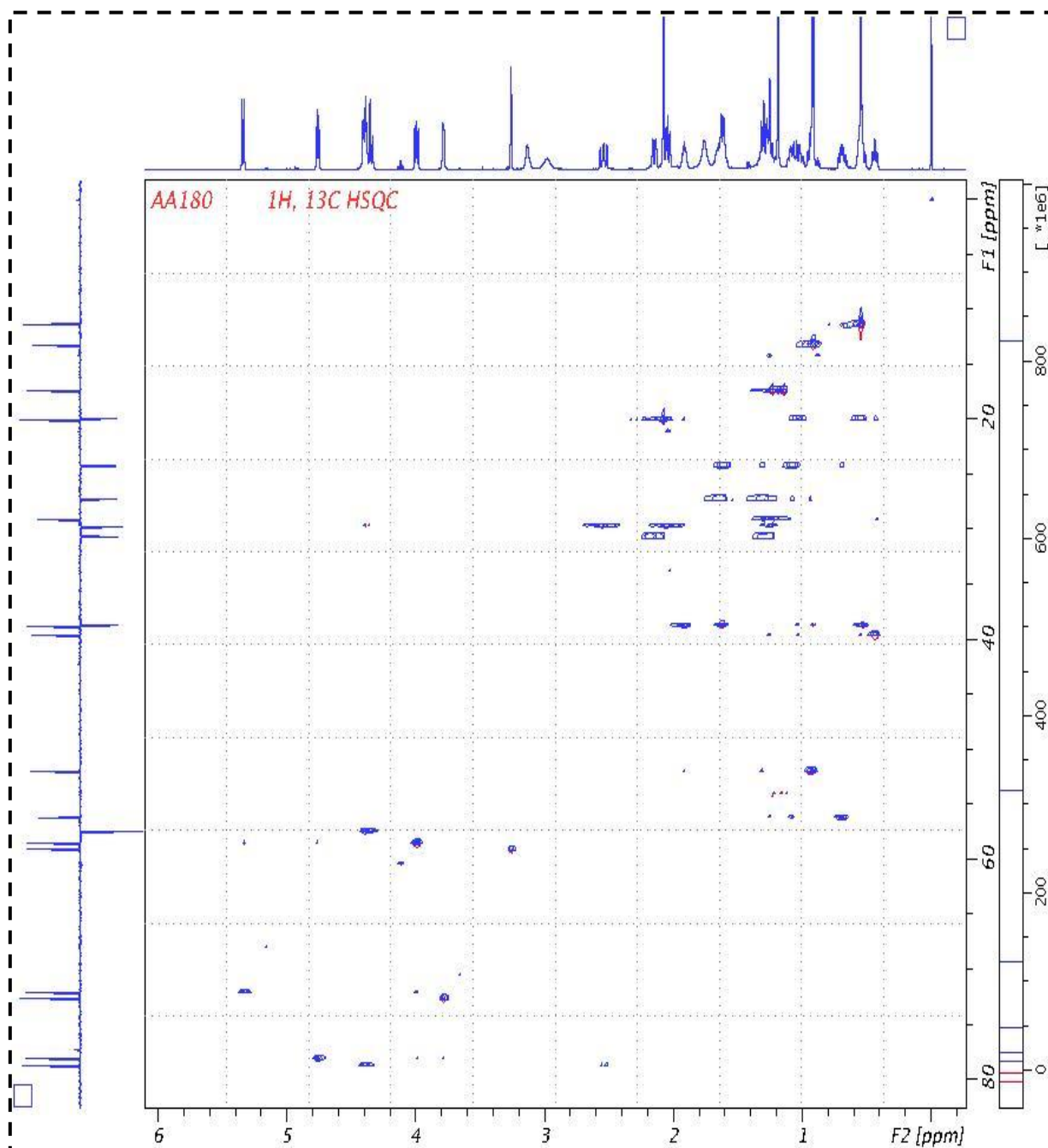


Figure S21: HPLC Profile of Compound 3B



Analysis Report

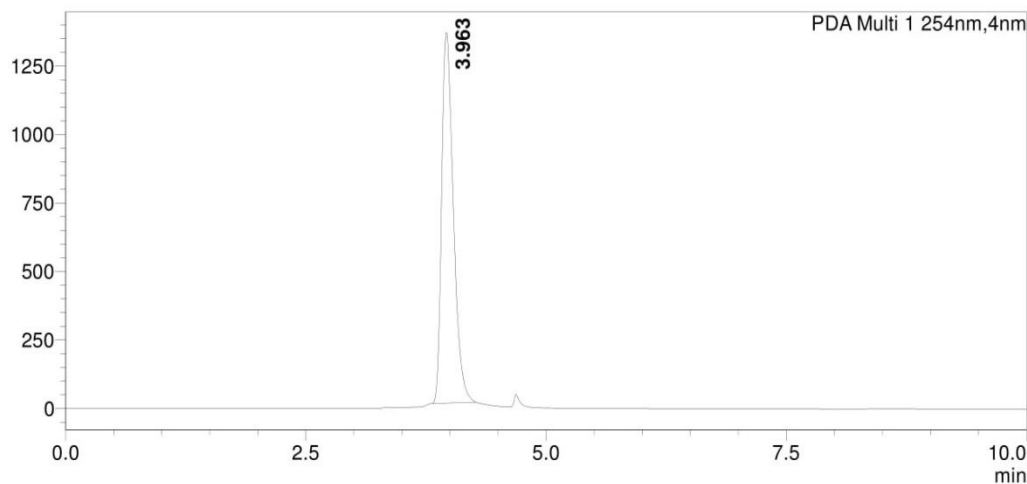
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 Method Filename : BASELINE.lcm
 Batch Filename :
 Vial # : 1-2
 Injection Volume : 10 µL
 Date Acquired : 2/6/2018 3:33:06 PM
 Date Processed : 2/6/2018 3:53:09 PM

Sample Type : Unknown
 Acquired by : user
 Processed by : user

<Chromatogram>

mAU



<Peak Table>

PDA Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
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Total		11436622	1351555	100.000	100.000

Figure S22: Mass Spectra of Compound 3B

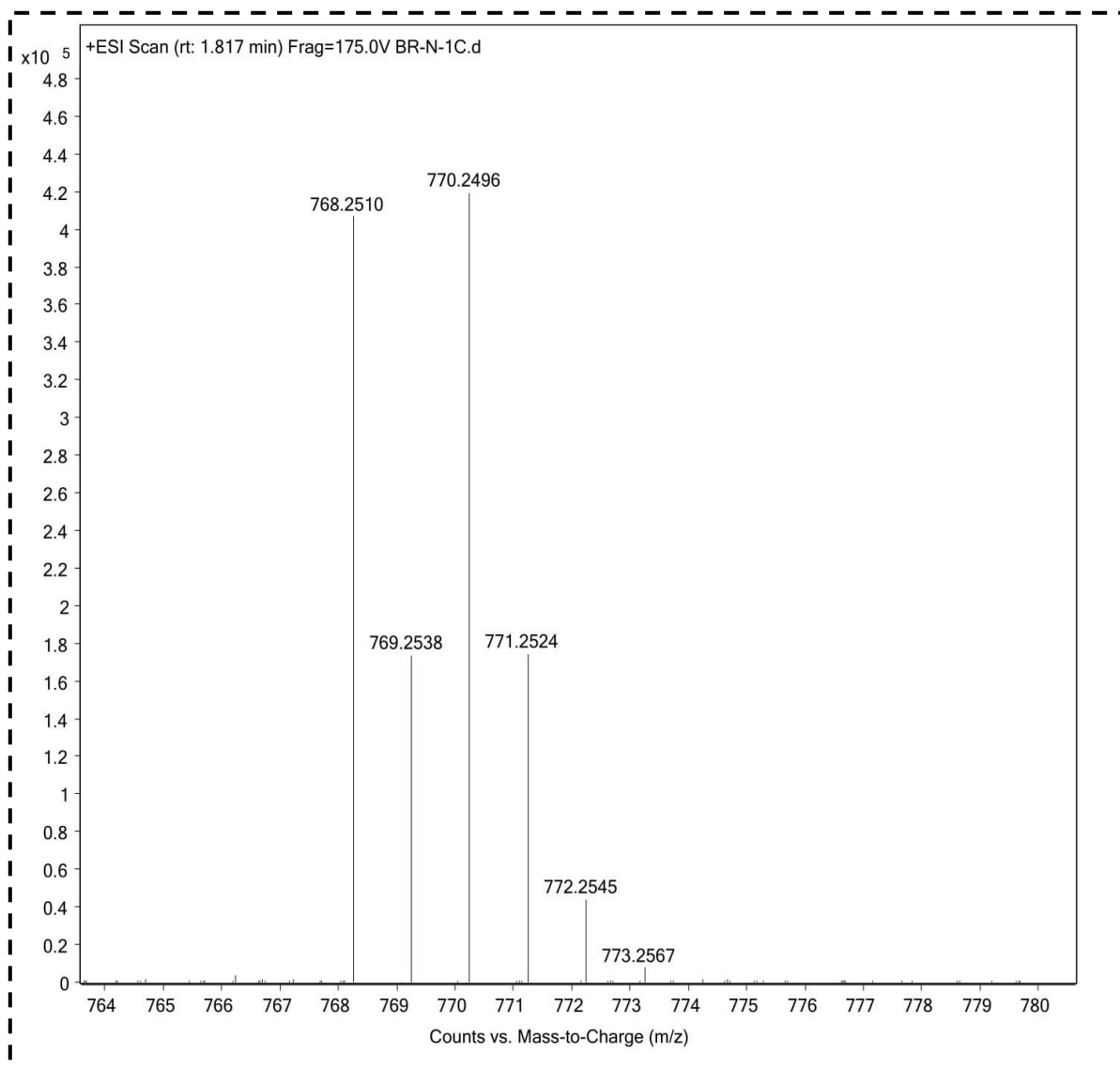


Figure S23: ^1H NMR of Compound 3B

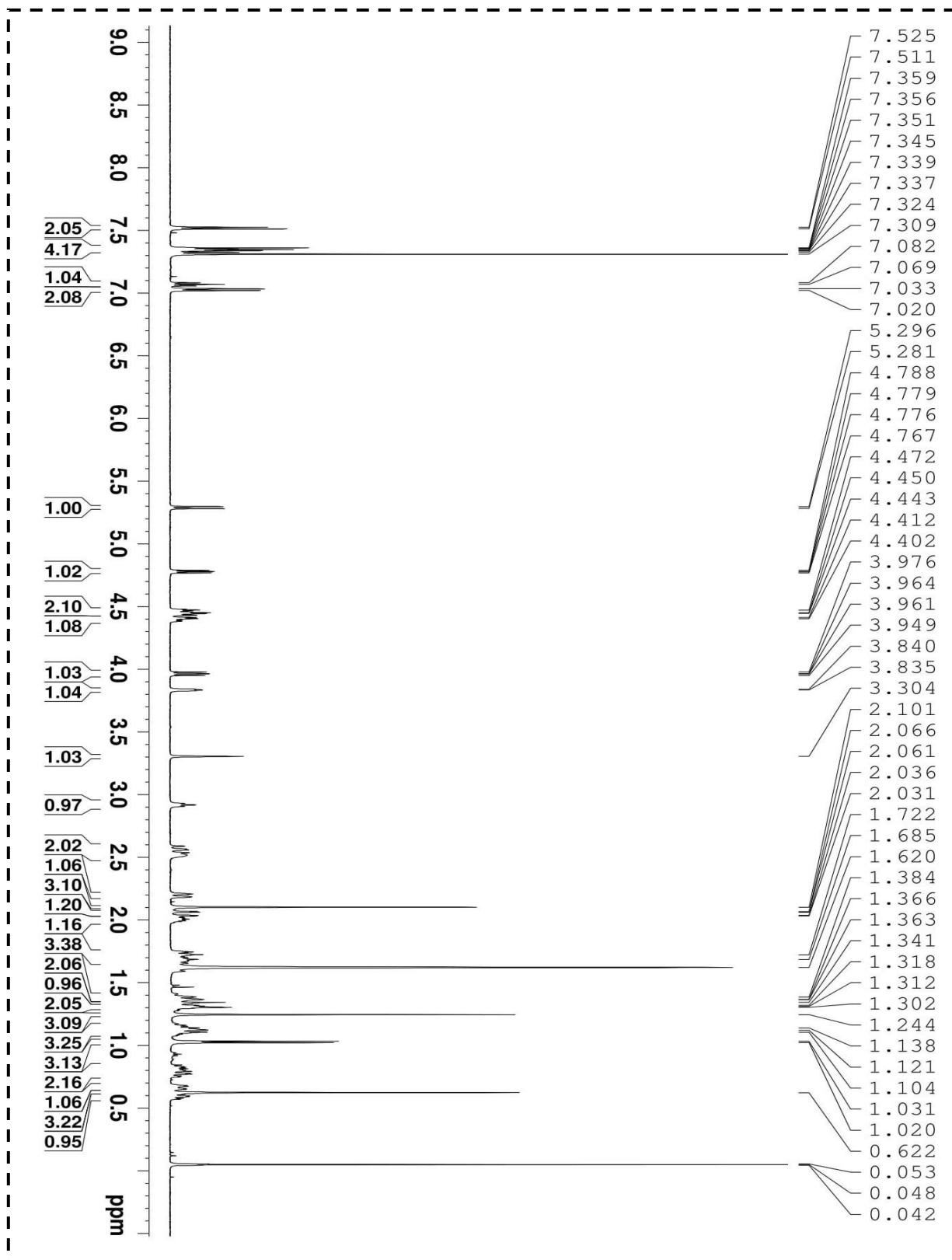


Figure S24: ^1H NMR of Compound 3B

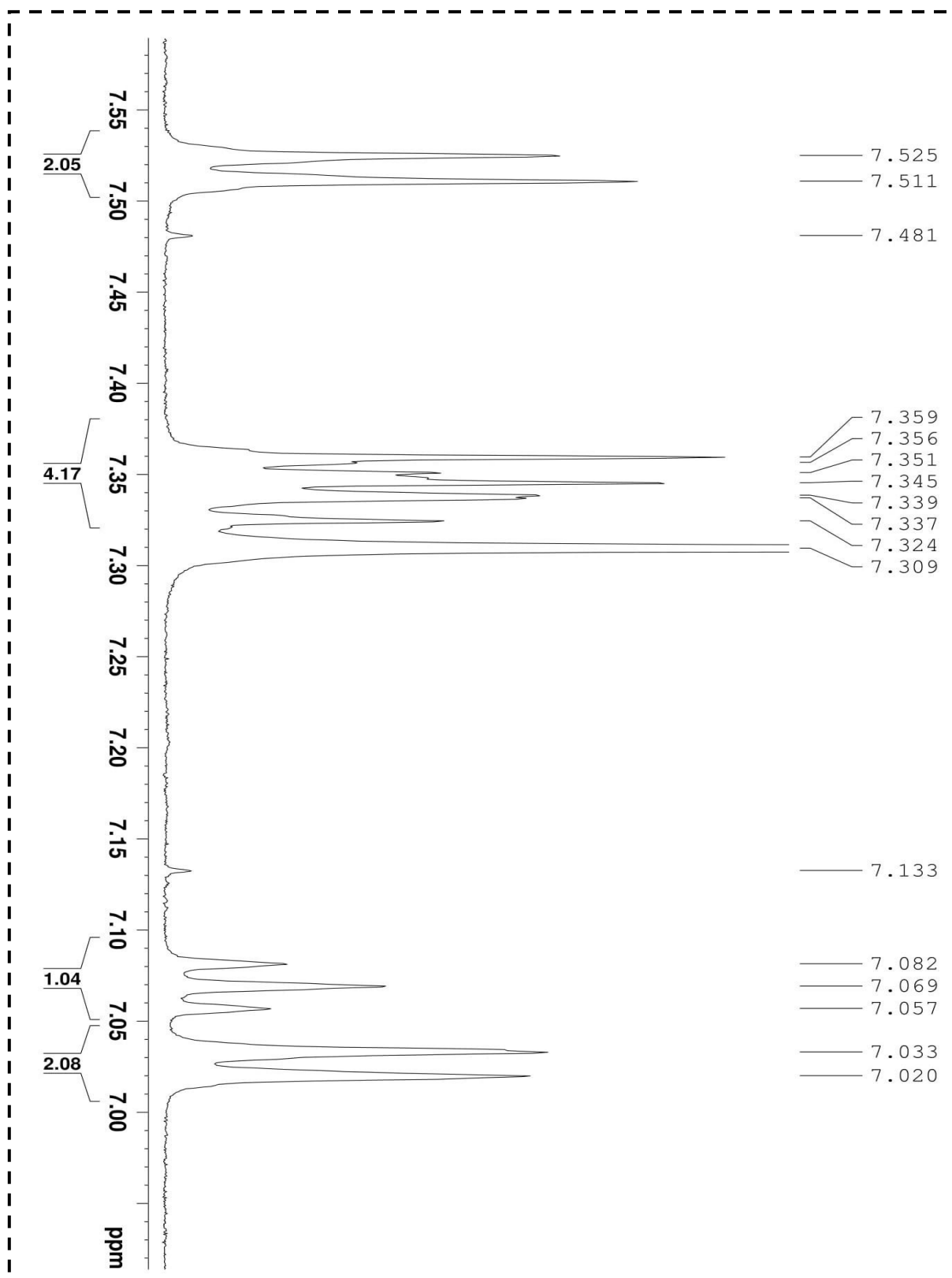


Figure S25: ^1H NMR of Compound 3B

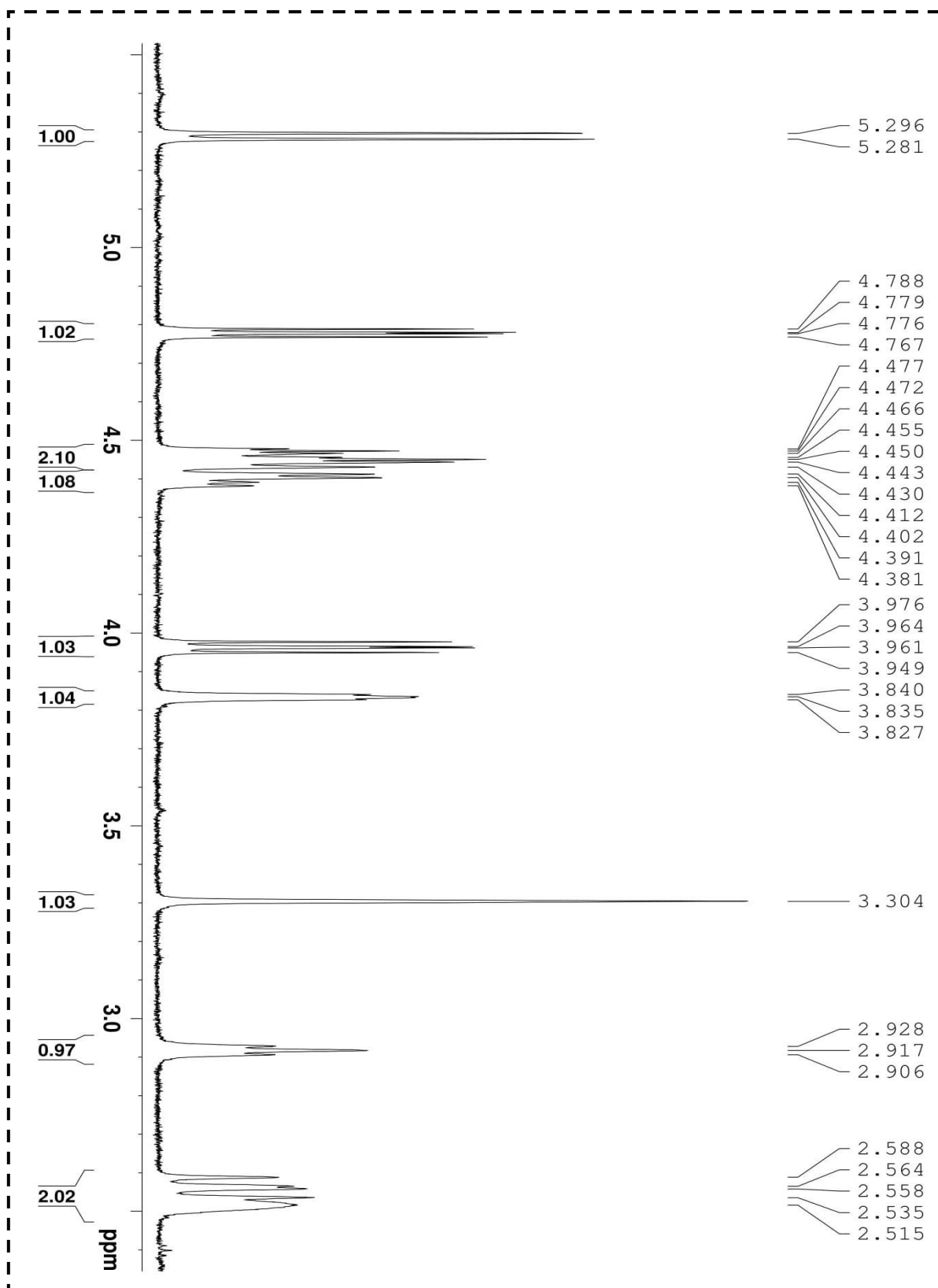


Figure S26: ^1H NMR of Compound 3B

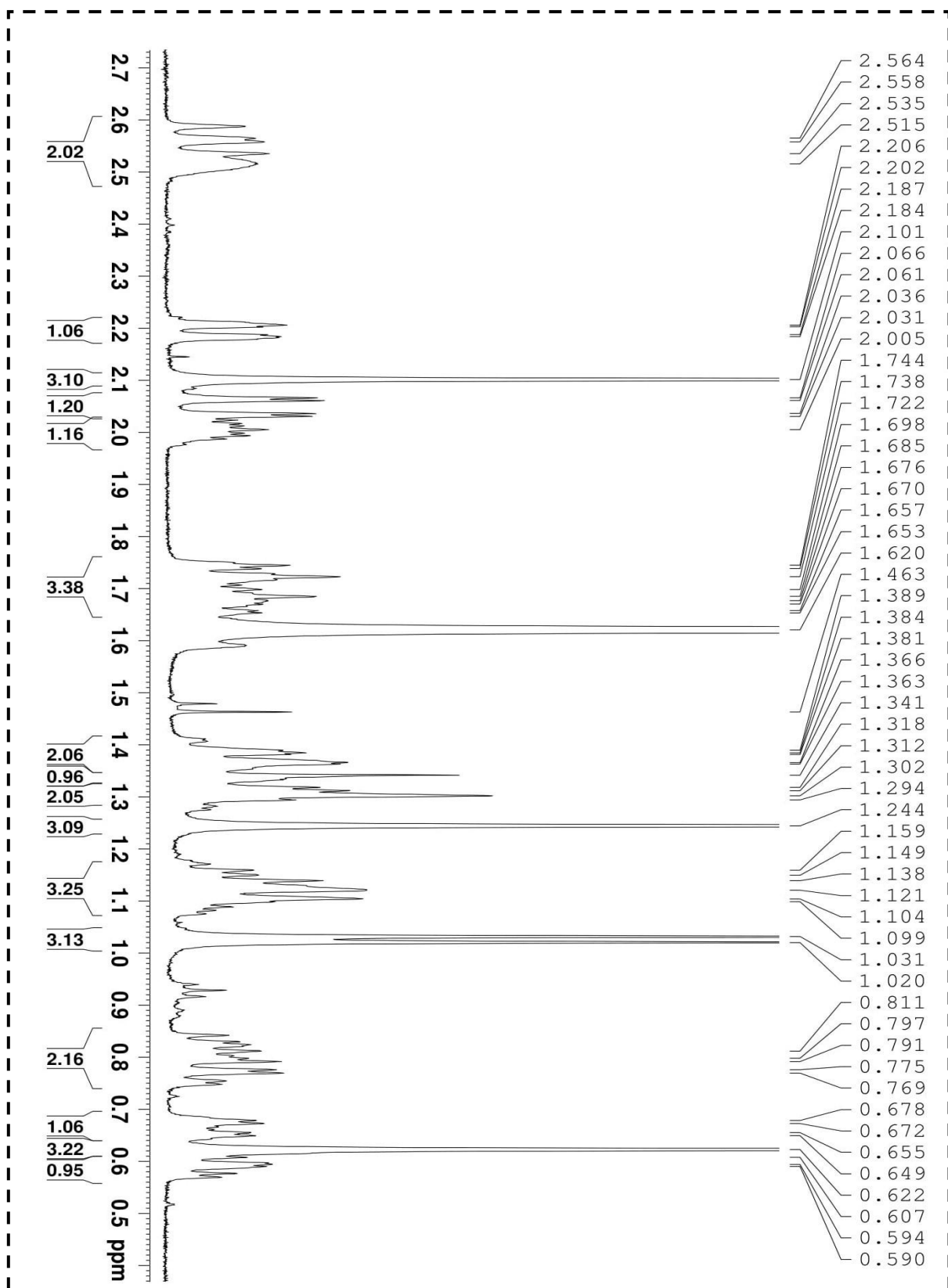


Figure S27: ^{13}C NMR of Compound 3B

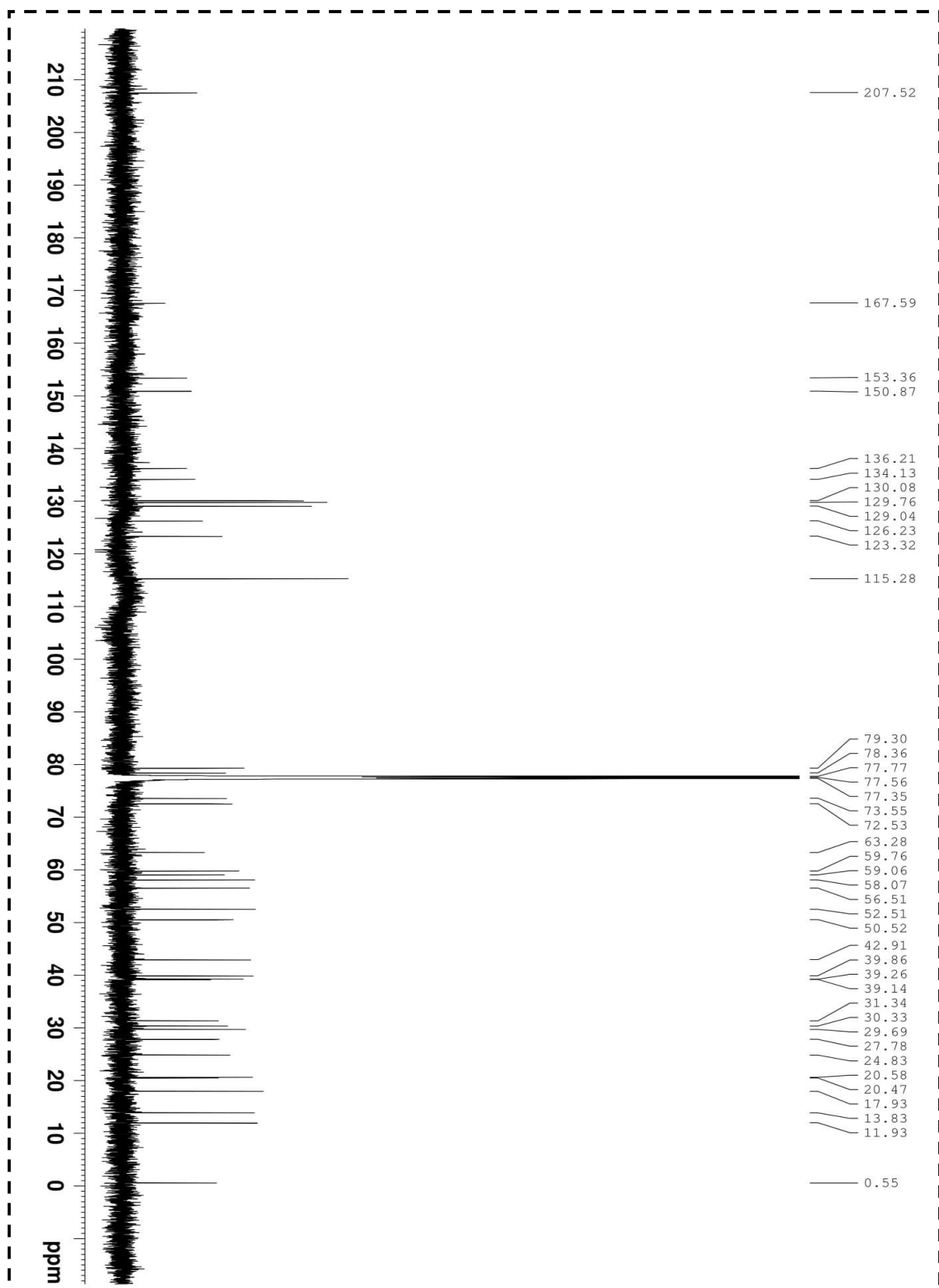


Figure S28: DEPT 90 of Compound 3B

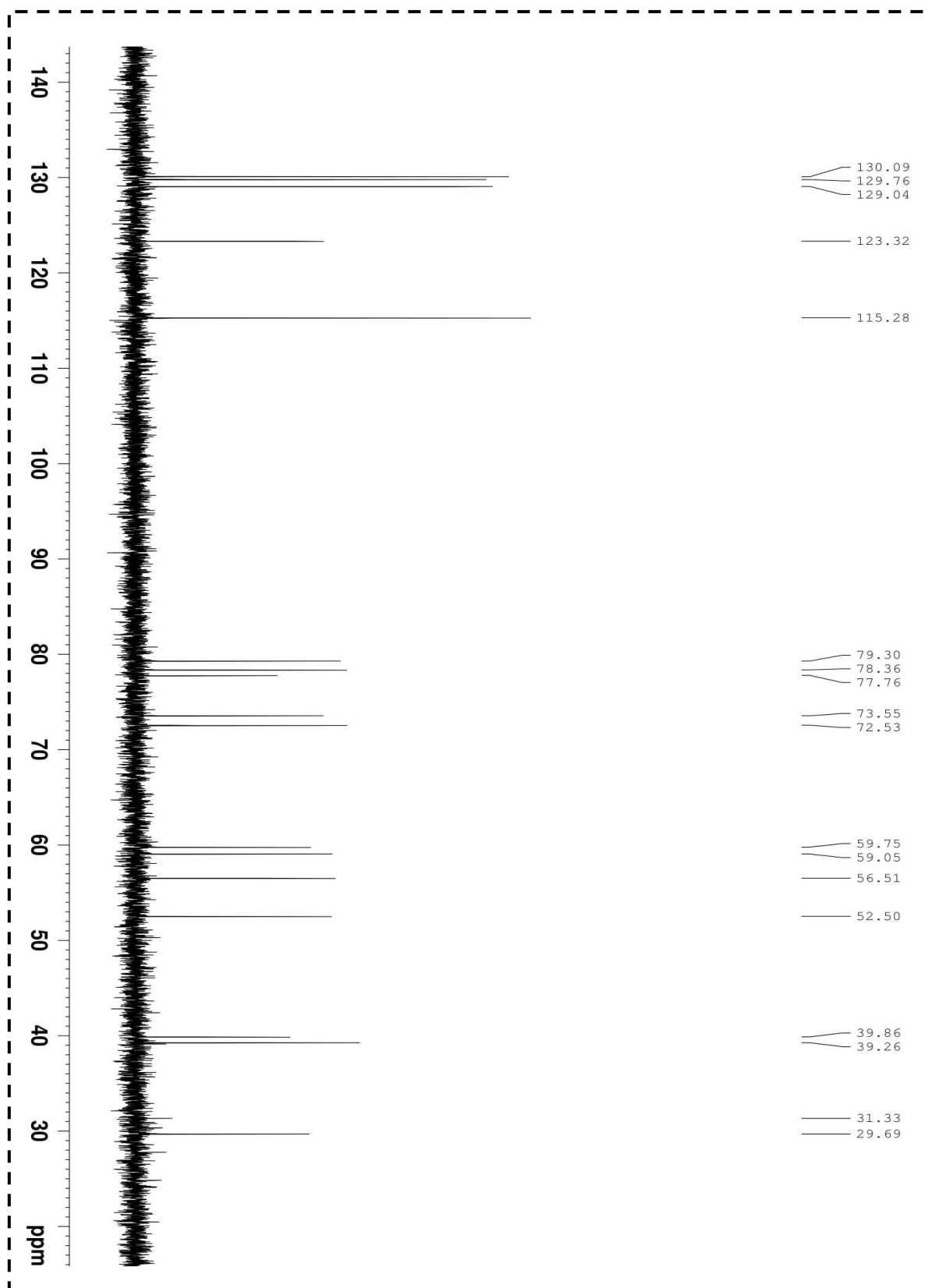


Figure S29: DEPT 135 of Compound 3B

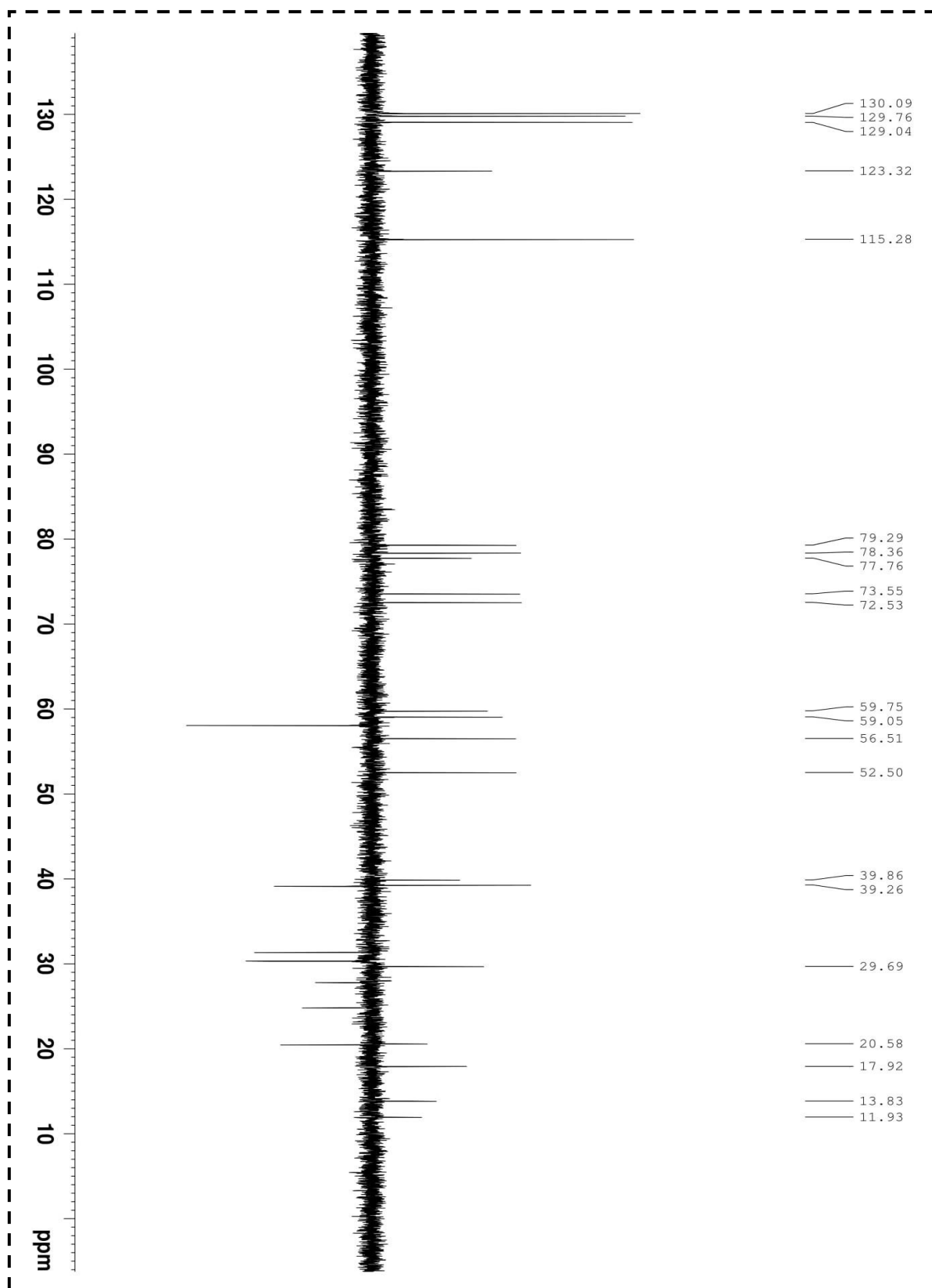


Figure S30: HPLC Profile of Compound 3C

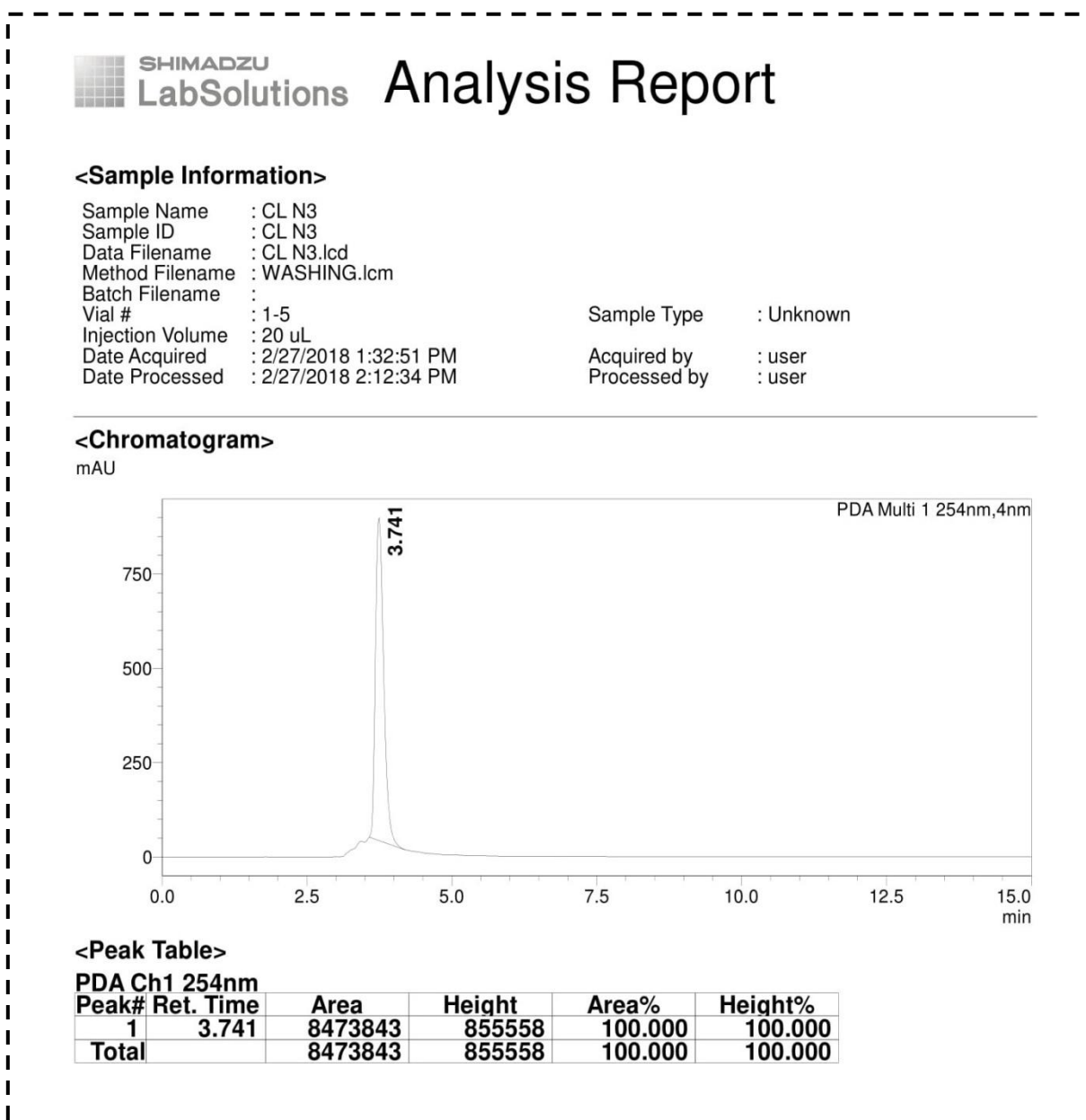


Figure S31: Mass Spectra of Compound 3C

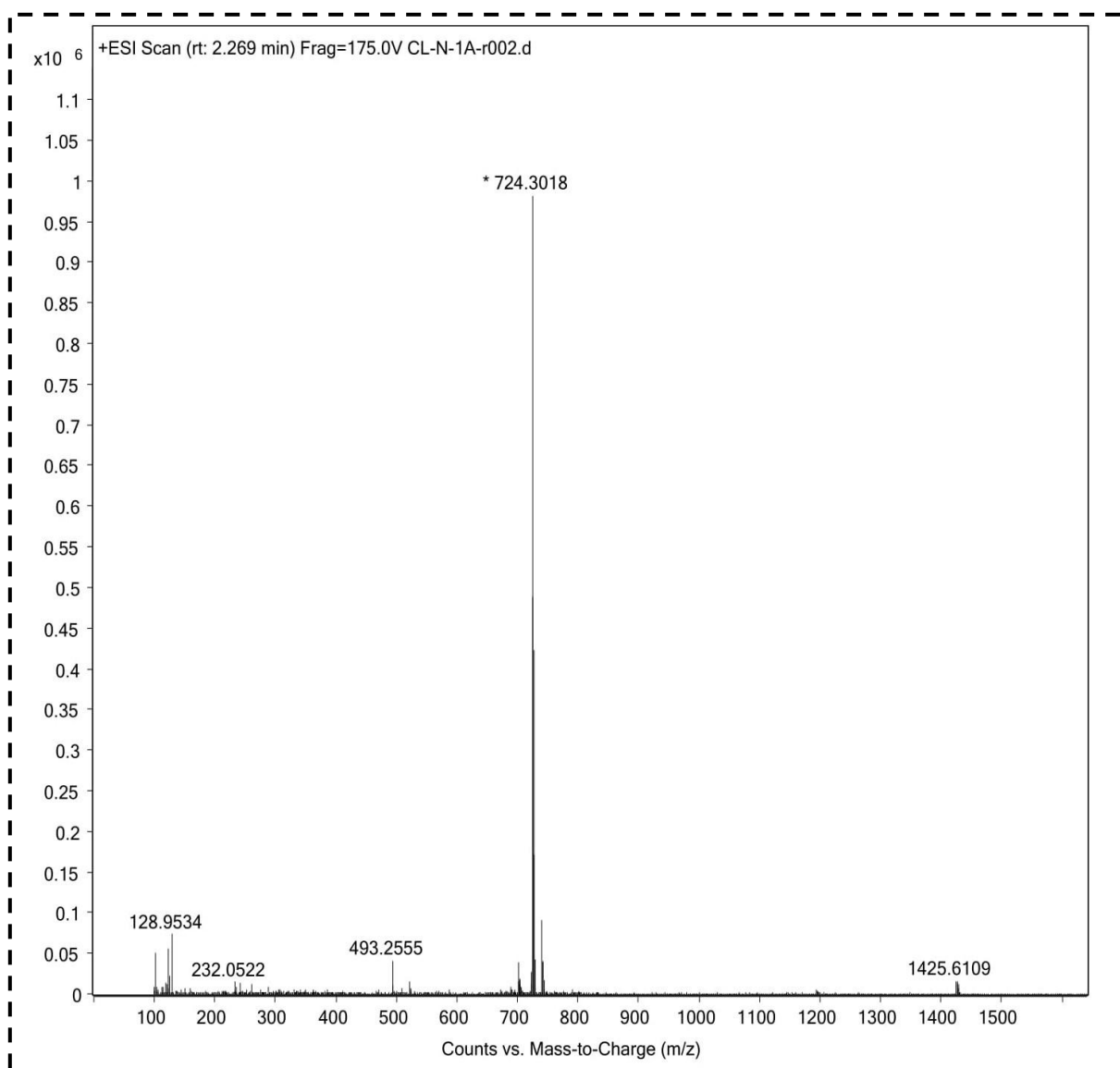


Figure S32: ^1H NMR of Compound 3C

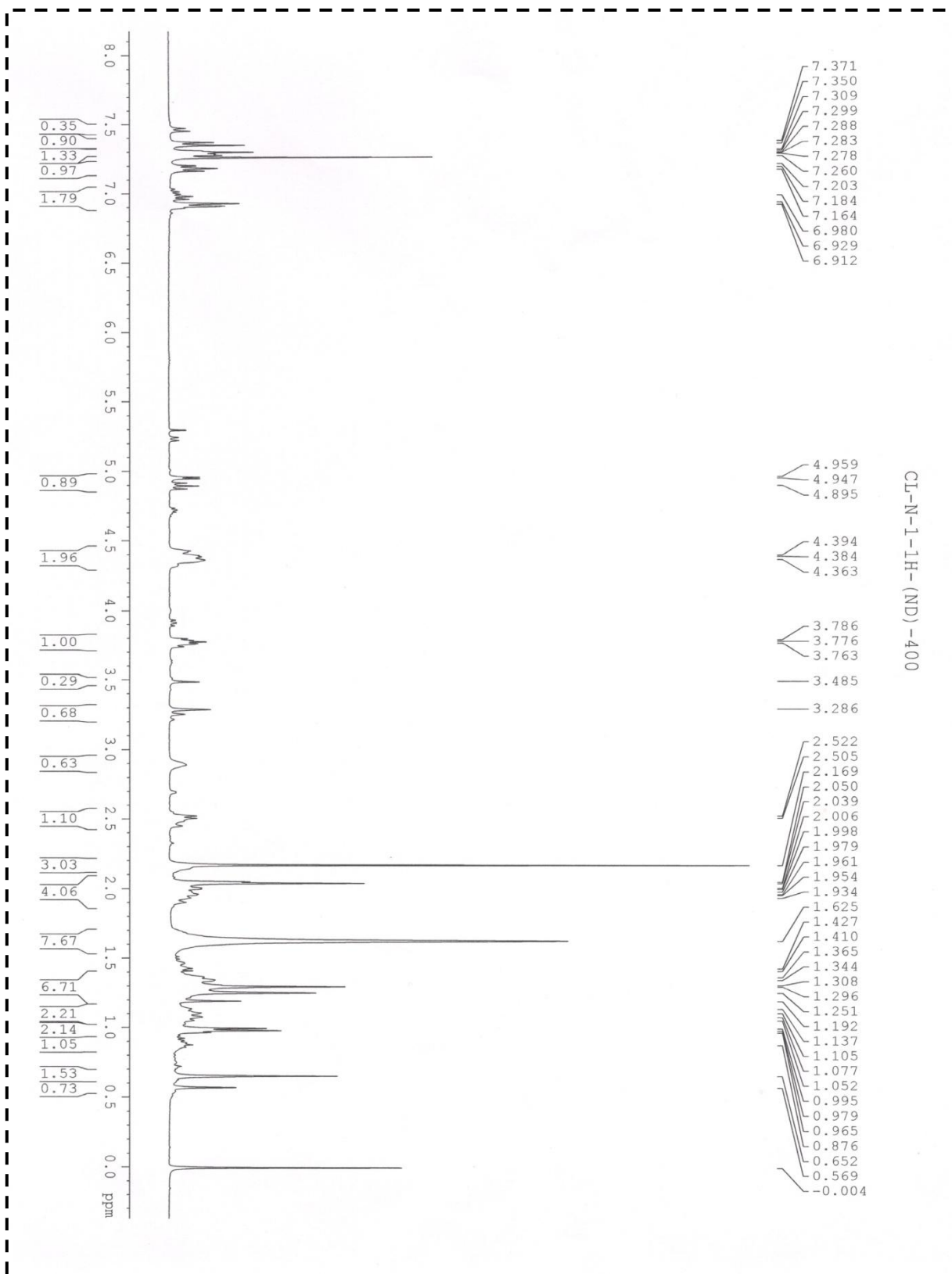


Figure S33: ^{13}C NMR of Compound 3C

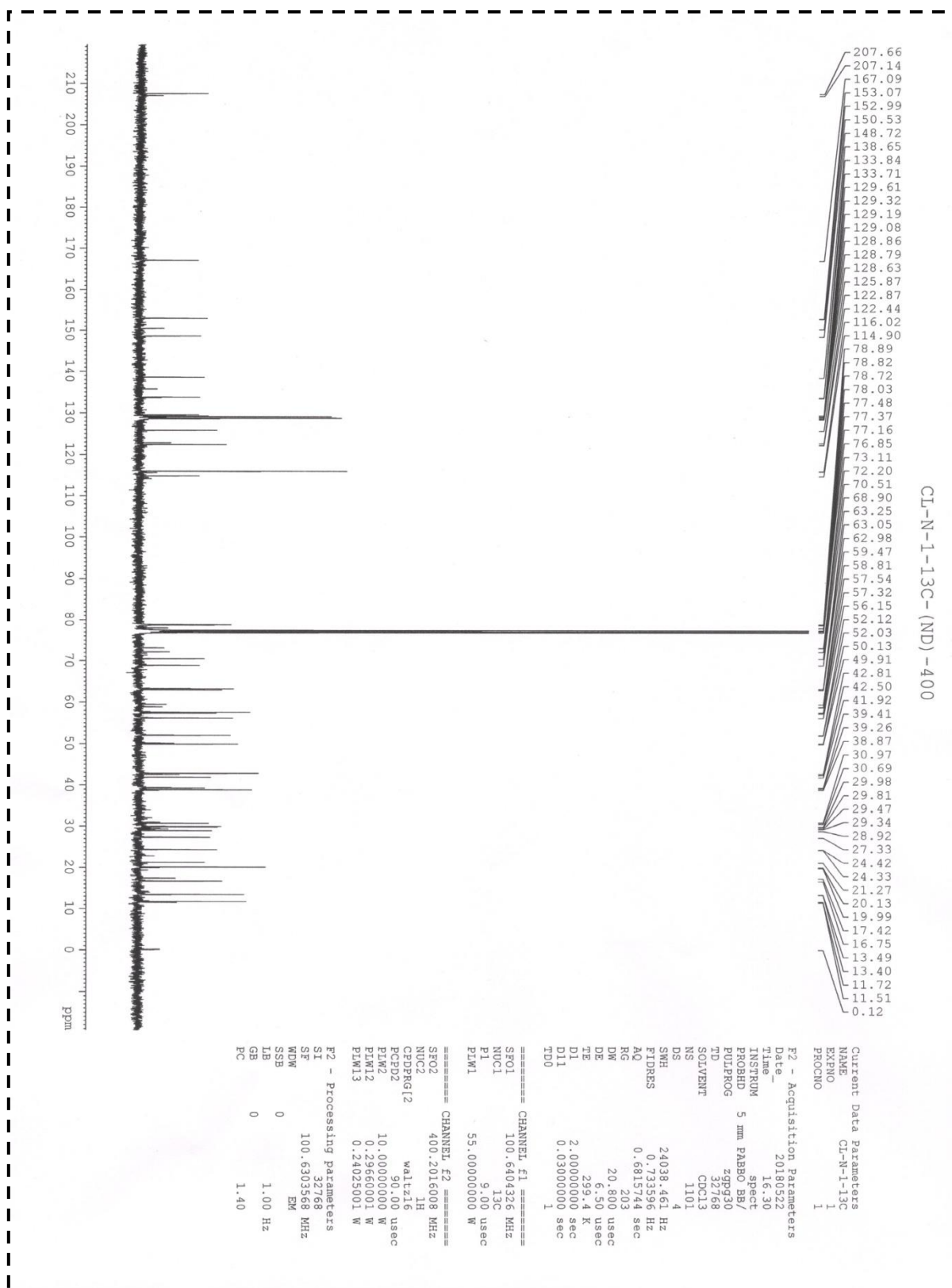


Figure S34: DEPT 90 of Compound 3C

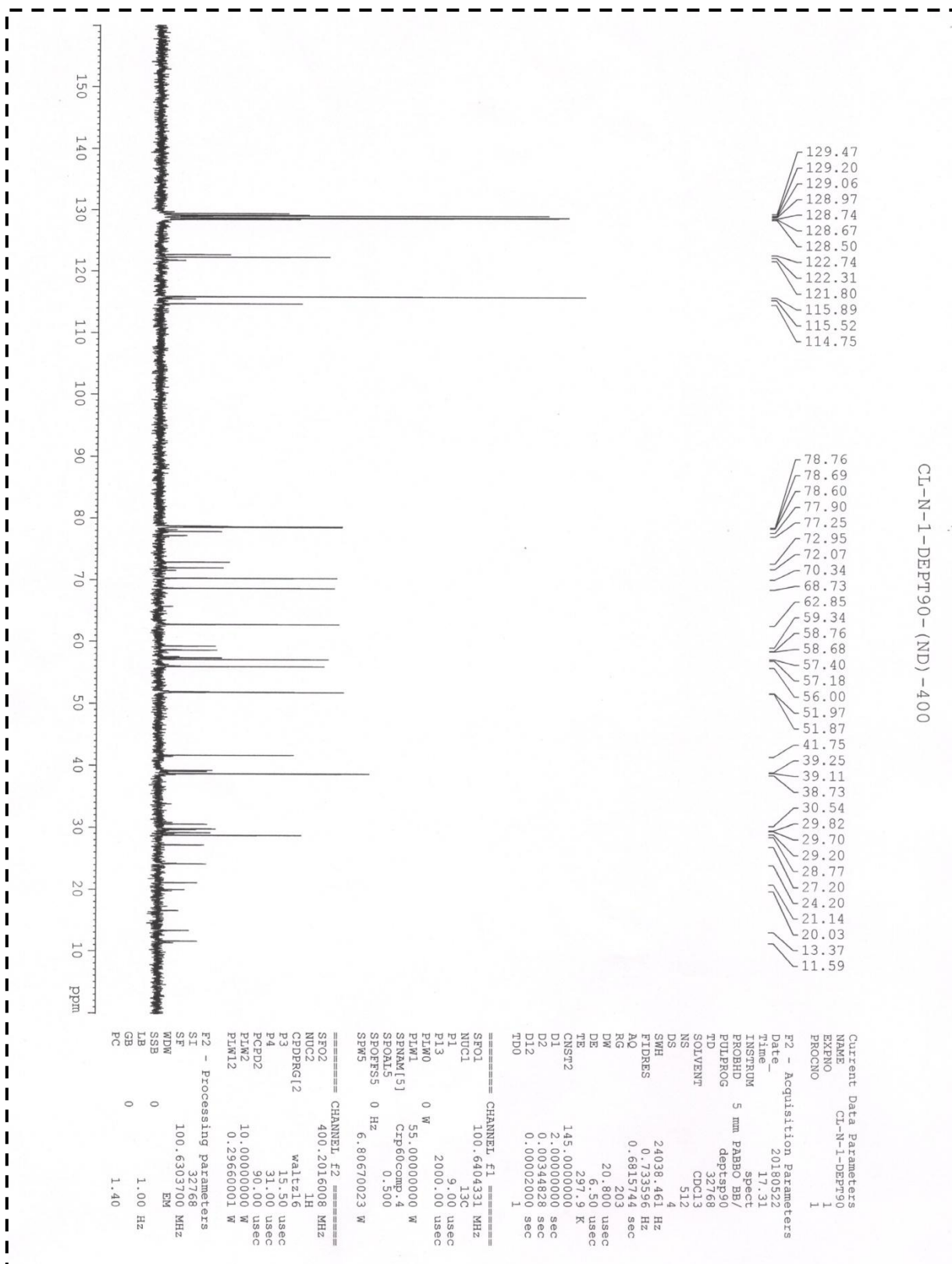


Figure S35: DEPT 135 of Compound 3C

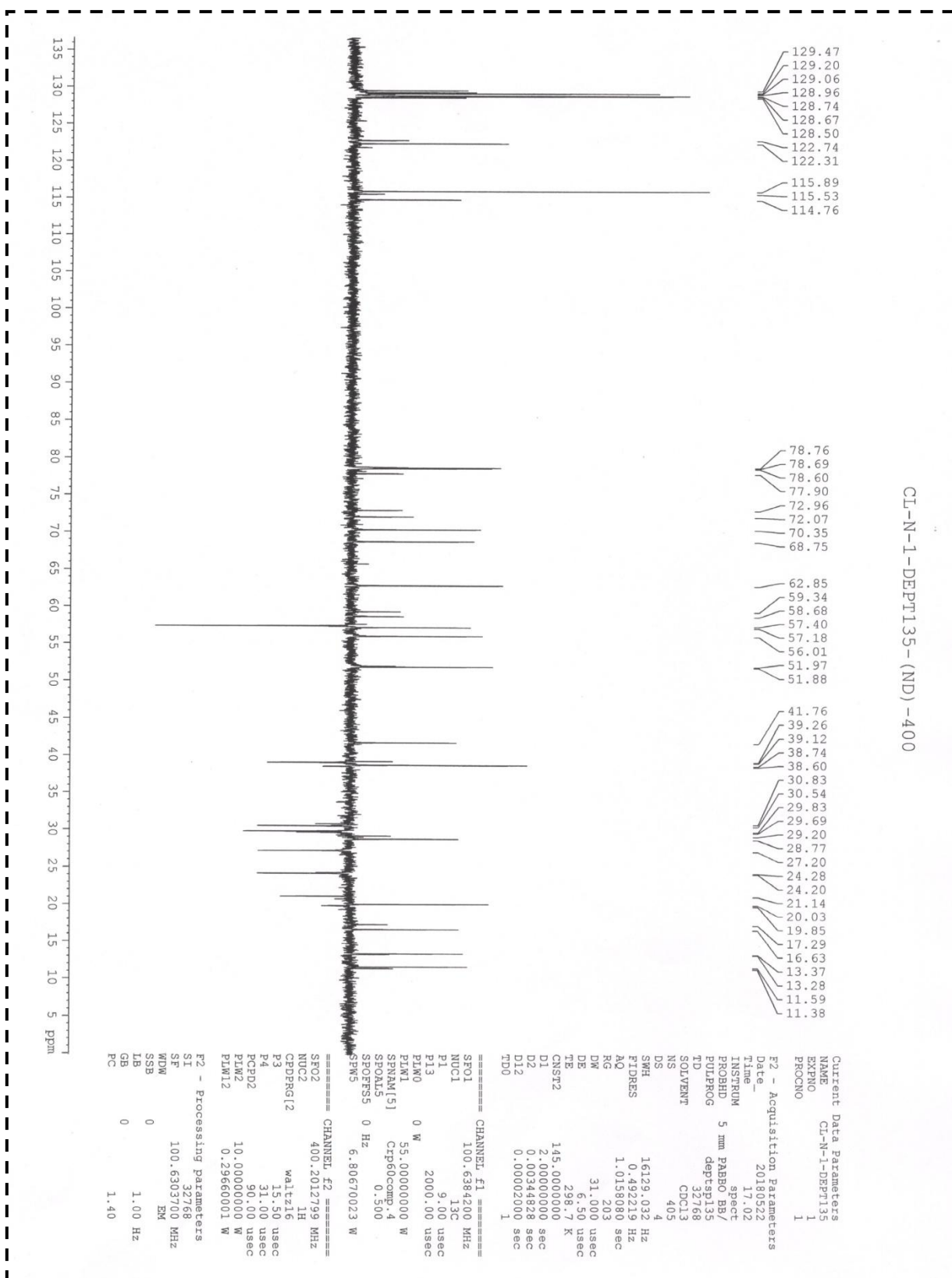


Figure S36: Mass Spectra of Withaferin-Dinitrone Adduct 5

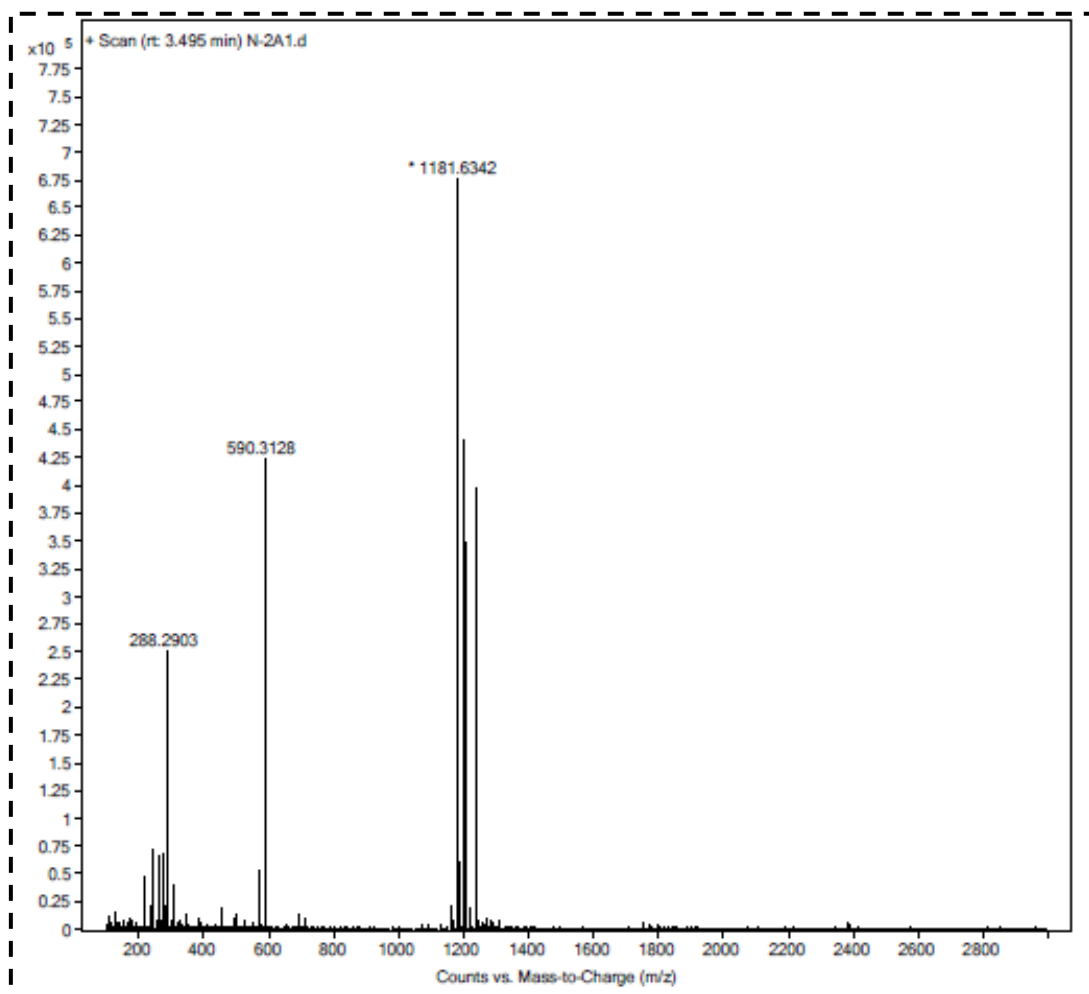


Figure S37: ^1H NMR Spectra of Withaferin-Dinitrone Adduct 5

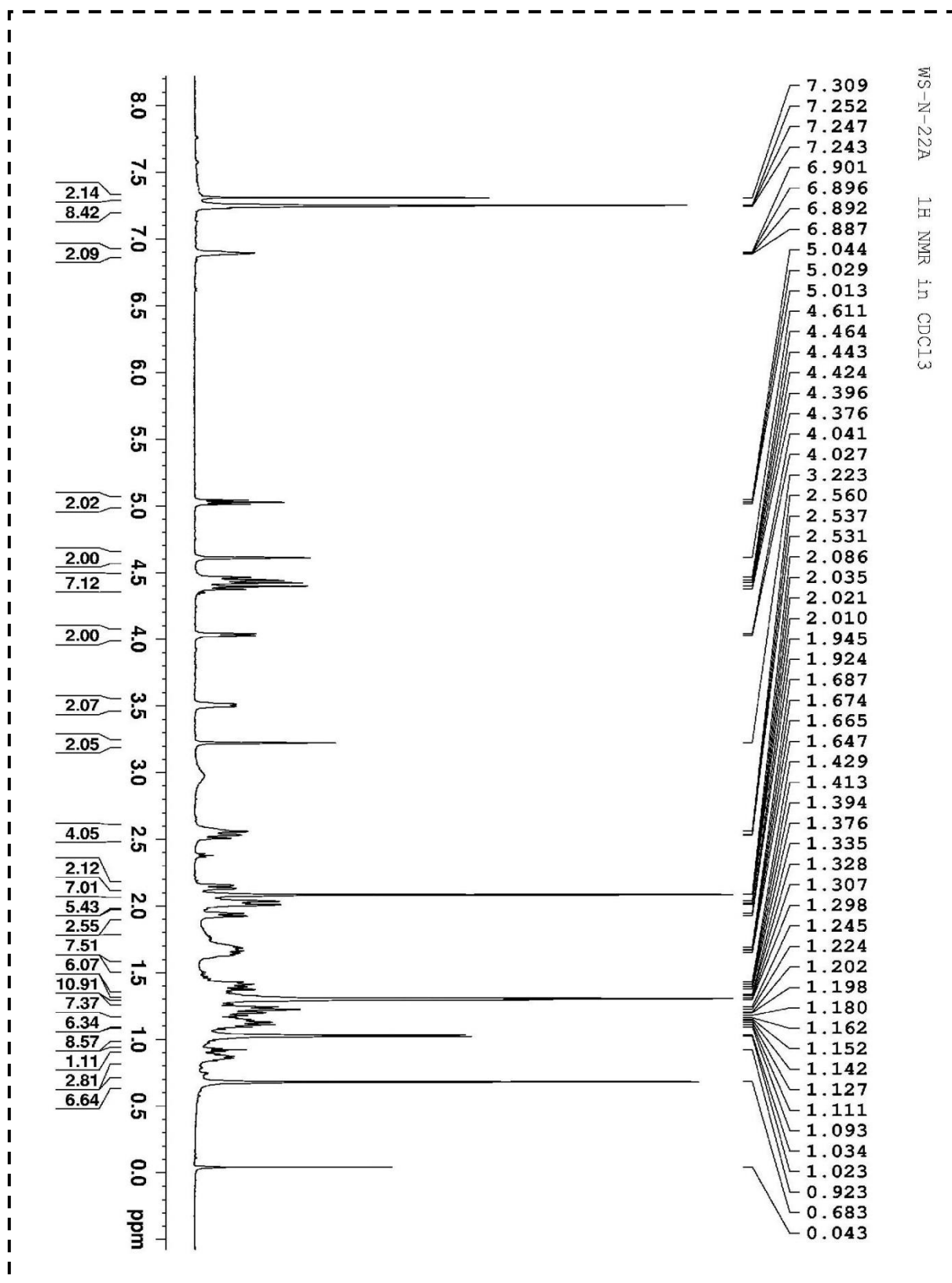


Figure S38: ^1H NMR Spectra of Withaferin-Dinitrone Adduct 5

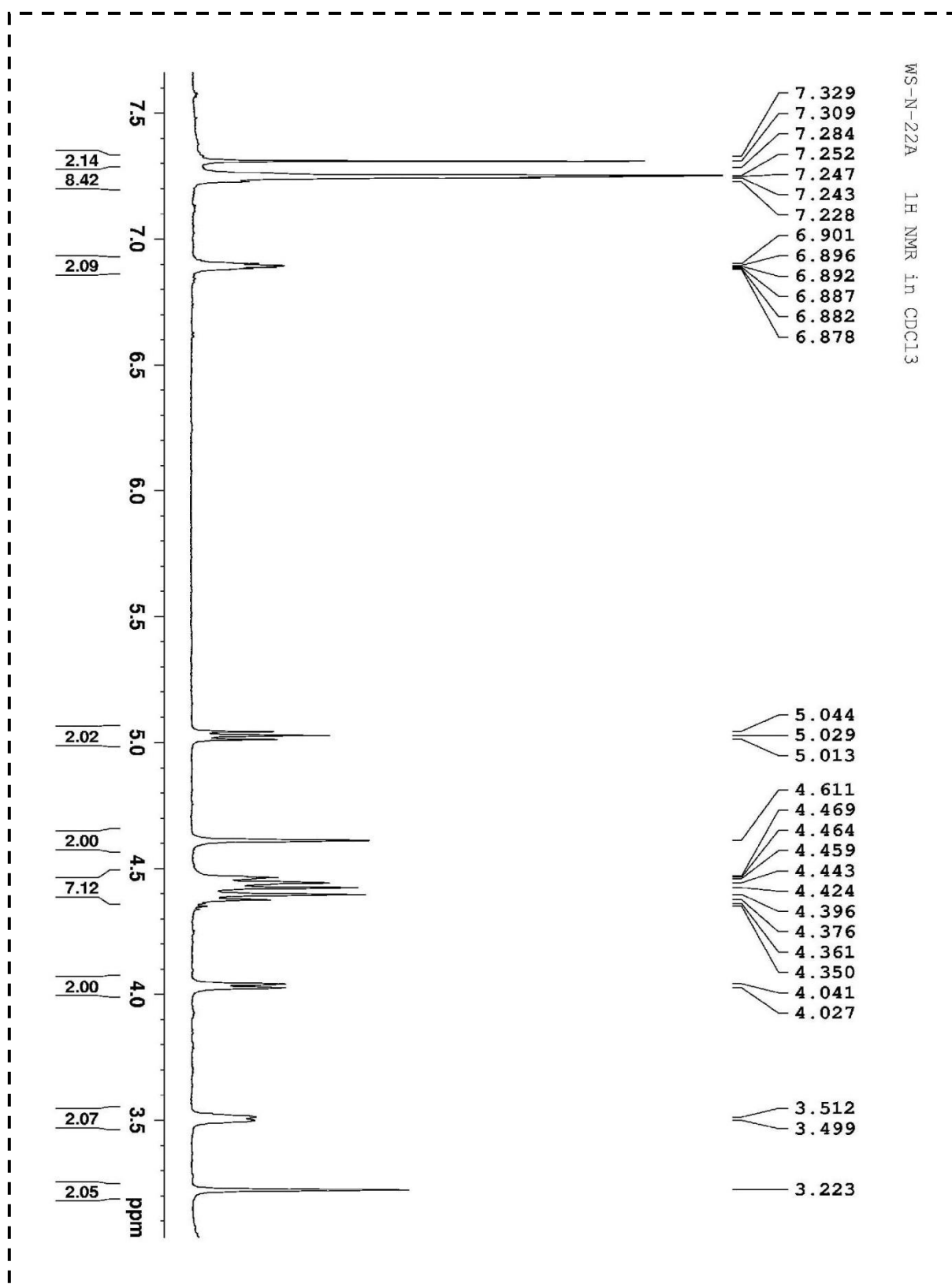


Figure S39: ^1H NMR Spectra of Withaferin-Dinitrone Adduct 5

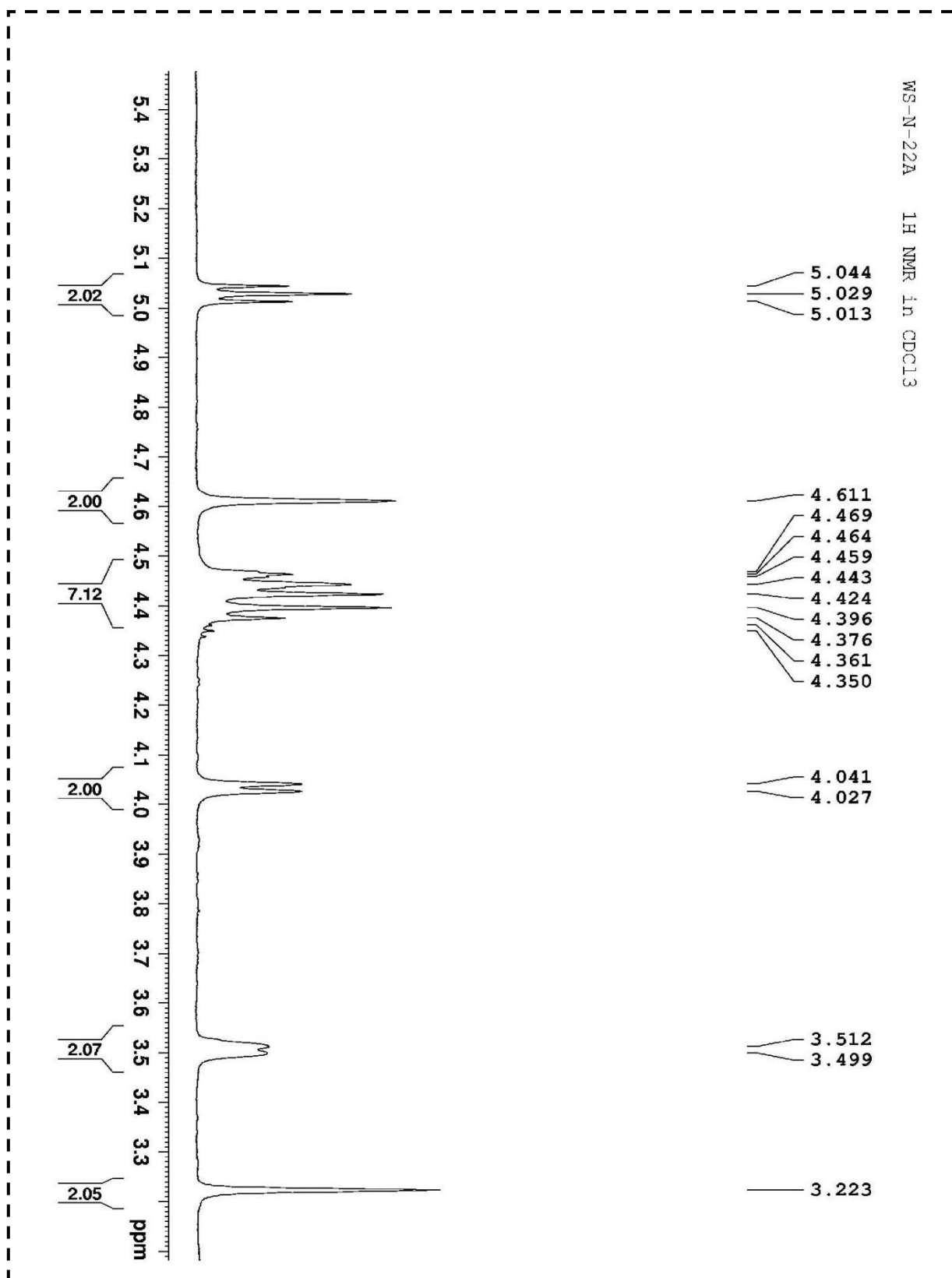


Figure S40: ^1H NMR Spectra of Withaferin-Dinitrone Adduct 5

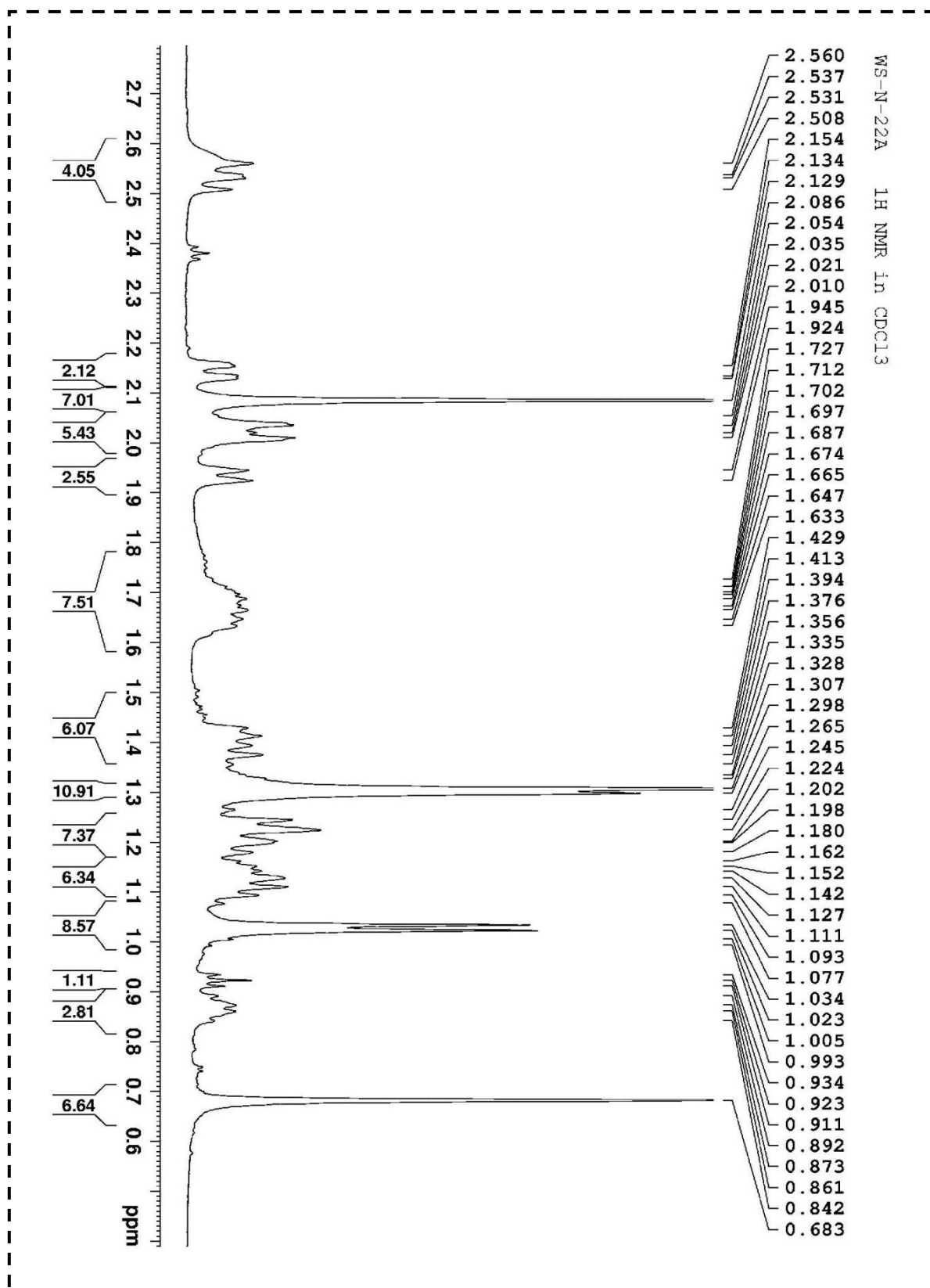


Figure S41: ^{13}C NMR Spectra of Withaferin-Dinitrone Adduct 5

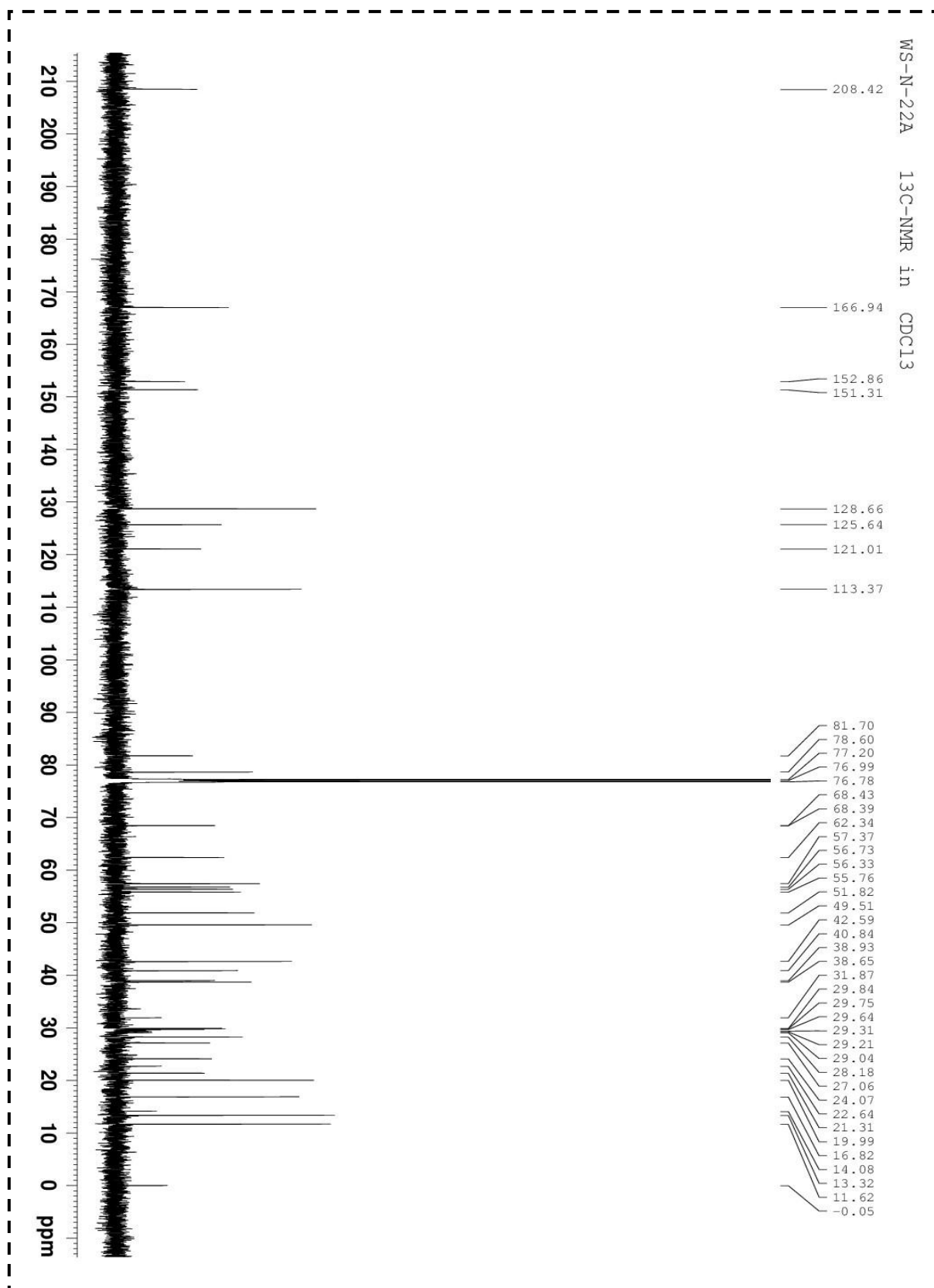


Figure S42: DEPT 90 of Withaferin-Dinitrone Adduct 5

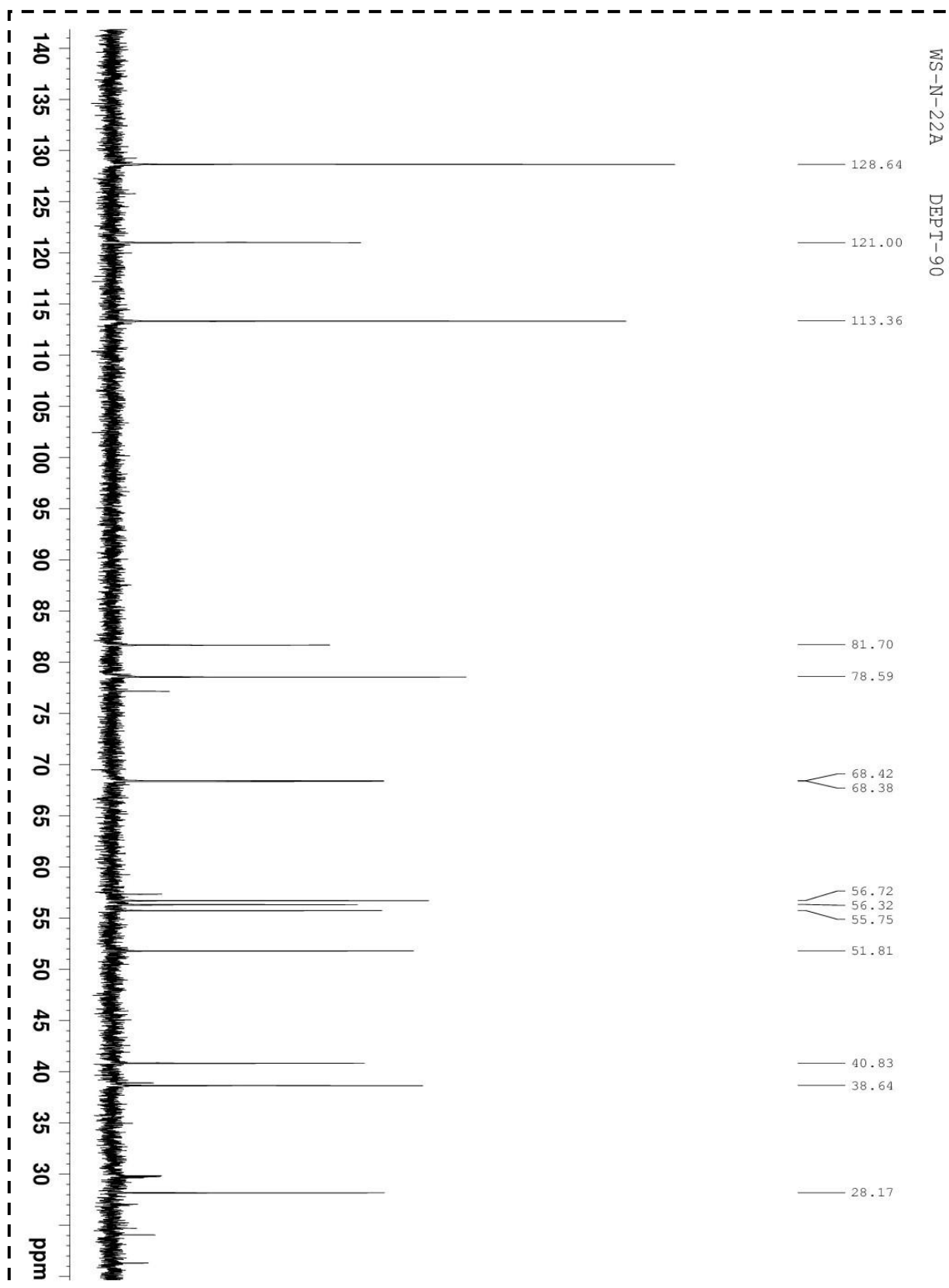


Figure S43: DEPT 135 of Withaferin-Dinitrone Adduct 5

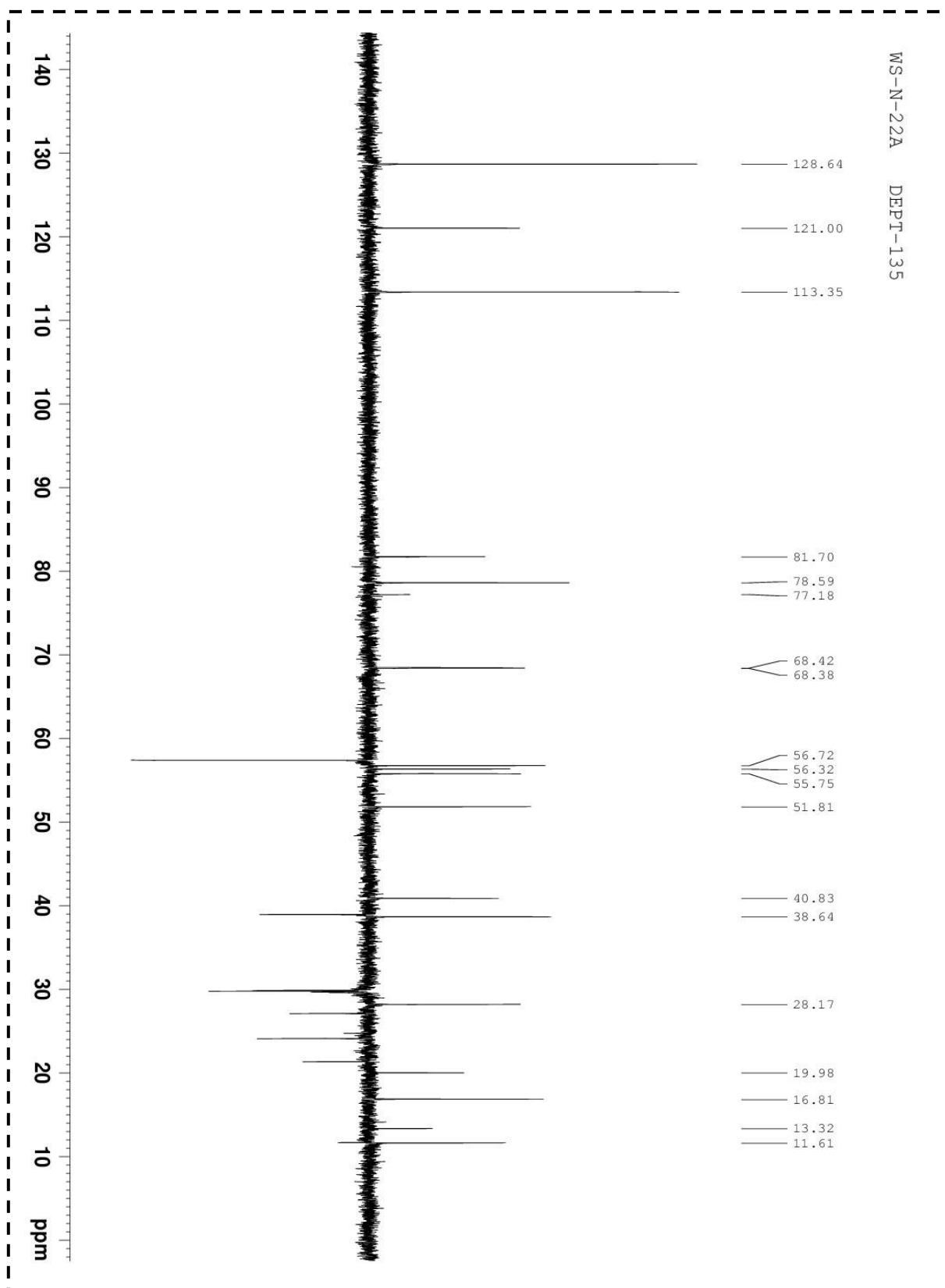


Figure S44: COSY of Withaferin-Dinitrone Adduct 5

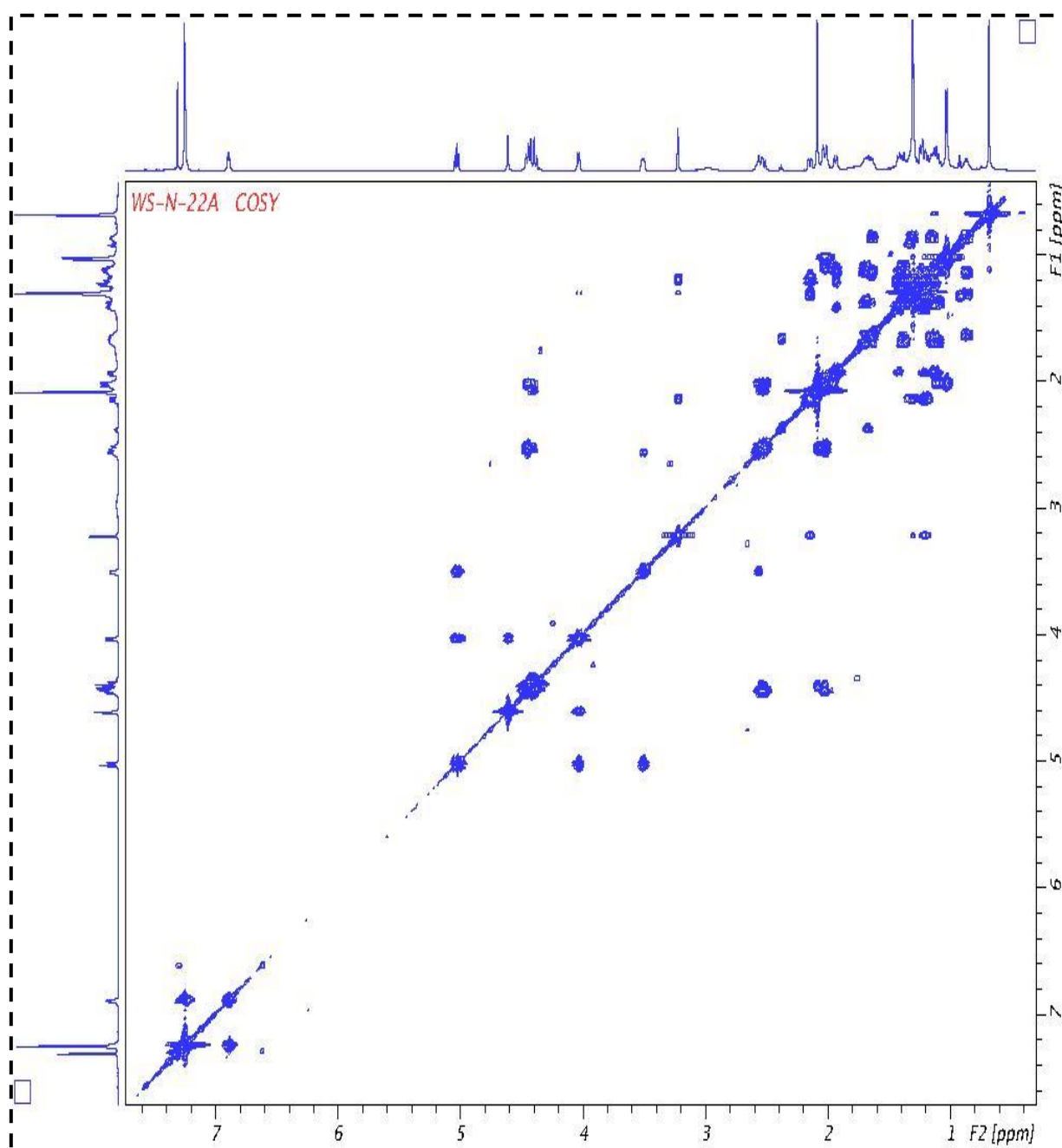


Figure S45: NOESY of Withaferin-Dinitrone Adduct 5

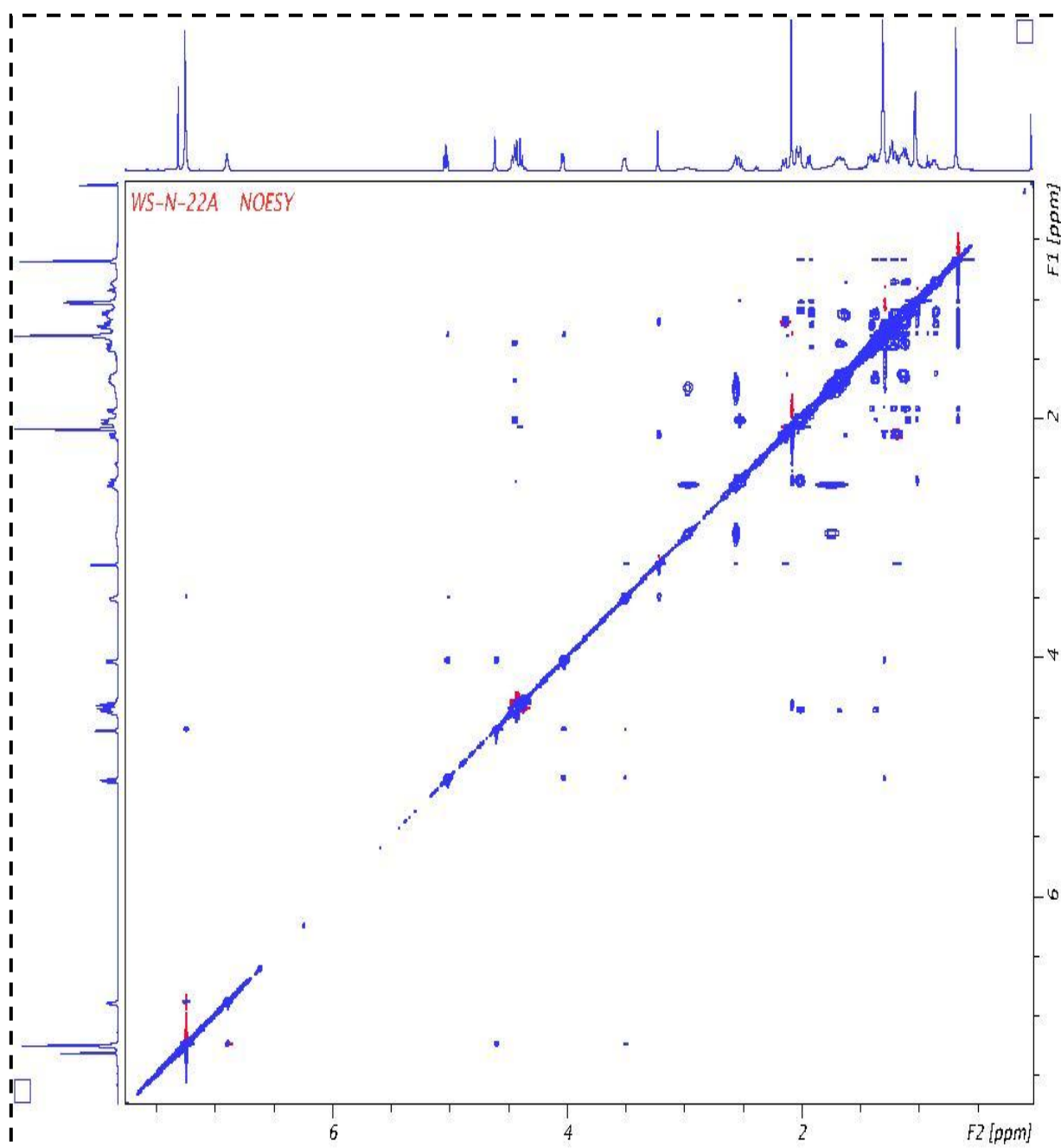


Figure S46: NOESY of Withaferin-Dinitrone Adduct 5

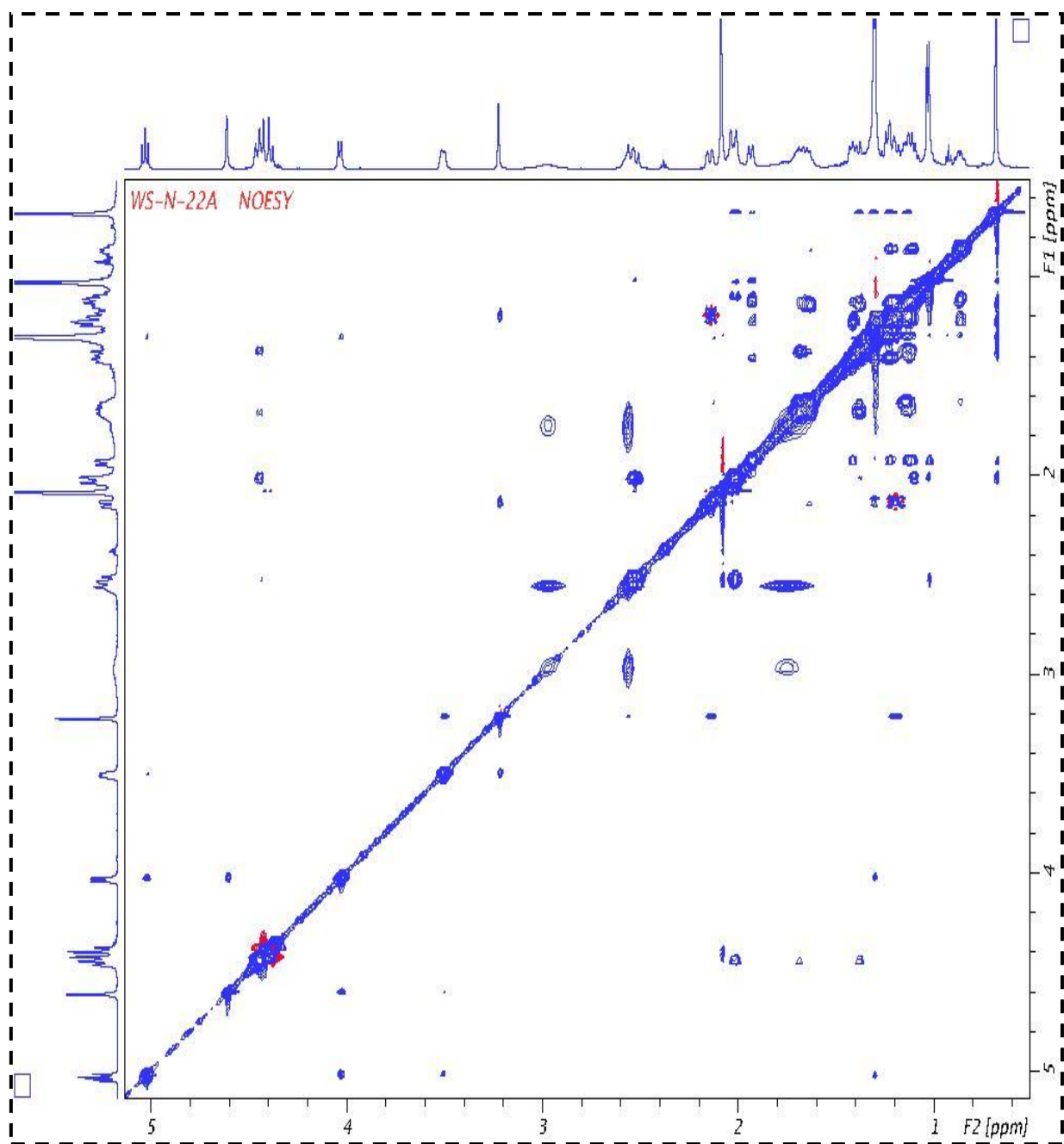


Figure S47: HMBC of Withaferin-Dinitrone Adduct 5

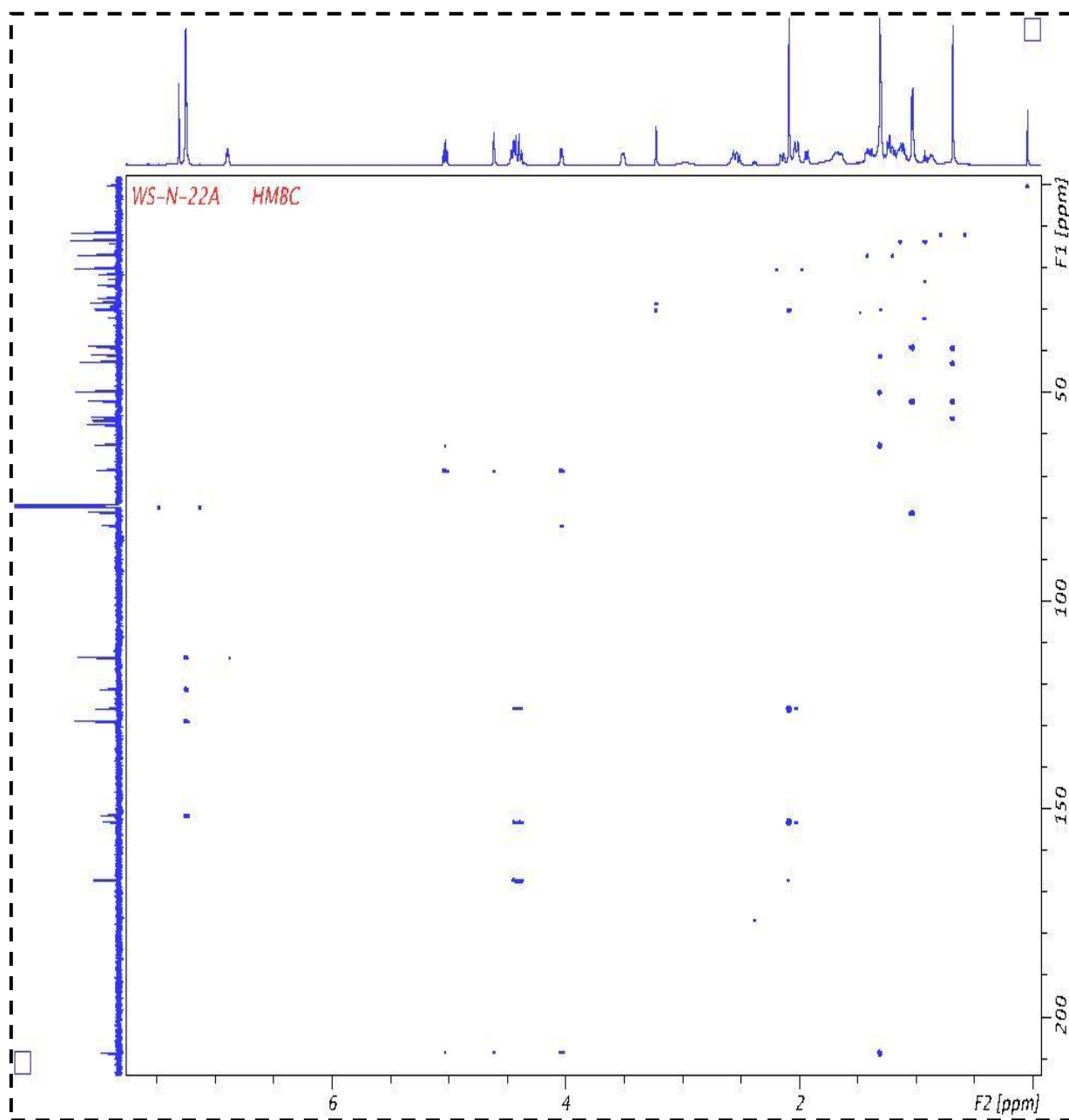


Figure S48: HSQC of Withaferin-Dinitrone Adduct 5

