Electronic Supplementary Material (ESI) for Chemical Science

Open flask and scaleable catalytic asymmetric α-amination of carboxylic acids using isothioureas at low catalyst loadings

*Louis C. Morrill, Alexandra M. Z. Slawin and Andrew D. Smith **

EaStCHEM, School of Chemistry, University of St Andrews, North Haugh, St Andrews, KY16 9ST, UK.

e-mail: ads10@st-andrews.ac.uk, lcm56@st-andrews.ac.uk

SUPPORTING INFORMATION

Contents

Appendix I: ^{1}H and ^{13}C NMR Spectra for Novel Compounds and HPLC data

1.1 General Information

Reactions involving moisture sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques in addition to freshly distilled solvents. All glassware used was flame dried and cooled under vacuum.

Solvents (THF, CH_2Cl_2, toluene, hexane and Et_2O) were obtained anhydrous and purified by an alumina column (Mbraun SPS-800). Petrol is defined as petroleum ether 40-60 °C. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise.

Room temperature (rt) refers to 20-25 °C. Temperatures of 0 °C and -78 °C were obtained using ice/water and CO_2(s)/acetone baths respectively. Temperatures of 0 °C to -50 °C for overnight reactions were obtained using an immersion cooler (HAAKE EK 90). Reflux conditions were obtained using an oil bath equipped with a contact thermometer. *In vacuo* refers to the use of a Büchi Rotavapor R-2000 rotary evaporator with a Vacubrand CVC_2 vacuum controller or a Heidolph Laborota 4001 rotary evaporator with a vacuum controller.

Analytical thin layer chromatography was performed on pre-coated aluminium plates (Kieselgel 60 F_{254} silica). TLC visualisation was carried out with ultraviolet light (254 nm), followed by staining with a 1% aqueous $KMnO_4$ solution. Flash column chromatography was performed on Kieselgel 60 silica in the solvent system stated.

^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were acquired on either a Bruker Avance 300 (300 MHz, ^1H, 75 MHz ^{13}C), Bruker Avance II 400 (400 MHz, ^1H, 100 MHz ^{13}C) or a Bruker Avance II 400 (500 MHz, ^1H, 125 MHz ^{13}C) spectrometer at ambient temperature in the deuterated solvent stated. All chemical shifts are quoted in parts per million (ppm) relative to the residual solvent as the internal standard. All coupling constants, *J*, are quoted in Hz. Multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), ABq (AB quartet), sept (septet), oct (octet), m (multiplet), dd (doublet of doublets), ddd (doublet of doublet of doublets, dt (doublet of triplets) and td (triplet of doublets). The abbreviation Ar is used to denote aromatic, br to denote broad and app. to denote apparent.

Infrared spectra (ν_{max}) were recorded on a Perkin-Elmer Spectrum GX FT-IR spectrometer using either thin films on NaCl plates or KBr discs. Only the characteristic peaks are quoted. Melting points were recorded on an Electrothermal apparatus and are uncorrected.

HPLC analyses were obtained on two separate machines; a Gilson HPLC consisting of a Gilson 305 pump, Gilson 306 pump, Gilson 811C dynamic mixer, Gilson 805 manometric module, Gilson 401C dilutor, Gilson 213XL sample injector and sample detection was performed with a Gilson 118 UV/vis detector while the temperature was assumed to be 20 °C; a Shimadzu HPLC consisting of a DGU-20A5 degasser, LC-20AT liquid chromatograph, SIL-20AHT autosampler, CMB-20A communications bus module, SPD-M20A diode array detector and a CTO-20A column oven which allowed the temperature to be set from 25-40

°C. Separation was achieved using Chiralcel OD-H and OJ-H columns or Chiralpak AD-H, AS-H, IA, IB, IC and ID columns.

Mass spectrometry (*m/z*) data were acquired by electrospray ionisation (ES), electron impact (EI) or nanospray ionisation (NSI) either at the University of St Andrews or the EPSRC National Mass Spectrometry Service Centre, Swansea. At the University of St Andrews, low and high resolution ESI MS were carried out on a Micromass LCT spectrometer. At the EPSRC National Mass Spectrometry Service Centre, low resolution NSI MS was carried out on a Micromass Quattro II spectrometer and high resolution NSI MS on a Thermofisher LTQ Orbitrap XL spectrometer.

Optical rotations were measured on a Perkin Elmer Precisely/Model-341 polarimeter operating at the sodium D line with a 100 mm path cell.

1.2 General Experimental Procedures

General procedure A: *Cu(I) mediated N-arylation.*

To a flask under inert atmosphere was charged the requisite aryl iodide, copper iodide, 1,10-phenanthroline, cesium carbonate, benzyl carbazate and anhydrous dimethyl formamide and the reaction mixture was heated at 80 °C for 1 h. Once cool the reaction mixture was filtered and concentrated *in vacuo* to give the crude reaction mixture.

General procedure B: *Hydrazine acylation.*

Following the procedure outlined by Bowman *et al*.,[1] to a solution of requisite hydrazine and triethylamine in Et_2O at 0 °C was added the requisite acid chloride dropwise. The reaction mixture was stirred at 0 °C for 30 minutes before being filtered. The residue was washed with water and recrystallised from ethanol to give the hydazide.

General procedure C: *Diazene formation.*

Following the procedure outlined by Bowman *et al*.,[1] to a solution of requisite hydrazide and pyridine in CH_2Cl_2 at -78 °C was added *N*-bromosuccinimide portion wise. The reaction mixture was warmed to rt and stirred for 30 minutes before being filtered. The filtrate was concentrated *in vacuo* and the resulting solid was triturated with Et_2O. The mixture was filtered and the filtrate was washed with 1M HCl followed by sat. aq. $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude reaction mixture.

General procedure D: *Michael addition-lactonization (racemic).*

To a solution of requisite acid in DCM were added DIPEA and either benzoyl chloride or p-methoxybenzoyl chloride at rt. The reaction mixture was allowed to stir at rt for 20 minutes.

The requisite Michael acceptor, Lewis base (1-20 mol%), and DIPEA were then added in that order at the required temperature. The reaction mixture was stirred at the required temperature until complete by TLC and was subsequently quenched by addition of 1M HCl. Once warmed to rt, the reaction mixture was poured into water and extracted twice with CH_2Cl_2. The combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude reaction mixture.

General procedure E: *Michael addition-lactonization (asymmetric).*

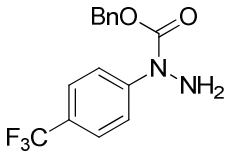
To a solution of requisite acid in DCM were added DIPEA and either benzoyl chloride or p-methoxybenzoyl chloride at rt. The reaction mixture was allowed to stir at rt for 20 minutes. The requisite Lewis base (1-20 mol%), Michael acceptor and DIPEA were then added in that order at the required temperature. The reaction mixture was stirred at the required temperature until complete by TLC and was subsequently quenched by addition of 1M HCl. Once warmed to rt, the reaction mixture was poured into water and extracted twice with CH_2Cl_2. The combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude reaction mixture.

General procedure F: *Samarium iodide N-N bond cleavage.*

To a solution of starting material in MeOH was added 0.1M SmI_2 and the reaction mixture was allowed to stir at -78 °C for 10 minutes. The reaction mixture was poured into sat. aq. $NaHCO_3$ and extracted twice with ethyl acetate. The combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude reaction mixture.

1.3 Experimental Procedures

benzyl 1-(4-(trifluoromethyl)phenyl)hydrazinecarboxylate

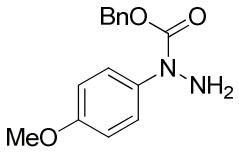


46

Following general procedure A 4-iodobenzotrifluoride (1.08 mL, 7.35 mmol), copper iodide (140 mg, 0.74 mmol), 1,10-phenanthroline (265 mg, 1.47 mmol), cesium carbonate (3.35 g, 10.3 mmol), benzyl carbazate (1.46 g, 8.82 mmol) and anhydrous dimethyl formamide (10 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75), amine **46** as a white solid (1.02 g, 45%); mp 62-64 °C; ν_{max} (KBr) 3367 (N-H), 2956 (C-H), 1684 (C=O), 1616, 1512; δ_H (500 MHz, $CDCl_3$) 4.52 (2H, s, NH_2), 5.29 (2H, s, CH_2), 7.38-7.41 (5H, m,

Ar*H*), 7.58 (2H, d, *J* 8.7, Ar*H*), 7.74 (2H, d, *J* 7.8, Ar*H*); δ_C (125 MHz, $CDCl_3$) 68.7 (*C*H_2), 122.4 (*ArC*), 124.2 (q, *J* 270, *C*F_3), 125.5 (q, *J* 3.5, *ArC*), 126.3 (q, *J* 32.1, 4ry *ArC*), 128.4 (*ArC*), 128.6 (*ArC*), 128.7 (*ArC*), 135.5 (4ry *ArC*), 145.6 (4ry *ArC*), 155.5 (*C*=O); *m*/*z* (CI^+) 311 ($[M+H]^+$, 100%); HRMS (CI^+) $C_{15}H_{14}F_3N_2O_2^+$ ($[M+H]^+$) requires 311.1002; found 311.1005 (+1.0 ppm).

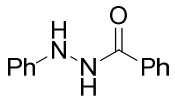
benzyl 1-(4-methoxyphenyl)hydrazinecarboxylate



47

Following general procedure A, 4-iodoanisole (10.0 g, 42.7 mmol), copper iodide (0.81 g, 4.27 mmol), 1,10-phenanthroline (1.54 g, 8.55 mmol), cesium carbonate (19.5 g, 59.8 mmol), benzyl carbazate (8.51 g, 51.3 mmol) and anhydrous dimethyl formamide (45 mL) gave, after chromatographic purification (eluent Et_2O:petrol 50:50), amine **47** as a yellow solid (11.2 g, 96%); mp 69-71 °C; {lit.[7] mp 74-75 °C}; δ_H (300 MHz, $CDCl_3$) 3.73 (3H, s, CH_3), 4.30 (2H, br s, NH_2), 5.13 (2H, s, CH_2), 6.77-6.80 (2H, m, Ar*H*), 7.23-7.29 (7H, m, Ar*H*).

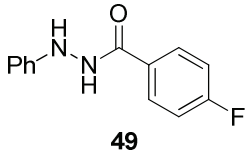
N'-phenylbenzohydrazide



48

Following general procedure B, phenylhydrazine (1.82 mL, 18.5 mmol), triethylamine (2.58 mL, 18.5 mmol) and benzoyl chloride (2.18 mL, 15.6 mmol) in Et_2O (35 mL) gave, after recrystallisation from ethanol, hydazide **48** as a white solid (1.60 g, 45%); mp 163-165 °C; {lit.[1] mp 171-172 °C}; δ_H (400 MHz, $CDCl_3$) 6.30 (1H, br s, N*H*), 6.84-6.86 (3H, m, Ar*H*), 7.15-7.19 (2H, m, Ar*H*), 7.40 (2H, t, *J* 7.6, Ar*H*), 7.49 (1H, t, *J* 7.4, Ar*H*), 7.77 (2H, d, *J* 7.4, Ar*H*), 7.94 (1H, br s, N*H*).

4-fluoro-N'-phenylbenzohydrazide

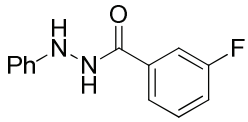


49

Following general procedure B, phenylhydrazine (0.55 mL, 5.59 mmol), triethylamine (0.78 mL, 5.59 mmol) and 4-fluorobenzoyl chloride (0.60 mL, 5.08 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **49** as a white solid (378 mg, 32%); mp 171-

173 °C; {lit.[3] mp 177-179 °C}; δ_H (300 MHz, $CDCl_3$) 6.35 (1H, d, *J* 3.5, N*H*), 6.96-7.00 (3H, m, Ar*H*), 7.20 (2H, t, *J* 8.6, Ar*H*), 7.27-7.33 (2H, m, Ar*H*), 7.85-7.93 (3H, m, Ar*H* and N*H*).

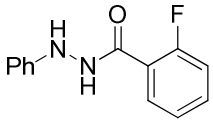
4-fluoro-N'-phenylbenzohydrazide



50

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 3-fluorobenzoyl chloride (1.01 mL, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **50** as a white solid (654 mg, 34%); mp 120-122 °C; ν_{max} (KBr) 3251 (N-H), 3026 (C-H), 1646 (C=O), 1588, 1551; δ_H (300 MHz, CD_3OD) 6.79-6.88 (3H, m, Ar*H*), 7.16-7.22 (2H, m, Ar*H*), 7.29-7.35 (1H, m, Ar*H*), 7.51 (1H, td, *J* 8.0, 5.7, Ar*H*), 7.62 (1H, dt, *J* 9.6, 2.0, Ar*H*), 7.71-7.74 (1H, m, Ar*H*); δ_C (75 MHz, CD_3OD) 114.3 (*ArC*), 115.5 (d, *J* 30.9, *ArC*), 119.9 (d, *J* 28.5, *ArC*), 121.3 (*ArC*), 124.3 (d, *J* 3.9, *ArC*), 130.0 (*ArC*), 131.8 (d, *J* 10.6, *ArC*), 136.5 (d, *J* 9.2, 4ry *ArC*), 150.0 (4ry *ArC*), 164.2 (d, *J* 326, 4ry *ArC*), 168.8 (*C*=O); *m*/*z* (NSI^+) 231 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{13}H_{12}FN_2O^+$ ($[M+H]^+$) requires 231.0928; found 231.0930 (+0.8 ppm).

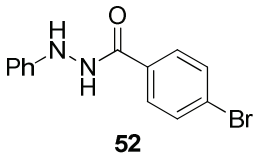
4-fluoro-N'-phenylbenzohydrazide



51

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 2-fluorobenzoyl chloride (1.01 mL, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **51** as a white solid (1.07 mg, 55%); mp 107-109 °C; ν_{max} (KBr) 3272 (N-H), 3024 (C-H), 1639 (C=O), 1546, 1499; δ_H (400 MHz, CD_3OD) 6.80-6.84 (1H, m, Ar*H*), 6.91 (2H, m, Ar*H*), 7.18-7.31 (4H, m, Ar*H*), 7.53-7.58 (1H, m, Ar*H*), 7.72-7.76 (1H, m, Ar*H*); δ_C (75 MHz, CD_3OD) 114.3 (*ArC*), 117.3 (d, *J* 29.9, *ArC*), 121.3 (*ArC*), 123.1 (d, *J* 19.7, 4ry *ArC*), 125.8 (d, *J* 4.6, *ArC*), 130.1 (*ArC*), 131.5 (d, *J* 3.3, *ArC*), 134.5 (d, *J* 11.4, *ArC*), 149.9 (4ry *ArC*), 161.4 (d, *J* 331, 4ry *ArC*), 167.2 (*C*=O); *m*/*z* (NSI^+) 231 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{13}H_{12}FN_2O^+$ ($[M+H]^+$) requires 231.0928; found 231.0930 (+0.8 ppm).

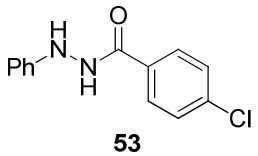
4-bromo-N'-phenylbenzohydrazide



52

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 4-bromobenzoyl chloride (1.85 g, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **52** as a white solid (828 mg, 34%); mp 196-198 °C; {lit.[3] mp 198-199 °C}; δ_H (400 MHz, $CDCl_3$) 6.35 (1H, d, *J* 3.4, N*H*), 6.94-6.98 (3H, m, Ar*H*), 7.26-7.30 (2H, m, Ar*H*), 7.65 (2H, d, *J* 8.5 Ar*H*), 7.74 (2H, d, *J* 8.5, Ar*H*), 7.96 (1H, br s, N*H*).

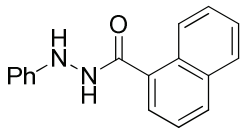
4-chloro-N'-phenylbenzohydrazide



53

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 4-chlorobenzoyl chloride (1.08 mL, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **53** as a white solid (1.17 g, 56%); mp 166-168 °C; {lit.[3] mp 193-195 °C}; δ_H (400 MHz, $CDCl_3$) 6.35 (1H, d, *J* 3.5, N*H*), 6.94-6.99 (3H, m, Ar*H*), 7.27-7.31 (2H, m, Ar*H*), 7.49 (2H, d, *J* 8.5 Ar*H*), 7.82 (2H, d, *J* 8.5, Ar*H*), 7.93 (1H, br s, N*H*).

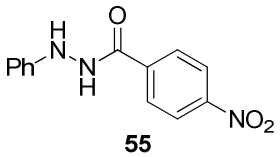
N'-phenyl-1-naphthohydrazide



54

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 1-naphthoyl chloride (1.27 mL, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **54** as a white solid (740 mg, 34%); mp 194-196 °C; {lit.[5] mp 240 °C}; δ_H (300 MHz, $CDCl_3$) 6.52 (1H, d, *J* 4.3, N*H*), 6.99-7.05 (3H, m, Ar*H*), 7.32-7.37 (2H, m, Ar*H*), 7.52-7.64 (3H, m, Ar*H*), 7.77-7.79 (2H, m, Ar*H*), 7.92-7.96 (1H, m, Ar*H*), 8.03 (1H, d, *J* 8.3, Ar*H*), 8.36-8.39 (1H, m, N*H*).

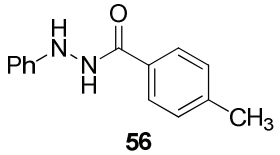
4-nitro-N'-phenylbenzohydrazide



55

Following general procedure B, phenylhydrazine (1.82 mL, 18.5 mmol), triethylamine (2.58 mL, 16.8 mmol) and 4-nitrobenzoyl chloride (3.12 g, 16.8 mmol) in Et_2O (35 mL) gave, after recrystallisation from ethanol, hydazide **55** as an orange solid (2.06 g, 48%); mp 198-200 °C; {lit.[2] mp 206 °C}; δ_H (400 MHz, $CDCl_3$) 6.37 (1H, d, *J* 3.0, N*H*), 6.96-7.00 (3H, m, Ar*H*), 7.31-7.33 (2H, m, Ar*H*), 8.01-8.06 (3H, m, Ar*H* and N*H*), 8.38 (2H, d, *J* 8.8, Ar*H*).

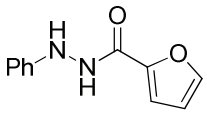
4-methyl-N'-phenylbenzohydrazide



56

Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and p-toluoyl chloride (1.11 mL, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **56** as a white solid (0.83 g, 44%); mp 166-167 °C; {lit.[2] mp 172 °C}; δ_H (300 MHz, $CDCl_3$) 2.36 (3H, s, CH_3), 6.26 (1H, d, *J* 3.5, N*H*), 6.87 (2H, d, *J* 8.2, Ar*H*), 7.15-7.22 (5H, m, Ar*H*), 7.68 (2H, d, *J* 8.2, Ar*H*), 7.76 (1H, br s, N*H*).

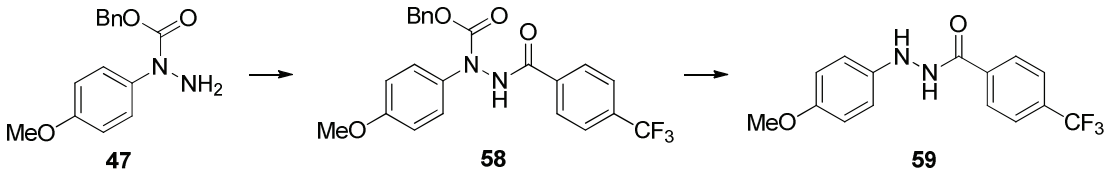
N'-phenylfuran-2-carbohydrazide



57

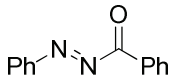
Following general procedure B, phenylhydrazine (0.91 mL, 9.25 mmol), triethylamine (1.29 mL, 9.25 mmol) and 2-furoyl chloride (0.83 mL, 8.41 mmol) in Et_2O (20 mL) gave, after recrystallisation from ethanol, hydazide **57** as a white solid (0.80 g, 47%); mp 141-142 °C; {lit.[6] mp 144-145 °C}; δ_H (300 MHz, $CDCl_3$) 6.24 (1H, br s, N*H*), 6.60 (1H, dd, *J* 3.5, 1.7, Ar*H*), 6.94-6.98 (3H, m, Ar*H*), 7.24-7.35 (3H, m, Ar*H*), 7.56 (1H, d, *J* 1.0, Ar*H*), 8.10 (1H, br s, N*H*).

N'-(4-methoxyphenyl)-4-(trifluoromethyl)benzohydrazide



To a solution of **47** (11.1 g, 40.8 mmol) and triethylamine (6.25 mL, 44.9 mmol) in EtOAc (100 mL) at 0 °C was added 4-trifluoromethylbenzoyl chloride (6.06 mL, 40.8 mmol). The reaction mixture was stirred at rt for 1 h. The reaction mixture was washed with 1M HCl and sat. aq. $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude acylated product **58** which was used without purification. To a solution of crude acylated product **58** (17.7 g, 40.8 mmol assuming 100% conversion) and 10% palladium on charcoal (4.27 g, 4.08 mmol, 10 mol%) in EtOAc (100 mL) was appended a balloon of hydrogen gas. The hydrogen gas was allowed to bubble through the reaction mixture at rt for 4 h. The reaction mixture was filtered through celite and concentrated *in vacuo*. Recrystallisation from ethanol gave hydrazide **59** as a white solid (7.95 g, 63% over 2 steps); mp 158-160 °C; ν_{max} (KBr) 3270 (N-H), 3068 (C-H), 1649 (C=O), 1551, 1510; δ_H (300 MHz, $(CH_3)_2S$=O) 3.67 (3H, s, C*H*$_3$), 6.79 (4H, s, Ar*H*), 7.69 (1H, d, *J* 2.5, N*H*), 7.89 (2H, d, *J* 8.2, Ar*H*), 8.11 (2H, d, *J* 8.1, Ar*H*), 10.6 (1H, d, *J* 2.2, N*H*); δ_C (75 MHz, $(CH_3)_2S$=O) 55.2 (*C*H$_3$), 113.9 (*ArC*), 114.3 (*ArC*), 123.9 (q, *J* 271, *C*F$_3$), 125.5 (q, *J* 3.7, *ArC*), 128.2 (*ArC*), 131.4 (q, *J* 31.7, 4ry *ArC*), 136.9 (4ry *ArC*), 143.0 (4ry *ArC*), 152.8 (4ry *ArC*), 165.1 (*C*=O); *m/z* (NSI$^+$) 311 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{15}H_{14}F_3N_2O_2^+$ ([M+H]$^+$) requires 311.1002; found 311.1005 (+1.0 ppm).

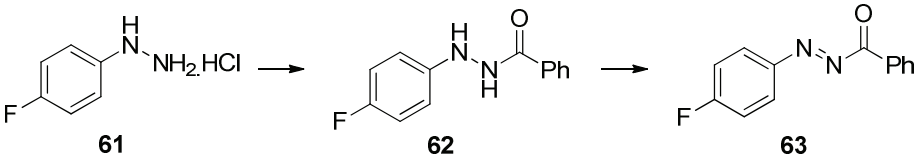
(E)-phenyl(phenyldiazenyl)methanone



60

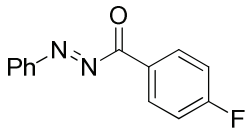
Following general procedure C, hydrazide **48** (1.5 g, 7.08 mmol), pyridine (0.63 mL, 7.79 mmol) and *N*-bromosuccinimide (1.26 g, 7.08 mmol) in CH_2Cl_2 (7 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **60** as a red oil (1.17 g, 79%); δ_H (400 MHz, $CDCl_3$) 7.43-7.63 (6H, m, Ar*H*), 7.91-8.02 (4H, m, Ar*H*).

(E)-((4-fluorophenyl)diazenyl)(phenyl)methanone



To a solution of 4-fluorophenylhydrazine hydrochloride **61** (2.00 g, 12.3 mmol) and triethylamine (3.43 mL, 24.6 mmol) in Et_2O (30 mL) at 0 °C was slowly added benzoyl chloride (1.29 mL, 11.2 mmol). After stirring at rt for 30 minutes the reaction mixture was concentration *in vacuo*. The solid was dissolved in CH_2Cl_2 and washed with 1M HCl. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a crude hydrazide **62** which was used without purification. Following general procedure C, hydrazide **62** (2.57 g, 11.2 mmol assuming 100% conversion), pyridine (1.07 mL, 12.3 mmol) and *N*-bromosuccinimide (1.98 g, 11.2 mmol) in CH_2Cl_2 (15 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **63** as a red solid (545 mg, 21% over 2 steps); mp 48-50 °C; ν_{max} (KBr) 3067 (C-H), 1702 (C=O), 1591, 1503; δ_H (300 MHz, $CDCl_3$) 7.26-7.32 (2H, m, Ar*H*), 7.54-7.60 (2H, m, Ar*H*), 7.68-7.74 (1H, m, Ar*H*), 8.06-8.12 (4H, m, Ar*H*); δ_C (75 MHz, $CDCl_3$) 116.5 (d, *J* 23.0, *ArC*), 126.0 (d, *J* 9.5, *ArC*), 128.9 (*ArC*), 130.6 (*ArC*), 130.9 (4ry *ArC*), 134.6 (*ArC*), 148.7 (d, 2.9, 4ry *ArC*), 165.9 (d, *J* 254, 4ry *ArC*), 181.7 (*C*=O); *m*/*z* (ES^+) 251 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{13}H_9FN_2NaO^+$ ($[M+Na]^+$) requires 251.0597; found 251.0590 (-2.5 ppm).

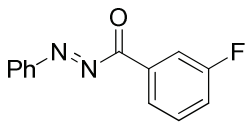
(E)-(4-fluorophenyl)(phenyldiazenyl)methanone



64

Following general procedure C, hydrazide **49** (370 mg, 1.61 mmol), pyridine (0.14 mL, 1.77 mmol) and *N*-bromosuccinimide (0.29 g, 1.61 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **64** as a red oil (280 mg, 76%); ν_{max} (thin film) 3068 (C-H), 1707 (C=O), 1597, 1507; δ_H (400 MHz, $CDCl_3$) 7.20-7.26 (2H, m, Ar*H*), 7.58-7.67 (3H, m, Ar*H*), 8.02-8.05 (2H, m, Ar*H*), 8.12-8.17 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 116.3 (d, *J* 21.9, *ArC*), 123.7 (*ArC*), 127.4 (d, *J* 2.7, 4ry *ArC*), 129.4 (*ArC*), 133.4 (d, *J* 9.7, *ArC*), 133.7 (*ArC*), 152.1 (4ry *ArC*), 166.6 (d, *J* 256, 4ry *ArC*), 180.5 (*C*=O); *m*/*z* (ES^+) 251 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{13}H_9FN_2NaO^+$ ($[M+Na]^+$) requires 251.0597; found 251.0602 (+2.1 ppm).

(E)-(3-fluorophenyl)(phenyldiazenyl)methanone

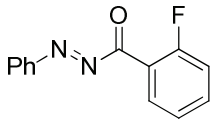


65

Following general procedure C, hydrazide **50** (488 mg, 2.13 mmol), pyridine (0.19 mL, 2.34 mmol) and *N*-bromosuccinimide (0.38 g, 2.13 mmol) in CH_2Cl_2 (5 mL) gave, after

chromatographic purification (eluent Et_2O:petrol 20:80), diazene **65** as a red oil (362 mg, 75%); ν_{max} (thin film) 3073 (C-H), 1716 (C=O), 1589, 1499; δ_H (400 MHz, $CDCl_3$) 7.37-7.42 (1H, m, Ar*H*), 7.54 (1H, td, *J* 8.0, 5.4, Ar*H*), 7.58-7.68 (3H, m, Ar*H*), 7.81 (1H, ddd, *J* 9.0, 2.6, 1.5, Ar*H*), 7.88-7.90 (1H, m, Ar*H*), 8.02-8.05 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 117.2 (d, *J* 22.8, *ArC*), 121.7 (d, *J* 21.3, *ArC*), 123.8 (*ArC*), 126.4 (d, *J* 3.0, *ArC*), 129.5 (*ArC*), 130.7 (d, *J* 7.4, *ArC*), 133.0 (d, *J* 6.7, 4ry *ArC*), 133.8 (*ArC*), 152.1 (4ry *ArC*), 162.7 (d, *J* 247, 4ry *ArC*), 180.6 (*C*=O); *m*/*z* (ES^+) 251 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{13}H_9FN_2NaO^+$ ($[M+Na]^+$) requires 251.0597; found 251.0602 (+2.1 ppm).

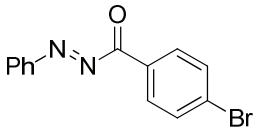
(E)-(2-fluorophenyl)(phenyldiazenyl)methanone



66

Following general procedure C, hydrazide **51** (800 mg, 3.49 mmol), pyridine (0.31 mL, 3.84 mmol) and *N*-bromosuccinimide (0.62 g, 3.49 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **66** as a red oil (540 mg, 68%); ν_{max} (thin film) 3066 (C-H), 1695 (C=O), 1609, 1586, 1505; δ_H (300 MHz, $CDCl_3$) 7.20 (1H, ddd, *J* 10.6, 8.4, 1.0, Ar*H*), 7.36 (1H, td, *J* 7.6, 0.9, Ar*H*), 7.56-7.71 (4H, m, Ar*H*), 7.98-8.02 (2H, m, Ar*H*), 8.13 (1H, ddd, *J* 7.8, 7.1, 1.8, Ar*H*); δ_C (75 MHz, $CDCl_3$) 117.2 (d, *J* 29.3, *ArC*), 119.3 (d, *J* 15.0, 4ry *ArC*), 123.6 (*ArC*), 124.6 (d, *J* 4.8, *ArC*), 129.4 (*ArC*), 132.5 (*ArC*), 133.4 (*ArC*), 136.4 (d, *J* 12.0, *ArC*), 152.1 (4ry *ArC*), 162.5 (d, *J* 346, 4ry *ArC*), 180.9 (d, *J* 7.8, *C*=O); *m*/*z* (ES^+) 251 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{13}H_9FN_2NaO^+$ ($[M+Na]^+$) requires 251.0597; found 251.0593 (-1.4 ppm).

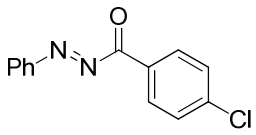
(E)-(4-bromophenyl)(phenyldiazenyl)methanone



67

Following general procedure C, hydrazide **52** (0.82 g, 2.82 mmol), pyridine (0.26 mL, 3.10 mmol) and *N*-bromosuccinimide (0.50 g, 2.82 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **67** as a red solid (669 mg, 82%); mp 39-40 °C; {lit.[4] mp 38-39.5 °C}; δ_H (300 MHz, $CDCl_3$) 7.57-7.66 (3H, m, Ar*H*), 7.68-7.72 (2H, m, Ar*H*), 7.95-7.99 (2H, m, Ar*H*), 8.01-8.04 (2H, m, Ar*H*).

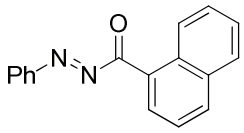
(E)-(4-chlorophenyl)(phenyldiazenyl)methanone



68

Following general procedure C, hydrazide **53** (1.16 g, 4.71 mmol), pyridine (0.42 mL, 5.18 mmol) and *N*-bromosuccinimide (0.84 g, 4.71 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **68** as a red oil (0.91 g, 76%); ν_{max} (thin film) 3064 (C-H), 1701 (C=O), 1591, 1500; δ_H (300 MHz, $CDCl_3$) 7.50-7.55 (2H, m, Ar*H*), 7.57-7.67 (3H, m, Ar*H*), 8.01-8.07 (4H, m, Ar*H*); δ_C (75 MHz, $CDCl_3$) 123.8 (*ArC*), 129.4 (*ArC*), 129.5 (*ArC*), 131.9 (*ArC*), 131.9 (4ry *ArC*), 133.7 (*ArC*), 141.2 (4ry *ArC*), 152.1 (4ry *ArC*), 180.8 (*C*=O); *m*/*z* (ES^+) 267 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_9H_{13}{}^{35}ClN_2NaO_3^+$ ($[M+Na]^+$) requires 267.0303; found 267.0302 (-0.3 ppm).

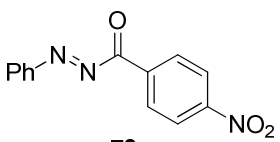
(E)-naphthalen-1-yl(phenyldiazenyl)methanone



69

Following general procedure C, hydrazide **54** (0.74 g, 2.81 mmol), pyridine (0.26 mL, 3.10 mmol) and *N*-bromosuccinimide (0.50 g, 2.81 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **69** as a red solid (575 mg, 79%); mp 76-78 °C; ν_{max} (KBr) 3061 (C-H), 1697 (C=O), 1591, 1500; δ_H (400 MHz, $CDCl_3$) 7.54-7.66 (5H, m, Ar*H*), 7.76 (1H, ddd, *J* 8.6, 7.0, 1.4, Ar*H*), 7.96 (1H, dd, *J* 8.2, 0.4, Ar*H*), 8.05-8.07 (2H, m, Ar*H*), 8.15 (1H, d, *J* 8.2, Ar*H*), 8.31 (1H, dd, *J* 7.3, 1.2, Ar*H*), 9.25 (1H, d, *J* 8.7, Ar*H*); δ_C (100 MHz, $CDCl_3$) 123.7 (*ArC*), 124.4 (*ArC*), 126.2 (*ArC*), 126.9 (*ArC*), 127.1 (4ry *ArC*), 128.8 (*ArC*), 129.0 (*ArC*), 129.4 (*ArC*), 131.6 (4ry *ArC*), 133.3 (*ArC*), 133.4 (*ArC*), 134.1 (4ry *ArC*), 135.6 (*ArC*), 152.1 (4ry *ArC*), 183.1 (*C*=O); *m*/*z* (ES^+) 283 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{17}H_{12}N_2NaO^+$ ($[M+Na]^+$) requires 283.0847; found 283.0848 (+0.2 ppm).

(E)-(4-nitrophenyl)(phenyldiazenyl)methanone

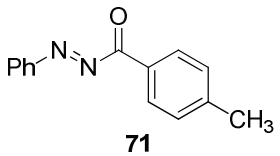


70

Following general procedure C, hydrazide **55** (2.00 g, 7.78 mmol), pyridine (0.69 mL, 8.56 mmol) and *N*-bromosuccinimide (1.39 g, 7.78 mmol) in CH_2Cl_2 (10 mL) gave, after

chromatographic purification (eluent Et_2O:petrol 50:50), diazene **70** as a red solid (0.91 g, 46%); mp 127-129 °C; ν_{max} (KBr) 3080 (C-H), 1711 (C=O), 1605, 1529, 1499; δ_H (300 MHz, $CDCl_3$) 7.50-7.62 (3H, m, Ar*H*), 7.94-7.97 (2H, m, Ar*H*), 8.19-8.23 (2H, m, Ar*H*), 8.29-8.33 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 124.0 (*ArC*), 124.0 (*ArC*), 129.6 (*ArC*), 131.7 (*ArC*), 134.3 (*ArC*), 136.1 (4ry *ArC*), 151.1 (4ry *ArC*), 152.1 (4ry *ArC*), 179.7 (*C*=O); *m*/*z* (APCI$^+$) 256 ([M+H]$^+$, 100%); HRMS (APCI$^+$) $C_{13}H_{10}N_3O^+$ ([M+H]$^+$) requires 256.0717; found 256.0714 (-1.0 ppm).

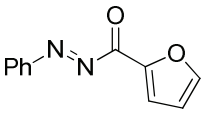
(E)-(phenyldiazenyl)(p-tolyl)methanone



71

Following general procedure C, hydrazide **56** (0.82 g, 3.63 mmol), pyridine (0.32 mL, 4.00 mmol) and *N*-bromosuccinimide (0.65 g, 3.63 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 15:85), diazene **71** as a red oil (0.63 g, 77%); δ_H (400 MHz, $CDCl_3$) 2.38 (3H, s, C*H*$_3$), 7.25 (2H, d, *J* 8.0, Ar*H*), 7.47-7.55 (3H, m, Ar*H*), 7.87-7.94 (4H, m, Ar*H*).

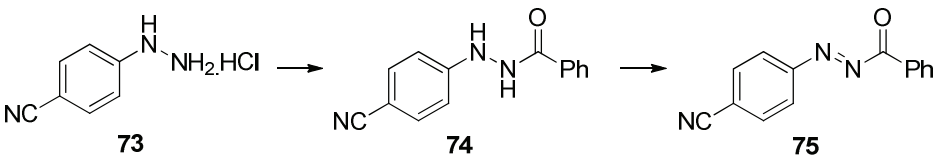
(E)-furan-2-yl(phenyldiazenyl)methanone



72

Following general procedure C, hydrazide **57** (0.79 g, 3.91 mmol), pyridine (0.35 mL, 4.30 mmol) and *N*-bromosuccinimide (0.69 g, 3.91 mmol) in CH_2Cl_2 (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **72** as a red oil (405 mg, 52%); δ_H (300 MHz, $CDCl_3$) 6.70 (1H, dd, *J* 3.6, 1.7, Ar*H*), 7.45 (1H, dd, *J* 3.6, 0.7, Ar*H*), 7.58-7.69 (3H, m, Ar*H*), 7.84 (1H, dd, *J* 1.7, 0.7, Ar*H*), 8.03-8.07 (2H, m, Ar*H*).

(E)-4-(benzoyldiazenyl)benzonitrile

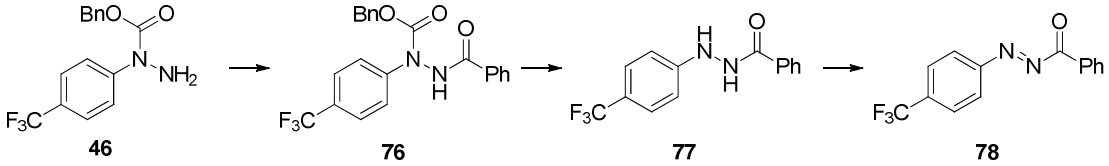


73 **74** **75**

To a solution of 4-cyanophenylhydrazine hydrochloride **73** (2.00 g, 11.8 mmol) and triethylamine (3.29 mL, 23.6 mmol) in Et_2O (30 mL) at 0 °C was slowly added benzoyl chloride (1.24 mL, 10.7 mmol). After stirring at rt for 30 minutes the reaction mixture was

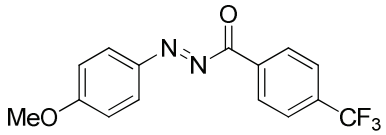
concentration *in vacuo*. The solid was dissolved in CH_2Cl_2 and washed with 1M HCl. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a crude hydrazide **74** which was used without purification. Following general procedure C, hydrazide **74** (2.54 g, 10.7 mmol assuming 100% conversion), pyridine (0.97 mL, 11.8 mmol) and *N*-bromosuccinimide (1.90 g, 10.7 mmol) in CH_2Cl_2 (15 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **75** as a purple solid (258 mg, 10% over 2 steps); mp 110-112 °C; ν_{max} (KBr) 3043 (C-H), 2229 (C≡N), 1706 (C=O), 1598, 1506; δ_H (400 MHz, $CDCl_3$) 7.57 (2H, t, *J* 7.7, Ar*H*), 7.73 (1H, t, *J* 7.4, Ar*H*), 7.91 (2H, d, *J* 8.4, Ar*H*), 8.05 (2H, d, *J* 7.3, Ar*H*), 8.09 (2H, d, *J* 8.4, Ar*H*); δ_C (75 MHz, $CDCl_3$) 116.5 (*C*≡N), 117.9 (4ry *ArC*), 123.9 (*ArC*), 129.1 (*ArC*), 130.2 (4ry *ArC*), 130.6 (*ArC*), 133.5 (*ArC*), 135.0 (*ArC*), 153.5 (4ry *ArC*), 181.5 (*C*=O); *m/z* (ES^+) 236 ($[M+H]^+$, 100%); HRMS (ES^+) $C_{14}H_{10}N_3O^+$ ($[M+H]^+$) requires 236.0824; found 236.0824 (+0.2 ppm).

(E)-phenyl((4-(trifluoromethyl)phenyl)diazenyl)methanone



To a solution of **46** (1.00 g, 3.226 mmol) and triethylamine (0.49 mL, 3.55 mmol) in EtOAc (10 mL) at 0 °C was added benzoyl chloride (0.37 mL, 3.23 mmol). The reaction mixture was stirred at rt for 1 h. The reaction mixture was washed with 1M HCl and sat. aq. $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give the crude acylated product **76** which was used without purification. To a solution of crude acylated product **76** (1.34 g, 3.23 mmol assuming 100% conversion) and 10% palladium on charcoal (0.34 g, 0.32 mmol, 10 mol%) in EtOAc (10 mL) was appended a balloon of hydrogen gas. The hydrogen gas was allowed to bubble through the reaction mixture at rt for 4 h. The reaction mixture was filtered through celite and concentrated *in vacuo* to give the hydrazide **77** which was used without purification. Following general procedure C, hydrazide **77** (903 mg, 3.23 mmol assuming 100% conversion), pyridine (0.29 mL, 3.55 mmol) and *N*-bromosuccinimide (0.57 g, 3.23 mmol) in CH_2Cl_2 (10 mL) gave, after chromatographic purification (eluent Et_2O:petrol 10:90), diazene **78** as a red oil (601 mg, 66% over 3 steps); ν_{max} (thin film) 3070 (C-H), 1716 (C=O), 1599; δ_H (500 MHz, $CDCl_3$) 7.46 (2H, t, *J* 7.8, Ar*H*), 7.61 (1H, t, *J* 7.5, Ar*H*), 7.76 (2H, d, *J* 8.3, Ar*H*), 7.94-7.96 (2H, m, Ar*H*), 8.00 (2H, d, *J* 8.2, Ar*H*); δ_C (125 MHz, $CDCl_3$) 123.6 (q, *J* 271, *C*F_3), 123.7 (*ArC*), 126.7 (q, *J* 3.5, *ArC*), 129.0 (*ArC*), 130.3 (4ry *ArC*), 130.6 (*ArC*), 134.4 (q, *J* 32.5, 4ry *ArC*), 134.9 (*ArC*), 153.6 (4ry *ArC*), 181.7 (*C*=O); *m/z* (ES^+) 301 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{14}H_9F_3N_2NaO^+$ ($[M+Na]^+$) requires 301.0565; found 301.0566 (+0.4 ppm).

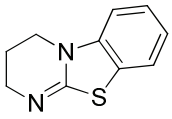
(E)-((4-methoxyphenyl)diazenyl)(4-(trifluoromethyl)phenyl)methanone



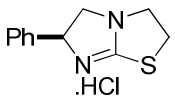
79

Following general procedure C, hydrazide **59** (3.50 g, 11.3 mmol), pyridine (1.02 mL, 12.4 mmol) and *N*-bromosuccinimide (2.00 g, 11.3 mmol) in CH_2Cl_2 (50 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80), diazene **79** as a red solid (2.57 g, 74%) mp 56-58 °C; ν_{max} (KBr) 2936 (C-H), 1696 (C=O), 1597, 1504; δ_H (300 MHz, $CDCl_3$) 3.97 (3H, s, C*H*$_3$), 7.07-7.11 (2H, m, Ar*H*), 7.82 (2H, d, *J* 8.2, Ar*H*), 8.04-8.10 (2H, m, Ar*H*), 8.29 (2H, d, *J* 8.1, Ar*H*); δ_C (100 MHz, $CDCl_3$) 55.8 (*C*H$_3$), 114.7 (*ArC*), 123.5 (q, *J* 271, *C*F$_3$), 125.8 (q, *J* 3.6, *ArC*), 126.6 (*ArC*), 131.0 (*ArC*), 134.9 (4ry *ArC*), 135.3 (q, *J* 32.7, 4ry *ArC*), 146.8 (4ry *ArC*), 164.8 (4ry *ArC*), 179.9 (*C*=O); *m*/*z* (ES^+) 331 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{15}H_{11}N_2NaO_2F_3^+$ ($[M+Na]^+$) requires 331.0670; found 331.0675 (+1.4 ppm).

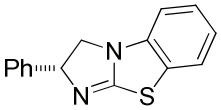
Isothiourea catalysts used



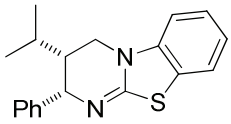
DHPB **80**



Tetramisole.HCl (2*S*)-**81**



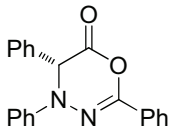
Benzotetramisole (2*R*)-**82**



(2*S*,3*R*)-**5**

Optimization studies on compound 3

triphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**3**

Following general procedure D, phenylacetic acid (54.5 mg, 0.40 mmol), DIPEA (104 μL, 0.60 mmol) and p-methoxybenzoyl chloride (102 mg, 0.60 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (±)-**3** as a colourless oil (41.0 mg, 63%); ν_{max} (thin film) 3063, 2977 (C-H), 1791 (C=O), 1596, 1495; δ_H (400 MHz, $CDCl_3$) 5.96 (1H, s, C(5)*H*), 6.89-6.92 (1H, m, Ar*H*), 7.15-7.28 (9H, m, Ar*H*), 7.31-7.34 (3H, m, Ar*H*), 7.86-7.89 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.5 (*C*(5)), 114.5 (*ArC*), 121.9 (*ArC*), 125.6 (*ArC*), 126.7 (*ArC*), 128.6 (*ArC*), 128.9 (4ry *ArC*), 129.1 (*ArC*), 129.4 (*ArC*), 129.4 (*ArC*), 130.3 (*ArC*), 131.2 (4ry *ArC*), 141.0 (*C*(2)), 144.3 (*ArC*), 160.4

(*C*(6)); *m*/*z* (APCI$^+$) 328 ([M]$^+$, 12%); HRMS (APCI$^+$) $C_{21}H_{16}N_2O_2^+$ ([M]$^+$) requires 328.1206; found 328.1201 (-1.6 ppm).

Asymmetric Catalyst Screen:

Tetramisole hydrochloride (2*S*)-**81** (4.82 mg, 0.02 mmol, 10 mol%) gave approximately 65% conversion to the desired product after 16 h at rt.

Benzotetramisole (2*R*)-**82** (5.04 mg, 0.02 mmol, 10 mol%) gave approximately 20% conversion to the desired product after 16 h at rt.

Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (6.17 mg, 0.02 mmol, 10 mol%) gave full conversion to the desired product after 1 h at rt. Chromatographic purification (eluent Et_2O:petrol 2:98) gave (5*R*)-**3** as a colourless oil (43.0 mg, 66%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.9 min, t_R(5*R*): 14.6 min, 95% *ee*.

Temperature Screen:

All reactions with Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (6.17 mg, 0.02 mmol, 10 mol%)

Reaction for 2 h at 0 °C gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (5*R*)-**3** as a colourless oil (42.3 mg, 65%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.8 min, t_R(5*R*): 14.4 min, 98% *ee*.

Reaction for 16 h at -30 °C gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (5*R*)-**3** as a colourless oil (39.7 mg, 61%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.8 min, t_R(5*R*): 14.5 min, 99% *ee*.

Reaction for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (5*R*)-**3** as a colourless oil (53.2 mg, 81%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 9.0 min, t_R(5*R*): 14.8 min, 99% *ee*.

Catalyst Loading Screen:

All reactions at -78 °C for 16 h.

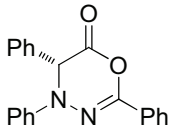
Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (3.09 mg, 0.01 mmol, 5 mol%) gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (5*R*)-**3** as a colourless oil (54.3 mg,

83%); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.8 min, t_R(5*R*): 15.2 min, >99% *ee*.

Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (1.23 mg, 0.004 mmol, 1 mol%) gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (5*R*)-**3** as a colourless oil (58.6 mg, 89%); $[\alpha]_D^{20}$ -621.7 (*c* 1.075, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.8 min, t_R(5*R*): 14.8 min, >99% *ee*.

Optimal asymmetric reaction conditions for compound 3

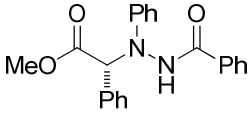
(R)-2,4,5-triphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**3**

Following general procedure E, phenylacetic acid (40.8 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 2:98) (5*R*)-**3** as a colourless oil (57.0 mg, 87%); $[\alpha]_D^{20}$ -621.7 (*c* 1.075, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.8 min, t_R(5*R*): 14.8 min, >99% *ee*.

methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-phenylacetate

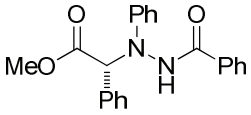


(±)-**4**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) a rotameric mixture (ratio 91:9) of (±)-**4** as a white solid (67.8 mg, 94%); mp 148-150 °C; ν_{max} (KBr) 3355 (N-H), 3075, 2950 (C-H), 1729 (C=O), 1687 (C=O), 1599; Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.74 (3H, s, C*H*$_3$), 5.82 (1H, s, C(2)*H*), 6.90-6.96 (3H, m, Ar*H*), 7.18-7.31 (7H, m, Ar*H*), 7.36-7.42 (3H, m, Ar*H*), 7.44-7.48 (2H, m, Ar*H*), 8.43 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.62 (3H, s, C*H*$_3$), 5.50 (1H, s, C(2)*H*), 7.90 (1H, s, N*H*); Data for major rotamer δ_C (100 MHz,

$CDCl_3$) 52.5 (*C*H_3), 66.7 (*C*(2)), 114.8 (*ArC*), 121.7 (*ArC*), 127.0 (*ArC*), 128.6 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 129.1 (*ArC*), 129.5 (*ArC*), 131.8 (*ArC*), 133.0 (4ry *ArC*), 133.3 (4ry *ArC*), 148.4 (4ry *ArC*), 166.6 (*C*=O), 173.1 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 52.4 (*C*H_3), 68.0 (*C*(2)), 115.4 (*ArC*), 122.3 (*ArC*), 127.8 (*ArC*), 129.9 (*ArC*), 130.2 (*ArC*), 130.4 (*ArC*); *m*/*z* (NSI$^+$) 361 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{22}H_{21}N_2O_3^+$ ([M+H]$^+$) requires 361.1547; found 361.1546 (-0.2 ppm).

(R)-methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-phenylacetate



(2*R*)-**4**

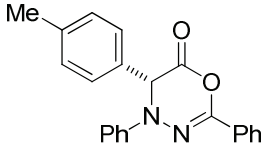
Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) a rotameric mixture (ratio 91:9) of (2*R*)-**4** as a white solid (67.8 mg, 94%); $[\alpha]_D^{20}$ -37.6 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 12.7 min, t_R(2*R*): 15.0 min, 99% *ee*.

The same procedure using Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.31 mg, 0.001 mmol, 0.5 mol%) for 16 h at -78 °C gave (2*R*)-**4** as a white solid (61.0 mg, 85%), >99% ee.

The same procedure using Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.16 mg, 0.0005 mmol, 0.25 mol%) for 40 h at -78 °C gave (2*R*)-**4** as a white solid (60.0 mg, 83%), >99% ee.

The same procedure using Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.062 mg, 0.0002 mmol, 0.1 mol%) for 40 h at -78 °C gave (2*R*)-**4** as a white solid (43.0 mg, 60%), 99% ee. The conversion was determined to be 65% by analysis of the crude ^{1}H NMR.

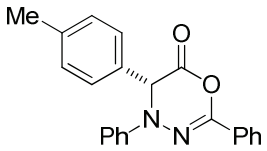
2,4-diphenyl-5-(p-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**6**

Following general procedure D, p-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**6** as a white solid (45.1 mg, 66%); mp 120-122 °C; ν_{max} (KBr) 3059, 2931 (C-H), 1789 (C=O), 1597, 1494; δ_H (400 MHz, $CDCl_3$) 2.18 (3H, s, C*H*$_3$), 5.92 (1H, s, C(5)*H*), 6.89-6.93 (1H, m, Ar*H*), 7.01 (2H, d, *J* 8.1, Ar*H*), 7.13-7.18 (4H, m, Ar*H*), 7.21-7.25 (2H, m, Ar*H*), 7.31-7.35 (3H, m, Ar*H*), 7.85-7.90 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 21.1 (*C*H$_3$), 59.3 (*C*(5)), 114.5 (*ArC*), 121.8 (*ArC*), 125.6 (*ArC*), 126.6 (*ArC*), 128.1 (4ry *ArC*), 128.6 (*ArC*), 128.9 (4ry *ArC*), 129.4 (*ArC*), 130.0 (*ArC*), 130.2 (*ArC*), 139.0 (4ry *ArC*), 140.9 (*C*(2)), 144.4 (4ry *ArC*), 160.6 (*C*(6)); *m*/*z* (APCI$^+$) 343 ([M+H]$^+$, 23%); HRMS (APCI$^+$) $C_{22}H_{19}N_2O_2^+$ ([M+H]$^+$) requires 343.1441; found 343.1438 (-0.9 ppm).

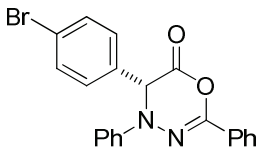
(R)-2,4-diphenyl-5-(p-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**6**

Following general procedure E, p-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**6** as a white solid (53.3 mg, 78%); $[\alpha]_D^{20}$ -603.3 (*c* 0.75, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.7 min, t_R(5*R*): 20.2 min, >99% *ee*.

5-(4-bromophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

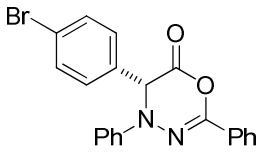


(±)-**7**

Following general procedure E, p-bromophenylacetic acid (64.5 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**7** as a white solid (41.2 mg, 51%); mp 38-40 °C; ν_{max} (KBr) 3060, 2934 (C-H), 1789 (C=O), 1597,

1486; δ_H (300 MHz, $CDCl_3$) 5.92 (1H, s, C(5)*H*), 6.92-6.97 (1H, m, Ar*H*), 7.13-7.18 (4H, m, Ar*H*), 7.22-7.28 (2H, m, Ar*H*), 7.33-7.37 (5H, m, Ar*H*), 7.86-7.89 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.1 (*C*(5)), 114.5 (*ArC*), 122.1 (*ArC*), 123.4 (4ry *ArC*), 125.6 (*ArC*), 128.4 (*ArC*), 128.6 (4ry *ArC*), 128.6 (*ArC*), 129.5 (*ArC*), 130.2 (4ry *ArC*), 130.5 (*ArC*), 132.5 (*ArC*), 141.2 (*C*(2)), 144.0 (4ry *ArC*), 160.0 (*C*(6)); *m*/*z* (NSI^+) 439 ($[M+CH_5O]^+$, 95%); HRMS (NSI^+) $C_{22}H_{20}{}^{79}BrN_2O_3^+$ ($[M+ CH_5O]^+$) requires 439.0652; found 439.0655 (+0.7 ppm).

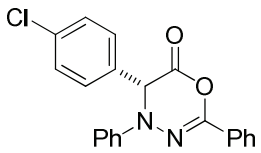
(R)-5-(4-bromophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**7**

Following general procedure E, p-bromophenylacetic acid (64.5 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**7** as a white solid (64.9 mg, 80%); $[\alpha]_D^{20}$ -572.0 (*c* 0.50, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 10.1 min, t_R(5*R*): 19.0 min, 99% *ee*.

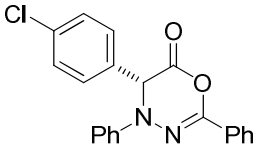
5-(4-chlorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**8**

Following general procedure D, p-chlorophenylacetic acid (51.2 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 µL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**8** as a white solid (38.9 mg, 54%); mp 40-42 °C; ν_{max} (KBr) 2933 (C-H), 1790 (C=O), 1598, 1490; δ_H (300 MHz, $CDCl_3$) 5.93 (1H, s, C(5)*H*), 6.93 (1H, t, *J* 7.2, Ar*H*), 7.13-7.28 (8H, m, Ar*H*), 7.30-7.38 (3H, m, Ar*H*), 7.84-7.90 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.0 (*C*(5)), 114.5 (*ArC*), 122.1 (*ArC*), 125.6 (*ArC*), 128.1 (*ArC*), 128.6 (4ry *ArC*), 128.6 (*ArC*), 129.5 (*ArC*), 129.6 (*ArC*), 129.6 (4ry *ArC*), 130.5 (*ArC*), 135.2 (4ry *ArC*), 141.2 (*C*(2)), 144.1 (4ry *ArC*), 160.1 (*C*(6)); *m*/*z* (NSI^+) 395 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}{}^{35}ClN_2O_3^+$ ($[M+ CH_5O]^+$) requires 395.1157; found 395.1157 (+0.0 ppm).

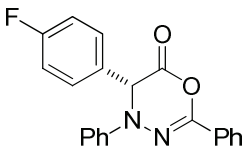
(R)-5-(4-chlorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**8**

Following general procedure E, p-chlorophenylacetic acid (51.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**8** as a white solid (47.8 mg, 66%); $[\alpha]_D^{20}$ -613.5 (*c* 0.2, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 9.2 min, t_R(5*R*): 16.9 min, >99% *ee*.

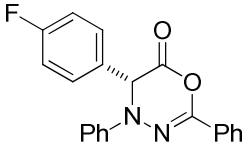
5-(4-fluorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**9**

Following general procedure D, p-fluorophenylacetic acid (46.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60**(42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1.5:98.5) (±)-**9** as a colourless oil (37.2 mg, 54%); ν_{max} (thin film) 3063, 2928 (C-H), 1791 (C=O), 1597, 1506; δ_H (400 MHz, $CDCl_3$) 5.94 (1H, s, C(5)*H*), 6.89-6.96 (3H, m, Ar*H*), 7.15-7.28 (2H, m, Ar*H*), 7.23-7.27 (4H, m, Ar*H*), 7.33-7.37 (3H, m, Ar*H*), 7.87-7.90 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 58.9 (*C*(5)), 114.5 (*ArC*), 116.4 (d, *J* 21.8, *ArC*), 122.0 (*ArC*), 125.6 (*ArC*), 126.9 (d, *J* 3.0, 4ry *ArC*), 128.5 (*ArC*), 128.6 (*ArC*), 128.7 (4ry *ArC*), 129.4 (*ArC*), 130.4 (*ArC*), 141.1 (*C*(2)), 144.1 (4ry *ArC*), 160.3 (*C*(6)), 163.1 (d, *J* 247, 4ry *ArC*); *m*/*z* (NSI^+) 379 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}FN_2O_3^+$ ($[M+ CH_5O]^+$) requires 379.1452; found 379.1454 (+0.4 ppm).

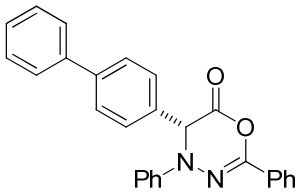
(R)-5-(4-fluorophenyl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**9**

Following general procedure E, p-fluorophenylacetic acid (46.2 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1.5:98.5) (5*R*)-**9** as a colourless oil (53.6 mg, 77%); $[\alpha]_D^{20}$ -634.2 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.5 min, t_R(5*R*): 12.7 min, >99% *ee*.

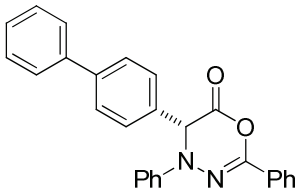
5-([1,1'-biphenyl]-4-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**10**

Following general procedure D, biphenylacetic acid (63.6 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**10** as a white solid (40.3 mg, 53%); mp 39-41 °C; ν_{max} (KBr) 3059, 2925 (C-H), 1790 (C=O), 1597, 1494; δ_H (400 MHz, $CDCl_3$) 6.01 (1H, s, C(5)*H*), 6.92-6.96 (1H, m, Ar*H*), 7.20-7.37 (12H, m, Ar*H*), 7.40-7.44 (4H, m, Ar*H*), 7.90-7.92 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.3 (*C*(5)), 114.5 (*ArC*), 121.9 (*ArC*), 125.6 (*ArC*), 127.1 (*ArC*), 127.1 (*ArC*), 127.7 (*ArC*), 128.1 (*ArC*), 128.6 (*ArC*), 128.6 (4ry *ArC*), 128.8 (*ArC*), 129.4 (*ArC*), 130.1 (4ry *ArC*), 130.3 (*ArC*), 140.1 (4ry *ArC*), 141.1 (*C*(2)), 142.0 (4ry *ArC*), 144.3 (4ry *ArC*), 160.4 (*C*(6)); *m*/*z* ($APCI^+$) 405 ($[M+H]^+$, 100%); HRMS ($APCI^+$) $C_{27}H_{21}N_2O_2^+$ ($[M+H]^+$) requires 405.1598; found 405.1591 (-1.6 ppm).

(R)-5-([1,1'-biphenyl]-4-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

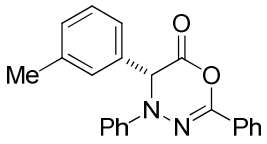


(5*R*)-**10**

Following general procedure E, biphenylacetic acid (63.6 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20

mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**10** as a white solid (70.8 mg, 88%); $[\alpha]_D^{20}$ -532.2 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 13.5 min, t_R(5*R*): 16.7 min, 98% *ee*.

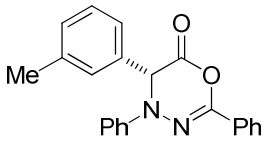
2,4-diphenyl-5-(m-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**11**

Following general procedure D, m-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**11** as a white solid (44.8 mg, 65%); mp 130-132 °C; ν_{max} (KBr) 3030, 2926 (C-H), 1789 (C=O), 1597, 1494; δ_H (400 MHz, $CDCl_3$) 2.19 (3H, s, CH_3), 5.91 (1H, s, C(5)*H*), 6.91 (1H, tt, *J* 7.2, 1.1, Ar*H*), 7.00-7.03 (2H, m, Ar*H*), 7.06-7.11 (2H, m, Ar*H*), 7.14-7.17 (2H, m, Ar*H*), 7.21-7.26 (2H, m, Ar*H*), 7.31-7.35 (3H, m, Ar*H*), 7.86-7.90 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 21.5 (CH_3), 59.5 (*C*(5)), 114.5 (*ArC*), 121.8 (*ArC*), 123.6 (*ArC*), 125.6 (*ArC*), 127.2 (*ArC*), 128.6 (*ArC*), 128.9 (4ry *ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 129.9 (*ArC*), 130.2 (*ArC*), 131.2 (4ry *ArC*), 139.3 (4ry *ArC*), 140.9 (*C*(2)), 144.3 (4ry *ArC*), 160.5 (*C*(6)); *m*/*z* ($APCI^+$) 343 ($[M+H]^+$, 92%); HRMS ($APCI^+$) $C_{22}H_{19}N_2O_2^+$ ($[M+H]^+$) requires 343.1441; found 343.1438 (-0.9 ppm).

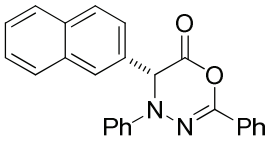
(R)-2,4-diphenyl-5-(m-tolyl)-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**11**

Following general procedure E, m-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**11** as a white solid (53.8 mg, 79%); $[\alpha]_D^{20}$ -651.6 (*c* 0.25, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 7.7 min, t_R(5*R*): 8.9 min, >99% *ee*.

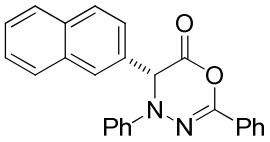
5-(naphthalen-2-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**12**

Following general procedure D, 2-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**12** as a white solid (40.3 mg, 53%); mp 40-42 °C; ν_{max} (KBr) 3058, 2935 (C-H), 1788 (C=O), 1596, 1494; δ_H (400 MHz, $CDCl_3$) 6.12 (1H, s, C(5)*H*), 6.90-6.94 (1H, m, Ar*H*), 7.20-7.27 (4H, m, Ar*H*), 7.32-7.42 (6H, m, Ar*H*), 7.64-7.74 (4H, m, Ar*H*), 7.88-7.91 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.8 (*C*(5)), 114.6 (*ArC*), 121.9 (*ArC*), 123.7 (*ArC*), 125.6 (*ArC*), 126.2 (*ArC*), 126.7 (*ArC*), 126.8 (*ArC*), 127.7 (*ArC*), 128.2 (*ArC*), 128.6 (4ry *ArC*), 128.6 (*ArC*), 128.8 (*ArC*), 129.4 (*ArC*), 129.5 (*ArC*), 130.3 (*ArC*), 133.2 (4ry *ArC*), 133.4 (4ry *ArC*), 141.1 (*C*(2)), 144.3 (4ry *ArC*), 160.4 (*C*(6)); *m/z* (APCI$^+$) 379 ([M+H]$^+$, 100%); HRMS (APCI$^+$) $C_{25}H_{19}N_2O_2^+$ ([M+H]$^+$) requires 379.1441; found 379.1433 (-2.1 ppm).

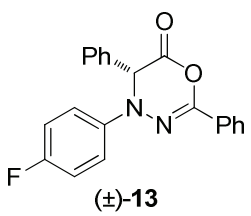
(R)-5-(naphthalen-2-yl)-2,4-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**12**

Following general procedure E, 2-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**12** as a white solid (57.6 mg, 76%); $[\alpha]_D^{20}$ -540.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 13.0 min, t_R(5*R*): 22.5 min, 99% *ee*.

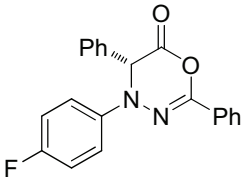
4-(4-fluorophenyl)-2,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**13**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **63** (45.4 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**13** as a white solid (49.6 mg, 72%); mp 48-50 °C; ν_{max} (thin film) 3062, 2924 (C-H), 1791 (C=O), 1600, 1506; δ_H (400 MHz, $CDCl_3$) 5.88 (1H, s, C(5)*H*), 6.90-6.95 (2H, m, Ar*H*), 7.08-7.12 (2H, m, Ar*H*), 7.20-7.26 (5H, m, Ar*H*), 7.31-7.35 (3H, m, Ar*H*), 7.85-7.87 (2H, m, Ar*H*); δ_C (75 MHz, $CDCl_3$) 59.9 (*C*(5)), 116.0 (d, *J* 22.6, *ArC*), 116.0 (d, *J* 7.7, *ArC*), 125.6 (*ArC*), 126.7 (*ArC*), 128.6 (*ArC*), 128.7 (4ry *ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 130.4 (*ArC*), 131.0 (4ry *ArC*), 140.7 (d, *J* 2.1, 4ry *ArC*), 141.1 (*C*(2)), 158.4 (d, *J* 240, 4ry *ArC*), 160.3 (*C*(6)); *m*/*z* (NSI^+) 379 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}FN_2O_3^+$ ($[M+CH_5O]^+$) requires 379.1452; found 379.1450 (-0.7 ppm).

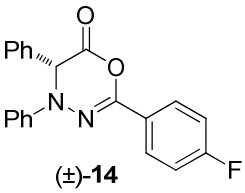
(R)-4-(4-fluorophenyl)-2,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**13**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **63** (45.4 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**13** as a white solid (56.7 mg, 82%); $[\alpha]_D^{20}$ -604.2 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 11.9 min, t_R(5*R*): 16.5 min, >99% *ee*.

2-(4-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

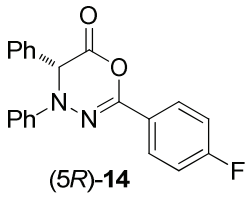


(±)-**14**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **64** (45.4 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**14** as a colourless oil

(48.5 mg, 70%); ν_{max} (thin film) 3064, 2920 (C-H), 1790 (C=O), 1597, 1496; δ_H (300 MHz, $CDCl_3$) 5.96 (1H, s, C(5)*H*), 6.89-6.94 (1H, m, Ar*H*), 6.98-7.04 (2H, m, Ar*H*), 7.13-7.17 (2H, m, Ar*H*), 7.20-7.28 (7H, m, Ar*H*), 7.83-7.89 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.5 (*C*(5)), 114.4 (*ArC*), 115.8 (d, *J* 21.9, *ArC*), 121.9 (*ArC*), 125.0 (d, *J* 3.2, 4ry *ArC*), 126.6 (*ArC*), 127.7 (d, *J* 8.4, *ArC*), 129.1 (*ArC*), 129.4 (*ArC*), 129.4 (*ArC*), 131.1 (4ry *ArC*), 140.4 (*C*(2)), 144.2 (4ry *ArC*), 160.2 (*C*(6)), 164.0 (d, *J* 250, 4ry *ArC*); *m*/*z* (NSI^+) 379 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}FN_2O_3^+$ ($[M+CH_5O]^+$) requires 379.1452; found 379.1456 (+0.9 ppm).

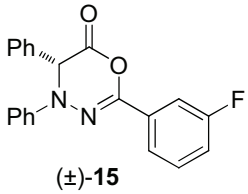
(R)-2-(4-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**14**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **64** (45.4 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**14** as a colourless oil (60.9 mg, 88%); $[\alpha]_D^{20}$ -609.2 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 9.9 min, t_R(5*R*): 18.6 min, 99% *ee*.

2-(3-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

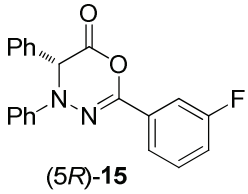


(±)-**15**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **65** (45.4 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**15** as a colourless oil (39.4 mg, 57%); ν_{max} (thin film) 3062 (C-H), 1792 (C=O), 1597, 1498; δ_H (400 MHz, $CDCl_3$) 5.96 (1H, s, C(5)*H*), 6.91-6.95 (1H, m, Ar*H*), 7.02 (1H, tdd, *J* 8.3, 2.6, 0.9, Ar*H*), 7.14-7.17 (2H, m, Ar*H*), 7.20-7.31 (8H, m, Ar*H*), 7.56-7.59 (1H, m, Ar*H*), 7.63-7.65 (1H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.5 (*C*(5)), 112.6 (d, *J* 24.4, *ArC*), 114.6 (*ArC*), 117.2 (d, *J* 21.4, *ArC*), 121.2 (d, *J* 2.7, *ArC*), 122.2 (*ArC*), 126.6 (*ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 129.4 (*ArC*), 130.2

(d, *J* 8.1, *ArC*), 131.0 (d, *J* 5.6, 4ry *ArC*), 131.0 (4ry *ArC*), 139.9 (4ry *ArC*), 144.1 (4ry *ArC*), 160.0 (*C*(6)), 162.9 (d, *J* 245, 4ry *ArC*); *m*/*z* (NSI^+) 379 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}FN_2O_3^+$ ($[M+CH_5O]^+$) requires 379.1452; found 379.1456 (+0.9 ppm).

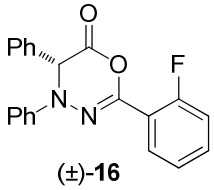
(R)-2-(3-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**15**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **65** (45.4 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**15** as a colourless oil (52.5 mg, 76%); $[\alpha]_D^{20}$ -608.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 8.1 min, t_R(5*R*): 10.5 min, 99% *ee*.

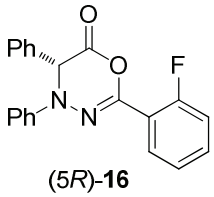
2-(3-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**16**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **66** (45.4 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**16** as a colourless oil (40.3 mg, 58%); ν_{max} (thin film) 3064 (C-H), 2925, 1791 (C=O), 1597, 1495; δ_H (300 MHz, $CDCl_3$) 5.99 (1H, s, C(5)*H*), 6.92 (1H, tt, *J* 6.9, 1.4, Ar*H*), 7.04-7.12 (2H, m, Ar*H*), 7.16-7.34 (10H, m, Ar*H*), 7.69 (1H, td, *J* 7.7, 1.7, Ar*H*); δ_C (75 MHz, $CDCl_3$) 59.6 (*C*(5)), 114.5 (*ArC*), 117.0 (d, *J* 28.8, *ArC*), 117.3 (d, *J* 12.8, 4ry *ArC*), 122.1 (*ArC*), 124.1 (d, *J* 5.1, *ArC*), 126.7 (*ArC*), 128.7 (*ArC*), 129.1 (*ArC*), 129.4 (*ArC*), 129.4 (*ArC*), 131.1 (4ry *ArC*), 131.7 (d, *J* 11.2, *ArC*), 137.7 (d, *J* 9.1, 4ry *ArC*), 144.2 (4ry *ArC*), 160.2 (*C*(6)), 160.3 (d, *J* 342, 4ry *ArC*); *m*/*z* (NSI^+) 379 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}FN_2O_3^+$ ($[M+CH_5O]^+$) requires 379.1452; found 379.1456 (+0.9 ppm).

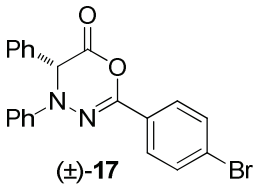
(R)-2-(2-fluorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**16**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **66** (45.4 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**16** as a colourless oil (48.5 mg, 70%); $[\alpha]_D^{20}$ -599.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 10.4 min, t_R(5*R*): 13.0 min, 99% *ee*.

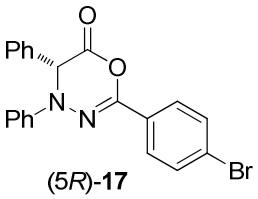
2-(4-bromophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**17**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **67** (57.8 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**17** as a white solid (51.4 mg, 63%); mp 44-46 °C; ν_{max} (KBr) 3062 (C-H), 1789 (C=O), 1597, 1497; δ_H (300 MHz, $CDCl_3$) 5.95 (1H, s, C(5)*H*), 6.89-6.95 (1H, m, Ar*H*), 7.13-7.27 (9H, m, Ar*H*), 7.42-7.47 (2H, m, Ar*H*), 7.70-7.75 (2H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 59.5 (*C*(5)), 114.5 (*ArC*), 122.1 (*ArC*), 124.7 (4ry *ArC*), 126.6 (*ArC*), 127.0 (*ArC*), 127.8 (4ry *ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 129.4 (*ArC*), 131.0 (4ry *ArC*), 131.8 (*ArC*), 140.3 (*C*(2)), 144.1 (4ry *ArC*), 160.1 (*C*(6)); *m*/*z* (NSI^+) 439 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}{}^{79}BrN_2O_3^+$ ($[M+CH_5O]^+$) requires 439.0652; found 439.0655 (+0.7 ppm).

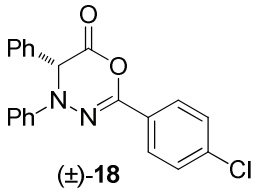
(R)-2-(4-bromophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**17**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **67** (57.8 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**17** as an off-white solid (63.3 mg, 78%); $[\alpha]_D^{20}$ -609.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 12.8 min, t_R(5*R*): 24.1 min, >99% *ee*.

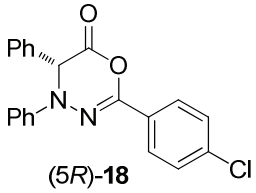
2-(4-chlorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**18**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **68** (48.9 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**18** as an off-white solid (48.9 mg, 67%); mp 80-82 °C; ν_{max} (KBr) 2966 (C-H), 1777 (C=O), 1595, 1497; δ_H (300 MHz, $CDCl_3$) 5.95 (1H, s, C(5)*H*), 6.89-6.95 (1H, m, Ar*H*), 7.13-7.32 (11H, m, Ar*H*), 7.77-7.82 (2H, m, Ar*H*); δ_C (75 MHz, $CDCl_3$) 59.5 (*C*(5)), 114.5 (*ArC*), 122.1 (*ArC*), 126.6 (*ArC*), 126.8 (*ArC*), 127.3 (4ry *ArC*), 128.9 (*ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 129.4 (*ArC*), 131.1 (4ry *ArC*), 136.4 (4ry *ArC*), 140.2 (*C*(2)), 144.1 (4ry *ArC*), 160.1 (*C*(6)); *m*/*z* (NSI^+) 395 ($[M+CH_5O]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}ClN_2O_3^+$ ($[M+CH_5O]^+$) requires 395.1157; found 395.1158 (+0.3 ppm).

(R)-2-(4-chlorophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one

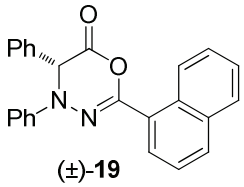


(5*R*)-**18**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **68** (48.9 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**18** as an off-white solid (56.3 mg, 78%); $[\alpha]_D^{20}$ -

614.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 11.5 min, t_R(5*R*): 22.8 min, >99% *ee*.

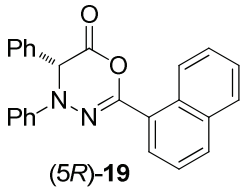
2-(4-bromophenyl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(±)-**19**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), diazene **69** (52.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (±)-**19** as an off-white solid (45.5 mg, 60%); mp 138-140 °C; ν_{max} (KBr) 3063 (C-H), 1791 (C=O), 1599, 1506; δ_H (400 MHz, $CDCl_3$) 6.05 (1H, s, C(5)*H*), 6.93 (1H, tt, *J* 6.9, 1.4, Ar*H*), 7.20-7.28 (7H, m, Ar*H*), 7.33-7.40 (3H, m, Ar*H*), 7.44 (1H, ddd, *J* 8.0, 6.9, 1.2, Ar*H*), 7.51 (1H, ddd, *J* 8.5, 6.9, 1.6, Ar*H*), 7.78-7.83 (2H, m, Ar*H*), 7.86 (1H, dd, *J* 7.4, 1.2, Ar*H*), 8.80-8.82 (1H, m, Ar*H*); δ_C (75 MHz, $CDCl_3$) 59.5 (*C*(5)), 114.6 (*ArC*), 122.1 (*ArC*), 124.9 (*ArC*), 125.4 (4ry *ArC*), 125.8 (*ArC*), 126.3 (*ArC*), 126.8 (4ry *ArC*), 127.4 (*ArC*), 127.5 (*ArC*), 128.9 (*ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 129.5 (*ArC*), 130.3 (4ry *ArC*), 131.2 (4ry *ArC*), 131.4 (*ArC*), 134.1 (4ry *ArC*), 141.5 (*C*(2)), 144.5 (4ry *ArC*), 160.6 (*C*(6)); *m*/*z* (NSI^+) 397 ($[M+H_3O]^+$, 100%); HRMS (NSI^+) $C_{25}H_{21}N_2O_3^+$ ($[M+H_3O]^+$) requires 397.1547; found 397.1548 (+0.3 ppm).

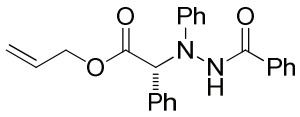
(R)-2-(naphthalen-1-yl)-4,5-diphenyl-4H-1,3,4-oxadiazin-6(5H)-one



(5*R*)-**19**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and p-methoxybenzoyl chloride (77 mg, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **69** (52.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 1:99) (5*R*)-**19** as an off-white solid (53.5 mg, 71%); $[\alpha]_D^{20}$ -611.5 (*c* 1.0, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (2% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(5*S*): 15.7 min, t_R(5*R*): 16.9 min, >99% *ee*.

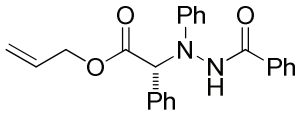
allyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-phenylacetate



(±)-**20**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of allyl alcohol (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 91:9) of (±)-**20** as a colourless oil (48.6 mg, 63%); ν_{max} (thin film) 3287 (N-H), 3064, 2948 (C-H), 1733 (C=O), 1683 (C=O), 1599; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 4.75 (2H, d, *J* 5.1, CH_2), 5.26-5.32 (2H, m, CH_2=CH), 5.87-5.93 (2H, m, C(2)*H* and CH_2=C*H*), 6.98-7.06 (3H, m, Ar*H*), 7.31-7.43 (7H, m, Ar*H*), 7.48-7.59 (5H, m, Ar*H*), 8.51 (1H, s, N*H*); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 5.61 (1H, s, C(2)*H*), 7.98 (1H, s, N*H*); Data for major rotamer δ_C (100 MHz, $CDCl_3$) 66.2 (*C*H_2), 66.8 (*C*(2)), 114.9 (*ArC*), 119.6 (*C*H_2=CH), 121.7 (*ArC*), 127.0 (*ArC*), 128.6 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 129.1 (*ArC*), 129.4 (*ArC*), 131.2 (CH_2=*C*H), 131.7 (*ArC*), 133.0 (4ry *ArC*), 133.2 (4ry *ArC*), 148.3 (4ry *ArC*), 166.5 (*C*=O), 172.3 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 65.8 (*C*H_2), 68.1 (*C*(2)), 115.4 (*ArC*), 122.3 (*ArC*), 127.8 (*ArC*), 129.8 (*ArC*), 130.2 (*ArC*); *m*/*z* (NSI^+) 387 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{24}H_{23}N_2O_3^+$ ($[M+H]^+$) requires 387.1703; found 387.1711 (+2.0 ppm).

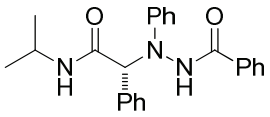
(R)-allyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-phenylacetate



(2*R*)-**20**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of allyl alcohol (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 91:9) of (2*R*)-**20** as a colourless oil (63.8 mg, 83%); $[\alpha]_D^{20}$ -30.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*R*): 18.1 min, t_R(2*S*): 21.8 min, 98% *ee*.

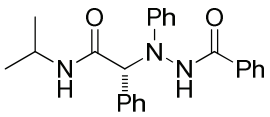
2-(2-benzoyl-1-phenylhydrazinyl)-N-isopropyl-2-phenylacetamide



(±)-**21**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of isopropylamine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 75:25) a rotameric mixture (ratio 93:7) of (±)-**21** as a white solid (53.4 mg, 69%); mp 64-66 °C; ν_{max} (KBr) 3235 (N-H), 3064, 2971 (C-H), 1653 (C=O), 1598; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 1.15 (3H, d, *J* 6.6, C*H*$_3$), 1.21-1.26 (3H, m, C*H*$_3$), 4.13 (1H, s, *J* 6.5, C*H*), 5.29 (1H, s, C(2)*H*), 6.85 (2H, d, *J* 6.8, Ar*H*), 7.00 (1H, t, *J* 7.3, Ar*H*), 7.20-7.35 (11H, m, Ar*H*), 7.50 (1H, t, *J* 7.3, Ar*H*), 7.59 (1H, s, N*H*), 9.38 (1H, s, N*H*); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 1.04 (6H, d, *J* 6.6, C*H*$_3$), 3.96-4.03 (1H, m, C*H*); Data for major rotamer δ_C (100 MHz, $CDCl_3$) 22.4 (*C*H$_3$), 22.5 (*C*H$_3$), 41.6 (*C*H), 72.0 (*C*(2)), 112.5 (*ArC*), 120.7 (*ArC*), 127.0 (*ArC*), 128.7 (*ArC*), 128.9 (*ArC*), 129.0 (*ArC*), 129.5 (*ArC*), 129.7 (*ArC*), 132.0 (4ry *ArC*), 132.3 (*ArC*), 134.2 (4ry *ArC*), 147.3 (4ry *ArC*), 168.9 (*C*=O), 169.5 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 22.6 (*C*H$_3$), 41.5 (*C*H); *m*/*z* (NSI$^+$) 388 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{24}H_{26}N_3O_2^+$ ([M+H]$^+$) requires 388.2020; found 388.2027 (+1.9 ppm).

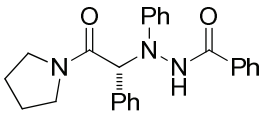
(R)-2-(2-benzoyl-1-phenylhydrazinyl)-N-isopropyl-2-phenylacetamide



(2*R*)-**21**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of pyrrolidine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 75:25) a rotameric mixture (ratio 93:7) of (2*R*)-**21** as a white solid (71.0 mg, 92%); $[\alpha]_D^{20}$ -132 (*c* 0.125, CH_2Cl_2); Chiral HPLC Chiralpak IB (20% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 6.6 min, t_R(2*R*): 7.6 min, 99% *ee*.

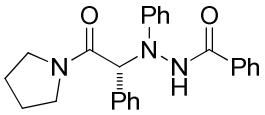
N'-(2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)-N'-phenylbenzohydrazide



(±)-**22**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of pyrrolidine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O) a rotameric mixture (ratio 96:4) of (±)-**22** as a colourless oil (71.3 mg, 89%); ν_{max} (thin film) 3344 (N-H), 3063 (C-H), 1687 (C=O), 1582; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 1.74-1.92 (4H, m, 2CH_2), 3.07-3.10 (1H, m, C*H*H), 3.42-3.54 (3H, m, CH_2 and CH*H*), 5.77 (1H, s, C(2)*H*), 6.85-6.93 (3H, m, Ar*H*), 7.19-7.27 (7H, m, Ar*H*), 7.36 (1H, t, *J* 7.1, Ar*H*), 7.45 (2H, d, *J* 7.1, Ar*H*), 7.50 (2H, d, *J* 7.4, Ar*H*), 9.41 (1H, s, N*H*); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 5.44 (1H, s, C(2)*H*), 8.65 (1H, s, N*H*); Data for major rotamer δ_C (100 MHz, $CDCl_3$) 24.1 (*C*H_2), 26.1 (*C*H_2), 45.8 (*C*H_2), 46.3 (*C*H_2), 65.7 (*C*(2)), 114.9 (*ArC*), 121.4 (*ArC*), 127.1 (*ArC*), 128.4 (*ArC*), 128.7 (*ArC*), 128.8 (*ArC*), 129.4 (*ArC*), 129.5 (*ArC*), 131.5 (*ArC*), 133.2 (4ry *ArC*), 133.4 (4ry *ArC*), 149.2 (4ry *ArC*), 166.4 (*C*=O), 170.7 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 23.9 (*C*H_2), 26.0 (*C*H_2), 67.7 (*C*(2)), 115.7 (*ArC*), 121.8 (*ArC*), 126.9 (*ArC*), 127.8 (*ArC*), 129.7 (*ArC*), 130.5 (*ArC*); *m/z* (NSI^+) 400 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{25}H_{26}N_3O_2^+$ ($[M+H]^+$) requires 400.2020; found 400.2026 (+1.6 ppm).

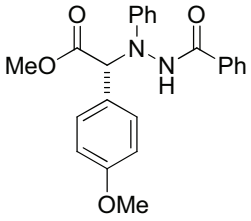
(R)-N'-(2-oxo-1-phenyl-2-(pyrrolidin-1-yl)ethyl)-N'-phenylbenzohydrazide



(2*R*)-**22**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of pyrrolidine (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O) a rotameric mixture (ratio 96:4) of (2*R*)-**22** as a colourless oil (69.7 mg, 87%); $[\alpha]_D^{20}$ -96.6 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 6.3 min, t_R(2*R*): 11.1 min, 99% *ee*.

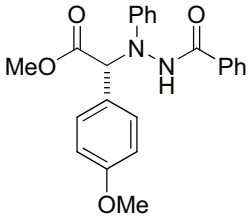
methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(4-methoxyphenyl)acetate



(±)-**23**

Following general procedure D, 4-methoxyphenylacetic acid (49.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 35:65) a rotameric mixture (ratio 89:11) of (±)-**23** as a light yellow solid (58.3 mg, 75%); mp 36-38 °C; ν_{max} (KBr) 3368 (N-H), 3060, 2952 (C-H), 1734 (C=O), 1675 (C=O), 1612, 1514; Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.66 (3H, s, C*H*$_3$), 3.71 (3H, s, C*H*$_3$), 5.75 (1H, s, C(2)*H*), 6.75-6.79 (2H, m, Ar*H*), 6.85-6.95 (3H, m, Ar*H*), 7.18-7.24 (2H, m, Ar*H*), 7.26-7.34 (4H, m, Ar*H*), 7.36-7.42 (1H, m, Ar*H*), 7.48-7.52 (2H, m, Ar*H*), 8.43 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.60 (3H, s, C*H*$_3$), 3.71 (3H, s, C*H*$_3$), 5.45 (1H, s, C(2)*H*), 6.56-6.59 (2H, m, Ar*H*), 7.85 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 52.5 (*C*H$_3$), 55.2 (*C*H$_3$), 66.1 (*C*(2)), 114.0 (*ArC*), 114.8 (*ArC*), 121.6 (*ArC*), 125.2 (4ry *ArC*), 127.1 (*ArC*), 128.6 (*ArC*), 129.5 (*ArC*), 130.4 (*ArC*), 131.8 (*ArC*), 133.0 (4ry *ArC*), 148.4 (4ry *ArC*), 159.9 (4ry *ArC*), 166.6 (*C*=O), 173.3 (*C*=O); Selected data for minor rotamer δ_C (75 MHz, $CDCl_3$) 52.4 (*C*H$_3$), 55.4 (*C*H$_3$), 67.2 (*C*(2)), 115.3 (*ArC*), 122.2 (*ArC*), 127.8 (*ArC*), 129.9 (*ArC*), 131.4 (*ArC*); *m*/*z* (NSI$^+$) 391 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{23}H_{23}N_2O_4^+$ ([M+H]$^+$) requires 391.1652; found 391.1655 (+0.7 ppm).

(R)-methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(4-methoxyphenyl)acetate

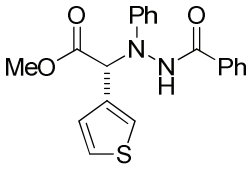


(2*R*)-**23**

Following general procedure E, 4-methoxyphenylacetic acid (49.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2

mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 30:70) a rotameric mixture (ratio 89:11) of (2*R*)-**23** as a light yellow oil (59.3 mg, 76%); $[\alpha]_D^{20}$ -30.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 19.3 min, t_R(2*R*): 26.2 min, 98% *ee*.

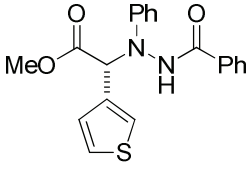
methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(thiophen-3-yl)acetate



(±)-**24**

Following general procedure D, thiophene-3-acetic acid (42.7 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **60** (42.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) a rotameric mixture (ratio 92:8) of (±)-**24** as a light yellow solid (67.2 mg, 92%); mp 128-130 °C; ν_{max} (KBr) 3355 (N-H), 3078, 2952 (C-H), 1727 (C=O), 1685 (C=O), 1600, 1514; Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.72 (3H, s, C*H*$_3$), 5.83 (1H, s, C(2)*H*), 6.87-6.95 (3H, m, Ar*H*), 7.16-7.23 (4H, m, Ar*H*), 7.28-7.33 (3H, m, Ar*H*), 7.38-7.42 (1H, m, Ar*H*), 7.49-7.51 (2H, m, Ar*H*), 8.47 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.59 (3H, s, C*H*$_3$), 5.56 (1H, s, C(2)*H*), 6.57 (1H, dd, *J* 5.0, 1.3, Ar*H*), 7.89 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 52.6 (*C*H$_3$), 62.7 (*C*(2)), 114.8 (*ArC*), 121.8 (*ArC*), 125.0 (*ArC*), 126.3 (*ArC*), 127.1 (*ArC*), 128.2 (*ArC*), 128.7 (*ArC*), 129.5 (*ArC*), 131.9 (*ArC*), 133.0 (4ry *ArC*), 133.8 (4ry *ArC*), 148.1 (4ry *ArC*), 166.8 (*C*=O), 173.0 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 52.5 (*C*H$_3$), 62.8 (*C*(2)), 115.4 (*ArC*), 122.3 (*ArC*), 126.1 (*ArC*), 127.8 (*ArC*), 129.9 (*ArC*), 130.6 (*ArC*); *m*/*z* (NSI$^+$) 367 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{20}H_{19}N_2O_3S^+$ ([M+H]$^+$) requires 367.1111; found 367.1114 (+0.8 ppm).

(R)-methyl 2-(2-benzoyl-1-phenylhydrazinyl)-2-(thiophen-3-yl)acetate

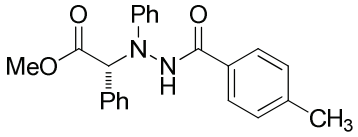


(2*R*)-**24**

Following general procedure E, thiophene-3-acetic acid (42.7 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **60** (42.0 mg, 0.20

mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent EtOAc:petrol 25:75) a rotameric mixture (ratio 91:9) of (2*R*)-**24** as a light yellow oil (63.1 mg, 86%); $[\alpha]_D^{20}$ -26.2 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 28.0 min, t_R(2*R*): 31.5 min, >99% *ee*.

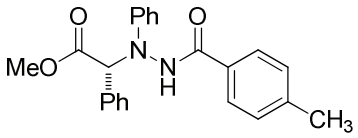
methyl 2-(2-(4-methylbenzoyl)-1-phenylhydrazinyl)-2-phenylacetate



(±)-**25**

Following general procedure D, phenylacetic acid (81.7 mg, 0.60 mmol), DIPEA (156 μL, 0.90 mmol) and benzoyl chloride (104 μL, 0.90 mmol) in DCM (2 mL), diazene **71** (44.8 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 2 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 92:8) of (±)-**25** as a white solid (66.0 mg, 88%); mp 36-38 °C; ν_{max} (KBr) 3374 (N-H), 3030, 2924 (C-H), 1750 (C=O), 1708 (C=O), 1599; Data for major rotamer δ_H (400 MHz, $CDCl_3$) 2.28 (3H, s, C*H*$_3$), 3.73 (3H, s, C*H*$_3$), 5.80 (1H, s, C(2)*H*), 6.86-6.95 (3H, m, Ar*H*), 7.08 (2H, d, *J* 7.9, Ar*H*), 7.19-7.27 (5H, m, Ar*H*), 7.34-7.39 (4H, m, Ar*H*), 8.40 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 2.18 (3H, s, C*H*$_3$), 3.61 (3H, s, C*H*$_3$), 5.51 (1H, s, C(2)*H*), 6.70-6.80 (2H, m, Ar*H*), 7.84 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 21.5 (*C*H$_3$), 52.5 (*C*H$_3$), 66.7 (*C*(2)), 114.8 (*ArC*), 121.6 (*ArC*), 127.1 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 129.1 (*ArC*), 129.2 (*ArC*), 129.5 (*ArC*), 130.0 (4ry *ArC*), 133.3 (4ry *ArC*), 142.3 (4ry *ArC*), 148.5 (4ry *ArC*), 166.5 (*C*=O), 173.1 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 22.7 (*C*H$_3$), 52.4 (*C*H$_3$), 68.0 (*C*(2)), 115.4 (*ArC*), 122.2 (*ArC*), 127.8 (*ArC*), 128.0 (*ArC*), 129.8 (*ArC*), 130.2 (*ArC*); *m*/*z* (NSI^+) 375 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{23}H_{23}N_2O_3^+$ ($[M+H]^+$) requires 375.1703; found 375.1706 (+0.7 ppm).

(R)-methyl 2-(2-(4-methylbenzoyl)-1-phenylhydrazinyl)-2-phenylacetate

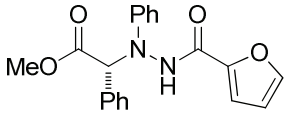


(2*R*)-**25**

Following general procedure E, phenylacetic acid (81.7 mg, 0.60 mmol), DIPEA (156 μL, 0.90 mmol) and benzoyl chloride (104 μL, 0.90 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **71** (44.8 mg, 0.20 mmol) and

DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 92:8) of (2*R*)-**25** as a white solid (49.2 mg, 66%); $[\alpha]_D^{20}$ -24.3 (*c* 1.0, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 11.9 min, t_R(2*R*): 14.3 min, >99% *ee*.

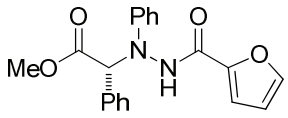
methyl 2-(2-(furan-2-carbonyl)-1-phenylhydrazinyl)-2-phenylacetate



(±)-**26**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78.0 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.90 mmol) in DCM (2 mL), diazene **72** (40.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 93:7) of (±)-**26** as a white solid (50.3 mg, 72%); mp 148-150 °C; ν_{max} (KBr) 3345 (N-H), 3097, 2950 (C-H), 1729 (C=O), 1695 (C=O), 1598; Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.72 (3H, s, C*H*$_3$), 5.77 (1H, s, C(2)*H*), 6.36 (1H, dd, *J* 3.5, 1.8, Ar*H*), 6.86-6.96 (4H, m, Ar*H*), 7.18-7.24 (5H, m, Ar*H*), 7.34-7.38 (3H, m, Ar*H*), 8.67 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.65 (3H, s, C*H*$_3$), 5.65 (1H, s, C(2)*H*), 6.14 (1H, dd, *J* 3.5, 1.7, Ar*H*), 7.82 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 52.5 (*C*H$_3$), 66.7 (*C*(2)), 112.0 (*ArC*), 115.0 (*ArC*), 115.5 (*ArC*), 121.8 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 129.2 (*ArC*), 129.4 (*ArC*), 133.1 (4ry *ArC*), 144.4 (4ry *ArC*), 146.6 (4ry *ArC*), 148.4 (4ry *ArC*), 157.2 (*C*=O), 172.7 (*C*=O); Selected data for minor rotamer δ_C (75 MHz, $CDCl_3$) 52.5 (*C*H$_3$), 67.6 (*C*(2)), 112.0 (*ArC*), 115.2 (*ArC*), 117.2 (*ArC*), 122.4 (*ArC*), 128.5 (*ArC*), 129.8 (*ArC*), 130.0 (*ArC*), 144.9 (*ArC*); *m*/*z* (NSI$^+$) 351 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{20}H_{19}N_2O_4^+$ ([M+H]$^+$) requires 351.1339; found 351.1339 (-0.1 ppm).

(R)-methyl 2-(2-(furan-2-carbonyl)-1-phenylhydrazinyl)-2-phenylacetate

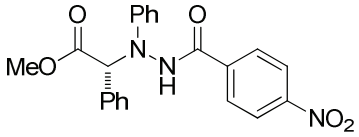


(2*R*)-**26**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78.0 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **72** (40.0 mg, 0.20 mmol) and

DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 93:7) of (2*R*)-**26** as a white solid (59.5 mg, 85%); $[\alpha]_D^{20}$ -38.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 16.2 min, t_R(2*R*): 21.5 min, 99% *ee*.

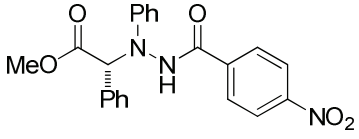
methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-phenylacetate



(±)-**27**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 69:31) of (±)-**27** as a light yellow solid (66.0 mg, 81%); mp 58-56 °C; ν_{max} (KBr) 3412 (N-H), 3075, 2953 (C-H), 1735 (C=O), 1678 (C=O), 1599, 1525 (N-O), 1346 (N-O); Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.74 (3H, s, C*H*$_3$), 5.81 (1H, s, C(2)*H*), 6.91-6.95 (3H, m, Ar*H*), 7.21-7.28 (5H, m, Ar*H*), 7.35-7.39 (2H, m, Ar*H*), 7.55-7.58 (2H, m, Ar*H*), 8.10-8.13 (2H, m, Ar*H*), 8.62 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.61 (3H, s, C*H*$_3$), 5.46 (1H, s, C(2)*H*), 7.77-7.80 (2H, m, Ar*H*), 8.12 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 52.6 (*C*H$_3$), 66.8 (*C*(2)), 114.9 (*ArC*), 122.1 (*ArC*), 123.8 (*ArC*), 128.3 (*ArC*), 128.7 (*ArC*), 129.1 (*ArC*), 129.1 (*ArC*), 129.6 (*ArC*), 133.1 (4ry *ArC*), 138.5 (4ry *ArC*), 148.0 (4ry *ArC*), 148.6 (4ry *ArC*), 164.8 (*C*=O), 173.1 (*C*=O); Selected data for minor rotamer δ_C (75 MHz, $CDCl_3$) 52.6 (*C*H$_3$), 68.4 (*C*(2)), 115.8 (*ArC*), 122.3 (*ArC*), 123.0 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 130.1 (*ArC*), 130.3 (*ArC*), 132.4 (4ry *ArC*), 138.6 (4ry *ArC*), 149.7 (4ry *ArC*), 171.4 (*C*=O), 171.5 (*C*=O); *m*/*z* (NSI^+) 406 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{22}H_{20}N_3O_5^+$ ($[M+H]^+$) requires 406.1397; found 406.1399 (+0.4 ppm).

(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-phenylacetate

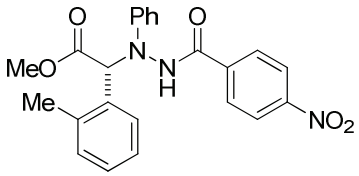


(2*R*)-**27**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea

catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **70** (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 69:31) of (2*R*)-**27** as a light yellow solid (67.8 mg, 84%); $[\alpha]_D^{20}$ -47.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 20.9 min, t_R(2*R*): 30.6 min, 99% *ee*.

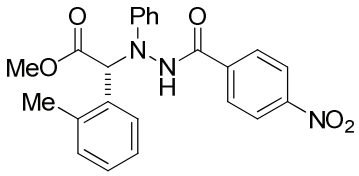
methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(o-tolyl)acetate



(±)-**28**

Following general procedure D, o-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 55:45) of (±)-**28** as a light yellow solid (63.0 mg, 75%); mp 56-58 °C; ν_{max} (KBr) 3333 (N-H), 3085, 2962 (C-H), 1721 (C=O), 1679 (C=O), 1598, 1529 (N-O), 1348 (N-O); Data for both rotamers δ_H (400 MHz, $CDCl_3$) 1.69 (3H, s, C*H*$_3$), 2.53 (3H, s, C*H*$_3$), 3.60 (3H, s, C*H*$_3$), 3.73 (3H, s, C*H*$_3$), 5.64 (1H, s, C(2)*H*), 5.91 (1H, s, C(2)*H*), 6.74-6.76 (1H, m, Ar*H*), 6.82-6.85 (2H, m, Ar*H*), 6.90-7.07 (7H, m, Ar*H*), 7.12-7.21 (6H, m, Ar*H*), 7.23-7.27 (2H, m, Ar*H*), 7.36-7.40 (2H, m, Ar*H*), 7.55-7.58 (2H, m, Ar*H*), 7.79-7.82 (2H, m, Ar*H*), 8.10-8.13 (2H, m, Ar*H*), 8.18 (1H, s, N*H*), 8.50 (1H, s, N*H*); Data for both rotamers δ_C (100 MHz, $CDCl_3$) 18.5 (*C*H$_3$), 19.2 (*C*H$_3$), 52.5 (*C*H$_3$), 52.6 (*C*H$_3$), 63.8 (*C*(2)), 65.2 (*C*(2)), 114.3 (*ArC*), 115.5 (*ArC*), 121.7 (*ArC*), 122.3 (*ArC*), 123.0 (*ArC*), 123.8 (*ArC*), 125.5 (*ArC*), 126.7 (*ArC*), 127.7 (*ArC*), 128.2 (*ArC*), 128.4 (*ArC*), 129.3 (*ArC*), 129.6 (*ArC*), 129.7 (*ArC*), 129.9 (*ArC*), 130.2 (*ArC*), 130.8 (*ArC*), 130.8 (4ry *ArC*), 131.2 (*ArC*), 131.3 (4ry *ArC*), 138.2 (4ry *ArC*), 138.6 (4ry *ArC*), 138.7 (4ry *ArC*), 139.8 (4ry *ArC*), 148.0 (4ry *ArC*), 148.6 (4ry *ArC*), 14.8.8 (4ry *ArC*), 149.7 (4ry *ArC*), 164.7 (*C*=O), 171.7 (C=O), 171.9 (C=O), 173.6 (*C*=O); *m*/*z* (NSI^+) 442 ($[M+Na]^+$, 42%); HRMS (NSI^+) $C_{23}H_{21}N_3NaO_5^+$ ($[M+Na]^+$) requires 442.1373; found 442.1375 (+0.4 ppm).

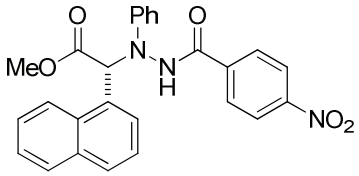
(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(o-tolyl)acetate



(2*R*)-**28**

Following general procedure E, o-tolylacetic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **70** (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 55:45) of (2*R*)-**28** as a light yellow solid (67.7 mg, 81%); $[\alpha]_D^{20}$ -30.0 (*c* 0.25, CH_2Cl_2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 11.7 min, t_R(2*R*): 16.1 min, 99% *ee*.

methyl 2-(naphthalen-1-yl)-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate

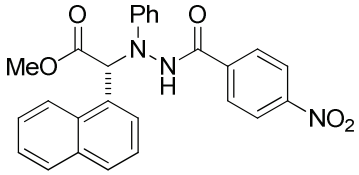


(±)-**29**

Following general procedure D, 1-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 78:22) of (±)-**29** as a light yellow solid (68.0 mg, 75%); mp 74-76 °C; ν_{max} (KBr) 3415 (N-H), 3062, 2953 (C-H), 1735 (C=O), 1670 (C=O), 1599, 1522 (N-O), 1344 (N-O); Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.66 (3H, s, C*H*$_3$), 6.30 (1H, s, C(2)*H*), 6.53-6.56 (2H, m, Ar*H*), 6.96-7.00 (1H, m, Ar*H*), 7.10 (1H, t, *J* 7.3, Ar*H*), 7.16-7.19 (1H, m, Ar*H*), 7.23-7.32 (6H, m, Ar*H*), 7.41-7.47 (3H, m, Ar*H*), 7.59 (1H, d, *J* 8.1, Ar*H*), 7.75-7.79 (1H, m, Ar*H*), 8.16 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.76 (3H, s, C*H*$_3$), 6,52 (1H, s, C(2)*H*), 7.03-7.05 (2H, m, Ar*H*), 8.04-8.07 (2H, m, Ar*H*), 8.18 (1H, d, *J* 8.7, Ar*H*), 8.57 (1H, s, N*H*); Data for both rotamers δ_C (100 MHz, $CDCl_3$) 52.7 (*C*H$_3$), 52.7 (*C*H$_3$), 63.5 (*C*(2)), 63.9 (*C*(2)), 114.5 (*ArC*), 115.0 (*ArC*), 122.0 (*ArC*), 122.1 (*ArC*), 122.1 (*ArC*), 122.9 (*ArC*), 123.7 (*ArC*), 123.7 (*ArC*), 124.3 (*ArC*), 125.3 (*ArC*), 125.8 (*ArC*), 126.2 (*ArC*), 126.6 (*ArC*), 126.8 (*ArC*), 127.3 (*ArC*), 127.4 (*ArC*), 127.4 (*ArC*), 128.2 (4ry *ArC*), 128.5 (*ArC*), 128.7 (*ArC*), 128.7

(*ArC*), 129.3 (4ry *ArC*), 129.8 (*ArC*), 130.4 (*ArC*), 130.4 (*ArC*), 130.5 (*ArC*), 131.7 (4ry *ArC*), 132.3 (4ry *ArC*), 133.6 (4ry *ArC*), 133.8 (4ry *ArC*), 137.5 (4ry *ArC*), 138.5 (4ry *ArC*), 148.0 (4ry *ArC*), 148.0 (4ry *ArC*), 148.5 (4ry *ArC*), 149.6 (4ry *ArC*), 164.3 (*C*=O), 171.6 (C=O), 172.0 (C=O), 173.5 (*C*=O); *m/z* (NSI^+) 478 ([M+Na]$^+$, 97%); HRMS (NSI^+) $C_{26}H_{21}N_3NaO_5^+$ ([M+Na]$^+$) requires 478.1373; found 478.1377 (+0.7 ppm).

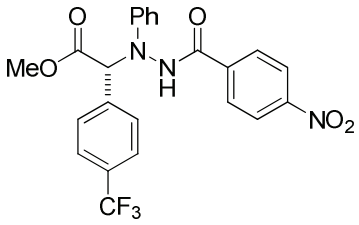
(R)-methyl 2-(naphthalen-1-yl)-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate



(2*R*)-**29**

Following general procedure E, 1-naphthylacetic acid (55.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **70** (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 78:22) of (2*R*)-**29** as a light yellow solid (72.0 mg, 79%); $[\alpha]_D^{20}$ +20.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 13.2 min, t_R(2*R*): 29.0 min, 99% *ee*.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(4-(trifluoromethyl)phenyl)acetate

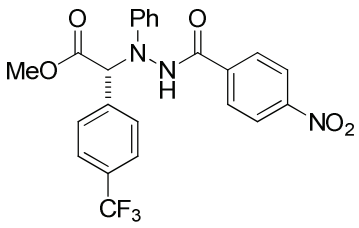


(±)-**30**

Following general procedure D, 4-trifluoromethylphenylacetic acid (61.3 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 74:26) of (±)-**30** as a light yellow solid (74.0 mg, 78%); mp 150-152 °C; ν_{max} (KBr) 3412 (N-H), 3085, 2956 (C-H), 1735 (C=O), 1680 (C=O), 1600, 1524 (N-O), 1323 (N-O); Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.77 (3H, s, C*H*$_3$), 5.83 (1H, s, C(2)*H*), 6.93-6.97 (2H, m, Ar*H*), 7.23-7.28 (2H, m, Ar*H*), 7.34-7.41 (1H, m, Ar*H*), 7.52 (4H, s, Ar*H*), 7.58-7.61 (2H, m,

Ar*H*), 8.11-8.15 (2H, m, Ar*H*), 8.71 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.65 (3H, s, CH_3), 5.12 (1H, s, C(2)*H*), 6.90-6.92 (2H, m, Ar*H*), 7.03-7.10 (3H, m, Ar*H*), 7.15-7.18 (2H, m, Ar*H*), 7.78-7.81 (2H, m, Ar*H*), 8.17 (1H, s, N*H*); Data for both rotamers δ_C (100 MHz, $CDCl_3$) 52.8 (*C*H_3), 52.9 (*C*H_3), 66.4 (*C*(2)), 67.9 (*C*(2)), 115.1 (*ArC*), 115.8 (*ArC*), 122.4 (*ArC*), 122.6 (*ArC*), 123.4 (*ArC*), 123.9 (*ArC*), 125.1 (4ry *ArC*), 125.6 (q, *J* 3.6, *ArC*), 125.7 (q, *J* 3.6, *ArC*), 128.2 (*ArC*), 128.6 (*ArC*), 129.4 (*ArC*), 129.7 (*ArC*), 130.2 (*ArC*), 130.6 (*ArC*), 131.0 (4ry *ArC*), 131.3 (4ry *ArC*), 136.4 (4ry *ArC*), 137.3 (4ry *ArC*), 138.1 (4ry *ArC*), 147.7 (4ry *ArC*), 148.2 (4ry *ArC*), 148.8 (4ry *ArC*), 149.9 (4ry *ArC*), 164.6 (*C*=O), 170.7 (C=O), 171.1 (C=O), 172.5 (*C*=O); *m/z* (NSI^+) 396 ($[M+Na]^+$, 65%); HRMS (NSI^+) $C_{23}H_{18}F_3N_3NaO_5^+$ ($[M+Na]^+$) requires 496.1091; found 496.1094 (+0.7 ppm).

(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(4-(trifluoromethyl)phenyl)acetate

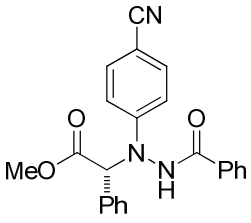


(2*R*)-**30**

Following general procedure E, 4-trifluoromethylphenylacetic acid (61.3 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S,*3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **70** (51.0 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 74:26) of (2*R*)-**30** as a light yellow solid (78.5 mg, 83%); $[\alpha]_D^{20}$ -26.6 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (80% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 40 °C) t_R(2*S*): 7.5 min, t_R(2*R*): 17.8 min, 97% *ee*.

* Enantiomeric excess was 92% when methanolysis carried out at rt. When the product is re-subjected to the reaction conditions at rt the ee drops with time.

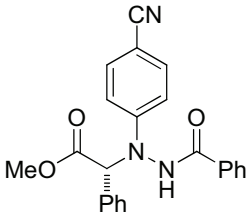
methyl 2-(2-benzoyl-1-(4-cyanophenyl)hydrazinyl)-2-phenylacetate



(±)-**31**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **75** (47.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 60:00) a rotameric mixture (ratio 94:6) of (±)-**31** as a white solid (52.5 mg, 68%); mp 72-74 °C; ν_{max} (KBr) 3412 (N-H), 2954 (C-H), 2220 (C≡N), 1748 (C=O), 1684 (C=O), 1604, 1508; Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.76 (3H, s, C*H*$_3$), 5.83 (1H, s, C(2)*H*), 6.89-6.94 (2H, m, Ar*H*), 7.21-7.49 (12H, m, Ar*H*), 8.37 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.65 (3H, s, C*H*$_3$), 5.56 (1H, s, C(2)*H*), 6.78 (2H, dd, *J* 8.2, 1.0, Ar*H*), 7.81 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 52.9 (*C*H$_3$), 66.4 (*C*(2)), 103.7 (4ry *ArC*), 114.1 (*ArC*), 119.4 (*C*≡N), 127.0 (*ArC*), 128.7 (*ArC*), 128.8 (*ArC*), 129.3 (*ArC*), 129.4 (*ArC*), 132.0 (4ry *ArC*), 132.1 (4ry *ArC*), 132.2 (*ArC*), 133.8 (*ArC*), 151.5 (4ry *ArC*), 166.4 (*C*=O), 172.2 (*C*=O); Selected data for minor rotamer δ_C (75 MHz, $CDCl_3$) 52.9 (*C*H$_3$), 67.5 (*C*(2)), 115.2 (*ArC*), 127.3 (*ArC*), 127.5 (*ArC*), 130.4 (*ArC*), 134.2 (*ArC*); *m*/*z* (NSI$^+$) 386 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{23}H_{20}N_3O_3^+$ ([M+H]$^+$) requires 386.1499; found 386.1502 (+0.7 ppm).

(R)-methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-phenylacetate

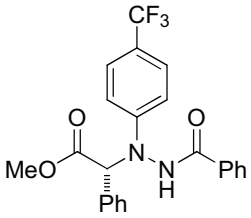


(2*R*)-**31**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **75** (47.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 60:40) a rotameric mixture (ratio 94:6) of (2*R*)-**31** as a white solid (71.5 mg, 93%); $[\alpha]_D^{20}$ -46.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (80% IPA:hexane, flow rate 1 mL min^{-1}, 254 nm, 40 °C) t_R(2*R*): 5.8 min, t_R(2*S*): 12.9 min, 98% *ee*.

* Enantiomeric excess was 91% when methanolysis carried out at rt. When the product is re-subjected to the reaction conditions at rt the ee drops with time.

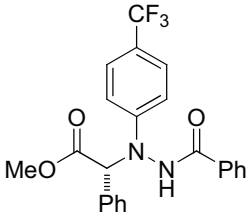
methyl 2-(2-benzoyl-1-(4-(trifluoromethyl)phenyl)hydrazinyl)-2-phenylacetate



(±)-**32**

Following general procedure D, phenylacetic acid (204 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), diazene **78** (278 mg, 1.00 mmol), DHPB **80** (38.0 mg, 0.20 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 1 h at rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 30:70) a rotameric mixture (ratio 94:6) of (±)-**32** as a white solid (278 mg, 65%); mp 120-122 °C; ν_{max} (KBr) 3392 (N-H), 2952 (C-H), 1738 (C=O), 1682 (C=O), 1616; Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.82 (3H, s, C*H*$_3$), 5.97 (1H, s, C(2)*H*), 7.07 (2H, d, *J* 8.6, Ar*H*), 7.32-7.38 (5H, m, Ar*H*), 7.47-7.58 (7H, m, Ar*H*), 8.67 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.72 (3H, s, C*H*$_3$), 5.70 (1H, s, C(2)*H*), 8.04 (1H, s, N*H*); Data for major rotamer δ_C (75 MHz, $CDCl_3$) 52.7 (*C*H$_3$), 66.8 (*C*(2)), 114.0 (*ArC*), 122.8 (q, *J* 32.9, 4ry *ArC*), 124.5 (q, *J* 269, *C*F$_3$), 126.8 (q, *J* 3.5, *ArC*), 127.1 (*ArC*), 128.7 (*ArC*), 128.7 (*ArC*), 129.2 (*ArC*), 129.3 (*ArC*), 132.1 (*ArC*), 132.4 (4ry *ArC*), 132.7 (4ry *ArC*), 151.0 (4ry *ArC*), 166.6 (*C*=O), 172.4 (*C*=O); Selected data for minor rotamer δ_C (75 MHz, $CDCl_3$) 52.7 (*C*H$_3$), 67.8 (*C*(2)), 114.9 (*ArC*), 127.3 (*ArC*), 127.7 (*ArC*), 130.3 (*ArC*), 130.8 (*ArC*); *m*/*z* (NSI^+) 429 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{23}H_{20}F_3N_2O_3^+$ ($[M+H]^+$) requires 429.1421; found 429.1422 (+0.3 ppm).

(R)-methyl 2-(2-benzoyl-1-(4-(trifluoromethyl)phenyl)hydrazinyl)-2-phenylacetate

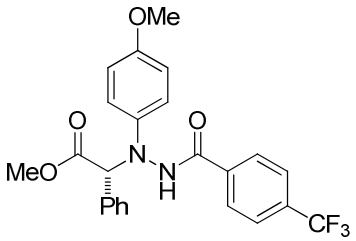


(2*R*)-**32**

Following general procedure E, phenylacetic acid (204 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (3.08 mg, 0.01 mmol, 1 mol%), diazene **78** (278 mg, 1.00 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 16 h at -78 °C followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 30:70) a rotameric mixture (ratio 94:6) of (2*R*)-**32** as a white solid (336 mg, 86%); $[\alpha]_D^{20}$ -48.6 (*c* 0.5,

CH_2Cl_2); Chiral HPLC Chiralpak IA (30% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*R*): 9.0 min, t_R(2*S*): 15.5 min, 99% *ee*.

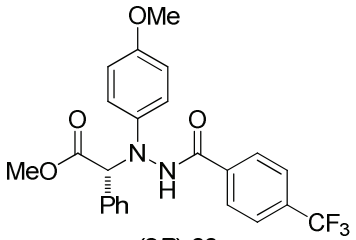
methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-phenylacetate



(±)-**33**

Following general procedure D, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **79** (61.6 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 76:24) of (±)-**33** as a light yellow oil (69.3 mg, 76%); ν_{max} (thin film) 3283 (N-H), 2955 (C-H), 1737 (C=O), 1674 (C=O), 1511; Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.69 (3H, s, CH_3), 3.72 (3H, s, CH_3), 5.69 (1H, s, C(2)*H*), 6.77-6.79 (2H, m, Ar*H*), 6.93-6.95 (2H, m, Ar*H*), 7.07-7.11 (1H, m, Ar*H*), 7.21-7.28 (3H, m, Ar*H*), 7.37-7.39 (1H, m, Ar*H*), 7.54 (4H, m, Ar*H*), 8.63 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.60 (3H, s, CH_3), 3.75 (3H, s, CH_3), 5.32 (1H, s, C(2)*H*), 6.87-6.92 (2H, m, Ar*H*), 8.15 (1H, s, N*H*); Data for both rotamers δ_C (100 MHz, $CDCl_3$) 52.4 (*C*H_3), 52.5 (*C*H_3) 55.6 (*C*H_3), 55.6 (*C*H_3), 67.7 (*C*(2)), 69.3 (*C*(2)), 114.7 (*ArC*), 115.1 (*ArC*), 117.3 (*ArC*), 117.7 (*ArC*), 124.0 (q, *J* 3.8, *ArC*), 125.6 (q, *J* 3.5, *ArC*), 127.5 (*ArC*), 128.1 (*ArC*), 128.7 (*ArC*), 128.8 (*ArC*), 128.9 (*ArC*), 129.0 (*ArC*), 129.0 (*ArC*), 130.0 (*ArC*), 131.7 (4ry *ArC*), 132.6 (4ry *ArC*), 133.2 (4ry *ArC*), 133.5 (4ry *ArC*), 136.2 (4ry *ArC*), 136.4 (4ry *ArC*), 142.0 (4ry *ArC*), 142.4 (4ry *ArC*), 155.2 (4ry *ArC*), 158.9 (4ry *ArC*), 165.3 (*C*=O), 171.6 (*C*=O), 172.3 (*C*=O), 173.3 (*C*=O); *m*/*z* (NSI^+) 459 ($[M+H]^+$, 100%); HRMS (NSI^+) $C_{24}H_{22}F_3N_2O_4^+$ ($[M+H]^+$) requires 459.1526; found 459.1520 (-1.3 ppm).

(R)-methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-phenylacetate



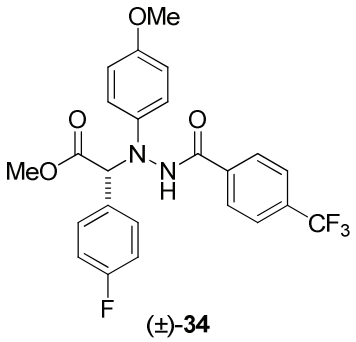
(2*R*)-**33**

Following general procedure E, phenylacetic acid (40.9 mg, 0.30 mmol), DIPEA (78 µL, 0.45 mmol) and benzoyl chloride (52.2 µL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **79** (61.6 mg, 0.20 mmol) and DIPEA (52 µL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 76:24) of (2*R*)-**33** as a light yellow oil (68.8 mg, 75%); $[\alpha]_D^{20}$ -34.6 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (50% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*R*): 19.0 min, t_R(2*S*): 34.7 min, 99% *ee*.

Scale-up:

Following general procedure E, phenylacetic acid (1.33 g, 9.74 mmol), DIPEA (2.53 mL, 14.6 mmol) and benzoyl chloride (1.70 mL, 14.6 mmol) in DCM (40 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (20.0 mg, 0.065 mmol, 1 mol%), diazene **79** (2.00 g, 6.49 mmol) and DIPEA (1.69 mL, 9.74 mmol) for 16 h at -78 °C rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 76:24) of (2*R*)-**33** as a light yellow oil (2.83 g, 95%); 99% *ee*.

methyl 2-(4-fluorophenyl)-2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)acetate

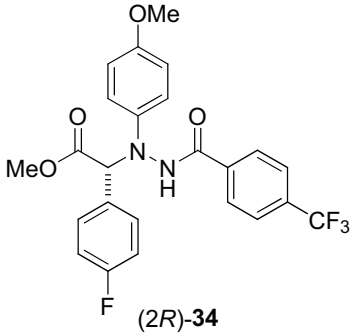


(±)-**34**

Following general procedure D, 4-fluorophenylacetic acid (231 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), diazene

79 (308 mg, 1.00 mmol), DHPB **80** (38.0 mg, 0.20 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 1 h at rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 81:19) of (±)-**34** as a white solid (347 mg, 73%); mp 68-70 °C; ν_{max} (KBr) 3363 (N-H), 2956 (C-H), 1741 (C=O), 1674 (C=O), 1513; Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.75 (3H, s, C*H*$_3$), 3.78 (3H, s, C*H*$_3$), 5.77 (1H, s, C(2)*H*), 6.86 (2H, d, *J* 9.0, Ar*H*), 6.98-7.05 (4H, m, Ar*H*), 7.47 (2H, dd, *J* 8.4, 5.3, Ar*H*), 7.59 (2H, d, *J* 8.2, Ar*H*), 7.66 (2H, d, *J* 8.2, Ar*H*), 8.96 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.68 (3H, s, C*H*$_3$), 3.81 (3H, s, C*H*$_3$), 5.43 (1H, s, C(2)*H*), 7.19 (2H, d, *J* 9.0 Ar*H*), 7.36 (2H, d, *J* 8.1, Ar*H*), 8.29 (1H, s, N*H*); Data for both rotamers δ_C (75 MHz, $CDCl_3$) 52.4 (*C*H$_3$), 52.5 (*C*H$_3$), 55.4 (*C*H$_3$), 55.5 (*C*H$_3$), 67.1 (*C*(2)), 68.5 (*C*(2)), 114.7 (*ArC*), 115.1 (*ArC*), 115.7 (d, *J* 21.7, *ArC*), 115.7 (d, *J* 21.7, *ArC*), 117.6 (*ArC*), 117.7 (*ArC*), 123.6 (q, *J* 271, *C*F$_3$), 124.0 (q, *J* 3.5, *ArC*), 125.6 (q, *J* 3.6, *ArC*), 127.6 (*ArC*), 128.2 (*ArC*), 128.7 (d, *J* 3.2, 4ry *ArC*), 129.6 (d, *J* 3.2, 4ry *ArC*), 130.8 (d, *J* 8.3, *ArC*), 131.9 (d, *J* 8.5, *ArC*), 133.4 (q, *J* 32.5, 4ry *ArC*), 136.2 (4ry *ArC*), 136.2 (4ry *ArC*), 141.9 (4ry *ArC*), 142.1 (4ry *ArC*), 155.3 (4ry *ArC*), 155.7 (4ry *ArC*), 162.8 (d, *J* 247, 4ry *ArC*), 162.8 (d, *J* 248 4ry *ArC*), 165.4 (*C*=O), 171.7 (*C*=O), 172.0 (*C*=O), 172.9 (*C*=O); *m/z* (NSI$^+$) 477 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{24}H_{21}F_4N_2O_4^+$ ([M+H]$^+$) requires 477.1432; found 477.1420 (-2.5 ppm).

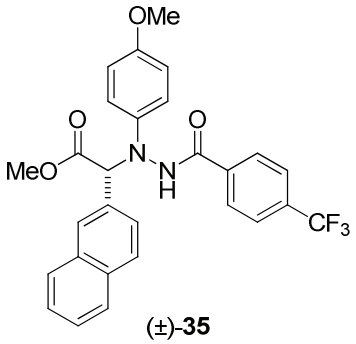
(R)-methyl 2-(4-fluorophenyl)-2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)acetate



(2*R*)-**34**

Following general procedure E, 4-fluorophenylacetic acid (231 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (3.08 mg, 0.01 mmol, 1 mol%), diazene **79** (308 mg, 1.00 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 16 h at -78 °C followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 79:21) of (2*R*)-**34** as a white solid (377 mg, 79%); $[\alpha]_D^{20}$ -43.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (50% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 17.0 min, t_R(2*R*): 26.4 min, 99% *ee*.

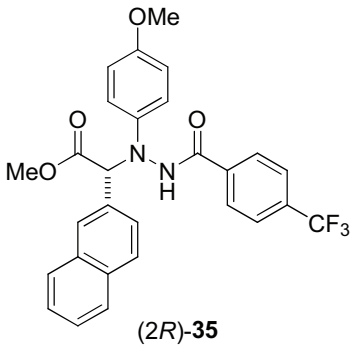
methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-(naphthalen-2-yl)acetate



(±)-**35**

Following general procedure D, 2-naphthylacetic acid (279 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), diazene **79** (308 mg, 1.00 mmol), DHPB **80** (38.0 mg, 0.20 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 1 h at rt followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 45:55) a rotameric mixture (ratio 75:25) of (±)-**35** as a light yellow solid (302 mg, 59%); mp 74-76 °C; ν_{max} (KBr) 3414 (N-H), 2954 (C-H), 1735 (C=O), 1670 (C=O), 1510; Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.79 (3H, s, C*H*$_3$), 3.85 (3H, s, C*H*$_3$), 6.03 (1H, s, C(2)*H*), 6.92 (2H, d, *J* 9.0, Ar*H*), 7.16 (2H, d, *J* 9.1, Ar*H*), 7.48-7.59 (6H, m, Ar*H*), 7.73-7.93 (5H, m, Ar*H*), 9.07 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.76 (3H, s, C*H*$_3$), 3.85 (3H, s, C*H*$_3$), 5.68 (1H, s, C(2)*H*), 6.77 (2H, d, *J* 8.1 Ar*H*), 7.04 (2H, d, *J* 9.0, Ar*H*), 7.29 (2H, d, *J* 9.0, Ar*H*), 7.66 (2H, d, *J* 8.3, Ar*H*), 8.42 (1H, s, N*H*); Data for both rotamers δ_C (75 MHz, $CDCl_3$) 52.5 (*C*H$_3$), 52.6 (*C*H$_3$), 55.5 (*C*H$_3$), 55.6 (*C*H$_3$), 68.1 (*C*(2)), 69.2 (*C*(2)), 114.7 (*ArC*), 115.2 (*ArC*), 117.6 (*ArC*), 117.8 (*ArC*), 123.8 (q, *J* 3.5, *ArC*), 125.5 (q, *J* 3.6, *ArC*), 126.5 (*ArC*), 126.6 (*ArC*), 126.7 (*ArC*), 126.7 (*ArC*), 126.7 (*ArC*), 126.8 (*ArC*), 127.2 (*ArC*), 127.5 (*ArC*), 127.8 (*ArC*), 127.9 (*ArC*), 128.1 (*ArC*), 128.2 (*ArC*), 128.2 (*ArC*), 128.4 (*ArC*), 128.6 (*ArC*), 129.9 (4ry *ArC*), 130.1 (*ArC*), 131.3 (4ry *ArC*), 133.0 (4ry *ArC*), 133.1 (4ry *ArC*), 133.3 (4ry *ArC*), 133.4 (4ry *ArC*), 136.0 (4ry *ArC*), 136.4 (4ry *ArC*), 142.2 (4ry *ArC*), 142.4 (4ry *ArC*), 155.3 (4ry *ArC*), 155.6 (4ry *ArC*), 165.5 (*C*=O), 171.7 (*C*=O), 172.1 (*C*=O), 173.1 (*C*=O); *m*/*z* (NSI$^+$) 509 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{28}H_{24}F_3N_2O_4^+$ ([M+H]$^+$) requires 509.1683; found 509.1680 (-0.5 ppm).

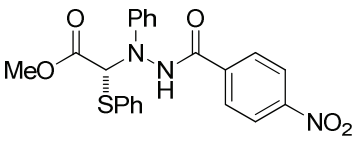
(R)-methyl 2-(1-(4-methoxyphenyl)-2-(4-(trifluoromethyl)benzoyl)hydrazinyl)-2-(naphthalen-2-yl)acetate



(2*R*)-**35**

Following general procedure E, 2-naphthylacetic acid (279 mg, 1.50 mmol), DIPEA (0.39 mL, 2.25 mmol) and benzoyl chloride (0.26 mL, 2.25 mmol) in DCM (10 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (3.08 mg, 0.01 mmol, 1 mol%), diazene **79** (308 mg, 1.00 mmol) and DIPEA (0.26 mL, 1.5 mmol) for 16 h at -78 °C followed by addition of MeOH (10 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 45:55) a rotameric mixture (ratio 70:30) of (2*R*)-**35** as a light yellow solid (408 mg, 80%); $[\alpha]_D^{20}$ -75.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (20% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 20 °C) t_R(2*S*): 12.5 min, t_R(2*R*): 14.5 min, 98% *ee*.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(phenylthio)acetate

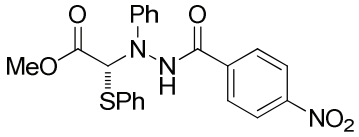


(±)-**36**

Following general procedure D, (phenylthio)acetic acid (50.5 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and DIPEA (52 μL, 0.3 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 87:13) of (±)-**36** as an orange oil (62.8 mg, 72%); ν_{max} (Diamond Cell) 3269 (N-H), 3061, 2953 (C-H), 1736 (C=O), 1682 (C=O), 1597, 1523 (N-O), 1348 (N-O); Data for major rotamer δ_H (300 MHz, $CDCl_3$) 3.70 (3H, s, C*H*$_3$), 5.69 (1H, s, C(2)*H*), 6.82-6.91 (3H, m, Ar*H*), 7.13-7.25 (5H, m, Ar*H*), 7.60-7.64 (2H, m, Ar*H*), 7.95-8.00 (2H, m, Ar*H*), 8.22-8.25 (2H, m, Ar*H*), 8.81 (1H, s, N*H*); Selected data for minor rotamer δ_H (300 MHz, $CDCl_3$) 3.57 (3H, s, C*H*$_3$), 5.60 (1H, s, C(2)*H*), 7.50 (2H, d, *J* 8.8, Ar*H*), 7.83 (2H, d, *J* 8.8, Ar*H*), 8.17 (1H, s, N*H*); Data for major rotamer δ_C (100 MHz, $CDCl_3$) 53.1 (*C*H$_3$), 72.1 (*C*(2)), 115.7 (*ArC*), 122.7 (*ArC*), 124.0 (*ArC*), 128.8 (*ArC*), 129.1 (*ArC*), 129.4 (*ArC*), 129.5 (*ArC*), 132.6 (4ry *ArC*), 133.7 (*ArC*), 138.6 (4ry *ArC*),

146.8 (4ry *ArC*), 150.0 (4ry *ArC*), 165.2 (*C*=O), 169.7 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 53.1 (*C*H_3), 72.3 (*C*(2)), 116.4 (*ArC*), 122.8 (*ArC*), 123.8 (*ArC*), 127.3 (*ArC*), 127.8 (*ArC*), 130.2 (*ArC*), 139.4 (4ry *ArC*), 147.5 (4ry *ArC*), 168.6 (*C*=O), 172.4 (*C*=O); *m/z* (ES^+) 460 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{22}H_{19}N_3NaO_5S^+$ ($[M+Na]^+$) requires 460.0943; found 460.0932 (-2.4 ppm).

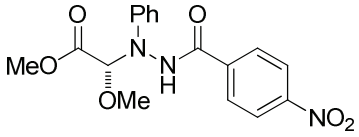
(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-2-(phenylthio)acetate



(2*R*)-**36**

Following general procedure E, (phenylthio)acetic acid (50.5 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (0.62 mg, 0.002 mmol, 1 mol%), diazene **70** (51.0 mg, 0.20 mmol) and DIPEA (52 μL, 0.3 mmol) for 16 h at -78 °C followed by addition of MeOH (2 mL) and stirring for 1 h at -78 °C gave, after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 87:13) of (2*R*)-**36** as an orange oil (72.7 mg, 83%); $[\alpha]_D^{20}$ +5.0 (*c* 0.2, CH_2Cl_2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*R*): 13.1 min, t_R(2*S*): 20.2 min, 98% *ee*.

methyl 2-methoxy-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate

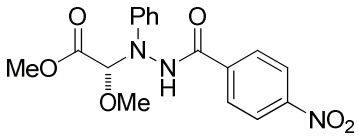


(±)-**37**

Following general procedure D, methoxyacetic acid (23.0 μL, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 70:30) a rotameric mixture (ratio 94:6) of (±)-**37** as an orange solid (38.9 mg, 54%); mp 122-124 °C; ν_{max} (Diamond Cell) 3278 (N-H), 3071, 2960 (C-H), 1748 (C=O), 1676 (C=O), 1597, 1525 (N-O), 1346 (N-O); Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.56 (3H, s, C*H*$_3$), 3.73 (3H, s, C*H*$_3$), 5.28 (1H, s, C(2)*H*), 6.93-7.00 (3H, m, Ar*H*), 7.22-7.26 (2H, m, Ar*H*), 7.93-7.96 (2H, m, Ar*H*), 8.21-8.24 (2H, m, Ar*H*), 8.41 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.45 (3H, s, C*H*$_3$), 3.67 (3H, s, C*H*$_3$), 4.93 (1H, s, C(2)*H*); Data for major rotamer δ_C (100 MHz, $CDCl_3$) 53.0 (*C*H_3), 57.5 (*C*H_3), 89.3 (*C*(2)), 115.8 (*ArC*), 122.8 (*ArC*), 124.0 (*ArC*), 128.7 (*ArC*), 129.5 (*ArC*), 138.4

(4ry *ArC*), 146.2 (4ry *ArC*), 150.0 (4ry *ArC*), 165.2 (*C*=O), 168.3 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 53.4 (*C*H_3), 90.7 (*C*(2)), 114.0 (*ArC*), 121.9 (*ArC*), 127.3 (*ArC*); *m*/*z* (ES^+) 382 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{17}H_{17}N_3NaO_6^+$ ($[M+Na]^+$) requires 382.1015; found 382.1023 (+2.0 ppm).

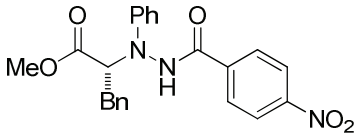
(R)-methyl 2-methoxy-2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)acetate



(2*R*)-**37**

Following general procedure E, methoxyacetic acid (23.0 μL, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (6.16 mg, 0.02 mmol, 10 mol%), diazene **70** (51.0 mg, 0.20 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 16 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 70:30) a rotameric mixture (ratio 95:5) of (2*R*)-**37** as an orange solid (38.7 mg, 54%); $[\alpha]_D^{20}$ +15.5 (*c* 0.2, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (20% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 22.4 min, t_R(2*R*): 24.7 min, 83% *ee*.

methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-3-phenylpropanoate

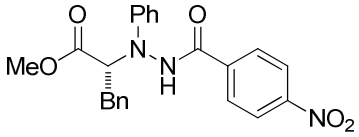


(±)-**38**

Following general procedure D, 3-phenylpropionic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52 μL, 0.45 mmol) in DCM (2 mL), diazene **70** (51.0 mg, 0.20 mmol), DHPB **80** (7.60 mg, 0.04 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 1 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 35:65) a rotameric mixture (ratio 90:10) of (±)-**38** as a light yellow solid (44.3 mg, 53%); mp 42-44 °C; ν_{max} (Diamond Cell) 3279 (N-H), 3065, 2943 (C-H), 1728 (C=O), 1686 (C=O), 1597, 1522 (N-O), 1344 (N-O); Data for major rotamer δ_H (400 MHz, $CDCl_3$) 3.10 (1H, dd, *J* 13.6, 8.2, C*H*H), 3.39 (1H, dd, *J* 13.6, 6.1, CH*H*), 3.52 (3H, s, CH_3), 4.71 (1H, dd, *J* 8.2, 6.1 C*H*), 6.83-6.92 (3H, m, Ar*H*), 7.16-7.26 (7H, m, Ar*H*), 7.99-8.02 (2H, m, Ar*H*), 8.26-8.29 (2H, m, Ar*H*), 8.86 (1H, s, N*H*); Selected data for minor rotamer δ_H (400 MHz, $CDCl_3$) 3.47 (3H, s, CH_3), 7.42 (2H, d, *J* 8.9, Ar*H*), 8.20 (1H, s, N*H*); Data for major rotamer δ_C (100 MHz, $CDCl_3$) 37.1 (*C*H_2), 52.1 (*C*H_3), 65.2 (*C*(2)), 115.3 (*ArC*), 122.3 (*ArC*), 124.1 (*ArC*), 127.2 (*ArC*), 128.6 (*ArC*), 128.7 (*ArC*), 129.2

(*ArC*), 129.5 (*ArC*), 136.5 (4ry *ArC*), 138.2 (4ry *ArC*), 147.9 (4ry *ArC*), 150.1 (4ry *ArC*), 164.8 (*C*=O), 174.2 (*C*=O); Selected data for minor rotamer δ_C (100 MHz, $CDCl_3$) 35.6 (CH_2), 52.1 (CH_3), 66.3 (*C*(2)), 116.4 (*ArC*), 122.8 (*ArC*), 128.2 (*ArC*), 128.5 (*ArC*), 130.0 (*ArC*); *m*/*z* (ES^+) 442 ($[M+Na]^+$, 100%); HRMS (ES^+) $C_{23}H_{21}N_3NaO_5^+$ ($[M+Na]^+$) requires 442.1379; found 442.1363 (-3.6 ppm).

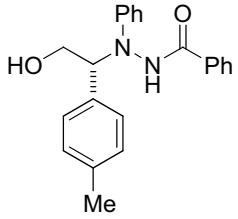
(R)-methyl 2-(2-(4-nitrobenzoyl)-1-phenylhydrazinyl)-3-phenylpropanoate



(2*R*)-**38**

Following general procedure E, 3-phenylpropionic acid (45.1 mg, 0.30 mmol), DIPEA (78 μL, 0.45 mmol) and benzoyl chloride (52.2 μL, 0.45 mmol) in DCM (2 mL), Ph/*i*-Pr isothiourea catalyst (2*S*,3*R*)-**5** (6.16 mg, 0.02 mmol, 10 mol%), diazene **70** (51.0 mg, 0.20 mmol) and PS-BEMP (227 mg, 0.5 mmol) for 16 h at rt followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave, after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 90:10) of (2*R*)-**38** as a light yellow solid (51.8 mg, 62%); $[\alpha]_D^{20}$ -28.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*R*): 9.8 min, t_R(2*S*): 18.1 min, 99% *ee*.

N'-(2-hydroxy-1-(p-tolyl)ethyl)-N'-phenylbenzohydrazide

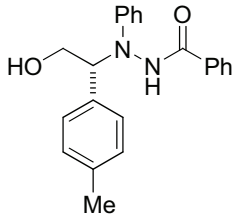


(±)-**39**

To a solution of (±)-**6** (68.4 mg, 0.20 mmol) in THF (1 mL) was added 2M $LiAlH_4$ (1.0 mL, 2.0 mmol) and the reaction mixture was allowed to stir at rt for 10 mins. The reaction mixture was quenched by addition of sat. aq. NH_4Cl and extracted with Et_2O. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Chromatographic purification (eluent Et_2O:petrol 60:40) gave (±)-**39** as a white solid (67.8 mg, 98%); mp 148-150 °C; ν_{max} (KBr) 3551 (O-H), 3412 (N-H), 2933 (C-H), 1662 (C=O), 1597, 1497; δ_H (500 MHz, $CDCl_3$) 2.23 (3H, s, C*H*$_3$), 3.78 (1H, td, *J* 11.7, 3.6, C(2)*H*H), 3.94 (1H, t, *J* 10.5, C(2)H*H*), 4.61 (1H, br s, O*H*), 5.18 (1H, d, *J* 7.2, C(1)*H*)), 6.82 (1H, t, *J* 7.3, Ar*H*), 6.94 (2H, d, *J* 8.1, Ar*H*), 7.02-7.05 (4H, m, Ar*H*), 7.17-7.20 (2H, m, Ar*H*), 7.41 (2H, t, *J* 7.6 Ar*H*), 7.51 (1H, t, *J* 7.4, Ar*H*), 7.74 (2H, d, *J* 7.6, Ar*H*); δ_C (125 MHz, $CDCl_3$) 21.1 (*C*H$_3$), 61.2 (*C*(2)), 65.2 (*C*(1)), 114.2 (*ArC*),

120.6 (*ArC*), 127.3 (*ArC*), 127.5 (*ArC*), 129.0 (*ArC*), 129.5 (*ArC*), 129.7 (*ArC*), 131.8 (4ry *ArC*), 132.4 (4ry *ArC*), 132.7 (*ArC*), 138.3 (4ry *ArC*), 148.6 (4ry *ArC*), 168.7 (*C*=O); *m*/*z* (NSI$^+$) 347 ([M+H]$^+$, 35%); HRMS (NSI$^+$) $C_{22}H_{23}N_2O_2^+$ ([M+H]$^+$) requires 347.1754; found 347.1760 (+1.7 ppm).

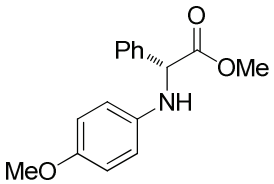
(R)-N'-(2-hydroxy-1-(p-tolyl)ethyl)-N'-phenylbenzohydrazide



(1*R*)-**39**

To a solution of (2*R*)-**6** (33.9 mg, 0.10 mmol) in THF (1 mL) was added 2M $LiAlH_4$ (0.5 mL, 1.0 mmol) and the reaction mixture was allowed to stir at rt for 10 mins. The reaction mixture was quenched by addition of sat. aq. NH_4Cl and extracted with Et_2O. The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. Chromatographic purification (eluent Et_2O:petrol 60:40) gave (±)-**39** as a white solid (33.6 mg, 97%); $[\alpha]_D^{20}$ -73.2 (*c* 0.25, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (30% IPA:hexane, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(1*R*): 7.4 min, t_R(1*S*): 10.7 min, >99% *ee*.

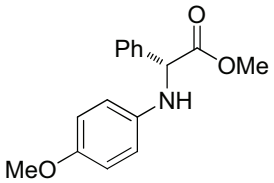
methyl 2-((4-methoxyphenyl)amino)-2-phenylacetate



(±)-**40**

Following general procedure F, ester (±)-**33** (400 mg, 0.88 mmol) and 0.1M SmI_2 (26.4 mL, 2.64 mmol) in MeOH (10 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80) (±)-**40** as a light yellow solid (167 mg, 70%); mp 104-106 °C; {lit.[8] mp 107-108 °C}; δ_H (300 MHz, $CDCl_3$) 3.73 (3H, s, C*H*$_3$), 3.75 (3H, s, C*H*$_3$), 4.69 (1H, br s, N*H*), 5.05 (1H, s, C(2)*H*), 6.54-6.59 (2H, m, Ar*H*), 6.72-6.76 (2H, m, Ar*H*), 7.33-7.41 (3H, m, Ar*H*), 7.50-7.53 (2H, m, Ar*H*).

(R)-methyl 2-((4-methoxyphenyl)amino)-2-phenylacetate

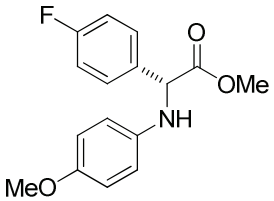


(2*R*)-**40**

Following general procedure F, ester (2*R*)-**33** (229 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 20:80) (2*R*)-**40** as a colourless oil (112 mg, 83%); $[\alpha]_D^{20}$ -99.2 (*c* 0.125, $CHCl_3$); {lit.[9] $[\alpha]^{20}_D$ +97.6 (c 1.29 in $CHCl_3$) for a 98% ee sample (2*S*)-configuration}; Chiral HPLC Chiralcel OJ-H (30% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(2*R*): 28.1 min, t_R(2*S*): 30.9 min, 99% *ee*.

* Enantiomeric excess was 91% when reaction carried out at rt.

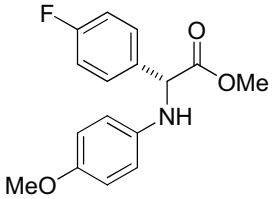
methyl 2-(4-fluorophenyl)-2-((4-methoxyphenyl)amino)acetate



(±)-**41**

Following general procedure F, ester (±)-**34** (238 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (±)-**41** as a light yellow solid (107.9 mg, 75%); mp 102-104 °C; {lit.[8] mp 99-100 °C}; δ_H (300 MHz, $CDCl_3$) 3.64 (3H, s, C*H*$_3$), 3.66 (3H, s, C*H*$_3$), 4.60 (1H, br s, N*H*), 4.92 (1H, s, C(2)*H*), 6.42-6.45 (2H, m, Ar*H*), 6.64-6.67 (2H, m, Ar*H*), 6.94-7.00 (2H, m, Ar*H*), 7.37-7.42 (2H, m, Ar*H*).

(R)-methyl 2-(4-fluorophenyl)-2-((4-methoxyphenyl)amino)acetate

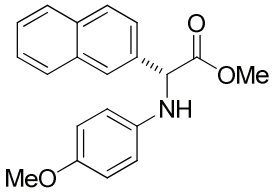


(2*R*)-**41**

Following general procedure F, ester (2*R*)-**34** (238 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (2*R*)-**41** as a light yellow solid (110 mg, 76%); $[\alpha]_D^{20}$ -86.8 (*c* 0.25, CH_2Cl_2); {lit.[9] $[\alpha]^{20}_D$ +70.4 (c 1.40 in $CHCl_3$) for a 93% ee sample (2*S*)-configuration}; Chiral HPLC

Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 13.7 min, t_R(2*R*): 15.9 min, 98% *ee*.

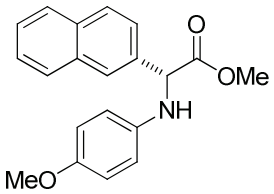
methyl 2-((4-methoxyphenyl)amino)-2-(naphthalen-2-yl)acetate



(±)-**42**

Following general procedure F, ester (±)-**35** (254 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (±)-**42** as a light yellow oil (111 mg, 69%); δ_H (300 MHz, $CDCl_3$) 3.59 (3H, s, C*H*$_3$), 3.62 (3H, s, C*H*$_3$), 4.73 (1H, br s, N*H*), 5.09 (1H, s, C(2)*H*), 6.47-6.51 (2H, m, Ar*H*), 6.59-6.65 (2H, m, Ar*H*), 7.36-7.41 (2H, m, Ar*H*), 7.51 (1H, dd, *J* 8.6, 1.8, Ar*H*), 7.71-7.76 (3H, m, Ar*H*), 7.87 (1H, s, Ar*H*).

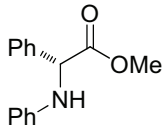
(R)-methyl 2-((4-methoxyphenyl)amino)-2-(naphthalen-2-yl)acetate



(2*R*)-**42**

Following general procedure F, ester (2*R*)-**35** (254 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (2*R*)-**42** as a colourless oil (131 mg, 82%); $[\alpha]_D^{20}$ -180.4 (*c* 0.25, CH_2Cl_2); {lit.[9] $[\alpha]^{20}_D$ +130.6 (c 1.60 in $CHCl_3$) for a 97% ee sample (2*S*)-configuration}; Chiral HPLC Chiralcel OJ-H (30% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(2*R*): 30.4 min, t_R(2*S*): 33.0 min, 98% *ee*.

methyl 2-phenyl-2-(phenylamino)acetate

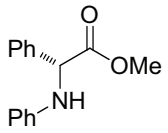


(±)-**43**

Following general procedure F, ester (±)-**4** (150 mg, 0.42 mmol) and 0.1M SmI_2 (12.5 mL, 1.25 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (±)-**43** as a white solid (59.8 mg, 60%); mp 73-74 °C; {lit.[12] mp 79-80 °C}; δ_H (300

MHz, $CDCl_3$) 3.63 (3H, s, C*H*$_3$), 4.87 (1H, d, *J* 5.7, N*H*), 5.00 (1H, d, *J* 5.9, C(2)*H*), 6.47 (2H, dd, *J* 8.6, 0.9, Ar*H*), 6.58-6.64 (1H, m, Ar*H*), 7.00-7.06 (2H, m, Ar*H*), 7.21-7.29 (3H, m, Ar*H*), 7.39-7.43 (2H, m, Ar*H*).

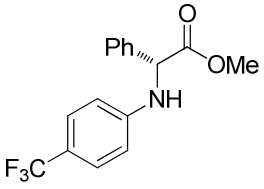
(R)-methyl 2-phenyl-2-(phenylamino)acetate



(2*R*)-**43**

Following general procedure F, ester (2*R*)-**4** (180 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (2*R*)-**43** as a colourless oil (109.7 mg, 91%); $[\alpha]_D^{20}$ -51.5 (*c* 0.2, CH_2Cl_2); {lit.[9] $[\alpha]^{20}_D$ +49.9 (c 0.9 in $CHCl_3$) for a 97% ee sample (2*S*)-configuration}; Chiral HPLC Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 23.7 min, t_R(2*R*): 26.1 min, 99% *ee*.

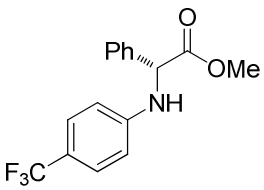
methyl 2-phenyl-2-((4-(trifluoromethyl)phenyl)amino)acetate



(±)-**44**

Following general procedure F, ester (±)-**32** (214 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (±)-**44** as a colourless oil (133 mg, 86%); δ_H (300 MHz, $CDCl_3$) 3.66 (3H, s, C*H*$_3$), 5.01 (1H, d, *J* 5.7, C(2)*H*), 5.28 (1H, d, *J* 5.5, N*H*), 6.47 (2H, d, *J* 8.5, Ar*H*), 7.23-7.31 (5H, m, Ar*H*), 7.37-7.40 (2H, m, Ar*H*).

(R)-methyl 2-phenyl-2-((4-(trifluoromethyl)phenyl)amino)acetate

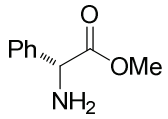


(2*R*)-**44**

Following general procedure F, ester (2*R*)-**32** (214 mg, 0.50 mmol) and 0.1M SmI_2 (15.0 mL, 1.50 mmol) in MeOH (5 mL) gave, after chromatographic purification (eluent Et_2O:petrol 25:75) (2*R*)-**44** as a colourless oil (117 mg, 76%); $[\alpha]_D^{20}$ -98.0 (*c* 0.25, CH_2Cl_2); Chiral HPLC

Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*R*): 13.6 min, t_R(2*S*): 14.7 min, 98% *ee*.

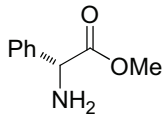
methyl 2-amino-2-phenylacetate



(±)-**45**

To a solution of PMP protected amine (±)-**40** (84.0 mg, 0.31 mmol) in MeCN:H_2O (1:1, 10 mL) was added periodic acid (70.5 mg, 0.31 mmol) and 1M H_2SO_4 (0.31 mL, 0.31 mmol) and the reaction mixture was allowed to stue for 16 h at rt. The reaction mixture was washed with CH_2Cl_2. The aqueous layer was retained, basified with sat. aq. $NaHCO_3$ and extracted twice with ethyl acetate. The combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give (±)-**45** as a yellow oil (16.0 mg, 31%); δ_H (300 MHz, $CDCl_3$) 1.97 (2H, br s, N*H*$_2$), 3.63 (3H, s, C*H*$_3$), 4.55 (1H, s, C(2)*H*), 7.23-7.30 (5H, m, Ar*H*).

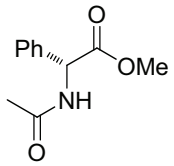
(R)-methyl 2-amino-2-phenylacetate



(2*R*)-**45**

To a solution of PMP protected amine (2*R*)-**40** (34.5 mg, 0.13 mmol) in MeCN:H_2O (1:1, 10 mL) was added periodic acid (28.9 mg, 0.13 mmol) and 1M H_2SO_4 (0.13 mL, 0.13 mmol) and the reaction mixture was allowed to stir for 16 h at rt. The reaction mixture was washed with CH_2Cl_2. The aqueous layer was retained, basified with sat. aq. $NaHCO_3$ and extracted twice with ethyl acetate. The combined organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give (2*R*)-**45** as a yellow oil (9.8 mg, 47%); $[\alpha]_D^{20}$ -192 (*c* 0.025, CH_2Cl_2); {lit.[10] $[\alpha]^{20}_D$ +202.3 (c 0.49 in $CHCl_3$) for a 91% ee sample (2*S*)-configuration}.

methyl 2-acetamido-2-phenylacetate

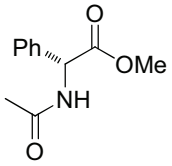


(±)-**83**

To a solution of amine (±)-**45** (15.0 mg, 0.09 mmol) and triethylamine (14.0 µL, 0.1 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added acetic anhydride (9.44 µL, 0.1 mmol) and the reaction mixture was stirred at rt for 30 minutes. The reaction mixture was washed several times with

water and the organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give acylated amine (±)-**83** as a yellow oil (15.1 mg, 80%); δ_H (300 MHz, $CDCl_3$) 1.97 (3H, s, C*H*$_3$), 3.66 (3H, s, OC*H*$_3$), 5.52 (1H, d, *J* 7.3, C(2)*H*), 6.42 (1H, br s, N*H*), 7.27-7.29 (5H, m, Ar*H*).

(R)-methyl 2-acetamido-2-phenylacetate



(2*R*)-**83**

To a solution of amine (2*R*)-**45** (6.0 mg, 0.036 mmol) and triethylamine (5.58 μL, 0.04 mmol) in CH_2Cl_2 (1 mL) at 0 °C was added acetic anhydride (3.78 μL, 0.04 mmol) and the reaction mixture was stirred at rt for 30 minutes. The reaction mixture was washed several times with water and the organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo* to give acylated amine (±)-**83** as a yellow oil (6.8 mg, 90%); $[\alpha]_D^{20}$ -188 (*c* 0.05, CH_2Cl_2); {lit.[11] $[\alpha]^{20}_D$ -36 (c 1.00 in $CHCl_3$) for a 24% ee sample (2*R*)-configuration}; Chiral HPLC Chiralcel OJ-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*): 16.1 min, t_R(2*R*): 17.9 min, 90% *ee*.

1.4 NMR Analysis

NMR analysis illustrating that hydrazide **4** and its analogues are rotameric

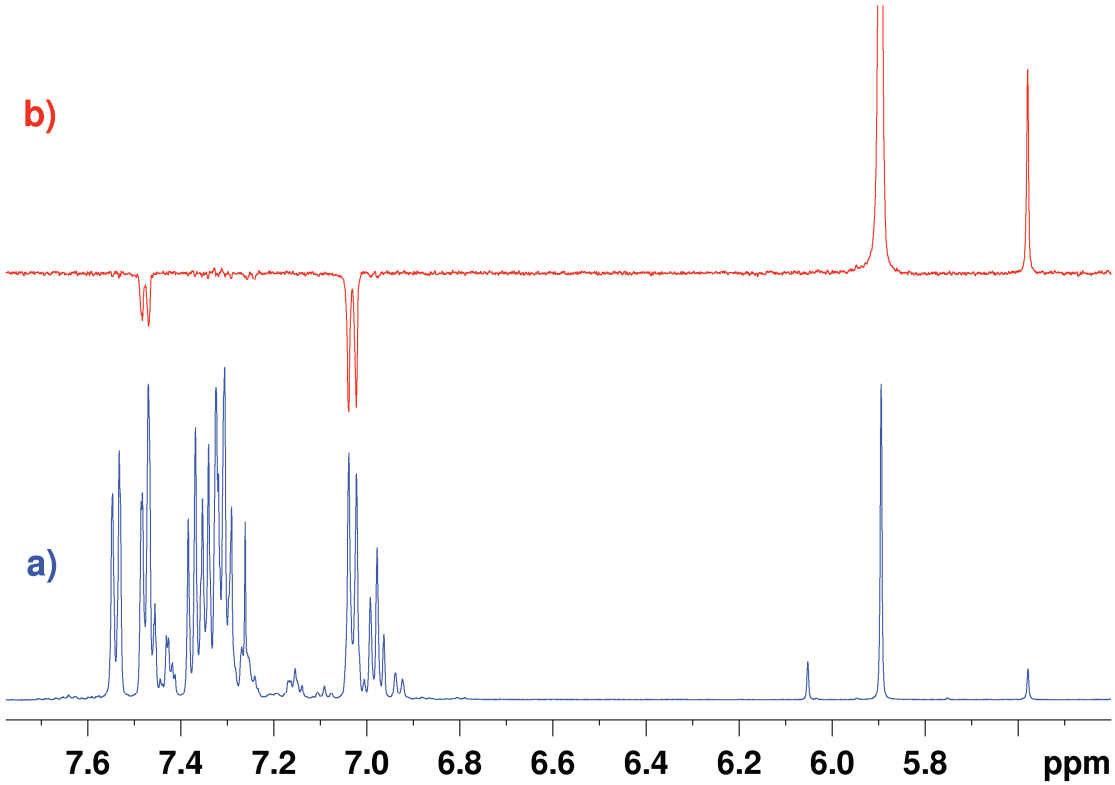


Fig. 1 a) Expansion of ^{1}H NMR spectrum of compound **4**. **b)** 1D gs-NOESY/EXSY spectrum acquired upon selective irradiation of aliphatic CH resonance at 5.89 ppm. The positive phased peak at 5.58 ppm indicates that hydrazide **4** exists in solution in the form of two fast exchanging species, likely rotamers. The negative phased doublets at 7.03 and 7.48 ppm appear in the spectrum due to NOE between the aliphatic CH resonance and adjacent *ortho*-phenyl protons for both major and minor rotamer.

1.4 References and Notes

[1] W. R. Bowman, J. A. Forshaw, K. P. Hall, J. P. Kitchin and A. W. Mott, *Tetrahedron*, 1996, **52**, 3961.

[2] B. Laude, M. Souflaoui and J. Arriau, *J. Heterocycl. Chem.*, 1977, **14**, 1183.

[3] Z. V. Molodykh, B. I. Buzykin, M. A. Kudrina, L. P. Sysoeva, N. G. Gazetdinova, I. D. Neklesova and Y. P. Kitaev, *Pharm. Chem. J.*, 1980, **14**, 162.

[4] Y-S. Niu and J-P. Li, *J. Chem. Res., Synop.*, 2005, **9**, 551.

[5] K. Issleib and O. Low, *Z. Anorg. Allg. Chem.*, 1966, **346**, 241.

[6] K. Hisler, A. G. J. Aurelien, S-Z. Zhuo and J. A. Murphy., *Tetrahedron Letters,* 2009, **50**, 3290.

[7] S. Karady, M. G. Ly, S. H. Pines, J. Chemerda and M. Sletzinger, *Synthesis,* 1973, 50.

[8] N. Kise and S. Morimoto, *Tetrahedron*, 2008, **64**, 1765.

[9] C. Zhu and T. Akiyama, *Adv. Synth. Catal.*, 2010, 352, 1846.

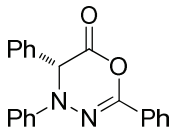
[10] G. Shang, Q. Yang and X. Zhang, *Angew. Chem.*, 2006, **118**, 6508.

[11] A. R. Katritzky, D. Fedoseyenko, M. S. Kim and P. J. Steel, *Tetrahedron: Asymmetry*, 2010, **21**, 51.

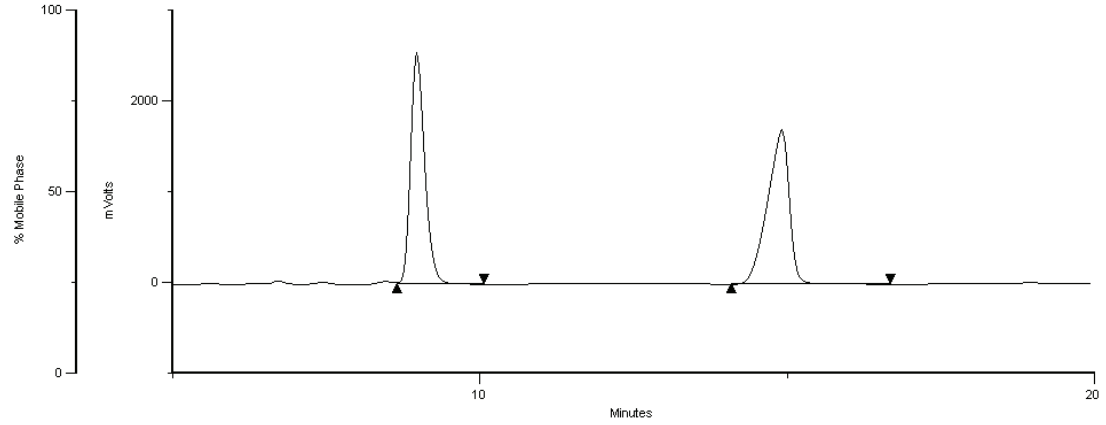
[12] H. E. Bartrum, C. J. Moody, C. J. Hayes and D. C. Blakemore, *Chem. Eur. J.*, 2011, 17, 9586.

HPLC Data

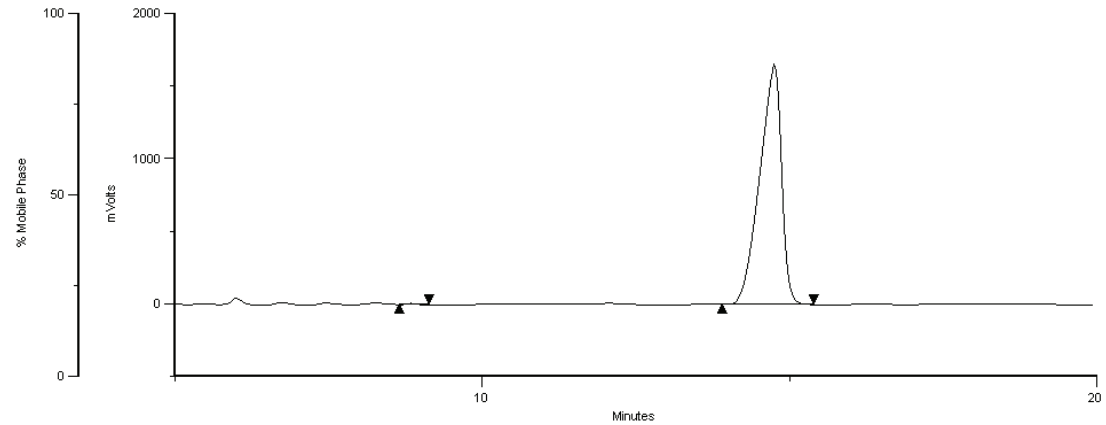
HPLC data compound **3**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



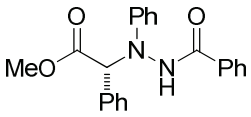
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.97	38149680.00	49.37
2	1.00	*2	14.91	39892360.00	50.63



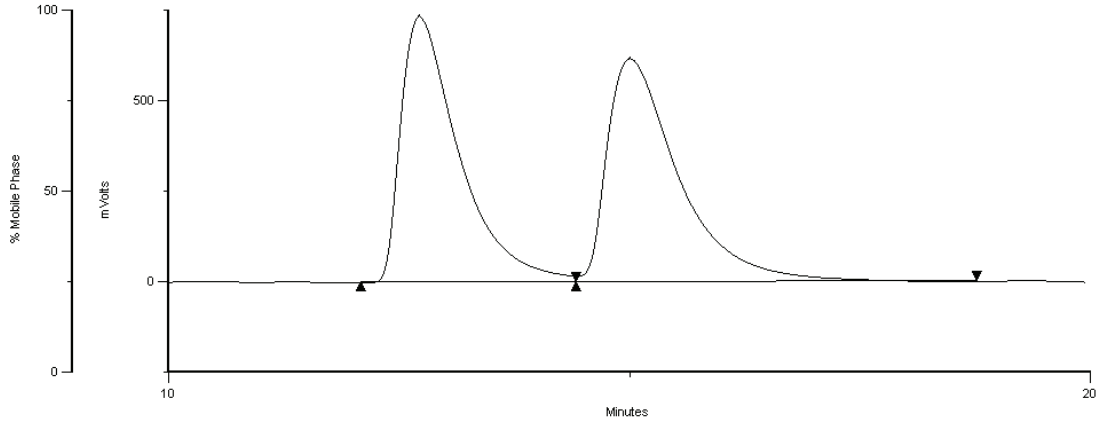
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.84	119161.32	0.17
2	1.00	*2	14.75	38126640.00	99.83



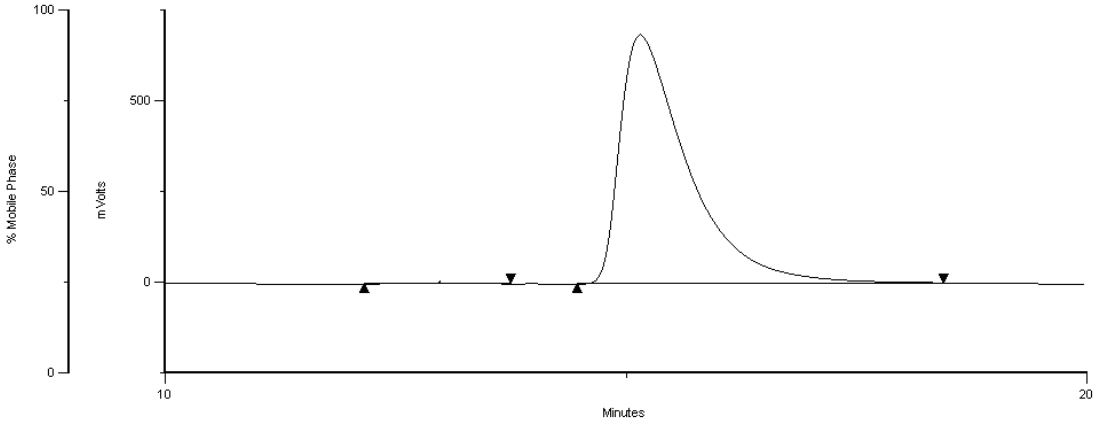
HPLC data compound **4**: Chiralpak IB 10% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



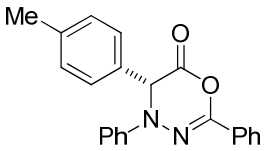
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	12.72	4284232.00	49.17
2	1.00	2	15.01	6125892.00	50.83



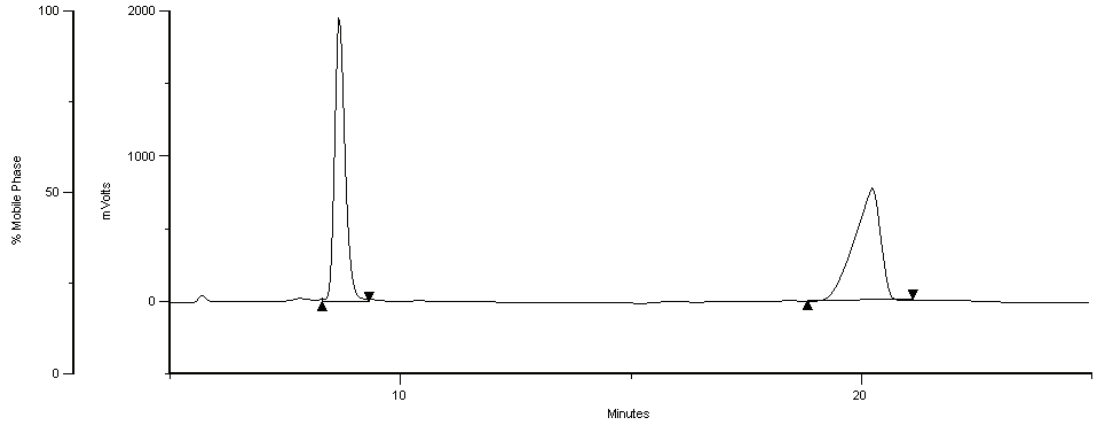
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.16	321664.56	0.54
2	1.00	*2	15.16	5914218 8.00	99.46



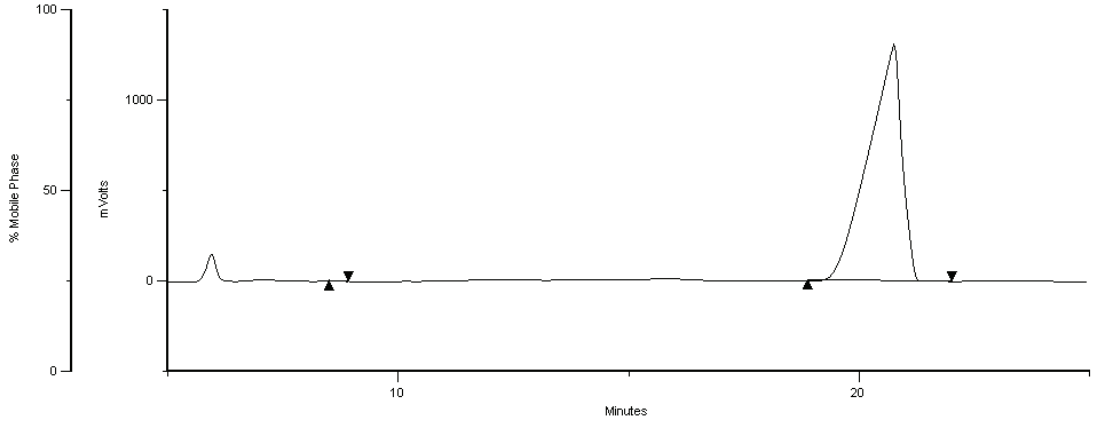
HPLC data compound **6**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



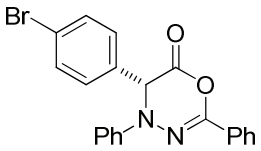
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.67	51800880.00	50.19
2	1.00	*2	20.24	51415304.00	49.81



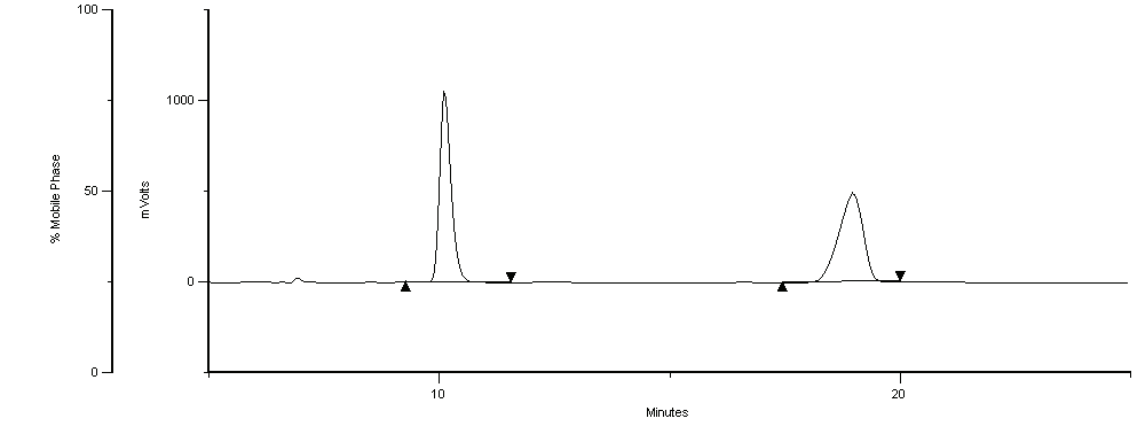
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.67	94316.68	0.09
2	1.00	*2	20.76	10163560.00	99.91



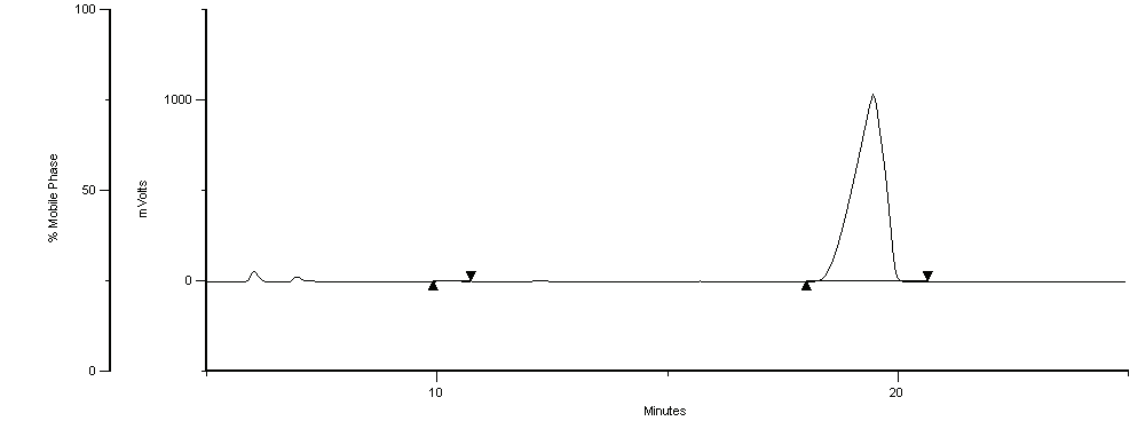
HPLC data compound **7**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



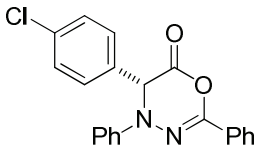
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	10.12	30899266.00	50.66
2	1.00	*2	18.98	30091176.00	49.34



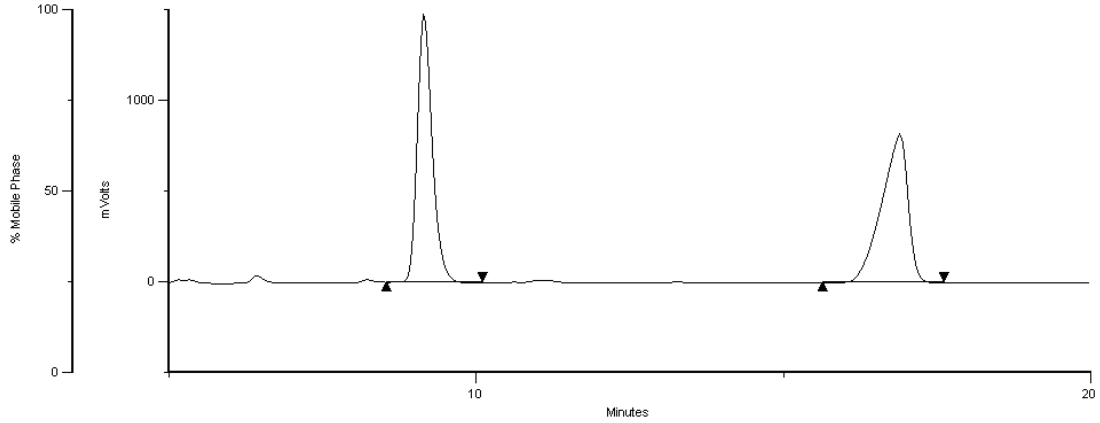
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	10.15	238250.17	0.30
2	1.00	*2	19.47	30005520.00	99.70



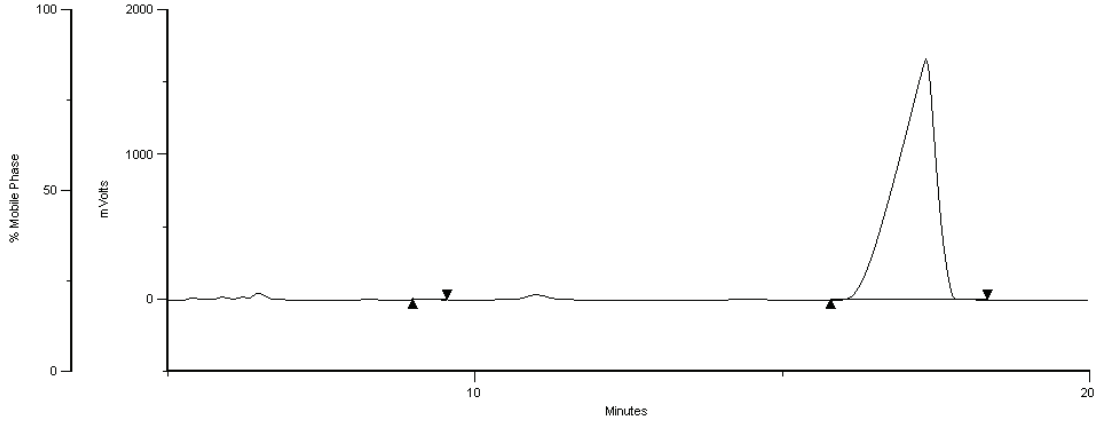
HPLC data compound **8**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



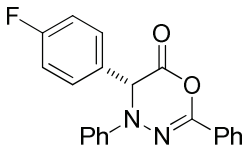
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	9.15	42294556.00	50.86
2	1.00	*2	16.89	40859416.00	49.14



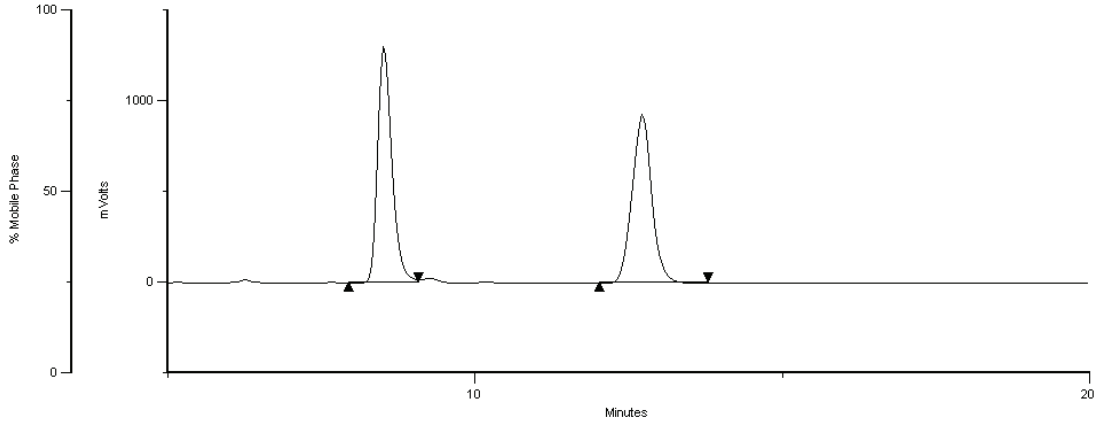
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	9.13	214503.36	0.17
2	1.00	*2	17.34	23265856.00	99.83



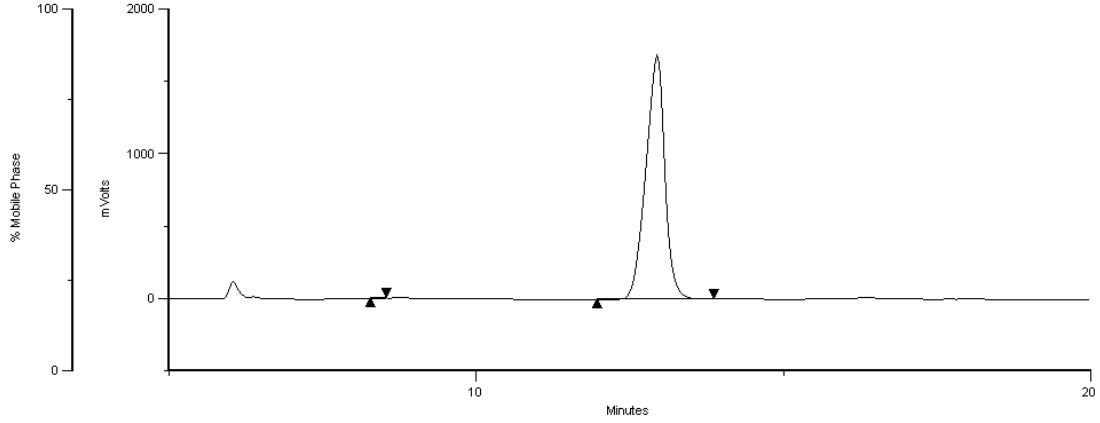
HPLC data compound **9**: Chiralpak AD-H 5% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, >99% ee



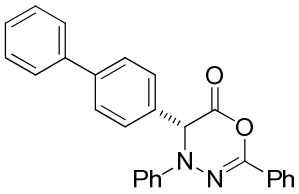
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.51	35436920.00	50.62
2	1.00	*2	12.72	34567096.00	49.38



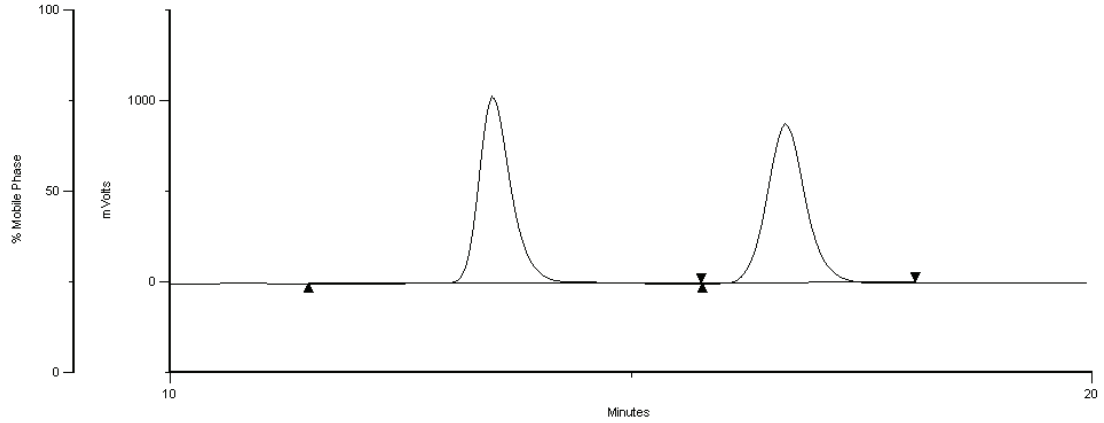
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.56	86740.42	0.14
2	1.00	*2	12.94	60603816.00	99.86



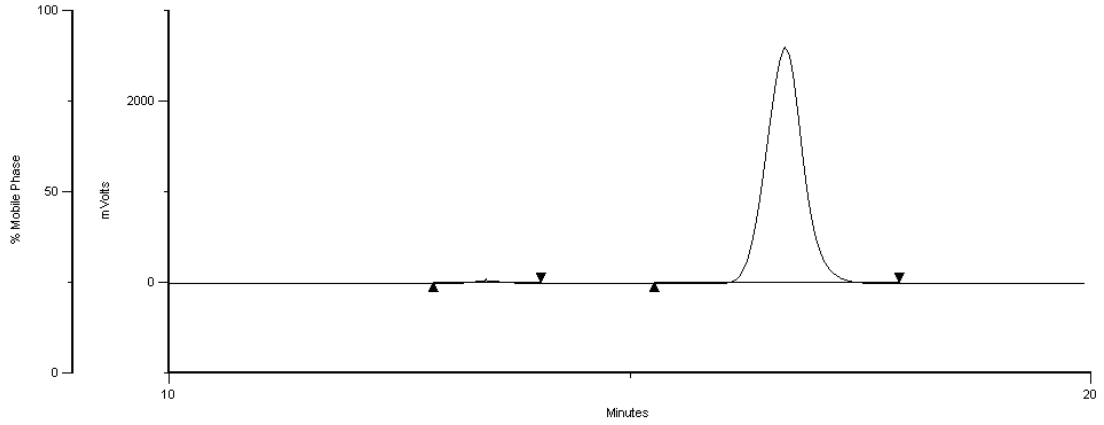
HPLC data compound **10**: Chiralpak AD-H 5% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, 98% ee



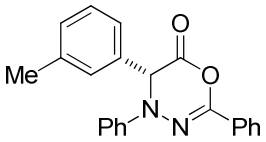
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.50	12698000.00	49.74
2	1.00	2	16.68	13136540.00	50.26



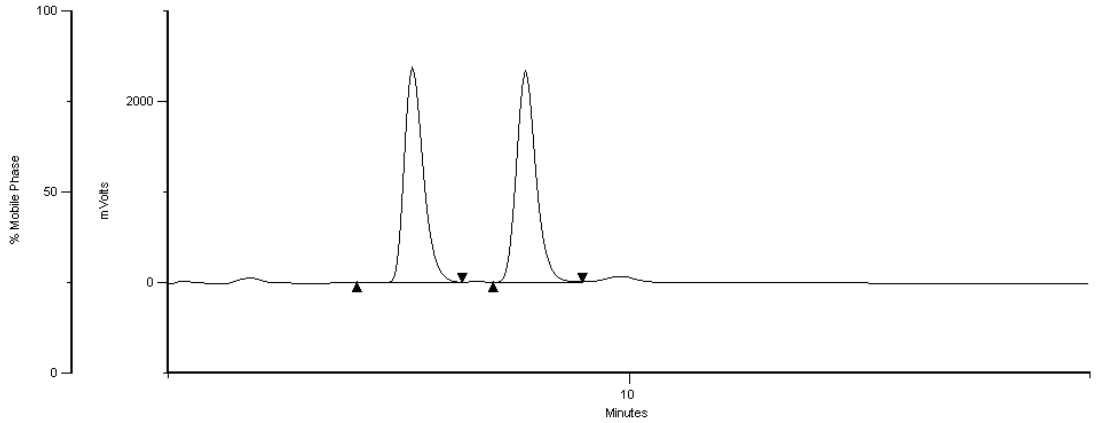
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.45	1328711.88	1.07
2	1.00	*2	16.69	22346144.00	98.93



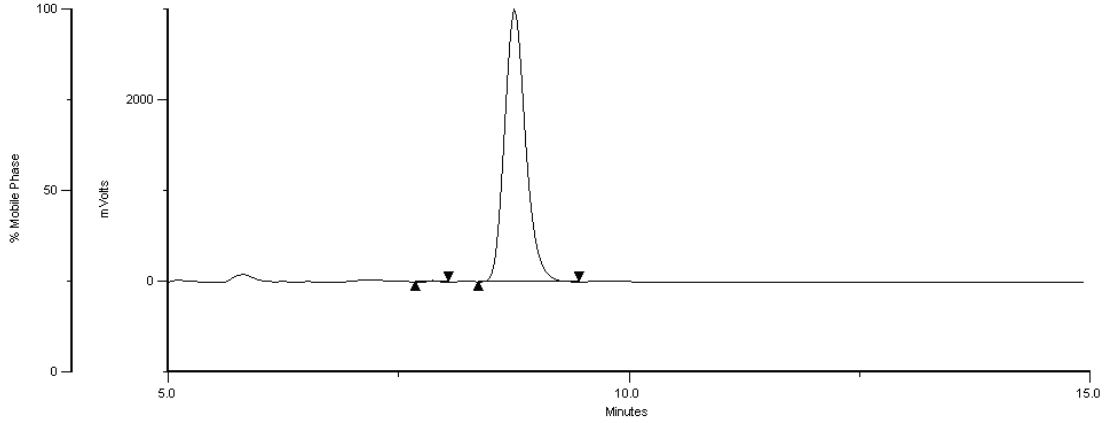
HPLC data compound **11**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



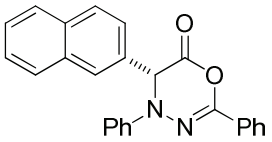
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	7.65	58555336.00	49.70
2	1.00	*2	8.88	59260780.00	50.30



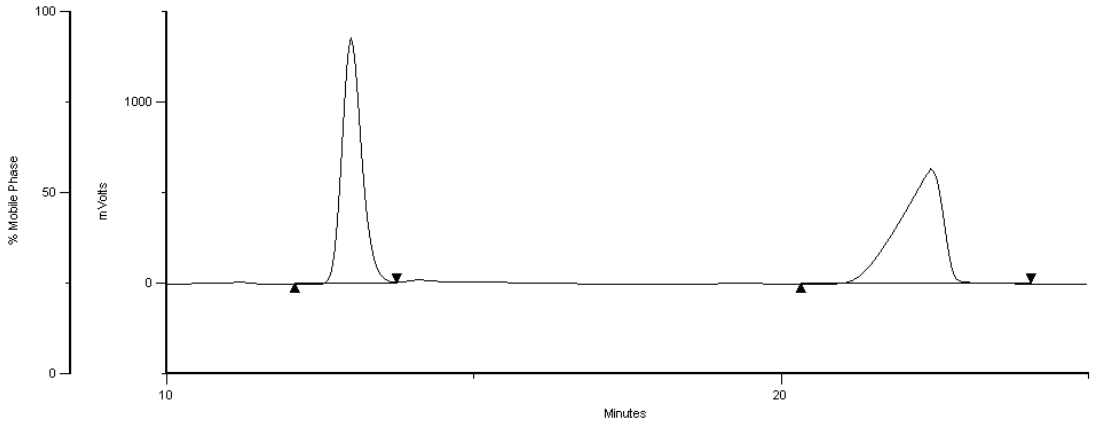
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	7.87	123616.59	0.15
2	1.00	*2	8.76	79818408.00	99.85



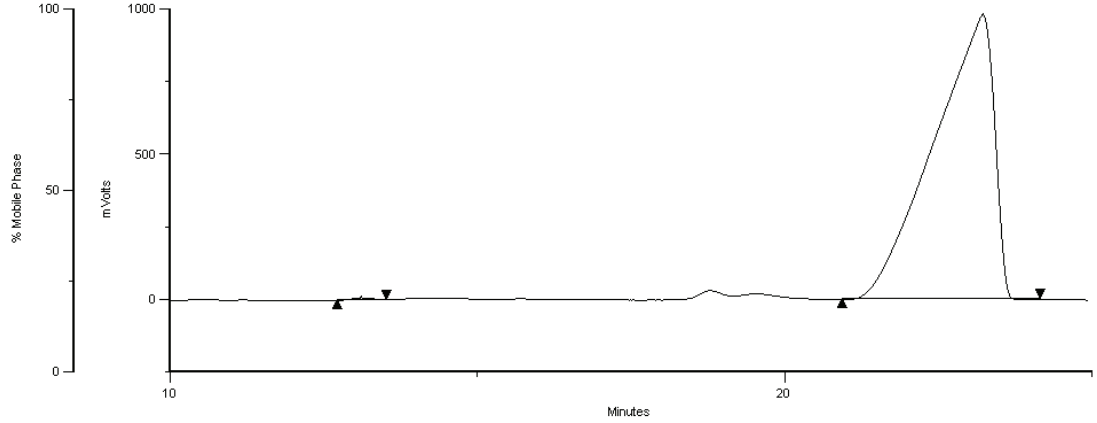
HPLC data compound **12**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



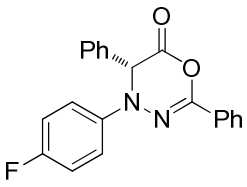
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.00	51101828.00	48.97
2	1.00	*2	22.45	53241888.00	51.03



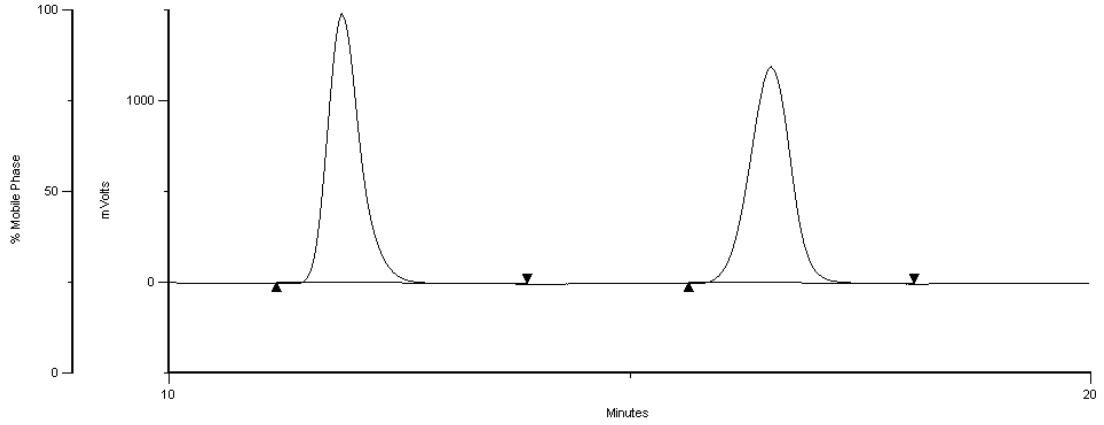
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.12	417392.94	0.37
2	1.00	*2	23.23	11715296.00	99.63



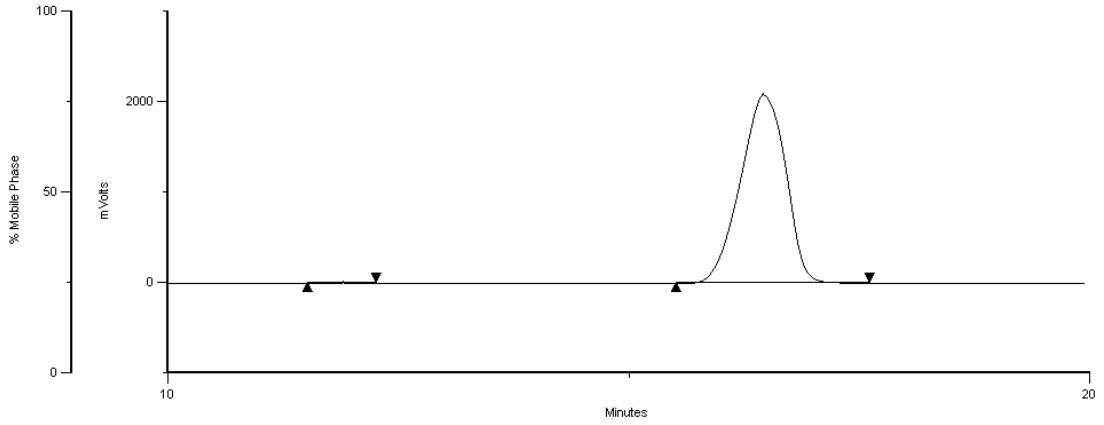
HPLC data compound **13**: Chiralpak AD-H 5% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, >99% ee



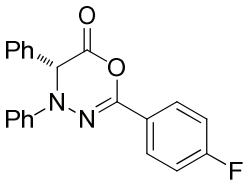
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.88	51871968.00	49.78
2	1.00	*2	16.53	52423600.00	50.22



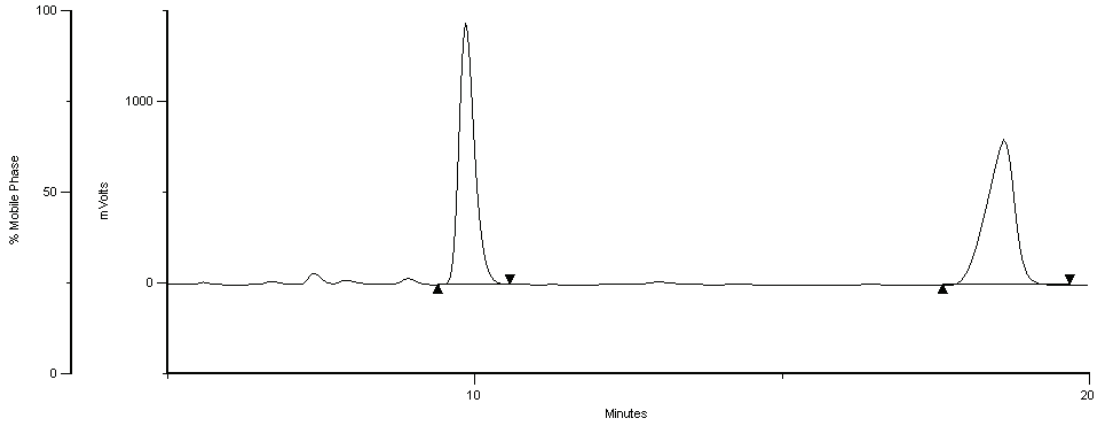
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.89	227088.08	0.19
2	1.00	*2	16.47	18728992.00	99.81



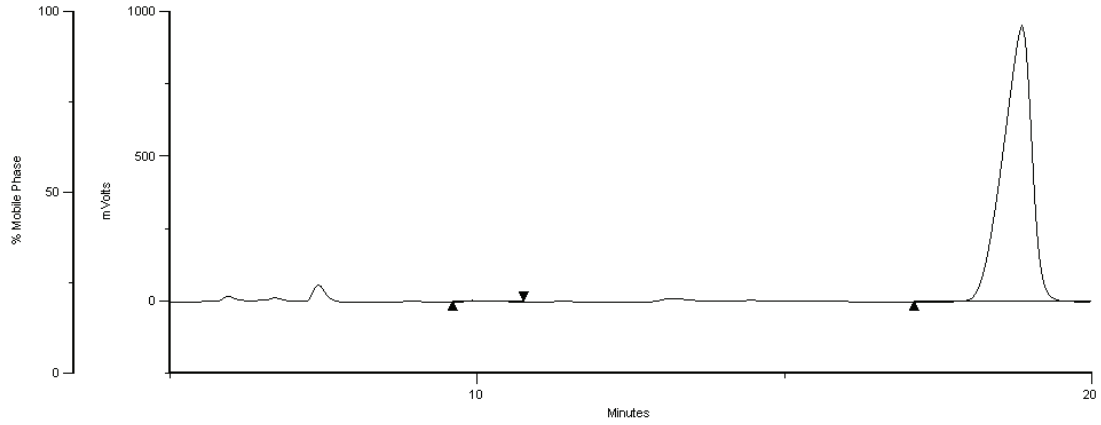
HPLC data compound **14**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



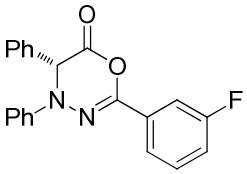
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	9.85	12655704.00	49.94
2	1.00	*2	18.61	12754988.00	50.06



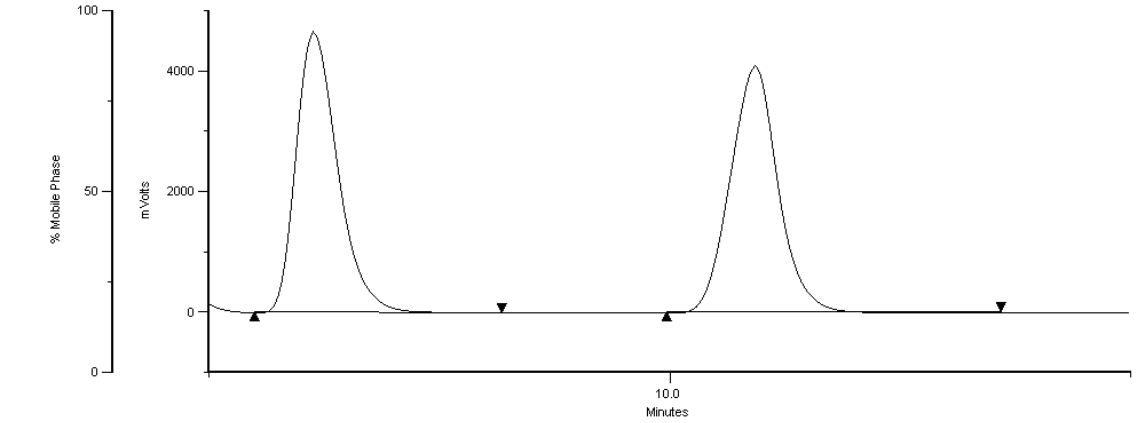
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	9.91	209480.56	0.40
2	1.00	*2	18.86	52050228.00	99.60



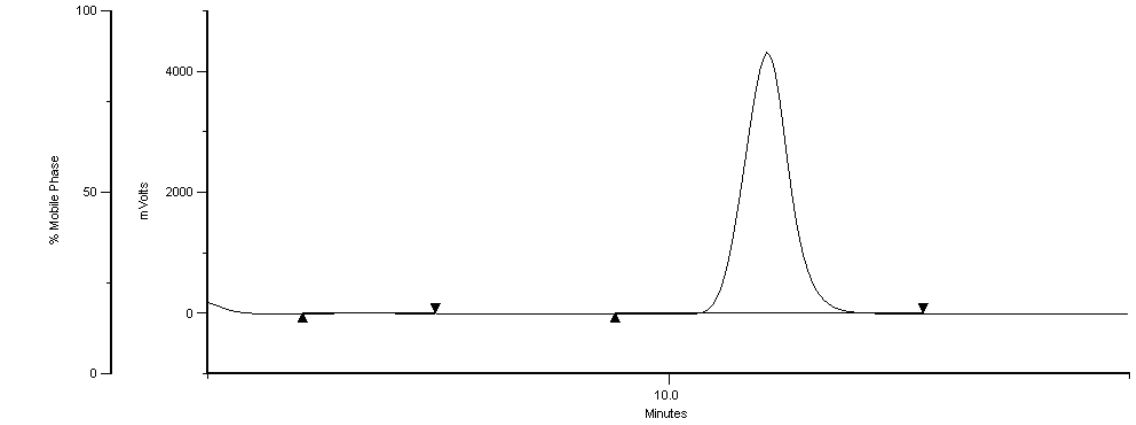
HPLC data compound **15**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



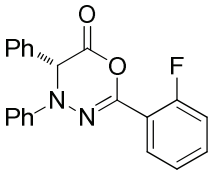
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.07	23199312.0(	49.96
2	1.00	*2	10.46	23372184.0(	50.04



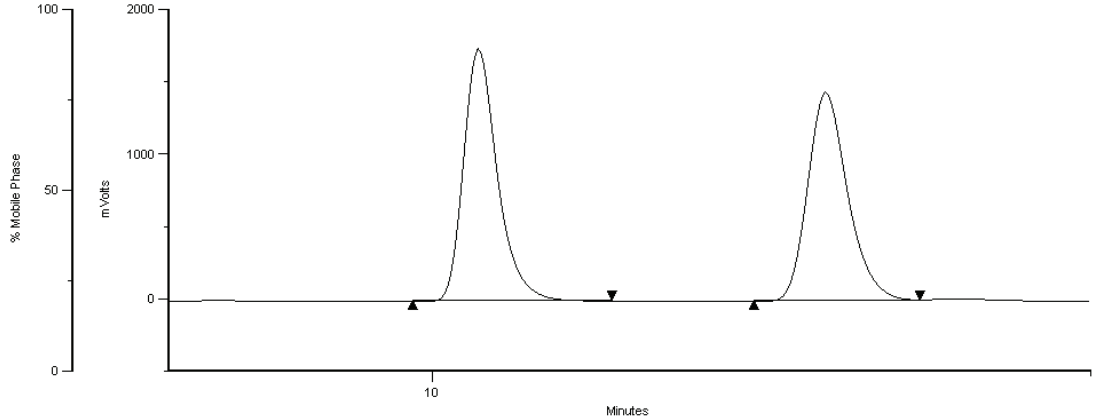
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.34	762609.56	0.60
2	1.00	*2	10.54	25357336.0(	99.40



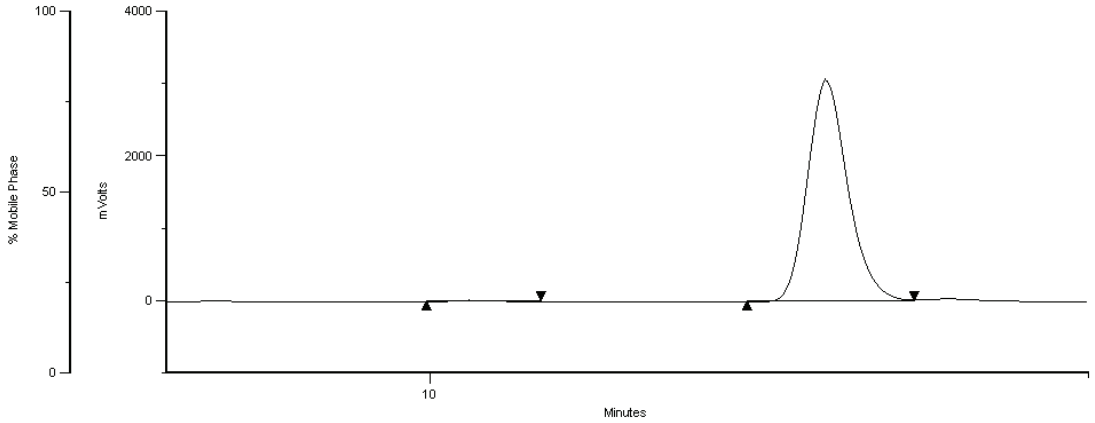
HPLC data compound **16**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



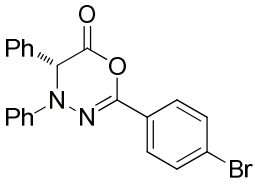
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	10.35	52643232.00	50.68
2	1.00	*2	12.99	51229808.00	49.32



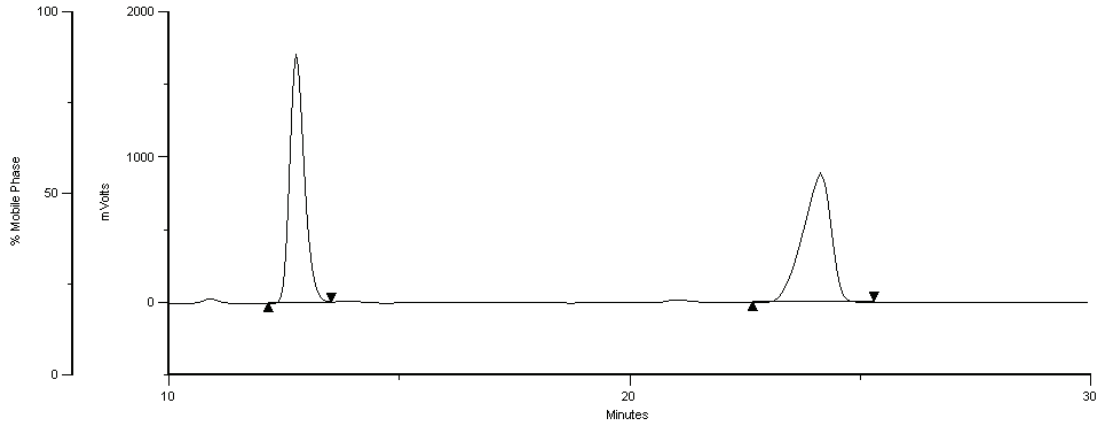
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	10.30	607907.19	0.55
2	1.00	*2	13.01	09373896.00	99.45



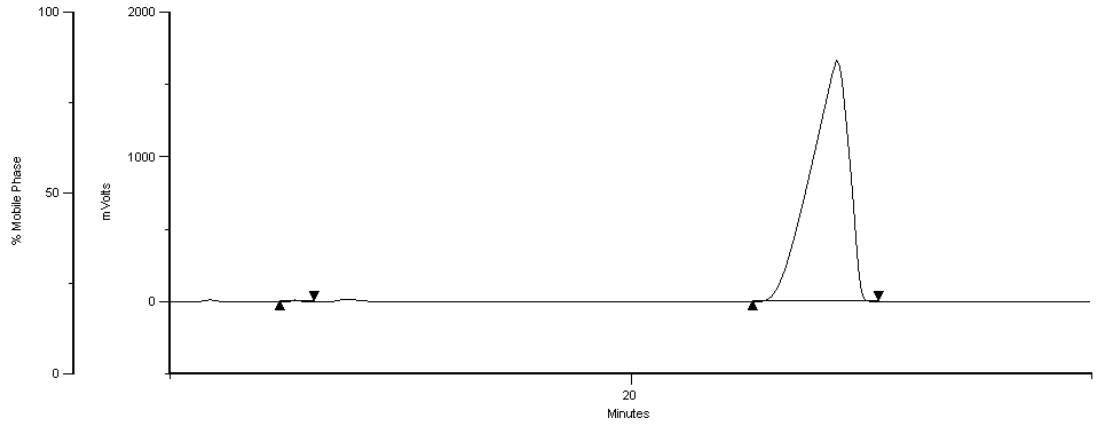
HPLC data compound **17**: Chiralpak AD-H 5% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



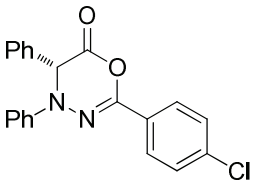
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	12.76	53235372.00	50.03
2	1.00	*2	24.14	53163196.00	49.97



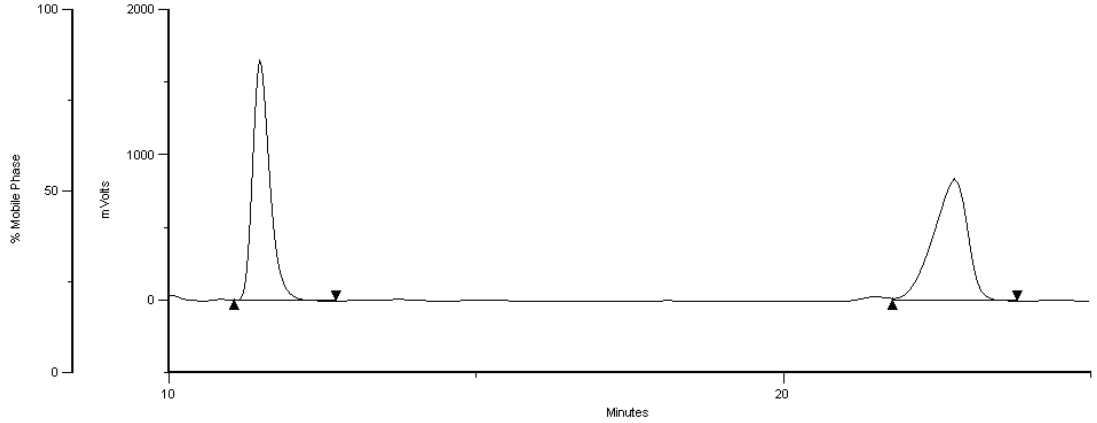
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	12.72	298010.69	0.19
2	1.00	*2	24.48	60513664.00	99.81



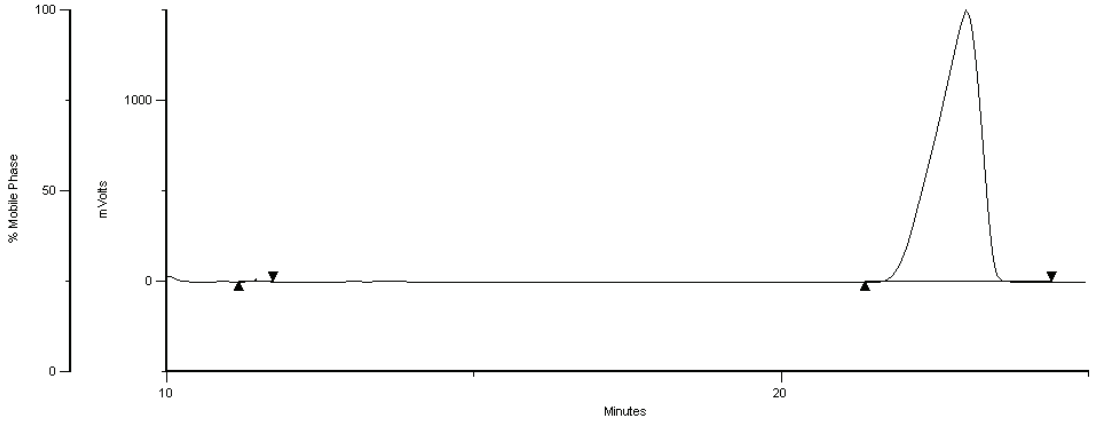
HPLC data compound **18**: Chiralpak AD-H 5% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, >99% ee



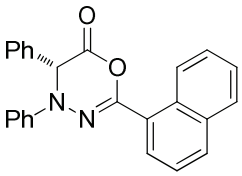
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.48	53839756.00	49.70
2	1.00	*2	22.79	54500632.00	50.31



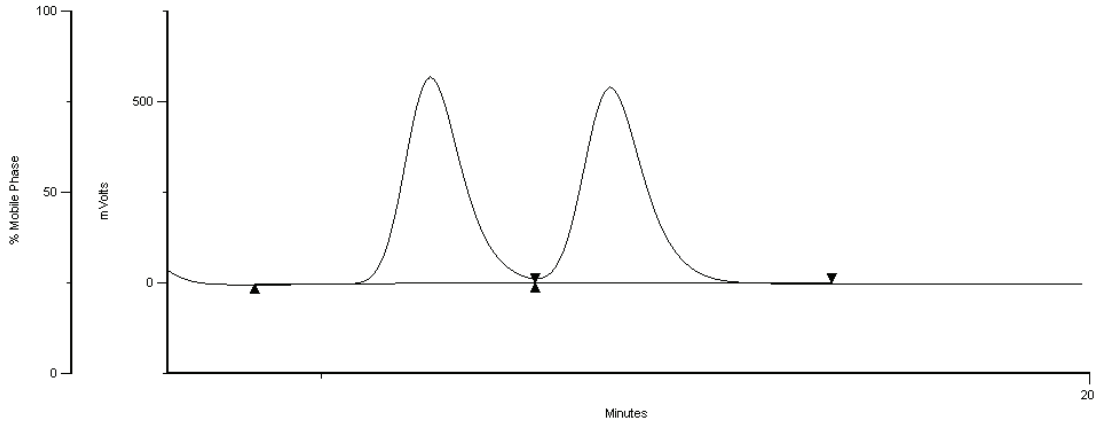
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.47	193277.06	0.15
2	1.00	*2	23.02	25874208.00	99.85



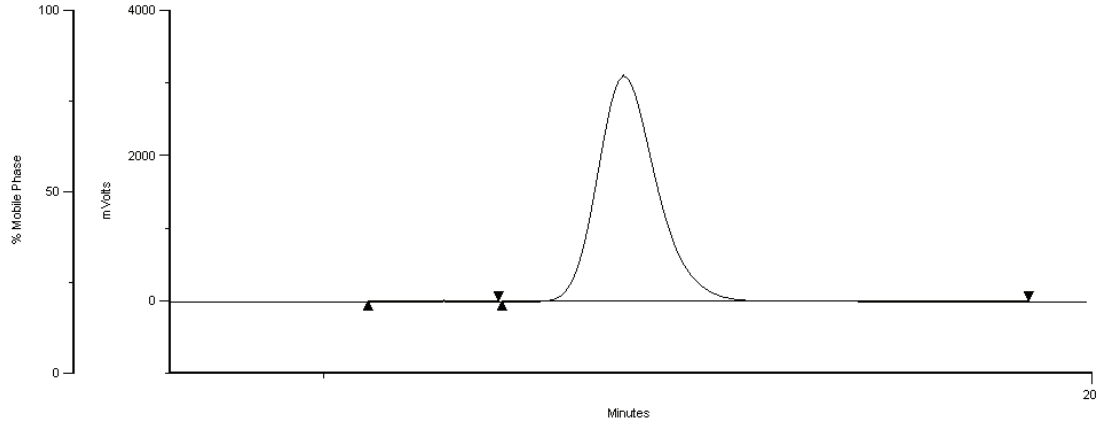
HPLC data compound **19**: Chiralpak AD-H 2% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



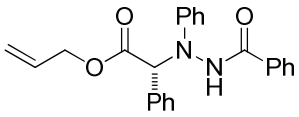
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	15.71	25713628.00	49.90
2	1.00	2	16.88	25819118.00	50.10



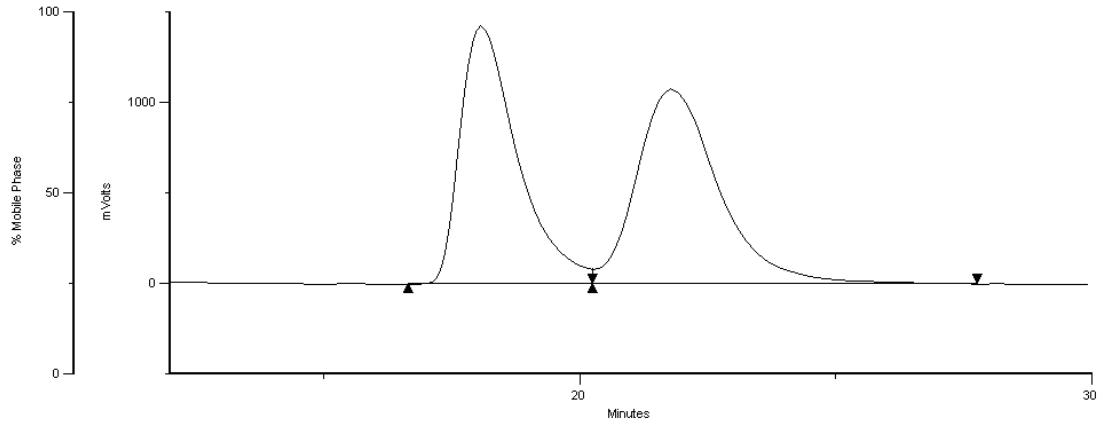
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	15.77	96360.26	0.07
2	1.00	*2	16.96	39902784.00	99.93



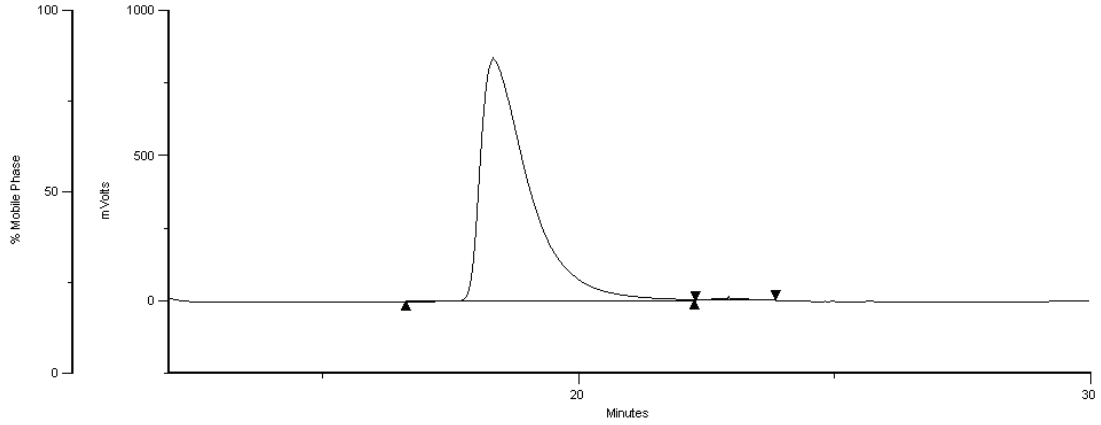
HPLC data compound **20**: Chiralpak IB 10% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 98% ee



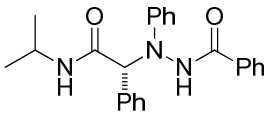
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	18.07	85810256.00	48.21
2	1.00	2	21.78	99611376.00	51.79



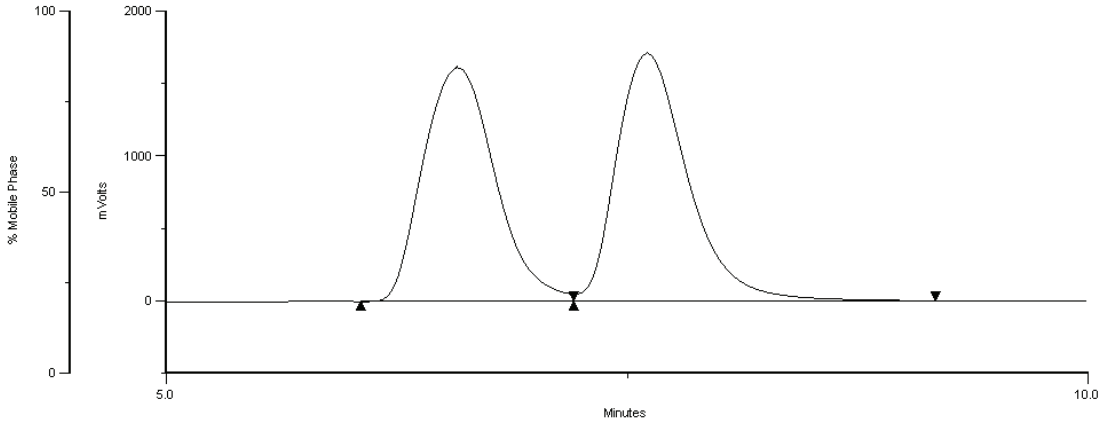
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	18.34	93232328.00	99.12
2	1.00	*2	22.94	823436.62	0.88



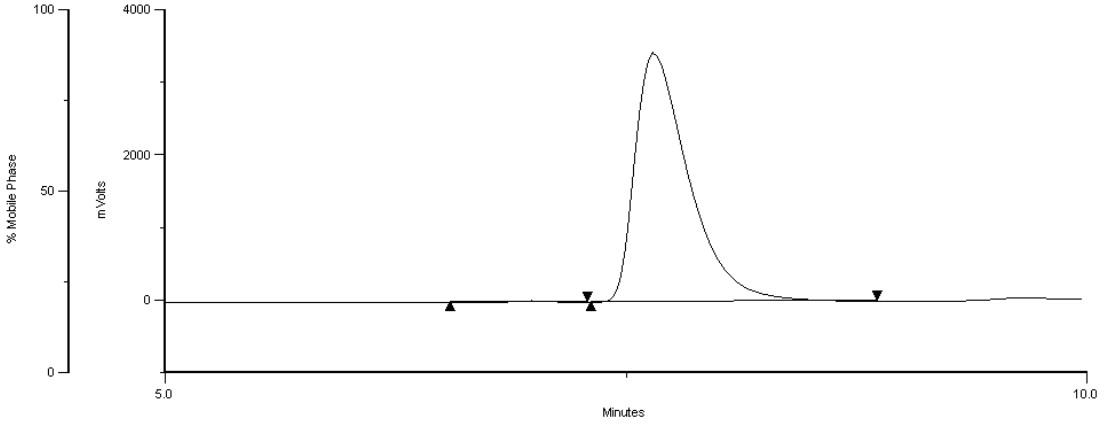
HPLC data compound **21**: Chiralpak IB 20% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



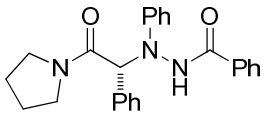
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	6.58	73329576.00	48.69
2	1.00	*2	7.61	77290104.00	51.31



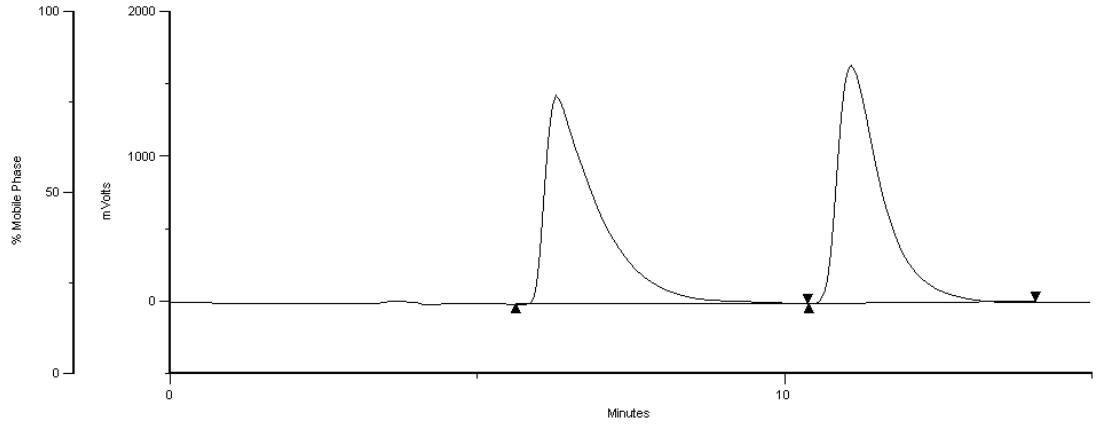
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	6.99	401518.41	0.34
2	1.00	2	7.65	16458616.00	99.66



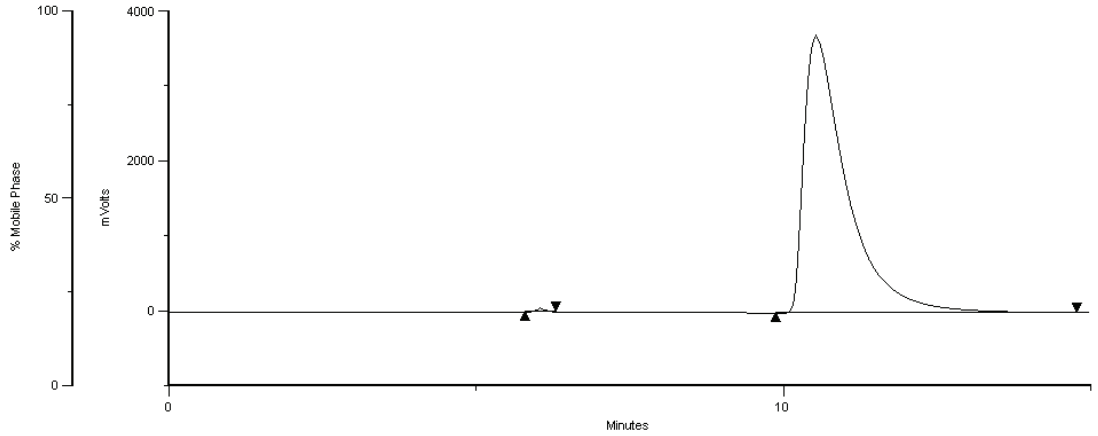
HPLC data compound **22**: Chiralpak IB 40% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



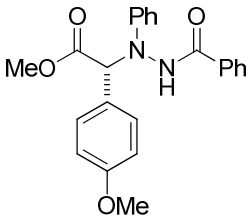
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	6.29	41210352.0(	50.68
2	1.00	2	11.09	37403904.0(	49.32



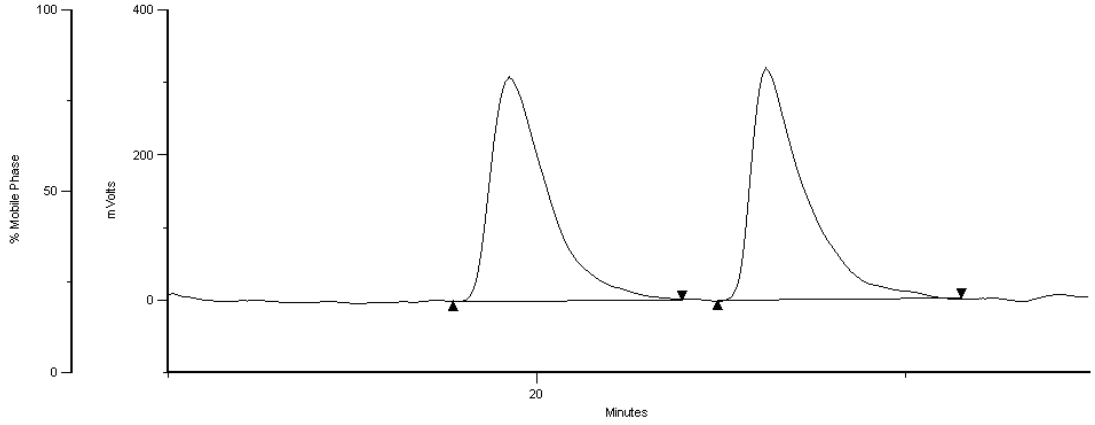
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	6.04	1234009.12	0.41
2	1.00	*2	10.53	00682560.0(	99.59



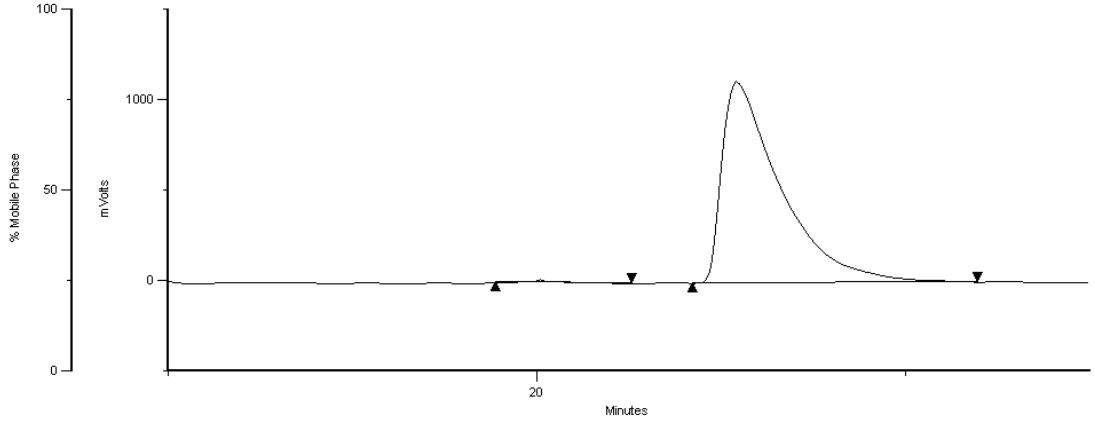
HPLC data compound **23**: Chiralpak IB 10% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, 98% ee



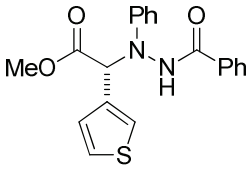
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	19.26	5718732.00	50.56
2	1.00	*2	26.23	4485904.00	49.44



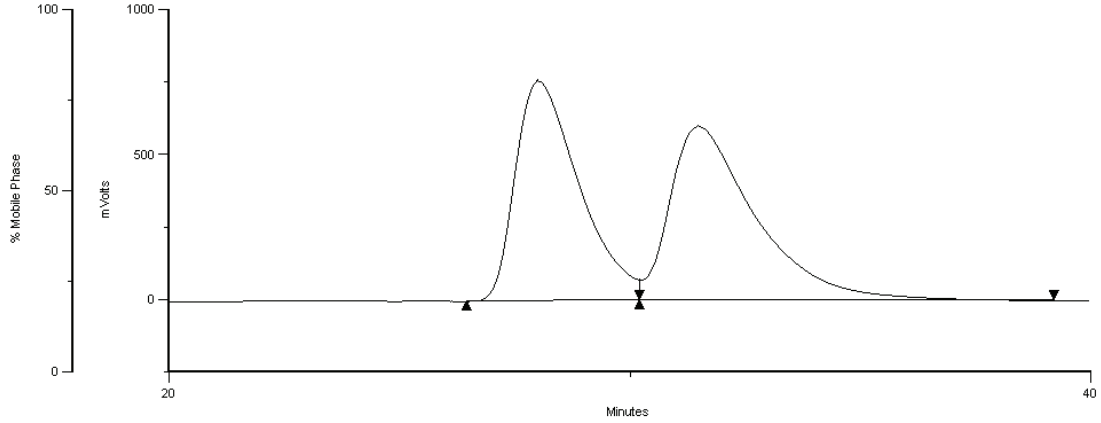
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	20.10	2015943.62	0.97
2	1.00	2	25.43	05419680.00	99.03



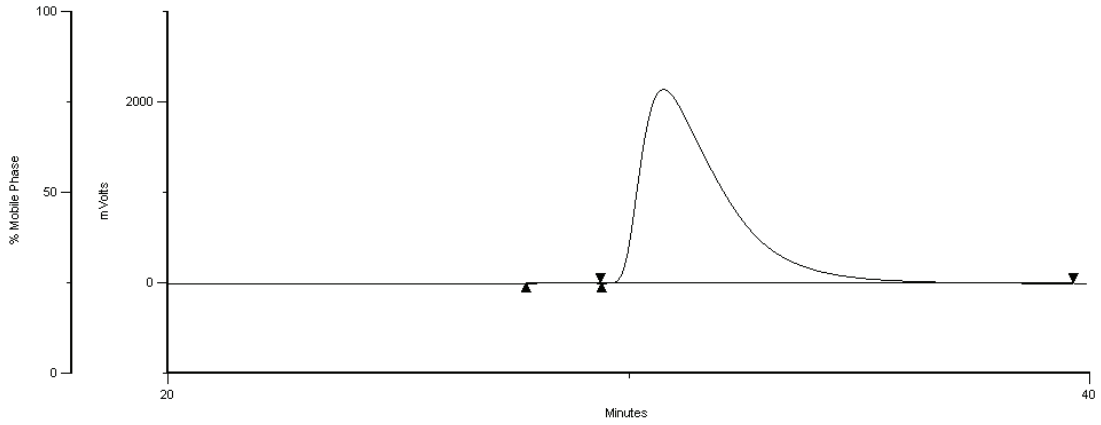
HPLC data compound **24**: Chiralcel OD-H 10% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, >99% ee



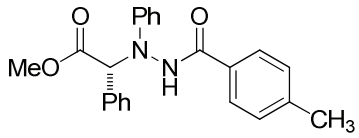
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	28.02	22289712.00	48.13
2	1.00	2	31.50	31778216.00	51.87



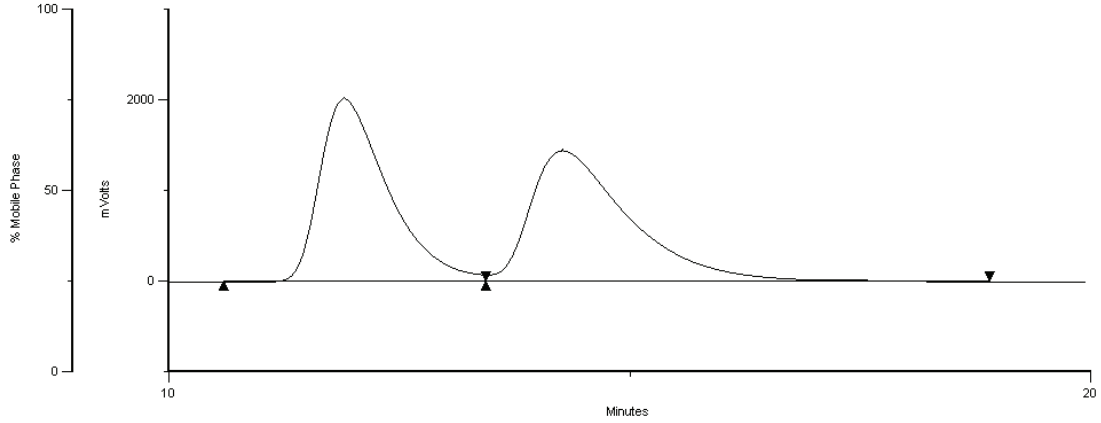
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	28.56	868532.81	0.20
2	1.00	*2	30.76	42654976.00	99.80



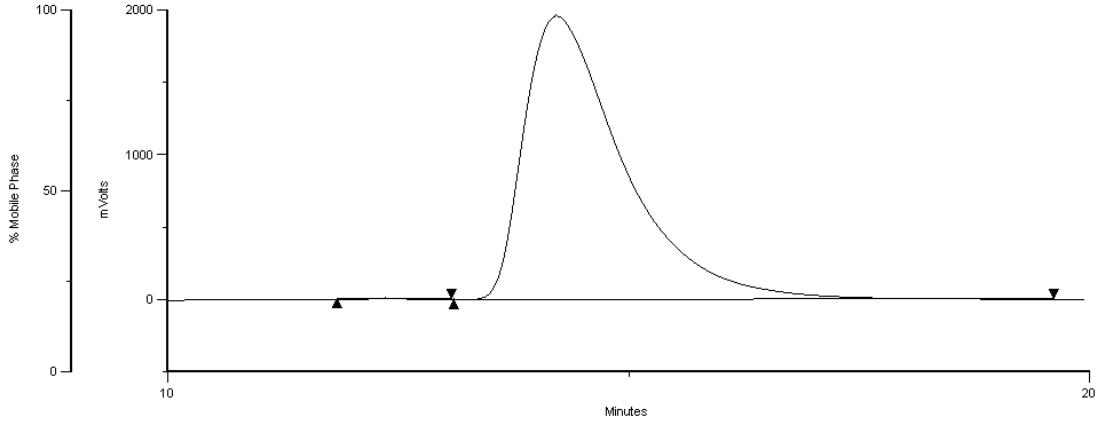
HPLC data compound **25**: Chiralcel OD-H 10% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, >99% ee



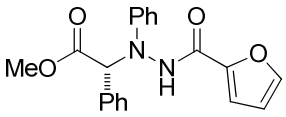
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.90	76088096.00	49.03
2	1.00	2	14.27	83044944.00	50.97



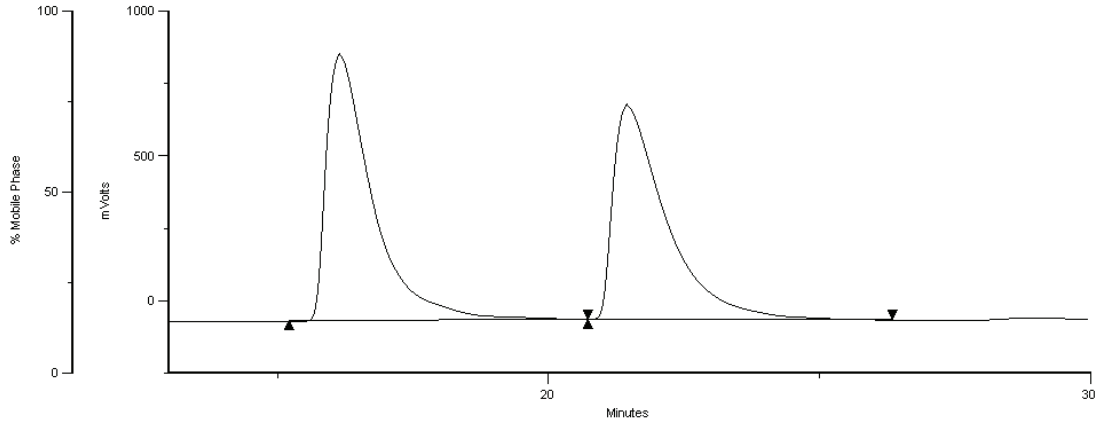
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	12.36	522850.00	0.21
2	1.00	*2	14.22	47685904.00	99.79



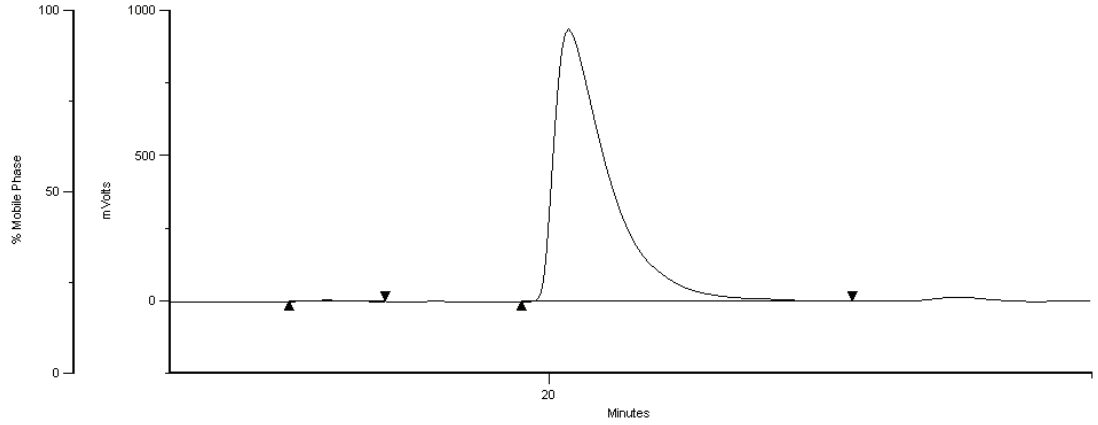
HPLC data compound **26**: Chiralpak IB 10% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



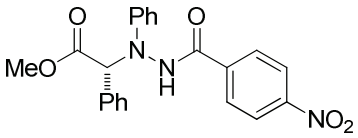
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	16.15	92587504.00	51.92
2	1.00	2	21.45	85727664.00	48.08



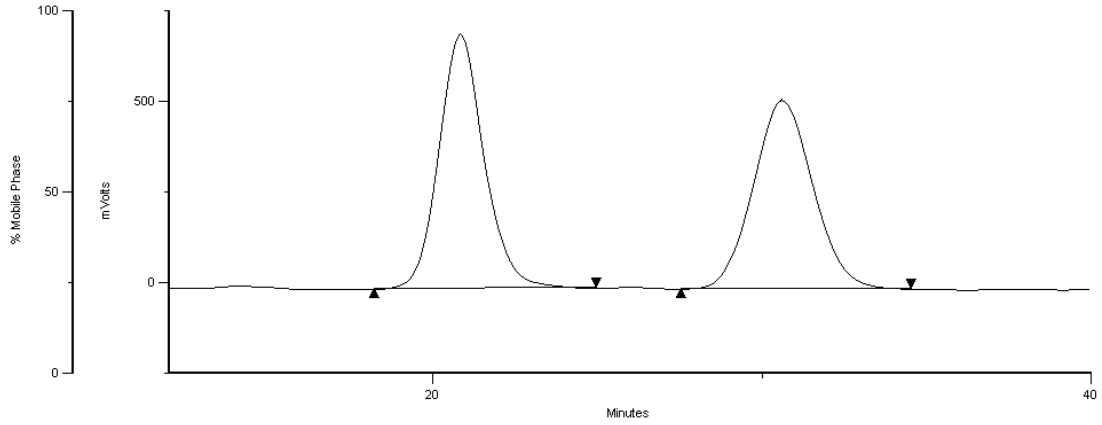
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	15.92	479216.22	0.44
2	1.00	*2	20.35	08939312.00	99.56



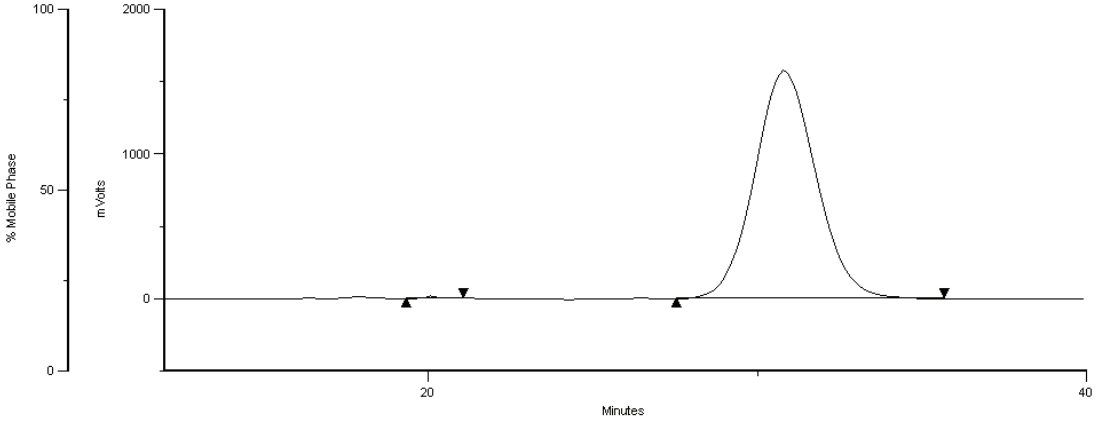
HPLC data compound **27**: Chiralpak IA 40% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, 99% ee



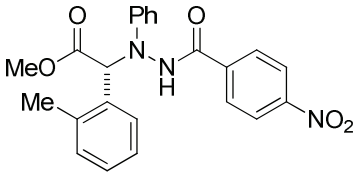
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	20.85	12706840.00	50.68
2	1.00	2	30.61	09684272.00	49.32



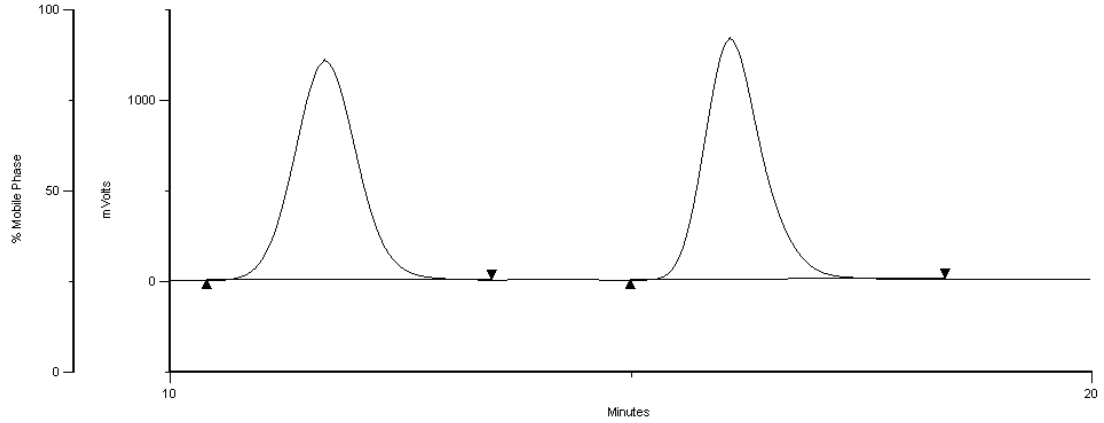
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	20.08	1152797.50	0.33
2	1.00	*2	30.81	43330560.00	99.67



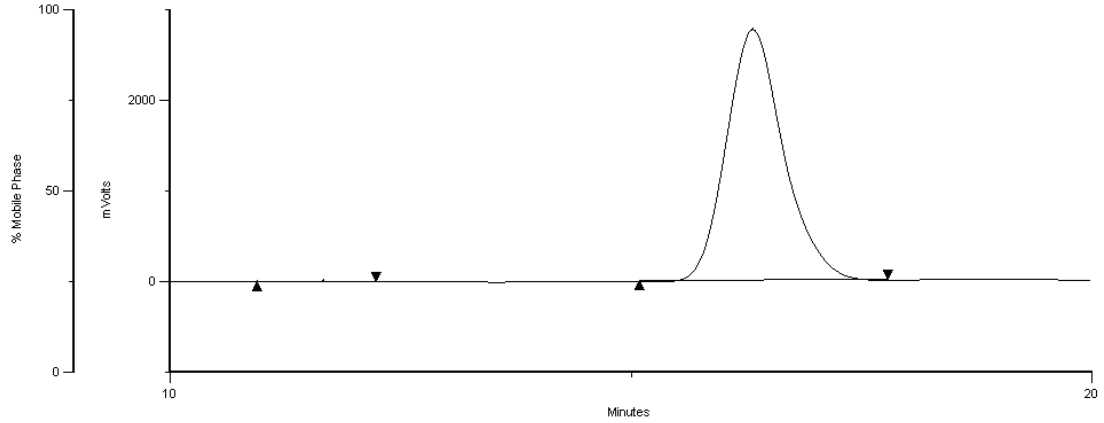
HPLC data compound **28**: Chiralpak IA 40% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



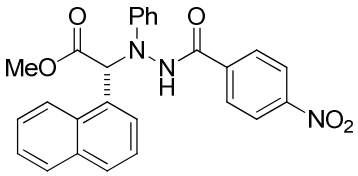
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.68	38162592.00	49.96
2	1.00	*2	16.08	38300576.00	50.04



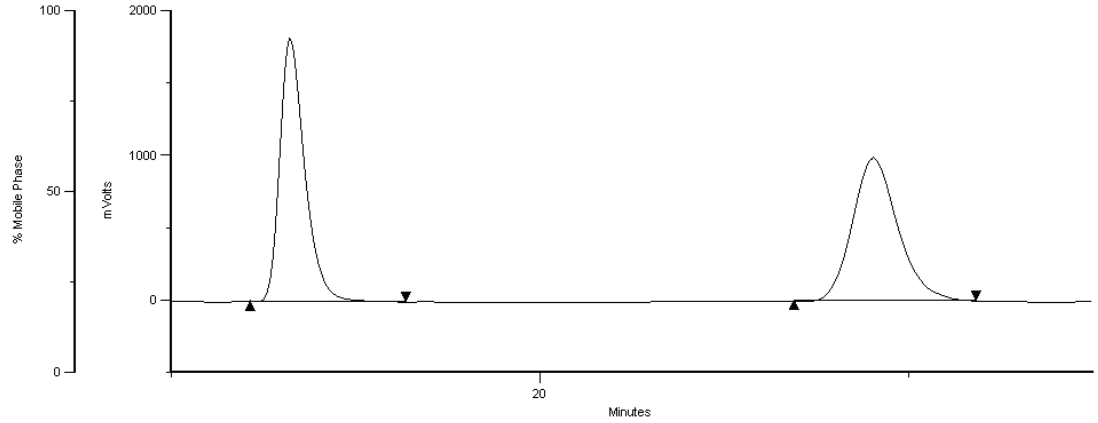
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	11.67	655594.69	0.33
2	1.00	*2	16.32	00501328.00	99.67



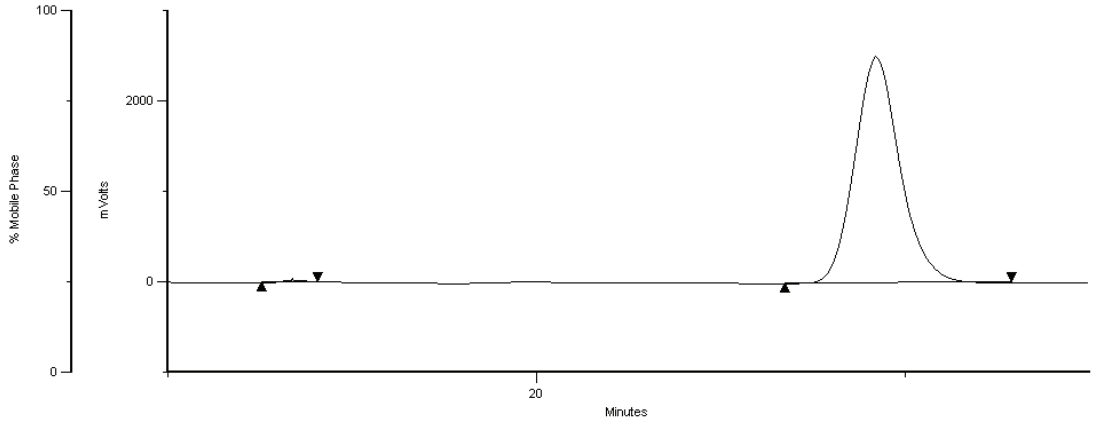
HPLC data compound **29**: Chiralpak IA 40% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



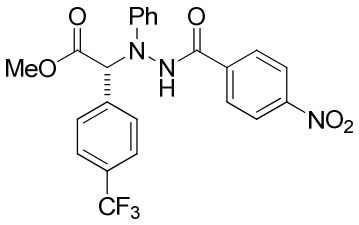
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.22	43556432.00	50.27
2	1.00	*2	29.04	42019296.00	49.73



	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	13.41	2681767.75	0.74
2	1.00	*2	29.22	57990976.00	99.26

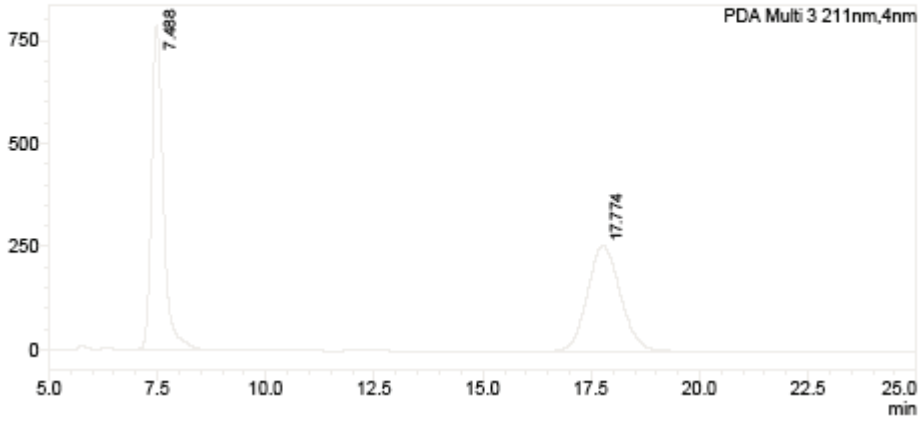


HPLC data compound **30**: Chiralpak IA 80% IPA:hexane, 1 mL min^{-1}, 211 nm, 40 °C, 97% ee



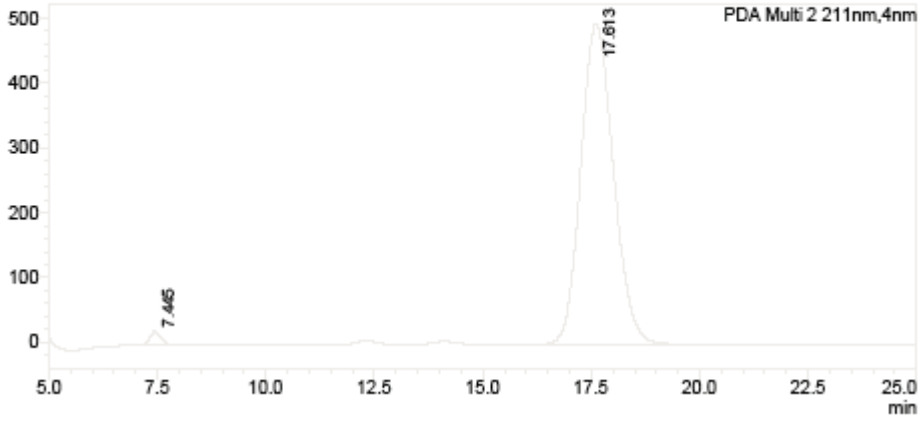
PDA Ch3 211nm

Peak#	Ret. Time	Area%
1	7.488	50.993
2	17.774	49.007
Total		100.000

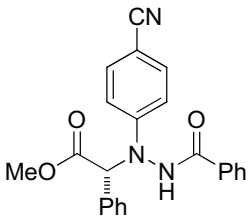


PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	7.445	1.368
2	17.613	98.632
Total		100.000

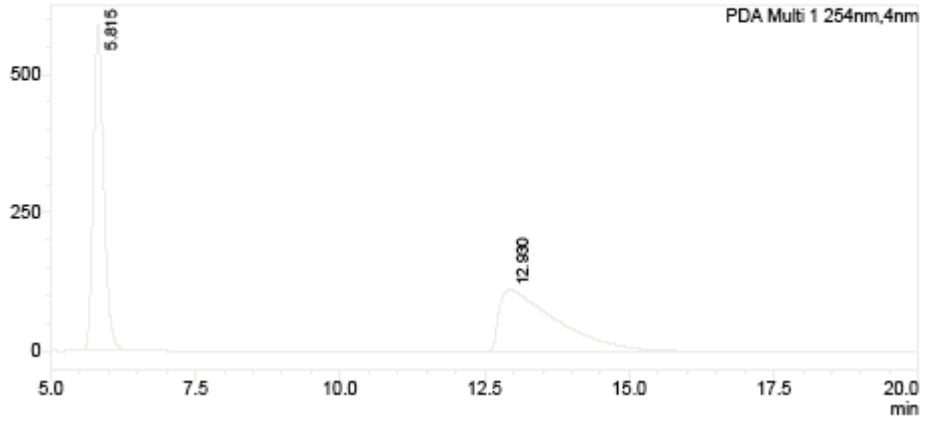


HPLC data compound **31**: Chiralpak IA 80% IPA:hexane, 1 mL min^{-1}, 254 nm, 40 °C, 98% ee



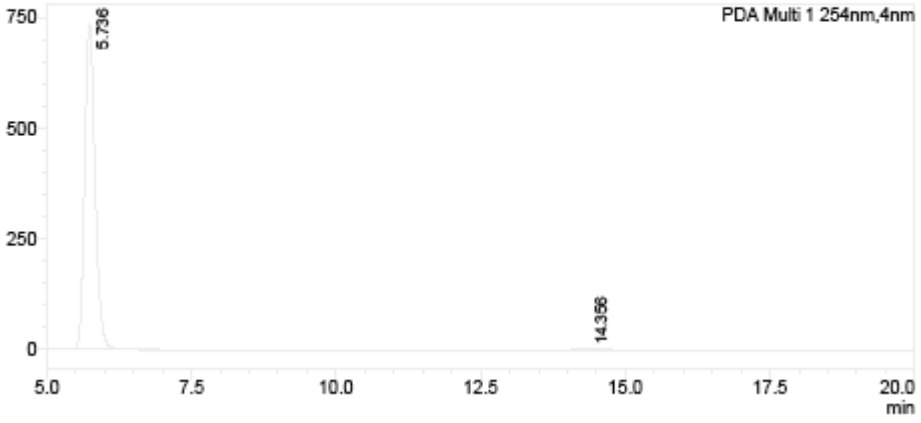
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	5.815	49.634
2	12.930	50.366
Total		100.000

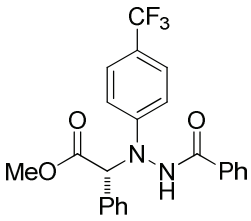


PDA Ch1 254nm

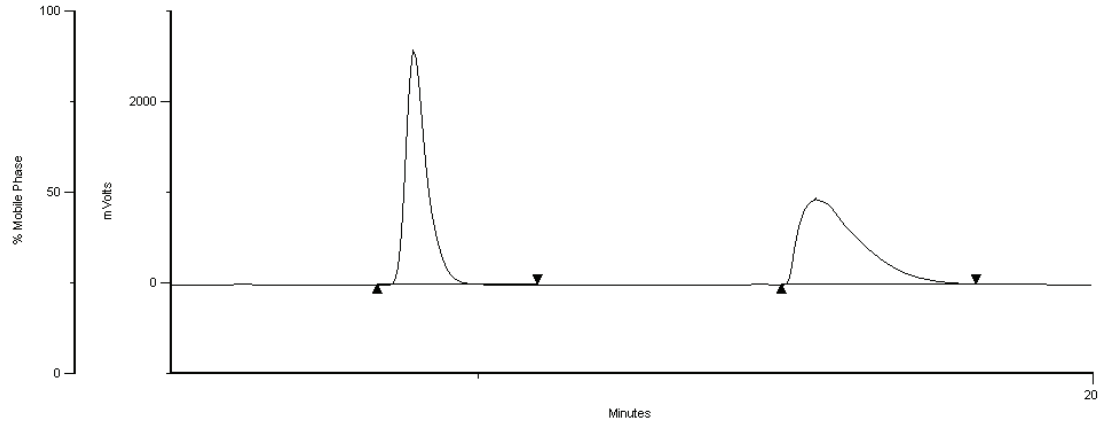
Peak#	Ret. Time	Area%
1	5.736	98.918
2	14.356	1.082
Total		100.000



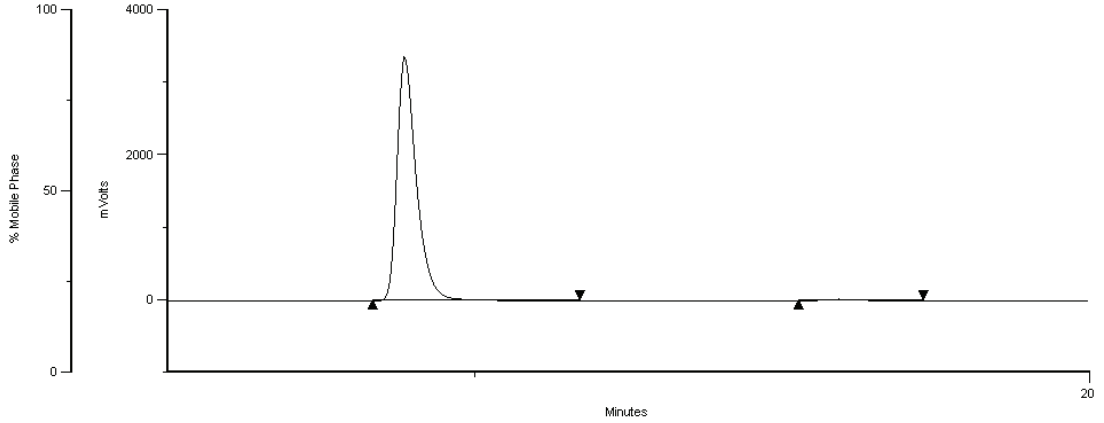
HPLC data compound **32**: Chiralpak IA 30% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, 99% ee



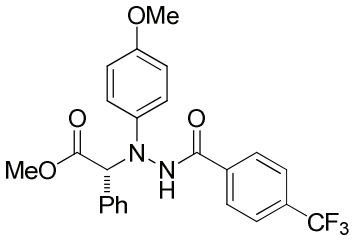
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	8.95	02382880.00	48.58
2	1.00	*2	15.50	08357416.00	51.42



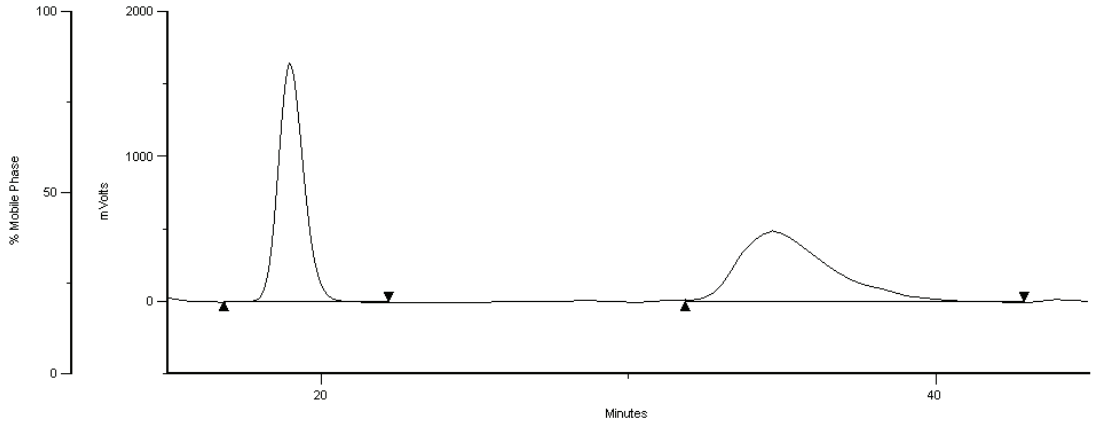
	Inj. Number	Peak Name	R. Time	Area	Area %
1	6.00	*1	8.85	22938440.00	99.38
2	6.00	2	15.92	766629.19	0.62



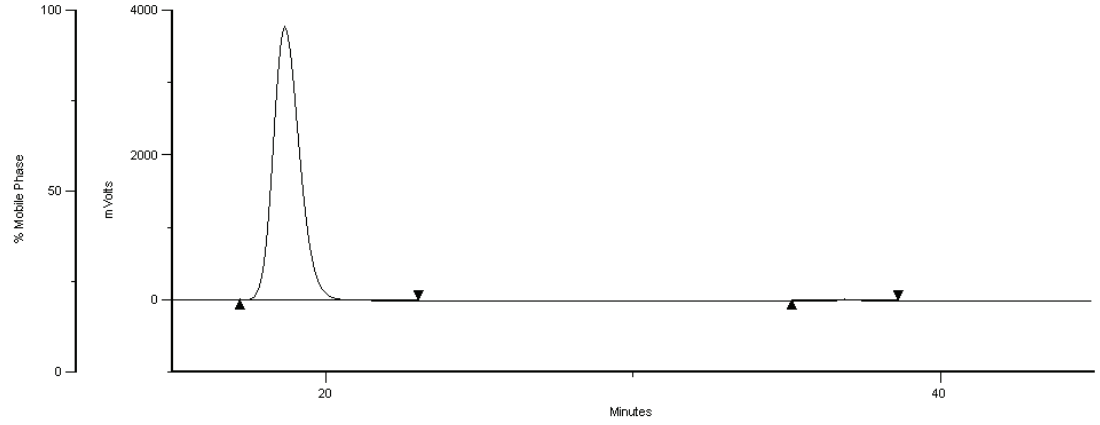
HPLC data compound **33**: Chiralpak IA 50% IPA:hexane, 2 mL min^{-1}, 211 nm, 20 °C, 99% ee



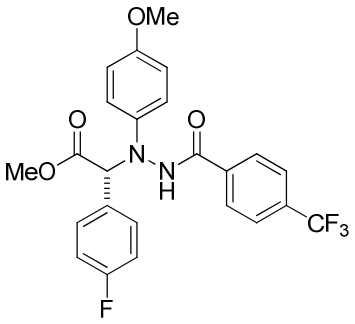
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	18.97	60329136.0(	48.51
2	1.00	*2	34.69	70188032.0(	51.49



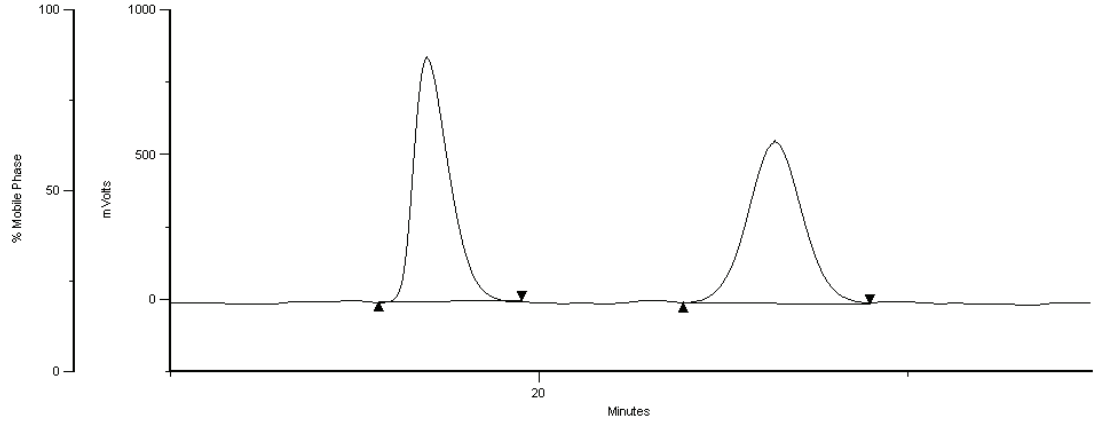
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	18.66	79143200.0(	99.63
2	1.00	*2	36.86	1418129.75	0.37



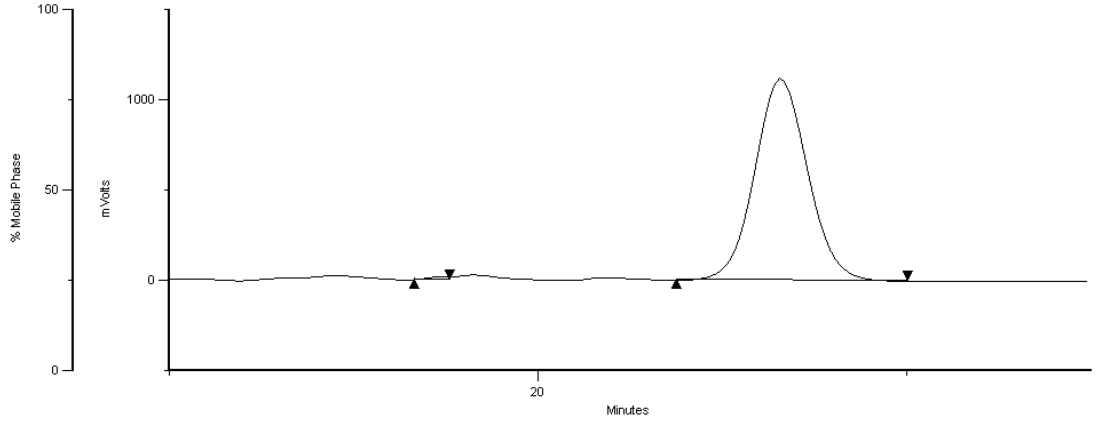
HPLC data compound **34**: Chiralpak IA 50% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 99% ee



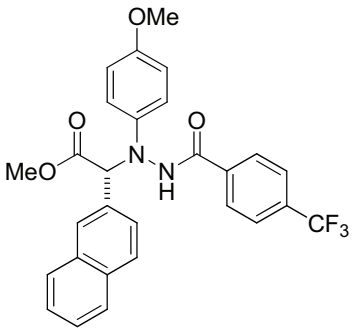
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	16.96	34616840.00	49.03
2	1.00	*2	26.41	36373592.00	50.97



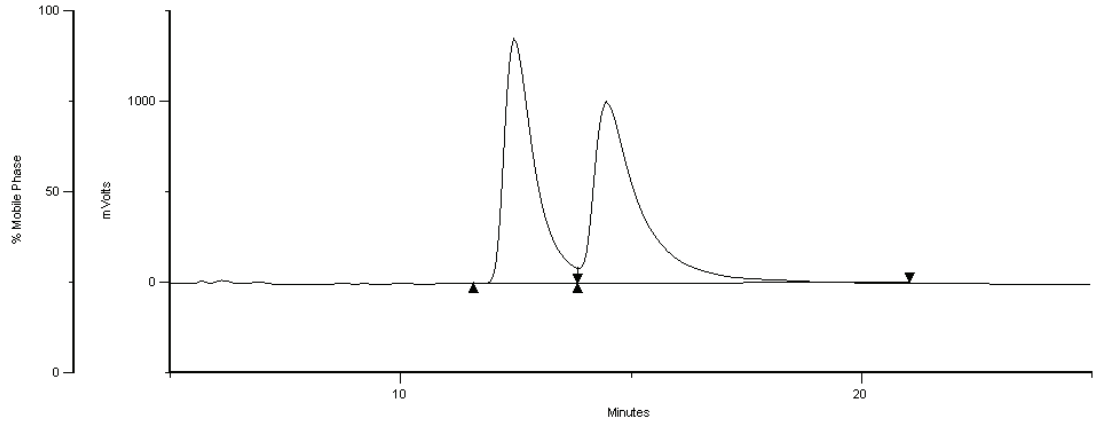
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	17.62	1103944.62	0.59
2	1.00	*2	26.58	87317104.00	99.41



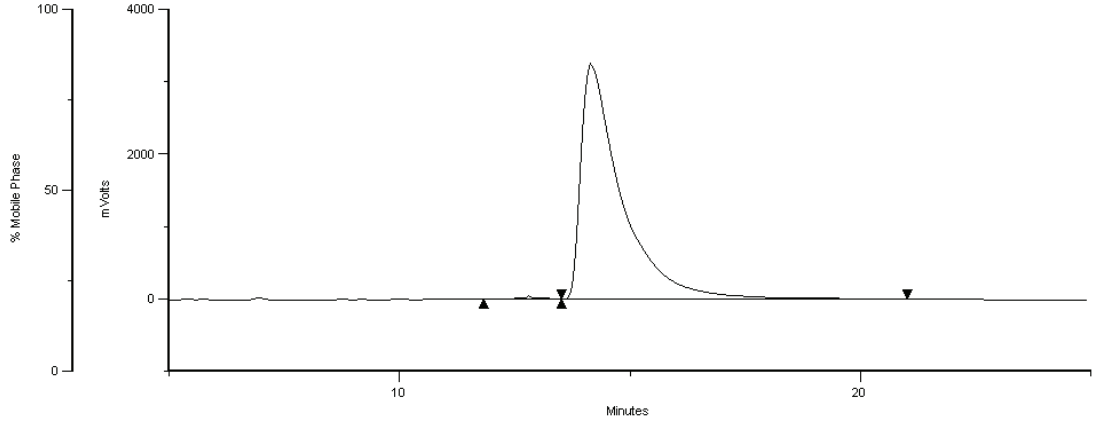
HPLC data compound **35**: Chiralpak IB 20% IPA:hexane, 1 mL min^{-1}, 211 nm, 20 °C, 98% ee



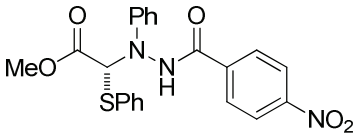
	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	12.47	04331272.0(	47.00
2	1.00	2	14.47	17663008.0(	53.00



	Inj. Number	Peak Name	R. Time	Area	Area %
1	1.00	*1	12.80	2883634.50	0.85
2	1.00	*2	14.16	37361120.0(	99.15

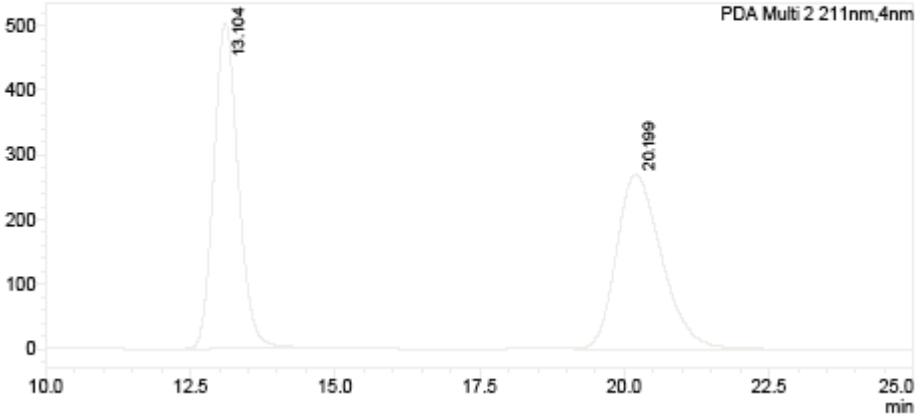


HPLC data compound **36**: Chiralpak IA 40% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 98% ee



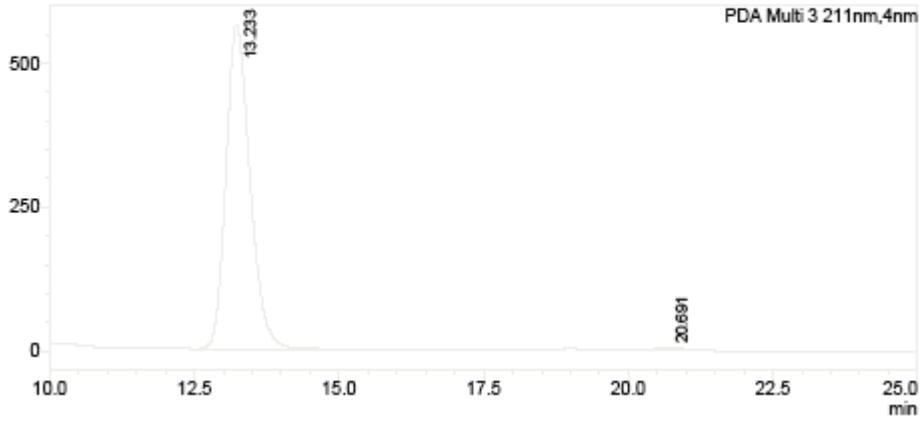
PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	13.104	50.269
2	20.199	49.731
Total		100.000

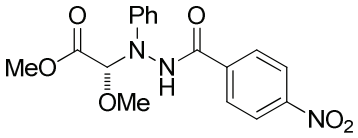


PDA Ch3 211nm

Peak#	Ret. Time	Area%
1	13.233	98.797
2	20.691	1.203
Total		100.000

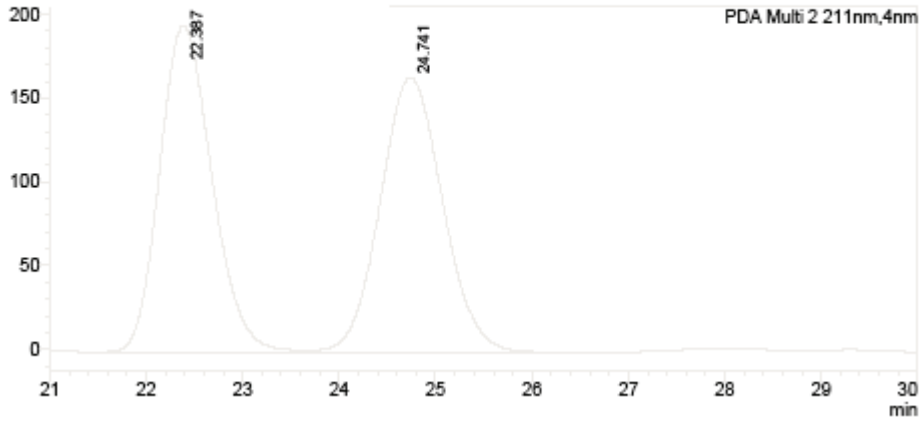


HPLC data compound **37**: Chiralpak AD-H 20% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 83% ee



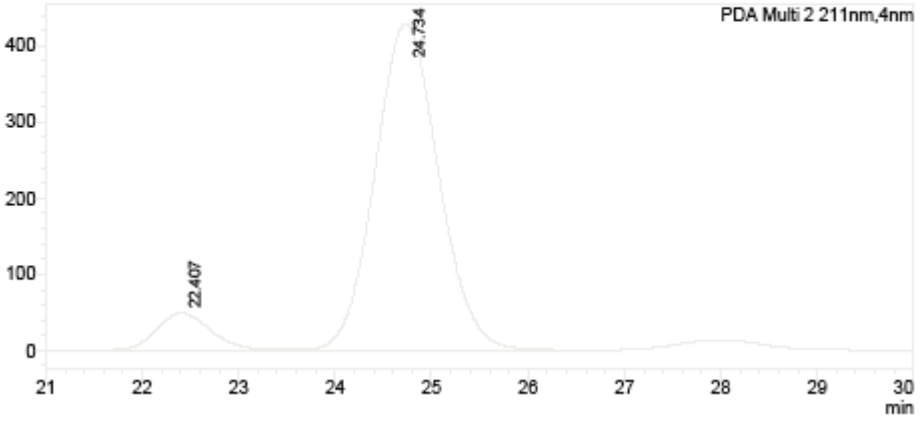
PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	22.387	49.935
2	24.741	50.065
Total		100.000

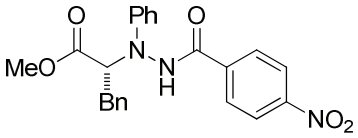


PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	22.407	8.706
2	24.734	91.294
Total		100.000

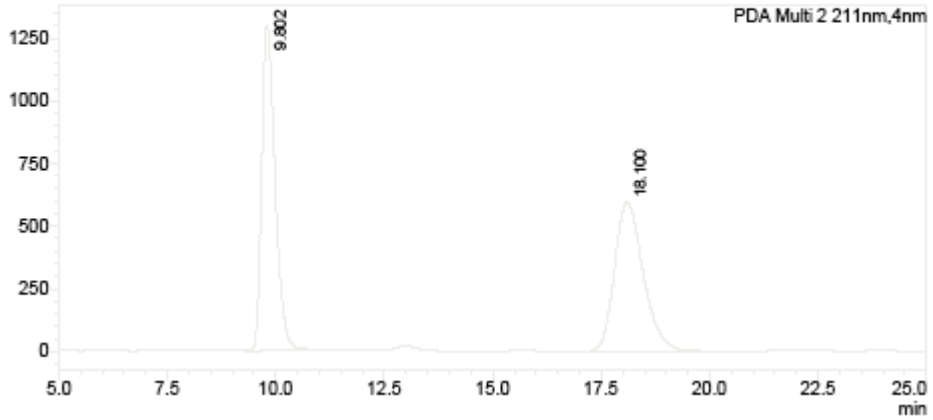


HPLC data compound **38**: Chiralpak IA 40% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 99% ee



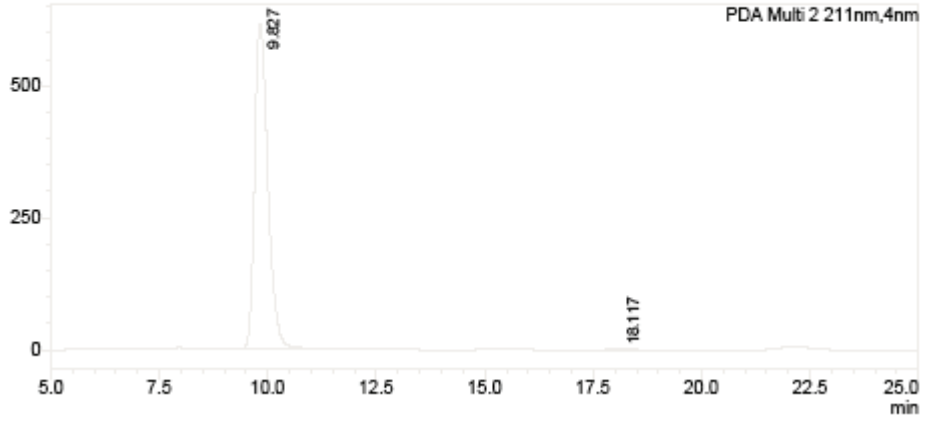
PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	9.802	50.319
2	18.100	49.681
Total		100.000

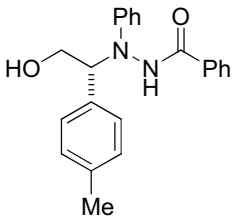


PDA Ch2 211nm

Peak#	Ret. Time	Area%
1	9.827	99.395
2	18.117	0.605
Total		100.000

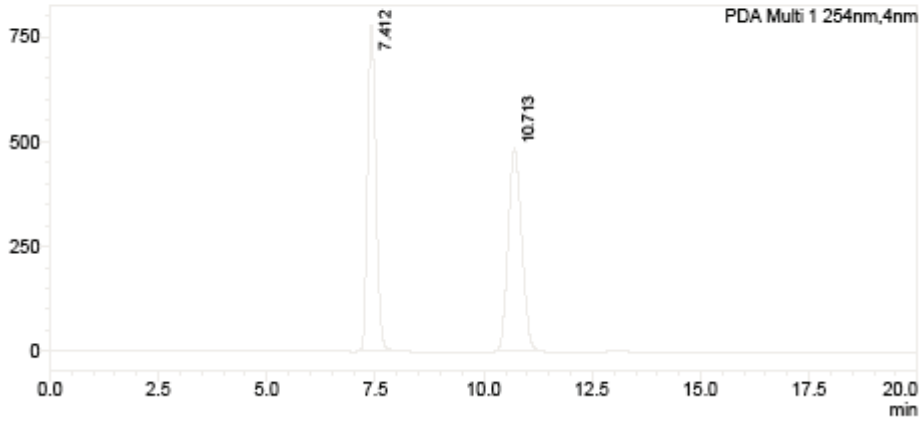


HPLC data compound **39**: Chiralpak AD-H 30% IPA:hexane, 1 mL min^{-1}, 254 nm, 30 °C, >99% ee



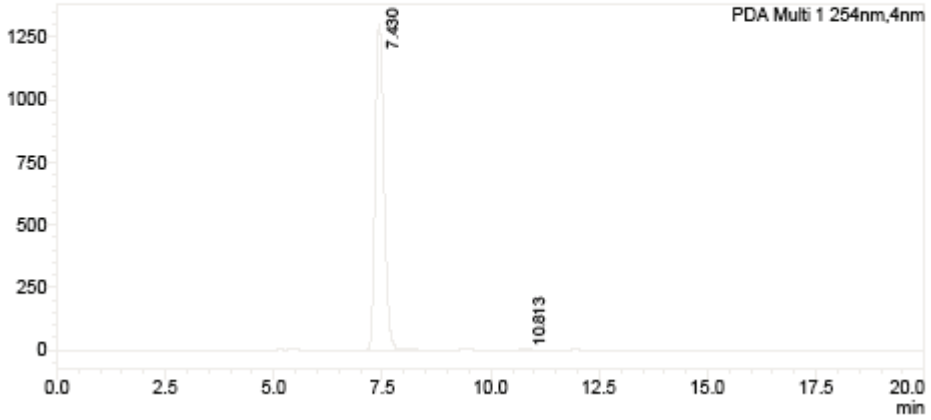
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.412	49.859
2	10.713	50.141
Total		100.000

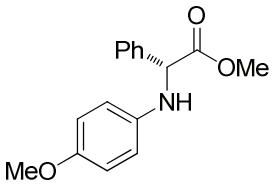


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.430	99.789
2	10.813	0.211
Total		100.000

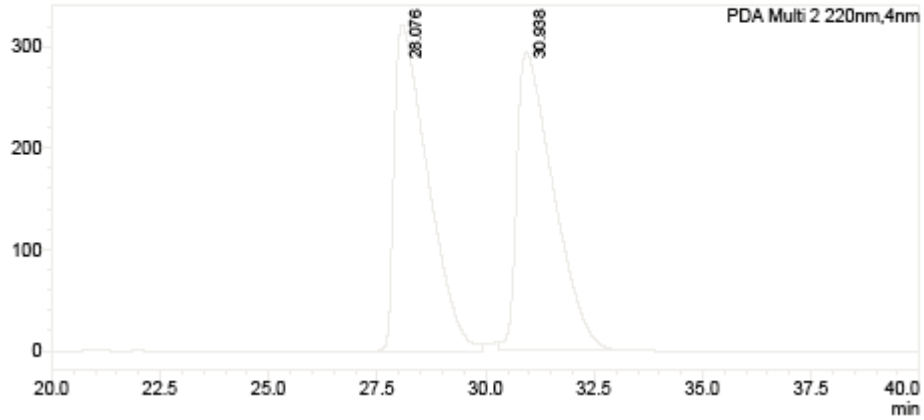


HPLC data compound **40**: Chiralcel OJ-H 30% IPA:hexane, 1 mL min^{-1}, 220 nm, 30 °C, 99% ee



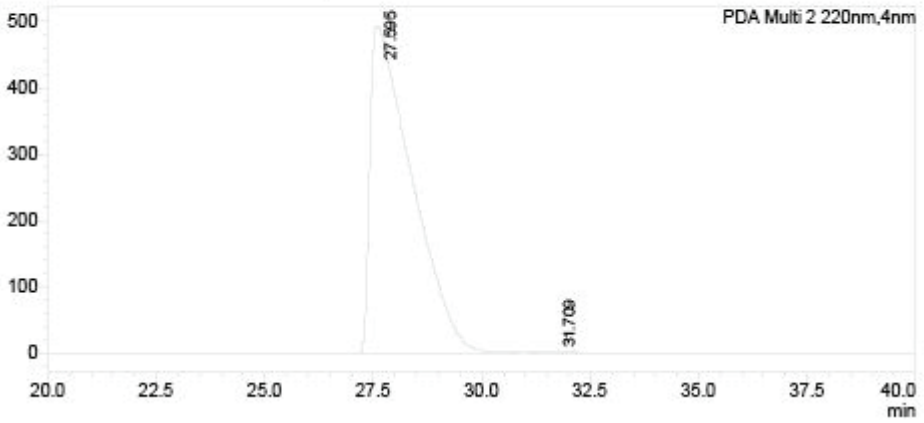
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	28.076	50.021
2	30.938	49.979
Total		100.000

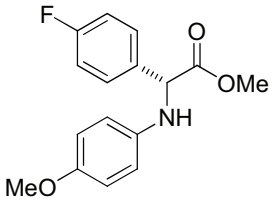


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	27.595	99.647
2	31.709	0.353
Total		100.000

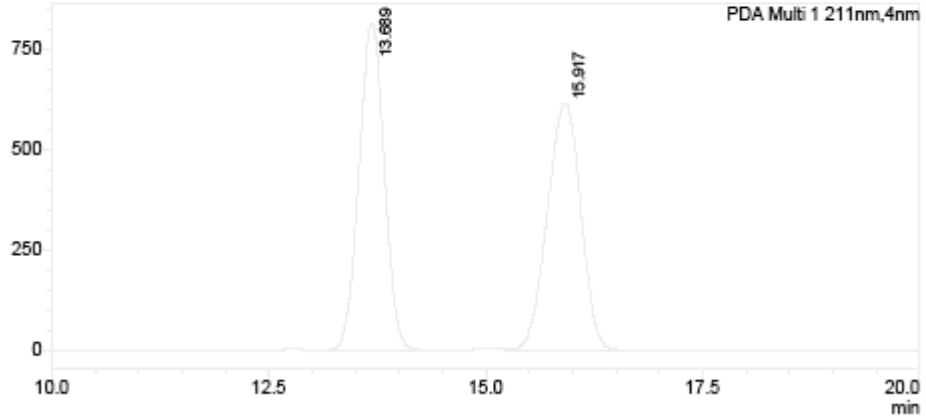


HPLC data compound **41**: Chiralpak AD-H 10% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 98% ee



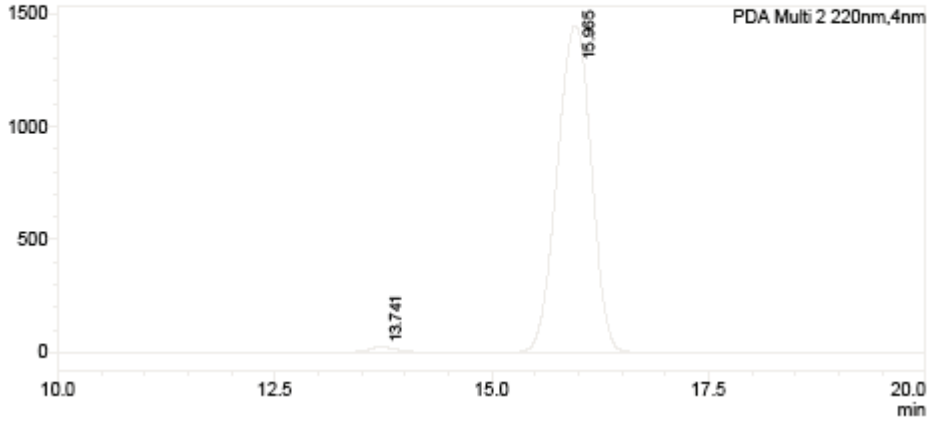
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.689	50.092
2	15.917	49.908
Total		100.000

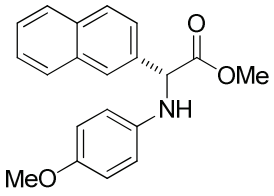


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	13.741	1.057
2	15.965	98.943
Total		100.000

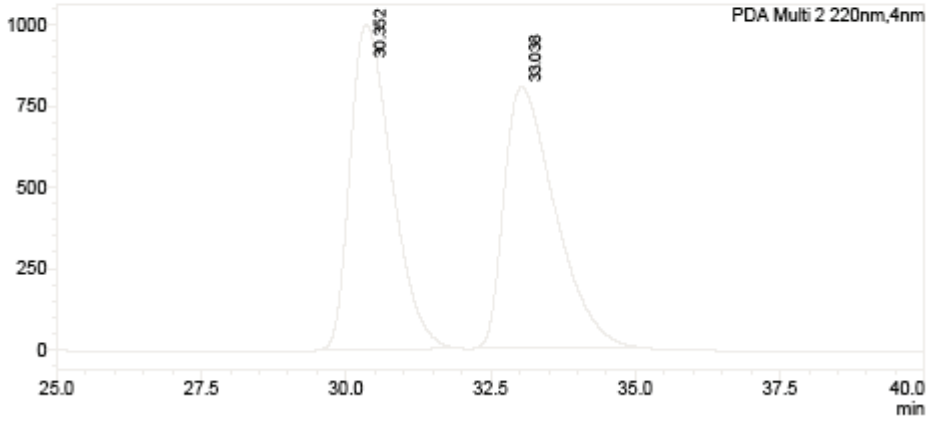


HPLC data compound **42**: Chiralpak IB 20% IPA:hexane, 1 mL min^{-1}, 220 nm, 30 °C, 98% ee



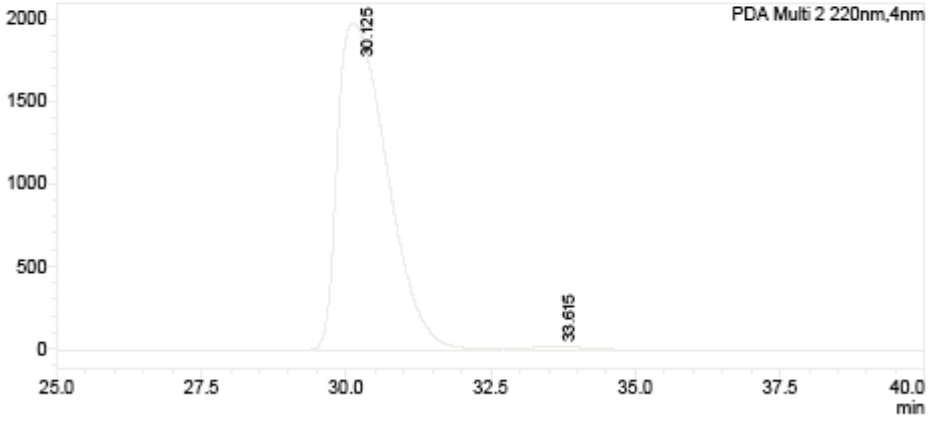
PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	30.352	50.173
2	33.038	49.827
Total		100.000

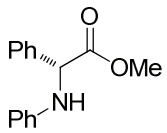


PDA Ch2 220nm

Peak#	Ret. Time	Area%
1	30.125	98.847
2	33.615	1.153
Total		100.000

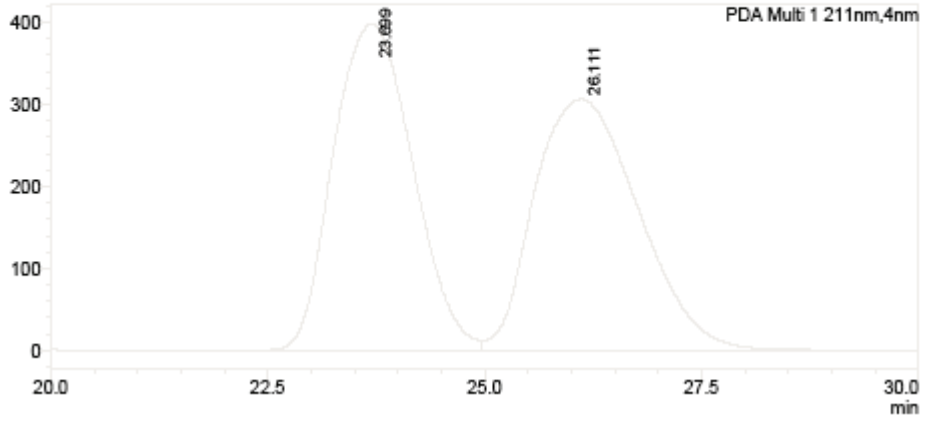


HPLC data compound **43**: Chiralcel OD-H 1% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 99% ee



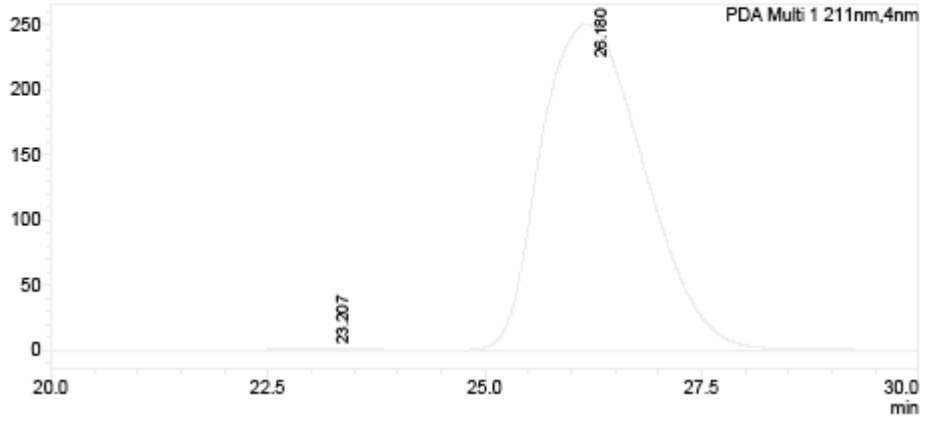
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	23.699	49.953
2	26.111	50.047
Total		100.000

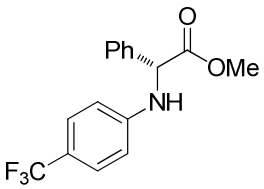


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	23.207	0.488
2	26.180	99.512
Total		100.000

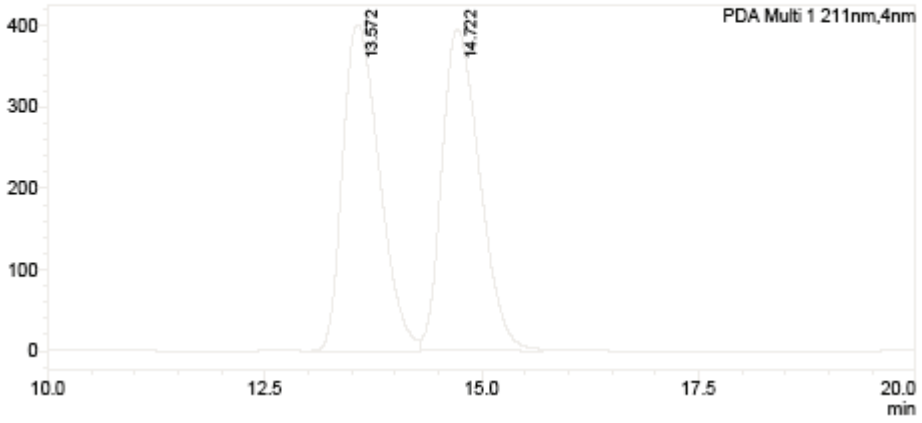


HPLC data compound **44**: Chiralcel OD-H 1% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 98% ee



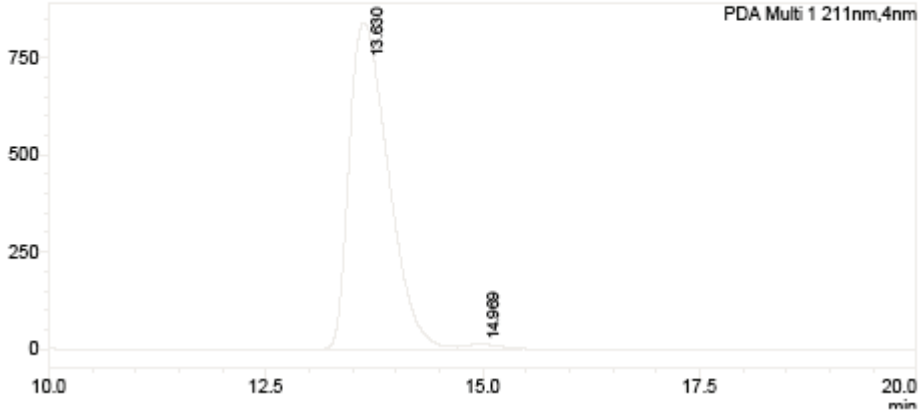
PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.572	49.641
2	14.722	50.359
Total		100.000

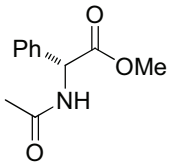


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	13.630	98.763
2	14.969	1.237
Total		100.000

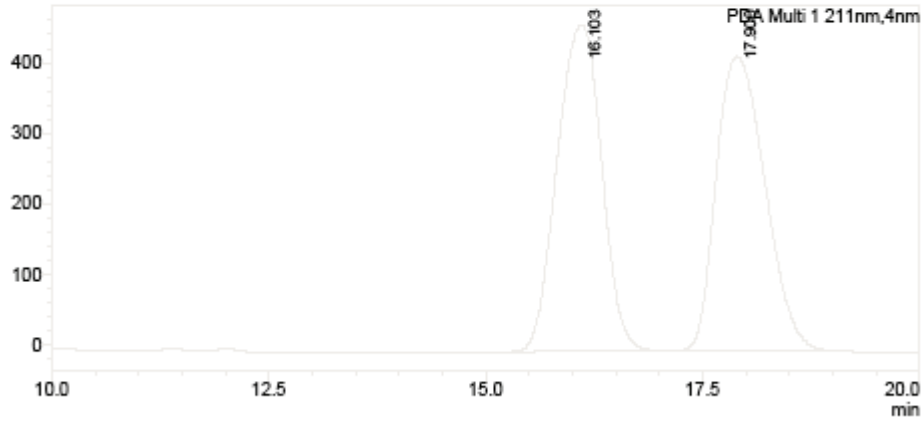


HPLC data compound **83**: Chiralcel OJ-H 10% IPA:hexane, 1 mL min^{-1}, 211 nm, 30 °C, 90% ee



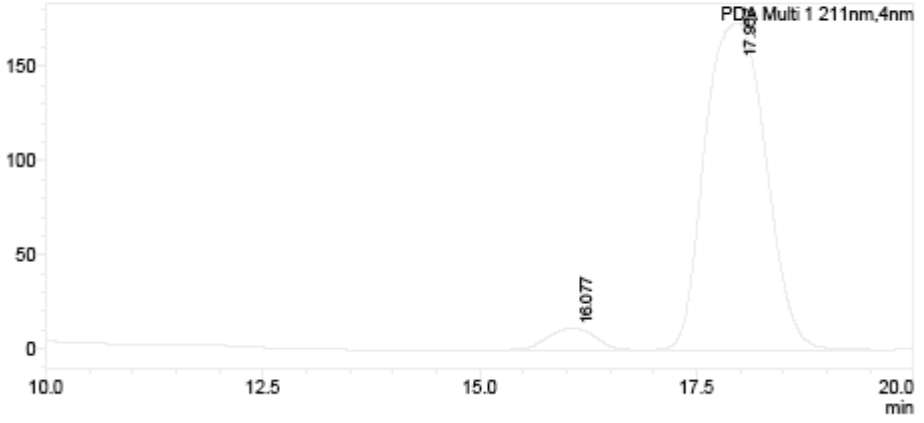
PDA Ch1 211nm

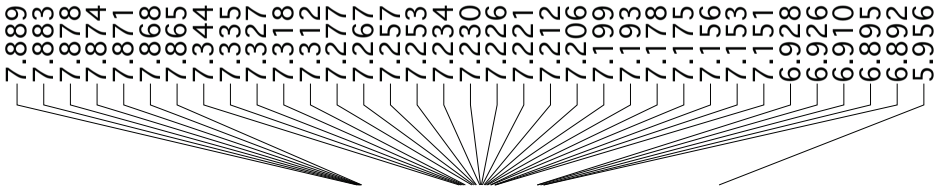
Peak#	Ret. Time	Area%
1	16.103	50.227
2	17.900	49.773
Total		100.000

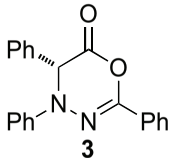


PDA Ch1 211nm

Peak#	Ret. Time	Area%
1	16.077	4.872
2	17.957	95.128
Total		100.000

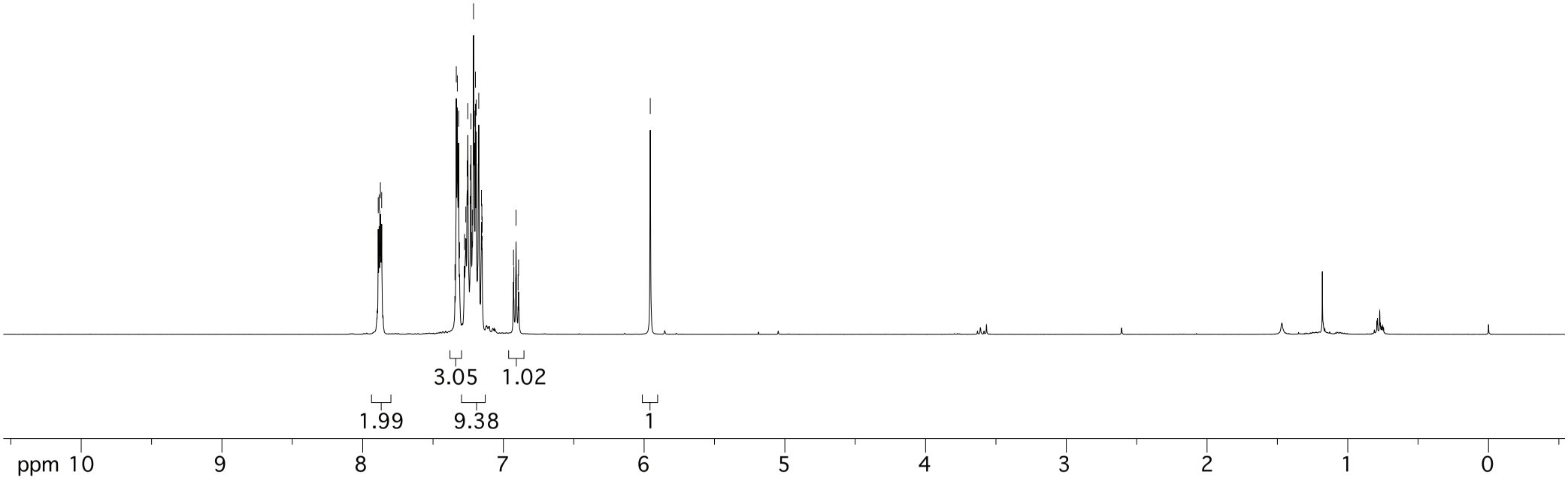


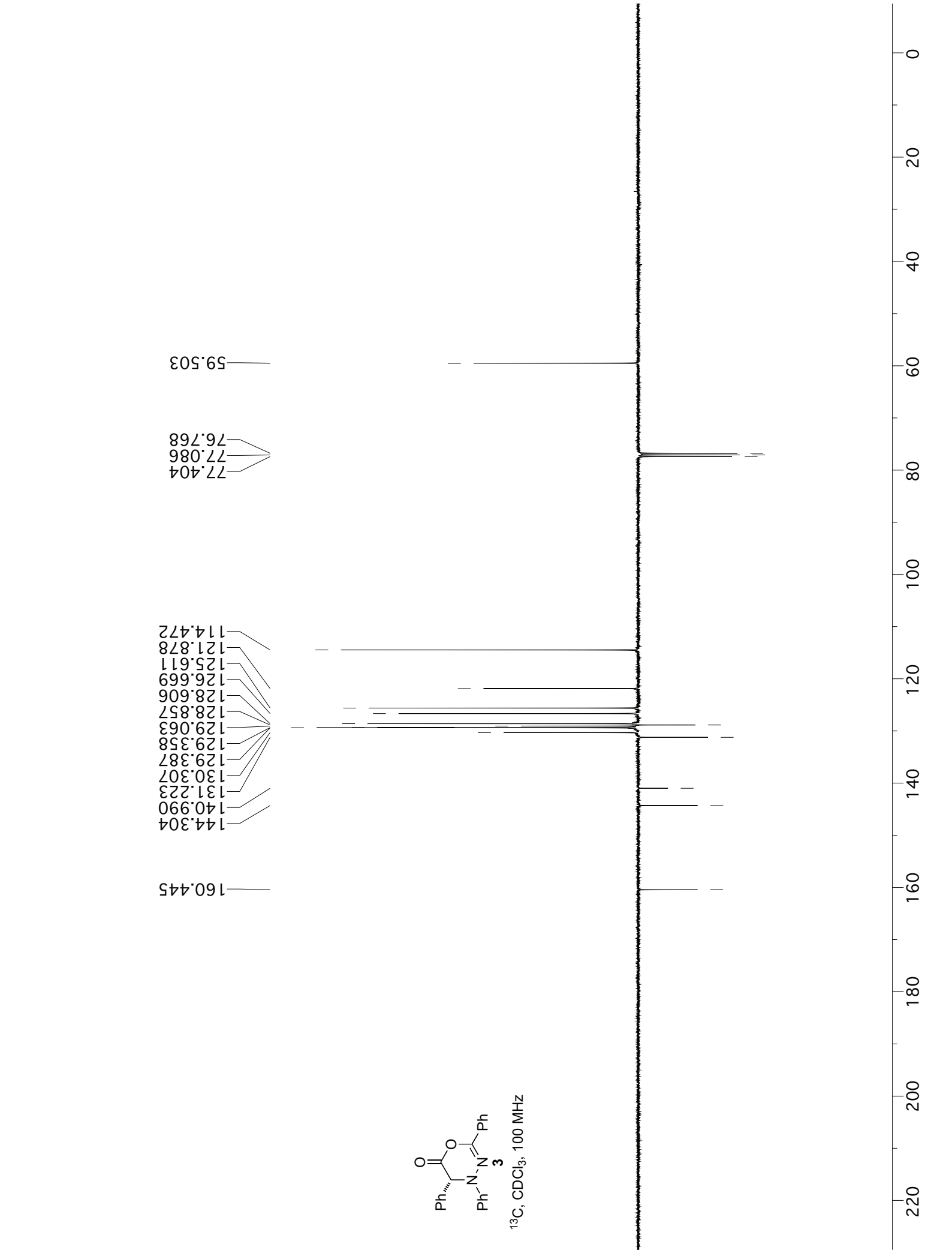


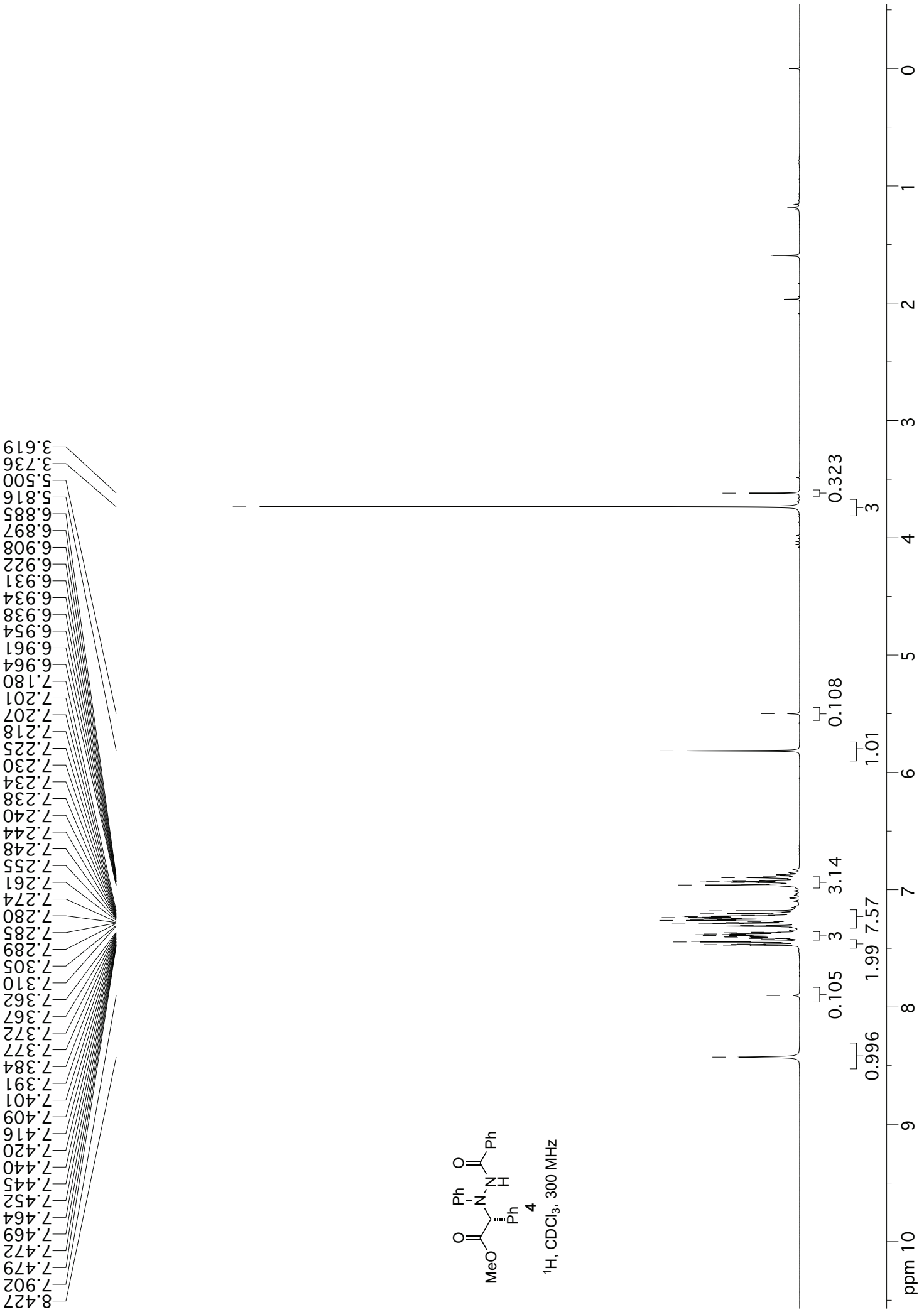


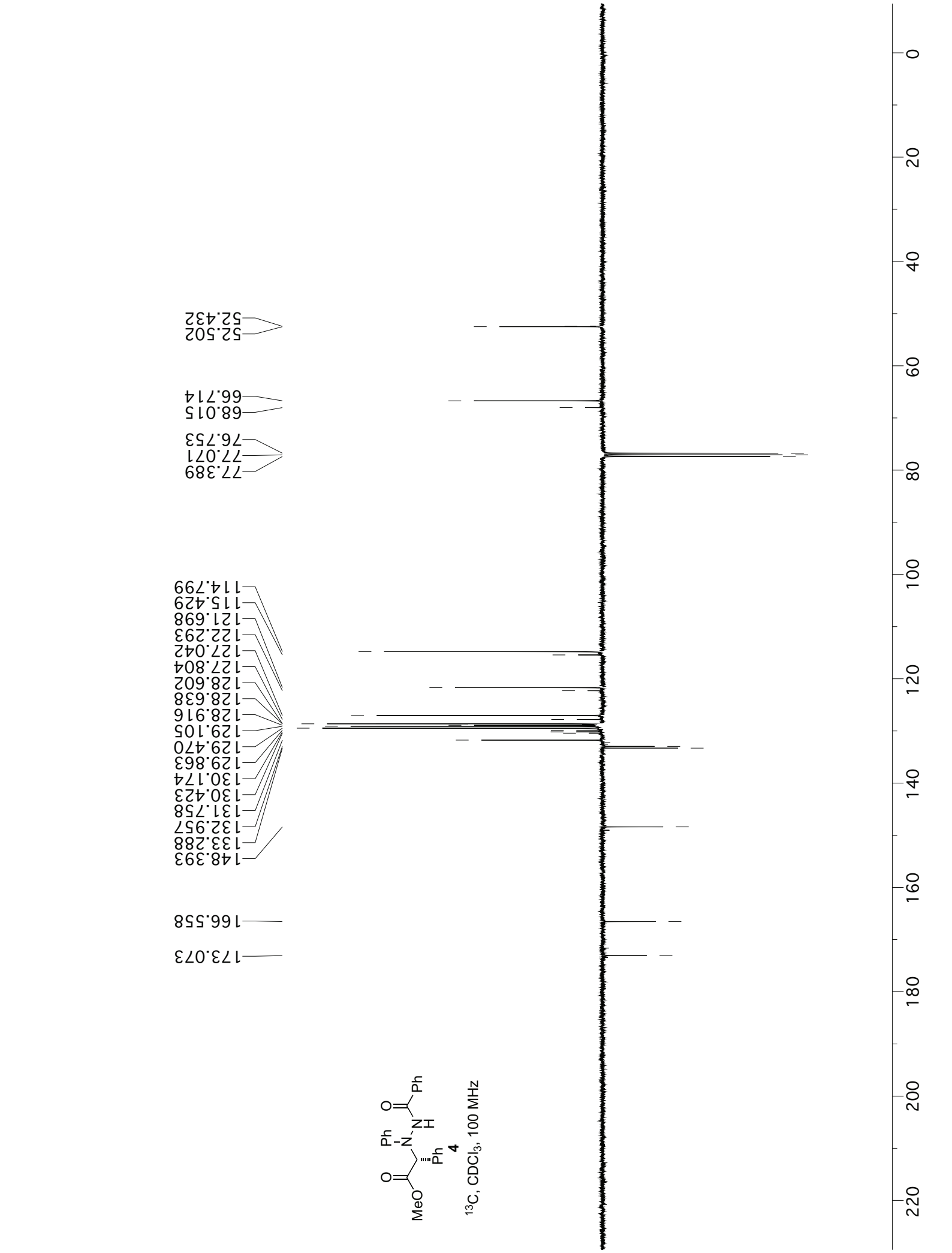
3

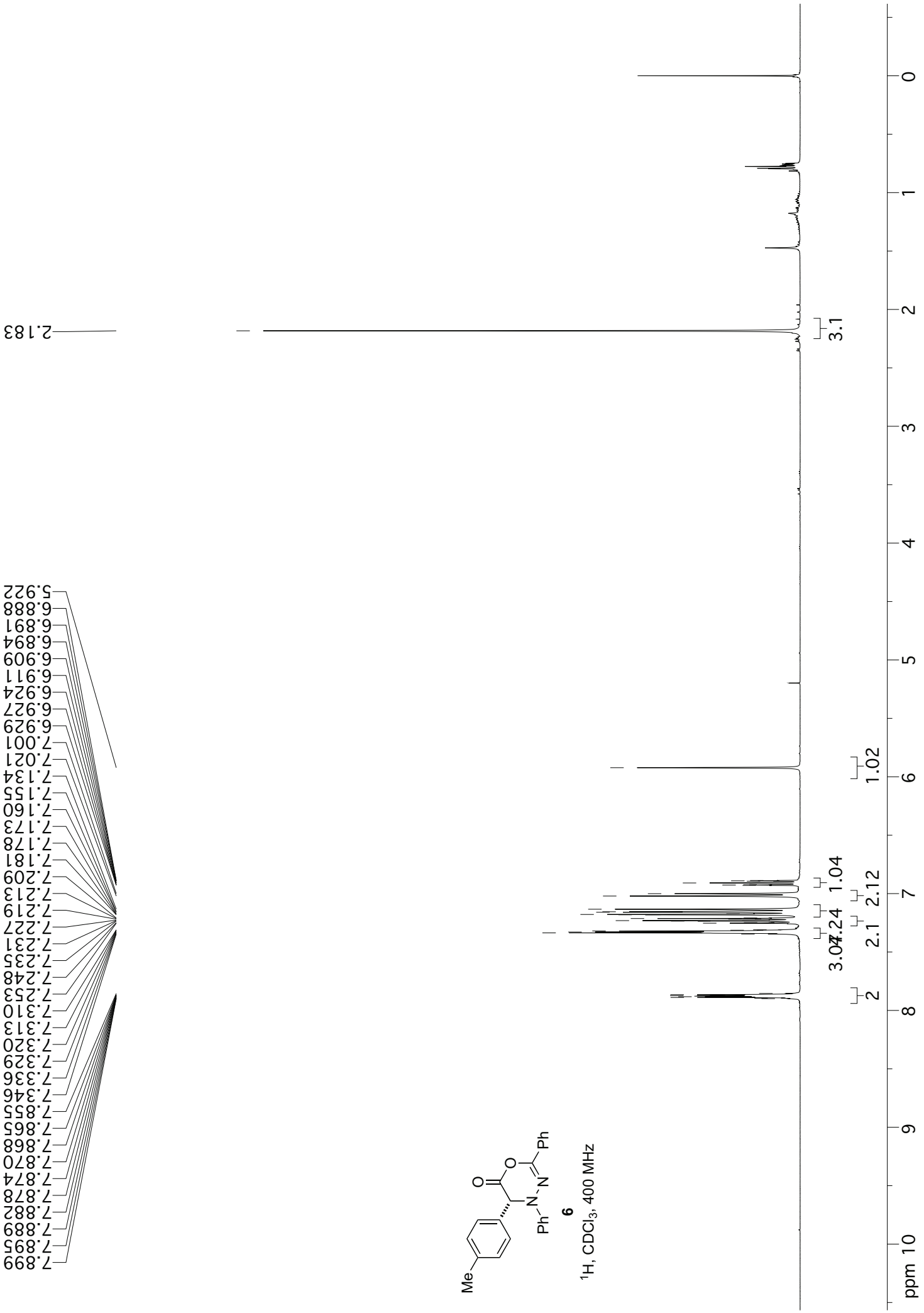
^{1}H, $CDCl_3$, 400 MHz

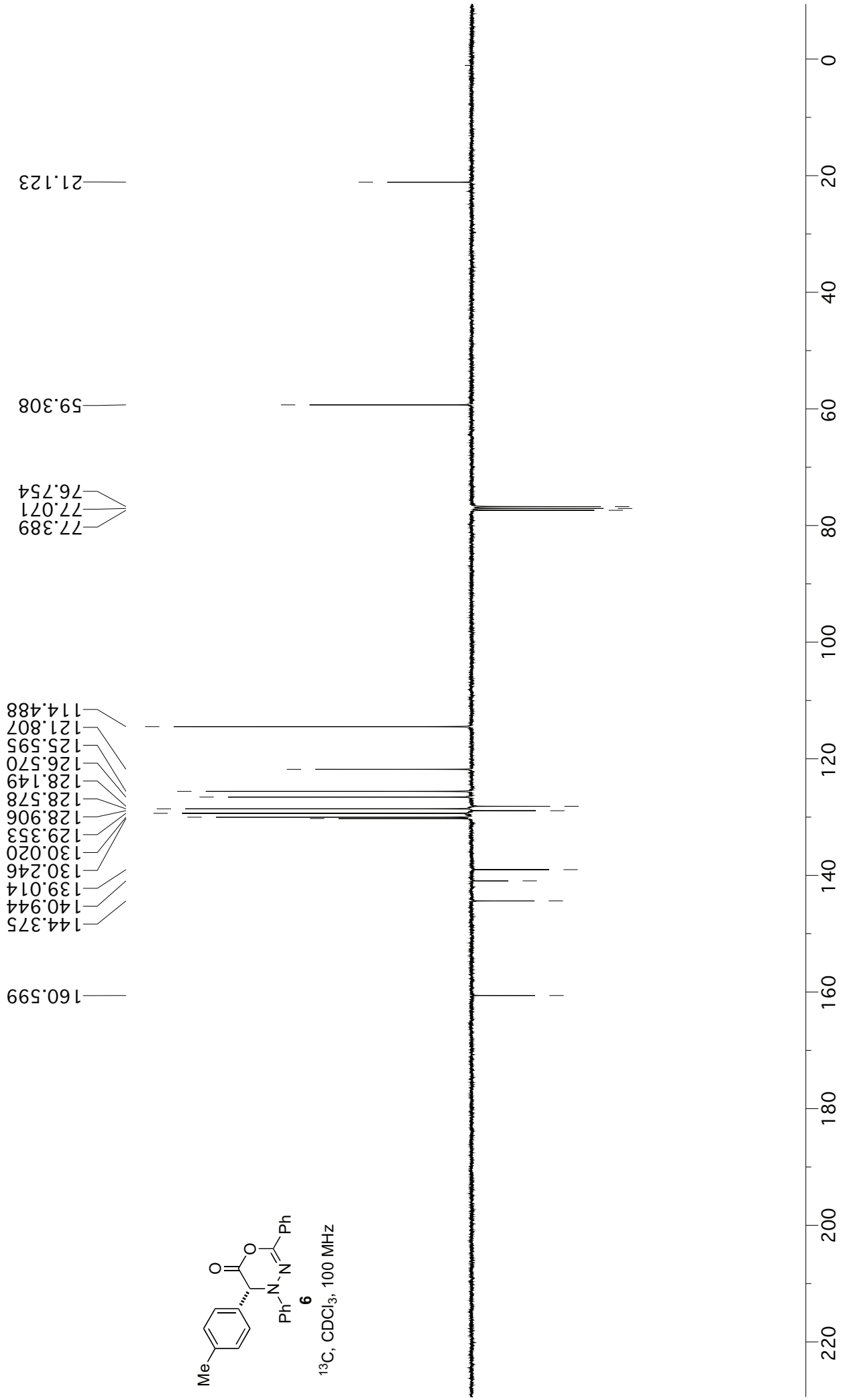


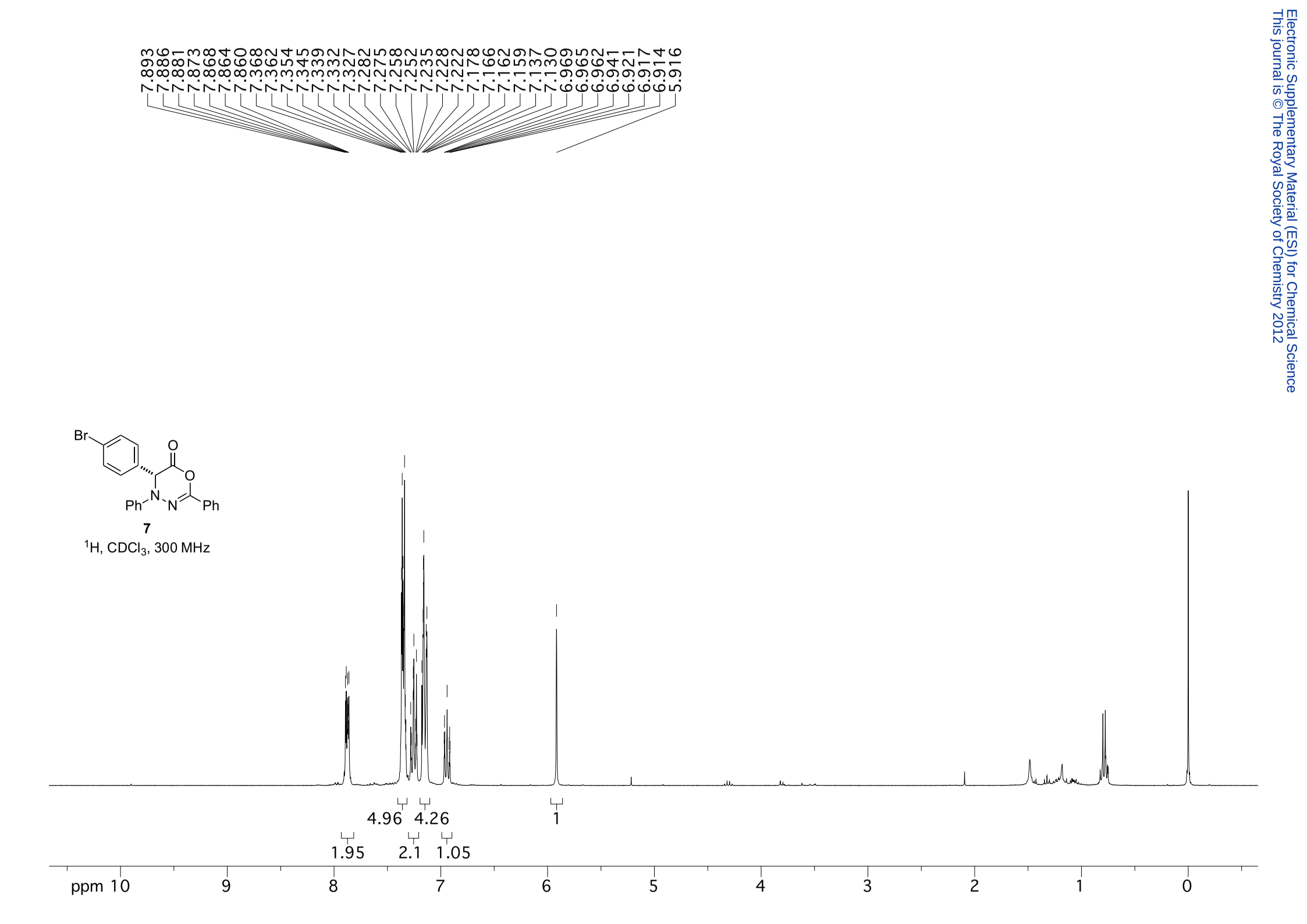


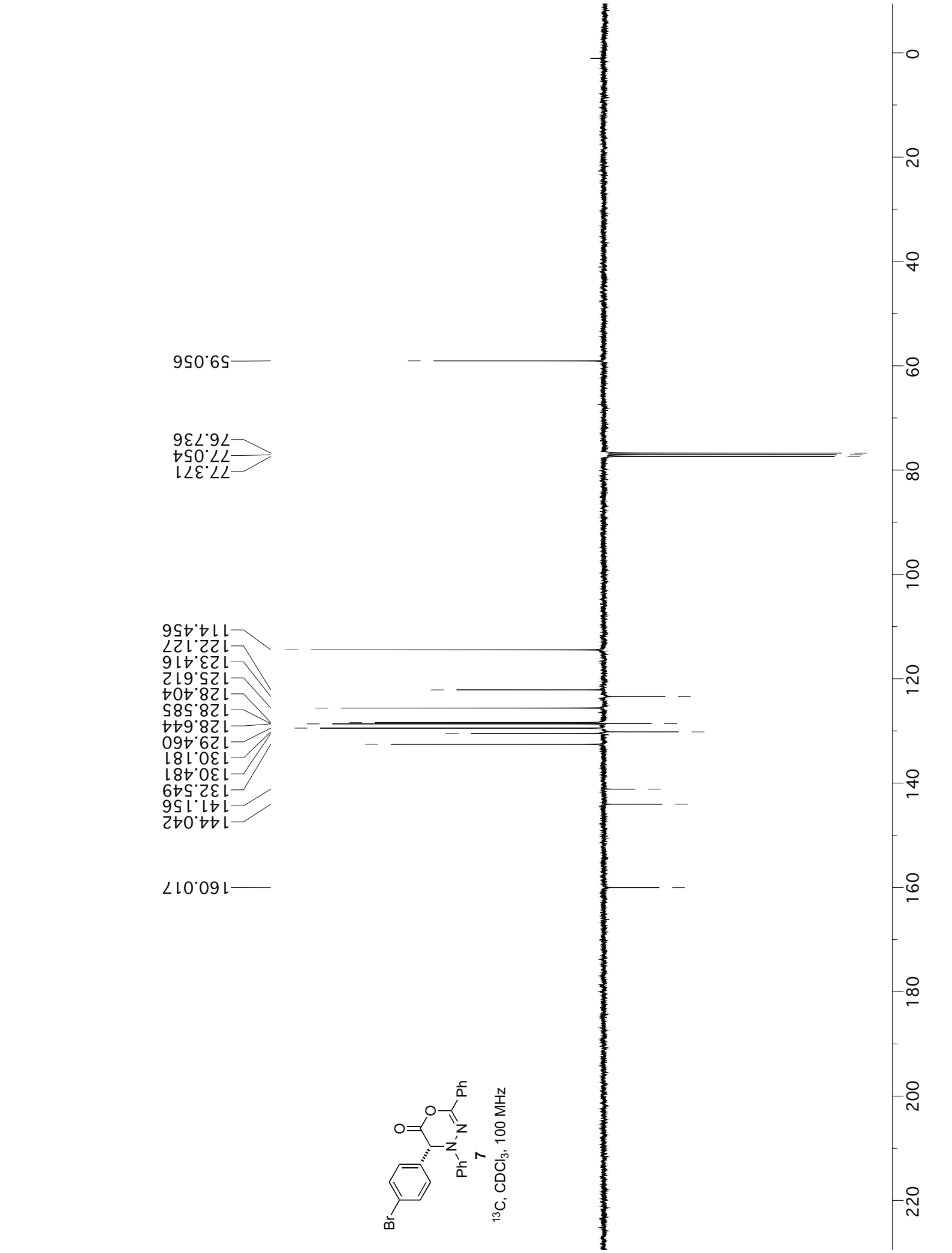


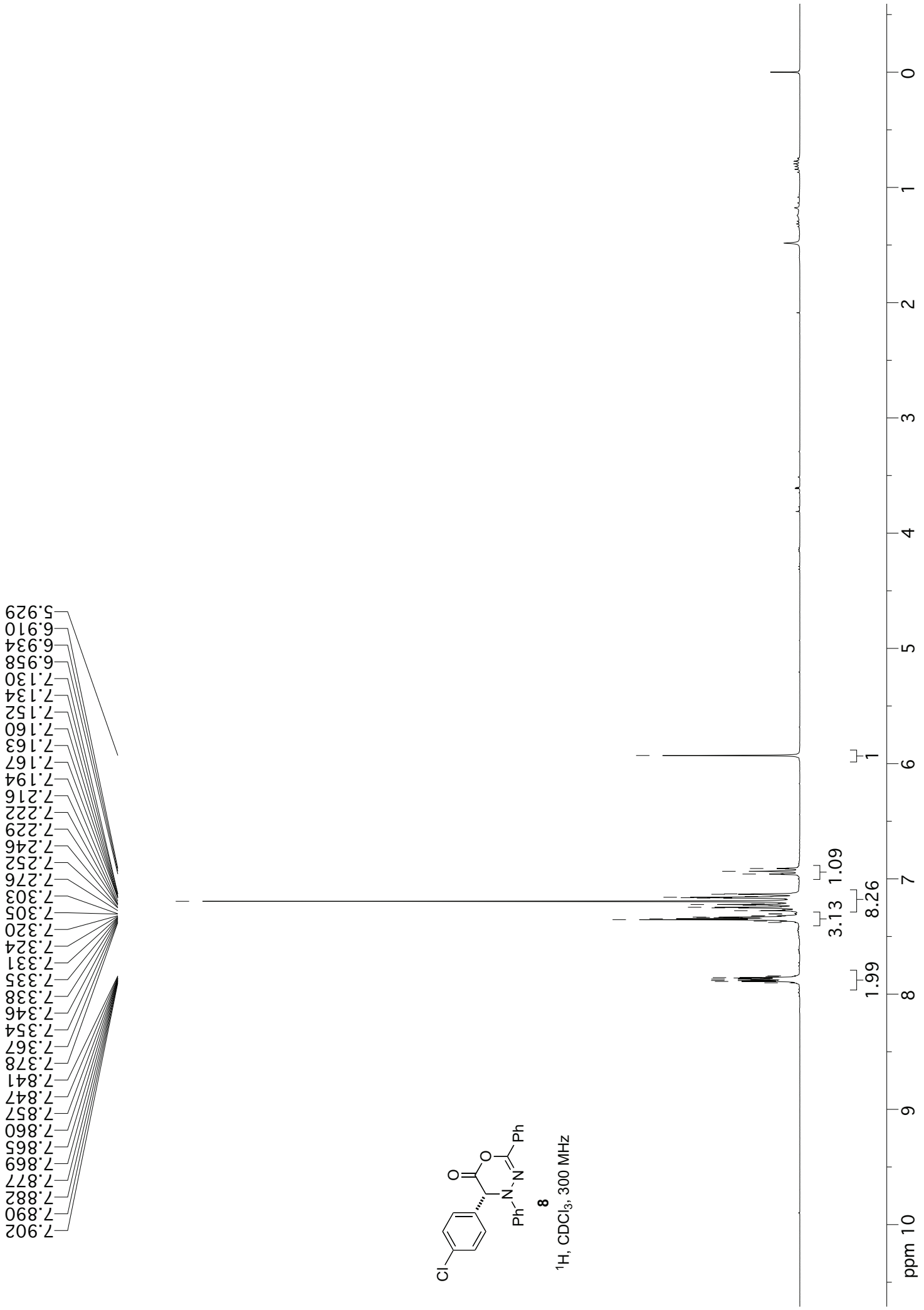


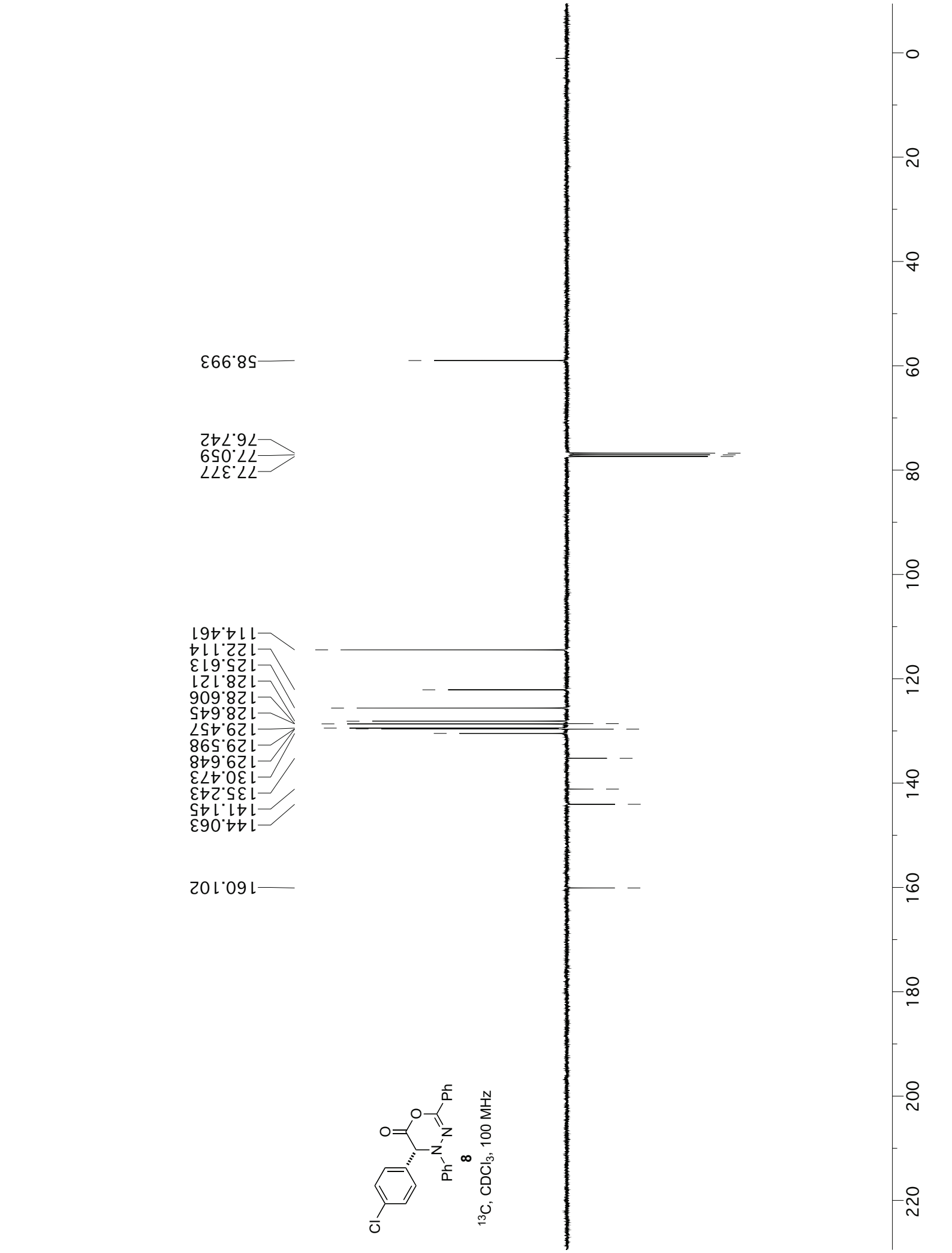


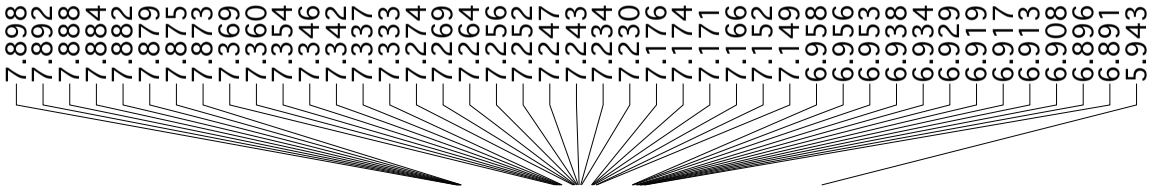


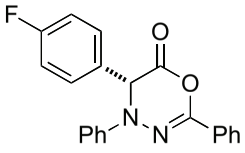






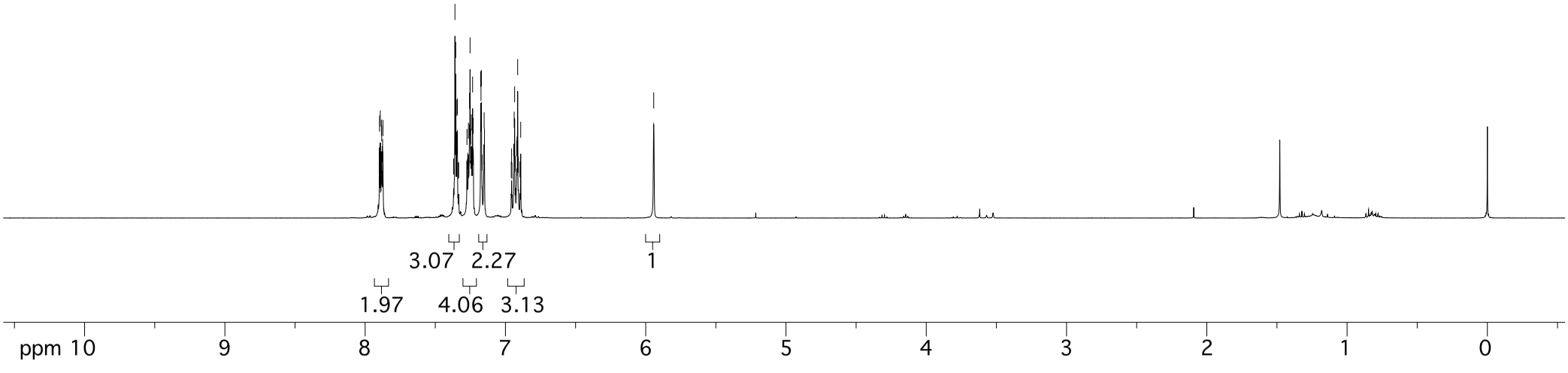


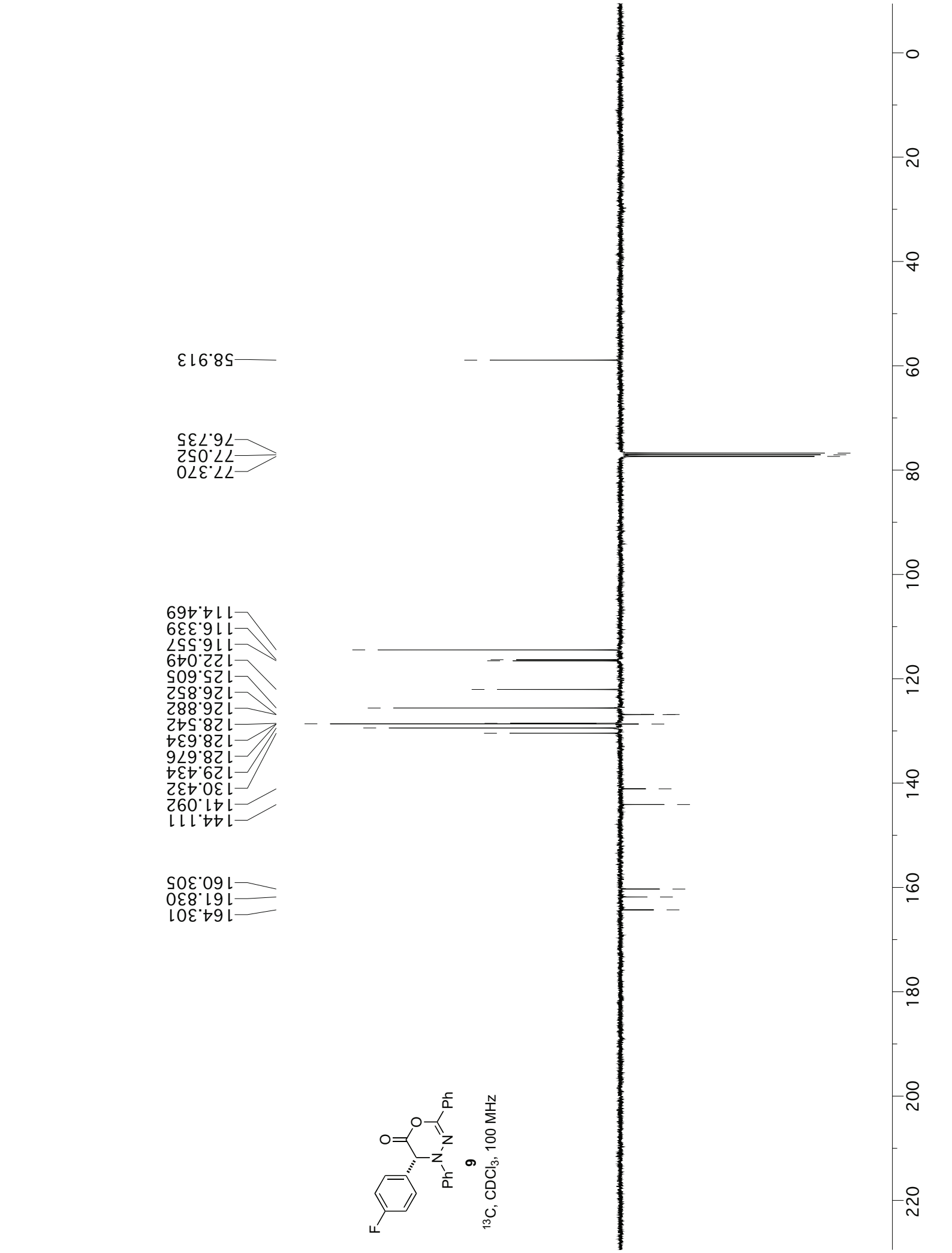


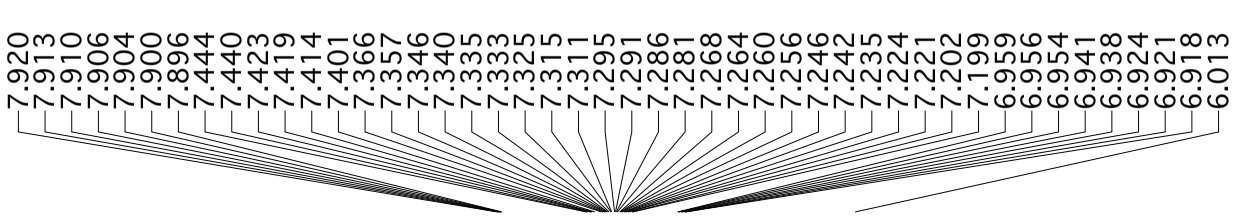


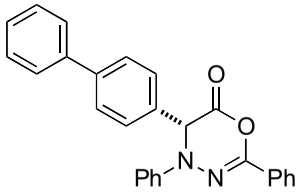
9

^{1}H, $CDCl_3$, 400 MHz



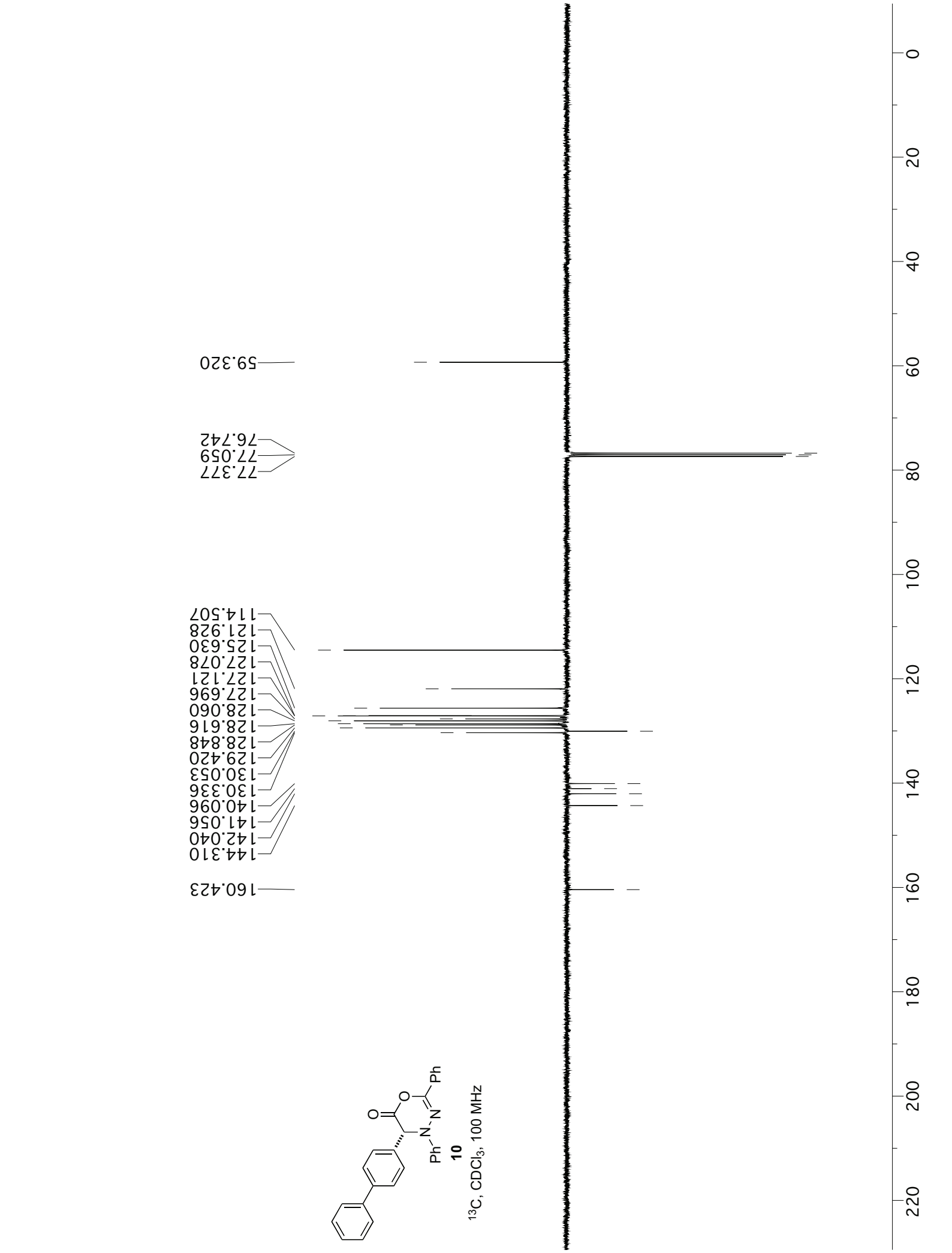


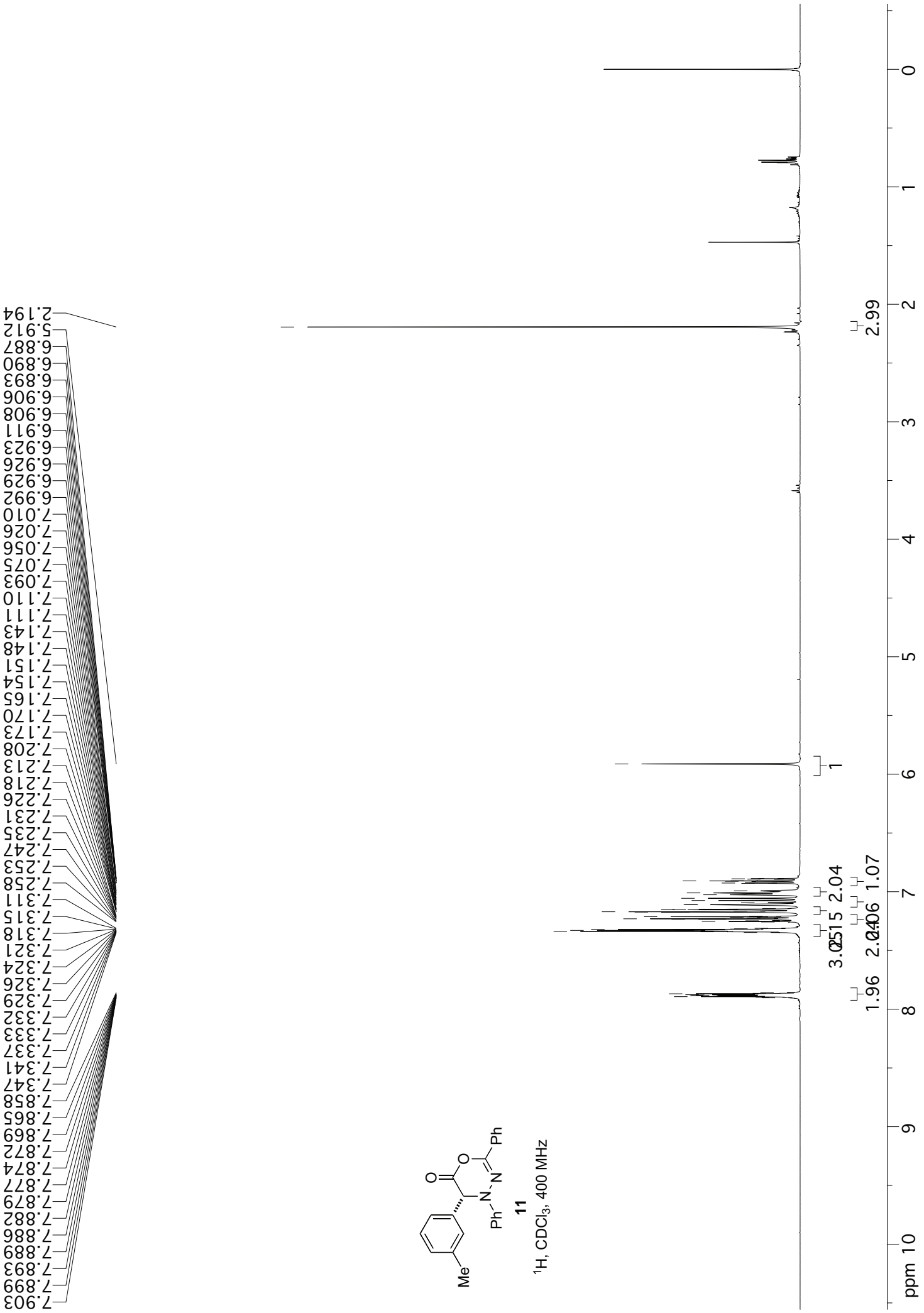


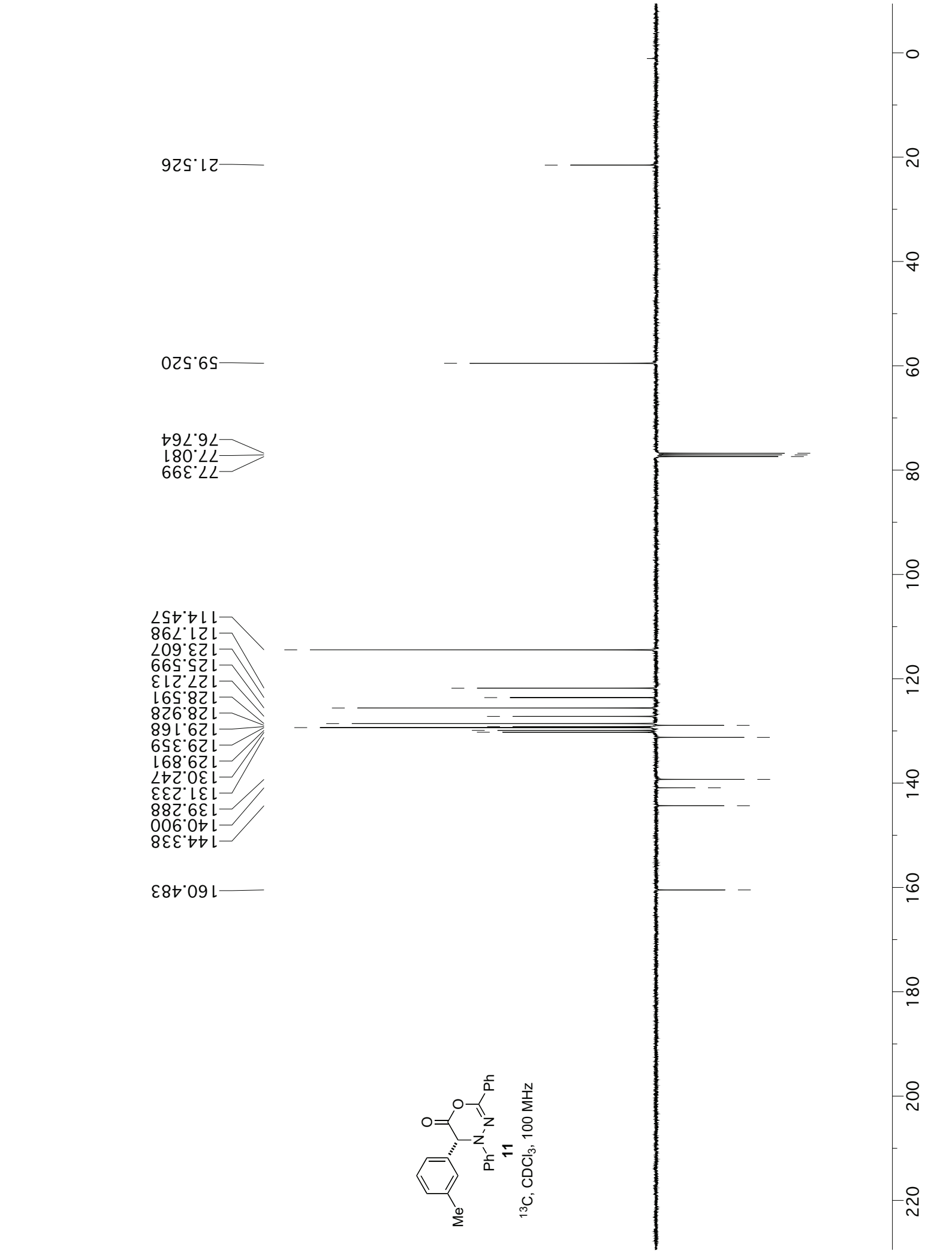


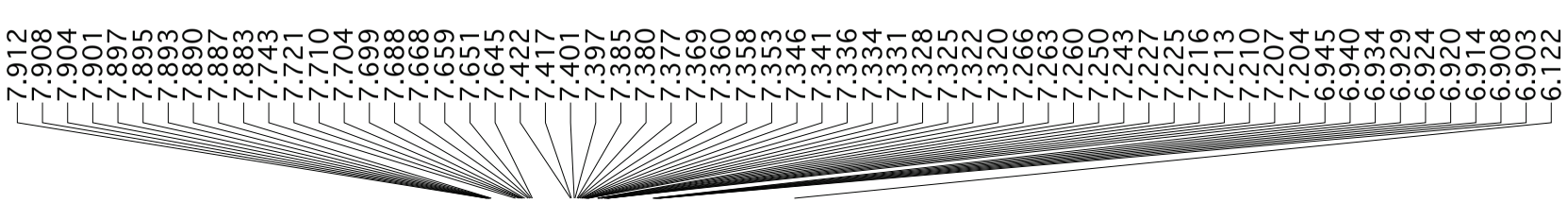
10

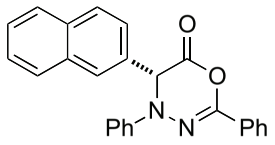
^{1}H, $CDCl_3$, 400 MHz




2.194
5.912
6.887
6.890
6.893
6.906
6.908
6.911
6.923
6.926
6.929
6.992
7.010
7.026
7.056
7.075
7.093
7.110
7.111
7.143
7.148
7.151
7.154
7.165
7.170
7.173
7.208
7.213
7.218
7.226
7.231
7.235
7.247
7.253
7.258
7.311
7.315
7.318
7.321
7.324
7.326
7.329
7.332
7.333
7.337
7.341
7.347
7.858
7.865
7.869
7.872
7.874
7.877
7.879
7.882
7.886
7.889
7.893
7.899
7.903
Me
Ph
N
N
O
O
Ph
11
^{1}H, CDCl$_3$, 400 MHz
2.99
1
3.02
2.15
2.04
2.04
2.06
1.07
1.96
ppm 10
9
8
7
6
5
4
3
2
1
0

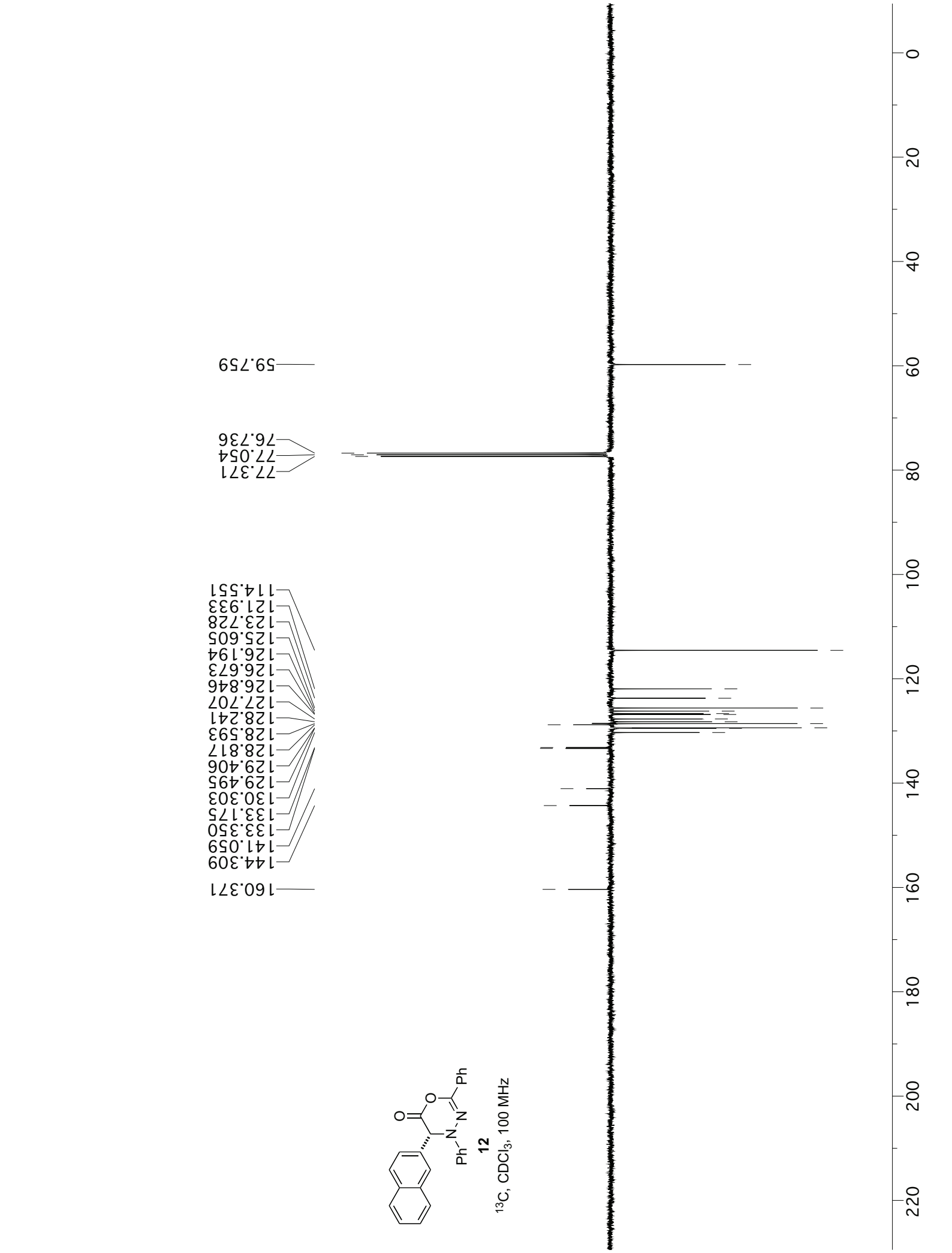


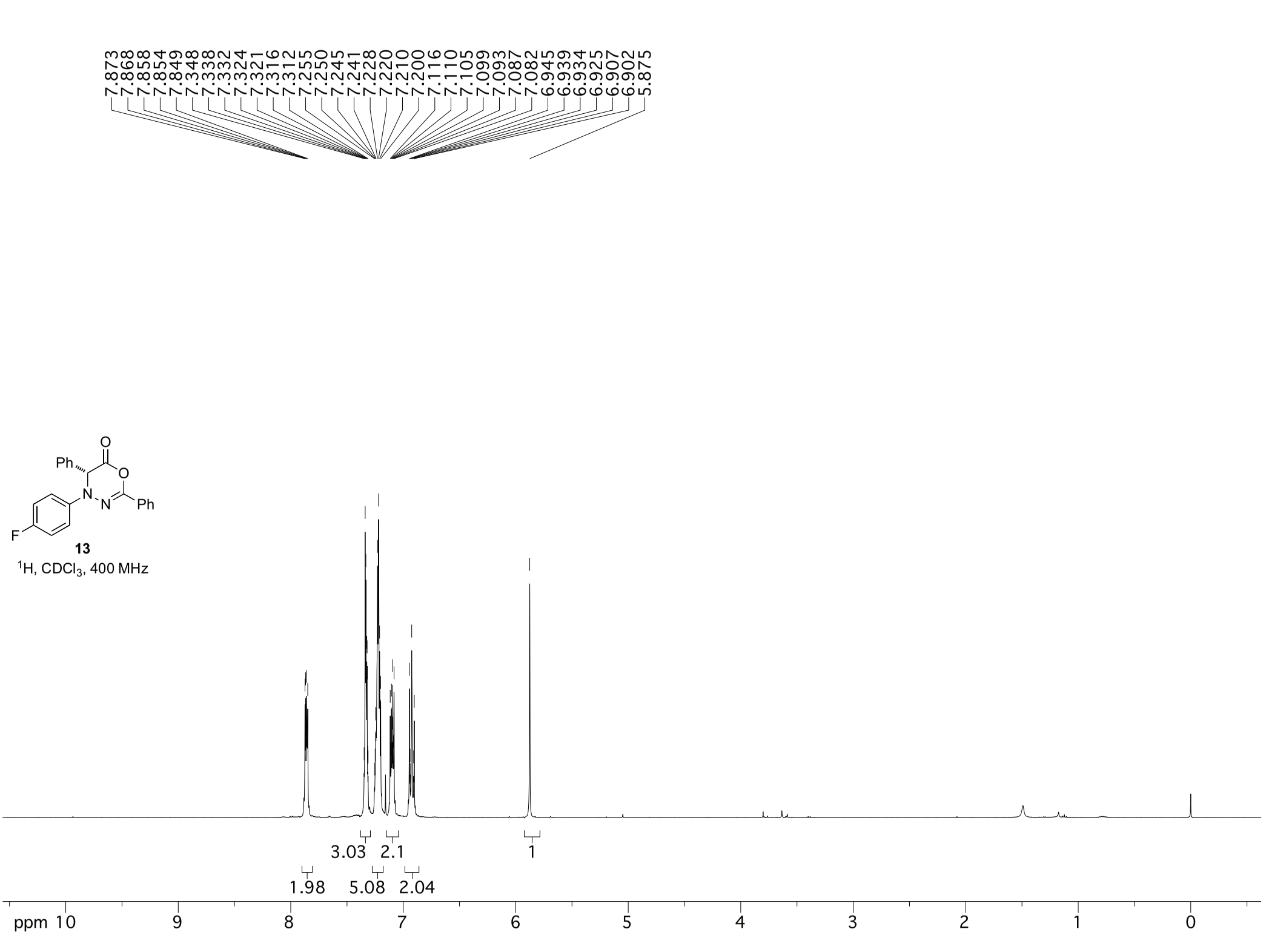


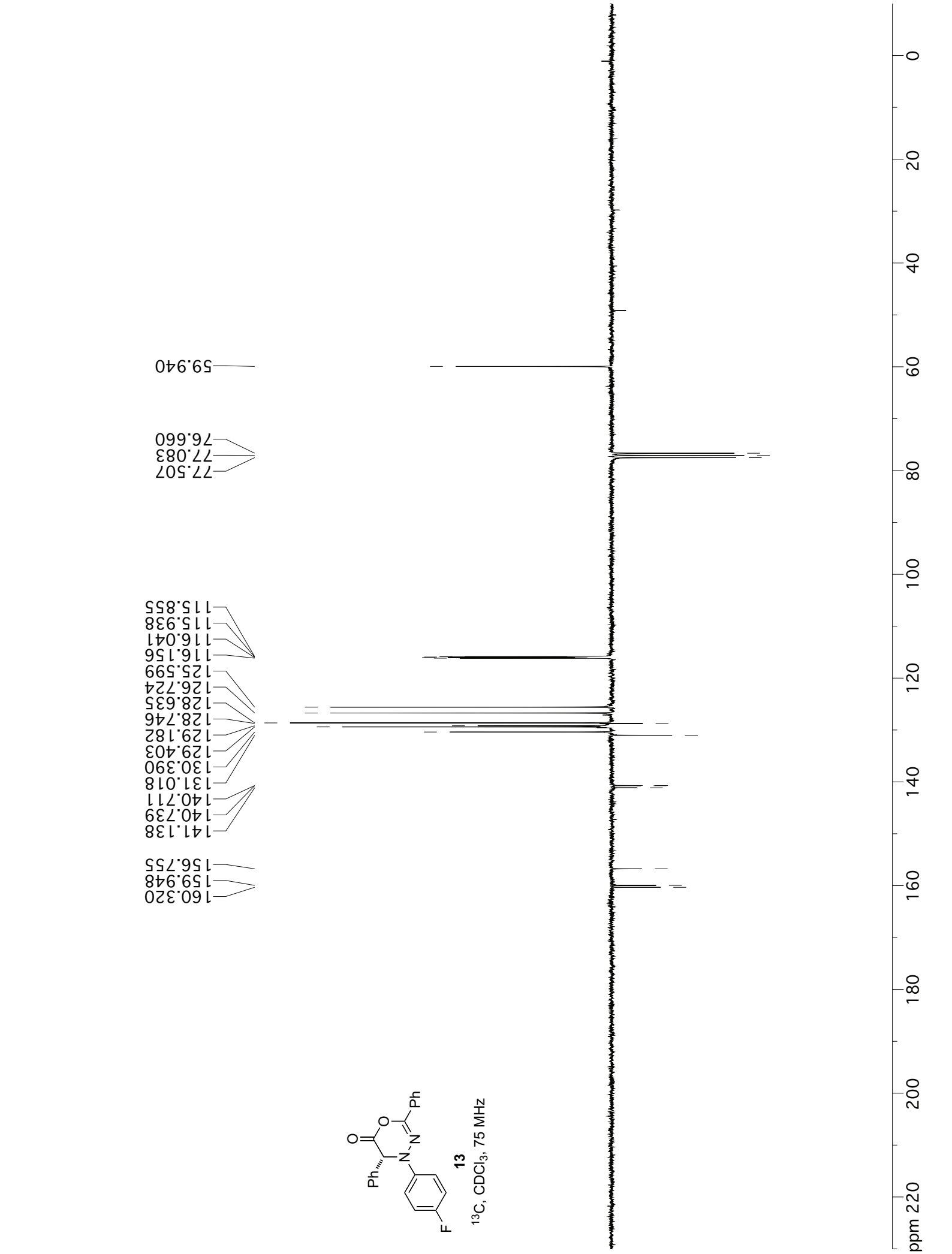


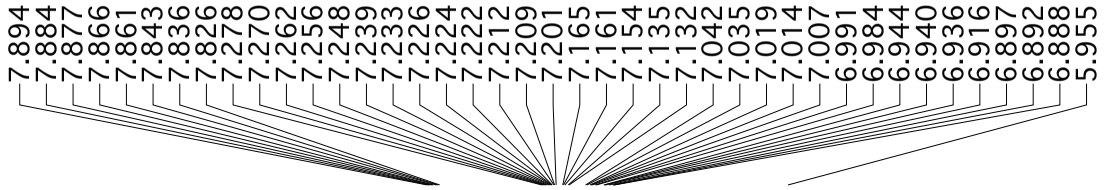
12

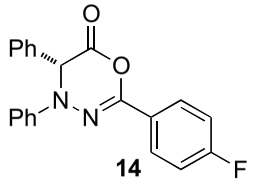
^{1}H, $CDCl_3$, 400 MHz





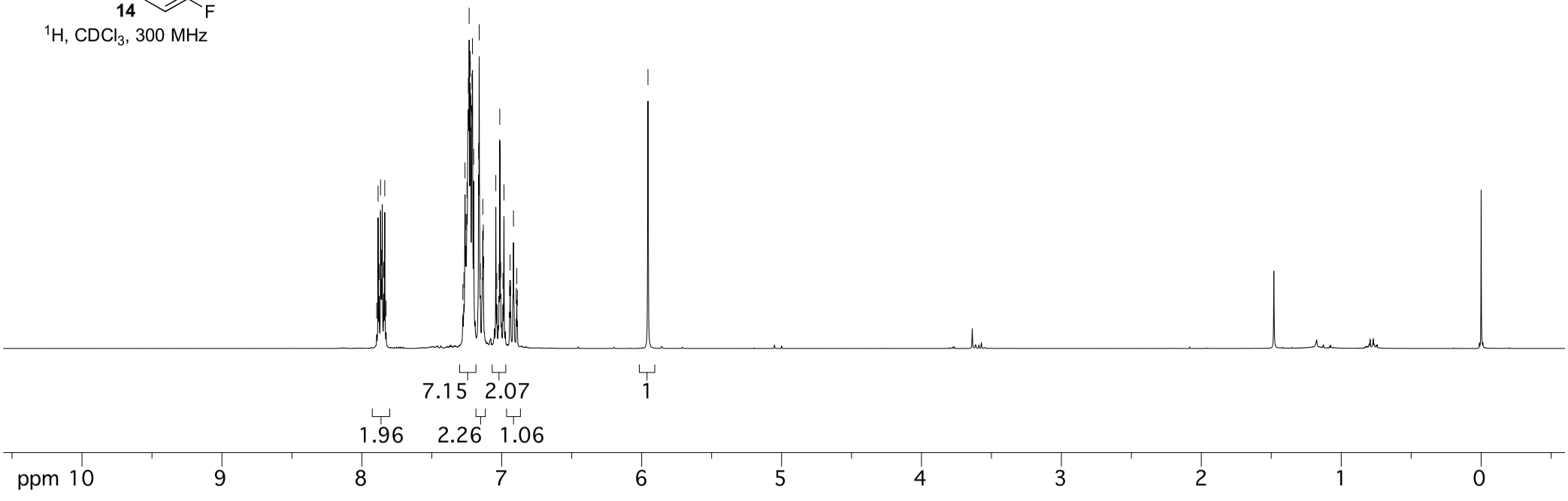

59.940
76.660
77.083
77.507
115.855
115.938
116.041
116.156
125.599
126.724
128.635
128.746
129.182
129.403
130.390
131.018
140.711
140.739
141.138
156.755
159.948
160.320
0
20
40
60
80
100
120
140
160
180
200
ppm 220
Ph
O
O
N
N
F
13
^{13}C, $CDCl_3$, 75 MHz

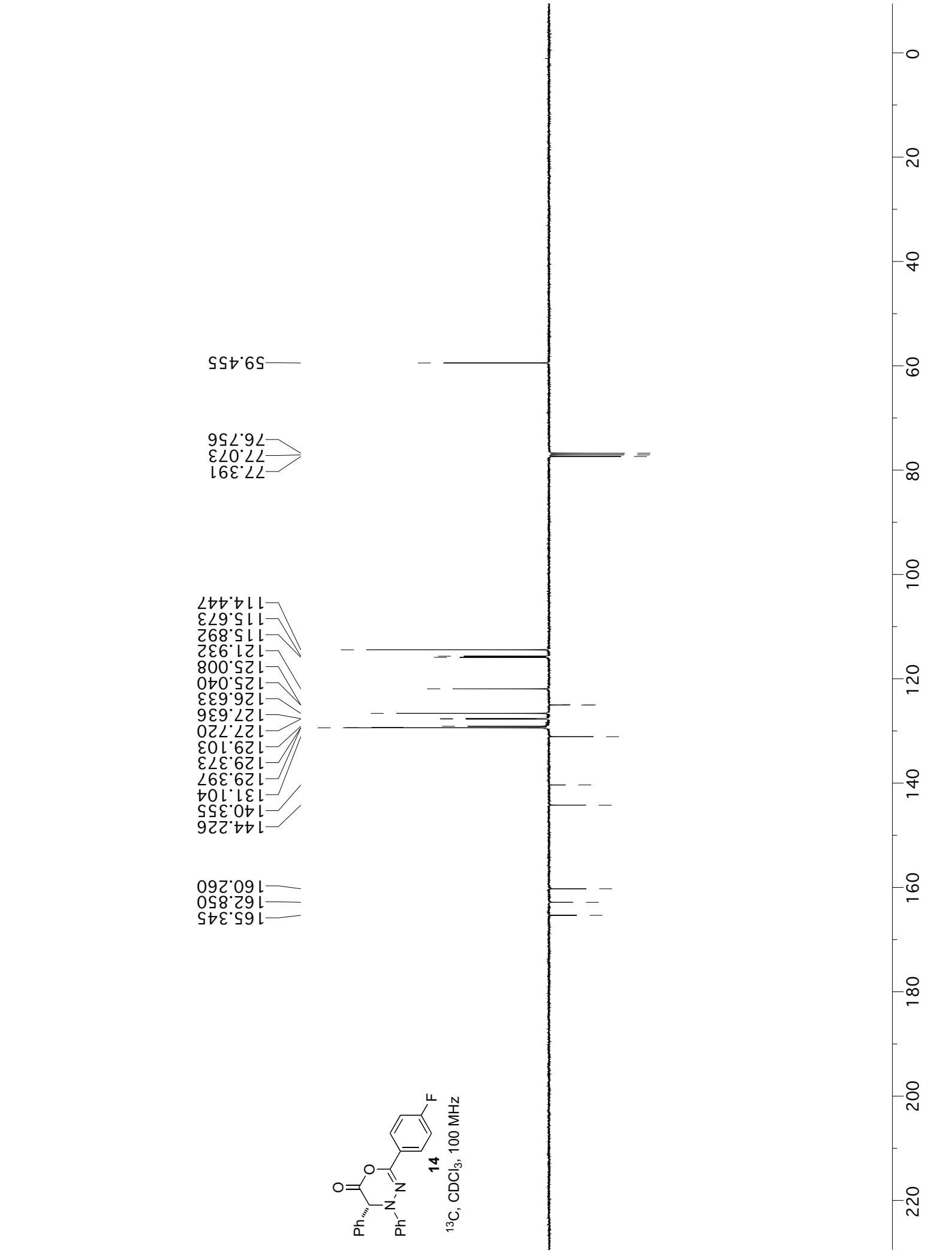


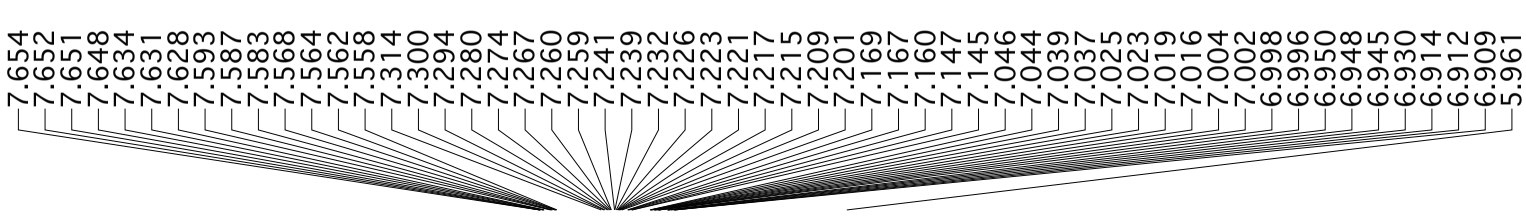


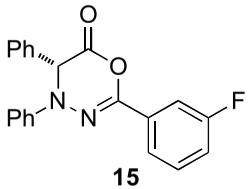
14

^{1}H, $CDCl_3$, 300 MHz



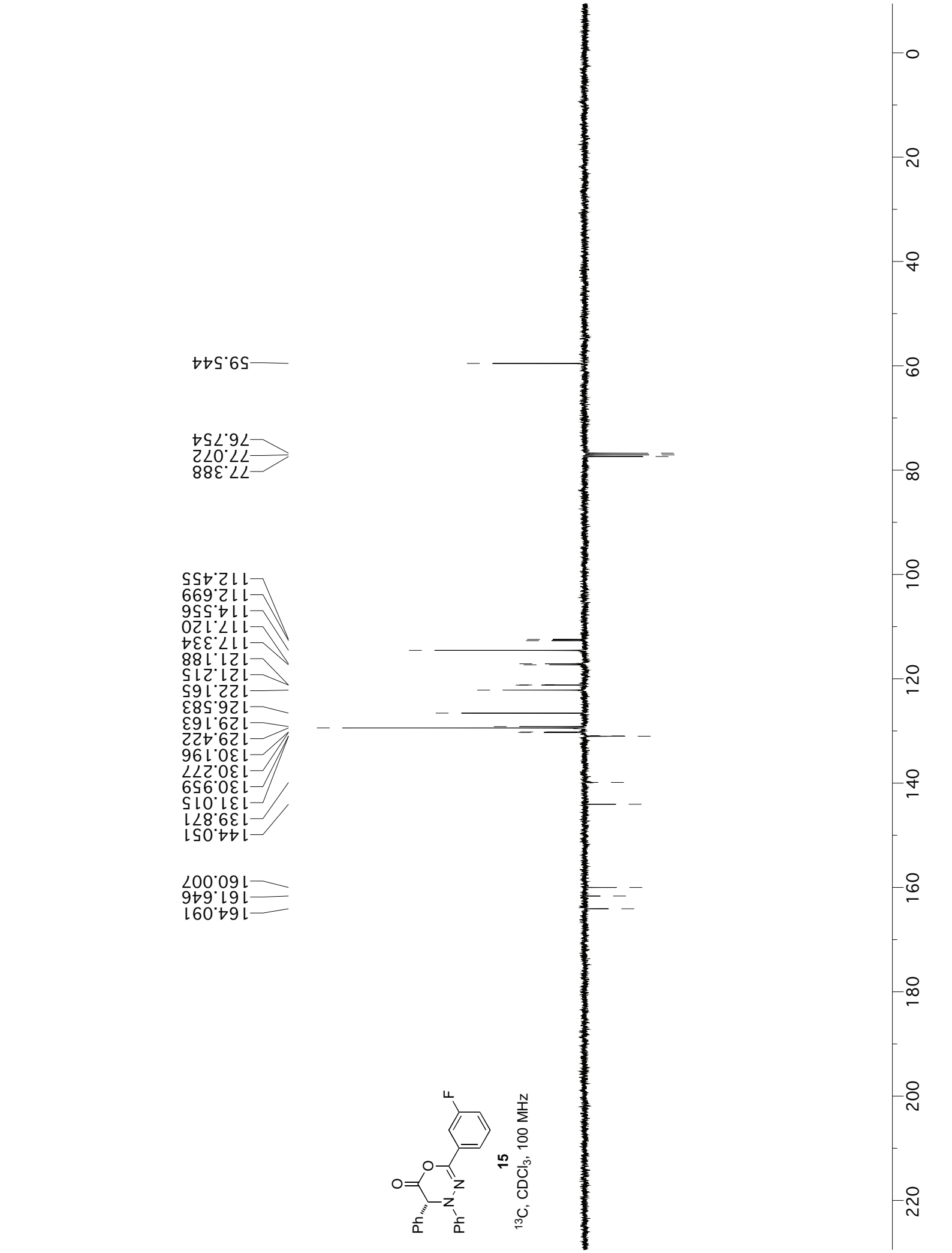


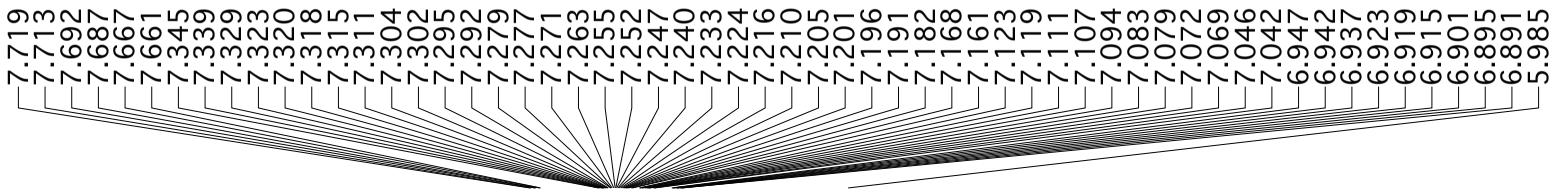


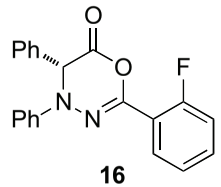


15

^{1}H, $CDCl_3$, 400 MHz

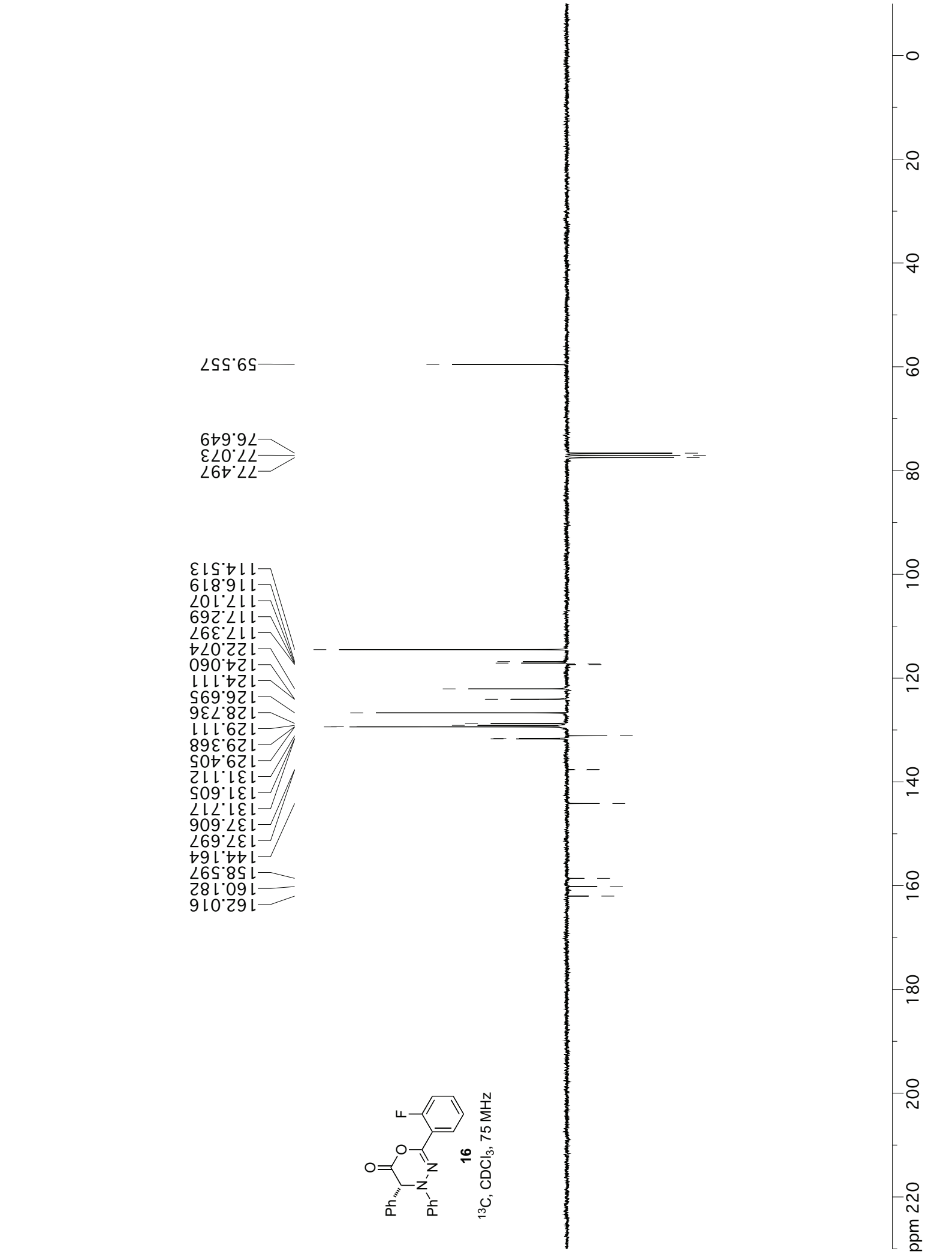


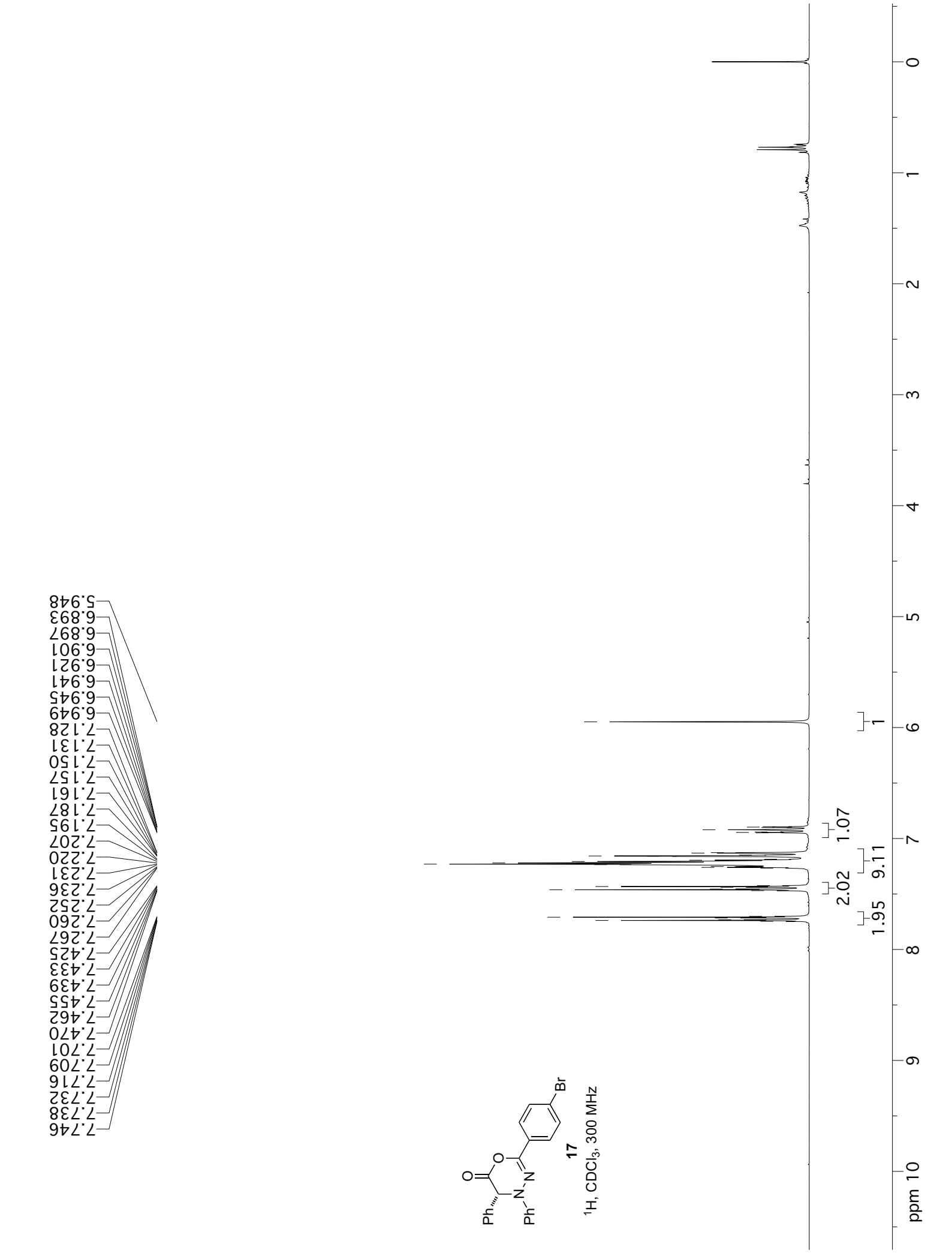


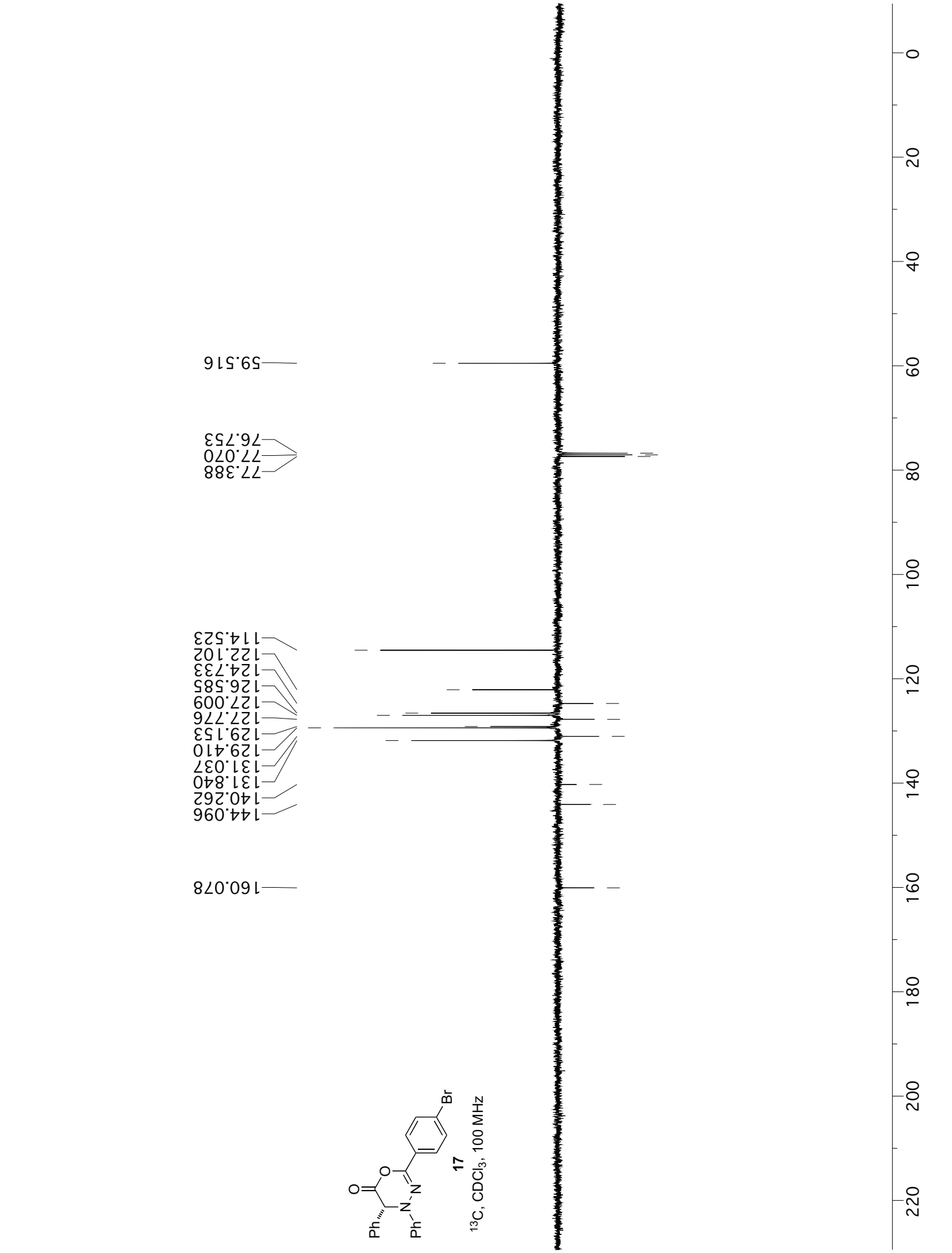


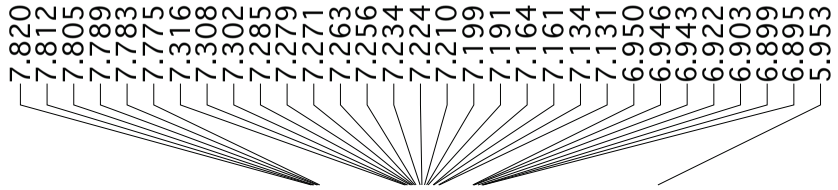
16

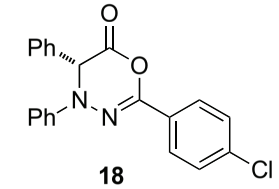
^{1}H, $CDCl_3$, 300 MHz





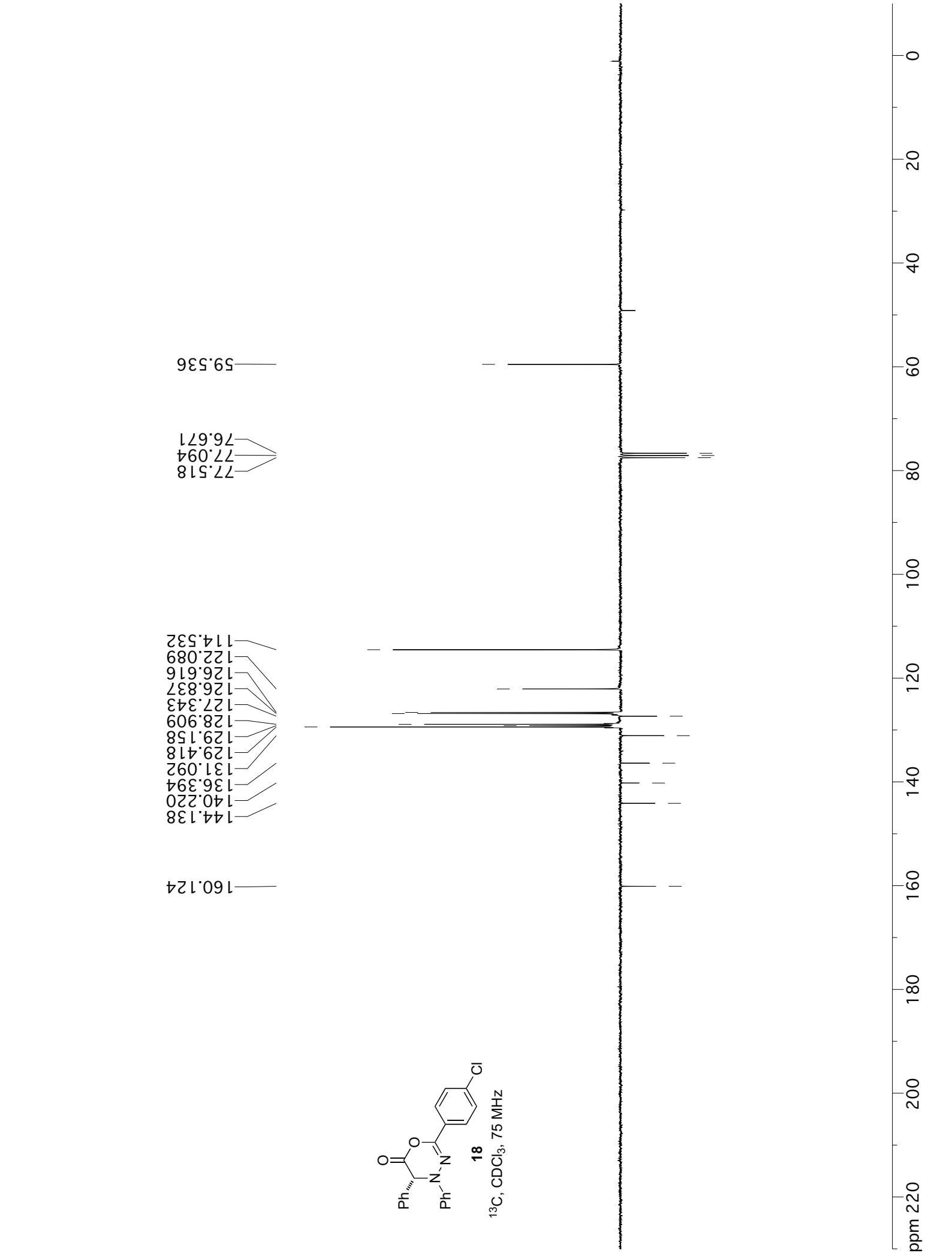


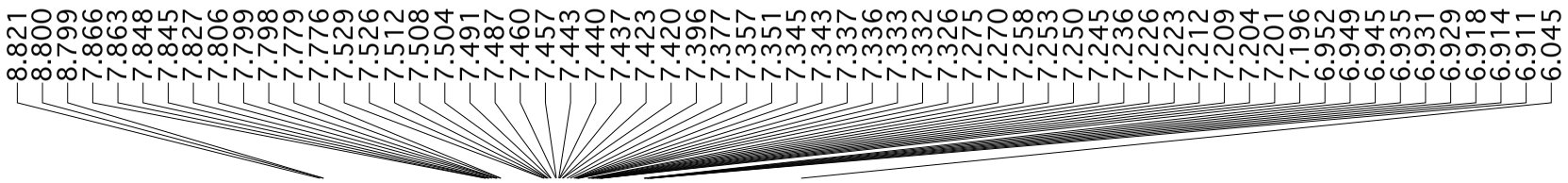


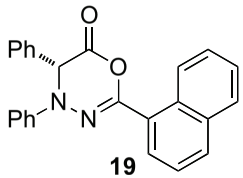


18

^{1}H, $CDCl_3$, 300 MHz

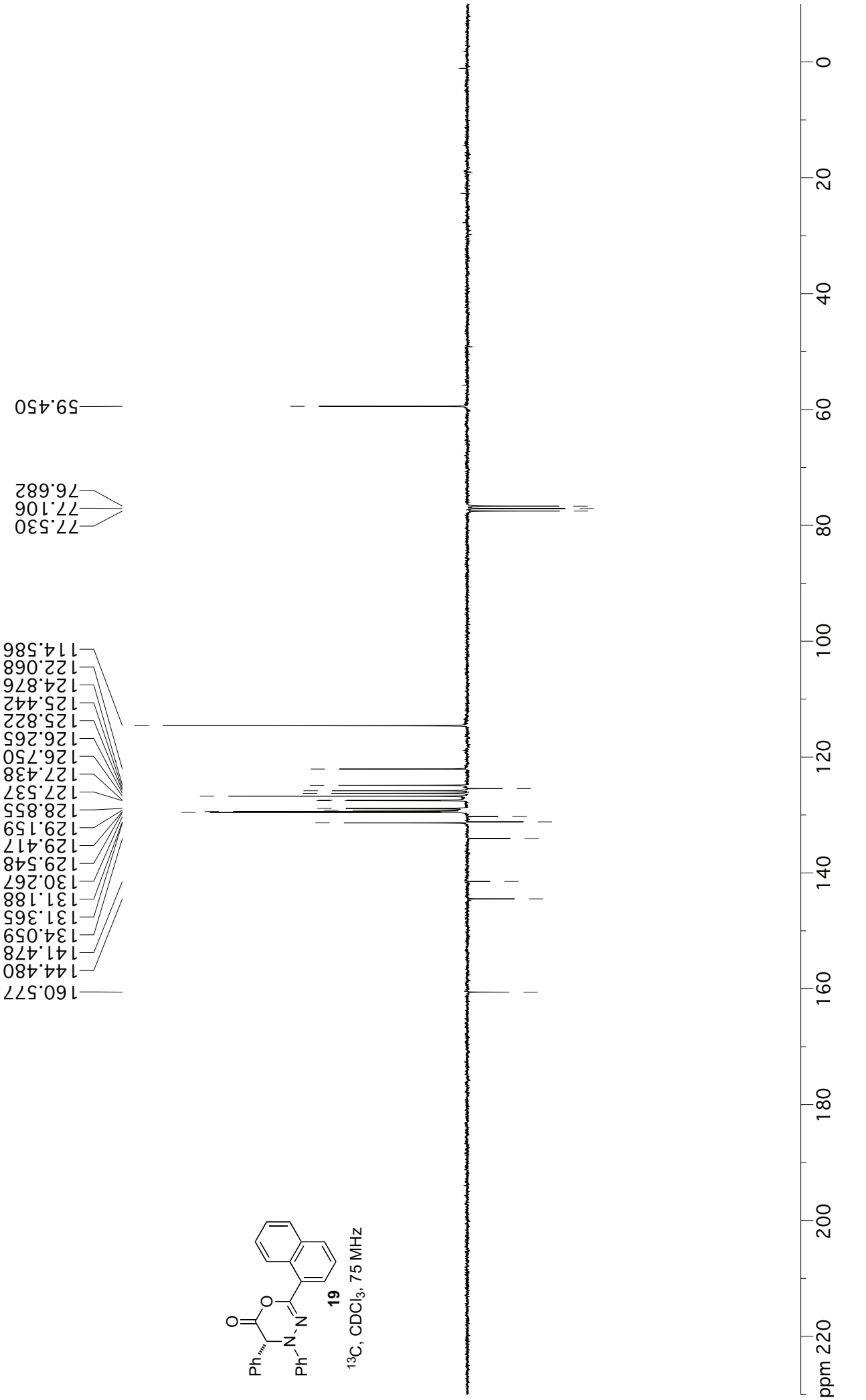


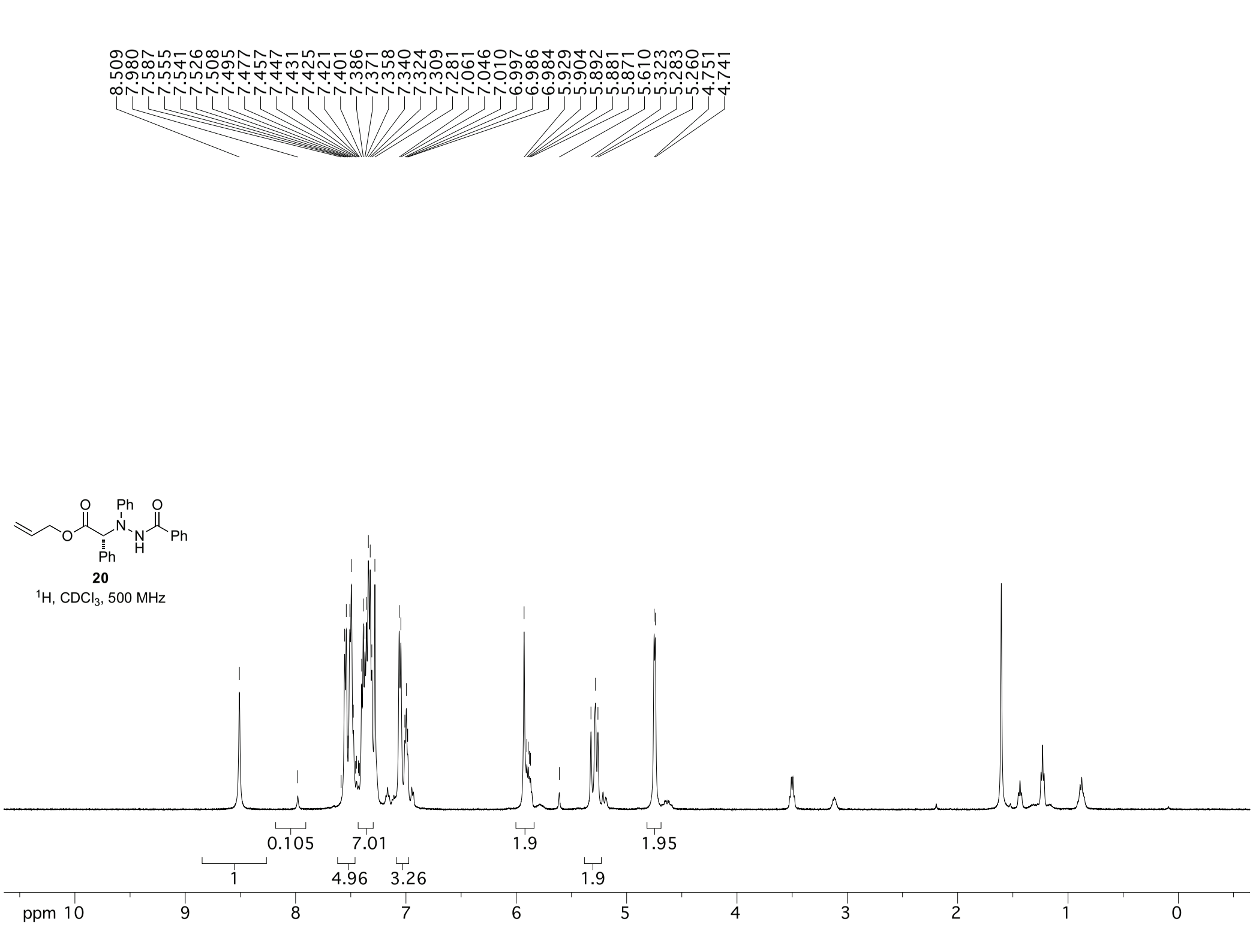


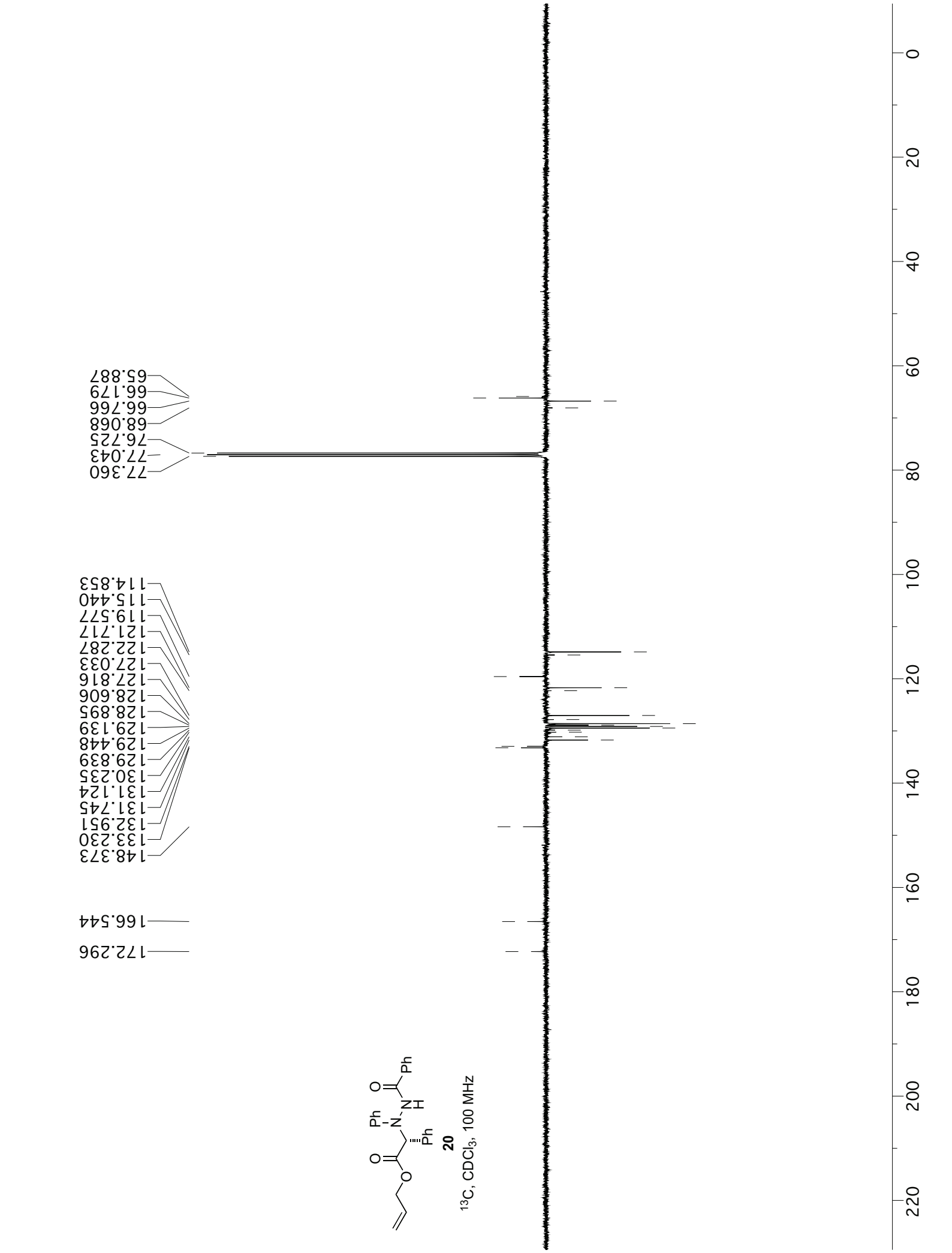


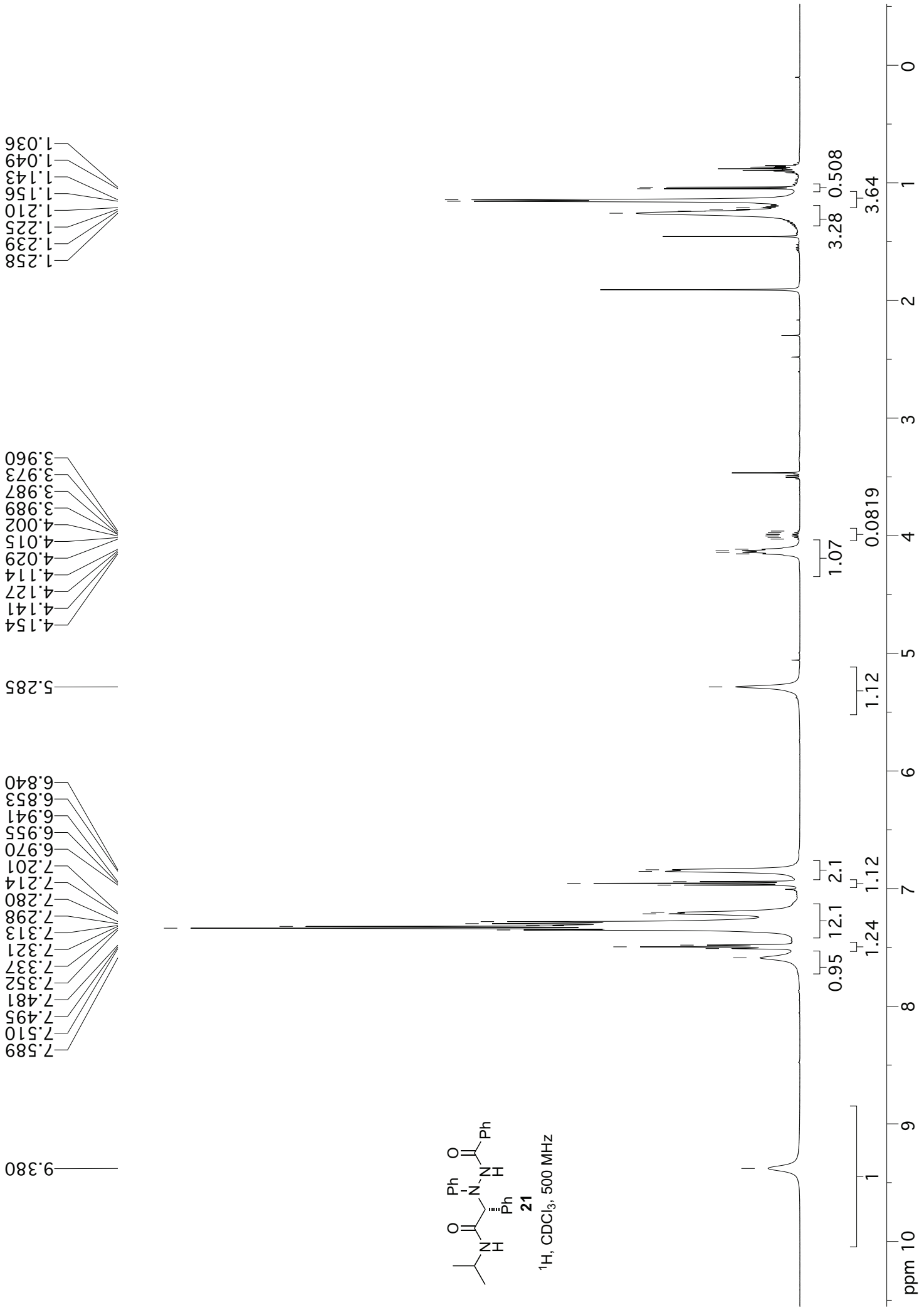
19

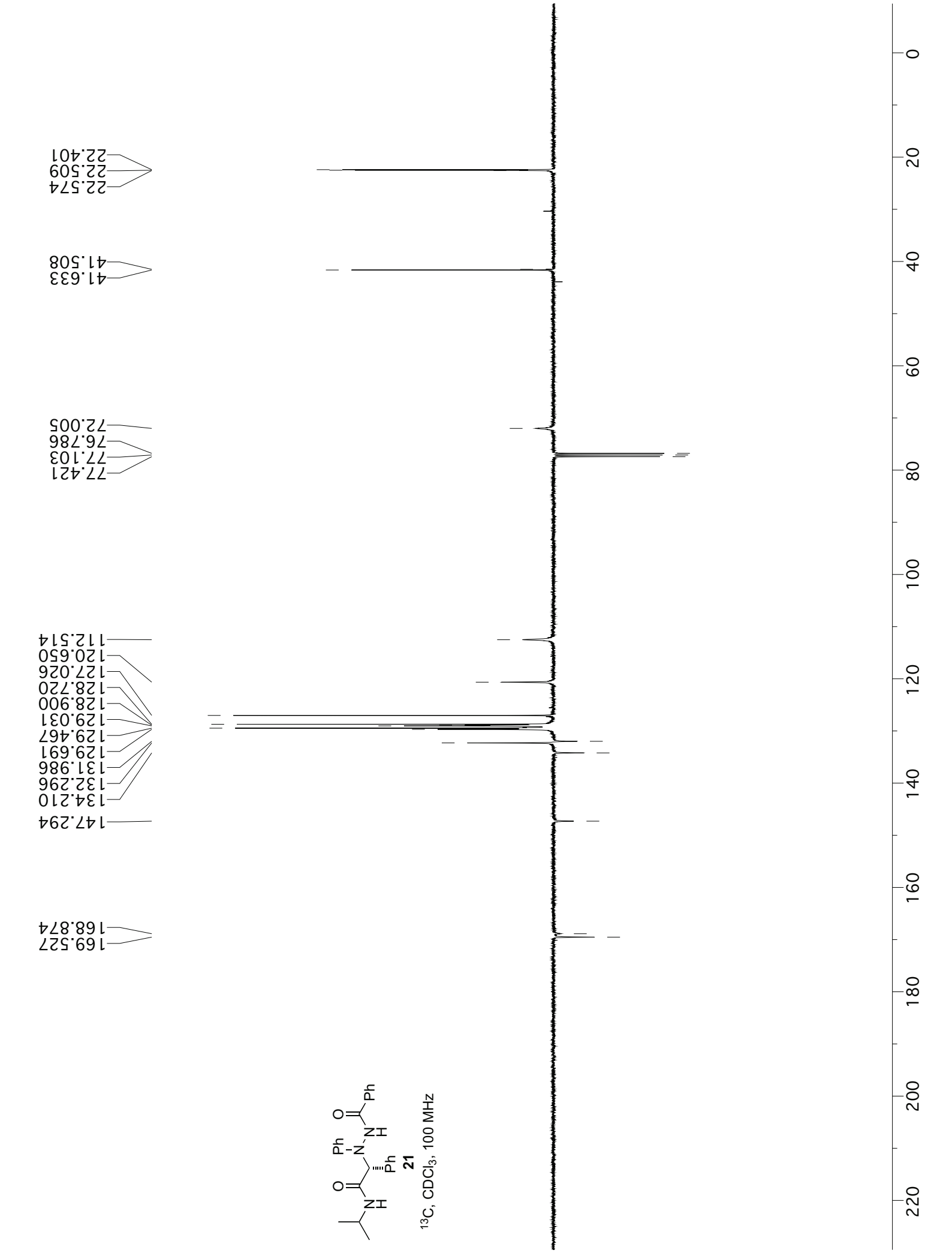
^{1}H, $CDCl_3$, 400 MHz

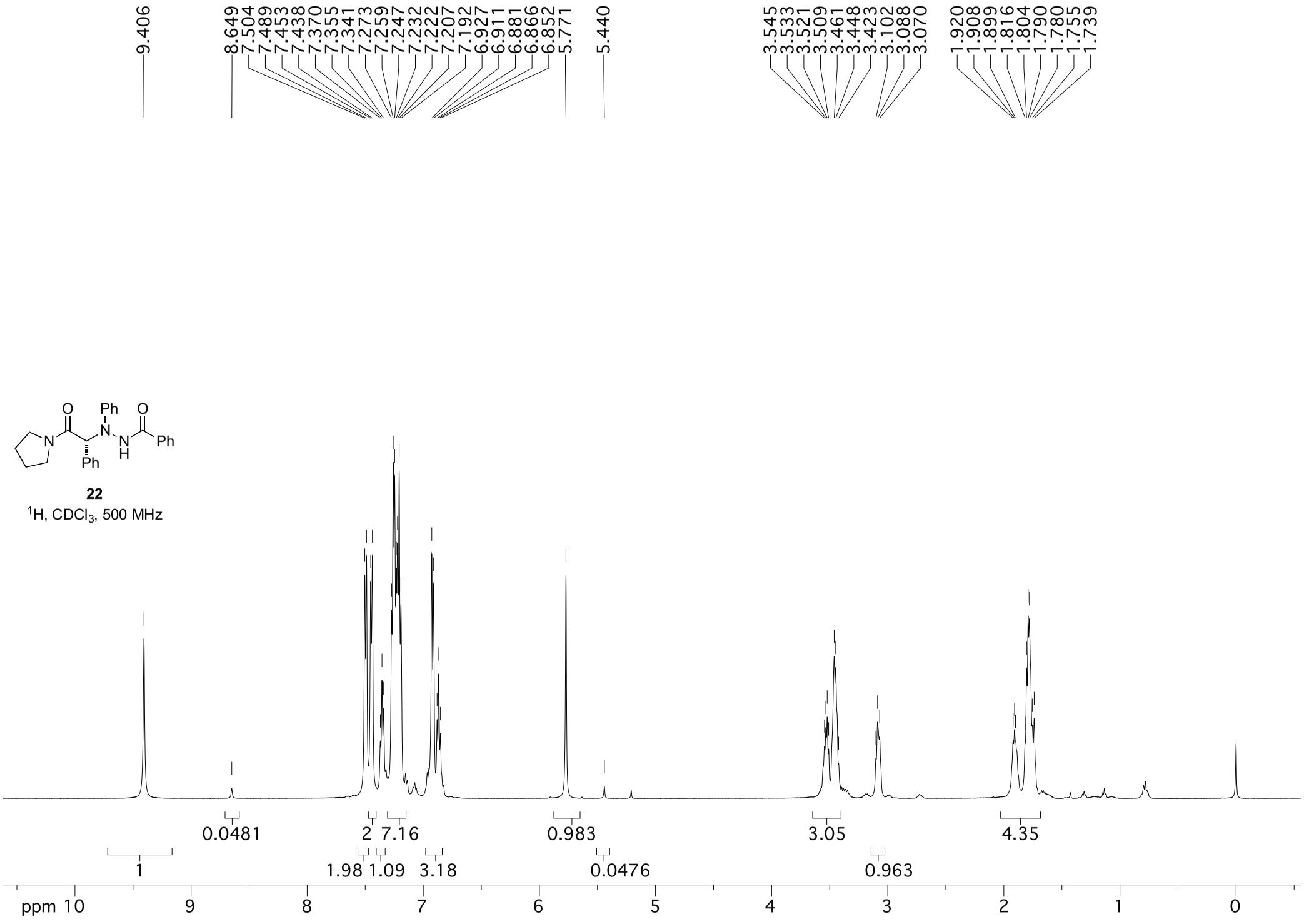


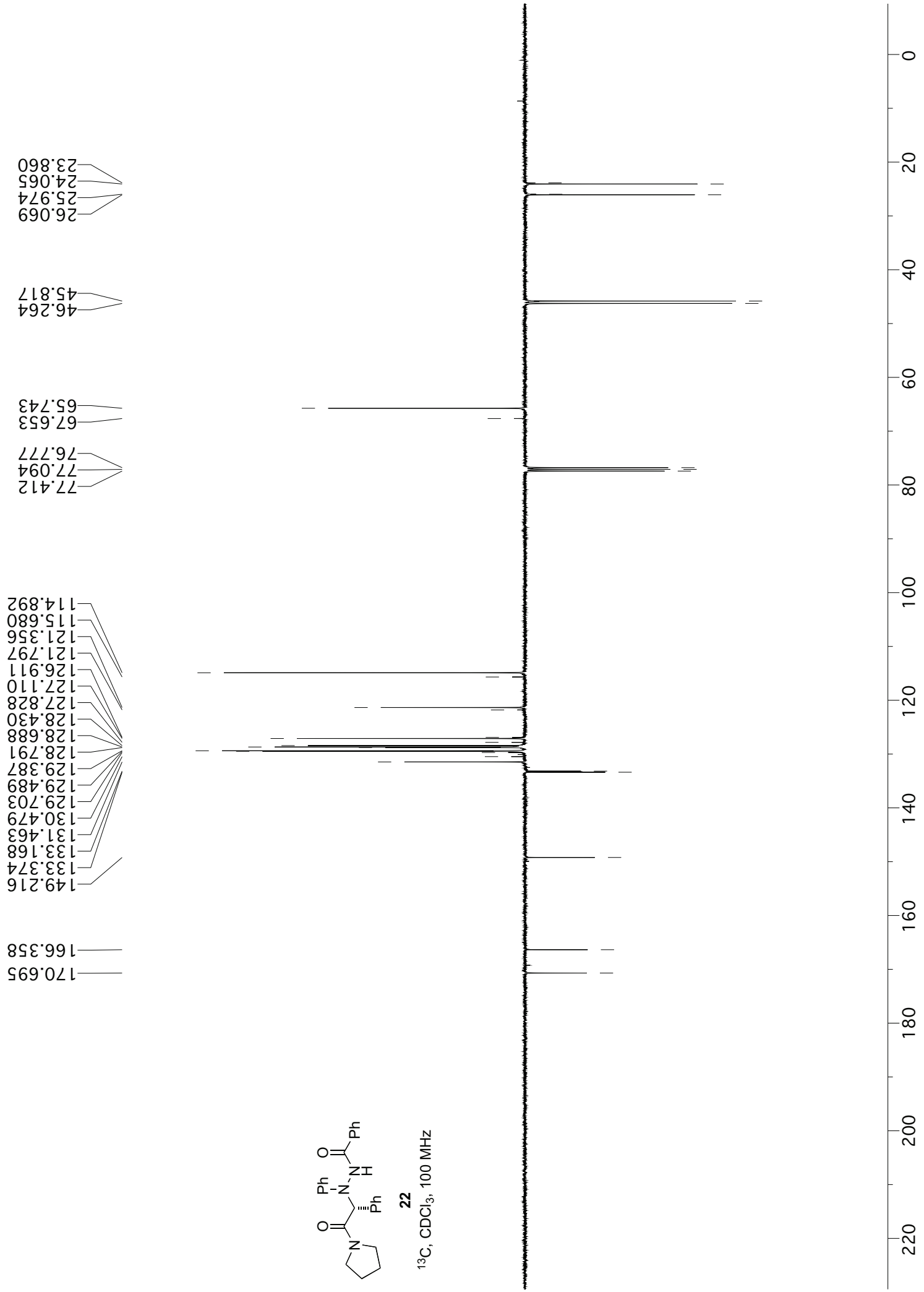


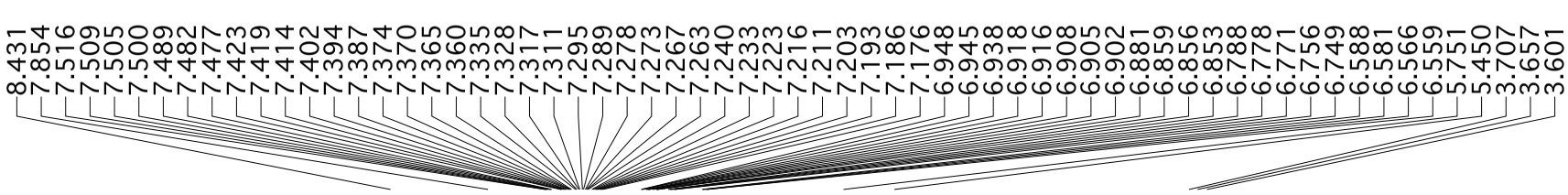


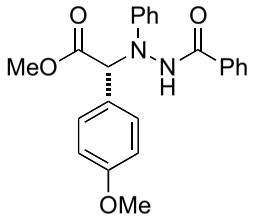






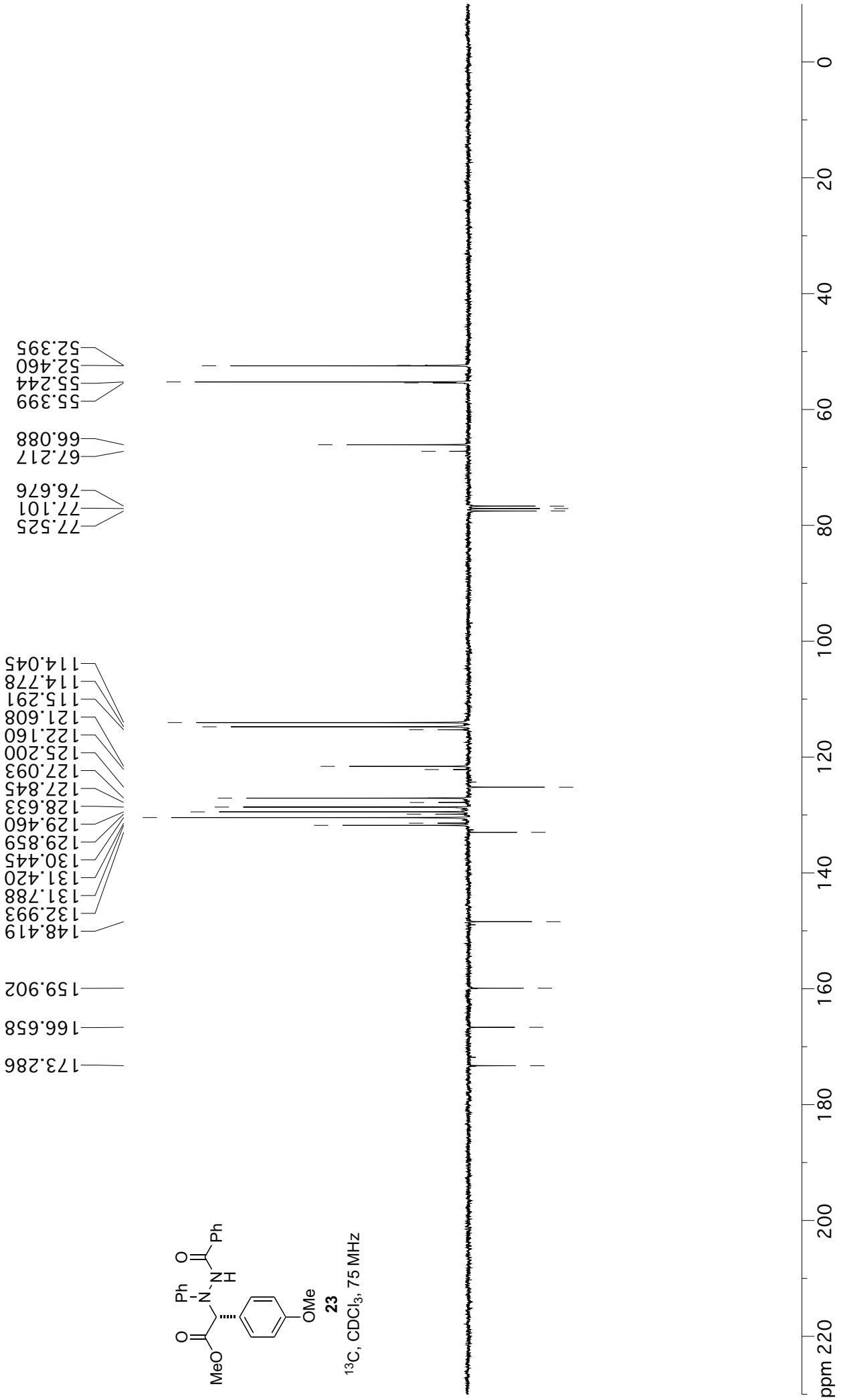


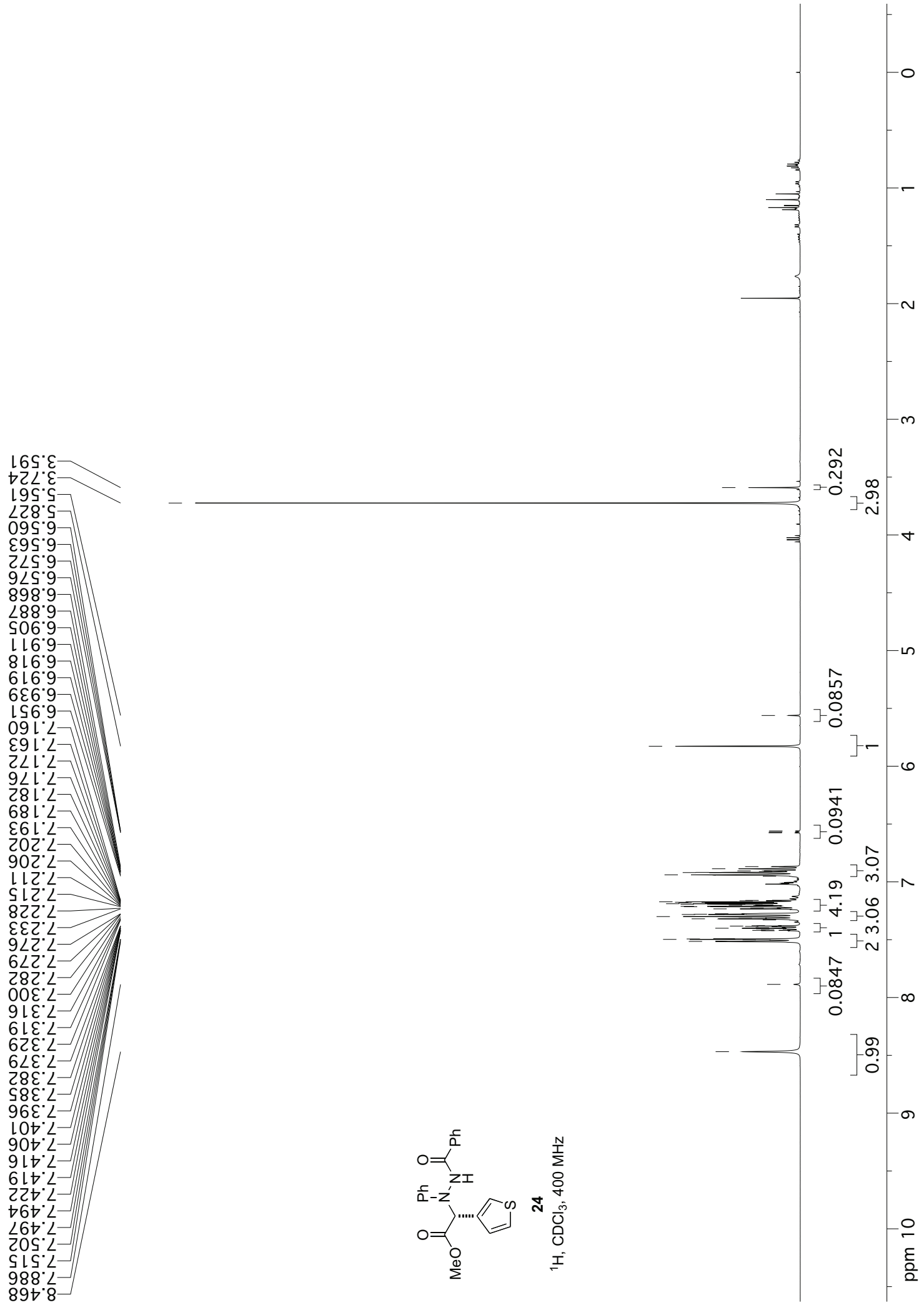


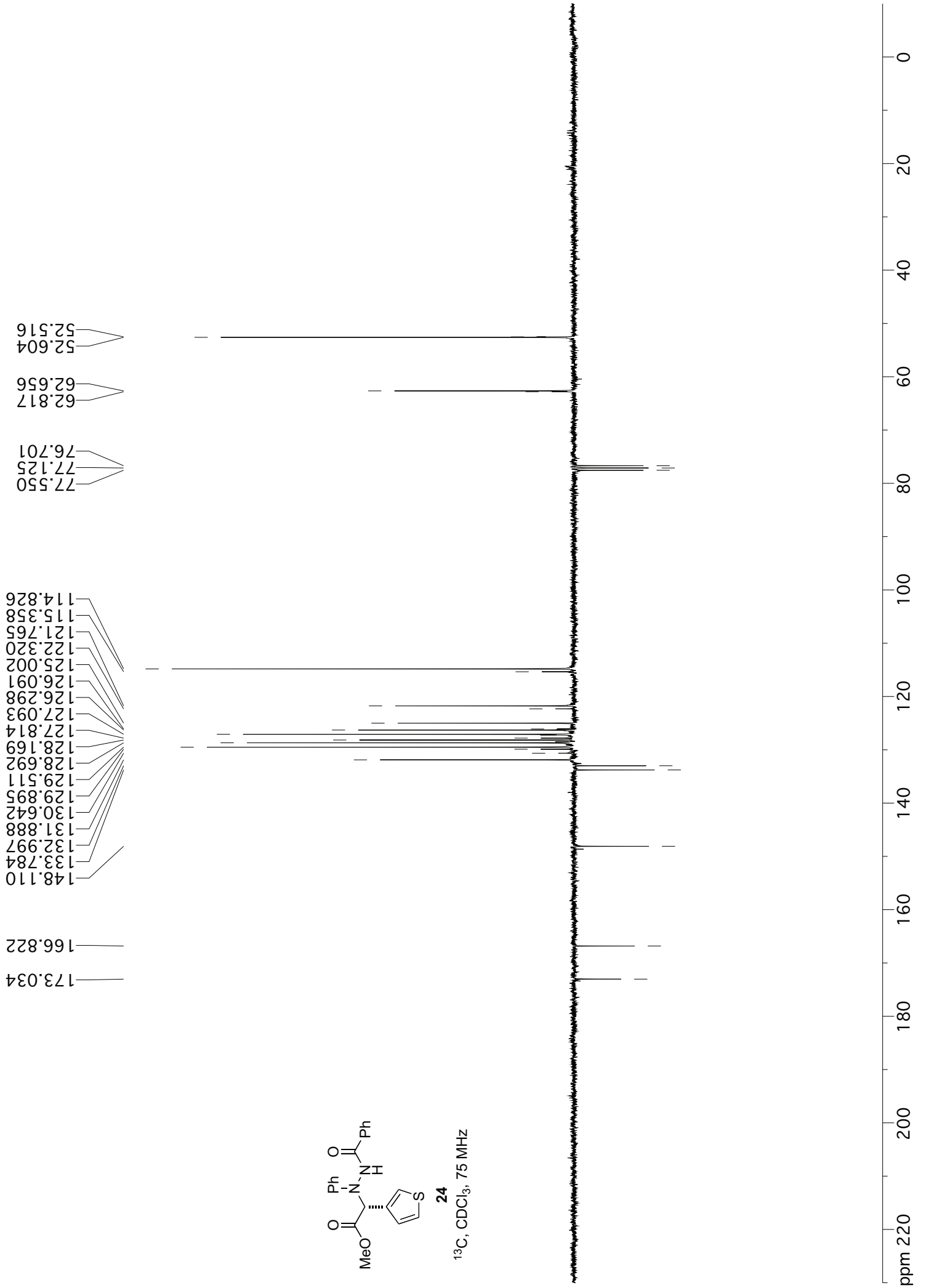


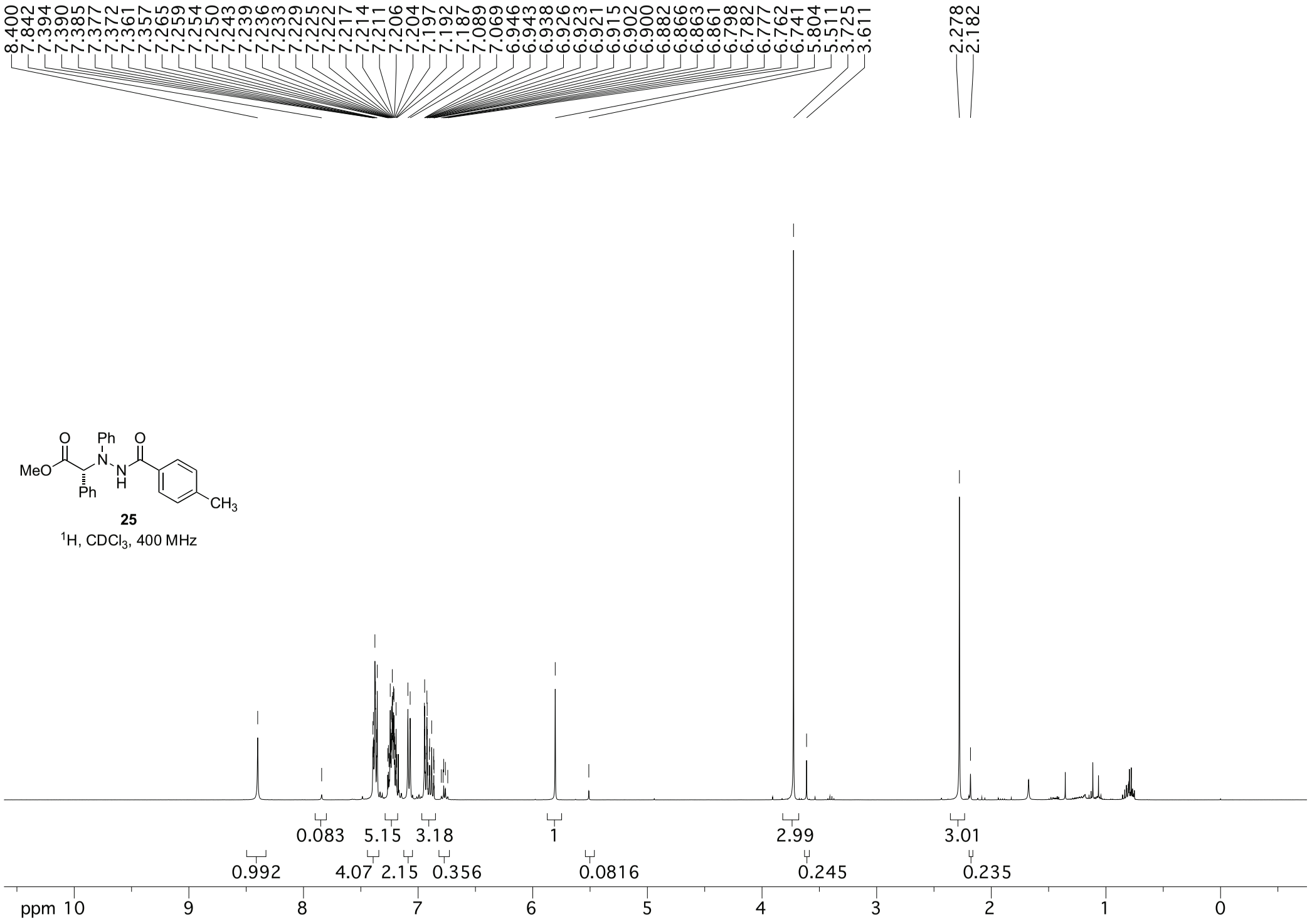
23

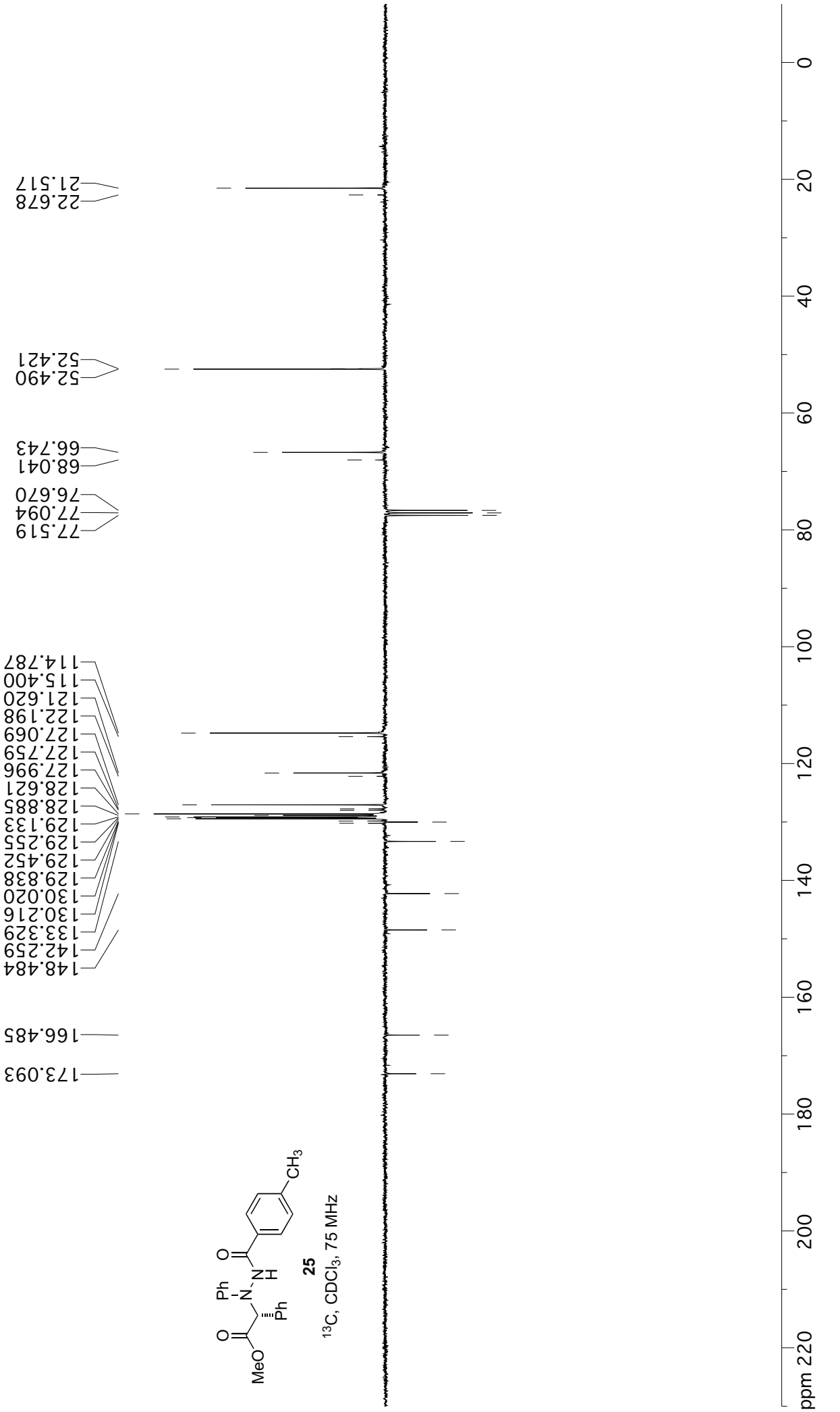
^{1}H, $CDCl_3$, 300 MHz

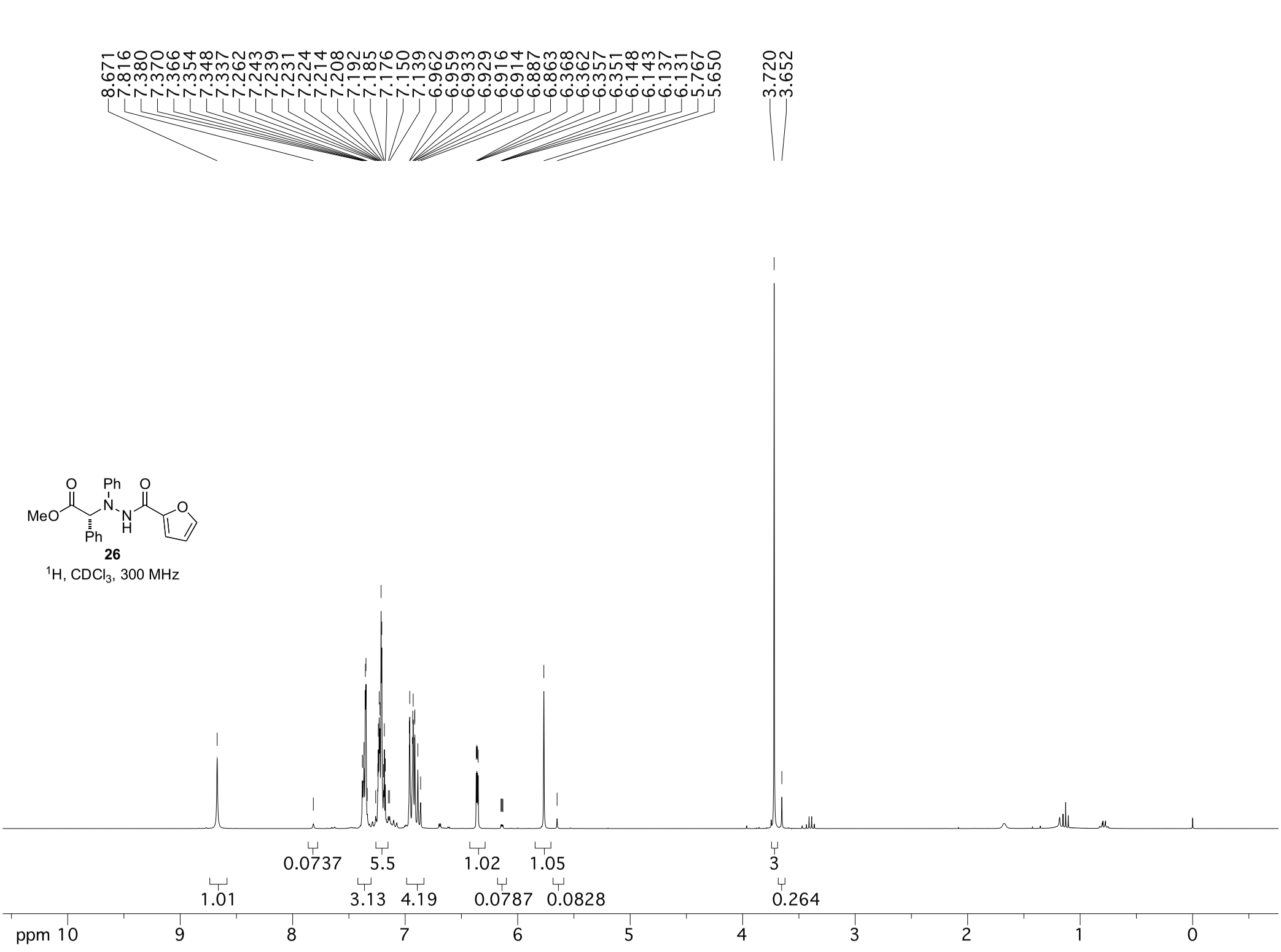


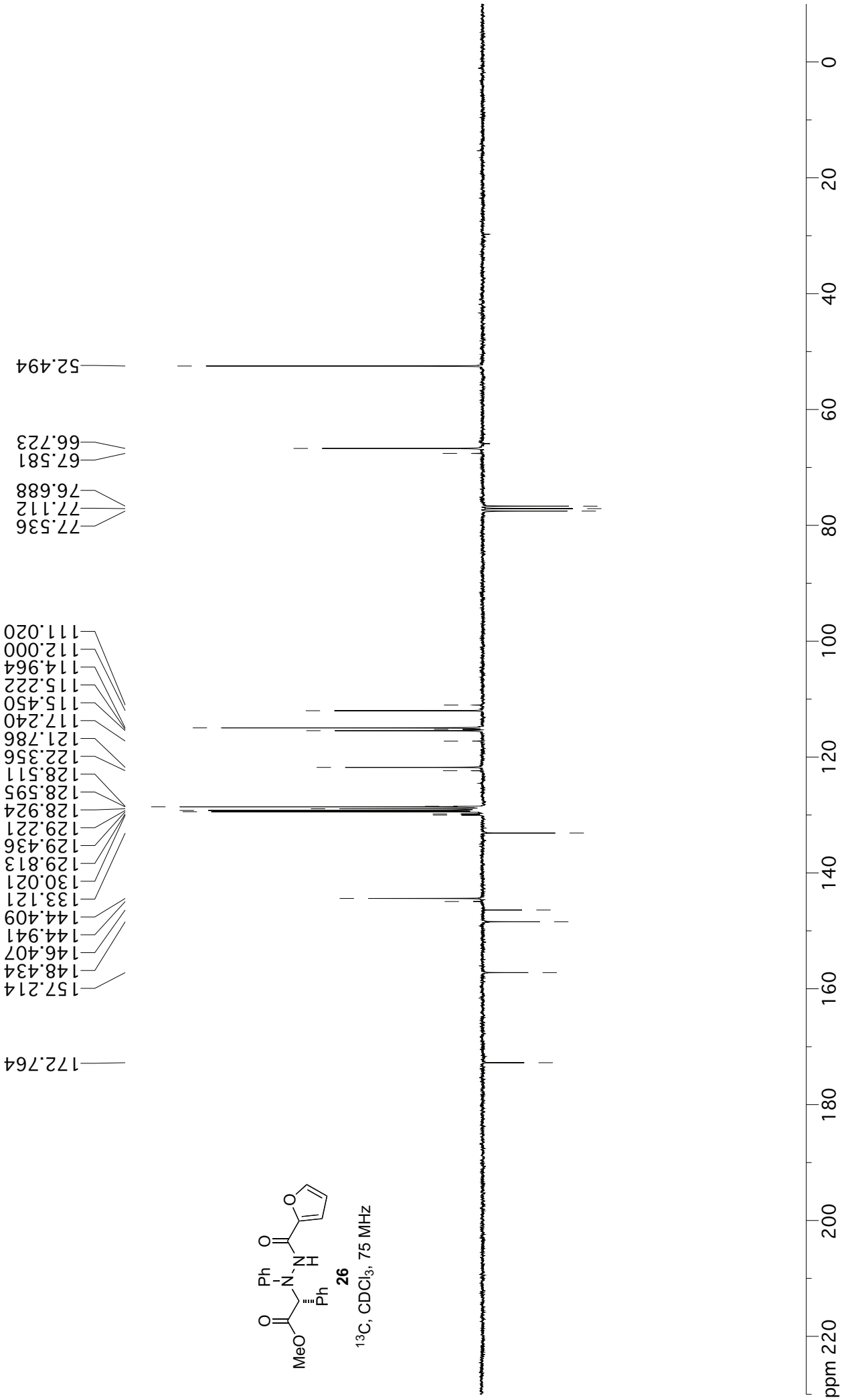


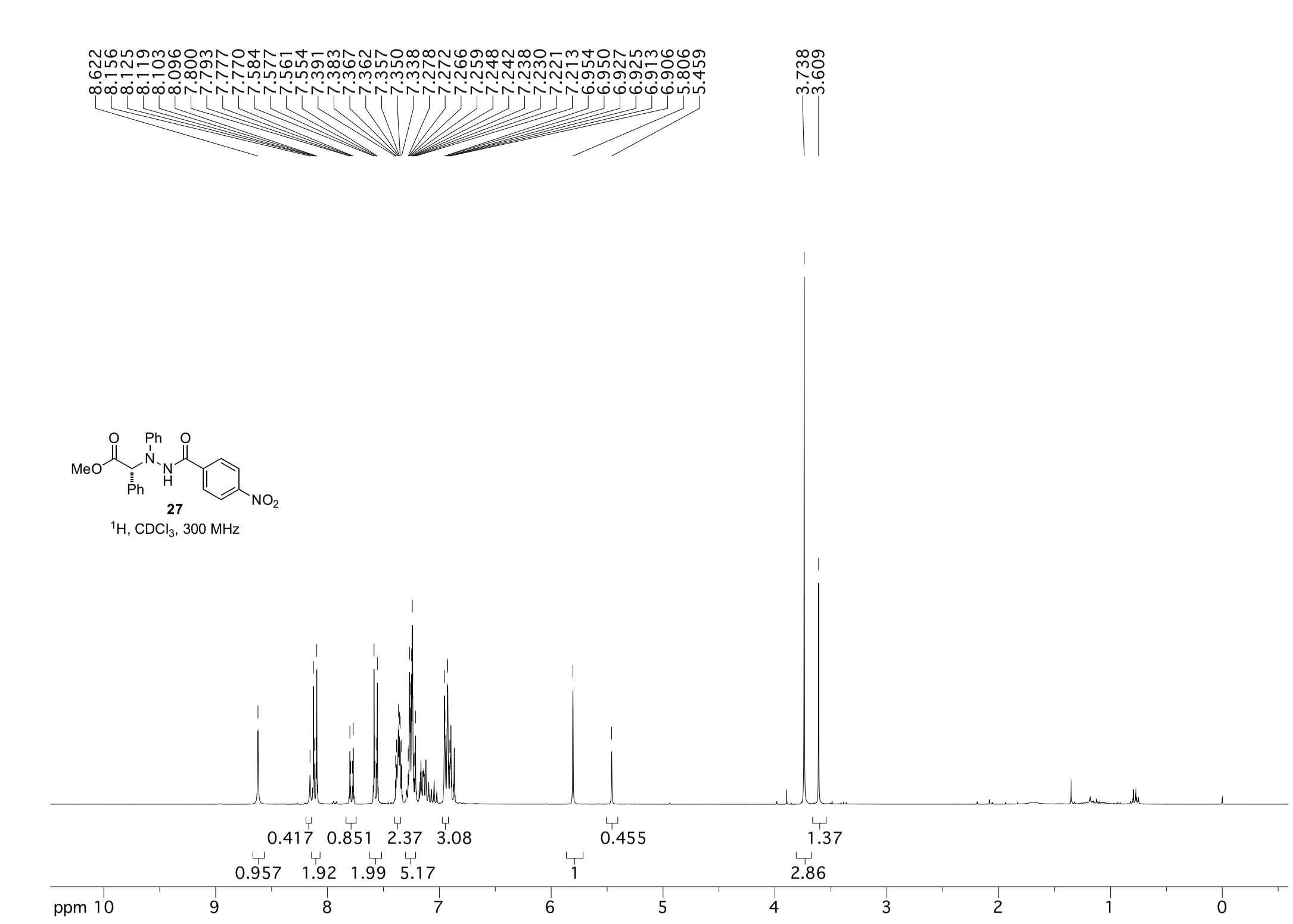


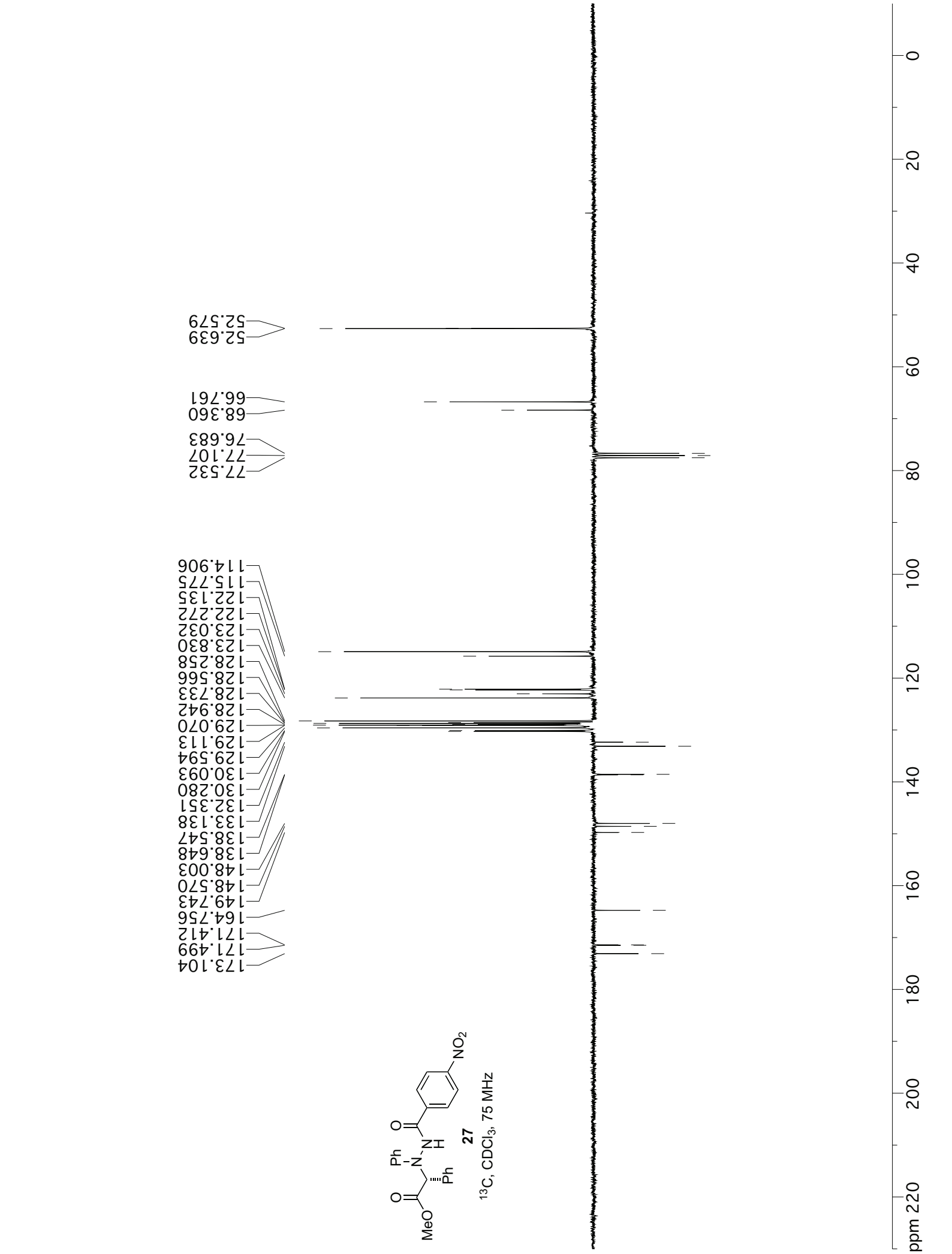


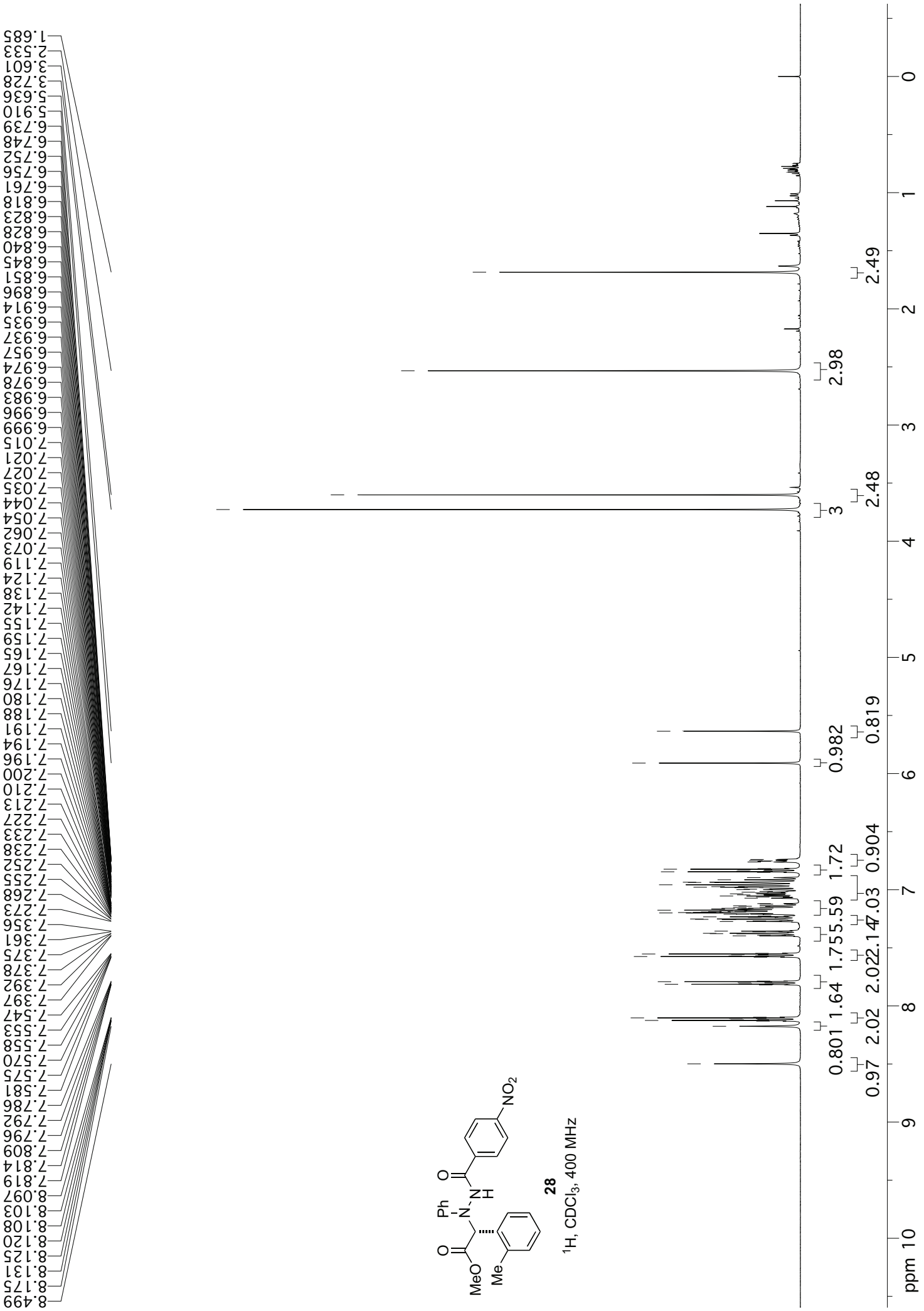


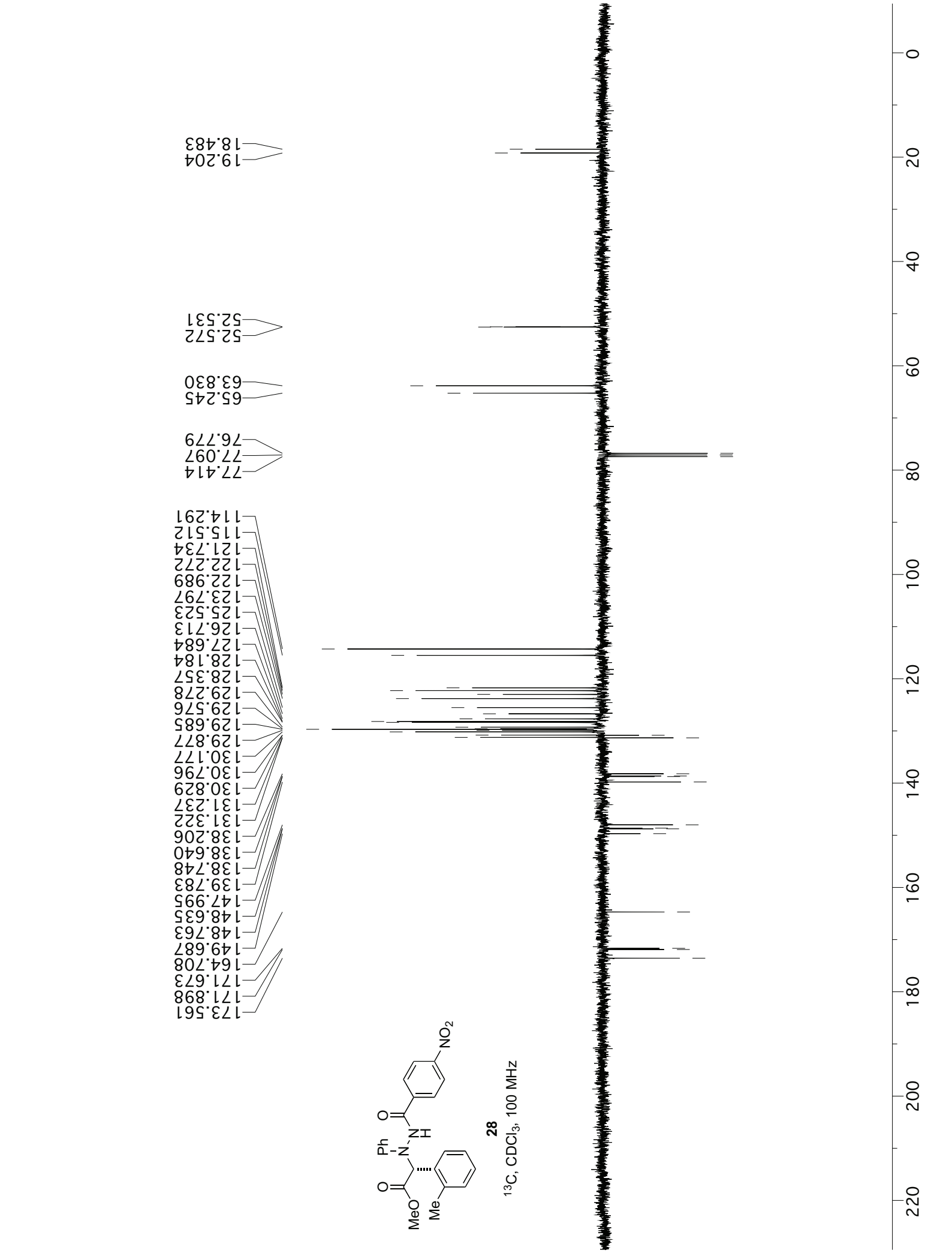


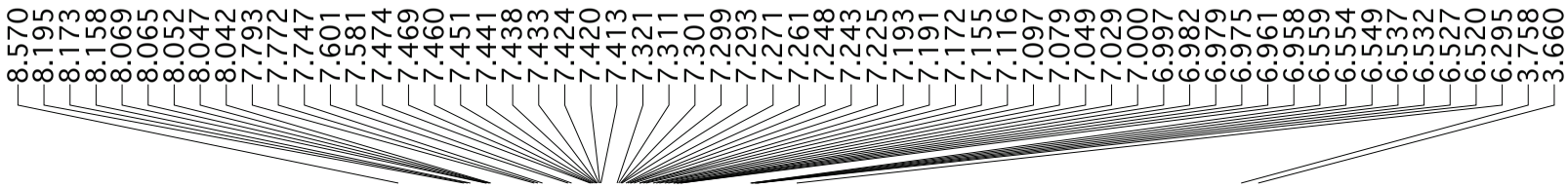


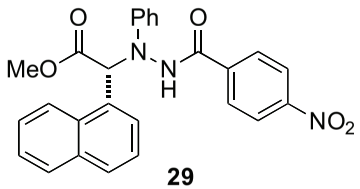






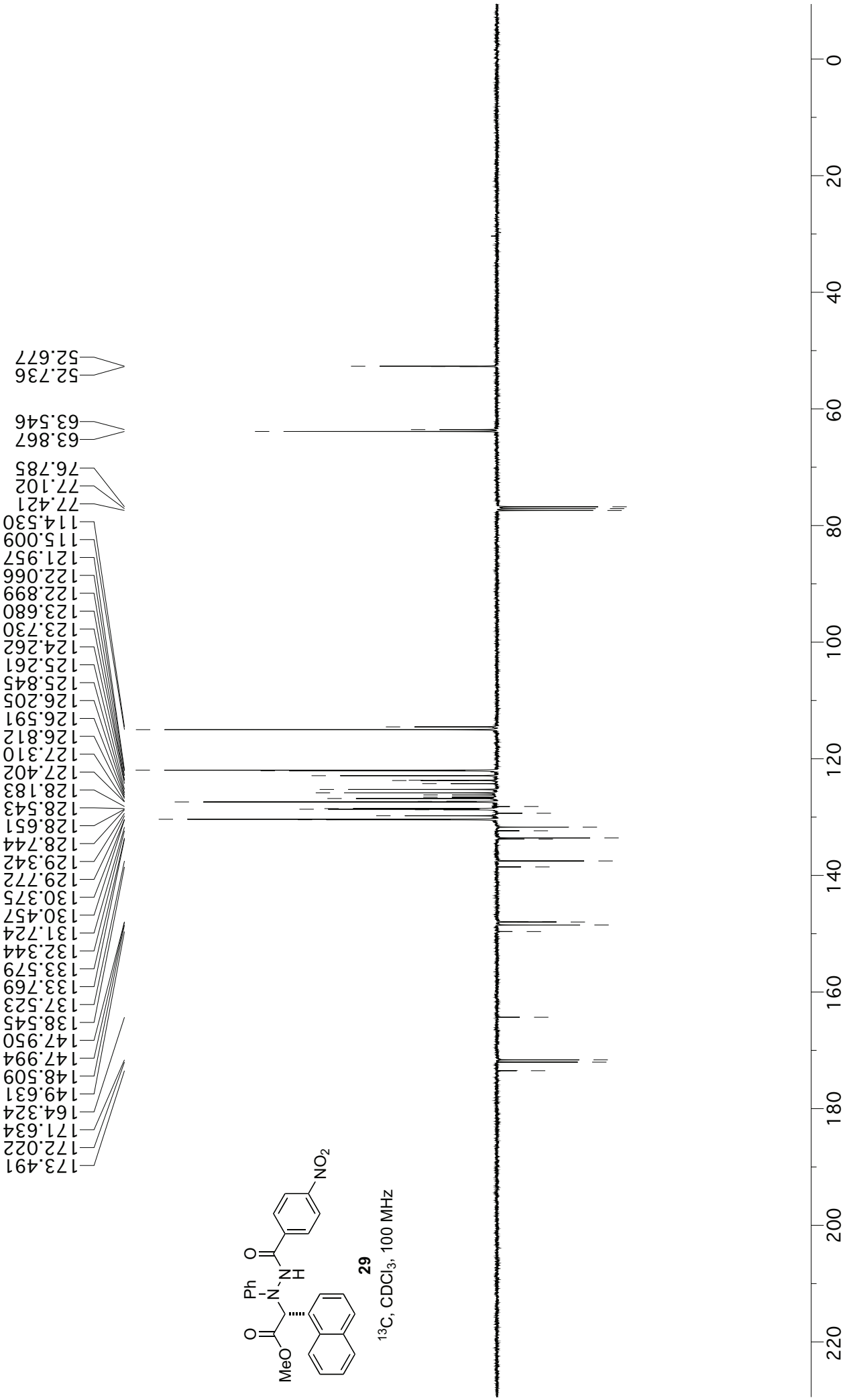


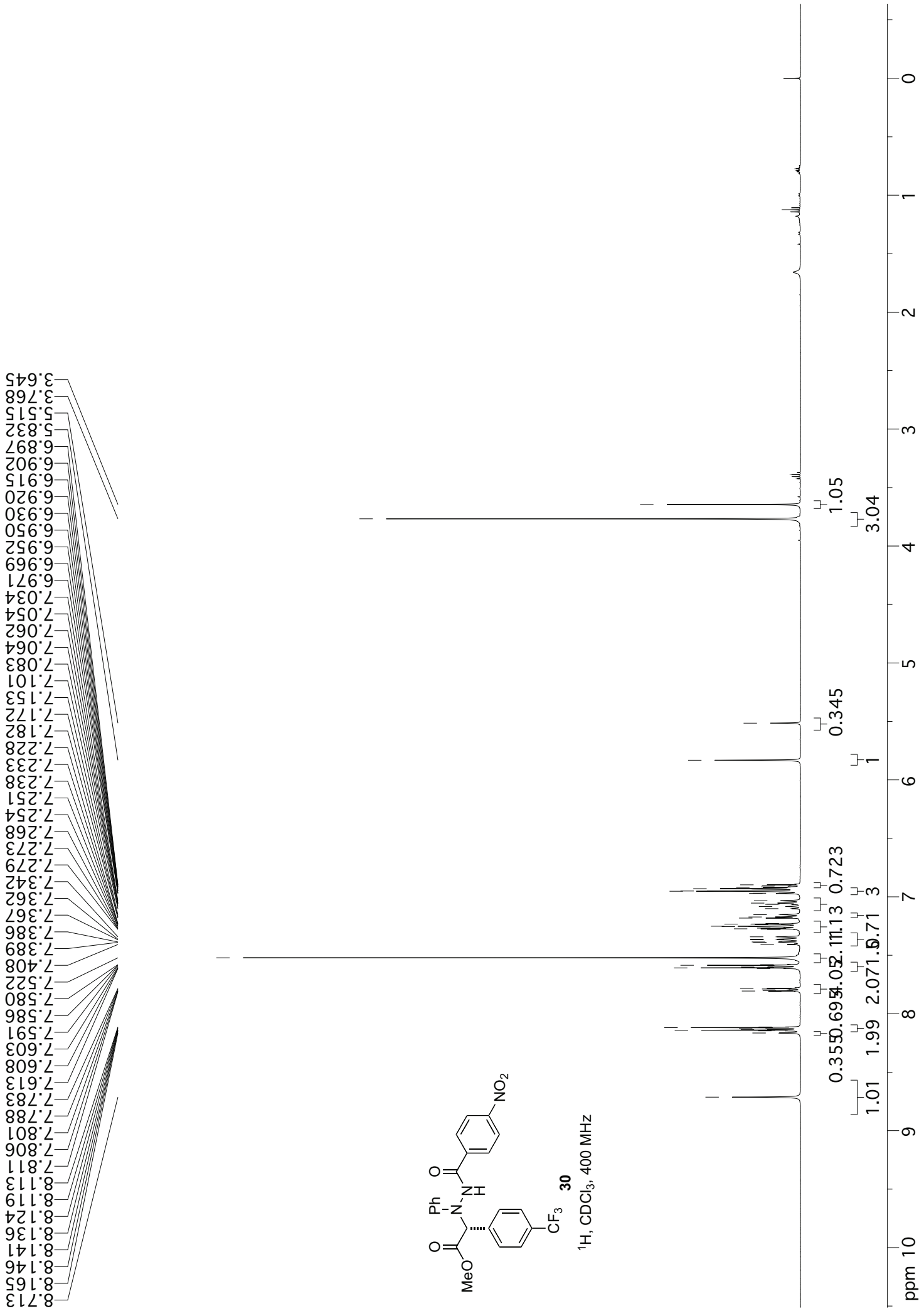


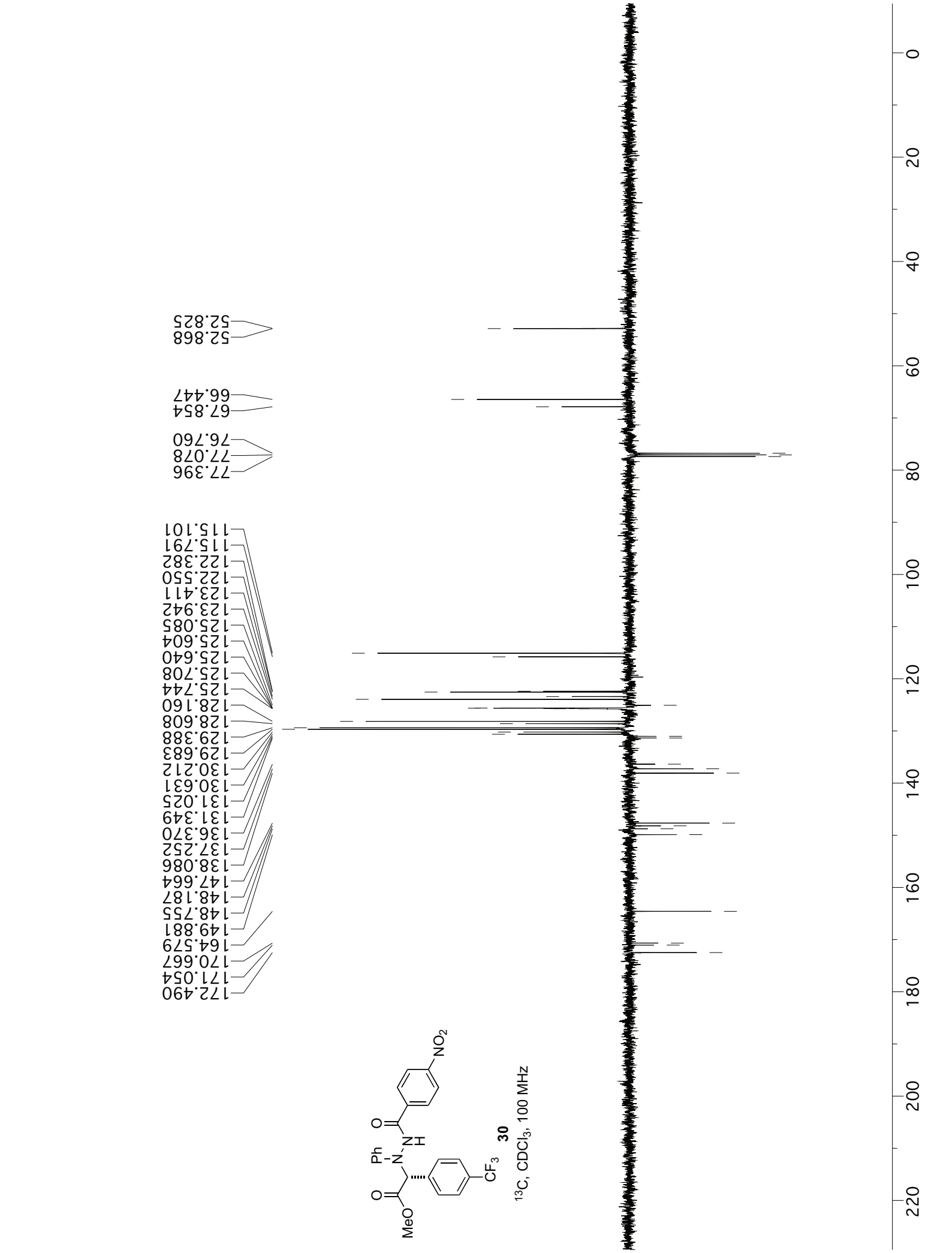


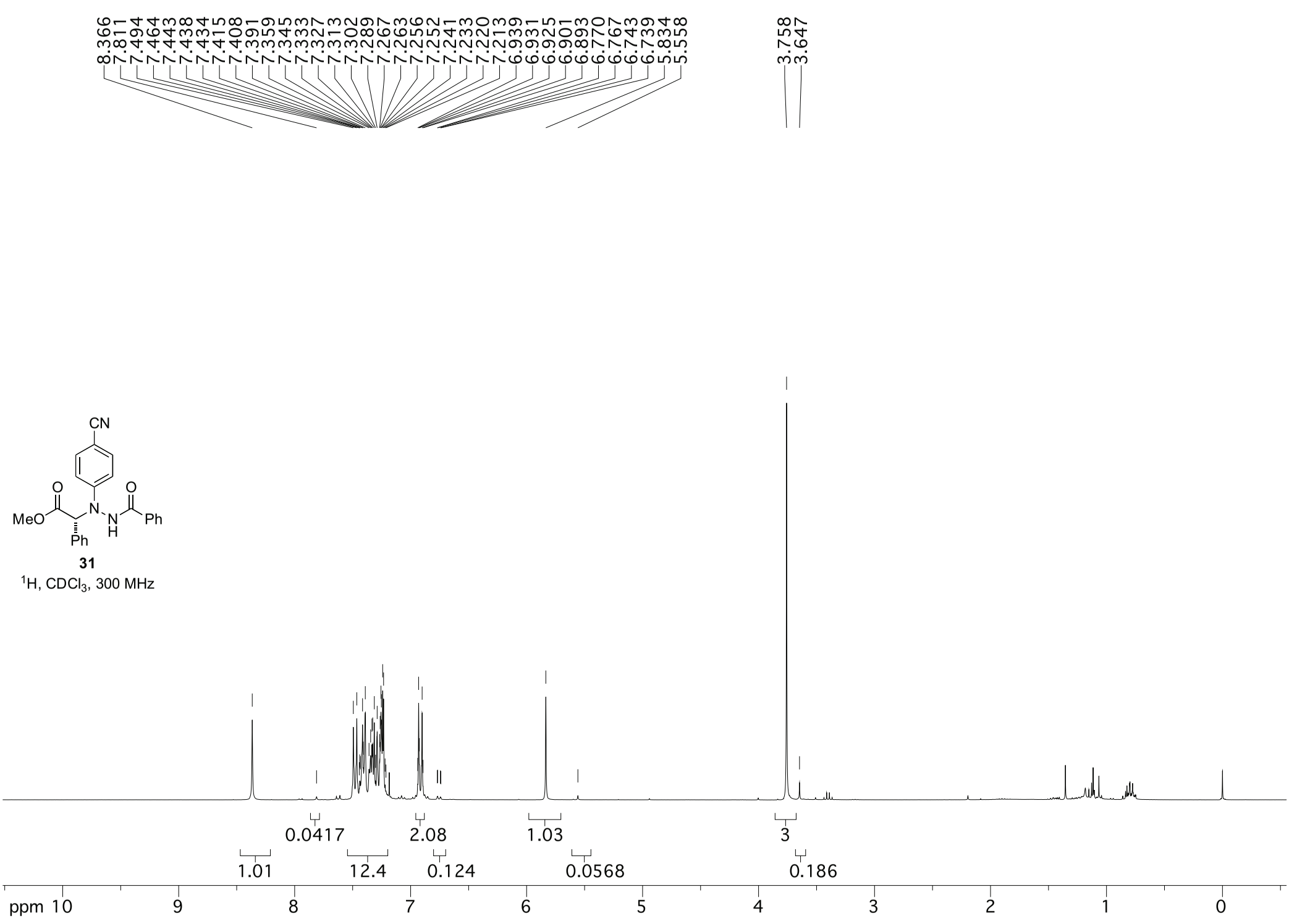
29

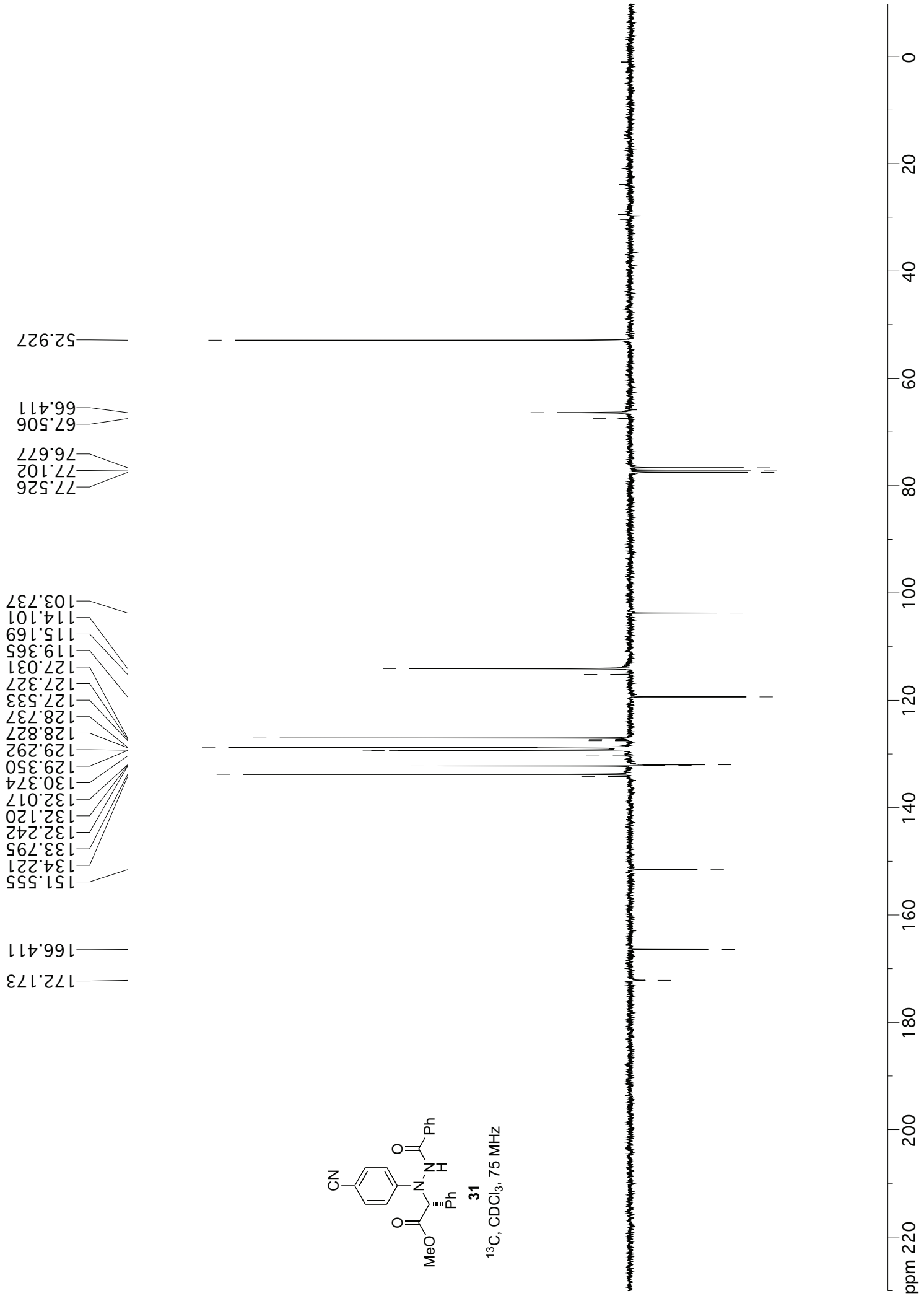
^{1}H, $CDCl_3$, 400 MHz

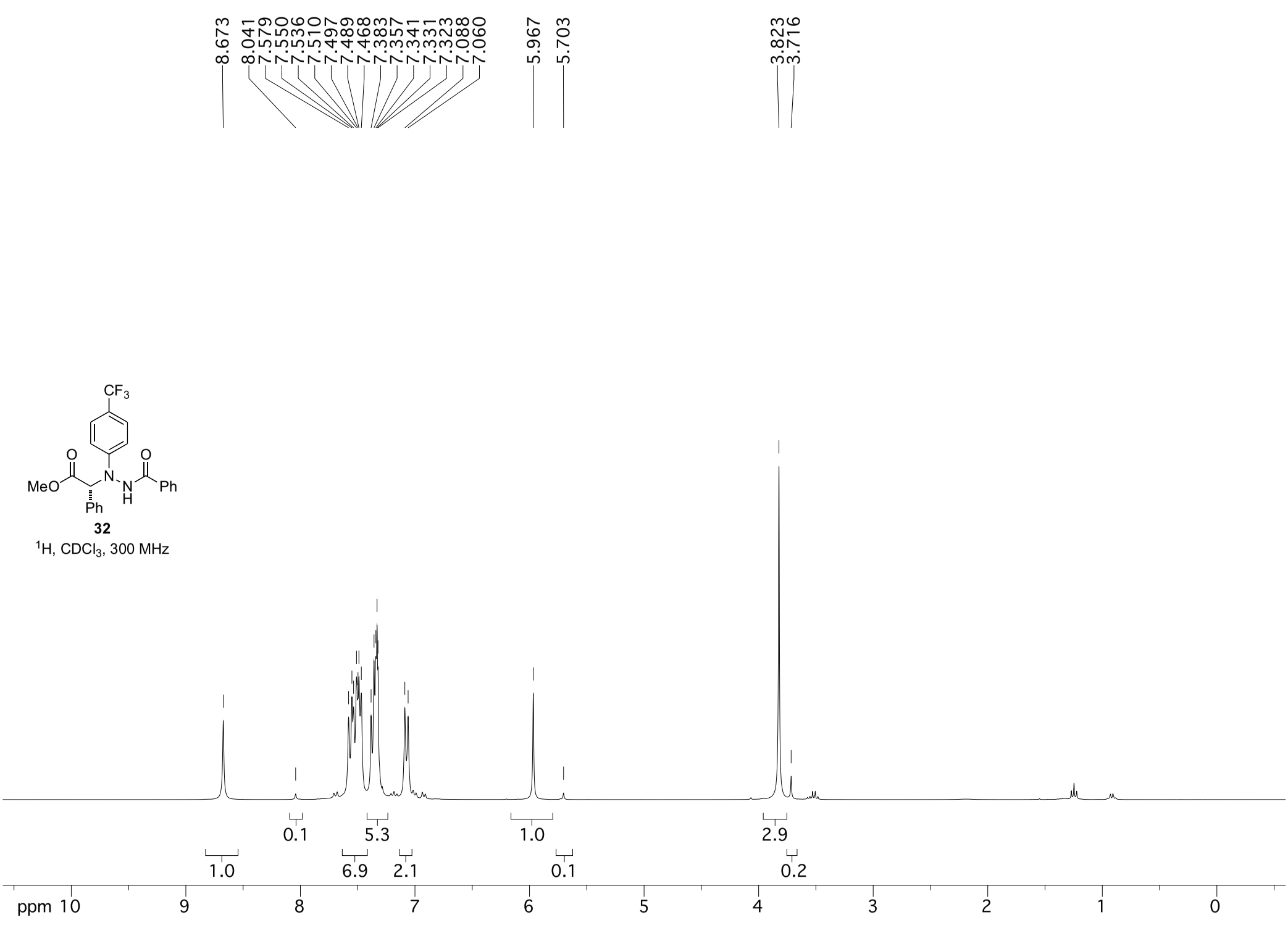

52.677
52.736
63.546
63.867
76.785
77.102
77.421
114.530
115.009
121.957
122.066
122.899
123.680
123.730
124.262
125.261
125.845
126.205
126.591
126.812
127.310
127.402
128.183
128.543
128.651
128.744
129.342
129.772
130.375
130.457
131.724
132.344
133.579
133.769
137.523
138.545
147.950
147.994
148.509
149.631
164.324
171.634
172.022
173.491
0
20
40
60
80
100
120
140
160
180
200
220
29
^{13}C, $CDCl_3$, 100 MHz

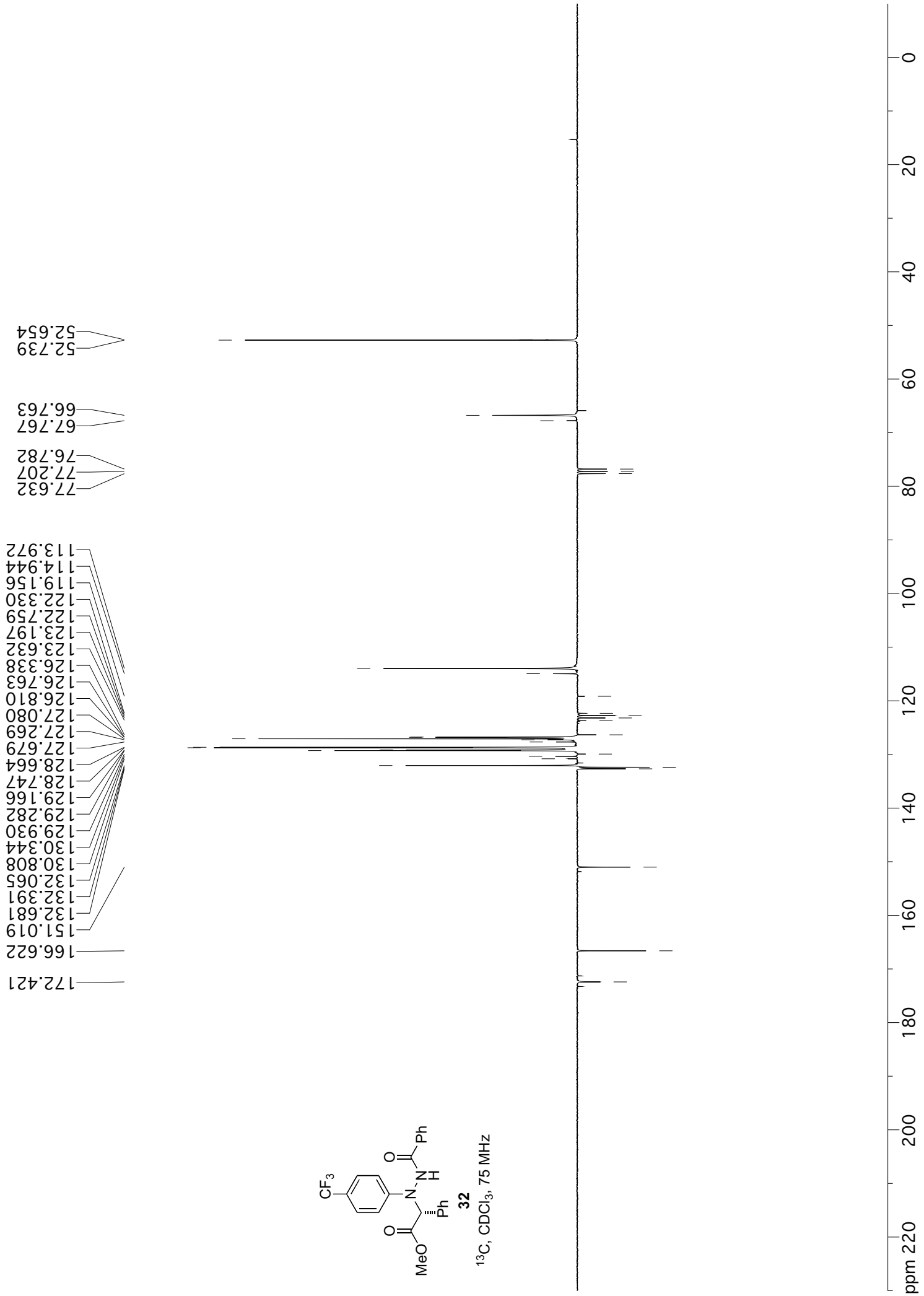


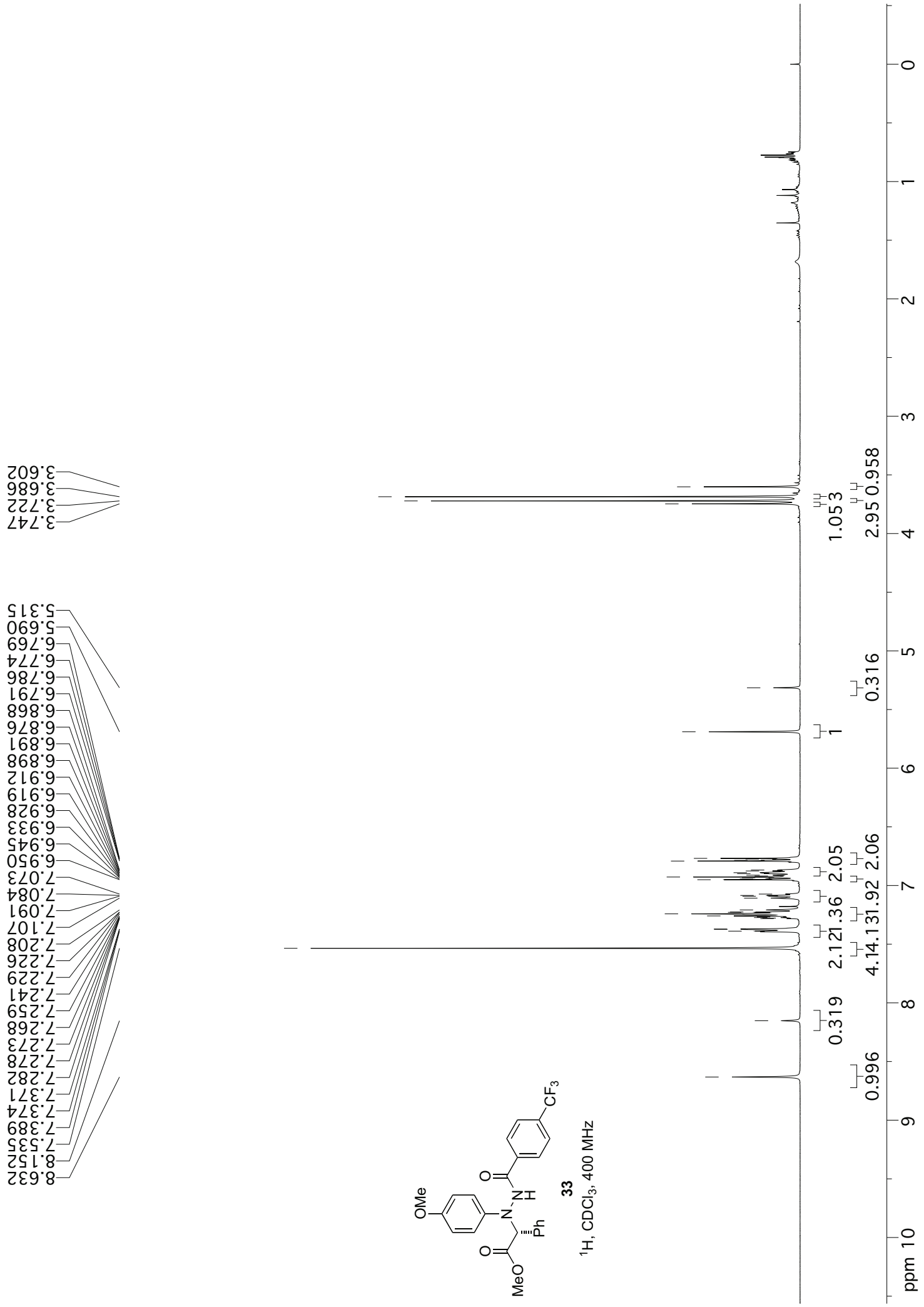


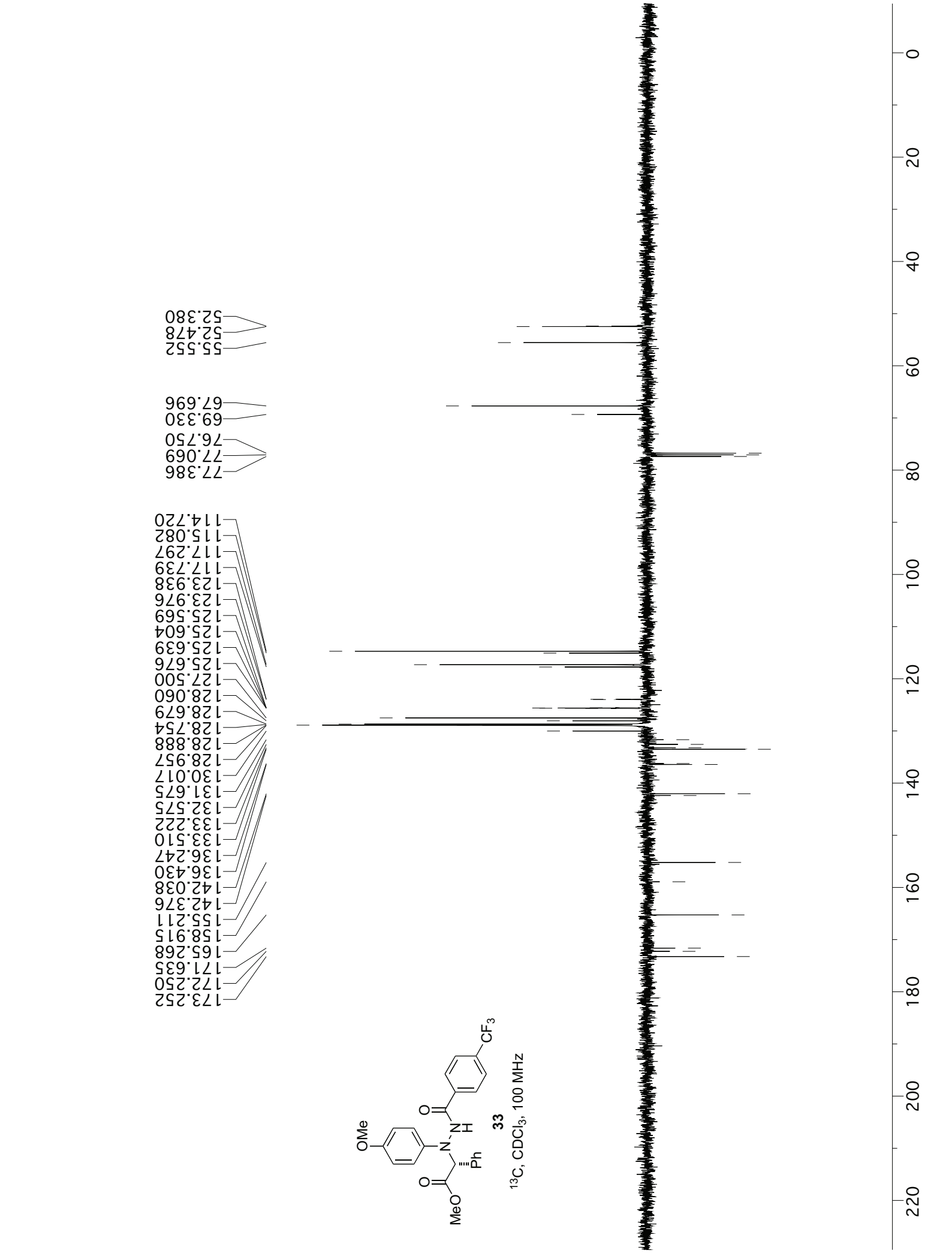


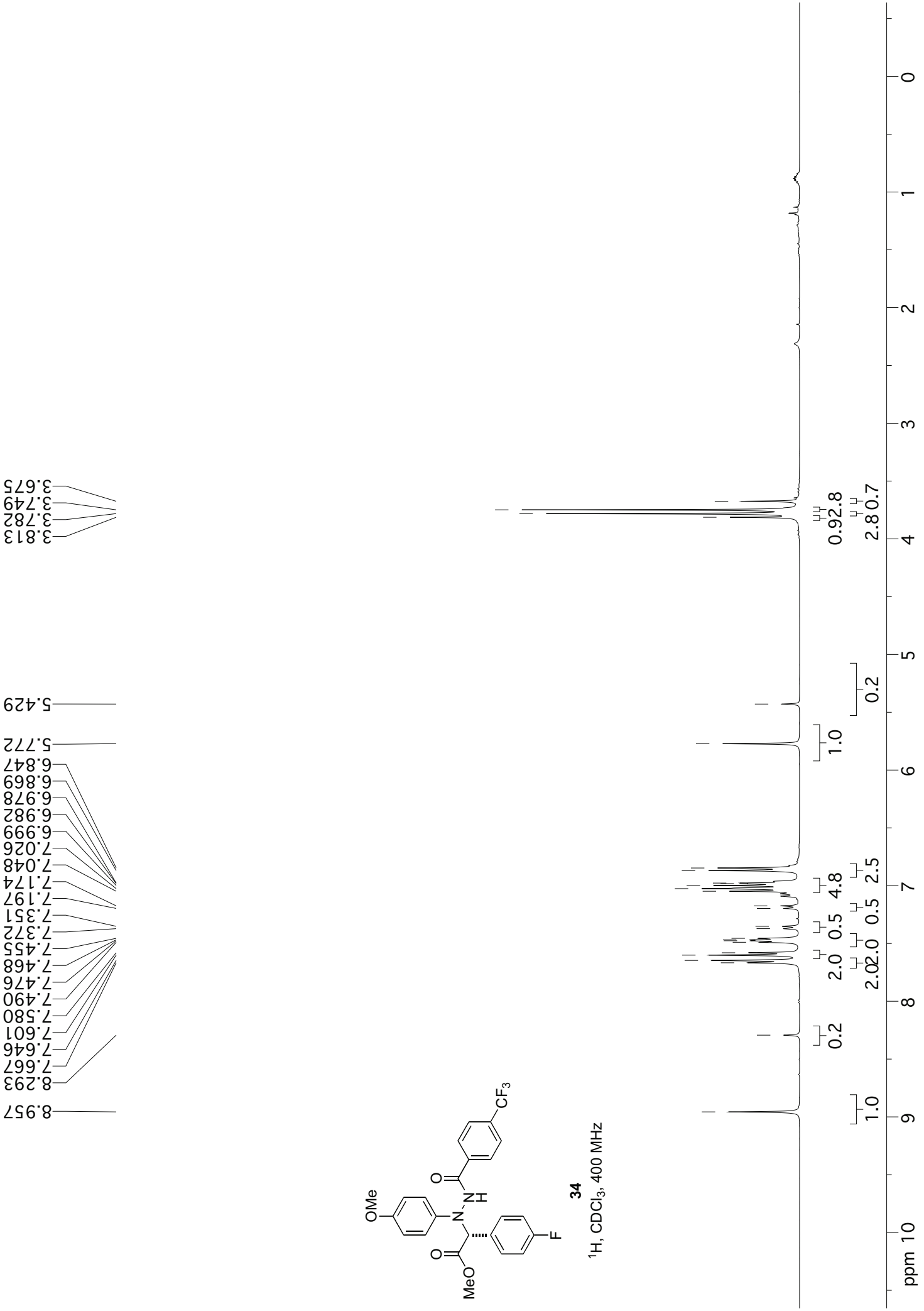


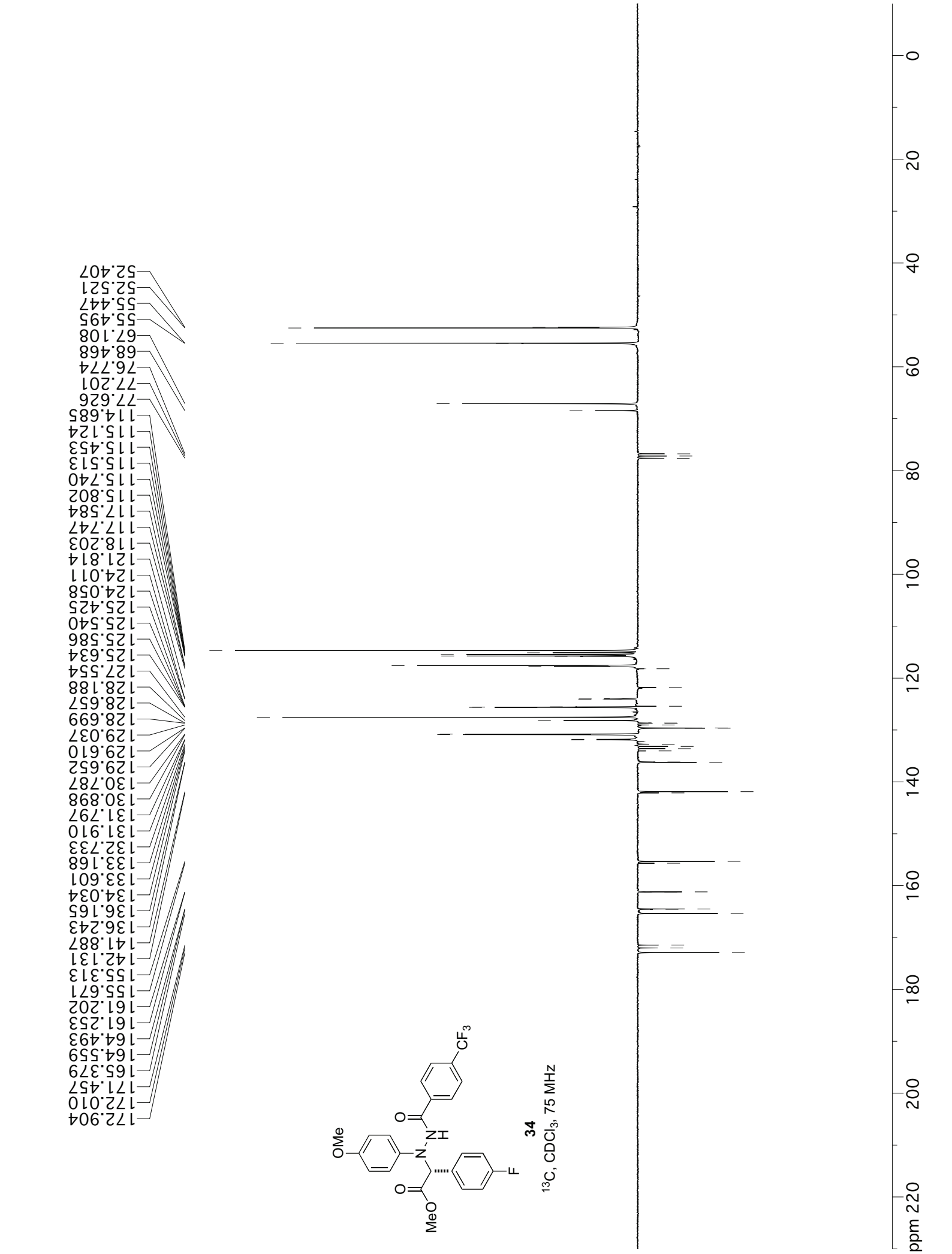


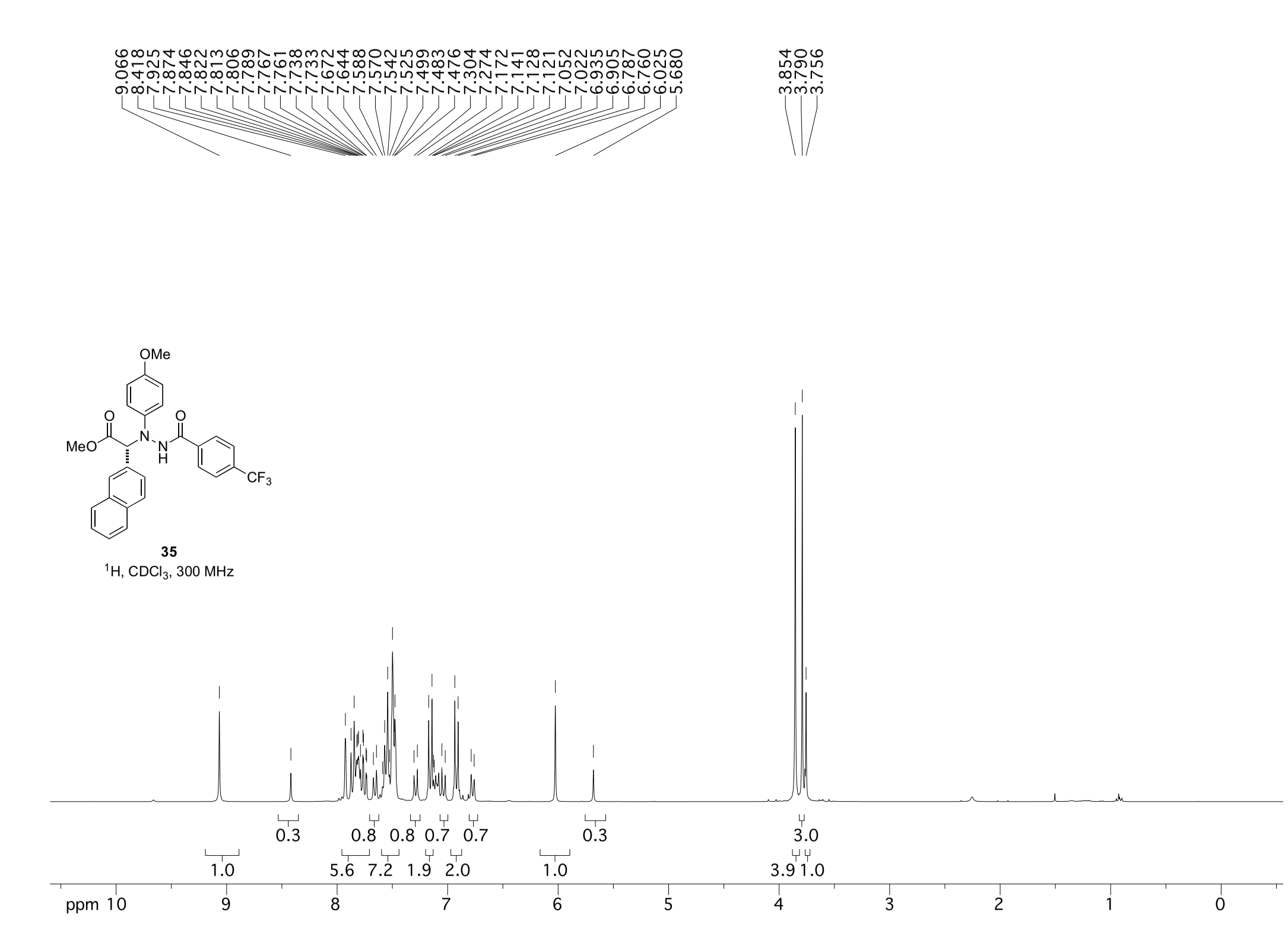


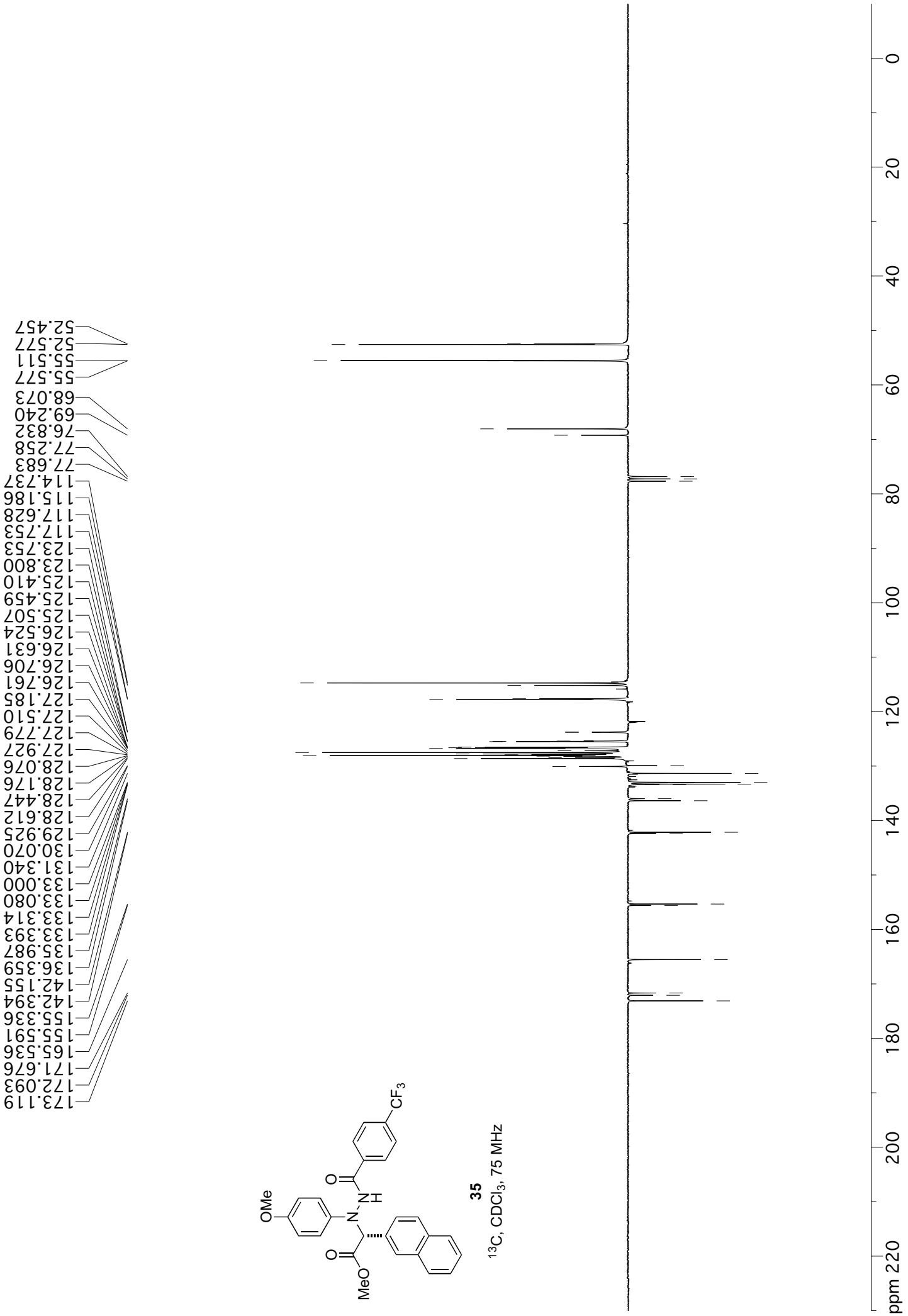


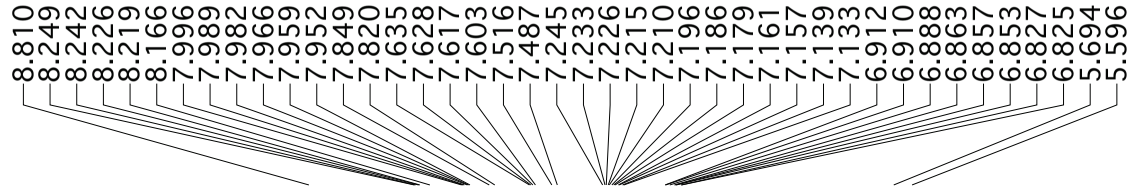


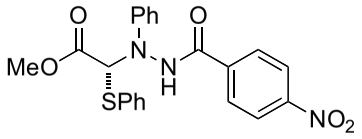






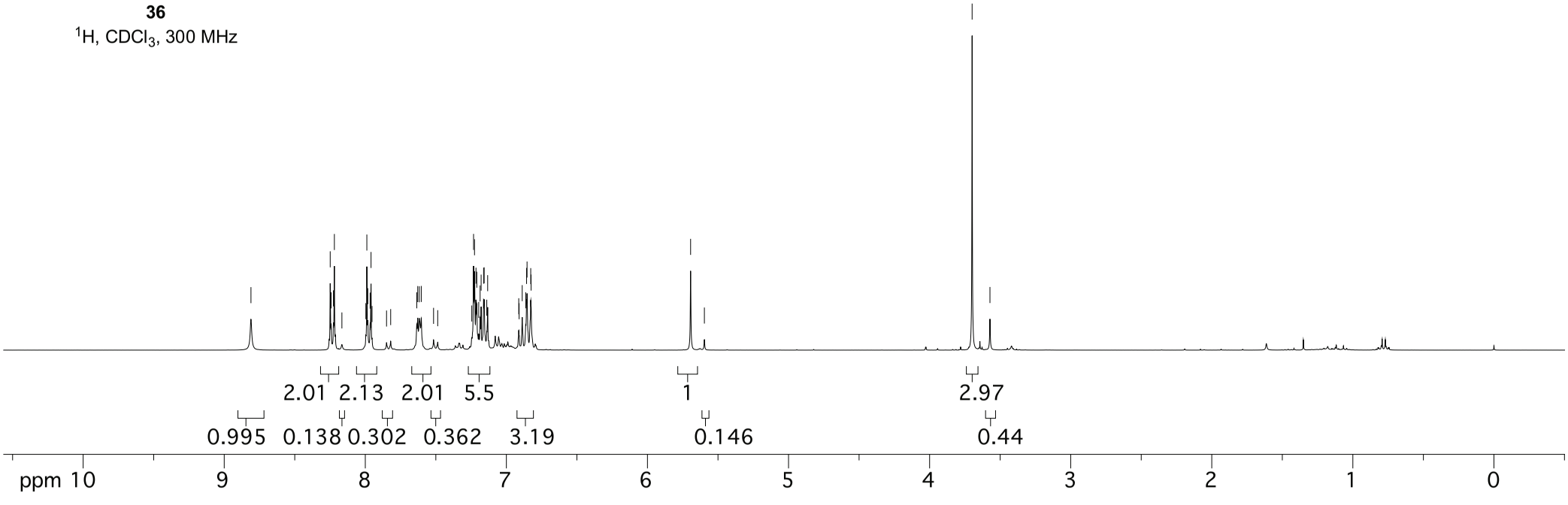

52.457
52.577
55.511
55.577
68.073
69.240
76.832
77.258
77.683
114.737
115.186
117.628
117.753
123.753
123.800
125.410
125.459
125.507
126.524
126.631
126.706
126.761
127.185
127.510
127.779
127.927
128.076
128.176
128.447
128.612
129.925
130.070
131.340
133.000
133.080
133.314
133.393
135.987
136.359
142.155
142.394
155.336
155.591
165.536
171.676
172.093
173.119
OMe
MeO
O
O
N
H
N
CF3
35
13C, CDCl3, 75 MHz
ppm
220
200
180
160
140
120
100
80
60
40
20
0

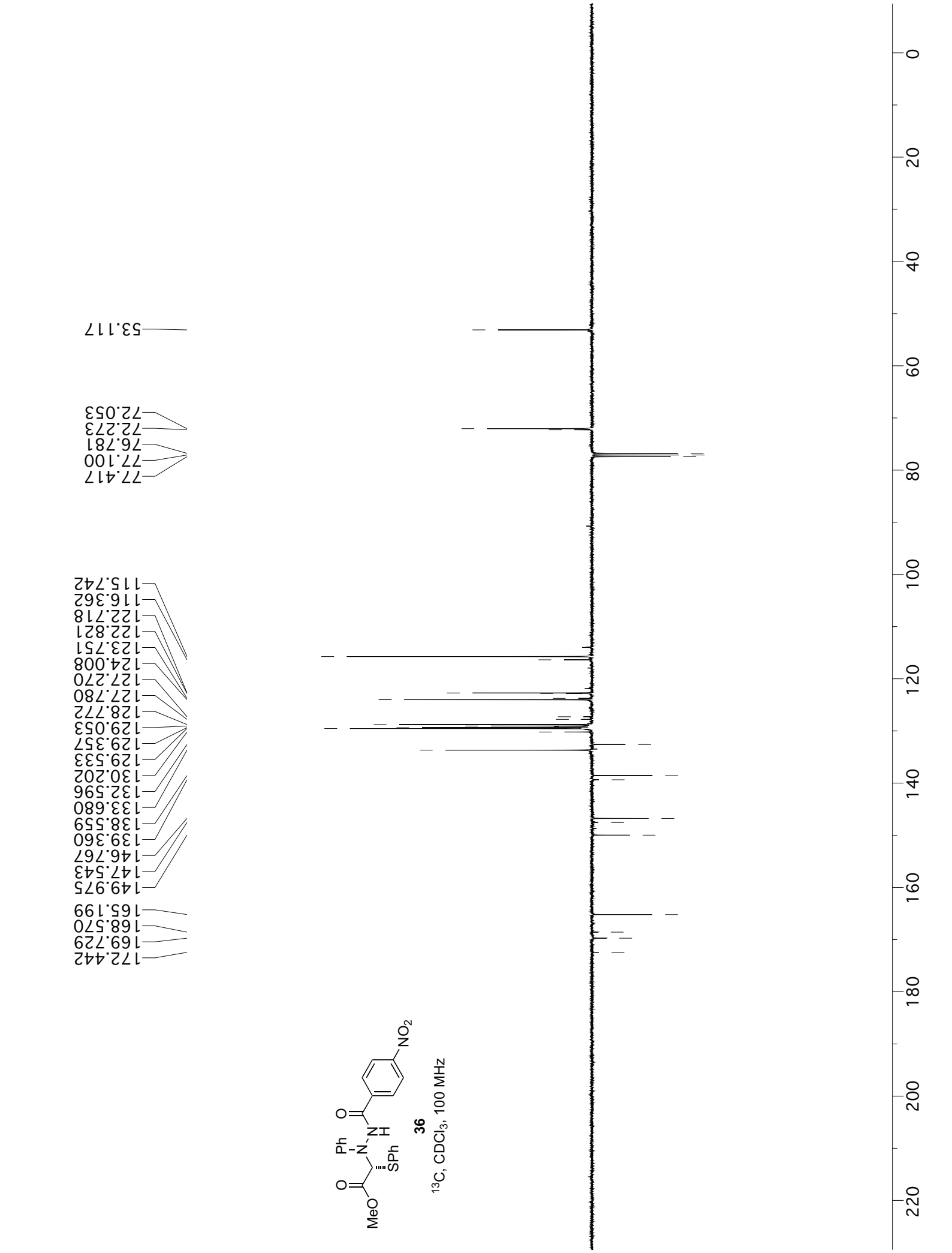


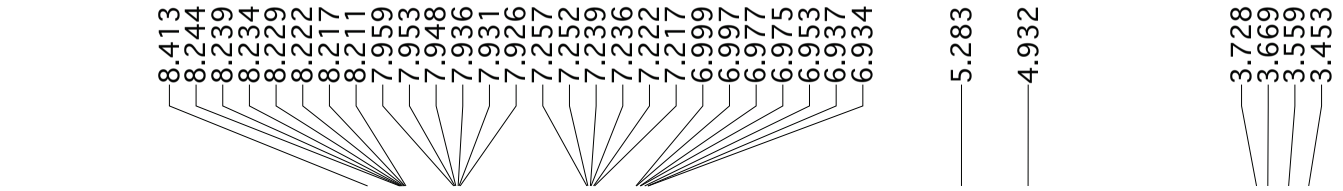


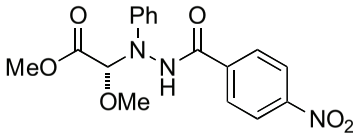
36

^{1}H, $CDCl_3$, 300 MHz



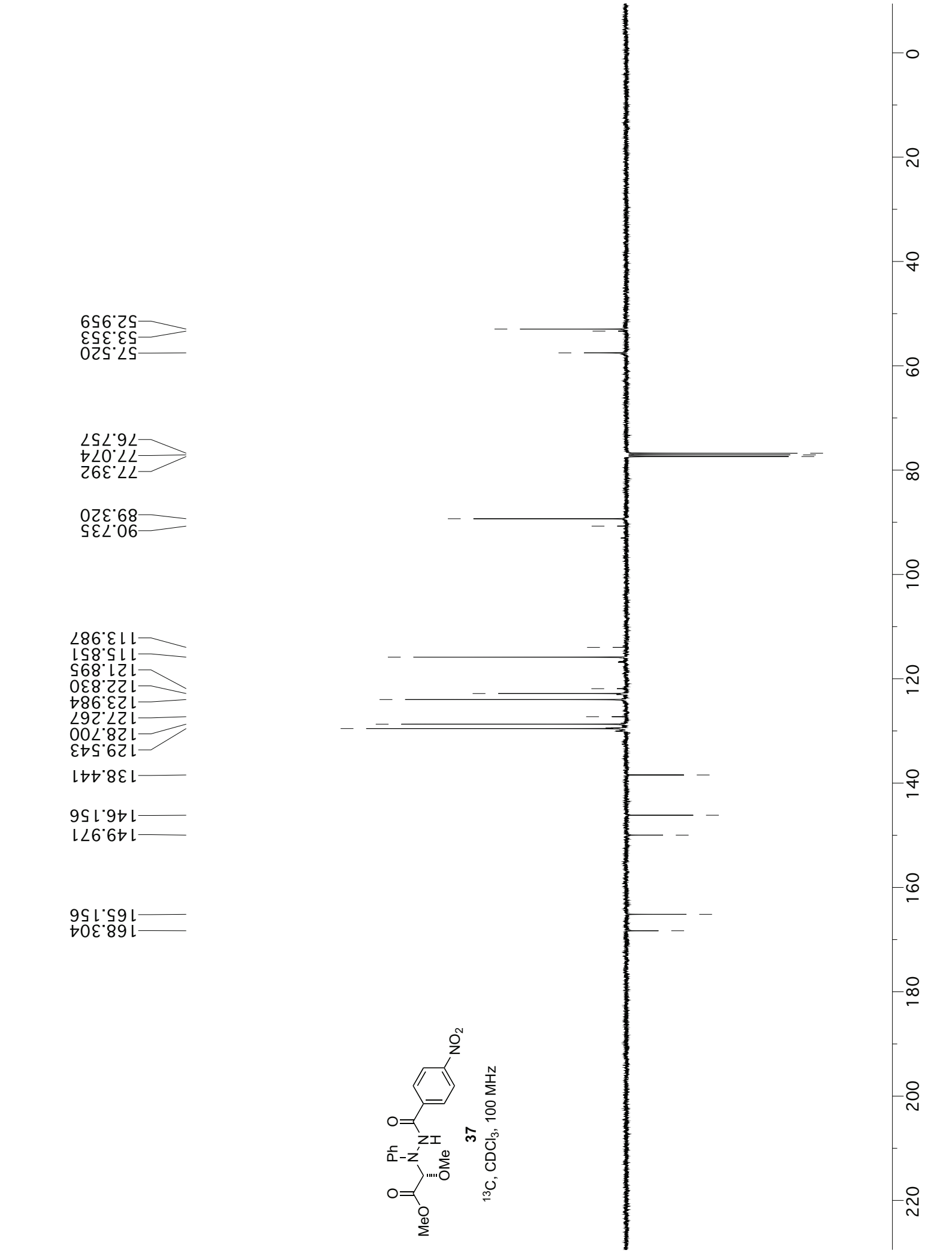


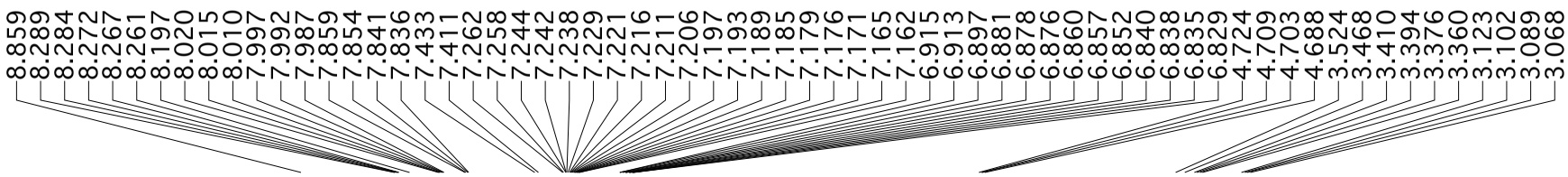


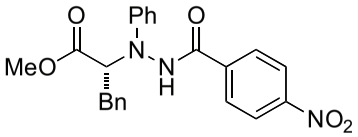


37

^{1}H, $CDCl_3$, 400 MHz

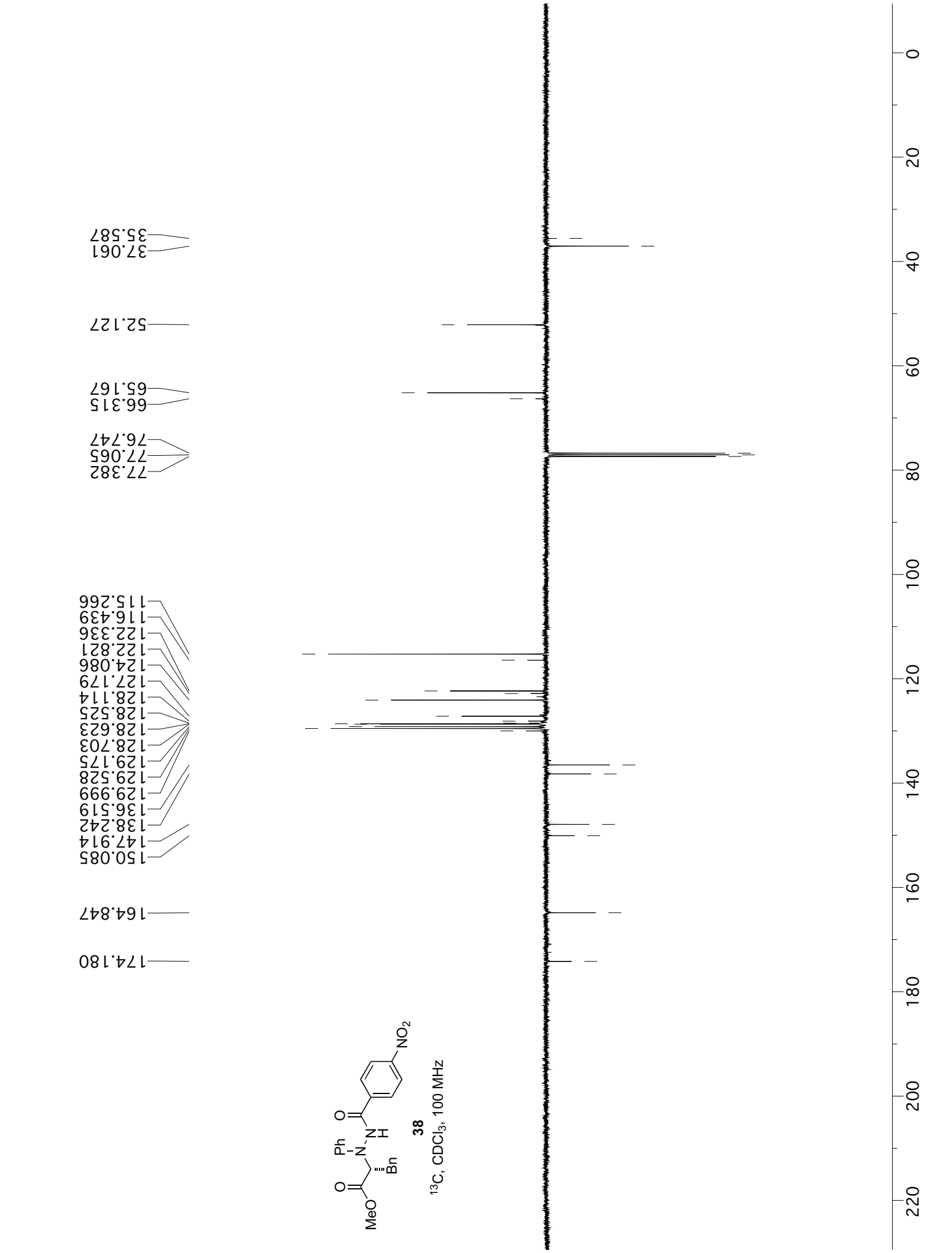


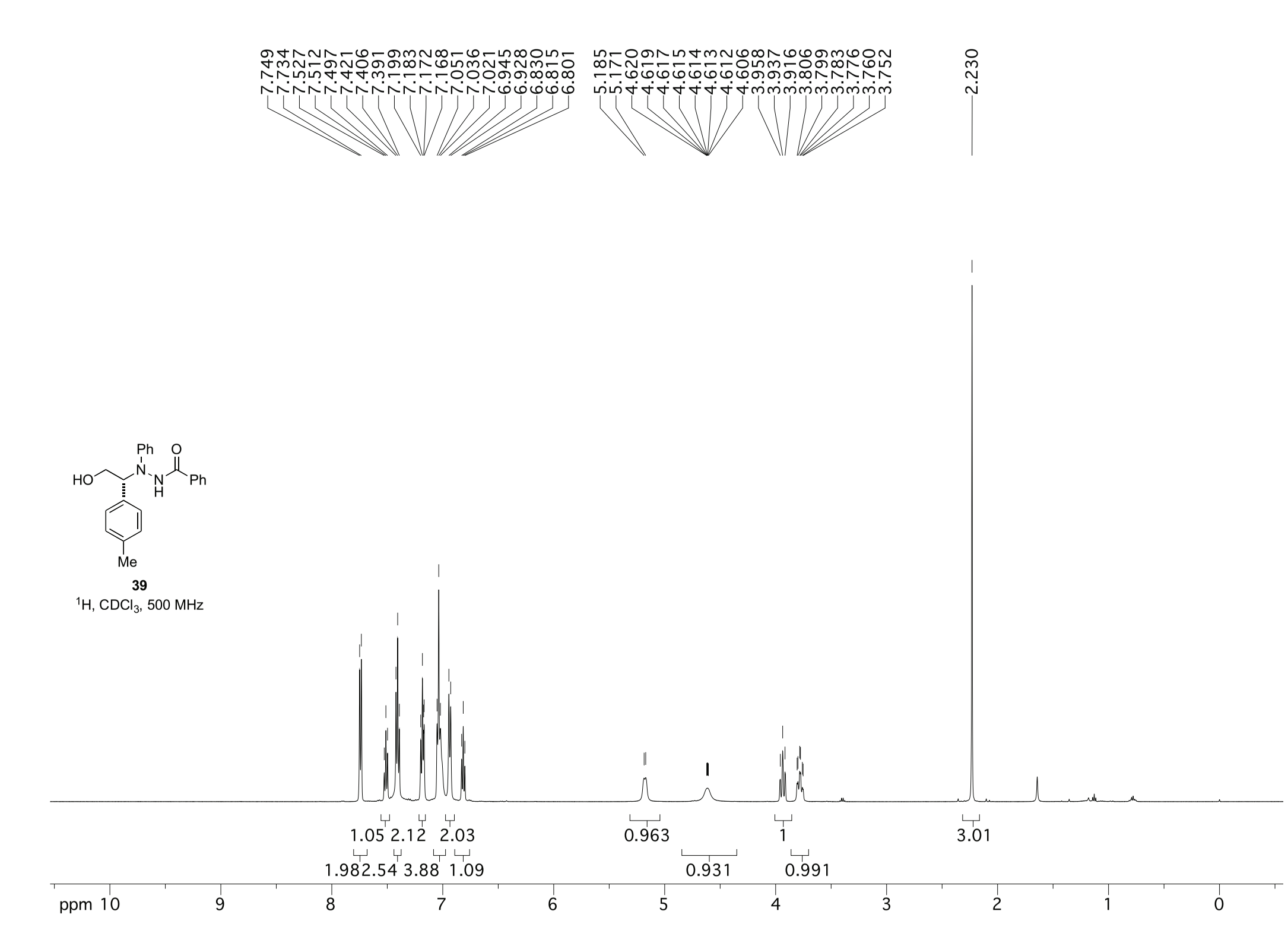


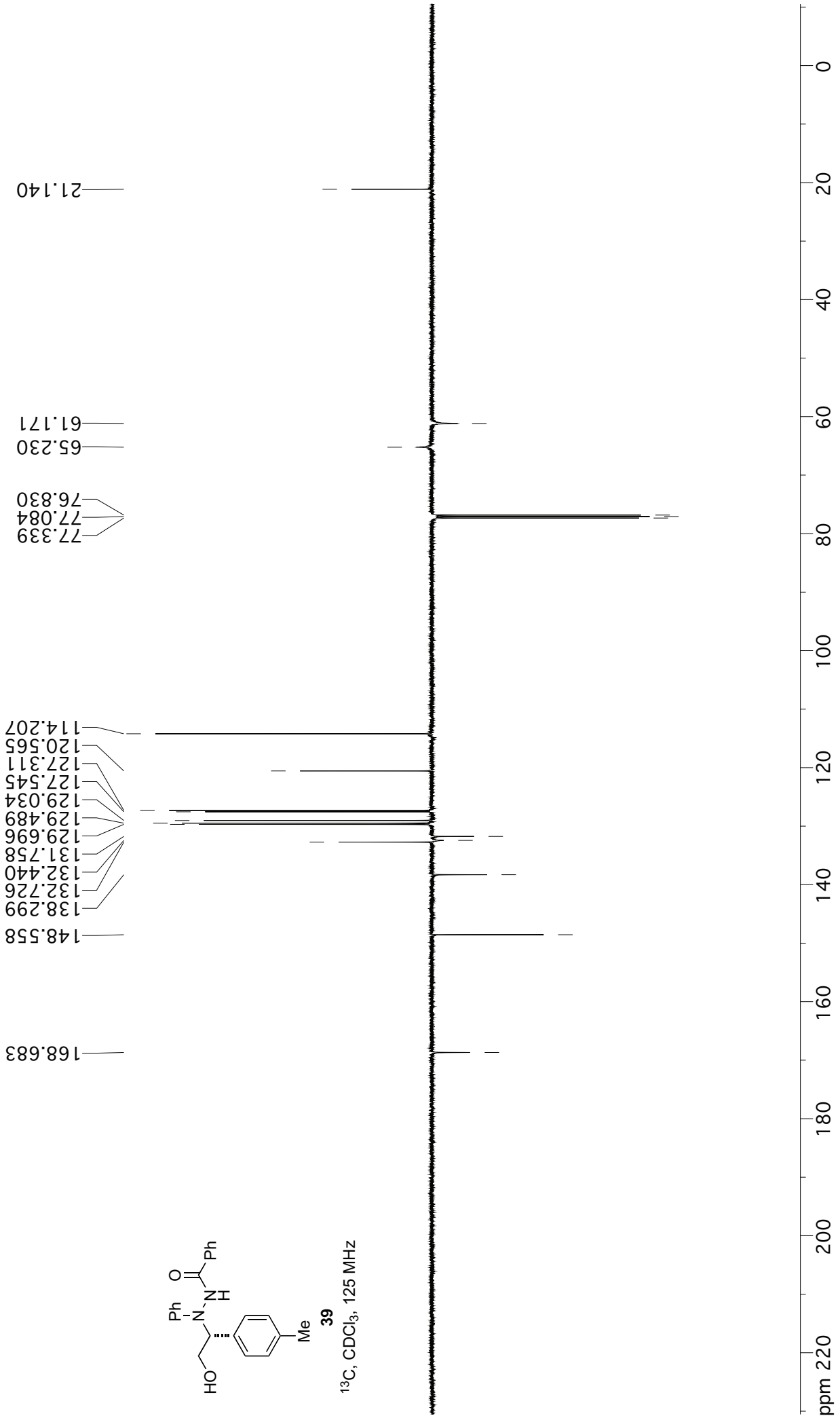


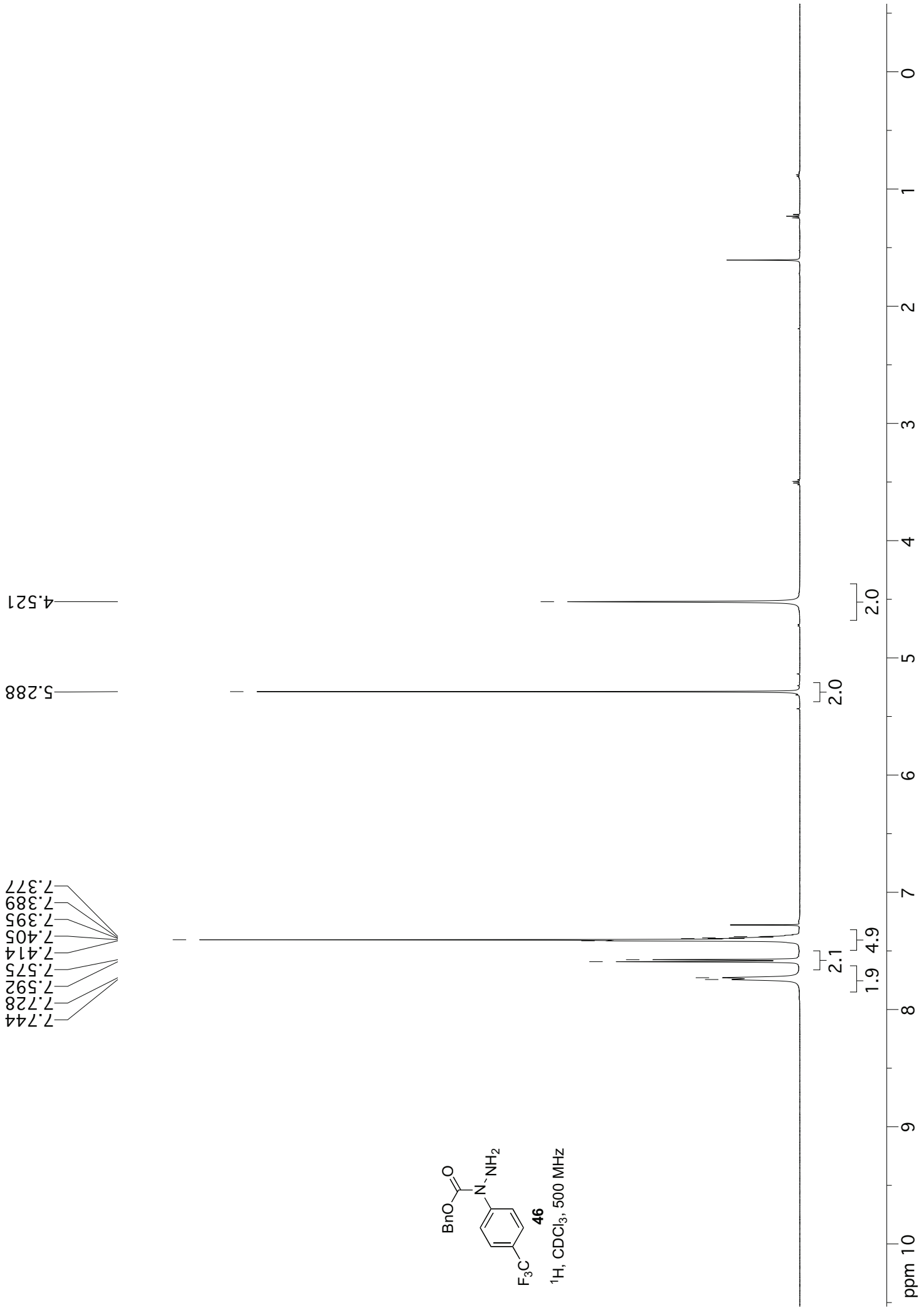
38

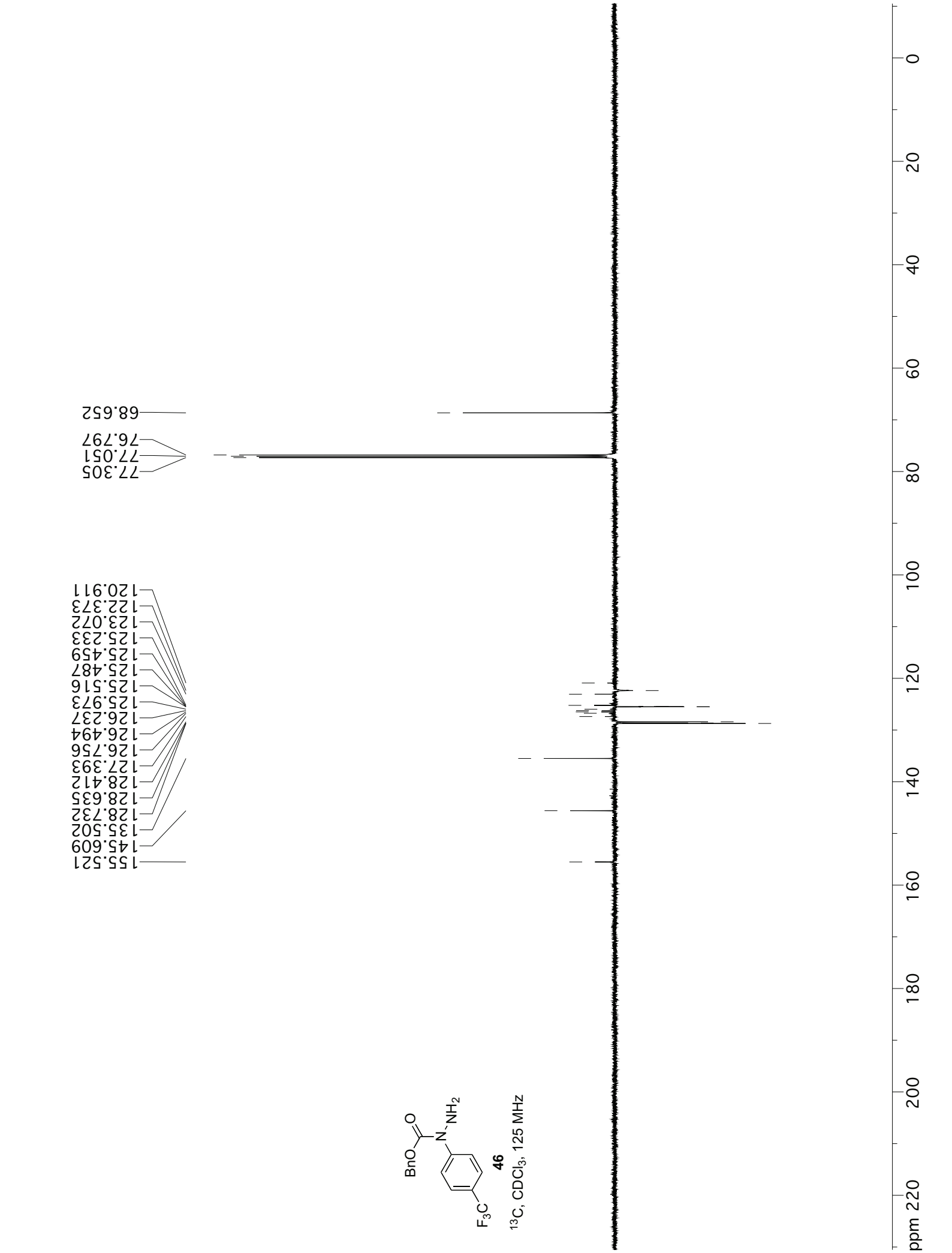
^{1}H, $CDCl_3$, 400 MHz

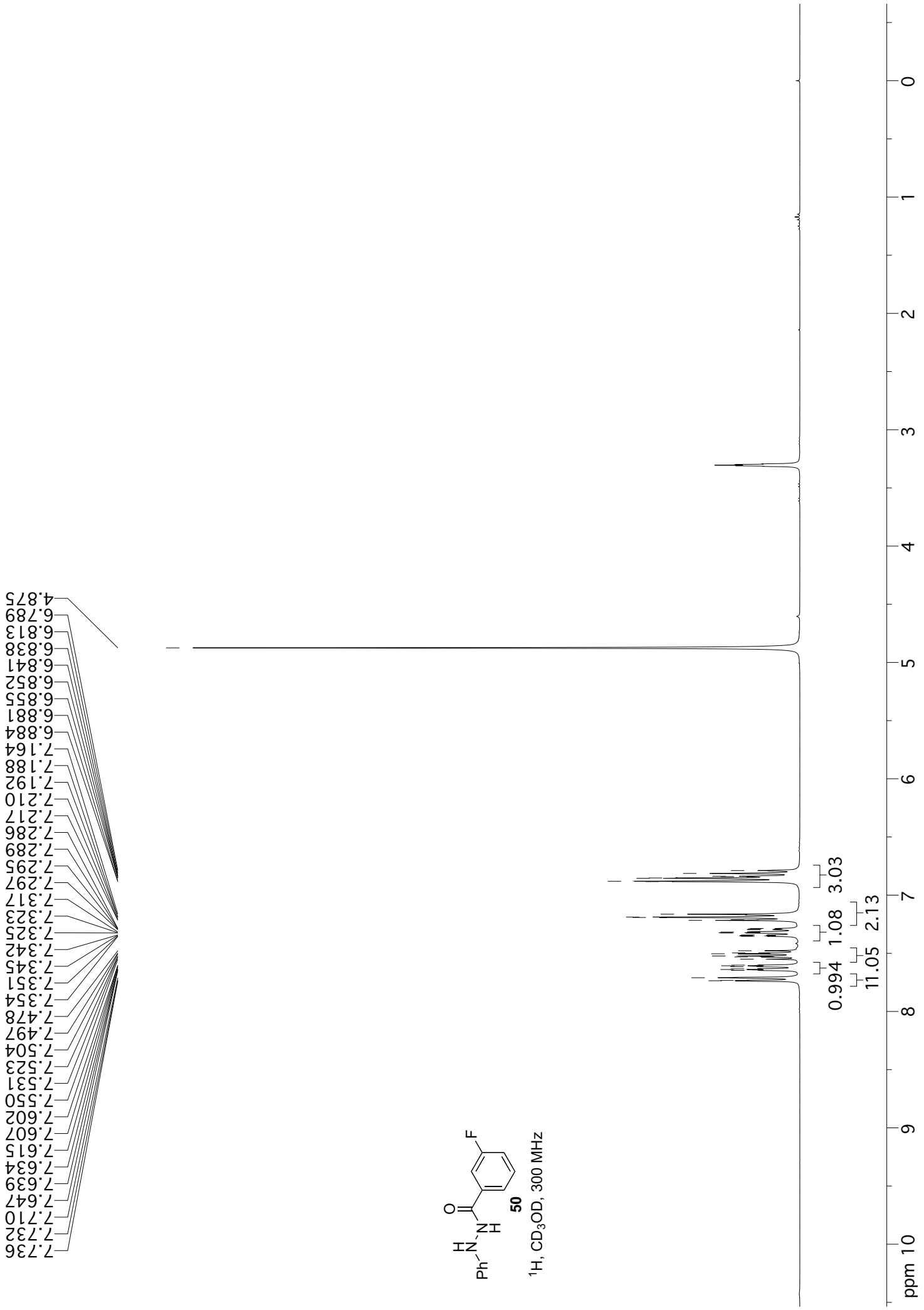


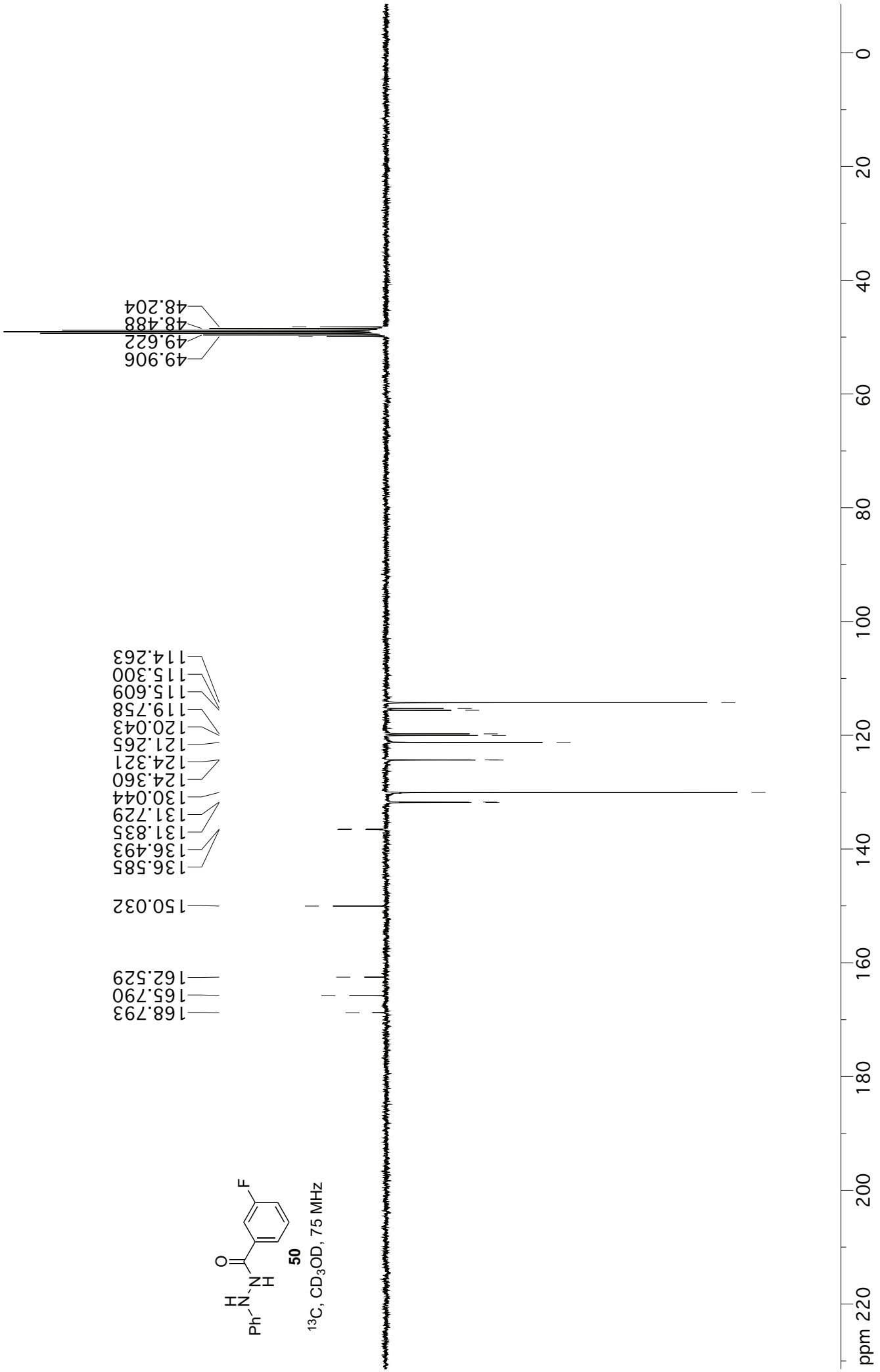


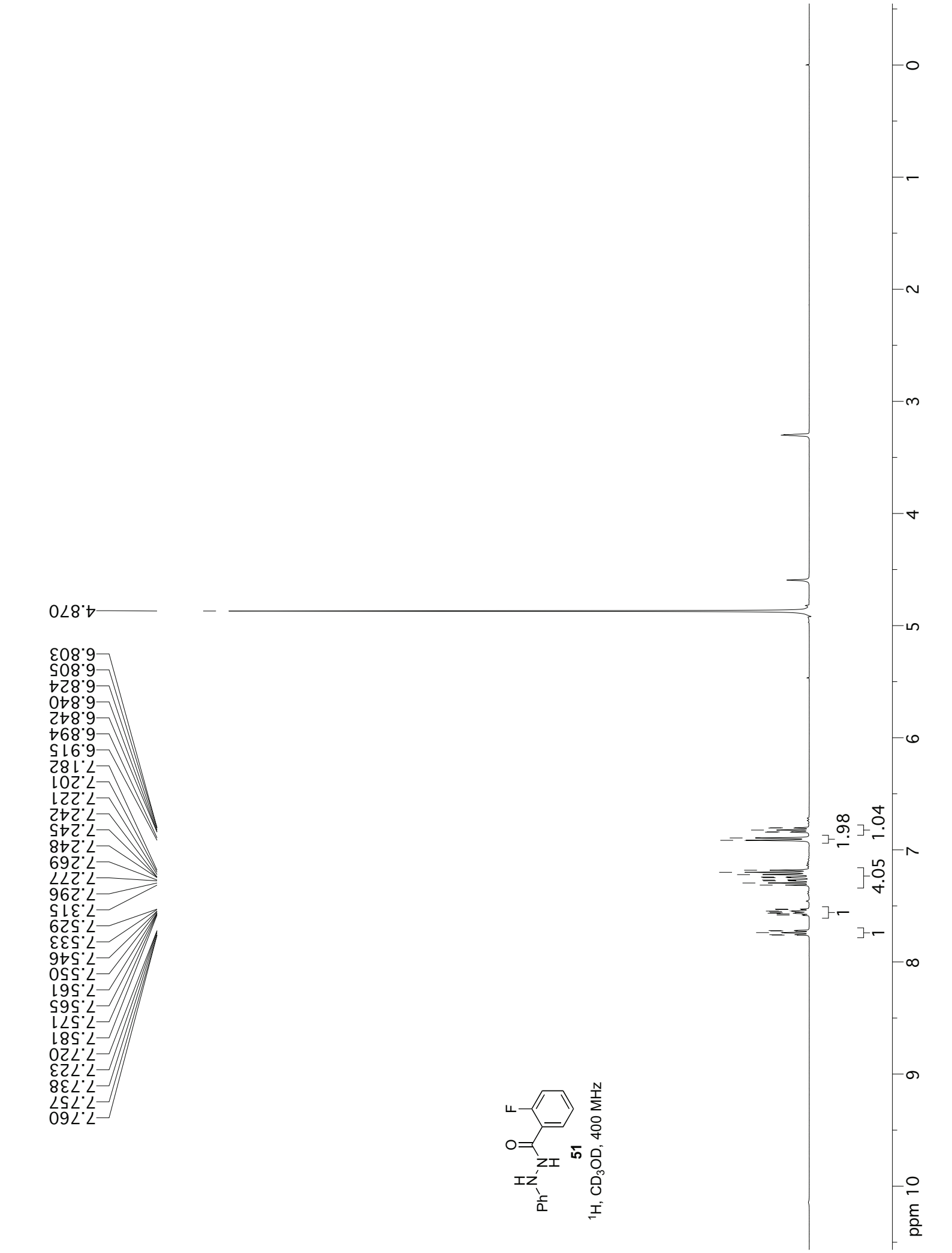


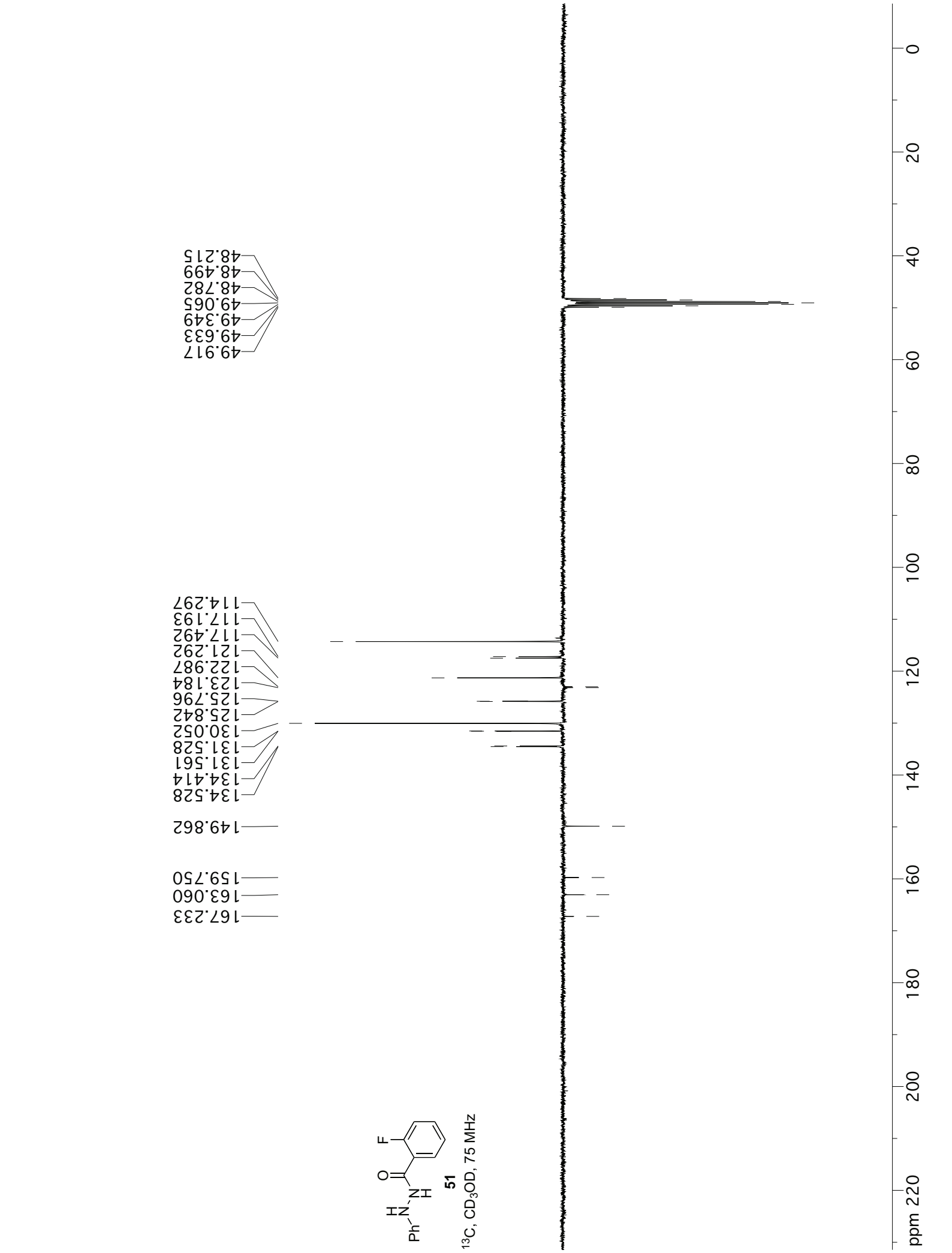


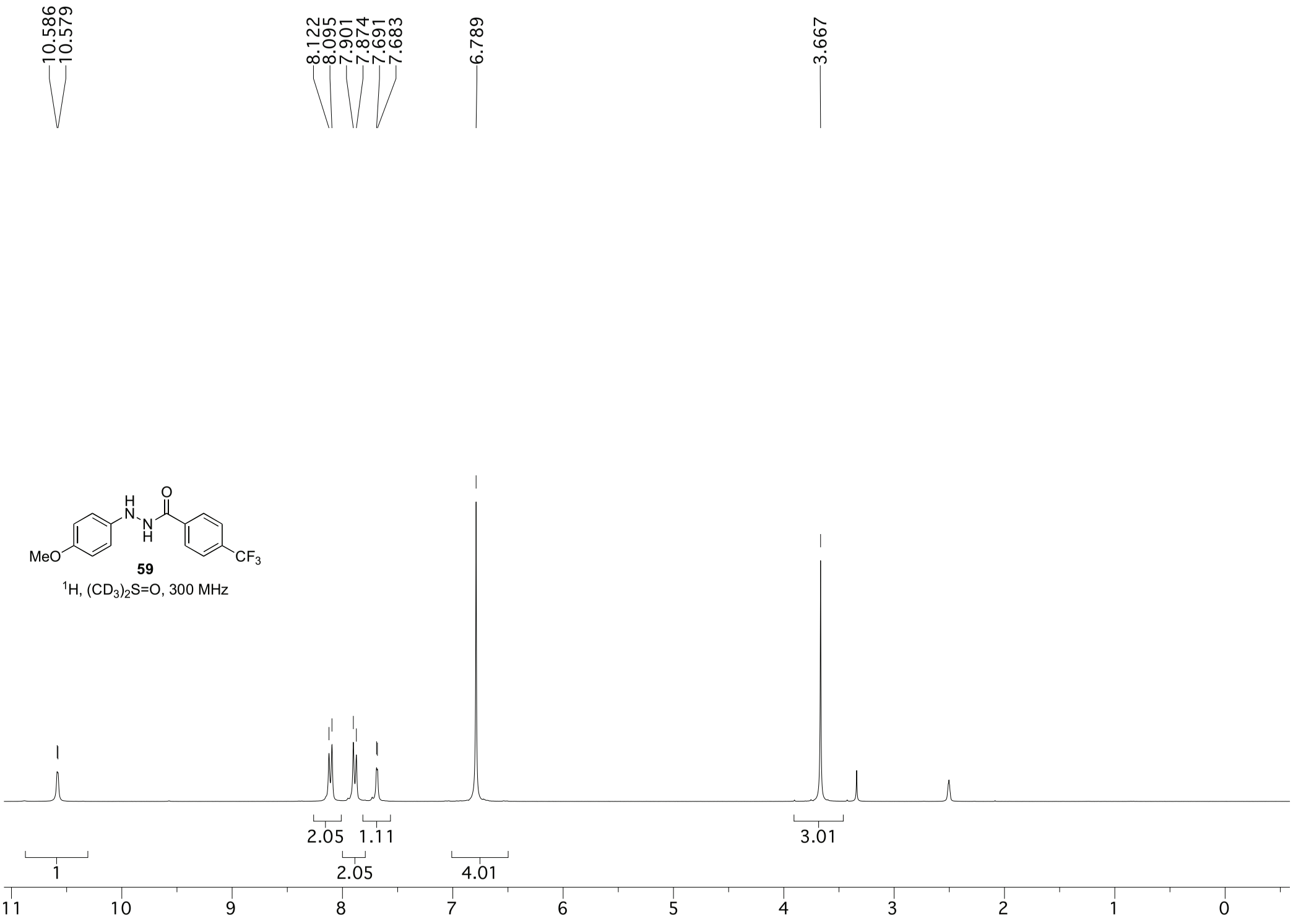


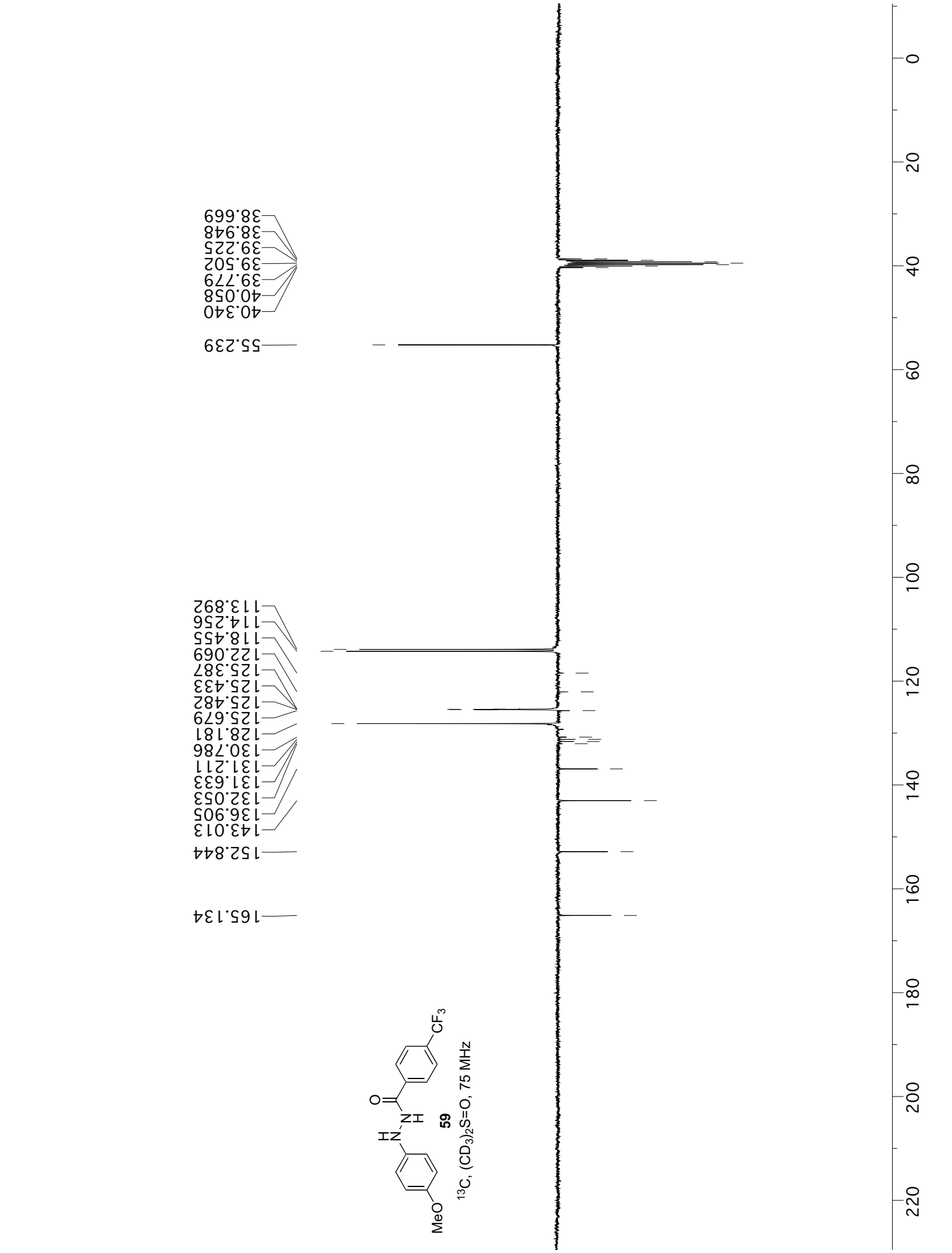


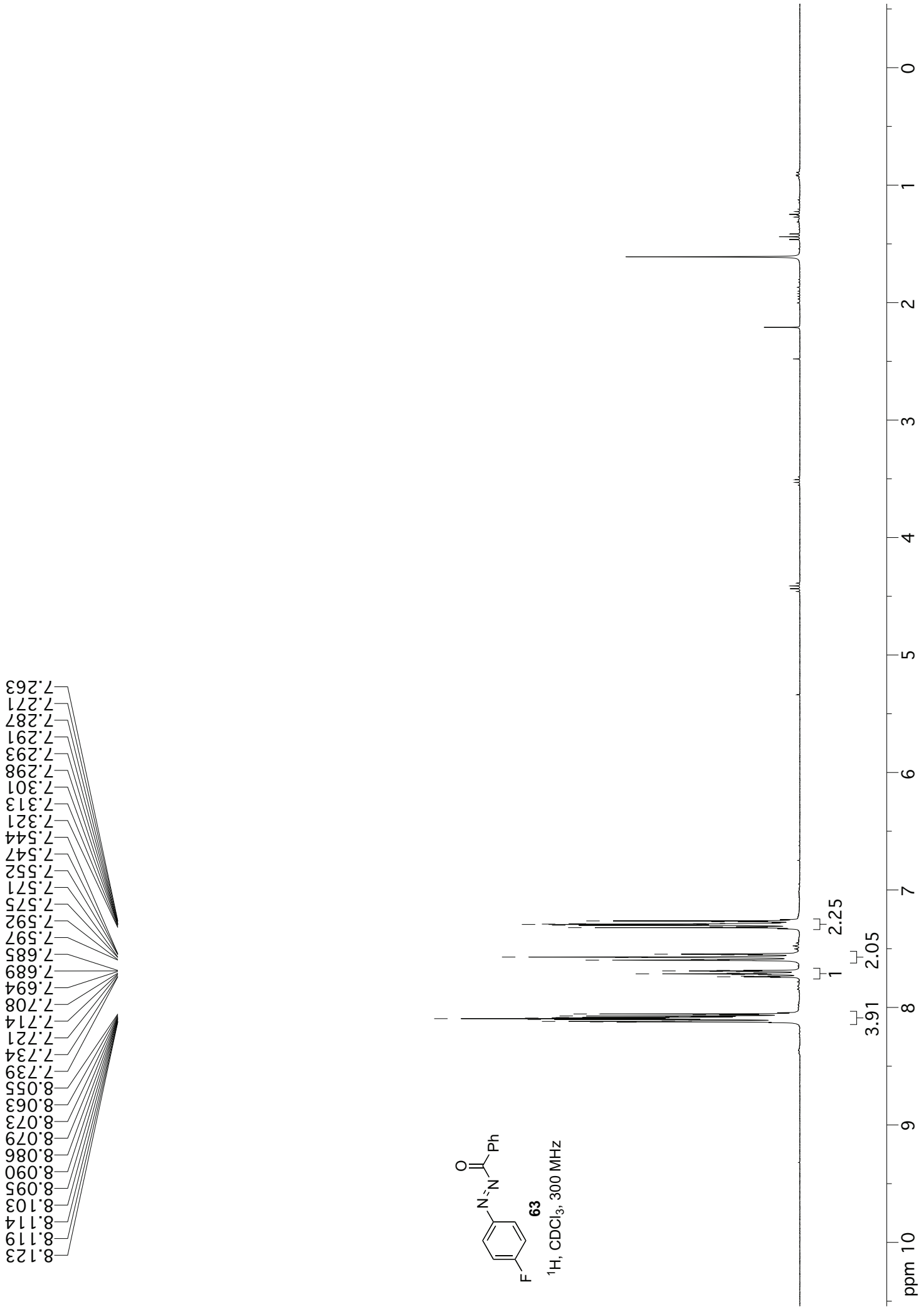


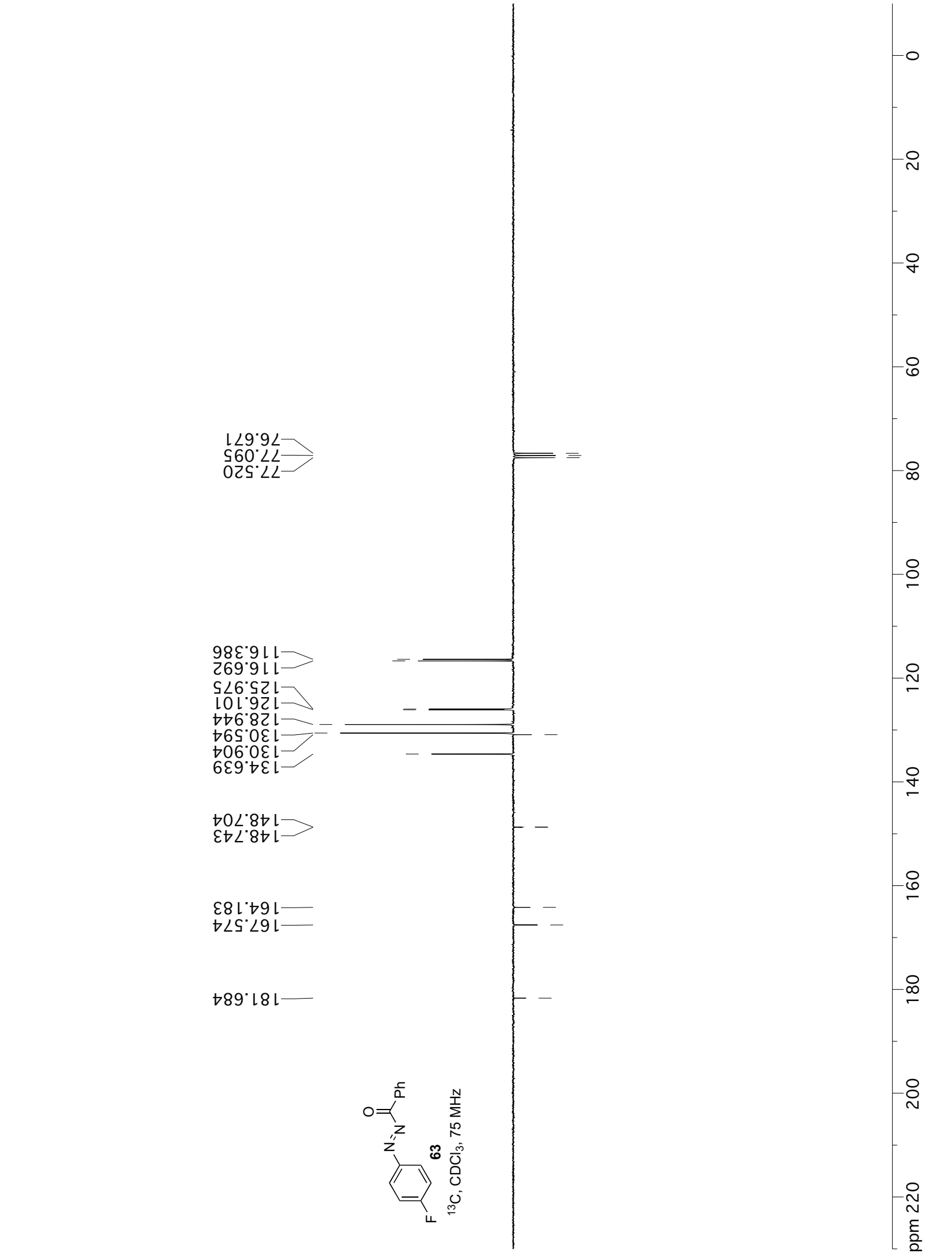


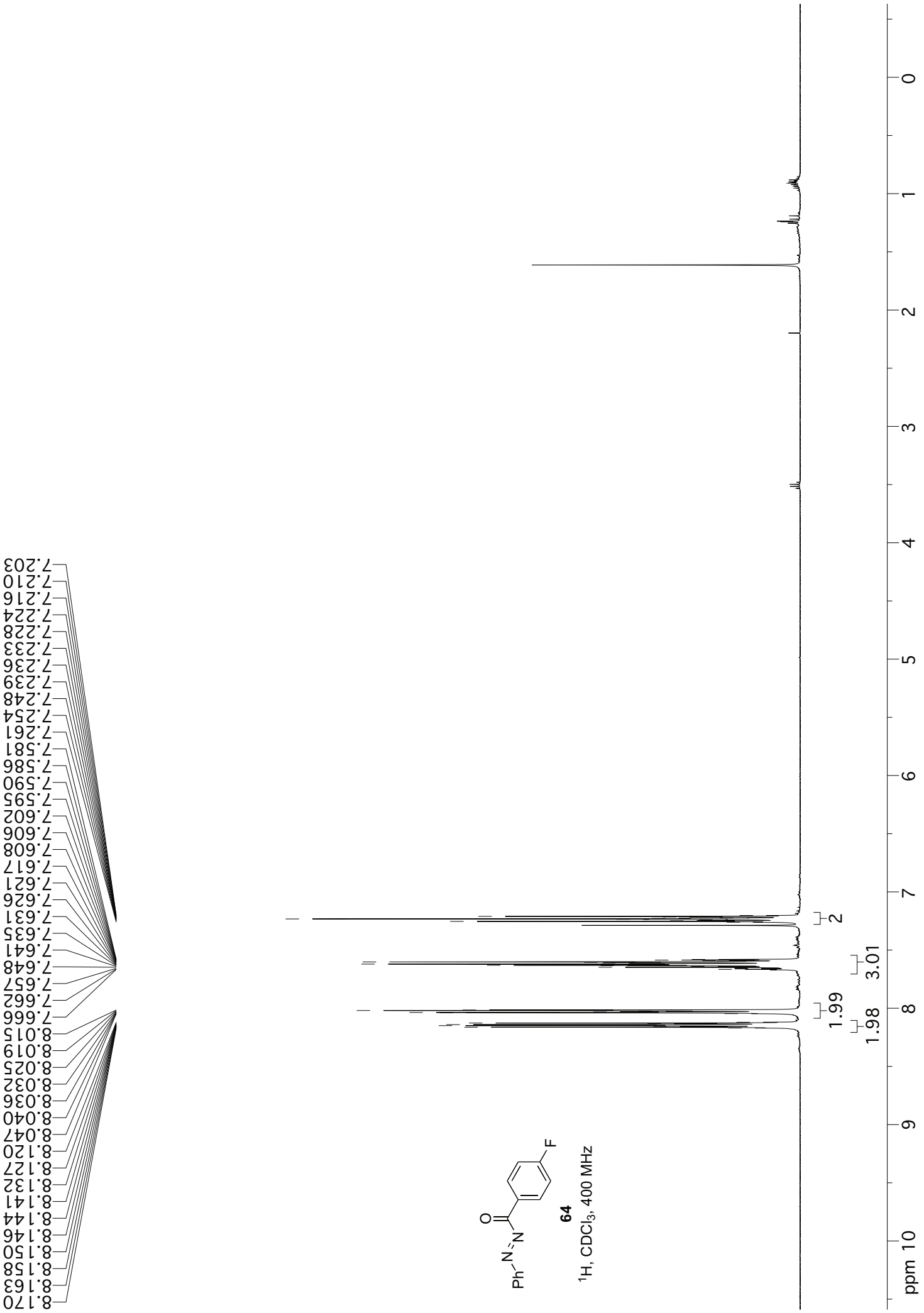


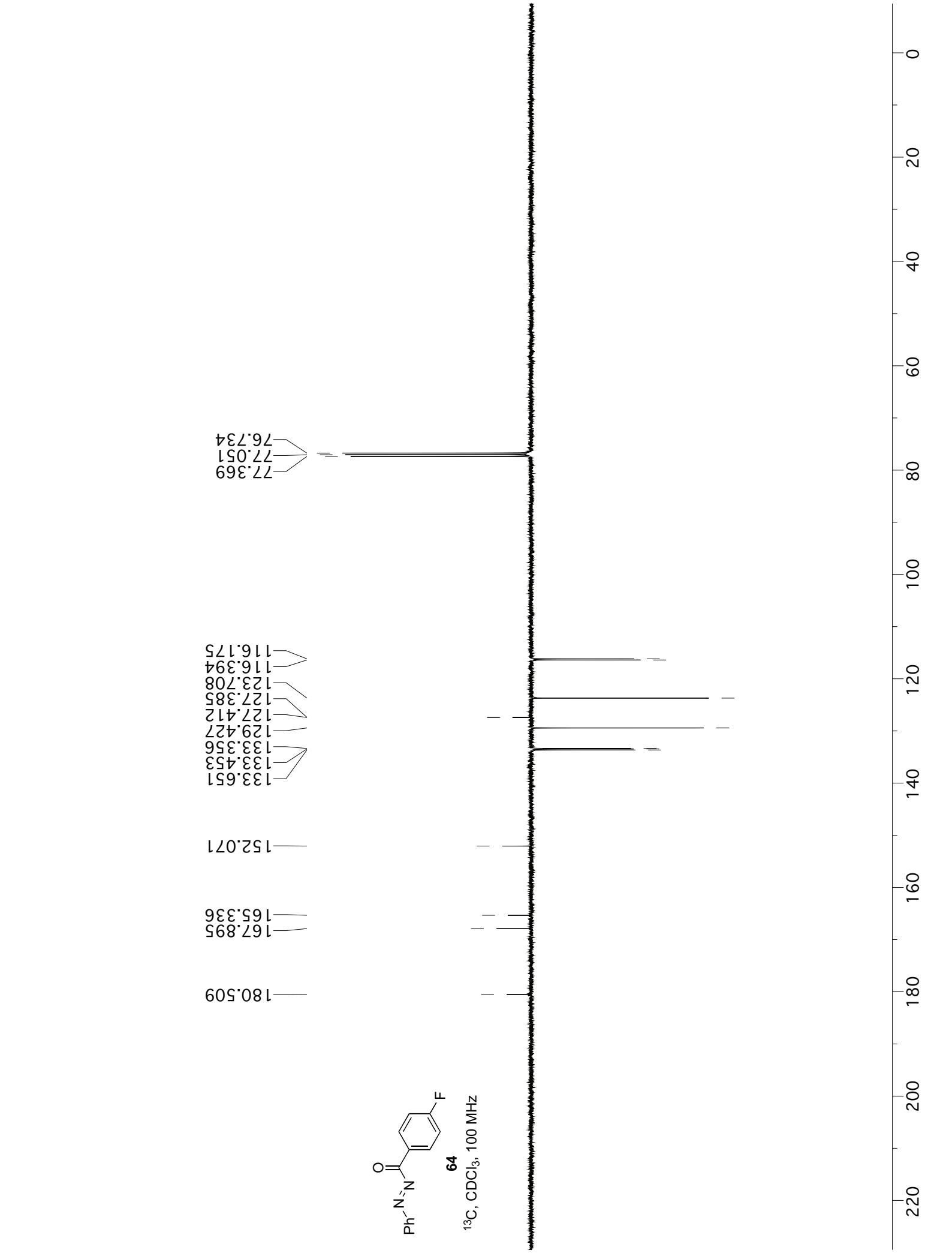


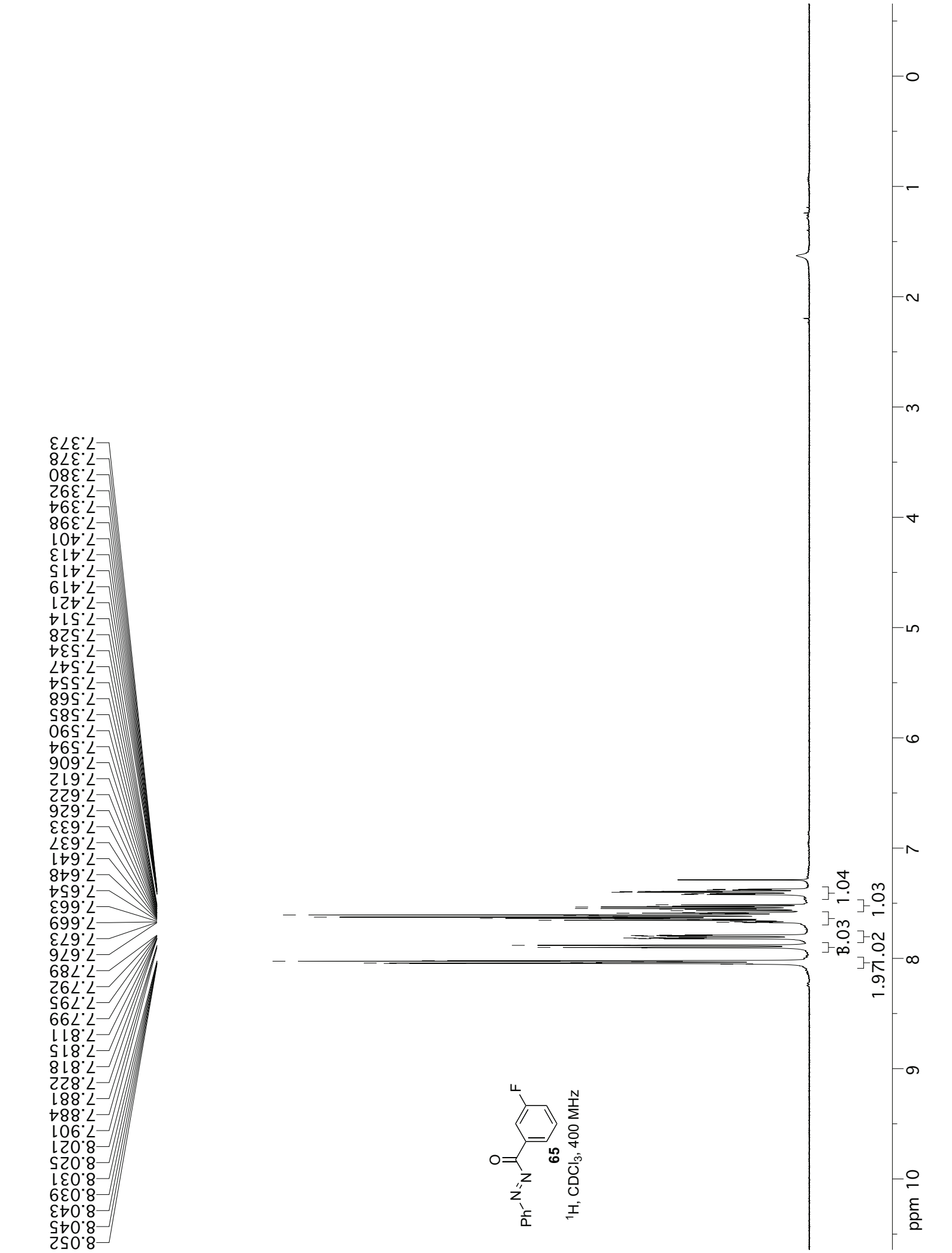


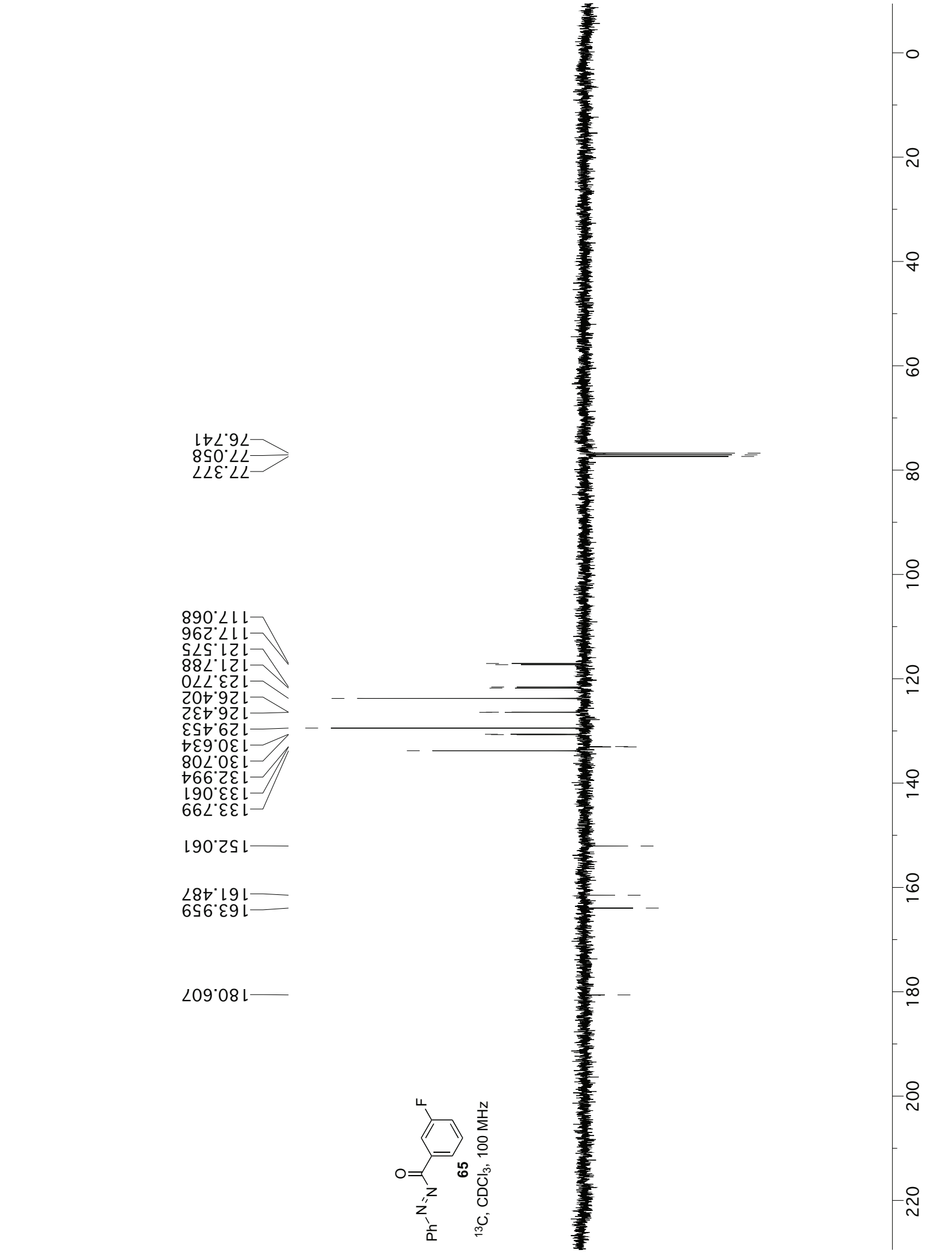


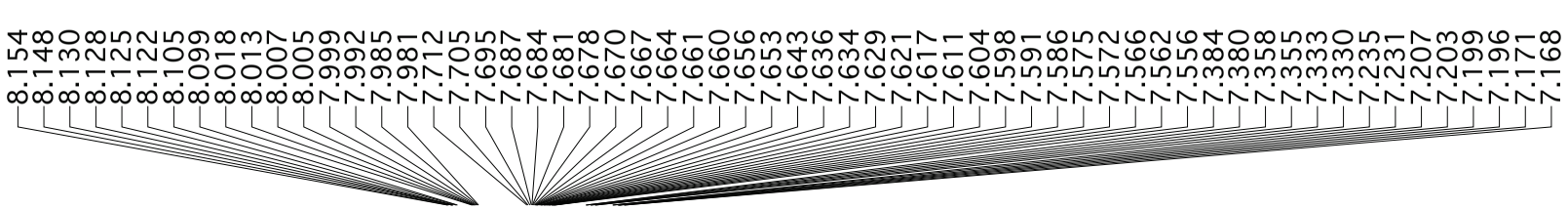


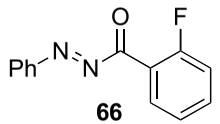






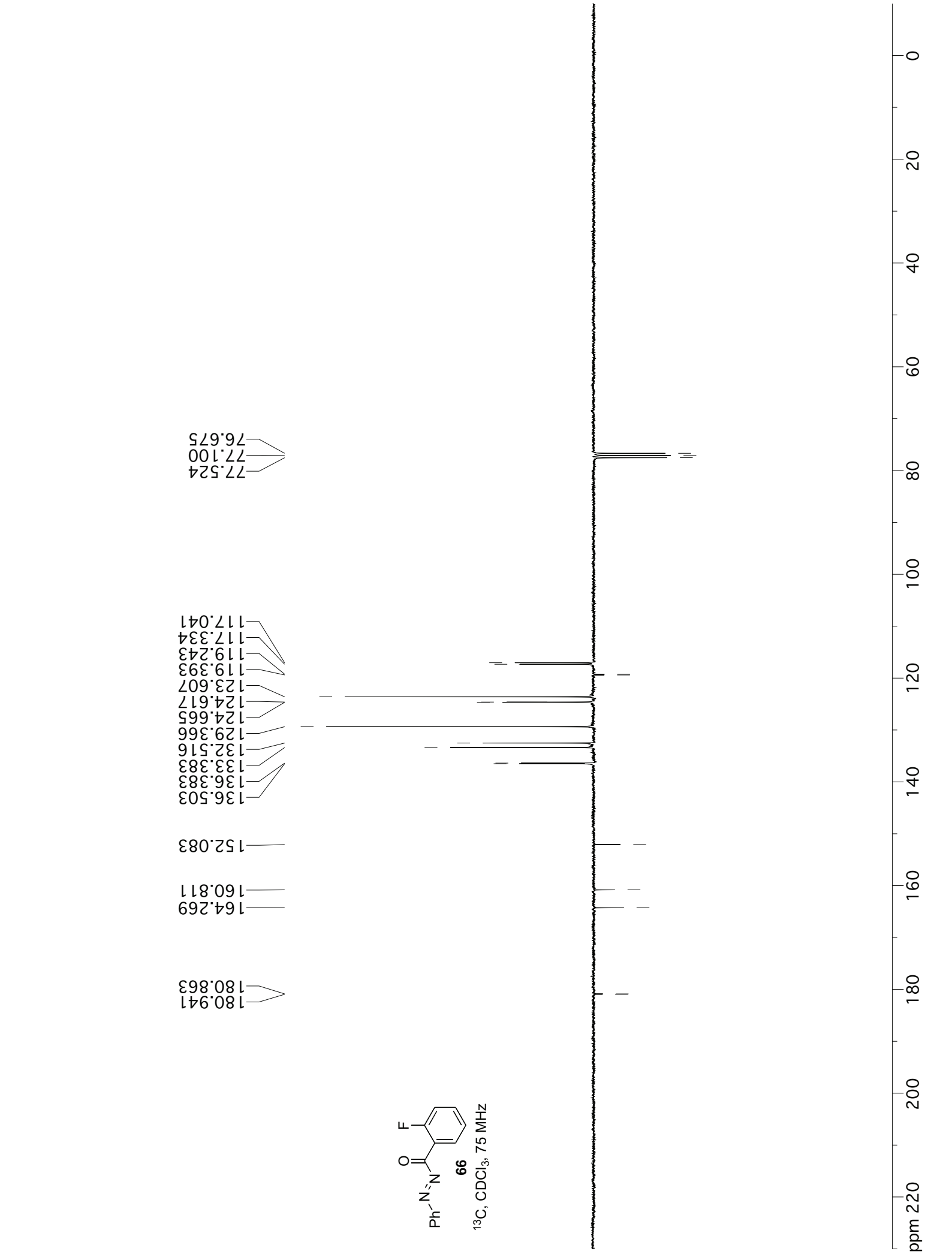


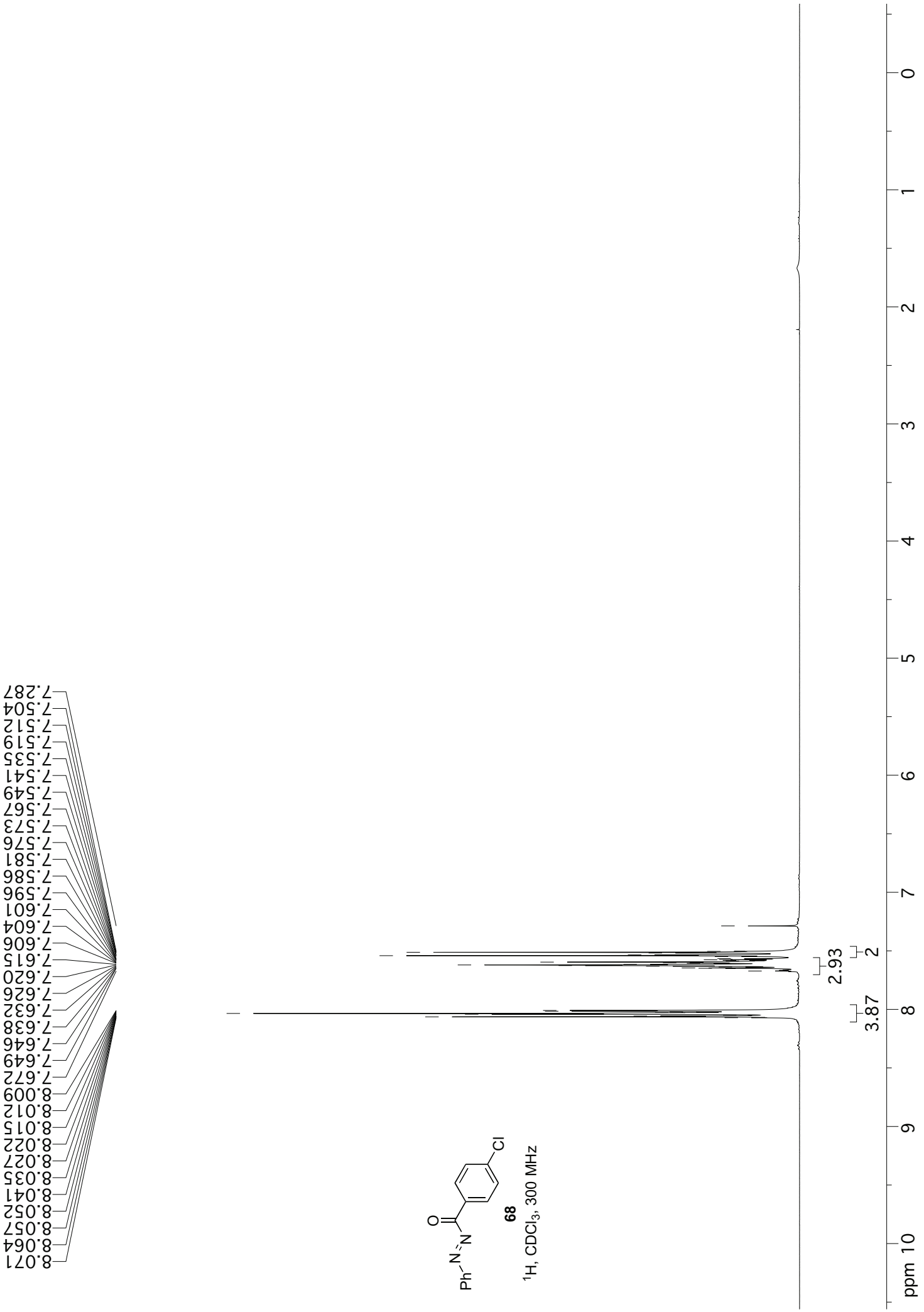


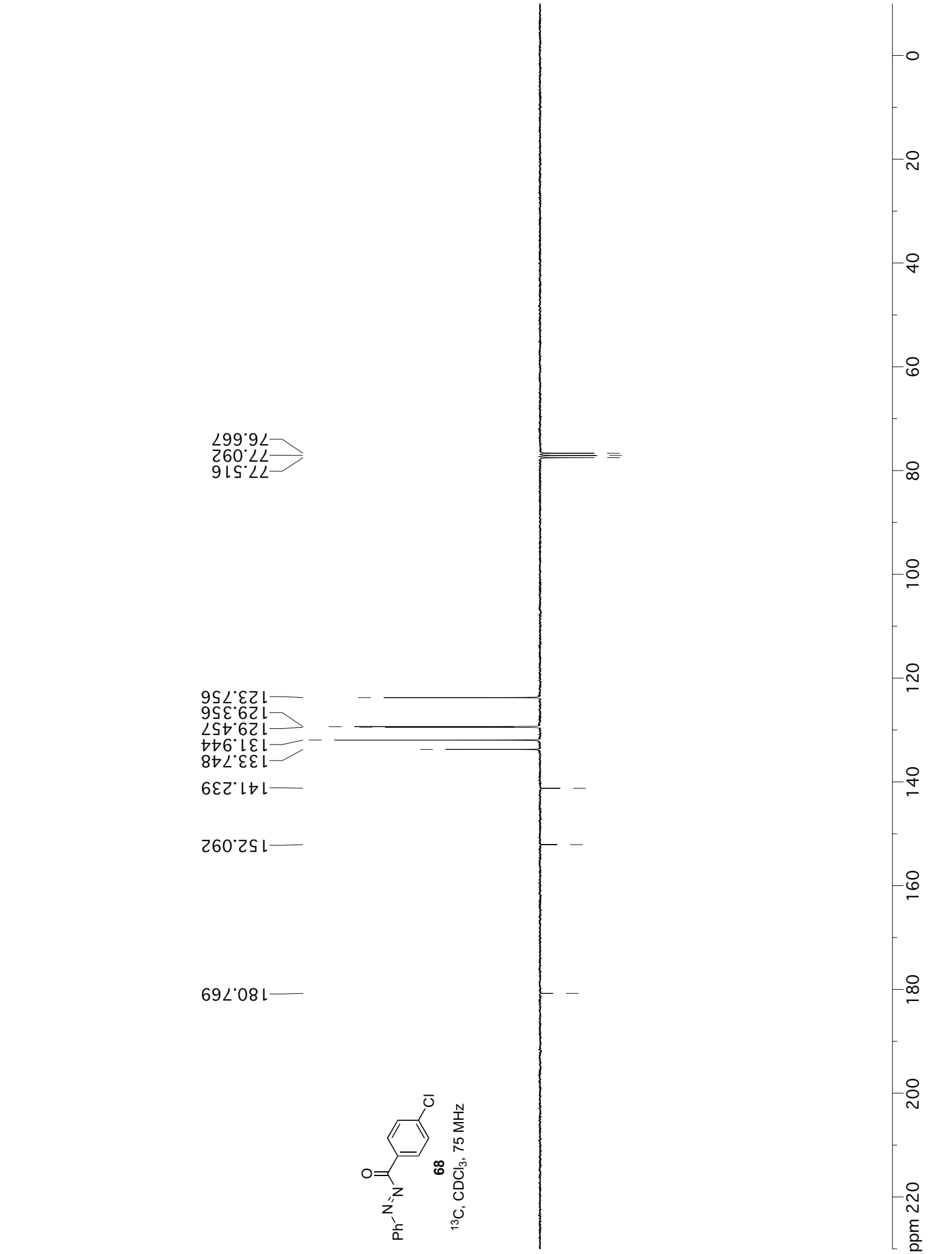


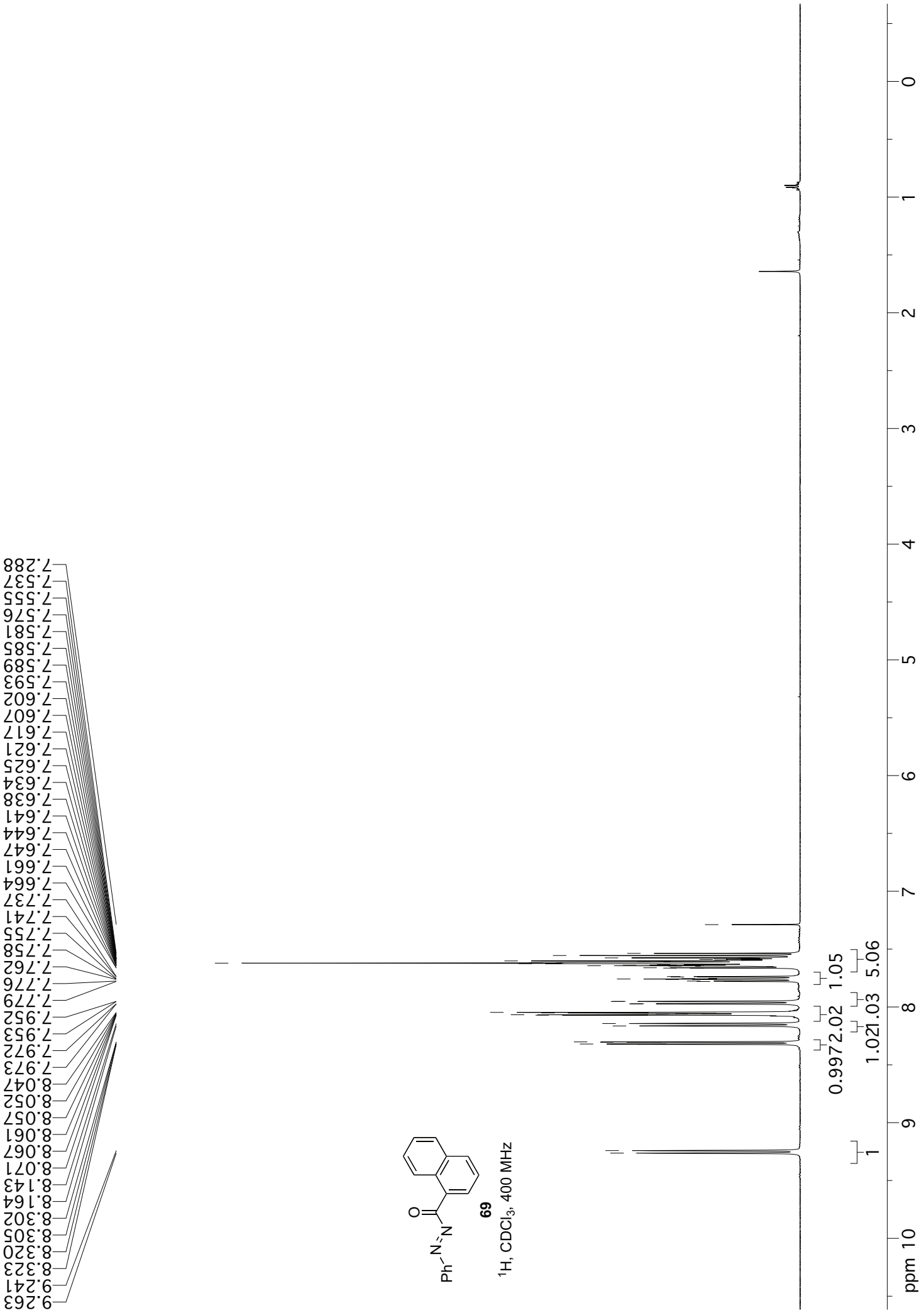
66

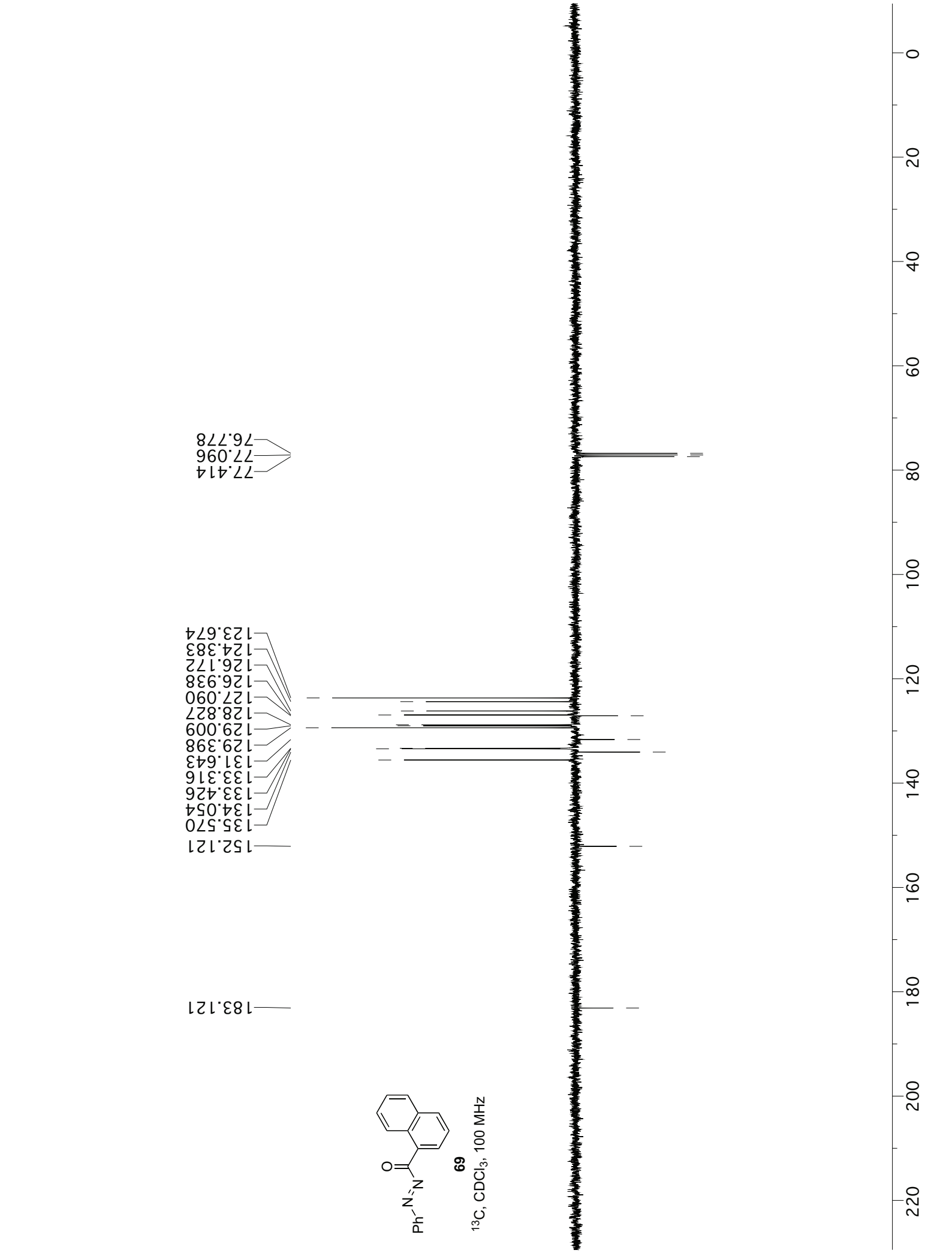
^{1}H, $CDCl_3$, 300 MHz

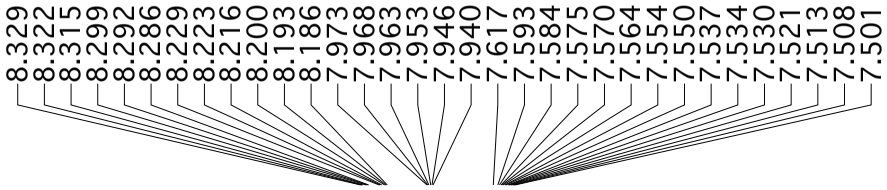


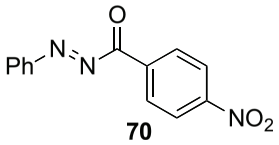






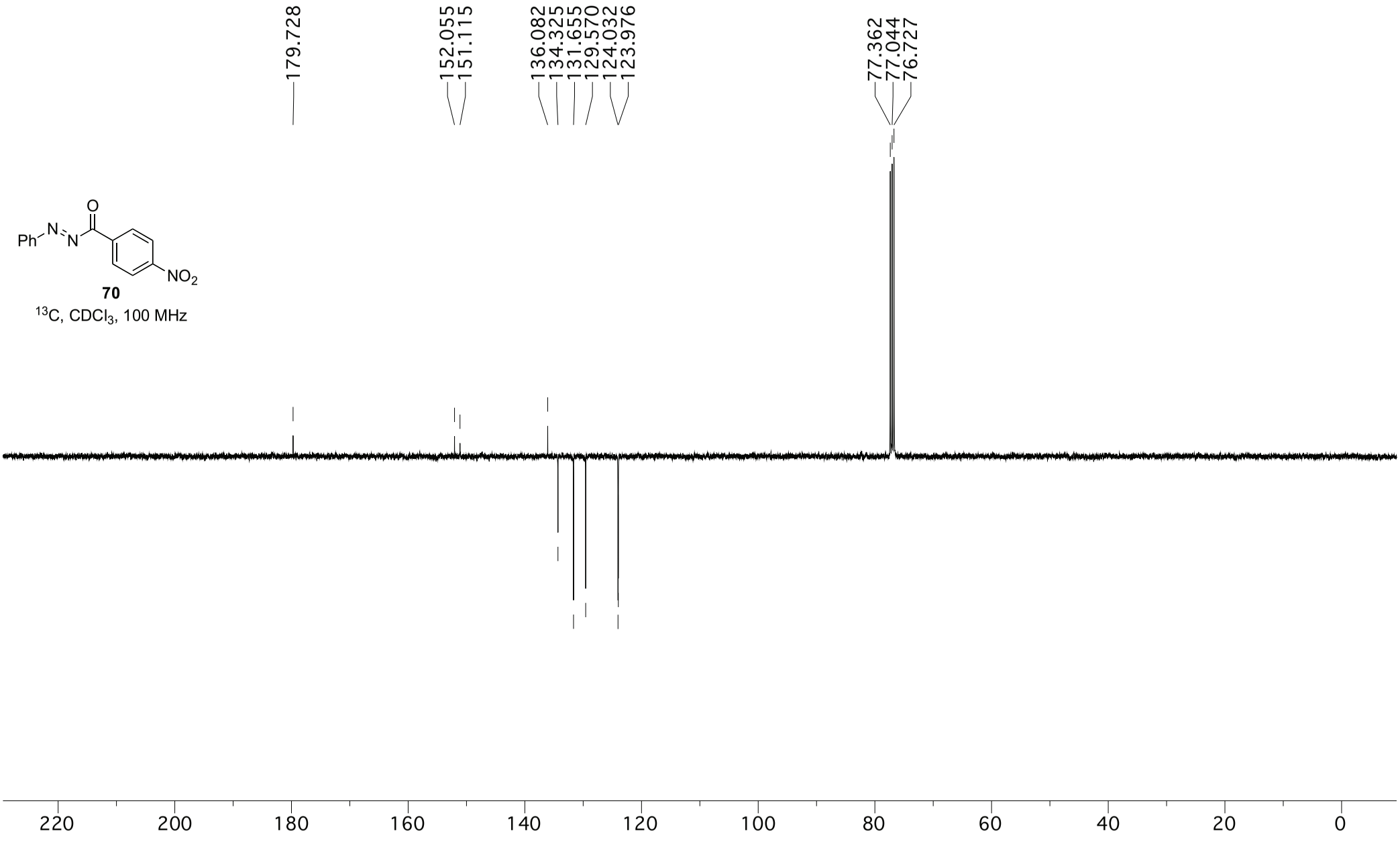






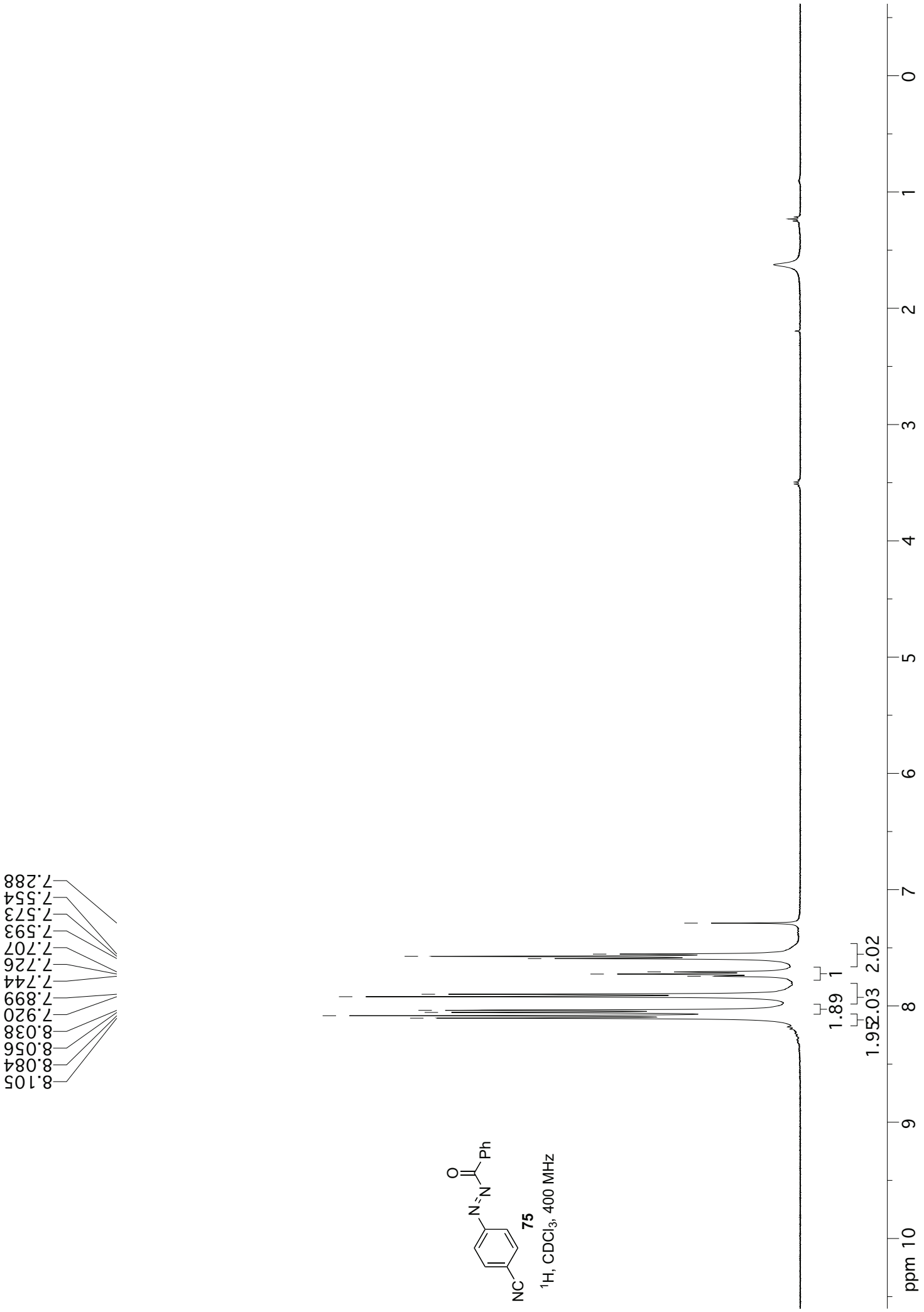
70

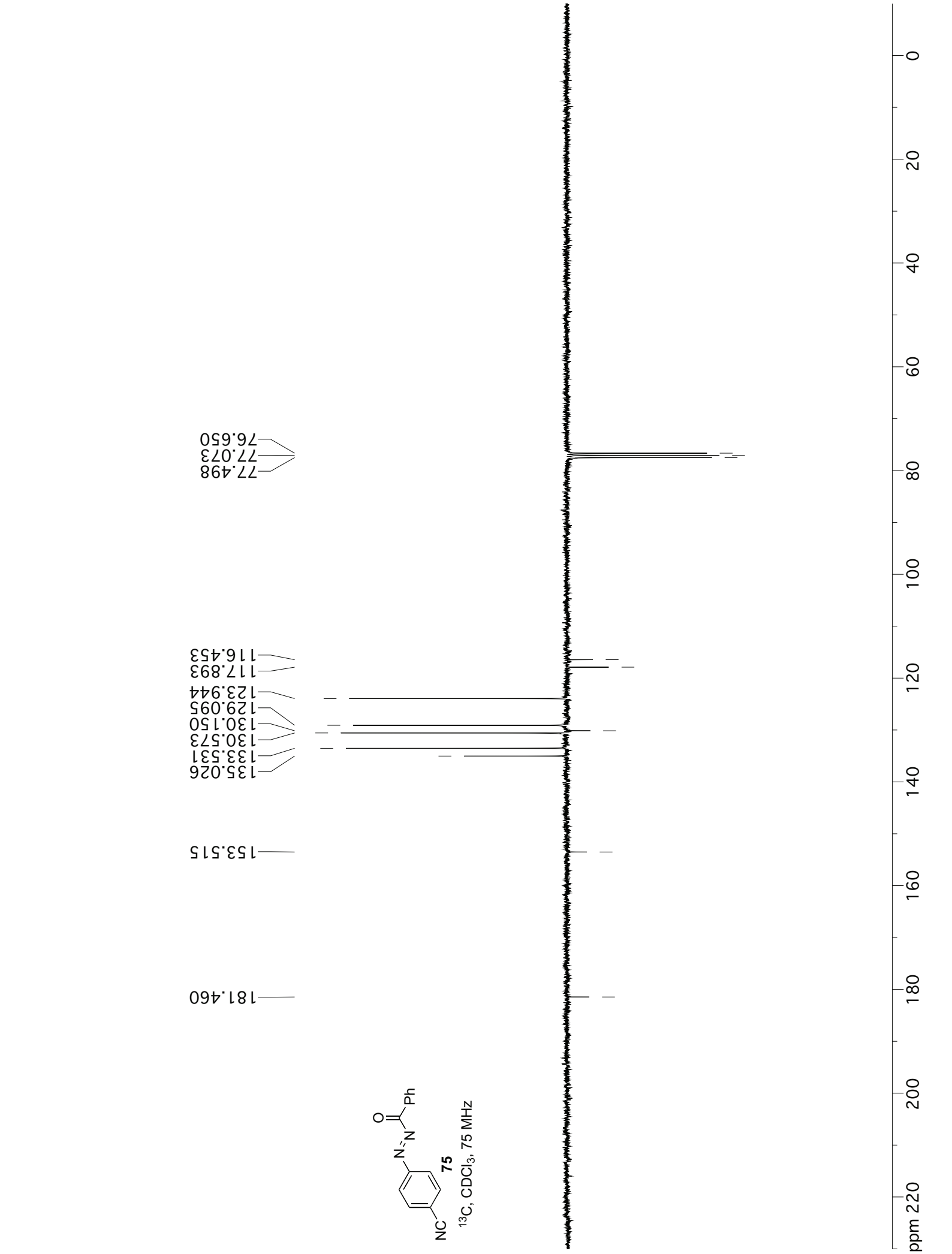
^{1}H, $CDCl_3$, 300 MHz

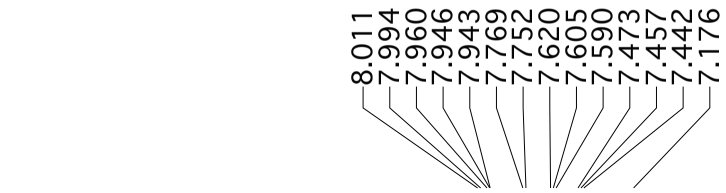


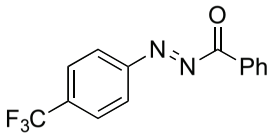
70

^{13}C, $CDCl_3$, 100 MHz









78

^{1}H, $CDCl_3$, 500 MHz